Inline monitoring of high ammonia concentrations in methanol with a customized 3D printed flow cell

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Abstract
A novel system for inline monitoring of ammonia (NH₃) suitable for methanol is presented. An optical ammonia sensor with a response time t₉₀ of 33 s was combined with a tailor-made, 3D printed flow cell and allowed efficient measurements under continuous flow. The optical sensor includes a fluorescent indicator dye that is physically immobilized into a polyurethane hydrogel. A protective layer made of hydrophobic polyether sulfone (PES) shields the ammonia sensitive material against interfering substances and guarantees long-term stability in methanol. The sensor can be read out via a compact phase fluorimeter. Measurements in continuous flow are enabled by a flow cell manufactured via selective laser melting (SLM) of stainless steel. Stainless steel was chosen for the flow cell due to its good heat transfer properties and relatively good chemical resistance of NH₃ in methanol. The measurements were successfully carried out with ammonia concentrations between 0.3 and 5.6 mol L⁻¹ NH₃ in methanol at 25 °C up to 80 °C. Additionally, different flow-rates (0.5–2.0 mL min⁻¹), varying internal pressure (0.5–2.0 bar) as well as reversibility of the measurements at 25 and 60 °C were studied in detail. The sensor did not degrade indicated by sufficient signal and low drift over a period of two weeks, thus indicating the high potential of the novel set-up for real-time measurements in continuous flow applications.

Keywords Organic solvent • 3D printing • Flow chemistry • Optical sensing • Selective laser melting • NH₃

Introduction
Monitoring of ammonia is an important tool in various technological and industrial applications. Because of its toxic and hazardous characteristics this compound is not easy to handle. In chemical industry as well as in scientific research, ammonia is a widely used reagent in different reactions [1–3]. It is a key component in the synthesis of heterocyclic compounds [4–7], derivatization of carboxylic acid derivatives into acid amides [8] and further into nitrile compounds [9, 10] as well as reductive amination to generate various amine species [11, 12] or amination of aryl halides [13–16]. Some of these reactions can be substantially improved by transferring them into flow chemistry where the control of various parameters such as different reactants (in this work ammonia), solvents and reaction parameters is desirable. Most ammonia sensors operating in industry measure in the gas phase and are often used in leakage alarm systems [17–23]. These types of ammonia sensors are well established and available by various suppliers on the market but reaction monitoring by using ammonia sensors which operate in solution are rare. Here, the ion selective electrode (ISE) is one described method. This electrode can measure ammonia very precisely and in low concentrations (up to 0.05 mol L⁻¹) in aqueous media and is therefore often used in environmental or medical applications [24]. Nevertheless, it is very difficult to use this electrode for reproducible measurements in organic media. It is influenced by different parameters which are hard to handle in organic solvents. Additionally, it measures the ammonium ion and due to the fact that there is hardly any data on the ammonia...
ammonium equilibrium in organic media because of the lack of free protons in solution it is difficult to verify the exact ammonium ion concentration in such media [25]. Also several luminescent based ammonia sensors working in aqueous systems have been published in the last two decades, [26–33], to the best of our knowledge, so far no optical ammonia sensors have been reported in literature as being suitable for measurements in organic solvents.

To overcome measurement limitations, this work presents an optical ammonia sensor that is able to operate in methanol under continuous flow. The sensor is based on a fluorescent BF$_2$-chelated tetraarylazadipyrromethene (aza-BODIPY) dye which is incorporated in a polyurethane hydrogel layer [34]. A porous protection layer on top of the sensing layer shields the sensing material against interfering substances such as protons relying on variations in the pH of the sample and other hydrophilic, ionic, gaseous species which can deprotonate the dye. The sensor’s mechanical design is based on an existing arrangement which fixates the membrane to an optical fibre [28]. Since the overall goal of this work was to apply the sensor in continuous flow applications, a suitable way to implement it in these set-ups was needed. The chosen solution for this challenge was a 3D printed flow cell made of stainless steel via selective laser melting (SLM) because of its wide solvent capability, well post-processing properties and prior knowledge for manufacturing. This technique provides the needed freedom of design as well as chemical and mechanical resistance to organic solvents as already shown in other flow chemistry applications [35–37]. The 3D printable flow cell was designed to accommodate the hole sensor head and guide a fluid stream to the sensor’s membrane. The cell guides the analyte through an internal microchannel to the sensor tip. This cell design can also act as a sensor port for future 3D printed reactors and allows similar implementations for continuous flow measurements of ammonia as it was shown in a previous work on oxygen [38].

In this new study, the performance of the developed set-up for sensor and flow cell was studied in a temperature range of 25–80 °C and ammonia concentrations between 0.3 and 5.6 mol L$^{-1}$. This concentration range was chosen on considerations on possible chemical reactions [4–16]. Furthermore, reversibility as well as two system relevant parameters, internal pressure and flow rate, were investigated in detail. The response time of the sensor was studied in batch measurements.

Results and discussion

Sensor performance in batch

The sensor response to ammonia dissolved in methanol at concentrations between 0.0007 and 7 mol L$^{-1}$ was first investigated in a temperature-controlled vessel and is shown in Fig. 1. This concentration range represents the hole dynamic range of the sensor which is limited by the pK$_a$ value of the dyes hydroxy group. The highest NH$_3$ concentration is limited by the highest commercially available amount of ammonia dissolved in methanol. The schematic design of the developed optical ammonia sensor is shown in Figure S1 b. During a measurement, ammonia is penetrating the hydrophobic barrier and diffuses into the sensing layer where it deprotonates the dye’s hydroxy group shutting off its fluorescence. Dual-lifetime referencing is chosen as readout method. Thereby, the overall phase angle dphi is measured. It originates from the luminescence intensity ratio between the indicator dye with a short lifetime and the reference dye having a comparable long lifetime (further information in ESI). An increase of the phase angle dphi indicates an increase in ammonia concentration and vice versa (Fig. 1a). The sensor shows a fast t$_{90}$, which represents the time the sensor needs for 90% of the respective maximal signal change, of 33 s and at each measured calibration solution a stable signal, where a plateau of the measured dphi value is reached (Fig. 1b). The relationship between the analyte concentration and the measured signal is described by a typical sigmoid shaped calibration curve (Figure S2), which can be described by a Boltzmann fit (see Equation S1). Since chemical reactions often need high ammonia concentrations, further inline experiments were performed at high analyze concentrations.

Inline measurements in the flow cell set-up

A micro fluidic flow cell (Fig. 2a-c) was designed to incorporate the sensor arrangement for continuous flow applications. While the design of the existing sensor head (Fig. 2d) was predefined, [28] a suitable and leak proof way to withstand organic solvents at high concentrations of ammonia (up to 7 mol L$^{-1}$ NH$_3$ in methanol) was needed. This was achieved by utilizing the design freedom given by 3D printing of stainless steel. 3D printing allowed to manufacture a part with internal structures which cannot be created with common machining tools. With this method, the internal channel can have almost any shape and was therefore the perfect possibility to design a flow cell including a reaction channel, fluid connector ports, coolant (water) guidance and a connector port for the sensor, all of these features combined within one part.

The stainless steel flow cell shown in Fig. 2 consists of a two-part system: A thermally controlled base part (Fig. 2a) with a 0.8 mm U-shaped micro channel (highlighted in red, Fig. 2a) guiding the solvent flow to the sensor head which is fixated in a connecting screw and enables the inline ammonia measurements. The solvent channel can be connected to 1/16” capillaries with standard fittings as found for high
performance liquid chromatography (HPLC) applications. Temperature control of the flowing solvent and the whole flow cell is possible by a guided coolant flux (water) which passes 2.5 mm channels perpendicular to the solvent flow (Fig. 2b). The sensor head (Fig. 2d) with a diameter of 8 mm can be mounted to the base with the second part, a 3D printed connecting screw. A commercial M6 screw is used to fixate the sensor head with the 3D printed screw (Fig. 2c). Base and connecting screw were sealed by an O-ring (perfluoroelastomer, FFKM, 8 × 1.5 mm). Additionally, all threads were sealed with the aid of polytetrafluoroethylene (PTFE) sealing tape. The U-shaped channel (see Fig. 2a) directing the fluid to the sensor tip allows a fast response of the sensor. As this channel can also be seen as a possible reaction channel in a micro reactor, only slight adaptations will be necessary to directly implement this flow cell in such an application. Therefore, a U-shaped bend similar like within the flow cell and the used sensor housing needs to be added at a suitable position of a micro reactor. This can be done by directly re-using this existing design (Fig. 2a).

To show the applicability of the developed set-up for common reaction temperatures in methanol, the sensor response was measured at 25 (ambient temperature), 60 (close to the boiling point of methanol) and 80 °C (above the boiling point of methanol) with an experimental set-up as shown in the ESI Figure S10. As a result, Fig. 3a shows the sensor response curve while measuring inline at 60 °C with a flow rate of 1 mL min⁻¹ of methanol stream. This measurement started with pure methanol and the ammonia concentrations were increased stepwise up to 5.6 mol L⁻¹ NH₃ by mixing solutions of pure methanol and 7 mol L⁻¹ NH₃ in methanol with an HPLC and a syringe pump. Corresponding response curves at 25 and at 80 °C are shown in the ESI (Figure S4 and S5). At the investigated temperatures, the sensor shows stable signals at each chosen ammonia concentration. These high analyte concentrations bring the sensor to its upper dynamic limit. Above this highest measured ammonia concentration, all hydroxy groups of all fluorescent dye molecules in the sensing layer will be deprotonated by ammonia and the fluorescence is therefore shut off completely. As a consequence, higher ammonia concentrations are not resolved anymore by this sensor. This behaviour is mathematically described via a one-phase exponential decay function (Equation S7) was used as fitting function in the data evaluation process. Figure 3b shows the calibration plots at the different temperatures indicating a negligible temperature influence on the sensor’s performance. We clearly see an influence of the set-up on the response time of the sensor at lower concentrations. Here, the response time t₉₀ increases up to 73 s when changing the ammonia concentration from 0.6 to 1.2 mol L⁻¹. Contrary, there is no considerable difference at higher ammonia concentrations (33 s in batch vs. 38 s in flow). This behaviour might be attributed to the slow mass transfer of a compound which is needed to equilibrate the sensor interaction site with analyte molecules at low analyte concentrations. This presumption is based on the time which is needed to equilibrate the sensor membrane.

Sensor reversibility and stability at 60 °C is shown in Fig. 4. The sensor was exposed to alternating ammonia concentrations of approximately 2.0 and 1.2 mol L⁻¹. The sensor signal shows barely any drift at the higher concentration and only a small one at the lower concentration. A similar result is achieved after seven cycles at 25 °C (see Figure S6).

Reliable and trustworthy data can only be achieved when the system parameters (internal pressure, flow-rate) do not influence the sensor signal. Different flow rates ranging from 0.5 up to 2.0 mL min⁻¹ of the methanol stream at 25 °C were investigated (Figure S7). The flow rate settings were on the one hand limited by the maximal force of the syringe pump which does not cause bending at the plastic syringe and on the other hand reduced to the fact that ammonia needs an internal pressure to prevent the creation of

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**Fig. 1** a Response curve of the optical sensor in methanol measured in batch over the full dynamic range (0.0007–7 mol L⁻¹ NH₃) of the ammonia sensor. b Response time t₉₀ for the sudden concentration change from 0.7 to 7 mol L⁻¹ ammonia in methanol highlighted in red.
bubbles. No considerable influence caused by the flow rate on the sensor signal was detected. The fairly small changes in the recorded sensor signal can be attributed to the operation behaviour of the used HPLC and the syringe pump. After an equilibration phase to the next flow rate, the sensor signal is at a stable plateau.

In addition to these experiments, the influence of changing internal pressure at the sensor on its signal at a defined NH$_3$ concentration at 25 °C was investigated (Figure S8). The studied internal pressure values of 0.5 up to 2.0 bar show only a negligible impact on the sensing signal of the ammonia sensor. No long-term effect on the sensing properties were detected afterwards.

**Conclusions**

A novel methanol resistant optical ammonia sensor in a new and self-designed 3D printed stainless steel flow cell was tested successfully under different conditions. Our measurements show the huge potential of inline ammonia sensors in continuous flow systems working with methanol. This work is a first proof of concept for optical sensors for the detection of ammonia in a polar organic solvent. We know that solvent vapours which can diffuse through the hydrophobic porous membrane influence the swelling behaviour of the hydrogel. These differences in swelling influence the respective sensor baseline signal and therefore the calibration. Therefore, we are planning to investigate different organic solvents which are essential for organic synthesis and can be applied in flow chemistry. Promising options are ether, ethanol or acetone. Tetrahydrofuran in contrast, will partly dissolve the used hydrogel which causes a degradation of the sensor. The signal of the ammonia sensor is only minimally influenced by varying temperatures up to 80 °C and shows no dependency on different flow rates up to 2.0 mL min$^{-1}$ and varying internal pressures up to 2.0 bar. However, the response time of the sensor within inline measurements is especially at low ammonia concentrations (below 1 mol L$^{-1}$) increased compared to batch measurements. Detailed experiments at higher pressures (above 20 bar), which are essential for applications in chemical industry, and faster flow rates (above 5 mL min$^{-1}$) are planned for the future. The reversibility measurements showed promising results up to 60 °C indicating a long-term stability of the sensor in methanol. Furthermore, with the developed flow cell it is possible to reuse its design in other (3D printed) reactors and thus, for example the real-time monitoring of reaction progresses inside customized microreactors.
Experimental

Sensor manufacturing process

We used a layer-by-layer concept for sensor manufacturing (see Figure S1 b). The sensing layer consists of a fluorescent BF₂-chelated tetraarylazadipyrromethene dye (aza-BODIPY, Figure S1 a) which is mixed with an internal reference dye (silanized Egyptian Blue). Both are physically immobilized into a polyurethane hydrogel (HydroMed D4) and knife-coated (25 µm wet film) on top of a transparent support. This enables the system to be read-out via a compact phase fluorimeter and also allows for dual-lifetime referencing (DLR) as the referencing method [39]. A protective layer out of hydrophobic PES at the top shields the sensing material against interfering substances and guarantees long-term stability in methanol. After the knife-coating process, a hydrophobic protection layer is laid on the still wet polymer layer. After two hours, the organic solvent is fully evaporated and the sensor can be stored in the measuring media. After additional 24 h of storing in methanol, the sensor is ready to be used for calibration. As read-out device a commercially available compact phase fluorimeter is used. This is based on a luminescence lifetime measurement principle in the frequency domain and yields in an overall phase angle signal \( \text{dphi} \). More detailed information on the sensor composition and read-out method can be found in the supplementary information.

3D printed flow cell

The newly designed flow cell consists of two parts. One is equipped with a fluid guiding and temperature-controlled flow cell and the second one is based on a connecting screw for mounting the sensor tip inside the flow cell (Fig. 2). A special focus was kept on the possibility to use standard laboratory equipment like flat bottom \( \frac{1}{4} \)"-28 connectors for 1/16" capillaries and simple hose nozzle connectors for the temperature regulation with a thermostat. The design process as well as a first test version made of polylactic acid (PLA) can be seen in Figure S9. Before flow cell and connecting screw can be additive manufactured, it was necessary to generate a standard triangle language (STL) file and to prepare external support structures, in case of the stainless steel version generated by Materialise’s Magics software, which connect the parts to the building platform.

A selective laser melting (SLM) system from EOS (Krailling near Munich, Germany) was used for the additive manufacturing of the flow cell and the connecting screw. This system utilizes an Ytterbium fibre laser with 400 Watt maximum power input, which scans through each of the 40 µm high sliced layers of a 316L stainless steel powder bed with a mean particle size of 35.9 µm. After printing, post-processing needed to be carried out including cutting the parts from the
building platform, stress relief annealing, several cleaning procedures with compressed air, treatments within an ultrasonic bath to free entrapped particles, sandblasting of the outer surfaces and cutting of threads.

Further information on the used materials and chemicals can be found in the respective section in the supplementary information.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s41981-021-00141-w.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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References

1. Klinkenberg JL, Hartwig JF (2011) Catalytic organometallic reactions of ammonia. Angew Chem Int Ed 50:86–95. https://doi.org/10.1002/anie.201002354
2. Kim J, Kim HJ, Chang S (2013) Synthetic uses of ammonia in transition-metal catalysis. Eur J Org Chem :3201–3213. https://doi.org/10.1002/ejoc.201300164
3. Kim H, Chang S (2017) The use of ammonia as an ultimate amino source in the transition&metal-catalyzed&nbsp;C–H&nbsp;amination. Acc Chem Res 50:482–486. https://doi.org/10.1021/acs.accounts.6b00489
4. Chen X, Yang H, Hülshey MJ, Yan N (2017) One-step synthesis of N-heterocyclic compounds from carbohydrates over tungsten-based catalysts. ACS Sustain Chem Eng 5:11096–11104. https://doi.org/10.1021/acssuschemeng.7b03048
5. Lichtenthaler FW (2002) Unsaturated O- and N-Heterocycles from carbohydrate feedstocks. Acc Chem Res 35:728–737. https://doi.org/10.1021/ar010071i
6. Forberg D, Schwob T, Zaher M, Friedrich M, Miyajima N, Kempe R (2016) Single-catalyst high-weight % hydrogen storage in an N-heterocycle synthesized from lignin hydrogenolysis products and ammonia. Nat Commun 7:13201. https://doi.org/10.1038/ncomms13201
7. Li H, Guo H, Fang Z, Aida TM, Smith RL (2020) Cycloamination strategies for renewable N-heterocycles. Green Chem 22:582–611. https://doi.org/10.1039/C9GC03655E
8. Cabrero-Antonino JR, Adam R, Beller M (2019) Catalytic reductive N-Alkylations using CO2 and carboxylic acid derivatives: recent progress and developments. Angew Chem Int Ed 58:12820–12838. https://doi.org/10.1002/anie.201810121
9. Ruggiero A, Fuchter MJ, Kokas OJ, Negru M, White AJP, Haycock PR, Hoflinan BM, Barrett AGM (2009) A ‘push–pull’ tropylum-fused aminoporphyrinazone. Tetrahedron 65:9690–9693. https://doi.org/10.1016/j.tet.2009.09.105
10. Eby CJ, Hauser CR (1957) Acylations of nitriles with esters by sodium amide in liquid ammonia to form β-ketonitriles. Consideration of amide formation. J Am Chem Soc 79:723–725. https://doi.org/10.1021/ja01560a060
11. Hahn G, Kunnas P, de Jonge N, Kempe R (2019) General synthesis of primary amines via reductive amination employing a reusable nickel catalyst. Nat Catal 2:71–77. https://doi.org/10.1038/s41929-018-0202-6
12. Gross B, Lockwood SY, Spence DM (2017) Recent advances in analytical chemistry by 3D printing. Anal Chem 89:57–70. https://doi.org/10.1021/acs.analchem.6b04344
13. Shen Q, Hartwig JF (2006) Palladium-catalyzed coupling of ammonia and lithium amide with aryl halides. J Am Chem Soc 128:10028–10029. https://doi.org/10.1021/ja064005t
14. Schulz T, Torborg C, Enthaler S, Schäffner B, Dumrah A, Spannenberg A, Neumann H, Börner A, Beller M (2009) A general palladium-catalyzed amination of aryl halides with ammonia. Chem Eur J 15:4528–4533. https://doi.org/10.1002/chem.200802678
15. Li Y, Shi R, Lin W, Cheng H, Zhang C, Arain M, Zhao F (2019) A green and recyclable ligand-free copper (I) catalysis system for amination of halonitrobenzenes in aqueous ammonia solution. Mol Catal 475:110462. https://doi.org/10.1016/j.mcat.2019.110462
16. Sury DS, Buchwald SL (2007) Selective palladium-catalyzed amination of ammonia: Synthesis of anilines as well as symmetrical and unsymmetrical Di- and triarylamines. J Am Chem Soc 129:10354–10355. https://doi.org/10.1021/ja074681a
17. Jerger A, Kohler H, Becker F, Keller HB, Seifert R (2002) New applications of tin oxide gas sensors: II. Intelligent sensor system for reliable monitoring of ammonia leakages. Sensors Actuators B Chem 81:301–307. https://doi.org/10.1016/S0925-4005(01)00970-4
18. Gangopadhyay RK, Das SK (2008) Ammonia leakage from refrigeration plant and the management practice. Process Saf Prog 27:15–20. https://doi.org/10.1002/prs.10208
19. Sensidyne, Ammonia Gas Detection | Sensidyne, (n.d.). https://www.sensidyne.com/support/application-support/ammonia-gas-detection-and-monitoring.php. Accessed 2 Oct 2020
20. Sensidyne (NH3) Ammonia Gas Detection | Sensidyne (n.d.). https://www.sensidyne.com/support/application-support/ammonia-gas-detection.php. Accessed 2 Oct 2020
21. Ammonia Detectors and Monitors | Draeger (n.d.) https://www.draeger.com/en-us/Safety/Hazmat-Handling/Ammonia-Gas-Detection. Accessed 2 Oct 2020
22. Ammonia Gas Detection | Refrigeration Systems | RC Systems (n.d.). https://www.rcsystemsco.com/ammonia-gas-detection-in-refrigeration-systems. Accessed 2 Oct 2020
23. Gas detection for industrial refrigeration (n.d.). https://www.danfoss.com/en/products/sensors-and-transmitters/des/gas-detecting-sensors/gas-detection-for-industrial-refrigeration/. Accessed 2 Oct 2020
24. Mettler-Toledo International Inc all rights reserved, GSE Ammonia Electrode (n.d.). https://www.mt.com/en/home/products/Laboratory_Analytics_Browse/pH-meter/sensor/ion-selective-electrode/NH3-GSE.html. Accessed 7 Apr 2020
25. Pungor E, Tóth K, Klatsmanyi PG, Izutsu K (1983) Applications of ion-selective electrodes in nonaqueous and mixed solvents. Pure Appl Chem 55:2029–2065. https://doi.org/10.1351/pac198355122029
26. Müller BJ, Steinmann N, Borisov SM, Klimant I (2017) Ammonia sensing with fluoroionophores – A promising way to minimize interferences caused by volatile amines. Sensors Actuators B Chem. https://doi.org/10.1016/j.snb.2017.08.209
27. Strobl M, Walcher A, Mayr T, Klimant I, Borisov SM (2017) Trace ammonia sensors based on fluorescent near-infrared-emitting aza-BODIPY dyes. Anal Chem 89:2859–2865. https://doi.org/10.1021/acs.analchem.6b04045
28. Maiherhofer M, Rieger V, Mayr T (2020) Optical ammonia sensors based on fluorescent aza-BODIPY dyes— a flexible toolbox. Anal Bioanal Chem. https://doi.org/10.1007/s00216-020-02891-3
29. Waich K, Mayr T, Klimant I (2008) Fluorescence sensors for trace monitoring of dissolved ammonia. Talanta 77:66–72. https://doi.org/10.1016/j.talanta.2008.05.058
30. Waich K, Mayr T, Klimant I (2007) Microsensors for detection of ammonia at ppb-concentration levels. Meas Sci Technol 18:3195. https://doi.org/10.1088/0957-0233/18/10/S22
31. Waich K, Borisov SM, Mayr T, Klimant I (2009) Dual lifetime referenced trace ammonia sensors. Sensors Actuators B Chem 139:132–138. https://doi.org/10.1016/j.snb.2008.10.010
32. Mader HS, Wolbeis OS (2010) Optical ammonia sensor based on upconverting luminescent nanoparticles. Anal Chem 82:5002–5004. https://doi.org/10.1021/ac1007283
33. Abel T, Ungerböck B, Klimant I, Mayr T (2012) Fast responsive, optical trace level ammonia sensor for environmental monitoring. Chem Cent J 6:124. https://doi.org/10.1186/1752-153X-6-124
34. Strobl M, Rappitsch T, Borisov SM, Mayr T, Klimant I (2015) NIR-emitting aza-BODIPY dyes – new building blocks for broad-range optical pH sensors. Analyst 140:7150–7153. https://doi.org/10.1039/C5AN01389E
35. Gutmann B, Köckinger M, Glotz G, Ciaglia T, Slama E, Zadravec M, Pfanner S, Maier MC, Gruber-Wölfler H, Kappe CO (2017) Design and 3D printing of a stainless steel reactor for continuous difluoromethylation using fluoroform. React Chem Eng 2:919–927. https://doi.org/10.1039/C7RE00176B
36. Reintjens R, Ager DJ, De Vries AHM (2015) Flow chemistry, how to bring it to industrial scale? Chim Oggi - Chemistry Today 33:21–24
37. Maier MC, Valotta A, Hiebler K, Soritz S, Gavric K, Grabner B, Gruber-Wöfler H (2020) 3D printed reactors for synthesis of active pharmaceutical ingredients in continuous flow, org. Process Res Dev 24:2197–2207. https://doi.org/10.1021/acs.oprd.0c00228
38. Maier MC, Lebl R, Sulzer P, Lechner J, Mayr T, Zadravec M, Slama E, Pfänner S, Schmölzer C, Pöchlauer P, Kappe CO, Gruber-Wöfler H (2019) Development of customized 3D printed stainless steel reactors with inline oxygen sensors for aerobic oxidation of Grignard reagents in continuous flow. React Chem Eng 4:393–401. https://doi.org/10.1039/C8RE00278A
39. Klimant I, Huber C, Liebsch G, Neurauter G, Stangelmayer A, Wolbeis OS (2001) Dual Lifetime Referencing (DLR) — a new scheme for converting fluorescence intensity into a frequency-domain or time-domain information. In: Valeur B, Brochon J-C (eds) New Trends in Fluorescence Spectroscopy: Applications to Chemical and Life Sciences. Springer Berlin Heidelberg, Berlin, pp 257–274. https://doi.org/10.1007/978-3-642-56853-4_13

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