

GLASS-SURFACE AS IN-SITU CATALYST IN REACTION CHIPS

M. Brivio, R. E. Oosterbroek, W. Verboom, M. H. Goedbloed, A. van den Berg and D. N. Reinhoudt

Mesa⁺ Research Institute, University of Twente, The Netherlands

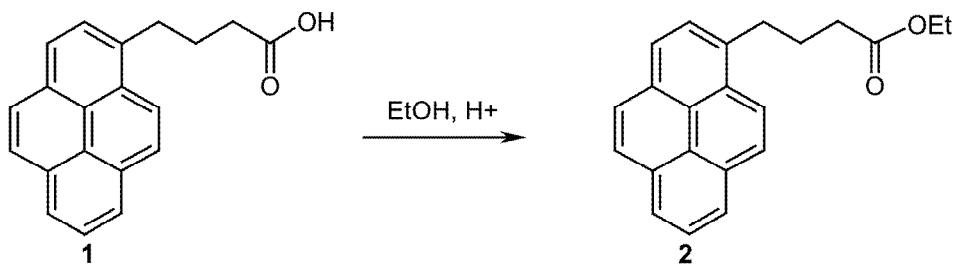
ABSTRACT

In a systematic study of the acid-catalyzed esterification of 9-pyrenebutyric acid (**1**) with ethanol, we demonstrate the significant contribution of surface phenomena to the “chip-effect”, leading to considerably higher product yield and shorter reaction time.

Keywords: Microfluidics, on-chip synthesis, pressure-driven, surface phenomena

1. INTRODUCTION

After the massive takeoff in the fields of analytical chemistry [1-4], microfluidics have also been applied more recently to synthetic chemistry, leading to the extension of the μ -TAS concept to the so-called lab-on-a-chip. Advantages that miniaturization brings to synthetic chemistry have been recently demonstrated for a number of liquid and gas phase reactions [5]. For most of the microscale syntheses, the improved reactivity has been mainly attributed to the high reaction control and mixing speed, achievable in electrokinetically driven micro reactors [6], as well as the fast diffusive mixing under laminar flow conditions and the high efficiency of heat transfer [7]. In our contribution we present the considerable enhancement of reaction efficiency observed in a systematic study of the acid-catalyzed esterification of 9-pyrenebutyric acid **1** with ethanol (Scheme 1), performed in a glass microchannel [8].



Scheme 1. The esterification reaction

2. EXPERIMENTAL

The target reaction was carried out in a pressure-driven borosilicate micro reactor (Figure 1a). During the experiments the chip was placed in a holder (Figure 1b) designed for fitting fused silica fibers into the inlet/outlet chip reservoirs by means of commercially available Upchurch Nanoport™ assemblies.

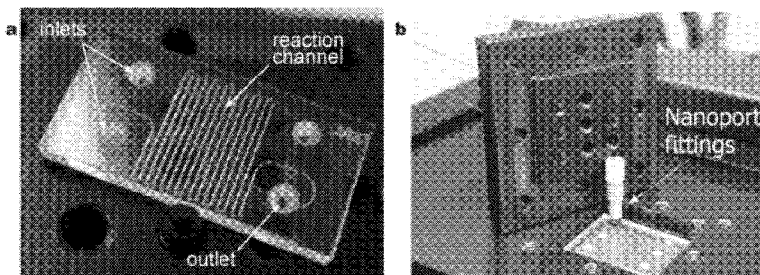


Figure 1. Picture of (a) the glass micro reactor and (b) the self-developed chip holder.

The reaction mixtures were transferred, in a continuous flow fashion, from the outlet silica fiber to a Matrix-Assisted Laser Desorption ionization Time of Flight (MALDI-TOF) sample plate where, upon quick solvent evaporation, no further reaction could take place. In this way the reaction-to-analysis delay time was eliminated, which is inherent to off-line chip analysis. High Pressure Liquid Chromatography (HPLC) was used for the quantitative determination of the conversions.

The on-chip conversions of acid **1** into ester **2** were compared with those obtained performing the reaction in conventional lab-scale glassware. All experiments were carried out under the same conditions using solutions of 10^{-4} M 9-pyrenebutyric acid **1** in ethanol and of 10^{-4} M sulfuric acid in ethanol both at room temperature and at 50 °C.

3. RESULTS AND DISCUSSION

Analysis of the samples showed that 15-20% of ester **2** was formed on chip after 40 min at room temp while higher yields were obtained when performing the on-chip reaction at 50 °C (Figure 2). However, no product was formed in the lab-scale experiments up to 20 min residence time, revealing a considerably increased reactivity of the on-chip versus the lab-scale experiments.

To study the observed “chip-effect”, the on-chip esterification was repeated without injecting the sulfuric acid. No ester **2** was formed at the residence times summarized in table 1. However, when activating the channel inner surface with a solution of sulfuric acid and hydrogen peroxide (3:1), 9% of ester **2** was formed in the glass microchannel after 40 min at 50 °C.

Aliquots of a premixed 1:1 solution of carboxylic acid **1** and sulfuric acid in ethanol were injected in a 100 μ m-diameter fused silica fiber, and heated at 50 °C. Analysis of

the samples showed that ester **2** was formed in yields comparable with those obtained in the on-chip experiment at comparable residence times. The same experiment performed in a fused silica fiber, the inner surface of which was coated with the hydrophobic octadecyltrichlorosilane self-assembled monolayer, showed no ester formation in any of the samples, excluding a partial contribution of the mixing dynamics to the observed “chip-effect”.

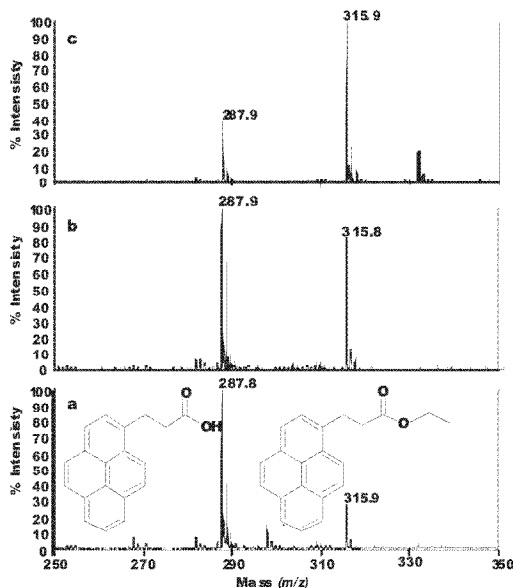


Figure 2. MALDI-TOF mass spectra of samples collected from on-chip reactions carried out at 50 °C at residence times of 4 (a), 10 (b), and 20 (c) min, respectively

Finally, the target reaction was performed at lab-scale in the presence of silica gel, imitating the same glass-surface to chemical-volume ratio (1:34) of the chip. Substantially lower conversions (Table 1) than those obtained at the same residence times in the on-chip experiments were obtained at 50 °C, indicating a higher efficiency of the catalytic process in the microchannel.

4. CONCLUSIONS

We have presented a systematic study of the influence of the channel surface in pressure-driven glass microchips, illustrated on the acid-catalyzed esterification of 9-pyrenebutyric acid **1**. Our results show a considerable reduction of reaction time at high glass surface to volume ratios (on chip, in the uncoated fiber and in silica gels) substantiating the important contribution of surface phenomena to the “chip-effect”,

giving rise to much shorter reaction times and higher yields than on conventional lab scale. Though similar glass-surface to chemicals-volume ratios were used, the conversions when using silica gel were considerably lower than on chip, clearly demonstrating the higher efficiency of the micro- over the macroscale reaction.

Table 1. Yields of ester **2** obtained in the on-chip and lab scale (with silica gel) experiments carried out at 50 °C

Residence times (min)	Flow rates (µl/min)	Yields (%)	
		On-chip	Lab SiO ₂ gel
4	1	17	8
10	0.4	33	9
20	0.2	51	10
33	0.12	71	n.d.
40	0.1	83	15

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