

DAMIETTA UNIVERSITY

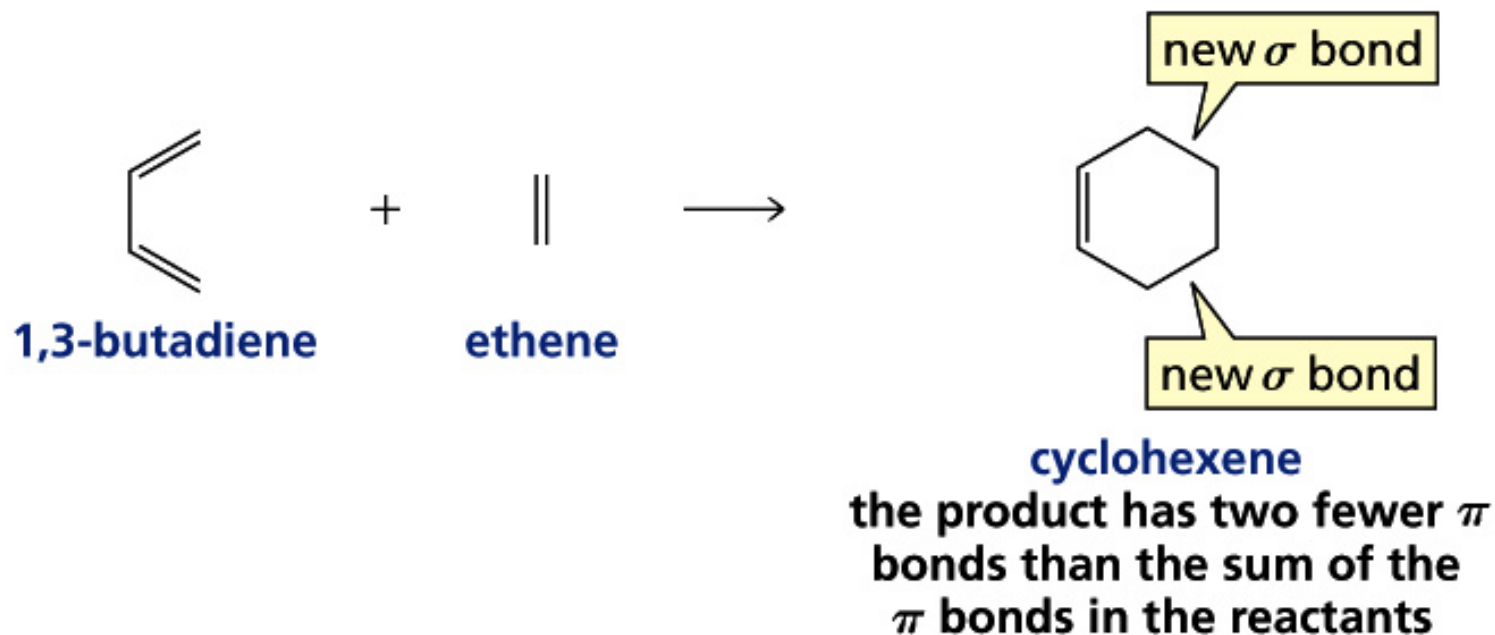
CHEM-405: PERICYCLIC REACTIONS

LECTURE 4

Dr Ali El-Agamey

Pericyclic Reaction II

a cycloaddition reaction

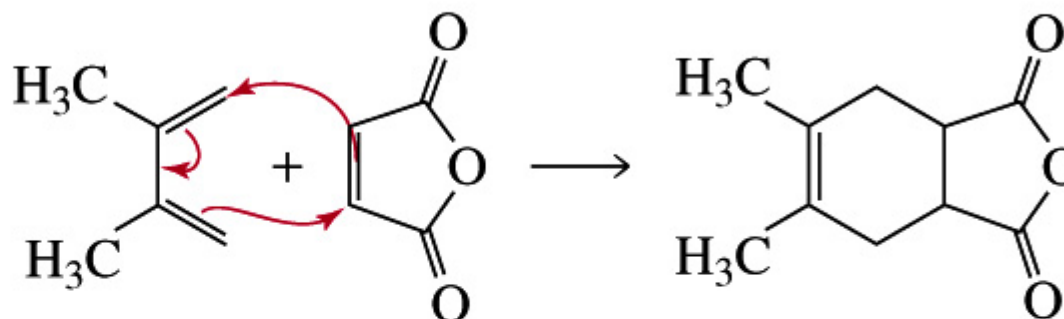


- Two different π bond-containing molecules react to form a cyclic compound

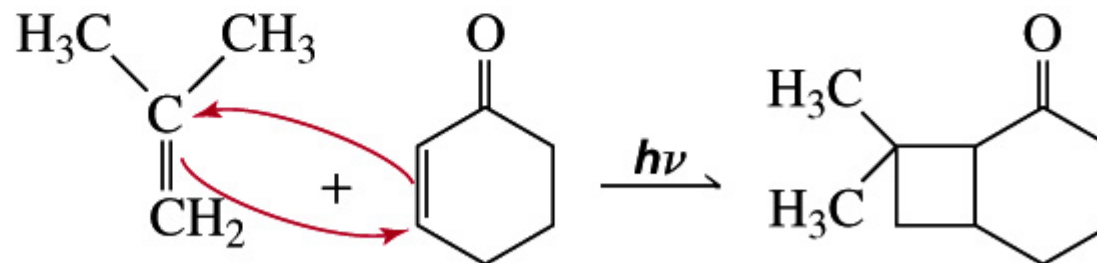
Cycloaddition reactions

Cycloadditions are classified according to **the number of π electrons** that interact in the reaction

[4 + 2] cycloaddition (a Diels–Alder reaction)



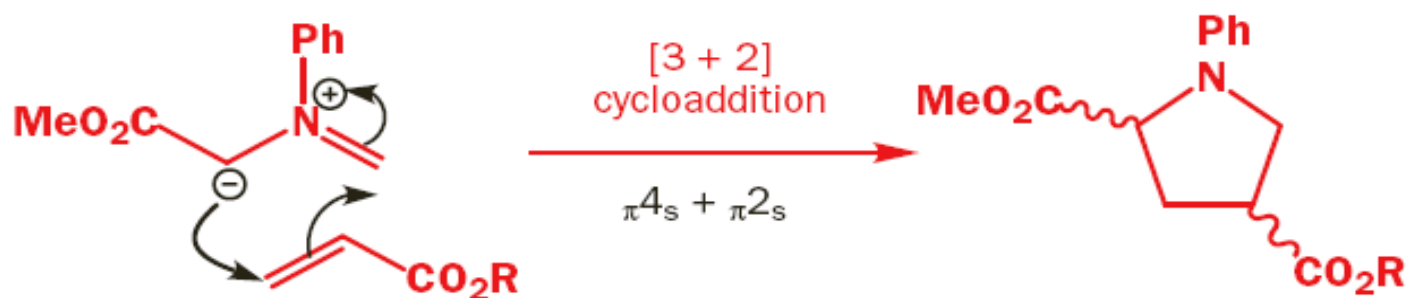
[2 + 2] cycloaddition



Electrocyclic reactions of cations and anions

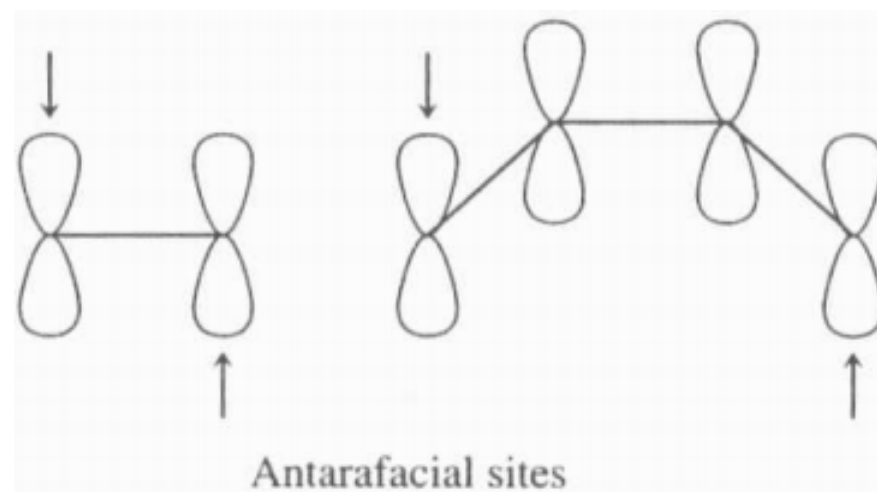
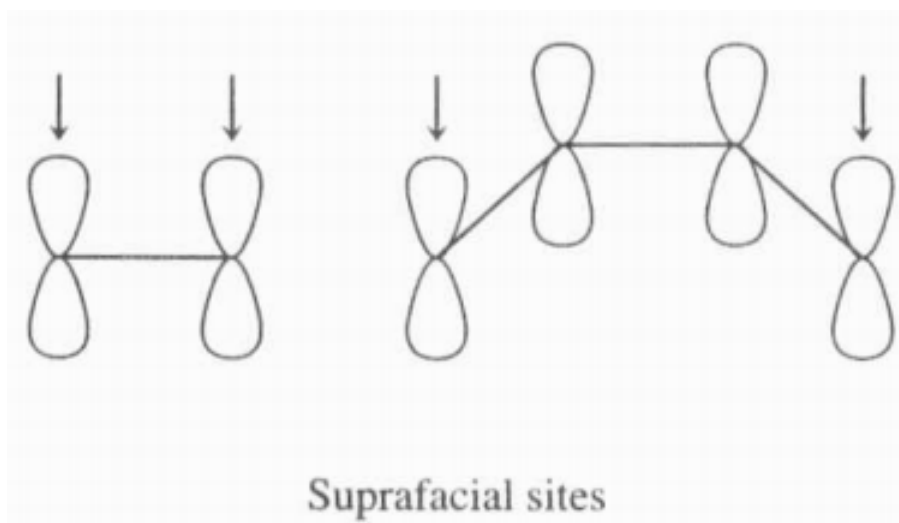
Three-atom electrocyclizations (4 electrons)

- Azomethine ylids can be trapped by [3 + 2] cycloaddition reactions with **dipolarophiles**.⁴

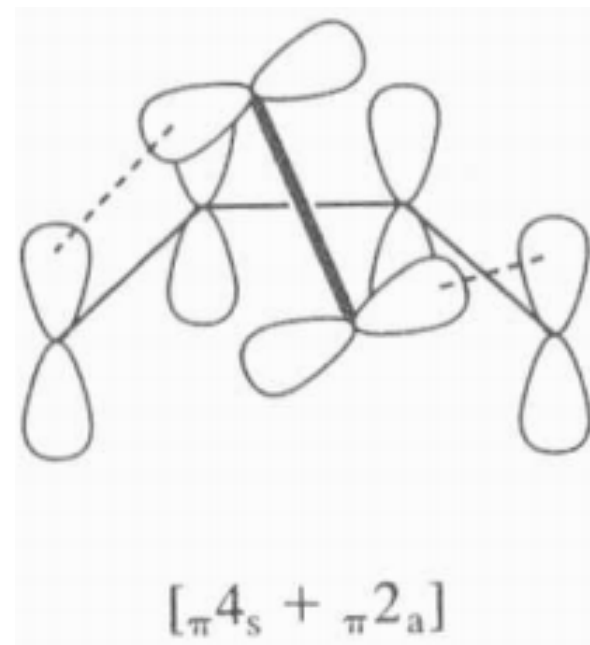
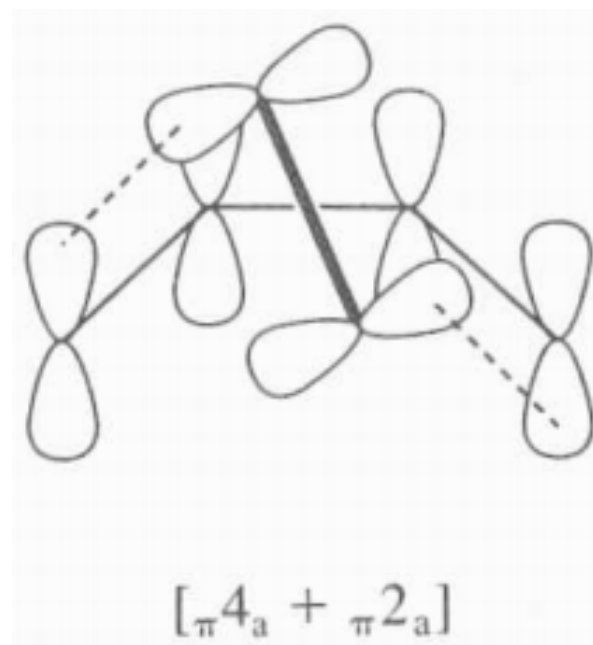
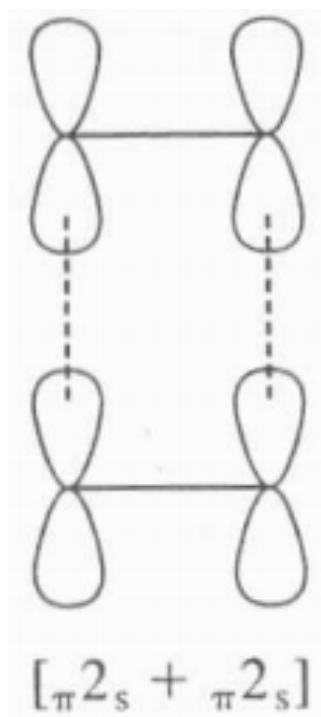


There are two possible ways to form bonds to the atoms of a pi bond.¹

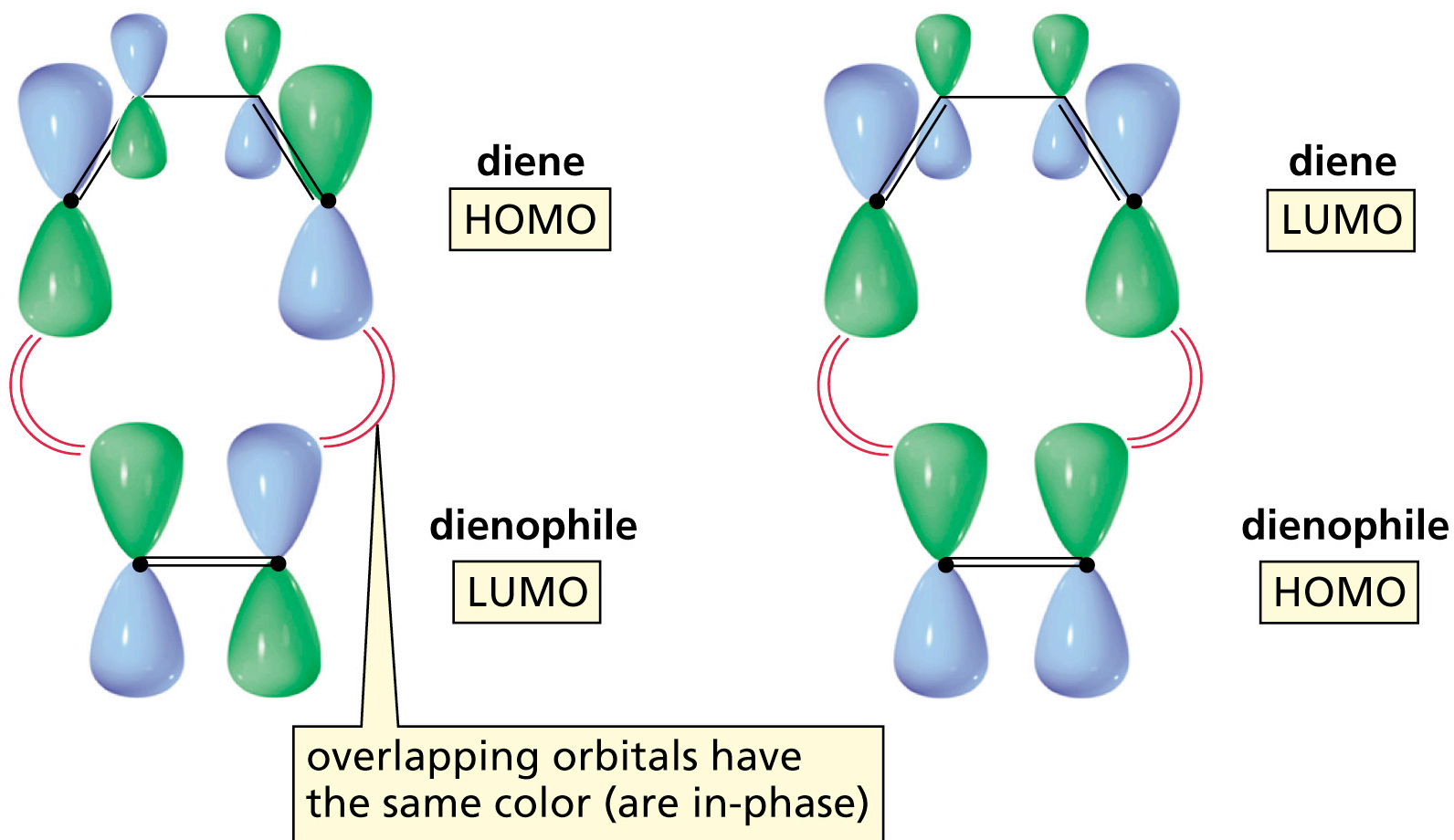
Woodward and Hofmann designated addition to lobes on the **same side** of a pi system as **suprafacial** addition on that pi system and called addition to lobes on **opposite sides** of a pi system **antarafacial** addition.¹ These modes of addition are identified by the symbols s and a, respectively.



Cycloaddition of a four-electron unit reacting antarafacially with a two-electron unit reacting suprafacially would be classified as a $[\pi 4_a + \pi 2_s]$ reaction.¹



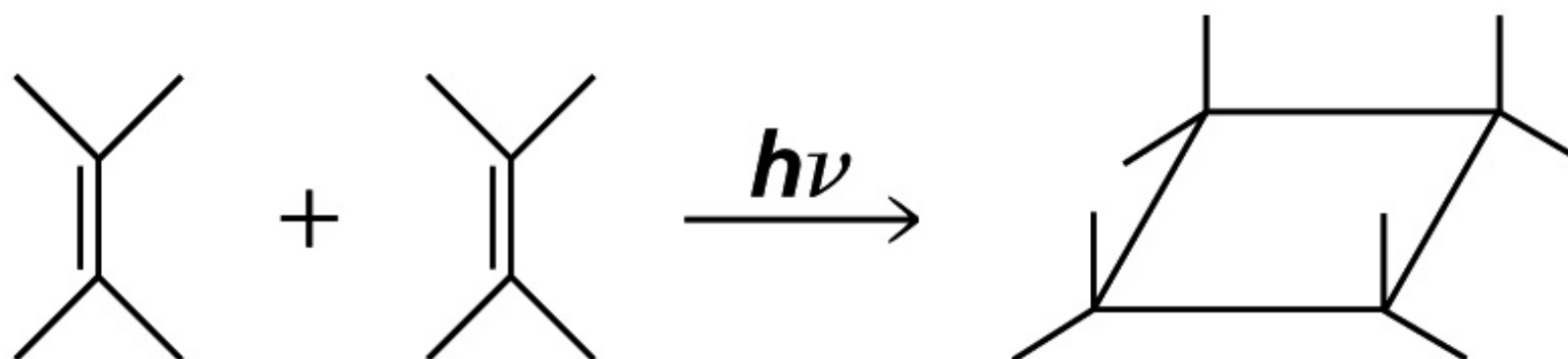
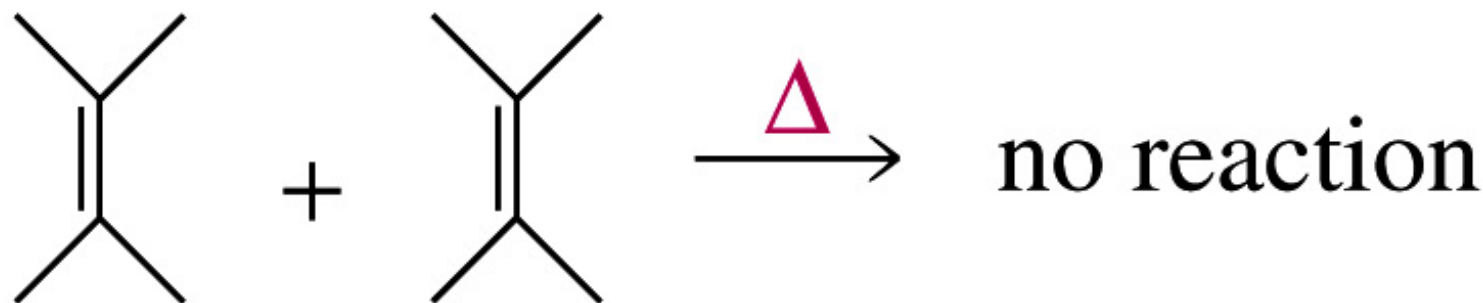
Frontier Orbital Analysis of a [4 + 2] Cycloaddition Reaction



Supra, supra

Supra, supra

A [2 + 2] Cycloaddition Reaction



Frontier MO Analysis of the [2 + 2] Cycloaddition Reaction

Thermal

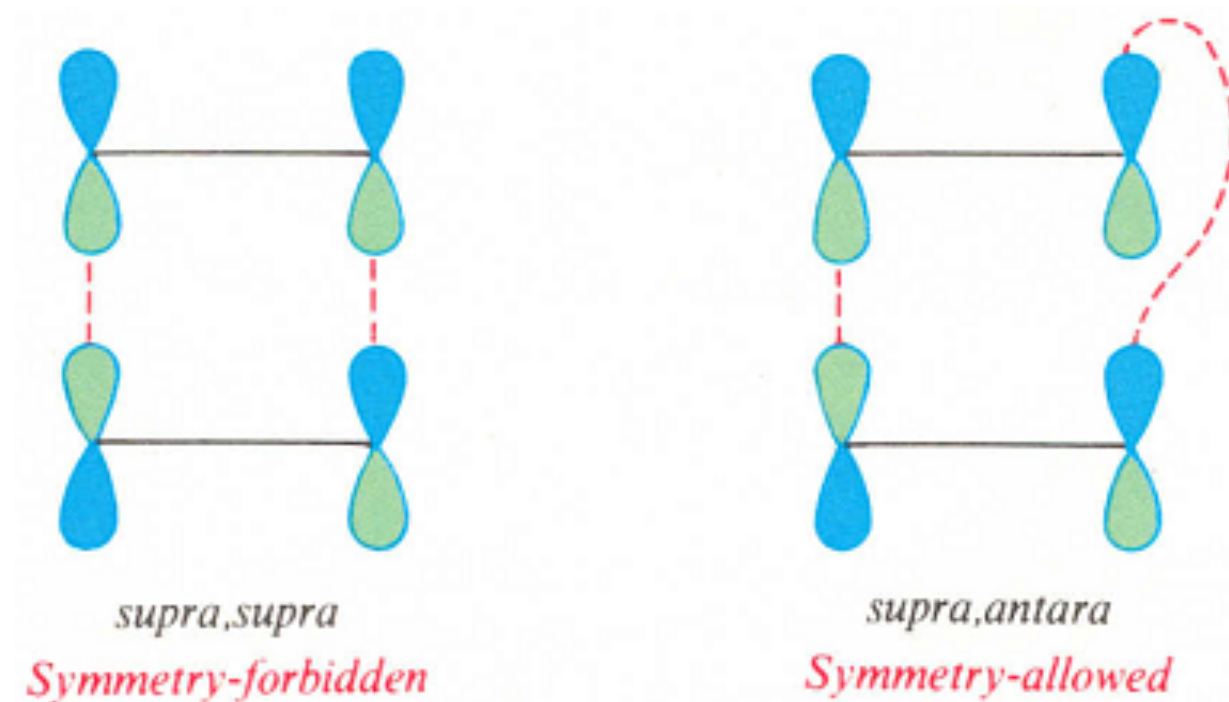


Fig 33.23 [2 + 2] thermal cycloaddition. **Supra, supra**: geometrically possible, but symmetry-forbidden. **Supra, antara**: symmetry-allowed, but geometrically difficult.

Frontier MO Analysis of the [2 + 2] Cycloaddition Reaction

Photochemical

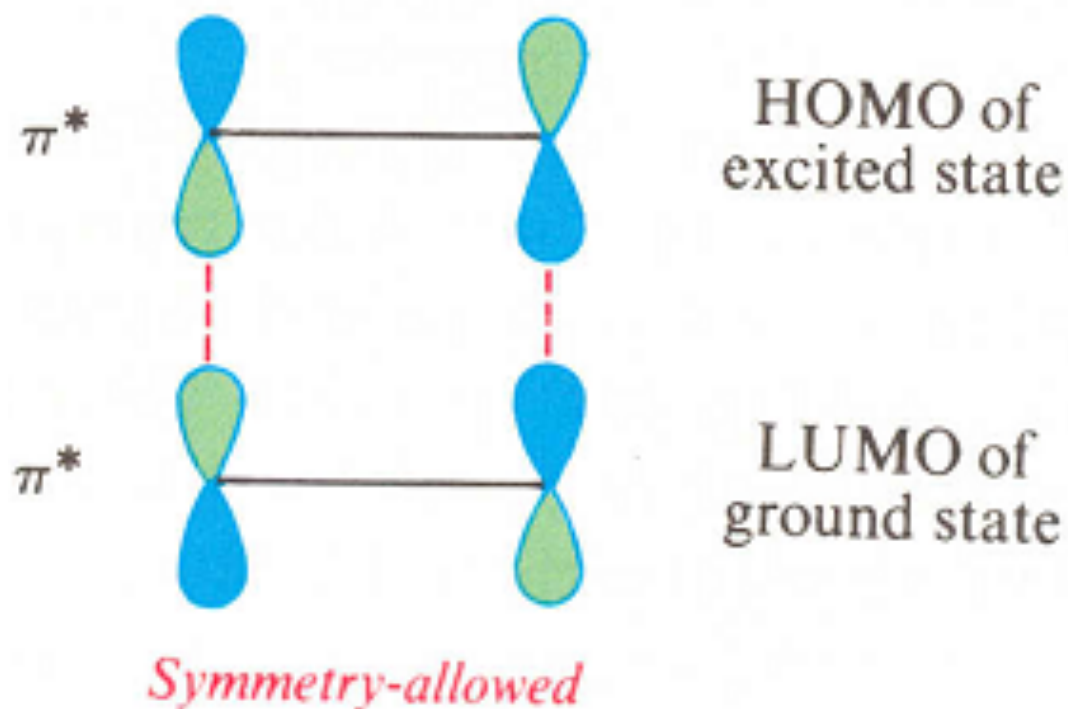


Fig 33.22 symmetry-allowed photochemical [2 + 2] cycloaddition: two molecules of ethylene, one excited and one in the ground state. **Interaction is bonding.**

Woodward-Hoffmann rules for $[i + j]$ cycloadditions¹

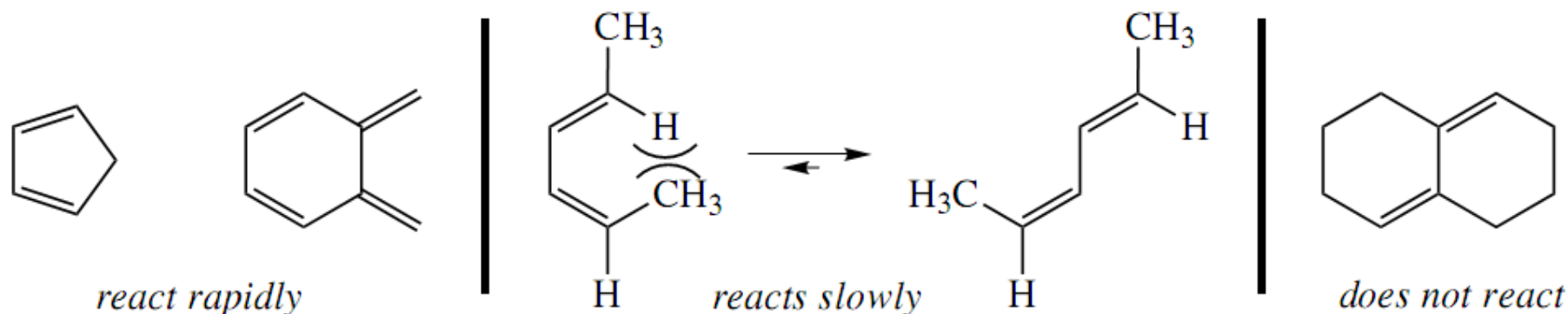
No. of electrons ($i + j$)	Thermal	Photochemical
$4n$	<i>supra, antara antara, supra</i>	<i>supra, supra antara, antara</i>
$4n + 2$	<i>supra, supra antara, antara</i>	<i>supra, antara antara, supra</i>

Factors affecting the rate of the Diels-Alder reaction

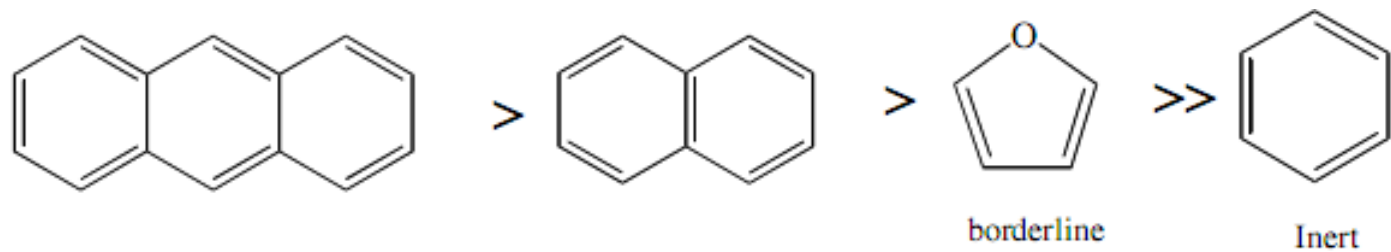
(1) The diene

(a) Conformation of the diene

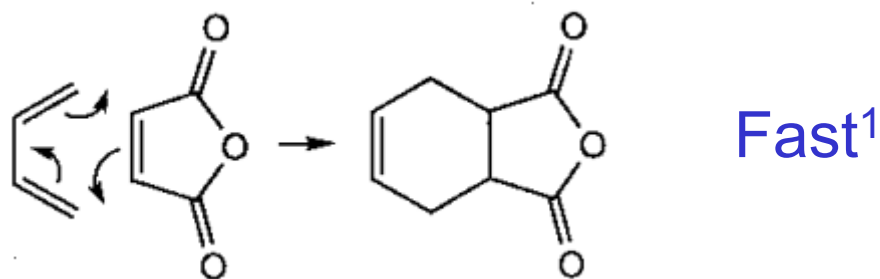
- The dienes must have the *s-cis* conformation.²
- The most reactive dienes are those in which the diene unit is **forced to** maintain an *s-cis* conformation e.g. cyclopentadiene undergoes Diels-Alder dimerization at RT.^{1,2}
- Dienes in which one or both substituents at C1 and C4 are *cis* to the other double bond react very slowly.¹
- Fixed *transoid* dienes are unreactive.^{2a,2}



(b) Aromaticity¹



(2) Electron-demand in Diels-Alder reactions



- Most Diels–Alder reactions occur with what is called **normal electron-demand**, in which an **electron-rich** (bears electron-donating group) **diene** reacts with an **electron-poor** (bearing electron-withdrawing group e.g. carbonyl, CN, sulfonyl, NO₂) **dienophile**.²

Electron-demand in Diels-Alder reactions¹

The smaller the difference in energy between the two MOs



the stronger their interaction



the lower the energy of the TS



the faster the reaction

Electron-demand in Diels-Alder reactions¹

The $\text{HOMO}_{\text{diene}}$, being a bonding orbital, is lower in energy than the $\text{LUMO}_{\text{dienophile}}$.

Substitution of the diene with electron-donating groups



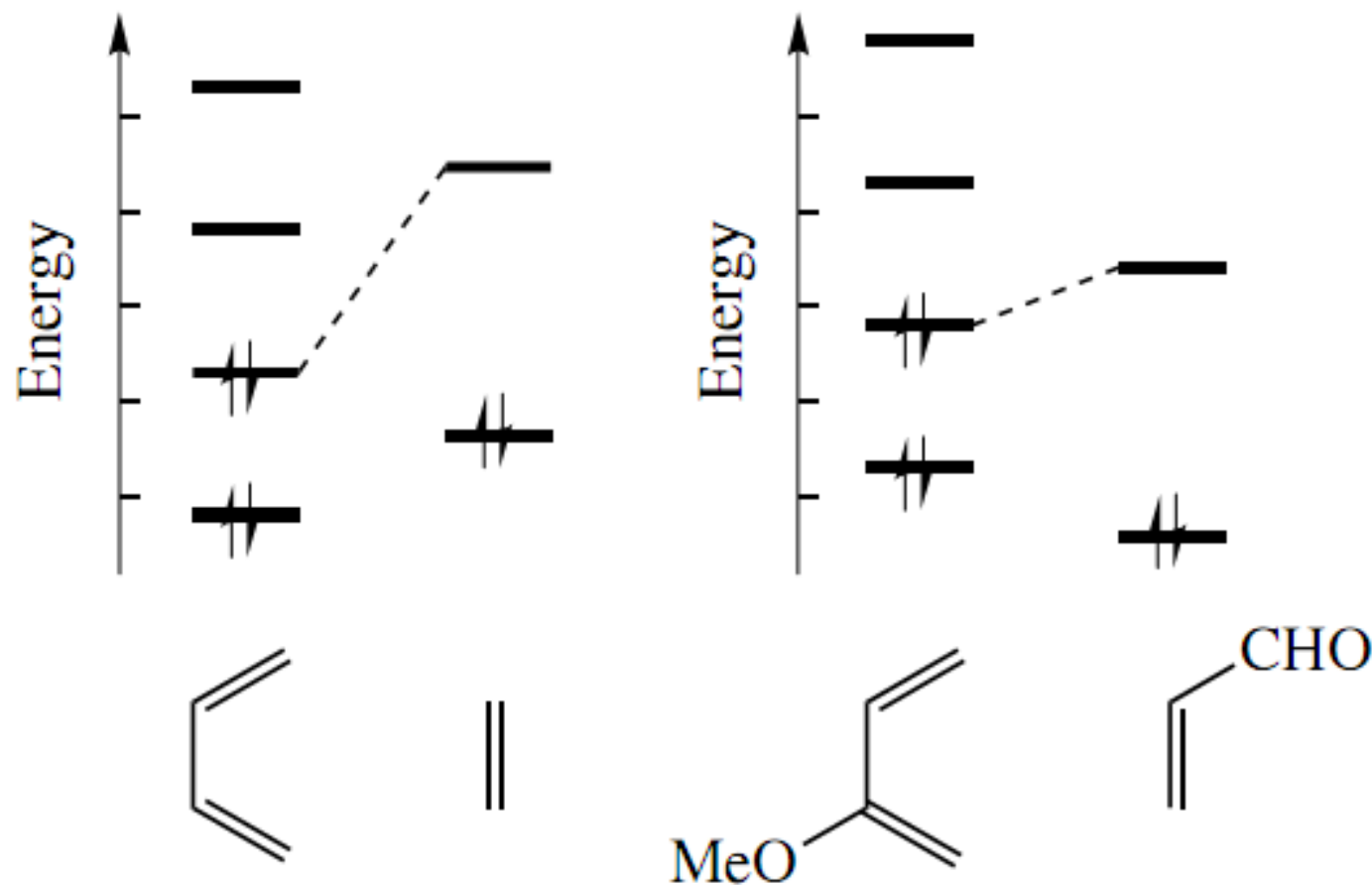
raises the HOMO and LUMO energies

Substitution of the dienophile with electron-withdrawing groups



lowers the HOMO and LUMO energies

Electron-demand in Diels-Alder reactions

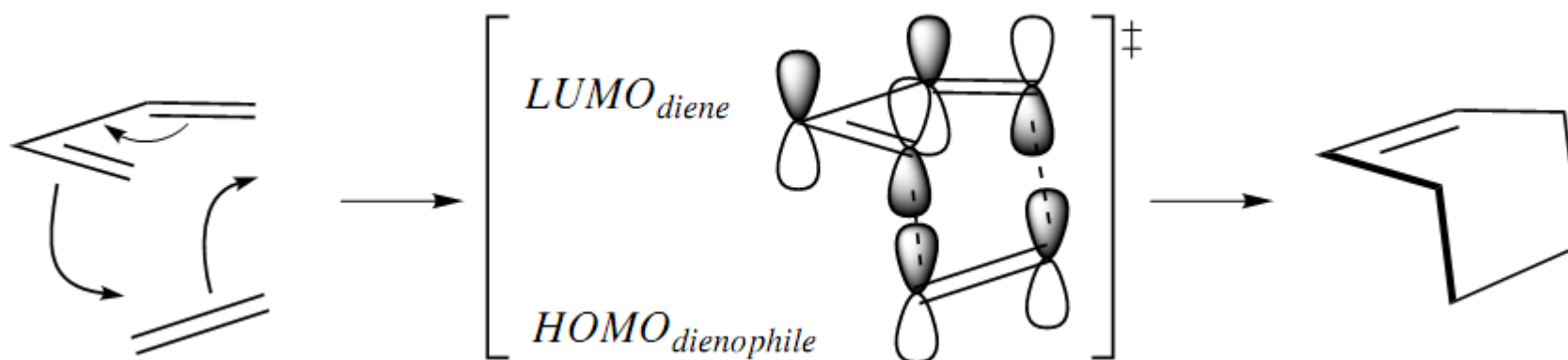


*HOMO-LUMO difference
decreases with electron-rich diene
and electron-poor dienophile, so
reaction rate increases*

Electron-demand in Diels-Alder reactions

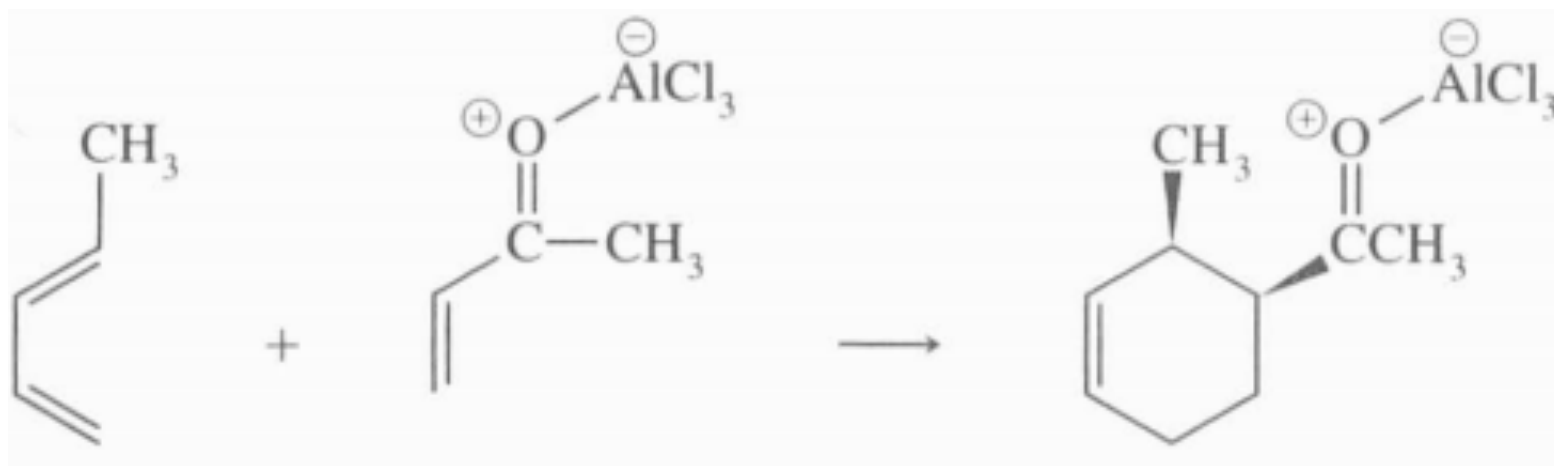
Very electron-poor dienes can undergo Diels–Alder reactions with electron-rich dienophiles in the *inverse electron-demand* Diels–Alder reaction.

The dominant interaction in the TS of inverse electron-demand Diels–Alder reactions is between the $LUMO_{\text{diene}}$ and the $HOMO_{\text{dienophile}}$.¹



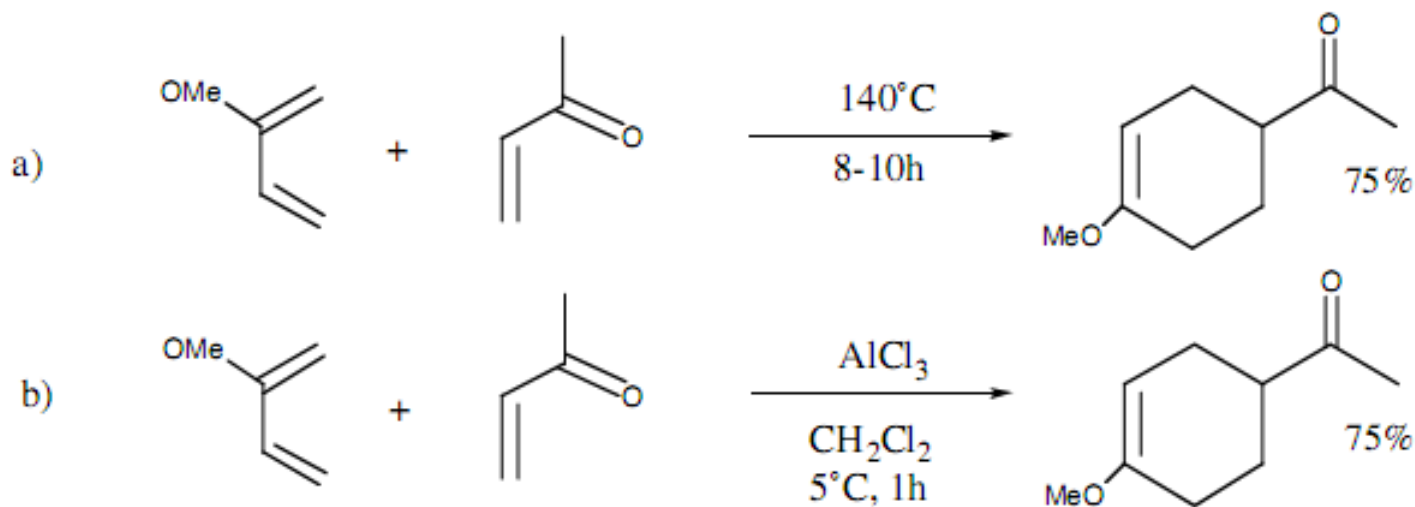
(3) Lewis-acid catalysis of the Diels-Alder reactions

- Lewis acids (e.g. BF_3 , AlCl_3 , TiCl_4 , SnCl_4 ,...) are known to catalyse Diels–Alder reactions. They coordinate to a Lewis base site, normally a heteroatom such as a carbonyl oxygen of the dienophile. The coordination of a Lewis acid makes the dienophile **more electron-deficient**.¹



(3) Lewis-acid catalysis of the Diels-Alder reactions

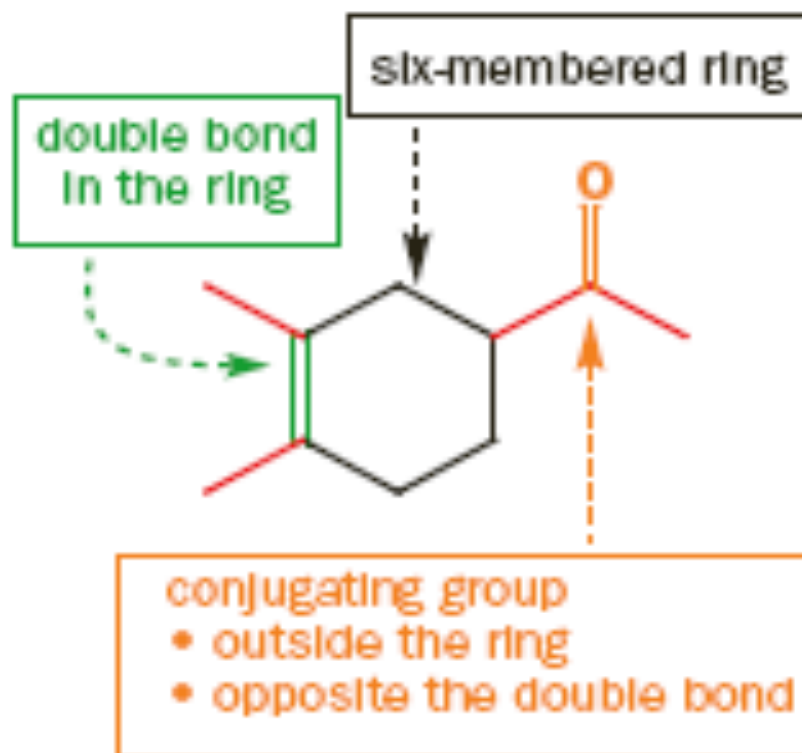
➤ **The energy of the HOMO and LUMO of the dienophile is decreased** compared to the uncomplexed dienophile and hence the $\text{HOMO}_{\text{diene}} - \text{LUMO}_{\text{dienophile}}$ gap is further reduced. Consequently, the rate of the Diels-Alder reactions is further enhanced.¹



Recognizing a Diels–Alder product¹

- We can easily recognize a Diels–Alder product as follows:

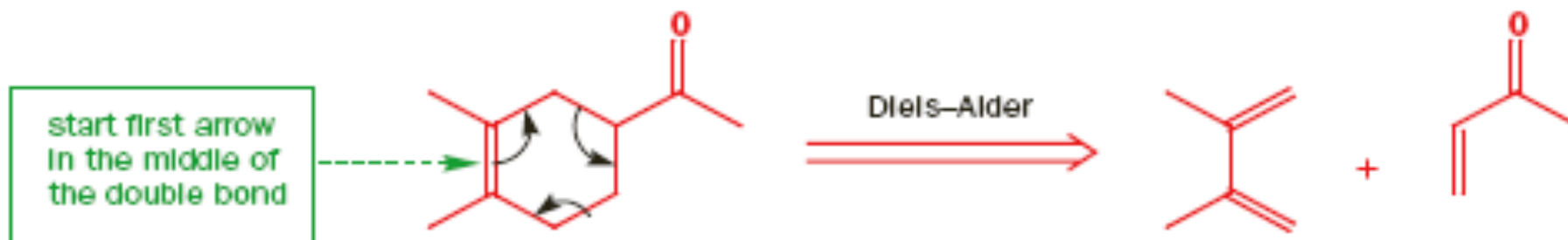
recognizing a Diels–Alder product:



Recognizing a Diels–Alder product¹

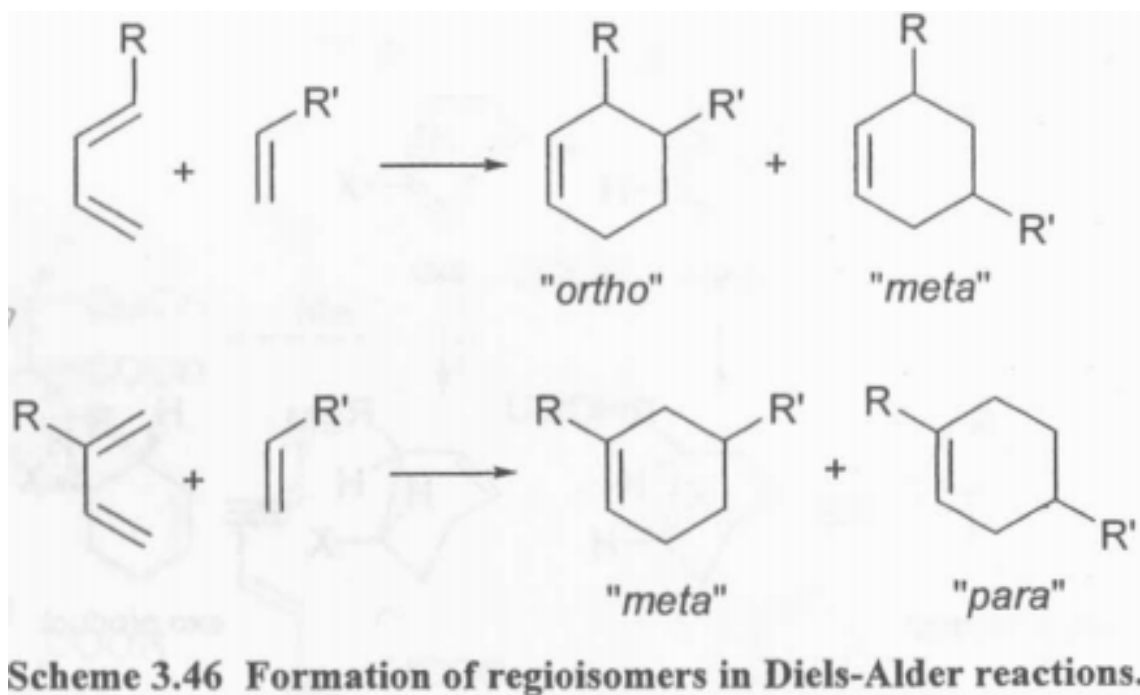
- The simplest way to find the starting materials is to draw the reverse Diels–Alder reaction.

the disconnection is the imaginary reverse Diels–Alder reaction



Regioselectivity

- The Diels-Alder reaction between an unsymmetrical diene and an unsymmetrical dienophile can lead to the formation of a mixture of regioisomers depending upon the **relative orientation** of the diene and the dienophile in the TS.¹



- Generally, the **more powerful** the electron-donating and electron-withdrawing substituents, the **more regioselective** is the reaction.²

Regioselectivity

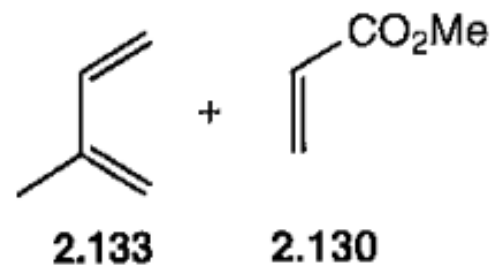
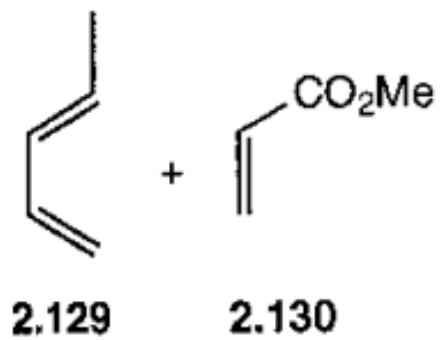
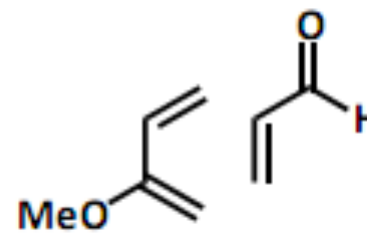
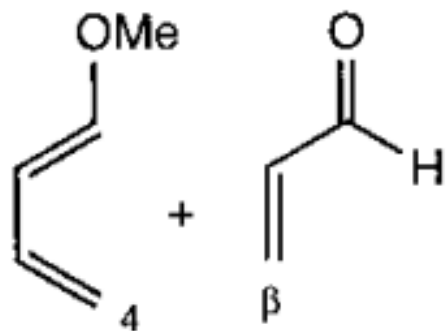
How can we determine the regioselectivity of the reaction?

- (1) Draw an “ionic” stepwise mechanism.
- (2) Orbital coefficient arguments.

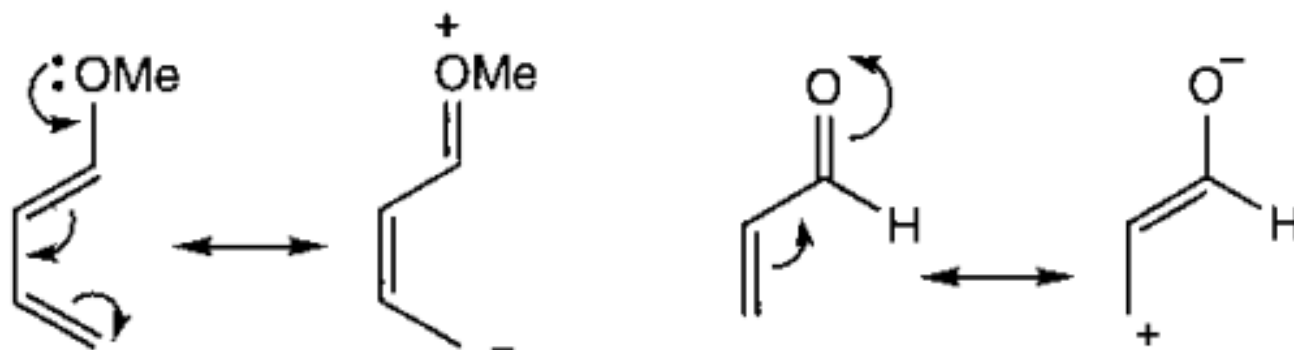
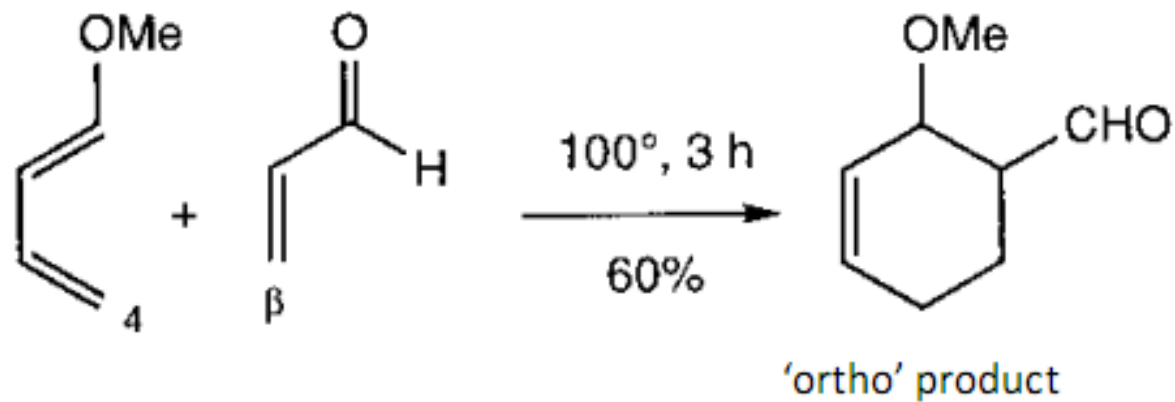
Regioselectivity

- (1) Draw an “ionic” stepwise mechanism.
- The **simplest way** to predict which product will be formed is to draw an “ionic” stepwise mechanism for the reaction to establish which end of the diene will react with which end of the dienophile.
- Of course this stepwise mechanism **is not completely correct** but it does lead to the correct orientation of the reagents.

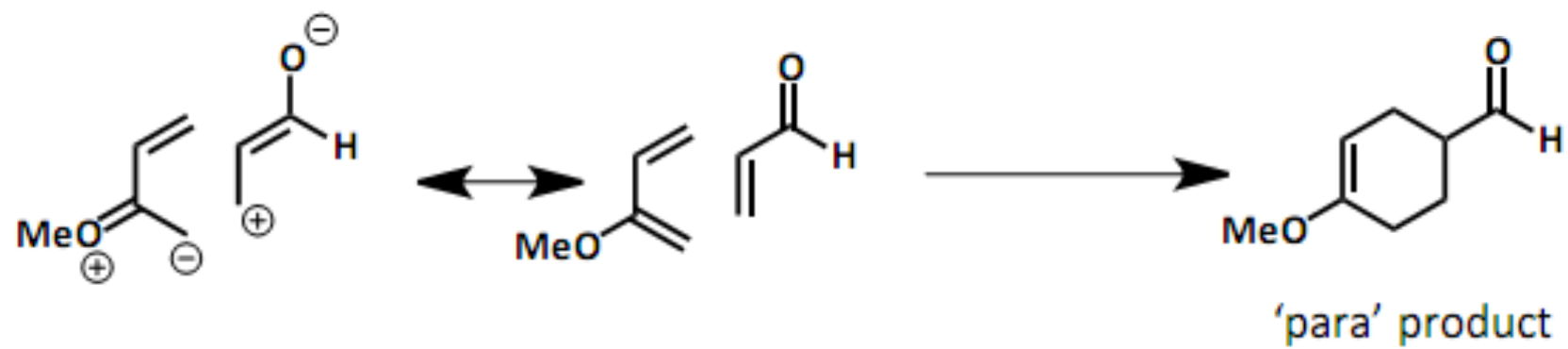
Regioselectivity



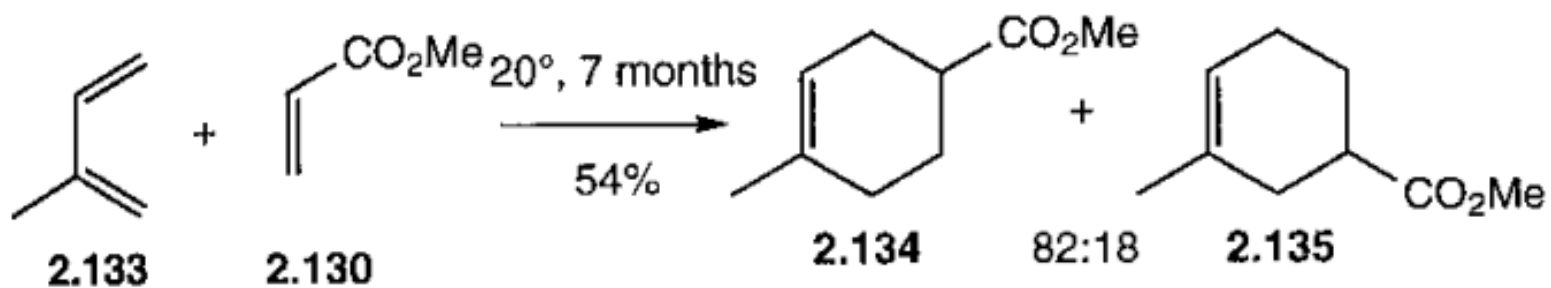
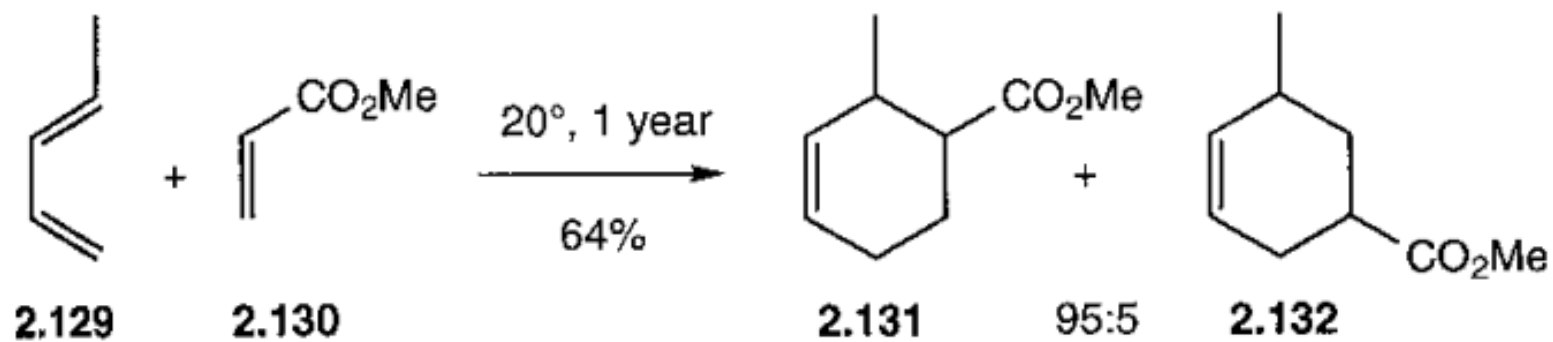
Regioselectivity



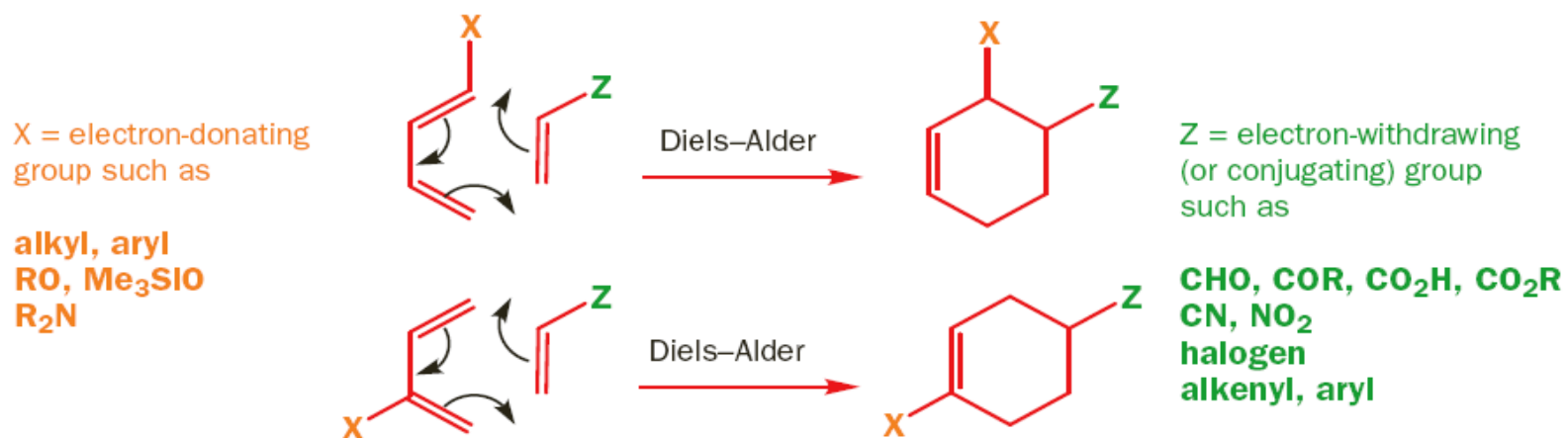
Regioselectivity



Regioselectivity

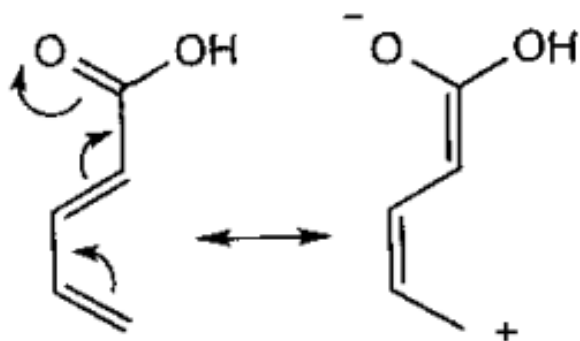
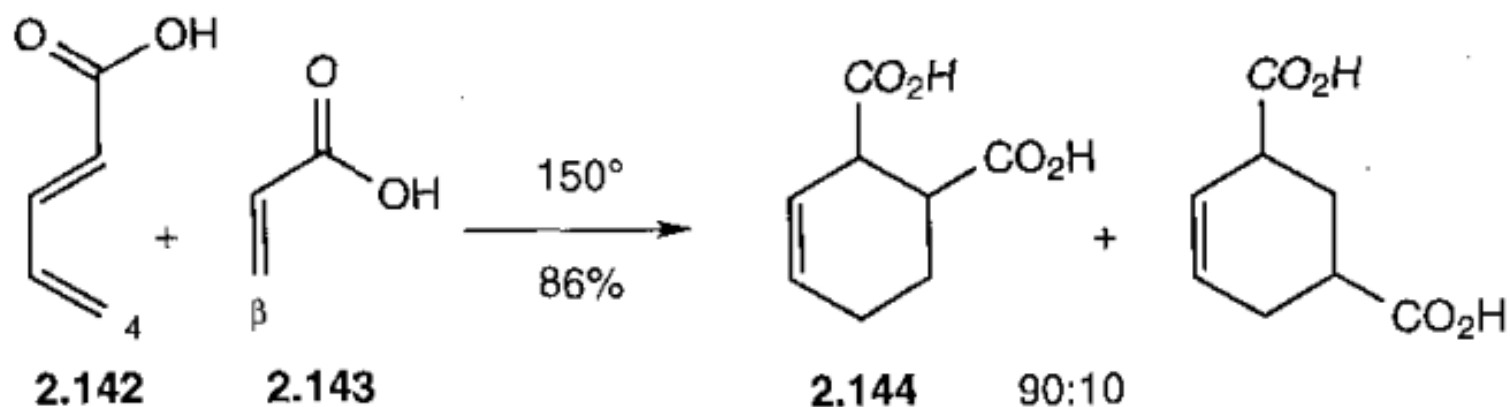


Regioselectivity



□ The Diels-Alder reaction is generally **highly regioselective** and the formation of **ortho and para adducts predominate** over the meta adduct.²

Regioselectivity¹



- Sometimes, looking at the resonance structures **can not** explain many cases.
- In such cases, orbital coefficient arguments should be used.¹

Regioselectivity¹

- The regioselectivity of inverse electron-demand Diels–Alder reactions, 1,3-dipolar cycloadditions, and other cycloadditions can similarly be explained by resonance and orbital coefficient arguments.

