

SuFEx on the Surface: A Flexible Platform for Postpolymerization Modification of Polymer Brushes

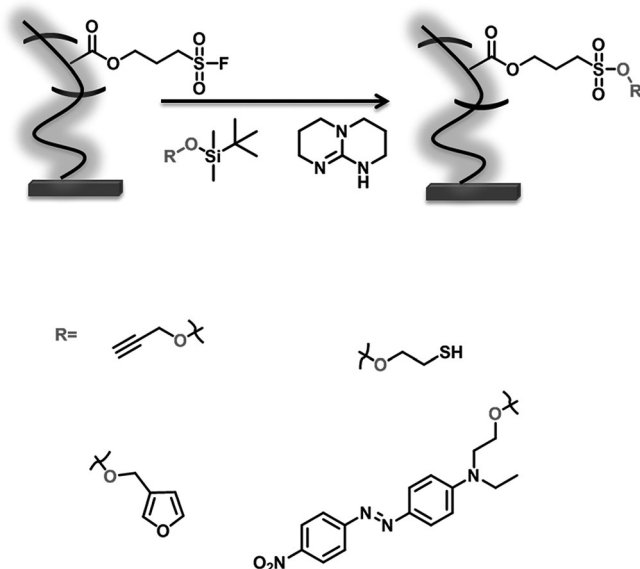
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Abstract: Polymer brushes present a unique architecture for tailoring surface functionalities due to their distinctive physicochemical properties. However, the polymerization chemistries used to grow brushes place limitations on the monomers that can be grown directly from the surface. Several forms of click chemistry have previously been used to modify polymer brushes by postpolymerization modification with high efficiency, however, it is usually difficult to include the unprotected moieties in the original monomer. We present the use of a new form of click chemistry known as SuFEx (sulfur(VI) fluoride exchange), which allows a silyl ether to be rapidly and quantitatively clicked to a polymer brush grown by free-radical polymerization containing native $-SO_2F$ groups with rapid pseudo-first-order rates as high as 0.04 s^{-1} . Furthermore, we demonstrate the use of SuFEx to facilely add a variety of other chemical functional groups to brush substrates that have highly useful and orthogonal reactivity, including alkynes, thiols, and dienes.

Over the past decade, reactions involving click chemistry have become essentially a standard coupling strategy used to covalently immobilize or conjugate a variety of simple and complex molecules in the chemical and biological sciences.^[1–3] These chemistries have also had an equally important impact on surface science, as they allow the attachment of complex or delicate molecules with high fidelity, speed, and conversion to solid or particle supports.^[3–7] Conversely, click chemistries can be used to attach polymers to substrates, one another, or add functionality along the backbone in an efficient and orthogonal manner.^[8–10] Polymer brushes have emerged at the forefront of surface functionalization due to the unique physicochemical properties of stretched polymer chains and the ability to have a high density of functional groups in a given area. Also, the functionalization of reactive polymer brushes through highly efficient forms of postpolymerization modification (PPM) reactions has emerged as an expanding field.^[11–17] By combining the unique properties of polymer brushes and click chemistry PPM, surfaces with desirable and unique properties can be quickly generated without laborious monomer or polymer synthesis. The ability to use a variety of coupling strategies, especially highly robust and efficient click chemistries, is particularly important for decorating surfaces

with multiple functionalities.^[18–21] However, some click reactions have inherent drawbacks such as oxygen sensitivity or difficult synthetic access. Our lab has already demonstrated several uses of PPM click chemistry on polymer brushes to design complex interfaces.^[21] Herein, we demonstrate the application of a new form of click chemistry, sulfur(VI) fluoride exchange (SuFEx), for the efficient functionalization of polymer brushes, with the aim towards increasing the ability to functionalize surfaces in an orthogonal fashion. We also believe that SuFEx provides a simple platform to graft other challenging functional groups that are intolerant of the required polymerization conditions, such as other click motifs, to brush surfaces.

The sulfur–fluoride exchange reaction, which was recently revived from an unrecognized state by the Sharpless group,^[22] is based on the unique reactivity of sulfonyl fluorides. Unlike electrophilic sulfonyl chlorides, sulfonyl fluorides are generally unreactive under a wide variety of harsh reaction conditions.^[22] However, in the presence of certain non-nucleophilic bases, such as diazabicycloundec-7-ene (DBU), or 2-*tert*-butyl-imino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diaza-phosphorine (BEMP), it has been previously demonstrated that sulfonyl fluorides will undergo exchange with silyl ethers in a highly selective fashion to form a new S–O bond (Scheme 1). This reaction is driven by the thermodynamically favorable formation of a Si–F bond (bond dissociation energy 565 kJ mol^{-1}).^[23] Other sulfonyl



Scheme 1. Top: Synthetic scheme for SuFEx brushes. Bottom: Selection of reactive functionalities for PPM of p(FSPMA) brushes.

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halides are much less suitable for this reaction due to their higher degree of $\text{SO}_2\text{-X}$ bond hydrolyzability and the lower Si-X bond formation energy (Si-Cl 456 kJ mol^{-1} , Si-Br 343 kJ mol^{-1} , Si-I 399 kJ mol^{-1}). The exact mechanism of the exchange has not been completely elucidated, but Gembus et al. hypothesized that a sulfonyl ammonium fluoride salt is formed by the reaction of an amine with the sulfonyl fluoride, which can then react with the silyl ether to form a sulfonate ester plus inert silyl fluoride.^[24]

In order to explore SuFEx chemistry on surfaces, a sulfonyl fluoride monomer, 3-(fluorosulfonyl)propyl methacrylate (FSPMA) monomer, was synthesized in two steps from sodium 3-(methacryloyloxy)propane-1-sulfonate (Supporting Information). Next, p(FSPMA) brushes were grown from an azo-based silane initiator monolayer using radical polymerization initiated with UV light.^[25] Brushes of ca. 25 nm were grown by this method, and the solution polymer was isolated and analyzed by GPC to obtain molecular weight data in order to estimate the grafting density of the brushes (0.14 chains/ nm^2). The p(FSPMA) brushes demonstrated excellent reactivity with silyl ethers in the presence of certain non-nucleophilic amines, which is consistent with the SuFEx reaction in solution, albeit with some interesting differences. These brushes were then explored to examine the suitability for efficient and highly specific postpolymerization modification. Triazabicyclodecene (TBD), a new catalyst for this reaction, was also investigated for its suitability for SuFEx.

Many of the chemical functional groups involved in the most widely used click chemistries are either incompatible or lead to complications with free radical polymerization. These functionalities include unprotected terminal alkynes and azides for CuAAC (Cu^I catalyzed azide/alkyne cycloaddition), thiols and alkenes for Michael addition, and dienes or dienophiles for Diels–Alder. Thiol–ene/yne chemistry, which, while not strictly a click reaction, shares several important traits such as fast kinetics and modularity, and is also not compatible with radical polymerization to high molecular weight because of chain transfer and/or cross-linking. Sulfonyl fluorides are tolerant of free radical polymerization conditions, and we also illustrate that p(FSPMA) brushes are an excellent platform to add some of these other reactive moieties to surface through easily synthesized *tert*-butyldimethylsilyl (TBDMS) protected alcohol precursors (Scheme 1).

Figure 1 shows the grazing incidence attenuated total reflection infrared spectrum (GATR-IR) of the p(FSPMA) brushes grown by free radical polymerization along with subsequent PPM with the different TBDMS precursors shown in Scheme 1. The p(FSPMA) brushes (Figure 1A) display the spectral features apparent in the monomer, such as C=O ester stretches at 1731 and 1236 cm^{-1} , symmetrical and asymmetrical S=O stretches of the sulfonyl fluoride at 1405 and 1200 cm^{-1} , and an S-F stretch at 816 cm^{-1} . After immersion in acetonitrile (MeCN) with DBU or TBD and a silyl ether protected molecule (propargyloxy-TBDMS, mercaptoethoxy-TBDMS, furfuryloxy-TBDMS, Figure 1B–D, respectively) at ambient temperature and open to atmosphere, spectral features of sulfonate ester formation appear. The S=O symmetrical stretch completely shifts to 1338 cm^{-1} , while the peaks at 1158 and 1038 cm^{-1} are assigned to the S-O

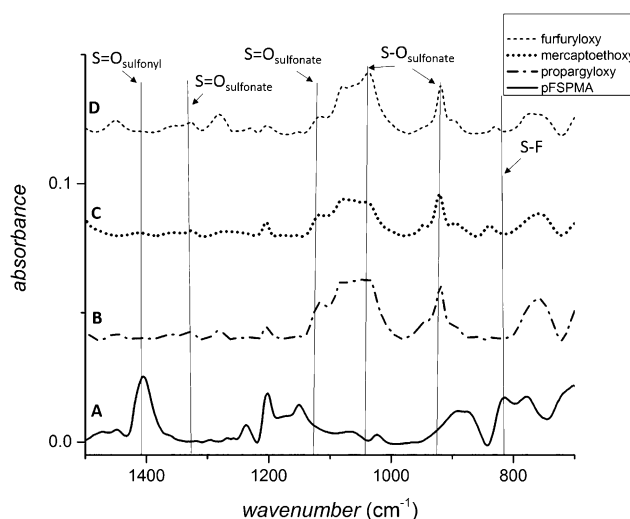


Figure 1. GATR-FTIR spectra of p(FSPMA) brush and PPM brushes. A) p(FSPMA), B) propargyloxy brush, C) mercaptoethoxy brush, D) furfuryloxy brush. Spectra were vertically shifted for clarity; y axis corresponds to spectrum (A).

stretches. Also in each case, the S-F stretch at 816 cm^{-1} disappears. We also observed the complete disappearance of fluorine (0.7 keV) on the surface by electron dispersive X-ray spectroscopy after each functionalization (Supporting Information).

UV/Vis data was obtained by dipping p(FSPMA) brush functionalized glass slides in solutions containing a catalyst and silyl ether protected Disperse Red 1, rinsing with good solvent, then monitoring the appearance of the Disperse Red 1 dye peak at 486 nm. These studies established that in the brush system, assuming pseudo-first-order kinetics, the rates of reaction for the TMS (trimethylsilyl) and TBDMS protected Disperse Red 1 (DR1) in the presence of DBU were similar ($k_{\text{TMS}} = 0.001 \text{ s}^{-1}$ vs $k_{\text{TBDMS}} = 0.0007 \text{ s}^{-1}$) (Figure 2). Rate constants were obtained during the portion of the functionalization reaction where substrate absorbance increased linearly with reaction time, before steric constraints and lowered SO_2F availability changed reaction dynamics (Supporting Information). The similarity of DBU surface reaction rate constants of TMS and TBDMS derivatives contradicts other reports where the reaction is carried out in homogeneous solution, and it was observed that SuFEx reactions with TBDMS derivatives are generally less favorable and may require heating to start the reaction.^[24,26] Also, we observed when using TBD as a catalyst, the reaction rate increased more than an order of magnitude ($k' = 0.038 \text{ s}^{-1}$) with the same TBDMS-DR1. The fact that TBD exhibits more than an order of magnitude faster SuFEx kinetics than DBU while still using the TBDMS derivative makes it a superior choice as a catalyst for SuFEx. A brush reaction rate constant of $k' = 0.038 \text{ s}^{-1}$ is comparable to the rate constant previously established for CuAAC in polymer brushes ($k' = 0.02 \text{ s}^{-1}$).^[27] The functional group density of dye molecules on the surface after reaction completion is similar to what was obtained using activated ester brushes

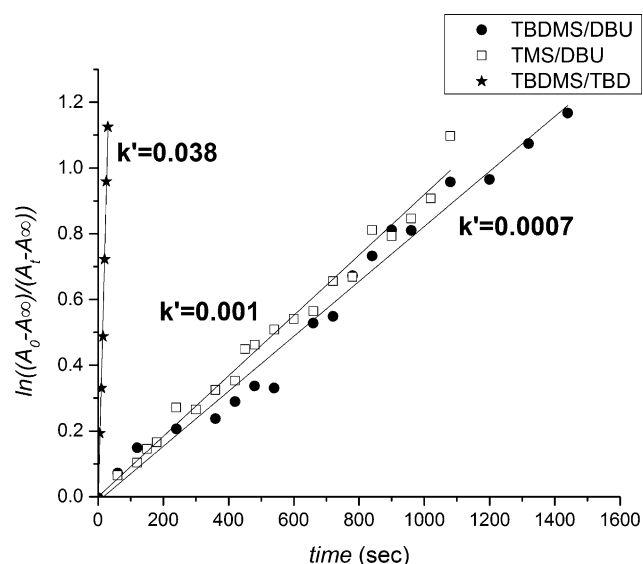


Figure 2. Pseudo-first-order kinetic plot of the linear region of DR1-silyl ether derivatives undergoing SuFEx with p(FSPMA) brush glass substrates. (●) TMS-DR1 catalyzed by DBU, (□) TBDMS-DR1 catalyzed by DBU, (★) TBDMS-DR1 catalyzed by TBD.

(3.62 dye molecules/nm³ for SuFEx vs 3.60 dye molecules/nm³ for pentafluorophenol based activated esters),^[25] indicating that the reaction has proceeded to very high conversion.

With the much greater hydrolytic stability of the TBDMS protecting group (which can survive aqueous workup), and the high reaction rate constant in the presence of TBD, it was selected as the silyl ether protecting group of choice for surface SuFEx. Dry MeCN was used to start the experiments, but no precautions were taken to exclude air or water in any of the PPM experiments.

In the interest of widening the scope of molecules that can be attached to polymer brush coatings, we used SuFEx to graft a cross-section of moieties that are suitable for additional PPM reactions. After synthesizing the TBDMS protected versions, propargyl alcohol, mercaptoethanol, and furfuryl alcohol were all successfully reacted with brush surfaces by SuFEx. Table 1 shows the increase in thickness measured by spectroscopic ellipsometry and changes in the contact angle of the substrates for each PPM, along with the GATR-IR spectra in Figure 1B–D. These functionalities can then be used for subsequent PPM through CuAAC, thiol-ene/yne, thio-Michael addition, and furan/maleimide Diels–Alder cycloaddition.

The use of SuFEx to functionalize polymer brushes is simple, quantitative and proceeds with rapid reaction kinetics.

Table 1: Thickness increases and contact angle changes after PPM of p(FSPMA) brush surfaces with reactive molecules.

Substrate coating	Thickness increase [%]	Contact angle [°]
p(FSPMA) brush (25 nm)	N/A	78
propargyloxy	38	67
mercaptoethoxy	34	15
furfuryloxy	27	83

In fact, in our experience, surface PPM using SuFEx is even more facile to conduct than previously reported SuFEx in homogenous solution as the reaction proceeds rapidly with TBDMS derivatives at room temperature, which are considerably more hydrolytically stable than TMS derivatives. In addition, the surface reaction requires only minute amounts of catalyst and reagent. We have also confirmed that TBD, which is a commonly available commercial ring opening polymerization catalyst, is an excellent new choice for the expedient SuFEx functionalization of brushes. Using TBD, PPM is completed in just a few minutes and should replace DBU as an economical catalyst for these reactions, and perhaps in solution SuFEx as well. Sharpless et al. also noted the efficacy of 2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine (BEMP), an organic phosphazene base, as a catalyst for SuFEx bulk or solution polymerization,^[26] which was not explored in this study.

The selection of highly efficient, robust, and specific chemistries available for efficient PPM of polymer brush surfaces has generally been limited to systems with oxygen sensitivity or incompatibility with free-radical polymerization conditions (CuAAC, Diels–Alder, thio-Michael addition, and thiol-ene/yne), hydrolytic instability (activated esters), or more difficult handling or synthesis (oximes and tetrazoles). SuFEx appears to be an alternative click chemistry with a broad functionality scope, tolerance to ambient conditions, easy synthesis, and compatibility with a wide variety of reaction conditions, most notably radical polymerization. The reaction is unidirectional, fast, high yielding, and produces only inert silyl fluorides as a byproduct. In addition, the functional group counterparts (TBDMS ethers and sulfonyl fluorides) can coexist in a dormant state under ambient conditions until activated by the addition of a catalyst. SuFEx is highly suitable for the addition of new functionalities to polymer brush backbones, especially other click moieties, which opens a vast library of compounds that can now be attached to polymer surfaces after a single facile PPM step.

Experimental Section

Equipment: FTIR studies were done using a Thermo-Nicolet model 6700 spectrometer equipped with a variable angle grazing angle attenuated total reflection (GATR-ATR) accessory (Harrick Scientific) at 64 scans with 4 cm^{−1} resolution. Polymerization was conducted in a Rayonet RPR-600 Mini UV reactor using 350 nm bulbs. Thickness was determined on a J. A. Woollam M-2000 V spectroscopic ellipsometer with a white light source at three angles of incidence (65°, 70°, and 75°) to the silicon wafer normal. A Cauchy model was used to fit the film thickness, extinction coefficient, and refractive index of the polymer brush layer. Static contact angle measurements were taken on a Krüss DSA 100 using a 1 μL drop of 18 MΩ water (pH 7). UV/Vis studies were performed on a Varian Cary 50 UV-Vis Spectrophotometer.

Synthesis of p(FSPMA) brushes: In a glovebox, plasma cleaned slides were immersed for 16 hr in a 10 mM dry toluene solution of azo-based silane initiator prepared according to Arnold et al. to form an photoinitiator monolayer.^[25] Slides were removed from the glovebox and sonicated in dry toluene. FSPMA was degassed with Ar for 2 h. Both the slides and degassed FSPMA were then brought into the glovebox. Slides were placed in glass vials with 0.3 mL FSPMA and tightly sealed using Teflon tape. Vials were removed from the

glovebox and irradiated with 350 nm light (1.25 mW cm^{-2}) in a UV reactor for 2 h. Slides were removed from the vials and sonicated with THF to remove any physisorbed polymer.

Postpolymerization modification of brushes: 0.1 mmol of a silyl ether protected molecule was dissolved in 2 mL of MeCN, and the substrate was added along with a small stir bar. 0.02 mmol of either DBU or TBD was added, and the p(FSPMA) substrate immersed in the solution for 2 h at room temperature for DBU or 3 min for TBD. The substrate was then washed with CH_2Cl_2 and isopropanol.

UV/Vis study: p(FSPMA) brush functionalized glass slides were measured on a UV-Vis spectrometer using a slide holder accessory with a sample window area of 19.6 mm^2 . The functionalized slide was immersed in 2 mL of 0.1 mmol Disperse Red 1 silyl ether and 0.02 mmol DBU or TBD in 2 mL MeCN. The slides were rinsed thoroughly prior to each measurement. The rate of substitution of Disperse Red 1 onto the polymer brush was measured by monitoring the appearance of the dye peak at 486 nm with time, and a kinetic plot was generated.

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- [1] H. C. Kolb, M. G. Finn, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2001**, *40*, 2004–2021; *Angew. Chem.* **2001**, *113*, 2056–2075.
- [2] H. C. Kolb, K. B. Sharpless, *Drug Discovery Today* **2003**, *8*, 1128–1137.
- [3] P. Espeel, F. E. Du Prez, *Macromolecules* **2015**, *48*, 2–14.
- [4] H. Nandivada, X. Jiang, J. Lahann, *Adv. Mater.* **2007**, *19*, 2197–2208.
- [5] R. K. Iha, K. L. Wooley, A. M. Nyström, D. J. Burke, M. J. Kade, C. J. Hawker, *Chem. Rev.* **2009**, *109*, 5620–5686.
- [6] B. S. Sumerlin, A. P. Vogt, *Macromolecules* **2010**, *43*, 1–13.
- [7] D. P. Nair, M. Podgórski, S. Chatani, T. Gong, W. Xi, C. R. Fenoli, C. N. Bowman, *Chem. Mater.* **2014**, *26*, 724–744.
- [8] C. J. Hawker, V. V. Fokin, M. G. Finn, K. B. Sharpless, *Aust. J. Chem.* **2007**, *60*, 381–383.
- [9] C. Barner-Kowollik, A. J. Inglis, *Macromol. Chem. Phys.* **2009**, *210*, 987–992.
- [10] C. Barner-Kowollik, F. E. Du Prez, P. Espeel, C. J. Hawker, T. Junkers, H. Schlaad, W. Van Camp, *Angew. Chem. Int. Ed.* **2011**, *50*, 60–62; *Angew. Chem.* **2011**, *123*, 61–64.
- [11] W. Senaratne, L. Andruzzi, C. K. Ober, *Biomacromolecules* **2005**, *6*, 2427–2448.
- [12] H. Murata, O. Prucker, J. Rühle, *Macromolecules* **2007**, *40*, 5497–5503.
- [13] S. V. Orski, K. H. Fries, G. R. Sheppard, J. Locklin, *Langmuir* **2010**, *26*, 2136–2143.
- [14] L. Q. Xu, D. Wan, H. F. Gong, K.-G. Neoh, E.-T. Kang, G. D. Fu, *Langmuir* **2010**, *26*, 15376–15382.
- [15] T. N. Gevrek, T. Bilgic, H.-A. Klok, A. Sanyal, *Macromolecules* **2014**, *47*, 7842–7851.
- [16] M. Dübner, T. N. Gevrek, A. Sanyal, N. D. Spencer, C. Padeste, *ACS Appl. Mater. Interfaces* **2015**, *7*, 11337–11345.
- [17] A. de Los Santos Pereira, N. Y. Kostina, M. Bruns, C. Rodriguez-Emmenegger, C. Barner-Kowollik, *Langmuir* **2015**, *31*, 5899–5907.
- [18] R. M. Hensarling, V. A. Doughty, J. W. Chan, D. L. Patton, *J. Am. Chem. Soc.* **2009**, *131*, 14673–14675.
- [19] P. L. Golas, K. Matyjaszewski, *Chem. Soc. Rev.* **2010**, *39*, 1338–1354.
- [20] S. B. Rahane, R. M. Hensarling, B. J. Sparks, C. M. Stafford, D. L. Patton, *J. Mater. Chem.* **2012**, *22*, 932–943.
- [21] R. M. Arnold, D. L. Patton, V. V. Popik, J. Locklin, *Acc. Chem. Res.* **2014**, *47*, 2999–3008.
- [22] J. Dong, L. Krasnova, M. G. Finn, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2014**, *53*, 9430–9448; *Angew. Chem.* **2014**, *126*, 9584–9603.
- [23] J. E. Huheey, E. A. Keiter, R. L. Keiter, *Inorganic Chemistry: Principles of Structure and Reactivity*, Harper Collins, New York, **1983**.
- [24] V. Gembus, F. Marsais, V. Levacher, *Synlett* **2008**, *2008*, 1463–1466.
- [25] R. M. Arnold, G. R. Sheppard, J. Locklin, *Macromolecules* **2012**, *45*, 5444–5450.
- [26] J. Dong, K. B. Sharpless, L. Kwisnek, J. S. Oakdale, V. V. Fokin, *Angew. Chem. Int. Ed.* **2014**, *53*, 9466–9470; *Angew. Chem.* **2014**, *126*, 9620–9624.
- [27] S. V. Orski, G. R. Sheppard, S. Arumugam, R. M. Arnold, V. V. Popik, J. Locklin, *Langmuir* **2012**, *28*, 14693–14702.

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