Supporting Information for:

Synthesis of Thiol-Clickable and Block Copolyptide Brushes via Nickel-Mediated Surface Initiated Polymerization of α-Amino Acid N-Carboxyanhydrides (NCAs)

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Materials and Methods. All reagents and solvents were obtained at the highest purity available from Aldrich Chemical Company or Acros Organics and used without further purification unless otherwise specified. Allyl chloroformate and (H-(Lys)Z-OH) were purchased from Fluka and triphosgene was purchased from TCI.

Characterization. A Varian Mercury Plus 200MHz NMR spectrometer operating at a frequency of 200.13 MHz with VNMR 6.1C software was used for proton analysis. Ellipsometric measurements were carried out using a Gaertner Scientific Corporation LSE ellipsometer with a 632.8 nm laser at 70° from the normal. Refractive indices of 3.89 for silicon, 1.46 for silicon oxide, 1.5 for alloc-L-leucine-APS, 1.46 for poly(benzyl glutamate), 1.37 for poly(lysine), and 1.5 for poly(cysteine) and block copolymers were used. ATR-FTIR spectra of surface polymers were carried out using a Nicolet 8700 with a gradient angle ATR attachment using Omnic software. Spectra were taken with a resolution of 4 cm⁻¹ by accumulating a minimum of 64 scans per run. Nitrogen was constantly purged through the attachment to reduce interference of carbon dioxide and water. XPS measurements were performed using a Kratos Axis Ultra Spectrometer (Kratos Analytical, Manchester, UK) with a monochromatic Al K X-ray source (1486.6 eV) operating at 150 W under 1.0 × 10⁻⁹ Torr. Measurements were performed in hybrid mode using electrostatic and magnetic lenses, and the pass energy of the analyzer was set at 40 eV for high-resolution spectra and 160 eV for survey scans, with energy resolutions of 0.1 eV and 0.5 eV, respectively. Generally, total acquisition times of 180 s and 440 s were used to obtain high resolution and survey spectra, respectively. For a 0° take off angle (angle between sample surface normal and the electron optical axis of the spectrometer), the maximum information depth of the measurements was approximately 8 nm. All XPS spectra were recorded using the Kratos Vision II software; data files were translated to VAMAS format and processed using the CasaXPS software package (v. 2.3.12). Binding energies were calibrated with respect to C 1s at 285 eV.

Cleaning Process of Silicon Wafers. Wafers were cut into appropriate size pieces and placed into a glass test tube. The wafers were ultrasonically cleaned with acetone, ethanol, and toluene for 10 min., respectively. The wafers were dried under a N₂ stream and placed in a UVO cleaner, where they were exposed to ozone for 30 minutes. Substrates were used immediately after exposure.
**Synthesis of NCA of S-tertbutylmercapto-L-cysteine.** This compound was prepared according to literature.\textsuperscript{2} Under N\textsubscript{2} flow, S-tertbutylmercapto-L-cysteine (2g, 9.56mmol, 1eq) and α-pinene (3.36mL, 2.89g, 21.21mmol, 2.22eq) were dissolved in 25mL of ethyl acetate in a RBF equipped with a Schlenk line attachment. In a scintillation vial, triphosgene (1.98g, 6.65mmol, 0.69eq) was dissolved in a minimal amount of ethyl acetate. The amino acid solution was refluxed (75°-80° C) and triphosgene solution was added slowly using a syringe. The solution became clear. Solvent was removed under a nitrogen flow until 1/3 of the original solution remained. The NCA solution was then precipitated into hexanes. The product was filtered, redissolved, and precipitated again for further purification. Finally, the product was filtered and dried in a vacuum oven overnight or until dry. Spectroscopic data was identical to that reported in the literature.\textsuperscript{2}

**Synthesis of NCA of γ-benzyl-L-glutamate.** This compound was prepared according to literature.\textsuperscript{3, 4} γ-benzyl-L-glutamate (2g, 8.43mmol, 1eq) was weighed out into a RBF equipped with a Schlenk line attachment. The amino acid was dried under vacuum and purged with N\textsubscript{2} each for 10-15 minutes. THF was added to the RBF (1 mL solvent/0.1g of amino acid) and the solution was stirred and heated to approximately 65° C. Triphosgene (1.14g, 3.8mmol, 0.45eq) was weighed out in a separate scintillation vial and dissolved with minimal THF. When the reaction mixture reached the appropriate temperature, the triphosgene solution was added to the RBF slowly. In order to keep the reaction dry, a flow of N\textsubscript{2} and a drying column equipped with glass wool and dri-rite was placed on top of the RBF. The reaction was refluxed until 20-25% of the original solution remained. The resulting mixture was added dropwise into hexanes (10:1 hexanes to reaction mixture). The flask was capped and left in the freezer overnight. The precipitate was collected by vacuum filtration. A faint yellow color indicates residual HCl. To remove residual HCl, the product was redissolved in a small amount of THF, activated charcoal was added and the mixture was stirred for 2 hours, and the placed in the freezer overnight. The charcoal was removed by filtration and the filtrate was added to hexanes to precipitate. The product was collected by filtration and dried in vacuum oven overnight or until dry. Spectroscopic data was identical to that reported in the literature.\textsuperscript{3, 4}

**Synthesis of NCA of H-(Lys)Z-OH.** This compound was prepared according to literature.\textsuperscript{3, 4} H-(Lys)Z-OH (2g, 7.13mmol, 1eq) was weighed out into a RBF equipped with a Schlenk line attachment. The amino acid was dried under vacuum and purged with N\textsubscript{2} each for 10-15 minutes. THF was added to the RBF (1mL solvent/0.1g of amino acid) and the solution was stirred and heated to approximately 65° C. Triphosgene (0.96g, 3.2mmol, 0.45eq) was weighed out in a separate scintillation vial and dissolved with minimal THF. When the reaction mixture reached the appropriate temperature, the triphosgene solution was added to the RBF slowly. In order to keep the reaction dry, a flow of N\textsubscript{2} and a drying column equipped with glass wool and dri-rite was placed on top of the RBF. The reaction was refluxed until 20-25% of the original solution remained. The resulting mixture was added dropwise into hexanes (10:1 hexanes to reaction mixture). The flask was capped and left in the freezer overnight. The precipitate was collected by vacuum filtration. A faint yellow color indicates residual HCl. To remove residual HCl, the product was redissolved in a small amount of THF, charcoal was added and the mixture was stirred for 2 hours, and the placed in the freezer overnight. The charcoal was removed by filtration and the filtrate was added to hexanes to precipitate. The product was collected by filtration and dried in vacuum oven overnight or until dry. Spectroscopic data was identical to that reported in the literature.\textsuperscript{3, 4}
**Synthesis of Alloc-L-leucine.** This compound was prepared according to literature.\(^5\) L-leucine (5g, 38mmol) was suspended in 25mL of DI water. The L-leucine was completely dissolved by adding 4N NaOH (9.5mL, 38mmol). The solution was cooled down in an ice bath and allyl chloroformate (4.96mL, 46.7mmol) was added to the vigorously stirred solution along with additional 4N NaOH (in order to retain a pH 9) over a period of an hour. Once equilibrated, the solution was stored in the refrigerator overnight. The solution was acidified to a pH ≈ 2-3 using H\(_2\)SO\(_4\). The product was extracted using ethyl acetate (3X) and dried using magnesium sulfate. The product was isolated using a rotary evaporator and dried under a high vacuum pump. Spectroscopic data was identical to that reported in the literature.\(^5\)

**Synthesis of Alloc-L-leucine-N-Hydroxysuccinimidyl Ester.** This compound was prepared according to literature.\(^5\) Alloc-L-leucine (0.5g, 2.3mmol) and N-Hydroxysuccinimide (NHS) (0.27g, 2.3mmol) were added to a round bottom flask (RBF) with dry THF. The solution stirred for 5-10 minutes in an ice bath. N,N'-dicyclohexylcarbodiimide (DCC) (0.48g, 2.3mmol) was weighed out and dissolved in a scintillation vial. The DCC was added to the stirred solution (white precipitate formation). The resulting solution was stored in the refrigerator overnight. The solution was then filtered to remove the precipitate. The solution was extracted (3X) using ethyl acetate and washed with NaCO\(_3\), H\(_2\)O, and NaCl/H\(_2\)O and dried over magnesium sulfate. The product was isolated using a rotary evaporator. Spectroscopic data was identical to that reported in the literature.\(^5\)

**Synthesis of Alloc-L-leucine-3-Aminopropyltriethoxysilane (Alloc-L-leucine-APS).** Alloc-L-leucine-NHS (0.45g, 1.4mmol) was dissolved in a scintillation vial with dry THF. 3-Aminopropyltriethoxysilane (APS) (0.305mL, 0.287g, 1.29mmol) was added to the solution and stirred overnight. The white precipitate formed was filtered from the solution and the product was isolated using a rotary evaporator. The product was used without further purification. The product was characterized using \(^1\)H and \(^{13}\)C NMR: \(^1\)H NMR (CDCl\(_3\)): \(\delta\) ppm 6.83 (s, 1H), 5.81 (m, 2H), 5.28 (d, 1H), 5.15 (d, 1H), 4.49 (m, 3H), 3.76 (q, 6H), 3.19 (m, 2H), 1.55 (m, 5H), 1.17 (t, 9H), 0.88 (m, 6H), 0.57 (t, 2H), \(^{13}\)C NMR (CDCl\(_3\)): \(\delta\) ppm 172.90, 156.35, 132.45, 117.69, 65.85, 58.41, 53.54, 41.97, 41.41, 25.37, 24.62, 22.55, 18.19, 7.53.
NMR

Figure S1. a)$^1$H NMR and b)$^{13}$C NMR of Alloc-L-leucine-3-Aminopropyltriethoxysilane (Alloc-L-leucine-APS).

Silicon Substrate Surface Modification with Alloc-L-leucine-APS. A stock solution (25 mg/mL) of alloc-L-leucine-APS in dry toluene was prepared. In a test tube capped with a septum, a clean Si-substrate was added into 5 mL of dry toluene containing 0.156 mL of the stock alloc-L-leucine solution. The test tube was placed on a rotation mixer for 1 hour. The substrate was rinsed in fresh toluene and dried under a N$_2$ stream. Ellipsometry was used to measure the thickness of the resulting film.

Complexing Ni with the Surface.$^6$ In an dry box under an inert atmosphere, a solution of bis(cyclooctadiene) nickel(0) (Ni(COD)$_2$) and 1,10-phenanthroline (1.49 mmol Ni(COD)$_2$):1.54
mmol 1,10-phenanthroline ratio) in dry DMF was stirred for 1 hour in a scintillation vial. The alloc-amide functionalized substrates were then suspended in the resulting solution (dark burgundy) and stirred at 80°C for 48 hours. The substrates were then rinsed thoroughly with DMF.

**Ni-Mediated Surface-Initiated Polymerization.** The nickel-complexed substrates were added into a 0.26 M monomer/DMF solution in a test tube. The reaction was allowed to proceed for 24 hours. The substrates were then rinsed Soxhlet extracted in THF for 24 hours. The film thickness was measured to by ellipsometry after drying under a stream of nitrogen. Block copolymers were prepared in an analogous manner by submerging (after rinsing extensively in DMF) a polypeptide brush substrate into an additional 0.26 M NCA monomer solution for 24 hours. The block copolypeptides were Soxhlet extracted in THF for 24-48 hours prior to characterization.

**Deprotection of Cysteine.** Dithiothreitol (0.324 mmol, 0.005g) was dissolved in dry DMF (5 mL) in a scintillation vial. The solution was added to a test tube containing a tert-butyl protected poly(cysteine) functionalized substrate. The test tube was heated to 60°C in an oil bath while N₂ is bubbled through the solution. The solution was maintained at 60°C for 5 days. After 5 days, the substrates were removed from the solution, washed with THF and toluene and dried with a stream of N₂. Upon deprotection, a decrease in ellipsometric film thickness was observed consistent with the loss of the t-butyl group.

**Thiol-Michael Post Modification.** The freshly deprotected poly(cysteine) brush substrate was submerged in a THF solution containing a fluorinated maleimide (0.02mmol, 0.0048g). The substrate was stirred overnight at room temperature. The substrates were then rinsed extensively in THF and Soxhlet extracted for 24 hours prior to analysis. The functionalization was monitored using ellipsometry and XPS.
X-ray Photoelectron Spectroscopy.

Figure S2. XPS spectrum of Alloc-L-leucine-APS

Figure S3. High resolution S2p XPS spectra of the cysteine-containing block copolypeptides.
References:


Figure S4. gATR-FTIR spectra of (a) poly(N-carbonyloxy-L-lysine), (b) poly(S-tertbutylmercapto-L-cysteine), (c) poly(γ-benzyl-L-glutamate) and (d) tethered alloc-amide initiator precursor.