



**Monolithic and flexible fluoropolymer film microreactor for organic synthesis applications**

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Complete List of Authors:	Kim, Jin-Oh; Center of Applied Microfluidic Chemistry, ; Kyungpook National University, Polymer Science and Engineering Kim, Heejin; Center of Applied Microfluidic Chemistry, ; Pohang University of Science and Technology, Chemical Engineering Ko, Dong-Hyeon; Center of Applied Microfluidic Chemistry, ; Pohang University of Science and Technology, Chemical Engineering Min, Kyoung-Ik; Center of Applied Microfluidic Chemistry, ; Pohang University of Science and Technology, Chemical Engineering Im, Do Jin; Pohang University of Science and Technology, Chemical Engineering Park, Soo-Young; Kyungpook National University, Polymer Science and Engineering Kim, Dong-Pyo; Center of Applied Microfluidic Chemistry, ; Pohang University of Science and Technology, Chemical Engineering

## PAPER

## Monolithic and flexible fluoropolymer film microreactor for organic synthesis applications

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Jin-Oh Kim,<sup>a,b</sup> Heejin Kim,<sup>a</sup> Dong-Hyeon Ko,<sup>a</sup> Kyoung-Ik Min,<sup>a</sup> Do Jin Im,<sup>c</sup> Soo-Young Park<sup>b</sup> and Dong-Pyo Kim<sup>a\*</sup>

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Photocurable and viscous fluoropolymer with chemical stability is a highly desirable material for fabrication of microchemical devices. Lack of reliable fabrication method, however, limits actual applications for organic reactions. Herein, we report fabrication of a monolithic and flexible fluoropolymer film microreactor and its use as a new microfluidic platform. The fabrication involves facile soft lithography techniques that enable partial curing of thin laminates, which can be readily bonded by conformal contact without any external forces. We demonstrate fabrication of various functional channels (~300  $\mu\text{m}$  thick) such as those embedded with either a herringbone micromixer pattern or a droplet generator. Organic reactions under strongly acidic and basic conditions can be carried out in this film microreactor even at elevated temperature with excellent reproducibility. In particular, the transparent film microreactor with good deformability could be wrapped around a light-emitting lamp for close contact with the light source for efficient photochemical reactions with visible light, which demonstrates easy integration with optical components for functional miniaturized systems.

### Introduction

Microfluidic devices, including lab-on-a-chip systems, have been utilized in various areas of chemistry, because of their unique features such as miniaturized reaction volume, extremely large surface to volume ratio, and efficient mass and heat transfer capability.<sup>1</sup> Advent of new microfluidic platforms has improved the safety and efficiency not only in bench scale chemical processes but also in industrial pharmaceutical research where synthesis of libraries of compounds is needed in mg scale. Robust and rigid materials such as silicon, metal and glass have generally been employed for the manufacture of microfluidic devices.<sup>2</sup> However, sophisticated fabrication techniques such as etching and micromachining required highly intensive process and expensive equipment. On the other hand, inexpensive polymers such as poly(dimethylsiloxane) (PDMS) or poly(methylmethacrylate) (PMMA) have also been used. But they are not suitable for application in organic chemical processes due to their low chemical stability and easy swelling behaviour, although it has been widely used in biological areas due to easy fabrication, high transparency and gas permeability.<sup>3-6</sup> Coating with a resistant material is one way of overcoming the problem.<sup>7, 8</sup> However, this intuitive process requires elaborate fabrication steps and careful control of thickness of coated material.

It is highly desirable to have a thermally and chemically stable polymer material as a matrix of microfluidic chip that can be fabricated by user-friendly and economic techniques.<sup>9-11</sup> Therefore, fluoropolymer based materials such as perfluorinated acid (PFA) and polytetrafluoroethylene (PTFE) are quite attractive because they are highly solvent-resistant and

thermo-resistant with low friction characteristics.<sup>12, 13</sup> However, their very low surface energy and non-adhesiveness make it difficult to seal the channels by interfacial chemical bonding. Several attempts have been made to overcome the problem. DeSimone *et al.* reported a microreactor fabricated with a photocurable, solvent-free, and low viscous perfluoropolyether (PFPE) with urethane dimethacrylate end groups using soft lithography technique.<sup>12</sup> The PFPE microfluidic chip is highly compatible with popular PDMS-based devices in terms of low surface energy, low toxicity, high elasticity, and high gas permeability. Nevertheless, bonding between thick and rigid laminates was problematic, leading to poor fidelity and inferior flexibility. Moreover, high cost of the polymer resin limited broad applications of the devices that required more than 10 gram of the polymer for fabrication of a thick plate type of microreactor.<sup>14</sup> In addition, there have been no actual organic reaction studies on fluoropolymer based microreactors except for simple solvent resistance tests.<sup>15, 16</sup>

Herein, we report facile and economic fabrication of monolithic and flexible fluoropolymer film microreactors with PFPE resin. The reproducibility of bonding process is highly improved by adapting flexible film-based fabrication process that facilitates the conformal contact bonding between partially cured laminates with no external force. We demonstrate the versatility of the process by fabricating various functional channels embedded with a herringbone micromixer pattern or a droplet generator. The highly chemical-resistant fluoropolymer film microreactor is utilized for various synthetic reactions under strongly acidic and basic conditions and at elevated temperature. In particular, the transparent film microreactor with high deformability was wrapped around a light bulb for a closer exposure to light, which is led to superior performance in

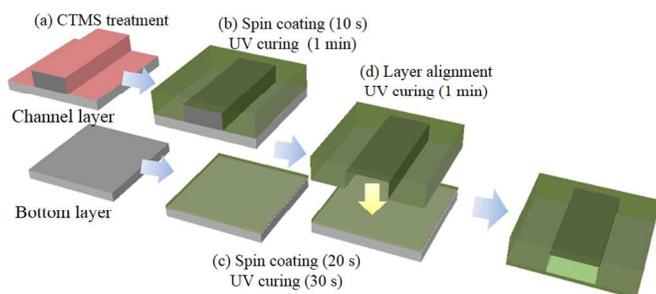
photochemical reactions. It is quite possible that this monolithic thin-film chip can readily be integrated with electrodes, heaters, light-emitting diodes, and various electronics for miniaturized systems.

## Experimental

### Materials

PFPE (Fluorolink MD 700, viscosity 581 cP) was bought from Solvay-solexis (Milan, Italy); 2-hydroxy-2-methyl-1-phenyl-propan-1-one (Darocur 1173) as a photoinitiator was bought from BASF (Ludwigshafen, Germany), and SU-8 50 photoresists were bought from Microchem (Seattle, USA). Unless stated otherwise, general-use chemicals and solvents were bought from Sigma-Aldrich (St. Louis, USA).

### Fabrication of a fluoropolymer film microreactor



**Fig. 1** A scheme for fabrication of monolithic and flexible fluoropolymer film microreactor: (a) non-adhesive coating on SU-8 master by chlorotrimethylsilane (CTMS) treatment, (b) spin coating of PFPE resin on the SU-8 master and UV irradiation for curing, (c) spin coating of PFPE resin on Si wafer and UV irradiation for partial curing, (d) conformal contact bonding to seal the channel by additional UV radiation for full cross-linking.

Various microchannels with 300 or 500  $\mu\text{m}$  width and 50  $\mu\text{m}$  height were prepared by replication of SU-8 masters which were obtained by photolithography process on silicon wafers according to previously reported method<sup>3</sup> (Electronic supporting information (ESI), † Fig. S1). Firstly, the PFPE resin for the fabrication of microfluidic chip was prepared by mixing Fluorolink MD 700 and Darocur 1173 ® in 10 to 1 ratio in wt. %. The low viscous and solvent-free mixture was readily homogenized by a vortexer (Dubuque10WA 52001, USA) for 10 min, then bubbles were removed by Rotavapor (R-210 BUCHI). Prior to replication of the microchannel pattern, the SU-8 mold on Si wafer was treated by chlorotrimethylsilane (CTMS) for 10 min to prevent the adhesion of fluoropolymer resin (Fig. 1-(a)).<sup>17</sup> The 1.5 mL of PFPE mixture was spin-coated (500 rpm, 10 sec) on the master to form a coating layer with up to 180  $\mu\text{m}$  thickness and exposed to UV irradiation for only 1 min under nitrogen atmosphere to be solidified in a fully curing manner (Fig.1-(b)). The flexible microchannel part with sufficient mechanical stability to retain the pattern was ripped off from the mold. Alternative PFPE film with 100  $\mu\text{m}$  thickness was made by spin-coating on a flat silicon wafer at 500 rpm for 20 sec and was partially cured with UV irradiation for 30 sec under nitrogen condition (Fig. 1-(c)). Inlet and outlet

parts of the microchannel should be punched to make holes using a puncher (Uni-Core 1.2 mm Harris). The free-standing and partially cured laminate with microchannel pattern was gently placed on another partially cured bottom film layer. And both thin laminates readily became intimate and in conformal contact, and then were irradiated by additional UV exposure for 1 min for complete cross-linking, resulting in strong chemical bonding at the interface between films (Fig. 1-(d)).

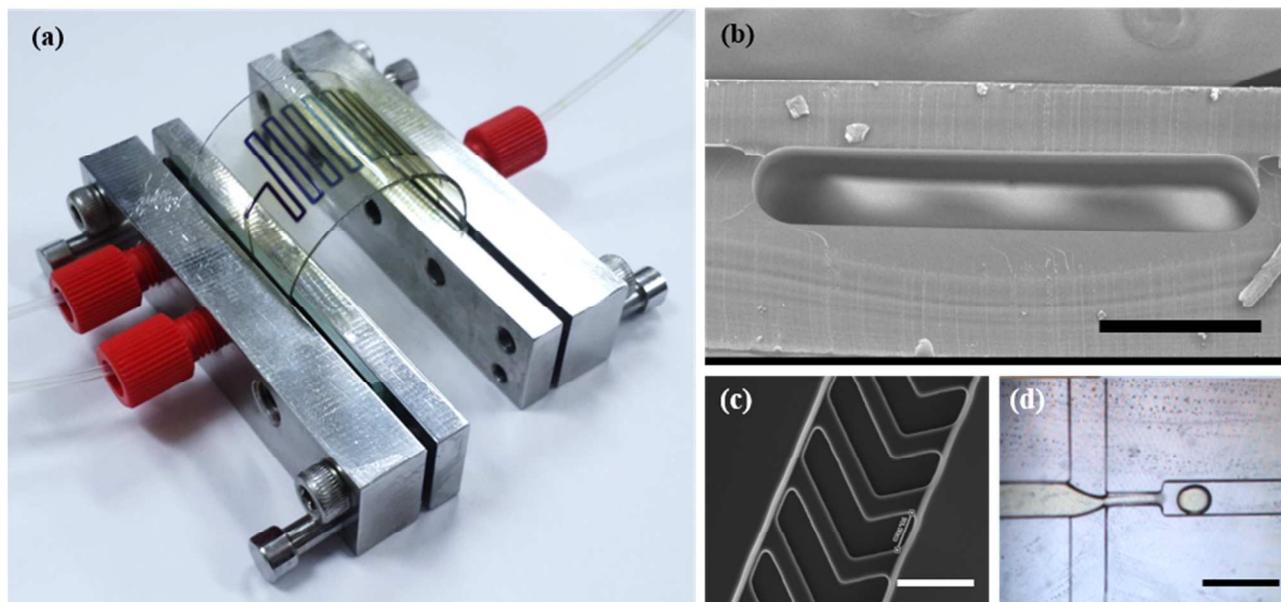
### Characterization and tolerance test

The dimension of microchannels was measured by scanning electron microscopy (SEM, SNE-1500/JEOL) and optical microscopy (SV 32, Sometch). The PFPE microfluidic devices with functional components such as a mixer and a droplet generator were also fabricated with different design of molds by identical replication and bonding steps. In order to investigate comparative solvent resistance of the cured PFPE under various organic reaction conditions, rectangular pieces of PFPE (1 cm x 1 cm x 1 mm) and PDMS (1 cm x 1 cm x 1 mm) were prepared by pouring into the mold and UV irradiation for 5 min, then immersed into various solvents in 10 mL glass vials at room temperature or 60 °C for 12 hrs. The swelling ratios of fluoropolymer and PDMS were calculated as  $100(W-W_0)/W_0$  ( $W$ : weight after swelling,  $W_0$ : weight before swelling).<sup>18-20</sup> In order to determine the bonding stability of the fabricated microchannels (300  $\mu\text{m}$  x 50  $\mu\text{m}$  x 30 mm), burst pressure was tested by connecting the inlet of microreactor to a high pressure pump (SP-930D, Younglin, Korea) with open outlet. Water was injected into the microchannel with very high flow rate in the range of 0.1 mL/min to 10 mL/min. Then the pressures at which the microchannel part was delaminated by flow induced force were determined as a measure of bonding strength. Moreover, burst pressures under organic reactions were also measured after performing continuous flow with various kinds of organic solvents (65% nitric acid, 40% methylamine solution and chloroform) for 1 hr. In addition, transparency of the fluoropolymer film (300  $\mu\text{m}$  thickness) was determined by a UV-Vis absorption spectrum (Nano Drop 2000c, Thermo scientific, Korea), which was compared with that of quartz glass (1.2 mm thickness).

### Application for organic synthesis under various conditions

To test the fluoropolymer film microreactor under various chemical conditions, we conducted reactions under strongly acidic (nitration of thiophene, pH = 1) and strongly basic (Schotten-Baumann amidation of benzoyl chloride, pH = 11) conditions at RT, and in corrosive organic media (Vilsmeier-Haack formylation) at 100 °C.

Nitration of thiophene<sup>21</sup> was conducted at RT. A solution of nitric acid (65 wt% in H<sub>2</sub>O, 50  $\mu\text{L}/\text{min}$ ) and a solution of thiophene (0.2 M in acetic anhydride, 50  $\mu\text{L}/\text{min}$ ) were introduced into a Y-shaped fluoropolymer film microreactor (300  $\mu\text{m}$  x 50  $\mu\text{m}$  x 50 mm) with or without a built-in herringbone mixer pattern (30 cm length) using separate syringe pumps (PHD-2000, Harvard). After a steady state was reached, the product was collected for 10 min while being quenched with 1 mL saturated NaHCO<sub>3</sub> aqueous solution. The crude solution was extracted with ether and washed with brine. The extracts were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated.



**Fig. 2** (a) A full set of monolithic and flexible fluoropolymer film microreactor with metal frame connection for chemical reaction. (b) Cross-sectional view of the film microchannel with 300  $\mu\text{m}$  width (scale bar: 100  $\mu\text{m}$ ). (c) Herringbone mixer pattern in the film microchannel (scale bar: 200  $\mu\text{m}$ ). (d) Droplet generator made by fluoropolymer film microreactor (scale bar: 200  $\mu\text{m}$ )

Schotten-Baumann amidation<sup>22</sup> was conducted using benzoyl chloride and methylamine. A solution of benzoyl chloride (0.1M in chloroform, 5  $\mu\text{L}/\text{min}$ ), (300  $\mu\text{m}$  channel width for continuous phase of benzyl chloride in  $\text{CHCl}_3$ , 100  $\mu\text{m}$  channel width for dispersion phase of methylamine in  $\text{H}_2\text{O}$ ) was used for reaction of the two immiscible phases at interface which were introduced into a T-Shaped fluoropolymer film microreactor (50  $\mu\text{m}$  height, 30 cm length) with droplet generator (300  $\mu\text{m}$  channel width for continuous phase) using syringe pumps at RT. The product was collected for 20 min while being quenched with 2 mL of saturated  $\text{NH}_4\text{Cl}$  aqueous solution. The crude solution was extracted using ether and washed using brine. Then, the extracts were dried over  $\text{Na}_2\text{SO}_4$  and concentrated.

Vilsmeier–Haack formylation<sup>23</sup> was conducted using a mixture solution of dimethylformamide (13 eq) and phosphoryl chloride (1.35 eq) (1.47  $\mu\text{L}/\text{min}$ ) and *N,N*-dimethylaniline (1 eq, 0.17  $\mu\text{L}/\text{min}$ ). In this reaction, a Y-shaped microreactor (300  $\mu\text{m}$  width, 50  $\mu\text{m}$  height, 55 cm length of reaction part) with two inlets was used. A mixture of dimethylformamide and phosphoryl chloride was infused through the inlet of the fluoropolymer film microreactor (flow rate: 1.47  $\mu\text{L}/\text{min}$ ), and *N,N*-dimethylaniline (1 eq) was injected to the other inlet (flow rate: 0.17  $\mu\text{L}/\text{min}$ ). The product was collected for 20 min while being quenched with 4 mL of  $\text{H}_2\text{O}$ . The crude solution was extracted with ether and washed with brine. Then, the extracts were dried over  $\text{Na}_2\text{SO}_4$  and concentrated.

Photochemical cyclization<sup>24</sup> was conducted using a mixture solution (0.1 M in acetonitrile based on starting compound) including (2*E*,7*E*)-1,9-diphenylnona-2,7-diene-1,9-dione as a starting compound, tris(2,2'-bipyridyl)dichlororuthenium(II) hexahydrate (5 mol%), lithium tetrafluoroborate (2 eq) and *N,N*-diisopropylethylamine (2 eq). The solution was introduced into the fluoropolymer film microreactor (300  $\mu\text{m}$  x 50  $\mu\text{m}$  x 88 mm) using a syringe pump (flow rate: 15  $\mu\text{L}/\text{min}$ ). After a steady state was reached under irradiation with visible light from a flat 30-W white LED lamp (HV-4-18, Huvit-LED, Korea), the product was collected for 10 min while being

quenched with 1 mL of saturated  $\text{NH}_4\text{Cl}$  aqueous solution. The crude solution was extracted with ether and washed with brine. The extracts were dried over  $\text{Na}_2\text{SO}_4$  and concentrated. The reaction conversion was calculated using  $^1\text{H}$  NMR by comparing the integral of the peak between desired cyclized product (3.87 ppm, 2H) and starting compound (2.40 ppm, 4H).

## Results and Discussion

### Fabrication of fluoropolymer film microreactor

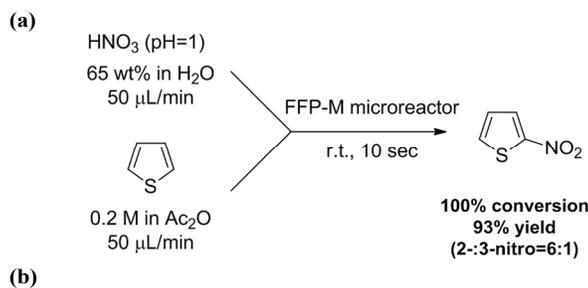
Elastic fluoropolymer film microreactors were fabricated by soft lithography process using commercially available and photocurable PFPE resin. The microchannel was formed by laminating two pieces of the partially cured films that were obtained by spin-coating the low viscosity (581 cP) PFPE polymer on the Si master with channel pattern and the Si wafer without the pattern. The film thickness was adjusted by controlling the rate and the time of spin coating (refer to ESI, † Fig. S2-(a)). For instance, 180  $\mu\text{m}$  and 100  $\mu\text{m}$  thick polymer films were obtained by spinning at 500 rpm for 10 sec, 20 sec, respectively. Absence or presence of channel pattern (300–500  $\mu\text{m}$  width, 50  $\mu\text{m}$  height) did not make any appreciable difference. Bending angle up to 120 degree could be maintained as long as the total thickness of the laminated PFPE film was less than 500  $\mu\text{m}$ . This thin film technique for microfluidic device saves the amount of the expensive fluoropolymer needed in fabrication. It also contributes to enhancing reproducibility and fidelity of the microchannel fabrication process by facilitating conformal and intimate contact bonding between two flexible and partially cured films, not requiring any external force for the bonding. Actually, 5 cm long microchannel with reliable bonding was fabricated with a thin patterned laminate (180  $\mu\text{m}$ ), while the channel with a thick laminate (3 mm) often caused no intimate bonding at several locations under the identical conditions of chemistry and fabrication techniques (refer to ESI, † Fig. S3). In addition to the thickness, the degree of curing is also very important to form strong covalent bond at the interface. The photocurable PFPE resin required 30 sec of UV radiation at least to solidify the viscous phase into a mechanically rigid film. It could easily be detached from the master without

damage by pre-treating the mold surface with CTMS to prevent the strong adhesion of the PFPE resin onto the mold, performing upto 20 times of repeated molding step. The bonding durability of PFPE film microreactor was tested by measuring the burst pressure at which the microchannel (300  $\mu\text{m}$  wide, 50  $\mu\text{m}$  high and 5 cm long) was delaminated. The flow rates were increased in the range 0.1 mL/min to 10 mL/min using a high pressure pump to generate the pressure for the delamination. The highest burst pressure was measured at 610 psi which is high enough for the range of flow rates typically encountered in organic synthesis in the film microreactor. Even after 1 hr continuous-flow by organic solvents there was no difference in burst pressure. However, when the partial curing time was further increased from 30 to 40, 50 and 60 sec, the burst pressure gradually decreased to 525 psi, 257 psi and 160 psi, respectively (refer to ESI,† Fig. S2-(b)). It could be interpreted that the extended UV curing consumed the functional group, thereby reducing the chemical activity of the film surface, and presumably leading to the weaker bonding strength. It is worth noting that fully cured PFPE (MD 700) had a modulus of 63.1 MPa at room temperature as reported<sup>19</sup> which is nearly 30 times higher than 2.4 MPa of PDMS (Sylgard 184).<sup>25</sup> The high mechanical strength preserves the structural integrity of the thin film with microchannel cavity against gravitational force as well as flow-induced force, unlike the PDMS-based film microchannel (500  $\mu\text{m}$  width, 50  $\mu\text{m}$  thickness) that was heavily deformed and clogged by saggy lid (refer to ESI, † Fig. S4).

For organic syntheses, little amount (about 1.8 g) of PFPE precursor was used and low cost (~1.0 US\$ resin per reactor) monolithic and flexible microfluidic device with 5 or 50 cm long microchannel was prepared by assembling a set of transparent fluoropolymer film microreactor (Fig. 2-(a)) with rectangular microchannel (Fig. 2-(b)). The metal frame with screw holes was used for tube connections into inlet and outlet of the microreactor so as to prevent leakage (refer to ESI,† Fig. S5). These thin film techniques can be utilized to embed various functional structures in the microchannel. An example is shown in Fig. 2-(c) for a built-in staggered herringbone mixer pattern (30 mm length) on fluoropolymer microchannel (50 mm length). The mixing efficiency of the mixer structure was experimentally demonstrated by generating a chaotic flow from two laminar flows of dye solutions at low flow rate of 10  $\mu\text{L}/\text{min}$  (refer to ESI,† Fig. S6), which is consistent with the reported result.<sup>26</sup> Another example is X-shape junction for a droplet generator, which produces two-phase droplet in a continuous-flow manner. Water droplets in toluene were generated with toluene as a continuous medium (Fig. 2-(d)), which was made possible due to organic solvent resistance and surface hydrophobicity that are offered by the fluoropolymer.

#### Application for organic synthesis under various conditions

To evaluate the performance of the fluoropolymer film microreactor under various chemical conditions, we carried out 3 types of well-known organic syntheses under harsh conditions as model reactions.

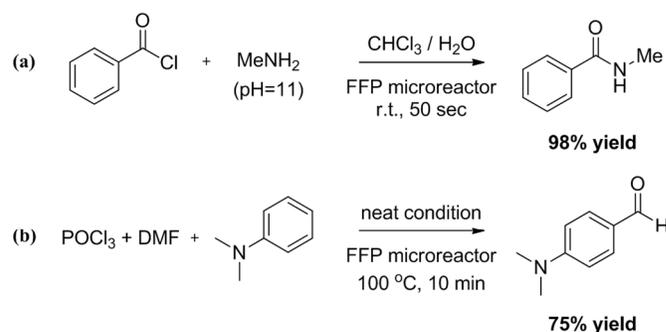


Entry	Microfluidic device	Conversion (Yield)
1	FF	70
2	FF-M <sup>a</sup>	100 (93) <sup>b</sup>

<sup>a</sup> FF with built-in herringbone mixer pattern. <sup>b</sup> Isolated yield.

**Fig. 3** (a) Scheme for mono-nitration of thiophene by fluoropolymer film microreactor (300  $\mu\text{m}$  wide, 50  $\mu\text{m}$  high, 30 cm long mixer pattern in 50 cm long microreactor) under concentrated nitric acid at room temperature. (b) Conversion comparison between plain fluoropolymer film microreactor (FF) and fluoropolymer film microreactor with herringbone mixer pattern (FF-M).

Mono-nitration of thiophene was chosen first to test the durability of the film microreactor under strongly acidic aqueous nitric acid (65%  $\text{HNO}_3$ , pH=1) with acetic anhydride (pH=1) as a solvent (Fig. 3). In this reaction, two types of Y-shaped microreactor (300  $\mu\text{m}$  wide, 50  $\mu\text{m}$  high, 50 cm long reaction part) with or without the built-in staggered herringbone mixer pattern (30 cm long) were used. The microreactor with the mixer pattern produced a 100% conversion and 93% yield of product with only 10 sec of reaction time at a total flow rate of 100  $\mu\text{L}/\text{min}$ :  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) of 2-nitrothiophene  $\delta$  7.98-7.90 (m, 1H), 7.60-7.52 (m, 1H), 7.12-7.03 (m, 1H) ppm;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) of 3-nitrothiophene  $\delta$  8.34-8.27 (m, 1H), 7.68-7.62 (m, 1H), 7.40-7.33 (m, 1H) ppm (ESI, † Fig. S8). While the microreactor without the mixer pattern showed a lower conversion of 70%. Intrinsic advantages of the chemical tolerant microreactor such as excellent heat conduction with high surface-volume ratio completed the nitration of thiophene at room temperature in a short time without leakage and delamination problems. Note that this highly exothermic nitration reaction generally required a low temperature cooling bath (-10 to 0  $^\circ\text{C}$ ) and a long reaction time.<sup>21</sup>



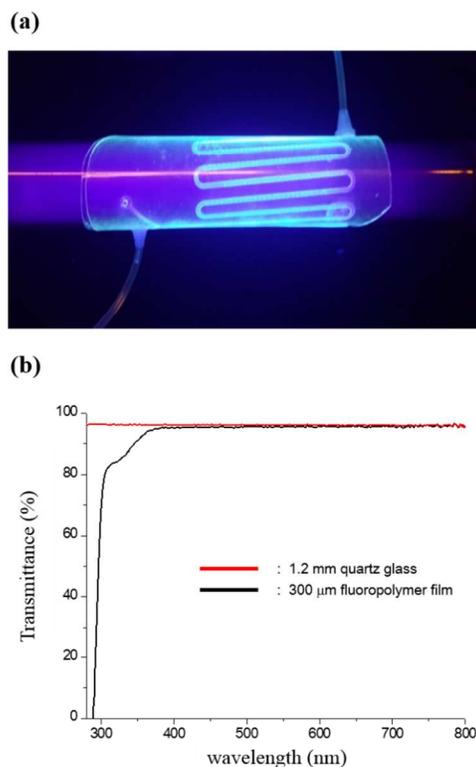
**Fig. 4** Two schemes of chemical reactions carried out in fluoropolymer film microreactor. (a) Schotten-Baumann amidation reaction at room temperature by T-shape droplet generator (300  $\mu\text{m}$  wide channel for continuous phase, 100  $\mu\text{m}$  wide channel for dispersion phase, 30 cm length of reaction part) (b) Vilsmeier-Haack formylation reaction at 100  $^\circ\text{C}$  by Y-shaped microreactor (300  $\mu\text{m}$  wide, 50  $\mu\text{m}$  high, 55 cm long)

Secondly, Schotten-Baumann amidation<sup>22</sup> of benzoyl chloride was selected to perform the reaction under extremely basic condition of neat aqueous methylamine solution (40 wt%  $\text{MeNH}_2$ , pH=11) as shown in (Fig. 4-(a)). The film microreactor (50  $\mu\text{m}$  height, 30 cm length) with a T-shape droplet generator (300  $\mu\text{m}$  wide channel for continuous phase of benzoyl chloride in  $\text{CHCl}_3$ , 100  $\mu\text{m}$  wide channel for dispersion phase of methylamine in  $\text{H}_2\text{O}$ ) was used for interfacial reaction between the two immiscible phases. After 50 sec of reaction time (total flow rate: 10  $\mu\text{L}/\text{min}$ ), the desired

amide product was obtained with 98% yield:  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.80-7.70 (m, 2H), 7.55-7.39 (m, 3H), 5.30 (s, 1H), 3.02 (d,  $J = 5.1$  Hz, 3H) ppm. It is demonstrated that the fluoropolymer film microreactor can be used not only for a corrosive reaction under extremely basic condition but also for two phase reaction with organic solvent without any leakage or observable degradation. Thirdly, in order to confirm thermal stability of the film microreactor at elevated reaction temperature, Vilsmeier–Haack formylation in corrosive organic medium was carried out at 100 °C. In this reaction, Y-shaped microreactor (300  $\mu\text{m}$  wide, 50  $\mu\text{m}$  high, 55 cm long reaction part) with two inlets was used. A mixture of dimethylformamide and phosphoryl chloride was infused through inlet part of the fluoropolymer microreactor (flow rate: 1.47  $\mu\text{L}/\text{min}$ ), and *N,N*-dimethylaniline (1 eq) was injected to the other inlet part (flow rate: 0.17  $\mu\text{L}/\text{min}$ ). As shown in (Fig. 4-(b)), the reaction for 10 min at 100 °C successfully produced the desired formylated product with 75% yield:  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.86 (2H,  $J = 8.1$  Hz, d), 7.25 (2H,  $J = 8.1$  Hz, d), 2.58 (s, 3H), 2.41 (s, 3H) ppm, which is compatible with previous report.<sup>23</sup> In addition, the chemical durability of the fluoropolymer film microreactor was also proven with absence of any observable defects on inner surface of microchannel when continuously infused by 65% nitric acid, 40% methylamine solution and chloroform upto 1 hr, respectively (refer to ESI, † Fig. S7). Furthermore, in order to confirm the long-term chemical stability, the UV-cured fluoropolymer pieces were immersed for 12 hrs into typical organic solvents such as DMF, THF, benzene, hexane, chloroform and trichloroethylene. Not much swelling occurred in most cases (< ca. 5 wt% at room temperature, < ca. 10 wt% at 60 °C), revealing much superior chemical stability to conventional polymers such as PDMS (refer to ESI, † Table. S1).

### Photochemistry application

In general, the radiation absorption for photoreaction conversion is directly affected by the distance between light source and reaction medium. Therefore, we envisaged that facile deformability of the film microreactor would be effectively applied for photochemical reaction in a visible wavelength region. And the optically transparent fluoropolymer film with no absorbance in visible light range (380 to 780 nm), as confirmed by UV-Vis transmittance spectrum in (Fig 5-(a)), allowed to achieve the closest proximity to the light source by wrapping the cylindrical light lamp as shown in (Fig. 5-(b)). The effectiveness of the fluoropolymer film microreactor (300  $\mu\text{m}$  wide, 50  $\mu\text{m}$  high, 88 cm long reaction part) was tested by conducting a reaction of photochemical cycloaddition using visible light from a flat 30 W white LED lamp in comparison to conventional flask reaction. Generally, a shorter distance between light source and reactor led to a higher reaction conversion as shown in Table. 1, which is consistent with the reported result.<sup>24</sup> In particular, for the case of 5 cm distance from the light source, the film microfluidic device delivered a conversion of 80% for the [2+2] photochemical cyclized product in 1 min whereas the conventional flask yielded a 66% conversion in 30 min of reaction time (entry 1 and 4). It is apparent that the reactants in the shallow (50  $\mu\text{m}$  high) and long (88 cm long) microchannel as well as high optical transparency of thin fluoropolymer led to highly efficient exposure to radiation.



**Fig. 5** (a) Fluoropolymer film microreactor wrapping a cylindrical LED lamp. (b) Comparison of UV-Vis transmittance spectrum between quartz glass (1.2 mm thickness) and fluoropolymer film microreactor (300  $\mu\text{m}$  thickness)

**Table. 1** Photochemical cyclization in the fluoropolymer film microreactor (300  $\mu\text{m}$  wide, 50  $\mu\text{m}$  high, 88 cm long reaction part) under various distances from a flat LED light source.

entry	reactor	reaction time (min)	temperature (°C)	distance from light (cm)	conversion <sup>a</sup> (%)
1	flask	30	r.t.	5	68
2	flask	30	70	-	<5
3	FF microreactor	1	r.t.	30	30
4	FF microreactor	1	r.t.	5	80
5	FF microreactor	1	r.t.	0.5 <sup>b</sup>	100
6	FF microreactor	1	0	0.5 <sup>b,c</sup>	98

<sup>a</sup> The reaction conversions were obtained by  $^1\text{H}$  NMR.

<sup>b</sup> The FF microreactor was attached to the surface of light source. The reaction temperature was checked during the reaction and maintained to r.t. by cooling fan.

<sup>c</sup> Cooling jacket as well as cooling fan was used to maintain to 0 °C.

The proximity contact to the light source at a distance of 0.5 cm gave the product in full conversion in 1 min of retention time (flow rate: 15  $\mu\text{L}/\text{min}$ ) at room temperature (entry 5):  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) 7.85-7.58 (m, 4H), 7.55-7.25 (m, 8H), 3.92-3.80 (m, 2H), 3.35-3.15 (m, 2H), 2.25-1.95 (m, 2H) ppm (ESI, † Fig. S9). The reaction also showed similar conversion (98%) when the reaction was carried out at 0 °C by placing an

ice cooling jacket at the opposite side of the irradiated part, proving high photochemical efficiency of the film reactor with negligible thermal effect (entry 6). It is pointed out that this thin film microreactor provides a photochemical platform alternative to conventional glass microreactors as well as falling film reactors where an efficient light irradiation is needed.<sup>27</sup>

## Conclusions

In summary, we have developed a monolithic and flexible fluoropolymer film microreactor with chemical resistance as a new platform for microchemical applications. The excellent deformability and high chemical activity of partially cured laminate films allowed conformal and intimate contact bonding in a reproducible and cost-saving manner, enabling fabrication of functional microchannels embedded with either a herringbone micromixer or a droplet generator. The performance of the fluoropolymer film microreactors with excellent chemical stability was demonstrated by conducting various organic reactions under both extreme acidic and basic conditions (pH 1, pH 11), as well as at elevated temperature. Moreover, it was found that the transparent and flexible thin microreactor was useful as an efficient photochemical platform for close proximity to flat or curved light source, which suggests its utilization for miniaturization and integration of the reaction systems.

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## Notes and references

<sup>a</sup> Department of Chemical Engineering, Pohang University of Science and Technology, Pohang, Korea. dpkim@posetech.ac.kr

<sup>b</sup> Department of Polymer Science and Engineering, Kyungpook National University, Daegu, Korea.

<sup>c</sup> Department of Chemical Engineering, Pukyong National University, Busan, Korea.

† Electronic Supplementary Information (ESI) available: [Detailed fabrication figure of various chip image, controlled chip thickness, pressure resistance, built-in herringbone mixer pattern in microreactor and its performance, products <sup>1</sup>H-NMR spectrum.] See DOI: 10.1039/b000000x/

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