SUPPLEMENTARY INFORMATION

Photodegradable and Size-Tunable Single-Chain Nanoparticles from a Single Main-Chain Coumarin-Containing Polymer Precursor

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1. Materials

All chemicals were purchased from Aldrich and used as received unless otherwise noted. Pyridinium-4-toluenesulfonate (DPTS) was synthesized using a literature method.[S1]

2. Instruments and Measurements

^{1}H NMR spectra were recorded on a Bruker AC400 (400MHz) spectrometer with *DMSO-d6* and $CDCl_3$ as the solvent. Size exclusion chromatograph (SEC) measurements were performed on a Waters system equipped with a photodiode array detector (PDA 996) and a refractive index detector (RI 410). THF was used as the eluent at an elution rate of 1 mL/min, while polystyrene standards were used for calibration. Dynamic light scattering (DLS) measurements were performed on a Malvern Zetasizer Nano ZS ZEN3600 with a helium−neon laser (wavelength, λ= 633 nm). All measurements were carried out at a scattering angle of 173°. The polymer was crosslinked by UV irradiation by OmniCure@ Series 1000 UV lamp (approximately 900mW/cm^2) with 320-480nm filter. The SCNPs were degraded under short wavelength UV light from a UVS-28 EL Series UV lamp (254nm, approximately 0.1W/cm^2). The photodimerization degree of coumarin was monitored by recording UV-vis spectra on a Varian 50 Bio UV-vis spectrophotometer. The morphology of nanoparticles was examined using a Hitachi H-7500 transmission electron microscope (TEM) operating at 80 kV. Samples were prepared by casting 3–5 mL solution on a carbon-coated copper grid, followed by drying at room temperature. Atomic force microscopy (AFM) images were recorded on a Dimension Icon AFM instrument equipped with a NanoScope V controller (Veeco/Digital Instruments, Santa Barbara, CA). AFM topographical images were done under ScanAsyst mode at room temperature using a silicon nitride (force constant 0.4 N/m) cantilever tips.

3. Coumarin Monomer and Polymer Synthesis

3.1 Synthesis of the coumarin monomer

Synthesis of 7-hydroxy-4-(chloromethyl) coumarin (**a** in Scheme S1):

To a solution under stirring of resorcinol (10 g 91 mmol, 1 eq) and 4-chloromethyl acetoacetate (17 g, 103 mmol, 1.14 eq) in toluene (150 mL) was added p-toluene sulfonic acid (3.6 g, 19 mmol, 0.21 eq). The solution was connected to a Dean-Stark apparatus and heated to reflux at 110 ^{o}C for 45 minutes. The reaction mixture was concentrated and purified by column chromatography (EtOAC:Hexane 1:9) to yield a white solid **(a),** (13.4g, 70% yield). ^{1}H NMR (300 MHz, *DMSO-d6*): 4.92 (s, 2H), 6.40 (s, 1H), 6.80 (s, 1H), 6.93 (d, 1H), 7.71-7.74 (d, 1H).

Synthesis of 7-hydroxy-4-4(hydroxymethyl) coumarin (**b**):

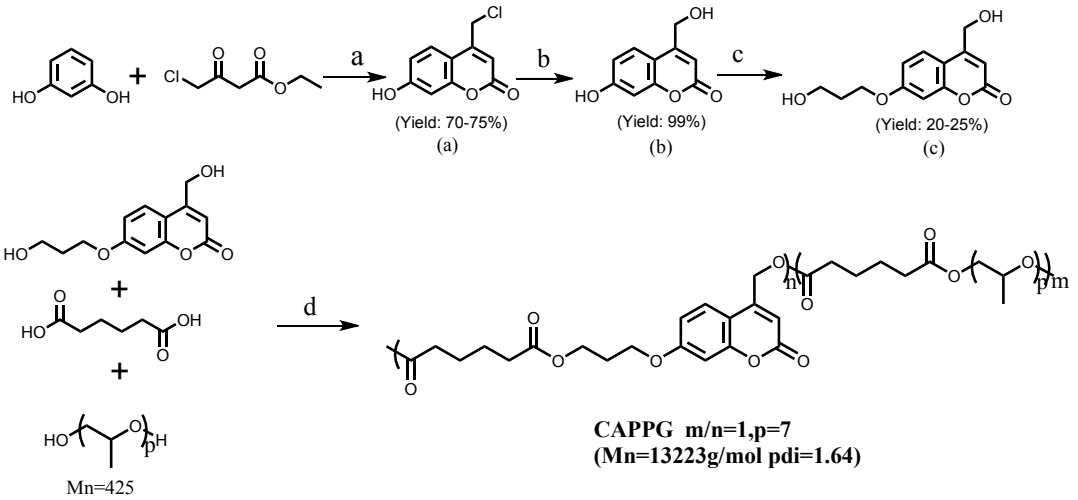
To water (350 mL) was added **a** (2.95g, 14 mmol) under stirring. The reaction mixture was refluxed for 3 days, filtered while hot and cooled to room temperature over 12 hrs to yield off-white needles **(b)**. The product was filtered and connected to vacuum overnight (2.67g, 99%). The product was used further without purification. ^{1}H NMR (300 MHz, *DMSO-d6*): 4.87 (s, 2H), 6.35 (s, 1H), 6.76 (s, 1H), 6.84 (d, 1H), 7.53-7.56 (d, 1H).

Synthesis of 7-(hydroxypropoxy)-4-(hydroxymethyl) coumarin (**c**):

To a solution of anhydrous acetone (15 mL), **b** (1.0 g, 5.2 mmol, 1 eq), potassium carbonate (2 g, 14.5 mmol, 2.8 eq), 3-bromo 1-propanol (1.5 g, 10.8 mmol, 2.1 eq) was added 18-crown-6 (0.7 g, 2.65 mmol, 0.5 eq) in a N_2 condition. The mixture was stirred for 30 minutes at room temperature and then was refluxed at 53°C for 18h and filtered. The solvent was removed under reduced pressure to yield a light yellow solid. Purification by column chromatography (EtOAC:Hexane 4:1) yielded a white solid**,** (0.29 g, 22%) **(c)**. ^{1}H NMR (300 MHz, *DMSO-d6*): 1.86-1.92 (d, 2H), 3.53-3.58 (m, 2H), 4.12-4.16 (t, 2H), 4.57-4.61 (t, -OH, 1H), 4.72-4.74 (d, 2H), 5.60-5.63 (t, -OH, 1H), 6.29 (s, 1H), 6.92-6.95 (d, 1H), 6.99 (s, 1H), 7.59-7.62 (d, 1H)

3.2 Synthesis of the coumarin-containing polymer precursor

A two neck round bottom flask was charged with **c** (62.5mg, 0.25mmol, 1 eq), poly(propylene glycol) (106.5mg, 0.25mmol, 1eq), adipic acid (73mg, 0.5mmol, 2eq) and DPTS (58.5mg, 0.8eq). The flask was vacuum backfilled three times with N_2. Dichloromethane (2.5 mL) was added while cooling the flask at 0 °C. After 15 minutes, N,N-diisopropylcarbodiimide (DIC) (470µl, 3 eq) was added and the reaction was allowed to take place at room temperature for 36-48 hrs. The polymer was precipitated three times in mixture of alcohols (MeOH:EtOH:PrOH 1:1:1). The polymer was collected, centrifuged, dried under vacuum to yield a white solid (208mg, 87% M_n=13220)**.**



(a) p-Toluenesulfonic acid (PTSA), Toluene, Reflux, 45min
(b)H_2O, Reflux, 3 days
(c) K_2CO_3, 18-Crown-6, Acetone, 3-bromopropanol-1, 55°C, 18h
(d) Diisopropyl carbodiimide (DIC), Dimethylaminopyridinium-p-toluenesulfonate (DPTS), CH_2Cl_2, R.T., 48-72hrs

Scheme S1 Synthesis procedure for the CAPPG polymer precursor.

4. Preparation of SCNPs

To fabricate the SCNPs of CAPPG, 10mg of the copolymer was dissolved in 50mL of $CHCl_3$ or THF and kept under stirring overnight. After being filtered with a 200nm pore size Teflon filter, the solution was then exposed to >320 nm UV light (900mW/cm^2, distance from the solution: 5cm) for various times. The solution could be concentrated under vacuum distillation and polymer nanoparticles precipitated in hexane were then dried under vacuum overnight. Nanoparticles can be re-dispersed in THF or $CHCl_3$ to form a homogenous solution with a desired concentration.

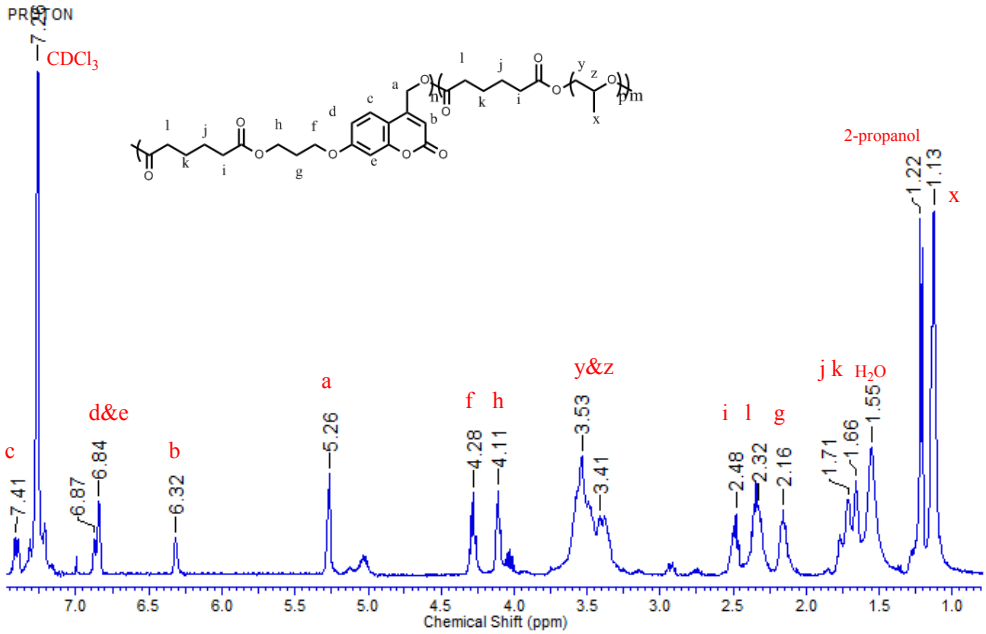


Fig. S1 ^{1}H NMR spectrum of the CAPPG polymer precursor (in $CDCl_3$).

5. SEC Measurements of CAPPG Polymer Precursor, SCNP and SCNP after Photodegradation

CAPPG polymer (5mg) was dissolved in THF (10 mL) and kept under stirring overnight. After being filtered with a 200nm pore size Teflon filter, the solution was then exposed to > 320 nm UV light (900mW/cm^2, distance from the solution: 5cm) for a chosen time. In the case of photodegraded SCNPs, a THF solution of the SCNP prepared upon >320nm UV irradiation for 120 min, was first prepared (5mg SCNP in 10 mL THF). The solution was then sonicated for 10 min before being exposed to the 254 nm UV light (100mW/cm^{-2}, distance from the solution: 5cm) for 3h. In all cases, the SCNP solution was directly injected into SEC for the measurement.

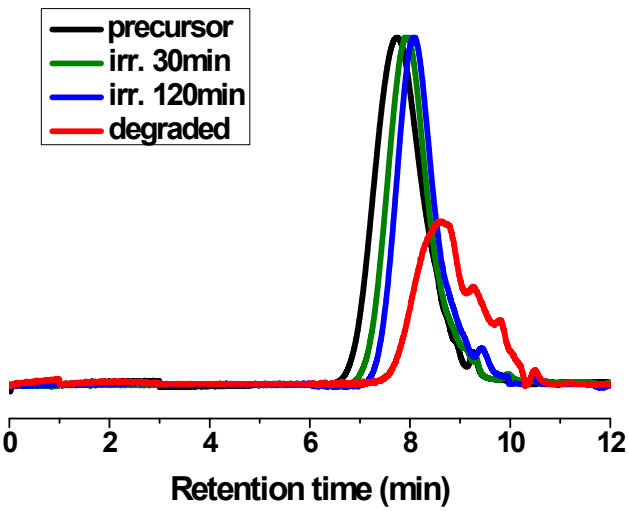
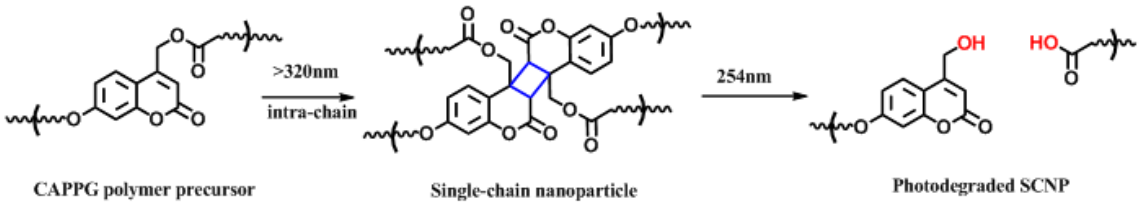


Fig.S2 SEC traces over the full retention time scale for the CAPPG precursor, its SCNPs prepared upon 30 and 120 min >320 nm UV irradiation, respectively, and the photodegraded SCNP obtained after 254 nm UV irradiation.

6. Photodegradation of SCNPs



Scheme S2: Photo-crosslinking and photo-degradation of SCNP of the main-chain coumarin-containing polymer. Under the 254 nm UV irradiation, cleavage of the coumarin-4-yl methyl ester, resulting in chain scission, can occur with coumarin in the monomeric form (as drawn in the scheme) or in the dimer form (not shown).

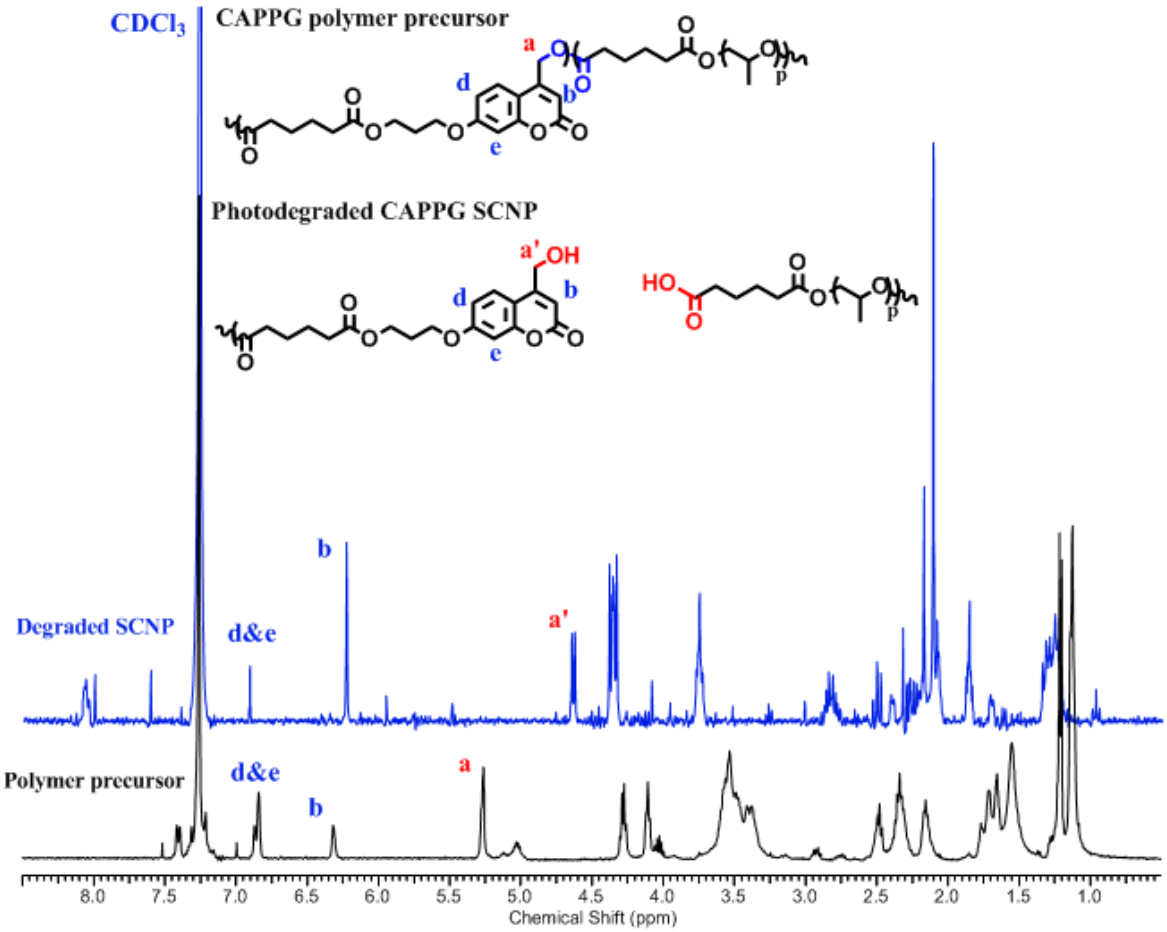


Fig. S3 ^{1}H-NMR spectra of the CAPPG precursor and the SCNP after photodegradation. The spectral changes upon 254 nm UV irradiation provide evidence for the photoinduced scission of chain backbone leading to the photodegradation of SCNP: peak *a* in the polymer precursor being replaced by peak *a*′ for the SCNP after photodegradation. We were unable to obtain a good ^{1}H NMR spectrum of the SCNPs before photodegradation due to the solid-like state of the nanoparticles as well as the dilute concentration.

7. AFM Images of SCNPs

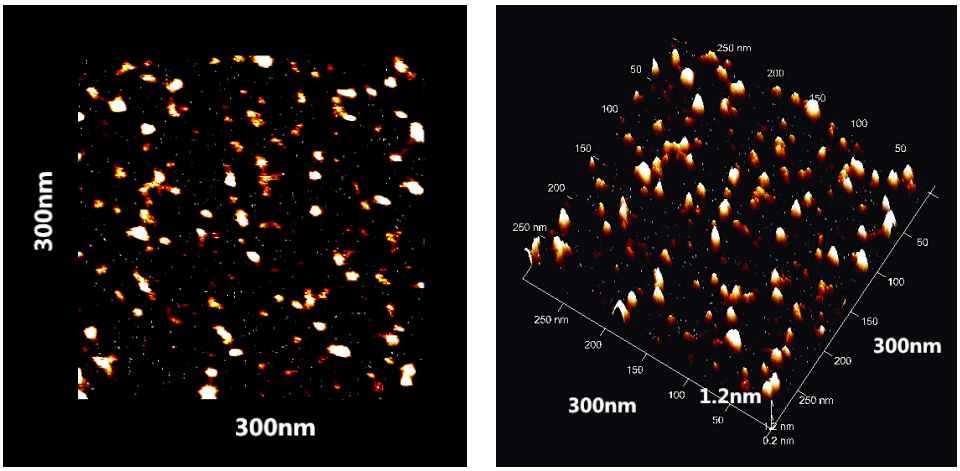


Fig.S4 AFM images of SCNPs (after 120min UV irradiation) dispersed in water.

8. DLS Measurements of SCNPs

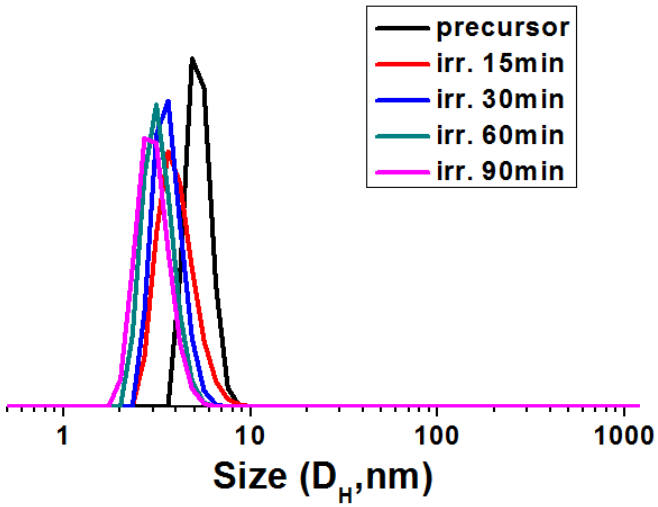


Fig. S5 Number-weighted size distribution of the precursor and SCNPs with different >320 nm UV irradiation times.

References

S1: J. S. Moore, S. I. Stupp, *Macromolecules* 1990, **23**, 65