CAMURE-11 11th International Symposium on Catalysis in Multiphase Reactors
ISMR-10 10th International Symposium on Multifunctional Reactors
MILANO, ITALY - 21-24 March, 2021

Development of multiphasic segmented flow for compartmentalized chemo-enzymatic cascade reaction

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1. Introduction

Combining several reactions in one reactor can provide major benefits in term of safety, costs and efficiency. The European ONE-FLOW project [1] aims to implement cascade reaction in continuous flow processes by using compartmentalized flow reactor. A promising approach for flow reactor compartmentalization is the segmented multiphasic flow. Gas/liquid or liquid/liquid segmented flow have already been extensively explored in the literature. Moreover more than two fluid phases can be contacted (gas/liquid/liquid for example) and heterogeneous catalyst can also be introduced [2]. Such diversity of multiphasic flows could have many applications for multistep synthesis.

This work aims at developing compartmentalization inside milli-channels by using multiphasic segmented flow. A case study was conducted on the chemo-enzymatic cascade reaction to form 1-phenylethanol by coupling the Wacker oxidation of styrene and the enzymatic reduction of acetophenone (Figure 1a). The main issue of the coupled process is the enzyme deactivation by the Cu catalyst hence the need to compartmentalize the two reactions. Sato et al. [3] have already performed this cascade reaction in a one pot process using a PDMS membrane to separate both reactions. To implement this cascade reaction in a flow system, a multiphasic segmented flow called the **alternated segmented flow** was developed (Figure 1b). The idea is to generate two aqueous droplets corresponding to the two mixtures used for each step. These two aqueous compartments would be separated by an organic inert phase that would allow acetophenone to transfer while confining copper ions inside the Wacker oxidation droplet.

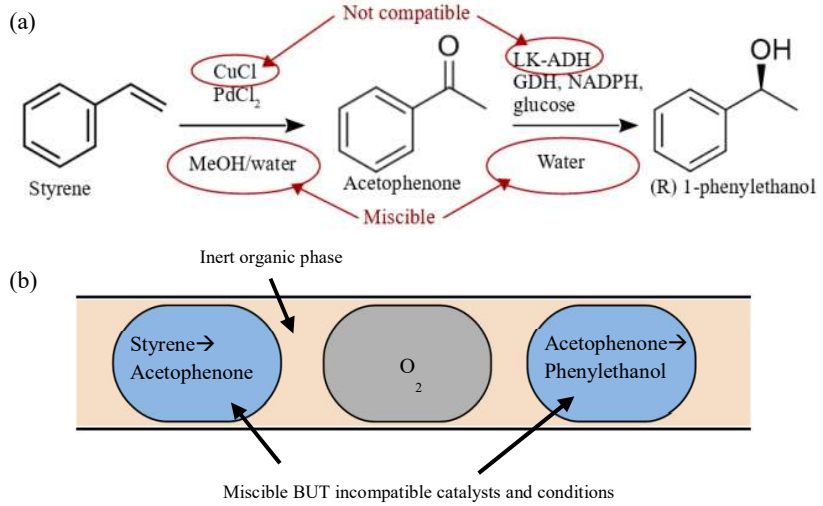

Figure 1: (a) Chemo-enzymatic cascade reaction combining the Wacker oxidation of styrene to acetophenone and the enzymatic reduction of acetophenone to 1-phenylethanol. This cascade reaction was developed in a one pot process by Sato et al. [3].
(b) Proposed multiphasic segmented flow to perform the chemo-enzymatic cascade in a one flow process

In the literature a few publications can be found on Aq./Aq./Org alternated segmented flow [4, 5]. However no work has been done on how to maintain the alternated segmented flow for a long resident time (~30 min)

without having coalescence of aqueous droplets. The objective was therefore to develop and characterize such an operational flow system capable of performing the described chemo-enzymatic cascade reaction.

2. Methods

A preliminary hydrodynamic study was first needed to obtain experimental conditions where robust alternated segmented flows can be maintained for a relatively long resident time (~30 minutes). Furthermore mass transfer of organic molecules from one droplet to the other has also been investigated using a colorimetric method. The transfer of acetic acid is characterized by the discoloration of the basic droplet which contains a pH indicator (Figure 2 (e)).

3. Results and discussion

For the hydrodynamic study, different injector geometries were tested to avoid coalescence of the two aqueous phases (Figure 2 (a) and (b)). Experimental conditions to obtain alternated segmented flow at the injection are presented in a flow map (Figure 2 (d)). The outcome of the alternated flow was observed in a 10 meter coiled reactor (Figure 2 (c)) and adjustments were made to avoid coalescence inside the reactor. In the end, we obtained experimental conditions to perform an Aq./Aq./Org./Gas segmented flow with a residence time of 30 min. Concerning the mass transfer study, the presence of gas between the two droplets doesn't hinder the transfer of acetic acid from one droplet to the other (Figure 2 (f)).

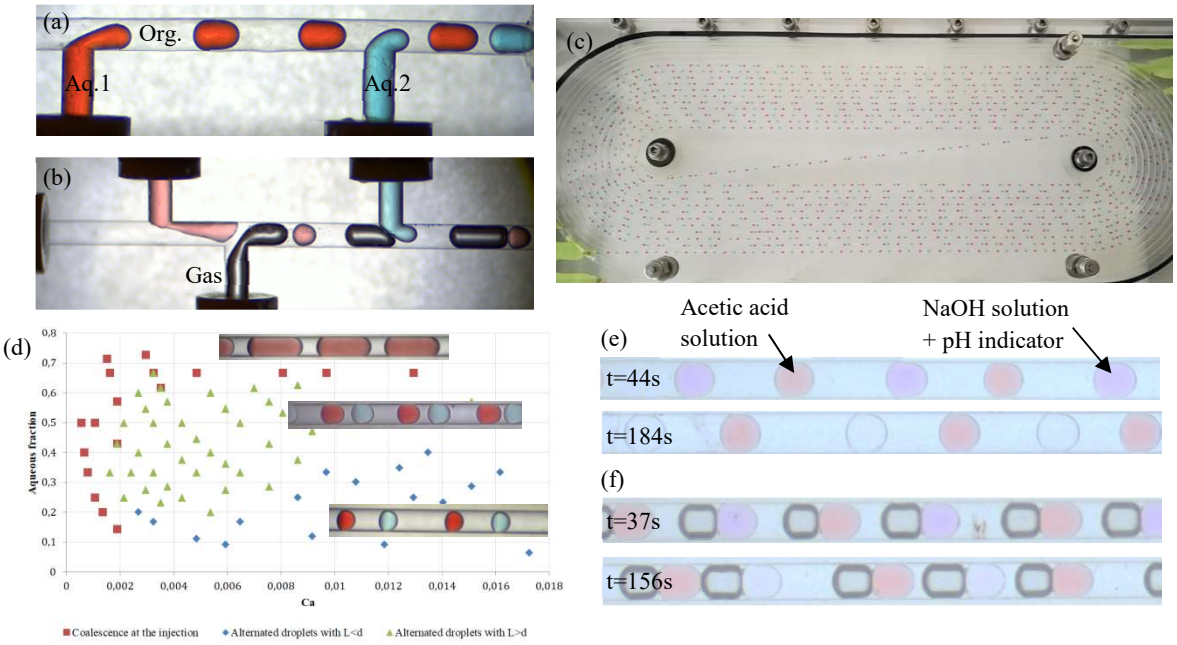

Figure 2: (a) Injection system for Aq.1/Aq.2/Org. alternated segmented flow, (b) Injection system for Aq.1/Aq.2/Org./Gas alternated segmented flow, (c) Coiled reactor used for the hydrodynamic study, (d) Mapping of flow regime, (e) Discoloration of basic droplet for Aq./Aq./Org segmented flow, (f) Discoloration of basic droplet for Aq./Aq./Org /Gas segmented flow.

4. Conclusions

In conclusion, we present a viable and operational system to compartmentalize two miscible phases inside a G-Aq.-Org.-Aq. multiphase flow reactor. Ongoing studies concern the implementation of this compartmentalization system to desired cascade reaction system.

References

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