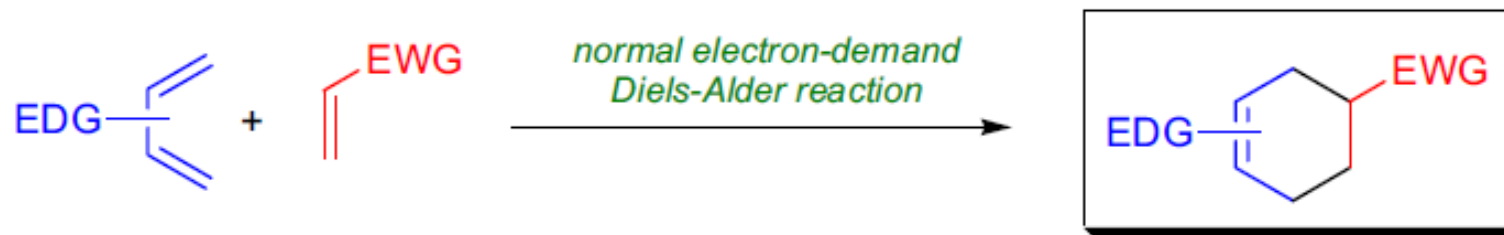


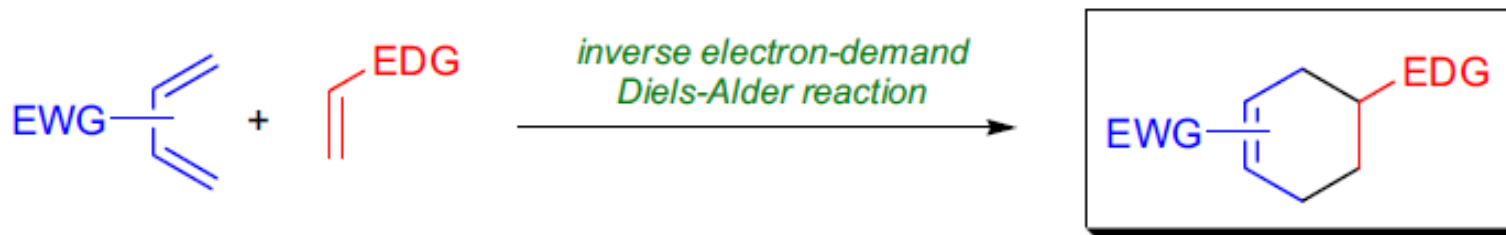
Name Reactions
Cycloaddition Reactions
(4+2)

Diels-Alder Cycloaddition

- **1928:** O. Diels and K. Alder
- The $[4\pi + 2\pi]$ cyclization of a diene and alkene to form a cyclohexene derivative is known as the Diels-Alder cycloaddition (D-A cycloaddition).
- The diene component is usually electron rich, while the alkene (dienophile) is usually electron poor and the reaction between them is called the **normal electron-demand D-A**
- When the diene is electron poor and the dienophile is electron rich then an **inverse electron demand D-A** cyclization takes place.



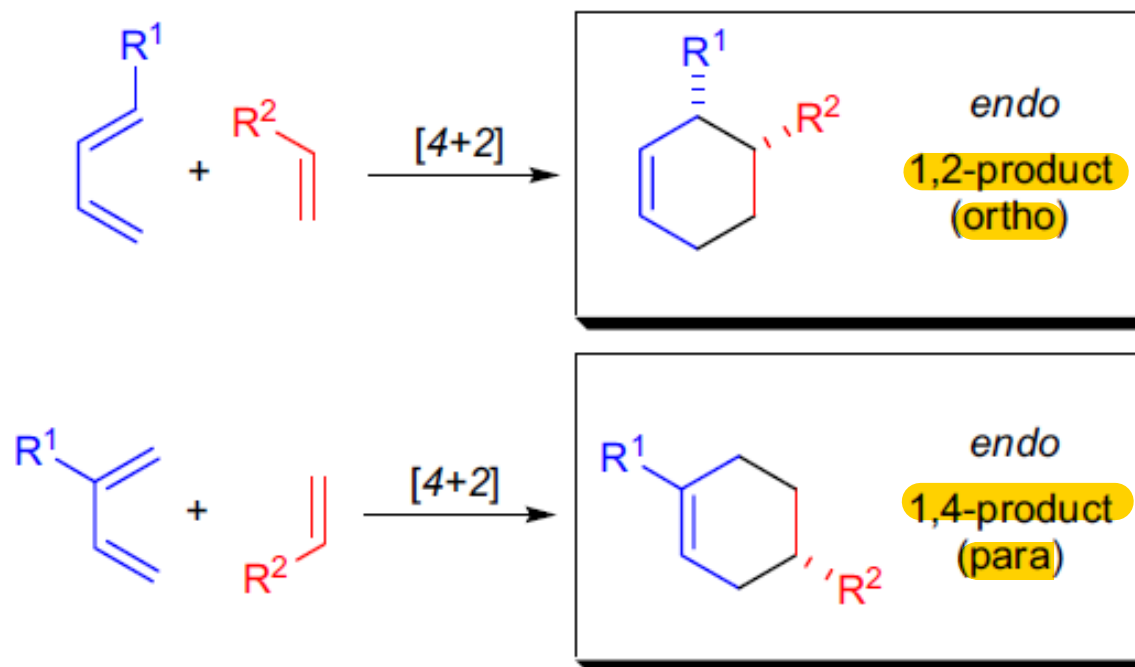
EDG (electron-donating group)
= alkyl, O-alkyl, N-alkyl, etc.



EWG (electron-withdrawing group) = CN, NO₂, CHO, COR, COAr, CO₂H, CO₂R, COCl etc.

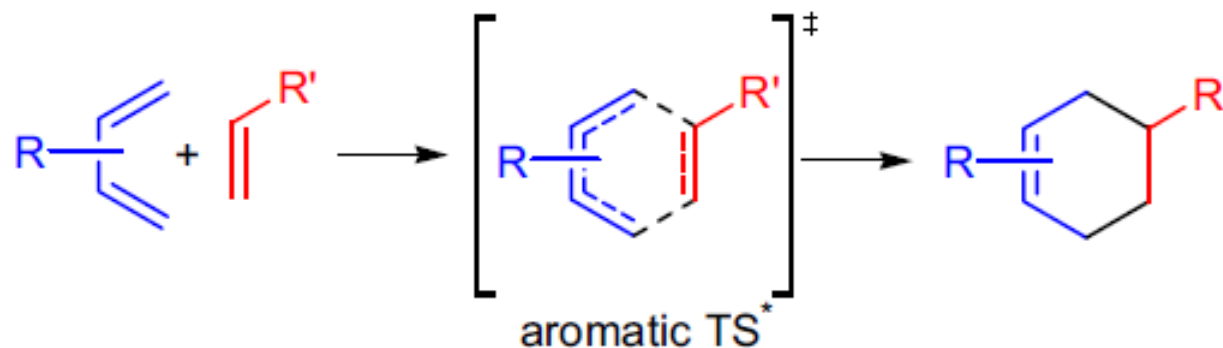
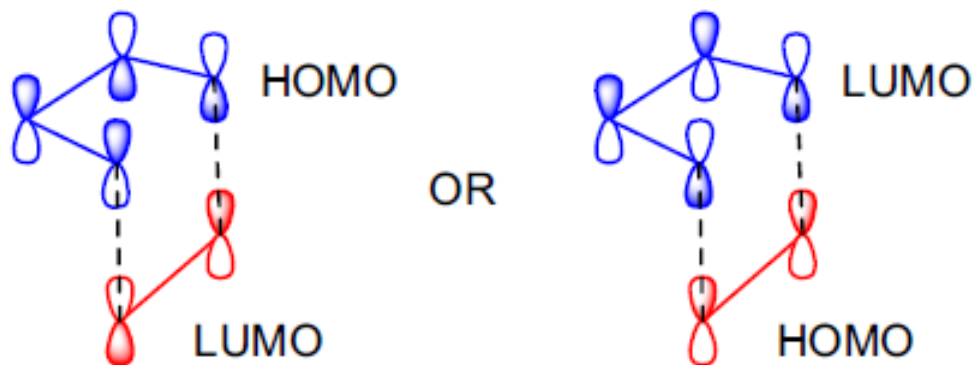
Diels-Alder Cycloaddition

- Besides alkenes, substituted alkynes, benzyne, and allenes are also good dienophiles.
- If one or more of the atoms in either component is other than carbon, then the reaction is known as the hetero-D-A reaction.
- In the retro-D-A reaction unsaturated six-membered rings break down to yield dienes and dienophiles
- the predominant product is the endo cycloadduct



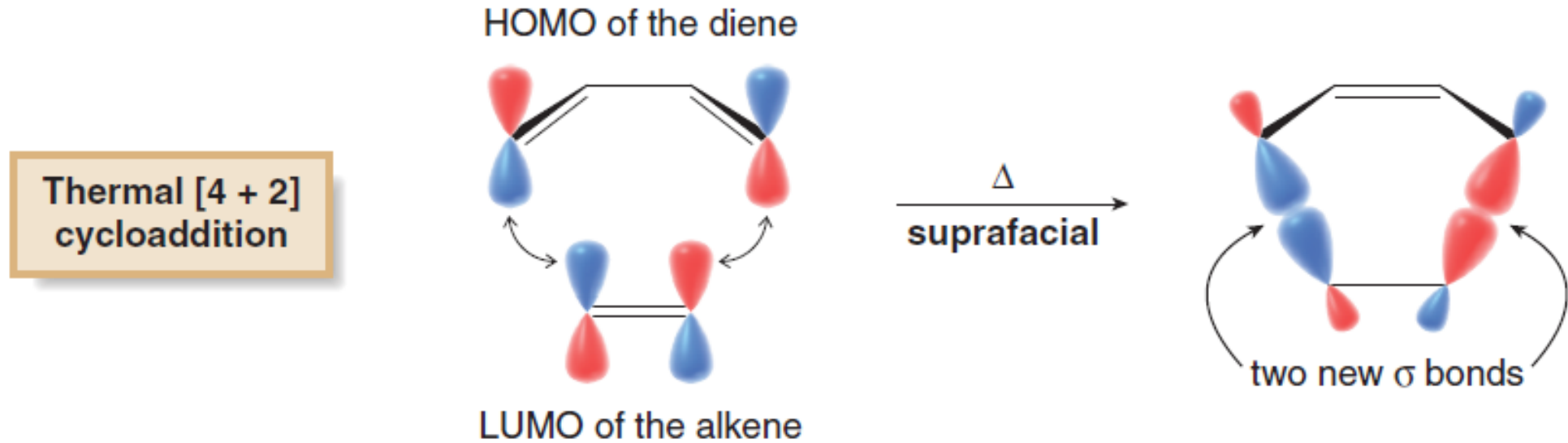
Diels-Alder Cycloaddition

- Mechanistically the D-A reaction is considered a concerted, pericyclic reaction with an aromatic transition state.
- The driving force is the formation of two new σ -bonds.



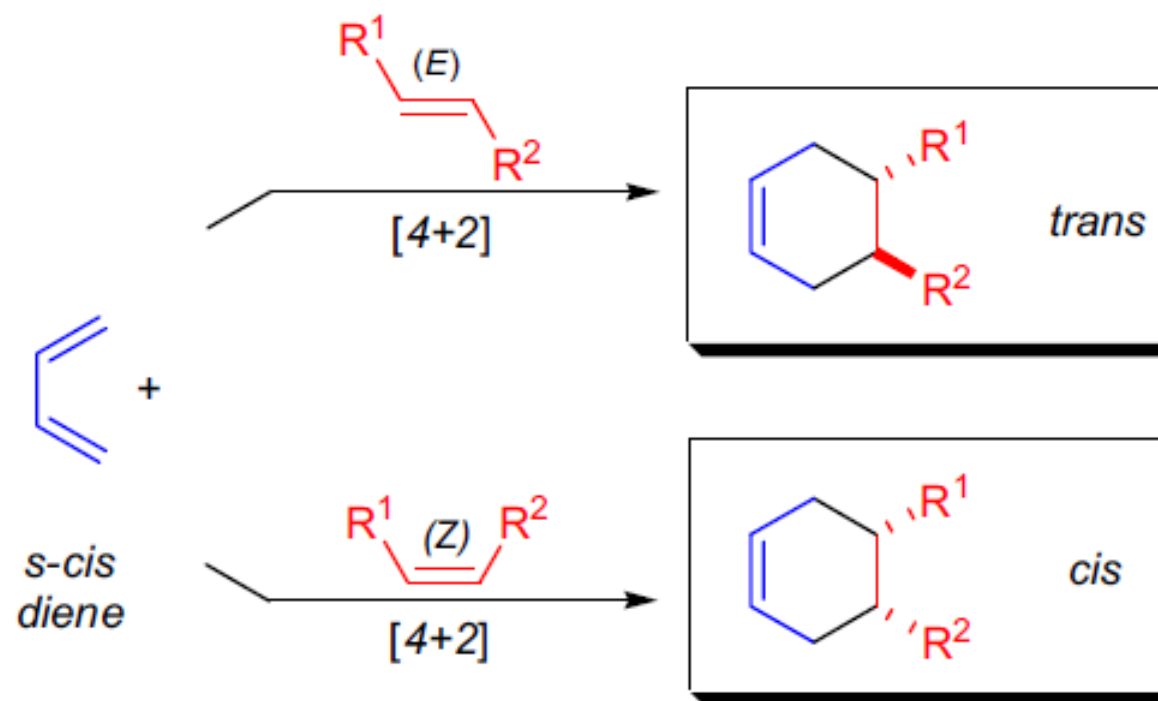
Diels-Alder Cycloaddition: Orbital Symmetry

- $[4 + 2]$ cycloaddition occurs readily by suprafacial reaction under thermal conditions.



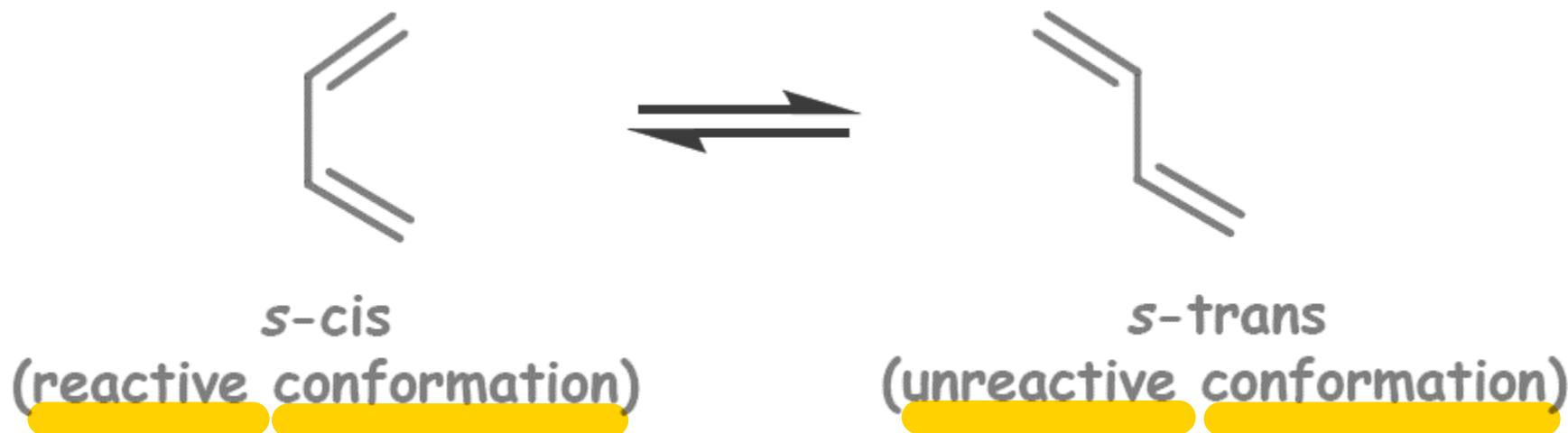
Diels-Alder Cycloaddition

- if a disubstituted cis (Z) alkene is used, the stereochemistry of the two substituents in the product will be cis and when an (E) alkene is used, the stereochemistry in the product will be trans; the stereochemical information (E or Z) in the diene is also transferred to the product



Diels-Alder Cycloaddition: Requirement of Diene

- Diene can be open chain or cyclic
- Diene should be electron rich and reactivity should be enhanced by electron donating group substituents
- The diene must adopt an s-cis conformation to be reactive

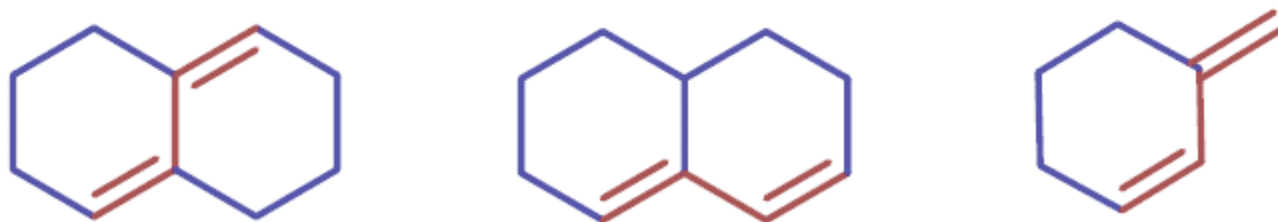


Diels-Alder Cycloaddition: Requirement of Diene

- Cyclic dienes which adopt s-cis conformation are very reactive

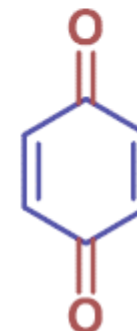
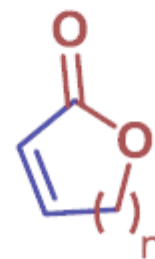
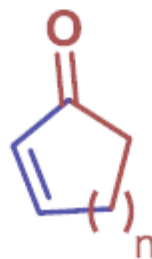
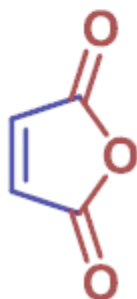
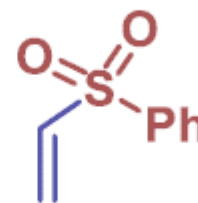
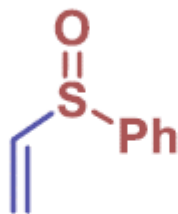
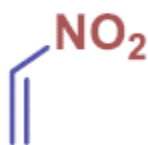
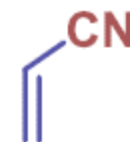
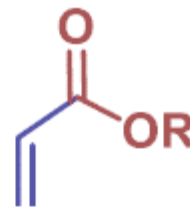
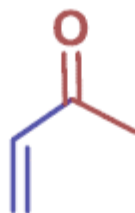
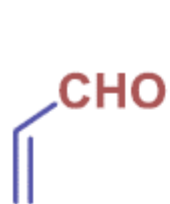


- Cyclic dienes which are permanently in s-trans conformation are unreactive in Diels-Alder reaction

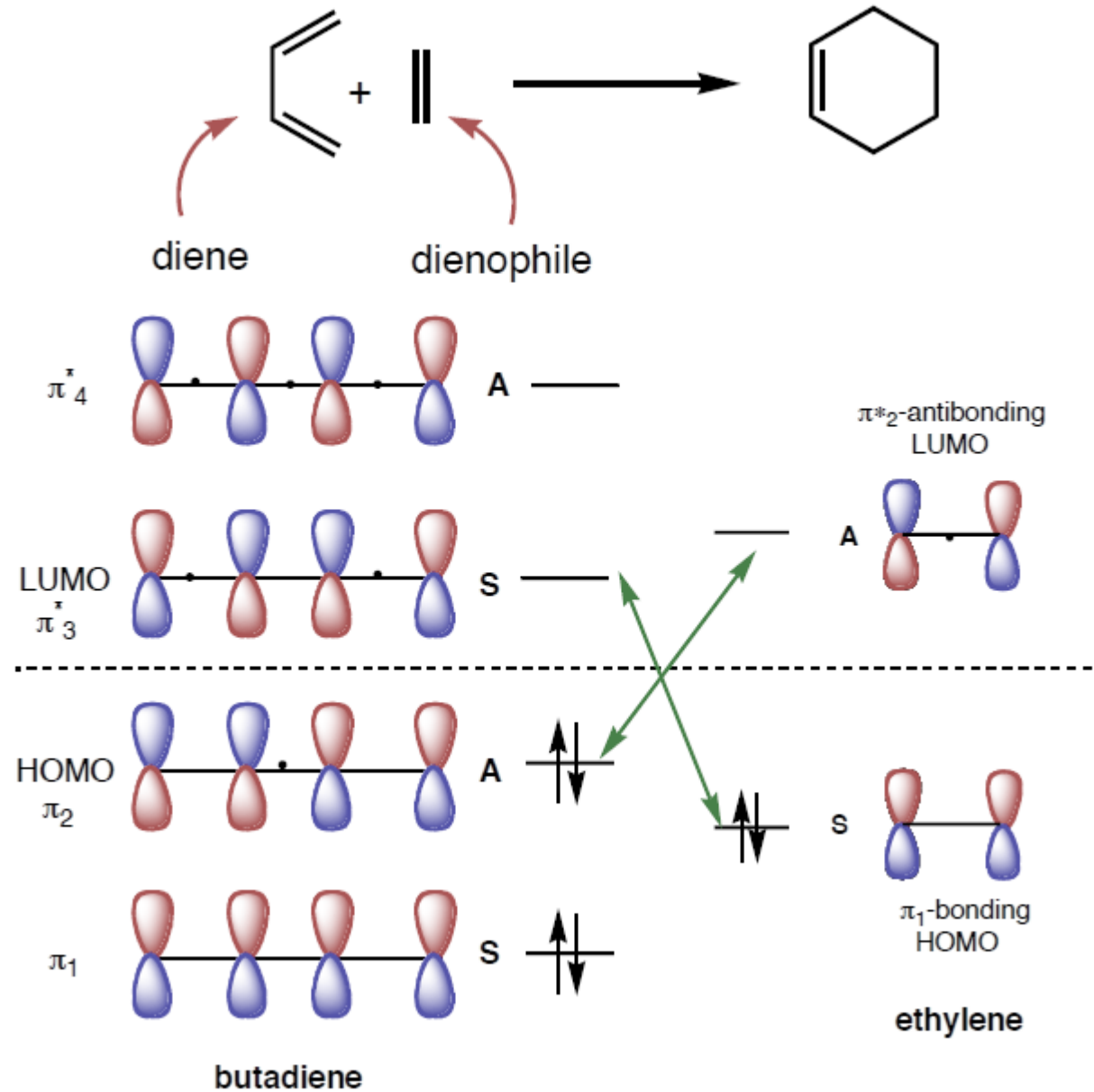


Diels-Alder Cycloaddition: Requirement of Dienophile

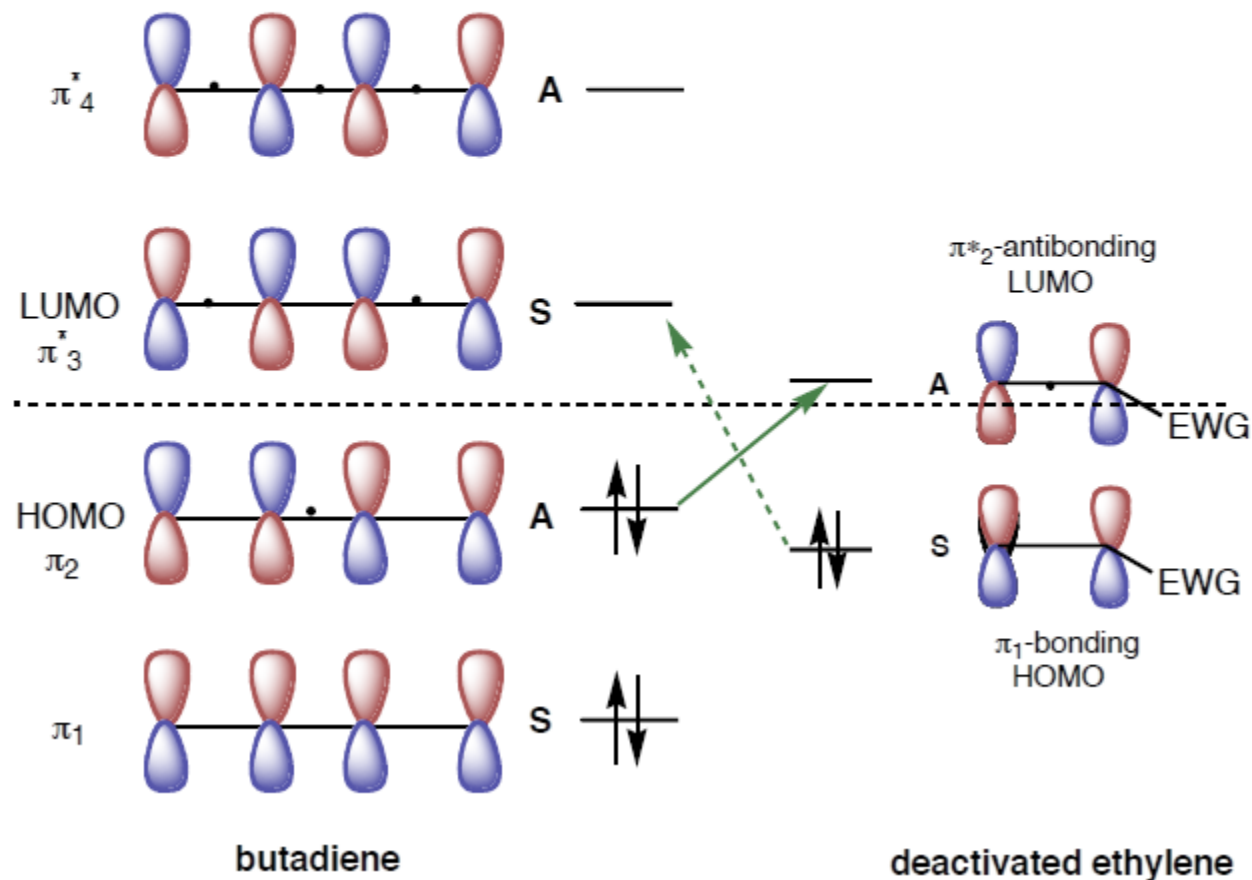
- Dienophile can be open chain or cyclic
- Dienophile should be electron deficient and reactivity should be enhanced by electron withdrawing substituents



Diels-Alder Cycloaddition: An allowed [4+2] Cycloaddition

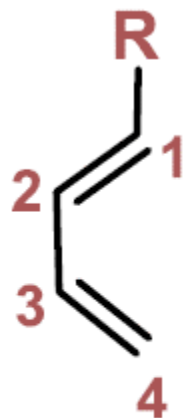


Diels-Alder Cycloaddition: Effect of EWG group

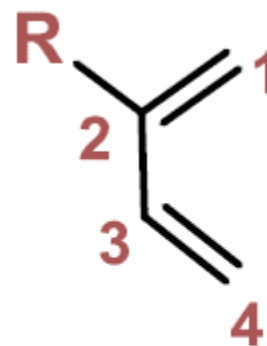


Diels-Alder Cycloaddition: 'Regioselectivity'

- For a mono-substituted diene, outcome of the product depends on the carbon atom where it is substituted
- Consider two classical cases, where the electron donating substituent could be present at carbon 1 or carbon 2



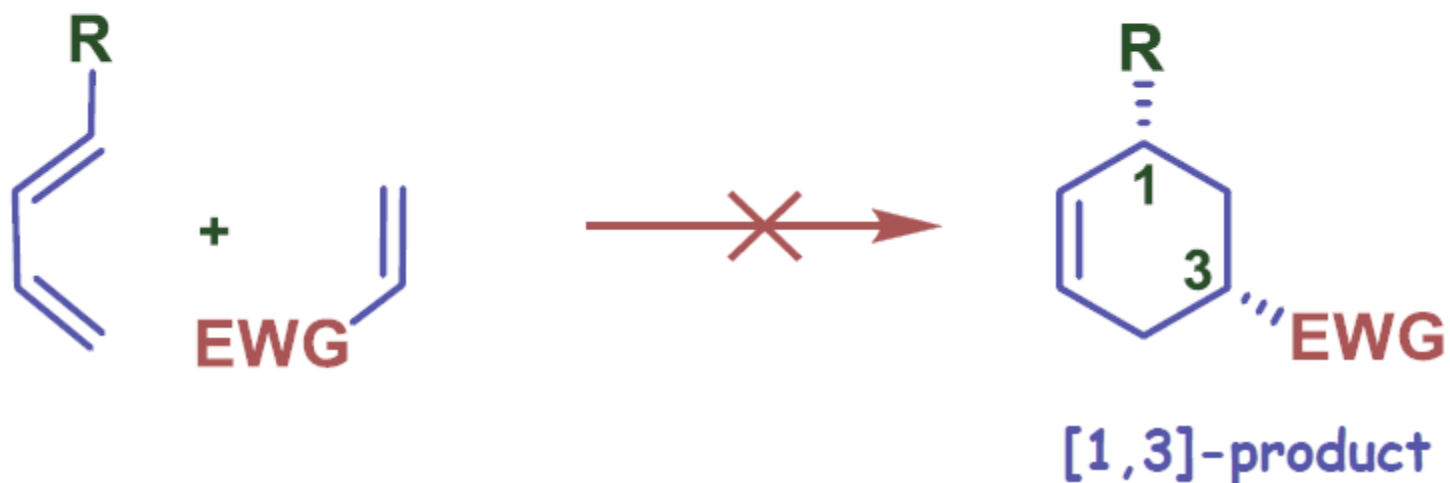
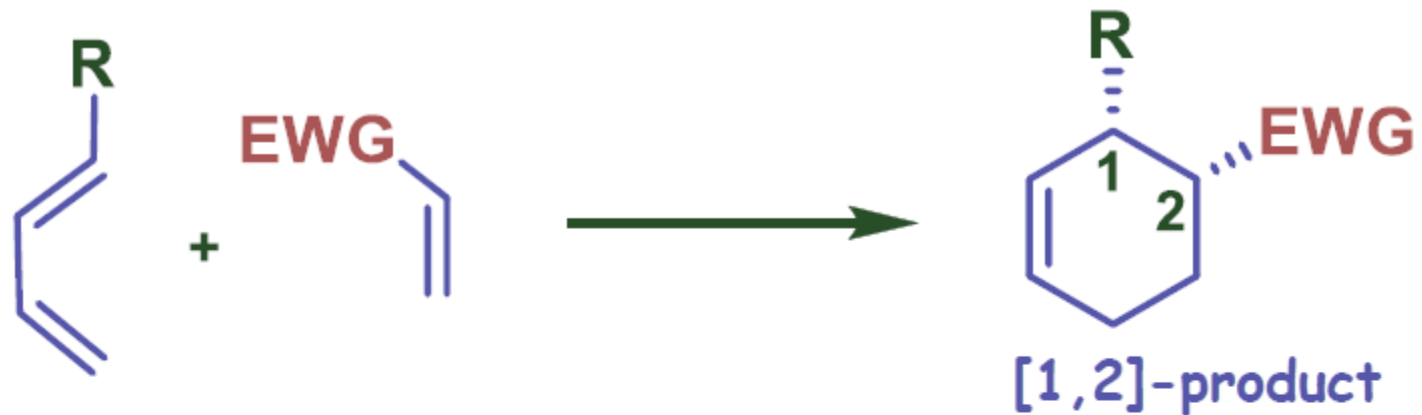
1-substituted diene



2-substituted diene

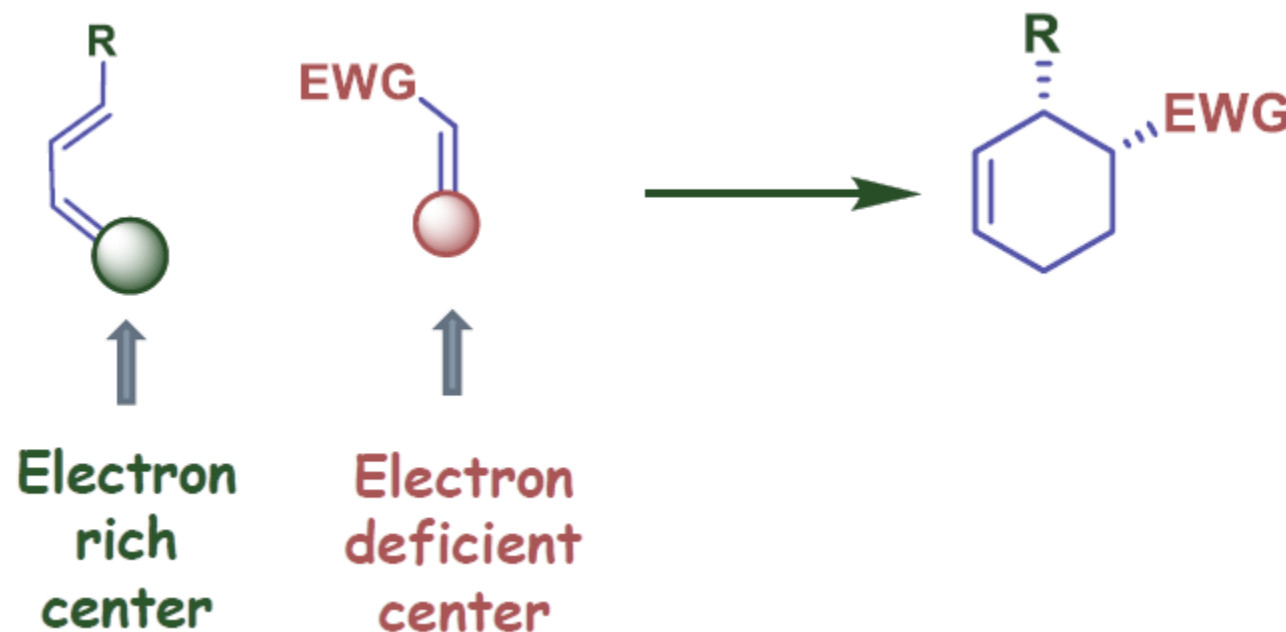
Diels-Alder Cycloaddition: 'Regioselectivity'

- 1-substituted diene react to give mainly [1,2]-product



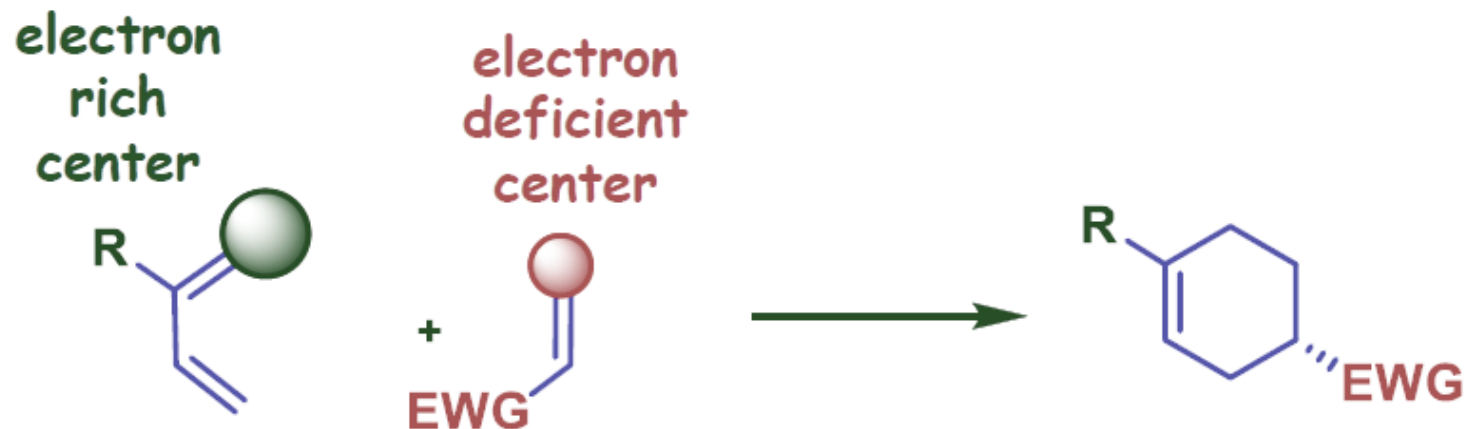
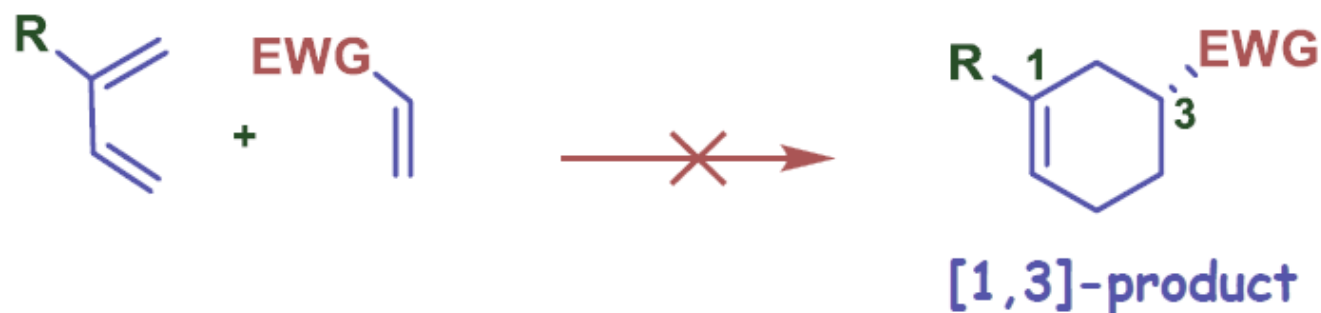
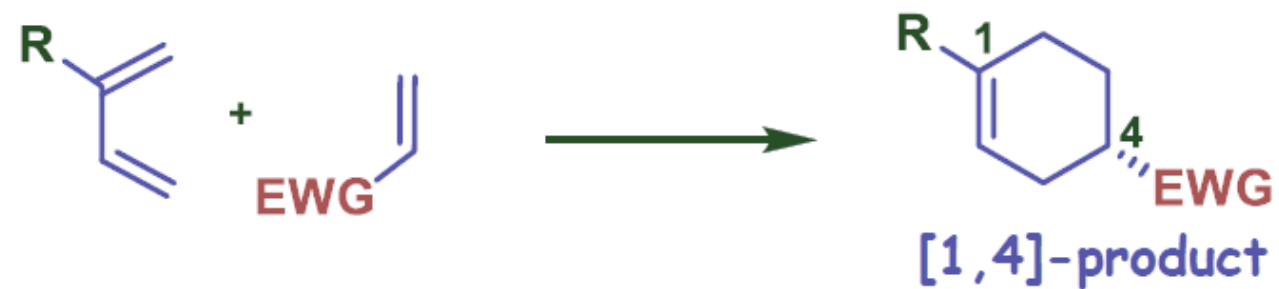
Diels-Alder Cycloaddition: 'Regioselectivity'

- Regioselectivity for the preference of [1,2]-product can be explained by considering the polarization of diene and dienophile
- Connect the electron rich center of diene to electron deficient center of dienophile



Diels-Alder Cycloaddition: 'Regioselectivity'

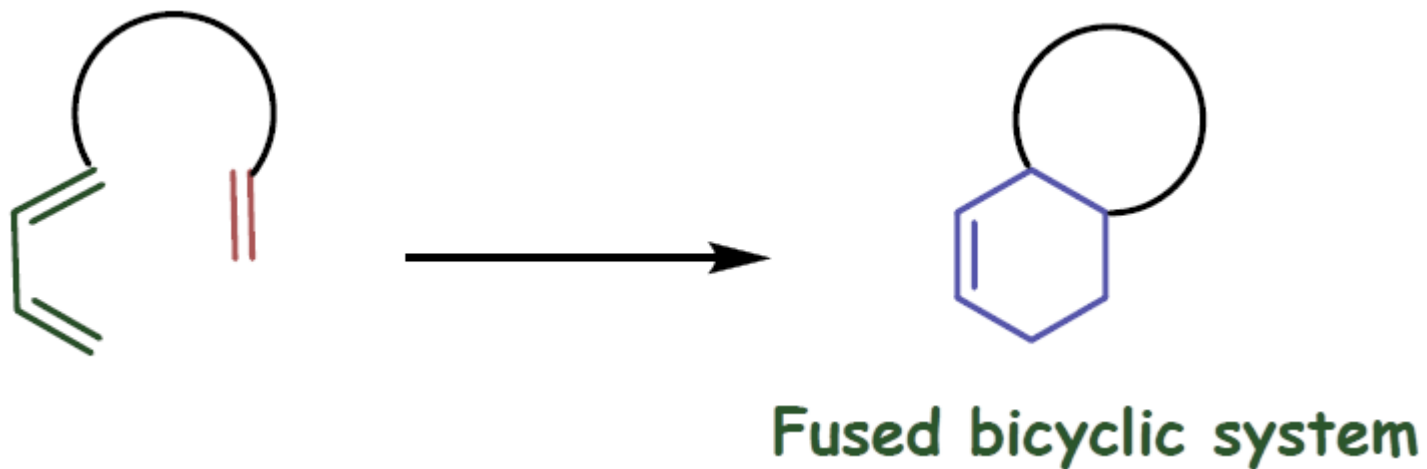
- 2-substituted diene react to give mainly [1,4]-substituted product



Intramolecular Diels-Alder Cycloaddition (IMDA)

Type I IMDA:

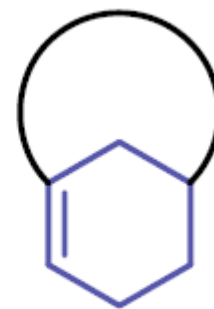
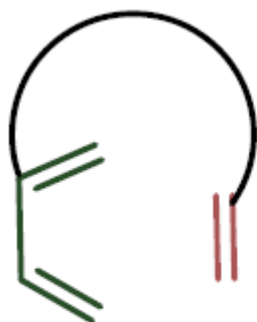
- Dienophile is attached to **C-1 atom of diene**
- Results in the formation of **fused bicyclic system**



Intramolecular Diels-Alder Cycloaddition (IMDA)

Type II IMDA:

- Dienophile is attached to **C-2 atom of diene**
- Type II IMDA generally results in the formation of **bridged bicyclic system**, provided the ring formed other than six member should be minimum seven member ring

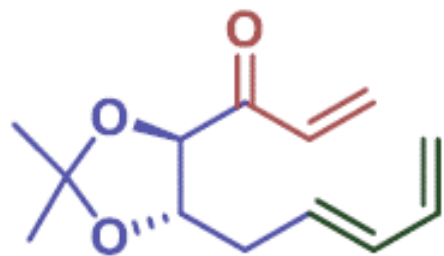


Bridged bicyclic system

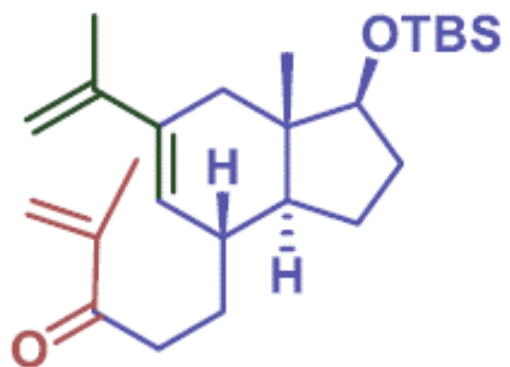
Intramolecular Diels-Alder Cycloaddition (IMDA): IMDA Type I Examples



Intramolecular Diels-Alder Cycloaddition (IMDA): IMDA Type I Examples



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Hetero Diels-Alder Cycloaddition

- If one or more of the atoms in either diene or dienophile component is other than carbon, then the reaction is referred to as the **hetero D-A cycloaddition (HDA)**.
- The first example of an **imine participating as a heterodienophile** was reported by K. Alder in 1943.
- **Diene does not contain a heteroatom and the heterodienophile is electron-deficient:** normal electron-demand D-A reaction (diene HOMO interacts with the LUMO of the heterodienophile).
- **Diene contains one or more heteroatoms and/or electron-withdrawing substituents, and dienophile is electron-rich:** inverse electron-demand D-A reaction (heterodiene LUMO interacts with the HOMO of the dienophile).
- **Heterodiene is substituted with one or more strongly electron-donating groups and dienophile is electron-deficient:** normal electron-demand D-A reaction
- HDA reactions can be catalyzed by Lewis acids

Hetero Diels-Alder Cycloaddition

□ **Hetero Diene**: Hetero atom is part of the diene



Hetero Diels-Alder Cycloaddition

□ **Hetero Dienophile**: Hetero atom is part of the dienophile

V. V IMP

