DIRECTORATE OF DISTANCE & CONTINUING EDUCATION

MANONMANIAM SUNDARANAR UNIVERSITY

TIRUNELVELI - 627 012

OPEN AND DISTANCE LEARNING (ODL) PROGRAMMES

(FOR THOSE WHO JOINED THE PROGRAMMES FROM THE ACADEMIC YEAR 2023–2024)

M. Sc. Chemistry

Course Material

Core IX – Organic Synthesis and Photochemistry

Course Code: SCHM31

Compiled and Edited by

Dr. K. Muthu

Assistant Professor

Department of Chemistry

Manonmaniam Sundaranar University

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Organic Synthesis and Photochemistry

Unit I: Planning an Organic Synthesis and Control elements: Preliminary Planning – knowns and unknowns of the synthetic system studied, analysis of the complex and interrelated carbon frameworkinto simple rational precursors, retrosynthetic analysis, alternate synthetic routes, key intermediates that would be formed, available starting materials and resulting yield of alternative methods. Linear Vs convergent synthesis based on umpolung concepts of Seeback, regiospecific control elements. Examples on retrosynthetic approach, calculation of yield, advantages of convergent synthesis, synthesis of stereochemistry-controlled products.

Unit II: Organic Synthetic Methodology: Retrosynthetic analysis; Alternate synthetic routes. Synthesis of organic mono and bifunctional compounds via disconnection approach. Key intermediates, available starting materials and resulting yields of alternative methods. Convergent and divergent synthesis, Synthesis based on umpolung concepts of Seebach. Protection of hydroxyl, carboxyl, carbonyl, thiol and amino groups. Illustration of protection and deprotection in synthesis.Controlelements:Regiospecific contro lelements.Use of protective groups , activating groups, and bridging elements. Stereo specific control elements. Functional group alterations and transposition.

Unit III: Pericyclic Reactions: Woodward Hoffmann rules; The Mobius and Huckel concept, FMO, PMO method and correlation diagrams. Cycloaddition and retrocycloaddition reactions; [2+2], [2+4], [4+4, Cationic, anionic, and 1,3-dipolar cycloadditions. Cheletropic reactions. ; Electrocyclization and ring opening reactions of conjugated dienes and trienes. Sigma tropic rearrangements: (1,3), (1,5), (3,3) and (5,5)-carbon migrations, degenerate rearrangements. Ionic sigma tropic rearrangements. Group transfer reactions. Regioselectivity, stereos electivity and periselectivity in pericyclic reactions.

Unit IV: Organic Photochemistry-I: Photochemical excitation: Experimental techniques; electronic transitions; Jablonskii diagrams; inter system crossings; energy transfer processes; SternVolmer equation. Reactions of electronically excited ketones; $\pi \rightarrow \pi^*$ triplets; Norrishtype-I and Norrishtype-II cleavage reactions; photo reductions; Paterno – Buchi reactions

Unit V: Organic Photochemistry-II: Photochemistry of α,β- unsaturated ketones; cis-trans isomerisation. Photon energy transfer reactions, Photo cycloadditions, Photochemistry of aromatic compounds; photochemical rearrangements; photostationery state; di- π-methane rearrangement; Reaction of conjugated cyclohexadienone to 3,4-diphenylphenols; Barton's reactions.

Recommended Text Books:

1. F. A.Carey and Sundberg,AdvancedOrganicChemistry,5thed, Tata McGraw-Hill, New York, 2003.
2. J.March and M.Smith,AdvancedOrganicChemistry,5thed., John-Wiley and sons, 2007.
3. R.E.Ireland,Organic synthesis,Prentice Hall India,Goelpublishing house, 1990.
4. Clayden,Greeves,Warren,Organic Chemistry, Oxford University Press, Second Edition, 2016.
5. M.B.Smith,OrganicSynthesis3rdedn,McGrawHillInternational Edition,2011.

UNIT I

Preliminary Planning: Knowns and Unknowns in Organic Synthesis

Organic synthesis involves constructing complex organic molecules from simpler ones, using controlled chemical reactions. The design and execution of an efficient synthetic pathway require a thorough understanding of the known variables (knowns) as well as the ability to identify and address potential challenges (unknowns) in the synthetic system. In this essay, we will explore the concept of preliminary planning in organic synthesis, focusing on the key aspects of knowns and unknowns that shape the success of a synthetic process.

Knowns in Organic Synthesis

Starting material

One of the most significant known factors in synthetic planning is the availability of starting materials. These compounds are typically chosen based on their structural similarity to the target molecule and their functional group compatibility with the planned reactions. Knowledge of the reactivity of the starting materials provides a foundation for designing the sequence of reactions. For instance, common reagents like alcohols, aldehydes, and carboxylic acids are widely used due to their well-documented reactivity patterns. Additionally, commercially available precursors or naturally derived compounds can offer economic and practical advantages.

Reaction Mechanisms and Pathways

A well-established aspect of organic synthesis is the mechanistic understanding of the reactions employed. Synthetic chemists rely on known reaction pathways—such as nucleophilic substitution, electrophilic addition, radical reactions, and pericyclic processes—to guide the transformation of starting materials into desired intermediates or products. For example, the mechanism of a nucleophilic substitution (S_N2 or S_N1) is well-characterized, and the outcome can be predicted based on the nature of the nucleophile and leaving group. The predictive power of reaction mechanisms is one of the central pillars of organic synthesis, enabling chemists to anticipate stereochemical outcomes, reaction rates, and selectivity.

Reaction Conditions

Another crucial "known" aspect in synthetic systems is the optimization of reaction conditions, including temperature, solvent choice, and the use of catalysts or reagents. Understanding the impact of these conditions on the reaction is vital for maximizing yield and minimizing side reactions. For example, polar aprotic solvents like DMSO and DMF are often chosen to favor nucleophilic substitution, while solvents like water can be beneficial for reactions involving ionic intermediates. Similarly, the choice of temperature can be used to drive reactions toward kinetic or thermodynamic products. Knowledge of these parameters allows chemists to tailor reactions to specific needs and constraints.

Functional Group Compatibility

During synthesis, functional groups must be carefully considered to prevent unwanted reactions or degradation of the molecule. Known functional group tolerance under specific reaction conditions is critical. For example, protecting groups are often used to shield sensitive functionalities (like alcohols or amines) during transformations, and their removal later in the synthetic sequence is another known step. The proper selection of these protective groups, based on their stability under different conditions, is essential for the overall success of the synthesis.

Unknowns in Organic Synthesis

Reaction Selectivity and Stereochemistry

Despite a thorough understanding of mechanisms and conditions, selectivity, especially regioselectivity and stereoselectivity, often presents an element of uncertainty. Organic molecules frequently contain multiple reactive sites, and predicting the exact site of reaction can be challenging. For example, in the synthesis of complex molecules like natural products or pharmaceuticals, controlling the stereochemistry of each reaction step is vital. While catalysts or chiral auxiliaries are employed to improve stereoselectivity, the degree of control and the possibility of by-products remain unknown until experimentally determined.

Reaction Yield and Efficiency

Another unknown in organic synthesis is the reaction yield. Although reaction mechanisms suggest possible outcomes, the actual yield is often influenced by a variety of factors, including side reactions, reagent purity, and reaction kinetics. Yield optimization frequently

requires trial and error, as unforeseen competing reactions or incomplete conversions may reduce the expected product yield. For example, unexpected side reactions like polymerization or rearrangement can significantly decrease the efficiency of a synthetic route.

Reactivity of Novel Intermediates

Many synthetic routes involve the generation of reactive intermediates (e.g., radicals, carbenes, or organometallic complexes), whose behavior may not always be predictable. These intermediates may undergo reactions other than the desired transformation, leading to the formation of undesired products. In cases where novel intermediates are involved, their stability and reactivity remain unknown until the reaction is performed. This unpredictability requires careful monitoring of reaction progress and sometimes necessitates the development of new reaction conditions or protective strategies to ensure the successful progression of the synthesis.

Unknown Side Reactions and Complications

Organic syntheses often face complications from side reactions that are not predicted by reaction mechanisms or the nature of the starting materials. For example, adventitious water in the reaction system can promote hydrolysis or other undesired pathways, or reactive intermediates may decompose before participating in the desired transformation. These side reactions not only reduce the yield but can also complicate purification and isolation of the product. While chemists may anticipate some side reactions based on experience, many issues remain unknown until the reaction is conducted in the lab.

Purification and Isolation Challenges

Even when a desired product is formed, purification can present significant challenges, especially when the product exists as a mixture of regioisomers, stereoisomers, or when trace impurities are difficult to remove. Techniques such as column chromatography, recrystallization, and distillation are often employed, but their efficiency in separating complex mixtures may be unpredictable. The unknowns associated with purification can prolong the synthetic process and reduce the overall efficiency of the route.

Scalability and Reproducibility

An additional unknown is the scalability of a synthetic process. While a reaction may work well on a small scale in the lab, its behavior on a larger scale can be quite different due to

factors like heat transfer, mixing efficiency, and reagent handling. Reproducibility is another concern, as subtle changes in reaction conditions (e.g., atmospheric moisture, reagent grade) can lead to variations in product yield and purity. Addressing these issues often requires iterative refinement of the synthetic procedure and testing on larger scales.

Conclusion

Preliminary planning in organic synthesis involves carefully considering the known aspects—such as starting materials, reaction mechanisms, and functional group compatibility—while remaining prepared for the unknowns, including reaction selectivity, yield unpredictability, and the challenges of purification and scalability. Successful organic synthesis requires a balance between leveraging established knowledge and addressing uncertainties through experimentation, optimization, and adaptation. By identifying and planning for the potential unknowns in a synthetic system, chemists can improve the likelihood of achieving their desired synthetic targets, while also developing a deeper understanding of the behavior of organic molecules in complex reaction environments.

Analysis of the complex and interrelated carbon framework into simple precursors

In organic synthesis, the analysis of the complex and interrelated carbon framework into simple precursors is essential for efficient chemical transformations.

Complex Carbon Frameworks:

Organic molecules often feature intricate carbon skeletons, including rings, branches, and functional groups, making their synthesis challenging.

Retrosynthetic Analysis:

This technique involves working backward from the target molecule to identify simpler precursors and intermediates. It helps in planning synthetic routes efficiently.

Functional Group Manipulation:

Transforming complex structures often requires modifying functional groups to achieve desired reactivity or stability, enabling the breakdown of intricate frameworks into simpler components.

Key Strategies:

Disconnection Strategies: Identifying strategic bond disconnections to simplify complex molecules into more accessible fragments.

Building Blocks:

Utilizing readily available simple precursors (e.g., alkenes, alcohols, acids) as starting materials to construct more complex architectures.

Synthesis of Intermediates: Many reactions produce intermediates that can be further transformed into target molecules, allowing for stepwise construction of complexity.

Catalysis and Reagents:

The use of catalysts and selective reagents is critical for efficiently transforming complex structures into simple precursors, minimizing side reactions.

Analytical Techniques:

Techniques such as NMR, IR, and mass spectrometry help identify and confirm the structures of intermediates and products, guiding the synthesis process.

Sustainability:

The simplification process can also focus on using renewable resources and green chemistry principles to minimize waste and improve efficiency.

By analyzing and simplifying complex carbon frameworks, chemists can streamline organic synthesis, enhance reaction yields, and develop innovative compounds more effectively.

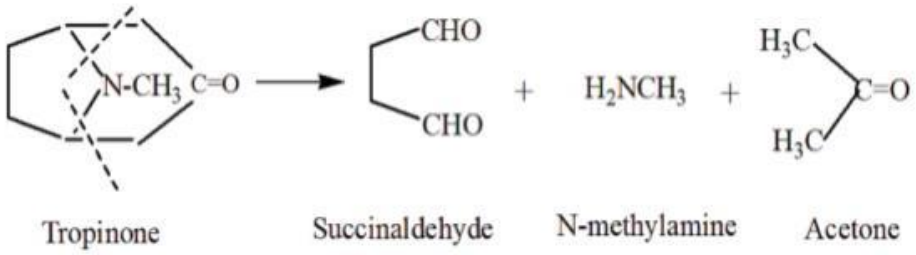
RETROSYNTHETIC ANALYSIS

Retrosynthetic analysis is a technique in organic chemistry used to plan the synthesis of complex molecules by breaking them down into simpler precursor structures. It involves working backwards from the target molecule ™ to simpler or commercially available starting materials through a series of disconnections. The goal is to identify strategic bonds to break (disconnections) that simplify the structure without losing important functional groups or stereochemistry.

The concept of retrosynthetic analysis was developed by the British chemist E.J. Corey in the 1960s. It revolutionized the way chemists think about organic synthesis, particularly for complex molecules such as natural products, pharmaceuticals, and materials. Corey's retrosynthesis method allowed for a systematic approach to simplifying complex molecules into more manageable pieces, making the planning of multi-step syntheses much more efficient and logical.

Retrosynthetic analysis is the exact reverse of a synthetic reaction. However, the first notable example of a product being transformed into it's synthetic precursors was that of Robinson's tropinone synthesis.

Tropinone was submitted to imaginary hydrolysis at the points indicated by the dotted lines below and resolved into succinaldehyde, methylamine and acetone.



Tropinone Succinaldehyde N-methylamine Acetone

The precursors were identified from the starting material, and then a suitable path was devised to convert these starting materials into the target molecule using known reactions.

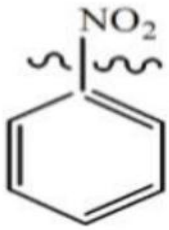
TERMS AND DEFINITIONS:

Target molecule (TM) : The molecule to be synthesized.

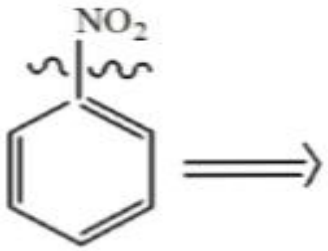
Retro synthetic analysis: The process of imaginary break down of a molecule into progressively simpler starting materials. The reactions are viewed in the retro synthetic direction i.e, starting with the product and going back to the reactants along a pathway that is reverse of a synthetic direction.

Disconnection: Imaginary bond cleavage corresponding to the reverse of a forward reaction leading to the immediate precursor. This is also known as transformation and is indicated by a wavy line.

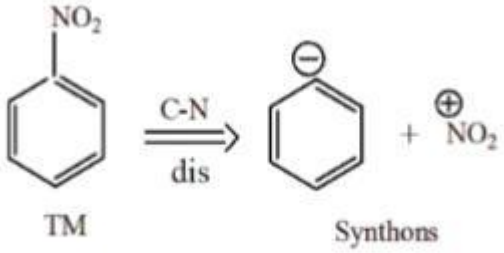
Retrosynthetic arrow: Disconnection is represented by a double line closed arrow which



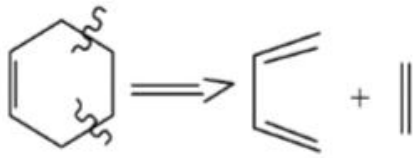
indicates the transformation of the molecule into it's immediate precursor.



Synthons: Synthons are the imaginary fragments obtained by disconnections. Synthons are not real compounds but are idealized ionic or neutral fragments, and they are not reagents.



The following reaction shows a concerted cycloaddition reaction, where the synthons are neutral fragments.



Retron: Each reaction generates a characteristic structural element in the product, such as the enone resulting from aldol condensation. This substructure, called the retron, must be present in a target molecule to be able to apply the corresponding transformation to that target.

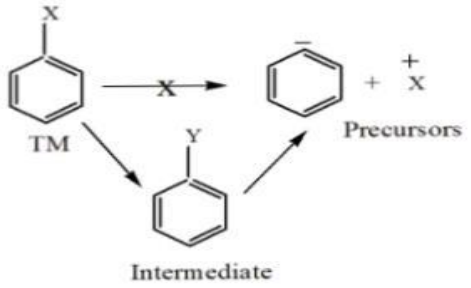
GROUP ORIENTED STRATEGY:

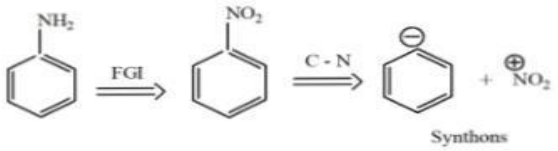
Whenever disconnection does not lead to reliable reactions, then the following changes have to be carried out with a functional groups- **FGI, FGA, FGR –** and the unmasking of the latent functional groups by deprotection or other conversions.

FUNCTIONAL GROUP INTERCONVERSION (FGI):

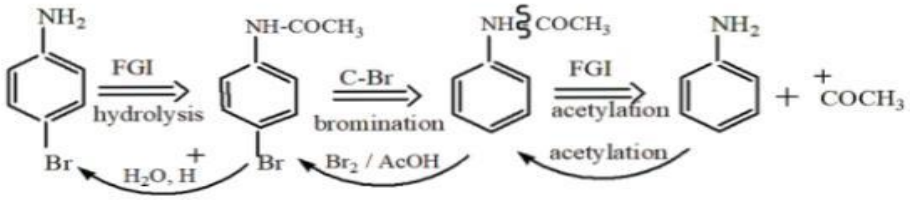
Functional Group Interconversion (FGI) is a key concept in retrosynthetic analysis. It refers to the transformation of one functional group into another, often to facilitate easier disconnections or to introduce a group that allows for a known synthetic route. FGIs are crucial when the target molecule has a functional group that doesn't immediately suggest a straightforward disconnection but can be converted into one that does.

Aniline on bromination gives 2,4,6 – tribromoaniline so the group interconversions has to be carried. Amino group is readily obtained by the reduction of Nitro group.





Preparation of p-bromoaniline from aniline is shown below.

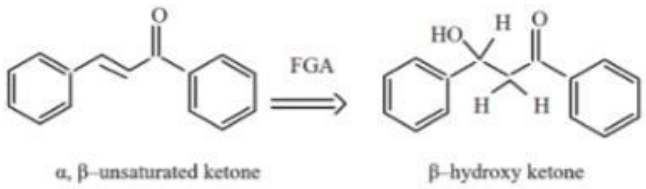


The synthetic route for the target molecule is the exact reverse of these retro steps.

FUNCTIONAL GROUP ADDITION (FGA):

Functional Group Addition refers to introducing new functional groups into a molecule, either to make it more reactive or to enable further synthetic transformations. This technique is widely used in organic synthesis, especially in retrosynthetic analysis, where it can simplify or enable specific disconnections that otherwise wouldn't be feasible.

Some functional groups need the addition of a group to the immediate precursor suitable for disconnection.



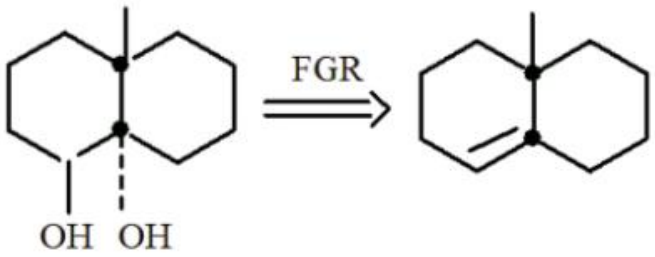
α, β–unsaturated ketone β–hydroxy ketone

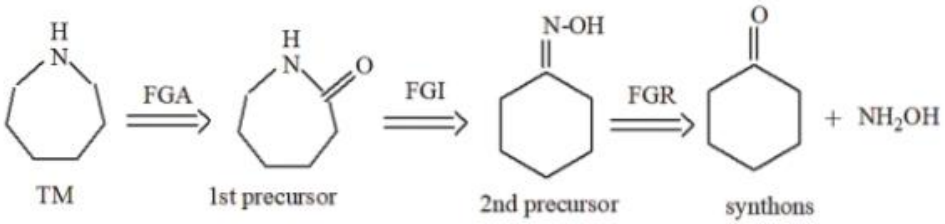
An example is the facile dehydration of β–hydroxy ketone that yields α, β–unsaturated ketone.

FUNCTIONAL GROUP REMOVAL (FGR):

Functional Group Removal refers to the process of eliminating a functional group from a molecule, typically to simplify the structure or to make the molecule less reactive. This technique is important in organic synthesis, especially when you need to “deactivate” or remove unnecessary functional groups after key reactions have taken place.

The target molecule caprolactam is obtained by Beckmann rearrangement from the lactam. So, the first retro step is the addition of a keto group to obtain a lactam. This reaction involves both FGR and FGI.





The aim of retrosynthetic analysis to not only simplify but also aid the discovery of new synthetic routes and compare them for the development of an efficient synthetic strategy for a complex molecule.

ALTERNATE SYNTHETIC ROUTES

Alternate Synthetic Routes refer to different possible pathways to synthesize a target molecule. These routes may vary in the type of reactions, reagents used, or the sequence of steps. Exploring alternative routes is crucial in organic synthesis to find the most efficient, cost-effective, or environmentally friendly pathway.

Why Consider Alternate Synthetic Routes?

1. **Efficiency:** Some routes may require fewer steps, making the synthesis quicker and cheaper.

2. **Yield**: Alternate routes may offer higher yields or better selectivity for the desired product.
3. **Availability of Starting Materials**: Certain routes may use more readily available or less expensive starting materials.
4. **Reaction Conditions:** Different routes may use milder conditions, reducing the risk of side reactions or decomposition.
5. **Environmental and Safety Concerns**: Avoiding toxic reagents or hazardous conditions can be essential for sustainable chemistry.

Steps to Develop Alternate Synthetic Routes:

1. **Identify Different Disconnections:** During retrosynthetic analysis, explore multiple ways to break down the target molecule into simpler precursors.
2. **Consider Functional Group Interconversions (FGI)**: Functional groups can often be transformed into each other. For example, an alcohol could be oxidized to a ketone or converted into a leaving group like a halide, allowing for different synthetic strategies.
3. **Use Different Reaction Mechanisms:** Some transformations can be achieved using various reaction mechanisms (e.g., nucleophilic substitution vs. elimination).
4. **Explore Protecting Group Strategies:** Protecting groups can be used differently in alternate routes to simplify selective reactions.
5. **Use Different Reagents/Catalysts:** Different reagents or catalysts may offer alternative pathways, especially in asymmetric synthesis or catalysis.

Example of Alternate Synthetic Routes:

Synthesis of 2-Phenylethanol

Route 1: Grignard Reaction

Route 1: Grignard Reaction

Step 1: Start with benzaldehyde (C_6H_5CHO).

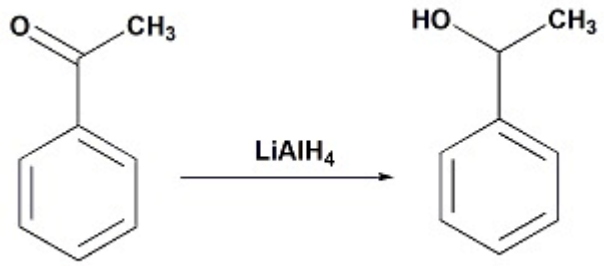
Step 2: React it with ethylmagnesium bromide (Grignard reagent) to form 2-phenylethanol.

Reaction: $C_6H_5CHO + CH_3CH_2MgBr \rightarrow C_6H_5CH_2CH_2OH$.

Route 2: Reduction of Ethyl Phenyl Ketone

Step 1: Start with ethyl phenyl ketone (acetophenone, $C_6H_5COCH_3$).

Step 2: Use hydride reduction (e.g., $LiAlH_4$ or $NaBH_4$) to reduce the ketone to 2-phenylethanol.



Reaction: $C_6H_5COCH_3 \rightarrow C_6H_5CH_2CH_2OH$.

Route 3: Hydrolysis of Phenyl Ethyl Ether

Step 1: Start with phenyl ethyl ether ($C_6H_5OCH_2CH_3$).

Step 2: Hydrolyze the ether bond to produce 2-phenylethanol.

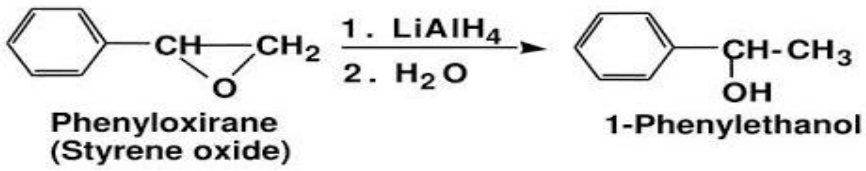
Reaction: $C_6H_5OCH_2CH_3 + H_2O \rightarrow C_6H_5CH_2CH_2OH + H_2O$.

Route 4: Reduction of Styrene Oxide

Step 1: Start with styrene ($C_6H_5CH=CH_2$).

Step 2: Perform epoxidation to form styrene oxide ($C_6H_5CH(O)CH_2$).

Step 3: Reduce styrene oxide to 2-phenylethanol using a hydride reducing agent.

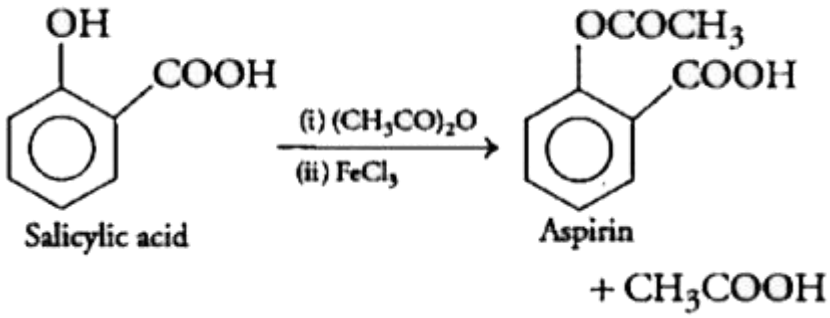


Reaction: $C_6H_5CH(O)CH_2 + LiAlH_4 \rightarrow C_6H_5CH_2CH_2OH$.

Example of Alternate Routes for Aspirin Synthesis:

Route 1: Acetylation of Salicylic Acid

Step 1: React salicylic acid with acetic anhydride in the presence of an acid catalyst (e.g., H_2SO_4) to acetylate the phenol group, forming aspirin.



Reaction: $C_6H_4(OH)COOH + (CH_3CO)_2O \rightarrow C_6H_4(OCOCH_3)COOH$ (Aspirin) + CH_3COOH.

Route 2: Acylation of Sodium Salicylate

Step 1: Start with sodium salicylate.

Step 2: React with acetyl chloride to form aspirin.

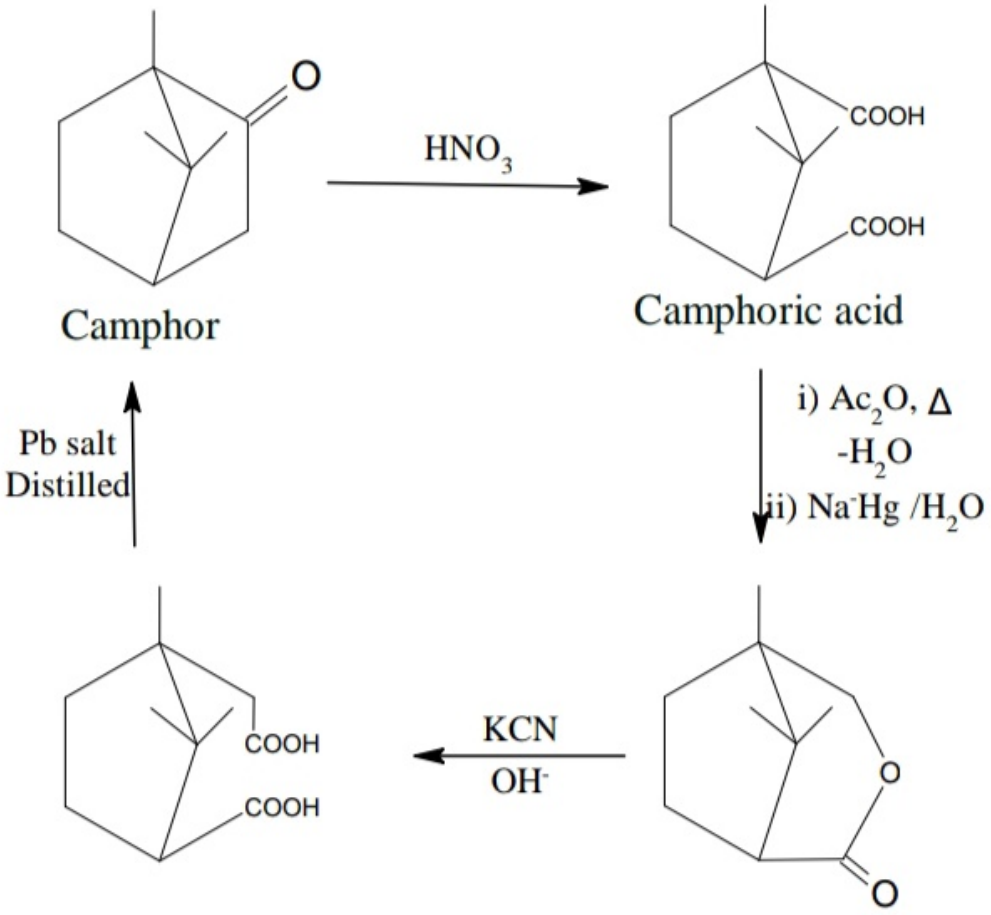
Reaction: $C_6H_4(OH)COONa + CH_3COCl \rightarrow C_6H_4(OCOCH_3)COOH + NaCl.$

Exploring alternate synthetic routes allows chemists to optimize the synthesis for cost, yield, safety, and environmental concerns. Multiple pathways to a target molecule often exist, and choosing the best route depends on a balance of practical and theoretical considerations.

KEY INTERMEDIATES

Sometimes during the degradative work of a natural substance, a key substance may be Obtained. From the key substance the synthesis of the natural material may be accomplished. This type of synthetic method is termed as “Relay approach” to synthesis. Now the synthesis Of the key substance forcommercially available material may complete the cyclic operation.

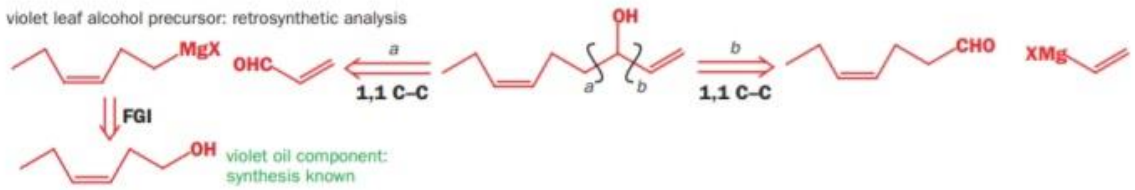
Systematic degradation of camphor gave camphoric acid. To establish the structural Change that attends this degradation, camphoric acid is reconverted to camphor through a series Of reactions.



AVAILABLE STARTING MATERIALS AND RESULTING YIELDS OF ALTERNATIVE METHODS

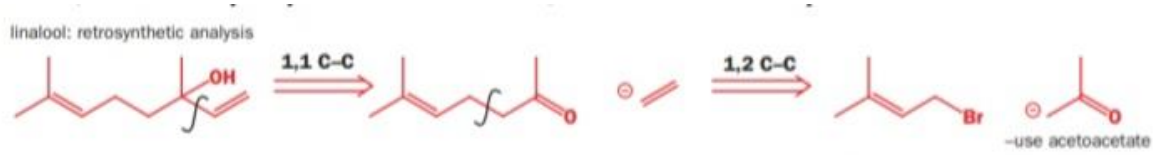
Some starting materials become available because other chemists have made them.

Our target is an allylic alcohol that produces the perfumery compound ‘violet leaf Alcohol’ by a rearrangement step. Two disconnections are possible, but one of them, (a), leads Back to a Grignard reagent that can be made by FGI on the violet oil component whose Synthesis.



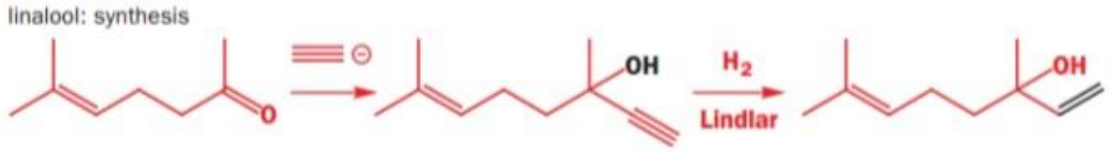
The synthesis was best carried out using the alkyl magnesium iodide and the iodide was Made from the alcohol via the chloride.

Linalool is another perfumery compound. Disconnection of the vinyl group leads to the Ketone, best made by alkylation of acetoacetate, an acetone enolate equivalent.



On an industrial scale it was best to introduce the vinyl anion synthon as acetylene and

On an industrial scale it was best to introduce the vinyl anion synthon as acetylene and then hydrogenate the alkyne. The unsaturated ketone was chosen as the starting material because its synthesis was already known.



Linear Synthesis Vs Convergent Synthesis

Linear Synthesis:

In linear synthesis, the target molecule (TM) is synthesized through a series of linear transformations. The TM is assembled in a stepwise manner.

$$\text{E.g., A} \rightarrow \text{B} \rightarrow \text{C} \rightarrow \text{D} \rightarrow \text{E} \rightarrow \text{F} \rightarrow G \rightarrow H$$

For the above seven step synthesis, there are total eight components (A to H). If the yield of the intermediate at each step is 80% then, Overall yield of H = 80/100*80/100*80/100*80/100*80/100*80/100 =0.21

Therefore, overall yield % of H = 21%.

Convergent Synthesis

A convergent synthesis is a strategy that aims to improve the efficiency of multistep organic synthesis. In this case, the key fragments of the target molecule are synthesized separately or independently and then joined together at a later stage in the synthesis to make the target molecule.

E.g., In this sequences of convergent synthesis:

$$\text{A} \rightarrow \text{B}$$

$$\text{C} \rightarrow \text{D}$$

$$\text{B} + \text{D} \rightarrow E$$

There are five components in two steps (A to E) each with a yield of 50% The overall yield is given by (50/100)*(50/100) =0.21 =21%

	Illustrative Example	Overall Yield
Linear Synthesis	$\text{A} \xrightarrow{85\%} \text{B} \xrightarrow{85\%} \text{C} \xrightarrow{85\%} \text{Product}$	61.4%
Convergent Synthesis	$\left.\begin{array}{l}\text{A} \xrightarrow{85\%} \text{B} \\ \text{D} \xrightarrow{85\%} \text{E}\end{array}\right\} \longrightarrow \text{Product}$	72.3%

	Linear Synthesis	Convergent Synthesis
DEFINITION	Linear synthesis is a chemical synthesis process in which a series of linear transformation reactions are used to convert a reactant or some reactants into a product or multiple products	Convergent synthesis is a chemical synthesis process in which pieces of the desired product are made by a set of reactions, and the pieces are combined with each other via another set of reactions
EFFICIENCY	Low	High
PROCESS LENGTH	Longer	Shorter
OVERALL YIELD	Lower than expected	Higher than expected

SYNTHESIS BASED ON UMPOLUNG CONCEPTS

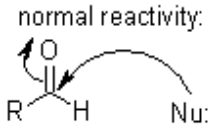
In organic chemistry, **Umpolung** or **polarity inversion**is the chemical modification of a functional group with the aim of the reversal of polarity of that group. The concept was introduced by D. Seebach (hence the German word umpolung for reversed polarity) and E. J.

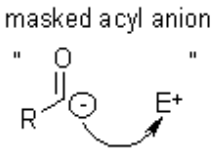
Corey. Polarity analysis during retrosynthetic analysis tells a chemist when umpolung tactics are required to synthesize a target molecule,

Polarity Inversion

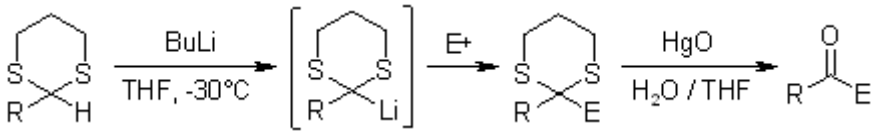
In normal polarisation, Generally in ketone or Aldehyde the bond shifts from carbon atom to oxygen atom, hence there is a formation of Carbon electrophile and this electrophilic carbon needs a nucleophile to react.

While in the Umpolang Polarisation, Generally in ketone or Aldehyde the bond shifts from Hydrogen atom to carbon ayom, hence there is a formation of Carbon Nucleophile and this nucleophilic carbon needs a electrophile to react.





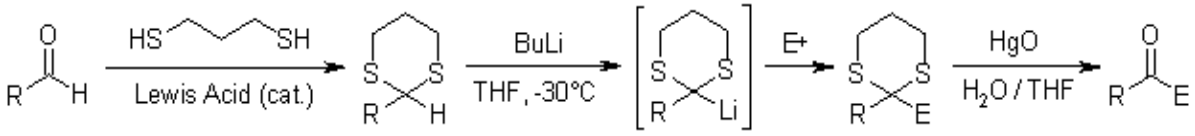
Seebach Umpolung



The Corey-Seebach Reaction uses lithiated 1,3-dithianes as nucleophilic acylating agents.

Mechanism of the Corey-Seebach Reaction

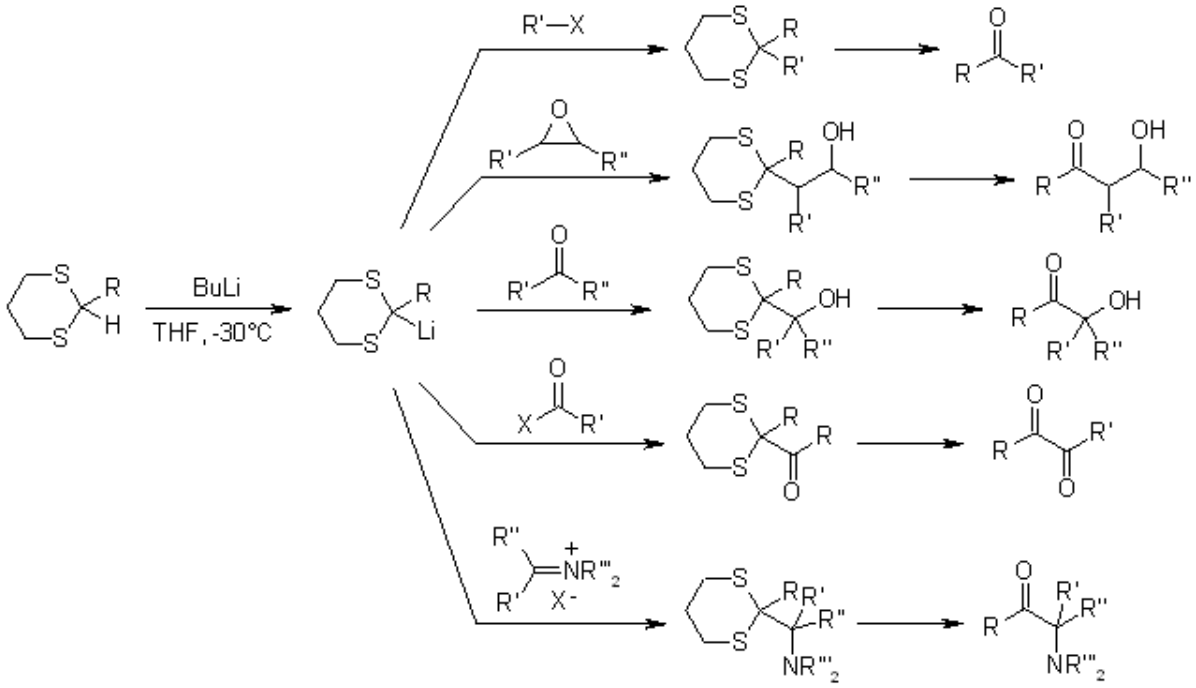
The Corey-Seebach Reaction allows a reversal of the normal reactivity of acyl carbon atoms, which combine only with nucleophiles. The German term "Umpolung" is widely used for this inversion of reactivity.



The lithiated 1,3-dithiane can be viewed as an masked acyl anion that is able to react with various electrophiles.

The acidity difference of hydrogen atoms adjacent to divalent sulfur compared to oxygen stems from the greater polarizability of sulfur and the longer C-S-bond length; d-orbitals are not involved. In most cases treatment of dithianes with *n*-BuLi at temperatures of -30 °C is

sufficient for the preparation of the lithio-derivatives. With pK_A values of approximately 30, lithiated dithianes can react with aldehydes or ketones, epoxides and acid derivatives, but also with alkyl halides without competing elimination reactions.



Umpolung offers access to a wide range of products, especially 1,2-diketones and α-hydroxy ketones, products that cannot be obtained using the normal reactivity (for example through aldol addition).

Regiospecific Control elements

Regiospecific reactions are those reactions where the same choice isn't there. A regiospecific reaction exclusively gives only one, specific product. A regioselective reaction can be made regiospecific by controlling the factors affecting the reaction, like temperature, pressure, presence of a catalyst.

Protective Groups, Activating groups and Bridging Elements

Protecting Agents:

Organic synthesis involves polyfunctional substrates. It is therefore necessary to protect a functional group in order to carry out a reaction at some other functional group without any interference. After the reaction is completed, the protected group can be deprotected.

Protection Reagent:

A molecular framework used to block the reactivity of a particular functional group in a substrate with polyfunctional groups under specified conditions.

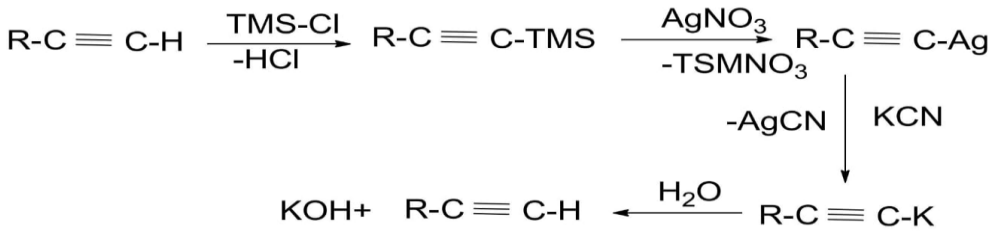
Example : alcohols are protective agent for acids.

Characteristics of Protective agent:

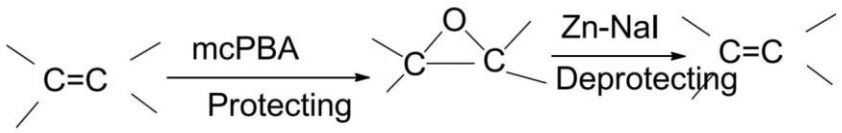
- It should be chemo selective in its reaction with the functional group to be protected.
- The protected group should be stable/resistant enough to survive the reaction conditions maintained for performing the desired reactions.
- After the reaction, the protected group should be easily and chemo selectively removed under mild conditions without affecting the rest of the molecule.

Example 1 :

Protection of active C-H bond. Terminal alkynes are protected with chloro trimethyl silane and deprotected by AgNO3/KCN –Corey' s method.



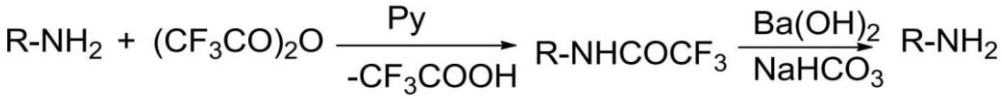
Alkenes can be protected by epoxidation reaction and deprotected by treatment with ZnI-NaI acetic acid.



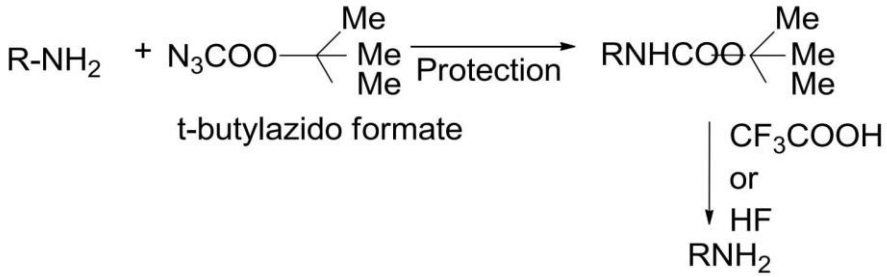
Example 2

Protection of Amino groups:

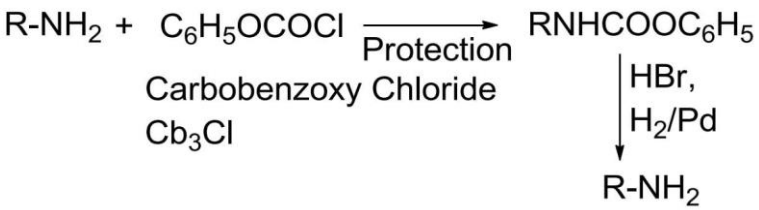
1) Trifluoroacetic anhydride:



2) tert-butyl azido formate:



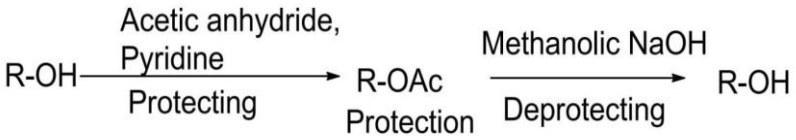
3)Carbobenzoxy chloride:



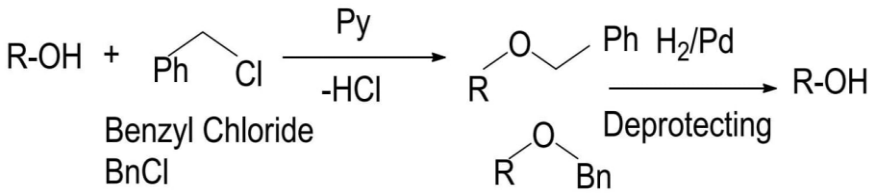
Example 3

Protection of alcohol group:

1)Acetic anhydride:



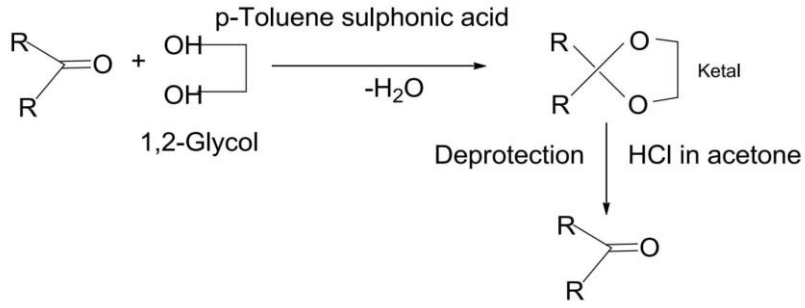
2) Benzyl chloride



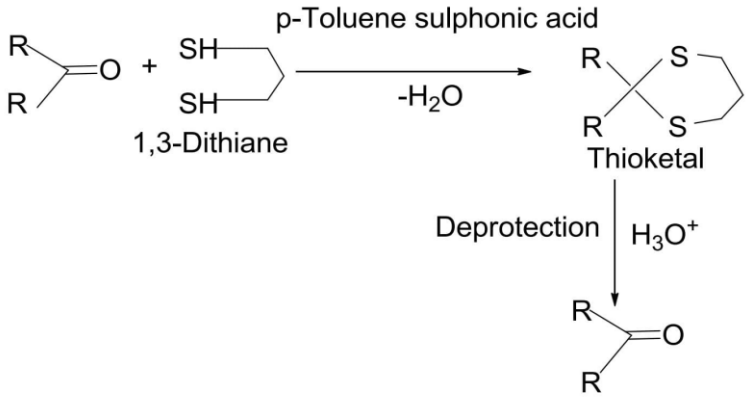
Example 4:

Protection of aldehydes and ketones

1) 1,2 glycol



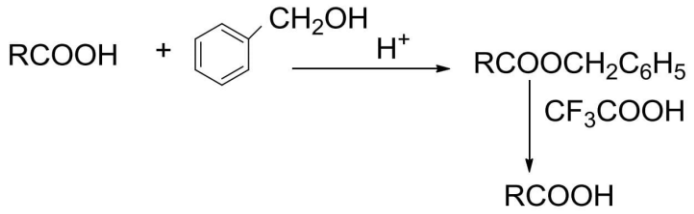
2)1,3-Dithiane



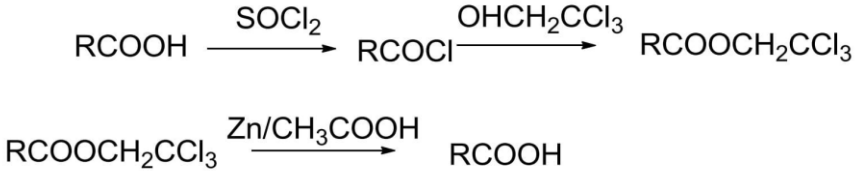
Example 5

Protection of acid group

1) Benzyl alcohol



2)Trichloro ethyl alcohol



Activating Groups :

The group which increases reactivity of benzene nucleus toward further electrophilic substitution reaction is called activating group.All ortho-para directing group except halogens are activating groups.These groups donate electrons to benzene ring. This increases electron density and make the benzene ring more reactive toward further electrophilic substitution reaction.

Examples :- NH2, -NHR, -O-, -OH, -OCH3, -CH3 etc

Deactivating Group

The group which decreases reactivity of benzene nucleus toward further electrophilic substitution reaction is called activating group .All meta directing group and halogens are deactivating groups. These groups withdraw electrons to benzene ring. This decreases electron density and make the benzene ring less reactive toward further electrophilic substitution reaction. Hence these groups are called deactivating groups.

Examples :- NO2, -SO3H, -CN, -CHO, -COOH, -CI, -Br. Etc

Activating groups	**Deactivating groups**
Activating groups increase the rate of reaction in electrophilic aromatic substitution reactions, relative to H Examples: hydroxy, alkoxy ,amine ,amide ,alkyl	Deactivating groups decrease the rate of reaction in electrophilic aromatic substitution reactions, relative to H Example: cyano, carbonyl ,halo, nitro sulfonyl ,haloalkyl

Bridging elements:

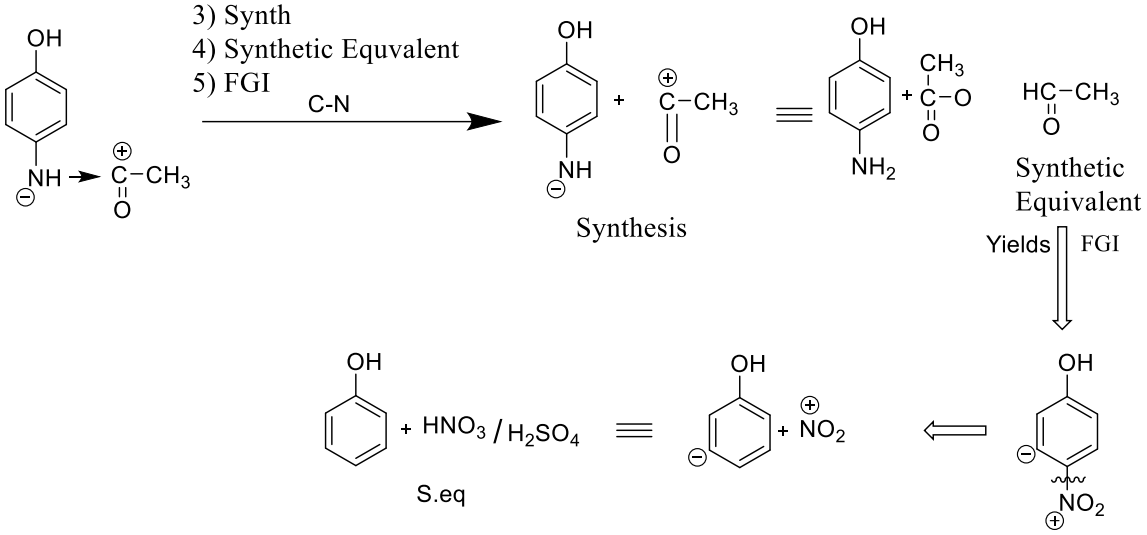
- Bridge elements are the elements of the second period of the periodic table.
- These elements show a relationship with the third-period elements or the typical elements, because of similarity in their properties.
- They show similarities in characteristics such as electronegativity and ion polarization.
- They are diagonally related to each other.

Examples of bridge elements:

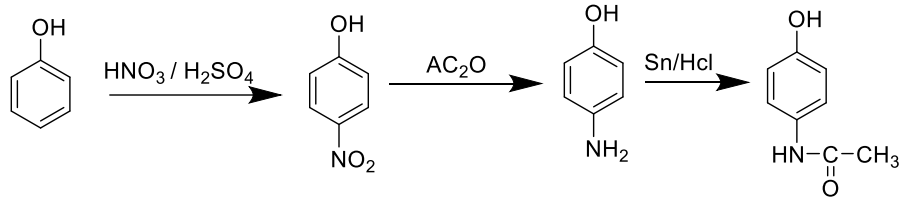
- Lithium (Li) and Magnesium (Mg) are bridge elements.
- Beryllium (Be) and Aluminium (Al) are bridge elements.

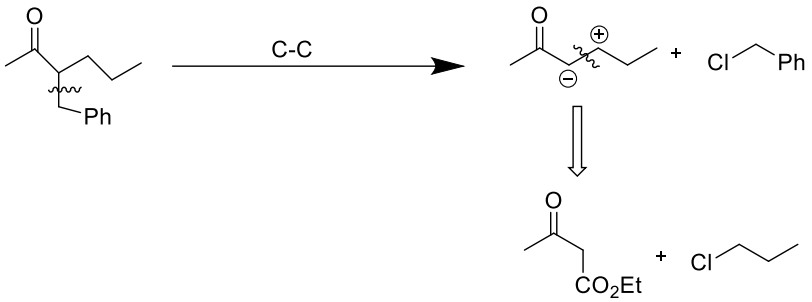
Retrosynthetic Analysis (R.A)

1) T.M
2) Disconnection
3) Synth
4) Synthetic Equvalent
5) FGI

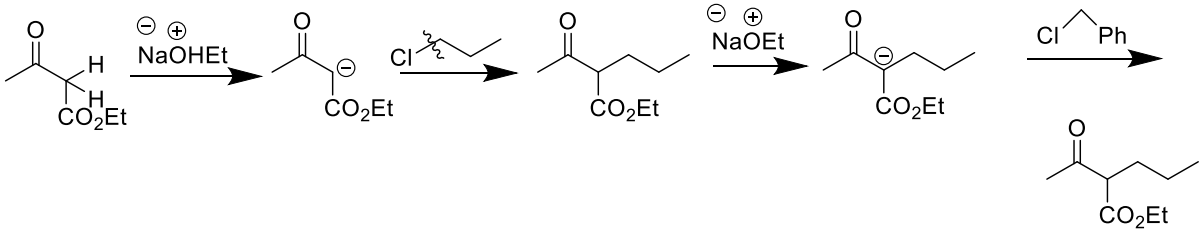


Synthesis:



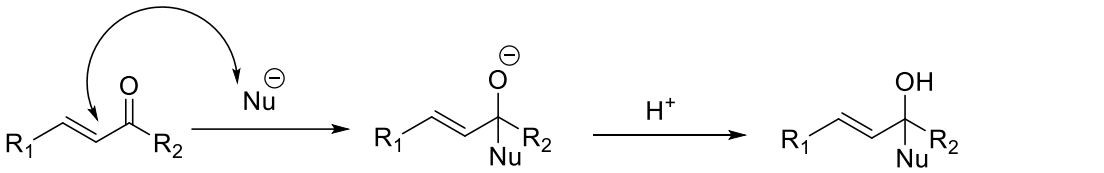


Synthesis:



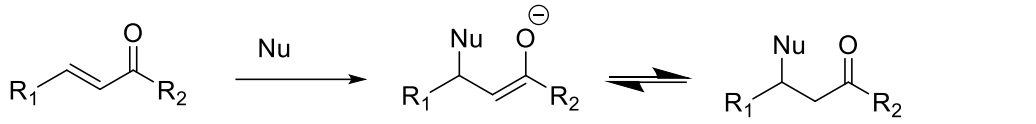
Regioselectivity dissconnection approach

1) 1,2 direct addiction



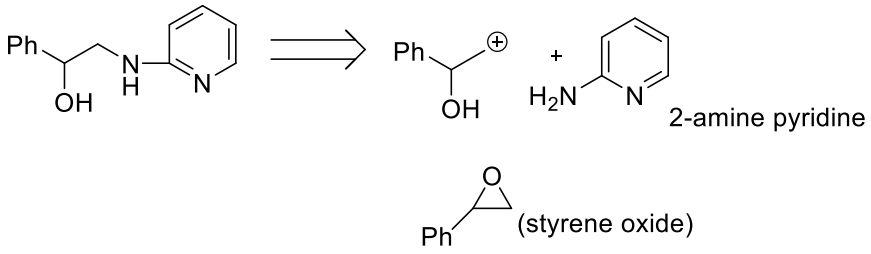
1,2-addiction kinetically favour

2) (1,4 Addiction) bidirect

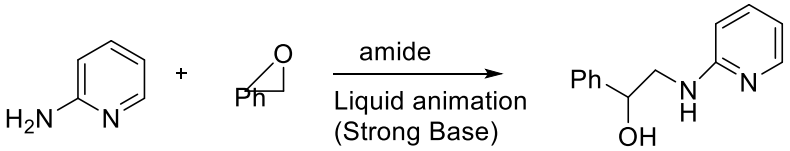


(1,4 addiction)
Thermodynamical stable

1,2 disconnection

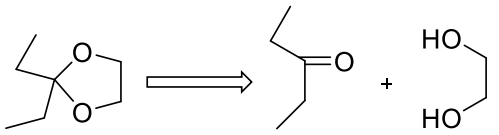


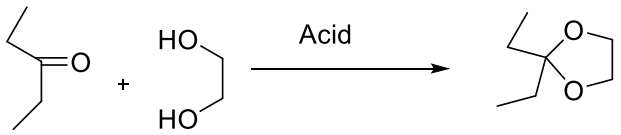
Sythesis



1,1 disconnection

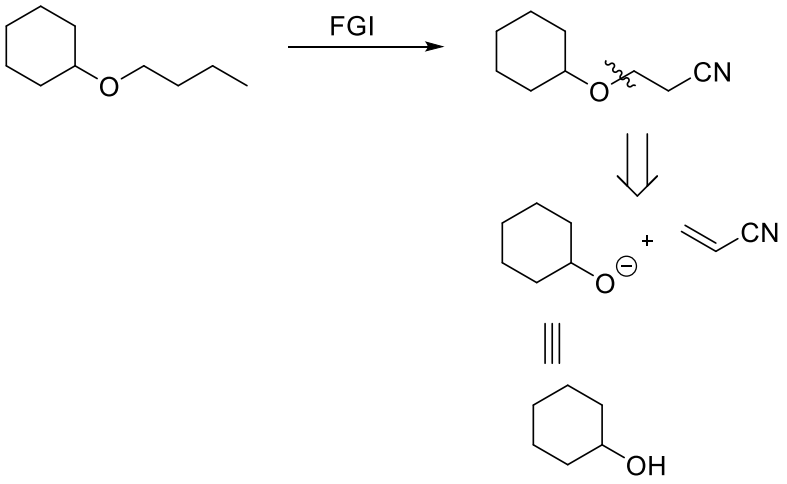
Same carbon attached to the functional group actone in synthesis is as proctecting group for aldehyde or ketone



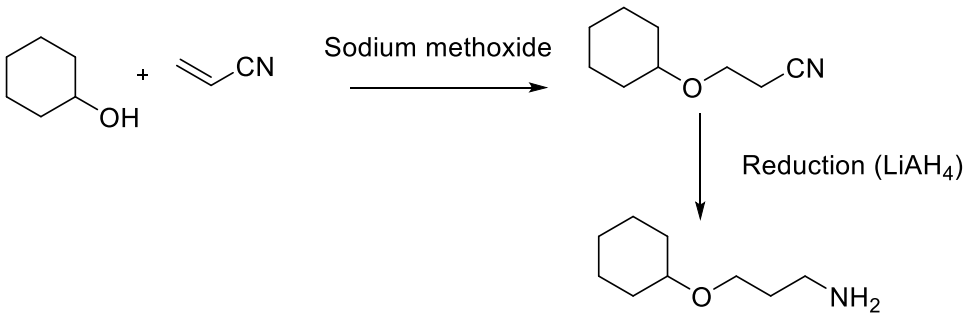


1,3 disconnection

1,3 disfunctional compound applicable eg: 1,3 amino acid



Synthesis



%Yield = Experimental yield / Theoritical yield *100

) calculate the %yield given reaction, where expeimental Yield 50g

$$mg + s \longrightarrow mgs$$

34g 30g

% = 50g / 56 * 100 = 89.28%56g

) 20g $CaCO_3$ is decomposed and 9.8g CaO is obtained what is %yield G CaO?

$$caco_3 \longrightarrow Cao + CO_2$$

coo g ⟶ 56g

20g ⟶ ?

20g = 56 * 20 / 100 g = 11.26 . cao

theoritical Yield

= 9.8 / 11.2 * 100

= 87.5%

ADVANTAGES OF CONVERGENT SYNTHESIS

Efficiency and Speed

1. Reduced number of steps: Convergent synthesis combines multiple components in a single step, decreasing overall synthesis time.

2. Increased yield: Fewer steps minimize cumulative losses, resulting in higher overall yields.

3. Faster optimization: Convergent synthesis allows for rapid evaluation of different components.

Simplification and Flexibility

1. Modular design: Convergent synthesis enables the assembly of complex molecules from smaller, interchangeable modules.

2. Easy modification: Individual components can be modified or replaced without affecting the overall synthesis.

3. Diversity-oriented synthesis: Convergent synthesis facilitates the generation of diverse compound libraries.

Improved Purification

1. Reduced impurities: Convergent synthesis minimizes the introduction of impurities at each step.

2. Simplified purification: Fewer steps result in fewer purification steps.

Economic Benefits

1. Cost savings: Reduced number of steps and reagents minimizes costs.

2. Atom economy: Convergent synthesis maximizes atom utilization, reducing waste.

Environmental Benefits

1. Reduced waste: Convergent synthesis generates less waste and byproducts.

2. Greener chemistry: Fewer reagents and steps minimize environmental impact.

Complex Molecule Synthesis

1. Enables synthesis of complex molecules: Convergent synthesis facilitates the assembly of intricate structures.

2. Natural product synthesis: Convergent synthesis is particularly useful for natural product synthesis.

CONVERGENT SYNTHESIS – SYNTHETIC ROUTE

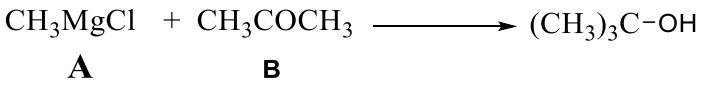
A →B

C→ D

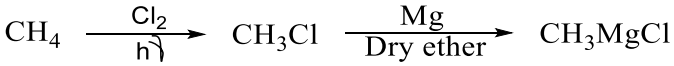
B+ D → *E*

SYNTHESIS OF STEREOCHEMISTRY CONTROLLED PRODUCT

1. <u>Synthesis of t-butyl alcohol</u>



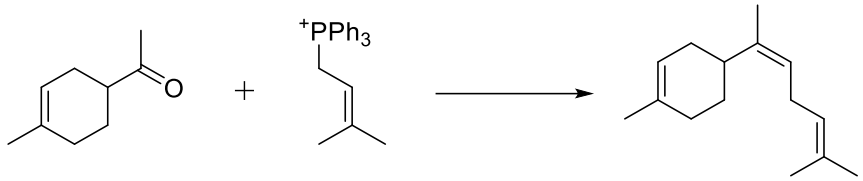
I. Preparation of methyl magnesium chloride (compound A)



II. Preparation of acetone(compound B)

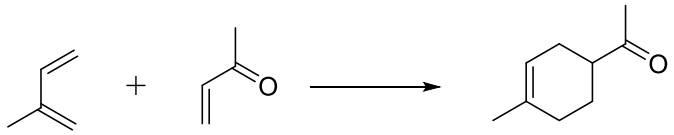
Synthesis of t-butyl alcohol is by reacting methyl magnesium chloride and acetone, two of them are prepared by different reactions. Methyl magnesium chloride is prepared by the reaction of methane with chlorine molecule methyl chloride is formed and methyl chloride reacted with magnesium and dry ether gives methyl magnesium chloride (compound A). Acetone is prepeared by reacting acetic acid with calcium hydrixide gives calcium acetate this on distillation gives acetone (compound B). Compound A and B reacted to give t-butyl alcohol.

2. <u>Synthesis of α-Bisabolene</u>

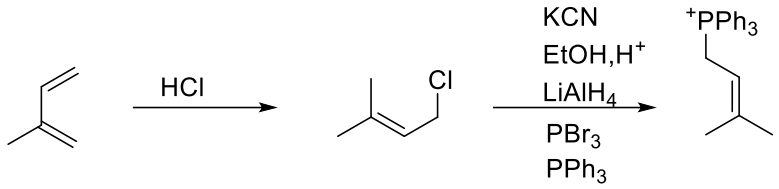


A **B**

<u>I. Synthesis of Compound A</u>



II. <u>Synthesis of compound B</u>



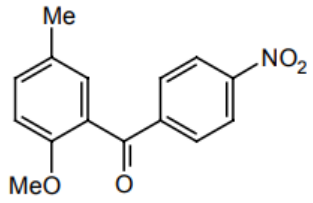
Synthesis of α-Bisabolene is obtained by reacting compound A and B in the above equation. Compound A is synthesized by Diels-Alder reaction by reacting isoprene with but-3-ene-2-one gives compound A (but-3-ene-2-one-1-(4-methylcyclohex-3-ene-1-yl)ethan-1-one). Compound B is synthesized by reacting isoprene with HCl gives 1-chloro-3-methyl-2-butene, this on reaction with KCN, EtOH, $LiAlH_4$, PBr_3,PPh_3 gives compound B (3-methylbut-2-en-1-yl tiphenylphosphonium ion. Compound A and compound B reacted by Wittig reaction to give α-Bisabolene.

UNIT II

Organic Synthetic Methodology

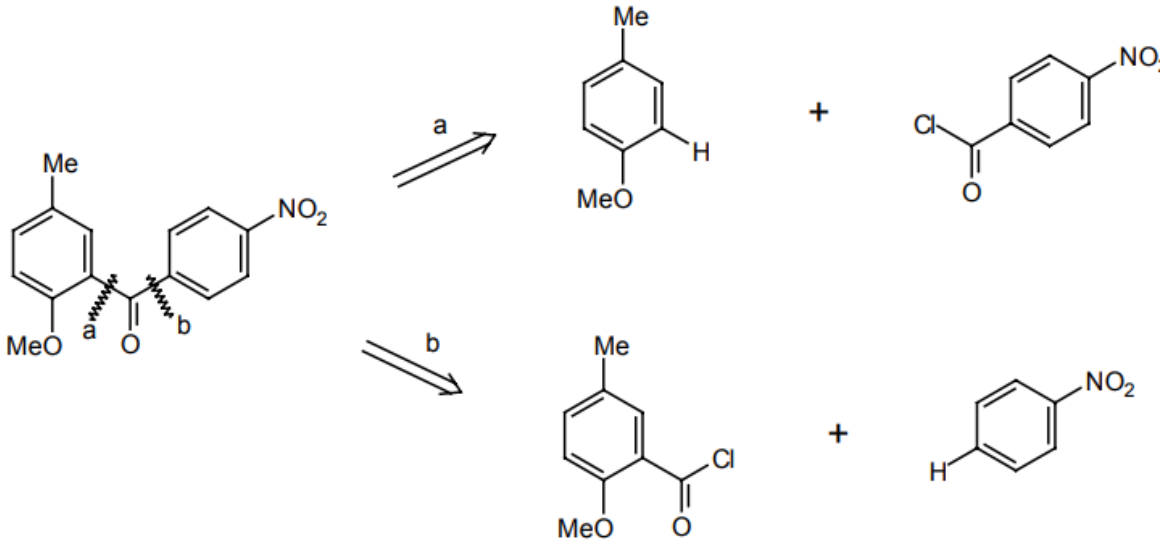
Retrosynthetic Analysis – Alternative Synthetic Routes

Example 1:



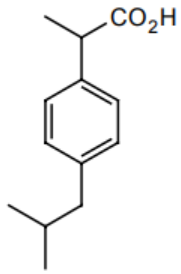
Analysis

There are two possible disconnections



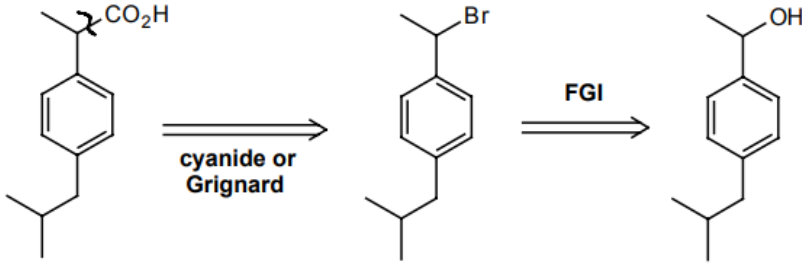
Disconnection b will not do as the nitro group is meta-directing and in any case nitro benzene will not react under Friedel-Crafts conditions. Disconnection a is fine as the MeO group is more powerfully ortho-directing than the Me group.

Example 2:

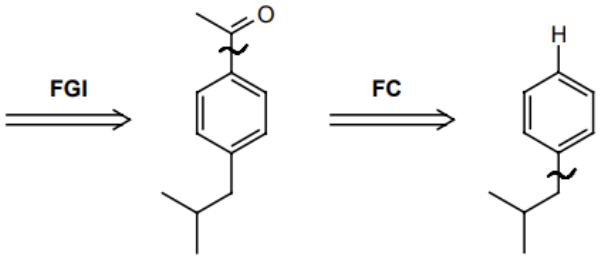


Analysis:

The carboxylic acid is the only FG so we can start there:

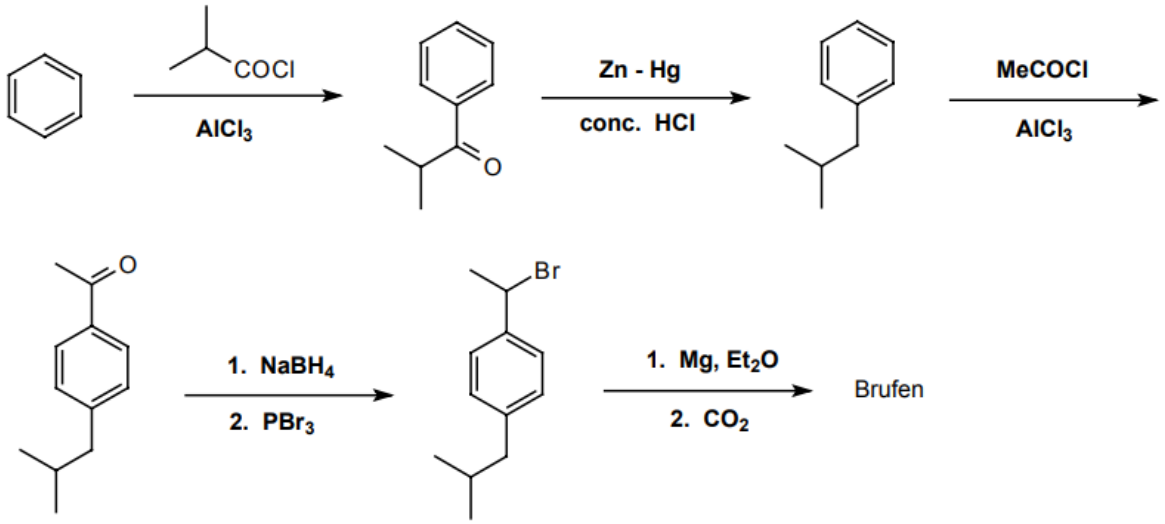


We now have a benzyl alcohol so we use Friedel-Crafts rather than Grignard

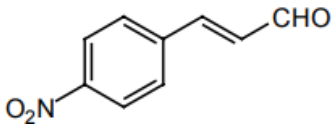


Again, we want to use Friedel-Crafts but we must use acylation rather than alkylation or we shall get rearrangement.

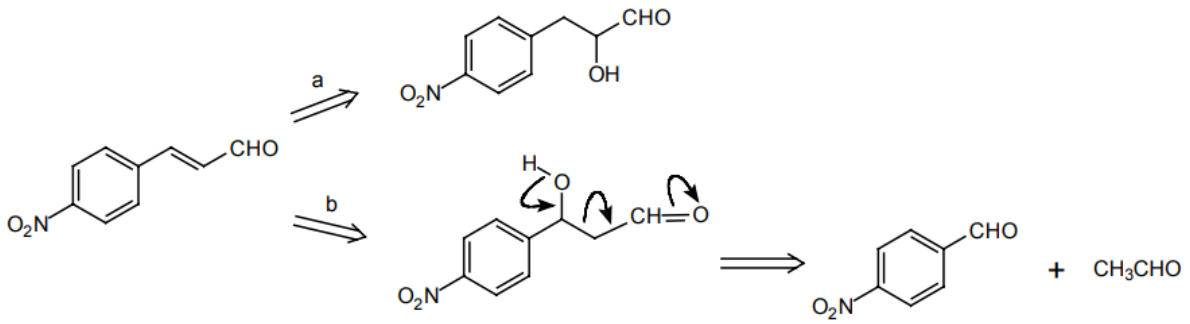
Synthesis:



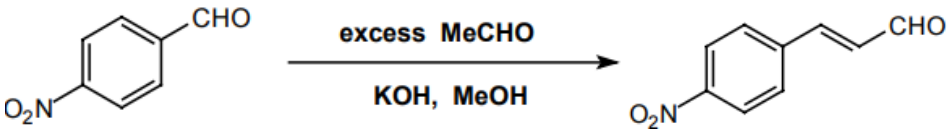
Example 3:



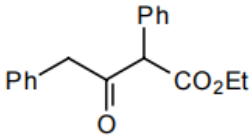
Analysis



The synthesis uses rather more vigorous conditions than those which gave the β-hydroxy carbonyl compounds. In fact, you can either treat the β-hydroxy compound with HCl in acetic acid or do the condensation in base:

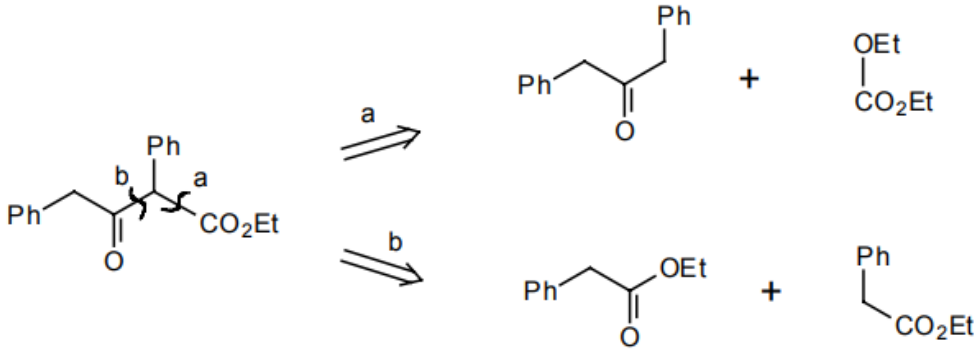


Example 4:

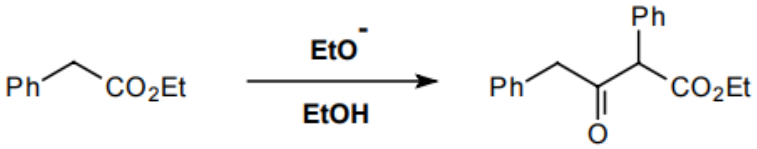


Analysis

B has the advantage of greater simplification. It also has an advantage of symmetry: both starting materials are actually the same molecule. The synthesis is therefore the Claisen ester condensation.



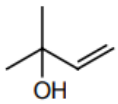
Synthesis



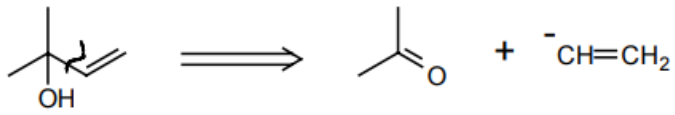
Synthesis Of Mono and Bifunctional Molecules Via Disconnection Approach

Monofunctional Molecules

Example 1

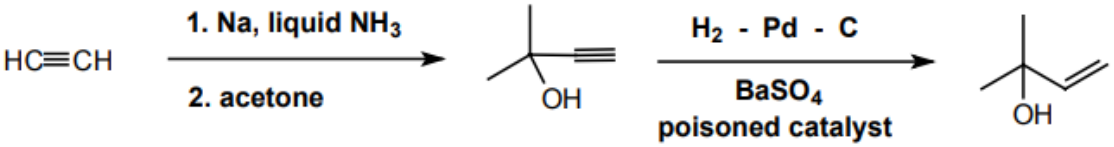


Analysis

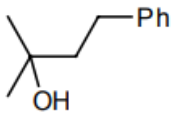


Synthesis

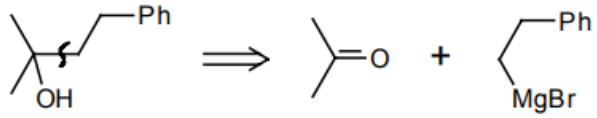
Partial reduction of the acetylene gives the olefin.



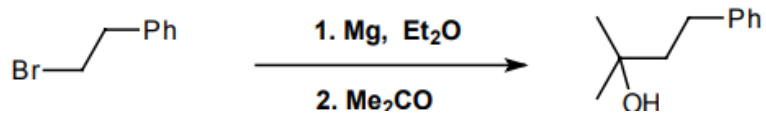
Example 2



Analysis

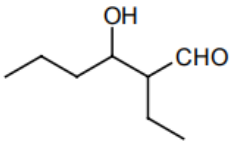


Synthesis

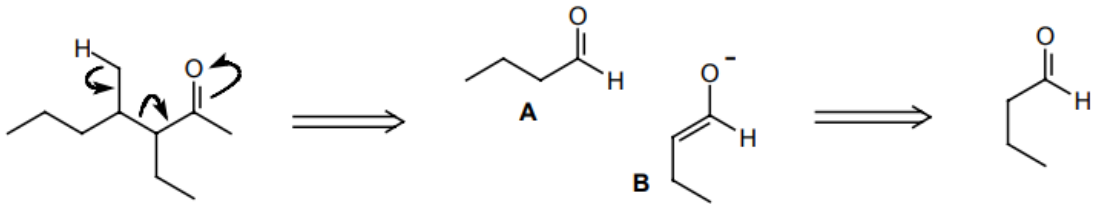


Bifunctional molecules

Example 1

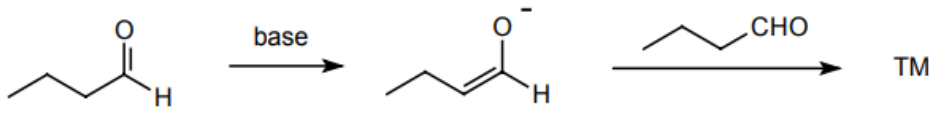


Analysis

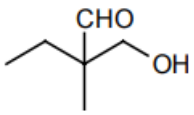


Synthesis

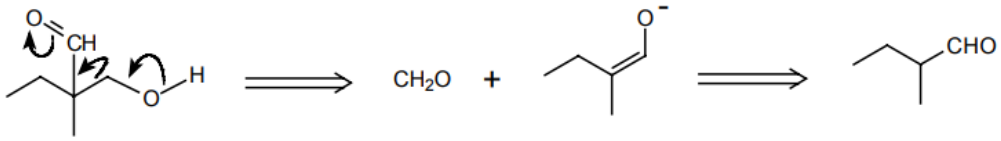
The anion B is just the enolate anion of a carbonyl compound, actually the same as A. So there is no need to use a Grignard reagent or any other synthetic equivalent in this reaction: anion B itself can be the intermediate and we simply treat the aldehyde with mild base:



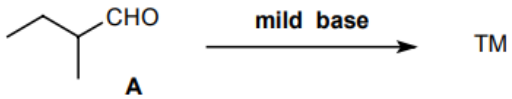
Example 2



Analysis



Synthesis



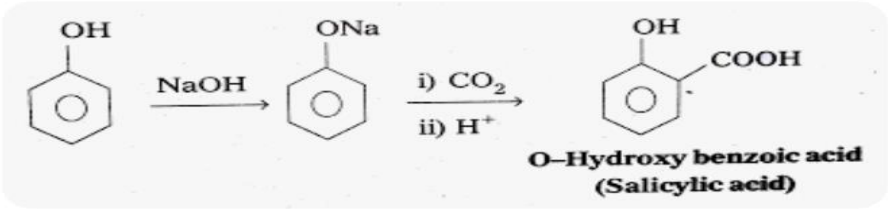
KEY INTERMIDIATES, AVALILABLE STARTING MATERIALS AND RESULTING YIELD OF ALTERNATIVE METHODS

Key Intermediate:

In organic synthetic methodology, a key intermediate is a crucial compound that forms during a multi-step chemical synthesis and is essential for producing the final desired product. A key intermediate is a compound that is necessary for the subsequent reactions leading to the target compound. It acts as a stepping stone. It connects the starting materials and product. They are often reactive and can undergo further transformations to yield the final product.

Example: Acetylsalicylic acid (Aspirin) synthesis

Kolbe-Schmitt reaction – Sodium phenoxide reacts with carbon dioxide to yield salicylic acid. When phenol is treated with sodium hydroxide, sodium phenoxide is produced. It is a carboxylation chemical reaction. Sodium phenoxide is a key intermediate.



Available Starting Materials and Resulting Yield of Alternative Methods

The choice of starting materials is crucial in organic synthesis, as it directly influences the efficiency and yield of the desired product. Some common starting materials like simple organic molecules (Alkenes, alkynes, aromatic compound, alcohols, aldehyde etc..), naturally occurring compounds (Sugar, amino acid, terpenes) etc.

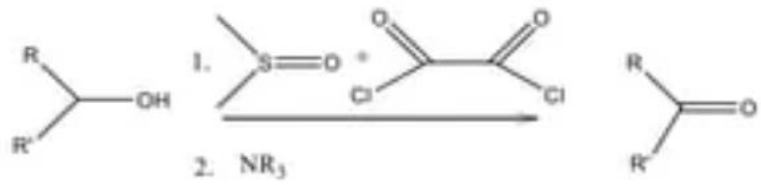
Example:

Oxidation of alcohols:

Starting material: primary or secondary alcohols

Swern oxidation: The swern oxidation of alcohols avoids the toxic metals such as chromium, and can be carried out under very mild conditions.(80-90%)yield.

This reaction allows the preparation of aldehyde and ketone from primary and secondary alcohols, respectively. Aldehydes do not react further to give carboxylic acids.



Swern oxidation requires low temperature (-78). Using dimethyl sulfoxide (DMSO), oxalyl chloride and a base (usually triethylamine).

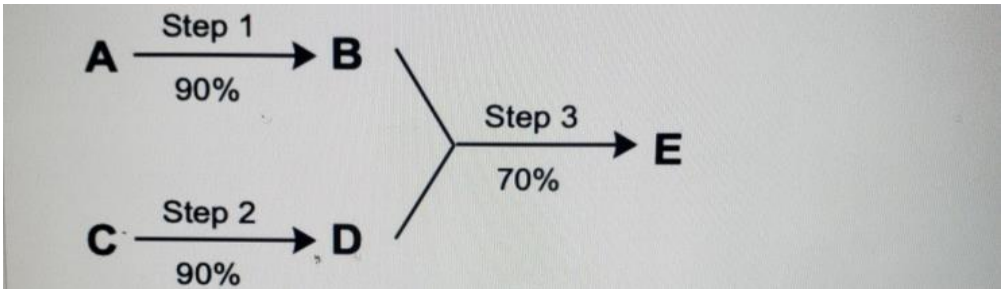
CONVERGENTS AND DIVERGENT SYNTHESIS AND SYNTHESIS BASED ON UMPOLUNG CONCEPTS OF SEEBACH

CONVERGENTS AND DIVERGENT SYNTHESIS

Convergent synthesis:

In convergent synthesis, key fragments of the target molecule are synthesized separately molecule. A convergent synthesis is shorter and more efficient than a linear synthesis leading to higher overall yield.

Where multiple fragments or building blocks are combined to form a larger complex molecule. It is flexible and easier to execute due to the independent synthesis of the fragments of the target molecule.



Longest sequence is 3 steps.

In this synthesis where two or more fragment of molecule are synthesized separately and then combined to form final product.

It have some advantages

1) Simplify the synthesis of complex molecules.
2) Improve overall yield and efficiency.
3) Modification can made individual fragments without affecting the entire synthesis .

A and B fragment it combined to final product.

Example: synthesis of aspirin

Salicylic acid synthesis to salicyloyl with hydrogen chloride and acetic anhydride to acetyl chloride with hydrogen chloride then combine these two steps to form a Target molecule.

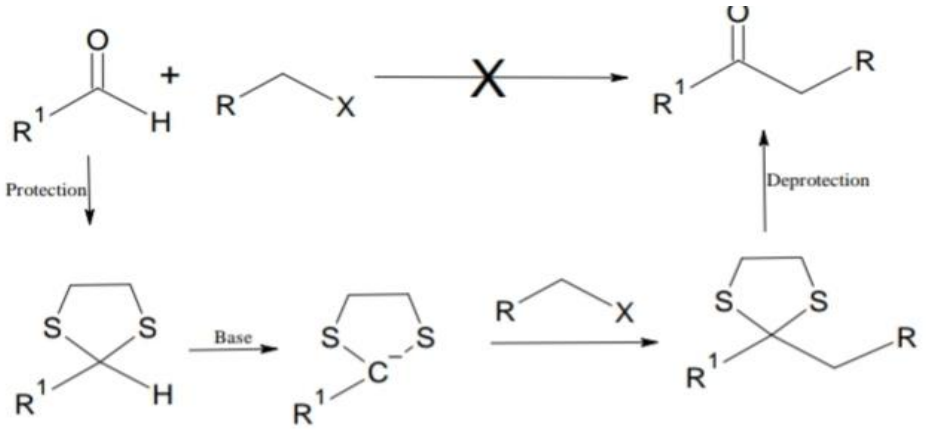
DIVERGENT SYNTHESIS

It is alternative the convergent synthesis. In divergent synthesis a single starting material is trans form into multiple product. A divergent synthesis is a strategy with the aim to improve the efficiency of chemical synthesis aims to generate a chemical compound by first reacting a molecule with a Set of reactants. The next generation of compound in generation. This methodology quickly diverges to large number of new compounds.

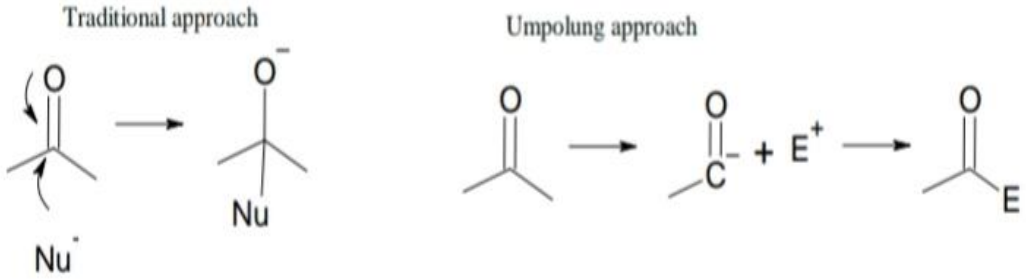
A fragment to give multi product

SYNTHESIS BASED ON UMPOLUNG CONCEPTS OF SEE BACH

Polarity inversion in organic chemistry is the chemical modification of a polarity of that group. The concept was introduced by D. Seebach and E.J Corey polarity analysis during restrosynthetic analysis tells a chemist. When umploung tactics are required to synthesis a Target molecule. It is also known as polarity inversion and also called Corey- Seebach reaction.



The temporary modification of a carbonyl group so that the carbon atom behaves as nucleophile in displacement and addition reaction would be of great utility in organic synthesis.



The carbonyl group is electrophilic at the carbon atom and is susceptible to attack by nucleophilic reagents. Thus, the carbonyl group so it act as a formula cation or as an acyl

cation. A reversal of the positive polarity of the carbonyl group so it act as a formula or acyl anion would be synthetically very attractive.To achieve, this the carbonyl group is converted to a derivative whose carbon atom has the negative polarity. After its reaction with an electrophilic reagent, the. Carbonyl is generated.

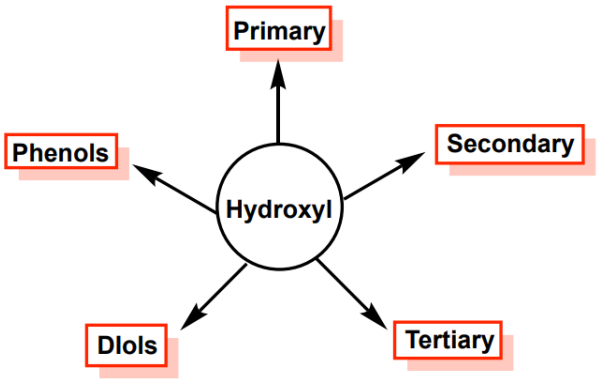
Hydroxyl and Carboxyl Protecting Groups

Protecting Groups

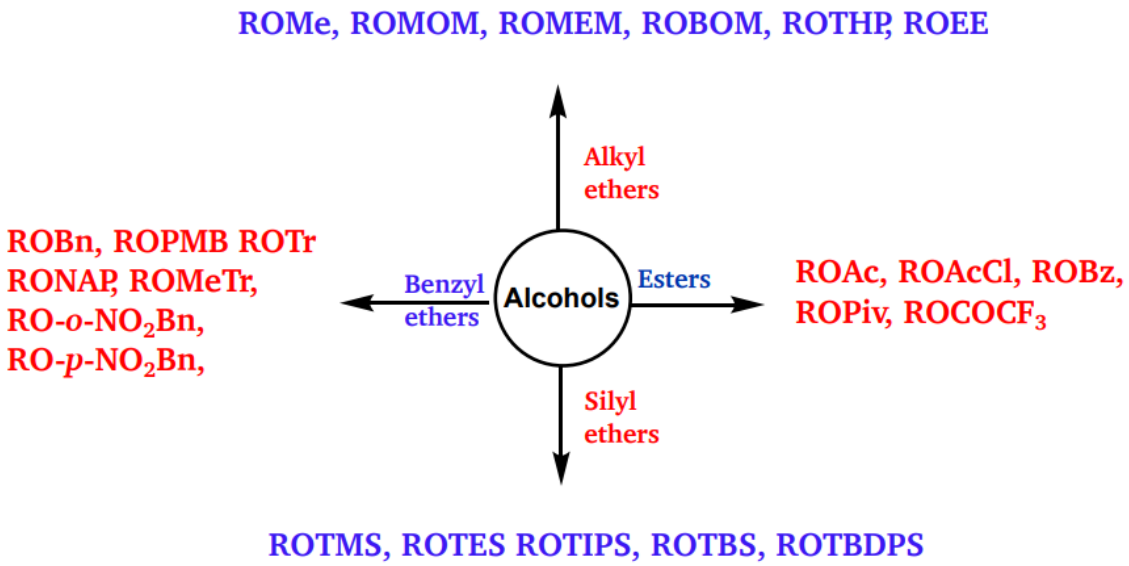
Protecting Groups are those groups which are temporarily attached to a functional group. These groups make the functional groups not to react under certain reaction conditions in subsequent steps. These groups can be cleaved after its job is done.

When a molecule has more than one functional group, then there is a likely possibility that functional groups interfering with each other while carrying out a reaction. When principles of selectivity can’t be applied, then protection of one functional group is really necessary to carry out a reaction on the other functional group.

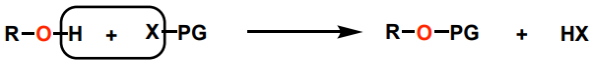
Hydroxyl Groups – Types



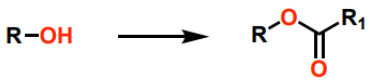
Protecting Group for Alcohols



Introduction of Protecting Groups



Acetates

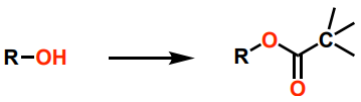


Properties: Stable to acid and mild base, not compatible with strong nucleophiles such as organometallic reagents

Formation: Ac_2O, pyridine

Acetyl chloride, pyridine

Pivaloates

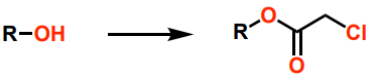


Properties: Selective for primary alcohols, Removed with mild bases

Formation: t-Butylacetyl chloride, Py

t-Butylacetic anhydride, Base

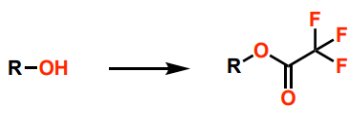
Chloroacetates



Properties: Removed with Zn dust or thiourea

Formation: Chloroacetyl chloride, Base

Trifluoroacetates

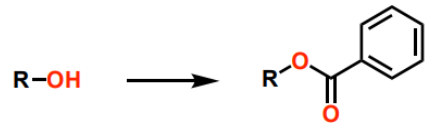


Properties: Removed with base

Formation: Trifluoroacetyl chloride, Base

Trifluoroacetic anhydride, Base

Benzoates



Properties: More stable than acetates wrt hydrolysis

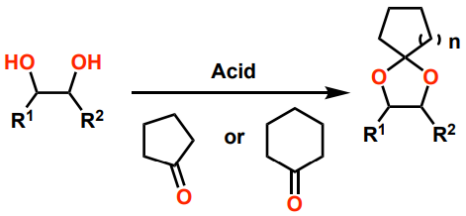
Formation: Benzoyl Chloride, Base

Benzoyl Cyanide, Base

Benzoic Anhydride, Base

For 1,2 Diols

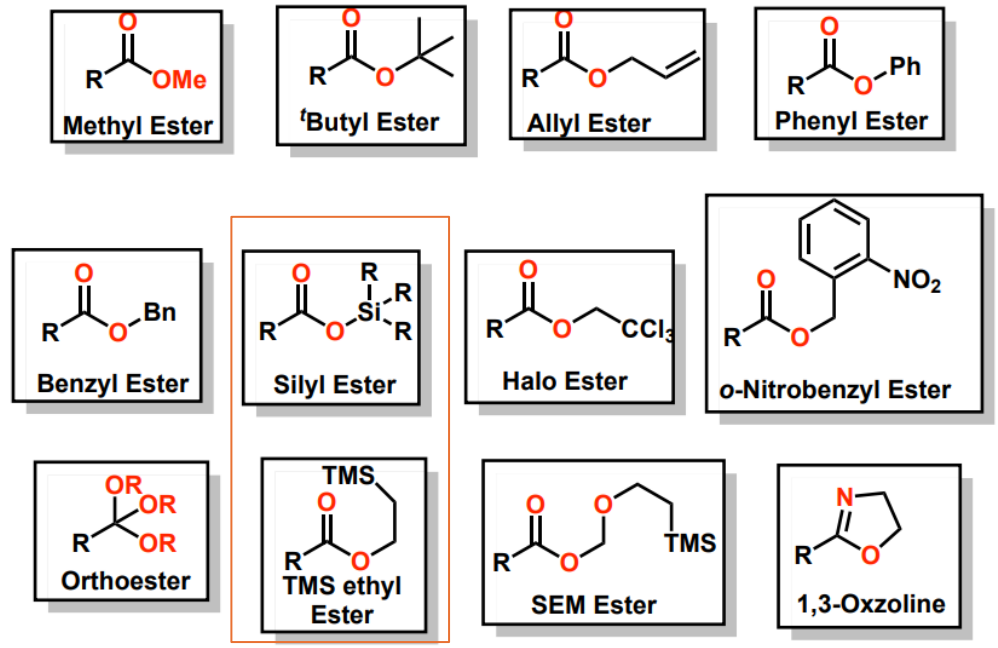
Cycloalkylidene ketals



Cyclopentylidenes are slightly easier to cleave than acetonides

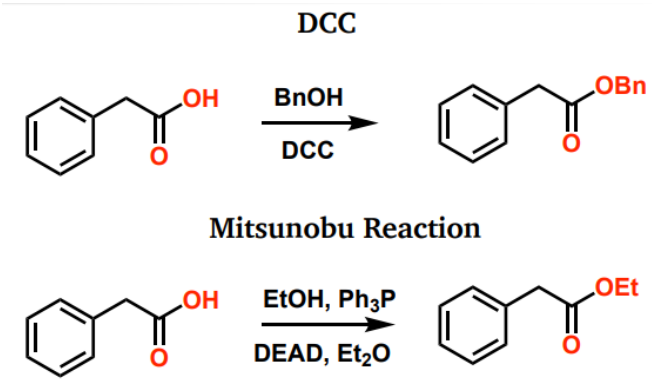
Cyclohexylidenes are slightly harder to cleave than acetonides

Protecting Group for Carboxylic Acids



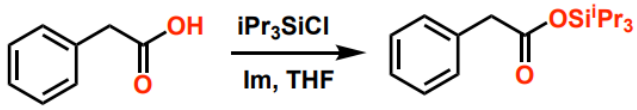
Alkyl esters:

Formation: Fischer esterification (RCOOH + R'OH + H^+), Acid chloride + ROH, pyridine t-Butyl esters: Isobutylene & acid Methyl esters: Diazomethane



Sillyl Esters

Bulky silyl esters do not react with organometallic reagents; fluorides are required to hydrolyse



PROTECTING GROUPS

Protecting groups are chemical entities used to temporarily mask functional groups in a molecule during synthetic reactions. They prevent unwanted reactions that could occur at those sites, allowing for selective modification to other parts of the molecule. Once the desired transformation are complete , the protecting groups can be removed to regenerate the original functional group.

Some common examples,

- Boc for protecting amine group.
- Diols for protecting carbonyl group.
- Triphenyl methyl for protecting alcohol group.
- Trityl for protecting thiol group.

ADVANTAGES:

- Easy to introduce.
- It leaves easily.
- Cheaply available.
- It does not react with other component in a reaction.
- After introduction of protecting group asymmetric carbon should not generate.

PROTECTION OF CARBONYL GROUP:

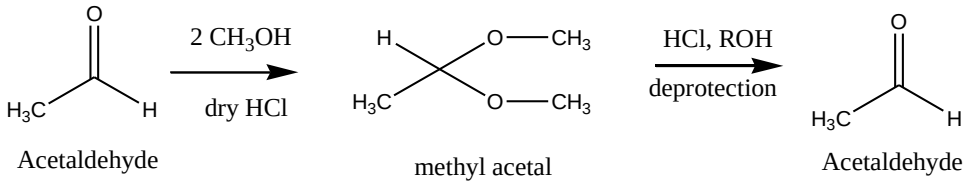
Protecting groups for carbonyl group are alcohol, diol, thiol, dithiol, hemiacetal. Semi carbazides, cyanohydrins, imines, hydrazones can protect carbonyl group but its deprotection is difficult.

Following compounds are formed while using protecting groups,

- Acyclic acetal or ketal
- Cyclic acetal or ketal
- Dithio acetal or ketal
- Hemithio acetal or ketal

ACYCLIC ACETAL OR KETAL:

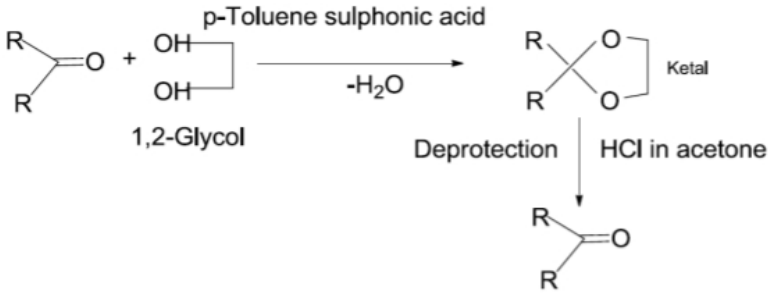
It is formed by using alcohol as protecting group in the presence of acid.



Acetaldehyde methyl acetal Acetaldehyde

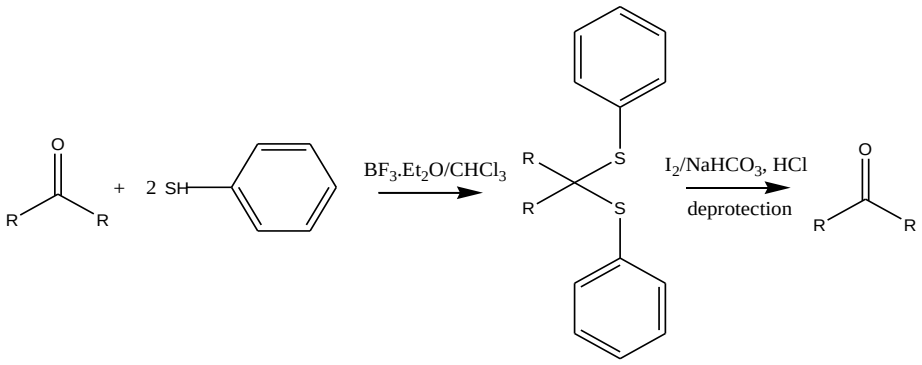
CYCLIC ACETAL OR KETAL:

It is acid catalyzed reaction for carbonyl group and solvents can be dry HCl or p-TsOH, acetone.

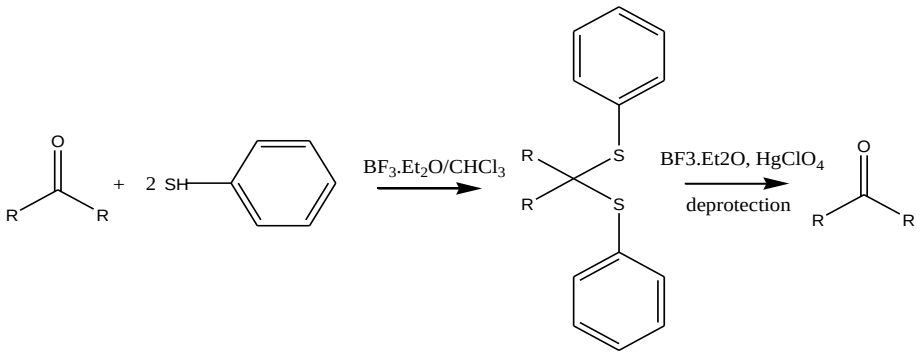


DITHIO ACETAL OR KETAL:

It can be protected by Sulphur derivative and it is deprotected by two ways. One way is using Hg^{2+} salt like $HgCl_2$ or $HgClO_4$ in the presence of $BF_3.Et_2O$ complexes as a solvent and another way is through oxidation by using oxidizing agents like $I_2/NaHCO_3$, HCl or $NaIO_4$,$BF_3.Et_2O$, HCl.



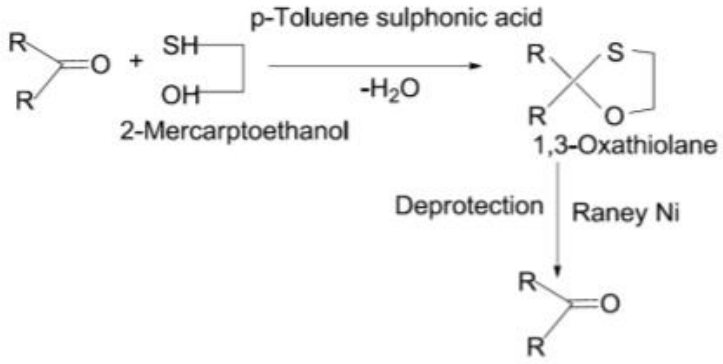
dithio ketal



dithio ketal

HEMITHIO ACETAL OR KETAL:

It is formed by using 2-mercarptoethanol as a protecting group in the presence of p-toluene sulphonic acid.

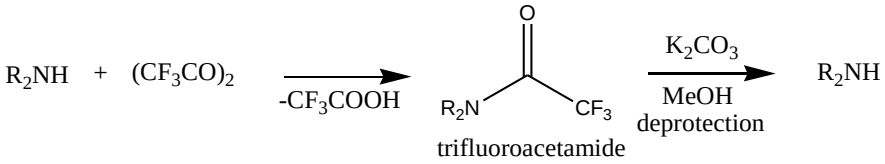


PROTECTION OF AMINO GROUP:

- Amino groups easily undergo rection with oxidizing agents and alkylating reagents.
- Primary and secondary amines are deprotonated easily with alcohol.
- Organometallic group easily remove hydrogen from primary and secondary amines.
- Basic groups also remove hydrogen.
- So, protecting group is required to avoid all those type of reactions during synthesis.
- It is not possible to build a peptide of specific structure from its component amino acids unless amino group can be protected.

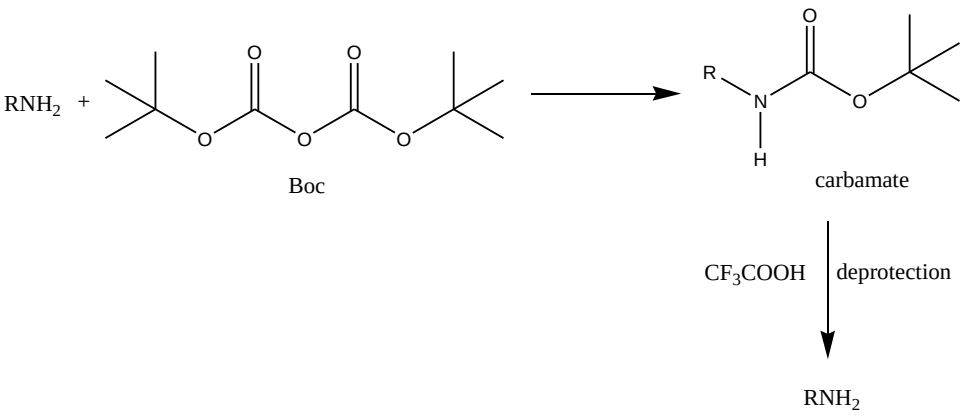
Examples,

Trifluoroacetic anhydride:

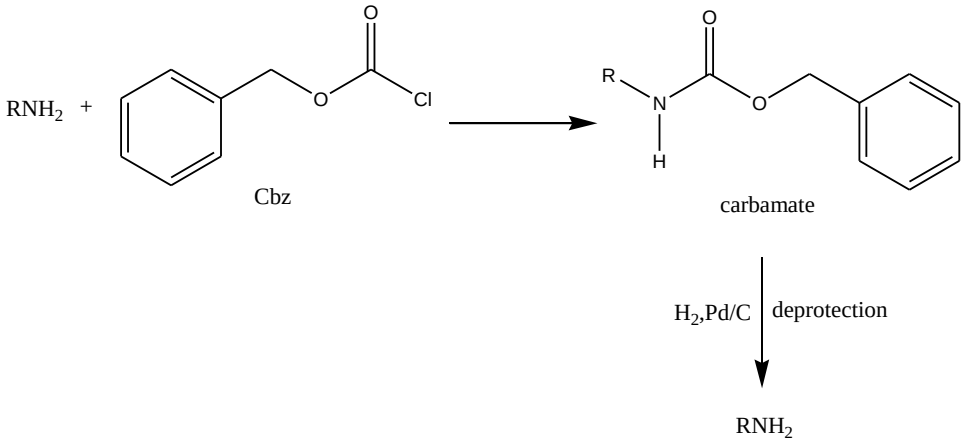


Tert-butyl azido formate:

Tert-butyl carbamate (Boc group):



Cbz or z-carbobenzyl:



PROTECTION OF THIOL GROUPS:

Protecting groups for thiols are chemical modifications that temporarily block the reactivity of thiol (-SH) groups, preventing unwanted side reactions, dimerization, or oxidation. This allows for:

- Selective modification of other functional groups
- Prevention of disulphide bond formation
- Improved stability and shelf-life.

Common protecting groups for thiols:

Acetyl (Ac) group:

- Protection: Acetic anhydride (Ac_2O) or acetyl chloride (AcCl)

  R-SH + Ac_2O ⟶ R-S-Ac + HOAc

- Deprotection: Base (e.g., NaOH) or ammonia (NH3)

  R-S-Ac + NaOH ⟶ R-SH + NaOAc

Example: Protection of cysteine thiol in peptide synthesis

Benzyl (Bn) group:

- Protection: Benzyl bromide (BnBr) or benzyl chloride (BnCl)

  R-SH + BnBr ⟶ R-S-Bn + HBr

- Deprotection: Hydrogenolysis (H_2, Pd/C) or acid (e.g., TFA)

  R-S-Bn + H_2 ⟶ R-SH + BnH

Example: Protection of thiol in 2-mercaptoethanol

$HS\text{-}CH_2\text{-}CH_2\text{-}OH \longrightarrow Bn\text{-}S\text{-}CH_2\text{-}CH_2\text{-}OH$ (protected 2-mercaptoethanol)

Tert-Butyl (t-Bu) group:

- Protection: tert-Butyl bromide (t-BuBr) or tert-butyl chloride (t-BuCl)

  $R\text{-}SH + t\text{-}BuBr \longrightarrow R\text{-}S\text{-}t\text{-}Bu + HBr$

- Deprotection: Acid (e.g., TFA) or base (e.g., NaOH)

  $R\text{-}S\text{-}t\text{-}Bu + TFA \longrightarrow R\text{-}SH + t\text{-}BuOH$

Example: Protection of thiol in 1-butanethiol

$HS\text{-}CH_2\text{-}CH_2\ CH_2\text{-}CH_3 \longrightarrow t\text{-}Bu\text{-}S\text{-}CH_2\text{-}CH_2\ CH_2\text{-}CH_3$ (protected 1-butanethiol)

Trityl (Tr) group:

- Protection: Trityl chloride (TrCl)

  $R\text{-}SH + TrCl \longrightarrow R\text{-}S\text{-}Tr + HCl$

- Deprotection: Acid (e.g., TFA) or silver nitrate ($AgNO_3$)

  $R\text{-}S\text{-}Tr + TFA \longrightarrow R\text{-}SH + TrOH$

Example: Protection of thiol in 2-mercaptoethylamine

$HS\text{-}CH_2\text{-}CH_2\text{-}NH_2 \longrightarrow Tr\text{-}S\text{-}CH_2\text{-}CH_2\text{-}NH_2$ (protected 2-mercaptoethylamine)

Illustration of protection and Deprotection in synthesis

Protection group

Protection in organic synthesis is a process that involves temporarily blocking a reactive site on a molecule with a protecting group. This is done to prevent unwanted reactions from occurring. The protecting group is then chemically removed in a later step, regenerating the reactive functional group. Then it enhance the chemical stability.

Purpose of protection groups

Prevent unwanted side reaction.

Enhance reaction efficiency.

Protect sensitive functional group (eh:- alcohols, amines)

Facilitate chemical reaction.

Improve yield and selectivity.

Allow for complex molecule synthesis.

Some common protection groups are:

For Alcohol – Tetrahydropyranyl (THP), Methoxy methyl(MOM)

For Amine – Tret-Butoxycarbonyl (BOC), Benz good u at bon um (Cbz)

For Carboxylic acid – Methyl ester (Me), Benzyl ether (Bn), Tert-dimethylsilyl(TBDMS)

For Phenols – Methyl ether, Benzyl ether.

Example:-

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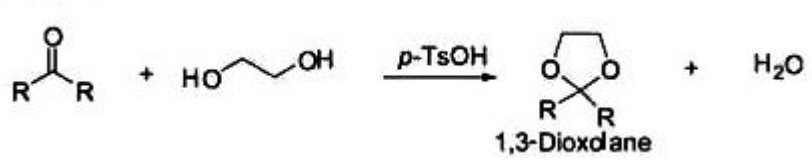
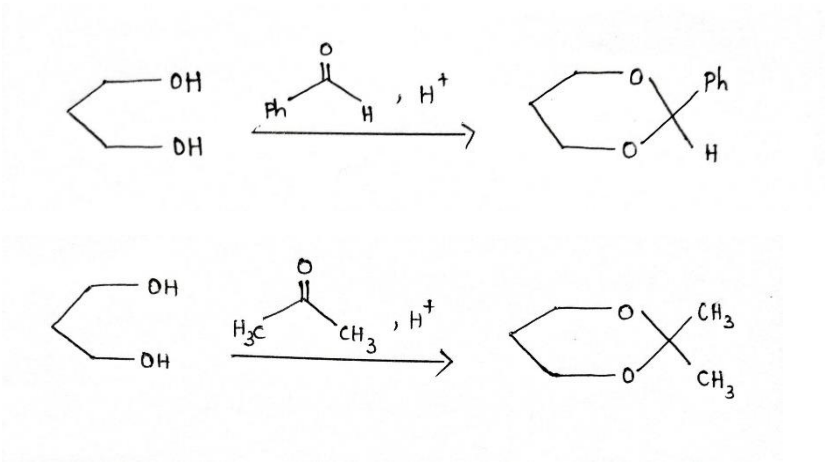


2. Protecting group of 1,2 and 1,3 diols



Deprotection in synthesis is the process of removing a protection group (PG) from a molecule to reveal the original functional group.

Purpose of Deprotection

1. Regenerates the original functional group
2. Allows further chemical reactions
3. Enables isolation of the final product
4. Enhances chemical diversity

Factors Influencing Deprotection

1. PG stability
2. Reaction conditions (temperature, solvent)
3. Substrate structure
4. Steric effects
5. Electronic effects

Importance of Deprotection

1. Regenerates original functional groups
2. Enables further synthesis
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5. Facilitates drug discovery and development

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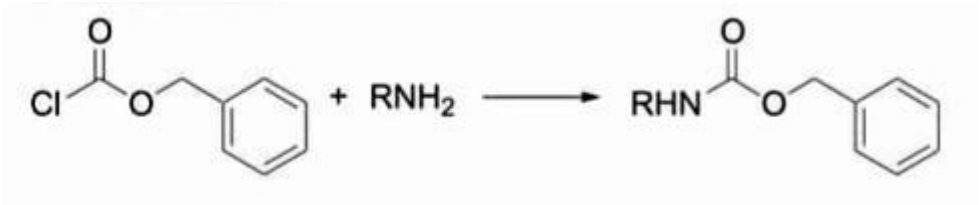
1. HCl (hydrochloric acid)
2. NaOH (sodium hydroxide)
3. Et3N (triethylamine)
4. H2 (hydrogen gas)
5. LiAlH4 (lithium aluminum hydride)
6. TBAF (tetrabutylammonium fluoride)
7. HF (hydrofluoric acid)

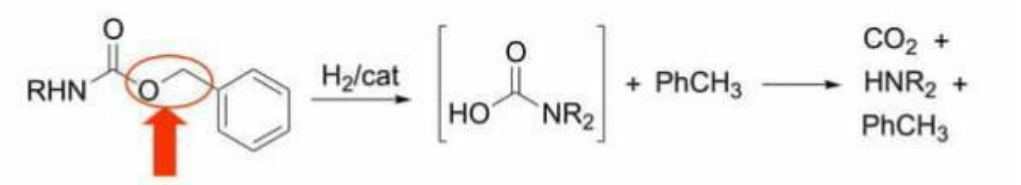
Examples:-

1. Protection of amino group as carbamates

Protection



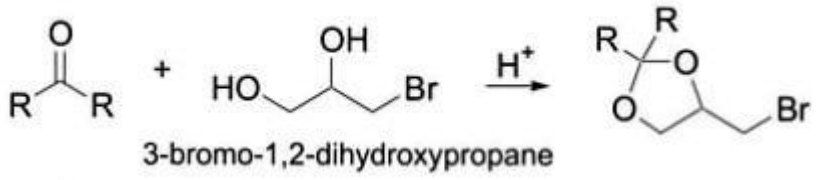
Deprotection



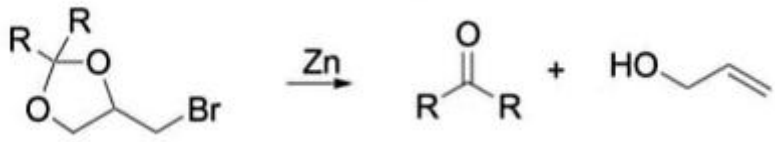
2. Protection of Carbonyl group as acetals and thioacetals

   A) Non hydrolytic conditions

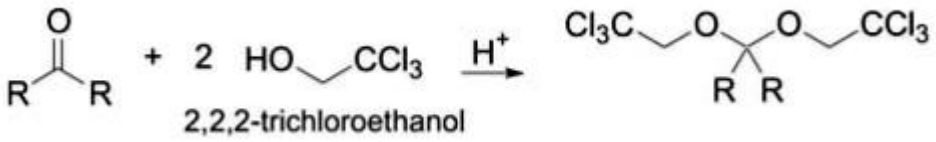
Protection



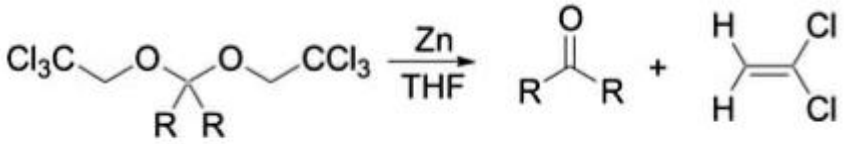
Deprotection



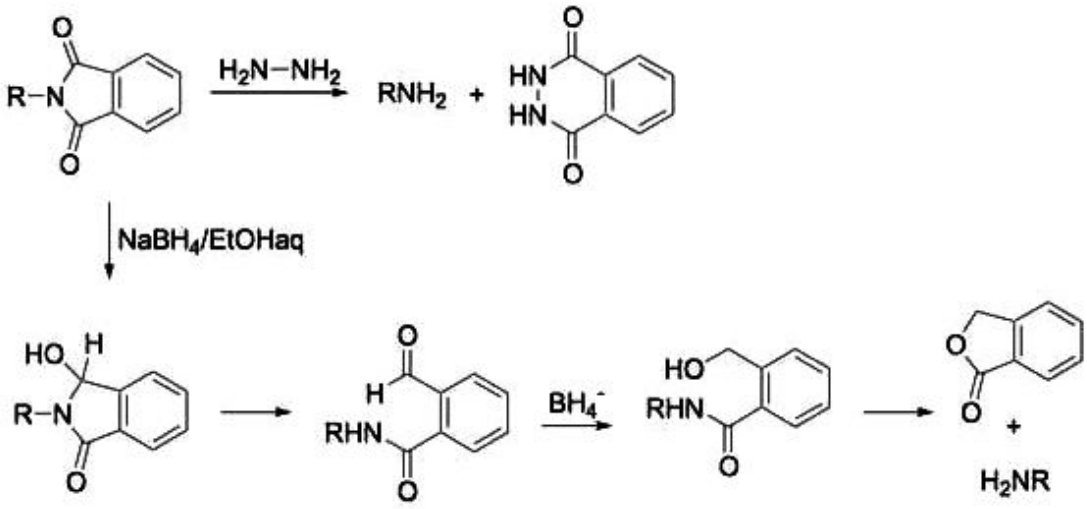
Protection



Deprotection



3. Protection of amino group as amide



CONTROL ELEMENTS:REGIOSPECIFIC CONTROL ELEMENTS

CONTROL ELEMENTS:

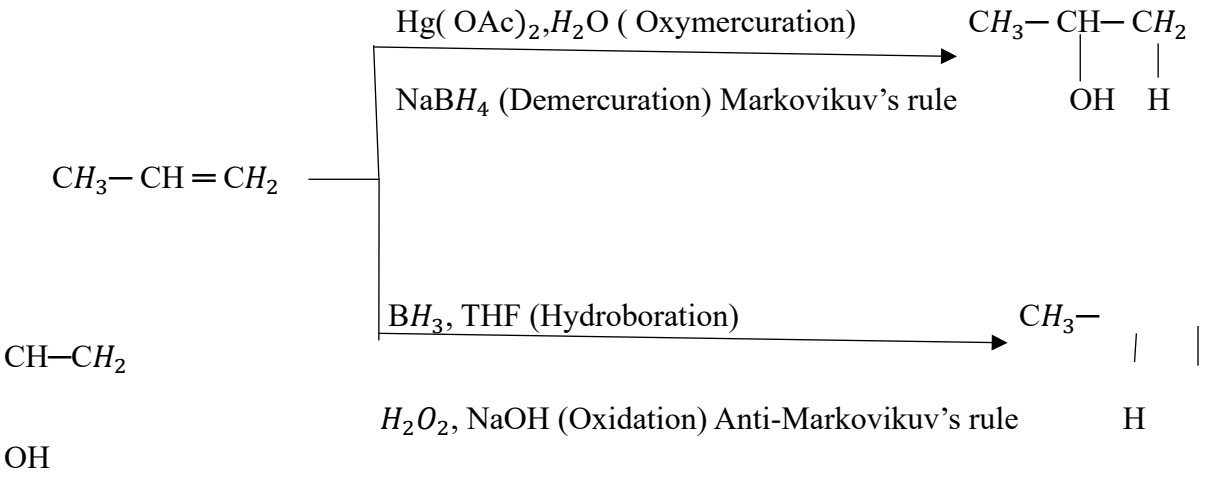
A control elements may be an atom or a group of atoms that are introduced in same stage of synthesis. So that the given reaction can be carried out selectively. The purpose of such control elements is to secure and efficient conversion of the starting material to the target molecule. They are divided into four type,

- Regiospecific control element
- Regioselective control element
- Stereospecific control element
- Stereoselective control element

REGIOSPECIFIC CONTROL ELEMENTS:

A regiospecific reaction exclusively gives only one, specific product. A regiospecific reaction can be made regiospecific by controlling the factors affecting the reaction, like temperature, pressure, presence of catalyst etc… i.e only one side is attacked completely and gives 100% yield.

EXAMPLE:



Markovikuv's rule:

In addition of unsymmetrical reagent to an unsymmetrical alkene, negative part of reagent add to the carbon (SP^2) of alkene having less hydrogen atom or more substitutent.

Anti- Markovikuv's rule:

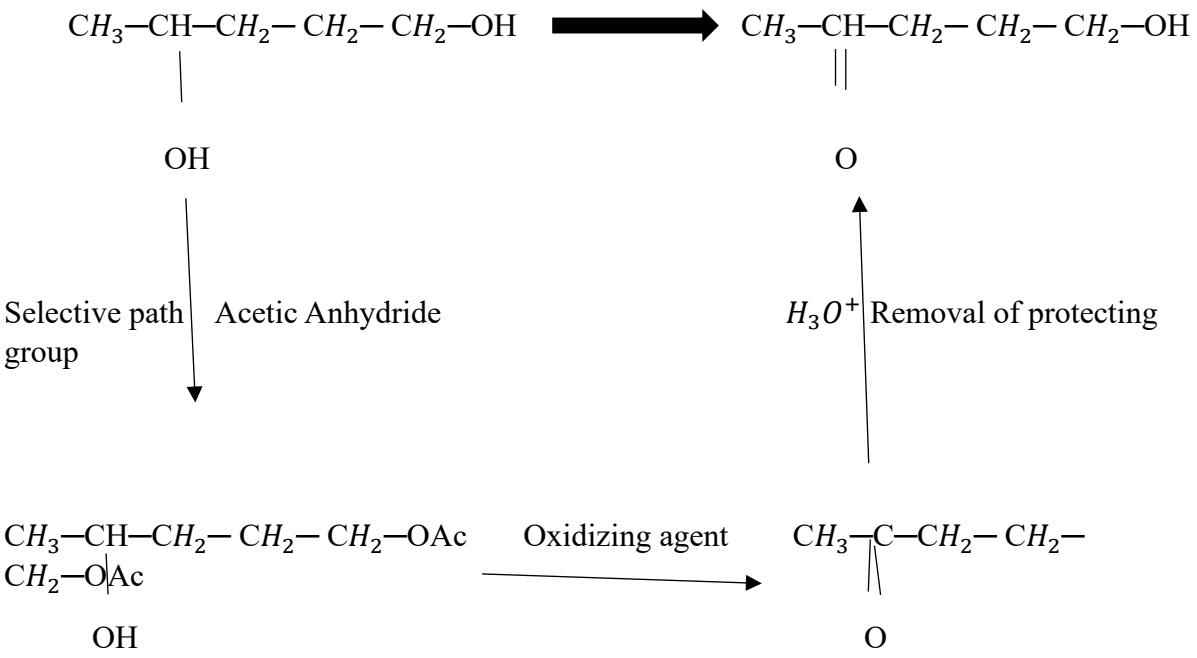
In addition of unsymmetrical reagent to an unsymmetrical alkene, negative part of reagent add to the carbon (SP^2) of alkene having more hydrogen atom or less substitutent.

USE OF AN PROTECTING GROPU:

Protecting groups are groups which are temporarily attached to a functional group and make that functional group not to react under certain condition in subsequent steps, cleaved after its job is done.

When a molecule has a more than one functional group, then there is likely possibily that functional group interfering with each other while carrying out a reaction. When principle of selectivity can't be applied then protection of one functional group is really catty but a reaction on the other functional group.

EXAMPLE:



USE OF A BRIDGING GROUP:

A regiospecific control element as a bridging group refers to a group or structural feature that connects two or more parts of a molecule influencing the regioselectivity of reaction. Bridging group can control the position where chemical reaction occur by enforcing structural constraint, electron distribution or steric hindrance.

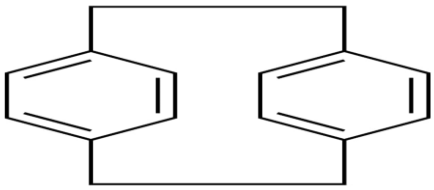
A bridging group links two different parts of a molecule, often stabilizing certain conformations and influencing how the molecule reacts. These groups can control regiospecificity by:

- Directing the formation of a particular regioisomer.
- Restricting the freedom of certain parts of the molecule to move or react.

- Modifying electronic or steric environments, thereby guiding chemical reactions to occur at specific positions in the molecule.

EXAMPLE:

In molecules like [2,2] paracyclophane, the bridging methylene chains lock two benzene rings in close proximity. This structural arrangement controls the electronic properties and reactivity of the aromatic rings, leading to regiospecific reactions.



[2,2] PARACYCLOPHANE

USE OF AN ACTIVATING GROUP:

This reaction involves Micheal condensation of Carvomenthone with methyl vinyl ketone to give adduct which contain formyl group present in the unsubstituted position. Hence the formyl group present in the unsubstituent position is called activating group. Finally the activating group gets eliminated under the some condition of the reaction.

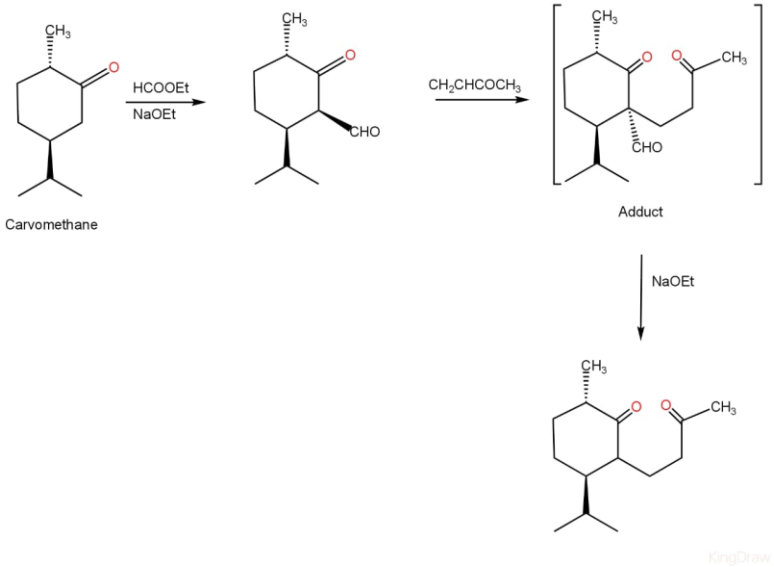


Illustration of protection and Deprotection in synthesis

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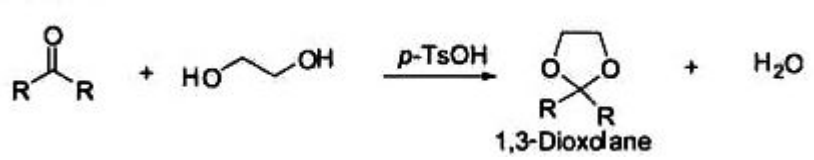

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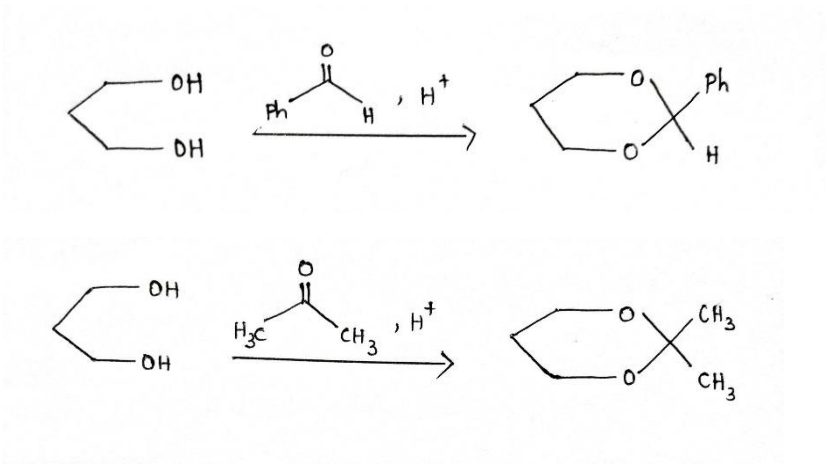

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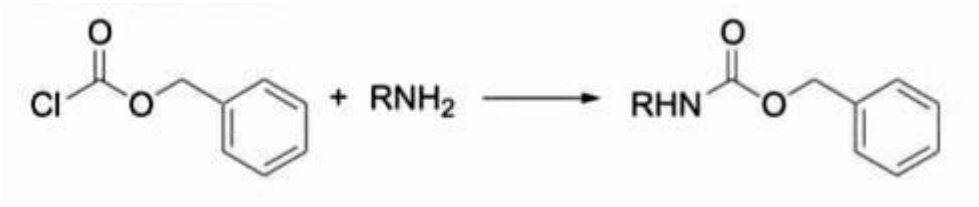
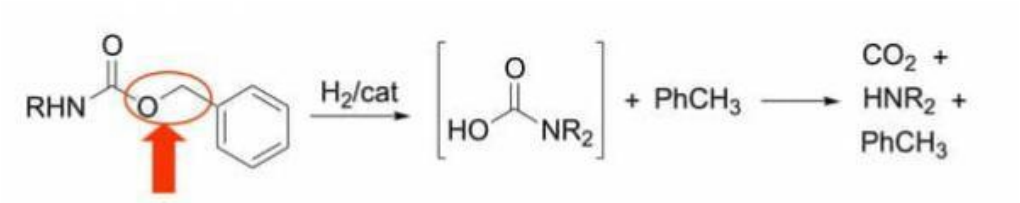
1. Protection of amino group as carbamates

Protection



Deprotection



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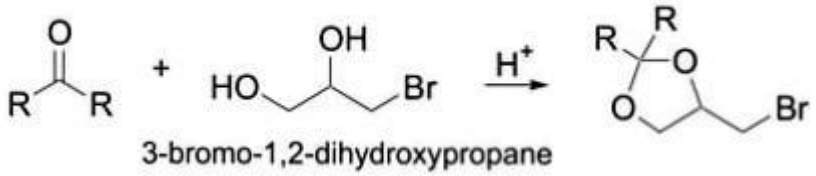
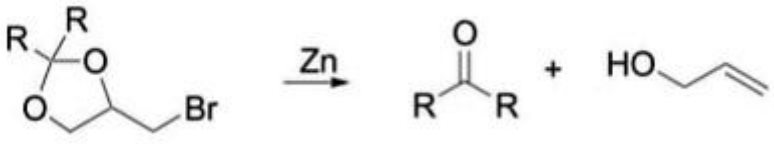
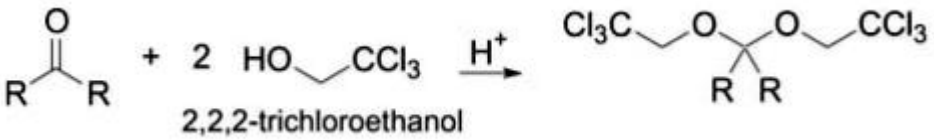


Deprotection



Protection



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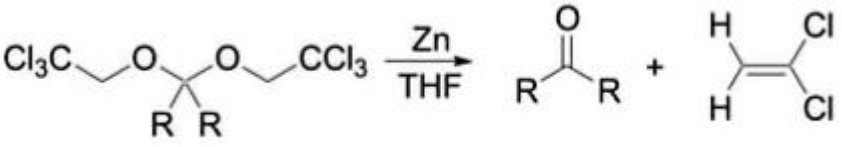

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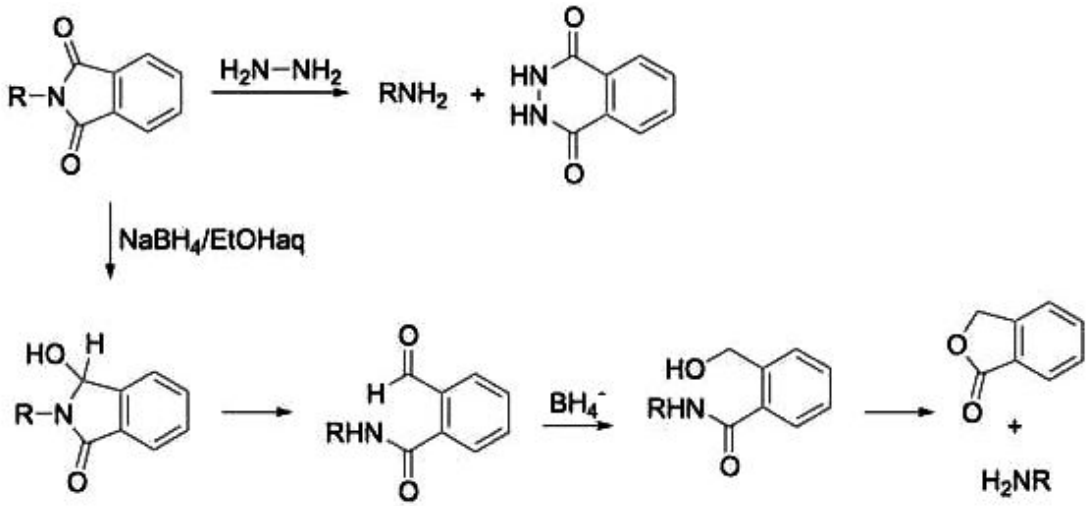


UNIT III

PERICYCLIC REACTIONS

WOODWARD HOFF MANN RULES:

To predict whether a pericyclic reaction is allowed or not under given condition, Woodward and Hoffmann proposed following set of rules based on *conservation of orbital symmetry* concept.

A thermal pericyclic reaction is allowed in the ground state, when the total number of $(4q + 2)_s$ and $(4r)_a$ components is odd.

Otherwise, if the total of $(4q + 2)_s$ and $(4r)_a$ components is even, the pericyclic reaction is allowed in the excited state i.e., under photochemical conditions.

Number of $(4q + 2)_s$ and $(4r)_a$ components	**The condition under which the reaction is allowed**
Odd	Thermal
Even	Photochemical

Component: A bond(s) or an orbital(s) taking part in the pericyclic reaction as a single unit can be considered as a component. It can have any number of electrons but may not have mixtures of π and σ electrons.

E.g.

A double bond is considered as a $_{\pi}2$ component, since there are two π electrons.

A conjugated diene can be considered as $_{\pi}4$ component, since there are four π electrons.

's' represents **suprafacial**. A suprafacial component forms new bonds on the same face at its both ends. In some cases suprafacial is equivalent to "dis-rotation".

'a' represents **antarafacial**. An antarafacial component forms new bonds on the opposite faces of its both ends. In some cases antarafacial is equivalent to "con-rotation".

E.g.

$_{\pi}2_s$ represents a component containing two π electrons and forming new bonds in suprafacial manner.

$_{\pi}4_a$ represents a component containing four π electrons and is going to form new bonds in antarafacial manner.

q & r: These are integers.

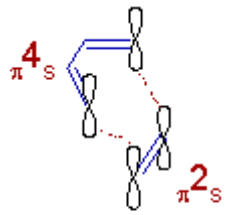
$(4q + 2)_s$ component: The suprafacial component, which may have either 2 or 6 or 10 or _ _ _ electrons of same type. These numbers are obtained by substituting 'q' by 0 or 1 or 2 or _ _ _.

$(4r)_a$ component: The antarafacial component, which may have either 4 or 8 or 12 or _ _ _ electrons of same type. These numbers are obtained by substituting 'r' by 1 or 2 or 3 or _ _ _.

Likewise the meanings of **$(4q + 2)_a$ & $(4r)_s$** can be understood.

Application:

Let us assume the diene and dienophile in Diels-Alder reaction are approaching suprafacially as shown below.



thermally allowed
suprafacial addition

Since there are 4 π electrons in diene, which is making bonds in suprafacial manner, it is a **$(4r)_s$** component**.**

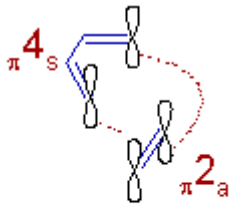
And the alkene is a **$(4q + 2)_s$** component, since it has 2 π electrons and is approaching the diene suprafacially.

i.e, there is **one** $(4q + 2)_s$ component and there are **no** $(4r)_a$ components.

Hence, the total number of $(4q + 2)_s$ and $(4r)_a$ components = 1 + 0 = 1, an odd number.

Therefore Diels-Alder reaction is thermally allowed in ground state when both the components are approaching suprafacially. Hence it is termed as $_\pi4_s + _\pi2_s$ cycloaddition.

Antarafacial addition, for this reaction, is not allowed under thermal conditions. But it is theoretically allowed under photochemical conditions in the excited state. However, the strain in the transition state while doing so forbids to do so.



photochemically allowed
antarafacial addition
but never takes place
under these conditions

Note: The orbitals shown in above diagrams are simple 'p' orbitals and are not the frontier molecular orbitals. Do not mix descriptions of FMO theory with Woodward-Hoffmann rules.

Since application of above Woodward-Hoffmann rules to pericyclic reactions is tedious and cumbersome, the following simplified rules based on aromatic transition state proposed by Zimmerman can be used to predict theoretically allowed modes of pericyclic reactions under given conditions.

These rules are based on the concept of topology of aromatic transition state. The cyclic transition state with **4n+2π** electrons has Huckel topology under thermal conditions and Mobius topology under photochemical conditions. Hence supra facial interaction between orbitals is allowed under thermal conditions, whereas antara facial interaction is allowed under photochemical conditions.

Whereas, the cyclic transition state with **4nπ** electrons has Mobius topology under thermal conditions and Huckel topology under photochemical conditions. Hence antara facial interaction between orbitals is allowed under thermal conditions, whereas supra facial interaction is allowed under photochemical conditions.

No. of π electrons	**Reaction conditions**	**Type of Aromaticity in Transition state**	**Allowed mode**
(4n+2) A Huckel number	Thermal	Huckel	Supra (or) Dis
	Photochemical	Mobius	Antara (or) Con
(4n) A non Huckel number	Thermal	Mobius	Antara (or) Con
	Photochemical	Huckel	Supra (or) Dis

Remember that even though the pericyclic reactions are allowed theoretically under both the conditions, most of the times the factors like steric hindrance and strain in the transition state may forbid the reaction in particular mode, especially the antara facial.

FRONTIER MOLECULAR ORBITAL

Frontier Molecular Orbital (FMO) theory proposed by Kenichi Fukui in 1952, explains whether a pericyclic reaction is allowed or not under given set of reactions conditions based on interactions between frontier molecular orbitals (FMOs) like HOMO, LUMO & SOMO.

HOMO = Highly Occupied Molecular Orbital

LUMO = Lowest Unoccupied Molecular Orbital

SOMO = Singly Occupied Molecular Orbital

The interaction between one FMO of one molecule with one FMO of another molecule results in two types of new Molecular Orbitals (MOs) i.e., bonding and antibonding. The bonding orbitals possess low energy, whereas the antibonding orbitals possess higher energy.

If both of these resulting MOs are filled with electrons, the bonding interaction is cancelled by the anti bonding interaction. Hence the net result is **no bonding** between molecules.

However, if only bonding orbitals are filled with electrons, the two molecules **attract** with each other.

* Interaction between HOMO & HOMO causes repulsion i.e., no bonding interaction since both bonding and antibonding MOs are filled with electrons.

* Interaction between HOMO & LUMO causes attraction i.e., bonding interaction, since only the bonding MO is filled with electrons.

* Interaction between LUMO & LUMO causes neither attraction nor repulsion since all the resulting MOs are empty.

* Interaction of SOMO with either HOMO or LUMO or another SOMO also causes attraction between the interacting species.

The effects of interactions between frontier molecular orbitals is summarized in the following table.

Interacting Frontier Molecular Orbitals	**Type of Interaction**
HOMO + HOMO	No bonding
HOMO + LUMO	Attraction - Bonding
LUMO + LUMO	No electrons, null interaction - No bonding
SOMO + HOMO SOMO + LUMO SOMO + SOMO	Attraction - Bonding

CORRELATION DIAGRAM

A correlation diagram is a tool used to identify the stereochemistry and preferred reaction pathways of pericyclic reactions. It's constructed by matching the molecular orbitals of the reactants and products that have similar symmetry. The diagram shows how the levels transform during the reaction, and can be used to predict if a reaction is feasible thermally or photochemically:

- Thermally feasible: If the molecular orbitals of the reactants and products match in the ground state
- Photochemically allowed : If the molecular orbitals of the reactants match the excited state of the products, or vice versa
- The diagram uses orbital symmetry as a guiding principle.
- An orbital in the starting material must feed into an orbital of the same symmetry in the product.
- The diagram can also be used to predict the height of transition state barriers.
- The symmetry present in an unsubstituted analog can be used to simplify the construction of the diagram.

- Orbital correlations can still be made even if there are no conserved symmetry elements.

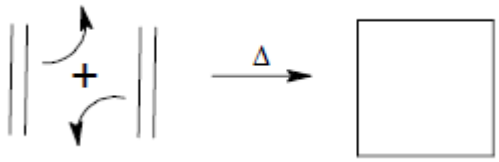
Pericyclic reactions are a unique group of reactions that are characterized by a cyclic transition state, concerted mechanism, and high stereospecificity.

Cycloaddition reaction

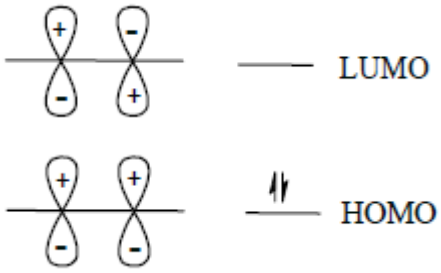
Cycloaddition reaction: A reaction in which two or more π-electron systems react to form a ring at the expense of one π- bond in each of the reacting partners. In this reaction formation of two new σ (*sigma*) bonds takes place which close a ring. Overall there is loss of two π (*pi*) bonds in reactants and gain of two σ (*sigma*) bonds in a product.

2+2 cycloaddition reactions

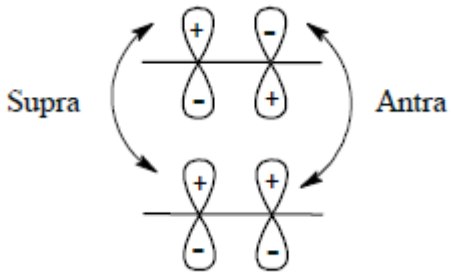
Consider the 2+2 cycloaddition reaction of two ethylene molecule



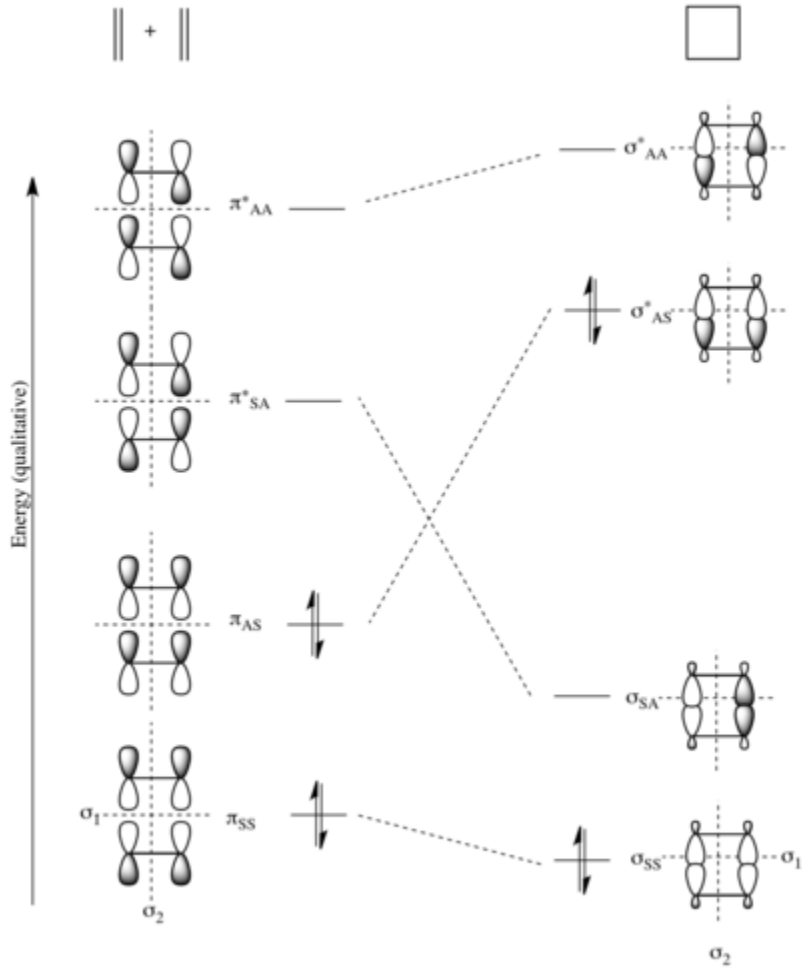
To know about the feasibility of the reaction, we have to draw the correlation diagram of the above reaction. In cycloaddition reactions the HOMO of one of the reactants is overlapped with the LUMO of the other reactant



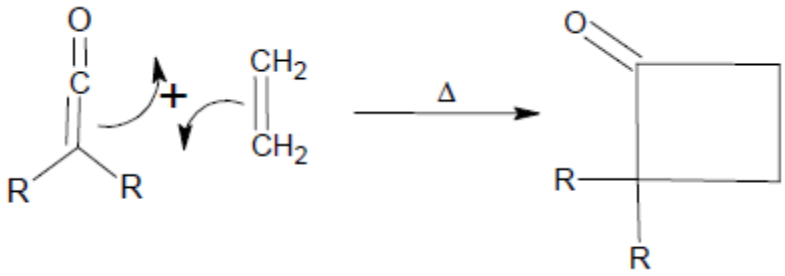
Hence the HOMO (□1) and LUMO (□2) overlaps with each other.



Since the above reaction involves supra-antra interaction the reaction needs some external favourability for the reaction to takes place. Therefore the cycloaddition of two ethylene molecules is not possible, however the ketene and ethylene molecule will undergo [2+2] cycloaddition reactions to give cyclic ketones. Due to the presence of □ electrons in the –C=O group the reaction is feasible at thermal condition.

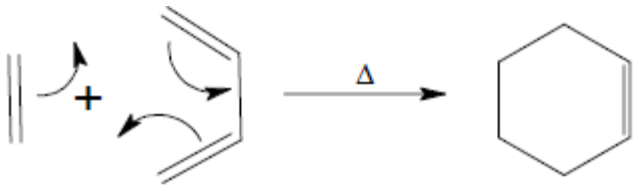


Example:

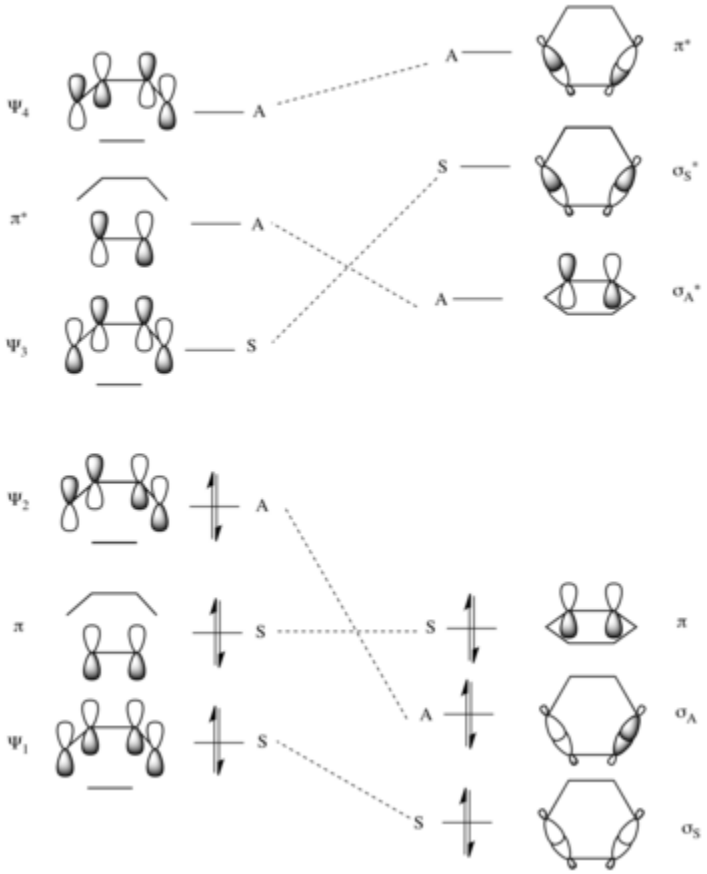


[2+4] cycloaddition

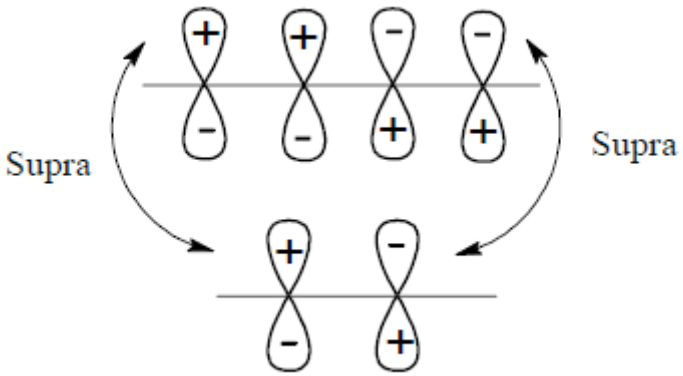
Consider the 2+4 cycloaddition of ethylene and butadiene molecules.



To analyse the feasibility of the 2+4 cycloaddition, we have to draw the correlation diagram of the above reaction.

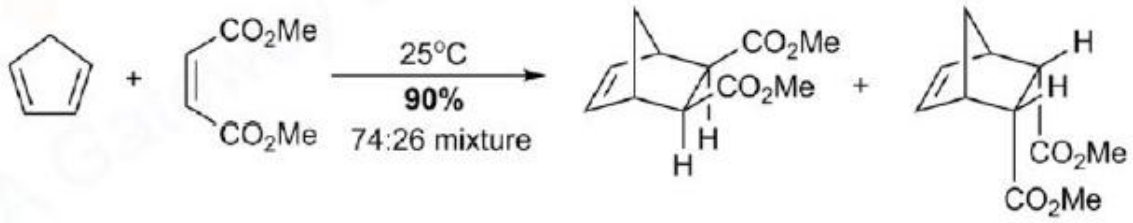


In which the HOMO of butadiene interacts with the LUMO of ethylene molecule.

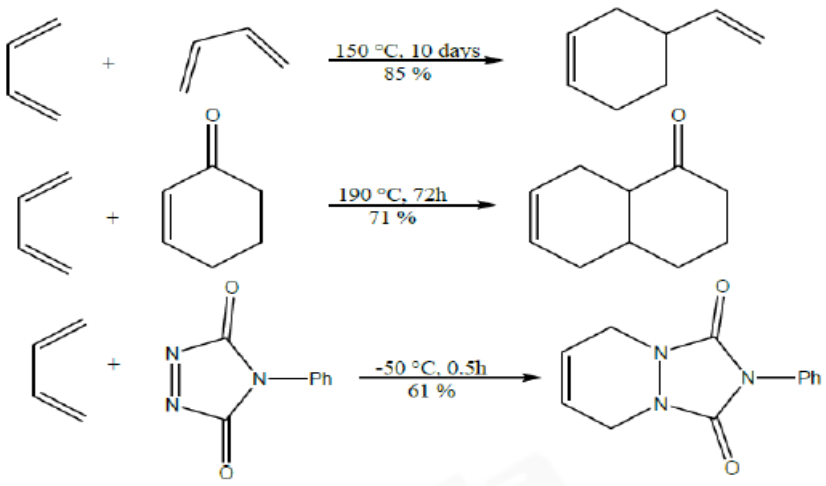


It undergoes supra – supra interaction, hence, the reaction is thermally allowed.

The most important type of cycloaddition reactions are Diels-Alder reactions. It is defined as the cycloaddition between a conjugated diene and a dienophile [4+2] leading to formation of a cyclic product.



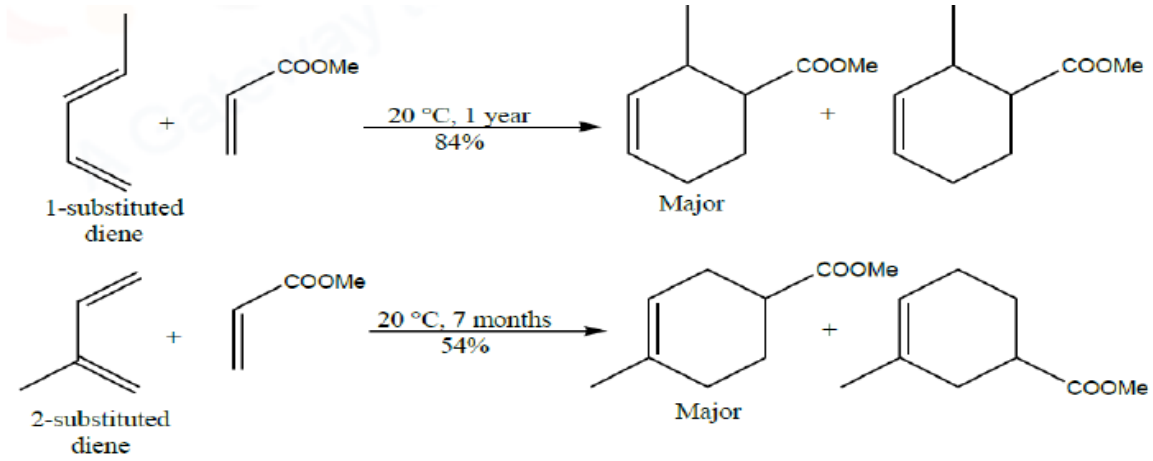
Like other pericyclic reactions, Diels-Alder reactions are concerted and stereospecific, i.e. stereochemical information in the reactants is retained in the products. The dienophiles which are in configuration E- and Z, results in adducts which has stereochemistry Syn or anti respectively. The reaction is slow for unsubstituted dienophiles and rate of reaction is enhanced by attaching suitable electron withdrawing substituents (carbonyl, nitrile and nitro) at the terminal alkenes. Substitution on the diene also enhances rate of reaction, provided the substituents are electron donating (methyl, alkoxy and amine). Following are examples of some reactions, where due to change in nature of the dienophile, there were drastic changes in the rate of reaction.



For the dienes along with electron donating substituents, cyclization also greatly enhances the rate of cycloaddition reactions, owning to proper geometric orientation of double bonds. This is because a diene can participate in Diels Alder reaction only when it is in the s-cis conformation

If it were to react in the s-trans conformation then the resulting cyclohexene would have a trans double bond in the cyclohexene system which is very high energy.

The regioselectivity of Diels Alder reaction depends on the number and nature of substituent on diene and dienophile along with the reaction conditions such as catalyst, temperature, pressure, solvent etc. Generally 1- and 2- substituted buta-dienes reacts with mono-substituted dienophiles to give mainly ortho and para adducts, respectively. Even with a small substituent such as methyl the degree of regioselectivity is high. The important feature of this pattern is the fact that whether a substituent is electron withdrawing or donating, it holds good for almost all combinations.



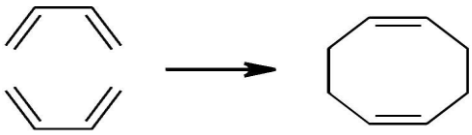
4+4 CYCLOADDITION AND 1,3 DIPOLAR CYCLOADDITIONS

Cycloaddition:

Cycloaddition is a chemical reaction in which two or more unsaturated molecule combine with the formation of a cyclic adduct in which there is a net reduction of the obond multiplicity. The resulting reaction is a cyclization reaction.

4+4 Cycloaddition:

4+4 cycloaddition reaction is a photochemical reaction that join two unsaturated molecules to form eight membered rings.

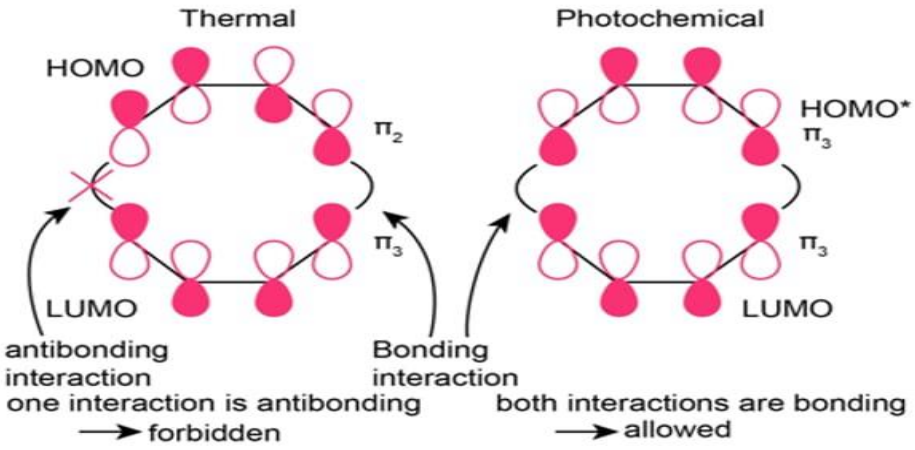


Thermal addition:

In the 4+4 cycloaddition of two butadiene molecules, one interaction is bonding and the other is antibonding. This type of addition is thermally forbidden .

Photochemical addition:

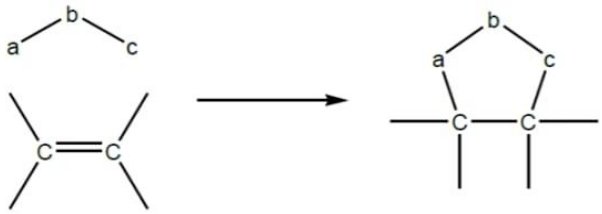
In the photochemical reaction both the interactions are bonding, which is photochemically allowed .



1,3 Dipolar cycloaddition:

- Thermal [$4\pi_s + 2\pi_s$] reaction involving 6π electrons.
- Involves an aromatic transition state (6e system).
- 4π electron component is referred to as 1,3 dipole.
- 2π electron component is called dipolsrphile.
- Used in the synthesis of 5 membered heterocyclic ring system.

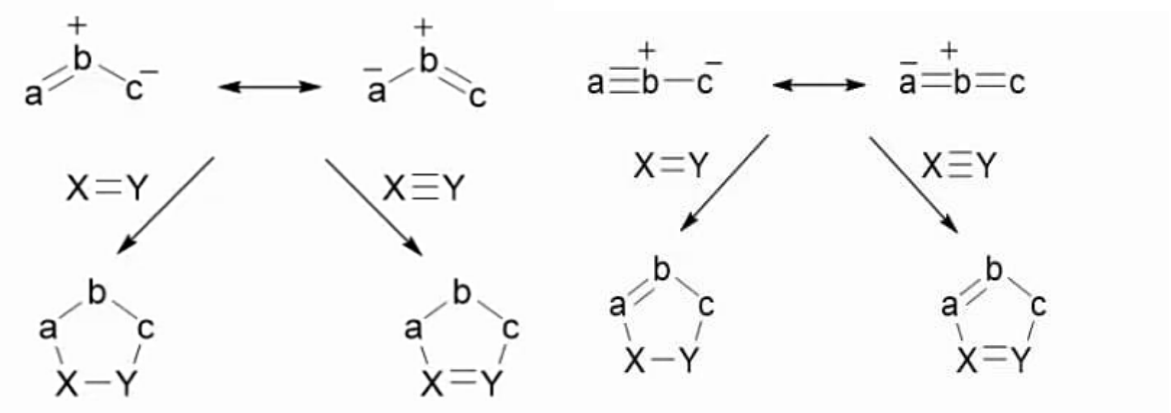
1,3 dipole + Dipolarophile → Cycloproduct



Two types :

1.Allyl anion type

2. Propargyl allenyl type



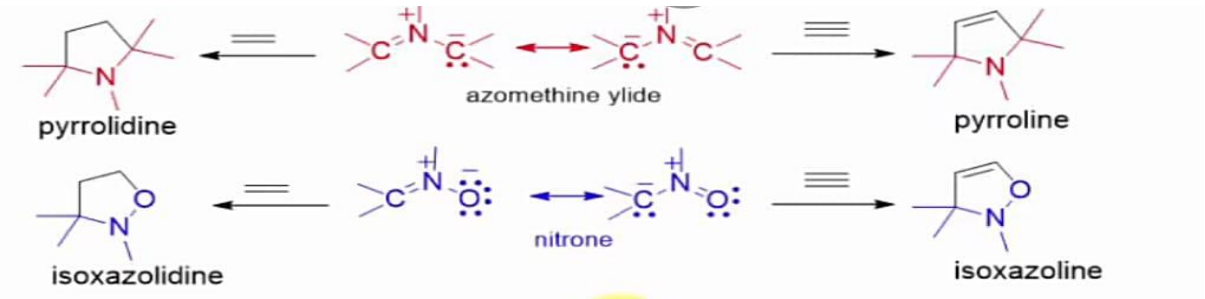
1,3 Dipole:

- Nitrile oxides
- Nitrile imines
- Azides
- Carbonyl ylides
- Nitrones

Dipolarphiles:

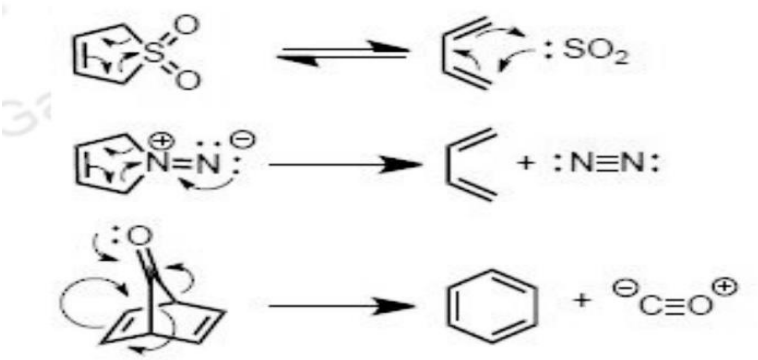
- Alkene
- Alkynes
- Heterocumulenes eg: isocyanates

Examples:



CHELETROPIC REACTIONS :

- Cheletropic reactions are a class of pericyclic cycloaddition reaction.
- Cheletropic reactions are those reaction where two sigma bonds are made or broken to the same atom in the reagent.
- Like all other pericyclic reactions , cheletropic reactions are also reversible, concerted and include a cyclic transition state.
- Cheletropic extrusion reactions are the reverse of cheletropic addition reaction these are assisted by elimination of a stable molecule from the reactant such as nitrogen or carbon monoxide.
- The addition of sulfur dioxide to a diene is a classical example of [4+1] cycloaddition.
- Cheletropic reactions follow woodward-hoffmann rules. According to the rules the conjugated fragment of (4n+2) pi electrons system react in a disrotatary (conrotatary) mode in linear(non linear)reactions. In (4n) pi electron system it reacts in a disrotatory (conrotatory) mode in non linear reaction.
- Cheletropic addition reactions involve two geometries linear and non linear based on orientation of incoming molecule relative to the diene.
- Ramberg – Buckland reaction is an important example of cheletropic extrusion reaction that leads to transformation of a carbon-sulfur bond to a carbon-carbon double bond.
- Example of cheletropic reactions



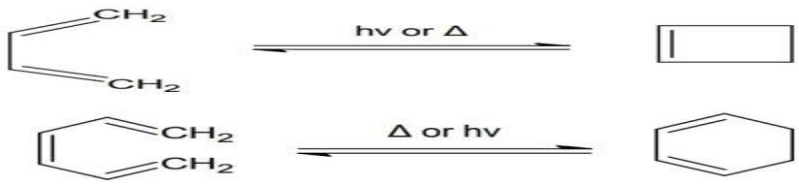
Selective Rules for Cheletropic Reactions :

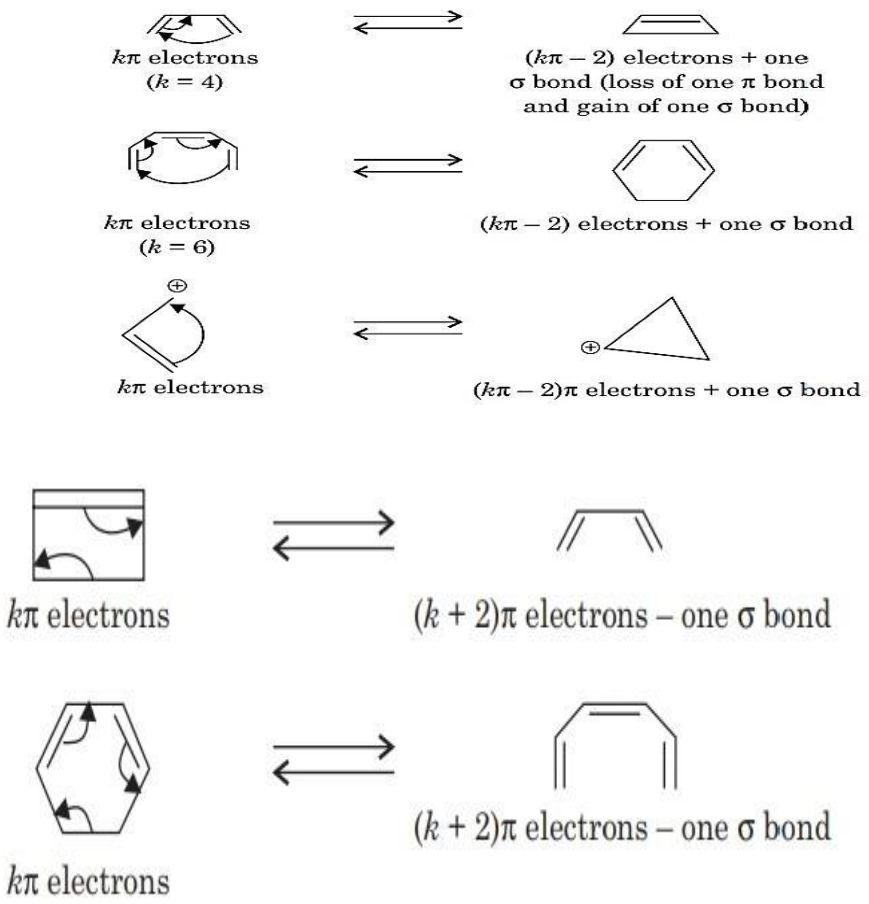
π electrons	**Allowed Ground State reaction**	
	Linear	Non linear
4n	disrotatory	conrotatory
4n+2	conrotatory	disrotatory
	Allowed Excited State Reaction	
4n	conrotatory	disrotatory
4n+2	disrotatory	conrotatory

Electrocyclic Reaction :

- It is a the concerted interconversion of a conjugated polyene and cycloalkane.
- Electrocyclic reaction are induced either thermally or photochemically.
- All electrocyclic reactions are reversible reactions.
- Open-chain partner of the reaction is always conjugated system whereas cyclic partner may or may not contain conjugated system.
- In electrocyclic reaction either a ring is formed with the generation of a new sigma bond and a loss of a pi bond(i.e gain of one sigma bond and loss of one pi bond) or ring is broken with the loss of one sigma bond and gain of one pi bond.

Examples :





The electrocyclic reaction can be classified into two categories

i) Electrocyclic opening of the ring and

ii) Electrocyclic closure of the conjugated system

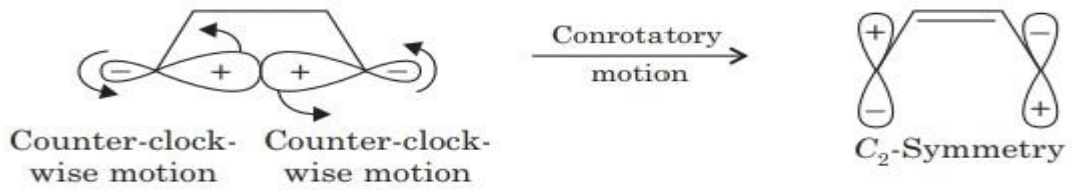
In the ring opening electrocyclic reaction if the ring partner contains kπ electrons, the open partner will contain (k+2) π electron with the loss of one sigma bond.

In the ring closing electrocyclic reaction if the π system of the open-chain partner contains kπ electrons the corresponding cyclic partner contains (k-2)π electrons and formation of sigma bond.

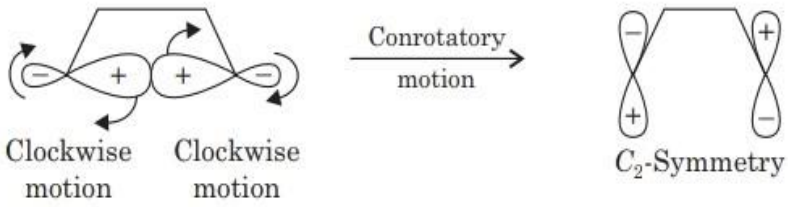
There are two possible stereochemistry for the ring opening and ring closing of electrocyclic reaction.

Con-rotatory Process :

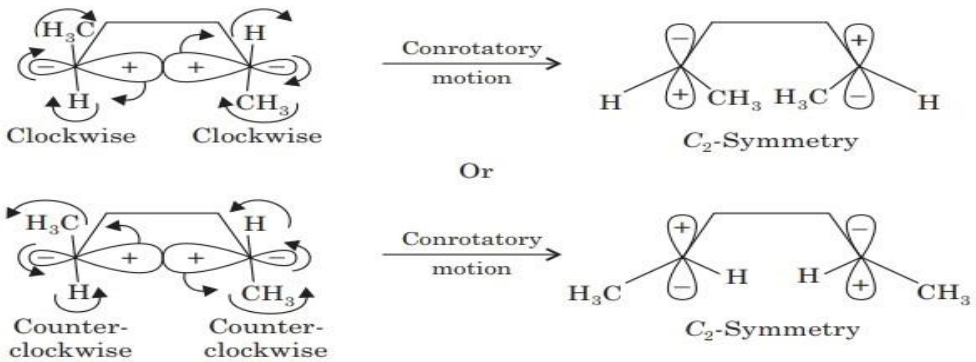
The two atomic orbital components of the sigma bond may both rotate in the same direction(either clockwise or counter clockwise). This is called con-rotatory process.



or

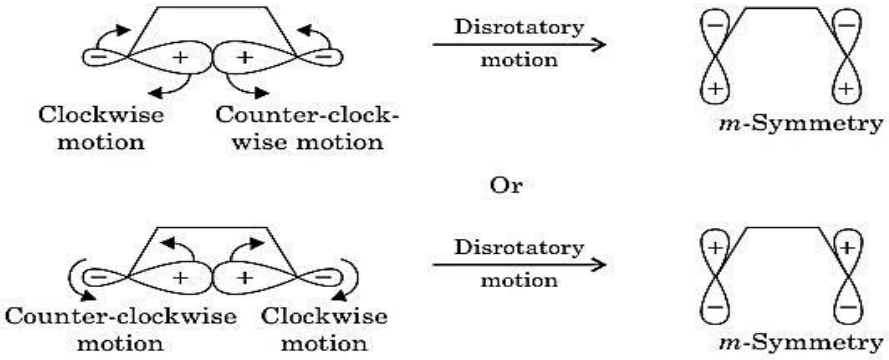


Conrotatory ring opening orbitals and group migrate in same direction

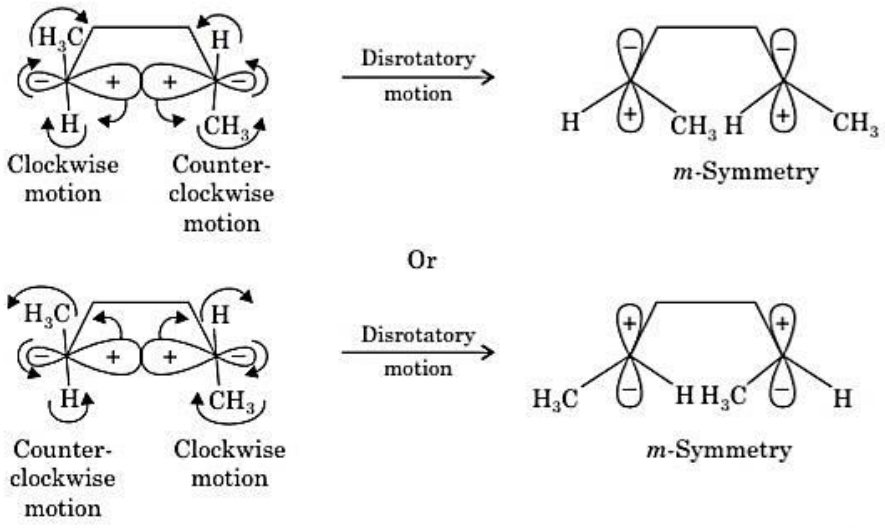


Dis-Rotatory :

The atomic orbitals may rotate in opposite directions, one clockwise and other counter-clockwise. This process of ring-opening is known as disrotatory motion



Disrotatory ring opening, orbitals and groups migrate in the opposite directions.

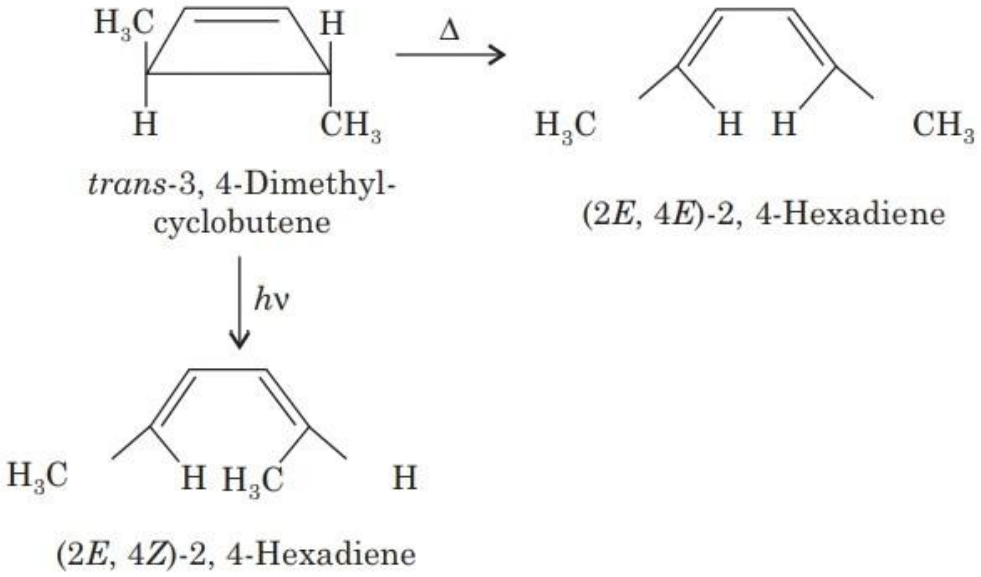


Open Chain Conjugated System having 4nπ Conjugated Electrons :

Let us consider the simplest example in which the cyclobutene derivative, i.e., Open-chain conjugated system has 4n conjugated π electrons.

In the thermal condition trans3,4-dimethylcyclobutene gives (2E,4E)-2,4-hexadiene. Thus this reaction is completely stereospecific.

In the photochemical condition the same substrate gives (2E,4Z)-2,4-hexadiene. In this case too, the reaction is completely stereospecific. Thus the reaction can be performed thermally or photochemically, and under either condition the reaction is completely stereospecific.

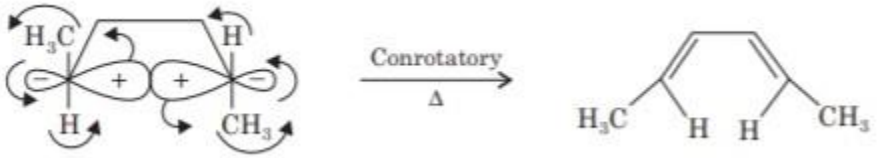


trans-3, 4-Dimethyl-cyclobutene

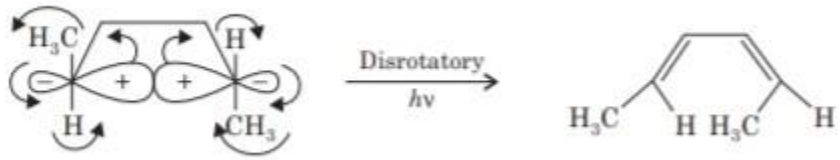
(2*E*, 4*E*)-2, 4-Hexadiene

(2*E*, 4*Z*)-2, 4-Hexadiene

Stereochemistry of the thermal reaction-1 (of the 4nπ system) can only be explained if process should be conrotatory.



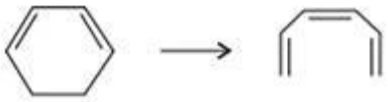
Stereochemistry of the photochemical reaction-2 (of the 4n,π system) can only be explained if process should be disrotatory.



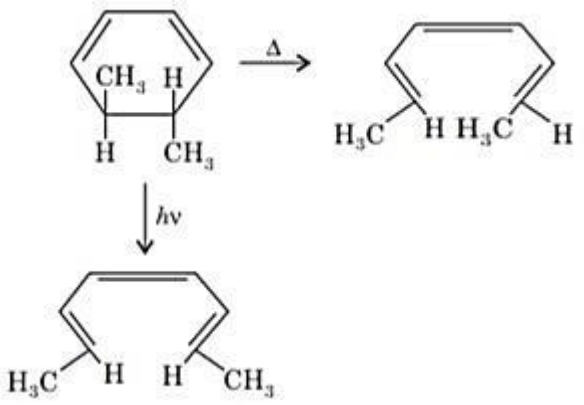
From the above two examples it is clear that thermally induced electrocyclic reaction involving 4nπ conjugated electrons require conrotatory motion and photochemically induced electrocyclic reactions require disrotatory motion.

Open Chain Conjugated System having (4n+2) π Conjugated Electrons :

The simplest example of this category is the ring-opening of 1, 3-cyclohexadiene into 1, 3, 5-hexatriene.



In thermal condition 5, 6-trans-dimethyl-1, 3-cyclohexadiene is converted exclusively to (2E, 4Z, 6Z)-2, 4, 6-octatriene. In the photochemical condition the same substrate is converted exclusively to (2E, 4Z, 6E)-2, 4, 6-octatriene.



These two conversions are also highly stereospecific. Stereochemistry of these two reactions can only be explained if process should be disrotatory in thermal condition and conrotatory in photochemical condition.

On the basis of these experimental results the stereochemistry of electrocyclic reactions can be summarised by noting that thermally induced electrocyclic reactions involving 4nπ electrons require conrotatory motion. Under similar conditions, electrocyclic reactions involving (4n + 2)π electrons follow disrotatory motion. Similarly, photo-induced electrocyclic reactions involving 4nπ electrons require disrotatory motion. Under similar conditions, electrocyclic reactions involving (4n + 2)π electrons follow conrotatory motion

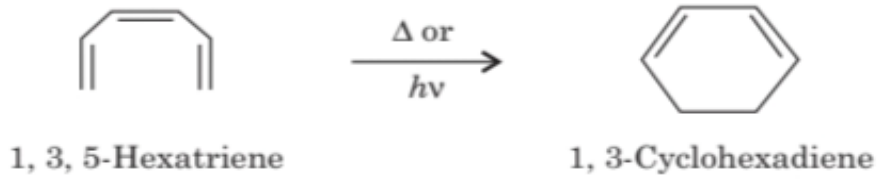
A summary of the type of motion to be expected from different polyenes under thermal and photochemical condition is shown in the table.

Number of π electrons	**Condition** **(Mode of activation)**	**Motion**
4n	i) Thermal ii) Photochemical	Conrotatory Disrotatory
4n+2	i) Thermal ii) Photochemical	Disrotatory Conrotatory

ELECTROCYLIZATION AND RING OPENING AND CLOSER REACTION COJUCATED TRIENES

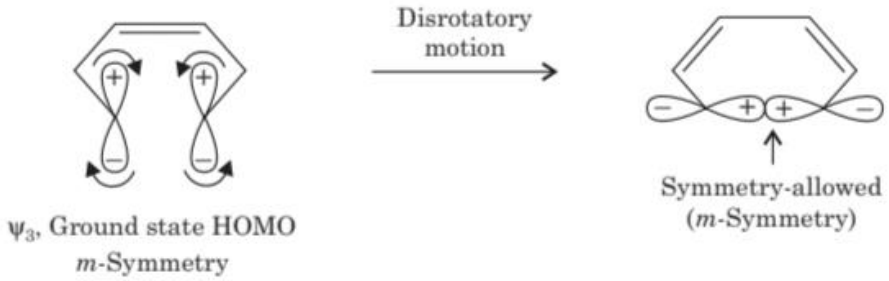
Electrocyclic ring closer reaction given by 1,3,5 hexatrien:

1,3,5 hexatriene is the most common example of the polyene having conjucated electrons.



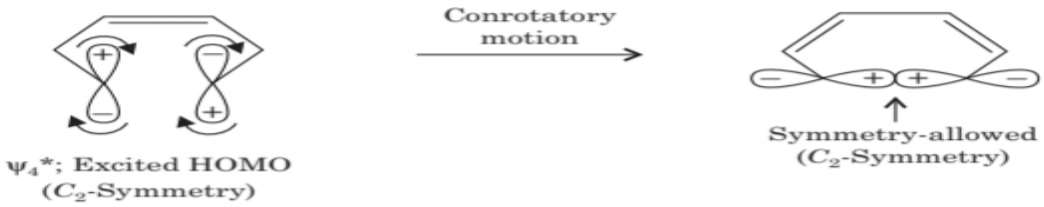
A)Thermal induced cyclisation:

1, 3, 5 hexatrien has m-symmetry the cyclisation proceeds by disrotatory motion.



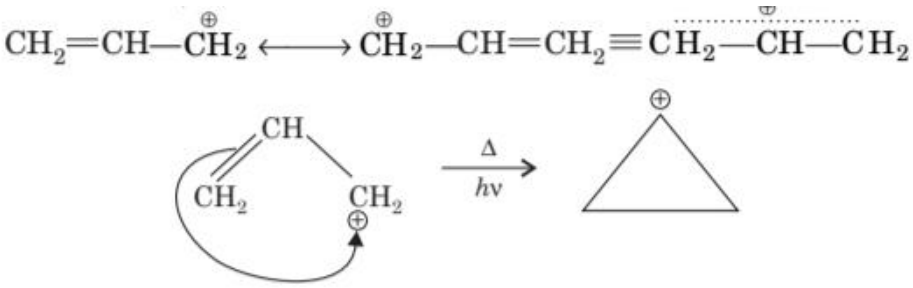
B) Photo-induced cyclisation:

When an electron 1, 3, 5 hexatriene is promoted by photon absorption becomes the HOMO. The excited state HOMO has C2 symmetry. Photo induced cyclisation proceeds by conrotatory motion.



2) Electrocyclic ring closer reaction given by allyl carbocation

Allyl carbocation contion conjugated electrons.



THERMAL INDUCED CYCLISATION

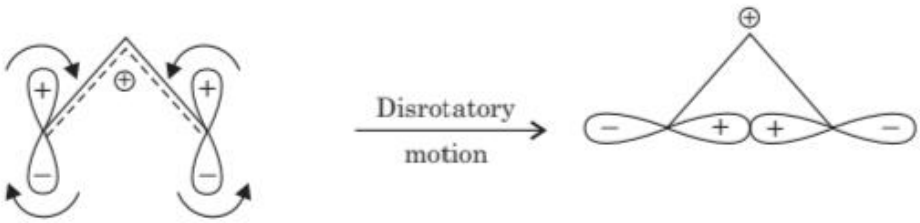
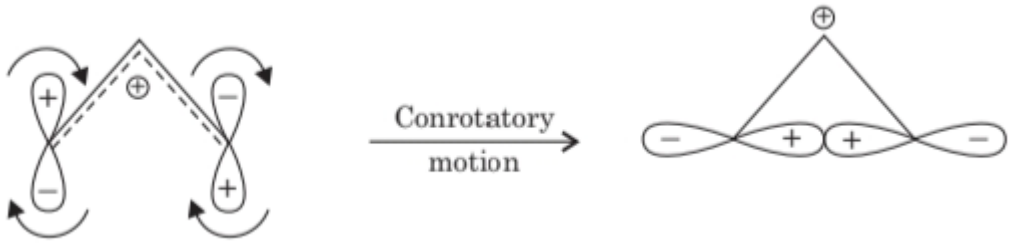


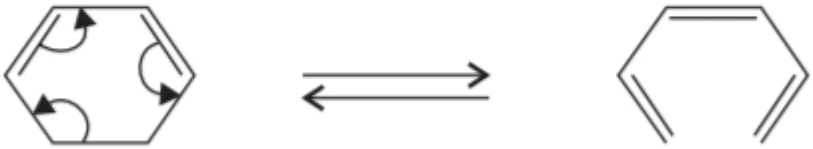
PHOTO INDUCED CYCLISATION



ELECTROCYCLIC RING OPENING

1) Conversion of 1,3 cyclohexadiene to 1,3,5hexarien system

1,3 cyclohexadiene to 1,3,5 cyclohexadiene in to 2,4,6 octatriene.



Two modes of disrotatory motion can be takeplaces:

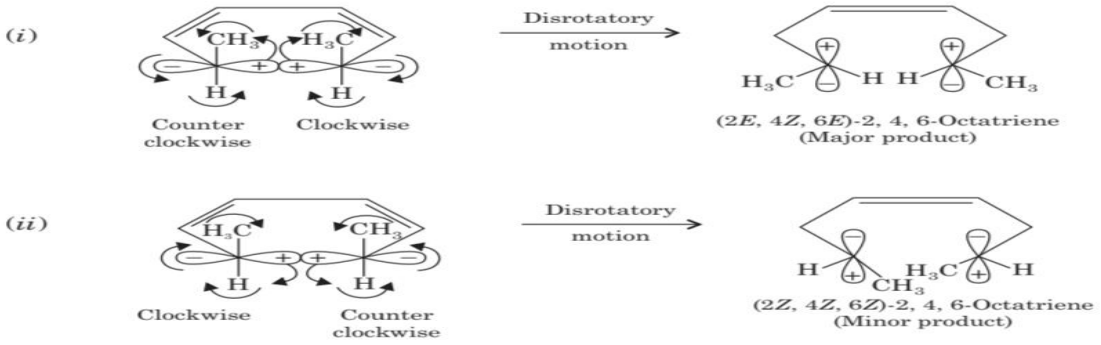
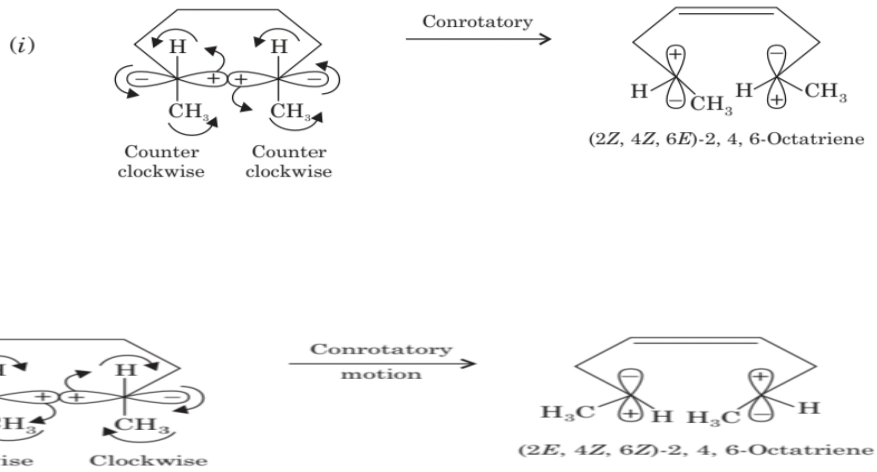


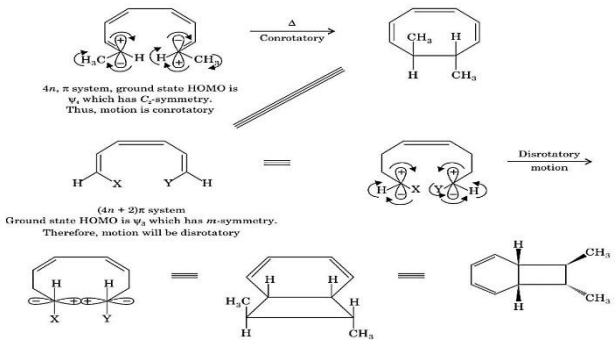
PHOTO INDUCED RING OPENING:

The two modes of conrotatory motions



2)THERMAL ELECTROCYCLIC REACTION GIVEN BY 2,4,6,8 DECATETRAENE:

Tetrane forms a cyclotatriene at room temperature. The electrocyclic reactions proceed disrotatory motion cis junction is formed.



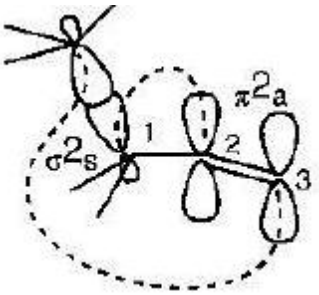
SIGMATROPIC REARRANGEMENT

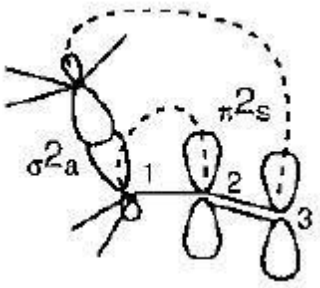
Sigmatropic rearrangement is a pericyclic reaction in which a σ-bonded group or atom migrates from one end of a π-system to other in an uncatalyzed intramolecular process.

Classes of sigmatropic rearrangements

[1,3] shifts

Thermally the antarafacial shift of carbon is symmetrically allowed with double bond acting as the antarafacial component but this does not happen because of difficulties of achieving effective orbital overlap. In practice, suprafacial shift of carbon occurs with inversion of configuration, where σ bond takes up the role of antarafacial component. This was not possible for hydrogen atom as it has only s orbital and lacks p-orbital. If we look at the orbital picture it becomes clear that the newly formed bond is a little longer and thus should not be very plausible.



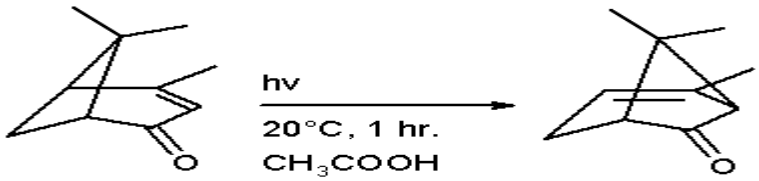


Symmetry allowed but barely Reasonable

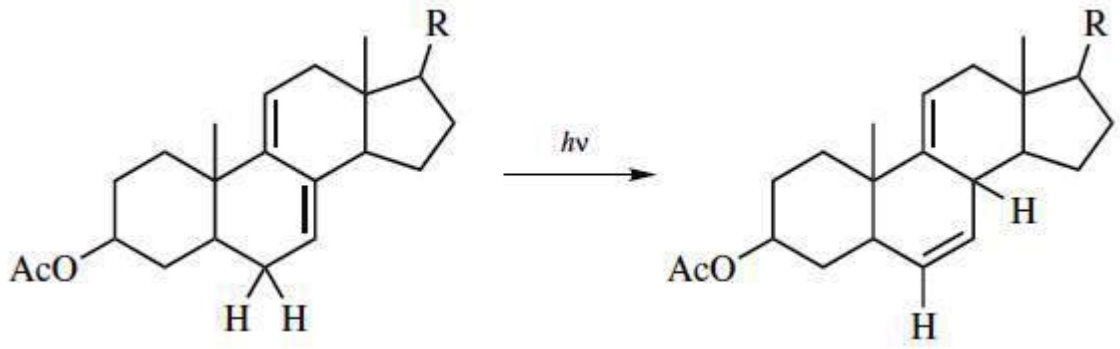
Takes place with silyl group migration

Nevertheless, the reaction has been shown to take place for suprafacial shift of silyl groups at 500°C with long Si-C bonds making it feasible.

Photochemically, a suprafacial shift with retention of configuration in the migrating group is allowed and a number of such examples are known. A reversible [1, 3] shift in verbenone (a plant derived terpene) to give chrysanthenone is such an example of photochemical alkyl shift.

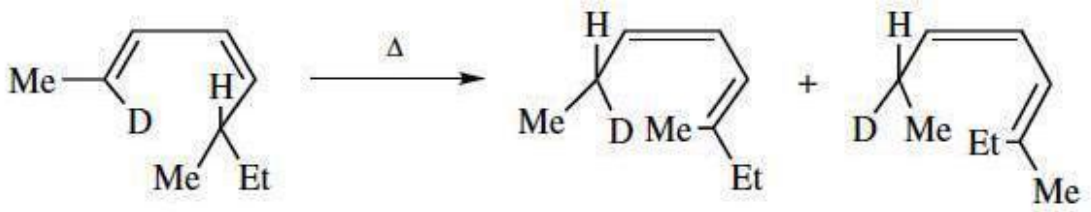


Another example of photochemically allowed [1, 3] sigmatropic shift in steroids is shown below.

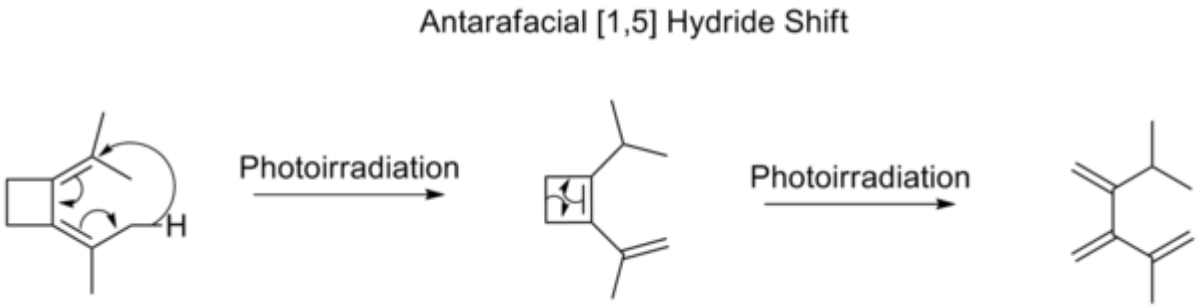


[1,5] shifts

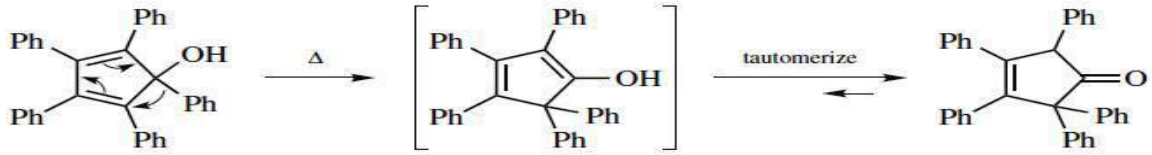
As compared to [1, 3] shifts, in the case of [1, 5] shift the suprafacial thermal rearrangements are quite common, while photochemical rearrangements are rarely observed. Following reaction gives an example of [1, 5] shift.



Antarafacial [1, 5] hydride shifts are possible although less commonly observed under photochemical irradiation.



[1, 5] migration of functional groups such as methyl and phenyl are thermally allowed.

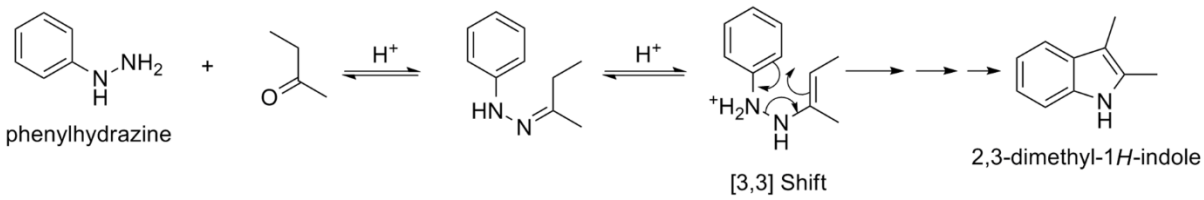


[3, 3] shift

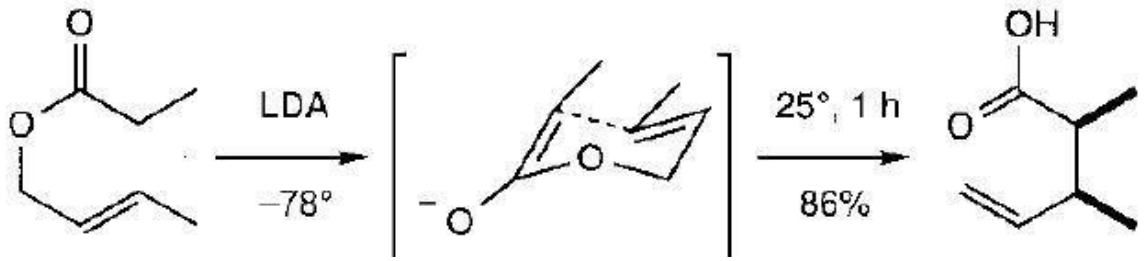
These are synthetically useful and there are several name reactions that fall under [3, 3] sigmatropic shift category. The popularity of [3, 3]-sigmatropic rearrangements in organic synthesis is due to the ability of such reactions to generate stereogenic centers from the sp2-hybridized carbons. Claisen and Cope rearrangements are important name reactions of this class;however, they will be discussed in the next module. Following are a few examples of other most common [3, 3] sigmatropic rearrangement reactions.

Fisher Indole synthesis: It is a chemical reaction that involves synthesis of the aromatic heterocycle indole from a (substituted) phenylhydrazine and an aldehyde or ketone. This reaction takes place under acidic conditions.

Fischer Indole Synthesis

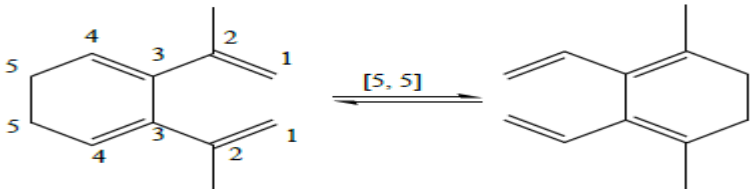


Ireland-Claisen rearrangement: This is an organic reaction of great utility as it creates two stereogenic centers with high levels of specificity arises as the transition state involves a chair like structure

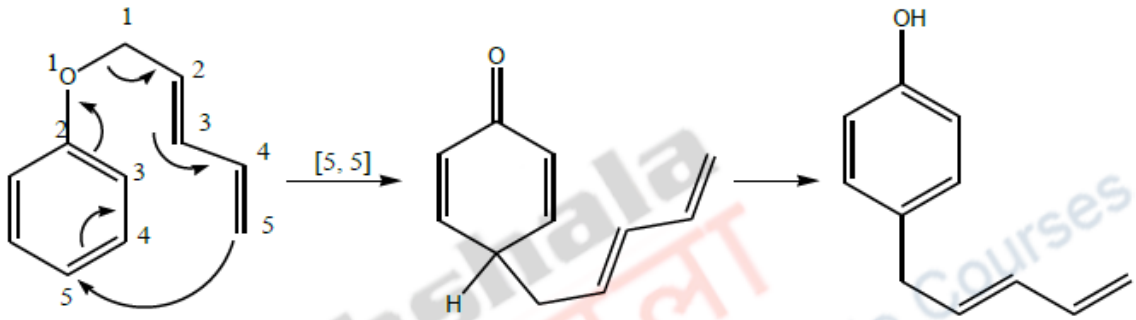


[5, 5] shift

Now let us consider the 10 electron systems that include [5, 5] sigmatropic shifts.



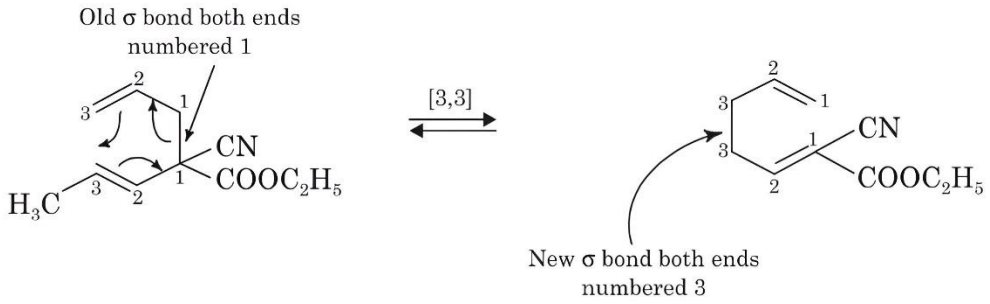
The [5, 5] sigmatropic rearrangement of 2, 4-pentadienylphenyl ethers can be considered a homologous to Claisen rearrangement.



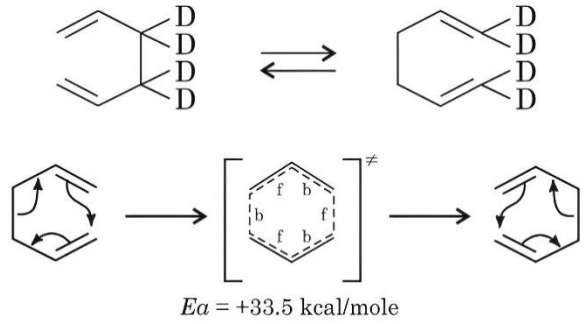
Ionic Sigmatropic shifts :

Cope Rearrangement:

The most important sigmatropic rearrangement are the [3, 3] process involving carbon-carbon bond. The thermal rearrangement of 1, 5-dienes by [3, 3] sigmatropy is called Cope rearrangement. The reaction proceeds in the thermodynamically favoured direction.



This particular reaction is called a [3, 3] sigmatropic rearrangement because the new s bond has a 3, 3 relationship to the old σ (sigma) bond. The equilibrium in this case is controlled by the conjugation present in the product. The rearrangement of the simplest possible case, 1, 5-hexadiene, has been studied using Deuterium labelling. For this reaction activation energy is 33.5 kcal/mole and the entropy of activation is -13.8 eu. The substantially negative entropy conforms the formation of cyclic transition state.



Conjugated substituents at C-2, C-3, C-4 or C-5 accelerate the rearrangement. Donor substituents at C-2 and C-3 have an accelerating effect. The effect of substituents can be rationalised in terms of the stabilisation of the transition state by depicting their different effect on two interacting system (Fig. 1).

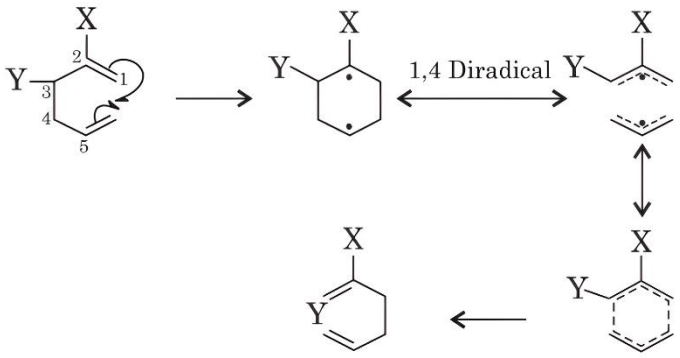


Figure 1

The transition state involves six partially delocalised electrons being transformed from one 1, 5-diene system to another. The transition state could range in character from a 1, 4-diradical to two nearly independent allyl radical, depending on whether bond making or bond breaking is more advanced. The general framework for understanding the substituent effects is that the reaction are concerted with relatively late transition state with well developed C-1-C-6 bonds (Figs 2 and 3).

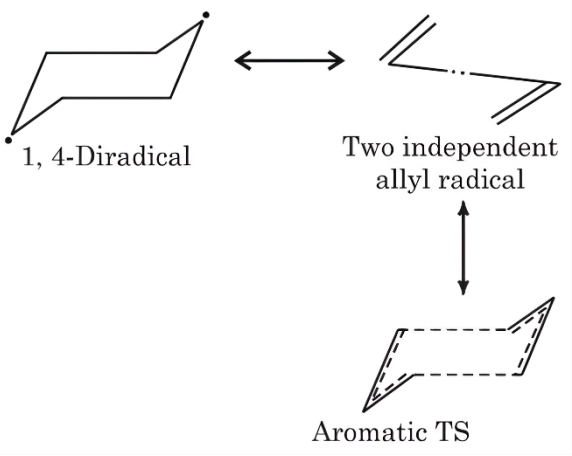


Figure 2

The most advanced molecular orbital calculations support the idea of an aromatic transition state having six partially delocalised electrons. The net effect on reaction rate of any substituent is determined by whether it stabilises the transition state or the ground state more effectively. The aromatic concept of transition state predicts that it could be stabilised by conjugated substituents at all positions.

n Cope rearrangement the migrating group is allyl radical. An analysis of the symmetry of the orbitals involved shows why this reaction is a relatively facile thermal process but is not commonly observed on photochemical activation. As we break the C(1)–C(1) bond (Fig. 3)

the phases of the overlaping lobes must be the same. The HOMO of the allyl radical is y2 and that information allows us to fill the symmetries of the two allyl radicals making up of transition state (Fig. 3).

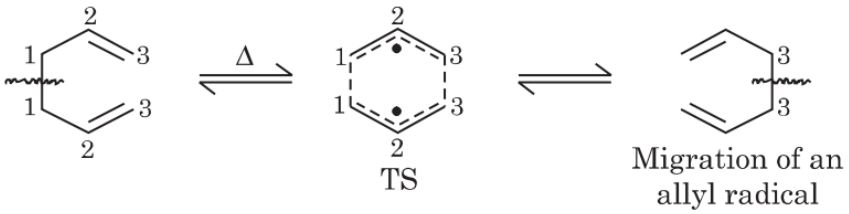


Figure 3

Reattachment at the two C(3) positions (Fig. 3) is allowed because the interaction of the two lobes on the two C(3) carbons is bonding (Fig. 4).

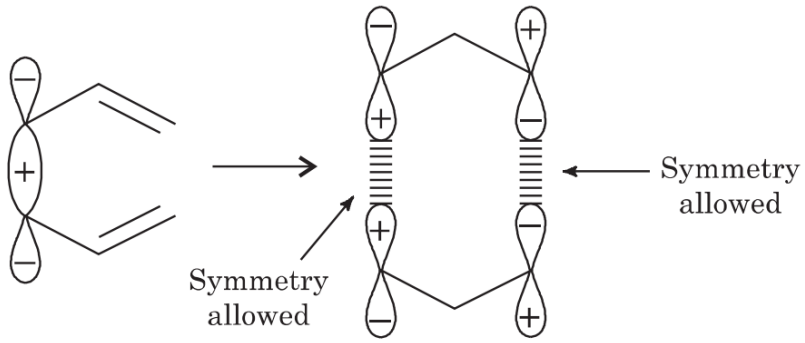


Figure 4

If interaction is carried out in the presence of UV light then one electron is promoted from the HOMO to the LUMO and LUMO will become photochemically HOMO (Fig. 5).

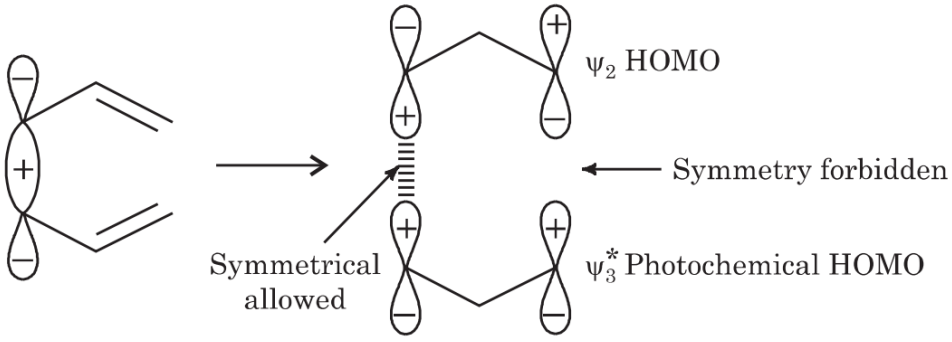
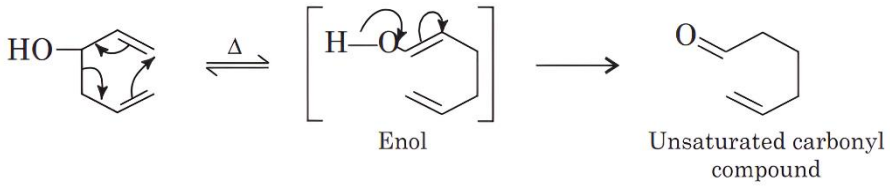


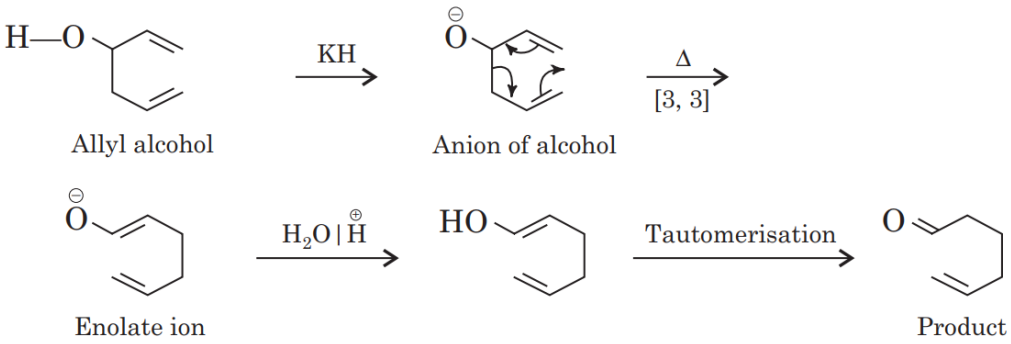
Figure 5

Preparation of Carbonyl Compounds from Cope Rearrangement:

1, 5-Hexadiene-3-ol on heating undergoes Cope rearrangement with formation of unsaturated carbonyl compounds. Cope rearrangement given by such compounds is known as oxy-Cope rearrangement.

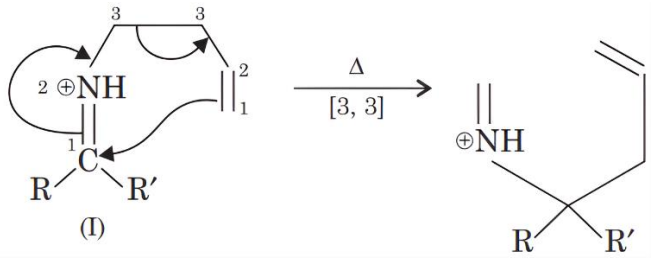


The reaction is accelerated when it is carried out in the presence of strong base. In the presence of strong base allyl alcohol converts into alkoxide ion which is very stable. Cope rearrangement given by anion of 1, 5-hexadiene-3-ol is known as anionic oxy-Cope rearrangement.

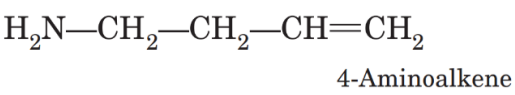


Alkoxide ion undergoes Cope rearrangement to give the product in which negative charge is in conjugation to π (pi) bond. This conjugation makes the anion very stable.

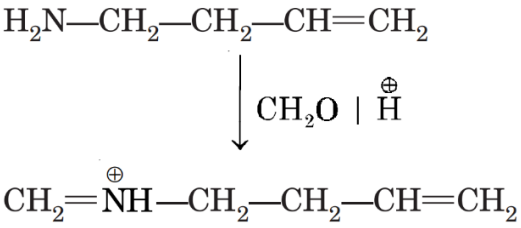
Iminium compound of type (I) also gives Cope rearrangement. Which is known as Aza Cope rearrangement.



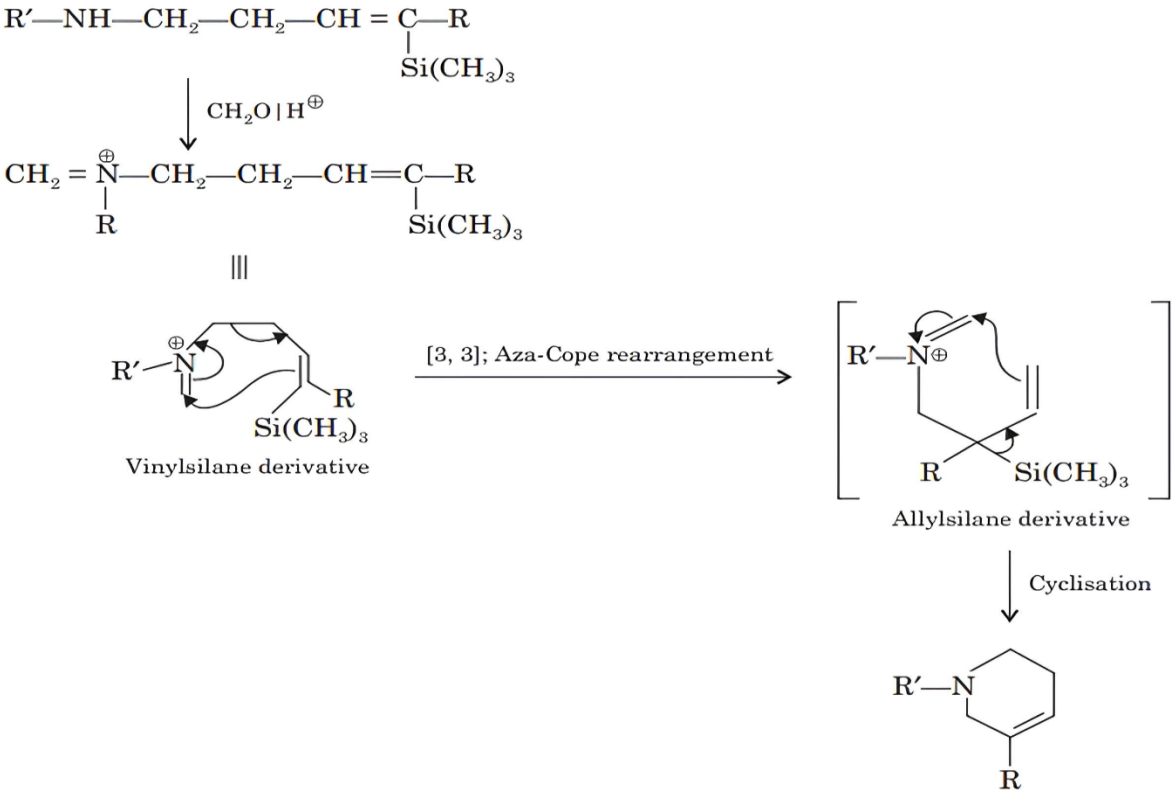
Compound (I) can be prepared from 4-aminoalkenes.



4-Aminoalkenes react with carbonyl compounds to give iminium compound of type (I).



Iminium compound of type (I) is very useful when it is prepared from 4-(trimethylsilyl)- 3-alkenylamines because in this case rearranged product undergoes cyclisation to give six membered nitrogen heterocyclic compound. Thus, the overall reaction is as follows:



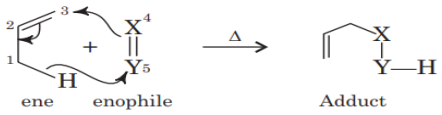
Group Transfer Reactions

A pericyclic process involving the transfer of one or more groups or atoms from one molecule to another is known as group transfer reaction. There are only a few reactions in this class. Ene reaction is one of the most common group transfer reaction. The other well known group transfer reaction is reduction of alkenes and alkynes by diimide.

Ene Reactions:

Ene reaction involves the thermal reaction of an alkene (called ene) having an allylic hydrogen with a compound having multiple bond (X Y, X Y), called enophile.

During the reaction, transfer of allylic hydrogen (1, 5 migration of hydrogen), shift of allylic double bond and bonding between two unsaturated termini (one terminus of ene and other terminus of enophile) takes place to form 1 : 1 adduct.

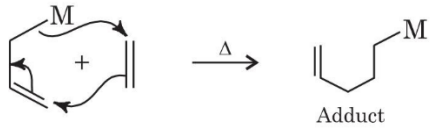


...(1)

In this reaction

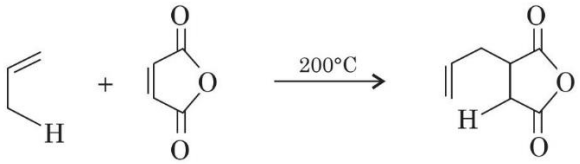
X═Y is	X≡Y is
C═C	C≡C
C═O	C≡N
C═S	
C═N	
N═O	
—N═N—	
O═O	

In ene reaction hydrogen atom of allylic carbon moves from ene to enophile. In principle atom other than hydrogen from allylic carbon can move from ene to enophile. In practice the only elements other than hydrogen commonly employed in this kind of reaction are metals like lithium, magnesium or palladium. When metal moves the reaction is known as metalla-ene reaction.

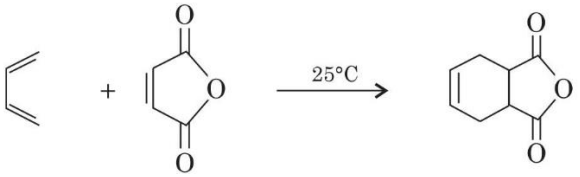


...(2)

In ene reaction there is a loss of a π (pi) bond and gain of two σ (sigma) bonds. In this reaction π (pi) bond of enophile is replaced by two σ (sigma) bonds with ene, therefore, this reaction resembles with cycloaddition reaction. This reaction also resembles with [1, 5] sigmatropic rearrangement because hydrogen migrates on atom-5 (equation-1) but reaction is neither sigmatropic nor cycloaddition reaction. This reaction is six electrons cycloaddition reaction. In this reaction hydrogen moves from ene to enophile. Due to this reason this reaction is an example of group transfer reaction. This reaction is like Diels-Alder addition. In DielsAlder addition all six electrons are π (pi) electrons. In this reaction, out of six electrons, four electrons are π (pi) electrons but two electrons are σ (sigma) electrons. Thus, activation energy of this reaction is greater than the Diels-Alder reaction. Due to this reason ene reactions take place at higher temperature than Diels-Alder reaction.

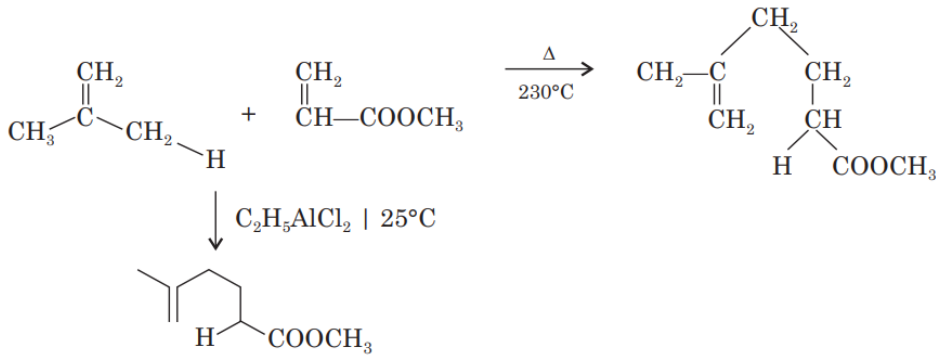


...(3)



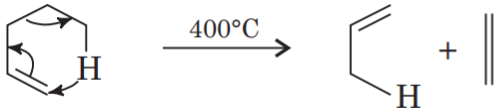
...(4)

Fortunately many ene reactions can be catalysed by Lewis acids. In the presence of Lewis acids as catalyst reaction proceeds under milder conditions. As far as catalyst is concerned the best result is obtained with alkyl aluminium halides.



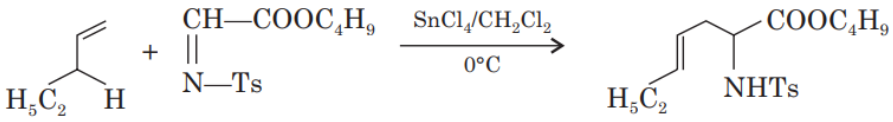
...(5)

Like Diels-Alder addition ene reaction is also reversible reaction. 1-pentene gives ethene and propene at 400°C.

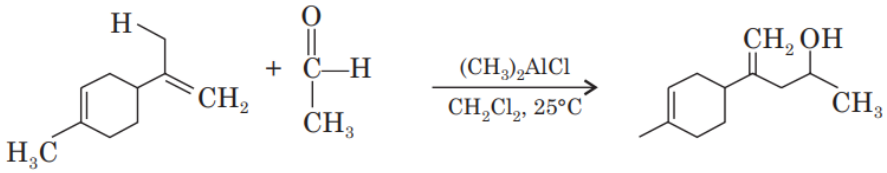


...(6)

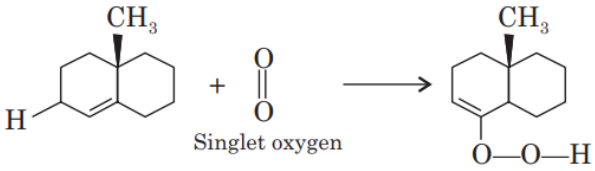
As mentioned earlier that enophile need not be alkene or alkyne derivatives heteroenophiles are also known.



...(7)

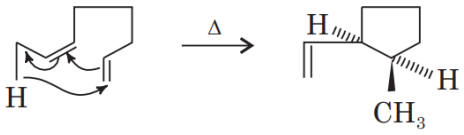


...(8)



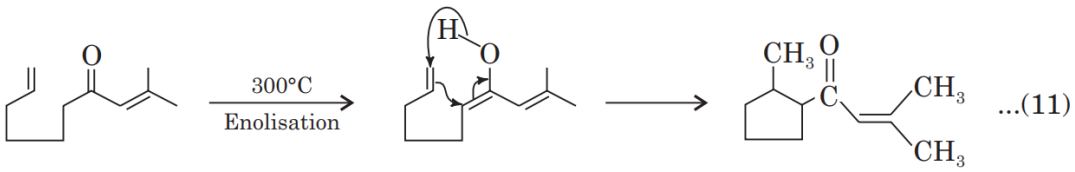
...(9)

Intramolecular ene reaction has great potential for the synthesis of cyclic compounds, particularly for the synthesis of five membered ring compounds from 1, 6-dienes.



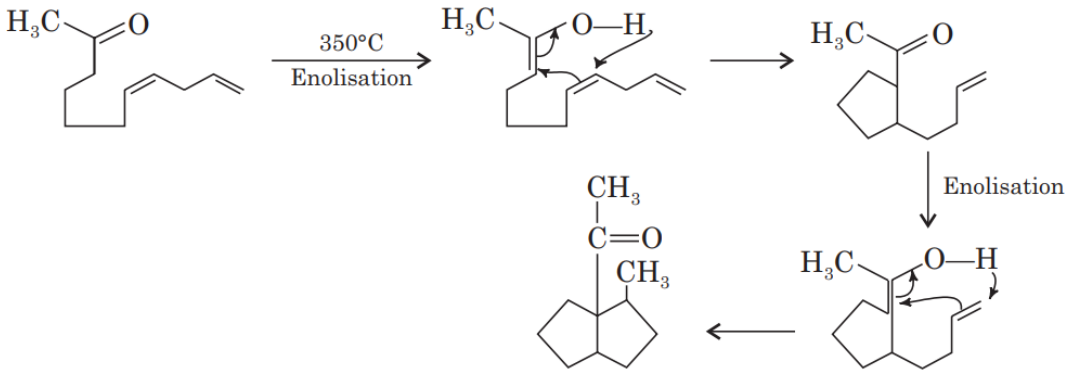
...(10)

Thermal cyclisation of 1, 8-diene-3-one provides a useful method for the preparation of cyclopentyl vinyl ketones by intramolecular ene reaction.



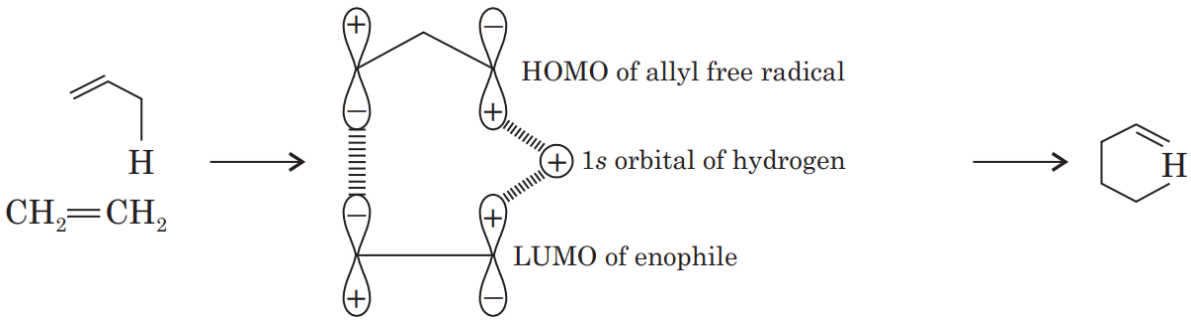
...(11)

Similarly 7, 10-alkadiene-2-one gives intramolecular ene reaction.



...(12)

The concerted mechanism is allowed by Woodward-Hoffmann rules. The transition state involves the π (pi) electrons of the ene and enophile and the σ (sigma) electrons of the C—H bond of ene.



The ene reaction is bimolecular therefore a concerted ene reaction corresponds to the interaction of a hydrogen atom with the HOMO of an allyl radical and the LUMO of the enophile and is allowed.

REGIOSELECTIVITY, STEREOSELECTIVITY AND PERISELECTIVITY IN PERICYCLIC REACTION

PERICYCLIC REACTON :

Reaction in which a reactant is converted to a product through cyclic transition state without giving any intermediate either thermally or photochemically.

It is highly stereospecific – i.e., diastereoselective , regioselective ,periselective

STEREOSELECTIVITY :

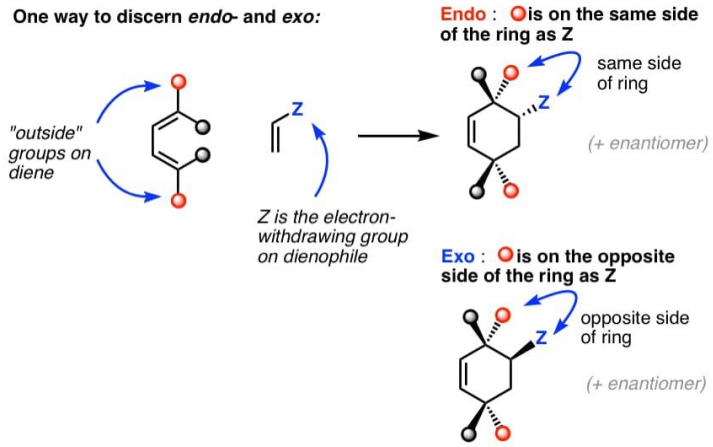
Stereoselective refers to the preferential formation of one stereoisomer over other due to stereochemical constraints.

Stereoisomer – same molecular formula and arrangement of atoms but differ from one another in 3- Dimensional space.

In Diel's Alder reaction , **endo** products tend to be favoured over **exo** products.

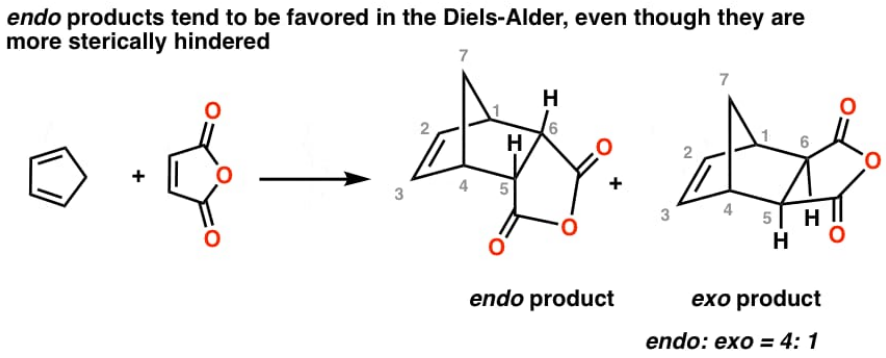
Endo – EWG points **towards** the conjugated system.

Exo – EWG points **away** from the conjugated system.



For eg,

Diel's Alder reaction of cyclopentadiene and maleic anhydride



Here Endo product is favoured over Exo .

Reason :

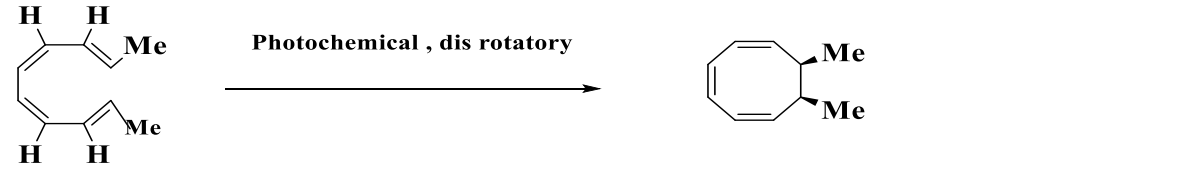
- Endo product is more sterically hindered but there comes a **Stabilizing interaction** in a endo transition state between a pi orbital from dienophile and extended pi-orbital of the HOMO of the diene. This is known as **Secondary Orbital Overlapping.**
- This overlapping or interaction can lower the energy of the transiton state. [Lower energy transition state = faster rate]
- This stabilizing electronic interaction compensates for greater steric Hindrance.
- But in exo ,secondary overlap is not possible as pi orbitals are too far away.
- **Kinetic or thermodynamic control** : Most exo products are in fact more stable than endo products for steric reasons but endo products are tend to be formed faster.

Endo - Kinetic product , **Exo** –Thermodynamic product.

PERISELECTIVITY :

If a reaction possibly can proceed in different pathways (including orientation and interaction of reacting species) and one is predominantly preferred ,the reaction is said to be peri-selective.

The orientation can be explained by conrotatory and disrotatory of the system.

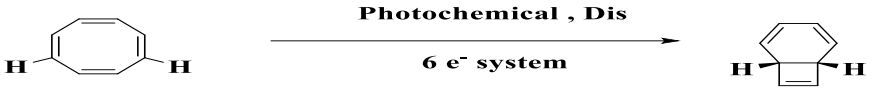


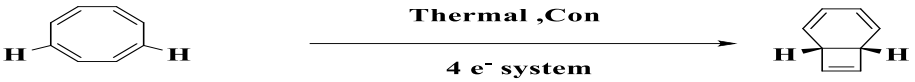
8 pi electron system

This structure is preferred as it is largely conjugated amd has large coefficeint than 4 pi and 6 pi electron system.

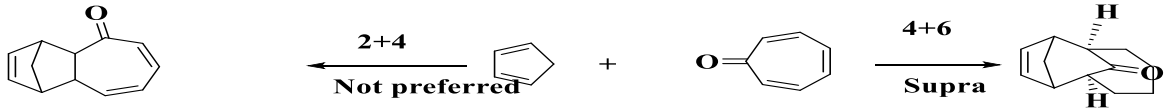
Thus disrotatory tends to give more conjugated product and being periselective.

	Thermal	Photochemical
4 n	Con	Dis
4n +2	Dis	Con





Periselectivity follows **WOODWARD –HOFFMANN RULES,** according to the rule all cycloaddition reactions are suprafacial when the total number of electrons are 6,10,14,etc.But it did not tell us which of 6 or 10 electrons is preferred if both are feasible. Thus in the reaction of cyclopentadiene and tropone there is a possibility of a Diel's Alder reaction (4+2=6e) which is not observed and (4+6=10e) cycloaddition is actually observed.



The product formed is not due to thermodynamic reason but due to frontier-orbital co-efficient. In General ,the ends of the conjugated system carry the largest co-efficients in the frontier orbital and we therefore expect pericyclic reaction to use the longest part of a conjugated system compatible with Woodward – Hoffmann Rule.

REGIOSELECTIVITY :

Refers to the preferential formation of one regioisomer over other where more regioisomers are formed .

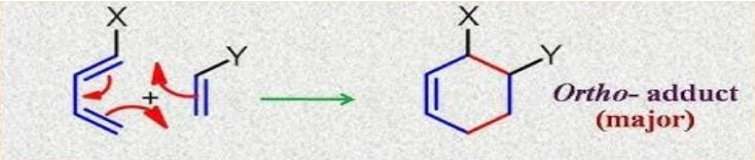
Regioisomer – Same molecular group ,same fuctional group but different attachment of points of functional group [ortho or para in this case].

Regioselectivity can be seen in unsymmetrical diene and unsymmetrical dienophile.

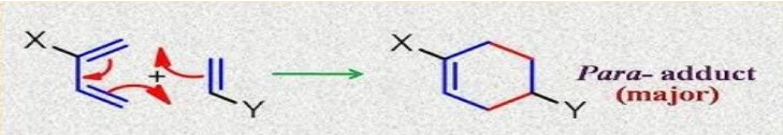
X = Electron Donating Group

Y = Electron Withdrawing Group

CASE 1,



Here EDG in diene is present at the terminal carbon, Thus the obtained product would be Ortho.



Here EDG in diene is present at the internal carbon, Thus the obtained product would be Para.

UNIT IV

ORGANIC PHOTOCHEMISTRY – 1

Photochemical Excitation of the Molecule

Photochemical excitation is the first step in a photochemical process, where a reactant is elevated to a higher energy state, called an excited state. This happens when a molecule absorbs light energy, which creates transient excited states with different chemical and physical properties than the original molecules.

Experiment technique

Photochemistry begins with absorption of light in the 200–800 nm region of spectrum. In order to know what wavelength of light we should employ in a particular photochemical experiment we must determine the UV 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 wavelength. The fraction of light absorbed (I/I_0) is given by the Beer's-Lambert's law. Lambert's law states that the fraction of the incident light absorbed by a compound is independent of the intensity of the source. Beer's law states that the absorption of light is proportional to the number of absorbing molecules. The absorption at a particular wavelength is defined by the equation

$A = log\ I_0/I$

Where, A = absorbance

I_0 = intensity of the reference light

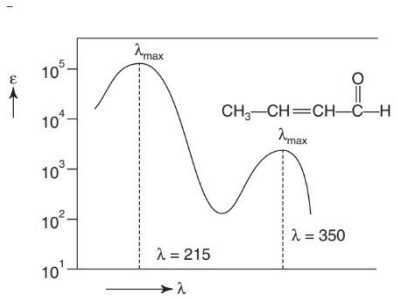
I = intensity of the beam coming out of the sample cell

The absorbance by a compound at a particular wavelength increases with increasing number of molecules undergoing transitions. Therefore, absorbance depends upon the electronic structure of the compound and also upon the concentration of the sample and length of the sample cell. For this reason, energy absorption is reported as molar absorptivity, ε, also known as molar excitation coefficient rather than actual absorbance. Often UV spectra are reported to show ε or log ε instead of A. The log ε value is specially useful when value for ε is very large.

$\varepsilon = A / C\,l$

where C = concentration of solution in mole/L

l = length of tube in cm



UV spectrum of CH3-CH=CH-CHO

General wavelength ranges for lowest energy absorption band of some classes of photochemical substrates

Substrate	**λ_{max} (nm)**
Alkenes	220 – 250
Acyclic dienes	199 – 200
Cyclic dienes	250 – 270

Styrene	270 – 300
Ketones	270 – 280
α, β-Unsaturated ketones	310 – 330
Aromatic aldehydes and ketones	280 – 300

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. Mercury arc lamp has three principle emission lines are 253.7 nm, 313 nm, 366 nm. Filters are available which permit selection of either of these lines. For example, if system is constructed so that light must pass through borosilicate glass (Pyrex) only wavelength longer than 300 – 310 nm will reach the sample because the glass absorbs below this wavelength. Pure fused quartz which transmits down to 220 nm must be used if the 254 nm radiation is desired. Other materials have cut off points between those of quartz and Pyrex. Filter solutions that absorb in specific wavelength ranges can also be used to control the energy if light reaching the sample.

Electronic transition

when molecule absorbs a quantum of light the electronic configuration changes to correspond to an excited state. Three general points about this process should be emphasised.

1. The excitation promotes an electron from filled orbital to an empty orbital. In most cases the promotion of electron is from the HOMO (highest occupied molecular orbital) to the LUMO (lowest unoccupied molecular orbital i.e., antibonding MO).

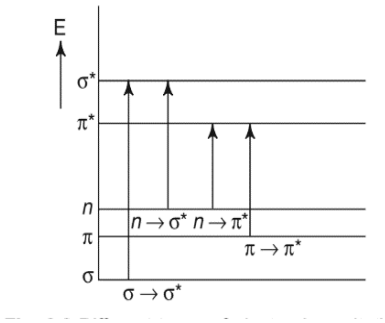
2. At the instance of excitation, only electrons are reorganised (i.e., from HOMO to LUMO). The heavier nuclei retain their ground state geometry according to Frank-Condon principle.

3. The electron do not undergo spin-inversion at the instant of excitation. Inversion is forbidden by quantum-mechanical selection rules, which require that there be conservation of spin during the excitation process. Although a subsequent spin state change may occur, it is a separate step from excitation. Thus, in the very short time (10–16s) required for excitation, the molecule does not undergo changes in nuclear position or in the spin state of the

promoted electron. After the excitation these changes can occur very rapidly when excited state comes in thermal equilibrium with its surrounding.

Types of electronics excitations

Let us consider the different types of electronic excitations which take place on absorption of light in UV and visible region. The ground state of organic compound contains valence electrons in three



Different types of electronic excitations

principle types of molecular orbitals: Sigma (σ) MO's, pi (π) MO's and filled but non-bonding (n or p) orbitals. Both σ and π MO's are formed from overlap of two atomic or hybrid orbitals. Each of these MO's therefore has an antibonding σ* and π* orbitals associated with it. An orbital containing nonbonding electrons or lone pair of electrons does not have an antibonding MO because it is not formed by overlap between two atomic orbitals. Electron transition involved the promotion of an electron from one of the three ground state (σ, π or n) to one of the antibonding (σ* or π*) MO's. The four important transitions are shown in figure. The usual order of energy required for various electronic transitions is as follows: σ → σ* > n → σ* > π → π* > n → π* Out of four excitations the π → π* and n → π*are more important in organic photochemistry than the other two σ → σ* and n → σ*.

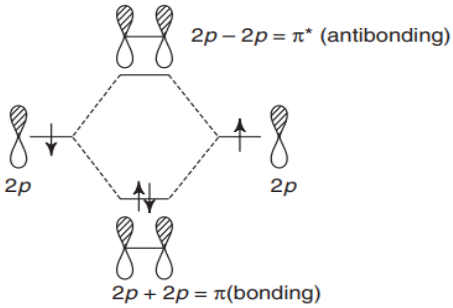
Types **of excitation in organic compound**

Type of excitation	**Type of organic compound**
(i) σ → σ*	Alkanes which have only σ bonds
(ii) n → σ*	Alcohols, amines, ethers thioethers etc.

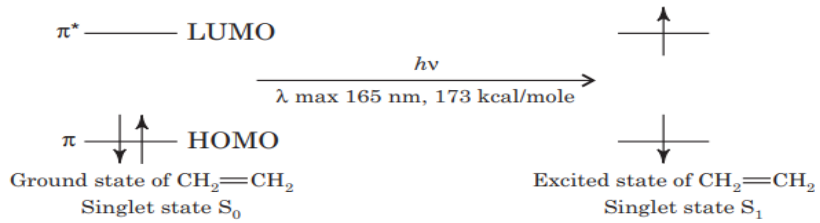
(iii) π → π*	Alkenes, carbonyl compounds Aromatic compounds etc.
(iv) n → σ*	Carbonyl compounds, acids and acid derivatives

Molecular orbital diagram view

To understand the electronic excitation in molecular orbital terms is possible only if we consider bonding as well as antibonding MO's. The bonding and antibonding MO's of ethylene and the electronic configuration of ethylene in the ground state and excited state are shown in Figure.



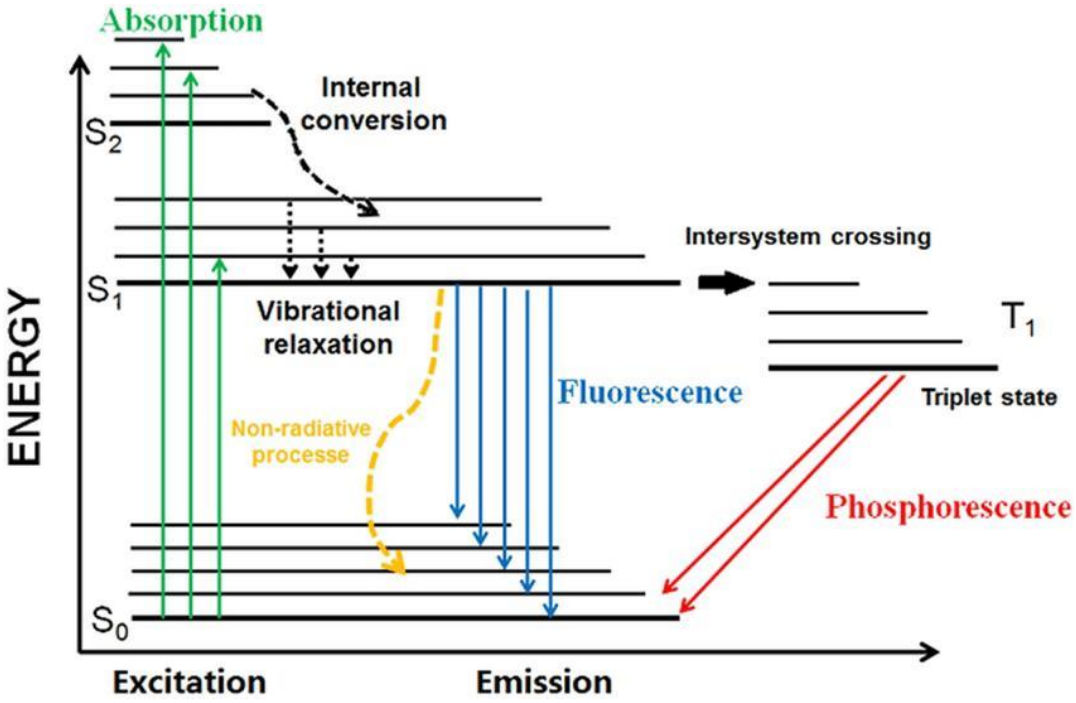
Molecular orbital diagram of ethylene



Excitation of ethylene molecule

Jablonski diagram

A Jablonski diagram is a graphical representation of the electronic states of a molecule and the transitions between them due to absorption or emission of light. It is used to explain the processes of fluorescence, phosphorescence, and non-radiative decay in photophysics and photochemistry.



Energy Levels:

The vertical axis of the diagram represents energy. The higher the position on the diagram, the higher the energy of the state.

The diagram shows three main types of electronic states:

Ground State (S_0): The lowest energy state, where the molecule is most stable.

Excited Singlet States (S_1, S_2, etc.): Higher energy states where the molecule can exist after absorbing a photon. These are called "singlet" states because the electron spins are paired.

Triplet States (T_1): These are lower in energy than the singlet excited states but are still higher than the ground state. In triplet states, the electron spins are unpaired.

1.Absorption:

When a molecule absorbs a photon, it transitions from the ground state (S_0) to an excited singlet state (S_1 or higher). This process is represented by an upward arrow.

2.Relaxation:

After excitation, the molecule can relax to lower energy states through several pathways:

3.Internal Conversion (IC):

A non-radiative process where the molecule loses energy through vibrational relaxation, dropping from a higher excited state (e.g., S_2) to a lower one (S_1).

4.Vibrational Relaxation:

After absorption, the molecule often relaxes to the lowest vibrational level of the excited state.

5.Fluorescence:

The molecule can release energy by emitting a photon and return to the ground state from an excited singlet state ($S_1 \rightarrow S_0$). This process is called fluorescence, and it is depicted by a downward arrow between singlet states.

6.Intersystem Crossing (ISC):

The molecule can undergo a transition from an excited singlet state (S_1) to a triplet state (T_1). This process is called intersystem crossing, represented by a diagonal arrow.

7.Phosphorescence:

The molecule can also return to the ground state from the triplet state ($T_1 \rightarrow S_0$), emitting a photon. This process is slower and is called phosphorescence, shown by a downward arrow from the triplet state to the ground state.

Energy transfer process

In photochemistry, energy transfer refers to the process by which energy is transferred from one molecule (the donor) to another molecule (the acceptor) without the emission of photons. It typically occurs after one molecule has absorbed light and entered an excited state. Energy transfer processes are fundamental in many photochemical reactions and are key mechanisms in biological systems like photosynthesis. There are two primary types of energy transfer mechanisms:

1.Forster Resonance Energy Transfer (FRET):

Mechanism: FRET involves the transfer of energy between two molecules through dipole-dipole interactions. The energy transfer occurs when the donor molecule, in an excited singlet state, transfers its energy directly to the acceptor molecule, causing the acceptor to transition from its ground state to an excited state.

Distance Dependence: FRET is highly dependent on the distance between the donor and acceptor molecules. The efficiency of FRET decreases with the sixth power of the distance between them, meaning it is effective only when the donor and acceptor are in close proximity (typically 1-10 nm apart).

Spectral Overlap: FRET requires the emission spectrum of the donor to overlap with the absorption spectrum of the acceptor, enabling energy transfer without the emission of a photon.

Applications: FRET is commonly used in biological research to study molecular interactions, such as protein-protein interactions, due to its sensitivity to distance changes.

2.Dexter Energy Transfer:

Mechanism: Dexter energy transfer is a quantum mechanical process that involves the exchange of electrons between the donor and acceptor molecules. In this process, the donor and acceptor must come into very close contact (typically less than 1 nm) because it involves an overlap of their electronic wave functions. The transfer occurs via a direct electron exchange between the excited donor and the acceptor, leading to the transfer of energy.

Distance Dependence: Unlike FRET, Dexter energy transfer is much more distance-sensitive and only occurs when the donor and acceptor molecules are very close.

Spin Requirements: Dexter transfer is more sensitive to the spin states of the donor and acceptor. It can occur between singlet-singlet or triplet-triplet states, and hence it is an important mechanism for triplet-triplet energy transfer.

Applications: Dexter energy transfer is often involved in processes where triplet states are relevant, such as in organic light-emitting diodes (OLEDs) or in some photochemical reactions.

3.Radiative Energy Transfer:

Mechanism: This process involves energy transfer through the emission and subsequent reabsorption of a photon. The donor molecule, after absorbing energy and entering an excited state, emits a photon. The acceptor molecule absorbs this photon and is excited to a higher energy level.

Distance Dependence: Radiative energy transfer is not limited by the proximity of the donor and acceptor. It can occur over long distances, as long as the emitted photon reaches the acceptor molecule.

Applications: This process is relevant in systems where light emission and reabsorption are feasible, such as in certain photonic devices or artificial photosynthesis.

Applications of Energy Transfer in Photochemistry:

Photosynthesis: In plants, energy transfer processes are crucial for capturing light energy and transferring it through the photosystems to drive the production of chemical energy.

Photovoltaics: Energy transfer is vital in solar cells, where absorbed light energy is converted into electrical energy.

Fluorescence Imaging: FRET is widely used in fluorescence-based imaging techniques to study molecular interactions and distances at the nanoscale.

Sensitization Reactions: In photochemical sensitization, energy transfer allows a donor molecule to activate an acceptor molecule, leading to chemical reactions that would not happen otherwise.

Intersystem crossing(ISC)

Intersystem crossing (ISC) is a non-radiative process in which a molecule transitions from an excited singlet state to a triplet state. This transition involves a change in the spin state of the electrons and is important in many photophysical and photochemical processes.

Singlet and Triplet States:

In a singlet state, the two electrons in the molecule are paired, meaning they have opposite spins (one up, one down). The total spin of the system is zero ($S = 0$).

In a triplet state, the spins of the two electrons are parallel (either both up or both down). This gives the molecule a net spin of 1 ($S = 1$).

Spin-Forbidden Transition:

A transition between states with different spin multiplicities (e.g., from a singlet to a triplet) is considered spin-forbidden by quantum mechanical selection rules. However, intersystem crossing still occurs due to a phenomenon called spin-orbit coupling, where the spin and orbital motions of electrons interact, allowing for some probability of this transition.

Because ISC is a spin-forbidden process, it typically happens more slowly than spin-allowed transitions, like fluorescence, but it still plays an important role in photophysics.

Process of Intersystem Crossing:

When a molecule absorbs light, it gets excited from the ground singlet state (S_0) to an excited singlet state (S_1 or S_2).

Intersystem crossing can occur from an excited singlet state (S_1) to a triplet state (T_1). During this process, the electron spin flips, and the molecule moves to a triplet state with a different spin configuration. After the molecule transitions to the triplet state, it may return to the ground state (S_0) by emitting light in the form of phosphorescence or by undergoing non-radiative decay.

Energy and Lifetime:

Triplet states generally have lower energy than the corresponding singlet states due to exchange energy, but their transitions back to the ground state are slow because they are spin-forbidden. As a result, molecules in the triplet state can remain in that state for a relatively long time (microseconds to seconds), which is why phosphorescence often persists after the exciting light source is removed.

Intersystem crossing competes with other deactivation pathways like fluorescence and internal conversion, influencing the behavior of the excited molecule.

STERN VOLMER EQUATION

Quenching

A process that leads to a reduction in fluorescence intensity is referred to as quenching. Quenching may occur due to energy transfer, charge transfer reaction or due to formation of complexes in the ground state.

Quenching may be classified as a) collisional quenching

b) static quenching

1. Excited state molecule returns to ground state via emission of a photon

2. Excited state molecule collides with quencher molecule and returns to ground state non-radiatively. The other routes through which the molecule may relax non-radiatively are internal conversion, intersystem crossover.

Stern-Volmer Plot

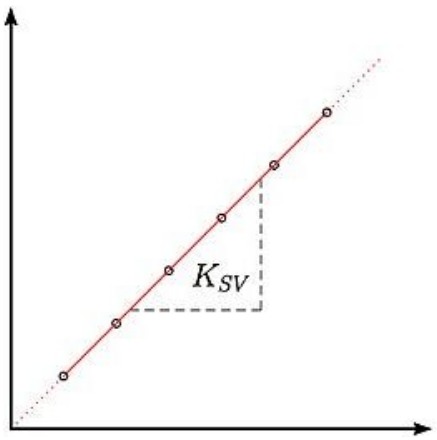
In case of simple collisional quenching Stern-Volmer equation or the following equation holds

$$\Phi^0/\Phi = 1+K_{SV}[Q]$$

Φ^0 - Quantum yield in the absence of quencher

Φ - Quantum yield in the presence of quencher

K_{SV} – Stern Volmer constant



Derivation

Suppose a molecule M absorbs energy and is excited to M*. The excited molecule may return to the ground state through a number of routes including both radiative and non-radiative process.

	Process	Rate
$^{S}M \rightarrow {}^{S}M^*$	Absorption	Ia
$^{S}M^* \rightarrow {}^{S}M + h\upsilon$	Fluorescence	$K_F[^{S}M^*]$
$^{S}M^* \rightarrow {}^{S}M$	Internal conversion	$K_{IC}[^{S}M^*]$
$^{S}M^* \rightarrow {}^{T}M^*$	Intersystem crossover	$K_{ISC}[^{S}M^*]$

Quantum yield of Fluorescence in the absence of quencher

$$\Phi^0 = \frac{\text{number of photons emitted as fluorescence}}{\text{Total number of photons absorbed}}$$

Or

Rate of all deactivation process

$$= \frac{K_F[{}^S M^*]}{K_F[{}^S M^*] + K_{IC}[{}^S M^*] + K_{ISC}[{}^S M^*]}$$

$$= \frac{K_F}{K_F + K_{IC} + K_{ISC}}$$

Quantum yield of Fluorescence in the presence of quencher

$$\Phi = \frac{\text{number of photons emitted as fluorescence}}{\text{Total number of photons absorbed}}$$

$$= \frac{K_F[{}^S M^*]}{K_F[{}^S M^*] + K_{IC}[{}^S M^*] + K_{ISC}[{}^S M^*] + Kq\,[Q]}$$

$$= \frac{K_F}{Kq\,[Q] + K_F + K_{IC} + K_{ISC}}$$

$$\Phi^0/\Phi = \frac{K_F}{K_F + K_{IC} + K_{ISC}} \Bigg/ \frac{K_F}{Kq\,[Q] + K_F + K_{IC} + K_{ISC}}$$

$$= \frac{Kq\,[Q] + K_F + K_{IC} + K_{ISC}}{K_F + K_{IC} + K_{ISC}}$$

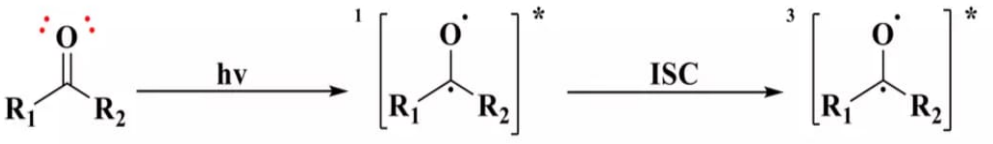
$$= \frac{Kq\,[Q + 1}{K_F + K_{IC} + K_{ISC}}$$

$$= 1 + K_q\,[Q]\,T_0$$

It is similar to the y=mx+c where it can also be writtern as $1+K_{SV}\,[Q]$ which is known as the derived form of Stern Volmer Equation.

NORRISH TYPE -1 AND NORRISH TYPE- 2 CLEAVAGE REACTIONS :

- Carbonyl compounds undergo various photochemical reactions in both gas and liquid phases.
- Carbonyl compounds are best suited for Photochemical reactions because ketones are much stable and undergo number of interesting reactions.
- The initiation of photochemical reaction depends on the capacity of reactants to absorb the light from an emitting source.
- The light photon energy must match with the energy necessary to excite one electron from HOMO to LUMO of a ground state molecule a quantized process to its exited state.
- It involves an n ➡ π^* excitation of an oxygen lone pair electron (n) to the π^* lowest unoccupied molecular orbital of the c=o chromophore.
- Excitation is from the S0 electronic ground state to the first singlet excited state ,S1, which correlates to excited state products.
- Dissociation on both T1 and S0 leads to ground state radical products.
- Internal conversion (IC) from S1 or two ISC steps. S1 –T1- S0, can also lead to photolysis on the S0 ground state .
- ISC is spin forbidden , the geometries of S1 and T1 excited state carbonyls are generally very similar and the energy separation between the states is small ,leading to fast S1-T1 ISC rates .
- The reactive excited states of saturated ketones are the n - π^* states ,whereas that of conjugated ketones are π- π^* states . Both these n - π^* and π- π^* transitions of carbonyl compounds may occur by singlet or triplet excited states.
- Both singlet and triplet excited states of a carbonyl compound react in different rates to give same type of products in different ratios.



NORRISH TYPE REACTIONS :

- Kirkbride and Norrish identifying α – bond cleavage as the dominant photolysis pathway in small carbonyls in 1931.
- The hemolytic cleavage of covalent bonds in carbonyl compound under photochemical conditions known as Norrish type reactions .
- They are divided into two types

1. Norrish type 1
2. Norrish type 2

Norrish type 1:

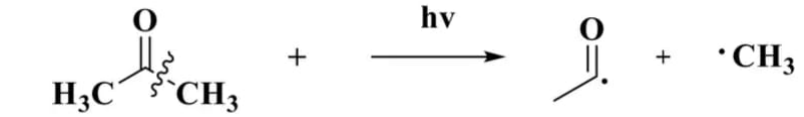
- ✓ The Norrish type 1 reaction is a photochemical cleavage or hemolysis of aldehyde and ketones into two free radical intermediates.
- ✓ The carbonyl groups accepts a photon and excited to a photochemical singlet state.
- ✓ Light energy is sufficient to break the alpha bond.
- ✓ Through intersystem crossing the triplet state can be obtained .
- ✓ On cleavage of the α-carbon bond from either state ,two eadical fragments are obtained which are alkyl or acyl radical.

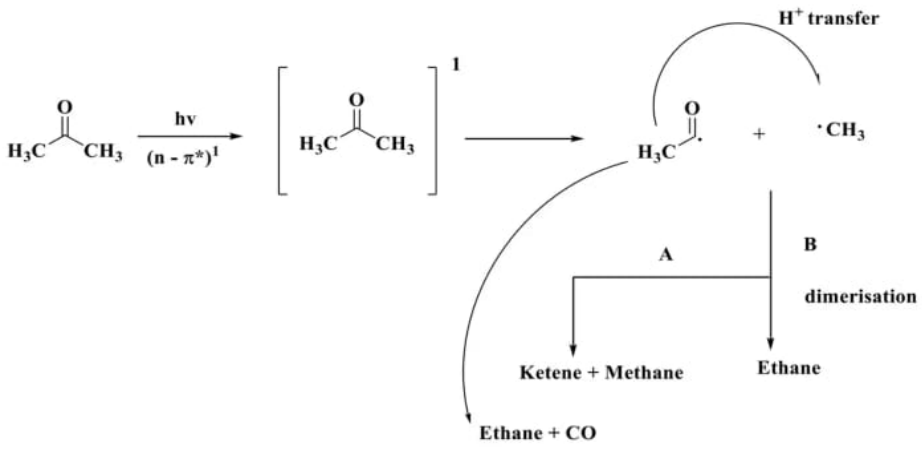
Distinctive features of Norrish type 1 reaction :

- ✓ Reaction intermediate are free radicals – acyl ,alkyl
- ✓ Reaction proceeds to form more stable free radical
- ✓ Reaction is more effective on vapour state
- ✓ The SP2 and SP of alpha carbon never participated in Norrish type 1 reaction

- ✓ Compound which are formed stable free radicals undergoes Norrish type 1 reaction even in liquid state

Reaction mechanism:

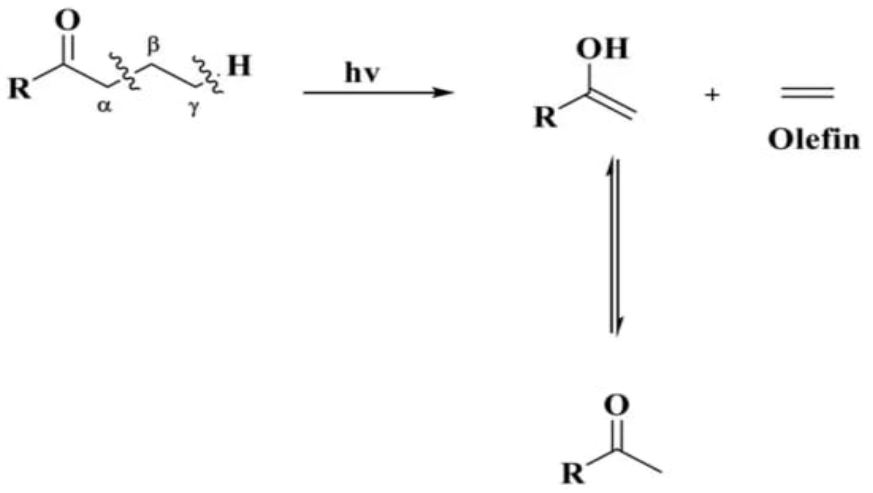




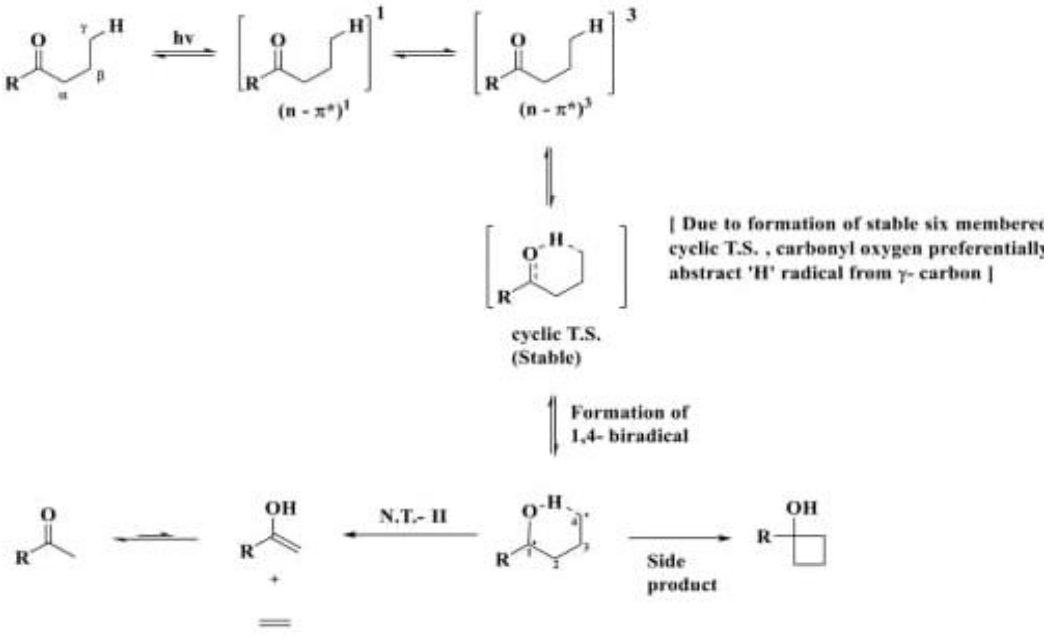
Norrish type 2 reaction :

- ❖ Photochemical reactions of aldehydes or ketones bearing γ –hydrogens
- ❖ It is a photochemical intramolecular abstraction of a γ- hydrogen (a hydrogen atom three carbon positions removed from the carbonyl group) by the excited carbonyl compound to produce a 1,4 – biradical a primary photoproduct
- ❖ The resulting diradical species can undergo a subsequent ring closure reaction to yield a cyclobutanol or suffer fragmentation to yield an enol and an alkene

- γ –hydrogens can undergo the intramolecular hydrogen abstraction from the singlet excited S1 state as well as the triplet T1 state
- β,γ - carbon always converted to olefins



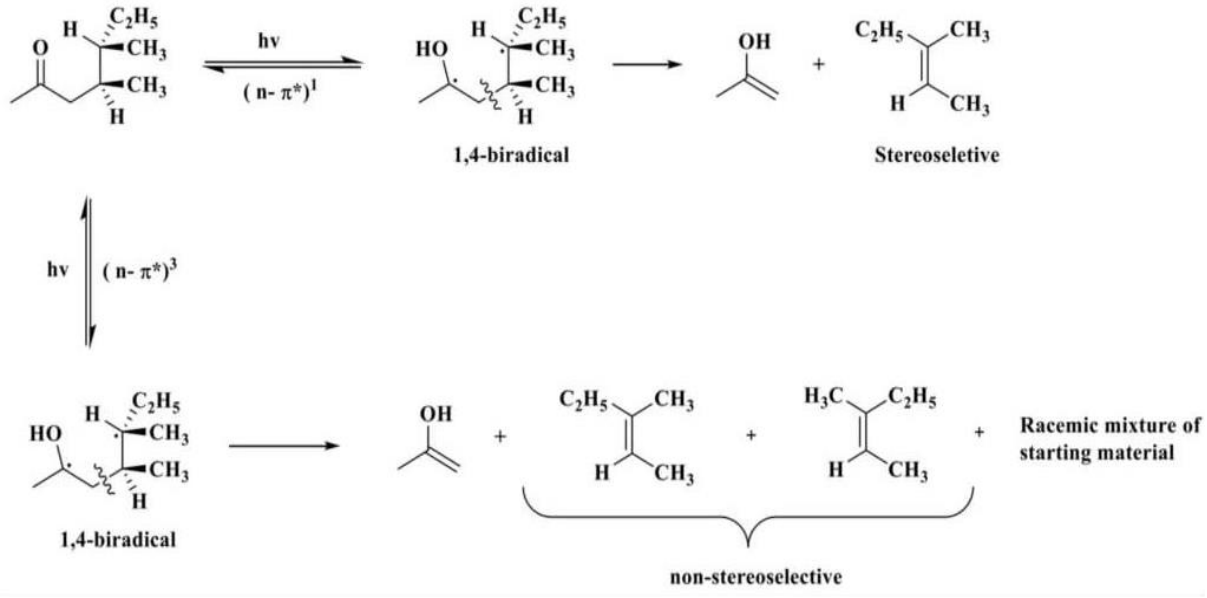
Reaction mechanism :



Distinctive features of Norrish type 2 reaction:

- $[n\text{-}\pi^*]^1$ and $[n\text{-}\pi^*]^3$ give rise to γ – hydrogen transfer
- However , the singlet and triplet reactions are quit distinguishable

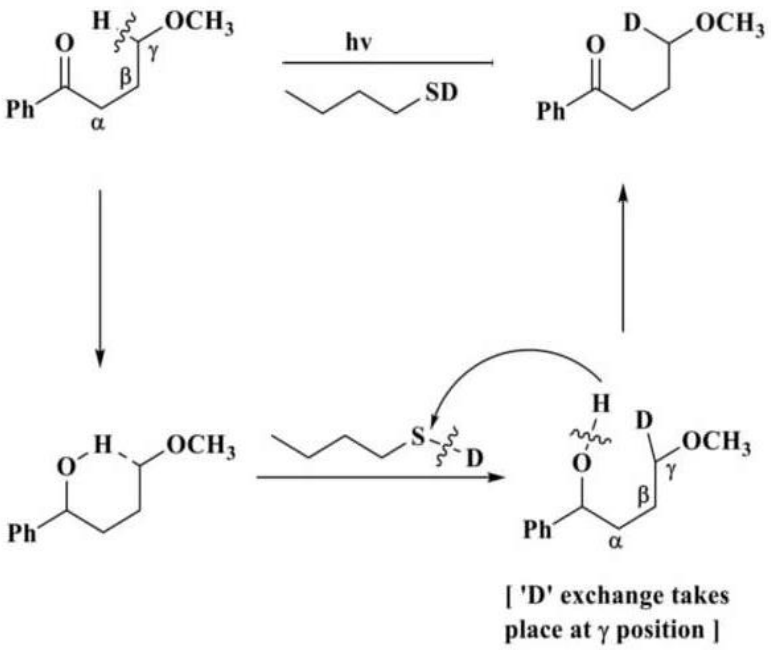
- Photochemical elimination is highly stereospecific when intermediate biradicals is $[n\text{-}\pi^*]^1$



- Photochemical elimination is non stereoselective when biradical intermediate is $[n\text{-}\pi^*]^3$

Stabilization of 1,4 –biradical:

- It may undergo photo- elimination and form olefins/ enols
- It may directly cyclize and form cyclobutanol byproduct derivative
- It may convert into starting material which may due to reversible formation of 1,4- biradical



Paterno-Buchi Reaction

Principle

Oxetane (four membered heterocycle with oxygen as hetero atom) is synthesised by the cycloaddition of an alkene to carbonyl compound upon exposure to UV-radiations. The reaction is known as Paterno-Buchi reaction. In general, it is photochemical (2+2) electrocyclisation of carbonyl group to an olefin under the influence of near UV-radiation to yield substituted oxetane ring system.

Mechanism

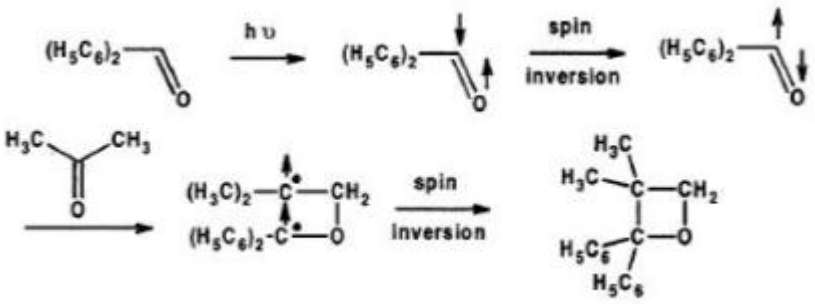
The mechanism of Paterno-Buchi reaction has not been explored thoroughly. However the mechanism outlined below is generally accepted .

1. Light catalysed stimulation of n-t transition of carbonyl group upon exposure to UV-radiations to form singlet or triplet excited carbonyl species.

2. Spin inversion of triplet state.

3. Addition of an olefin to form exciplex which is converted to more stable diradical.

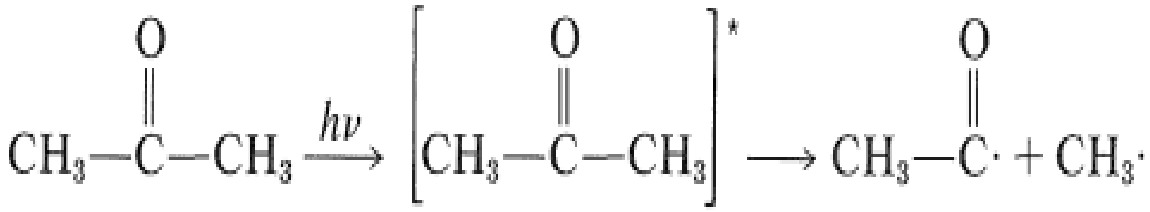
4. Spin inversion leading to the formation of regioselective oxetane.



UNIT – 5

Photochemistry of α,β unsaturated ketone

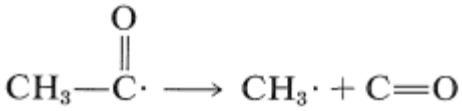
Carbonyl compounds undergo various photochemical reactions in both gas and liquid phases. The electronic excited states of saturated ketones are n → π* states, whereas of conjugated ketones are π → π* states. Both these excited states in singlet or triplet states take part in chemical reactions. The activation energies for singlet and triplet states of saturated ketones are about 80–85 and 75–80 kcal/mol, respectively, whereas of unsaturated ketones, these are in the range of 45–75 kcal/mol. For this reason, the photoreactions of saturated ketones occur in the UV region, 270–290 nm, and of unsaturated ketones in the UV region, 310–330 nm. The excited carbonyl compounds have radical characters at both carbon and oxygen atoms of the carbonyl group, and hence most of their photoreactions proceed through radical intermediates. The important photoreactions of carbonyl compounds are the reduction of carbonyl compounds by hydrogen abstraction, fragmentation including the *Norrish types I and II cleavages*, cycloaddition to alkenes (the *Paterno- Büchi reaction*), and rearrangement (the *lumiketone and oxa-di- π-methane rearrangements*)



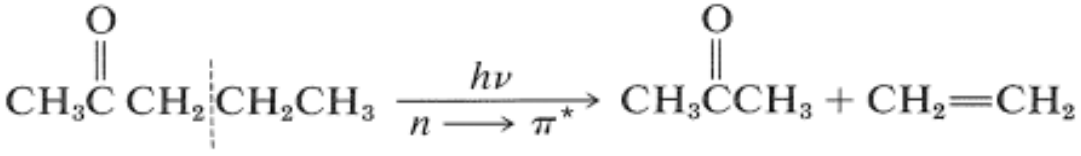
We have mentioned how chlorine molecules dissociate to chlorine atoms on absorption of near-ultraviolet light and thereby cause radical-chain chlorination of saturated hydrocarbons.. Photochemical chlorination is an example of a photochemical reaction that can have a high *quantum yield* - that is, many molecules of chlorination product can be generated per quantum of light absorbed. The quantum yield of a reaction is said to be unity when 1mol1mol of reactant is converted to product(s) per einstein11 of light absorbed. The symbol for quantum yield is usually ΦΦ.2-Propanone (acetone) vapor undergoes a photodissociation reaction with 313313-nmnm light with ΦΦ somewhat less than unity. Absorption of light by 2-propanone results in the formation of an excited state that has sufficient energy to undergo cleavage of a C=C bond (the weakest bond in the molecule) and form a methyl radical and an ethanoyl radical. This is a *primary* photochemical reaction:

The subsequent steps are dark reactions.

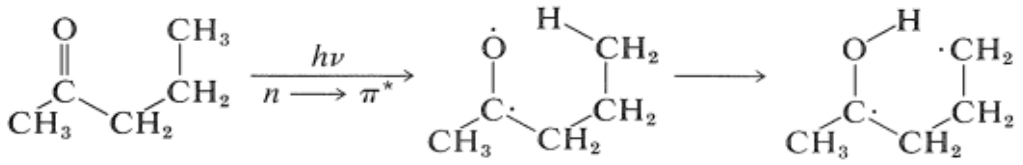
At temperatures much above room temperature, the ethanoyl radical breaks down to give another methyl radical and carbon monoxide:



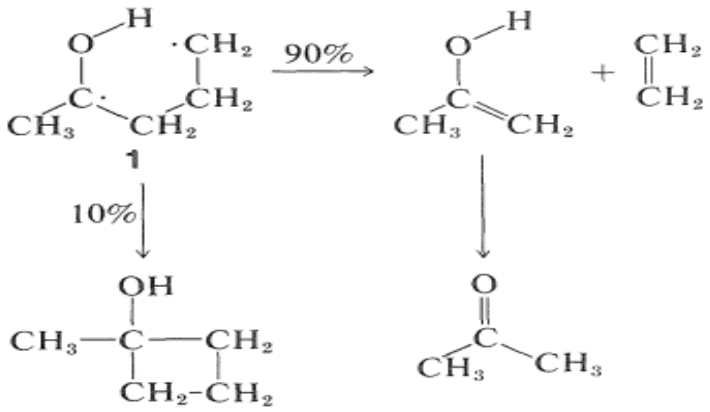
In this pathway (*Norrish type II process*), cleavage occurs at the Cα−Cβ bond to give, as the major product, a ketone of shorter chain length and an alkene. Thus for 2-pentanone:



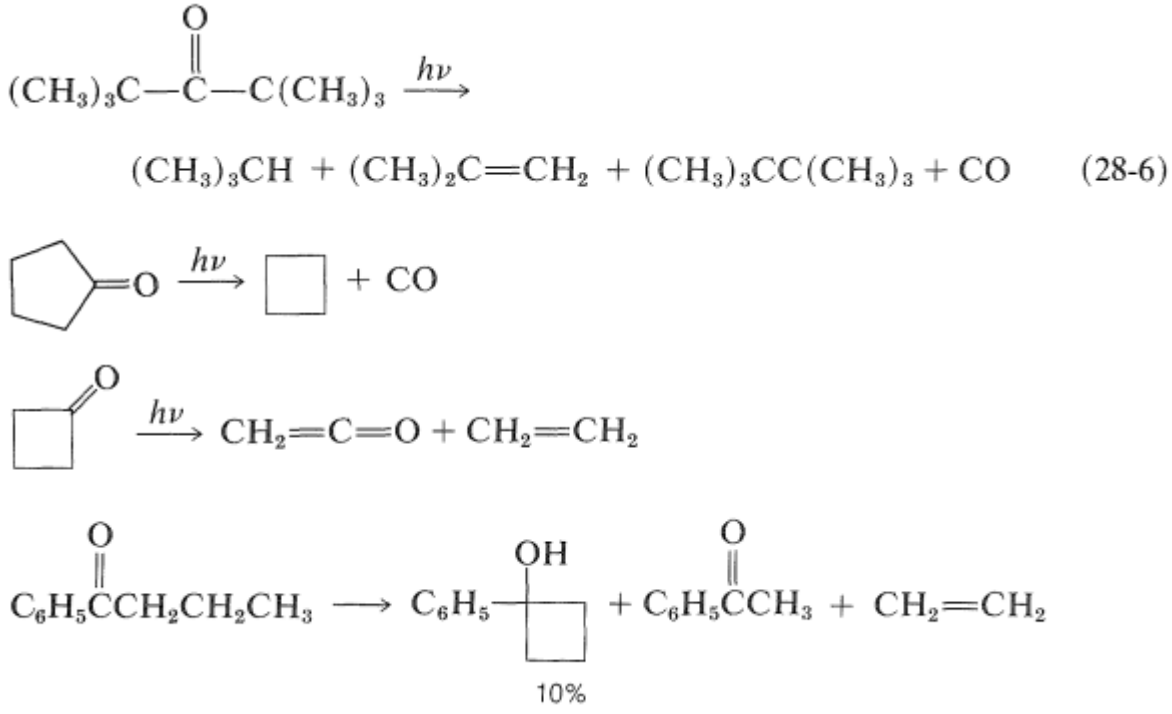
This reaction occurs in an interesting way. Whatever the nature of then n→π∗ excited state, S11 or T11, the primary photochemical reaction is the abstraction of a hydrogen atom from the γ carbon by the carbonyl oxygen to give the diradical,



The subsequent dark reactions readily are understood as typical of diradicals. Cleavage of 11 at Cα−CβC gives ethene and an enol, which rearranges to the ketone. Alternatively, 11 can cyclize to a cyclobutanol

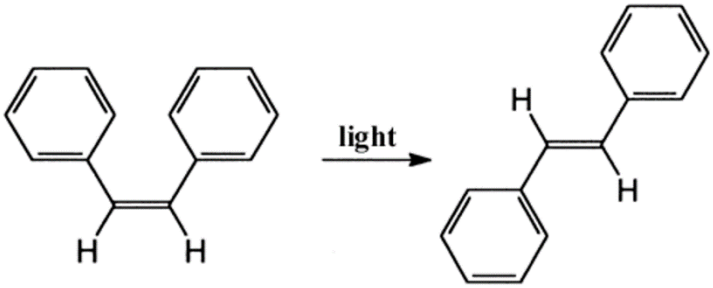


A variety of photodissociation reactions have been found to take place with ketones, but the products almost always can be explained as the result of Norrish type I and/or II cleavage. Examples are:



Photochemical Isomerization of Cis and Trans Alkenes

An important problem in many syntheses is to produce the desired isomer of a cis-trans pair of alkenes. The problem would not arise if it were possible to isomerize the undesired isomer to the desired isomer. In many cases such isomerizations can be carried out photochemically. A typical example is afforded by *cis*- and *trans*-1,2-diphenylethene (stilbene):



cis-stilbene **trans-stilbene**

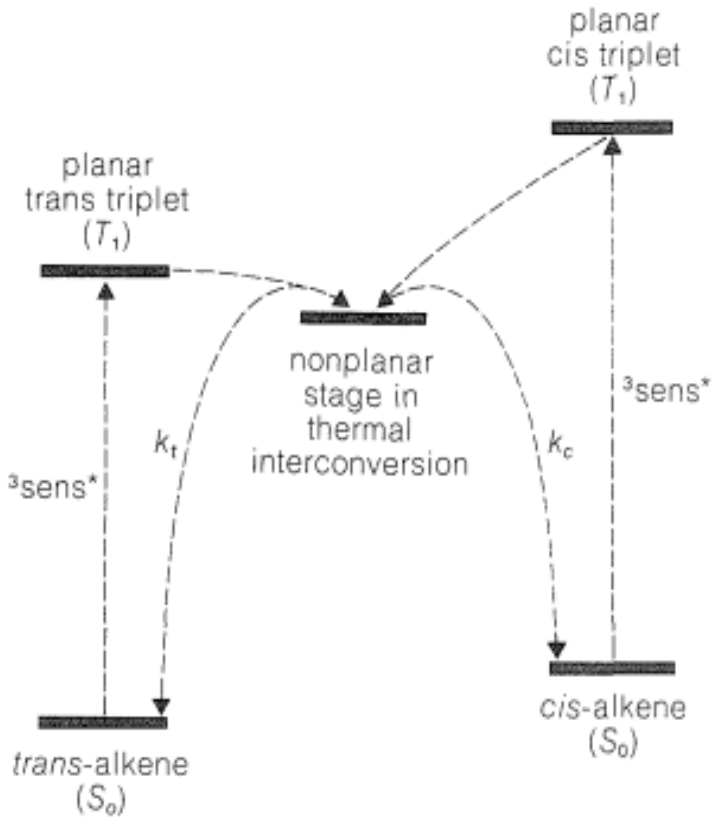
Here the trans form is easily available by a variety of reactions and is more stable than the cis isomer because it is less sterically hindered. However, it is possible to produce a mixture containing mostly cis isomer by irradiating a solution of the trans isomer in the presence of a suitable photosensitizer. This process in no way contravenes the laws of thermodynamics because the input of radiant energy permits the equilibrium point to be shifted from what it would be normally.

Isomerization appears to occur by the following sequence: The sensitizer, usually a ketone such as benzophenone or 1-(2-naphthyl)ethanone, is raised by an n→π∗ transition from the singlet ground state (S0)(0) to an excited state (S1)(1) by absorption of light. Intersystem crossing then occurs rapidly to give the triplet state (T1)(1) of the sensitizer:

$$^1\text{Sens} \xrightarrow[n \longrightarrow \pi^*]{h\nu} {}^1\text{Sens}^* \xrightarrow{\text{intersystem crossing}} {}^3\text{Sens}^*$$

(Sens = $C_6H_5\overset{\overset{O}{\|}}{C}C_6H_5$; ^{1}Sens = singlet state; ^{3}Sens* = triplet state)

The next step is excitation of the alkene by energy transfer from the triplet state of the sensitizer. Remember, the net electron spin is conserved during energy transfer, which means that the alkene will be excited to the triplet state:



Schematic energy levels for cis- and trans-1,2-diphenylethene. The upward transitions are achieved by transfer of energy from triplet sensitizer. The downward transitions from the nonplanar stage marked with the rate constants ktand kc involve loss of thermal energy to the solvent, or phosphorescence. The lower energies assigned to the S00 and T11 states of trans-*1,2-diphenylethene relative to the S00 and T11 states of the cis isomer reflect steric hindrance between the phenyl groups of the cis isomer.*

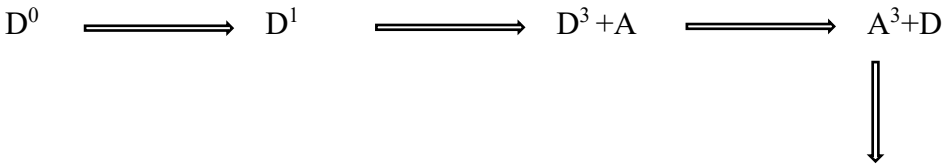
Photon energy transfer reaction

Photon energy transfer reaction involves the conversion of low energy photons into higher energy photons. In this process, one molecule absorbs light energy gets existed & transfers to another molecule. The donor molecule returns to its ground state, While the acceptor gets excited which undergoes photo -chemical reactions.

Conditions:

Energy of donor molecule should be 5 kcal/mode more energy than the energy needed for excitation of acceptor molecule.

hv ISC

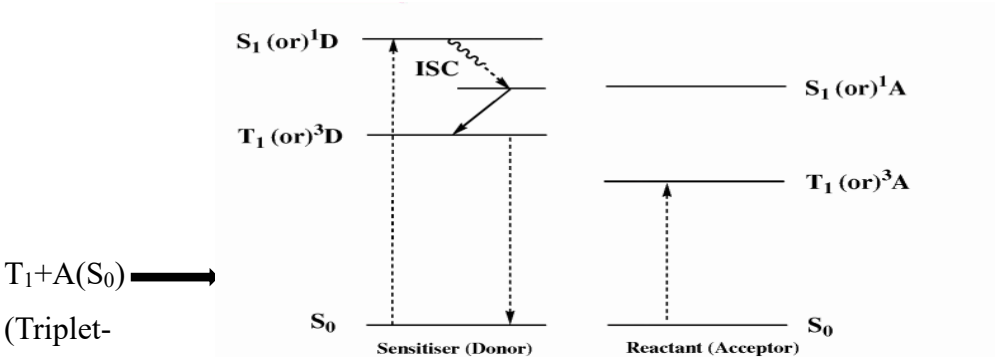


Product

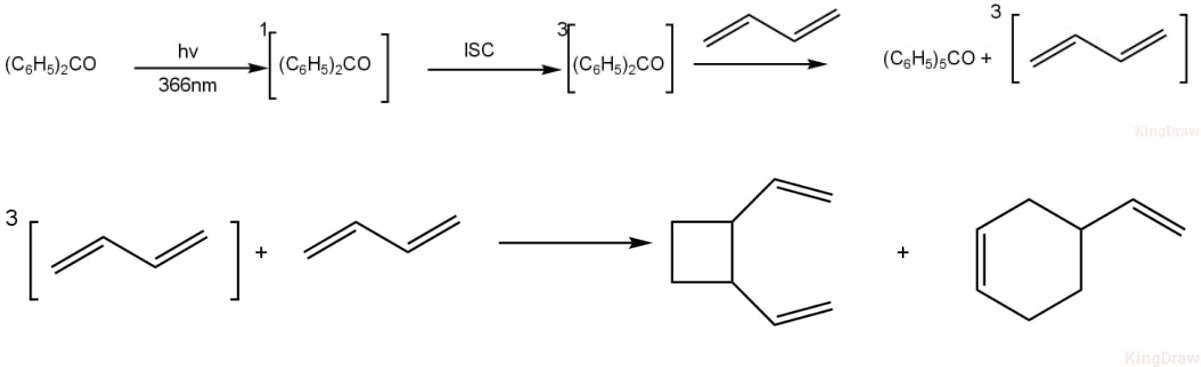
Transfer of energy from excited singlet state produces singlet and transfer from excited Triplet produces Triplet.

In other words. if the acceptor molecule possesses a state of same multiplicity and lower energy than that of donor molecule. Energy transfer will occur from donor to acceptor. This provides a versatile method for forming triplet by triplet to triplet energy transfer.

Eg :1,3butadine with donor.

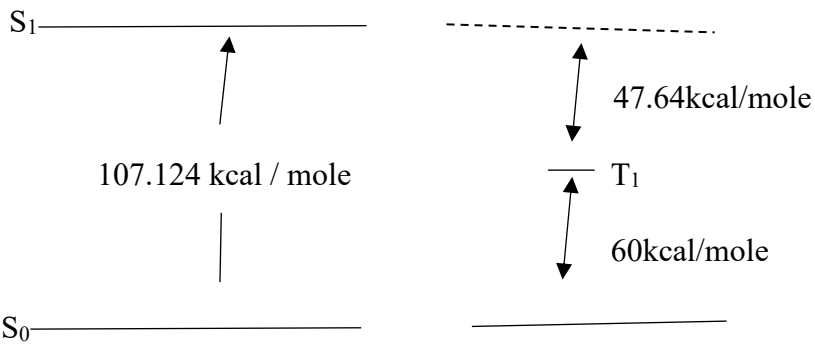


(Triplet-Transfer)

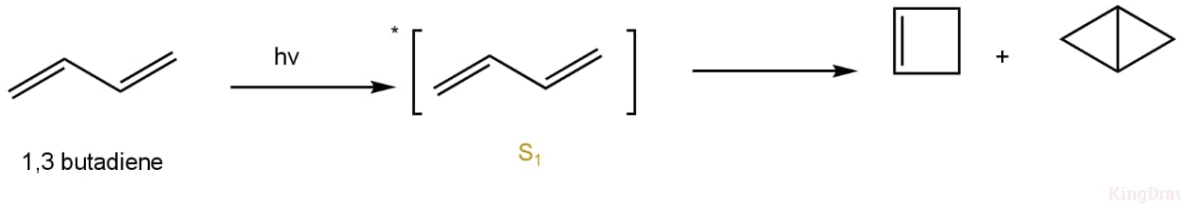


Triplet excited butadiene produced by energy transfer from triplet excited benzophenone gives only dimers.

Eg:1,3 butadiene without donor.



1,3 butadiene



The sensitizer should meet the following criteria:

- Must be excited by the Irradiation to be used.
- Must be present in sufficient concentration & absorb more. strongly than the other reactants under the condition of the experiment so that it is the major light absorber.
- The energy of triplet state of sensitizer must be greater than that, of reactant. if this condition is not met the energy transfer becomes endothermic.
- Must be able to reactant to transfer energy to the desired reactant.
- The sensitizer should possess high ISC, absorb at lower wavelength & does not interfere with analytical procedure.

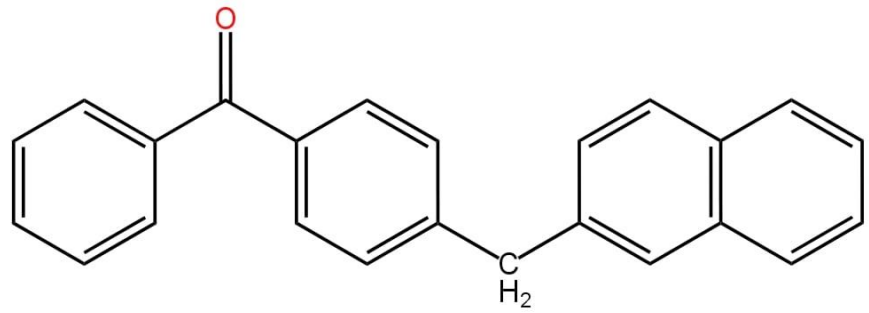
Useful features using a photosensitizer are,

- Reaction proceeding via singlet state can be avoided & the quantum yield of product is increased.
- Substance which are unable to absorb light of conveniently longer wavelength may after be sensitized by additives.

In terms of energetics, it implies that common compound whose upper singlet (s_1) & (T_1) are widely separated thereby making ISC difficult may be excited to their Triplet state by sensitizer is appropriate intermediate energy levels.

INTRAMOLECULAR ENERGY TRANSFER:

There are certain complex molecules, like substituted aromatic ketones or aldehydes which shows electronic excitation of one part of the molecule and transfer of this excitation energy from one part to the another part, in the Same molecule this phenomenon is known as Intramolecular energy transfer.



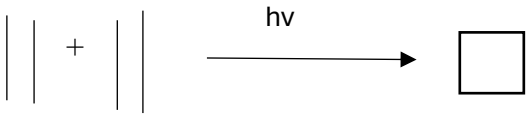
4-(1-naphthyl methyl) - benzophonone

During irradiation of the above mentioned compound with radiation of wavelength 366nm absorbed by benzophenone moiety gets excited and goes to Triplet excited state by ISC.

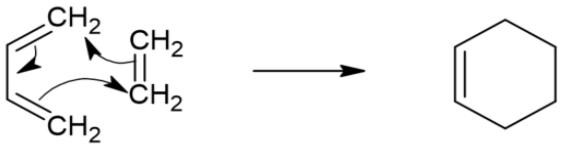
This Triplet excited shows efficient transfer from benzophenone moiety to naphthalene moiety.

PHOTOCYCLOADDITION:

Cycloaddition is a reaction on which two unsaturated molecules undergoes an addition reaction to give a cycle product, formation of cycle product takes place at the expenses of one pi bond each of the reactant & gain of two sigma bond. Thus in this reaction there is a loss of two pi bond of the reaction & gain of two sigma bond in the product.



The above reaction in the equation (2+2) cycloaddition reaction because the reaction involves 2 e^- from one reacting component and also 2 e^- from the other



The above reaction is (4+2) cycloaddition reaction.

The cycloaddition reactions are classified with respect to three facts of the reactions.

1. Number of e^- of each reactant participating in cycloaddition reaction.
2. The nature of orbitals undergoing change. (sigma or pi).
3. Stereochemical mode of cycloaddition

The stereochemical mode is given by s or a which indicates whether the addition occurs in a super or anthra mode on each reaction.

The cycloaddition reaction may occur either across the same or across the opposite faces of the planes in each reaction.

If the reaction occurs of the same face of the pi system the reaction is said to be suprafacial.

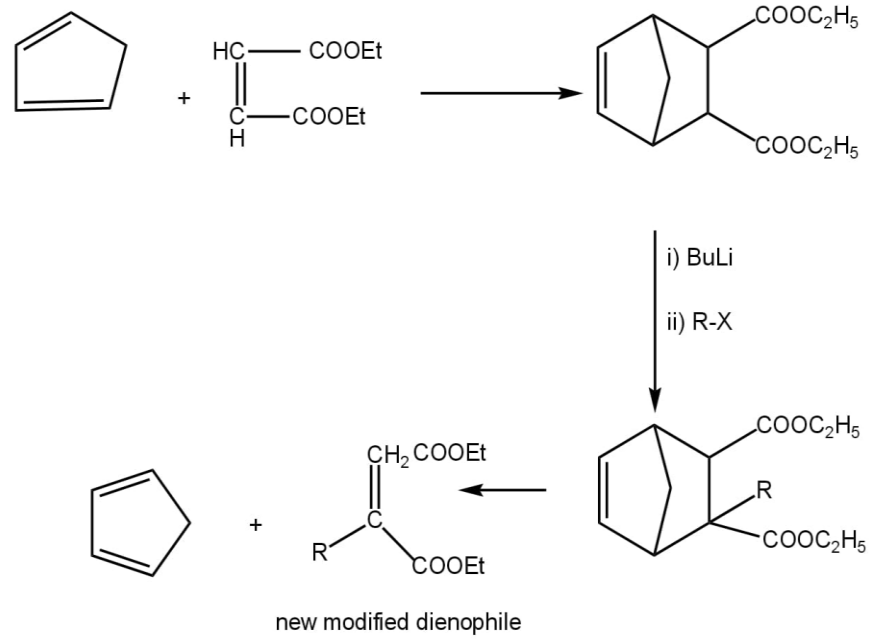
The suprafacial is nothing more than the syn addition.

The revers of cycloaddition reaction are called as cycloreversion or retro grade cycloaddition.

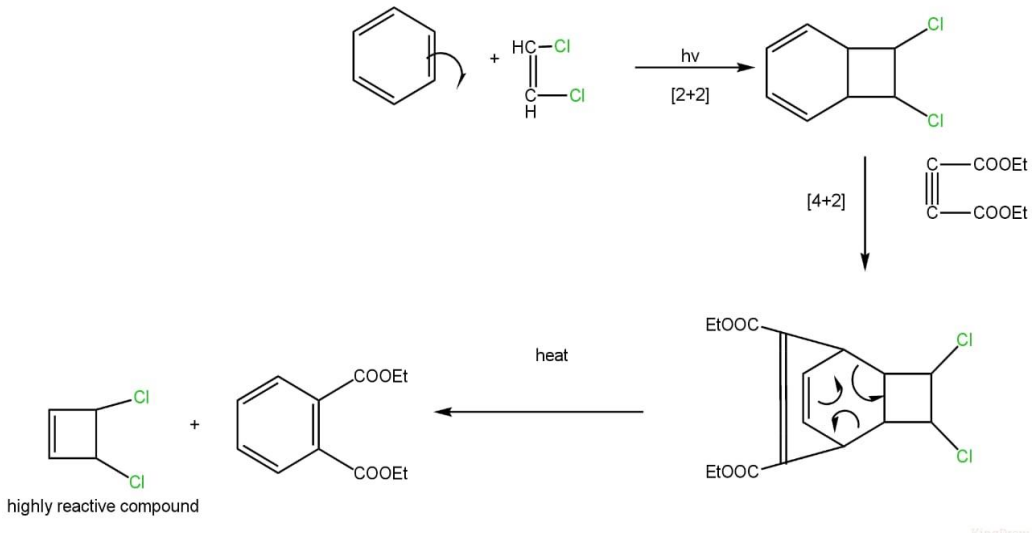
There are 2 types of addition reaction occurs in aromatic compound,

1. (2+2) cycloaddition on cycloreversion.
2. (4+2) cycloaddition.

(-) sign in both indicates cycloreversion reaction. (4+6) cyclo reversion reaction is most common and also known as retro diles alder reaction.



By retro-Diles alder reaction some highly reactive compounds can be formed which are difficult to prepare by other, methods and are used as a reagent for the preparation of various other compounds.



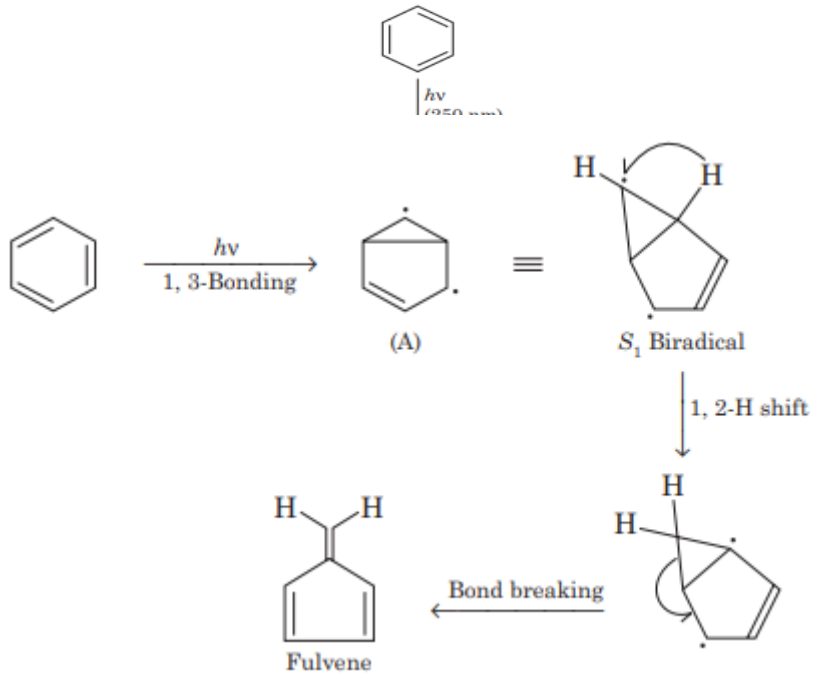
THE PHOTOCHEMISTRY OF AROMATIC COMPOUNDS

The photochemistry of aromatic compounds involves various reactions that occur when these compounds absorb light and become excited.

Photochemical Reactions of Aromatic Compounds

1. **Photoisomerization**: This involves the structural rearrangement of an aromatic comp ound upon light absorption. For example, benzene can isomerize to benzvalene u nder UV light.
2. **Photocycloaddition**: Aromatic compounds can undergo cycloaddition reactions with alkenes or other unsaturated compounds. This includes [2+2] and [4+2] cycloaddition s, leading to the formation of various adducts.
3. **Photodimerization**: This reaction involves the formation of dimers from two identical aromatic molecules upon exposure to light.
4. **Photooxidation and Photoreduction**: Aromatic compounds can undergo oxidation or reduction reactions when excited by light.
5. **Photorearrangement**: This includes rearrangement reactions such as the photo-Fries rearrangement, where an aryl ester is converted to a hydroxyaryl ketone
6. **Photoinduced Electron Transfer**: Aromatic compounds can participate in electron transfer reactions, leading to the formation of radical ions and other intermediate

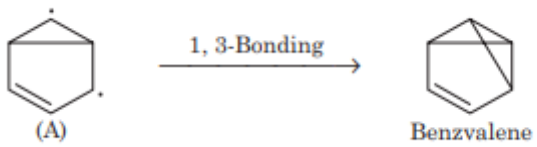
Benzene and substituted benzene undergoes valence isomerisation by irradiation. Selective excitation into S1 gives preferentially meta and ortho product while excitation into S2 gives para bonded products by valence isomerisation. These processes are described by biradical intermediate for case of visualisation



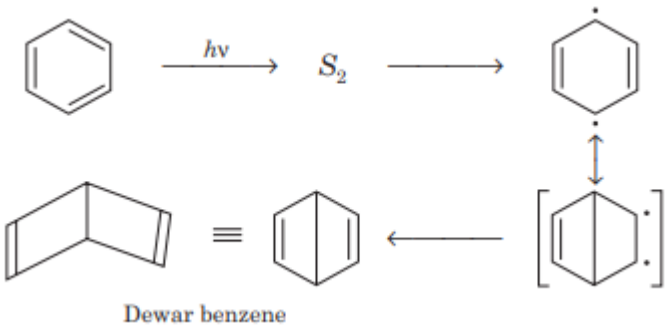
Irradiation of liquid benzene under nitrogen at 254 nm causes excitation to S1 state and the products, benzvalene and fulvene are formed via 1, 3-biradical

The formation of fulvene can now be considered to arise by reaction of the biradical (A) by a 1, 2-hydrogen migration and bond breaking

Formation of benzvalene can take place as follows:

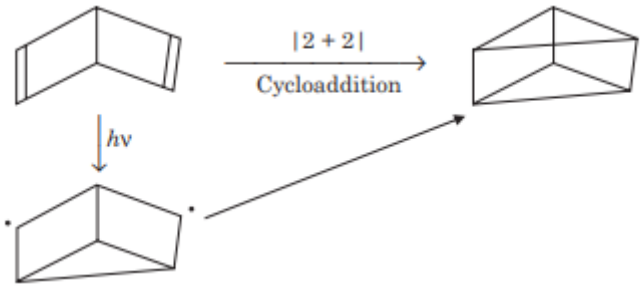


Dewar benzene is formed via S2 state upon short wavelength irradiation (205 nm).

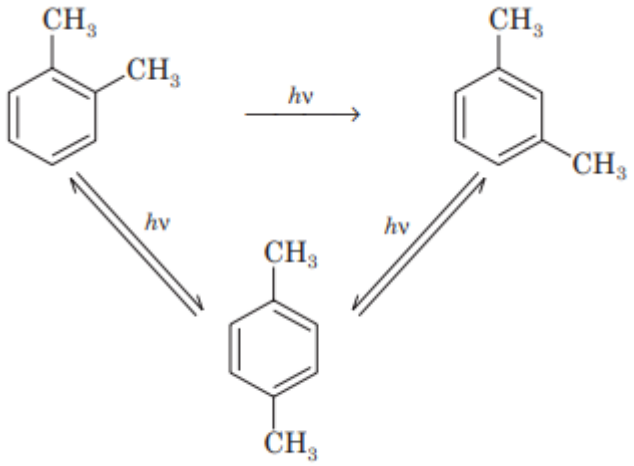


Dewar benzene

It has been confirmed that Dewar benzene is converted into prismane either by concerted path or by formation of a biradical.



All these strained intermediates are thermally labile and ultimately isomerises into benzenoid compounds. Monocyclic aromatic compounds undergo remarkable photochemical rearrangements. For example, o-xylene on irradiation gives mixture of o, m and p-xylenes.



Conversion of o-xylene into m-xylene and m-xylene into p-xylene is due to 1, 2-alkyl group shift. Similarly conversion of o-xylene into p-xylene and vice-versa is due to the 1, 3-alkyl

group shift. 1, 2-Alkyl group shift takes place by benzvalene as well as prismane intermediates whereas 1, 3-alkyl group shift takes place only by prismane intermediate.

Photochemical Rearrangements and Photostationary State

Photochemical rearrangements

Many photoreactions are known to interconvert isomeric compounds. The term "rearrangement" is more general than "isomerization" but for the reactions under photochemical rearrangement will not be concerned with a distinction between these terms.

Photochemical rearrangement is a chemical reaction that occurs when a molecule is exposed to light, resulting in a change in its chemical structure. This process involves the absorption of light energy by a molecule, leading to the breaking and forming of chemical bonds, resulting in a new molecular arrangement.

Light absorption: A molecule absorbs light energy (photons) from a specific wavelength range (e.g., ultraviolet, visible, or infrared).

Excitation: The absorbed light energy excites the molecule, promoting an electron to a higher energy state.

Reactive state: The excited molecule enters a reactive state, allowing it to undergo chemical transformations.

Bond breaking and forming: The excited molecule undergoes bond breaking and forming, leading to a new molecular arrangement.

Product formation: The resulting molecule is the product of the photochemical rearrangement reaction.

Types of photochemical rearrangements:

Photoisomerization: A molecule changes its shape or configuration (e.g., cis-trans isomerization).

Photocycloaddition: Two or more molecules combine to form a new ring structure.

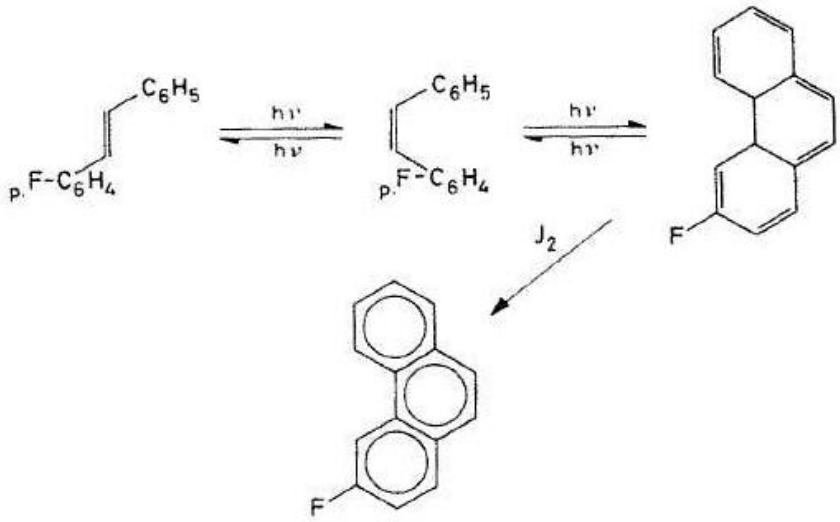
Photoelimination: A molecule loses a functional group or atom, resulting in a simpler structure.

Photorearrangement: A molecule undergoes a structural change, often involving ring opening or closure.

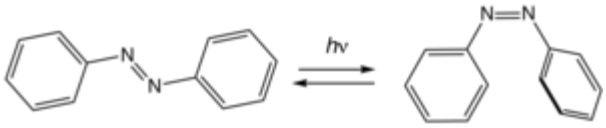
Photoisomerization

In chemistry, **photoisomerization** is a form of isomerization induced by photoexcitation.[2] Both reversible and irreversible photoisomerizations are known for photoswitchable compounds. The term "photoisomerization" usually, however, refers to a reversible process.

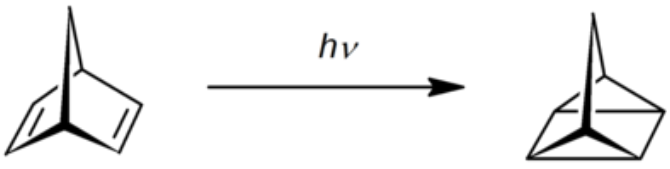
The photoisomerization of E-stibenes has been applied in the preparation of phenanthrenes, as Z-stilbenes undergoes electrocyclic ring closure to dihydrophenanthrenes which in easily oxidized to phenanthrenes.



Photoisometization of Azobenzene



Azobenzenes, stilbenes, spiropyrans, are prominent classes of compounds subject to photoisomerism.



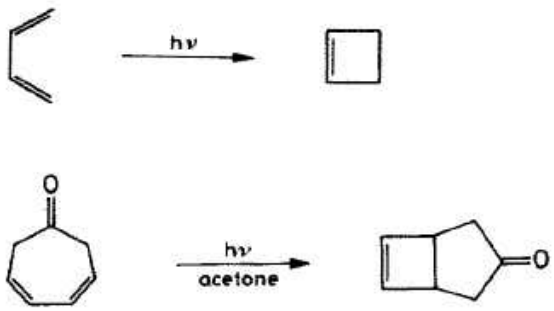
Photoisomerization of norbornadiene to quadricyclane. In the presence of a catalyst, norbornadiene converts to quadricyclane via ~300nm UV radiation . When converted back to norbornadiene, quadryicyclane's ring strain energy is liberated in the form of heat ($\Delta H = -89$ kJ/mol). This reaction has been proposed to store solar energy (photoswitchs).

Electrolytic Reactions of Dienes and Trienes

Electrolytic reactions were first described by Woodward and Hoffmann in their classic series of articles. One very interesting aspect of such reactions is that

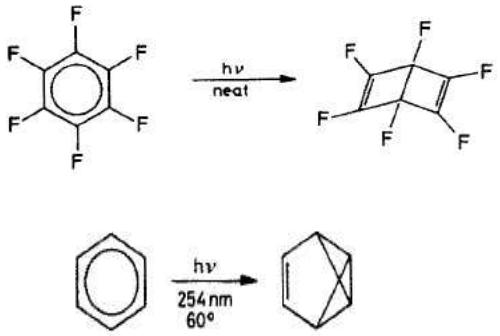
for a given conjugated polyene photochemical transformations leads to the steriochemical outcome than the thermal one.

The ring closure of 1,3 butadienes to cyclobutenes has been utilized for synthetic purposes as in the preparation of cyclobutene itself or a bicylocheptanone.



Photorearrangement of Arenes

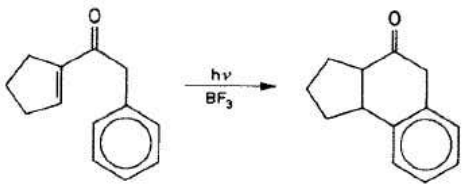
Benzene is commonly used as solvent un photochemical reactions; nevertheless one has to take into consideration that arenes do undergo photorearrangment. Benzene isomers as Dewar Benzene or Benzavalene have been prepared by photolysis of benzene.



Photorearrangement of α,β- and β,γ- unsaturated Ketones

Enones undergo a variety of photorearrangements. In contrast to **α,β-** Unsaturated ketones which react in many different ways, β,γ- unsaturated Ketones undergo the oxadi-pi-methane rearrangement in sensitized irradiation, in complete analogy the products formed are cyclopropyl ketones.

Cyclopentanyl ketones can undergo photoarylation when irradiated in the presence of a Lewis Acid Catalyst



Photostationary State

The photostationary state (PSS) refers to an equilibrium state reached between different chemical species under the influence of light irradiation. It is a crucial concept in photochemistry, where the rates of formation and destruction of specific compounds reach a balance due to competing reactions driven by light and thermal processes.

The **photostationary state** of a reversible photochemical reaction is the equilibrium chemical composition under a specific kind of electromagnetic irradiation (usually a single wavelength of visible or UV radiation).

Suppose a substance change ino a substance B by the absorption of light i.e., the reaction A→B is a photochemical reaction. The reverse can also occur either as a photochemical reaction or thermal reaction (dark reaction).

In either case, a stage may rate of the rate of forwards reaction may become equal to the rate of backward reaction. Now the absorption of light produces no further chemical change. The reaction then said to have attained a 'photochemical equilibrium' or a 'photostationary state'.

Two Types:

First Category: Only one reaction is light-sensitive

$$A + B \xrightleftharpoons[\text{dark}]{\text{light}} C + D$$

Exampes:

- Photochemical decompositiion of Nitrogen dioxide

$$2NO2 \xrightleftharpoons[\text{dark}]{\text{light}} 2NO + O2$$

- Dimerization of Anthracene

$$2C14H10 \xrightleftharpoons[\text{dark}]{\text{light}} C2H8H2O$$

Second Category: Both the reactions are light-sensitive

$$A + B \underset{\text{dark}}{\overset{\text{light}}{\Longleftrightarrow}} C + D$$

Examples:

i. Formation of Sulphur Trioxide

$$SO2 + O2 \underset{\text{dark}}{\overset{\text{light}}{\Longleftrightarrow}} 2SO3$$

ii, Isomerization of Maleic Acid into Fumaric Acid

$$\text{cis} - (CH - COOH)2 \underset{\text{dark}}{\overset{\text{light}}{\Longleftrightarrow}} \text{trans} - (CH - COOH)2$$

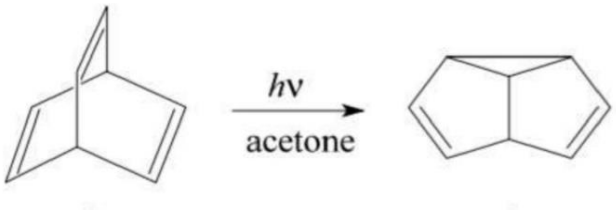
- **Equilibrium:** A Photostationary state (PSS) is an equilibrium state between chemical species.
- **Factors that influence PSS**: Factors that can affect a PSS include light intensity, reaction quantum yields, and the nature of the chemical system.
- **Applications:** PSS can be used in polymer networks to control the extent of a reaction and maintain mechanical properties. In atmospheric chemistry, deviations from the expected PSS can indicate missing oxidants.
- **Visualization:** An energy diagram can be used to visualize a PSS.
- **Leighton ratio:** The Leighton ratio can be used to describe a PSS

Di-π methane rearrangement

Di-π methane rearrangement is an intramolecular rearrangement reaction in 1,4-diene system. Which the diene is converted to vinyl cyclopropane. In this reaction, a three-membered

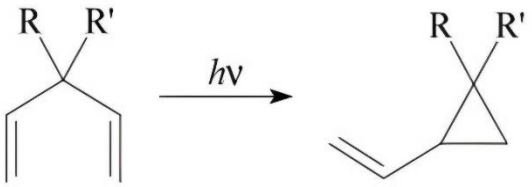
cyclopropane ring is formed by 1,2 migration. It is a photochemical reaction that requires π–π* electronic transition.

It has been reported in 1966 by Zimmerman and Grunewald with the isomerization of barrelene to semibullvalene. This rearrangement occurs in the presence of acetone as a photosensitizer.



Barrelene Semibullvalene

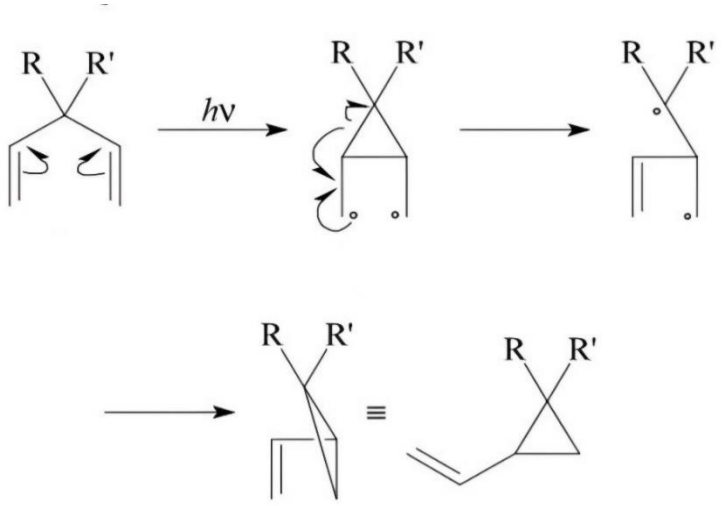
General Reaction



Mechanism

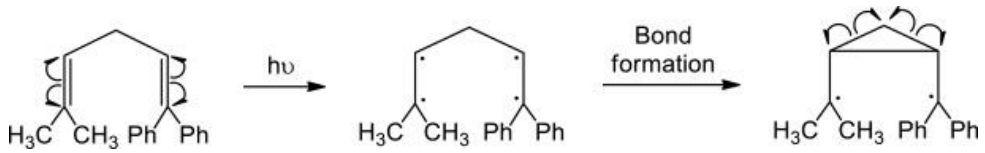
Di-π methane rearrangement reaction is a concerted reaction, that is, the formation of new bonds and the breaking of old bonds take place in a single step. First, in the presence of sunlight, the 1,4-diene is converted into radicals by the hemolytic cleavage of π-bonds, forming carbon-free radicals on C1, C2, C4, and C5.

Radicals on C2 and C4 then combine to form cyclopropane rings and diradicals at C1 and C5. Due to strains in the cyclopropane ring, it breaks down by homolytic fission, in the presence of sunlight, to form vinyl cyclopropane through intramolecular rearrangement.

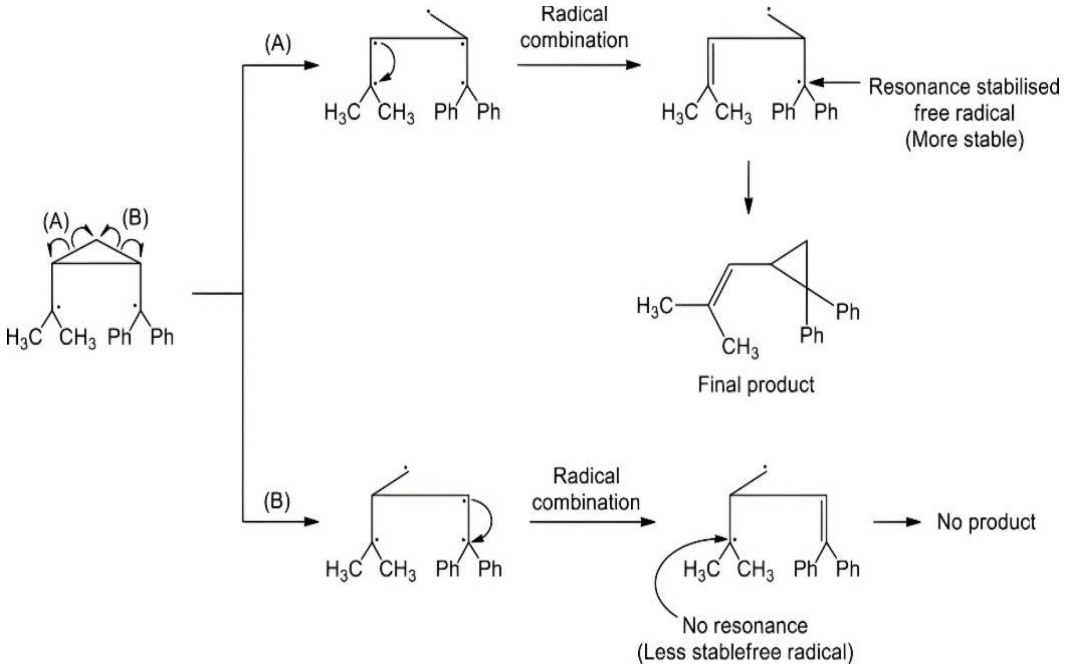


Selectivity in the breaking of cyclopropane ring

After the cyclopropane ring is formed, there is a possibility of it breaking on either side.



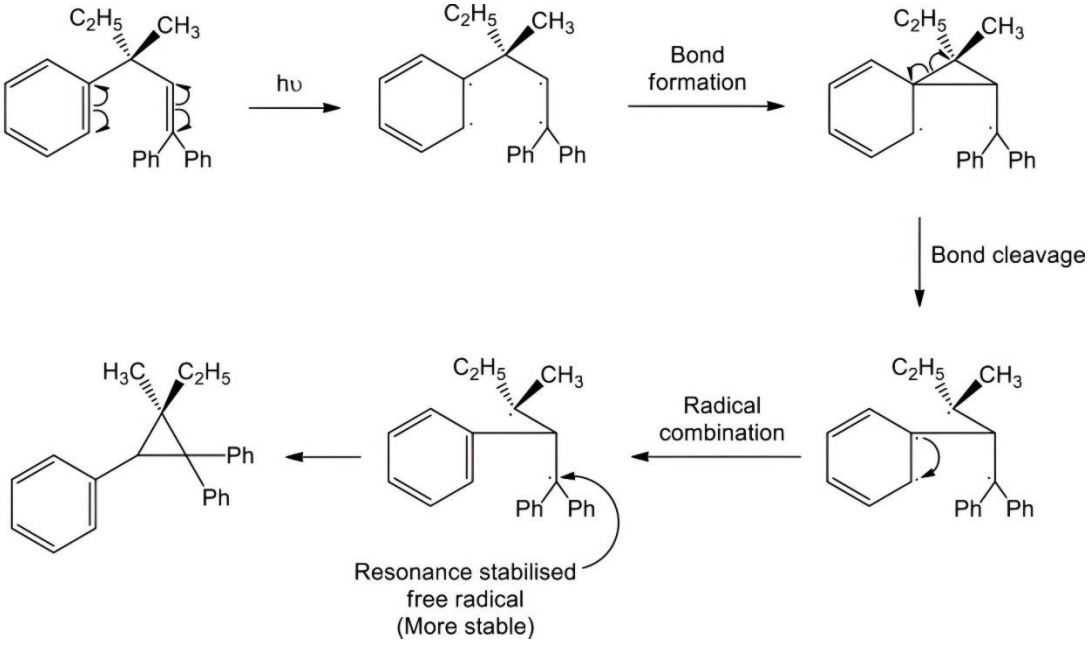
When a di-π methane rearrangement reaction occurs in 1,4-diene, in which different groups in C1 and C5 are attached, the bond is dissociated from the side from which the free radical formed after separation is more stable.



Stereo Chemistry of di-π methane rearrangement:

The Di-π methane rearrangement reaction is a stereospecific reaction in which the same type of product is formed. There is no change in the configuration of C1 and C5 in the product formed, while the configuration of C3 is inverted after rearrangement as follows:

(ii)



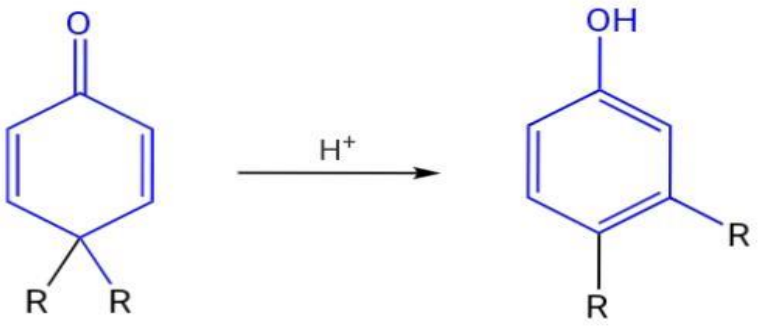
Reaction of conjugated cyclohexidienone to 3,4 diphenyl phenol:

4,4 dialkyl cyclohexidienone is treated with acid converted to phenol with migration one of the alkyl group to adjacent carbon this known as dienone – phenol rearrangement.

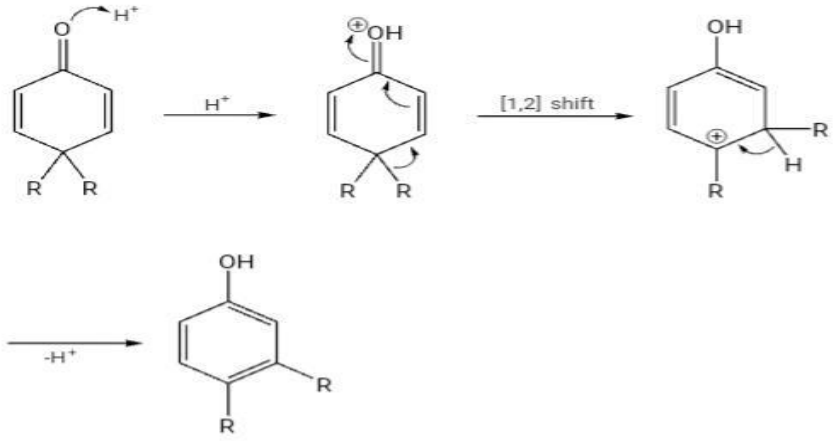
Dienone phenol rearrangement first reported in 1921 **karl von Auwers** and **karl Ziegler .**

Reaction:

In this rearrangement 4,4 disubstituted cyclohexidienone converted into to a stable 3,4 disubstituted phenol in the presence of acid.



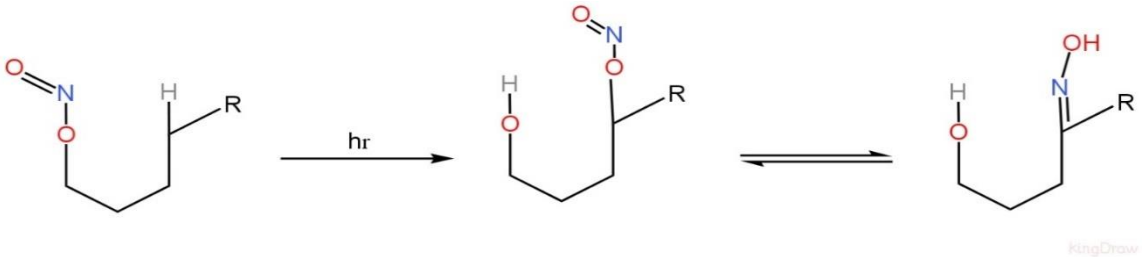
Mechanism:



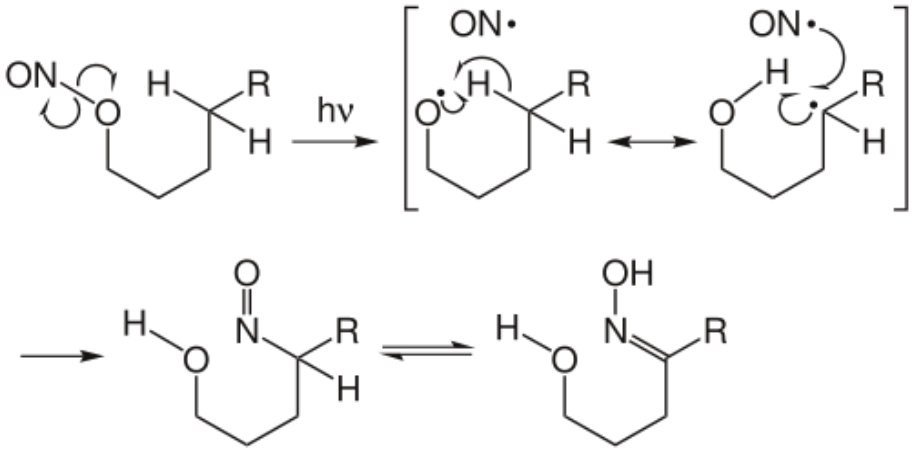
BARTON REACTION

REACTION:

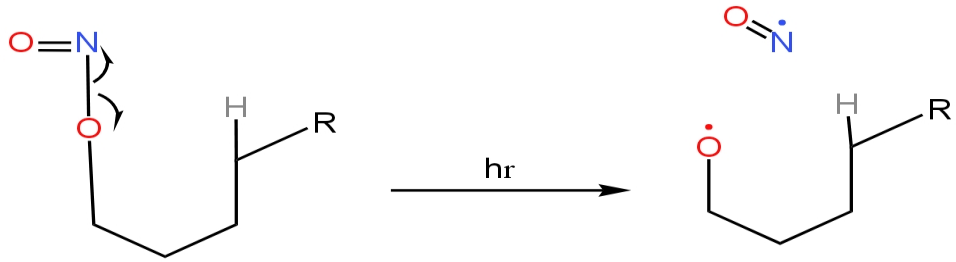
Barton reaction is a photochemical reaction in which Organic nitrates with delta-Hydrogen under photochemical condition gets converted into delta-nitrosyl alcohol which further tautomerize to corresponding oxime.



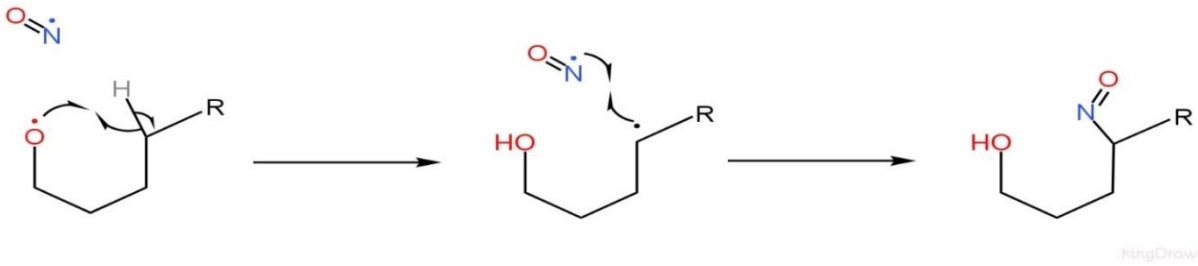
MECHANISM:



1. Homolytic cleavage of N-O bond to produce alkoxy radical and ·N=O radical



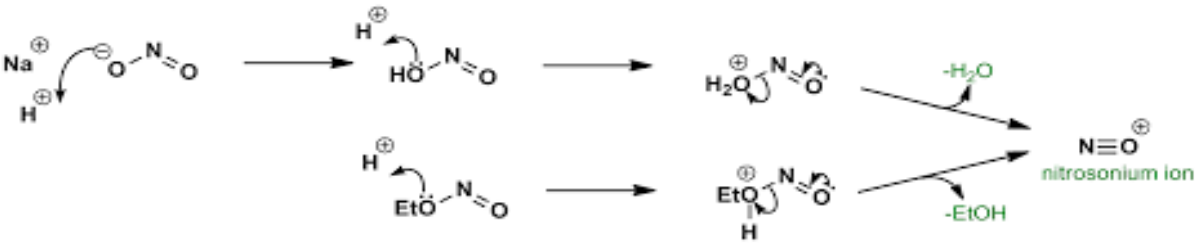
2. Alkoxy radical abstract delta-Hydrogen to give alcohol with radical at delta-carbon atom. Then this radical carbon react with ·N=O to form a covalent bond which results in the formation of nitrosyl alcohol.



3. This nitrosyl alcohol which is in nitroso form which tautomerize to more stable oxime tautomer.

PREPARATION OF ORGANIC NITRITES:

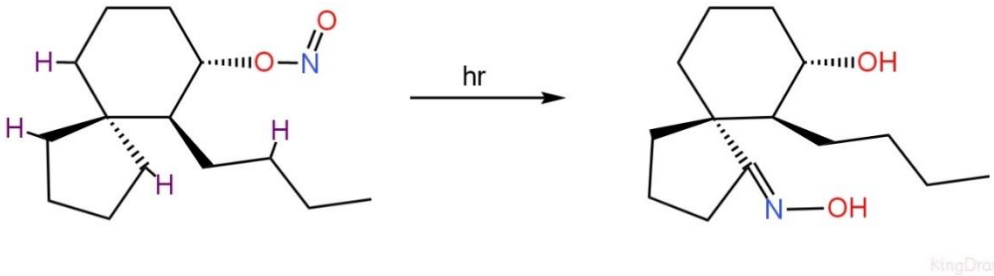
1. On reacting HCl and HNO_2 (nitrous acid) will gives NOCl (nitrosyl chloride) which can be prepared in insitu



2. This nitrosyl chloride on reacting with any organic alcohols to give organic nitrites.

EXAMPLES:

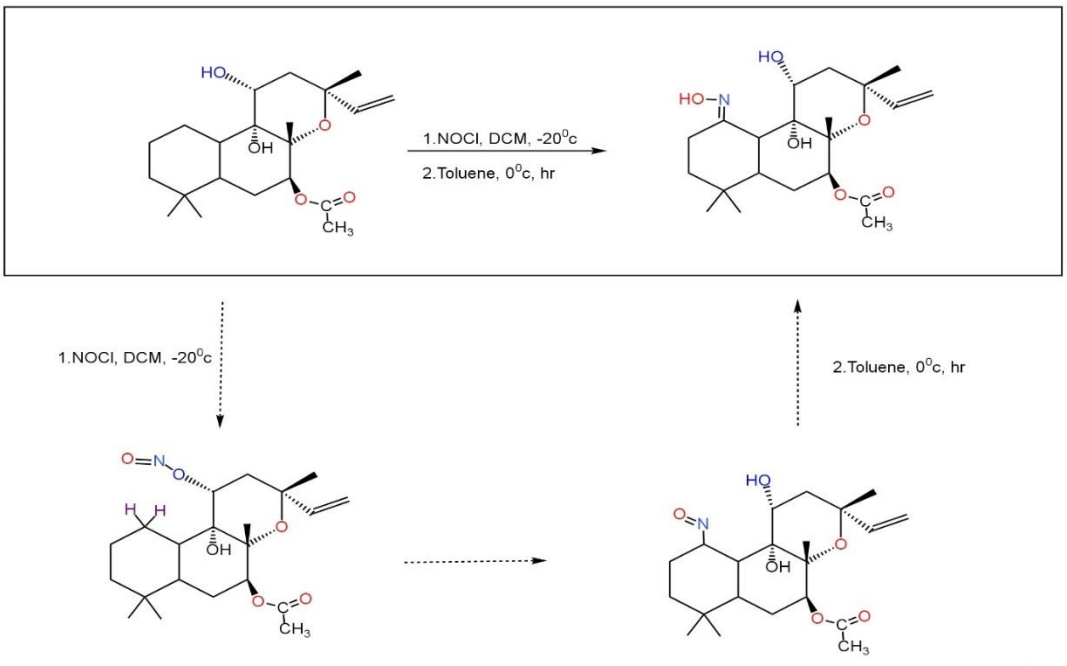
Reaction:1



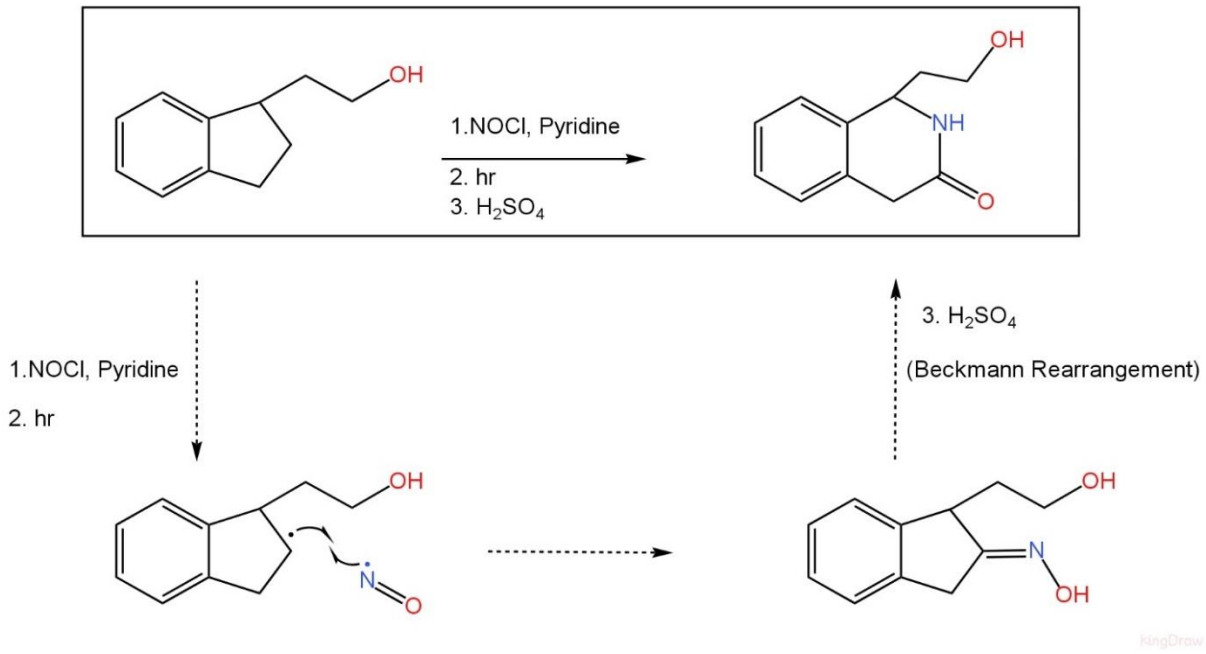
In barton reaction out of all possible delta-Hydrogen atoms, delta-Hydrogen which is closer in space to nitrosyl group will be abstracted by delta-carbon radical.

Reaction:2

Reaction:3



Reaction:4



Reaction:5