School of Industrial and Information Engineering

Course 096125 (095857)

Introduction to Green and Sustainable Chemistry

POLITECNICO DI MILANO

Catalysis in Sustainable Chemistry.

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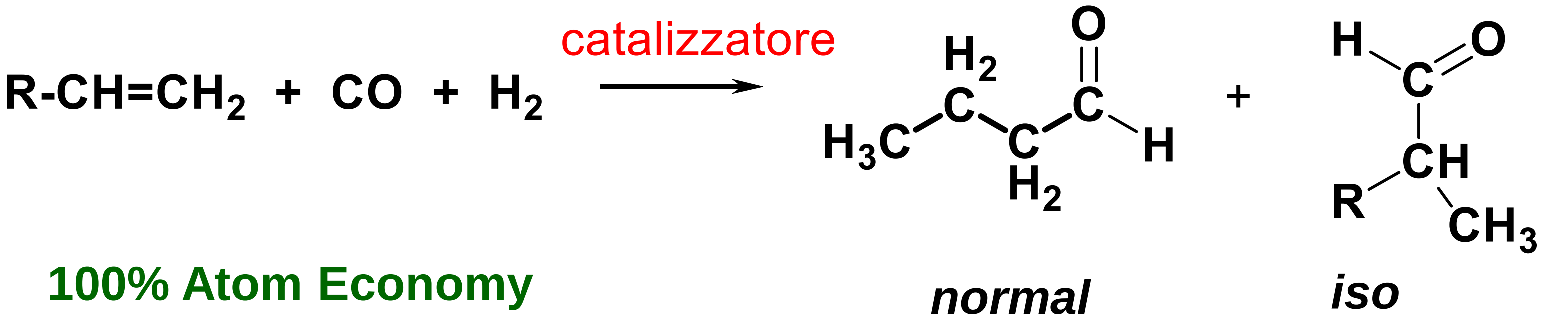
https://iscamapweb.chem.polimi.it/citterio/it/education/course-topics/

Use of Catalysts in Chemical Reaction.

- **Speed up the chemical reaction rate.**
- **Speed up selectively one of the several thermodynamically possible reactions and yield selectively specific products.**
- **Namely, the use of catalysts can control the selectivity towards specific products.**
- **Control the enantio-selectivity of a reaction.**
- **Catalyst has been called as “molecular machine”:**
  - Synthesize the special conformation of chiral isomers
  - Incorporate with reaction conditions, and control the selectivity of chemical reaction.
  - It is relevant for the high selectivity and atom economy in bio-processes, and all reactions in living organisms are catalyzed by enzymes.
  - high specificities, selectivity and atom economy.

Example of Relevant Catalysis: Hydroformilation Reaction.

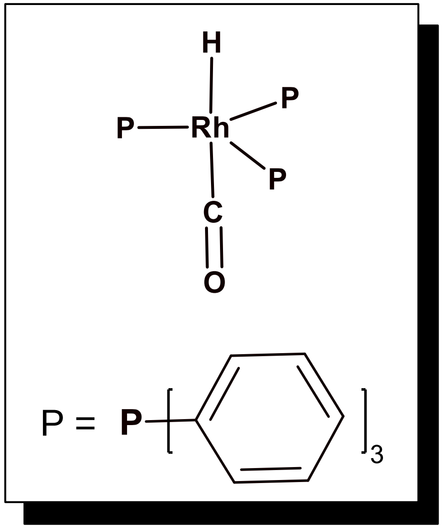


100% Atom Economy

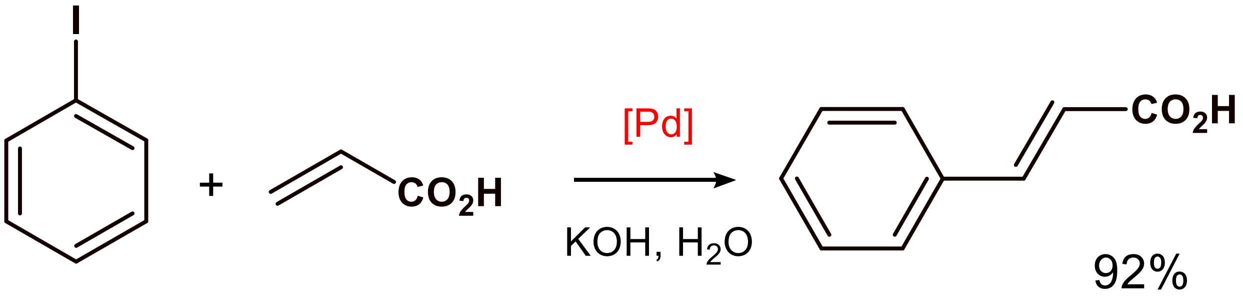
100 - 300 psi CO/H_2, 100°C, P:Rh = 1000

Catalysts:

- **$HRh(CO)(PPh_3)_3$**
- **$Rh(acac)(CO)_2$**
- **$Rh(acac)(CO)(PPh_3)$**
- **$Rh(acac)[P(OPh)_3]_2$**



Example of Relevant Catalysis: Synthesis of Cinnamic acid in H_2O.

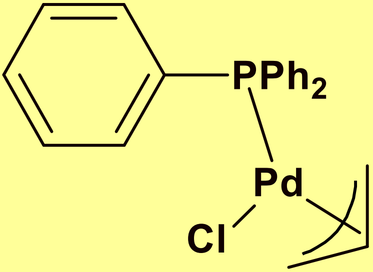


Heck Reaction*

↑

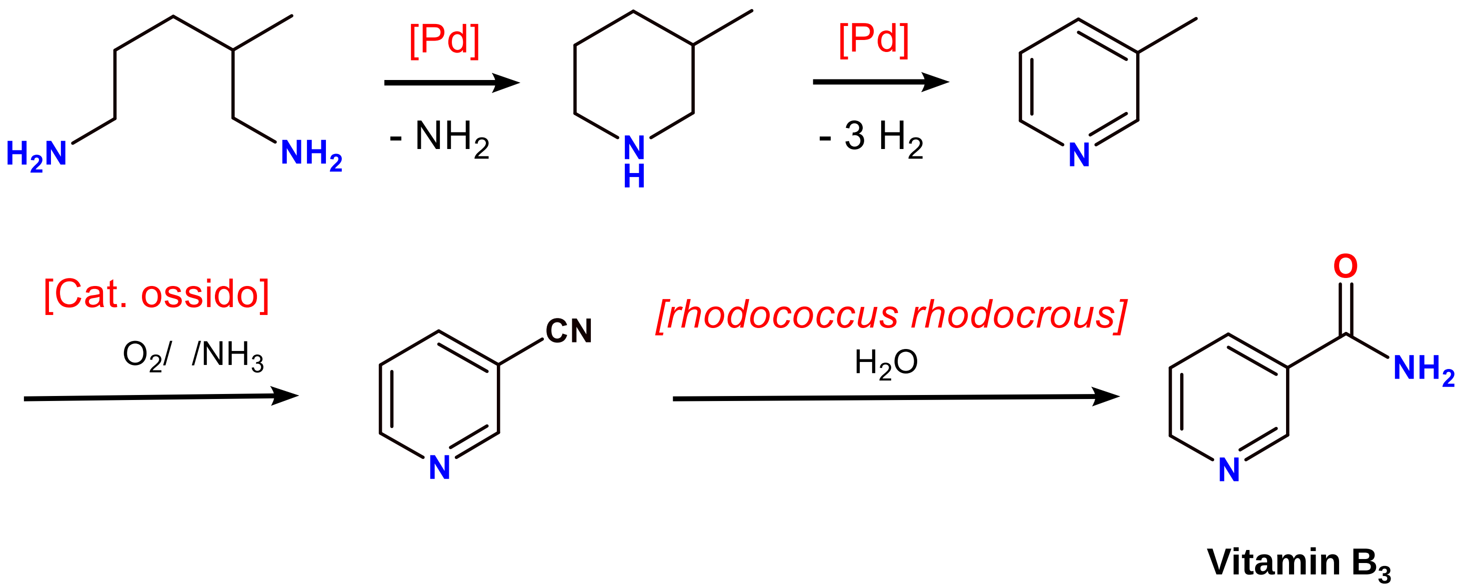
Use
(UV filters, fragrances)

[Pd] = i.e. PS-PEG-NH-CO--



Y. Uozumi, J. Org. Chem., 1999
***Nobel price 2010**

Example of Relevant Catalysis: Lonza Process – Synthesis of Nicotinamide.



Vitamin B_3

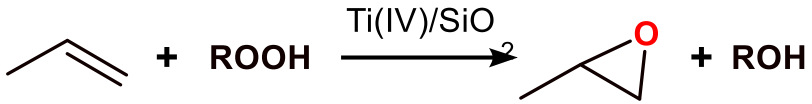
$$C_6H_{16}N_2 + 3/2\ O_2 \rightarrow C_6H_6N_2O + 2\ H_2O + 3\ H_2$$

catalysis and biocatalysis

Advanced in Chemical Catalysis.

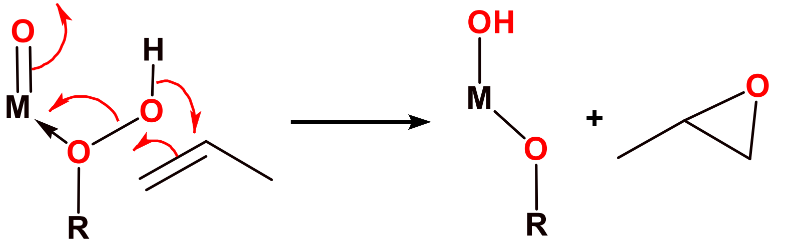
Metal Catalyzed Epoxidation

Shell SMPO process 1973



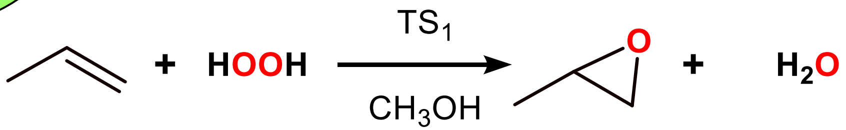
Sheldon and van Doorn, *J.Catal.* 31, 427, 1973

Peroxometal mechanism 1973



Sheldon, *Rec.Trav.Chim.Pays-Bas*, 92, 253, 1973

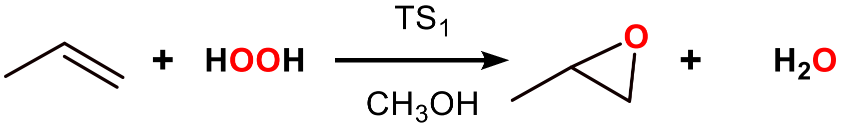
Mimoun, Sharpless



Enichem 1985

Ti-beta, Ti-MCM41, Ti-ITQ, etc.
van Bekkum, Corma
Dakka, Sato, LeBars

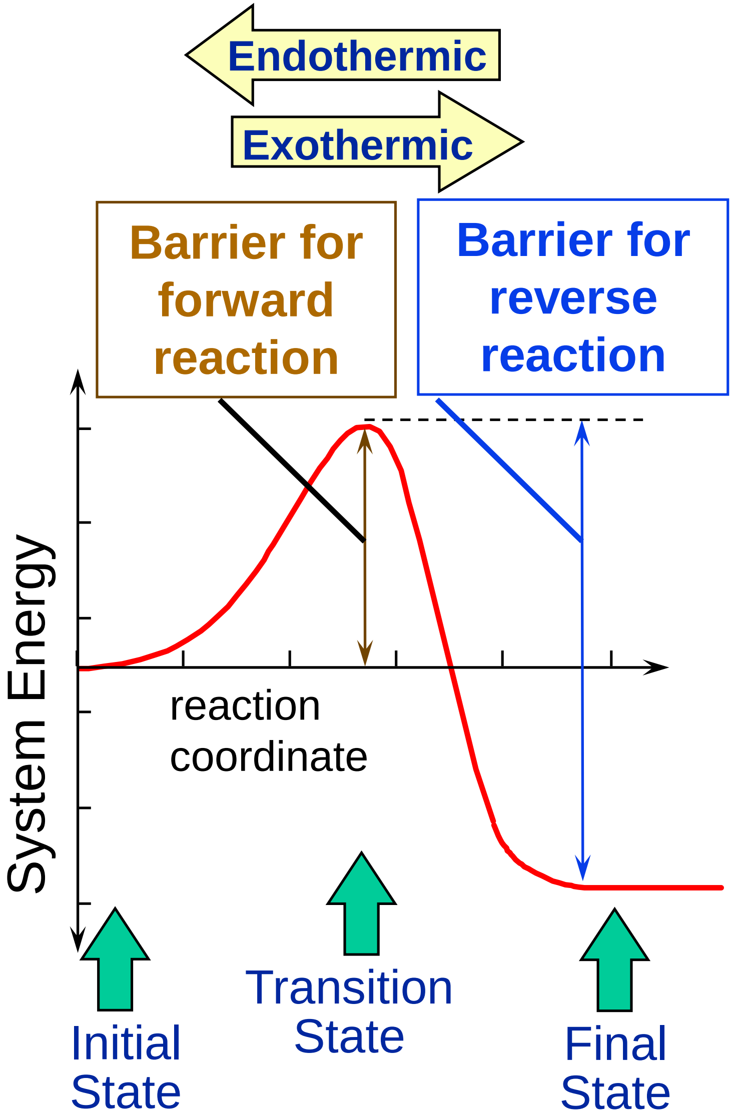
$$O_2 + H_2 \xrightarrow{\text{Pd/Pt (4 nm)}} HOOH$$



Headwaters/Evonik 2006

Kinetics of Chemical Reactions and Catalysis.

- Quantifies how fast a system evolves from an initial state to the equilibrium state.
- Kinetics primarily interest in overcoming the energy barrier. It does not deal of thermodynamics (i.e. energy of reactants and products).
- An exothermic reaction often has a lower barrier to its reverse reaction and therefore proceeds faster.



Rate and Reaction Order.

Generally, reaction rate depends on concentration of reagents. The number of reagents which determines the rate depends on the order of reaction:

$$R + R' \rightarrow P + P'$$

$$(CH_3)_3CBr + C_2H_5OH \xrightarrow{\text{probably 1° order}} (CH_3)_3C^+ + Br^- + C_2H_5OH$$

- *First* order: rate = k·[R]

  Typical for a dissociation reaction.

- *Second* order: rate = k·[R]·[R']

  Typical for interexchange and associative reactions.

$$Cl^- + CH_3F \xrightarrow{\text{probably 2° order}} CH_3Cl + F^-$$

Kinetics: Constraints to Reaction Rate.

Under normal considerations on the kinetics assumes that the products are removed quickly and that the reagents are in excess.

But reaction rates are limited also by transport of species by diffusion.

$$rate = k \cdot \frac{d[R]}{dx}$$

or

$$rate = k \cdot \frac{d\mu_R}{dx}$$

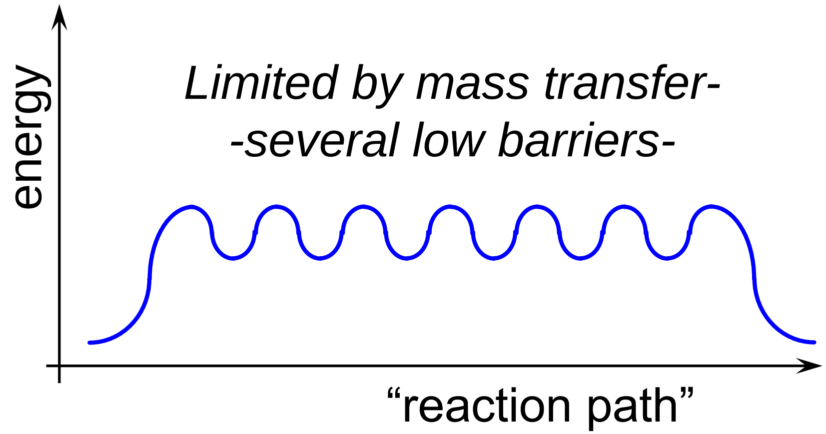
driven by concentration

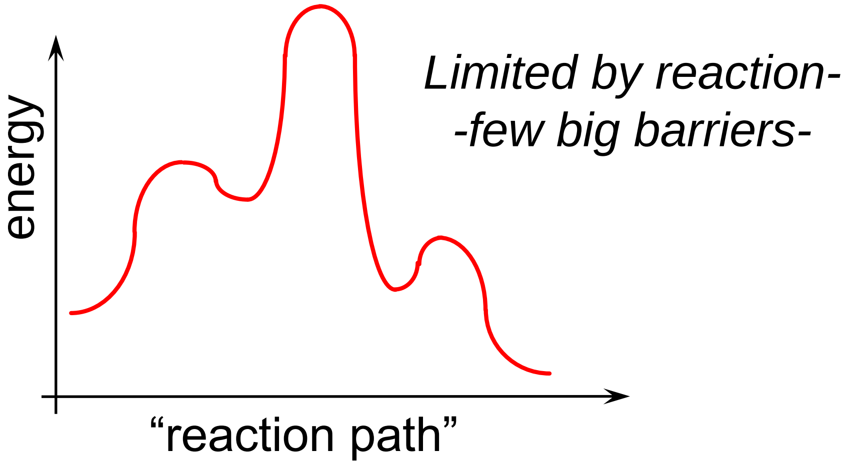
driven by chemical potential

Typically, diffusion of a species (reagent or product) is slower and the overall rate of a reaction limited by mass transfer depends only from that species.

Kinetics: Constraints to Reaction Rate.

- The energy of processes has a different behavior depending if the reaction is controlled by mass transfer or by energy barrier.
- Processes limited by mass transfer depend on how far a reagent must travel (rate $\propto x^{1/2}$).
- Processes limited by reaction depend on how much energy a reaction needs to be able to perform.





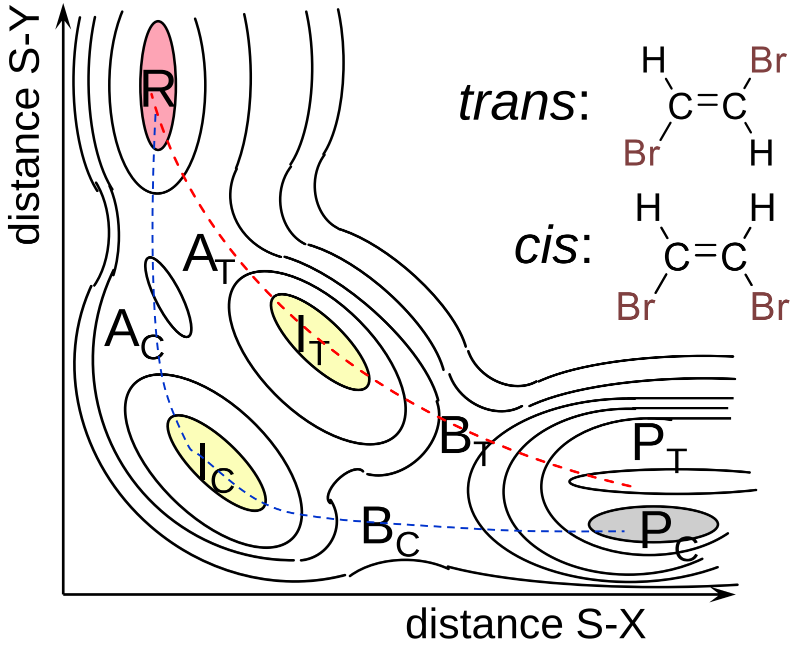
Activation Energy.

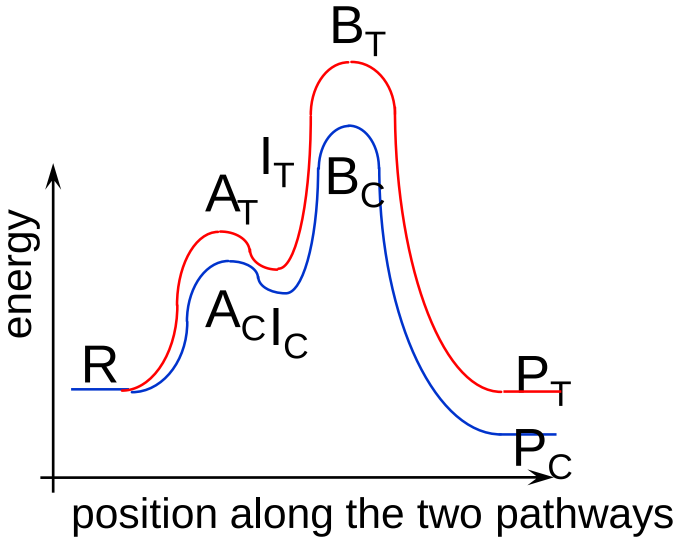
In some reactions alternative reaction pathways are possible resulting in different products, for example different isomers:

Example:

For a substitution reaction

$$H_2C{=}CHBr + Br_2 \rightleftharpoons BrCH{=}CHBr + HBr$$





Kinetics and Catalysis.

Increasing the rate of passing the energy barrier (transition state):

Increase of the sampling rate (pre-factor k_0):

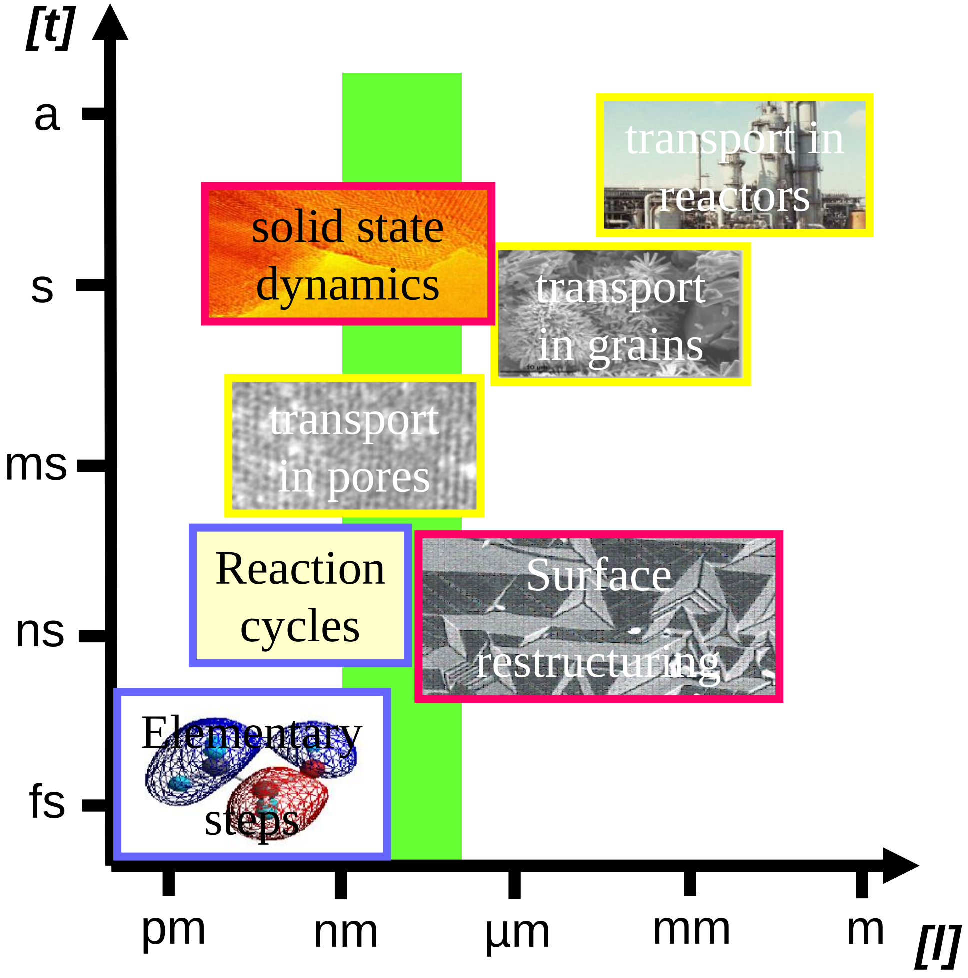
Decrease of the energy of the transition state (E).

$$k = k_0 e^{-\frac{E}{k_B T}}$$

Change of reagent configuration in order to provide more efficient interaction in order to react faster (typically, from 100 to 1000 more fast).

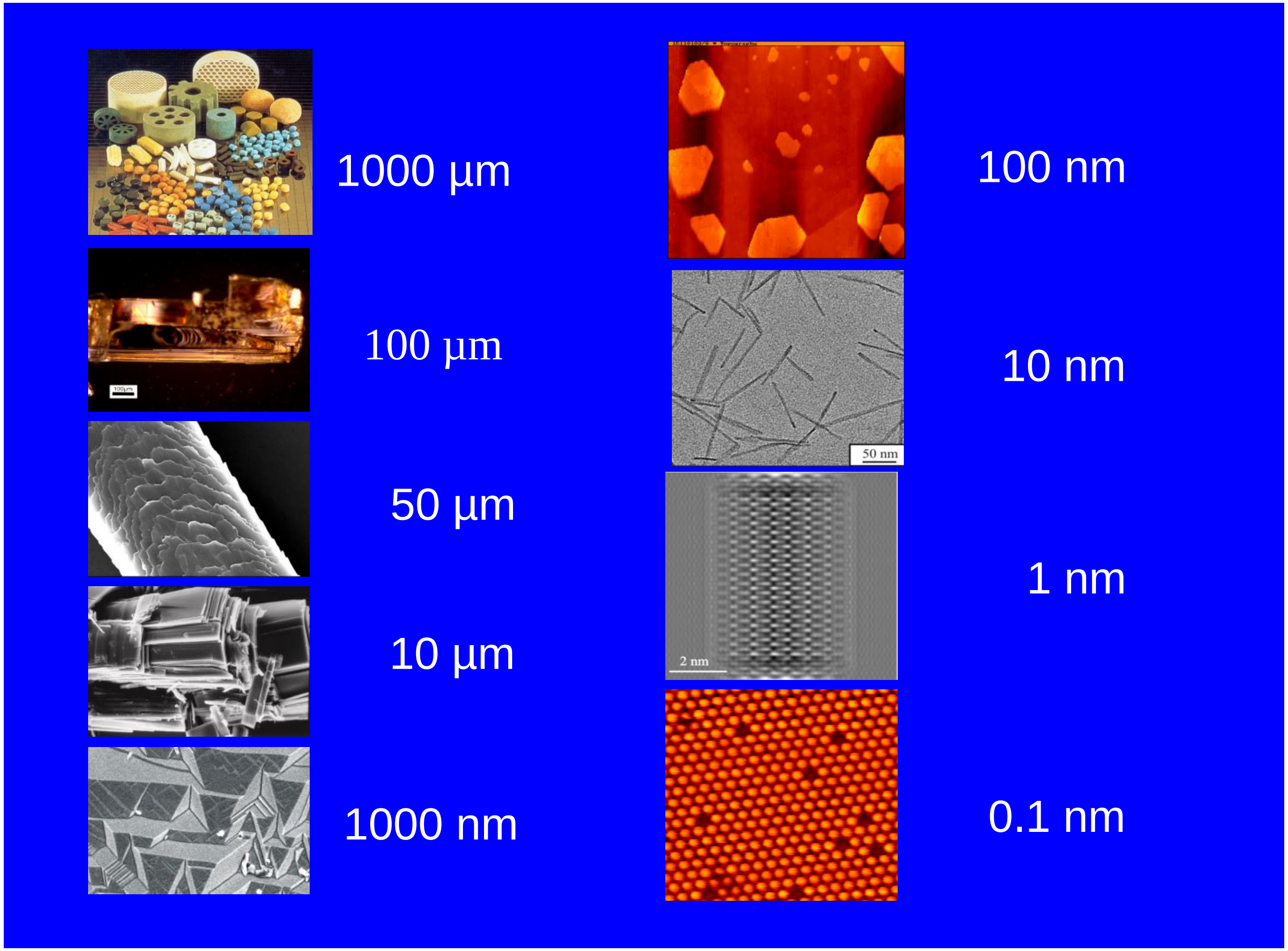
Forming a complex with the configuration of the transition state decreases the energy, typically more than 0.9 eV!

Multi-scale Phenomenon.



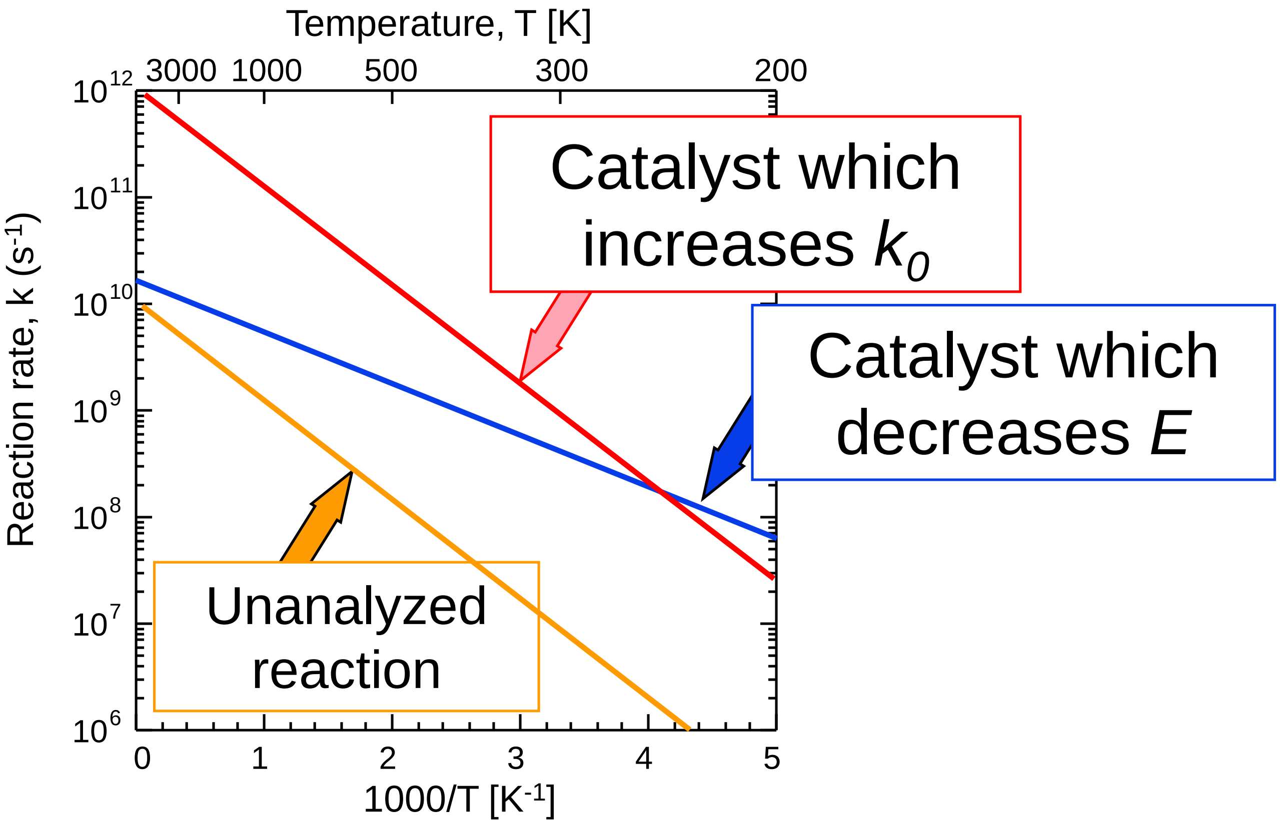
- Most of catalyst is not active (bulk).
- Even most of the surface is not active.
- Active are defects.
- There are many types of defects.
- Catalysts are dynamically behaving matrices for metastable minority structural elements that are active sites.

Detail Levels in Catalysis.



Catalysis.

Effect on overall reaction rate on temperature for catalysis in the rate determining step of kinetics:



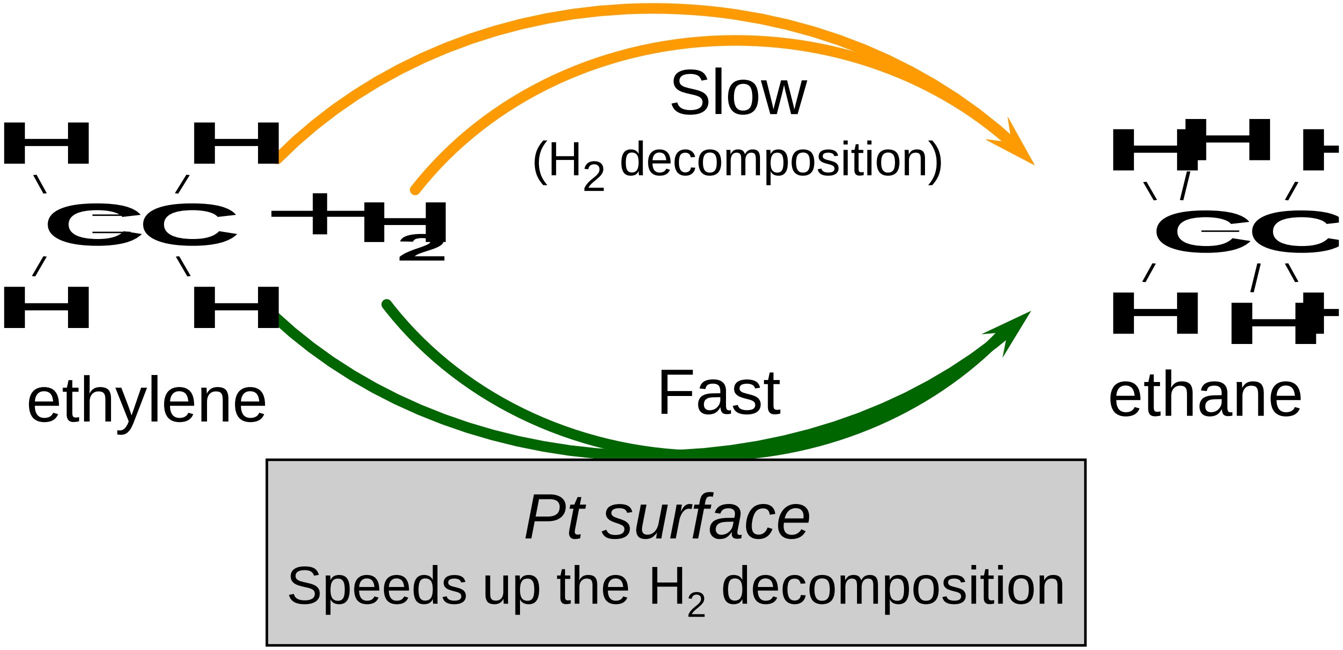
Catalyst which increases k_0

Catalyst which decreases E

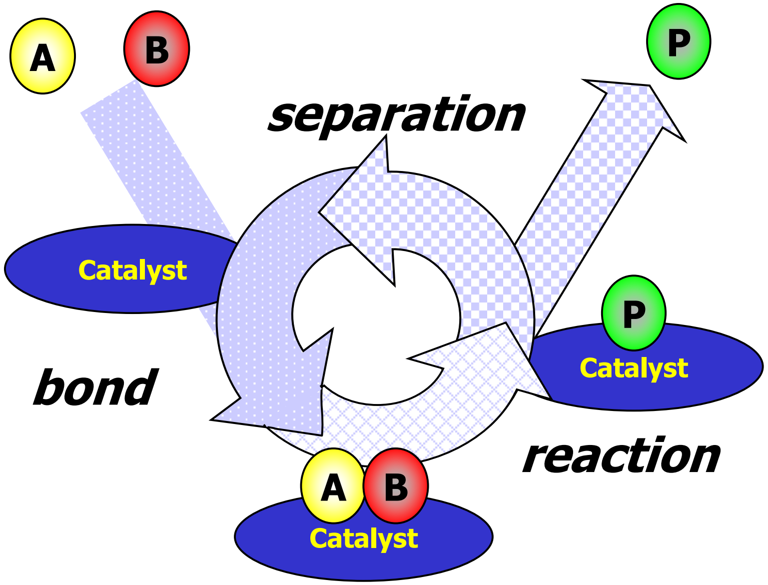
Unanalyzed reaction

Catalysts.

- Catalysts are compounds or materials which accelerate a reaction but are not consumed by reaction – they are nor reagents nor products. Typically they are substrates.
- In some cases they are intermediates which are processed by a reaction but regenerated by a subsequent reaction and then released.



Notion of Catalytic Reaction: Cycle.



In general terms:

1- bonding of 2 molecules A and B to catalyst,

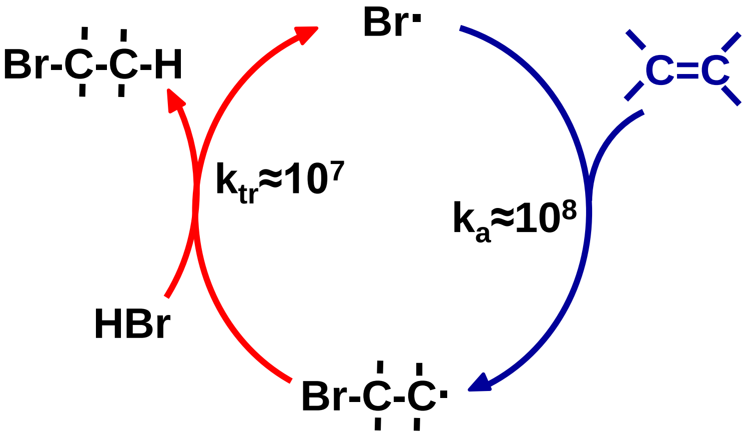
2- A and B react and afford P, bonded to catalyst,

3- P is detached from the catalyst, freeing it for a new cycle

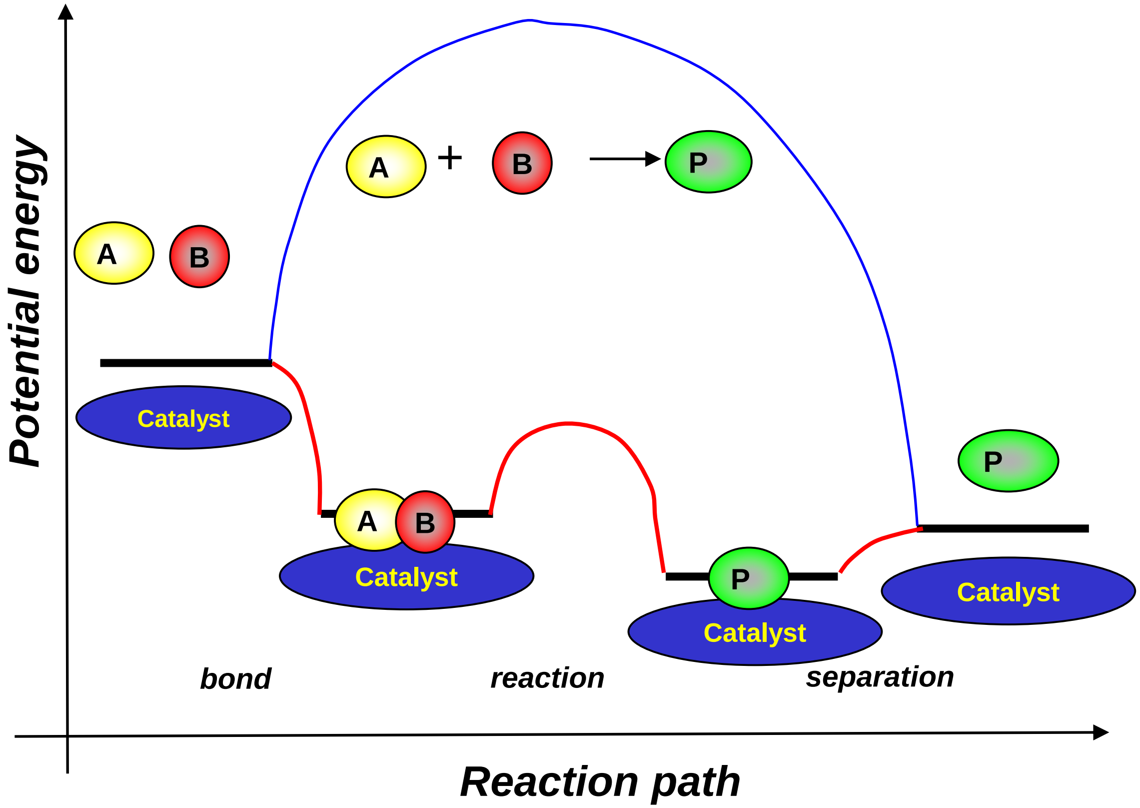
Radical chain reactions:

1- A radical intermediate adds to double bond.

2- The radical adduct regenerates the starting radical.



The Catalyst Role: Potential Energy Diagram.



For the uncatalyzed reaction:

reaction occurs when A and B collide with sufficient energy to overcome the activation barrier.

For the catalyzed reaction:

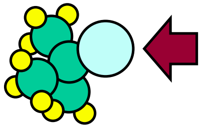
Adsorption of reagents is spontaneous and the activation barrier of reaction over the catalyst is remarkably lower, the product however must desorb from catalyst.

Homogeneous Catalysis – Mechanisms.

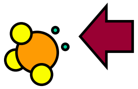
- **Change of charge distribution, orientation, or shape** of a molecule making more easily attacked during reaction.
- **Occupying a reactive site** force the reaction to take place at another site.
- **Bond together two molecules** until they react.
- **Stabilize an unstable intermediate** until it reacts.
- **Decompose a small molecule** making it reactive.

N.B. **Change of equilibrium constants** (stabilizing a reagent or a product can modify the reaction yield – *N.B. this is not a true catalysis because it is used stoichiometrically*).

Terms.



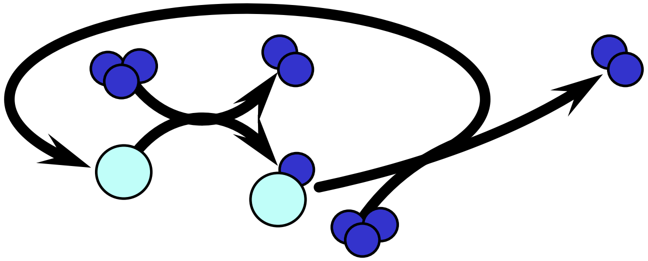
- Functional group: a reactive part of a molecule.
- Nucleophile: a negatively charged part of a molecule, reacts with positive charges of another molecule.
- Lewis Base: an electron pair donor, i.e.: NH_3



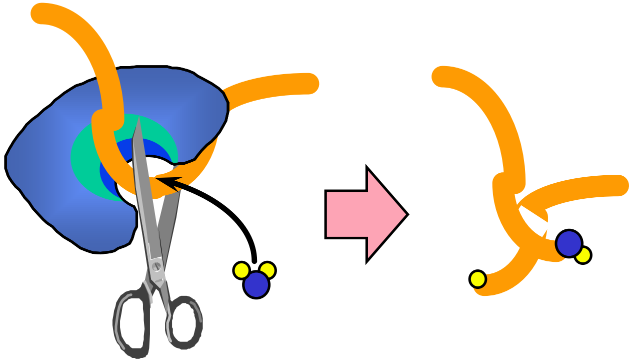
- Electrophile: a positively charged part, reacts with negatively charged parts of an another molecule.
- Lewis Acid: acceptor of an electron pair, i.e.: $\boxed{H^+}$
- Ligand: a Lewis base bonded to a metal atom, i.e. CN^- in $[Fe(CN)_6]^{4-}$
- Radical: A molecule incompletely bonded, it presents unpaired electrons, i.e.: $H_3C\text{-}CH_2^{\bullet}$
- Cation/Anion: charged ions positively/negatively, i.e.: H^+ / OH^- .

Classes of Catalysts.

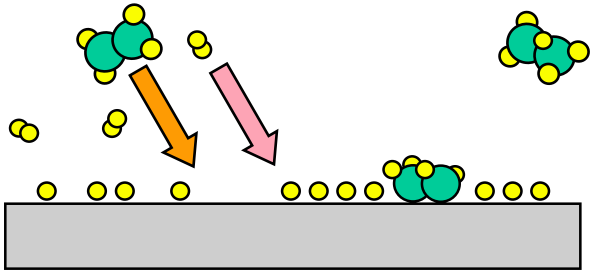
Homogeneous – catalysts and reagents are in the same phase.



Enzymes – protein molecules accelerating biologic reactions.



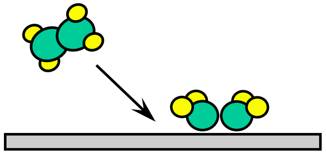
Heterogeneous – catalyst and reagents are in different phases.



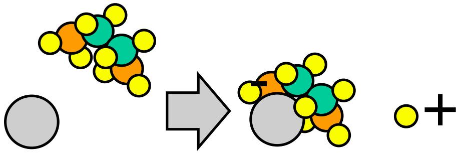
Catalysis Mechanism.

Mechanisms:

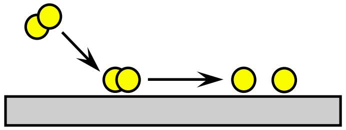
- **Conformational Organization**



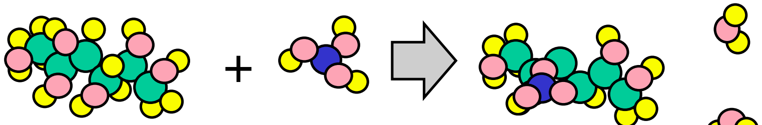
- **Charge change/electron-transfer**



- **Promotion of reagents decomposition**



- **Formation of reactive complexes**



complex
(more easily ionized)

- **Formation of free radicals**

$$Fe^{2+} + H_2O_2 \rightarrow FeOH^{2+} + \bullet OH$$

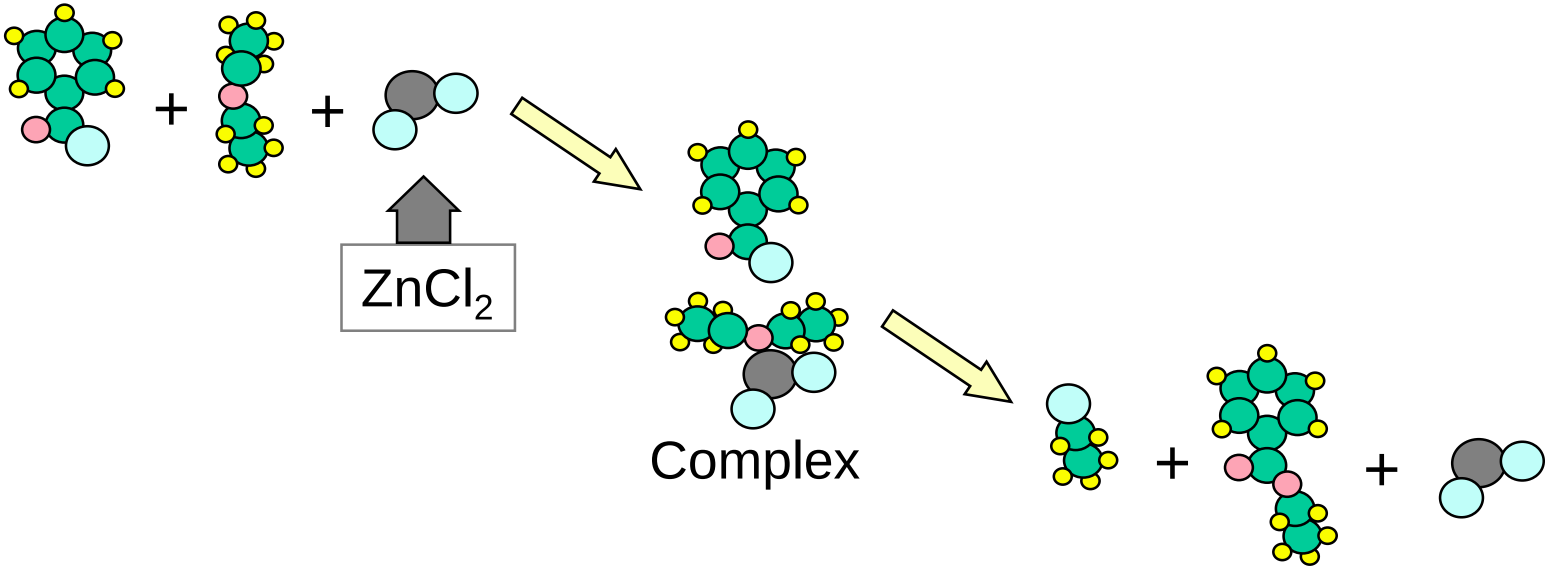
Catalysis: Another View.

- Specific mechanisms used to lower activation energies:
  1. **Binding and orienting substrates (binding energy)**
  2. **General Acid-Base catalysis**
  3. **Covalent catalysis**
  4. **Metal ion assisted catalysis**
  5. **Organization of the reaction environment (take away water).**

Homogeneous Catalysis.

Catalysis in the same phase.

These catalysts form complexes with molecules in a given phase (normally in a liquid solution) and modify the reaction process.



$$\mathrm{PhCOCl} + (C_2H_5)_2O \xrightarrow{ZnCl_2} \mathrm{PhCOOC_2H_5} + C_2H_5Cl$$

Homogeneous Catalysis

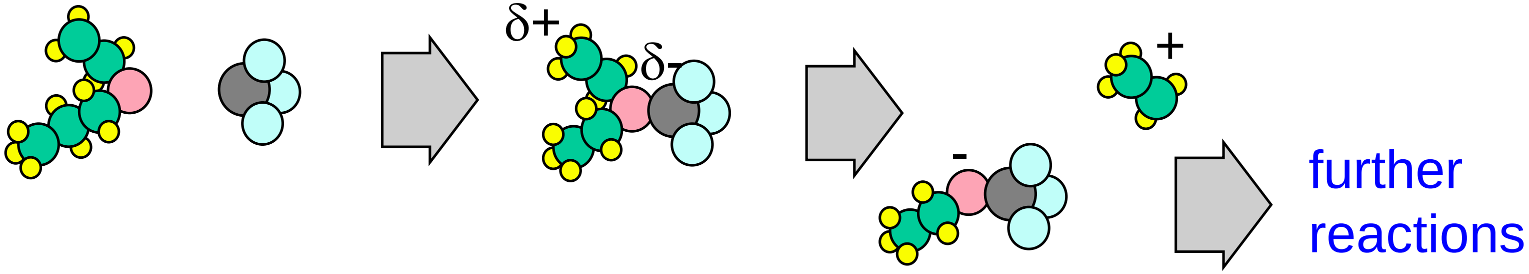
(Catalysis by changing the charge distribution).

- Reactions often involve the attack of a molecule by another that has both:
  - positive charge therefore attracts electrons (electrophile)
  - negative charge therefore attracts positive charges (nucleophile)
  - N.B. Charges can be also fractional
- Homogeneous catalysts often modify **the degree of charge** in interested molecules making the attack faster.

Homogeneous Catalysis

(Polarization of reagents with metal ions).

The formation of a complex between the organic molecule and a metal halide generally results in electron transfer to metal (when σ-bonded):



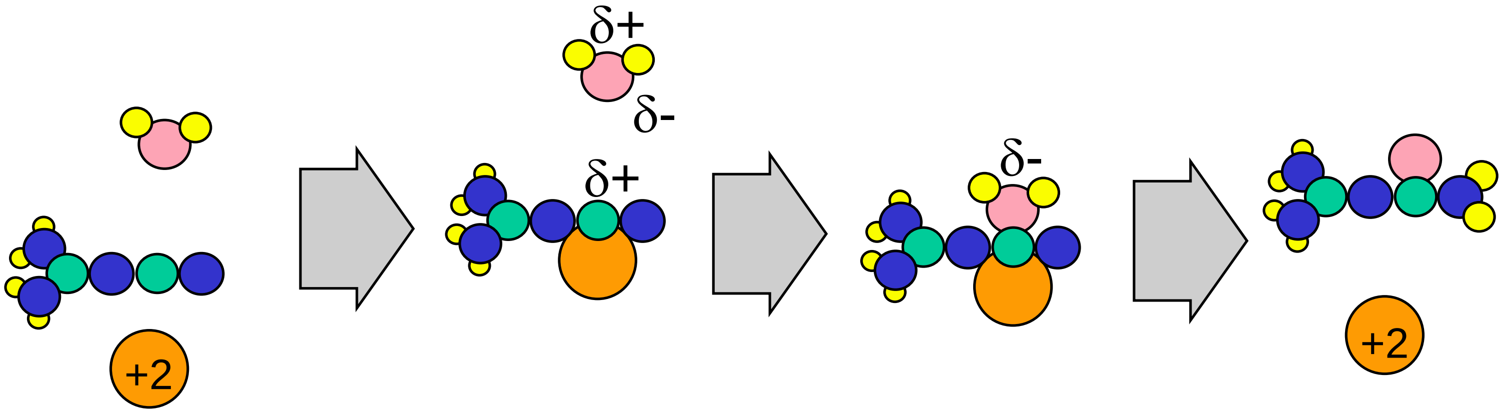
$C_2H_5OC_2H_3 + AlCl_3 \rightarrow [C_2H_5OAlCl_3]^- + C_2H_5^+$

Complexes formed via π bonds or incorporating *d* states can transfer charge from metal rather than accept it.

Homogeneous Catalysis

(Polarization of reagents with metal ions).

Example:



$(H_2N)_2C=N\text{-}C\equiv N + H_2O\ [+ CuSO_4] \rightarrow (H_2N)_2C=N\text{-}CO\text{-}NH_2$

(In the example SO_4^{-2} group does not participates in the process).

Homogeneous Catalysis

(Polarization of reagents with metal ions).

- Move electrons from a ligand (reagent molecule) in a metal can:
  - Facilitate the attack by nucleophiles (negatively charged).
  - Delaying the attack by electrophiles (positively charged).
- Oxidant species are generally electrophiles therefore coordination typically slow down the oxidation reactions and accelerate reduction reactions!

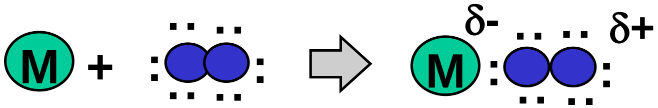
[Note: The effectiveness of various metal ions depends on pH].

Homogeneous Catalysis
(Polarization of reagents with metal ions).

Several important effects occur in small molecule as a result of complex formation:

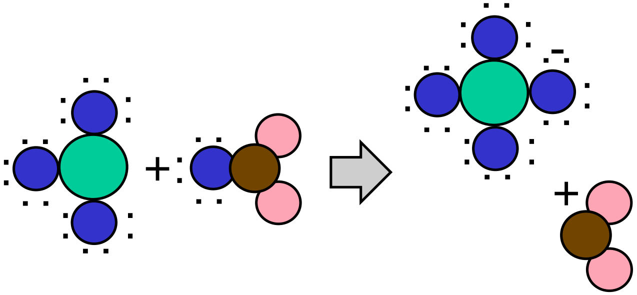
- polarization (formation of a dipole as before)

$$\boxed{Cl_2 \xrightarrow{M} Cl^{\delta+} - Cl^{\delta-}}$$



- ionization by charge transfer or decomposition:

$$\boxed{NO_2Cl + FeCl_3 \rightarrow NO_2^{+} + FeCl_4^{-}}$$



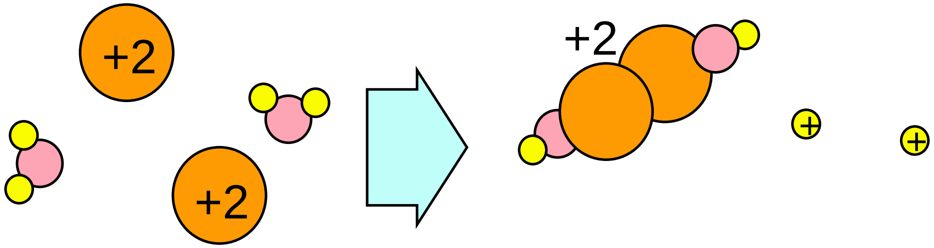
- Generation of free radicals:

$$\boxed{H_2O_2 \xrightarrow{M^+} 2\ HO\bullet}$$

Homogeneous Catalysis

(Complexes able to change reagent acidity).

Example:



$$2\ Cu^{+2} + 2H_2O \rightarrow Cu_2(OH)_2^{2+} + 2H^+$$

- Electrons exchange from water to Cu^{+2} which reduces electronic density on the hydrogens of H_2O, making easier the proton removal.

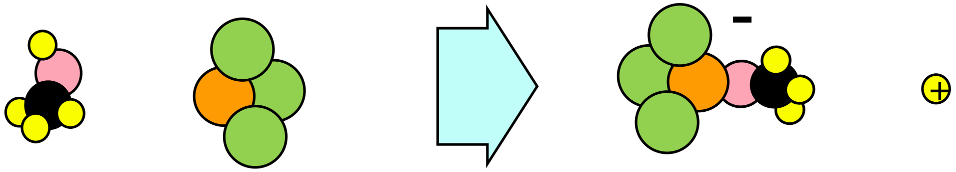
This can increase the acidity (H^+ donation) of 10^7 or more!

Homogeneous Catalysis

(Complexes able to change reagent acidity).

- When a molecule carrying an hydrogen atom (which can be removed as ion) forms a complex with an electron pairs acceptor (Lewis acid), hydrogen ion is removed much more easily.
- This increases the reactivity. After the reaction the Lewis acid is recovered by decomposition of the complex.

Example:

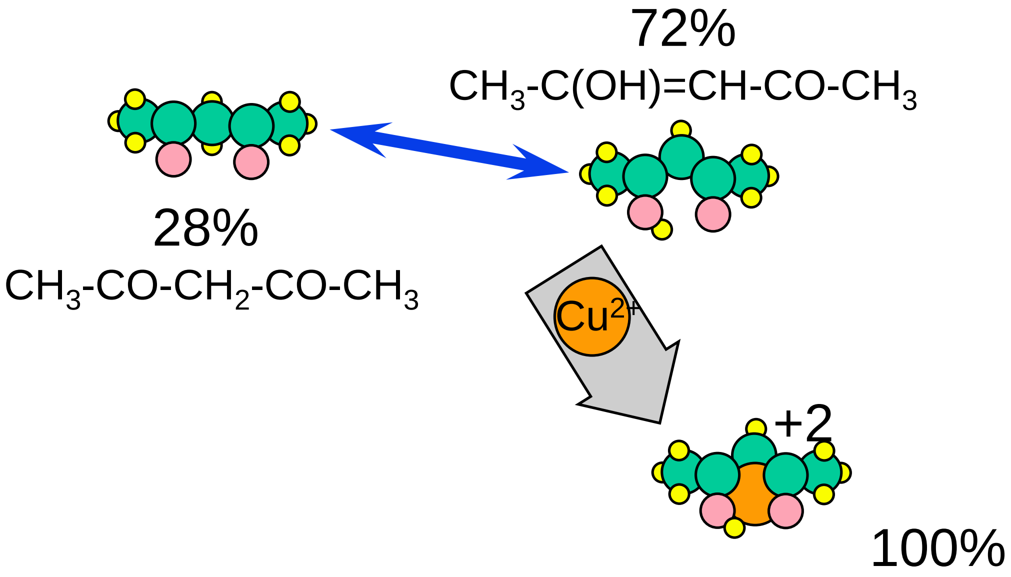


$CH_3OH + AlCl_3 \rightarrow AlCl_3(OCH_3)^- + H^+$

Homogeneous Catalysis
(Tautomeric Equilibria).

Selection of a specific structure of a compound in equilibrium with others (common by hydrogen relocation):

when two structures are in equilibrium, only a specific form can provide a complex, stabilizing only that form.



72%

CH_3-C(OH)=CH-CO-CH_3

28%

CH_3-CO-CH_2-CO-CH_3

100%

Keto-enol tautomerism

Homogeneous Catalysis

(factors affecting the $\Delta G^{\#}$ of reaction).

$$\Delta G^{\#} = \Delta H^{\#} - T\Delta S^{\#}$$

- The factors must affect ΔH, μ, or ΔS!
  - Changes of bond energy (via μ)
  - Changes of $\Delta H^{\#}$ for state change
  - Changes in $\Delta S^{\#}$ for change in:
    - particle number
    - symmetry
    - possible motions
    - state/phase
    - charge

Homogeneous Catalysis

(entropy change by electrostatic interactions).

The entropy difference between isolated reagents and the electrostatically bound transition state is:

$$\boxed{\Delta S = F \cdot Z_A \cdot Z_B}$$

Where F is a constant and Z are the charges of the ligand.

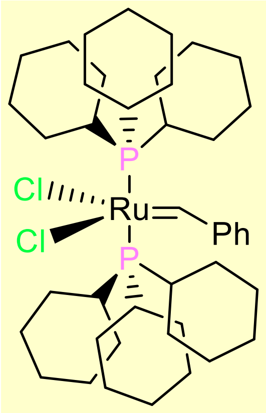
The entropy change ΔS for the formation of the complex with a charged ion (normally a metal) is:

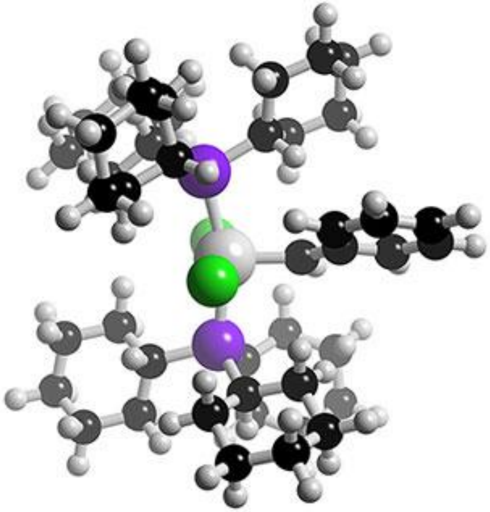
$$\boxed{\begin{aligned}\Delta(\Delta S) &= F \cdot [Z_A + Z_M] \cdot Z_B - F \cdot Z_A \cdot Z_B \\ &= F \cdot Z_B \cdot Z_M\end{aligned}}$$

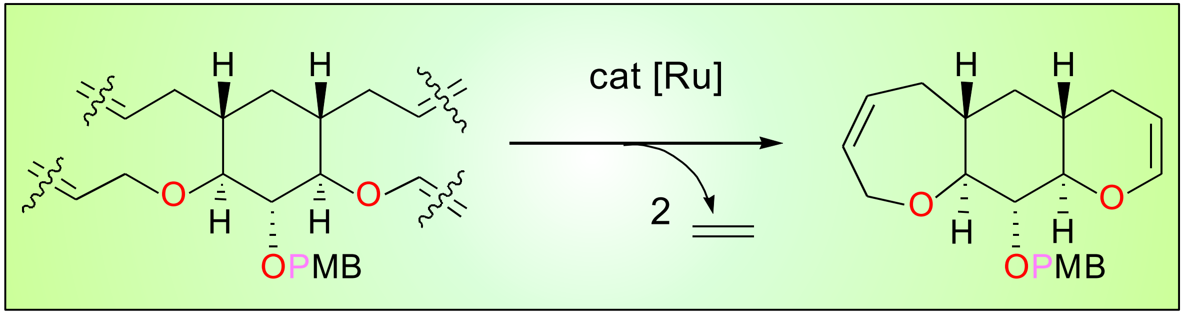
The sign of entropy change for catalyst determines whether the reaction is accelerated or delayed. This depends on the sign of Z_B and Z_M.

Homogeneous Catalysis in Metathesis by Ring Closure (RCM).

- Homogeneous catalysis is often used for the production of pharmaceuticals and the synthesis of natural products and organic materials.
- A relevant example (between others …) is the Metathesis of olefins on Schrock and Grubbs catalyst (Nobel 2006).







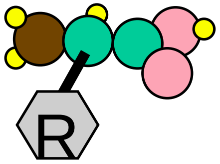
Ring Closure Metathesis RCM

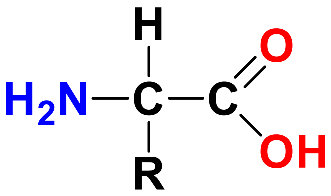
MILESTONES IN ASYMMETRIC CATALYSIS.

- 1939 Cinchonine-modified Pt (Lipkin and Stewart)
- 1956 Pd modified with silk fibroin (Akabori, Izumi)
- 1963 Raney Ni/tartrate (Izumi)
- 1966 Asymmetric cyclopropanation catalyzed by a chiral Schiff's base complex, 10% ee (Nozaki, Noyori)
- 1968 Asymmetric hydrogenation with a rhodium-chiral phosphine complex, 15% ee (Knowles and Sabacky; Horner)
- 1970 Monsanto L-Dopa process
- 1971 DIOP ligand (Kagan)
- 1980 Asymmetric epoxidation, Ti/TBHP/tartrate (Sharpless)
- 1984 Takasago l-menthol process, Rh-Binap (Otsuka, Akutagawa, Noyori)
- 1988 Asymmetric dihydroxylation of olefins, OsO_4/quinine (Sharpless)
- 1991Jacobsen-Katsuki epoxidation
- 2001Nobel prize in Chemistry for Knowles,Noyori and Sharpless

Homogeneous Catalysis
(Biocatalysis or Enzymatic Catalysis).

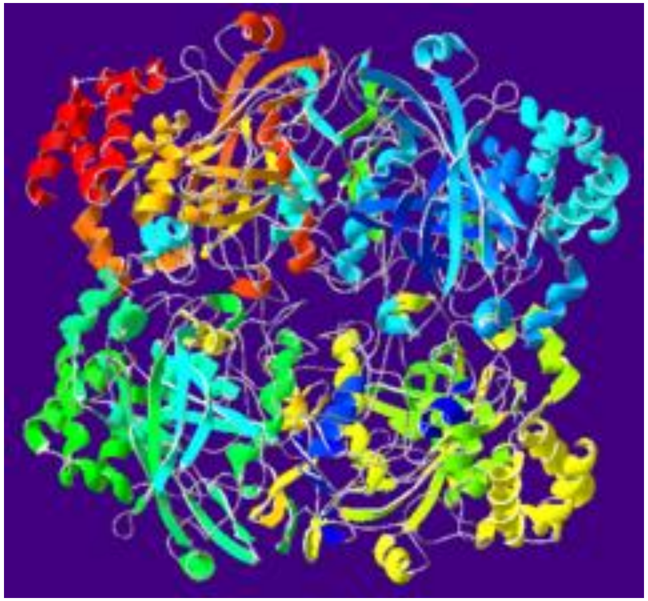
- Enzymes are essential catalysts of living organisms.
- Enzymes use several major catalytic approaches concurrently:
  - Polarization trough formation of metal complexes.
  - Keep neighboring desired reaction sites.
  - Use steric hindrance to prevent unwanted reactions.
- Enzymes are proteins formed from amino acids:





$$H_2N-\overset{\displaystyle H}{\underset{\displaystyle R}{C}}-C(=O)OH$$

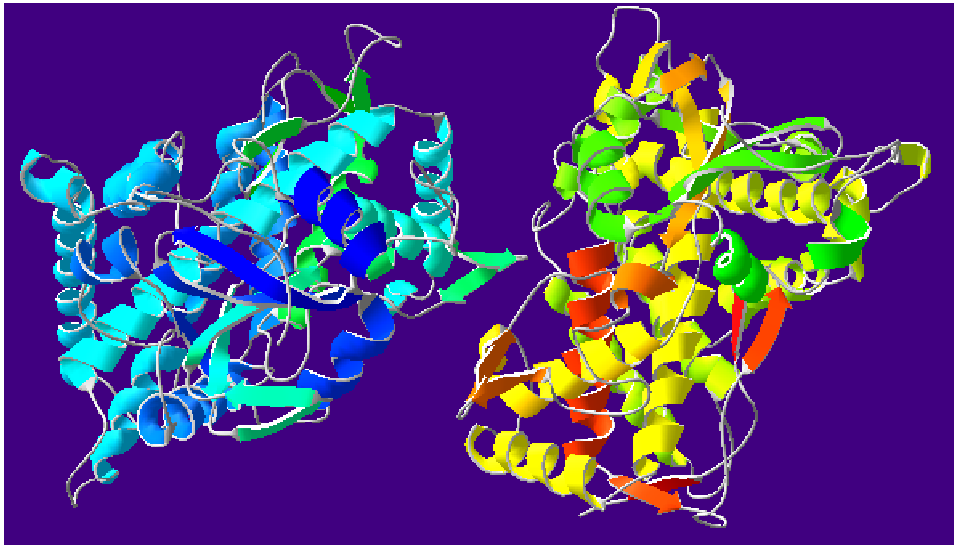
Biocatalysis: Examples.



Catalase enzyme accelerates the decomposition of hydrogen peroxide in water and oxygen

$2\ H_2O_2 \rightarrow 2\ H_2O + O_2$

→ 10^7 molecules are converted each second!!!



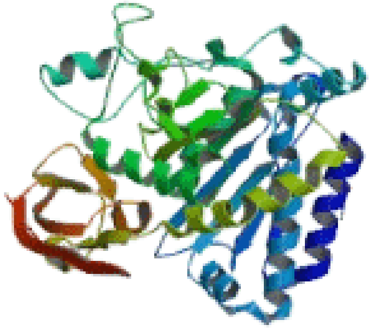
Cytochrome P450 = enzyme for oxidation and detoxification of toxic compounds.

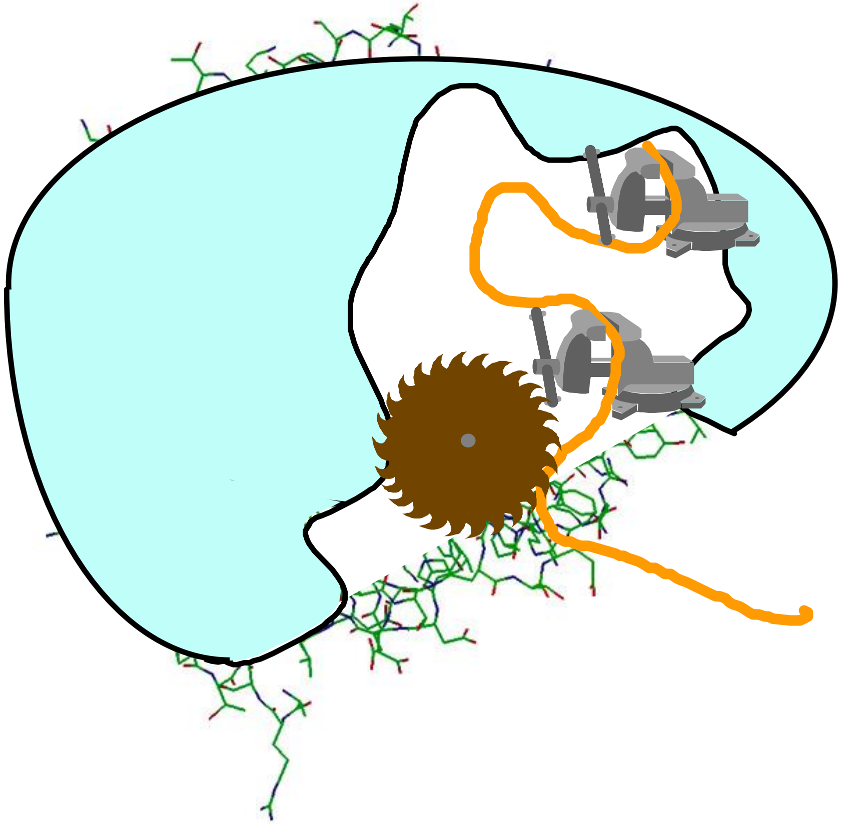
Homogeneous Catalysis

(enzymatic catalysis - Carboxypeptidase-A).

Carboxypeptidase-A is a protein with 307 amino acids. Breaks other proteins, i.e.:

- **Links the substrate protein**
- **Zn^{2+} ion polarizes the interested bond (C=O)**
- **Polarized water is provided to hydrolyze the bond (CO-NH).**



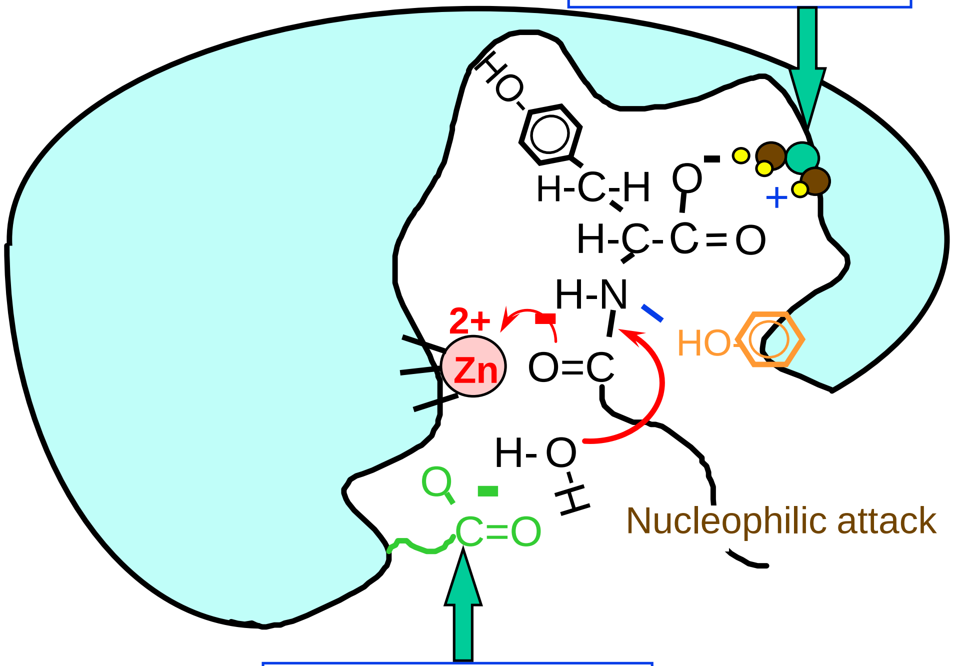


Homogeneous Catalysis
(enzymatic catalysis - carboxypeptidase-A).

In more detail:

- **Links the protein**
- **Zn^{2+} ion polarizes the bond of interest**
- **Polarized water is provided to hydrolyze the bond.**

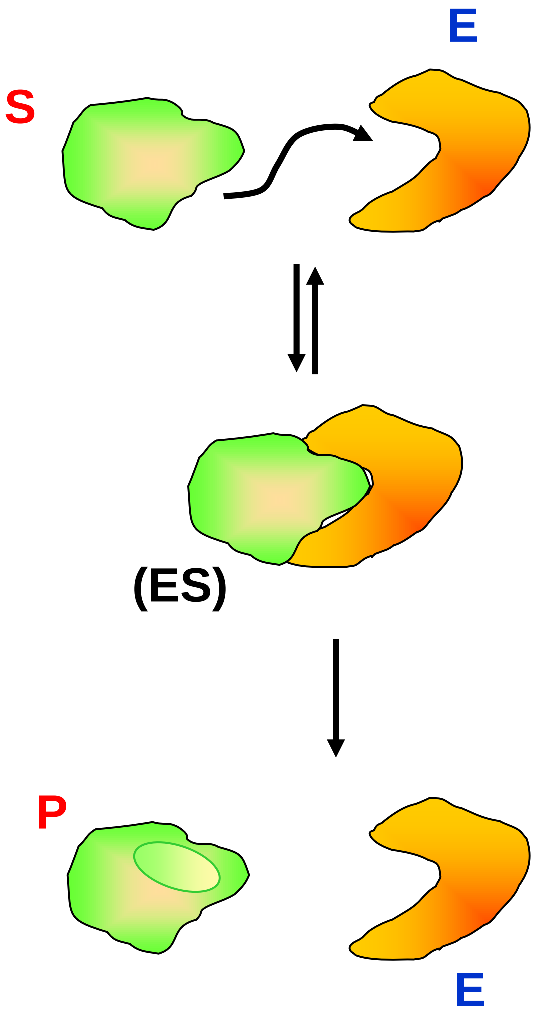
[amine terminal ($-NH_2$) of Enzyme]



Nucleophilic attack

[carboxylate terminal (COO^-) of Enzyme]

Enzyme Mechanism.



A typical kinetic law for enzymatic reactions is:

Rate of product formation = k [E][S]/([S] + K_M) where [E] is the concentration of enzyme and [S] is the concentration of substrate. K_M is constant known as **Michaelis constant.**

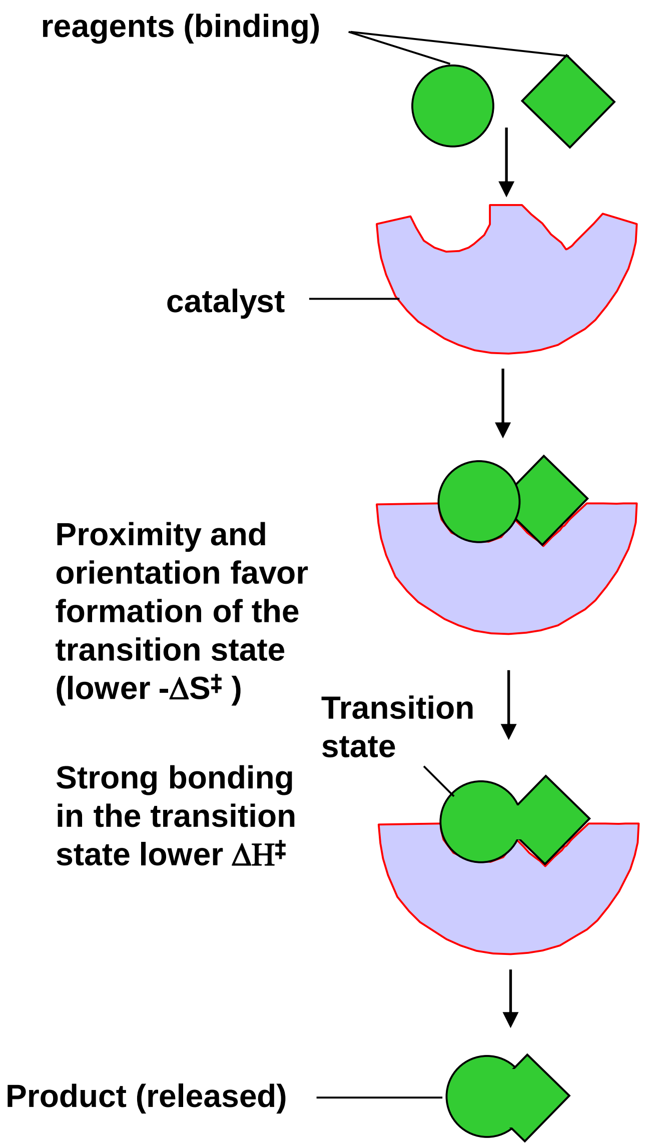
Note: The reaction is first-order in E but does not have a specific order in S.

The proposed mechanism is

- 1. Formation of complex ES:
  E + S $\rightleftharpoons$ ES (k_a)
- 2. Decomposition of ES:
  ES $\rightleftharpoons$ E + S (k_a')
- 3. Formation of products and release of enzyme:
  ES $\rightleftharpoons$ P + E (k_b)

1. Bonding and Orienting Substrates.

- **Bind reactants close together and hold them in proper orientation for reaction.**
- **Especially effective when 3 or more reactants need to be in place for reaction to occur.**

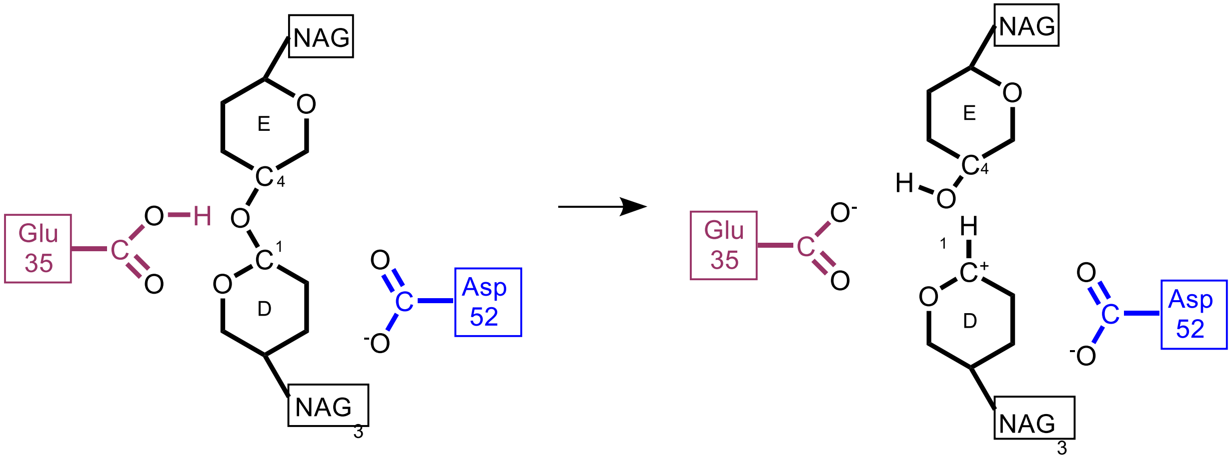


2. Acid-Base Catalysis.

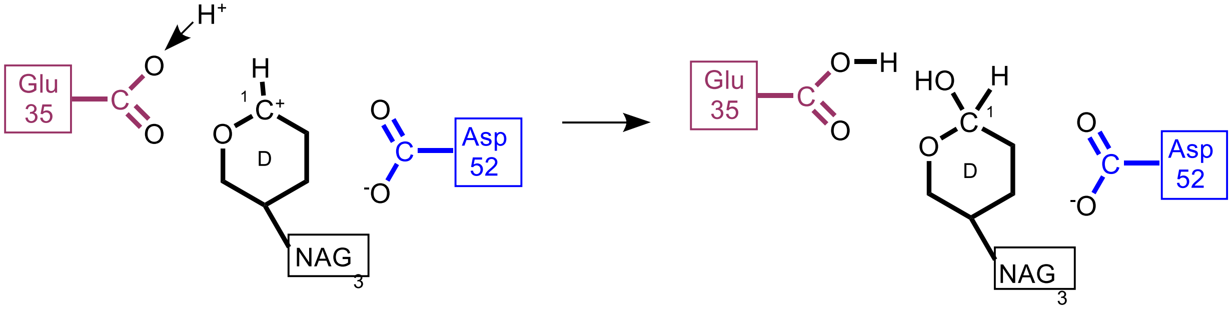
Amino acids in the enzyme donate H$^+$ ion to the reactant or accept H$^+$ ion from the reactant.

- Donate H$^+$ = general acid,
- Accept H$^+$ = general base.

Ex. Cleavage by lysozyme:



1st step: Glu35 acts as a general acid.



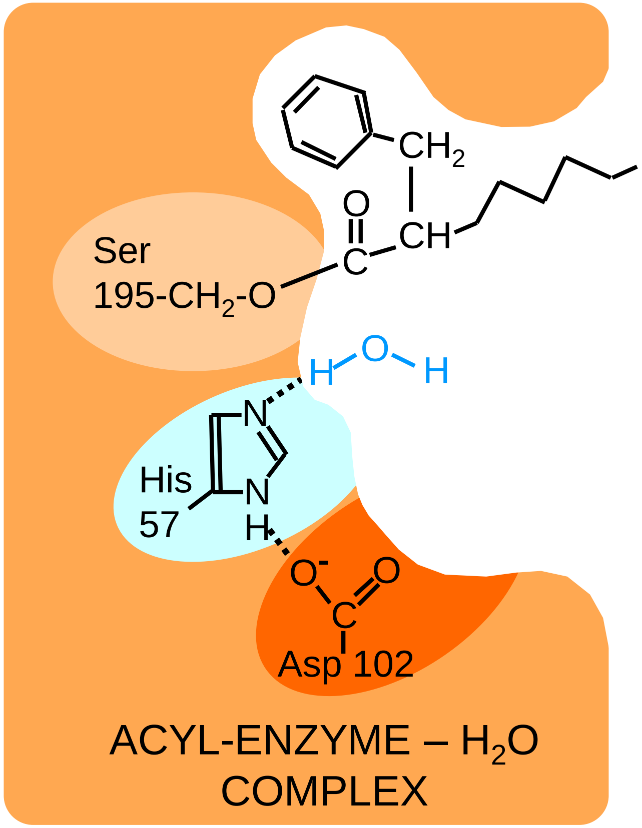
2nd step: Glu35 acts as a general base.

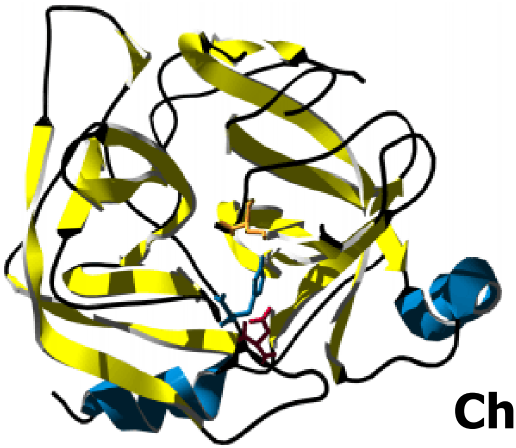
3. Covalent Catalysis.

A (transient) covalent bond is formed between the reactant(s) and the enzyme.

Example: Serine proteases form a covalent bond to part of the protein they are cleaving.

This is the 'Acyl-Enzyme' Intermediate.



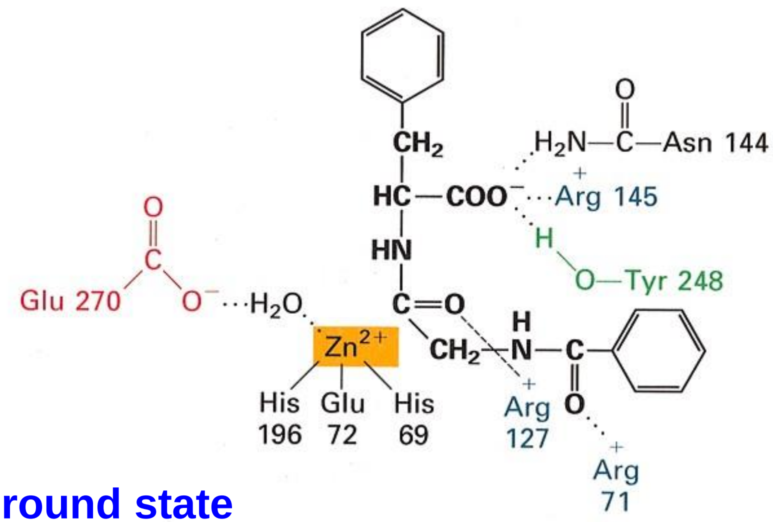


Chymotrypsin

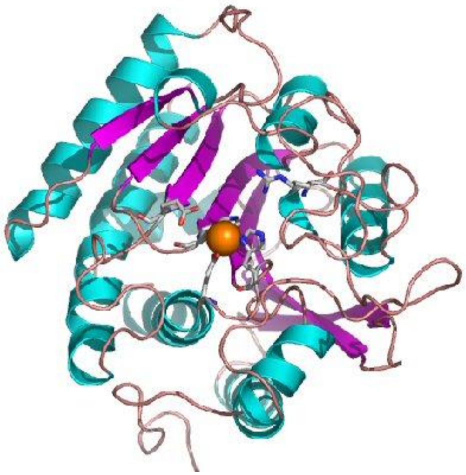
4. Metal-ion Assisted Catalysis

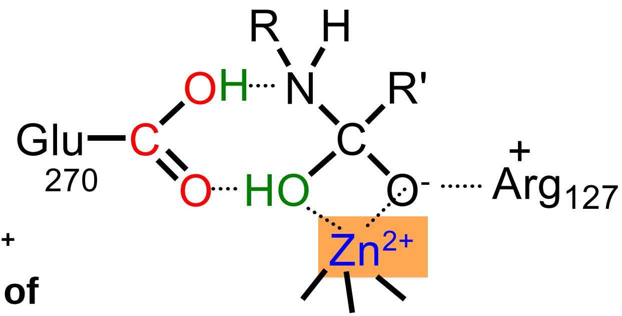
Coordination to metal centers favors reactions via metal-substrate (ligand) bond able to activate the process.

Example: Carboxypeptidase A uses a Zn^{2+} ion.



Ground state



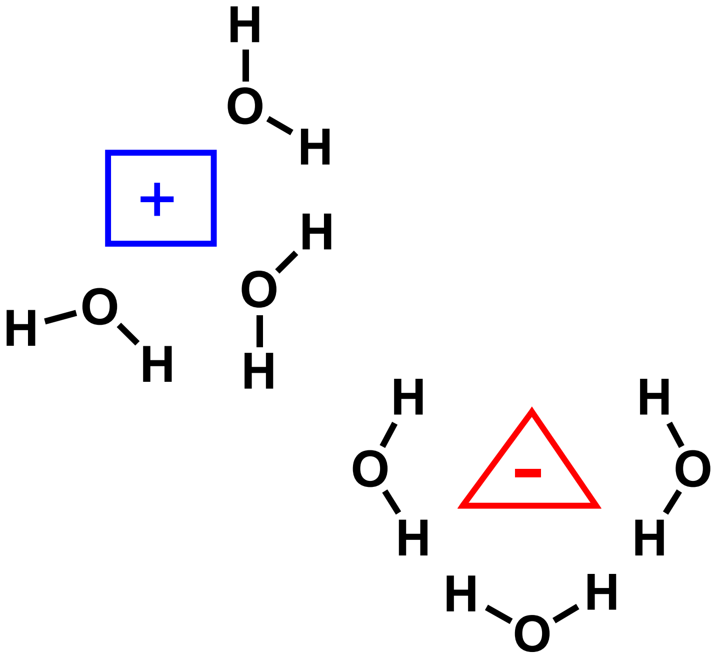


Transition state: Zn^{2+} stabilizes formation of hydroxide (OH) from water, and stabilizes the negative charge on oxygen (COO^-).

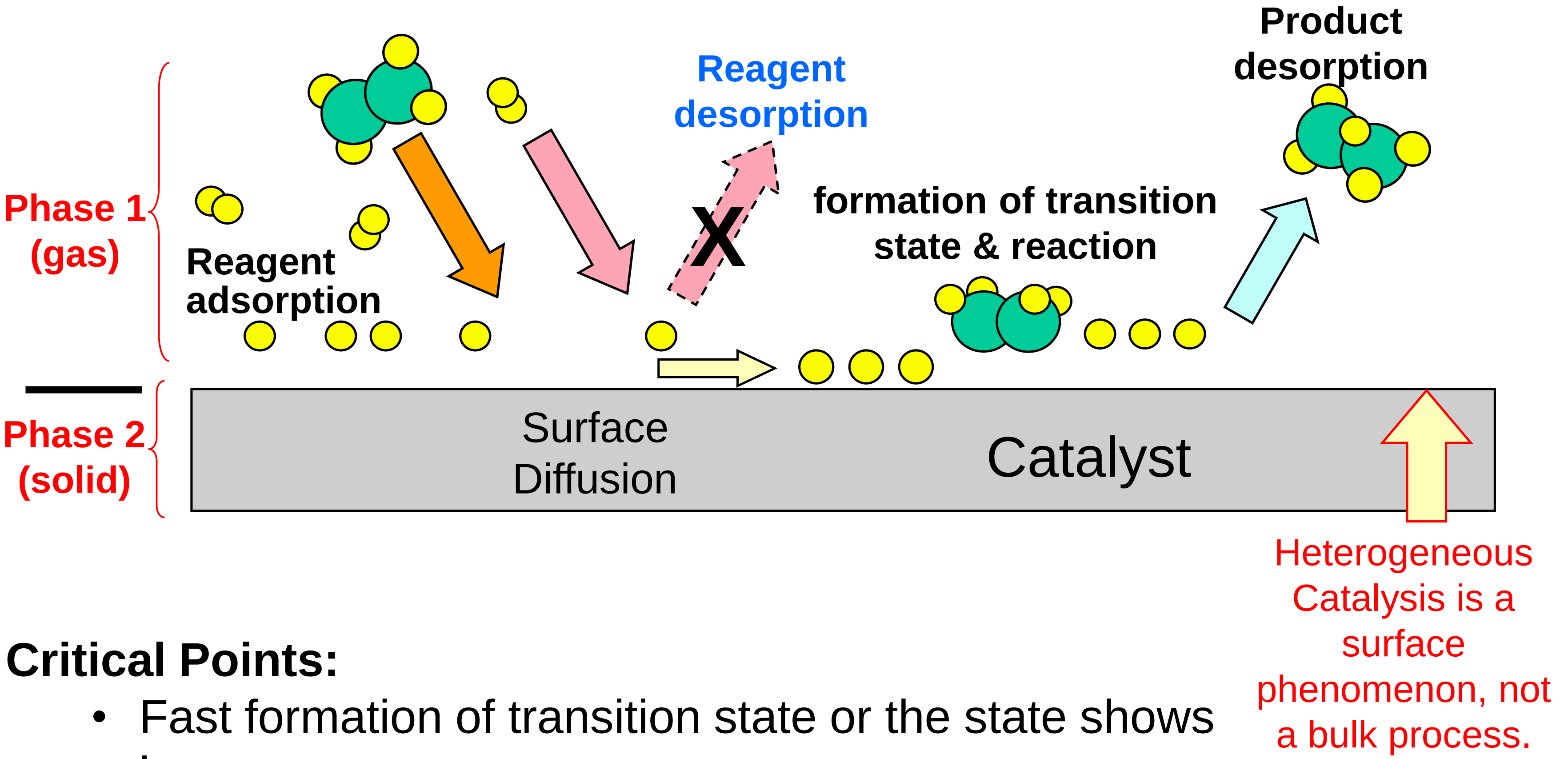
5. Organizing the Reaction Environment (take away water molecules).

Water molecules (solvation) prevent reactants to interact each other.

If the enzyme can bind the reactants without the associated water molecules, they can react easier.



Heterogeneous Catalysis.



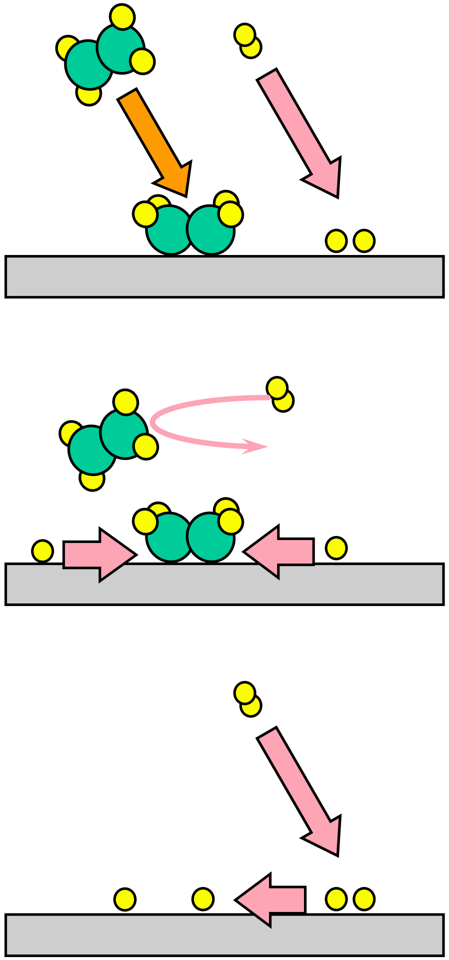
Critical Points:

- Fast formation of transition state or the state shows low energy.
- Fast adsorption of reagents, desorption of products, and slow desorption of reagent.

Heterogeneous Catalysis (2).

Energy, Entropy, and Steric Effects in heterogeneous catalysis:

- Entropy generally decreases because reagents are confined on the surface (a bad aspect for fast reactions).
- Steric effects are generally reduced by reagent organization on surface.
- Reaction energy barrier is generally reduced by catalytic surface. The set of states can be made essentially instantaneous.



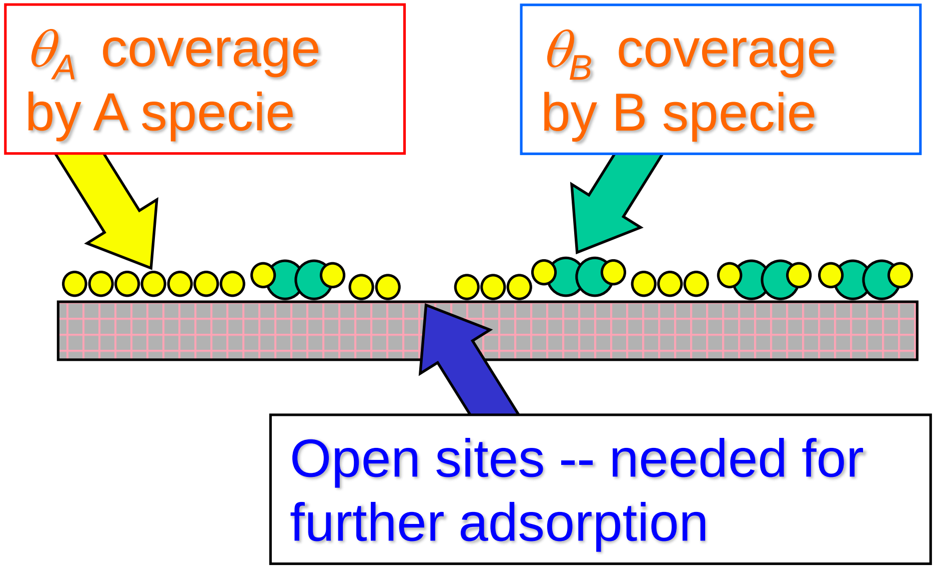
Heterogeneous Catalysis (3).

The reaction rate in an heterogeneous catalyzed process depends on density of adsorbed molecules.

$$r = k\cdot\theta_A\cdot\theta_B$$

r : rate, *k* : specific constant

- Faster for $\theta_A = \theta_B$.
- The best catalyst adsorbs reagents more strongly.
- Reagents should not be grouped together for an optimal reactivity at high coverage.



θ_A coverage by A specie

θ_B coverage by B specie

Open sites -- needed for further adsorption

$$\left[\frac{mol}{\min\ \ g_{catalyst}}\right] \qquad \left[\frac{mol}{\min\ \ m^2_{catalyst\ surface}}\right]$$

Turn Over Frequency.

low site density　　high site density

- Rate with respect to number of active sites

Turnover frequency is the number of molecules formed per active site per second (in a stage of saturation with reactant, i.e. a zero order reaction with respect to the reactant)

$$\textbf{TOF} = \left[\frac{molecules}{site \cdot s}\right] = \left[s^{-1}\right]$$

TOF, TON, Catalysis.

- TON

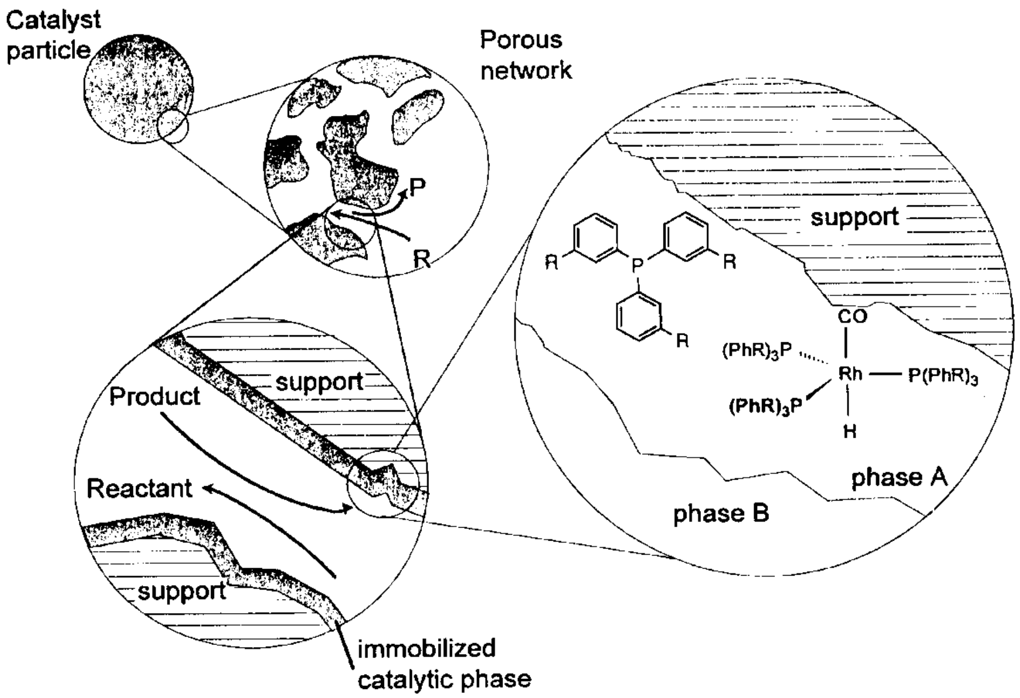
  Total number of product formed molecules per active site

  TON = TOF × catalyst life time

  - TON = 1 stoichiometric reaction
  - TON $\geq 10^2$ catalytic reaction
  - TON = 10^6-10^7 industrial application

Reaction	Substrate	TOF Molecule/site·sec	Relative TOF
Cracking	**Hexane**	**0.0469**	**1**
	Nonane	**0.150**	**3.2**
	Dodecane	**1.07**	**23**
Isomerization	**m-Xilene**	**10.6**	**226**
Poyimerization	**Propylene**	**40.7**	**868**
Cracking	**1-Hexene**	**36.7**	**782**
	1-Heptene	**56.7**	**1209**
skeletral Isomeriz.	**1-Hexene**	**$>5x10^3$**	**$> 1x10^5$**
Double-bond shift	**1-Hexene**	**$4.7x10^4$**	**$1x10^6$**

Immobilization via Supported Liquids.



Schematic of a supported liquid phase catalyst.

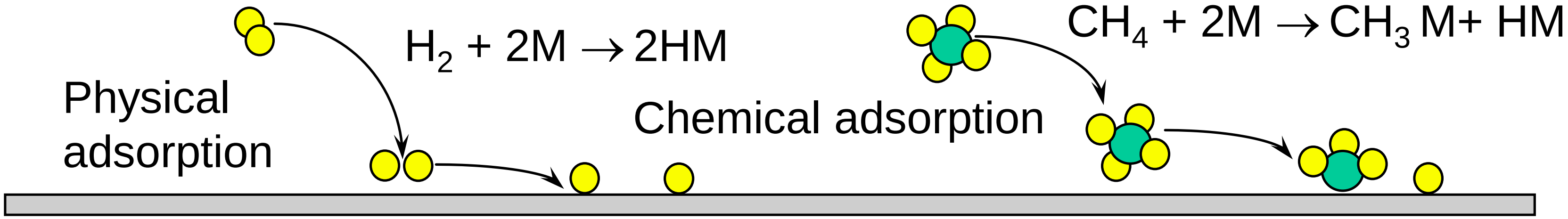
The liquid or water absorbed on the porous support forms a film on the inner surface of the support.

SLPC: phase A: nonvolatile organic solvent (R = H); phase B is a gas phase (light olefins and CO/H_2).

SAPC: phase A is water (R = SO_3Na); phase B is an organic liquid (higher olefin).

Chemtech, 2 (1992) ACS

Heterogeneous Catalysis – (gas adsorption).

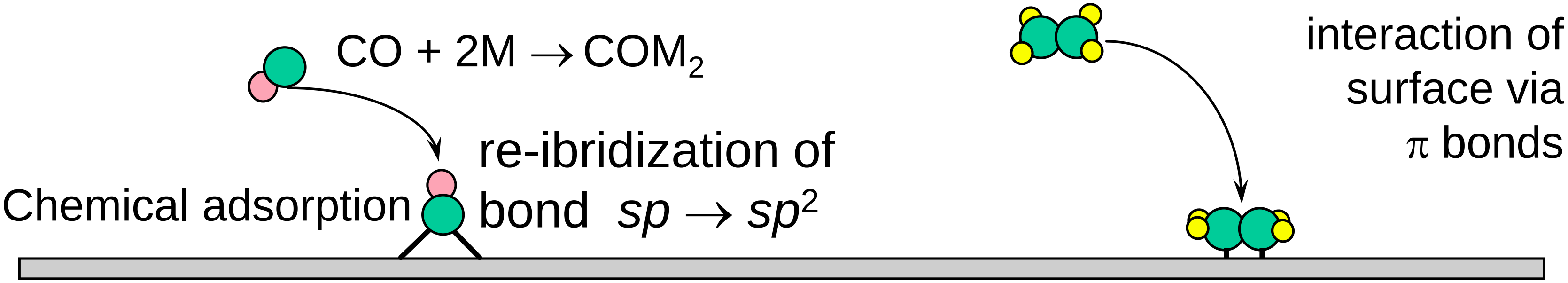


$H_2 + 2M \rightarrow 2HM$

Physical adsorption

$CH_4 + 2M \rightarrow CH_3M + HM$

Chemical adsorption



$CO + 2M \rightarrow COM_2$

Chemical adsorption

re-ibridization of bond $sp \rightarrow sp^2$

interaction of surface via π bonds

Heterogeneous Catalysis –
(gas adsorption) (2).

- Dissociative Chemisorption
  - Increase the reactivity and decrease the reaction activation energy by violent separation of reagent molecules.
- Associative Chemisorption
  - Increase the reactivity and decrease the reaction activation energy favoring the re-ibridization of bonds following the reaction requirements.

Heterogeneous Catalysis in Reactions.

- **Catalysts of oxidation**: must not be oxidizable. Therefore most oxides and metal salts in high oxidation state catalyze well several oxidation processes.
- **Catalysts of reduction** (hydrogenation): must not be reducible by hydrogen and other reducing agents. Metals are good catalysts for reactions with H_2.
- **Catalysts of dehydrogenation**: good are some insulating oxides (i.e.: Al_2O_3).
- **Catalysts of isomerization**: oxides of acid nature with high surface area (internal pores and channels – zeolites, clays)
- **Catalysts of polymerization**: quite good are several types of acids.

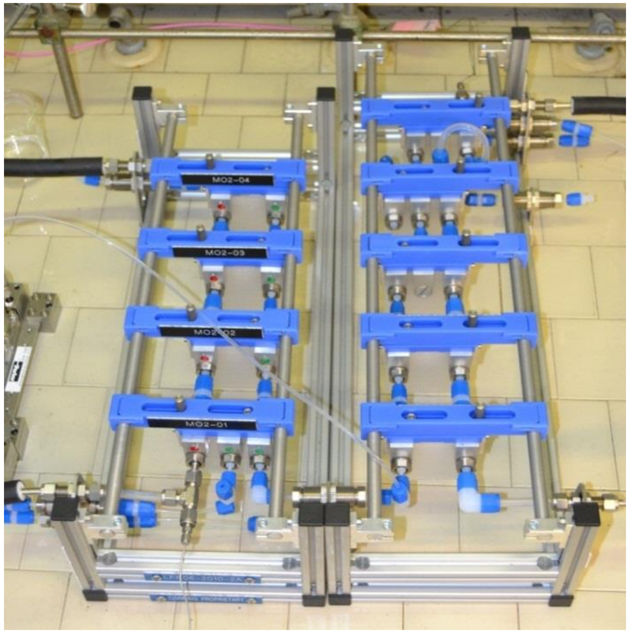
Catalysis and Metal Nature.

The ability of some metal centers to adsorb gases controls their catalytic activity – the higher is the adsorption, more effective is the catalysis:

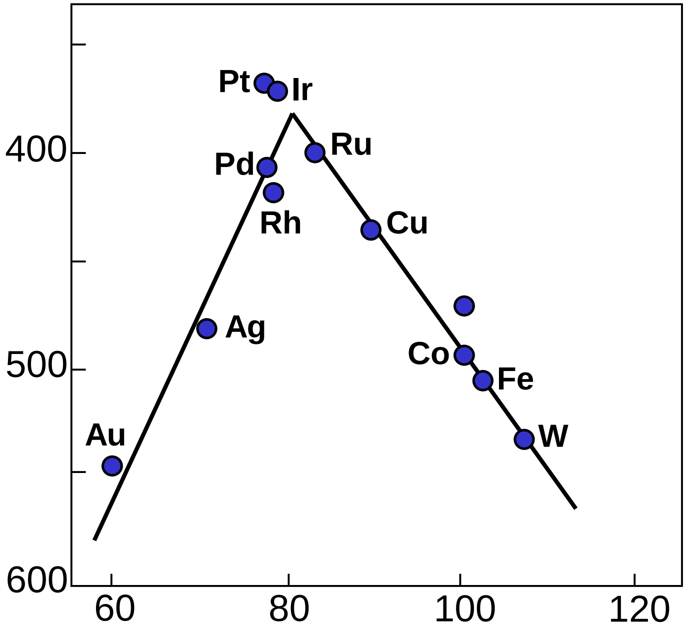
Catalyst Group	Metal	O_2	C_2H_2	C_2H_4	CO	H_2	CO_2	N_2
A	**Ti, Zr, HF, V, Nb, Ta, Cr, Mo, W, Fe, Ru, Os**	+	+	+	+	+	+	+
B_1	**Ni, Co**	+	+	+	+	+	+	-
B_2	**Rh, Pd, Pt, Ir**	+	+	+	+	+	-	-
B_3	**Mn, Cu**	+	+	+	+	±	-	-
C	**Al, Au**	+	+	+	+	-	-	-
D	**Li, Na, K**	+	+	-	-	-	-	-
E	**Mg, Ag, Zn, Cd, In, Si, Ge, Sn, Pb, As, Sb, Bi**	+	-	-	-	-	-	-

Strategies in the Use of Catalysts

- Auto segregation from reaction medium;
- Heterogeneization of homogeneous catalysts;
- Nano-structured catalytic materials;
- Biocatalysis and biotransformation;
- Catalytic technologies :
  - Fluid bed reactors
  - Membrane reactors
  - Catalytic bed spinning reactors
  - Micro reactors.

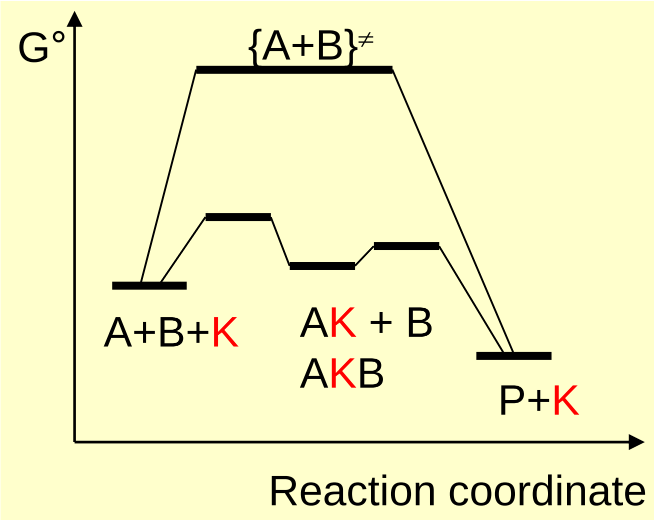


Catalysis and the Sabatier Principle.



Sabatier's principle: volcano curves Tv/K. The temperature at which the rate of decomposition of formic acid (vertical axis) has a set value v, correlated with the heat of formation of the bulk metallic formate, in kcal per equivalent (horizontal axis).

- ❖ Catalyst must have affinity for reactant,
- ❖ .... but not too much!



Homogeneous vs. Heterogeneous Catalysis.

Homogeneous Catalyst

- ☑ High activity & selectivity
- ☑ Wide variety of reactions (enantio-selective)
- ☑ Active site clearly defined and well characterized (number of atoms <, = molecules or clusters)
- ☑ Efficient heat transfer

- ☒ Toxic, corrosive
- ☒ Contamination by reaction products
- ☒ Cumbersome separation (distillation, etc.) → recyclability <<<
- ☒ Mainly batch processes

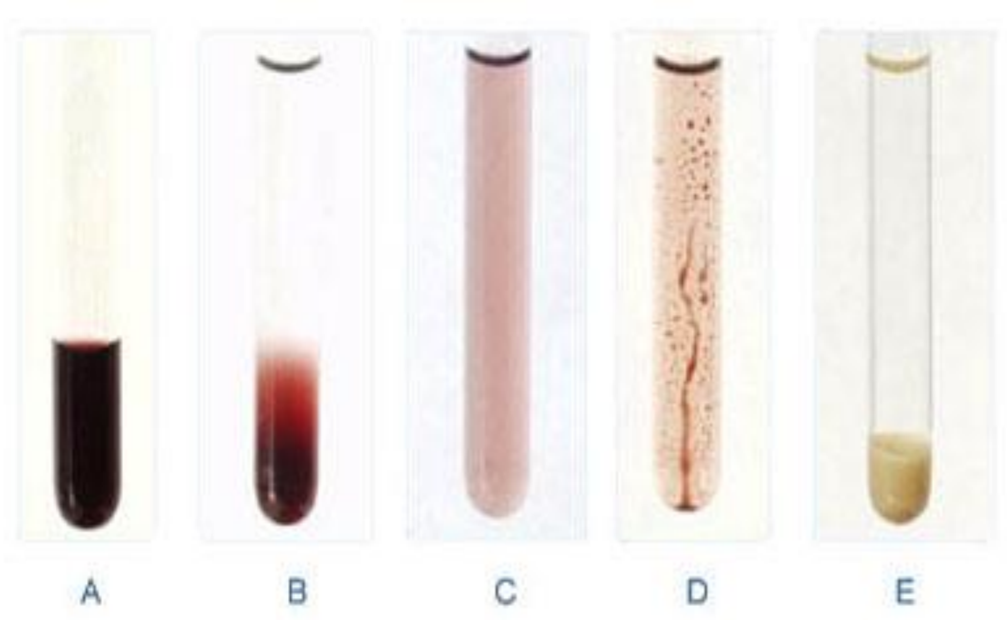
Heterogeneous Catalyst

- ☑ Facile separation
- ☑ → Reusable - recyclables
- ☑ Confined use
- ☑ → Less toxic and not corrosive
- ☑ Less wastes
- ☑ Continuous processing
- ☑ Several type of reactors

- ☒ Applications more limited (in fine chemicals) (enantio-selectivity <)
- ☒ Generally less active and/or selective
- ☒ Can contain a large variety of active sites (difficult to characterize/quantify)

Auto Separation of Catalyst.

A careful design allows to auto-separate products using physic/chemical intrinsic properties i.e. solubility, volatility, etc.



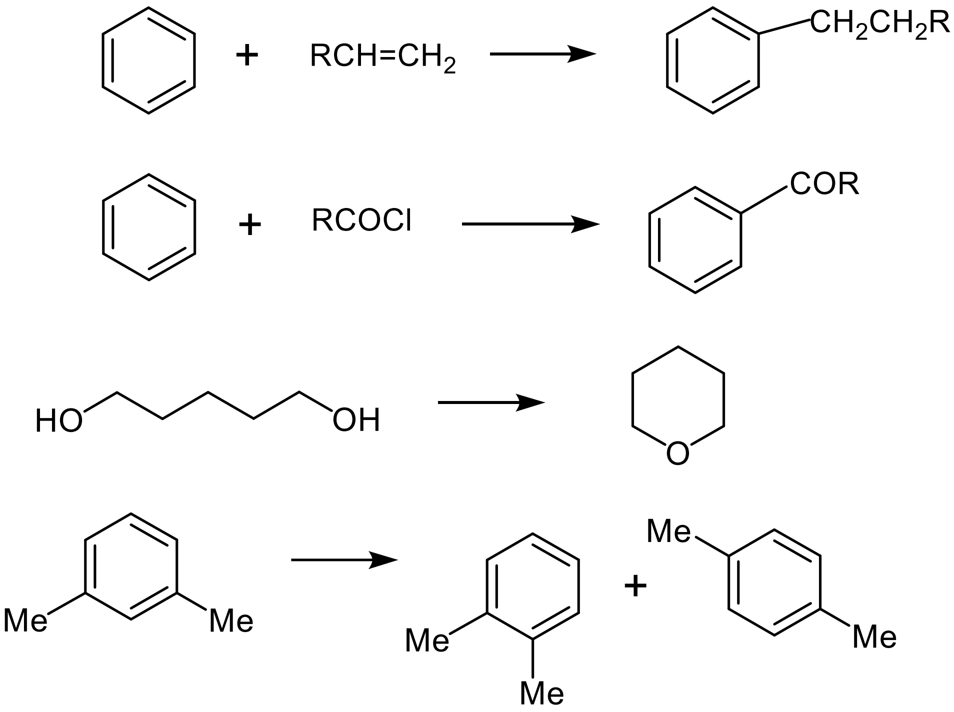
The catalyst is soluble in one of reagents and remains soluble when the other reagent is added. In the course of the reaction, and product accumulate, the catalyst separate from the mixture as oil. This clathrate oil—liquid—retains the catalytic activity, because reagents can penetrate inside. When all reagents are transformed into products, the catalytic oil become again a sticky solid, which can be easily separated and recycled.

Dioumaev, VK, and RM Bullock. July 31, 2003. *Nature* 424(6948):530-531

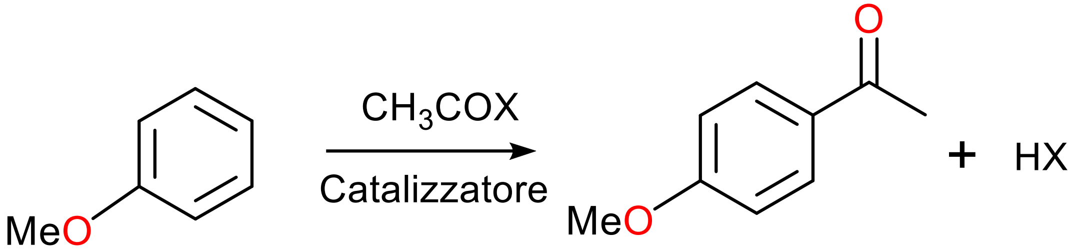
Acid-Catalyzed Reactions.

- Widely used type of catalysis
- Can be applied to all sectors of chemical industry, pharmaceutical and similar.
- Largely based on inexpensive Brönsted and Lewis Acids

  - H_2SO - HF - $AlCl_3$ - BF_3
- Continuous processes of larger scale in gas phase are moving towards solid acids
- A quite variable chemistry.



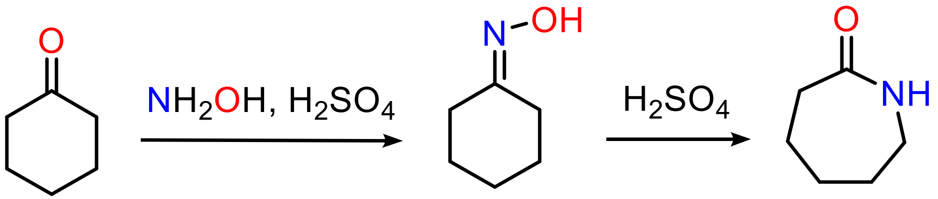
Aromatic Acylation by Various Catalysts.



	$AlCl_3$	H-beta	$H_3PW_6Mo_6O$	$Yb(OTf)_3$
X	Cl	OAc	Cl	OAc
Solvent	CS_2	-	-	CH_3NO_2
S/C (g/g)	0.7	2.9	2.6	8.5
Productivity	0.26	25	7	0.4
Yield by Volume (g/l)	47	162	51	17
STY (g/l/day)	560	648	303	22
E factor (g/g)	3	0.4	0.24	0.43
Atomic Efficiency (%)	25	71	80	71
Byproducts	$AlCl_3.nH_2O$ HCl	HOAc	HCl	HOAc

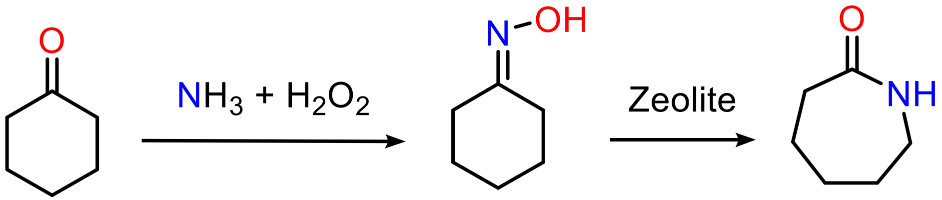
Synthetic Routes to Caprolactam
(intermediate of nylon-6).

Traditional



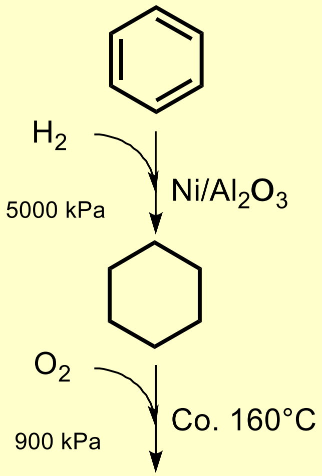
- relevant waste of $(NH_4)_2SO_4$
- E = 8 (kg waste for kg of product)

Improved (use of environmentally compatible catalysts)



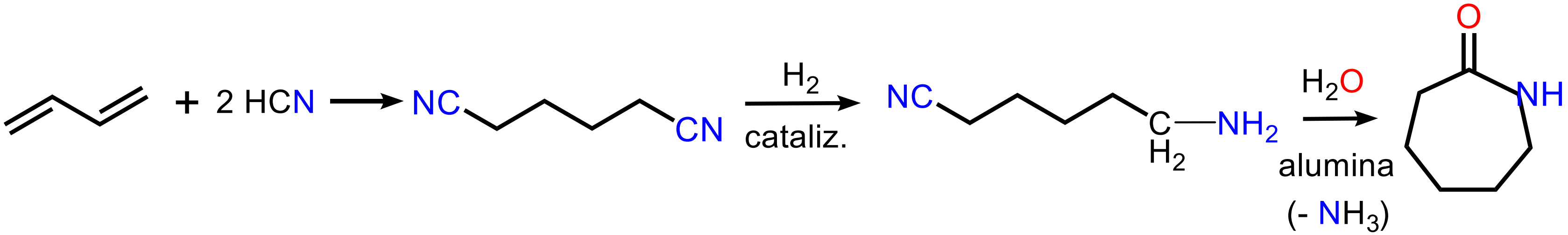
- minimal waste (water)
- without salts
- E = 0.32

Du Pont Process



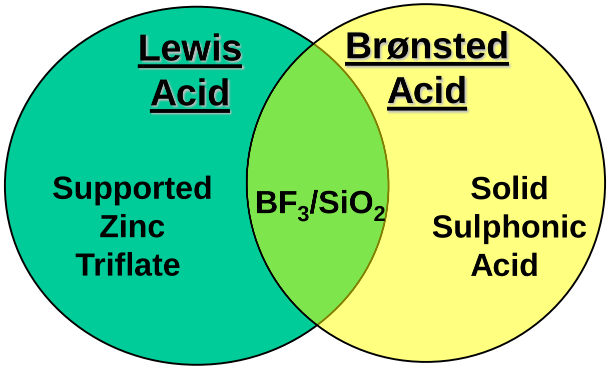
Further Route to Caprolactam.

New process (alternative starting material):

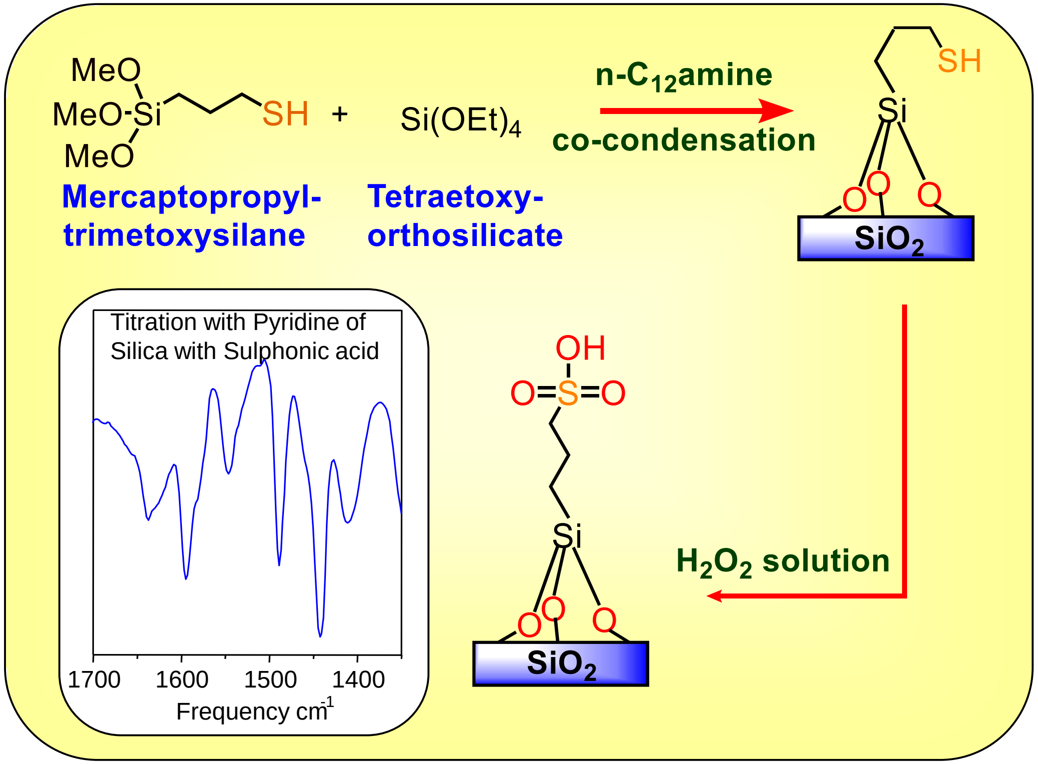


- **Minimal waste**
- **Does not use the harmful raw material benzene (via cyclohexane/cyclohexanone)**
- **Without salts**
- **E = 0.13**

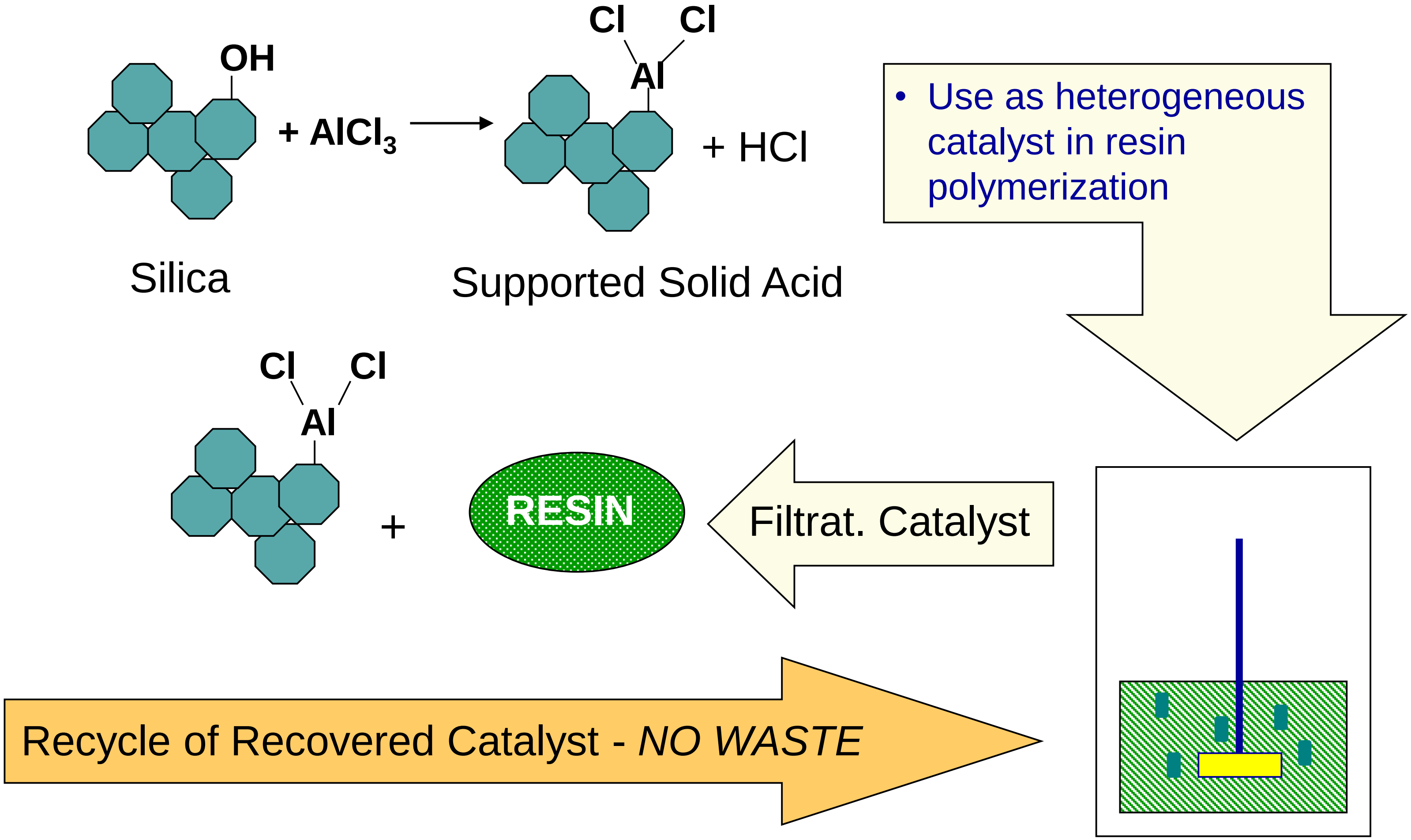
Heterogeneization of Acid Catalysts.



Preparation of Sulphonic Acid



Heterogeneous Acid Catalysts for Polymer Synthesis.



Silica

Supported Solid Acid

- Use as heterogeneous catalyst in resin polymerization

Filtrat. Catalyst

Recycle of Recovered Catalyst - *NO WASTE*

Strength of Representative Solid Acids.

$AH + B \rightleftarrows BH^+ + A^-$

$H^0 = pK_a + \log[B]/[BH^+]$

Hammett acidity constant

Solid acids	$H^{0(a)}$	$-\Delta H_{ads}$ (NH_3)/kJ mol^{-1}
$H_3PW_{12}O_{40}$	-13.16	195
$Cs_{2.5}H_{0.5}PW_{12}O_{40}$	-13.16	-
SO_4^{2-}/ZrO_2	-14.52	165-150
H-ZMS-5	-12.70	145
SiO_2-Al_2O_3	-12.70	
Nafion®	ca. -12	

Homogeneous Acids	CF_3SO_3H	-14.1
	H_2SO_4 c.	-12.0

Industrial Applications of Solid Acid-Base Catalysts.

- 127 industrial processes use solid acid-base catalysts
  - Mainly in the production of bulk/petrochemicals, i.e. dehydration, condensation, alkylation and etherification
- 180 different catalysts used
  - 74 of them are zeolites, with ZSM-5 the main group
  - The second wider group is represented by Al / Si / Ti and Zr oxides

Product	**Company**	**Catalyst**
Cumene	Mobil, Enichem	Zeolite
LABs	UOP	Zeolite
Cyclohexanol	Asahi	H-ZMS-5
Vinylbicycloheptene	Sumitomo	Na/alumina
Ethyleneimine	Nippon Shokubai	Si/Ba/Cs/P/O

* Review : K Tanabe & W F Holderich, Applied Cat. A 1999, 181, 399

Origin of Zeolite Acidity.

Acid Catalysis:

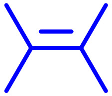
$$A + H^+ \rightarrow AH^+$$

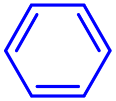
$$AH^+ + B \rightarrow ABH^+$$

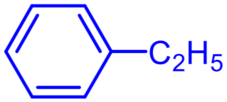
$$ABH^+ \rightarrow AB + H^+$$

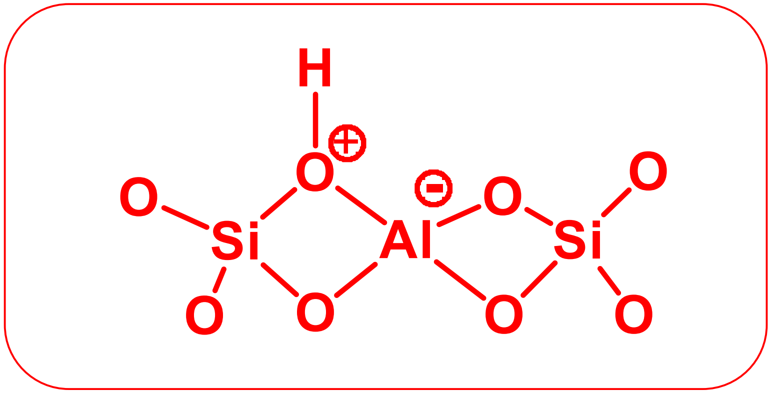
$$A + B \rightarrow AB$$

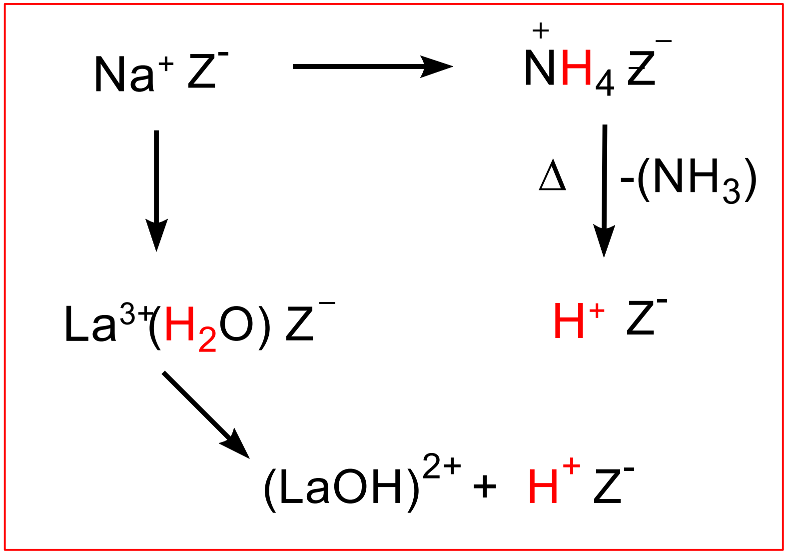
For example:

A is 

B is 

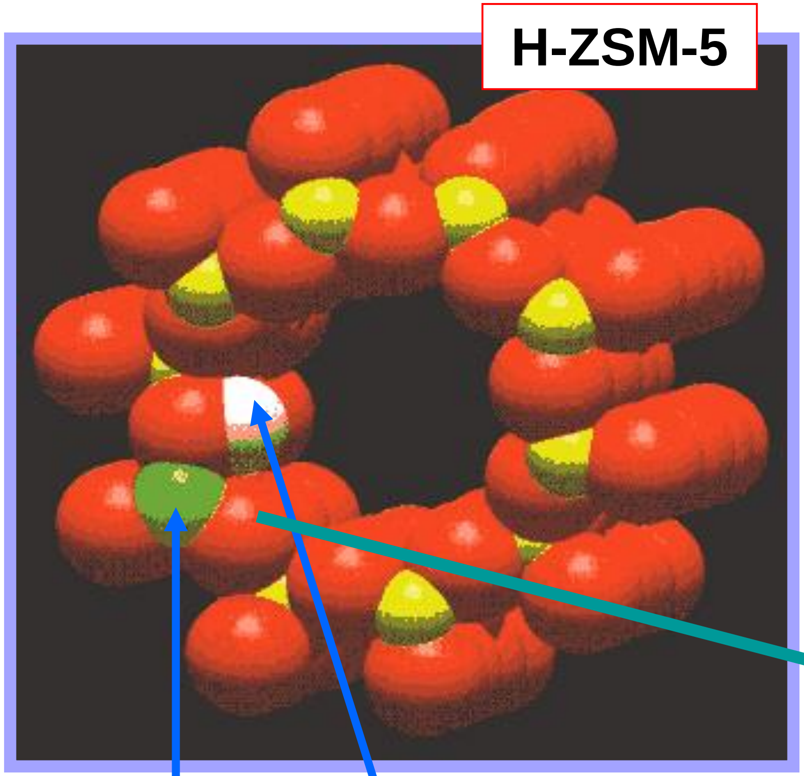
AB is 





$$\begin{tikzcd} Na^+ Z^- \arrow[r] \arrow[d] & \overset{+}{N}H_4 Z^- \arrow[d, "\Delta"', "-(NH_3)"] \\ La^{3+}(H_2O) Z^- \arrow[dr] & H^+ Z^- \\ & (LaOH)^{2+} + H^+ Z^- \end{tikzcd}$$

Structure/Acid Strength Relationship.

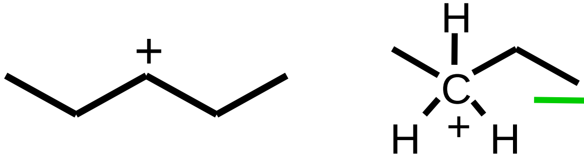


Proton affinity :

$H\text{-}Z \rightleftarrows H^+ + Z^-$

$H\text{-}Z + B \rightleftarrows HB^+ + Z^-$

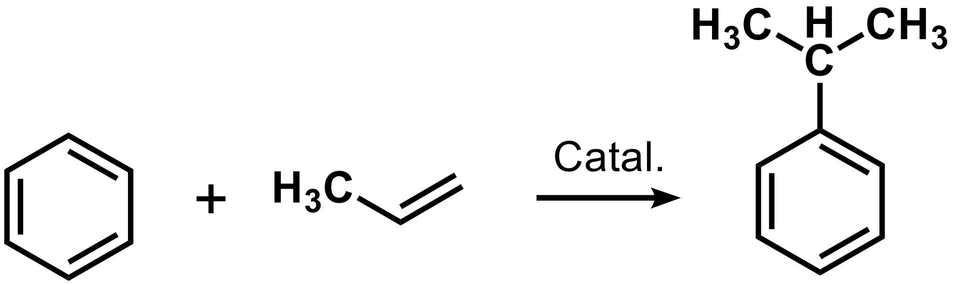
HB^+: carbenium ion, carbonium ion



Solvation of HB^+

Monomolecular conversion of alkane intermediates

Catalysis in Cumene Process.



- Important until 1950 for phenol production
- Initial process use $AlCl_3$ or H_2SO_4
  - Relevant amount of acid wastes
- Huls developed the HF process
  - Greener but dangerous
- UOP Process in gas phase with H_3PO_4/ SiO_2 and BF_3
  - Good but quite corrosive
- Mobil Process with Zeolites
  - No acid waste, not-corrosive, yield close to 100%.

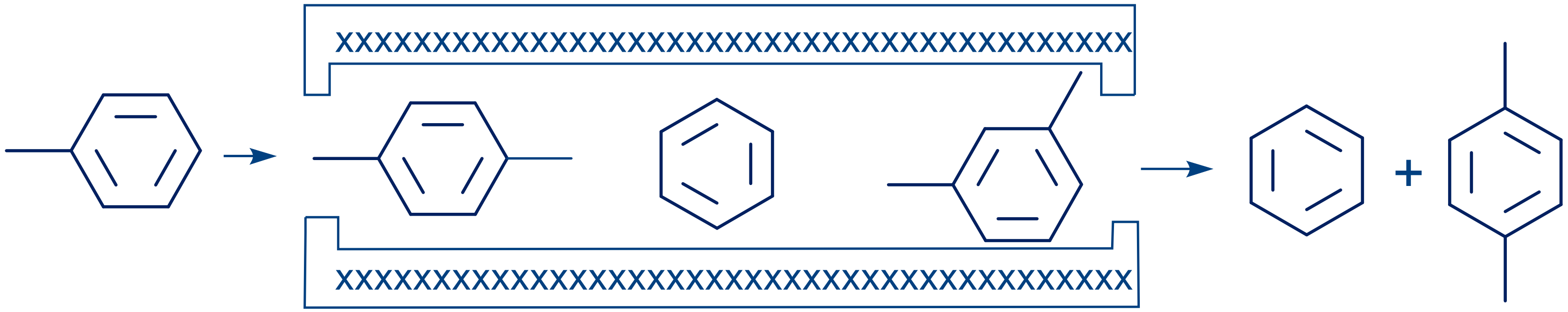
Synthesis of AlkylBenzenes.

$$\text{Benzene} + \text{Olefin} \xrightarrow{\text{Cat.}} \text{Alkylbenzene}$$

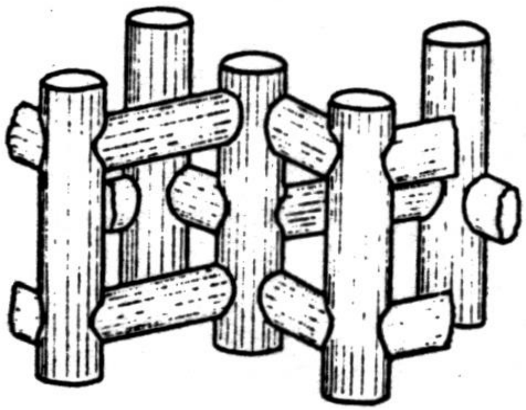
- These are converted in sulphonates to be used for cleaning
- Until the end of 1960 iso-$C_{12}H_{24}$ was used with H_3PO_4/ SiO_2
  - Low biodegradability owing to the branched structure and corrosive properties
- Linear hydrocarbons C_{10} - C_{12} were obtained with HF or $AlCl_3$
  - Biodegradability improved, but overall waste was increased
- UOP technology with zeolites becomes popular in 1980-90 years
- Several issues remain to be solved in the degradation
  - Compounds are not easy biodegraded and alcohol sulfates can be preferred or new bio-surfactants?

Catalysis with Zeolites (Shape selectivity).

Toluene disproportionation with HZSM-5

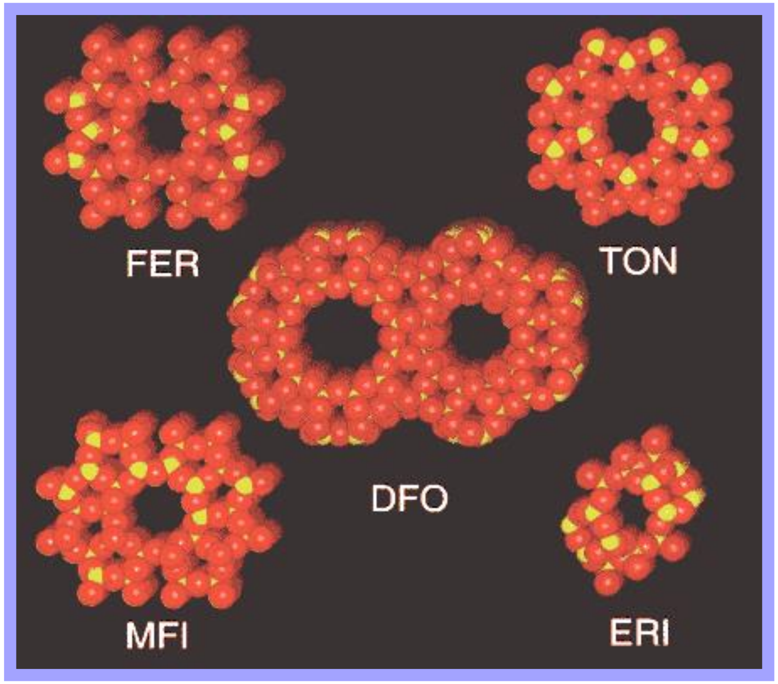


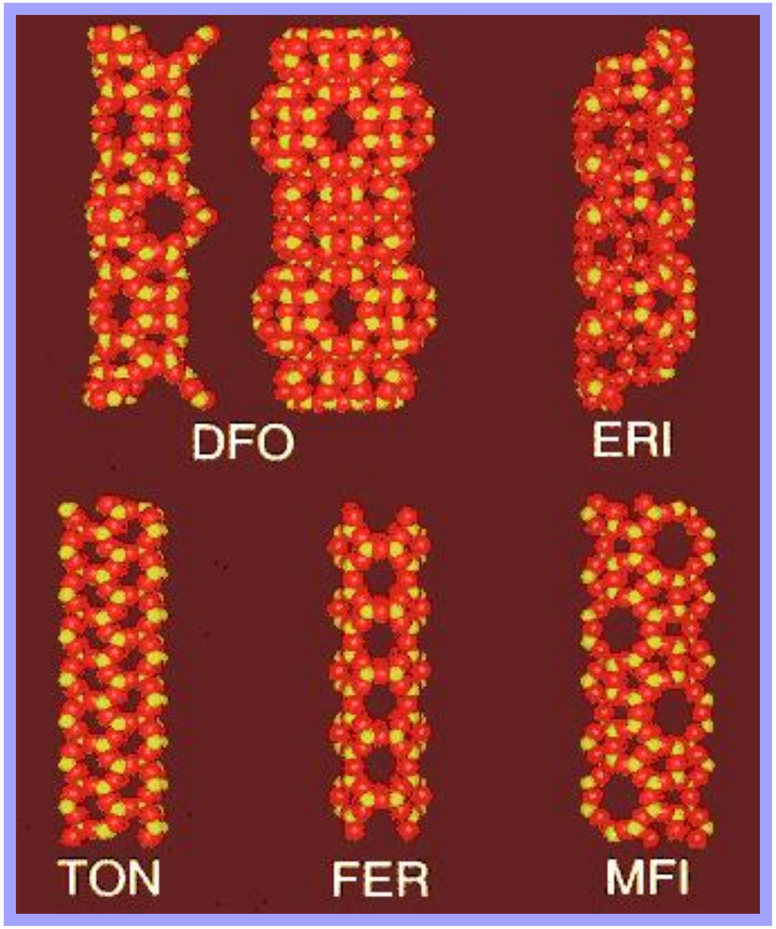
Shape selectivity allows to the only *p*-xylene to travel inside the channel of the material.



Channel structure Of ZMS-5

Zeolites – Tertiary Structure.

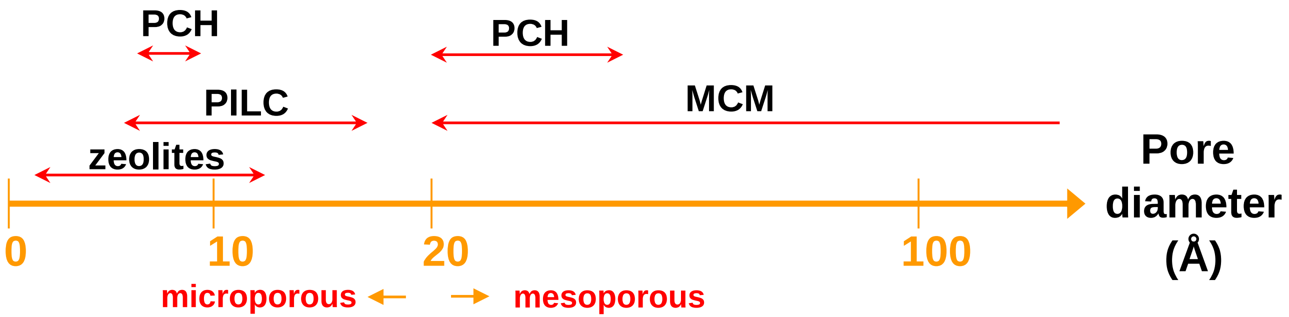




Porous Siliceous Materials.

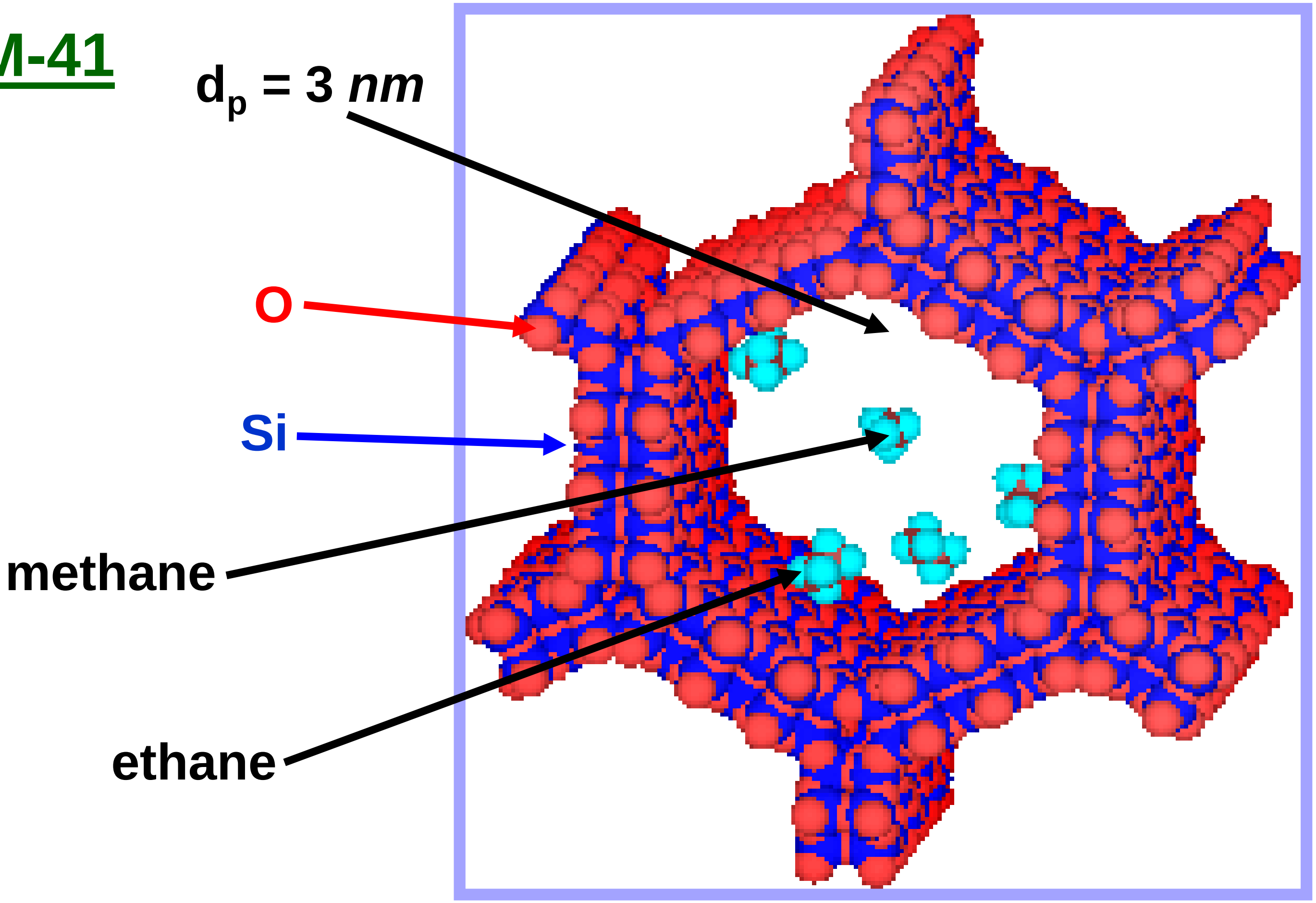
Historical Evolution

- 1756 - discovery of natural zeolites
- 1938 - synthetic zeolites (Prof. R.M. Barrer)
- 1950 - industrial interest (adsorption and catalysis)
  - pore size changed via controlled synthesis
- 1973 - oil crisis → need of materials with higher porosity ↗
- 1980 – first stable super microporous Pillared Clays (PILCs)
- 1992 – controlled mesoporous MCM (Mobil Oil Corporation)
- 1995 – controlled micro/mesoporous PCH (Michigan University)



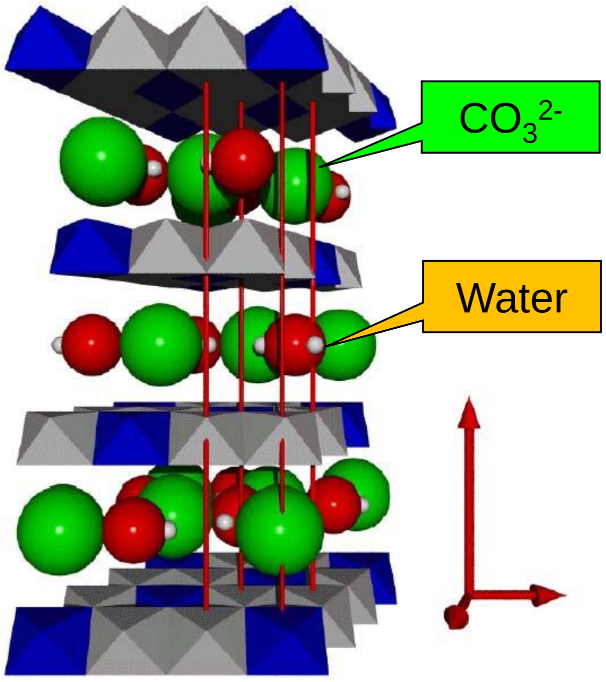
Mesoporous Materials.

MCM-41

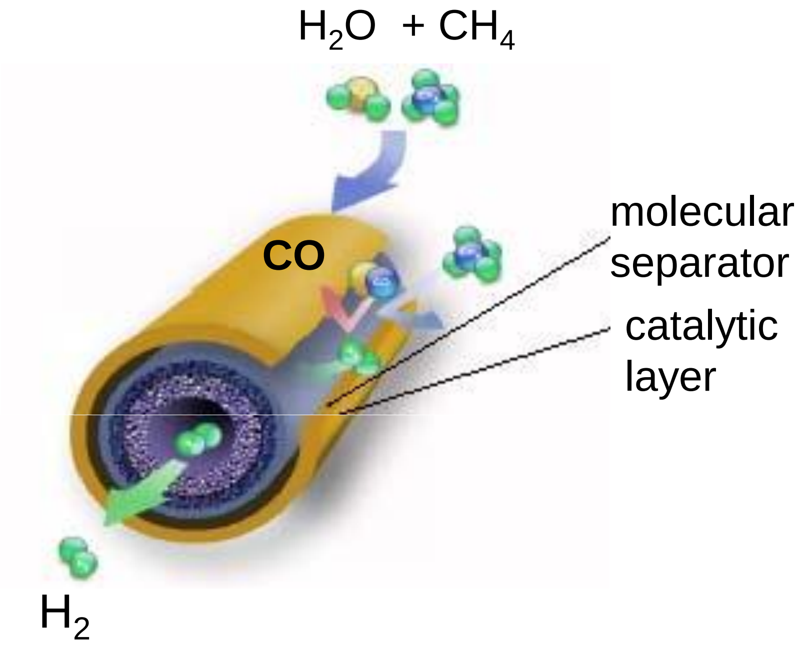


Heterogeneous Catalysis by Solid Bases.

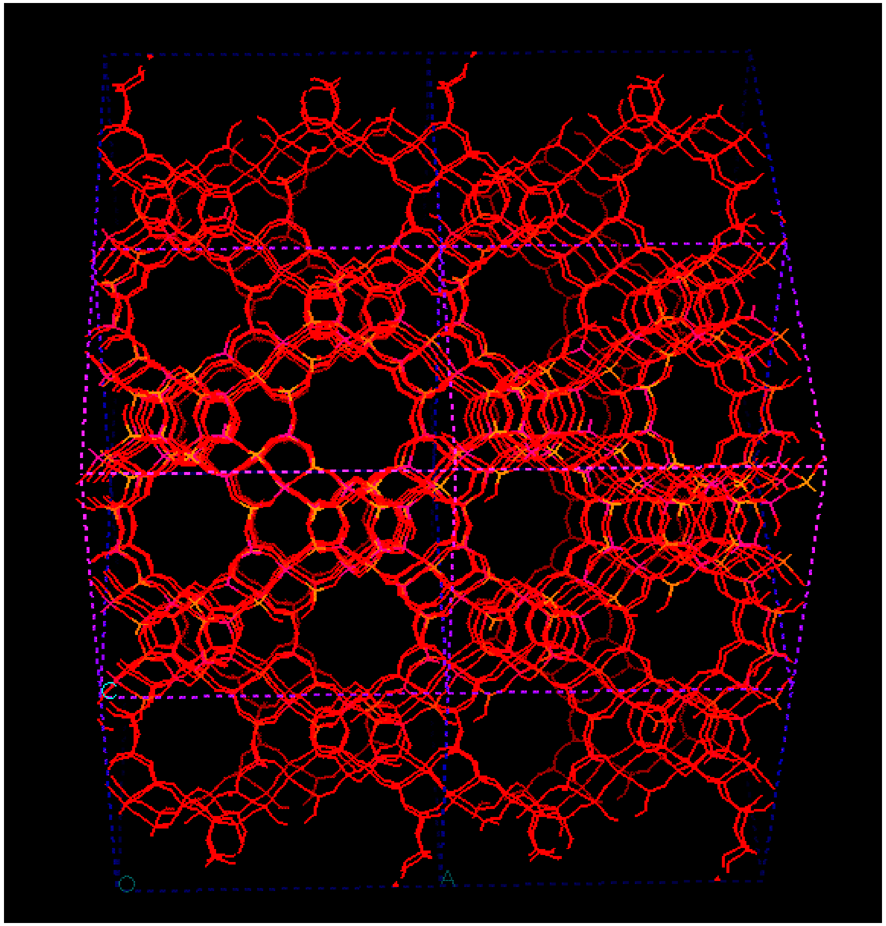
CO_2 membrane candidate: Hydrotalcite



Layered metal oxides (LDO)



Zeolites as Alternative to Classical Routes.



- Alumino-silicates
- 3D crystalline structure
- Uniform pore sizes
- Green applications in:
  - > Catalysis
  - > Water treatment
  - > Remediation
  - > Odor control

Redox Reactions and Oxidant Agents.

- **Dangerous …**
  - CrO_3 / H_2SO_4 (Jones)
  - $(py)_2 CrO_3$ (Collins)
  - $(pyH)+ClCrO_3^-$ (Corey)
  - $(CH_3)_2S$ / Cl_2
  - $(CH_3)_2SO$ / $(COCl)$
  - $Pb(OAc)_4$ /pyridine
- **Dirty …**
  - MnO_2
  - Ag_2CO_3
  - $Al(OiPr)_3$ / Me_2CO
- **Clean**
  - Titanium silicalite / H_2O_2

Stoichiometric vs. Catalytic Oxidations.

- **Traditional Method :**

i.e. $3PhCH(OH)CH_3 + 2CrO_3 + 3H_2SO_4 \rightarrow 3PhCOCH_3 + Cr_2(SO_4)_3 + 6H_2O$

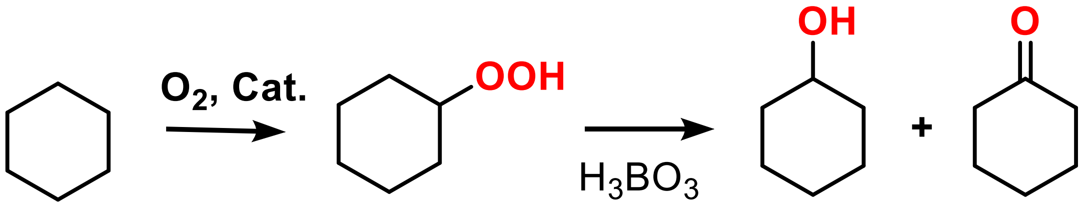
  - great amount of reagents consumed
  - hazardous conditions (toxic oxidant, toxic waste)
  - less than half of atoms in the process go into the desired product.

- **Green Method (catalytic):**

$$PhCH(OH)CH_3 + 1/2O_2 \rightarrow PhCOCH_3 + H_2O$$

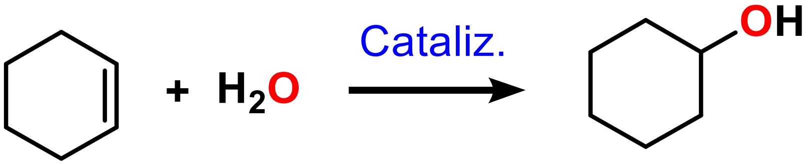
  - only oxygen (air) consumed
  - non-hazardous conditions (?)
  - environmentally benign waste
  - most atoms in the process go into the desired product.

Catalysis in the Cyclohexanol Production.

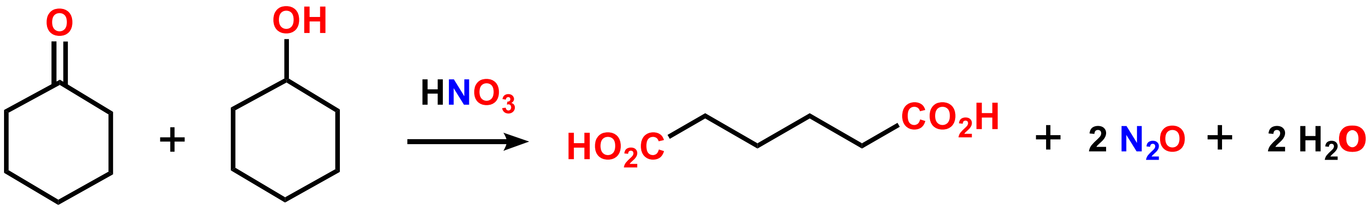


- Used in the production of adipic acid – nylon 6,6
- First stage: typical catalyst Co or Mn naphthenate
  - Catalyst not recovered
- Second stage carried out with boric acid
  - Again acid wastes

Asahi process overcomes these issues performing the hydration of cyclohexene with water on HZSM-5 - selectivity: 95%



Nitrous Oxide and Adipic Acid.



- N_2O is a greenhouse gas 200 times more powerful than CO_2
- It is also involved in the depletion of the stratospheric ozone layer
- Its atmospheric concentration is 310 ppb and increases 6% per year.
- Bifore1998, 10% of N_2O resulted from the adipic acid production.

Control Options

- $CH_4 + 4N_2O = 4N_2 + CO_2 + 2H_2O$
- $N_2O + 0.5O_2 = N_2 + O_2$
- $N_2O + 0.5O_2 = 2NO$ (Nitric acid)

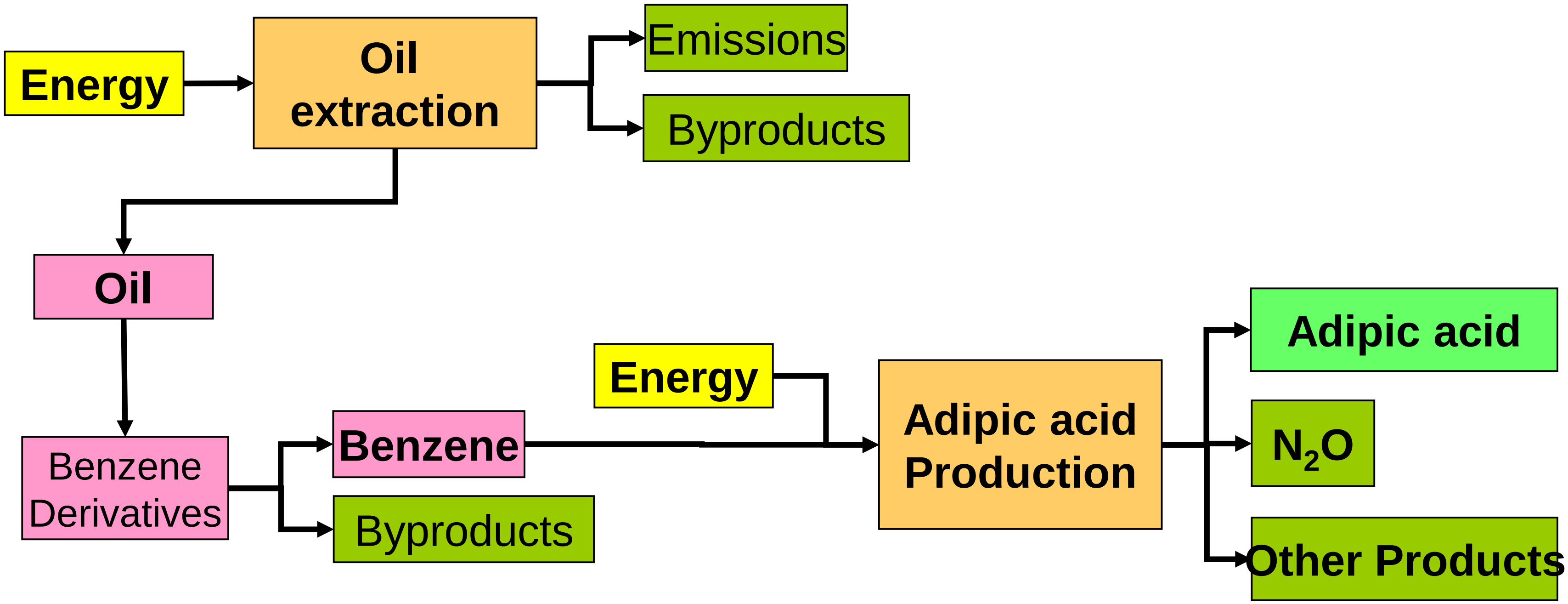
Long term option

glucose $\xrightarrow{\text{enzyme}}$ $HO_2CCH_2CH_2CH_2CH_2CO_2H$

$\xrightarrow{H_2\ Pt}$ Adipic acid

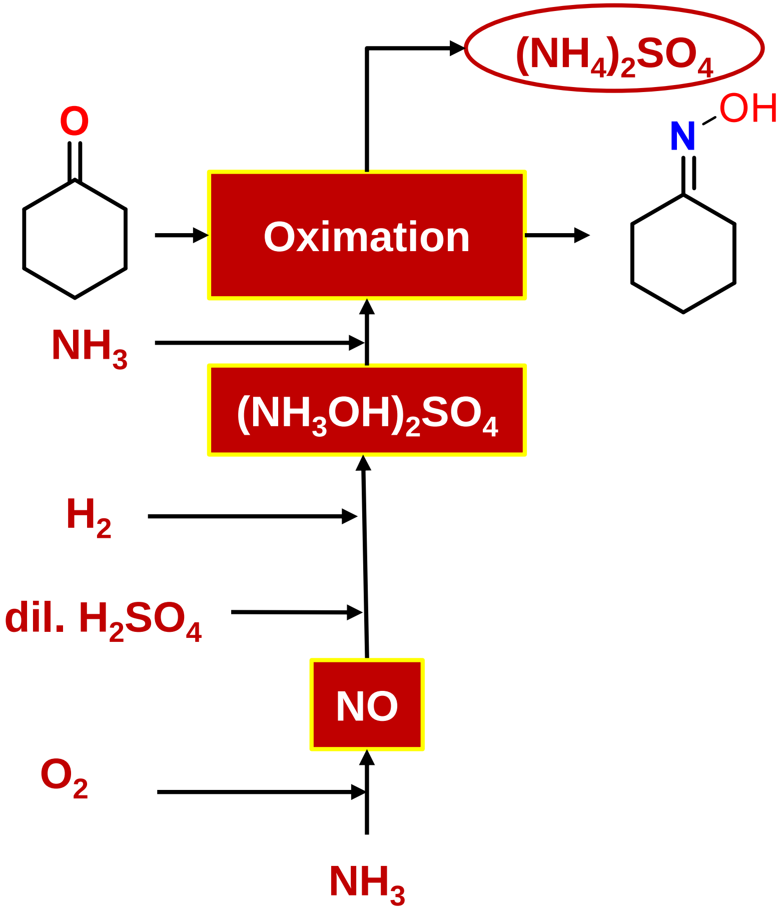
J W Frost & K M Draths, Chem. Br.1995, 31 206

Life Cycle of the Traditional Process of Adipic Acid Production.

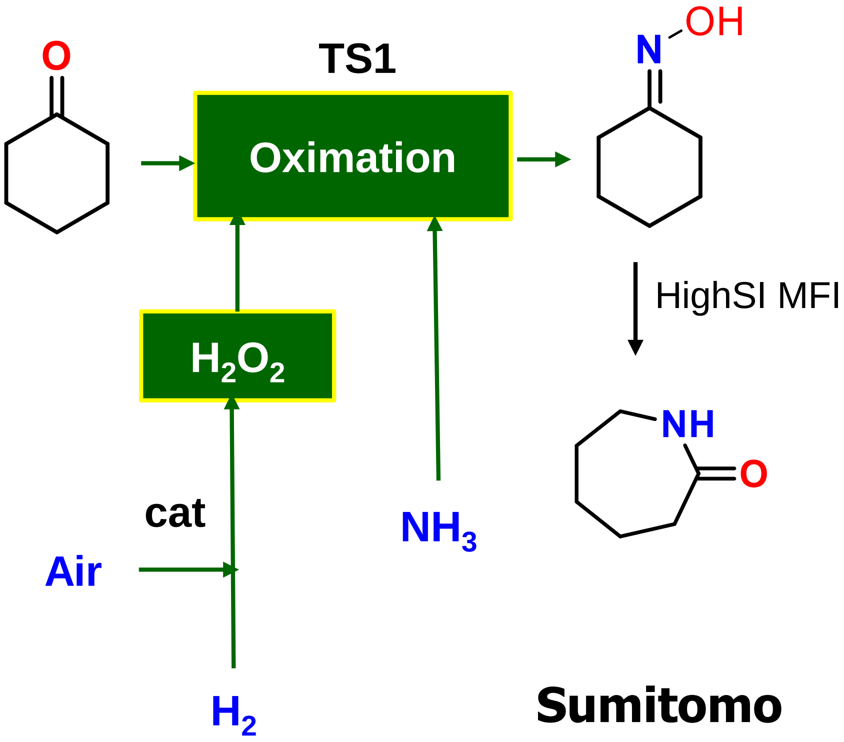


Cyclohexanone Oxime Manufacturing Process.

Current Process



Ammoximation Process

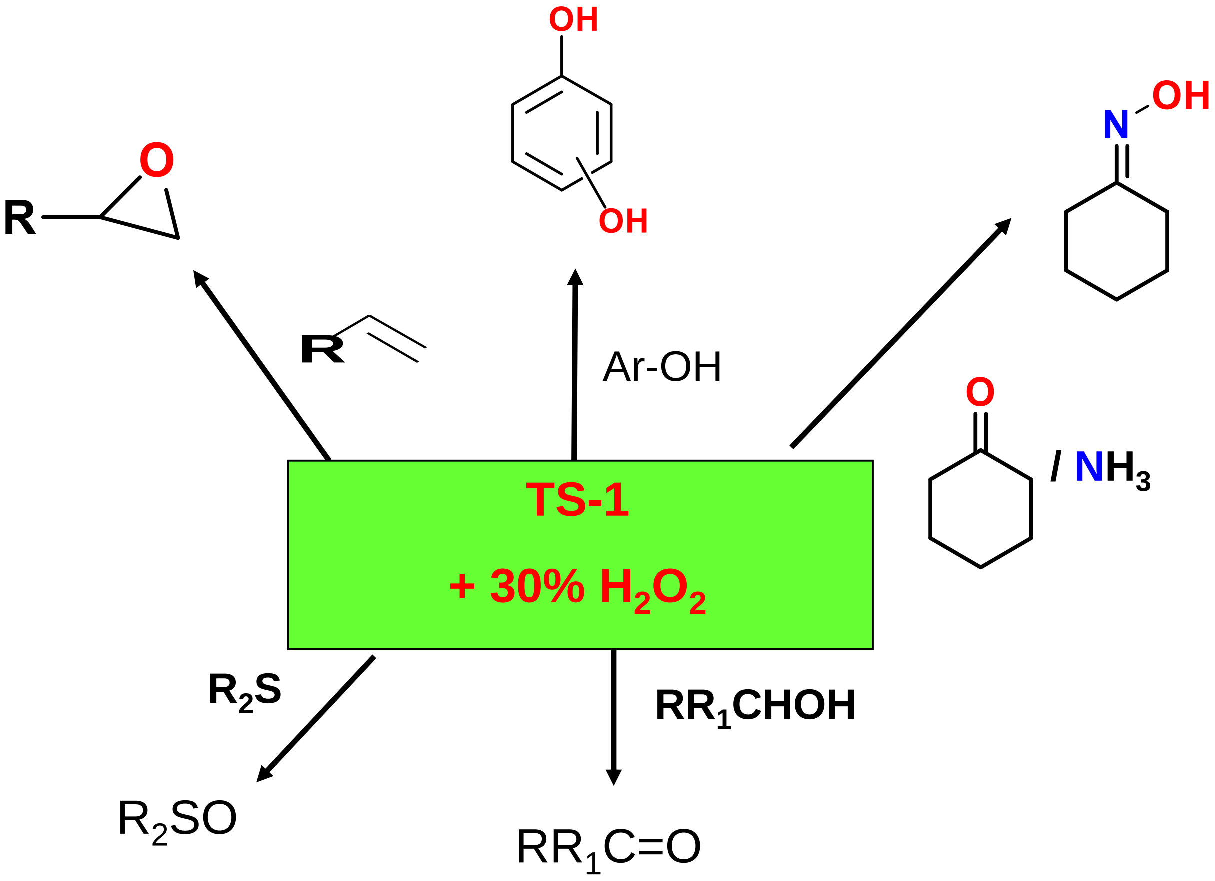


Sumitomo

Atom efficiency = 29% ; E = 4.5

Atom efficiency = 75% ; E = 0.32 (<0.1)

Oxidations Catalyzed by Titanium Silicalite.



TS-1

+ 30% H_2O_2

Ar-OH

/ NH_3

R_2S

R_2SO

RR_1CHOH

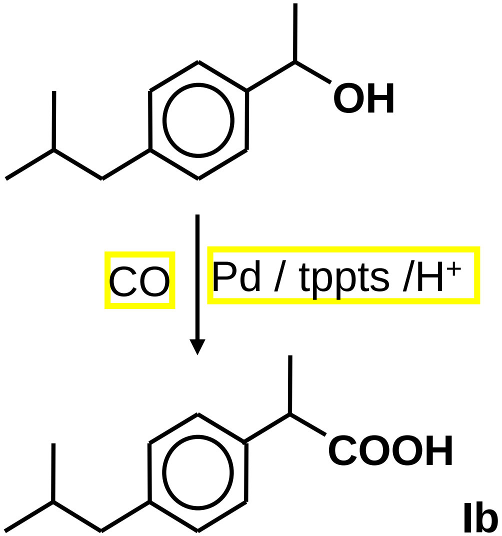
$RR_1C=O$

1983 – discovered ENIChem

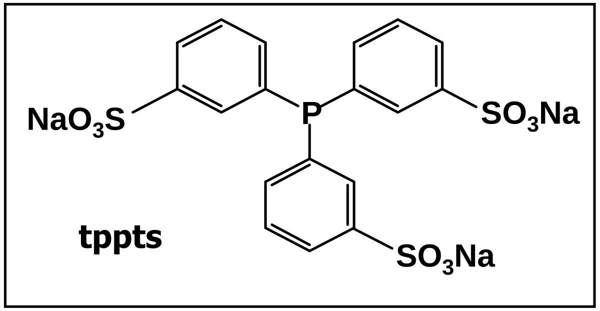
(B. Notari, *Stud. Surf. Sci. Catal*., 1988, **37**, 413)

Aqueous Biphasic Catalysis.

1. Carbonylation



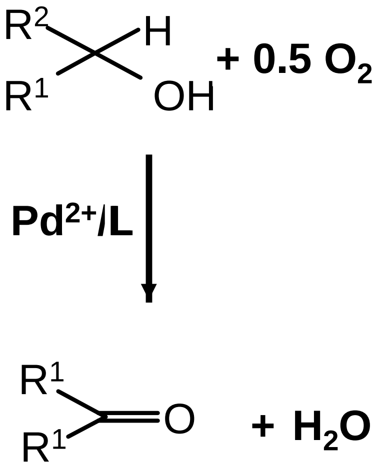
Ibuprofen

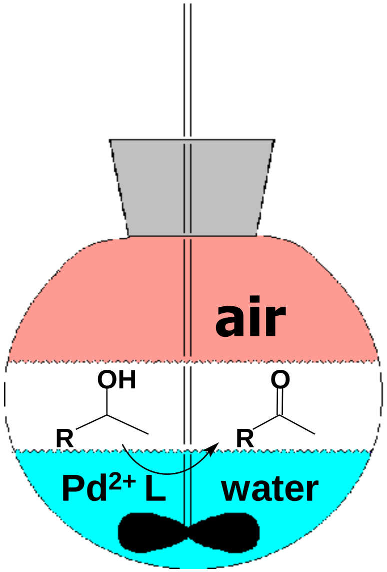


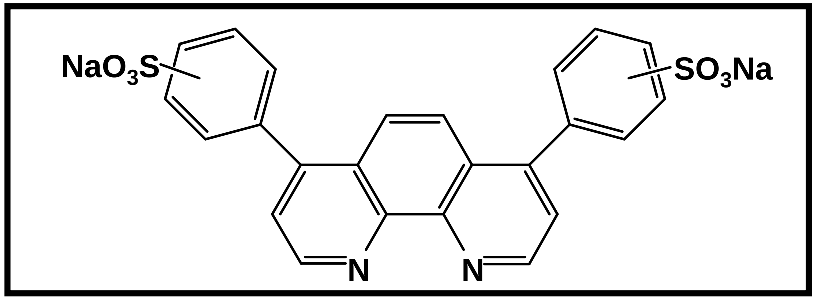
tppts

Papadogianakis, Verspui (2001)

2. Aerobic Oxidation





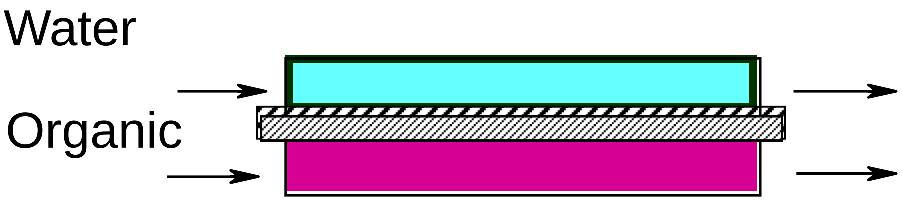


Moiseev

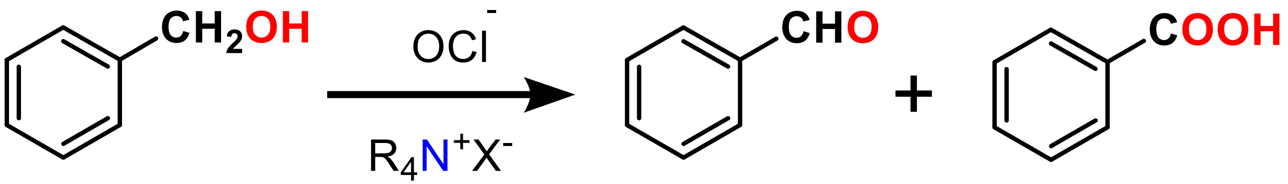
ten Brink (2001)

Membrane Reactor: Selective Oxidation of Benzyl Alcohol.

Membrane reactor:

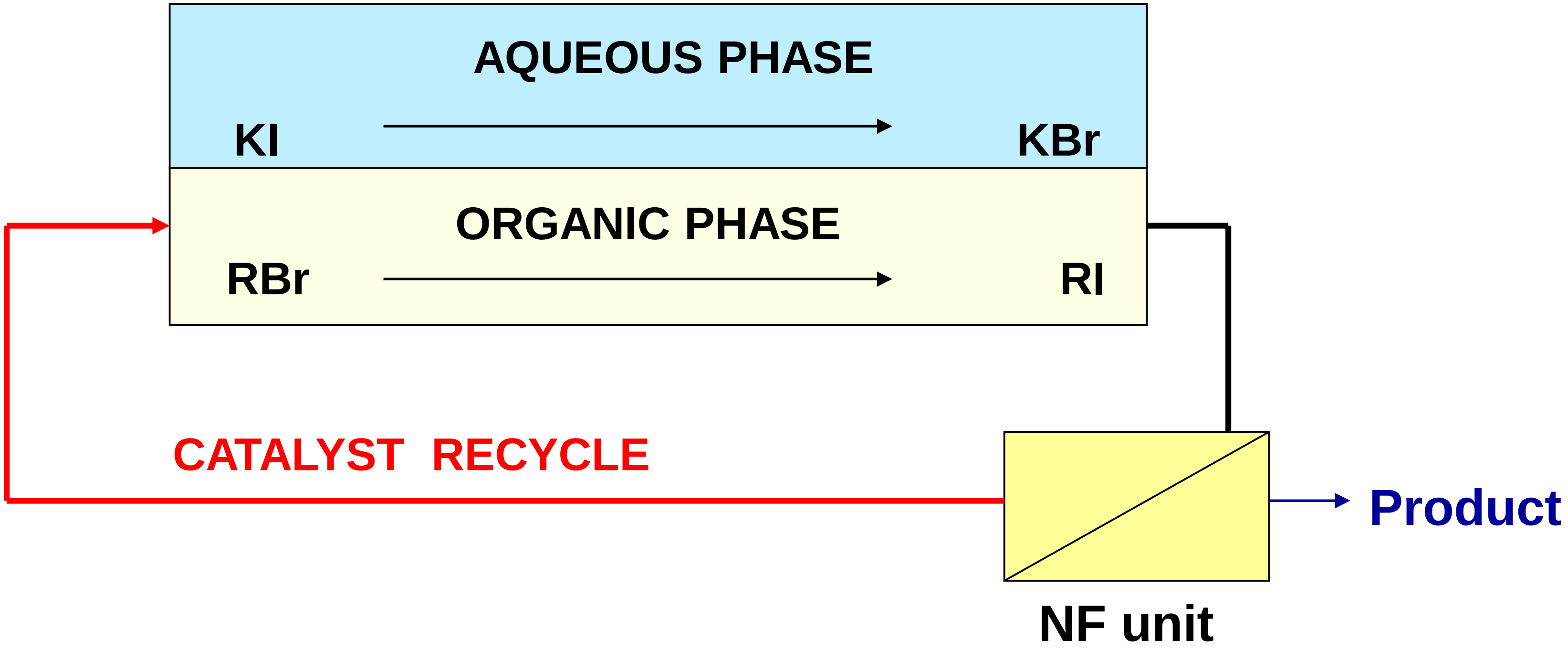


Catalyzed Oxidation via phase transfer (PCT)



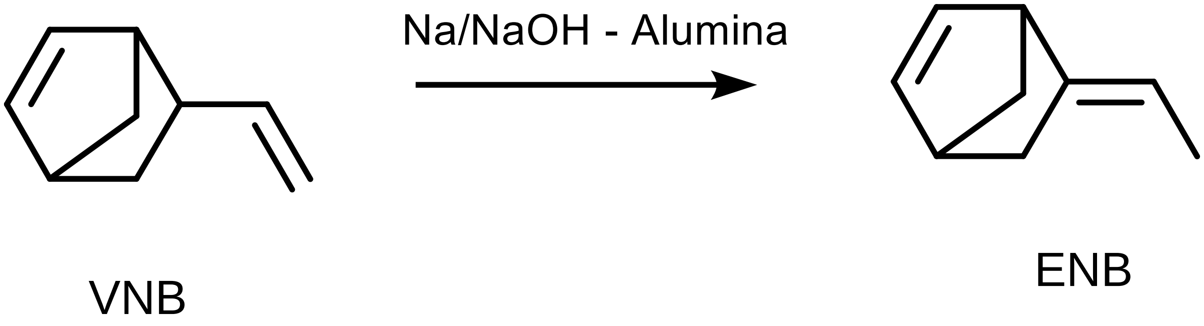
- Different kinetic for alcohol to aldehyde and for aldehyde to acid.
- Under optimal flow conditions a selectivity of 100% in aldehyde can be reached.

Phase Transfer Catalysis – Systems with Nanofiltration.



Luthra et al, Chem. Commun., 2001, 1468

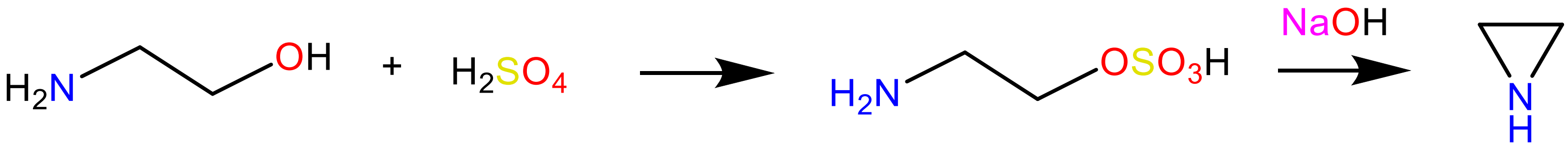
Solid Base Catalyzed Isomerization.



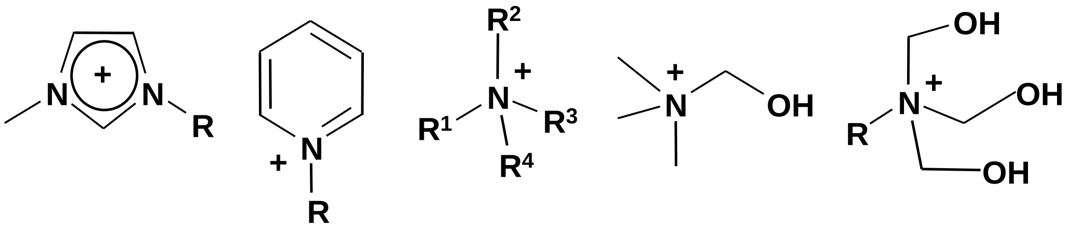
- Industrial processes catalyzed by solid bases are relatively rare
- Sumitomo developed a process to convert VNB into ENB
- This process removes the use of Na/K in liquid ammonia
- ENB is used as key component in EPDM rubber.

Acid-Base Catalysis / Ethyleneimine.

- Used as intermediate for drugs
- Conventional production generates 4 ton. of sodium sulfate per 1 ton. of ethyleneimine
- Nippon Shokubai process cleanly combines the two stages using a Si/Ba/Cs/P oxide solid catalyst.
  - Selectivity: 81% at conversion: 86%

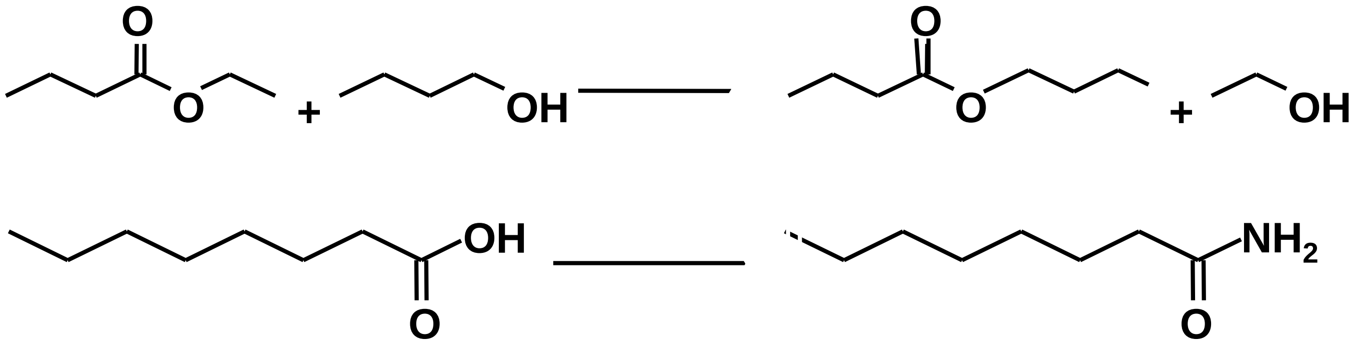


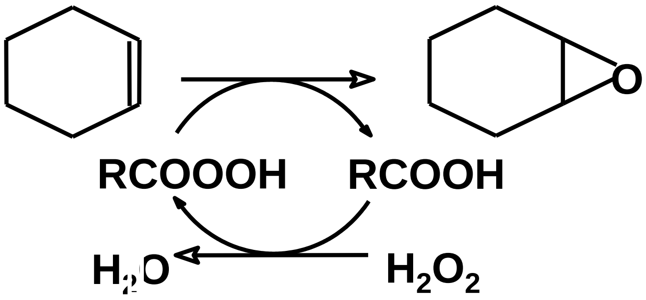
Catalysis in Ionic Liquids.



Anions : BF_4, PF_6 , RCO_2 , H_2PO_4 , NO_3 , $HOCH_2CO_2$

- Negligible vapor pressure
- Designer solvents
- Catalytic hydroformylation, carbonylation, hydrogenation and biocatalysis



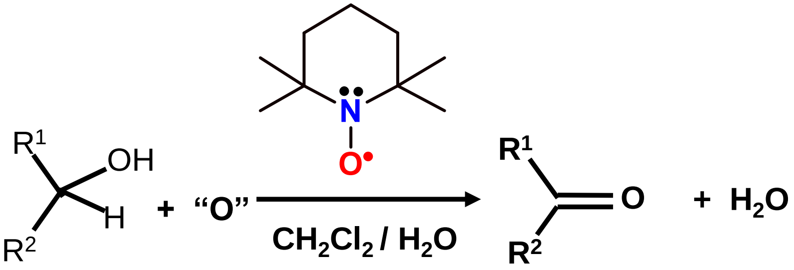


CaLB in [bmim][BF_4] and [bmim][PF_6]

Madeira Lau (2003) Seddon

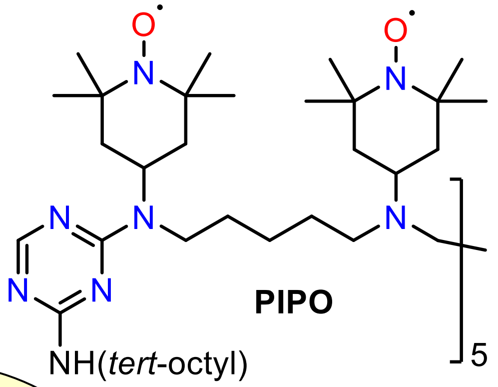
Product recovery?

Organocatalytic Oxidations.



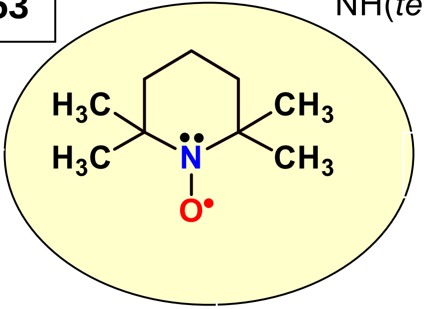
"O" = NaOCl, m-CPBA, oxone (+ Br$^-$)

van Bekkum et al , Synthesis, 1996, 1153



- No solvent
- No Br$^-$
- NaOCl
- Recyclable
- Cheap raw material

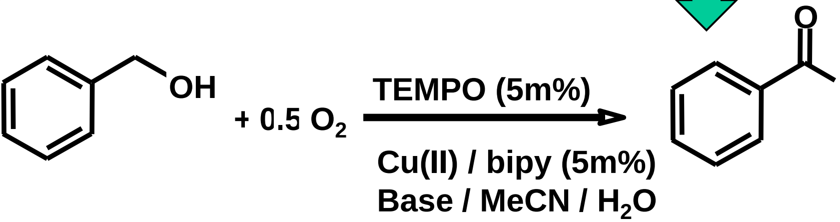
Chimassorb 944



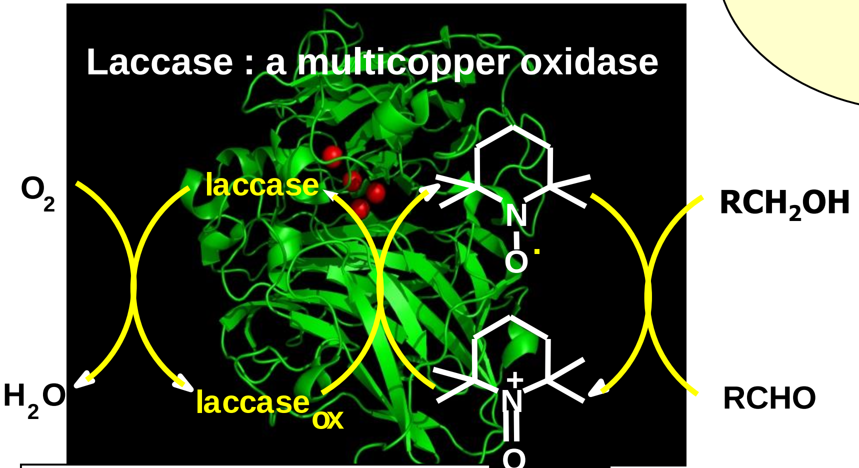
PIPO

Dijksman (2001)

Cu(II) / PIPO / O$_2$



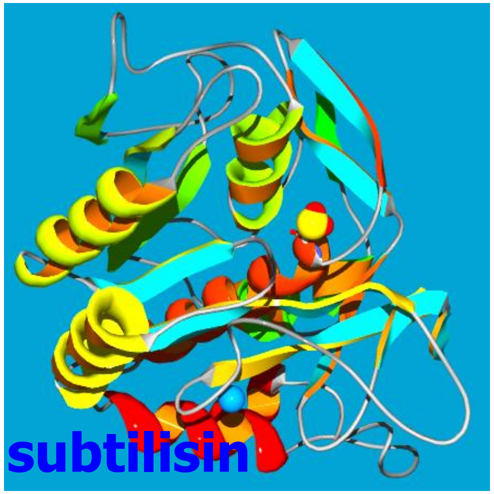
Gamez

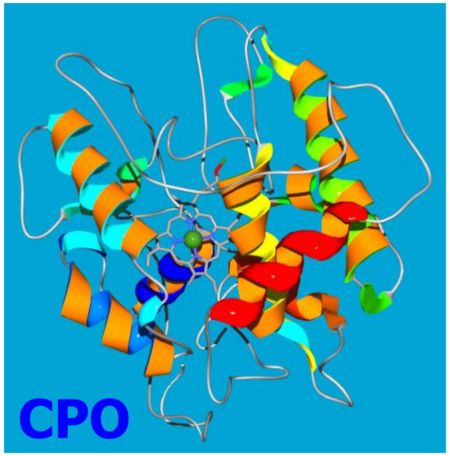


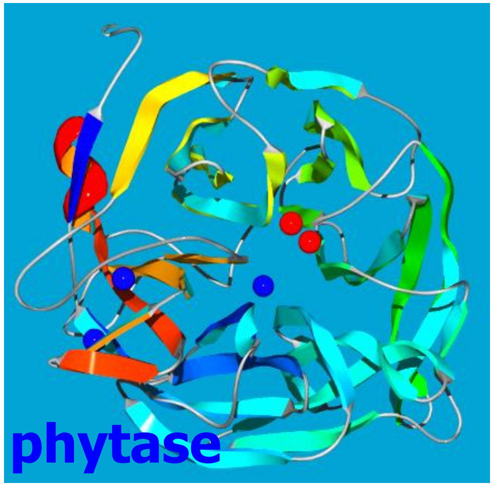
Li (2004), Matijosyte

de Vries/Hagen

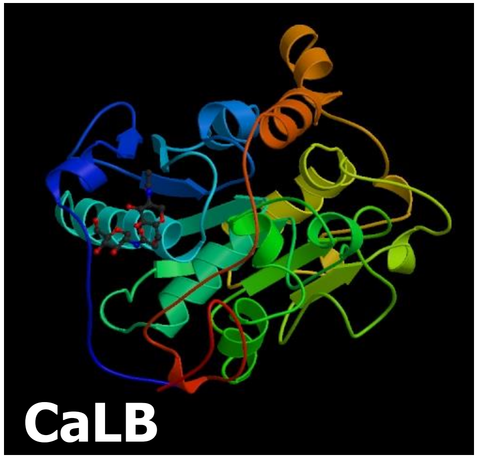
Biocatalysis.

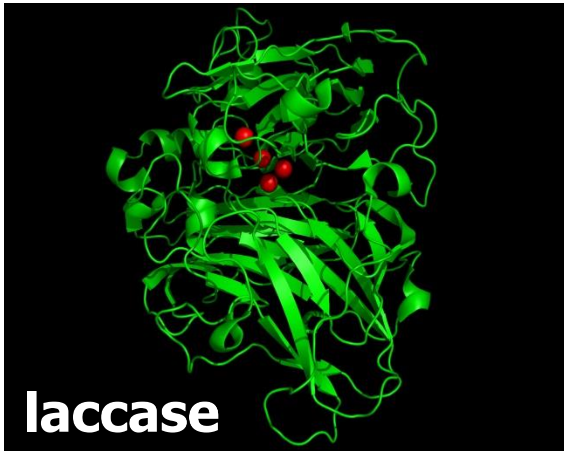


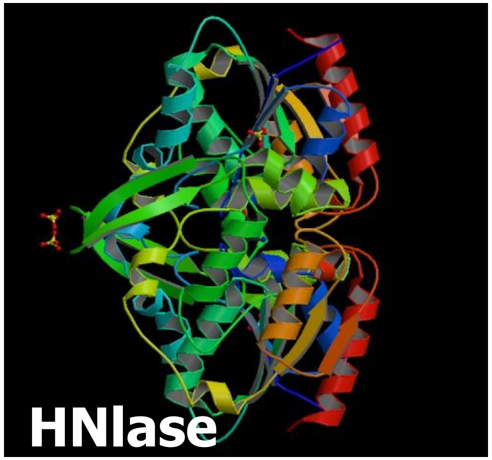




Inventing New Enzymes & Enzymatic Reactions

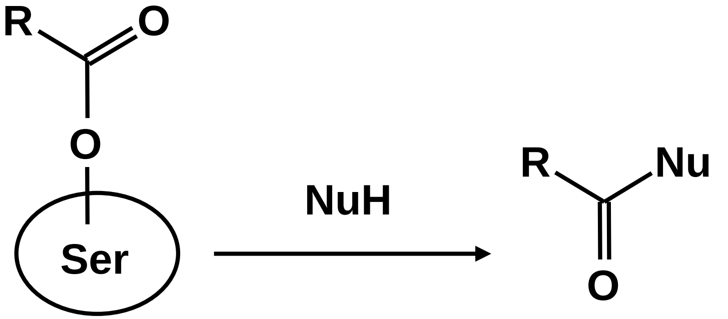




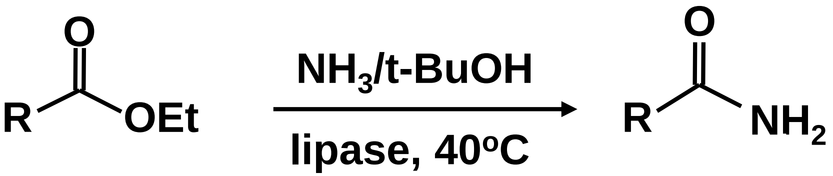


Applications of Biocatalysis.

Enzymatic Ammonolysis



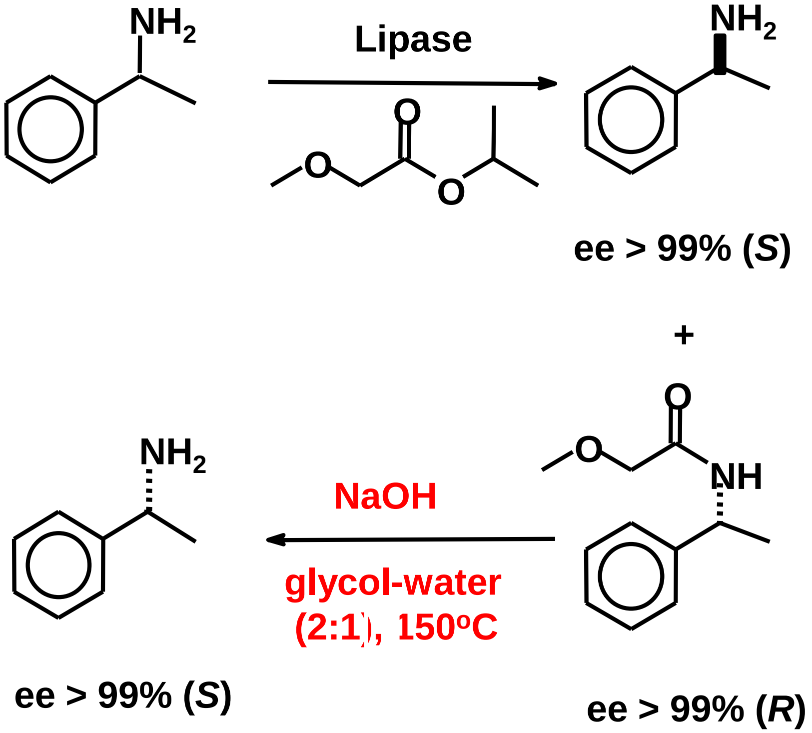
Nu = OH, OR, NH_2 , RNH, OOH, etc.



- Green amide synthesis
- Enantioselective with amino acid esters

Steverink(1995), Hacking (1999)
Wegman(2001)

BASF Process



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References on Catalysis.

- Hagen, J. Industrial Catalysis: A Practical Approach, Wiley (2015)
- Schmal, M. Heterogeneous Catalysis and its Industrial Applications, Springer 2016.
- K. V. Raghavan, B. M. Reddy (Ed.) Industrial Catalysis and Separations: Innovations for Process Intensification, CRC press 2014.
- Crawley, M. L.; Trost B. M. (Ed.) Applications of Transition Metal Catalysis in Drug Discovery and Development: An Industrial Perspective, Wiley, 2012.
- Viswanathan, B., et al. (2002). Catalysis: Principles and Applications, Narosa Publishing House.
- Kirk-Othmer (1992) Encyclopedia of Chemical Technology, J. Wiley, New York. (\bi. 5, 324: .. Homogeneous Catalysis ").
- Davies, S.C. (1982) Organotransition Metal Application to Organic Synthesis, Pergamon Press.
- Kochi, J.K. (1978) Organometallic Mechanisms und Catalysis, Academic Press, London.