RECYCLABLE PHASE-ANCHORED SILYLATION REAGENTS

An Undergraduate Research Scholars Thesis

by

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TABLE OF CONTENTS

ABSTRACT

Polyisobutyldimethylchlorosilane as a Recyclable Phase-Anchored Silylation Reagent

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Chlorosilanes are common protecting groups. However, in use, they introduce an extra step and after use they are discarded. As part of an effort to make these species' use greener, we have been exploring effective ways to efficiently isolate silyl-protected species and to recycle and regenerate trialkylsilylchlorides after the protecting group is removed from its substrate. Prior work in the Bergbreiter group has shown that attaching a highly nonpolar group to molecules makes them selectively soluble in nonpolar solvents. This selective solubility allows such phase-anchored species to be separated from the reaction mixture with a biphasic extraction. We have extended this work to silyl species showing that a chlorosilane with a long alkyl chain, octadecyldimethylchlorosilane can make silylated species phase-selectively soluble. This was shown by allowing octadecyldimethylchlorosilane to react with several primary alcohols to form dimethyloctadecylsilyl ethers. These ethers were placed in a DMF/cyclohexane solvent system where they showed >96% retention of the silylated alcohols in the nonpolar phase. Octadecyldimethylchlorosilane was also used as a protecting group in a palladium-catalyzed cross-coupling reaction. In this case, the silylated product could be removed from polar phase soluble catalyst residues by a simple extraction, avoiding a waste generating chromatographic purification step. To further improve phase-selectivity, we replaced the octadecyl group with

PIB, a soluble polymer support. PIB-chlorosilane was synthesized using hydrosilylation and chlorination reactions and ongoing work involves removing unreacted PIB with a PEG protection and precipitation. Octadecyldimethylsilyl triflate, a Lewis acid catalyst, was also synthesized.

ACKNOWLEDGMENTS

I would like to acknowledge my research advisor, Dr. David E. Bergbreiter, for giving me a chance to do my own research. In the course of my work, I have learned so much more about research, graduate school, and life as a chemist than I could have imagined otherwise. I can honestly say that I would not be where I am as a person without the opportunities that he has given me.

I would also like to thank Chih-Gang Chao, my research mentor, for putting up with me through the years, teaching me the practical aspects of chemistry research and helping me to develop processes to conduct research on my own.

NOMENCLATURE

DCM	Dichloromethane
DMF	Dimethylformamide
THF	Tetrahydrofuran
PIB	Polyisobutylene
PEG	Polyethylene Glycol

CHAPTER I

INTRODUCTION

Chlorosilanes are used in organic synthesis as protecting groups for various functional groups such as alcohols, alkynes, and enolates.[1-4] Other trimethylsilyl derivatives like trimethylsilyl triflate are also useful as catalysts. The attachment and deprotection of organosilyl compounds can be affected under mild conditions and can be very selective, making chlorosilanes extremely useful protecting groups. However, such reagents are discarded as waste after a reaction. As part of an effort to make these species' use greener, we have been exploring effective ways to efficiently isolate silyl-protected species and to recycle and regenerate the protecting group after it is removed from its substrate. Similar issues affect use of silyl-containing catalysts and existing silylated catalysts are typically not reusable or recyclable.

Reuse of silyl protecting groups

A few studies have attempted to recycle organosilyl species. Darling investigated cross-linked polystyrene supported chlorosilanes used as protecting groups in solid phase synthesis. These chlorosilanes can be regenerated upon treatment with BCl_3. This heterogeneous support suffers from low efficiency, and is difficult to characterize.[5] Lickiss and coworkers showed that *tert*-butyldimethyl-silanol can be converted to *tert*-butyldimethylchlorosilane, allowing it to be recycled. However, due to the volatile nature of the hemihydrate of *tert*-butyldimethylsilanol the silylating agent cannot be efficiently recycled.[6] An alternative approach that avoids the problems described above would be desirable.

Phase selective supports to facilitate product purification and reagent reuse

Prior work in the Bergbreiter group has shown that reactions can be effected using a phase-selective catalyst or reagent.[7] Phase selectivity for a catalyst or reagent is achieved by anchoring it to a highly phase-selective group, typically a soluble polymer support (Figure 1.1). Others have shown that long chain alkyl groups are also sometimes effective in achieving similar separations. After a reaction, the reaction mixture is placed in a biphasic solvent system to facilitate purification.[8,9] In this technique, solvents are chosen so that the products are in one phase and the catalyst or reagent is in the other phase. A gravity separation of the phases thus allows the reaction products to be separated from the phase-anchored species.[10] The catalyst or reagent can then be regenerated and reused.[11]

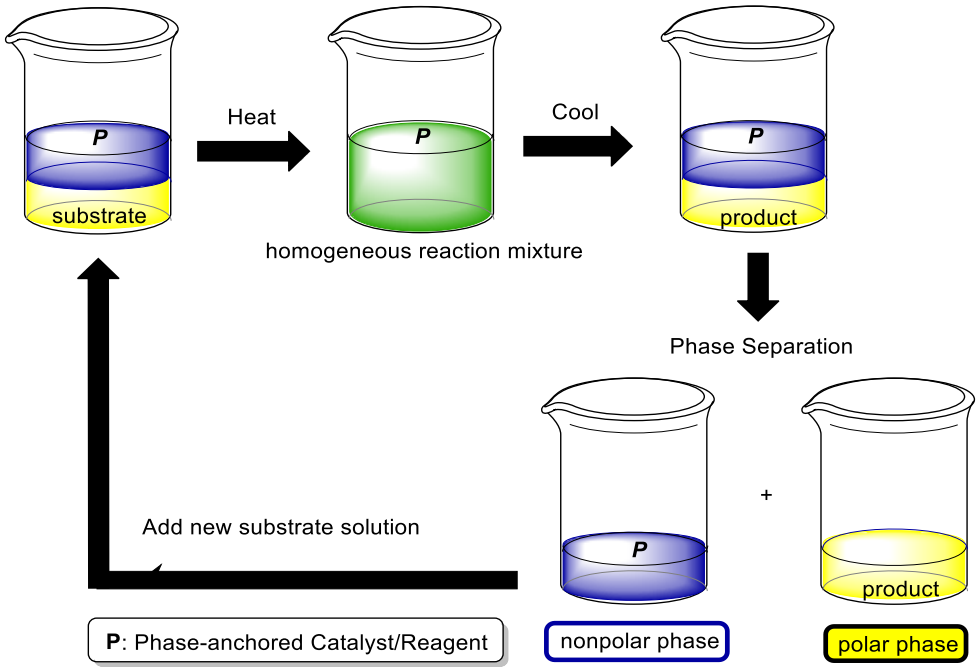


Figure 1.1. Biphasic catalysis using a thermomorphic solvent system

CHAPTER II

METHODS

General methods

All reagents were purchased from commercial sources and used without further purification unless otherwise stated. Primary alcohols were dried over 3Å molecular sieves for 4 h prior to use. THF and toluene were dried in solvent stills. Thionyl chloride ($SOCl_2$) was distilled prior to use.

^{1}H NMR spectra were recorded using Inova 300 and 500 MHz spectrometers. ^{13}C NMR spectra were recorded using Inova 75 and 125 MHz spectrometers. Data are expressed as chemical shifts in parts per million (ppm) relative to residual chloroform and $CDCl_3$ (^{1}H 7.26 ppm, ^{13}C 77.2 ppm respectively). Coupling constants (J) are given in Hertz (Hz) and rounded to the nearest 0.1 Hz. Multiplicities are as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Infrared spectra were obtained using an ATR-FTIR spectrometer. Vibrational frequencies are given in cm^{-1}.

CHAPTER III

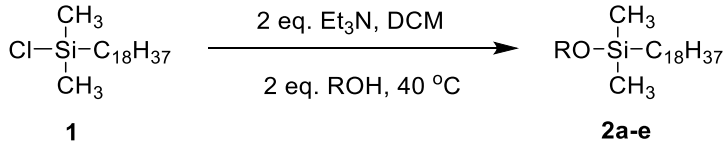
RESULTS AND DISCUSSION

Octadecyldimethylchlorosilane as a phase selective reagent

Silylating agents containing octadecyl groups are used widely to modify silica supports. The resulting supports are hydrophobic, allowing for reversed-phase chromatography (RPC). In RPC, the solid support is hydrophobic and the mobile phase is hydrophilic, making it possible to enact a larger variety of separations. We reasoned that these same molecules could be used in synthesis as phase selectively soluble silylating agents and that they could serve as handles to phase anchor suitable products in an alkane versus a polar phase.

These same silylating agents could also be recycled after use. Often, silylating agents used in chemical synthesis are discarded as waste. The phase-selectivity of octadecyldimethyl silyl groups would make them able to be separated from the product mixture, so they could be regenerated with a simple chlorination reaction. This would make the silylating agents greener, reducing the waste produced and the total amount of silylating agents used.

Scheme 3.1. Synthesis of phase-selective silyl ethers **2a-e**



1 **2a-e**

R = $-CH_3$ (85%); $-CH_2CH_3$ (85%); $-CH_2(CH_2)_2CH_3$ (87%); $-CH_2(CH_2)_4CH_3$ (89%); $-CH_2(CH_2)_8CH_3$ (87%);

To test this concept, we applied the phase-selectivity approach used in the Bergbreiter group to the issue of recycling organosilyl compounds using these same octadecyldimethyl silyl groups. In preliminary work, we successfully used octadecyldimethylchlorosilane (**1**) as a recyclable silylation reagent. This reagent was used to protect primary alcohols (Scheme 3.1).

To determine how effective a biphasic separation would be, we measured the leaching of these octadecyldimethylsilyl ethers using a DMF/cyclohexane thermomorphic solvent system. 5 mmol of an octadecyldimethylsilyl ether was dissolved in 5 mL of cyclohexane, then heated with 5 mL of DMF until a single phase was formed.

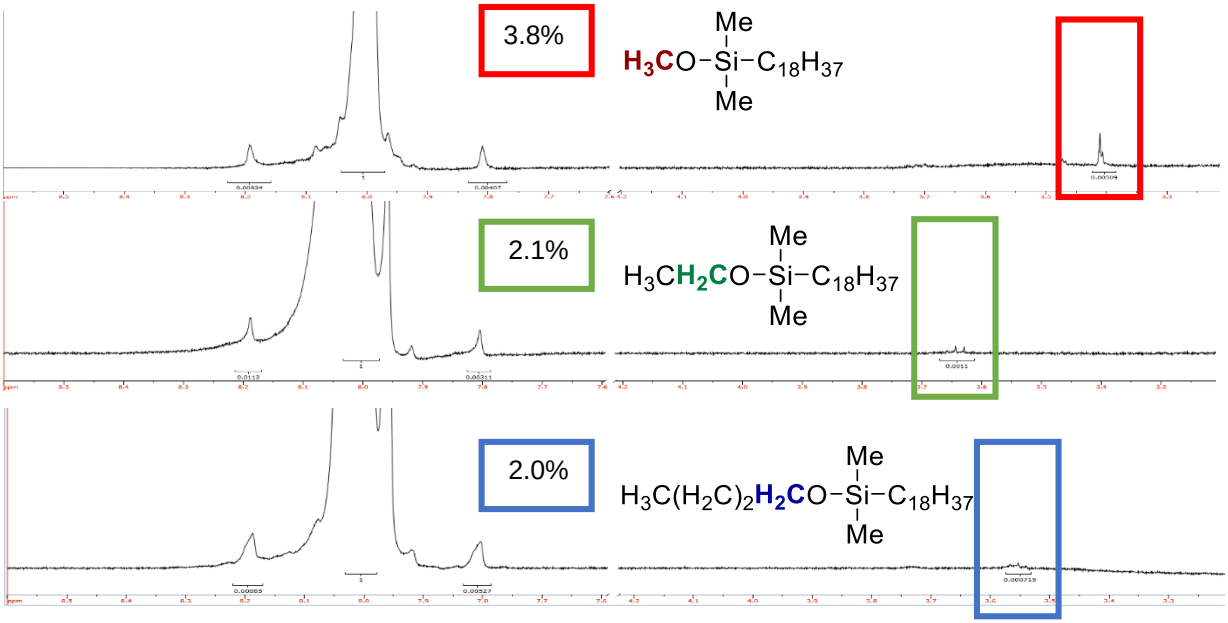
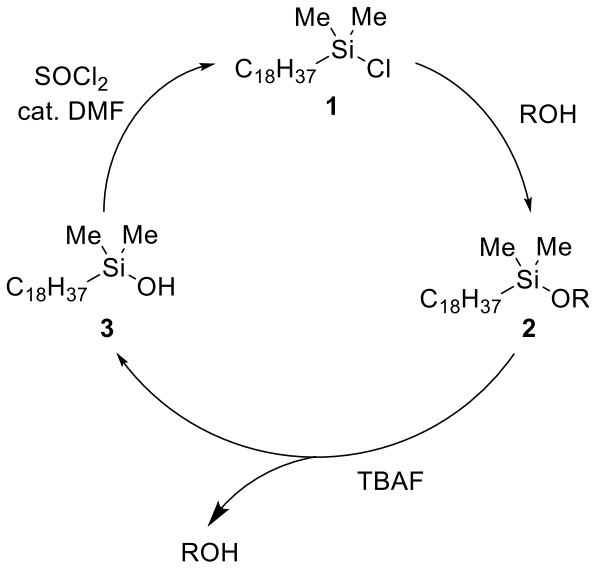


Figure 3.1. Phase-Selective Solubility Tests in DMF/cyclohexane

Upon cooling, the phases separated and the concentration of each of the silyl ethers (**2a**-**2e**) in the DMF phase was determined using NMR spectroscopy by comparing the DMF peak at 8.0 ppm to the silyl ether peak at approximately 3.5 ppm as shown in Figure 3.1. The concentration

of silyl ether in the DMF phase was then compared to the initial concentration in the cyclohexane phase and a leaching percentage was calculated by dividing the concentration in the DMF phase by the concentration in the cyclohexane phase. Methoxyoctadecyldimethylsilane (**2a**) showed 3.8% leaching, ethoxyoctadecyldimethylsilane (**2b**) showed 2.1% leaching, and butoxyoctadecyldimethylsilane (**2c**) showed 2.0% leaching. This means that greater than 96% of simple octadecyldimethylsilyl ethers are held in the cyclohexane phase.

Scheme 3.2. Regeneration cycle for **1**



We next developed a procedure to cleave silyl ethers, recover the alcohols, and regenerate **1** (Scheme 3.2). Octadecyldimethylsilyl ethers were cleaved to form alcohols and octadecyldimethylsilanol (**3**) using TBAF in THF. After this solution was concentrated at reduced pressure, an equivolume mixture of heptane and 90% aqueous ethanol was added. Then, the alcohol was separable from **3** using a biphasic extraction because **3** preferentially dissolved in heptane and the alcohols preferentially dissolved in the ethanol phase. Finally, **3** was chlorinated

with thionyl chloride in the presence of catalytic DMF.[12] In this process, **1** could be regenerated in near quantitative yield and reused in subsequent protection reactions.

We also used isomeric octadecyl groups for these protection and regeneration reactions. Isomeric octadecyldimethylchlorosilane is commercially available and less expensive than n-octadecyldimethylchlorosilane. While it is likely formed by a hydrosilylation reaction using $HSiCl(Me)_2$, its formation presumably involves use of a catalyst for the hydrosilylation that isomerizes the starting 1-octadecene (terminal olefins or so-called alpha olefins are articles of commerce made from reactions like the classical Aufbau process first explored by Ziegler or Shell's higher olefin process).[13,14] In general we used n-octadecyl groups for the work here since the products formed from isomeric octadecyldimethylchlorosilane will consist of a product mixture – a mixture that is not quite as characterizable as the single product formed using *n*-octadecyl groups. For example, the $–CH_2OSi-$ group in a silyl ether formed from n-octadecyldimethylchlorosilane is expected to be a single triplet. However, a 2-octadecylgroup would have a small chemical shift difference in ^1H NMR spectroscopy. The problems would also be exacerbated if chiral groups were present, leading to the presence of diastereomers.

Nonetheless, we did briefly examine the use of isomeric octadecyldimethyl chlorosilane since its products have similar solubility and the starting chlorosilane is less expensive. Those experiments involved the protection of primary alcohols, their corresponding leaching studies, and the recycling of octadecyldimethylchlorosilane. The results using isomeric octadecyldimethylchlorosilane were identical to those found using n-

octadecyldimethylchlorosilane, that is comparative yields were the same and >96% of the silyl ethers were selectively soluble in a hydrocarbon phase.

To further explore the utility of hydrocarbon soluble silylating agents, we next explored their use in reactions where trialkylsilyl groups serve as protecting groups and where the octadecyl group of **1** could serve as a purification agent. This chemistry was envisioned as being equivalent to chemistry that uses solid phase extraction as a purification process. Those processes usually use a functionalized, insoluble solid support that reacts with an intermediate or product, separating it from byproducts or excess reagent.[15] In our scheme, we imagined that the phase selectively soluble silylating agent could serve in a similar manner but in a liquid/liquid separation.

In the same way organic acids are separated from neutral or basic by-products and organic impurities by extraction from an organic solvent into aqueous base, we hypothesized that **1** could render a suitable product or intermediate lipophilic and heptane soluble. Since most inorganic reagents and most organic compounds are too polar to dissolve in heptane, **1** would effect a similar purification. Then, as is the case with aqueous base or aqueous extractions where addition of acid or base regenerates the organic phase soluble species, **1** could be removed to regenerate a polar organic phase soluble product in a scheme like that shown in Figure 3.2 below.

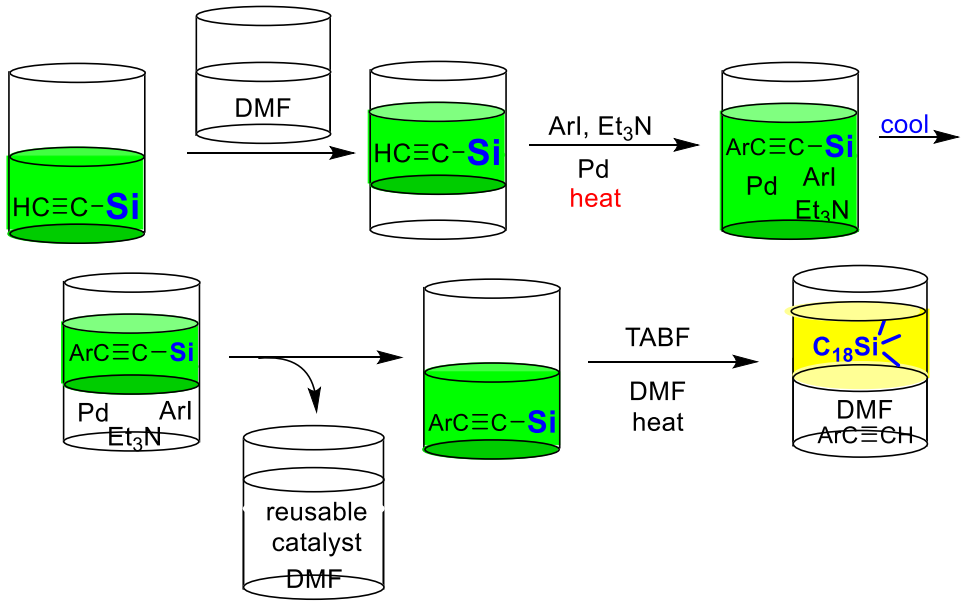
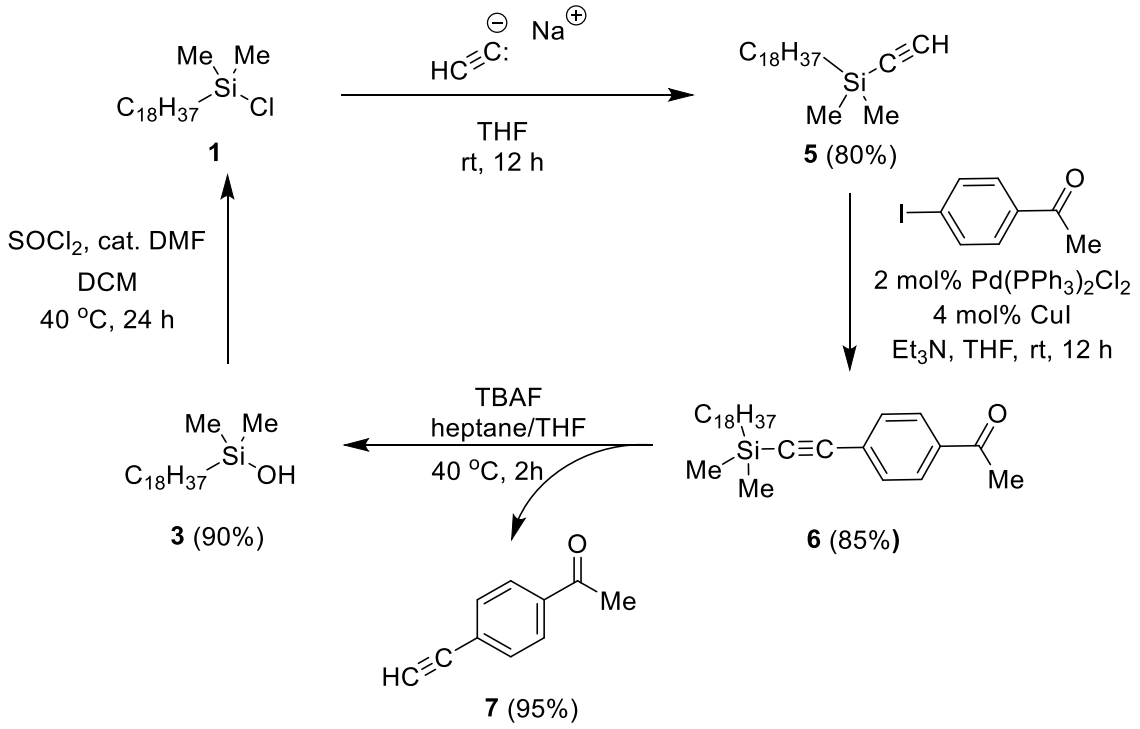


Figure 3.2. Separation scheme showing product isolation after a cross-coupling reaction using **1** as a hydrocarbon phase anchor

The concept of using a soluble sequestrating silylating agent that purifies an intermediate by a simple extraction was explored initially using the Sonogashira reaction as an example. The Sonogashira reaction, is widely used to couple alkynes with arenes.[16] Commonly, this procedure uses trimethylsilyl-protected acetylene as a reagent to form terminal alkyne products.[17,18] In these cases, column chromatography is needed to separate the product from catalyst residues.[19,20] We have shown that trimethylsilyl groups can be replaced by **1** in these sorts of coupling reactions. As shown in Scheme 3.3, **1** was reacted with sodium acetylide[21] to form octadecyldimethylsilylacetylene (**5**), which was subsequently coupled with 4-iodoacetophenone. The silylated product (**6**) was able to be separated from catalyst residues using a simple biphasic extraction, avoiding a waste-generating column chromatography step. After cleavage to form the product (**7**), octadecyldimethylchlorosilane (**1**) was regenerated in high yield and reused.

Scheme 3.3. Palladium-catalyzed cross-coupling reaction using **1** as a protecting group



The issue of whether this protecting group is always a sufficiently efficient phase anchor was tested by attaching larger, more polar molecules to the octadecyldimethylsilyl group. We reacted para-butyl red, a relatively common azo dye, with **1**. This silylated dye (**8**) shows significant leaching into the polar phase of a biphasic solvent system consisting of heptane and 90% aqueous ethanol (Figure 3.3). The results show that the octadecyl group is not large enough to ensure that a derivative of a larger polar molecule such as para-butyl red will selectively partition into the nonpolar phase. This is presumably because the azo dye group is both polar and has a mass that is approximately the same as the octadecyl group. Since the group is sufficiently large, its polar nature cannot be offset by the nonpolar octadecyl group.

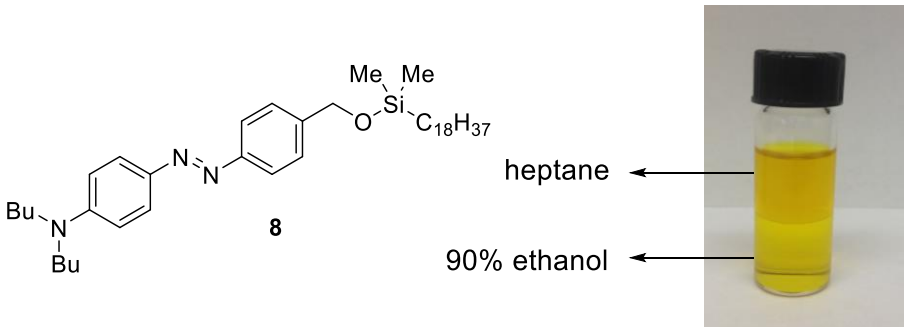


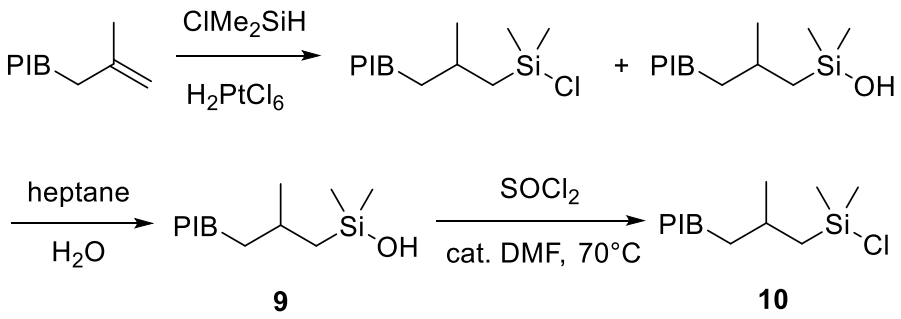
Figure 3.3. Phase selectivity of **8** at 25 °C in a thermomorphic 1/1 (vol/vol) mixture of heptane and 90% aqueous ethanol.

To solve this problem, we began to consider attaching a nonpolar polymer, polyisobutylene (PIB), to the protecting group to increase its phase-selectivity. For this purpose, we chose a commercially available polyisobutylene, PIB-1000, with a molecular weight of 1000 g/mol and a degree of polymerization of about 17 that contains a vinyl end group.

Synthesis of PIB-chlorosilane

We used a hydrosilylation reaction catalyzed by chloroplatinic acid to attach chlorodimethylsilane to PIB (Scheme 3.3). This reaction formed a mixture of PIB-silanol (**9**) and PIB-chlorosilane (**10**). After stirring with heptane and water, pure **9** was formed. Finally, we chlorinated the PIB-silanol with thionyl chloride and catalytic DMF to form pure **10**. A major problem with this reaction was how the product turned a very dark brown after chlorination. We believe this is possibly due to impurities in the thionyl chloride that are left behind after the reaction. Purification with extraction or column chromatography was not possible due to the high reactivity of **10**. Any contact of the product with water, in solution or in the air, would cause it to hydrolyze, reforming **9**.

Scheme 3.3. Synthesis of PIB-chlorosilane (**10**)



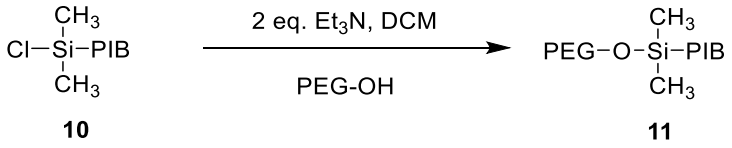
In an attempt to counteract this and improve the purity of **10**, thionyl chloride was distilled according to a literature procedure[22] and used in the chlorination reaction, to give a clearer product.

Another problem with this synthesis is the presence of unreacted PIB in the product, since not all of the PIB reacts during the hydrosilylation reaction even when excess silane is used. The PIB cannot be removed by column chromatography, since it is so similar in polarity, or by distillation, since it has such a high boiling point. Alternate methods had to be examined.

PIB-chlorosilane purification

We are currently working on a procedure to purify **10** by removing any unreacted PIB. **10** was attached to polyethylene glycol (PEG) by a simple protection reaction of the alcohol end group using Et_3N as shown in Scheme 3.4. The PIB-silyl protected PEG (**11**) could then be precipitated in heptane, allowing the unreacted PIB to be washed away. The PIB-silyl protected PEG could then be deprotected and chlorinated, giving pure PIB-chlorosilane (**10**). A disadvantage of this approach is that it uses several time-consuming steps that give the product in very low yields. This method and others are still being looked into.

Scheme 3.4. Synthesis of PIB-Si-O-PEG (**11**)

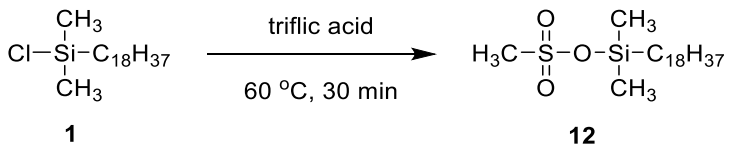


Octadecyldimethylsilyl triflate as a recyclable Lewis acid catalyst

Lewis acids have recently been explored as catalysts. These molecules are used to catalyze reactions such as the Diels-Alder, Mukaiyama aldol, and Sakurai reactions. Substrates that contain carbonyl groups can be activated by lowering the LUMO energy, namely the C-O π* orbital, towards nucleophilic attack. Silyl Lewis acids in particular can catalyze aldol and ester cleavage reactions.[23,24] Benefits of silyl Lewis acid catalysts over metal catalysts include cost and environmental considerations.[25] Transition metal catalysts can be very expensive and harmful to the environment.

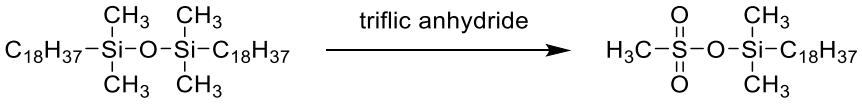
One major problem with Lewis acid catalyst is the need for very strong Lewis acids and large catalyst loadings. Silyl Lewis acids, such as silyl triflates, are known for their high acidity and reactivity as Lewis acid catalysts; they would be ideal Lewis acid catalysts if a separation scheme could be designed to make them easily recyclable. If silyl Lewis acids could be recycled efficiently, we would be able to overcome, or at least offset, the need for high catalyst loadings.

Scheme 3.5. Synthesis of octadecyldimethylsilyl triflate (**12**) using triflic acid



We decided to apply our octadecyl silane chemistry to the issue of recycling Lewis acid catalysts, to develop an efficient separation scheme. Octadecyldimethylsilyl triflate (**12**) was synthesized by stirring **1** with excess triflic acid at 60°C for 30 minutes[26] (Scheme 3.5). The remaining triflic acid would be removed by vacuum during the last 10 minutes of the reaction. When we tried this route, we were having problems removing all of the triflic acid without damaging the vacuum pump or hydrolyzing the product.

Scheme 3.6. Synthesis of octadecyldimethylsilyl triflate **12** using anhydrides



3b **12**

As a safer alternative, we are in the process of synthesizing **12** by reacting octadecyldimethylsilyl anhydride (**3b**) with triflic anhydride (Scheme 3.6). **3b** is formed by stirring **1** with 5:1 heptane/water for two hours; triflic anhydride can be found commercially or by vacuum distillation of triflic acid using P_4O_{10}. The product will be purified by vacuum distillation.

CHAPTER IV

CONCLUSION

Common protecting groups such as chlorosilanes are typically discarded as chemical waste after use. We have been exploring effective ways to facilitate separations of silylated species and to regenerate silyl reagents to make their use greener. The Bergbreiter group has previously demonstrated that attaching a highly nonpolar group to a molecule makes the product preferentially soluble in nonpolar solvents. These phase-anchored species can be separated from reaction mixtures by extraction with a hydrocarbon solvent due to their selective solubility. We have extended this work to chlorosilane protecting groups showing that octadecyldimethylchlorosilane, a chlorosilane with a long nonpolar chain, can make silylated species phase-selectively soluble. Our studies showed that in DMF/cyclohexane solvent system, >96% of simple silylated alcohols are retained in the cyclohexane phase. We further showed that we could cleave this silyl group and then regenerate the original protecting group in high yield. Octadecyldimethylchlorosilane was also used as a protecting group in a Sonogashira cross-coupling reaction. In this case, the silylated product could be removed from catalyst residues using a simple biphasic extraction step. Ongoing work has a goal of further improving phase-selectivity by replacing the octadecyl group with a polyisobutyl group. The synthesis of Lewis acid catalyst, octadecyldimethylsilyl triflate, was also explored.

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APPENDIX

Octadecyldimethylsilyl ether synthesis

To a mixture of alcohol (10 mmol) and Et_3N (1.5 g, 15 mmol) in 15 mL of DCM, was added 10 mL of octadecyldimethylchlorosilane (**1**) (10 mmol, 1.0 M in DCM). The mixture was stirred for 18 h at 40 °C. After the solvent was removed *in vacuo*, the residue was dissolved in 30 mL of hexane and washed by 90% ethanol (10 mL x 3). The hexane phase was dried over Na_2SO_4 and the solvent was removed *in vacuo* to give the product.

Methoxy(octadecyldimethyl)silane (2a). 3.0 g (89 %). Clear liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.42 (s, 3 H), 1.28-1.22 (br, 32 H), 0.85 (t, J = 6.9 Hz, 3 H), 0.60 (t, J = 7.0 Hz, 2 H), 0.09 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 50.1, 32.0, 29.7, 29.5, 29.4, 22.9, 16.0, 14.1, -2.73. IR (neat, cm^{-1}) 2920, 2853, 1466, 1250, 1188, 1092, 837, 781, 721. HRMS (ESI+) calculated for $C_{21}H_{46}OSi$ [M+H]+ : 343.3396, found: 343.3380

Ethoxy(octadecyldimethyl)silane (2b). 3.3 g (93 %). Clear liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.66 (q, J = 6.9 Hz, 2 H), 1.28-1.22 (br, 32 H), 1.19 (t, J = 7.2 Hz, 3 H), 0.88 (t, J = 6.9 Hz, 3 H), 0.59 (t, J = 8.0 Hz, 2 H), 0.09 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 58.2, 32.0, 29.7, 29.6, 29.4, 22.7, 18.5, 16.4, 14.1, -2.12. IR (neat, cm^{-1}) 2920, 2853, 1466, 1250, 1107, 1080, 945, 837, 779, 721. HRMS (ESI+) calculated for $C_{22}H_{48}OSi$ [M+H]+ : 357.3553, found: 357.3539

Butoxy(octadecyldimethyl)silane (2c). 3.5 g (94 %). Clear liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.57 (t, J = 6.9 Hz, 2 H), 1.5 (m, 2 H), 1.40-1.20 (br, 34 H), 0.91 (t, J = 7.3 Hz, 3 H), 0.88 (t, J

= 7.0 Hz, 3 H), 0.58 (t, J = 7.8 Hz, 2 H), 0.08 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 62.2, 46.2, 29.8, 29.7, 29.6, 29.5, 22.6, 18.7, 16.4, 14.1, -2.14. IR (neat, cm^{-1}) 2920, 2853, 1466, 1250, 1094, 1038, 980, 889, 837, 779, 719. S3 HRMS (ESI+) calculated for $C_{24}H_{52}OSi$ [M+H]+ : 385.3866, found: 385.3868

Hexyloxy(octadecyldimethyl)silane (2d). 3.7 g (90 %). Clear liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.56 (t, J = 6.6 Hz, 2 H), 1.51 (m, 2 H), 1.35-1.20 (br, 38 H), 0.90-0.87 (m, 6 H), 0.58 (t, J = 8.0 Hz, 2 H), 0.08 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 62.8, 31.9, 29.7, 29.6, 29.4, 22.7, 16.4, 14.1, -2.10. IR (neat, cm^{-1}) 2920, 2853, 1466, 1248, 1096, 1041, 951, 837, 781, 719. HRMS (ESI+) calculated for $C_{26}H_{56}OSi$ [M+H]+ : 413.4179, found: 413.4242

Decyloxy(octadecyldimethyl)silane (2e). 4.2 g (89 %). Clear liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.56 (t, J = 6.9 Hz, 2 H), 1.48 (m, 2 H), 1.30-1.20 (br, 46 H), 0.88 (m, 6 H), 0.60 (t, J = 7.2 Hz, 2 H), 0.08 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 62.8, 29.8, 29.5, 29.4, 29.1, 25.9, 23.2, 22.7, 16.4, -2.14. IR (neat, cm^{-1}) 2920, 2853, 1466, 1248, 1098, 837, 779, 719. HRMS (ESI+) calculated for $C_{26}H_{56}OSi$ [M+H]+ : 469.4805, found: 469.4945

General procedures of phase selectivity studies

The octadecyldimethylsilyl ether that was to be analyzed (1 mmol) was placed in a vial and dissolved in 10 mL of cyclohexane, hexane, heptane or cyclooctane. Then 10 mL of DMF or 90 % ethanol was added to this hydrocarbon solution. The mixture was sealed and heated to 80 °C to generate a homogeneous solution. The solution was cooled to room temperature to produce a biphasic solution. An aliquot of the polar solution was then analyzed by ^{1}H NMR spectroscopy.

When the polar solvent is DMF, we integrated the α-C-H next to the ether linkage and divided the integral by the numbers of the α-C-H. We then compared this number with the integration of the satellite peak of the aldehyde proton in the DMF solvent to determine the leaching of the silyl ethers into the polar solvent. These satellite peaks are due to the coupling of the aldehyde proton to the adjacent ^{13}C isotope, which is present in 1% of all molecules naturally. Thus, each of these satellite peaks represents 0.5% of the concentration of DMF. Thus, the concentration of silyl ethers in DMF solution can be calculated by using integral ratio of the α-C-H versus aldehyde proton. Then used the concentration to calculate the amount of silyl ethers leaching into DMF solution to compare to the original amount of silyl ethers, thus, the leaching percentage can be obtained. When the polar solvent is 90% ethanol, we integrated the CH3 attached on Si and divided the integral by the numbers of the C-H. We then compared this number with the integration of CH2 in the ethanol solvent to determine the leaching of the silyl ethers into the polar solvent.

Cleavage of decyloxy(octadecyldimethyl)silane (2e)

To 2.0 g of **2e** (4.4 mmol) and 10 mL of heptane, 10 mL of TBAF was added (10 mmol, 1 M in THF). The mixture was stirred for 6 h at 40 °C. After the solution was cooled down to ambient temperature, the solvent was removed at reduced pressure and 20 mL of heptane was added. The mixture was washed by 10 mL of water three times to remove TBAF. The heptane solution was then extracted with 90% ethanol. The ethanol phase was concentrated *in vacuo* to give 493 mg (73%) of decanol (**4**). Clear liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 3.62 (t, J = 7.2 Hz, 2 H), 1.63 (m, J = 6.9 Hz, 2 H), 1.44 (m, J = 7.2 Hz, 2 H), 1.25 (br, 12 H), 0.85 (t, J = 6.9 Hz, 3 H). IR (neat, cm^{-1}) 3320, 2956, 2864, 1466, 1378, 1120, 1065, 877. The heptane phase was concentrated

in vacuo to give 1.32 g (94%) of octadecyldimethylsilanol (**3**). White solid. This compound has no signal in ^{19}F NMR. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (br, 32 H), 0.88 (t, J = 6.6 Hz, 3 H), 0.49 (t, J = 6.6 Hz, 2 H), 0.03 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.5, 31.9, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 22.7, 18.4, 14.1, 0.39. IR (neat, cm^{-1}) 3500, 2914, 2848, 1469, 1249, 1066, 840, 810, 788, 775, 717, 709; mp 35-40 ^{o}C This product was further purified by a recrystallization from pentane at -20 ^{o}C to give bis(octadecyldimethylsilyl)disiloxane (**3b**). White solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (br, 32 H), 0.88 (t, J = 6.6 Hz, 3 H), 0.49 (t, J = 6.6 Hz, 2 H), 0.03 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.5, 32.0, 30.4, 30.1, 29.7, 29.6, 29.5, 29.4, 29.1, 23.3, 22.7, 18.4, 0.43, 0.35. IR (neat, cm^{-1}) 2914, 2848, 1469, 1249, 1066, 840, 810, 788, 775, 717, 709; mp 41-42 ^{o}C. Elemental analysis (%): calcd C 75.15, H 13.56; found: C 75.28, H 13.65

Regeneration of 1 from 3

To 1.4 g of **3** (3.6 mmol) and 20 mL of DCM, 3 drops of dry DMF and 3 mL of thionyl chloride were added. The mixture was stirred under nitrogen for 2 days at 40 °C. The solution was concentrated *in vacuo* to give 1.48 g (98 %) of **1**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (m, 32 H), 0.88 (t, J = 6.8 Hz, 3 H), 0.81 (t, J = 8.0 Hz, 2 H), 0.39 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 50.3, 33.7, 32.1, 29.9, 23.3, 22.9, 16.0, 14.2, 6.0.

Preparation of octadecyldimethylsilylacetylene (5).

To a flame-dried 100 mL three-necked round bottom flask, 4.16 g of **1** (11.9 mmol) in 25 mL of heptane was added. 0.58 g of sodium acetylide (11.9 mmol in 18 % of xylene slurry) in 25 mL of freshly dried THF was added to the mixture via syringe. The mixture was stirred at rt under N_2 atmosphere for 24 h then 50 mL of water was added. The heptane phase was washed with water

(25 mL × 2) and 90% ethanol (25 mL × 3). The heptane phase was dried over Na_2SO_4 and concentrated *in vacuo* to give 3.2 g (80 %) of **5**. White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.38 (s, 1 H), 1.25 (br, 32 H), 0.88 (t, J = 6.6 Hz, 3 H), 0.63 (t, J = 7.8 Hz, 2 H), 0.17 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 93.3, 89.5, 33.3, 31.9, 30.1, 29.7, 29.6, 29.4, 29.3, 29.0, 22.71, 15.87, -1.96. IR (neat, cm^{-1}) 3271, 2916, 2847, 2035, 1464, 1250, 866, 842, 824, 787, 772, 716, 694, 683; mp: 24-25 ^{o}C. Elemental analysis (%): calcd C 78.48, H 13.17; found: C 78.69, H 13.20.

4-((Dimethyl(octadecyl)silyl)ethynylacetophenone (6).

To a flame-dried 50 mL two-necked round bottom flask, 246 mg of 4-iodoacetophenone (1.0 mmol), 404 mg of **7** (1.2 mmol), 23 mg of $Pd(PPh_3)_4$ (0.02 mmol), and 7.6 mg of CuI (0.04 mmol) in 10 mL of freshly dried THF were added. 0.21 mL of Et_3N was added to the mixture then it was stirred at rt under N_2 atmosphere 24 h. The solvent was removed by rotary evaporation then 30 mL of heptane was added. The heptane phase was washed by water (25 mL × 2) and 90 % ethanol (25 mL × 3). The heptane phase was dried over Na_2SO_4 and concentrated *in vacuo* to give 417 mg of mixture which contains 85% of **6** (The yield is 82 %) and 15% of acetylene dimers. Brown solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 8 Hz, 2 H), 7.53 (d, J = 8 Hz, 2 H), 2.60 (s, 3 H), 1.28- 1.24 (br, 32 H), 0.88 (t, J = 6.6 Hz, 3 H), 0.59 (m, 2 H), 0.09 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.8, 136.2, 132.0, 128.0, 127.9, 104.4, 97.61, 33.21, 31.90, 30.04, 29.69, 29.65, 29.59, 29.35, 29.32, 28.99, 26.42, 23.75, 22.66, 15.95, -1.89. IR (neat, cm^{-1}) 2914, 2849, 2160, 2066, 1682, 1601, 1470, 1265, 844, 831, 818, 808, 785, 773, 718, 586. HRMS (ESI+) calculated for $C_{30}H_{50}OSi$ [M+H]+ : 455.3709, found: 455.3728

Preparation of 4-ethynylacetophenone (7).

To 417 mg of the mixture obtained from previous procedure and 10 mL of heptane and 10 mL of THF, 1.0 mL of TBAF (1.0 mmol, 1 M in THF) was added. The mixture was stirred for 2 h at rt then 20 mL of heptane and 20 mL of NH_4Cl aqueous solution was added. The heptane phase was washed with water (20 mL × 2). The product was extracted by 90 % ethanol and the ethanol phase was concentrated *in vacuo* to give 126 mg (95 %) of **7**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (d, J = 9 Hz, 2 H), 7.61 (d, J = 9 Hz, 2 H), 2.60 (s, 3 H). IR (neat, cm^{-1}) 3350, 2961, 2916, 2874, 2212, 1674, 1599, 1400, 1288, 1261, 1221, 1177, 817. The heptane phase was concentrated *in vacuo* to give 303 mg (90 %) of **3**.

4-(N,N-Dibutyl-4-aminophenyl) azophenylmethoxy(octadecyl)dimethylsilane (11). 255 mg (0.74 mmol) of octadecyldimethylchlorosilane (**1**) in 10 mL of DCM was added to a mixture of S6 250 mg (0.74 mmol) of 4-(N,N-dibutyl-4-aminophenyl) azophenylmethanol and 0.15 mL of triethylamine in 15 mL of DCM. The mixture was stirred for 18 h at 40 °C. After the mixture was cooled to the ambient temperature, the solvent was removed *in vacuo*. The residue was dissolved in 30 mL of DCM and washed by water (10 mL x 2). The DCM was removed *in vacuo* to give the crude product. The crude was purified by silica gel column chromatography (eluent: ethyl acetate/dichloromethane = 1/9, Rf = 0.8) to give the 270 mg (53 %) of product. Red solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 10 Hz, 2 H), 7.79 (d, J = 10 Hz, 2 H), 7.41 (d, J = 10 Hz, 2 H), 6.68 (d, J = 10 Hz, 2 H), 4.75 (s, 2 H), 3.36 (t, J = 7.5 Hz, 4 H), 1.62, (m, 4 H), 1.39 (m, 4 H), 1.29-1.23 (br, 32 H), 0.98 (t, J = 7.5 Hz, 6 H), 0.88 (t, J = 5.0 Hz, 3 H), 0.64 (t, J = 7.5 Hz, 1 H), 0.60 (t, J = 7.5 Hz, 1 H), 0.14 (s, 3 H), 0.13 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.4, 150.3, 143.0, 142.1, 127.3, 126.8, 125.1, 122.0, 110.96, 50.87, 33.42, 31.90, 29.69, 29.35,

23.13, 22.67, 20.25, 17.80, 16.35, 13.90, 0.39, -2.03. IR (neat, cm^{-1}) 3300, 2916, 2849, 1599, 1514, 1396, 1365, 1250, 1153, 1138, 1109, 1086, 1061, 868, 837. HRMS (ESI+) calculated for $C_{41}H_{71}N_3OSi$ [M+H]+ : 650.5445, found: 650.5487

Hydrosilylation of PIB-1000 with chlorodimethylsilane

A pressure vessel containing 2.9 g of PIB-1000 (3 mmol) was placed under vacuum and flushed with nitrogen for several minutes. To the vessel, 5 drops of chloroplatinic acid, 0.6mL of chlorodimethylsilane, and 10 mL of dry toluene were added. The vessel was capped and stirred at 80°C. After 1 h, the solution turned black. After 2 days, the mixture was transferred to a round bottom flask and rinsed with heptane, then concentrated *in vacuo*. The product was stirred with 10 mL of heptane and 10mL of distilled water for 1 h, then filtered through celite, dried with sodium sulfate, and concentrated *in vacuo* to give 2.9g of PIB-silanol (**9**). 2.9 g. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.50-0.74 (m, 662H), 0.08 (s, 6H).

Synthesis of PIB-chlorosilane (10)

The 2 g of PIB-silanol (**9**) (2 mmol) was transferred to a pressure vessel using DCM that was later evaporated. To the vessel, 1 pipet of freshly distilled thionyl chloride and 5 drops of DMF were added. The vessel was sealed and stirred at 70°C for 2 days. The solution was transferred to a round bottom flask and rinsed with DCM, then concentrated *in vacuo* to give 2 g of PIB-chlorosilane (**10**) 2 g. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.50-0.74 (m, 662H), 0.42 (s, 6H).

Synthesis of PIB-Si-O-PEG (11)

To a mixture of PEG-5000 (5 mmol) and Et_3N (1.5 g, 10 mmol) in 25 mL of DCM, was added 10 mL of PIB-chlorosilane (**10**) (5 mmol, 1.0 M in DCM). The mixture was stirred for 18 h at 40 °C. After the solvent was removed *in vacuo*, the residue was dissolved in 10 mL of DCM and pipetted into 500 mL of heptane. The precipitate was filtered and dried to give PIB-Si-O-PEG (**11**) 5.2g.

Synthesis of octadecyldimethylsilyl triflate (12) using triflic acid

To a 25 mL round-bottom flask, 1.0 g of **1** (3 mmol) and 0.6 mL of triflic acid (6 mmol) were added. The flask was stirred at 60°C for 30 minutes. The mixture was placed under vacuum for 10 minutes to give 1.0 g of octadecyldimethylsilyl triflate (**12**) ^{1}H NMR (300MHz, $CDCl_3$) δ 3.42 (s, 3H), 1.25(m, 32H), 0.85(t, J = 6.9Hz, 3H), 0.77 (t, J = 7.2Hz, 2H), 0.51(s, 6H).