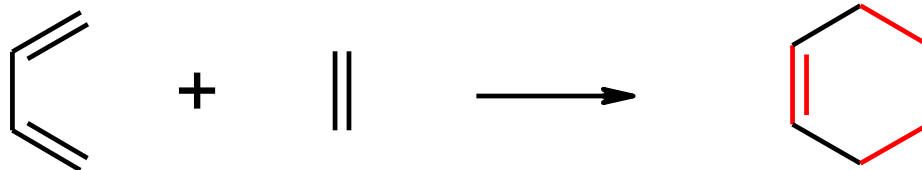


# Diels-Alder Reaction

- Method for synthesis of 6-membered ring
- One-step, concerted reaction
- Termed [4+2] cycloaddition reaction where  $4\pi$  and  $2\pi$  electrons react.



# Diels-Alder Reaction

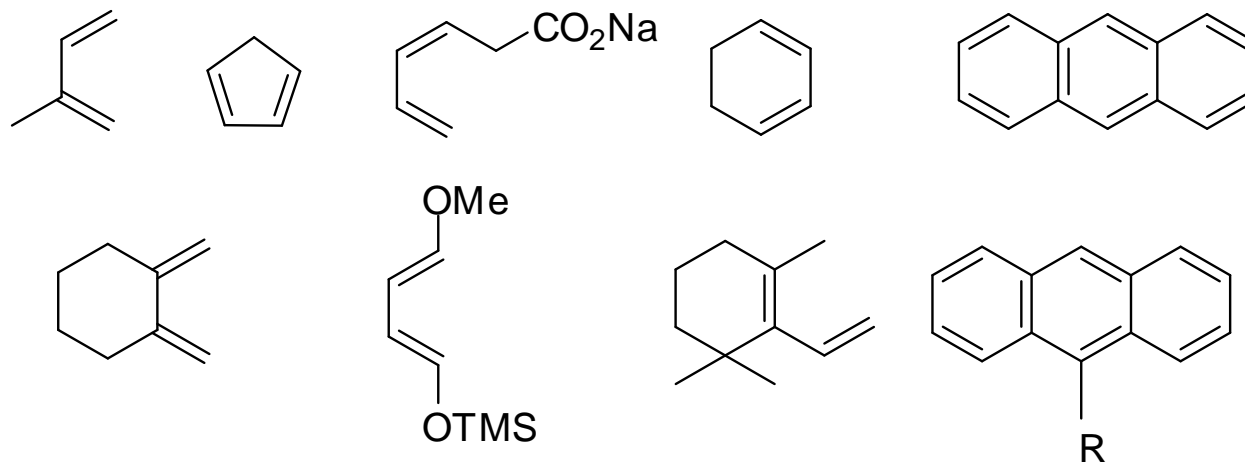
- Discovered by O. Diels and K. Alder in 1928.
- Occur between a conjugated diene and substituted alkene (dienophile) to form cyclohexene ring system.
- Concerted reaction (single step), can be accelerated by heating or using some catalysts.
- [ 4+2 ] cycloaddition reaction.
- In retro Diels-Alder reaction, the six membered ring is break down to regenerate the diene and dienophile using high temperature usually.
- Stereoselective reaction (mainly one product formed).

# Diels-Alder Reaction

- Stereospecific reaction ( reactants can keep their stereochemistry).
- No transition states or charged intermediates.
- All electrons moving in same time to form two new  $\sigma$  bonds.
- 100 % economic ( No. of reactants atoms = No. of products atoms).
- If one or more of diene or dienophile atoms are not carbon ,the reaction is hetero-Diels-Alder reaction.

# The dienes

- Can be cyclic , acyclic carrying many kinds of substituents.
- Must have *s-cis* conformation.
- +I substituted dienes are more reactive than others.



Danishefsky diene

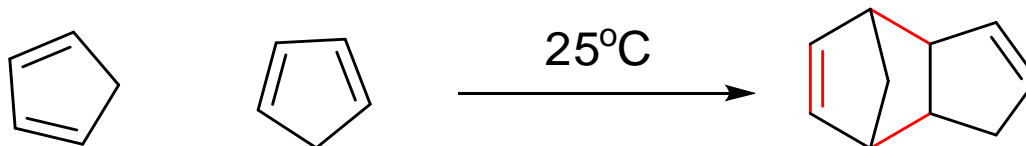
R= Me, OMe, CH(Me)OMe

OTMS = Octadecyltrimethoxysilane

Danishef's sky diene = 1-Methoxy, 1,3-butadiene

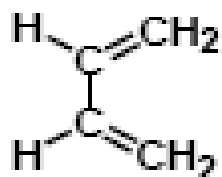
# Cyclopentadiene

- Cyclopentadiene which is well known as a standard diene can undergo self D.A at R.T.

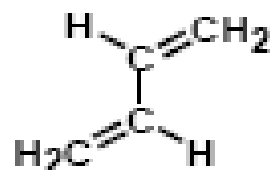


## The Diene

- must adopt *s-cis* conformation about single bond

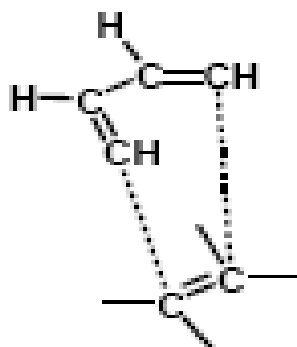


*s-cis* conformation

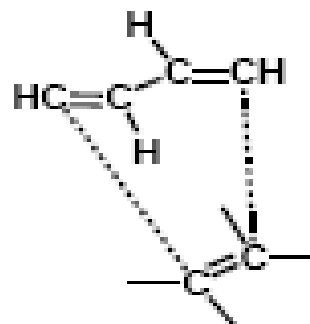


*s-trans* conformation

- in the alternative *s-trans* conformation, the ends of the diene are too far apart to overlap with the dieneophile *p orbitals*



reaction

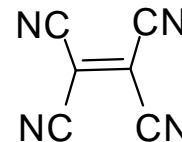
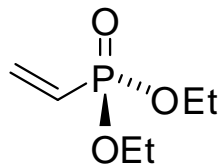
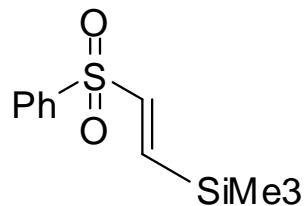
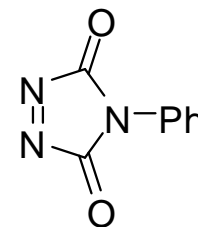
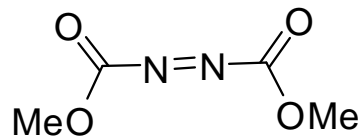
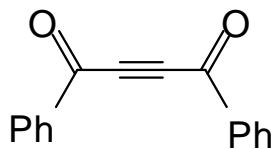
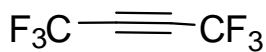
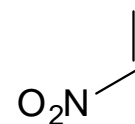
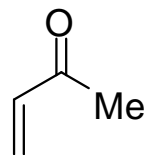
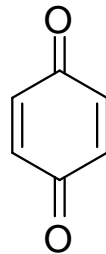
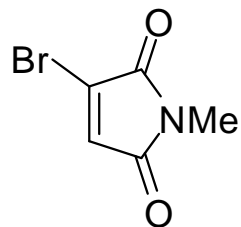
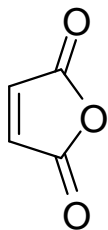


no reaction

# The dienophiles

- Wide range of dienophiles can be used including cyclic, acyclic and hetero compounds for the Diels-Alders reaction.
- Perfect dienophiles are alkenes conjugated to electron withdrawing groups such as carbonyl, nitro, nitrile, and halogen
- *Certain* groups can increase the rate of Diels-Alder reaction.
- Diels-Alder reactions between alkene and diene without any substituents can take place but with low yield.

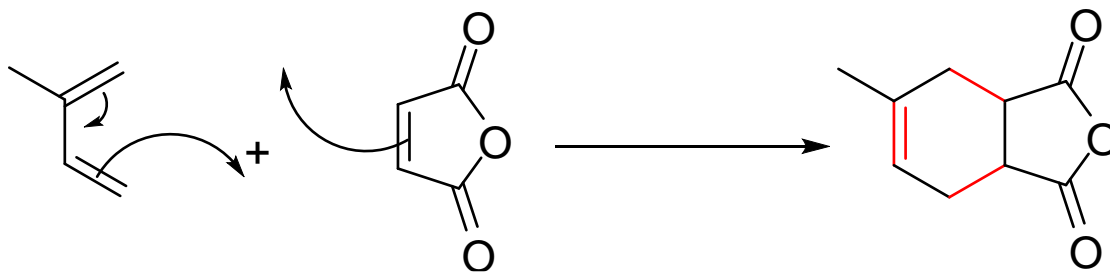
# The dienophiles





# How to know its Diels-Alder reaction?

- Since it's {4+2} cycloaddition, the product is, six membered ring, **double bond inside the ring**, conjugate group outside the ring opposite to double bond.

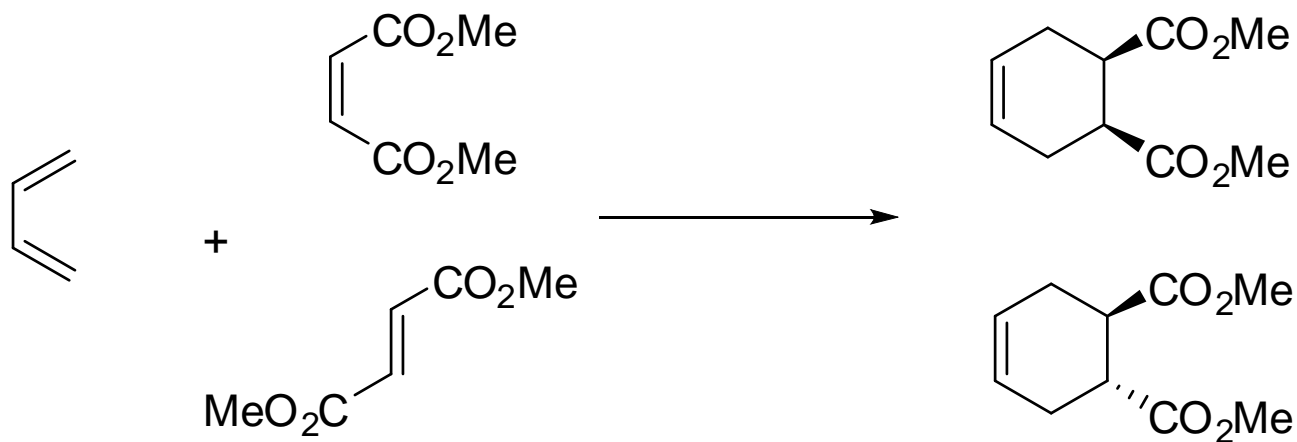


# How it works?

- Concerted reaction via aromatic transition state.
- There are two approaches, the first depends on the interaction between **HOMO** of The diene and **LUMO** of the dienophile.
- The second, depends on +I, -I groups affect, since they form negative and positive charges on the diene and dienophile.

# Stereochemistry

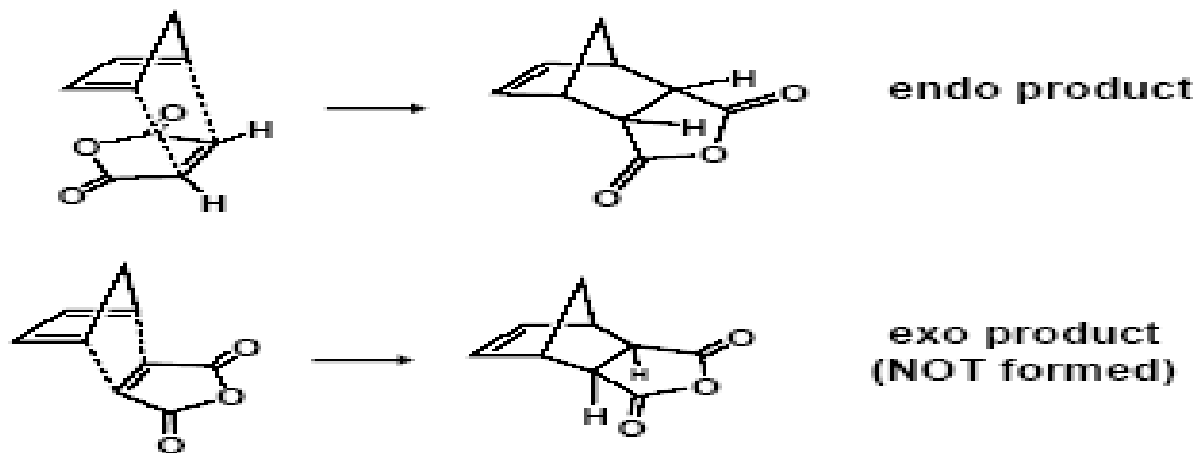
- The stereochemistry of substituents can be retained in the product.
- Cyclic dienes must be in *s-cis* are highly reactive .



# Endo rule

- Diels-Alder between cyclic dienes and dienophiles can lead two diastereomers, *endo* and *exo*.
- Endo product is kinetically controlled product.
- Exo product is thermodynamically product.

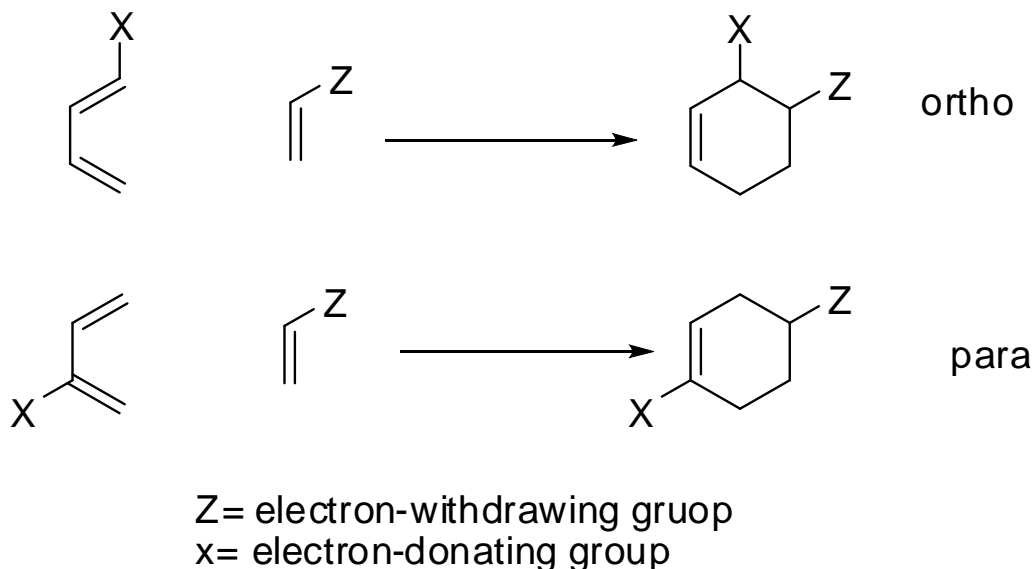
- *endo* product results because orbital overlap is best when the reactants lie directly on top of one another so that the electron-withdrawing substituent on the dienophile is underneath the diene



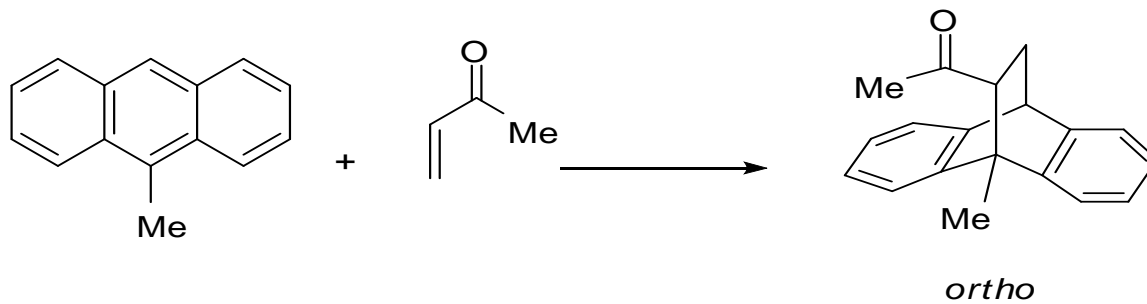
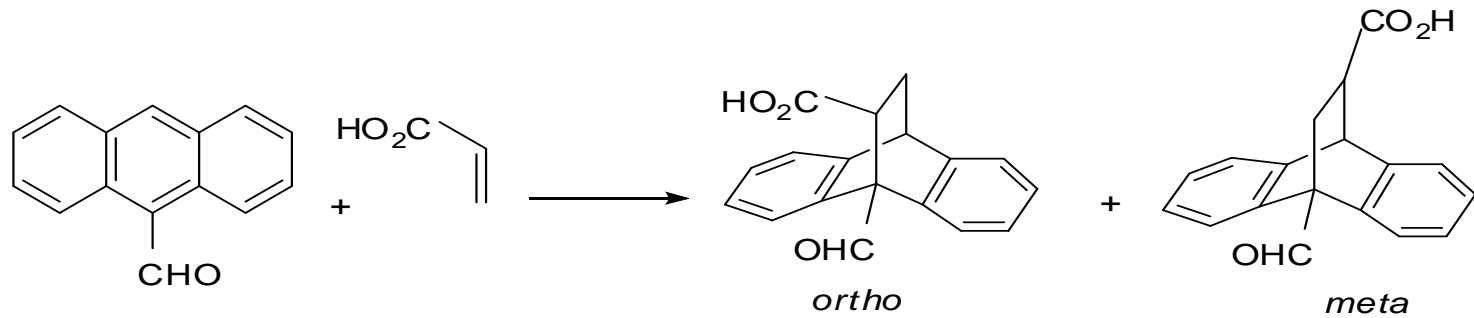
- bicyclic product is known as a norbornane -

# Regioselectivity

- Diels-Alder reaction can lead to different structural isomers.
- Electronic and steric effects of the substituents.
- Position of these groups is the main factor.
- Usually its *ortho* and *para* directiong.



# Regioselectivity



# Catalysed Diels-Alder reaction

- To increase the rate of the reaction.
- To reduce high temperature and long reaction times.
- To improve the regioselectivity.
- As a source of enantioselectivity.

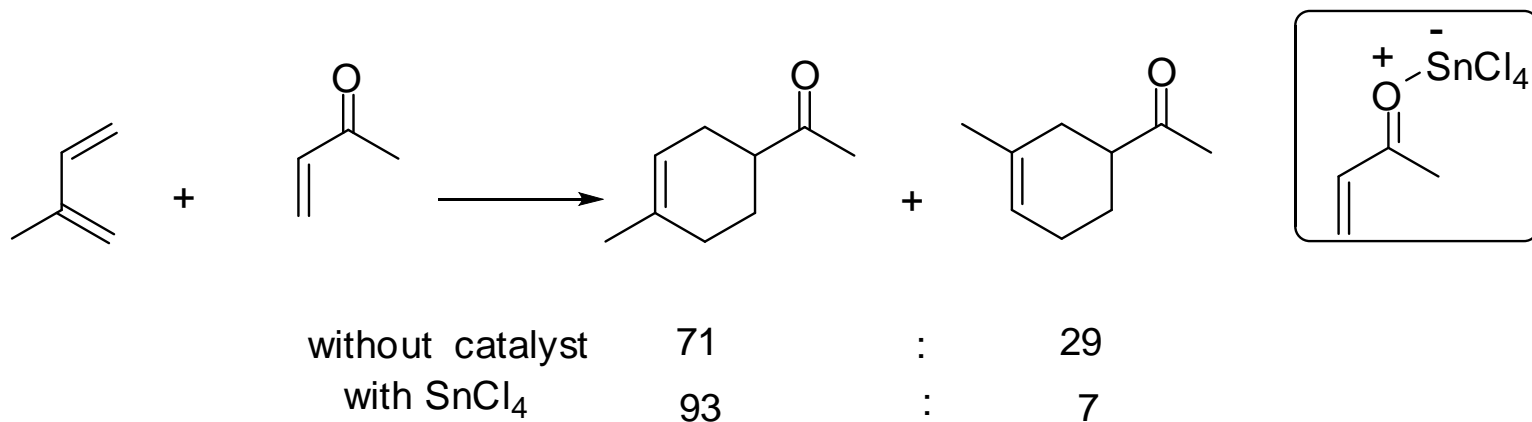
# Catalysed Diels-Alder reaction

- Using Lewis acids catalysts (including chiral members).
- $\text{AlCl}_3$  and its derivatives,  $\text{M}(\text{OTf})$ ,  $\text{BF}_3 \cdot \text{OEt}$ .....
- Using organic catalysts (organic molecules can be used individually or combined with Lewis Acids).
- Imidazolidinone derivatives, thiourea derivatives, BINOL and its derivatives.....



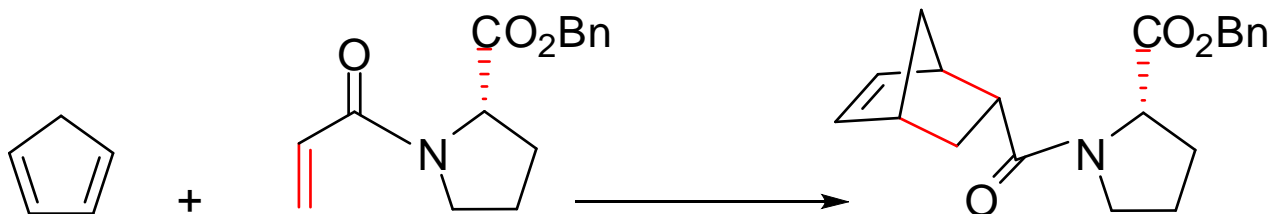
# Lewis Acid catalysis

- L.A binding with EWD group then make the dienophile more electron deficient.
- Then, decrease LUMO energy, strong interaction with diene's HOMO.

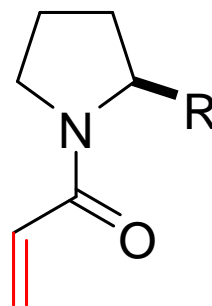
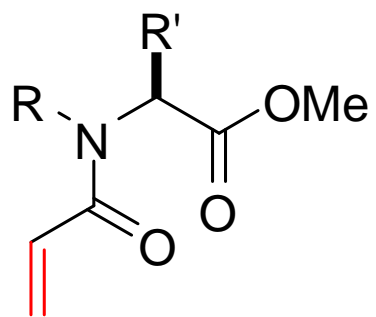
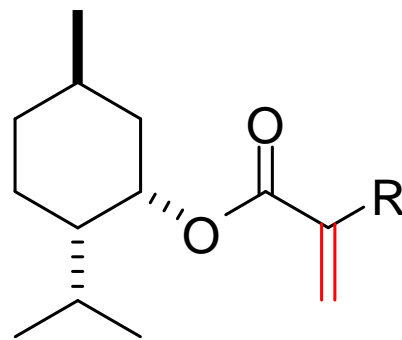
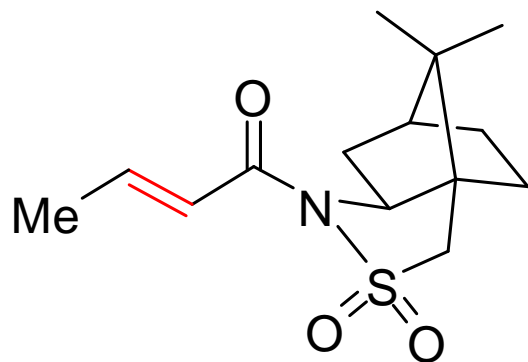


# Asymmetric Diels-Alder reaction

- Preparation of chiral cyclohexene derivatives .
- **Using chiral dienes or dienophiles**
- Using chiral Lewis Acids.

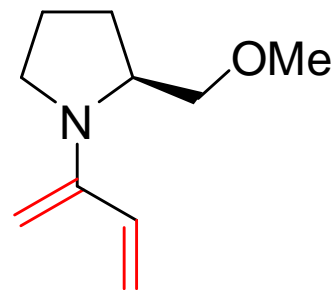
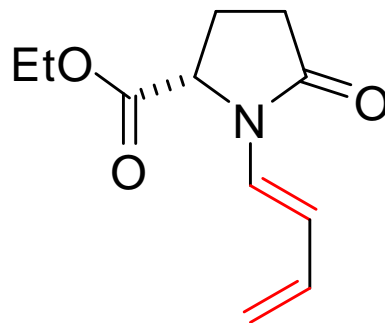
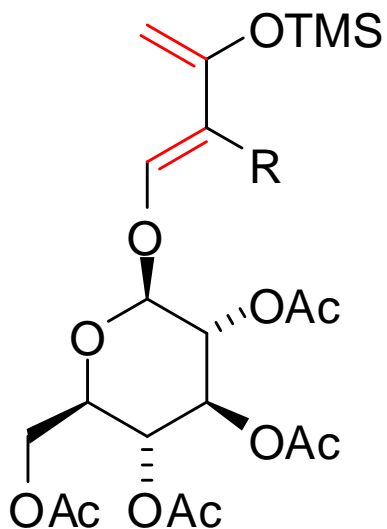


# Chiral dienophiles



# Chiral dienes

- Using chiral dienes is less developing as the use of chiral dienophiles.



# Chiral Lewis Acids

