MODULAR ATR FT-IR MICROREACTOR CHIP FOR OPTIMIZING REACTION CONDITIONS

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ABSTRACT

A silicon chip for attenuated total reflection (ATR) Fourier transform infrared (FT-IR) spectroscopy in combination with a modular PDMS herringbone mixer and a microreactor has been successfully fabricated and tested. The modular design allows the chip to be used for a variety of reactions. A model synthesis of 1-butyl-2,5-dimethyl-1H-pyrrole from hexane-2,5-dione with 1-butylamine has been performed on chip. When plotting the natural logarithm of the peak area corresponding to the ketone stretch vibration at 1710cm^{-1}, against the residence time, a linear curve can be fitted, suggesting this step to be a first order reaction.

KEYWORDS: Infrared spectroscopy, attenuated total reflection, online reaction monitoring

INTRODUCTION

Optimizing chemical reaction parameters can be an expensive and time consuming process. Microfluidic flow chemistry is an established method to obtain better control over temperature, concentrations and mass transport [1]. Integrating such a microfluidic-chip with an analytical method allows for direct characterization of the (intermediate) products. ATR FT-IR is chosen as analytical technique since it can be used online, is not destructive and generates both quantitative and qualitative information about the sample. Combinations of microfluidic-chips with ATR FT-IR spectroscopy have been proposed in the past [2,3], but these are often limited to a specific application and can be difficult to fabricate.

We propose a modular, easy-to-fabricate design, consisting of a silicon ATR crystal that can be combined with one or several stacks of PDMS microreactor and herringbone mixer layers [4]. On the side of the chip, two resistors are placed that can be used to heat up the chip, allowing control over the reaction temperature. With this modular design several parameters of the reaction can easily be adjusted, allowing one to optimize a large variety of multi-step reactions.

A schematic representation of two possible combinations of PDMS layers for the microfluidic-chip are shown in Figure 1. In Figure 1A, a silicon ATR crystal in combination with a single PDMS layer, consisting of both a mixer and reaction chamber, is shown. A simple reaction where reactant A plus reactant B becomes product C, can be performed on this chip. In Figure 1B the same ATR crystal is shown, but now with 3 PDMS layers. The top two layers consist of only mixers, and the bottom layer consist of a mixer and a reaction chamber. By selectively punching holes in the PDMS chips and carefully planning where the tubing's connect to, several reactants can be introduced and mixed in the chip. In the top mixer layer, reactant A and B are mixed, forming product C. Product C will flow into the middle mixer layer, where it is mixed with reactant D to form product E. Product E is introduced to the final, bottom layer where it is mixed with reactant F, to form the end product G.

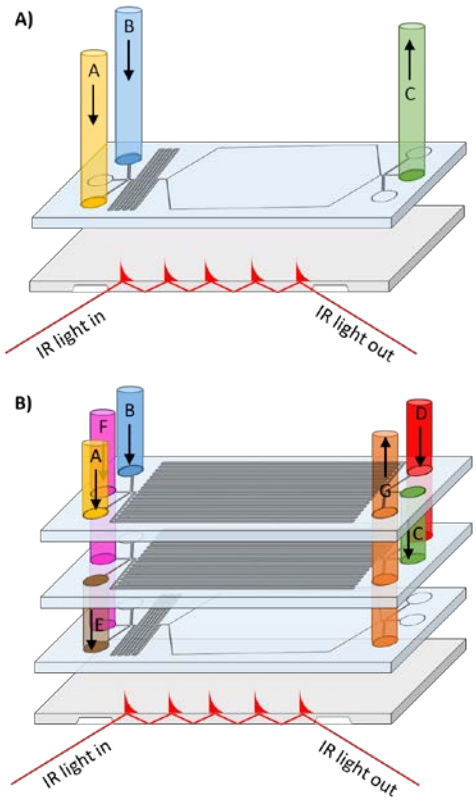

Figure 1: schematic representation of the chip. (A) ATR crystal with single PDMS layer. (B) ATR crystal with three layers of PDMS, capable of handling a larger number of reactants

EXPERIMENTAL

The silicon ATR crystal is partly based on the design of Karabudak et al. [3]. A 525µm thick silicon wafer with a {100} crystal orientation is anisotropically etched with KOH, creating facets with an angle of 54.7°. Etching is stopped when 75µm of silicon remains, creating increased structural support for the addition of the PDMS microfluidic chip. The created facets are used to couple IR light into the crystal, as schematically represented in Figure 1. The PDMS microfluidic-chips are bonded with oxygen plasma on top of the silicon ATR crystal.

As a proof of concept, a model reaction is performed using a chip with a single PDMS layer configuration, as shown in Figure 1A. For this design, the mixing channel is 70mm long, 200µm wide and 85µm high. The herringbone mixer on top of the channel has grooves with a depth of 15µm [4]. The reaction chamber is approximately 13mm long, 10mm wide and 85µm high, corresponding with a total volume of 12.25µL.

A Paal-Knorr synthesis of 1-butyl-2,5-dimethyl-1H-pyrrole from hexane-2,5-dione with 1-butylamine is chosen as model reaction, of which the mechanism is shown in Figure 2. A custom build aligner with integrated mirrors is used to put the ATR-chip in the beam path of a commercially available FT-IR spectrometer (Bruker Vertex 70). Tubing is connected to the PDMS chip and a syringe pump (neMESYS) is used to introduce both reactants into the chip, each with a flow of 5µl/min (total flow of 10µl/min.). After mixing, the solution is introduced to the reaction chamber and the flow is stopped. The reaction chamber is directly above the sensing area of the ATR crystal. IR spectra is recorded every 3.5 minutes over a period of 21 minutes. The reaction is performed at room temperature so the integrated heaters are not used for this experiment.

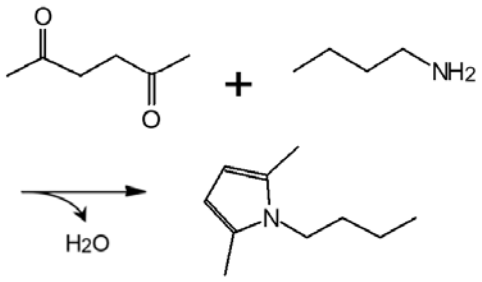

Figure 2: Synthesis of 1-butyl-2,5-dimethyl-1H-pyrrole from hexane-2,5-dione with 1-butylamine

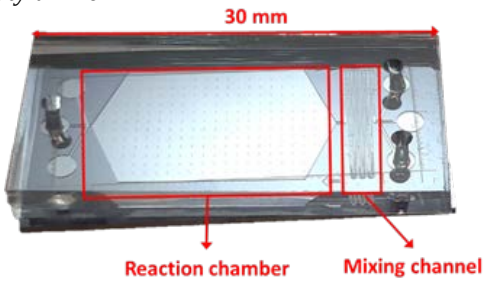

Figure 3: fabrication result of one of the PDMS chips bonded on the silicon ATR crystal.

RESULTS AND DISCUSSION

Fabrication results of the chip are shown in Figure 3. On the bottom part of the chip the silicon ATR crystal with dimensions of 30mm by 15mm is clearly visible. Highlighted is the mixing chamber and the reaction chamber. The dots in the reaction chamber are pillars for increased structural support.

The results of the IR spectra are shown in Figure 4A and Figure 4B. On the x-axis the wavenumber is shown which is plotted against the absorbance on the y-axis. Spectra at t=3.5 min (red), t=10.5min (blue) and at 21.0min (yellow) after the start of the reaction are shown. In Figure 4A the spectra from 4000cm^{-1} to 2500cm^{-1} are shown. One can clearly see the broad peak around 3400cm^{-1} increasing, this corresponds to the O-H bond stretching vibration, suggesting either the formation of water (side-product), alcohol (intermediate-product), or a combination of both [5]. The peaks around 3000cm^{-1}, associated with the alkyl-stretches, are decreasing and changing in ratio. This could correspond to the pyrrole formation [5].

Figure 4B shows the spectra from 1800cm^{-1} to 1000cm^{-1}. Notable peaks that increase in signal are the peak at 1525cm^{-1}, assigned to the skeleton vibration of the pyrrole, the peak at 1410cm^{-1}, likely to be an CH_2-C=O deformation vibration and the peak at 1300cm^{-1}, which could be assigned to the C-N stretch vibration [5]. Interesting peaks with decreasing intensities are the initially strong peak at 1710cm^{-1}, which can be assigned with certainty to the ketone stretch vibration, the peak at 1360cm^{-1}, which is a decrease in the CH_3 symmetrical deformation and the peak at 1160cm^{-1}, which can be assigned to the OH bending vibration from the isomeric form of hexane-2,5-dione [5,6].

In Figure 4C the natural logarithm of the peak-area of the ketone stretch vibration at 1710cm^{-1} is plotted against the residence time in the chip. The peak area is decreasing in time at a logarithmic rate, indicating a first order reaction. The same trend is not obtained when integrating the O-H peak at 3400cm^{-1} or the peak at 1525cm^{-1}. This suggests that different intermediate products are formed with different reaction orders.

CONCLUSION

We have demonstrated that it is feasible to fabricate a modular, cheap and user friendly chip that can be used for optimizing reaction conditions while monitoring chemical species with IR spectroscopy. The combination of integrated heaters and modular PDMS mixers, allow the chip to be used for a wide range of reactions. A model synthesis of 1-butyl-2,5-dimethyl-1H-pyrrole from hexane-2,5-dione with 1-butylamine proves that reactions can be monitored with the device, and that it can be used to get insight in the reaction order.

Future plans include adding confocal mirrors to the setup to increase light coupling into the ATR crystal, creating a grating coupler to improve the coupling efficiency of specific wavelengths, and improving the limit-of-detection by adding structures for surface enhanced infrared spectroscopy.

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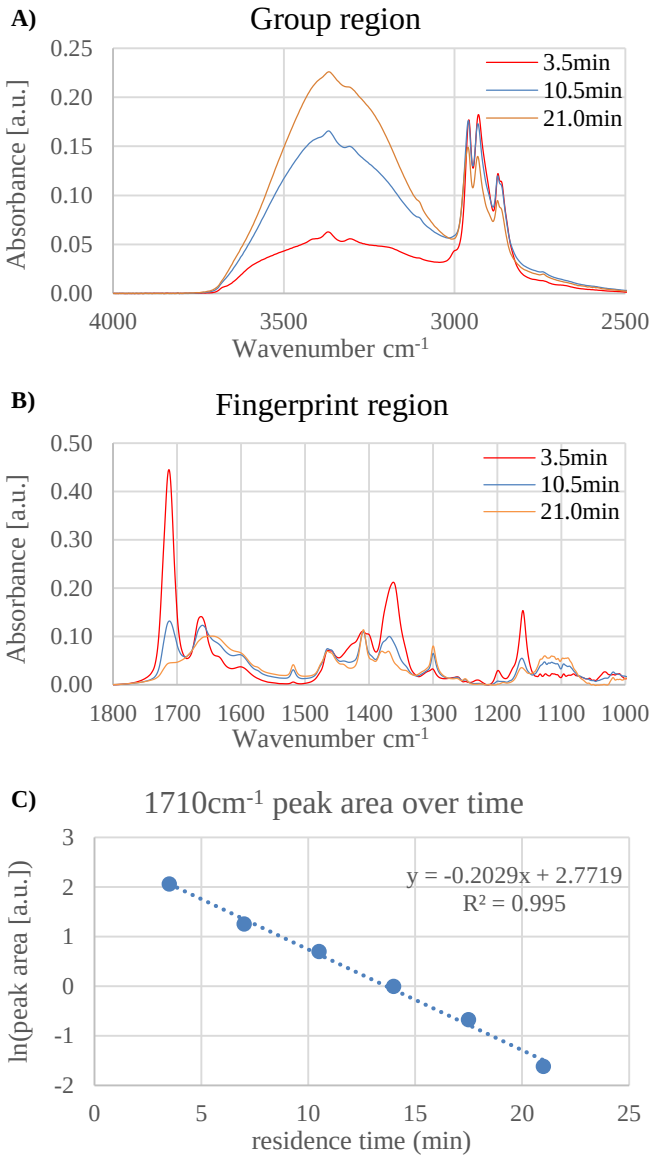

Figure 4: (A) FT-IR spectra at 4000-2500cm^{-1}, red line after 3.5min, blue line after 10.5min and yellow line after 21.0min. (B) FT-IR spectra at 1800-1000cm^{-1}, red line after 3.5min, blue line after 10.5min and yellow line after 21.0min. (C) The natural logarithm of the peak area at 1710cm^{-1}, corresponding with the ketone stretch vibration, against the residence time.

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