



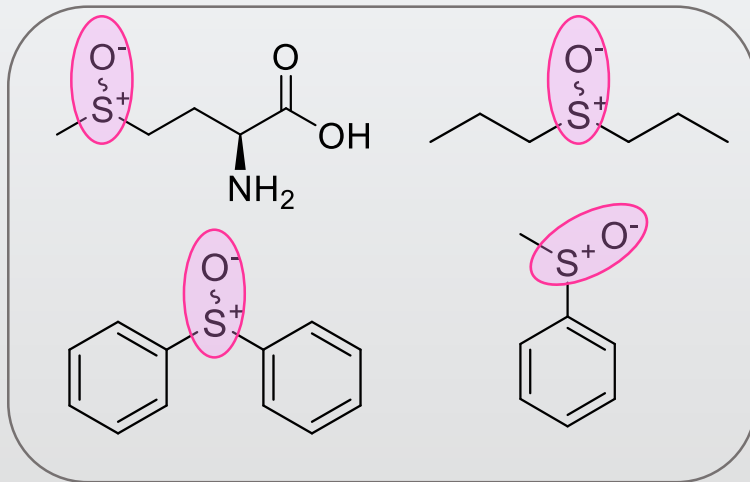
Integrated Continuous-flow Photoreactors : Photooxidation with singlet oxygen

N. Emmanuel - J-C. M. Monbaliu

CiTOS – ULiège

Introduction

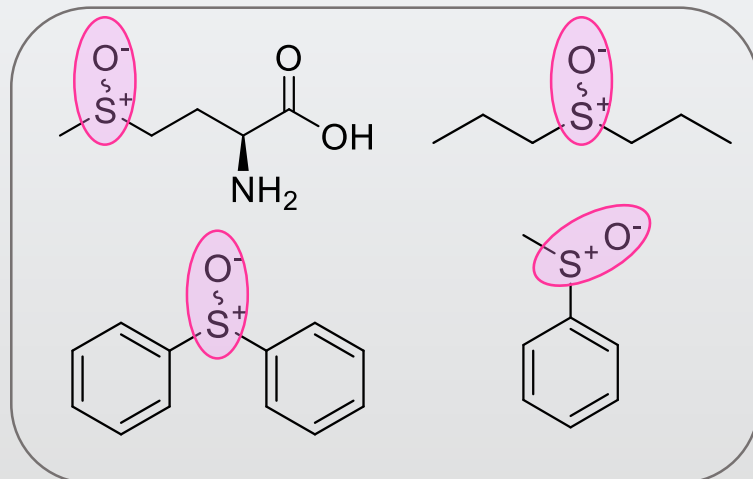
Overview of the project



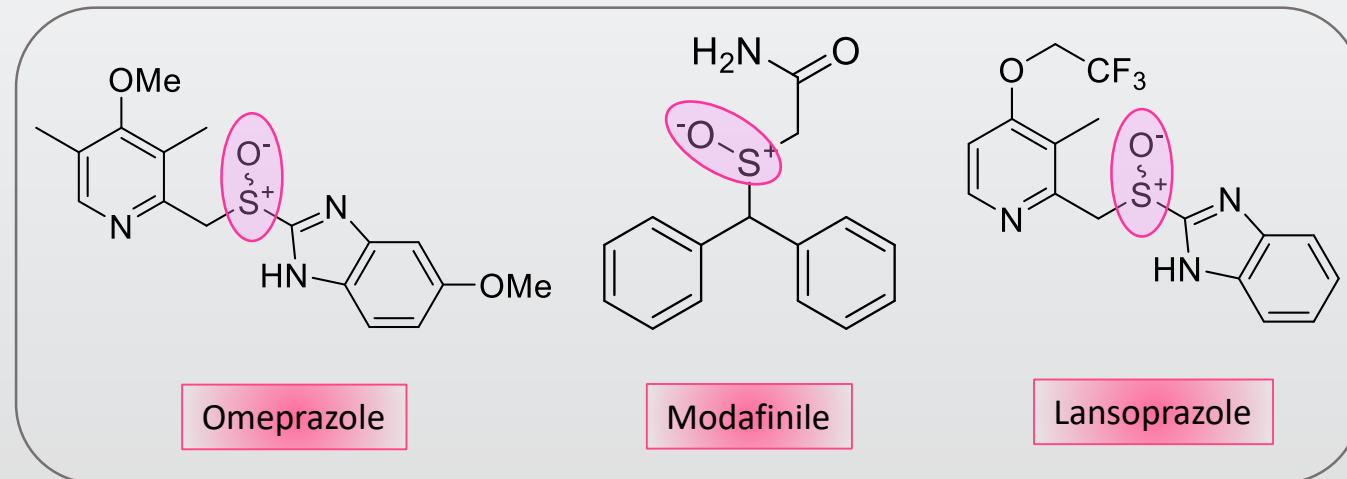
Examples of model sulfoxides

Introduction

Overview of the project



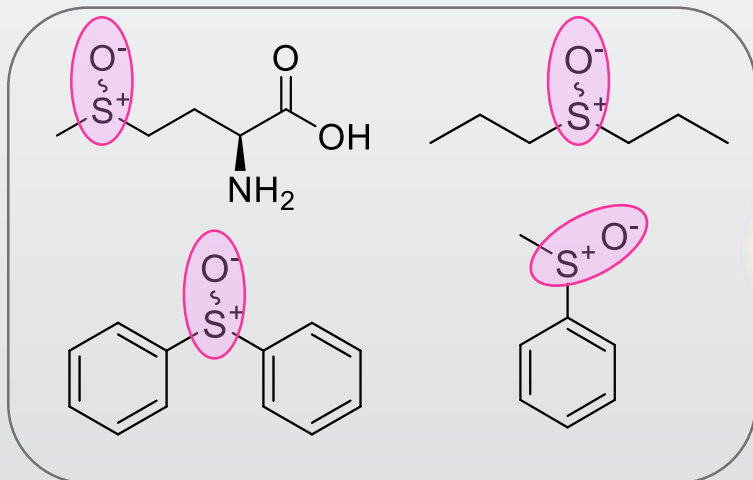
Examples of model sulfoxides



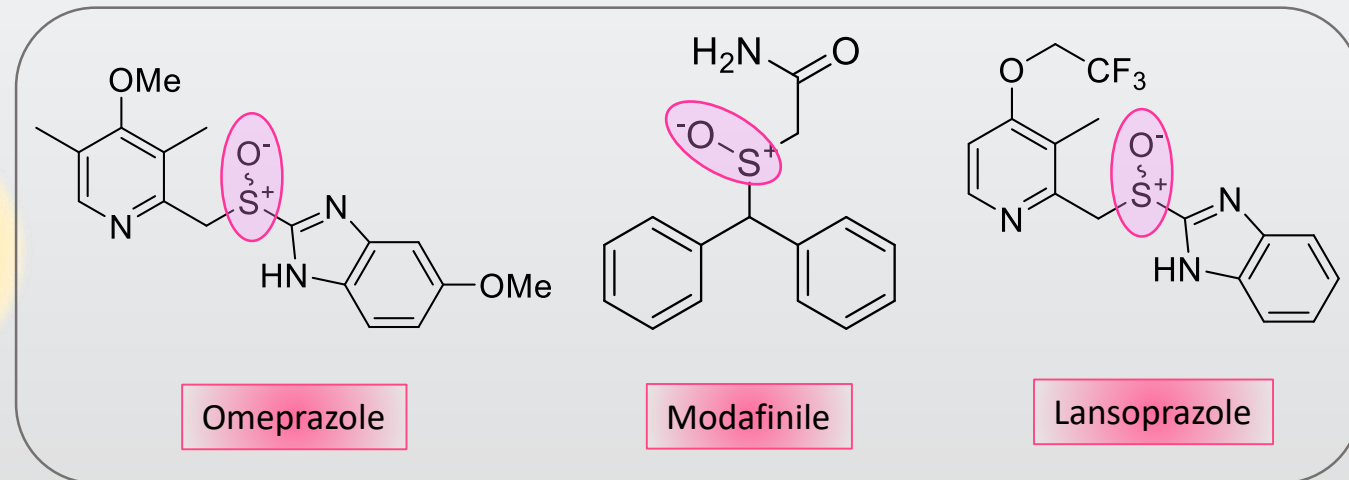
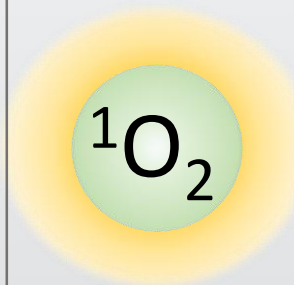
Examples of pharmaceuticals sulfoxides → **high-added value**

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Overview of the project



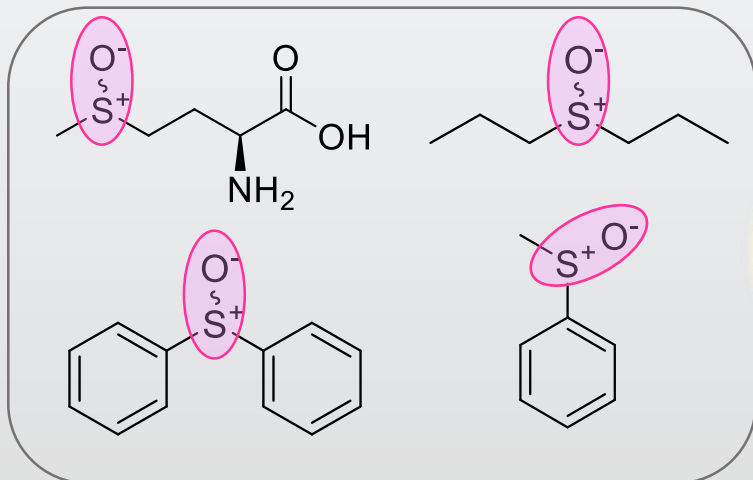
Examples of model sulfoxides



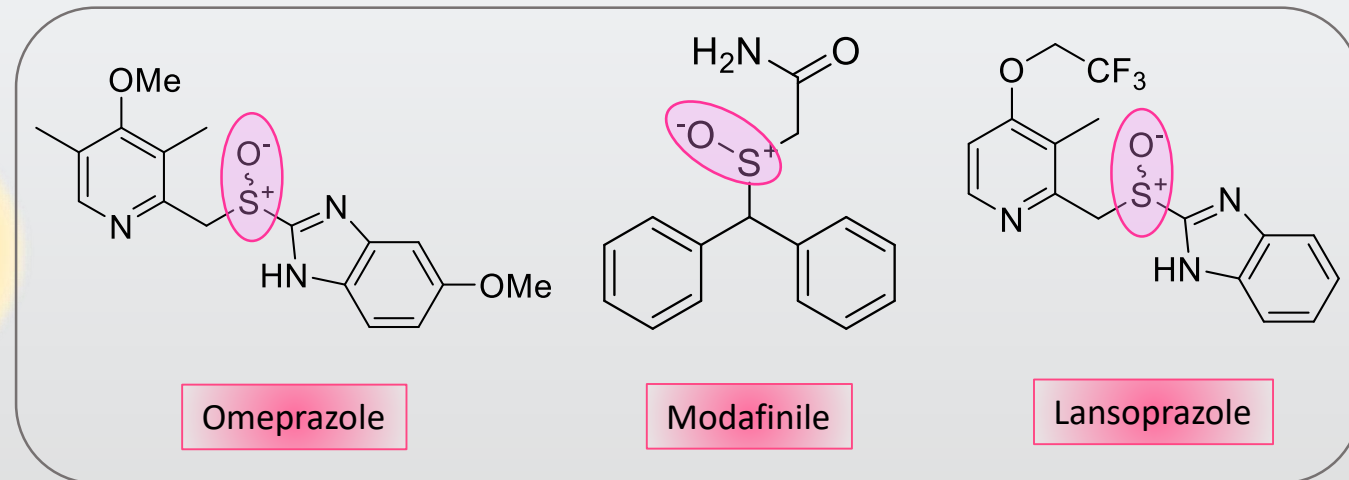
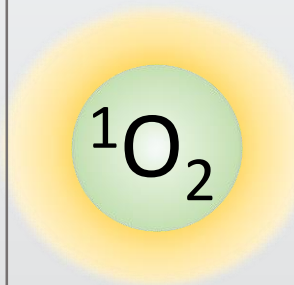
Examples of pharmaceuticals sulfoxides → **high-added value**

Introduction

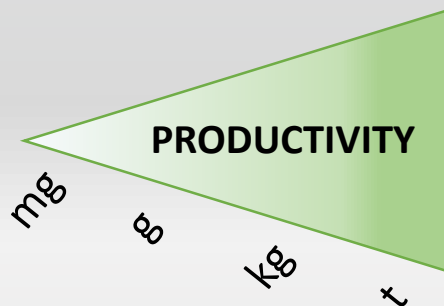
Overview of the project



Examples of model sulfoxides



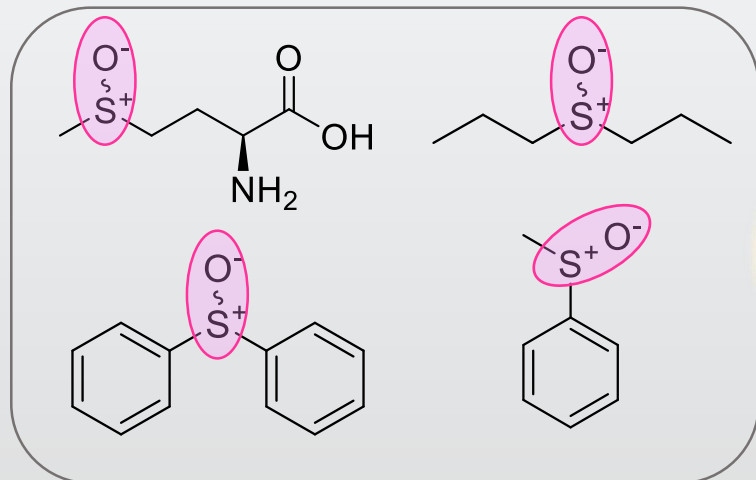
Examples of pharmaceuticals sulfoxides → **high-added value**



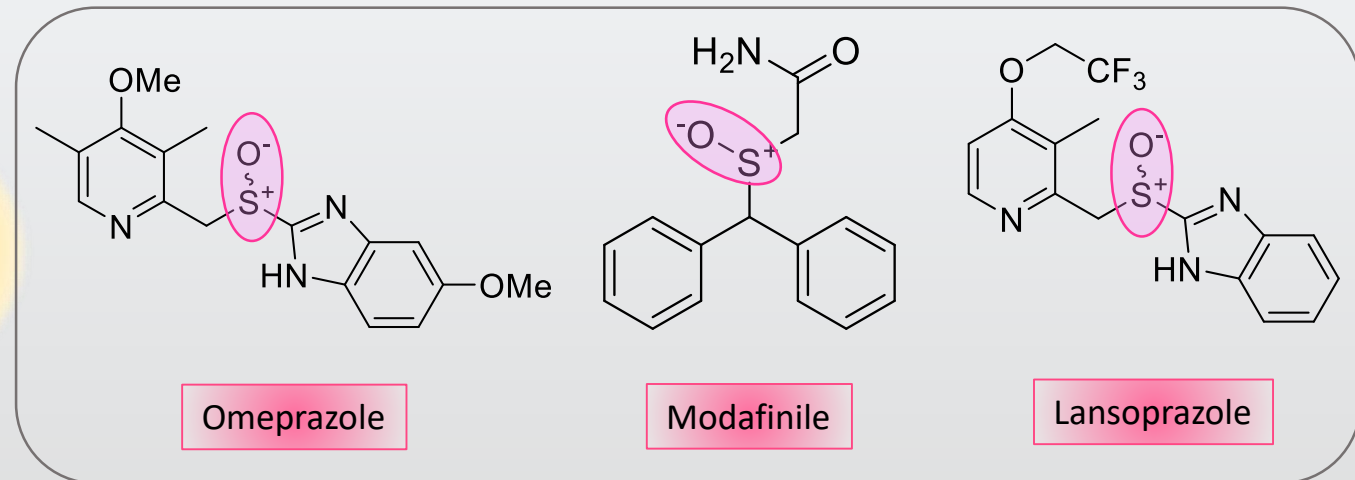
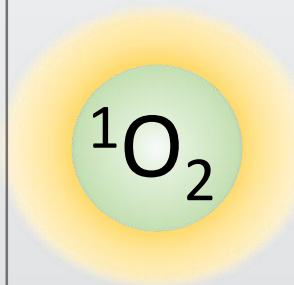
Seamless scale-up

Introduction

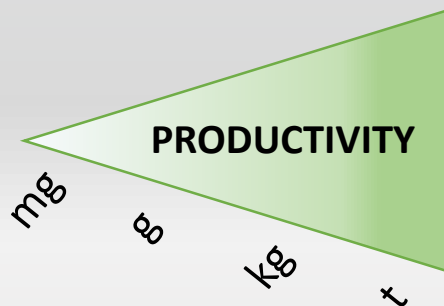
Overview of the project



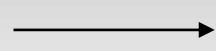
Examples of model sulfoxides



Examples of pharmaceuticals sulfoxides → **high-added value**



Seamless scale-up



Continuous-Flow Chemistry

Introduction

What is continuous-flow chemistry?

Batch reactors

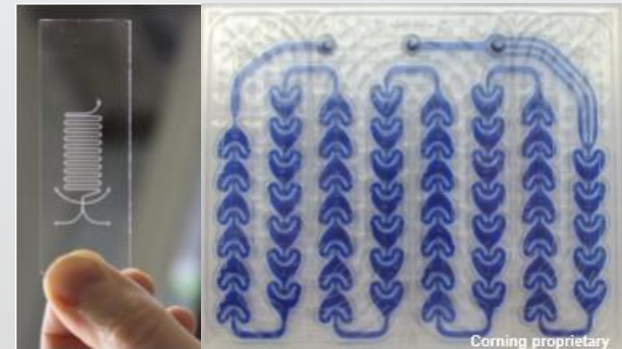


3D internal structure $\gg 10^4 \mu\text{m}$

mL < internal volume < kL

Finite volume of chemicals

Continuous-Flow micro/mesofluidic reactors



3D internal structure $< 10^3 \mu\text{m}$

μL < internal volume < mL

Infinite volume (flow) of chemicals

Introduction

What is continuous-flow chemistry?

Batch reactors



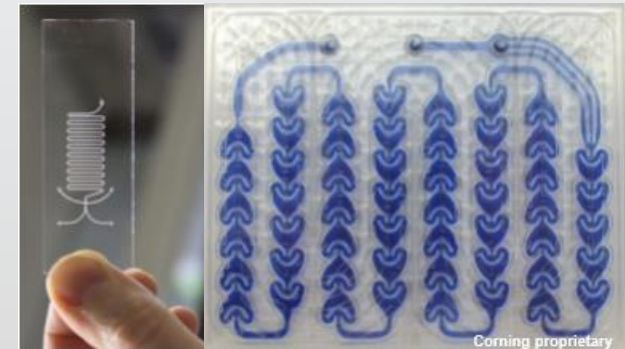
3D internal structure $\gg 10^4 \mu\text{m}$

mL < internal volume < kL

Finite volume of chemicals

Reactor Type	Surface/Volume Ratio (cm^2/cm^3)
1 m ³ reactor	0.06
100 mL reaction bulb	1
microchannel 100 μm	200

Continuous-Flow micro/mesofluidic reactors



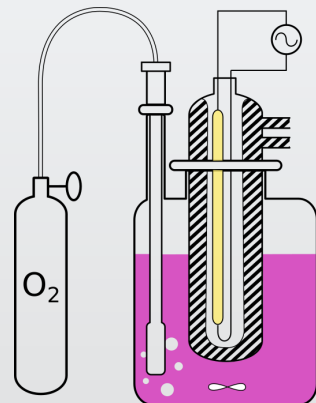
3D internal structure $< 10^3 \mu\text{m}$

μL < internal volume < mL

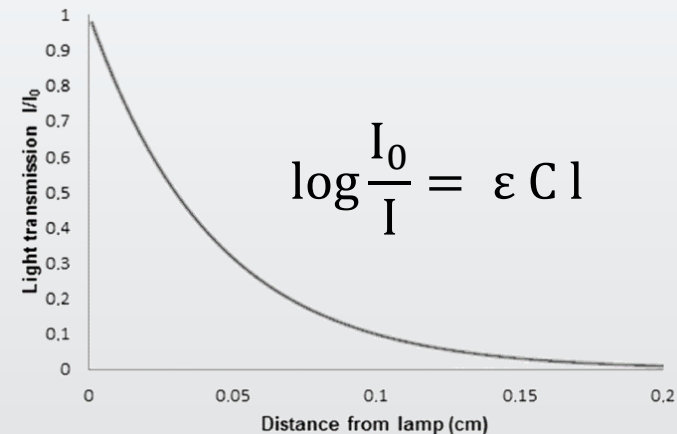
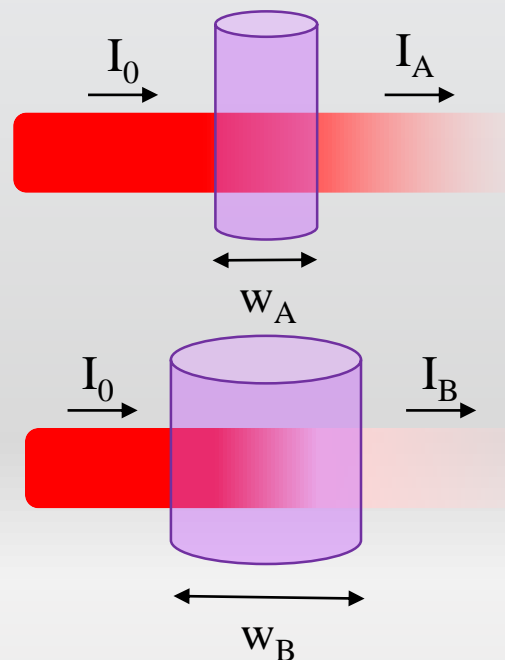
Infinite volume (flow) of chemicals

Introduction

Batch photochemistry



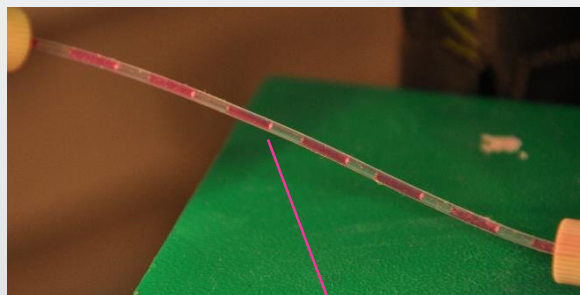
- Lack of uniformity in irradiation
 - Control of exposure time?
 - Mixing efficiency ?
 - Thickness of solution ?
 - Concentration ?
- Only for low concentrations
- Tricky scale-up



$$W_A < W_B$$
$$I_A > I_B$$

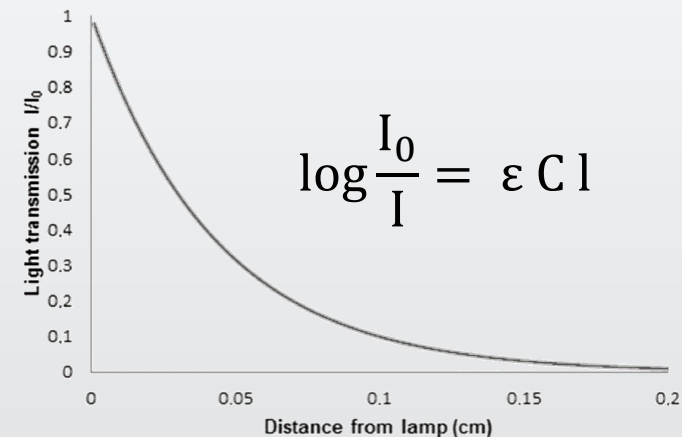
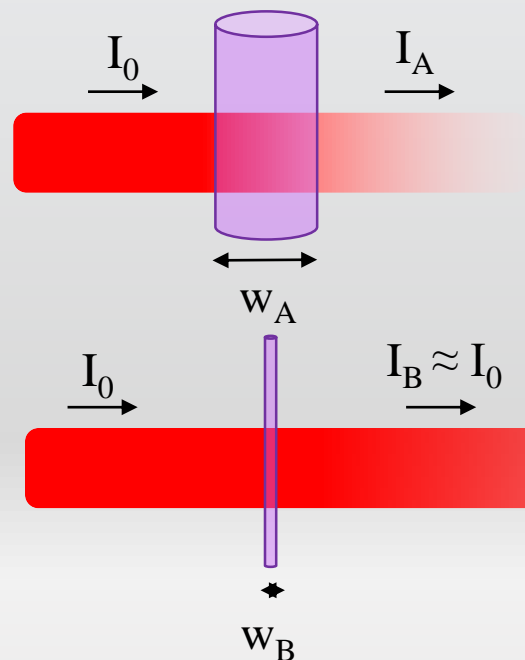
Introduction

Flow photochemistry



Ø 750 µm

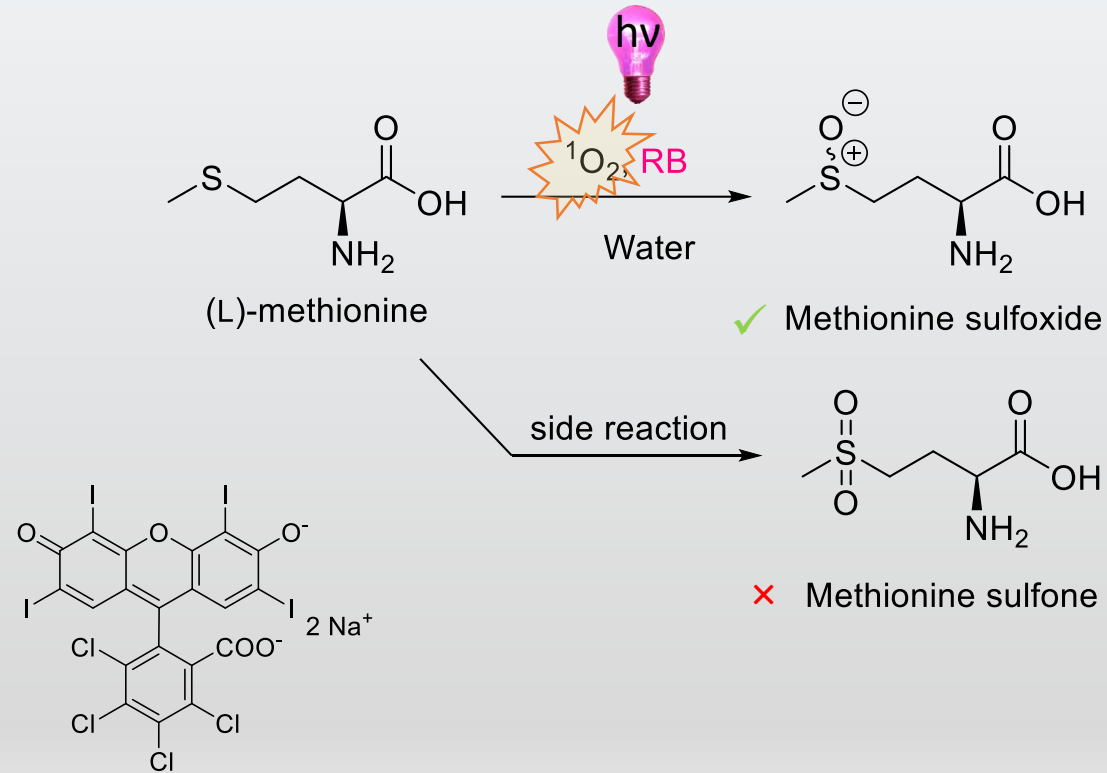
- Uniform irradiation
 - Precise control of exposure time (residence time)
 - High or low concentrations
 - Thin layer of solution
- Easy scale-up



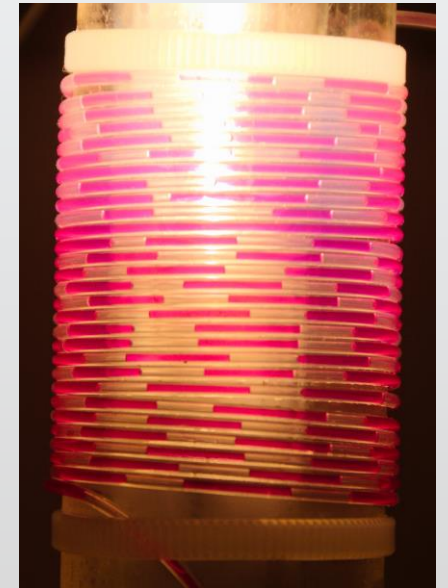
$$\begin{matrix} W_A > W_B \\ I_A < I_B \approx I_0 \end{matrix}$$

Introduction

Our project : First step model reaction

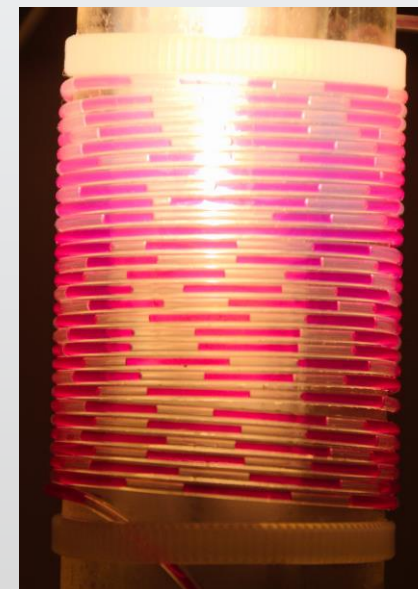
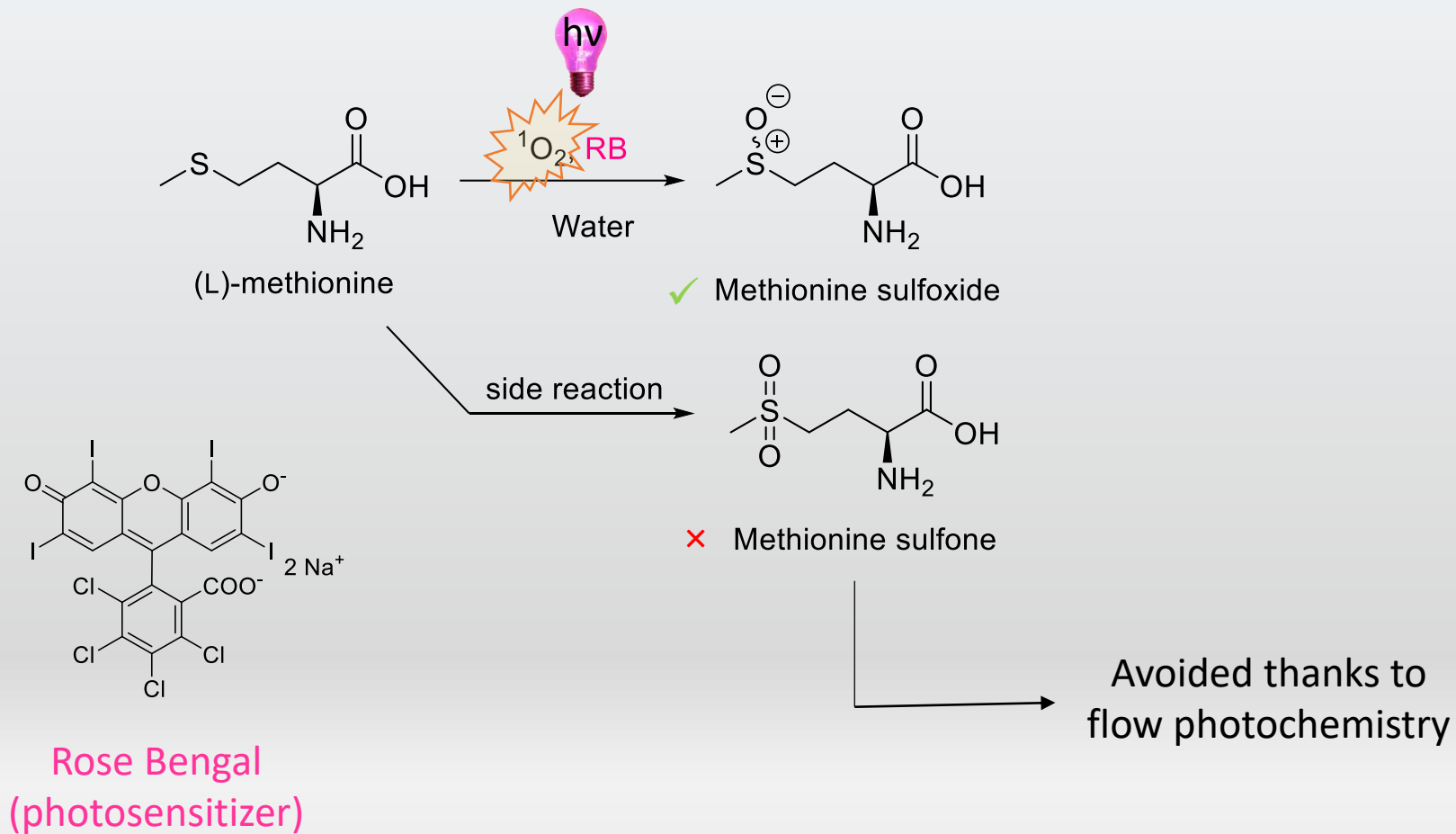


Rose Bengal
(photosensitizer)



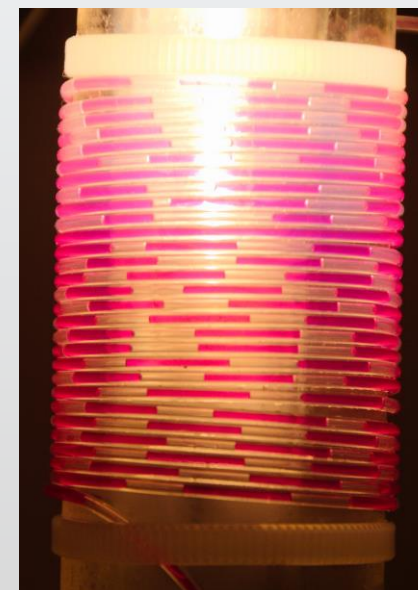
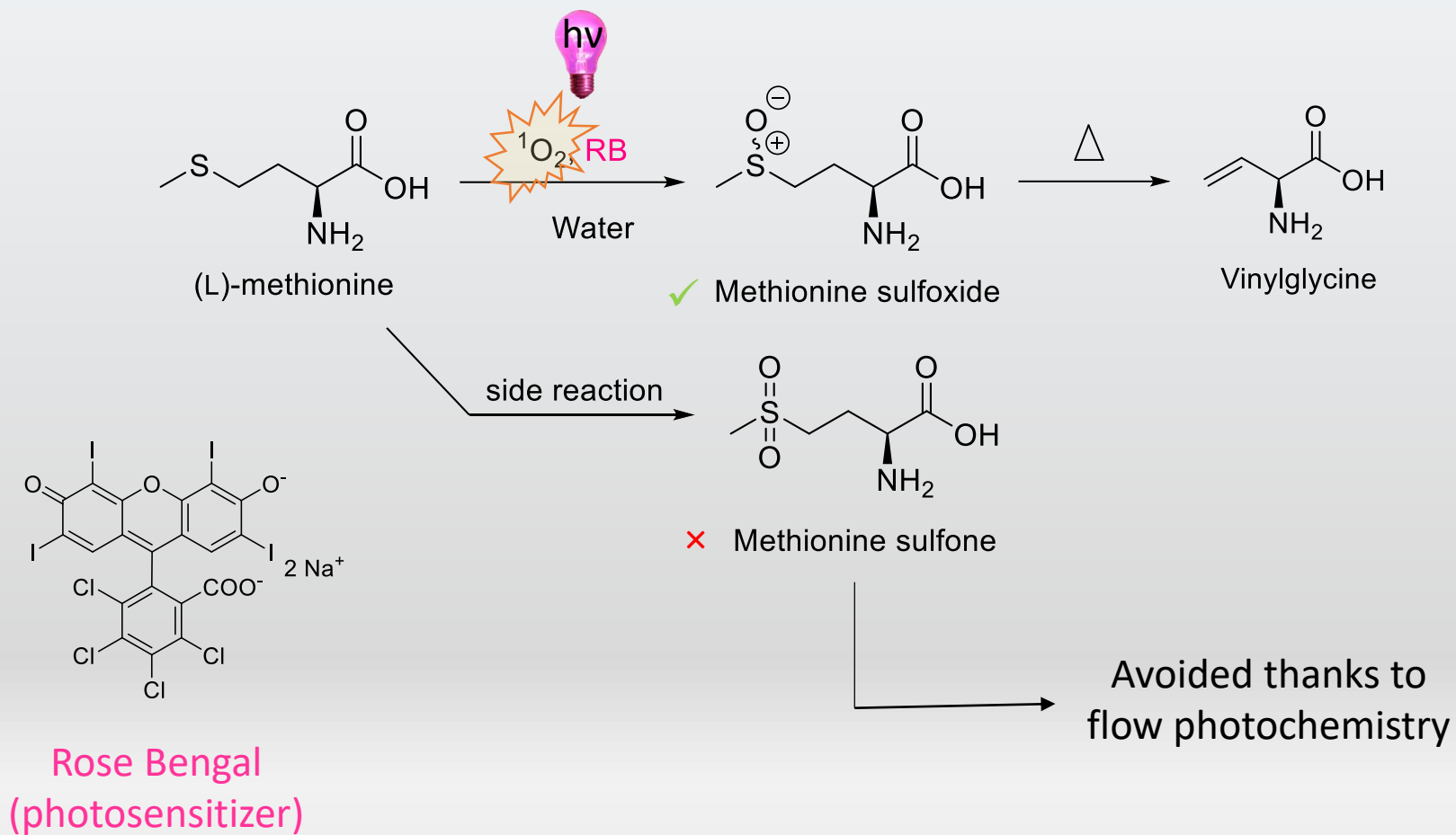
Introduction

Our project : First step model reaction



Introduction

Our project : First step model reaction

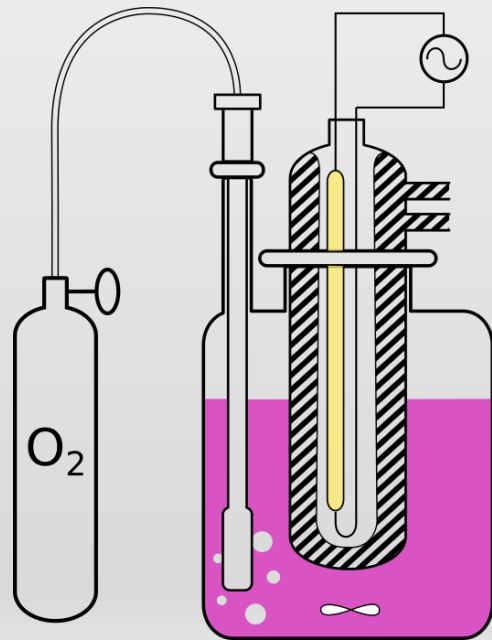


Photooxidation of (L)-methionine

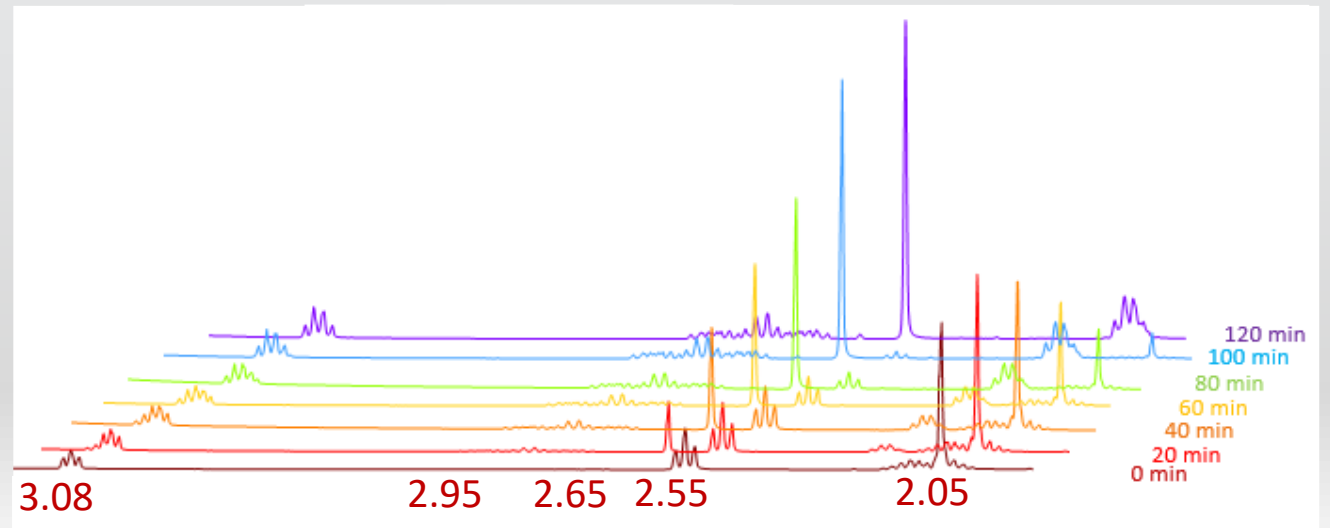
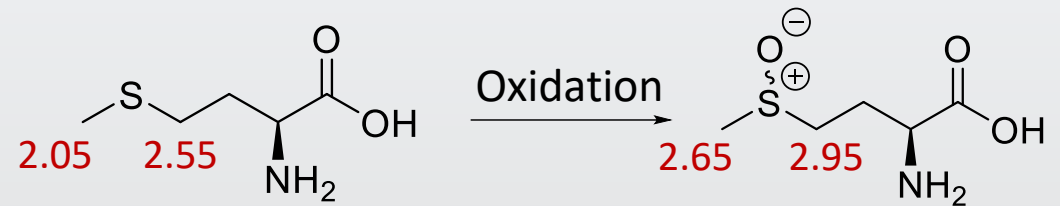
Results in batch



Methionine
Rose Bengal
water

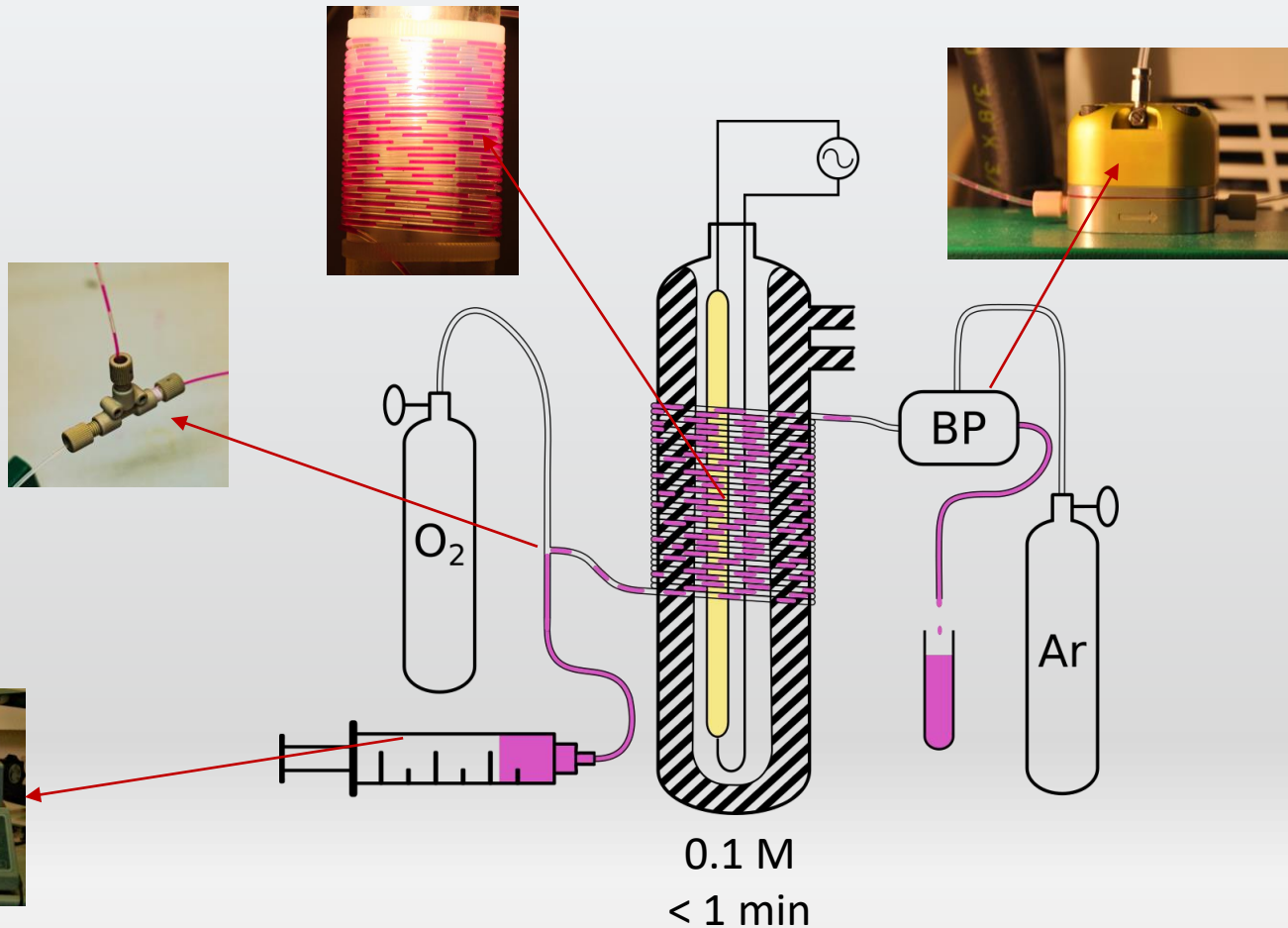


0.1 M
2h

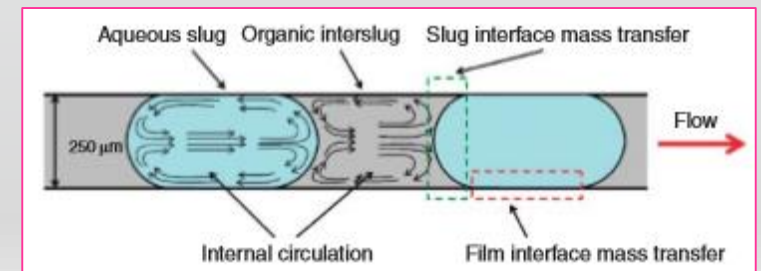


Photooxidation of (L)-methionine

Results in a home-made microreactor



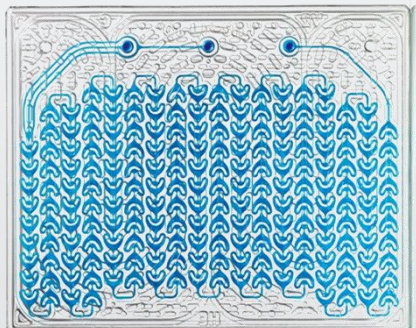
Segmented flow for an excellent exchange between liquid and gas



(*Discovering the Future of Molecular Sciences*, 2014)

Corning Photoreactor

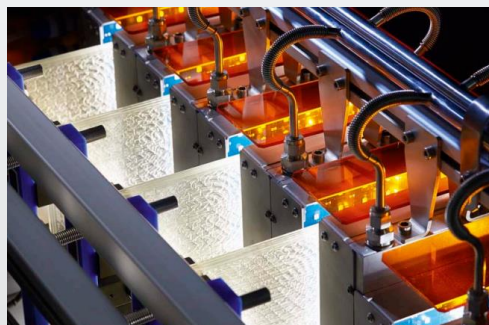
Corning© Photoreactors : Laboratory to industrial scale



Low-flow

Lab scale

1 plate : 155 x 125 mm



G1

Pilote (transition)

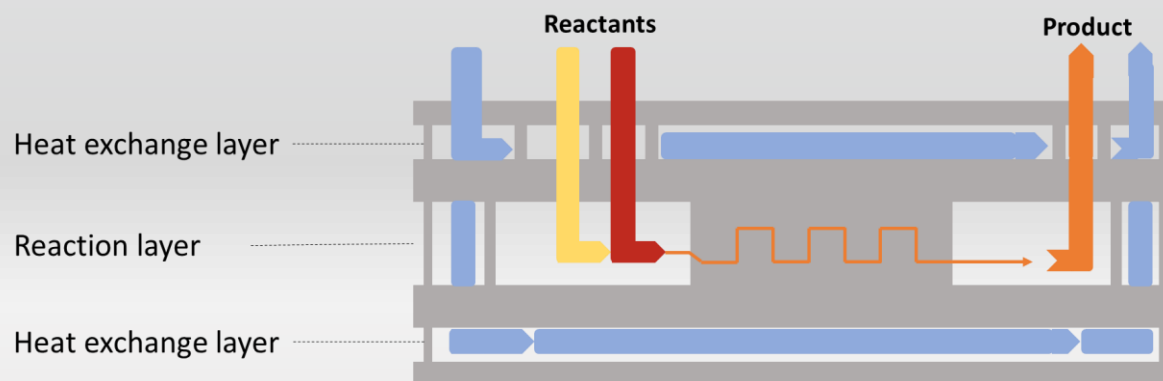
5 plates : 155 x 125 mm



G3

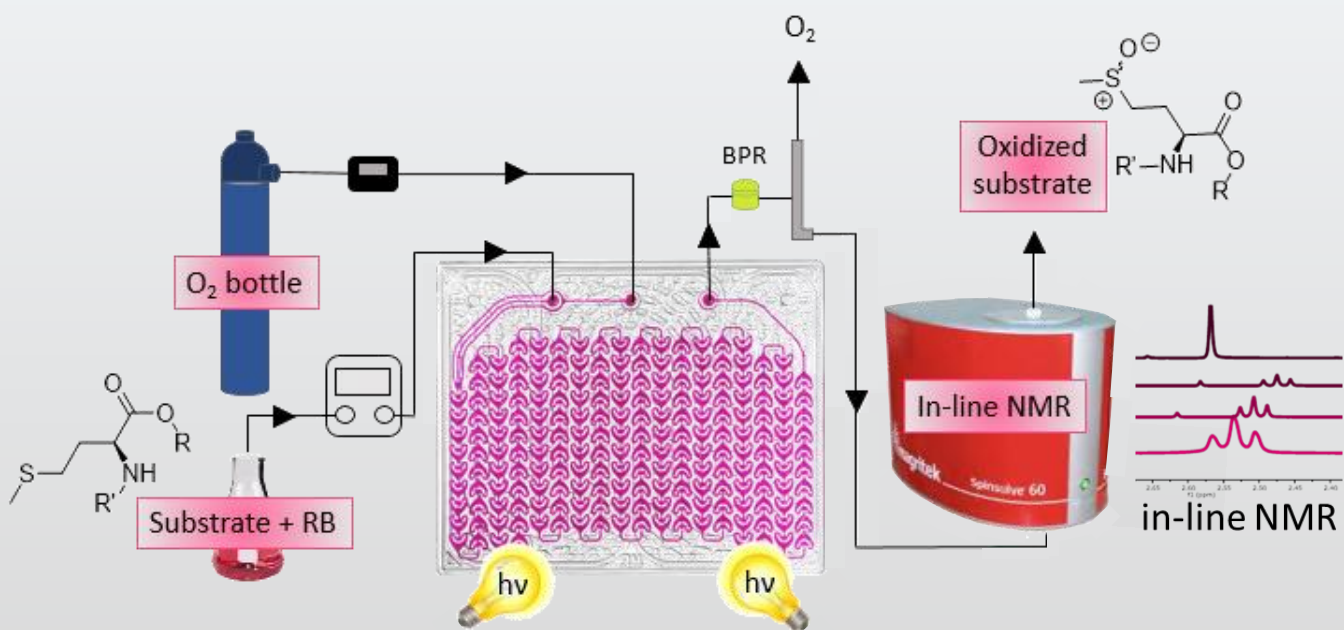
Industrial scale

5 plates : 310 x 250 mm



Corning Photoreactor

Results in a Corning© Advanced-Flow™ Lab Photo Reactor

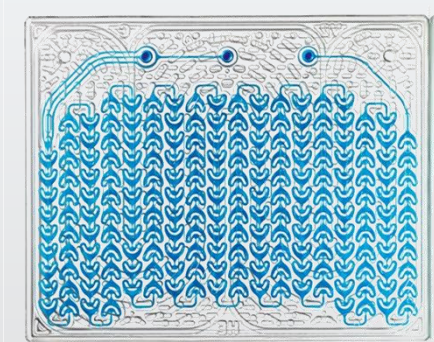


1.2 min residence time
1.1 O_2 equivalent
>99% conversion

N. Emmanuel, C. Mendoza, M. Winter, C. R. Horn, A. Vizza, L. Dreesen, B. Heinrichs, J-C. M. Monbaliu, *Org. Process Res. Dev.*, 21 (2017) 1435–1438.

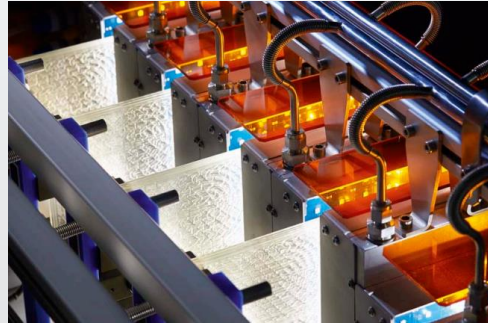
Corning Photoreactor

Corning© Photoreactors : Laboratory to industrial scale



Low-flow
Lab scale

1 plate : 155 x 125 mm



G1

Pilote (Transition)

5 plates : 155 x 125 mm



G3

Industrial scale

5 plates : 310 x 250 mm

productivity

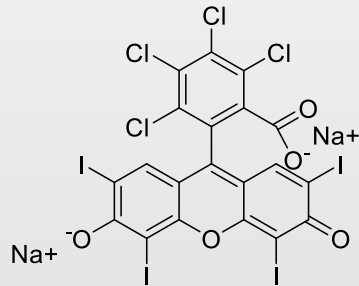
0.13 Kg day⁻¹

5.1 Kg day⁻¹

16.5 Kg day⁻¹

Corning Photoreactor

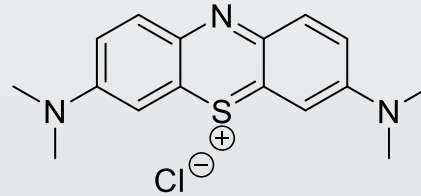
Test of 3 water-soluble photosensitizers



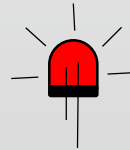
Rose Bengal



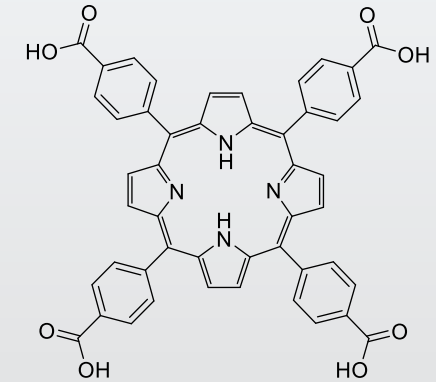
λ_{\max} : ~ 540 nm



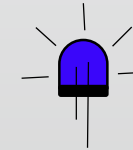
Methylene blue



λ_{\max} : ~ 670 nm



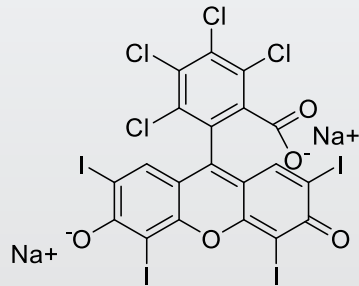
tetrakis(4-carboxyphenyl)porphyrin



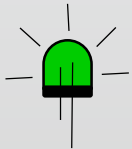
λ_{\max} : 410 to 420 nm

Corning Photoreactor

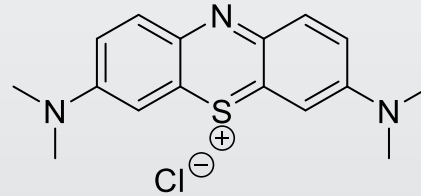
Test of 3 water-soluble photosensitizers



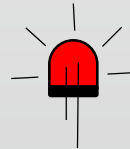
Rose Bengal



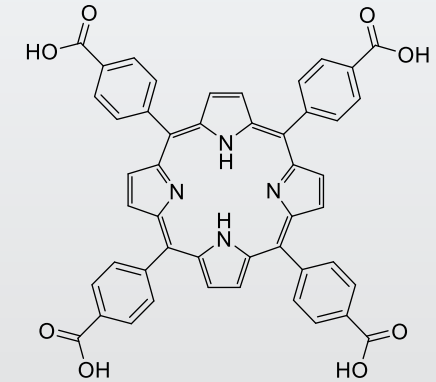
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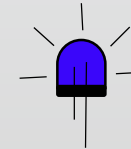
Methylene blue



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tetrakis(4-carboxyphenyl)porphyrin

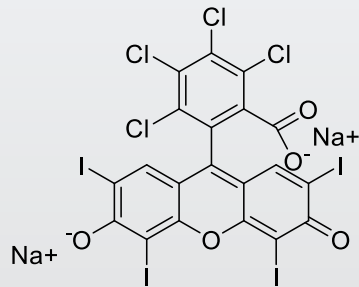


λ_{\max} : 410 to 420 nm



Corning Photoreactor

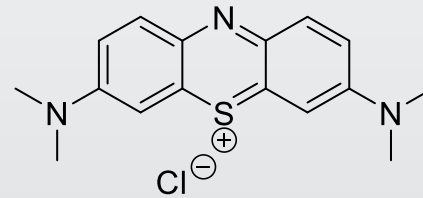
Test of 3 water-soluble photosensitizers



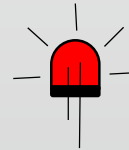
Rose Bengal



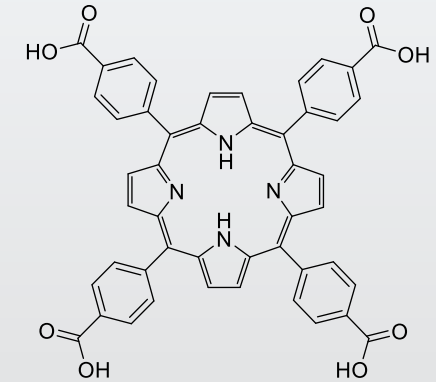
λ_{\max} : ~ 540 nm



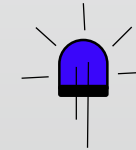
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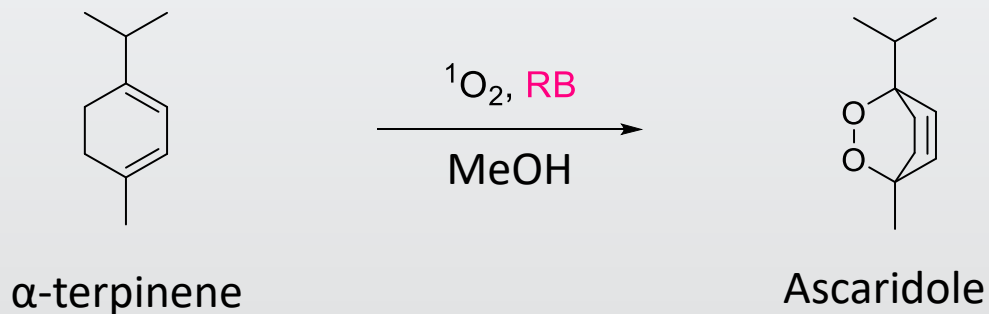


λ_{\max} : 410 to 420 nm

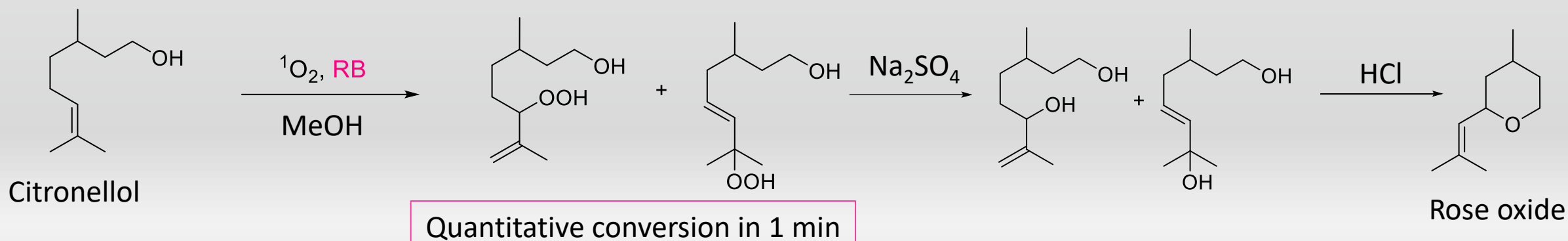
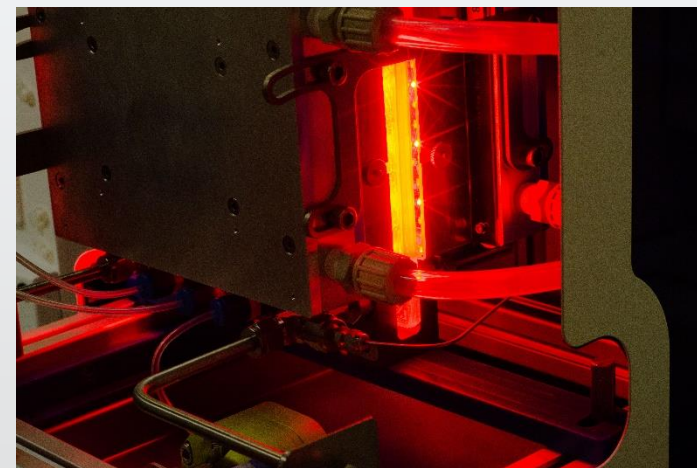


Corning Photoreactor

Transposition to other compounds



Quantitative conversion in 2 min



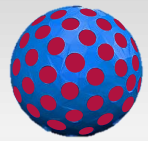
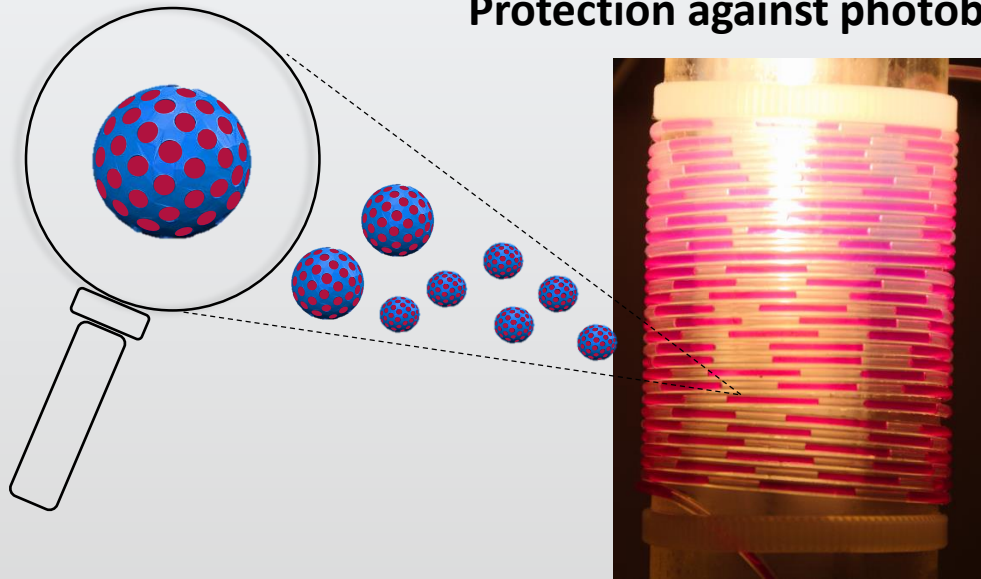
Quantitative conversion in 1 min

N. Emmanuel, C. Mendoza, M. Winter, C. R. Horn, A. Vizza, L. Dreesen, B. Heinrichs, J-C. M. Monbaliu, *Org. Process Res. Dev.*, 21 (2017) 1435–1438.

Recovery of photosentizer

Rose Bengal in silica nanoparticles

Protection against photobleaching



Pore size : 2.96 nm

wt% of RB : 8%

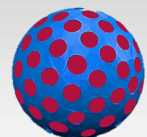
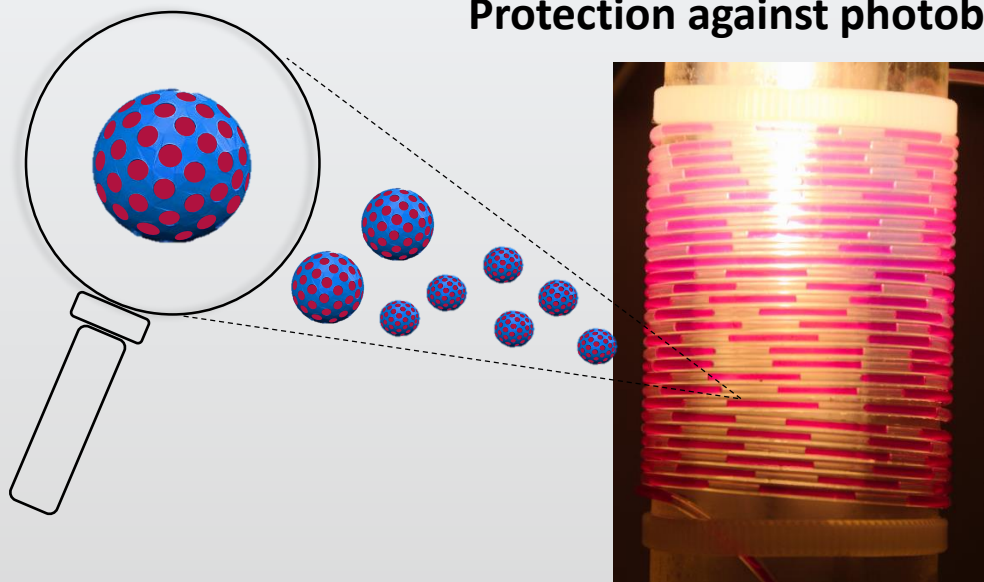
Produced by C. Mendoza

45 nm

Recovery of photosensitizer

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Protection against photobleaching

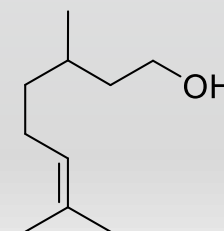
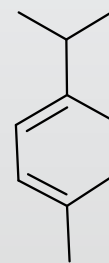
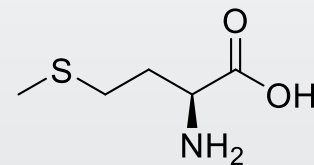


45 nm

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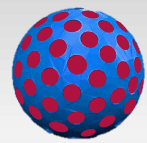
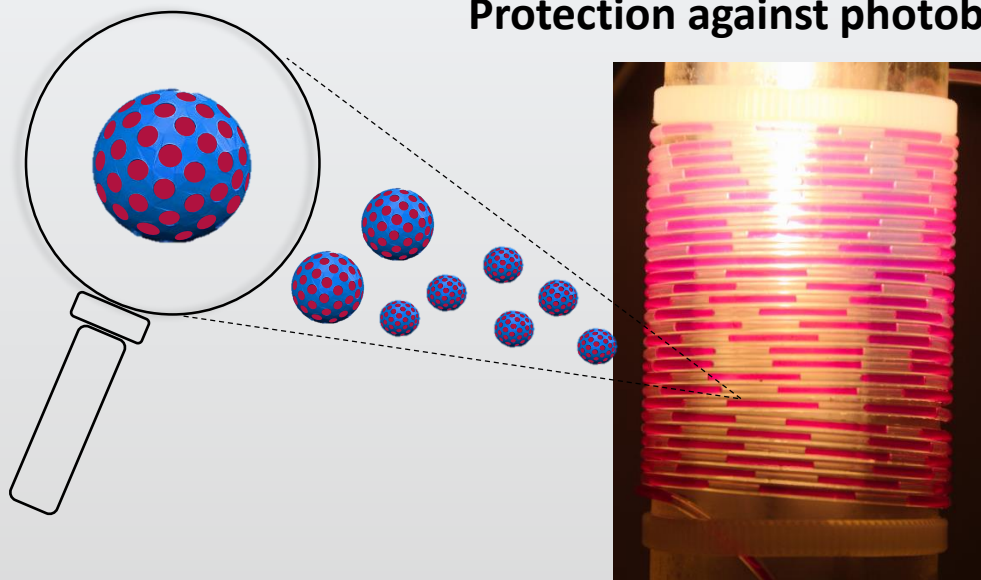
RB-Si

Free RB

Recovery of photosensitizer

Rose Bengal in silica nanoparticles

Protection against photobleaching

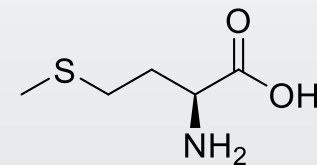


45 nm

Pore size : 2.96 nm

wt% of RB : 8%

Produced by C. Mendoza

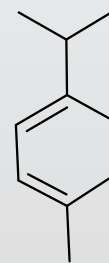


RB-Si

47%

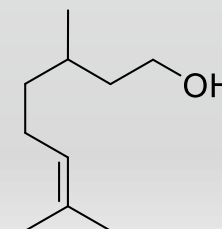
Free RB

Quantitative



90%

Quantitative

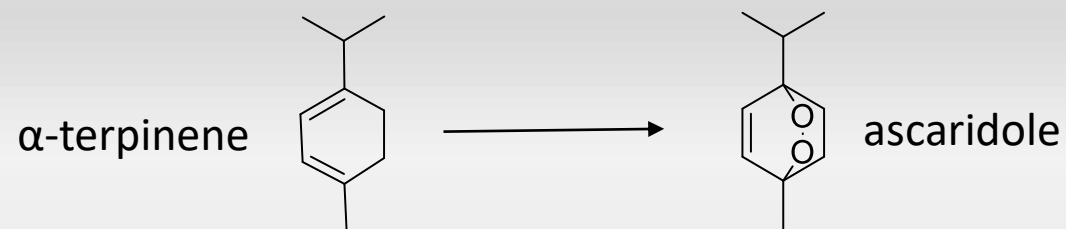
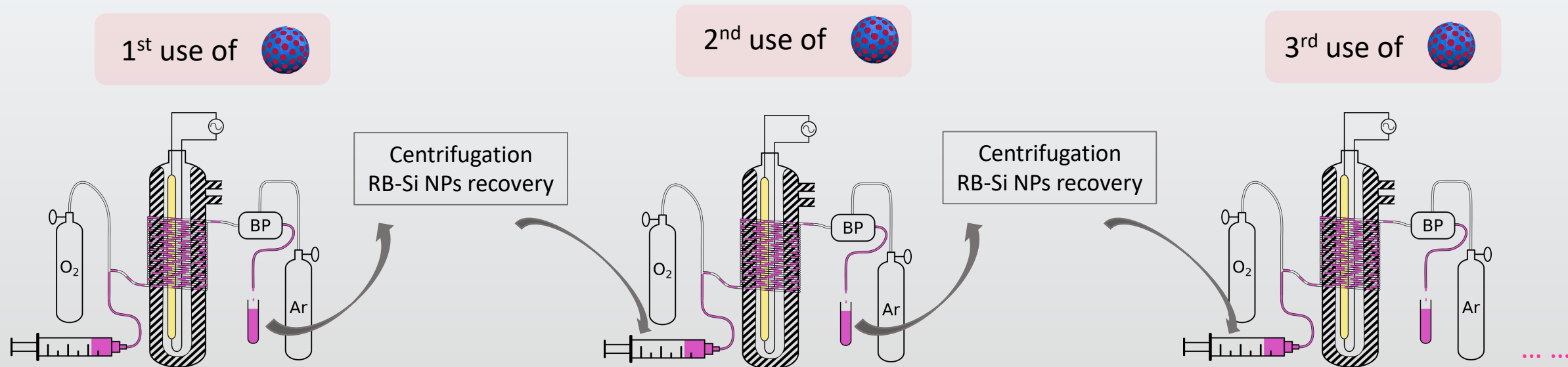


34%

Quantitative

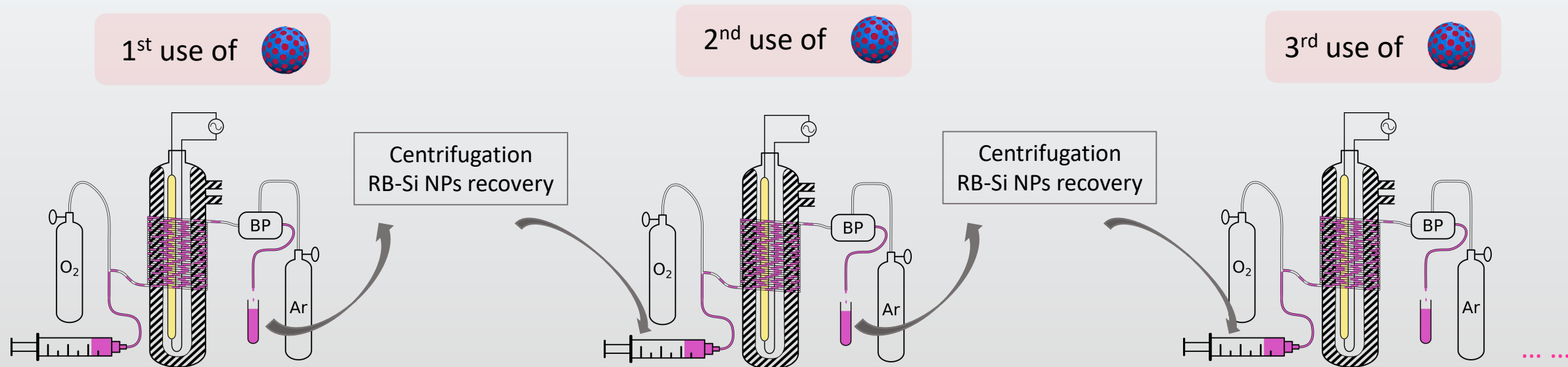
Recovery of photosensitizer

Rose Bengal in silica nanoparticles

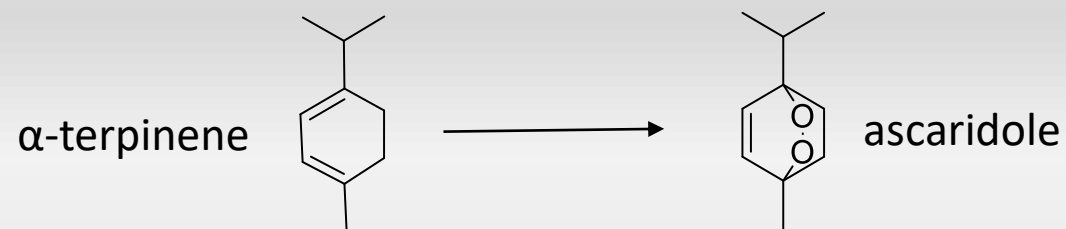


Recovery of photosensitizer

Rose Bengal in silica nanoparticles

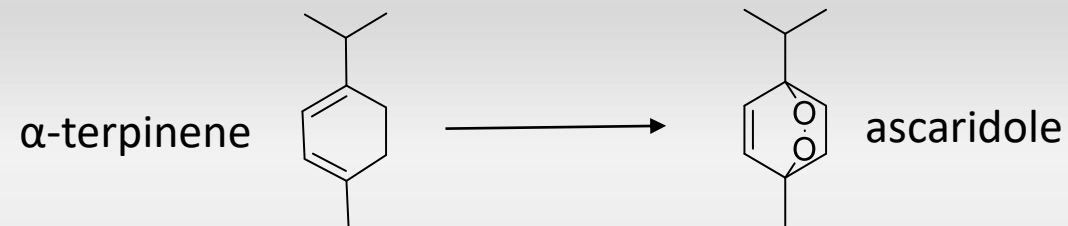
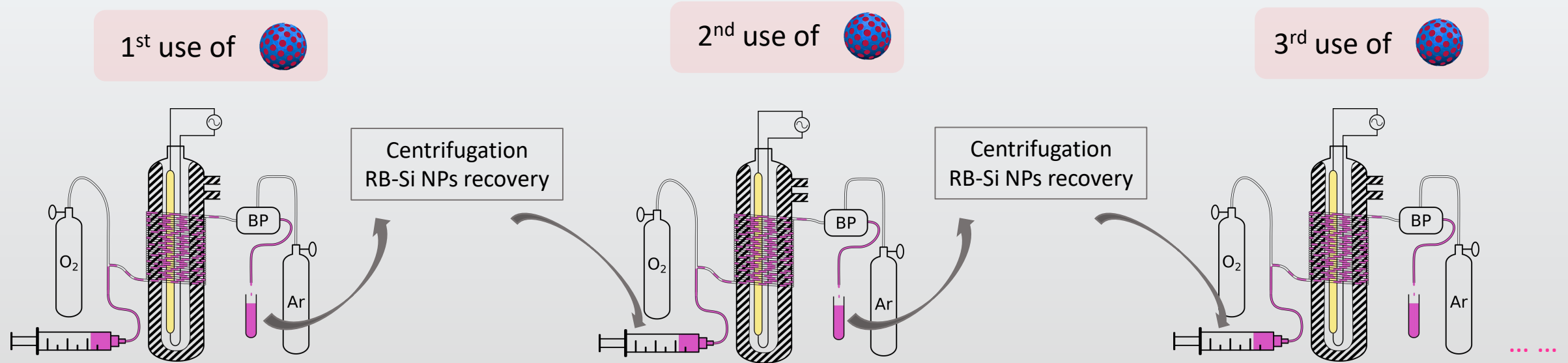


90%



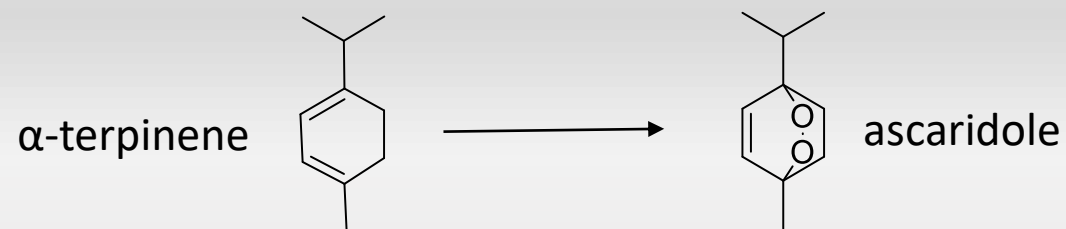
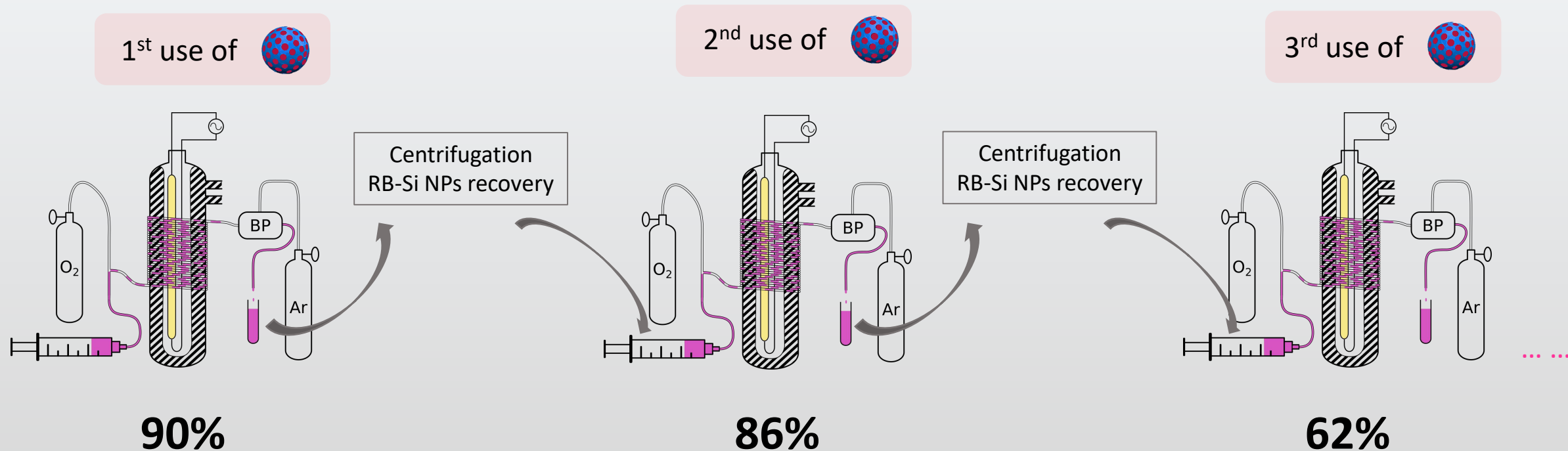
Recovery of photosensitizer

Rose Bengal in silica nanoparticles



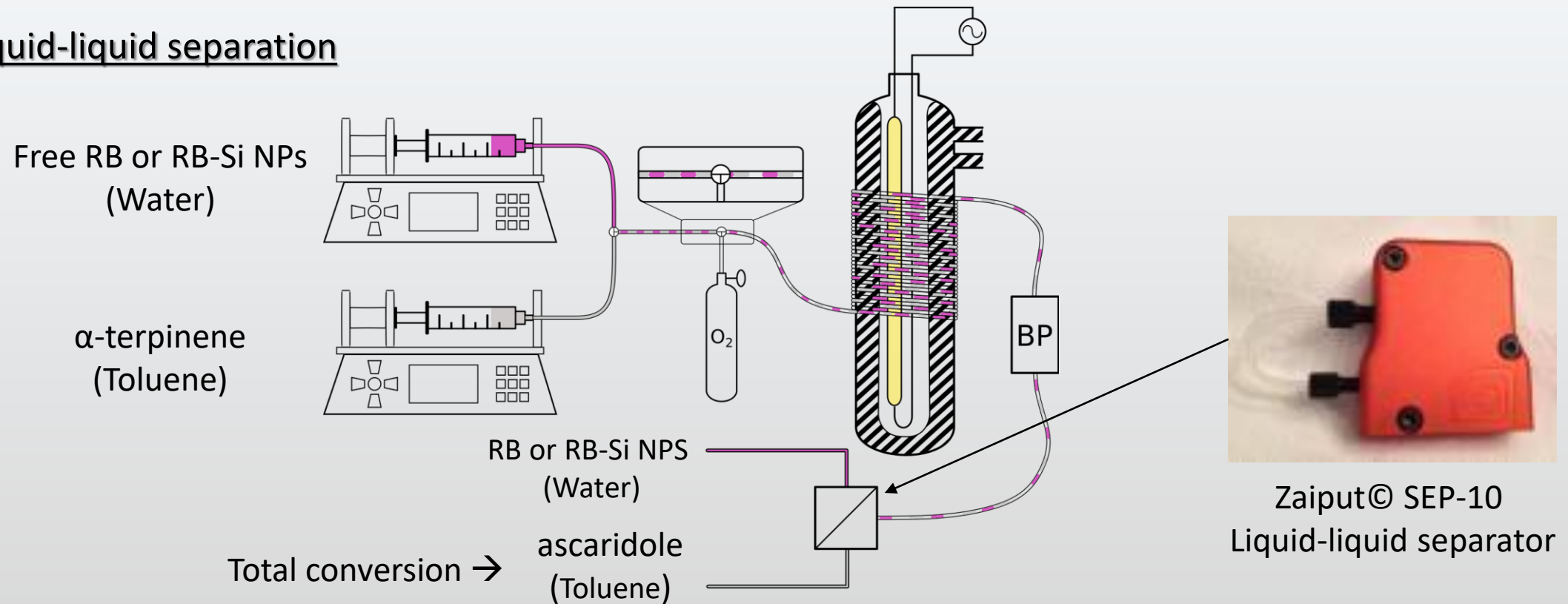
Recovery of photosensitizer

Rose Bengal in silica nanoparticles



Recovery of photosensitizer

In-line liquid-liquid separation

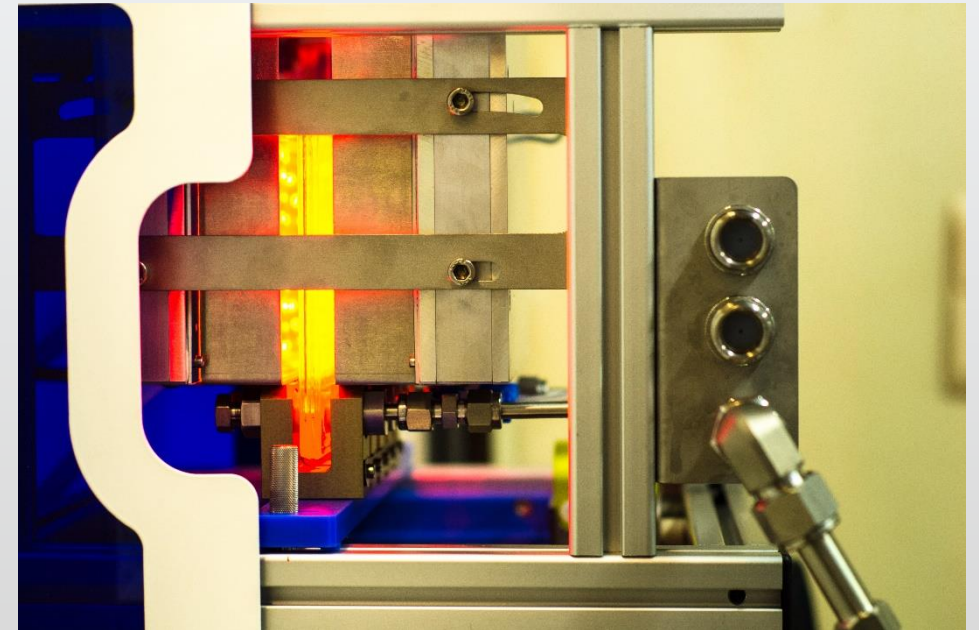


- **Multi-phasic system** : aqueous phase, organic phase, gas phase, solid phase (NPs)
- Higher **affinity** of free RB (or RB-Si NPs) for aqueous vs organic phase
- In-line separation could allow **successive uses of photosensitizer**

Conclusion

Photooxidation in continuous-flow reactor

- Benefits from microreactor's assets
 - Control of irradiation, residence time, temperature, pressure, ...
- Total conversion in short times (min)
- Green conditions : Rose Bengal, Water, light, oxygen, ...
- Highly eased scale-up
- Versatility
 - Substrate, photosensitizer, conditions, ...
- Opens to plenty of possibilities



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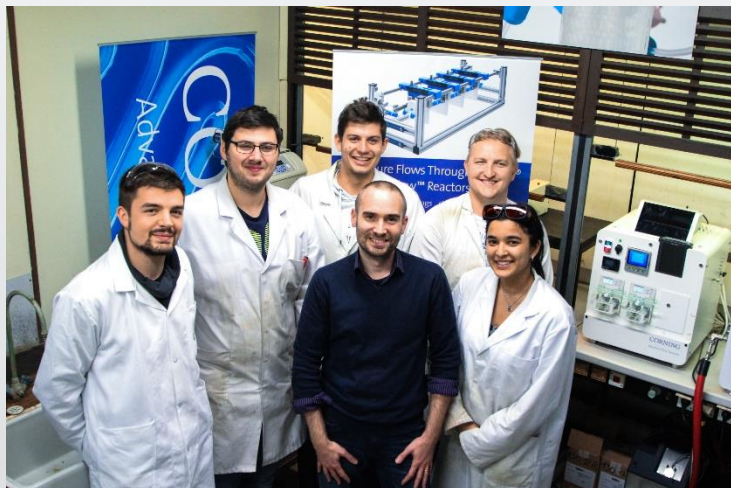
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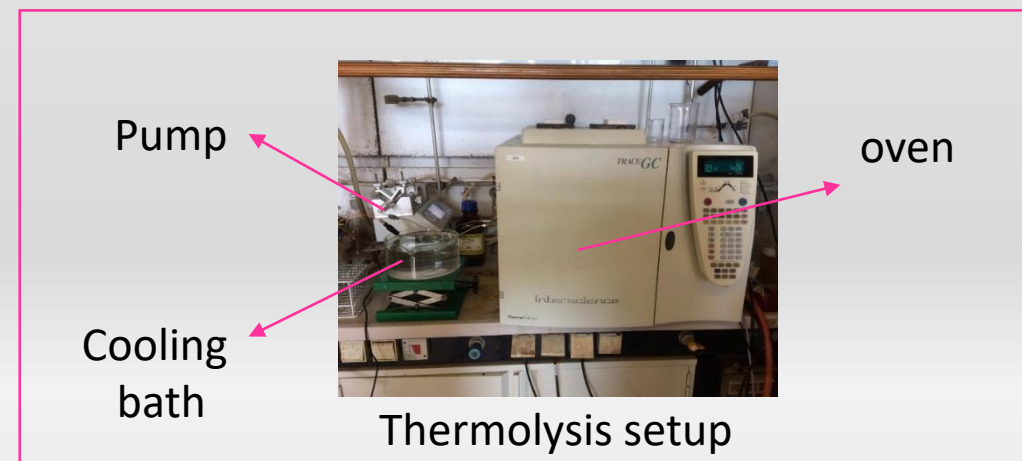
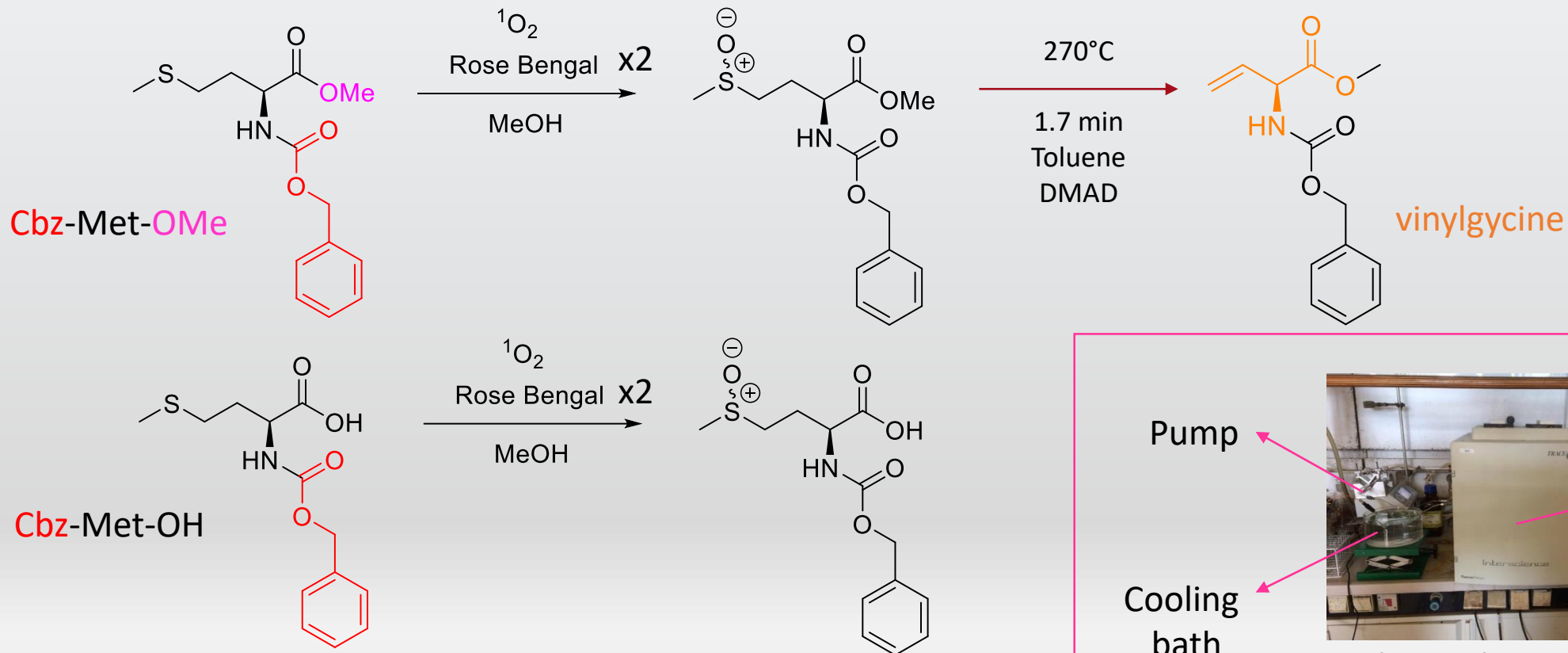
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Thank you for your kind attention

Photooxidation of (L)-methionine

Thermolysis to vinylglycine



¹ N. Lamborelle, J. F. Simon, A. Luxen, J-C. M. Monbaliu, *Org. Biomol. Chem.*, 2015, **13**, 11602