

# Fast Hydrogenation: Systematic development and optimisation of hydrogen reductive processes in a Corning Advanced-Flow Reactor.

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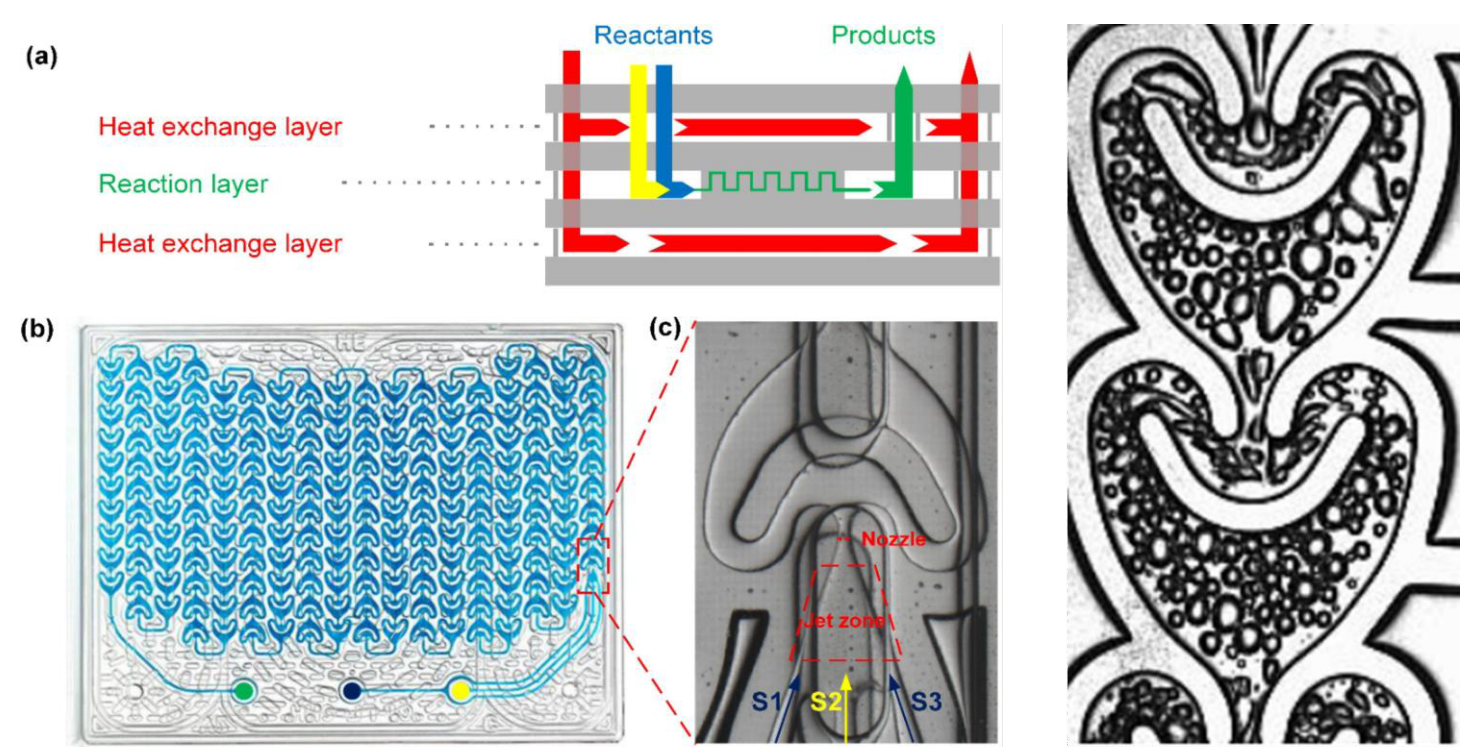
## Introduction & Research Gap

Replacing hazardous batch hydrogenation with a safer, highly selective AFR platform offering tight reaction control.

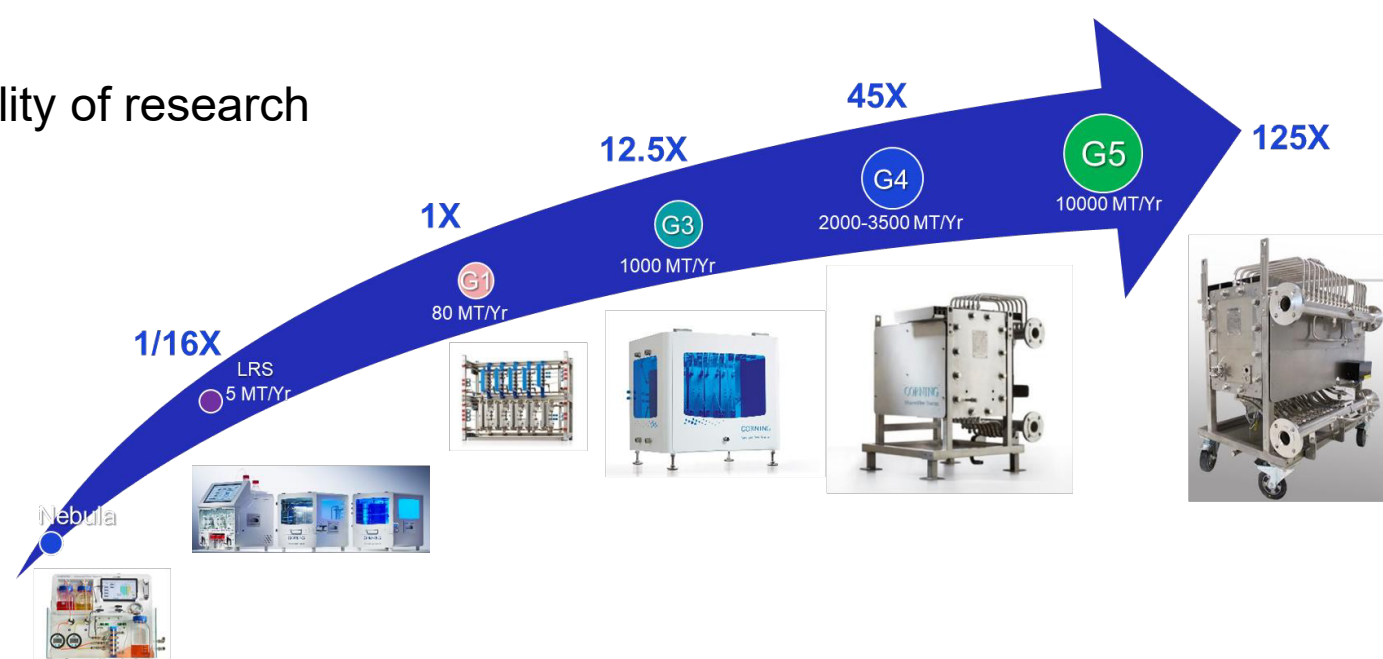
### Batch Hydrogenation Dangers



### Structured Microreactors: A possible solution



Potential scalability of research



## OBJECTIVES

IMPLEMENT AFR AS A PLATFORM FOR HYDROGENATION

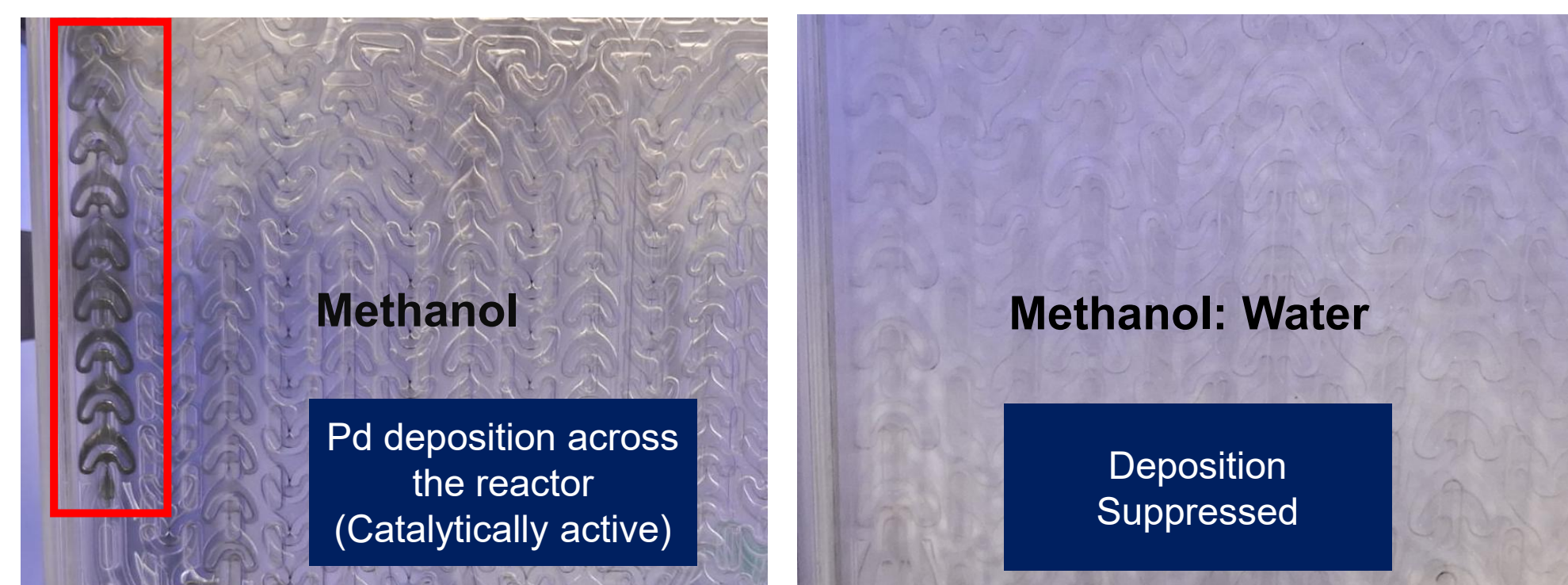
USE AFR MIXING TO CONTROL REACTION OUTCOMES

EVALUATE CATALYST SYSTEMS WITH SYSTEMATIC METHODS

## Palladium Deposition Control

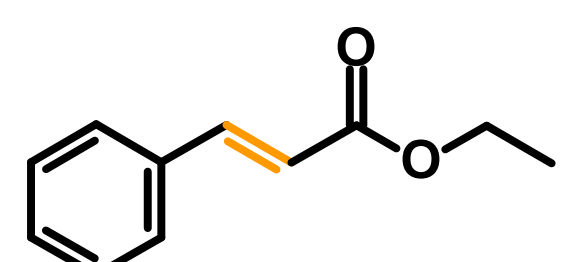
Methanol : Water Yield >99%	Ethanol : Water Yield >99%	IPA : Water Yield >99%	Butanol : Water* Yield >19%	Toluene : Water* Yield >81%
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Reaction conditions: 50 °C, back pressure: 5 bar.g, ethyl cinnamate (0.022 M), Pd(OAc)<sub>2</sub> : 1 mol %, liquid flow rate 0.5 ml/min, gas flow rate 5 ml/min (normalised), residence time 29 secs, 3:2 v/v of organic : aqueous solvent, Yield determined by GC, \* two separate organic and water solvent feed streams.



Post-reaction reactor

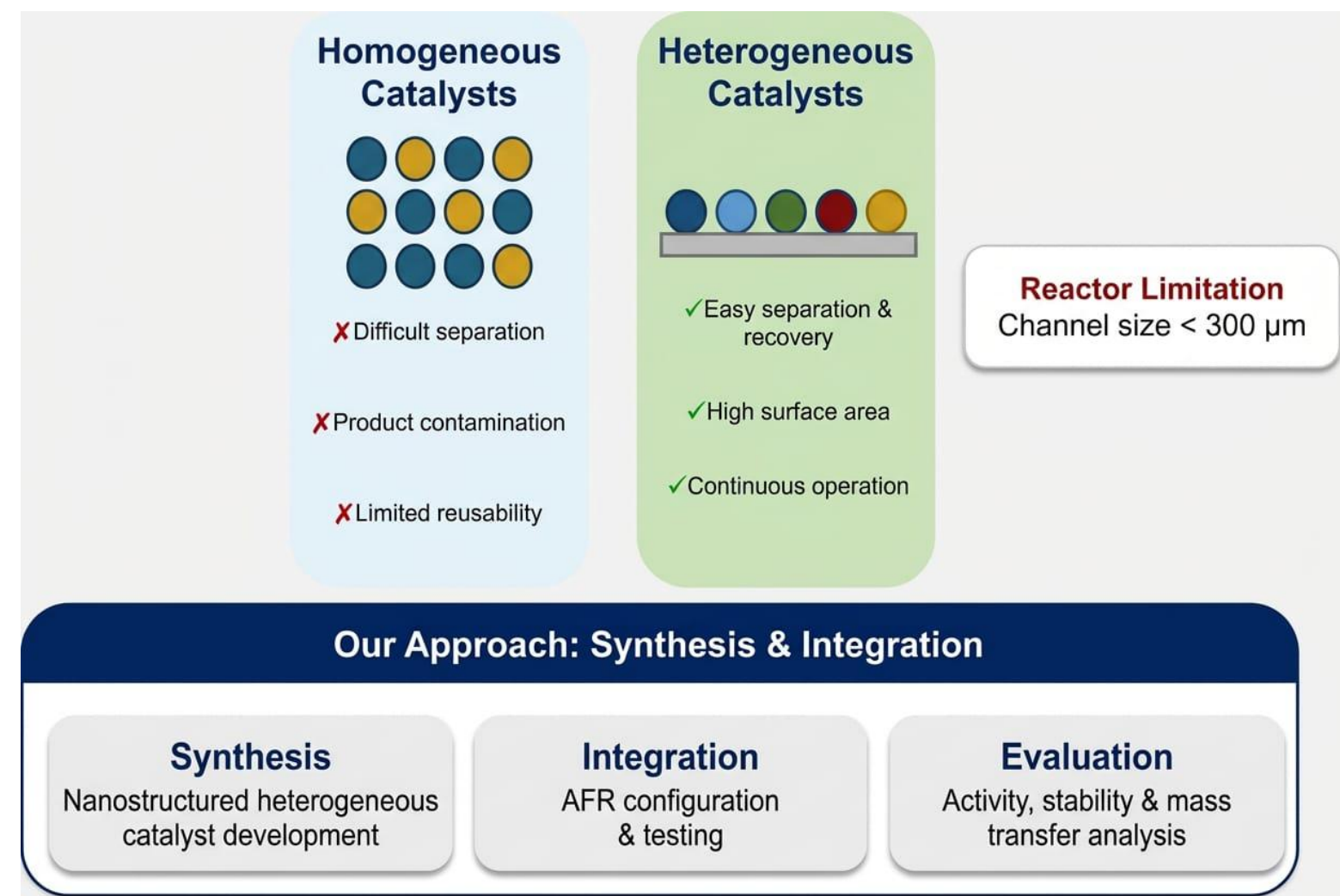
## Concentration Studies



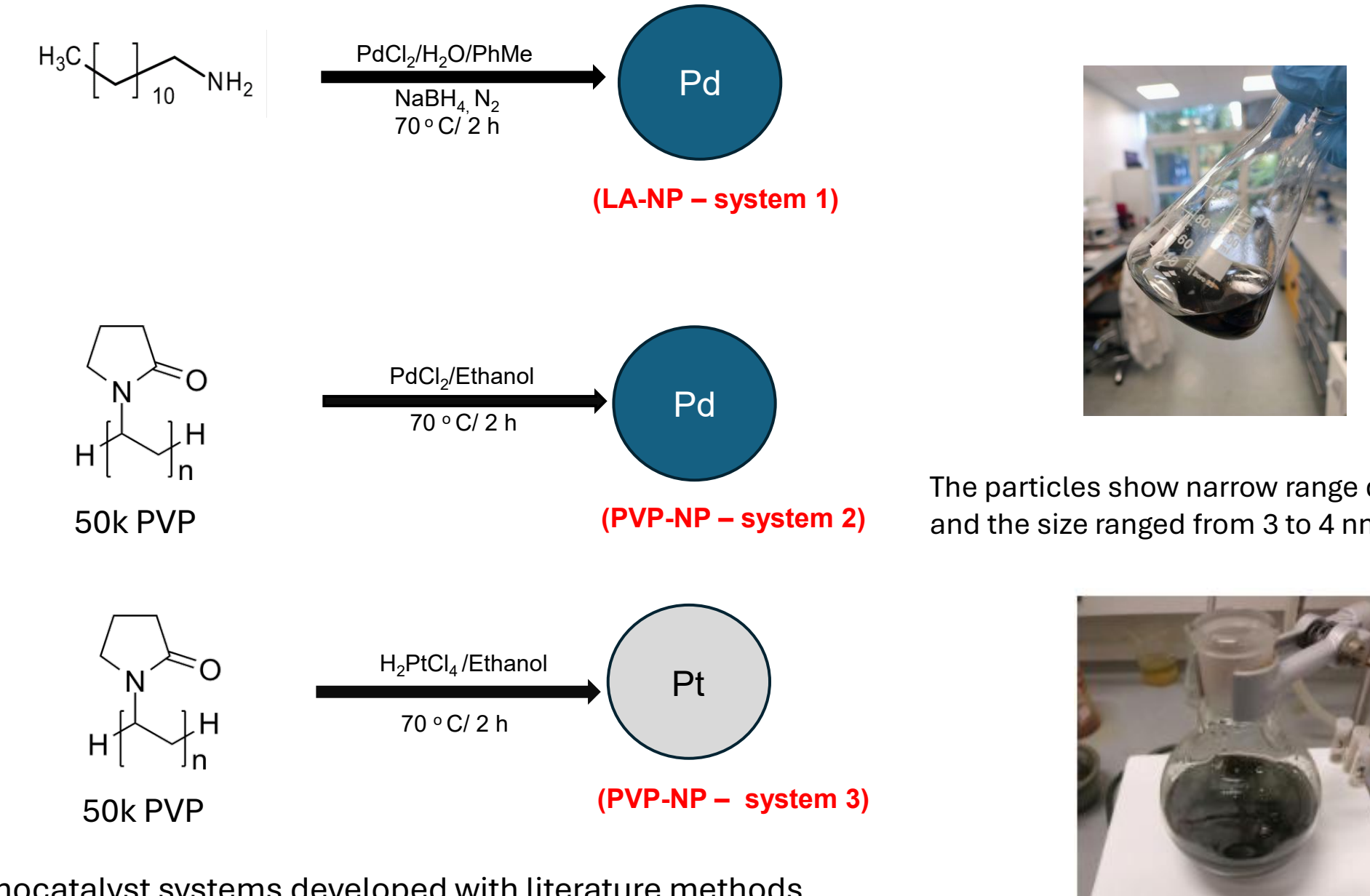
Concentration of Ethyl cinnamate (M)	Yield (%)
0.022	>99
0.075	>99
0.125	>99
0.15	>99

Reaction conditions: 60 °C, Pd(OAc)<sub>2</sub> : 0.5 mol % eq., backpressure 5 bar.g, 0.5 mL/min liquid, H<sub>2</sub> : 4 ml/min (normalised), theoretical residence time 36 secs. Yield determined by GC.

## Heterogeneous Nano catalysis



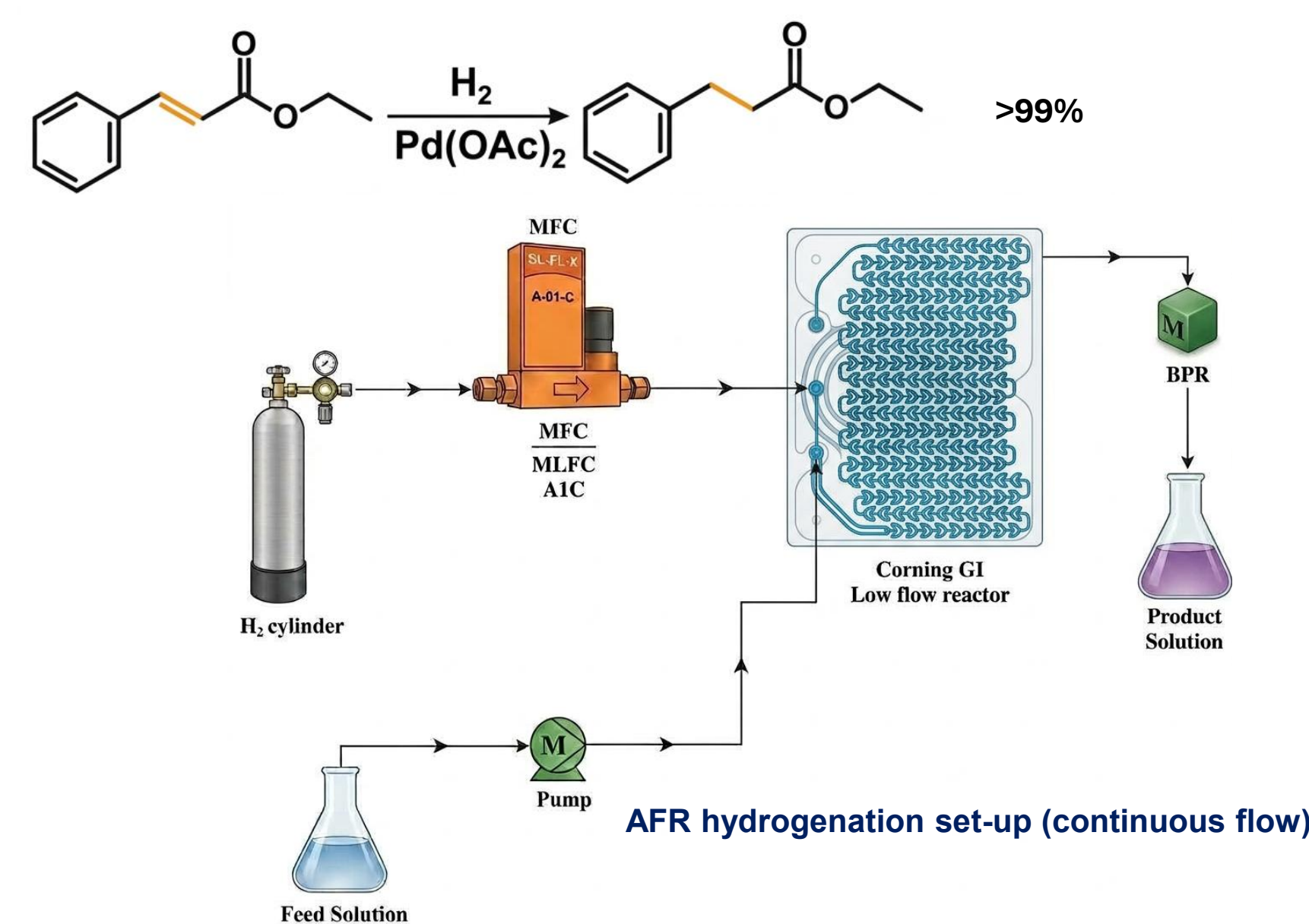
## Nano catalyst Synthesis



The particles show narrow range distribution and the size ranged from 3 to 4 nm

Nanocatalyst systems developed with literature methods

## Case Study 1: Feasibility in Flow

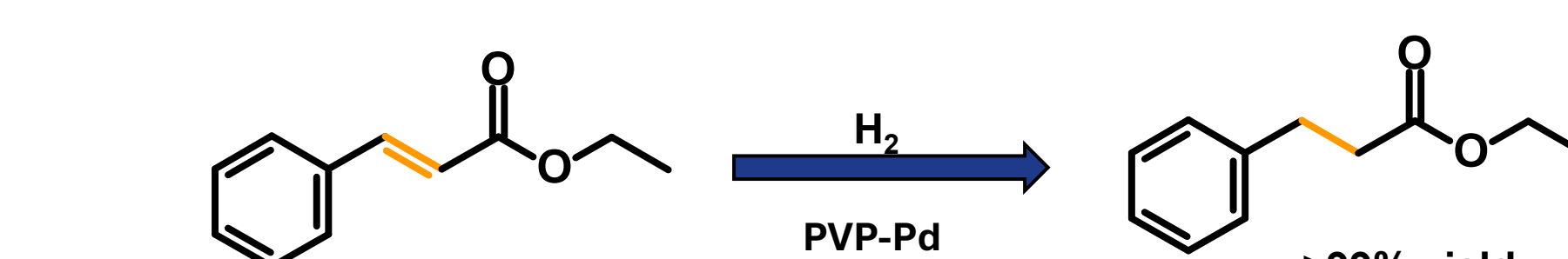


## Substrate Scope

% Yield >99%	% Yield >99%	% Yield >99%	% Yield >99%, >90%
% Yield >99%	% Yield >99%	% Yield >99%, >90%	% Yield >99%

Reaction conditions: Pd(OAc)<sub>2</sub> 0.5 mol%, 90 °C, backpressure 5 bar.g, 0.5 mL/min liquid, H<sub>2</sub> : 4 nL/min, residence time 36 secs

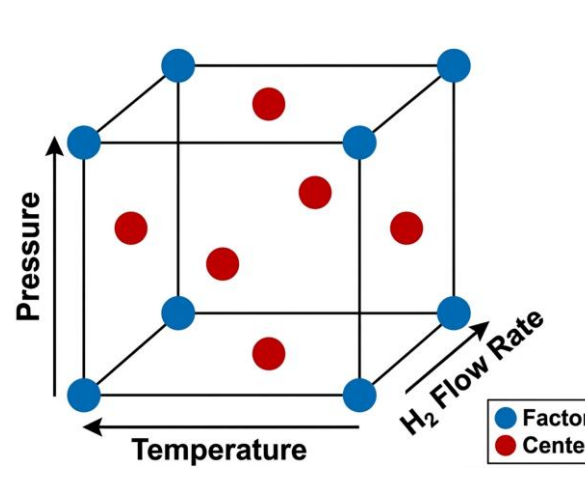
## Investigation in AFR (Nanocat)



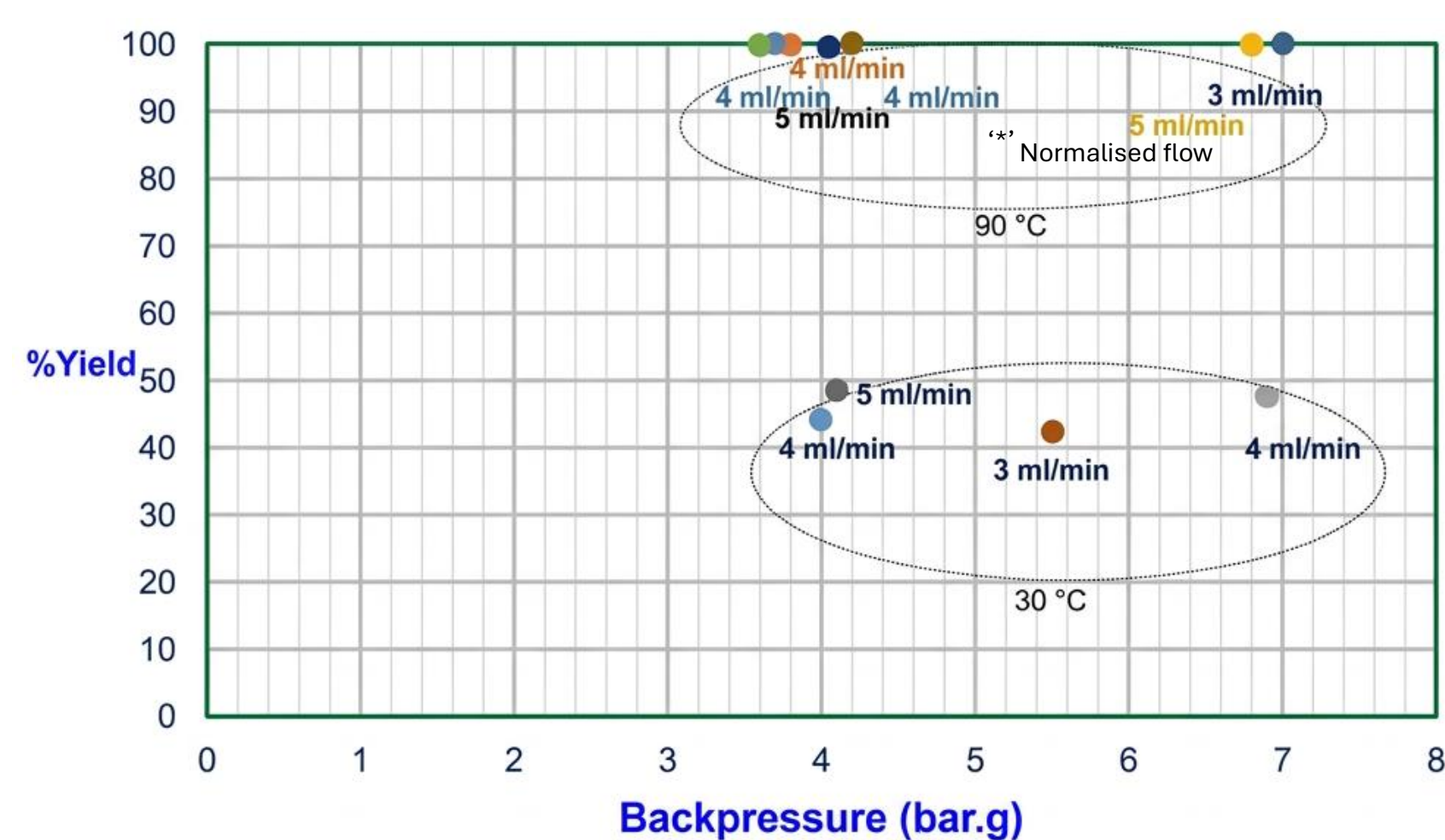
Reaction Conditions:  
 Liquid flow rate: 0.5 mL/min,  
 H<sub>2</sub> flow rate: 4 nL/min, residence time ~30  
 Back pressure: 7 bar.g, Temperature: 100 °C.



## Design of Experiments



Factor	Low Level (-1)	Mid Level (0)	High Level (1)
Temperature (°C)	30	60	90
H <sub>2</sub> Flow (ml/min)	3	4	5
Backpressure (bar.g)	4	5.5	7



Strong yield dependence only on the temp at higher temp

## DOE Model and Verification

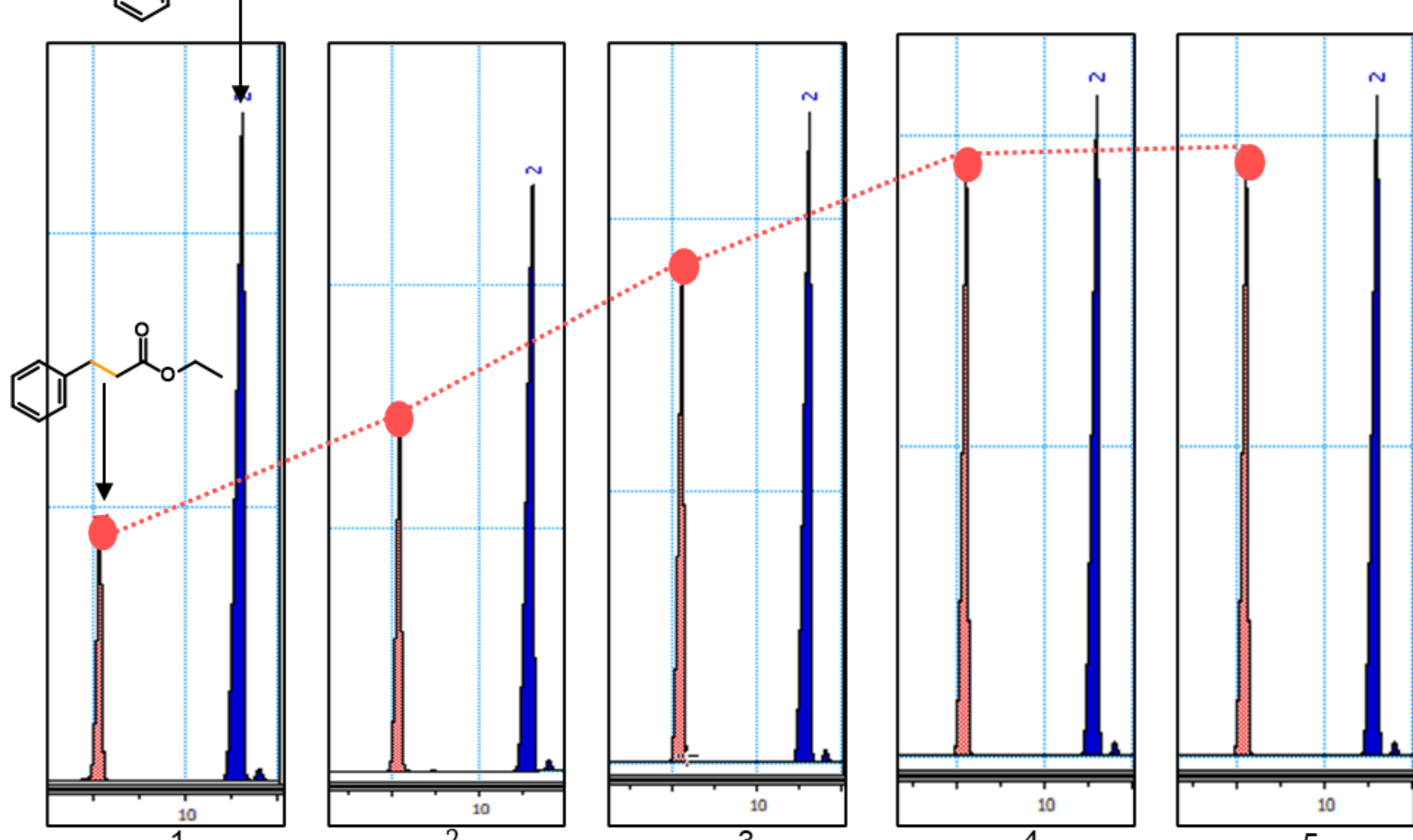
$$\% \text{Yield} = -86.93 + 5.1646T - 0.034431T^2$$

Model Experiment	1	2
Temperature	40 °C	80 °C
% Actual Yield	57%	99%
% Predicted Yield	60%	105%

Elemental Pd deposition made H<sub>2</sub> flow rate (mL/min) and back pressure (bar.g) less dominant and altered the steady-state

Effect minimised at high temps

Example of steady state operation at 30°C

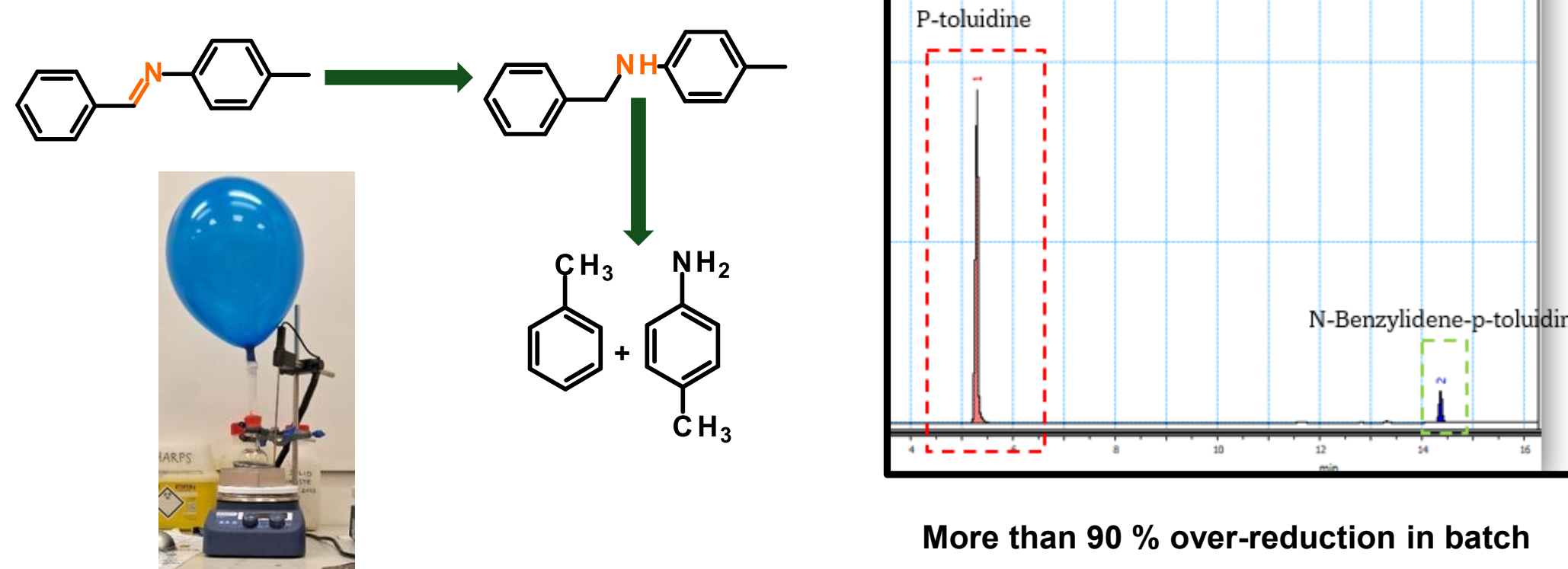


Sample chromatograms

## Imine Hydrogenation

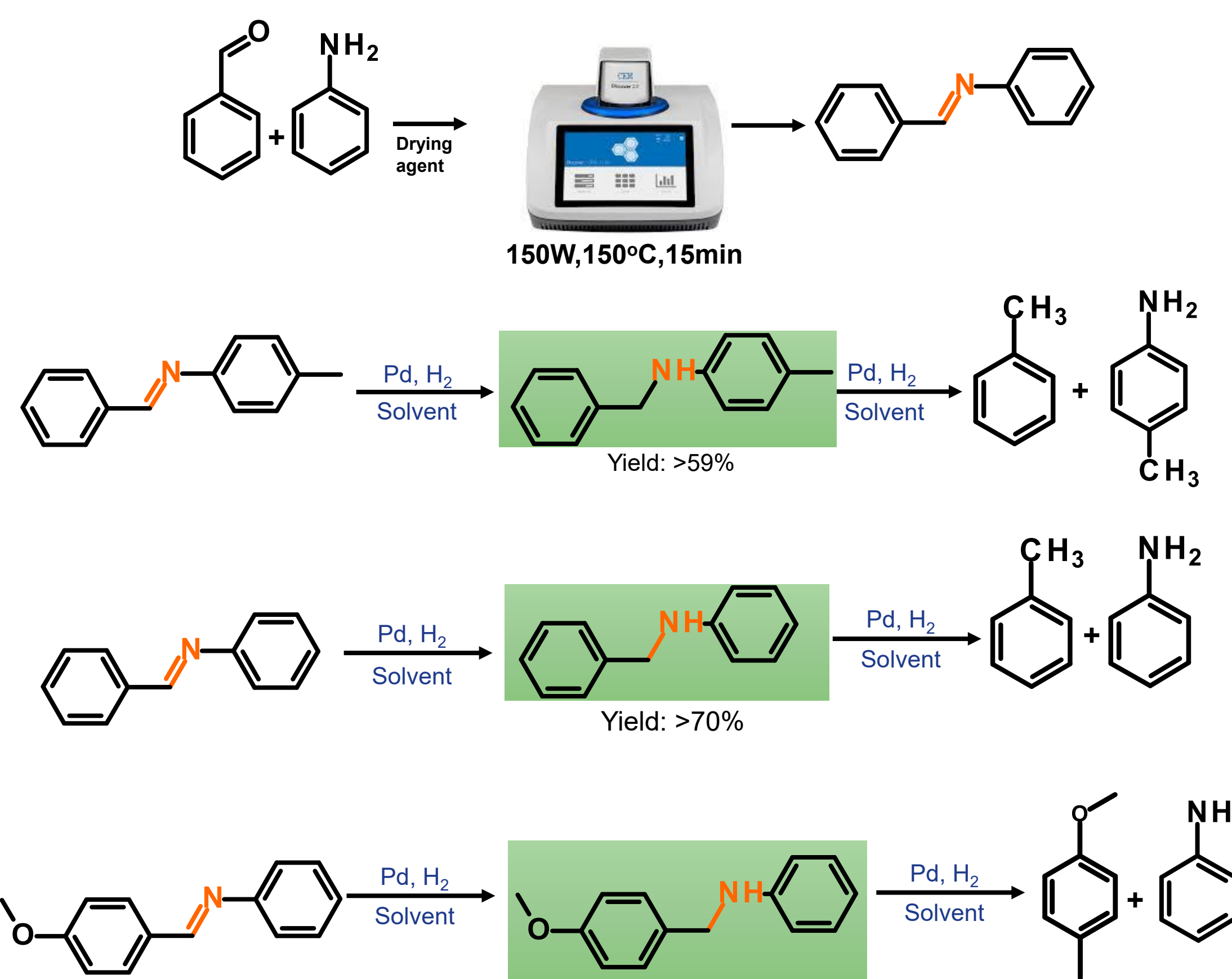


- Critical for pharmaceutical synthesis.
- Synthesized by transfer hydrogenation. (atom inefficient)
- vulnerable to over-reduction
- Robust heat & mass transfer
- Selectivity directing



More than 90 % over-reduction in batch

## Microwave Imine Synthesis and AFR Hydrogenation



Reaction Conditions: Reagent (0.018 M), Catalyst: Pd(OAc)<sub>2</sub> 5 mol % eq., Residence Time: 23 sec (Liq. Flow rate: 0.5 mL/min, H<sub>2</sub> : 3 mL/min), T - 50 °C Back Pressure : 5 bar.g

## Nano catalyst Imine Hydrogenation

Reagent	PVP-Pd	LA-Pd	PVP-Pt
(Hydrogen/Reagent) <sub>mol ratio</sub>	4.42	4.42	4.42
Reagent (1)	0.47%	0.5%	11.7
Product (2)	95.86%	96.3%	15.7
Analysis Byproduct	3.66%	3.2%	73%*

Reagent	PVP-Pd	LA-Pd	PVP-Pt
(Hydrogen/Reagent) <sub>mol ratio</sub>	4.33	4.33	4.33
Residence Time Theoretical	40.5 sec	40.5 sec	40.5 sec
Reagent (1)	<0.5%	<0.5%	<10.3*
Product (2)	62.44	79.6%	84.7
Analysis (GC) Byproduct	37.56%	19.9%	<5%

Reagent Concentration: 0.03 M, 90 °C, Backpressure: 5 bar.g, H<sub>2</sub> : 3 nL/min, liquid: 1 mL/min, Residence Time: 40.5 sec

## References

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