

Safety Study of Single-Phase Aerobic Oxidations in 3D-Printed Reactors

Frederik Norman^{a*}, Lana Borukhova^b, Raf Reintjens^b, Bas Ritzen^b, Dennis Heemkerk^b, Tom Segers^a, Filip Verplaetsen^a

^aAdinex NV, Brouwerijstraat 11, 2200 Noorderwijk, Belgium,

^bInnosyn BV, Urmonderbaan 22, 6167 RD Geleen, the Netherlands
frederik.norman@adinex.be

Molecular oxygen is a green, inexpensive and very abundant oxidant on earth. Until recently, classical oxidations were executed using toxic (in)organic oxidants such as CrO₃, KMnO₄, MnO₂, activated DMSO (Dimethyl sulfoxide) and bleach. Recent social concerns regarding the environmental impact and sustainability of chemical processes have shifted the attention to green alternatives. O₂ fits this role perfectly, as it is readily available, non-toxic, and displays high atom economy in oxidation reactions.

New advances in reactor technologies have made it possible to perform continuous aerobic oxidations in flow reactors. Performing chemistry in continuous flow reactors offers significant improvements over batch reactors regarding mixing, heat transfer, ease of pressurization, scalability, and more (Gavriilidis et al., 2016). The exothermic nature of aerobic oxidations can be controlled using the superior heat transfer of flow reactors, and the oxygen pressure in the reaction medium can be easily increased to increase the oxygen concentration, thus boosting reaction productivity.

In order to operate safely the continuous aerobic oxidation of acetonitrile and oxygen inside the micro 3D-printed reactors at elevated pressures and temperature, a safety study was performed. 3D-printed reactors can safely withstand up to 100 bar system pressure. The safety tests were performed in an autoclave filled with 5 gr of pure acetonitrile and pressurized with a respective oxygen pressure of 20, 48 and 102 bar. The autogenous ignition temperature (AIT) was determined according to ISO 11114-3 at different conditions as a safety limit for the continuous flow set-up.

1. Introduction

Oxidation chemistry using pure oxygen as oxidant has already been studied in the pharmaceutical and fine chemical industry. However, due to associated productivity issues and safety concerns, oxidations using pure oxygen have not been widely implemented yet. Although liquid-phase aerobic oxidations generally take 5 to 30 minutes for sufficient conversion, this does not hold true for aerobic oxidations in batch reactors. Not only is the reaction rate limited by the mass transfer rate of oxygen to the liquid phase, the reactor headspace is filled with oxygen, which produces several safety concerns. Glace et al. (2020) reported that as a result, diluted concentrations of oxygen were used (5-10 v/v% O₂/N₂) to cope with the hazardous nature of the gas phase, which in turn drastically decreases the reaction productivity (5-41 hours to achieve an acceptable conversion). The exothermic nature of aerobic oxidations can be controlled using the superior heat transfer of flow reactors (Lavric and Cerato-Noyerie 2012), and the oxygen pressure in the reaction medium can be easily increased to increase the oxygen concentration, thus boosting reaction productivity.

The proposed approach is built on the work of Stahl (Hill 2013). The goal of the study was to investigate the feasibility of aerobic oxidation as a continuous process in terms of safety and productivity. Herein, we describe a green method where close to stoichiometric amounts of oxygen is used in combination with modest catalyst loadings to afford the conversion of alcohols to oxygen. The process results in increased spacetime yield improving the foot print. Oxidation of benzyl alcohol in acetonitrile served as a model reaction during initial

parameter screening and further optimization. Rather simple setup shown in Figure 1 demonstrated fast solubility of oxygen at room temperature.

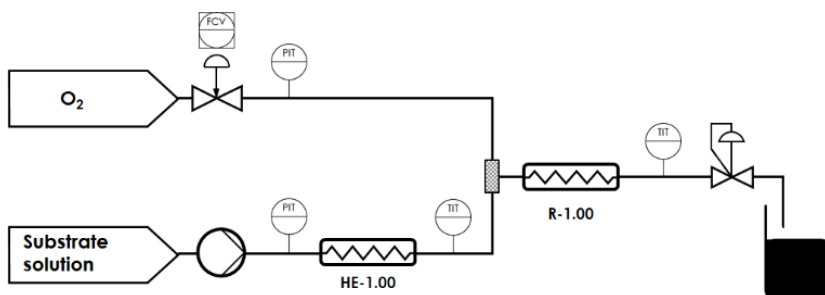
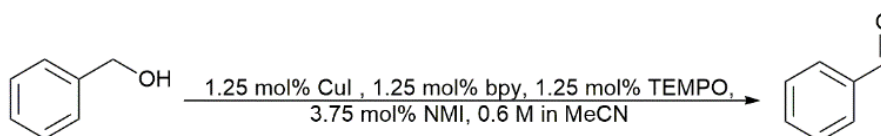


Figure 1. Simplistic view of continuous flow setup*. *A detailed process and instrumentation diagram can be found in (Hill 2013)

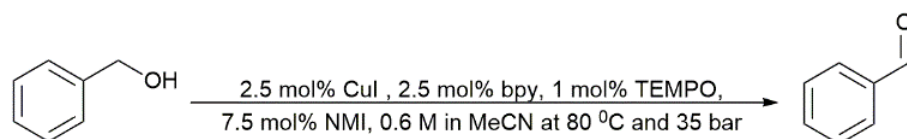
Table 1. Parameter screening of Benzyl alcohol oxidation (bpy =2,2'-bipyridine; TEMPO =Tetramethylpiperidine-1-oxyl ; NMI = N-methylimidazole)



Entry	O ₂ excess (mol %)	T (°C)	p (bar)	τ (min)	Conversion(%)
1	-50	80	20	1	44
2	-20	80	20	1	64
3	0	80	10	1	46
4*	0	80	20	1	67
5	0	100	20	1	58
6*	0	100	35	1	66
7	-20	100	35	2	71
8	0	100	35	2	82

Table 1 shows the results obtained under conditions where all oxygen was dissolved and reactor operated as a single phase system. Thus, at higher pressures due to the higher solubility of oxygen higher conversions were reached. Longer residence times similarly lead to higher conversions at otherwise same conditions. Increasing the temperature, however, led to a decrease in conversion. This observation could be a result of thermal instability of TEMPO (Tetramethylpiperidine-1-oxyl). Ciriano et al. (1999) have reported the conversion of the TEMPO-nitroxyl-group to its amine at 380 K, which would result in a loss of catalyst activity. Thus, catalyst decomposition may be the cause for the loss in yield.

In an industrial setting, it is important that all oxygen is dissolved in the solvent, so that potential hazards of gaseous oxygen are removed. The flow of oxygen was chosen in such a way that the solution was nearing its saturation limit with respect to oxygen (MeCN as solvent, 35 bar). The maximum substrate concentration was 0.6M. Figure 2 shows the results from the screening of oxygen excess effect on the oxidation. It appears that 20 mol% excess of oxygen with respect to benzyl alcohol is needed to reach full conversion within 4 minutes residence time.



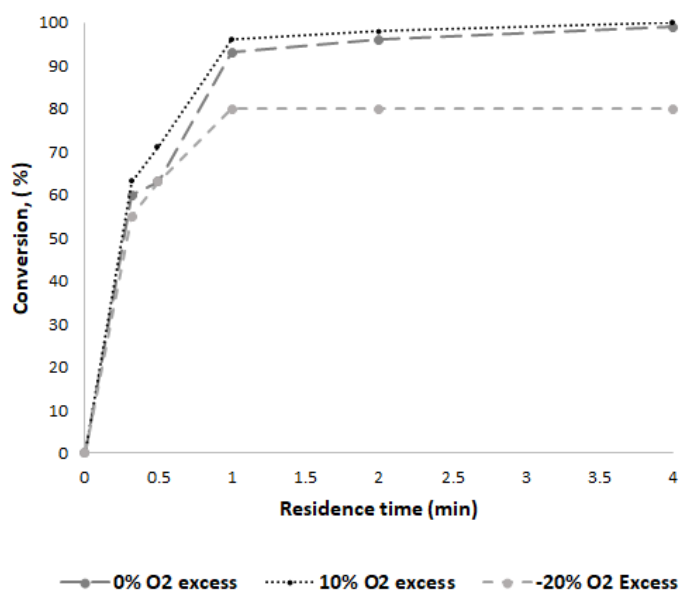


Figure 2. Conversion in function of oxygen excess.

3D printed zig-zag reactor

How it looks like:
inside and outside

Zig-zag assures turbulent (non-laminar) flow despite the commercially relevant millimeter diameter scale of the tube

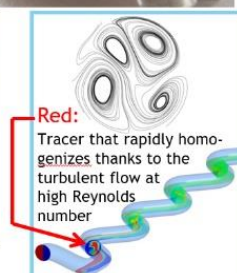
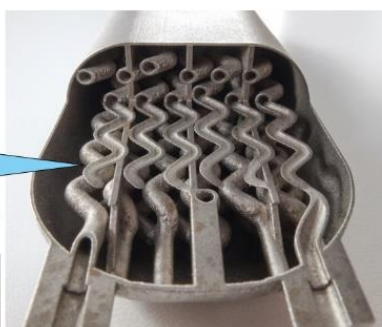


Figure 3. 3D printed reactors used as heat exchangers and reactors within the study.

2. Safety Study

A safety study of acetonitrile as a solvent under pressurized oxygen atmosphere was performed in order to determine the operational limits of the potential system. 3D-printed reactors, see Figure 3, can safely withstand up to 100 bar system pressure. The safety tests were performed in an autoclave filled with 5 gr of pure acetonitrile and pressurized with a respective oxygen pressure of 20, 48 and 102 bar. The autogenous ignition temperature (AIT) was determined according to ISO 11114-3 (2010) at different conditions as a safety limit for the continuous flow set-up. Tests were performed under isochoric (constant volume) conditions. The AIT is defined as the lowest temperature at which a sample reacts with the oxygen and/or decomposes exothermally in the absence of any ignition source. Figure 4 shows the setup used in the measurements.



Figure 4. Photograph of a setup assembly a) 5 g Acetonitrile in glass tube, b) Mini-autoclave set-up inside heating block.

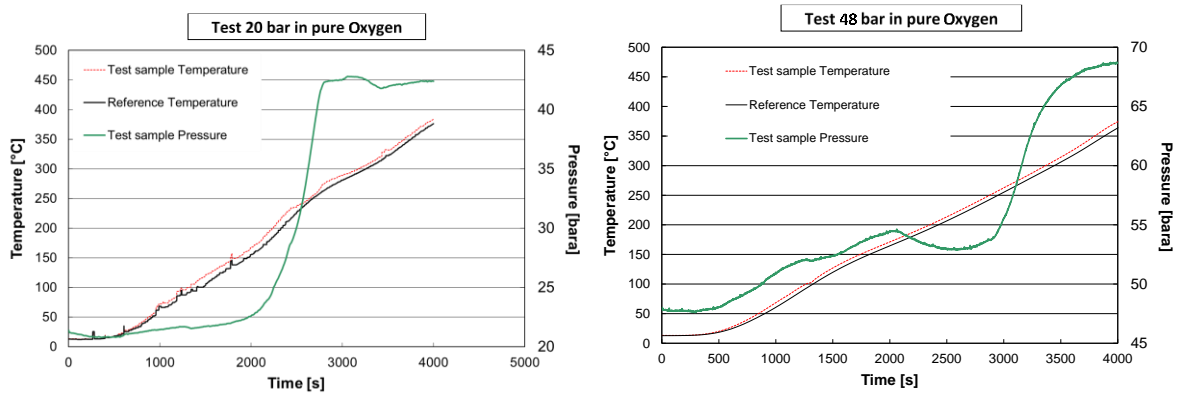


Figure 5. Autogenous ignition test curve at an oxygen pressure of 20 bara (5a) and 48 bara (5b)

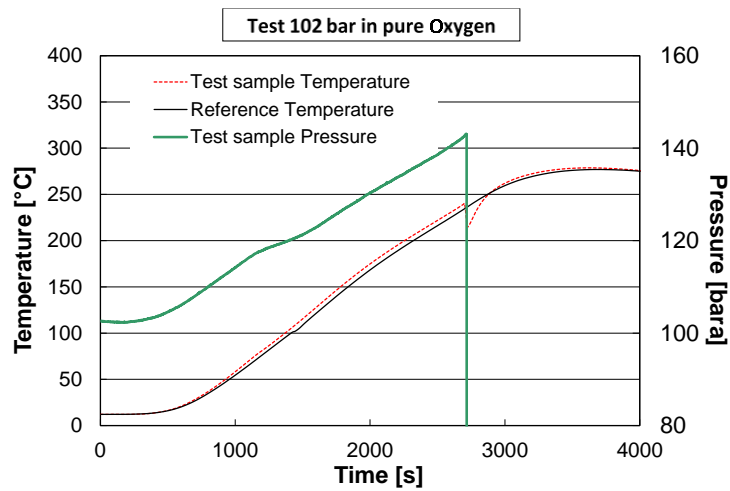


Figure 6. Autogenous ignition test curve at an oxygen pressure of 102 bara

The measured AIT values for tested pressure levels are shown in Table 2. Both 20 and 48 bar overpressure resulted in smooth and expected pressure increases due to the thermal expansion under isochoric conditions as temperature increased from 25 to 350 °C, see Figure 5a and 5b. When the sample pressurized to 100 bar was heated in the similar dynamic manner of 5 K/min, loss of containment (LOC) occurred at 235 °C, see Figure 6 and 7. The upper valve and pressure transducer with a maximum pressure of 350 bar was destroyed by the loss of containment, see Figure 7.

Table 2. *Autogenous Ignition temperature of acetonitrile under oxygen pressure*

Test	Overpressure [bar]	Autogenous ignition temperature (AIT) (°C)
1	20	> 350
2	48	> 350
3	100	235



Figure 7: Photograph of the pressure transducer affected by the loss of containment at 100 bar at 235 °C.

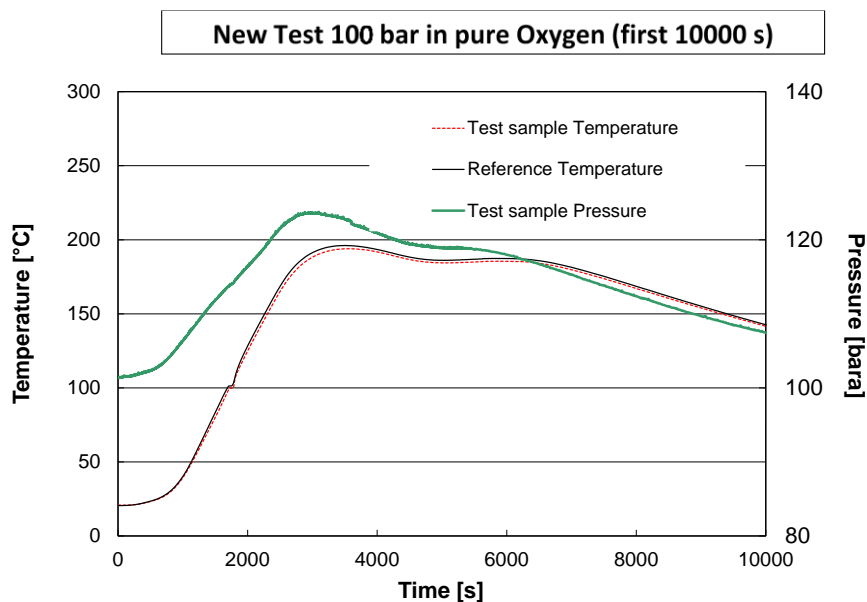


Figure 8 Autogenous ignition test curve at an Oxygen pressure of 100 bara and 186 °C (30 min)

As next, the test was repeated with heating up to 196 °C, with subsequent equilibration and isothermal hold at minimum 186 °C for 30 min, see Figure 8. As such, the system remained under pressure and no ignition or LOC was observed. Under the tested conditions, it can be concluded that a pressure of 100 bar, 186 °C is a safe operating condition without autogenous ignition of the acetonitrile/oxygen mixture.

Continuous flow processes are open systems with reactants flowing in and out. With a system pressure of 100 bar any gradual pressure build-up would take place at the outlet of the reactor. However, in case of detonation the acceleration of the pressure build-up would affect the entire system as a whole and the relief would occur at the most stressed (weakest) point of the assembly.

Here, flow processes provide the safety advantage due to their small operating volume. Based on the information gathered we can conclude that safe operation of aerobic processes in acetonitrile under pure oxygen pressure of 100 bar is safe at temperature up to 150 °C in once-flow through systems. In this study only the reaction of acetonitrile with oxygen is studied. Attention must be paid if other exothermic reactions with other chemicals can take place or higher safety margins must be applied.

3. Conclusions

The focus of the project was on the development of a safe and productive single-phase process. A reactor setup was successfully developed in the initial phases, taking into account elements such as safety and productivity. Benzaldehyde was successfully produced in the reactor with 89% yield using 10% excess O₂, $\tau = 1$ min, 80 °C and 35 bar at a substrate concentration of 0.6 M.

The safety study revealed that at a pressure of 20 or 48 bar the autogenous ignition temperature of acetonitrile under pure oxygen is higher than 350°C. At a pressure of 100 bar autogenous ignition or loss of containment was observed at a temperature of 235°C. It can be concluded that a safe operation of aerobic processes in acetonitrile under pure oxygen pressure of 100 bar is safe at temperature up to 150 °C.

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