

## **COURSE FILE (Chem-22341)**

### ***Organic Special (MSc-III)***

#### **Contents**

1. Teaching Plan
2. Syllabus
3. Time Table
4. Lecture Notes
5. Class Test
6. Assignments
7. Presentations Topics for Students
8. Mid-Semester/Final Exam Question Paper



# *The Islamia University Bahawalpur*

## **Department of Chemistry**

M. Sc. (III Semester) CHEM-22341  
Chemistry-I  
Credit Hours: 04

Advance Organic

Instructors:	Prof. Dr. Shazia Anjum	Class Room:	Room No.
Class Day:	Monday-Thursday	Class Timing:	08:30-09:30 am

### **Chem. 21341      Advance Organic Chemistry – I**

#### **Reactive Intermediates:**

Structure, formation and reactions of Carbocations, Carbanions, Carbenes, Nitrenes and Benzyne.

#### **Photochemistry:**

Concept of photochemical and photophysical processes, Analysis of Pericyclic reactions; Electrocyclic and Cycloaddition reactions; Sigma-tropic rearrangements using Frontier Molecular Orbital Approach.

#### **TEACHING METHODOLOGY**

The class will be conducted in lecture and discussion environment. The instructor will deliver the lecture and the students will be encouraged to critically evaluate the information and participate by asking questions.

#### **GRADING AND EXAMS**

Regular class tests will be conducted at the end of each chapter to assess understanding of the subject matter. The assignments, quizzes, surprise tests will evaluate conceptual learning through multiple choice and problem based questions. Final assessment will be done in the annual examination conducted by the university.

#### **COURSE CONTENT**

Week 1	Introduction of Reactive Intermediates
Week 2	Structure, Formation and Reactions of Carbocations
Week 3	Structure, Formation and Reactions of Carbanions
Week 4	Structure, Formation and Reactions of Carbenes
Week 5	Structure, Formation and Reactions of Nitrenes
Week 6	Structure, Formation and Reactions of Benzyne
Week 7	Introduction to Concept of Photochemical and Photophysical Processes
Week 8	Review

Week 9	<b>Mid Term Examination</b>
Week 10	Introduction to Concept of Photochemical and Photophysical Processes
Week 11	Analysis of Pericyclic Reactions
Week 12	Analysis of Cycloaddition Reactions & Frontier Molecular Orbital Approach
Week 13	Analysis of Cycloaddition Reactions & Frontier Molecular Orbital Approach
Week 14	Analysis of Electrocyclic Reactions & Frontier Molecular Orbital Approach
Week 15	Analysis of Electrocyclic Reactions & Frontier Molecular Orbital Approach
Week 16	Sigma-tropic Rearrangements & Ene-Reactions
Week 17	Review
Week 18	<b>Final Term Examination</b>

### **APPOINTMENT WITH THE INSTRUTORS**

Prof. Dr. Shazia Anjum will be available in her office Monday to Friday during office hours.

### **BOOKS RECOMMENDED**

(Latest available editions of the following books are recommended)

1. Francis A. Carey, Richard J. Sundberg, **2007**, 5<sup>th</sup> Edition, Advanced Organic Chemistry Part A: Structure and Mechanism, Springer- Verlag Berlin Heidelberg .
2. Peter Sykes, A Guide Book to Organic Chemistry, **1985**, 6<sup>th</sup> Edition, John Wiley & Sons, New Jersey, USA.
3. Milton Orchin, Roger S. Maccomber, Allan E. Pinhas, R. Marshall Wilson, The Vocabulary and Concept of Organic Chemistry, **2005**, 2<sup>nd</sup> Edition, A John Wiley & Sons, Inc., Publication, New Jersey.
4. J. Cleyden N. Greeves. S. Warren and P. Wothers, "Organic Chemistry" Oxford University Press (**2001**).

### **Lecture Notes**

## Introduction of Reactive Intermediates

### OUTLINE

**Definition:** a reaction intermediate or an intermediate as a molecular entity (atom, ion, molecule...) with a lifetime appreciably longer than a molecular vibration that is formed (directly or indirectly) from the reactants and reacts further to give (either directly or indirectly) the products of a chemical reaction.

**Main carbon reactive intermediates:**

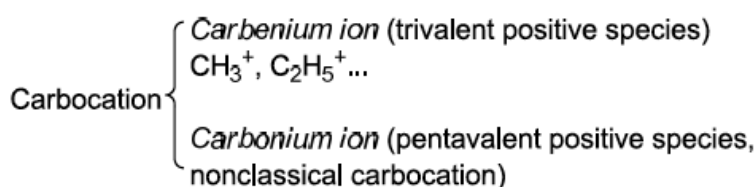
- Carbocations and their stabilized equivalents such as oxonium ions
- Carbanions and their stabilized equivalents such as enolates
- Free radicals
- Carbenes

### Common features

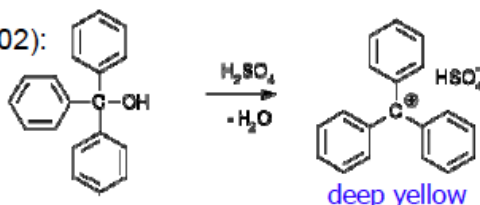
- ◆ Low concentration
- ◆ Do not obey the Lewis octet rule with the exception of carbanions, hence the **high reactivity**
- ◆ Often generated on chemical decomposition
- ◆ It is often possible to prove the existence of this species by spectroscopic means
- ◆ **Cage effects** have to be taken into account
- ◆ Often stabilisation by conjugation or resonance
- ◆ Often difficult to distinguish from a transition state
- ◆ Prove existence by means of chemical trapping

## Structure, Formation and Reactions of Carbocations

- A **carbocation** is an ion with a positively-charged carbon atom.



Norris and Kehrman (1902):



In 1962 **Olah** directly observed the *tert*-butyl carbocation by **NMR** as a stable species on dissolving *tert*-butyl fluoride in magic acid.

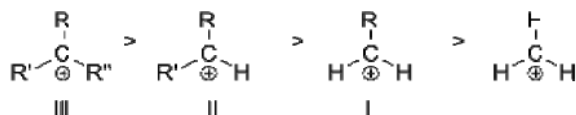


## I. STRUCTURE AND STABILITY

In solution, the carbocation may be free (this is more likely in polar solvents, in which it is solvated) or it may exist as an **ion pair**. Ion pairs are more likely in nonpolar solvents.

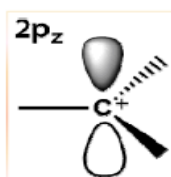
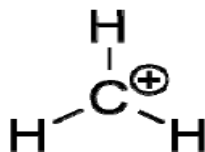
### A. Simple alkyl carbocations

Stability: tertiary > secondary > primary

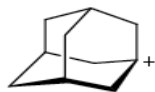


The most stable of all alkyl cations is the *tert*-butyl cation. Methane, ethane, and propane, treated with superacid, also yield *tert*-butyl cation as the main product.

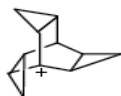
### CARBOCATION STRUCTURES: PLANAR $sp^2$ HYBRID



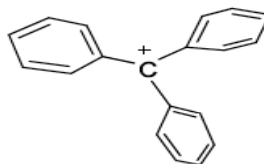
*tert*-butyl cation  
demonstrating planar geometry



adamantyl

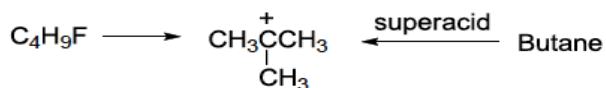
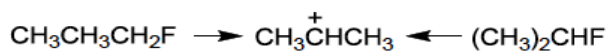
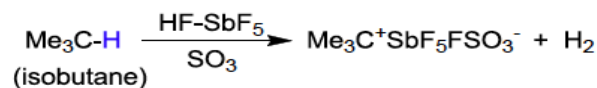
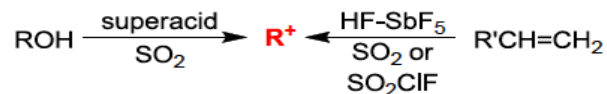


1-trishomobarrellyl

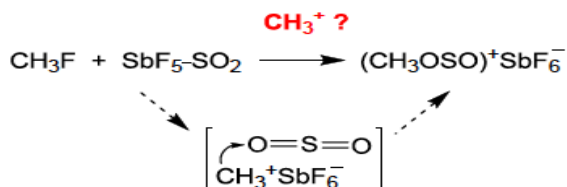


triphenylmethyl  
propeller-shaped

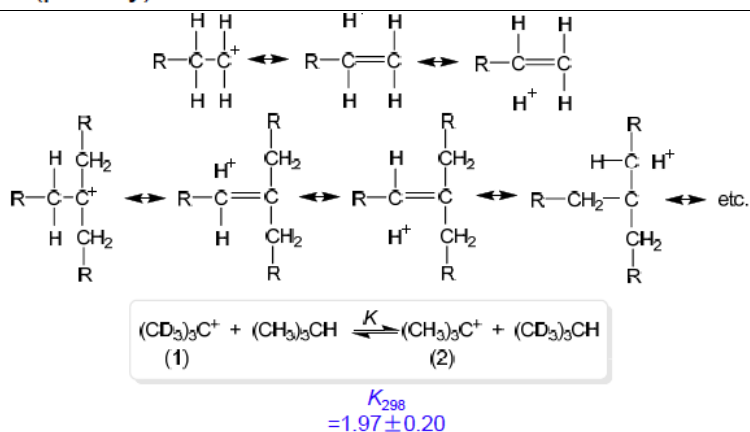
No matter how they are generated, study of the simple alkyl cations has provided dramatic evidence for the stability. Both propyl fluorides gave the isopropyl cation; all four butyl fluorides gave the *tert*-butyl cation. Butane, in superacid, gave only the *tert*-butyl cation.



To date, no primary cation has survived long enough for detection.



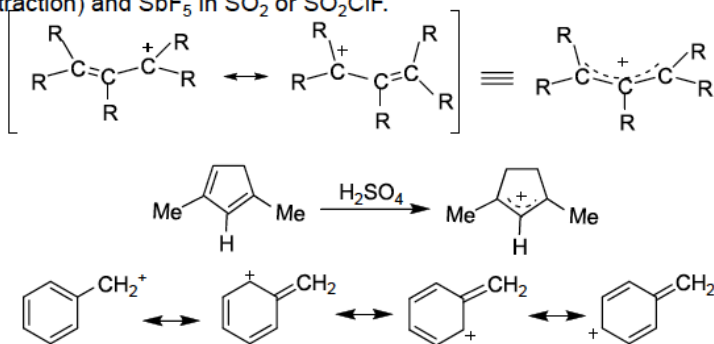
- ♦ **The field effect.** The electron-donating effect of alkyl groups increases the electron density at the charge-bearing carbon, reducing the net charge on the carbon, and in effect spreading the charge over the  $\alpha$  carbons.
- ♦ **Hyperconjugation.** Tertiary carbocations are more stable (and form more readily) than secondary carbocations; primary carbocations are highly unstable because, while ionized higher-order carbons are stabilized by **hyperconjugation**, unsubstituted (primary) carbons are not.

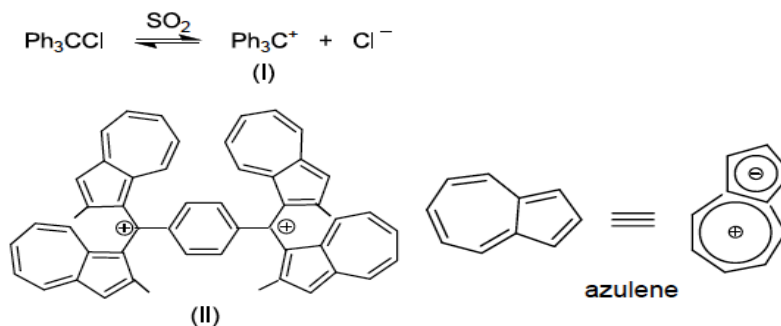


$K$  is 1.97, showing that **2** is more stable than **1**. This is a secondary isotopic effect; there is less hyperconjugation in **1** than **2**.

## B. STABLE ALLYLIC-TYPE CATIONS

Allyl cation and benzyl cation are more stable than most other carbocations. Molecules which can form allyl or benzyl carbocations are especially reactive. Stable allylic cations have been obtained by the reaction between alkyl halides, alcohols, or alkenes (by hydride extraction) and  $\text{SbF}_5$  in  $\text{SO}_2$  or  $\text{SO}_2\text{ClF}$ .



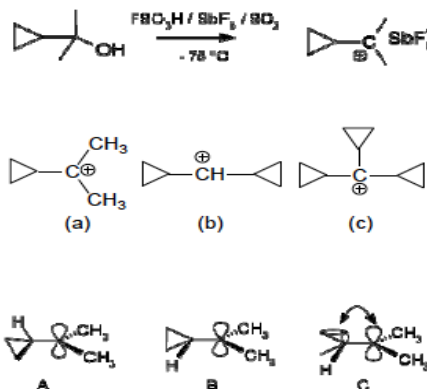


Both triphenylmethyl (I) and diphenylmethyl cations have been isolated as solid salts and, in fact,  $\text{Ph}_3\text{C}^+\text{BF}_4^-$  and related salts are available commercially. Positively charged benzylic carbon (II) is stabilized by two azulene rings.

### C. CYCLOPROPYLMETHYL CATIONS

Cyclopropylmethyl cations are even more stable than the benzyl type. Compound (c) has been prepared by solution of the corresponding alcohol in  $\text{H}_2\text{SO}_4$ . Compounds a, b, and similar ions have been prepared by solution of the alcohols in  $\text{FSO}_3\text{H}-\text{SO}_2-\text{SbF}_5$ .

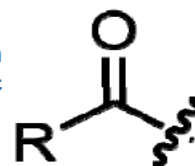
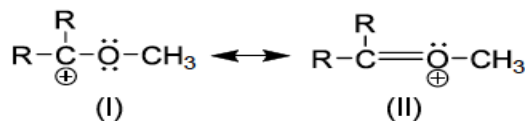
NMR spectrum of a dimethyl derivative (a), identical signals are found for the two methyl groups.



*J. Am. Chem. Soc.* 1970, 92, 3234–3235

### E. OTHER STRUCTURAL TYPES

Another structural feature that increases carbocation stability is the presence, adjacent to the cationic center, of a heteroatom bearing an unshared pair.



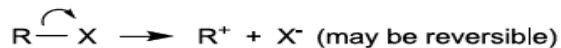
♦ Simple acyl cations ( $\text{RCO}^+$ ) have been prepared in solution and the gas state. The acetyl ( $\text{CH}_3\text{CO}^+$ ) is about as stable as the *tert*-butyl cation. The 2,4,6-trimethylbenzoyl cations are especially stable (for steric reasons) and are easily formed in 96%  $\text{H}_2\text{SO}_4$ .



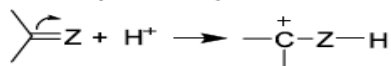
## II. THE GENERATION AND FATE OF CARBOCATIONS

### Two general ways to form carbocations:

i. A direct ionization:

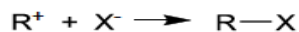


ii. Addition of a positive species to an unsaturated system:

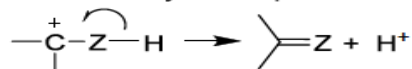


### The reaction of carbocations:

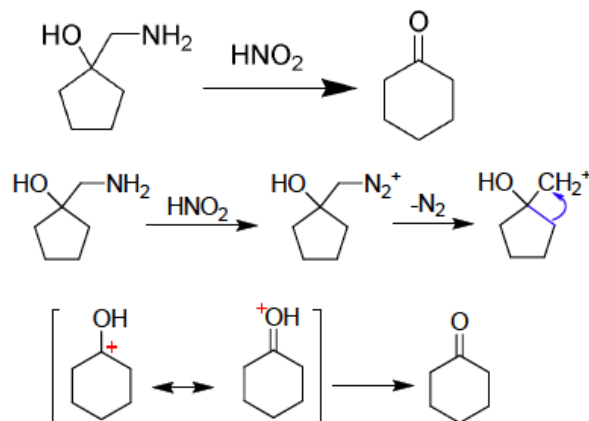
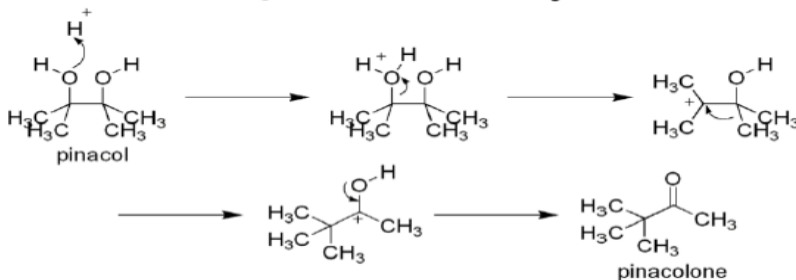
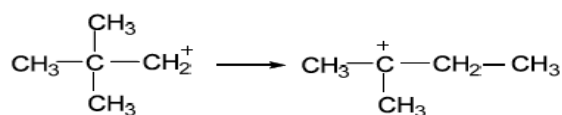
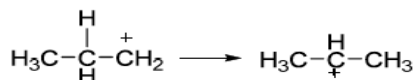
i. Combination with a species possessing an electron pair.



ii. The carbocation may lose a proton from the adjacent atom.

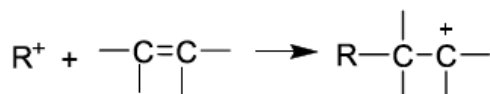


iii. Rearrangement



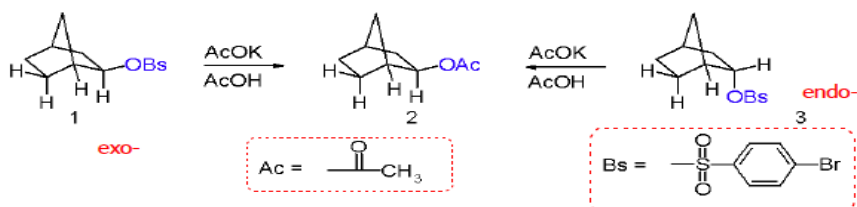
iv.

Addition



**Non-classical ions** are a special type of carbonium ions displaying delocalization of sigma bonds in **3-center-2-electron bonds** of bridged systems.

S. Winstein (1949): Acylation (solvolysis) of norbornyl brosylate

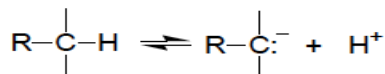


A key observation is that in this nucleophilic displacement both isomers give the same reaction product an exo-acetate 2. Also the reaction rate for the exo-reaction is 350 times the reaction rate for the endo reaction.

## Structure, Formation and Reactions of Carbanions

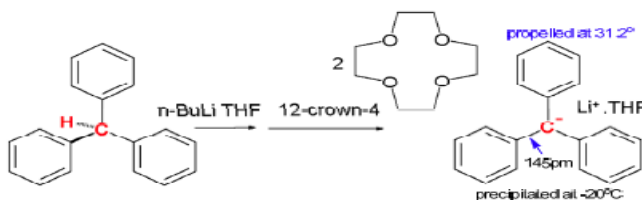
A **carbanion** is an anion in which carbon has an unshared pair of electrons and bears a negative charge usually with three substituents for a total of eight valence electrons.

Formally a carbanion is the **conjugate base** of a carbon acid.



Stable carbanions do however exist although in most cases they are reactive.

Olmstead (1984):



### I. STABILITY AND STRUCTURE

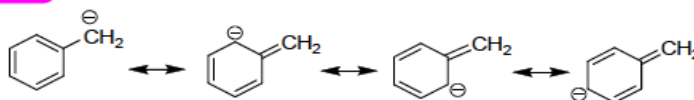
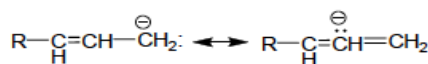
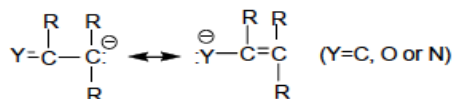
The stability of the carbanion is directly related to the strength of the conjugate acid. The weaker is the acid, the greater is the base strength and the lower is the stability of the carbanion.

**Factors determining the stability and reactivity of a carbanion:**

- **The inductive effect.** Electronegative atoms adjacent to the charge will stabilize the charge;
- **Hybridization** of the charge-bearing atom. The greater the s-character of the charge-bearing atom, the more stable the anion;
- **The extent of conjugation of the anion.** Resonance effects can stabilize the anion. This is especially true when the anion is stabilized as a result of aromaticity.

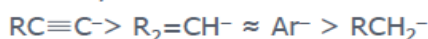
## RELATIVELY STABLE CARBANIONS WITH CERTAIN STRUCTURAL FEATURES

Conjugation of the unshared pair of electrons with an unsaturated bond

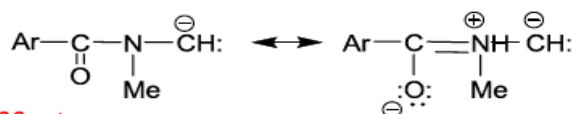
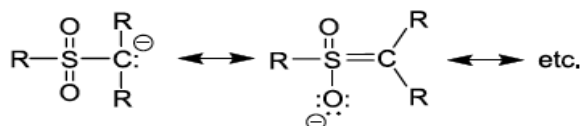


Carbanions increase in stability with an increase in the amount of *s* character at the carbanionic carbon.

Stability:



Stabilization by sulfur or phosphorus.

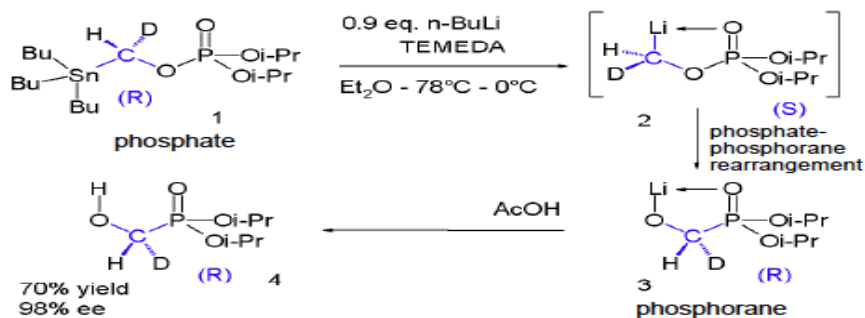


Field effect:

- Ylides are more stable than the corresponding simple carbanions.
- Carbanions are stabilized by a field effect if there is any hetero atom (O, N or S) connected to the carbanionic carbon, provided that the hetero atom bears a positive charge in at least one important canonical form.



Question:  
Whether or not carbanions can display chirality?



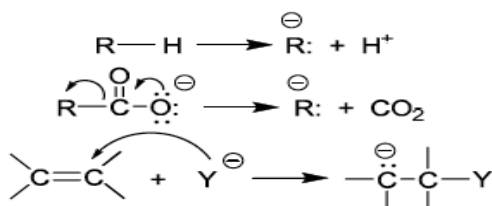
In the range of  $-78$  to  $0^\circ\text{C}$  the chirality is preserved in this reaction sequence.

*J. Am. Chem. Soc.*; **2007**; 129(4), 914-923

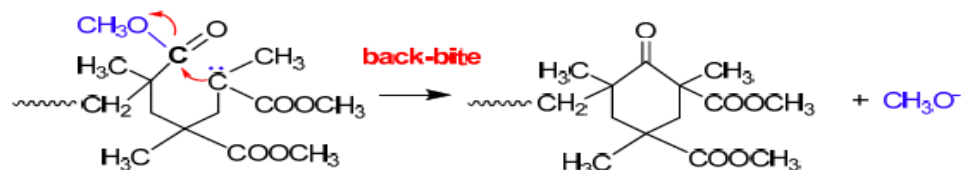
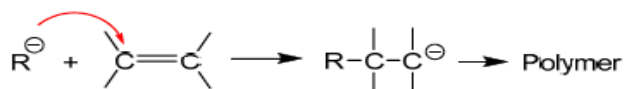
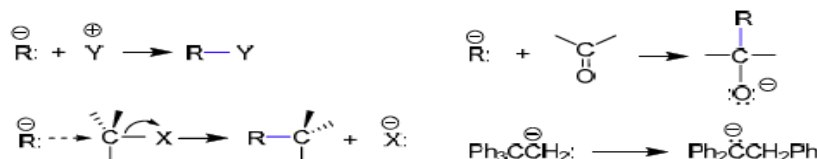
## II. THE GENERATION AND FATE OF CARBANIONS

a) A group attached to a carbon leaves without its electron pair.

b) A negative ion adds to a carbon-carbon double or triple bond.



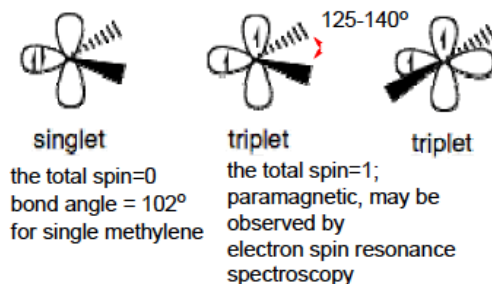
Reactions:



## Structure, Formation and Reactions of Carbenes

- A **carbene** is a highly reactive species containing a carbon atom with six valence electrons and having the general formula  $\text{RR}'\text{C}^{\cdot}$ , practically all having lifetimes considerably under 1 sec.

i. Structure and bonding

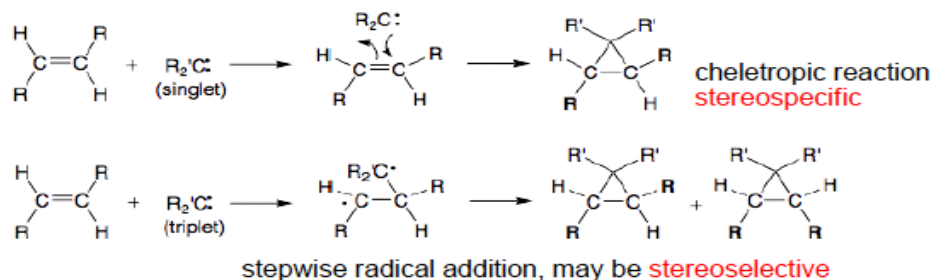


*Triplet carbenes are generally stable in the gaseous state, while singlet carbenes occur more often in aqueous media.*

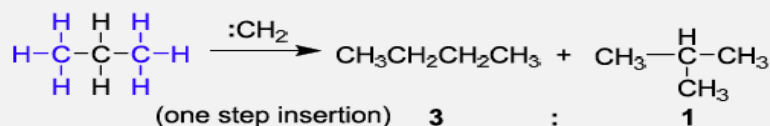
## II. REACTIVITY

- Singlet and triplet carbenes exhibit divergent reactivity. Singlet carbenes generally participate in **cheletropic reactions**. Singlet carbenes with unfilled *p*-orbital should be **electrophilic**. Triplet carbenes can be considered to be diradicals, and participate in stepwise radical additions.

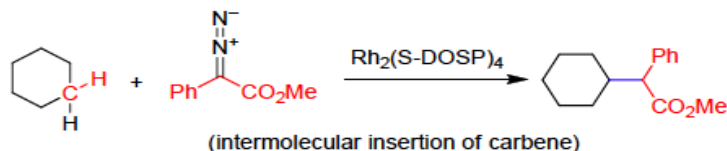
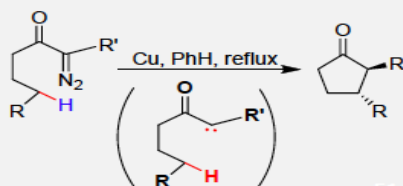
Addition to C=C:



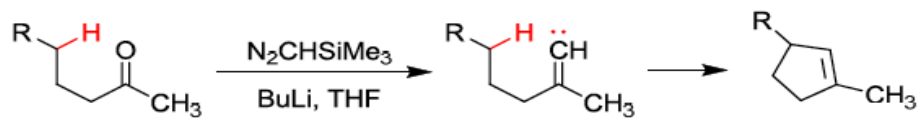
### INSERTION REACTION



- The order of preference: X-H (where X is not carbon) > C-H > C-C. Insertions may or may not occur in single step.
- When an intramolecular insertion is possible, no intermolecular insertions are seen. *In flexible structures, five-membered ring formation is preferred to six-membered ring formation.*



- **Alkylidene carbenes** are alluring in that they offer formation of cyclopentene moieties. To generate an alkylidene carbene a ketone can be exposed to **trimethylsilyl diazomethane**.

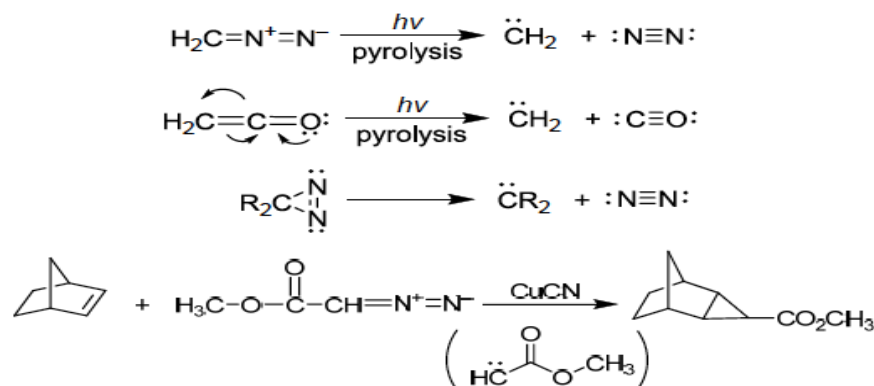


An alkylidene carbene

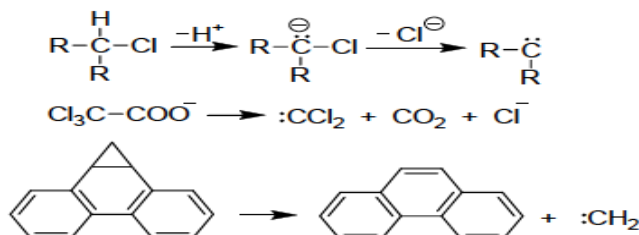


### III. GENERATION OF CARBENES

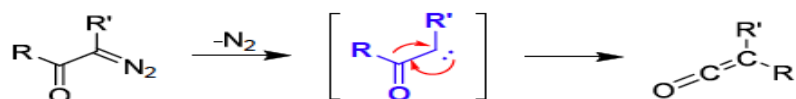
- Disintegration of diazoalkanes and their analogs, via photolytic, thermal, or transition metal (Rh, Cu)-catalyzed routes.



- Base-induced  $\alpha$ -elimination

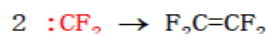


- Carbenes are intermediates in the *Wolff rearrangement*.

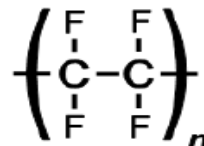


### IV. APPLICATIONS OF CARBENES

- A large scale application of carbenes is the industrial production of **tetrafluoroethylene**. Tetrafluoroethylene is generated via the intermediacy of difluorocarbene:



- Polytetrafluoroethylene (PTFE, mp 327°C the DuPont brand name **Teflon**) is a synthetic fluoropolymer of tetrafluoroethylene which finds numerous applications: used as a non-stick coating for pans and other cookware.



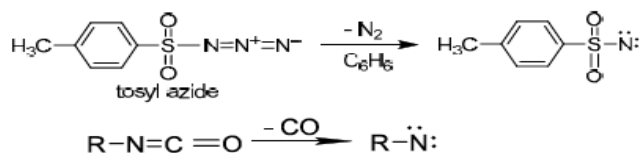
## Structure, Formation and Reactions of Nitrenes

- A **nitrene** ( $R-\dot{N}:$ ) is the nitrogen analogue of a carbene. The nitrogen atom has only 6 electrons available and is therefore considered an electrophile. A nitrene is a reactive intermediate and is involved in many chemical reactions.



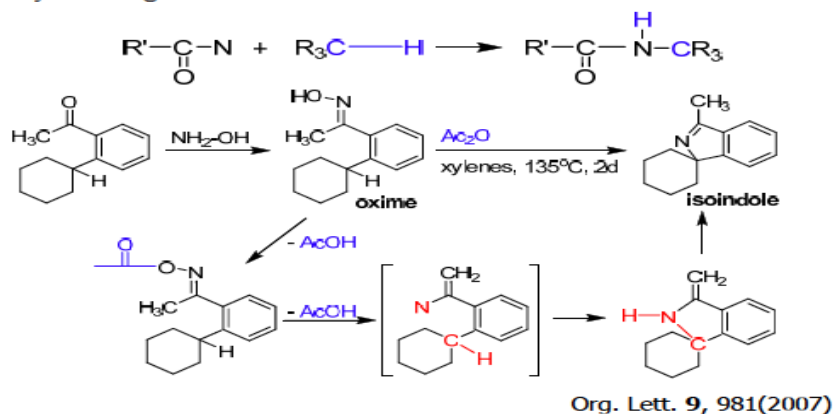
The structure of a typical nitrene group

- **Formation of nitrenes**
  - from **thermolysis** or photolysis of **azides**.
  - from **isocyanates**, with expulsion of CO.

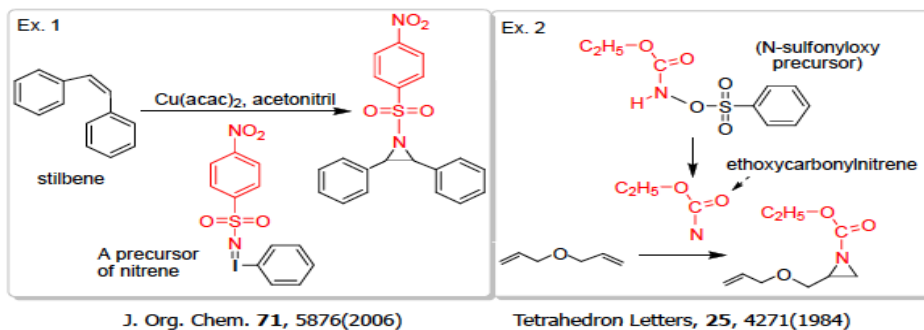
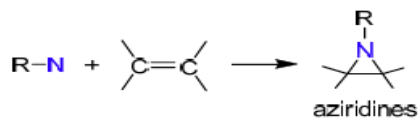


### REACTIONS OF NITRENE

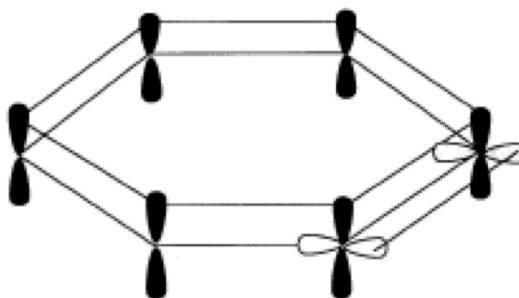
- **Nitrene C-H insertion.** A nitrene can easily insert into a C-H bond yielding an amine or amide.



- **Nitrene cycloaddition.** With alkenes, nitrenes react to aziridines.



# Structure, Formation and Reactions of Benzyne



Benzyne

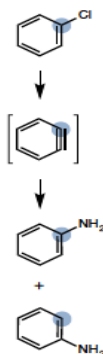
1954: Official Introduction of the Benzyne Concept

## REARRANGEMENT IN THE REACTION OF CHLORO-BENZENE-1-C<sup>14</sup> WITH POTASSIUM AMIDE<sup>1</sup>

Sir:

No satisfactory explanation has been published for the rearrangements which often occur in the amination of "non-activated" aryl halides with alkali-metal amides.<sup>2</sup> The pattern of the rearrangements shows a considerable disregard for the influences governing the usual aromatic substitutions and is well illustrated by the products obtained from the amination of the methoxy- and trifluoromethyl-halobenzenes. These facts as well as the orientation data for various substituents can be accommodated by an elimination-addition mechanism involving at least transitory existence of an electrically neutral "benzyne" intermediate (II).

J. D. Roberts *et al.* *J. Am. Chem. Soc.* **1953**, 75, 3290

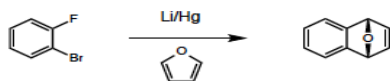


■ <sup>14</sup>C label shows a 1:1 mixture of products: reaction proceeds through symmetrical intermediate

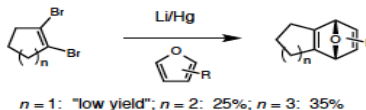
## Further Proof of Triple Bond-Containing Structure

over the next decade, evidence for "the benzyne" grows

■ 1955: the first benzyne Diels-Alder



■ 1960: aliphatic cycloalkynes postulated

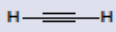


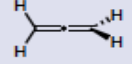


■ early reports: dimerization and trimerization products always present



### Further Proof of Triple Bond-Containing Structure

spectroscopic advances allow for more rigorous structural evaluation

				
$^{13}\text{C}$ ( $\delta$ )	70	95	182	75/214 (terminal/internal)
IR ( $\text{cm}^{-1}$ )	2100	2216	1846	1950

■  $^{13}\text{C}$  NMR and IR data imply significant resonance contributions of both triple-bond and cumulene-type structures:

consistent  
with  $^{13}\text{C}$  data

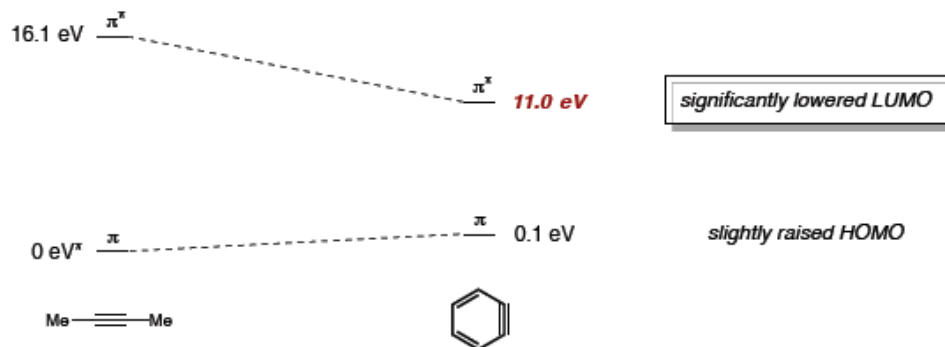


consistent  
with IR data

### So Why is Benzyne Electrophilic?

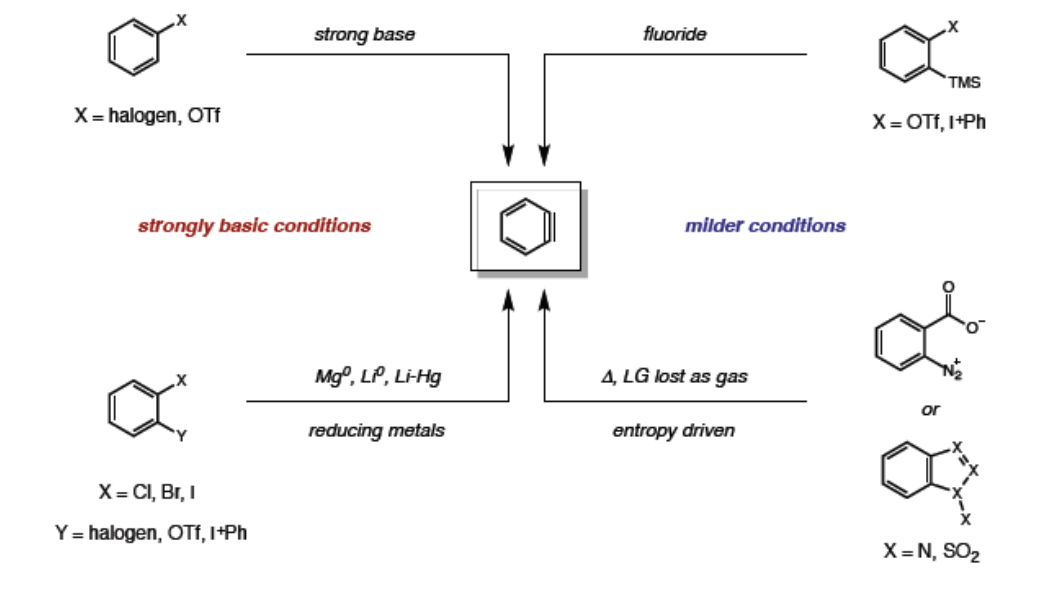
why is a highly strained triple bond inherently electrophilic?

■ Hoffman's application of extended Hückel theory sheds light



- significant deviation from preferred 180° bond angle results in a low-lying LUMO
- low LUMO explains extreme reactivity towards nucleophiles and dienes

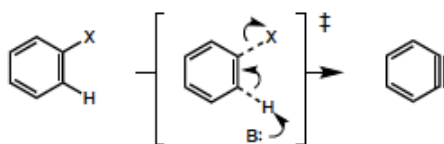
## Generation of Aryne Intermediates



## Mono- and o-Dihalobenzenes as Precursors

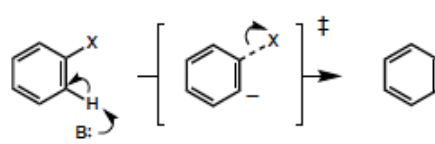
variable trends depending on nature of base and solvent or metal

■ protic solvents: concerted mechanism



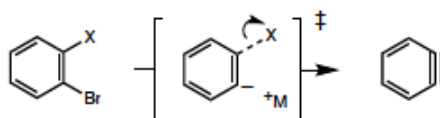
rate:  $Br > I > Cl > F$

■ aprotic solvents: stepwise mechanism



rate:  $F > Cl > Br > I$

■ dihalides: rate mainly affected by choice of metal



X = F, Cl, Br, I, OTf, I+Ph

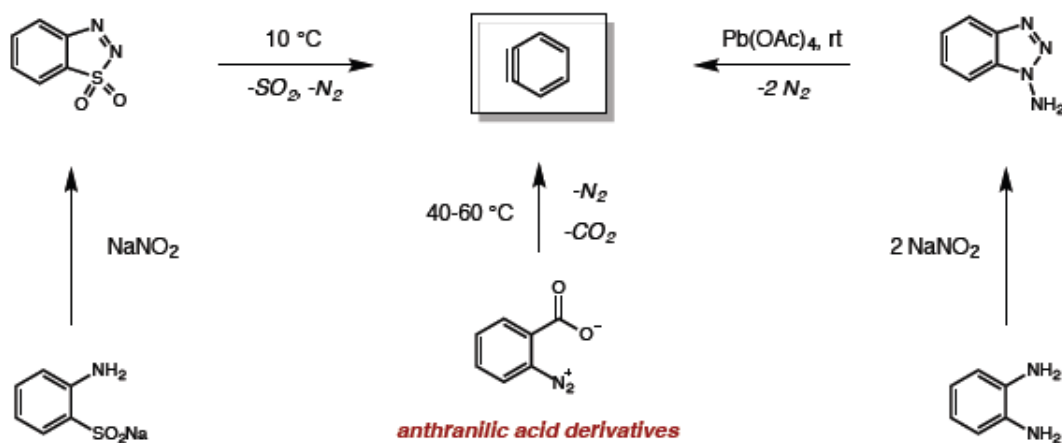
rate:  $Na > Mg > Li \gg Cu^+$

\*elimination not observed with o-chloro aryl copper intermediates!

## Diazotization of o-Disubstituted Anilines Provides Labile Benzyne Precursors

*mild thermal/oxidative cleavage provides access to benzyne derivatives*

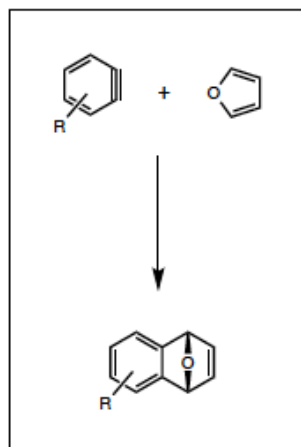
- loss of 2 gas molecules drives benzyne formation under relatively mild conditions



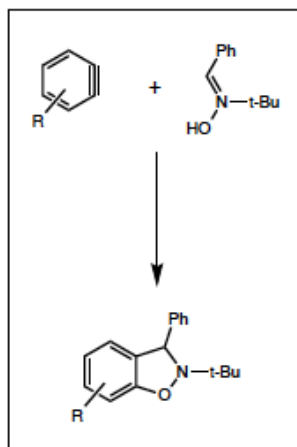
## Benzyne Reactivity: Cycloadditions

*extremely low LUMO provides high reactivity in a variety of cycloaddition reactions*

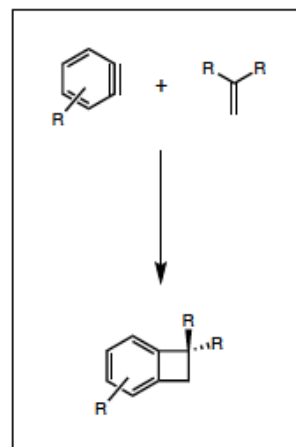
- [4+2] and Diels-Alder



- [3+2] cycloadditions



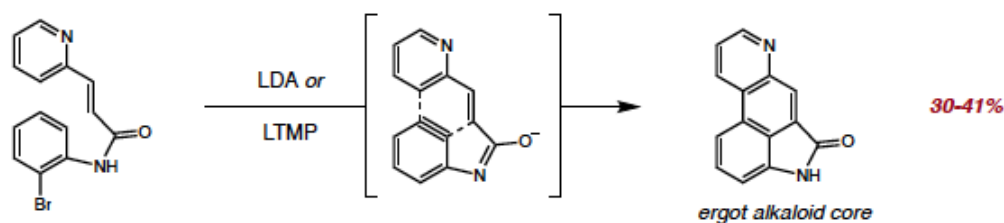
- [2+2] cycloadditions



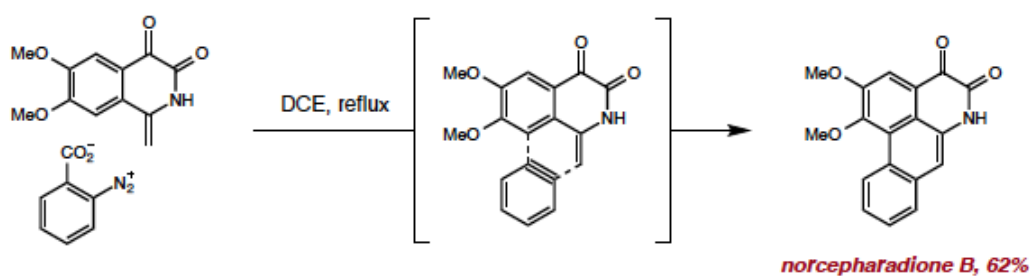
## Benzyne Diels-Alder and [4+2] Cycloadditions

literature is flush with intra- and intermolecular annulations

### ■ intramolecular example towards ergot alkaloids



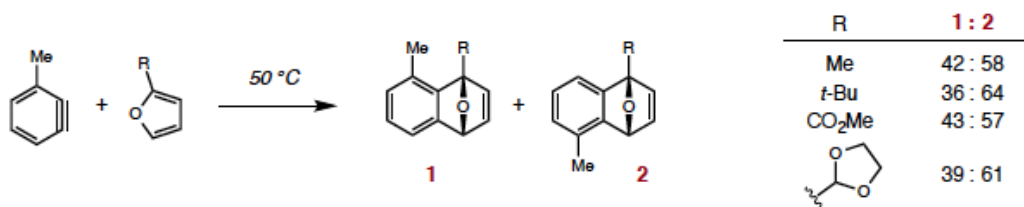
### ■ intermolecular example towards aporphinoids



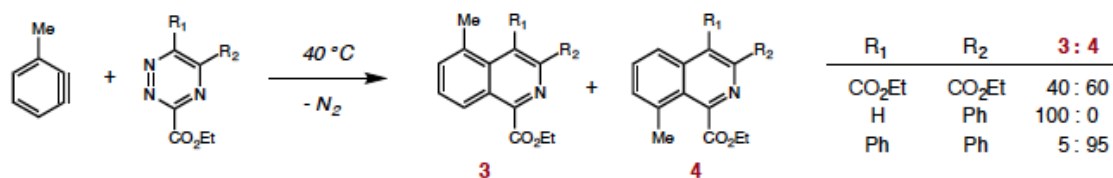
## Benzyne Diels-Alder and [4+2] Cycloadditions

literature is flush with intra- and intermolecular annulations

### ■ non-symmetrical dienes often display little selectivity:



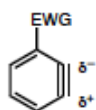
### ■ less reactive dienes appear to be under steric control



## Can Selectivity be Induced with Benzyne Intermediates?

*biasing of the aryne intermediate can powerfully affect selectivity*

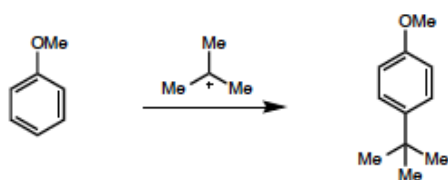
- introduction of polar group at 3-position dramatically influences selectivity



- dipoles arranged to be stabilized by electron withdrawing group

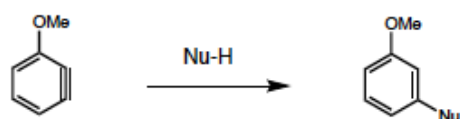
- due to orthogonal nature, typical donating groups are withdrawing!

- Friedel-Crafts chemistry:



*OMe is activating as EDG*

- benzyne chemistry:

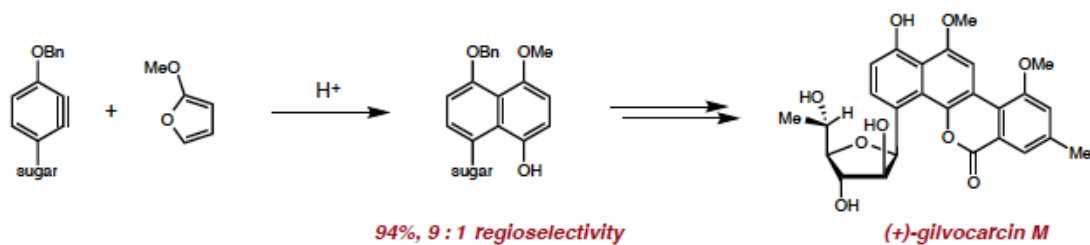


*OMe is activating as EWG*

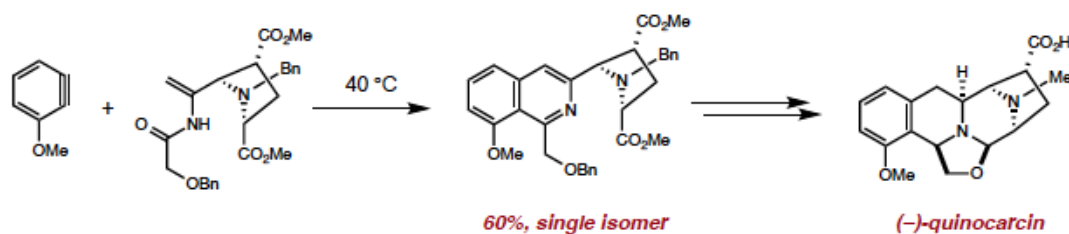
## Applications in Total Synthesis

*high selectivity achieved with 3-methoxy arynes*

- Suzuki *et al.*, 1992:



- Stoltz *et al.*, 2008:

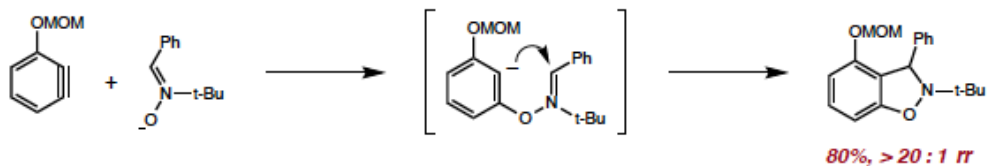




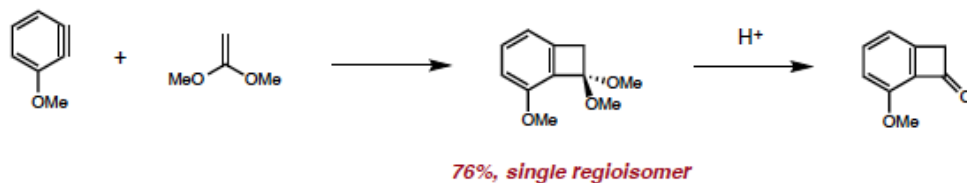
## [2+2] and [3+2] Cycloadditions

high selectivity achieved with 3-methoxy arynes

- stepwise [3+2] cycloadditions proceed with same regiochemistry:



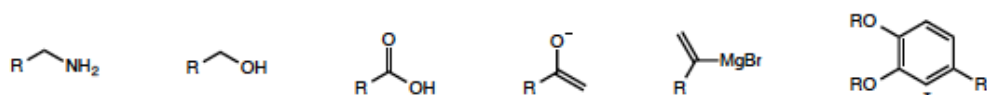
- [2+2] cycloadditions with enol ethers provide convenient access to benzocyclobutenones



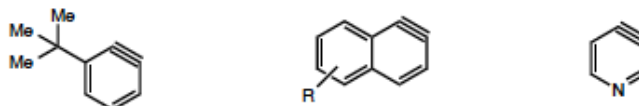
## Nucleophilic Attack on Arynes

the most common reactivity of arynes

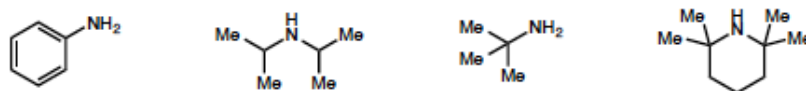
- nearly any nucleophile will react with benzyne:



- nature of the aryne has little effect on reactivity:



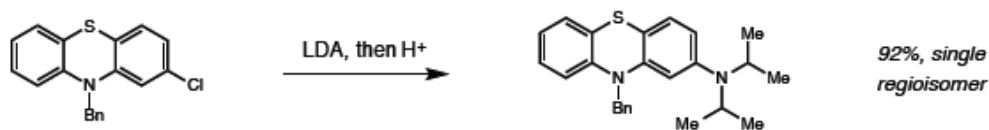
- even sterically-hindered and electronically-deactivated nucleophiles are highly reactive:



## Nucleophilic Attack on Arynes: Selectivity Trends

high selectivity sometimes observed in bicyclic systems

- again, adjacent EWG will dictate selectivity:



- theory provides a predictive model based on bond angle distortion:

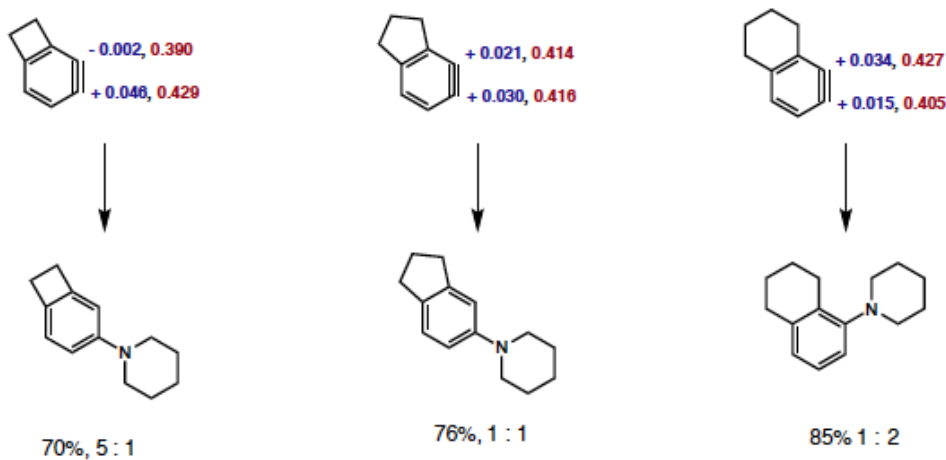


*smaller bond angle has more s-character ( $\delta^-$ ); larger bond angle has more p character ( $\delta^+$ )*

## Effect of Ring Strain on Regioselectivity

- calculation of charge and LUMO coefficients matches predictions of bond angle strain with selectivity trends

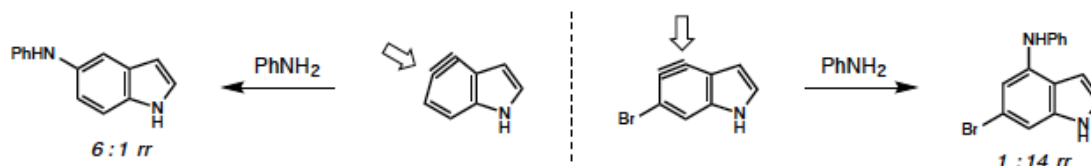
*DFT calculated charge, LUMO coefficient*



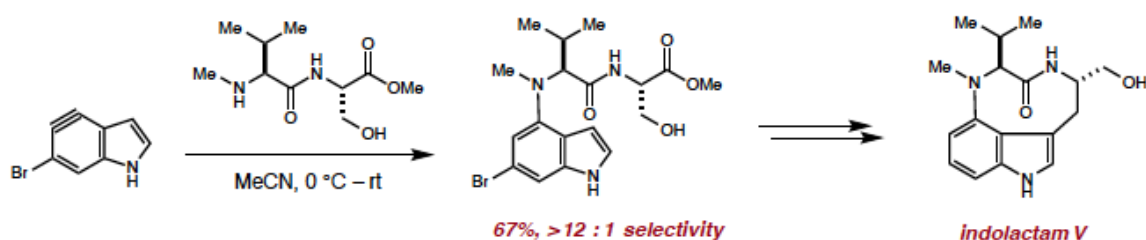
## Nucleophilic Attack on Arynes: Selectivity Trends

can inherent selectivity be reversed?

- introduction of bromide to indole strongly influences site of nucleophilic attack

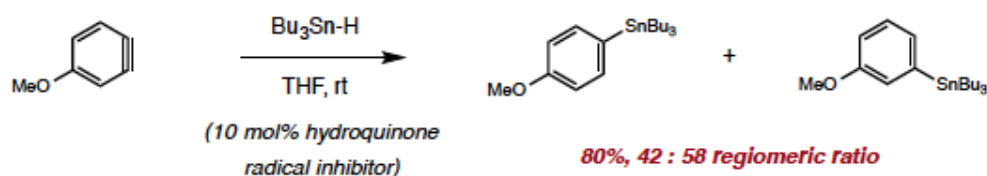


- application to the total synthesis of indolactam V

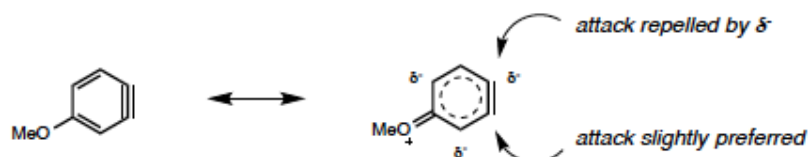


## More Distal Polar Group Results in Greatly Diminished Selectivity

- recent example: 4-methoxybenzyne provides products in only a 1.5 : 1 ratio

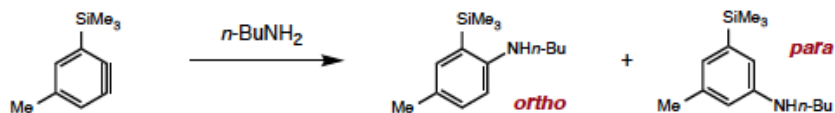


- possible cause: electrostatic repulsion of electron rich  $\pi$ -system

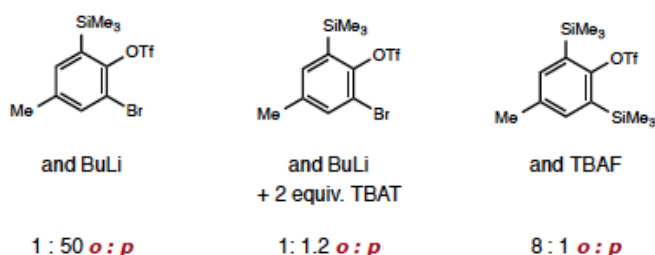


## Reversing Selectivity: Formation of ate-Complex

- introduction of silyl group produces *meta*-product, likely due to non-bonding interactions



- method of generation and presence of fluoride strongly influences selectivity:



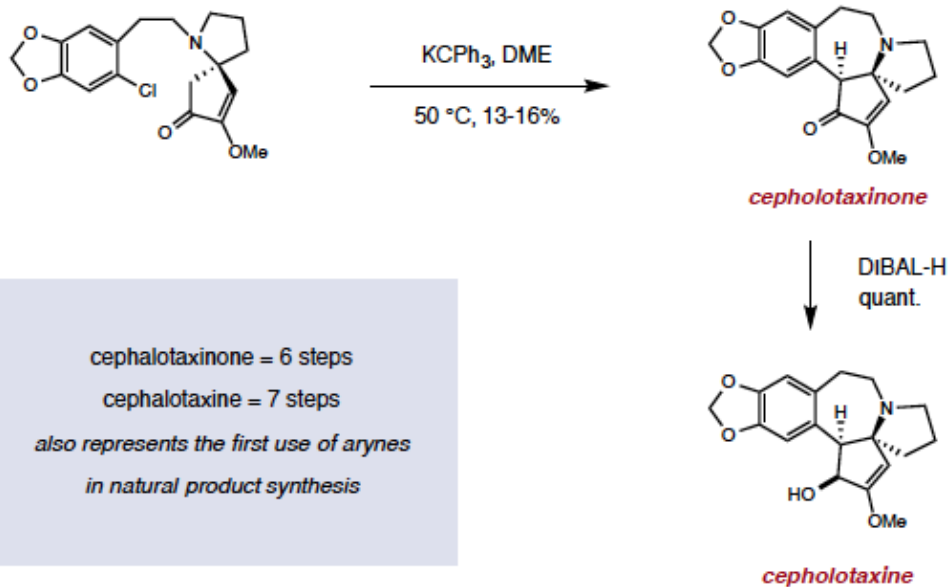
- DFT predicts significantly increased charges in ate-complex



## Nucleophilic Attack on Arynes by Enolates

notable appearances in natural product synthesis

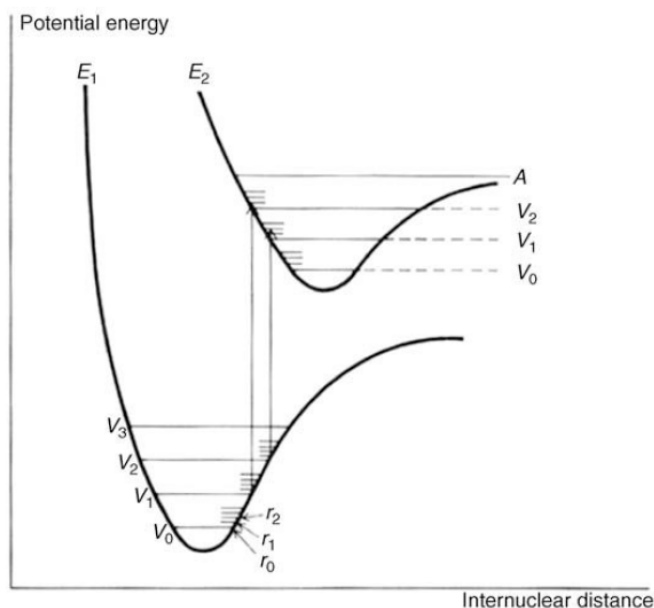
- first report: Semmelhack, 1972



## Introduction to Concept of Photochemical and Photophysical Processes

Most reactions carried out in organic chemistry laboratories take place between molecules, all of which are in their ground electronic states. In a photochemical reaction, however, a reacting molecule has been previously promoted to an electronically excited state by absorption of light. A molecule in an excited state must lose its extra energy in some manner; it cannot remain in the excited state for long. The subject of electronic spectra is closely related to photochemistry. A chemical reaction is not the only possible means of relinquishing the extra energy in a photochemical process. Electrons can move from the ground-state energy level of a molecule to a higher level (i.e., an unoccupied orbital of higher energy) if outside energy is supplied. In a photochemical process, this energy is in the form of light. Light of any wavelength has an energy value associated with it given by  $E=h\nu$ , where  $\nu$  is the frequency of the light ( $\nu$ = velocity of light  $c$  divided by the wavelength  $\lambda$ ), and  $h$  is Planck's constant. Since the energy levels of a molecule are quantized, the amount of energy required to raise an electron in a given molecule from one level to a higher one is a fixed quantity. Only light with exactly the frequency corresponding to this amount of energy will cause the electron to move to the higher level. If light of another frequency (too high or too low) is sent through a sample, it will pass out without a loss in intensity, since the molecules will not absorb it. However, if light of the correct frequency is passed into a sample, molecules will use that energy for electron promotion, and the light that leaves the sample will be diminished in intensity or altogether gone. A **spectrophotometer** is an instrument that allows light of a given frequency to pass through a sample and that detects (by means of a phototube) the amount of light that has been transmitted, that is, not absorbed. A spectrophotometer compares the intensity of the transmitted light with that of the incident light. Automatic instruments gradually and continuously change the frequency, and an automatic recorder plots a graph of absorption versus frequency or wavelength. When an electron moves from one electronic level to another, it moves from a given vibrational and rotational level within that electronic level to some vibrational and rotational level at the next electronic level. A given sample contains a large number of molecules, and even if all of them are in the ground electronic state, they are still distributed among the vibrational

and rotational states (though the ground vibrational state,  $V_0$ , is most heavily populated). This means that not just one wavelength of light will be absorbed, but a number of them close together, with the most probable transition causing the most intense peak. But in molecules containing more than a few atoms, there are so many possible transitions, and these are so close together that what is observed is a relatively broad band.



1. *Spin-Forbidden Transitions.* If the spin of an electron changes, transitions are not allowed, because a change from one spin to the opposite involves a change in angular momentum. Such a change would violate the law of conservation of angular momentum. Therefore, singlet–triplet and triplet–singlet transitions are forbidden, whereas singlet–singlet and triplet–triplet transitions are allowed.
2. *Symmetry-Forbidden Transitions.* Among the transitions in this class are those in which a molecule has a center of symmetry. In such cases, a  $g \rightarrow g$  or  $u \rightarrow u$  transition (see Sec. 1.A.) is “forbidden”, while a  $g \rightarrow u$  or  $u \rightarrow g$  transition is allowed.

### 7.A.iii. Types of Excitation

When an electron in a molecule is promoted (normally only one electron in any molecule), it usually goes into the lowest available vacant orbital, though promotion to higher orbitals is also possible. For most organic molecules, there are consequently four types of electronic excitation:

1.  $\sigma \rightarrow \sigma^*$ . Alkanes, which have no  $n$  or  $\pi$  electrons, can be excited only in this way.<sup>8</sup>
2.  $n \rightarrow \sigma^*$ . Alcohols, amines,<sup>9</sup> ethers, and so on can also be excited in this manner.

3.  $\pi \rightarrow \pi^*$ . This pathway is open to alkenes as well as to aldehydes, carboxylic esters, and so on.
4.  $n \rightarrow \pi^*$ . Aldehydes, ketones, carboxylic esters, and so on can undergo this promotion, as well as the other three.

#### 7.A.vi. The Fate of the Excited Molecule: Physical Processes

When a molecule has been photochemically promoted to an excited state, it does not remain in the excited state for long. Most promotions are from the  $S_0$  to the  $S_1$  state. As seen previously, promotions from  $S_0$  to triplet states are “forbidden”. Promotions to  $S_2$  and higher singlet states take place, but in liquids and solids these higher states usually drop very rapidly to the  $S_1$  state ( $\sim 10^{-13}$  to  $\sim 10^{-11}$  s). The energy lost when an  $S_2$  or  $S_3$

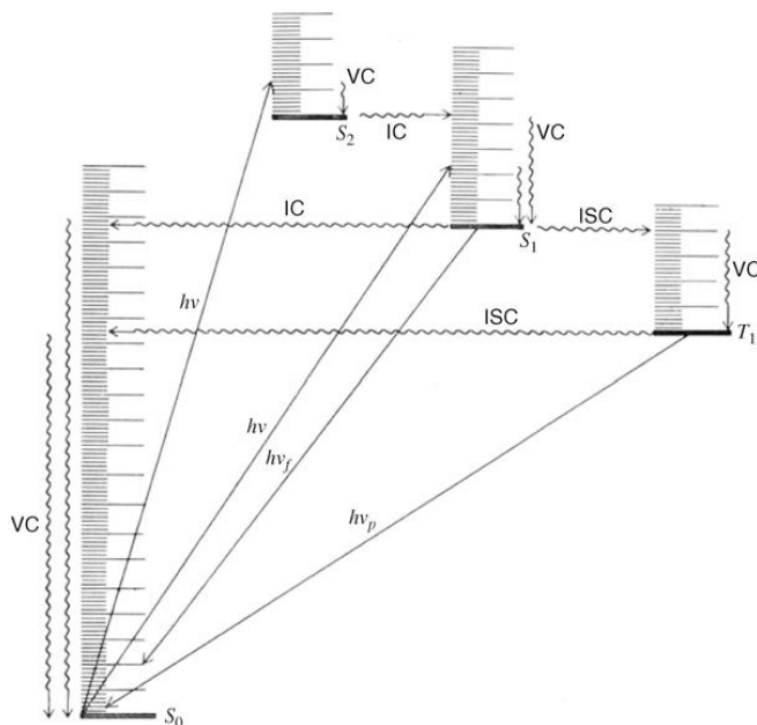


FIG. 7.4. Modified Jablonski diagram showing transitions between the excited and the ground state. Radiative processes are shown by straight lines, radiationless processes by wavy lines. vc = vibrational cascade;  $h\nu_f$  = fluorescence;  $h\nu_p$  = phosphorescence.

molecule drops to  $S_1$  is given up in small increments to the environment by collisions with neighboring molecules. Such a process is called an *energy cascade*. In a similar manner, the initial excitation and the decay from higher singlet states initially populate many of the vibrational levels of  $S_1$ , but these also cascade, down to the lowest vibrational level of  $S_1$ . Therefore, in most cases, the lowest vibrational level of the  $S_1$  state is the only important excited singlet state.<sup>21</sup> This state can undergo various physical and chemical processes. In the following list, we describe the physical pathways open to molecules in the  $S_1$  and excited triplet states. These pathways are also shown in a modified *Jablonski diagram* (Fig. 7.4) and in Table 7.4.



2. A molecule in the  $S_1$  state can drop to some low vibrational level of the  $S_0$  state all at once by giving off the energy in the form of light. This process, which generally happens within  $10^{-9}$  s, is called *fluorescence*. This pathway is not very common either (because it is relatively slow), except for small molecules (e.g., diatomic) and rigid molecules (e.g., aromatic). For most other compounds, fluorescence is very weak or undetectable. For compounds that do fluoresce, the fluorescence emission spectra are usually the approximate mirror images of the absorption spectra. This comes about because the fluorescing molecules all drop from the lowest vibrational level of the  $S_1$  state to various vibrational levels of  $S_0$ , while excitation is from the lowest vibrational level of  $S_0$  to various levels of  $S_1$  (Fig. 7.5). The only peak in common is the one that results from transitions between the lowest vibrational levels of the two states (called the 0–0 peak). In solution, even the 0–0 peak may be noncoincidental because the two states are solvated differently. Fluorescence nearly always arises from a  $S_1 \rightarrow S_0$  transition, although azulene (Sec. 2.I.iii) and its simple derivatives are exceptions,<sup>23</sup> emitting fluorescence from  $S_2 \rightarrow S_0$  transitions.

Because of the possibility of fluorescence, any chemical reactions of the  $S_1$  state must take place very fast, or fluorescence will occur before they can happen.

3. Most molecules (but by no means all) in the  $S_1$  state can undergo an *intersystem crossing* (ISC, see Fig. 7.4) to the lowest triplet state  $T_1$ .<sup>24</sup> An important example is benzophenone, of which 100% of the molecules that are excited to the  $S_1$  state cross over to the  $T_1$ .<sup>25</sup> Intersystem crossing from singlet to triplet is of course a “forbidden” pathway, since the angular-momentum problem (Sec. 7.A.ii) must

be taken care of, but this often takes place by compensations elsewhere in the system. Intersystem crossings take place without loss of energy. Since a singlet state usually has a higher energy than the corresponding triplet, this means that energy must be given up. One way for this to happen is for the  $S_1$  molecule to cross to a  $T_1$  state at a high vibrational level and then for the  $T_1$  to cascade down to its lowest vibrational level (see Fig. 7.4). This cascade is very rapid ( $10^{-12}$  s). When  $T_2$  or higher states are populated, they too rapidly cascade to the lowest vibrational level of the  $T_1$  state.

4. A molecule in the  $T_1$  state may return to the  $S_0$  state by giving up heat (ISC) or light (this is called *phosphorescence*).<sup>26</sup> Of course, the angular momentum difficulty exists here, so that both ISC and phosphorescence are very slow ( $\sim 10^{-3}$ – $10^1$  s). This means that  $T_1$  states generally have much longer lifetimes than  $S_1$  states. When they occur in the same molecule, phosphorescence is found at lower frequencies than fluorescence (because of the higher difference in energy between  $S_1$  and  $S_0$  than between  $T_1$  and  $S_0$ ) and is longer-lived (because of the longer lifetime of the  $T_1$  state).
5. If nothing else happens to it first, a molecule in an excited state ( $S_1$  or  $T_1$ ) may transfer its excess energy all at once to another molecule in the environment, in a process called *photosensitization*.<sup>27</sup> The excited molecule, which we will call D for donor, thus drops to  $S_0$  while the other molecule (A for acceptor) becomes excited:





### 7.A.vii. The Fate of the Excited Molecule: Chemical Processes

Although both excited singlet and triplet species can undergo chemical reactions, they are much more common for triplets, simply because these generally have much longer lifetimes. Excited singlet species, in most cases, have a lifetime of  $<10^{-10}$  s and undergo one of the physical processes already discussed before they have a chance to react chemically. Therefore, photochemistry is largely the chemistry of triplet states.<sup>41</sup> Table 7.5<sup>42</sup> lists many of the possible chemical pathways that can be taken by an excited molecule.<sup>43</sup> The first four of these are unimolecular reactions; the others are bimolecular. In

TABLE 7.5 Primary Photochemical Reactions<sup>a</sup> of an Excited Molecule A—B—C<sup>b</sup>

Reactions	Reaction Type	Example Number
$(A-B-C) \rightarrow A-B\cdot + C\cdot$	Simple cleavage into radicals <sup>46</sup>	(1)
$(A-B-C) \rightarrow E + F$	Decomposition into molecules	(2)
$(A-B-C) \rightarrow A-C-B$	Intramolecular rearrangement	(3)
$(A-B-C) \rightarrow A-B-C'$	Photoisomerization	(4)
$(A-B-C) + RH \rightarrow A-B-C-H + R\cdot$	Hydrogen-atom abstraction	(5)
$(A-B-C) \rightarrow (ABD)_2$	Photodimerization	(6)
$(A-B-C) + A \rightarrow ABX + A^*$	Photosensitization	(7)

the case of bimolecular reactions, it is rare for two excited molecules to react with each other (because the concentration of excited molecules at any one time is generally low); reactions are between an excited molecule and an unexcited molecule of either the same or another species. The reactions listed in Table 7.5 are primary processes. Secondary reactions often follow, since the primary products are frequently radicals or carbenes; even if they are ordinary molecules, they are often in upper vibrational levels and so have excess energy. In almost all cases, the primary products of photochemical reactions are in their ground states, though exceptions are known.<sup>44</sup> Of the reactions listed in Table 7.5, the

## Pericyclic Reactions

An important body of chemical reactions, differing from ionic or free radical reactions in a number of respects, has been recognized and extensively studied. Among the characteristics shared by these reactions, three in particular set them apart.:

1. They are relatively unaffected by solvent changes, the presence of radical initiators or scavenging reagents, or (with some exceptions) by electrophilic or nucleophilic catalysts.
2. They proceed by a simultaneous (concerted) series of bond breaking and bond making events in a single kinetic step, often with high stereospecificity.
3. In agreement with 1 & 2, no ionic, free radical or other discernible intermediates lie on the reaction path.

Since reactions of this kind often proceed by nearly simultaneous reorganization of bonding electron pairs by way of cyclic transition states, they have been termed **pericyclic reactions**. The four principle classes of pericyclic reactions are termed: **Cycloaddition**, **Electrocyclic**, **Sigmatropic**, and **Ene Reactions**.

## Analysis of Cycloaddition Reactions

### (a) *Diels–Alder reaction*

The reaction between butadiene and ethylene



is the simplest example of a general procedure for forming six-membered rings, developed by Diels and Alder, in which a conjugated diene reacts with a compound containing a  $C=C$  or  $C\equiv C$  bond (a *dienophile*). The reactions are described as  $[\pi 4 + \pi 2]$  cycloadditions, denoting the numbers of interacting  $\pi$ -electrons in each component. They are normally brought about by heating the components alone or in an inert solvent, the temperature required depending on the structures of the reactants.

Diels–Alder reactions have large negative entropies of activation, reflecting not only the loss of translational entropy when two molecules come together but also the high degree of ordering which corresponds to the mutual orientation of four atomic centres. However, the activation enthalpy is often small, so that rates of reaction are large even at moderate temperatures. The reverse reaction can often be brought about at high temperatures (i.e. as the  $T\Delta S$  term becomes increasingly important).

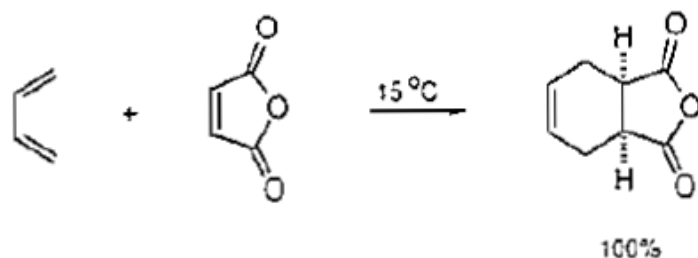
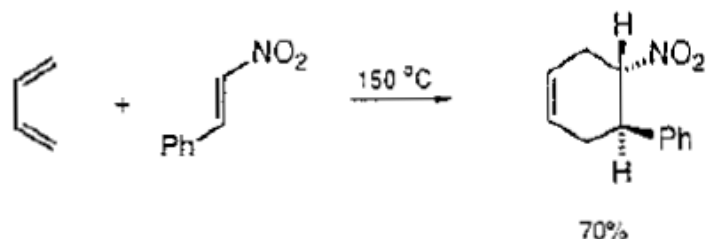
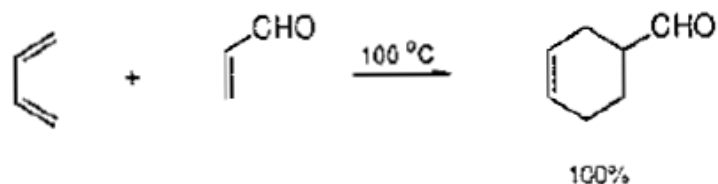
A brief account of these reactions in terms of frontier-orbital analysis was given earlier (section 4.8). A more detailed treatment of the interaction between the highest-occupied molecular orbital (HOMO) of one reactant and the lowest-unoccupied molecular orbital (LUMO) of the other will be given here.

(i) *The dienophile.* Although the Diels–Alder reaction between butadiene and ethylene is successful (in low yield), it is generally unsatisfactory, or fails completely, with other simple alkenes or alkynes. However, when the unsaturated bond of the dienophile is conjugated to a group of  $-M$  type, such as carbonyl, nitro, or cyano, reaction occurs under milder conditions and normally gives good yields. It is thought that this is because the substituent lowers the energy of the LUMO of the dienophile, thereby bringing it closer in energy to the HOMO of the diene and increasing the bonding interaction in the transition state. Sometimes

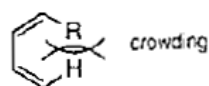
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greater reactivity can be achieved by carrying out the reaction in the presence of a Lewis acid such as  $BF_3$ , which complexes with the  $-M$  substituent and so serves to withdraw electrons even more strongly; such reactions can occur at room temperature or below. The following reactions of butadiene with various dienophiles are illustrative:

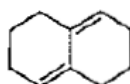
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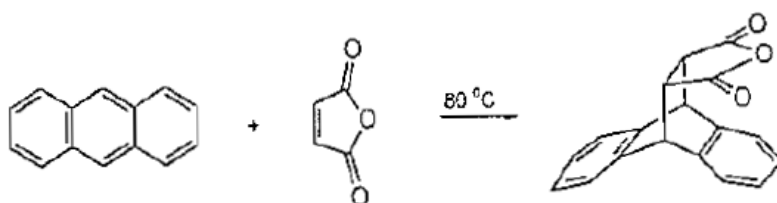
(ii) *The diene.* In order for reaction to occur, the diene must be capable of achieving the *s-cis* conformation which the formation of a six-membered ring requires. This is always possible for acyclic dienes but it can result in wide variations in reactivity. For example, *cis*-1-substituted butadienes are less reactive than their *trans*-isomers because the substituent in the former suffers steric crowding in the *s-cis* conformation which raises the activation energy:



Cyclic dienes react only if they are of *cis* type; for example,

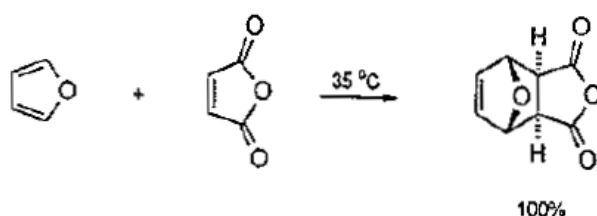


Aromatic compounds are effective dienes providing that the loss of aromatic stabilization energy is not too great. For example, although benzene is inert, anthracene reacts with maleic anhydride at 80°C,



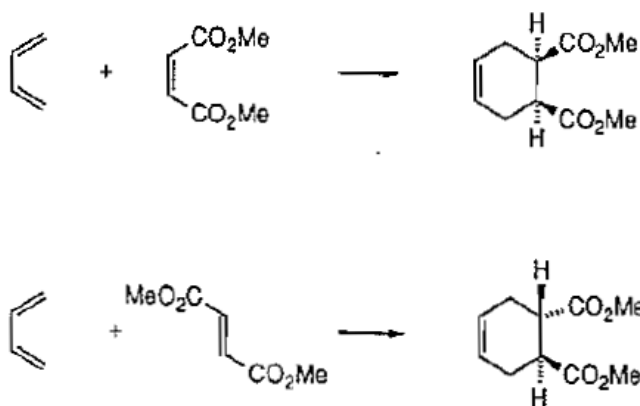
the difference reflecting the fact that whereas a reaction with benzene would result in the loss of  $150 \text{ kJ mol}^{-1}$  of stabilization energy, only  $(349 - (2 \times 150))$ , i.e. about  $50 \text{ kJ mol}^{-1}$  is lost on addition to anthracene.

Amongst monocyclic heteroaromatic compounds, furan is reactive, e.g.



whereas the more stabilized aromatic, thiophene, is inert. Pyrrole reacts with maleic anhydride, but not in the Diels–Alder manner (p. 358).

(iii) *Stereochemistry*. The cycloadditions are stereospecific. For example, dimethyl maleate and dimethyl fumarate react with butadiene to give, respectively, *cis*- and *trans*-dimethyl cyclohexene-4,5-dicarboxylates:

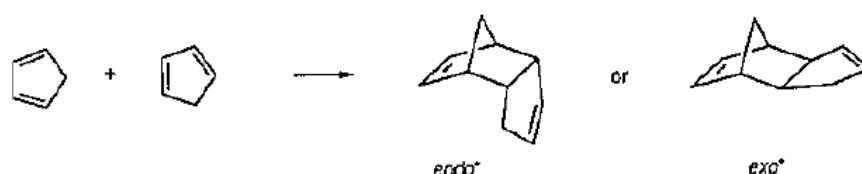


This is a result of the concerted nature of the reaction. The diene and dienophile can only achieve appropriate orbital overlap if they come together with their

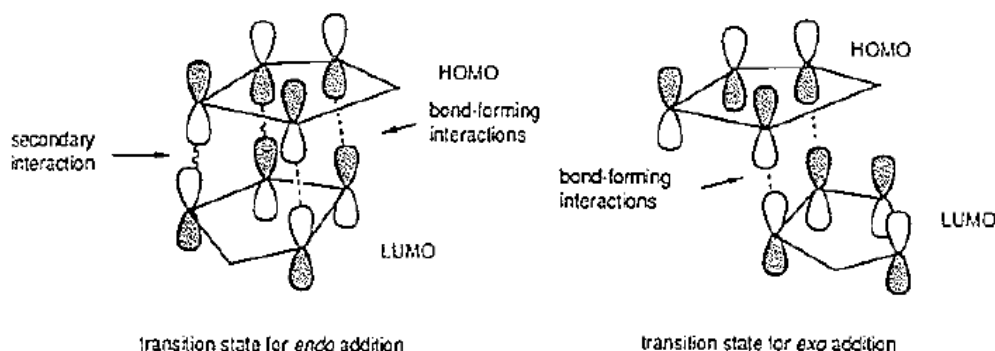
molecular planes (nearly) parallel; the orbital interaction is suprafacial with respect to both reactants:



A further stereochemical factor applies with suitably substituted reactants. For example, in the dimerization of cyclopentadiene, where one molecule acts as diene and the other as dienophile, two orientations in the product are possible, each of which arises from suprafacial-suprafacial interaction of the reactants:

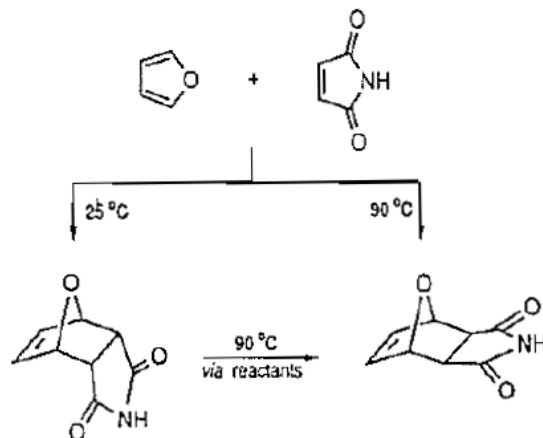


In practice, in this and most other cases the thermodynamically less stable *endo* product predominates. This has been accounted for in terms of a secondary interaction of the HO and LU orbitals in the transition state for *endo* addition which is sterically impossible for *exo* addition:



This secondary interaction does not lead to bonding in the product, but, because the overlapping orbitals are of like phase, it can stabilize the transition state.

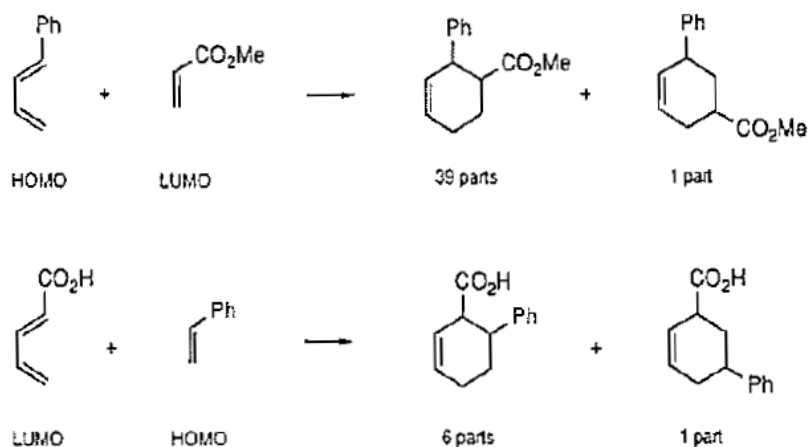
Since, usually, the *exo* product is thermodynamically more stable, it is sometimes possible to form it by the use of conditions under which formation of the kinetically favoured adduct is reversible. The reaction of furan with maleimide is an example:



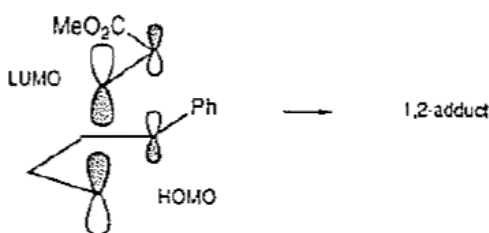
The less stable *endo* isomer is formed the faster and predominates at 25°C, where the reaction is effectively irreversible. At 90°C, this product is in fairly rapid equilibrium with the reactants, and the less rapidly formed but more stable *exo* isomer gradually accumulates.

Maleic anhydride and furan give the *exo*-adduct even at low temperatures (p. 272). This is because, although the *endo*-adduct is formed about 500 times faster than the *exo*-isomer, it reverts to reactants about 10000 times faster and *exo*-product accumulates.

(iv) *Regiochemistry*. When both diene and dienophile contain substituents, more than one product can be formed, e.g.

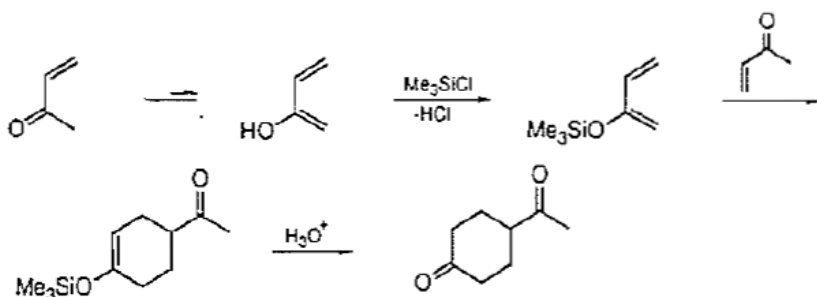


It is believed that 1,2-products predominate in these cases because bonding at the transition state is not only more effective when the HOMO of one reactant and the LUMO of the other are more closely matched in *energy* (whence the pairings noted above and as described earlier) but also when the *sizes* of the orbitals at the reacting termini are the more closely matched, e.g.

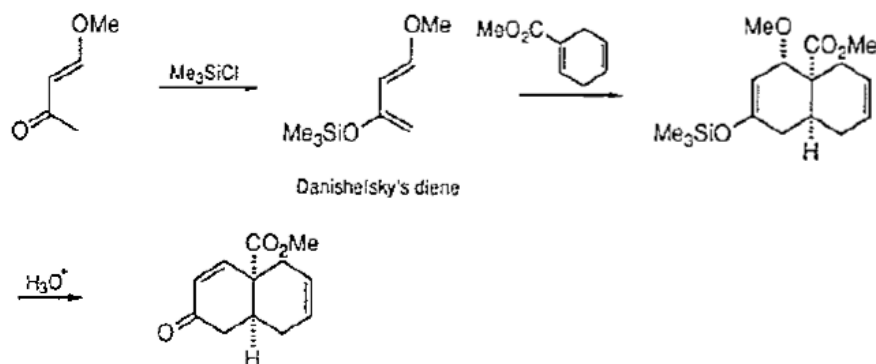


is a better match than the alternative that leads to the 1,3-adduct.

Regioselectivity is particularly marked with butadiene containing a 2-OSiMe<sub>3</sub> substituent, e.g.

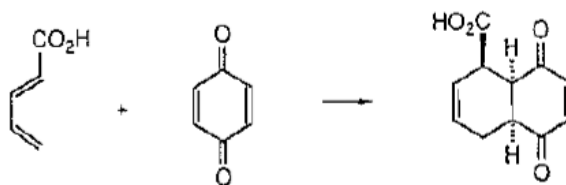


A modification of this reaction, employing *Danishefsky's diene*, enables  $\alpha\beta$ -unsaturated ketones to be formed, e.g.



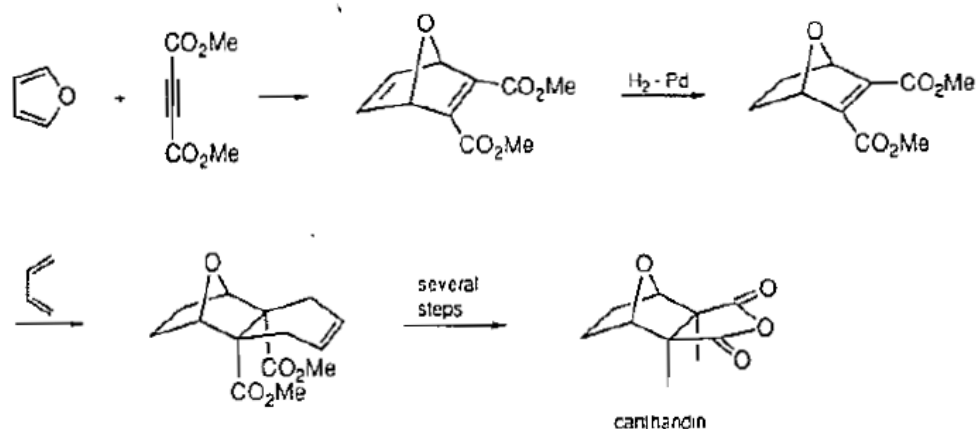
(v) *Applications.* The Diels–Alder reaction is of very great importance in the synthesis of naturally occurring compounds, partly because of the large number of structures to which it is applicable and partly because of its stereospecificity. By the appropriate choice of starting materials, it is often possible in one step to assemble a product with several groupings in the required stereochemical configuration. Some examples are:

(1) The reaction



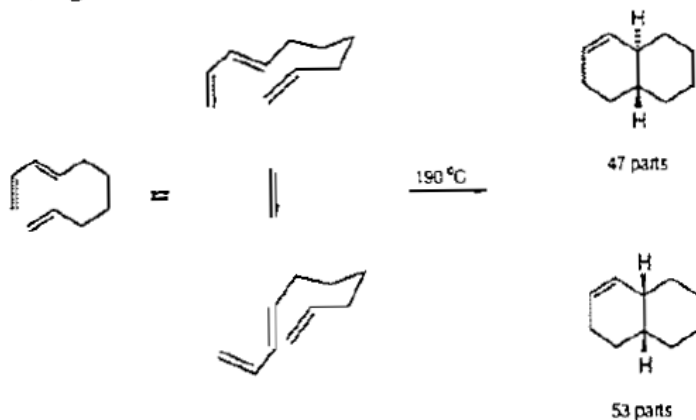
was employed in the synthesis of the alkaloid reserpine to assemble three stereocentres (p. 731).

(2) The reaction between furan and dimethyl acetylenedicarboxylate, in a synthesis of cantharidin (from the body fluid of cantharides beetles such as the Spanish fly). Catalytic hydrogenation of the product gave a new dienophile which

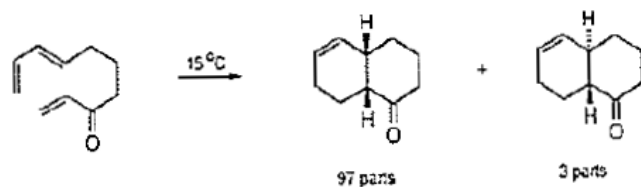


reacted with butadiene in a second Diels–Alder reaction.\* The required stereochemistry having been established, the ester groups were converted into methyl and the ring derived from butadiene was oxidized in several steps to the required anhydride.

(3) Intramolecular Diels–Alder reactions can be used to assemble bicyclic compounds, e.g.

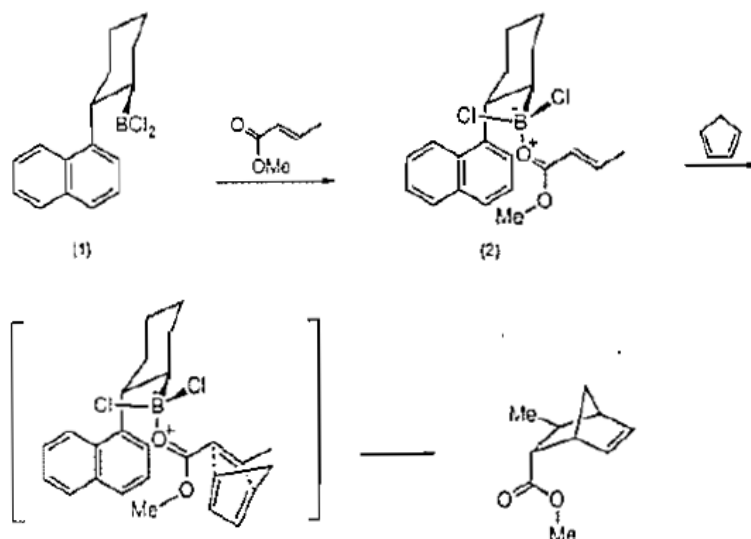


The activating effect of a carbonyl group conjugated to the dienophile is shown by



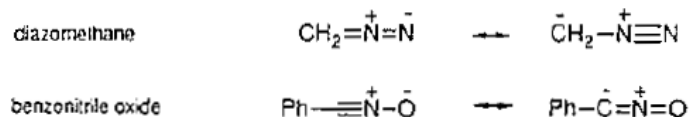


(vi) *Enantioselective synthesis.* Although stereocentres can be created in Diels–Alder reactions (e.g. three in example (1) above), racemic mixtures are obtained unless one or both reactants is asymmetric. An approach being developed to induce enantioselectivity is the use of a chiral catalyst. For example, the optically active alkyldichloroborane (1) complexes with (*E*)-methyl crotonate to give (2). The approach of cyclopentadiene from the rear face of the dienophile is strongly hindered by the naphthyl group and attack from the front gives product in almost optically pure state:



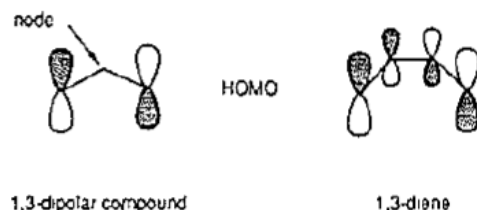
### (b) 1,3-Dipolar additions

A large number of types of five-membered ring may be formed by the reaction of '1,3-dipolar' compounds with unsaturated bonds (dipolarophiles) such as  $C=C$ ,  $C\equiv C$ ,  $C=O$ , and  $C\equiv N$ . The 1,3-dipolar components are compounds whose representation requires ionic structures which include ones with charges on atoms bearing a 1,3-relationship, e.g.



The 1,3-dipole is a structural variant of the diene component in the Diels–Alder reaction; in the dipolar compound, four  $\pi$ -electrons are distributed over three atoms instead of the four in a diene. Moreover, the HOMO and LUMO of a 1,3-dipole are of similar symmetry to those of a diene with respect to the two-fold axis and to the mirror plane which bisects the molecule:

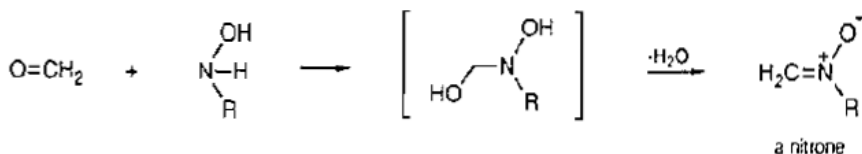
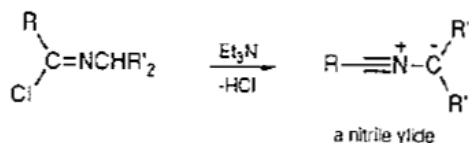
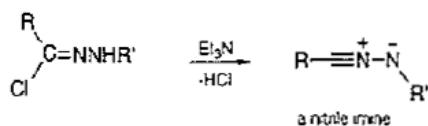
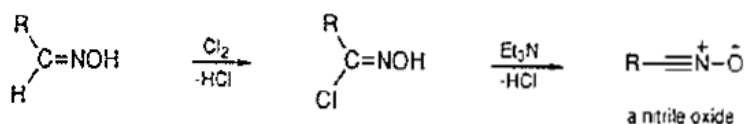




Consequently, concerted cycloaddition to an alkene is symmetry-allowed.

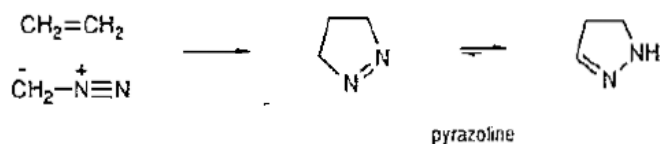
Unlike dienes which are stable, isolable molecules, 1,3-dipoles are often short-lived species which must necessarily be generated *in situ* and trapped as soon as they are formed; even those which are isolable, such as diazoalkanes,  $R-\bar{C}H-\dot{N}\equiv N$ , and azides,  $R-\bar{N}-\dot{N}\equiv N$ , often tend to be thermally labile materials, best handled in solution and used immediately after synthesis.

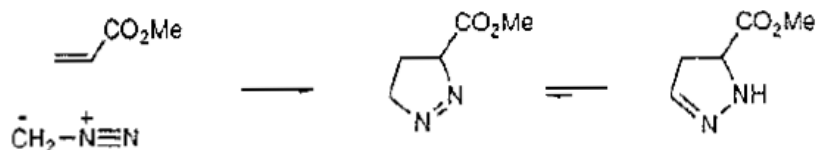
The following reactions illustrate those which are used for preparing 1,3-dipolar compounds *in situ*:



(i) *Applications.* A variety of heterocyclic compounds can be constructed by reactions of 1,3-dipolar compounds with alkenes and alkynes. Some examples are:

(1) Diazoalkanes yield pyrazole derivatives, e.g.





(2) Azides yield triazole derivatives,



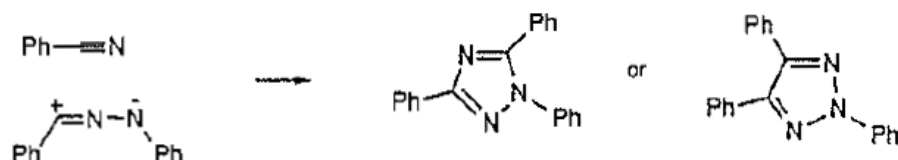
(3) Nitrile oxides yield isoxazole derivatives,



(4) Nitrile ylides yield pyrrole derivatives,

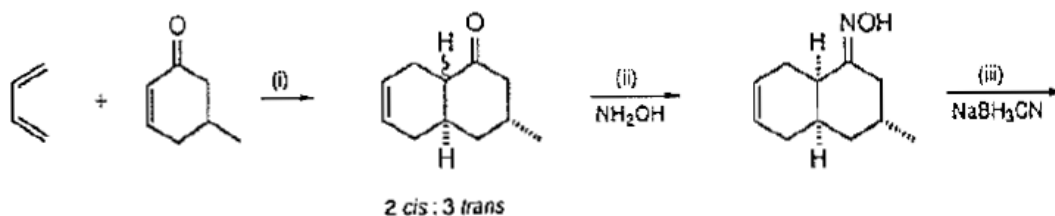


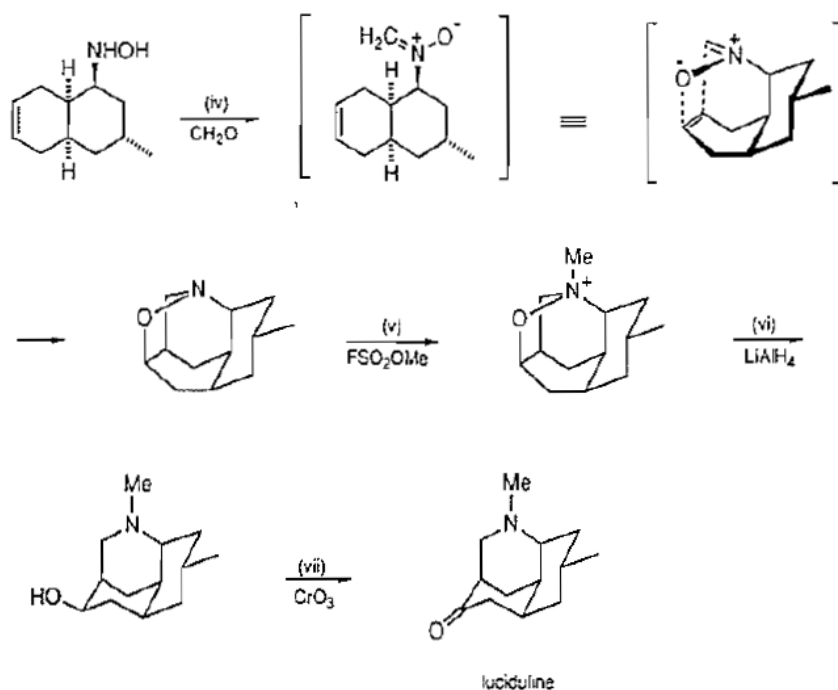
The dipolarophile may also be a carbonyl compound or a nitrile. In these cases, there are two possible orientations for the addition, e.g.



One product usually predominates: in the above example it is the first of the two. This and related results can be accounted for by considering the energies of the bonds being formed. For example, in the first product above, two C—N bonds are formed, whereas in the second, one C—C and one N—N bond are formed; the first combination corresponds to the greater bonding energy and this is reflected in the preceding transition states.

The value of 1,3-dipolar cycloaddition in the synthesis of natural products is now well recognized. An elegant example, the synthesis of (racemic) luciduline (an alkaloid whose dextrorotatory enantiomer occurs in *Lycopodium lucidulum*), made use of both 1,3-dipolar and Diels–Alder cycloaddition:



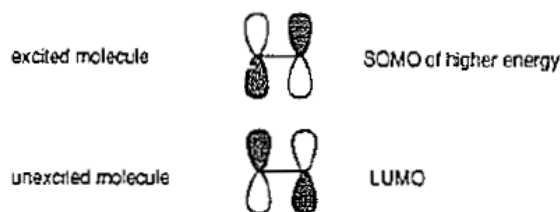


The Diels–Alder reaction – step (i) – was carried out at room temperature in the presence of tin(IV) chloride. This results initially in the formation of a *cis*-ring junction and also in a *cis* relationship between the hydrogen atoms at the ring junction and the methyl substituent (the latter because the suprafacial addition of the diene is to the less hindered face of the dienophile). However, the bridgehead hydrogen adjacent to the carbonyl group undergoes acid-catalyzed enolization and the major product was the (unwanted) *trans*-isomer. It was found that the *cis*-isomer reacted the faster of the two with hydroxylamine in step (ii), and by conducting this reaction at high pH so as to effect rapid *cis-trans* isomerization *via* the enolate, it was possible to obtain almost entirely the required *cis*-ring-fused oxime. This was reduced with sodium cyanoborohydride in methanol: this is a hydride-transfer agent (p. 651) which delivered  $\text{H}^-$  from the less hindered side of the oxime, to create a hydroxylamine function stereoselectively as shown. The nitrone, generated in step (iv) with paraformaldehyde in hot toluene, underwent a spontaneous cycloaddition to give a bridged oxazolidine. In step (v) this was methylated with methyl fluorosulfonate and the resulting salt was reduced in step (vi) with lithium aluminium hydride (p. 651). In the final step, the secondary alcohol was oxidized to carbonyl with chromium(VI) oxide in acetone.

### (c) $[\pi 2 + \pi 2]$ Cycloadditions

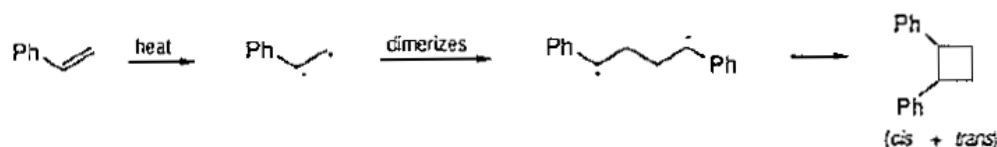
As described in chapter 4, cycloaddition of alkenes to form cyclobutanes is a symmetry-forbidden process when the geometry of the transition state requires suprafacial-suprafacial interaction of the orbitals.

However, alkenes do combine in the  $[\pi 2 + \pi 2]$  manner photochemically. The simplest interpretation of this is as follows. When an alkene absorbs a quantum of light, an electron is promoted from the HOMO to the LUMO, so that there are now two singly occupied molecular orbitals (SOMO). The highest occupied orbital now therefore has the symmetry of the LUMO and consequently can interact with the LUMO of a second molecule of the alkene which is in its ground state to give a cyclobutane in its first excited state; this loses energy and returns to the ground state by fluorescence or collisional deactivation.

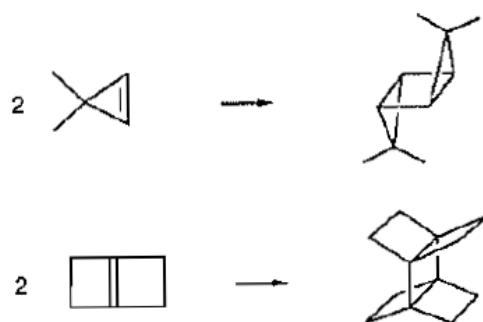


These photochemical reactions are considered in more detail in chapter 16.

The formation of cyclobutanes from alkenes also occurs in two circumstances by routes which are neither photochemical nor concerted, but involve thermally generated diradicals. First, alkenes with radical-stabilizing substituents react on heating to give head-to-head adducts, e.g.



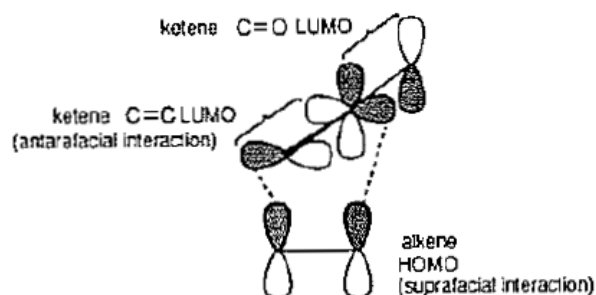
Second, highly strained cycloalkenes dimerize, sometimes spontaneously, e.g.



(i) *Cumulenes*. Cumulenes – compounds which contain adjacent double bonds, such as allene ( $\text{CH}_2=\text{C}=\text{CH}_2$ ), ketene ( $\text{CH}_2=\text{C}=\text{O}$ ), and isocyanates ( $\text{RN}=\text{C}=\text{O}$ ) – participate readily in  $[\pi 2 + \pi 2]$  cycloadditions which have been proved in a number of cases to be concerted. For example, ketene reacts with dienes to give  $[2 + 2]$  cycloadducts in a concerted reaction, to the exclusion of the formation of  $[4 + 2]$  adducts.

From the earlier analysis of the  $[\pi 2 + \pi 2]$  cycloaddition of alkenes,  $[\pi 2 + \pi 2]$  addition for ketenes is forbidden when the geometry of approach is suprafacial-

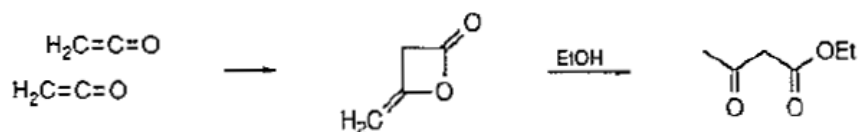
suprafacial. However, consider the alternative suprafacial-antarafacial interaction. The efficiency of bonding interaction is very low unless one of the components undergoes twisting about its original  $\pi$ -bond, and this is the constraint which makes a transition state derived from this array inaccessible for alkenes. On the other hand, if the component whose  $\pi$  orbital interacts in an antarafacial manner is a cumulene, one of the carbons involved is  $sp$ -hybridized. This reduces the geometric constraint but, more importantly, makes available another orbital whose participation stabilizes the transition state. This further orbital is the LUMO of the adjacent double bond. This is very low-lying, in ketene especially, and its participation accounts for the preference by ketene of  $[\pi 2 + \pi 2]$  over  $[\pi 4 + \pi 2]$  cycloaddition.



The propensity for  $[\pi 2 + \pi 2]$  cycloaddition amongst cumulenes causes them readily to dimerize. Substituted ketenes form cyclobutanediones,

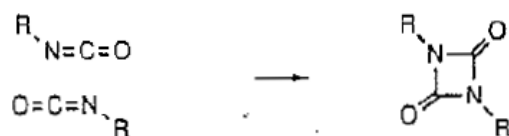


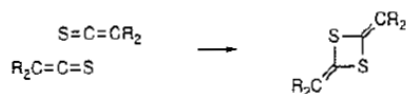
but ketene itself dimerizes in the liquid phase to a  $\beta$ -lactone, the  $[2 + 2]$  addition involving the carbonyl group of one component:



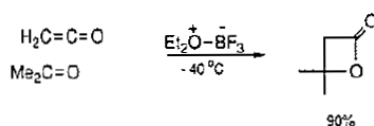
This dimerization forms part of the industrial synthesis of acetoacetic ester; the ketene is obtained by the pyrolysis of acetone, and the dimer is converted into acetoacetic ester by reaction with ethanol, as shown.

Other examples of dimerizations of cumulenes and of  $[2 + 2]$  cycloadditions involving cumulenes are the following:

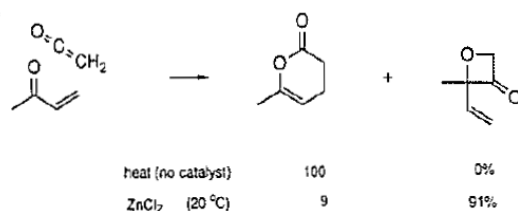




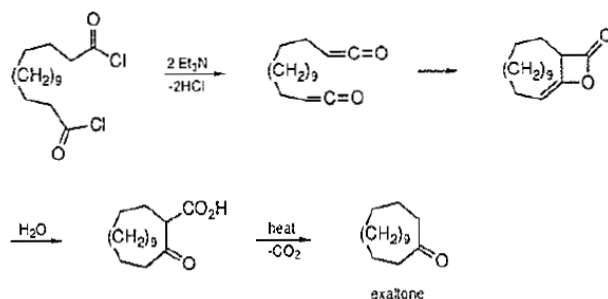
Ketenes also undergo  $[\pi 2 + \pi 2]$  cycloadditions with ketones, catalyzed by Lewis acids, e.g.



and Lewis acids can also divert  $[\pi 4 + \pi 2]$  cycloadditions to  $[\pi 2 + \pi 2]$  reactions, e.g.

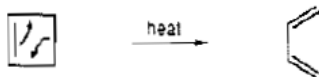


Finally, the intramolecular cyclization of diketenes forms the basis of a method for making large-ring ketones, e.g.



## Analysis of Electrocyclic Reactions

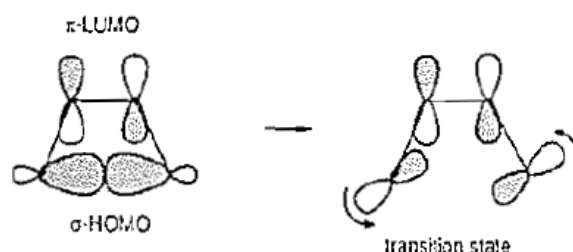
Electrocyclic reactions are those in which either a ring is formed with the generation of a new  $\sigma$ -bond and the loss of a  $\pi$ -bond or a ring is broken with the opposite consequence, e.g.



The reactions are stereospecific. For example, *cis*-3,4-dimethylcyclobutene gives solely *cis,trans*-2,4-hexadiene, which is not the thermodynamically most stable isomer:



Considerations of orbital symmetry again offer an explanation. In the transition state for ring opening of a cyclobutene, the HOMO of the  $\sigma$ -bond that is undergoing fission interacts with the LUMO of the  $C=C$  bond. This can only happen if the  $\sigma$ -bond opens in a *conrotatory* manner:\*



For the reverse reaction – the ring closure – precisely the opposite path is followed (principle of microscopic reversibility) so that conrotatory motion of the termini is likewise required.

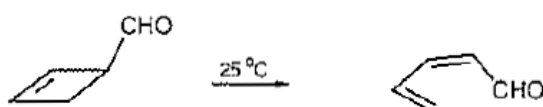
Conrotatory ring opening of *trans*-3,4-dimethylcyclobutene could in principle lead to two products, depending upon the sense of the rotation: the *trans,trans*-dimethyl diene and the *cis,cis*-isomer. However, severe steric crowding would result from the conrotatory movement which turns both methyl groups inwards in the formation of the latter compound,



\* This also follows if the  $\sigma$ -LUMO and the  $\pi$ -HOMO are considered.

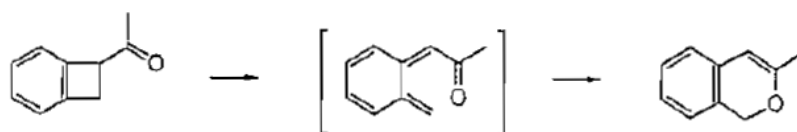
so raising the activation energy relative to that for the *trans,trans*-isomer. Consequently, only the *trans,trans*-compound is formed.

In contrast, strongly electron-withdrawing groups preferentially rotate inward, e.g.

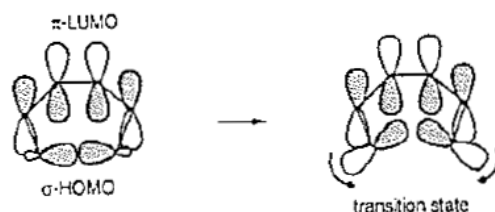




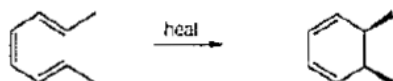
This can be exploited in synthesis, e.g.



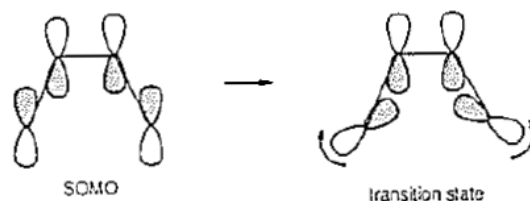
The theory is readily extended to polyenes. For example, the opening of a 1,3-cyclohexadiene, and likewise the ring closure, require *disrotatory* motion:



It can be understood why, for example, *trans,cis,trans*-2,4,6-octatriene gives specifically *cis*-5,6-dimethylcyclohexadiene:



When the ring closures of dienes and trienes are carried out photochemically, the stereospecificity is the opposite to that of the thermal reaction: the symmetry of the SOMO of higher energy governs the reaction and the observed stereochemical course follows, e.g.



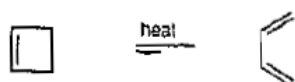
However, it is recognized that this is an oversimplified treatment: a full understanding requires examination of all the  $\pi$  orbitals of polyene and product, as well as of the  $\sigma$  orbital of the bond formed between the termini.

The stereochemistry of electrocyclic reactions is summarized in Table 9.1:

**Table 9.1** Direction of motion of the termini in electrocyclic ring closure or the reverse ring opening

Number of $\pi$ -electrons in ring closure reaction	Rotatory motion	
	Thermal reaction	Photochemical reaction
4	con	dis
6	dis	con

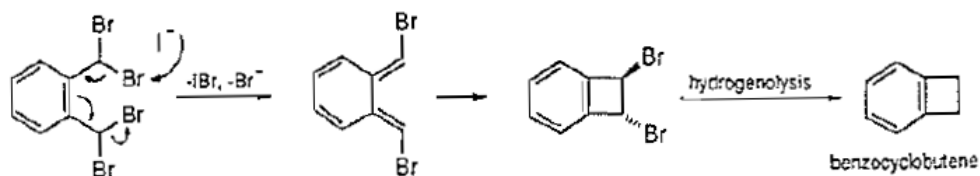
(i) *Applications.* The direction taken by an electrocyclic reaction depends on the relative stabilities of the ring and open-chain reactants. With cyclobutenes, the latter is favoured because of the strain in the ring, e.g.



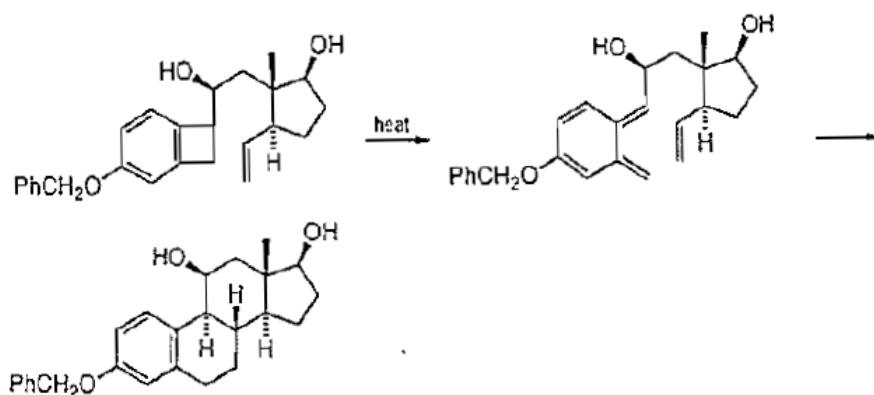
In contrast, with benzocyclobutenes the ring structure is favoured because the loss of aromatic stabilization energy on ring opening outweighs the strain in the ring, e.g.



The latter equilibrium opens up two synthetic routes. First benzocyclobutenes can be synthesized, e.g.



Second, a benzocyclobutene is a masked conjugated diene; a reagent that reacts only with the diene can trap it as it is formed. This principle was applied in an elegant steroid synthesis in which two of the rings were formed with a predetermined *trans* stereochemistry:

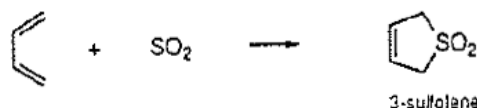


(ii) *Valence tautomerism.* Electrocyclic equilibria that occur at ambient temperature give rise to the phenomenon of valence tautomerism. For example, cyclooctatetraene is in equilibrium with *cis*-bicyclo[4.2.0]octa-2,4,7-triene, which it forms by the symmetry-allowed disrotatory ring closure:\*



## Cheletropic Reactions

Cheletropic reactions are ones in which two  $\sigma$ -bonds which terminate at a single atom are made or broken in a concerted reaction, e.g.



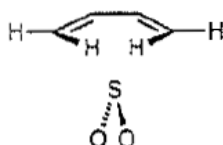
Cheletropic addition is related to Diels–Alder addition in that the  $2\pi$ -electron system in the dienophile of the latter is replaced by an unshared pair of electrons on a single atom in the former.

### (a) Cheletropic reactions of dienes

The HOMO of a molecule like sulfur dioxide or carbon monoxide is that which has a lone-pair of electrons in the plane containing the atoms; the LUMO is a  $p$  orbital perpendicular to this plane:

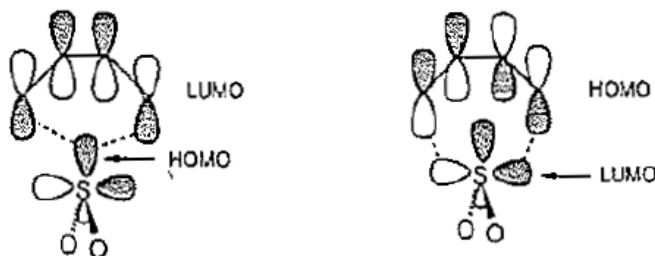


For a symmetry-allowed cycloaddition of sulfur dioxide to a diene, the SO<sub>2</sub> lies in a plane which bisects the *s-cis* conformation of the diene, and the reaction is suprafacial with respect to both diene and SO<sub>2</sub>:

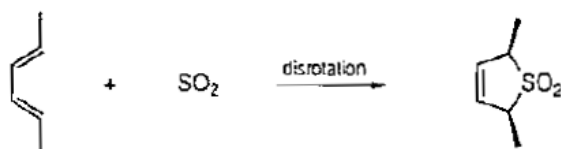


\* Valence tautomerism can be studied by NMR spectroscopy. If equilibrium occurs slowly with respect to the NMR time scale, the spectrum of each tautomer is observed; if it is fast, a time-averaged spectrum of the two is observed. At intermediate rates, line-broadened spectra are obtained, analysis of which enables the rate of interconversion to be derived.

The appropriate matching of orbitals is:

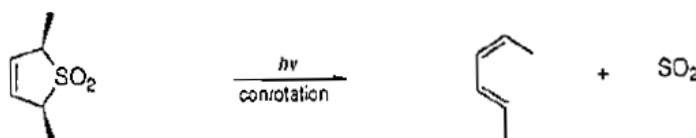


In the transition state, the terminal carbon atoms of the diene must move in the disrotatory manner so that the HOMO of  $\text{SO}_2$  can interact with the LUMO of the diene, or the LUMO of  $\text{SO}_2$  with the HOMO of the diene. The reality of this prediction of frontier-orbital theory is proved by the fact that *trans,trans*-1,4-disubstituted dienes give specifically the more crowded *cis*-substituted 3-sulfolenes, e.g.



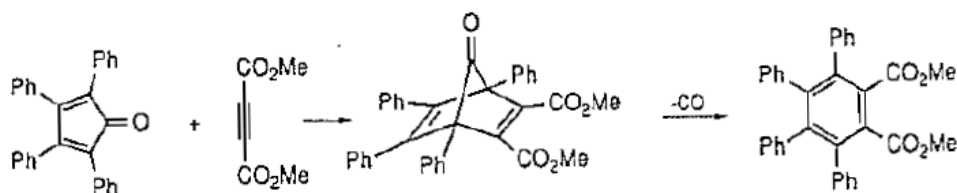
and *cis,trans*-disubstituted dienes give *trans*-substituted 3-sulfolenes.

As with electrocyclic reactions, the opposite stereochemistry is observed if the reaction is photochemical rather than thermochemical:



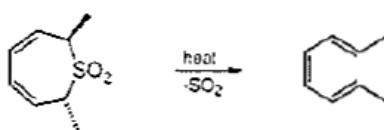
(i) *Applications.* The reaction between butadiene and sulfur dioxide and the reverse reaction which occurs at high temperatures, provide a useful method for 'carrying' butadiene, so avoiding the experimental inconvenience of handling gaseous butadiene at the elevated temperatures which may be needed for reaction. For example, when 3-sulfolene is heated in the presence of a dienophile, butadiene is released and immediately trapped in a Diels-Alder reaction.

There are few other reactions where a molecule like sulfur dioxide is sequestered by a diene, but there are others where the reverse process – extrusion of a, usually, stable molecule – occurs. For instance, Diels-Alder adducts of cyclopentadienones extrude carbon monoxide, e.g.

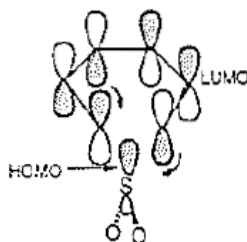


### (b) *Cheletropic reactions of trienes*

2,7-Dihydrothiepin dioxides undergo thermolysis with a high degree of stereospecificity, e.g.

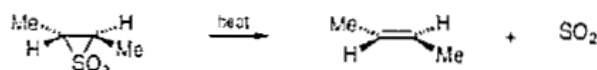


The reaction therefore occurs with a conrotatory motion of the triene termini. If the cheletropic reaction is linear, i.e. if the HOMO of  $\text{SO}_2$  reacts suprafacially as it does in the case of dienes, the triene must react antarafacially, which is consistent with the observed conrotation:

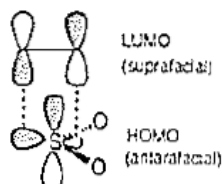


### (c) Cheletropic reactions of simple alkenes

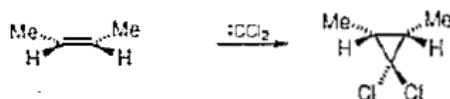
Cheletropic reaction of sulfur dioxide with alkenes is symmetry-forbidden if both components interact suprafacially. Antarafacial reaction of a simple alkene is sterically very unlikely (cf. discussion of  $[\pi 2 + \pi 2]$  cycloaddition of alkenes), so that the reaction is likely to involve the  $\text{SO}_2$  antarafacially. It is known in the stereospecific extrusion of  $\text{SO}_2$  from episulfones, e.g.



The orbital interaction in the transition state is represented by:



The reactions of singlet carbenes and nitrenes with alkenes are also of this type, e.g.



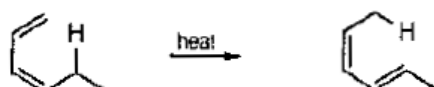

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Only singlet carbenes and nitrenes behave in this way: the addition of triplet carbenes or nitrenes to a double bond results in a diradical which is sufficiently long-lived, during the time required for spin-inversion, for stereospecificity to be lost as a result of rotations about bonds.

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## Sigma-tropic Rearrangements

A sigmatropic rearrangement is a pericyclic reaction which involves the migration of a  $\sigma$ -bonded atom or group within a  $\pi$ -electron system; overall, the numbers of  $\pi$ - and  $\sigma$ -bonds remain separately unchanged. The rearrangements can be divided into two classes: (1) those where the group which migrates is bonded through the same atom in both reactant and product, (2) those where the migrating group is bonded through different atoms in the reactant and the product. An example of the former is,



where hydrogen is transferred from the methylene group to the alternative terminus of the diene; the latter is exemplified by the Claisen rearrangement, e.g.

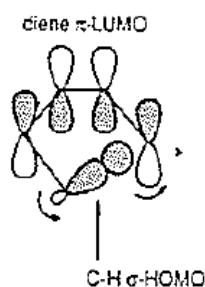


where the allyl group which migrates is bound by different atoms before and after the reaction. The first reaction is thermodynamically favourable because a dialkyl-substituted diene is more stable than a mono-alkylated one (p. 34) and the second reaction reflects the strength of the  $\text{C}=\text{O}$  bond.

These two reactions illustrate, respectively, a [1,5]-shift and a [3,3]-shift. The figures in parentheses denote the numbers of essential interacting centres in the two groups which are formed by breaking the migrating  $\sigma$ -bond.

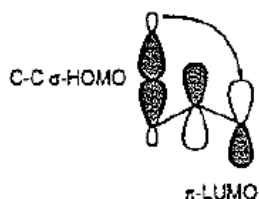
### (a) [1,*j*]-Sigmatropic rearrangements

The occurrence and stereochemistry of sigmatropic rearrangements can be accounted for, like other pericyclic reactions, in terms of the symmetry of frontier orbitals. Consider the [1,5]-shift of hydrogen as in the first example:



For a maximum of bonding to occur in the transition state when the HOMO (or LUMO) of the C—H  $\sigma$ -bond interacts with the LUMO (or HOMO) of the diene  $\pi$ -system, the hydrogen is transferred suprafacially. Since this arrangement is easily accessible geometrically, the [1,5]-shift of hydrogen in dienes readily occurs thermally.

Owing to the difference in symmetry between the LUMO of a simple alkene and that of a diene, a similar suprafacial [1,3]-transfer of hydrogen in a substituted alkene is symmetry-forbidden. A [1,3]-hydrogen transfer would be allowed if the  $\pi$ -bond were to interact antarafacially,

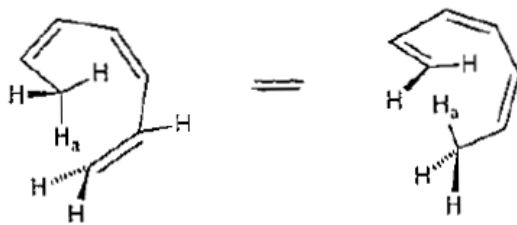


but the geometric constraint that this imposes is too great and concerted [1,3]-transfer of hydrogen is not observed. The stability of the triene,

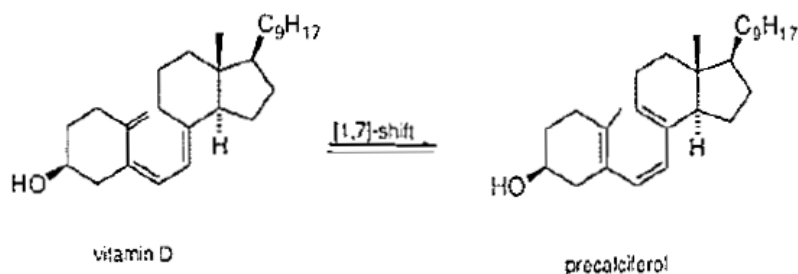


derives from the fact that concerted thermal isomerization to toluene, which is thermodynamically much the more stable, is a symmetry-forbidden process.

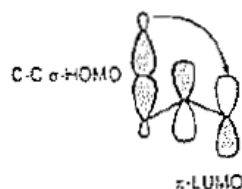
On the other hand, a [1,7]-transfer of hydrogen in a triene, which must also be antarafacial if it is to be symmetry-allowed, is sterically feasible when the system can form a helical structure:



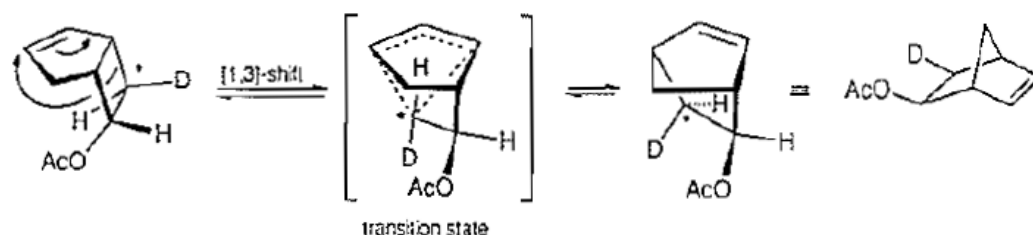
The classic example is the thermal interconversion of vitamin D and precalciferol:



In sigmatropic shifts of hydrogen, only the polyene can participate in an antarafacial manner on account of the spherical symmetry of the hydrogen  $s$  orbital. With other functions such as alkyl groups, the migrating group can be the antarafacial component and this expands the possibility for reaction. Consider the [1,3]-shift of an alkyl group in an alkene:



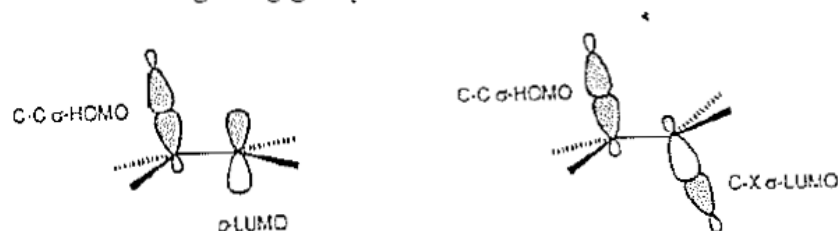
As shown, there is the possibility of an interaction which is antarafacial for the C—C  $\sigma$ -bond and suprafacial for the  $\pi$ -bond. Again, this is likely to require a transition state with a geometrically difficult access, particularly for flexible molecules, but this interaction is known in molecules whose rigid framework builds into the ground state of the reactant much of the ordering which would otherwise have to be achieved at the expense of an unfavourable entropy of activation in a flexible analogue. An example is:



The antarafacial character of the interaction of the alkyl  $\sigma$ -bond is demonstrated by the fact that the configuration of the migrating carbon (marked \*) is inverted in the change.

Alkyl migrations occur with carbocations and compounds with a good leaving group, X. Interaction of the HOMO of the migrating  $\sigma$ -bond with the LUMO of

the empty  $p$  orbital or of the C—X  $\sigma$ -bond is consistent with the retention of configuration of the migrating group:



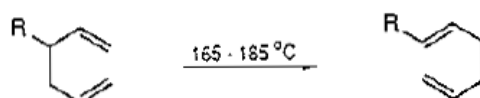
In contrast, the concerted [1,2]-shift in a carbanion is predicted to be symmetry-forbidden.\* Such rearrangements do, however, occur but not by a concerted mechanism (p. 447).



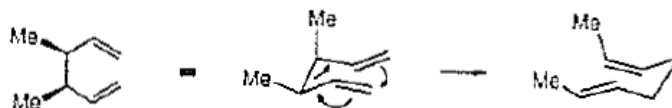
(b) *[i,j]*-Sigmatropic rearrangements

The most frequently encountered sigmatropic rearrangements of this category are [3,3]-shifts for, as the notation implies, the transition state involves the stereochemically favourable six-membered ring.

The *Cope rearrangement* is the [3,3]-sigmatropic rearrangement of 1,5-dienes, e.g.

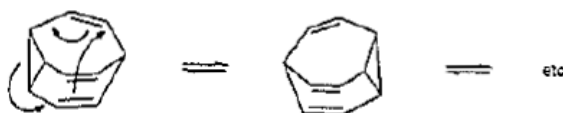


The stereochemical outcome of the rearrangements of acyclic compounds is consistent with their occurrence through chair-shaped transition states. For example, *meso*-3,4-dimethyl-1,5-hexadiene gives *cis,trans*-2,6-octadiene,

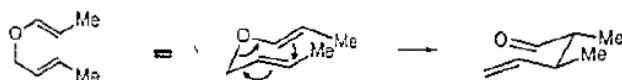


whereas a boat-shaped transition state would give *trans,trans*- or *cis,cis*-product.

The valence tautomers of bullvalene undergo interconversion (between over a million identical forms) by Cope rearrangement, e.g.

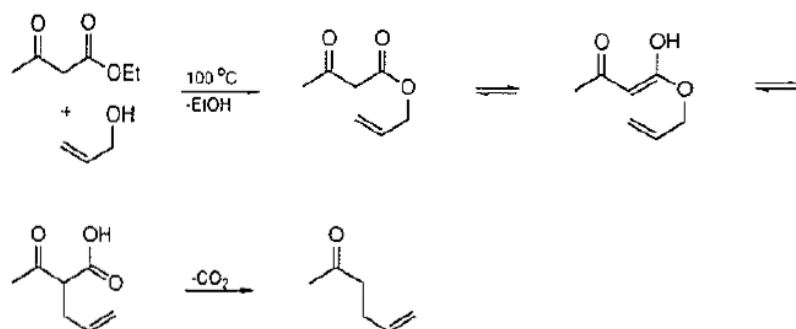


The *Claisen rearrangement* of allyl alkenyl ethers is another example of a [3,3]-sigmatropic rearrangement, differing from the Cope rearrangement in the replacement of a CHR fragment by oxygen but having the same stereochemical outcome, e.g.

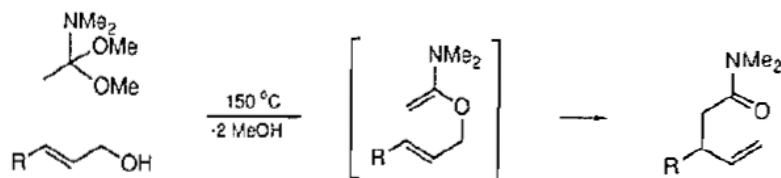


The reaction is widely employed for building up bi- and polyfunctional carbon chains, for example:

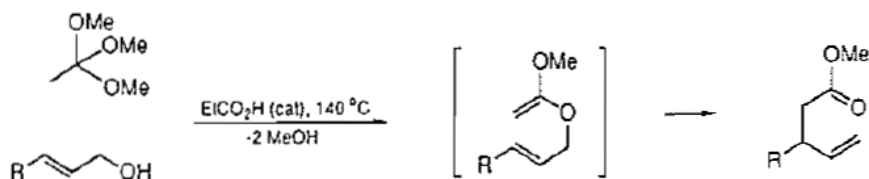
(1)  $\beta$ -Keto-esters to  $\gamma\delta$ -unsaturated ketones, e.g.



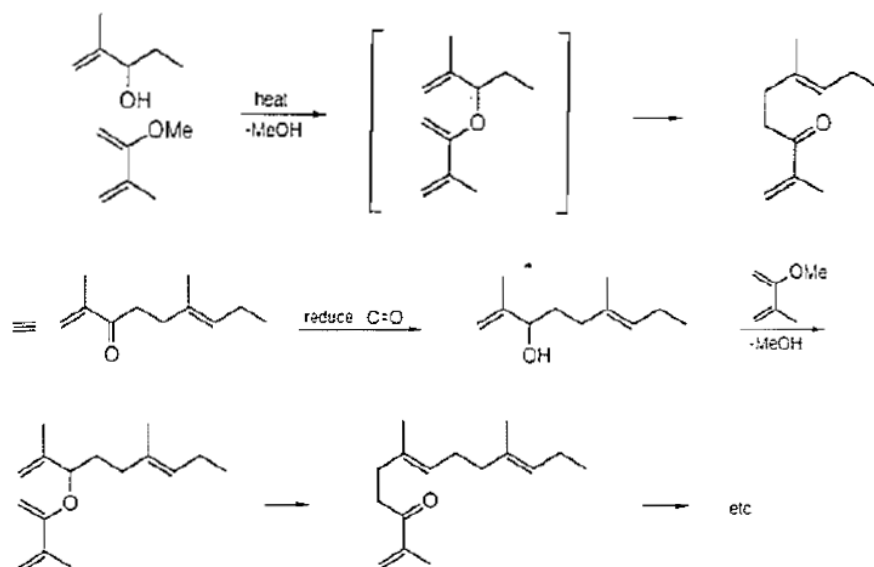
(2) Allyl alcohols to  $\gamma\delta$ -unsaturated amides (*Eschenmoser reaction*), e.g.



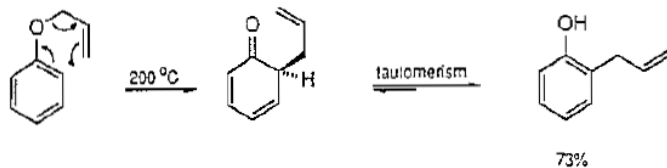
or  $\gamma\delta$ -unsaturated esters, e.g.



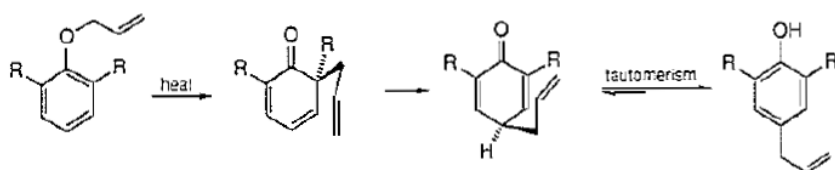
(3) Prenylation, e.g.



Claisen rearrangements of aryl allyl ethers also occur, e.g.

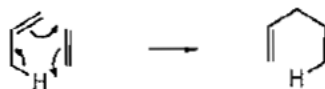


If both *ortho*-positions are substituted, the cyclohexadienone intermediate undergoes a second [3,3]-shift, giving a *p*-allylphenol:

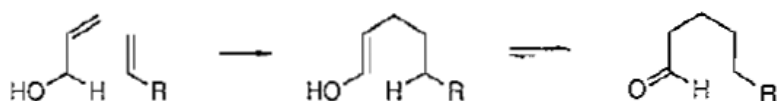


## Ene- Reactions

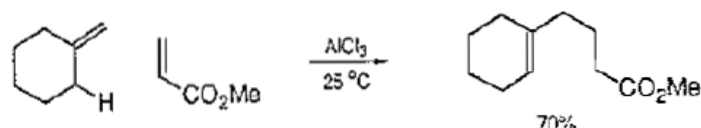
The ene-reaction is a reaction of an allylic compound with an alkene in a manner which resembles both cycloaddition and a [1,5]-sigmatropic shift of hydrogen, e.g.



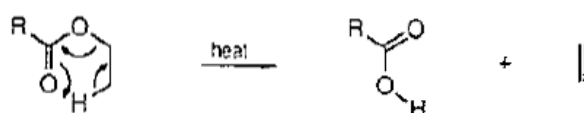
For example, allyl alcohols form aldehydes,



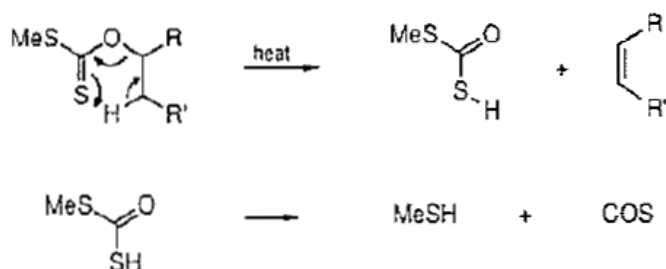
The reactions require higher temperatures than Diels–Alder reactions but occur faster with conjugated enones, especially (as in Diels–Alder reactions) with Lewis-acid catalysis, e.g. .



The reverse process also occurs, as in the pyrolysis of esters:

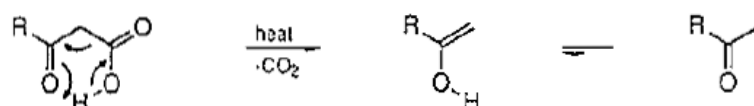


The temperature required for this reaction is high (300–500°C), which restricts its utility. Conditions are much milder, however, for the related *Chugaev reaction* in which a xanthate ester is heated at 100–200°C:



The synthetic value of the Chugaev reaction lies in the stereospecificity which its concertedness confers.

The ready decarboxylation of  $\beta$ -keto-acids has been shown to occur analogously, e.g.



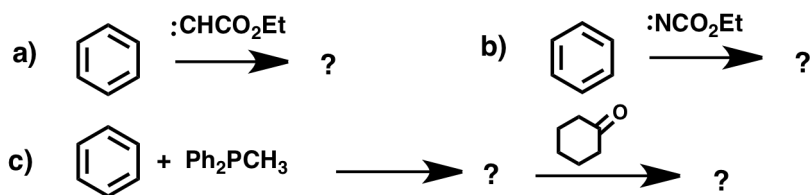
The *Cope reaction* is a related pericyclic reaction of amine oxides which involves a five-membered cyclic transition state. It occurs under mild conditions and is useful in the generation of non-conjugated polyenes, e.g.



## **Class Tests**

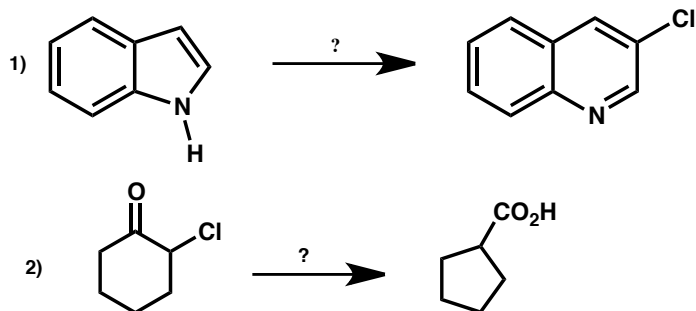
### Class Test:1

Write products of following reactions:



### Class Test:2

Write down mechanism of following reactions:



### Class Test:3

Write a note on angle strain of benzyne molecular structure and how does it effect on chemical reactivity?

## *Assignments*

Solving problems at page number 951 (10.1 to 10.20) of “Francis A. Carey, Richard J. Sundberg, **2007**, 5<sup>th</sup> Edition, Advanced Organic Chemistry Part A: Structure and Mechanism, Springer- Verlag Berlin Heidelberg” with the help of cited references.



## **Class Presentations**

## **Topics for Presentations**

**(MSc 3<sup>rd</sup> Semester)**

1.	Bushra Shabbir	Reactive Intermediates and their Role in Organic Chemistry
2.	Aiman Javeria	Structure and Formation of Carbocations in Organic Chemistry
3.	Asma Gulzar	Carbocations in Organic Syntheses
4.	Rabia Zakir	Structure and Formation of Carbenes in Organic Chemistry
5.	Danish Ali	Carbenes in Organic Syntheses
6.	Sana Afzal	Structure and Formation of Nitrenes in Organic Chemistry
7.	M. Naveed Hameed	Nitrenes in Organic Syntheses
8.	Muhammad Mujahid	Structure and Formation of Benzyne
9.	M. Naveed Irshad	Benzyne in Organic Syntheses
10.	Amina Noreen	Regioselectivity of Mono- and Di-substituted Benzyne

**Mid-Semester/Final Exam Question Paper**

# The Islamia University of Bahawalpur


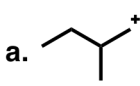
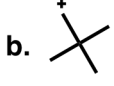
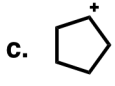
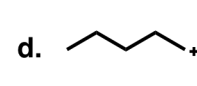
## Department of Chemistry



### MSc (Semester III)- Course (CHEM-22341) Organic Chemistry; Mid Term Examination

Total Marks 30	Time Allowed: 75 min
<b>NOTE:</b> Time allowed will be strictly observed. You will have to hand over answer sheet (MCQs) after 20 min and before getting the next part of the question paper and its answer sheet.	
Name of the Candidate and Roll No.	

#### PART-I (MCQs) Pick the best answer (Marks 10)

- Carbenes can be generated from:-  
a.  $\alpha$ -Elimination      b. Hydrazone      c. Ylide      d. All of these
- Singlet carbene is:-  
a. Electrophile      b. Nucleophile      c. Ambiphilic      d. None of these
- Which of the following carbocations provides this carbocation   
a.       b.       c.       d. 
- Hybridization in singlet carbene is:  
a.  $sp^3$       b.  $sp^2$       c.  $sp$       d.  $sd^3$
- What is **NOT TRUE** about triplet nitrene?  
a. paramagnetic      b. diamagnetic      c.  $sp$  hybridized      d.  $2S+1=3$
- In general.....groups are present in singlet carbene?  
a. Bulky      b. Acidic      c. +I (inductively  $e^-$  donating)      d. -I (inductively  $e^-$  withdrawing)
- What is **TRUE** about reactivity of triplet carbene?  
a. diradical mechanism      b. stereospecific      c. concerted      d. both b & c
- What is **NOT TRUE** about reactivity of singlet nitrene?  
a. concerted      b. stereospecific      c. diradical mechanism      d. both a & b
- The structure of benzyne was determined by:  
a. Georg Wittig      b. John D. Robert      c. F. W. Bergstrom      d. J. F. Bunnett
- Regioselectivity of unsymmetrical arynes mainly depends on:  
a. Inductive effect of R      b. Mesomeric effect of R      c. Steric effect of R      d. both c & b



**The Islamia University of Bahawalpur**  
**Department of Chemistry**

**MSc (Semester III)- Course (CHEM-22341)**  
**Organic Chemistry; Mid Term Examination**

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**PART-II**

**(Marks 10)**

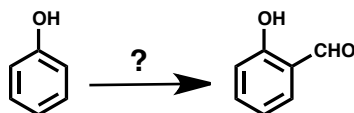
**Q. No. 2      Write short answers to following questions**

1.      Write key differences carbanions and carbocations. (2 marks)
2.      Write any 02 methods of carbenes generation (2 marks)
3.      Write any 02 methods of nitrene generation (2 marks)
4.      Write any 02 methods of benzyne generation (2 marks)
5.      How to overcome undesirable side products while synthesizing benzyne from aryl halides with strong bases? (2 marks)

**PART-III**

**(Marks 10)**

1.      Write a note on the hybridization in carbenes, nitrenes and benzyne (6 marks)
2.      Account for the following: (4 marks)
  - i)      Show how benzyne react in electrophilic reactions.
  - ii)     Write mechanism of formation of following product:



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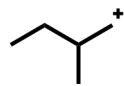



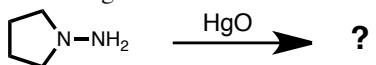

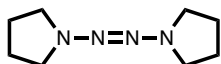
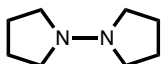
### MSc (Semester III)- Course (CHEM-22341) Organic Chemistry; Final Term Examination

<b>Total Marks 50</b>	<b>Time Allowed: 120 min</b>
<b>NOTE:</b> Time allowed will be strictly observed. You will have to hand over answer sheet (MCQs) after 30 min and before getting the next part of the question paper and its answer sheet.	
<b>Name of the Candidate and Roll No.</b>	

#### **PART-I (MCQs) Pick the best answer**

**(Marks 20)**

- ONE** is **WRONG** about the theory of Photochemistry
  - Initially the molecule is present in GS (Ground state) which then energized to ES (excited state)
  - The energy of the product is always higher than that of the ES
  - The energy of the product may be higher than that of reactant
  - The excited state is also called the transition state
- Intramolecular photochemical reaction that involves abstraction of  $\gamma$ -hydrogen is called:
  - Norrish Type I
  - Diels Alder
  - Sigmatropic Rearrangement
  - Norish Type II
- A reaction in which a conjugated molecule forms two single bonds from terminal atoms of the conjugated system to a single atom on another molecule to give a cyclic adduct is called:
  - Diels Alder
  - Electrocyclic
  - Cheletropic
  - Sigmatropic rearrangement
- ONE** among the following is **TRUE** for the Pericyclic Reactions
  - These reaction cannot be completed without free radical or ionic intermediate
  - The reactions are completed through concerted mechanism (single step reactions)
  - These reactions are mostly affected by the use of solvents or catalysts
  - These reactions love the involvement of electrophilic or nucleophilic reagents
- All are **WRONG** for Electrocyclic Reactions **Except:**
  - Intermolecular cyclization takes place through the displacement of electron in the compound
  - The Con-rotatory motions, both the terminal rotate anti-clockwise rotation
  - There is no control of stereochemistry during these reactions
  - In these reactions, shuffling of electrons takes place and terminal rotations result into cyclization
- ONE** is **TRUE** for Norrish Type Reactions in Photochemistry
  - These reactions stand only for alkenes
  - These reactions give only the cyclic product
  - Only the carbonyl compounds undergo these reactions
  - None of these
- Carbenes can be generated from:-
  - $\alpha$ -Elimination
  - Hydrazone
  - Ylide
  - All of these

8. Singlet carbene is:-  
 a. Electrophile      b. Nucleophile      c. Ambiphilic      d. None of these
9. Which of the following carbocations provides this carbocation 
- a.       b.       c.       d. 
10. Carbenes are:  
 a. acidic, trivalent species      b. neutral, divalent species      c. basic, monovalent species      d. a & c
11. Hybridization in singlet carbene is:  
 a.  $sp^3$       b.  $sp^2$       c.  $sp$       d.  $sd^3$
12. What is **NOT TRUE** about singlet carbene?  
 a. paramagnetic      b. diamagnetic      c. no signal in esr      d.  $2S+1=1$
13. What is **NOT TRUE** about triplet nitrene?  
 a. paramagnetic      b. diamagnetic      c.  $sp$  hybridized      d.  $2S+1=3$
14. In general.....groups are present in singlet carbene?  
 a. Bulky      b. Acidic      c. +I (inductively  $e^-$  donating)      d. -I (inductively  $e^-$  withdrawing)
15. What is **TRUE** about reactivity of triplet carbene?  
 a. diradical mechanism      b. stereospecific      c. concerted      d. both b & c
16. What is **NOT TRUE** about reactivity of singlet nitrene?  
 a. concerted      b. stereospecific      c. diradical mechanism      d. both a & b
17. What is true about carbanions?  
 a. Complete octet      b. Diamagnetic      c. Paramagnetic      d. both a & b
18. N-Nitrosomethyl urea is equivalent to:  
 a. Ylides      b.  $CH_2N_2$       c. Oxiranes      d. All
19. What is the right product of following reaction?  
  
 a.       b.       c.       d. None
20. *ortho*-Formylation of phenols involves:  
 a. carbenes      b. carbocations      c. carbanions      d. None



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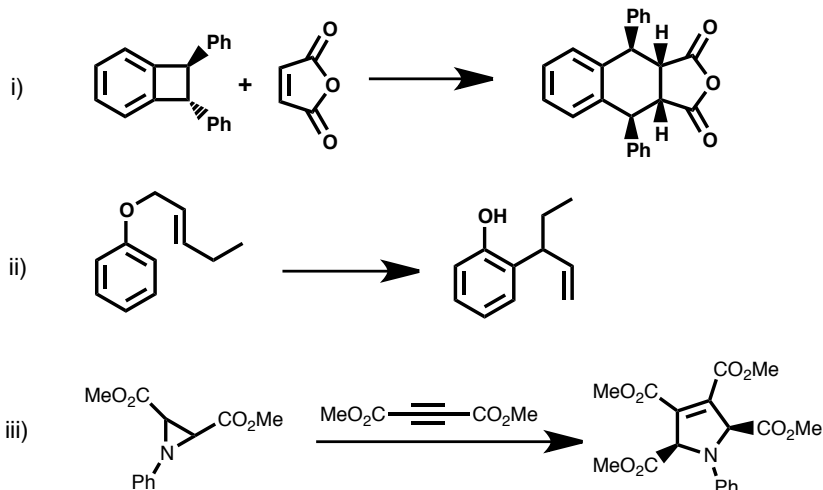
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### PART-II

(Marks 14)

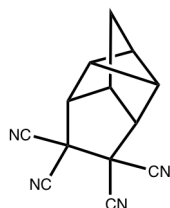
**Q. No. 2** Write short answers to following questions

1. Write key differences between Cope rearrangement and Claisen rearrangement (2 marks)
2. How would you describe an Inverse Demand for Diels Alder Reaction? (2 marks)
6. During the 2+2 cycloaddition reaction when mode of reaction is photochemical, it gave symmetry allowed product. How? (2 marks)
7. Rationalize the formation of: (2+2+2 marks)



5. How would you employ pericyclic reaction in the synthesis of following?

(2 marks)







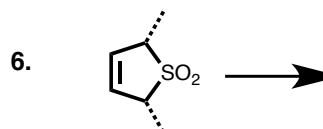
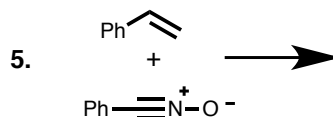
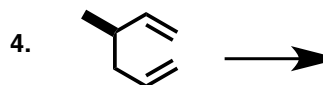
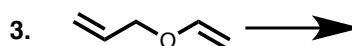
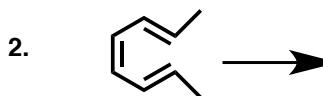
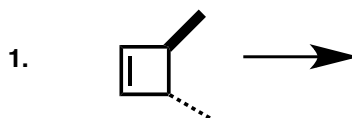
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**PART-III**

**(Marks 16)**

1. Write a note on photophysical processes with special emphasis on Florescence and Phosphorescence. (4 marks)
2. Draw the structure of the chief products of following thermal reactions:- (6 marks)



3. How regio- and stereochemistry is controlled in Diels Alder reactions? (3 marks)
4. Rationalize formation of less stable *endo* product that predominates in following reaction: (3 marks)

