Effect of Gas Flow on Liquid Flow in a Cocurrent Downflow Trickle Bed Reactor

Huibo Sheng[1], Tomislav A. Ljubicic[1], David Pfisterer[1], Howard W. Ward II[2], Mark A. Hardink[2], Angel R. Diaz[2], Frank Riley[2], Joel M. Hawkins[1]*, and Jason Mustakis[1]*
[1]*Chemical Research and Development, Pfizer, Groton, CT*
[2]*Analytical Research and Development, Pfizer, Groton, CT*
*Jason.mustakis@pfizer.com

Introduction

Trickle bed reactors (TBRs) are fixed bed reactors that widely used in chemical and petroleum industries for gas-liquid-solid three-phase reactions, [1] and they have been extensively studied under the conditions for these industrial applications on large scale. [2-3] Pharmaceutical applications are on a much smaller scale, and the general flow hydrodynamics together with the multiphase interaction can be very different compared to the petrochemical studies. For instance, the effect of gas flow has been generally reported as no effect on the liquid holdup or only negligible effect on dispersion coefficient by many authors. [4-6] However, these claims are mostly based on studies over large scales reactions on petrochemical process that may not be applicable to pharmaceutical applications, where the liquid phase reactants, active pharmaceutical ingredients (APIs), only possess a small percentage of the total liquid volume while the remaining solvent is inert to the reaction. During the reaction, while gas is consumed along the packed bed, the liquid volumetric flow remains almost constant. As a result, the gas to liquid ratio decreases dramatically along the reactor. The effect of gas phase becomes important and needs to be investigated to ensure a steady reaction and consistent results. In this work, we have developed a trickle bed reactor for flow hydrogenation and an optic fiber probe was employed to illustrate the axial temperature distribution during the reaction. Further investigations on the liquid phase residence time distribution was carried out to present the effect of gas flow on the liquid flow.

Materials and Methods

The experiments were carried out in a trickle bed reactor that is designed for hydrogenation processes for the synthesis of active pharmaceutical ingredients (APIs). The reactor was placed in vertical position, allowing gas and liquid flow downward cocurrently. Liquid phase residence time distribution was studied by injections of a tracer chemical (ethanol) into nitrogen-methanol system in the activated carbon packed reactor. Online IR was employed to track the liquid phase concentration change to obtain the residence time distribution function. Benzyl alcohol hydrogenation to toluene was investigated as a model reaction over commercial 5% Pd/C catalysts and the reaction results were analyzed by UPLC-MS.

Results and Discussion

We have found that the gas flow plays an important role for the conversion of benzyl alcohol and the reaction stability. An optimum gas to liquid (G/L) ratio was determined for the best benzyl alcohol conversion. Higher G/L ratios shortened the liquid residence time and consequently resulted in lower benzyl alcohol conversions. Meanwhile lower G/L ratios led to significantly lowered conversions and even catalyst deactivation. At low G/L, the reactor axial temperature profile showed that the performance of bottom catalyst was lowered as observed by a loss of high reaction temperature, and it was not restored when G/L ratio returned later on (Figure 1). The effect of gas flow on liquid flow was further evaluated by calculating the hydrodynamic parameters at different gas to liquid ratios, such as liquid holdup and liquid phase mean residence time. Finally, three hydrodynamic zones were identified as a function of G/L ratios, which indicates the flow regime transit in the trickle bed reactor.

Significance

This work discusses the effect of gas phase flow on the liquid flow in a pharmaceutical scale trickle bed reactor, in comparison to negligible gas effect [4-6] on large scale reactors in petrochemical industries. The result of three hydrodynamic zones provides guidance on the criteria of determining the optimum gas to liquid ratio, which is of great importance in pharmaceutical applications for both efficient and economical considerations.

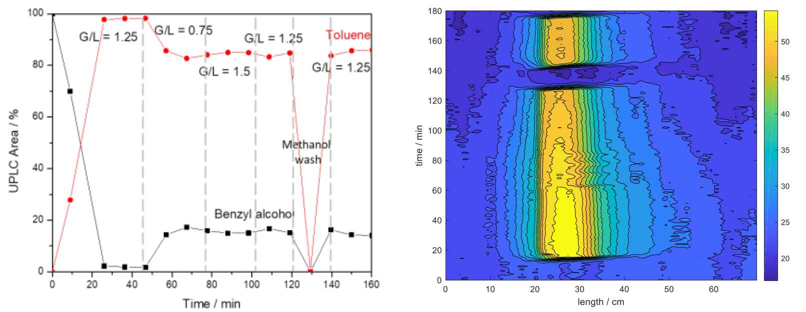

Figure 1. (Left) the effect of G/L on benzyl alcohol conversion to toluene and (Right) trickle bed reactor axial temperature contour plot during the reaction

References

1. Al-Dahhan, M. H., Larachi, F., Dudukovic, M. P., & Laurent, A. (1997). *Ind. Eng. Chem. Res.*, 36(8), 3292-3314.
2. Satterfield, C. N. (1975). *AIChE J.*, 21(2), 209-228.
3. Losey, M. W., Schmidt, M. A., & Jensen, K. F. (2001). *Ind. Eng. Chem. Res.*, 40(12), 2555-2562.
4. Hochman, J. M., & Effron, E. (1969). *Ind. Eng. Chem. Fund.*, 8(1), 63-71.
5. Cassanello, M. C., Martinez, O. M., & Cukierman, A. L. (1992). *Chem. Eng. Sci.*, 47(13-14), 3331-3338.
6. Pant, H., Saroha, A., & Nigam, K. (2000). *Nukleonika*, 45(4), 235-241.