PERICYCLIC REACTIONS

PART-3, PPT-14, SEM-5, CC-12 Cycloaddition Reaction I

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Cycloaddition Reaction I CONTENTS (PART-3)

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Theory of Cycloadditions and Cycloreversions

- In order to derive the selection rules for one type of simple twocomponent cycloaddition, woodward and Hoffmann introduced the terms *suprafacial* (*supra; subscript s*) and *antarafacial* to indicate geometrical relationship of the bonding (or fission) mode.
- A *suprafacial* process is one in which bonds made or broken lie on the same face of the system undergoing reaction. For example, in an ethylenic (A) or *cisoid* diene system (B), formation of bonds in the senses indicated by the arrows takes place in a *suprafacial* manner. These are illustrated in Figure 1.



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Theory of Cycloadditions and Cycloreversions

• The alternative, *antarafacial (antara; subscript a)* processes one in which the newly formed or broken bonds lie on opposite faces of the reacting systems. For example, in an ethylenic (C) or *cisoid* diene system (D), formation of bonds in the senses indicated by the arrows takes place in an *antarafacial* manner. These are illustrated in Figure 2.



• There are, in fact, four possible modes of combination of the termini of two unlike components in a cycloaddition reaction. Each mode has a characteristic stereochemical consequence, displayed in Figure 3.

Theory of Cycloadditions and Cycloreversions



• When the two reactants are identical the supra, antara and the antara, supra processes arc indistinguishable and give the same product. Also, for each process there are two possible cases, one producing the *endo* product, the other the *exo*. The diagrams in **Figure 3** are purely schematic, and do not reflect the actual geometry of the *transition states*.

Analysis of Cycloaddition Reactions and Selection Rules

- In order to analyze cycloaddition reactions, the possible geometric or stereochemical modes in terms of *suprafacial/antarafacial* components are determined. Let us consider, the Diels-Alder reaction between a diene and a dienophile to illustrate the stereochemical features of cycloaddition reactions. The diene is a $_{\pi}4$ component and the dienophile is a $_{\pi}2$ component. The type of electron (π) is usually indicated as a subscript to the left of the electron number.
- Assuming bond-formation on the same face or opposite faces of the diene and dienophile, there are four possible stereochemical modes of diene/dienophile interactions as shown in Figure 4. These are designated as: (A) *supra/supra* or [_π4_s+_π2_s], (B) *supra/antara* or [_π4_s+_π2_a], (C) *antara/supra* or [_π4_a+_π2_s] and (D) *antara/antara* or [_π4_a+_π2_a].

Analysis of Cycloaddition Reactions and Selection Rules



• The developing new σ bonds clearly identify a diene or a dienophile component to be *supra* or *antara*. This is clearly pictured in Figure 4.

Analysis of Cycloaddition Reactions and Selection Rules

- A *suprafacial* or *antarafacial* component is specified by electron number, type of electron (left subscript to electron number) and *suprafacial* or *antarafacial* (*s* or *a* as right subscript to electron number).
- As such, the *suprafacial* diene component is designated as ${}_{\pi}4_{s}$, and the *suprafacial* dienophile component is designated as ${}_{\pi}2_{s}$. The *supra/supra* mode of the reaction is then represented as $[{}_{\pi}4_{s}+{}_{\pi}2_{s}]$. The other modes are designated similarly.
- In general, for any two-component cycloadditions, four stereochemical modes (*supra/supra*, *supra/antara*, *antara/supra* and *antara/antara*) are possible. Geometrically, a particular mode may be highly favourable, or difficult to achieve but not impossible, or very unfavourable. A symmetry-allowed but geometrically impossible mode of a pericyclic reaction would not occur in reality.

Application of the Woodward-Hoffmann Generalized Rules

• The application of the Woodward-Hoffmann generalized rules were illustrated taking a representative case from (4n+2)- and (4n)-electron cycloadditions (Figure 5).



- Of the four possible stereochemical modes of the Diels-Alder reaction, the $[{}_{\pi}4_{s}+{}_{\pi}2_{s}]$ mode is most favourable geometrically as it requires an easy parallel approach of the diene and the dienophile. This parallel approach for the *supra/sup*ra mode leads to a *boat* geometry of the TS (Figure 6).
- For the purpose of analysis, counting of only $(4q+2)_s$ and $(4r)_a$ components is needed. There is no need to count $(4q+2)_a$ and $(4r)_s$ components, if any.



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- Then, the total number of $(4q+2)_s$ and $(4r)_a$ components, i.e., $[(4q+2)_s+(4r)_a]$ are calculated (vide Figure 6). If the total is an odd number, the reaction is symmetry-allowed thermally, and when the total is zero or an even number, the reaction is symmetry-allowed photochemically. Therefore, $(4n+2) \pi$ -electron cycloaddition is a thermally allowed process under (*s*,*s*) mode.
- It should be noted that the type of electrons $(\pi, \sigma \text{ or } \omega)$ does not matter in the analysis. For the sake of simplicity, some countable and not countable components are given in **Table 1**.

Table 1: Countable and Non-countable Components in		
Cycloaddition Reactions		
Countable Component	Non countable Component	

Countable Component	Non-countable Component
$(4q+2)_{s}: 2_{s}, 6_{s}, 10_{s}, 14_{s}$	$(4q+2)_{a}: 2_{a}, 6_{a}, 10_{a}, 14_{a}$
$(4r)_{a}: 0_{a}, 4_{a}, 8_{a}, 12_{a}$	$(4r)_{s}: 0_{s}, 4_{s}, 8_{s}, 12_{s}$
(taking q, r = 0, 1, 2, 3)	
(taking q, r = 0, 1, 2, 3)	

- The analysis of the $[_{\pi}4_{s}+_{\pi}2_{s}]$ mode shows that $[(4q+2)_{s}+(4r)_{a}] = 1$ (odd number), and hence the process is symmetry-allowed thermally (Figure 6). Almost all thermal Diels-Alder reactions proceed through this symmetry-allowed and geometrically favourable $[_{\pi}4_{s}+_{\pi}2_{s}]$ mode. In general, the *supra/supra* mode is thermally allowed for cycloadditions involving '4n+2' electrons.
- The other modes of the Diels-Alder reaction can be analyzed in the similar manner. For the $[{}_{\pi}4_{a} + {}_{\pi}2_{a}]$ process, $[(4q+2)_{s} + (4r)_{a}] = 0+1 = 1$ (odd), and hence symmetry-allowed thermally. This *antara/antara* interaction is very difficult to achieve geometrically (Case D, Figure 4) and examples are rare but known.

- The $[_{\pi}4_{a}+_{\pi}2_{a}]$ mode gives $[(4q+2)_{s}+(4r)_{a}] = 0$, and is, therefore, symmetry-forbidden thermally but symmetry-allowed photochemically.
- The $[_{\pi}4_{a}+_{\pi}2_{s}]$ mode is also photochemically allowed because $[(4q+2)_{s}+(4r)_{a}] = 2$ (even number). These photochemically allowed modes are geometrically quite unfavourable and photochemical Diels-Alder reactions are indeed rare.
- The $[_{\pi}4_{s}+_{\pi}2_{s}]$ Diels-Alder reaction can alternatively be represented as the $[_{\pi}2_{s}+_{\pi}2_{s}+_{\pi}2_{s}]$ or $[_{\pi}2_{s}+_{\pi}2_{a}+_{\pi}2_{a}]$ reaction. This can be explained as the following:
- In the $[{}_{\pi}4_{s}+{}_{\pi}2_{s}]$ description, the diene is regarded as a single ${}_{\pi}4$ component. However, for the purpose of analysis, each π bond of the diene can be artificially treated as a separate ${}_{\pi}2$ component.

The Diels-Alder Reaction

• The analysis then involves three π^2 components (two from diene and one from dienophile), which provide alternative representations of the same *supra/supra* addition of diene and dienophile. The orbital interactions in this three-component analysis indicate developing overlaps in the TS for the formation of two σ bonds as well as one π bond as shown below.



• The analyses (Figure 7) show that $[_{\pi}2_{s}+_{\pi}2_{s}+_{\pi}2_{s}]$ and $[_{\pi}2_{s}+_{\pi}2_{a}+_{\pi}2_{a}]$ representations are symmetry-allowed thermally.

'4n' Electron System:[2+2] Cycloaddition of Alkenes

- The [2+2] cycloaddition of two alkenes is a 4-electron cycloaddition that forms a cyclobutane (Figure 5B). For the prototype reaction between two ethylene molecules, *supra/antara* and *antara/supra* modes are equivalent. Therefore, there will be three distinct stereochemical modes (*supra/supra*, *supra/antara* and *antara/antara*) for the prototype reaction. The orbital picture representations of these modes and their analyses are shown in Figure 8.
- It is seen that the $[_{\pi}2_{s}+_{\pi}2_{s}]$ and $[_{\pi}2_{a}+_{\pi}2_{a}]$ processes are symmetry allowed photochemically. The $[_{\pi}2_{s}+_{\pi}2_{s}]$ mode is highly favourable geometrically by the parallel approach of the two components and allows photochemical cycloaddition of alkenes to take place readily.



• In general, the *supra/supra* mode is photochemically allowed for cycloadditions involving 4n electrons. However, the *antara/antara* interaction for two small π components is geometrically impossible to achieve and the photochemical cycloaddition of alkenes cannot occur through this mode.

'4n' Electron System:[2+2] Cycloaddition of Alkenes

- As shown in **Figure 8**, the $[_{\pi}2_{s}+_{\pi}2_{a}]$ mode is symmetry-allowed thermally. The geometric requirement for this interaction is attained when the two components can approach in an *orthogonal* fashion and thermal $[_{\pi}2_{s}+_{\pi}2_{a}]$ cycloaddition can take place.
- The Woodward-Hoffmann selection rules for two-component cycloadditions are obtained as shown in **Table 2**. The selection rules clearly predict which cycloadditions are symmetry allowed thermally or photochemically. A thermally allowed process is photochemically forbidden, and vice versa.

Table 2: Selection Rules for two-component Cycloadditions			
Total Number of Electrons	Thermally Allowed	Photochemically Allowed	
4n+2	supra/supra	supra/antara	
	antara/antara	antara/supra	
4 n	supra/antara	supra/supra	
	antara/supra	antara/antara	

- Analysis of a *retro*-cycloaddition includes σ components, besides the π component. To illustrate, let us consider the *retro*-Diels-Alder reaction. Here the reactant cyclohexene possesses three components comprising two σ bonds and one π bond.
- As the microscopic reverse of the forward reaction, the *retro*-Diels-Alder reaction also proceeds through the formation of *boat* TS. The developing overlaps (dashed lines) in the *boat* TS with respect to formation of three new π bonds (two for 'diene' and one for 'ene') are shown in **Figure 9**. Based on the developing overlaps, the two σ and one π components can be designated as *supra* or *antara*.

• As shown in Figure 9, two inner lobes of both σ bonds are involved in the interactions, and hence both σ components are *supra*, that is, ${}_{\sigma}2_{s}$ and ${}_{\sigma}2_{s}$. The π component is also supra (${}_{\pi}2_{s}$) as two lower lobes on the same face of the π bond are involved. The analysis then shows that the *retro*-Diels-Alder reaction is a thermally allowed [${}_{\pi}2_{s}$ + ${}_{\sigma}2_{s}$ + ${}_{\sigma}2_{s}$] reaction.



- The lobe interactions in the TS may be shown in multiple ways for the allowed *retro*-Diels-Alder reaction. Figure 10A shows that lobe interactions for the formation of three π bonds involve two outer lobes of each σ bond and two upper lobes on the same face of the π bond. The designation is then also $[\pi 2_s + \sigma 2_s + \sigma 2_s]$, as in Figure 9.
- Another way of depicting lobe interactions is shown in Figure 10B. In this diagram, the interactions involve two inner lobes of one σ bond, the inner and outer lobes of the other σ bond, and the upper and lower lobes on the opposite faces of the π bond in the same TS geometry. The designation is now $[_{\pi}2_{a}+_{\sigma}2_{s}+_{\sigma}2_{a}]$, which is also thermally allowed.



- It should be noted that multiple versions of representation or designation can arise from more than one choice of lobe interactions in the same TS geometry, which do not indicate the different allowed pathways. A π bond orbital has four lobes (two upper and two lower) and a σ bond orbital too has four lobes (two inner and two outer).
- Out of four lobes, two lobes are needed to identify a component to be *supra* or *antara*, and therefore provide scope for multiple choices of two lobes in the interacting bond orbitals. The two designations $[_{\pi}2_{s}+_{\sigma}2_{s}+_{\sigma}2_{s}]$ and $[_{\pi}2_{a}+_{\sigma}2_{s}+_{\sigma}2_{a}]$ here indicate two representations or drawings of the same allowed pathway of the *retro*-Diels-Alder reaction.

- In a bimolecular process, all molecular orbitals of one component can interact with all molecular orbitals of the other component. Of these, the interaction of an occupied orbital with an unoccupied orbital leads to a net stabilization by lowering of energy (Figure 11A). The extent of stabilization is greater when the energies of the interacting orbitals are closer. Therefore, the predominant contribution to stabilization is effected by the interacting orbitals with the lowest energy separation.
- Evidently, this dominant interaction happens to be between the highest occupied molecular orbital (HOMO) of one component and the lowest unoccupied molecular orbital (LUMO) of the second component (Figure 11B). This HOMO/LUMO interaction is popularly known as the FMO interaction where HOMO and LUMO orbitals are called frontier orbitals.



The frontier orbital theory developed and named by Fukui is the most accessible theory to analyzing organic chemical reactions. For the two interacting components A and B, there are two possible frontier orbital pairs: HOMO_A/LUMO_B and HOMO_B/LUMO_A.

- In terms of FMO interactions, a cycloaddition reaction is allowed when the orbital interactions at the ends of the components indicate bonding interactions with the in-phase (same sign) overlap. If any one of the interactions is antibonding with an out-of-phase (different sign) overlap, the concerted process is forbidden. It is the orbital symmetry (not the size of coefficients) of frontier orbitals that decides the bonding/antibonding interaction.
- The analysis of the thermal $[_{\pi}4_{s}+_{\pi}2_{s}]$ Diels-Alder reaction by the FMO approach is shown in **Figure 12**. Here, the favourable interactions between the frontier orbital pairs, such as, HOMO_{diene}/LUMO_{dienophile} and LUMO_{diene}/HOMO_{dienophile} are shown. It is seen that both FMO interactions are bonding at the two ends of the diene and dienophile. The $[_{\pi}4_{s}+_{\pi}2_{s}]$ process is, therefore, thermally allowed.



• The other stereochemical modes of the Diels-Alder reaction can be analyzed similarly.

• The FMO analyses of thermal $[_{\pi}2_{s}+_{\pi}2_{s}]$ and $[_{\pi}2_{s}+_{\pi}2_{a}]$ cycloadditions are shown in **Figure 13.** The $[_{\pi}2_{s}+_{\pi}2_{s}]$ process is thermally forbidden due to an antibonding interaction (**Case A; Figure 13A**), whereas the $[_{\pi}2_{s}+_{\pi}2_{a}]$ process is thermally allowed (**Case B; Figure 13B**), but geometrically improbable as it involves strained TS.



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Photochemical Reactions in General

- In most bimolecular photochemical reactions, the first step is the photoexcitation of one component, usually the one with the chromophore which most efficiently absorbs the light. Typically, if a conjugated system of carbon atoms is present in one component, it can absorb a photon of relatively long wavelength, and in doing so an electron leaves the HOMO and arrives in the LUMO.
- The second step of the reaction, if it is bimolecular, is between the photochemically excited molecule and a second molecule, which may or may not be the same compound, in its *ground state*. For this kind of reaction, there will generally be two energetically profitable orbital interactions (**Figure 14**):
- 1. the interaction between the singly occupied π^* orbital of the excited molecule, labelled 'LUMO' and the LUMO of the molecule which is in its *ground state*; and

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Photochemical Reactions in General

- 2. the interaction of the singly occupied π orbital of the excited molecule, labelled 'HOMO' and the HOMO of the molecule which is in its *ground state*.
- Both the said interactions will usually be strong, because the interacting orbitals are likely to be close in energy. Partly for this reason, this step of a photochemical reaction is often very fast.
- Therefore, the important frontier orbitals in a photochemical reaction are HOMO/'HOMO' and LUMO/'LUMO'. 'HOMO' and 'LUMO' are associated with the excited molecule when it is in its *ground state*. Photochemical reactions often seem to do the opposite of what is expected of the equivalent thermal reaction. In the latter it is the HOMO/LUMO interactions which predominate in bond-making processes, and in the former it is HOMO/'HOMO' and LUMO/'LUMO' interactions.



• The $[_{\pi}2_{s}+_{\pi}2_{s}]$ cyclodimerization of ethylene is a photochemically allowed process. The frontier orbital approach can provide a suitable explanation for the allowed photochemical reaction. Since molecules in the *excited singlet state* have short lifetimes, the probability of two excited state molecules interacting one another is quite low.

- Consequently, photochemical cycloaddition results from the interaction of an *excited state* molecule with a *ground state* molecule.
- As shown in Figure 14, the most important interactions under photochemical conditions are π/π and π^*/π^* , each of which is energy-lowering. The π/π interaction is the HOMO/'HOMO' interaction, and π^*/π^* is the LUMO/'LUMO' interaction.
- It should be kept in mind that the *excited state* HOMO and LUMO, both are actually SOMO (Singly Occupied Molecular Orbital), are singly occupied. Thus, frontier orbital analysis for photochemical cycloaddition refers to HOMO/'HOMO' and LUMO/'LUMO' interactions.

• The FMO picture for the photochemical $[_{\pi}2_{s}+_{\pi}2_{s}]$ process is shown in Figure 15.



• Both HOMO/HOMO (actually HOMO/'HOMO') and LUMO/LUMO (actually LUMO/'LUMO') interactions involve bonding interactions and the $[{}_{\pi}2_{s} + {}_{\pi}2_{s}]$ reaction is, therefore, allowed under photochemical conditions. The FMO approach also gives the same predictions as obtained from other approaches, and leads to the same selection rules (Table 2).

- In the dimerization of an alkene under photochemical conditions combination of the *excited state* of one alkene with the *ground state* of another solves the symmetry problem.
- Mixing the two π orbitals leads to two molecular orbitals and two electrons go down in energy while only one goes up. Mixing the two π^* orbitals is also good, as one electron goes down in energy and none goes up. The result is that three electrons go down in energy and only one goes up. Bonding can occur. This is illustrated in Figure 14.