UV-Responsive Degradable Polymers Derived from 1-(4-Aminophenyl) ethane-1,2-diol

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ABSTRACT: A UV-responsive polymer was prepared via condensation polymerization of 2-nitrobenzyl(4-(1,2-dihydroxyethyl)-phenyl)carbamate and azalaic acid dichloride. When the polymer was irradiated with UV light, the nitrobenzyl urethane protecting group was removed and the deprotected aniline underwent spontaneous 1,6-elimination reactions, resulting in degradation of the polymer. Nanoparticles with encapsulated Nile Red were formulated with the degradable polymer and triggered burst release of Nile Red was observed when the nanoparticles were irradiated by UV light. © 2015 Wiley Periodicals, Inc. J. Polym. Sci., Part A: Polym. Chem. **2015**, *00*, 000–000

KEYWORDS: degradable materials; depolymerization; nanoparticles; photochemistry; polyester; self immolative; stimuli-sensitive polymer; triggered release

INTRODUCTION Polymers that can be degraded in response to external triggers have been used in many applications, such as controlled release, self-healing, tissue engineering, sensors, and smart surface coatings.[1–15] Substantial effort has been devoted to developing degradable polymers with stimuli-responsive groups incorporated into the polymer backbones to control their degradation. Recently, there is growing interest in designing polymers whose degradation is controlled by the terminal or side-chain trigger-responsive groups.[16–24] Representative examples include the self-immolative polymers developed by Shabat and coworkers that can be degraded through removal of the terminal trigger-responsive protecting group[25,26] and the polymers developed by the Almutairi[24,27–30] and Gillies groups[17,31,32] with trigger-responsive domains placed on the side groups which control the polymer degradation. Inspired by these works, we recently designed 2,6-bis(hydroxymethyl)aniline (BHA), an analog of the key block of the self-immolative polymers ((4-aminophenyl)methanol), and used it to develop chain-shattering-polymers (CSPs)[33] and chain-shattering polymeric therapeutics.[34] By removing the pendant urethane protecting groups, CSPs undergo a spontaneous self-elimination reaction which eventually breaks down the polymer into smaller molecular weight species [Scheme 1(a)].

CSPs derived from BHA undergo a double 1,4-elimination reactions [Scheme 1(a)] on each residue, leading to complete backbone degradation; however, even one of the two self-elimination reactions of the BHA would result in polymer backbone degradation. Thus, it is excessive to use the BHA for the design of the trigger responsive domain (TRD) of CSPs, as any benzyl alcohol can possibly be such a TRD as long as the TRD has the (4-aminophenyl)methanol structure [Scheme 1(b)]. Herein, we report the use of 2-nitrobenzyl (4-(1,2-dihydroxyethyl)phenyl) carbamate (**1**) and azalaic acid dichloride (**2**) for the design of the degradable poly(**1**/**2**) [Scheme 1(c)]. The resulting polymer undergoes a 1, 6-elimination reaction upon removal of the nitrobenzyl protecting group with UV irradiation. This polymer can be used for future applications and materials in microcapsule shells for self-healing applications and in environmentally responsive coatings whose wettability and adhesion change in response to a stimulus.

EXPERIMENTAL

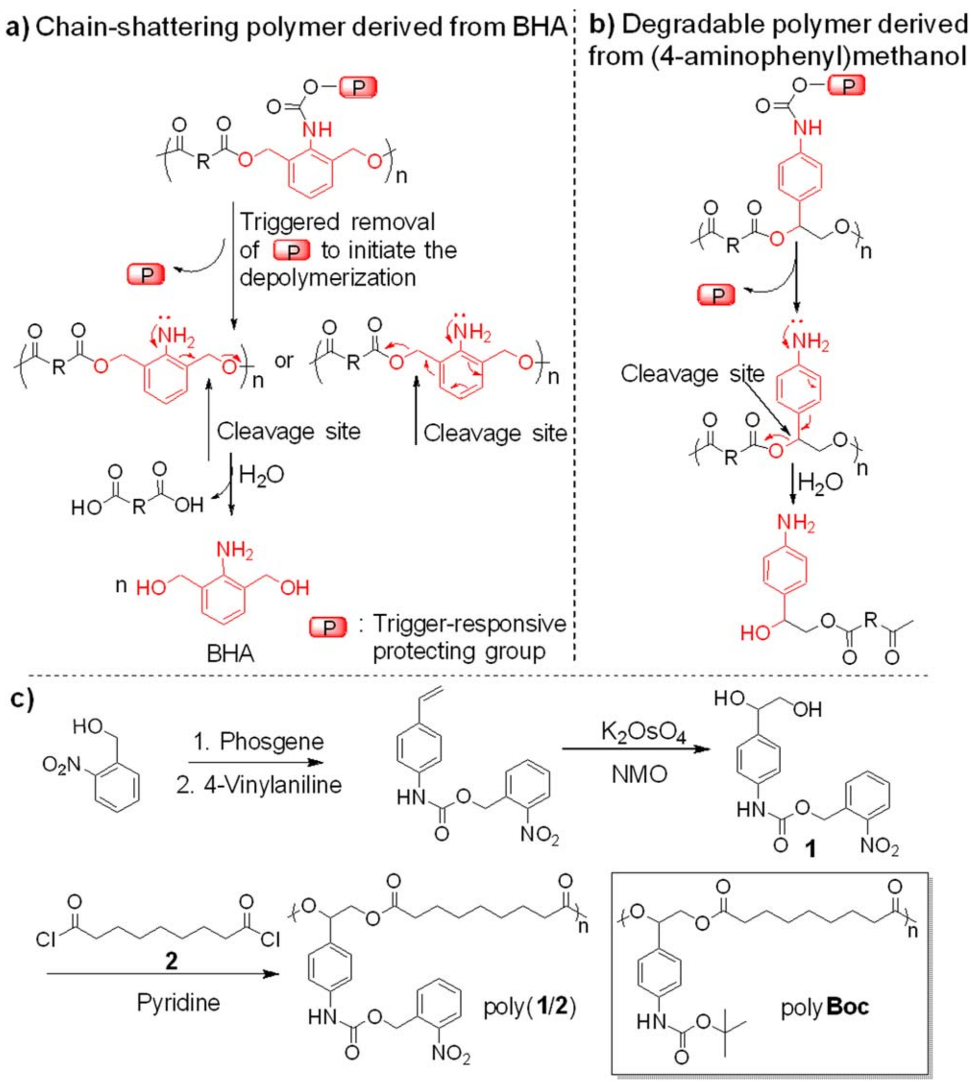
Materials

All chemicals were purchased from Sigma-Aldrich (St. Louis, MO, USA) and used as received unless otherwise specified. Anhydrous dichloromethane (DCM) and tetrahydrofuran (THF) were dried by a column packed with alumina. Anhydrous dimethylformamide (DMF) was dried by passing the solvent through a column packed with 4Å molecular sieves.

Instrumentation

NMR spectra were recorded on a Varian U500, a VXR500 or on a UI500NB 500 MHz NMR spectrometer. High resolution

Additional Supporting Information may be found in the online version of this article.



SCHEME 1 Illustration of the degradation of 2, 6-bis(hydroxymethyl) aniline (BHA) (a) and 1-(4-aminophenyl) ethane-1,2-diol based polymers (b); (c) Synthesis of degradable poly(**1**/**2**) and chemical structure of control polyBoc.

electrospray ionization mass spectrometry (HR-ESI-MS) experiments were conducted on a Waters Quattro II mass spectrometer. Size-exclusion chromatography experiments were performed on a system equipped with an isocratic pump (Model 1100, Agilent Technology, Santa Clara, CA, USA), a DAWN HELEOS multiangle laser light scattering (MALLS) detector, and an Optilab rEX refractive index detector (Wyatt Technology, Santa Barbara, CA). The detection wavelength of HELEOS was set at 658 nm. Separations were performed using serially connected size exclusion columns (50, 100, 500, and 10^3 Å Phenogel columns, 5 μm, 300 × 7.8 mm, Phenomenex, Torrance, CA) at 60 °C using DMF containing 0.1 M LiBr as the mobile phase. The MALLS detector is calibrated using pure toluene with no need for calibration using polymer standards and can be used for the determination of the absolute molecular weights (MWs). The molecular weight of polymer was determined from the d*n*/d*c* value calculated offline by means of the internal calibration system processed by the ASTRA V software (Version 5.1.7.3, Wyatt Technology). Scanning electron microscopy (SEM) images were collected using a Hitachi S-4800 SEM at an operating voltage of 15 kV. Particle size and dispersity were measured with a ZetaPlus dynamic light scattering detector (15 mW laser, incident beam at 676 nm, Brookhaven Instruments, Holtsville, NY). UV irradiation was performed using a high pressure mercury vapor short arc bulb from an Omnicure S1000 with the adjustable collimating adaptor. The beam irradiating the sample was at a power of 50 mW cm^{-2}. The probe sonication was performed using a probe sonicator (700 W, 20 kHz, Fisher Scientific, Pittsburg, PA, USA). HPLC was performed on a Shimadzu HPLC system (LC-20AT) connected with PDA detector (SPD-M20A) and fluorescence detector (RF-20A). Shimadzu C18 column (3 μm, 50 × 4.6 mm^2 dimension) was used for analysis. The mobile phase consisted of 0.1% TFA/Water and acetonitrile with flow rate 1.5 mL/min. The UV wavelength for detecting pyrene derivatives was set at 343 nm. UV–vis absorption was recorded by Cary 5000 spectrophotometer from Agilent Technologies.

Polymer Synthesis

Synthesis of 2-Nitrobenzyl(4-vinylphenyl)carbamate

2-Nitrobenzyl alcohol (0.92 g, 6 mmol) in 5 mL anhydrous THF was added to a stirred solution of phosgene (15 wt % in toluene, 9 mL, 12.6 mmol) in 10 mL anhydrous THF under nitrogen at 0 °C. The reaction was stirred for 6 h and then the solvent and excess phosgene was removed under vacuum. The resulting oil was used directly without further purification. 4-Vinylaniline (0.60 g, 5 mmol) was dissolved in a 15 mL anhydrous THF and then added to 10 mL THF solution of above oil-like compound (1.29 g, 6 mmol). The resulting mixture was stirred at room temperature for 48 h. The solvent was removed after filtration and the residue was purified by silica gel column chromatography (hexane: ethyl acetate = 2:1, v/v) to afford the product as a white solid. (1.0 g, yield 56%). ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.97 (s, 1H, Ar—N*H*—CO—O—), 8.13 (d, 1H, Ar*H*), 7.87–7.71 (m, 2H, Ar*H*), 7.68–7.59 (m, 1H, Ar*H*), 7.48–7.35 (m, 4H, Ar*H*), 6.64 (d, 1H, —Ph—C*H*=CH$_2$), 5.70 (d, 1H, —Ph—CH=C*H*$_2$), 5.48 (s, 2H, Ph—C*H*$_2$—O—CO), 5.13 (d, 1H, —Ph—CH=C*H*$_2$).^{13}C NMR (DMSO-d_6, 500 MHz): δ 153.5, 148.0, 139.2, 136.8, 134.9, 132.9, 132.3, 129.9, 127.4, 125.6, 118.9, 113.2, 63.2. ESI-MS (low resolution, positive mode): calculated for $C_{16}H_{15}N_2O_4$, m/z, 299.1 $[M + H]^+$; found 299.1 $[M + H]^+$.

Synthesis of 2-Nitrobenzyl(4-(1,2-dihydroxyethyl)phenyl)carbamate (1)

2-Nitrobenzyl (4-vinylphenyl)carbamate (1.0 g, 3.3 mmol) and K_2OsO_4 (62 mg, 0.165 mmol) were dissolved in acetone/H_2O (3:1, v/v, 100 mL), and then 4-methylmorpholine N-oxide (NMO) (586 mg, 5 mmol) was added. The mixture was stirred at room temperature overnight and saturated aqueous solution of $Na_2S_2O_3$ (10 mL) was then added to quench the reaction. After 12 h, the resulting solution was extracted by ethyl acetate (3 × 100 mL). The crude product was obtained after removal of ethyl acetate. The product was then purified by silica gel column chromatography using a gradient elution (hexane: ethyl acetate = 1:1 to 0:1, v/v) to give compound **1** (0.87 g, yield 80%) as a white solid. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.83 (s, 1H, Ar—N*H*—CO—O—), 8.13 (d, 1H, Ar*H*), 7.81 (d, 1H, Ar*H*), 7.76–7.71 (m, 2H, Ar*H*), 7.66–7.58 (m, 1H, Ar*H*), 7.38 (d, 2H, Ar*H*), 7.26–7.19 (m, 2H, Ar*H*), 5.47 (s, 2H, Ph—C*H*$_2$—O—CO), 5.12 (d, 1H, —CH—O*H*), 4.65 (t, 1H, —CH$_2$—C*H*—OH), 4.49–4.42 (m, 1H, —CH$_2$—O*H*), 3.40–3.34 (m, 2H, —C*H*$_2$—OH).^{13}C NMR (DMSO-d_6, 500 MHz): δ 153.6, 147.9, 138.4, 138.1, 134.8, 133.0, 129.9, 127.3, 125.5, 118.5, 74.1, 68.1, 63.0. ESI-MS (low resolution, positive mode): calculated for $C_{16}H_{16}N_2O_6Na$ 355.1, m/z, $[M + Na]^+$; found 355.1 $[M + Na]^+$.

Synthesis of Poly (1/2)

To the solution of compound **1** (332 mg, 1 mmol) and azelaic acid dichloride (225 mg, 1 mmol) in DCM (3 mL), anhydrous pyridine (0.483 mL, 6 mmol) was added dropwise over 10 min under nitrogen. The solution was stirred for 22 h at room temperature. The reaction mixture was concentrated to 0.5 mL under vacuum, and precipitated into cold methanol (10 mL). The precipitate was collected by centrifugation at 4000 r.p.m. and dried under vacuum. Poly (**1/2**) was obtained as a light yellow solid (400 mg, yield 80%). $M_n = 11{,}200$ g mol^{-1}; $M_w/M_n = 1.24$. ^{1}H NMR (CDCl$_3$, 500 MHz): δ 8.09 (d, 1H, Ar*H*), 7.67–7.21 (m, 7H, Ar*H*), 5.95 (s, 1H, Ar—N*H*—CO—O—), 5.58 (d, 2H, Ph—C*H*$_2$—O—CO), 4.28 (s, 2H, —CH—C*H*$_2$O—CO—), 3.65 (s, 1H, Ph—C*H*—CH$_2$—), 2.35–2.23 (m, 4H, —CO—C*H*$_2$—CH$_2$—), 1.59–1.19 (m, 10H, —OCO—CH$_2$— (C*H*$_2$)$_5$—CH$_2$—).

General Procedure for the Photolysis of Poly(1/2) or PolyBoc and Analysis of the MWs by GPC

A DMF/H_2O (95:5, v/v) solution (1 mL) of poly (**1/2**) or polyBoc (10 mg/mL) in a quartz cuvette was placed under illumination from the UV source (365 nm, 50 mW cm^{-2}) and irradiated for 40 min or 2 h. The resulting solution was then incubated under dark at 37 °C for 96 h before it was dried under vacuum. The residue was dissolved in DMF (1 mL) and used for the MW analysis by GPC.

General Procedure for Analysis of Degradation Kinetics of 3 by ^{1}H NMR

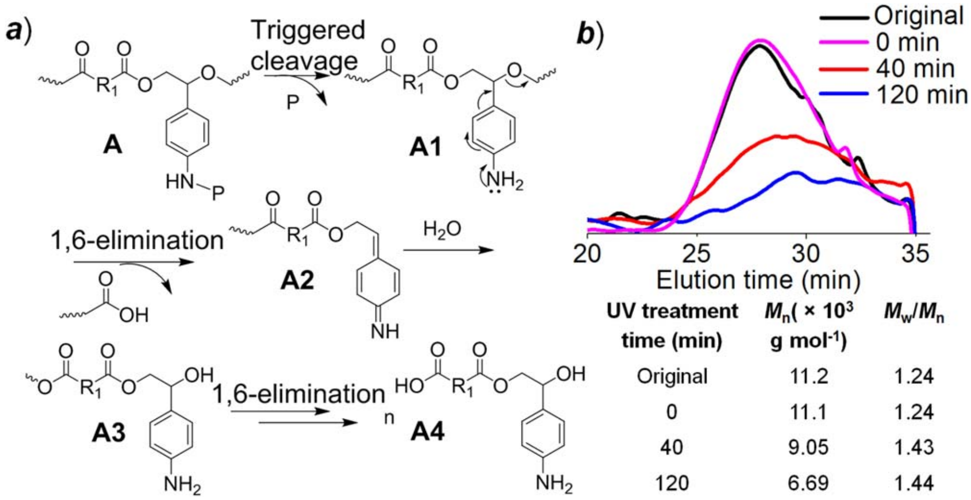
The solution of **3** in DMSO-d_6: D_2O (5:1, v/v, 1.3 mM) in a quartz cuvette was placed inside a photoreactor and irradiated by UV light (365 nm, 50 mW cm^{-2}) for different time (0, 40 min, 80 min) and then the resulted solution was incubated at 37 °C for different period of time. The solution was used for the degradation analysis of **3** by ^{1}H NMR.

General Procedure for Analysis of Degradation Species of 3 by HPLC

A CH_3CN/H_2O (9:1, v/v) solution of **3** (0.2 mg mL^{-1}) in a quartz cuvette was placed under illumination from the UV source (365 nm, 50 mW cm^{-2}) and irradiated for 1 h. The resulting solution was incubated at 37 °C under dark. At different time point (0, 22, 44, 66, and 90 h), a small aliquot of the solution (250 μL) was diluted with 500 μL CH_3CN and 100 μL DMF before analysis by HPLC. F2 peak was confirmed by ESI (high resolution mode; calculated for $C_{48}H_{40}NO_4$ 694.2964, m/z, $[M + H]^+$; found 694.2957 $[M + H]^+$.) and F5 peak was confirmed by comparison with standard.

General Procedure for the Preparation of Nile Red Encapsulated Polymer (1/2) Based Nanoparticles and UV-Triggered Release of Nile Red from the Nanoparticles

Poly (**1/2**) (20 mg) and Nile Red (0.5 mg) were dissolved in DCM (2 mL), and the solution was added to DI-water (40 mL) containing 1% poly(vinylalcohol) (PVA). The mixture was stirred at 1000 rpm for 10 min. The above mixture was sonicated by probe sonication for 5 min (40 W, 1 s pulse with 1 s delay) under ice bath. The suspension was further stirred at 500 rpm using a magnetic stirrer to evaporate DCM overnight. The nanoparticles were collected by ultracentrifugation at 12 000 rpm for 20 min and washed twice with water to remove PVA and dried by lyophilization. An aqueous solution of Nile Red loaded nanoparticles of poly (**1/2**) (50 μg mL^{-1}) in a quartz cuvette was irradiated at 50 mW cm^{-2} for a specific period of time. The resulting solution was used for fluorescence analysis ($\lambda_{ex} = 556$ nm; $\lambda_{em} = 634$ nm). Known amount of dry Nile Red loaded



UV treatment time (min)	M_n (× 10^3 g mol^{-1})	M_w/M_n
Original	11.2	1.24
0	11.1	1.24
40	9.05	1.43
120	6.69	1.44

FIGURE 1 (a) Proposed degradation mechanism for poly(**1**/**2**); (b) GPC curves of poly(**1**/**2**) treated under UV irradiation (365 nm, 50 mW cm^{-2}) for 0, 40, and 120 min in DMF/H_2O (95: 5, v/v) and incubated for 96 h thereafter in the dark. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

nanoparticles was dissolved in DMSO and its UV-vis absorption was measured by spectrophotometer. Nile Red content in nanoparticles was calculated based on its optical density at 552 nm in DMSO (extinction coefficient = 19,600 cm^{-1} M^{-1})[35] by using following equation.

$$\text{Nile Red Content in Nanoparticles } (\%) = \frac{\text{mass of Nile Red in nanoparticles}}{\text{mass of nanoparticles}} \times 100\%$$

RESULTS AND DISCUSSION

We started with commercially available 2-nitrobenzyl alcohol and treated it with phosgene to form 2-nitrobenzyl carbonochloridate which was then used to react with 4-vinyl aniline to give 2-nitrobenzyl (4-vinylphenyl)carbamate [Scheme 1(c)]. The alkene of 2-nitrobenzyl (4-vinylphenyl)carbamate was oxidized to form diol **1**. Two-step yield for synthesizing monomer **1** is about 45%. Protecting the aniline group before generation of the hydroxyl groups avoided the protection/deprotection of hydroxyl groups, which occurred in the preparation of precursors for self-immolative polymers and BHA based CSPs.[27,28,30,33,34] Compound **1** was then copolymerized with **2** in DCM in the presence of pyridine to afford poly(**1**/**2**) with M_n of 11,200 g mol^{-1} and PDI of 1.24 [Fig. 1(b)] by polycondensation.[33] For a control study, we adopted same method by using Boc protected monomer to prepare a photostable polyBoc (M_n = 8000 g mol^{-1} and PDI = 1.31). (Supporting Information Scheme S1).

We next evaluated the degradation of poly(**1**/**2**) in response to UV irradiation by gel permeation chromatography (GPC). Poly(**1**/**2**) in DMF/H_2O (95: 5, v/v) was irradiated with UV light (365 nm, 50 mW cm^{-2}) for 0, 40, and 120 min, respectively, and then incubated at 37 °C for 96 h. Such long incubation time used here is based on degradation kinetics result of our model compound **3** (see below) and previous studies on self-immolative linkers based degradable polymers.[27,28] The solvent was then removed under vacuum followed by dissolution of the residue in DMF. The changes in polymer molecular weights (MWs) were then monitored using GPC. As shown in Figure 1(b), the MWs of UV-irradiated samples for 40 and 120 min were 9050 and 6 690 g mol^{-1}, corresponding to 19 and 40% reduction of their original MWs, respectively. UV light induced degradation of poly(**1**/**2**) was also confirmed by ^{1}H NMR spectrum of poly(**1**/**2**) in DMSO-d_6/D_2O (10:1, v/v) (365 nm, 50 mW cm^{-2}) after the UV treatment for 40 min and followed by incubation at 37 °C for 96 h (Supporting Information Fig. S1). In a control experiment, we irradiated the polymer solution of polyBoc for 120 min with UV light and incubated the resulting solution at 37 °C for 96 h. As shown by the GPC trace in Supporting Information Figure S2(a), no remarkable change of molecular weight was observed. Moreover, after incubation of the solution of poly(**1**/**2**) in the same conditions in the dark for one week, the molecular weight of the polymer remained unchanged [Supporting Information Fig. S2(b)]. Taken together, these data indicate that polymer backbone fragmentation is controlled exclusively by the removal of the triggering groups through UV light and that no side reactions such as hydrolysis occurred during the long UV irradiation time or dark incubation time.

The degradation of poly(**1**/**2**) likely occurs by means of a 1,6-elimination at deprotected repeating unit [Fig. 1(a)].[23,36] The degradation starts when the aniline moiety [**A**, Fig. 1(a)] is unmasked by cleavage of the protecting group (P) to form **A1**, which then undergoes spontaneous 1,6-elimination reaction to cleave the ester at the benzylic position and form a reactive azaquinone-methide intermediate (**A2**). Intermediate **A2** is then trapped by H_2O to form **A3**. Ideally, when the P group is removed from all the repeating units, the resulting P-depleted polymer (**A1**) becomes unstable and shatters to **A4**.

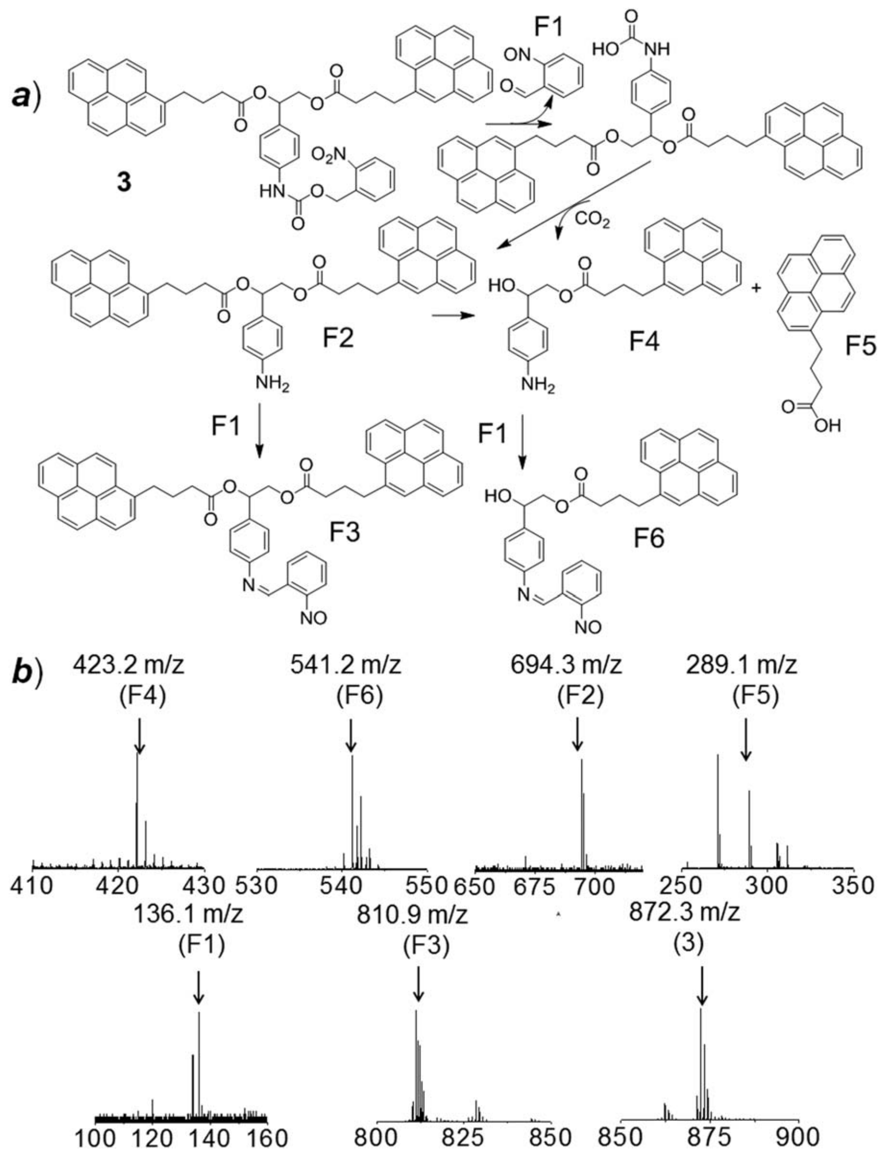


FIGURE 2 (a) Proposed degradation mechanism of **3** upon exposure to UV treatment; (b) LC-MS analysis of degradation fragments of **3** after UV treatment (365 nm, 50 mW cm^{-2}, 2 h).

To confirm this degradation mechanism, we prepared **3** [Fig. 2(a)], a small-molecule analogue containing the triggering structure of the poly(**1**/**2**) but with an easily detectable pyrene moiety via the reaction of TRD **1** and 1-pyrenebutyric chloride [SI, Scheme S2]. Analysis of a solution of **3** in DMSO-d_6/D_2O (5: 1, v/v) by LC-MS after UV irradiation (365 nm, 50 mW cm^{-2}) for 2 h showed F4, F5, and F6 were the major degradation products, suggesting the desired degradation occurred at the majority of repeating unit sites. Interestingly both the nitrosobenzaldehyde (F1) was observed, along with the detection of small amounts of the unstable species F2. In our previous work with the BHA,[33] we did not observe the aniline intermediate after UV irradiation. The discrepancy suggests that 1,6-elimination reaction mentioned herein to form F4 is not as fast as the 1, 4-elimination reaction in CSPs prepared with BHA [Scheme 1(a)]. As such, it is not surprising that a small peak of F3 was also detected because of trapping F2 by F1 before its 1, 6-elimination to form F4.

We then investigated the degradation kinetics of **3** by monitoring the released percentage of final fragments via ^{1}H NMR spectrum in DMSO-d_6/D_2O (5:1, v/v). A solution of **3** was irradiated with UV light for 40 and 80 min, respectively, and then incubated at 37 °C at dark. ^{1}H NMR analysis of the resulting solution was recorded at appropriate time intervals. Figure 3(b) reveals the spectrum of **3** after UV irradiation for 80 min following incubation under dark for 80 h. To identify the major peaks, we synthesized 2-hydroxy-2-phenylethyl octanoate (**4**) for comparison (Supporting Information Scheme S3 and Fig. S3) and its structure was confirmed by gHMBC and mass spectrometry. F5 is chosen as the target molecule since it is the final degradation fragment and its peak assignments can be exclusively identified by

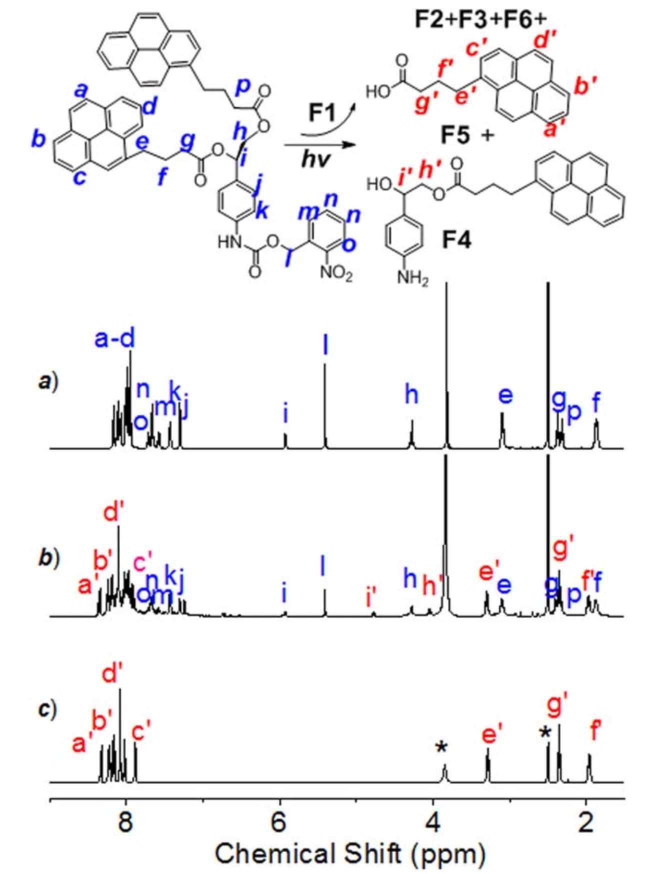


FIGURE 3 [1]H NMR spectra in DMSO-d_6: D_2O (5: 1, v/v) of (a) **3** before UV irradiation; (b) **3** after UV irradiation (365 nm, 50 mW cm^{-2}) for 80 min with incubation under dark at 37 °C for 80 h; (c) authentic **F5**. Asterisks represent peaks due to solvents. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

taking the ^{1}H NMR spectrum of standard F5 [Fig 3(c)]. After UV light irradiation (365 nm, 50 mW cm^{-2}) for 80 min, the integration of peak l (5.41 ppm) decreased to 25%, which means 75% of the nitrobenzyl group was removed after UV light irradiation [Supporting Information Fig. S4]. At the same time, a new peak e′ (3.31 ppm) assigned to F5 appeared whose integration increased with incubation time. The percentage of released F5 was calculated by the integration of peak e′ versus the total integration of peak f′ and peak f. (Supporting Information). As a comparison, without any treatment, **3** showed no hydrolysis in one month as demonstrated by unchanged ^{1}H NMR spectra (Supporting Information Fig. S5), revealing the release of F5 was due to the cleavage of protecting group. Figure 4 shows the release profile of F5 with incubation time after UV irradiation. After about 90 h, target molecule F5 was released to reach its saturated concentration. As we expected, 75% of F5 was released from **3** when 75% of protecting group was removed. In the case where UV irradiation was carried out for 40 min, 45% of the nitrobenzyl group was cleaved and after about 90 h postreaction incubation in the dark, the

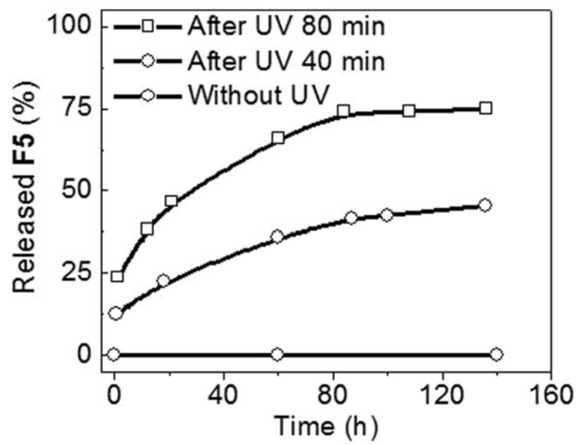


FIGURE 4 Degradation kinetics of **3**, as measured by ^{1}H NMR spectroscopy in DMSO-d_6: D_2O (5: 1, v/v) after the UV irradiation (365 nm, 50 mW cm^{-2}) for different time followed by incubation at 37 °C in the dark.

amount of F5 released was also found to 45% in the final solution. The half-life of 1,6-elimination reaction in our study is thus close to 40 h.

It should be mentioned that typical reaction-rate of 1, 6-elimination using 4-aminobenzyl alcohol as a spacer is fast and typically the substrate is able to be fully released within 1 - 2 h after de-masking the protecting group in aqueous solution.[37,38] The unexpected slow degradation kinetics of **3** likely arises from the effect of $-CH_2OCO-$ substitution at the benzylic methylene position. It has been reported that electron donating substituents, such as a methyl group, increase the elimination rate and it is expected that electron withdrawing effects of the ester group in our work have the opposite effect, leading to prolonged lifetime of the deprotected aniline moiety (F2).[39,40] To confirm our hypothesis, time course monitoring presence of the key intermediate (F2) and final product (F5) was conducted by HPLC as shown in Figure 5 and Supporting Information Figure S6. As expected, F2 showed corresponding opposite change trend as F5 indicating the substantial elongated lifetime of the

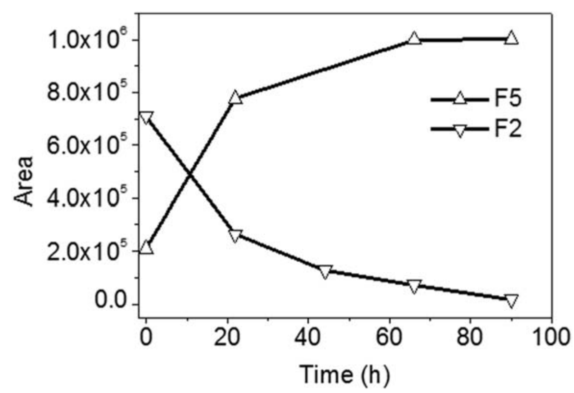


FIGURE 5 HPLC peak areas of F2 and F5 as a function of incubation time after 60 min UV irradiation (365 nm, 50 mW cm^{-2}) of **3** in CH_3CN/H_2O (9:1, v/v).

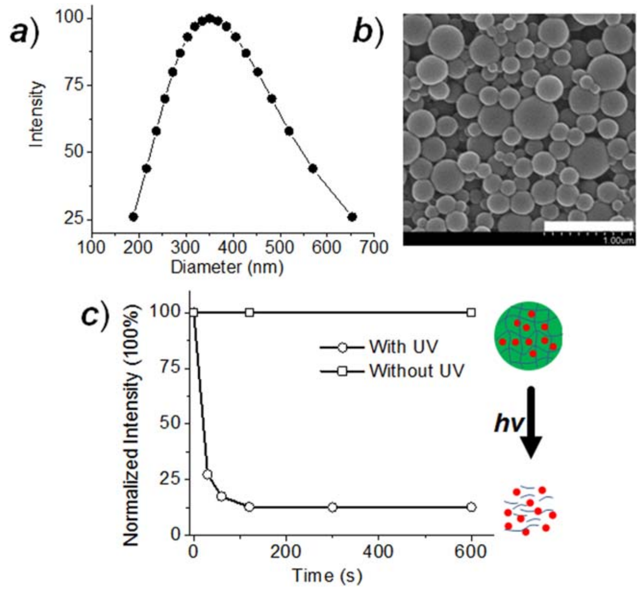


FIGURE 6 (a) Size distribution of Nile Red loaded poly(**1**/**2**) nanoparticles determined by DLS. (b) SEM image of Nile Red loaded poly(**1**/**2**) nanoparticles. Scale bar: 1.0 μm. (c) Normalized fluorescent intensity of Nile Red encapsulated poly(**1**/**2**) nanoparticles upon UV irradiation (365 nm, 50 mW cm^{-2}). (λ_{Em} = 643 nm; λ_{Ex} = 556 nm). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

intermediates. This result may imply that different rates of 1, 6-elimination can be achieved by tuning the substituents at the benzylic methylene position.

We then explored the use of the trigger-responsive poly(**1**/**2**) for controlled release applications. We first attempted to control the release of the dye Nile Red from nanoparticles (NPs) prepared from the poly(**1**/**2**). NPs encapsulating Nile Red with 1.4% content were prepared from poly(**1**/**2**) by means of conventional emulsion methods due to the negligible solubility of poly(**1**/**2**) in water. The average diameter of the NPs was 351 nm ± 150, as determined by dynamic light scattering (DLS) and confirmed by SEM [Fig. 6(a,b)]. The release of the Nile Red payload from poly(**1**/**2**) NPs upon UV treatment was detected by fluorescence spectroscopy. As shown in Figure 6(c) and Supporting Information Figure S7, the fluorescence intensity decreased by 74%, showing the burst release of Nile Red from poly(**1**/**2**) based nanoparticles after UV treatment for 30 seconds. In a control study, the suspension of NPs without UV irradiation showed no dramatic change of fluorescence intensity over one week (Supporting Information Fig. S8). The fluorescence intensity dropped quickly, indicating the trigger-induced burst release of Nile Red from the NPs into a more polar environment (water) from hydrophobic NPs as reported in previous literature.[27,28]

CONCLUSIONS

In summary, we developed 1-(4-aminophenyl)ethane-1,2-diol based polymer (poly(**1**/**2**)) that could be degraded upon trigger-induced removal of the aniline protecting groups [Scheme 1(b)]. The degradation of these polymers contrasts with that of self-immolative polymers, which depolymerize sequentially from one chain end to the other. We used poly(**1**/**2**) to prepare dye-containing NPs from which the encapsulated molecules could be rapidly released upon trigger-induced degradation. This study revealed the feasibility of making stimuli-responsive polymer by utilizing the derivative of 1,4-aminobenzyl alcohol and its application as delivery vehicles. Since the protecting group of 1,4-aminobenzyl alcohol can be tuned easily and the degradation kinetics of such derivatives might be controlled by choosing different substituent groups on the benzylic methylene position, this strategy may be a promising way to prepare stimuli-responsive system owning both “on-demand” responsiveness and controlled degradation rate. Such programmable responsive system may have many potential applications as microcapsule shell materials that release healing reagents for self-repairing purpose[12,41,42] and in smart surface coatings that change wettability in response to environment.[43]

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