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Photo-selective chain end transformation of polyacrylate-iodide using cysteamine and its application to facile single-step preparation of patterned polymer brushes†

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Cysteamine, which is an inexpensive and non-toxic aminothiol, was successfully employed as a photo-selective chain end transformation agent of iodo-terminated polymer chains (polymer-I). Polymer-I was selectively transformed to hydrogen-terminated (polymer-H) and thiol-terminated (polymer-SH) polymers with and without UV irradiation, respectively. This method is applicable to acrylate polymers. This photo-selective reaction offered a single-step preparation of patterned polymer brushes with SH and H chain end functionalities as a unique application.

Selective reactions, in which different products are selectively generated from the same reactant in response to the applied environment, are useful tools in organic and polymer syntheses. Different products are targeted upon different external stimuli such as temperature, light, redox, force, and solvent polarity, enabling unique molecular design by simply switching the external stimuli.[1–6]

Living radical polymerization (LRP),[7–9] also known as reversible-deactivation radical polymerization, is a powerful approach for preparing polymers with narrow molecular weight distribution and well-defined structures. The obtained polymer (polymer-X) possesses a capping agent (X) at the chain end. The chain end functionalized polymers are obtainable *via* the conversion of X into functional groups.[10–13]

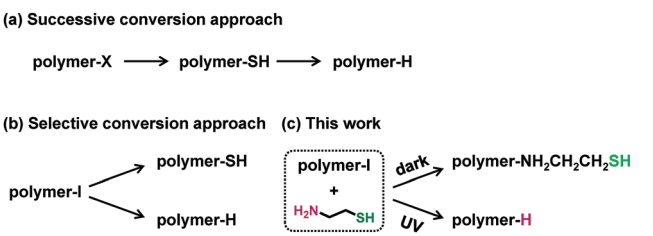
Thiol-terminated polymers can connect with other polymers and bio-molecules to create block copolymers, stars, and bio-conjugates,[14–18] and can also be anchored on gold surfaces to generate polymer brushes on the surfaces.[19]

The reactive chain end (capping agent X) of the polymer obtained *via* LRP often negatively influences the long-term stability and the post polymer processing. To address this negative aspect, the conversion of X into a simple hydrogen has been achieved through either a thermal or photo-induced reduction.[20,21]

Thiol- and hydrogen-terminated polymers (polymer-SH and polymer-H, respectively) were synthesized independently. Recently, an elegant approach was reported on the successive conversion of polymer-trithiocarbonate to polymer-SH and subsequently to polymer-H using a photo-redox catalyst and amine and phosphine additives (Scheme 1a).[22] Herein, we propose a simple and unique approach for synthesizing polymer-SH and polymer-H selectively under two different external stimuli (Scheme 1b).

Our group developed an organocatalyzed LRP using alkyl iodides as dormant species (X = iodide) and organic molecules as catalysts.[23–26] The post-modification of the terminal iodide was studied *via* treatment with primary amines (R–NH_2), yielding chain end functionalized polymers (polymer-NHR) with various functionalities at the R group.[27]

In the present work, we use bifunctional cysteamine ($NH_2CH_2CH_2SH$) containing thiol and primary amino groups as the chain end modification agents (Scheme 1c). Cysteamine is biosynthesized in mammals and biocompatible. Without photo irradiation, the chain end iodide reacts with the amino group of cysteamine *via* a substitution reaction, yielding a thiol-terminated polymer-SH (Scheme 1c). With the UV irradiation, the carbon–iodide bond is photo-cleaved to generate a carbon-centred radical (polymer•), which undergoes a radical transfer reaction with the thiol group of cysteamine and yields a hydrogen-terminated polymer-H (Scheme 1c). Therefore, by switching the UV irradiation



Scheme 1 (a) Successive and (b) selective conversion approaches for the synthesis of polymer-SH and polymer-H. (c) This work.

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on and off, polymer-H and polymer-SH are selectively obtained from the same reactant polymer-I (iodo-terminated polymer). Because the substitution occurs effectively for secondary alkyl chains but not for tertiary alkyl chains, this method is useful for acrylate polymers but not methacrylate polymers. This work focuses on acrylate polymers. This approach is a selective conversion (Scheme 1b) that is different from the successive conversion (Scheme 1a). The selective conversion enables a single-step preparation of patterned polymer brushes with SH and H chain end functionalities as a unique application described below. This approach is attractive for the use of only two reactants, *i.e.*, polymer-I and cysteamine without extra catalysts and additives. The non-toxic nature of cysteamine is further attractive for biological applications.

To probe this reaction, we first studied a low-mass model alkyl iodide, *i.e.*, ethyl 2-iodopropanoate (EA-I (Fig. 1)), which is a unimer model of poly(acrylate)-iodide. We studied a mixture of EA-I (80 mM) and cysteamine (400 mM) with and without UV irradiation (365 (±10) nm) at room temperature. The solvent was a mixed solvent (dielectric constant ε = 6.0) of toluene-d_8 (ε = 2.4) and methanol-d_4 (ε = 32.7) (w/w = 88/12), in which methanol-d_4 was added to dissolve cysteamine.

Under the dark condition (without UV) after 1 h, EA-I was virtually quantitatively (>99%) converted to the substitution product EA-SH (Fig. 1a, b, and d). In contrast, under UV irradiation for 10 min, EA-I was mainly converted to the radical transfer product EA-H (91%) with minor generation of the substitution product EA-SH (9%) (Fig. 1a, c, and e). (While this reaction was optimized, a higher UV intensity and a lower temperature may even suppress the generation of EA-SH.) These results clearly demonstrate high selectivity of the reaction with and without UV irradiation.

Mechanistically, with UV irradiation, EA-I is photo-dissociated to generate EA$^\bullet$, which subsequently abstracts a hydrogen from the SH group of cysteamine to generate EA-H and $NHCH_2CH_2S^\bullet$. Two molecules of $NHCH_2CH_2S^\bullet$ subsequently combine to form a disulfide (as observed at 2.51 and 2.72 ppm in Fig. 1c). Both with and without UV irradiation, HI was generated, forming a salt (precipitation) with cysteamine. HI changed the pH value, resulting in a slight difference in the NMR chemical shift among the samples (Fig. 1).

Instead of EA-I, the bromide analogue, *i.e.*, ethyl 2-bromopropanoate (EA-Br), was also studied. However, EA-Br was converted to only EA-SH but not EA-H. EA-SH was also slowly generated (85% for 1 h). Therefore, the dual (selective) and rapid reactions are unique to the alkyl iodide.

Both of the NH_2 and SH groups of cysteamine are nucleophiles and may undergo substitution with alkyl halides.[28] However, in our studied conditions, we observed only the substitution with NH_2 (hence EA-SH as a product) (in a mechanistic study in the ESI†), meaning that NH_2 is a much more reactive nucleophile than SH in our conditions.

We then studied polymer systems. Poly(butyl acrylate)-iodide (PBA-I) was prepared *via* the organocatalyzed LRP of butyl acrylate (BA) with 2-iodo-2-methylpropionitrile (CP-I) as an alkyl iodide initiator and tetrabutylammonium iodide (BNI) as a catalyst (ESI†). The PBA-I was purified by reprecipitation and subsequently by preparative GPC to remove trace amounts of impurities. The M_n and dispersity ($Đ = M_w/M_n$) of the purified PBA-I were 2900 and 1.29, respectively, where M_n and M_w are the number-average and weight-average molecular weights, respectively.

Subsequently, polymer-I (1 eq., 20 wt%) and cysteamine (20 eq.) were dissolved in a mixed solvent (ε = 12.3) of diglyme (ε = 7.2) and 1-butanol (ε = 17.4) (w/w = 1/1). An excess of cysteamine (20 eq.) was used, because the reaction is slower for a polymer (polymer-I) than a low-mass analogue (EA-I). A more polar solvent was used for polymer-I (ε = 12.3) than EA-I (ε = 6.0) to accelerate the substitution reaction. The reaction time was also prolonged to 12 h under dark conditions and 2 h under UV irradiation.

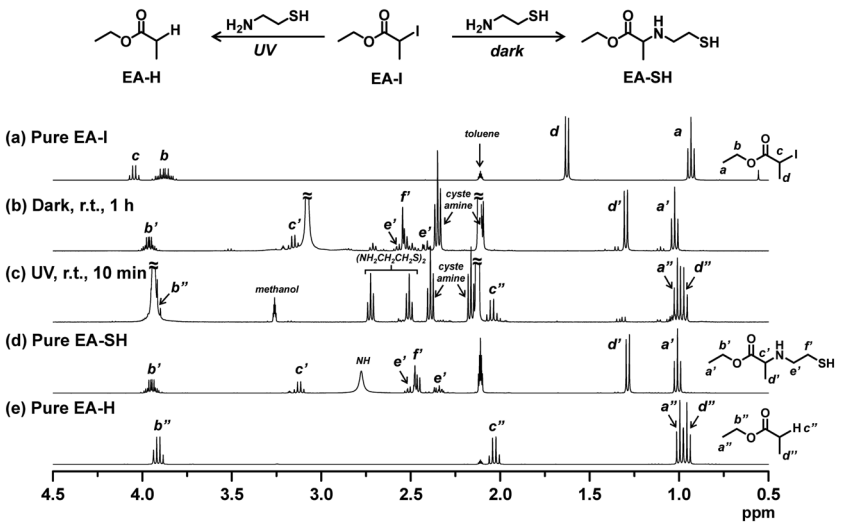
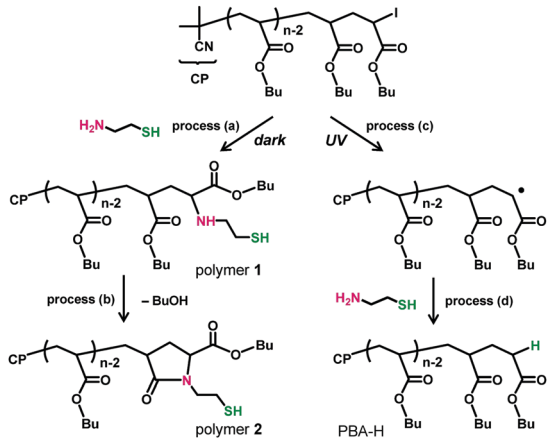


Fig. 1 ^{1}H NMR (400 MHz) spectra in a mixture of toluene-d_8 and methanol-d_4 (w/w = 88/12). (a) Pure EA-I. (b and c) A reaction mixture of EA-I (80 mM) and cysteamine (400 mM) (b) without UV after 1 h and (c) with UV (365 (±10) nm) after 10 min. (d) Pure EA-SH. (e) Pure EA-H.



Scheme 2 Detailed mechanisms for the selective reactions of PBA-I and cysteamine with and without UV irradiation.

Scheme 2 shows the detailed reaction mechanisms. Under dark conditions, PBA-I undergoes substitution with NH_2 of cysteamine to generate polymer **1** (process (a) in Scheme 2), followed by an intramolecular amidation to generate polymer **2** with a 5-membered ring at the chain end (process (b)). The chain end of polymer **2** possesses a SH group. Under UV irradiation, PBA-I was photo-dissociated to generate a polymer radical PBA$^{\bullet}$ (process (c)), followed by a radical transfer with SH of cysteamine to generate a hydrogen-terminated PBA-H (process (d)).

Fig. 2a shows the matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) spectrum of the product under the dark condition for 12 h. We used *trans*-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) as a matrix and CF_3COONa as an additive salt for the MALDI-TOF-MS analysis. Fig. 2a (right) shows the isotope distribution (^{13}C distribution) in the mass region of 2780–2790. Fig. 2c shows the theoretical isotope distribution of polymer **2**. The far left peak (experimental mass = 2782.34) corresponds to the polymer without a ^{13}C atom (only with ^{12}C atoms). The experimental mass matches the theoretical mass (2782.75). The second peak from the left (experimental mass = 2783.33) corresponds to the polymer possessing one ^{13}C atom, and the other peaks (experimental mass = 2784.32 and so on) correspond to those possessing two or more ^{13}C atoms. The experimental mass distribution (Fig. 2a (right)) well matched the theoretical one of polymer **2** (Fig. 2c). We also observed only a single series of repeated peaks (*i.e.*, only one product) (Fig. 2a (middle)), suggesting a nearly quantitative conversion of PBA-I to polymer **2**. The ^1H NMR spectrum (Fig. S3b, ESI†) also confirmed the successful attachment of the CH_2CH_2SH moiety.

In contrast, under UV irradiation for 2 h, we observed only PBA-H as a single species (Fig. 2b (middle)). The experimental mass (2781.60) (Fig. 2b (right)) matched the theoretical mass of PBA-H (2781.81 (Fig. 2d)). The difference in the theoretical masses of polymer **2** (2782.75 (Fig. 2c)) and PBA-H (2781.81 (Fig. 2d)) is only 0.94. Therefore, we look into the peak areas. The theoretical area ratio of the far left and second left peaks of PBA-H (2781.81 and 2782.81 (Fig. 2d)) is 0.571. The experimental area ratio (0.605) of those peaks (2781.60 and 2782.60 (Fig. 2b)) was close to the theoretical one. If polymer **2** is also generated, the experimental peak at 2782.60 should increase because the peak of polymer **2** is overlapped. The close matching of the experimental (0.605) and theoretical (0.571) ratios means a nearly quantitative conversion of PBA-I to PBA-H. These results show high selectivity of the reactions with and without UV irradiation.

To extend the scope of polymers, we also used this method for other polymers, *i.e.*, poly(2-methoxyethyl acrylate)-iodide (PMEA-I) (M_n = 3000 and $Đ$ = 1.16) and carboxyl acid terminated PMEA-I (HOOC-PMEA-I) (M_n = 3200 and $Đ$ = 1.79) (ESI†). We successfully obtained the thiol-terminated polymers (PMEA-SH and HOOC-PMEA-SH) and hydrogen-terminated polymers (PMEA-H and HOOC-PMEA-H) in a selective manner (Fig. S4 and S5, ESI†). These results indicate good compatibility with functional groups in this approach.

A unique application was the chain end functionalization of polymer brushes on surfaces. Polymer brushes provide surfaces with advanced mechanical, optical, electrical, and biological properties.[29] Surface-initiated LRP is a powerful method to synthesize concentrated polymer brushes with high surface densities.[30] Because of the steric hindrance of neighbouring chains, the polymer chains are forced to be extended and the growing chain ends tend to be localized at the outermost surface of the brush layer. The post chain end modification can afford functionalities at the outermost surface. In the present work, we used selective reactions (not multi-step modification or successive reactions) and prepared patterned polymer brushes with SH and

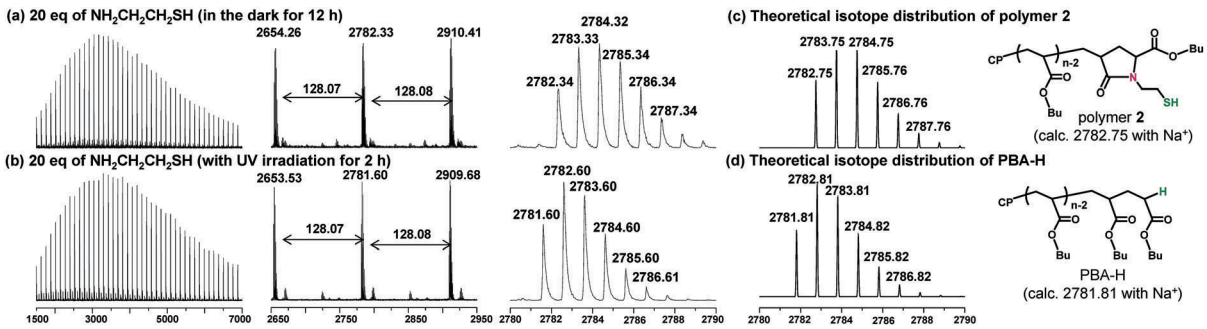


Fig. 2 MALDI-TOF-MS spectra of products obtained *via* a reaction of PBA-I and cysteamine (a) without UV after 12 h and (b) with UV after 2 h. The theoretical mass distributions of (c) polymer **2** and (d) PBA-H with n = 21.

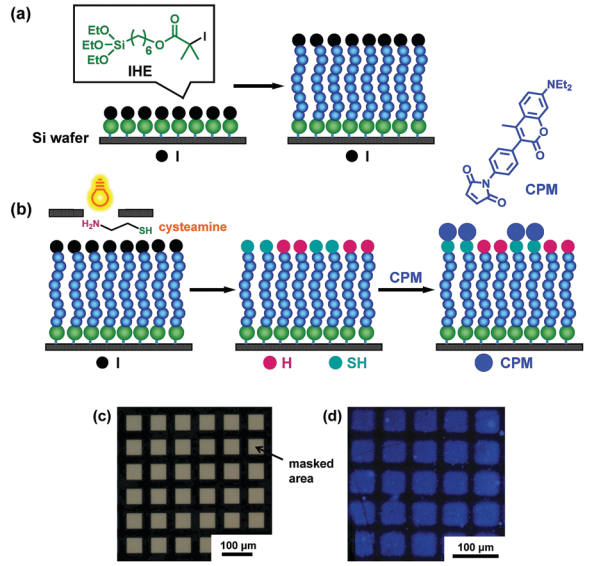


Fig. 3 (a) Synthesis of PBA-I brushes *via* surface-initiated organocatalyzed LRP. (b) Surface patterning of H and SH chain end functionalized polymer brushes and subsequent attachment of CPM. (c) Optical microscope image of the glass photomask. (d) Fluorescence microscope image of CPM-attached patterned PBA brushes.

H chain end functionalities in a single step. The single step manner is a unique advantage of this approach.

PBA-I brushes were uniformly fabricated on silicon wafers (without patterning) *via* surface-initiated organocatalyzed LRP (Fig. 3a). Concentrated polymer brushes (with surface occupancy (σ^*) > 10%) with different thicknesses (20 and 30 nm) were prepared (Table S1, ESI†). A cysteamine solution (5 wt% in diglyme/1-butanol (w/w = 1/1)) was dropped on the polymer brush, which was covered by a cover glass. A glass photomask containing repeating squares (Fig. 3c) or a copper grid (Fig. S6a, ESI†) was placed on the cover glass. After UV irradiation for 2 h, the chain end iodide was converted to SH in the masked area and to H in the unmasked area (Fig. 3b). We subsequently labelled SH with a fluorescence maleimide, 7-diethylamino-3-(4-maleimidophenyl)-4-methylcoumarin (CPM), *via* the thiol-maleimide Michael addition (Fig. 3b). A fluorescence pattern was clearly observed using a fluorescence microscope (Fig. 3d for 30 nm thick brush with the glass photomask), demonstrating the selective chain end modification of the polymer brush. A similarly clear fluorescence pattern was observed with the copper grid (Fig. S6b, ESI†) and for the brushes with different thicknesses (Fig. S7, ESI†). These results demonstrate the versatility in photomasks and brush thicknesses.

In conclusion, an inexpensive and non-toxic cysteamine was successfully employed as a photo-selective chain end modification agent of polymer-I. By simply switching UV light on and off, polymer-I was selectively transformed to polymer-H and polymer-SH, respectively, in a facile and quantitative manner. A unique application was a single-step preparation of patterned polymer brushes with SH and H chain end functionalities. Patterned surfaces with inert (hydrogen-terminated) and reactive/binding (thiol-terminated) areas may find sensing applications, *e.g.*, for biomolecular and ionic recognitions.

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Conflicts of interest

There are no conflicts to declare.

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