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Ambivalent Adhesives: Combining Biomimetic Cross-Linking With Antiadhesive Oligo(ethylene glycol)

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Abstract

Oligo(ethylene glycol) (OEG) and poly(ethylene glycol) (PEG) exhibit several desirable properties including biocompatibility and resistance to fouling by protein adsorption. Still needed are surgical glues and orthopedic cements, among several other materials, that display similar traits. However the very lack of interactions with other molecules that prevents toxicity and fouling also makes adhesion elusive. In work described here the cross-linking chemistry of marine mussel adhesive is combined with OEG to make a family of terpolymers. The effect of polymer composition upon bulk adhesion was examined. High strength bonding was found with a subset of the polymers containing appreciable OEG content. These structure-property insights may help the design of new materials for which the properties of OEG and high strength adhesion are both being sought.

Introduction

Poly(ethylene glycol) (PEG) and oligo(ethylene glycol) (OEG) are amongst the most widely studied synthetic polymers owing to several intriguing properties including hydrophilicity,¹ chain flexibility,¹ resistance to protein adsorption,² and biocompatibility.³ These characteristics lie at the heart of why OEG is seen so often in a biomedical context as well as several other fields.^{1,3} Cell growth scaffolds,^{4–6} drug delivery matrices,¹ nonfouling surfaces,^{2,7–10} nonionic surfactants,¹¹ and solid polymer electrolytes¹² are all being developed with OEG. Still very much in demand are plastics able to deter biomedical (e.g., bacteria) or marine (e.g., barnacles) fouling, water compatible adhesives, surgical glues, and bone cements.^{2–7,13–17}

At first glance, OEG may appear ideal for moving research in such directions. However, the very traits that allow one application can prevent another. For example, biocompatibility and the lack of protein adsorption of OEG are a result of the polymer not interacting with much more than solvent.¹ Developing a bulk adhesive from OEG thus brings about the seemingly opposed properties of strong chemical bonding to surfaces and polymer chains versus a lack of interactions with those same surroundings. Generally speaking, OEG is considered to prevent adhesion,¹⁸ although coatings and adhesives containing OEG have been reported.^{2,4,6–8,15–44} The simplest approach to adhering OEG is blending the polymer with a common glue such as an epoxy.³⁹ Significant adhesion can result, although potential

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Supporting Information Available: ¹H NMR spectra of monomers and polymers. This material is available free of charge via the Internet at <http://pubs.acs.org>.

problems include phase separation of polymers and domination of the physical properties by the host adhesive matrix.⁴⁵

An intriguing approach to materials design is to consider how marine mussels affix themselves to rocks.^{46–48} These shellfish generate a protein-based glue in which 3,4-dihydroxyphenylalanine (DOPA) provides access to cross-linking adhesive chemistry.^{46–48} A collection of OEG–DOPA copolymer systems⁴⁹ have been developed for surface coatings^{7,18,20,21} and hydrogels^{13,23–26,40} but less bulk adhesion has been reported (i.e., bonding two substrates together).^{4,15,29,36,41–44} For copolymers of OEG with DOPA or a pendant catechol (i.e., 1,2-dihydroxybenzene),⁴⁹ high strength adhesion has remained elusive. Common commercial materials such as white glue and “Super” glue can bond with strengths in the range of 4–11 MPa (see data below).⁵⁰ So far, experiments with OEG–DOPA copolymers have shown bulk adhesion only $\sim 1/10^{\text{th}}$ that of the established products.^{4,15,29,36,41–44}

The exact mechanism of adhesion for DOPA-containing proteins and catechol-containing polymers has yet to be described precisely. Both adhesive contacts to the surface and cohesive forces within the bulk must be considered. Oxidative cross-linking^{46,51,52} and metal chelation^{47,48,52,53} have been found within the bulk materials. With regard to surface adhesion, evidence for hydrogen bonding,⁵⁴ metal chelation,^{47,48,52,55,56} and radical-surface coupling^{47,48,52,53} has all been reported. Indeed, a combination of each process may be at play, thereby giving rise to the unique bonding properties of mussel adhesive and synthetic mimics thereof.

The contradictory nature of OEG–DOPA copolymers- with DOPA sticking and OEG preventing most interactions- makes for an interesting target of investigation. We embarked on a structure-function study in order to understand the interplay between these two intriguing components when contained within the same molecule. The ideal system will allow the amounts of DOPA (or catechol) and OEG to be varied systematically within a single copolymer chain. If the DOPA content is held constant but the OEG content is varied, what changes to bulk adhesive bonding may result? To the best of our knowledge, there are no systematic studies in which the direct influence of OEG upon copolymer adhesion has been examined. These efforts are not necessarily aimed at making the strongest glue just yet. Rather, we are seeking methodical insights and fundamental knowledge that will aid the design of future materials.

To obtain the desired structure-property insights, a framework was sought to have a flexible composition. Scheme 1 shows a copolymer design in which catechol-containing monomers provide cross-linking adhesive chemistry while, at the same time, OEG-containing monomers are likely to prevent this adhesion. A catechol-containing 3,4-dihydroxystyrene monomer represents the simplest possible mimic for the DOPA chemistry of mussel adhesive proteins (Scheme 2).^{57–60} Polystyrene proved to be a logical polymer host given the structural similarities between 3,4-dihydroxystyrene and styrene.^{57–60} Furthermore, polystyrene provides a clean baseline for these studies, with no appreciable adhesion to start with.^{57,59} According to results shown below, a styryl “filler” monomer helps to ameliorate the conflict between adhesion and antifouling. A further benefit of this copolymer design is potential distribution of catechol chemistry throughout the polymer chains, much like the random distribution of DOPA residues in mussel adhesive proteins.⁴⁶ A family of polymers was prepared in which the catechol content remained unchanged while the amount of OEG was varied. The bonding capability of each polymer was quantified. This systematic approach revealed compositions at which both high strength adhesion and significant OEG content could coexist.

EXPERIMENTAL SECTION

General Procedures

Nuclear magnetic resonance (NMR) spectroscopy was performed on a Varian INOVA 300 MHz spectrometer in CDCl₃. Full spectra are provided in the online Supporting Information. Gel permeation chromatography (GPC) was carried out on a Polymer Laboratories PL-GPC 20 using THF for the eluent. Styrene was purified prior to use with an alumina column to remove the polymerization inhibitor that is included when purchased.

Synthesis of 3,4-bis[*tert*-butyldimethylsilyl]oxy]benzaldehyde

Modification of literature methods was used to prepare this compound as well as the following vinyl derivative.^{58,61,62} *Tert*-butyldimethylsilyl chloride (30.4 g, 202 mmol) was dissolved in acetonitrile (200 mL). To this solution, 3,4-dihydroxybenzaldehyde (10.3 g, 74 mmol) was added and the mixture cooled to 0 °C for at least 10 minutes. Addition of 30.0 mL (198 mmol) 1,8-diazabicyclo[5.5.0]-undec-7-ene was followed by stirring for 48 hours at 4 °C. Solvent was removed to obtain the crude product. Purification was accomplished by silica gel column chromatography (6.3 cm × 45.7 cm) using dichloromethane (DCM) for the mobile phase. The final product was obtained as a solid 15.2 g (41% yield). ¹H NMR (CDCl₃, Figure S1): δ 0.31 (d, *J* = 6.2 Hz, 6H, SiCH₃)₂, 1.07 (d, *J* = 1.0 Hz, 18H, SiC(CH₃)₃), 7.02 (d, *J* = 8.7 Hz, 1H, aromatic), 7.39–7.50 (m, 2H, aromatic), 9.88 (s, 1H, CHO).

Synthesis of 3,4-bis[*tert*-butyldimethylsilyl]oxy]styrene.^{58,61,62}

Methyltriphenylphosphonium bromide (44.4 g, 12 mmol) was dissolved in 176 mL of THF followed by dropwise addition of *n*-butyllithium (45.0 mL, 112 mmol). The solution was stirred for 4 hours at room temperature to allow formation of the ylide. Slow addition of 3,4-bis[*tert*-butyldimethylsilyl]oxy]benz-aldehyde (15.2 g, 41.5 mmol) over 10 minutes was completed and the reaction stirred overnight at 40 °C. Solvent was removed under vacuum and the resulting solid dissolved in DCM. An extraction with water was carried out. The organic phase was collected and dried over MgSO₄. Silica gel column chromatography (6.3 cm × 45.7 cm) with DCM eluent provided the product, 9.6 g (64% yield). ¹H NMR (CDCl₃, Figure S2): δ = 2.3 Hz, 6H, SiCH₃)₂, 1.11 (d, *J* = 3.8 Hz, 18H, SiC(CH₃)₃), 5.22 (d, *J* = 10.8 Hz, 1H, alkene), 5.67 (d, *J* = 17.5 Hz, 1H, alkene), 6.70 (dd, 1H, *J* = 17.5 Hz, alkene), 6.85–7.07 (m, 2H, aromatic), 7.44 (s, 1H, aromatic).

Synthesis of 4-vinylbenzyl[tetra(ethylene glycol)]

This compound was prepared according to a literature procedure.⁶³ Tetra(ethylene glycol) (200.0 mL, 1158 mmol) was added to a 1 L flask that contained (2.1 g, 12.6 mmol) of 4-*tert*-butylcatechol and NaOH (16.2 g, 405 mmol). The reaction mixture was heated to 110 °C, followed by dropwise addition of 4-vinylbenzylchloride (20.0 mL, 138.7 mmol) over 5 minutes. The solution mixture was stirred at 110 °C for 2 hours and allowed to cool to room temperature. This mixture was then combined with 250 mL of toluene and an aqueous-organic extraction was performed. The organic phase was dried over MgSO₄ and solvent removed under vacuum. The yellow oil was purified by silica gel column chromatography (6.3 cm × 45.7 cm) using 2% methanol in toluene. The final product was a yellow oil, 7.1 g (21% yield). ¹H NMR (CDCl₃, Figure S3): δ 3.57–3.70 (m, 16H, OCH₂CH₂O), 4.55 (s, 2H, ArCH₂O), 5.23 (d, *J* = 11.9 Hz, 1H, alkene), 5.74 (d, *J* = 16.5 Hz, 1H, alkene), 6.71 (dd, *J* = 10.9 Hz, *J* = 17.4 Hz, 1H, alkene), 7.29 (d, *J* = 6.9 Hz, 2H, aromatic), 7.42 (d, *J* = 6.9 Hz, 2H, aromatic).

Synthesis of 4-vinylbenzyl[methyltetra(ethylene glycol)]

A literature procedure was followed to obtain this compound.⁶³ 4-Vinylbenzyl[tetra(ethylene glycol)] (7.3 g, 28.9 mmol) was dissolved in 600 mL of benzene and sodium hydride in mineral oil was added (6.62 g, 165.5 mmol). After 2 hours, iodomethane (23.0 mL, 369.5 mmol) was added dropwise over 15 minutes and the solution was stirred for 4 days at room temperature. Solvent was removed and the solid dissolved in DCM. An extraction was performed with a saturated solution of sodium bicarbonate and the organic phase was dried over CaCl₂ followed by removal of solvent under vacuum. A silica gel column (6.3 cm × 45.7 cm) and 2% MeOH in DCM were used to purify the final product, 4.2 g (59% yield). ¹H NMR (CDCl₃, Figure S4): δ 3.38 (s, 3H, OCH₃), 3.54–3.69 (m, 16H, OCH₂CH₂O), 4.56 (s, 2H, ArCH₂O), 5.20 (d, *J* = 10.9 Hz, 1H, alkene), 5.75 (d, *J* = 17.6 Hz, 1H, alkene), 6.71 (dd, *J* = 10.9 Hz, *J* = 17.4 Hz, 1H, alkene), 7.32 (d, *J* = 6.9 Hz, 2H, aromatic), 7.43 (d, *J* = 6.9 Hz, 2H, aromatic).

Synthesis of poly{(3,4-di(OTBDMS)styrene)-co-[4-vinyl-benzyl[methyltetra(ethylene glycol)]]-co-styrene}

In order to obtain the desired polymers, radical polymerizations (AIBN) were performed. Polymerizations were typically carried out in benzene but for polymers containing higher percentages of OEG (~30+%), anhydrous toluene or freshly distilled THF were used. Polymerizations were performed in an air free flask and sealed for 7 or 10 days at 80 °C.

A typical polymerization consisted of styrene (0.8560 g, 8.2 mmol), 3,4-di(OTBDMS)styrene (0.3688 g, 1.0 mmol) and 4-vinylbenzyl[methyltetra(ethylene-glycol)] (0.4687 g, 1.4 mmol) dissolved in 10.0 mL of benzene. The radical initiator AIBN (0.0044 g, 0.03 mmol) was added and the solution stirred for 7 days at 80 °C. Once cooled to room temperature, polymers were precipitated with MeOH (or hexanes) at least three times to remove starting materials. Solvent was removed under vacuum to obtain the polymer, 1.5 g (88.6 % yield). ¹H NMR (CDCl₃, Figure S5): δ 0–1.2 ppm (broad, TBDMS groups), 1.2–2.3 ppm (broad, polymer backbone), 3.1–4.6 ppm (broad, OEG groups), and 6.0–7.4 ppm (broad, aromatic). These ¹H NMR spectra were used to determine the monomer ratios in the final polymers (Table 1). GPC provided molecular weights of the polymers, shown in Table 2.

Synthesis- of- poly{(3,4-dihydroxystyrene)-co-[4-vinyl-benzyl[methyltetra(ethylene glycol)]]-co-styrene}

The polymers were deprotected to expose the pendant catechol groups. In a general procedure, a protected polymer (1.5 g) was dissolved in 60.0 mL dioxane and 13.0 mL of concentrated HCl were added. The reaction was stirred overnight at 80 °C and allowed to cool to room temperature. Solvent was removed under vacuum and the solid dissolved in 1:1 acetone/DCM. An extraction was performed with water and the organic phase dried over MgSO₄. Solvent was removed under vacuum to provide 1.2 g of product (80% yield). ¹H NMR (CDCl₃, Figure S6): δ 1.2–2.3 ppm (broad, polymer backbone), 3.1–4.6 ppm (broad, OEG groups), and 6.0–7.4 ppm (broad, aromatic).

Adhesion studies

Bonding performance was quantified with lap-shear adhesion.⁶⁴ Each terpolymer (13.5 mg in 45 μL of 1:1 acetone/DCM) was added to two polished aluminum adherends. The adherends were overlapped with an area of 1.2 × 1.2 cm and allowed to set for one hour at room temperature. Weights (~54 g) were applied to hold the assemblies together. Samples were cured in an incubator for 22 hours at 70 °C and then cooled at room temperature for one hour. The shear tests were performed using an Instron 5544 materials testing system.

Each measurement was repeated 10 times, averaged, and error bars of 90% confidence intervals are shown.

RESULTS AND DISCUSSION

Polymer Synthesis and Characterization

Scheme 2 shows the six step synthetic route developed to obtain the target terpolymers. A catechol monomer was realized in two steps by modifying published methods, starting from an aldehyde, progressing through silyl protection, and a Wittig reaction to reveal the vinyl group (Scheme 2A).^{58,61,62} A literature approach was used to couple vinylbenzyl chloride and OEG, followed by CH₃I capping, for the styryl OEG monomer (Scheme 2B).⁶³ This OEG monomer was combined with the protected catechol monomer, styrene, and a radical initiator to obtain the protected terpolymer (Scheme 2C). Acid removed the silyl protecting groups, thereby yielding the final poly{(3,4-dihydroxystyrene)-*co*-(4-vinylbenzyl [methyl-tetra(ethylene glycol)])-*co*-styrene} polymers.

Polymer characterization was accomplished by ¹H NMR spectroscopy and GPC. The ratio of monomers in the final polymer was revealed with ¹H NMR spectroscopy (Table 1). Generally speaking, the polymeric monomer mole percent was a reflection of the ratios in the starting feed (Table 1). The GPC data for all of the terpolymer derivatives showed number average molecular weights (*M_n*'s) within a range of 13,000–40,000 and polydispersity indices (PDI's) between 1.2 and 1.7, indicating consistency amongst the polymers (Table 2). These low PDI values are likely a result of the long OEG substituents shielding propagating radicals from chain termination.⁶⁵

Thermal characterization by methods such as differential scanning calorimetry (DSC) was complicated by some polymers appearing to exhibit *T_g* values below room temperature. With low OEG content the copolymers were solid but when the OEG monomer percentage increased the copolymers were oils. Consequently, a melting temperature apparatus was used in an effort to gain some insight on the thermal behavior. For a 100% polystyrene control, the polymer deformed at ~140 °C and was still solid up to 230 °C. With 3% OEG in poly-[(3,4-dihydroxystyrene)-*co*-(4-vinylbenzyl [methyl-tetra(ethylene glycol)])-*co*-styrene], melting at ~71–73 °C was observed. Increasing the OEG content to 9% brought the melting temperature down to ~43 °C. At 42% OEG the copolymer was already an oil at room temperature.

Adhesion Measurements

With a synthetic route to cross-linking OEG polymers in hand, an exploration of bonding properties was then carried out. To see if both high strength adhesion and high OEG content could coexist, a family of seven different polymers was prepared. For each case, the catechol monomer content was maintained at close to 10 mole percent, approximating the DOPA found in mussel adhesive proteins.⁶⁶ The OEG monomer was placed into the polymer at 0%, 88%, and several intermediate loadings. Styrene comprised the reminder.

Adhesion of each polymer was examined by bonding together two pieces of polished aluminum in a lap shear configuration (Figure 1).⁶⁴ Several methods exist for testing adhesive bonding including lap shear, tensile, peel, and burst.^{50,67} Lap shear is used the more often than other bonding schemes.^{50,67} Making direct comparisons between different adhesion studies can be difficult (see below), but lap shear bonding of metal substrates will provide what may be the closest thing to a general condition.

The polymers were dissolved in solvent for application onto the adherends. The second adherend was overlapped onto the first and the assembly was cured. Bonding strengths were

quantified by pulling apart the glued substrates until failure. This failure force (in Newtons) was divided by the measured adherend overlap area (in m^2) and is reported in Pascals ($\text{Pa} = \text{N}/\text{m}^2$). Adhesion data for each polymer are provided in Figure 2.

A 100% polystyrene control adheres only weakly, at $\sim 0.2\text{--}0.6$ MPa.^{57,59} For another control without OEG, the 10% catechol, 90% styrene copolymer adhered at 1.3 ± 0.2 MPa. Comparing the performance of these two polymers indicates that introduction of the catechol group enhances adhesion.

For the poly{(3,4-dihydroxystyrene)-*co*-(4-vinylbenzyl [methyl-tetra(ethylene glycol)])-*co*-styrene} copolymers, addition of 2% OEG monomer (and removal of 2% styrene), displayed comparable attachment at 1.8 ± 0.4 MPa (Figure 2). The strongest bonding of 2.3 ± 0.5 MPa was found with 13% OEG. Total OEG monomer content could be pushed to 18% without any major penalty on adhesion (1.6 ± 0.2 MPa). Higher OEG loadings, however, did inhibit adhesion significantly (Figure 2). The 35% OEG derivative only stuck at 0.26 ± 0.04 MPa. At 88% OEG there was not even sufficient bonding of the substrates to allow handling for measurements.

When examining adhesion as a function of OEG content, we must also be mindful of effects from varying the styrene monomer content. Recently, we showed that incorporation of 3,4-dihydroxystyrene into polystyrene to form poly[(3,4-dihydroxystyrene)-*co*-styrene] can generate high strength adhesives, with bonding up to ~ 7 MPa.⁵⁹ Polystyrene exhibits minimal adhesion of $\sim 0.2\text{--}0.6$ MPa when measured under conditions similar to those used here.^{57,59} For data presented in the current study, decreased adhesion with increased OEG content coincided with less styrene in the polymer. These results lead us to believe that the styrene monomers are providing a “filler” for the polymer composition and are not necessarily bringing about any detriment to adhesion.

Overall, these data are consistent with the general notion that OEG typically prevents adhesion. To provide a perspective on this adhesive performance, three established commercial glues were measured under similar conditions. White glue (polyvinyl acetate, Elmer's) adhered at 4 ± 1 MPa, “Krazy Glue” (cyanoacrylate) at 7 ± 1 MPa, and a two part epoxy (Loctite) at 11 ± 2 MPa.

Comparisons to Other OEG-Containing Adhesives

Bulk adhesion data for OEG-containing copolymers have been reported in some cases. These OEG adhesives include a hydrogel composed of cross-linked OEG-aldehyde able to bond at 0.7 MPa,³³ a poly(acrylic acid)–OEG sticking at ~ 0.15 MPa,¹⁶ scaffolds of OEG-DOPA-polycaprolactone with adhesion of 0.11 MPa,⁴ four-arm OEG-(DOPA)₄-type systems bonding with strengths of 0.035¹⁵ or 0.030³⁶ MPa, and an eight-arm OEG aldehyde matrix at 0.019 MPa.³⁷ A recent report with both OEG and dopamine yielded impressive bonding at 1.2 MPa, although juxtaposition may not be appropriate here given that each component was in a separate polymer chain.²⁹

Results shown for the poly{(3,4-dihydroxystyrene)-*co*-(4-vinylbenzyl[methyltetra(ethylene glycol)])-*co*-styrene} terpolymers appear to display the strongest bonding for an OEG-DOPA-type copolymer. That said, direct correlations can be difficult to make. Differences in bonding modes, substrates, cure conditions, and sample environments prevent putting various materials on equal footing. The lap shear bonding of a high energy substrate used in this current study was chosen to provide the most broadly applicable insights on polymer adhesive performance. Nonetheless, the results presented do show that significant bonding and appreciable OEG copolymer content need not to be mutually exclusive. OEG-containing copolymers can be turned into high strength adhesives.

CONCLUSIONS

The compelling properties of OEG have driven development of applications in several fields of study. High strength adhesion, however, has remained elusive given that OEG prevents interactions with other molecules. Here a systematic structure-property study was carried out to provide insights on how OEG and a DOPA mimic influence each other when contained within a polymer chain. At the maximum possible OEG content adhesion was not detectable. Lower loadings of OEG did display adhesion with no discernable penalty relative to the starting polymer without any OEG. We hope that these results will aid the design of new materials such as coatings, hydrogels, and bulk glues for which both OEG and DOPA can be so well suited.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Knop K, Hoogenboom R, Fischer D, Schumbert US. *Angew Chem Int Ed*. 2010; 49:6288–6308.
2. Banerjee I, Pangule RC, Kane RS. *Adv Mater*. 2011; 23:690–718. [PubMed: 20886559]
3. Alcantar NA, Aydil ES, Israelachvili JN. *J Biomed Mater Res*. 2000; 51:343–351. [PubMed: 10880075]
4. Murphy JL, Vollendweider L, Xu F, Lee BP. *Biomacromolecules*. 2010; 11:2976–2984.
5. Castillo AJ, Borchmann DE, Cheng AY, Wang Y, Hu C, García AJ, Weck M. *Macromolecules*. 2012; 45:62–69. [PubMed: 22279245]
6. Song A, Rane AA, Christman KL. *Acta Biomaterialia*. 2012; 8:41–50. [PubMed: 22023748]
7. Dalsin JL, Lin L, Tosatti S, Vörös J, Textor M, Messersmith PB. *Langmuir*. 2005; 21:640–646. [PubMed: 15641834]
8. Statz AR, Meagher RJ, Barron AE, Messersmith PB. *J Am Chem Soc*. 2005; 127:7972–7973. [PubMed: 15926795]
9. Statz AR, Finlay J, Dalsin J, Callow M, Callow JA, Messersmith PB. *Biofouling*. 2006; 22:391–399. [PubMed: 17178572]
10. Balamurugan S, Ista LK, Yan J, López GP, Fick J, Himmelhaus M, Grunze M. *J Am Chem Soc*. 2005; 127:14548–14549. [PubMed: 16231888]
11. Lin HY, Thomas JL. *Langmuir*. 2003; 19:1098–1105.
12. Wuelfing WP, Gross SM, Miles DT, Murray RW. *J Am Chem Soc*. 1998; 120:12696–12697.
13. Yates CC, Whaley D, Babu R, Zhang J, Krishna P, Beckman E, Pasculle WA, Wells A. *Biomaterials*. 2007; 28:3977–3986. [PubMed: 17561250]
14. Cai L, Wang K, Wang S. *Biomaterials*. 2010; 31:4457–4466. [PubMed: 20202682]
15. Burke SA, Jones MR, Lee PB, Messersmith PB. *Biomed Mater*. 2007; 2:203–210. [PubMed: 18458476]
16. Choi HK, Kim OJ, Chung CK, Cho CS. *J Appl Polym Sci*. 1999; 73:2749–2754.
17. Pechey A, Elwood CN, Wignall GR, Dalsin JL, Lee BP, Vanjcek M, Welch I, Ko R, Razvi H, Cadieux PA. *J Urol*. 2009; 182:1628–1632. [PubMed: 19683735]
18. Yuan S, Wan D, Liang B, Pehkonen SO, Ting YP, Neoh KG, Kang ET. *Langmuir*. 2011; 27:2761–2774.

19. Holten-Andersen N, Harrington MJ, Birkedal H, Lee BP, Messersmith PB, Lee KYC, Waite JJ. *Proc Natl Acad Sci USA*. 2011; 108:2651–2655. [PubMed: 21278337]
20. Black KCL, Liu ZQ, Messersmith PB. *Chem of Mater*. 2011; 23:1130–1135. [PubMed: 21666825]
21. Finlay AS, Dalsin J, Callow M, Callow JA, Messersmith PB. *Biofouling*. 2006; 22:391–399. [PubMed: 17178572]
22. Dalsin JL, Hu BH, Lee BP, Messersmith PB. *J Am Chem Soc*. 2003; 125:4253–4258. [PubMed: 12670247]
23. Bae KH, Kim YB, Lee Y, Hwang J, Park H, Park TG. *Bioconjugate Chem*. 2010; 21:505–512.
24. Strehin I, Nahas Z, Arora K, Nguyen T, Elisseeff J. *Biomaterials*. 2010; 31:2788–2797. [PubMed: 20047758]
25. Chawla K, Lee S, Lee BP, Dalsin JL, Messersmith PB, Spencer ND. *J Biomed Mater Res A*. 2009; 90A:742–749. [PubMed: 18570317]
26. Brubaker CE, Messersmith PB. *Biomacromolecules*. 2011; 12:4326–4334. [PubMed: 22059927]
27. Burke SA, Ritter-Jones M, Lee BP, Messersmith PB. *Biomed Mat*. 2007; 2:203–210.
28. Brubaker CE, Kissler H, Wang LJ, Kaufman DB, Messersmith PB. *Biomaterials*. 2010; 31:420–427. [PubMed: 19811819]
29. Sarbjit K, Weerasekare GM, Stewart RJ. *ACS Appl Mater Interfaces*. 2011; 3:941–944. [PubMed: 21410239]
30. Lee H, Lee KD, Pyo KB, Park SY, Lee H. *Langmuir*. 2010; 26:3790–3793. [PubMed: 20148541]
31. Malisova B, Tosatti S, Textor M, Gademann K, Zurcher S. *Langmuir*. 2010; 26:4018–4026. [PubMed: 20146501]
32. Saxer S, Portmann C, Tosatti S, Gademann K, Zurcher S, Textor M. *Macromolecules*. 2010; 43:1050–1060.
33. Oelker AM, Berlin JA, Wathier M, Grinstaff MW. *Biomacromolecules*. 2011; 12:1658–1665. [PubMed: 21417379]
34. Degoricija L, Bansal PN, Sontjens SHM, Joshi NS, Takahashi M, Synder B, Grinstaff MW. *Biomacromolecules*. 2008; 9:2863–2872. [PubMed: 18800810]
35. Bencherif SA, Gao H, Srinivasan A, Siegwart DJ, Hollinger JO, Washburn NR, Matyjaszewski K. *Biomacromolecules*. 2009; 10:1795–1803. [PubMed: 19518096]
36. Brubaker CA, Messersmith PB. *Biomacromolecules*. 2011; 12:4326–4334. [PubMed: 22059927]
37. Chenault HK, Bhatia SK, DiMaio WG Jr, Vincent GL, CamachoWB, Behrens A. *Curr Eye Res*. 2011; 36:997–1004. [PubMed: 21999226]
38. Strehin I, Nahas Z, Arora K, Nguyen T, Elisseeff J. *Biomaterials*. 2010; 31:2788–2797. [PubMed: 20047758]
39. Mukherjee GS, Shukla N, Singh RK, Mathur GN. *Def Sci J*. 2004; 54:249–255.
40. Lee BP, Huang K, Nunalee FN, Shull KR, Messersmith PB. *J Biomater Sci Polym Edn*. 2004; 15:449–464.
41. Brodie M, Vollenweider L, Murphy JL, Xu FM, Lyman A, Lew WD, Lee BP. *Biomed Mat*. 2011; 6:015014.
42. Lee BP, Chao CY, Nunalee FN, Motan E, Shull KR, Messersmith PB. *Macromolecules*. 2006; 39:1740–1748.
43. Hu B, Messersmith PB. *Orthod Craniofacial Res*. 2005; 8:145–149.
44. Ryu JH, Lee Y, Kong WH, Kim TG, Park TG, Lee H. *Biomacromolecules*. 2011; 12:2653–2659. [PubMed: 21599012]
45. Ryan AJ. *Nature Mat*. 2002; 1:8–10.
46. Sagert, J.; Sun, C.; Waite, JH. *Biological Adhesives*. Springer-Verlag; Berlin: 2006. p. 125-143.
47. Wilker JJ. *Curr Opin Chem Biol*. 2010; 14:276–283. [PubMed: 20036600]
48. Wilker JJ. *Angew Chem Int Ed*. 2010; 49:8076–8078.
49. Moulay S. *C R Chim*. 2009; 12:577–601.
50. Pocius, AV. *Adhesion and Adhesives Technology*. 2. Hanser Gardner; Ohio: 2002.
51. Yu J, Wei W, Danner E, Ashley RK, Israelachvili JN, Waite JH. *Nature Chem Biol*. 2011; 7:588–590. [PubMed: 21804534]

52. Wilker JJ. *Nature Chem Biol.* 2011; 7:579–580. [PubMed: 21849996]
53. Sever MJ, Weisser JT, Srinivasan S, Wilker JJ. *Angew Chem Int Ed.* 2004; 43:447–450.
54. Mian SA, Saha LC, Jang J, Wang L, Gao XF, Nagase S. *J Phys Chem C.* 2010; 114:20793–20800.
55. Ooka AA, Garrell RL. *Biopolymers.* 2000; 57:92–102. [PubMed: 10766960]
56. Lee H, Scherer NF, Messersmith PB. *Proc Natl Acad Sci USA.* 2006; 103:12999–13003. [PubMed: 16920796]
57. Westwood G, Horton TN, Wilker JJ. *Macromolecules.* 2007; 40:3960–3964.
58. White JD, Wilker JJ. *Macromolecules.* 2011; 44:5085–5088.
59. Matos-Pérez CR, White JD, Wilker JJ. *J Am Chem Soc.* 2012; 134:9490–9505.
60. Cristescu R, Kocourek T, Doraiswamy A, Mihaiescu D, Narayan R, Stamatini I, Wilker JJ, Jelinek M, Mihaiescu IN, Chrisey DB. *Appl Surface Sci.* 2009; 255:5496–5498.
61. Menichetti S, Aversa MC, Cimino F, Contini A, Viglianisi C, Tomaino A. *Org Biomol Chem.* 2005; 3:3066–3072. [PubMed: 16186941]
62. Fakar CA, Joulié MM. *Org Lett.* 2007; 9:1987–1990. [PubMed: 17447776]
63. Kros A, Gerritsen M, Murk J, Jansen JA, Sommerdijk NAJM, Nolte RJM. *J Polym Sci A.* 2001; 39:469–474.
64. ASTM International D1002-05. Standard Test Method for Apparent Shear Strength of Single-Lap-Joint Adhesively Bonded Metal Specimens by Tension Loading (Metal-to-Metal). ASTM International; West Conshohocken, PA: 2005.
65. Krstina J, Moad G, Rizzardo E, Winzor CL. *Macromolecules.* 1995; 28:5381–5385.
66. Rzepecki LM, Hansen KM, Waite HJ. *Biol Bull.* 1992; 183:123–137.
67. Mays, GC.; Hutchinson, AR. *Adhesives in Civil Engineering.* Cambridge University Press; Cambridge, UK: 1992.

Figure 1.

(A) Two aluminum adherends bonded together with 225 mg of a 15% OEG-containing polymer, able to support a 25 pound (~11 kg) weight. (B) Representative data from a lap shear adhesion test in which a sample is pulled apart until failure. The plot rises with increasing force applied to the bond until a sudden drop, indicating that the joint has broken, thereby providing the maximum adhesive force. (C) Photograph of two bonded substrates in the materials testing system, ready to be pulled apart for measurement of adhesive strength.

Figure 2.

Influence of OEG monomer content on adhesive bonding of poly{(3,4-dihydroxystyrene)-*co*-{4-vinylbenzyl-[methyl-tetra(ethylene-glycol)]}-*co*-styrene} terpolymers. The adhesive catechol-containing monomer was held constant at ~10% while the amount of OEG-containing monomer was varied. Styrene provided the remainder.

Scheme 1.

Design of polymers containing both adhesive promoting groups as well as OEG chains that typically deter bonding.

Scheme 2.

(A) Synthesis of the protected adhesive monomer. (B) Preparation of the OEG-containing monomer. (C) Polymerization and deprotection to yield the poly{(3,4-dihydroxystyrene)-*co*-{4-vinylbenzyl[methyltetra(ethylene-glycol)]}}-*co*-styrene} terpolymers.

Table 1

Monomers in the starting feeds compared to composition of the final polymers.

feed	final polymer composition			
	OEG	catechol	styrene	styrene
0%	9%	91%	0%	90%
2%	10%	88%	2%	87%
8%	8%	84%	9%	82%
14%	9%	77%	13%	78%
15%	9%	76%	18%	73%
38%	12%	50%	35%	52%
91%	9%	0%	88%	0%

Table 2

Molecular weights and polydispersity data for each poly {[3,4-di(OTBDMS)styrene]-*co*-[4-vinylbenzyl[methyltetra-(ethylene-glycol)]]-*co*-styrene} terpolymer.

OEG	catechol	styrene	<i>Mn</i>	<i>Mw</i>	PDI
0%	10%	90%	39,792	49,712	1.2
2%	11%	87%	16,612	19,255	1.2
9%	9%	82%	16,927	19,722	1.2
13%	9%	78%	20,673	25,295	1.2
18%	9%	73%	19,626	22,119	1.1
35%	13%	52%	12,627	21,240	1.7
88%	12%	0%	13,711	19,972	1.5