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## ARTICLE

# Continuous Heterogeneously Catalysed Oxidation of Benzyl Alcohol Using a Tube-in-Tube Membrane Reactor

Gaowei Wu<sup>1</sup>, Achilleas Constantinou<sup>1</sup>, Enhong Cao<sup>1</sup>, Simon Kuhn<sup>2</sup>, Moataz Morad<sup>3</sup>, Meenakshisundaram Sankar<sup>3</sup>, Donald Bethell<sup>4</sup>, Graham J. Hutchings<sup>3</sup>, Asterios Gavriilidis<sup>1,\*</sup>

<sup>1</sup> Department of Chemical Engineering, University College London, Torrington Place, London, WC1E 7JE, U.K.

<sup>2</sup> Department of Chemical Engineering, KU Leuven, W. de Croylaan 46, 3001 Leuven, Belgium

<sup>3</sup> School of Chemistry, Cardiff University, Main Building, Park Place, Cardiff, CF10 3AT, U.K.

<sup>4</sup> Department of Chemistry, University of Liverpool, Crown Street, Liverpool L69 7ZD, U.K.

\* Corresponding Author: E-mail: [a.gavriilidis@ucl.ac.uk](mailto:a.gavriilidis@ucl.ac.uk).

## Abstract

In this work, a Teflon AF-2400 tube-in-tube microreactor is investigated for the continuous, solvent-free, catalytic oxidation of benzyl alcohol with oxygen. The semi-permeable Teflon AF-2400 tube acts as the interface between the gaseous oxidant and the liquid substrate. Due to the inherent safety of this contacting method, the use of pure oxygen is possible. The semi-permeable tube was packed with 1 wt% Au-Pd/TiO<sub>2</sub> catalyst particles and placed inside a PTFE tube to provide an annular region which is pressurised with pure oxygen. This design allowed continuous penetration of oxygen through the inner tube during the reaction, resulting to higher oxygen concentration in the catalyst bed and significantly improved conversion compared to a reactor operating with an oxygen pre-saturated feed. The amount of oxygen available for reaction in the tube-in-tube microreactor was two orders of magnitude higher, as compared to the non-permeable reactor with oxygen pre-saturated feed. The semi-permeable tube reactor performance in terms of both conversion and selectivity was enhanced by increasing the gas pressure, the average residence time of liquid in the bed and by dilution of the catalyst. The highest conversion of benzyl alcohol obtained for the range of conditions investigated was 44.1 %, with 73.0 % selectivity to benzaldehyde, at 120 °C, catalyst contact time 115 g<sub>cat</sub>·s/g<sub>alcohol</sub> and catalyst dilution factor 4.

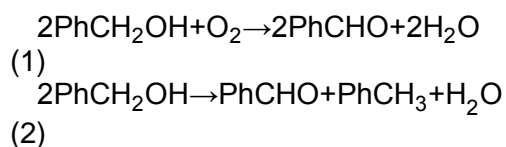
## 1. Introduction

Heterogeneous catalytic gas-liquid reactions are an important category in synthetic chemistry, with great significance for both laboratory research and industrial applications. Conventionally such reactions are performed in a batch reactor, and the phases are brought in contact by mechanical stirring. However, this results in a poorly defined interfacial contact area and renders scale-up more complex<sup>1, 2</sup>. Additionally, the immediate contact of the phases raises safety concerns for hazardous reactions like oxidation reactions. Over the past decade, microreactor technology has emerged as an efficient tool for chemical synthesis<sup>3</sup>. The intrinsic advantages associated with such reactors are the high efficiency of heat and mass transfer, due to the high surface-area-to-volume ratio, as well as the high-resolution reaction time control<sup>1, 2, 4</sup>. The small physical scale can also significantly enhance

safety<sup>5, 6</sup>. Several types of microreactors have been developed for gas-liquid-solid reactions<sup>7</sup>, including the coated-wall microreactor<sup>5</sup>, the packed-bed microreactor<sup>8</sup> and the “slurry Taylor” flow microreactor<sup>9</sup>.

Recently, membrane microreactors have drawn growing interest, as they combine the benefits of both the membrane reactor and the microreactor<sup>10, 11</sup>. Gas and liquid phases can flow separately with a well-defined contacting interface and high mass and heat transfer rates. A tube-in-tube configuration employing a semipermeable Teflon AF-2400 tube as the contact interface for gas and liquid has recently been proposed by Ley's group<sup>12, 13</sup>. This material is permeable to a wide range of gases but is impermeable to liquids. This controlled method of gas/liquid contact could enhance safety, especially for hazardous reactions. Furthermore, due to the transfer process consisting of gas permeation solely through the Teflon AF-2400 tube and the laminar liquid flow, the mass transfer of gas in the tube-in-tube microreactor can be accurately simulated, providing insight into reactor operation<sup>14</sup>. Various gas-liquid reactions have been successfully performed in this type of reactor, such as ozonolysis<sup>12</sup> and hydrogenation<sup>15</sup> of alkenes, synthesis of styrenes using ethylene<sup>16</sup>, carboxylation of Grignard reagents with CO<sub>2</sub><sup>17</sup>. Skowerski *et al.*<sup>18</sup> reported heterogeneous olefin metathesis in a tube-in-tube microreactor through packing the solid catalyst in the annulus between the inner and outer tube and improved yield and selectivity due to the efficient removal of ethylene during the reaction. O'Brien *et al.*<sup>19</sup> carried out three-phase heterogeneous catalytic reactions, where the liquid was first saturated with gas in a tube-in-tube configuration and subsequently reacted in a catalyst packed column. However, with this approach the amount of gas available for the reaction is limited by its solubility in the reaction mixture as it is not supplied in the downstream reaction section<sup>14</sup>. This severely affects the productivity of the tube-in-tube microreactor.

Selective oxidation of alcohols is an important reaction in chemical synthesis<sup>20, 21</sup>, and the aerobic oxidation of benzyl alcohol using molecular oxygen is one of the most intensively studied<sup>5, 6, 22, 23</sup>. A few studies investigated this reaction under flow condition using a gold-based catalyst. Wang *et al.*<sup>5</sup> prepared a gold-immobilized capillary column reactor through cross-linking of copolymer for the oxidation of various alcohols. In our previous studies<sup>8, 24</sup>, silicon-glass micropacked-bed reactors were used for aerobic oxidation of benzyl alcohol, with a Au-Pd/TiO<sub>2</sub> catalyst. Conversions of benzyl alcohol obtained from conventional stirred batch reactor and micropacked reactor were found to be comparable. Oxidation of solvent-free benzyl alcohol on Au-Pd/TiO<sub>2</sub> catalyst is considered to comprise of two main steps<sup>8, 25, 26</sup>, the oxidation reaction (eqn 1) and the disproportionation reaction (eqn 2).



In this work, oxidation of benzyl alcohol was investigated on Au-Pd/TiO<sub>2</sub> catalyst, which was directly packed in a Teflon AF-2400 tube-in-tube microreactor. Thus, the gas transport process and the reaction section were integrated, and gas was supplied as the reaction progressed. Operating parameters were studied, with the aim to understand reactor behaviour and improve its performance.

## 2. Experimental

### 2.1 Catalyst preparation

1 wt% Au-Pd/TiO<sub>2</sub> catalyst with weight ratio of Au to Pd equivalent to 1:19 was used and was prepared by a modified impregnation method as described previously<sup>27, 28</sup>. The gold precursor (HAuCl<sub>4</sub>·3H<sub>2</sub>O, Sigma Aldrich, USA) was dissolved in deionized water to form a solution with a gold concentration of 9.8 mg/mL, and the palladium precursor (PdCl<sub>2</sub>, Sigma Aldrich, USA) was dissolved in a 0.58 M aqueous HCl solution (conc. HCl, diluted using the

requisite amount of deionized water) with vigorous stirring to form a solution with a Pd concentration of 6 mg/mL. Then, the requisite amount of each metal precursor solution was charged into a 50 mL round-bottom flask fitted with a magnetic stirrer bar. The volume of the mixture was adjusted using deionized water to a total volume of 15 mL. The flask was immersed into an oil bath placed on a magnetic stirrer hot plate. The solution was stirred vigorously at 1000 rpm and the temperature of the oil bath was raised from 27 to 60 °C over a period of 10 min. At 60 °C, 1.98 g of the TiO<sub>2</sub> support (Degussa Evonik P25, Germany) was added slowly over a period of 8 to 10 min with constant stirring. After the completion of addition of the support material, the slurry was stirred at 60 °C for an additional 15 min. Following this, the temperature of the oil bath was raised to 95 °C, and the slurry was stirred at that temperature for a further 16 h until all the water evaporated leaving a dry solid. Subsequently the resultant solid powder was transferred into a mortar and pestle and was ground thoroughly to form a uniform mixture. A 400 mg portion of the uncalcined sample was transferred and spread out over a glass calcination boat (13 cm in length). This boat was then placed inside a calcination furnace fitted with an inlet and outlet valve. The temperature of the furnace was raised from 30 to 400 °C at a heating rate of 10 °C/min and then kept at 400 °C for 4 h under a steady flow of 5 % H<sub>2</sub> in Ar. After the furnace was cooled, the resultant solid powder was pelletized, crushed and sieved to the desired particle size range.

## 2.2 Tube-in-tube microreactor set-up

The schematic representation of the tube-in-tube microreactor used in this work is shown in Figure 1. The reactor is comprised of an inner Teflon AF-2400 tube (Biogeneral, USA) and an outer PTFE tube (Agilent, USA). The inner diameter (ID) of the Teflon AF-2400 tube is 0.8 mm, and the outer diameter (OD) is 1.0 mm. The ID and OD of the PTFE tube are 1.59 mm and 3.18 mm, respectively. For the measurement of oxygen permeation, a 100 cm-length tube was used without any packing. For the catalytic oxidation reaction, the total length of the reactor was 30 cm. Packing the inner tube was achieved by placing in the tube outlet a piece of silica wool which was supported by a 5 cm-length stainless steel tube. Au-Pd/TiO<sub>2</sub> catalyst particles (63-75 μm) were sucked into the inner tube by a vacuum pump. The amount of catalyst used in all experiments was 20 mg. The bed length was maintained at ca. 3.0 cm. The catalyst was also mixed with silica beads (63-75 μm) before packing, to investigate the effect of catalyst dilution. The inner semi-permeable tube and the outer PTFE tube were assembled together by a union and a T-piece to make up the tube-in-tube microreactor. The outlet of the inner tube was connected to a 7.9 bara back pressure regulator (Upchurch, USA) (all pressures reported in this study are absolute). The pressure of the gas and liquid phases was monitored by pressure sensors placed upstream of the reactor (Zaiput, USA). The effluent was collected in a small vial which was placed in an ice-water bath. The reactor was immersed in a stirred oil bath, whose temperature was controlled by a hotplate fitted with a thermocouple (Stuart US152, UK). The reaction was carried out at 120 °C. Oxygen was fed in the annulus between the inner and outer tube, and the pressure was maintained by a gas pressure regulator (Swagelok, USA). When the temperature reached the desired value, liquid benzyl alcohol (99.0 %, Sigma-Aldrich, USA) was supplied into the tube-in-tube microreactor by a HPLC pump (Knauer P2.1S, Germany). The temperature of the fluid reached the required reaction temperature before entering the catalyst bed, as observed by temperature measurements inside the inner tube. The collected sample was quantitatively analysed by a gas chromatograph (Agilent 6890, USA) fitted with a HP-INNOWax capillary column and a FID detector. Benzyl alcohol conversion ( $X_{total}$ ) and selectivity (S) of each product were calculated according to the following equations:

$$X_{total} = \frac{C_{alcohol,in} - C_{alcohol,out}}{C_{alcohol,in}} \times 100 \% \quad (3)$$

where  $C_{alcohol,in}$  and  $C_{alcohol,out}$  were the concentration of benzyl alcohol at the inlet and outlet, respectively,

$$S_i = \frac{C_i \cdot v_i}{C_{\text{alcohol, in}} \cdot X_{\text{total}}} \times 100 \% \quad (4)$$

where  $v_i$  was the number of moles of benzyl alcohol giving rise to 1 mole of product  $i$ .

Catalyst contact time was used to characterise the reaction time of benzyl alcohol, and was defined as:

$$\text{CCT} = \frac{\text{Mass of catalyst (g}_{\text{cat}})}{\text{Mass flowrate of benzyl alcohol (g}_{\text{alcohol}}/\text{s)}} \quad (5)$$

For each experiment, at least three samples were collected and the results were averaged. The relative error was less than  $\pm 1.0$  %. Reproducibility of the experiments and the stability of the catalyst were checked every day by a standard run (120 °C, catalyst contact time 115 g<sub>cat</sub>·s/g<sub>alcohol</sub>, gas pressure 6 bara, liquid flow rate 0.01 mL/min, liquid pressure 7.9 bara) and the relative differences were less than  $\pm 2$  %.

For comparison, a PTFE tube with the same ID and length as the Teflon AF-2400 tube was also packed with the same catalyst and tested. Three different feeding modes (shown in Figure 2) were investigated for the PTFE reactor: benzyl alcohol a) exposed to air before use, b) presaturated with oxygen at given gas pressure by an unpacked tube-in-tube contactor, and c) mixed with oxygen. The liquid pressure for the liquid-only-feed design (Figure 2a&b) was kept at 7.9 bara using a fixed back pressure regulator (Upchurch, USA). An adjustable back pressure regulator (Zaiput, USA) was used for the mixed gas/liquid feed design (Figure 2c) to maintain the gas/liquid mixture pressure at 6 bara.

### 3. Results and Discussion

#### 3.1 Oxygen permeation

The amount of oxygen dissolved in benzyl alcohol is an important factor for the evaluation of the tube-in-tube microreactor<sup>14</sup>. When the benzyl alcohol leaves the BPR, the dissolved oxygen escapes from the liquid, due to the pressure difference between the reactor and the outlet. Assuming the residual gas in the fluid at the outlet is the same to that in the inlet (benzyl alcohol presaturated with oxygen at 1 bara and room temperature), the volume of oxygen released per unit volume of benzyl alcohol equates approximately to the oxygen permeated while the liquid is passing through the reactor. This was measured using the traditional burette method<sup>19</sup>. During the measurement, the tube-in-tube microreactor was kept at 120 °C, and the liquid outlet was connected to a burette filled with benzyl alcohol (presaturated with oxygen at 1 bara and room temperature). The duration for collecting a fixed volume of oxygen in the burette was recorded for different liquid flow rates and absolute gas pressures in the annulus. Thus, the outgassing rate of oxygen could be calculated. The average liquid residence time was calculated by the tube length divided by the superficial velocity of the liquid in the inner tube.

From Figure 3, it can be noted that initially the outgassing rate increased gradually with residence time at each set gas pressure, and stabilised after 50 s, indicating saturation of benzyl alcohol with oxygen. O'Brien *et al.*<sup>19</sup> reported a similar behaviour for a hydrogen/dichloromethane system. The final outgassing rates at different gas pressure varied almost linearly with the gas pressure difference (between annulus and burette). These measurements show that the permeation of oxygen through the semi-permeable tube can be altered by changing the liquid residence time and gas pressure.

### 3.2 Performance of different reactors

Reaction experiments of benzyl alcohol were first performed in the packed PTFE tube at 120 °C. Using the substrate without presaturation or mixing with oxygen (Figure 2a), the conversion was very low, just 1.45 % (Table 1a) in the packed PTFE reactor. Equimolar amounts of benzaldehyde and toluene were formed, due to the disproportionation of benzyl alcohol (eqn 2)<sup>8, 25</sup>. Relatively high selectivity to dibenzyl ether was observed, which was formed by the intermolecular dehydration of benzyl alcohol<sup>25</sup>. These results indicate that practically no oxidation reaction was taking place in the absence of oxygen. To test the packed PTFE reactor under oxidative condition, benzyl alcohol was first saturated with oxygen by a tube-in-tube contactor (100 cm long, gas pressure 6 bara, liquid flow rate 0.01 mL/min, Figure 2b). The residence time in the tube-in-tube contactor was about 3000 s, which was long enough for the alcohol to reach saturation. Under this condition, no obvious improvement in conversion was obtained. The main difference between the two feed approaches was the higher selectivity to benzaldehyde compared to toluene. This was due to the additional oxidation of benzyl alcohol (eqn 1), besides the disproportionation reaction, because of the small amount of dissolved oxygen present in the liquid substrate.

These results confirm the two main reactions of the overall oxidation of benzyl alcohol, according to previous studies<sup>8, 24-26</sup>. Benzaldehyde, the target product, is formed by both the oxidation and disproportionation of benzyl alcohol, while another main product, toluene, is only obtained from the disproportionation. We can quantify the amount of benzaldehyde produced by the oxidation, and further calculate the amount of benzyl alcohol consumed by the oxidation reaction ( $X_O$ )<sup>8, 25</sup>:

$$X_O = X_{total} \cdot (S_{benzaldehyde} - S_{Toluene}) \quad (6)$$

This conversion in Table 1b was just 0.07 %. Assuming that all the oxygen dissolved in the liquid flow ( $\sim 0.5 \text{ mL/mL}_{\text{alcohol}}$  estimated from Figure 3) was consumed through oxidation reaction, the theoretical maximum  $X_O$  would be 0.43 %.

Next, the reactor with the catalyst packed in the semi-permeable tube-in-tube microreactor was evaluated (Figure 1). From Table 1c, it can be seen that the conversion of benzyl alcohol increased dramatically compared to the other two approaches at the same reaction temperature and gas pressure. The selectivity to benzaldehyde was about 30 % higher than that of toluene. This improvement in the performance of the tube-in-tube microreactor was due to the increased amount of oxygen participating in the reaction, based on the corresponding  $X_O$ . The amount of consumed oxygen calculated from  $X_O$  is  $12.4 \text{ mL/mL}_{\text{alcohol}}$ , which is ca. 150 times higher than  $0.08 \text{ mL/mL}_{\text{alcohol}}$  calculated for oxygen presaturated benzyl alcohol. Comparing this value ( $12.4 \text{ mL/mL}_{\text{alcohol}}$ ) with the outgassing rate in Figure 3 ( $\sim 0.5 \text{ mL/mL}_{\text{alcohol}}$ ) shows that oxygen permeation during the reaction was enhanced, since an oxygen concentration gradient was sustained across the semi-permeable tube wall. This makes the packed tube-in-tube microreactor more efficient for three-phase reactions compared with non-permeable PTFE reactor configurations with oxygen presaturated feed (Figure 2b).

The amount of benzyl alcohol consumed by the disproportionation reaction can be estimated by subtracting  $X_O$  from  $X_{total}$ . It was 1.78 % for the conditions of Table 1b and 26.6 % for those of Table 1c. This indicates that adding oxygen can accelerate the disproportionation reaction, which agrees well with previous studies that suggest two distinct pathways to disproportionation<sup>25</sup>. Selectivities of other products are also listed in Table 1, and the values were all lower than 2 %.

To further explore the effect of oxygen concentration on the reaction performance, a mixture of oxygen and benzyl alcohol was fed into the packed PTFE reactor (Figure 2c). The gas to liquid volume ratio (at standard temperature and pressure, 0 °C, 1.0 bara) was 100, and the

outlet pressure was kept at 6 bara. Two-phase slug flow was observed upstream of the packed bed. It can be seen from Table 1d that the conversion was two-fold higher than that in the tube-in-tube microreactor, with 12 % higher selectivity to benzaldehyde. The difference between the two approaches clearly indicates the deficiency of oxygen for the packed tube-in-tube microreactor for the conditions of Table 1c. However, the packed tube-in-tube microreactor is intrinsically safer as gaseous oxygen does not come in contact with the organic mixture.

### 3.3 Effect of gas pressure in packed tube-in-tube microreactor

In order to alter the amount of oxygen available for the reaction, the oxidation of benzyl alcohol was carried out with the gas pressure in the annulus changing from 3 to 7 bara. The liquid pressure was maintained at 7.9 bara by the BPR, and the catalyst contact time and reaction temperature were kept the same. The conversion and selectivities of benzyl alcohol ( $S_B$ ) and toluene ( $S_T$ ) are shown in Figure 4; other minor products (not shown) were all lower than 2.0 %. The total conversion of benzyl alcohol increased gradually with the gas pressure. The highest conversion was 41.5 % at 7 bara gas pressure. The same trend was observed for the selectivity to benzaldehyde, which reached 65.1 % at 7 bara. As for the selectivity to toluene, it showed an opposite dependence on the gas pressure, decreasing from 36.2 % to 32.4 %. Similar behaviour was also observed in a batch<sup>26</sup> and packed-bed microreactor<sup>8, 24</sup>. The conversion increased from 78.5 % at 2.1 bara to ca. 95 % at 5 bara, and the selectivity to benzaldehyde increases from 57.7 % to 77.8 % in a packed-bed microreactor with oxygen/alcohol mixture feed<sup>8</sup>.

Additionally,  $X_O$  varied approximately linearly with the gas pressure. This directly proves that more oxygen participated in the reaction at higher gas pressure. Furthermore, it is reasonable to deduce that the oxygen concentration in the liquid was maintained at low level, and the plot of  $X_O$  also quantitatively reflects the amount of oxygen penetrating through the inner tube. Hence, increasing the gas pressure can enhance the oxygen concentration gradient between the annulus and the inner tube, thus more oxygen permeates and results to more benzyl alcohol reacting.

### 3.4 Effect of catalyst contact time in packed tube-in-tube microreactor

The effect of catalyst contact time was investigated by changing the flow rate of benzyl alcohol, keeping the same mass of catalyst. The results are shown in Figure 5. The conversion increased from 26.1 % to 46.9 %, with selectivity to benzaldehyde from 58.6 % to 67.5 %, when catalyst contact time increased from 46  $\text{g}_{\text{cat}} \cdot \text{s} / \text{g}_{\text{alcohol}}$  to 230  $\text{g}_{\text{cat}} \cdot \text{s} / \text{g}_{\text{alcohol}}$ . Correspondingly, the selectivity to toluene decreased from 38.4 % to 29.3 % at the investigated catalyst contact time range. This conversion trend agrees with that in a batch and packed-bed microreactor. However, the selectivities to benzaldehyde and toluene in both batch and microreactor, where oxygen was in excess, remained practically constant with catalyst contact time<sup>8</sup>. The selectivity differences in the tube-in-tube microreactor are probably caused by the insufficient amount of oxygen in the liquid. It should be noted that the plot of  $X_O$  also showed a linear trend. Considering the bed length was the same due to the same amount of catalyst packed, longer catalyst contact time was due to lower flow rate of the liquid, and the average residence time for the liquid through the bed was correspondingly longer. Thus, oxygen had more time to permeate and react due to longer catalyst contact time, and this resulted to increase of the oxygen consumed by the oxidation reaction,  $X_O$ .

### 3.5 Effect of catalyst dilution in packed tube-in-tube microreactor

The effect of catalyst dilution was investigated by diluting the same amount of catalyst with different amounts of silica beads. The catalyst dilution factor is defined as the total mass of catalyst bed (catalyst + silica beads) divided by the mass of catalyst. In this case, catalyst contact time was kept constant (inlet benzyl alcohol flowrate was constant), while the bed length (and hence bed residence time) was changed. The actual bed length was about 3.0 cm for every 20 mg of packing. In Figure 6, reaction performance is shown, when the

catalyst was mixed with the same mass of silica beads (catalyst dilution factor 2). The conversion (42.3 %) and selectivity to benzaldehyde (68.4 %), as well as  $X_{\text{O}}$  (18.1 %) were close to those when catalyst contact time was  $230 \text{ g}_{\text{cat}} \cdot \text{s} / \text{g}_{\text{alcohol}}$  (46.9 %, 67.5 % and 18.0 %). Assuming the porosity of the bed was the same for both conditions, the average residence time for the liquid passing through the bed with the catalyst contact time  $115 \text{ g}_{\text{cat}} \cdot \text{s} / \text{g}_{\text{alcohol}}$  and catalyst dilution factor 2 equaled to that when catalyst contact time was  $230 \text{ g}_{\text{cat}} \cdot \text{s} / \text{g}_{\text{alcohol}}$  and catalyst dilution factor was 1. Thus, the time for oxygen permeation was also the same. However, the main difference was that half of the bed in the former case did not contain catalyst. Therefore, similar results under these two conditions further support that oxygen permeation is a key factor controlling the performance of the tube-in-tube microreactor. Further dilution did not change the total conversion of benzyl alcohol very much, while the selectivity to benzaldehyde increased gradually, as well as the amount of benzyl alcohol converted by oxygen. Notably, the selectivity to benzaldehyde at catalyst dilution factor 4 reached 73.0 %, which is close to the premixed alcohol/oxygen conditions (75.0 %, Table 1d). This also approached the selectivity to benzaldehyde in a micropacked bed reactor (77.8 %, 6 bara gas pressure, gas to liquid volume ratio 200)<sup>8</sup>. Thus, dilution of the catalyst bed allowed increasing the surface area available for oxygen transfer without increasing the oxygen demand by the catalytic bed, resulting in higher conversion and selectivity.

#### 4. Conclusions

A semi-permeable Teflon AF-2400 tube-in-tube microreactor was developed for the continuous solvent-free aerobic heterogeneous oxidation of benzyl alcohol. By comparison with non-permeable PTFE configurations, the packed tube-in-tube microreactor allowed the continuous supply of oxygen during the reaction, and therefore significantly improved both conversion and selectivity. The amount of oxygen that permeated played a vital role in reactor performance. Oxygen permeation increased by increasing the gas pressure and catalyst contact time. By diluting the catalyst, the average residence time of liquid in the bed increased, allowing larger oxygen permeation, also resulting in improved reactor performance. Even though the amount of oxygen available for the reaction was not enough to achieve the same total conversion of benzyl alcohol as in a packed non-permeable PTFE reactor with a mixture of oxygen/benzyl alcohol feed, the selectivity for both reactors was similar. As gas does not come directly into contact with the organic mixture in the packed tube-in-tube microreactor, its intrinsic safety makes this type of reactor promising for wider applications in heterogeneous reactions.

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#### References

1. Elvira, K. S.; i Solvas, X. C.; Wootton, R. C. R.; deMello, A. J., The Past, Present and Potential for Microfluidic Reactor Technology in Chemical Synthesis. *Nat. Chem.* **2013**, *5*, 905-915.
2. Jähnisch, K.; Hessel, V.; Löwe, H.; Baerns, M., Chemistry in Microstructured Reactors. *Angew. Chem. Int. Ed.* **2004**, *43*, 406-446.
3. Pastre, J. C.; Browne, D. L.; Ley, S. V., Flow Chemistry Syntheses of Natural Products. *Chem. Soc. Rev.* **2013**, *42*, 8849-8869.
4. Hartman, R. L.; McMullen, J. P.; Jensen, K. F., Deciding Whether To Go with the Flow: Evaluating the Merits of Flow Reactors for Synthesis. *Angew. Chem. Int. Ed.* **2011**, *50*, 7502-7519.
5. Wang, N.; Matsumoto, T.; Ueno, M.; Miyamura, H.; Kobayashi, S., A Gold-Immobilized Microchannel Flow Reactor for Oxidation of Alcohols with Molecular Oxygen. *Angew. Chem.* **2009**, *121*, 4838-4840.

6. Zotova, N.; Hellgardt, K.; Kelsall, G. H.; Jessiman, A. S.; Hii, K. K., Catalysis in Flow: the Practical and Selective Aerobic Oxidation of Alcohols to Aldehydes and Ketones. *Green Chem.* **2010**, *12*, 2157-2163.
7. Kiwi-Minsker, L.; Renken, A., Microstructured Reactors for Catalytic Reactions. *Catal. Today* **2005**, *110*, 2-14.
8. Cao, E. H.; Sankar, M.; Firth, S.; Lam, K. F.; Bethell, D.; Knight, D. K.; Hutchings, G. J.; McMillan, P. F.; Gavriilidis, A., Reaction and Raman Spectroscopic Studies of Alcohol Oxidation on Gold-Palladium Catalysts in Microstructured Reactors. *Chem. Eng. J.* **2011**, *167*, 734-743.
9. Liedtke, A.-K.; Bornette, F.; Philippe, R.; de Bellefon, C., Gas-Liquid-Solid "Slurry Taylor" Flow: Experimental Evaluation through the Catalytic Hydrogenation of 3-methyl-1-pentyn-3-ol. *Chem. Eng. J.* **2013**, *227*, 174-181.
10. Noël, T.; Hessel, V., Membrane Microreactors: Gas-Liquid Reactions Made Easy. *ChemSusChem* **2013**, *6*, 405-407.
11. Tan, X.; Li, K., Membrane Microreactors for Catalytic Reactions. *J. Chem. Technol. Biotechnol.* **2013**, *88*, 1771-1779.
12. O'Brien, M.; Baxendale, I. R.; Ley, S. V., Flow Ozonolysis Using a Semipermeable Teflon AF-2400 Membrane To Effect Gas-Liquid Contact. *Org. Lett.* **2010**, *12*, 1596-1598.
13. Petersen, T. P.; Polyzos, A.; O'Brien, M.; Ulven, T.; Baxendale, I. R.; Ley, S. V., The Oxygen-Mediated Synthesis of 1,3-Butadiynes in Continuous Flow: Using Teflon AF-2400 to Effect Gas/Liquid Contact. *ChemSusChem* **2012**, *5*, 274-277.
14. Yang, L.; Jensen, K. F., Mass Transport and Reactions in the Tube-in-Tube Reactor. *Org. Process Res. Dev.* **2013**, *17*, 927-933.
15. Mercadante, M. A.; Kelly, C. B.; Lee, C.; Leadbeater, N. E., Continuous Flow Hydrogenation Using an On-Demand Gas Delivery Reactor. *Org. Process Res. Dev.* **2012**, *16*, 1064-1068.
16. Bourne, S. L.; Koos, P.; O'Brien, M.; Martin, B.; Schenkel, B.; Baxendale, I. R.; Ley, S. V., The Continuous-Flow Synthesis of Styrenes Using Ethylene in a Palladium-Catalysed Heck Cross-Coupling Reaction. *Synlett* **2011**, 2643-2647.
17. Polyzos, A.; O'Brien, M.; Petersen, T. P.; Baxendale, I. R.; Ley, S. V., The Continuous-Flow Synthesis of Carboxylic Acids Using CO<sub>2</sub> in a Tube-In-Tube Gas Permeable Membrane Reactor. *Angew. Chem. Int. Ed.* **2011**, *50*, 1190-1193.
18. Skowerski, K.; Czarnocki, S. J.; Knapkiewicz, P., Tube-In-Tube Reactor as a Useful Tool for Homo- and Heterogeneous Olefin Metathesis under Continuous Flow Mode. *ChemSusChem* **2014**, *7*, 536-542.
19. O'Brien, M.; Taylor, N.; Polyzos, A.; Baxendale, I. R.; Ley, S. V., Hydrogenation in Flow: Homogeneous and Heterogeneous Catalysis Using Teflon AF-2400 to Effect Gas-Liquid Contact at Elevated Pressure. *Chem. Sci.* **2011**, *2*, 1250-1257.
20. Hashmi, A. S. K.; Hutchings, G. J., Gold Catalysis. *Angew. Chem. Int. Ed.* **2006**, *45*, 7896-7936.
21. Della Pina, C.; Falletta, E.; Prati, L.; Rossi, M., Selective oxidation using gold. *Chem. Soc. Rev.* **2008**, *37*, 2077-2095.
22. Kesavan, L.; Tiruvalam, R.; Rahim, M. H. A.; bin Saiman, M. I.; Enache, D. I.; Jenkins, R. L.; Dimitratos, N.; Lopez-Sanchez, J. A.; Taylor, S. H.; Knight, D. W.; Kiely, C. J.; Hutchings, G. J., Solvent-Free Oxidation of Primary Carbon-Hydrogen Bonds in Toluene Using Au-Pd Alloy Nanoparticles. *Science* **2011**, *331*, 195-199.
23. Obermayer, D.; Balu, A. M.; Romero, A. A.; Goessler, W.; Luque, R.; Kappe, C. O., Nanocatalysis in Continuous Flow: Supported Iron Oxide Nanoparticles for the Heterogeneous Aerobic Oxidation of Benzyl Alcohol. *Green Chem.* **2013**, *15*, 1530-1537.
24. Cao, E. H.; Sankar, M.; Nowicka, E.; He, Q.; Morad, M.; Miedziak, P. J.; Taylor, S. H.; Knight, D. W.; Bethell, D.; Kiely, C. J.; Gavriilidis, A.; Hutchings, G. J., Selective Suppression of Disproportionation Reaction in Solvent-less Benzyl Alcohol Oxidation Catalysed by Supported Au-Pd Nanoparticles. *Catal. Today* **2013**, *203*, 146-152.
25. Sankar, M.; Nowicka, E.; Tiruvalam, R.; He, Q.; Taylor, S. H.; Kiely, C. J.; Bethell, D.; Knight, D. W.; Hutchings, G. J., Controlling the Duality of the Mechanism in Liquid-Phase



Oxidation of Benzyl Alcohol Catalysed by Supported Au-Pd Nanoparticles. *Chem. Eur. J.* **2011**, *17*, 6524-6532.

26. Meenakshisundaram, S.; Nowicka, E.; Miedziak, P. J.; Brett, G. L.; Jenkins, R. L.; Dimitratos, N.; Taylor, S. H.; Knight, D. W.; Bethell, D.; Hutchings, G. J., Oxidation of Alcohols Using Supported Gold and Gold-Palladium Nanoparticles. *Faraday Discuss.* **2010**, *145*, 341-356.

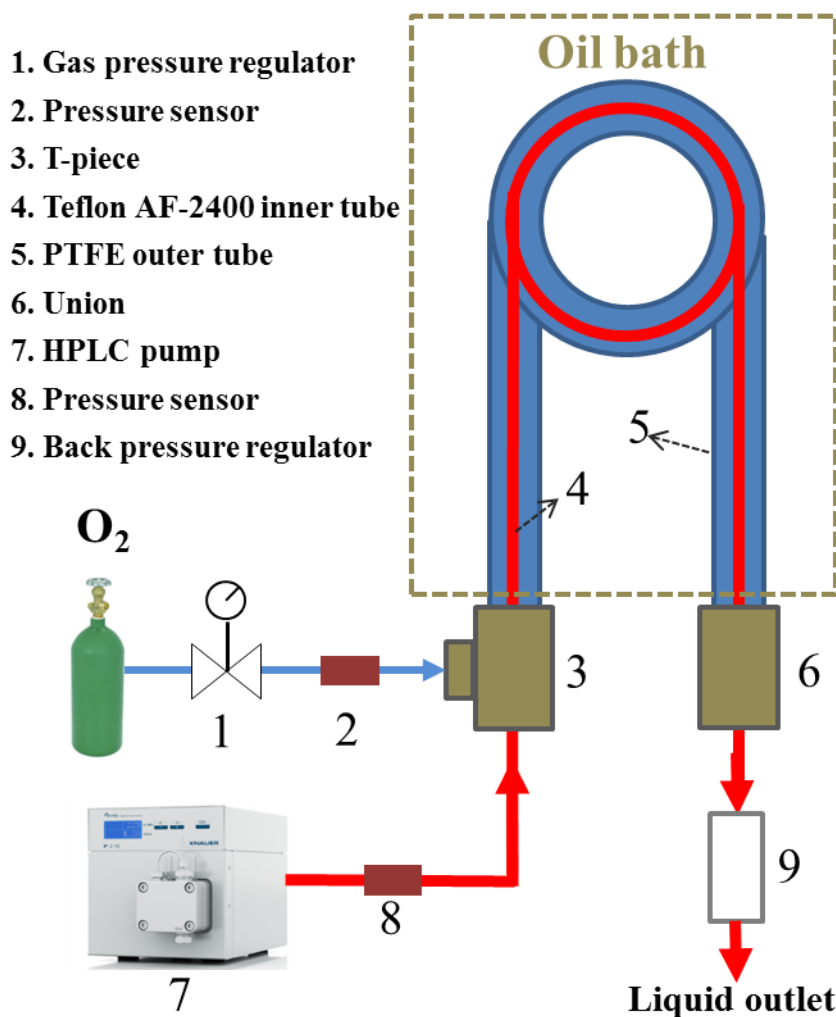
27. Morad, M.; Sankar, M.; Cao, E.; Nowicka, E.; Davies, T. E.; Miedziak, P. J.; Morgan, D. J.; Knight, D. W.; Bethell, D.; Gavriilidis, A.; Hutchings, G. J., Solvent-free Aerobic Oxidation of Alcohols Using Supported Gold Palladium Nanoalloys Prepared by a Modified Impregnation Method. *Catal. Sci. Tech.* **2014**, *4*, 3120-3128.

28. Sankar, M.; He, Q.; Morad, M.; Pritchard, J.; Freakley, S. J.; Edwards, J. K.; Taylor, S. H.; Morgan, D. J.; Carley, A. F.; Knight, D. W.; Kiely, C. J.; Hutchings, G. J., Synthesis of Stable Ligand-free Gold-Palladium Nanoparticles Using a Simple Excess Anion Method. *ACS Nano* **2012**, *6*, 6600-6613.

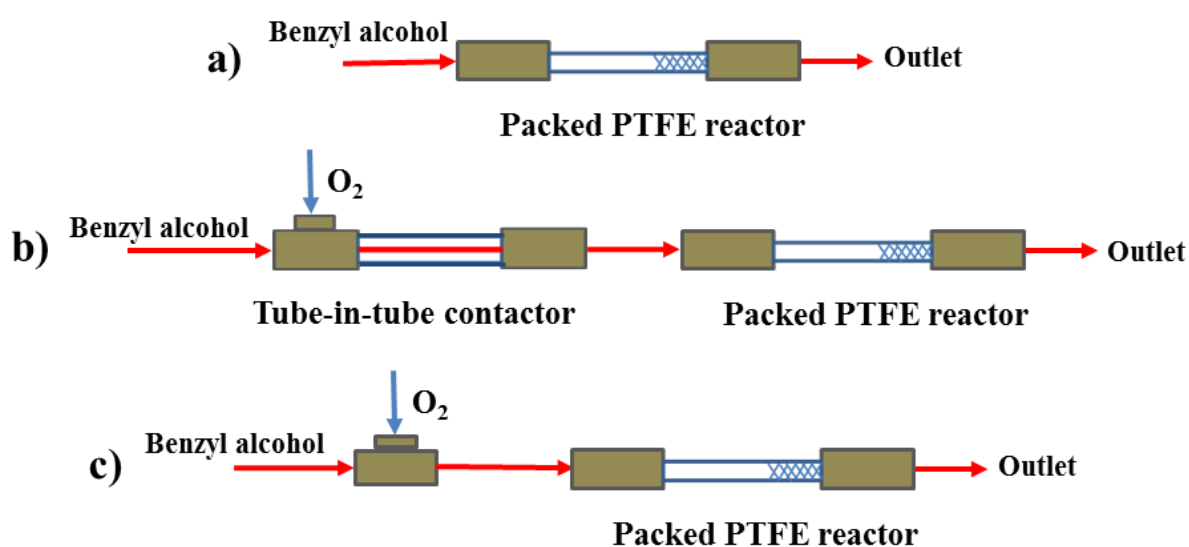
**Table 1** Conversions and selectivities (%) of oxidation of benzyl alcohol in different reactors. Reaction conditions: 120 °C, catalyst contact time 115 g<sub>cat</sub>\*s/g<sub>alcohol</sub>, liquid flow rate 0.01 mL/min, gas pressure 6 bara, catalyst dilution factor 1.

Reaction conditions	X <sub>Total</sub>	X <sub>O</sub>	S <sub>Benzaldehy</sub> de	S <sub>Toluen</sub> e	S <sub>Benzen</sub> e	S <sub>Dibenzyl ether</sub>	S <sub>Benzoic</sub> acid	S <sub>Benzyl benzoate</sub>
a	1.45	0.01	40.6	40.0	0	17.6	0.32	1.51
b	1.85	0.07	44.5	40.8	0	14.2	0	0.48
c	37.3	10.7	63.1	34.4	0.74	0.98	0.23	0.65
d	78.1	45.8	75.0	16.4	0.08	0.36	1.04	7.34

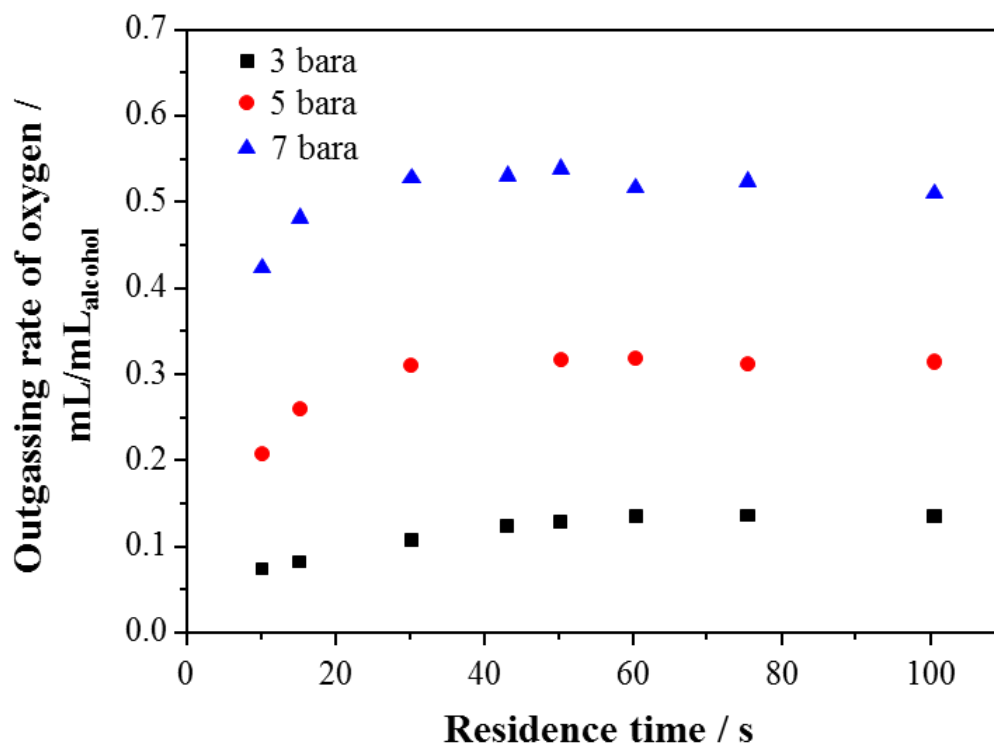
a: Reaction in packed bed PTFE reactor with benzyl alcohol exposed to air before use, liquid pressure 7.9 bara;  
b: Reaction in packed bed PTFE reactor with benzyl alcohol presaturated with oxygen at 6 bara gas pressure, liquid pressure 7.9 bara;  
c: Reaction in packed bed tube-in-tube microreactor, liquid pressure 7.9 bara;  
d: Reaction in packed bed PTFE reactor with mixture of oxygen and benzyl alcohol feed, liquid pressure 6.0 bara.



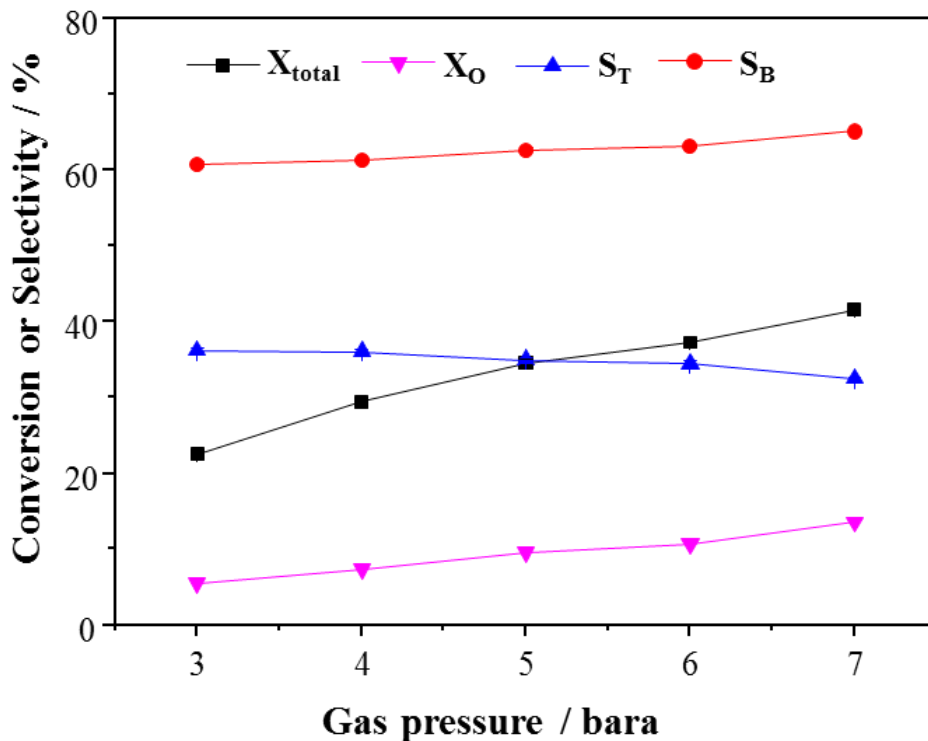
**Figure 1** Schematic of the Teflon AF-2400 tube-in-tube microreactor set-up.



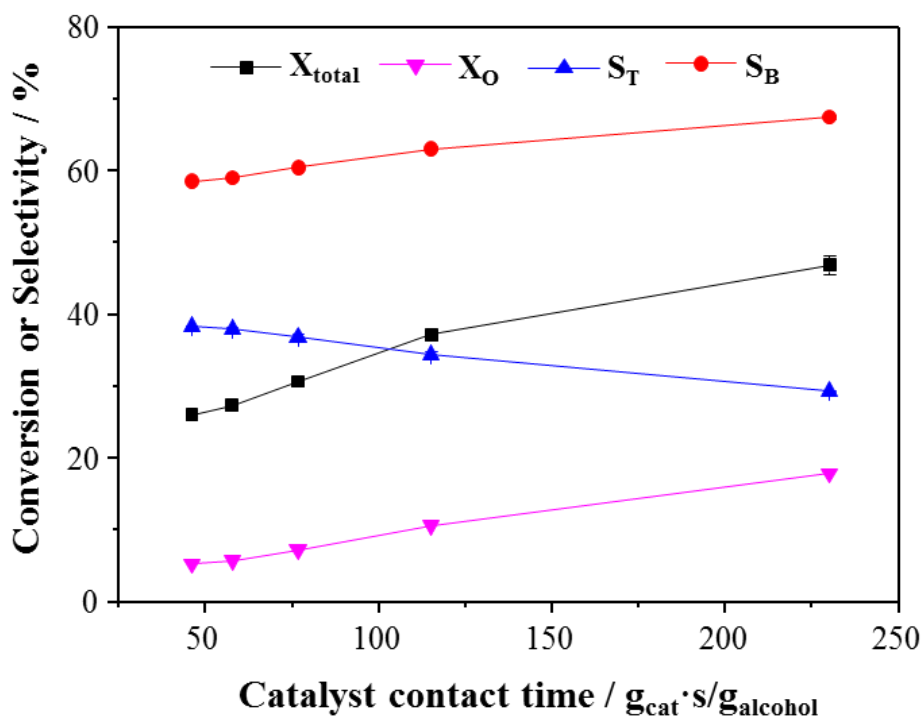
**Figure 2** Packed bed PTFE reactors with different gas/liquid feed. a) Benzyl alcohol exposed to air before use; b) Benzyl alcohol presaturated with oxygen by a tube-in-tube contactor; c) Mixture of oxygen and benzyl alcohol.



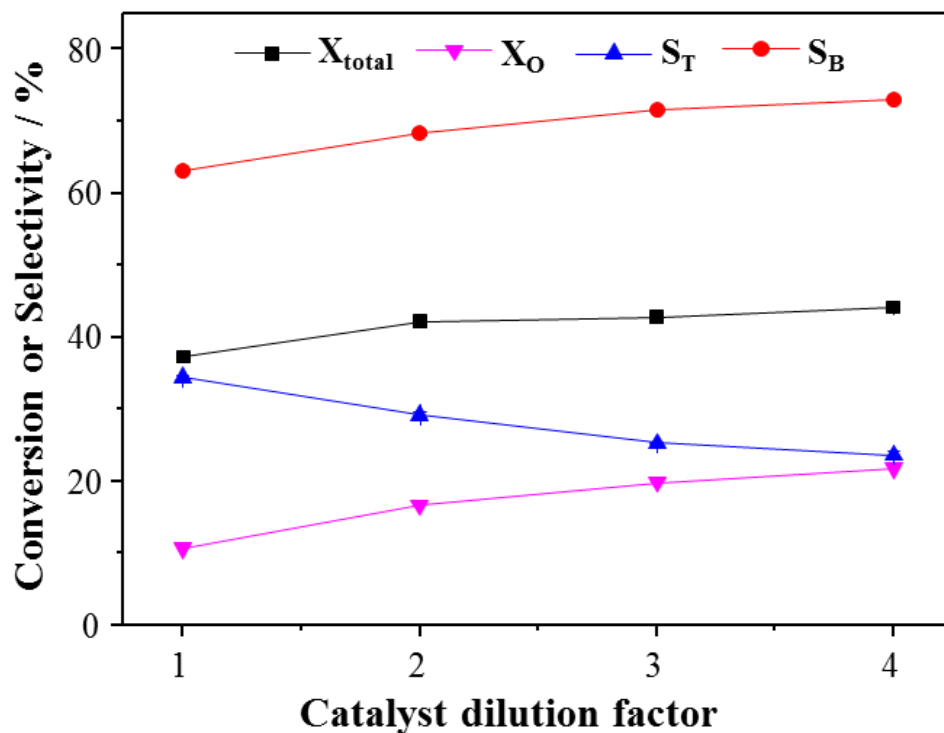
**Figure 3** Outgassing rate of oxygen as a function of residence time and gas pressure in the annulus. Liquid pressure 7.9 bara, temperature of the tube-in-tube microreactor 120 °C.



**Figure 4** Effect of gas pressure in the annulus on the conversion and selectivities during benzyl alcohol oxidation. Reaction conditions: catalyst contact time 115 g<sub>cat</sub>·s/g<sub>alcohol</sub>, liquid flow rate 0.01 mL/min, reaction temperature 120 °C, liquid pressure 7.9 bara, catalyst dilution factor 1. X<sub>total</sub> = Total benzyl alcohol conversion, X<sub>O</sub> = Benzyl alcohol conversion through oxidation reaction, S<sub>T</sub> = Selectivity to toluene, S<sub>B</sub> = Selectivity to benzaldehyde.



**Figure 5** Effect of catalyst contact time on the conversion and selectivities during benzyl alcohol oxidation. Reaction conditions: gas pressure in the annulus 6 bara, reaction temperature 120 °C, liquid pressure 7.9 bara, catalyst dilution factor 1.  $X_{\text{total}}$  = Total benzyl alcohol conversion,  $X_{\text{O}}$  = Benzyl alcohol conversion through oxidation reaction,  $S_{\text{T}}$  = Selectivity to toluene,  $S_{\text{B}}$  = Selectivity to benzaldehyde.



**Figure 6** Effect of catalyst dilution on the conversion and selectivities during benzyl alcohol oxidation. Reaction conditions: catalyst contact time  $115 \text{ g}_{\text{cat}} \cdot \text{s} / \text{g}_{\text{alcohol}}$ , liquid flow rate  $0.01 \text{ mL/min}$ , gas pressure in the annulus  $6 \text{ bara}$ , liquid pressure  $7.9 \text{ bara}$ , reaction temperature  $120 \text{ }^\circ\text{C}$ .  $X_{total}$  = Total benzyl alcohol conversion,  $X_O$  = Benzyl alcohol conversion through oxidation reaction,  $S_T$  = Selectivity to toluene,  $S_B$  = Selectivity to benzaldehyde.