

CYI101

Common CHEMISTRY(Organic)

Pericyclic reactions: Cycloaddition Reactions

Cycloaddition Reaction:

A concerted combination of two π -electron systems to form a ring of atoms having two new σ bonds and two fewer π bonds is called a cycloaddition reaction.

Two important classifications of cycloaddition reactions

(i) **[4 + 2] Cycloaddition** (ii) **[2+2] Cycloaddition**

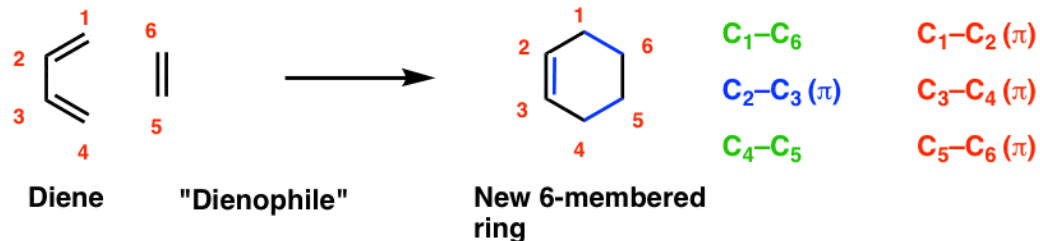
The most common cycloaddition reaction is the $[4\pi+2\pi]$ cyclization known as the **Diels-Alder reaction**. Discovered by Professor Otto Diels and his student Kurt Alder in 1928 and received Nobel prize in 1950.



- *Reaction between a conjugated diene and dienophile*
- *Highly effective method for the formation of cyclohexene ring*

Diels-Alder Reaction: $\Delta\sigma = \pm 2$

The Diels-Alder Reaction:



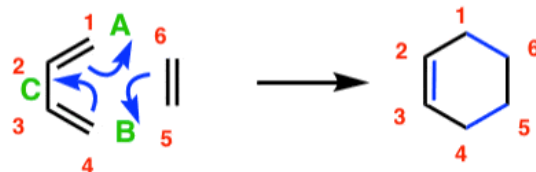
ALWAYS this pattern

- break 3 C-C pi bonds
- form 2 C-C single bonds and 1 C-C pi bond

Diels-Alder Mechanism

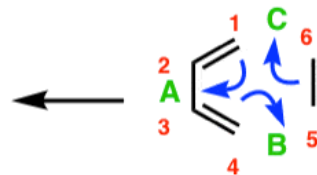
Can draw the direction of electron flow two ways (both give same result)

"clockwise" flow:



- A Break $C_1-C_2 (\pi)$, form C_1-C_6
- B Break $C_5-C_6 (\pi)$, form C_4-C_5
- C Break $C_3-C_4 (\pi)$, form $C_2-C_3 (\pi)$

"counter-clockwise" flow:

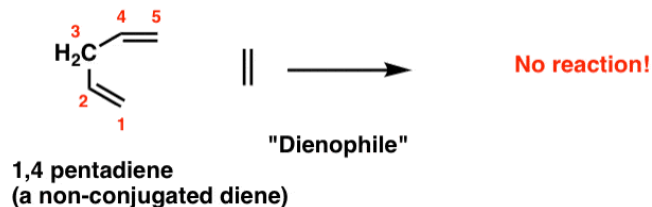


- A Break $C_1-C_2 (\pi)$, form $C_2-C_3 (\pi)$
- B Break $C_3-C_4 (\pi)$, form C_4-C_5
- C Break $C_5-C_6 (\pi)$, form C_1-C_6

Diels-Alder Reaction: “Diene” & “Dienophile”

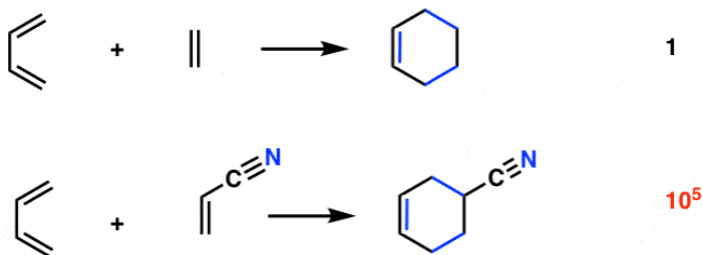
In general: **Diene** should be **e⁻-rich** & **Dienophile** should be **e⁻-deficient** (or *Vive-versa*) for better reaction.

The diene must be conjugated in order for the Diels-Alder to occur:

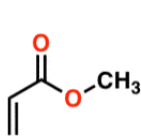


Electron withdrawing groups on the dienophile increase the reaction rate

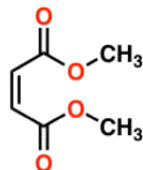
Relative Rate



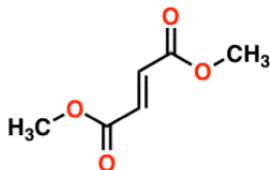
Examples of common dienophiles



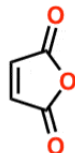
Methyl acrylate



Dimethyl maleate

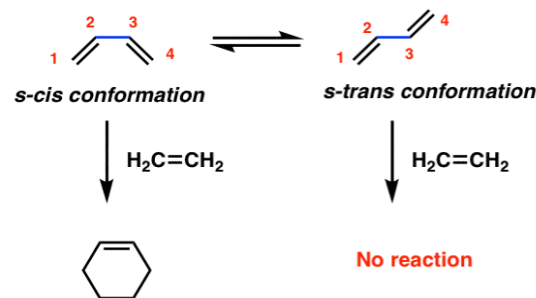


Dimethyl fumarate



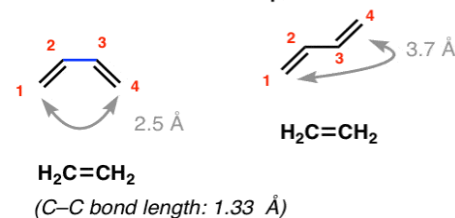
Maleic anhydride

The diene **must** be in the *s-cis* conformation to participate in the Diels-Alder reaction

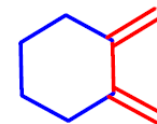
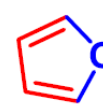


Why?

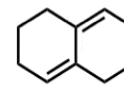
Geometry. In the *s-trans* conformation, C₁ and C₄ are too far apart to be able to react with the dienophile



Reactive Diene:

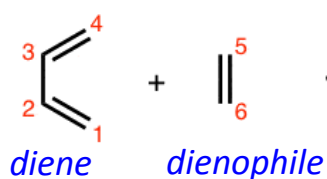


Dienes locked in the *s-trans* conformation cannot undergo the Diels Alder

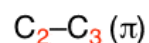
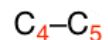
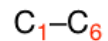


Diels-Alder Reaction: *Diversity*

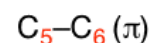
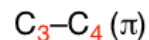
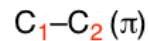
The Diels-Alder Reaction



Bonds Formed



Bonds Broken



Intermolecular

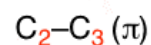
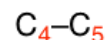
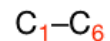
The Intramolecular Diels Alder Reaction Results In Two New Rings

diene and
dienophile attached
by linker

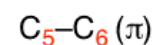
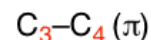
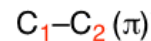
new ring!

new ring!

Bonds Formed



Bonds Broken



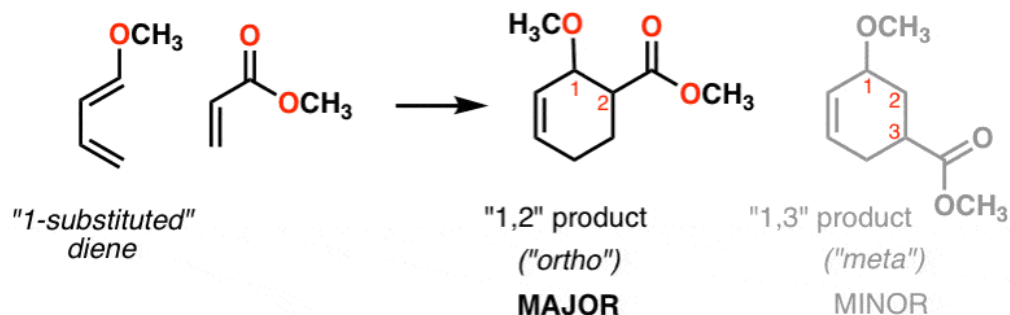
Intramolecular

Diels-Alder Reaction: *Regioselectivity*

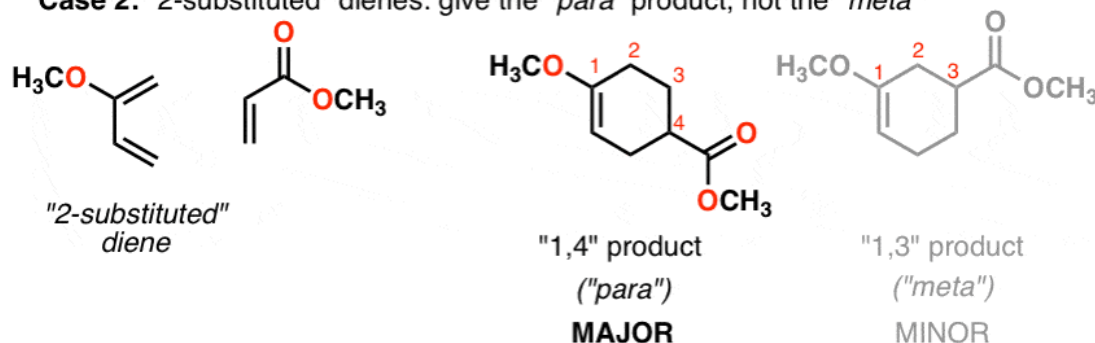
Regioselectivity In The Diels Alder

When non-symmetrical dienes react with non-symmetrical dienophiles, two "regioisomers" are possible

Case 1: "1-substituted" dienes: give the "*ortho*" product, not the "*meta*"

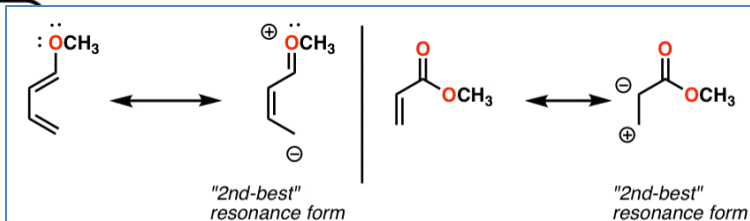


Case 2: "2-substituted" dienes: give the "*para*" product, not the "*meta*"

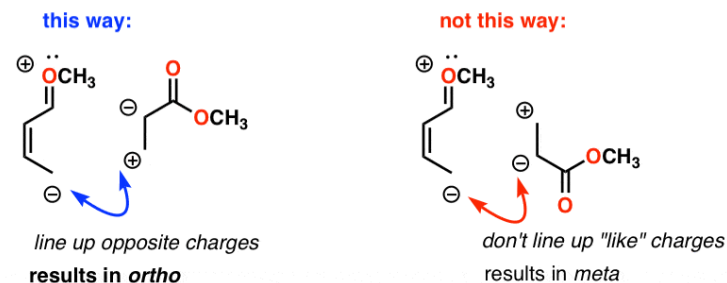


The "1,3" ("*meta*-") product is **disfavored** in both cases

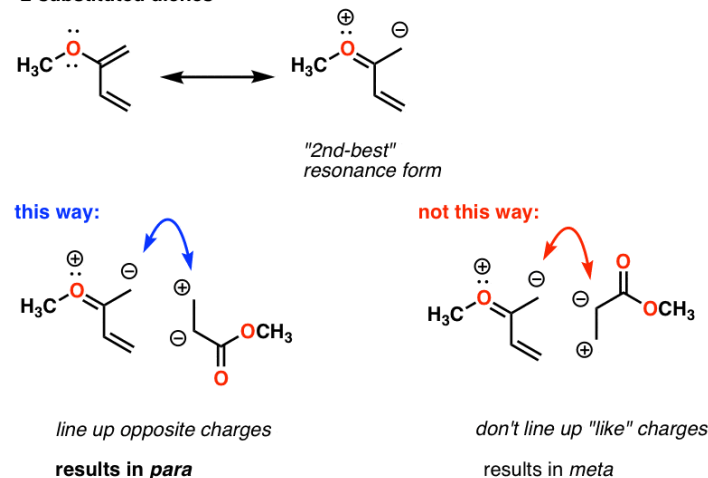
<https://www.MasterOrganicChemistry.com>



Now, line up the **negative charge from the diene** with the **positive charge on the dienophile**



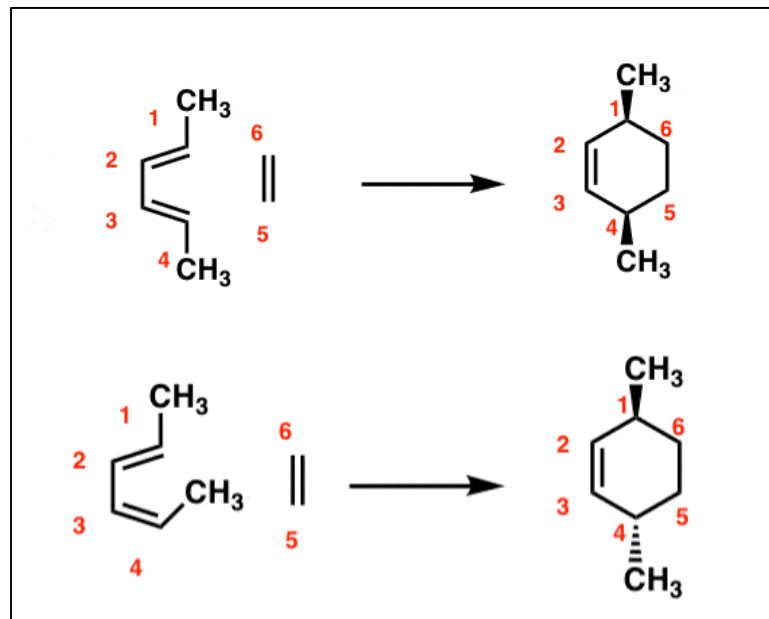
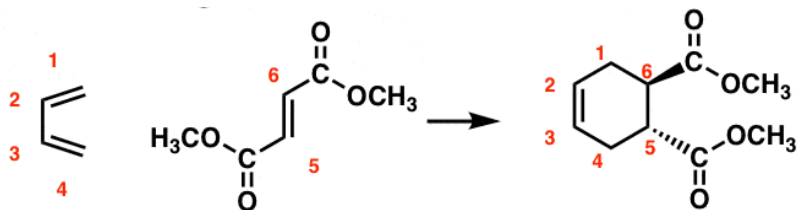
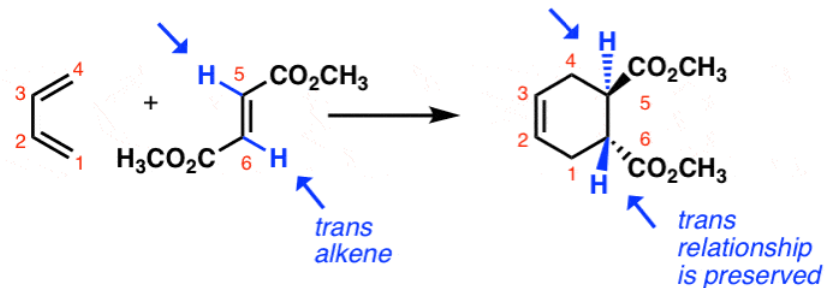
2-substituted dienes



Diels-Alder Reaction: Stereochemistry

- Stereochemistry of both *diene* and *dienophile* retained in the product

In The Diels Alder Reaction The Stereochemistry Of The Dienophile Is Preserved

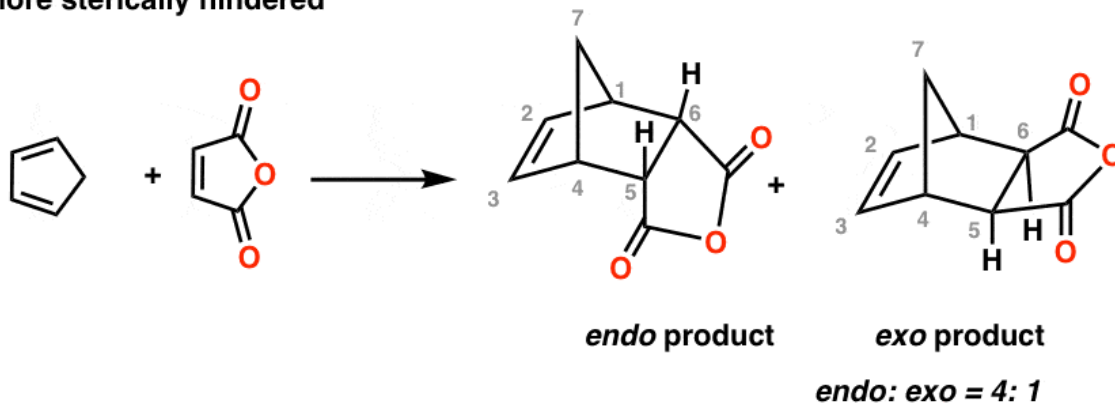


Diels-Alder reaction of a cyclic dienophile

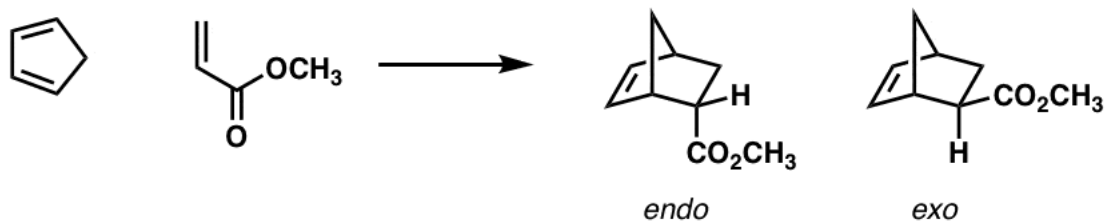


Diels-Alder Reaction of Cyclic Diene: *Regioselectivity*

endo products tend to be favored in the Diels-Alder, even though they are more sterically hindered



Lewis acid catalysis improves selectivity for *endo*:



CH_2Cl_2 , 0°C

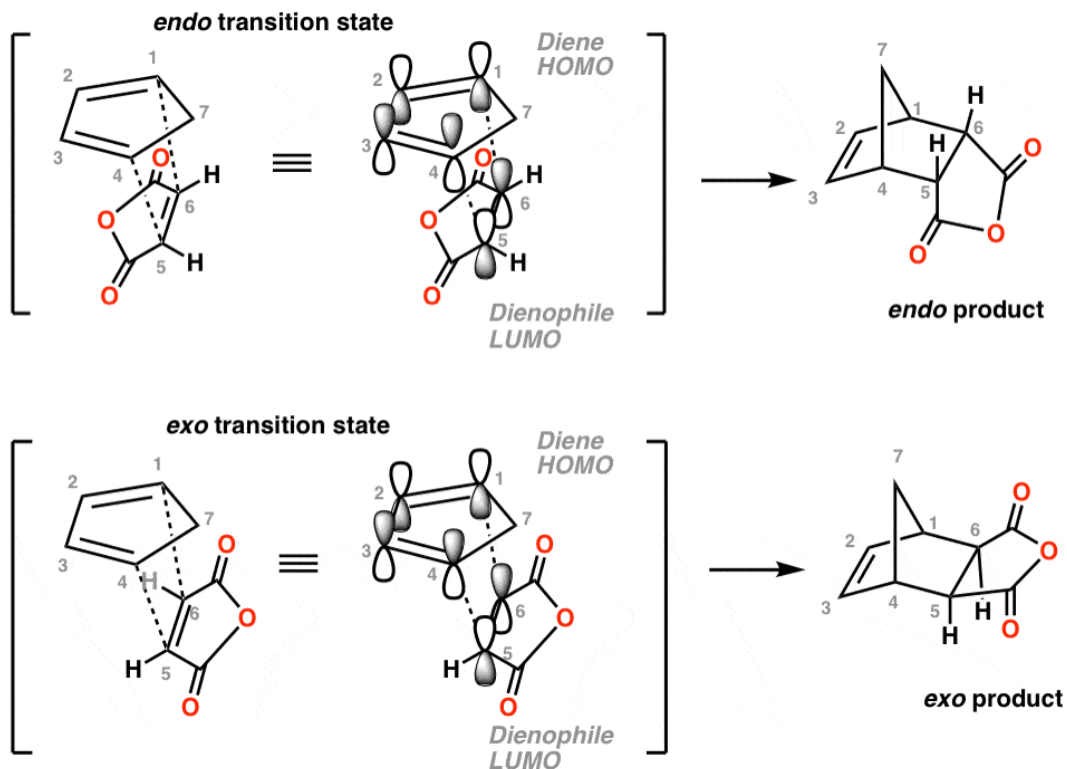
80:20

benzene, SnCl_4 , 25°C

95:5

Diels-Alder Reaction: *Endo* vs *Exo* Products

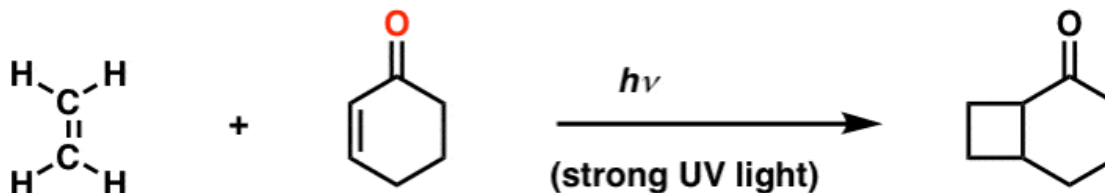
exo and *endo* Transition States and Molecular Orbitals



Because the C₂-C₃ orbitals of the diene HOMO are positioned close to the C=O orbitals of the dienophile LUMO, they can interact: "*secondary orbital interaction*"

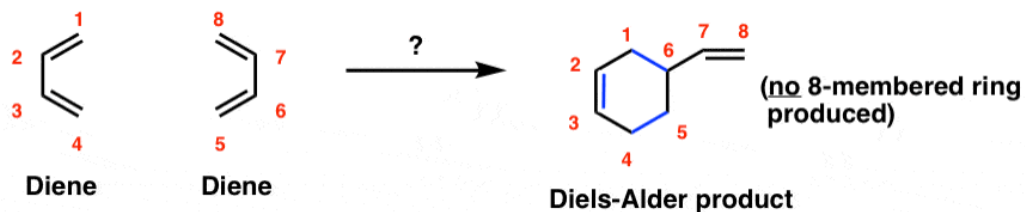
[2+2] Cycloaddition: *Under Photo-irradiation*

Example of a [2+2] Cycloaddition



no reaction in the absence of UV light

Q. What about dienes? Can we combine two dienes to make an 8-membered ring?



A. Doesn't work. We get a Diels-Alder product instead!

Diels-Alder Reaction: *[4+2] Cycloaddition*

