Supporting Information for

Modular Synthesis and Facile Network Formation of Catechol Functionalized Triblock Copolymers

Fahed Albreiki,[a] Tobias Göckler,[a,b] and Samanvaya Srivastava[a,c,d,e*]

Contents

[a.] *Department of Chemical and Biomolecular Engineering, University of California, Los Angeles, Los Angeles, CA 90095, USA*
[b.] *Institute of Functional Interfaces, Karlsruhe Institute of Technology (KIT), 76344 Eggenstein- Leopoldshafen, Germany*
[c.] *California NanoSystems Institute, University of California, Los Angeles, Los Angeles, CA 90095, USA*
[d.] *BioPACIFIC MIP, University of California, Los Angeles, Los Angeles, CA 90095, USA*
[e.] *Institute for Carbon Management, University of California, Los Angeles, Los Angeles, CA 90095, USA*
** Email: samsri@ucla.edu*

1. Materials and methods:

1.1. Materials:

Potassium (99.5% trace metal basis), naphthalene, poly(ethylene glycol) ($M_n \sim 5.4$ kg/mol), allyl glycidyl ether (AGE), 2,2-dimethoxy-2-phenyl- acetophenone (DMPA), calcium hydride, dopamine hydrochloride, sodium bicarbonate $NaHCO_3$, γ-thiobutyrolactone, silica sand, and magnesium sulfate $MgSO_4$ were purchased from Sigma Millipore. Tetrahydrofuran (THF), ethyl acetate (EA), and heptane were purchased from Fischer Scientific.

1.2. Chemical characterizations:

1.2.1. Nuclear magnetic resonance ^{1}H NMR spectroscopy:

^{1}H NMR spectroscopy was conducted in Bruker NMR spectrometer equipped with a 400 MHz NMR magnet and 5 mm probe. The samples were dissolved in their deuterated solvents mentioned in the synthesis procedure section.

1.2.2. Diffusion Order Spectroscopy (DOSY):

DOSY ^{1}H NMR experiments were conducted on a Bruker NMR spectrometer NEO instrument equipped with a 400 MHz NMR magnet. All DOSY experiments were conducted with a pulse length of 1.25 ms (δ = 1250 μs), diffusion time of 210 ms (Δ = 0.210 s), and the linear gradient was split into 32 steps from 2% to 95% strength at $T = 298$ K.

1.2.3. Fourier transform infrared (FTIR) spectroscopy:

Solid-state attenuated total reflection Fourier transform infrared (ATR-FTIR) spectroscopy was performed using a Spectrum Two FT-IR Spectrometer (Perkin Elmer). Powdered samples were pressed with 90 N of force on a diamond/ZnSe composite crystal to generate total internal reflection with wavenumbers ranging from 4000 to 400 cm^{-1}.

1.2.4. Ultraviolet-visible (UV-Vis) spectroscopy:

UV-Vis absorbance was performed in a Thermo Scientific Varioskan LUX multimode microplate reader. Absorbance spectra were collected in the 200-800 nm range in 1 nm

increments. For these measurements, dopamine **1** was dissolved in water (39.5 mM), whereas DOPA-thiol **2** (29.5 mM) was dissolved in a water/methanol mixture (50%/50%, v/v). Oxidization of catechol in **1** and **2** was done by the addition of sodium periodate $NaIO_4$ to achieve 0.9 mM in each solution.

1.2.5. Gel Permeation Chromatography (GPC):

GPC was performed using Waters Alliance HPLC System with e2695 Separation Module as the pumping system coupled with Tosoh TSKgel SuperHZM-N mixed bed columns (MW range: 200-700,000 g/mol). Differential Refractometer (RI) (Waters 2410) and Photodiode Array Detector (PDA) (Waters 2998) were used to produce the size exclusion chromatographs. THF was used as the solvent, and a total volume of 30 μL of sample was injected at a flow rate of 0.35 mL/min.

1.3. Hydrogel preparation:

Samples were prepared by first dissolving dry tbPC in Mili-Q water to create a stock solution (C_{tbPC} = 50 wt%). Hydrogelation was initiated by further dilution to desired C_{tbPC} at pH = 7.0, followed by adding pre-determined amounts of $NaIO_4$ to achieve a desired [$NaIO_4$]/[DOPA] stoichiometric ratio.

1.4. Shear rheology:

Shear rheology measurements were performed on an Anton Paar MCR 302 rheometer. A cone-and-plate assembly (diameter = 10 mm; cone angle = 2°) was used. Appropriate amounts of oxidized samples were loaded into the lower plate, and the excess sample was trimmed after the cone reached the measuring gap. The elastic G' and loss $G"$ moduli were measured as a function of time while the sample was subjected to an oscillatory strain at an angular frequency ω = 1 rad/s and strain γ = 1%.

1.5. Adhesion testing:

Lab shear adhesion test was conducted using an Instron 5944 universal testing machine (UTM) equipped with a 2 kN load cell. Glass substrates were prepared by soaking in isopropanol for 10 minutes prior to drying at room temperature. Collagen casings were soaked in deionized (DI) water and were gently dried with Kimwipes at room temperature. To prepare the specimens, 70 μL of oxidized samples were injected on one surface (either glass or collagen) covering an area of 25 × 10 mm, and the second surface was placed immediately on top of the sample to allow for curing between the substrates for 7 hours. Collagen specimens were left to cure while pressed with a 100 g weight, whereas glass substrates were joined with clip binders during curing. After curing, one end of the specimen was stretched at a constant rate ($V = 5$ mm.min^{-1}), and the stretching force F was measured until failure. The stress $\tau = F/A$ and strain $\gamma = (D_{0+i} - D_0)/l$ relationship obtained from these lap shear adhesion tests (where D and l are the displacement and overlap length, respectively).

2. Synthesis procedure:

2.1. General procedure for the synthesis of N-(3,4-dihydroxyphenetyl)-4-mercapto-butanamide – DOPA-thiol 2. DOPA–thiol was produced following the protocol described previously[1] but with slight modifications. Dopamine HCl (17.9 g, 94 mmol), sodium bicarbonate $NaHCO_3$ (16.4 g, 195 mmol), and γ-thiobutyrolactone (8.8 mL, 100 mmol) were dissolved in 176 mL deionized (DI) water. The reaction mixture was heated to 95 °C and was allowed to reflux for 2 hours in a Graham condenser before being cooled down to room temperature. 176 mL brine was added to the mixture and the product was extracted twice with THF using a separatory funnel. The organic phase was obtained and dried over $MgSO_4$. The mixture was filtered, and the solvent was evaporated under reduced pressure. An additional purification step was carried out using flash chromatography on silica using ethyl acetate/heptane (80%/20%, v/v) as the mobile phase. Thin layer chromatography (TLC) was also performed periodically during the purification on TLC plates using ethyl acetate/heptane (80%/20%, v/v) as the mobile phase to confirm the purity of the product. Ethyl acetate/heptane solvents were removed under reduced pressure. The final product, a slightly yellow solid, was obtained after solvent removal under reduced pressure. ^{1}H NMR (400 MHz, CD_3OD) δ(ppm): 6.66 (d, 1H, Ar), 6.60 (d, 1H, Ar), 6.50 (dd, 1H, Ar), 2.60 (t, 2H, Ar-CH_2–), 3.28 (t, –CH_2–NHCO), 2.43 (t, 2H, –CH_2–SH), 2.23 (t, 2H, –NHCO–CH_2–), 1.81 (p, 2H, –CH_2–CH_2–SH); (M_w = 255 g/mol).

2.2. General procedure for the synthesis of P(AGE-b-EG-b-AGE), 4. Synthesis of precursor triblock polymers was performed by modifying previously described protocols.[2] 10 mL allyl glycidyl ether (AGE) was transferred to an oven-dried distillation flask, followed by the addition of 0.4 g calcium hydride to dry the AGE. The mixture was stirred overnight before AGE was distilled and collected. 100 mL dry tetrahydrofuran (THF) was added to a two-neck flask, followed by the addition of 3.0 g potassium and

10.0 g naphthalene to make potassium naphthalenide (0.4 M in THF). 15 g PEG was dried *in vacuo* overnight and added to an oven-dried round bottom flask (reaction flask). The flask was filled with Ar and evacuated several times. Dry THF was added to the reaction flask at 40 °C and stirred to dissolve the PEG. Potassium naphthalenide was added dropwise to the reaction flask until a light green color persisted, indicating that hydroxyl groups were deprotonated. 3.5 mL of AGE was added to the reaction mixture, and the reaction was allowed to proceed for 20 hours. The reaction was quenched by the addition of 10 mL of distilled methanol. The final product was precipitated in hexanes. ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 3.50 – 3.70 (–OCH_2CH_2O–, –OCH_2CH–, and –OCH_2CH_2–), 3.99 (d, –$OCH_2CH{=}CH_2$), 5.71 (d, –$OCH_2CH{=}CH_2$), 5.29 (d, –$OCH_2CH{=}CH_2$), 5.89 (m, –$OCH_2CH{=}CH_2$).

2.3. General procedure for thiol-ene reaction, to synthesize catechol-functionalized P(AGE-b-EG-b-AGE), 5. Triblock precursor polymer **4** and 8 equivalents per alkene of DOPA-thiol **2** were dissolved in THF (10 mL per 1.0 g of precursor). A radical initiator, 2,2-Dimethoxy-2-phenylacetophenone (DMPA) was added to the mixture (0.1 equivalent per alkene), and the reaction mixture was sparged with N_2 for 30 minutes. The degassed solution was irradiated with ultraviolet light (UV) at $\lambda = 365$ nm while stirring overnight. The solution was placed in dialysis tubes (MWCO: 3.5 k) and dialyzed against deionized (DI) water for 8 cycles (8 hours each). The solution was filtered and lyophilized, yielding white powder. ^{1}H NMR (400 MHz, D_2O) δ(ppm): 3.50 – 3.70 (–OCH_2CH_2O–, –OCH_2CH-, and –OCH_2CH_2–), 6.71 (d, 1H, Ar), 6.65 (d, 1H, Ar), 6.56 (dd, 1H, Ar), 2.57 (t, 2H, Ar-CH_2–), 3.28 (t, –CH_2–NHCO), 2.42 (t, 2H, –CH_2–SH), 2.25 (t, 2H, –NHCO–CH_2–), 1.65 (p, 2H, –CH_2–CH_2–SH), 2.13 (t, 2H, SH–CH_2–).

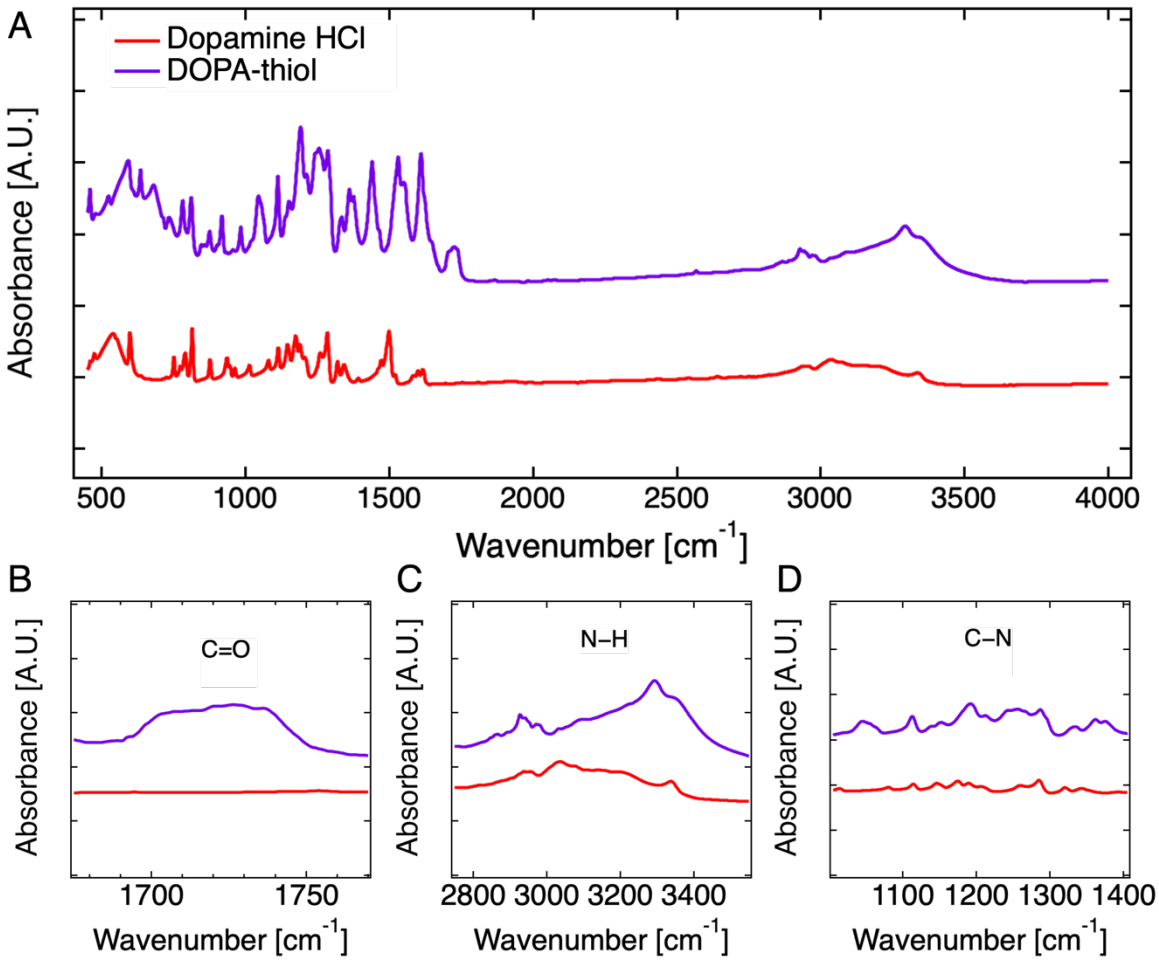

Figure S1. (A) Fourier transform infrared (FTIR) spectra of dopamine **1** and DOPA-thiol **2**. **(B-D)** The same spectra, shown over small wavenumber ranges to highlight the differences.

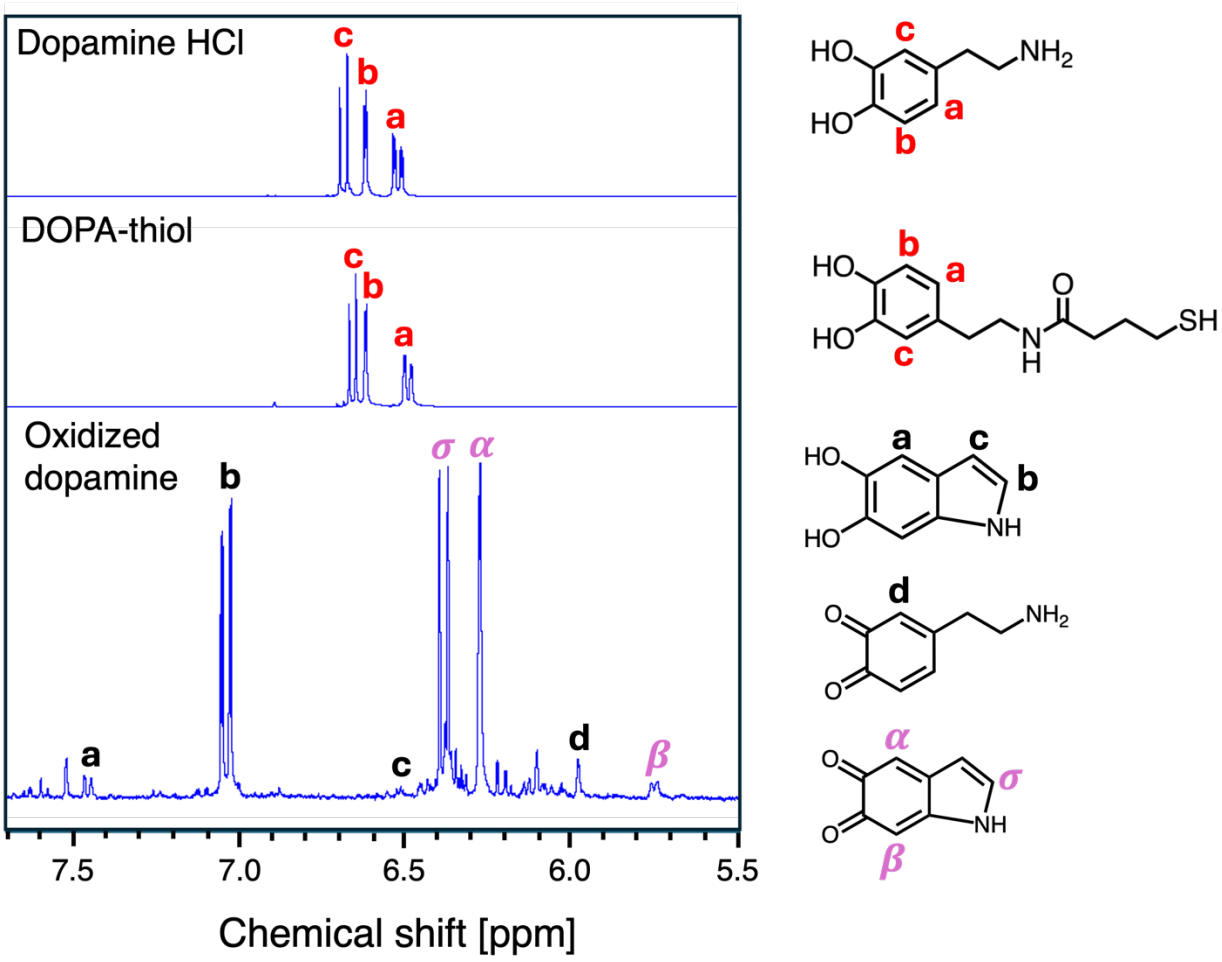

Figure S2. ^{1}H NMR spectra contrasting dopamine **1**, DOPA-thiol **2**, and oxidized dopamine. The benzene ring peaks in **1** and **2** are identical. The oxidized dopamine exhibited changes in the aromatic ring peaks corresponding to a combination of oxidized derivatives (*e.g.*, dopamine quinone, 5,6-dihydroxyindole, 1 *H*-indole-5,6-dione).

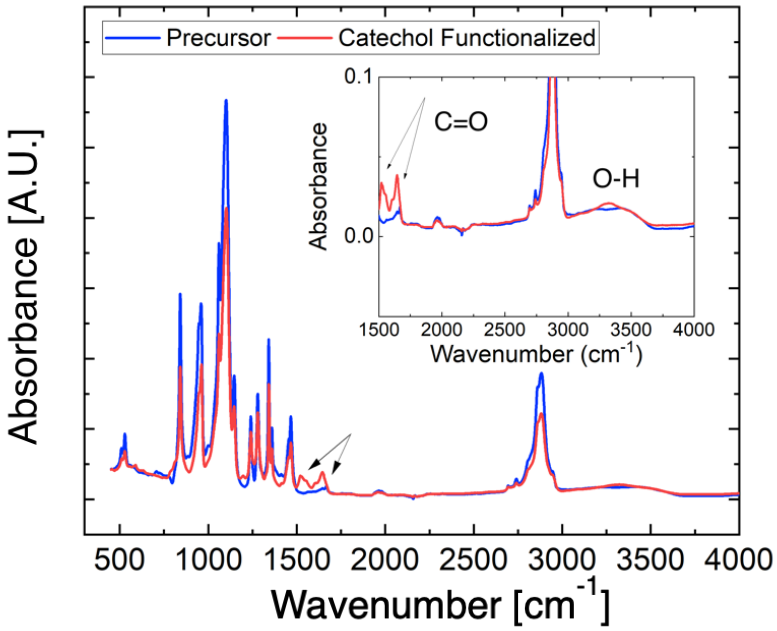

Figure S3. Fourier transform infrared (FTIR) spectra of the precursor $PAGE_6$-PEG_{136}-$PAGE_6$ **4** and after functionalization with catechol to obtain tbPC **5**. *Inset*: FTIR spectra highlighting the difference over a smaller wavenumber range.

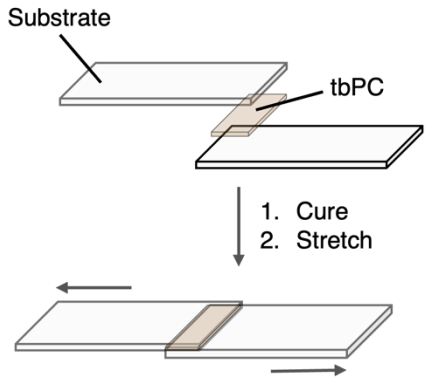

Figure S4. Schematic showing the preparation of lap shear adhesion test specimen using triblock polycatechol or tbPC as the adhesives.

References:

1. K. Olofsson, V. Granskog, Y. Cai, A. Hult and M. Malkoch, *RSC Advances*, 2016, **6**, 26398-26405.
2. J. N. Hunt, K. E. Feldman, N. A. Lynd, J. Deek, L. M. Campos, J. M. Spruell, B. M. Hernandez, E. J. Kramer and C. J. Hawker, *Advanced Materials*, 2011, **23**, 2327-2331.