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Title: 3D Micropatterned all Flexible Microfluidic Platform for Microwave Assisted Flow Organic Synthesis (MAFOS)

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This manuscript has been accepted after peer review and appears as an Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). This work is currently citable by using the Digital Object Identifier (DOI) given below. The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: ChemPlusChem 10.1002/cplu.201700440

Link to VoR: http://dx.doi.org/10.1002/cplu.201700440



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# **3D Micropatterned all Flexible Microfluidic Platform for Microwave Assisted Flow Organic Synthesis (MAFOS)**

Deniz Hür,\*,a,b Mehmet G. Say,b,c Sibel E. Diltemiz,a,b Fatma Duman,a Arzu Ersöz,a,b Rıdvan Saya,b

#### Dedication ((optional))

**Abstract:** In present work, we have fabricated large area, all flexible and microwaveable PDMS microfluidic reactor that has printed via 3D bioplotter system. The sacrificial microchannels have printed on Polydimethoxylane (PDMS) substrates by direct ink writing method using water soluble Pluronic F-127 ink and encapsulated between PDMS layers. The structure of micrometer sized channels has analyzed by optical and electron microscopy techniques. The fabricated flexible microfluidic reactors have utilized for acetylation of different amines under microwave irradiation to get acetylamides in shorter reaction time and good yields in Microwave Assisted Flow Organic Synthesis (MAFOS).

#### Introduction

Based on their excellent mass and heat transfer rates, short reaction times and selective reaction ability; microfluidic systems which are fabricated using several materials (i.e. glass, polypropylene (PP), polydimethoxysilane (PDMS), Teflon (PTFE), steel etc.) in different shapes, have large application area in synthesis of organic [1-6] and pharmaceutical [7-9] products as well as inorganic nanoparticles <sup>[10-17]</sup>. Micron scaled electromagnets have prepared in PDMS microfluidic [18]. Additionally, continuous microfluidic reactors have developed for polymer particles <sup>[19]</sup>. Several bio application methods of microfluidics have been reviewed in 2011<sup>[20]</sup>. Enzymatic catalysis works have been conducted using flow reactors [21]. Among different fabrication methods, three dimensional (3D) printing of microfluidic systems have great application area [22-24].

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the document.((Please delete this text if not appropriate))

Different 3D printing methods have been applied in literature. These are: a) Inkjet 3D printing in which both drop on demand and continuous printing modes are applicable <sup>[25]</sup>, b) Stereo lithography, where objects are printed layer-by-layer using photo polymerization of monomers <sup>[26]</sup>, c) Two-photon polymerization method, where near-infrared femtosecond laser is applied on material for polymerization <sup>[27, 28]</sup>.

3D printing has been used to use in the area of microfluidics <sup>[29, 30]</sup>, in order to fabricate microfluidic networks and chips utilizing microvascular networks<sup>29</sup>, tissue engineering <sup>[31-34]</sup> and chemical synthesis applications <sup>[35]</sup>. On the other hand 3D printed mesoreactors are available in literature <sup>[36]</sup>. These applications can be realized by using different types of 3D printing technologies such as STL based printing <sup>[37]</sup>, Fused Deposition Modelling <sup>[33]</sup> and direct-ink writing of sacrificial inks <sup>[38, 39]</sup>. Details of these techniques and applications have been published as a review by Au and co-workers <sup>[40]</sup>.

3D printing/writing of sacrificial hydrogels and fugitive inks are one of the escalating technologies to create microfluidic channels. Liquid metals <sup>[41]</sup>, bio-polymer based hydrogels <sup>[42, 43]</sup> and Pluronic based <sup>[32, 44]</sup> inks have been used to fabricate sacrificial patterned micro networks. Among these techniques, Pluronic F-127 based inks are chosen for superior properties such as easy to print, room temperature writing of the inks and controlled ink rheology. In addition, printed networks with this material can be removed easily after encapsulation because of thermally reversible gelation properties of the Pluronic F-127 <sup>[45]</sup>. These properties make Pluronic F-127 inks excellent candidate for creating fugitive networks for microfluidic application.

PDMS is one of the superior material for production of microfluidic devices based on its transparency, non-toxicity, flexibility, chemical inertness, and non-flammable properties. This widely used material in microfluidics field is generally bonded to a glass slide or sandwiched between another PDMS layer by oxygen plasma. Additionally, three aspects of compatibility (swelling, dissolution of PDMS oligomers in a solvent and solute dispersion between solvent and PDMS)

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for PDMS were investigated and shown that PDMS can be useful fabrication material for microfluidics area <sup>[46]</sup>. Previously PDMS was used for fabrication of microfluidic devices with different fabrication techniques and various applications in literature <sup>[47-50]</sup>.

Presented work here, describes and introduces a novel 3D micro patterning method for creating microfluidic reactors using Pluronic F-127 ink by direct ink-writing technique and PDMS encapsulation. We demonstrated fabrication procedure of all-flexible, transparent, low cost microfluidic reactor, which is completely compatible for microwave flow synthesis conditions. In particular, high reusability of these devices allows us to run experiments in MAFOS without losing efficiencies. MAFOS has been employed in research laboratories and industry based on their safe process at elevated temperatures and pressures, and also acceleration effect of microwave (MW) on reactions<sup>[51-55]</sup>.

#### **Results and Discussion**

#### **3D Fabrication of all Flexible Microfluidic**

In the present work, 3D micro patterns we plotted using water soluble Pluronic F-127 ink and encapsulated this printed structures in PDMS matrix to fabricate microwaveable, all flexible, low cost PDMS based microfluidic reactors. Aqueous solution of highly concentrated co-polymer, wax like Pluronic F127, which consists Poly(propylene oxide) (PPO) center with Poly(ethylene oxide) (PEO) side chains, was used as sacrificial ink. Fabrication of 3D printed microfluidic reactors consisted of several steps (Figure 1). The fabrication started with preparation of flexible substrate. 15-20 mL of PDMS mixture was poured into 12 cm petri dishes and cured at 70 °C for 5 h. The Pluronic F-127 (40 w/v %) sacrificial ink was printed using 3D-Bioplotter (EnvisionTEC, Germany) onto substrate with optimized bio printing parameters (Table 1, see movie S1). Next, 3D bio printed pattern was encapsulated with PDMS (15-20 ml) and cured at room temperature overnight (see sup. Fig. 4). Finally, withdrawal of the Pluronic F-127 was performed by constantly circulation of cold water and ethanol throught the channel in minutes. The removal of the ink was controlled with UV-Vis spectra at 220 nm after washing microfluidic with 10, 20, 30 mL water in flow rate of 2 mLmin<sup>-1 [56]</sup> Subsequently, micro reactors were connected with standard PTFE tubing by plugging PTFE tubing and insulation with household construction silicon.



Printing of Sacrificial Networks



**Encapsulation of Fugitive Network** 



#### **PDMS Microreactor**

**Figure 1.** 3D microfabrication method of all flexible PDMS micro reactor. a) Plotting cold, gel Pluronic F-127 on PDMS in petri dish. b) Covering and curing printed micro channels with second layer of PDMS. c) Removal of Pluronic F-127 ink by pumping cold water in micro channel. Inset shows SEM image of PDMS channel (scale bar 400 μm)

Detailed Optical microscope and SEM images were recorded for Pluronic F-127 microchannel to analyze dimensions of printed structure dimensions (Figure 2). Printed networks were fabricated by using 250  $\mu$ m plastic needle tips. As depicted in figure 2, direct ink written layers demonstrated perfect shape and precise dimensions. Thus, smooth lines of Pluronic F-127 inks can be printed having channel widths vary from 300  $\mu$ m to 570  $\mu$ m (figure

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S5). The total lenght of channel is 58.4 cm and volume is 0.35 mL.

Table 1. Printing parameters for 40 w/v % Pluronic F-127 ink to fabricate microfluidic networks.

	Pluronic F-127 Sacrificial Ink		
Needle Diameter (mm)	0.25		
Printing Temperature ( <sup>0</sup> C)	14 °C – 22 °C		
Printing (XY) Speed (mm/s)	8 – 10		
Pressure (bar)	0.4 - 0.9		
Postflow & Preflow delay (s)	- 0.1 - 0.1		
Amount of Ink Used (µI)	~ 100		
Printing time (s)	40		
Dimensions (mm)	65 x 17 x 0.3		



Figure 2. (a) Optical microscope image of Pluronic F-127 networks (b) SEM image of printed line.

All previous literature for fabrication of micro reactor and microfluidics via PDMS were based on lithographic method where microchannel was produced by photoresist SU-8 shaped PDMS mold. Afterward this lithographed PDMS was stacked on glass using plasma to prepare half-flexible PDMS-glass integrated microfluidic. Since adhesion between glass and PDMS has limitations this microfluidics cannot be used in heated systems with organic solvent due to after swelling and peeling of PDMS cause leakage of liquid. In another fabrication method, a microfiber was embedded in PDMS, after curing, microfiber was pulled away for tunneling microchannel in PDMS block<sup>[57]</sup>. This method has disadvantage due to pulling away procedure needs straight microfiber. Thus, channels has to be line shaped.

Presented fabrication method, in this research, deals with preventing of these disadvantages of previous methods by introducing all flexible and unlimited shaped microchannel in PDMS microfluidic devices. Although, swelling of PDMS in organic solvents has been judged as a disadvantage before, since our 3D plotted microfluidics fabricated from only PDMS, swelling will not be caused to leakage and deformation. According to figure 3, small change was observed on structure of microchannel after five reactions (swelling and deswelling). Detailed SEM investigations showed that width of microchannel is 571.0 µm and 590.8  $\mu m$  before reaction and after reactions, respectively. In the image of cross section of hollow microchannel as shown in Figure 3c, the width of semi-circular structure is between 400 µm - 1 mm that can be changed by applying different 3D printing parameters. Supporting Figure S5 and Figure S6 provide additional optical and SEM images for further analysis of printed and encapsulated layers.

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Figure 3. SEM images of microfluidic device (a) before reaction (b) after reaction (swelling and deswelling) (c) cross-section view of PDMS microchannel. Scale bars show 200 µm.

#### Usage of Fabricated Microfluidic in Microwave Organic Synthesis

To demonstrate effectiveness of flexible micro-reactors in MAFOS applications, PTFE tubings were plugged into inlets and outlet of microfluidic device, then the micro-reactor was used for the organic synthesis of acetylamides. In microwave setup, microreactor was placed in microwave chamber and reagents were pumped in with a peristaltic pump (Figure 4). Reaction between

N-acetylbenzotriazole, 1, and several amines, 2, under 100 W microwave irradiation in tetrahydrofuran (THF) at 0.3 mLmin<sup>-1</sup> flow rate at 67 °C was given 3a-e in 92-96 % yields, to prove the usability of fabricated microfluidic reactor in microwave system with organic solvents.

Structure of products were characterized by <sup>1</sup>H and <sup>13</sup>C NMR. (see Supp.Info.)





Microwave Reactor



R:-Ph, PhCH, ,n-Butyl-, Cyclohexyl, 4-OMe-Ph-

Figure 4. Schematic representation of MAFOS procedure, synthesis procedure of Acetylamides 3a-e.

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By using fabricated microfluidic reactor under microwave irradiation, positive effects of both flow and microwave on organic reactions were applied. Reaction yield and times were comparable with both conventional and microwave reflux methods (Table 2).

Table 2. Structure,	yields and	reaction t	times of	products	За-е.
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a) overall microwave flow reaction 15 min., residual time 1.16 min., reflux under microwave in 30 min. resulted in 90% yield, conventional heating in 5 hours resulted in 73% yield.

Since PDMS is microwave transparent, reaction temperature is easily followed using IR sensor which has minimum surface area of 8-14  $\mu$ m implemented in CEM Discover Microwave Reactor. Only one microfluidic device was used for all reactions and no deformation was observed. Thus, it can be concluded that PDMS micro-reactor has high usability in these reaction conditions.

#### Conclusions

Several additive manufacturing techniques have been used to fabricate submillimeter and millimeter fluidics. However, our technique allows that user defined, computer aided design micropattern generation, which paves the way of large area, flexible and stretchable microfluidics applications.

In this work, we introduced a novel 3D fabrication method of all flexible (Figure 5), PDMS microfluidic reactor. This microfluidic device successfully used in microwave flow organic synthesis for acetylation of several amines.



**Figure 5.** Images of all flexible, PDMS microfluidic device, is filled with red food dye solution. (a) straight (b) bended.

Introduced microwave flow reaction in microfluidic reactor have been dramatically reduced reaction time and increased yields compared with microwave and conventional heating. Same microfluidic reactor was used for all reactions without causing any problem. Thus, durability and effectiveness of this concept has been proven. We believe that combining with microwave transparent solvents, transparency of PDMS will be great opportunity for MAFOS. In future works, we plan to modify PDMS surface with organic catalysis bearing trimethoxysilyl (-Si(OMe)3) moiety to coat microfluidic's walls with different heterogeneous catalysts<sup>[58]</sup>.

#### **Experimental Section**

# General Synthesis of N-acetylamides in PDMS Microfluidic under Microwave Irradiation

THF (15 mL) dissolved N-acetylbenzotriazole (3 mmol) and amines (3 mmol) were pumped in PDMS microfluidic reactor with 0.3 mLmin<sup>-1</sup> flow rate in CEM Discover microwave instrument. Continuous 100 W MW was applied with continuous air cooling during the reaction. The overall reaction time was 15 min and residual reaction time was calculated as 1.16 min (volume of microfluidic / flow rate = 0.35 mL / 0.3 mLmin<sup>-1</sup>= 1.16 min) After finishing reaction, solvent was removed under vacuum. Crude product was dissolved in ethyl acetate and extracted with 20 % aqueous Na<sub>2</sub>CO<sub>3</sub> solution to remove 1H-benzotriazole. Organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> to give N-acetylamides in 92-96 % isolated yield. Structure of products were characterized using <sup>1</sup>H and <sup>13</sup>C NMR analyses (see supp. info.).

**Keywords:** all flexible microfluidic • microwaveable microfluidic • 3D printed PDMS microfluidic • flow synthesis • acetylation

#### References

- J. Kobayashi, Y. Mori, S. Kobayashi, *Chem. Asian. J.*, **2006**, 1 –2, 22– 35.
- [2] H. P. L. Gemoets, Y. Su, M. Shang, V. Hessel, R. Luque, T. Noël, *Chem. Soc. Rev.*, **2016**, 45, 83-117.
- [3] R. Singh, H. J. Lee, A. S. Singh, D. P. Kim, Korean Journal of Chemical Engineering, 2016, 33(8), 2253-2267.
- [4] J. J. Heiland, R. Warias, C. Lotter, L. Mauritz, P. J. W. Fuchs, S. Ohla, K. Zeitler, D. Belder, *Lab Chip*, 2017, 17, 76-81.
- [5] H. Kim, H-J. Lee, D.-P. Kim, Angew. Chem. Int. Ed., 2015, 54, 1877 1880.
- [6] P. W. Miller, L. E. Jennings, A. J. deMello, A. D. Gee,
- N. J. Long, R. Vilara, Adv. Synth. Catal. 2009, 351, 3260 3268.
- [7] M. Wang, L. Hu, C. Xu, *Lab Chip*, 2017, 17, 1373-1387.

 [8] J. Y. Sim, M. P. Haney, S. II Park, J. G. McCall, J.-W. Jeong , *Lab Chip*, 2017, 17, 1406-1435.

[9] L. Kang, B. G. Chung, R. Langer, A. Khademhosseini, *Drug Discov. Today*, **2008**, 13(1-2), 1–13.

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- [10] Ma, J.; Lee, S. M.-Y.; Yi, C.; Wing, C. Controllable synthesis of functional nanoparticles by microfluidic platforms for biomedical applications – a review, *Lab Chip*, 2017, 17, 209-226.
- [11] H. Nagasawa, K. Mae, Ind. Eng. Chem. Res., 2006, 45, 2179–2186.

[12] L. Yu, Y. C. Pan, C. Q. Wang, L. X. Zhang, *Chem. Eng. J.*, **2013**, 219, 78–85.

[13] B.K.H. Yen, N.E. Stott, K.F. Jensen, M.G. Bawendi, *Adv. Mater.*, 2003, 15: 1858–1862.

[14] H.Z. Wang, H. Nakamura, M. Uehara, Y. Yamaguchi, M. Miyazaki, H. Maeda, Adv. Funct. Mater., 2005, 15, 603–608.

[15] E. M. Chan, A. P. Alivisatos, R. A. Mathies, J. Am. Chem. Soc., 2005, 127, 13854–13861.

[16] A. Abou-Hassan, O. Sandre, V. Cabuil, *Angew. Chem. Int. Ed.*, **2010**, 49, 6268 – 6286.

[17] J. Wan, L. Shi, B. Benson, M. J. Bruzek, J. E. Anthony, P. J. Sinko, R. K.
 Prudhomme, H. A. Stone, *Langmuir*, **2012**, 28 (37), 13143–13148.

[18] A. C. Siegel, S. S. Shevkoplyas, D. B. Weibel, D. A. Bruzewicz, A. W. Martinez, G. M. Whitesides, *Angew. Chem. Int. Ed.*, **2006**, 45, 6877 -6882.

- [19] M. Seo, Z. Nie, S. Xu, M. Mok, P. C. Lewis, R. Graham, E. Kumacheva, Langmuir, 2005, 21 (25), 11614–11622.
- [20] L. Y. Yeo, H.-C. Chang, P. P. Y. Chan, J. R. Friend, Small, 2011, 7, 12–48.

[21] O. Cascon, G. Richter, R. K. Allemann, T. Wirth, *ChemPlusChem*, **2013**, 78 (11), 1334-1337

[22] S. Waheed, J. M. Cabot, N. P. Macdonald, T. Lewis, R. M. Guijt, B. Paullab, M. C. Breadmore, *Lab Chip*, **2016**, 16, 1993-2013.

[23] R. Amin, S. Knowlton, A. Hart, B. Yenilmez, F. Ghaderinezhad, S. Katebifar, M. Messina, A. Khademhosseini, S. Tasoglu, *Biofabrication*, **2016**, 8, 022001.

[24] S. Rossi, A. Puglisi, M. Benaglia, *ChemCatChem*, DOI: 10.1002/cctc.201701619.

[25] M. Singh, H. M. Haverinen, P. Dhagat, G. E. Jabbour, *Adv. Mater.*, 2010, 22, 673-685.

Y. Pan, C. Zhou, Y. Chen, J. Manuf. Sci. Eng., 2012, 134, 051011, 1-9.
 W. Kaiser, C. Garrett, Phys. Rev. Lett., 1961, 7, 229-232.

[28] S. Kawata, H.-B. Sun, T. Tanaka, K. Takada, *Nature*, **2001**, 412, 697–698.

[29] F. Li, P. Smejkal, N. P. Macdonald, R. M. Guijt, M. C. Breadmore, *Anal. Chem.* 2017, 89, 4701–4707.

[30] M. Sun, Y. Xie, J. Zhu, J. Li, J. C. T. Eijkel, Anal. Chem. 2017, 89, 2227–2231.

[31] L. E. Bertassoni, M. Cecconi, V. Manoharan, M. Nikkhah, J. Hjortnaes,
 A. L. Cristino, G. Barabaschi, D. Demarchi, M. R. Dokmeci, Y. Yang, A.
 Khademhosseini, *Lab Chip*, **2014**, 14, 2202–2211.

[32] D. B. Kolesky, R. L. Truby, A. S. Gladman, T. A. Busbee, K. A. Homan, J. A. Lewis, *Adv. Mater.*, **2014**, 26, 3124–3130.

[33] B. N. Johnson, K. Z. Lancaster, I. B. Hogue, F. Meng, Y. L. Kong, L. W.
 Enquist, M. C. McAlpine, *Lab Chip*, **2016**, 16, 1393-1400.

- [34] C. Colosi, S. R. Shin, V. Manoharan, S. Massa, M. Costantini, A. Barbetta, M. R. Dokmeci, M. Dentini A. Khademhosseini, *Adv. Mater.*, **2016**, 28, 677–684.
- [35] P. J. Kitson, M. H. Rosnes, V. Sans, V. Dragone, L. Cronin, *Lab Chip*, 2012, 12, 3267-3271.

[36] S. Rossi, R. Porta, D. Brenna, A. Puglisi, M. Benaglia, Angew. Chem. Int. Ed., 2017, 56, 4290 -4294.

[37] A. Urrios, C. Parra-Cabrera, N. Bhattacharjee, A. M. Gonzalez-Suarez,

L. G. Rigat-Brugarolas, U. Nallapatti, J. Samitier, C. A. DeForest, F. Posas, J. L. Garcia-Cordero, A. Folch, *Lab Chip*, **2016**, 16, 2287-2294.

- [38] J. A. Lewis, Adv. Funct. Mater., 2006, 16, 2193–2204.
- [39] D. Therriault, R. F. Shepherd, S. R. White, J. A. Lewis, *Adv. Mater.*, 2005, 17, 395–399.

[40] A. K. Au, W. Huynh, L. F. Horowitz, A. Folch, *Angew. Chem. Int. Ed.*, 2016, 55, 3862 – 3881.

[41] D.P. Parekh, C. Ladd, L. Panich, K. Moussa, M. D. Dickey, *Lab Chip*, **2016**, 16, 1812-1820.

[42] V. K. Lee, D. Y. Kim, H. Ngo, Y. Lee, L. Seo, S. S. Yoo, P. A. Vincent, G. Dai, *Biomaterials*, **2014**, 35, 8092–8102.

- [43] Q. Gao, Y. He, J. Z. Fu, A. Liu, L. Ma, Biomaterials, 2015, 61, 203–215.
- [44] C. J. Hansen, W. Wu, K. S. Toohey, N. R. Sottos, S. R. White, J. A. Lewis, *Adv. Mater.*, **2009**, 21, 4143–4147.
- [45] W. Wu, A. Deconinck J. A. Lewis, *Adv. Mater.*, **2011**, 23, 178–183.
- [46] J. N. Lee, C. Park, G. M. Whitesides, Anal. Chem., 2003, 75, 6544-6554.
- [47] T. Fujii, Microelectronic Engineering, 2002, 61, 907–914.

[48] K. Hosokawa, T. Fujii, I. Endo, Anal. Chem., **1999**, 71 (20), 4781–4785.

[49] M. Bender, U. Plachetka, J. Ran, A. Fuchs, B. Vratzov, H. Kurz, J. Vac. Sci. Technol. B, 2004, 22, 3229-3232.

[50] M. M. Picher, S. Küpcü, C-J. Huang, J. Dostalek, D. Pum, U. B. Sleytr, P. Ertl, Lab Chip, 2013, 13, 1780-1789.

[51] C.Strauss, R. Trainor, Aust. J. Chem. 1995, 48, 1665-1692.

[52] E. Comer, M. G. Organ, J. Am. Chem. Soc. 2005, 127, 8160-8167.

[53] T. M. Barnard, N. E. Leadbeater, M. B. Boucher, L. M. Stencel, B. A. Wilhite, Energy and Fuels, **2007**, 21, 1777-1781.

[54] R. Baxendale, J. Hayward, V. Ley, S. Comb. Chem. High Throughput Screen., 2007, 10, 802-836.

[55] P. Öhrngren, A. Fardost, F. Russo, J. S. Schanche, M. Fagrell, M. Larhed, Org. Process Res. Dev. 2012, 16, 1053-1063.

[56] M. Callan, E. Jang, J. Kelly, K. Nguyen, C. Marmorat, M. Rafailovich, "Characterization of Pluronic F127 for the Controlled Drug Release Vancomycin in the Spinal Column", to be found under https://you.stonybrook.edu/jucer/files/2017/04/1-Kim-F127-Pg-9-19-y289nt.pdf
[57] S. Takeuchi, P. Garstecki, D. B. Weibel, G. M. Whitesides, *Adv.Mater.*, 2005, 17, 1067–1071.

[58] R. Munirathinam, J. Huskens, W. Verboom, *Adv. Synth. Catal.*, 2015, 357, 1093-1123.

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3D Fabricated all flexible PDMS microfluidic was used for the Microwave Assisted Flow Organic Synthesis (MAFOS) of acetylation of several amines.



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