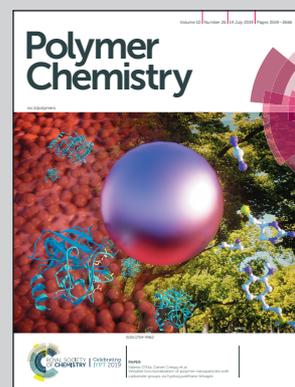


Showcasing research from Professor Qian Zhang's laboratory, Department of Applied Chemistry, Xi'an University of Technology, Xi'an, Shaanxi Province, P.R. China.

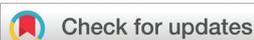
Photo-controlled release of metal ions using triazoline-containing amphiphilic copolymers

Photo-controlled release that shows quick response and high spatial/temporal accuracy has become attractive given its potential applications for biomedicines. However, the encapsulation and controlled release of metal ions using polymer micelles are challenging. We report an interesting example of photo-controlled release of metal ions *via* triazoline-containing amphiphilic polymers. The triazoline moieties could coordinate to Co^{2+} , thus encapsulating the metal ions in the core of the micelles. Photo-induced denitrogenation of triazoline can disrupt the coordination, therefore leading to the release of Co^{2+} . The mechanism is potentially useful for the delivery of essential ions *in vivo*.

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Photo-controlled release of metal ions using triazoline-containing amphiphilic copolymers

Xiaoying Xu,^a Qian Zhang,^{id} *^a Kang Liu,^a Nailiang Liu,^a Ying Han,^{*b} Weixing Chen,^c Chao Xie,^b Pengfei Li^{id} ^d and Jie He^{id} *^e

Photo-controlled release that shows a quick response and high spatial/temporal accuracy has become attractive given its potential applications for biomedicines. A few metal complexes are known for their uses in detoxification, sterilization, and diagnosis and treatment of diseases, but, the encapsulation and controlled release of those metal ions using polymer micelles are challenging. We report an interesting photo-controlled release of metal ions *via* photo-responsive triazoline-containing amphiphilic polymers. Amphiphilic random copolymers of glycidyl methacrylate and oligo(ethylene oxide) methyl ether methacrylate were prepared through free radical copolymerization. The glycidyl pendants were converted to azide, followed by a 1,3-dipolar cycloaddition reaction to form triazoline with norbornene. The resulting random copolymers containing triazoline formed micelles with a critical micellar concentration (CMC) of 7.68×10^{-3} mg mL⁻¹. The triazoline moieties could coordinate to transition metal ions, *e.g.* Co²⁺, and thus encapsulate the metal ions to the core of micelles. Photo-induced denitrogenation of triazoline was able to disrupt the coordination of Co²⁺ and triazoline, therefore leading to the release of Co²⁺. Solution viscosity, UV-vis/NMR spectroscopy and TEM were used to show that the coordination and release of Co²⁺ ions were successful upon exposure to light. The photo-controlled release profile was found to be linearly dependent on the irradiation time, which is potentially useful for the delivery of essential ions *in vivo*.

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1. Introduction

Metal ions play an important role in biological systems. They are involved in many physiological processes.^{1,2} For example, as a trace element in our bodies, cobalt (Co) is present in vitamin B₁₂, known as cobalamin which is the only vitamin containing metal. Without the participation of Co, the efficacy of vitamin B₁₂ will be greatly suppressed or even reduced to nothing. In addition, metal ion complexes can also be used for detoxification,³ sterilization,⁴ and diagnosis⁵ and treatment of diseases.⁶ In ancient civilization, copper and gold were used to cure disease and arsenic was applied for treating epilepsy.⁷

Another typical example is cisplatin, the platinum containing molecule that has been widely used as an efficient drug for chemotherapy treatment.^{8–11} The focus of our study is on the controlled release of Co²⁺ ions specifically by light irradiation. The selection of cobalt is mainly for a proof-of-concept study of the light-induced release mechanism, taking into consideration easy availability, high coordinating ability and the importance of this trace metal in human bodies which can be read about in review articles.^{1,12} For example, administration of cobalt could affect the production and release of red cells into the circulation.¹³

Light is a form of propagating energy. Its wavelength and intensity can be precisely and conveniently tuned, and the irradiation time and illuminated area can be controlled accurately. Therefore, light has been a type of stimulus of great interest for responsive polymers and the pharmaceutical industry.^{14–18} For example, Chen *et al.*¹⁹ reported that amphiphilic polymer micelles containing cisplatin and a photosensitizer could be used in chemotherapy. It is anticipated that photo-controlled release can be of great help to decrease the serious side effects of cisplatin, such as nephrotoxicity, nausea, hearing damage and irreversible peripheral nerve damage.^{8–11} Nevertheless, it is unusual to see photoinduced release of metal ion species, which can be an interesting topic for the conveniently combined time and space accuracy by means of light irradiation; consequently, physiological activity

^aDepartment of Applied Chemistry, Xi'an University of Technology, Xi'an, Shaanxi, 710048, P. R. China. E-mail: qzh@xaut.edu.cn

^bState Key Laboratory of Military Stomatology, National Clinical Research Center for Oral Diseases, Shaanxi Engineering Research Center for Dental Materials and Advanced Manufacture, Department of Oral Implantology and School of Stomatology, The Fourth Military Medical University, Xi'an, Shaanxi, 710032, P. R. China. E-mail: hany722@fjmmu.edu.cn

^cSchool of Materials and Chemical Engineering, Xi'an Technological University, Xi'an, Shaanxi, 710021, P. R. China

^dFrontier Institute of Science and Technology (FIST), Xi'an Jiaotong University, Xi'an, Shaanxi, 710054, P.R. China

^eDepartment of Chemistry and Institute of Materials Science, University of Connecticut, Storrs, Connecticut 06269, USA. E-mail: jie.he@uconn.edu

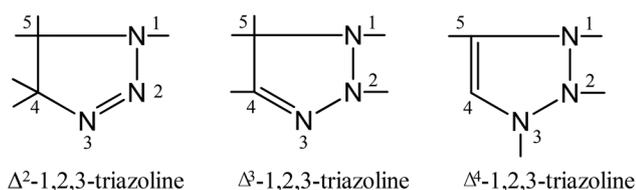
can be regulated accordingly *via* light-triggered release of metal ions.

The current contribution aims at this goal through the photolysis chemistry of triazoline. In 1912, Wolff^{20,21} reported the structure of 1,2,3-triazoline for the first time. Now it is known that the five-membered ring molecule can have three different classes, as shown in Scheme 1.²²

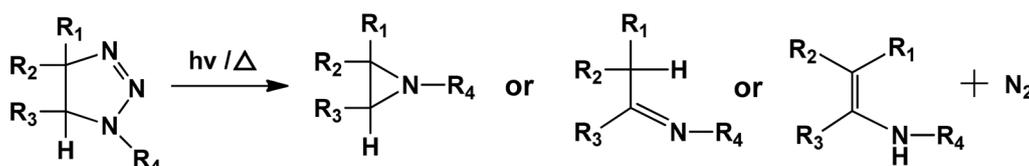
In the past few decades, this heterocyclic compound has attracted much attention due to its extensive biological activities, such as anti-cancer,^{23,24} anti-convulsion,^{22,25–29} and soothing blood vessels.³⁰ In 1984, Kadaba *et al.* found that triazoline can be used as a unique anticonvulsant drug.^{25–28} Compared to other prototype anticonvulsants, it has an excellent anticonvulsant effect and low neurotoxicity.²⁶ In addition, the heterocyclic compound can also be used as a precursor for antibacterial, antiviral, antirheumatic drugs and the like by further functional group reaction modification.²⁸ Besides the pharmaceutical applications, triazoline is also a very interesting molecule for its photo- and thermo-induced nitrogen-elimination process.

The five-membered ring of triazoline is an intermediate state.³¹ It can decompose upon heating or acidic conditions, *via* releasing a dinitrogen to form aziridine. Light is another very efficient driving force for dinitrogen elimination. Garcia-Garibay *et al.* successfully applied photo-induced denitrogenation on the solid state of the crystalline structure of triazoline derivatives, and consequently solid-to-solid conversion was achieved.^{32–34} Luo *et al.* took advantage of the N₂ elimination process to obtain an aziridine-containing polymer for electrooptic applications.³⁵ To date and based on our knowledge, the conditions for decomposition are mainly above 100 °C or upon UV irradiation. The nitrogen elimination of triazoline nitrogen is illustrated in Scheme 2. It is noted that Schiff base and enamine are other possible byproducts from denitrogenation.^{36–38}

Through denitrogenation, the five-membered ring shrinks to a much smaller three-membered ring (main product). The decrease in metal coordination is anticipated. Therefore we



Scheme 1 Nomenclature of 1,2,3-triazoline.²²



Scheme 2 The dinitrogen elimination of triazoline.^{36–38}

propose an interesting photo-controlled release of metal ions upon the photolysis of triazoline to aziridine. The main idea including the synthetic routes is shown in Scheme 3. We synthesized random copolymers of glycidyl methacrylate (GMA) and oligo(ethylene oxide) methyl ether methacrylate (OE), denoted as PGO. The glycidyl moieties were then converted to azide by reacting with sodium azide to yield PGO-N₃. PGO-N₃ then reacted with norbornene through a 1,3-dipolar cycloaddition reaction to form a triazoline-containing polymer with norbornene pendant moieties (PTA, TA refers to triazoline). PTA can coordinate through N-Co binding (PTA-Co) between Co²⁺ and triazoline as confirmed by the change in solution viscosity upon coordination. To elucidate photo-triggered release of Co²⁺ ions, PTA-Co was subjected to UV radiation and the changes in polymer structures as well as the release profile of Co²⁺ ions were investigated in detail.

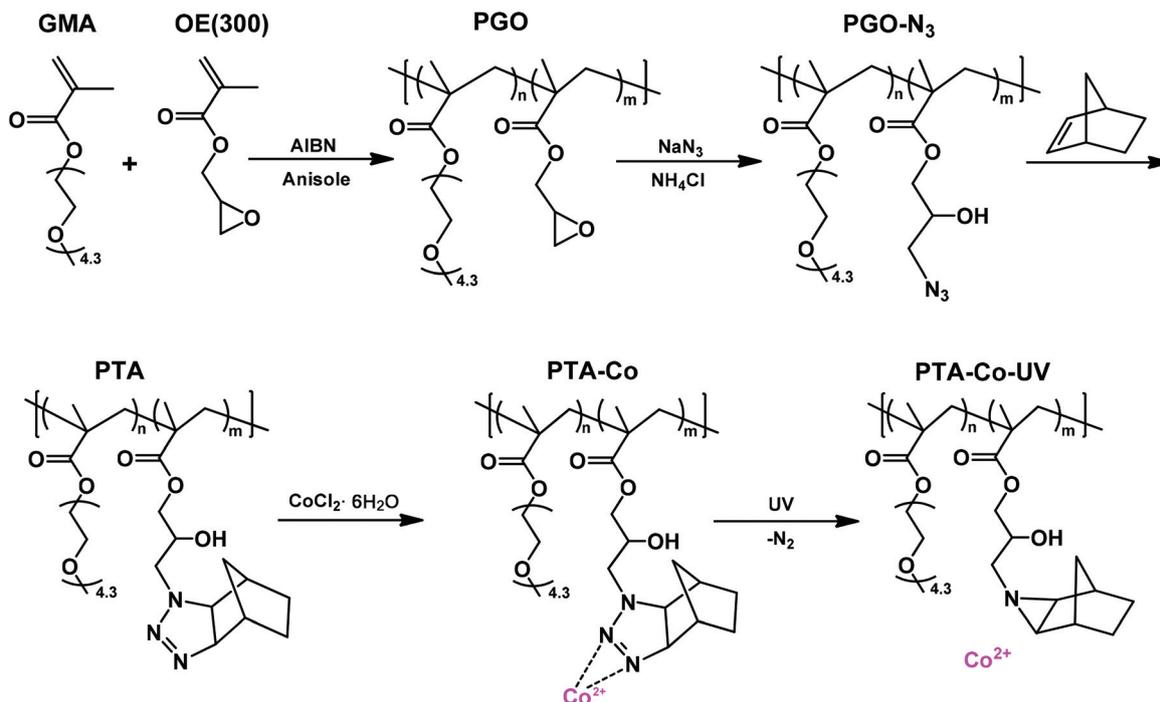
2. Experimental section

2.1 Materials and characterization

Oligo(ethylene oxide) methyl ether methacrylate (OE, average $M_n = 300$) was purchased from Sigma-Aldrich and glycidyl methacrylate (GMA, 96%) was from J & K Technology. Anisole was from Aladdin. Norbornene was from Tokyo Chemical Industry (TCI). Cobalt chloride hexahydrate (CoCl₂·6H₂O), ammonium chloride (NH₄Cl) and azobisisobutyronitrile (AIBN) were from Sinopharm Chemical Reagent. All monomers were passed through an activated basic alumina column to remove the inhibitor before polymerization. AIBN was recrystallized from methanol and stored in a refrigerator before use.

¹H-NMR spectra were recorded using a Bruker Advance III 400 MHz spectrometer equipped with an autosampler. The CDCl₃ singlet at 7.26 ppm was used as the reference standard. Spectral features were tabulated in the following order: chemical shift (ppm), multiplicity (s – singlet, d – doublet, t – triplet, m – complex multiplet, broad-broad peaks), number of protons and its position on the chemical structure.

The relative molecular weight (MW) and the dispersity index (*D*) were determined by using a gel permeation chromatograph (GPC, Malvern Viscotek 270MAX) from Malvern Instruments Ltd. It is equipped with a VE 3580 refractive index (RI) detector. Two PolyAnalytik columns (LT3000L and LT6000L) were used with THF as the eluent at 35 °C at a flow rate of 1 mL min⁻¹. Linear polystyrene (PS) standards were used for calibration up to 2 500 000 g mol⁻¹. Aliquots of polymer samples were dissolved in THF (THF/anisole = 70/1 (v/v)) and anisole was added



Scheme 3 The polymers containing triazoline are synthesized by the “click” reaction between azide and olefin. The coordination and light-triggered release of Co²⁺ ions are proposed through the denitrogenation of triazoline.

as a flow rate marker, and filtered with a 0.22 μm PTFE membrane to remove the insoluble prior to injection.

Transmission electron microscopy (TEM) was used to characterize the morphology and particle size of polymer micelles. A JEM-3010 with a point-to-point resolution and a line resolution of 0.19 nm and 0.14 nm, respectively, was operated at 300 kV. Samples for TEM observations were prepared by dropping the diluted dispersion onto copper grids (230 mesh, 10–20 nm carbon coating), and drying in air.

The Fourier-transform infrared spectroscopy (FTIR) spectra of the samples were recorded on a Shimadzu Prestige-21 ATR spectrometer equipped with ZnSe crystals by single reflection in the range of 4000–650 cm⁻¹. The resolution is 4 cm⁻¹ and the number of scans is 16.

The size of polymer micelles was measured by dynamic light scattering (DLS) using a Malvern Nano-ZS90. 1.0–1.5 mL sample volume was used for each measurement. The UV-vis spectrograph was recorded on a MAPADA UV-3200 spectrophotometer using a 1 cm quartz cuvette.

UV-irradiation was applied using a thin-layer-chromatography (TLC) lamp from Anting electronics Shanghai Co. Ltd working at 245 nm. The sample was placed in a 20 mL vial right below the center of the lamp, and the distance between the lamp and the bottom of the container was controlled at 11 cm. In the release tracking experiment by UV, a 50 mL beaker was used.

Rheological properties of the sample were determined using a Discovery HR-2 hybrid rheometer from TA instruments

with flat plate geometry. The shear rate was from 0.01 to 360 s⁻¹. The temperature was set at 20 °C.

Fluorescence spectroscopy was performed on a Shimadzu RF-6000 spectrometer. The excitation wavelength was set at 595 nm, and the emission was recorded from 600 to 800 nm. The data interval was 1.0 nm, and the scanning speed was at 200 nm min⁻¹.

2.2 Polymer synthesis and post-polymerization functionalization

2.2.1 Synthesis of polymer PGO.

GMA (200 mg, 1.33 mmol), OE (2 g, 6.67 mmol), AIBN (13.4 mg, 0.08 mmol) and anisole (8.3 mL) were mixed in a round-bottomed flask. The oxygen in the mixture was removed by bubbling with N₂ for 30 min, and then the mixture was placed in an oil bath preheated at 75 °C for polymerization for 24 h. After polymerization, the reaction mixture was purified by precipitation in *n*-hexane. The supernatant was discarded, the precipitate was redissolved in THF and this process was repeated three times. At the end, the residual solvent was eliminated by using a rotary evaporator under reduced pressure. The product was further dried in a vacuum oven at room temperature. Finally, a transparent viscous liquid polymer was obtained (1.937 g, yield 97%). The ratio of GMA/OE was calculated based on the integral ratio of 3.39 ppm and 3.21 ppm from ¹H NMR. ¹H NMR (400 MHz, CDCl₃) δ: 4.5–4.0 (broad, -COO-CH₂-), 4.0–3.5 (broad, -COO-CH₂-CH₂-O-), 3.39 (s, -O-CH₃), 3.21 (s, -COO-CH₂-CH-), 2.84 and 2.63 (s, -CH-CH₂-), 2.2–1.5 (broad, back-

bone $-\text{CH}_2-$), 1.5–0.5 (broad, backbone $-\text{CH}_3$). Likewise, random copolymers having different GMA/OE ratios of 1/10, 1/12, and 1/15 were prepared accordingly.

2.2.2 Synthesis of PGO- N_3 . The synthesis of PGO- N_3 was carried out according to previous literature.^{39–41} PGO (1.01 g, 0.68 mmol), NaN_3 (443.2 mg, 6.8 mmol), NH_4Cl (181.5 mg, 3.4 mmol), acetonitrile (9 mL) and deionized water (3.9 mL) were mixed in a thick-wall flask, and sealed with a Viton ring and PTFE cap. The reaction was carried out in an oil bath at 75 °C for 7 h. After reaction, anhydrous magnesium sulfate was added to remove the water. The mixture was then extracted with ethyl acetate and water. The organic phase was rinsed with water at least three times, and then anhydrous NaSO_4 was added and the mixture was stirred overnight. Then, it was filtered and the solvent was stripped. The product was dried under vacuum at room temperature to afford a yellowish jelly solid (873.2 mg, yield = 84.0%). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 4.5–4.0 (broad, $-\text{COO}-\text{CH}_2-$), 4.0–3.5 (broad, $-\text{COO}-\text{CH}_2-\text{CH}_2-\text{O}-$), 3.39 (s, $-\text{O}-\text{CH}_3$), 2.2–1.5 (broad, backbone $-\text{CH}_2-$), 1.5–0.5 (broad, backbone $-\text{CH}_3$). The three other polymers with different GMA/OE ratios of 1/10, 1/12, and 1/15 were prepared similarly using PGO/ NaN_3 / NH_4Cl of 1/10/5, respectively, to yield PGO- N_3 .

2.2.3 Synthesis of PTA. The triazoline polymer was synthesized using a reported procedure.⁴² PGO- N_3 (750 mg, 0.490 mmol) was mixed with an excess of norbornene (478.2 mg, 5.079 mmol) in 1.5 mL THF in a 20 mL vial protected against light with alumina foil. The reaction was monitored by FTIR until the azide group was consumed completely. Then, the mixture was quickly added to the *n*-pentane to precipitate. The supernatant was discarded and the precipitate was dissolved in THF. The purification was repeated three times. At the end, the precipitate was dried in a vacuum oven at room temperature to obtain a transparent light brownish solid (642.5 mg, yield = 85.7%). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 4.4–4.25 (broad, norbornene $-\text{N}-\text{CH}<$), 4.25–3.8 (broad, $-\text{COO}-\text{CH}_2-$), 3.75–3.5 (broad, $-\text{COO}-\text{CH}_2-\text{CH}_2-\text{O}-$), 3.39 (s, $-\text{O}-\text{CH}_3$), 2.75–2.0 (broad, norbornene $-\text{CH}<$), 1.55–1.1 (broad, norbornene $-\text{CH}_2-$), 2.0–1.6 (broad, backbone $-\text{CH}_2-$), 1.1–0.5 (broad, backbone $-\text{CH}_3$). Other PGO- N_3 with varying GMA/OE = 1/10, 1/12, and 1/15 was converted to triazoline-containing polymers similarly.

2.2.4 Synthesis of PTA-Co in the mixture of methanol and H_2O . PTA (100 mg, 0.067 mmol) was mixed with methanol (200 μL) and kept in a refrigerator for 10 h, and then vortexed to make a solution. At the same time, $\text{CoCl}_2\cdot 6\text{H}_2\text{O}$ (5.3 mg, 0.022 mmol) was dissolved in deionized water (200 μL). It was then mixed with PTA solution to form a viscous solution immediately. The solution was then taken to the rheological experiment immediately. When used for UV-vis spectroscopy measurements, all the solutions were diluted at the same time to maintain the relative concentration.

2.2.5 Preparation of the micellar dispersion

PTA micellar dispersion. PTA (11.4 mg) was dissolved in THF (1 mL) and added dropwise to deionized water (10 mL). The dispersion was then stirred at room temperature under ventilation for 24 h until THF evaporates completely in the dark. A

turbid dispersion was obtained and filtered with a 0.45 μm membrane. The micellar dispersion was diluted to 0.04 mg mL^{-1} for TEM and DLS measurements.

PTA-Co micellar dispersion. PTA (20.6 mg) was dissolved in THF (1 mL) and added dropwise to deionized water (20 mL). The dispersion was then stirred at room temperature in ventilation for 24 h until THF evaporated completely in darkness; then $\text{CoCl}_2\cdot 6\text{H}_2\text{O}$ (0.928 mg) was added and quickly stirred. A turbid dispersion was obtained and it was filtered with a 0.45 μm membrane. 6 mL of dispersion was not further purified and taken for illumination at 245 nm for 7 h, the sample including that before illumination was diluted to 0.04 mg mL^{-1} for DLS and TEM experiments.

2.2.6 Determination of the critical micellar concentration (CMC). Nile Red (NR) was used as a probe to determine the CMC through fluorescence spectroscopy according to literature procedures.^{43,44} Stock solutions of PTA (1 mg mL^{-1}) and NR (1 mg mL^{-1}) were prepared with THF separately in advance. Deionized water (10 mL) was added dropwise into a series of mixtures consisting of the stock solutions of PTA and NR. The amount of NR used was fixed at 0.5 mL, and a variety of amounts of PTA stock solution were used. The resulting dispersions were stirred for 30 h to evaporate THF, followed by filtering with a 0.45 μm PES membrane. A series of NR-loaded PTA micelles at various concentrations from 2.0×10^{-4} to 7.0×10^{-2} mg mL^{-1} were prepared. Their fluorescence intensities were recorded by excitation at 653 nm.

2.2.7 Light-induced release experiment. The kinetics of light-induced release for PTA-Co when exposed to UV light was investigated according to previously reported procedures.^{45–47} The aqueous solution of PTA-Co was charged into a dialysis bag (cutoff molecular weight of 500 daltons from Spectra/Por). It was then placed into a small beaker containing 4 mL of deionized water. The dialysis bag containing PTA-Co solution was completely immersed in water and placed under UV light at 254 nm. The control experiment was conducted at the same time with samples placed in the dark.

3. Results and discussion

3.1 Synthesis of polymers

The random copolymer PGO of GMA and OE was synthesized through free radical polymerization. It is noted that block copolymers have been extremely promising in the area of light-induced drug release; however, their synthesis is onerous. The current study is focused on the performance of random copolymers with a simple synthetic process and facile post-polymerization functionalization.^{45,47,48} As shown in Scheme 3, the glycidyl groups were then converted to azide (PGO- N_3), which was followed by a 1,3-dipolar cycloaddition reaction with norbornene to form triazoline (PTA) according to a previous report.⁴² The FTIR, GPC and NMR results are shown in Fig. 1. The molecular weight (MW) and dispersity (\bar{D}) of the copolymers were also measured by GPC. PGO has $M_n = 48.6 \text{ kg mol}^{-1}$ vs. polystyrene standard in THF. PGO- N_3 shows

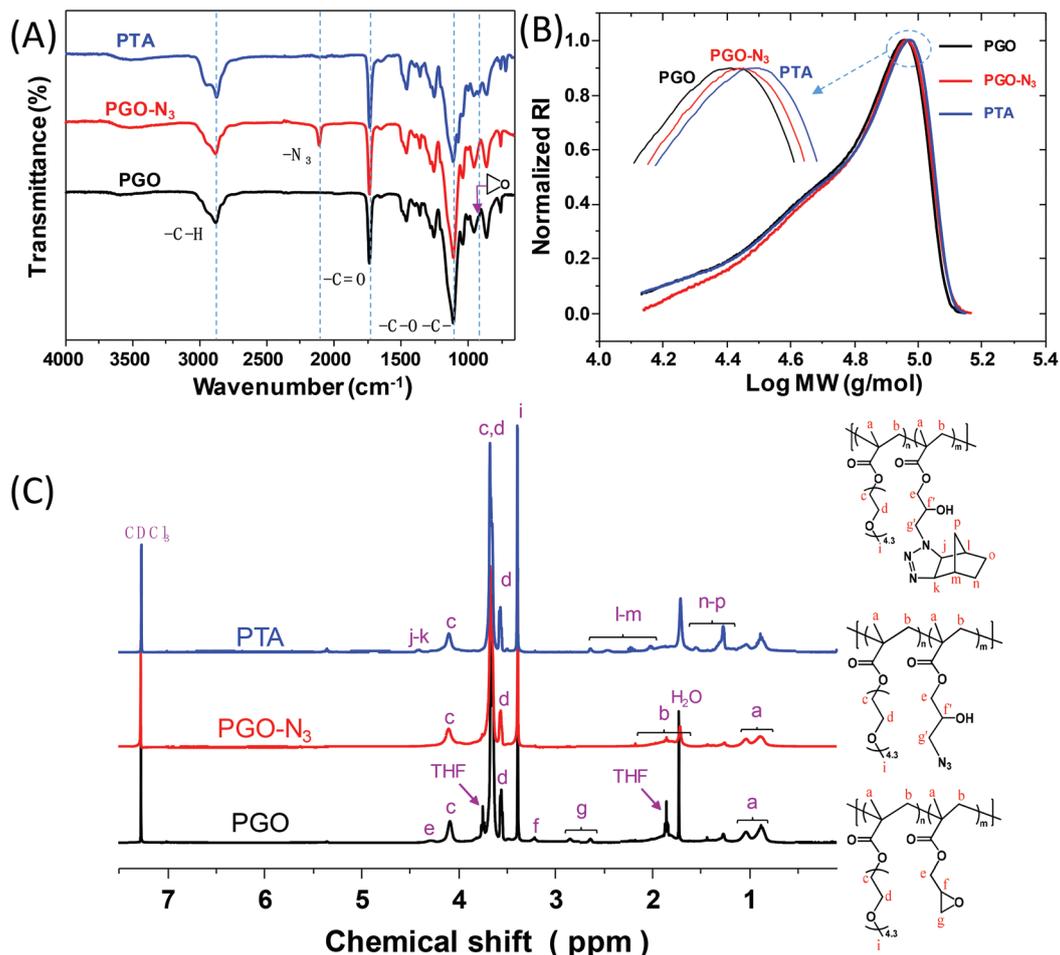


Fig. 1 The FTIR spectra (A), GPC chromatograms (B) and NMR spectra (C) of PGO, PGO-N₃, and PTA.

a small increase of M_n to 51.0 kg mol⁻¹. The M_n of the triazoline-containing PTA increased further to 53.3 kg mol⁻¹. This increase of MW can be identified by a shift of the elution peak from GPC, as indicated by M_p in Table 1 and the inset in Fig. 1 (B). Assuming that 48.6 kg mol⁻¹ (relative molecular weight vs. PS standard used in GPC calibration) is close to the real M_n of PGO and taking into account the ratio of GMA/OE = 1/4.49 (see below), one can calculate the theoretical molecular weight of PGO-N₃'s M_n to be 50.0 kg mol⁻¹ and PTA's M_n to be 53.1 kg mol⁻¹. This fits very well with the experimental results of M_n in Table 1.

The conversion of functional groups in those polymers was further confirmed using FTIR and NMR. As shown in Fig. 1(A), the FTIR of PGO shows the C-H stretching vibration of -CH₃,

-CH₂- and -CH- around 2870 cm⁻¹. A characteristic stretching of carbonyl (C=O) can be seen at 1730 cm⁻¹. 1103 cm⁻¹ is attributed to the stretching of C-O. The signal from the glycidyl group is expected to be around 910 cm⁻¹;⁴⁹ unfortunately, this area overlaps with other signals and only a tiny shoulder can be identified to differ from other spectra (purple arrow). The existence of glycidyl can also be confirmed by the reaction of PGO with sodium azide to afford PGO-N₃. An intense peak of azide is found at 2100 cm⁻¹;⁵⁰ at the same time the tiny shoulder at 910 cm⁻¹ disappeared. In the next step, PGO-N₃ reacted with norbornene to form a triazoline-containing polymer (PTA). The disappearance of azide is evidenced, but unfortunately, no typical peaks from triazoline can be identified.

Fig. 1(C) shows the ¹H NMR spectra for all the polymers with protons assigned. For PGO, the GMA/OE ratio can be calculated by the integrals from the protons on the glycidyl group (3.21, 2.84 and 2.63 ppm) and on the end-capped methyl group (3.39 ppm). This ratio is slightly higher than the feeding ratio of GMA/OE = 1/5, implying a lower reactivity of OE probably due to the bulky side chain of ethylene oxide. The appearance of protons on glycidyl moieties also confirmed the

Table 1 Summary of GPC results of polymer samples

	M_n , GPC	M_p , GPC	D (M_w/M_n)	Yield
PGO	48.6 k	90.9 k	1.51	96.7%
PGO-N ₃	51.0 k	92.5 k	1.48	84.0%
PTA	53.3 k	94.7 k	1.34	85.7%

success of copolymerization. As for PGO-N₃, the complete consumption of glycidyl can be confirmed by the disappearance of signals “f” and “g” at 2.63–3.21 ppm in Fig. 1(C). The appearance of new characteristic protons on –CH₂–N₃ which is possibly in the range of 3.39–3.50 ppm as reported elsewhere^{51–54} can be hardly observed due to overlap with other signals. PTA shows a much more complicated NMR spectrum for the incorporation of the norbornene group, and a complete resolving of the spectrum is challenging. The new appearance of signals from 2.0–2.7 ppm implies the existence of protons from substituted norbornene.⁴² And fortunately, the emergence of a signal centered at 4.40 ppm (“j” and “k”) indicated very well the formation of triazoline groups, as can be referred to in other triazoline-containing molecules.^{32,34,35,42,55,56} Besides, its response to light also confirmed its relationship with triazoline groups (*vide infra*).

The reaction of 1,3-dipolar cycloaddition between azide and norbornene was carried out at room temperature. The efficiency of the 1,3-dipolar cycloaddition reaction is known to be enhanced by strained cycloalkane like norbornene.^{42,57} The reaction kinetics can be followed by FTIR (Fig. 2). Four parallel experiments were conducted with polymers having different GMA/OE feeding ratios from 1/5 to 1/15. The molar ratio of norbornene/azide was fixed at 10/1. All FTIR spectra in Fig. 2 were normalized using the C=O stretching at 1730 cm⁻¹ as an internal standard to measure the peak intensity of azide. The evolution of azide concentration (integral) was calculated relative to that when the reaction just started, and the plot was made *vs.* day. It was found that the reaction can be approximately first order (Fig. 2B), with a rate constant *k* in the range of 0.02–0.035 d⁻¹. This reaction is very slow, but the reaction rate seems to be independent of the concentration of azide per polymer chain.

3.2 Photo-induced nitrogen elimination of PTA

The five-membered ring is unstable,^{42,55} and can decompose upon heating or irradiation with UV light to release dinitrogen.^{32,33,58} The sample was dissolved in CDCl₃ and irradiated using a fluorescent UV lamp. The dinitrogen elimination can be monitored using ¹H NMR (Fig. 3a). The NMR spectra were normalized using the peak at 4.1 ppm as an internal standard to measure the protons on the triazoline at 4.35–4.45 ppm. The peak at 4.43 ppm (see the previous text) was used to calculate the release of dinitrogen of PTA. Fig. 3(B) shows that the peak at 4.43 ppm on the normalized NMR spectra decreased gradually with the irradiation of UV light, and eventually disappeared after 7 h. The kinetic curve of the decomposition reaction was constructed with time (*t*) according to the integral of the peak that is directly proportional to the concentration (*C_t* and *C₀*) of triazoline moieties, and *k_d* is the denitrogenation constant. By fitting the data, a linear relationship can be identified as a first order reaction (see eqn (1) and Fig. 3) with a *k_d* value of 3.85 × 10⁻³ min⁻¹.

$$\ln \frac{C_0}{C_t} = k_d \times t \quad (1)$$

3.3 Light-induced coordination disruption of PTA-Co

To validate the light-induced Co release of PTA-Co complexes, UV-vis spectroscopy was used to study the change of the coordination of Co²⁺ species within PTA. Fig. 4(A) shows the spectra of PTA, CoCl₂, PTA-Co and PTA-Co-UV. The PTA solution (in methanol) is nearly transparent from 500 to 650 nm. Pure CoCl₂ solution (in water) showed a typical pink color with a maximum absorbance at 512 nm due to

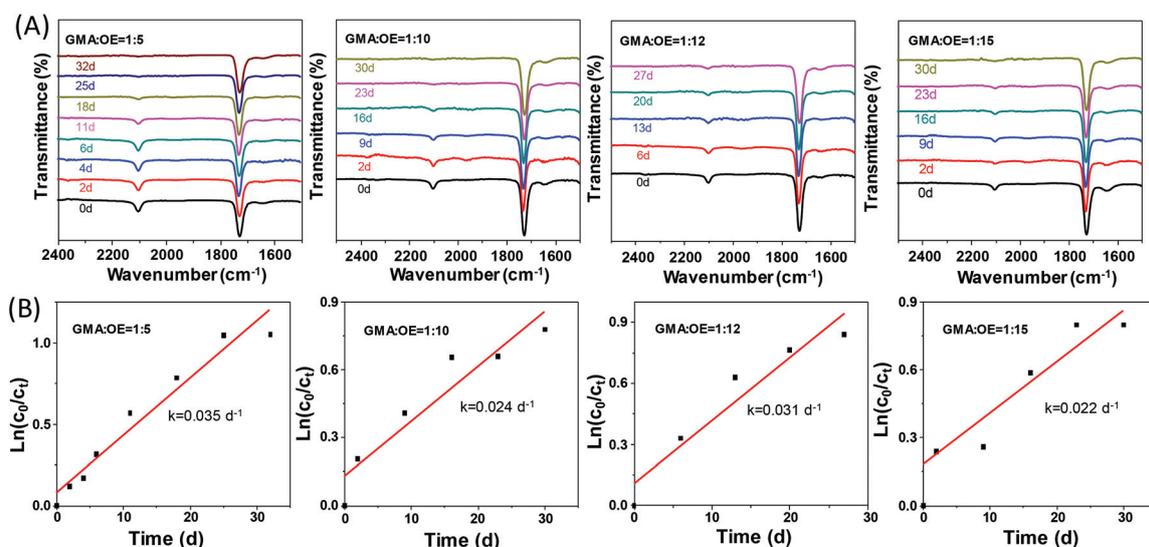


Fig. 2 The tracking by FTIR (A) of the “3 + 2” cycloaddition of PGO-N₃ and norbornene. Wavenumber in the range of 2500–1500 cm⁻¹ is shown to elucidate the kinetic curve (B). The FTIR spectra are normalized by the peak at 1730 cm⁻¹, and the integral of the peak of azide at 2100 cm⁻¹ is used for the construction of kinetic curves.

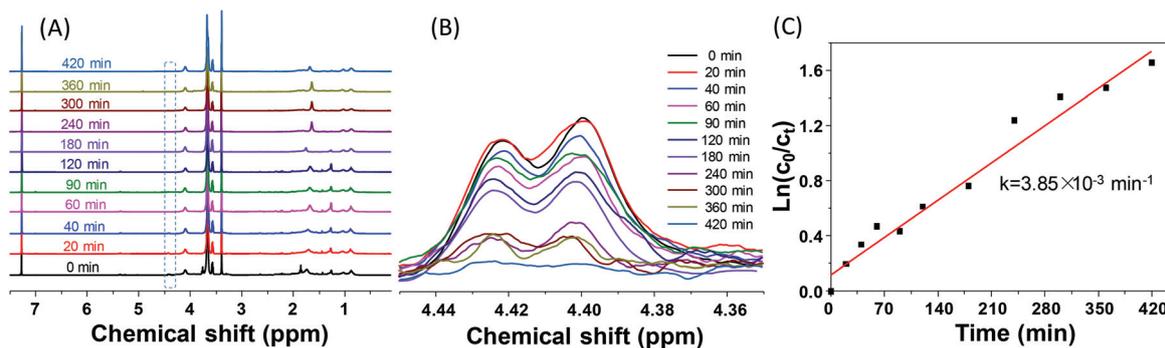


Fig. 3 The NMR spectra (A) of PTA evolve with irradiation time, and are highlighted (B) from 4.35 to 4.45 ppm. The kinetic curve (C) is constructed using the integration value of the peak in the mentioned range.

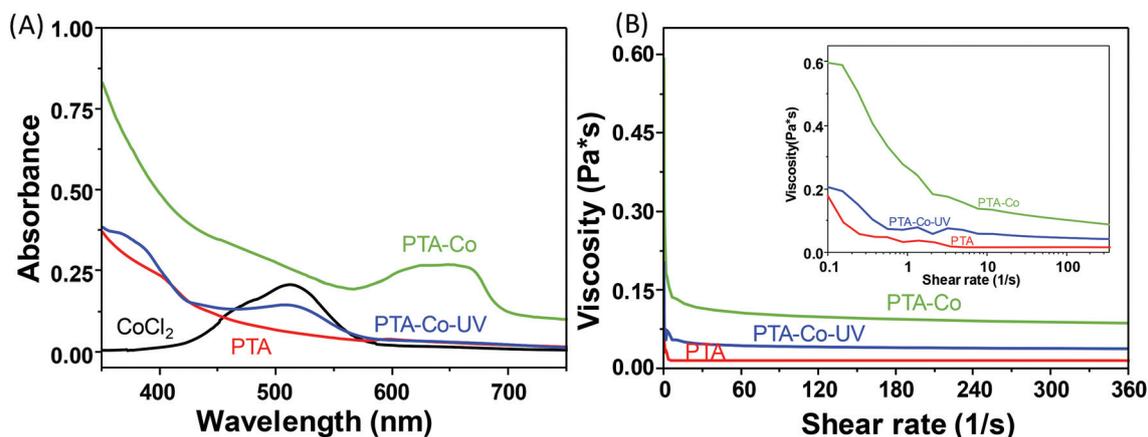


Fig. 4 The comparison of UV-vis spectra (A) and rheological profiles (B) of polymer samples.

the hydration. When mixed, the maximum absorbance shifted to 645 nm, implying the occurrence of Co–N coordination and an enhanced metal–ligand charge transfer.⁵⁹ After UV irradiation for 7 h, the sample (PTA-Co-UV) showed a much decreased absorption in the same range (the blue curve in Fig. 4A) compared to that of PTA-Co, while the absorbance of hydrated Co^{2+} species at 512 nm reappeared.

The solution of PTA-Co was typically shear-thinning as for many polymer solutions. Fig. 4(B) shows the typical viscosity plotted vs. the shear rate. As control, the pure PTA shows very low viscosity. As soon as it was mixed with CoCl_2 , the viscosity increased nearly 3 times at a shear rate of 0.1 rad s^{-1} as a result of the physical cross-linking of polymer chains *via* cobalt–N coordination. After irradiation, PTA-Co-UV displayed a decreased viscosity, which was close to that of the pure PTA solution. The shift of the maximum absorption peak and viscosity increase in the preparation of PTA-Co suggested that the Co–N coordination was present in PTA-Co and the light irradiation disrupted the Co–N coordination due to the elimination of dinitrogen.

3.4 Light-induced morphology change of micelles

The PTA contains both bulky hydrophobic norbornene pendant groups and hydrophilic polyethylene glycol (PEG). This is a typical amphiphilic random copolymer. Its CMC was determined to be $7.68 \times 10^{-3} \text{ mg mL}^{-1}$ by the fluorescence method using Nile Red as the probe according to the literature (Fig. 5).^{43,44}

The morphological change of PTA micelles upon coordination with Co and after denitrogenation was studied using DLS and TEM. The micellar dispersion of 1 mg mL^{-1} for PTA in water and PTA-Co was prepared by the evaporation method detailed in the Experimental section. The dispersions were diluted (to 0.04 mg mL^{-1}) before the experiment, and the results are shown in Fig. 6. When shone with a laser pointer at 633 nm, a clear light path can be identified for all the samples, indicating a stable micellar dispersion. PTA showed a diameter of $11.0 \pm 2.2 \text{ nm}$. After addition of Co^{2+} ions, it increased to $21.6 \pm 3.8 \text{ nm}$. The bigger aggregates can be observed in the TEM image. After exposure to UV for 7 h, the aggregate diameter decreased to $12.7 \pm 3.3 \text{ nm}$ and at the same

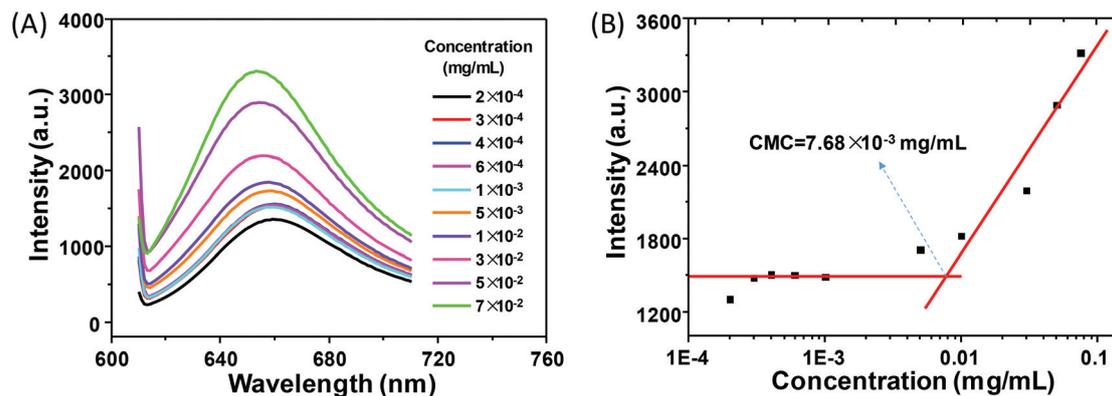


Fig. 5 Determination of the CMC of PTA in water through fluorescence spectroscopy using NR as a probe.

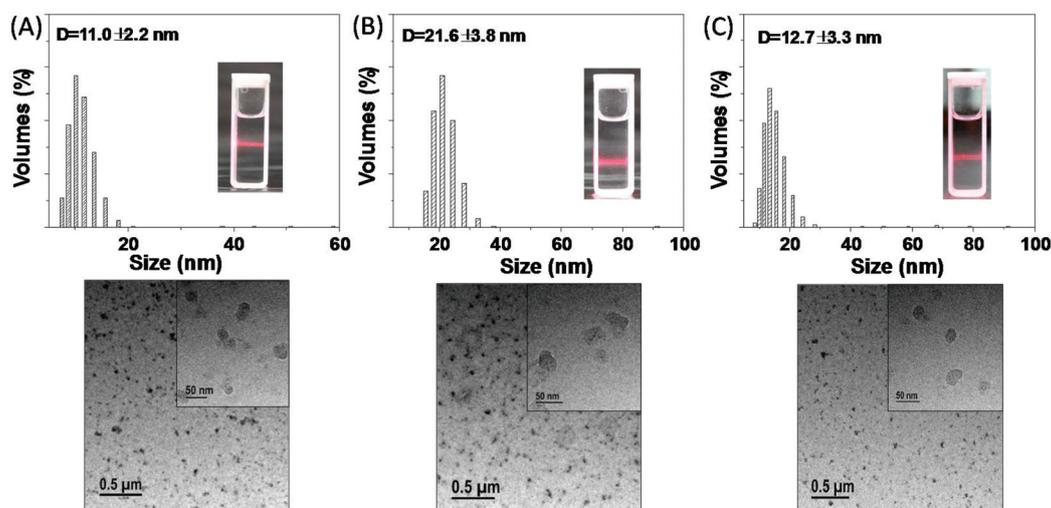


Fig. 6 DLS diagrams and TEM images of PTA, PTA-Co and PTA-Co-UV. The inset picture shows the red laser beam (633 nm) crossing the dispersion.

time, the TEM image showed a narrow dispersion. The increase in the diameter for PTA-Co micelles may be due to the addition of Co^{2+} ions into the micellar cores, therefore more solvation by water. After exposure to UV light, PTA-Co-UV showed an obvious decrease of micelle sizes, likely due to the removal of Co^{2+} ions.

3.5 Determination of the binding constant

The binding constant of PTA and Co^{2+} ions was measured according to a titration method as reported in previous references.^{60,61} Briefly, the copolymer was dissolved in methanol and CoCl_2 solution in methanol was added to the PTA solution. The absorption of the mixed solution at 645 nm was measured until absorption saturation was reached. The binding constant of the cobalt ion to the polymer was calculated based on the fractional saturation θ that can be calculated from absorbance change ΔA , ΔA_{max} is the maximum

change in absorbance (eqn (2)) and the results are shown in Fig. 6.

$$\theta = \frac{\Delta A}{\Delta A_{\text{max}}} \quad (2)$$

An “S”-shaped curve of θ vs. $[\text{Co}^{2+}]$ can be found, and the binding constant (K) can be found as the reciprocal of the slope (k) of the curve of $1/\theta$ vs. $1/[\text{Co}^{2+}]$ in Fig. 7(B): $K = 99.3 \text{ M}^{-1}$ ($\log K = 2.00$).

3.6 Kinetic study of the release rate of PTA-Co

To investigate the release kinetics of PTA-Co when exposed to UV light, a previously reported controlled release method was used.^{45–47} A dialysis bag was used to isolate the free Co^{2+} in beaker water that is tracked using UV-vis every 10 min at 512 nm for free Co^{2+} ions. The results are shown in Fig. 8(A). The recorded release profile with time is given in Fig. 8(B). The

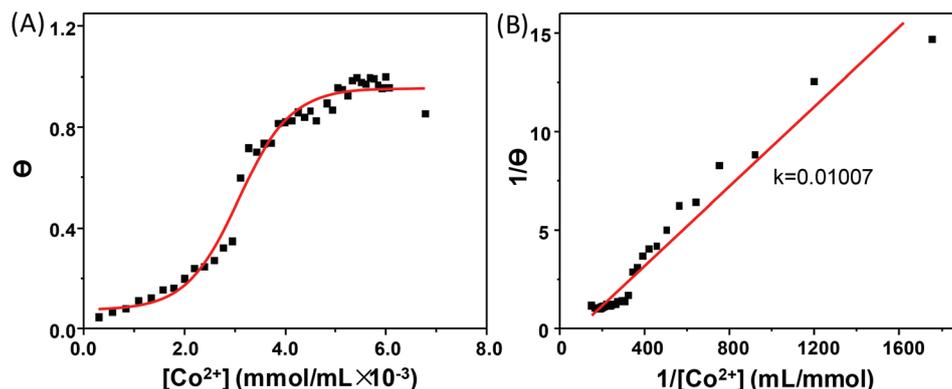


Fig. 7 Determination of the binding constant between Co^{2+} and PTA. The slope of the curve $1/\theta$ vs. $1/[\text{Co}^{2+}]$ was found to be 0.01007, so its reciprocal gives the binding constant $K = 99.3 \text{ M}^{-1}$. The loading capacity was calculated to be 15.3 mol%.

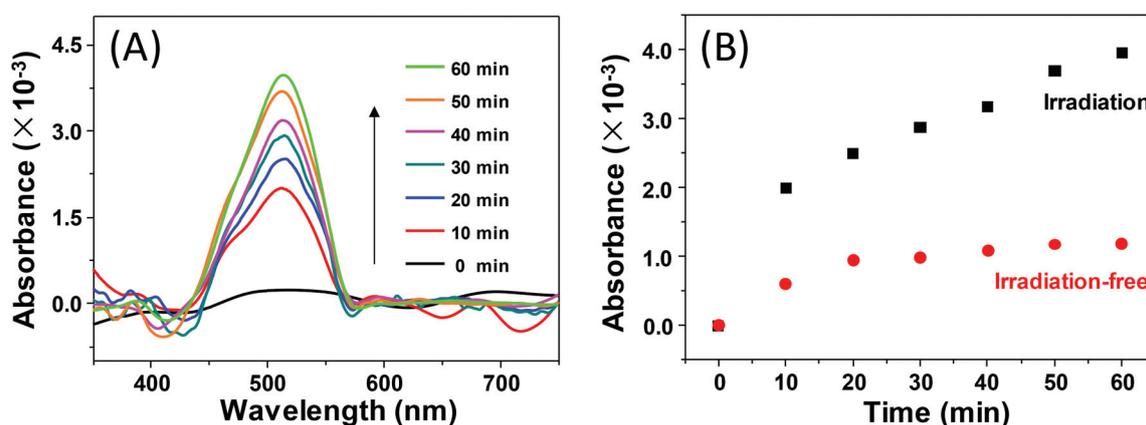


Fig. 8 The UV-vis spectra (A) of PTA-Co were recorded with irradiation time. The maximum absorption at 512 nm is displayed (B) with time as well.

release of Co^{2+} ions upon light exposure from PTA-Co increased linearly with irradiation time after 10 min, in contrast to the control sample without irradiation that almost achieved a plateau after 20 min. This suggests that the release of Co^{2+} ions from the disruption of triazoline-containing amphiphilic polymers is highly controllable.

4. Conclusions

To summarize, we demonstrated a new mechanism for photo-controlled release of metal ions using triazoline-containing amphiphilic polymers. Taking advantage of the efficient reaction of 1,3-dipolar cycloaddition between azide and norbornene, novel triazoline-containing amphiphilic PTA copolymers were successfully synthesized. The syntheses including the conversion kinetics were studied in detail using FTIR. The “3 + 2” cycloaddition of PGO- N_3 and norbornene is slow and approximately first order, with a rate constant k in the range of 0.02–0.035 d^{-1} . The light-induced denitrogenation kinetics of triazoline in PTA analyzed by ^1H NMR spectroscopy was found to be first order as well with a rate constant of $3.85 \times 10^{-3} \text{ min}^{-1}$

under irradiation at 254 nm. The amphiphilic copolymer PTA formed micelles in the aqueous dispersion and the CMC was found to be $7.68 \times 10^{-3} \text{ mg mL}^{-1}$. We showed that the triazoline-containing PTA can coordinate with Co^{2+} ions (PTA-Co) as confirmed by UV-vis spectroscopy and the increase in solution viscosity. Both the micellar dispersion of PTA and PTA-Co also displayed a size evolution from DLS and TEM. Since the triazoline is light sensitive, the micelles of PTA-Co can release Co^{2+} ions upon irradiation with UV light. Our results illustrate a novel way for the design of light-induced controlled release of metal ions, which could be promising in the regulation of trace essential ions in human bodies.

Conflicts of interest

There are no conflicts of interest to declare.

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