Programme

- Introduction
- Carbonylation of olefins to aldehydes, etc.
- Oxidation of ethylene to acetaldehyde (Wacker Process)
- Hydrolysis of nitriles to carboxamides
- Oxidation of ketones to esters or lactones (Baeyer-Villiger reaction)
- Coupling reactions from organohalides
- Metathesis of olefins
- Activation and functionalization of alkanes to alcohols, ketones and carboxylic acids
GENERAL BIBLIOGRAPHY

Various ch. in general books on Catal., Organomet. or Coord. Chem. e.g.:


A – The role of the catalyst and the catalytic cycle

Catalysis consists basically on the repetition of a cycle (catalytic cycle) of reactions (reaction steps) in which the substrate(s) is(are) consumed leading to the product(s) with regeneration of the catalyst whose role is to promote the rate of the desired reaction.

Sometimes the catalyst is generated in situ from a catalyst precursor.

One catalytic turnover is completed each time the complete catalytic cycle is performed.

The reaction steps in the catalytic cycle correspond to the known types of reactions in non-catalytic processes: dissociation and addition of ligands, insertion, elimination, nucleophilic attack at ligands, oxidative addition (OA), reductive elimination (RE), etc.
Kinetic role of the catalyst: increase of the rate by inducing a new route, usually a new multistep mechanism whose steps have lower activation energies ($\Delta G^\neq$).
**B – Properties of the catalyst**

<table>
<thead>
<tr>
<th>SELECTIVITY</th>
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<tr>
<td>Capacity (ability) to produce the desired product with the minimum yield of by-products</td>
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<table>
<thead>
<tr>
<th>ACTIVITY</th>
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<tr>
<td>Expressed by</td>
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</table>

- **Turnover number (TON)**: \( \frac{\text{moles of product}}{\text{mole of catalyst}} \)
- **Turnover frequency (TOF)**: \( \frac{\text{TON}}{\text{unit of time (h)}} \)

\[
\text{Reagent} \xrightarrow{\text{cat.}} \text{Product} \quad \text{In heterogeneous processes, concentrations are replaced by the corresponding amounts}
\]

\[
v = \frac{d[\text{Product}]}{dt} \quad \text{TOF} = \frac{v}{[\text{cat.}]}
\]

**Yield (relative to the substrate) (%)**:
\[
\left( \frac{\text{moles of product}}{\text{mole of substrate}} \right) \times 100
\]

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LIFETIME
Can be measured by the total turnovers before deactivation

HOMOGENEOUS CATALYST
Present in the same phase (liquid) as the substrate

HETEROGENEOUS CATALYST
In a different phase, usually solid. *Will not be considered in the course.*

SUPPORTED CATALYST
A catalyst that is supported on a solid surface, either inorganic (*e.g.* silica) or organic (*e.g.* cross-linked polystyrene beads).

If the unsupported catalyst is homogeneous the method allows to benefit from its selectivity (see below) jointly with the easy separation associated to the heterogeneous catalysts.
C – Homogeneous vs. heterogeneous catalyses. Applications and trends

Catalysis has relevant applications in industrial, laboratory and biological (enzymes) syntheses, making processes accessible by increasing their rates. Otherwise, they could not be performed unless under much more energy demanding and unfavourable conditions.

Catalysis has a key role for the production of both commodity chemicals (bulk large scale) and fine or speciality chemicals (high added-value products, smaller scale production).

Among the top-20 commodity chemicals with the highest industrial production (based on mass), 13 are obtained by catalytic processes (usually heterog.).

Shift of industrial interest from traditional commodity chemicals to fine chemicals production.

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Advantages of homogeneous vs. heterogeneous catalysis

→ Higher selectivity: higher capacity to produce the desired product with minimum of by-products

→ Amenable to mechanistic studies and understanding at the molecular level

→ Easier establishment and control of the catalyst structure

→ Easier heat transfer and diffusion

Disadvantages of homogeneous vs. heterogeneous catalysis

→ More difficult product separation and catalyst recovery

→ Lower operating temperature limit

→ Common lower activity

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D – Supported and biphasic catalyses

Fixation (heterogenization) of a homogeneous catalyst (M) to a solid support (see supported catalyst) can overcome the difficulty of separation inherent to homogeneous catalysis, still benefiting from its high selectivity.

This can also be achieved by:
- Liquid/liquid biphasic catalysis:

- Phase transfer catalysis: use of a transfer agent (salt of a bulky cation, NR$_4^+$ or PR$_4^+$, with long alkyl chains) that transports to organic phase (where is the substrate) an anionic catalyst (e.g. metal polyoxide) that otherwise is only soluble in aqueous phase.
CARBONYLATION

• CO incorporation reactions.
• High interest for organic synthesis (aldehydes, alcohols, ketones, esters, carboxylic acids, amides, etc.).
• Industrial application of olefin hydroformylation.

A – Types of carbonylation reactions

- Hydrocarbonylation
  - $\text{H} - \overset{\text{C}}{\text{C}} - \overset{\text{O}}{\text{C}} - \overset{\text{H}}{\text{C}}$ formyl

- Oxocarbonylation
  - $\overset{\text{O}}{\text{C}} - \overset{\text{O}}{\text{C}} - \overset{\text{O}}{\text{C}}$ acyloxy

- Carbocarbonylation
  - $\overset{\text{O}}{\text{C}} - \overset{\text{C}}{\text{C}} - \overset{\text{O}}{\text{C}}$ ketone, quinone

- Azacarbonylation
  - $\overset{\text{O}}{\text{C}} - \overset{\text{N}}{\text{C}} - \overset{\text{O}}{\text{C}}$ N-acyl

- Halocarbonylation
  - $\overset{\text{O}}{\text{C}} - \overset{\text{C}}{\text{C}} - \overset{\text{X}}{\text{C}}$ $X = \text{halogen}$
B – General types of mechanisms

a – Via formal *insertion* of the substrate (*e.g.* alkene or alkyne) into a M-H bond (formation of a M-C bond)

\[ \text{YCOZ} \quad \xrightarrow{\text{nucleophile}} \quad \text{ZH} \quad \xrightarrow{\text{M-H}} \quad \text{M} = \text{C} \quad \xrightarrow{\text{acyl}} \quad \text{M-Y} \]

ZH = H₂, H₂O, ROH, RNH₂, XH

b – Via oxidative addition (OA) of the substrate or a derivative.
C – Hydroformylation (oxo or hydrocarbonylation) of alkenes

Reaction of the alkene with CO and H\textsubscript{2} leading to an aldehyde with one further C

\[
\text{RCH}=\text{CH}_2 + \text{CO} + \text{H}_2 \rightarrow \text{RCH}_2\text{CH}_2\text{C}=\text{H}
\]

Denomination based on the formal addition of formaldehyde (H-CHO) to the double bond (anti-Markownikov type reaction).

The alternative Markownikov type addition (OHC-H) would form the branched (iso) aldehyde H-(C=O)-CHR-CH\textsubscript{3} usually of lower commercial value

Discovered by Otto Roelen (1938), at Ruhrchemie

Accounts for the largest amount of products from a homogeneous transition-metal catalysed reaction (ca. 6 mte/year of products)

The aldehydes are commonly hydrogenated to alcohols

\[
\text{RCH}_2\text{CH}_2\text{C}=\text{H} + \text{H}_2 \xrightarrow{\text{catal.}} \text{R(CH}_2)\text{2CH}_2\text{OH}
\]
Types of catalysts

• Carbonyl (or hydrido-carbonyl) Co complexes e.g. [CoH(CO)₄] (original Roelen process)

  • Catalyst precursor:

  \[
  [\text{Co}_2(\text{CO})_8] + \text{H}_2 \rightarrow 2[\text{CoH(\text{CO})}_4]
  \]

  2 isomers:

  \[
  (\text{OC})_3\text{Co} - \text{Co(\text{CO})}_3 \quad \text{and} \quad \text{OC} \rightarrow \text{Co} - \text{Co} \rightarrow \text{Co} - \text{CO}
  \]
• Phosphine-modified Co catalyst e.g. [CoH(CO)₃(PR₃)] (Shell).

• Analogous Rh/P complexes e.g. [RhH(CO)(PPh₃)₃] (Union Carbide): higher selectivity and activity (at lower P and T), but more expensive, relatively to the Co catalyst.

• Biphasic phosphine-modified Rh complexes e.g. [RhH(CO)(PR₃)₃] (R = m-C₆H₄SO₃Na) with a water-soluble sulphonated phosphine (Rhône Poulenc-Ruhrchemie).

  Easy separation of the insoluble aldehydes. Easy recovery and recycle of the expensive catalyst by simply decanting the aqueous phase.
(1) Dissociation

(2) Addition

(3) 1,2-insertion

(4) Addition

(5) CO insertion

(6) OA

(7) RE

H - C - (CH₂)₂R

CoH(CO)₄

CoH(CO)₃

CH₂=CHR

H

(CO)₃Co(Ill) - C - (CH₂)₂R

H₂

(CO)₃Co - C - (CH₂)₂R

16-e

16-e

16-e

16-e

(CO)₄Co - (CH₂)₂R

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Step (3)

*(CO)₃Co → (CO)₃Co(CH₂)₂R → ...

* Anti-Markownikov type

# Markownikov type

Formation of *iso* aldehyde (usually less valuable) can be hampered by stereochemical effects: bulky R, CO replacement by bulky phosphine.

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D – Carbonylation of methanol. Monsanto acetic acid process

Overall reaction requires a metal catalyst

\[
\text{CH}_3\text{OH} + \text{CO} \xrightarrow{\text{cat.}} \text{CH}_3\text{COOH}
\]

and an iodide promoter

\[
\text{CH}_3\text{OH} + \text{HI} \rightleftharpoons \text{CH}_3\text{I} + \text{H}_2\text{O}
\]

which cleaves the methanol C-O bond forming a more reactive species (CH₃I) which can oxidatively add to the metal catalyst and then undergo carbonylation (insertion of CO into metal-CH₃).

Cat. = Rh-based (Monsanto), Ir-based (Cativa process)

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\[
\text{Rh}^{\text{III}}X_3 + 3\text{CO} + \text{H}_2\text{O} \rightarrow [\text{Rh}^1X_2(\text{CO})_2]^- + \text{CO}_2 + 2\text{H}^+ + X^-
\]

(if \(X \neq I\))

1,1-insertion

rate limiting

16-e

18-e

18-e

16-e

[\text{Rh}^1X_2(\text{CO})_2]^- 

[\text{Rh}^1X_2(\text{CO})_2]^- 

[\text{Rh}^1X_2(\text{CO})_2]^- 

[\text{Rh}^1X_2(\text{CO})_2]^- 

[\text{Rh}^1X_2(\text{CO})_2]^- 

[\text{Rh}^1X_2(\text{CO})_2]^-
Oxidation of ethylene to acetaldehyde
(Wacker Process)

\[
\text{H}_2\text{C}=\text{CH}_2 + \text{PdCl}_2 + \text{H}_2\text{O} \xrightarrow{\text{(a)}} \text{CH}_3\text{CHO} + \text{Pd}^0 + 2\text{HCl}
\]

(a) Stoichiometric Pd\text{II}-mediated oxidation known since long (F.C. Phillips, 1894), but without commercial interest (expensive PdCl\text{2})

(b) Recycling of palladium by oxidation of Pd(0) before it precipitates (J. Smidt at Wacker Chemie, 1956)
Rate equation:

\[ v = k \cdot \frac{[\text{PdCl}_4^{2-}][\text{C}_2\text{H}_4]}{[\text{Cl}^-]^2[H^+]} \]

suggests that the conversion of [PdCl\(_4\)]\(^{2-}\) (the normal form of palladium chloride in solution) into the transition state limiting the turnover, involves the gain of a C\(_2\)H\(_4\) molecule and a loss of 2 Cl\(^-\) and of one H\(^+\).
Wacker Process

1,2-insertion into Pd-H

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Catalytic Nitrile Hydrolysis to Carboxamides

\[
\text{N} \equiv \text{CR} + \text{H}_2\text{O} \rightarrow \text{H}_2\text{N} - \text{C} - \text{R}
\]

**Uses of carboxamides:** Intermediates in synthesis of products with application in medicine, agriculture, polymers, dyes, and fine chemicals

**Difficulties:** Faster hydrolysis of carboxamides lead to carboxylates or carboxylic acids

Formation of inorganic waste (polluting salts derived from the final neutralization). In concentrated acid, the reaction can stop at the amide stage but a tight control of temperature (exothermic reaction) and reagents ratio is required to avoid polymerization

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Advantages and effects of a metal catalyst

- Acceleration of the nitrile hydrolysis
  Factor $= 10^6 - 10^8$ (usual), $10^{18}$ (Hg$^{II}$)

- (a) Activation of NCR towards direct nucleophilic addition of water or
- (b) activation (OA) of water

Neutral conditions. No salt formation
- No need for a high water excess (can be < 3 molar equiv.) which would hamper the isolation of the amides
- But usually low activity

Zn(II) / oxime catalyst

\[
R\equiv N + H_2O \xrightarrow{\Delta} R\equiv CNH_2
\]

\[
Zn(II)/R'_2C=NOH \xrightarrow{\Delta} R\equiv CNH_2
\]

Isolated active intermediates: \([ZnX_2(oxime)_2]\)

Postulated mechanism:

- High isolated yields (up to 90%)
- TON up to 1000 (upon catalyst recycle)
- High simplicity, cheap, easily available and non-polluting (environmentally friend) chemicals, operation in air

* or direct displacement by NCR


Patent PT 102618 P (2001)

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Pt(II) or Pd(II) complexes with phosphines or related ligands

e.g. the dimethylphosphineoxide-derived phosphinito/hydroxyphosphine chelate

\[
\begin{align*}
[\text{Pt}(\text{PPh}_3)_4] & \xrightarrow{\text{O=PHMe}_2} [\text{PtH(Me}_2\text{PO}\cdots\text{H}\cdots\text{OPMe}_2](\text{PMe}_2\text{OH})] \\
\text{dry toluene} & \text{RT}
\end{align*}
\]

Refluxing solvent (NCR, EtOH or THF) conditions (~90 – 100 °C)
High TON (up to 77000) for the selective hydration of acrylonitrile (H$_2$C=CHC≡N) to acrylamide (H$_2$C=CHCONH$_2$)

Proposed mechanism via a cationic intermediate and intramolecular nucleophilic attack of the hydroxy group of the hydroxyphosphine

Baeyer-Villiger (B-V) Reaction

Direct oxidation of cyclic and acyclic ketones to lactones and esters

Application in the production of monomers for polymers, pharmaceuticals, aromas and perfumes, pheromones (agrochemicals)
Platinum(II)–CF$_3$ Catalysts (B-V Reaction)

Platinum(II) CF$_3$ complexes developed by Strukul et al. in the early 90’s

\[
\text{Pt}^+ = [(\text{dppe})\text{Pt}(\text{CF}_3)(\text{solv})]^+ 
\]

• C-C or C-heteroatom bond formation from a variety of sources.
• Can be applied to asymmetric synthesis

**Coupling Reactions from OrganoHalides**

- **Heck Reaction**
  - \( R\rangle R' + HX \)

- **Suzuki Coupling**
  - \( R\rangle Ar + XB(OH)_2 \)

- **Stille Coupling**
  - \( R\rangle Ar + XSnR'_{3} \)

- **Hartwig-Buchwald Coupling**
  - \( R\rangle NR'_{2} + HX \)
Catalyst – Pd$^{\text{II}}$ complex e.g. Pd(OAc)$_2$ / PR$_3$
Mechanism – Usual initial reduction to a Pd$^0$ complex, PdL$_2$, followed by OA of R–X to give a Pd$^{\text{II}}$–R intermediate.
R – usually aryl (Ar–X) or vinyl ( ) to avoid decomposition of the Pd – R intermediate by β-elimination.
PR$_3$ – basic and bulky phosphine to promote the OA step and the unsaturation of the metal site.

**Heck reaction:**

$$R' \text{ vinyl} + \text{HX} \rightarrow \text{base} \rightarrow \text{OA} \rightarrow \text{PdL}_2 \rightarrow \text{reductive elim. by β-elimination} \rightarrow 1,2\text{-insertion} \rightarrow \text{R–X}$$
Suzuki, Stille or Hartwig-Buchwald couplings:

Ar-B(OH)$_2$ (Suzuki),
Ar-SnR$_3$ (Stille)
R$_2$N-H (Hartwig-Buchwald)
**METATHESIS**

\[
\begin{align*}
\text{a} & \quad \text{b} \\
\text{c} & \quad \text{d} & + & \quad \text{e} & \quad \text{f} \\
\text{g} & \quad \text{h} & \quad & \text{cat.} & \quad & \text{b} & \quad \text{e} \\
\text{a} & \quad \text{f} & + & \quad \text{c} & \quad \text{g} \\
\text{d} & \quad \text{h}
\end{align*}
\]

- No equivalent in pure organic chemistry
- Discovered in the mid 1950s (workers at *Du Pont*, *Standard Oil*, *Phillips Petroleum*) for simple olefins

**Mechanism (Chauvin)**: via carbene and metalacyclobutane intermediates

\[
\begin{align*}
\text{a} & \quad \text{M} \\
\text{b} & \quad + \\
\text{e} & \quad \text{g} \\
\text{f} & \quad \text{h} & \quad \rightarrow & \quad \text{a} & \quad \text{b} & \quad \text{M} \\
\text{e} & \quad \text{f} & \quad \text{g} & \quad \rightarrow & \quad \text{a} & \quad \text{b} \\
\text{f} & \quad \text{e} & \quad \text{g} & \quad \text{h} & \quad + & \quad \text{M}
\end{align*}
\]

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CATALYSTS: Carbene complexes

Schrock
R = -C(CH₃)(CF₃)₂
Ar = C₆H₃ᵢPr-2,6

Osborn
The Lewis acid creates a vacant site at W

Grubbs
Tolerant of olefin functionality (late transition metal)
Metathesis Types

Cross-metathesis (CM):

\[ R' + R'' \xrightarrow{\text{CM}} R \xrightarrow{\text{-CH}_2=\text{CH}_2} R' \]

Ring-opening metathesis (ROM):

\[ R + R' \xrightarrow{\text{ROM}} \text{cyclic structure} \]

Ring-closing metathesis (RCM):

\[ \text{cyclic structure} \xrightarrow{\text{-CH}_2=\text{CH}_2} \text{cyclic structure} \]

Cross-metathesis (CM):

\[ \xrightarrow{\text{CM}} \]

Enyne metathesis (EYM):

\[ R \xrightarrow{\text{EYM}} R' \]

Ring-opening metathesis polymerization (ROMP):

\[ \xrightarrow{\text{ROMP}} \ldots \]

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**ACTIVATION AND FUNCTIONALIZATION OF ALKANES**

**Alkane unreactivity**
unavailability of lone pairs and of empty orbitals
low energy lying HOMO (σ)
high energy lying LUMO (σ*)

Two-component:
σ-donation + π-back donation

\[
\begin{align*}
\text{(a)} & \quad M - H \quad \text{OA} \\
\text{(b)} & \quad M - H^+ \quad \text{heterolytic cleavage} \\
\text{(c)} & \quad \text{R}^* \quad \text{homolysis}
\end{align*}
\]

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a) C-H Oxidative addition

- Thermodynamically unfavourable (→): low M-C bond energy + entropically unfavourable (1 molec. from 2). Alkyl-hydride product thermodynamically unstable towards alkane elimination (←)
- Requirement for equilibrium shift (→): further reactions of the alkyl-hydride.

![Chemical diagram showing the reaction mechanism of C-H Oxidative addition](IP-Erasmus_Pombeiro)
b) Heterolytic C-H cleavage

Predominant $\sigma$-donation over $\pi$-backbonding

Electrophilic attack of M to C-H: R$^-$ abstraction

1) Shilov Pt system

Since 1970, the first alkane functionalization catalysis based on a transition metal: reversal with D$^+$ $\Rightarrow$ alkane deuteriation

$$\text{M-Cl} + \text{RH} \rightleftharpoons \text{M-R} + \text{H}^+ (\text{D}^+)$$

$$\text{M-Cl} = [\text{PtCl}_4]^{2-}$$
$$\text{Pt}^{IV} = [\text{PtCl}_6]^{2-}$$

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Heterolytic C-H cleavage

2) Fujiwara Pd$^\text{II}$ carboxylation system

\[ \text{Pd(OAc)}_2 / \text{K}_2 \text{S}_2 \text{O}_8 \text{ (peroxydisulfate) / CF}_3 \text{COOH (TFA, solvent)} \]

\[ \text{C}_n \text{H}_{2n+2} + \text{CO} \xrightarrow{\text{cat.} 80 \ ^\circ \text{C}} \text{C}_n \text{H}_{2n+1} \text{C} = \text{O} \]

\[ n \geq 1 \quad \text{(includes gaseous alkanes)} \quad \text{(high yield)} \]

[Y. Fujiwara et al., Synlett, 1996, 591]
Heterolytic C-H cleavage

One-Step Oxidative Condensation of CH₄ to CH₃COOH

\[ 2^{13}\text{CH}_4 + 4\text{H}_2\text{SO}_4 \xrightarrow{\text{Pd}^{\text{II}}\text{oxidant}} \text{Pd}^{\text{II}}\text{H}_2\text{SO}_4 \xrightarrow{180 ^\circ\text{C}} ^{13}\text{CH}_3^{13}\text{COOH} + 4\text{SO}_2 + 6\text{H}_2\text{O} \]

12 % yield \((\text{CH}_3\text{COOH} + \text{CH}_3\text{OH})\)
TON \(\leq 18\)

Periana et al., Science, 2003, 301, 814
Aerobic Oxidation of CH₄ via ET Chain
Pd²⁺ / Q / NaNO₂ / O₂ / TFA system

CH₃OH → CF₃COOH → CF₃COOCH₃

1 – CH₄ oxidation by Pd²⁺
2 – Regeneration of Pd⁰
3 – Regeneration of benzoquinone (oxidant)
4 – Formation of nitrogen dioxide (oxidant) by oxidation of nitrous oxide (NO)

Net reaction (compare with Wacker)
CH₄ + 1/2O₂ → CH₃OH

Source of NOₓ: nitrite decomposition (ac. medium)

Ester: Low TON (up to 7, 10h) yield (≤ 0.1 %)

Bao et al., JACS, 2006, 128, 16028

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c) Homolytic C-H cleavage

Formation of R* by H-atom abstraction from RH

- By a reactive species generated upon metal activation of the other reagent (instead of the alkane)
  Typical: reactive hydroxyl radical (HO*) from H₂O₂

  - Alkane oxidation by the Fenton’s reagent: Fe²⁺ + H₂O₂
  - Alkane oxidation by the Vanadate–H₂O₂ Shulpin’s system
  - Alkane oxidation by the [MeReO₃] (MTO)–H₂O₂ system (our work)

- By a high valent metal oxide (bio and mimetic systems)

  RH + O=Mⁿ → R* + HO–Mⁿ⁻¹ → ROH + Mⁿ⁻²

  *Rebound mechanism*

  IP-Erasmus_Pombeiro
Homolytic C-H cleavage

Shulpin’s Vanadate–PCA–O$_2$–H$_2$O$_2$–NCMe System

RH + [Bu$_4$N][VO$_3$] + pyrazine-carboxylic acid

\[ \text{oxidant} \quad \text{promoter (HO$^\circ$ source)} \]

RH + O$_2$ \xrightarrow{H$_2$O$_2$ \text{NCMe} \ (< 40 \, ^\circ\text{C})} \text{ROOH} \xrightarrow{\Delta \text{time}} \frac{1}{2} \text{ROH} + \frac{1}{2} \text{R}(\text{H})=\text{O} \quad \text{Yield up to 30 \%}

TON up to 1.3x10$^3$

Radical mechanism

(a) H$_2$O$_2$ (H donor)
(b) HOO$^\circ$ (H donor)
(c) $\text{ROO}^-$


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V-assisted formation of HOO• and OH• radicals from H₂O₂

\[ \text{[V]} + \text{H}_2\text{O}_2 \xrightarrow{1-3} \text{[V]IV} + \text{HOO•} + \text{H}^+ \text{ (to O-ligand)} \]

oxidant

\[ \text{[V]IV} + \text{H}_2\text{O}_2 \xrightarrow{4-6} \text{[V]} + \text{HO•} + \text{O}^2- \text{ (ligand)} + \text{H}^+ \text{ (to O-ligand)} \]

reducer

\[ \text{[V]} = \text{[V}^\text{IV}_2\text{(pca)] (pca = pyrazine-carboxylate)} \]

pca role: H⁺-transfer promoter

"robot's arm"

Proton-transfer promoting role of pyrazine-carboxylate ligand in Shulpin’s “robot’s arm” mechanism


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MTO - water assisted formation of HOO$^\cdot$ and HO$^\cdot$ radicals from H$_2$O$_2$
(MTO-aq.H$_2$O$_2$-NCMe system)

Water as H$^\cdot$-transfer promoter
(via 6-membered metallacycles)

* H-shift from H$_2$O$_2$

Re$^{\text{VII}}$ + H$_2$O$_2$ $\rightarrow$ Re$^{\text{VI}}$ + HOO$^\cdot$ + H$^+$
Re$^{\text{VI}}$ + H$_2$O$_2$ $\rightarrow$ Re$^{\text{VII}}$ + HO$^\cdot$ + OH$^-$

No additives or N,O-ligands are required

Kuznetsov, Pombeiro,
Coordination Chemistry and Catalysis in AQUEOUS media

Hydrosoluble ligands
Amino-polyalcohols / base (NO\textsubscript{x}, O\textsubscript{x})
Benzene-polycarboxylic acids / base (O\textsubscript{x})
Scorpionates (N\textsubscript{x}, N\textsubscript{x}O)

Water soluble tris(pyrazolyl)methanesulfonate (Tpms)

“this creature grabs its prey with two claws and ...with its overarching tail.”, S. Trofimenko
Half-sandwich Scorpionate Complexes as Catalysts for Cyclohexane Peroxidative Oxidation

Hydrosoluble Fe catalyst active in water without any organic solvent ⇒ green catalytic system


Patent: PT 104153

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<table>
<thead>
<tr>
<th></th>
<th>TON</th>
<th>Yield</th>
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<tr>
<td>Fe</td>
<td>690</td>
<td>25%</td>
</tr>
<tr>
<td>V</td>
<td>170</td>
<td>13%</td>
</tr>
<tr>
<td>Cu</td>
<td>43</td>
<td>&lt;1%</td>
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Amavadine and other V complexes as catalysts for the partial oxidation of alkanes

Amavadine
intriguing natural bare V complex present in some amanita toadstools

Hydrosoluble

Other simpler V complexes with O, N or O,O ligands exhibit similar catalytic activity

R = Me (basic form of 2,2’-(hydroxyimino)dipropionic acid
R = H (basic form of 2,2’-(hydroxyimino)diacetic acid
Partial oxidation of alkanes by *Amavadin* and other V-complexes

\[
\text{H}_2\text{O}_2 / \text{H}^+ \xrightarrow{-\text{H}_2\text{O}} \text{C} = \text{O} \quad \text{TON 50, 10\% yield}
\]

\[
\text{RT, H}_2\text{O} / \text{NCMe}
\]

\[
\text{H}_2\text{O}_2 / \text{H}^+ / \text{Br}^- \xrightarrow{-\text{H}_2\text{O}} \text{C} - \text{Br}
\]

\[
\text{haloperoxidase}
\]

\[
\text{CO} / \text{TFA} \xrightarrow{\text{S}_2\text{O}_8^{2-}} \text{C} = \text{O}
\]

\[
\text{TON over } 10^4 \quad \text{Yield over 90\%}
\]

Kirillova, Kuznetsov, Martins, Alegria, da Silva, Kirillov, Reis, Fraústo Silva, Pombeiro

*Chem. Commun.*, 2000, 1845


IP-Erasmus_Pombeiro
Self-assembled Multi-Cu(II) Coordination Compounds and Polymers Derived from Aminopolyalcohols and Benzenepolycarboxylates

General scheme of self-assembly synthesis


IP-Erasmus_Pombeiro
SELF-ASSEMBLY SYNTHESIS of HYDROSOLUBLE Cu COORDINATION POLYMERS

Karabach, Guedes Silva, Kirillov, Kopylovich, Pombeiro,
Crystal Growth & Design, 2006, 6, 2200

IP-Erasmus_Pombeiro
**Self-assembled Multinuclear Cu Complexes as Catalysts for Peroxidative Oxidation of Alkanes**

Cu-catalyst with H$_2$O$_2$, HNO$_3$, 20-40 °C in H$_2$O/MeCN


39%, 380 TON

2.2%, 47 TON

2.1%, 23 TON

IP-Erasmus_Pombeiro
C- and O-Centred Radical Mechanism for Alkane Oxidation and Carboxylation

Radical Trap Experiments

Supression of catalytic activity by a radical trap

- Trichlorobromomethane ($\text{CBrCl}_3$)
- 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO)
- Diphenylamine ($\text{Ph}_2\text{NH}$)
- di-tert-butyl-hydroxytoluene (BHT)
- 5,5-dimethyl-1-pyrroline N-oxide
Trinuclear Triangular Cu$^{II}$ Complexes as Catalysts for Peroxidative Oxidation of Cycloalkanes

$$[\text{Cu}_3(\mu_3\text{-OH})(\mu\text{-pz})_3(\text{RCOO})_2L_x]$$

R = H, alkyl
L = Hpz, H$_2$O, MeOH, EtOH
x = 1, 2

Radical pathway (radical trap experiments) via ROOH

SINGLE-POT CARBOXYLATION of ALKANES to CARBOXYLIC ACIDS under mild/moderate conditions

\[ {^{13}\text{C}} \text{nH}_{2n+2} + \text{CO} \xrightarrow{\text{K}_2\text{S}_2\text{O}_8, \text{TFA}, 80^\circ\text{C}} {^{13}\text{C}} \text{nH}_{2n+1}\text{COOH} \]

Alkane as source of alkyl group of acid proved by \(^{13}\text{C}\) labelled studies

Pioneered by Y. Fujiwara
Pd, Cu – much lower activity than our systems

Amavadine and other alkane carboxylation V-(N,O or O,O) catalysts / \(\text{K}_2\text{S}_2\text{O}_8 / \text{CF}_3\text{COOH (TFA) (our systems)}\)

Low P (5 – 30 atm) Moderate T (80\(^\circ\)C)

High acid yield and TON :
- \(> 50\%\) 6 \(\times 10^3\) \(\text{CH}_4\)
- \(93\%\) 2 \(\times 10^4\) \(\text{C}_2\text{H}_6\)
- \(70\%\) 1.8 \(\times 10^4\) \(\text{C}_3\text{H}_8\)

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CH₄ as the Methyl Source for CH₃COOH

P(^{13}\text{CH}_4) = 2 \text{ atm} , \ P(\text{CO}) = 20 \text{ atm} . \ K_2\text{S}_2\text{O}_8 : [\text{VO}\{\text{NCH}_2\text{CH}_2\text{O}\}_3] = 20 : 1

CF₃COOH , 80 °C , 20 h

IP-Erasmus_Pombeiro

JACS, 2007, 129, 10531
Conversion of methane into acetic acid

\[
\begin{align*}
\text{CH}_4 \quad &\rightarrow \quad \text{CH}_3^\cdot \quad \text{CO} \\
\Delta \quad &\rightarrow \quad \text{SO}_4^{2-} (\text{HSO}_4^+) \\
\text{Yield} \quad &55\% \\
\text{TON} \quad &6 \times 10^3 \\
\text{J. Am. Chem. Soc., 2007, 129, 10531}
\end{align*}
\]
Energy profile

CPCM-B3LYP/6-31G* level of theory

JACS, 2007, 129, 10531

IP-Erasmus_Pombeiro
Single-pot Carboxylation (and Oxidation) of Ethane into Propionic and Acetic Acids

\[ C_2H_6 + CO \xrightarrow{\text{V catalyst}} C_2H_5COOH + CH_3COOH \]

Typical 80% yield, 5%

\[ pC_2H_6 = 10 \text{ atm} \quad pCO = 30 \text{ atm} \]

20 h

Overall yields up to 93%

TONs up to $2 \times 10^4$

$^{13}$C-labelled experiments

Kirillova, Kuznetsov, Silva, Guedes da Silva, Fraústo da Silva, Pombeiro,

IP-Erasmus_Pombeiro
Single-pot Carbonyl. (Oxid.) of Ethane to Propionic and Acetic Acids

$^{13}$C-labelled experiments

$^{13}$CH$_3^{13}$CH$_3$ + CO $\xrightarrow{\text{V catalyst}}$ K$_2$S$_2$O$_8$, TFA $^{13}$CH$_3^{13}$CH$_2$COOH + $^{13}$CH$_3^{13}$COOH + $^{13}$CH$_3$COOH  
16 : 1

carbonylation oxidation C-C cleavage carbonylation

CH$_3$CH$_3$ + $^{13}$CO $\xrightarrow{\text{V catalyst}}$ K$_2$S$_2$O$_8$, TFA CH$_3$CH$_2^{13}$COOH + CH$_3$COOH + CH$_3^{13}$COOH  
20 : 1

carbonylation oxidation C-C cleavage carbonylation

Propionic acid: carbonylation of ethane by CO (or TFA in absence of CO)
Acetic acid: oxidation of ethane
C-C cleavage and carbonylation by CO (and TFA)

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CARBOXYLATION
Single-pot direct conversion of methane to acetic acid

\[
\text{CH}_4 + \text{CO} \xrightarrow{\text{cat. oxidant}} \text{CH}_3\text{COOH}
\]

Much simpler than the 3 separate stage industrial processes

\[
\begin{align*}
\text{CH}_4 + \text{H}_2\text{O} & \xrightarrow{\text{high T. cat.}} \text{CO} + 3\text{H}_2 \\
\text{CO} + 2\text{H}_2 & \xrightarrow{\text{high T. cat.}} \text{CH}_3\text{OH} \\
\text{CH}_3\text{OH} + \text{CO} & \xrightarrow{\text{cat.}} \text{CH}_3\text{COOH}
\end{align*}
\]

Monsanto (Rh)  
Cativa (Ir)

But need for cheaper and less toxic solvent and oxidant

IP-Erasmus_Pombeiro
Alkanes Hydrocarboxylation in Aqueous Medium

\[ \text{C–H} + \text{CO} + \text{H}_2\text{O} + \text{S}_2\text{O}_8^{2-} \rightarrow \text{C–COOH} + 2\text{HSO}_4^- \]

Mild conditions, no acid

\( \text{H}_2\text{O} \) with hydroxylating role

Both gaseous (except \( \text{CH}_4 \)) and liquid alkanes

Both metal-free and metal-promoted

Water soluble Cu\textsuperscript{II} promoter

\[ [\text{O}\subset\text{Cu}_4\{\text{N}({\text{CH}_2\text{CH}_2\text{O}})_3\}\{\text{BOH}\}_4][\text{BF}_4]_2 \]

\( \text{K}_2\text{S}_2\text{O}_8 \) – radical initiator and oxidant (yield of carboxylic acid based on oxidant up to 48 %)

2° C-atoms carbonylate preferably to 1° C-atoms

Suppression of acid formation by a radical trap (CBrCl\textsubscript{3})


IP-Erasmus_Pombeiro
Proposed Main Radical Mechanism

1 → 2: acyl radical formation
3 → 4: metal-free pathway
5/5’ → 7: metal-promoted pathway

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