Process Intensification of Photochemical Oxidations using a High Throughput Rotor-Stator Spinning Disk Reactor: A Strategy for Scale Up

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Abstract This paper presents a novel high-throughput reactor for intensification of photochemical conversion processes. The photocatalyzed gas-liquid oxidation of $\alpha$-terpinene to the drug ascaridole with rose-bengal was achieved with throughputs of over 1 kg·day\textsuperscript{-1} (71 kg·day\textsuperscript{-1}·m\textsuperscript{-2}) under visible light irradiation. The performance of the reactor is correlated to rotation speed, liquid flowrate, gas flowrate, catalyst concentration, substrate concentration, gas holdup, gas bubble size, and energy dissipation rate. The conversion and selectivity increase from 37% to 97% and 75% to 90% respectively with an increase of rotation speed from 100 to 2000 RPM. Compared to conventional photochemical reactors such as the batch reactor or the microreactor, the photo-rotor-stator spinning disk reactor has much higher productivity (270 mmol·h\textsuperscript{-1} or 19.2 mol·h\textsuperscript{-1}·m\textsuperscript{-2}) and higher selectivity (> 90%), with the latter illustrating the impact of mixing on selectivity. The findings of this study can be used to study, design, optimize and scale photochemical processes using the rotor-stator spinning disk reactor.

Keywords: Process Intensification, Scale-Up of Photochemical Reactors, Rotor-Stator Spinning Disk Reactors, Photocatalysis, Visible Light, Multiphase Reactors

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Graphical Abstract

- Facile scale up and intensification
- 1 kg/day
- Gas-liquid multiphase flow
- High mixing efficiency
- High selectivity (up to 95%)
1 Introduction

The use of light as a source for the activation of reactants can be a sustainable alternative to the conventional use of thermochemical activation\cite{1}, for instance for cross-coupling reactions\cite{2}. Light can also be used to access reactive intermediates under milder conditions, e.g., the photocatalytic pathway to generate singlet oxygen or trifluoromethyl radicals\cite{3}. Various studies have already illustrated the potential for the synthesis of fine chemicals and pharmaceuticals through photochemical means\cite{4-6}; however, one of the challenges which prevents the ubiquitous use of this technology is that organic molecules tend to only absorb photons in the ultraviolet (UV) region. With energy efficient UV light sources being developed, this issue can soon be circumvented, but other challenges such as the presence of unproductive decomposition and the need for the specially designed reactors which can safely handle high intensity UV radiations, remain\cite{7}. Various solutions have been proposed to improve on these apparent limitations in photochemistry. For instance, an alternative to using UV activation is the use of visible light photocatalysis\cite{1,7}. This method involves the activation of metal complexes or organic dyes by light and the subsequent single-electron transfer or energy transfer from/to the substrate through various pathways\cite{8,9}. Furthermore, the combination of photochemistry with microflow reactors, has shown promise for the wide spread application of photochemical reactions\cite{6}. These reactors not only improve on the safety but also improve mass transfer and light penetration, leading to an accessible method for the continuous production of chemicals through photochemistry. While the throughput of a single microreactor is quite low, various scale up strategies, e.g. using longer operation times, external and internal numbering up, can be used to bring the throughputs closer to industrial scale. There are however, challenges associated with each scale up strategy, i.e. higher pressure drops, need for multiple autonomous reaction systems, and the issues with flow maldistribution, respectively\cite{10-12}. Nonetheless, microreactors have been widely investigated for photocatalytic systems \cite{10-12,13-15}. In addition other reactor designs such as tube reactors\cite{16,17}, plate-based reactors\cite{14}, a vortex reactor\cite{18}, gas phase reactors\cite{19,20} and rotating disk reactors \cite{21-24} have also been tested for photochemistry. It should be noted for these rotating disk reactors, the operating principle relies on the formation of a thin film to intensify mass transfer and heat transfer rates. Due to the formation of such a thin film, only low throughputs were achieved. In contrast, the reactor described in this work, the rotor-stator spinning disk reactor relies on generating intense turbulence in an enclosed
housing to intensify mass and heat transfer rates. Scaling up of such reactors have mostly focused on single phase liquid reactions as gas-liquid systems are traditionally more challenging. In 2016, a collaboration between Knowles and Merck led to the development of a photo-redox-mediated indoline dehydrogenation for the synthesis of Elbasvir, a compound used for the treatment of chronic hepatitis\cite{25}. They achieved 100 g of product within 5 hours for this radical chain reaction. In the same year, Stephenson et al. were able to produce 0.5 kg\textperiodcentered day\textsuperscript{-1} of a fluorinated compound\cite{26}. In 2018, Booker-Milburn et al. obtained 1.5 kg of product in 9 hours in a continuous flow Firefly reactor\cite{27} by applying a \([2+2]\) cycloaddition under UV irradiation of very high intensity (3 kW)\cite{28}. Using a similar method, Britton et al. produced 45 g of fluorinated leucine in 2 h\cite{13}. Recently, researchers at AbbVie were able to reach kg\textperiodcentered day\textsuperscript{-1} scale for a C-N coupling reaction in a CSTR using a catalyst with a low absorption coefficient, therefore making it possible to irradiate the reactor efficiently\cite{29}. However, even though these studies show that an effective reactor design significantly improves the performance of photochemical systems by increasing interfacial area and/or light penetration, only a few examples of industrial scale photochemical production are known\cite{29–31}, due to the absence of effective photochemical reactors with high productivity.

We show here the use of a rotor-stator spinning disk reactor (RS-SDR) for photochemical production on industrial scale. The RS-SDR generates intense turbulence by the rotation of a disk between two closely spaced stators, which results in high rates of mass and heat transfer\cite{32–36}. For gas-liquid systems, Meeuwse et al. found values as high as 23 m\textsuperscript{L}\textperiodcentered m\textsuperscript{G}\textperiodcentered s\textsuperscript{-1} for the RS-SDR, 40 times higher than in conventional reactors\cite{37,38}. More recently, Kleiner and Hinrichsen also observed improved productivities for the multiphase epoxidation of methyl oleate in a RS-SDR\cite{39}. In addition to high mass transfer rates, a high illuminated interfacial area and light penetration per volume reactor can be achieved\cite{40,41}. This combination makes the RS-SDR ideal for industrial scale photochemical conversions. Furthermore, the RS-SDR has minimal pressure drop across the reactor\cite{37}.

The productivity of a continuous photochemical reactor depends on parameters such as oxygen mass transfer, dissolved oxygen concentration, reaction kinetics, and the residence time in the reactor. These parameters are controlled by process conditions such as gas flowrate, gas pressure, liquid flowrate, catalyst concentration, and substrate concentration. By optimization of these parameters we illustrate how the photo-rotor-stator spinning disk reactor (pRS-SDR) facilitates production scale up while retaining high selectivity.
In this work, we focus on oxidations mediated by singlet oxygen. These reactions are easily performed with a visible light source, require inexpensive photosensitizers, and have a widespread application\textsuperscript{[6,42]}. We specifically investigate the oxidation of $\alpha$-terpinene to ascaridole, a benchmark reaction to characterize photoreactor performance\textsuperscript{[43]}. Ascaridole has applications as a pharmaceutical drug due to its anthelmintic properties and antitumor activity\textsuperscript{[44]}. The photosensitizer of choice for this reaction, is the organic dye Rose Bengal (RB). The overall scheme of the reaction is presented in Fig 1. The primary product of the photooxygenation is ascaridole; however, side reactions can result in the formation of various products such as p-cymene, isoascaridole, allylic epoxides, as well as enals\textsuperscript{[45,46]}.

When studying the mechanism (Fig 1) of the photooxygenation of $\alpha$-terpinene to ascardidole we identified multiple steps in the process that might be susceptible for improvement by more efficient mixing; e.g., the formation of singlet oxygen via excited RB and the subsequent oxidation of $\alpha$-terpinene to ascardidole due to the short life time of singlet oxygen (16 $\mu$s in ethanol).
2 Results & Discussion

2.1 Kinetics in a Batch, Microreactor, and pRS-SDR

Our first experiments involved investigations into the kinetic characterization of batch and microflow reactors; the two most commonly used photoreactors. From the results, illustrated in Fig 2, there were two very apparent findings: (1), the mass transfer and light penetration have important effects on the yield and selectivity of this reaction. With the batch reaction, much lower values for the yield/selectivity were obtained in comparison to the microreactor: the selectivity increased from 50% to 70%, for the longer residence times; (2), the reaction was much faster in a microreactor in comparison to batch. This has
previously been illustrated by other researchers\cite{47} and is attributed to better light penetration and improvements in mass transfer and mixing.

![Figure 2: Left) Conversion, yield and selectivity of the oxidation of $\alpha$-terpinene in a 5 mL batch reactor (reaction vial). Right) Conversion, yield and selectivity of the reaction in a 1 mL microflow reactor (inner diameter 0.76 mm).](image)

The microreactor results indicate that residence times in the range of 20-40 s are interesting to investigate in the pRS-SDR, with a 3:1 mole-flow ratio of oxygen: substrate. This ratio was also used in the microreactor (a higher oxygen concentration showed more selective ascaridole formation\cite{48}). The findings, illustrated in Fig 3, were quite interesting. As expected, with longer residence times, i.e. with lower liquid flowrates, the yield was improved. This result was similar to what was obtained in the microreactor. However, we observed that the rotation speed had a huge influence on yield and selectivity. This is most likely due to the improvements in mass transfer and the more effective mixing that occurs with high rotation speeds. With more effective mixing, we ensure that an excited oxygen species is more efficient in meeting a substrate before falling back to its ground state, i.e. within 16 $\mu$s. Similarly, with higher mass transfer rates, we can guarantee that the maximum dissolved oxygen concentration is reached quickly, and that the oxygen consumed due to reaction, can be quickly replenished in the liquid phase. This assures that we reach as close to intrinsic kinetic rates as possible. Furthermore, it is possible that with a higher turnover rate of the liquid close to the quartz plate, the light penetration improves, therefore also improving the yields.
2.2 Effects of Flow Ratio, Catalyst & Substrate Concentration, and Pressure

We investigated various process conditions to observe how these parameters affect the observed kinetics. We expected that the gas flowrate should influence the mixing and mass transfer due to the hydrodynamics of a RS-SDR [33]; therefore, we used varying gas-to-liquid flow ratios to discern the effects of lower relative gas flows. As the results illustrate in Fig 4, the flow ratio is an important factor not only for the yield, but also for the selectivity. This is likely due to the enhanced mass transfer with an increase in relative gas velocities, as was demonstrated in the work of Meeuwse et al. [33]. However, there are limits due to the solubility of oxygen in our solvent, and therefore, it seems as we go from a 2:1 ratio to a 3:1 ratio, this effect on the kinetics, becomes less pronounced. For a low gas flow ratio as is the case for a 1:1 ratio, we are also at a flow ratio below the stoichiometric requirement for the reaction. Therefore, this will also kinetically limit our reaction and possibly promote side reactions due to the unavailability of oxygen.
Figure 4: Yield (left) and selectivity (right) of the oxidation of α-terpinene (0.1M, 1 mol% Rose Bengal) at 60 mL·min⁻¹ with different gas-to-liquid volumetric flow ratios. (Conversion plot is presented in Supporting Information)

Experiments with varying liquid flowrates (Fig 3) implied that at rotation speeds of around 2000 RPM, kinetically limited conditions were reached, as the yield flattened out with increasing rotation speeds, regardless of the residence time. Since the light source was already fixed for the system, we investigated if increasing the catalyst concentration could further enhance the productivity by improving the kinetics. In a system with RB as catalyst, the decay of the transmittance of light is an important factor (Supporting Information). Since, the light penetration decreases with an increasing catalyst concentration, simply increasing this parameter will not necessarily lead to improved kinetics. We wanted to investigate if with more effective mixing, higher catalyst concentrations would be within reach, therefore offering the potential to boost the productivity. However, as can be observed in the results in Fig 5; this was not the case. Either due to the issue of transmittance or the limitation of the photon flux, the yield was not boosted by doubling catalyst concentration. On the other hand, while lowering the catalyst concentration, yields predictably decreased due to the now imposed kinetic limitations, it seemed to slightly improve selectivity; especially apparent at the higher rotation speeds for 0.25 mol%. This is mostly likely due to the lower catalyst concentration having better light transmittance throughout the reactor, therefore preventing “dark reactions” (Fig 1B) from proceeding. Nonetheless, it seems that further optimization of the catalyst concentration for a given light source, is an important strategy to further improve the achieved yields and selectivity[29].
Another parameter of consideration is the effective substrate concentration. We have investigated this parameter halving the substrate concentration and the results obtained, illustrated in Fig 6, were as expected. As ratio of substrate decreased relative to the oxygen flowrate, we observed an increase in yield and conversion. Therefore, by imposing a higher relative oxygen concentration we have effectively improved the availability of oxygen. The rotation speed still influences the conversion; however, by around 1000 RPM, the effect is much less pronounced for 0.05M. This implies that due to the relative excess of oxygen, the mass transfer is of less importance. Interestingly, the selectivity does not seem to be influenced by the decrease in substrate concentration once mass transfer limitations are overcome.

The kinetic rates will also be dictated by the maximum solubility of oxygen in the solvent. Therefore, we investigated the system at higher pressures to discern if further intensification can be possible with a more intense light source in the future, when we plan to further optimize this system.
From Fig 7, it can be observed that at a higher pressure, i.e., with a higher limit for the dissolved oxygen concentration, we reach what appears to be kinetically limited regimes at lower rotation speeds. Even at low rotation speeds, the mass transfer limitations can be easily overcome. Therefore, if the photon flux were to be increased for these cases, the productivity could be improved even further.
A visual comparison of the gas-liquid characteristics with increasing rotation speed can be observed in Fig 8. As expected, we observed smaller bubbles, therefore increasing interfacial areas, as the rotation speed increased. From our observation, the bubbles were smallest at the edge of the disk and increased in size as the flow moved closer to the exit of the reactor. This can also be expected since the shear forces are the highest at the rim of the rotating disk. Analysis of these bubble sizes with a high-speed camera resulted in histograms which we used to better understand how the average interfacial area was changing with the rotation speed (Fig 9). As expected, with increasing rotation speed we saw an increase in interfacial area. At high, RPMs, however, the analysis suggests a plateau of the bubble sizes. This is most likely due to the inability of the camera/MATLAB to observe bubble size less than 0.2 mm, which compares to 5 pixels in the images. Nevertheless, the theoretical bubble size, which is obtained from Eq.1 \[ a_{GL} \propto \omega^{1.4} \frac{\omega}{h^{0.8} V^{0.5}} \] could be matched to the obtained sizes up to 2000 RPM. In this equation, derived from the correlation between the energy dissipation and mass transfer coefficient; $h$ represents the gap distance and $V_r$ the reactor volume therefore, we can say with reasonable certainty that the theoretical trend should also be followed up to 3000 RPM. This implies that the specific interfacial area in the reactor at 3000 RPM was approximately 1000 m$^2$/m$^3$. More illustrations and videos of the gas-liquid characteristics are presented in Supporting Information.
In the pRS-SDR, energy is required to rotate the disk, which increases the overall energy requirements of the system. The energy dissipation with rotation speed can be estimated from the correlation of de Beer et al.\cite{50}, presented in Eq. 2, where $G$ represents the gap ratio and $Re_\omega$, the rotational Reynolds number. From this analysis (Fig 10), we can see that the excess energy taken for mixing will only account for a fraction of the light source. For our system, where we seem to reach kinetic limitations around 2000 RPM, the energy dissipation is approximately 15 W, which is 11% of the total energy consumption when taking the 120 W rated light source into account. Therefore, in a photochemical process the light source will most likely be the source of the highest energy consumption.
\[ E_d = 5.73 \cdot 10^{-12} G^{-0.14} \text{Re}^{2.12} \]  \hspace{1cm} (2)

Figure 10: Energy dissipation values for pRS-SDR at different rotation speeds obtained through the correlation in Eq.2.

2.4 Comparison & Scale-Up

A comparison of the specific productivity which can be achieved with our three reactor types is illustrated in Fig 11. As can be observed, the specific productivity obtained in the pRS-SDR is approximately 2.6 times higher than the microflow reactor. This was obtained with a 50 ml min\(^{-1}\) liquid flowrate (1 mol\% RB, 0.1 M substrate, 3:1 gas-to-liquid ratio) for full conversion in the pRS-SDR and with a residence time of 60 s for full conversion in the microflow reactor (1 mol\% RB, 0.1 M substrate, 3:1 gas-to-liquid ratio). Therefore, to obtain the same total productivity as obtained with the pRS-SDR, the microflow reactor would have to be scaled up 71 times. This would be challenging due to reasons previously mentioned. On the other hand, the pRS-SDR works without any significant pressure drops across the reactor \[^{37}\] and the dispersed type flow, essential for effective mass transfer, was consistently observed at high rotation speeds for the high throughputs used.

As illustrated in the experiments with pressure, as expected, an increase in pressure resulted in an increase of reaction rates. This particular pRS-SDR had pressure limits due to the design of the reactor, but in the future we expect that this can be overcome with a thicker quartz window and higher pressure rated sealings. Secondly, from Henry’s law, it is obvious that an increase in pressure will result in an increase of oxygen solubility limits.
Therefore, if the solubility is not the limiting factor, then the two parameters that will determine the productivity will be the kinetics and mass transfer. For photochemistry, the kinetics can be boosted with a more powerful light source and therefore the reaction can be operated at mass transfer limited conditions. Thus, with a high pressure pRS-SDR we can further boost the productivities obtained here.

To compare the values obtained using the pRS-SDR to those of other reactors which carried out the photooxygenation of α-terpinene, we compared the reported productivity (Table 1). As can be seen, the pRS-SDR far outperforms other reactors reported in literature and it does not rely on specialized operating conditions as the nebulizer reactor\[^{20}\], where aerosols are generated for high productivity; or the thin film rotary reactor, which operates in a semi-batch fashion\[^{19}\].

![Figure 11: Comparison for the productivity normalized by the energy input for batch, microflow and the pRS-SDR (all this work).](image-url)
| Reactor Type                                      | Productivity (mmol·h⁻¹) |
|-------------------------------------------------|-------------------------|
| Batch<sup>51</sup>                               | 0.1                     |
| Batch (this work)                                | 0.375                   |
| Capillary<sup>52</sup>                           | 3.4                     |
| Capillary (this work)                            | 4.2                     |
| LSC-PM<sup>52</sup>                              | 8.9                     |
| Thin Film Rotary<sup>19</sup>                    | 45                      |
| Nebulizer<sup>20</sup>                           | 84.6                    |
| Falling Film Microreactor<sup>51</sup>            | 0.137                   |
| Vortex Reactor<sup>18</sup>                      | 2.73                    |
| pRS-SDR (this work)                              | **270**                 |

Table 1: Literature comparison of the productivity of the oxidation of α-terpinene to ascaridole. The space time yield values obtained in the pRS-SDR (this work) was 10 M·h⁻¹ (1 bar), whereas for the capillary reactor (this work) this value was 4.2 M·h⁻¹ (1 bar).

3 Conclusion

The results of this study illustrate that photochemical oxidations can be carried out effectively with high productivity in a pRS-SDR. By improving mass transfer and with enhanced mixing in our reactor system, we were able to reach 1.1 kg·day⁻¹ levels of productivity with full conversion of the substrate, without even optimizing the reactor design and photo intensity. Furthermore, we reached selectivity of over 90%, thus reducing the need of downstream processes for purification, and increasing the efficiency of the overall process. Therefore, the pRS-SDR can be used as a novel photochemical reactor for the facile scale up and intensification of multiphase, photocatalytic processes. In recent years, microreactors have been shown to intensify photochemical processes and therefore have been proposed as a scale up method. However, the challenges associated with microreactors, such as high pressure drops and changing flow patterns often prevent the technology from being applied at industrial/pilot scale. On the other hand, the pRS-SDR operates without any significant pressure drop across the reactor and the formation of dispersed bubbles are dependent on the rotation speed of the disk, rather than the imposed flowrate. As a consequence, this allows the pRS-SDR to be very suitable for the scale up of photochemical reactions. Throughout this paper we have investigated various process parameters which we believe influence the efficiency of the reaction. With further optimization of such
parameters (i.e. photon flux, backpressure, substrate concentrations and mass transfer), further improvements in productivity are expected to be gained. Furthermore, the applicability of RS-SDRs for multiphase reactions\cite{32,36,53} makes it particularly interesting for further investigations of other kinds of photochemical reactions.

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**References**

[1] T. P. Yoon, M. A. Ischay, J. Du, *Nat. Chem.* **2010**, *2*, 527–532.
[2] R. C. McAtee, E. J. McClain, C. R. J. Stephenson, *Trends Chem.* **2019**, *1*, 111–125.
[3] C. Sambiagio, T. Noël, *Trends Chem.* **2019**, *1*, 1–15.
[4] P. Esser, B. Pohlmann, H.-D. Scharf, *Angew. Chemie Int. Ed. English* **1994**, *33*, 2009–2023.
[5] B. Pohlmann, H. D. Scharf, U. Jarolimek, P. Mauermann, *Sol. Energy* **1997**, *61*, 159–168.
[6] D. Cambié, C. Bottecchia, N. J. W. Straathof, V. Hessel, T. Noël, *Chem. Rev.* **2016**, *116*, 10276–10341.
[7] D. M. Schultz, T. P. Yoon, *Science (80).* **2014**, *343*, 1239176–1239176.
[8] L. Marzo, S. K. Pagire, O. Reiser, B. König, *Angew. Chemie - Int. Ed.* **2018**, *57*, 10034–10072.
[9] D. M. Arias-Rotondo, J. K. McCusker, *Chem. Soc. Rev.* **2016**, *45*, 5803–5820.
[10] Y. Su, K. Kuipers, V. Hessel, T. Noël, *React. Chem. Eng.* **2016**, *1*, 73–81.
[11] I. Rossetti, M. Compagnoni, *Chem. Eng. J.* **2016**, *296*, 56–70.
[12] F. Zhao, D. Cambié, J. Janse, E. W. Wieland, K. P. L. Kuipers, V. Hessel, M. G. Debije, T. Noël, *ACS Sustain. Chem. Eng.* **2018**, *6*, 422–429.
[13] S. D. Halperin, D. Kwon, M. Holmes, E. L. Regalado, L. C. Campeau, D. A. Dirocco, R. Britton, *Org. Lett.* **2015**, *17*, 5200–5203.
[14] J. D. Williams, M. Nakano, R. Gérardy, J. A. Rincón, Ó. De Frutos, C. Mateos, J. C. M. Monbaliu, C. O. Kappe, *Org. Process Res. Dev.* **2019**, *23*, 78–87.
[15] E. B. Corcoran, F. Lévesque, J. P. McMullen, J. R. Naber, *ChemPhotoChem* **2018**, *2*, 931–937.
[16] R. A. Bourne, X. Han, M. Poliakoff, M. W. George, *Angew. Chemie - Int. Ed.* **2009**, *48*, 5322–5325.
[17] J. F. B. Hall, R. A. Bourne, X. Han, J. H. Earley, M. Poliakoff, M. W. George, *Green Chem.* **2013**, *15*, 177–180.
[18] D. S. Lee, Z. Amara, C. A. Clark, Z. Xu, B. Kakimpa, H. P. Morvan, S. J. Pickering, M. Poliakoff, M. W. George, *Org. Process Res. Dev.* **2017**, *21*, 1042–1050.
[19] C. A. Clark, D. S. Lee, S. J. Pickering, M. Poliakoff, M. W. George, *Org. Process Res. Dev.* **2016**, *20*, 1792–1798.
[20] G. I. Ioannou, T. Montagnon, D. Kalaitzakis, S. A. Pergantis, G. Vassilikogiannakis, *ChemPhotoChem* **2017**, *1*, 173–177.
[21] J. D. Tibbetts, D. R. Carbery, E. A. C. Emanuelsson, *ACS Sustain. Chem. Eng.* **2017**, *5*, 9826–9835.
[22] D. D. Dionysiou, G. Balasubramanian, M. T. Suidan, A. P. Khodadoust, I. Baudin, J. M. Laîné, *Water Res.* **2000**, *34*, 2927–2940.
[23] T. Van Gerven, G. Mul, J. Moulijn, A. Stankiewicz, *Chem. Eng. Process. Process Intensif.* **2007**, *46*, 781–789.
[24] I. Boiarkina, S. Norris, D. A. Patterson, *Chem. Eng. J.* **2013**, *225*, 752–765.
[25] H. G. Yayla, F. Peng, I. K. Mangion, M. McLaughlin, L. C. Campeau, I. W. Davies, D. A. Dirocco, R. R. Knowles, *Chem. Sci.* **2016**, *7*, 2066–2073.
[26] J. W. Beatty, J. J. Douglas, R. Miller, R. C. McAtee, K. P. Cole, C. R. J. Stephenson, *Chem* **2016**, *1*, 456–472.
[27] L. D. Elliott, M. Berry, B. Harji, D. Klauber, J. Leonard, K. I. Booker-Milburn, *Org. Process Res. Dev.* **2016**, *20*, 1806–1811.
[28] L. D. Elliott, J. P. Knowles, C. S. Stacey, D. J. Klauber, K. I. Booker-Milburn, *React. Chem. Eng.* **2018**, *3*, 86–93.
[29] K. C. Harper, E. G. Moschetta, S. V. Bordawekar, S. J. Wittenberger, *ACS Cent. Sci.* **2019**, *5*, 109–115.
[30] J. Turconi, F. Griollet, R. Guevel, G. Oddon, R. Villa, A. Geatti, M. Hvala, K. Rossen, R. Göller, A. Burgard, *Org. Process Res. Dev.* **2014**, *18*, 417–422.
[31] T. Noël, *J. Flow Chem.* **2017**, *7*, 87–93.
[32] F. Visscher, J. van der Schaaf, M. H. J. M. de Croon, J. C. Schouten, *Chem. Eng. J.* **2012**, *185–186*, 267–273.
[33] M. Meeuwse, J. van der Schaaf, J. C. Schouten, *Ind. Eng. Chem. Res.* **2010**, *49*, 18.
1605–1610.

[34] F. Haseidl, J. Pottbäcker, O. Hinrichsen, Chem. Eng. Process. Process Intensif. 2016, 104, 181–189.

[35] M. Meeuwse, J. van der Schaaf, B. F. M. Kuster, J. C. Schouten, Chem. Eng. Sci. 2010, 65, 466–471.

[36] M. Meeuwse, S. Lempers, J. van der Schaaf, J. C. Schouten, Ind. Eng. Chem. Res. 2010, 49, 10751–10757.

[37] M. Meeuwse, J. van der Schaaf, J. C. Schouten, AIChE J. 2012, 58, 247–255.

[38] J. Van Der Schaaf, J. C. Schouten, Curr. Opin. Chem. Eng. 2011, 1, 84–88.

[39] J. Kleiner, O. Hinrichsen, Chem. Eng. Process. - Process Intensif. 2019, 136, 152–162.

[40] E. Boix-Garriga, B. Rodríguez-Amigo, O. Planas, S. Nonell, in Singlet Oxyg. Appl. Biosci. Nanosci. Vol. 1, The Royal Society Of Chemistry, 2016, pp. 23–46.

[41] L. Petrizza, M. Le Bechec, E. Decompte, H. El Hadri, S. Lacombe, M. Save, Polym. Chem. 2019, 10, 3170–3179.

[42] H. P. L. Gemoets, Y. Su, M. Shang, V. Hessel, R. Luque, T. Noël, Chem. Soc. Rev. 2016, 45, 83–117.

[43] R. C. R. Wootton, R. Fortt, A. J. De Mello, Org. Process Res. Dev. 2002, 6, 187–189.

[44] D. P. Bezerra, J. D. B. Marinho Filho, A. P. N. N. Alves, C. Pessoa, M. O. De Moraes, O. D. L. Pessoa, M. C. M. Torres, E. R. Silveira, F. A. Viana, L. V. Costa-Lotufo, Chem. Biodivers. 2009, 6, 1224–1231.

[45] J. Rudbäck, M. A. Bergström, A. Börje, U. Nilsson, A. T. Karlberg, Chem. Res. Toxicol. 2012, 25, 713–721.

[46] F. Ronzani, N. Costarramone, S. Blanc, A. K. Benabbou, M. Le Bechec, T. Pigot, M. Oelgemöller, S. Lacombe, J. Catal. 2013, 303, 164–174.

[47] C. Y. Park, Y. J. Kim, H. J. Lim, J. H. Park, M. J. Kim, S. W. Seo, C. P. Park, RSC Adv. 2015, 5, 4233–4237.

[48] R. Radjagobalou, J. F. Blanco, O. Dechy-Cabaret, M. Oelgemöller, K. Loubière, Chem. Eng. Process. - Process Intensif. 2018, 130, 214–228.

[49] M. Meeuwse, E. Hamming, J. van der Schaaf, J. C. Schouten, Chem. Eng. Process. Process Intensif. 2011, 50, 1095–1107.

[50] M. M. de Beer, L. Pezzi Martins Loane, J. T. F. Keurentjes, J. C. Schouten, J. van der Schaaf, Chem. Eng. Sci. 2014, 119, 88–98.

[51] O. Shvydkiv, K. Jähnisch, N. Steinfeldt, A. Yavorskyy, M. Oelgemöller, Catal. Today 2018, 308, 102–118.

[52] D. Cambié, J. Dobbelaar, P. Riente, J. Vandespikken, C. Shen, P. H. Seeberger, K. Gilmore, M. G. Debije, T. Noël, Angew. Chemie Int. Ed. 2019, 58, 14374–14378.
[53] K. M. P. van Eeten, D. H. J. Hülsman, J. van der Schaaf, J. C. Schouten, *AIChE J.* 2015, 61, 3656–3665.