Integrated Microfluidics for Targeted Applications
Including Polymerization, Carbon Dioxide Sequestration,
and Gas Separation

by

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Abstract

The work presented in this thesis explores the utilization of microfluidic (MF) reactors fabricated in different materials for targeted applications and capitalizes on the various fundamental advantages inherent to MF reactors for studying chemical reactions.

In Chapter 3, we describe the fabrication of MF reactors in different polymer materials, including polycarbonate, cyclic olefin polymer, poly(methyl methacrylate), polyethylene, poly(vinyl chloride), and polystyrene to address the previous lack of MF reactor materials that are chemically stable in polar and nonpolar solvent, have gas impermeability, are cost-efficient, and biocompatible. We investigated polymer performance under specific conditions and optimized the conditions for the fabrication of MF reactors following well-defined requirements.

Chapter 4 focuses on work that developed and utilized a MF platform with integrated online attenuated total reflection Fourier transform infrared spectroscopic characterization to study the kinetics of an exemplary reaction, namely, the
polymerization of N-isopropyl acrylamide in the presence of accelerator N',N',N,N-tetramethylethylenediamine, and initiator ammonium persulfate. The polymerization reaction was studied in flow in a throughput manner at various reagent concentrations and different pH values. By monitoring the rate of disappearance of the IR band corresponding to the monomer concentration as a function of time, we obtained reaction orders with respect to each reagent and found good correlation to values reported in the literature.

In Chapter 5, we utilized MF reactors by generating segmented flow of CO\textsubscript{2} gas and solvent (bromobenzene) to investigate fundamental information, such as thermodynamics and reaction efficiency, of the reaction involving CO\textsubscript{2} gas and Frustrated Lewis pairs (FLPs). Studies of the reaction thermodynamics using batch scale methods are challenging. We developed a method to overcome the challenges inherent in batch processes to successfully obtain fundamental information (\(\Delta G\), \(\Delta H\), \(\Delta S\), and enhancement factors) in the temperature range from 0 to 40 °C. This information is vital for future optimization and development of FLPs.

Finally, Chapter 6 explores the use of FLPs to effectively separate gases from their mixtures by extracting the gas in a reactive solvent phase. We used MFs to assess the efficiency of the separation of ethylene from its mixture with ethane, due to the reaction of ethylene with FLP. We found that increasing the FLP concentration, as well as reducing the temperature of the separation from 25 to 0 °C, led to significant increase of separation of ethylene from the mixture. The resultant separation factor for ethylene was 7.3 with an ethylene purity of 88%.
I gratefully acknowledge and express my deepest appreciation for my supervisor Prof. Eugenia Kumacheva, without whom this thesis would not be possible. My 8+ years under Eugenia’s guidance, first as an undergraduate and then as a Ph.D, has taught me countless lessons in science as well as in human relations. Prof. Kumacheva’s unending patience and enthusiasm for science has made every single day of my Ph.D a pleasurable learning experience and has taught me valuable lessons for the future. I am deeply indebted to her.

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<table>
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<tbody>
<tr>
<td>APS</td>
<td>Ammonium persulfate</td>
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<tr>
<td>ATR</td>
<td>Attenuated total reflection</td>
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<tr>
<td>ATR-FTIR</td>
<td>Attenuated total reflection Fourier transform infrared</td>
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<td>BB</td>
<td>Bromobenzene</td>
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<td>B(C(_6)F(_5))(_3)</td>
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<tr>
<td>IR</td>
<td>Infrared</td>
</tr>
<tr>
<td>MF</td>
<td>Microfluidic</td>
</tr>
<tr>
<td>MOF</td>
<td>Metal organic framework</td>
</tr>
<tr>
<td>NIPAAm</td>
<td>N-isopropyl acrylamide</td>
</tr>
<tr>
<td>NMR</td>
<td>Nuclear magnetic resonance</td>
</tr>
<tr>
<td>PC</td>
<td>Polycarbonate</td>
</tr>
<tr>
<td>PDMS</td>
<td>Polydimethylsiloxane</td>
</tr>
<tr>
<td>PE</td>
<td>Polyethylene</td>
</tr>
<tr>
<td>PS</td>
<td>Polystyrene</td>
</tr>
<tr>
<td>PVC</td>
<td>Poly(vinyl chloride)</td>
</tr>
<tr>
<td>(t)Bu(_3)P</td>
<td>tri-(t)ert-butylphosphine</td>
</tr>
<tr>
<td>TEMED</td>
<td>(N,N,N,N)-tetramethylethylenediamine</td>
</tr>
<tr>
<td>THF</td>
<td>Tetrahydrofuran</td>
</tr>
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# Physical Parameters

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\theta$</td>
<td>Contact angle</td>
</tr>
<tr>
<td>$\beta_L$</td>
<td>Liquid volume fraction in segmented flow</td>
</tr>
<tr>
<td>$C$</td>
<td>Total concentration</td>
</tr>
<tr>
<td>$Ca$</td>
<td>Capillary number</td>
</tr>
<tr>
<td>$CO_2_{tot}$</td>
<td>Total carbon dioxide concentration</td>
</tr>
<tr>
<td>$C_r$</td>
<td>Reacted carbon dioxide concentration</td>
</tr>
<tr>
<td>$D_H$</td>
<td>Hydrodynamic radius</td>
</tr>
<tr>
<td>$d_f$</td>
<td>Thickness of liquid film surrounding plug</td>
</tr>
<tr>
<td>$E$</td>
<td>Enhancement factor</td>
</tr>
<tr>
<td>$K$</td>
<td>Degrees Kelvin</td>
</tr>
<tr>
<td>$k_d$</td>
<td>Dissociation constant</td>
</tr>
<tr>
<td>$K_{eq}$</td>
<td>Equilibrium constant</td>
</tr>
<tr>
<td>$k_p$</td>
<td>Polymerization constant</td>
</tr>
<tr>
<td>$k_t$</td>
<td>Termination constant</td>
</tr>
<tr>
<td>$H$</td>
<td>Channel height</td>
</tr>
<tr>
<td>$\eta$</td>
<td>Viscosity</td>
</tr>
<tr>
<td>$n$</td>
<td>Number of moles</td>
</tr>
<tr>
<td>$n_{slug}$</td>
<td>Number of moles in the slug</td>
</tr>
<tr>
<td>$\lambda$</td>
<td>Wavelength</td>
</tr>
<tr>
<td>$\rho$</td>
<td>Density</td>
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<tr>
<td>$f_{slug}$</td>
<td>Friction factor</td>
</tr>
<tr>
<td>$L$</td>
<td>Total length of the channel</td>
</tr>
<tr>
<td>$L_P$</td>
<td>Length of plug</td>
</tr>
<tr>
<td>$L_S$</td>
<td>Length of slug</td>
</tr>
<tr>
<td>$P$</td>
<td>Pressure</td>
</tr>
<tr>
<td>$Q$</td>
<td>Flow rate</td>
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<tr>
<td>$T$</td>
<td>Temperature</td>
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<tr>
<td>$R$</td>
<td>Gas Constant</td>
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<tr>
<td>$Re$</td>
<td>Reynold’s number</td>
</tr>
<tr>
<td>Symbol</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>$R_p$</td>
<td>Rate of polymerization</td>
</tr>
<tr>
<td>$t$</td>
<td>Time</td>
</tr>
<tr>
<td>$T_g$</td>
<td>Glass transition temperature</td>
</tr>
<tr>
<td>$T_m$</td>
<td>Melting temperature</td>
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<tr>
<td>$\Delta H$</td>
<td>Enthalpy</td>
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<tr>
<td>$\Delta S$</td>
<td>Entropy</td>
</tr>
<tr>
<td>$\Delta G$</td>
<td>Gibbs free energy</td>
</tr>
<tr>
<td>$U_p$</td>
<td>Plug velocity</td>
</tr>
<tr>
<td>$U_s$</td>
<td>Slug velocity</td>
</tr>
<tr>
<td>$V_e$</td>
<td>Experimental plug volume</td>
</tr>
<tr>
<td>$w$</td>
<td>Channel width</td>
</tr>
</tbody>
</table>
Author Contributions

Portions of this thesis are based on projects that have been previously published in peer-reviewed scientific journals. All manuscripts were written by Danut Voicu with revisions by Eugenia Kumacheva and corresponding collaborators. The contributions of all authors involved in each project are provided in detail below.

Chapter 3: Polymer Microfluidic Devices for Targeted Applications

Authors: Danut Voicu, Michael DeBono, Gabriella Lestari, and Eugenia Kumacheva.

Contribution: Danut Voicu contributed by designing, carrying out all experiments, data analysis and interpretation. Michael DeBono assisted in fabrication of microfluidic reactors. Gabriella Lestari provided assistance for chemical compatibility studies involving polyethylene. Eugenia Kumacheva provided significant guidance and advice on experiments, interpretation, and writing.

Chapter 4: Kinetics of a Multicomponent Polymerization Reaction Studied in a Microfluidic Format

Portions of Chapter 4 have been previously published as: Voicu, D., Scholl, C., Li, W., Jagadeesan, D., Nasimova, I., Greener, J., Kumacheva, E. Macromolecules 2012, 45, 4469-4475.

Authors: Danut Voicu, Clement Scholl, Wei Li, Dinesh Jagadeesan, Irina Nasimova, Jesse Greener, and Eugenia Kumacheva.

Contribution: Danut Voicu designed and carried out all experiments, data analysis, interpretation, and writing. Clement Scholl assisted with carrying out experiments and with data analysis. Wei Li assisted with designing the experiments. Dinesh Jagadeesan
assisted in designing the experiments and in data analysis. Irina Nasimova assisted in interpretation of results and in guidance. Jesse Greener assisted in designing experiments, in interpretation of results, and with writing. Eugenia Kumacheva provided guidance and assistance for rationalizing experiments, data interpretation, and with writing.

Chapter 5: Using Frustrated Lewis Pairs For Carbon Dioxide Sequestration in a Microfluidic Format


Authors: Danut Voicu, Milad Abolhasani, Rachelle Choueiri, Gabriella Lestari, Caroline Seiler, Gabriel Menard, Jesse Greener, Axel Guenther, Douglas W. Stephan, and Eugenia Kumacheva.

Contribution: Danut Voicu designed and carried out all experiments, data analysis, interpretation, and writing. Milad Abolhasani assisted in designing and carrying out experiments involving diethanolamine as well as with data analysis. Rachelle Choueiri assisted in carrying out experiments and in experiment preparation. Caroline Seiler assisted in conducting experiments and in data analysis. Gabriel Menard assisted in providing chemical reagents and providing guidance on the chemistry of the reactions. Jesse Greener assisted in designing experiments. Axel Guenther provided technical guidance. Douglas W. Stephan provided guidance and advice on data interpretation and in designing experiments. Eugenia Kumacheva provided guidance in designing experiments and with data interpretation and writing.
Chapter 6: Microfluidic Separation of Ethylene and Ethane Using Frustrated Lewis Pairs

Authors: Danut Voicu, Douglas W. Stephan, and Eugenia Kumacheva

Contribution: Danut Voicu designed and conducted all experiments, data analysis, interpretation, and writing. Douglas W. Stephan provided guidance in designing experiments and in interpretation of data. Eugenia Kumacheva provided guidance in designing experiments, data interpretation, critical assessment, and writing.
Other publications during the Ph.D Study

Refereed Journal Papers


Chapter 1

Introduction

1.1 Microfluidic Studies of Chemical Reactions

1.1.1 Overview of Microfluidics

Microfluidics (MFs) is a broad, multidisciplinary field that deals with the control and manipulation of small quantities of fluids (on the order of $10^{-9}$ to $10^{-18}$ liters) that are geometrically constrained in narrow channels or thin films with length scales in the typical range from tens to hundreds of micrometers. The field of MFs emerged in the 1980s, when it was utilized in inkjet print heads and lab-on-a-chip technologies. Today, this area of fundamental research and technology bridges engineering, synthetic chemistry, physics, biochemistry, materials science, cell biology and point-of-care devices.

Microfluidics may employ passive fluid control methods, e.g., capillary forces that cause fluid to flow through the channels, or active fluid control that utilizes fluidic pumps or pressure-driven flow along with valves and other components required for fluid manipulation. Microfluidics can involve a single phase flow or multiphase systems. Single-phase systems involve one fluid, typically a pure liquid or a solution. Multiphase systems involve two or more fluid phases, such as liquid-gas systems or two immiscible liquids. In multiphase systems, the fluids are not miscible and form distinct interfacial boundaries.

Microfluidic platforms have numerous advantages over batch scale (or macroscale processes). The small diffusion length scales and high surface-to-volume
ratios in MFs lead to fast diffusive mixing and heat transfer. Microfluidics consume low reagent volumes, which is important when dealing with dangerous or expensive chemicals and MFs offer throughput capabilities resulting in fast replication rates and quick parameter space analysis. Table 1.1 compares characteristics of MFs and macroscale processes.

Table 1.1. Comparison of microscale and macroscale characteristics.

<table>
<thead>
<tr>
<th>Microscale</th>
<th>Macroscale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low reagent consumption</td>
<td>High reagent consumption</td>
</tr>
<tr>
<td>Fast heat transfer</td>
<td>Slow, uneven heat transfer</td>
</tr>
<tr>
<td>Improved mass transfer</td>
<td>Limited mass transfer</td>
</tr>
<tr>
<td>Cost efficient</td>
<td>Expensive</td>
</tr>
<tr>
<td>Rapid mixing</td>
<td>Slow, uneven mixing</td>
</tr>
<tr>
<td>Throughput</td>
<td>Low replication rate</td>
</tr>
</tbody>
</table>

These advantages of MFs make it an ideal tools for studying fast reactions (on the order of hundreds of milliseconds) and obtaining fundamental information such as their kinetics and thermodynamics. The distinct features of microfluidics include the dominant role of the surface tension and fluid resistance. Laminar flow is predominant in MF systems and it is characterized by the dimensionless Reynolds number, \( Re \), as

\[
R_e = \frac{\rho v D_H}{\eta}
\]

where \( \rho \) is the density of the fluid, \( v \) is the velocity, \( D_H \) is the hydraulic diameter, and \( \eta \) is the dynamic viscosity of the fluid. The Reynonld’s number describes the ratio of inertial forces to viscous forces for flow conditions and is used to characterize different flow
regimes (laminar vs. turbulent). As the Reynold’s numbers are typically low (below 2100) in MF systems and flow is laminar, fluids that are flowing side by side in a straight channel do not mix by convection. Diffusion is the primary mode of mixing in laminar flow. In macroscopic systems where the magnitude of Re is greater than 2100. Flow can become turbulent and mixing can occur via both diffusion and convection. Although macroscale reactors may benefit from turbulent flow where mixing occurs by convection, the large diffusion length scales leads to mass transfer limitations which results in slow and inhomogeneous mixing. Due to this limitation, the study of intermediate stages of chemical reactions or physical processes is challenging in macroscale systems. MFs, due to their small diffusion length scales, significantly reduce mass transfer limitation and lead to more homogeneous mixing. MFs also lend themselves well to visual characterization.

In MF synthesis, the productivity of a MF reactor is determined by the flow rate, usually not exceeding several mL/hr. Once stable MF synthesis is enabled, it may continue for extended periods of time, thereby generating relatively large amounts of synthetic product. Further increasing the product yield, or optimizing formulations in a throughput manner, can be achieved by coupling several MF reactors together via the "numbering up" approach. This strategy can lead to production of grams of desired product per hour. Still, the MF "numbering up" approach can be used for high-value products that require precise control over reaction parameters and environment.

Microfluidic reactors became popular in the late 1990s due to the availability of methods for rapid prototyping and fabricating MF reactors, primarily in polydimethylsiloxane (PDMS), using a soft lithography approach. The method of
fabricating PDMS MF reactors involves first, creating a reactor design in a CAD program and converting this to a transparent mask, in which the channels are printed in black ink. Next, photolithography is used to generate a positive relief photoresist master replicate on a silicon wafer. The PDMS is cast on the mold and, upon curing in 4 hours at 70 °C, yields an exact replica of the features of the master. This cast is oxidized in oxygen plasma along with a planar PDMS sheet, which allows the surfaces to seal tightly and form a strong bond when pressed together. Although quick and easy to fabricate, PDMS has several important limitations including the adsorption and absorption of small biomolecules such as proteins, uptake of organic solvents (e.g., hexane and alcohols), and high gas permeability. Thus it has been realized that PDMS is not suitable for many MF applications. New materials were needed to use MF devices in chemistry.

It was immediately realized that glass and silicon are excellent materials that can be utilized in microfabrication of MF reactors, however, the high cost and labor-intensive fabrication leads to long turnaround times. Furthermore, these materials are not suitable for quick prototyping. Over the last decade, new polymer materials have been utilized in MF reactors, including polycarbonate, cyclic olefin polymer, polyurethane, and polyethylene. The choice of material becomes especially important when non-aqueous systems involving aggressive organic solvents are used. Another area of concern is biomedical applications of MFs in which precise analytical characterization of biomolecules can be hampered by adhesion of these species to the walls of the MF device.
1.1.2 Chemical Reactions in Flow

An important application of MFs includes fundamental studies and screening of chemical reactions. Such studies can be performed in a single phase or two-phase systems. Microfluidics have been used for exploratory studies of glycosylation, synthesis of carbamates, polymers, polymer particles, oxidation, reduction, fluorination, bromination, and hydrogenation reactions. Excellent control over heat and mass transfer has led to high selectivity, improved yield, and increased purity of products. In addition, the use of MF systems is ideal for dealing with explosive or dangerous chemicals since only small quantities are required.

Microfluidic synthesis of complex substances is facilitated by the capability to conduct multi-step sequential reactions without the exposure of reactive intermediates to ambient conditions. Multistep reactions are facilitated by creating multiple on-chip zones with different reaction conditions, such that a product formed between two phases can move and encounter an additional reagent (which is introduced from an additional inlet). The products then exit the reactor via an outlet. This approach allows for a continuous multi-step synthesis to be achieved on-chip. Moreover, MFs allow the capability for on-chip, real-time analysis of reaction products or intermediates. Several analytical tools have been integrated with MFs to provide such characterization including FTIR, UV/Vis, surface enhanced Raman spectroscopy, and fluorescence microscopy. Importantly, MFs used for continuous flow synthesis allows products to be constantly generated (with different properties as the reagents are introduced at different conditions), which allows for throughput rapid screening of reaction parameters.
1.1.3 Microfluidic Polymerization Reactions

Due to the short diffusion length scales and the reduction of the mass transfer limitation, MF reactors offer homogeneous mixing of different fluids, which is necessary for avoiding concentration gradients and non-uniform heat transfer often present in batch-scale reactors. In MF reactors, complete mixing can be achieved within several milliseconds, compared to conventional macroscale reactors that achieve mixing on the timescale of seconds. Figure 1.1a shows a schematic of a conventional setup for batch scale polymerization. The monomer and initiator are introduced in a round bottom flask containing a solvent and the system is purged with an inert gas. The solution is stirred by a mechanical stirrer. The measurement of temperature with a thermometer precludes the probability of overheating. When the reaction is complete, it is quenched by cooling, and aliquots of the solution of the product are removed for later analysis. The process must be repeated for each concentration of reagents and temperatures studied, in order to find optimal conditions for the desired product.

Figure 1.1b shows a schematic of a flow microreactor used for polymerization studies. The system is composed of two syringe pumps, which supply the monomer and initiator at well-defined volumetric flow rates, a mixing T-junction (M1), a polymerization channel that provides sufficient time for the reaction (R2), and a short quenching zone (R3), where the reaction is halted by reducing the temperature. The polymerization channel (R2) is heated to the desired temperature, in order to initiate the polymerization. This temperature can be readily controlled in order to increase or decrease the initiation rate. The polymer solution is collected continuously from the
outlet of the reactor and analyzed off-chip. In a batch scale process, each experiment requires a new reaction mixture with distinct concentrations of the initiator and monomer. Continuous MF synthesis illustrated in Figure 1.1b provides throughput capabilities for assessing reaction parameters. The time required to obtain valuable data optimization of conditions is significantly shortened.

**Figure 1.1.** Schematics of (a) conventional polymer synthesis setup and (b) microreactor system for polymerization. The conventional system (a) involved adding the monomer and initiator in a round bottom flask and stirring it while monitoring the temperature. In the MF setup (b), the monomer and initiator are supplied by syringe pumps through tubings that converge to a T-junction used for mixing. The mixture enters the polymerization channel (R2), which is heated, inducing the polymerization, and then enters a termination, or quenching zone (R3) where the reaction is stopped by lowering the temperature. Finally, the polymer solution exits the MF device via the outlet.
In contrast to macroscale polymerization reactors, the concentrations of the monomer and/or initiator in the MF reactor can be tuned continuously by varying the flow rate of the stock solutions, and thereby the MF reactor can produce polymers of differing composition and characteristics in a continuous mode. The reaction time, which controls the degree of polymerization, can also be tuned by changing the total flow rate of the system, thereby increasing or decreasing the residence time of the polymer in the polymerization channel (R2).

Microfluidics can be very efficient in studies of polymerization reactions due to their throughput capabilities that allow for quick assessment of reaction parameters and characteristics such as fast heat and mass transfer that is required for polymerization reactions. Another major drawback of batch-scale processes is the difficulty in controlling highly exothermic reactions, due to insufficient, non-uniform heat distribution and the occurrence of hot spots\textsuperscript{36}. The efficient heat removal in MF reactors leads to a lower probability of side reactions and provides greater control over the reaction. For example, MF reactions can be quickly quenched due to the high surface to volume ratio, which is difficult to achieve for the large-volume reaction medium in batch scale processes.

Polymerization reactions carried out in MFs were used for the preparation of polymer particles with controllable shapes, sizes, and compositions\textsuperscript{37-42}, controlled radical polymerization for block copolymers\textsuperscript{43}, continuous atom transfer radical polymerization\textsuperscript{44}, coordination polymerization\textsuperscript{45}, polycondensation\textsuperscript{46}, anionic polymerization\textsuperscript{47,48}, and ring-opening polymerization\textsuperscript{49,50}. 
Typically, polymerization product is removed from the MF chip and studied off chip. The integration of real-time characterization of all species would allow for quick analysis and feedback on reaction parameters.

1.1.4 Gas Liquid Reactions Using Microfluidics

Conventional macroscale techniques for studies of dissolution and solubility of gases in liquid phases include pressure decay\(^5\), static methods\(^5\,^5\) and gas chromatography\(^5\). These techniques have mass transfer limitations and large uncertainties in measurements, due to poorly defined gas-liquid interfaces\(^5\,^5\). The accurate characterization, using infrared spectroscopy (IR) or nuclear magnetic resonance (NMR), of kinetic and thermodynamic properties of such reactions in bulk systems are highly problematic due to the mass transfer limitation that leads to inhomogeneous mixing and, as a result, inaccurate data. To produce new and efficient catalysts and chemical formulations, fundamental knowledge concerning mechanisms, kinetics, and thermodynamics of gas-liquid reactions must be acquired. With macroscale experiments, rate constants have large (up to 35%) variation\(^5\,^5\) due to inhomogeneous mixing caused by large diffusion length scales and to poorly defined interfacial boundaries. Large diffusion length scales lead to long data acquisition times, sometimes up to 24 hr for obtaining solubility data for aqueous solutions\(^5\).

Gas-liquid segmented flow, which is the flow of alternating gas bubbles (plugs) and liquid segments (slugs) is a MF approach to studying gas-liquid reactions while it provides well-defined gas-liquid interfaces and a very significant reduction in diffusion length scales. Segmented flow is formed when a liquid stream and gas stream are
introduced at a T-junction. The liquid stream periodically breaks up the gas segment to form alternating plugs and slugs. Figure 1.2 compares a large-scale apparatus used for studies of the dissolution and solubility of gases and the equivalent MF gas-liquid segmented flow process. In large-scale reactions, the dissolution and solubility of the gas in a liquid is analyzed by bubbling gas through a liquid chamber (the bubble column)\(^6\), as shown in Figure 1.2a. The liquid exits the chamber and the concentration of gas in the liquid, \(C_L\), is characterized off-chip. Batch-scale solubility experiments are conventionally done in static methods, as illustrated in Figure 1.2b. Here, a chamber is filled with solvent and a gas is introduced atop this liquid. The chamber is sealed by a pressure sensor. As gas mass transfers into the liquid, the pressure in the chamber changes and this change is detected by the pressure sensor. The change in pressure is related to the change in moles of gas in the gas phase. This characterization is used to obtain the data on equilibrium solubility, however, due to the large volumes of liquid and gas and the limited surface boundary, this method is extremely time-consuming.
Figure 1.2. Macroscale and microscale methods for determining CO\textsubscript{2} dissolution (mass transfer) and solubility of gases in solvents. (a) Batch scale measurement of gas dissolution in a bubble column. The outgoing solvent is characterized to obtain the dissolved CO\textsubscript{2} concentration in the liquid. (b) Schematic of static gas-liquid solubility measurement. (c) Schematic of two adjacent gas plugs in microscale segmented flow of CO\textsubscript{2}. The mass transfer of CO\textsubscript{2} from the plug to the liquid segment leads to a reduction in the length of the plug. The convective currents inside the liquid segment ensures even dissolution of gas. (d) Schematic of 3D representation of the microchannel showing the solubility of gas in the liquid segments (arrows) as well as the shrinking plugs (transparent plug overlap). Reproduced with permission from Ref. 61.

Figure 1.2 c and d. show segmented gas-liquid flow in a MF reactor channel, which is utilized for studies of dissolution and solubility of a gas in a liquid. The MF approach can accomplish these studies within 1 hr, that is, significantly faster than in a macroscopic batch processes. In addition, the MF approach offers versatility and throughput capability.
Microfluidic gas-liquid reactions involve the generation of a dispersed phase, the gas bubbles, in a continuous phase, the liquid. Typically, the gas bubble lengths exceed the MF channel diameter, which causes them to form oblong plugs (Figure 1.3). The gaseous plugs and liquid segments exhibit well-defined interfaces, reduced axial dispersion, enhanced mixing, and reduced mass transfer time, due to the convective stirring in the liquid segments between the plugs (Figure 1.3). When the gas transfers from the plugs to the liquid segments, the plugs shrink. This shrinkage is proportional to the quantity of gas transferred to the liquid and can be used to obtain valuable information, including solubility and dissolution, kinetics and thermodynamics, conversion information, and equilibrium constants (Figure 1.3). Microfluidics therefore offer a suitable platform for studies reactions and processes involving reactive gases such as sequestration of CO$_2$ or gas separation.

**Figure 1.3.** Schematic showing a T-junction microchannel and segmented flow of gas plugs (dark segments) and liquid segments (light regions). Reproduced with permission from Ref. 66.
1.1.4.1 Carbon Dioxide Sequestration Reactions in MF Systems

Carbon dioxide is a major greenhouse gas and a leading contributor to global warming. The anthropogenic sources of CO₂ are so vast that by the middle of the 21st century, the concentration of CO₂ in the atmosphere is expected to double. It is anticipated that this change will lead to the increase in global mean temperatures, deglaciation, rise in sea levels, and the potential extinction of species now living in colder climates. To reduce and prevent these negative effects, CO₂ sequestration and storage have been two areas of active research. Currently, CO₂ sequestration is achieved by gas scrubbing from flue gas streams, typically with amine solutions, at industrial sites where CO₂ is emitted. Amine scrubbing uses aqueous solutions of amines to chemically react with CO₂ and produce a zwitterion product as

The reaction is reversible and upon heating (typically to 130 °C, depending on the amine), the CO₂ gas can be released from the solution leaving behind, and regenerating, the amine. The gas can then be compressed and stored in underground aquifers or can be used in chemical reactions as a feedstock, for example in hydrogenation reactions to produce methanol. The scrubbing process, which has been used for over 80 years, is sensitive to the presence of oxygen and sulfur gases due to side reactions that can produce soluble products and cause corrosion problems. Amines can also be degraded at elevated temperatures which are required for the sequestration reaction. In addition, the method requires high energy input for regeneration of the solvent and release of the CO₂.
These disadvantages necessitate the development of new, more efficient technologies and chemical reagents for CO$_2$ sequestration. Recently, MFs has been successfully used to assess the efficiency and feasibility of new technologies, as well as new formulations of amine solutions.

In 2012, a MF system was used to study kinetics of fast gas-liquid reactions involving CO$_2$ and secondary amines$^{71}$. The authors used the reversible reaction between CO$_2$ and a secondary amine$^{72}$ to demonstrate the feasibility and capabilities of the MFs platform in measurements of the reaction rate constants. Figure 1.4 shows a schematic of the MF reactor and segmented flow (a), the characteristics of the forward reaction to produce the CO$_2$-amine adduct (b) and the reverse reaction that liberated CO$_2$ (c). Segmented flow generates highly monodispersed plugs and liquid slugs, which leads to well-defined gas-liquid interfaces$^{73-75}$. To characterize the mass transfer of gas to the adjacent liquid segments, the length and volume of plugs were monitored with distance from the Y-junction which was converted to reaction time.

Figure 1.4a shows the experimental setup and the reaction zones for the forward and reverse reactions, illustrated in Fig. 1.4b and c. In the forward reaction, the amine, R$_1$NHR$_2$ dissolved in acetonitrile, reacts with CO$_2$ gas from the plugs (leading to plug shrinkage as gas is consumed in the reaction) and produces the zwitterionic carbamate salt. In region 2 (Figure 1.4c), heating causes the reaction to reverse, expelling CO$_2$ from the solution and yielding R$_1$NHR$_2$. This process leads to plug expansion. The shrinkage and expansion of plugs was the basis for characterizing the reactions. Using the ideal gas law, and assuming ideal gas behavior, allowed the authors to obtain the concentration of CO$_2$ in the liquid segments from the plug volumes at each reaction time. In this manner,
the authors were able to obtain rates, at which CO$_2$ mass transferred from the plugs to the liquid segments at varying amine concentrations and reaction temperatures were analyzed. Yet, in these early studies, the importance of comparison of gas mass transfer rate vs. reaction rate was not explored. These studies also did not focus on thermodynamics of the reaction.

**Figure 1.4.** Schematics representing the MF system used to study the reversible binding of CO$_2$ to secondary amines. (a) Schematic of the MF reaction showing segmented flow of alternating liquid amine segments and gas CO$_2$ plugs. The reaction involving the binding of CO$_2$ to amine (b) occurs in Region 1 of the MF reactor while the reverse reaction (c) occurs in Region 2. Reaction 1 leads to bubble shrinkage as CO$_2$ transfers from the gas to the liquid segments. Reaction 2, which is heated to 60°C, leads to bubble expansion as CO$_2$ is liberated and amine is regenerated. Reproduced with permission from Ref. 71.

The physical dissolution of CO$_2$ in various solvents, in the absence of chemical characterization, was also recently investigated. The authors utilized an automated MF approach to image and simultaneously analyze the shrinkage of CO$_2$ plugs with time due to the physical mass transfer of CO$_2$ from the gaseous phase to the liquid phase. The
automated data acquisition and analysis enabled measurements of the volume of 20,000 CO₂ plugs within tens of minutes. As in the previous work by Li et al., the authors assumed an ideal gas behaviour and converted the change in volume of CO₂ bubbles (or the number of moles of dissolved CO₂) into the concentration of CO₂ in the adjacent liquid segments. The authors found that mass transfer was enhanced with increasing plug velocity, $U_B$, due to the convection currents in the liquid segments. The dissolution and solubility characteristics found for CO₂ using a MF approach, were in agreement with the literature data within 2-5%.

**Figure 1.5.** Schematic illustrating the MF setup for automated approach. The setup consisted of pressure regulator supplying the CO₂ gas, a syringe pump supplied the solvent, and an inert gas cylinder for purging the solvent prior to dissolution experiments. Inset: optical image showing segmented flow and the shrinkage of gas plugs. Reproduced with permission from Ref. 61.
The two examples showcased above are representative, and by no means comprehensive, of chemical and physical sequestration reactions in a MF format. MFs allow rapid screening and optimization of reaction conditions for gas-liquid reactions where interfaces are well defined and reaction parameters are strictly controlled. The role of MFs therefore is to provide a platform that can simplify and speed up analysis of reactions involving mass transfer of gases and to obtain fundamental information on such reactions, including their reversibility. MFs is the essential first step in analyzing a reaction and can be used as a tool to obtain the limits of a system and its feasibility prior to upscaling.

1.2. Frustrated Lewis Pair Reactions

Lewis pairs are composed of a Lewis acid, the electron acceptor, and a Lewis base, the electron donor. In terms of molecular orbitals, a Lewis acid has a low lying unoccupied molecular orbital (LUMO), while a Lewis base has a high energy occupied molecular orbital (HOMO). Lewis bases react with Lewis acids to form classical neutralization adducts. When Lewis acids and bases have bulky side groups, or steric congestion, they are termed “frustrated” Lewis Pairs (FLPs), which do not undergo direct reaction to form an adduct due to their steric hindrance. The term frustrated Lewis Pair was introduced by Stephan et al, who discovered that a Lewis acid and Lewis base were able to cleave a dihydrogen molecule under ambient conditions. The combination of bulky Lewis acid and base that heterolytically cleaved the H-H bond to activate dihydrogen led to a rapid expansion in FLP research as it paves the way for metal-free
catalytic reactions. Figure 1.6 illustrates the various reactions with FLPs studied and showcases the versatility of the system.

**Figure 1.6.** Illustration showing the various reactions of an FLP system consisting of a phosphine and a borane with H₂, N₂O, THF, alkenes, and alkynes.

The frustrated Lewis pair, namely, tBu₃P and B(C₆F₅)₃, was found to react with CO₂ to give a stable adduct, tBu₃PCO₂B(C₆F₅)₃. The adduct evolved CO₂ above 70 °C or when treated with H₂ gas. Further work revealed that reaction of CO₂ with tBu₃P and ClB(C₆F₅)₂ yielded a stable complex. Although the physical characteristics of the complex have been studied in bulk using NMR and X-ray diffraction providing high confidence of the products formed, important information about the system such as reaction kinetics and thermodynamics was lacking. This fundamental information is required to assess the propensity of the reaction under various conditions and its reversibility. The probing of the reaction under different conditions allows for optimization of FLP structure and increased efficiency of CO₂ reaction.

Furthermore, the ability of sterically encumbered phosphines and boranes to react with hydrogen prompted investigation of reactions with other small molecules including
ethylene. It was found that the reaction of tBu₃P and B(C₆F₅)₃ with ethylene resulted in a zwitterionic product [tBu₃P(C₂H₄)B(C₆F₅)₃]. Following this result, it was found that propene and hexane also react with the same FLP to give [tBu₃P(CHCH₂CH₂B(C₆F₅)₃] and [tBu₃P(CHC₄H₉CH₂B(C₆F₅)₃], respectively. For the reactions involving olefins, the boron added to the terminal carbon, while the phosphine added to the secondary carbon center. The reaction of FLPs and olefins was also lacking full characterization in terms of kinetic and thermodynamic information and, as a result, the optimization of reaction conditions was yet to be investigated.

The reaction of FLPs with small molecules such as CO₂ and alkenes has many potential applications in terms of CO₂ sequestration and gas separation. Fundamental studies of these reactions, to obtain kinetic and thermodynamic information, is crucial for assessing the feasibility and efficiency of these reactions and comparing them with currently used methods. Due to the limitations of conventional batch reactions, which mainly stem from the large diffusion length scales, inhomogeneous mixing, and slow replication rate, the kinetics and thermodynamics of FLP reactions with CO₂ or alkenes has not been studied. These challenges can be readily addressed by using MF reaction, if an appropriate platform and data analysis are performed.

1.3 Summary

Currently used batch-scale processes lack the necessary capability to acquire, in a throughput manner, fundamental information such as thermodynamics from two-phase reactions. The lack of information regarding kinetics and thermodynamics of chemical reactions prevents optimization of chemical reagent structures and conditions. Having
this information would enable directed effort in developing new and more efficient reagents as well as optimal reaction conditions to maximize productivity.

Microfluidic studies offer numerous advantages in fundamental studies and screening of single-phase and multi-phase chemical reactions and physical processes over traditionally used batch-scale studies, including significantly reduced mass transfer limitation due to the small diffusion length scales, fast heat transfer, rapid diffusive mixing, and precise control over reaction parameters such as temperature, reagent concentrations, and reaction time. Microfluidics allow throughput studies by working in the continuous mode with the capability of changing reaction conditions such as reagent concentrations, on the fly. This feature allows rapid generation of products that can be screened and analyzed. The use of MFs significantly reduces reaction time, compared to macroscale experiments, and allows for rapid analysis of the parameter space of chemical reactions. Microfluidics may also be integrated to powerful, online and real-time characterization tools such as Fourier transfer infrared spectroscopy that provides full spectrum characterization of all reaction intermediates.

The objective of this work then was to develop optimal MF systems in order to bridge the gap between what is already known about gas-liquid reactions involving CO$_2$ and alkenes to the information that is required in order to fully understand the chemistry. Our MF approach aimed to address the lack of fundamental information necessary for comparing the reaction methods with currently used protocols and assessing the feasibility of these reactions. The thesis begins by developing and optimizing the fabrication conditions of polymer materials for MF reactors (Chapter 3). Next, we developed and validated a MF approach to studying an exemplary chemical reaction
(Chapter 4). We then employed the MF strategy by designing a methodology to study the reaction between FLPs and CO$_2$ with the aim of obtaining fundamental thermodynamic information about the reaction and contributing to the understanding of the thermodynamic driving forces (Chapter 5). Finally, we utilized the same MF approach to study a new application of FLPs: the separation of olefins and paraffins. We used MFs to assess the reaction of FLPs with ethylene for use in gas separation applications and characterized its efficiency.
References


(64) Oskooei, S. A. K.; Sinton, D. Lab Chip 2010, 10, 1732-1734.


Chapter 2

Materials and Methods

This chapter describes the materials and methods that were used for all microfluidic experiments described in Chapters 3 – 6.

2.1 Materials

2.1.1. Materials for Fabrication of Microfluidic Devices

Photoresist SU-8 3050 was purchased from Microchem Corp. (MA). Single-side polished copper sheets were purchased from McMaster Carr Supply Co. (IL). Polycarbonate (Lexan 9034-112) was purchased from Sabic Polymershapes (NC). Poly(vinyl chloride) (PVC), Type 1, sheets were purchased from McMaster Carr Supply Co. (IL). Polystyrene (PS) sheets were purchased from Plaskolite Inc. (A-81, USA). Methanol, acetone, and isopropyl alcohol were purchased from Sigma Aldrich (Canada). A spin coater (WS-400-6NPP) was purchased from Laurell Technologies Corp. (PA). NanoPort connections (model M-333) were purchased from IDEX Health & Science (WA). Epoxy resin (Clearweld) was purchased from J-B Weld Co. (TX).

2.1.2. Materials for Microfluidic Polymerization

N-isopropylacrylamide (NIPAAm) was purchased from Sigma-Aldrich Canada and recrystallized prior to use. Ammonium persulfate (APS), N,N,N’,N’-tetramethylethylenediamine (TEMED), and ethanolamine were purchased from Sigma Aldrich Canada and used as received. Phosphoric acid was purchased from Caledon Laboratories Ltd. (Canada). Hydrochloric acid was purchased from VWR (PA).
Dihydrogen phosphate monosodium and sodium hydroxide were purchased from ACP Chemicals (Quebec, Canada).

2.1.3. Materials for Frustrated Lewis Pair Reactions with CO$_2$ and Ethylene

Tri-tert-butylphosphine, tBu$_3$P, and tris(pentafluorophenyl)borane, B(C$_6$F$_5$)$_3$, were purchased from Sigma Aldrich Canada. Chlorobis(pentafluorophenyl)borane, ClB(C$_6$F$_5$)$_2$, was synthesized as described in previous literature$^{1,2}$. Bromobenzene was purchased from Caledon Laboratories Ltd. (Canada). Carbon dioxide gas (grade 4.0) was purchased from Linde (Germany).

2.2 Methods

2.2.1. Fabrication of Microfluidic Devices

2.2.1.1 Stamp Fabrication

Thermoplastic polymer microfluidic devices were fabricated by thermal embossing and bonding. The embossing stage utilized a photoresist-coated metal stamp. The method for the fabrication of the stamp has been published elsewhere$^3$. Figure 2.1 illustrates the fabrication process. Stamps were fabricated by a multi-step photolithography in order to create bas-relief features. A single-side polished copper sheet was rinsed with acetone, methanol, and isopropyl alcohol and dried with compressed nitrogen. The sheet was coated with a 50 µm thick SU-8 photoresist layer (the seed layer) by spin coating. After coating, the sheet was baked at 96 °C for 15 min and subjected to 30 s of UV radiation in order to crosslink the resist (Hg lamp with 350-
450 nm output supplied from a mask aligner (Suss Microtec)), as shown in Figure 2.1 a.

After irradiation, the stamp was baked for 5 minutes.

**Figure 2.1.** A schematic of the multi-step fabrication of copper stamps containing bas-relief features of a desired channel design. A copper plate (a) was used as a substrate. A thin seed layer of SU-8 3050 was coated on the surface to a thickness of 50 µm and crosslinked by UV exposure for 30 s (b). A second coat of SU-8, having the same thickness as the height of the target channels, was coated on top of the seed layer (c). A mask containing the channel features was placed over the stamp and subjected to UV exposure for the appropriate length of time, depending on the channel layer thickness (d). The stamp was developed using SU-8 developer (e).

A second layer of SU-8, the feature layer, was applied to the seed layer to the desired thickness (or height of channel). After baking at 96 °C for 15 min, a photomask of the microfluidic channels was placed on top of this layer and the stamp was subjected to 50 s of UV radiation. The stamp was then baked for 5 min at 96 °C and developed using SU-8 developer purchased from Microchem Corp. Finally, the stamp was baked for
1 hour at 175 °C to enhance durability of the features and to fuse the channel layer to the seed layer.

2.2.1.2 Microfluidic Reactor Fabrication in Thermoplastic Materials

Microfluidic reactors were fabricated by thermal embossing and bonding as described elsewhere\(^3\). Figure 2.2 shows a schematic for embossing a thermoplastic sheet and bonding it to a second planar sheet. In the embossing stage, the copper-SU-8 stamp was sandwiched with a planar thermoplastic sheet and placed in a custom built vacuum chamber which was placed on a hot press (Model M, Carver, IN). For polycarbonate reactors, the hot press platens were heated to 165 °C for 5 min without any applied pressure to allow the polymer to soften. After 5 min pressure of 1.5 MPa was applied to the stack for 5 min. The platens were then cooled with circulating water to 145 °C and pressure was released, the vacuum chamber was opened, and the polycarbonate sheet was detached from the stamp.

The embossed polycarbonate sheet was drilled at the outlets and inlets with a 1/16\(^{th}\) inch drill bit to allow the channels to be accessed via tubings. The polycarbonate was rinsed in isopropyl alcohol and subjected to a 5 min sonication bath (Branson 1510, Emerson Industrial Automation, MO). The embossed sheet was joined with a planar sheet and placed in the vacuum chamber and heated on the hot press at 143 °C for 5 min. A pressure of 1.55 MPa was applied to the stack immediately and the temperature was maintained. After 5 min, the platens were cooled to 60 °C with circulating water while maintaining the applied pressure of 1.55 MPa. Pressure was then released and the vacuum chamber was opened. The bonded reactor was inspected and stored.
The microfluidic reactor was interfaced with tubings either by using NanoPorts or by interfacing with our custom built manifold (see Section 2.2.2.). The Nanoports were attached to the reactors using epoxy resin.

![Diagram of Embossing and Sealing Process]

**Figure 2.2.** Schematic of the thermal embossing procedure (a-c) and the bonding/sealing procedure (d-e). (a) The stamp and a planar thermoplastic sheet was subjected to heat for several minutes to soften the plastic. (b) Pressure was applied in order to imprint the plastic sheet with the stamp features. (c) The embossed plastic sheet was separated from the stamp and (d) coupled with a planar sheet and heated. (e) Pressure was applied to form a seal between the two substrates.

### 2.2.2. Integration of Microfluidic Devices with ATR-FTIR Probe

For the experiments described in Chapter 3 we utilized an attenuated total reflection (ATR) diamond crystal with the shape of a circular trapezoid that protruded 175 µm from a metal base plate. For proper sample measurement, the surface of the crystal had to be in
contact with the sample, located in the channel of the microfluidic device. Ideally, the surface of the crystal should be flush with the bottom of the microchannel wall such that any fluid traversing the channel can flow over the crystal. With a protruding crystal, this meant that the MF reactor needed to have an access hole from the bottom, where the crystal would fit.

Based on these requirements, we established a protocol to interface the crystal with the MF reactor. Figure 2.3 shows a schematic outlying the procedure required in preparing a device containing an access hole for the ATR crystal.

<table>
<thead>
<tr>
<th>a)</th>
<th>Embossed thermoplastic sheet</th>
<th>Metal stamps with ATR replica</th>
</tr>
</thead>
<tbody>
<tr>
<td>b)</td>
<td>De-embossed sheet</td>
<td></td>
</tr>
<tr>
<td>c)</td>
<td>ATR access hole is punched out</td>
<td></td>
</tr>
<tr>
<td>d)</td>
<td>Sheet is sanded down</td>
<td></td>
</tr>
<tr>
<td>e)</td>
<td>Sheet bonded to a channel patterned sheet</td>
<td></td>
</tr>
<tr>
<td>f)</td>
<td>Device is integrated with ATR crystal</td>
<td></td>
</tr>
</tbody>
</table>

*Figure 2.3.* The fabrication steps required to integrate the ATR crystal with the reactor. A planar thermoplastic substrate is embossed with a stamp containing a replica of the ATR crystal feature (a). The film is de-embossed (b) and the ATR crystal hole is punched out (c). The film is sanded to remove excess thickness (d) and is bonded with an embossed sheet containing the channel features (e). The bonded reactor contains a hole at the bottom where the ATR crystal fits.
The exact 3D shape of the ATR crystal was replicated in a metal stamp by machining a blank stainless steel disk. The stamp was used to thermally emboss the ATR feature into a thin thermoplastic sheet, Figure 2.3 (a). For the crystal with the height of 175 µm tall, the embossed films were 180 µm thick. Following de-embossing (Figure 2.3b), the ATR crystal access hole was punched out using a metal punch with the same diameter as the top of the ATR crystal (Figure 2.3. c). The film was then sanded on both sides (d). Sanding was necessary to 1) remove the excess material covering the crystal feature and to create the access hole and 2) to reduce the film to the correct thickness (the height of the ATR crystal). Finally, the film was bonded to a previously embossed reactor chip (e). After bonding, the reactor was coupled to the Fourier transform infrared (FTIR) spectrometer (f). The ATR crystal (red) was aligned with the access hole on the bottom side of the reactor and the top of the crystal was flush with the bottom microchannel wall.

In order to ensure a tight seal was formed when the ATR crystal was inserted in the bottom of the reactor, we applied pressure to the top of the reactor. This was accomplished using a custom-built plastic manifold. The manifold provided screw-in capabilities for connecting tubings to the MF reactor. Figure 2.4 shows a side view of the fully-coupled device with tubing connections.
Figure 2.4. The fully integrated microfluidic reactor to the ATR-FTIR instrument. Tubings connected to syringe pumps (not shown) deliver the reagents on chip. A CCD camera and light source were positioned atop the setup to. This allowed for optical characterization of the MF channels.

2.2.2.1 ATR-FTIR Optical Characterization

A custom made optical characterization setup was used to provide real-time images of the ATR characterization zone (the channel running across the ATR crystal). A CCD camera (Infinity 2, Lumenera Corp., Canada) was connected to a variable zoom optical tube (custom made). Illumination was provided by a high intensity light source (MI-150, Edmond Optics, US). The horizontal movement of the CCD camera was enabled by two connected linear rack and pinion stages.
2.2.3. Error Analysis

The work in Chapters 3-6 contains a lot of experimental studies and, as a result, some information on the inherent operational and systematic errors is required. Table 2.1 shows the operational errors of each measured variable used in the work.

Table 2.1. The operational errors of the measured experimental variables.

<table>
<thead>
<tr>
<th>Measured Variables</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optical width measurements</td>
<td>2 μm</td>
</tr>
<tr>
<td>Optical Profiling</td>
<td>100 nm</td>
</tr>
<tr>
<td>IR peak intensity</td>
<td>1.7 x10^{-5} a.u.</td>
</tr>
<tr>
<td>Temperature water bath</td>
<td>1 °C</td>
</tr>
<tr>
<td>Gas Pressure</td>
<td>0.01 psig</td>
</tr>
<tr>
<td>Contact angle</td>
<td>0.2 °</td>
</tr>
<tr>
<td>Reagent weights (NIPAAm project)</td>
<td>1x10^{-4} g</td>
</tr>
<tr>
<td>Reagent weights (FLP work)</td>
<td>1x10^{-3} g</td>
</tr>
<tr>
<td>Length of plugs and slugs</td>
<td>8 μm</td>
</tr>
</tbody>
</table>

To obtain the precision of each measured variable, 10 measurements were conducted and the standard deviation was obtained. There were also some systematic errors in our work such as the calibration of the MATLAB software code that was used to automatically scan optical images and measure the lengths of the gas plugs and liquid slugs. Another systematic error arose from the oscillatory nature of syringe pumps, which were used to supply the liquid reagents in all the work in this thesis.
2.2.4 Reproducibility of Experiments

The experiments conducted in Chapter 3 (embossing and bonding of polymers) were conducted at least 10 times. The optimized conditions listed in Table 3.2 were taken after at least 5 reactors were successfully fabricated using the conditions to ensure reproducibility.

Experiments in Chapter 4 were conducted in triplicate on different occasions and the results were within the error obtained (which is incorporated in all figures). Similarly, the experiments for Chapters 5 and 6 were conducted in triplicate, on different days and the results were found to be reproducible.

2.2.5. Time Limitations of Experiments

The throughput capability of the experiments conducted in Chapter 4 allowed for the reaction-analysis process to be finished in 10 min for each experiment. This total time included 5 min for stabilization of flow, 1 minute for acquiring data and 4 minutes for analysis. The primary limitation to the analysis-to-reaction time was the time required for flow to stabilize. For the work in Chapter 4, we utilized syringe pumps to supply the liquid reagents. Due to the oscillatory nature of the pump flow, we used long tubings (3 feet) to increase the fluidic resistance and decrease the oscillatory behavior. The result of the long tubing was that there was a longer lag time from the point of changing flow rate parameters to when the new changes reached the MF reactor. Therefore, the limitation of this process was based on the usage of syringe pumps. Using pressure driven flow, which does not have oscillatory behavior and therefore does not require long tubings, would enable even faster reaction-to-analysis times.
References


Chapter 3

Polymer Microfluidic Devices For Targeted Applications

3.1 Introduction

Exploratory applications of microfluidics (MFs) in chemistry and biology offer the advantages of low reagent consumption, enhanced control over heat and mass transfer, the ability to carry out multi-step reactions without exposure to the ambient environment, and the ability to change reagent concentrations in a throughput manner. A broad range of applications of MFs imposes specific and stringent requirements for the material from which MF reactors are fabricated.

The key characteristics of the materials used for the fabrication of MF reactors are summarized in Table 3.1. While some of these features, e.g., the cost and the ease of fabrication, are the desirable characteristics regardless of the application of the MF reactor, other features are determined by its particular application. For example, polydimethylsiloxane (PDMS) has a high gas permeability\(^1,2\) which is beneficial for MF cell culture\(^3-5\), yet gas diffusion across the device walls would adversely influence the results of experimental studies of gas-liquid reactions and processes. Microfluidic devices fabricated in glass or silicon offer gas impermeability, as well as compatibility with organic solvents, however the high cost and long time of fabrication do not satisfy the needs of academic research.
Table 3.1. Key characteristics of polymer materials used for the fabrication of MF reactors.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Requirements</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fabrication</td>
<td>High-fidelity, low cost, rapid prototyping.</td>
<td>Ability to scale up.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Important for optical inspection in MF experiments.</td>
</tr>
<tr>
<td>Optical Properties</td>
<td>Transparent (~ 90% transmission) at desired wavelength.</td>
<td>Important for photo-initiated reactions, spectroscopy-based sensing, and fluorescence-based analysis.</td>
</tr>
<tr>
<td></td>
<td>No absorption and auto-fluorescence in specific wavelength range.</td>
<td>Important for optical inspection in MF experiments.</td>
</tr>
<tr>
<td>Mechanical Properties</td>
<td>Flexible or rigid (application specific)</td>
<td>High temperature experiments require higher $T_g$ polymer.</td>
</tr>
<tr>
<td></td>
<td>Typical glass transition temperature $T_g &gt; 100 , ^\circ C$.</td>
<td></td>
</tr>
<tr>
<td>Chemical resistance</td>
<td>Compatible with application-specific solvent (nonpolar, polar).</td>
<td>In some applications, minimal swelling is allowed.</td>
</tr>
<tr>
<td>Gas permeability</td>
<td>High gas permeability for cell culture experiments and UV-polymerization.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low gas permeability for studies of gas-liquid reactions and physical processes,</td>
<td></td>
</tr>
<tr>
<td>Biocompatibility</td>
<td>Modifiable surface (to improve cell adhesion),</td>
<td>The surface chemistry of the material determines its wetting properties.</td>
</tr>
<tr>
<td></td>
<td>Non-toxic to cells.</td>
<td></td>
</tr>
</tbody>
</table>

There is a growing interest in the fabrication of MF devices from polymer materials, since they offer the advantages of rapid and cost-efficient fabrication$^6$ and, potentially, can meet the requirements of most MF applications. Polymers such as polycarbonate (PC) and cyclic olefin polymer (COP) are chemically stable in aqueous systems, however, for applications involving organic solvents, these polymers are not suitable. Furthermore, most of the polymers that are used for the fabrication of MF
devices have relatively high gas permeability. The fabrication of MF devices in polymers with low gas permeability can enable studies of gas-liquid mass transfer and gas-liquid reactions at long time scales that are currently not accessible. These applications of MFs would enable efficient studies of greenhouse gases such as carbon dioxide\(^7\), methane, and nitrous oxide, as well as studies involving biologically-relevant gases such as oxygen and nitric oxide.

Recent work\(^6\) has shown promise for using PC, COP, and poly(methyl methacrylate) (PMMA) in aqueous systems, yet further analysis on their chemical compatibility and material properties is required in assessing the full range of applicability of these materials. Furthermore, more demanding applications requiring nonpolar and several polar solvents, present a challenge. For example, MF studies of reactions of frustrated Lewis pairs with \(\text{CO}_2\)\(^8\) or \(\text{CO}_2\)-mediated liquid-liquid phase separation\(^9\) are conducted in bromobenzene (BB) and tetrahydrofuran (THF), respectively; these are not compatible with PC, COP, or PMMA. Furthermore, the gas permeability of COP, PC, and PMMA may preclude their utilization in studies of gas-liquid reactions involving long reaction times on the order of hours\(^10\).

Therefore, each application requires a different material for the fabrication of MF reactors. In the present work, we fabricated MF devices in materials that satisfy the specific requirements of compatibility with polar solvents, organic solvents, low gas permeability, and bio-compatibility, in order to expand the usage of polymers to additional targeted MF applications. We selected PC, COP, and PMMA for reactions in aqueous systems. High-density polyethylene (HDPE) was the material of choice to fabricate MF reactors compatible with organic nonpolar, polar aprotic, and polar protic
solvents in a range of temperatures. To address the requirement of low gas permeability, we utilized poly(vinyl chloride) (PVC), a robust and cost-efficient glassy polymer with low gas permeability determined by the high-density packing of the polymer chains and low segmental motion of the chains\textsuperscript{11}. To address the biological compatibility requirements, we fabricated MF devices in polystyrene (PS), a prevalent polymer extensively used in the biomedical field for labware such as petri dishes, well plates, test tubes, and medical trays. The work described in this chapter aims to provide guidance for the fabrication and operation conditions for MF devices fabricated in robust polymer materials, as well as the MF reactor performance under conditions that are specific for their projected applications.

3.2 Experimental

Microfluidic devices were fabricated by hot embossing and thermal bonding using custom-made SU-8 photoresist on copper metal stamps. Below, we describe the various stages involved in fabricating reactors in PC, COP, PMMA, HDPE, PVC, and PS.

3.2.1 Stamp Fabrication

Thermal embossing of polymers requires a stamp, which contains bas-relief features of the desired channels, and is used to impress these features into the polymer. Upon embossing, the stamp must resist high temperature and pressure, and therefore must be fabricated from robust materials.

In our work, stamps were fabricated by multi-step photolithography. The procedure for the fabrication of the stamps was similar to the method previously
developed in our group by Li et al. A polished square copper sheet, with a width of 4”, was cleaned thoroughly with acetone, methanol, and isopropyl alcohol, and subsequently dried with compressed nitrogen. A 50 µm layer of the photoresist, SU-8 3050, was deposited on the copper surface using a spin coater (WS-400-6NPP, Laurell Technologies, PA, USA) at 3000 rpm for 30 sec. After baking the coating for 5 min at 95 °C, the stamp was subjected for 50 sec to UV irradiation (Hg lamp, 350-450 nm, supplied from a Mask Aligner 6 (Suss Microtec) and then baked for 15 min on a hot plate at 95 °C, a second 50 µm thick layer of SU-8 50, was applied to the surface at 3000 rpm for 30 sec. A mask containing the desired channel features was placed on top of this layer and the system was subjected to the same UV source for 50 sec. The stamp was developed using SU-8 developer purchased from Microchem Corp. (MA, USA) and then baked for 1 hr at 175 °C to enhance durability of the features.

3.2.2 Hot Embossing of Polymers

The procedure for thermal embossing was similar for all polymers used in the present work, that is PC, COP, PMMA, HDPE, PVC, and HDPE, and involved using a hot press (Carver, Model M, Wabash, USA) to apply heat and pressure to the polymer that was placed against a stamp containing channel features.

Polymer samples were first cut into 5.5 cm diameter disks using a lathe. The disks were washed and sonicated in an isopropyl alcohol bath to remove any debris from the surface. The embossing process was conducted in a vacuum chamber that was situated on the hot press in order to remove any air bubbles from becoming trapped between the polymer and stamp.
The polymer was placed atop the stamp and the sandwich was placed on the hot press, which was heated to a specific temperature, above the glass transition \( (T_g) \) temperature for amorphous polymers, or above the melting temperature \( (T_m) \) for semicrystalline polymers. The embossing temperature and pressure varied for each sample based on the polymer (the detailed embossing parameters are given in Table 3.2). After embossing, the samples were cooled to several degrees below the \( T_g \) (or below the \( T_m \) in the case for HDPE) to allow the polymers to solidify and maintain the newly-embossed patterns. The embossed sheet was removed from the stamp and visually inspected for any defects. The temperature, pressure, and time were optimized to achieve high feature reproducibility from the stamp to the polymer disks.

For experiments involving HDPE, the 0.5 cm thick sheets supplied by the manufacturer required thinning in order to improve their optical clarity. The thinning of the HDPE material was carried out prior to embossing features. The HDPE sheet was placed between two silicon wafers (which are atomically smooth on the surface), heated to 150 °C (above its \( T_m \)) and subjected to a pressure of 2500 psi. Metal shims were placed next to the sample to provide a way to control the height of the resulting film. The film was released upon cooling to 90 °C. Films with several thicknesses were fabricated to assess the transparency of the polymer and suitability for the fabrication of MF reactors.

### 3.2.3 Thermal Bonding of Polymers for MF reactors

Embossed reactors were thoroughly cleaned in a sonication bath of isopropyl alcohol, prior to bonding, to remove any debris trapped in the channels. The inlets and
outlets were drilled using a 1/16\textsuperscript{th} inch drill bit. The two MF reactor components (embossed sheet and planar sheet) were sandwiched between a rubber silicon sheet and a metal plate. These were placed in a vacuum chamber and subjected to a specific temperature and pressure, based on the mechanical properties and $T_g$ of the polymers (and $T_m$ in the case for HDPE), for a specific amount of time. The newly bonded reactor was then removed and allowed to cool to room temperature under 1 lb of pressure. Prior to experimental use, the bonded reactors were sonicated in isopropyl alcohol for 1 minute and then dried for 30 min in a convection oven at 75 °C.

3.2.4 Surface Modification of Polyethylene

High-density polyethylene sheets were exposed to different gases in a plasma cleaner (PDC-32G, Harrick Plasma, USA). Plasma was created by using high frequency voltage to ionize a gas at low pressure. The plasma can remove organic contaminants by chemical reaction (O\textsubscript{2} or air plasma) or by physical ablation (argon plasma). In this manner, it can clean surfaces without the use of solvents and also render surfaces hydrophilic, especially when O\textsubscript{2} plasma is used, due to the oxidation of the surface. Ambient air, oxygen (Linde, USA), or nitrogen (Linde, USA) were supplied to the chamber under 600 mTorr for 45 to 180 sec. The surface properties of the samples were investigated by measuring the contact angle of water on the polymer surface immediately following plasma treatment. Contact angles of water on each polymer sample were measured using a drop shape analyzer (DSA100S, KRUSS GmbH, Germany) with fitting method.
3.2.5 Examination of Compatibility of PC, COP, and PMMA Reactors with Solvents

The compatibility of MF reactors fabricated in PC, COP, and PMMA with xylene, diethyl ether, ethanol isopropyl alcohol, and water was investigated by exposing small, 1x1 cm, pieces of the specific polymer to each solvent for 24 hr. The polymer samples were weighed before and after exposure to solvent and the weight change (swelling ratio) was determined.

3.2.6 Examination of Compatibility of Polyethylene Reactors with Organic Solvents

The compatibility of MF reactors fabricated in HDPE was investigated by injecting a particular solvent, tetrahydrofuran, bromobenzene, dichloromethane, and hexanes, into a MF reactor for 5 h, the typical duration of MF experiments, and inspecting the change in dimensions of the microchannel width. The solvent uptake was also determined for polymer sheets and is discussed in the results section.

3.2.7 Gas Permeability Experiments with PVC MF Reactors

Poly(vinyl chloride) MF reactors were tested for gas permeability by first generating segmented flow of alternating plugs of CO\textsubscript{2} or N\textsubscript{2} gas and aqueous liquid slugs. Subsequently, stopping the flow of the liquid segments by pressurizing the inlets and the outlet with a pressure, 5 to 15 psig allowed the segmented species to remain stationary, and available for optical characterization. The lengths of the gaseous plugs were subsequently measured as a function of time.
3.3 Results and Discussion

3.3.1 Stamp Fabrication

In order to emboss MF features into polymer sheets, we fabricated and utilized stamps composed of a SU-8 photoresist coating on a rigid metal substrate. A copper plate was coated with a seed primer layer of SU8-3050 photoresist, and subsequently by a second, feature layer, with the thickness equal to the height of the desired channels. Unlike in soft-lithography, fabrication of bas-relief features of channels in polymers required pressure and heat. The applied pressure would easily crack and break traditional silicon wafer stamps (which are used as mold masters for PDMS). Therefore, we selected 1 mm-thick copper sheets as the base plates onto which we applied the SU-8 coating. We chose SU-8 3050 for the fabrication of stamps since, based on the manufacturer’s data, this specific photoresist has superior adhesion to copper, in comparison with other photoresists.

Furthermore, we found that fabricating stamps by coating one layer, the feature layer in contact with the copper stamp led to the channel features peeling off during embossing of polymer sheets and, as a result, short stamp lifetime. This problem occurred because the surface contact area of the channel photoresist layer with the copper stamp was small (as wide as the channel), which did not provide enough adhesion between the photoresist and the copper to resist the embossing stage. To overcome this problem, we first applied a seed layer of SU-8 on the copper stamp, which covered the entire stamp surface. Subsequently, we deposited a second channel feature layer on the first SU-8 layer. We found that the adhesion between two SU-8 layers (the channel layer to the seed
layer) is stronger than the adhesion between photoresist and copper and therefore the stamp containing a seed layer was more robust and lasted longer than a stamp without a seed layer.

In the course of fabrication, we found several limitations in channel dimensions. First, the aspect ratio, defined as the ratio of the height of the channel to its width could not exceed 3. Figure 3.1. shows a schematic of the cross-section of a stamp with features with three aspect ratios of the topographic features. In the embossing stage, when the temperature was above the glass transition temperature, $T_g$, for amorphous polymers (or above $T_m$ for HDPE), and pressure was applied, the stamp features became imbedded into the softened polymer. Once the stamp and polymer cooled to the de-embossing temperature (below the $T_g$) the polymer became glassy and rigid. In the case for HDPE, the de-embossing temperature was below the $T_m$. Since higher aspect-ratio stamp features with the same width have a higher surface area in contact with the polymer, due to taller features, the force required to remove the polymer from the stamp at the de-embossing temperature, was increased when the aspect ratio was too high. The adhesion between the feature walls and the stamp was greater than the adhesion of the photoresist channel layer to the stamp seed layer. In such a case, the stamp feature layer peeled off the seed layer. Thus, in the present work, the stamp feature aspect ratio was limited in the range 0.16 to 1.
Figure 3.1. A schematic of a SU-8 on copper stamp showing three channel features of different aspect ratios (0.25, 1, and 2).

3.3.2 Polymer Reactor Fabrication

The fabrication conditions for the PC, COP, PMMA, HDPE, PVC, and PS, are listed in Table 3.2. The parameters, such as pressure, temperature, and time, were optimized to ensure high fidelity embossing of channel features and strong bonding between the embossed and planar polymer sheets, to produce durable MF reactors. Each polymer required specific embossing and bonding conditions, such as pressure and temperature. For example, PS required an embossing temperature of 125 °C while PC required a temperature of 165 °C, since these amorphous polymers have a different $T_g$ and different mechanical properties.

The embossing step for amorphous polymers was carried out at a temperature several degrees above the $T_g$ to allow the polymer to soften (and become viscous) and to conform to the stamp upon the application of pressure. All polymers were heated for a particular amount time, usually 5 min, prior to any pressure being applied, in order to adequately soften the polymer. Applying pressure to the polymer on the stamp before sufficiently heating the sample resulted in cracking of the stamp features. After pressure was applied and maintained during the embossing stage, the hot press was cooled to several degrees (10 to 20 °C) below the $T_g$ for amorphous polymers, or several tens of
degrees below the $T_m$ for HDPE, in order to preserve the embossed features during de-embossing. It was easier to de-emboss a ductile polymer sheet (that was relatively close to its $T_g$) vs. a hard rigid one (that was several tens of degrees below its $T_g$). Allowing the polymer and stamp to cool to room temperature before de-embossing resulted in the stamp features tearing off the stamp when removed. Thus, we optimized the de-embossing temperatures for each of the polymers to ensure preservation of features in the embossed reactor, as well as to limit any damage to the stamp.

Bonding of the topographically patterned polymer sheet and a planar sheet was achieved at the temperature several degrees below the $T_g$ of the particular polymer used (for HDPE, the temperature was several degrees below its $T_m$). For example, 143 °C was used for PC which has $T_g$ of 149 °C. The temperature chosen for each polymer for bonding was such that the polymer was close to the glass transition range, to allow chain mobility at the interface between the embossed reactor and planar sheet, but preserved the topographical features.
### Table 3.2. Optimized fabrication conditions for the fabrication of MF devices

<table>
<thead>
<tr>
<th>Structure</th>
<th>Polycarbonate</th>
<th>Cyclic Olefin Polymer</th>
<th>Poly(methyl methacrylate)</th>
<th>Polyethylene (HDPE)</th>
<th>Poly(vinyl chloride)</th>
<th>Polystyrene*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glass transition temperature (°C)</td>
<td>149(^a)</td>
<td>136(^b)</td>
<td>120(^{19,21})</td>
<td>-123(^{22-24})</td>
<td>90(^{25})</td>
<td>95(^a)</td>
</tr>
<tr>
<td>Melting Temperature (T&lt;sub&gt;m&lt;/sub&gt;) (°C)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>146(^{26-28})</td>
<td>210</td>
<td>-</td>
</tr>
<tr>
<td>Embossing temperature (°C)</td>
<td>165</td>
<td>155</td>
<td>125</td>
<td>145</td>
<td>125</td>
<td>125</td>
</tr>
<tr>
<td>Embossing time (min)</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>1</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Embossing pressure (MPa)</td>
<td>1.55</td>
<td>1.55</td>
<td>1.55</td>
<td>2.24</td>
<td>2.07</td>
<td>1.55</td>
</tr>
<tr>
<td>De-embossing temperature (°C)</td>
<td>145</td>
<td>135</td>
<td>105</td>
<td>120</td>
<td>65</td>
<td>105</td>
</tr>
<tr>
<td>Bonding temperature (°C)</td>
<td>143</td>
<td>133</td>
<td>105</td>
<td>120</td>
<td>88</td>
<td>90</td>
</tr>
<tr>
<td>Bonding time (min)</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>6</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Bonding pressure (MPa)</td>
<td>1.55</td>
<td>1.55</td>
<td>1.38</td>
<td>2.24</td>
<td>1.38</td>
<td>1.21</td>
</tr>
</tbody>
</table>

* Polystyrene MF reactors were fabricated for potential biological applications, however, the biocompatibility of reactors was not assessed in this work.

\(^{a}\) Glass transition temperatures were obtained from the manufacturer.

\(^{b}\) Information provided by the manufacturer.

### 3.3.3 Characteristics of Embossed MF Reactors

To ensure the fidelity and reproduction of channel features from the copper stamp to the polymer sheets after embossing, optical microscopy and profilometry analyses were carried out. Figure 3.2 shows a comparison of features on the stamp (a,c) taken in the reflection mode and the MF reactor (b,d) features taken in the transmission mode. After embossing the reactor, the channel imprints were characterized for fidelity and
reproduction of topographic features (the channel widths of the features on the stamp (left) and the features embossed in the polymer (right) differed by less than 2%).

**Figure 3.2.** Optical reflectance images of the two regions of the copper stamp (a,c) and of the embossed polymer sheet (b,d). These images provide two-dimensional characterization in order to ensure fidelity of features from the stamp to the microreactor. The scale bar is 200 µm.

Figure 3.3 shows a three-dimensional profile of a channel bend in an embossed PC MF reactor. The colours (red and blue) indicate the height of features with blue and red colours corresponding to low and high features, respectively. Profiles of the embossed channel features were obtained after the embossing stage to ensure channel feature fidelity. The height of the channels fabricated on the copper stamp, for the PC experiments, was 51 µm as measured by profilometry immediately after stamp fabrication. The average depth of the embossed polymer channel features in the MF reactor was 50 µm (Figure 3.3). We observed consistent reproducibility of channel
feature heights with maximum variation of 1-2 µm from the polymer features and stamp features.

Figure 3.3. A three-dimensional image of the channel bend in the embossed MF reactor. The image was taken with an optical profilometer to ensure that the correct heights were achieved in the embossed reactor.

3.3.4 Bond Strength of MF Reactors

In order to optimize the temperatures and pressures of polymer bonding to fabricate polymer reactors, we examined the bond strength following the bonding stage. Pressurized N₂ gas was supplied at pressures in the range 0 to 500 kPa, to a MF reactor to determine the pressure at which the seal between the embossed and planar sheets began to detach. Polymer sheets with embossed features were sealed with a planar sheet after only one inlet was drilled at one end of a channel, such that the channel connected to this inlet was a “dead-end”. Tubing was glued to this inlet using epoxy resin and connected to a compressed nitrogen tank. The device was placed under water and the pressure of nitrogen gas was gradually increased in steps of 10 kPa/min. After a critical pressure was reached, the bond between the embossed reactor and the planar sheet of polymer started
to fail and bubbles exiting the reactor were observed. As an example, typical de-bonding pressures for PC were in the range from 320 to 400 kPa. To compare these pressures with the pressures experienced in the MF experiments, we connected a pressure gauge to one of the inlets of our MF reactor and introduced water at various flow rate in the range 1 to 10 mL/hr. We observed that the reactor remained operation up to 10 mL/hr.

3.3.5 Solvent Compatibility of Polymer MF Reactors

Although there are many polymers that can be used for the fabrication of MF reactors, the typical challenge is to choose the material that is compatible with the solvents and reagents to be used in MF synthesis. A compatible material is one that does not swell, dissolve, or react in any way with the solvents being used. Swelling of the MF reactor material or a chemical reaction between the solvent and the polymer used for the fabrication of the reactor can lead to a change in the channel geometry and weaken the bond between the embossed reactor and the planar sheet. We focused our efforts on finding and testing MF materials for polar solvent and organic solvents.

3.3.5.1. Microfluidic Reactors Operating in Polar Solvents

The material compatibility of PC, COP, and PMMA was assessed with several different solvents, including xylene, diethyl ether, hydrochloric acid, isopropyl alcohol, and water, to gauge the usability of PC for MF reactors operating in different solvents. We first tested the swelling behavior of PC by cutting pieces (1x1 cm) and measuring dry weight change before and after solvent exposure. Figure 3.4 shows the percentage of
weight change, \( \delta \), for PC pieces after 24 h incubation in the xylene, diethyl ether, hydrochloric acid, isopropyl alcohol, and water. It was found that xylene led to the most weight change, i.e \( \delta \), (43%), followed by diethyl ether (14%). Hydrochloric acid, isopropyl alcohol, and water resulted in minimal (less than 2%) weight change after 24 hr. The results of the solvent uptake experiments was useful for determining which solvents were compatible with polycarbonate MF reactors and assessing the potential applicability of PC reactors.

![Figure 3.4](image)

**Figure 3.4.** Solvent uptake of polycarbonate of xylene (red), diethyl ether (orange), hydrochloric acid (teal), isopropyl alcohol (blue), and water (green).

The results of testing chemical compatibility for PC, COP, and PMMA are shown in Table 3.3. A check mark in Table 3.3 indicates that the material is compatible (solvent uptake is less than 2%). An “X” indicates that swelling greater than 2% (weight) occurs upon exposure to solvent.
Table 3.3. Chemical compatibility of COP, PC, and PMMA to a range of solvent.

<table>
<thead>
<tr>
<th></th>
<th>COP</th>
<th>PC</th>
<th>PMMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isopropyl Alcohol</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Hydrochloric Acid</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Ethanol</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Xylene</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Water</td>
<td>✓</td>
<td>✗</td>
<td>✓</td>
</tr>
</tbody>
</table>

Based on the solvent uptake results presented in Table 3.3, we selected PC as the material of choice for aqueous MF synthesis. Specifically, we utilized a PC MF reactor for studying kinetics of the aqueous polymerization reaction of $N$-isopropyl acrylamide (NIPAAm) in the presence of $N',N',N,N'$-tetramethylene diamine and ammonium persulfate (the details of this study as described in Chapter 4). We verified that the PC reactor used in the polymerization study was compatible with the solvent and reagents by measuring the channel widths before and after polymerization (Figure 3.5). The channel widths did not change appreciably (the change was less than 1%) after the MF reactor was used in polymerization reactions.

Figure 3.5. Optical microscopy images of channel bends in a PC reactor before NIPAAm polymerization experiments (a), and after experiments (b). Scale bar is 400 µm.
3.3.5.2. Microfluidic Reactors Operating in Organic, Aromatic, and Hydrocarbon Solvents

Aromatic and linear hydrocarbon solvents are used in organic synthesis and are not compatible with the majority of polymers, such as PC, PMMA, and COP that are currently used for the fabrication of MF reactors, as shown in Table 3.3. In the present work, we selected PE as the material for organic solvent compatibility experiments.

The compatibility of the PE reactor with different hydrocarbon and aromatic solvents, such as tetrahydrofuran (THF), dichloromethane (DCM), hexanes, and bromobenzene (BB), was assessed by fabricating a MF reactor and examining the change in the width of the microchannel. The width of the channel was measured every 30 min for 4.5 h (approximately the duration of a typical experiment), in order to assess the extent of PE swelling and the results are presented in Figure 3.6a for THF, DCM, hexanes, and BB. The extent of swelling of the microchannel width was inferred by calculating the relative reduction in channel width as $(w-w_0)/w_0$, where $w_0$ was the initial channel width and $w$ was the channel width after the specific time. Figure 3.6a shows that the maximum swelling of channel walls of 1.5% for $w_0= 300$ µm occurred in DCM after 4.5 h. No de-bonding, visible channel distortion, or compromised reactor structural integrity were observed.

To evaluate the chemical resistance of the MF reactor fabricated in PE at elevated temperatures, we examined the compatibility of PE with BB by measuring the relative change in the width of the channel upon exposure to solvent. To conduct these tests we submerged the PE reactor in an oil bath at different temperatures from 25 to 80 °C. Figure 3.6b shows the change in channel width (as a percentage) at the after 4.5 hr
exposure to bromobenzene at 25, 60, and 80 °C. The MF reactor channel width decreased by 1.2, 1.9, and 2.7 % at 25, 60, and 80 °C, respectively. No de-bonding or change in structural integrity of the PE reactor was observed.

**Figure 3.6.** Chemical compatibility of HDPE reactors for THF, DCM, hexanes, and BB (a) and for BB at elevated temperatures (b). The width of the channel, \( w = 300 \, \mu m \), was measured over a period of 4.5 hours while several solvents flowed through the reactor channel.

As specified in Table 3.1, optical transmission can be a crucial requirement for the performance of MF reactors, as it allows for online optical microscopy characterization of chemical reactions\(^8,9\). Since PE is a translucent polymer, due to the scattering of light by its crystalline domains, the transmission of light through the MF reactor fabricated in PE would depend on the thickness of the reactor walls.

We examined the variation in light transmission in the spectral range from 300 to 800 nm of a PE film with the thickness varying from 325 to 1500 \( \mu m \) (Figure 3.7a). The transmission of light (corresponding to the optical transparency of PE) increased with a reduction in PE film thickness. For example, for the wavelength of 500 nm, it increased from 12.2 to 64 % for the sheet thickness reducing from \( \sim 1500 \) to \( 325 \, \mu m \), respectively. Yet, with reduced thickness, the PE films became more flexible, which led to difficulties
in the embossing stage, e.g., sagging and warping of the reactor walls and ceiling. Thus the lower PE film thickness limit for fabrication was determined to be \(~300 \, \mu\text{m}\).

To determine the upper limit in PE sheet thickness, we fabricated a MF reactor with the thickness of reactor walls in the range from 325 to \(\sim1500 \, \mu\text{m}\) and determined the maximum thickness of the reactor wall, at which segmented gas-liquid flow could not be discerned using optical microscopy. For 150 \(\mu\text{m}\) tall channels, the maximum thickness of a single PE sheet was determined to be \(\sim1500 \, \mu\text{m}\).

Next, we examined the ability to vary the surface energy of PE sheets. Since PE is a hydrophobic material and has a low surface energy, it may not be suitable, in its original state, for applications in which a high energy surface is required. The PE sheet was subjected to gas plasma treatment and the subsequent change in contact angle, \(\theta\), of water was examined as a function of plasma exposure time.

![Figure 3.7](image-url)

**Figure 3.7.** Variation in transmission of PE films of increasing thickness from 300 to 1500 \(\mu\text{m}\), in the spectral range 300 to 800 nm, plotted as a function of wavelength (a). Contact angles measurements of PE after plasma treatment under oxygen, nitrogen, or air, at varying exposure durations (b).

Figure 3.7b shows the variation in the value of \(\theta\) after plasmas of several gases. After exposure of PE sheets to oxygen plasma for 50 s, the value of \(\theta\) was reduced from
92 to 53 °; and did not significantly decrease at longer exposure times. This value of θ remained constant for at least 7 days, when the PE sheets were stored under ambient conditions. Plasma treatment of PE sheets with nitrogen and air plasma yielded similar θ values (Fig 3.7b).

A MF reactor was fabricated in PE and used for gas-liquid reaction of CO₂ and BB (Figure 3.8a). The MF reactor utilized a T-junction to generate segmented flow of alternating has plugs (CO₂) and liquid segments (BB), as shown in Figure 3.8b. The segmented flow was maintained for 2 hr. After that, the width of the microchannel at the T-junction (denoted as “D” in Figure 3.8a, inset) was measured before and after the reaction. The width difference before and after reaction was 1%. This result indicated that PE is the material of choice for MF studies involving organic solvents.

**Figure 3.8.** Schematic of the MF reactor for gas-liquid studies (a). The inset shows an optical image of the T-junction and the location of the measurements of the channel width, D. Segmented flow generation in the MF reactor at the T-junction (b).

PE was investigated for chemical compatibility with organic solvents, DCM, BB, THF, and hexanes, and was found to be suitable for MF studies. This polymer can be used for fabrication of MF reactors for studying chemical reactions.
3.3.6. Microfluidic Reactors with Low Gas Permeability

The ability of a gas to permeate polymer substrates depends on the type of polymer, the type of gas, the temperature, and the pressure gradient across the substrate. The flexibility of polymer chain increases the free volume in the polymer that allows gas to diffuse into the network\textsuperscript{29}. Gas diffusion in the polymer occurs as gas molecules migrate through free volume of the polymer. Some polymers such as low-density polyethylene (LDPE) and PDMS are easily permeated by gases, while polymers such as poly(vinyl chloride) (PVC) and biaxially stretched polyethylene terephthalate are relatively impermeable.

The permeability of a polymer to a gas, or penetrant, is generally expressed as\textsuperscript{30}

\[ P = \frac{NI}{p_2 - p_1} \]  

where \( P \) is the permeability coefficient (cm\(^2\)/s), \( p_2 \) is the upstream pressure, \( p_1 \) is the downstream pressure, \( l \) is the film thickness, and \( N \) is the steady-state penetrant flux through the polymer.

Gas permeation in MF reactors has received increased attention in applications ranging from studying hypoxic effects on cells, evaporation-based protein crystallization\textsuperscript{31}, polymerase chain reaction MF studies\textsuperscript{32}, and supercritical fluid extractions. The requirement for low gas permeability of MF devices becomes important when either a gas remains inside a microchannel for a relatively long period of time (several hours) or gas diffusion in and out of a channel must be strictly controlled – as is the case for gas-liquid reactions\textsuperscript{8}. On the other hand, gas permeation through MF reactor walls may be beneficial as in the case of cell culture in the MF device\textsuperscript{33}. 
We selected PVC as the material for the fabrication of MF reactors with low gas permeability. PVC has reduced gas permeability compared to more common polymers such as PC. For example the permeability of PC to CO$_2$ gas is $6.0 \text{ m}^3 \text{(STP)} \text{ m}^{-1} \text{ m}^{-2} \text{ Pa}^{-1} \left(10^{17}\right)^{34}$ compared to $0.15 \text{ m}^3 \text{(STP)} \text{ m}^{-1} \text{ m}^{-2} \text{ Pa}^{-1} \left(10^{17}\right)$ for PVC$^{35}$.

Since PDMS is one of the standard materials used in MFs, we used it as a reference material in studies of gas permeability, to compare it with PVC. The PVC MF reactor consisted of two inlets that converged to a T-junction (the channel geometry is shown in Figure 3.8a). The fabrication of the reactor consisted in bonding a 1/4 inch thick PVC embossed sheet, containing the channel features, to a 100 $\mu$m thick PVC film. The same stamp template was used to fabricate a MF reactor in PDMS. Sufficient material thickness of at least ¼” was allowed for the side walls and floor of the channel in order to allow for the assumption that the majority of gas diffusion occurred through the 100 $\mu$m thick (top ceiling of the channel) during the time span of the experiments.

Segmented flow of gas and liquid was generated in the MF channel using pressure driven flow. After alternating N$_2$ plugs and liquid slugs were generated, the inlets and outlet of the MF reactor were both pressurized at 1.73 atm which stopped flow and maintained the gas plugs stationary. The pressure difference of 1.7 atm in the plugs to 1 atm (outside the reactor, at the outlet) was the driving force for gas mass transfer across the 100 $\mu$m-thick PVC or PDMS film. We monitored the volume change of the stationary plugs in the reactor channel as a function of time for the PDMS reactor at 1.73 N$_2$ pressure (Figure 3.9) and observed bubble volume decay with time. We chose the length of experiment to be 5 hr (typical for most MF studies). After 5 hr, there was a 45% reduction of the plug volume, in the PDMS reactor.
The shrinkage of gas plugs eventually resulted in plugs with a diameter smaller than the width of the microchannels which led to liquid seeping between plugs. At this point (typically after 5 hr), the experiments were stopped. To ensure that the shrinkage of plugs over time was not a result of physical dissolution of N\textsubscript{2} in water, the segmented flow was generated 15 cm upstream of the characterization zone to allow the system sufficient time to reach equilibrium. Since physical dissolution occurs within 10 s, based on previous MF studies\textsuperscript{8}, any subsequent plug shrinkage was attributed to gas mass transfer out of the reactor across the 100 \(\mu\text{m}\)-thick ceiling of the MF reactor.

![Figure 3.9](image.png)

**Figure 3.9.** Gas plug volume as a function of time for PDMS reactor at 1.73 atm N\textsubscript{2}. Optical images of bubbles are superimposed at two time points, 50 min and 300 min, to show the length of bubbles.

Following PDMS experiments, experiments were repeated for PVC MF reactor under the same conditions.

The experiments were repeated at pressure of 2.44 atm and the time-dependent plug volumes were normalized and plotted together in Figure 3.10. The decay in plug volume was more pronounced for 2.44 atm vs. 1.73 atm for the PDMS reactor: at 300 min, the volumes at 1.73 and 2.44 atm were 45 and 21% of the initial plug volumes,
respectively. In comparison, plug volume decay in the PVC reactor under both 1.73 and 2.44 atm N\textsubscript{2}, was negligible (less than 2 % difference).

![Normalized plug volumes as a function of time for PDMS reactor at 1.73 atm N\textsubscript{2} (blue diamond), PDMS reactor at 2.44 atm N\textsubscript{2} (purple circles), PVC reactor at 1.73 atm N\textsubscript{2} (red squares), and PVC reactor at 2.44 atm N\textsubscript{2} (green triangles).](image)

**Figure 3.10.** Normalized plug volumes as a function of time for PDMS reactor at 1.73 atm N\textsubscript{2} (blue diamond), PDMS reactor at 2.44 atm N\textsubscript{2} (purple circles), PVC reactor at 1.73 atm N\textsubscript{2} (red squares), and PVC reactor at 2.44 atm N\textsubscript{2} (green triangles).

We note that the pressures used in these experiments, up to 2.44 atm, was above pressures used in previous gas-liquid studies involving CO\textsubscript{2}\textsuperscript{7-9}. The experiments conducted illustrate the inapplicability of PDMS reactors for reactions involving gas at the pressures studied. On the other hand, PVC is an ideal polymer for long-term reactions involving requiring gas impermeability.
3.4 Conclusions

The results described in this chapter allows simple fabrication techniques to be applied to a number of polymers including PC, COP, PMMA, HDPE, PVC, and PS, each of which can impart useful chemical and mechanical properties to a MF reactor. We developed a reproducible, cost-efficient, and time-efficient method for fabricating reliable and durable MF reactors in which the methodology can be tuned for different polymer material. Each material is tailor-fabricated for the specific application, depending on the solvents used, optical characteristics and gas permeability requirements.

We showed that PC, COP, and PMMA are applicable to polar solvent systems but not for organic solvents. High-density polyethylene was used in MF compatibility experiments involving organic solvents such THF, DCM, BB, and hexanes and shown to be compatible in a gas-liquid reaction involving CO2 and BB. Poly(vinyl chloride) was used to showcase gas impermeability of MF reactor and compared to PDMS reactor for the segmented flow of N2 and water. Finally, PS MF reactor was fabricated for biological applications.

The work in this chapter paves the way for chemical reactions, previously limited to batch scale, to be conducted in a MF format while removing the limitations of currently employed MF materials.
References


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Chapter 4

Kinetics of a Multicomponent Polymerization Reaction Studied in a Microfluidic Format

4.1 Introduction

A systematic exploration of a broad range of experimental variables for multicomponent reactions is time-consuming and is cost-inefficient, especially when the parameter space includes varying concentrations of multiple reagents and the changes in temperature, pH, or pressure. Numerous reiterations are needed to evaluate and quantify the effect of superposition of multiple reaction variables.

Studies of chemical reactions in a microfluidic (MF) format provide an efficient experimental platform for the exploration of a large parameter space and optimization of formulations, due to the ability to vary the concentrations of reagents in a throughput manner, especially when this is complemented by rapid on-chip characterization of reaction products. In MF synthesis, the type and the concentrations of multiple reagents introduced in the reaction system are controlled in a throughput manner by varying the ratio of their volumetric flow rates. Advantages of MFs as a chemical discovery platform also include reduced consumption of reagents, excellent control over heat and mass transfer, improved safety in handling dangerous species, and the ability to carry out multi-step reactions without exposure of the system to ambient conditions. Moreover, in comparison with the challenge in scaling up of conventional multi-reagent reactions, a combination of multiple MF reactors working in parallel (the “scaling up” strategy) offers high reproducibility and an increase in productivity.
Continuous in-flow polymerization in microreactor systems has been demonstrated for radical polymerization of vinyl monomers, coordination polymerization, polycondensation, anionic, and ring-opening polymerization. Advantages of polymerization reactions in a MF format included excellent control of reaction conditions, the capability to vary the degree of polymerization by modulating the monomer-to-initiator ratio by changing their relative flow rates, and the ability to generate, in a throughput manner, large libraries of polymer samples for rapid evaluation.

The potential applications of the MF platform for studies and optimization of chemical formulations for polymerization reactions would not be fully realized without rapid, on-chip characterization of reagents and products. Implementation of in situ chemical characterization opens the possibility for (i) the rapid screening of the effect of reaction variables, (ii) feedback for reaction control parameters, (iii) detection of transient species, which may not exist upon their removal from the MF reactor, and (iv) kinetic studies with sufficient time resolution, specifically during the initial stage of the reaction.

Various characterization tools have been utilized for MF polymerization reactions. Continuous online size exclusion chromatography enabled monitoring of the molecular weight and molecular weight distribution of polymers synthesized in a tubular reactor by nitroxide-mediated polymerization. Multi-detection gel permeation chromatography of polymer samples collected at the outlet of a micro-reactor was used for the characterization of linear and branched polymers by combining a concentration- and a mass-sensitive detection technique. In situ Raman spectroscopy was used to characterize, with acceptable accuracy, the change in composition and degree of conversion of methacrylate compartmentalized in droplets in a MF reactor. Small-angle
light scattering was utilized to monitor and characterize the formation and size
distribution of multi-lamellar vesicles of a diblock copolymer in aqueous solutions\textsuperscript{11}.

Here we present the results of the first in situ MF study of the kinetics of a
polymerization reaction using infrared spectroscopy. This approach builds upon other IR-
based analytical approaches to MFs\textsuperscript{13}. We conducted a throughput systematic study of the
kinetics of a multi-component polymerization reaction at different pH values by using a
MF reactor interfaced with a Fourier transform infrared (FTIR) spectrometer. Fourier
transform infrared spectroscopy is a well-established technique that is applicable to full-
spectrum characterization of chemical species, as it allows quantitative analysis of
multiple reagents and products\textsuperscript{12}. Infrared spectroscopy can also be used to characterize
solvent–analyte interactions, hydrogen bonding, changes to protonation states,
conformation of macromolecules, and effects of temperature or electromagnetic fields.
These factors affect vibrational spectra by changing absorbance peak intensity and peak
position or by causing subtle changes in spectral line shape, which can be revealed
through second derivative spectroscopy\textsuperscript{14}.

We examined an exemplary polymerization reaction: the polymerization of N-
isopropylacrylamide (NIPAAm) in water, which was initiated by ammonium persulfate
(APS) in the presence of the accelerator $N,N,N',N'$-tetramethylethylenediamine
(TEMED). This important reaction is used for the preparation of gels in cell biology\textsuperscript{15},
gel electrophoresis\textsuperscript{16}, and the encapsulation of cells\textsuperscript{17}. 

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Based on previous work, the reaction that takes place is\textsuperscript{23}

\begin{equation}
S_2O_8^{2-} + (CH_3)_2NCH_2CH_2N(CH_3)_2 \rightarrow (CH_3)_2NCH_2CH_2\dot{N}^+ (CH_3)_2 + SO_4^- + SO_4^{2-} \quad (1)
\end{equation}

\begin{equation}
CH_2 = CHCONHC\dot{H}(CH_3)_2 \rightarrow [-CH_2 - CHCONHC\dot{H}(CH_3)_2]_n \quad (2)
\end{equation}

The APS and TEMED initiate the reaction and lead to the formation of two radical species which initiate polymerization. TEMED acts as an accelerator to increase the decomposition of APS at ambient temperature as well as participates in radical production\textsuperscript{23}.

We show the capability of synthesis in MFs integrated with infrared spectroscopy to rapidly examine the effects of varying the concentration of the monomer, initiator, and accelerator and the effect of pH of the solution on the kinetics of this polymerization reaction.

\subsection*{4.2 Experimental}

\subsubsection*{4.2.1. Experimental Design}

Figure 4.1 shows the design of the MF reactor used to study the kinetics of the polymerization of NIPAAm. The MF reactor was fabricated in polycarbonate, as described elsewhere\textsuperscript{18}. Fluid reagents were introduced into the MF reactor via a threaded interface system\textsuperscript{19}, which connected 1.6 mm poly(ether ether ketone) tubing (IDEX Corp.) to inlets on the reactor.

We followed the protocol of integration of the ATR-FTIR with the MF reactor described in our earlier work\textsuperscript{20}. The reactor had a microchannel width and height of 200 and 50 \(\mu\text{m}\), respectively. Unless specified, the cross-sectional area of the microchannel was \(10^4 \text{ \(\mu\text{m}^2\)}\). Aqueous solutions of APS, TEMED, and NIPAAm with initial
concentrations $C_{\text{APS},i}$, $C_{\text{TEMED},i}$, and $C_{\text{NIPAAm},i}$, respectively, and water were introduced into four syringes and supplied to the MF reactor through inlets (i)–(iv), respectively. The mixing between the reagent streams was carried out in a stepwise manner: first, by mixing the liquids supplied through inlets (i) + (ii) and (iii) + (iv) and then by combining the two streams in the reaction chamber in the serpentine channel (v), where the liquid reagents mixed and the reaction took place. The chemical changes in the reaction mixture were characterized after it flowed through the reaction chamber (v) and reached the ATR crystal (IR probe), a temperature probe, and a pH probe, located at positions P1, P2, and P3, respectively. The solution containing the polymer product and unreacted reagents exited the MF reactor through the outlet (vi).

Figure 4.1. Schematic of the MF reactor used for studying the polymerization reaction. Solutions of APS, TEMED, NIPAAm, and water were supplied via inlets (i)–(iv), respectively. Four small wavy channels following the inlets were used to increase hydrodynamic resistance in order to stabilize flow and avoid cross-talk between the channels. The reagents streams joined at a T-junction and flowed through a long serpentine channel in the mixing zone (v). The composition of the reaction mixture was characterized by ATR-FTIR using a probe placed at point P1. A temperature and a pH probe were placed at points P2 and P3, respectively. The solution of the polymer product and unreacted reagents were evacuated from the MF reactor via outlet (vi). The scale bar is 1 cm.
The cross-sectional area of the mixing channels in zone (v) was reduced from $10^4$ to $7.5 \times 10^3 \, \mu m^2$, due to protrusions from the channel walls, introduced to enhance mixing of the reagents (Figure 4.2).

**Figure 4.2.** Schematic of the segment of the mixing serpentine channel within the reaction compartment. Dimensions of microchannel features a, b, and c are 200, 100, and 200 µm, respectively.

### 4.2.1.1. Reaction Time and Reagent Concentrations

The reaction time was determined by the time it took the fluid to move between the T-junction (prior to the mixing channel) and the moment the mixture reached the ATR crystal. The reaction time was calculated as

$$t = DA/Q_T$$  \hspace{1cm} (3),

where $D$ is the distance between the beginning of the reaction chamber (v) and the ATR-FTIR probe (P1) ($D = 160$ mm); $A$ is the average area of the cross section of the microchannel in the reaction compartment, $A = 7.5 \times 10^3 \, \mu m^2$; and $Q_T$ is the flow rate of the entire reaction mixture. The value of $Q_T$ is defined as:

$$Q_T = Q_{NIPAAm} + Q_{TEMED} + Q_{APS} + Q_{H2O}$$  \hspace{1cm} (4),

where $Q_{NIPAAm}$, $Q_{TEMED}$, $Q_{APS}$, and $Q_{H2O}$ are the individual volumetric flow rates of the solutions of NIPAAm, TEMED, APS, and water, respectively. After on-chip mixing in the mixing channel (Figure 4.1, (v)), the solutions of the reagents were diluted to the initial on-chip concentrations.
\[ C_{\text{NIPAAm,d}} = C_{\text{NIPAAm,i}} \times \frac{Q_{\text{NIPAAm}}}{Q_T} \]  
\[ C_{\text{TEMED,d}} = C_{\text{TEMED,i}} \times \frac{Q_{\text{TEMED}}}{Q_T} \]  
\[ C_{\text{APS,d}} = C_{\text{APS,i}} \times \frac{Q_{\text{APS}}}{Q_T} \]

After a reaction time \( t \), the concentrations of the reagents changed to \( C_{\text{NIPAAm,t}} \), \( C_{\text{TEMED,t}} \), and \( C_{\text{APS,t}} \).

### 4.2.1.2. Correlation of Absorbance to Concentration

The flow rate of the solutions of each reagent solution was independently controlled using a separate syringe pump (PHD2000, Harvard Apparatus). All reactions were conducted at \( 21 \pm 1 \) °C. An attenuated total reflection Fourier transform infrared (ATR-FTIR) spectrometer (Vertex 70, Bruker Corp.) was interfaced with the MF reactor using a single reflection diamond ATR crystal (MIRacle, Pike Technologies). Unless otherwise specified, the spectra were generated from 32 scans at 10 kHz scan speed with 4 cm\(^{-1}\) spectral resolution. Infrared absorbance of chemical species of interest was determined by measuring the intensity of an absorption peak and relating it to the molar concentration using a calibration curve. The spectrometer was purged with air supplied from a purge gas generator (model 75-45, Parker Balston) to limit absorption by ambient \( \text{CO}_2 \) and \( \text{H}_2\text{O}(g) \). Detection was accomplished using a deuterated L-alanine-doped triglycine sulfate detector (DLATGS/D301, Bruker Inc.). Opus 6.5 software was used for computer-control of data acquisition and analysis. Measurements of \( \text{pH} \) were conducted using a VWR Symphony SB70P \( \text{pH} \) meter connected to a probe (MI408C, Microelectrode Inc.) with flow-through reference probe (ME16730, Microelectrode Inc.).
Probes and fluidic connections were interfaced with a customized microfluidic reactor (FlowJEM Inc.) using an interface component (PCIC, FlowJEM Inc., Toronto).

The use of *in situ* ATR-FTIR characterization enables measurements of reagent and product concentrations. Figure 4.3a shows representative IR spectra collected for the individual solutions of APS, TEMED, NIPAAm, and PNIPAAm. The arrows specify characteristic IR peaks for each species. Prior to the reaction, we verified that the spectrum of the reaction mixture was a weighted average of the individual reagent spectra. Figure 4.3b shows the variation in the intensity of the IR peaks, labeled in Figure 4.3a, for solutions with solute concentrations ranging from 1 to 150 mM. We verified that the linear trend of IR peak intensity *vs.* monomer concentration held until $C_{\text{NIPAAm}} = 300$ mM, which was the maximum on-chip concentration used in the present work (Section 4.3.4).

**Figure 4.3.** (a) Characteristic IR spectra for independent reagents acquired for the aqueous solutions of (i) APS, (ii) TEMED, (iii) NIPAAm, and (iv) PNIPAAm, collected at $Q_T = 3$ mL h$^{-1}$. Arrows mark characteristic “fingerprint” peaks chosen for subsequent intensity measurements. The groups responsible for the characteristic vibrations were (i) $S_2O_8^{2-}$ (1270 cm$^{-1}$), (ii) C–N (1020 cm$^{-1}$), (iii) C=C–H (975 cm$^{-1}$), and (iv) N–H (1560 cm$^{-1}$). All spectra were acquired *in situ* by averaging five spectra, each composed of 32 scans at 10 kHz. (b) Variation in concentration-dependent absorbance of the IR bands marked in (a). The inset shows the absorbance of the corresponding solutions at concentrations below 20 mM. Error bars represent one standard deviation.
In the range of monomer concentrations studied, the intensity of the absorbance peak at 975 cm\(^{-1}\) was related to the concentration of the monomer in solution by the slope of our calibration plot, which held constant up to 300 mM. We used the variation in absorbance of the double bond of NIPAAm vs. \(t\) to measure the time-dependent concentration of the monomer during the reaction (that is, conversion of monomer to polymer). We used our calibration plot, along with calculations of the effective path length of the ATR evanescent wave, to find the molar extinction coefficient of NIPAAm (see Appendix 4.1).

4.2.1.3. Determination of the Rate of Polymerization

We modulated the total flow rate of the reaction mixture to tune the reaction time within the interval \(0 \leq t \leq 6.75\) s, which limited the extent of conversion to less than 30\% for all reagent concentrations. A relatively low conversion enabled us to avoid problems associated with increase in viscosity of the polymer solution, due to the formation of high-molecular weight PNIPAAm, as well as polymer adsorption on the ATR crystal. We prepared three stock aqueous solutions with \(C_{\text{NIPAAm},i} = 525\) mM, \(C_{\text{TEMED},i} = 180\) mM, and \(C_{\text{APS},i} = 180\) mM and introduced them in the MF reactor. The manipulation of the flow rate of water (the fourth inlet) enabled controlled dilution of the reagent streams. For example, we used \(Q_{\text{NIPAAm}} = 0.235\) mL h\(^{-1}\), \(Q_{\text{TEMED}} = 0.118\) mL h\(^{-1}\), \(Q_{\text{APS}} = 0.235\) mL h\(^{-1}\), and \(Q_{\text{H2O}} = 0.118\) mL h\(^{-1}\) (\(Q_T = 0.706\) mL h\(^{-1}\)) to calculate the reaction time \(t = 6.75\) s using eq. 3. Using eq. 5, we determined initial on-chip reagent concentrations to be \(C_{\text{NIPAAm},d} = 175\) mM, \(C_{\text{TEMED},d} = 30\) mM, and \(C_{\text{APS},d} = 60\) mM.
The reaction was allowed to run for 5 min, after which the FTIR spectra were acquired and the concentration of NIPAAm was determined from the intensity of NIPAAm absorbance peak at 975 cm\(^{-1}\) by using eq. 6. Following data acquisition, the value of \(Q_T\) was changed to achieve a new reaction time, without changing the ratio between \(C_{\text{NIPAAm},d}\), \(C_{\text{TEMED},d}\), and \(C_{\text{APS},d}\), by modulating all reagent flow rates by the same multiplicative factor. In this manner, we examined the effect of four different reaction times in the range from 2.25 to 6.75 s. Table 4.1. shows the flow rates of the solutions of individual reagents and their corresponding residence times in the channel. Using eq. 5, the initial reagent concentrations of \(C_{\text{NIPAAm},i} = 525\) mM, \(C_{\text{TEMED},i} = 90\) mM, and \(C_{\text{APS},i} = 180\) mM were diluted to \(C_{\text{NIPAAm},d} = 175\) mM, \(C_{\text{TEMED},d} = 30\) mM, and \(C_{\text{APS},d} = 60\) mM with residency times ranging from 2.25 to 6.25 s.

As NIPAAm was consumed over the course of polymerization, the variation of \(C_{\text{NIPAAm},t}\) vs. \(t\) yielded an exponentially decaying curve. Such curves were plotted for varying \(C_{\text{NIPAAm},d}\), \(C_{\text{TEMED},d}\), and \(C_{\text{APS},d}\). Each decay curve \((C_{\text{NIPAAm},t}\) vs. \(t\)) was fit to an exponential decay function \(C_{\text{NIPAAm},t} = C_{\text{NIPAAm},d}e^{-bt}\), where \(C_{\text{NIPAAm},d} = 175\) mM, and \(b\) is the exponential decay constant (determined from fitting). The initial rate of decay at \(t = 0\) was acquired by taking the derivative of the decay function with respect to time and setting \(t = 0\) (that is, \(dM/dt|_0 = -b \times 175\) mM s\(^{-1}\)). We converted the initial rate of decay of the monomer to the initial polymerization rate as \(-dM/dt|_0 = dP/dt|_0\), where the terms on the left and right side are the rate of change of the monomer concentration and the rate of change of the polymer concentration at \(t = 0\), respectively.
Table 4.1. Calculated residence times in the reaction compartment and flow rates.

<table>
<thead>
<tr>
<th>Residence Time (s)</th>
<th>$Q_T$ (mL h$^{-1}$)</th>
<th>$Q_{APS}$ (mL h$^{-1}$)</th>
<th>$Q_{TEMED}$ (mL h$^{-1}$)</th>
<th>$Q_{NIPAAm}$ (mL h$^{-1}$)</th>
<th>$Q_{H2O}$ (mL h$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.25</td>
<td>2.12</td>
<td>0.71</td>
<td>0.35</td>
<td>0.71</td>
<td>0.35</td>
</tr>
<tr>
<td>3.38</td>
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<td>0.47</td>
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<td>0.24</td>
</tr>
<tr>
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<td>0.35</td>
<td>0.18</td>
</tr>
<tr>
<td>6.75</td>
<td>0.71</td>
<td>0.24</td>
<td>0.12</td>
<td>0.24</td>
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</table>

Table 4.2 summarizes the flow rate ratios and the corresponding initial reagent concentrations for every series of experiments conducted in this work, as well as the required flow rate ratios to achieve those concentrations.

Table 4.2. Concentrations of the reagents and their respective flow rate ratios.

<table>
<thead>
<tr>
<th>Figure</th>
<th>$C_{APS,d}$ (mM)</th>
<th>$C_{TEMED,d}$ (mM)</th>
<th>$C_{NIPAAm,d}$ (mM)</th>
<th>$Q_{APS}/Q_T$</th>
<th>$Q_{TEMED}/Q_T$</th>
<th>$Q_{NIPAAm}/Q_T$</th>
<th>$Q_{H2O}/Q_T$</th>
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<td>0.333</td>
<td>0.167</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>30</td>
<td>175</td>
<td>0.250</td>
<td>0.167</td>
<td>0.333</td>
<td>0.250</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>30</td>
<td>175</td>
<td>0.167</td>
<td>0.167</td>
<td>0.333</td>
<td>0.333</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>30</td>
<td>175</td>
<td>0.083</td>
<td>0.167</td>
<td>0.333</td>
<td>0.417</td>
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<tr>
<td>4.5</td>
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<td>175</td>
<td>0.167</td>
<td>0.333</td>
<td>0.333</td>
<td>0.167</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>45</td>
<td>175</td>
<td>0.167</td>
<td>0.250</td>
<td>0.333</td>
<td>0.250</td>
</tr>
<tr>
<td></td>
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<td>30</td>
<td>175</td>
<td>0.167</td>
<td>0.167</td>
<td>0.333</td>
<td>0.333</td>
</tr>
<tr>
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<td>15</td>
<td>175</td>
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<td>0.333</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>45</td>
<td>175</td>
<td>0.250</td>
<td>0.250</td>
<td>0.333</td>
<td>0.167</td>
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<td></td>
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<td>0.333</td>
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<td>0.500</td>
<td>0.167</td>
</tr>
<tr>
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<td>305</td>
<td>0.167</td>
<td>0.167</td>
<td>0.583</td>
<td>0.083</td>
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4.2.1.4. Determining the Reaction Order of the Reagents

In a steady-state approximation, the rate of initiation is equal to the rate of termination, such that the concentration of radical species remains constant and polymerization rate of free radical polymerization can be written as

\[
\frac{-d[M]}{dt} = R_p = k_p \left( \frac{f k_d}{k_t} \right)^{1/2} [M]^{1/2} \]

(7),

where \([M]\) is the concentration of monomer, \(R_p\) is the rate of polymerization, \(f\) is the fraction of initiator radicals reacting with the monomer, and \(k_p\), \(k_d\), and \(k_t\) are the rate constants for chain propagation, initiator decomposition, and chain termination, respectively.\(^{22}\) This equation holds true for initiators that produce two radical species.

In the absence of the accelerator, TEMED, eq. 7 can be rewritten to incorporate the initiator, APS, and monomer, NIPAAm as

\[
\frac{dP}{dt} \bigg|_0 = k_p \left( f \frac{k_d}{k_t} \right)^{1/2} C_{\text{APS,d}}^{1/2} C_{\text{NIPAAm,d}}
\]

(8),

where \(dP\) is the rate of polymerization.

In the present work, TEMED accelerated the reaction by enhancing decomposition of APS and by forming its own radical species.\(^{23}\) The rate of the polymerization was determined as

\[
\frac{dP}{dt} \bigg|_0 = k' C_{\text{APS,d}} \times C_{\text{TEMED,d}} \times C_{\text{NIPAAm,d}}^{z}
\]

(9),

where \(k' = k_p [f(k_d/k_t)]^{1/2}\). The equivalent form of eq. 9 is

\[
\ln \left( \frac{dP}{dt} \bigg|_0 \right) = x \ln(C_{\text{APS,d}}) + y \ln(C_{\text{TEMED,d}}) + z \ln(C_{\text{NIPAAm,d}}) + \ln k'
\]

(10)
To test the reaction order with respect to a particular reagent, $\frac{dP}{dt}|_0$ was determined for several concentrations of that reagent, while the concentrations of the other two reagents were maintained constant. For example, when $C_{APS,d}$ changed and $C_{TEMED,d}$ and $C_{NIPAAm,d}$ were maintained constant, eq. 10 took the form of eq. 11a. Similarly, when $C_{TEMED,d}$ or $C_{NIPAAm,d}$ was changed and the concentrations of two other reagents were maintained constant, eq. 10 took the form of eqs. 11b and 11c, respectively.

$$\ln\left(\frac{dP}{dt}|_0\right) = x \ln(C_{APS,d}) + \ln(w_a)$$  \hspace{1cm} (11a)

$$\ln\left(\frac{dP}{dt}|_0\right) = y \ln(C_{TEMED,d}) + \ln(w_b)$$ \hspace{1cm} (11b)

$$\ln\left(\frac{dP}{dt}|_0\right) = z \ln(C_{NIPAAm,d}) + \ln(w_c)$$ \hspace{1cm} (11c)

where $w_a$, $w_b$, and $w_c$ are constants with the values $\ln(w_a) = \ln k' + y \ln(C_{TEMED,d}) + z \ln(C_{NIPAAm,d})$, $\ln(w_b) = \ln k' + x \ln(C_{APS,d}) + z \ln(C_{NIPAAm,d})$, and $\ln(w_c) = \ln k' + x \ln(C_{APS,d}) + y \ln(C_{TEMED,d})$. Plotting $\ln(dP/dt|_0)$ vs. $\ln(C)$ yields a linear plot with a slope equal to the reaction order with respect to the reagent with changing concentration.

**4.3 Results and Discussion**

**4.3.1. Effect of the Initiator Concentration on the Polymerization Kinetics**

In the first series of experiments, we tested the effect of the concentration of the initiator APS, $C_{APS,d}$, on the rate of NIPAAm polymerization. Figure 4.4a shows
representative overlaid spectra of the NIPAAm double bond peak for different reaction time, \( t \), during the polymerization reaction. The arrow shows that in the time interval \( 0 \leq t \leq 6.75 \) s the characteristic NIPAAm absorbance peak decreased with reaction time, indicating consumption of the monomer.

**Figure 4.4.** (a) Absorbance spectra acquired in the course of polymerization of NIPAAm at different reaction times. The rate of decay of the peak at 975 cm\(^{-1}\) (C=C−H) of NIPAAm corresponds to the rate of consumption of the monomer (the rate of polymerization). The arrow indicates the direction of the peak intensity. \( C_{\text{NIPAAm,d}} = 175 \) mM, \( C_{\text{TEMED,d}} = 30 \) mM, and \( C_{\text{APS,d}} = 60 \) mM. (b) Decay curves for monomer absorbance for \( C_{\text{APS,d}} \) of 15 (●), 30 (□), 45 (▲), and 60 (○) mM. \( C_{\text{TEMED,d}} = 30 \) mM; \( C_{\text{NIPAAm,d}} = 175 \) mM. The slopes, acquired at \( t = 0 \) from exponential fits, provide the respective initial rates of polymerization, \( \frac{dP}{dt}|_{t=0} \). (c) A plot of \( \ln(\frac{dP}{dt}|_{t=0}) \) vs. \( \ln(C_{\text{APS,d}}) \) generated based on the data shown in (b). All measurements were conducted three times. Error bars represent one standard deviation.

The experiments were conducted at four values of \( C_{\text{APS,d}} \), while other reagents’ concentrations remained unaltered (Table 4.2). Figure 4.4b shows the variation in \( C_{\text{NIPAAm,t}} \) vs. \( t \). The initial rate of monomer consumption (−dM/dt|\(_{t=0}\)) from each curve was
determined by fitting the decay curves and determining the initial slope, as discussed in Section 4.2.1.3. Table 4.3 summarizes the fitting results for Figure 4.4b.

Table 4.3 Fitting results from curves shown in Figure 4.4a.

<table>
<thead>
<tr>
<th>( C_{\text{APS,d}} ) (mmol L(^{-1}))</th>
<th>( C_{\text{NIPAAm,t}} ) (mmol L(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>( y = 175e^{-0.029t} )</td>
</tr>
<tr>
<td>30</td>
<td>( y = 175e^{-0.042t} )</td>
</tr>
<tr>
<td>45</td>
<td>( y = 175e^{-0.047t} )</td>
</tr>
<tr>
<td>60</td>
<td>( y = 175e^{-0.059t} )</td>
</tr>
</tbody>
</table>

By using \(-dM/dt|_0 = dP/dt|_0\), we plotted \(\ln(dP/dt|_0)\) vs. \(\ln(C_{\text{APS,d}})\) (Figure 4.4c) and determined the slope to be 0.50. On the basis of eq. 11a, we determined the order of reaction with respect to APS to be \(\sim 0.5\), which is the expected value for free radical polymerization reactions\(^{22}\).

4.3.2. Effect of the Accelerator Concentration on the Polymerization Kinetics

In the next series of experiments, the values of \(C_{\text{APS,d}}\) and \(C_{\text{NIPAAm,d}}\) were maintained at 30 and 175 mM, respectively, and the decay curves for monomer concentration were collected at four values of \(C_{\text{TEMED,d}}\). The value of \(dP/dt|_0\) was determined for each monomer concentration decay curve, as described in section 4.3.1. Figure 4.5 shows the acquired data and the linear fit for \(\ln(dP/dt|_0)\) vs. \(\ln(C_{\text{TEMED,d}})\).
By using eq. 11b, we determined from the slope of the plot in Figure 4.5 that the order of the reaction with respect to TEMED was 0.38. This finding indicated that the rate of polymerization was affected by the concentration of TEMED. Consistent with previous work\textsuperscript{23}, TEMED can participate in the initiation of polymerization by producing radicals and thus affect $dP/dt$.

### 4.3.3. Effect of the Initiator + Accelerator Complex on the Polymerization Kinetics

We simultaneously changed the molar concentrations of both APS and TEMED, while keeping the ratio $C_{\text{APS,d}}: C_{\text{TEMED,d}}$ at 1:1. The concentration of the “initiator + accelerator” complex immediately after dilution (at the entrance of the reaction chamber (v), Figure 4.2) was denoted as $C_{\text{m,d}}$. 

![Figure 4.5. Logarithmic plot of the variation of the initial rate of polymerization, $\ln(dP/dt)_0$, vs. the concentration of TEMED, $\ln(C_{\text{TEMED,d}})$. $C_{\text{APS,d}} = 30$ mM; $C_{\text{NIPAAm,d}} = 175$ mM. Error bars represent one standard deviation.](image)
To examine the effect of the change in $C_{m,d}$ on the polymerization kinetics, we rearranged eq. 10 as

$$\ln \left( \frac{dP}{dt} \bigg|_{t_0} \right) = x \ln(C_{m,d}) + y \ln(C_{m,d}) + \ln(w_d)$$

(12a),

where $\ln(w_d) = \ln(k') + y \ln(C_{TEMED,d})$. Rearranging eq. 12a yielded

$$\ln \left( \frac{dP}{dt} \bigg|_{t_0} \right) = (x + y) \ln(C_{m,d}) + \ln(w_d)$$

(12b),

which is the equation of a line with the slope equal to $x + y$, the sum of the orders of reactions with respect to APS and TEMED. (In the previous sections, we found that $x = 0.50$ and $y = 0.38$, respectively.) For $C_{NIPAAm,d} = 175$ mM, we collected decay curves and determined the initial rate of decay for varying concentrations of $C_{m,d}$ (Figure 4.6). A
linear fit of the data points gave a slope of 0.83, which was within ∼5% of the expected value of 0.88 obtained from eq. 12b.

4.3.4. Effect of the Monomer Concentration on the Polymerization Kinetics

To investigate the effect of monomer concentration on the polymerization kinetics, we used $C_{APS,d} = C_{TEMED,d} = 30$ mM and modulated $C_{NIPAAm,d}$ in the range of 90–305 mM (Table 4.2). The initial rate of decay of the monomer concentration was measured for each $C_{NIPAAm,d}$, and a plot of $\ln(dP/dt)$ vs. $\ln(C_{NIPAAm,d})$ was generated (Figure 4.7). We used eq. 11c and the slope of the graph in Figure 4.7 to determine the reaction order with respect to NIPAAm.

![Figure 4.7](image.png)

**Figure 4.7.** Variation in $\ln(dp/dt_0)$ vs. $\ln(C_{NIPAAm,d})$. The reaction mixture included $C_{APS,d} = C_{TEMED,d} = 30$ mM. Error bars represent one standard deviation.

This method gave us the order of 1.09, with respect to the monomer. This value was close to 1.00, the order of free radical polymerization reaction with respect to the monomer$^{24}$. 

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4.3.5. Effect of the pH on the Polymerization Kinetics

For pH-dependent polymerization experiments, we used three buffer solutions with pH values of 2.23, 7.26, and 9.50. The pH 2.23 phosphate buffer solution was prepared by mixing H$_3$PO$_4$ with the pre-dissolved aqueous reagent solution (either NIPAAm, TEMED, or APS) and titrating it to pH = 2.23 with a 1 M HCl solution. The pH 7.26 phosphate buffer solution was prepared by dissolving NaH$_2$PO$_4$ in the pre-dissolved aqueous reagent solution and titrating it with 1 M HCl to pH = 7.26. To prepare pH 9.50 buffer, ethanolamine was mixed with the aqueous reagent solution and titrated with a 10 M NaOH solution to pH = 9.50.

We conducted the polymerization reaction at three different pH values, in order to monitor changes to polymerization kinetics as a function of pH. To maintain a particular value of pH, we used three buffer solutions of pH 2.23, 7.26, and 9.50. First, we ensured that the pH value was maintained at the original value during the polymerization reaction, by monitoring the pH in real-time off-chip (bulk) experiments at $C_{\text{NIPAAm},d} = 175$ mM, $C_{\text{APS},d} = 30$ mM, and $C_{\text{TEMED},d} = 30$ mM. Next, the buffered reagent solutions were injected into the MF reactor, and their flow rates were adjusted to achieve different reaction times until the reaction mixture reached the IR probe. The absorbance peak of NIPAAm was measured for each reaction time, as discussed in Section 4.3.1., and the corresponding $C_{\text{NIPAAm}}$ was calculated using eq. 6. Figure 4.8 shows the change in $C_{\text{NIPAAm}}$ in each buffer solution.

The initial reaction rates, $dP/dt|_0$, in pH 2.23, 7.26, and 9.50 buffer solutions were determined to be 2.27, 2.97, and 3.50 M L$^{-1}$ s$^{-1}$, respectively. This trend was in agreement with previously reported increase in $dP/dt|_0$ with increasing pH of the reaction.
Increasing pH leads to consumption of sulfuric acid, which is one of the products generated by the initiation step of this reaction (eq. 1).

Figure 4.8. Variation in C_{NIPAAm} vs. time at different pH values of the reaction mixture: 2.23 (●), 7.26 (□), 9.50 (▲). The initial concentrations of monomer, initiator, and accelerator were 175, 30, and 30 mM, respectively, for all pH values. Error bars represent one standard deviation.

4.4 Conclusions

We demonstrated a systematic, throughput study of a multicomponent polymerization reaction in a MF reactor integrated with in situ FTIR. The technique was used to study the kinetics of an exemplary free-radical polymerization reaction of N-isopropylacrylamide, which was initiated in water by ammonium persulfate in the presence of the accelerator N,N,N′,N′-tetramethylethylenediamine. The MF format of these studies allowed rapid exploration of the reaction parameter space such as reagent concentrations and reaction time (manipulated by changing the total system flow rate) and thus enabled the determination of the reaction kinetics. The MF study was also used
to examine the effect of pH of the reaction mixture on polymerization kinetics. This work opens the way for the kinetic measurements of complex polymer systems. With the use of feedback control of programmable syringe pumps this work opens the way for fully automated on-chip characterization of polymerization reactions for optimization of chemical formulations.
References


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Chapter 5

Using Frustrated Lewis Pairs for Carbon Dioxide Sequestration in a Microfluidic Format

5.1 Introduction

Elevated levels of carbon dioxide (CO$_2$) in the atmosphere are clearly influencing the progression of global warming. Strategies to manage atmospheric CO$_2$ concentrations include reducing emissions, sequestration and storage (e.g., in underground aquifers), or utilization of CO$_2$ as a C$_1$ chemical feedstock$^{1-3}$. The conversion of CO$_2$ to products such as formic acid and carbon monoxide$^4$ or to readily usable fuels such as methanol$^5,6$ remains a challenge due to the relatively low reactivity and high thermal stability of the CO$_2$ molecule. While a series of transition metal systems have been reported to effect reduction chemistry of CO$_2$$^{7-11}$, a unique alternative involves the use of frustrated Lewis pairs (FLPs)$^{12-14}$. These systems, comprising sterically hindered Lewis acids and bases, act in concert to capture CO$_2$ under mild reaction conditions, a discovery led by professor Douglas W. Stephan, at the University of Toronto$^{15}$. Moreover, tuning the Lewis acidity and basicity of the FLPs alters their reactivity in reactions with CO$_2$ from reversible sequestration to stoichiometric and even catalytic reduction to methanol$^{16}$ or carbon monoxide$^{17-20}$. Strategies to predict and design FLPs capable of the effective sequestration and activation of CO$_2$ necessitate a deeper understanding of the factors that influence the reaction. To this end, the deliberate studies of the effects of FLP structure, concentrations, and reaction temperatures on the reactivity of FLP reagents are required. As the initial FLPs afforded reversible binding to CO$_2$, the determination of equilibrium
constants and thermodynamic parameters of these reactions should enable assessment of the efficiency of a particular FLP system for CO\(_2\) sequestration and provide predictive insights for design strategies targeting new and efficient formulations of FLP catalysts for CO\(_2\) capture and reduction. Currently used batch-scale characterization methods\(^{21,22}\) for gas–liquid reactions involving CO\(_2\) are time-consuming and plagued with an insufficient control over gas–liquid interfaces and diffusion control challenges associated with the large volumes of the reactors used. Measurements of a particular physical or chemical property require a relatively large quantity of reagents. Common spectroscopic characterizations of reaction products may be challenged by chemical exchange processes with the atmosphere. Moreover, when equilibrium constants of FLP–CO\(_2\) reactions are high, the equilibrium thermodynamic characterization cannot be achieved using batch-scale methods\(^{23}\). This information, if available, would enable intelligent tuning of FLP chemistry to enhance the reaction or to tune the reversibility of the CO\(_2\) capture.

Recently, the utilization of microfluidic (MF)-based platforms has been proposed to address some of these challenges by dramatically shrinking the dimensions of the reaction vessel from centimeters to micrometers, thereby reducing the diffusion length and time scales. Integration of in-line characterization tools with different MF devices has enabled throughput screening of the physical and chemical processes\(^{24-30}\). In particular, a reduced mass transfer limitation and well-defined interfacial areas achieved in gas–liquid segmented flows have been utilized for chemical\(^{31}\) and physical\(^{32-35}\) screening of gas–liquid processes involving CO\(_2\).

We developed a MF strategy for fundamental thermodynamic studies of reactions of CO\(_2\) with FLP reagents. The approach utilized segmented flow, that is flow of
alternating segments of CO$_2$ and solution, using a MF approach, and we calculated equilibrium constants of a reaction between CO$_2$ and a FLP at different temperatures. We assessed the thermal stability of the adduct and determined the thermodynamic characteristics of the reaction, such as the enthalpy, entropy, and the Gibbs free energy. The method we developed and employed for this reaction can be used to acquire thermodynamic data for FLP–CO$_2$ reactions in 10–15 min and can be applied to fundamental studies of other reactions that include reactive gases. This work was reported as a paper in the Journal of the American Chemical Society$^{36}$.

5.2 Experimental

5.2.1. Materials

The reagents tri-tert-butylphosphine, $t$Bu$_3$P, and chlorobis(penta-fluorophenyl)borane, ClB(C$_6$F$_5$)$_2$, were synthesized as described elsewhere$^{23}$ and dissolved in bromobenzene to various concentrations ranging from 0 to 50 mM. These solutions were prepared in a glovebox (1.2 – 2 ppm O$_2$) to avoid exposure to oxygen or water vapour which would react with the FLP. Bromobenzene was purchased from Caledon (Canada) and distilled prior to use.

5.2.2. Experimental Design

The solutions of individual FLP reagents in bromobenzene were supplied to the MF reactor from two 1 mL gastight syringes (SGE Analytical Science), using the same syringe pump.
5.2.2.1 Microfluidic Experimental Setup

The individual solutions containing FLP reagents dissolved in bromobenzene were supplied to the MF reactor (R150.332.2, Micronit Microfluidics) using two glass syringes coupled to a syringe pump (PHD2000, Harvard Apparatus). The tubings connected to the syringes supplying equal concentrations of tBu₃P and Cl(C₆F₅)₂ solutions, met at an off-chip T-junction. The solutions were mixed before entering the inlet to the MF reactor. In order to account for reagent dilution upon mixing, each syringe contained a solution of tBu₃P or Cl(C₆F₅)₂ with the concentration twice as large as the on-chip concentration. For example, to study a 20 mM FLP solution, the syringes were loaded with 40 mM tBu₃P and 40 mM Cl(C₆F₅)₂ solutions, each, and the individual solutions were supplied to the MF reactor. This flow rate was maintained for all experiments. The CO₂ (Grade 4.0, Linde) gas was supplied from a gas cylinder to the second inlet of the MF reactor via a servo pressure regulator (Marsh Bellofram Type 3000) at P=118.5 kPa. The reactor was clamped in a custom-made acrylic manifold containing embedded NanoPort connections (IDEX Health Science, USA). Polyether ether ketone tubings with an internal diameter of 0.001” and length of 5’ were used to supply reagents and gas to the MF reactor via the NanoPort connections. The FLP solution and CO₂ met at the on-chip Y-junction, where they generated alternating gas and liquid segments (Figure 1). We used 1.25X magnification on an inverted microscope (Olympus IX71, Olympus Canada) to image segments of CO₂ and FLP solution flowing through the MF reactor and measure the length of the CO₂ plugs. This examined field of view encompassed only a fraction of the MF reactor, as illustrated in Figure 5.1. The inset in Figure 5.1 illustrates the field of view (FOV) that incorporates only a portion of
the overall reactor. We did not analyze the change in the length of CO\textsubscript{2} outside the designated area, which led to the gaps in experimental data points for the reaction time 1.2 - 2 s (Figure 5.5).

**Figure 5.1.** Schematic of the glass MF reactor. The reactor consisted of two inlets that converged at a Y-junction. The field of view used to acquire optical images is shown with a dashed box. The microchannel had the width, height, and length of 150 µm, 150 µm, and 30.4 cm, respectively, and a total volume of 6 µL. The inset shows an optical image of alternating segments of gaseous CO\textsubscript{2} (dark) and the FLP solution (light). The scale bar is 500 µm.

Prior to MF experiments, the reactor was purged with dry CO\textsubscript{2} for 10 min at 2 psig to remove air. The inverted microscope was coupled to a CCD camera (Photometrics CoolSnap ES) and was used for optical characterization of the CO\textsubscript{2} bubbles and liquid segments. ImagePro (Media Sybernetics) software was used to acquire multiple sequences of bright-field images of the segmented flow on-chip. Analysis of the image sequence was carried out using a custom-developed MATLAB- based image processing
code, which automatically measured the CO₂ plug length and plug position in a region of interest\textsuperscript{34,35}.

The pressure drop along the microchannel was calculated based on the CO₂ plug velocity, void fraction, microchannel length, liquid viscosity, and the atmospheric pressure of 101.3 kPa at the outlet of the reactor. The individual solutions of ClB(C₆F₅)₂ and tBu₃P in bromobenzene with equal molar concentration were supplied to the MF reactor at a flow rate of 2.5 µL/min (the total volumetric flow rate of the mixed reagent solution was 5 µL/min). The total FLP concentration, C_{FLP}, in the mixed solution was changed from 0 to 50 mM. Experiments were performed at temperatures, T, of 273, 283, 293, 303, and 313 K in an oil bath.

5.2.2.2 Data Acquisition and Analysis

For each concentration of FLPs, three sequences of 300 images were acquired in the field of view, with at least 4000 bubbles detected. The plug length, L_P, the slug length, L_S, and the velocity of CO₂ plugs, U_P at different microchannel locations, X, were calculated from the images using a Matlab-based program code described elsewhere\textsuperscript{37}. The average value of L_P at a particular location was determined and standard deviation was calculated. The MATLAB program did not detect plugs flowing through the channel bends, which led to small gaps in the experimental points, e.g., at 0.7 s in Figure 5.5b. The average velocity, \( v \), of the CO₂ plugs was calculated as

\[
  v = \frac{d_2-d_1}{t_2-t_1}
\]

(1),

where \( d_1 \) is the distance from the center of the plug to the Y-junction at time \( t_1 \) and \( d_2 \) is the distance of the center of the plug from the Y-junction one image frame later, at \( t_2 \). By
using the value of \( v \) and the distance-to-time transformation, we determined the reaction time. The value of \( L_p \) was converted to plug volume, \( V_e \), as

\[
V_e = H \cdot w \left( L_p - (H - 2d_f) \right) + \pi \cdot w \left( \frac{H}{2} - d_f \right)^2
\]

(2),

where \( V_e \) is the plug volume, \( H \) and \( w \) are the height and the width of the microchannel, respectively (\( H= 150 \mu m, w = 150 \mu m \)), and \( d_f \) is the thickness of the liquid film surrounding the plug (\( d_f = 1.5 \mu m \)). The volume change of the CO\(_2\) plug was due to (i) the drop in pressure along the channel, leading to plug expansion, (ii) physical dissolution of CO\(_2\) in the adjacent liquid slug, and (iii) chemical reaction of CO\(_2\) with FLP in the adjacent solution slug. All three effects exist in the FLP-CO\(_2\) system studied in the MF format (Figure 5.2). The experimentally determined plug volume, \( V_e \), depended on both factors and related as

\[
\Delta V_d = \Delta V_e + \Delta V_p
\]

(3),

where \( \Delta V_d \) is the change in volume change due to the physical and reaction-induced dissolution of CO\(_2\), \( \Delta V_e \) is the experimentally determined volume change of the plug, and \( \Delta V_p \) is the CO\(_2\) plug volume expansion caused by the pressure drop along the channel. We calculated \( \Delta V_p \) as

\[
\Delta V_p = \frac{P_0 - P_X}{n_X RT}
\]

(4),

where \( P_0 \) is the initial pressure at the Y-junction and \( P_X \) is the pressure at distance \( X \) from the Y-junction. Using eqn 3, we obtained values of \( \Delta V_d \) from \( \Delta V_e \) and \( \Delta V_p \). Although we supplied CO\(_2\) to the MF reactor at a pressure of 118.5 kPa, the actual pressure at the Y-junction, \( P_0 \), was lower, due to the pressure drop along the supplying tubing.
The initial pressure at the Y-junction was calculated as

\[ P_0 = P_{\text{out}} + \left( \frac{dP}{dX} \right) L \]  

(5),

where \( P_{\text{out}} \) is the atmospheric pressure, \( \frac{dP}{dX} \) is the pressure drop along the channel, and \( L \) is the total channel length of the microchannel from the Y-junction to the outlet. The pressure drop along the channel was calculated using the correlation proposed by Kreutzer et al.\textsuperscript{38,39} as

\[ \frac{\Delta P}{X} = \beta_L f_{\text{slug}} \left( \frac{2\rho UB^2}{D_h} \right) \]  

(6),

\[ f_{\text{slug}} = \frac{16}{Re} \left[ 1 + 0.17 \frac{w}{L_s} \left( \frac{Re}{Ca} \right)^{0.33} \right] \]  

(7),

where \( \Delta P/X \) is the pressure drop along the channel, \( \beta_L \) is the liquid volume fraction in the entire length of the channel, \( f_{\text{slug}} \) is the friction factor for segmented flow, \( Ca \) is the capillary number, \( Re \) is the Reynolds number, and \( \rho \) is the liquid density.

![Figure 5.2. Illustration of the changes in plug volume due to (i) the drop in pressure along the channel, leading to plug expansion, (ii) physical dissolution of CO\(_2\) in the](image-url)
adjacent liquid slug, and (iii) chemical reaction of CO$_2$ with FLP in the adjacent solution slug. All three effects exist in the FLP-CO$_2$ system studied in the MF format.

Based on the volume of gaseous plugs, we calculated the number of moles of CO$_2$ in the plugs at each position along the microchannel using the ideal gas law. With reducing plug length, the number of moles of CO$_2$ transferred into the adjacent liquid segment was determined as

$$n_{\text{slug}(x)} = n(x) - n_0$$

(8),

where $n_{\text{slug}(x)}$ is the number of moles of CO$_2$ in the liquid slugs, $n_x$ is the number of moles in each gaseous plug at position $X$, and $n_0$ is the initial number of moles of CO$_2$ in the first plug generated at the Y-junction. The liquid volume, $V_S$, was determined as

$$V_S = H \cdot w \cdot L_s + \left[ H \cdot w (H - 2d_t) - \frac{4}{3} \pi \left( \frac{H}{2} - d_t \right)^3 \right]$$

(9)

We found that the length of the liquid segments did not change with time (Figure 5.3), which allowed us to assume that the plugs and the slugs moved with the same velocity.

![Figure 5.3](image)

Figure 5.3. The slug length normalized over channel width, plotted as a function of reaction time. Error bars represent one standard deviation.
5.2.2.3. Infrared Spectroscopy Experiments

A customized home-built gas-tight chamber was placed around the ATR crystal, and purged with dried CO₂ for 10 min. The chamber was then sealed using a rubber membrane and was pressurized with CO₂ at a pressure of 108.2 kPa. A 100 µL-volume droplet of the liquid sample (with a radius of ~3 mm) was placed on the crystal using a syringe that penetrated the rubber membrane of the chamber. The pressure in the chamber was maintained at constant pressure for the duration of the experiment. The variation in intensity of the IR peak at 2343 cm⁻¹, which corresponded to the physically dissolved CO₂⁴⁰ was monitored over the course of 2 hrs. The variation in the peak 2 intensity was studied for bromobenzene, a 80 mM tBu₃P solution in bromobenzene, a 80 mM Cl(C₆F₅)₂ solution in bromobenzene, and a 160 mM FLP solution in bromobenzene, vs. time (Figure 5.5.a). For all four systems we observed the same intensity of the IR peak at 2343 cm⁻¹ at equilibrium.

5.3 Results and Discussion

5.3.1. Segmented Flow and Mass Transfer of CO₂

Figure 5.4a shows the chemical reaction of CO₂ with the FLP reagents, that is, ClB(C₆F₅)₂ and tBu₃P, leading to the FLP−CO₂ adduct. Figure 5.4b illustrates the reaction conducted in a macroscopic format. The conventionally-used macroscale process involves bubbling CO₂ into the FLP solution at a fixed pressure, which is followed by the isolation, drying, and analysis of the precipitated product, ClB(C₆F₅)₂−CO₂−tBu₃P.²³ Generally, one experiment involving the synthesis, isolation, and analysis of the product
takes ~2 h. For screening of several FLP concentrations and temperatures, multiple experiments are required, which requires ever longer time. The isolated product may undergo a facile loss of CO$_2$, which is accelerated with increasing temperature.

**Figure 5.4.** Reversible FLP–CO$_2$ reaction conducted in a MF reactor. (a) Reaction of FLP reagents, ClB(C$_6$F$_5$)$_2$ and tBu$_3$P, with CO$_2$ in bromobenzene forming the FLP–CO$_2$ adduct. (b) Schematic of the batch-scale experiment. (c) Illustration of the CO$_2$ plugs and liquid slugs of FLP reagents with lengths $L_P$ and $L_S$, respectively, forming at the Y-junction.

Figure 5.4c illustrates the same reaction conducted in the continuous mode in a MF reactor using alternating flow of CO$_2$ plugs and slugs. In our work, the solution of FLP reagents in bromobenzene and the CO$_2$ gas were supplied via two inlets into the MF reactor. The ClB(C$_6$F$_5$)$_2$ and tBu$_3$P reagents were mixed in-line, using a T-junction, before entering the MF device. The liquid reagents and CO$_2$ converged at the Y-junction, where the gas stream periodically broke up to produce gaseous CO$_2$ plugs separated by liquid reagent slugs (Figure 5.1 inset). Following dissolution of CO$_2$ in an adjacent liquid slug, the CO$_2$ reacted with the FLP reagents. As a result of these two processes, the
gaseous CO₂ plugs shrank with time. Two recirculation zones inside each liquid segment enhanced mixing and mass transfer of CO₂ molecules into the liquid phase by convective transport (Figure 5.4c).

The total change in dimensions of the CO₂ plugs was determined by three factors: (i) the drop in pressure along the microchannel, (ii) the physical dissolution of CO₂ in bromobenzene, and (iii) the chemical reaction of CO₂ with FLP reagents (Figure 5.2). The first effect led to the expansion of CO₂ plugs, while the other two effects led to gaseous plug shrinkage. At equilibrium, the physical dissolution and reaction-induced reduction in CO₂ plug dimensions were temporarily balanced by the pressure drop along the channel, and the size of the CO₂ plugs remained constant. This volume of CO₂ plugs was used to calculate the amount of CO₂ that transferred to the liquid slugs at equilibrium.

In the course of our experiments, we monitored the variation in the length of CO₂ plugs, \( L_P \), when CO₂ dissolved in the adjacent liquid segment with the length \( L_S \) (\( L_S \) remained approximately constant as seen in Figure 5.3). By accounting for the expansion of the gas plug due to the pressure drop\(^{32} \), we evaluated the amount of CO₂ transferred from the gas plugs to the liquid slugs. Since the initial size of the generated CO₂ plugs was sufficiently large to retain their plug-like shape after CO₂ dissolution, we assumed that the gas plugs and the liquid slugs moved with the same velocity, and in this manner, we converted the distance traveled by the plugs and slugs into reaction time, \( t \).

Assuming an ideal gas behavior, we calculated the time-dependent volume of CO₂ plugs, \( V_P \), and the number of moles of CO₂, \( n_{CO₂}(t) \), in the plug at time \( t \) as

\[
n_{CO₂}(t) = \frac{PV_P}{RT} \tag{10}
\]
where \( P \) is the pressure in the plug after accounting for pressure drop at each \( X \) position, \( R \) is the gas constant \( (R = 8.314 \, \text{J} \, \text{mol}^{-1} \, \text{K}^{-1}) \), and \( T \) is the temperature of the system. The total number of moles of CO\(_2\) transferred from the plug equaled the number of CO\(_2\) moles entering the liquid segment, and the concentration of CO\(_2\) in the liquid was calculated as

\[
C_{\text{tot}}(t) = \frac{n_{\text{CO}_2}(t = 0) - n_{\text{CO}_2}(t)}{V_s}
\]

(11),

where \( C_{\text{tot}}(t) \) is the total concentration of CO\(_2\) in the liquid slug at time \( t \); \( n_{\text{CO}_2}(t = 0) \) and \( n_{\text{CO}_2}(t) \) correspond to the number of moles of CO\(_2\) in the plug at time \( t = 0 \) and \( t \), respectively, and \( V_s \) is the volume of the adjacent liquid slug.

### 5.3.2. Infrared Spectroscopy Experiments

Prior to MF experiments, we ensured that physical dissolution of CO\(_2\) in the liquid medium does not change in the presence of FLP reagents. We conducted attenuated total reflection Fourier transform infrared (ATR-FTIR) spectroscopy characterization of the physical dissolution of CO\(_2\) in reagent-free bromobenzene, as well as in bromobenzene solutions containing 80 mM \( t\text{Bu}_3\text{P} \), 80 mM \( \text{ClB}(\text{C}_6\text{F}_5)_2 \), and 160 mM of the FLP reagents (Figure 5.5a). Figure 5.5b shows the representative variation in the normalized length, \( L_p/L_0 \), of the CO\(_2\) plugs in bromobenzene and an FLP solution, where \( L_0 \) is the initial CO\(_2\) plug length formed after the Y-junction. Figure 5.5b, inset, illustrates the shrinkage of CO\(_2\) plugs. Under similar pressure and temperature, the ratio \( L_p/L_0 \) was significantly smaller for the system containing FLP reagents than for the FLP-free system, as a result of FLP reaction with CO\(_2\).
We monitored the intensity of the IR peak corresponding to physically dissolved CO$_2$, $I_{CO2}$, at 2343 cm$^{-1}$. The equilibrium intensity of the peak was reached after 80 min, with identical peak intensity for all the four solutions tested. This result indicated that the physical uptake of CO$_2$ by bromobenzene was not affected by the presence of individual FLP reagents or a 1:1 mixture of the reagents. On the basis of these results, we used the dissolution of CO$_2$ in bromobenzene as a reference system for the MF studies of the FLP–CO$_2$ reaction. We note that the time scale difference between the ATR-FTIR and MF experiments (90 min and 1 s in Figure 5.5a,b, respectively, needed for liquid saturation with CO$_2$) is associated with the CO$_2$ diffusion length difference for these experiments. Similar time scales for both experiments can be achieved if the ATR-FTIR
characterization was performed on the same length scale as the MF experiments (see Appendix A5.1).

5.3.3. Reacted Carbon Dioxide

Using eqs 10 and 11, we converted the change in volume of the CO₂ plugs into $C_{tot}$ for different FLP concentrations (Figure 5.6a).

![Figure 5.6](image)

**Figure 5.6.** (a) Variation in total molar concentration of CO₂ transferred at 273 K from the gas phase to the solution with FLP concentration of 0 mM (black), 10 mM (red), 20 mM (blue), 30 mM (pink), 40 mM (green), and 50 mM (orange). The gaps in the data points appear due to the MF reactor geometry (see Figure 5.1). (b) Variation in the equilibrium concentration of chemically reacted CO₂, plotted as a function of the initial FLP concentration at $T = 273$ K. Each experimental point is the average of three experiments conducted under identical conditions. Three hundred images were acquired for each experiment with at least 4000 CO₂ plugs. Error bars represent one standard deviation.

With increasing reaction time, $t$, the concentration of CO₂ in the liquid slugs increased, and the equilibrium was reached after ~2 s. The equilibrium CO₂ uptake by the
liquid slugs increased with increasing concentrations of tBu₃P and ClB(C₆F₅)₂, indicating that the FLP reagents were the limiting reagents. The CO₂ uptake caused by the chemical reaction, $C_r$, was determined by subtracting the equilibrium $C_{tot}$ (for the CO₂–bromobenzene system) from the total equilibrium uptake of CO₂, $C_{tot}$, for the FLP–CO₂ system. Figure 5.6b shows that the value of $C_r$ increased linearly with FLP concentration.

Since the reaction between ClB(C₆F₅)₂, tBu₃P, and CO₂ is exothermic, local heat accumulation immediately downstream of the Y-junction could be expected if the rate of heat generation was faster than heat distribution and dissipation through the walls of the MF reactor. Such accumulation could affect the reaction kinetics and the gas plug size over the course of the reaction but would not affect the thermodynamics of the reaction.

### 5.3.4. Temperature Control for the FLP-CO₂ Reaction

We studied the FLP-CO₂ reaction at 273±2 K, 283±2 K, 293±2 K, 303±2 K, and 313±2 K. To achieve temperatures other than room temperature, 293 K, we submerged the acrylic manifold containing the MF reactor and 3 feet-long supplying tubings in an oil bath to allow the FLP solution and CO₂ to reach the desired temperature before entry into the reactor. Reaching the desired temperature before the reaction occurs is especially important for the gas stream in order to avoid on-chip bubble expansion as the gas warms up to temperature. If the gas reaches the proper temperature prior to the reactor Y-Junction where it creates segmented flow, any expansion in the bubble will be attributable only to pressure drop (Figure 5.2).
Figure 5.7 shows the temperature distribution within the immersed tubings obtained through a two-dimensional numerical model (COMSOL multiphysics 4.3a) for bromobenzene (a) and CO$_2$ (b). For increasing liquid flow rate (Figure 5.7a), the time of heating or cooling decreases and the required tubing length to reach the target temperature increases. The flow rate used in our work was 5 µL/min, resulting in the requirement for tubing length of 10 mm. The temperature of water in the bath was increased using a bendable heating element (McMaster Carr, Catalog No. 3540K31), which was connected to a digital temperature regulator (Omega, CN8200 series). A type-K thermocouple probe (Sper Scientific, 14003-116) allowed feedback to the temperature controller. To achieve the lower temperatures of 273 K and 283 K, we used a copper heat exchange coil submersed in our water bath coupled to a circulating ethanol-water reservoir pump.

Figure 5.7. Numerically calculated temperature distribution along PEEK tubing supplying fluids to the MF reactor and immersed into a water bath at a particular temperature, plotted as a function of tubing length, $X$. (a) Bromobenzene: heating from 293.15 to 313.15 K (solid lines, left Y-axis); cooling from 293.15 to 273.15 K (dashed lines, right Y-axis). The lowest flow rate was 5 µL/min, the highest flow rate was 30 µL/min (with a 5 µL/min change step). (b) CO$_2$: heating from 293.15 to 313.15 K (solid line, left Y-axis); cooling from 293.15 to 273.15 K (dashed line, right Y-axis). Inlet pressure was 118.5 kPa.
Since the reaction between FLP reagents and CO$_2$ is exothermic, there is an expected generation of heat at the gas-liquid interface. This may result in local moderate accumulation of heat (hot spots) in the microchannel immediately downstream of the Y-junction. This heat will be released to the water bath, which maintains the desired temperature, through conduction via the top and bottom glass surfaces of the MF reactor. Since we are interested in the evaluation of equilibrium constants and the total reaction enthalpy, only the initial volumes at t=0, at the Y-junction, and equilibrium volumes, after 3 s, of CO$_2$ plugs were considered in our work. According to Figure 5.5b, the CO$_2$ plug volume did not change after reaching the equilibrium condition, thereby confirming the constant temperature within the micro-channel equal to the water bath temperature, after the equilibrium point. The invariance of CO$_2$ plug volume with time after the equilibrium point (Figure 5.5a) indicated that the heat generated during the CO$_2$–FLP reaction has been dissipated before the reaction reached the equilibrium.

5.3.5. Obtaining Equilibrium and Thermodynamic Information

Following the approach established in section 5.3.1. for the CO$_2$–FLP reaction at 273 K, we studied the equilibrium chemical uptake of CO$_2$ by the FLP reagents at 283, 293, 303, and 313 K. The submersion of the tubing in the oil bath was especially important for the CO$_2$ gas in order to avoid temperature-mediated, rather than reaction-induced, changes in the CO$_2$ plug volume. Figure 5.8 shows that the value of $C_r$ varied linearly with the FLP concentration in the entire temperature range studied.
Figure 5.8. Variation in the equilibrium reaction-induced chemical CO$_2$ uptake, plotted as a function of the initial concentration of FLP reagents in the adjacent liquid slugs for 273 K (red), 283 K (blue), 293 K (green), 303 K (orange) and 313 K (black). Error bars represent one standard deviation.

For similar concentrations of FLP reagents, the value of $C$ reduced with increasing temperature. This trend resulted from the reverse FLP–CO$_2$ reaction (Figure 5.4.a), which was favored at elevated temperatures$^{10}$ and led to the release of CO$_2$ from the adduct. As a result, the highest conversion of FLP reagents was achieved at 273 K.

Using the data plotted in Figure 5.8, the equilibrium constant, $K_{eq}$, of the FLP–CO$_2$ reaction at a particular temperature was determined as

$$
K_{eq} = \frac{[\text{ClB}(C_6F_5)_2 - \text{CO}_2 - t\text{Bu}_3\text{P}]}{[\text{ClB}(C_6F_5)_2][t\text{Bu}_3\text{P}]C_{\text{tot}}(\text{bromobenzene})}
$$

(12),

where [ClB$(C_6F_5)_2$−CO$_2$−tBu$_3$P] is the concentration of the FLP–CO$_2$ adduct, equal to $C_t$ (determined from Figure 5.6b), [ClB$(C_6F_5)_2$] and [tBu$_3$P] are the equilibrium
concentrations of the reagents, calculated as $C_r = [\text{ClB(C}_6\text{F}_5)_2]_{\text{initial}}$ and $C_r = [t\text{Bu}_3\text{P}]_{\text{initial}}$, respectively, and $C_{\text{tot(bromobenzene)}}$ is the equilibrium concentration of CO$_2$ dissolved in bromobenzene (Figure 5.6a). For the calculation of $K_{eq}$, the reaction of CO$_2$ with ClB(C$_6$F$_5$)$_2$ and tBu$_3$P was assumed to be stoichiometric and side reactions were ignored. Upon the reaction with FLP reagents, CO$_2$ is replenished by the continuous dissolution of CO$_2$ from gaseous plugs, thus maintaining the total supply of CO$_2$ in the solution. Using eq 12, the equilibrium constants for the FLP–CO$_2$ reaction carried out at 273, 283, 293, 303, and 313 K were calculated to be 687, 431, 223, 141, and 75 M$^{-2}$, respectively.

Next, we calculated the Gibbs free energy of the reaction, $\Delta G$, at 273, 283, 293, 303, and 313 K as

$$\Delta G = -RT\ln(K_{eq})$$ (13),

and obtained the values of $\Delta G$ to be $-14.8$, $-14.3$, $-13.2$, $-12.5$, and $-11.2$ kJ mol$^{-1}$, respectively.

We then determined the enthalpy and the entropy of the FLP–CO$_2$ reaction, $\Delta H$ and $\Delta S$, by using the van’t Hoff equation$^{41}$

$$\ln(K_{eq}) = -\frac{\Delta H^0}{RT} + -\frac{\Delta S^0}{R}$$ (14),

and plotting $\ln(K_{eq})$ versus $1/T$, a graph with the slope of $-\Delta H/R$ and the y-intercept of $\Delta S/R$ (Figure 5.9). A linear dependence of $\ln(K_{eq})$ versus $1/T$ indicated that $\Delta H$ does not appreciably change with temperature over the range studied.
Figure 5.9. Variation of ln(K_{eq}) with reaction temperature. Based on eq 17, the slope of the graph yields \(-\Delta H/R\).

The best fit of the linear dependence \(\ln(K_{eq})\) versus \(1/T\) yielded a \(\Delta H\) value of \(-39.3\) kJ mol\(^{-1}\). We independently estimated \(\Delta S\) as \(-\left(\Delta G - \Delta H\right)/T\) and obtained the values of \(-89.3\), \(-88.1\), \(-88.8\), \(-88.2\), and \(89.3\) J mol\(^{-1}\) K\(^{-1}\), for the temperatures 273, 283, 293, 303, and 313 K, respectively. Table 5.1 shows the summary of thermodynamic characteristics of the FLP–CO\(_2\) reaction.

<table>
<thead>
<tr>
<th>(T) (K)</th>
<th>273</th>
<th>283</th>
<th>293</th>
<th>303</th>
<th>313</th>
</tr>
</thead>
<tbody>
<tr>
<td>(K_{eq}) (M(^{-2}))</td>
<td>687</td>
<td>431</td>
<td>223</td>
<td>141</td>
<td>75</td>
</tr>
<tr>
<td>(\Delta H^a) (kJ mol(^{-1}))</td>
<td>(-39.3)</td>
<td>(-39.3)</td>
<td>(-39.3)</td>
<td>(-39.3)</td>
<td>(-39.3)</td>
</tr>
<tr>
<td>(\Delta S) (J mol(^{-1}) K(^{-1}))</td>
<td>(-89.3)</td>
<td>(-88.1)</td>
<td>(-88.8)</td>
<td>(-88.2)</td>
<td>(-89.3)</td>
</tr>
<tr>
<td>(\Delta G) (kJ mol(^{-1}))</td>
<td>(-14.8)</td>
<td>(-14.3)</td>
<td>(-13.2)</td>
<td>(-12.5)</td>
<td>(-11.2)</td>
</tr>
</tbody>
</table>

\(^a\)The value of \(\Delta H\) is determined from the slope of the graph in Figure 5.
The thermodynamic characteristics of the reaction, obtained here, are essential for the formulation and optimization of FLP reagents to control the strength of the FLP – CO$_2$ intermolecular associations as well as to fine-tune the reversibility of the reaction. The thermodynamic characteristics provide information on whether the reaction is favourable and its temperature dependence. The temperature at which the reaction becomes unfavourable, that is, when the reverse reaction is favoured and CO$_2$ is released, is significant since a higher temperature requires additional energy spent on releasing CO$_2$ once captured. By adjusting the chemical structure of the FLP such as the electronegativity of the side groups, the Lewis acid and base strengths can be tuned which affects the FLP-CO$_2$ association strength as well as the energy required to reverse the reaction.

Finally, we calculated the enhancement factor, $E$, which describes the influence of a reaction on mass transfer and is defined as the ratio of total absorption of gas by a reactive liquid to the physical absorption of the gas under identical conditions$^{42,43}$. The positive deviation of $E$ from unity reflects the effect of a chemical reaction on increased uptake of a gas by the liquid medium$^{44}$. We determined the value of $E$ as the number of moles of CO$_2$, $\Delta n_{CO_2,\text{chem-phys}}$, transferred into the FLP solution divided by the number of moles of CO$_2$, $\Delta n_{CO_2,\text{phys}}$, transferred in bromobenzene as

$$E = \left(\frac{\Delta n_{CO_2,\text{chem-phys}}}{\Delta n_{CO_2,\text{phys}}}\right)$$

(15)

The enhancement factor was determined for different FLP concentrations and different temperatures and is summarized in Table 5.2. As expected, the value of $E$ increased with an increase in FLP reagent concentration and with decreasing temperature.
We validated the MF methodology by applying it to the well-characterized reaction between CO$_2$ and diethanolamine and comparing the experimentally obtained enthalpy with the reported literature values.

**Table 5.2. Enhancement Factor of the FLP–CO$_2$ Reaction**

<table>
<thead>
<tr>
<th>T (K)</th>
<th>[FLP] (mM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10</td>
</tr>
<tr>
<td>273</td>
<td>1.05</td>
</tr>
<tr>
<td>283</td>
<td>1.04</td>
</tr>
<tr>
<td>293</td>
<td>1.02</td>
</tr>
<tr>
<td>303</td>
<td>1.01</td>
</tr>
<tr>
<td>313</td>
<td>1.01</td>
</tr>
</tbody>
</table>

The value of $\Delta H$ of $-69$ kJ mol$^{-1}$ obtained in the MF CO$_2$–diethanolamine experiments compared favorably with the values of $\Delta H$ in the range of $-71 \pm 4$ kJ mol$^{-1}$, obtained by calorimetry, NMR, and solubility methods (Table 5.3).

**5.3.6. Validation of the MF Methodology**

In order to validate a MF approach for the thermodynamic characterization of CO$_2$-FLP reactions, we examined a well-established and well-characterized reaction between CO$_2$ and an aqueous solution of diethanolamine (DEA). Using the approach developed for the FLP experiments, we studied the CO$_2$ mass transfer to the slugs of DEA solutions and obtained information on the equilibrium constants and enthalpy of this reaction. Figure 5.10 illustrates the volume mass transfer of CO$_2$ vs. distance from the Y-junction, at 273 K in experiments conducted for four solutions of DEA with varying concentrations in water. Experiments were repeated at 283, 293, and 303 K.
Figure 5.10. Variation in CO₂ plug shrinkage (normalized by the liquid slug volume) 
\((dV_p/V_S)\), plotted as a function of the distance from the Y-junction at 273 °K. The 
concentrations of the aqueous DEA solutions are 0 mM (●), 75 mM (●), 100 mM (●), 
and 125 mM (●). The volumetric flow rate of the DEA solution was 6 uL/min, and CO₂ 
pressure was 119.96 kPa.

In order to calculate the equilibrium constant at each temperature we followed the 
method described by Donnellan and Crooks\(^{45}\), whereby the reaction between 
diethanolamine (DEA) and CO₂ is described as

\[
\begin{align*}
R_2NH + CO_2 &\leftrightarrow R_2N^+HCO_2^- \quad (16) \\
R_2N^+HCO_2^- + R_2NH &\leftrightarrow R_2NCO_2^- + R_2NH_2^+ \quad (17)
\end{align*}
\]

According to this mechanism, \(R_2NH\) reacts with CO₂ to produce a zwitterion 
intermediate. This intermediate reacts with DEA to produce the CO₂-DEA adduct and a 
cation, \(R_2NH_2^+\). The equilibrium constant for this reaction is expressed as

\[
K_{DEA} = \frac{[R_2NH_2^+][R_2NCO_2^-]}{[CO_2][R_2NH_2]^2} \quad (18)
\]
The reaction requires two mols of DEA for every 1 mol CO\textsubscript{2} reacted, since one mol DEA reacts with one mol of CO\textsubscript{2} to generate the experimentally-measured product, R\textsubscript{2}NCO\textsuperscript{2-}, and one mol DEA reacts with the zwitterion intermediate to form the cation R\textsubscript{2}NH\textsubscript{2}\textsuperscript{+}.

Using equation 18, we calculated an equilibrium constant at each temperature and plotted ln \( k_{eq} \) vs. \( 1/T \) to obtain the enthalpy of reaction, as shown in Figure 5.9 in the main text. The value of \( \Delta H \) of -69 kJ mol\textsuperscript{-1} obtained for the CO\textsubscript{2}-DEA MF experiments compared favorably with the values of \( \Delta H \) in the range of -67 to -75 kJ mol\textsuperscript{-1}, obtained by the calorimetry\textsuperscript{46,47,49}, NMR\textsuperscript{45} and solubility methods\textsuperscript{48} (Table 5.3).

Table 5.3. Comparison of the values of \( \Delta H \) for the CO\textsubscript{2}-DEA reaction obtained by different methods

<table>
<thead>
<tr>
<th>( \Delta H ) (kJ mol\textsuperscript{-1})</th>
<th>Method</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>-69.4</td>
<td>Microfluidic</td>
<td>This work</td>
</tr>
<tr>
<td>-72</td>
<td>NMR</td>
<td>45</td>
</tr>
<tr>
<td>-69</td>
<td>Isothermal Flow Calorimetry</td>
<td>46</td>
</tr>
<tr>
<td>-75</td>
<td>Isoperibol Calorimetry</td>
<td>47</td>
</tr>
<tr>
<td>-67</td>
<td>Solubility</td>
<td>48</td>
</tr>
<tr>
<td>-69</td>
<td>Isothermal Displacement Calorimetry</td>
<td>49</td>
</tr>
</tbody>
</table>

5.4 Conclusions

In summary, we developed a time- and labor-efficient MF platform for real-time, throughput studies of thermodynamics of FLP–CO\textsubscript{2} reactions. The approach presented
here was validated for the reaction between CO₂ and diethanolamine. The equilibrium constants, Gibbs energy, enthalpy, and entropy of the FLP–CO₂ reaction were determined at different temperatures. In addition, we determined the enhancement factor under different reaction conditions. The proposed MF strategy provides access to the thermodynamic characterization of FLP–CO₂ reactions that is not accessible otherwise and can be applied to other gas-liquid reactions. Future work will enable the examination of gas-liquid reactions using on-chip IR and microscopic characterization working in tandem. This approach will allow the acquisition and determination of equilibrium and thermodynamic information of reactions, from MF characterization, and the characterization and tracking of all chemical species, including side reactions, using on-chip IR characterization.
References


Chapter 6

Microfluidic Separation of Ethylene and Ethane Using Frustrated Lewis Pairs

6.1 Introduction

Separation of individual gases from their mixtures is used in the purification of air, the recovery of CO$_2$ from natural gas, hydrogen storage, and the reduction of greenhouse gas emissions from flue gas, to give just a few important examples. In particular, separation of saturated and unsaturated hydrocarbons such as olefins and paraffins is an ever growing sector in the chemical and petrochemical industries. Ethylene and propylene are important feedstock components for the synthesis of polyethylene, ethylene oxide, acetonitrile, and acrylic acid$^1$. Over the last decade, the demand for the production of ethylene and propylene has increased over 50%$^2$ as a result of increased global demand for feedstock chemicals and a growing global population.

Ethylene and propylene are produced by steam cracking of hydrocarbons, a process in which high temperature and pressure applied to a light hydrocarbon feed induce molecular breakdown and formation of olefins$^{2,3}$. This process produces approximately equal fractions of light paraffins and olefins that subsequently require separation into individual gaseous components. The separation is predominantly carried out using cryogenic distillation, in which the feed components, typically a hydrocarbon mixture, are distilled at their boiling points in a separation column. The demand for the high purity separation of olefins and paraffins that possess low boiling points and small
differences in volatilities necessitates the utilization of large cryogenic distillation columns. The energy required to maintain a temperature close to the boiling points of the gases can account for up to 85% of the total energy required for the separation\textsuperscript{2,4,5}. Research is ongoing to find less energy-consuming and more cost-effective options for this process, and include pressurized water scrubbing, amine swing absorption, pressure swing adsorption, and temperature swing adsorption\textsuperscript{6}.

Alternatively, olefins and paraffins can be separated using membranes and molecular sieves\textsuperscript{7,8}, zeolites\textsuperscript{9-12}, and metal organic frameworks\textsuperscript{13,14} (MOFs). The separation is achieved due to the selective affinity of olefins to these materials either by trapping and confining one of the gases in pores (\textit{via} physical or chemical adsorption), or by physically transiting the membrane. The utilization of MOFs and zeolites is typically limited by the amount of gas they can be adsorb. In addition, large temperature or pressure modulations are often required to obtain gas desorption\textsuperscript{15}. In general, there is a challenge to balance selectivity with permeability: highly selective membranes have low permeability and vice \textit{versa}\textsuperscript{8}. Currently, many of the materials used for gas separation are not commercially viable and not easy to implement on a large scale, either due to a high cost, or to problems with up-scaling the separation technology.

On the other hand, a method that is similar to reactive liquid extraction can be used for the separation of gases. In this method, extraction of one of the components from a liquid (feed phase) by another liquid phase (extract phase) is enhanced by the chemical reaction of the reagents in the extract phase with the solute-to-be-extracted\textsuperscript{16}. For mixtures of gases, gas-liquid reactions can be used for enhanced selective mass transfer.
of one of the gases in the liquid phase, with a subsequent release of this gas from the extract phase at elevated temperature.

Recently, it has been shown that frustrated Lewis pairs (FLPs) react with olefins such as ethylene\textsuperscript{17}, but not with paraffins. The reactivity of FLPs toward small molecules such as olefins stems from the bulky side groups preventing the Lewis acid from direct reaction with the Lewis base, while low molecular weight olefins donate electron density to the Lewis acid, thereby polarizing the olefin, which is then attacked by the Lewis base to form an FLP-olefin adduct\textsuperscript{17,18}. Thus, selective reactivity of FLPs with olefins can be used to transfer olefins in a liquid (extract) phase and, in this manner, can be utilized for the separation of olefins from paraffins from a gas mixture.

While the reaction between olefins and FLPs has been established for ethylene\textsuperscript{17,19}, the efficiency of separation of olefins from paraffins using frustrated Lewis pairs is yet to be studied. These studies are necessary to compare the efficiency of gas separation using reactive extraction with FLPs. The exploration of reaction conditions such as the FLP concentration and the reaction temperature would provide insight into the potential applications of FLPs for gas separation.

In the present work, we explored separation of ethylene from its mixture with ethane using tri-\textit{tert}-butylphosphine and tris(pentafluorophenyl)borane as FLP reagents. The separation process was studied using segmented gas-liquid microfluidic (MF) flow, using a strategy developed in our group\textsuperscript{20}. The MF approach offered inherent advantages over bulk (macroscopic) experimental methods, including reduced mass-transfer limitation, a well-defined interfacial area between the gas and the liquid segments, the ability to study chemical and physical processes in real time and throughput capability.
that is implemented by real-time manipulation of reagent and gas flow rates. The approach utilized periodic MF generation of uniformly sized bubbles (plugs) from the mixture of ethylene and ethane, which were separated with uniformly sized segments (slugs) of the solution of FLP. Shrinkage of the gaseous plugs occurred due to the physical dissolution of both gases in FLP solution and the reaction of ethylene with FLPs. An 88 % separation efficiency was achieved for the ethylene/ethane mixture by optimizing FLP concentration and by reducing the temperature of the system to 0 °C, which favored its reaction with FLP. The results of this work provide understanding of the performance of FLPs in olefin/paraffin separation and pave the way for future exploratory work on FLP applications in the separation of gases.

6.2 Experimental

6.2.1. Materials

Tri-tert-butylphosphine, tris(pentafluorophenyl)borane, and 1,2-dichloroethane were purchased from Sigma Aldrich Canada. Glass microfluidic reactors were purchased from Micronit Microfluidics (Model R150.332.2). Ethane (grade 2.0) and ethylene (99%) gas were purchased from Linde (Germany).

6.2.2. Experimental Design

The reagents tri-tert-butylphosphine and tris(pentafluorophenyl)borane in a one-to-one molar ratio were dissolved in dichloroethane (DCE) to concentrations in the range
from 0 to 200 mM. A 200 mM FLP solution therefore contained 200 mM tri-tert-butylphosphine and 200 mM tris(pentafluorophenyl)borane. The solutions were prepared on the day of experiments and subsequently stored in a glovebox (1.2-2 ppm O₂) prior to experiments. A mixed solution was supplied to the MF reactor at a flow rate of 2.5 µL min⁻¹ using a 1 mL gas-tight syringe (SGE Analytical Science) coupled to a fluidic pump (PHD-2000, Harvard Apparatus). To remove ambient air from the reactor, prior to experiments, it was purged with dry ethylene or ethane, depending on the experiment being conducted. For experiments with the gas mixture, the reactor was purged with a dry mixture of ethylene/ethane in a 1:1 vol ratio. A CCD camera (Photometrics CoolSnap ES) coupled to an inverted microscope (Olympus IX71) was used for imaging gas plugs and liquid segments slugs. ImagePro (Media Sybernetics) software was used to acquire multiple sequences of bright-field images of the segmented flow. The analysis of each image was carried out with a custom-programmed MATLAB-based image processing code, which allowed for measurements of plug length and position.

In experiments with individual gases, ethylene or ethane were supplied to the MF reactor under gauge pressure 11 kPa. In experiments with the mixture of ethylene and ethane, the total gauge pressure of the system was 22 kPa. The pressure difference along the microchannel was calculated based on the gaseous plug velocity, the liquid volume fraction in the channel, the channel length, the viscosity of the liquid, and the atmospheric pressure of 101.3 kPa at the outlet of the reactor.
The initial pressure at the Y-junction was calculated as

\[ P_o = P_{\text{out}} + \left( \frac{dP}{dX} \right) L \]  

(1),

where \( P_{\text{out}} \) is the atmospheric pressure at the outlet of the MF reactor, \( dP/dX \) is the pressure drop along the microchannel, and \( L \) is the total channel length from the Y-junction to the outlet of the reactor. The pressure drop along the channel was calculated as \(^{21,22}\)

\[ \frac{\Delta P}{X} = \beta_L f_{\text{slug}} \left( \frac{2\rho u_p^2}{D_h} \right) \]  

(2)

\[ f_{\text{slug}} = \frac{16}{Re} \left[ 1 + 0.17 \frac{w}{L_S} \left( \frac{Re}{Ca} \right)^{0.33} \right] \]  

(3),

where \( \Delta P/X \) is the pressure drop along the channel, \( \beta_L \) is the liquid volume fraction in the channel from the Y-junction to the outlet, \( f_{\text{slug}} \) is the friction factor for segmented flow, \( Ca \) is the capillary number, \( Re \) is the Reynold’s number, and \( \rho \) is the liquid density.

6.3 Results and Discussion

6.3.1 Infrared Spectroscopy Experiments

Prior to MF experiments, we conducted bulk IR experiments to ensure that physical dissolution of ethylene in DCE did not change in the presence of ethane, or vice versa. IR spectroscopic experiments were conducted after (i) ethylene and ethane were individually bubbled through 1 mL of DCE at 11 kPa for 3 hr and (ii) after 1:1 vol mixture of ethylene and ethane was bubbled through 1 mL of DCE at 22 kPa for 3 hr. Figure 6.1a shows off-line IR absorption spectra of physically dissolved ethylene (green curve), ethane (red curve), and ethylene/ethane mixture (beige curve), for the spectral
range 1820 to 1580 cm$^{-1}$. Importantly, for the ethylene/ethane mixture, the pressure was 22 kPa, corresponding to the same partial pressure of the individual gases used in MF experiments. The peak at 1725 cm$^{-1}$ corresponding to symmetrical vibration of ethane$^{24}$, had a similar area under the peak for the gas mixture and for ethane only (the area under the peak differed by 10 %). Based on this result, we conclude that the physical dissolution of ethane in the presence of ethylene is not significantly impacted.

Figure 6.1b shows IR spectra for the same three systems in the spectral range 3150 to 2500 cm$^{-1}$. The peak at 2857 cm$^{-1}$ corresponding to asymmetrical vibration of ethylene$^{25}$ had a 9.7 % difference in area under the peak for the gas mixture and the individual ethylene, suggesting that the amount of physically dissolved ethylene did not significantly change in the presence of ethane.

**Figure 6.1.** IR absorbance spectra in the ranges 1820 to 1580 cm$^{-1}$ (a) and 3100 to 2500 cm$^{-1}$ (b) for physical dissolution of ethane in DCE at 11 kPa (red curve), physical dissolution of ethylene in DCE at 11 kPa (green curve), and physical dissolution of ethylene/ethane mixture at 22 kPa in DCE (beige curve).
6.3.2 Reaction of Ethylene and FLPs in the MF Reactor

Figure 6.2a shows the equation of the reversible chemical reaction between tri-\textit{ tert}-butylphosphine (\(t\text{Bu}_3\text{P}\)) and tris(pentafluorophenyl)borane \(\text{B}(\text{C}_6\text{F}_5)_3\) and ethylene gas, \(\text{C}_2\text{H}_4\), to form the zwitterionic FLP-ethylene adduct. The reaction is exothermic\textsuperscript{17,19}, that is, based on the Le Châtelier's principle, it is favored under reduced temperatures. Thus by increasing the temperature, the reaction can be reversed\textsuperscript{17,19} and thus can be used for the release of the reacted (extracted) gas. In the present work, DCE was selected as a solvent for the preparation of FLP solution to fulfill the following requirements: to provide sufficient solubility for FLP reagents and the FLP-ethylene product, to exhibit chemical inertness toward the FLP reagents, and to provide relatively low physical solubility for ethane.

Figure 6.2b shows a schematic of the MF reactor used in this work. The reactor was fabricated in glass and contained two inlets that converged to a Y-junction, a wavy channel, and an outlet. An FLP solution was supplied to the MF reactor via inlet 1. Inlet 2 supplied ethane or ethylene from a gas regulator or the 1:1 vol mixture of ethylene and ethane. The convergence of the FLP solution and the gas stream at the Y-Junction led to the periodic breakup of the gas stream into regularly spaced gaseous plugs separated with liquid segments, due to the shear stress imposed by the liquid stream\textsuperscript{23}.

The inset in Figure 6.2b shows an optical microscopy image of gaseous plugs (dark segments) and liquid slugs (light segments) in the MF channel. As gas plugs travelled along the channel from the Y-junction, their lengths reduced due to the transfer of the gas to the liquid slugs. The lengths of liquid segments along the microchannel
remained constant, as shown previously\(^{20}\). Three factors contributed to the change in plug dimensions, namely, (i) the physical dissolution of the gases in DCE (favoring plug shrinkage), (ii) the chemical reaction of ethylene with FLP (favoring plug shrinkage), and (iii) the pressure drop along the microchannel (favoring plug expansion). At equilibrium, the shrinkage of plugs resulting from physical and chemical gas dissolution was balanced by the expansion of plugs as a result of pressure drop.

Figure 6.2. The chemical reaction between the FLP, B(C\(_6\)F\(_5\))\(_3\) and P(t-Bu)\(_3\), and ethylene to form the FLP-ethylene zwitterion adduct (a). An optical image of the reactor showing the channels (blue), the inlets (1) and (2), and outlet (3), and the region of interest (ROI) (dotted square) (b). The inset shows an optical microscopy image of the ROI with gaseous plugs (dark segments) and liquid slugs (light segments). The scale bar is 450 µm.

For quantitative characterization of reactive extraction of ethylene, we defined a unit cell, which consisted of a gaseous plug and an adjacent liquid slug, as shown in Figure 6.3. The variation in the length of the plug, \(L_P\), was monitored from the Y-junction along the microchannel. The linear distance from the Y-junction was transformed into
reaction time using the average plug velocity, \( U_B \), and the distance-to-time transformation as

\[
U_B = \frac{d_2 - d_1}{t_2 - t_1}
\]

(4),

where \( d_1 \) is the distance from the center of the plug to the Y-junction at time \( t_1 \) and \( d_2 \) is the distance of the center of the plug from the Y-junction one image frame later, at \( t_2 \). Each image frame was labeled with the time at which it was taken, and for each time, we measured the distance of the plug from the Y-junction. By measuring the change in distance and time from one image frame to the next one, we obtained the velocity \( U_P \) of the gaseous plugs and liquid segments.

![Figure 6.3. Illustration of the formation of gaseous plugs and liquid slugs. The unit cell includes one gaseous plug with length \( L_P \) and one liquid segment with length \( L_s \). \( U_P \) is the plug velocity and \( X \) is the distance from the Y-junction. The channel width was 150 \( \mu \)m.](image)

Assuming an ideal gas behavior, we utilized the ideal gas law to calculate the number of moles of ethylene or ethane in each gaseous plug along the microchannel as

\[
n_{c=c} (t) = \frac{p_{c=c}V_P}{RT}
\]

(5)

\[
n_{c-c} (t) = \frac{p_{c-c}V_P}{RT}
\]

(6),
where \( n_{C=C}(t) \) or \( n_{C-C}(t) \) is the total numbers of moles of ethylene and ethane, respectively, in the corresponding gaseous plug at time \( t \), \( P_{C=C} \) and \( P_{C-C} \) are the pressures of ethylene and ethane, respectively, in the plugs at time \( t \) (after accounting for pressure drop), \( V_p \) is the plug volume, \( R \) is the gas constant, 8.314 J mol\(^{-1}\) K\(^{-1}\), and \( T \) is the temperature of the system.

The concentration of ethylene (eqn. 7) or ethane (eqn. 8) in the adjacent liquid segment was determined as

\[
C_{C=C} = \frac{n_{C=C}(t=0) - n_{C=C}(t)}{V_s}
\]  

(7) \[
C_{C-C} = \frac{n_{C-C}(t=0) - n_{C-C}(t)}{V_s}
\]  

(8),

where \( C_{C=C} \) and \( C_{C-C} \) are the total concentrations of ethylene and ethane, respectively, in the adjacent liquid segment at time \( t \); \( n_{C=C}(t=0) \) and \( n_{C-C}(t=0) \) are the number of moles of ethylene or ethane, respectively, in the gas plug at time \( t=0 \); \( n_{C=C}(t) \) and \( n_{C-C}(t) \) are the number of moles of ethylene or ethane, respectively, in the gas plug at time \( t \), and \( V_s \) is the volume of the liquid segment.

### 6.3.3 Reaction of Ethylene or Ethane Individually

We first examined the transfer of individual gases - ethylene and ethane - from their plugs to the FLP solution. Figure 6.4 shows the variations of the total concentration of ethylene (a) and ethane (b) transferred to the solution with varying FLP concentration, plotted as a function of time. In Figure 6.4a, the increase in the concentration of ethylene
in the liquid segment was the result of physical and chemical dissolution of ethylene. For the concentrations of FLP reagents in the range from 0 to 200 mM, the amount of ethylene, $C_{c=c}$, transferred to the solution increased at higher FLP concentrations, which indicated that the FLP was the limiting reagent. Overall, the total uptake of ethylene was 83 mM at 200 mM FLP, in comparison with 20.3 mM transferred in the FLP-free solvent, due to physical dissolution only.

Figure 6.4b shows the variation in ethane concentration, $C_{c-c}$, in the liquid segments, plotted as a function of time for FLP concentrations in the range from 0 to 200 mM. The concentration of ethane in the solution did not appreciably change when FLP reagents were introduced in DCE, which implied that no reaction occurred between the FLP and ethane, and plug shrinkage occurred predominantly as a result of physical dissolution of ethane in DCE. This result was in agreement with previously reported findings$^{17}$.

To determine the concentration of reacted ethylene, $C_{c=c,r}$, the equilibrium value of $C_{c=c}$ for the FLP-free solution was subtracted from the equilibrium values of $C_{c=c}$ for each FLP concentration, based on the results shown in Figure 6.4a. The same subtraction was applied to the dissolution of ethane, based on Figure 6.4b.
Figure 6.4. Variation in the total concentration of ethylene (a), plotted as a function of time for the FLP solutions with concentrations of 0 (black), 10 FLP (red), 20 FLP (green), 30 (blue), 40 (teal), 50 (orange), 100 (purple), 150 (pink), and 200 mM (light green lines). Variation in the total concentration of ethane (b), plotted as a function of time for the FLP solutions with concentrations of 0 (blue), 50 (red), 100 (purple), and 200 mM (green).

Figure 6.5a shows the variation in the total equilibrium concentration of ethylene and ethane at 0 °C and 25 °C, plotted as a function of the FLP concentration in the solution. Figure 6.5b shows the dependence of the concentration of reacted ethylene,
$C_{c=c,r}$ as well as the reacted ethane $C_{c=c,r}$ as a function of FLP concentration. We found that $C_{c=c,r}$ was negligible for all FLP concentrations. Notably, to maximize the chemically mediated uptake of ethylene over physical consumption of ethane, we increased the concentration of FLP reagents in the solution to 200 mM, making it significantly higher than in earlier experiments. Further increase in FLP concentration beyond 200 mM led to precipitation of the product from the solution.

Secondly, we rationalized that the reduction of temperature would shift the equilibrium for the FLP-ethylene reaction (Figure 6.2a) and increase the amount of adduct for the same concentration of FLP, thus overall, consuming more ethylene. We decreased the temperature of the reaction from 25 to 0 °C by immersing the MF reactor in an ethylene glycol/water bath. A circulating water cooler was used to flow cooled fluid through a circular network of copper tubes that were submerged in the bath. The copper piping facilitated heat exchange between the cooled circulating fluid and the water/ethylene glycol bath.

Figure 6.5b shows that the concentration of reacted ethylene, $C_{c=c,r}$, at 0 °C was significantly higher than at 25 °C, signifying the exothermic nature of the reaction of FLPs with ethylene and Le Chatelier’s principle. At 200 mM FLP, the total concentration of ethylene uptaken by the system (both physical and chemical) was 154 mM compared to 21 mM for ethane under similar conditions.
Figure 6.5. Variation in the total (physical and chemical) mass transfer of ethylene at 0 °C (green), ethylene at 25 °C (blue), and ethane at 25 °C (red), and ethane at 0 °C (orange), plotted as a function of initial FLP concentration (a). Chemically mediated transfer of ethylene at 0 °C (green) and 25 °C (blue), and ethane at 0 °C (orange), and 25 °C (red) as a function of initial FLP concentration (b). Error bars represent one standard deviation.

Thus we conclude that the separation of ethylene and ethane was based on the difference between the physical dissolution of ethane in DCE and the chemically mediated dissolution of ethylene as a result of its reaction with the FLPs. Two features favored the enhanced reactive separation of ethylene and ethane: a reduced temperature of the system, at which the physical dissolution of ethane did not significantly change, and a high concentration of FLP of up to 200 mM.
For the maximum total ethylene uptake \( C_{c=c} \) at 0 °C of 154 mM and \( C_{c-c} \) of 21 mM, the separation factor, \( S \), defined as \( C_{c=c} / C_{c-c} \) was found to be 7.3. We defined the purity of ethylene from the resultant separation factor as \( S/S+1 \). In other words, 7.3 parts ethylene were extracted from the gas mixture for every 1 part ethane. For our system we calculated the purity of ethylene, based on the individual gas experiments, which was expected to be 88 % for a 1:1 vol gas mixture of ethylene/ethane.

6.3.4 Gas Mixture Experiments

To assess the accuracy of this prediction, we conducted MF separation from an ethylene/ethane mixture (1:1 volume ratio) at the FLP concentrations varying from 0 to 200 mM. The two gases were mixed in a tubing, prior to their entry in the MF device. Ethane and ethylene were supplied at a total pressure of 22 kPa, that is, two-fold higher than the pressure used in the individual gas experiments, in order to obtain the same partial pressure of each gas as in the experiments with individual gases (and hence the same number of moles of gas). Based on Dalton’s law, the total pressure exerted by a mixture of gases is

\[
P_{\text{total}} = p_{c=c} + p_{c-c}
\]

(9),

where \( P_{\text{total}}=22 \) kPa, and \( p_{c=c} \) and \( p_{c-c} \) are the partial pressures of ethylene and ethane, respectively.

Figure 6.6 shows the temporal variation in the total concentration of gas mixture (ethylene and ethane) uptaken by the solution at various FLP concentrations. For the ethylene/ethane mixture, physical gas dissolution in the pure solvent was 43 mM. Since
the ethylene and ethane do not affect each other’s physical dissolution, as verified by IR spectroscopy (Figure 6.1), the sum of the individual gas physical solubilities was expected to be similar to the total physical gas solubility of the mixture. For example, at 0 °C, the individual physical uptake of ethylene and ethane by DCE were 25 and 21 mM, respectively. Thus, the expected total physical uptake of the 1:1 gas mixture of ethylene/ethane supplied at the same partial pressure was expected to be 46 mM. Figure 6.6 shows the physical uptake of both gases to be 43 mM, which was only 7% lower than the expected value.

![Graph](image)

**Figure 6.6.** Variation in the total uptake of the 1:1 vol ratio ethylene/ethane mixture at by the solution with initial FLP concentrations of 0 (blue), 50 (red), 100 (green), and 200 mM (purple) at 0 °C.

Table 6.1 shows the total uptake (physical plus chemical) of individual ethylene and ethane gases, as well as a 1:1 ethylene/ethane mixture, at 0 °C, by solutions with four FLP concentrations ranging from 0 to 200 mM. For the 1:1 vol mixture of ethylene and ethane, the expected values (based on Dalton’s law and on the fact that the physical dissolution of each gas does not affect the other, as shown in Figure 6.1), are tabulated and are compared to the actual results obtained from MF experiments. The last column in
the table, denoted as the percent ratio actual data over the expected value indicates the variation between actual results and expected results. The experimental and expected results differed by an average 8% for 4 FLP concentrations studied.

### Table 6.1. Total uptake of ethylene, ethane, or ethylene/ethane mixture

<table>
<thead>
<tr>
<th>[FLP] (mM)</th>
<th>Individual Gases</th>
<th>Mixture [Gas]_{total}</th>
<th>Actual/Expected</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[C-C]_{total} (mM)</td>
<td>[C=C]_{total} (mM)</td>
<td>Expected (mM)</td>
</tr>
<tr>
<td>0</td>
<td>21</td>
<td>25</td>
<td>46</td>
</tr>
<tr>
<td>50</td>
<td>20</td>
<td>57</td>
<td>77</td>
</tr>
<tr>
<td>100</td>
<td>20</td>
<td>92</td>
<td>112</td>
</tr>
<tr>
<td>200</td>
<td>20.5</td>
<td>154</td>
<td>174</td>
</tr>
</tbody>
</table>

The MF strategy allowed for the separation of ethylene from a 1:1 vol mixture of ethane/ethylene with a separation factor of 7.3 and a resulting ethylene purity of 88%, which favourably compares with other separation systems. For example, the separation of ethylene from ethane using 6FDA-based polyimide membranes\(^8\) have yielded a separation factor for ethylene/ethane between 3.3 and 4.4 at feed pressures up to 17 atm (1.72 MPa) and 308 K (34.8 °C). The use of copper-doped MCM-48 molecular sieves led to a separation factor for ethylene/ethane of 3.8\(^7\) A MOF (ZIF-8) membrane was recently used to separate an equimolar ethylene/ethane mixture at room temperature and 1 atm with a separation factor of 2.8\(^26\). Compared to these recently reported systems, reactive extraction using FLPs allows for a higher separation factor at milder reaction conditions (temperature and pressure).
6.4 Conclusions

In summary, we developed a MF methodology to study the separation of ethylene from ethane using Frustrated Lewis pairs. We utilized a glass MF reactor with a Y-junction to generate segmented flow of alternating plugs and slugs with well-defined interfacial areas. The system was studied at high (up to 200 mM) FLP concentration in solution and at temperature reduced to 0 °C. Both factors resulted in shift of equilibrium of the direct reaction of ethylene with FLP and enabled a greater separation efficiency with a separation factor of 7.3 and 88% ethylene purity. The use of FLPs and a MF platform opens the door for numerous studies of gas separation, with a comprehensive throughput exploration of a large parameter space of reaction conditions.
References


Chapter 7

Summary and Outlook

7.1 Summary

The unifying theme of this work was the development and use of MF platforms for fundamental studies of chemical reactions, including their kinetics and thermodynamics. Exemplary reactions studied in the present work included polymerization of N-isopropyl acrylamide, CO₂ sequestration by Frustrated Lewis pairs (FLPs), and ethylene separation from its mixture with ethane due to the reaction of ethylene with FLPs.

Microfluidics offered several key advantages over batch scale reactors such as the cost effectiveness, improved heat and mass transfer, and throughput capability, which make MFs ideal for studying kinetics and thermodynamics of fast reactions occurring on the time scale of several seconds. Microfluidic platforms act primarily as screening tools that use low reagent volumes (picolitres) and allow quick assessment of reaction parameters. Thus we utilized MFs for investigating chemical reactions.

Chapter 3 described the fabrication of MF reactors by thermo-embossing different polymer materials, such as polycarbonate, cyclic olefin polymer, poly(methyl methacrylate), high-density, poly(vinyl chloride), and polystyrene, and tested them under exemplary experimental conditions. The goal of this work was to expand the potential applicability of MFs to reactions involving polar and organic solvents, gas impermeability experiments, and biological applications. We described the optimization
of fabrication protocols and addressed the challenges and limitations of microfabrication. Importantly, each polymer used in the present work required different embossing and bonding conditions, based on the mechanical properties and glass transition temperature, and thus we provided detailed and optimized fabrication conditions for each polymer (Table 3.2).

In Chapter 4, we utilized a custom-made polycarbonate MF reactor integrated to an attenuated total reflection Fourier transform infrared (ATR-FTIR) spectrometer to study the aqueous polymerization of \( N \)-isopropyl acrylamide in the presence of \( N'N,N,N' \)-tetramethylethylenediamine and ammonium persulfate. The integration of the reactor to the spectrophotometer allowed for full spectrum characterization of all reagents in the solution. We tracked the disappearance of the IR band corresponding to the monomer concentration in order to obtain the rate of polymerization under different reagent concentrations and pH values. We obtained reaction orders with respect to each reagent, which compared favourably to values published in the literature.

In Chapter 5, we utilized segmented flow of alternating gas plugs and liquid slugs, in a MF reactor, to obtain fundamental information such as thermodynamic parameters \( \Delta G \), \( \Delta H \), and \( \Delta S \) and reaction efficiency of the gas-liquid reaction involving CO\(_2\) and FLPs. We optically tracked the plug volumes as a function of time to investigate the mass transfer of CO\(_2\) from the gas plugs to the liquid slugs where the chemical reaction occurred. We dissected the total uptake of CO\(_2\) by the liquid segments to physical dissolution in the solvent and to chemical reaction with FLPs, both of which contributed to the mass transfer of CO\(_2\) from the plugs. We utilized ATR-FTIR spectroscopy to verify that the physical dissolution of CO\(_2\) was unaffected by the presence of the FLP. Finally,
we conducted the reaction at different temperatures and, in a throughput manner, calculated $\Delta G$, $\Delta H$, and $\Delta S$ for 5 temperatures.

In Chapter 6 we described the results of studies of the capacity of FLPs to facilitate the separation of gases, namely, extraction of ethylene from an ethylene/ethane gas mixture. Segmented flow was generated of alternating gas plugs of the mixture of ethylene and ethane, with alternating slugs of the solution of FLPs in dichloroethane. Due to the reaction of ethylene with FLP, ethylene was chemically uptaken by the solution where it formed a stable, yet reversible, zwitterionic product. By monitoring the volume of plugs using optical microscopy, we studied the physically and chemically mediated transfer of gases into the liquid medium. Similar to the work described in Chapter 5, we dissected the effects of physical dissolution of gas in the solvent and the chemical reaction between ethylene and FLPs. We showed, through MF experiments, that FLPs react with ethylene yet not with ethane. By increasing the concentration of FLP reagent in the liquid and reducing the temperature of the system to 0 °C, we obtained a separation factor for ethylene of 7.3 and a purity of 88% from a 1:1 vol ethylene/ethane mixture.

7.2 Future Work

Microfluidic platforms serve primarily as characterization tools that aid in the development of reagents for increased reaction efficiency and for studying reactions in various conditions. Although MFs can be used successfully to obtain fundamental information on chemical reactions, such as kinetics and thermodynamic information, several areas of MFs require further work.
The exemplary polymerization of NIPAAm studied in the current work did could have benefited from light scattering or GPC measurements to supply additional information of the reaction products.

Exothermic reactions occurring in single-phase and segmented multi-phase flow, similar to the reactions described in Chapters 4, 5, and 6, result in generation of heat that may lead to local hot spots. These hot spots may alter the kinetics of the reaction as well as the temperature of the system. Although we used a temperature probe to measure the reaction temperature of polymerization product in Chapter 4, on-chip, measurements of temperature have not been conducted for the FLP work involving sequestration of CO₂ and separation of ethylene, which are also exothermic reactions. Future work could implement temperature probes at the region of interest to ensure that heat generated is dissipated evenly by the MF reactor to the surrounding and that hot spots do not persist, which would result in inaccurate assessment of the reaction kinetics and thermodynamics.

One of the primary advantages of MF reactors is their low consumption of reagents. However, assessment of reaction products from MF synthesis sometimes requires large volumes, up to several mL, e.g., for NMR or gas chromatography studies. Therefore, the implementation of several reactors running in tandem to produce product would be beneficial.

A major area of future work will deal with the integration of polymer MF reactors (made of chemical resistant PE) to ATR-FTIR spectroscopy instrumentation, and at the same time utilizing an overhead CCD camera to simultaneously track the chemical reaction, in segmented flow, by optical characterization (similar to Chapters 5 and 6) as well as by full spectrum IR characterization. The combination of real-time IR assessment
will complement and support the optical characterization of gas migration from plugs to slugs. The optical characterization will provide information of the mass transfer of gas (physical and chemical), while the IR characterization will provide detailed information of the reaction intermediates in the solution. Together, the system is expected to provide full characterization of all species involved in the reaction.

The projects in Chapter 5 and Chapter 6, involving FLP reactions, explored only the forward reactions where gas chemically reacted with the FLP. Studying the reverse reaction is significant in assessing the reversibility of the reaction and how favourable it is to regenerate the FLP and release the gas. The reversibility of the reaction is important in assessing the economics of the reaction and its suitability in commercial applications.

Another major area of future research is acquiring information about the stoichiometry of the reaction between FLPs and CO$_2$. Current MF work that has been done to-date has not addressed any aspects of the reaction mechanism and how this trimolecular reaction occurs. It is not known whether the Lewis acid first reacts with CO$_2$ and then the product reacts with the Lewis base, or vice versa. Another possibility is the “pre-organization” of the FLP, that is, the Lewis acid and base can form intermolecular interactions (between the hydrogen atoms on the tert butyl group and the fluorine atoms on the pentafluorophenyl group) which can form a complex that then reacts with CO$_2$. The work in this thesis used equal concentrations of the Lewis acid and base together for each reaction (their molar ratios were kept constant). For future work, we aim to change the concentrations between Lewis acid and base in order to find whether any reaction occurs between just CO$_2$ and borane, CO$_2$ and phosphine, or the Lewis acid and the Lewis base (to form a pre-organized complex).
Finally, future fundamental studies, to obtain kinetics and thermodynamic information, of reactions involving FLPs and other small molecules (see Figure 1.6) is wanting in the community due to the challenges of using batch scale processes to attain this information. Since mixing in the batch scale is slow and inhomogeneous, studies to find kinetics and thermodynamics with characterization tools such as NMR lead to inaccurate results. Therefore, we propose that the MF platform be utilized in such cases for fast reactions.
Appendix

Appendix to Chapter 4

A4.1 Effective Path Length of ATR Evanescent Wave

In this section, we explain the calculations involved in determining the molar extinction coefficient of NIPAAm and the effective path length for the evanescent wave protruding into the sample atop the ATR crystal. The calibration plot for absorbance vs. NIPAAm concentration (Figure 4.3b) yielded a linear relationship and can be described by the Beer-Lambert law as

\[ A = \varepsilon l c \quad (1) \]

where \( A \) is the absorbance at 975 cm\(^{-1}\), \( \varepsilon \) is the molar extinction coefficient, \( l \) is the path length, and \( c \) is the NIPAAm concentration. The evanescent wave which protrudes out of the ATR crystal at the point of internal reflection of the IR beam, decays exponentially as it enters the sample, following the relation\(^1\)

\[ E = E_o \exp \left( \frac{-2\pi}{\lambda_1} (\sin^2 \theta - n_{21}^2) \frac{1}{z} \right) \quad (2) \]

where \( E_o \) is the initial electric field amplitude, \( \lambda_1 \) is the wavelength of radiation in the denser medium (ATR crystal), \( \theta \) is the incident angle, \( n_1 \) and \( n_2 \) are the indices of refraction of the ATR crystal and the sample, respectively, \( n_{21} = n_2/n_1 \), and \( z \) is the distance from the surface of the ATR crystal. A consequence of the exponential decay of the evanescent wave is that obtaining the effective path length, which may be used in the Beer-Lambert law, is not straightforward. The effective penetration length, \( d_e \), defined as
the equivalent path length in a transmission measurement that would lead to an absorption band of the same intensity\textsuperscript{2}, may be calculated using the equations first derived by Harrick\textsuperscript{2} for perpendicular polarized (eq. 3) and parallel polarized (eq. 4) IR radiation as

\[
d_{e\perp} = \frac{n_{21}\lambda_1 \cos\theta}{\pi(1-n_{21}^2)(\sin^2\theta-n_{21}^2)^2}
\]

\[
d_{e\parallel} = \frac{n_{21}\lambda_1(2\sin^2\theta-n_{21}^2)\cos\theta}{\pi(\sin^2\theta-n_{21}^2+n_{21}^4\cos^2\theta)(\sin^2\theta-n_{21}^2)^2}
\]

where \(\lambda_1 = \lambda/n_1\) and \(\lambda\) is the wavelength in vacuum. For un-polarized light, the equation for \(d_e\) becomes

\[
d_e = \frac{d_{e\perp}+d_{e\parallel}}{2}
\]

In order to find the effective path length, that is the path length that would give the same absorbance in transmission as obtained in ATR-FTIR experiments, we multiplied \(d_e\) by the number of internal reflections of our crystal, \(N\), (our diamond crystal had 1 internal reflection) and the Beer-Lambert law can thus be written as

\[
A = \varepsilon N d_e c
\]

The methodology of using the effective path length, calculated here, in conjunction with the Beer-Lambert law for quantitative ATR spectroscopy is widely used in the literature\textsuperscript{3-5}. Using eq. 5, we calculated the effective path length, \(Nd_e\), of the evanescent wave protruding from the ATR crystal and into the sample to be 1.94 \(\mu\)m. We used eq. 6 to calculate the molar extinction coefficient using our calibration plot (Figure 4.3b) as 8.57 x10\textsuperscript{3} M\textsuperscript{-1}cm\textsuperscript{-1}. 

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Appendix to Chapter 5

A5.1 Micro and Macroscale Physical Dissolution

In this section, we explain the difference in time scales of Figures 5.5a and 5.7a, corresponding to the macro- and microscale experiments, respectively. Since the diffusivity, $D$, of CO$_2$ within the solvent is the same for both macro- (IR experiment) and microscale experiments, the difference in the time scales results from the difference in diffusion length scales, $L_D$, of these two experiments:

(a) Macroscale. A stationary 100 µL-volume droplet on the ATR crystal: $L_D \approx 3$ mm. (b) Microscale. A 6 nL-volume liquid segment entrapped between two CO$_2$ plugs flowing along the microchannel: $L_D = 37.5$ µm. In the diffusive processes, time scales as $L_D^2$. Thus the ratio of the physical dissolution times of CO within the solvent for experiments (a) and (b) can be estimated as
where $t_{\text{Macro}}$ and $t_{\text{Micro}}$ are physical dissolution times of CO$_2$ within the solvent for the IR and MF experiments, respectively.

In order to estimate $t_{\text{Micro}}$, the liquid segment streamline patterns entrapped between two gas plug caps, while flowing in the microchannel are shown in the figure below.

![Figure A5.1](image)

**Figure A5.1.** Numerically obtained streamline patterns inside a liquid segment while flowing inside a microchannel.

Due to the convection and symmetric recirculation patterns inside the liquid segment in Figure 5.4, a quarter of the microchannel width, $W$, can be assumed as the characteristic diffusion length scale in the MF experiment. The diffusion coefficient of CO$_2$ molecules into bromobenzene, $D_{\text{CO}_2-\text{BB}}$, is estimated using Versteeg and Swaalj’s equation$^{39,40}$,

$$D_{\text{CO}_2-\text{BB}} = D_{\text{CO}_2-\text{Water}} \times \left( \frac{\mu_{\text{Water}}(T)}{\mu_{\text{BB}}(T)} \right)^{0.8}$$  \hspace{1cm} (2),
where, \( D_{\text{CO}_2-\text{Water}} \) is the diffusion coefficient of \( \text{CO}_2 \) in water, \( \mu_{\text{Water}}(T) \) and \( \mu_{\text{BB}}(T) \) are viscosities of water and bromobenzene at the temperature \( T \), respectively. Using the estimated \( D_{\text{CO}_2-\text{BB}} \), the physical dissolution time of a 600 \( \mu \text{m} \) long bromobenzene segment while flowing in a microchannel with a width of 150 \( \mu \text{m} \) can be calculated as:

\[
 t_{\text{Micro}} = \frac{(W / 4)^2}{D_{\text{CO}_2-\text{BB}}} = 0.85 \text{s} 
\]

(3)

Thus, in the MF experiment, the physical \( \text{CO}_2 \) uptake time within the solvent is less than 1 s, while the solvent \( \text{CO}_2 \) uptake time in the IR experiment would be: \( t_{\text{Macro}} = t_{\text{Micro}} \times 6400 = 90.6 \text{ min} \).