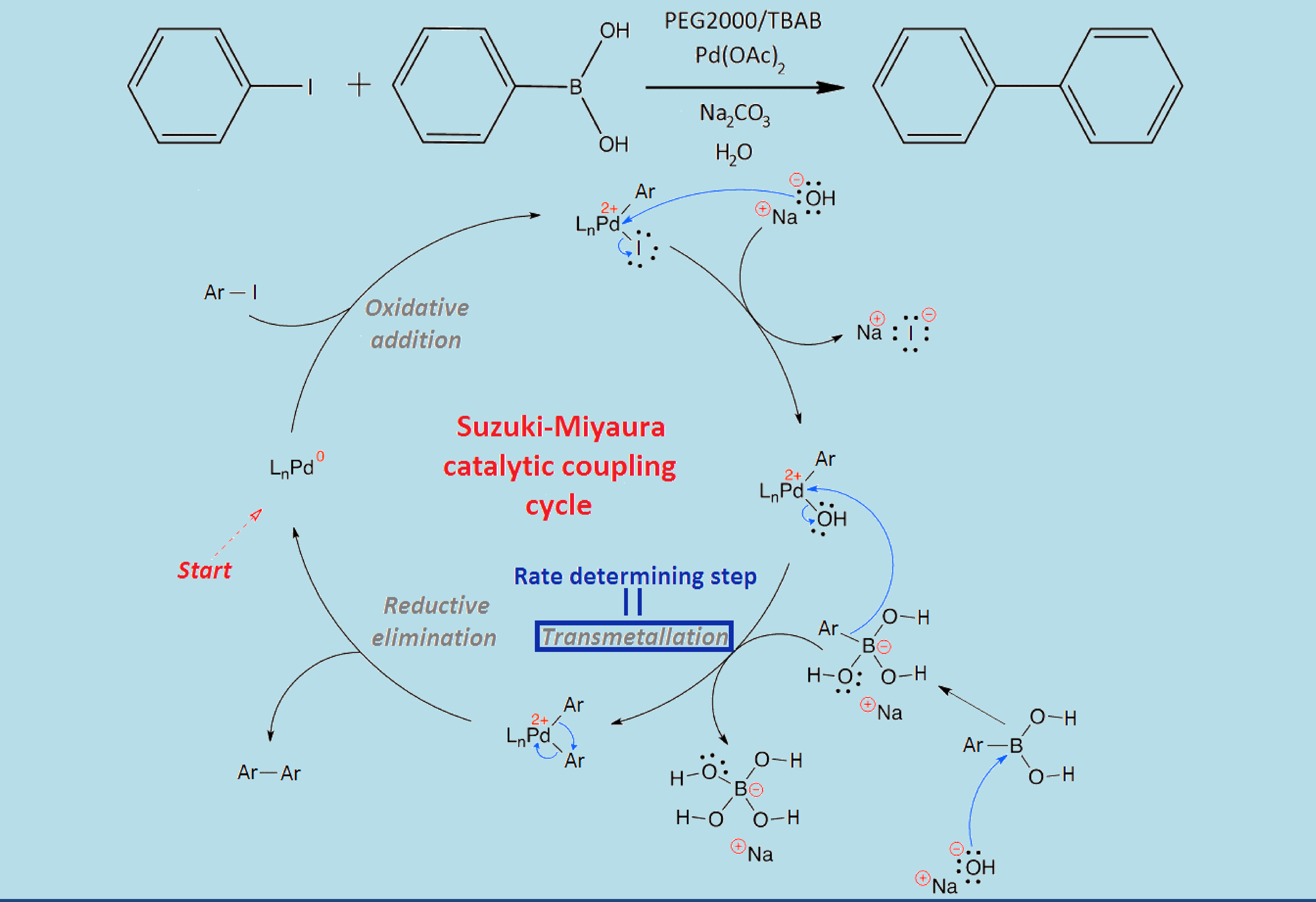
KU LEUVEN

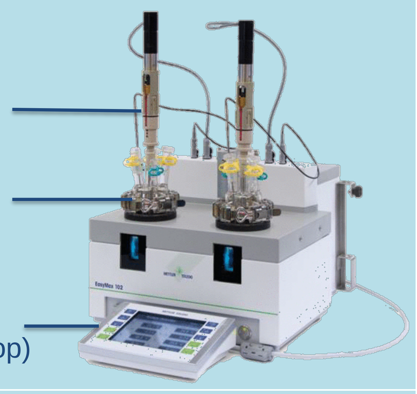
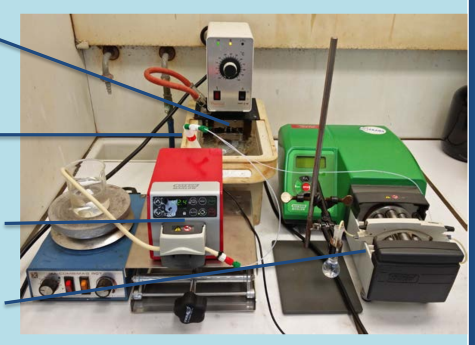
Kinetic investigation and development of a continuous microwave flow system for the Suzuki-Miyaura reaction

The increasing popularity of microwave radiation as energy source to fasten chemical reactions has led to this study on the Suzuki-Miyaura reaction where phenylboronic acid reacts with iodobenzene to form biphenyl. Palladium acetate serves as catalyst while tetrabutylammonium bromide (TBAB) or polyethylene glycol 2000 (PEG2000) acts as an additional phase transfer catalyst. UV-Vis spectrophotometry is used to quantify the reaction products. The coupling reaction is performed in four different reactor set-ups: the conventional and microwave batch and flow reactor. The batch reactors are used to study the reaction kinetics by varying the iodobenzene concentration and the reactor temperature. The experimental conversions in the conventional and microwave flow reactors are compared to the theoretical conversions based on the reaction kinetics, residence time and temperature.

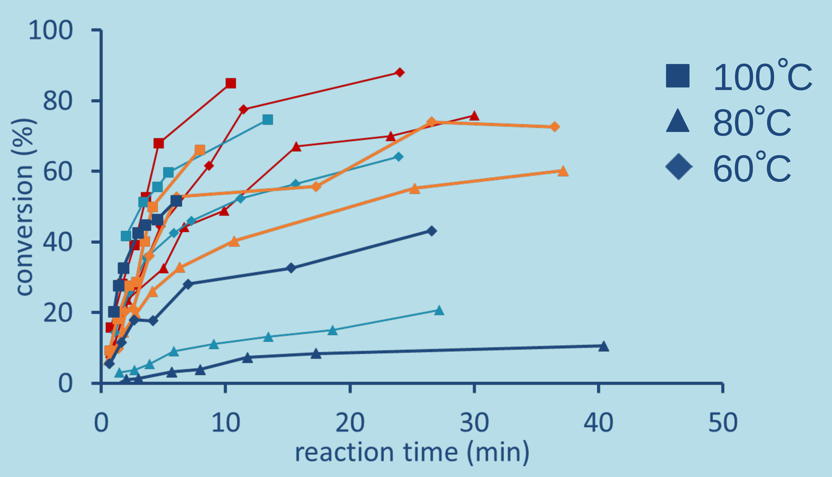
Reaction mechanism



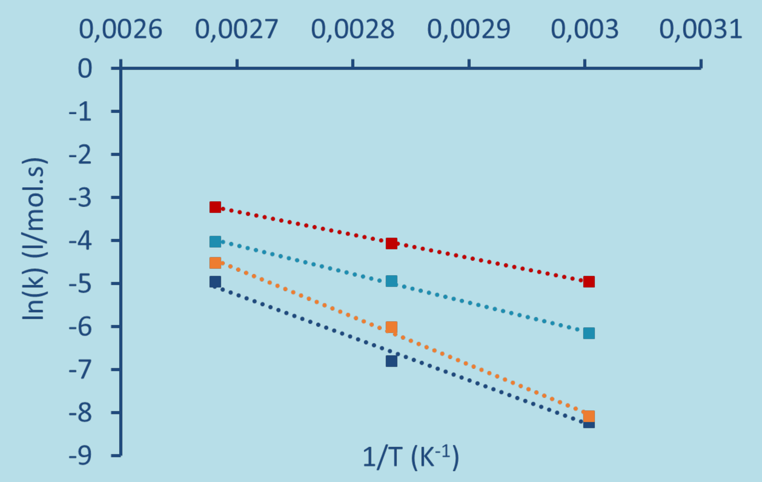
Reactor set-up

	Batch	Flow
Experiments	TBAB and PEG2000 T: 60, 70, 80, 90, 100 ºC Kinetic study	PEG2000 Power: 200W Residence time: 0.5 - 3 min
Conventional	EasyMax 102 Overhead stirrer 100 ml reactor Touch screen (+ control via laptop) 	Hot water bath flow reactor (L = 8m, ID = 1mm) T-piece mixer Peristaltic pump (reactor solution) Peristaltic pump (iodobenzene) 
Microwave	Sairem Miniflow 200SS 100 ml reactor Touch screen control 	Peristaltic pump (iodobenzene) µW flow reactor (L=8 m, ID=1 mm) T-piece mixer Peristaltic pump (reactor solution) 

Reaction kinetics



Concentration profiles



Kinetic profiles

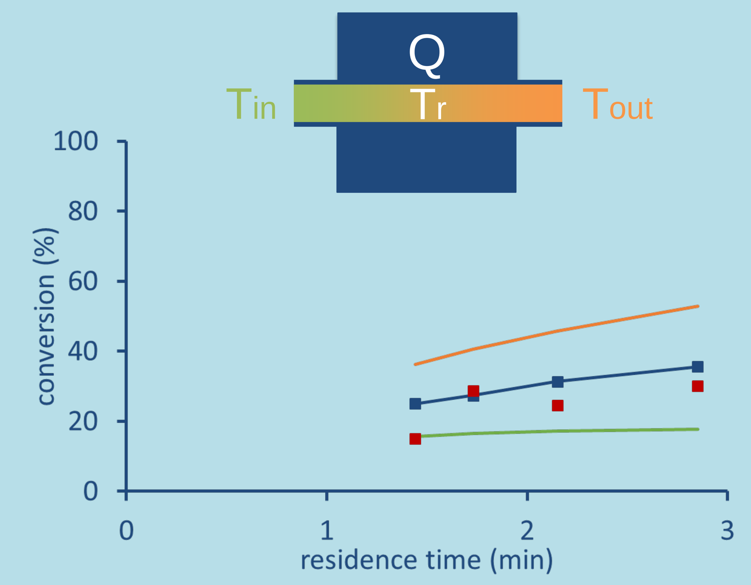
$$-r_a = k * C_{iodobenzene}^2$$

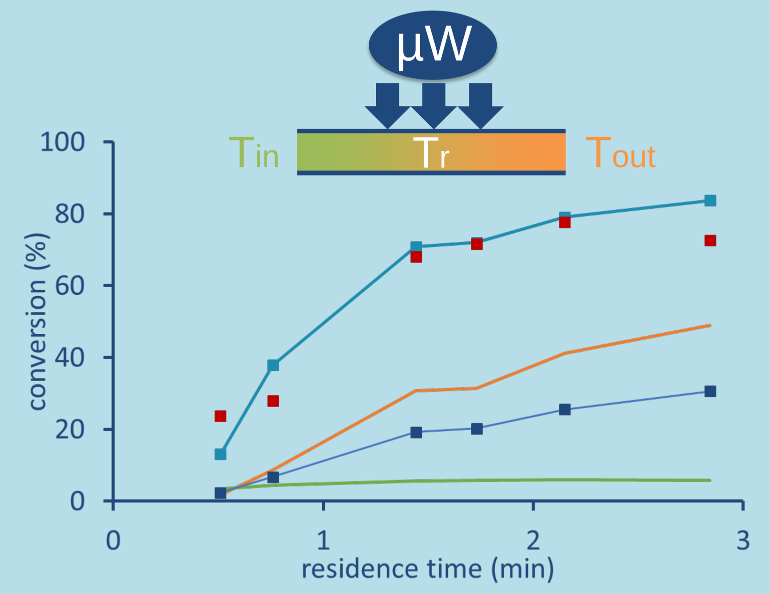
$$k = k_0 * e^{\frac{-Ea}{R*T}}$$

$$k_{PEG2000\ Conv.} = 7.57 * 10^4 * e^{\frac{-44.8*10^3}{R*T}} \quad k_{TBAB\ Conv.} = 9.43 * 10^{10} * e^{\frac{-92.2*10^3}{R*T}}$$

$$k_{PEG2000\ \mu W} = 9.37 * 10^5 * e^{\frac{-55.0*10^3}{R*T}} \quad k_{TBAB\ \mu W} = 2.27 * 10^9 * e^{\frac{-82.5*10^3}{R*T}}$$

Flow experiments and modelling





■ Lab experiments — Modeling T_{out} — Modelling T_{in} —■— Modelling T_r —■— Modelling $T_{r+40^\circ C}$

Conventional flow

Modelling T_r ≈ lab results

(between modelling of T_{in} and T_{out})

Microwave flow

modelling lab results ≈ 3.3 x modelling T_r

modelling lab results ≈ modelling T_r + 40˚C

Hypothesis

µW = heating bulk content + local hotspots (at metal catalyst)

reactivity ↗
conversion ↗

Conclusion

The reaction kinetics of the conventional and microwave batch reactor are determined and used to simulate the flow results. While the reaction conversion of the conventional flow matches with the modelling, higher conversions are obtained at the microwave flow system. A first hypothesis of this difference between the lab and modelled results is the that, possibly, a higher bulk reactor temperature occurs. The temperature is measured at the reactor outlet. However, it is possible that the fluid is not irradiated with microwaves at the end of the reactor which means that the fluid has already cooled down before the reactor temperature is measured. The second, and most plausible explanation is that local hotspots are formed. This formation occurs during the reaction: the metal catalyst absorbs more microwave energy which results in local zones of higher temperatures. Since the reaction occurs at the catalyst, the reactivity and thus also the conversion increase.

Ing. L. Camps[a]
Prof. dr. ir. L. Braeken[a,b] **Prof. dr. ir. L. Thomassen**[a,b]
[a]**KU Leuven** department FIIW technology campus Diepenbeek
[b]**KU Leuven** department CIT, Leuven

janssen PHARMACEUTICAL COMPANIES OF Johnson&Johnson