AN INTELLIGENT MICROREACTOR SYSTEM FOR REAL-TIME OPTIMIZATION OF A CHEMICAL REACTION

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ABSTRACT

We have developed a silicon microreactor system with online temperature and concentration monitoring, and have integrated this system with control and optimization algorithms to perform real-time, automated optimization of a chemical reaction network. We have demonstrated this principle experimentally by implementing an optimization algorithm to determine the optimal operating conditions of a series reaction.

KEYWORDS: Integrated microreactor, real-time optimization, reactions in series

INTRODUCTION

The ability to perform a myriad of chemical syntheses and the ease of integrating physical and chemical sensors makes silicon microreactor technology an ideal platform for automation of accurate optimization studies, as recently demonstrated for the synthesis of cadmium selenium nanoparticles [1]. In the current work, we expand automated optimization with microreactor technology to the field of chemical synthesis by performing multiple parameter (e.g. temperature, reactant concentration, reaction time) optimization for a series reaction. Furthermore, to reduce experimental set-up and analysis time, we automate other typical experimental procedures such as generating calibration curves and performing a preliminary search of the parameter space for initial conditions suitable for the optimization procedure.

BACKGROUND

The oxidation of benzyl alcohol to benzaldehyde with further oxidation to benzoic acid (Figure 1) served as model chemistry for demonstrating real-time optimization in microchemical systems. In addition to reaction temperature and time, both reactions are dependent on the concentrations of the aromatic compound, the chromium (VI), and acid. The latter concentration can be coupled with the reaction temperature via dissociation of acetic acid, or controlled independently by introducing a strong acid, such as perchloric acid, into the system. By implementing a traditional optimization algorithm for this model chemistry, the microfluidic platform performed the necessary experiments to determine the conditions that maximize the concentration of the intermediate, benzaldehyde.

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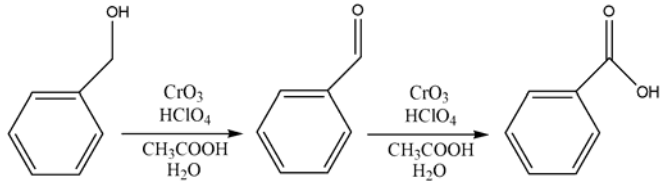


Figure 1. Model chemistry selected for platform validation

EXPERIMENTAL

This investigation used an integrated device with mixing, reaction, and quench sections that was designed and fabricated in silicon [Figure 2]. Reaction stoichiometry and residence time were controlled by adjusting the flow rates with syringe pumps (Harvard PHD 2000). Heating and cooling of the reaction was accomplished with thermoelectric modules (TE Technologies). Additionally, an aluminum housing/heat sink component was designed and machined to accurately provide a temperature range of -30 to 150°C. The quenched reaction stream was diluted and well-mixed by incorporating a pressure-driven stream and a micromixer before chemical detection via HPLC. Control and optimization algorithms were performed in Matlab scripts with LabVIEW software. The optimization algorithm used in all experiments was derived from a simple Nelder-Mead Simplex Method [2]. Termination of the optimization procedure occurred when increases in the benzaldehyde yield were marginal or when sequential experiments converged.

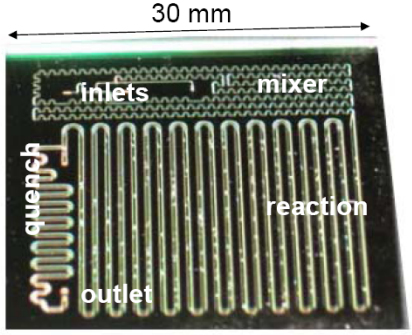


Figure 2. Integrated silicon microreactor contains a mixer, reaction, and reaction quench sections.

1-parameter (1D) optimization trials, in which only one reaction parameter was varied, were performed for reaction time and for temperature. Results of the temperature optimization are shown in Figure 3. To obtain more information about the reaction system, an automated preliminary scan of the reaction space was executed to characterize the reaction profile. The results from these scans can be used as starting points for the more complex, multi-variable optimizations (i.e., 2D, 3D, and 4D). Results from the 4-parameter (4D) optimizations are shown in Figure 4 with the use of a lumped variable defined by the product of the reaction time and the ratio of the initial concentrations of chromium trioxide to benzyl alcohol. Consolidation of variables in this manner enables 2D representation of data collected over a 4D optimization. After performing approximately 30 experiments, the automated microfluidic platform found the optimal benzaldehyde yield corresponding to 84%.

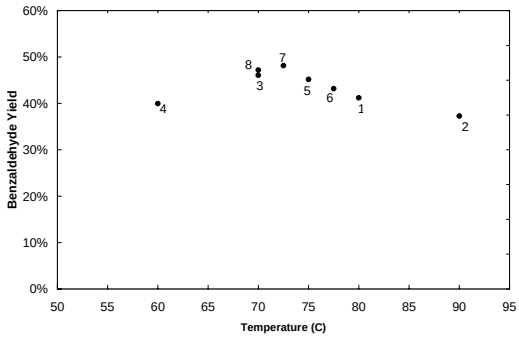
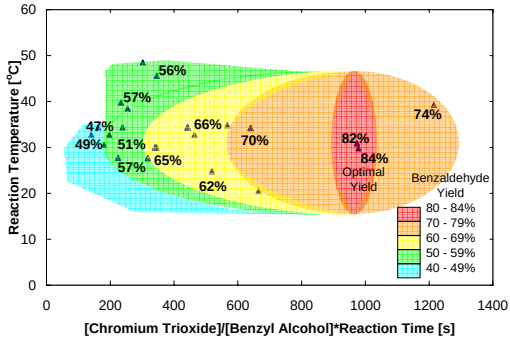


Figure 3. Results for 1D optimization of reaction temperature at reaction time of 20 seconds. Automated experimentation began at 80°C and 90°C. The optimization progressed (sequential experiments are numbered) from this data toward the optimal temperature of 72°C, corresponding to a benzaldehyde yield of 54%

Figure 4. Benzaldehyde yield for experimental conditions automatically performed by multiple parameter optimization platform. To aid in visualization of the data, projected contours of benzaldehyde yield are shown for different reaction temperatures, and for a lumped variable defined by the product of the ratio of the initial concentrations of chromium trioxide to benzyl alcohol and reaction time.



CONCLUSIONS

Real-time optimization by a microchemical system was demonstrated for oxidation reactions in series. This automated optimization, combined with the automation of other common laboratory tasks such as calibrations and preliminary experiments, decreases the amount of required starting material and increases experimental throughput. This ability to easily perform numerous optimization studies while only consuming ~100μg of reagents has significant applications in the pharmaceutical and fine chemistry fields.

REFERENCES

[1] Krishnadasan, S.; Brown, R.J.C.; deMello, A.J.; deMello, J.C.; *Lab Chip*, 2007, 7, 1434-41

[2] See Nelder-Mead Simplex in Himmelblau, D.H., *Applied Nonlinear Programming*, NY, McGraw-Hill, 1972.