CATALYSIS
Theory and Applications

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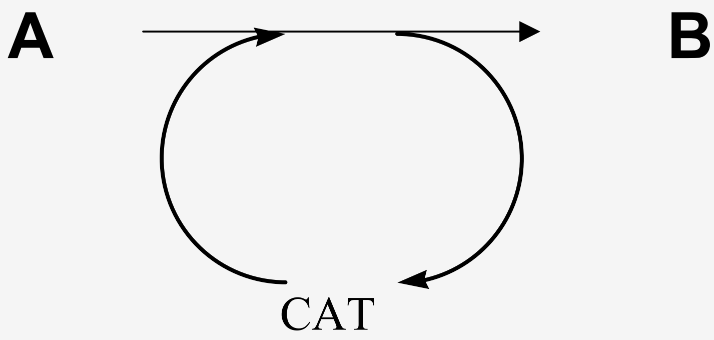
Definition of Catalysis and Catalyst

A catalyst is a substance that increases the rate of a reaction remaining itself unchanged

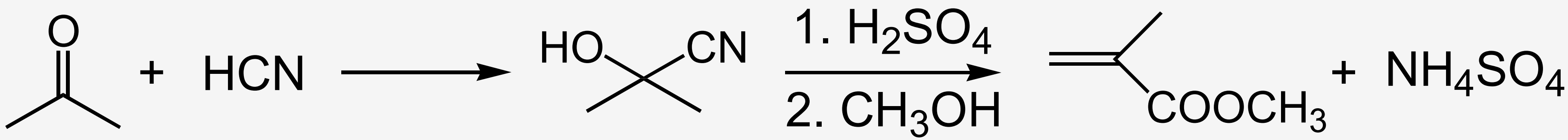


Importance of Catalysis

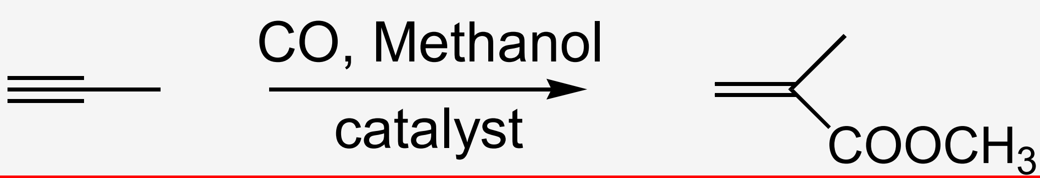
- increasingly important in synthesis
- selectivity in production of fine chemicals
- clean processes, high atom economy (bulk processes)
- production of high-tech products / materials
- mild conditions (low energy consumption)
- environmentally friendly

Example: methyl metacrylate (MMA)

Old process: 2.5 kg waste / kg product



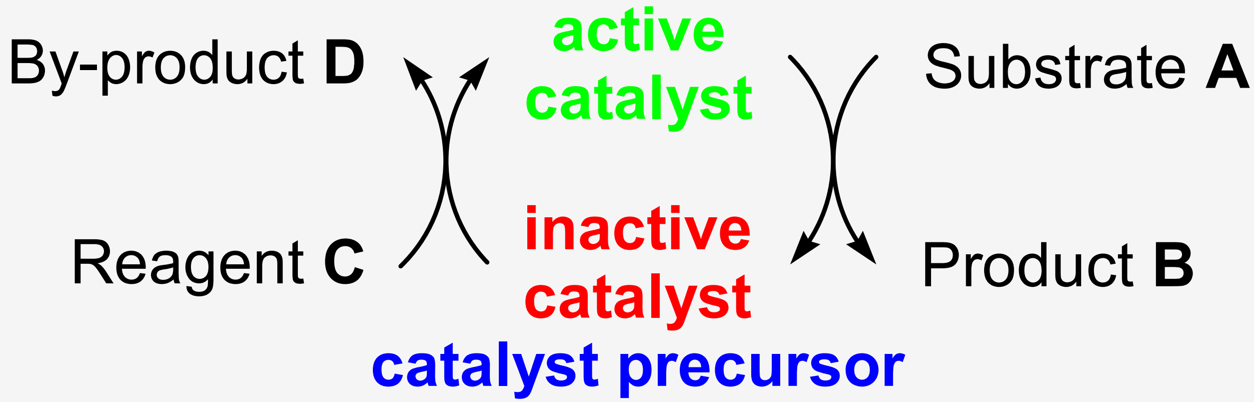
New catalytic process: 50 g waste / kg product



Catalyst Activation and Regeneration

A + catalyst $\longrightarrow$ B + catalyst

a catalytic reaction wherein the catalyst is unchanged



a catalytic reaction wherein the catalyst is deactivated and needs to be regenerated (re-activated) or requires an incubation time

How Does a Catalyst Work?

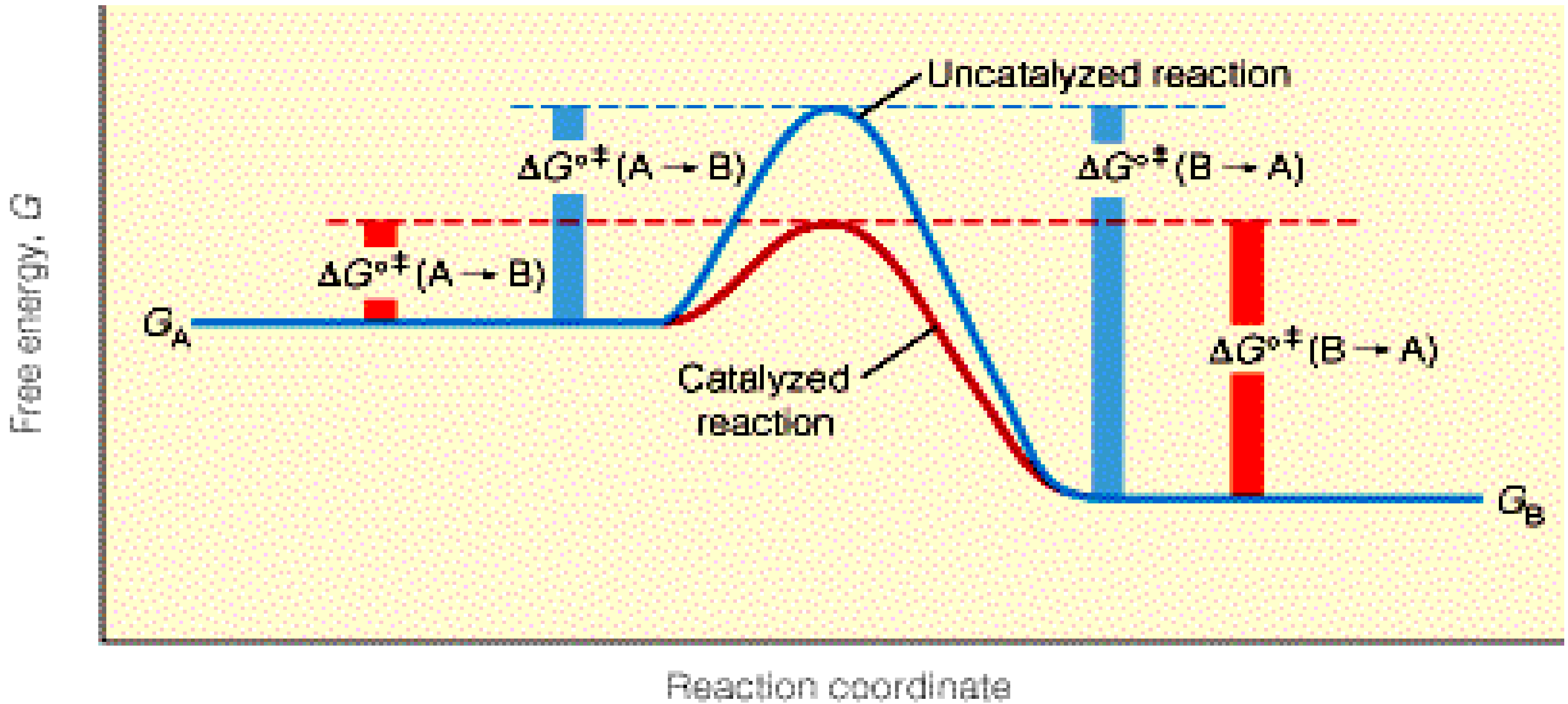
- Lowering activation energy

- Stabilization of a reactive transition state

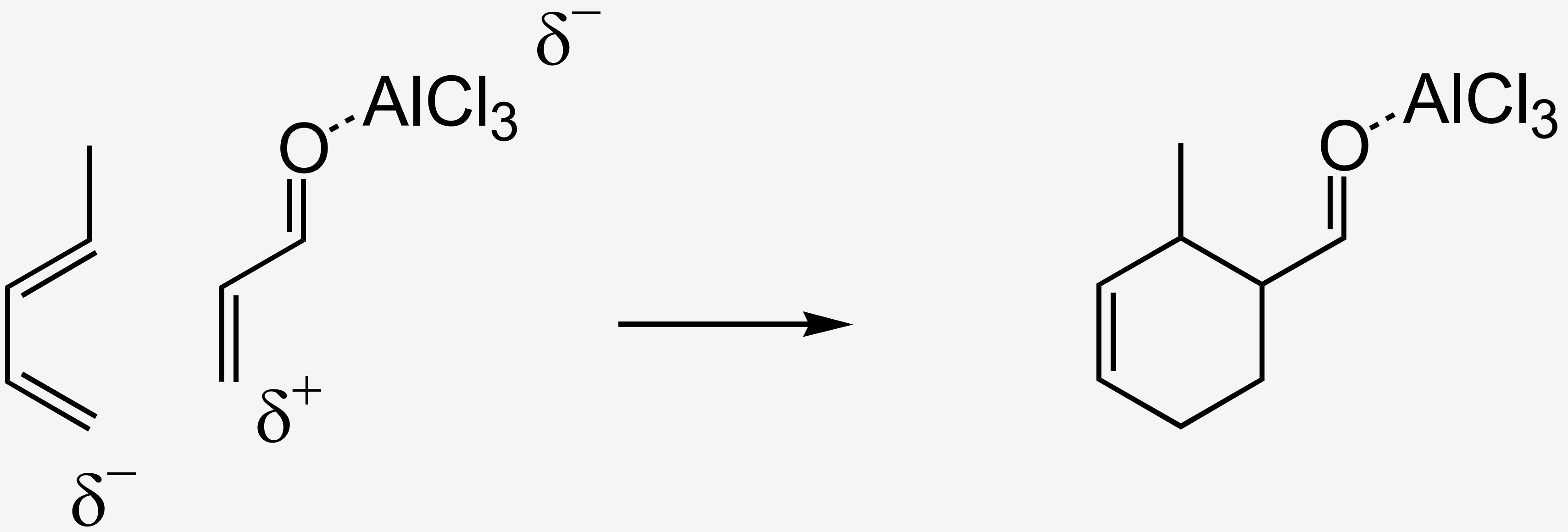
- Bringing reactants together
  - proximity effect
  - orientation effect

- Enabling otherwise inaccessible reaction paths

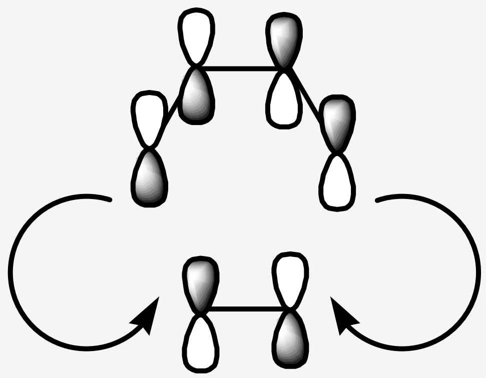
Energy profile of a reaction



Example: Lewis Acid Catalyzed Diels-Alder Reaction

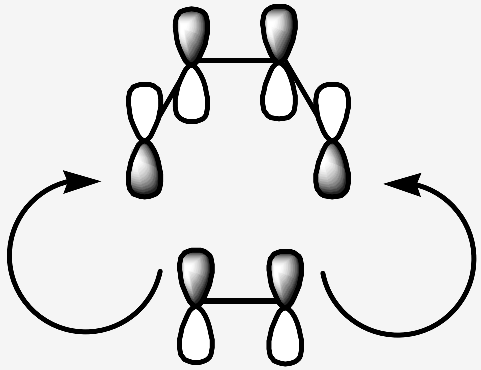


Frontier orbitals overlap



HOMO of butadiene (Ψ_2)

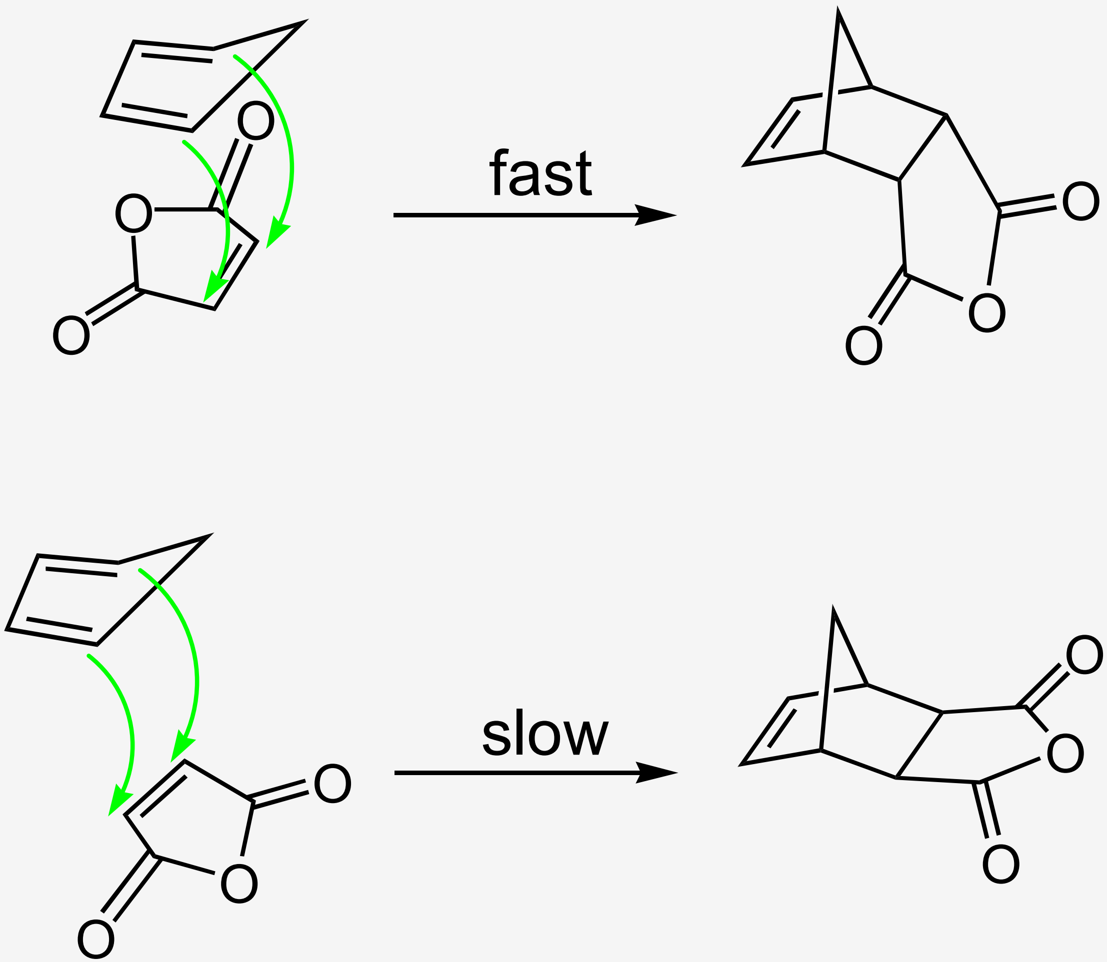
LUMO of ethylene (π^*)

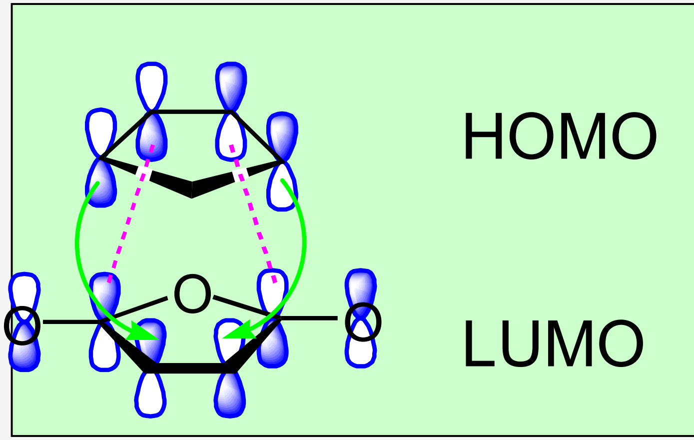


LUMO of butadiene (Ψ_3^*)

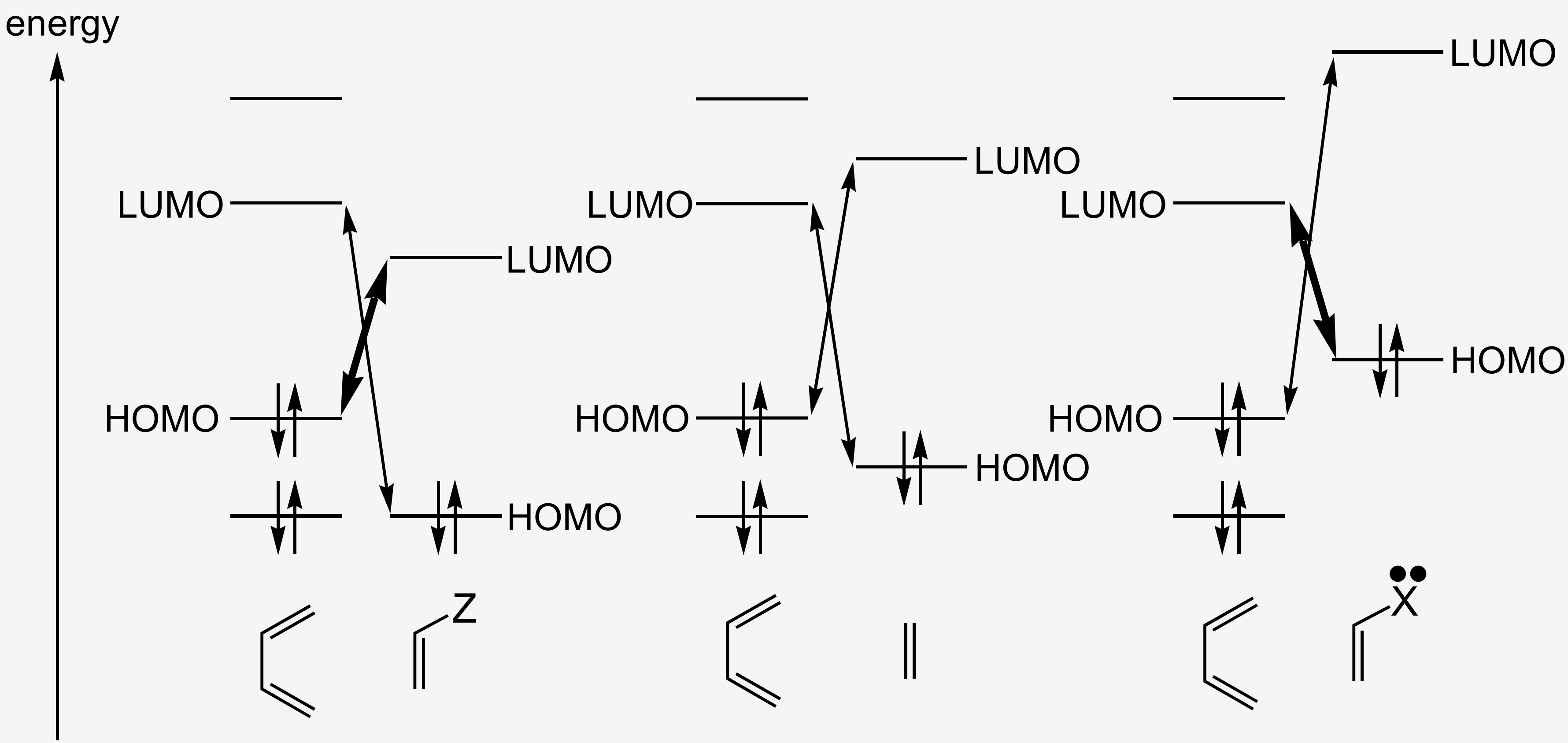
HOMO of ethylene (π)

Secondary overlap stabilizes *endo* transition state





Frontier orbital interactions for DA reactions

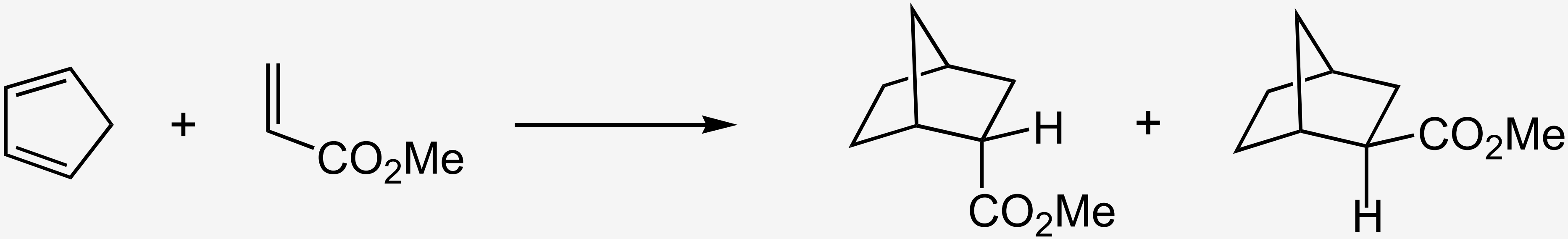


dienophile with a low energy LUMO

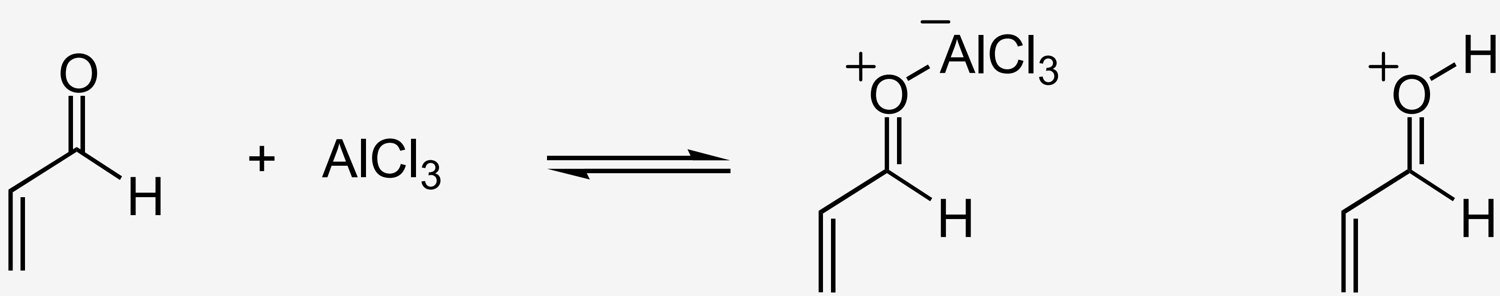
dienophile with neither a low energy LUMO nor a high energy HOMO

dienophile with a high energy LUMO

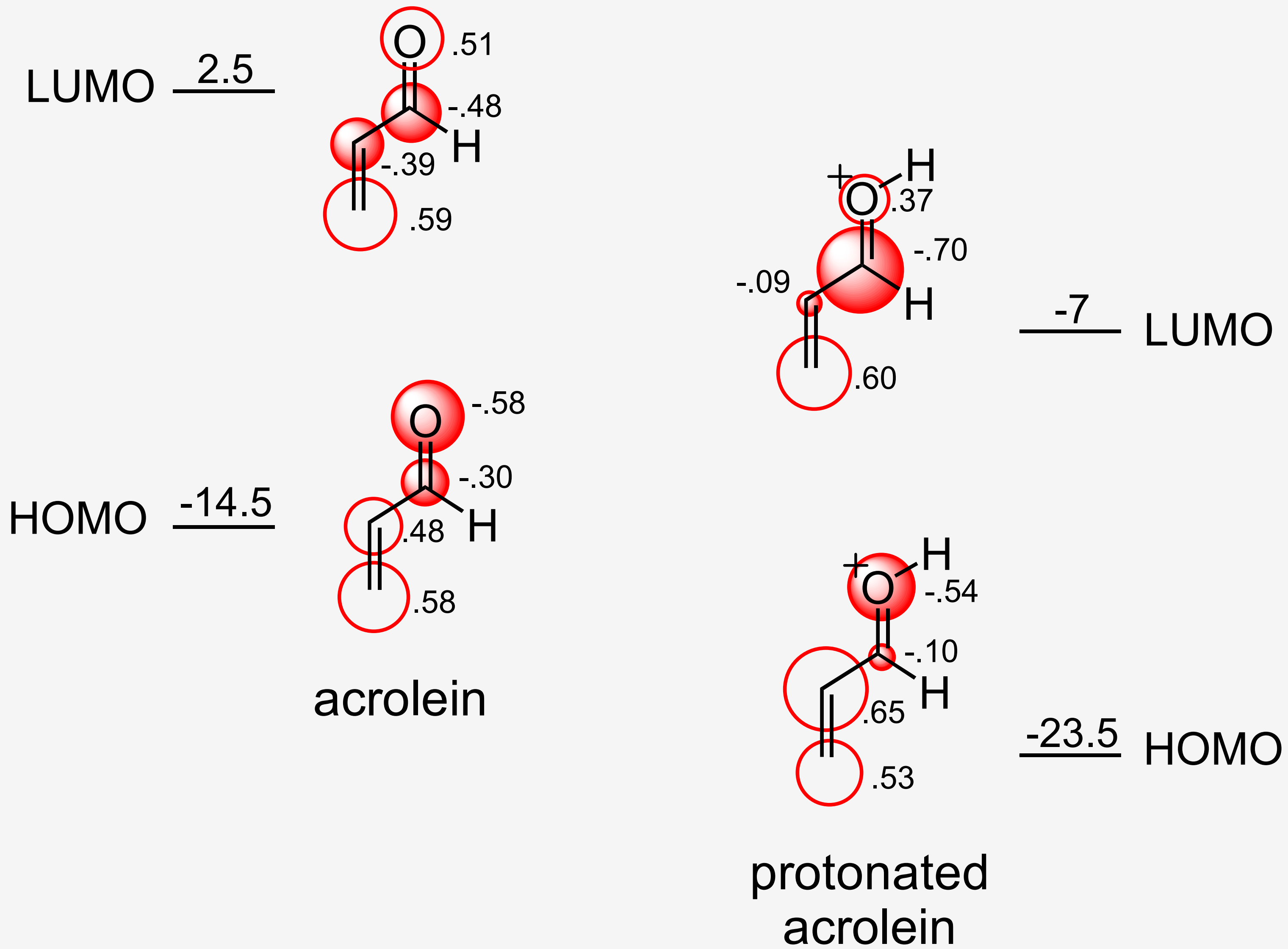
Influence Lewis Acids on endo-selectivity



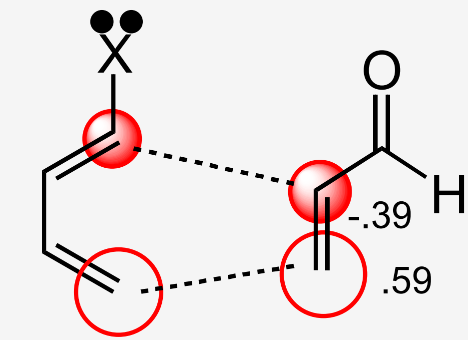
without $AlCl_3$ at 0°	88%	12%
with $AlCl_3$ at 0°	96%	4%
with $AlCl_3$ at -80°	99%	1%



Frontier orbital energies and coefficients acrolein

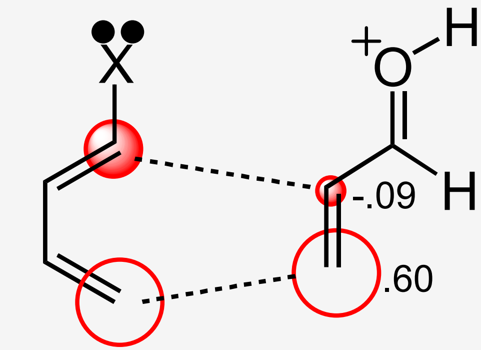


Increased regioselectivity acid catalyzed DA



HOMO LUMO

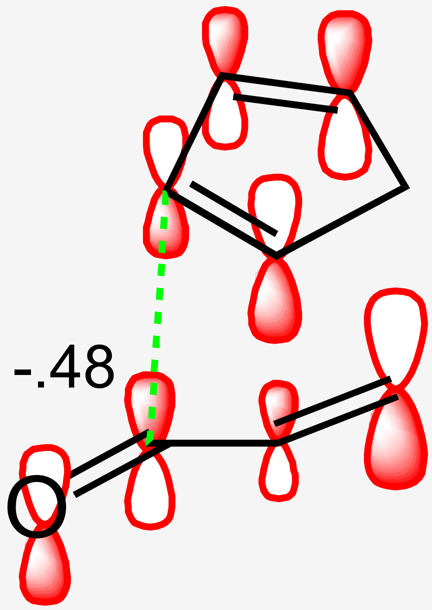
without catalysis



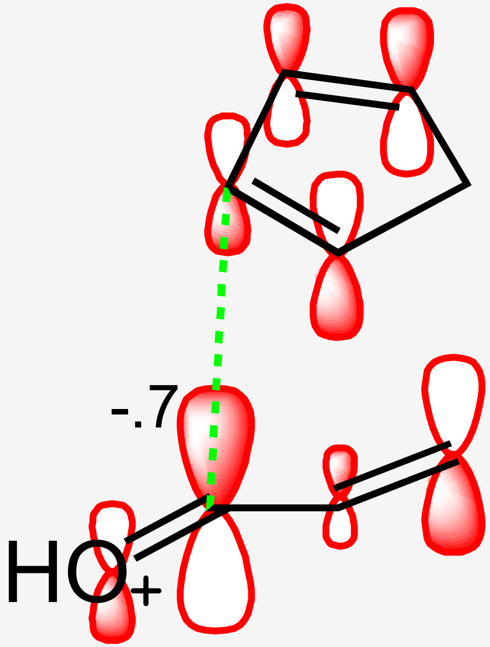
HOMO LUMO

with catalysis

Increased endo selectivity acid catalyzed DA



without catalysis



with catalysis

Catalysts

- general acid and base catalysis (ester hydrolysis),
- Lewis acids as catalysts (Diels-Alder reactions),
- organic catalysts (thiazolium ions in Cannizzarro reactions),
- porphyrin complexes (epoxidations, hydroxylations),
- enzymatic processes,
- co-ordination complexes (polyester condensations),
- catalytic antibodies

world market for catalysts: 9 billion USD

Catalysts affect both rate and selectivity

Reaction	A + B ⟶ P
uncatalyzed	$d[P]/dt = k_1[A][B]$
catalyzed	$d[P]/dt = k_2[Cat][A][B]$

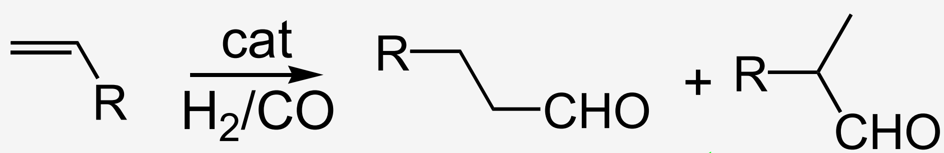
Atom economy $$\frac{\text{number of atoms ended up in product}}{\text{number of atoms from the reagents}}$$

E factor $$\frac{\text{mass units of waste}}{\text{mass units of product}}$$

Diels Alder

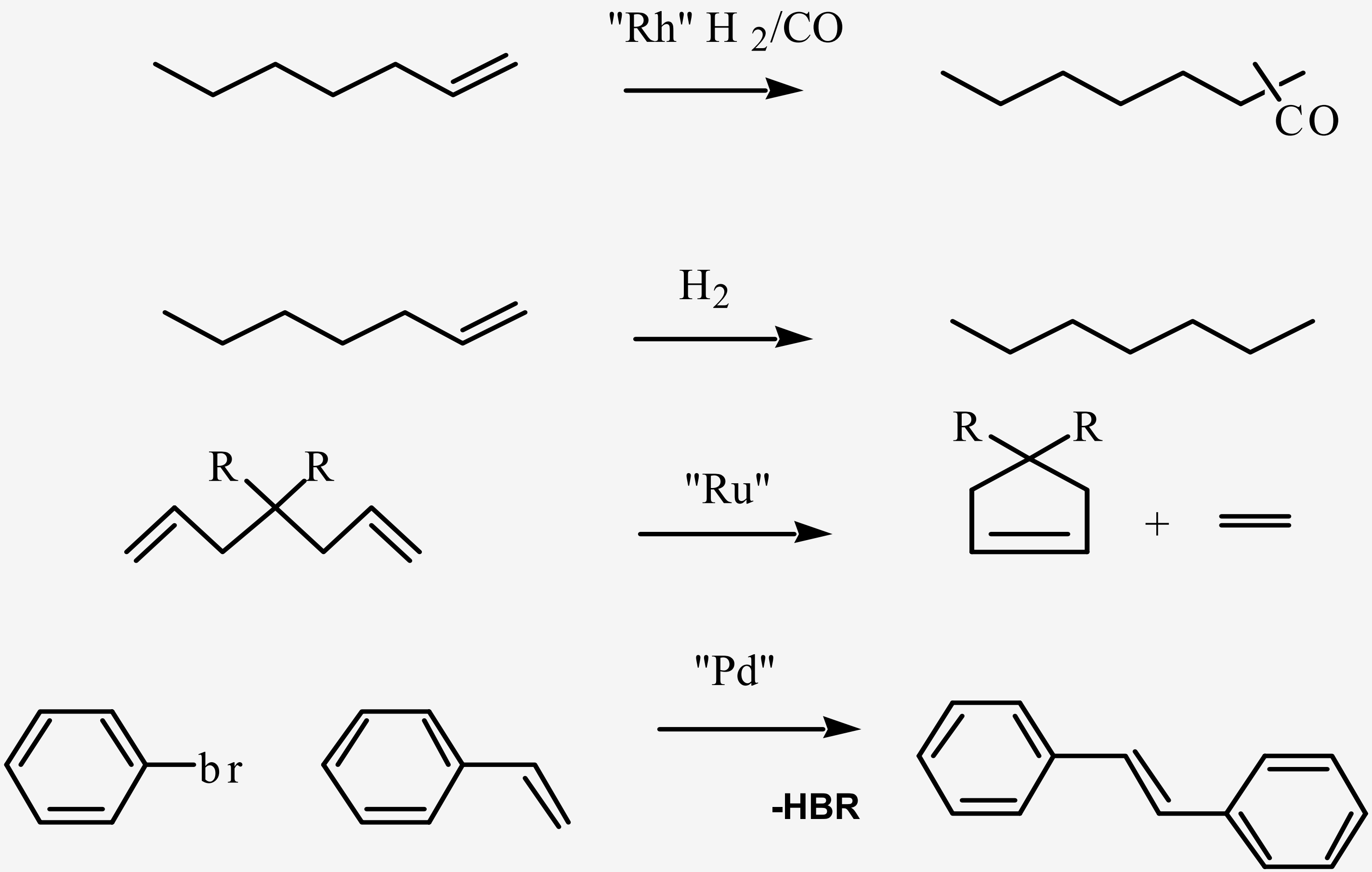
atom economy 100%

Hydroformylation



atom economy 100%

Examples atom economy



100%

100%

100%

26/28
(69 mass percent)

E factor

Industry	Production ton/year	waste/product ratio
Oil	10^6-10^8	0.1
Bulk	10^4-10^6	<1-5
Finechemicals	10^2-10^4	5-50
Pharmaceuticals	10-10^3	25- >100

Homogeneous catalysis

Definition: Catalyst components and substrates of the reaction are in the same phase, most often the liquid phase (some catalytic reactions in the gas phase are also known).

Generally homogeneous catalysis refers to the use of organometallic complexes as the catalysts.

Advantages / disadvantages

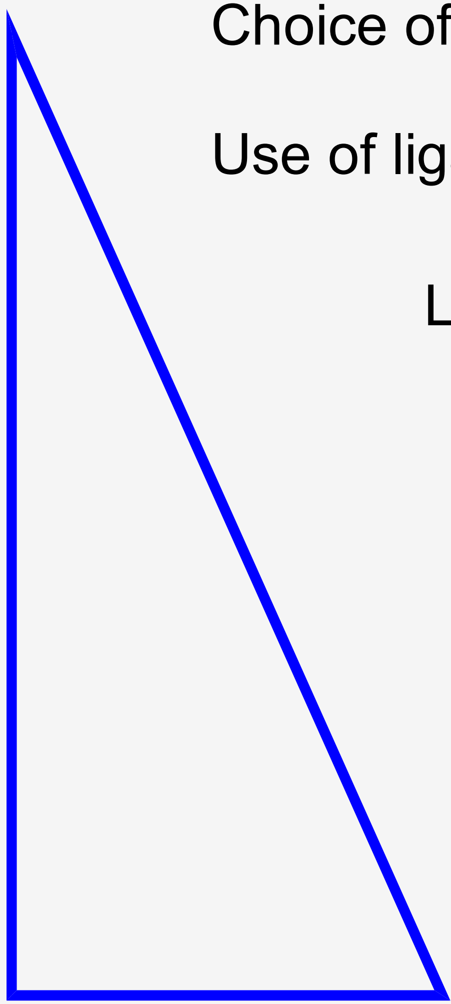
Advantages:

- understandable kinetics
- reproducibility
- relatively mild reaction conditions
- high selectivity
- easy modification of catalyst properties
- efficiency; all molecules are accessible
- mechanistic studies are relatively easy to perform (complex identification by IR, NMR, UV etc.)

Disadvantages:

- water and oxygen sensitivity
- separation of catalyst and products often difficult

Development of Transition Metal Catalysts



Choice of **metal**

Use of ligands with proper **donor atoms**

Ligand effects on activity and selectivity

Steric effects
Electronic effects
Bite Angle

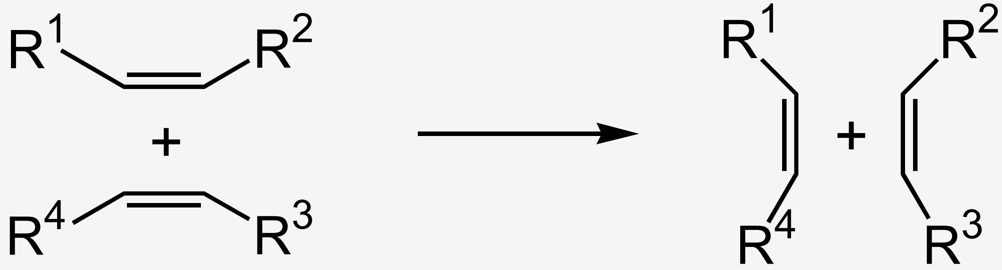
Secondary interactions

Substrate-metal
Substrate-ligand
Medium effects

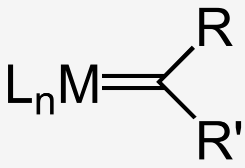
level of sophistication

Rational catalyst design

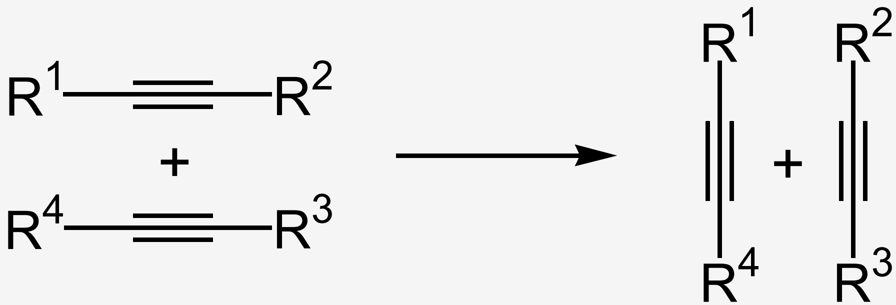
alkene metathesis



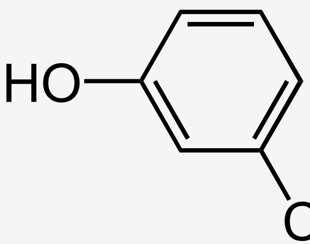
catalyst:



alkyne metathesis



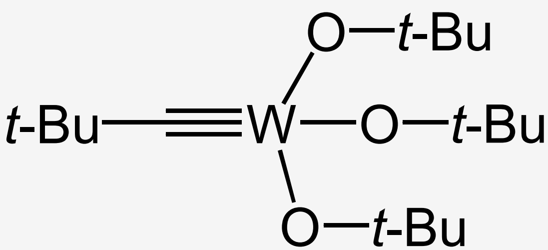
catalyst: $Mo(CO)_6$ +



rate: 2 mol / mol / h

Mortreux (1974)

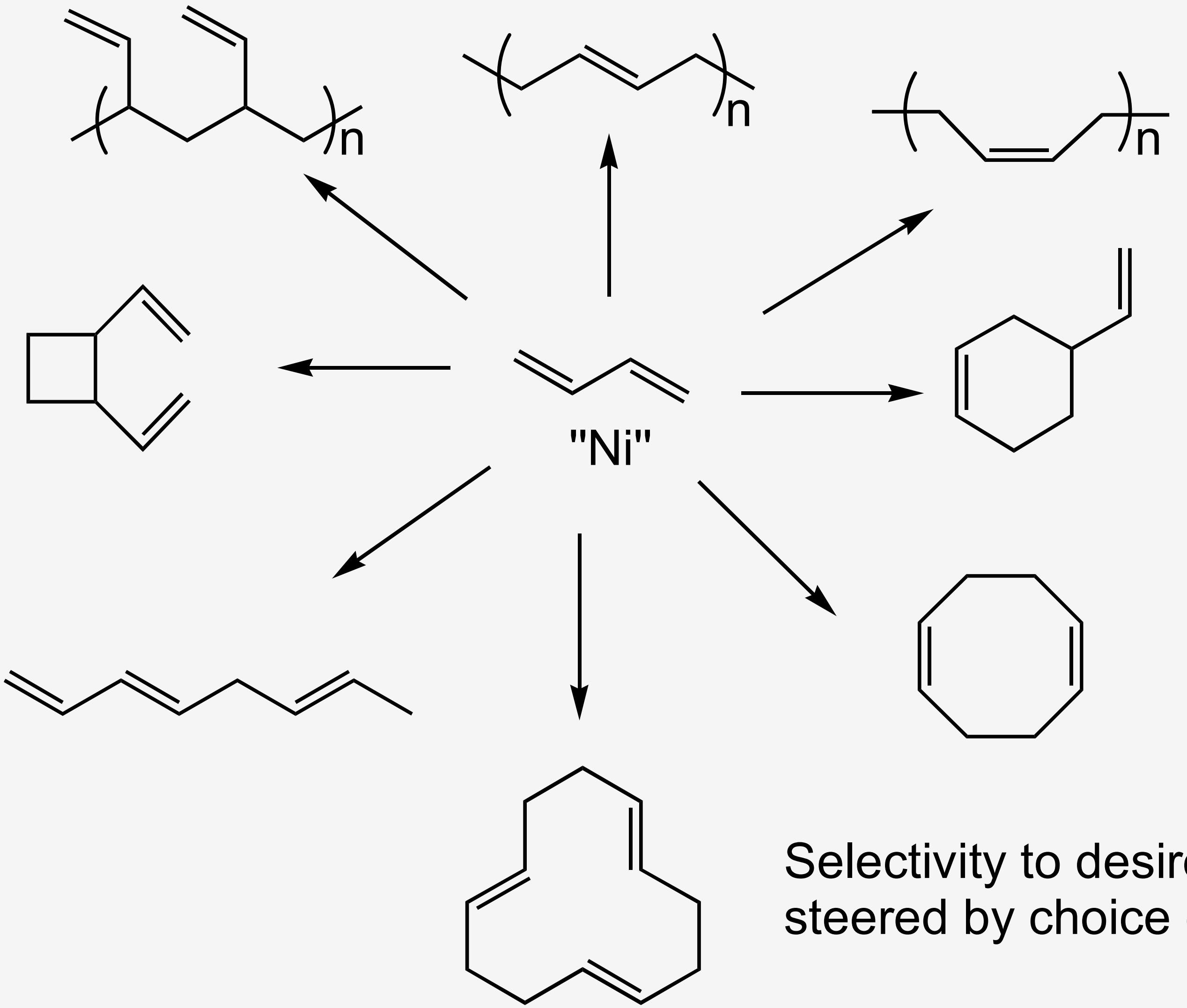
"designed catalyst":



rate: 300,000 mol / mol / h

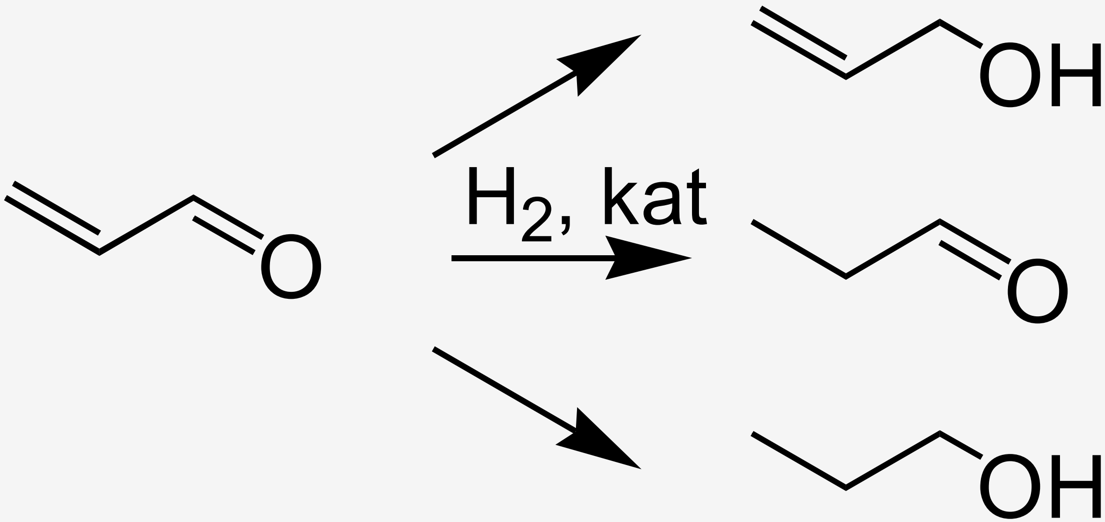
Schrock (1984)

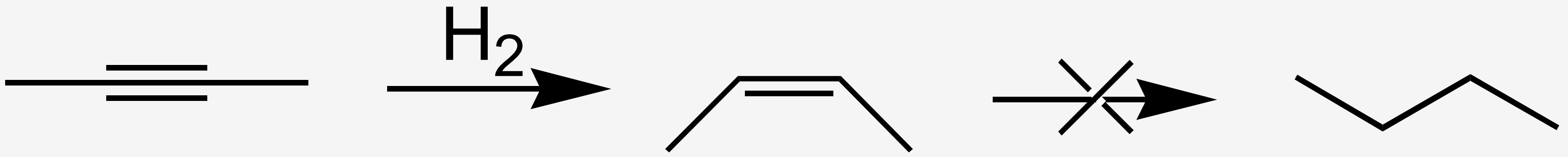
Selectivity in nickel catalyzed butadiene reactions



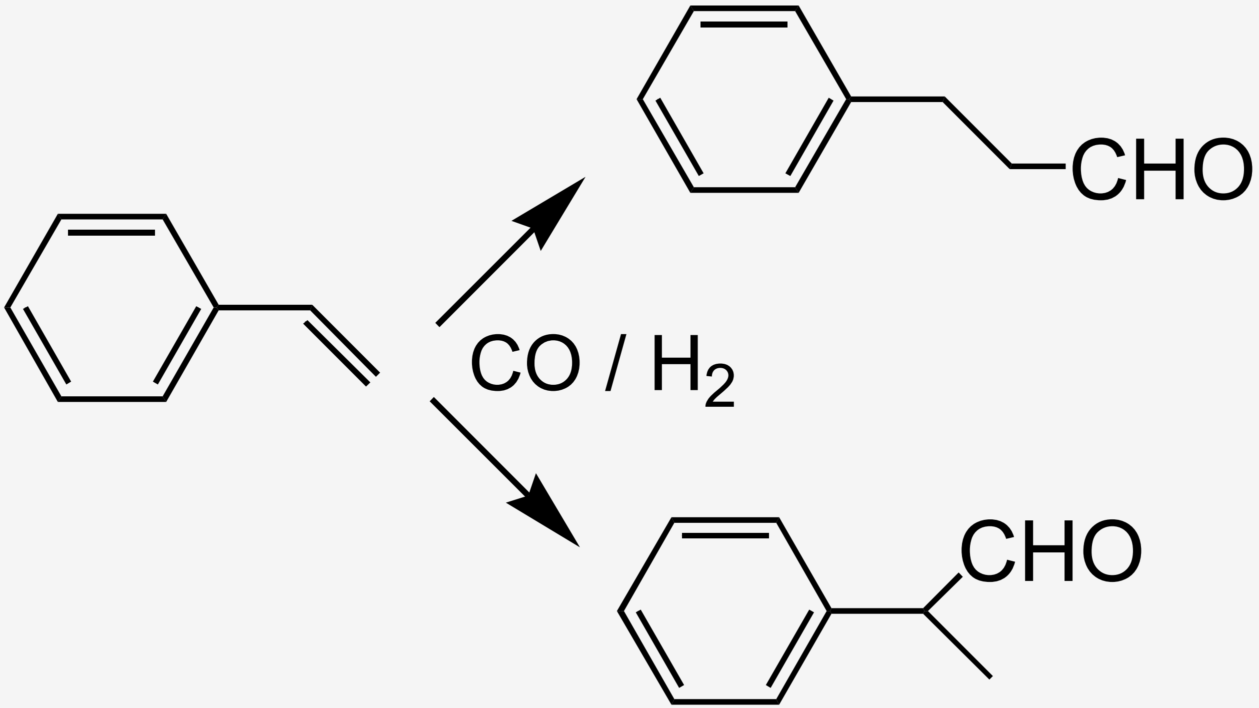
Selectivity to desired product steered by choice of ligands

Chemoselectivity

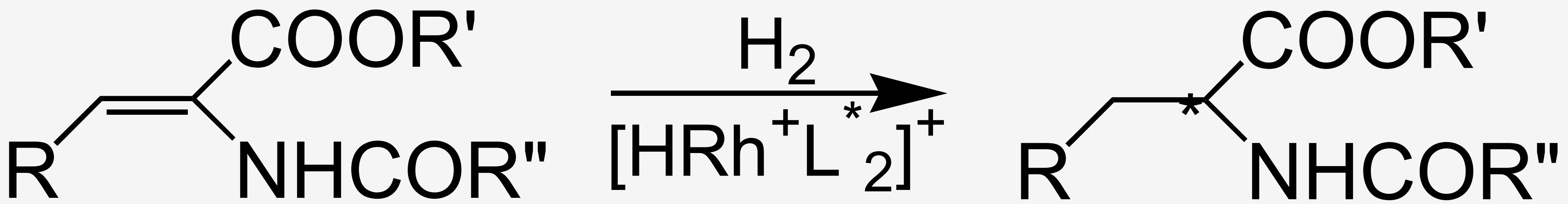




Regioselectivity

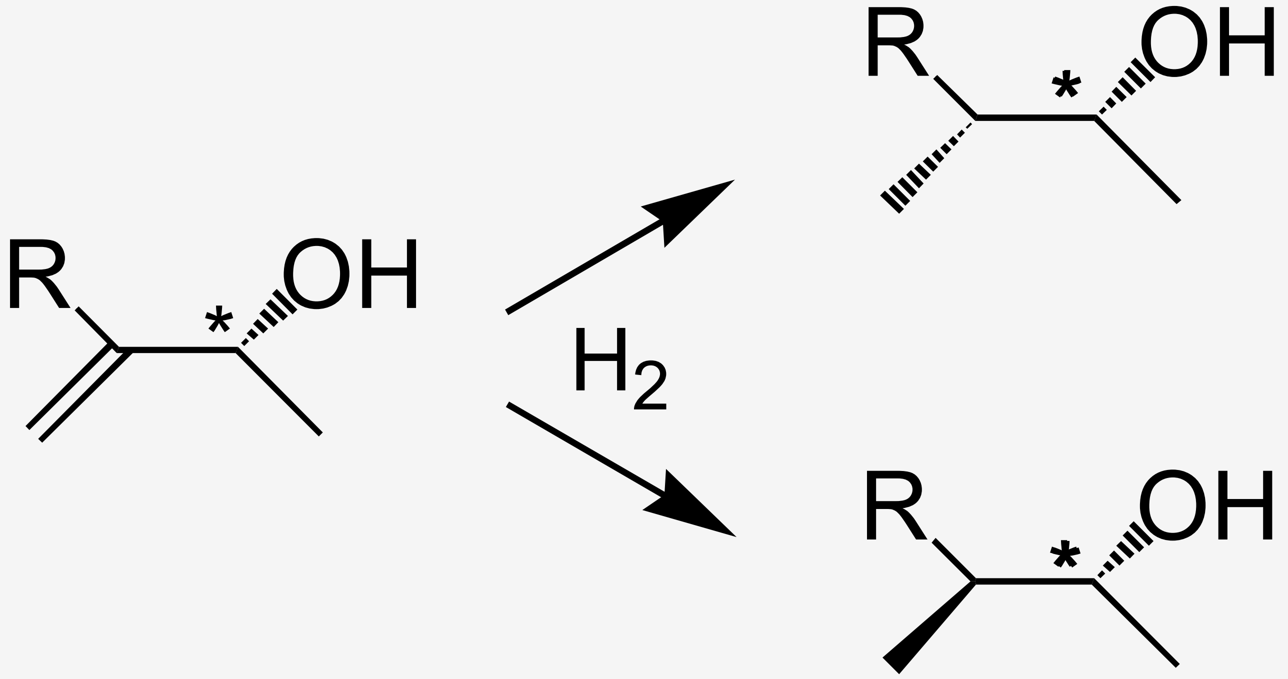


Enantioselectivity



99 % ee

Diastereoselectivity



Heterogeneous catalysis

Advantages:

- easy separation of catalyst and products
- low sensitivity to water and oxygen
- high temperature stability
- shape selectivity (zeolites)

Disadvantages:

- kinetics can be complex
- often high pressures and temperatures required
- catalyst poisoning by sulfur compounds
- sintering
- heat transfer
- surface chemistry; using a few atoms only

Immobilization of transition metal complexes

Supported Homogeneous Catalysts
- Organic Polymers
- Dendrimers
- Inorganic Metal Oxides

Supported Aqueous Phase Catalysis

Two-phase catalysis
- organic solvents (SHOP)
- fluorous phase
- aqueous phase

Sol-Gel catalysis

Extraction (acid / base)

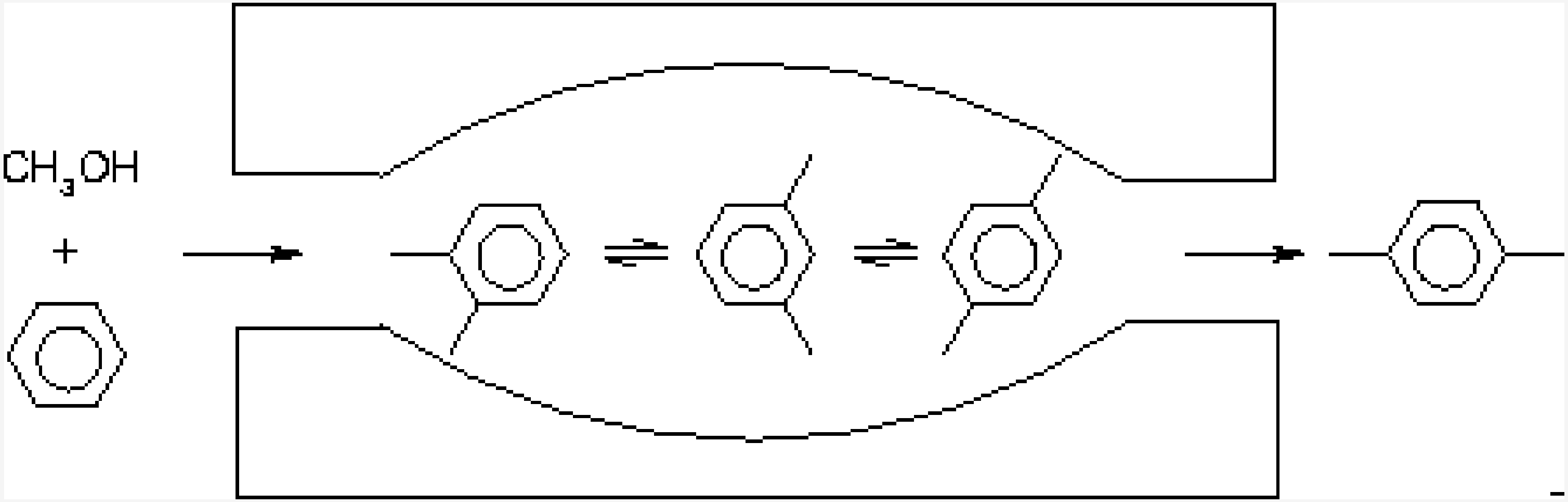
Ultrafiltration

disadvantages:

- degradation of polymer
- leaching of metal
- oxidation of anchored ligands

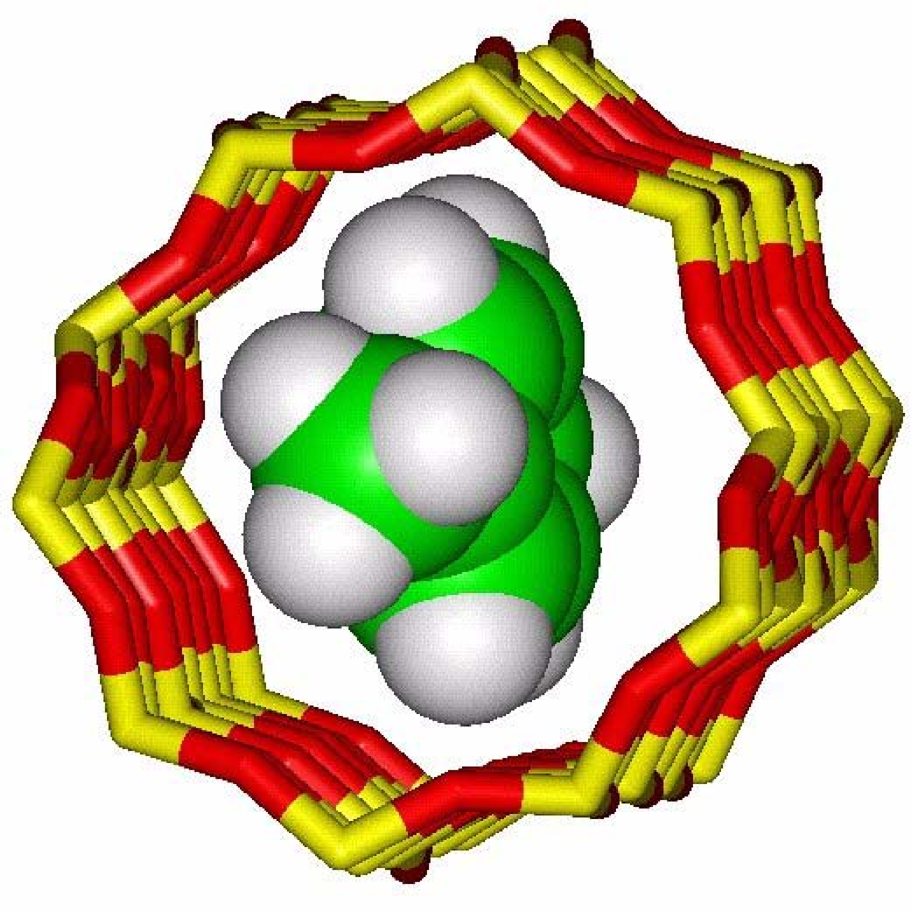
Product shape-selectivity

selective diffusion of *para*-xylene out of the pores of silicalite



Product shape-selectivity

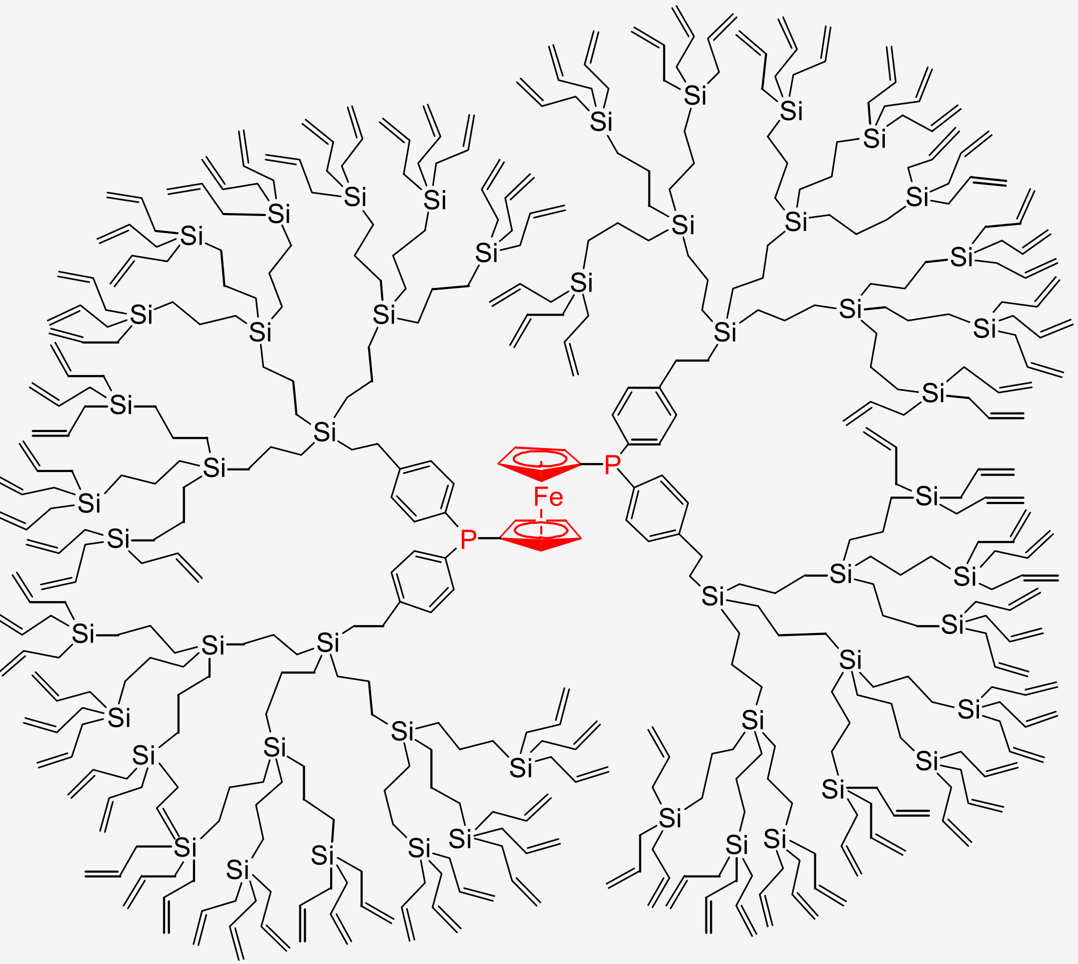
computer simulation of *para*-xylene in a silicalite pore



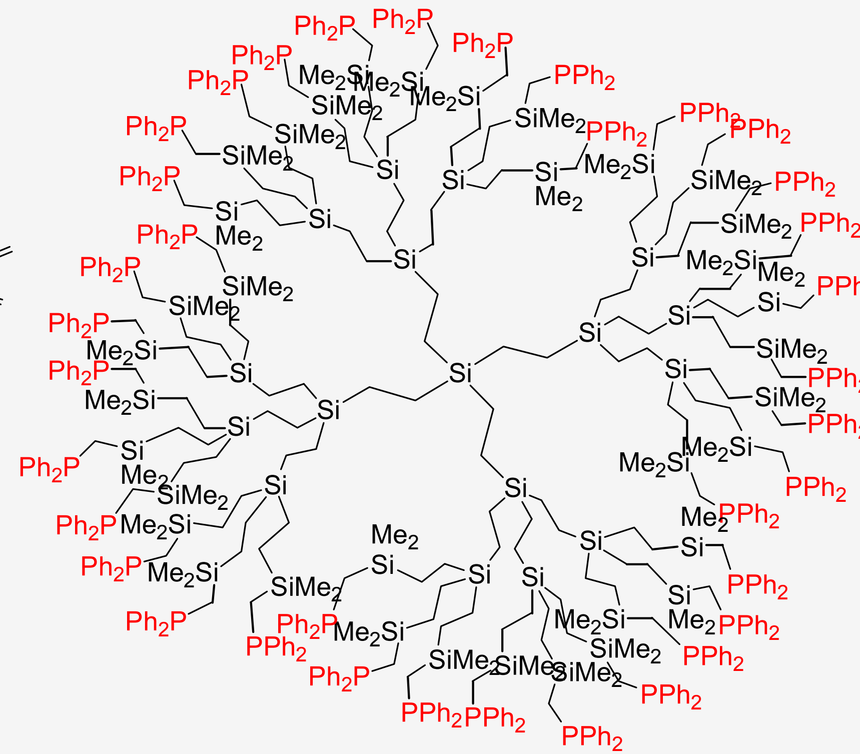
Dendrimers as support

Dendrimer particle that serves as a catalyst support

Catalyst immobilisation on dendrimers



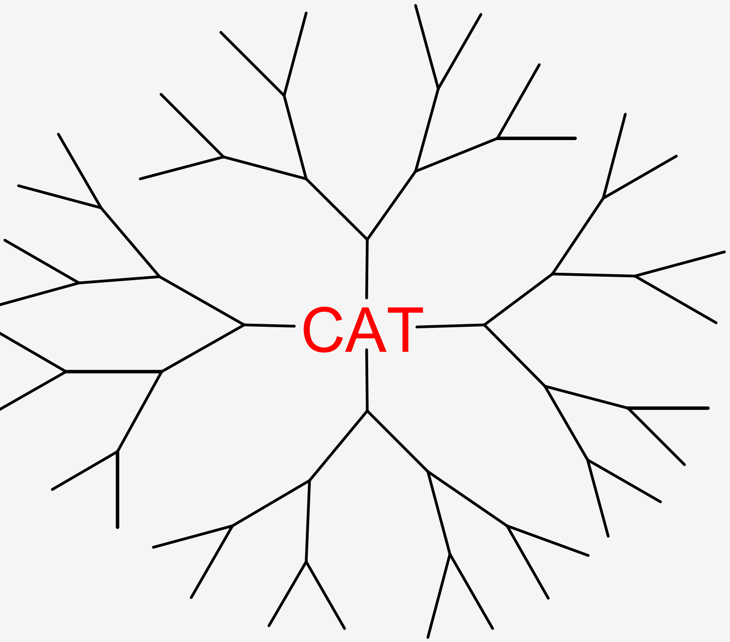
G.E. Oosterom et al. *Chem. Commun.* **1999**, 1119



D. de Groot et al. *Chem. Commun.* **2000**, 711

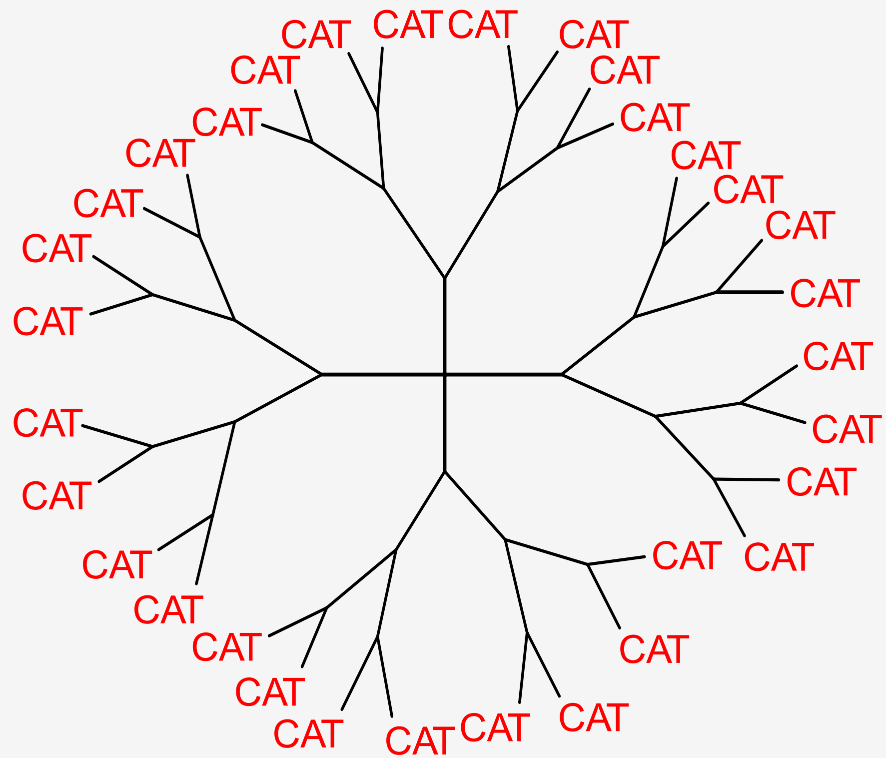
Dendritic transition metal catalysts: covalent approach

Core functionalization



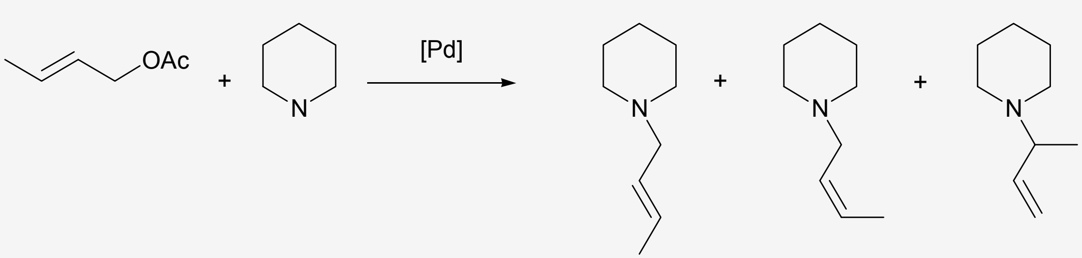
- site isolation
- micro-environment

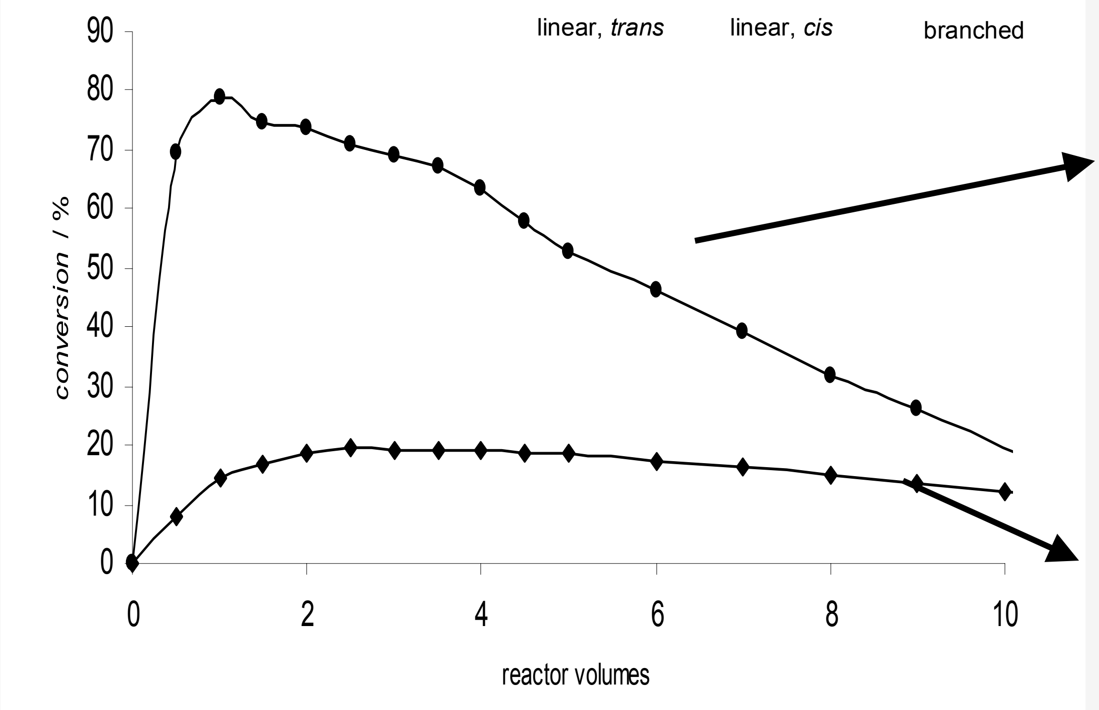
Periphery functionalization

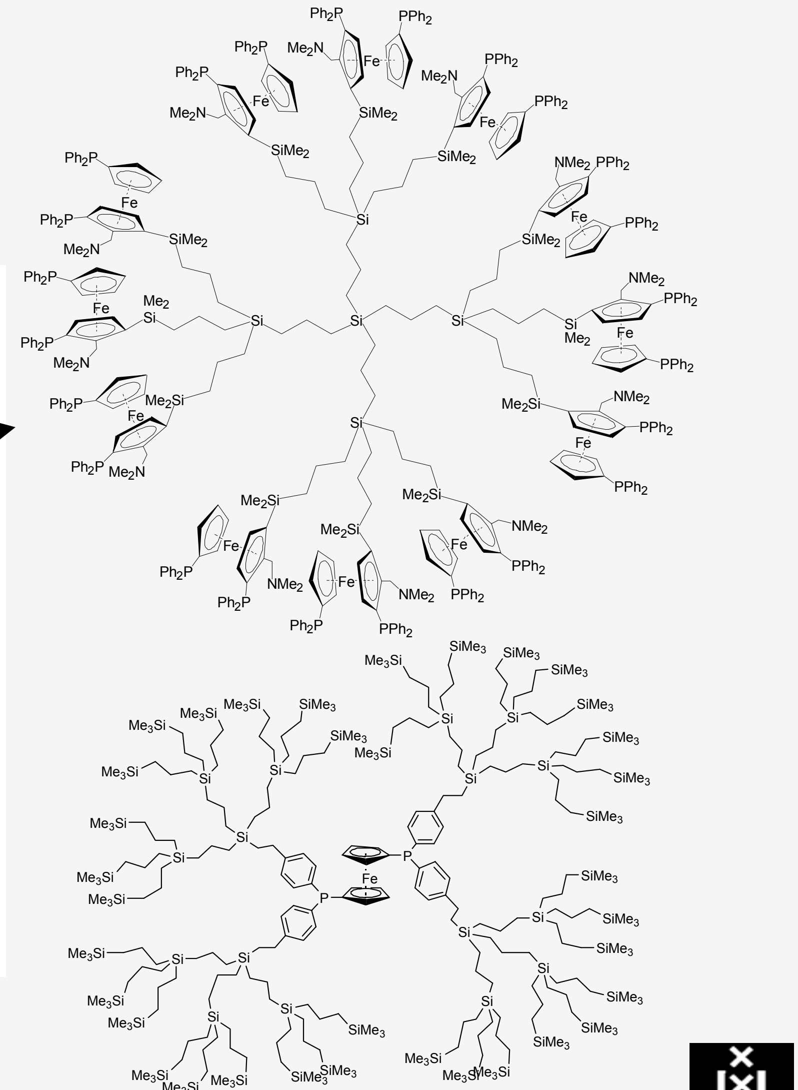


- multiple active sites
- potential cooperativity
- easy accessibility

Direct comparison core and periphery functionalized dendrimers







Room temperature, solvent: CH_2Cl_2, P/Pd=2.

Biocatalysis: the use of enzymes or cells

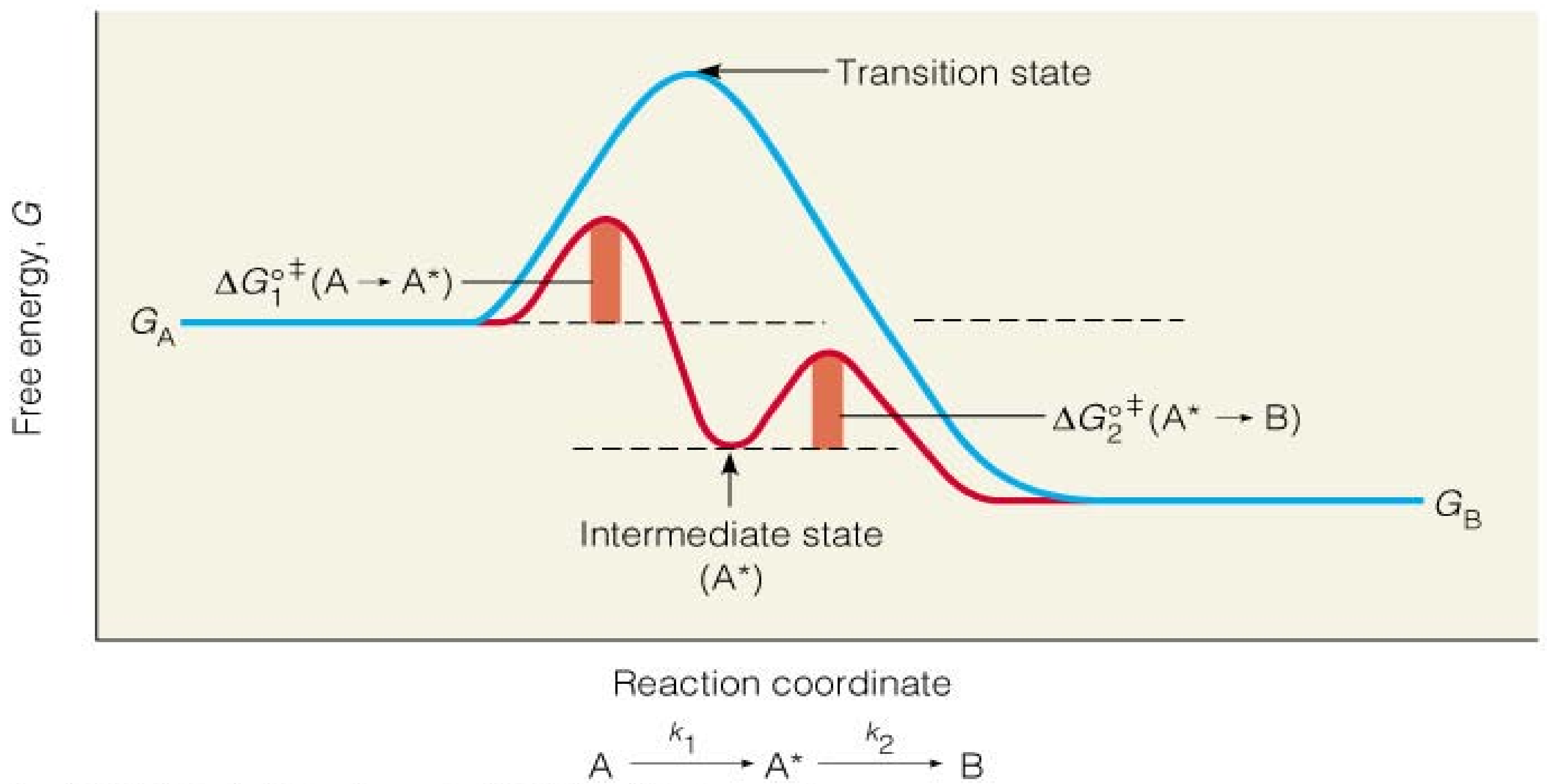
Enzyme optimization:

- protein "engineering"
- molecular evolution
- enzyme "engineering"

Enzymes can be applied in:

- Water
- Organic solvents
- Supercritical CO_2
- Ionic liquids

Energy profile of an enzyme catalyzed reaction

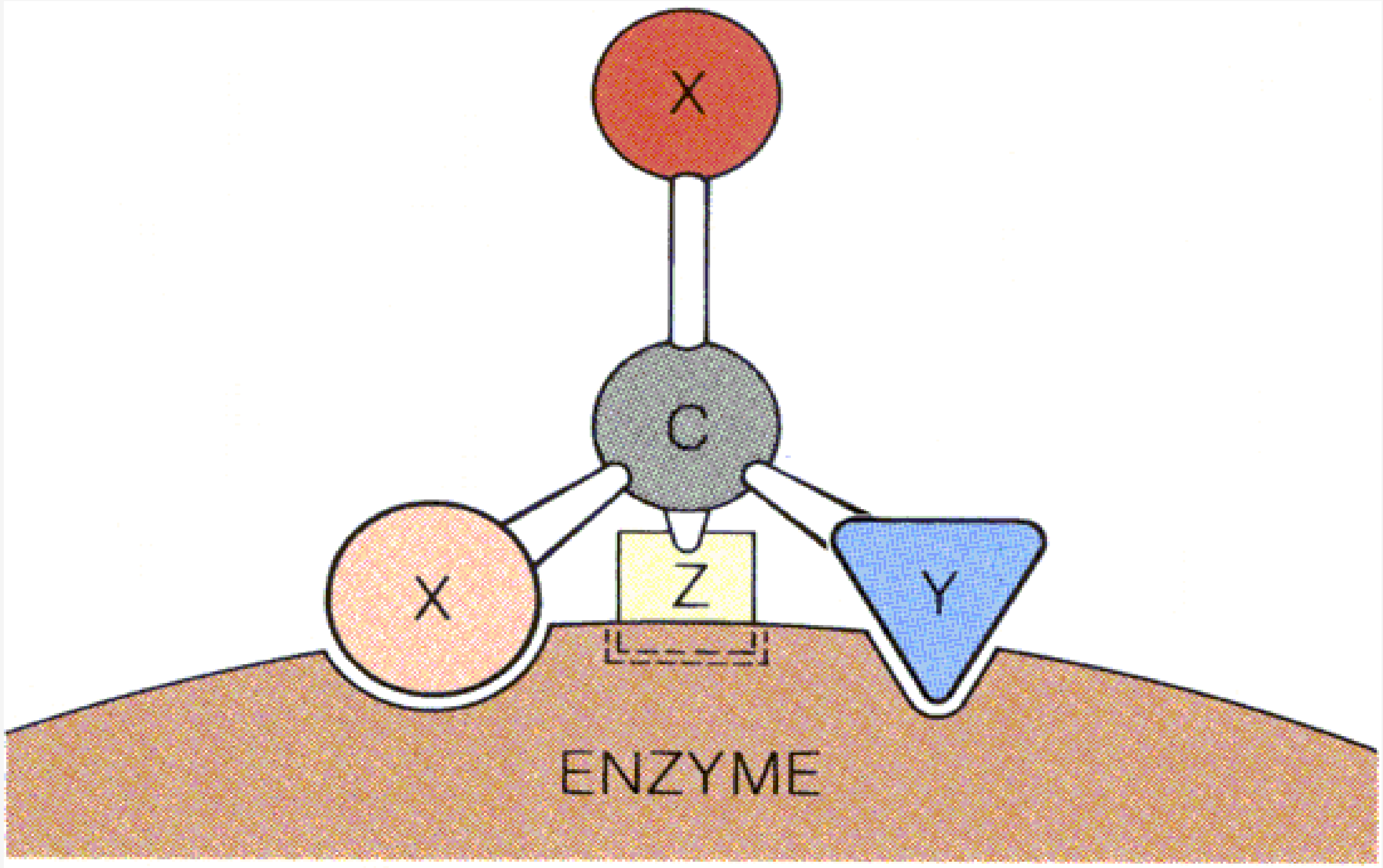


Enzymes give great rate enhancements

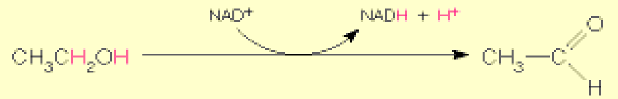
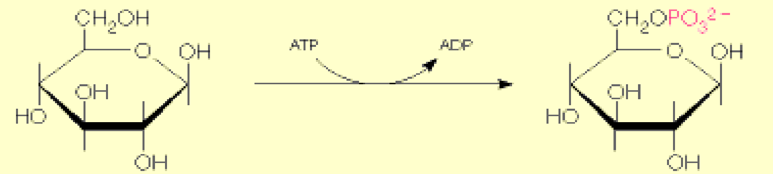
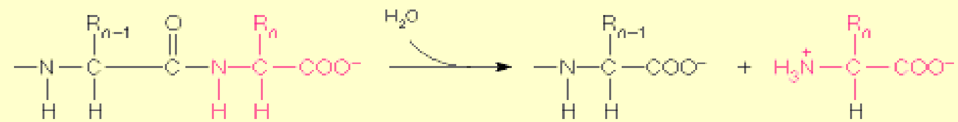
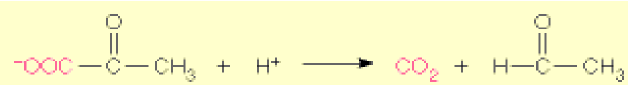
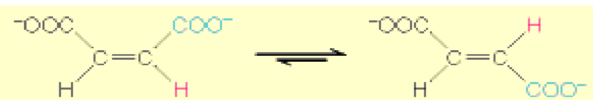
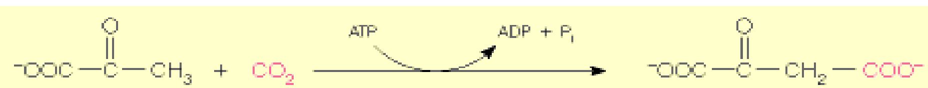
Michaelis-Menten parameters for selected enzymes

Enzyme	Reaction Catalyzed	K_M (mol/L)	k_{cat}(s^{-1})	k_{cat}/K_M [$(mol/L)^{-1} s^{-1}$]
Chymotrypsin	Ac–Phe–Ala $\xrightarrow{H_2O}$ Ac–Phe + Ala	1.5×10^{-2}	0.14	9.3
Pepsin	Phe–Gly $\xrightarrow{H_2O}$ Phe + Gly	3×10^{-4}	0.5	1.7×10^3
Tyrosyl-tRNA synthetase	Tyrosine + tRNA $\longrightarrow$ tyrosyl-tRNA	9×10^{-4}	7.6	8.4×10^3
Ribonuclease	Cytidine 2′, 3′ cyclic phosphate $\xrightarrow{H_2O}$ cytidine 3′-phosphate	7.9×10^{-3}	7.9×10^2	1.0×10^5
Carbonic anhydrase	$HCO_3^- + H^+ \longrightarrow H_2O + CO_2$	2.6×10^{-2}	4×10^5	1.5×10^7
Fumarase	Fumarate $\xrightarrow{H_2O}$ malate	5×10^{-6}	8×10^2	1.6×10^8

Enzyme specificity



Examples of classes of enzymes

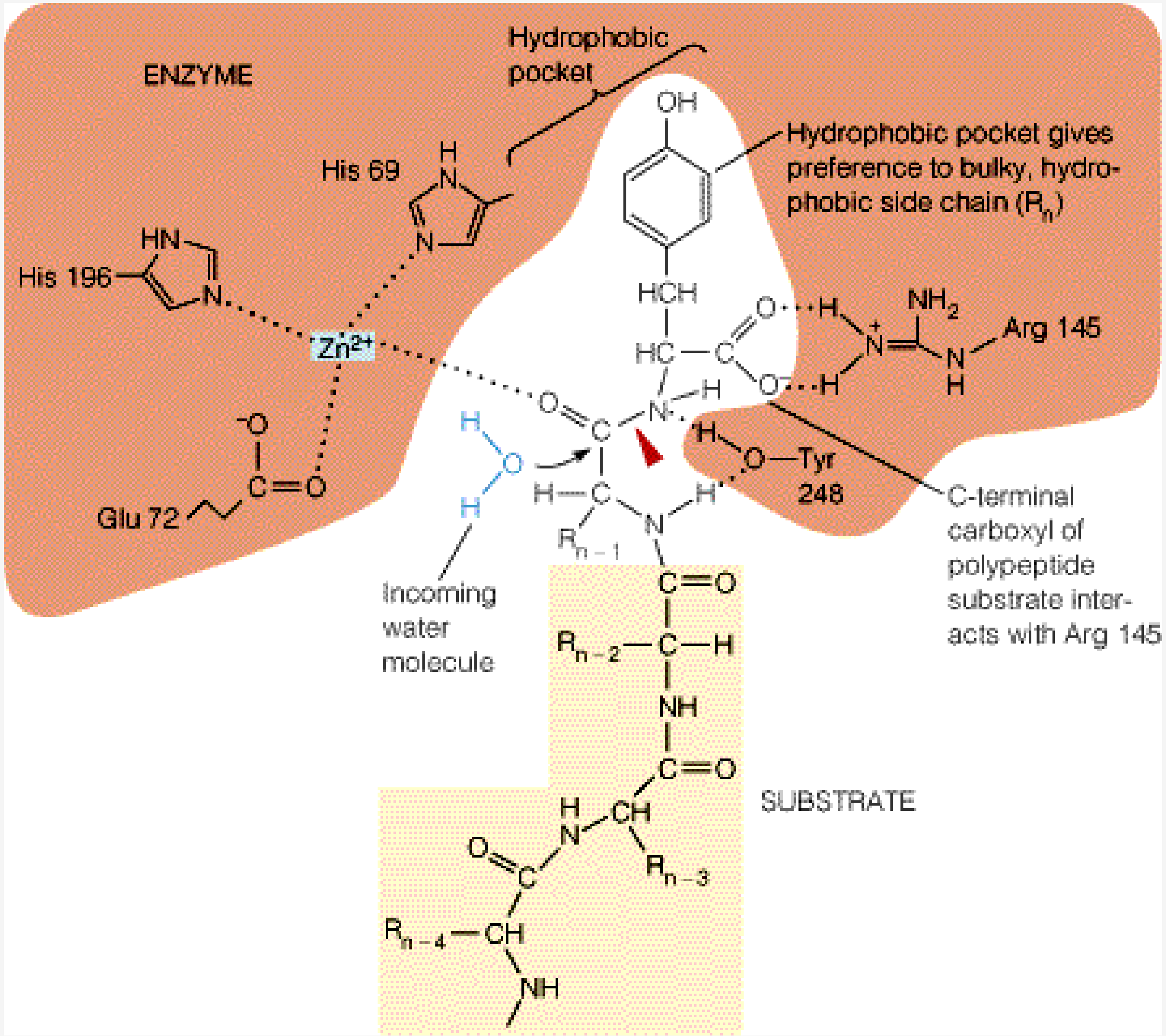
Class	Example (reaction type)	Reaction Catalyzed
1. Oxidoreductases	Alcohol dehydrogenase (EC 1.1.1.1) (oxidation with NAD^+)	 Ethanol → Acetaldehyde
2. Transferases	Hexokinase (EC 2.7.1.2) (phosphorylation)	 D-Glucose → D-Glucose-6-phosphate
3. Hydrolases	Carboxypeptidase A (EC 3.4.17.1) (peptide bond cleavage)	 C-terminus of polypeptide → Shortened polypeptide + C-terminal residue
4. Lyases	Pyruvate decarboxylase (EC 4.1.1.1) (decarboxylation)	 Pyruvate → Acetaldehyde
5. Isomerases	Maleate isomerase (EC 5.2.1.1) (*cis–trans* isomerization)	 Maleate ⇌ Fumarate
6. Ligases	Pyruvate carboxylase (EC 6.4.1.1) (carboxylation)	 Pyruvate → Oxaloacetate

Coenzymes, vitamins and metals

Some important coenzymes and related vitamins

Vitamin	Coenzyme	Reactions Involving These Coenzymes	Page Where Coenzyme Is Introduced
Thiamine (vitamin B_1)	Thiamine pyrophosphate	Activation and transfer of aldehydes	490
Riboflavin (vitamin B_2)	Flavin mononucleotide; flavin adenine dinucleotide	Oxidation–reduction	492
Niacin	Nicotinamide adenine dinucleotide; nicotinamide adenine dinucleotide phosphate	Oxidation–reduction	389, 423
Pantothenic acid	Coenzyme A	Acyl group activation and transfer	494
Pyridoxine	Pyridoxal phosphate	Various reactions involving amino acid activation	731
Biotin	Biotin	CO_2 activation and transfer	507
Lipoic acid	Lipoamide	Acyl group activation; oxidation–reduction	492
Folic acid	Tetrahydrofolate	Activation and transfer of single-carbon functional groups	732
Vitamin B_{12}	Adenosyl cobalamin; methyl cobalamin	Isomerizations and methyl group transfers	738

Active site of carboxypeptidase A



Ideal catalyst characteristics

- High activity (mild reaction conditions)
- High selectivity (chemo, regio, enantio)
- Stable catalyst
- Easy separation and reuse of catalyst

New “green” processes:

- Atom economic
- No or as little as possible waste
- decrease in solvent use
- Mild reaction conditions
- Catalytic use of reagents instead of stochiometrisch
- Non-toxic reagents,
- New sustainable starting materials