Advanced Catalysis and Organometallic Chemistry, Camerino, 16.08. – 27.08.2009

- **Green chemistry**

- Why green chemistry
- Green chemistry principles
- Ionic liquids as green solvents
- Ionic liquids as active components of the catalytic system
- Highly selective catalysis
- Alternative feedstock

SYNTHESIS of NEW COMPOUNDS

IS

a EXCLUSIVE DOMAIN of CHEMISTRY

(characterization, interactions studies, manipulations, transformations)

Efficiency, atom economy, *E* - factor

B. Trost, R. Sheldon

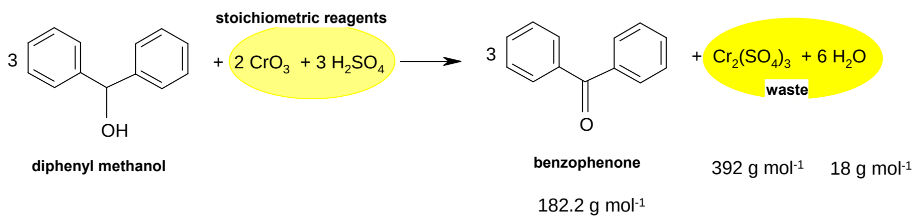
$$E = \frac{\Sigma \text{ waste}}{\Sigma \text{ product}} \quad \text{(kg/kg)}$$ Ecologic factor

$$E^{-1} = \frac{\Sigma \text{ substrates}}{\Sigma \text{ product}} \quad \text{(kg/kg)}$$ Material factor

Product	Production (ton)	*E*
bulk chemicals	**< 10^4 – 10^6**	**< 1 – 5**
fine chemicals	**10^2 - 10^4**	**5 – 50**
pharmaceuticals	**10 – 10^3**	**25 – 100**
oil refining	**10^6 - 10^8**	**0.1 - 1**

Efficiency, atom economy – *E* - factor

(example)



$$\begin{array}{ccc} 3 \times 182.2 & - & 392 + 6 \times 18 \\ 1 & - & X \\ \hline \end{array}$$

$$X = 0.915$$

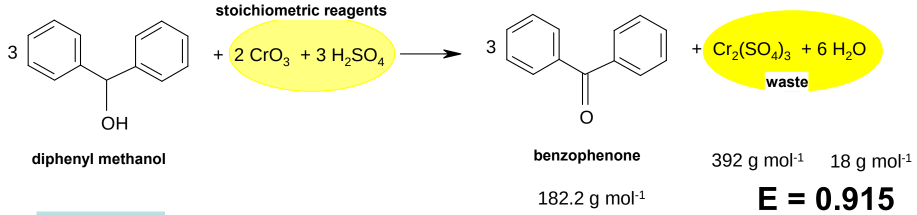
E = 0.915

1 kg of product - 0.915 kg waste

Efficiency, atom economy – *E* - factor

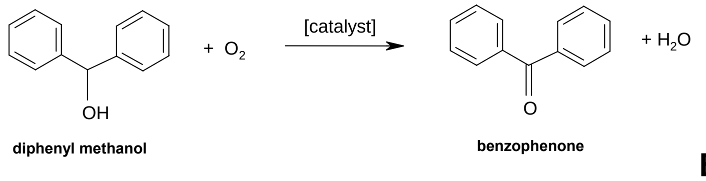
(example)

stoichiometric

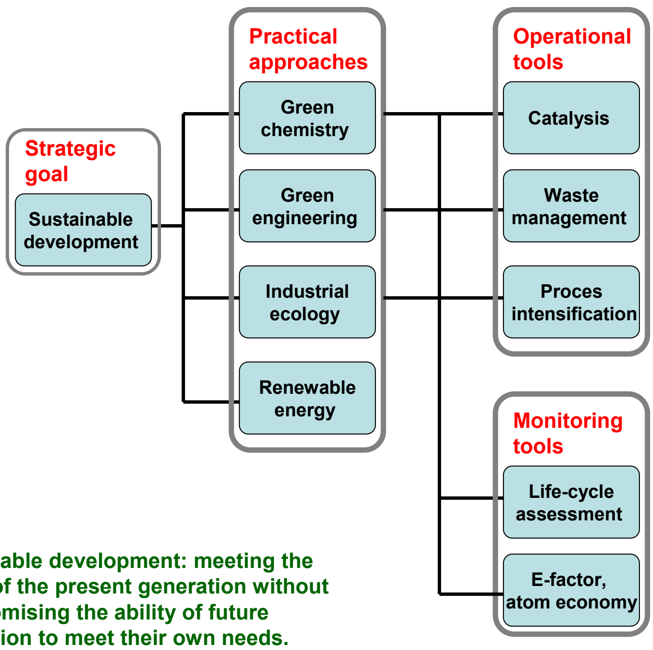


E = 0.915

catalytic



E = 0.099



Sustainable development: meeting the needs of the present generation without compromising the ability of future generation to meet their own needs.

NEW PROCESSES

IMPROVEMENT of the KNOWN PROCESSES

SEARCHING for the NEW PROCESSES

ROLE of CATALYSIS

CATALYSIS IS A MAIN TOOL OF GREEN CHEMISTRY

EVOLUTION of the ENVIRONMENTAL MOVEMENT

* dilution is the solution to pollution
  (but bioaccumulation, chronic toxicity)
* waste treatment through command and control
  - waste treatment prior to release
  - exposure control
  - abatement of the wastes subsequent to their release

„GREEN CHEMISTRY"

Green chemistry efficiently utilizes (preferably renewable) raw materials, eliminates waste and avoids the use of toxic and/or hazardous reagents and solvents in the manufacture and application of chemical products.
(P. Anastas, T. Warner)

Green chemistry eliminates waste at source, i.e. it is primary pollution prevention rather than waste remediation.

Green chemistry = environmentally friendly chemical synthesis

Sustainability is the goal and green chemistry is the means to achieve it.

Green chemistry principles

(P. Anastas and T. Warner, Green Chemistry, Theory and Practice, Oxford Univ. Press, 1998)

1. Prevent waste instead of treating it.
2. Design atom-efficient synthetic methods. (C)
3. Choose synthetic routes using nontoxic compounds where possible. (C)
4. Design new products that preserve functionality while reducing toxicity.
5. Minimize the use of auxiliary reagents and solvents. (C)
6. Design processes with minimal energy requirements. (C)
7. Preferably use renewable raw materials.
8. Avoid unnecessary derivatization. (C)
9. Replace stoichiometric reagents with catalytic cycles. (C)
10. Design new products with biodegradable capabilities. (C)
11. Develop real-time and on-line process analysis and monitoring methods.
12. Choose feedstocks and design processes that minimize the chance of accidents.

EXAMPLES of APPLICATION of GREEN CHEMISTRY PRINCIPLES in CATALYTIC REACTIONS

Atom economy - principle 2

Example: hydroformylation

$$R\text{-}CH{=}CH_2 + CO + H_2 \xrightarrow{\text{cat.}} R\text{-}CH_2\text{-}CH_2\text{-}\overset{\overset{O}{\|}}{C}H + R\text{-}\underset{\underset{\underset{O}{\|}}{C\text{-}H}}{\overset{|}{C}}H\text{-}CH_3$$

100% atom economy

Catalysts:

$HRh(CO)(PPh_3)_3$

$Rh(acac)(CO)_2$

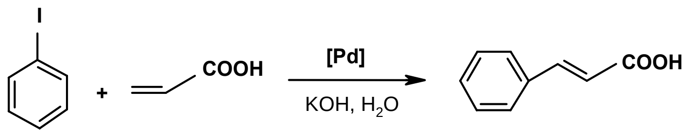
$Rh(acac)(CO)(PPh_3)$

$Rh(acac)[P(OPh)_3]_2$

Use of catalyst, innocuous solvent

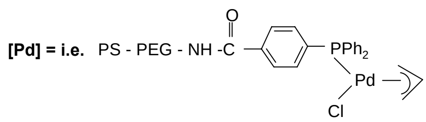
Synthesis of cinnamic acid in H_2O

(UV filters, fragnances)



92 %

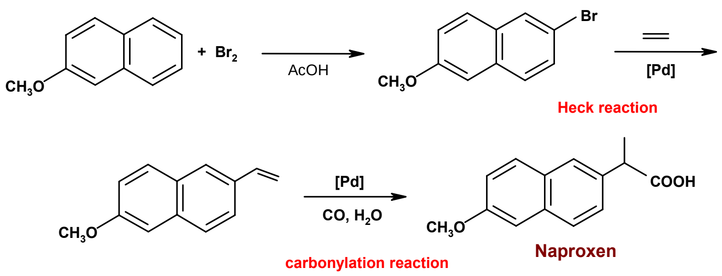
Heck reaction

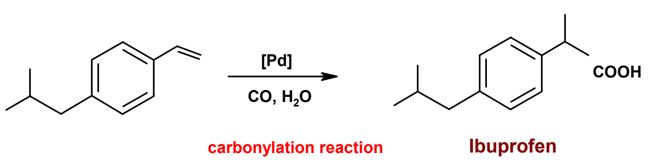


Y. Uozumi, J.Org.Chem., 1999

Use of catalytic reactions

Synthesis of Naproxen and Ibuprofen (antiflamable drugs)

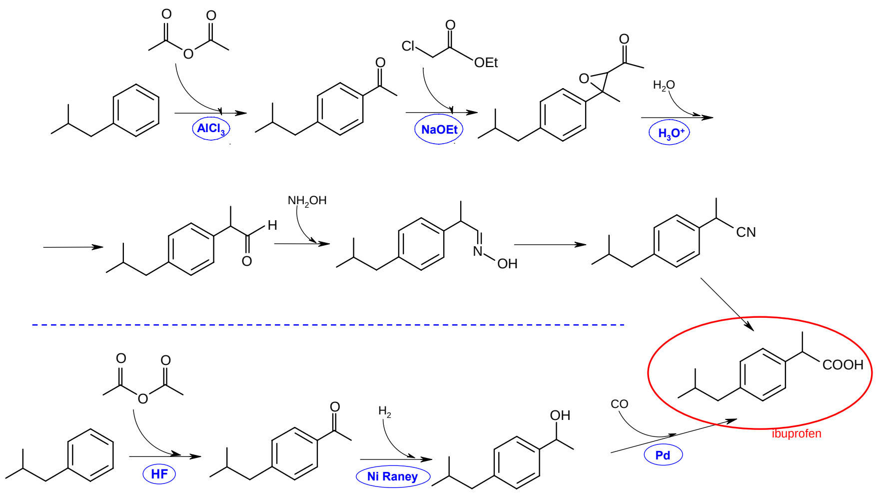




[Pd] = $PdCl_2(PPh_3)_2$

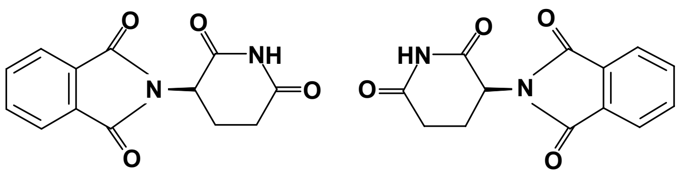
Nippon Petrochemicals Comp. Ltd., Ethyl Corp., Montedison, Albermarle

Two methods of ibuprofen synthesis



Green Chemistry Award, 1997

A CASE of THALIDOMIDE

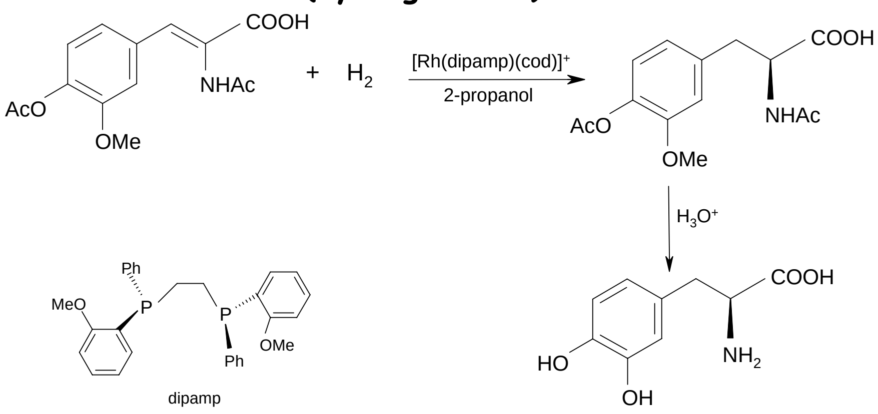


S - THALIDOMIDE R - THALIDOMIDE

Most of biological processes are stereospecific but usually only one optical isomer of a chiral compound is responsible for desired biological activity

ASYMMETRIC CATALYSIS

(hydrogenation)

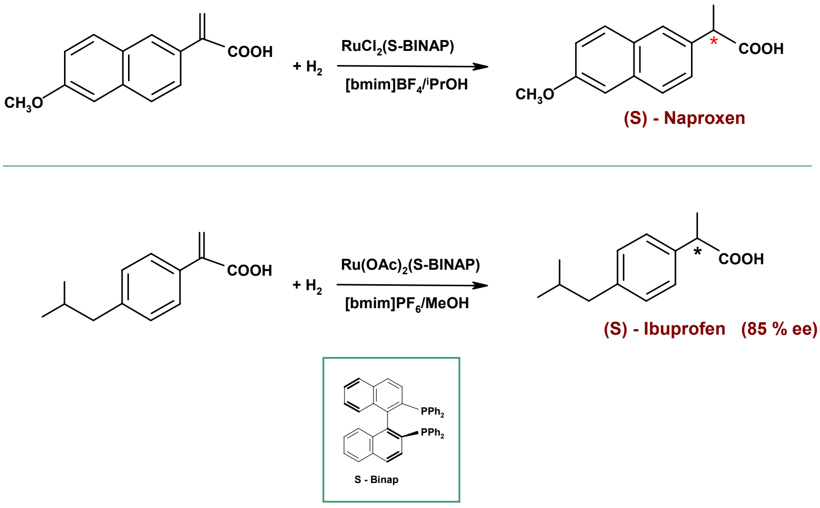


L - DOPA
(for Parkinson therapy)

pharmaceuticals

Use of catalytic reactions

Synthesis of Naproxen and Ibuprofen in asymmetric hydrogenation



IONIC LIQUIDS AS REACTION MEDIUM

of C-C CROSS-COUPLING

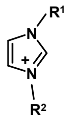
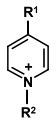
IONIC LIQUIDS

Ionic liquids are liquids fully composed of ions.

Ionic liquids are fluid around 100°C.

$[HNEt_3]NO_3$ – the first room – temperature ionic liquid was obtained in 1914 by Paul Walden

Examples of ionic liquids

	R^1, R^2,	Anion	t_t (°C)	name
	$R^1 = R^2 = CH_3$	Cl	125	mmim
	$R^1 = CH_3$, $R^2 = C_4H_9$	Cl	65	bmim
	$R^1 = CH_3$, $R^2 = C_2H_5$	Cl	87	emim
		Br	81	
		PF_6	62	
		NO_2	55	
		BF_4	6	
		CF_3SO_3	- 9	
	$R^1 = CH_3$, $R^2 = C_4H_9$	Cl	158	bmpy
		PF_6	45	
		BF_4	< 20	
	$R = CH_3$	Br	> 300	
	C_2H_5	Br	284	
$[NR_4]^+$	C_4H_9	Br	124	
	C_6H_{13}	Br	99	
	C_8H_{17}	Br	95	

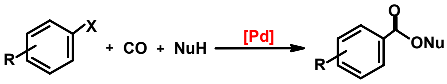
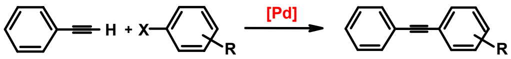
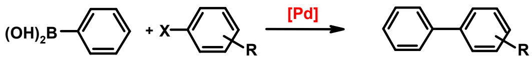
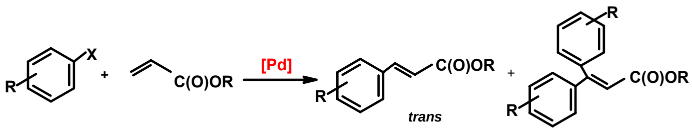
Widely tunable properties of ionic liquids

- high thermal stability
- little/no vapour pressure
- good solvents for organic and inorganic compounds
- good solvents for gases
- non-flammable
- possibility to use in multiphasic systems

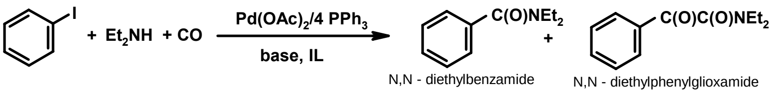
- coordination ability dependent on the kind of anion and cation
- ability to form carbene complexes with transition metals

P. Wasserscheid, W. Keim, 2000; R. Sheldon, 2001; W.Herrmann, 1995; J. Dupont, 1998; T. Welton, 1999; J. Dupont, 2002; H. Olivier – Bourbigou, 2002

Examples of C-C bond forming reactions in which ionic liquids can be used as solvents

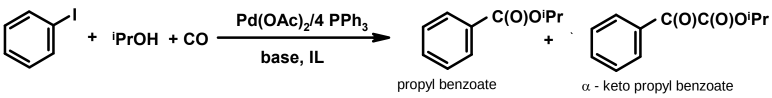
Reaction	Scheme
carbonylation	
Sonogashira	
Suzuki	
Heck	

Amino- and alkoxycarbonylation of iodobenzene



NuH = Et$_2$NH (= base)

solvent	yield (%)	
NEt$_2$H	18	82
[bmim]BF$_4$	17	83
[bmim]PF$_6$	24	76

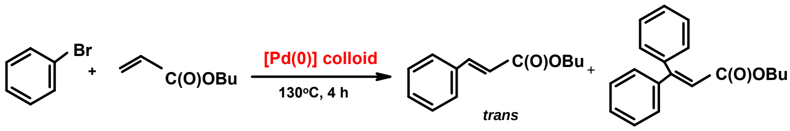


NuH = ^{i}PrOH

solvent	yield (%)	
^{i}PrOH	5	7
[bmim]BF$_4$	58	25
[bmim]PF$_6$	93	6

M. Tanaka, Green Chem., 2001

Pd(0) COLLOID CATALYZED HECK REACTION in MOLTEN SALT



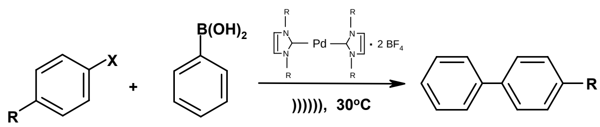
1 2

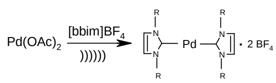
[PhBr] : [acrylate] = 2.3

Catalyst	yield (%)	
	1	2
Pd(0) colloid	28	0
Pd(0) colloid / $[Bu_4N]Br$	37	67

Trzeciak, Ziółkowski, 2005

Suzuki reaction under sonochemical conditions

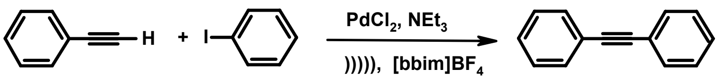




Substrate	time(min)	yield(%)
iodobenzene	20	92
4-methoxyiodobenzene	20	93
4-chloroiodobenzene	30	85
bromobenzene	45	82
4-methoxybromobenzene	10	85
chlorobenzene	60	42

R. Rajagopal, D.V. Jarikote, K.V. Srinivasan, Chem. Comm., 2002

Sonogashira reactions in ionic liquids under sonochemical conditions

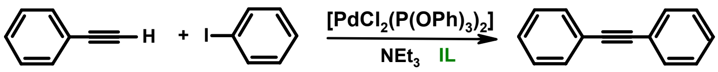


Reaction yield in subsequent cycles (%)

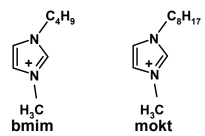
(1)	(2)	(3)	(4)	(5)
93	91	89	88	85

K.V. Srinivasan i inni, J. Org. Chem., 2005

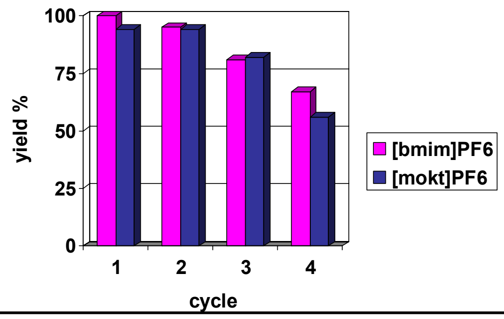
SONOGASHIRA REACTION in IONIC LIQUIDS



IL	Wydajność %
$[bmim]PF_6$	83
[mokt]Cl	0
$[mokt]PF_6$	100

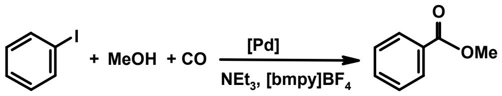


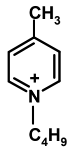
RECYCLING of CATALYST (possible in IL only)



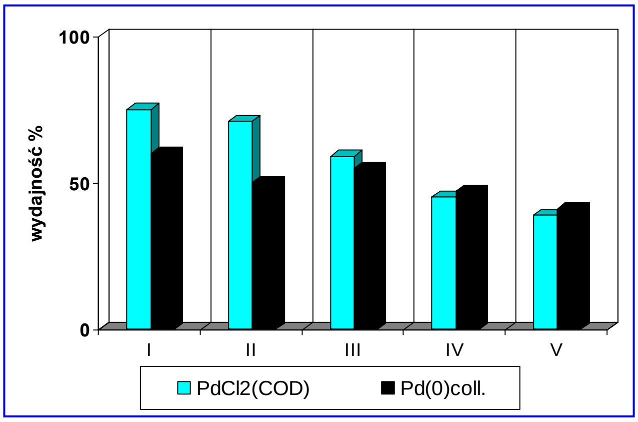
Trzeciak, Ziółkowski, 2006

Recycling of Pd catalysts in $[bmpy]BF_4$



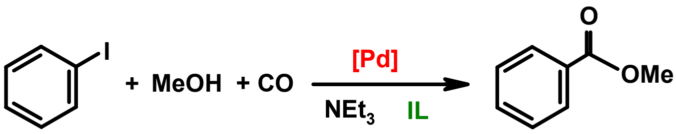


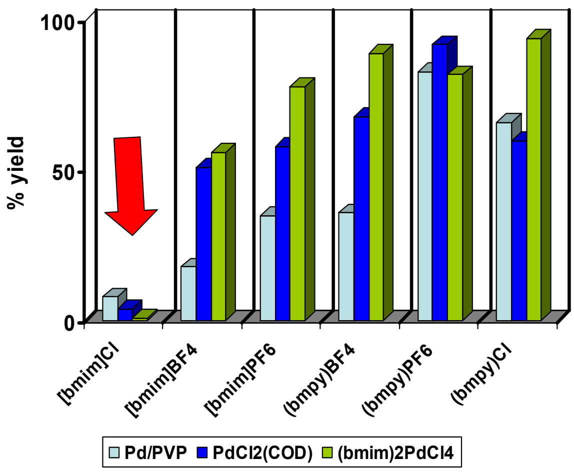
bmpy

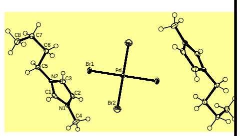


Trzeciak, Ziółkowski, 2004

Yield of methylbenzoate obtained in methoxycarbonylation of iodobenzene in IL



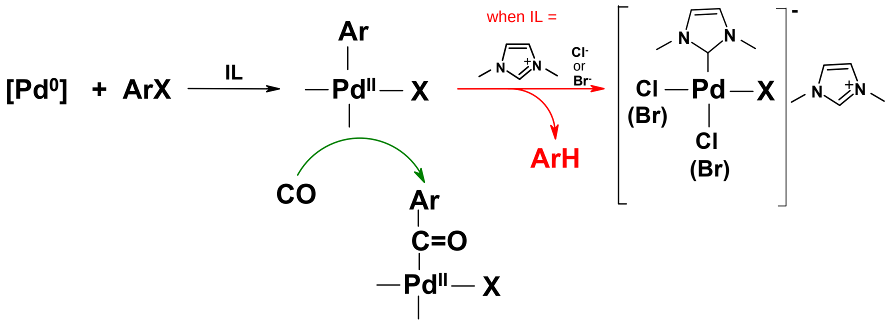




$[bmim]_2[PdBr_4]$

Trzeciak, Ziółkowski, 2004, 2006

NEGATIVE EFFECT of [bmim]X on METHOXYCARBONYLATION - reaction with Pd-aryl complex



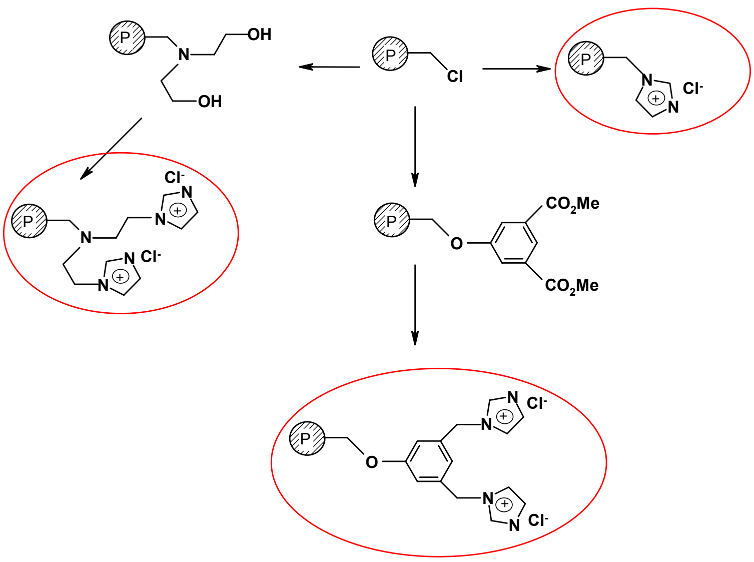
$[Pd^0] = [Pd^{(0)}L_{3,4}]$ or Pd^0 colloid

Zawartka, Trzeciak, Ziółkowski, 2008

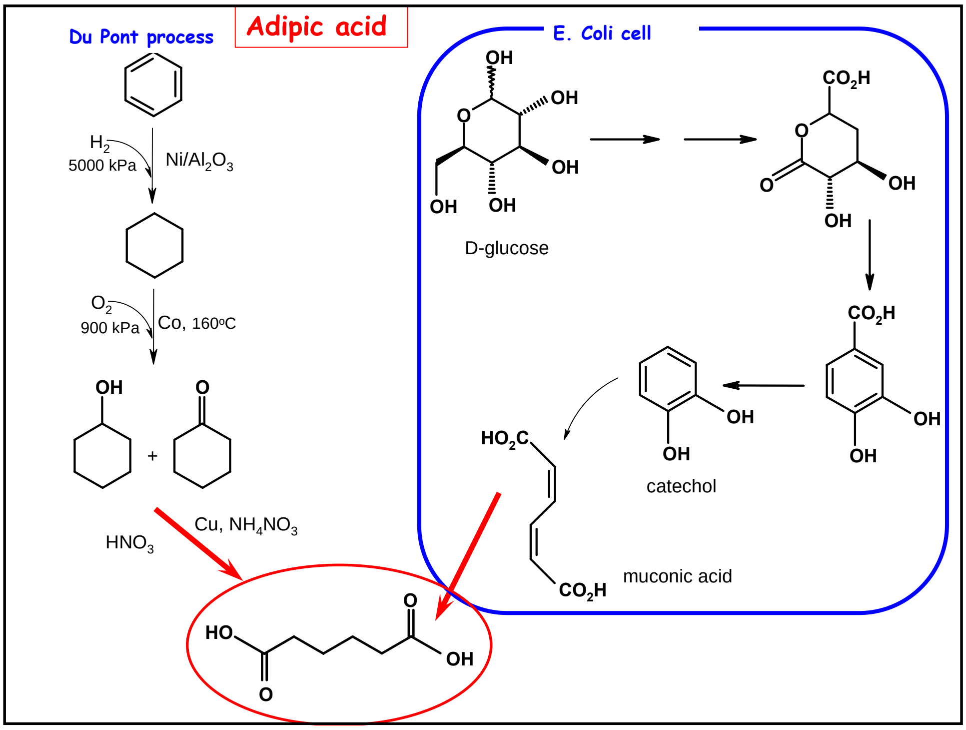
Advantages of ionic liquids application (principles 3, 5 and 9)

- replacement of VOC (*volatile organic compounds*)
- easy separation of catalyst from organic products

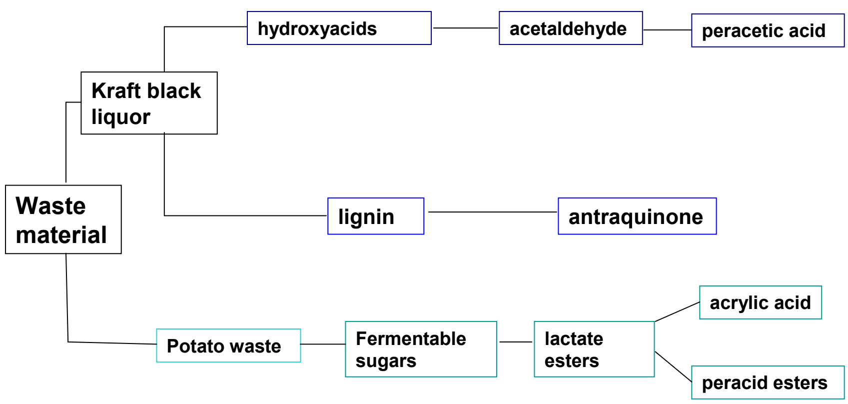
Immobilized ionic liquids



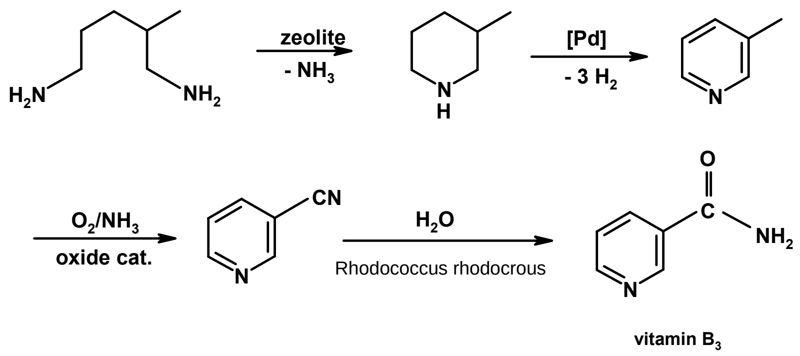
ALTERNATIVE FEEDSTOCK



Alternative (agricultural) feedstock



Lonza process – synthesis of nicotinamide



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

catalysis and biocatalysis