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Phase Transfer Catalyzed Wittig Reaction in the Microtube Reactor under Liquid−Liquid Slug-Flow Pattern

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ABSTRACT: Phase transfer catalysis (PTC) is an important method in synthetic two-phase chemistry. Stable liquid−liquid hydrodynamic flow in a microtube reactor offers considerable benefits over the conventional batch reactors. In this work, we attempted to conduct a two-phase organic solvent/aqueous sodium hydroxide solution PTC Wittig reaction of benzyltriphenylphosphonium bromide and *o*- and *p*-methoxybenzaldehydes in a microtube reactor under reproducible slug-flow pattern. Stable operating conditions and a defined specific interfacial area are crucial to study the interaction between kinetics and mass transfer effects. A strong impact of aqueous-to-organic (AO) phase volumetric flow ratio on the specific interfacial area and consequently on mass transfer between phases was observed. The increase of the specific interfacial area causes a higher overall reaction rate at the same residence time when 0.1 M sodium hydroxide solution was used, which confirms that mass transfer has an influence on the overall reaction rate. Increasing the aqueous sodium hydroxide solution concentration at the organic−water interface increased mass transport. At defined conditions, when the surface-to-volume ratio and concentration of OH^- ions were adequate, reaction kinetics came to be the rate-limiting step.

INTRODUCTION

The increasing demand of industry, for example chemical, pharmaceutical, analytical and biochemical, for novel technologies has led to the intensive development of the microreactor technology which is nowadays one of the most innovative and rapidly developing fields in chemical engineering, synthesis and process technology. In the past decade, microstructured devices have impressively demonstrated several decisive advantages, such as better heat and mass transfer due to a very large surface-to-volume ratio and superior mixing of the fluid phases.[1,2]

An important feature of microstructured reactors is the hydrodynamic flow in the microchannels. In liquid−liquid microchannel flow, different flow patterns such as annular flow, parallel flow, drop flow or slug flow are found. Circulation patterns vary with the physical properties of liquids as well as with operating parameters such as flow ratio of two immiscible liquids, mixing elements geometry, channel geometry and capillary dimensions.[3] In a microtube reactor with stable two-phase slug-flow regime, which is characterized by a reproducible slug flow, a high degree of control over the slug size distribution can be achieved, and the liquid−liquid interfacial surface-to-volume ratio is in the order of 5000 to 30 000 m^2/m^3.[1]

The migration of reactants in synthetic organic two-phase liquid−liquid chemistry from one phase into another phase where the reaction occurs is often accelerated by phase transfer catalysis (PTC). The key factor in PTC is the ability of small quantities of an agent to transfer one reactant across the interface between two immiscible liquid−liquid phases so that reaction can proceed.[4,5] The first study of a PTC reaction in a microchannel was performed by Hisamoto et al.[6] on a diazo-coupling reaction. Ueno et al.[7] investigated PTC alkylation, and Ahmed-Omer et al.[8] investigated a number of process-intensification techniques in a two-phase slug-flow reaction system in a microreactor. Previously published research studies of microdevices show decisive advantages in PTC.

The Wittig reaction is one of the most important and versatile reactions in organic chemistry for the synthesis of alkenes with unambiguous positioning of the double bond. Since its discovery,[9,10] the reaction has been studied very extensively,[11,12] also under PTC conditions.[13−15] The reaction, where benzaldehyde reacts with benzyltriphenylphosphonium salt (BTPP salt) to yield stilbene is generally classified as a PTC reaction[16] even though BTPP salt itself is a reactant. The liquid−liquid two-phase Wittig reaction of BTPP salt and benzaldehyde can be simplified as depicted in Figure 1. Since materials in the two separate phases must contact each other before reaction can occur, both the mass transfer and the chemical rates will enter the overall rate expression. Therefore, the reaction consists of mass transfer and kinetic steps. The BTPP salt transfers to the organic−aqueous interphase (mass transfer step) where it is deprotonated by base (kinetic step). The generated ylide transfers back to the organic phase (mass transfer step) and reacts with benzaldehyde to generate stilbene and phosphine oxide (kinetic step).

In this work, we attempted to conduct a two-phase PTC Wittig reaction in a fluorinated ethylene propylene (FEP) microtube reactor (Vici AG, Schenkon, Switzerland) with an internal diameter of 250 μm. The reaction was carried out at slug-flow regime. First, the stable flow operating regime characterized by a reproducible slug flow was investigated. In further investigations the influences of (i) flow rate, (ii) variation of the ratio between the aqueous and organic phase flow rates and (iii) different concentrations of aqueous sodium hydroxide solution on the overall rate of the PTC Wittig reaction were investigated. The overall rates of reaction at stable flow regime in a microtube reactor and in a standard batch reactor with a mechanical stirrer were also compared.

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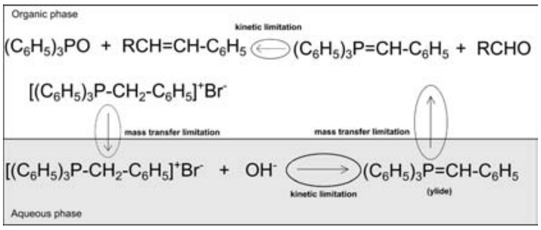

Figure 1. Wittig reaction of BTPP salt and benzaldehyde (mass transfer and kinetic steps).

EXPERIMENTAL SECTION

Materials. Benzyltriphenylphosphonium bromide (96%, Sigma Aldrich), *p*-methoxybenzaldehyde (98%, Sigma Aldrich), *o*-methoxybenzaldehyde (98%, Sigma Aldrich), sodium hydroxide (≥99%, Merck), dichloromethane (≥99.5%, Merck), hydrochloric acid (≥37%, Riedel-de Haen) and deionized water were used.

Batch Experiments. Batch experiments were carried out in a 250-mL glass reactor with four necks, equipped with a reflux condenser, a mechanical stirrer and a digital thermometer. All batch reactor experiments were performed at room temperature and at a stirring rate of 400 rpm. An amount of 0.03 mol of benzyltriphenylphosphonium bromide and equimolar amounts of *p*- and *o*-methoxybenzaldehydes were dissolved in 75 mL of dichloromethane. At vigorous stirring 75 mL of diluted sodium hydroxide was added. During the reaction, the fading of the color of the ylide (ranging from yellow to white) was observed. At a chosen time, 2 mL of sample was taken and put into the extraction sample bottle which contained 2 mL of diluted hydrochloric acid to quench the reaction. The extraction bottle was shaken vigorously for 15 s and then allowed to stand for a few minutes until the separation of organic and aqueous phases was obtained. The aqueous layer was washed with 2 mL of dichloromethane, and the combined organic layers were evaporated and analyzed by ^{1}H NMR.

Microreactor Experiments. Microreactor experiments were carried out in the microtube reactor connected to high-performance syringe pumps (Harvard Apparatus, Holliston, U.S.A.) with perfluoroalkoxy (PFA) tubes (with an internal diameter of 0.75 mm). Syringe pumps ensured highly controllable flow rates.

The reaction in the FEP microtube reactor with an internal diameter of 250 μm was carried out at a slug-flow regime. The organic-phase feed consisted of equimolar amounts (0.4 mol/L) of benzyltriphenylphosphonium bromide and *p*- and *o*-methoxybenzaldehydes dissolved in dichloromethane. The aqueous phase consisted of 1 or 0.1 M aqueous sodium hydroxide solution. The mixing of phases was done in a poly(ether)etherketone (PEEK) T-mixer (Vici AG, Schenkon, Switzerland) with an internal diameter of 250 μm. At the exit of the microtube reactor the reaction was quenched with aqueous hydrochloric acid solution. The resulting mixture was separated, and the aqueous phase was extracted with dichloromethane. The combined organic layers were evaporated and analyzed by ^{1}H NMR. Reactants residence times were determined by the length of the microtube reactor (from 90 cm to 17 m) and the overall flow rate which varied from 50 to 200 μL/min.

Analysis. The conversions of *p*- and *o*-methoxybenzaldehydes in samples were evaluated by ^{1}H NMR spectroscopy (BRUKER DPX 300 NMR). Different proton chemical shifts of MeO-substituent (singlet) for *p*-methoxybenzaldeyde (reactant) and (*Z*)-, (*E*)-1-methoxy-4-styrylbenzene (products) may be observed: (i) (*Z*)-1-methoxy-4-styrylbenzene at 3.77 ppm,[17] (ii) (*E*)-1-methoxy-4-styrylbenzene at 3.84 ppm,[18] (iii) *p*-methoxybenzaldeyde at 3.88 ppm (^{1}H NMR spectra of commercial compound). Similar chemical shifts of ortho MeO-substituents may be observed. The conversion of *p*- and *o*-methoxybenzaldeydes was determined by the surface area ratio between reactants and products MeO-substituens signals, respectively.

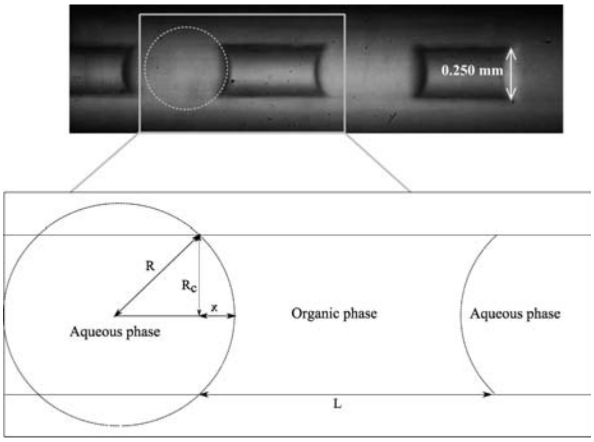

Figure 2. Stable two-phase slug flow with spherical cap-shaped domed ends of the slug in a 250-μm microtube reactor.

Surface, volume, and surface-to-volume ratio of organic phase were determined by microscopic flow imaging. For this purpose ImageJ 1.43u software was used. It may be assumed that the interfacial area between the organic and the aqueous slug, where mass transfer occurs, is limited only on a spherical cap-shaped domed end of the slug (Figure 2). The curved surface area is:

$$S_{\text{int}} = 2\pi Rx \tag{1}$$

The volume of the organic slug is defined as a volume of a cylinder with a subtracted volume of spherical caps:

$$V_{\text{org}} = \pi R_c^2 L - \frac{2\pi x^2(3R - x)}{3} \tag{2}$$

Surface-to-volume ratio is expressed as $S_{\text{int}}/V_{\text{org}}$.

To obtain an overall reaction rate at the chosen conversion of *p*- or *o*-methoxybenzaldehyde, the first derivative of the mathematical function that has the best fit to the experimental data points was calculated. For this purpose OriginPro 8 software was used.

RESULTS AND DISCUSSION

Stable Flow Regime. A microreactor study requires the stability and reproducibility of the specific liquid−liquid two-phase system flow pattern. A stable flow operating regime allows a high degree of control over the liquid−liquid interfacial area. In a microtube reactor, a stable regime is characterized by a reproducible slug flow, which allows a high control over the slug size distribution. To ensure a stable flow regime in a microtube reactor, the flow rate was varied from 50 to 200 μL/min. At this stable flow regime, aqueous-to-organic (AO) phase volumetric flow ratio was varied from 0.5 to 6 when 0.1 M aqueous sodium hydroxide solution was used, and from 0.25 to 2 when 1 M aqueous sodium hydroxide solution was used. At unstable flow

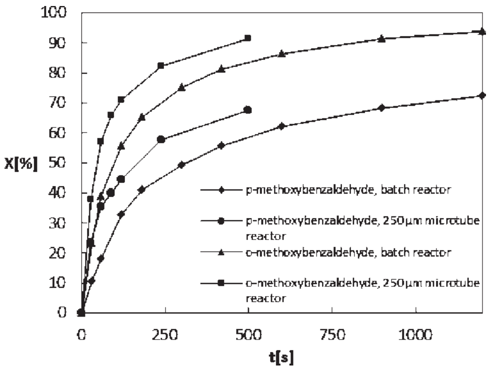

Figure 3. Conversion of *p*- and *o*-methoxybenzaldehydes as a function of residence time (0.1 M aqueous sodium hydroxide solution, flow rate 100 μL/min — microtube reactor, AO = 1).

regime slugs of different lengths without any reproducibility were observed. This became apparent when the flow rates were lower than 50 μL/min and microtube reactors were longer than 2 m, at all mentioned phase volumetric flow ratios. A similar phenomenon was also observed at flow rates higher than 50 μL/min, when the AO volumetric flow ratio was higher than 6. Only the stable regime was used for further investigations.

Batch Reactor versus Continuous Microtube Reactor. Overall rate of PTC reaction is often limited by the rate of catalyst phase transfer, usually from aqueous to organic phase, which depends on interfacial surface between organic and aqueous phases. The stirring of two immiscible phases in conventional batch reactors generates a wide range of drop sizes with diameters varying from tens of micrometers to millimeters. Therefore, the liquid—liquid interfacial surface area varies considerably from one drop to another.[19−21] On the other hand in the case of microtube reactor all slugs are almost of the same length and have defined interfacial surface, furthermore interfacial surface-to-volume ratio is much higher.

To compare the overall reaction rates in the microtube and batch reactors *p*- and *o*-methoxybenzaldehydes were used. The aqueous phase consisted of 0.1 M aqueous sodium hydroxide solution. The flow rate in the microtube reactor was constant (100 μL/min) at an aqueous-to-organic (AO) volumetric flow ratio of 1 (this same AO ratio in the batch reactor was also assured).

Figure 3 shows conversion of both aldehydes as a function of residence time. The overall rate of the chemical reaction of *o*-methoxybenzaldehyde is higher than that of *p*-methoxybenzaldehyde in the batch as well as in the microtube reactor. In the microtube reactor the overall reaction rate at conversion of 40% was calculated to be 0.00335 mol L^{-1} s^{-1} and 0.00063 mol L^{-1} s^{-1} when *o*- and *p*-methoxybenzaldehydes were used, respectively. On the other hand, in the batch reactor the overall reaction rate at the same conversion was calculated to be 0.00161 mol L^{-1} s^{-1} and 0.00049 mol L^{-1} s^{-1} when *o*- and *p*-methoxybenzaldehydes were used, respectively. Moreover, it was also observed that the ortho substituent tends to give a higher proportion of *cis* product than does the para substituent. The *cis*-to-*trans* isomer ratio determined was 1.7 for *p*-methoxybenzaldehyde and 2.4 for *o*-methoxybenzaldehyde.

It may be observed that the overall rate of chemical reaction for both used aldehydes was higher in the microtube than in the batch reactor (values calculated above). At a residence time of 1 min, 35.5% conversion of *p*-methoxybenzaldehyde was achieved in the microtube reactor, compared to only 18% in the batch reactor. To achieve 50% conversion, residence times of 300 and 180 s were needed in the batch reactor and microtube reactor, respectively (Figure 3).

Comparing the respective results obtained in batch and microtube reactors, one may observe that, at the residence time of 1 min, 57.1% conversion of *o*-methoxybenzaldehyde was achieved in the microtube reactor, compared to 39% in the batch reactor. To achieve 90% conversion, residence times of 900 and 500 s were needed in the batch reactor and microtube reactor, respectively (Figure 3). It may be assumed that the overall rate of the chemical reaction was higher in the microtube reactor than in the conventional batch reactor due to the higher surface-to-volume ratio of organic phase and consequently more efficient mass transport through the organic—water interface.

Because of the higher overall chemical reaction rate achieved in the microtube reactor than in the batch reactor for both aldehydes used, and the higher overall chemical reaction rate of *o*- than that of *p*-methoxybenzaldehyde (in the microtube and batch reactor), it may be assumed that, in the investigated liquid—liquid two-phase system, mass transfer and the chemical reaction rate have an effect on the overall rate of the chemical reaction and neither phenomenon may be ignored.

To define qualitatively the effect of process parameters on mass transfer and the overall chemical reaction rate, different flow rates, AO ratios, and concentrations of aqueous sodium hydroxide solution were used.

Table 1. Average surface-to-volume ratio of the organic phase in the microtube reactor at different volumetric aqueous-to-organic (AO) phase flow ratios (0.1 M aqueous sodium hydroxide solution, flow rate 100 μL/min)

AO vol. flow ratio	average org. slug length [μm]	average S/V ratio [m^2/m^3]
0.5	460	6500
1	390	8100
2	280	11 100
6	260	12 100

Influence of Changing AO Ratio in Microtube Reactor. The comparison between the standard batch reactor and the continuous microtube reactor showed the influence of a specific interfacial surface area on the overall rate of a chemical reaction. Therefore, the influence of changing the AO ratio on a specific interfacial surface area and, consequently, its effect on the overall rate of the chemical reaction were studied. Again, *p*-methoxybenzaldehyde and the aqueous phase, consisting of 0.1 M aqueous sodium hydroxide solution, were used. At a constant total flow rate (100 μL/min) AO ratios of 0.5, 1, 2, and 6 were used. To change the AO ratio the flow of one phase was decreased, and the other was increased.

Microscopic flow imaging showed that the average length of the organic slugs decreased from 460 to 260 μm when the AO ratio was increased from 0.5 to 6 (Table 1). Consequently, the average surface-to-volume ratio (of organic phase where reactants are dissolved) increased from 6500 to 12 100 m^2/m^3. The average organic slug length at an AO ratio of 2 (8100 m^2/m^3) is almost 40% higher than at an AO ratio of 1 (11 100 m^2/m^3). It can be seen (Figure 4) that the lengths of the organic phase at AO ratios 2 and 6 are similar (only 8% higher average organic slug

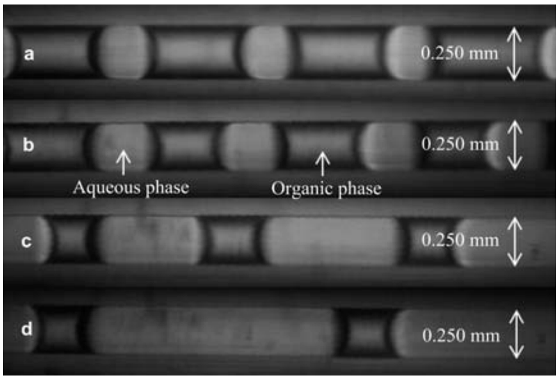

Figure 4. Stable slug-flow regime at different AO ratios: (a) AO = 0.5, (b) AO = 1, (c) AO = 2, (d) AO = 6. (0.1 M aqueous sodium hydroxide solution, flow rate 100 μL/min — microtube reactor).

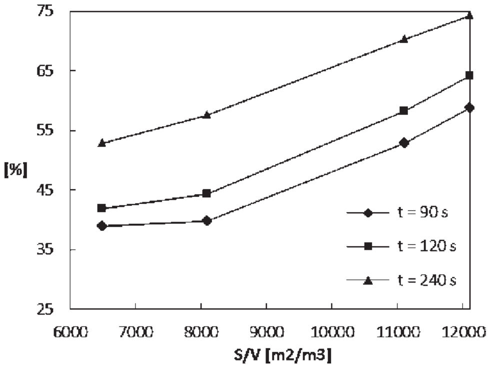

Figure 5. Conversion of *p*-methoxybenzaldehyde as a function of surface-to-volume ratio at different residence times (0.1 M aqueous sodium hydroxide solution, flow rate 100 μL/min).

length and 9% higher average surface-to-volume ratio at AO ratio of 6), while the lengths of aqueous phase increased in size.

In Figure 5 conversion of *p*-methoxybenzaldehyde as a function of surface-to-volume ratio at different residence times is shown. At a residence time of 4 min the conversions of *p*-methoxybenzaldehyde reached 52.8 and 74.2% at surface-to-volume ratios of 6500 and 12 100 m^2/m^3, respectively. Increasing the surface-to-volume ratio results in higher overall reaction rates. At a conversion of 40%, the overall reaction rate was calculated to be 0.00051 mol L^{-1} s^{-1}, 0.00063 mol L^{-1} s^{-1}, 0.00159 mol L^{-1} s^{-1}, and 0.00233 mol L^{-1} s^{-1} at AO ratios 0.5, 1, 2, 6, respectively. That confirms the prediction that the mass transfer has an influence on the overall reaction rate when 0.1 M aqueous sodium hydroxide solution is used.

Influence of Flow Rate. The mass transfer in the slug-flow regime depends on the physical properties of both phases such as viscosity, density and interfacial tension and operating parameters such as flow rates, AO ratio and geometric characteristics of the microchannel. There are two possible mechanisms of mass transfer within the slug or between two consecutive slugs. One is molecular diffusion and second is convection.[22] Molecular diffusion through the interfacial layer occurs because of concentration gradients between adjacent slugs, whereas convection within slugs arises while slugs move through the capillary. The shear between the wall surface and the slug produces internal circulation within the slug. It may be expected that increasing the flow rate will cause an increase in the internal circulation within the slug due to more extensive shear between the wall surface and the slug. However, the convection reduces the thickness of the boundary layer at the phase interface, thereby enhancing diffusive penetration.[23] The mass transfer between two phases therefore strongly depends on the effective interfacial area.

Table 2. Average surface-to-volume ratio of the organic phase in the microtube reactor at different flow rates (0.1 M aqueous sodium hydroxide solution, AO = 1)

flow rate [μL/min]	average org. slug length [μm]	nn.
50	380	8200
100	390	8100
200	380	8200

Two distinct cases of interfacial area are possible inside the hydrophobic microtube: with or without the organic wall film. Due to the superior organic phase wetting properties of the hydrophobic microtube wall material it may be expected that dichloromethane forms a thin organic wall film. In the case of the organic film formation the aqueous phase is not in contact with the microtube wall, and the whole enclosed aqueous slug surface takes part in the mass transfer, thus increasing the mass exchange between two phases.[23,24] The second possibility is that dichloromethane inside the hydrophobic microtube does not form a wall film. In this case the aqueous slug is in contact with the microtube wall, the two-phase interfacial area is reduced, and only domed ends of the slugs take part in the mass transfer.

The wall film thickness can be represented as a function of the capillary number (the ratio of viscous forces and surface tension forces) according to the Bretherton law:[25]

$$h = 1.34 R_c C_a^{2/3} = 1.34 R_c \left(\frac{\mu_{org} v_{slug}}{\gamma} \right)^{2/3} \tag{3}$$

$$C_a = \frac{\mu_{org} v_{slug}}{\gamma} \tag{4}$$

The dependence of flow rate on the organic slug length and surface-to-volume ratio was studied at flow rates 50, 100, and 200 μL/min (slug velocities 17, 34, and 68 mm/s). Capillary radius (R_c) was 125 μm. Again, *p*-methoxybenzaldehyde was used, and the aqueous phase consisted of 0.1 M aqueous sodium hydroxide solution. All experiments were carried out at AO ratio of 1. At these conditions the film thickness was calculated using eq 3 to be 0.7, 1.1, and 1.7 μm at slug velocities 17, 34, and 68 mm/s, respectively. For the calculation of the film thickness, the values of viscosity and interfacial surface tension between the organic and aqueous phases were taken at a temperature of 20 °C (μ_{org} = 0.430 mPa s, $\gamma = 28.3 \times 10^{-3}$ N/m).[26,27]

Microscopic flow imaging showed negligible slug velocity impact on average organic slug length. Slugs were almost of the same lengths and had a defined interfacial surface (Table 2). In Figure 6 conversion of *p*-methoxybenzaldehyde as function of residence time at different flow rates is shown. Although an increase of the overall rate of reaction due to the increase of flow rate was expected, negligible impact was observed. Considering similar average organic slug lengths and similar overall reaction rates at linear velocities of 17, 34, and 68 mm/s, it may be assumed that internal circulation within the slug was not affected by the increase of flow rate.

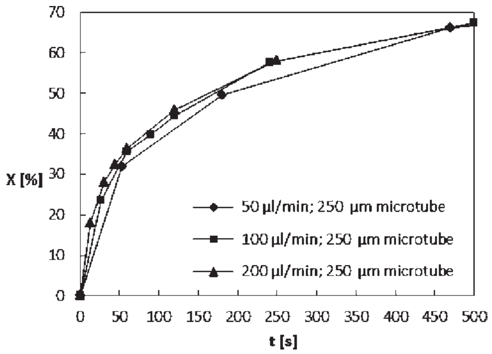

Figure 6. Conversion of *p*-methoxybenzaldehyde as function of residence time at different flow rates (0.1 M aqueous sodium hydroxide solution, AO = 1).

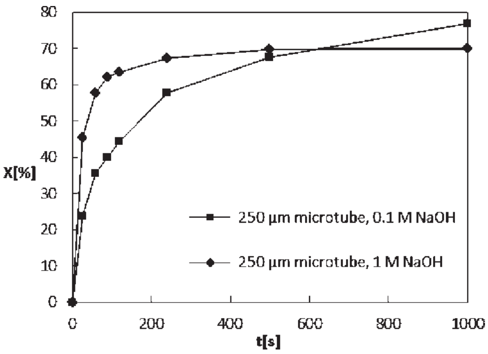

Figure 8. Conversion of *p*-methoxybenzaldehyde as function of residence time at different concentrations of aqueous sodium hydroxide solution (AO = 1, flow rate 100 μL/min).

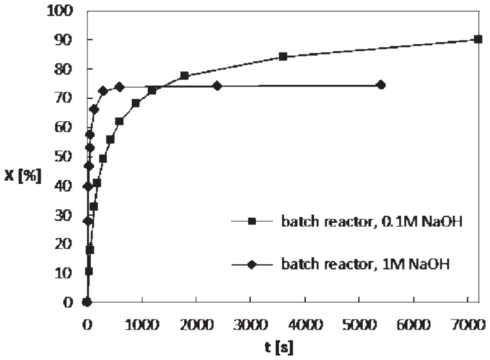

Figure 7. Conversion of *p*-methoxybenzaldehyde as function of residence time at different concentrations of aqueous sodium hydroxide solution (AO = 1).

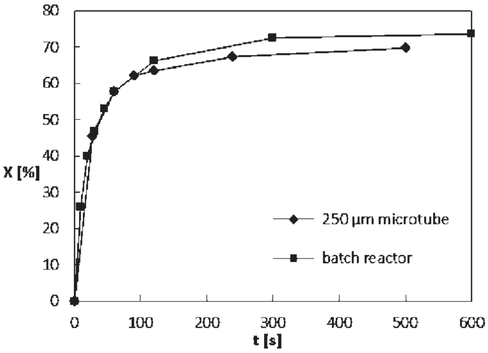

Figure 9. Conversion of *p*-methoxybenzaldehyde as a function of residence time (AO ratio = 1, 1 M aqueous sodium hydroxide solution, flow rate 100 μL/min − microtube reactor).

According to the results we cannot confirm the existence of an organic wall film and its influence on the overall rate of reaction. It may be assumed that mass transfer through the thin organic wall film (calculated using eq 3) may be neglected so that only the domed ends of the slugs take part in the mass transfer through the slug.

Sodium Hydroxide Solution Concentrations. The influence of aqueous sodium hydroxide solution of higher concentration on the overall rate of reaction in microtube and batch reactors at different AO ratios was investigated. In Figure 7 conversion of *p*-methoxybenzaldehyde as a function of residence time at two different concentrations of aqueous sodium hydroxide solution in a batch reactor at an AO ratio of 1 is shown. It was observed that a higher concentration of sodium hydroxide solution results in a higher overall rate of reaction in both the batch (Figure 7) and the microtube reactors (Figure 8). In the batch reactor the overall reaction rate at a conversion of 40% was calculated to be 0.00380 mol L^{-1} s^{-1} and 0.00049 mol L^{-1} s^{-1} when 1 and 0.1 M aqueous sodium hydroxide solutions were used, respectively. On the other hand, in the microtube reactor the overall reaction rate at the same conversion was calculated to be 0.00418 mol L^{-1} s^{-1} and 0.00063 mol L^{-1} s^{-1} when 1 and 0.1 M aqueous sodium hydroxide solution were used, respectively.

It may be seen that lower maximal conversion of *p*-methoxybenzaldehyde at a higher concentration of sodium hydroxide solution was achieved. This phenomenon was noticed in the batch reactor and also the microtube reactor. It may be assumed that the lower maximal conversion of *p*-methoxybenzaldehyde occurs due to the decomposition of the phosphonium salt in a hydroxide medium of higher concentration.[14]

Although the specific interfacial area in the microtube reactor is higher than in the batch reactor, the overall reaction rate at AO ratio of 1 is similar in both systems (Figure 9). It may be assumed that the higher concentration of OH^- ions at the organic−water interface increased mass transport and the higher interfacial area in the microtube reactor does not play a significant role anymore. It may be assumed that reaction kinetics is the rate-limiting step.

To test the influence of surface-to-volume ratio on the overall rate of reaction at 1 M aqueous sodium hydroxide solution, different AO ratios (2, 1, 0.5 and 0.25) in microtube reactor were investigated. Microscopic flow imaging (Figure 10) showed that the average length of the organic slugs decreased from 1500 to 330 μm when the AO ratio was increased from 0.25 to 2 (Table 3). Consequently, the average surface-to-volume ratio (of the organic phase where reactants are dissolved) increased from 1700 to 10 000 m^2/m^3. In Figure 11 the relatively weak influence of an almost 6 times higher average surface-to-volume ratio on the conversion of *p*-methoxybenzaldehyde at the same residence time may be observed. Only a few percent higher conversion of *p*-methoxybenzaldehyde was achieved at a residence time of 90 s when the surface-to-volume ratio was increased from 1700 to 5600 m^2/m^3. It has to be mentioned that, at residence times of 240 and 500 s, the lowest conversion of *p*-methoxybenzaldehyde was achieved at a surface-to-volume

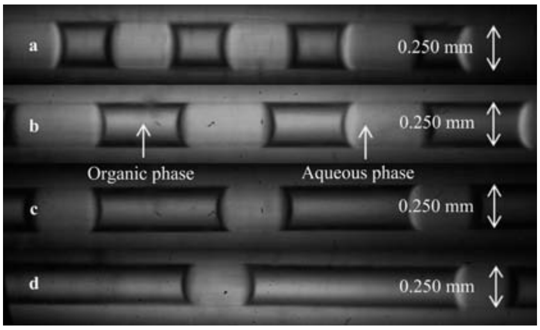

Figure 10. Stable slug-flow regime at different AO ratios: (a) AO = 2, (b) AO = 1, (c) AO= 0.5, (d) AO = 0.25 (1 M aqueous sodium hydroxide solution, flow rate 100 μL/min − microtube reactor).

Table 3. Average surface-to-volume ratio of the organic phase in the microtube reactor at different volumetric aqueous-to-organic (AO) phase flow ratios (1 M aqueous sodium hydroxide solution, flow rate 100 μL/min)

AO volumetric flow ratio	average org. slug length [μm]	average *S*/*V* [m^2/m^3]
0.25	1500	1700
0.5	810	3400
1	520	5600
2	330	10 000

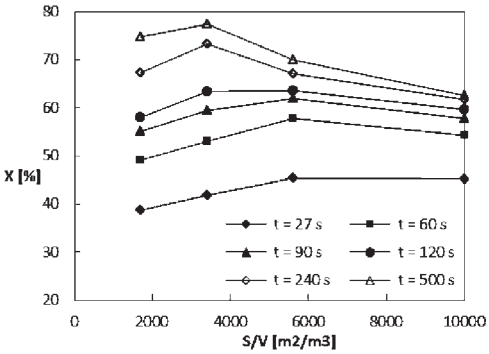

Figure 11. Conversion of *p*-methoxybenzaldehyde as function of surface-to-volume ratio at different residence times (1 M aqueous sodium hydroxide solution, flow rate 100 μL/min).

ratio of 10 000 m^2/m^3 and the highest conversion was achieved at 3000 m^2/m^3. It may be assumed that the decomposition of the phosphonium salt occurs on the organic−water interface where the concentration of OH^- is higher. Increasing the surface-to-volume ratio consequently increases also the rate of phosphonium salt decomposition.

■ CONCLUSIONS

In the present study the two-phase liquid−liquid PTC Wittig reactions of benzyltriphenylphosphonium bromide and *p*- and *o*-methoxybenzaldehydes in an FEP microtube reactor were studied.

In this case, when the mass transfer is the rate-limiting step, the overall rate of chemical reaction in the microtube reactor at slug-flow regime is much higher in comparison to that of the batch reactor due to higher surface-to-volume ratio and consequently more rapid mass transport. In the studied chemical reaction, mass transfer played a significant role when 0.1 M aqueous sodium hydroxide solution was used.

Negligible impact of flow rate on slug lengths, on the interfacial surface between organic and aqueous phase and on the overall rate of reaction was observed. Therefore, internal circulation and consequently mass transport were not affected by the increase in the flow rate. According to the results (microscopic flow imaging and determination of *p*- and *o*-methoxybenzaldehyde conversions with ^{1}H NMR spectroscopy), we cannot confirm the existence of an organic wall film and its influence on the overall rate of reaction.

At higher AO ratios the conversions of *p*- and *o*-methoxybenzaldehydes at constant total flow and the same residence time were increased. Microscopic flow imaging showed that aqueous slugs became longer, whereas the organic slugs decreased in size. Consequently, the specific interfacial area and overall chemical reaction rate increased.

A higher concentration of aqueous sodium hydroxide solution resulted in a higher overall reaction rate but lower maximal conversion that may be explained by the phosphonium salt decomposition in a hydroxide medium of higher concentration. This phenomenon was noticed in the batch reactor and also in the microtube reactor. Although the specific interfacial area in the microtube reactor is higher than in the batch reactor, the overall reaction rate at AO ratio of 1 is similar in both systems. Because of the higher concentration of OH^- ions at the organic−water interface, mass transfer through the interfacial area increases, and higher specific interfacial area in a microtube reactor does not play a significant role anymore. It may be assumed that reaction kinetics is the rate-limiting step. Nevertheless, specific interfacial area still has an influence. Final conversion was lower in the microtube reactor than in batch reactor. Because of the high concentration of OH^- ions at the interfacial area, the decomposition of phosphonium salt was more rapid in the microtube reactor, and final conversion was consequently lower than in the batch reactor. Lower conversion at higher specific interfacial area was confirmed in the microtube reactor at higher AO ratio.

In a two-phase system specific interfacial area is crucial for desired interactions between two phases. Mass transfer between phases and sometimes also the chemical reaction of reactants presented in different media is limited to this area. Known and precisely tuned specific interfacial area enables optimization of a chosen two-phase chemical reaction. A microreactor process with a stable flow pattern and, consequently, a known, specific interfacial area provides a great advantage over the standard batch method. A two-phase system can be more precisely controlled, predicted and finally optimized.

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NOMENCLATURE

Ca	capillary number
h	film thickness [m]
L	length of the organic phase slug [m]
R	radius of the sphere [m]
R_c	capillary radius [m]
S_{int}	interfacial area between organic and aqueous slug [m^2]
t	residence time [s]
V_{org}	volume of the organic slug [m^3]
v_{slug}	slug velocity [m/s]
x	height of the spherical cap [m]
γ	interfacial surface tension between the organic and aqueous phases [N/m]
μ_{org}	viscosity of organic phase [Pa s]

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