

Surface Confined Retro Diels–Alder Reaction Driven by the Swelling of Weak Polyelectrolytes

Beier Lyu,^{†,∇,○} Wenli Cha,^{†,#,○} Tingting Mao,[§] Yuanzi Wu,[†] Hujun Qian,^{||} Yitian Zhou,[†] Xiuli Chen,[⊥] Shen Zhang,[†] Lanying Liu,[§] Guang Yang,[⊥] Zhongyuan Lu,^{||} Qiang Zhu,^{*,§} and Hongwei Ma^{*,†,‡}

[†]Division of Nanobiomedicine, Suzhou Institute of Nano-Tech and Nano-Bionics, Chinese Academy of Science, Suzhou 215123, People's Republic of China

[‡]Collaborative Innovation Center of Suzhou Nano Science and Technology, Soochow University, Suzhou 215123, People's Republic of China

[§]State Key Laboratory of Respiratory Disease, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou 510530, People's Republic of China

^{||}State Key Laboratory of Theoretical and Computational Chemistry, Institute of Theoretical Chemistry, Jilin University, Changchun 130023, People's Republic of China

[⊥]College of Life Science and Technology, Huazhong University of Science & Technology, Wuhan 430074, People's Republic of China

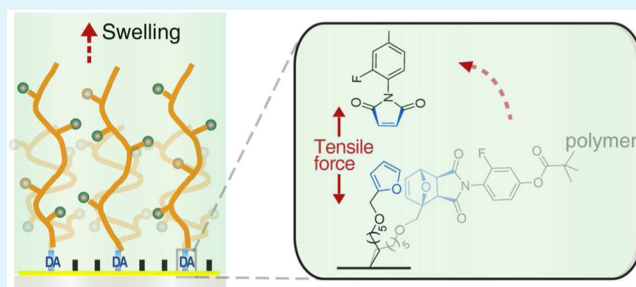
[#]Nano Science and Technology Institute, University of Science and Technology of China, Suzhou 215123, People's Republic of China

S Supporting Information

ABSTRACT: Recently, the type of reactions driven by mechanical force has increased significantly; however, the number of methods for activating those mechanochemical reactions stays relatively limited. Furthermore, in situ characterization of a reaction is usually hampered by the inherent properties of conventional methods. In this study, we report a new platform that utilizes mechanical force generated by the swelling of surface tethered weak polyelectrolytes. An initiator with Diels–Alder (DA) adduct structure was applied to prepare the polyelectrolyte-carboxylated poly(OEGMA-r-HEMA), so that the force could trigger the retro DA reaction.

The reaction was monitored in real time by quartz crystal microbalance and confirmed with atomic force microscopy and X-ray photoelectron spectroscopy. Compared with the conventional heating method, the swelling-induced retro DA reaction proceeded rapidly with high conversion ratio and selectivity. A 23.61 kcal/mol theoretical energy barrier supported the practicability of this retro DA reaction being triggered mechanically at ambient temperature. During swelling, the tensile force was controllable and persistent. This unique feature imparts this mechanochemical platform the potential to “freeze” an intermediate state of a reaction for in situ spectroscopic observations, such as surface-enhanced Raman spectroscopy and frequency generation spectroscopy.

KEYWORDS: mechanochemistry, retro Diels–Alder reaction, polyelectrolyte, polymer brush, quartz crystal microbalance



INTRODUCTION

Mechanically facilitated chemical deformations in polymers, such as bond dissociation and isomerization, have been realized with various methods.^{1–5} However, the understanding of the mechanisms of the mechanochemical deformations has been lagging behind, largely due to the difficulty in monitoring reactions in real time. As for the solution-state methods such as sonication and flow fields, reactions are usually characterized ex situ with optical/fluorescent spectroscopy, such as the gel permeation chromatography or nuclear magnetic resonance spectroscopy.^{6,7} Efforts have been taken to monitor reaction dynamics, but entirely in situ analyses are still highly wanted.

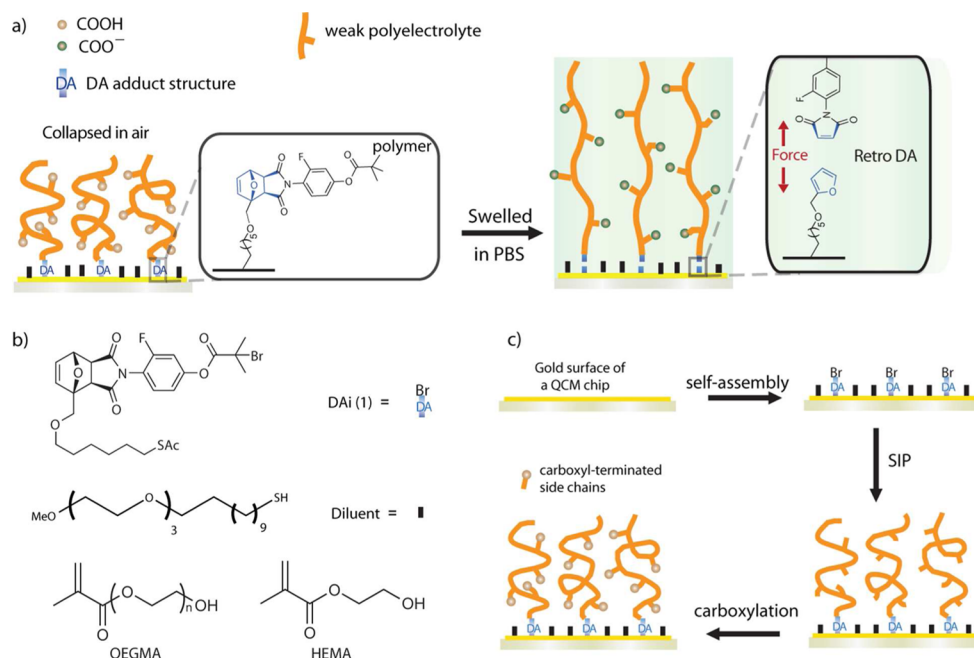
In the current study, we report a new mechanochemical platform that is potentially compatible with in situ analyzing techniques. In this platform, the target bond was embedded into the chains of surface-tethered weak polyelectrolyte brush-carboxylated poly(OEGMA-r-HEMA), which was tethered on gold surface on one end (Scheme 1a). When exposed to salt solutions, the ionized polyelectrolyte chains would repulse to each other and extend perpendicularly to the surface due to electrostatic interactions, which is referred to as the swelling

Received: January 18, 2015

Accepted: March 3, 2015

Published: March 3, 2015

Scheme 1. Design of the Swelling-Induced Retro DA Reaction



^aA DA adduct structure was linked on one end to the surface and on the other end to a weak polyelectrolyte chain. The cycloreversion was proposed to be driven by the swelling of the weak polyelectrolyte brushes. ^bChemical structure of DAi, EG₃, and monomers. ^cPreparation of carboxylated poly(OEGMA-r-HEMA) from DAi.

behavior.⁸ During swelling, a tensile force would be generated in the polymer chain to balance for the repulsion;⁸ such tensile force was adopted as the driving force for mechanochemical reaction. The advantage of this platform is that the force is controllable and persistent by maintaining the swelling equilibrium,⁹ making simultaneous spectroscopic analyses possible.

The retro DA reaction has been reported to be triggered mechanically both in solution¹⁰ and in bulk,^{11,12} with significantly reduced temperature requirement. Therefore, it was selected as the model reaction here. The swelling-induced ring-opening was demonstrated and compared with the same reaction driven by heating. Thus, we provided a mechanochemical platform that has the potential to “freeze” an intermediate state of a reaction for in situ spectroscopic observations, such as surface-enhanced Raman spectroscopy and frequency generation spectroscopy.

RESULTS AND DISCUSSION

Swelling-Induced Retro DA Reaction. Surface-initiated polymerization (SIP)¹³ was conducted from the mixed self-assembled monolayer (SAM) of initiator molecule (DAi, **1**) and diluent molecule 2,5,8,11-tetraoxadocosane-22-thiol (EG₃), followed by carboxylation to give carboxylated poly(OEGMA-HEMA)¹⁴ (Scheme 1b,c). The DAi was labeled with a F atom to facilitate confirmation of retro DA reaction with element analysis. To obtain polymer layers with ideal thicknesses, the molar ratio of DAi to EG₃ (indicated as the solution initiator density, $\chi^{\text{sol}}_{\text{I}}$, where $\chi^{\text{sol}}_{\text{I}} = n_{\text{DAi}} / (n_{\text{DAi}} + n_{\text{EG3}})$) was carefully tuned, and $\chi^{\text{sol}}_{\text{I}}$ was finally set to 95%. Films with thicknesses ($T_{\text{COOH,dry}}$) ranging from 50 to 110 nm were obtained.

To trigger the designed mechanochemical retro DA reaction, we sent the surface tethered weak polyelectrolyte to swelling by treatment with phosphate buffered saline (PBS) in ambient temperature. The salt concentration of Na⁺ ($[\text{Na}^+]$) in the PBS

was increased gradually to control the extent of swelling. Because the energy barrier for retro DA reaction was lower than that of Au–S degradation as reported by others^{15,16} and supported by our computation, the retro DA reaction was expected to happen before the breaking of Au–S bonds. The outcome of the PBS treatment was monitored in real time with QCM measurement (Figure 1).¹⁷

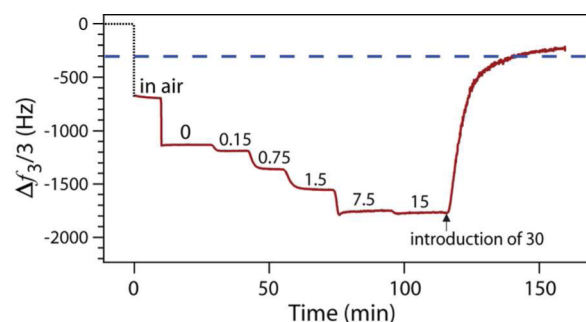


Figure 1. Characterization of the swelling-induced retro DA reaction by QCM. Real-time monitoring of the progressive swelling of a 90 nm thick carboxylated poly(OEGMA-r-HEMA) in a salt gradient at 37 °C and the swelling-induced retro-DA reaction. The numbers indicate $[\text{Na}^+]$ of PBS with the unit of mM. The blue dashed line indicates the Δf level of a bare chip in PBS.

Each time PBS with a higher salt concentration was introduced, the frequency would always first decrease due to intensified swelling and then, if it reached swelling balance, stay steady.¹⁸ It is clear from Figure 1 that an equilibrium of swelling could be easily achieved. Thus, it is reasonable to assume that the tensile force was controllable and persistent at each of these equilibrium states. This unique feature imparts this mechanochemical platform with the potential to “freeze” an

intermediate state of a reaction for in situ spectroscopic observations.

As shown in Figure 1, for a sample with a 90 nm weak polyelectrolyte film at 37 °C, frequency increase occurred at the introduction of 30 mM PBS, implying that the retro DA reaction was induced at that extent of swelling. The frequency rose to the same level as that of an unmodified gold sensor in PBS, which suggested that all the tethered polymer chains had detached from the surface. The reaction completed in about 50 min.

We further tested the response of samples with different $T_{\text{COOH,dry}}$ to PBS. The swelling-induced retro DA reaction was found to depend on film thickness. At 25 °C, only samples with $T_{\text{COOH,dry}} > 65$ nm underwent retro DA reaction. This fact supported the notion that the reaction was triggered by mechanical force, as the effect of sonication also depends on the degree of polymerization.¹⁰ The surface morphology before and after PBS treatment were compared using AFM (Figure S3a,b, Supporting Information), which suggested that after PBS treatment the surface morphology resembled a typical Au(111) surface.

The swelling-induced retro DA reaction is sensitive to temperature. Although the swelling of the 65 nm film could not induce retro DA reaction at 25 °C, even when salt concentration increased to 150 mM, it initiated the cycloreversion reaction when the temperature was further increased to 26 °C, in the midst of a heating process in which the temperature was elevated from 25 to 37 °C (Figure 2) which suggested that temperature has the potential to be another parameter other than the salt concentration to regulate the swelling-induced retro DA reaction.

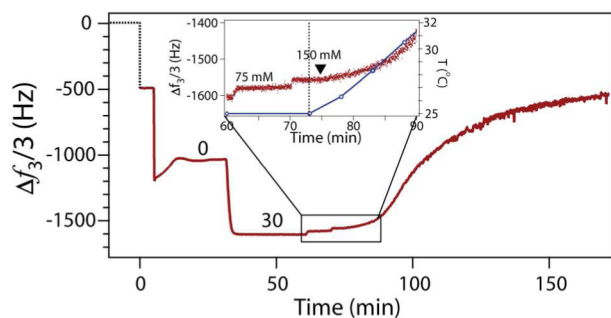


Figure 2. A 65 nm film underwent retro-DA only when temperature was raised. Real-time monitoring of swelling of a 65 nm thick carboxylated poly(OEGMA-r-HEMA) with the salt concentration from 0 to 30 mM. (Inset) The temperature was raised from 25 to 37 °C, as indicated by the blue curve; the black arrow indicated the starting point of retro-DA reaction at 26 °C.

To further confirm the cycloreversion of DAi, we adopted XPS to determine the surface element content of three states, namely, “SAM”, “COOH”, and “mechano-degraded” (Figure 3a). Specifically, the evolutions of the content of element S and F through these three states were monitored. The content of S showed no significant difference between SAM (6.94%) and mechano-degraded group (6.83%), while the content of F decreased significantly (from 0.69 to 0.15%). This result implied that retro DA reaction rather than the degradation of Au–S bond was the main cause for chain scission.

On the basis of the F content determined for SAMs the surface initiator density, we also calculated χ_1^{surf} (see Supporting Information): a $\chi_1^{\text{sol}} = 95\%$ gave a $\chi_1^{\text{surf}} = 23.1\%$, which should

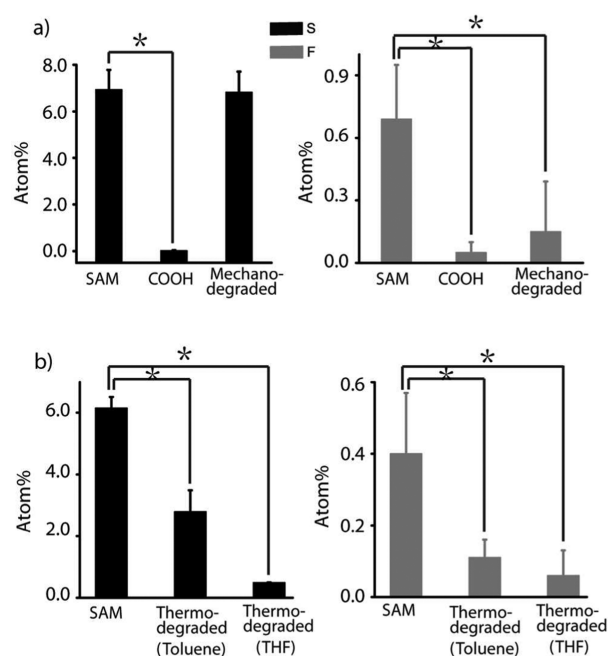


Figure 3. Changes in the surface content of element S and F after the swelling/thermo-driven retro DA reactions determined with XPS. (a) “SAM” represents the DAi and EG₃ mixed SAM-modified gold surface; “COOH” for the carboxylated poly(OEGMA-r-HEMA) grafted surface; “mechano-degraded” for the PBS-treated surface; (b) element contents of various surfaces after thermo treatment in two different solvents. * $p < 0.05$. In all the calculation of element contents in this study, the element Au was excluded.

be ascribed to the hindrance effect: initiator DAi is much bigger than the diluent EG₃. If the decrease of F were due to Au–S bond breakage,¹⁷ one should notice significant S loss. The almost unchanged S content of SAM and mechano-degraded samples thus strongly suggested that retro DA of DAi was the main event.

Retro DA Reaction Driven by Heating. For comparison, the retro DA reaction of DAi was also operated using a conventional heating method. The conventional thermo-triggering of retro DA reactions typically requires temperatures over 110 °C.^{19–24} Kiselev et al. reported that retro DA reaction shows distinct properties in solvents that are different in polarity.²⁵ Thus, we chose to subject the SAM-modified surfaces in two different solvents—toluene and tetrahydrofuran (THF)—refluxed (at 110 °C) for 14 h. The XPS results (Figure 3b) showed that retro DA reaction had been triggered on the SAM-modified surfaces, as the content of F dropped significantly after the heating treatment in both toluene (from 0.40 to 0.11%) and THF (from 0.40 to 0.06%). The small difference in F content indicated that XPS was unable to show if the two different solvents caused differences in retro DA reactions. However, the decrease in the content of S indicated that a notable amount of Au–S bonds had also been degraded in the heating process, which is understandable because the thermal instability of thiol SAMs on gold is a known issue.

The C peak of the XPS was also analyzed (Table 1), the contents of carbon (C 1s) slightly decreased from SAM to the COOH and swelling-induced states, as carboxylation of weak polyelectrolytes enhanced the oxygen content. In contrast, the decrease was more significant after heating in THF, which suggested that the reflux treatment might have caused oxidation

Table 1. Content of Carbon Atom of Different Surfaces in Different States

	atom content (%)			
	SAM	COOH	mechano-degraded	thermo-degraded (in THF)
C 1s	73.1	66.5	61.8	31.9
C–H	39.8 (54.4%) ^a	50.7 (76.2%)	31.1 (50.3%)	18.0 (56.4%)
C–O	32.3 (44.2%)	6.72 (10.1%)	24.5 (39.6%)	
C=O	1.01 (1.40%)	9.18 (13.8%)	6.23 (10.1%)	13.9 (43.6%)

^aValues in parentheses indicate the percentage of the content of C–H, C–O, or C=O relative to total C 1s.

of the thiol molecules, resulting in a content of C=O as high as 43.6% (relative to all C 1s). In addition, the peak of S_{2p} spectra of the SAM surface was at around 162.5 eV; however, after heating in THF, it migrated to around 168.4 eV (Figure S2, Supporting Information), also an indication of oxidation. The SAMs that have been treated by heating could no longer initiate polymerization.

The polyelectrolyte-grafted surfaces were also treated under the same condition. However, ellipsometric data (change in dry thickness from 95.2 to 97.1 nm) showed that the polymer films did not detach from surface after heating, which suggested that either (1) the retro DA reaction (as well as Au–S bond degradation) did not occur, or (2) recycloaddition had happened during the cooling stage. Because the molecular weight of the grafted polymer chains was particularly large (on the magnitude of 10^5 g/mol), the first assumption is more reasonable. It is interesting why retro DA reaction was hindered here by the attached polymer chains but not affected by the tethered poly(ethylene glycol) (PEG) chains, as reported by Barner-Kowollik.²⁶ The molecular weight may play a critical role, because the molecular weight of the PEG they used was only 2200 g/mol, which suggested it may have melted at 120 °C. In addition, there may be extensive cross-linking inside the polymer brush used in the current study mediated by hydrogen bonds, as demonstrated by its inhibiting effect on proton permeation in our previous study.²⁷

Computational Study. Computational studies were conducted to evaluate the energy barrier of the retro DA reaction used in the current study. All quantum chemistry (QM) calculations are carried out using the GAUSSIAN 09 program. To speed up the calculation, we simplified the reactants as a furan molecule and a succinimide molecule.

Figure 4 presents the potential energy curves for DA reaction pathways between the two model molecules. They take a face-to-face (FF) conformation in one pathway and an edge-to-edge (EE) conformation in the other. In the FF pathway, the forward DA reaction has a barrier of 21.70 kcal/mol. The product has an energy of –1.91 kcal/mol. Therefore, the reverse DA reaction has a barrier of 23.61 kcal/mol. Similarly, in the EE pathway, the forward reaction barrier is 21.10 kcal/mol, and the reverse reaction has a barrier of 25.83 kcal/mol (Figure 4). In both pathways, the forward DA and the reverse DA reactions have similar energy barriers, indicating the reversibility of the DA reaction. Although this model is simplified, we believe that the experimental system has similar energy barriers for forward DA and reverse DA reactions because the chemical attachments on both furan and succinimide molecules only contribute weak

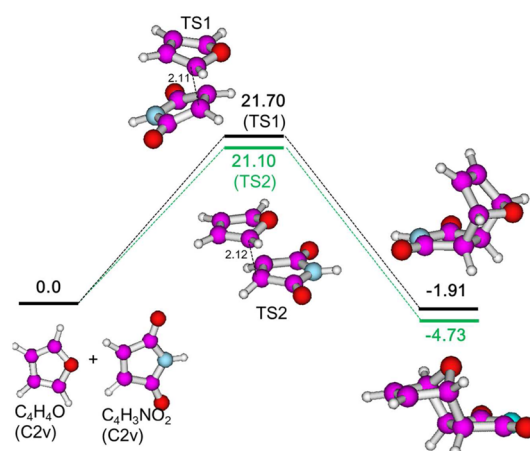


Figure 4. Schematic potential energy curves for the Diels–Alder reaction pathways in a model system of a furan ring and a succinimide molecule. The black curve denotes a pathway in which the two ring molecules adopting a face-to-face conformation, resulting in the formation of boat-like structure in product. In contrast, the green curve denotes a pathway forming a chairlike conformation in product. The structures of reactants (both have a C_{2v} symmetry), transition states (TS), and products are shown for clarity. The energies are indicated in the unit of kcal/mol near the respective energy bars. In both transition state structures, the dashed lines are drawn connecting two nearest carbon atoms on each ring, and a number is used to indicate the distance between the two atoms.

van der Waals dispersions, which may not influence the reaction barrier, especially in the extended configurations of the swollen state. Although the reverse DA reaction has a slightly higher energy barrier than the forward DA reaction, it still can be easily overcome by the swelling of the polymer film. Northrop and Boutelle indicated the reactivity and reversibility of furan-maleimidecycloadditions can be tuned significantly through the addition of appropriate substituents.²⁸

These energy barrier values were also close to the experimental and theoretical activation energy of the decomposition of a similar compound, 7-oxabicyclo-[2.2.1]hept-5-ene-2,3-dicarboxylic anhydride, reported by Friedli et al.¹⁵ Therefore, the energy barrier of the retro DA reaction was significantly lower than that of the Au–S bond degradation which has been reported to be ≤ 50 kcal/mol.¹⁶ By preparing polymer brushes from silicon substrates, one could adopt this swelling-based mechanochemical platform to chemical bonds that have higher bond energies than the Au–S bond.

CONCLUSION

In summary, surface confined retro DA reaction has been triggered at ambient temperature utilizing the mechanical force provided by the swelling of surface-tethered carboxylatedpoly-(OEGMA-r-HEMA) in PBS. The reaction was monitored in real time with liquid phase QCM measurement, which showed that the reaction proceeded rapidly with a high conversion ratio. The swelling-induced retro DA reaction was dependent on film thickness and sensitive to temperature. The critical film thickness for the reaction at 25 °C was 65 nm. A comparison with the heating-induced retro DA reaction revealed that the mechanochemical platform possessed higher selectivity and efficiency. The mechanical force generated during swelling was controllable and persistent, which imparts it with the potential of superior controllability over other mechanochemical treat-

ments. The range of chemical bonds that amenable for this platform is expandable.

■ EXPERIMENTAL METHODS

Synthesis of DA-Containing Initiator. To a well-stirred solution of 2-furan methanol (0.49 g, 5.0 mmol, 1.0 equiv) in dry THF (10 mL) was added dropwise an aqueous solution of NaOH (0.5 mL, 50 wt %) at room temperature. The mixture was stirred for half an hour, then tetrabutylammonium bromide (0.123 g, 0.47 mmol, 0.094 equiv) was added, and the resulting mixture was heated to 60 °C. Then, a solution of 6-bromo-1-hexanol (0.72 mL, 1.1 mmol, 1.1 equiv) in 2 mL of THF was added dropwise, and the reaction was stirred at 60 °C overnight. After 2-furan methanol was consumed, as monitored by TLC, the mixture was concentrated by rotary evaporation. The residue was diluted with ethyl acetate (40 mL), washed with water, and dried over MgSO₄. After removal of the solvent, the desired product 1-1 was obtained by flash column chromatography (silica gel, neutral, with PE/EA = 32:1, 297 mg, 30% yield).

Triethylamine (281 μL, 2.02 mmol, 2.0 equiv) was added to a solution of compound 1-1 (200 mg, 1.01 mmol, 1.0 equiv) in dry THF under Ar atmosphere. The mixture was cooled to 0 °C, then a solution of methanesulfonyl chloride (156 μL, 2.02 mmol, 2.0 equiv) in dry THF (2 mL) was added dropwise. After being stirred for half an hour at 0 °C, the reaction was stirred for another 12–16 h at room temperature. The reaction mixture was concentrated and diluted with ethyl acetate (40 mL). The solution was washed with brine and dried over Na₂SO₄. After removal of the solvent, the desired product 1-2 was obtained by flash column chromatography (silica gel, neutral, with PE/EA = 2:1, 200 mg, 72% yield).

Under Ar atmosphere, triethylamine (1.63 mL, 11.7 mmol, 2.0 equiv) was added to a solution of compound 1-2 (1.61 g, 5.84 mmol, 1.0 equiv) in dry THF. Then, the mixture was cooled to 0 °C, followed by addition of a solution of thioacetic acid (0.83 mL, 2.02 mmol, 2.0 equiv) in dry THF (4 mL). After being stirred at 0 °C for half an hour, the reaction was stirred for another 12–16 h at room temperature. Then, the reaction mixture was concentrated and diluted with ethyl acetate (40 mL). The solution was washed with brine and dried over Na₂SO₄. After removal of the solvent, the desired product 1-3 was obtained by flash column chromatography (silica gel, neutral, with PE/EA = 16:1, 1.24 g, 83% yield).

A solution of 4-amino-3-fluorophenol (763 mg, 6.0 mmol, 1.0 equiv) in 4 mL of DMF was added to a solution of maleic anhydride (590 mg, 6.0 mmol, 1.0 equiv) in 4 mL of DMF with stirring at room temperature. After 1 h, a solution of P₂O₅ (477 mg, 3.4 mmol, 0.56 equiv) and sulfuric acid (98%wt) in 2 mL of DMF was added dropwise to the mixture. The resulting mixture was heated to 110 °C for 2 h. The reaction mixture was extracted with ethyl acetate (3 × 100 mL) and washed with brine. The extract was dried over Na₂SO₄. The solution was concentrated, and the residue was purified by column chromatography on silica gel (DCM/MeOH = 30:1) to give 1-4 as a solid (310 mg, 25% yield).

Compounds 1-3 (0.512 g, 2.0 mmol, 1.0 equiv) and 1-4 (0.414 g, 2.0 mmol, 1.0 equiv) were added to a 10 mL seal tube, and the tube was vacuumed and charged with argon. Then, 4 mL of Et₂O was added, and the reaction mixture was refluxed at 40 °C overnight. The mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The residue was diluted with ethyl acetate (60 mL), and the solution was washed with brine. The organic phase was dried over Na₂SO₄. After removal of the solvent, the desired product 1-5 was obtained by flash column chromatography (silica gel, neutral, with PE/EA = 2:1, 720 mg, 77% yield).

To a solution of compound 1-5 (520 mg, 1.12 mmol, 1.0 equiv) in 2 mL of dry THF, was added triethylamine (471 μL, 3.38 mmol, 3.0 equiv) under argon atmosphere. The mixture was cooled to 0 °C, and then a solution of 2-bromo-2-methylpropanoyl bromide (417 μL, 3.37 mmol, 3.0 equiv) in 1 mL of dry THF was added dropwise. The reaction was stirred overnight at room temperature. The mixture was concentrated under reduced pressure, and the residue was diluted with ethyl acetate (40 mL). The solution was washed with brine and dried

over Na₂SO₄. After removal of the solvent, the desired product 1 was obtained by flash column chromatography (silica gel, neutral, with DCM/MeOH = 50:1, 168 mg, 25% yield).

Surface Preparation of Weak Polyelectrolyte from DAi. Surface tethered, carboxylated poly(OEGMA-*r*-HEMA) film was prepared as previously described.¹⁴ First, DA-containing initiator and diluents were immobilized on a QCM chip (AT cut, 5 MHz; HZDW, Hangzhou, China) via Au–S bonds as a SAM technique and incubated in the ethanol solution for 14 h at ambient temperature and protected from light. $n_{\text{initiator}} + n_{\text{diluent}} = 1$ mM. Second, the neutral polymer brushes were synthesized via SIP from the initiator-modified surfaces, using bipyridine as a ligand and water/ethanol = 1:1 as the solvent (the water used was Milli-Q water with resistivity of 18.2 MΩ cm⁻¹ in this study), with a molar ratio of OEGMA/HEMA/CuCl₂/bipyridine/ascorbic acid = 125/125/1/2/1 (i.e., 500/500/4/8/4 mM). For the monomer OEGMA used in this study, Mn = 526. The reaction mixture was degassed with Ar for 1 h before transferred to a glovebox for SIP. The reaction was terminated with water, and the chips were then rinsed thoroughly with water and ethanol and dried under a nitrogen flow.

Monitoring Retro DA Reaction by QCM. The swelling and/or swelling-induced retro DA reaction in PBS of various salt concentrations was monitored in real time by liquid phase QCM measurement. A home-built QCM was used with control software purchased from Resonant Probes GmbH (Goslar, Germany). Water or PBS was pumped through by a peristaltic pump at a speed of 80 μL min⁻¹, and the change in frequency and dissipation was recorded in real time. The primitive PBS solution (pH = 7.4, [Na⁺] = 150 mM) was prepared as follows: 8.00 g of NaCl, 0.20 g of KCl, 0.24 g of KH₂PO₄, and 3.63 g of Na₂HPO₄·12H₂O were dissolved into 1 L of water. The primitive PBS solution was then diluted to obtain solutions with the desired [Na⁺]. In this study, the increase of temperature has been realized in situ through semiconductor temperature control system.

Quantum Chemistry Calculations. All quantum chemistry (QM) calculations were carried out using the GAUSSIAN 09 program. The equilibrium geometries and frequencies of the reactants, products and transition states are calculated at the B3LYP/6-311G(d, p) level.^{29–31}

■ ASSOCIATED CONTENT

Supporting Information

Synthesis of DAi(1) and the compounds characterized by NMR, AFM micrographs of the surface before and after retro-DA reaction, high-resolution S 2p spectra of DAi SAM on Golds and SAM-contained DAi was oxidized S significantly by heat treatment in THF, and calculation of surface initiator density. This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: hwma2008@sinano.ac.cn.

*E-mail: zhu_qiang@gibh.ac.cn.

Present Address

[∇]Physical Chemistry I, Department of Chemistry and Biology, Siegen University, Adolf-Reichwein-Strasse 2, 57076 Siegen, Germany

Author Contributions

[○]These authors contributed equally.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This project was partially supported by an NSFC Grant (21174161), CAS Funds (KJZD-EW-J01, KJX2-YW-M21),

and JS Grants (BK20130008) to H.M. and by an NSFC Grant (21104092) to S.Z.

REFERENCES

- (1) Wiggins, K. M.; Brantley, J. N.; Bielawski, C. W. Methods for Activating and Characterizing Mechanically Responsive Polymers. *Chem. Soc. Rev.* **2013**, *42*, 7130–7147.
- (2) Hickenboth, C. R.; Moore, J. S.; White, S. R.; Sottos, N. R.; Baudry, J.; Wilson, S. R. Biasing Reaction Pathways with Mechanical Force. *Nature* **2007**, *446*, 423–427.
- (3) Beiermann, B. A.; Kramer, S. L. B.; Moore, J. S.; White, S. R.; Sottos, N. R. Role of Mechanophore Orientation in Mechanochemical Reactions. *ACS Macro Lett.* **2012**, *1*, 163–166.
- (4) White, S. R.; Moore, J. S.; Sottos, N. R.; Krull, B. P.; Santa Cruz, W. A.; Gergely, R. C. R. Restoration of Large Damage Volumes in Polymers. *Science* **2014**, *344*, 620–623.
- (5) Baytekin, H. T.; Baytekin, B.; Incorvati, J. T.; Grzybowski, B. A. Material Transfer and Polarity Reversal in Contact Charging. *Angew. Chem., Int. Ed.* **2012**, *124*, 4927–4931.
- (6) Lenhardt, J. M.; Ong, M. T.; Choe, R.; Evenhuis, C. R.; Martinez, T. J.; Craig, S. L. Trapping a Diradical Transition State by Mechanochemical Polymer Extension. *Science* **2010**, *329*, 1057–1060.
- (7) Brantley, J. N.; Wiggins, K. M.; Bielawski, C. W. Unclicking the Click: Mechanically Facilitated 1,3-Dipolar Cycloreversions. *Science* **2011**, *333*, 1606–1609.
- (8) Zhulina, E. B.; Birshtein, T. M. Theory of Ionizable Polymer Brushes. *Macromolecules* **1995**, *28*, 1491–1499.
- (9) Zhang, Y.; Lv, B.; Lu, Z.; He, J.; Zhang, S.; Chen, H.; Ma, H. Predicting Au-S Bond Breakage from the Swelling Behavior of Surface Tethered Polyelectrolytes. *Soft Matter* **2011**, *7*, 11496–11500.
- (10) Wiggins, K. M.; Syrett, J. A.; Haddleton, D. M.; Bielawski, C. W. Mechanically Facilitated Retro [4 + 2] Cycloadditions. *J. Am. Chem. Soc.* **2011**, *133*, 7180–7189.
- (11) Larsen, M. B.; Boydston, A. J. “Flex-Activated” Mechanophores: Using Polymer Mechanochemistry to Direct Bond Bending Activation. *J. Am. Chem. Soc.* **2013**, *135*, 8189–8192.
- (12) Gossweiler, G. R.; Hewage, G. B.; Soriano, G.; Wang, Q.; Welshofer, G. W.; Zhao, X.; Craig, S. L. Mechanochemical Activation of Covalent Bonds in Polymers with Full and Repeatable Macroscopic Shape Recovery. *ACS Macro Lett.* **2014**, *3*, 216–219.
- (13) Ma, H.; He, J.; Liu, X.; Gan, J.; Jin, G.; Zhou, J. Surface Initiated Polymerization from Substrates of Low Initiator Density and Its Applications in Biosensors. *ACS Appl. Mater. Interfaces* **2010**, *2*, 3223–3230.
- (14) Zhu, Y.; Lv, B.; Zhang, P.; Ma, H. Swelling Induced Au-S Bond Breakage Is Determined by the Molecular Composition of Surface Tethered Copolymers-Carboxylated Poly(OEGMA-HEMA). *Chem. Commun.* **2011**, *47*, 9855–9857.
- (15) Manka, J. T.; Douglass, A. G.; Kaszynski, P.; Friedli, A. C. Retro Diels–Alder Reactions of 5,6-Disubstituted-7-oxabicyclo[2.2.1]hept-2-enes: Experimental and Density Functional Theory Studies. *J. Org. Chem.* **2000**, *65*, 5202–5206.
- (16) Love, J. C.; Estroff, L. A.; Kriebel, J. K.; Nuzzo, R. G.; Whitesides, G. M. Self-Assembled Monolayers of Thiolates on Metals as a Form of Nanotechnology. *Chem. Rev.* **2005**, *105*, 1103–1170.
- (17) Ma, H.; He, J.; Zhu, Z.; Lv, B.; Li, D.; Fan, C.; Fang, J. A Quartz Crystal Microbalance-Based Molecular Ruler for Biopolymers. *Chem. Commun.* **2010**, *46*, 949–951.
- (18) Zhang, Y.; He, J.; Zhu, Y.; Chen, H.; Ma, H. Directly Observed Au-S Bond Breakage Due to Swelling of the Anchored Polyelectrolyte. *Chem. Commun.* **2011**, *47*, 1190–1192.
- (19) Zhang, Y.; Broekhuis, A. A.; Picchioni, F. Thermally Self-Healing Polymeric Materials: The Next Step to Recycling Thermoset Polymers. *Macromolecules* **2009**, *42*, 1906–1912.
- (20) Wijnen, J. W.; Engberts, J. B. Retro-Diels–Alder Reaction in Aqueous Solution: Toward a Better Understanding of Organic Reactivity in Water. *J. Org. Chem.* **1997**, *62*, 2039–2044.
- (21) Teplyakov, A. V.; Lal, P.; Noah, Y. A.; Bent, S. F. Evidence for a Retro-Diels–Alder Reaction on a Single Crystalline Surface: Butadienes on Ge(100). *J. Am. Chem. Soc.* **1998**, *120*, 7377–7378.
- (22) Horn, B. A.; Herek, J. L.; Zewail, A. H. Retro-Diels–Alder Femtosecond Reaction Dynamics. *J. Am. Chem. Soc.* **1996**, *118*, 8755–8756.
- (23) Goussé, C.; Gandini, A.; Hodge, P. Application of the Diels–Alder Reaction to Polymers Bearing Furan Moieties. 2. Diels–Alder and Retro-Diels–Alder Reactions Involving Furan Rings in Some Styrene Copolymers. *Macromolecules* **1998**, *31*, 314–321.
- (24) Chung, Y.; Duerr, B. F.; McKelvey, T. A.; Nanjappan, P.; Czarnik, A. W. Structural Effects Controlling The Rate of The Retro-Diels–Alder Reaction in Anthracene Cycloadducts. *J. Org. Chem.* **1989**, *54*, 1018–1032.
- (25) Kiselev, V. D.; Kashaeva, E. A.; Bolotov, A. V.; Shakirova, I. I.; Kononov, A. I. Energy and Volume Activation Parameters of The Retro-Diels–Alder Reaction in Different Solvents. *Russ. Chem. Bull.* **2009**, *58*, 21–24.
- (26) Preuss, C. M.; Goldmann, A. S.; Trouillet, V.; Walther, A.; Barner-Kowollik, C. Biomimetic Dopamine-Diels–Alder Switches. *Macromol. Rapid Commun.* **2013**, *34*, 640–644.
- (27) Wang, X.; Lv, B.; Cai, G.; Fu, L.; Wu, Y.; Wang, X.; Ren, B.; Ma, H. A Proton Shelter Inspired by The Sugar Coating of Acidophilic Archaea. *Sci. Rep.* **2012**, *2*, 892.
- (28) Boutelle, R. C.; Northrop, B. H. Substituent Effects on the Reversibility of Furan-Maleimide Cycloadditions. *J. Org. Chem.* **2011**, *76*, 7994–8002.
- (29) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*, Revision D.01; Gaussian, Inc.: Wallingford, CT, 2009.
- (30) Becker, A. D. A New Mixing of Hartree–Fock and Local Density-Functional Theories. *J. Chem. Phys.* **1993**, *98*, 1372–1377.
- (31) Lee, C.; Yang, W.; Parr, R. G. Development of The Colle–Salvetti Correlation-Energy Formula Into a Functional of The Electron Density. *Phys. Rev. B* **1988**, *37*, 785–789.