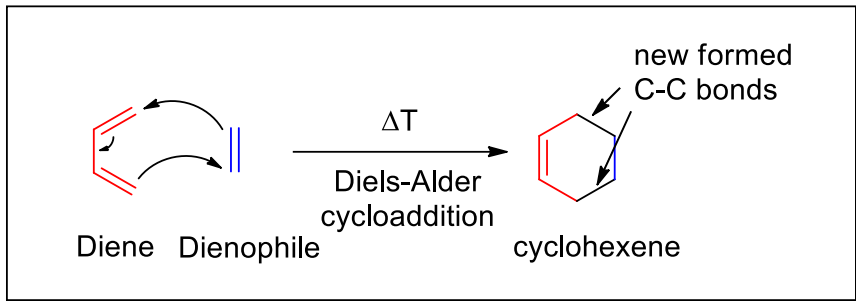


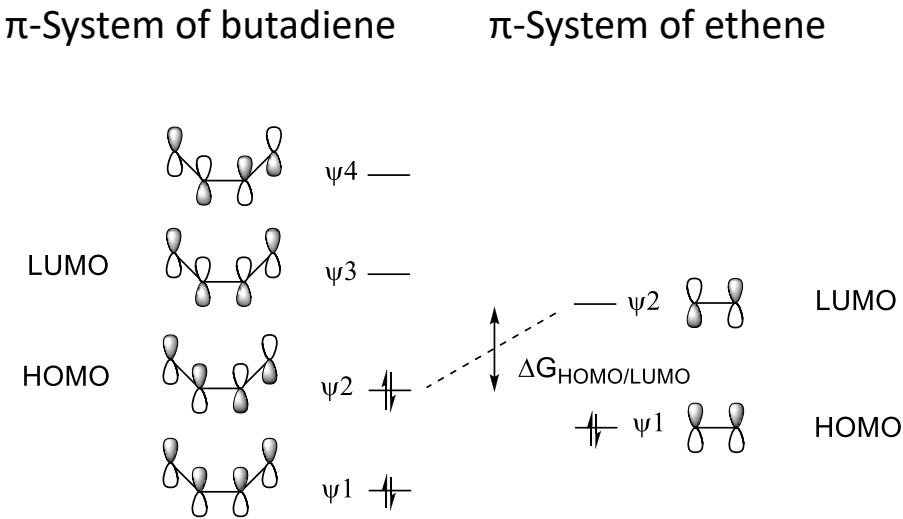
3.1.1. General reaction principle

The Diels-Alder reaction was discovered by Otto Diels and Kurt Alder (Nobel prize in 1950)



Diene: 4 π -electrons
Dienophile: 2 π -electrons
Diels-Alder reaction: [4+2]-cycloaddition

Molecular Orbital picture of the Diels-Alder Cycloaddition:

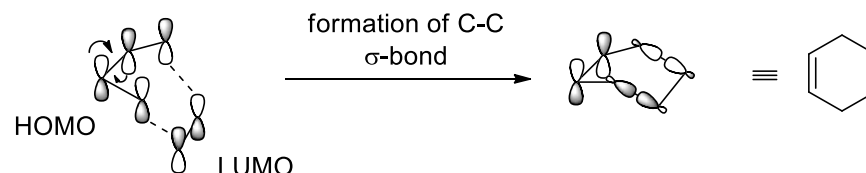


For the Diels-Alder cycloaddition, the interaction between the butadiene HOMO and the ethene LUMO is relevant.

➡ The smaller the Gap $\Delta G_{\text{HOMO/LUMO}}$, the easier and faster the cycloaddition reaction proceeds.

3.1.1. General reaction principle

Interaction of the HOMO of the diene with the LUMO of the olefin



Concerted cycloaddition, no intermediate

An interaction is possible when allowed by the orbital symmetry: $\text{HOMO}_{\text{Diene}}/\text{LUMO}_{\text{Dienophile}}$ and $\text{LUMO}_{\text{diene}}/\text{HOMO}_{\text{Dienophile}}$

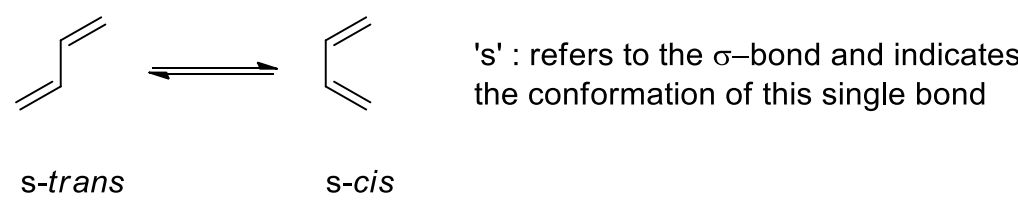
The better the energetic overlap, the better and faster the Diels-Alder reaction

Minimize energy difference between HOMO of the diene and LUMO of the dienophile:

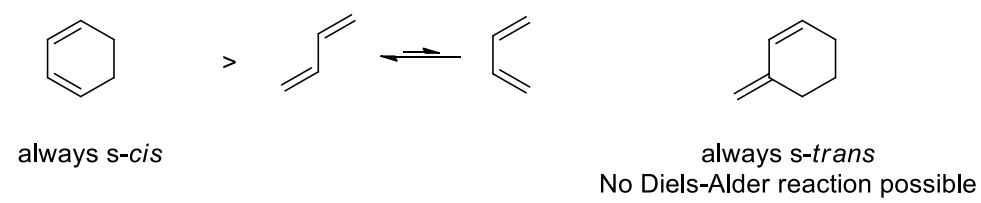
- Diene needs to be electron-rich = high lying HOMO
- Dienophile needs to be electron-poor = low lying LUMO

3.1.2 The nature of the diene

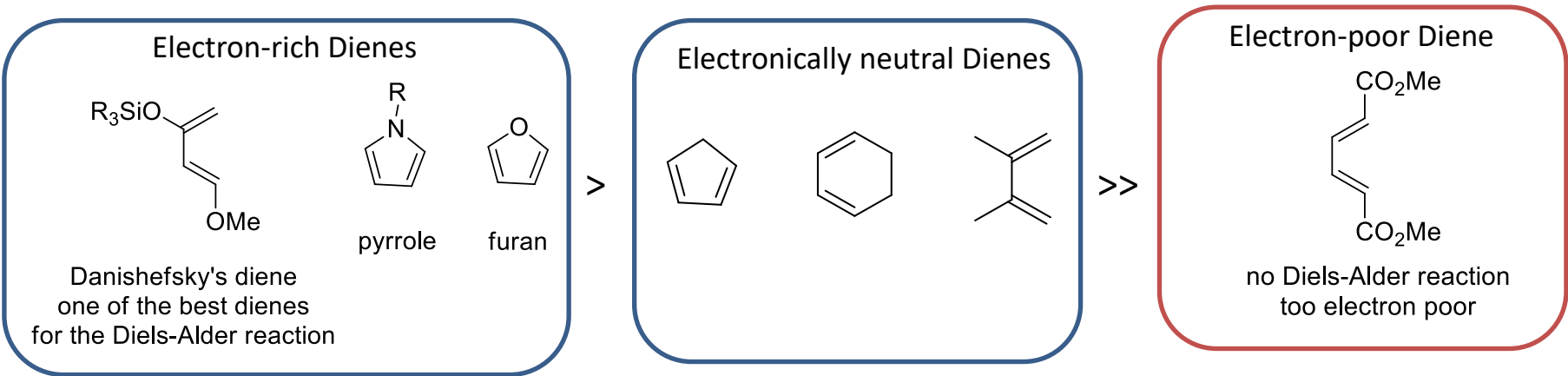
The diene component must be able to adopt *s-cis* conformation: A Diels-alder cycloaddition is only possible from the *s-cis* conformer.



Examples:



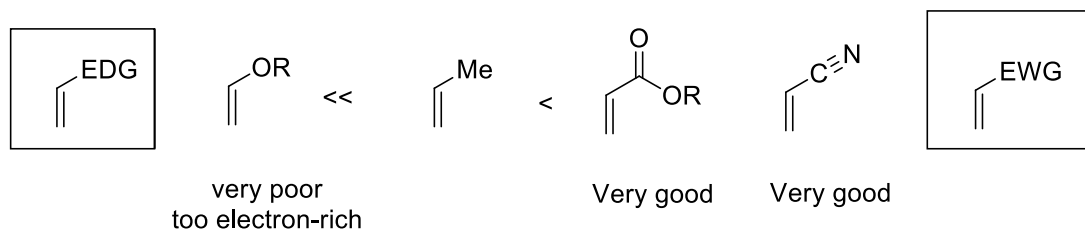
Electron-rich dienes react faster:



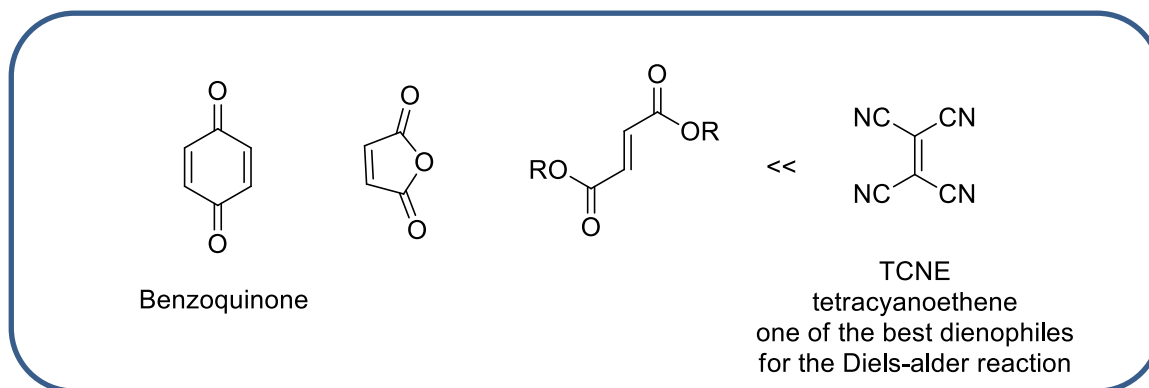
3.1.3. The nature of the dienophile

Electron-poor dienophiles are best suited and react fast

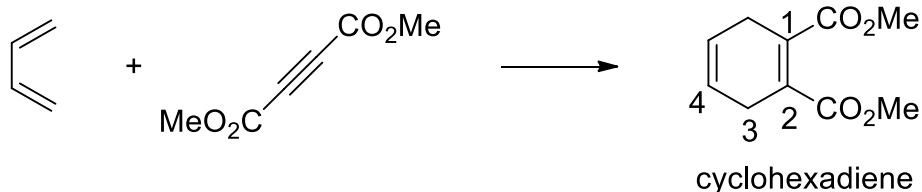
Examples of Dienophiles:



The effect of EWG-Substituents is additive:



- Electron-poor alkynes can be used as dienophiles as well, and yield 1,4-cyclohexadienes as products:



3.2.1. Diene and dienophile isomers

The Diels-Alder reaction is a concerted cycloaddition and obeys the Woodward-Hoffmann rules for pericyclic reactions.

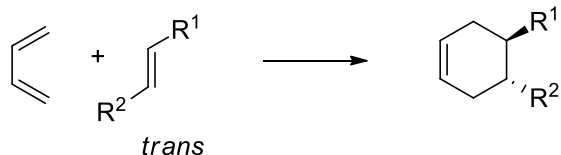
In that respect, the Diels-Alder cycloaddition is a thermally allowed process.

➡ The stereochemical information of the starting materials is conserved in the product:

cis-Olefins: substituents end up on the **same** face of the product:

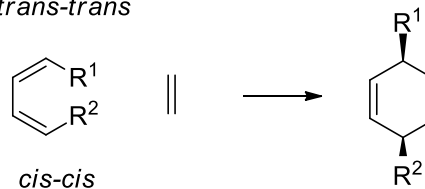
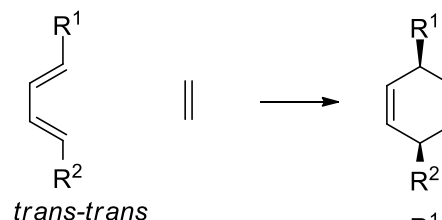


trans-Olefins: substituents end up on the **opposite** face of the product:



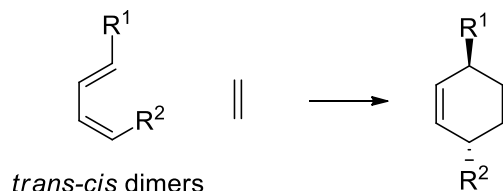
Dienes that have the same double bond isomers (*cis+cis* or *trans+trans*):

R¹ and R² end up on the **same** face



Dienes that have opposite double bond isomers (*cis+trans*):

R¹ and R² end up on the **opposite** face

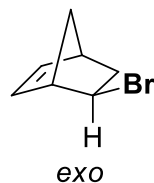
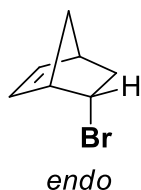


3.2.2. *Exo* / *Endo* selectivity

General and original explanation of the forms *exo/endo*:

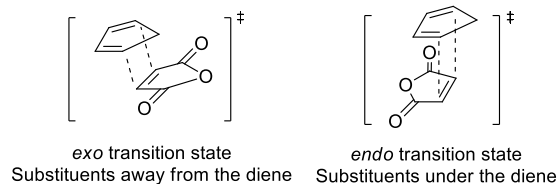
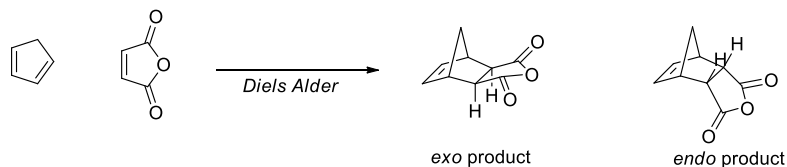
Substituent of a bicyclic molecule is

- Under the 'roof' = *endo*
- Out of the 'roof' = *exo*

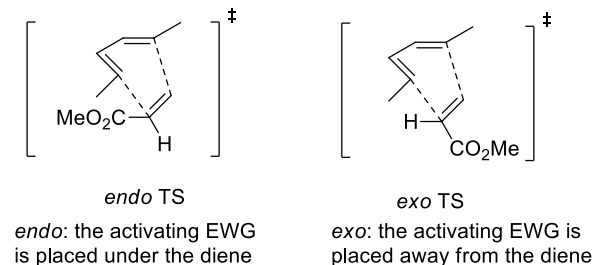
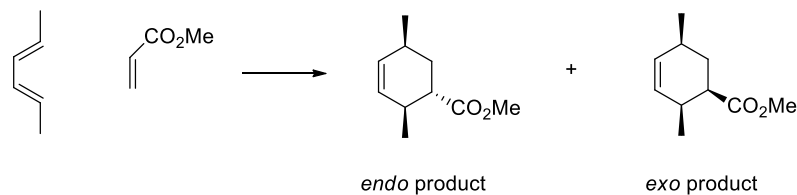


In the context of Diels Alder reaction:

Bicyclic products:



Monocyclic products:



3.2.2. *Exo* / *Endo* selectivity

Comparison between kinetic and thermodynamic product:

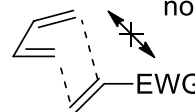
- *Endo* is the kinetic product: the transition state is stabilized by secondary orbital interactions.
- *Exo* is the thermodynamic product: more stable, less hindered product.

secondary orbitals interactions
between the diene and EWG
of the dienophile



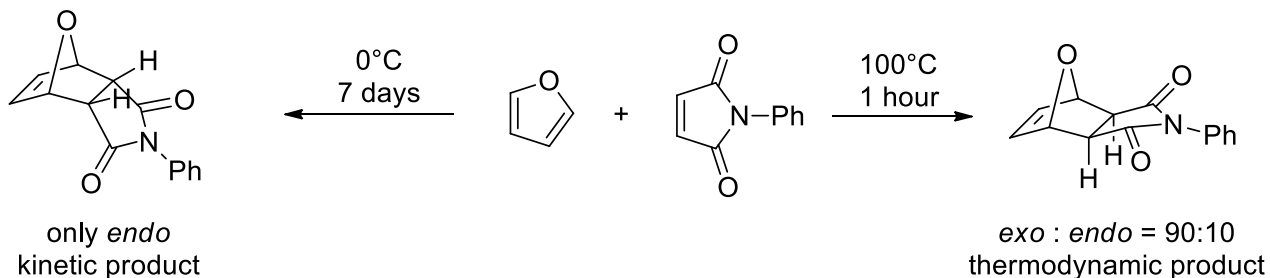
endo

no interaction
possible



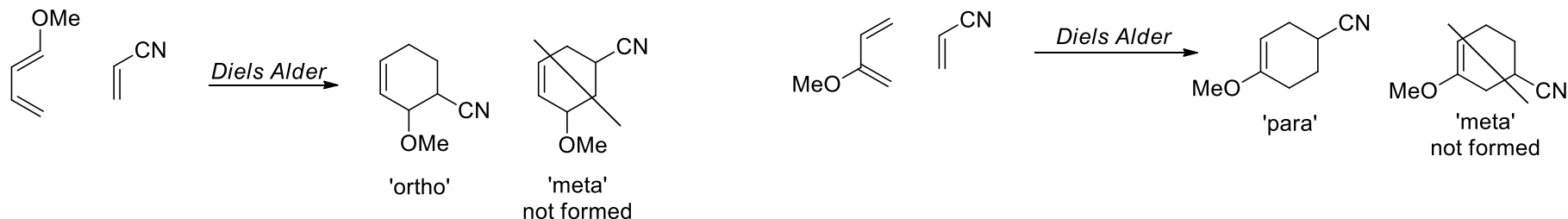
exo

Example:



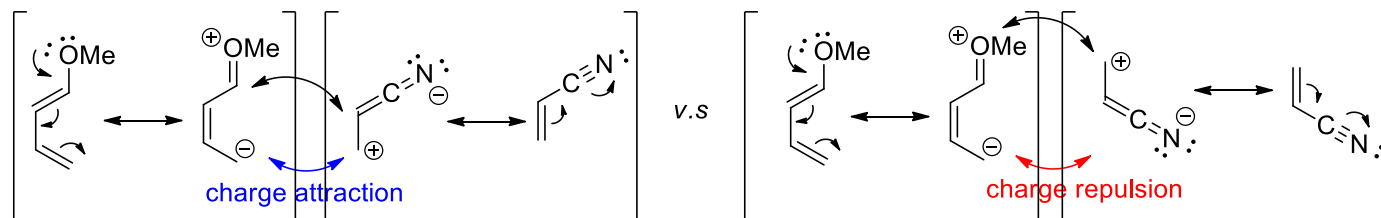
3.3. Diels-Alder regioselectivity

Observations:



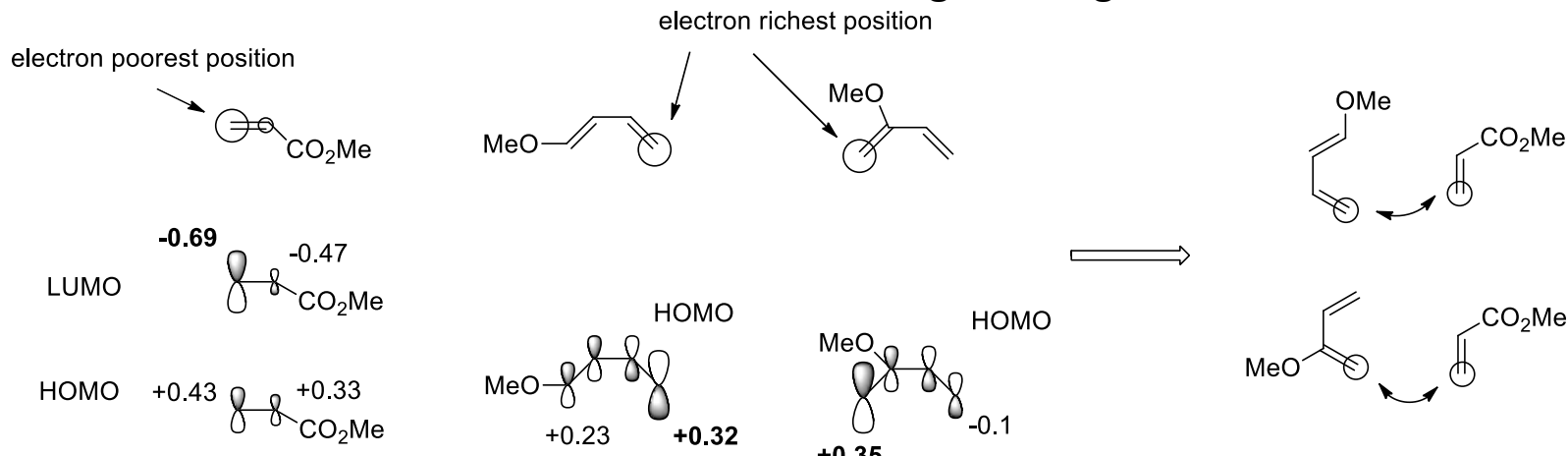
Rule: Electron-donating and electron-withdrawing groups are oriented 'ortho' or 'para' to each other.

Simple explanation with the mesomeric structures:



More accurate explanation with orbital coefficients:

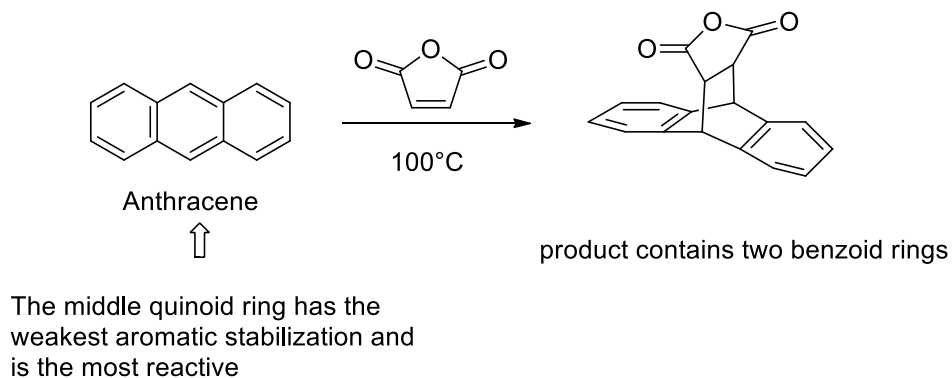
➡Favorable interaction: small coefficients with small, big with big



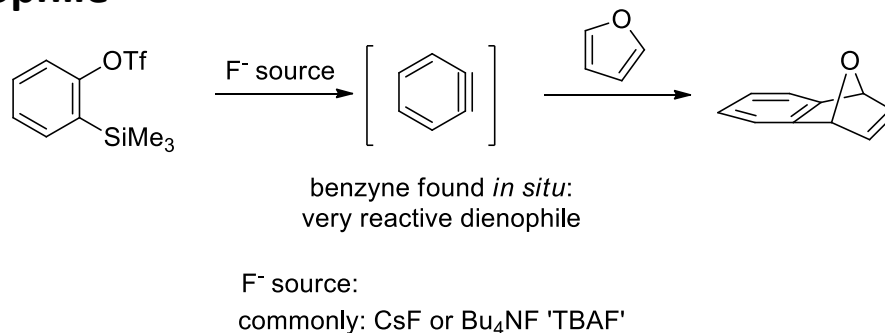
3.3. Additional examples of Diels-Alder cycloaddition

3.3.1. Extended polycyclic aromatics as diene component

Polycyclic arenes can react as diene-components in Diels-alder cycloaddition

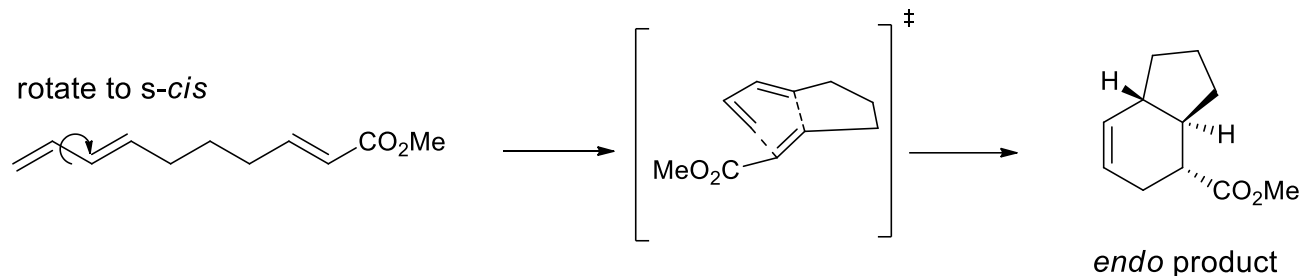


3.3.2. Benzyne as dienophile



3.3. Additional examples of Diels-Alder cycloaddition

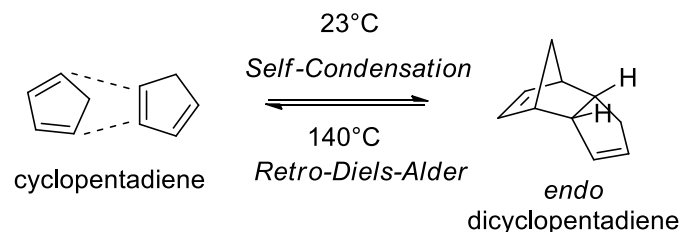
3.3.3. Intramolecular Diels-Alder reactions



➡ In intramolecular Diels-Alder reactions, even not very favorable Diene/Dienophile combinations which are unreactive for intermolecular Diels-Alder reactions react.

3.3.4. Self condensation and Retro-Diels-Alder reaction

Cyclopentadiene self-condenses at ambient temperature. The reaction is reversible above 140°C



➡ All Diels-Alder cycloadditions are principally reversible at a high enough temperature (>350°C) as the entropy increases (2 molecules v.s. 1 molecule)