Sustainable and Supramolecular Chemistry

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Multicatalytic processes based on Supported Ionic Liquid-Like Phases (SILLPs)

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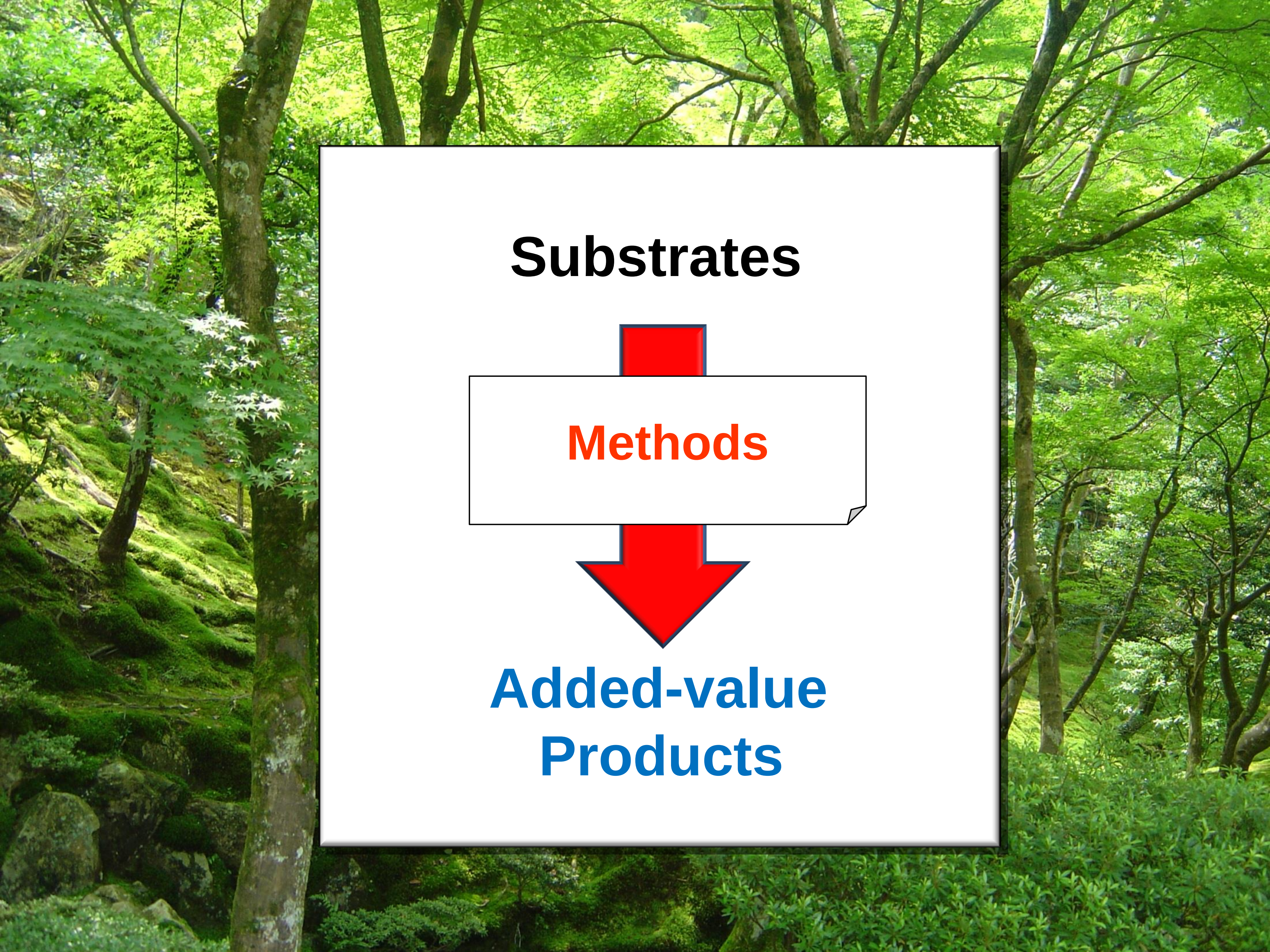
Substrates
Methods
Added-value
Products

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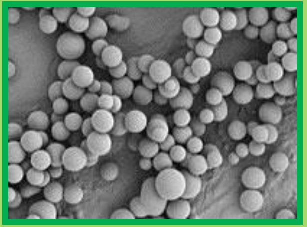
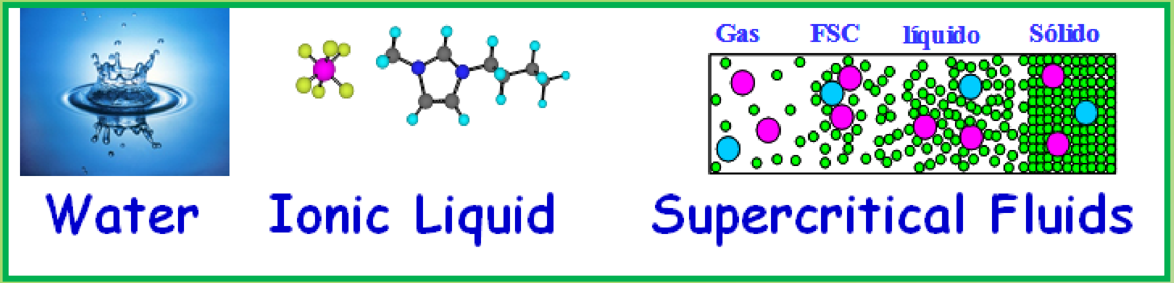
Tools

- **Catalysis**
  Heterogeneous catalysis

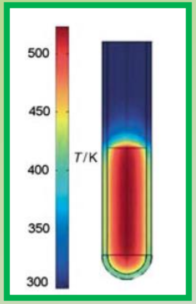


Green Chemistry Toolbox

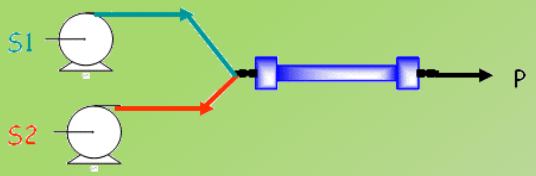
- **Alternative Solvents**



- **Microwave heating**



- **Flow Process**



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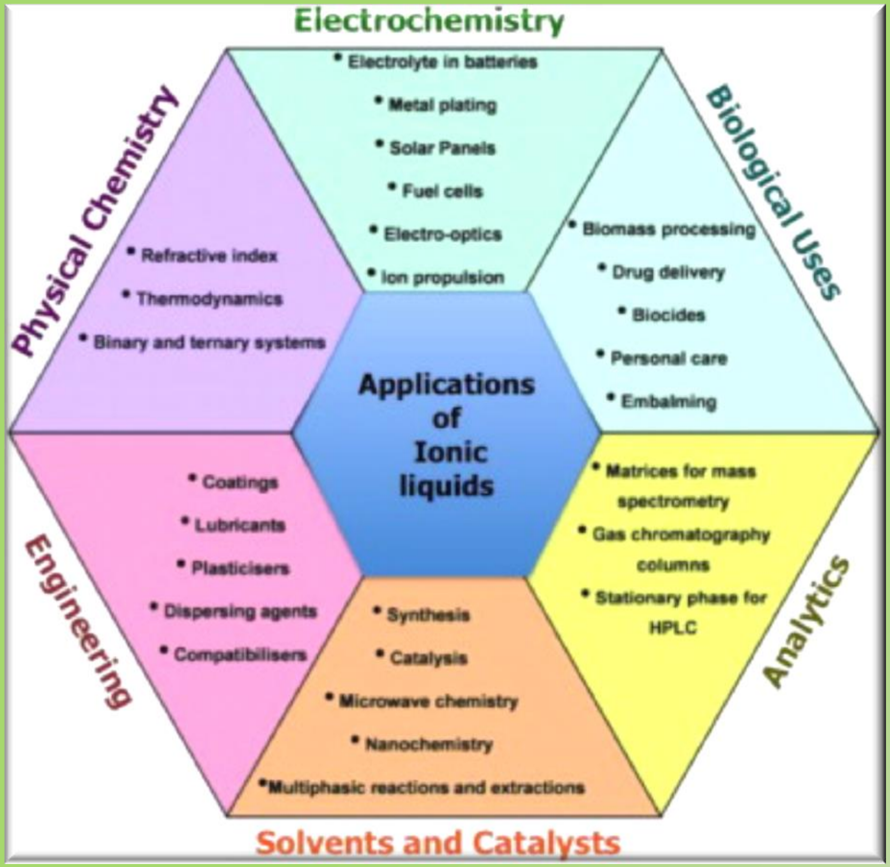
Why ILs?

It is possible to design ionic liquids of suitable properties by combining appropriate anions, cations, and varying their structure



N.V. Plechkova, K.R. Seddon Chem Soc Rev, 37 (1) (2008), pp. 123–150

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….Nobody is perfect!!

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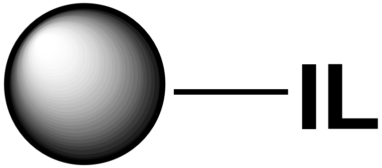
Ionic liquids as "Green Solvents"

Biphasic liquid-liquid systems:
✓ require relatively **large amounts** of IL.
✓ **relatively expensive**
✓ some of them show evidence of **low biodegradability** and high **(eco)toxicological** properties.
✓ require an extraction solvent

The immobilisation of ILs onto a support or structured material (*e.g*. by simple impregnation, covalent linking of the cation, sol-gel method, etc):
SILLP: Supported Ionic Liquid-Like Phases



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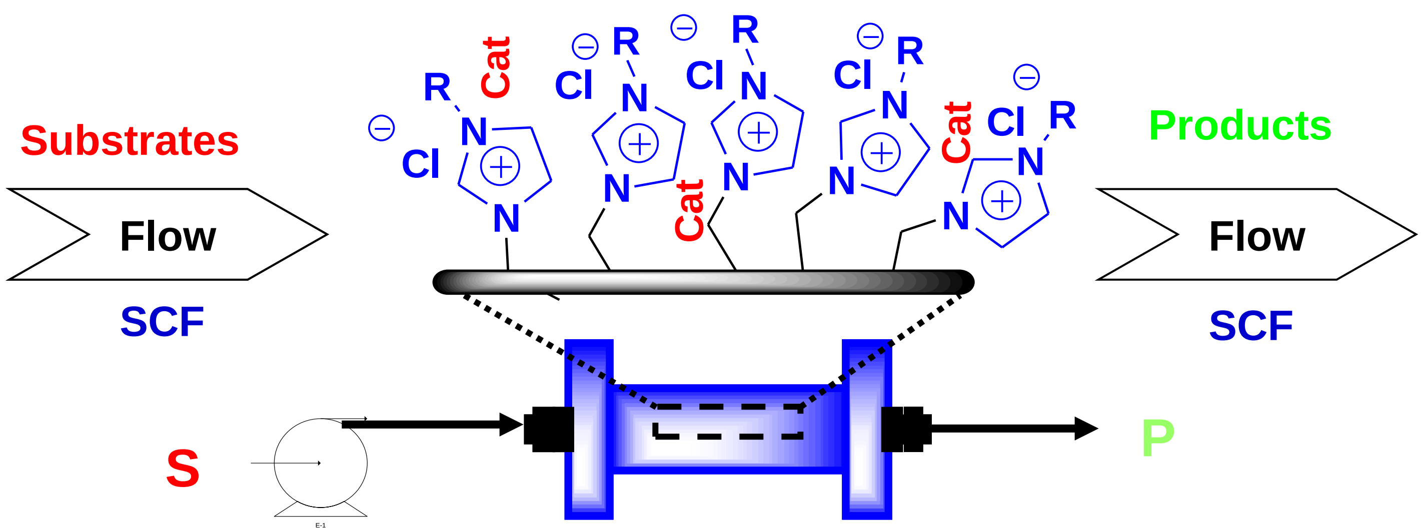
Ionic liquids as "Green Solvents": SILLPs

SILLPs: Immobilisation of ILs onto a support or structured materials (by covalent linking of the cation) to transfer the properties of the IL to an inert support

- ✓ **minimize the amount** of ILs used: lower cost
- ✓ **easy separation and recyclability**
- ✓ potential for the development of **continuous processes**
- ✓ **solventless reactions or in SCFs**



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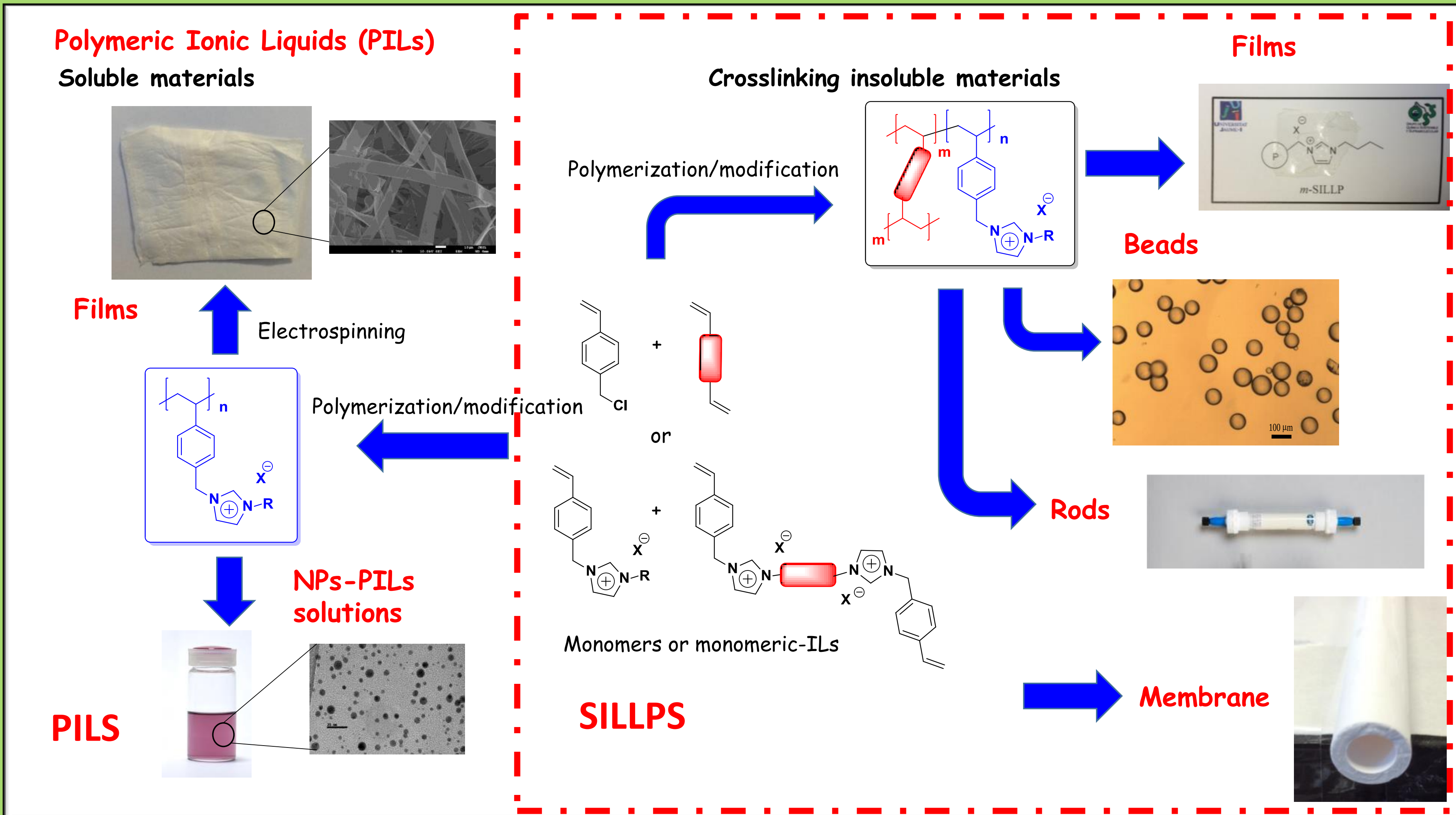
Ionic liquids as "Green Solvents": SILLPs



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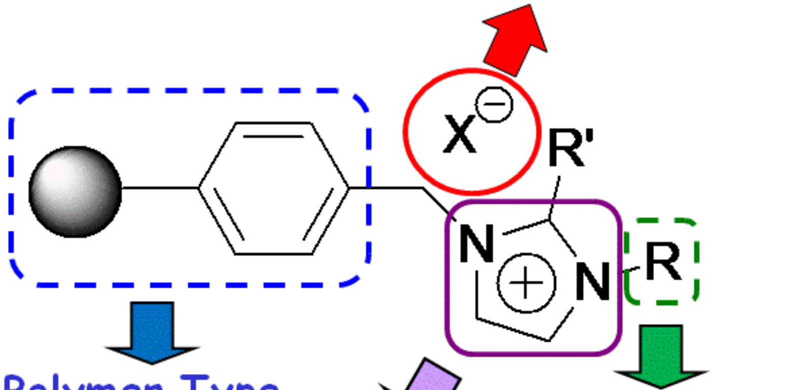
ILs vs. SILLPs:
How much do they look alike?

Transfer the properties of the IL to an inert support

What properties?

- modular
- thermal stability
- polarity
- Mw heating
- ability to stabilise different catalysts



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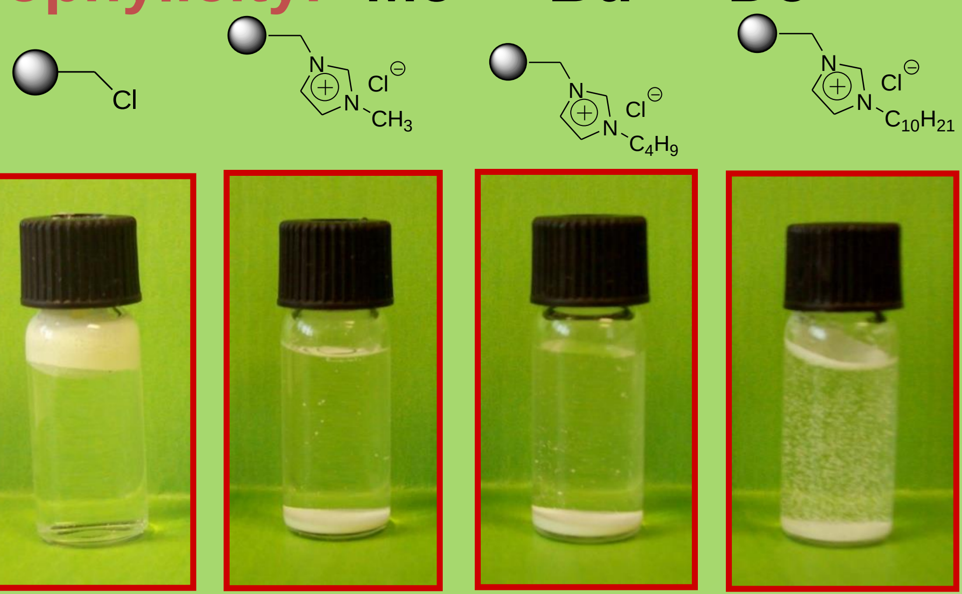
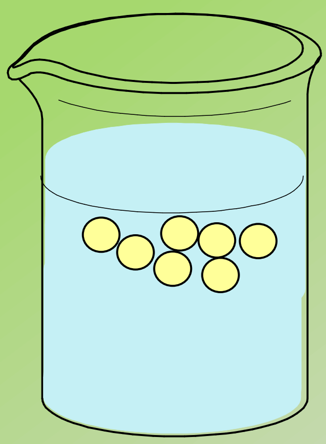
Properties of SILLPs:
Polarity/Behaviour in water

The length of the chain in the IL allows to modulate the polarity

*** Hydrophylicity: -Me > -Bu > -De**





***macro*-PS-DVB 1.2 mmol Cl/g**

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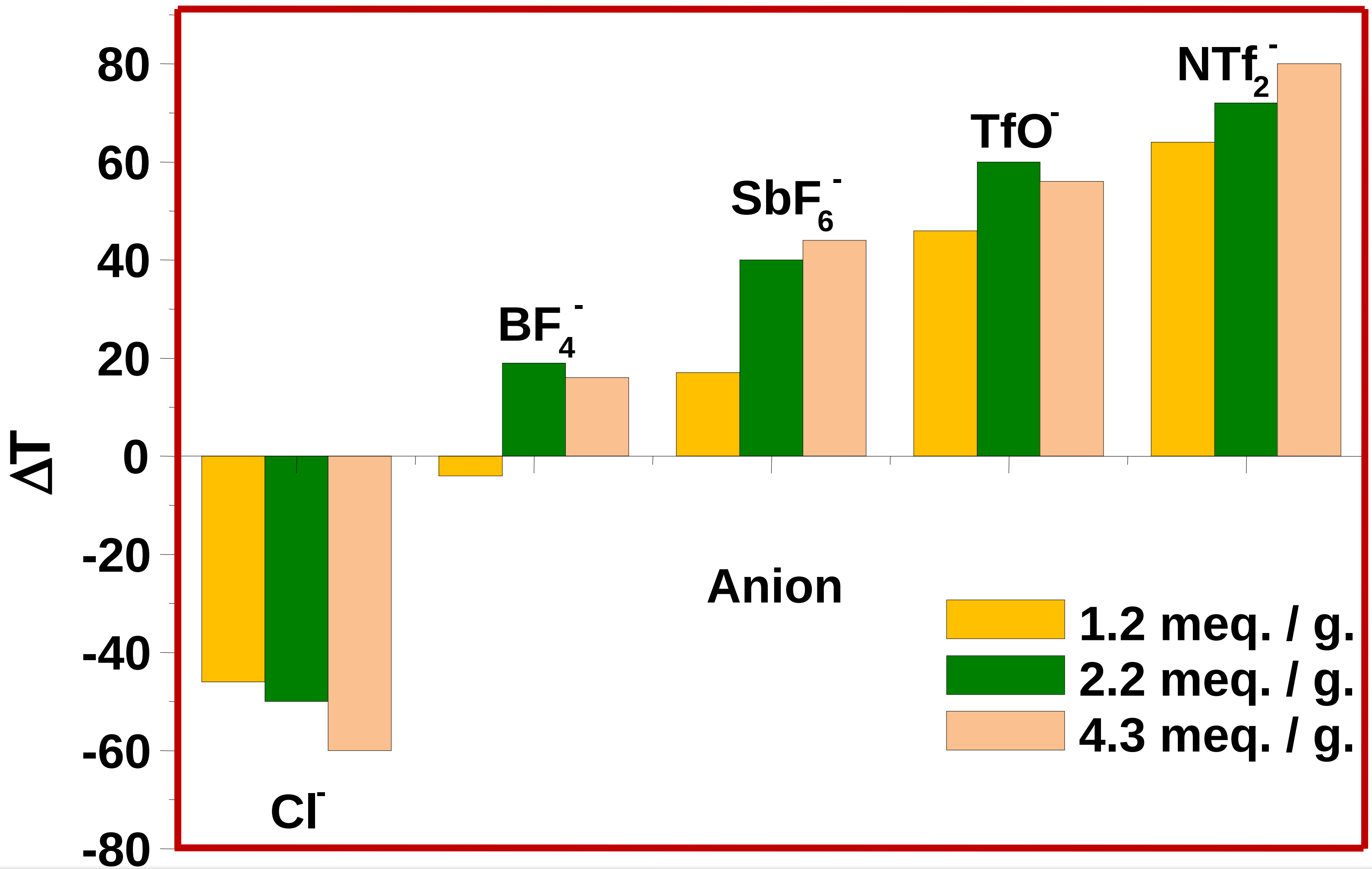
Synthesis of Supported Ionic Liquid-Like Phases: SILLPs



TGA

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Chem. Eur. J., 2011

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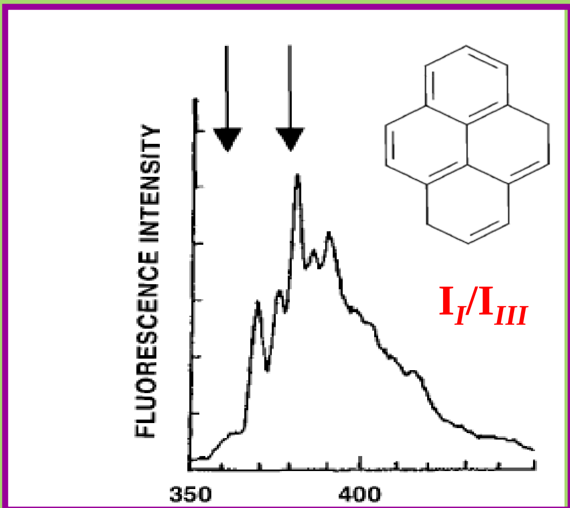
Properties of SILLPs: Polarity



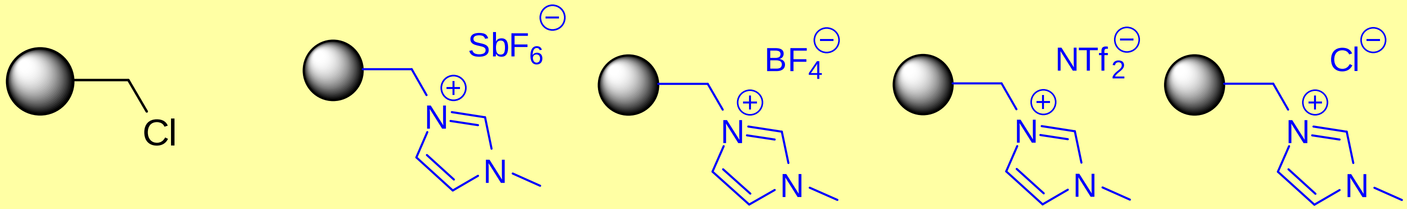
Pyrene as solvatochromic fluorescent probe

The pyrene solvent polarity scale is defined as the I_I/I_{III} emission intensity ratio

I_I/I_{III} increases with increasing solvent polarity

Hexane	Toluene	MeOH	CH_3CN	DMF
0.61	1.11	1.33	1.75	1.82

\- → +



Cl	SbF_6^-	BF_4^-	NTf_2^-	Cl^-
0.93	1.15	1.29	1.40	1.64

Chem. Eur. J., 2011

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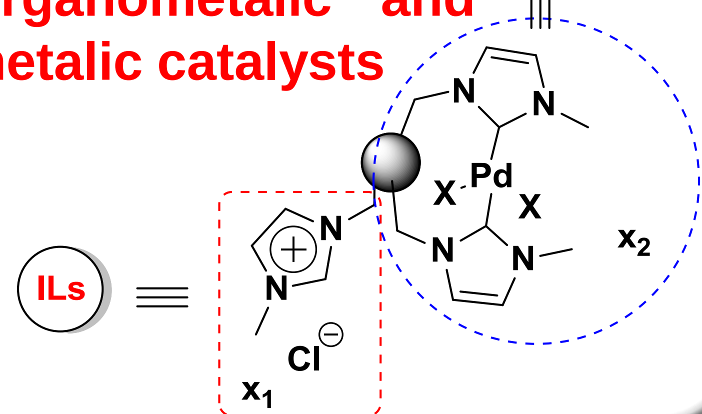
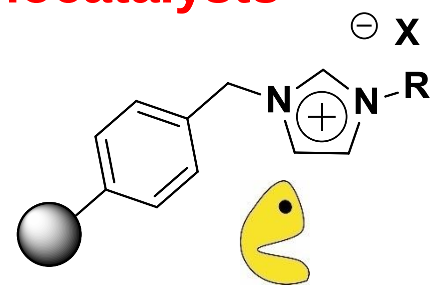
Supported Ionic Liquid-Like Phases (SILLPs)

Organometalic and metalic catalysts

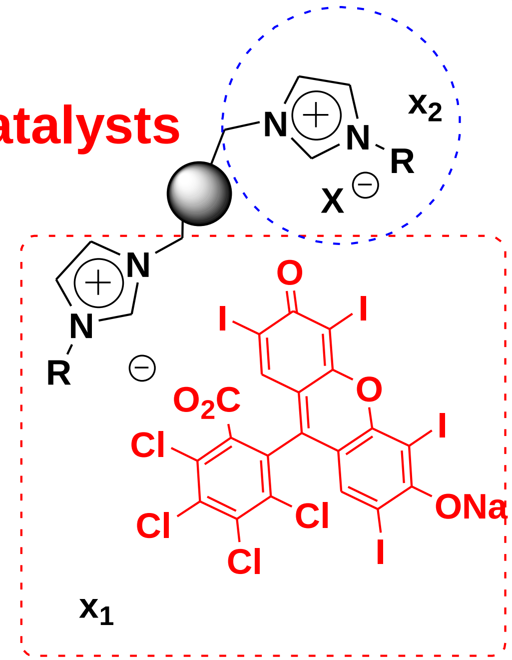
NHC-ligand



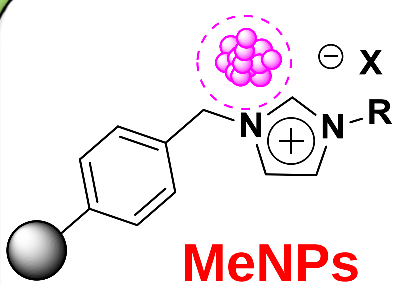
Biocatalysts



Photocatalysts

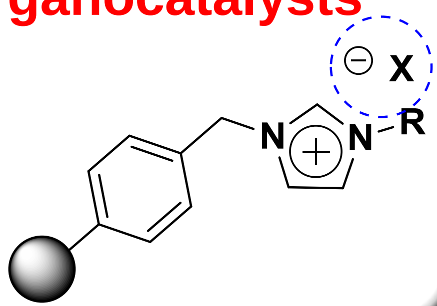


Rose Bengal



MeNPs

Organocatalysts



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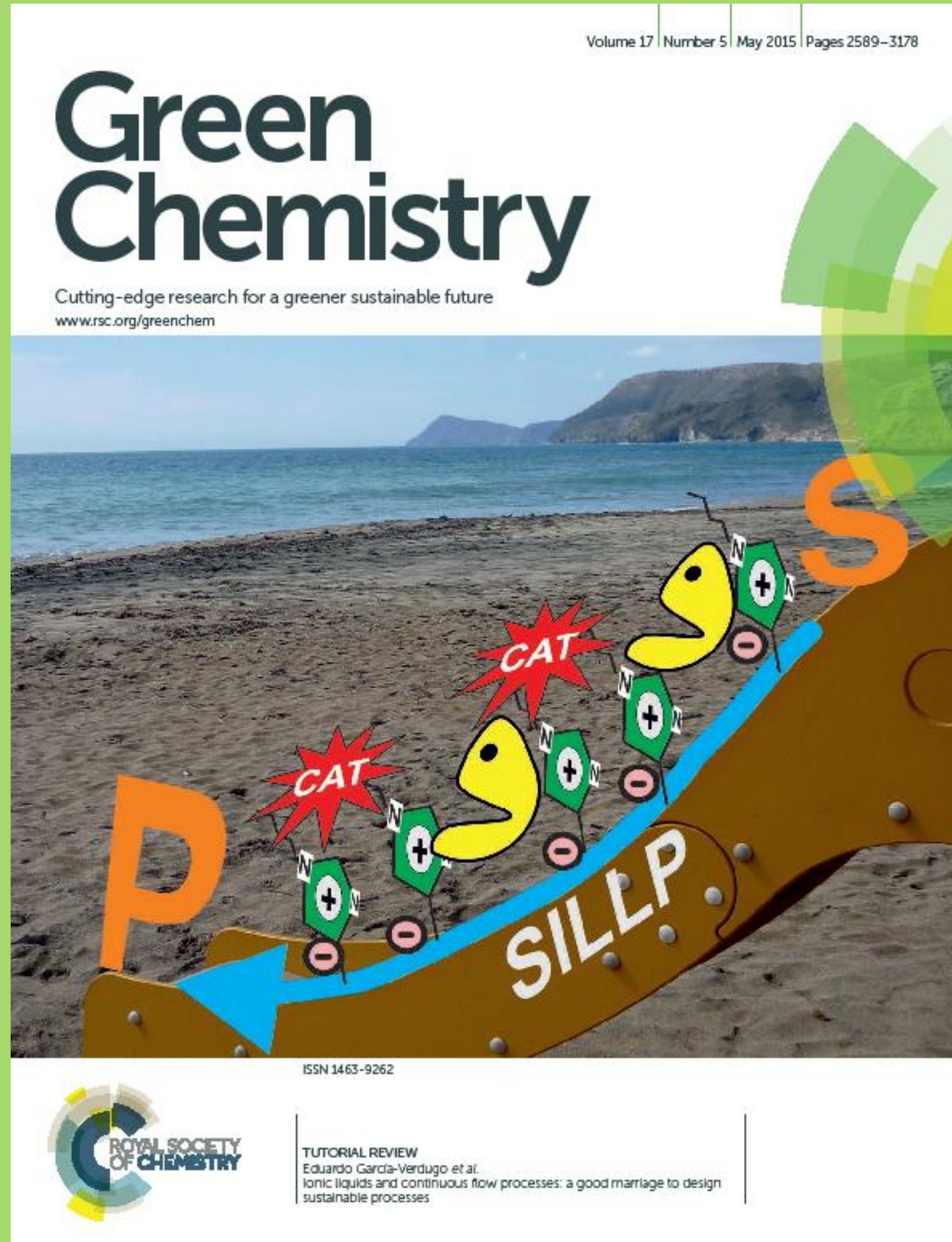

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Application of SILLPs: Catalytic supported PdNPs

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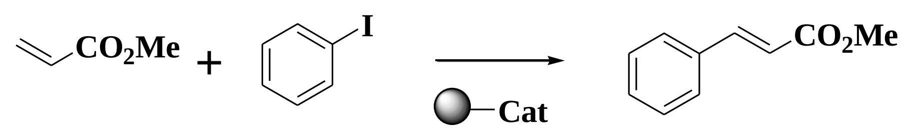
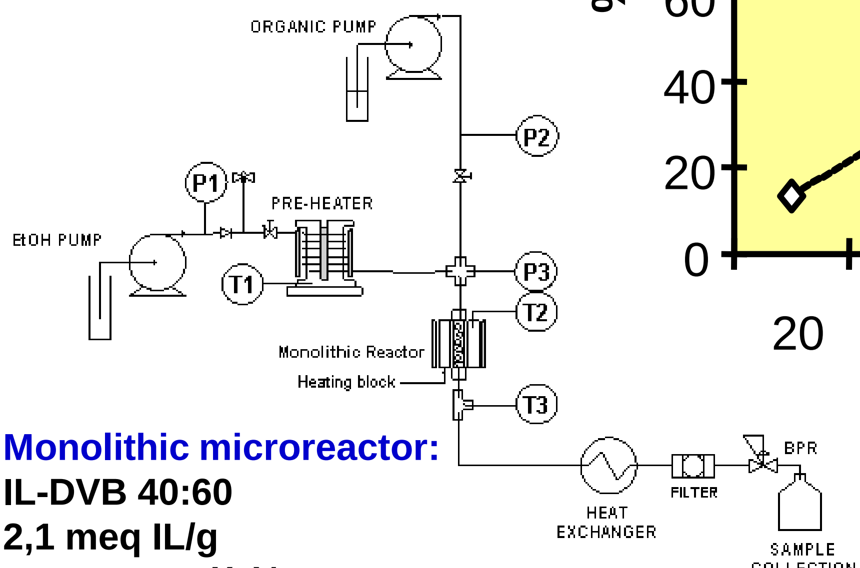
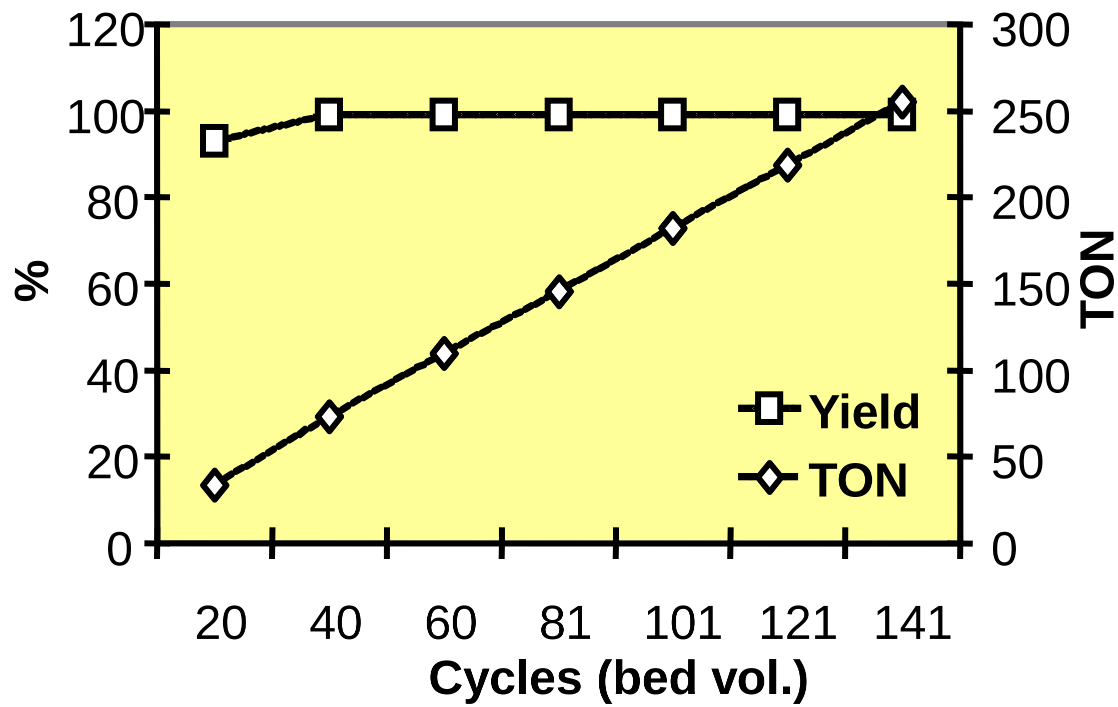


- T>150ºC
- T>250ºC transesterification.

scEtOH
(T_c=241ºC, P_c=61 bar)





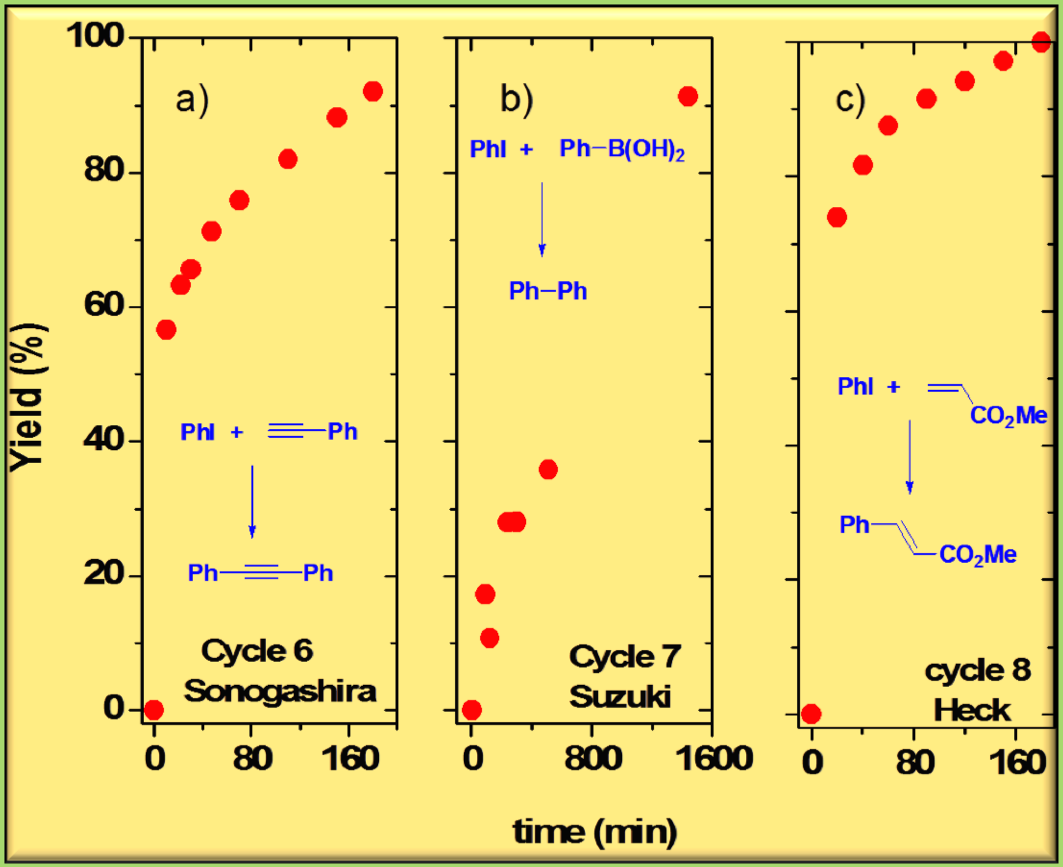
Monolithic microreactor:
IL-DVB 40:60
2,1 meq IL/g
0,21 meq Pd(0)/g

***J. Catal*., 2010**

- 100% trans
- high stability 420min (7h)
- TON/cycle: 2.28
- Residence time: 2.98min

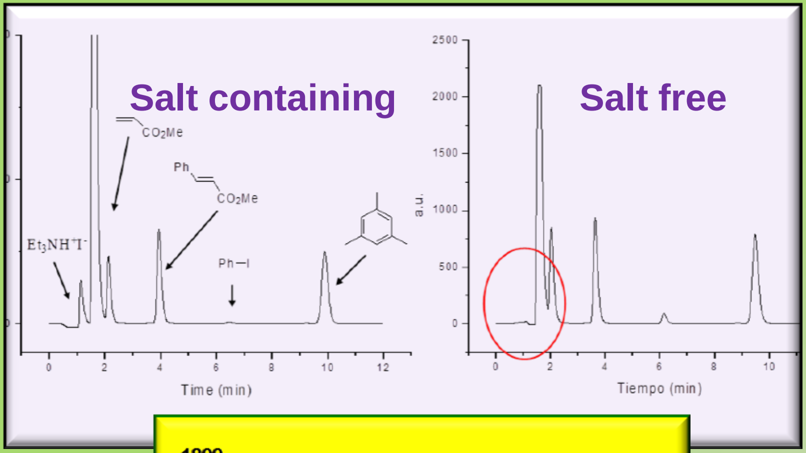
Application of SILLPs: Catalytic supported PdNPs

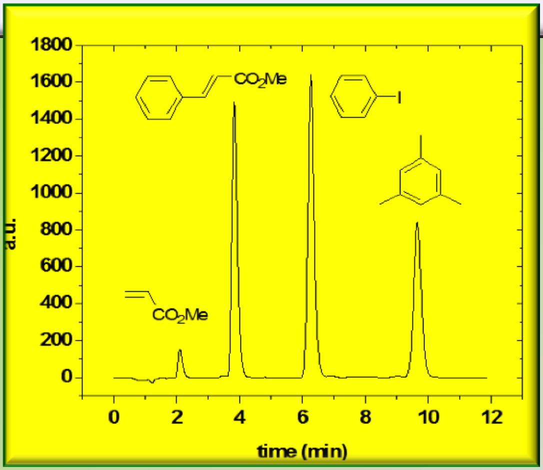
Polymeric cocktail



Entry	Cycle	Yield (%)	TOF_{50} (h^{-1})
1	2	99	2727
2	8	99	2970

HPLC chromatograms





Under continuous flow with $scCO_2$:
Salt free, solvent free

Adv. Synth. Catal., 2010

Application of SILLPs: Supported biocatalysts

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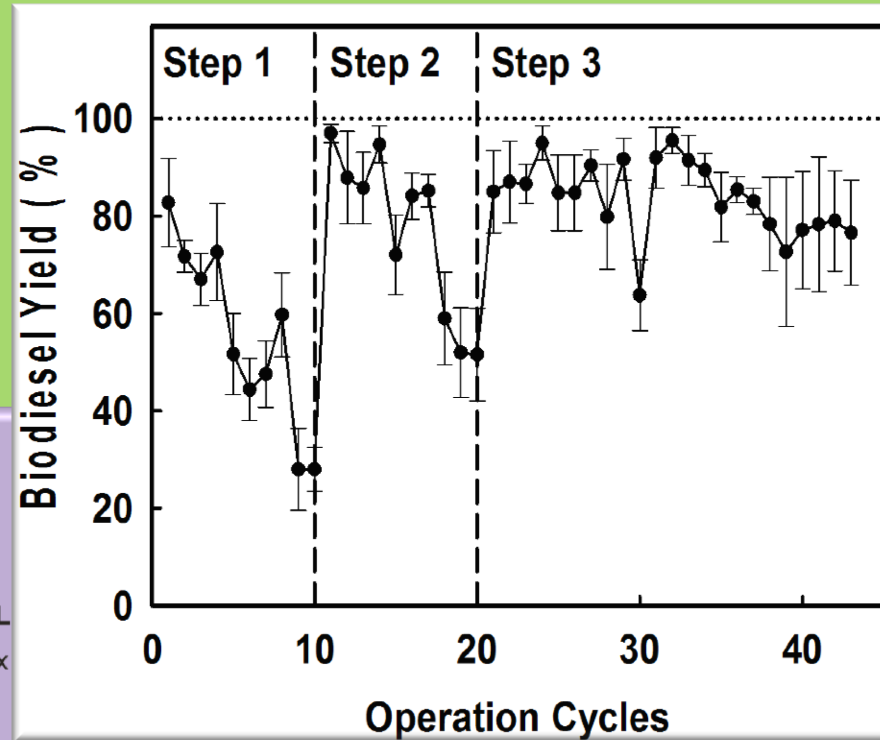
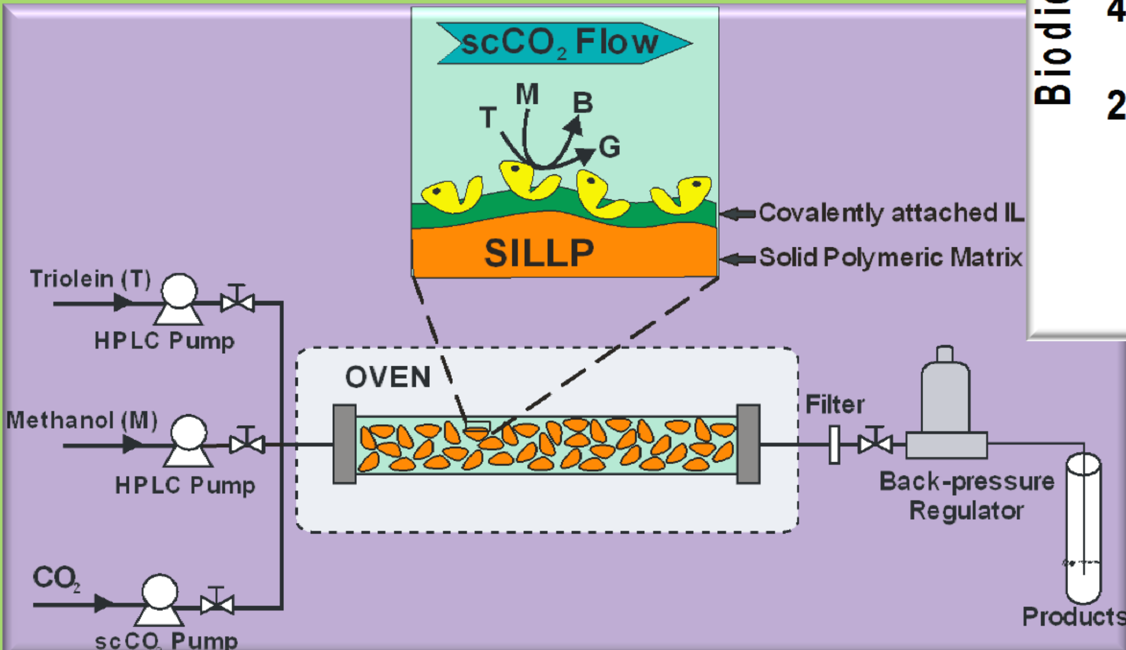
Biocatalytic continuous biodiesel synthesis in $scCO_2$





The presence of *t*-butanol as cosolvent avoids poisoning of the biocatalyst by the side product glycerol

***ChemSusChem* 2012**

Application of SILLPs: Supported photocatalysts

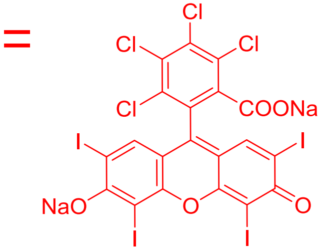
Why?

- Reaction induced by light.
- Clean and selective processes.

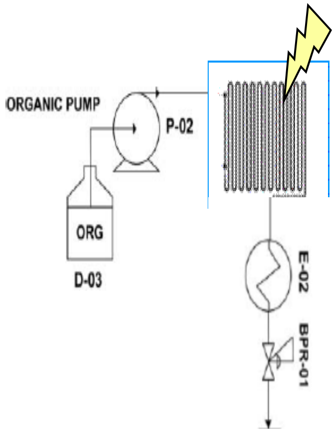
How?

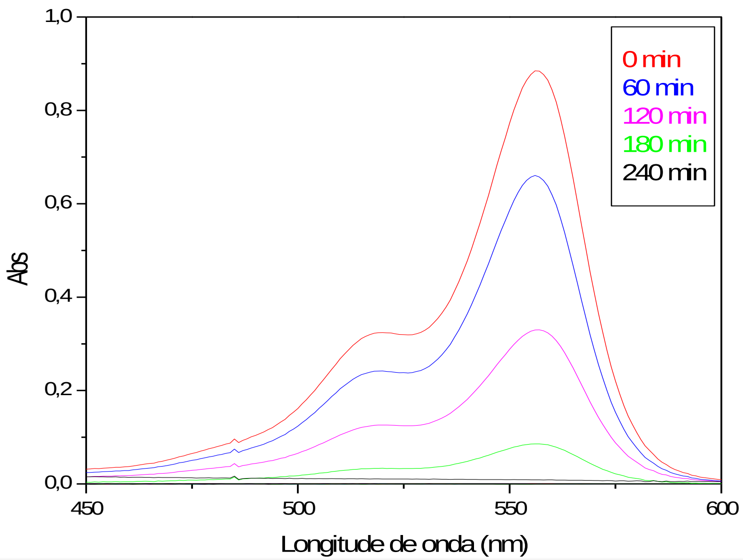
- adsorbing Rose of Bengal.

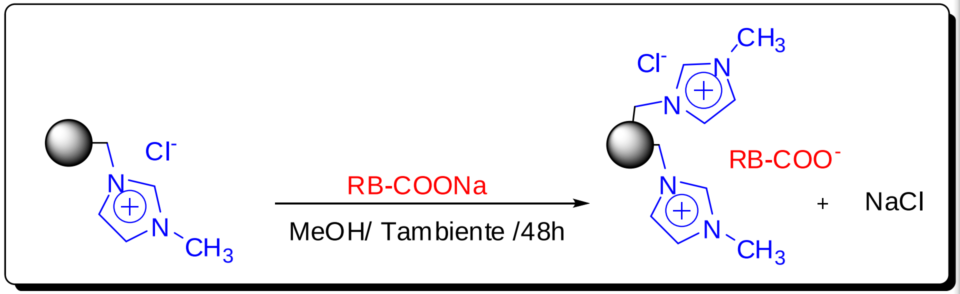
RB =

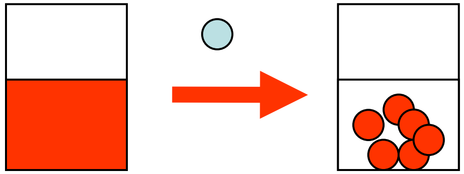


Rose Bengal









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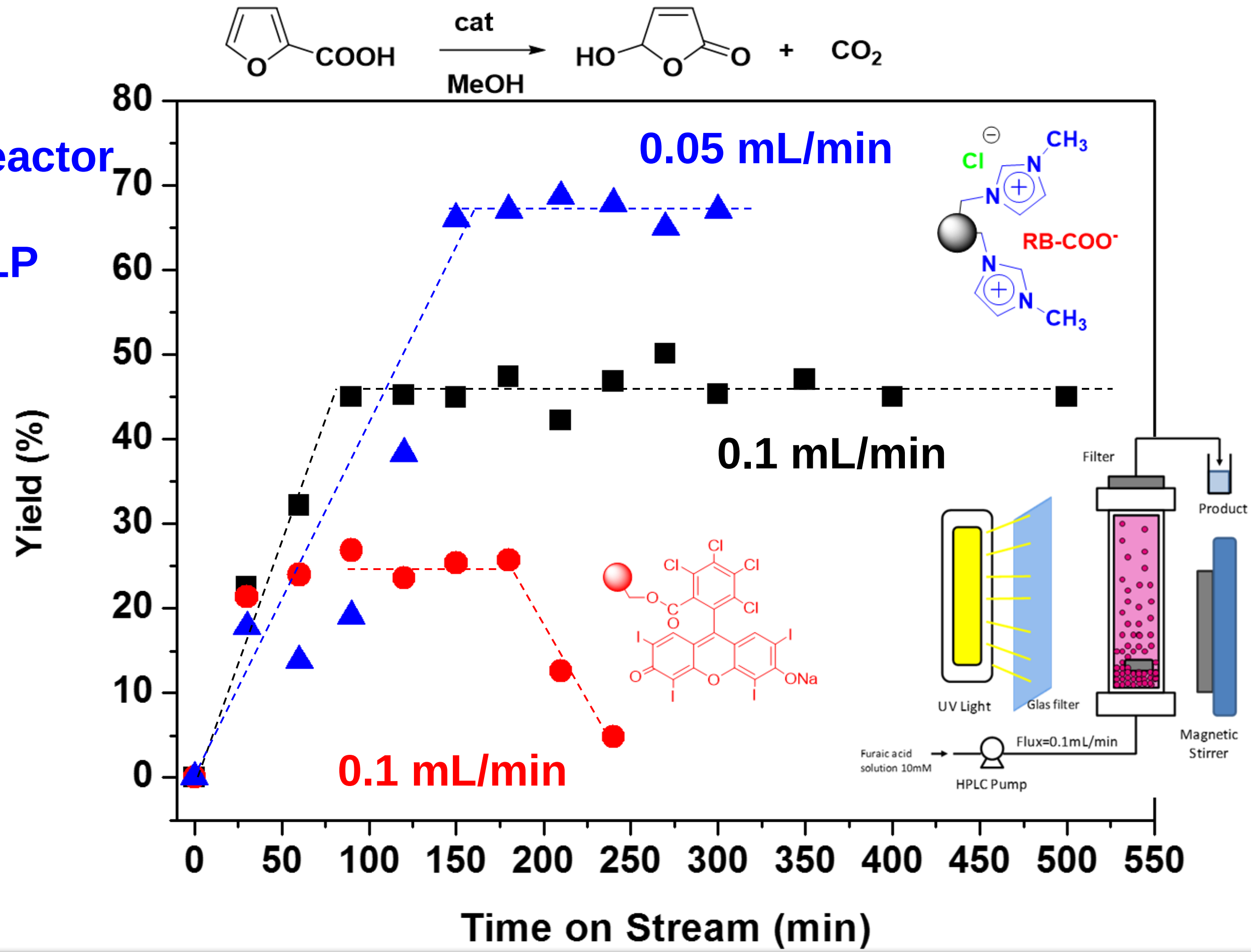
Application of SILLPs: Supported photocatalysts

Fluidized bed reactor
10 mL
250 mg RB-SILLP



Cyanosilylation of Carbonyl Compounds

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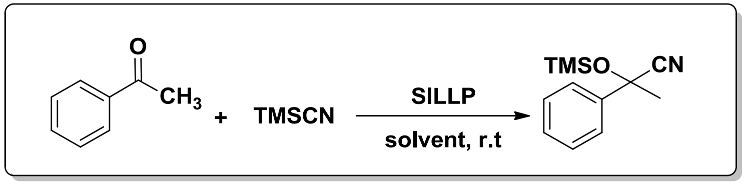
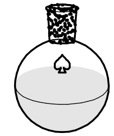
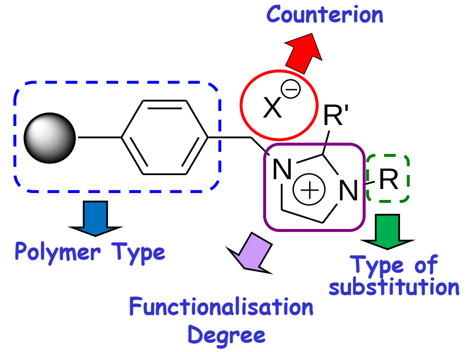
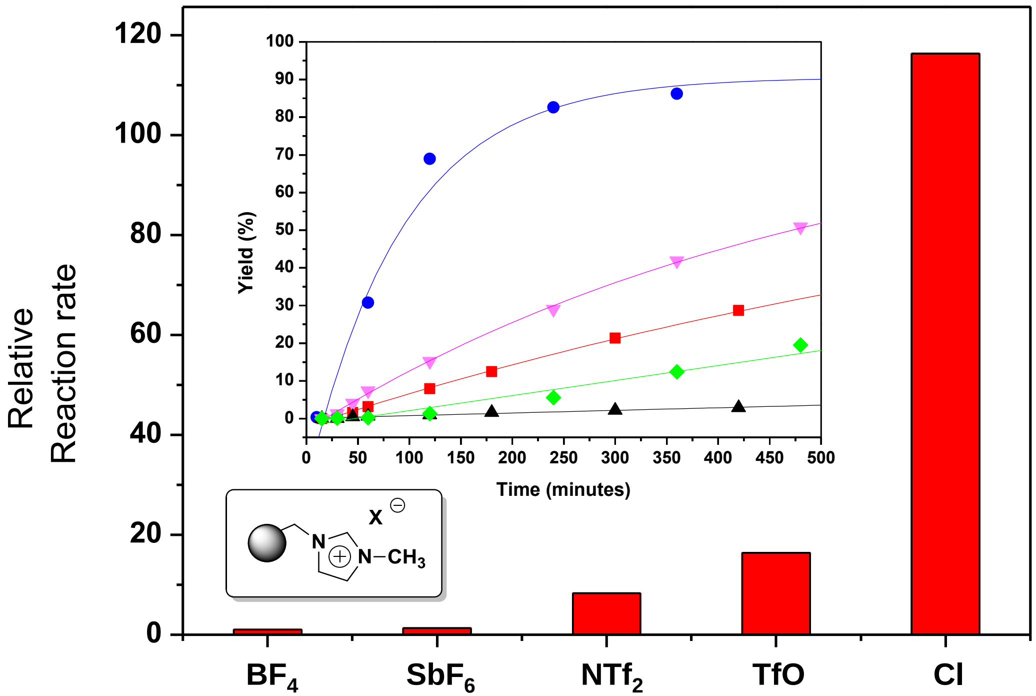
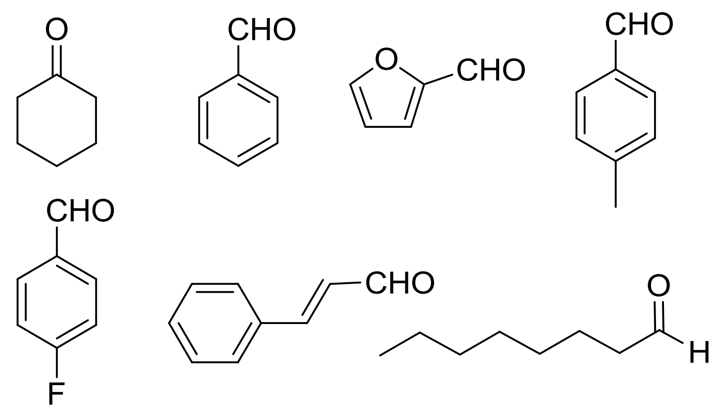








- ❑ More basic SILLP more active catalyst



- ❑ > 99% yield for different ketones and aldehydes

Green Chem., **2014**, 16, 1639.

Cyanosilylation of Carbonyl Compounds

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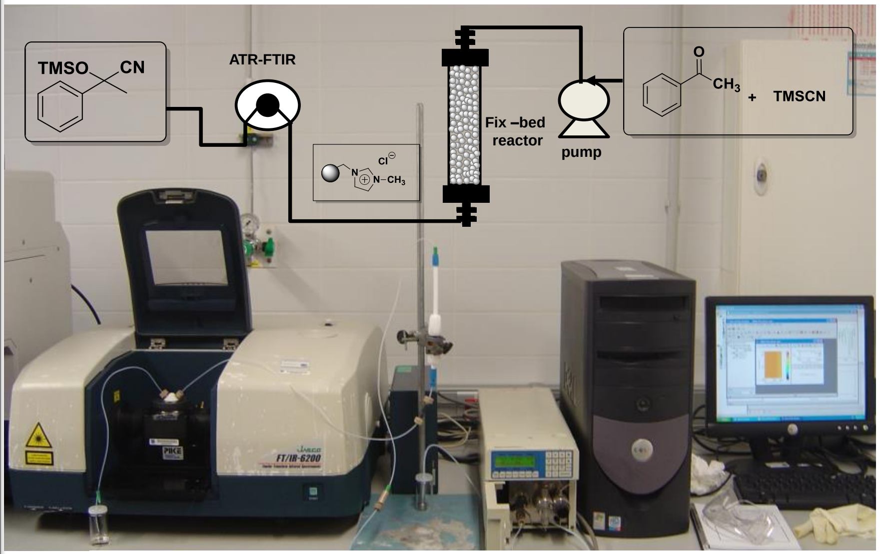
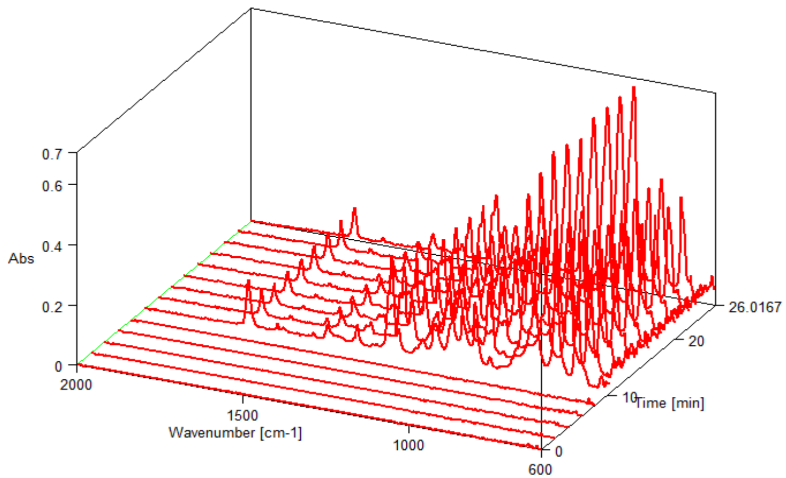
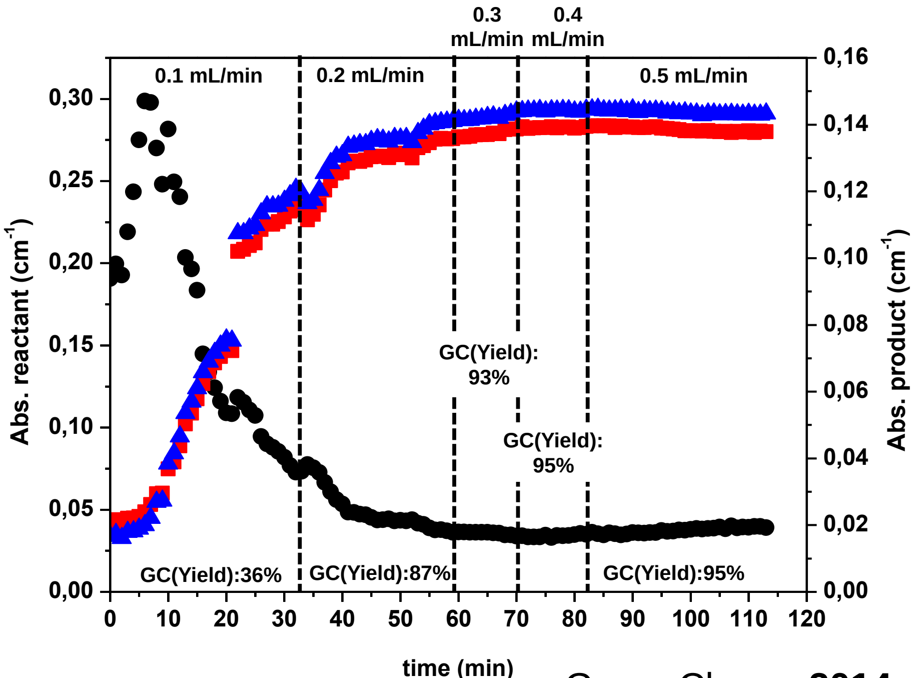




FLOW PROCESS

- ✓ **95% yield,**
- ✓ **solvent-free,**
- ✓ **excellent catalytic activity,**
- ✓ **continuous monitoring**



Green Chem., **2014**

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Natural biosynthetic systems

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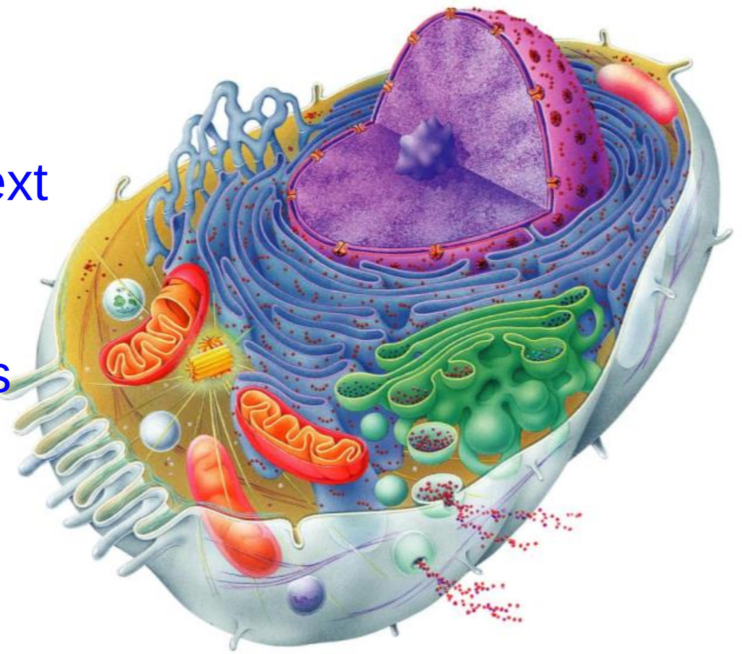
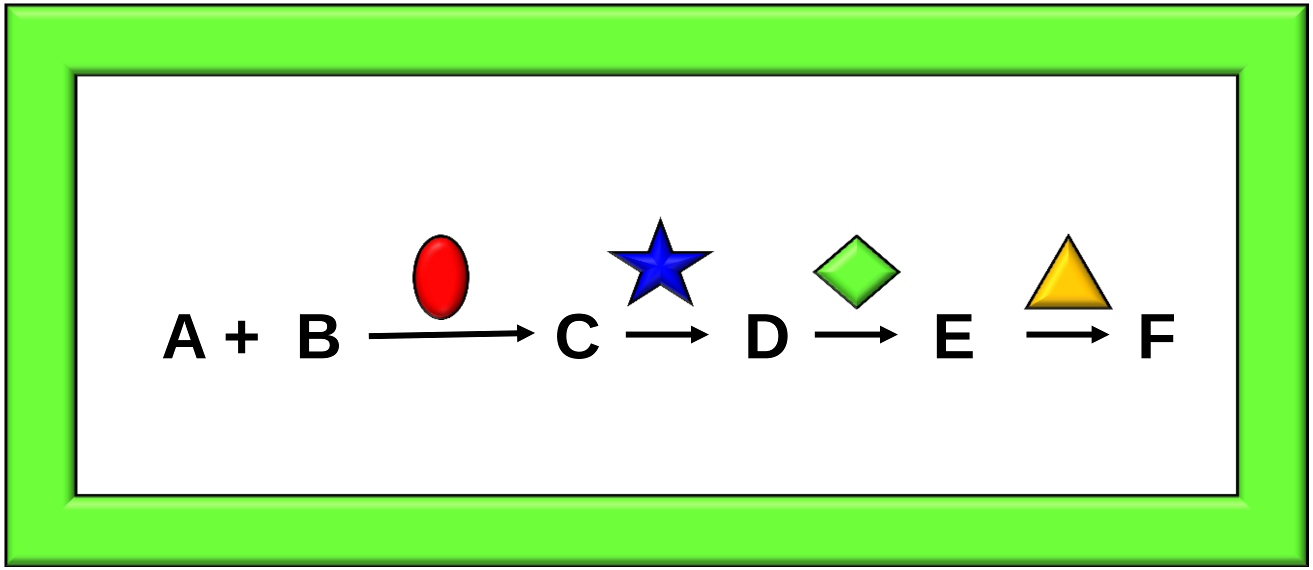
Cells produce complex compounds

- ✓ many catalytic reactions occurring in the same vessel
- ✓ products from one step do not inhibit the next one.
- ✓ Reagents compatibility: oxidants/reductants or nucleophile/electrophile together.
- ✓ linear combination of irreversible steps



Non-natural biosynthetic systems



- ✓ Isolation of incompatible catalysts
- ✓ Reagent(s)/product(s) compatibility.
- ✓ linear combination of irreversible steps

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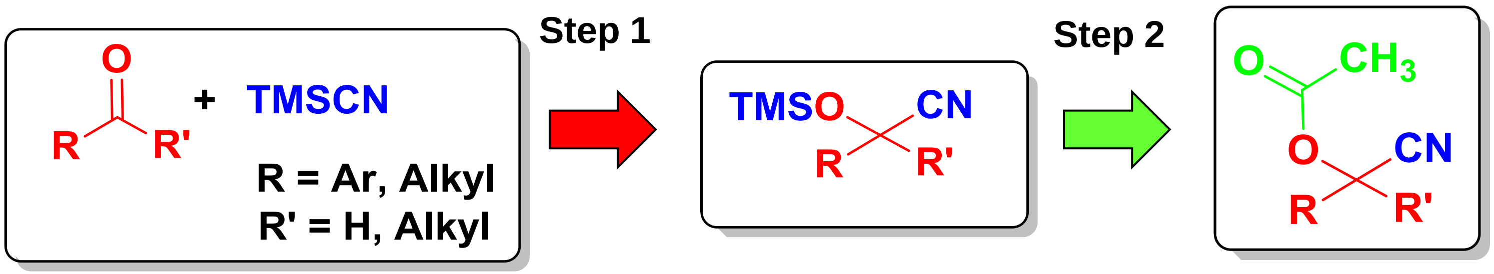
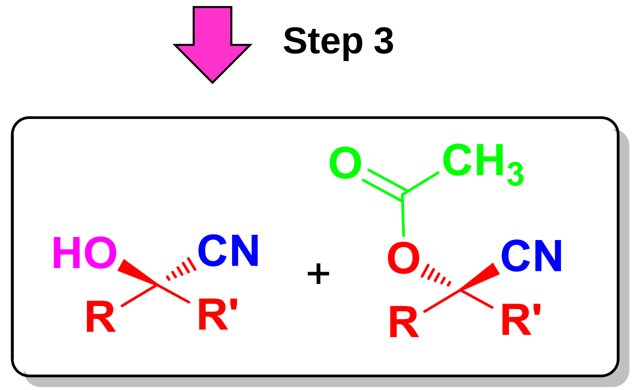
Synthesis of cyanohydrin





- **Step 2**: two reactions: hydrolysis of TMSOR and acetylation
- **Step 3**: Enzymatic trans-esterification, enantiopure cyanohydrins
- Overall: 4 reactions in 3 consecutive steps

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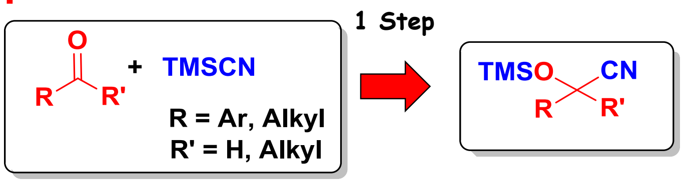
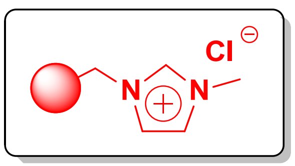
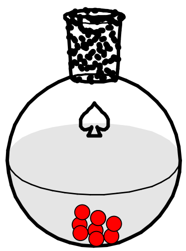
Synthesis of cyanohydrin

Batch process:

Step 1

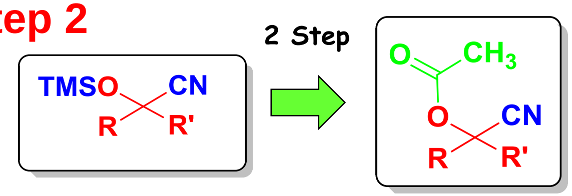


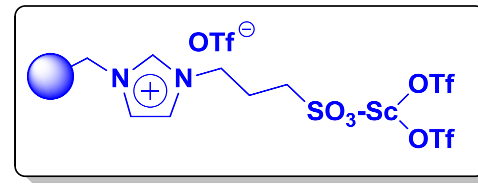


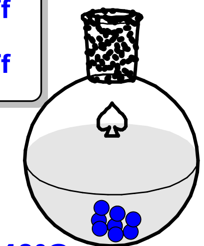


- 1 eq acetophenone 1,2 eq TMSCN; rt, 24h.
- Cat: 25 mg/mmol benzaldehyde
- Yield: >99%

Step 2

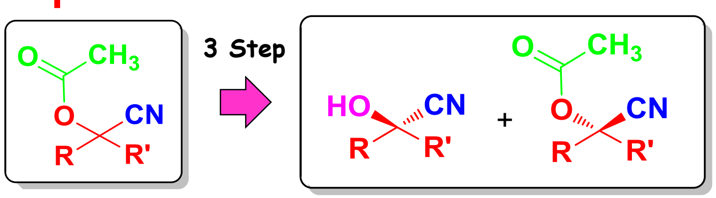


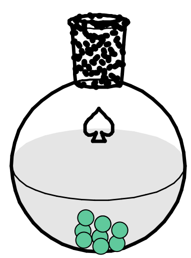




- 1 eq substrate, 2 eq Ac_2O, 40ºC, 24h.
- 50 mg cat / mmol substrate.
- Yield: >99%

Step 3



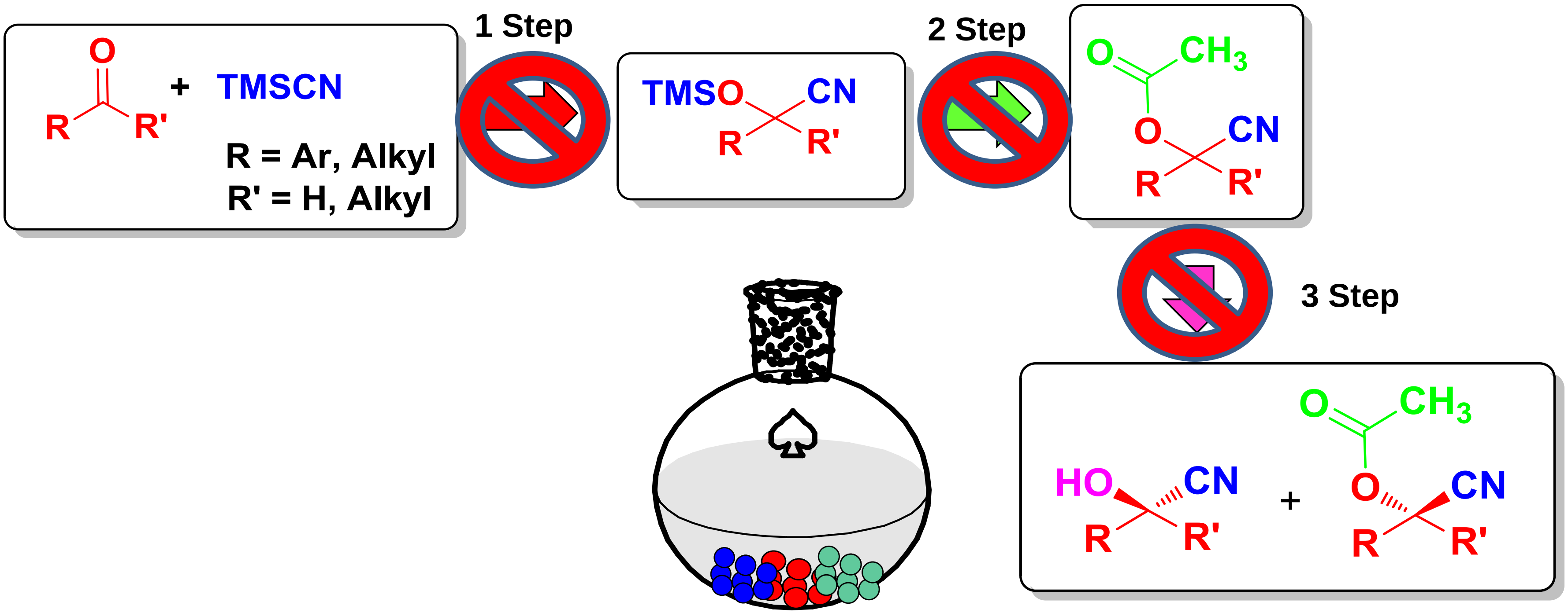


- 9,8 ml methyl-THF, 0,15ml n-propanol and 100 mg CAL-B (Novozyme 435) /mmol substrate; 60ºC, 24h.
- 50% conv.,
- ROH: 98% e.e., AcOR: 99% e.e.

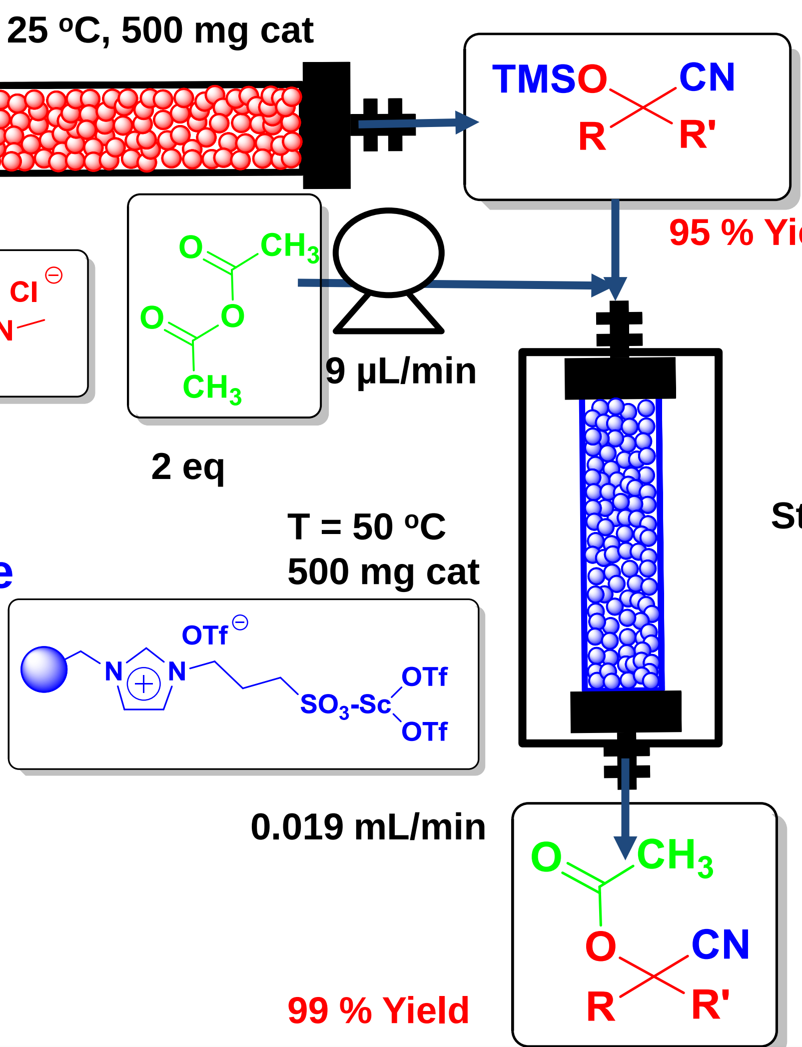
Synthesis of cyanohydrin

Batch process:

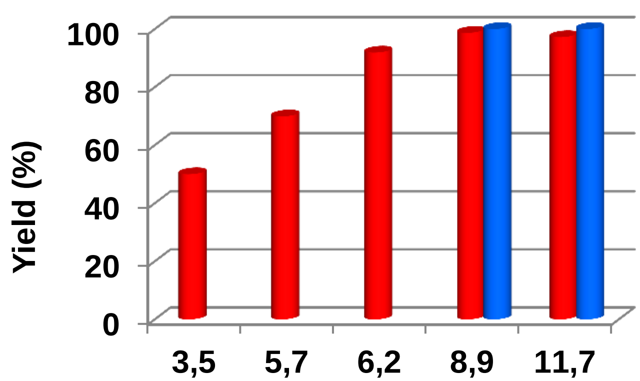
One-pot multistep batch process



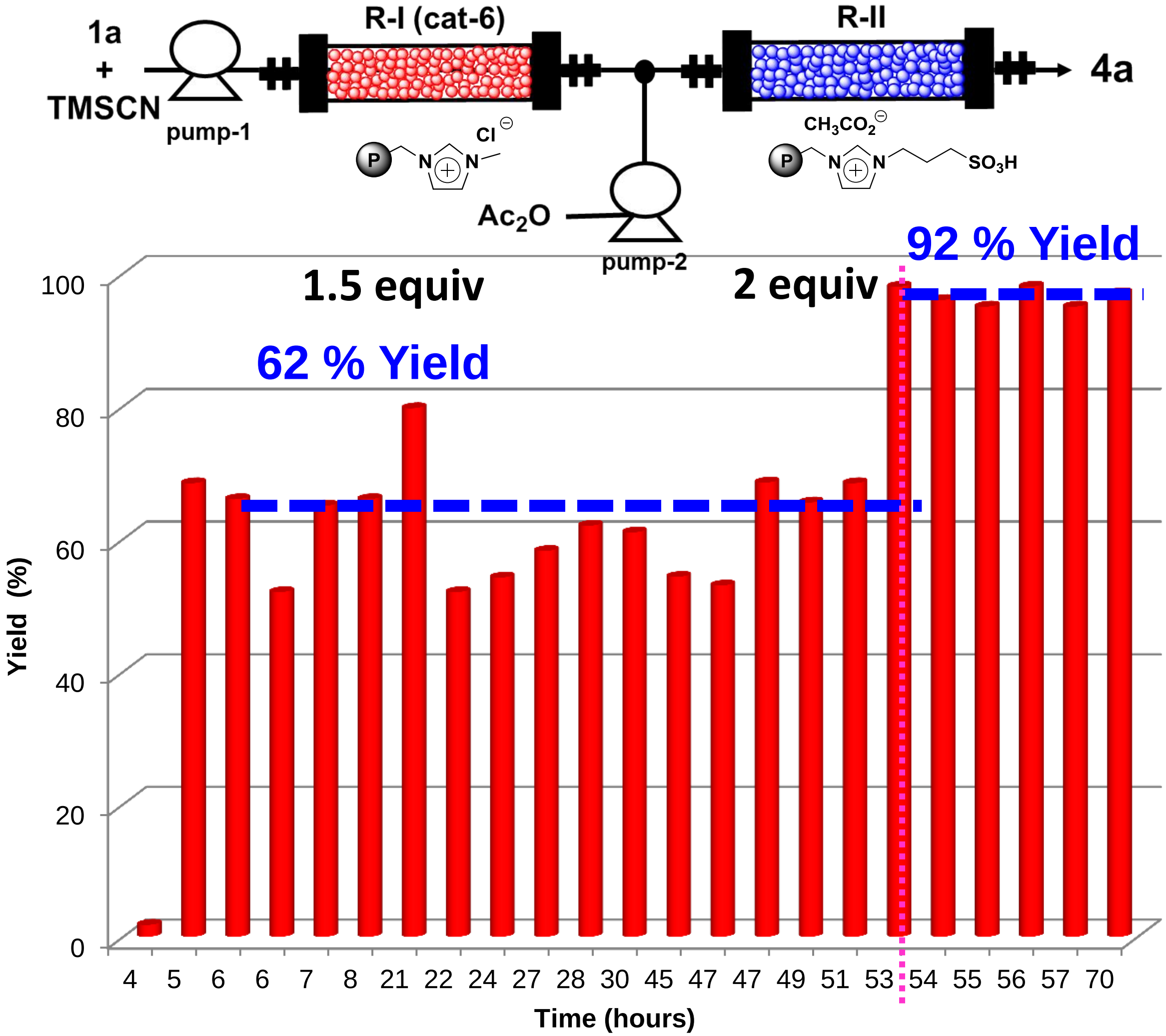
Synthesis of cyanohydrin- Flow process

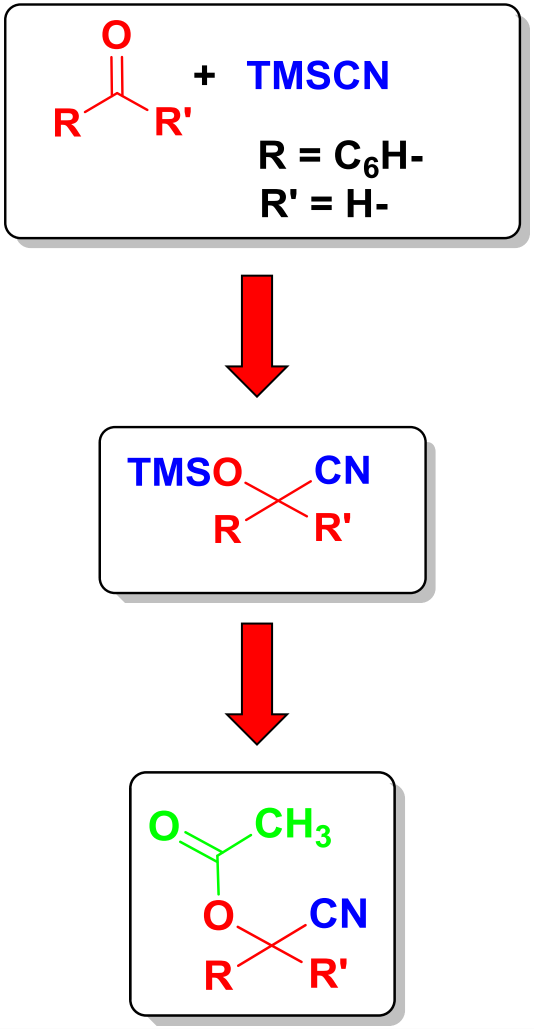


- ❑ Up to 85 overall yield for the two steps
- ❑ Single pot reactor mixing catalyst and reagents does not work
- ❑ Stable for up to 12h continuous use



Synthesis of cyanohydrin- Flow process





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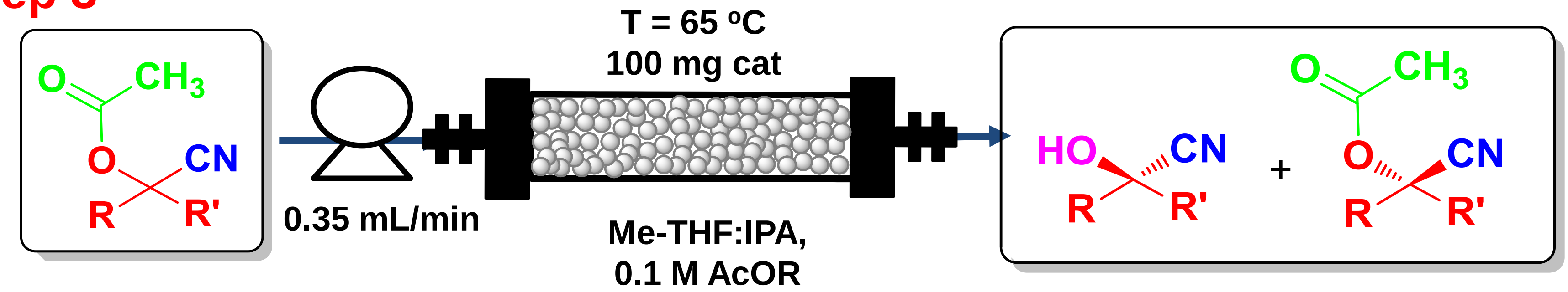
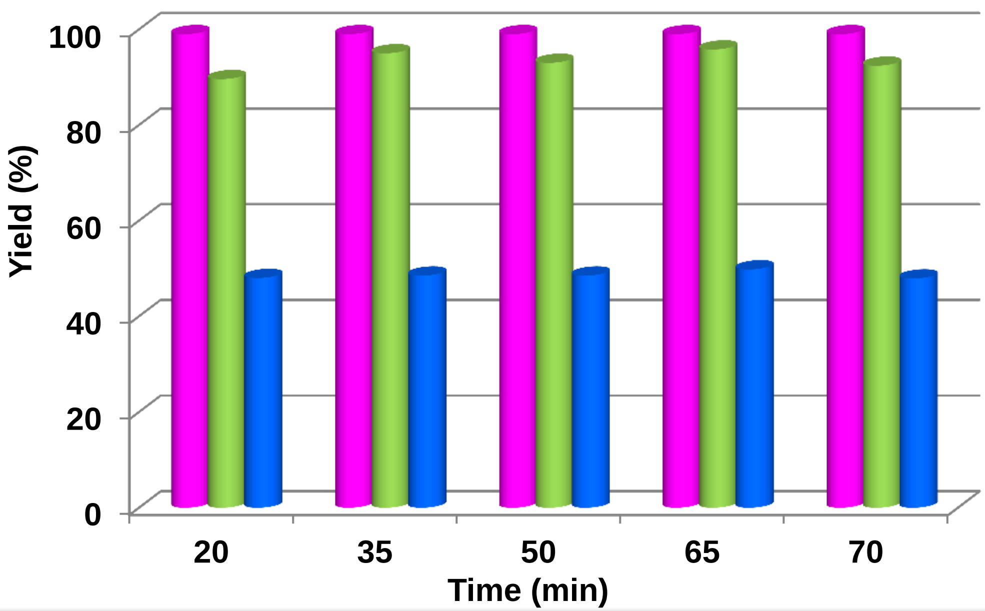
Synthesis of cyanohydrin- Flow process

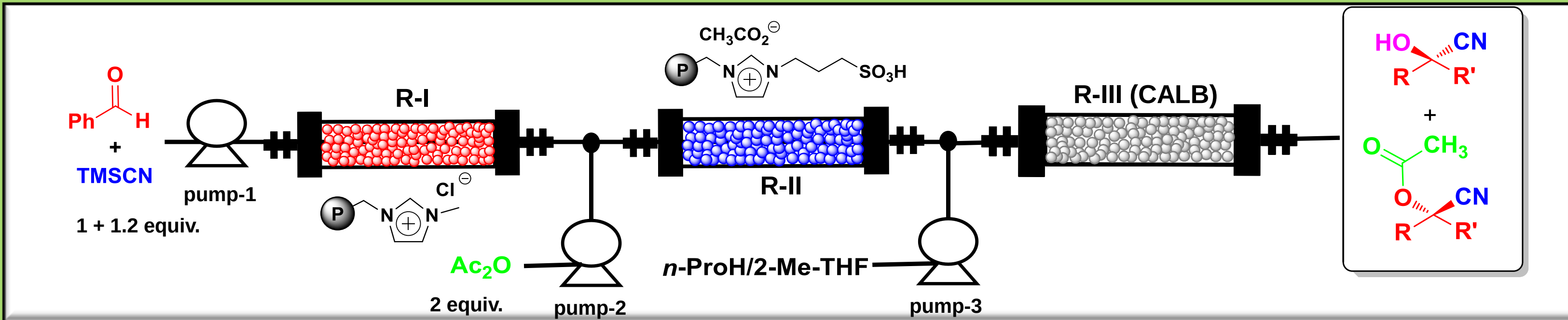
Step 3

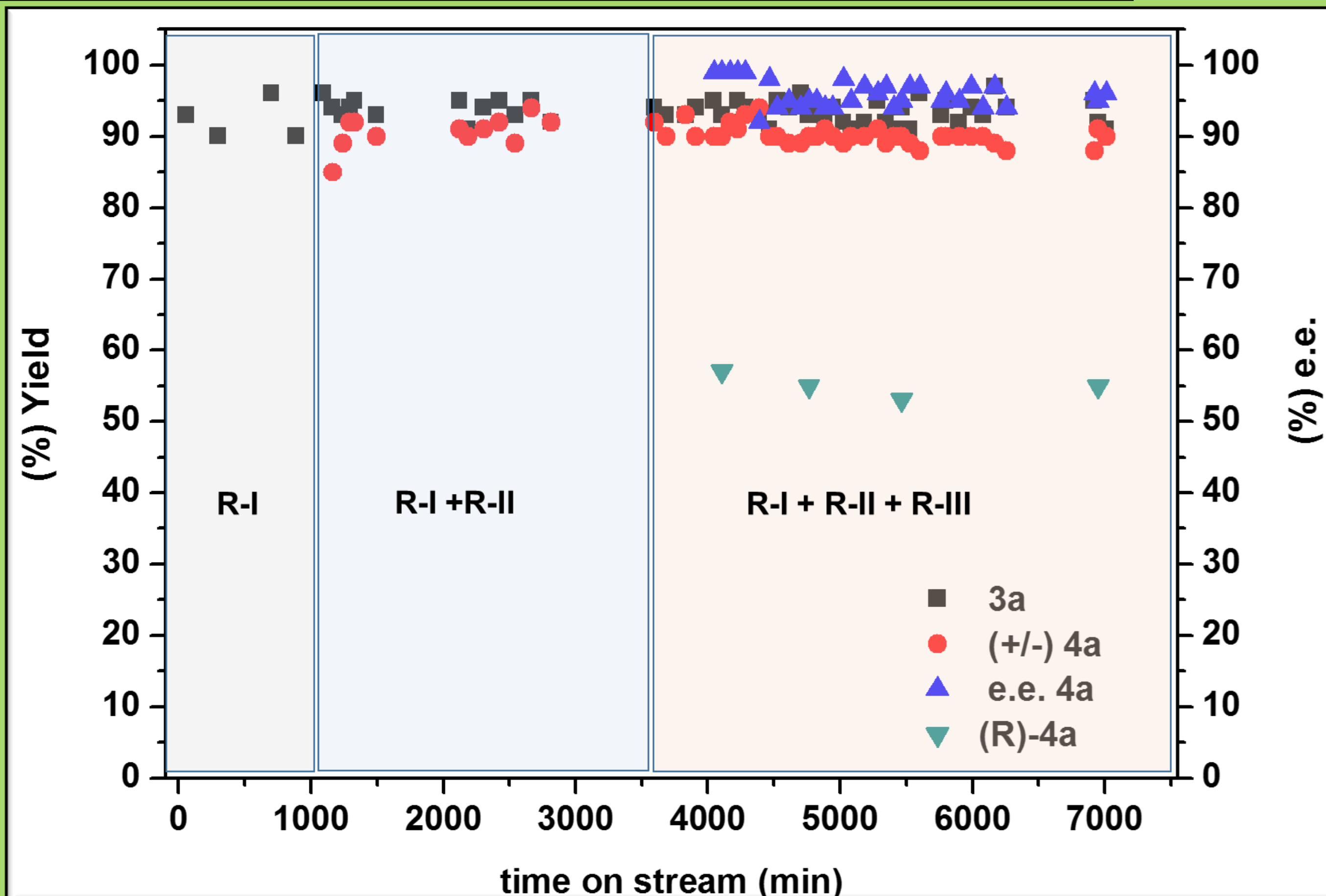




- ❑ Up to 48 % conversion
- ❑ 99% e.e. ROH
- ❑ 95% e.e. AcOR

Synthesis of cyanohydrin- Flow process





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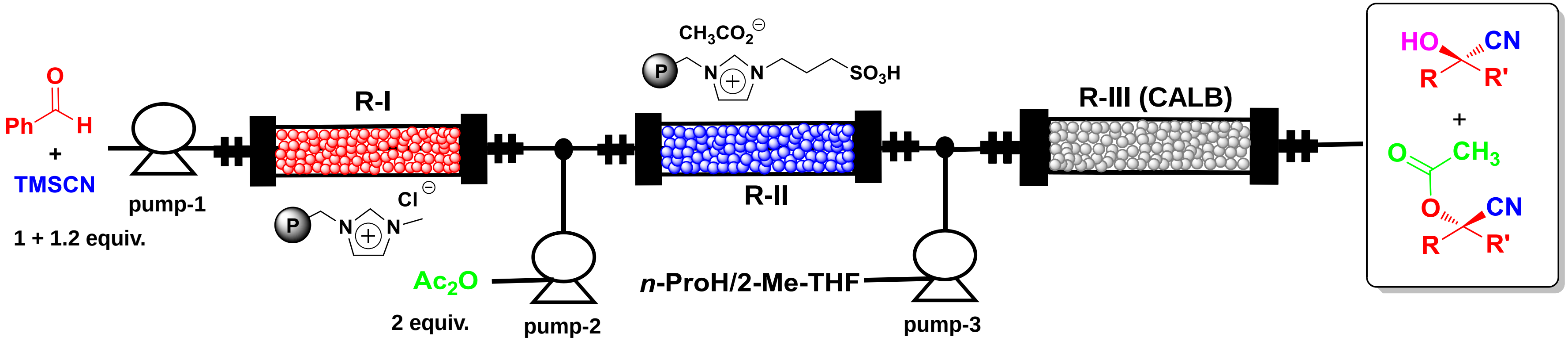
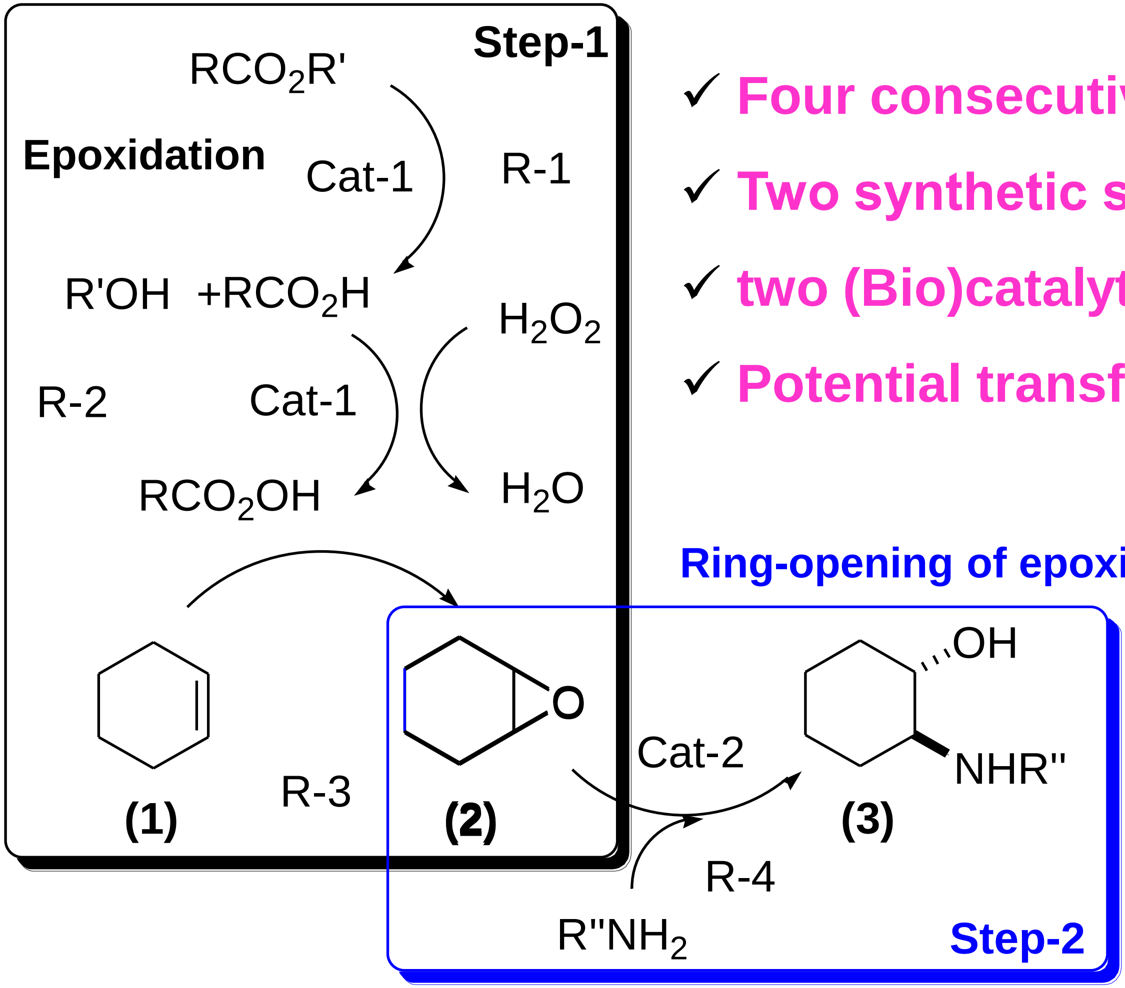
Synthesis of cyanohydrin- Flow process



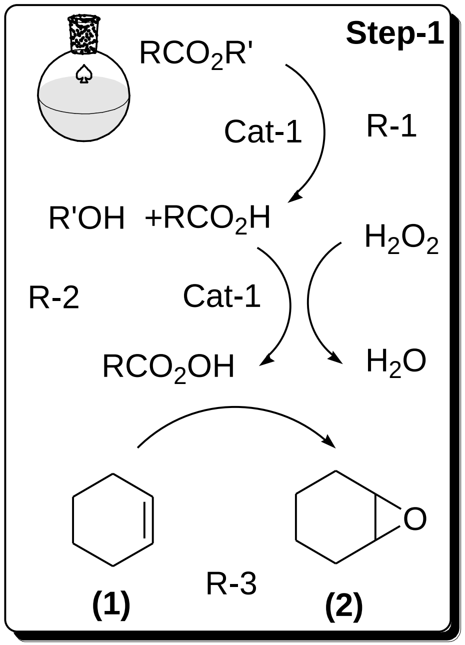
- ❑ Four consecutive reactions
- ❑ Three synthetic steps “one-pot”
- ❑ Metal free synthesis
- ❑ Five days ToS highly stable.
- ❑ Final product in high yield
- ❑ > 98%ee for the (*R*) acetylated product

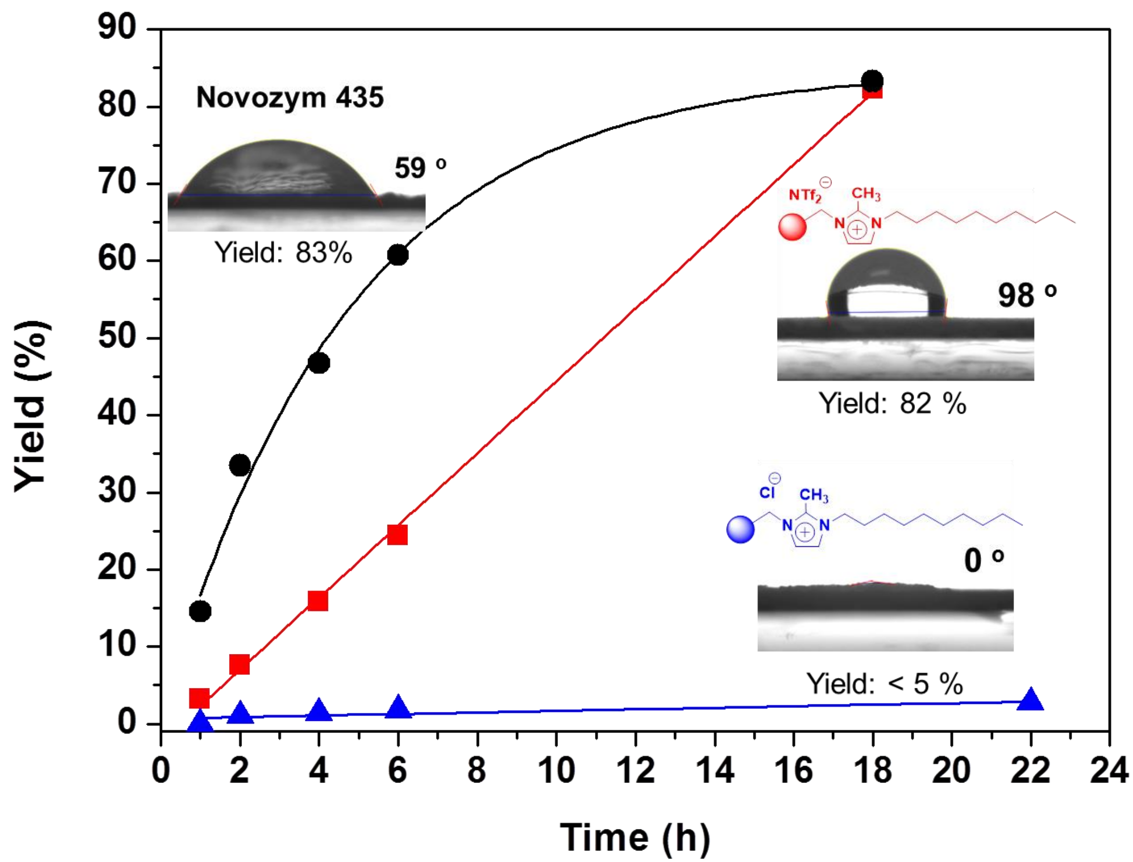
Synthesis of amino alcohols



- ✓ Four consecutive reactions
- ✓ Two synthetic steps “one-pot”
- ✓ two (Bio)catalytic steps (enz. and chemo)
- ✓ Potential transfer to flow conditions.

Synthesis of amino alcohols- Epoxidation





- **Step 1**: lipase-mediated epoxidation of cyclohexene
- **DMC** as solvent and source of peroxy acids (residues CO_2 and MeOH)

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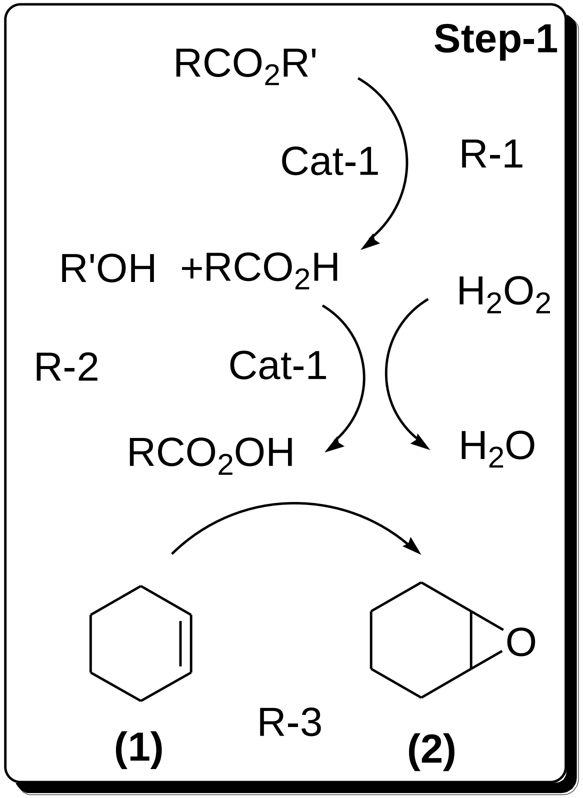
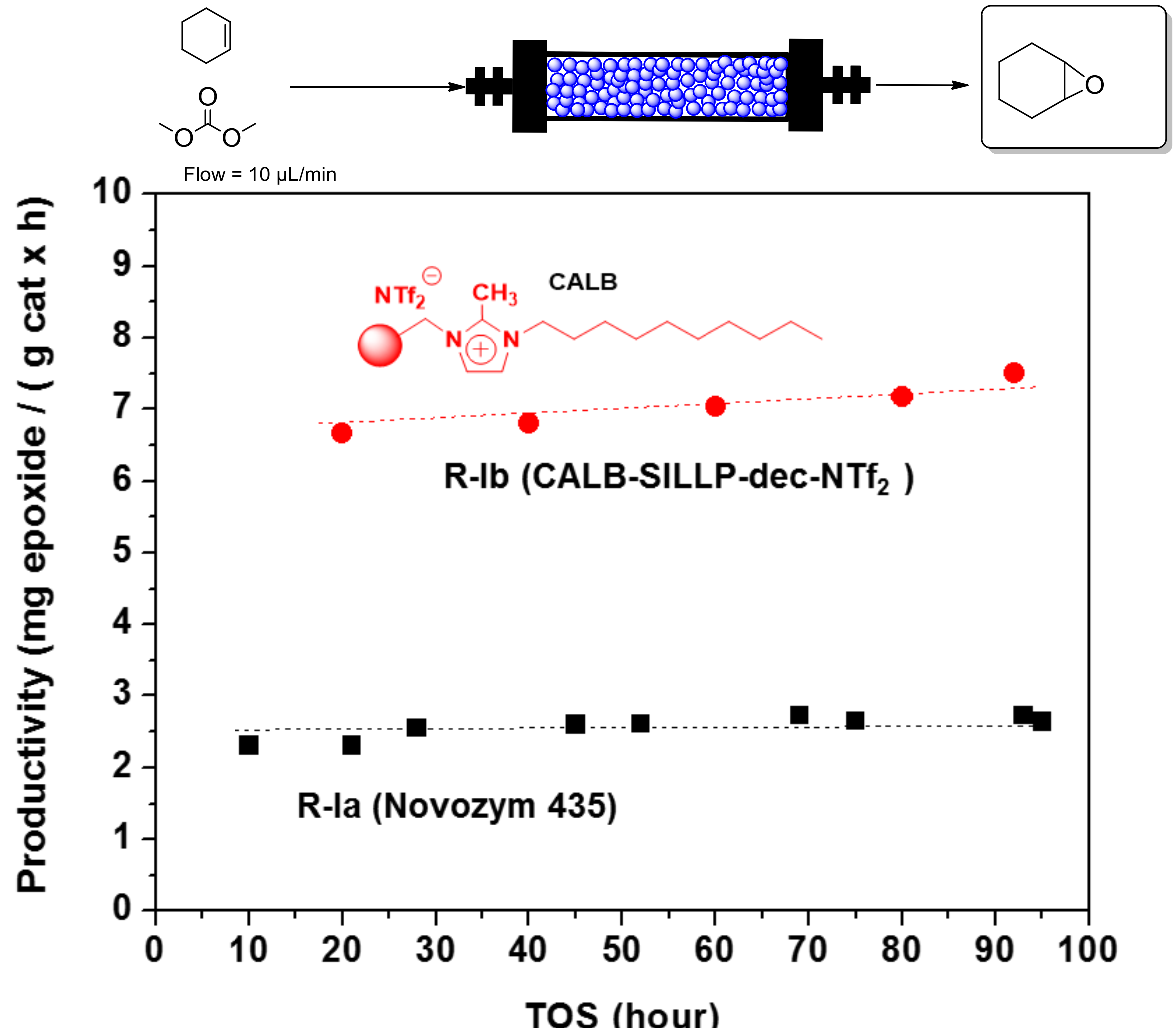
Synthesis of amino alcohols-
Flow Epoxidation





✓ **Stable catalyst for hydroperoxydation**

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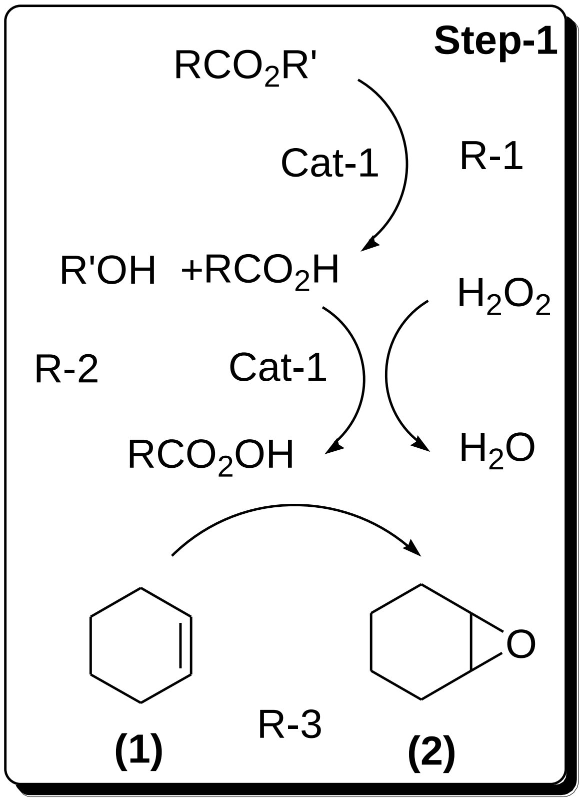
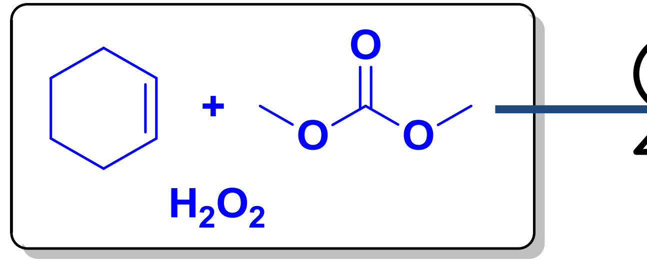
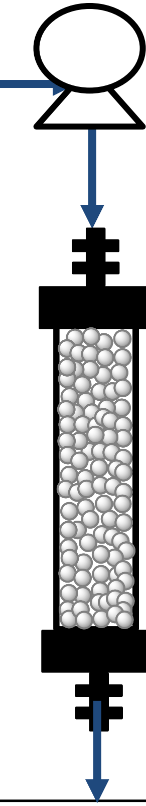
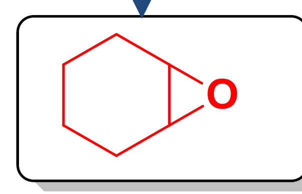
Synthesis of amino alcohols-
Flow Epoxidation





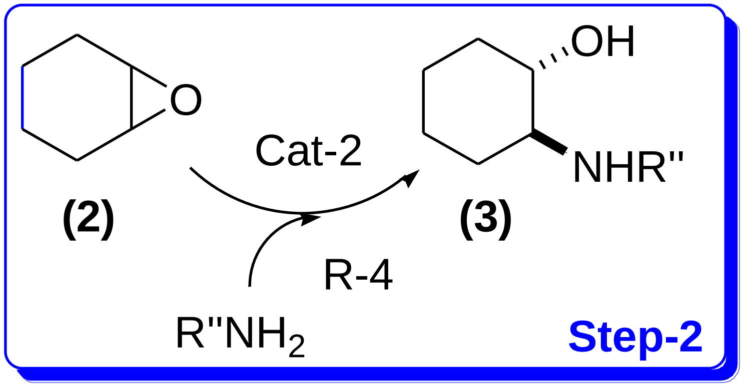


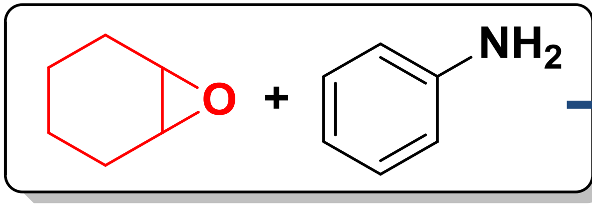
- ❑ cyclohexene (1equiv.), H_2O_2 (50%) (2.5 equiv.), dimethyl carbonate (0.1 mmol/mL), 1/8 TFA fix-bed reactor (180 mg), 45 ºC , 5µL/min, **97% of yield was obtained**.
- ❑ same conditions but 1 equiv. of H_2O_2 (50%), **72% of yield was obtained**.

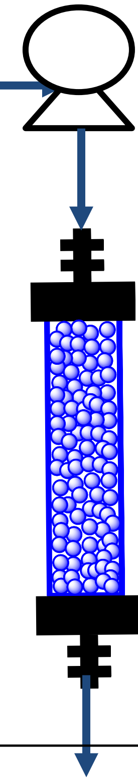


✓ Epoxidation feasible with CALB as catalyst for hydroperoxydation

Synthesis of amino alcohols-
Epoxide opening- Flow process

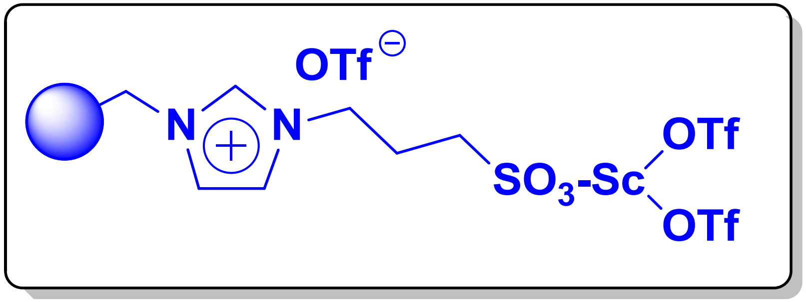


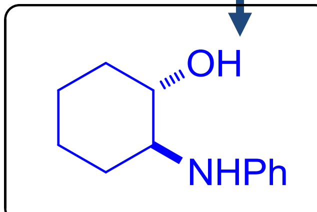




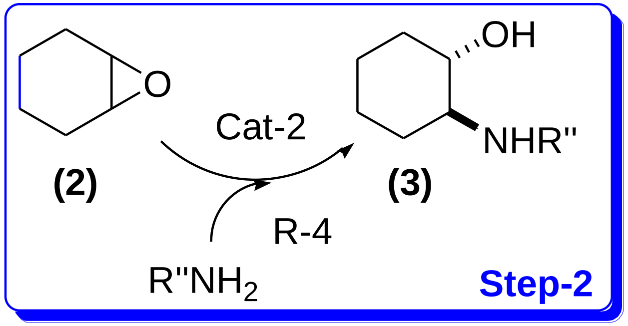
cyclohexene epoxide (1equiv) **aniline** (1equiv) in dimethyl carbonate (0.25 mmol/mL) (flow of 7µL/min), TFA reactor packed with SILLP-SO3-Sc (264 mg), at 45 ºC.

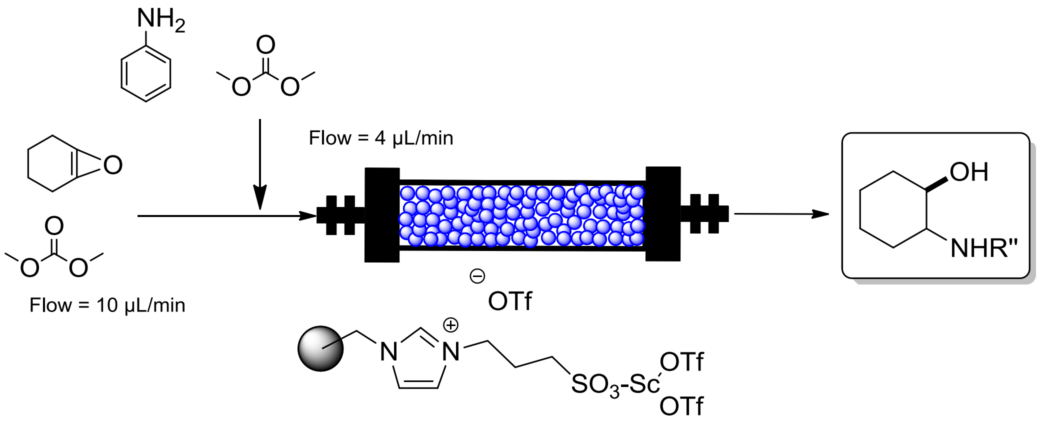
99% of yield was obtained.





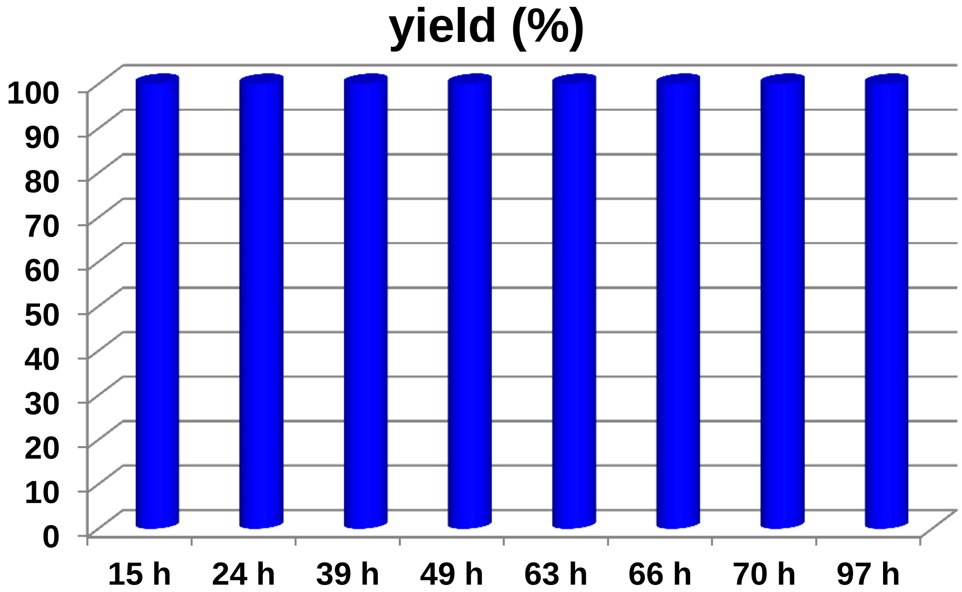
Synthesis of amino alcohols-
Epoxide opening- Flow process





cyclohexene epoxide (1equiv) **aniline** (1equiv) in dimethyl carbonate (0.25 mmol/mL) (flow of 10µL/min), SILLP-SO3-Sc (1g), at 45 ºC.

- ❑ **99% of yield was obtained.**
- ❑ Stable for 97 hours of continuous use



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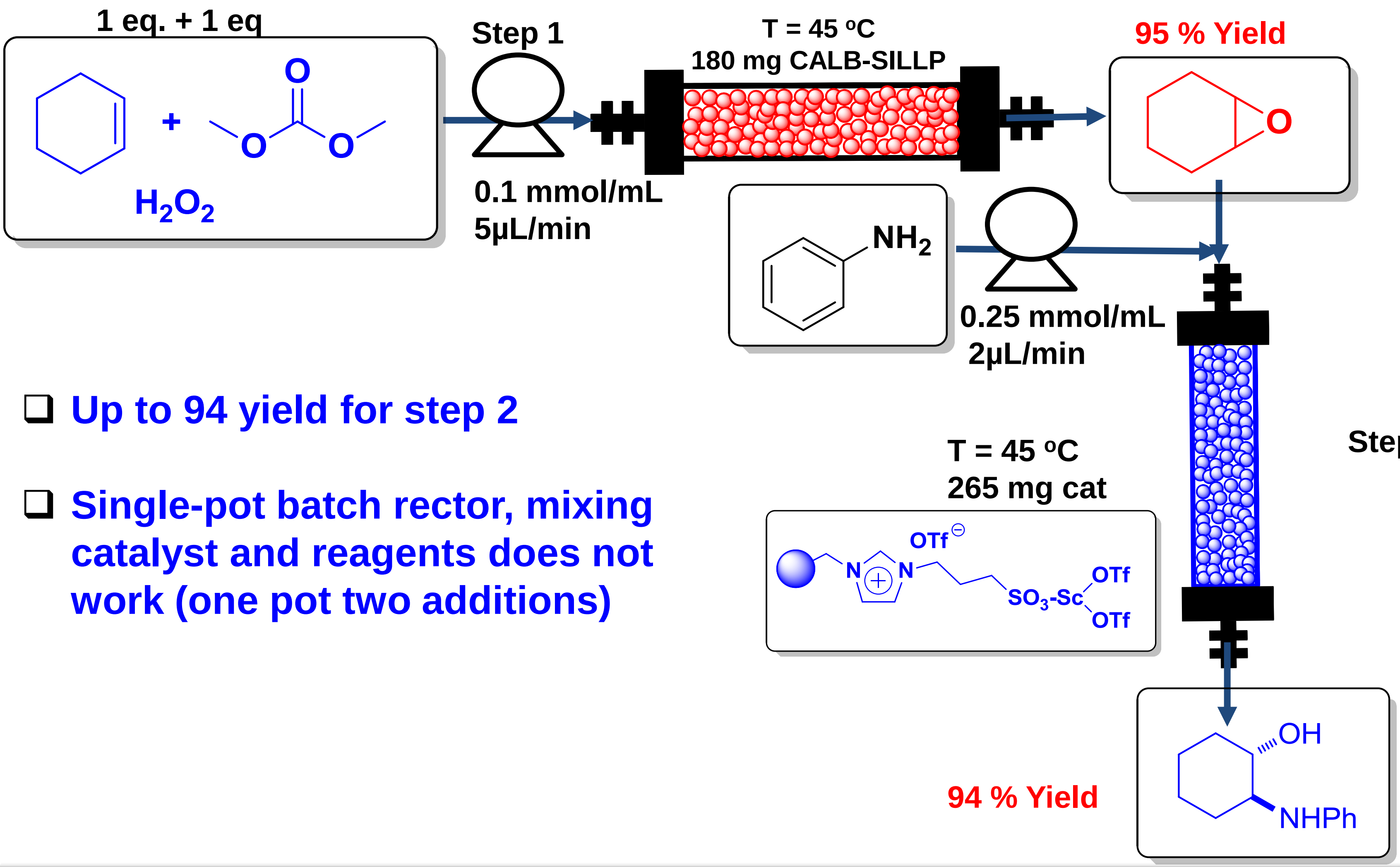
Synthesis of amino alcohols-
Coupled flow process



- Up to 94 yield for step 2
- Single-pot batch rector, mixing catalyst and reagents does not work (one pot two additions)

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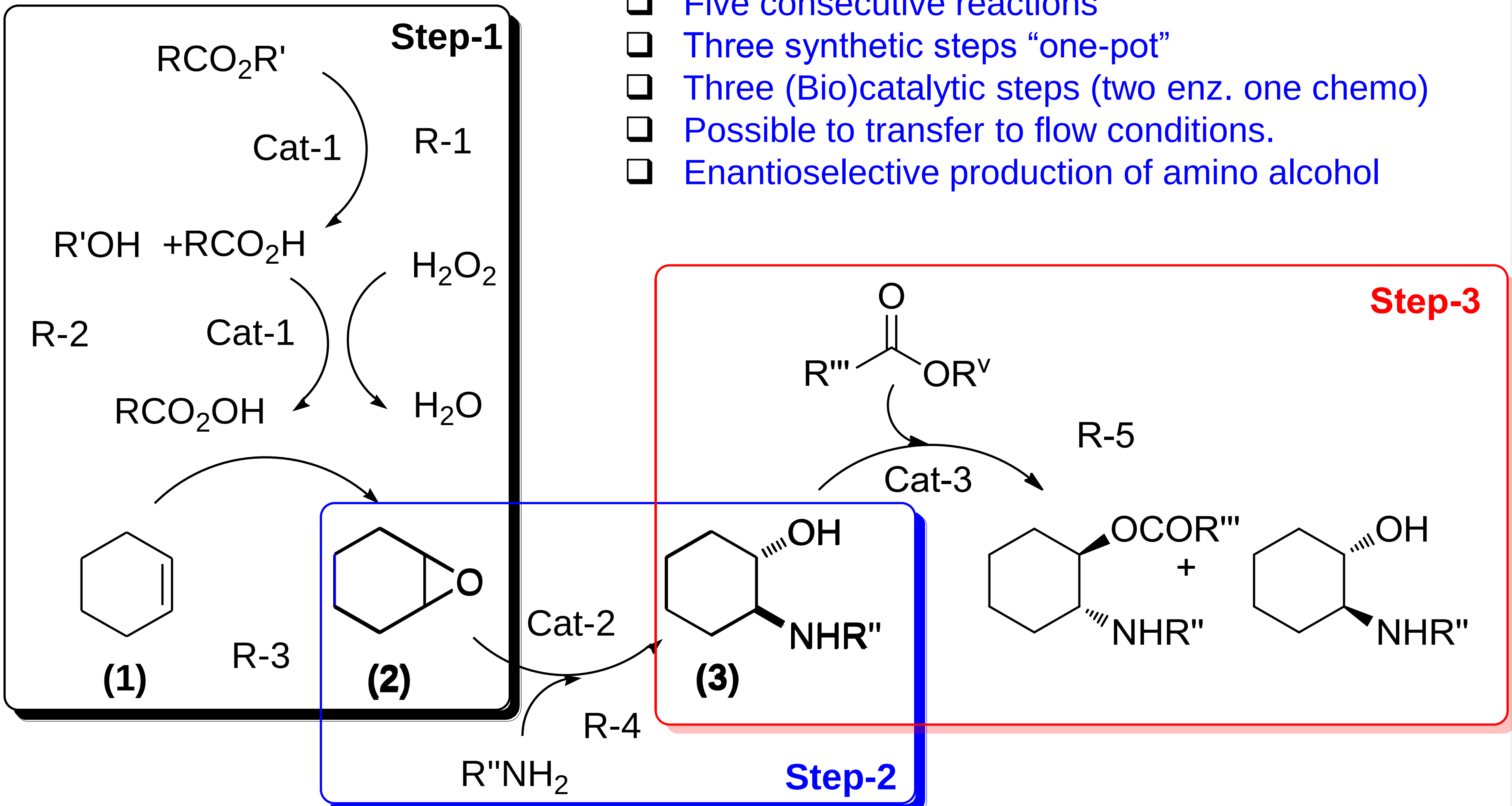
Synthesis of amino alcohols

- Five consecutive reactions
- Three synthetic steps "one-pot"
- Three (Bio)catalytic steps (two enz. one chemo)
- Possible to transfer to flow conditions.
- Enantioselective production of amino alcohol



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Synthesis of amino alcohols-Resolution Flow Process

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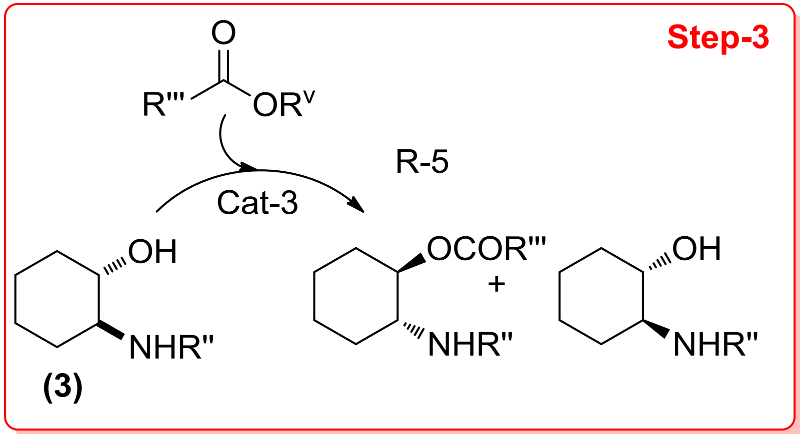
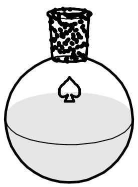
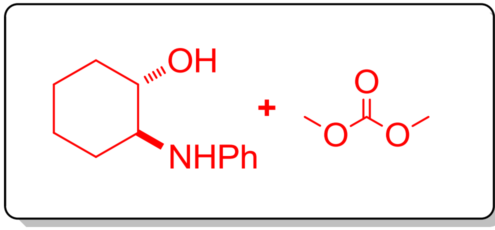
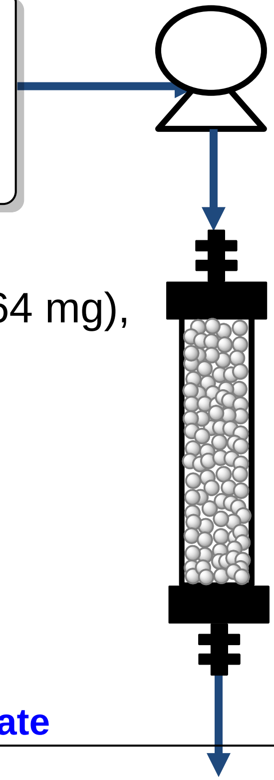




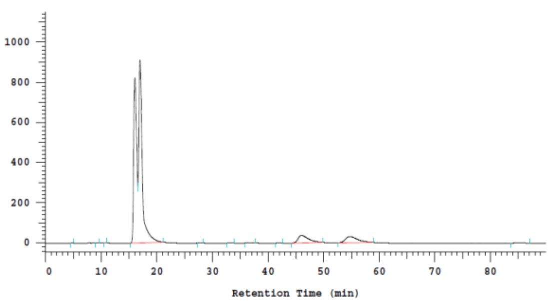
Step 1: aminoalcohol (1 eq), CAL-B (50 mg), dimethyl carbonate (1 mL) for 71 h at 50 ºC and 250 rpm.

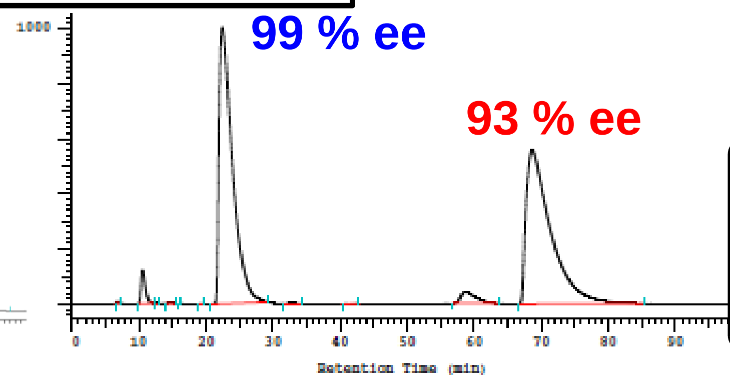




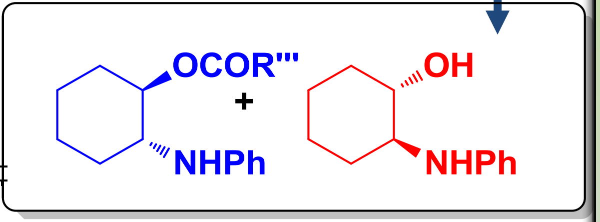
Aminoalcohol (0.25 mmol/mL) (flow of 7µL/min), Novozyme (264 mg), at 50 ºC.

47% of yield was obtained.





47% yield
99% ee carbonate



Synthesis of amino alcohols-Resolution Flow Process

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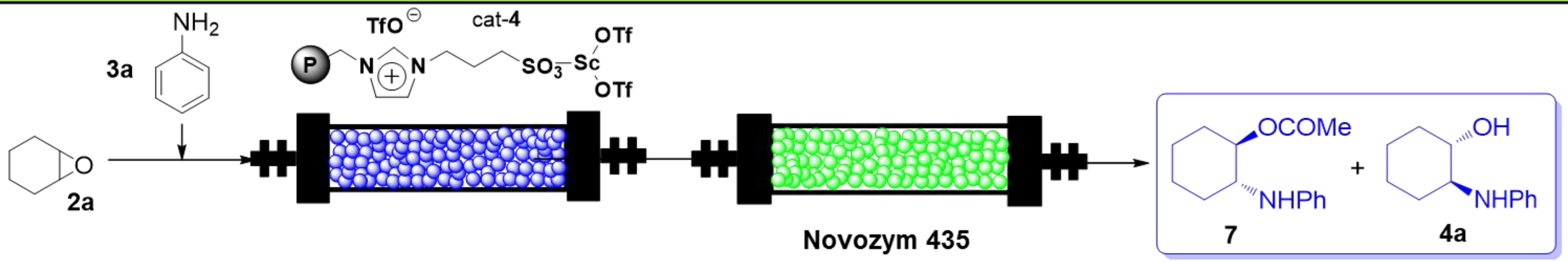
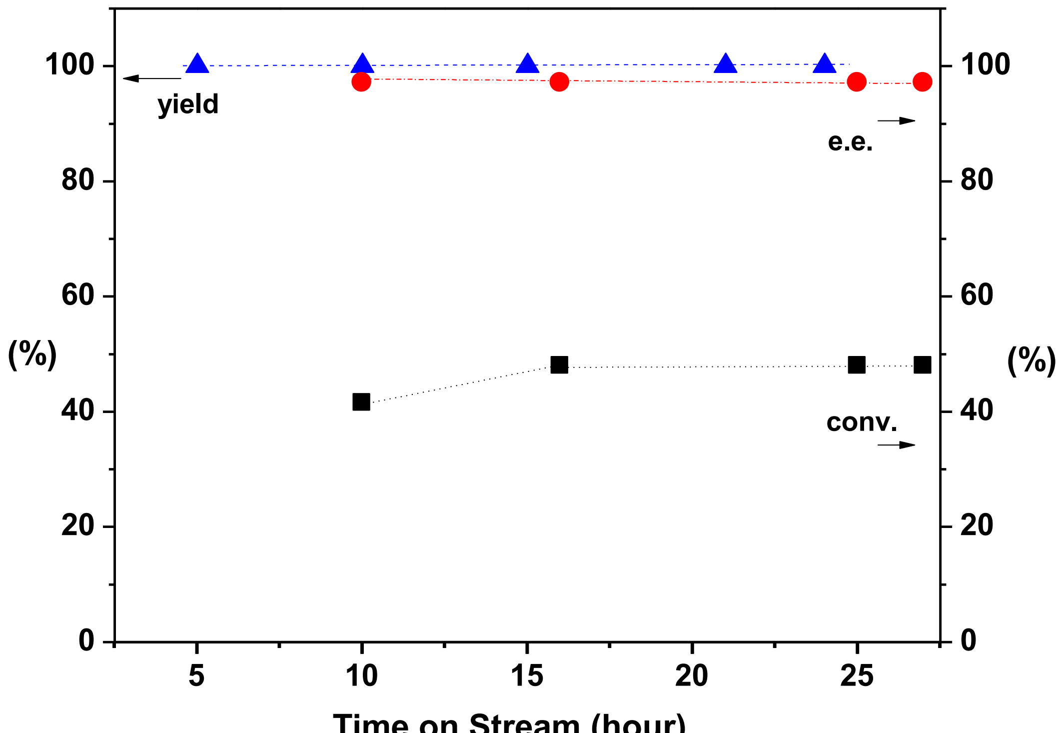
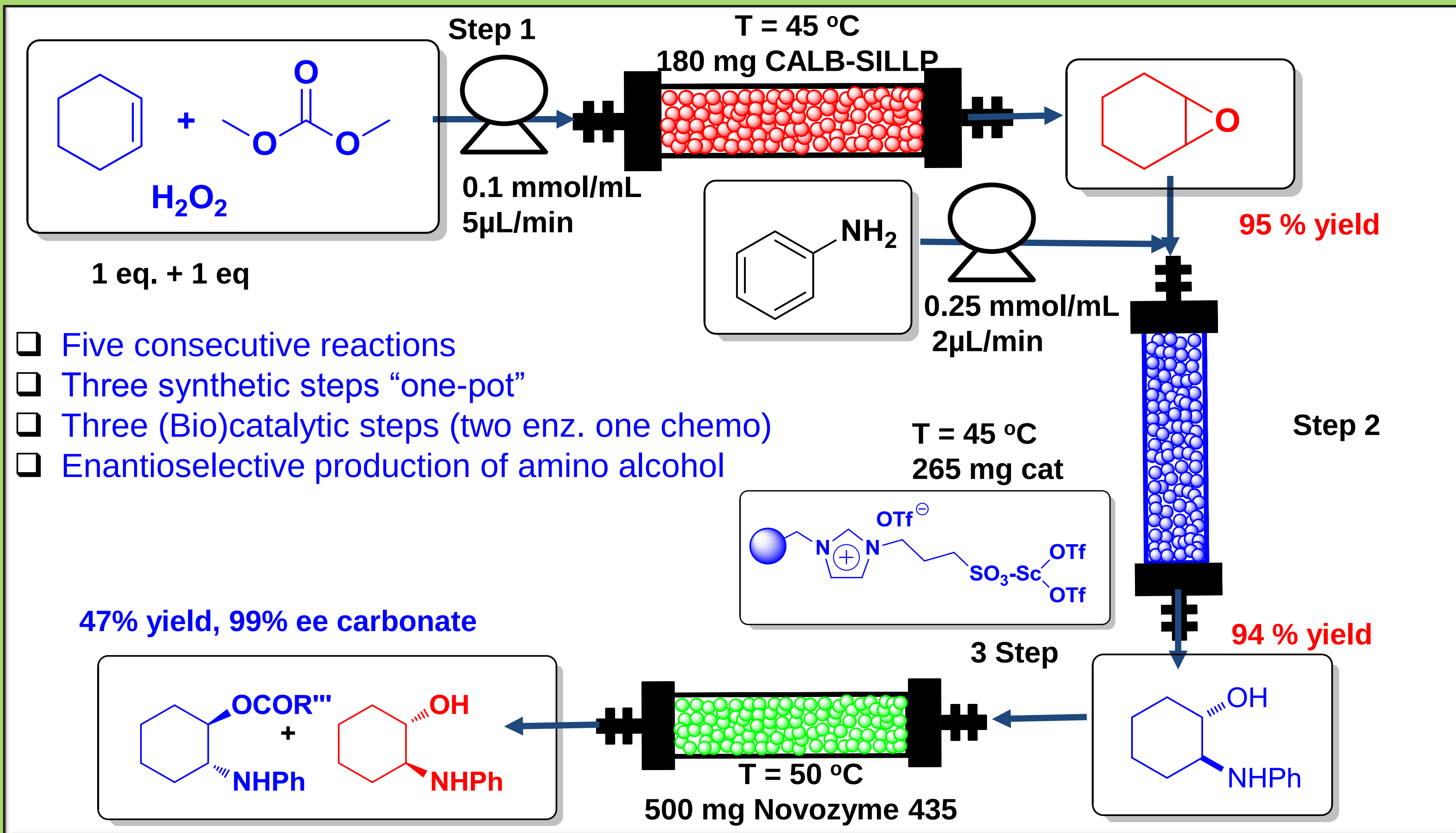


- 47 % conversion
- 99 % *e.e.* ester
- 97 % *e.e.* alcohol
- Stable 27 hours continuous use
- Enantioselective production of amino alcohol



Synthesis of amino alcohols Flow Process



- Five consecutive reactions
- Three synthetic steps “one-pot”
- Three (Bio)catalytic steps (two enz. one chemo)
- Enantioselective production of amino alcohol

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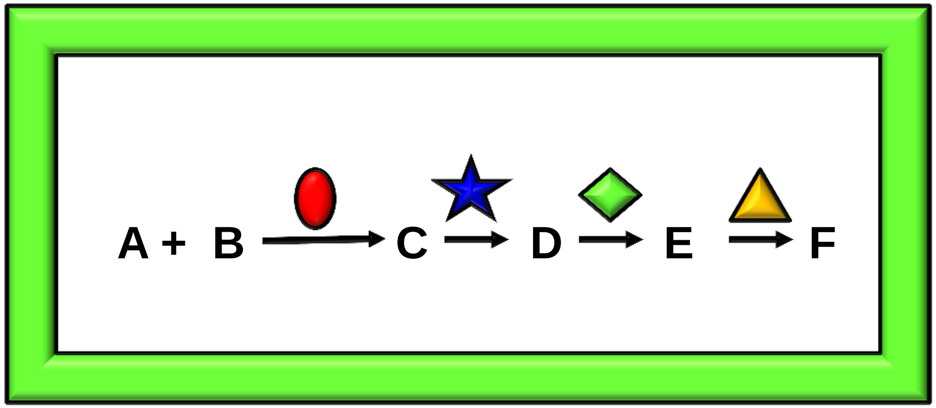
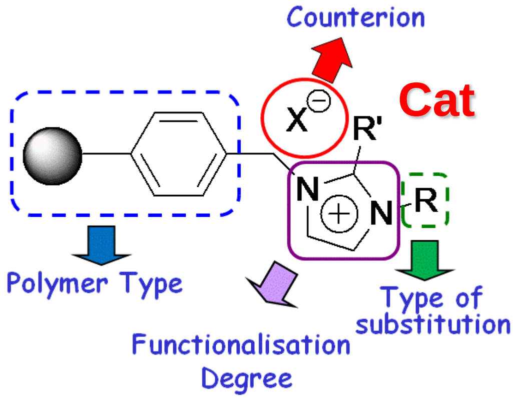
Conclusion

It is possible the immobilisation of ILs onto a support by covalent linking, transferring the IL properties to the solid phase leading to i.e. monolithic or gel-type polymer supported ionic liquid phases (SILLPs)

- minimize the amount of ILs used
- avoid toxicological concerns
- easy separation and recyclability
- mini-flow catalytic reactors for continuous processes in SCFs/green solvents
- can be applied to both Chemical Catalysis and Biocatalysis
- many potential applications beyond





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