Fonction et réaction organiques II

Fall Semester 2025

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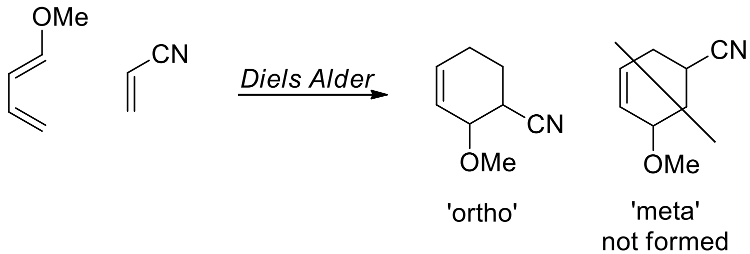
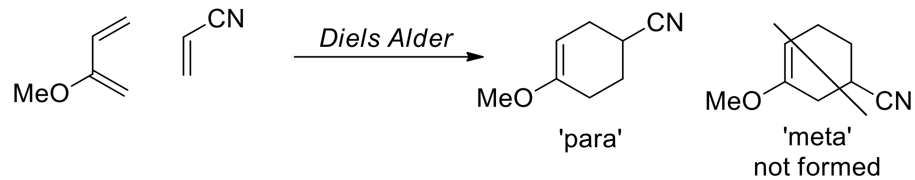
3.3. Diels-Alder regioselectivity

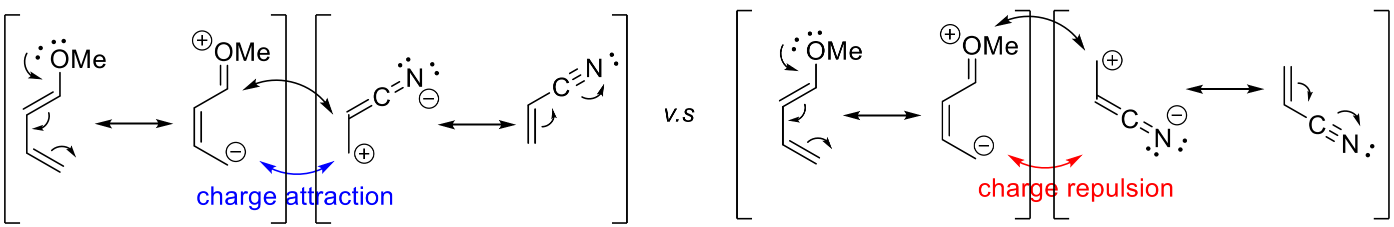
Observations:





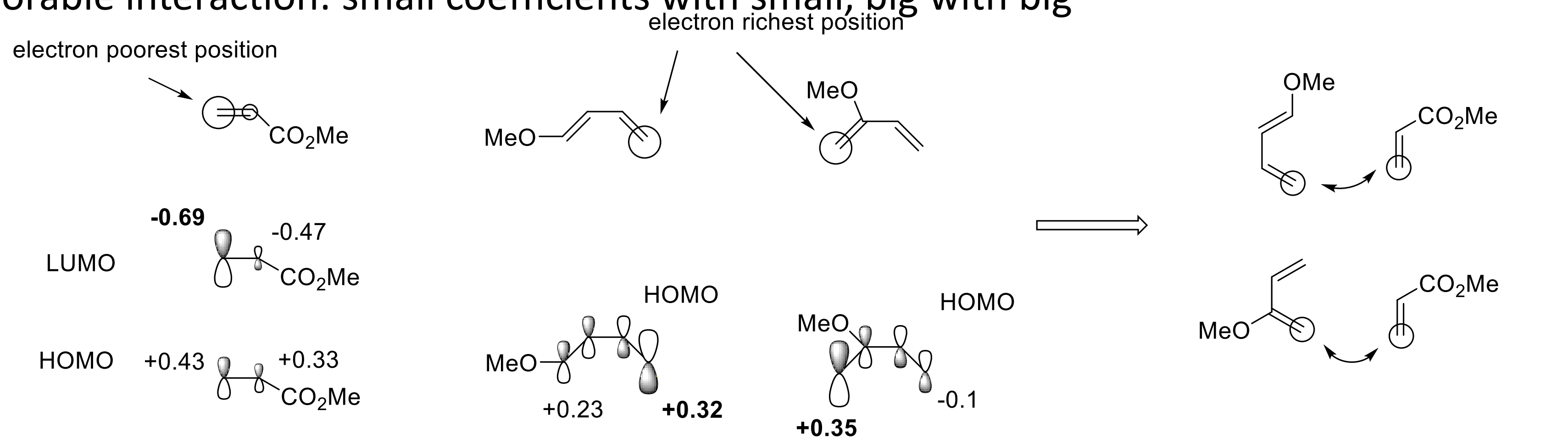
Rule: Electron-donating and electron-withdrawing groups are oriented 'ortho' or 'para' to each other.

Simple explanation with the mesomeric structures:



More accurate explanation with orbital coefficients:

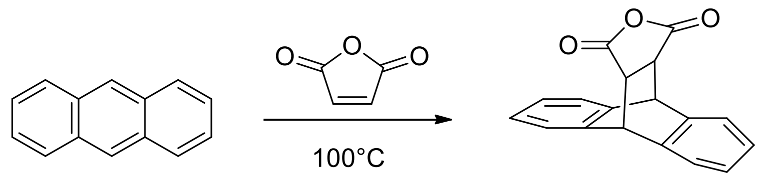
➡Favorable interaction: small coefficients with small, big with big



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



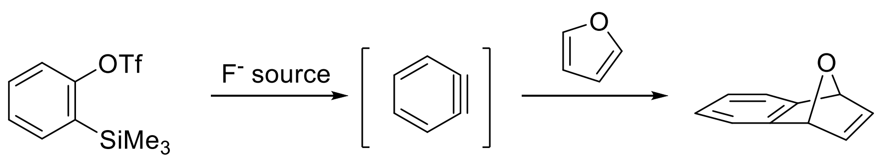
Anthracene

⇧

product contains two benzoid rings

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

3.3.2. Benzyne as dienophile

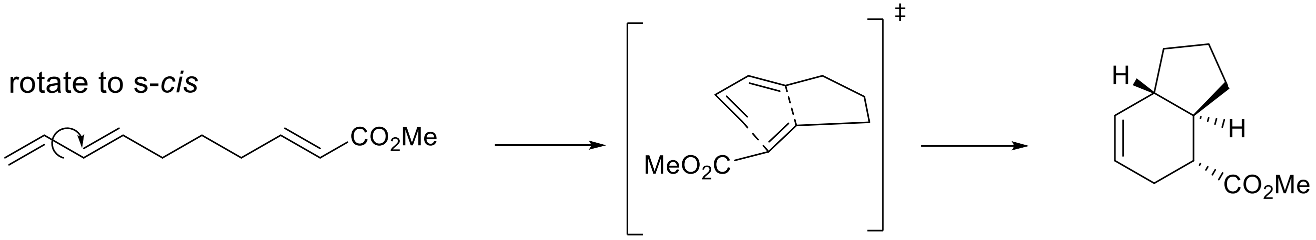


benzyne found *in situ*:
very reactive dienophile

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

3.3. Additional examples of Diels-Alder cycloaddition

3.3.3. Intramolecular Diels-Alder reactions

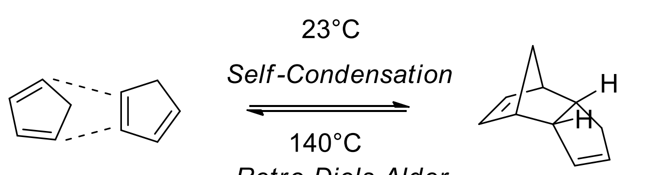


endo product

➡ 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



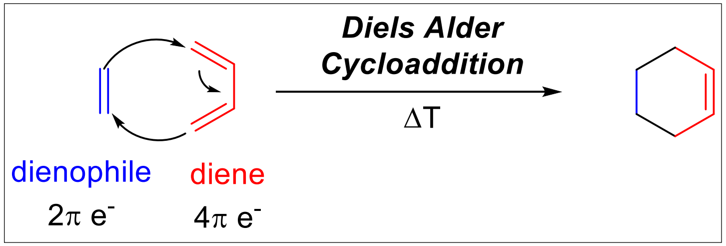
cyclopentadiene

endo dicyclopentadiene

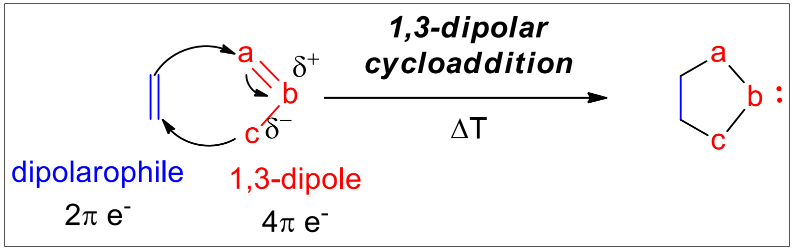
➡ All Diels-Alder cycloadditions are principally reversible at a high enough temperature (>350°C) as the entropy increases (2 molecules *v.s.* 1 molecule)

4.1.1. 1,3-dipolar cycloaddition

- Recap of the Diels-Alder cycloaddition:



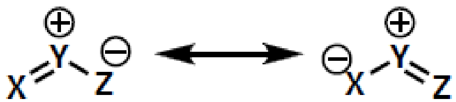
- Analogy for 1,3-dipolar cycloaddition:



Types and Classification of 1,3-Dipoles

Two Types of Dipoles:

(1) Allyl anion

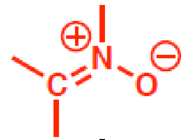


- Bent
- Y = N, O, S

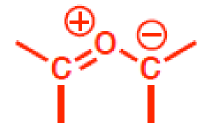
(2) Propargyl/allenyl anion

- Linear
- Y = Nitrogen

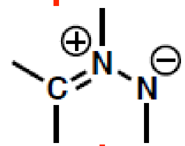
Classification of the Allyl Anion Type 1,3-Dipoles



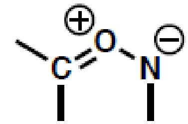
Nitrones



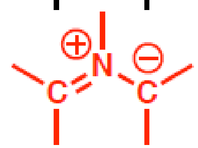
Carbonyl Ylide



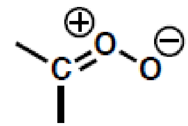
Azomethine Imines



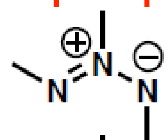
Carbonyl Imines



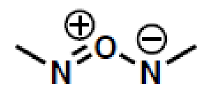
Azomethine Ylides



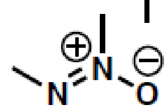
Carbonyl Oxides



Azimines

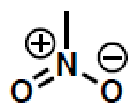


Nitrosimines

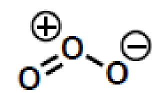


Azoxy Compounds

Nitrosoxides

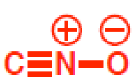


Nitro Compounds

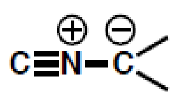


Ozone

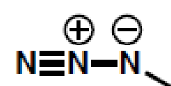
Classification of the Propargyl/Allenyl Anion Type 1,3-Dipoles



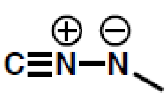
Nitrile Oxides



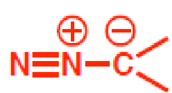
Nitrile Ylides



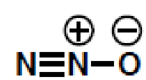
Azides



Nitrile Imines



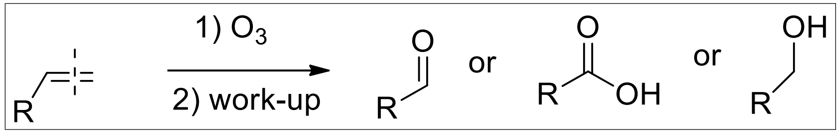
Diazoalkanes



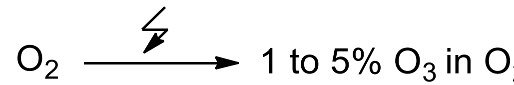
Nitrous Oxide

4.1.1. Ozonolysis

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

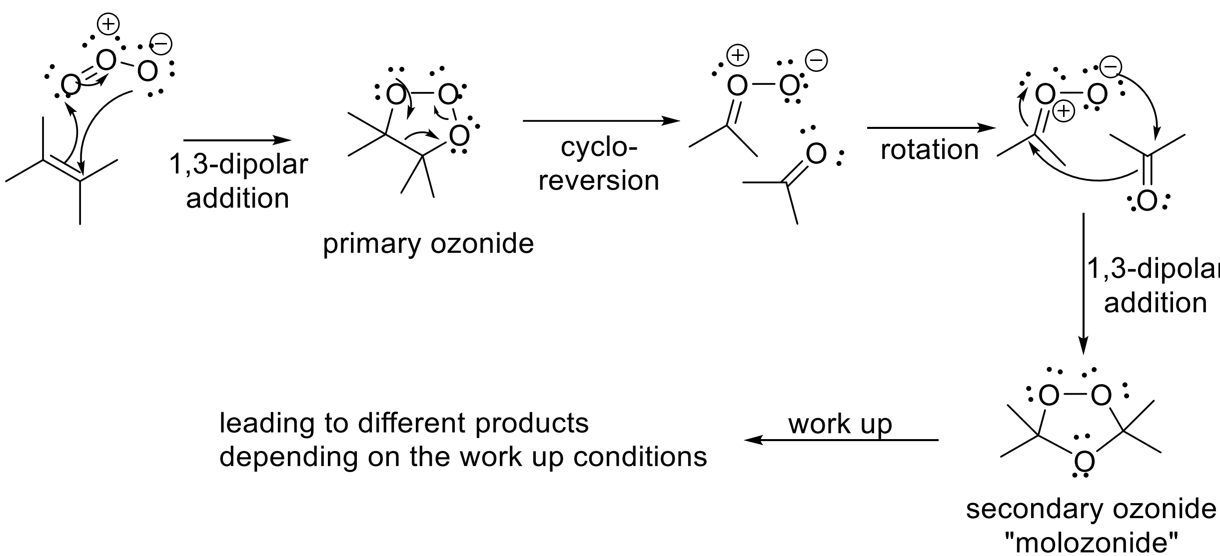


- Ozone O_3 is generated from O_2 (dry) by silent discharge:



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.
Careful: it is explosive in pure solution

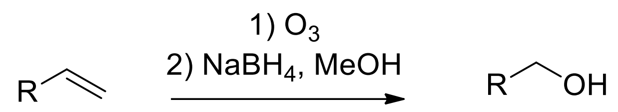
- Mechanism:



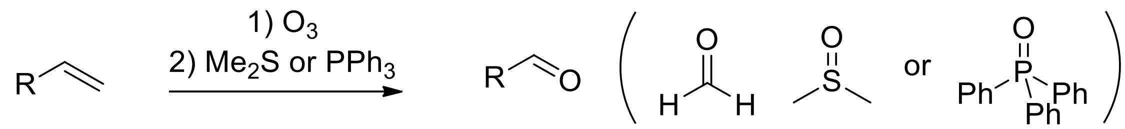
4.1.1. Ozonolysis

Different work-up strategies:

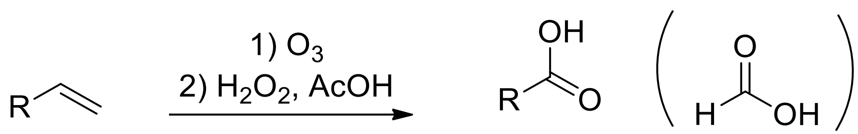
- Reductive work up with $NaBH_4$ + MeOH: formation of alcohols



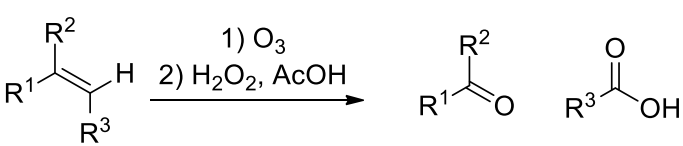
- Mildly reductive work up with Me_2S or PPh_3: formation of aldehydes or ketones

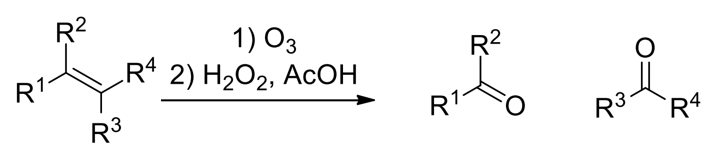


- Oxidative work-up with H_2O_2 + acetic acid: formation of carboxylic acids or ketones

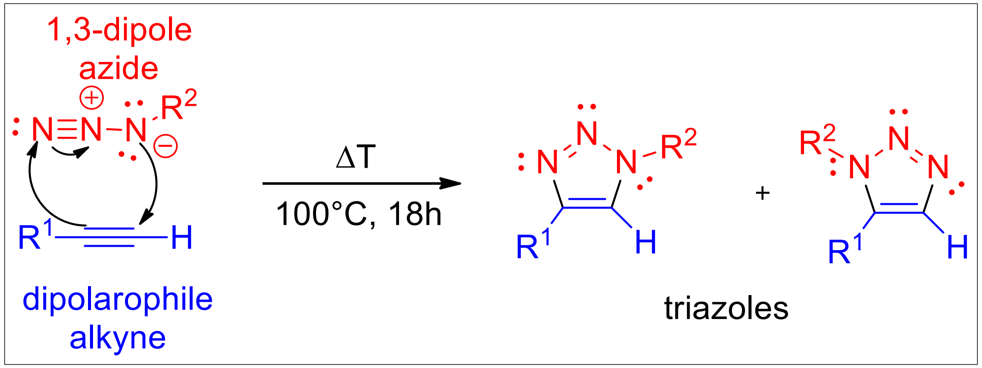


Careful with tri- or tetra-substituted alkenes:

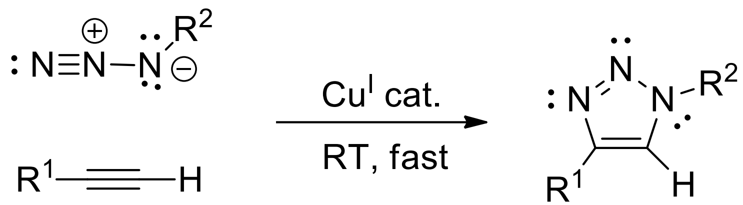




4.1.1. Huisgen azide-alkyne cycloadditions, Click chemistry



When catalyzed by copper(I), it is known as "Click chemistry" :



It is no longer a concerted mechanism but a stepwise metal-catalyzed process.

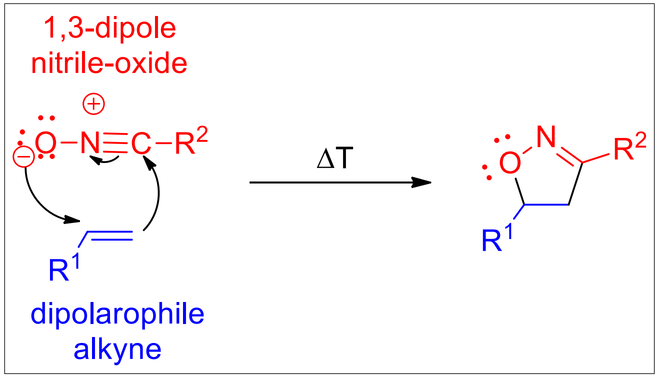
Usually: $Cu^{II}(OAc)_2$ + NaAscorbate ⟶ Cu^{I} source

reductant

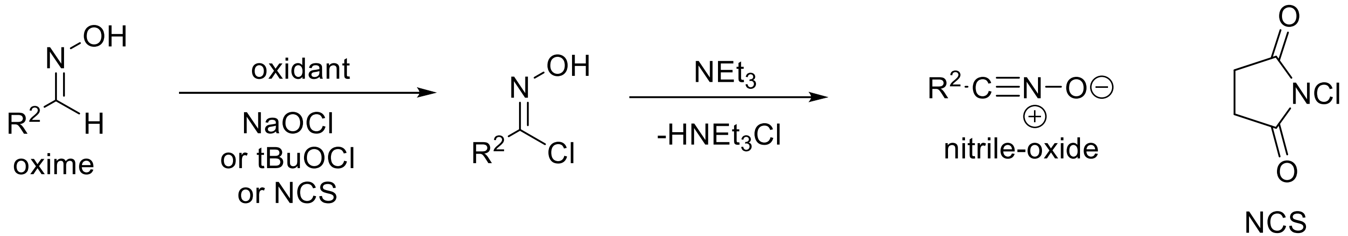
The reaction is very fast even at room temperature and it is proceeding in water as well.

It has found widespread applications in chemistry, chemical biology, material science, etc.

4.1.1. Nitrile-oxide cycloaddition



The nitrile-oxide dipole is not isolable, it needs to be generated in situ:



Example: