

Cite this: *Lab Chip*, 2011, **11**, 2035

www.rsc.org/loc

Micromolding of solvent resistant microfluidic devices^{†‡}

Theodorus J. A. Renckens,^a Dainius Janeliunas,^b Hilbert van Vliet,^a Jan H. van Esch,^b Guido Mul^{ac} and Michiel T. Kreutzer^{*a}

Received 1st November 2010, Accepted 3rd May 2011

DOI: 10.1039/c0lc00550a

We demonstrate a rapid fabrication procedure for solvent-resistant microfluidic devices based on the perfluoropolyether (PFPE) SIFEL. We carefully modified the poly-dimethylsiloxane (PDMS) micromolding procedure, such that it can still be executed using the standard facilities for PDMS devices. Most importantly, devices with a thin SIFEL layer for the patterned channels and a PDMS support layer on top offered the best of two worlds in terms of chemical and mechanical stability during fabrication and use. Tests revealed that these devices overcome two important drawbacks of PDMS devices: (i) incompatibility with almost all non-aqueous solvents, and (ii) leaching of oligomer into solution. The potential of our device is shown by performing a relevant organic synthesis reaction with aggressive reactants and solvents. PFPE-PDMS devices will greatly expand the application window of micromolded devices.

Introduction

This paper presents a facile recipe to produce solvent-resistant microfluidic devices using existing PDMS infrastructure. In the development of portable and robust microfluidic devices, PDMS (poly-dimethylsiloxane) is the material of choice in the field of biology and biochemistry.¹ Ease of fabrication by way of micromolding² and its elastomeric properties (used in *e.g.* valves³ and piezo pulse chambers⁴) have contributed to its success. The application of PDMS devices for synthesis in organic chemistry is, however, severely impeded by the swelling and oligomer leaching of PDMS in a large number of solvents.⁵ Glass and steel can be used and have rigid, non-permeable walls, high temperature operation and better heat conductivity, which for certain applications can be advantages in comparison to elastomers. The downside is that fluidic devices of these materials are more difficult, time-consuming and costly to fabricate.⁶ This paper describes a simple and cheap alternative using standard PDMS facilities.

Alternatives for PDMS have been found, both as devices with coated channels^{7–9} and various alternative materials.^{10–13}

However, coatings are difficult to apply homogeneously and chemical resistance of most polymers excludes widely used solvents. The material with the broadest proven chemical compatibility is perfluoropolyethers (PFPE). Two problems arise when replacing PDMS with PFPE's: lift-off from a master, typically SU-8-on-silicon, and bonding to solid substrates. An early micromolding recipe¹⁴ used a UV bonding step that suffered from a low yield due to quenching by oxygen.¹⁵ To improve yield, subsequent bonding was performed in a glove box under nitrogen atmosphere,¹⁶ severely limiting the ease of fabrication. A similar UV-based approach did produce leak tight devices, but was limited to very shallow features (~2 μm) lifted from a silicon master.¹⁷ Another PFPE molding technique uses a mold that does not require photolithography.¹⁸ An amorphous fluorinated thermoplastic was hot embossed to produce transparent devices,¹⁹ but with a bond strength ten times lower than that of PDMS devices. Maltezos *et al.*¹⁵ elegantly circumvented lift-off problems by using a sacrificial wax mold produced using a 3D printer, that was removed by melting it. Contrary to PDMS micromolding, this solution requires that a mold is made for every device and the present wax printing techniques do not offer the same resolution as photolithography.²⁰ In conclusion, there is still a need for an easy-to-use procedure for micromolding solvent resistant microfluidic devices.

In this work we present a method for the micromolding of high-aspect ratio, solvent-resistant devices from SU-8 masters that address the shortcomings mentioned above. We used SIFEL, a commercially available elastomeric PFPE with a proven chemical resistance and an elasticity that allows for production of microfluidic valves.^{15,21} A patterned SIFEL layer can be bonded to another flexible SIFEL layer on a rigid glass slide. The number of applications in chemically aggressive

^aDelft University of Technology, Dept. of Chemical Engineering, Product and Process Engineering, Julianalaan 136, 2628 BL Delft, The Netherlands. E-mail: m.t.kreutzer@tudelft.nl

^bDelft University of Technology, Dept. of Chemical Engineering, Self Assembling Systems, Julianalaan 136, 2628 BL Delft, The Netherlands

^cUniversity of Twente, IMPACT Institute, PCS group, Meander 229, 7500 AE Enschede, The Netherlands

[†]Published as part of a LOC themed issue dedicated to Dutch Research: Guest Editor Professor Sabeth Verpoorte.

[‡]Electronic supplementary information (ESI) available: A step-by-step guide and commentary for micromolding PDMS-SIFEL devices. See DOI: 10.1039/c0lc00550a

environments is significantly increased using PFPE's, as we demonstrate below. We expect that SIFEL micromolding significantly opens up miniaturization possibilities, prominently in the domain of continuous-flow chemical synthesis, and in other applications that have been impeded by the lack of solvent-resistant rapid prototyping.

Device production

Micromolding of SIFEL (2610 grade, Shin-Etsu) was carried out comparably to PDMS micromolding,²² with some crucial differences that we discuss here (Fig. 1, full details in the supplementary information.†) An SU-8-on-silicon mold was heated to 393 K after silanization, which was essential to prevent tearing of the SU-8 during liftoff of the SIFEL layer (see Fig. S1†). We fully covered the features on the mold with a layer of SIFEL, using spincoating as opposed to casting this opaque polymer, ensuring that the device is transparent. A layer of PDMS on top of the SIFEL layer provided additional mechanical strength.¹⁷ The two-layer approach also eliminated severe wrinkling problems during curing (see Fig. S2†) and, as PDMS is a lot cheaper than SIFEL, suppresses the materials cost. The bonding of SIFEL to PDMS is covalent (the same crosslinking agent is used in both materials). The SIFEL–PDMS bond was never a cause for device failure. Plasma bonding commonly used for PDMS devices does not work for bonding SIFEL. To bond SIFEL, a thin coating ($\sim 5 \mu\text{m}$) of diluted SIFEL pre-polymer coating is cured mildly on the substrate. This coating then acts as adhesive. The patterned device was hot-pressed to the coated glass slide as the curing was completed in an oven; without pressing the bonding was incomplete. Similarly, we found that leakage of solvents into the PDMS layer could be prevented by coating the outsides of the tubes with diluted SIFEL prior to insertion to create a leak-tight seal around the inlet. With this recipe, we were able to obtain leak-tight devices in more than 90% of all cases.

It was observed that the extent of lift-off problems does depend on aspect ratio of the channel features. For example, we could reliably produce SIFEL devices with aspect ratios up to

2.5 : 1 and feature sizes of $30 \mu\text{m}$. A ten by ten array of such features was successfully fabricated, demonstrating the reproducibility of the molding procedure (see Fig. 1B). In contrast, all pillars with aspect ratio 8 : 1 and 10 micrometre diameter broke off.

We also created fully flexible devices by bonding patterned SIFEL-PDMS devices to other SIFEL layers without solid support using the above method. We expect that the reproducible fabrication of monolithic microfluidic valves is possible by adapting our method, as the elastic properties of SIFEL closely resemble those of PDMS.

Device properties

Now that we demonstrated the production of SIFEL-PDMS devices, we investigated the physical and chemical properties of the obtained devices. After bonding to glass, the SIFEL layer is sufficiently thin for devices to be optically transparent and phenomena in the channels can be observed using a microscope. The delamination overpressure was 2.5 bar, which is high enough for most flow applications, and devices operated below this pressure with various solvents did not delaminate even when operated for several days or at elevated temperatures up to 100°C .

Our devices also had a long-term chemical stability. The stability of the surface energy was evaluated using contact angle measurements. The leaching of oligomers into solution is a known problem for PDMS.⁵ At the same swelling ratio, oligomer leaching was an order of magnitude lower for SIFEL compared to PDMS at similar swelling (see Fig. 2 and Table S2†), which makes SIFEL a much more suitable platform for chemical synthesis. The solvents used, as well as values for swelling and leaching can be found in the ESI.† SIFEL compatibility with several fluids, including aggressive acids and bases, is shown in Table 1. SIFEL, and by extension our devices, were found to be strongly resistant to acids, but somewhat less resistant to very strong bases.

To test the possibility to work under oxygen-free conditions inside the microchannels, and the possibility to feed oxygen

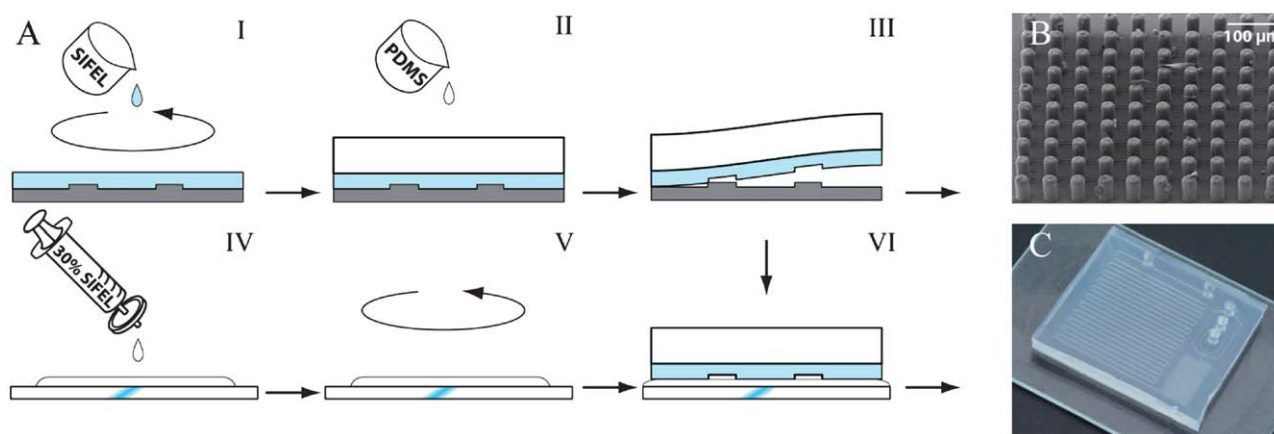


Fig. 1 Device production of a SIFEL microfluidic device, encased in PDMS (A). After salinizing, one or more layers of SIFEL are spincoated onto the mold and cured until it retains its shape (I). A layer of PDMS is cured over the layer of SIFEL (II) before demolding (III). A typical demolding result is shown in (B). After demolding, a filtered solution of SIFEL is spincoated onto a glass slide and briefly precured (IV–V). Both layers can be bonded by clamping, and curing overnight (VI). An example of the final device is shown in (C).

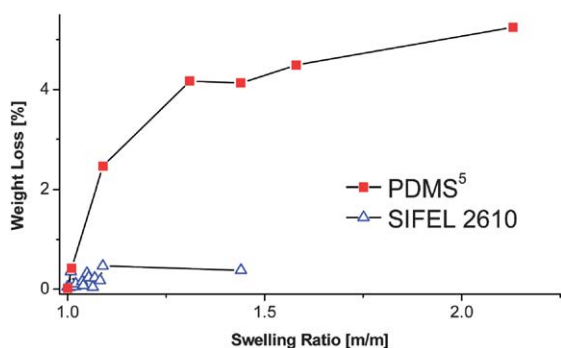


Fig. 2 Comparison of SIFEL 2610 and PDMS weight loss due to oligomer extraction in representative organic solvents. Leaching of oligomer is lower for SIFEL. With SIFEL's reduced swelling compared to PDMS, oligomer leaching is reduced by two orders of magnitude. A table that lists the data for this figure with the solvents used is in the ESI.†

through the device, the oxygen permeation through a thin SIFEL membrane was measured and found to be 3×10^{-14} mol·m/m²·s·Pa, *i.e.* similar to PDMS.²³ The methods to work under aerobic and anaerobic conditions with PDMS should then be equally applicable to SIFEL.

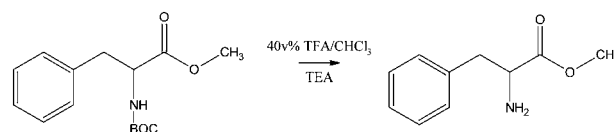
Compared to the method by Rolland,¹⁴ the device production discussed here is simpler because no synthesis step or glovebox conditions are needed, although that may well be related to our simpler designs compared with the elastomeric microvalve-containing designs of Rolland. Our method shows higher aspect ratio structures as well as a five times better delamination pressure compared to the 0.5 bar of Begolo.¹⁹ At the cost of 3D fabrication, the wax sacrificial mold Maltezos¹⁵ used is replaced by re-useable SU-8 on silicon molds.

Sample chemistry

To highlight possibilities of SIFEL as a platform for organic synthesis in aggressive media, we deprotected phenylalanine methyl ester in a SIFEL device. The aim of this experiment was to expose the device to a chemically aggressive environment used in organic synthesis. N-Boc was cleaved from Boc-L-phenylalanine methyl ester dissolved in chloroform using 40 vol% trifluoroacetic acid (TFA). Afterwards, the acidic mixture was quenched in triethylamine (see Scheme 1). The residence time was two hours at a flow of 4 μ L h⁻¹. Product identity was confirmed from MS and ¹H NMR spectroscopy. Conversion was

Table 1 Resistance at room temperature of micromolded SIFEL to acids and bases commonly applied in organic synthesis

Reagent/solvent	Weight change (%)	Colour change
1.6 M BuLi/hexane	Dissolved	
0.16 M BuLi/ 10% hexane, 90% THF	0.0	Yes
1.0 M ethyl-MgBr/THF	6.4	Yes
0.7 M triethylamine/THF	-1.5	No
1.3 M trifluoroacetic acid/THF	-0.4	No
2.6 M hydrochloric acid/ 25% water, 75% THF	0.8	No
1.7 M acetic acid/THF	0.3	No



Scheme 1 Deprotection of phenylalanine methyl ester. Boc-protected phenylalanine methyl ester is deprotected using trifluoroacetic acid (TFA) in chloroform. Triethylamine is used to quench the acidity.

determined by HPLC and was found to be 91%, compared to 76% in the flask at the same residence time (see the ESI.†). The device was operated for 40 h and was fully functional afterwards. The above example clearly demonstrates the potential of SIFEL-PDMS micromolded devices for organic synthesis.

It should be noted that, after prolonged operation, the fluidic connections are slowly damaged by exposure to TFA, as evidenced by white opaque stains. This leads to a small amount of PDMS being observed in our product NMR spectrum, which is equivalent to approx. 40 μ g h⁻¹. This highlights the importance of limiting contact with the PDMS support layer by tight fluidic connections.

Conclusions

In this paper, we present SIFEL as an alternative to PDMS in micromolding fabrication. We have adapted the procedure in use for PDMS to allow the facile production of PFPE-PDMS microreactors by using modifications readily accessible to cleanroom users. PFPE-PDMS microreactors offer significant advantages over PDMS: improved solvent resistance, stable contact angles and reduced oligomer leaching. Relevant organic chemistry using a strong solvent and aggressive reagents was successfully carried out in a PFPE-PDMS device. This work compares favorably to other methods to produce microfluidic devices from fluorinated materials.

Acknowledgements

The authors would like to gratefully acknowledge Michel Rosso for helpful discussions. This work was supported by the ACTS (PoaC project 053.65.006) program from NWO. MTK was supported by a Veni grant (700.56.404).

References

- G. M. Whitesides, *Nature*, 2006, **442**, 368–373.
- Y. N. Xia and G. M. Whitesides, *Angew. Chem., Int. Ed.*, 1998, **37**, 551–575.
- M. A. Unger, H. P. Chou, T. Thorsen, A. Scherer and S. R. Quake, *Science*, 2000, **288**, 113–116.
- M. T. Kreutzer, A. Gunther and K. F. Jensen, *Anal. Chem.*, 2008, **80**, 1558–1567.
- J. N. Lee, C. Park and G. M. Whitesides, *Anal. Chem.*, 2003, **75**, 6544–6554.
- H. Becker and L. E. Locascio, *Talanta*, 2002, **56**, 267–287.
- A. R. Abate, D. Lee, T. Do, C. Holtze and D. A. Weitz, *Lab Chip*, 2008, **8**, 516–518.
- B. Y. Kim, L. Y. Hong, Y. M. Chung, D. P. Kim and C. S. Lee, *Adv. Funct. Mater.*, 2009, **19**, 3796–3803.
- M. Kanai, D. Uchida, D. Sugiura, Y. Shirasaki, J. S. Go, H. Nakanishi, T. Funatsu, and S. Shoji, *Proceedings of microTAS 2003*, Squaw Valley CA, USA, 2003, 429–432.

- 10 Z. T. Cygan, J. T. Cabral, K. L. Beers and E. J. Amis, *Langmuir*, 2005, **21**, 3629–3634.
- 11 L. H. Hung, R. Lin and A. P. Lee, *Lab Chip*, 2008, **8**, 983–987.
- 12 K. I. Min, T. H. Lee, C. P. Park, Z. Y. Wu, H. H. Girault, I. Ryu, T. Fukuyama, Y. Mukai and D. P. Kim, *Angew. Chem., Int. Ed.*, 2010, **49**, 7063–7067.
- 13 J. Steigert, S. Haeberle, T. Brenner, C. Müller, C. P. Steinert, P. Koltay, N. Gottschlich, H. Reinecke, J. Ruehe, R. Zengerle and J. Ducrec, *J. Micromech. Microeng.*, 2007, **17**, 333.
- 14 J. P. Rolland, R. M. van Dam, D. A. Schorzman, S. R. Quake and J. M. DeSimone, *J. Am. Chem. Soc.*, 2004, **126**, 2322–2323.
- 15 G. Maltezos, E. Garcia, G. Hanrahan, F. A. Gomez, S. Vyawahare, R. M. van Dam, Y. Chen and A. Scherer, *Lab Chip*, 2007, **7**, 1209–1211.
- 16 Y. Y. Huang, P. Castrataro, C. C. Lee and S. R. Quake, *Lab Chip*, 2007, **7**, 24–26.
- 17 C. De Marco, S. Girardo, E. Mele, R. Cingolani and D. Pisignano, *Lab Chip*, 2008, **8**, 1394–1397.
- 18 P. H. Hoang, C. T. Nguyen, J. Perumal and D. P. Kim, *Lab Chip*, 2011, **11**, 329–335.
- 19 S. Begolo, G. Colas, J. L. Viovy and L. Malaquin, *Lab Chip*, 2011, **11**, 508–512.
- 20 G. Maltezos, M. Johnston, D. G. Maltezos and A. Scherer, *Sens. Actuators, A*, 2007, **135**, 620–624.
- 21 H. Koshikawa, Y. Tarumi and M. Shiono, *Sealing Technology*, 2006, **2006**, 7–12.
- 22 G. M. Whitesides and A. D. Stroock, *Phys. Today*, 2001, **54**, 42–48.
- 23 T. C. Merkel, V. I. Bondar, K. Nagai, B. D. Freeman and I. Pinnau, *J. Polym. Sci., Part B: Polym. Phys.*, 2000, **38**, 415–434.