

# Improved Catalytic Activity and Stability Using Mixed Sulfonic Acid- and Hydroxy-Bearing Polymer Brushes in Microreactors

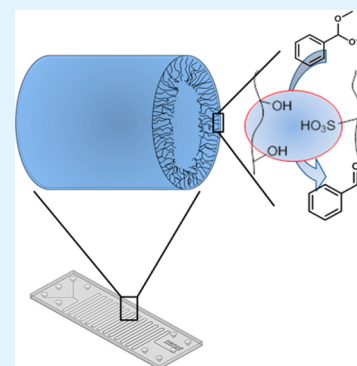
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## S Supporting Information

**ABSTRACT:** Sulfonic acid-bearing polymer brushes were grown on the inner walls of continuous flow glass microreactors and used in the acid-catalyzed hydrolysis of benzaldehyde dimethyl acetal as a test reaction. Randomly 1:1 mixed polymer brushes of poly-3-sulfopropyl methacrylate (PSPM) and poly-2-hydroxyethyl methacrylate (PHEMA) showed a 6-fold increase of the TOF value compared to the solely PSPM-containing microreactor. This remarkable improvement is attributed to the cooperative stabilizing effect of proximal OH groups on the active sulfonic acid moieties within the brush architecture. In fact, the rational mixing of SPM with methyl methacrylate (MMA) as an OH-free comonomer caused a drop in the activity of the resulting catalytic platform. A 5-fold increase of the TON of the 1:1 PSPM–PHEMA versus the PSPM homopolymer brush systems additionally demonstrates the substantial increase in the stability of the mixed brushes catalytic platform, which could be continuously run over 7 days without significant loss of activity. The 1:1 PSPM–PHEMA mixed brush catalytic system also showed a good activity in the deprotection of 2-benzyl tetrahydropyranyl ether.

**KEYWORDS:** catalytic coating, continuous flow, heterogeneous catalysis, microreactors, polymer brushes



## INTRODUCTION

Microreactor technology combined with continuous flow synthesis offer a favorable means to carry out heterogeneous catalysis.<sup>1</sup> The advantages derive directly from the features of a microfluidic device, notably the huge surface-to-volume ratio, which is of great interest for surface functionalization, and improved heat and mass diffusion phenomena, which yield overall a better control over the reaction conditions.<sup>2–6</sup>

Catalysts anchored within a microstructured reactor offer the possibility of easy product separation, reuse of the catalyst, and less waste, all aspects playing a central role in modern organic synthesis in adherence to the so-called “green parameters”.<sup>7,8</sup> However, despite the numerous examples of chemical reactions in microfluidic devices,<sup>9</sup> less effort has been put on the development of on-chip catalysis.<sup>10</sup> Within the field of supported catalysis, many studies have made use of packed-bed microreactors, where the catalyst is anchored to different supports and therefore “packed” within the chip.<sup>11–14</sup> Despite the increased active surface for catalyst anchoring, this approach suffers from the high back-pressure developed along the channel, random bead distribution, and broad residence time. By using microreactors with wall-catalysts, a good control over the reaction conditions can be achieved<sup>15</sup> as demonstrated for several examples.<sup>16–18</sup>

Polymer brushes offer a versatile method for surface functionalization.<sup>19</sup> They refer to polymeric structures tethered at one end to a solid substrate, and the distance between neighboring chains influences the architecture of the brush.<sup>20</sup> The great interest in polymer brushes arises from the possibility

of tuning the surface properties of a material by growing chains with the desired functionalities. With respect to this, polymer brushes bearing catalytic moieties have obtained considerable attention, combining a high local concentration of catalyst to the versatility of supported active sites.<sup>21–24</sup> Recently, our group has developed a new strategy for the anchoring of polymer brushes within microfluidic reactors bearing a wide range of catalysts, such as organic,<sup>17</sup> metallic,<sup>25</sup> enzymatic,<sup>26</sup> and Lewis-acidic.<sup>27</sup> Interestingly, this approach combines continuous flow supported-catalysis and the possibility to fine-tune the type of active catalytic sites employed as well as their loading.<sup>28</sup>

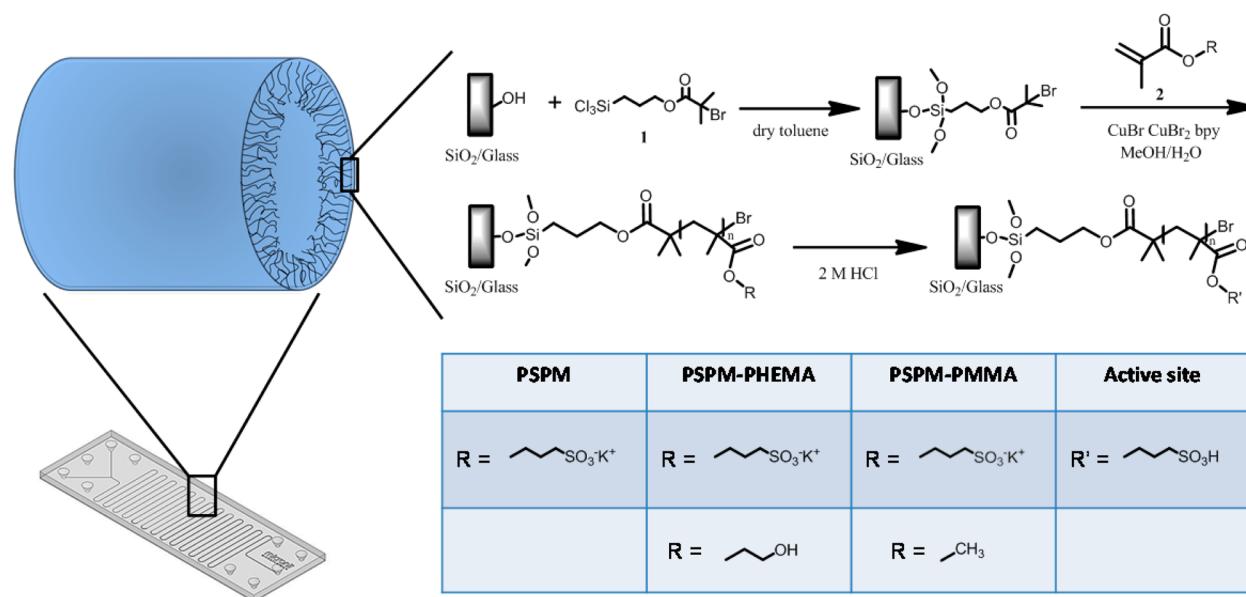
Acid catalysis plays a central role in organic synthesis, especially in industry. However, the use of mineral acids in a homogeneous fashion is still predominant. Nevertheless, the transition from homogeneous to heterogeneous acid catalysis is an active research field,<sup>29</sup> with sulfonic acid moieties supported onto ion-exchange resins,<sup>30</sup> ordered mesoporous materials,<sup>31–33</sup> and amorphous carbon.<sup>34</sup> To this regard, the use of solid acid catalysis using polymer brushes is well documented, grown onto silica,<sup>35</sup> mesoporous polymers,<sup>36</sup> and particles.<sup>37</sup>

At present, heterogeneous acid catalysis in continuous flow reactors is mostly carried out using packed-bed reactors of supported acids.<sup>38,39</sup> We have recently presented a single step functionalization of the inner walls of glass microreactors by a

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**Figure 1.** General procedure for the functionalization of a flat silicon dioxide surface and glass microreactors by poly-3-sulfopropyl methacrylate (PSPM), mixed brushes of PSPM with poly-2-hydroxyethyl methacrylate (PHEMA), and mixed brushes of PSPM with poly(methyl methacrylate) (PMMA).

strong perfluorosulfonic acid and shown its activity in different acid-catalyzed reactions.<sup>40</sup>

Herein, we present the use of sulfonic acid-bearing polymer brushes grafted onto the walls of microreactors and their use in a model reaction, the hydrolysis of benzaldehyde dimethyl acetal. 1:1 Mixed brushes of poly-3-sulfopropyl methacrylate (PSPM) with poly-2-hydroxyethyl methacrylate (PHEMA) remarkably improved the catalytic activity of the system compared to the use of a homopolymer of PSPM due to the proximity effect of the PHEMA OH groups on the sulfonic acid active sites of PSPM, which affect the activity as well as the stability of the catalysts. This was supported by the clear decrease in both the activity and stability when mixed brushes of PSPM with OH-free poly(methyl methacrylate) (PMMA) were used. To demonstrate the further applicability of the 1:1 PSPM–PHEMA catalytic brush system, it was successfully employed in the deprotection of 2-benzyl tetrahydropyranil ether.

## RESULTS AND DISCUSSION

**Flat Surface and Microreactor Functionalization.** The growth and characterization of sulfonic acid-bearing polymer brushes were first performed on a flat silicon dioxide surface. First, a self-assembled monolayer (SAM) of Atom Transfer Radical Polymerization (ATRP) initiator (**1**) was deposited following a literature procedure.<sup>41</sup> Afterward, different mixtures of methacrylate monomers (**2**) were grown via ATRP yielding homopolymer brushes of PSPM, mixed brushes of PSPM–PHEMA and PSPM–PMMA (Figure 1).

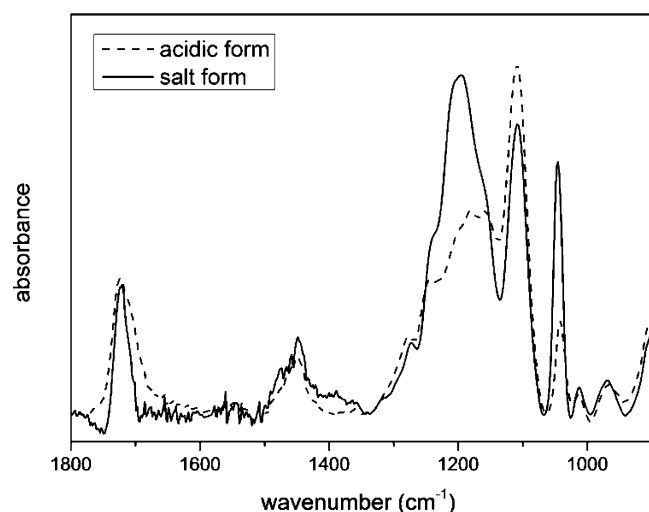
PSPM was grafted following a procedure reported in literature, where 3-sulfopropyl methacrylate potassium salt monomer (SPM) was dissolved in a degassed methanol/water solvent mixture with bipyridyl and copper salts.<sup>42</sup> The mixed brushes were synthesized using 1:1, 2:1, and 1:2 molar ratios of the two monomers, SPM–HEMA and a 1:1 molar ratio for SPM–MMA, which were dissolved in a degassed methanol/water (3:1 v/v) mixture containing bipyridyl and copper salts. Finally, all the polymer brush-functionalized surfaces were

treated with a 2 M HCl solution to obtain the catalytic  $\text{SO}_3\text{H}$  active sites.

Water contact angle measurements of the initiator-functionalized samples showed a static contact angle value of  $85^\circ$ . Upon polymerization the value decreased considerably to below  $30^\circ$ , due to the high hydrophilicity of the brushes, also in the case of the mixed PSPM–PMMA. The value of the contact angle stayed below  $30^\circ$  after activation of the sulfonic acid groups by HCl.

Transmission FT-IR of the PSPM homopolymer indicated the surface functionalization as demonstrated by the stretching of the carbonyl peak at around  $1720\text{ cm}^{-1}$ ,  $\text{CH}_2$  bending vibrations around  $1450\text{ cm}^{-1}$ , the asymmetric sulfonate stretching around  $1200\text{ cm}^{-1}$ , and the symmetric sulfonate stretching around  $1045\text{ cm}^{-1}$ .<sup>42</sup> The strong band at around  $1100\text{ cm}^{-1}$  belongs to the stretching of Si–O–Si of the silicon substrate. Upon treatment with HCl, the intensity of the carbonyl absorbance remained the same, indicating no substantial hydrolysis or polymer detachment from the surface, whereas both the asymmetric and the symmetric sulfonate stretching decreased (Figure 2). The FT-IR spectrum of the PSPM–PHEMA mixed brushes displayed the same peaks as PSPM as well as a broad band around  $3500\text{ cm}^{-1}$  belonging to the HEMA OH groups (Supporting Information Figure S1).

X-ray photoelectron spectroscopy (XPS) was performed after HCl treatment for the brush-functionalized surfaces. The experimental data reported in Table 1 support the expected random (co)polymerization for the (mixed) brushes, the experimental values being in excellent agreement with the theoretical atomic ratios. The sulfur content in the PSPM–PMMA brush was around 20% higher than the theoretical value for a 50:50 monomer mixture, suggesting a SPM:MMA 60:40 ratio. Potassium was not detected, thus confirming the sulfonic acid activation, supported by the sulfur S 2p spectra that showed a binding energy fitting the C– $\text{SO}_3$  bond. In all cases, the thickness of the brush exceeded 20 nm (vide infra for the exact values); thereby, the interference of the silicon substrate



**Figure 2.** Transmission FT-IR spectrum of a PSPM-functionalized flat SiO<sub>2</sub> surface.

and of the SAM of the initiator could be excluded from the analysis.

The thickness of the different polymer brushes on flat surfaces was determined with ellipsometry (Table 2). Using the same polymerization times in flow, the film thicknesses in the microreactors were estimated to have the same values, as proven in a previous study.<sup>17</sup>

The same procedures described for the flat surfaces were followed for the functionalization of several glass microreactors (Figure 1). After the activation of the inner surface, the solution of the ATRP initiator (1) in toluene was flowed through the channel overnight. The initiator-functionalized chip was subsequently reacted with the monomer mixtures (2) for the aforementioned polymerization times. A 2 M solution of HCl was finally flowed through the channel for 2 h to activate the sulfonate groups.

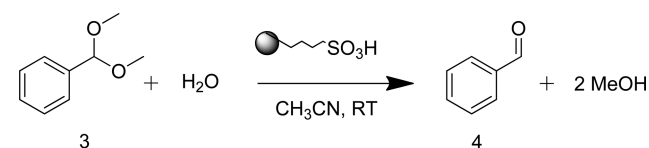
**Catalytic Activity.** To prove the validity of the catalytic systems, the hydrolysis of benzaldehyde dimethyl acetal (3, BDMA) was chosen as a model reaction (Scheme 1).<sup>43</sup> A mixture of BDMA (3) and water in acetonitrile was flowed continuously through the brush-functionalized microreactors at room temperature. The formation of benzaldehyde (4) was followed by GC, confirming that there are no side products forming during the course of the reaction.

At first, the catalytic activity of the sulfonic acid-bearing polymer brushes of PSPM homopolymer was investigated. Exploiting the high local concentration of catalyst created in the brush film, the system turned out to be highly active in the acid-catalyzed test reaction reaching conversions up to 90% within a few minutes of residence time. To perform a kinetic study for the hydrolysis of BDMA (3), its concentration was varied in the

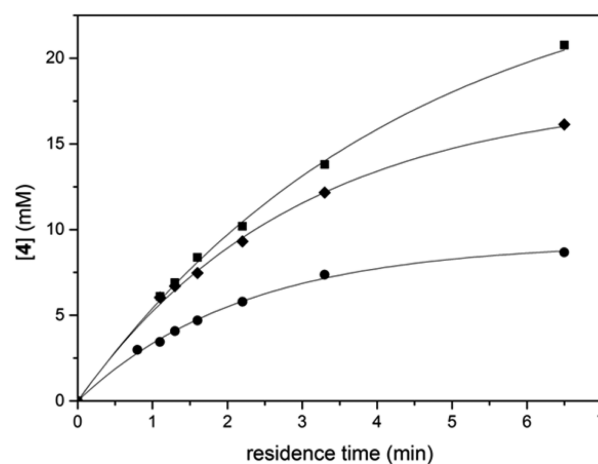
**Table 2.** Polymerization Times and Correspondent Ellipsometric Thicknesses for PSPM, PSPM-PHEMA, and PSPM-PMMA Polymer Brushes on Flat Silicon Dioxide Surfaces

system	polym. time (min)	thickness (nm)
PSPM	45	92
PSPM-PHEMA (1:1)	40	55
PSPM-PMMA	50	83

**Scheme 1.** Acid-Catalyzed Hydrolysis of Benzaldehyde Dimethyl Acetal (3)



range from 10 to 30 mM using an excess of water to achieve pseudo-first-order kinetics (Figure 3).



**Figure 3.** Formation of benzaldehyde (4) within a PSPM-functionalized microreactor at different BDMA (3) concentrations: (●) 10 mM, (◆) 20 mM, (■) 30 mM. [Water] = 100 mM.

For each BDMA concentration a pseudo-first-order rate constant was calculated, specifically 0.45 min<sup>-1</sup> at 10 mM, 0.34 min<sup>-1</sup> at 20 mM, and 0.22 min<sup>-1</sup> at 30 mM. The amount of catalyst loaded in the microreactor was calculated based on the volume that the brush architecture occupies, considering the internal surface available for functionalization (3.47 × 10<sup>14</sup> nm<sup>2</sup>) and a polymer thickness of 92 nm as calculated on flat surface using the same experimental conditions. Assuming a brush density close to that of the bulk material (1 g mL<sup>-1</sup>) results in a loading of 130 nmol. For all substrate concentrations a turnover frequency (TOF) value of around

**Table 1.** XPS data of PSPM, PSPM-PHEMA, and PSPM-PMMA-Functionalized Silicon Dioxide Surfaces<sup>a</sup>

atomic ratio	PSPM		PSPM-PHEMA						PSPM-PMMA	
			1:1		2:1		1:2		1:1	
	theor	exp	theor	exp	theor	exp	theor	exp	theor	exp
C/S	7	7.1	13	12.6	10	9.0	19	17.0	12	9.8
C/O	1.4	1.4	1.6	1.8	1.5	1.5	1.7	1.7	1.7	1.6

<sup>a</sup>See also Supporting Information Figure S2.

$1.0 \times 10^{-2} \text{ s}^{-1}$  was calculated, demonstrating that the amount of catalyst controls the rate of the reaction.

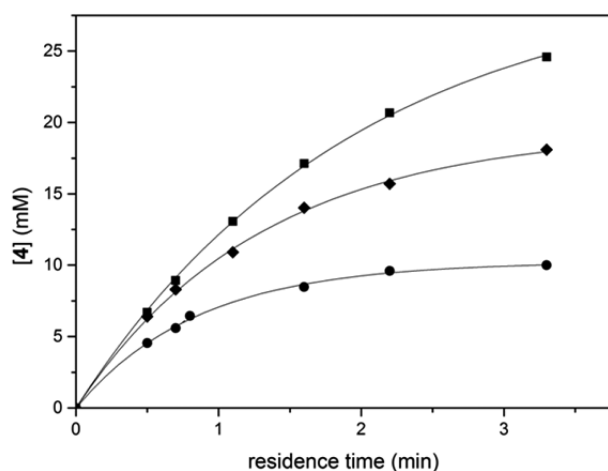
A control experiment was carried out to assess that the observed activity is due to the anchored brush. First, the microreactor was “deactivated” by an ion-exchange reaction with a 1 M aqueous  $\text{K}_2\text{CO}_3$  solution to obtain an inactive salt form of the brushes. Afterward, the test reaction was repeated under the same conditions showing a marginal conversion (<5%) for a residence time up to 7 min. Subsequently, the chip was reactivated with a 2 M solution of HCl and the pristine activity could be restored, thus confirming the role of the sulfonic acid moieties as active catalysts.

To study the effect of the temperature on the stability of the polymeric architecture, the brush-functionalized microreactors were kept at  $80^\circ\text{C}$  in acetonitrile for at least 6 h. Afterward, the hydrolysis of BDMA (3) was carried out under the standard conditions retaining the pristine activity, thus excluding any alteration of the catalytic active sites.

For potential applications, the long-term stability of the catalytic platform is of importance. To this respect, stability studies carried out with the PSPM-functionalized microreactor at a fixed residence time (3.25 min) showed that the system could be run for 3 days with a marginal decrease in activity for the test reaction. After this term, however, progressive deactivation of the catalytic active sites required reactivation by means of a fresh HCl solution, which restored the pristine activity. The reason for the deactivation may be found in the replacement of the active  $\text{SO}_3\text{H}$  protons with contaminant cations present.

To improve the stability of the brush-catalysts, the use of mixed brushes was considered. In this approach, an appropriate monomer is introduced to stabilize the catalytically active sites, exploiting the proximity effect created in the brush environment.<sup>44</sup> This was verified by introducing OH groups-bearing polymer brushes in the polymeric system, using the HEMA monomer. Therefore, a kinetic study of the catalytic test reaction (Scheme 1) was repeated with the 1:1 PSPM–PHEMA-functionalized microreactor under the same experimental conditions as used with the PSPM homopolymer (Figure 4).

In this case, pseudo-first-order rate constants of  $1.17 \text{ min}^{-1}$ ,  $0.77 \text{ min}^{-1}$ , and  $0.51 \text{ min}^{-1}$  were calculated for 10, 20, and 30



**Figure 4.** Formation of benzaldehyde (4) within a 1:1 PSPM–PHEMA-functionalized microreactor at different BDMA (3) concentrations: (●) 10 mM, (◆) 20 mM, (■) 30 mM. [Water] = 100 mM.

mM BDMA (3) concentrations, respectively. The amount of active sites for this microreactor was calculated based on the same assumptions as described for the homopolymeric system, taking into account the thickness measured on an equivalent flat surface (55 nm) and the presence of half of the sulfonic acid moieties (50:50 monomer ratio), giving a value of 51 nmol of catalyst. TOF values for the different concentrations of 3 are presented in Table 3, showing an average of  $6.0 \times 10^{-2} \text{ s}^{-1}$ .

**Table 3.** TOF Values for the Hydrolysis of BDMA (3) in PSPM and 1:1 PSPM–PHEMA-Functionalized Microreactors at Different Concentrations of BDMA (3)

3 (mM)	TOFs ( $10^{-2} \text{ s}^{-1}$ )		
	PSPM	PSPM–PHEMA 1:1	ratio
10	0.8	5.0	6.3
20	1.1	6.5	5.9
30	1.1	6.5	5.9

Comparing the TOFs of the two catalytic systems highlights a remarkable six times larger value for the 1:1 PSPM–PHEMA mixed brushes, compared with the use of PSPM (Table 3).

These results clearly show the influence of the proximal OH groups of PHEMA on the sulfonic acid moieties, most probably via hydrogen bonding. In fact, in a recent work by Kass et al. it is demonstrated that hydrogen bonds can improve the catalytic activity and enhance Brønsted acidities, especially through stabilization of the conjugate bases.<sup>45</sup> In a similar way, enzyme active sites make use of hydrogen bonds to stabilize transition-state structures by delocalizing negatively charged centers.<sup>46</sup>

In a similar way as described for the homobrushes, the 1:1 PSPM–PHEMA brushes could be deactivated and reactivated by treatment with a 1 M aqueous  $\text{K}_2\text{CO}_3$  solution and 2 M HCl, respectively. The two brush systems showed a similar behavior, also when a much lower concentration of  $20 \mu\text{M}$   $\text{K}_2\text{CO}_3$  was used. This means that the OH groups do not affect the blocking by cations.

In order to further study the influence of the number of OH groups on the activity of the system, 2:1 PSPM–PHEMA and 1:2 PSPM–PHEMA mixed brushes were prepared, having 33% less and more OH groups, respectively, as compared with the standard 1:1 mixed polymer. XPS data confirmed that the two monomers, SPM and HEMA, mix randomly and follow the ratio used in the feeding solution (Table 1). For both catalytic systems the TOF values of the model reaction were determined (Table 4).

**Table 4.** TOF Values for the Hydrolysis of BDMA (3, 10 mM) for Different PSPM–PHEMA-Functionalized Microreactors

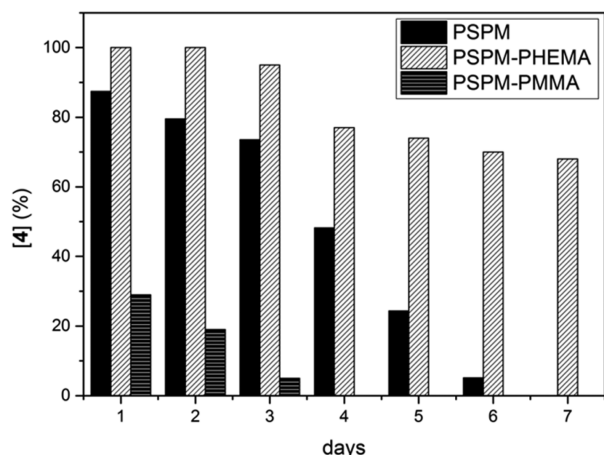
PSPM–PHEMA	TOF ( $10^{-2} \text{ s}^{-1}$ )
1:1	5.0
2:1	0.1
1:2	1.2

Clearly, the best activity was obtained with the 1:1 mixed system. The TOF value for the 2:1 PSPM–PHEMA system was considerably lower than that of the 1:1 mixed system. Apparently, the presence of fewer OH groups gives rise to a decrease of the stabilization. The 1:2 PSPM–PHEMA mixed system showed a higher activity than the 2:1 PSPM–PHEMA



mixed system, where the OH groups play their stabilizing role, however, with fewer active sites.

Interestingly, PSPM–PHEMA mixed brushes turned out to improve also the stability of the catalytic platform. As evident from Figure 5, the mixed brushes-functionalized microreactor



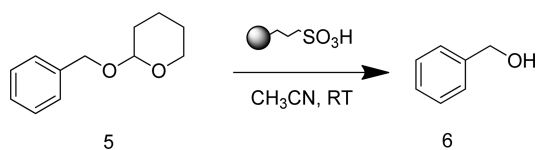
**Figure 5.** Hydrolysis of BDMA (3) in a PSPM, 1:1 PSPM–PHEMA, and PSPM–PMMA-functionalized microreactor. [3] = 10 mM; [water] = 100 mM; residence time = 3.25 min.

could be run for at least seven consecutive days maintaining a substantial activity in the catalytic test reaction. Direct comparison with the PSPM homopolymer strikingly highlights the stabilizing effect of the HEMA moieties. However, in case of a PSPM–PMMA mixed brush microreactor, containing OH-free methyl methacrylate (MMA), the overall activity for 3.25 min residence time was only around 30%, while the reusability was limited to 2 days of continuous use (Figure 5).

A TON of 470 was calculated for the PSPM catalytic system, while that for the mixed PSPM–PHEMA brush system was of 2200, involving an approximately 5-fold increase. The TON for the PSPM–PMMA microreactor was of only 82. This unequivocally assesses the improved catalytic activity and stability of the PSPM–PHEMA mixed brush system.

The 1:1 PSPM–PHEMA catalytic system was employed in another acid-catalyzed reaction to study its wider applicability. Preliminary results showed a good activity for the deprotection of tetrahydropyranyl (THP) ethers. THP is one of the most common and useful protecting groups for alcohols and phenols.<sup>47</sup> A variety of deprotection methods of THP groups in the presence of other functional groups were carried out using acidic, neutral, and reductive media. However, most of these methods involve tedious work-up, heating, highly toxic reagents, quantitative amounts of reagents, and formation of numerous side products. The use of a continuous flow solid acid catalyst may be beneficial to overcome these drawbacks. The deprotection of 2-benzyl-THP (5) to give benzyl alcohol (6) was chosen as test reaction (Scheme 2). This reaction performed in the 1:1 PSPM–PHEMA catalytic system reached

**Scheme 2.** Acid-Catalyzed Deprotection of Benzyl-THP (5)



70% conversion at a residence time of 6.5 min. No side products were detected during the course of the reaction, confirming the advantage of the mixed-brush catalytic system.

## CONCLUSIONS

In this study, we demonstrated the effective use of sulfonic acid-bearing polymer brushes (PSPM) in continuous flow microreactors for the hydrolysis of benzaldehyde dimethyl acetal. The grafting of a 1:1 mixed PSPM–PHEMA brush system resulted in a remarkable increase in catalytic activity and stability, evident from a 6-fold increase in the TOFs and 5-fold increase in TONs. This behavior was ascribed to the cooperative effect of the OH groups in stabilizing the sulfonic acid moieties, due to the environment created within the brush architecture. In fact, when PMMA was used as comonomer, thus, not having OH groups, the activity of the catalytic system dropped considerably. By using mixed-brush systems with different percentages of HEMA monomer, thus by varying the number of OH groups present, it turned out that the best catalytic activity was obtained for a presence of about 50% OH groups. Moreover, the 1:1 PSPM–PHEMA mixed system effectively catalyzed the deprotection of 2-benzyl tetrahydropyranyl ether (benzyl-THP).

This approach will be promising to study a wide range of acid-catalyzed reactions in a continuous flow microreactor since both the number of the active sites and the activity and stability of the catalytic system can be fine-tuned.

## EXPERIMENTAL SECTION

**Materials and Equipment.** The chemicals and solvents were purchased from Sigma-Aldrich unless otherwise stated and were used without purification unless specified. Single-side-polished silicon wafers were purchased from OKMETIC with (100) orientation. 3-(5'-Trichlorosilyl)pentyl 2-bromo-2-methylpropionate was synthesized following a literature procedure.<sup>41</sup> CuBr was purified by washing with glacial acetic acid and, after filtration, by rinsing with ethanol and acetone, it was stored in a vacuum desiccator. Methanol and ethanol (VWR, analytical reagent grade) were used without further purification, water was purified with the Milli-Q pulse (MILLIPORE, R = 18.2 MΩ cm) ultrapure water system, acetonitrile and toluene were purified through a solvent purification system dispensing ultra dry solvents (MBraun, MB-SPS-800). Contact angles were measured on a Krüss G10 contact angle measuring instrument, equipped with a CCD camera. Gas chromatography (GC) experiments were performed with an Agilent DB-SMS UI column (30 m × 0.32 mm i.d., 25 μm film thickness) with a constant pressure of 11.9 psi. Ellipsometry measurements were performed with a plasmon ellipsometer (λ = 632.8 nm) assuming a refractive index of 1.5 for the organic compound. For X-ray photoelectron spectroscopy (XPS) a Quanterra Scanning X-ray Multiprobe instrument was used, equipped with a monochromatic Al Kα X-ray source producing approximately 25 W of X-ray power. XPS-data were collected from a surface area of 1000 × 300 μm with a pass energy of 224 eV and a step energy of 0.8 eV for survey scan and 0.4 for high resolution scans. For quantitative analysis, high resolution scans were used. FT-IR analysis was performed using a Nicolet 6700 instrument (Thermo Scientific) in transmission mode.

**Flow Apparatus.** In all microreactor experiments, the sample solutions were mobilized by means of a PHD 22/2000 series syringe pump (Harvard Apparatus, U.K.) equipped with 500 μL flat tip syringes (Hamilton). Syringes were connected to fused silica capillaries (100 μm i.d., 362 μm o.d., Polymicro Technologies) by means of Upchurch Nanoport assembly parts (i.e., Nano-tight unions and fittings, Upchurch Scientific Inc. U.S.A.). During the experiments, the microreactor was placed in a home-built chip holder designed for fitting fused silica fibers into the inlet/outlet chip reservoirs by means of commercially available Upchurch Nanoport assembly parts. Glass

microreactors with a residual volume of 13  $\mu\text{L}$  (dimensions: 150  $\mu\text{m}$  width and 150  $\mu\text{m}$  depth) were purchased from Micronit Microfluidics (see Supporting Information Figure S3).

**Polymer Brush Functionalization of Flat Silicon Dioxide Surface and Microreactor.** *Poly-3-sulfopropyl Methacrylate.* Immobilization of the trichlorosilane initiator and the PSPM brushes were carried out following literature procedures.<sup>42</sup> A solution of 3-sulfopropyl methacrylate sodium salt (4.0 g, 16.2 mmol), 2,2'-bipyridyl (156 mg, 1 mmol), and  $\text{CuBr}_2$  (5 mg, 0.02 mmol) in a 2:1 mixture of methanol and water (9 mL) was degassed using the freeze–pump–thaw method (in a sealed Schlenk vessel). This solution was transferred in a degassed flask containing  $\text{CuBr}$  (60 mg, 0.42 mmol) and stirred for 30 min to ensure the complete dissolution of the solid. Afterward, an initiator coated silicon wafer was placed in a Schlenk tube and the flask sealed with a septum. The tube was filled with argon and the monomer solution was syringed inside. For the polymerization in the device, the same solution was syringed through the microchannel until the device was completely filled. The solution was kept in contact with the silicon wafer and with the microchannel at a flow rate of 0.1  $\mu\text{L}\cdot\text{min}^{-1}$  for 45 min. After the polymerization, the silicon wafer and the microchannel were rinsed with water and methanol, and dried with a stream of nitrogen. In the next step the silicon wafers were soaked in a 2 M solution of HCl. The same solution was flowed with a flow rate of 0.1  $\mu\text{L}\cdot\text{min}^{-1}$  through the microreactor. After 2 h they were rinsed with water, acetone, and acetonitrile, and subsequently dried with a stream of nitrogen.

*Mixed Brushes of Poly-2-hydroxyethyl Methacrylate and Poly-3-sulfopropyl Methacrylate.* A 1:1 molar ratio of the two monomers 2-hydroxyethyl methacrylate (1.95 g, 15 mmol) and 3-sulfopropyl methacrylate potassium salt (3.69 g, 15 mmol) were dissolved in a 3:1 solvent mixture of methanol and water (12 mL). To this solution were added 2,2'-bipyridyl (281 mg, 1.8 mmol) and  $\text{CuBr}_2$  (8.4 mg, 0.04 mmol). The resulting mixture was degassed using the freeze–pump–thaw method (in a sealed Schlenk vessel). This solution was transferred in a degassed flask containing  $\text{CuBr}$  (107 mg, 0.75 mmol) and stirred for 30 min to ensure the complete dissolution of the solid. Afterward an initiator coated silicon wafer was placed in a Schlenk tube and the flask sealed with a septum. The tube was filled with argon and the monomers solution was syringed inside. For the polymerization in the device, the same solution was syringed through the microchannel until the device was completely filled. The solution was kept in contact with the silicon wafer and with the microchannel at a flow rate of 0.1  $\mu\text{L}\cdot\text{min}^{-1}$  for 40 min. After the polymerization, the silicon wafer and the microchannel were rinsed with water and methanol, and dried with a stream of nitrogen. In the next step, the silicon wafers were soaked in a 2 M solution of HCl. The same solution was flowed with a flow rate of 0.1  $\mu\text{L}\cdot\text{min}^{-1}$  through the microreactor. After 2 h, they were rinsed with water, acetone, and acetonitrile, and subsequently dried with a stream of nitrogen.

The same procedure was followed for the growth of the 2:1 PSPM–PHEMA (20 mmol SPM, 10 mmol HEMA) and 1:2 PSPM–PHEMA (10 mmol SPM, 20 mmol HEMA) brush systems.

*Mixed Brushes of Poly(methyl methacrylate) and Poly-3-sulfopropyl Methacrylate.* These mixed polymer brushes were prepared using a 1:1 monomer molar ratio and following the same procedure as described for the PSPM–PHEMA mixed brushes.

**Catalytic Reactions Inside the Microreactor.** Benzaldehyde dimethyl acetal (3; BDMA, 10 mM) and water (100 mM) were dissolved in dry acetonitrile and passed through a 13  $\mu\text{L}$  internal volume microreactor kept at room temperature at flow rates varying from 10  $\mu\text{L}\cdot\text{min}^{-1}$  to 1  $\mu\text{L}\cdot\text{min}^{-1}$ . The reaction products were collected and analyzed off-line by GC. For the kinetic study within a PSPM and PSPM–PHEMA-functionalized microreactors, the concentration of BDMA was varied in the range 10–30 mM and the concentration of water was kept constant at 100 mM. Flow rates from 13  $\mu\text{L}\cdot\text{min}^{-1}$  to 2  $\mu\text{L}\cdot\text{min}^{-1}$  were used. The experimental error in these measurements is  $\pm 4\%$ .

2-Benzyl tetrahydropyranil ether (5) was synthesized according to a literature procedure.<sup>48</sup> A 10 mM solution of 5 in dry acetonitrile was passed through the 1:1 PSPM–PHEMA-functionalized microreactor

at room temperature at a flow rate of 1  $\mu\text{L}\cdot\text{min}^{-1}$ . The reaction product was collected and analyzed off-line by GC.

## ■ ASSOCIATED CONTENT

### Supporting Information

Transmission FT-IR spectrum of a 1:1 PSPM–PHEMA-functionalized flat  $\text{SiO}_2$  surface. XPS data measured on a flat  $\text{SiO}_2$  surface for PSPM, 1:1 PSPM–PHEMA, 2:1 PSPM–PHEMA, and 1:2 PSPM–PHEMA. Microreactor features. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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### Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

### Notes

The authors declare no competing financial interest.

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