

Competition between Oxidation and Coordination in Cross-Linking of Polystyrene Copolymer Containing Catechol Groups

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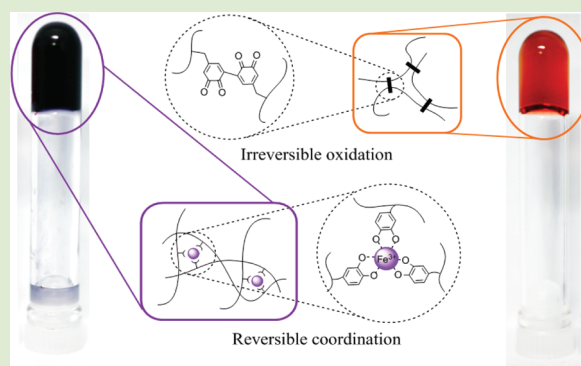
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Supporting Information

ABSTRACT: In gelation chemistry, catechol groups are used as cross-linking points. Both oxidation and coordination effects of catechol were investigated for their unique features in chemistry by spectroscopic measurements. Polystyrene copolymers containing catechol groups were synthesized by free radical copolymerization of styrene and *N*-2-(3',4'-ditriethylsilyloxyphenyl)ethyl methacrylamide, and the successive deprotection reaction was catalyzed by tetra-*n*-butylammonium fluoride. The copolymer containing catechol units afforded a dual cross-linking system based on completely different coordination and oxidation chemistries, and the competing cross-linking mechanisms are discussed. These findings are useful and important for paving the way for designing a novel bioinspired artificial adhesive surface coating and curing system.



Marine mussels are a fascinating species; they affix themselves to the turbulent intertidal zone by their byssus.¹ This amazing environment-tolerant bioadhesive system is supported by adhesive proteins containing a large number of 3,4-dihydroxyphenylalanine (DOPA) residues,^{2–4} which act as crucial adhesive functional groups on both organic and inorganic substrates.⁵ This bioadhesive system has become the focus of considerable attention for many researchers trying to clarify the essential mechanism of the adhesive route.^{6–11} 3,4-Dihydroxyphenethylamine (dopamine),^{12–15} which is a simple DOPA structure containing only 1,2-dihydroxybenzene (catechol) and primary amine, was applied in surface coating experiments. The curing behavior of the raw mussel protein extract was investigated by adding some oxidant and metal ions.^{9,16} These reports revealed that DOPA or dopamine can self-polymerize by some redox reactions in the presence of oxidizing agents under basic conditions. Catechol units in DOPA and dopamine are assumed to play an important role in these reactions, because catechol is not stable under basic conditions and is easily oxidized to quinone.^{6,7} Furthermore, the radical generation and oxidative coupling processes of catechol have also been confirmed.⁶ Although the complete reaction mechanism of catechol in a marine mussel adhesive system still remains vague, there is reliable evidence that the catechol groups can react with each other by an oxidative process under appropriate (pH 8.5) conditions.¹²

In addition, catechol ferric ion complexes were observed in marine mussel adhesive fibers, and these reversible coordinative cross-linking points were considered to enhance the fiber

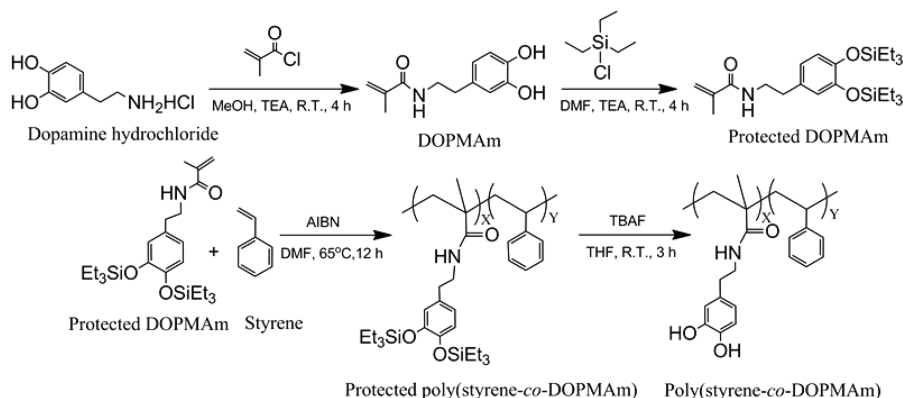
strength.^{17,18} The catechol–Fe³⁺ coordination system was discovered in siderophores of enteric bacteria in the 1970s.¹⁹ This coordination system is pH-sensitive, which means that the iron monocatecholate, bis-catecholate, and tris-catecholate complexes form in turn, as the pH is increased from 5.5 to 10 in aqueous systems.^{19,20} A reasonable interpretation is that the base can deprotonate the dihydroxy groups of catechol moieties, which leads to a stronger chelating ability with ferric ions.^{13,20} Self-healing polymer systems have recently been developed on the basis of reversible catechol–Fe³⁺ coordination.^{21,22} Studies have also reported that a single catechol or catecholamine group has a stronger interaction with titanium and stainless steel.^{13,23}

In the past decade, properties such as the metallic adsorption, redox activity, and adhesion promotion of the polymers bearing a dihydroxybenzene moiety were investigated on the basis of both the oxidative and the coordinative effects,²⁴ and biomimetic coatings and adhesive methods were consequently developed.²⁵ However, it is unclear how these two mechanisms compete with each other. In gelation chemistry, catechol groups act as cross-linking points, and, in this study, we designed a simple polystyrene copolymer containing catechol groups; both oxidative and coordinative effects were investigated according to their unique features in chemistry.

Received: December 10, 2011

Accepted: March 13, 2012

Published: March 19, 2012

Scheme 1. Synthetic Steps of Poly(styrene-*co*-DOPMAm)

N-(3,4-Dihydroxyphenethyl)methacrylamide (DOPMAm, Scheme 1), a catecholamine-based methacrylamide monomer, was synthesized using dopamine hydrochloride and methacryloyl chloride. The catechol group was then protected by chlorotriethylsilane. Free radical copolymerization of styrene and the protected DOPMAm (40/1, mol/mol) was carried out using azobisisobutyronitrile (AIBN) as an initiator at 60 °C for 14 h. Poly(styrene-*co*-protected DOPMAm) was obtained, and size exclusion chromatography (SEC) measurements showed that the molecular weight and their distribution were $M_n = 46800$ and $M_w/M_n = 1.96$, respectively. The composition of the protected DOPMAm unit in the copolymer was estimated to be 1.5% from the NMR spectrum. Poly(styrene-*co*-protected DOPMAm) was deprotected to afford poly(styrene-*co*-DOPMAm) by tetra-*n*-butylammonium fluoride (TBAF). The detailed synthetic steps of poly(styrene-*co*-DOPMAm) are shown in Scheme 1.

Ultraviolet–visible (UV–vis) spectroscopy was adopted to realize both oxidative and coordinative behaviors of catechol units in poly(styrene-*co*-DOPMAm). Oxidation was triggered by simply adding sodium methoxide (MeONa) to the copolymer THF solution. Figure 1a gives the UV–vis spectra of a 0.6 mM solution of catechol (calculated by the catechol ratio in the copolymer); 2.5 equiv of MeONa per catechol maintained the same species. The starting catechol was converted to the *o*-quinone type intermediate ($\lambda_{\max} = 425$ nm) within 30 min. The absorbance decreased in intensity over time, which indicates that *o*-quinone-type intermediates were consumed by the subsequent coupling oxidations that gave the typical oxidative behavior of catechol, as reported in previous literature.^{6,7}

For Fe^{3+} –catechol coordination, we used a THF/methanol (9/1) mixed solvent system due to the solubility problem, and iron(III) trifluoromethanesulfonate ($\text{Fe}(\text{SO}_3\text{CF}_3)_3$) was applied as Fe^{3+} . Figure 1b,c shows the UV–vis spectra of a 0.6/0.2 mM solution of catechol/ $\text{Fe}(\text{SO}_3\text{CF}_3)_3$ titrated with MeONa. When the base was increased, the same species was maintained up to 2.0 equiv of MeONa per catechol; an obvious increase in the peak around 571 nm was observed (Figure 1b), which corresponds to the formation of iron bis-catecholate complexes.^{19,20} Further addition of base, up to 4.0 equiv of MeONa, caused the peak to shift from 571 to 481 nm; iron tris-catecholate complexes were assumed to have formed (Figure 1c).^{19,20} Similar results were also confirmed by previous experiments in an aqueous system.^{19,20}

Based on these UV–vis results, catechol units can give completely different behaviors, from oxidation to coordination,

under nearly identical basic conditions, depending only on the presence of Fe^{3+} . Interestingly, a small peak around 425 nm was observed in Figure 1c to appear at higher concentrations of MeONa; this indicates that slight oxidation took place even though Fe^{3+} was present, when a large amount of MeONa (base) was added.

The color of each specimen at different equivalent bases (MeONa) per catechol is shown in Figure 2. The 2 wt % solution of poly(styrene-*co*-DOPMAm) without base was colorless and transparent (Figure 2a). When 0.33 equiv of ferric ion was added, the color changed slightly to pale yellow (Figure 2b). When 0.5 equiv of MeONa per catechol was also added, a pale blue color was observed. This was assumed to be a mixture of monocatecholate and bis-catecholate complexes (Figure 2c). When the amount of base was increased up to 1.5 equiv, a blue-violet color originating from the bis-catecholate complex became dominant (Figure 2d). Further addition of the base, up to 4.5 equiv, caused the solution color to turn wine-red; this was attributed to the tris-catecholate complexes (Figure 2e). After excessive acetic acid was added, this wine-red color suddenly returned to pale yellow. This was probably due to the collapse of the catecholate complexes under acidic conditions (Figure 2f).^{19,20} No obvious precipitate formed under the present experimental conditions, and these results were consistent with UV–vis data; thus, reversible catechol– Fe^{3+} complexes were revealed to exist in the present copolymer system.

The following gelation experiments were carried out to obtain further insight into the oxidation and coordination; a 10 wt % THF solution of poly(styrene-*co*-DOPMAm) in ambient air (presence of oxygen) was used. After 2.0 equiv of MeONa was added without Fe^{3+} , the viscosity gradually increased while the system remained homogeneous; an orange-colored gel formed after 12 h (Figure 3a, left). When 0.33 equiv of Fe^{3+} per catechol was dissolved in the poly(styrene-*co*-DOPMAm) solution in advance, a dark purple precipitate formed immediately after MeONa was added. After 12 h, the system became more homogeneous like a dark purple gel (Figure 3a, right).

These two extremely different phenomena indicate that completely different gelation mechanisms occurred in the present system. The addition of base can lead to the cross-linking of catechol groups by an oxidative process, in which unstable catechols couple to each other to form irreversible covalent bonds. This process is relatively slow but depends on the concentration of the base. On the other hand, if Fe^{3+} exists in the system, the catechols choose another cross-linking route

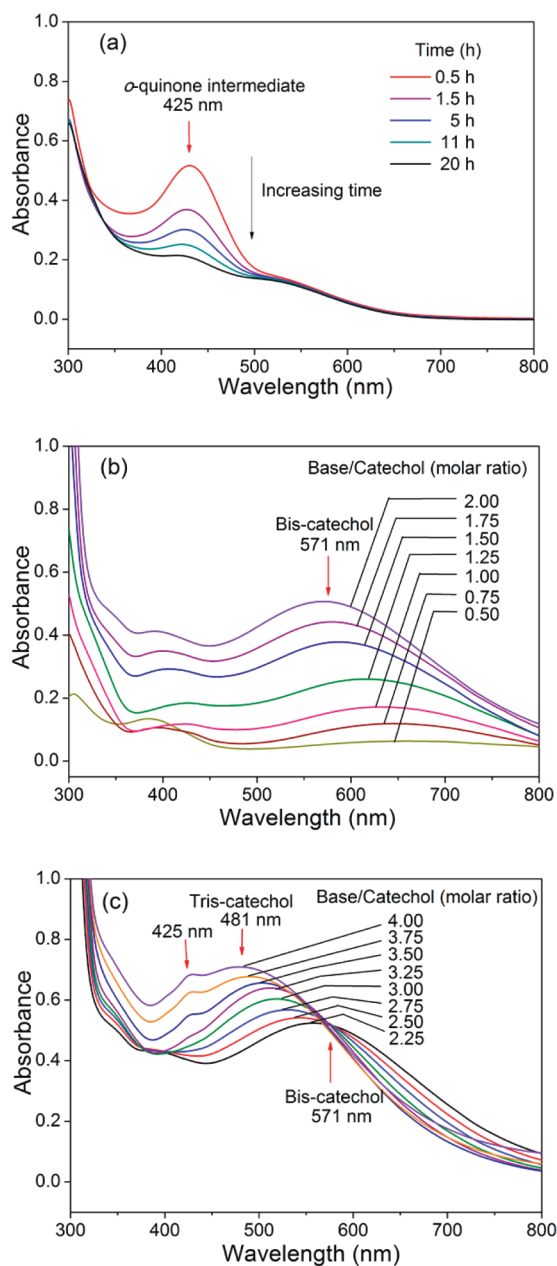


Figure 1. (a) Time-dependent UV-vis spectra of THF copolymer solution [catechol] = 0.6 mM, with 2.5 equiv of MeONa per catechol. (b, c) UV-vis spectra of catechol/ $\text{Fe}(\text{SO}_3\text{CF}_3)_3$ in THF/MeOH (9/1, v/v) solution titrated with MeONa/MeOH solution (18 mM); Initial concentration [catechol] = 0.6 mM, $[\text{Fe}(\text{SO}_3\text{CF}_3)_3]$ = 0.2 mM; (b) increase up to 2.0 equiv per catechol and (c) increase up to 4.0 equiv per catechol.

that is dominated by very fast reversible coordinative bonds, similar to the reported self-healing system based on catecholates complexes.^{21,22} The catechol- Fe^{3+} complex can form immediately, which affords the formation of the dark purple precipitate that appeared in the initial stage. Then, as the coordinative bonds break and recombine, the system gradually unifies to a homogeneous gel. To confirm this mechanism, excessive acetic acid was added to the dark purple gel. The gel gradually dissolved and finally changed to a light yellow solution (Figure 3b–f, right). In other words, negligible irreversible cross-linking occurred in the presence of ferric ions, indicating that ferric ions can stabilize catechols by coordination against oxidation.



Figure 2. Photographs of 2 wt % copolymer THF solution with different amount of Fe^{3+} and MeONa, (a) 2 wt % copolymer THF solution, (b) $[\text{Fe}^{3+}]/[\text{catechol}] = 0.33$, (c) $[\text{Fe}^{3+}]/[\text{catechol}] = 0.33$, $[\text{MeONa}]/[\text{catechol}] = 0.5$, (d) $[\text{Fe}^{3+}]/[\text{catechol}] = 0.33$, $[\text{MeONa}]/[\text{catechol}] = 1.5$, (e) $[\text{Fe}^{3+}]/[\text{catechol}] = 0.33$, $[\text{MeONa}]/[\text{catechol}] = 4.5$, and (f) $[\text{Fe}^{3+}]/[\text{catechol}] = 0.33$, $[\text{MeONa}]/[\text{catechol}] = 4.5$, with excessive acetic acid. UV-vis data for these samples at the lower concentrations are shown in Supporting Information, which gives the spectroscopic evidence for the reversible coordination in the copolymer system.

In contrast, the orange gel without ferric ions stayed in the gel state, even after the addition of excessive acetic acid (Figure 3b–f, left). This was undoubtedly due to the cross-linking by irreversible covalent bonds formed by the oxidation process.

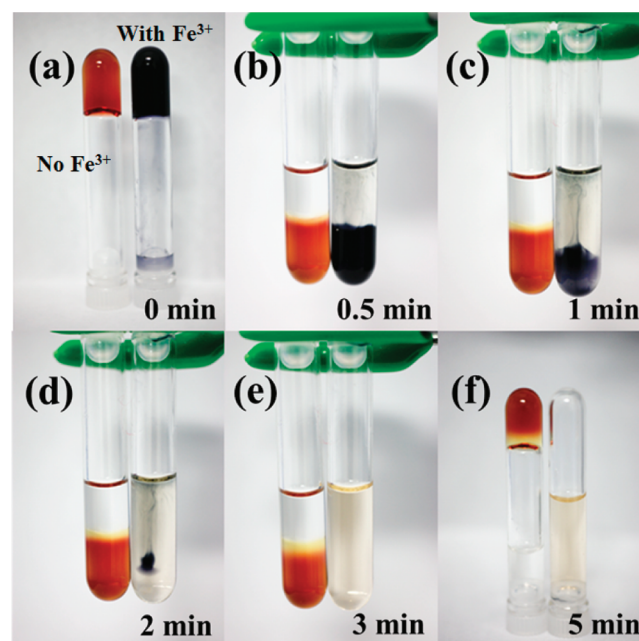


Figure 3. Photographs of (a) the final state of gels cross-linked by irreversible covalent bonds (left) and reversible coordinate bonds (right) after curing for 12 h; (b) 0.5 min after excessive acetic acid was added to (a), the coordinative cross-linked gel started to de-cross-link; (c–e) the coordinative cross-linked gel further de-cross-linked, while the covalently cross-linked gel remained in a gel state for the following 3 min; (f) the coordinative cross-linked gel completely dissolved after 5 min (right), while the covalently cross-linked gel (left) was stable.

We present a clear picture regarding the cross-linking mechanism of catechols in the present copolymer system in Figure 4.

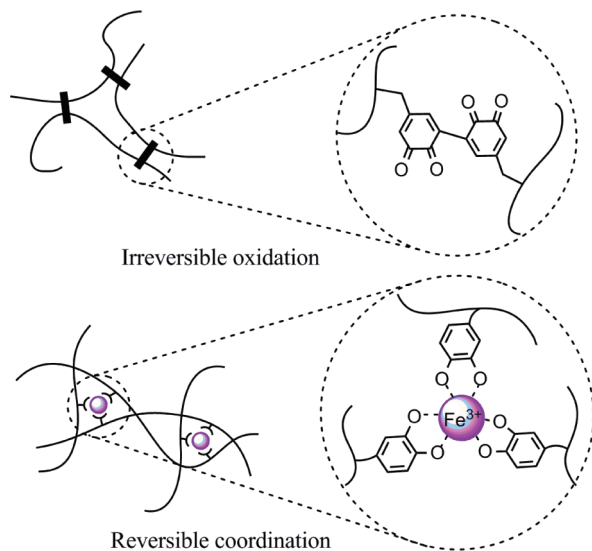


Figure 4. Plausible mechanism of the dual cross-linking system based on irreversible oxidation and reversible coordination.

However, it is difficult to completely avoid oxidation. In the plausible mechanism, a catechol-Fe³⁺ complex system is in dynamic equilibrium,¹⁹ which means that even if there is sufficient Fe³⁺, there is still a small number of free catechols in the system. Oxidation consumes the free catechols (shifts the equilibrium), which finally breaks down the complexes, and this process can be accelerated by further increasing the amount of base, which results in a higher oxidative rate. In most cases, hybrid gels were formed by dual cross-linking, and the ratio of each type of cross-linking may shift from coordinative bond to covalent bonds over time.

In summary, a copolymer containing catechol units could afford a dual cross-linking system, based on oxidative coupling with oxygen or coordinative coupling through Fe³⁺. The basic condition enhanced both of these mechanisms, and temporary cross-linking by coordination was dominant in the presence of Fe³⁺, because coordination is faster than the oxidation according to our observations. In other words, the Fe³⁺ could stabilize catechols through coordination against oxidation to some extent. We believe that these findings will be helpful and important to the design of a bioinspired artificial adhesive surface coating and curing system.

■ ASSOCIATED CONTENT

Supporting Information

Additional experimental details and figures. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The present work is supported by a Grant-in-Aid for the Global COE Program, "Science for Future Molecular Systems" and a Grant-in-Aid for Scientific Research on Innovative Areas (20106001) from MEXT.

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