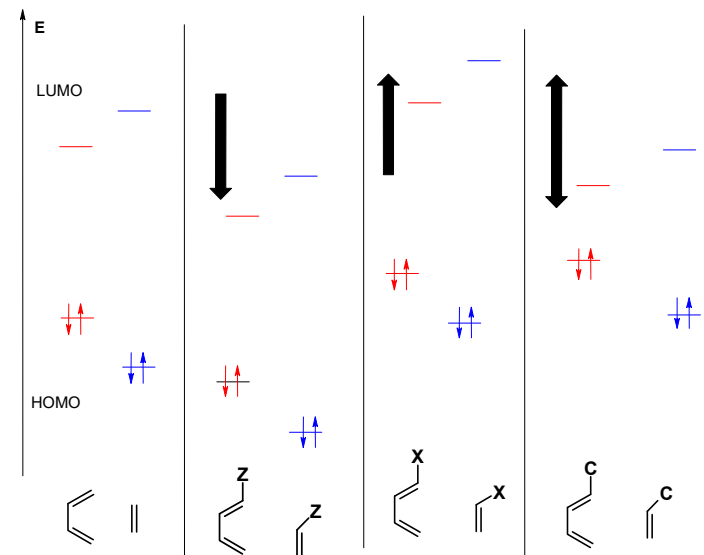
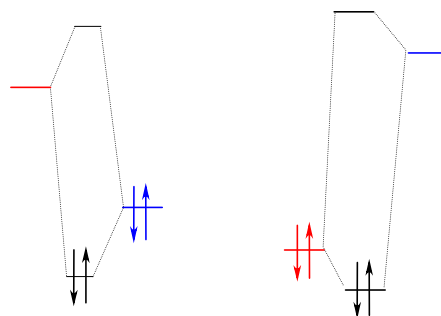
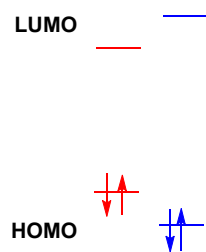
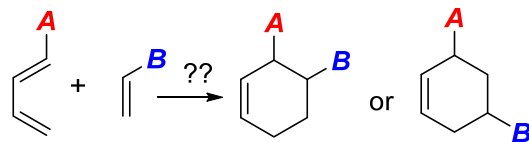
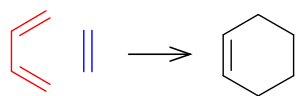


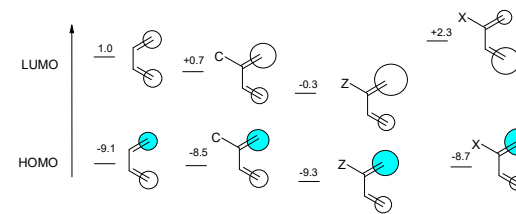
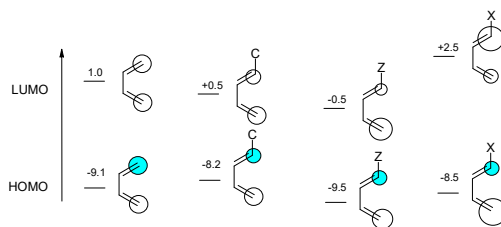
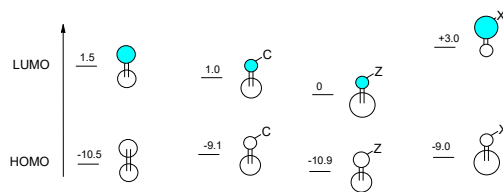
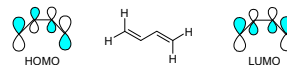
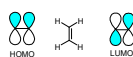
ORGANIC STEREOCHEMISTRY lecture 6



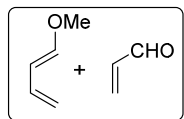
Energy gained during formation of new bonds is higher when HOMO and LUMO are closer

$$\Delta E \sim 1 / (E_1 - E_2)$$

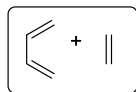
Typical energies (eV) and coefficients



## Diels – Alder Reaction

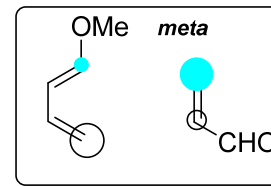
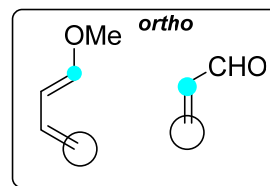


easy (smooth) reaction



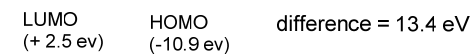
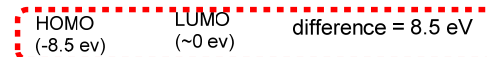
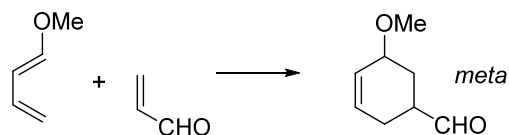
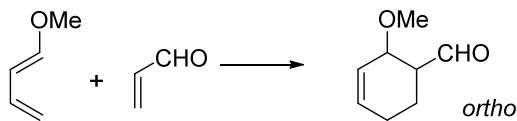
difficult process

**Analysis for Diene-X; Dienophile-Z**

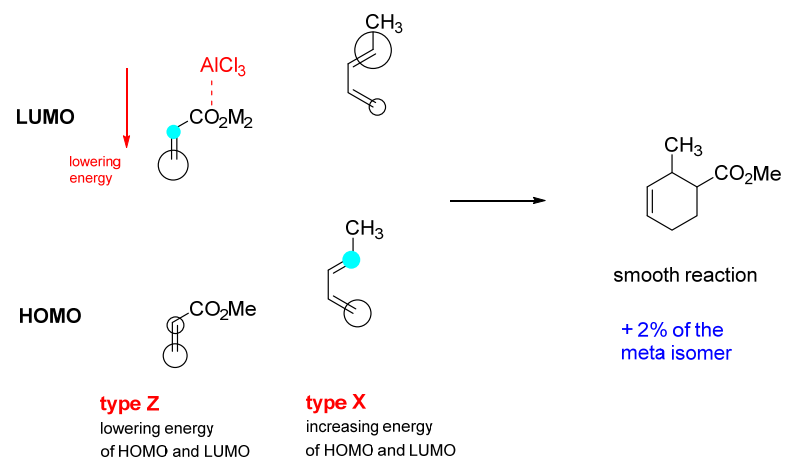
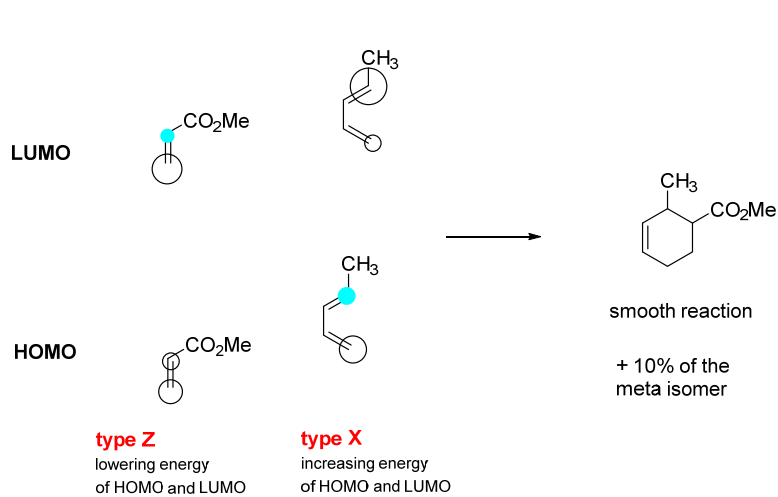


**Best overlapping when  $\Sigma C_{ij} = \max$**

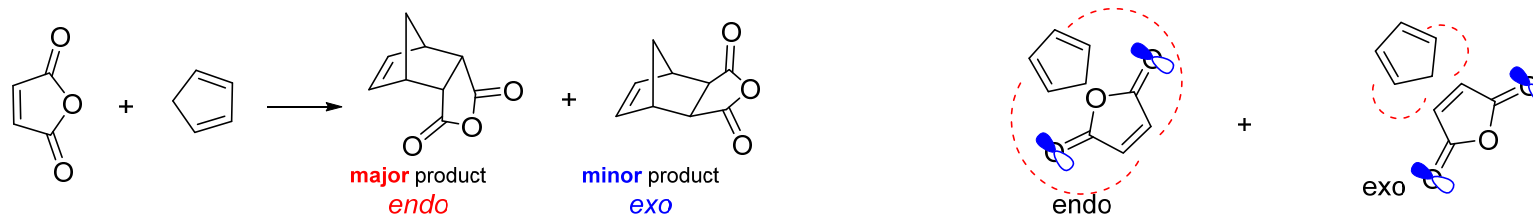
regioselectivity in D-A reactions



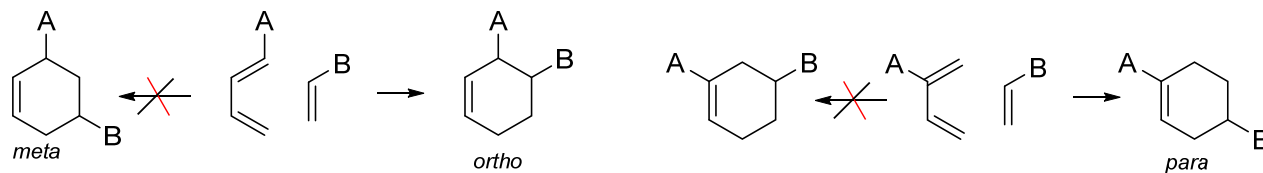
## Diels-Alder reaction catalyzed with Lewis acids



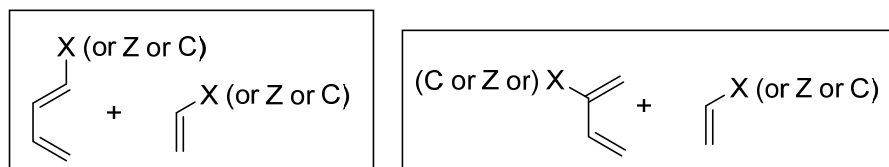
## Secondary effects in the Diels-Alder reaction



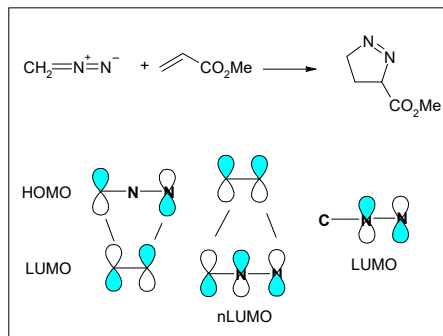
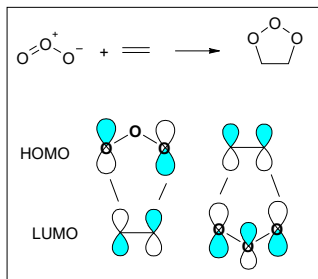
The simple way to estimate the regioselectivity in the D-A reactions



This analysis can be also performed for all other combinations

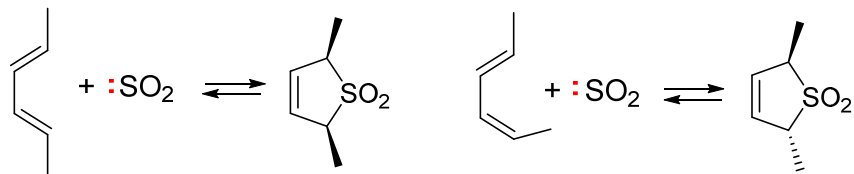
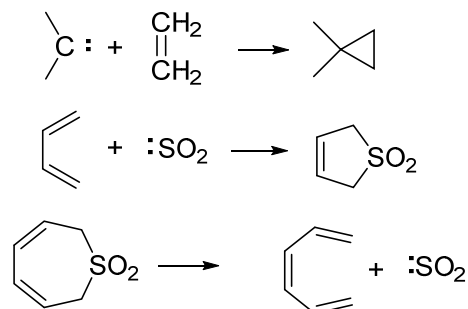


## 1,3-dipolar cycloaddition

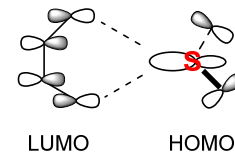
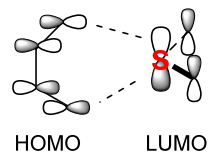


## cheletropic reactions

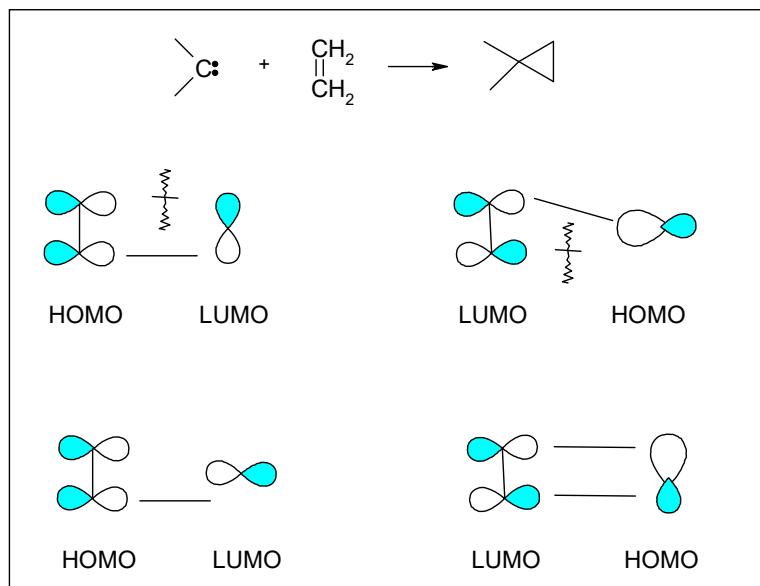
Sub-class of cycloaddition reactions. The only difference is that new bonds are created/broken at the same atom of the reactant



relation between  $\text{CH}_3$  points at the suprafacial attack

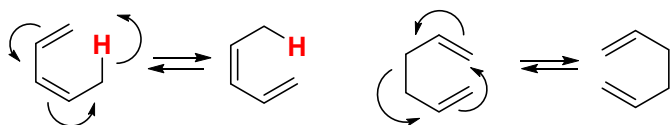


## Singlet carbene

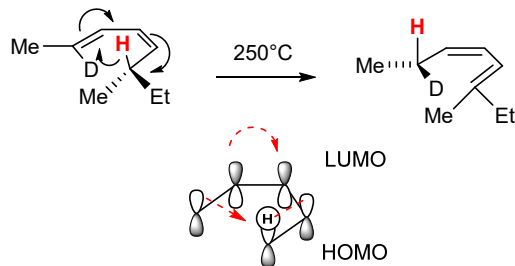


## Sigmatropic rearrangements

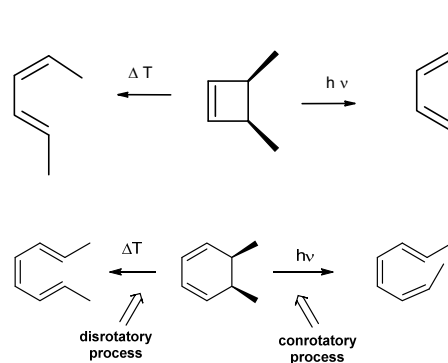
Reactions in which the bond is moving along the conjugated system to new position. Representative examples: [1,5] or [3,3] rearrangements



In the case of the concerted process all bonds MUST be created /broken at the same time.  
Since the number of the electron pairs is ODD ( $n = 3$ ) this process should be suprafacial



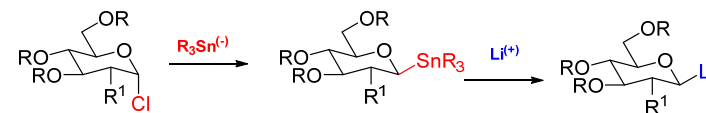
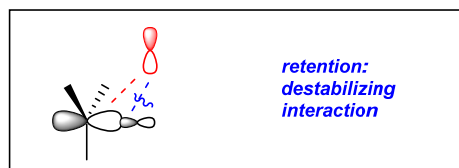
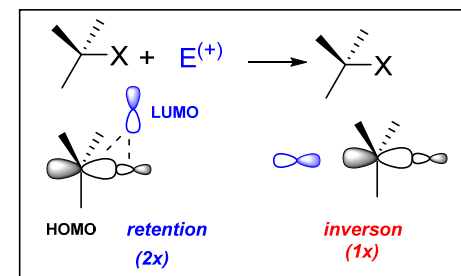
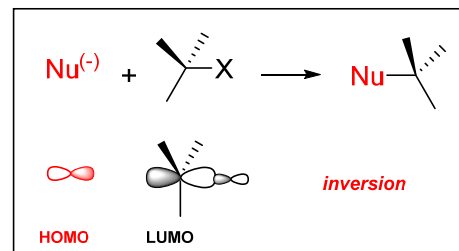
## Electrocyclic Reactions



**Review:** Recent Advances on the Application of Electrocyclic Reactions in Complex Natural Product Synthesis *Synthesis*, **2017**, 49, 4383–4413; Ming Bian et al..

## Nucleophilic Substitution ( $S_N2$ ) and Electrophilic Substitution ( $S_E2$ )

$S_N2$  reaction - inversion of the configuration;  $S_E2$  - usually retention of the configuration



Burkhart, Kessler, TL, 1998

## The origin of optically active and optically PURE compounds

Up to 1957 it was assumed that Nature is symmetrical at the atomic level

In 1957 Lee and Young proposed the 'parity violation' (different probability of existence of the process and its mirror image)

Biochemical homochirality is a consequence of the spontaneous violation of the symmetry and the existence of the L-aminoacids and D-sugars is incidental

Nowadays the commonly accepted concept postulates that homochirality is not of biogenic nature

There are experimental proofs of incidental generation of optical activity

Spontaneous resolution through a preferred crystallization of a racemate

In weak atomic interactions (*weak forces*) it was observed, that beta particles emitted by radioactive atomic nuclei have disturbed symmetry:  
the 'left-handed' electrons are slightly more common than their mirror images

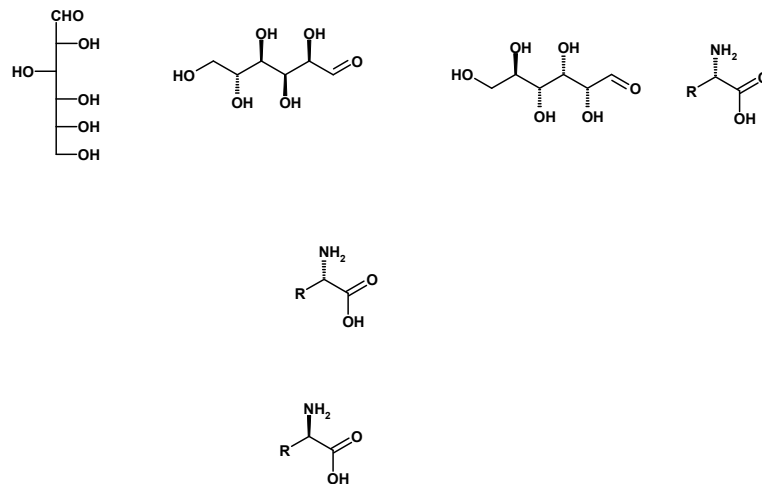
The main consequence of this fact:

**CHIRALITY is observed at the level of elementary particles**

Calculations show that the energy of enantiomers is DIFFERENT !

For D- and L-aminoacids this difference is:  $10^{-13}$  to  $10^{-16}$  J/mol

Review: B. Feringa *et.al.* Angewandte **1999**, 38, 3418-3438



In chemical reactions of optically inactive compounds, only the optically inactive derivatives are produced, without the external source of chirality

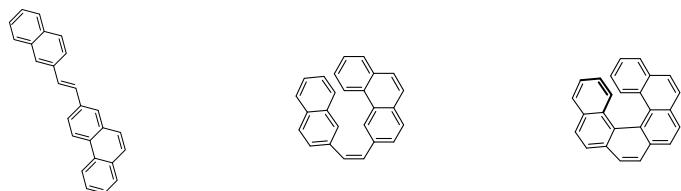
They can be either achiral (*i.e.* meso-tartaric acid) or chiral but racemic (*i.e.* D/L-tartaric acid; 50:50%)

Racemates can have different melting point than single enantiomers!!!

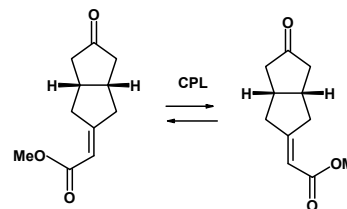
If we have, therefore 'enriched' racemate (i.e. a mixture of enantiomers in a ratio 85:15) it is possible to obtain pure enantiomer by crystallization.

**Several mechanism of obtaining optically pure compounds:**

Crystallization of an achiral derivative in a chiral form (quartz)



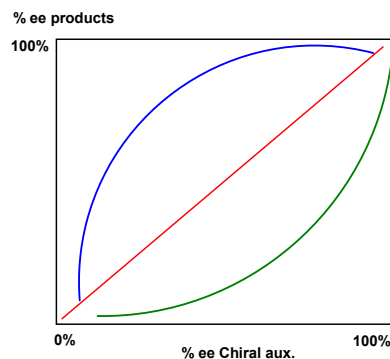
circularly polarized light, asymmetric synthesis, kinetic decomposition of a racemate



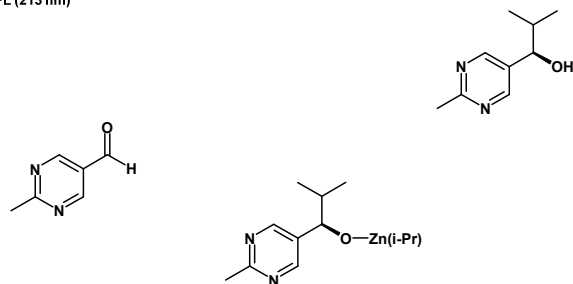
**‘CHIRAL AMPLIFICATION’**

It is a process in which the enantiomeric excess of the product is much much higher than that of a catalyst or chiral auxiliary

Kagan H.B.\* *JACS* **1994**, *116*, 9430-9439



DL-leucine  $\xrightarrow{(+)\text{CPL (213 nm)}}$  L-leucine (2% ee)



chiral initiator	ee% initiator	ee% product
<chem>CC(O)C(=O)OC1=CC=CC=C1</chem>		
<chem>CC(C)C(=O)OC1=CC=CC=C1</chem>		