Langmuir

Letter

pubs.acs.org/Langmuir

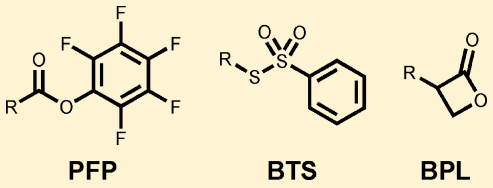
New Functionalizable Alkyltrichlorosilane Surface Modifiers for Biosensor and Biomedical Applications

Christophe Blaszykowski, Sonia Sheikh, Pasquale Benvenuto, and Michael Thompson*

Department of Chemistry, University of Toronto, 80 St. George Street, Toronto, ON, Canada M5S 3H6

Supporting Information

ABSTRACT: We report herein three unprecedented alkyltrichlorosilane surface modifiers bearing pentafluorophenyl ester (PFP), benzothiosulfonate (BTS), or novel β-propiolactone (BPL) functionalizable terminal groups. Evidence is provided that these molecules can be prepared in very high purity (as assessed by NMR) through a last synthetic step of Pt-catalyzed alkene hydrosilylation then directly employed, without further purification, for the surface modification of quartz and medical grade stainless steel. Subsequent on-surface functionalizations with amine and thiol model molecules demonstrate the potential of these molecular adlayers to be important platforms for future applications in the bioanalytical and biomedical fields.



Trichlorosilane self-assembling monolayer (SAM) chemistry constitutes a method of choice for the rapid and inexpensive preparation of thin organic films on various hydroxylated and oxide-bearing surfaces such as silicon or tin-doped indium oxides.[1] In practice, customizable molecules are engineered for surface modification purposes to spontaneously form ordered molecular assemblies with the aim of permanently altering the electronic,[2] surface energy,[3] or fouling properties[4] of underlying substrates. These properties are important in many surface science-related disciplines such as molecular optoelectronics and biosensor technology. Such molecules possess highly reactive trichlorosilyl tail functions (Cl_3Si-) that enable robust and durable anchorage to the substrate via covalent polysiloxane networks. They also contain long organic backbones, generally of the alkyl or oligoethylene glycol variety, to drive self-assembly and provide rigidity, order, and extra stability to the SAM through intermolecular interactions.[1,5] Molecules with distal functionalizable head groups can also be designed to covalently and site-specifically immobilize, post-assembly, various biomolecules such as polypeptides[6] and oligonucleotides,[7] in a single step without the need of preactivation. These features endow this type of surface-modifying molecule with a unique position for tethering biological entities to inorganic substrates, in a durable and controlled manner. This is of particular interest for the development of biosensing platforms and biomimetic hybrid materials.

There is, however, a recurrent practical issue associated with the trichlorosilyl moiety.[8] This concerns its high reactivity, which primarily renders trichlorosilane surface modifiers extremely moisture sensitive and requires that their synthesis, handling, and storage be performed under rigorously anhydrous conditions. Synthetically, the trichlorosilyl moiety only tolerates the presence of a limited number of functional groups. This restricts the diversity and complexity of surface modifiers, especially with respect to their functionalizable head group. Moreover, the purification of such sensitive molecules often constitutes a demanding and difficult task.[8] One convenient option to circumvent these drawbacks consists of installing the desired head groups post-assembly, onto SAMs constructed from simpler surface modifiers possessing chemically compatible and modifiable terminal groups. In fact, siloxane-anchored SAMs have long been shown to offer a stable foundation onto which various synthetic modifications can be reproduced from solution,[9] steadily diversifying the scope of available surface functionalities over the years.[9−11] This multistep alternative route is sometimes preferred over cumbersome synthetic and attendant purification procedures.[12]

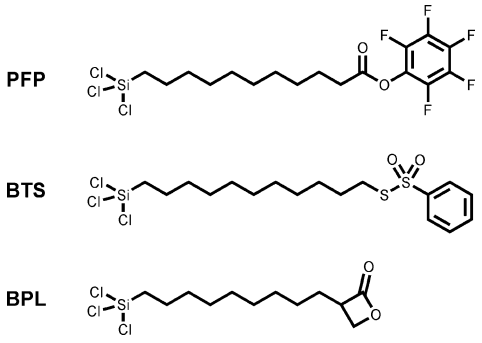
In this context, we describe herein the straightforward and purification-free synthesis of three unprecedented alkyltrichlorosilane surface modifiers possessing pentafluorophenyl ester (PFP), benzothiosulfonate (BTS), or novel β-propiolactone (BPL) functionalizable head groups (Scheme 1). The procedure produces very high purity molecules (as assessed by NMR) that can be directly engaged for the surface modification of quartz and medical grade stainless steel. Subsequent on-surface functionalizations, with amine and thiol probe molecules, are also presented.

Surface engineering using trichlorosilane chemistry for the development of selective biosensing platforms,[13] composite electrodes with high work function for photonic devices,[14] and antifouling biomaterials[4] is the current focus of research in our laboratory. Designing customized surface modifiers with specific attributes for a variety of purposes is thus an important component of our work. With respect to the backbone, we recently showed that incorporating single ether oxygen atoms within otherwise fully alkylated chains enables radical alteration of the fouling behavior of quartz against undiluted serum.[4] In the present paper, we present three new alkyltrichlorosilane

Received: November 1, 2011
Revised: January 17, 2012
Published: January 23, 2012

   dx.doi.org/10.1021/la2042839 | *Langmuir* 2012, 28, 2318−2322

Scheme 1. Structure of PFP, BTS, and BPL Surface Modifiers



surface modifiers, bearing pentafluorophenyl ester (PFP), benzothiosulfonate (BTS),[13] or novel β-propiolactone (BPL) functionalizable head groups for the purpose of subsequent biomolecule immobilization. The PFP moiety was selected for its ability to readily react with primary amine residues and form strong amide bonds, most importantly when implemented as head function at the surface of siloxane-anchored SAMs.[12] In this particular case, however, PFP groups were installed post-assembly using carbodiimide coupling chemistry.[12] We will later show that this extra activation step can be avoided. Thiosulfonates such as the BTS moiety are known for readily and regioselectively reacting with thiols to form disulfide bonds.[15] This feature may be of particular interest for the oriented immobilization of large biomacromolecules through cysteinyl residues.[16,17] Finally, the strained four-membered BPL ring was chosen for its potential to provide enhanced surface reactivity.

The trichlorosilyl moiety was installed last in the synthetic pathway, by Pt-catalyzed hydrosilylation of the corresponding alkene precursors [see Supporting Information (SI)].[18] These solvent-free reactions proceeded smoothly using (sub)catalytic amounts (0.1−1.0 mol %) of chloroplatinic acid hexahydrate ($H_2PtCl_6{\cdot}6H_2O$) and excesses of trichlorosilane (up to 6 equiv), at room temperature for 4.5−43 h. After removal of the volatiles under vacuum, the crude ^{1}H NMR spectra (recorded in $CDCl_3$) showed total consumption of the starting precursors as featured by the complete disappearance of their alkene moiety at $\delta \sim 5$−6 ppm (Figure 1). All three surface modifiers were obtained as thick oils in very high purity, with negligible to nondetectable amounts of the branched regioisomer or any other side-product[18] (Figure 1). In the particular case of BPL, the cleanliness of the hydrosilylation reaction was quite remarkable considering the propensity of this strained functional group to undergo ring-opening.[19] Not unexpectedly, however, an attempt to purify the BPL surface modifier (as well as BTS) by Kugelrohr distillation under vacuum (10^{-1} mmHg) produced intractable material presumably due to the low thermal stability of the compound. It is also important to note that, upon storage at ~ -10 °C, the initial oil turned into an amorphous solid that was poorly soluble into $CDCl_3$. This was

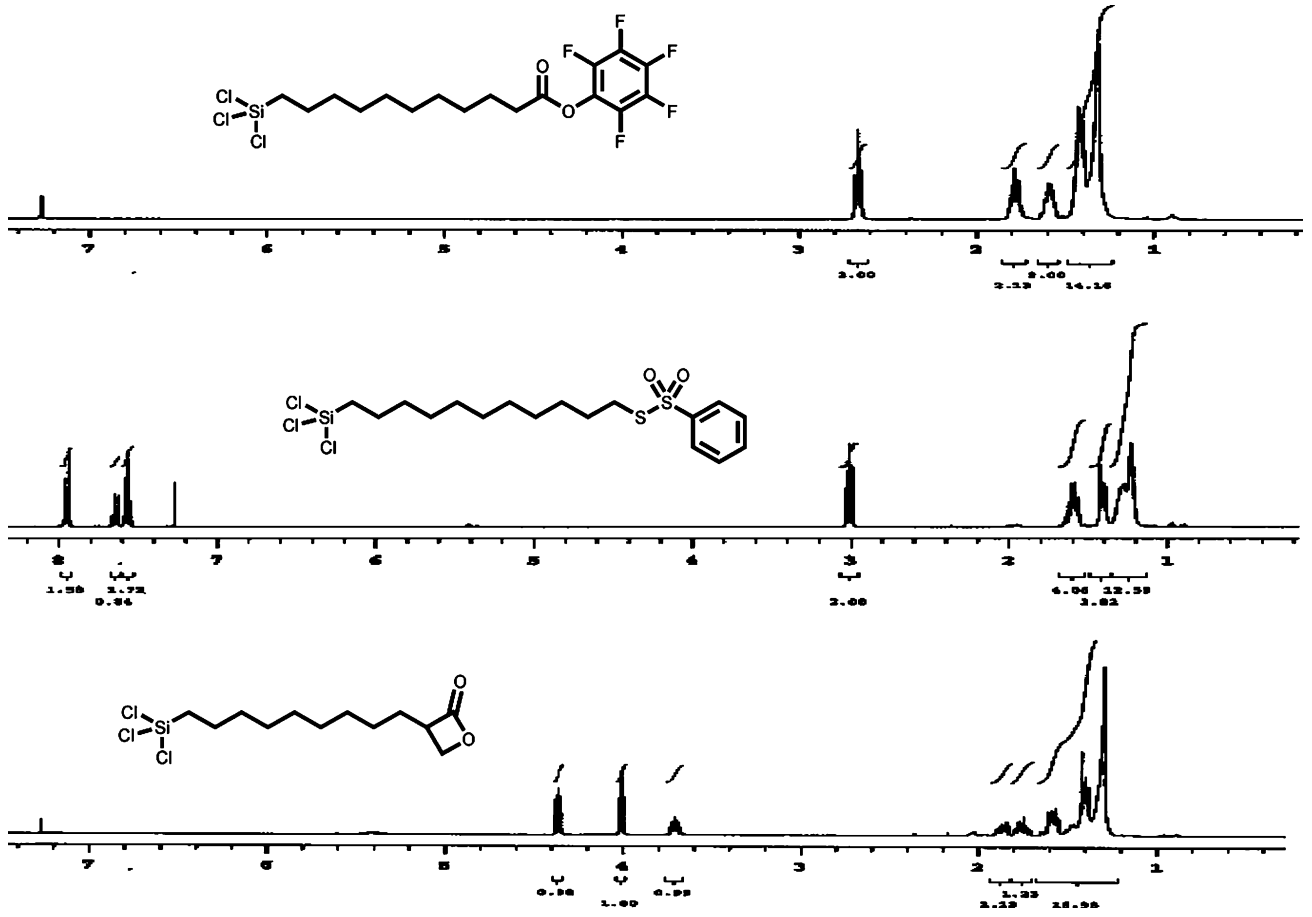
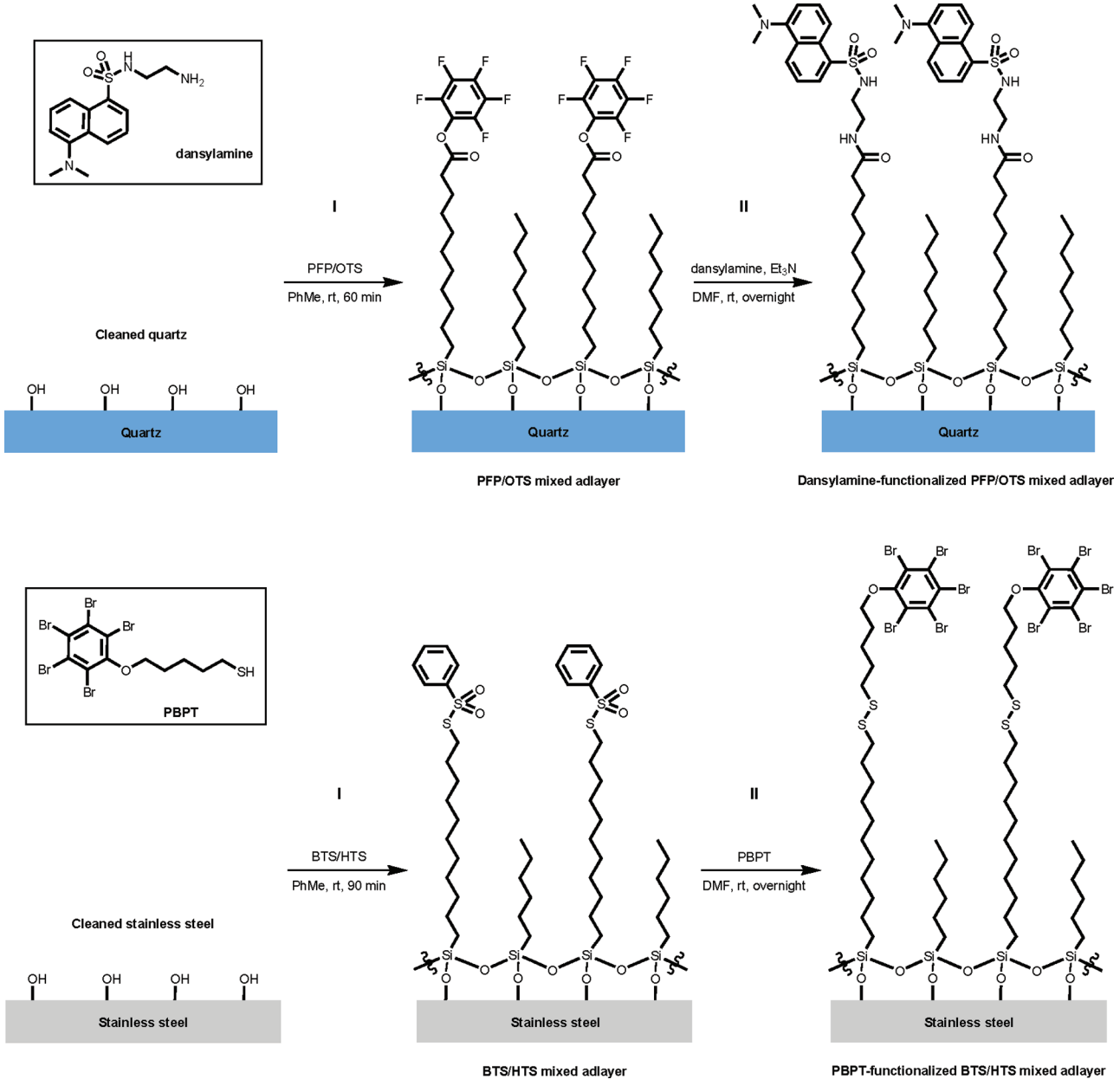


Figure 1. Crude ^{1}H NMR spectra in $CDCl_3$ for (top to bottom) PFP, BTS, and BPL surface modifiers formed by Pt-catalyzed hydrosilylation of the corresponding alkene precursors.

dx.doi.org/10.1021/la2042839 | *Langmuir* 2012, 28, 2318−2322

Scheme 2. Illustration of PFP/OTS (top) and BTS/HTS (bottom) Mixed Adlayer Formation onto Quartz and Stainless Steel, Respectively (steps I), and Their Subsequent Site-Specific Functionalization with Dansylamine and PBPT Probes, Respectively (steps II)



most likely a result of BPL engaging in a ring-opening polymerization-type reaction. ^{1}H NMR of the soluble fraction confirmed this suspicion by only displaying the characteristic signals of an opened four-membered ring at $\delta \sim 3.8-3.6$ and 2.8 ppm (see SI). No trace of intact BPL could be detected. This inopportune reactivity may unfortunately limit the potential and utility of BPL. Unlike BPL, however, PFP and BTS surface modifiers are not mere synthetic curiosities and can be successfully employed, directly as is, for the surface modification of quartz and medical grade stainless steel (Scheme 2). Quartz constitutes a substrate of choice for piezoelectric biosensors. Stainless steel is widely used in stent implant technology. Both fields are main areas of research in our laboratory.

PFP/OTS and BTS/HTS adlayers (Scheme 2) were respectively prepared upon immersion of cleaned quartz discs or stainless steel slides into 1/1/2000 (v/v/v) mixture solutions of PFP/OTS and BTS/HTS surface modifiers in anhydrous toluene, for 60−90 min at room temperature (steps I). OTS and HTS are shorter alkyltrichlorosilane codeposited "diluent" molecules whose intended role is to space out the PFP and BTS linking residues allowing them to protrude (Scheme 2).[20] This arrangement aims to decrease steric hindrance around the PFP and BTS head functions in order to offer enhanced binding ability compared to the otherwise congested undiluted assemblies. Substrate silanization was confirmed by X-ray photoelectron spectroscopy (XPS) following the appearance of the characteristic peaks of PFP (F_{1s} at 688 eV) and BTS [Si_{2p} at 103 eV, S_{2p} (sulfide) at 164 eV, and S_{2p} (sulfonyl) at 169 eV], as shown in Figure 2. However, the surface coverage and composition, degree of order, and thickness of these coatings are still unknown. As a consequence, PFP/OTS and BTS/HTS

dx.doi.org/10.1021/la2042839 | *Langmuir* 2012, 28, 2318−2322

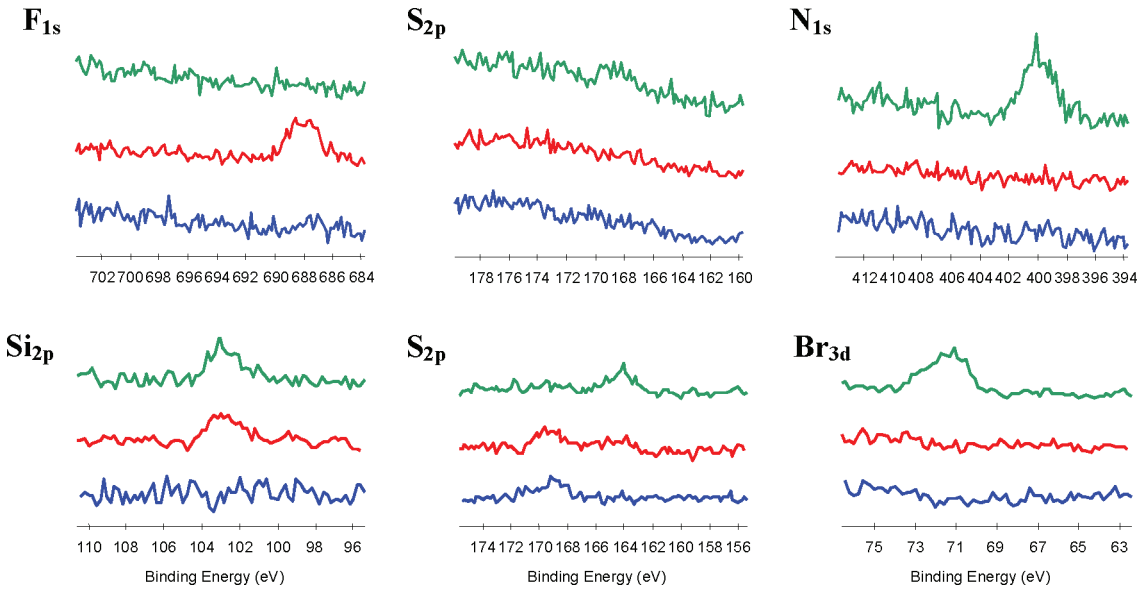


Figure 2. XPS narrow scans for the characteristic elements of (top) PFP (fluorine) and dansylamine (sulfur and nitrogen) as well as (bottom) those of BTS (silicon and sulfur) and PBPT (bromine), recorded for bare quartz and stainless steel (bottom blue curves), PFP/OTS and BTS/HTS mixed adlayers (middle red curves), as well as dansylamine- and PBPT-functionalized surfaces (top green curves). The takeoff angle is 70° relative to the normal (surface analysis).

films are herein more accurately referred to as "(mixed) adlayers" rather than genuine "SAMs". These mixed adlayers were then functionalized with dansylamine or PBPT probe in anhydrous DMF, overnight at room temperature (Scheme 2, steps II). Both modifications proceeded to completion as also determined by XPS (Figure 2). With respect to the PFP/OTS system, the F_{1s} peak completely disappeared while signals for the sulfur (S_{2p} at 169 eV) and nitrogen (N_{1s} at 400 eV) elements present in dansylamine appeared (Figure 2, top). This indicates that the probe had effectively bound through an amide bond with elimination of the PFP group. It is also worth noting that dansylthiol, the thiolated homologue of dansylamine (see SI), binds almost as well with only <10% of the F_{1s} signal remaining upon reaction. In the case of the BTS/HTS system, the appearance of a peak for bromine (Br_{3d} at 71 eV) and the sole disappearance of the S_{2p} sulfonyl peak at 169 eV collectively show that the PBPT probe had successfully bound through a disulfide bond, in place of the benzosulfonyl residue (Figure 2, bottom). Failure of the methyl thioether version of PBPT to bind corroborated that the thiol probe had attached covalently to the BTS/HTS adlayer and not merely physisorbed to its surface.

In summary, we have reported herein three new alkyltrichlorosilane surface modifiers bearing pentafluorophenyl ester (PFP), benzothiosulfonate (BTS), or novel β-propiolactone (BPL) functionalizable terminal groups. These molecules were prepared from the corresponding alkene precursors through a highly efficient and purification-free Pt-catalyzed hydrosilylation procedure that produced very high purity material (as assessed by NMR). It was also successfully demonstrated that both PFP and BTS surface modifiers could be directly utilized for the surface modification of quartz and medical grade stainless steel. Lastly, subsequent on-surface functionalizations with amine and thiol model molecules revealed the potential of these molecular adlayers to be important platforms for future applications in the bioanalytical and biomedical fields.

■ ASSOCIATED CONTENT

Supporting Information

Synthesis, characterization, and ^{1}H NMR spectra for PFP, BTS, and BPL surface modifiers as well as dansyl and PBPT probes. Procedures for quartz disc and stainless steel slide cleaning, substrate silanization, and probe immobilization. Angle-resolved X-ray photoelectron spectroscopy for substrate silanization and probe immobilization. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: mikethom@chem.utoronto.ca. Tel: (416) 978 3575.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the Natural Sciences and Engineering Research Council of Canada (NSERC) for support, Drs. Peter Brodersen and Rana Sodhi from *Surface Interface Ontario* for XPS analysis, as well as Sean F. Robertson for help with BTS/HTS experiments.

■ REFERENCES

(1) Ulman, A. *Adv. Mater.* **1990**, *2* (12), 573−582.
(2) Gozlan, N.; Haick, H. *J. Phys. Chem. C* **2008**, *112* (33), 12599−12601.
(3) Janssen, D.; De Palma, R.; Verlaak, S.; Heremans, P.; Dehaen, W. *Thin Solid Films* **2006**, *515* (4), 1433−1438.
(4) Sheikh, S.; Yang, D. Y.; Blaszykowski, C.; Thompson, M. *Chem. Commun.* **2012**, *48* (9), 1305−1307.
(5) Ulman, A. *Chem. Rev.* **1996**, *96* (4), 1533−1554.
(6) Lee, Y. W.; Reed-Mundell, J.; Zull, J. E.; Sukenik, C. N. *Langmuir* **1993**, *9* (11), 3009−3014.
(7) Wang, Y.; Prokein, T.; Hinz, M.; Seliger, H.; Goedel, W. A. *Anal. Biochem.* **2005**, *344* (2), 216−223.
(8) Barness, Y.; Gershevitz, O.; Sekar, M.; Sukenik, C. N. *Langmuir* **2000**, *16* (1), 247−251.

(9) Balachander, N.; Sukenik, C. N. *Langmuir* **1990**, *6* (11), 1621−1627.
(10) Haensch, C.; Hoeppener, S.; Schubert, U. S. *Chem. Soc. Rev.* **2010**, *39* (6), 2323−2334.
(11) See also: (a) Samanta, D.; Sarkar, A. *Chem. Soc. Rev.* **2011**, *40* (5), 2567−2592. (b) Li, J.; Thiara, P. S.; Mrksich, M. *Langmuir* **2007**, *23* (23), 11826−11835. (c) Sullivan, T.; Huck, W. T. S. *Eur. J. Org. Chem.* **2003**, *1*, 17−29. (d) Chechik, V.; Crooks, R. M.; Stirling, C. J. M. *Adv. Mater.* **2000**, *12* (16), 1161−1171.
(12) Cho, W. K.; Jung, Y. H.; Lee, K.-B.; Park, H. J.; Kim, Y.; Whang, D.; Choi, I. S. *Bull. Korean Chem. Soc.* **2006**, *27* (1), 111−114 and references therein.
(13) Sheikh, S.; Sheng, J. C.-C.; Blaszykowski, C.; Thompson, M. *Chem. Sci.* **2010**, *1* (2), 271−275.
(14) Blaszykowski, C.; Cheran, L.-E.; Thompson, M. *Can. J. Chem.* **2011**, *89* (12), 1512−1518.
(15) Parsons, T. F.; Buckman, J. D.; Pearson, D. E.; Field, L. *J. Org. Chem.* **1965**, *30* (6), 1923−1926.
(16) Bonroy, K.; Frederix, F.; Reekmans, G.; Dewolf, E.; De Palma, R.; Borghs, G.; Declerck, P.; Goddeeris, B. *J. Immunol. Methods* **2006**, *312* (1−2), 167−181.
(17) Camarero, J. A. *Biophys. Rev. Lett.* **2006**, *1* (1), 1−28.
(18) Hayashi, T. In *Comprehensive Asymmetric Catalysis I*; Jacobson, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer-Verlag Publisher: Berlin, Heidelberg, 1999; pp 319−333.
(19) Mead, K. T.; Samuel, B. *Tetrahedron Lett.* **1988**, *29* (50), 6573−6576.
(20) OTS and HTS are, respectively, octyl- and hexyltrichlorosilane.