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Jet Colliding and Mixing Efficiency

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Abstract: Two experimental methods, the Nile Red dye extraction and the Williamson ether synthesis in biphasic conditions, were used to characterize the mixing performance of a new cheap impinging jet colliding mixer from Gjosa and to compare it to other commercial micromixers (Caterpillar CPMM-R300, T-mixer, LTF MR-MX and LTF MR-MS). The Nile Red method shows that the Caterpillar mixer is the best one. Excellent results are also achieved with two Gjosa mixers in series. These results are not reflected in the Williamson ether synthesis, where the best mixer is the Gjosa one.

Keywords: Jet colliding · Nile Red · Mixing · Williamson ether synthesis

1. Introduction

Mixing is crucial for most chemical reactions: it ensures a good contact between reactants and reagents, it favors homogeneity and an efficient heat transfer.[1] This is even more important when biphasic reactions are performed, as mass transfer between phases is challenging. If the mixing quality is poor, the reaction will proceed very slowly no matter how well the other physico-chemical parameters are optimized. In that case, poor yield, low conversion and sometimes bad quality (formation of impurities) are observed.[2] On the other side, when optimal mixing is quickly achieved, the reaction is not limited by mass transfer. Mixing in chemistry is therefore a crucial parameter.

In a batch reactor, the reactor geometry, baffles, mixer types and size (*e.g.* anchor, impeller), and the agitation speed influence the mixing quality.[3] In flow chemistry, mixing is achieved by diffusion. When the reaction is very fast or when the channel diameter is too large, static or dynamic mixers are used to ensure proper mixing. Many different static mixers exist and some are more efficient than others.[4] These mixers are usually expensive even at small scale, ranging from several hundreds to several thousand Swiss francs (*e.g.* Dolomite micromixer chip[5] or Caterpillar micromixers[6]), hence there is a need to lower the costs. Moreover, most of the time these mixers are limited to a defined range of flow rate and are not suitable for scale up.

Mixers based on impinging jet colliding may be of great interest to solve both drawbacks.[7] Furthermore, this technique can be operated at high flow rates.[8] These mixers consist in spraying two phases against each other.[9]

To characterize the mixing, several methods can be used like the Nile Red (Fig.1). In this method, a water/methanol media containing the dye Nile Red is simply extracted with an organic phase. It is a stable dye that is soluble in several solvents with all kinds of polarity, from acidic water to hexane. Its absorption maximum varies as function of the solvent; hence, it is very easy to follow its extraction from the water

phase to the organic phase. The solvatochromic Nile Red shifts its absorption maximum from 581 nm in water/methanol to 489.3 nm in *n*-heptane (Fig. 2). The higher the absorbance, the better the mixing. In contrast to the single-phase 'Villermaux-Dushman method', the multiphase dye extraction method Nile Red is not based on competing parallel reactions but is only entropy controlled and does not require on-line spectroscopic measurements.[10] Since no chemical reaction is involved in this method, it is possible to exactly follow the mass transfer (that is proportional to the degree of mixing) without concerns about reaction kinetics.[11]
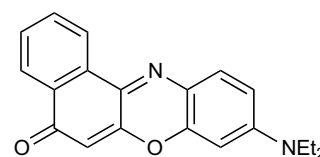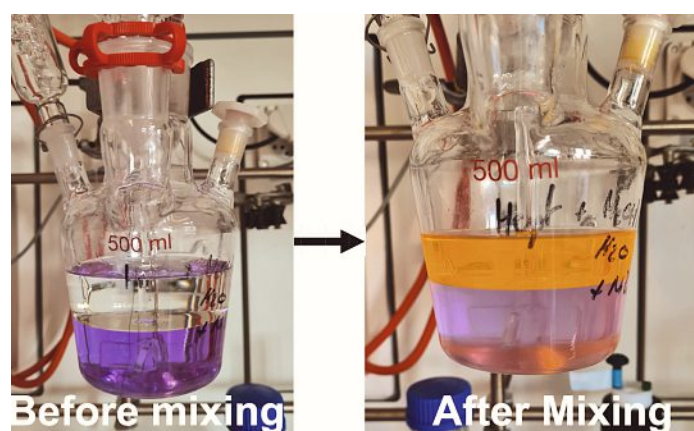

Fig. 1. Nile Red

Fig. 2. Colour change of the organic (top layer) and aqueous phase (bottom layer) during the batch extraction of Nile Red.

In this paper, we are using two biphasic methods to characterize the mixing provided by several static mixers: the Nile Red extraction[10] and the Williamson ether synthesis of **3** (Scheme 1).[12,13] The mixing efficiencies of T-mixers, LTF MR-MX and MR-MS,[14] Caterpillar CPMM-R300[6] are compared with the new impinging jet colliding mixers developed by Gjosa[15] (Fig. 3).

2. Results and Discussion

2.1 *Mixing Efficiency with the Nile Red Method*

The comparison of the mixing efficiency of two immiscible phases has been undertaken with the Nile Red method. The aqueous phase containing the dye is extracted with an organic phase (*n*-heptane) and the absorbance is measured by UV-vis at 489.3 nm.[10] The aqueous phase consists of a mixture water/methanol 1:1 because with pure water the dimerization of Nile Red occurs. Such aggregation tends to increase the initial aqueous solution's absorbance over time and affects the ex-
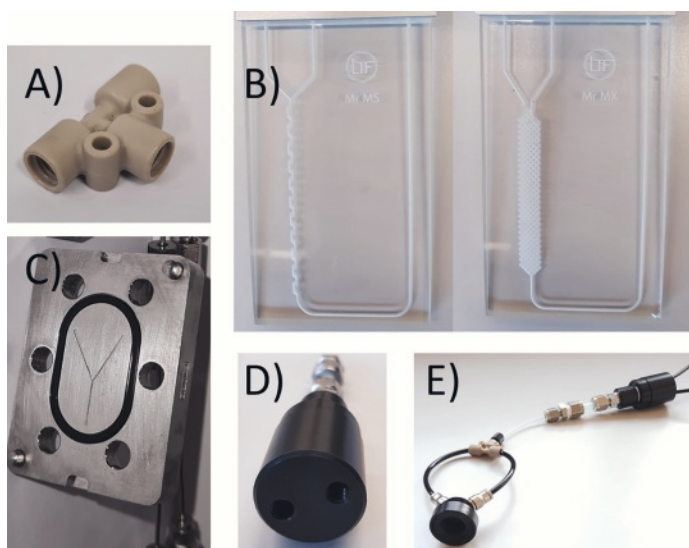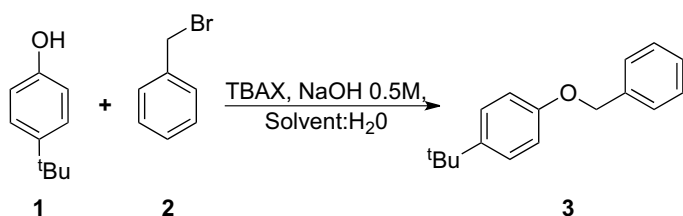
Fig. 3. Static mixers used. A) T-mixer, B) LTF mixers (MR-MS and MR-MX), C) Caterpillar CPMM-R300, D) Gjosa and E) 2x Gjosa mixers in series.

Scheme 1. Williamson ether synthesis of **3** under biphasic reaction conditions.

perimental reliability.[16]

Batch experiments at various mixing speeds (100, 200, 400 and 1000 rpm) over 30 minutes with a ratio aqueous to organic phase of 1:1 showed that the absorbance increases over time to reach a maximum value around 0.36 corresponding to the equilibrium partition of Nile Red in-between the aqueous phase and *n*-heptane (Fig. 4). This value indicates a very good mixing and will be used to benchmark the micromixers. Moreover, the absorption variation over time dA/dt at the beginning strongly increased with the mixing speed. This observation is correlated with the formation of smaller droplets, leading to an increase of the interphase's surface and an acceleration of the diffusion process. At 100 rpm, proper formation of an emulsion did not occur and the only contact surface was the initial interphase between the two liquids, leading to a linear increase of the absorbance over time.

As shown in Table 1, increasing the flow rate from 30 to 50 mL/min improved the efficiency of all the mixers tested in this paper. The T-mixer was not a good mixer for biphasic systems (entries 4, 5, 12, 13, 20), whereas the split-and-recombine mixer of Caterpillar showed the best performance (entries 1, 9, 17). Nonetheless, the combination in series of two jet colliding mixers with channels diameter of 0.4 mm from Gjosa gave very good results; as good as the Caterpillar mixer at low flow rate (entry 8), and even better at higher flow rate (entry 16). It even reached the equilibrium value of 0.36 within a second (entry 24), whereas it required 30 min under vigorous agitation for the batch experiment to reach this value (Fig. 4).

Apart from the efficiency of the mixing, there are other considerations when it comes to choosing a mixer: throughput, material of construction, cost, and the maximum pressure allowed (Table 2). The Gjosa mixer is attractive due to its good performance, its versatility, its cost and its throughput (high flow rate

can be achieved). In addition to the manufacturer limitation, the throughput is also limited by the pressure drop generated in the flow system. Among the mixers tested in this study, the Caterpillar CPMM-R300 is the only one that reached the limit of our system (21 bars) with a flow rate of 90 mL/min (Fig. 5). Due to this significant pressure drop, more expensive pumps like high pressure gear pumps are required.

As the jet colliding mixers of Gjosa were easier to modify, several mixers have been manufactured and tested. A larger channel diameter (0.4 mm) required a higher flow rate to achieve a similar performance than a mixer with small diameter (0.2 mm) at a slower flow rate (entries 6, 7, 14, 15, 22, 23).[17] However, achieving a diameter smaller than 0.2 mm is challenging with polyoxymethylene (POM). Nonetheless, the excellent performance observed with two Gjosa mixers in series (entries 8, 16, 24) offers interesting perspectives. The type of mixing (impinging colliding jet) is most probably altered in that case, because a small pre-mixing chamber between the feeds and the impinging jets of the first mixer is created by coupling two Gjosa mixers in series (see the first mixer on the lower right corner of the Fig. 3).
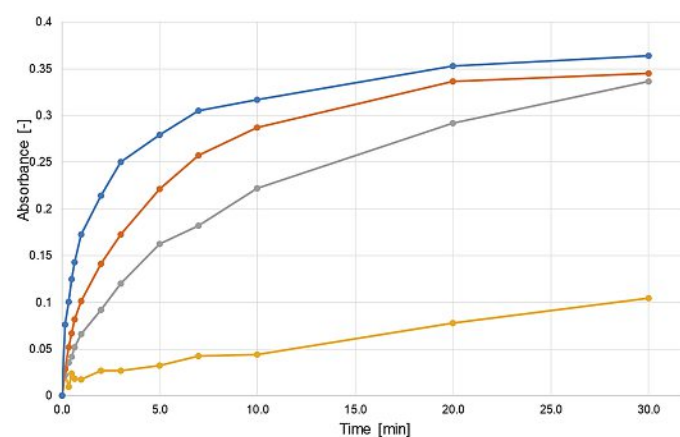

Fig. 4. Extraction kinetic of Nile Red in n-heptane for different agitation speeds. Reactions were performed in 500 mL flask with a mechanical impeller at 25 °C.
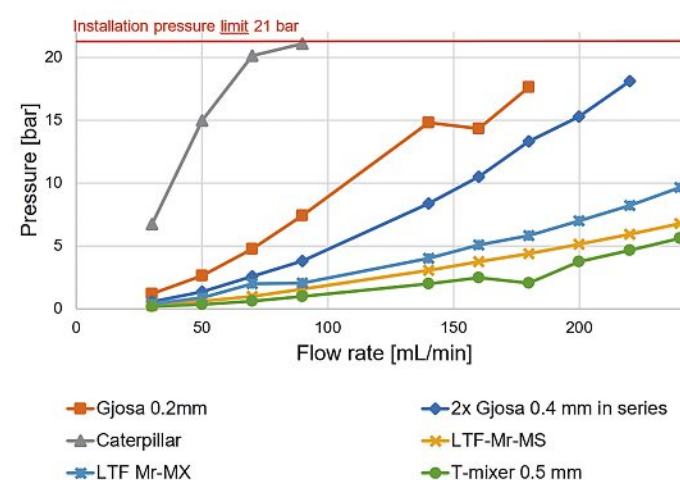

Fig. 5. Pressure profile over the flow rate for the Caterpillar 0.3 mm, LTF MR-MX/MS, the T-mixers 1 mm and 0.5 mm, Gjosa mixer 0.2 mm and 2 Gjosa mixers 0.4 mm in series. The maximum pressure on the testing system was set at 21 bar.

2.2 Mixing Efficiency with a Biphasic Williamson Ether Synthesis

The formation of **3** *via* a biphasic Williamson ether synthesis works well in $CHCl_3$ with TBAI as phase transfer catalyst

Entry	Mixer	Type	Channel size [mm]	Total flow rate [mL/min]	Absorbance of the organic phase [-]
1	Caterpillar CPMM-R300	Split-and-recombine	0.3	30	**0.24**
2	LTF Mr-MX	Split-and-recombine	1	30	**0.14**
3	LTF Mr-Ms	Chaotic	1	30	**0.18**
4	T-mixer	Impact jet	1	30	**0.02**
5	T-mixer	Impact jet	0.5	30	**0.11**
6	Gjosa	Collision jet	0.2	30	**0.12**
7	Gjosa	Collision jet	0.4	30	**0.08**
8	2 x Gjosa in series	Collision jet	0.4	30	**0.23**
9	Caterpillar CPMM-R300	Split-and-recombine	0.3	50	**0.27**
10	LTF Mr-MX	Split-and-recombine	1	50	**0.28**
11	LTF Mr-Ms	Chaotic	1	50	**0.24**
12	T-mixer	Impact jet	1	50	**0.03**
13	T-mixer	Impact jet	0.5	50	**0.13**
14	Gjosa	Collision jet	0.2	50	**0.21**
15	Gjosa	Collision jet	0.4	50	**0.11**
16	2 x Gjosa in series	Collision jet	0.4	50	**0.34**
17	Caterpillar CPMM-R300	Split-and-recombine	0.3	90[a]	**0.30**
18	LTF Mr-MX	Split-and-recombine	1	220[a]	**0.29**
19	LTF Mr-Ms	Chaotic	1	220[a]	**0.32**
20	T-mixer	Impact jet	1	70[a]	**0.06**
21	T-mixer	Impact jet	0.5	160[a]	**0.29**
22	Gjosa	Collision jet	0.2	90[a]	**0.22**
23	Gjosa	Collision jet	0.4	240[a]	**0.20**
24	2 x Gjosa in series	Collision jet	0.4	200[a]	**0.36**

[a]flow rate that gives the best absorbance of the organic phase

Table 1. Results of the Nile Red experiments for various micro-mixers at different flow rates.

Mixer	Material of construction	Flow rate range [mL/min]	Max pressure [bar]	Estimated price per unit [CHF]
Caterpillar CPMM-R300	Stainless steel 316	8-60	100	~ 4000
LTF Mr-Ms/MX	Glass	0.1-20	15	600 – 800
T-mixer	PEEK[a]	Up to max pressure	35	~ 20
Gjosa	POM[b]	Up to max pressure	20	100 – 200

[a]PEEK = Polyetheretherketone. [b]POM = Polyoxymethylene

Table 2. Features of the tested micromixers.

Table 3. Reaction yield of the Williamson ether synthesis of **3** with various micromixers. Conditions: solvent (CPME:water 1:1), 1.9 eq. of bromobenzyl **2** and 0.03 M of TBAI, 80°C.

Mixer	Flow rate [mL/min]	Yield[a] after 9 s residence time [%]	Yield[b] after 609 s residence time [%]
Gjosa 0.2 mm	200	6.2	19.2
Gjosa 0.4 mm	200	2.7	11.9
Caterpillar CPMM-R300	60	5.7	10.6
Batch[c]	–	–	85

[a] The residence time for Caterpillar mixer is 32 s.
[b] The residence time for the Caterpillar mixer is 632 s.
[c] Agitation speed : 1000 rpm.

(Scheme 1).[18] A yield of 93% is obtained after 60 min of residence time at 50 °C. As we are working with large solvent inventories and due to the high toxicity of CHCl₃, a solvent screening was performed to find greener alternative for our study. Data not shown here demonstrate that CPME gave good yield of **3** (85%) after 10 min in batch reaction under strong agitation (1000 rpm) at 80 °C.

Promising results have been obtained with static mixers. In a very short mixing time (less than 1s) and a few seconds of residence time in a tubular reactor (diameter:1/8''; length: 6 m), the product **3** has been obtained with a poor yield regardless of the mixers used. Increasing the residence time increased the yield of **3** (Table 3). Due to the non-optimal residence time (10 min without stirring in a 20 mL cylinder), a fast phase separation severely impacted the diffusion process and slowed down the formation of **3**. Despite this unfavorable setup, **3** was obtained with 19% yield when the Gjosa mixer 0.2 mm was used. This mixer showed better performances (yield and throughput) than the Caterpillar one.

Increasing the residence time to 10 min with a tubular reactor could improve this result, but it would require a minimum of 400 m of a thermostatized stainless steel tube with a diameter of 1/8''. A better approach to circumvent or minimize the decantation in the residence time zone would be to interpose several mixers in the reaction zone or to add several mixers in series, a strategy successfully adopted by Corning Advanced-Flow™ glass reactors with its patented HEART design.[19]

Comparing the results of the Nile Red experiments (Table 1) with the results of the Williamson ether synthesis of **3** (Table 3) showed that the best mixer for the Nile Red extraction is not the best mixer for the synthesis of **3**. Thus, the Nile Red method cannot be used to select the best mixer for a biphasic Williamson ether synthesis. One reason could be that the Nile Red method is based on phase transfer (physical interaction) without reaction kinetics (chemical reaction).

3. Conclusions

The Nile Red method was successfully used to characterize the mixing efficiency of several micromixers for biphasic systems. Chaotic and split-and-recombine mixers are more efficient than the impinging jet colliding mixers from Gjosa. In order to achieve comparable or superior results to the others mixers, two Gjosa mixers in series can be used. Moreover, the efficiency/cost ratio for the Gjosa mixers (even considering two of them in series) is very good. Unfortunately, the Nile Red method can not be used to select the best mixer for a reaction like a biphasic Williamson ether synthesis. All the mixers tested in this study gave **3**, but with poor yield. As the synthesis conditions and the residence time were not optimized, these low yields reflected much more the quality of the mixing than it would for a fully optimized synthesis. Additional improvements of the Gjosa mixer are ongoing. Moreover, the optimization of the Williamson ether synthesis for flow chemistry will also be further investigated.

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