Real-time Monitoring of Reaction Synthesis using an NMR Spectroscopy in Micro-flow Reactor Platform

Hemalaxmi Rajavelu[1], Sridharakumar Narasimhan[1]*, Nirav P Bhatt[2]

1 Department of Chemical Engineering, Indian Institute of Technology Madras, India;

2 Department of Biotechnology, Indian Institute of Technology Madras, India;

**sridharkrn@iitm.ac.in*

Highlights

- An automated flow reactor setup for real-time process monitoring and kinetic modelling.
- In-house built syringe pump assembly for automated reagent delivery.
- Online NMR spectroscopy for real- time product characterization.
- Process monitoring of the methylacetate synthesis.

1. Introduction

The discovery of chemical reactions is a time-consuming and expensive process. An automated Chemical reactor system controlled by an ML algorithm can quickly explore the space of chemical reactions in a well-trained manner [1]. The current work proposes a system for automated synthesis of chemical reactions and online analytical tools that can perform reactions quickly and real-time reaction monitoring for the further prediction of optimal reaction conditions like reaction time, stoichiometric ratio, temperature, and pressure. This approach helps to effectively navigate through the chemical reactions compared to the conventional way of performing it manually. For such an automated system, flow micro-reactors are the best option where the reagent is delivered to the reactor, and the product delivered by the reactor for online analysis happens continuously without any manual intervention. A programmable reagent delivery system connected to the flow microreactor ensures to explore the chemical reactions under different reaction times and stoichiometric ratios of reagents. Further, integration of benchtop low-field NMR spectroscopy can perform online real-time analysis of products and generate datasets required for process monitoring [2].

The present work approach can develop a much more robust and reliable system for automated reaction monitoring and kinetic study of chemical reactions. Also, eliminating human involvement thereby preserves the data quality that is crucial for kinetic study and process optimization. Hence, the present work will employ the proposed automated reactor system for the methyl acetate synthesis and study its performance by continuous monitoring [3].

2. Methods

Figure 1 shows the schematic of the automated reactor platform controlled via the LabView interface. The syringe pump assembly will perform the purpose of a reagent delivery system which can have control over the flow rate of reagents; thereby controlling the reaction time and stoichiometric ratio of the reagents. The reagent delivery system is expected to deliver the reagents into the continuous flow microcell (CFMC) and the product from the CFMC will be directed to the NMR probe. The NMR spectroscopy analyzes products delivered from CFMC and generates data in real time. For the automated synthesis of MeOAc, two syringe pumps have been separately filled with HOAc and the mixture of MeOH and sulphuric acid. Both the syringe pumps with HOAc and MeOH have been run at different flow rates corresponding to the stoichiometry ratio of 1:2.5, respectively. The sum flow rate of two pumps was varied between 0.5 to 1.9 mlpm, to study the reaction dynamics at different flow rates by keeping the stoichiometry ratio the same. At the end of each reaction, the corresponding NMR spectrum

has been saved automatically to a remote computer. Finally, a Python code will analyze the collected NMR spectrum and determine the concentration profile of the flow reactions.

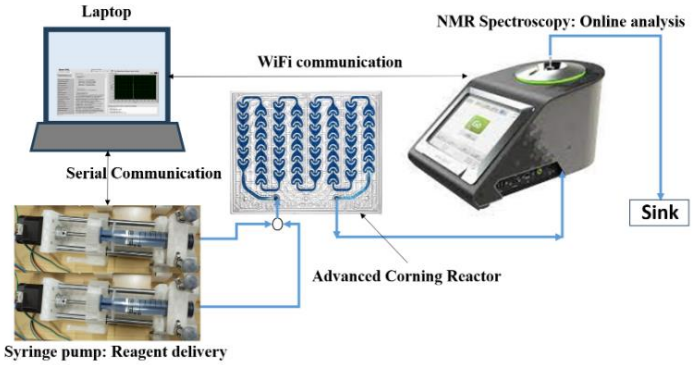

Figure 1. Schematic representation of automated reactor.

3. Results and discussion

Figure 2 shows the concentration profile of both the product (MeOAc) and reactant (MeOH). It is observed that, at longer residence time, the slowest flow rates produce more product quantity than the smaller residence time. At the longer residence time, both the product and reagent concentrations attain steady state value, because of the reversible nature of the reaction [24]. This is because the reactants were allowed with enough time for efficient mixing. Similar experimental data, at different reagent ratios, catalyst concentrations, and reaction temperatures also be studied with the current setup.

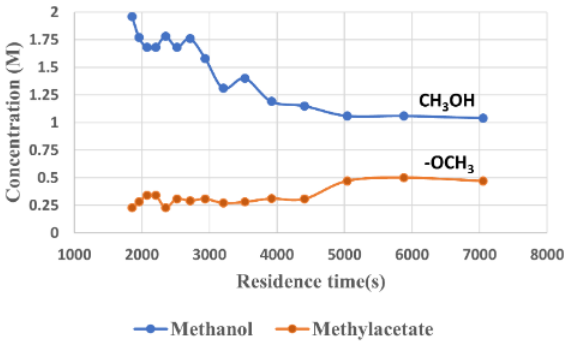

Figure 2. Concentration profiles of Methanol and Methyl acetate as a function of residence time.

4. Conclusions

The automated process monitoring setup has been built with an in-house built programmable syringe pump, micro flow reactor, and online NMR spectrometer with LabView control. Synthesis of methylacetate by the methanolysis of acetic acid reaction has been demonstrated successfully for automated process monitoring applications. Further, work will be focused on the development of automated kinetic modeling of chemical reactions.

References

[1] Volk, A. A., Abolhasani, *Trends Chem. 3*(7) (2021) 519-522
[2] Friebel, A., von Harbou, E., Münnemann, K., & Hasse, H. Ind. amp; Eng. Chem. Res *58*(39) (2019) 18125-18133.
[3] Ganesh, B., Rani, K. Y., Satyavathi, B., & Venkateswarlu, C. H. Int. J. Chem. Kinet. *43*(5) (2011) 263-277.

Keywords: Automated synthesis, real-time reaction monitoring, online NMR, Methylacetate.