EuCheMS
European Chemical Sciences

Organometallic Chemistry for Homogeneous Catalysis

Dedicated to all who suffer as a result of the Italian earthquakes, especially in Camerino

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Thanks to:

Paul Kamer
University of St Andrews

Bob Tooze
Sasol Technology UK Ltd (St. Andrews)

Piet van Leeuwen
University of Amsterdam, ICIQ Tarragona

EaStCHEM
The Edinburgh and St Andrews
Research School of Chemistry

Books

Homogeneous Catalysis: Understanding the Art

Piet W. N. M van Leeuwen, Kluwer Dordrecht, 2004

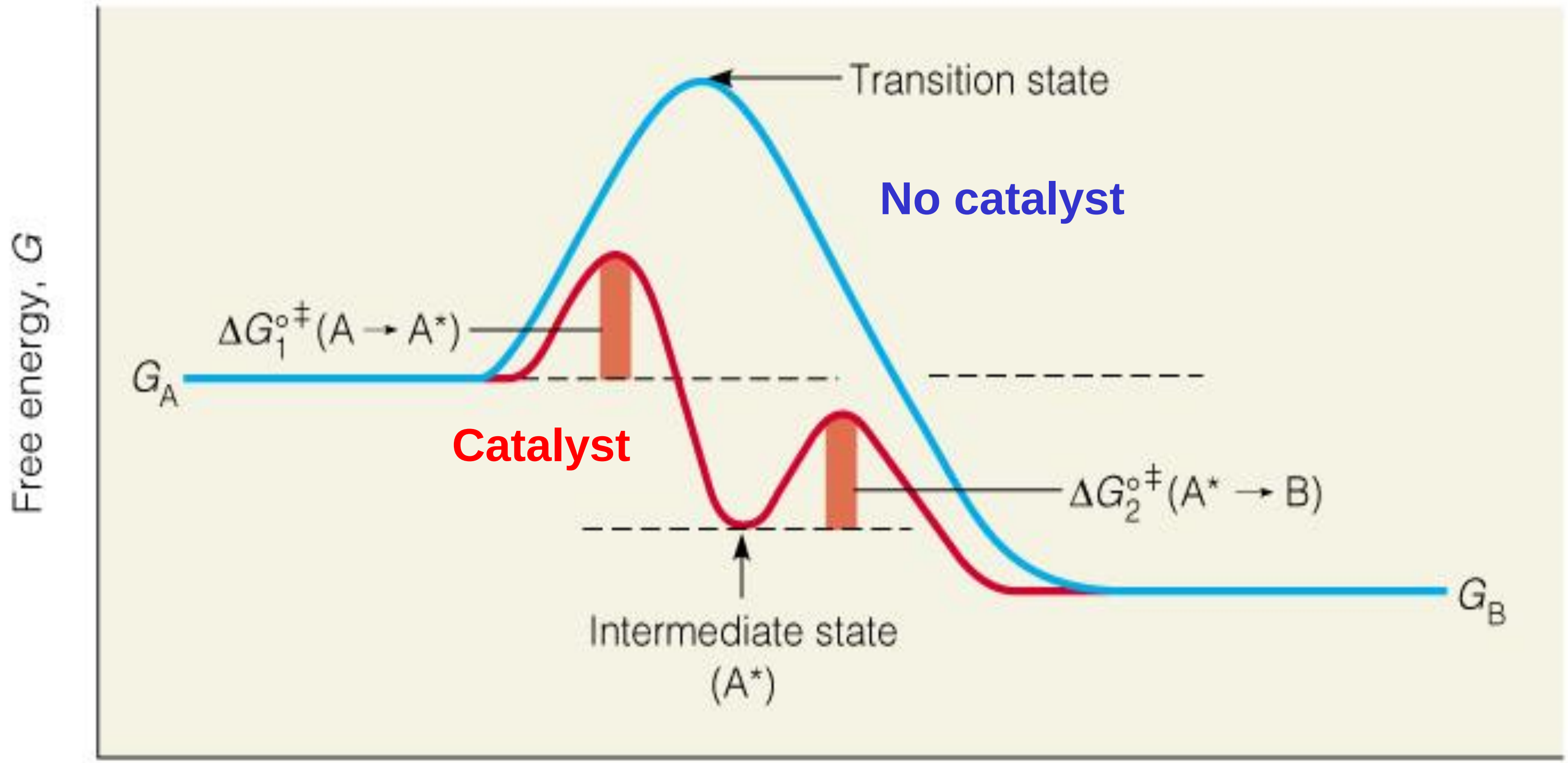
***Applied Homogenous Catalysis with Organometallic Compounds*,**

Eds. B. Cornils and W. A. Herrmann, Wiley, VCH, Weinheim, 2002

Outline

- Background to Catalysis
- Basic Principles of Homogeneous Catalysis
- Selected Examples
- Using Bioresources
- Catalysts Separation and recycling
- Flow homogeneous catalysis

Energy profile of a reaction



Reaction coordinate

$$A \xrightarrow{k_1} A^* \xrightarrow{k_2} B$$

A catalyst lowers the activation energy of a reaction

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

触媒
Tsoo Mei
Marriage broker - catalyst

12 Principles of Green Chemistry

P	Prevent waste	√
R	Renewable materials	√
O	Omit derivatisation	√
D	Degradable chemical products	
U	Use safe synthetic methods	√
C	Catalytic reagents	√
T	Temperature, pressure ambient	√
I	In-process monitoring	
V	Very few auxiliary substances	√
E	E-factor, maximise feed in product	√
L	Low toxicity of chemical products	
Y	Yes, it is safe	√

P. Anastas J. Warner

E Factor

E-Factor = total waste (kg) / product (kg)

E-Factors in the chemical industry

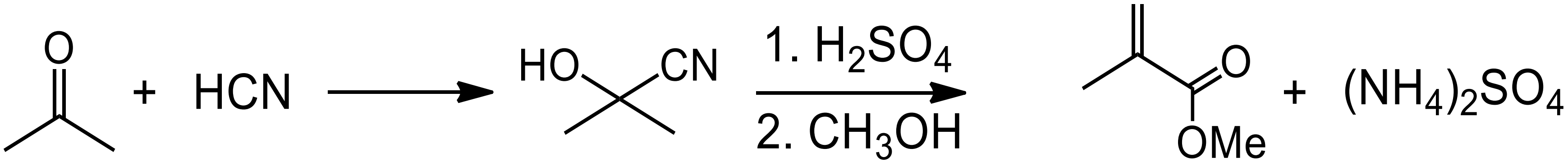
Industry segment	Product tonnage	E-Factor
Oil refining	10^6-10^8	<0.1
Bulk chemicals	10^4-10^6	<1-5
Fine chemicals	10^2-10^4	5-50
Pharmaceuticals	10-10^3	25-100

E-Factor in Pharmaceuticals:
Multiple step syntheses
Use of classical stoichiometric reagents
However, lower absolute amount (compared to bulk).

Advantages of Catalytic Process

Methyl Methacrylate (for Perspex)

Old process: 2.5 kg waste / kg product



Different types of Catalyts

Heterogeneous

- Usually a solid in a different phase from the reactants
- Usually metal or metal oxide

Homogeneous

- In the same phase as the reactants
- Usually a dissolved metal complex

Enzyme (Biological)

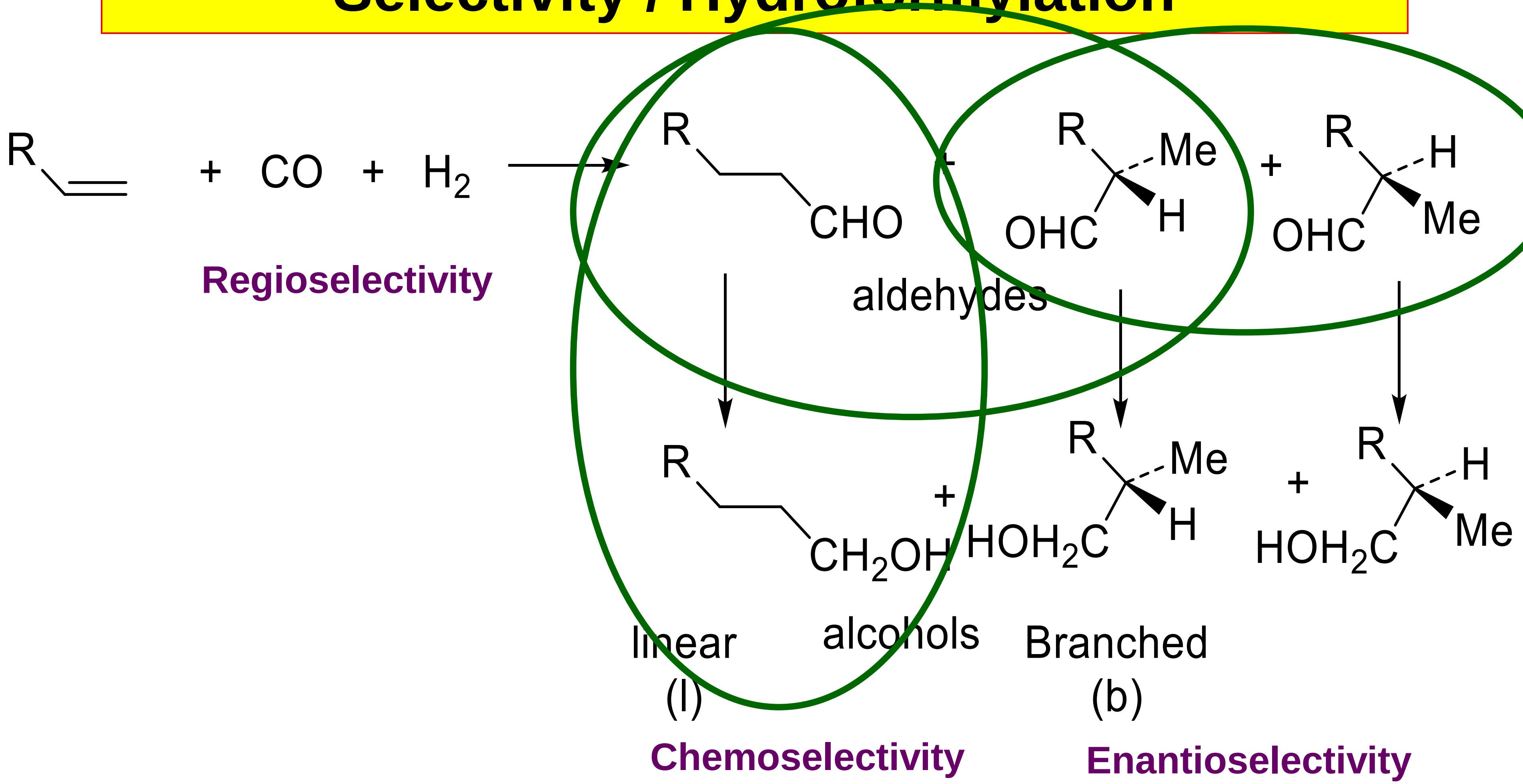
- Usually a complex system in water
- Highly active and selective
- Sometimes rather unstable
- Becoming increasingly popular

World Catalyts market $ 9 billion

Heterogeneous vs Homogeneous Catalysis

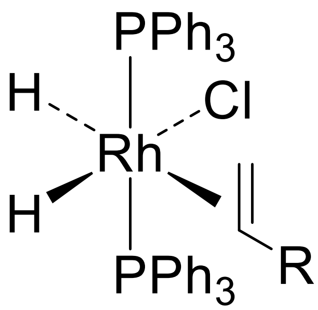
Heterogeneous	Homogeneous
Solid metal or metal oxide	Metal complex
Solvent not required	Solvent required (usually)
Thermally robust	Thermally sensitive
Only surface atoms available	All metal centres available
Selectivity can be poor	Selectivity can be tuned
Difficult to study while operating	In situ spectroscopy
Easy separation from products	Difficult product separation
Some processes only heterogeneous $N_2 + 3 H_2 \longrightarrow 2 NH_3$ Exhaust catalyst	Some processes only homogeneous $MeOH + CO \longrightarrow MeCO_2H$ Hydroformylation of alkenes

Selectivity / Hydroformylation



Counting electrons

- Determine the oxidation state of the metal and hence the number of d electrons.
- Add 2 for each ligand (note that benzene coordinates through the 3 double bonds so gives 6).
- Add electrons for overall negative charges, subtract electrons for overall positive charges.

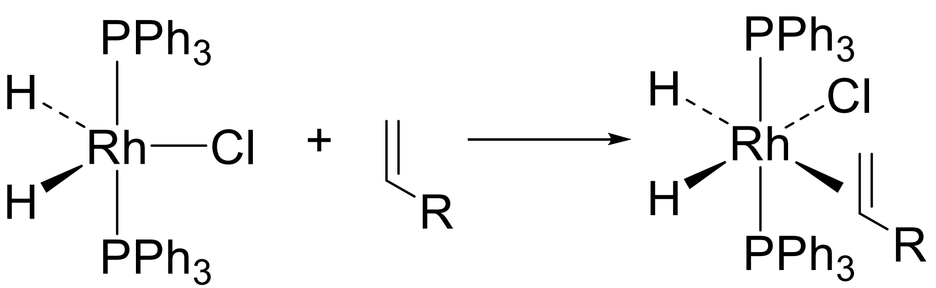


Rh^{III} $4d^6$	6 e
6 x 2e ligands	12 e
Total	18 e

Reactions in catalytic cycles

Coordination

- Need a vacant site (often 14 or 16 e intermediate)

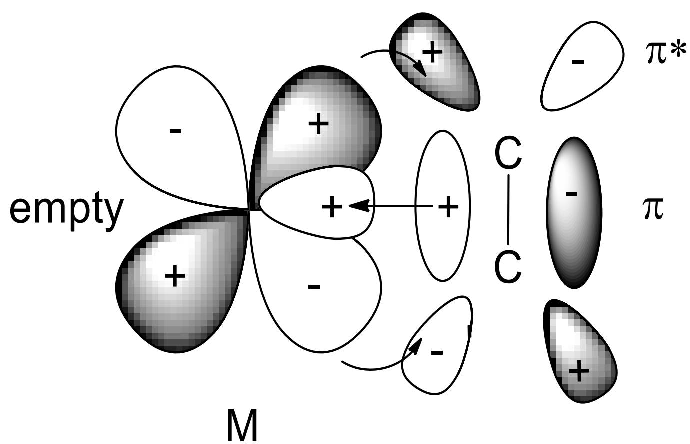


Rh^{III} $4d^6$	6 e	
5 2e ligands	10 e	18 e
Total	16 e	

Bonding of alkenes

• Donation of electron density from π orbital on C=C to an empty s, p or d orbital on the metal

• Back donation of electron density from the filled t_{2g} level on the metal to the empty π* orbital on C=C

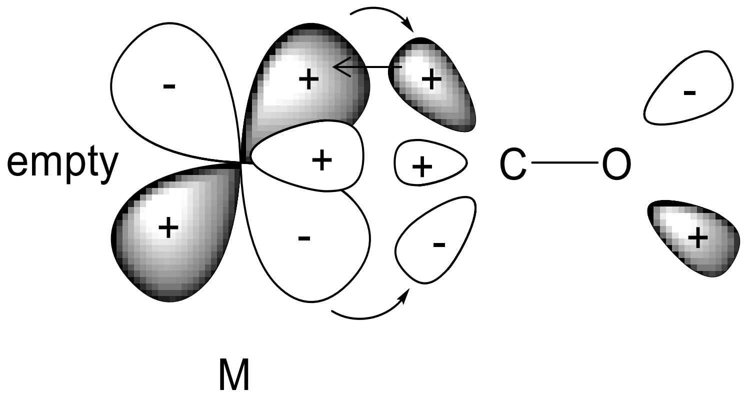


Adds 2 e

Bonding of CO

• Donation of a lone pair of electrons from the C atom of CO to an empty s, p or d orbital on the metal

• Back donation of electron density from the filled t_{2g} level to the empty π^* orbital on CO



Adds 2 e

Substitution

Octahedral complexes

Mechanism

$$[ML_6]^{n+} \;+\; L' \rightarrow [ML_5L']^{n+} \;+\; L$$

1) Dissociative (S_N1)

$$[ML_6]^{n+} \xrightarrow{-L} [ML_5]^{n+} \xrightarrow{L'} [ML_5L']^{n+}$$

square pyramidal

0 order in L[1].

$\Delta S^{\ddagger}$ will be positive

2) Associative (SN2)

$$[ML_6]^{n+} \;+\; L' \rightarrow [ML_6L']^{n+} \rightarrow [ML_5L']^{n+} \;+\; L$$

7 coordinate

1st order in L'

$\Delta S^{\ddagger}$ negative

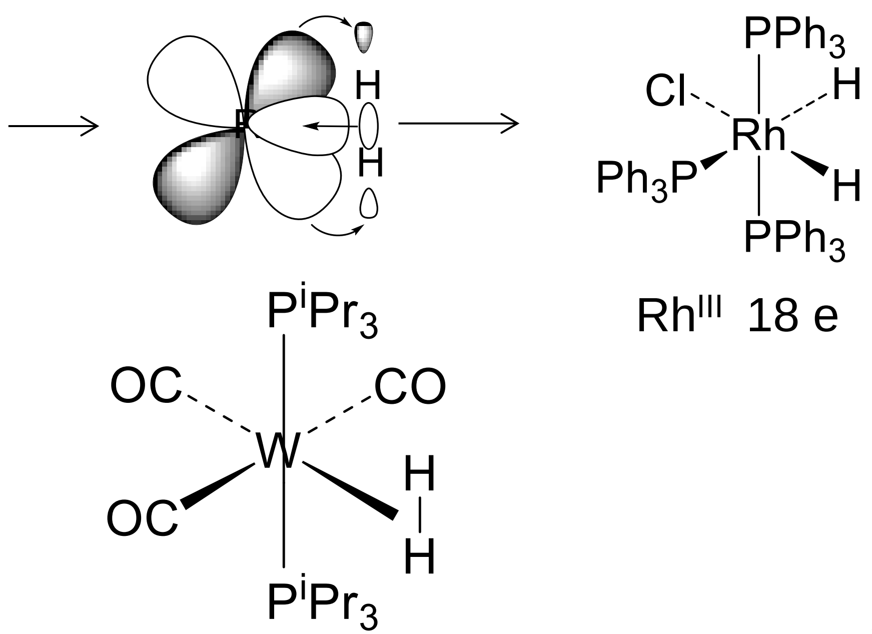
3) Hybrid mechanisms

No change in e count

Oxidative Addition

Concerted addition

$[RhCl(PPh_3)_3]$ + H_2



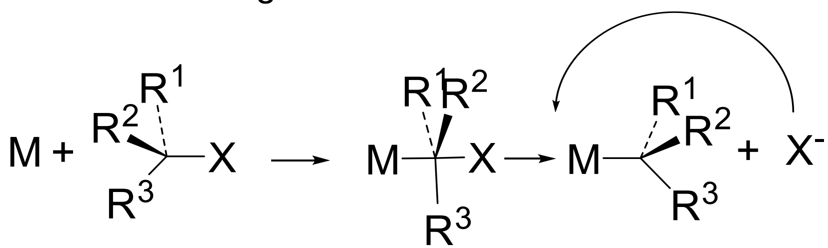
Rh^{I} 16 e

Adds 2 e

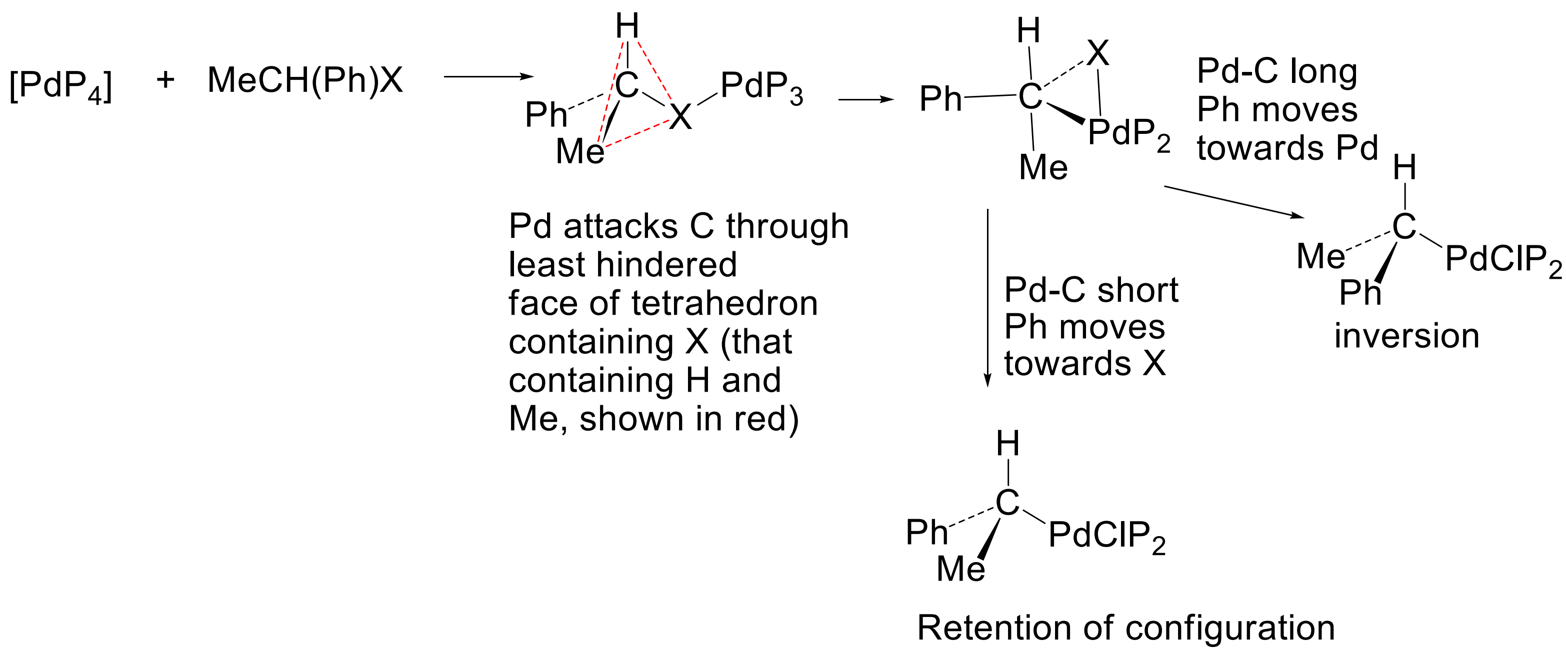
Kubas, G. J.; Ryan, R. R.; Swanson, B. I.; Vergamini, P. J.; Wasserman, H. J., *J. Am. Chem. Soc.*, 1984, 106, 451

Alkyl halides – S_n2

Should give inversion of configuration



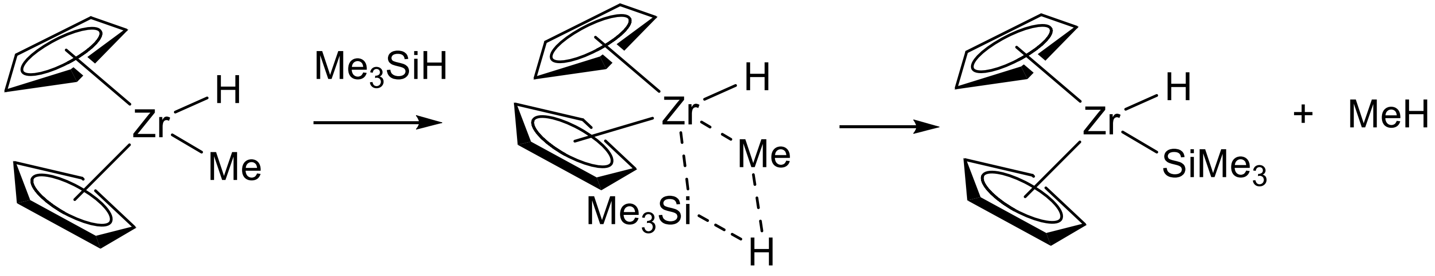
Trans **addition usually goes by this mechanism**



If both pathways have similar energy partial racemisation will occur

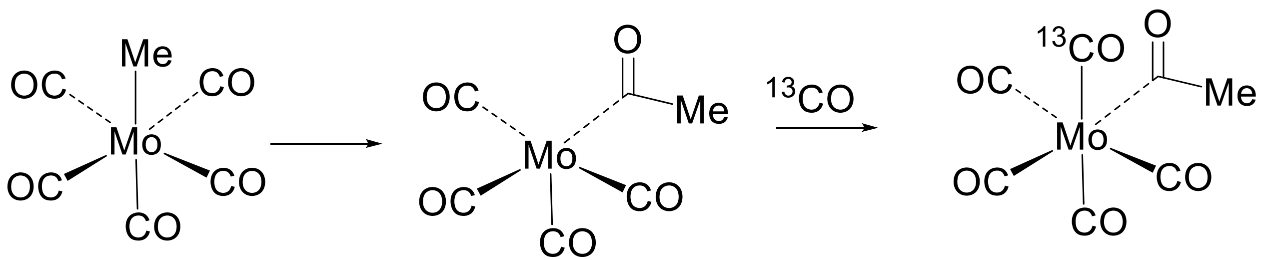
σ–bond metathesis

Occurs when metal is in highest oxidation state (d^0) and oxidative addition is not possible



No change in e count

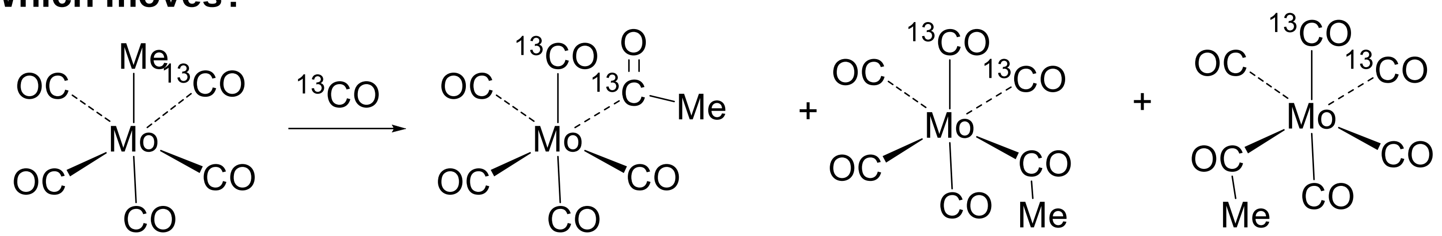
Migratory insertion



- **Incoming ligand does not insert**
- **Incoming ligand ends up *cis* to the acyl**
- **Me and CO involved in migration are mutually *cis***

Removes 2 e

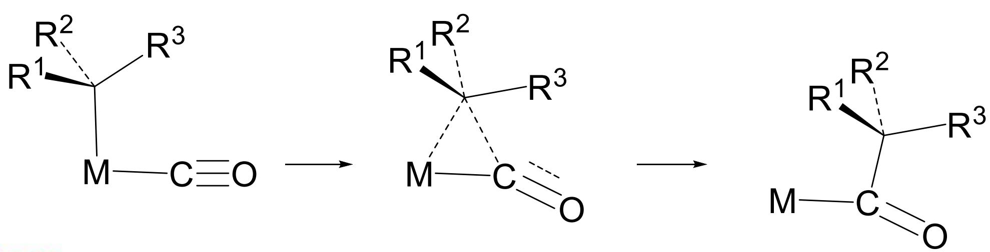
Which moves?



Ratio 1 **A** 2 **B** 1 **C**

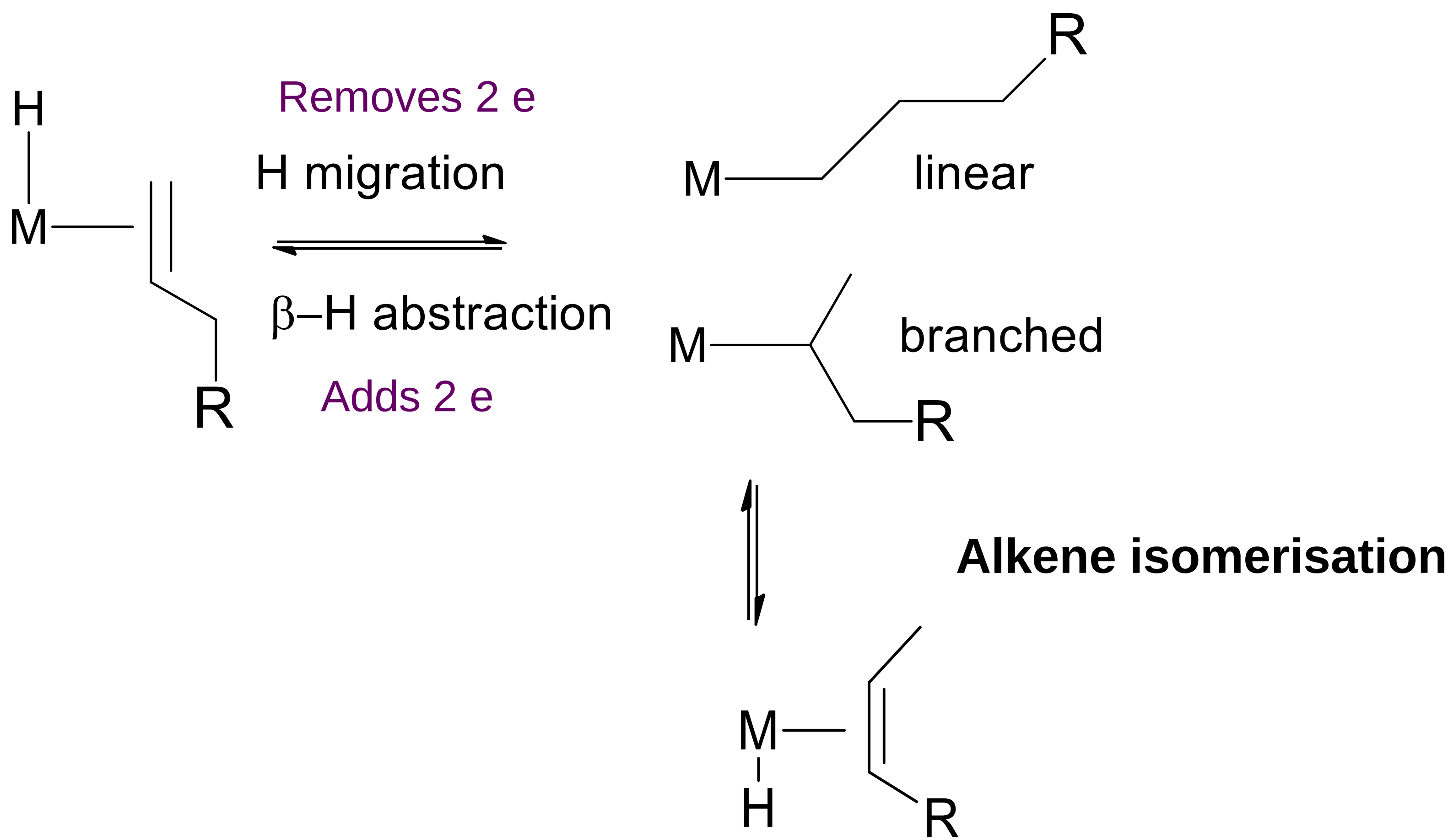
Me must move.

If CO moves cannot get C

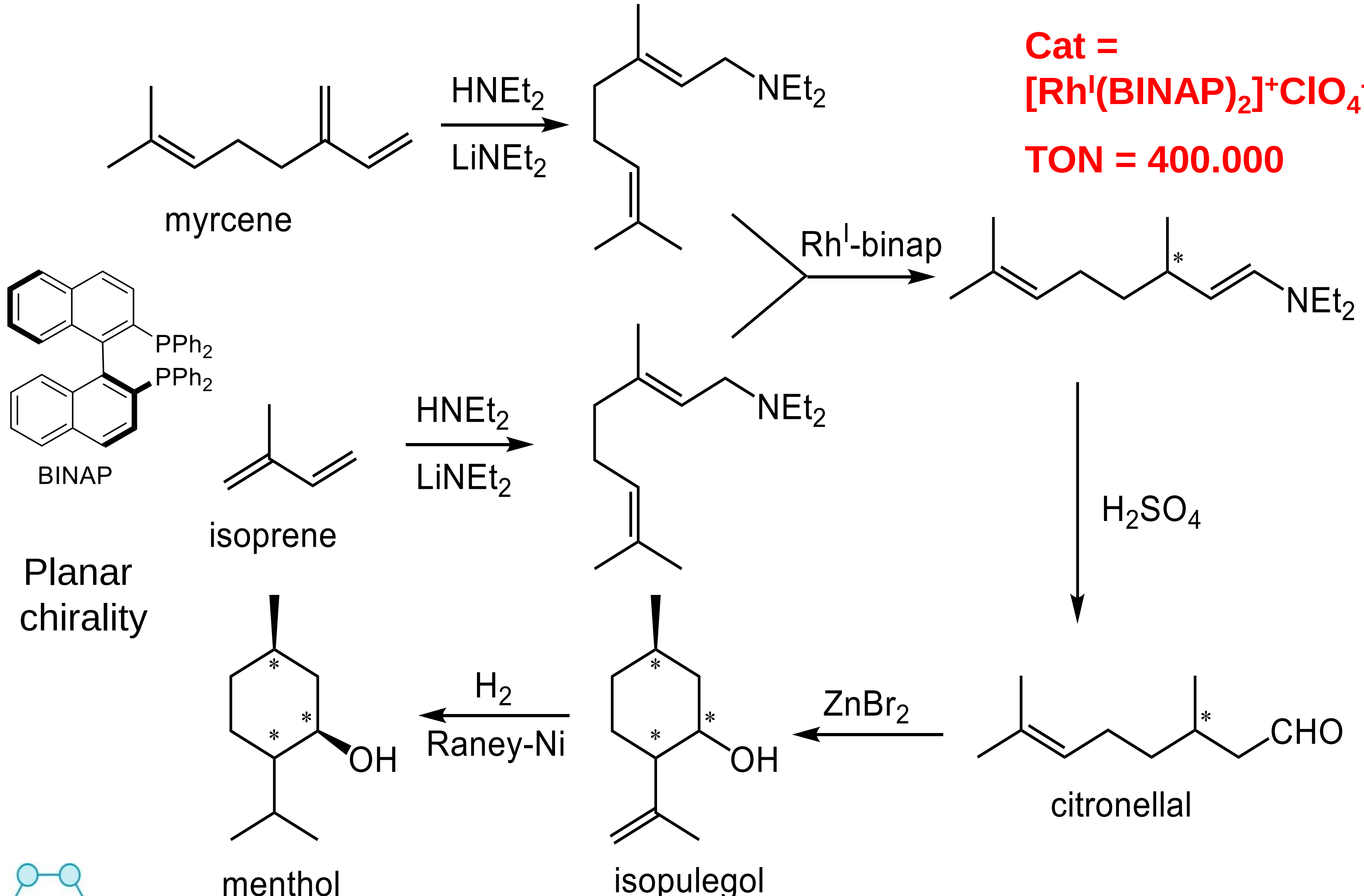


Retention of configuration

Hydride migration and β-hydrogen abstraction

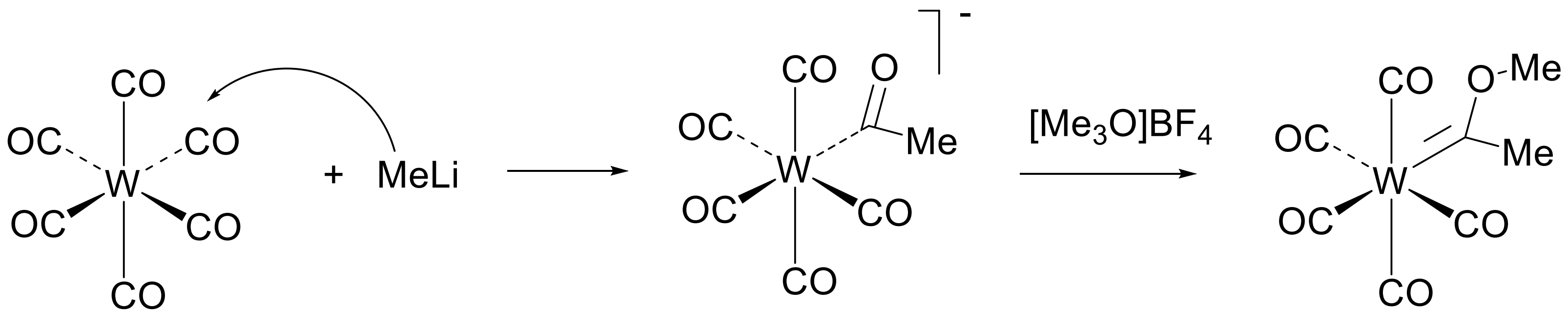


Takasago Menthol Synthesis



K. Tani, T. Yamagata, S. Akutagawa, H. Kumobayashi, T. Taketomi, H. Takaya. A. Miyashita, R. Noyori and S. Otsuka, *J. Am. Chem. Soc.*, 1984, **106**, 5208

Attack on Coordinated ligands



Fischer Carbene

Nucleophilic **Electrophilic**

E. O. Fischer and co-workers

No change in e count

The Wacker Process

$$[PdCl_4]^{2-} + C_2H_4 + H_2O \rightarrow CH_3CHO + Pd + 4\,Cl^- + 2\,H^+$$

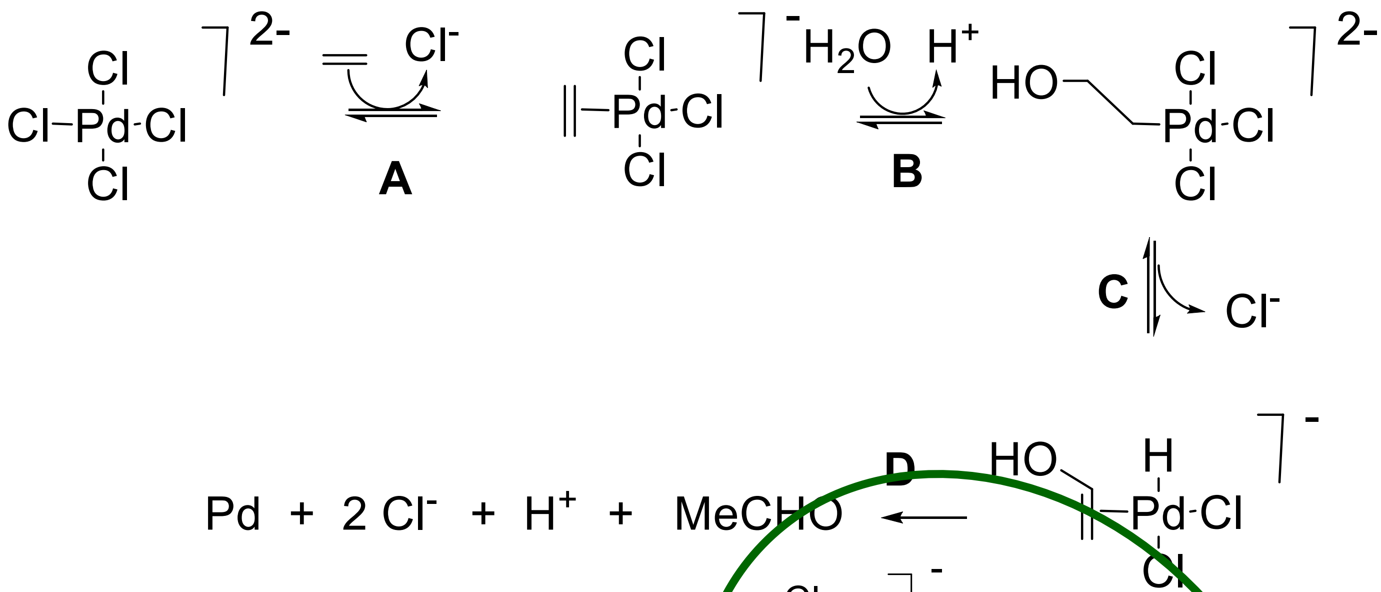
$$Pd + 2\,Cu^{2+} + 4Cl^- \rightarrow [PdCl_4]^{2-} + 2\,Cu^+$$

$$2\,Cu^+ + \tfrac{1}{2}\,O_2 + 2\,H^+ \rightarrow Cu^{2+} + H_2O$$

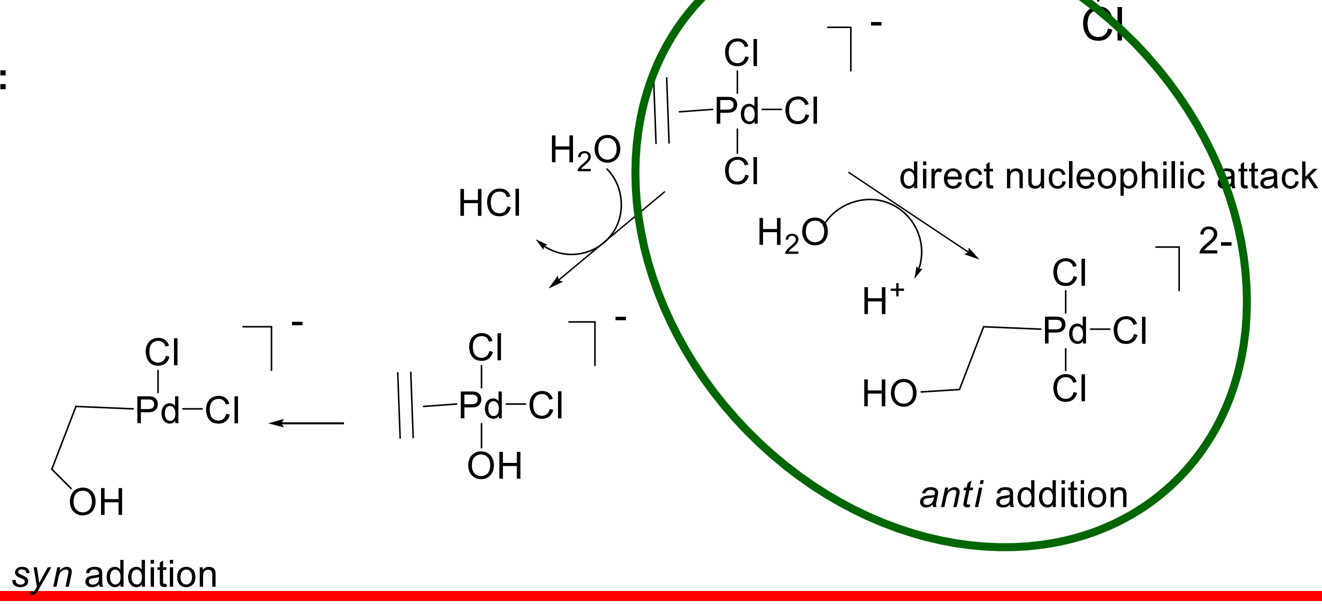
$$C_2H_4 + \tfrac{1}{2}\,O_2 \rightarrow CH_3CHO$$

1970’s 2 M tonnes per year - decreasing

Mechanism



Step B:



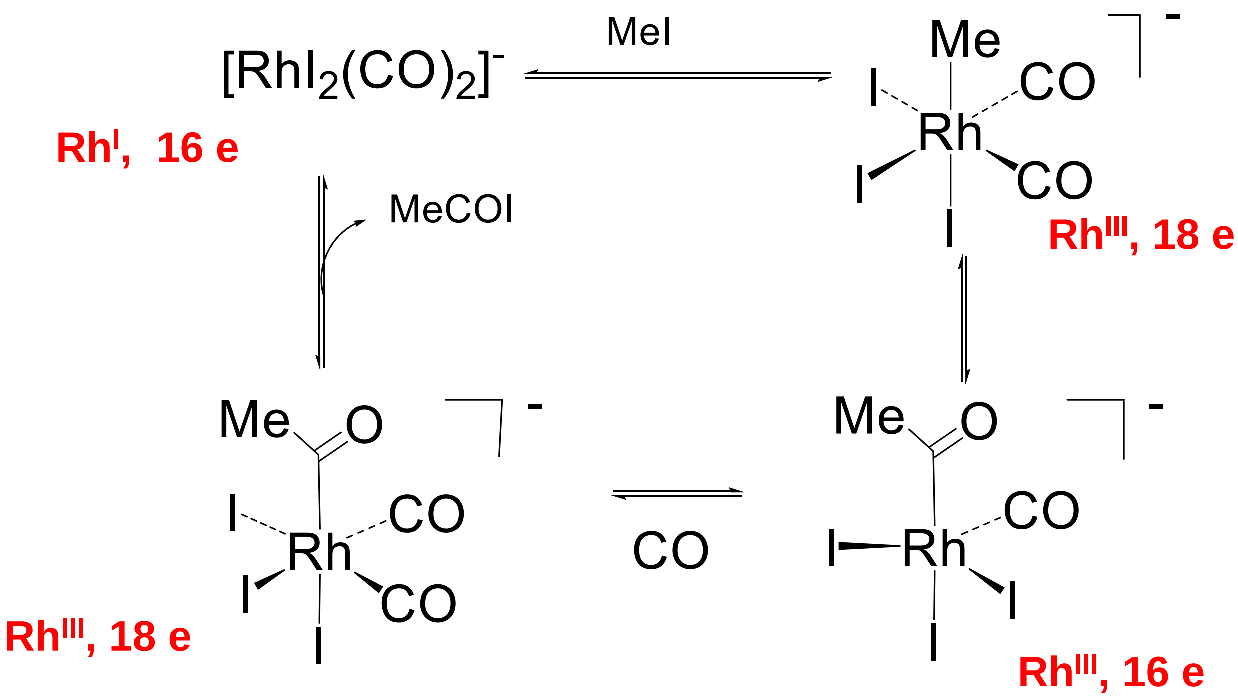
Unit steps in Catalytic reactions

	Change in No of electrons
Introduction of substrates onto metal centre	
- Simple Coordination	+2
- Substitution	0
- Oxidative Addition	+2
- Sigma bond metathesis	0
Reactions between substrates in coordination sphere.	
- Migratory insertion	-2
- Attack of Nucleophiles onto coordinated ligands	0
- β-H abstraction	+2
Releasing substrates from Metal Centre.	
- Decoordination	-2
- Substitution	0
- Reductive Elimination	-2
- Sigma bond metathesis	0

Reverse of introduction

16/18 e Rule

- Catalytic cycles often proceed through a variety of intermediates alternating between 16 and 18 electrons



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ABC chem
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23-26 January, 2018

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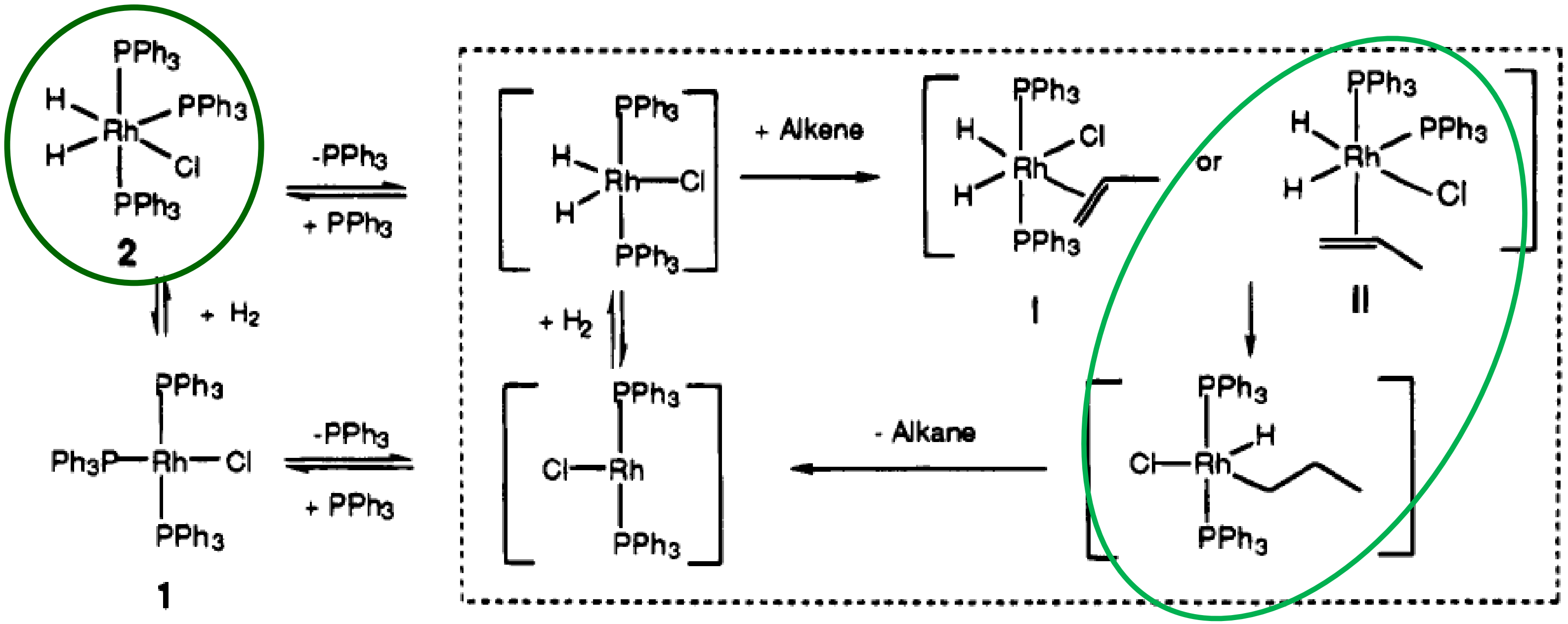
Catalytic hydrogenation (Wilkinson's catalyst)



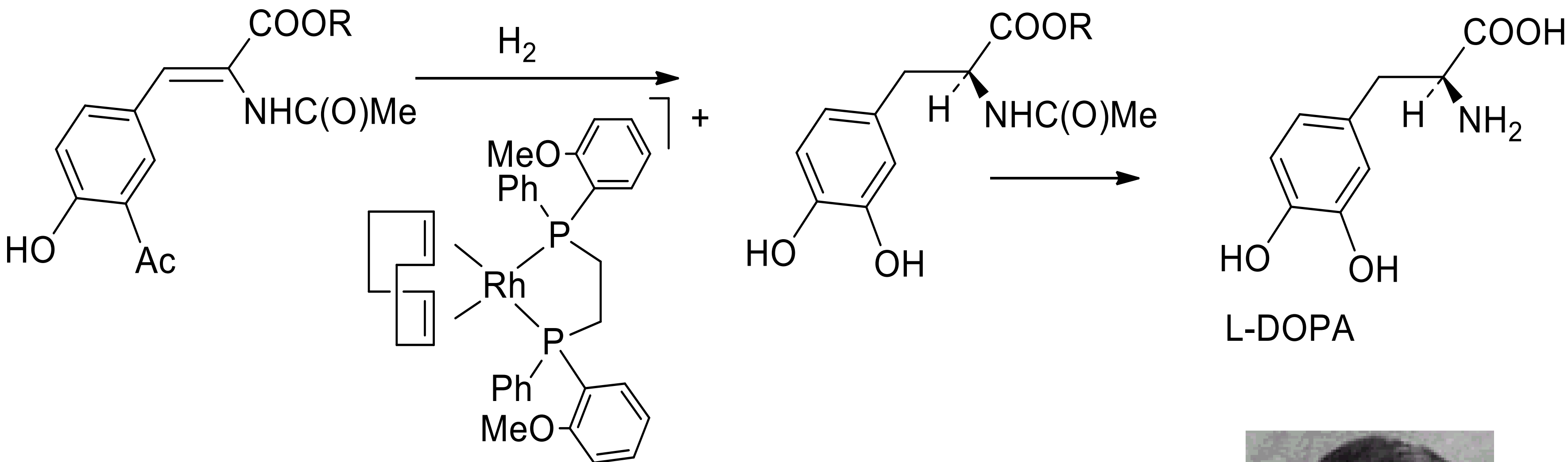
By ^{31}P and ^{1}H NMR spectroscopy see only compound 2 , a resting state outside the catalytic cycle – no information about cycle

Kinetics suggest H migration onto alkene is rate determining

Parahydrogen allows detection of II

Duckett et al, *J. Am. Chem. Soc,* 1994, **116,** 10548

Asymmetric hydrogenation



W. S. Knowles
Nobel Prize, 2001

W.S. Knowles and M.J. Sabacky, *Chem. Commun.*, 1968, 481

Ketone hydrogenation

Rhodium based catalysts are usually of very low activity unless very electron rich (e. g. $[RhH(CO)(PEt_3)_3]$ for aldehyde hydrogenation, J. K. MacDougall et al, *J. Chem Soc. Dalton Trans.,* 1996, 1161)

Ruthenium based catalysts are preferred

Asymmetric Catalysis by Architectural and Functional Molecular Engineering:

Practical Chemo and Enantioselective Synthesis of Ketones

R. Noyori
Nobel Prize, 2001

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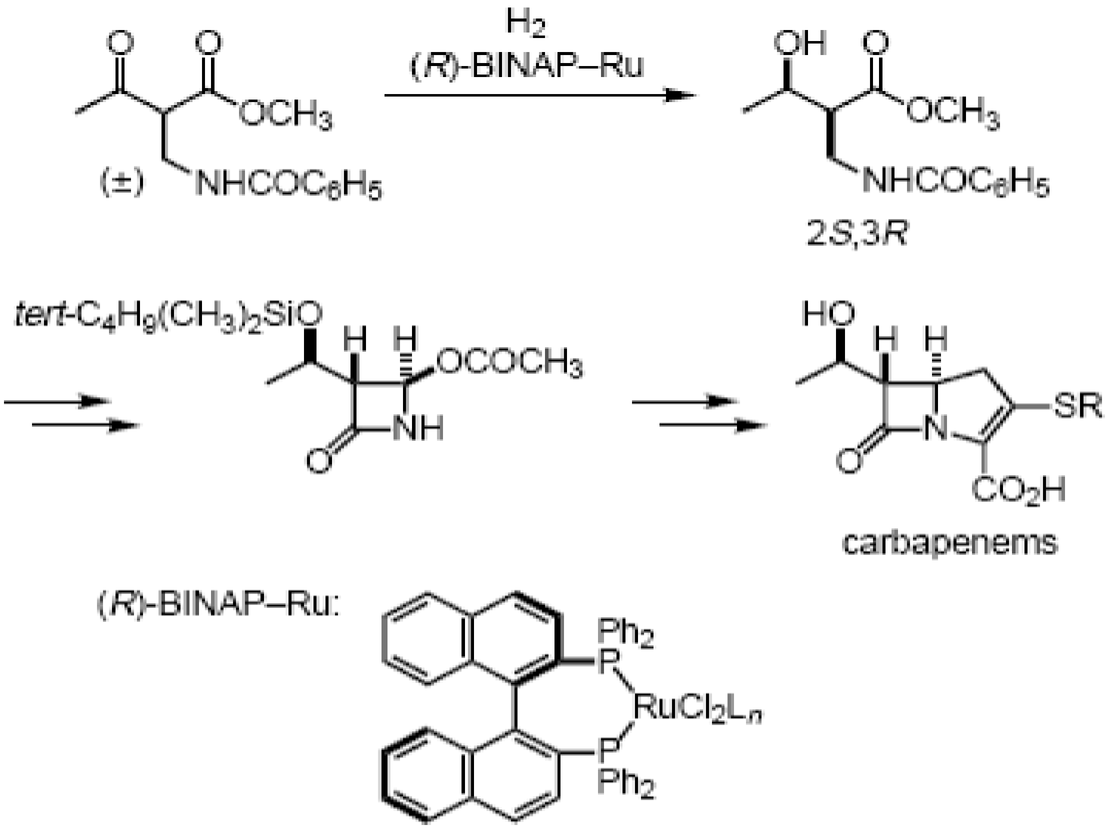
The Edinburgh and St Andrews Research School of Chemistry

R. Noyori and T. Ohkuma *Angew..Chem.Int. Edi.* 2001,**40,** 40-73.

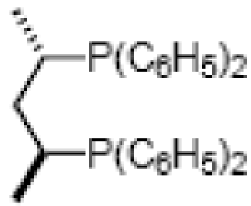
Hydrogenation of activated ketones



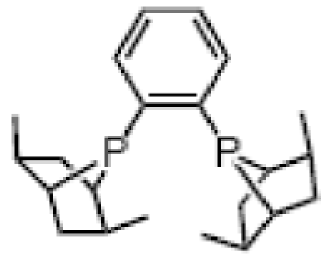
The Edinburgh and St Andrews Research School of Chemistry

R. Noyori and T. Ohkuma *Angew..Chem.Int. Edi.* 2001,**40,** 40-72

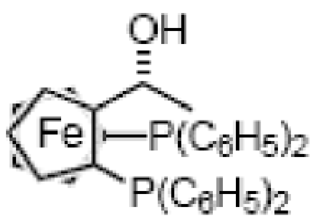
Ligands for asymmetric ketone hydrogenation



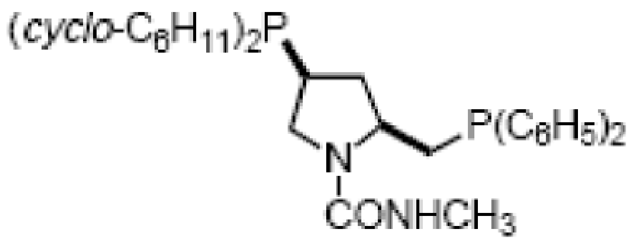
(*S*,*S*)-BDPP



(*R*,*S*,*R*,*S*)-Me-PennPhos

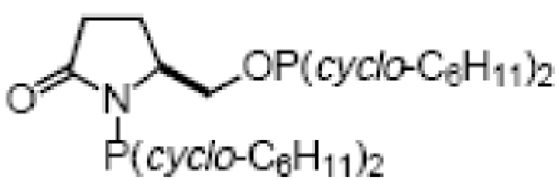


(*R*,*S*)-BPPFOH

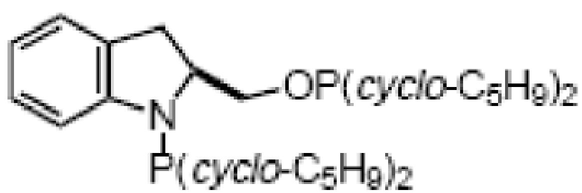


(2*S*,4*S*)-MCCPM

Non-classical ligands



(*S*)-Cy,Cy-OxoProNOP



(*S*)-Cp,Cp-IndoNOP

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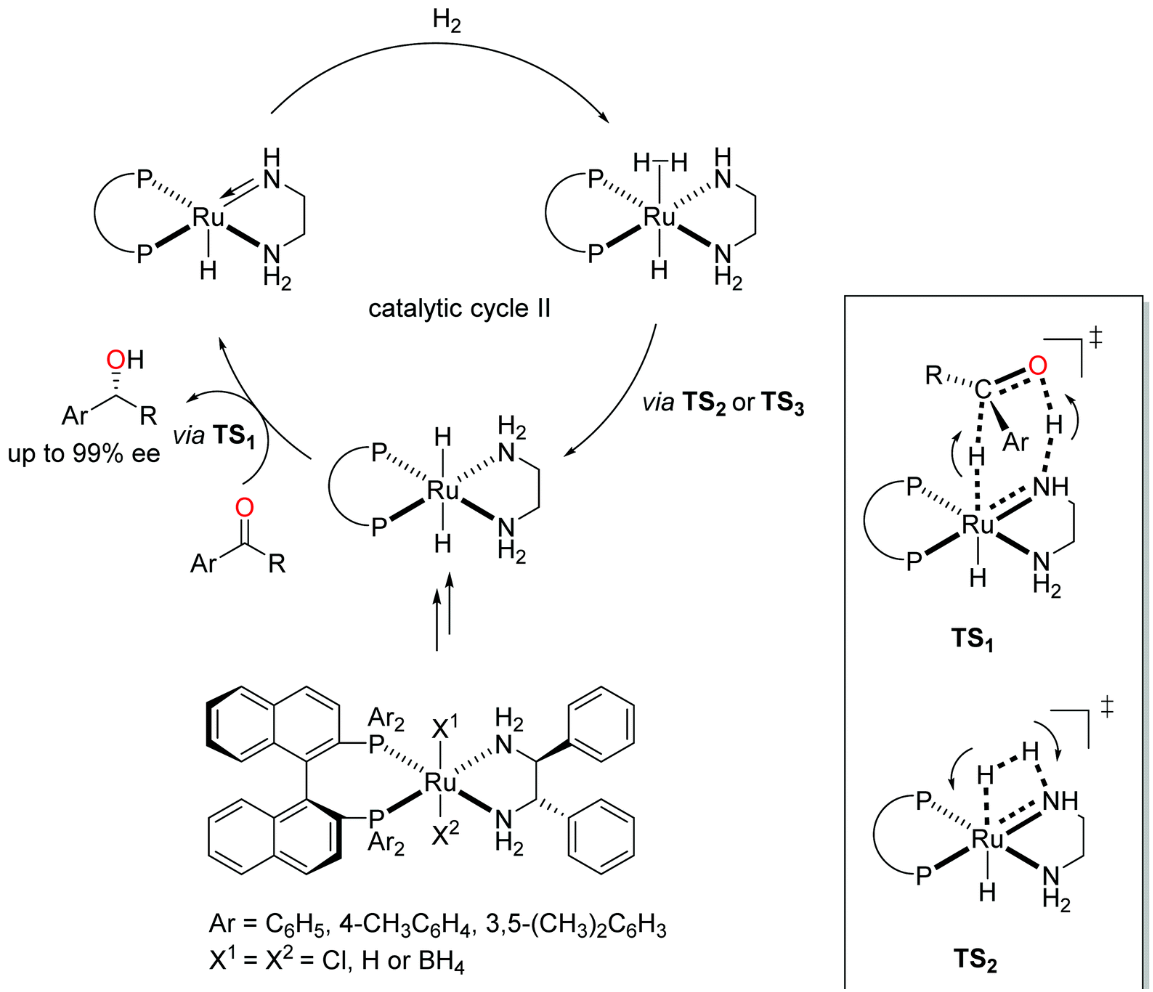
R. Noyori and T. Ohkuma *Angew..Chem.Int. Edi.* 2001,**40,** 40-73.

Outer sphere mechanism

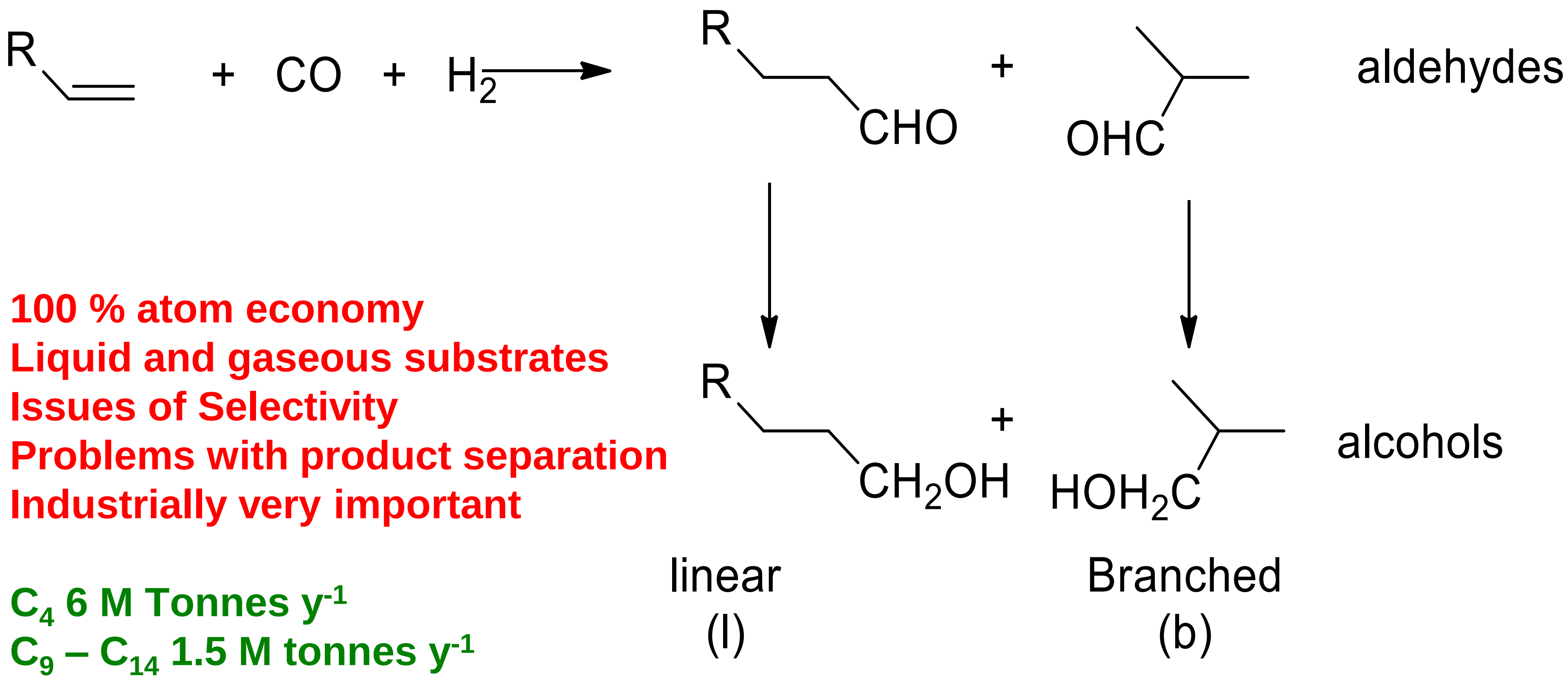
Addition of H^+ and H^-

Substrate does not bind to the metal



P. A. Dub and J. C. Gordon, *Dalton Trans.*, 2016,**45**, 6756

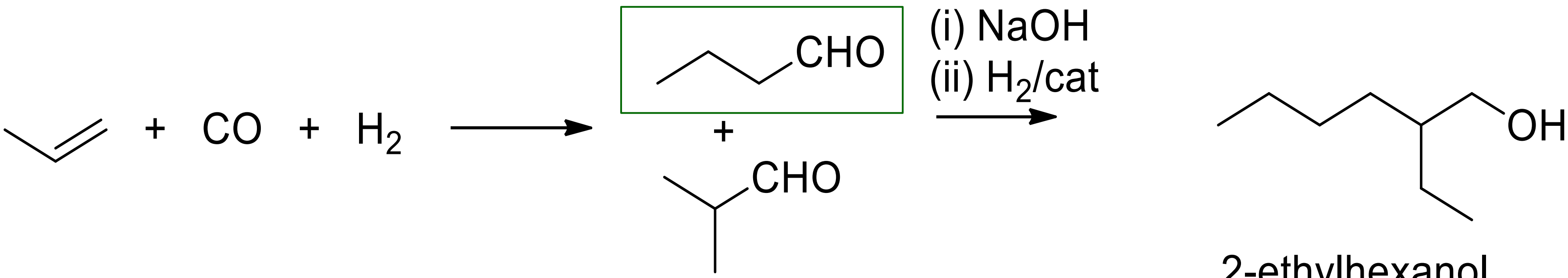
Hydroformylation



100 % atom economy
Liquid and gaseous substrates
Issues of Selectivity
Problems with product separation
Industrially very important

C_4 6 M Tonnes y^{-1}
C_9 – C_{14} 1.5 M tonnes y^{-1}
Plasticisers, soaps, detergents

Butanal

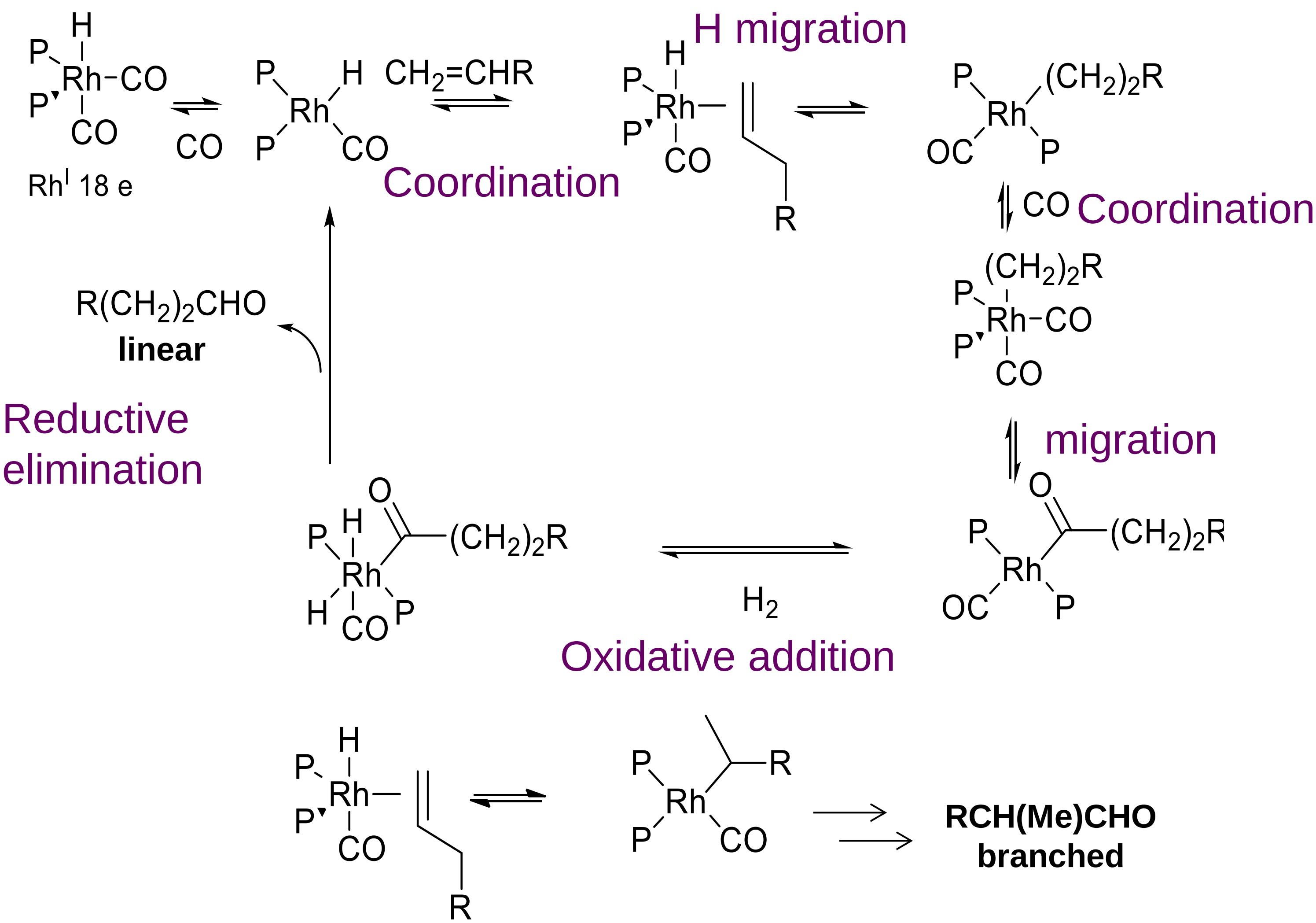


2-ethylhexanol

High linear selectivity is essential

Plasticiser for PET

Hydroformylation mechanism



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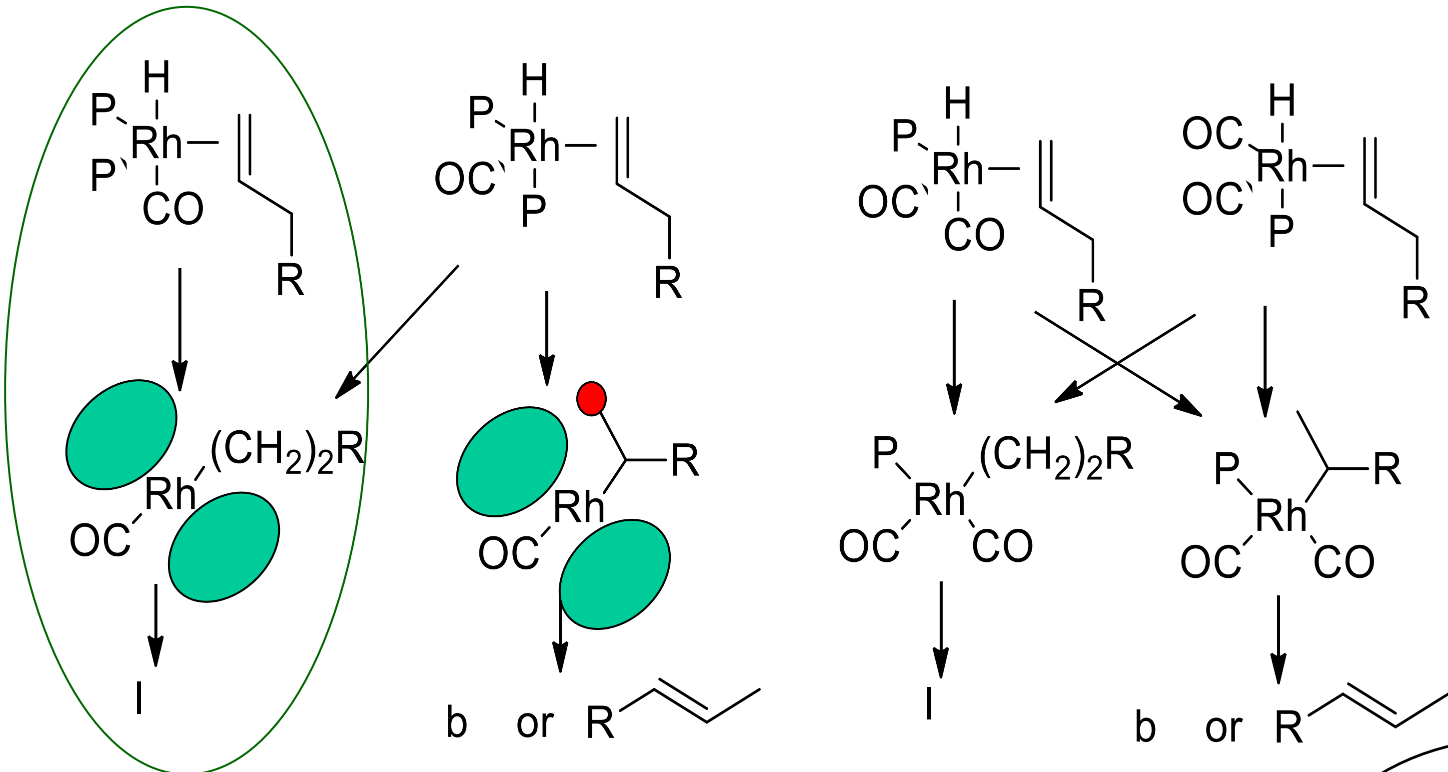
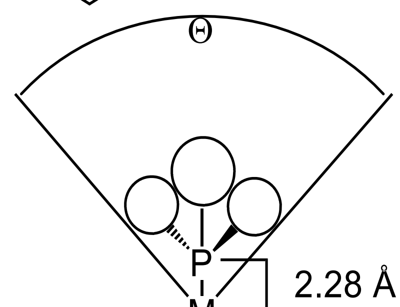
Linear branched selectivity



2 P equatorial (ee) – angle is 120º
1 P equatorial, 1 axial – angle is 90 º

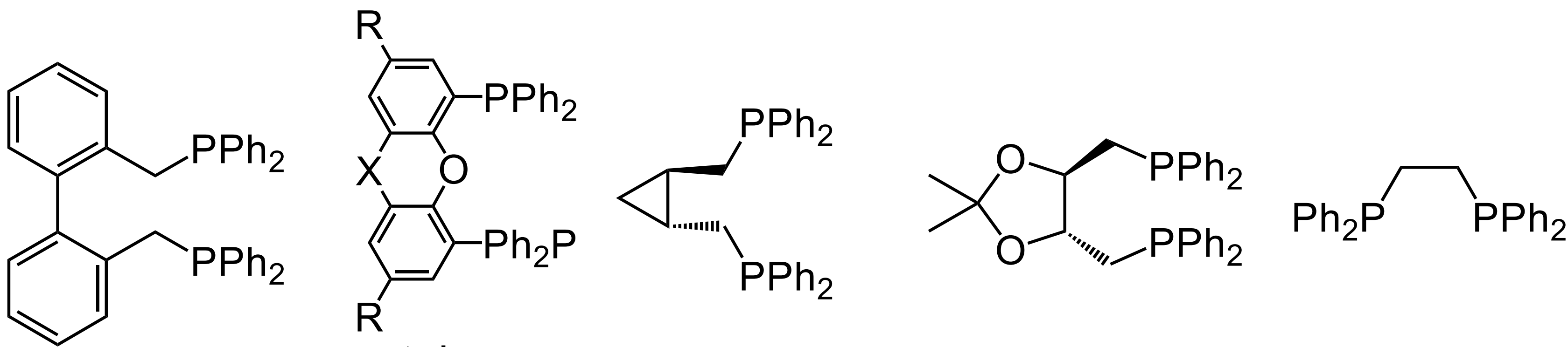


Tolman's cone angle Θ

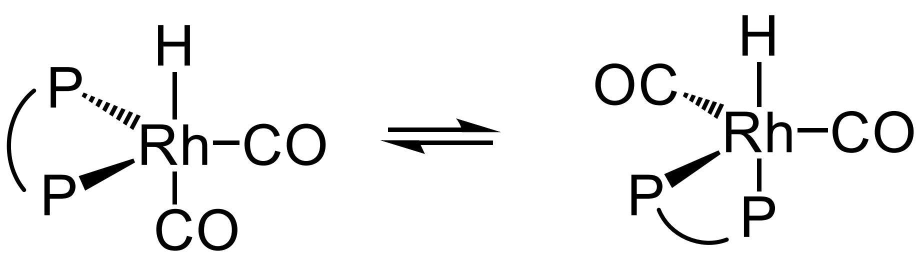
For high linear selectivity – need

- **excess of large ligands e. g. PPh_3 Rh:P = 30:1, l:b = 15**
- **Low p_{CO}**
- **OR bidentate ligand with a bite angle near 120º**

Structure-selectivity relation

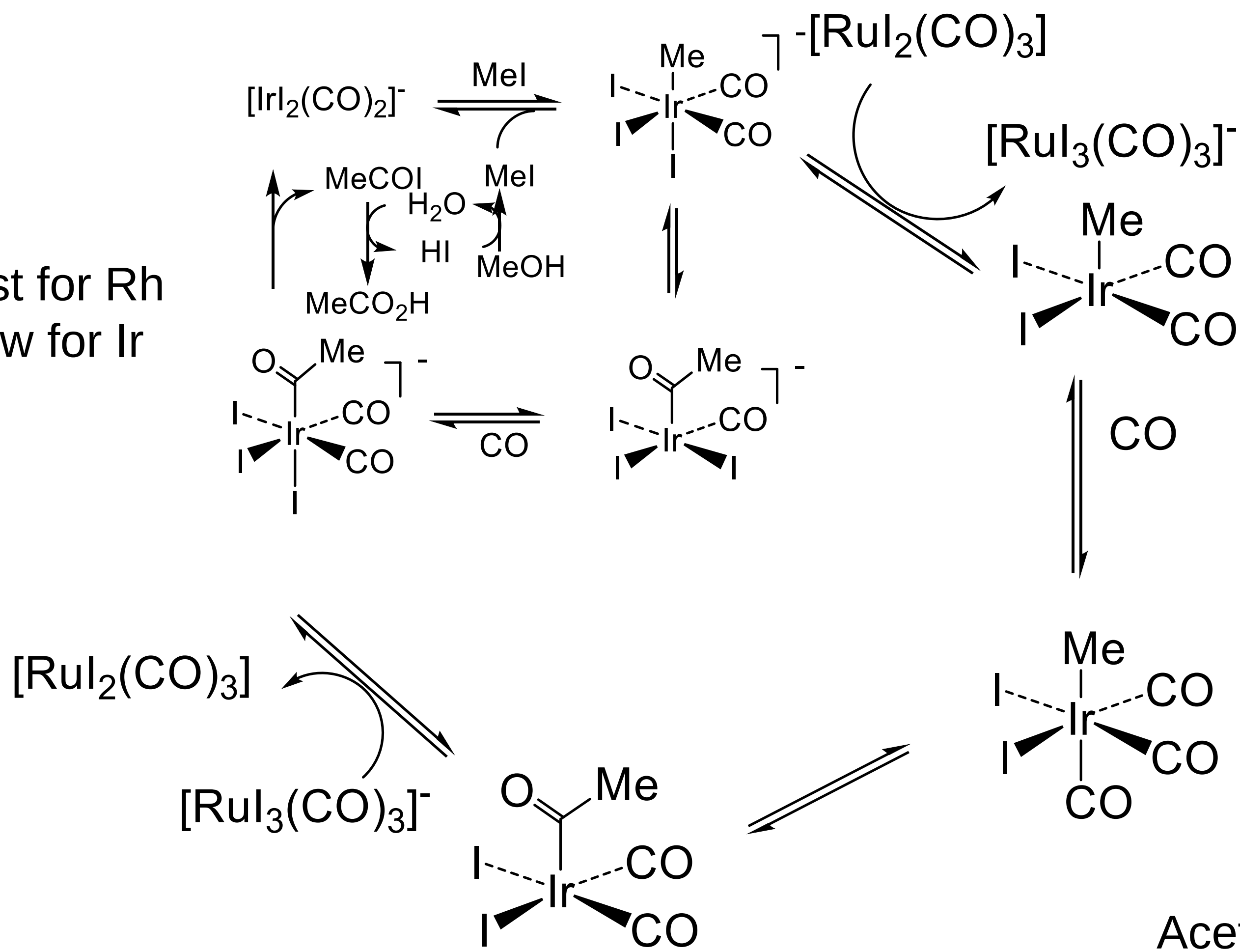


	BISBI	xantphos	*trans*-dppm-cyp	DIOP	dppe
bite angle	113°	111 °	107°	102°	85°
l : b	66	49	12	8.5	2.1



Carbonylation of methanol (Cativa)

Fast for Rh
Slow for Ir



Anionic
Ox Addn fast
Migration v slow

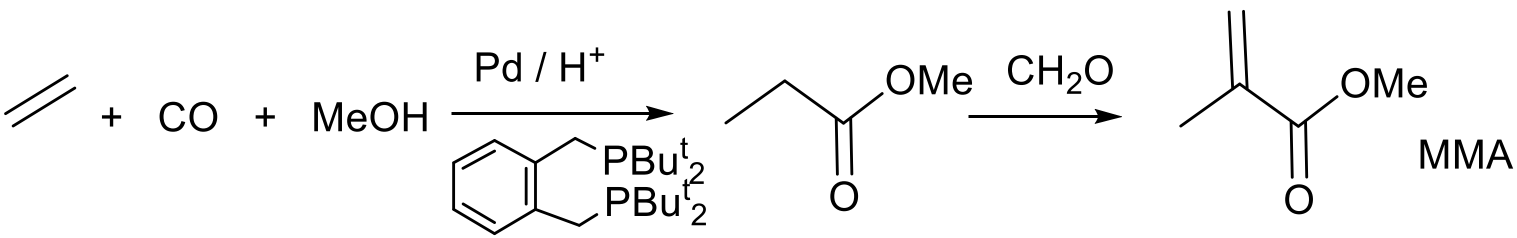
Neutral
Ox addn slow
Migration fast

Need to cycle
Between two

Acetic acid 16 M tonnes pa

A. Haynes, P. M. Maitlis, G. E. Morris, G. J. Sunley, et al*J. Am. Chem. Soc.*, 2004, **126**, 2847-2861.

Ethene carbonylation (Lucite)

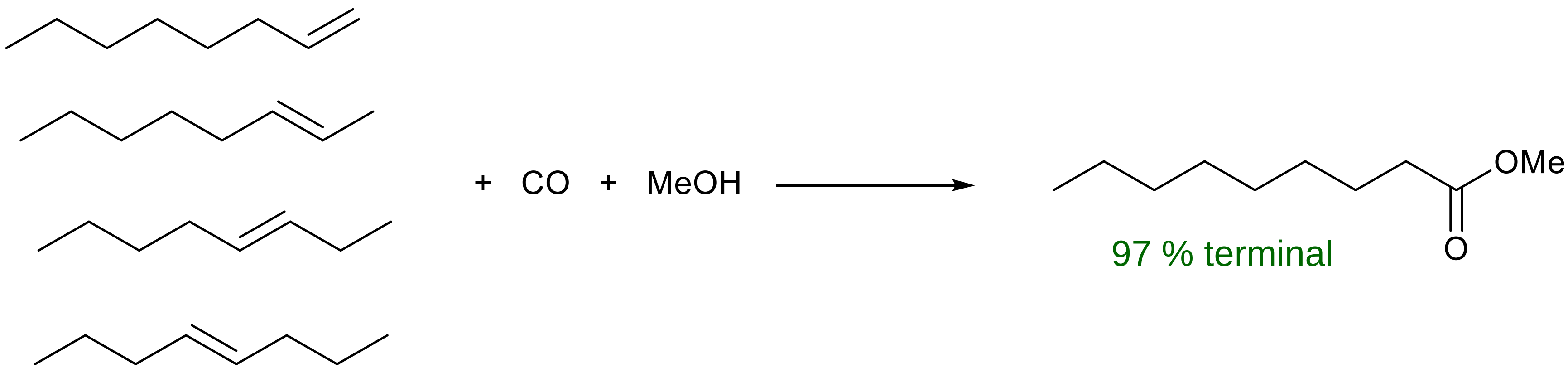


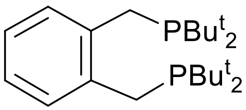
TOF = 12,000 h^{-1} TON = > 1,000,000 Selectivity = 99.9 %

120,000 tonnes per year
Singapore

D. Johnson, http://www.soci.org/chemistry-and-industry/cni-data/2009/20/a-winning-process

Methoxycarbonylation of alkenes



[$Pd_2(dba)_3$] (0.05 mmol) 

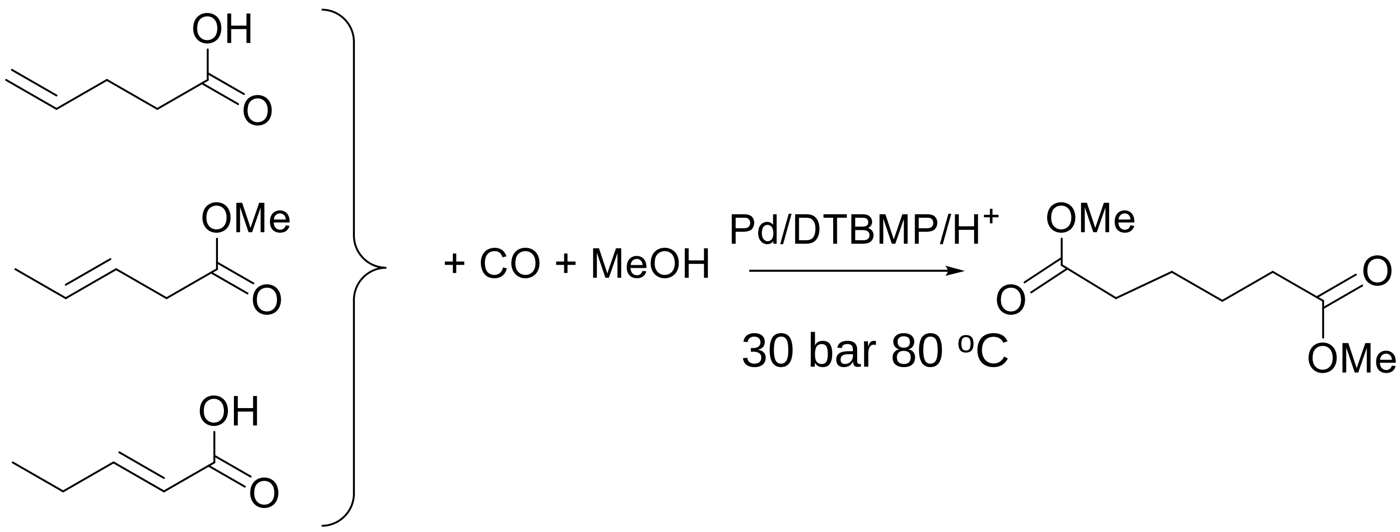
(0.5 mmol)

CH_3SO_3H (1 mmol), alkene (12.7 mmol), methanol (10 cm^3),

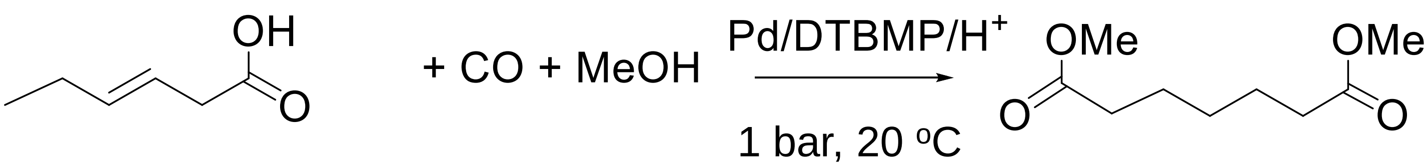
CO (1-4 bar) 20 ^oC, 3 h

C. Jiménez Rodriguez, D. F. Foster, G. R. Eastham, and D. J. Cole-Hamilton, *Chem. Commun.*, 2004, 1720-1721

Isomerisingmethoxycarbonylation of unsaturated esters



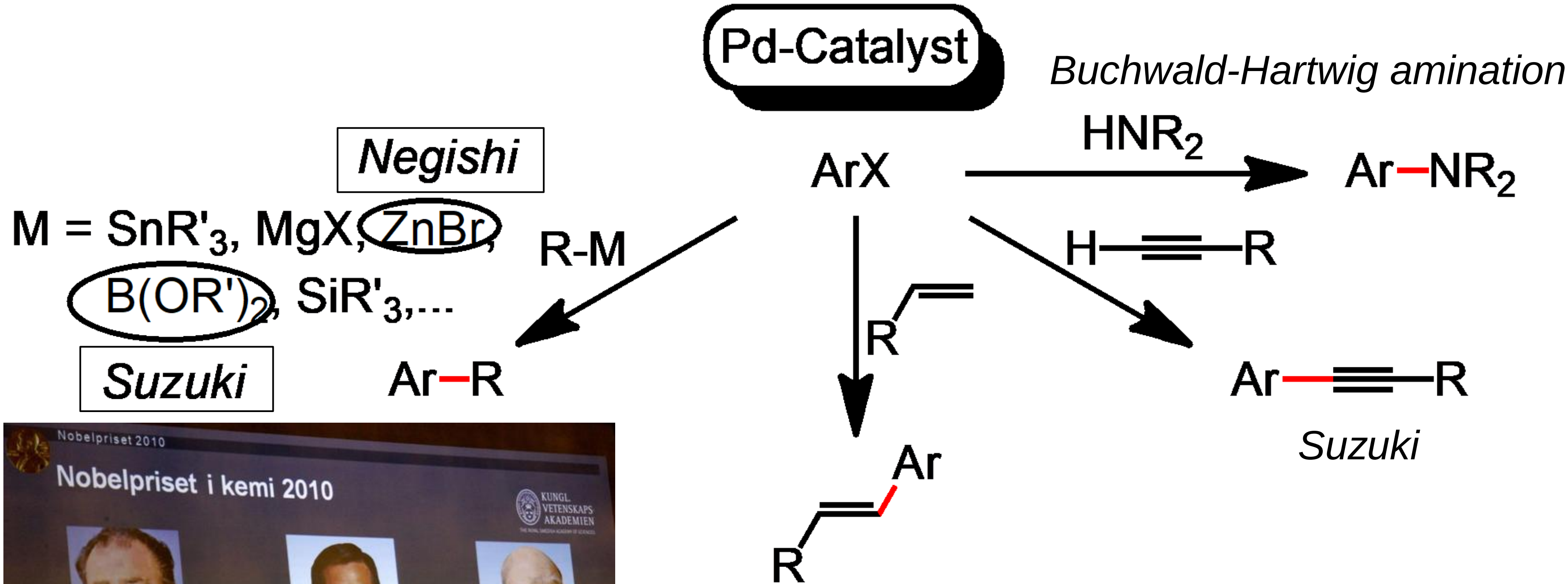
Conv %	Sel %
100	96.3
100	99
100	97.3



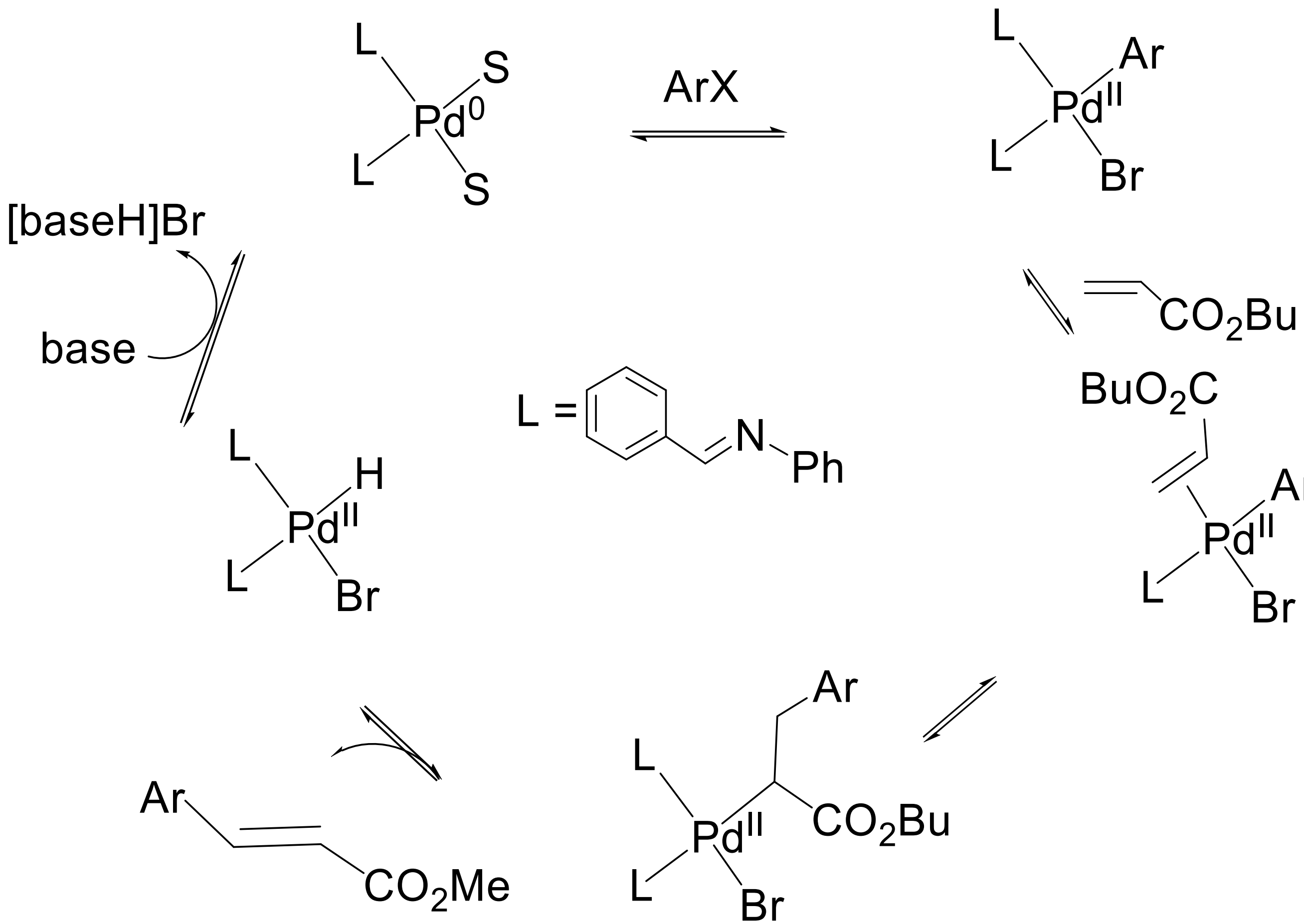
Conv %	Sel %
17.3	100

C. Jiménez Rodriguez, G. R. Eastham and D. J. Cole-Hamilton, *Inorg. Chem. Commun.*, 2005, **8**, 878.

Cross coupling reactions: a success story

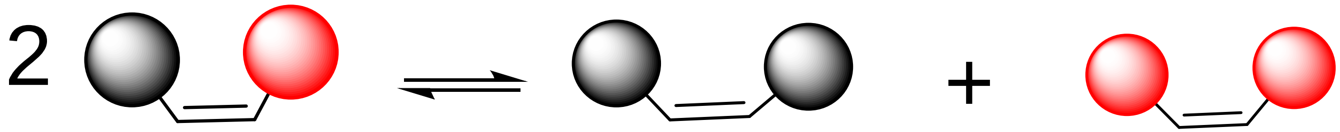


Heck Coupling Mechanism



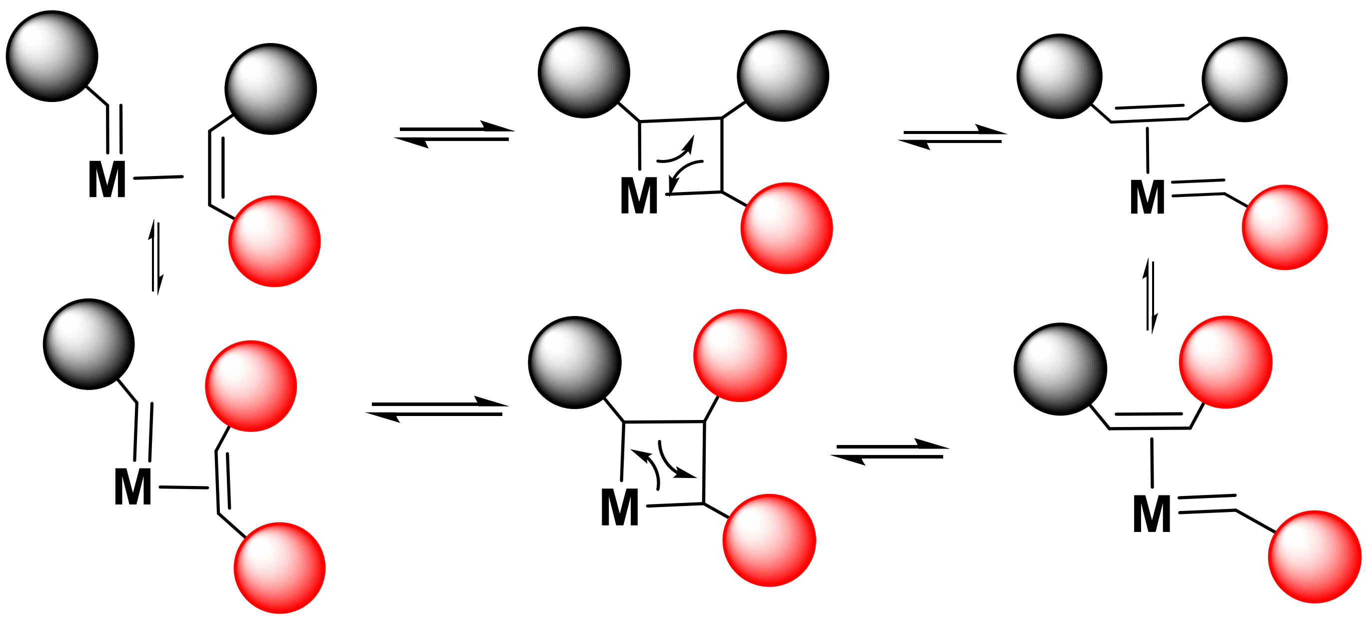
Blackmond and coworkers, *Angew Chem. Int. Ed*. 2005, **44**, 4302; *J. Am. Chem. Soc.*, 2001, **123**, 1848

Alkene Metathesis

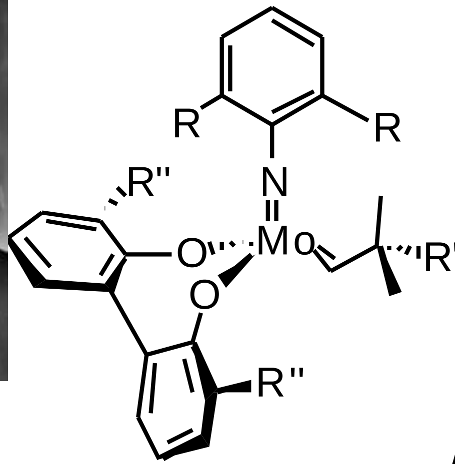


Cross-Metathesis

metathesis: from Greek *meta*, change; *tithenai*, place

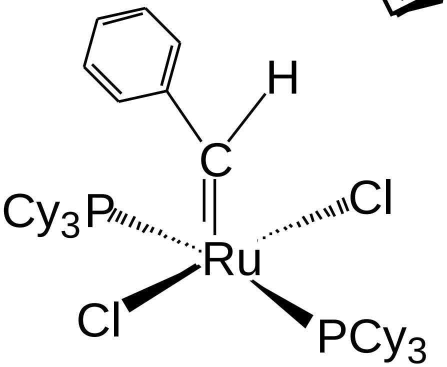


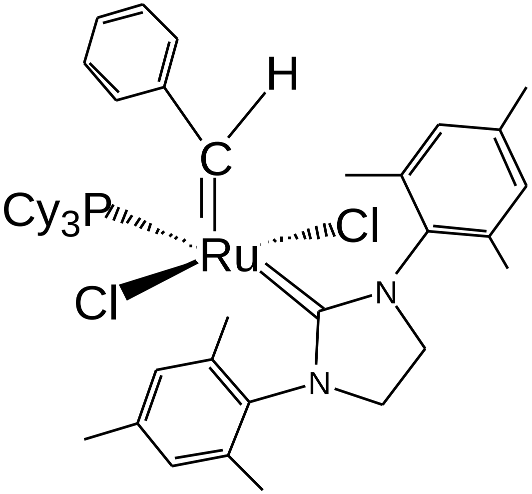
Well-Defined Metathesis Catalysts



- **Schrock**
- **Range of biphen / binaphtholates**
- **tunable: ARCM, chiral ROMP**

- **Grubbs “2nd generation”**





- **Grubbs I**
- **Robust (>> tolerant of air, water, polar functional-groups)**
- **Very wide range of processes catalyzed by Ru**

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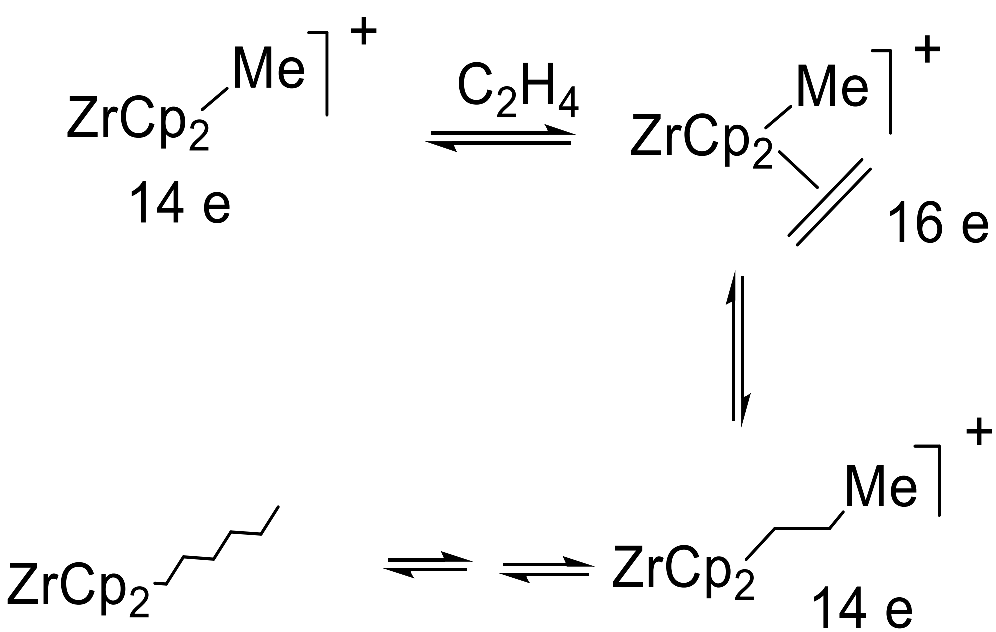
Nobel Prize, 2005 with Yves Chauvin

Ethene polymerisation

Cp_2ZrMe_2 + MAO ⟶ $[Cp_2ZrMe]^+$

partially hydrolysed Me_3Al



W. Kaminsky, K. Kulper, H. H. Brintzinger and F. Wild, *Angew. Chem.-Int. Edit. Engl.*, 1985, **24**, 507

Oil - What next?

Fuels ?

Demand is too high
Land use, fuel vs food
Contribution
10 % biodiesel in UK diesel

4 %
Chemicals ?

Using waste streams are best

Waste Oils

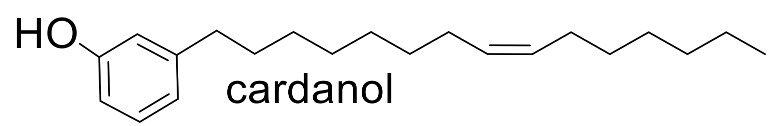
Tall Oil (paper)

Kraft Process

$NaOH$ / Na_2S

2 M tonnes per year

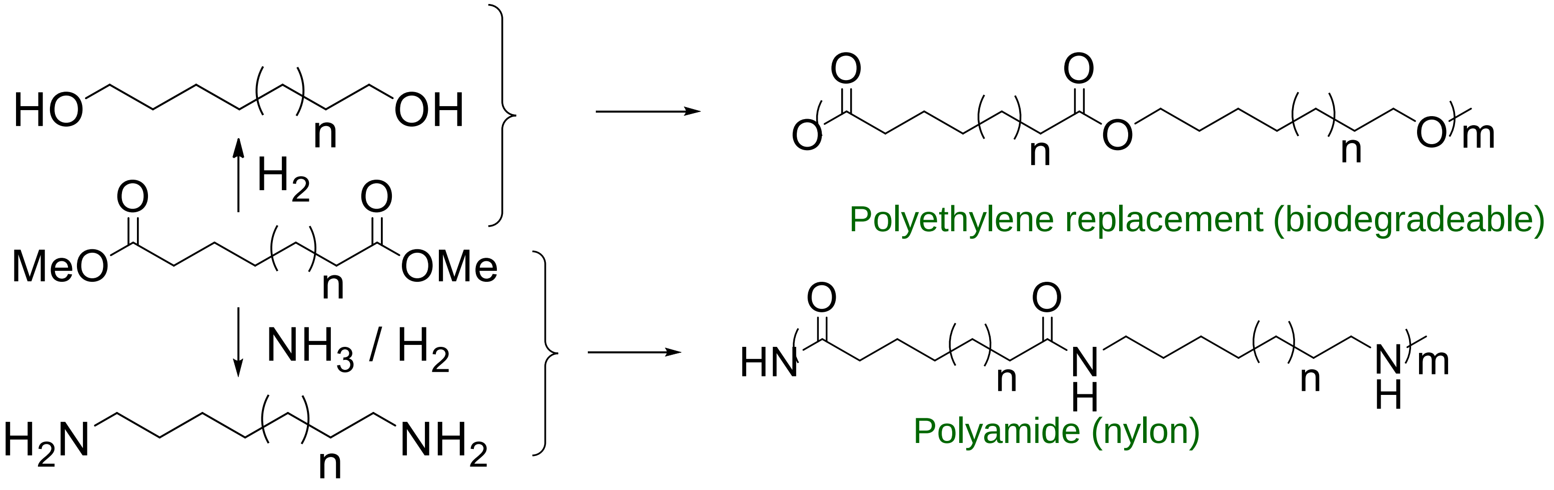
Cashew nut shell liquid (food)



300,000 tonnes per year

85 %

Uses of α,ω–difunctionalised compounds



Fibres | Elastomers
Thermoplastics | Melt adhesives
Coatings | Engineering plastics,
Nylons (2 M tonnes per year).

Overall 3 M tonnes per year

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D. Quinzler and S. Mecking, *Angew Chem.* 2010, **49**, 4306; F. Stempfle, D. Quinzler, I. Heckler, S. Mecking, *Macromolecules* 2011, **44**, 4159-4166

Biodegradable

Desirable

Undesirable

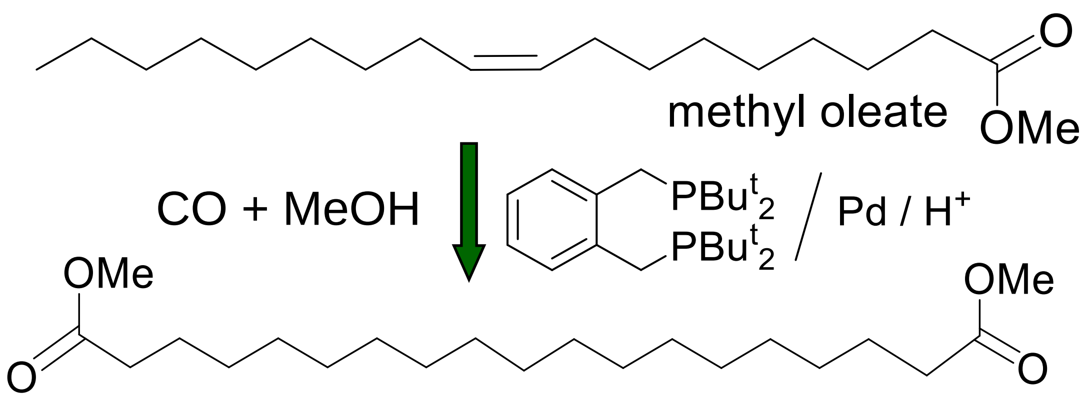
Manila Harbour

Oilprice.com

Gas pipeline

(HDPE 50 % of all polyethylene)

Oleochemicals



dimethyl nonadecanedioate

Methyl ester	Yield (sat diester)/%	linear selectivity / %	Other prods (%)
oleate	95	> 95	

25 g

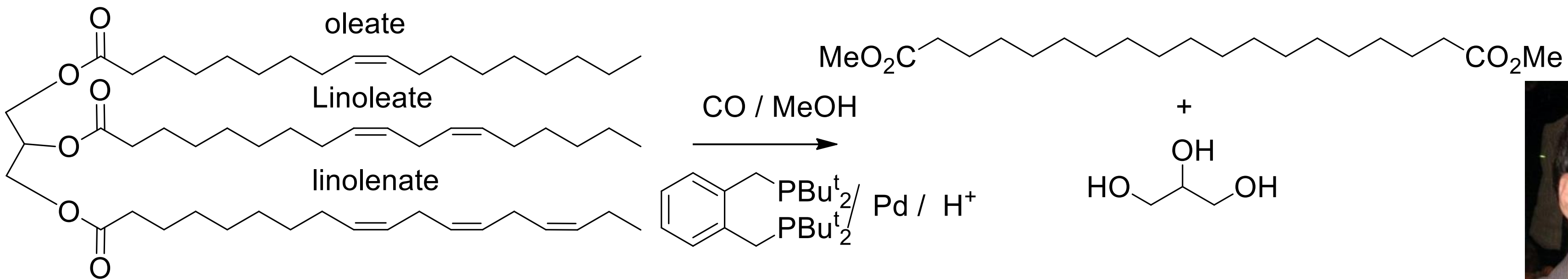
[Pd] = 0.008 mol dm^{-3}, [DTBPMB] = 0.04 mol dm^{-3}, [MSA] = 0.08 mol dm^{-3}, substrate (2 cm^3, 6 mmol), methanol (10 cm^3), p_{CO} = 30 bar, 80 °C, 22 h,

C. Jimenez-Rodriguez, G. R. Eastham and D. J. Cole-Hamilton, *Inorg. Chem. Commun.*, **2005,** *8*, 878

High oleic sunflower oil – 3.5 kg in 12 dm^3 autoclave

G. Walther, J. Deutsch, A. Martin, F.-E. Baumann, D. Fridag and A. Köckritz, *ChemSusChem*, 2011, **4**, 1052

Methoxycarbonylation of natural oils

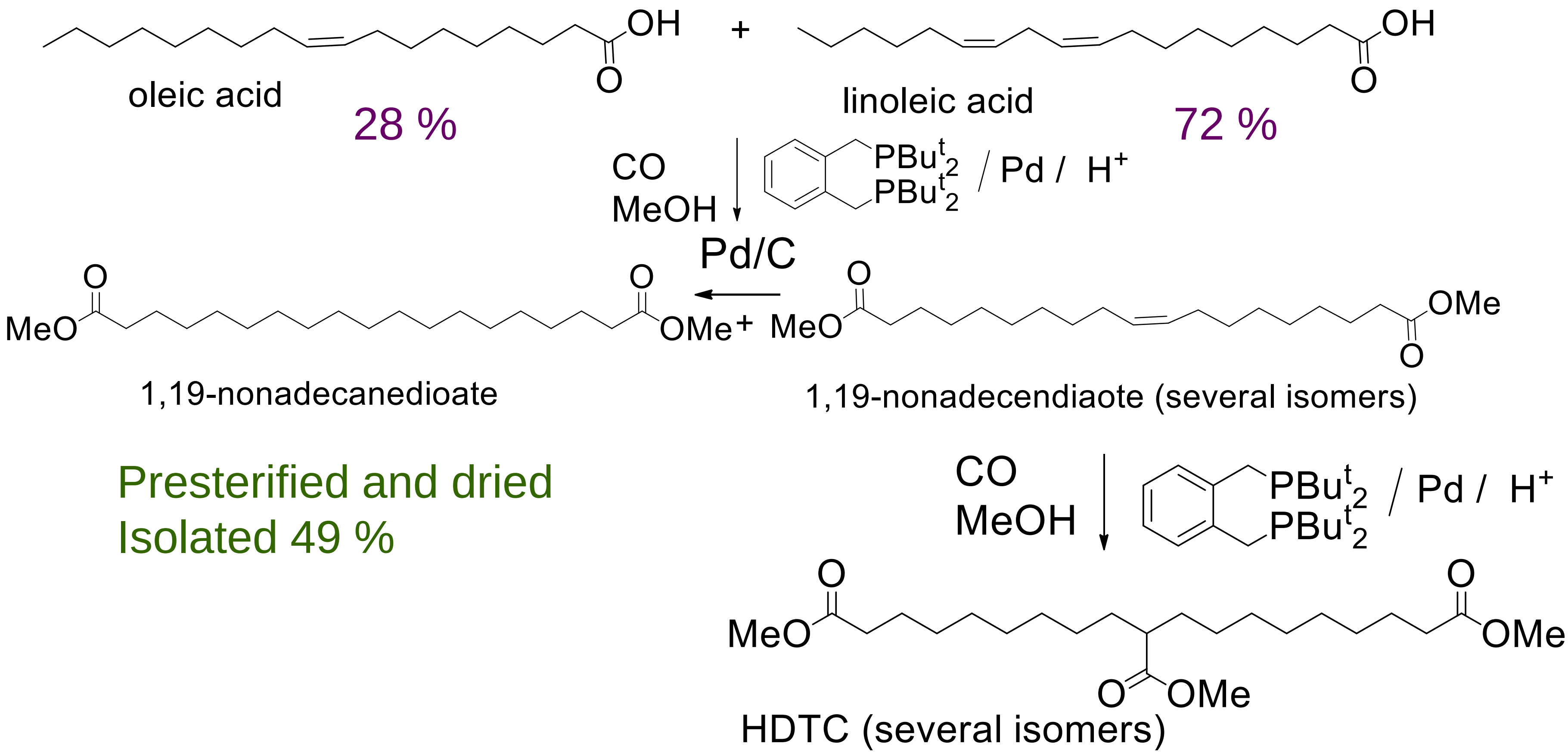


	Methyl oleate (Aldrich)	Olive (Tesco)	Rapeseed (Tesco)	Sunflower (Tesco)
Oleate / %	>90	73	64	38
Linoleate / %		2	19	50
Linolenate / %		3	10	2
Diester / g from 10 mL oil	9.0	6.9	6.4	3.4
Yield / % (from oleate)		74.7 102.3	69.3 108.3	36.8 96.8
Cost of diester / kg^{-1}	$ 6500 (>99 %) $ 50 (70 %)	$ 4.3	$ 1.3	

Marc Furst

M. R. L. Furst, R. le Goff, D. Quinzler, S. Mecking and D. J. Cole-Hamilton, *Green. Chem.* 2012, **14**, 472

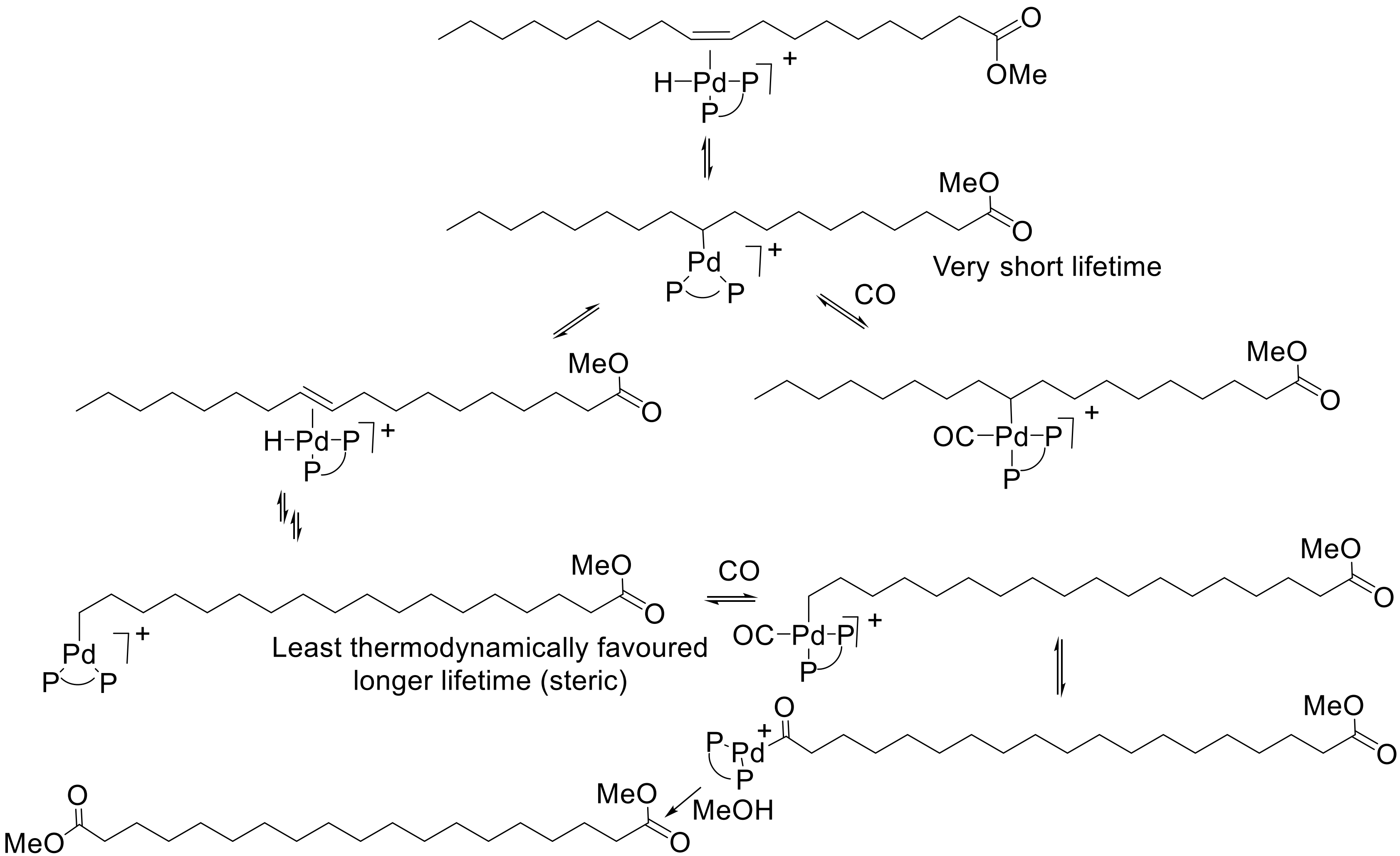
Tall Oil Fatty Acids (TOFA)



Presterified and dried
Isolated 49 %

M. R. L. Furst, T. Seidensticker and D. J. Cole-Hamilton, *Green Chem.*, 2013, **15**, 1218

Why so selective?



Catalyst recovery and recycling

D. J. Cole-Hamilton, *Science,* 2003*,* **299**, 1702

D. J. Cole-Hamilton and R. P. Tooze, eds.,
Catalyst Separation, Recovery and Recycling; Chemistry and Process Design, Springer, Dordrecht, 2006

Hydroformylation Conditions

Parameter	Cobalt /(+phosphine)	Rhodium / PPh_3
Temperature / ^oC	120-160 (150-190)*	80-120
Pressure / bar	270-300 (40-100)	12-25
l:b	3:1 (10:1)	12:1
Side reactions	(Alkanes, *alcohols*, esters, acetals)	Condensed aldehydes (used as solvent)
Stability	Stable to high T	Decomposes at 110 ^oC
Catalyst recovery	Difficult but possible	Easy <C_7

* Rate is reduced by a factor of 4-6

Problems with Homogeneous Catalysts

- - Separation of the solvent, catalysts and product
- - Recycling of the catalyst
- - The use of volatile organic solvents
- - Batch or batch continuous processing

The separation problem

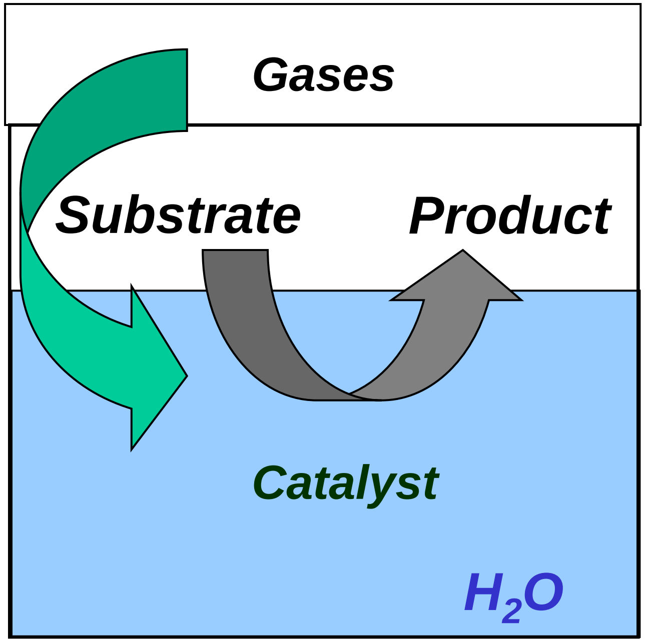
Please make me
a cup of coffee

Now please bring me:

- The pure coffee
- The pure sugar
- The pure milk
- The pure water

All from this cup of coffee
All with 100 % recovery

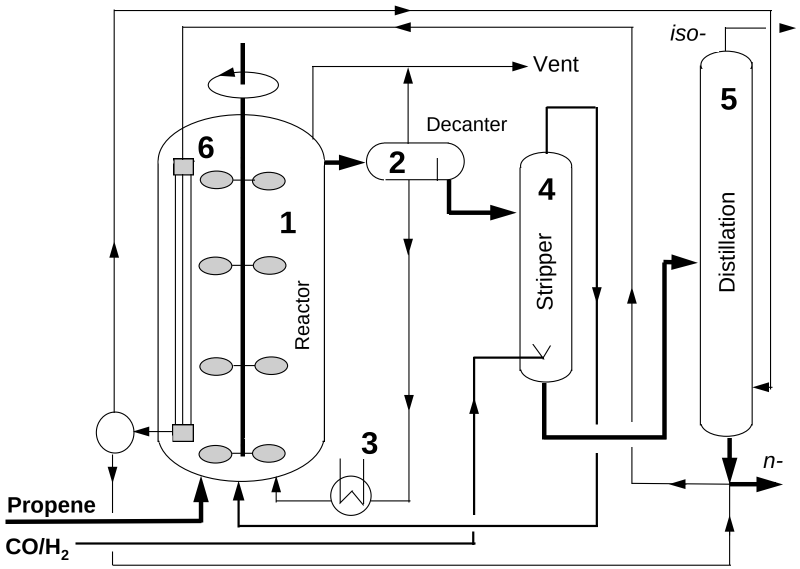
Aqueous biphasic catalysis



Originally proposed by **J. Manessan** in *Progress in Research*, Eds F. Basolo and R. L. Burwell, Plenum Press, London, 1973, p 183

Originally demonstrated by **E. Kuntz**, Fr. Demande, 1975, 2,314,910

Ruhrchemie Reactor

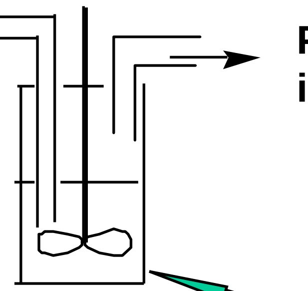


< 1 ppb Rh loss

Only operational for propene
Low solubility of higher alkenes limits mass transfer

E. Wiebus and B. Cornils in *Catalyst separation, recovery and recycling: Chemistry and process Design,* Eds D. J. Cole-Hamilton and R. P. Tooze, Springer, Dordrecht, 2006, p 105

Continuous flow reactor for low volatility substrates and products



Solvent

- \- Involatile
- \- Insoluble in $scCO_2$
- \- Dissolves catalyst

Catalyst

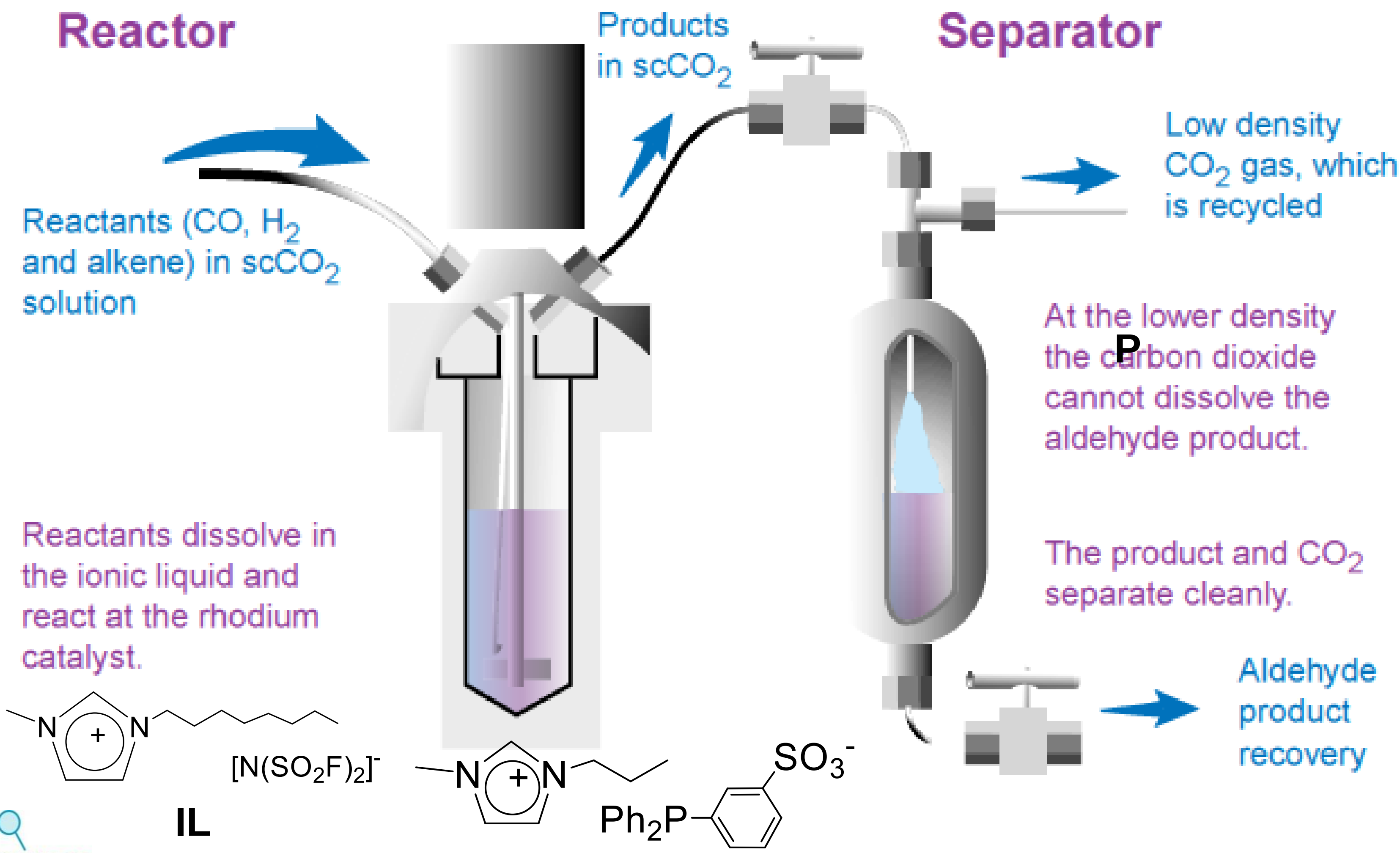
- \- Soluble in solvent
- \- Insoluble in $scCO_2$

IONIC LIQUID?

IONIC CATALYST

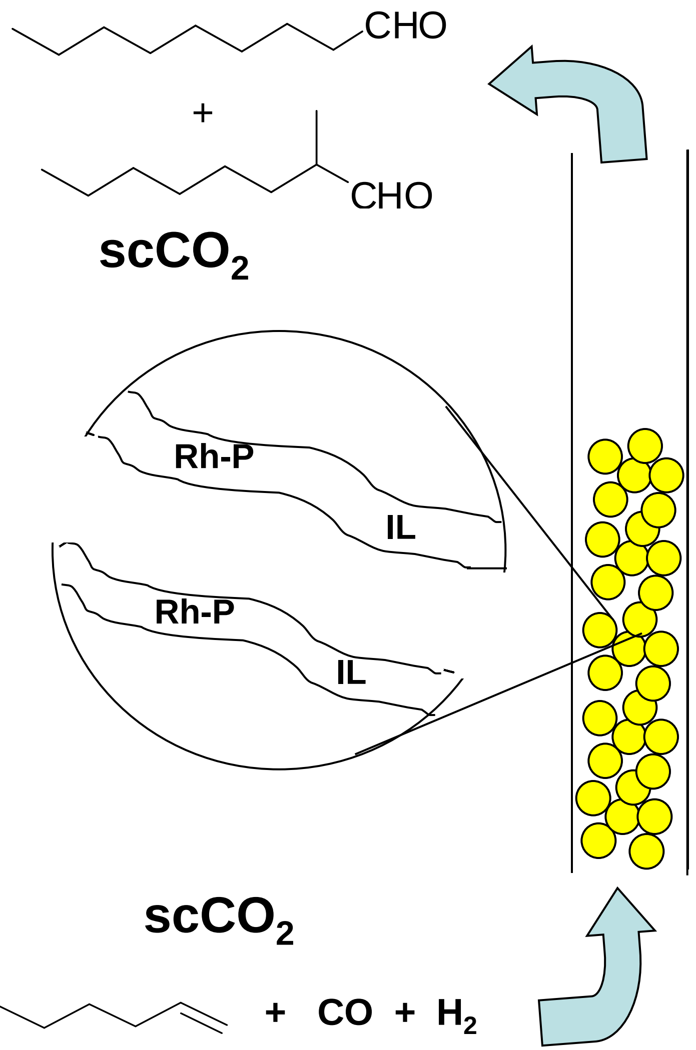
P. B. Webb, M. F. Sellin, T. E. Kunene, S. Williamson, A. M. Z. Slawin and D. J Cole-Hamilton, *J. Am. Chem. Soc.*, 2003, 125, 15577

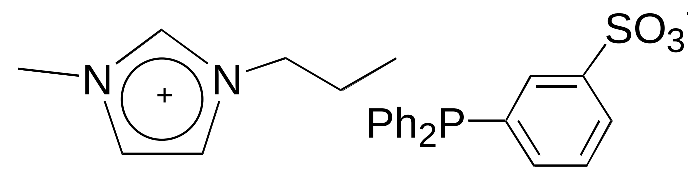
Flow homogeneous catalysis



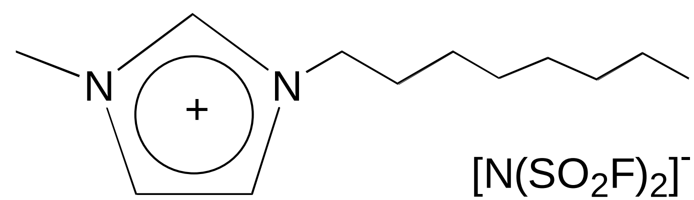
D. J. Cole-Hamilton, *Science*, 2003, **299**, 1702-1706

SILP hydroformylation with SCF flow





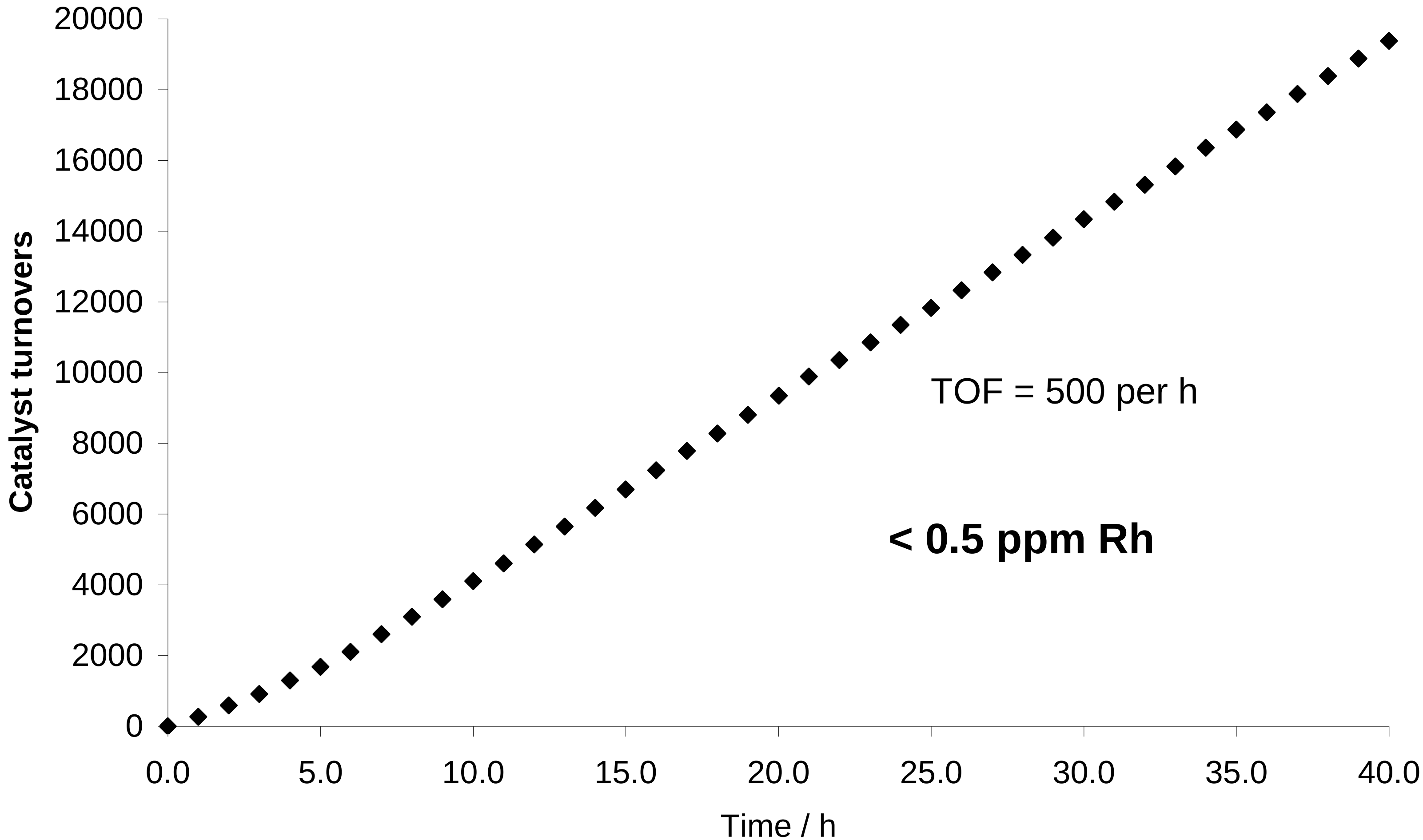
P



IL

U. Hintermair, Z. Gong, A. Serbanovic, M. J. Muldoon, C. C. Santini and D. J. Cole-Hamilton, *Dalton Trans*, 2010, 39, 8501

Catalyst stability



U. Hintermair, G. Y. Zhao, C. C. Santini, M. J. Muldoon, and D. J. Cole-Hamilton
Chem. Commun., 2007, 1462

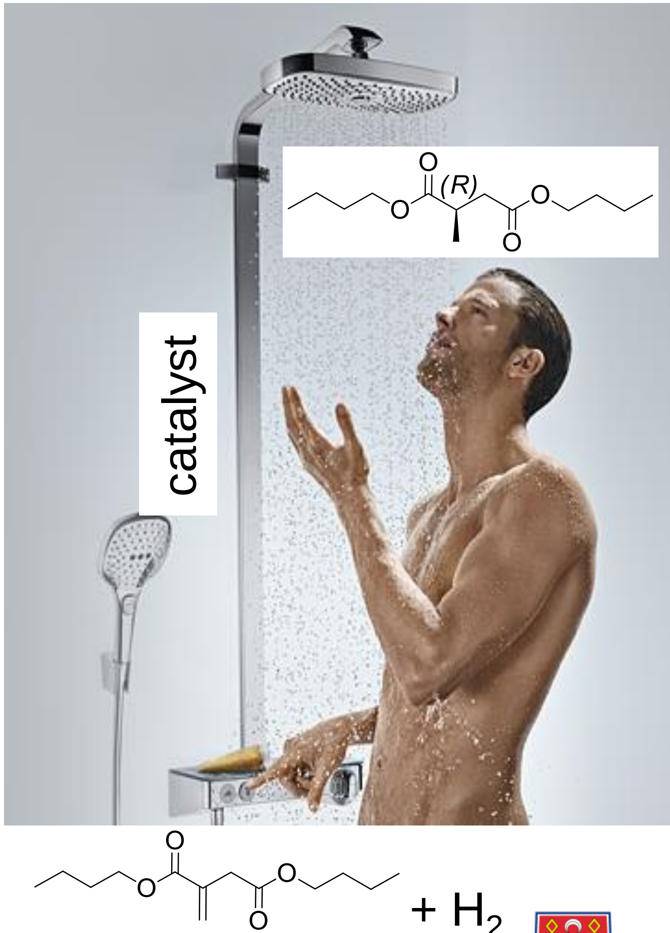
What we really want

It does, for example, no good to offer an elegant, difficult and expensive process to an industrial manufacturing chemist, whose ideal is something to be carried out in a disused bathtub by a one-armed man who cannot read, the product being collected continuously through the drain hole in 100% purity and yield.

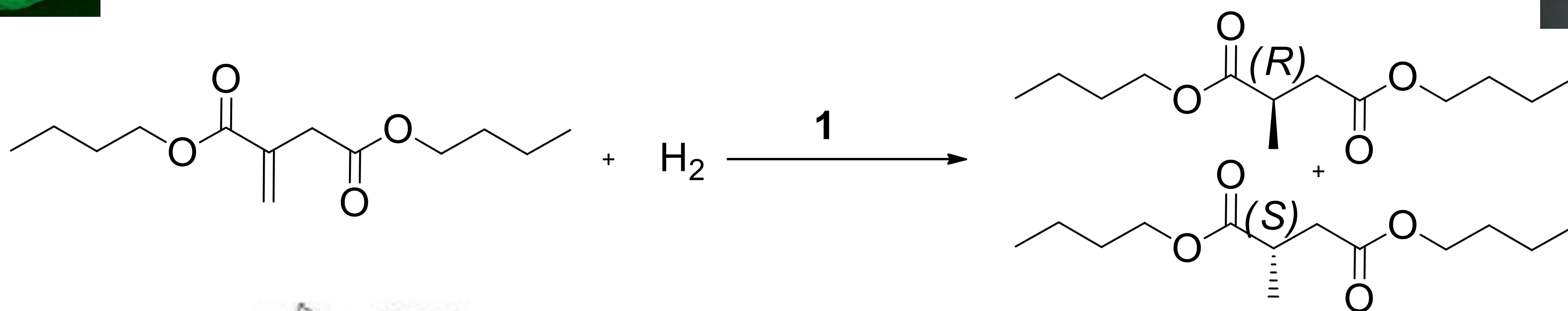
Sir John Cornforth, *Chemistry in Britain*, **1975**, 342.

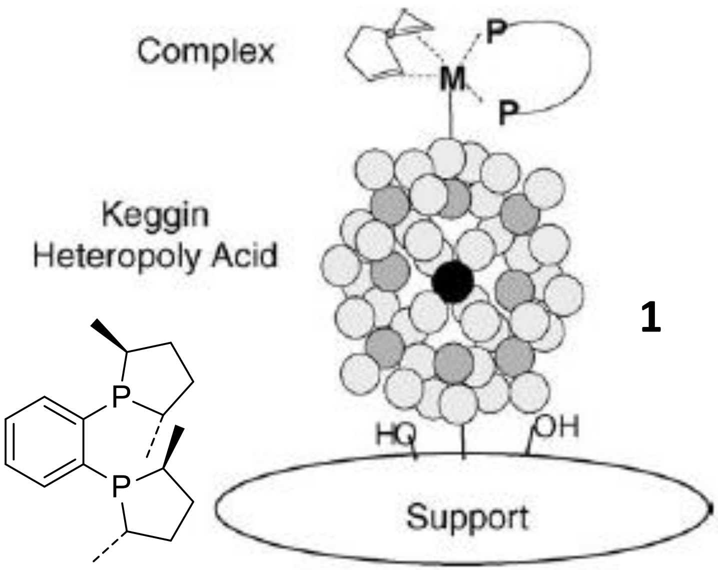
Continuous FLOW

Bath

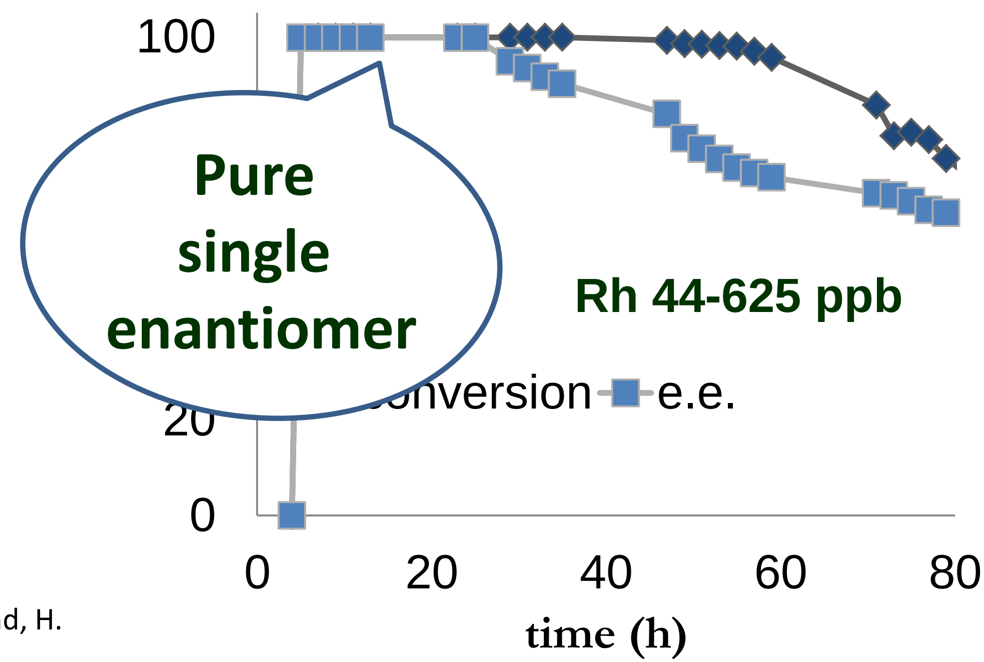


Solventless reaction Ruben Duque





1



R.L. Augustine*, S.K. Tanielyan, N. Mahata, Y. Gao, A. Zsigmond, H. Yang, *Applied Catalysis A: General* 2003, **256,** 69–76

22 ºC, H_2 (5 bar, 0.2 $dm^3\ min^{-1}$), substrate (neat, 0.05 $ml\ min^{-1}$)

9580 TON after 80.5 h, 400 $g\ week^{-1}$

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R. Duque, P. J. Pogorzelec and D. J. Cole-Hamilton, *Angew. Chem., Int. Ed.*, 2013, **52**, 9805

Conclusions

Homogeneous Catalysts

ROCK