University of Groningen

Mass Transfer and Reaction Characteristics of Homogeneously Catalyzed Aerobic Oxidation of 5-Hydroxymethylfurfural in Slug Flow Microreactors

Hommel, Arne; Disselhorst, Bas; Janssens, Minke; Stevelink, Ruben ; Heeres, Hero; Yue, Jun

Published in:
Chemical Engineering Journal

DOI:
[10.1016/j.cej.2020.127552](https://doi.org/10.1016/j.cej.2020.127552)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2021

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Hommel, A., Disselhorst, B., Janssens, M., Stevelink, R., Heeres, H., & Yue, J. (2021). Mass Transfer and Reaction Characteristics of Homogeneously Catalyzed Aerobic Oxidation of 5-Hydroxymethylfurfural in Slug Flow Microreactors. *Chemical Engineering Journal*, 413, [127552].
<https://doi.org/10.1016/j.cej.2020.127552>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Mass transfer and reaction characteristics of homogeneously catalyzed aerobic oxidation of 5-hydroxymethylfurfural in slug flow microreactors

Arne Hommes, Bas Disselhorst, Hermine Minke Margreet Janssens, Ruben Johannes Antonius Stevelink, Hero Jan Heeres, Jun Yue*

Department of Chemical Engineering, Engineering and Technology Institute Groningen, University of Groningen, Nijenborgh 4, 9747 AG Groningen, the Netherlands

ARTICLE INFO

Keywords:

2,5-Diformylfuran
2,5-Furandicarboxylic acid
5-Hydroxymethylfurfural
Co/Mn/Br catalyst
Oxidation
Microreactor

ABSTRACT

Oxidation of 5-hydroxymethylfurfural (HMF) using air or pure oxygen was performed in polytetrafluoroethylene capillary microreactors under gas–liquid slug flow, with Co/Mn/Br as the homogeneous catalyst in the acetic acid solvent. The temperature was varied from 90 to 165 °C at a pressure of 1 or 5 bar. At atmospheric pressure conditions (and 90 °C), acetaldehyde was further added as a co-oxidant to accelerate the reaction. At 150 °C, 5 bar oxygen and a residence time of 2.73 min, an HMF conversion of 99.2% was obtained, with the yields of 2,5-diformylfuran (DFF), 5-formylfurancarboxylic acid (FFCA) and 2,5-furandicarboxylic acid (FDCA) being 22.9%, 46.7%, and 23.8%, respectively. By operation under wetted slug flows and elevated partial oxygen pressures, mass transfer limitations and oxygen depletion in the microreactor could be eliminated. This allowed to run the microreactor under kinetically controlled conditions, where both the HMF consumption and DFF formation were found zero order in partial oxygen pressure and roughly first order in HMF. The total selectivity towards DFF/FFCA/FDCA was ca. 40% at low partial oxygen pressures due to the dominant occurrence of side reactions. By using pure oxygen at 5 bar the total selectivity was improved to 60–94%. The space time yields of DFF and FFCA in the microreactor exceeded those obtained in conventional (semi-)batch reactors at slightly elevated temperatures and pressures, due to the superior mass transfer and higher initial HMF concentrations in the microreactor. For highly efficient FDCA synthesis, more dedicated microreactor operations are needed to tackle its precipitation.

1. Introduction

The depletion of fossil sources urges a switch to renewable feedstocks. Biomass is an abundantly available renewable source of carbon that is essential for the production of fuels and chemicals [1]. In this respect, top value-added biobased platform chemicals have been identified, which can partially replace the existing petroleum-based ones in the chemical industry [2,3]. One typical example is 5-hydroxymethylfurfural (HMF), an easily obtained dehydration product of C₆-sugars derived from lignocellulosic biomass [4]. The oxidation of HMF can produce valuable (intermediate) products such as 2,5-diformylfuran (DFF), 5-formylfurancarboxylic acid (FFCA) and 2,5-furandicarboxylic acid (FDCA). The two reactive aldehyde groups of DFF make it an attractive platform chemical for a variety of applications [5]. It can be converted (e.g., by hydrogenation, oxidation, polymerization, hydrolysis) to phenolic resins, pharmaceutical intermediates, organic

conductors, ligands and polymer building blocks (e.g., for polypinacols and polyvinyls) [4–6]. FDCA is a well-known building block for biobased plastics such as polyethylene furanoate (PEF) [7–9]. PEF is an attractive alternative for the conventional petroleum-based polyethylene terephthalate (PET), commonly used for making beverage bottles. It is worth mentioning that an alternative route for PEF production is via dimethyl-2,5-furandicarboxylate (FDCM), obtained by the oxidative esterification of HMF and methanol [10–15]. FDCM has a lower boiling point than FDCA, and is thus easier retrieved in pure form by e.g., distillation [11]. Although FFCA utilization is not widely reported up to this date, it has potential as a building block to produce chemical intermediates, polymers, fuels and active pharmaceutical ingredients [16].

The HMF oxidation usually starts with the conversion of its alcohol group to an aldehyde, resulting in DFF and H₂O. The aldehyde groups of DFF can be further oxidized to FFCA and finally FDCA. Alternatively,

* Corresponding author.

E-mail address: yue.jun@rug.nl (J. Yue).

<https://doi.org/10.1016/j.cej.2020.127552>

Received 10 July 2020; Received in revised form 22 October 2020; Accepted 25 October 2020

Available online 1 November 2020

1385-8947/© 2020 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

FFCA can be formed from HMF via its oxidation to 5-hydroxymethylfuran-2-carboxylic acid (HMFCFA) first, depending on the catalyst's preference (Scheme 1) [7].

The oxidation of HMF has been examined extensively in the past decades using different catalysts and reactor configurations [4,17]. The majority of these researches focused on the catalytic performance and many recent works reported that HMF could be oxidized rapidly and selectively using heterogeneous (e.g., Au, Pt, Pd and Ru based) catalysts towards DFF [5,18–23], and FDCA [8,24–36]. The high-yield synthesis of FFCA was usually followed by its further oxidation towards FDCA [37–39]. This results in a multi-component mixture where energy-intensive separation procedures may be required to retrieve the pure FFCA product. However, some recent works report the highly selective (>90%) FFCA production from HMF [16,40,41]. Heterogeneous catalysts can selectively catalyze the HMF oxidation under relatively mild conditions and usually do not require additional steps to separate the catalyst from the product mixture (e.g., in a packed bed reactor configuration). Despite this, their use can be less favored due to high costs (especially for noble metals), usually slow reaction rates and the fact that the long-term stability is not widely examined for many catalysts. Furthermore, for the oxidation of HMF specifically, the FDCA product is poorly soluble in water and commonly used organic solvents. Hence its formation can cause catalyst blockage by the precipitation on the active sites [38]. In this case, the heterogeneously catalyzed oxidation of HMF is more technically feasible when low substrate concentrations are used. However, this has a negative effect on the product space time yield. Homogeneous catalysis is considered as a cheap and effective method for the conversion of biomass derivatives to value-added chemicals, despite its separation and reusability issues [42]. Homogeneous metal bromide complexes are widely used catalysts for the aerobic oxidation of hydrocarbons [43]. The industrial oxidation of *p*-xylene to terephthalic acid, a monomer for producing PET, is performed in the Amoco Mid-Century (MC) process using a homogeneous Co/Mn/Br catalyst with acetic acid as the solvent at elevated temperature and pressure conditions (200 °C and 15 bar) [44]. Such metal bromide catalysts in acetic acid are well recyclable in the current industrial process [44]. Metal bromide catalysts are also reported to effectively oxidize HMF towards (mainly) DFF at relatively low temperatures (50–90 °C) [45,46], and towards FFCA/FDCA at higher temperatures and pressures (120–200 °C and 15–70 bar) [47–49]. Co/Mn/Br catalyzed oxidations in acetic acid are free-radical chain reactions, where Co^{3+} (formed with oxygen or a peroxide via the Haber-Weiss cycle) and a bromide ion generate Co^{2+} and a bromine radical ($\text{Br}^\cdot$). This bromine radical then initiates the radicalization of HMF, DFF or FFCA (represented as RH to $\text{R}^\cdot$) along with hydrogen bromide [44].

Scheme 1. Reaction scheme of HMF to its oxidation products: DFF, HMFCFA, FFCA and FDCA. Molecular oxygen or a peroxide (e.g., H_2O_2) is typically used as the oxidant.

Saha et al. [45] performed the Co/Mn/Br (molar ratio of 1/0.075/1 with a 40 mM cobalt concentration) catalyzed oxidation of HMF in acetic acid. By adding 5 wt% trifluoroacetic acid (HTFA) to the reaction mixture, 32% DFF, 31% FFCA and 37% FDCA yields were obtained in 3 h reaction time at atmospheric pressure and 90 °C in a stirred glass flask with a continuous air feed. Without HTFA, solely DFF was formed (96% yield in 4.5 h). It was concluded that HTFA enhanced the reaction rate by forming $\text{Mn}(\text{TFA})_3$ salt with a higher oxidation performance than the $\text{Mn}(\text{AcO})_3$ salt formed in the acetic acid solvent [45]. Partenhimer and Grushin [46] used acetaldehyde as a co-oxidant in the Co/Mn/Br (molar ratio of 1/1/2 with a 26.8 mM Co concentration) catalyzed oxidation of HMF to DFF in acetic acid under mild conditions (75 °C, 1 bar). Air was fed continuously from the bottom of a glass reactor. Approximately 50% DFF yield was obtained in 8 h reaction time and the yield decreased towards 20% after 30 h reaction time, which may be due to the further oxidation towards FFCA/FDCA [46]. Acetaldehyde spontaneously formed peracetic acid in the presence of oxygen at ambient conditions [50], which accelerated the generation of free bromine radicals required for initiating the oxidation of HMF. The same researchers performed the HMF oxidation using the same catalytic system at a slightly elevated temperature in a batch glass autoclave operated at 70 bar [46]. In the absence of acetaldehyde, 63.0% DFF yield was obtained at 75 °C in 2 h and 35.2% FDCA yield at 125 °C in 2 h [46].

ADM patented the Co/Mn/Br catalyzed synthesis of FDCA by the oxidation of HMF in (fed-)batch reactors at elevated temperatures and pressures (160–180 °C, 30–60 bar) [47]. Elevated temperatures are generally used to induce evaporation of the acetic acid solvent in order to effectively regulate the temperature of this exothermic oxidation reaction [51]. Zuo et al. [48] performed the aerobic oxidation of HMF using Co/Mn/Br catalysts at relatively high temperatures and pressures (120–200 °C and 30–60 bar). Optimization studies were done in a semi-batch titanium Parr reactor. Herein, the liquid solution containing HMF was fed gradually to the reactor to prevent an excessive temperature increase by the highly exothermic reaction and O_2 was replenished continuously to compensate for its consumption and to maintain a constant reactor pressure. An FDCA yield of 90% was obtained in 30 min, using a 1/0.015/0.5 M ratio of Co, Mn and Br with 7 vol% water in acetic acid as the solvent at 180 °C and 30 bar (CO_2/O_2 as the gas phase with 1/1 M ratio) [48]. The presence of CO_2 in the gas phase reduced the oxidative decomposition of substrate and solvent towards CO and CO_2 and the formation of other byproducts, therewith increasing the selectivity towards FDCA. In a follow-up study [49], kinetics of the Co/Mn/Br catalyzed HMF oxidation to FDCA was investigated in the same semi-batch reactor. A simplified kinetic description was developed based on the assumed first order rate dependency in HMF and zero order in partial oxygen pressure [49]. Besides using HMF as the substrate, some studies reported the synthesis of FDCA by the Co/Mn/Br catalyzed oxidation of other biomass-derived furans (e.g., 5-methylfurfural, 5-methoxymethylfurfural and 5-acetoxymethylfurfural) [51–53].

In fed-batch reactors the oxidation of HMF towards DFF and FFCA was found limited by the mass transfer of oxygen to the liquid phase [49]. To improve the oxygen mass transfer, a spray oxidizer was used as a means of process intensification [54]. In this reactor tiny liquid droplets are formed, significantly increasing the gas–liquid interfacial area available for mass transfer. Spray processes have shown to be economically feasible for such oxidation reactions [55]. These generally require large amounts of hot recirculating air and thus a large reactor volume, making them especially attractive for large-scale production. Another process intensification method is microreactor technology that might be more suitable for distributed and/or flexible production (on a smaller scale). Continuous flow microreactors are capillary or chip-based reactors with an internal channel diameter of ca. 1 mm or below [56–58]. Microreactors offer several fundamental advantages over traditional reactors, including enhanced heat/mass transfer [59] and relatively easy upscaling by numbering-up [60]. Microreactors are particularly attractive for multiphase (gas–liquid) reactions [61], that are often limited by mass transfer in conventional reactors. Due to their small channel size, an enhanced interfacial area (a) and liquid phase mass transfer coefficient (k_L) are obtained in microreactors [62,63]. Regular multiphase flow patterns (e.g., slug flow) with well-defined hydrodynamics and mass transfer properties are easily generated in microreactors, which provide valuable insights in kinetics and allow for a significant reaction efficiency increase towards improved (space time) yields of the target product [56–58,64,65]. For slug flow processing, it is particularly attractive to generate gas bubbles that are fully surrounded by the liquid (hereafter referred to as wetted slug flow), therewith maximizing the specific gas–liquid interfacial area and thus the mass transfer rate [66–68]. The generation of a wetted slug flow is promoted by a high liquid affinity with the microreactor wall (i.e., characterized by a low contact angle) and operation at relatively high bubble or mixture velocities [68]. The liquid phase aerobic oxidation of hydrocarbons, alcohols and aldehydes has been extensively examined and intensified using microreactors [69–71]. Microreactor operation allows a precise temperature control of such (aerobic) oxidation reactions and enhances safety (additionally due to low inventory and explosion suppression e.g., when using pure O_2) [72]. Very recently, the aerobic oxidation of HMF over heterogeneous catalysts has received research attentions in microreactors [73–76]. A wall-coated tube-in-tube polytetrafluoroethylene (PTFE) microreactor was used for the oxidation of HMF to DFF in dimethyl sulfoxide (DMSO) over a salen-transition metal core-shell ($Fe_3O_4/SiO_2/Mn$) catalyst [74]. Herein, 93% HMF conversion and 84% DFF yield were obtained in 60 min. The oxidation of HMF to DFF, FFCA and FDCA was also reported in a PTFE capillary microreactor packed with TEMPO on silica as the solid catalyst in 1,2-dichloroethane (DCE) with O_2 as the oxidant and HNO_3 as a co-oxidant [75]. High yields of DFF (95% in 2 min) were realized under mild conditions (55 °C and 5 bar O_2). Further increasing the residence time to 8 min yielded ca. 35% FDCA, which resulted in crystal formation due to the low solubility of FDCA in the solvent. Also, the oxidative esterification of HMF and methanol to FDCM using oxygen as the oxidant benefitted from operation in a packed bed microreactor with nitrogen-doped carbon-supported bimetallic Co/Ru as the solid catalyst [76]. In the microreactor the FDCM production rate was found over 15-fold higher than in batch reactors [76].

For the HMF oxidation in microreactors, homogeneous catalysis represents also a feasible option, particularly when aiming for the (well-soluble) DFF/FFCA products. In this work, the homogeneously catalyzed aerobic oxidation of HMF towards DFF, FFCA (and FDCA to a lesser extent) is described for the first time using microreactors. The reaction was performed in PTFE capillary microreactors operated under gas–liquid slug flow, with Co/Mn/Br as the homogeneous catalyst in the acetic acid solvent and air or pure O_2 as the oxidant. Both atmospheric pressure conditions (at 90 °C) in the presence of acetaldehyde as a co-oxidant and at a slightly elevated temperature and pressure (5 bar and up to 165 °C; i.e., above the vapor pressure of acetic acid being 3.5 bar)

without acetaldehyde were investigated. Operating parameters (e.g., the phasic flow rate, gas–liquid flow ratio, microreactor inner diameter and partial oxygen pressure) were varied to reveal mass transfer and reaction characteristics in microreactors. Mass transfer limitations could be diminished by wetted slug flow processing in small inner diameter microreactors and oxygen depletion was prevented by increasing the partial oxygen pressure (e.g., using pure O_2 and/or increasing the pressure to 5 bar). This allowed to investigate the effect of temperature, partial oxygen pressure and initial HMF concentration under the kinetic regime. The intensification potential in the present microreactors was demonstrated by the increased space time yield towards DFF/FFCA as compared with those in (semi- and fed-)batch reactors tested in this work and the literature [45,46,48,49]. An optimization strategy is further proposed to allow for higher space time yields towards DFF/FFCA synthesis in microreactors. For the efficient synthesis of FDCA in microreactors, its precipitation at high yields remains a challenge to tackle.

2. Experimental

2.1. Chemicals

HMF ($\geq 99\%$) was obtained from Ava Biochem BSL AG. DFF (97%), FDCA (97%), 5-acetoxymethylfurfural (AMF; 97%), $Co(OAc)_2$ tetrahydrate (reagent grade), $Mn(OAc)_2$ tetrahydrate ($\geq 99.0\%$), NaBr ($\geq 99.0\%$), 2,4-pentanedione ($\geq 99.5\%$) and acetaldehyde ($\geq 99.5\%$) were obtained from Sigma-Aldrich. FFCA (90.3%) and acetic acid ($\geq 99.5\%$) were obtained from Acros chemicals. Compressed oxygen, nitrogen and air were purchased from Linde gas. Milli-Q water was used for HPLC sample preparation. The homogeneous catalyst complex was prepared at room temperature by dissolving $Co(OAc)_2$, $Mn(OAc)_2$ and NaBr in acetic acid at a molar ratio of 1/1/2 (catalyst mixture 1) or 1/1/3.3 (catalyst mixture 2), both using a cobalt concentration (C_{Co}) of 30 mM. The use of NaBr instead of HBr as a bromine source increases operation safety and minimizes corrosion of the process equipment [44]. The HMF substrate and acetaldehyde co-oxidant (if applicable) were consecutively mixed with the catalyst solution before starting the reaction procedure.

2.2. Microreactor setup and procedure

Experiments were performed in two different setups (i.e., at atmospheric pressure and elevated pressure (5 bar); Fig. 1), similar to those in our previous work [68]. A Hewlett Packard (Agilent series 1100) HPLC pump was used to feed the liquid solution containing the HMF substrate at a certain concentration ($C_{HMF,0} = 70$ –240 mM), acetaldehyde co-oxidant (if present, with a concentration, $C_{AcO,0}$, at 50 mM) and Co/Mn/Br catalyst in the acetic acid solvent. The cobalt concentration ($C_{Co} = 30$ mM) in the liquid feed was in excess (i.e., further increasing the catalyst concentration did not increase the reaction rate) for all experiments to maximize the kinetic performance and increase the selectivity towards DFF/FFCA/FDCA [46,48]. Compressed air or oxygen was fed by a Bronkhorst (High-Tech model F-200 CV) mass flow controller (MFC), through a small-diameter capillary (made of polyether ether ketone (PEEK); inner diameter of 50 μm and length of 20 cm) as the flow restrictor to stabilize the gas flow. Then, the two phases were mixed via a PEEK T-junction (inner diameter: 0.2 mm) to generate a gas–liquid slug flow in the attached PTFE capillary microreactor that was coiled and immersed in an oil bath (90–165 °C). Microreactors with inner diameters (d_C) of 0.5–1.0 mm and lengths (L_C) of 0.5–8.7 m (i.e., the effective length in the oil bath) were used. In experiments performed at room temperature, there was practically no reaction occurrence. As such, the reaction occurrence in the short microreactor sections before and after the oil bath (i.e., almost under room temperature) was expected negligibly low, given the rapid cooling due to the large surface to volume ratio and good air circulation around the setup (cf. Section S7 in

Fig. 1. Schematics of the experimental setup at atmospheric (see the dashed box) and elevated pressures.

the [Supplementary Information](#)).

Two types of experiments were conducted, i.e., one at atmospheric pressure (at the microreactor outlet) and 90 °C, the other at an elevated total pressure (p_{tot}) of 5 bar with temperatures (T) ranging from 90 to 165 °C. For the atmospheric pressure experiments, acetaldehyde was used as a co-oxidant and a 1/1/2 M ratio of Co, Mn and Br (catalyst mixture 1) was used, similar to the conditions used by Partenheimer and Grushin [46]. Liquid samples were collected continuously at the microreactor outlet in an open sampling vial while the gas phase was exhausted to air. Experiments conducted at elevated pressure (5 bar) were performed in the absence of acetaldehyde and a 1/1/3.3 M ratio of Co, Mn and Br (catalyst mixture 2) was used. The catalytic performance is not considerably influenced by the difference in the Co/Mn/Br molar ratios used in this work [44]. This facilitated a comparison with kinetic studies of the HMF oxidation towards DFF, FFCA and FDCA by Zuo *et al.* [49], who used the same catalyst composition. Here, the microreactor outlet was connected to either a waste or sample vessel (depending on the operation sequence) in which the liquid product was accumulated and separated from the gas phase. The gas phase was then exhausted through a back pressure regulator (BPR; Porter model 9000) into the atmosphere. Pressures were measured online with pressure indicators (PI; ESI-TEC of model GS4200-USB) before the flow restrictor and before the BPR. In the experiments, the microreactor was pressurized to the desired pressure beforehand with solely the gas phase before introducing the liquid feed. Liquid product from the microreactor was first led to a waste vessel before a steady state operation was obtained, i.e., after a stable gas–liquid flow profile was established in the PTFE microreactor and subsequently waiting for at least 3 times the residence time in the microreactor. Then, the waste vessel was closed and the microreactor outlet was directed using valves to a replaceable vessel where the liquid sample was collected. In some experiments, a 50 mL syringe was attached to the gas outlet in which a gas sample was collected under steady state conditions (Fig. 1). The gaseous molar composition was then analyzed (i.e., to determine CO/CO₂ formation and/or O₂ depletion; see below).

For each steady state flow operation, photos of the gas–liquid (slug) flow were taken at the microreactor outlet (and at the inlet in some cases) using a digital camera (Nikon D3300) with a Nikon lens (AF-S Micro Nikkor 60 mm f/2.8 G ED). For a better visualization, an LED illuminator (Fiber-Lite MI-LED A2 from Dolan-Jenner Industries) was used as the backlight.

2.3. Analysis

Samples were prepared by mixing 0.2 mL of the obtained acetic acid solution (i.e., the liquid product collected from the microreactor outlet or feed) with an *ex situ* internal standard solution containing 2 mg of 2,4-pentanedione in milli-Q water (1.6 mL). These were analyzed with both the ultraviolet (UV) detector and refractive index detector (RID) by high performance liquid chromatography (HPLC; Agilent 1200 series, Bio-Rad Aminex HPX-87H 300 mm × 7.8 mm column, 60 °C, with 0.5 mM H₂SO₄ as an eluent at a flow rate of 0.55 mL/min). The concentrations of HMF, DFF, FFCA and FDCA in the liquid sample were determined quantitatively by HPLC. Furthermore, traces of HMFCFA could be observed along with traces of side products such as furfural and formic acid. At long HPLC retention times unidentified peaks were detected, probably attributed to high molecular weight components (e.g., HMF dimers/oligomers and humins) [46,48,49]. Based on the analyses, the relative error from experiments performed at least in duplicate is usually within 5–10% and in exceptional cases as high as 20% due to the formation of somewhat unsteady flows (e.g., due to the somewhat significant gas compression by the oxygen depletion).

The molar fraction of O₂ (i.e., when using air as the gas), CO and CO₂ in the gas outlet was measured in some experiments by an offline gas chromatography (Hewlett Packard 5890 Series II) equipped with a thermal conductivity detector with a Porablot Q Al₂O₃/Na₂SO₄ column and a molecular sieve (5A) column. The injector temperature was set at 150 °C and the detector temperature at 90 °C. The oven temperature was kept at 40 °C for 2 min and heated at 20 °C/min to 90 °C and held for 2 min. A reference gas (containing 3% CO and 18% CO₂) and air were used for the calibration of CO/CO₂ and O₂, respectively.

2.4. Definitions

The HMF conversion (X_{HMF}) and the yield towards oxidative derivatives (e.g., DFF, FFCA and FDCA) (Y_i) are based on mol% and determined as follows

$$X_{HMF} = \left(1 - \frac{C_{HMF,1}}{C_{HMF,0}} \right) \times 100\% \quad (5)$$

$$Y_i = \frac{\xi_i C_{i,1}}{C_{HMF,0}} \times 100\% \quad (6)$$

Here C_{HMF} and C_i are the concentrations of HMF and component i (oxidation product of HMF), respectively. The subscripts 0 and 1 denote the microreactor inlet and outlet, respectively. ζ_i is the stoichiometric constant for oxidation products formed from HMF, being 1 for DFF, FFCA and FDCA.

The selectivity towards different oxidative derivatives (σ_i) of HMF is defined as

$$\sigma_i = \frac{Y_i}{X_{HMF}} \times 100\% \quad (7)$$

The total selectivity (σ_P) to the desired oxidation products (i.e., DFF, FFCA and FDCA) is

$$\sigma_P = \sigma_{DFF} + \sigma_{FFCA} + \sigma_{FDCA} \quad (8)$$

The residence time (τ) in the microreactor is defined as

$$\tau = \frac{V_C}{Q_{tot}} = \frac{\frac{\pi}{4}d_C^2 L_C}{Q_G + Q_L} \quad (9)$$

Here V_C is the capillary microreactor volume. Q_{tot} is the sum of the liquid and gas volumetric flow rates (Q_L and Q_G , respectively), based on the temperature and average pressure in the microreactor at the reaction conditions (without considering oxygen consumption; note that pressure drop through the microreactor was negligible (i.e., never exceeding 0.2 bar) under the investigated conditions).

The gas–liquid mixture velocity (U_M) is calculated by

$$U_M = \frac{Q_G + Q_L}{\frac{\pi}{4}d_C^2} \quad (10)$$

The space time yield of component i (STY_i) in the microreactor, based on the liquid volume, is defined as

$$STY_i = \frac{Y_i C_{HMF,0}}{\tau} \quad (11)$$

3. Results and discussion

3.1. Reaction profile and mass balance

Typical reaction profiles for the HMF oxidation in microreactors at different residence times and pressures are depicted in Fig. 2. The values of $Q_{G,0}$, $Q_{L,0}$ and $Q_{tot,0}$ relevant to this figure and elsewhere refer to the gas, liquid and total mixture volumetric flow rates at the microreactor inlet (i.e., at room temperature and local pressure; cf. Fig. 1). It should be noted that here the residence time was adjusted by varying the microreactor length ($L_C = 0.4$ – 5 m) for Fig. 2a and b, or by varying the flow rate ($Q_{tot,0}$) for Fig. 2c. At 1 bar air pressure and 90 °C with 50 mM acetaldehyde as the co-oxidant, ca. 23% HMF conversion with 10% DFF yield was achieved at a residence time of 35 s (Fig. 2a). FFCA was only formed in small quantities (ca. 1% yield) and FDCA was practically not observed. In the absence of acetaldehyde at 90 °C, no HMF conversion and product formation were observed in the microreactor for residence times up to 5 min, showing the slow reaction kinetics under such conditions. Acetaldehyde as a co-oxidant significantly enhances the kinetic rate, as already indicated in the oxidation of hydrocarbons (e.g., *p*-xylene to terephthalic acid and toluene to benzoic acid) [77,78]. Such enhancement has been also proven for the highly selective oxidation of benzyl alcohol to benzaldehyde in the current microreactors using the same catalytic system (see Section S1 in the Supplementary Material). To achieve the considerable HMF conversion and product yields without using acetaldehyde as a co-oxidant, elevated temperatures were required. At 150 °C and 5 bar air pressure, 67.4% HMF conversion,

Fig. 2. Typical reaction profiles of HMF oxidation in a PTFE microreactor at (a) atmospheric and (b-c) elevated pressures. Conditions in (a): $Q_{tot,0} = 3.6$ mL/min, $C_{HMF,0} = 90$ mM, $C_{AcO,0} = 50$ mM, catalyst mixture 1, 90 °C, 1 bar air. Conditions in (b): $Q_{tot,0} = 1.26$ mL/min, $C_{HMF,0} = 120$ mM, catalyst mixture 2, 150 °C, 5 bar air. Common conditions in (a-b): $d_C = 0.8$ mm, $Q_{G,0}/Q_{L,0} = 5$. Conditions in (c): $d_C = 1.0$ mm, $L_C = 8.7$ m, 150 °C, 5 bar O₂, $C_{HMF,0} = 240$ mM, catalyst mixture 2, $Q_{G,0}/Q_{L,0} = 5$. Error bars in (a), (c) and other figures are based on experiments performed at least in duplicate.

13.3% DFF yield and 6.4% FFCA yield were obtained in 44 s in the microreactor (Fig. 2b). Furthermore, 2.5% yield of FDCA was detected. Fig. 2b further shows that at prolonged residence times, the HMF conversion and product yields continued to increase (i.e., in the case of sufficient oxygen available). Yields towards DFF (22.9%), FFCA (46.7%) and FDCA (23.8%) were further improved by using pure oxygen at 5 bar as the gas phase at a prolonged residence time of 2.73 min (Fig. 2c). Once the majority of HMF was converted, the DFF yield decreased due to its further transformation towards FFCA and subsequently FDCA.

Not all consumed HMF was converted towards the desired oxidation products (i.e., DFF, FFCA, FDCA) (Fig. 2). The total selectivity towards DFF, FFCA and FDCA (σ_p) under most conditions is generally in a range of 35–50%. Only at relatively high partial oxygen pressures (i.e., when using pure O₂ at 5 bar), the total selectivity towards DFF, FFCA and FDCA was improved to 60–94% (Fig. 2c), which will be more elaborately discussed in Section 3.3.4. The total formation of the desired oxidation products never resulted in a closed carbon mass balance (cf. Section S2 in the Supplementary Material). From an experiment using nitrogen as the inert gas phase with the setup shown in Fig. 1, no significant decrease in the HMF concentration (<10% at $C_{\text{HMF},0} = 240$ mM; within the experimental uncertainty) was found at 150 °C and residence times up to 2 min, indicating that the thermal decomposition of HMF is negligibly low. This gap in the carbon balance is thus explained by the occurrence of side reactions, which are mainly the over-oxidation of HMF (as well as its derivatives) to CO_x (CO and CO₂) [46,48,49,79], the HMF condensation to dimers, oligomers and humins (e.g., HMF-derived humins have possibly complex polymer structures consisting of multiple furans with alcohol, aldehyde, ketone and acid functional groups [80,81]) and the oxidative ring-opening (Scheme 2) [79]. Typically, the (HMF, DFF, FFCA-derived) intermediates (e.g., furan radicals) can undergo unwanted side reactions, which might cause C–C cleavage to simple furans (e.g., to furfuryl alcohol, furfural, furoic acid or furan; where formic acid is a possible side product), the formation of bromide/alcohol groups on unwanted positions [52] and could eventually lead to an over-oxidation towards CO_x. Also, furan radicals might propagate with HMF (derivatives) to oligomeric radicals, eventually leading to dimers, oligomers or humins by their termination. FDCA is considered relatively stable in the reaction mixture up to temperatures of ca. 180 °C and is thus expected not to decompose into side products under the current experimental conditions [48,49,53,79]. In addition, AMF is reported to form by the esterification of HMF with the acetic acid solvent.

This AMF intermediate can be further converted to DFF, which represents another possible pathway for the HMF oxidation to DFF (Scheme 2) [46,48,49].

The high molecular weight components (e.g., HMF-derived dimers, oligomers and humins) could not be measured quantitatively by HPLC (cf. Fig. S2 in the Supplementary Material) [46,48,49,79]. Maleic and fumaric acids have also been observed as liquid phase side products, which are typically formed via maleic anhydride (a possible oxidation product of the furan radicals) by the oxidative ring opening of HMF (Scheme 2) [79]. These components might also undergo an over-oxidation into CO_x. The furan ring of HMF is more susceptible to oxidative decomposition than the benzylic ring (i.e., furan has a resonance energy of 17 kcal/mol vs. 36 kcal/mol for benzene) [46]. Therefore, the oxidation of HMF to DFF/FFCA/FDCA [46,48,49,79] appears to be less selective than the oxidation of benzyl alcohol to benzaldehyde [46,68,82] and *p*-xylene to terephthalic acid [44], both using a similar Co/Mn/Br catalytic system in acetic acid.

3.2. Microreactor studies at atmospheric pressure

Reactions were firstly conducted in the microreactor at 1 bar air pressure and 90 °C with acetaldehyde as a co-oxidant, in order to screen the reaction conditions and provide insights for further optimization. In this respect, mass transfer limitations should be eliminated as much as possible. Furthermore, the influence of partial oxygen pressure on the reaction performance and on the kinetics was tested. Since the main oxidation product was DFF under these conditions and FFCA/FDCA were formed to a lesser extent (Fig. 2a), the reaction performance is mainly described in terms of the DFF yield (Y_{DFF}) and selectivity (σ_{DFF}).

3.2.1. Mass transfer limitations

The oxidation of HMF was carried out under slug flow in the microreactor at different mixture flow rates ($Q_{\text{tot},0} = 0.3$ –4.8 mL/min) (Fig. 3), where the gas to liquid volumetric flow ratio was kept equal ($Q_{\text{G},0}/Q_{\text{L},0} = 5$). For a given flow rate, the residence time was altered by adjusting the microreactor length. The liquid-side volumetric mass transfer coefficient ($k_L a$) for a gas–liquid slug flow in microreactors is enhanced with increasing superficial/mixture velocities [62,63]. As such, the HMF oxidation will be faster at higher mixture flow rates under mass transfer limited conditions. At relatively high flow rates ($Q_{\text{tot},0} = 1.2$ –4.8 mL/min) and at a certain short residence times (of up to ca. 0.5

Scheme 2. Simplified reaction scheme of the Co/Mn/Br catalyzed HMF oxidation to DFF, FFCA, FDCA and possible side products based on the literature [53,79]. The components within the red dotted box may undergo an over-oxidation to CO_x.

Fig. 3. Influence of the inlet mixture volumetric flow rate ($Q_{tot,0}$) and residence time on (a) the DFF yield and (b) HMF conversion in PTFE microreactors of different lengths. Conditions: $d_C = 0.8$ mm, $L_C = 0.62$ – 10 m, $Q_{G,0}/Q_{L,0} = 5$, $C_{HMF,0} = 90$ mM, $C_{AcO,0} = 50$ mM, catalyst mixture 1, 90 °C, 1 bar air. Lines are for illustrative purposes.

min), the DFF yield (Fig. 3a) and HMF conversion (Fig. 3b) were unaffected by the flow rate, implying that the reaction rate is not considerably limited by mass transfer within this flow range. Thus, under these conditions the HMF conversion and DFF formation were probably governed by kinetics. This kinetic limitation is possibly caused by the relatively slow oxidation rate of the HMF radicals formed, given that the oxidation of acetaldehyde and thus the radical formation are very fast (even at room temperature) [83]. At lower flow rates ($Q_{tot,0} = 0.3$ – 0.6 mL/min), however, the DFF yield and HMF conversion were smaller at a certain residence time, probably due to mass transfer limitations of oxygen towards the liquid phase.

The presence of mass transfer limitations at such low mixture flow rates is further supported by the change in the slug flow profile therein (Fig. 4). At relatively high flow rates ($Q_{tot,0} = 1.2$ – 4.8 mL/min) and thus mixture velocities (Eq. (10)), bubble end caps appeared to have a (more or less) hemispheric shape, suggesting the presence of a complete liquid film around the bubble body (defined as the wetted slug flow; Fig. 4a–c). At relatively low flow rates ($Q_{tot,0} = 0.3$ – 0.6 mL/min), a flattening of the rear end cap of the bubble occurred, implying the (partial) dewetting of the lubricating liquid film (defined as the dewetted slug flow; Fig. 4d and e). This dewetting significantly reduced the reaction rate under mass transfer limited conditions by the lower effective interfacial area [68]. For gas–liquid slug flows operated at relatively low mixture velocities (or more precisely, low bubble velocities (U_B)), the liquid film becomes thinner corresponding with the decreasing capillary number [84]. There is a critical wetting velocity (U_{CW}) over which a fully wetted liquid film is maintained [68,85]. Dewetting takes place when $U_{CW} > U_B \approx U_M$ at very small capillary numbers. For an air–acetic acid slug flow, U_{CW} is ca.

30 mm/s (or ca. 0.9 mL/min) in PTFE microchannels ($d_C = 0.8$ mm, $Q_G/Q_L = 5$) at ambient conditions [68]. This is in agreement with the flow rate range (i.e., between 0.6 and 1.2 mL/min) where a transition between wetted and dewetted slug flows occurred in this work (Fig. 4).

The absence of mass transfer limitations was further confirmed by experiments conducted in a smaller inner diameter capillary microreactor ($d_C = 0.5$ mm) under otherwise similar reaction conditions. The specific interfacial area (a) is known to be higher in smaller diameter microreactors. Hence, under mass transfer limited conditions, an increase in the mixture velocity and/or a decrease in the microreactor diameter would result in an increased reaction rate. The DFF yield was found almost the same for both diameter microreactors at a certain residence time under a wetted slug flow profile, therefore it is concluded that the reaction regarding the DFF formation was conducted in a kinetic regime without mass transfer interference (see Section S3 in the [Supplementary Material](#) for more details).

For each mixture flow rate, the DFF yield increased with the residence time to a maximum of ca. 10% and for higher residence times a lower DFF yield was observed (Fig. 3a). This decrease could be partly attributed to the formation of FFCA, although its yield is low (ca. up to 1.5%). A more plausible explanation is that due to the fixed molar oxygen to HMF ratio, there was limited oxygen available in the microreactor. Once oxygen was depleted, the formed DFF radicals may be terminated towards side products (e.g., oligomers, humins or simple furans) [46], rather than being further oxidized to FFCA. This is supported by the fact that the HMF conversion still increased with increasing residence times (at least up to ca. 7 min; cf. Fig. 3b), accompanied by a decreased selectivity of DFF. This further implies that

Fig. 4. Influence of flow rate on the gas–liquid slug flow profile. Photos of wetted slug flow are shown in (a–c) and dewetted slug flow in (d–e). Other conditions: $d_C = 0.8$ mm, $Q_{G,0}/Q_{L,0} = 5$, $C_{HMF,0} = 90$ mM, $C_{AcO,0} = 50$ mM, catalyst mixture 1, 90 °C, 1 bar air. Flow direction is from left to right.

not all oxygen was effectively utilized in the formation of DFF/FFCA. Oxygen could be also consumed in the oxidation of acetaldehyde, acetic acid solvent [86] and side products derived from HMF. In Fig. 3, an inlet gas–liquid volumetric flow ratio of 5 was used, corresponding to an O_2 to HMF molar ratio of 0.48. The oxygen to HMF ratio could be increased by operation at higher gas to liquid flow ratios, towards achieving higher DFF yields. However, operating under such high flow ratios negatively affected the oxidation rate and thus the space time yield. This was presumably due to the formation of a dewetted slug flow for long bubbles, causing mass transfer limitations by a reduced effective interfacial area (see Section S4 in the [Supplementary Material](#)). A more feasible strategy is to increase the partial oxygen pressure by operation with pure O_2 and/or elevated pressure.

3.2.2. Influence of partial oxygen pressure

The influence of partial oxygen pressure (p_{O_2}) on the reaction characteristics was examined by performing the HMF oxidation under kinetically controlled conditions, (i.e., a wetted slug flow at $Q_{tot,0} = 2.51$ mL/min and $Q_{G,0}/Q_{L,0} = 5$), using pure O_2 ($p_{O_2} = 1$ bar) instead of air ($p_{O_2} \approx 0.21$ bar) as the gas phase (Fig. 5). The residence time was varied by adjusting the microreactor length. This increase in p_{O_2} for a given gas to liquid volumetric flow ratio enhances both the oxygen supply rate towards the liquid phase and the maximum attainable DFF yield in the case of limited oxygen available. Fig. 5a shows that an increase in p_{O_2} did not affect the DFF yield at low residence times (up to ca. 0.5 min). This illustrates the absence of mass transfer limitations and furthermore supports that the formation of DFF from HMF is zero order in oxygen. This zero order dependency is consistent with the previous reports on the Co/Mn/Br catalyzed oxidation of benzyl alcohol to benzaldehyde [68], and the oxidation of *p*-xylene to terephthalic acid using similar metal bromide catalysts in the acetic acid solvent [87]. Also in the previous kinetic studies on the oxidation of HMF, the formation rates of DFF, FFCA and FDCA were assumed zero order in oxygen under elevated pressures ($p_{O_2} = 2.8$ –7.6 bar) [49]. However, Fig. 5a reveals that the FFCA yield was higher at increased p_{O_2} for each residence time. This seems to suggest that the formation of FFCA is positively affected by an increase in p_{O_2} , as also confirmed by the enhanced formation of FFCA (or FDCA) under elevated pressures reported in the literature [48,49]. For more substantiated conclusions, dedicated kinetic studies need to be performed to support (e.g., by the synthesis of FFCA/FDCA using DFF as the substrate).

For experiments performed with air as the gas phase, the DFF yield approached a maximum of ca. 10% in 50 s, after which it dropped to 5.2% in ca. 100 s (Fig. 5a). While in the case of pure O_2 as the gas phase, the DFF yield continued to increase and reached 15.9% in ca. 100 s. In

both cases, the FFCA yield is not considerably affected by such DFF yield change and only increases slightly with the residence time. The HMF conversion increased similarly with the residence time and is not significantly affected by using air or pure O_2 as the gas phase (Fig. 5b). Only at higher residence times (e.g., 50 or 100 s), the HMF conversion is slightly lower with air than pure oxygen as the gas phase. This is possibly due to the actual residence time being somewhat higher in the latter case, given that the oxygen depletion could result in a more significant drop of the actual mixture velocity along the microreactor (as indicated by the more remarkable bubble shrinkage; cf. Section S5 in the [Supplementary Material](#)). In contrast, when using air as the gas phase, such drop in the actual mixture velocity is less significant due to the large presence of inert N_2 in the gas, and thus the actual residence time was less affected. The decrease in the DFF yield when using air as the gas phase, with the HMF conversion and FFCA yield being unaffected, strongly indicates that DFF was converted to not only FFCA (and subsequently FDCA). DFF was also converted to side products (e.g., furan-based oligomers), which may further explain the relatively low selectivity towards the desired oxidation products. The cause for this yield decrease was probably due to oxygen depletion. When most oxygen was consumed, the formation of DFF from HMF stopped, whereas the conversion of DFF (and HMF for that matter) to side products could continue. The occurrence of oxygen depletion was further proved by measuring the relative bubble size shrinkage at the microreactor outlet as compared to the inlet (see details in Section S5 of the [Supplementary Material](#)). From this, the effective oxygen utilization (i.e., oxygen consumed in the production of DFF/FFCA/FDCA) was estimated to be ca. 10–15%.

3.3. Microreactor studies at elevated pressure

The gas pressure was increased (using 5 bar air or oxygen) to enable performing the HMF oxidation at higher temperatures (the boiling point of acetic acid is 118 °C at 1 bar). The kinetic rate is strongly enhanced at increased temperatures, so that the acetaldehyde co-oxidant is no longer required. This results in less oxygen consumption (i.e., in the oxidation of acetaldehyde) and additional costs for these chemicals are avoided. Elevated temperature processing also facilitates the high-yield syntheses of FFCA and FDCA, which typically have slower kinetics than the formation of DFF from HMF [49].

3.3.1. Influence of temperature

The oxidation of HMF was performed under a wetted slug flow in the microreactor at different temperatures (90–165 °C) and a fixed inlet mixture flow rate ($Q_{tot,0} = 1.26$ mL/min and $Q_{G,0}/Q_{L,0} = 5$) and 5 bar air

Fig. 5. Influence of using air or pure O_2 as the oxidant on (a) the DFF and FFCA yields and (b) HMF conversion in the microreactor. Conditions: $Q_{tot,0} = 2.51$ mL/min, $Q_{G,0}/Q_{L,0} = 5$ (under wetted slug flow operation), $L_C = 0.62$ –5 m, $d_C = 0.8$ mm, $C_{HMF,0} = 90$ mM, $C_{AcO,0} = 50$ mM, catalyst mixture 1, 90 °C, 1 bar air or pure O_2 . Note that the actual residence time values may be slightly higher due to the compression of the gas phase by the oxygen consumption.

Fig. 6. Effect of reaction temperature on (a) the HMF conversion and product yields and (b) the corresponding product selectivity. Conditions: $d_C = 0.8$ mm, $L_C = 5$ m, $Q_{tot,0} = 1.26$ mL/min, $\tau = 86$ –100 s, $Q_{G,0}/Q_{L,0} = 5$, $C_{HMF,0} = 240$ mM, catalyst mixture 2, 5 bar air. Lines in (b) are for illustrative purposes.

(Fig. 6). The residence time varied slightly from 86 to 100 s, due to gas expansion at elevated temperatures (i.e., increased Q_G ; cf. Eq. (9)). For relatively low temperatures (90–110 °C), no appreciable HMF conversion and product yields were found (Fig. 6a). Under similar conditions at atmospheric pressure conditions in the presence of acetaldehyde, there was a somewhat considerable reaction occurrence (Fig. 2a). This further proves that acetaldehyde significantly enhanced the overall reaction rate under such conditions. For higher temperatures (130 °C and above), the HMF conversion and product yields increased exponentially. At 130 °C in 92 s, the HMF conversion reached 31.1% and the yields of DFF and FFCA are 11.7% and 1.9%, respectively. At 165 °C in 86 s, the yields of DFF, FFCA and FDCA are 28.3%, 11.2%, and 1.7%, respectively, at an HMF conversion of 85.8%.

The selectivity towards DFF at temperatures between 110 and 150 °C was not significantly affected ($\sigma_{DFF} = 35$ –40%; Fig. 6b). At 165 °C, where the majority of HMF was converted ($X_{HMF} = 85.8\%$) after 86 s, the DFF selectivity dropped slightly. This is because less DFF is typically formed at low HMF concentrations and a somewhat more significant transformation of DFF into among others FFCA occurred. This corresponds to the increasing selectivity towards FFCA (and to a lesser extent, FDCA) for higher temperatures. The reaction temperature seemingly did not have a significant effect on the total selectivity towards DFF/FFCA/FDCA

FDCA ($\sigma_P = 40$ –50%), suggesting that the overall reaction rates for the formation of the target oxidation products (DFF/FFCA/FDCA) and the side products are affected by the temperature to a more or less similar degree. The obtained total selectivity is similar to that in a fed-batch reactor ($\sigma_P = 31.5\%$) in 10 min with the same catalytic system under a slightly higher temperature and pressure (180 °C, 15.8 bar O_2/N_2 at a 0.28/1.3 M ratio) [49]. A strategy to optimize the selectivity towards DFF/FFCA/FDCA is proposed in Section 3.5.

3.3.2. Absence of mass transfer limitations

To investigate mass transfer limitations under the slightly higher temperatures and pressures (150 °C and 5 bar air), the HMF oxidation was performed in microreactors under wetted and dewetted slug flows (Fig. 7). A temperature of 150 °C was chosen, where HMF was not fully converted and sufficient oxygen was available, enabling a sound comparison of the reaction behavior under different conditions. The HMF conversion and DFF/FFCA yields at a certain residence time seem to be only slightly higher under the wetted slug flow pattern as compared with the dewetted slug flow (Fig. 7), whereas the volumetric liquid phase mass transfer coefficient ($k_L a$) under the dewetted slug flow pattern is considerably lower [66–68]. This suggests that mass transfer limitations were (largely) eliminated under such conditions, especially for the

Fig. 7. Influence of residence time for wetted ($Q_{tot,0} = 1.26$ mL/min) and dewetted ($Q_{tot,0} = 0.63$ mL/min) slug flows on (a) the product yields and (b) HMF conversion. (c) Photos of wetted (top) and dewetted (bottom) slug flows. Flow direction is from left to right. Other conditions: $d_C = 0.8$ mm, $L_C = 0.4$ –2.5 m, $Q_{G,0}/Q_{L,0} = 5$, $C_{HMF,0} = 120$ mM, catalyst mixture 2, 150 °C, 5 bar air.

wetted slug flow operation. Note that at the atmospheric pressure conditions (90 °C and 1 bar air; Fig. 3a), significant mass transfer limitations were found present under the dewetted slug flow operation and only absent at higher flow rates at which the wetted slug flow pattern was generated. However, those results were obtained in the presence of acetaldehyde that accelerated the reaction rate (Fig. 3a). The inappreciable presence of mass transfer limitations in both slug flow patterns as revealed in Fig. 7 is thus plausible, since i) the elevated oxygen pressure ($p_{O_2} = 1$ bar) largely increased the mass transfer rate; ii) the absence of acetaldehyde resulted in considerably slower kinetics despite the elevated temperature in use (150 °C). This is also supported by the same range of the HMF conversion and DFF yield under 90 °C with 50 mM acetaldehyde (Fig. 3) as that at 150 °C without acetaldehyde (Fig. 7).

The possible absence of mass transfer limitations under the elevated temperature is corroborated by experiments performed at different gas to liquid flow ratios. For $Q_{G,0}/Q_{L,0}$ ranging from 2.5 to 20, there is no significant difference in the DFF or FFCA yield. Thus, the reaction rate thereof was probably not affected by mass transfer (i.e., under kinetic control; cf. Section S6 in the Supplementary Material). This also indicates that there was enough oxygen available since in the case of

oxygen depletion lower yields would be obtained.

3.3.3. Influence of initial HMF concentration

The initial HMF concentration ($C_{HMF,0}$) was varied under the previously determined kinetically controlled conditions (i.e., under a wetted slug flow and $Q_{G,0}/Q_{L,0} = 5$). The flow conditions were kept unchanged and the residence time was altered by using microreactors of different lengths ($L_C = 0.4$ –5 m; Fig. 8). The HMF conversion was not considerably affected by $C_{HMF,0}$ being changed from 70 to 240 mM (Fig. 8a), implying that the HMF consumption rate is roughly first order in the HMF substrate. At relatively low residence times (up to ca. 30 s), the DFF/FFCA yields were not much influenced by changes in $C_{HMF,0}$ (Fig. 8b and c), indicating a first order substrate dependency on their respective formation rates. This first order dependency is in line with previous reports on the homogeneous Co/Mn/Br catalyzed oxidation reactions (e.g., the oxidation of benzyl alcohol to benzaldehyde [68], and *p*-xylene to terephthalic acid [87]). At longer residence times (30–90 s), the DFF yield dropped for $C_{HMF,0} = 70$ mM (Fig. 8b), whereas for higher $C_{HMF,0}$ values it kept rising. This is probably because the majority of HMF was already consumed at such long residence times in

Fig. 8. Influence of the initial HMF concentration on (a) the HMF conversion, (b and c) product yield and (d and e) selectivity for different residence times. Conditions: $d_C = 0.8$ mm, $L_C = 0.4$ –5 m, $Q_{tot,0} = 1.26$ mL/min, $Q_{G,0}/Q_{L,0} = 5$, catalyst mixture 2, 150 °C, 5 bar air.

the former case (Fig. 8a), which caused the formation of DFF to end while it was still further converted towards FFCA/FDCA. The reduced DFF formation also resulted in less FFCA being formed (Fig. 8c). FDCA was not formed in significant amounts for all conditions and is thus not depicted in Fig. 8.

Fine details of Fig. 8a reveal a somewhat higher HMF conversion at a given residence time for $C_{HMF,0} = 70$ mM compared to higher initial HMF concentrations, incurring a lower selectivity towards DFF and FFCA (Fig. 8d and e). This suggests that side reactions (i.e., the over-oxidation to e.g., CO_x and/or the formation of HMF dimers, oligomers, humins and simple furans; Scheme 2) are less accelerated than the preferred oxidation reaction at relatively high HMF concentrations. Since the formation rate of DFF/FFCA and the HMF consumption rate appear to be roughly first order in HMF, it is speculated that the reaction order of the most prevalent side reaction(s) is probably (slightly below) first order in HMF, an aspect that deserves further research. Partenhimer and Grushin [46] also observed a slightly higher selectivity towards DFF when using a higher initial HMF concentration (i.e., 67.5% DFF yield at 1.12 M vs. 61.6% yield at 0.375 M) after 2 h reaction time in a batch autoclave using Co/Mn/Br/Zr catalyst at 70 bar air and 75 °C [46]. However, more dedicated experiments focusing on the influence of the initial HMF concentration were not performed.

From the preliminary kinetic experiments in the microreactor operated under a wetted slug flow at 5 bar air or O_2 and 90–150 °C (Figs. 2b–c and 6–8), a simplified kinetic description was developed based on a first order in the HMF substrate and zero order in the partial oxygen pressure (cf. Section S7 in the Supplementary Material). At 150 °C and pure O_2 as the oxidant, the kinetic constants for the conversion of HMF to DFF ($k_1 = 1.62 \text{ min}^{-1}$), DFF to FFCA ($k_2 = 0.68 \text{ min}^{-1}$), FFCA to FDCA ($k_3 = 0.31 \text{ min}^{-1}$) and the formation of total side products from HMF ($k_5 = 0.49 \text{ min}^{-1}$) were roughly determined. Since there are limited data at different temperatures using pure O_2 as the oxidant, experiments with air (Fig. 6a) were used for a rough estimation of the activation energy ($E_a = 64 \text{ kJ/mol}$) and pre-exponential factor ($A = 5.8 \times 10^7 \text{ min}^{-1}$) for the overall HMF consumption. Given no significant effect of the temperature on the total selectivity of the desired oxidation products (Fig. 6b), the overall HMF oxidation rate to DFF/FFCA/FDCA and that to side products seem to be affected in a similar degree (i.e., for temperatures between 90 and 150 °C).

These roughly estimated kinetic parameters were used to calculate the Hatta number (Ha) which for a (0,1)-th order reaction is defined as

$$Ha = \sqrt{\frac{2D_{O_2}k_{OV}C_{HMF}}{k_L^2C_{O_2,LL}}} \quad (12)$$

where D_{O_2} is the diffusion coefficient of oxygen in acetic acid, k_{OV} is the kinetic constant for the overall HMF consumption, $C_{O_2,LL}$ is the liquid phase oxygen concentration at the gas–liquid interface, ζ_{HMF} is the stoichiometric constant of HMF (assumed to be roughly 0.5 as in most cases DFF is the major oxidation product) and k_L is the liquid phase mass transfer coefficient. The low Ha values (<2.5 or 1.25 when using air or pure oxygen as the gas phase; cf. Section S7 in the Supplementary Material) further support our previous assumption that mass transfer limitations were (largely) absent at least in the wetted slug flow operated at the elevated pressure (5 bar air or O_2 ; cf. Figs. 2b–c and 6–8).

The kinetic estimation here also allowed to perform a simplified energy balance analysis over the current microreactor system. The results further verify that the reactor could be considered nearly isothermal (cf. Section S7 in the Supplementary Material for more discussions and calculation details), despite the strongly exothermic nature of the reaction (e.g., reaction enthalpies of the HMF oxidation towards DFF, FDCA and CO_2 have been computed or measured to be -232.4 , -869.9 and -2781.2 kJ/mol , respectively [88]).

3.3.4. Further selectivity improvement by pure oxygen operation

The selectivities towards DFF and FFCA were calculated to be in the

range of 20–45% and 5–15%, respectively, under the above investigated conditions in the microreactor (i.e., 90–165 °C, 1–5 bar air or 1 bar pure O_2 ; cf. Figs. 3 and 5–8). These are on the same order of magnitude as those reported in a semi-batch reactor at atmospheric pressure and 75 °C with acetaldehyde as a co-oxidant ($\sigma_{DFF} = 42\text{--}63\%$) [46] and in the semi-batch reactor used in this work ($\sigma_{DFF} = 35\text{--}45\%$ at 50–90 °C and 1 bar air; cf. Section S8 in the Supplementary Material). The similar selectivity level obtained in the semi-batch reactor (under severe mass transfer limitations) as compared with microreactors (without mass transfer limitations) shows that such limitations did not significantly affect the selectivity (cf. Fig. S14b in the Supplementary Material), suggesting that the reaction mechanism is not (much) changed by the oxygen supply rate within these reaction conditions.

By operating at elevated partial oxygen pressures (p_{O_2}) in fed-batch reactors, a higher selectivity towards DFF/FFCA/FDCA was obtained [49]. At 15.5 bar ($p_{O_2} = 2.8$ bar) and 180 °C, the respective yields towards DFF, FFCA and FDCA are 6.6%, 19.4% and 5.5% after 10 min reaction time. This corresponds to a total product selectivity (σ_P) of 31.5% (Eq. (8)), which is in a similar value range as that obtained in the current microreactor ($\sigma_P = 35\text{--}50\%$). Further increasing p_{O_2} to 4.1 bar in the fed-batch reactor under otherwise the same conditions resulted in significantly higher yields and selectivity ($\sigma_P = 81.0\%$; DFF, FFCA and FDCA yields at 2.5%, 22.3% and 55.9%, respectively) [49]. At even higher p_{O_2} (5.5–7.6 bar), FDCA appeared as the main product ($Y_{FDCA} = 92.9\%$) [49].

In an attempt to improve selectivity towards the desired oxidation products, experiments were conducted at 150 °C with pure O_2 at relatively high partial oxygen pressures in the microreactor ($p_{O_2} = 5$ bar; Fig. 2c). To further increase the product yield, a larger volume PTFE microreactor ($d_C = 1.0 \text{ mm}$ and $L_C = 8.7 \text{ m}$) was used that enabled wetted slug flow operation at higher residence times. Additionally, the CO/CO_2 concentrations in the gas outlet were measured to gain additional insights into the reaction behavior (Fig. 9b). The HMF conversion at a certain residence time was not significantly affected when using air (Fig. 8a) or pure O_2 as the gas phase (Fig. 2c). This further confirms the zero-order dependency of the HMF consumption rate on the oxygen concentration, as also observed in atmospheric pressure experiments (Section 3.2.2). Remarkably, the yields towards DFF, FFCA and FDCA at a given residence time are considerably higher with pure O_2 than air as the gas phase at 5 bar (Fig. 2c, 8b and 8c). This also led to a higher total selectivity towards DFF/FFCA/FDCA ($\sigma_P = 60\text{--}94\%$) in the present case using relatively high partial oxygen pressures (Fig. 9a), which corresponds with fed-batch results reported in the literature [49]. The low selectivity at lower partial oxygen pressures was explained by the slow oxygen supply rate, which promoted the occurrence of unwanted side reactions [49]. However, under low partial oxygen pressures in this work the total selectivity was similar when the reaction was operated under (severely) mass transfer limited conditions (e.g., in a semi-batch reactor) or in the kinetic regime (cf. Fig. 9a and Section S8 in the Supplementary Material). It appears thus that the oxygen supply rate (within the partial oxygen pressure range of $p_{O_2} = 0.21\text{--}1.05$ bar) accelerates both the desired and side reactions at a similar rate. Hence, the increased total selectivity at elevated partial oxygen pressures might be better explained by mechanistic/kinetic effects (see below).

The CO_x formation is lower than 0.1 mol/mol HMF for all experiments in Fig. 9b, which shows that this is not a significantly formed side product (cf. Section S2 in the Supplementary Material). With 5 bar pure O_2 as the gas phase, the CO_x content at the gas outlet was higher than with air, while the HMF conversion was almost the same. This implies that the over-oxidation towards CO_x therein is more prevalent with pure oxygen (while the selectivity towards DFF/FFCA/FDCA is higher). This further confirms that substrate over-oxidation towards CO_x is not the main reason for the gap in the carbon mass balance.

The majority of side products are thus present in the liquid phase, possibly as dimers/oligomers, humins and simple furans (Scheme 2) [48,49,79]. The reaction mixture at the reactor outlet was much darker

Fig. 9. Influence of residence time on (a) the total selectivity towards DFF, FFCA and FDCA (σ_p) and (b) CO/CO₂ formation when using pure O₂ or air as the gas phase in the microreactor. Conditions: $d_c = 1.0$ mm, $L_c = 8.7$ m, 150 °C, 5 bar, $C_{HMF,0} = 240$ mM, catalyst mixture 2, $Q_{G,0}/Q_{L,0} = 5$.

with air as the gas phase than in the case with pure O₂, which is a strong indication of a higher concentration of oligomeric/polymeric furan components. These side products are thus formed more extensively at relatively low partial oxygen pressures. From a mechanistic perspective, a competition might exist between the HMF degradation to (oligomeric) side products and its oxidation to the desired products, in which the reaction preference is affected by the liquid phase oxygen concentration (and thus p_{O_2} [89]). In other words, once HMF is radicalized, O₂ is required to form the desired oxidation products. If the liquid concentration of O₂ is too low (i.e., at $p_{O_2} = 1.05$ bar and 150 °C the oxygen solubility in acetic acid is 9.1 mol/m³ [68,89]), oxidation reactions may be less favored and HMF radicals may react with other components (e.g., towards HMF dimers, oligomers and humins) or break down into e.g., simple furans to a relatively large extent (Scheme 2).

3.4. Intensification potential in microreactors

Despite the relatively low yield obtained towards FDCA (up to 23.8%) in this work, the current microreactor system illustrates its intensification potential to produce DFF and FFCA given the possibility of eliminating mass transfer limitations and short residence time operation (i.e., in a few minutes). The space time yield (STY) is a good indicator for this intensification potential as well as the industrial feasibility of a process (for better conclusions on the techno-economic feasibility of microreactor processes other aspects such as numbering-up should also be assessed). An increased STY requires less space for a given production capacity and thus reduces the required capital expenditure (CapEx) of a process. Values of STY for DFF, FFCA and FDCA based on the liquid volume in the microreactor were determined by Eq. (11) and compared with those estimated from the literature work in Table 1 [45,46,48,49], which also includes the additional experiments in semi-batch reactors conducted in this work (cf. Section S8 in the Supplementary Material) for a better comparison.

At atmospheric pressure and 90 °C, STY_{DFF} in the microreactor (10.3 mol m⁻³ min⁻¹ with air as the oxidant (entry 5) or 13.7 mol m⁻³ min⁻¹ with pure oxygen as the oxidant (entry 6)) far exceeded that in the semi-batch reactor (0.24 mol m⁻³ min⁻¹; entry 4) under otherwise similar reaction conditions. It should be noted that semi-batch experiments performed in this work were under (severely) mass transfer limited conditions due to the non-optimized gas–liquid distribution resulting in a relatively low specific interfacial area (cf. Section S8 in the Supplementary Material). For a better comparison with batch reactors, an oxidation reactor may be used. Herein, oxidation reactions can be performed without dilution while avoiding the generation of any dangerous explosive gas mixture [90]. STY_{DFF} in the microreactor is much higher than that obtained in a semi-batch reactor under the same reaction conditions and a 1/0.075/1 M ratio of Co, Mn and Br (entry 1) [45]. It is also ca. 15 times higher than the literature value obtained in a semi-

batch reactor at a slightly lower temperature (75 °C), but higher initial HMF concentration (806 mM; entry 2) [46]. It is ca. 3 times higher than in a batch autoclave operated at a much higher pressure (70 bar and 75 °C; entry 3) [46]. This indicates that even at relatively mild reaction conditions (i.e., 90 °C and below) with acetaldehyde as the co-oxidant, the HMF oxidation can be intensified via microreactor operation by the improved gas–liquid mass transfer therein.

The best microreactor results of this work were achieved at 150 °C and 5 bar pure O₂ and a residence time of 2.73 min, where yields towards DFF, FFCA and FDCA are 22.9%, 46.7%, and 23.8%, respectively, at an HMF conversion of 99.2% (Fig. 2c). The corresponding space time yields towards DFF, FFCA and FDCA are 20.1, 41.1, 20.9 mol m⁻³ min⁻¹, respectively (Table 1, entry 11). Despite the relatively low FDCA yield, STY_{FDCA} in the microreactor is ca. two times higher than that reported in a fed-batch reactor (i.e., being 11.3 mol m⁻³ min⁻¹; entry 7) operated at a higher temperature and pressure (180 °C and 30 bar O₂/CO₂ of a 1/1 M ratio). Herein, the liquid was fed to the initial reaction phase and the gas phase was replenished continuously to maintain a constant reactor pressure. However, STY calculations in these fed-batch reactors were based on the final reaction time ($t = 10$ –30 min) when HMF was already fully converted [48,49]. This is also the case for entry 10, where an 82.4% FDCA yield was obtained after 20 min operation at 160 °C and 15 bar air [79], corresponding to an STY_{FDCA} of 13.7 mol m⁻³ min⁻¹. Another study from the same group reported 86.5% FDCA yield at 140 °C, 10 bar air and $C_{HMF,0}/C_{Co} = 8.6$ [53], however, the total reaction time was not specified so that STY_{FDCA} could not be determined. A more appropriate comparison is at lower residence times, where FFCA (i.e., 45.8% yield in 1 min; entry 8) was the predominant product in the fed-batch reactor. In such case an STY_{DFF} of 19.8 mol m⁻³ min⁻¹ and an STY_{FFCA} of 27.9 mol m⁻³ min⁻¹ were obtained at 170 °C and 15.5 bar O₂/N₂ (at a 0.55/1 M ratio; entry 7) [49]. These STY values for DFF and FFCA are still lower than those in the microreactor (entry 11), despite the higher temperature and pressure employed in the former case. This is mainly due to a lower HMF feed concentration and a lower reaction rate limited by mass transfer in these batch reactors. A best STY_{FDCA} of 27.6 mol m⁻³ min⁻¹ was obtained in the fed-batch reactor (i.e., 90.7% FDCA yield in 2 min at 170 °C and 15.5 bar O₂/N₂ (entry 9) [49]. In the current microreactor, STY_{FDCA} is slightly lower since the yield of FDCA is not significant, indicating further room for improvement. This gives even more potential for process intensification in microreactors if the FDCA precipitation can be prevented or the formation of solids is handled accordingly (cf. Section 3.5), which may eventually lead to a high STY_{FDCA} at prolonged residence times. Besides mass transfer effects, the enhanced heat transfer in the microreactor should be noted. Despite the high exothermicity of the HMF oxidation [88], a tight temperature control is maintained in microreactors due to the excellent heat transfer therein [59], and the reaction operation in the current microreactor system can thus be considered almost isothermal (cf. Section S7 in the

Table 1
Comparison of space time yields with different reactor configurations on the Co/Mn/Br catalyzed HMF oxidation in an acetic acid solvent.

Entry	Reactor	Co/Mn/Br molar ratio	C _{Co} (mM)	C _{HMF,0} (mM)	C _{HMF,0} /C _{Co} (–)	Gas phase	P _{tot} (bar)	T (°C)	X _{HMF} (%)	Y _{DFF} (%)	Y _{FFCA} (%)	Y _{FDCA} (%)	Y _P (%)	t or τ (min)	STY ^d (mol m ^{−3} min ^{−1})			Reference
															DFF	FFCA	FDCA	
1	SB	1/0.075/1	40	240	6.0	Air	1	90	100	32	31	37	100	180	0.43	0.41	0.49	1.33 [45]
2	SB	1/1/2	27.3	806	29.5	Air	1	75	97	52			52	430	0.97			0.97 [46]
3	Batch	1/1/2	6.82	1120	164	Air	70	75	74	49.9			49.9	120	4.66			4.66 [46]
4	SB	1/1/2	30	180	6.0	Air	1	90	85	29.8	6.9		36.7	120	0.24	0.06		0.30 This work
5	MR	1/1/2	30	90	3.0	Air	1	90	26.4	9.9	0.9		10.8	0.87	10.3	0.9		11.2 This work
6	MR	1/1/2	30	90	3.0	O ₂	1	90	39.5	12.7	2.8		15.5	0.83	13.7	3.0		16.7 This work
7	FB	1/0.015/0.5	62.9 ^b	377 ^b	6.0	O ₂ /CO ₂ (1/1) ^c	30	180	>99			90	90	30		11.3		11.3 [48]
8	FB	1/1/3.3	13.4 ^b	60.8 ^b	4.5	O ₂ /N ₂ (0.55/1) ^c	15.5	170	>99	32.6	45.8	16.4	94.8	1	19.8	27.9	9.97	57.7 [49]
9	FB	1/1/3.3	13.4 ^b	60.8 ^b	4.5	O ₂ /N ₂ (0.55/1) ^c	15.5	170	>99			90.7	90.7	2		27.6		27.6 [49]
10	FB	10/1/10	64.3	333 ^b	5.2	Air	15	160	>99			82.4	82.4	20				13.7 [79]
11	MR	1/1/3.3	30	240	8.0	O ₂	5	150	99.2	22.9	46.7	23.8	93.4	2.73	20.1	41.1	20.9	82.1 This work

Other notes: In entry 1, 5 wt% HTFA was added to the reaction mixture. Acetaldehyde was added (0.5–1 M) in entries 2–3, 230 mM in entry 4 and 50 mM in entries 5–6. In entry 7, the solvent contained 7 vol% water. ^a SB, FB and MR in the column represent the semi-batch, fed-batch reactor and PTFE microreactor ($d_c = 0.8$ mm in entries 5–6 and 1.0 mm in entry 11), respectively.

^b C_{Co} and C_{HMF,0} for entries 7–10 are based on the total liquid volume (i.e., after the liquid feeding was stopped). HMF (13.2 mmol in 5 mL) was fed at 0.25 mL/min in 30 mL acetic acid for entry 7 and HMF (2.25 mmol in 2.5 mL) at 5 mL/min in 34.5 mL acetic acid for entries 8–9. In entry 10, the air feed rate was 5 L/min and the HMF feed rate was 0.85 g/min.

^c Ratio in brackets means the molar ratio.

^d The space time yield in the (semi- or fed-) batch reactors is determined by $STY_i = Y(N_{HMF,0}/(V_L t))$, where $N_{HMF,0}$ is the initial amount of moles of HMF, V_L is the total liquid volume in the reactor and t is the reaction time. The space time yield in the microreactor is calculated by Eq. (11).

^e STY of all the desired oxidation products (DFF/FFCA/FDCA).

Supplementary Material). In larger-scale (fed- or semi-)batch reactors, however, local hot spots may be formed resulting in an inhomogeneous temperature distribution in the reactor. As such, the actual (average) temperature in such reactors may be higher than the reported values, which may have increased product yields due to the faster reaction at elevated temperatures if selectivity is not much affected. However, when an excessive temperature rise is generated by hotspots, the product yield might decrease by the significant decomposition of the target oxidation products. In the semi-batch experiments of this work (cf. Section S8 of the Supplementary Material), the reaction rate was very low. As such, the temperature increase by the exothermic reaction is probably negligible there.

3.5. Microreactor optimization strategy

This work provides a rich information on mass transfer and reaction characteristics for the HMF oxidation in microreactors. Although the current preliminary results have highlighted the promising intensification potential for conducting this reaction in microreactors, flow and reaction conditions should be further optimized for the enhanced DFF/FFCA (and potentially FDCA) formation in high yields, though challenges remain for FDCA synthesis (see below).

Mass transfer limitations can be minimized in the microreactor by avoiding dewetted slug flow operation so that a superior interfacial area is ensured, allowing to run the reaction (largely) under kinetic control. Acetic acid is marginally wetted on PTFE (with a static contact angle of ca. 41°) [68]. This implies that U_{CW} for this system is relatively high and an improved wettability may result in wetted slug flow under a wider range of flow conditions. In other words, more hydrophilic microreactor materials on which acetic acid has a lower contact angle (e.g., glass, fused silica, stainless steel) may be more appropriate than PTFE when using acetic acid as the solvent. However, PTFE has advantages in terms of flexibility (e.g., more easily coiled than glass) and transparency that allows for visualizing multiphase flow profiles (e.g., in contrast to stainless steel). To prevent the film dewetting in PTFE microreactors, a sufficiently high mixture velocity (i.e., higher than U_{CW}) should be used [68]. Longer residence times, required to obtain higher DFF/FFCA yields, can then be realized by increasing the microreactor length.

The inclusion of HTFA in the liquid phase significantly accelerated the FDCA formation in semi-batch reactors [45]. Also, the addition of CO₂ in the gas phase reduced substrate burning and therewith improved the selectivity of the reaction [48]. Such alternative reaction conditions might also be used in microreactors for a further optimization of the HMF oxidation to DFF/FFCA/FDCA. Moreover, in this research an excess of catalyst was used in all microreactor experiments. To increase the feasibility of the Co/Mn/Br catalyzed oxidation of HMF in microreactors, optimization studies in catalyst utilization should be performed and a better understanding of the influence of catalyst concentration on reaction characteristics is required, which is part of our ongoing work. For more detailed studies on the effect of catalyst concentration and composition we refer to other works [46,48,49,79].

With pure O₂ at 5 bar as the oxidant, the highest FDCA yield of 23.8% was obtained in 2.73 min (Fig. 2c). By operating for >10 min under such conditions the microreactor tended to malfunction due to clogging of the PTFE capillary. This was probably caused by the excessive formation of FDCA, leading to its precipitation (given the poor FDCA solubility in the acetic acid solvent) and risks of solid accumulation to block the microchannel. For the high-yield FDCA synthesis (without using impractically low HMF feed concentrations), proper solid handling methods need to be implemented (e.g., via the in-situ integration of ultrasonic treatment with microreactor processing or the addition of an inert carrier phase to prevent solid contact with the wall) and their effectiveness needs to be well examined [91]. Alternatively, solvents in which FDCA has a higher solubility than acetic acid (e.g., methanol) [92,93] could be used to reduce precipitation and thus facilitate its production in microreactors [73]. However, such solvent might not be compatible with the Co/Mn/

Br catalysts [43] and requires the use of other (homogeneous) catalytic systems. In summary, the current microreactor system is well suited for the enhanced synthesis of DFF and FFCA which have a (much) higher solubility than FDCA in the acetic acid solvent. However, for industrial feasibility, the catalyst recycling and product purification require more dedicated research work. For highly efficient FDCA synthesis, more dedicated microreactor operations are still needed to address the above-mentioned challenges.

4. Conclusions

The homogeneously catalyzed aerobic oxidation of HMF to DFF, FFCA and (to a lesser extent) FDCA was performed for the first time in microreactors. The reaction was operated under gas–liquid slug flow in PTFE capillaries with Co/Mn/Br catalyst in the acetic acid solvent and air or pure oxygen as the oxidant. Under atmospheric conditions (at 90 °C with acetaldehyde as a co-oxidant), mass transfer limitations in the oxidation of HMF towards DFF could be eliminated in the microreactor by operating under wetted slug flows that were typically obtained at relatively high mixture velocities. To reduce the oxygen depletion, the molar oxygen to HMF ratio was increased by using pure O₂ as the gas phase or operating at elevated air pressures. Executing the reaction at a slightly elevated pressure (5 bar) additionally allowed operation at higher reaction temperatures (up to 165 °C) to enhance the kinetics for obtaining significant product yields without the need of acetaldehyde as a co-oxidant. Respective yields of 22.9%, 46.7%, and 23.8% towards DFF, FFCA and FDCA at an HMF conversion of 99.2% were obtained at a residence time of 2.73 min at 150 °C and 5 bar in the microreactor with pure O₂ as the gas phase.

Given no significant influence of the partial oxygen pressure (by using air or pure oxygen as the gas phase at 1 bar and 90 °C) on the HMF conversion and DFF yield for a given residence time, their respective consumption and formation rates are considered zero order in oxygen. Under slightly higher temperatures and pressures (5 bar air and 150 °C) without acetaldehyde, mass transfer limitations were (largely) diminished, given the presence of only a minor improvement in the reaction performance under wetted slug flows compared with the dewetted slug flow operation under otherwise similar conditions. By varying the initial HMF concentration under such conditions, a roughly first order dependency of the HMF consumption and DFF/FFCA formation in HMF was observed. The selectivities are ca. 30–40% towards DFF and 5–15% towards FFCA in most experiments (i.e., at low partial oxygen pressures), however, when using pure oxygen at 5 bar the total selectivity towards DFF/FFCA/FDCA was further improved to 60–94%.

The space time yields towards DFF and FFCA in the microreactor exceeded those in fed-batch reactors from the literature, despite more elevated temperatures and pressures used in the latter [48,49]. This is primarily attributed to diminishing mass transfer limitations in the microreactor, illustrating it to be a potential process intensification tool. Under such conditions the efficient production of FDCA in microreactors might also be possible, however, more dedicated operations are needed to overcome the challenge of handling its precipitation in flow.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

This work was financially supported by the University of Groningen (startup package in the area of green chemistry and technology for Jun Yue).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.cej.2020.127552>.

References

- [1] A. Corma, S. Iborra, A. Velty, Chemical routes for the transformation of biomass into chemicals, *Chem. Rev.* 107 (2007) 2411–2502, <https://doi.org/10.1021/cr050989d>.
- [2] T. Werpy, G. Petersen, Top value added chemicals from biomass: volume I - Results of screening for potential candidates from sugars and synthesis gas, No. DOE/GO 102004-1992. National Renewable Energy Lab., Golden, CO (US), 2004. doi: 10.2172/15008859.
- [3] I. Delidovich, P.J.C. Hausoul, L. Deng, R. Pfützenreuter, M. Rose, R. Palkovits, Alternative monomers based on lignocellulose and their use for polymer production, *Chem. Rev.* 116 (2016) 1540–1599, <https://doi.org/10.1021/acs.chemrev.5b00354>.
- [4] R.J. van Putten, J.C. van der Waal, E. de Jong, C.B. Rasrendra, H.J. Heeres, J.G. de Vries, Hydroxymethylfurfural, a versatile platform chemical made from renewable resources, *Chem. Rev.* 113 (2013) 1499–1597, <https://doi.org/10.1021/cr300182k>.
- [5] M. Sajid, X. Zhao, D. Liu, Production of 2,5-furandicarboxylic acid (FDCA) from 5-hydroxymethylfurfural (HMF): Recent progress focusing on the chemical-catalytic routes, *Green Chem.* 20 (2018) 5427–5453, <https://doi.org/10.1039/c8gc02680g>.
- [6] M. Cui, R. Huang, W. Qi, R. Su, Z. He, Synthesis of 2,5-diformylfuran from 5-hydroxymethylfurfural in ethyl acetate using 4-acetamido-TEMPO as a recyclable catalyst, *Catal. Today*. 319 (2019) 121–127, <https://doi.org/10.1016/j.cattod.2018.03.054>.
- [7] T. Xiang, X. Liu, P. Yi, M. Guo, Y. Chen, C. Wesdemiotis, J. Xu, Y. Pang, Schiff base polymers derived from 2,5-diformylfuran, *Polym. Int.* 62 (2013) 1517–1523, <https://doi.org/10.1002/pi.4452>.
- [8] Z. Zhang, K. Deng, Recent advances in the catalytic synthesis of 2,5-furandicarboxylic acid and its derivatives, *ACS Catal.* 5 (2015) 6529–6544, <https://doi.org/10.1021/acscatal.5b01491>.
- [9] M. Vannini, P. Marchese, A. Celli, C. Lorenzetti, Fully biobased poly(propylene 2,5-furandicarboxylate) for packaging applications: excellent barrier properties as a function of crystallinity, *Green Chem.* 17 (2015) 4162–4166, <https://doi.org/10.1039/c5gc00991j>.
- [10] Y. Sun, H. Ma, X. Jia, J. Ma, Y. Luo, J. Gao, J. Xu, A high-performance base-metal approach for the oxidative esterification of 5-hydroxymethylfurfural, *ChemCatChem*. 8 (2016) 2907–2911, <https://doi.org/10.1002/cctc.201600484>.
- [11] F. Li, X.L. Li, C. Li, J. Shi, Y. Fu, Aerobic oxidative esterification of 5-hydroxymethylfurfural to dimethyl furan-2,5-dicarboxylate by using homogeneous and heterogeneous PdCoBi/C catalysts under atmospheric oxygen, *Green Chem.* 20 (2018) 3050–3058, <https://doi.org/10.1039/c8gc01393d>.
- [12] A. Salazar, P. Hünemörder, J. Rabeah, A. Quade, R.V. Jagadeesh, E. Mejia, Synergetic bimetallic oxidative esterification of 5-hydroxymethylfurfural under mild conditions, *ACS Sustain. Chem. Eng.* 7 (2019) 12061–12068, <https://doi.org/10.1021/acssuschemeng.9b00914>.
- [13] F. Menegazzo, M. Signoretti, D. Marchese, F. Pinna, M. Manzoli, Structure-activity relationships of Au/ZrO₂ catalysts for 5-hydroxymethylfurfural oxidative esterification: Effects of zirconia sulphation on gold dispersion, position and shape, *J. Catal.* 326 (2015) 1–8, <https://doi.org/10.1016/j.jcat.2015.03.006>.
- [14] O. Casanova, S. Iborra, A. Corma, Biomass into chemicals: One pot-base free oxidative esterification of 5-hydroxymethyl-2-furfural into 2,5-dimethylfuroate with gold on nanoparticulated ceria, *J. Catal.* 265 (2009) 109–116, <https://doi.org/10.1016/j.jcat.2009.04.019>.
- [15] J. Deng, H.J. Song, M.S. Cui, Y.P. Du, Y. Fu, Aerobic oxidation of hydroxymethylfurfural and furfural by using heterogeneous Co₃O₄-N/C catalysts, *ChemSusChem*. 7 (2014) 3334–3340, <https://doi.org/10.1002/cssc.201402843>.
- [16] C. Zhang, X. Chang, L. Zhu, Q. Xing, S. You, W. Qi, R. Su, Z. He, Highly efficient and selective production of FFCA from CoTA-TJ102 laccase-catalyzed oxidation of 5-HMF, *Int. J. Biol. Macromol.* 128 (2019) 132–139, <https://doi.org/10.1016/j.ijbiomac.2019.01.104>.
- [17] Z. Zhang, G.W. Huber, Catalytic oxidation of carbohydrates into organic acids and furan chemicals, *Chem. Soc. Rev.* 47 (2018) 1351–1390, <https://doi.org/10.1039/C7CS00213K>.
- [18] J. Nie, J. Xie, H. Liu, Efficient aerobic oxidation of 5-hydroxymethylfurfural to 2,5-diformylfuran on supported Ru catalysts, *J. Catal.* 301 (2013) 83–91, <https://doi.org/10.1016/j.jcat.2013.01.007>.
- [19] J. Artz, S. Mallmann, R. Palkovits, Selective aerobic oxidation of HMF to 2,5-diformylfuran on covalent triazine frameworks-supported Ru catalysts, *ChemSusChem*. 8 (2015) 772–789, <https://doi.org/10.1002/cssc.201403078>.
- [20] K. Ghosh, R.A. Molla, M.A. Iqbal, S.S. Islam, S.M. Islam, Ruthenium nanoparticles supported on N-containing mesoporous polymer catalyzed aerobic oxidation of biomass-derived 5-hydroxymethylfurfural (HMF) to 2,5-diformylfuran (DFF), *Appl. Catal. A Gen.* 520 (2016) 44–52, <https://doi.org/10.1016/j.apcata.2016.03.035>.
- [21] R. Fang, R. Luque, Y. Li, Selective aerobic oxidation of biomass-derived HMF to 2,5-diformylfuran using a MOF-derived magnetic hollow Fe-Co nanocatalyst, *Green Chem.* 18 (2016) 3152–3157, <https://doi.org/10.1039/c5gc03051j>.
- [22] F. Neatu, N. Petrea, R. Petre, V. Somoghi, M. Florea, V.I. Parvulescu, Oxidation of 5-hydroxymethyl furfural to 2,5-diformylfuran in aqueous media over

- heterogeneous manganese based catalysts, *Catal. Today*. 278 (2016) 66–73, <https://doi.org/10.1016/j.cattod.2016.03.031>.
- [23] Y. Yan, K. Li, J. Zhao, W. Cai, Y. Yang, J.M. Lee, Nanobelt-arrayed vanadium oxide hierarchical microspheres as catalysts for selective oxidation of 5-hydroxymethylfurfural toward 2,5-diformylfuran, *Appl. Catal. B Environ.* 207 (2017) 358–365, <https://doi.org/10.1016/j.apcatb.2017.02.035>.
- [24] T. Pasini, M. Piccinini, M. Blosi, R. Bonelli, S. Albonetti, N. Dimitratos, J.A. Lopez-Sanchez, M. Sankar, Q. He, C.J. Kiely, G.J. Hutchings, F. Cavani, Selective oxidation of 5-hydroxymethyl-2-furfural using supported gold-copper nanoparticles, *Green Chem.* 13 (2011) 2091–2099, <https://doi.org/10.1039/c1gc15355b>.
- [25] J. Artz, R. Palkovits, Base-free aqueous-phase oxidation of 5-hydroxymethylfurfural over ruthenium catalysts supported on covalent triazine frameworks, *ChemSusChem*. 8 (2015) 3832–3838, <https://doi.org/10.1002/cssc.201501106>.
- [26] Y. Wang, K. Yu, D. Lei, W. Si, Y. Feng, L.L. Lou, S. Liu, Basicity-tuned hydrotalcite-supported Pd catalysts for aerobic oxidation of 5-hydroxymethyl-2-furfural under mild conditions, *ACS Sustain. Chem. Eng.* 4 (2016) 4752–4761, <https://doi.org/10.1021/acssuschemeng.6b00965>.
- [27] X. Tong, L. Yu, H. Chen, X. Zhuang, S. Liao, H. Cui, Highly efficient and selective oxidation of 5-hydroxymethylfurfural by molecular oxygen in the presence of Cu-MnO₂ catalyst, *Catal. Commun.* 90 (2017) 91–94, <https://doi.org/10.1016/j.cattom.2016.11.024>.
- [28] Z. Gui, W. Cao, S. Saravanamurugan, A. Riisager, L. Chen, Z. Qi, Efficient aerobic oxidation of 5-hydroxymethylfurfural in aqueous media with Au–Pd supported on zinc hydroxycarbonate, *ChemCatChem*. 8 (2016) 3636–3643, <https://doi.org/10.1002/cssc.201600852>.
- [29] K.R. Vuyyuru, P. Strasser, Oxidation of biomass derived 5-hydroxymethylfurfural using heterogeneous and electrochemical catalysis, *Catal. Today*. 195 (2012) 144–154, <https://doi.org/10.1016/j.cattod.2012.05.008>.
- [30] B. Liu, Y. Ren, Z. Zhang, Aerobic oxidation of 5-hydroxymethylfurfural into 2,5-furandicarboxylic acid in water under mild conditions, *Green Chem.* 17 (2015) 1610–1617, <https://doi.org/10.1039/C4GC02019G>.
- [31] Y.Y. Gorbanev, S. Kegnæs, A. Riisager, Selective aerobic oxidation of 5-hydroxymethylfurfural in water over solid ruthenium hydroxide catalysts with magnesium-based supports, *Catal. Lett.* 141 (2011) 1752–1760, <https://doi.org/10.1007/s10562-011-0707-y>.
- [32] L. Ardemani, G. Gibin, A.J. Dent, M.A. Isaacs, G. Kyriakou, A.F. Lee, C.M.A. Parlett, S.A. Parry, K. Wilson, Solid base catalysed 5-HMF oxidation to 2,5-FDCA over Au/hydrotalcites: fact or fiction? *Chem. Sci.* 6 (2015) 4940–4945, <https://doi.org/10.1039/c5sc00854a>.
- [33] H.A. Rass, N. Essayem, M. Besson, Selective aerobic oxidation of 5-HMF into 2,5-furandicarboxylic acid with Pt catalysts supported on TiO₂- and ZrO₂-based supports, *ChemSusChem*. 8 (2015) 1206–1217, <https://doi.org/10.1002/cssc.201403390>.
- [34] F. Neațu, R.S. Marin, M. Florea, N. Petrea, O.D. Pavel, V.I. Părvulescu, Selective oxidation of 5-hydroxymethylfurfural over non-precious metal heterogeneous catalysts, *Appl. Catal. B Environ.* 180 (2016) 751–757, <https://doi.org/10.1016/j.apcatb.2015.07.043>.
- [35] D.K. Mishra, H.J. Lee, J. Kim, H.S. Lee, J.K. Cho, Y.W. Suh, Y. Yi, Y.J. Kim, MnCo₂O₄ spinel supported ruthenium catalyst for air-oxidation of HMF to FDCA under aqueous phase and base-free conditions, *Green Chem.* 19 (2017) 1619–1623, <https://doi.org/10.1039/c7gc00027h>.
- [36] G. Yi, S.P. Teong, Y. Zhang, Base-free conversion of 5-hydroxymethylfurfural to 2,5-furandicarboxylic acid over a Ru/C catalyst, *Green Chem.* 18 (2016) 979–983, <https://doi.org/10.1039/c5gc01584g>.
- [37] Z.-W. Mei, L.-J. Ma, H. Kawafuchi, T. Okihara, T. Inokuchi, TEMPO-mediated oxidation of primary alcohols to carboxylic acids by exploitation of ethers in an aqueous-organic biphasic system, *Bull. Chem. Soc. Jpn.* 82 (2009) 1000–1002, <https://doi.org/10.1246/bcsj.82.1000>.
- [38] M.A. Lilga, R.T. Hallen, M. Gray, Production of oxidized derivatives of 5-hydroxymethylfurfural (HMF), *Top. Catal.* 53 (2010) 1264–1269, <https://doi.org/10.1007/s11244-010-9579-4>.
- [39] H.A. Rass, N. Essayem, M. Besson, Selective aqueous phase oxidation of 5-hydroxymethylfurfural to 2,5-furandicarboxylic acid over Pt/C catalysts: Influence of the base and effect of bismuth promotion, *Green Chem.* 15 (2013) 2240, <https://doi.org/10.1039/c3gc40727f>.
- [40] M. Ventura, M. Aresta, A. Dibenedetto, Selective aerobic oxidation of 5-(hydroxymethyl)furfural to 5-formyl-2-furancarboxylic acid in water, *ChemSusChem*. 9 (2016) 1096–1100, <https://doi.org/10.1002/cssc.201600060>.
- [41] M. Ventura, F. Lobefaro, E. de Giglio, M. Distaso, F. Nocito, A. Dibenedetto, Selective aerobic oxidation of 5-hydroxymethylfurfural to 2,5-diformylfuran or 2-formyl-5-furancarboxylic acid in water by using MgO-CeO₂ mixed oxides as catalysts, *ChemSusChem*. 11 (2018) 1305–1315, <https://doi.org/10.1002/cssc.201800334>.
- [42] P.J. Deuss, K. Barta, J.G. de Vries, Homogeneous catalysis for the conversion of biomass and biomass-derived platform chemicals, *Catal. Sci. Technol.* 4 (2014) 1174–1196, <https://doi.org/10.1039/c3cy01058a>.
- [43] W. Partenheimer, Methodology and scope of metal/bromide autoxidation of hydrocarbons, *Catal. Today*. 23 (1995) 69–158, [https://doi.org/10.1016/0920-5861\(94\)00138-R](https://doi.org/10.1016/0920-5861(94)00138-R).
- [44] R.A.F. Tomás, J.C.M. Bordado, J.F.P. Gomes, p-xylene oxidation to terephthalic acid: A literature review oriented toward process optimization and development, *Chem. Rev.* 113 (2013) 7421–7469, <https://doi.org/10.1021/cr300298j>.
- [45] B. Saha, S. Dutta, M.M. Abu-Omar, Aerobic oxidation of 5-hydroxymethylfurfural with homogeneous and nanoparticulate catalysts, *Catal. Sci. Technol.* 2 (2012) 79–81, <https://doi.org/10.1039/c1cy00321f>.
- [46] W. Partenheimer, V.V. Grushin, Synthesis of 2,5-diformylfuran and furan-2,5-dicarboxylic acid by catalytic air-oxidation of 5-hydroxymethylfurfural. Unexpectedly selective aerobic oxidation of benzyl alcohol to benzaldehyde with metal/bromide catalysts, *Adv. Synth. Catal.* 343 (2001) 102–111, [https://doi.org/10.1002/1615-4169\(20010129\)343:1<102::AID-ADSC102>3.0.CO;2-Q](https://doi.org/10.1002/1615-4169(20010129)343:1<102::AID-ADSC102>3.0.CO;2-Q).
- [47] A. Sanborn, Oxidation of furfural compounds, US Patent No. 8,558,018, 2013.
- [48] X. Zuo, P. Venkatasubramanian, D.H. Busch, B. Subramaniam, Optimization of Co/Mn/Br-catalyzed oxidation of 5-hydroxymethylfurfural to enhance 2,5-furandicarboxylic acid yield and minimize substrate burning, *ACS Sustain. Chem. Eng.* 4 (2016) 3659–3668, <https://doi.org/10.1021/acssuschemeng.6b00174>.
- [49] X. Zuo, A.S. Chaudhari, K. Snavely, F. Niu, H. Zhu, K.J. Martin, B. Subramaniam, Kinetics of homogeneous 5-hydroxymethylfurfural oxidation to 2,5-furandicarboxylic acid with Co/Mn/Br catalyst, *AIChE J.* 63 (2017) 162–171, <https://doi.org/10.1002/aic.15497>.
- [50] C.E.H. Bawn, J.B. Williamson, The oxidation of acetaldehyde in solution. Part I. The chemistry of the intermediate stages, *Trans. Faraday Soc.* 47 (1951) 721–734, <https://doi.org/10.1039/TF9514700721>.
- [51] J.C. van der Waal, E. Mazoyer, H.J. Baars, G.J.M. Gruter, From terephthalic acid to 2,5-furandicarboxylic acid: An industrial perspective, in: *Liquid phase aerobic oxidation catalysis: Industrial applications and academic perspectives*, John Wiley & Sons, 2016, pp. 311–329. doi:10.1002/9783527690121.ch19.
- [52] H. Ban, S. Chen, Y. Zhang, Y. Cheng, L. Wang, X. Li, Kinetics and mechanism of catalytic oxidation of 5-methylfurfural to 2,5-furandicarboxylic acid with Co/Mn/Br catalyst, *Ind. Eng. Chem. Res.* 58 (2019) 19009–19021, <https://doi.org/10.1021/acs.iecr.9b03573>.
- [53] H. Ban, Y. Zhang, S. Chen, Y. Cheng, T. Pan, L. Wang, X. Li, Production of 2,5-furandicarboxylic acid by optimization of oxidation of 5-methylfurfural over homogeneous Co/Mn/Br catalysts, *ACS Sustain. Chem. Eng.* 8 (2020) 8011–8023, <https://doi.org/10.1021/acssuschemeng.0c02574>.
- [54] B. Subramaniam, X. Zuo, D.H. Busch, P. Venkatasubramanian, Spray oxidation process for producing 2,5-furandicarboxylic acid from hydroxymethylfurfural, US Patent No. 9,586,923B2, 2017.
- [55] M. Li, T. Ruddy, D. Fahey, D.H. Busch, B. Subramaniam, Terephthalic acid production via greener spray process: Comparative economic and environmental impact assessments with Mid-Century process, *ACS Sustain. Chem. Eng.* 2 (2014) 823–835, <https://doi.org/10.1021/sc4004778>.
- [56] K. Jähnisch, V. Hessel, H. Löwe, M. Baerns, Chemistry in microstructured reactors, *Angew. Chemie - Int. Ed.* 43 (2004) 406–446, <https://doi.org/10.1002/anie.200300577>.
- [57] K.F. Jensen, Flow chemistry - Microreaction technology comes of age, *AIChE J.* 63 (2017) 858–869, <https://doi.org/10.1002/aic.15642>.
- [58] J. Yue, Multiphase flow processing in microreactors combined with heterogeneous catalysis for efficient and sustainable chemical synthesis, *Catal. Today*. 308 (2018) 3–19, <https://doi.org/10.1016/j.cattod.2017.09.041>.
- [59] E. Mielke, P. Plouffe, N. Koushik, M. Eyholzer, N. Kockmann, A. Macchi, D.M. Roberge, Local and overall heat transfer of exothermic reactions in microreactor systems, *React. Chem. Eng.* 2 (2017) 763–775, <https://doi.org/10.1039/c7re00085e>.
- [60] D.M. Roberge, M. Gottsponer, M. Eyholzer, N. Kockmann, Industrial design, scale-up, and use of microreactors, *Chim. Oggi*. 27 (2009) 8–11.
- [61] J.R. Burns, C. Ramshaw, The intensification of rapid reactions in multiphase systems using slug flow in capillaries, *Lab Chip*. 1 (2001) 10–15.
- [62] J. Yue, G. Chen, Q. Yuan, L. Luo, Y. Gonthier, Hydrodynamics and mass transfer characteristics in gas-liquid flow through a rectangular microchannel, *Chem. Eng. Sci.* 62 (2007) 2096–2108, <https://doi.org/10.1016/j.ces.2006.12.057>.
- [63] P. Sobieszuk, J. Aubin, R. Pohorecki, Hydrodynamics and mass transfer in gas-liquid flows in microreactors, *Chem. Eng. Technol.* 35 (2012) 1346–1358, <https://doi.org/10.1002/ceat.201100643>.
- [64] A. Günther, K.F. Jensen, Multiphase microfluidics: From flow characteristics to chemical and materials synthesis, *Lab Chip*. 6 (2006) 1487–1503, <https://doi.org/10.1039/b609851g>.
- [65] L. Amini-Rentsch, E. Vanoli, S. Richard-Bildstein, R. Marti, G. Vilé, A novel and efficient continuous-flow route to prepare trifluoromethylated N-fused heterocycles for drug discovery and pharmaceutical manufacturing, *Ind. Eng. Chem. Res.* 58 (2019) 10164–10171, <https://doi.org/10.1021/acs.iecr.9b01906>.
- [66] K. Hecht, G. Fröhlich, P. Pfeifer, R. Dittmeyer, B. Kraushaar-Czarnetzki, The influence of surface properties on chemical reaction in multiphase flow in capillaries, *Chem. Eng. J.* 225 (2013) 837–847, <https://doi.org/10.1016/j.cej.2012.11.092>.
- [67] X. Wang, Y. Yong, C. Yang, Z.S. Mao, D. Li, Investigation on pressure drop characteristic and mass transfer performance of gas-liquid flow in micro-channels, *Microfluid. Nanofluidics*. 16 (2014) 413–423, <https://doi.org/10.1007/s10404-013-1226-5>.
- [68] A. Hommes, B. Disselhorst, J. Yue, Aerobic oxidation of benzyl alcohol in a slug flow microreactor: Influence of liquid film wetting on mass transfer, *AIChE J.* 66 (2020), e17005, <https://doi.org/10.1002/aic.17005>.
- [69] H. Pennemann, G. Kolb, Review: Microstructured reactors as efficient tool for the operation of selective oxidation reactions, *Catal. Today*. 278 (2016) 3–21, <https://doi.org/10.1016/j.cattod.2016.04.032>.
- [70] H.P.L. Gemoets, Y. Su, M. Shang, V. Hessel, R. Luque, T. Noël, Liquid phase oxidation chemistry in continuous-flow microreactors, *Chem. Soc. Rev.* 45 (2016) 83–117, <https://doi.org/10.1039/c5cs00447k>.
- [71] A. Gavrilidis, A. Constantinou, K. Hellgardt, K.K.M. Hii, G.J. Hutchings, G.L. Brett, S. Kuhn, S.P. Marsden, Aerobic oxidations in flow: Opportunities for the fine chemicals and pharmaceuticals industries, *React. Chem. Eng.* 1 (2016) 595–612, <https://doi.org/10.1039/c6re00155f>.

- [72] J. Fischer, T. Lange, R. Boehling, A. Rehfinger, E. Klemm, Uncatalyzed selective oxidation of liquid cyclohexane with air in a microcapillary reactor, *Chem. Eng. Sci.* 65 (2010) 4866–4872, <https://doi.org/10.1016/j.ces.2010.05.028>.
- [73] A. Hommes, H.J. Heeres, J. Yue, Catalytic transformation of biomass derivatives to value-added chemicals and fuels in continuous flow microreactors, *ChemCatChem* 11 (2019) 4671–4708, <https://doi.org/10.1002/cctc.201900807>.
- [74] G.Y. Jeong, A.K. Singh, S. Sharma, K.W. Gyak, R.A. Maurya, D.P. Kim, One-flow syntheses of diverse heterocyclic furan chemicals directly from fructose via tandem transformation platform, *NPG Asia Mater.* 7 (2015), e173, <https://doi.org/10.1038/am.2015.21>.
- [75] C. Aellig, D. Scholz, S. Conrad, I. Hermans, Intensification of TEMPO-mediated aerobic alcohol oxidations under three-phase flow conditions, *Green Chem.* 15 (2013) 1975–1980, <https://doi.org/10.1039/c3gc40159f>.
- [76] A. Salazar, A. Linke, R. Eckelt, A. Quade, U. Kragl, E. Mejia, Oxidative esterification of 5-hydroxymethylfurfural under flow conditions using a bimetallic Co/Ru catalyst, *ChemCatChem* 12 (2020) 3504–3511, <https://doi.org/10.1002/cctc.202000205>.
- [77] T.V. Bukharkina, N.G. Digurov, Kinetics of aerobic liquid-phase oxidation of organic compounds, *Org. Process Res. Dev.* 8 (2004) 320–329, <https://doi.org/10.1021/op030012f>.
- [78] A.K. Suresh, M.M. Sharma, T. Sridhar, Engineering aspects of industrial liquid-phase air oxidation of hydrocarbons, *Ind. Eng. Chem. Res.* 39 (2000) 3958–3997, <https://doi.org/10.1021/ie0002733>.
- [79] S. Chen, Y. Cheng, H. Ban, Y. Zhang, L. Zheng, L. Wang, X. Li, Liquid-phase aerobic oxidation of 5-hydroxymethylfurfural to 2,5-furandicarboxylic acid over Co/Mn/Br catalyst, *Ind. Eng. Chem. Res.* 59 (2020) 17076–17084, <https://doi.org/10.1021/acs.iecr.0c01309>.
- [80] I. van Zandvoort, Y. Wang, C.B. Rasrendra, E.R.H. van Eck, P.C.A. Bruijninx, H. J. Heeres, B.M. Weckhuysen, Formation, molecular structure, and morphology of humins in biomass conversion: influence of feedstock and processing conditions, *ChemSusChem* 6 (2013) 1745–1758, <https://doi.org/10.1002/cssc.201300332>.
- [81] G. Tsilomelekis, M.J. Orella, Z. Lin, Z. Cheng, W. Zheng, V. Nikolakis, D.G. Vlachos, Molecular structure, morphology and growth mechanisms and rates of 5-hydroxymethyl furfural (HMF) derived humins, *Green Chem.* 18 (2016) 1983–1993, <https://doi.org/10.1039/c5gc01938a>.
- [82] W. Partenheimer, The high yield synthesis of benzaldehydes from benzylic alcohols using homogeneously catalyzed aerobic oxidation in acetic acid, *Adv. Synth. Catal.* 348 (2006) 559–568, <https://doi.org/10.1002/adsc.200505394>.
- [83] C.E.H. Bawn, J.B. Williamson, The oxidation of acetaldehyde in solution. Part II. Kinetics and mechanism of the formation of peracetic acid, *Trans. Faraday Soc.* 47 (1951) 735–743, <https://doi.org/10.1039/TF9514700735>.
- [84] P. Aussillous, D. Quéré, Quick deposition of a fluid on the wall of a tube, *Phys. Fluids* 12 (2000) 2367–2371, <https://doi.org/10.1017/S0022112060001055>.
- [85] B.M. Jose, T. Cubaud, Formation and dynamics of partially wetting droplets in square microchannels, *RSC Adv.* 4 (2014) 14962–14970, <https://doi.org/10.1039/c4ra00654b>.
- [86] W. Partenheimer, Chemistry of the oxidation of acetic acid during the homogeneous metal-catalyzed aerobic oxidation of alkylaromatic compounds, *Appl. Catal. A Gen.* 409–410 (2011) 48–54, <https://doi.org/10.1016/j.apcata.2011.09.025>.
- [87] M. Li, F. Niu, D.H. Busch, B. Subramaniam, Kinetic investigations of p-xylene oxidation to terephthalic acid with a Co/Mn/Br catalyst in a homogeneous liquid phase, *Ind. Eng. Chem. Res.* 53 (2014) 9017–9026, <https://doi.org/10.1021/ie403446b>.
- [88] S.P. Verevkin, V.N. Emel, E.N. Stepurko, R.V. Ralys, D.H. Zaitsau, A. Stark, Biomass-derived platform chemicals: Thermodynamic studies on the conversion of 5-hydroxymethylfurfural into bulk intermediates, *Ind. Eng. Chem. Res.* 48 (2009) 10087–10093, <https://doi.org/10.1021/ie901012g>.
- [89] X. Wu, Z. Deng, J. Yan, Z. Zhang, F. Zhang, Z. Zhang, Experimental investigation on the solubility of oxygen in toluene and acetic acid, *Ind. Eng. Chem. Res.* 53 (2014) 9932–9937, <https://doi.org/10.1021/ie5014772>.
- [90] A.K. Roby, J.P. Kingsley, Oxide safely with pure oxygen, *Chemtech.* 26 (1996) 39–46.
- [91] R.L. Hartman, Managing solids in microreactors for the upstream continuous processing of fine chemicals, *Org. Process Res. Dev.* 16 (2012) 870–887, <https://doi.org/10.1021/op200348t>.
- [92] Y. Zhang, X. Guo, P. Tang, J. Xu, Solubility of 2,5-furandicarboxylic acid in eight pure solvents and two binary solvent systems at 313.15–363.15 K, *J. Chem. Eng. Data* 63 (2018) 1316–1324, <https://doi.org/10.1021/acs.jced.7b00927>.
- [93] H. Ban, T. Pan, Y. Cheng, L. Wang, X. Li, Solubilities of 2,5-furandicarboxylic acid in binary acetic acid + water, methanol + water, and ethanol + water solvent mixtures, *J. Chem. Eng. Data* 63 (2018) 1987–1993, <https://doi.org/10.1021/acs.jced.7b01112>.