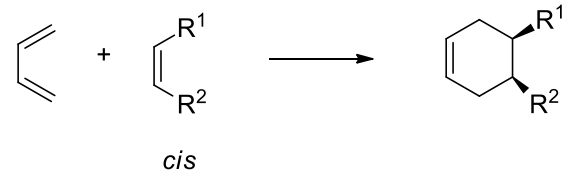
3.2.1. Diene and dienophile isomers

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.

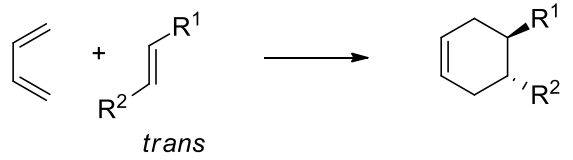
➡ The stereochemical information of the starting materials is conserved in the product:

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



cis

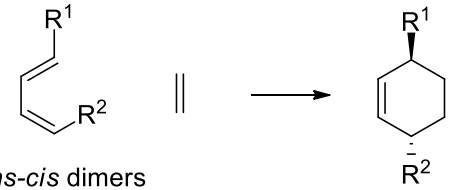
trans-Olefins: substituents end up on the **opposite** face of the product:



trans

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

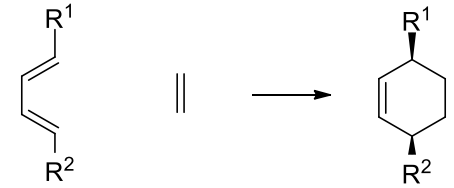
R^1 and R^2 end up on the **opposite** face



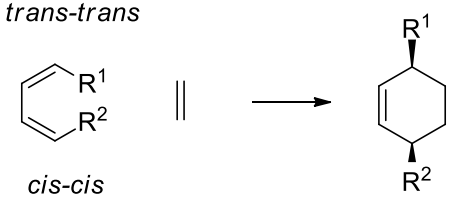
trans-cis dimers

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

R^1 and R^2 end up on the **same** face



trans-trans

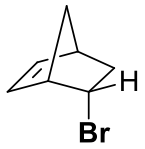


cis-cis

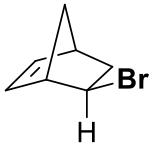
3.2.2. *Exo* / *Endo* selectivity

General and original explanation of the forms exo/endo:

Substituent of a bicyclic molecule is
- Under the 'roof' =endo
- Out of the 'roof' =exo



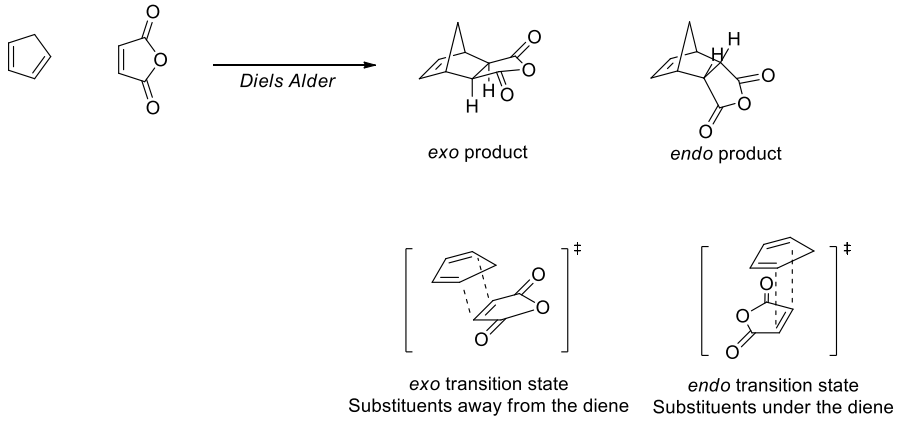
endo



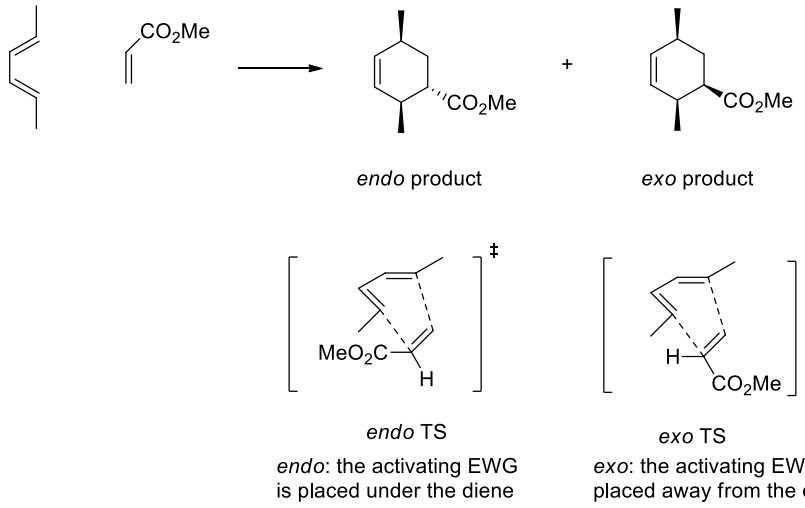
exo

In the context of Diels Alder reaction:

Bicyclic products:



Monocyclic products:

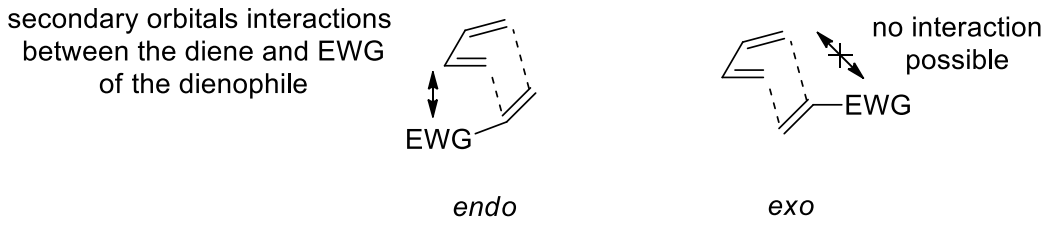


3.2.2. *Exo* / *Endo* selectivity

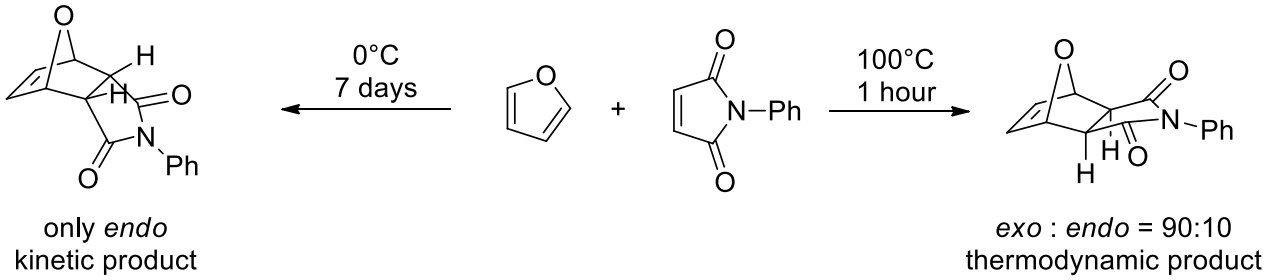
Comparison between kinetic and thermodynamic product:

→ *Endo* is the kinetic product: the transition state is stabilized by secondary orbital interactions.

→ *Exo* is the thermodynamic product: more stable, less hindered product.

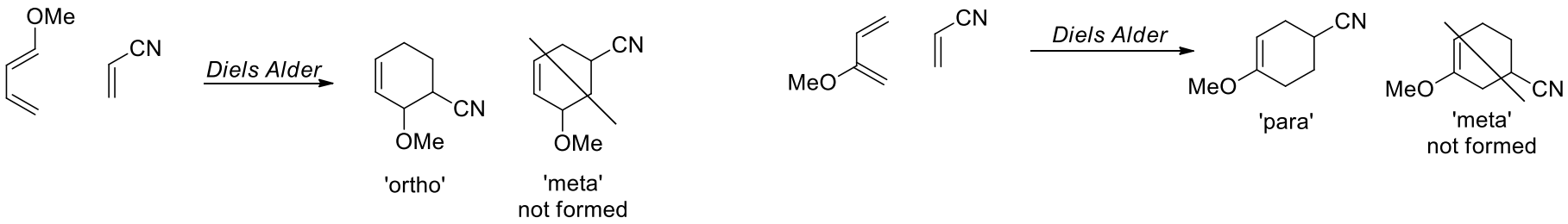


Example:



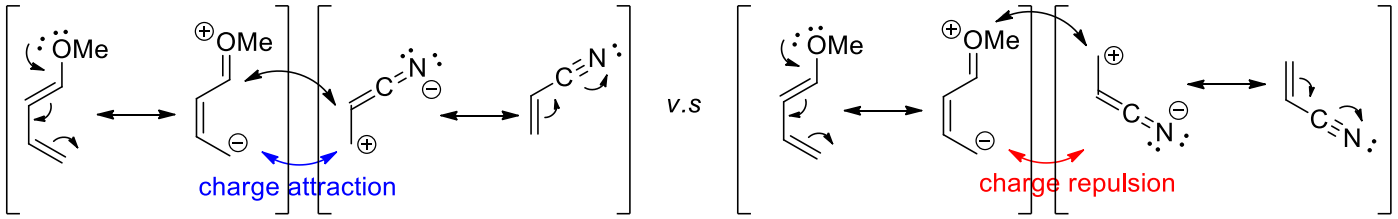
3.3. Diels-Alder regioselectivity

Observations:



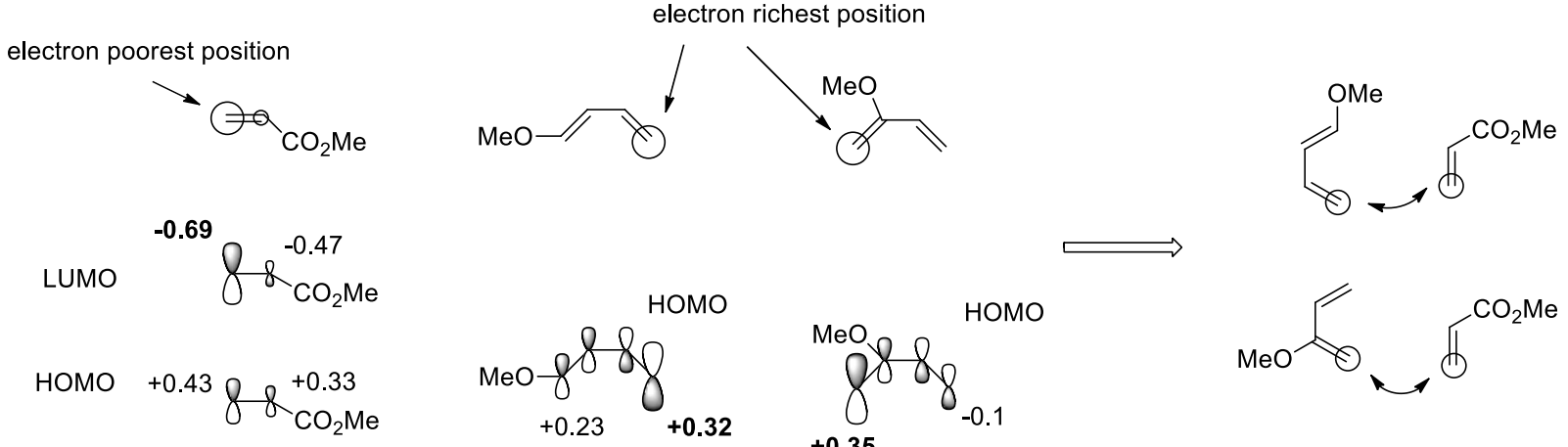
Rule: Electron-donating and electron-withdrawing groups are oriented 'ortho' or 'para' to each other.

Simple explanation with the mesomeric structures:



More accurate explanation with orbital coefficients:

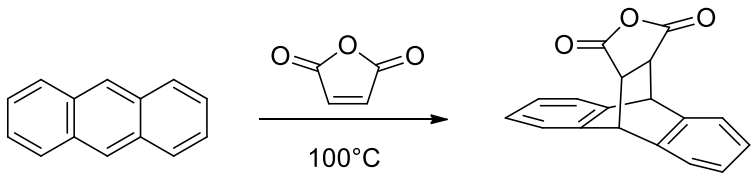
➡ Favorable interaction: small coefficients with small, big with big



3.3. Additional examples of Diels-Alder cycloaddition

3.3.1. Extented polycyclic aromatics as diene component

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



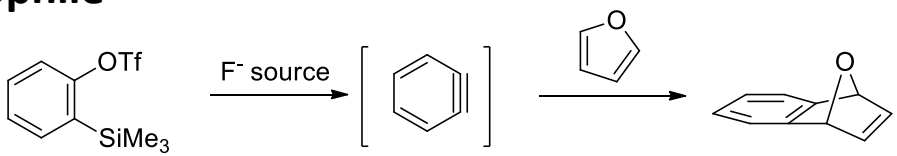
Anthracene

⇧

The middle quinoid ring has the weakest aromatic stabilization and is the most reactive

product contains two benzoid rings

3.3.2. Benzyne as dienophile

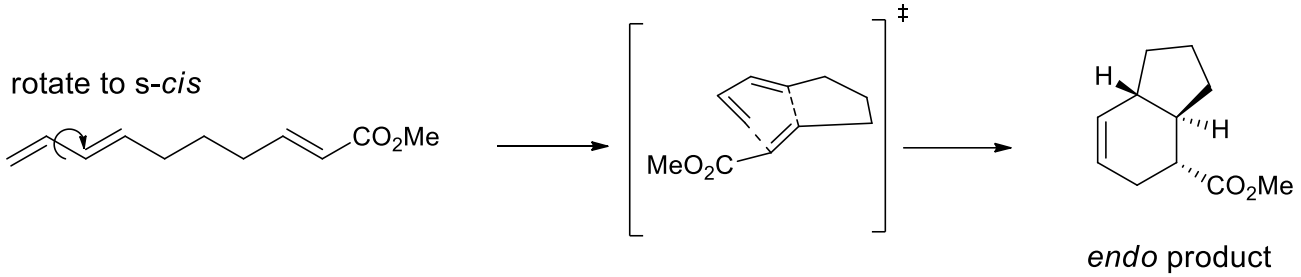


benzyne found *in situ*:
very reactive dienophile

F^- source:
commonly: CsF or Bu_4NF 'TBAF'

3.3. Additional examples of Diels-Alder cycloaddition

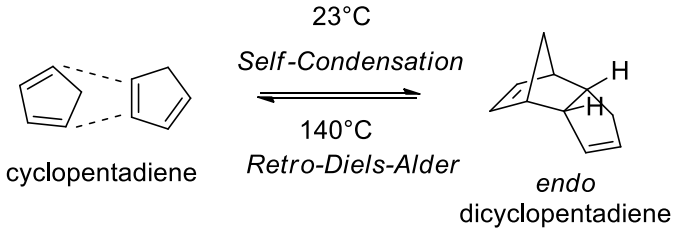
3.3.3. Intramolecular Diels-Alder reactions



➡ 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

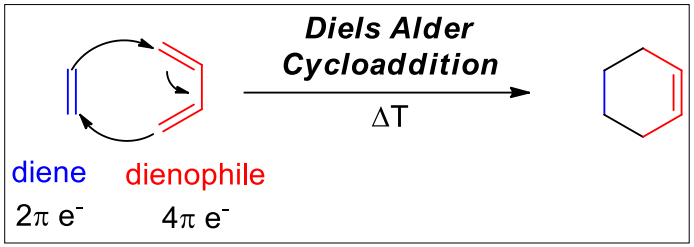
Cyclopentadiene self-condenses at ambient temperature. The reaction is reversible above 140°C



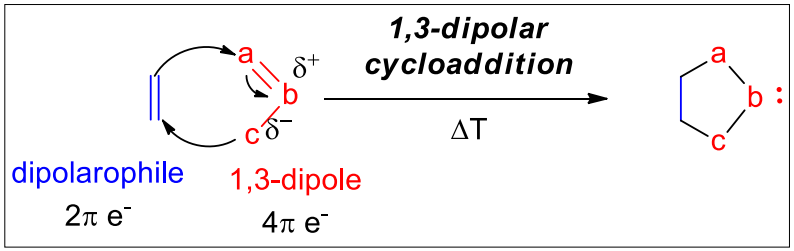
➡ All Diels-Alder cycloadditions are principally reversible at a high enough temperature (>350°C) as the entropy increases (2 molecules *v.s.* 1 molecule)

4.1.1. 1,3-dipolar cycloaddition

- Recap of the Diels-Alder cycloaddition:



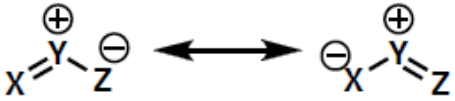
- Analogy for 1,3-dipolar cycloaddition:



Types and Classification of 1,3-Dipoles

Two Types of Dipoles:

(1) Allyl anion

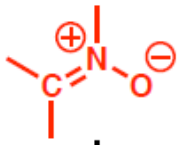


- Bent
- Y = N, O, S

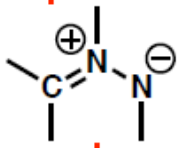
(2) Propargyl/allenyl anion

- Linear
- Y = Nitrogen

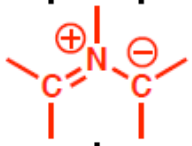
Classification of the Allyl Anion Type 1,3-Dipoles



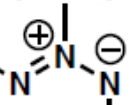
Nitrones



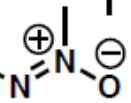
Azomethine Imines



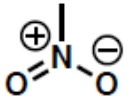
Azomethine Ylides



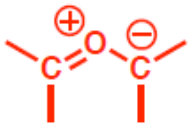
Azimines



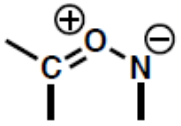
Azoxy Compounds



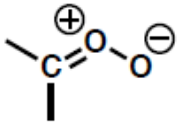
Nitro Compounds



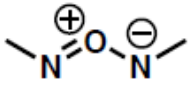
Carbonyl Ylide



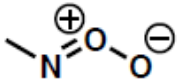
Carbonyl Imines



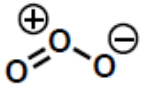
Carbonyl Oxides



Nitrosimines



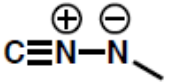
Nitrosoxides



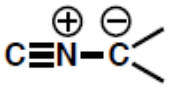
Ozone

Classification of the Propargyl/Allenyl Anion Type 1,3-Dipoles

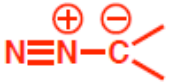
Nitrile Oxides



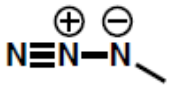
Nitrile Imines



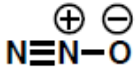
Nitrile Ylides



Diazoalkanes



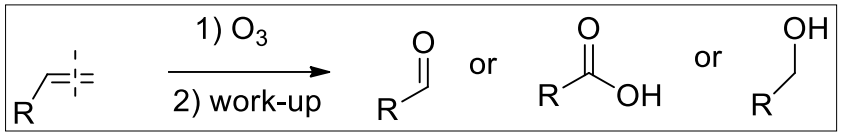
Azides



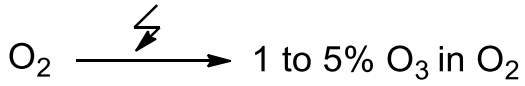
Nitrous Oxide

4.1.1. Ozonolysis

- Ozonolysis is a synthetically very important reaction converting olefins into alcohols, aldehydes, or carboxylic acids.

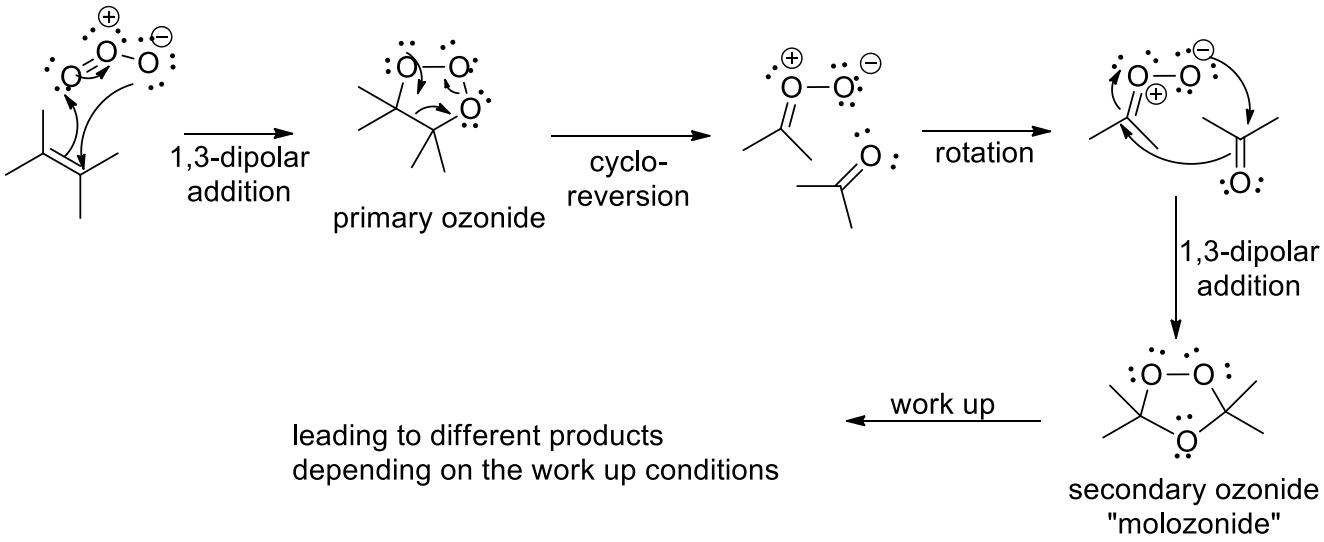


- Ozone O_3 is generated from O_2 (dry) by silent discharge:



Ozone has a blue color in solution, allowing to follow the progress of a reaction with it. When the reaction mixture turns light blue, it means that ozone is not consumed anymore and that the reaction is complete.
<u>Careful:</u> it is explosive in pure solution

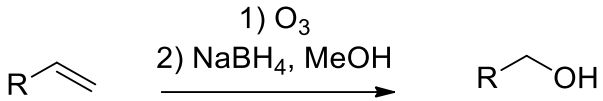
- Mechanism:



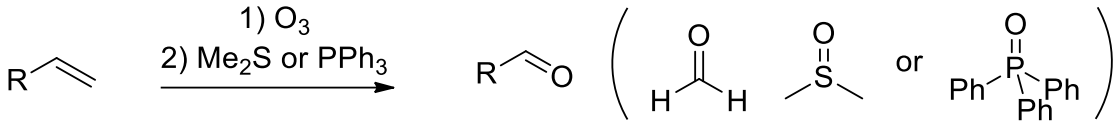
4.1.1. Ozonolysis

Different work-up strategies:

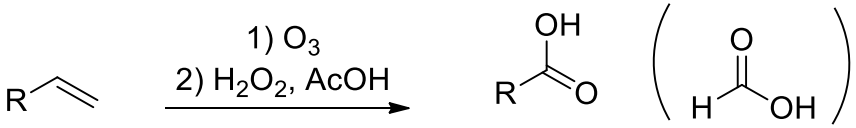
- Reductive work up with $NaBH_4$ + MeOH: formation of alcohols



- Mildly reductive work up with Me_2S or PPh_3: formation of aldehydes or ketones



- Oxidative work-up with H_2O_2 + acetic acid: formation of carboxylic acids or ketones



Careful with tri- or tetra-substituted alkenes: