Electronic Supplementary Material (ESI) for Chemical Communications.

Supporting Information

Chemical fuel driven transient polymeric micelles nanoreactors towards reversible trapping and reaction acceleration

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Experimental Procedures

Materials

2,2'-Azobisisobutyronitrile (AIBN) was recrystallized from ethanol. Acrylic acid (AA) is purified by vacuum distillation. 1,4-Dioxane and Dimethyl sulfoxide were percolated over basic alumina prior to use. Chain transfer agent (CTA) was prepared according to reference S1[1]. All other chemicals were commercially available and used without further purification.

Instruments.

Nuclear magnetic resonance (NMR) spectroscopy. ^{1}H NMR spectra were recorded on a JNM-ECZ400S/L1 400MHz NMR spectrometer. Deuterated dimethyl sulfoxide (DMSO-d^6), deuterated chloroform ($CDCl_3$) and deuterium oxide (D_2O) were used as solvents.

Fourier Transform Infrared Spectrometer (FTIR Spectrometer). FTIR Spectra were measured on Thermo Fisher Is50 FTIR Spectrometer.

UV-vis spectroscopy. UV absorbance spectra was performed by a SHIMADZU UV1900 UV spectrophotometer.

Fluorescence spectroscopy. Fluorescence spectra were recorded on a HITACHI F-4700 fluorescence spectrophotometer. Excitation wavelength: 355 nm, Slit width (ex/em): 5/10 nm.

Dynamic light scattering (DLS). DLS was carried out by a Malvern Zetasizer (Nano ZS90).

Transmission Electron Microscope (TEM). TEM images were recorded on JEOL JEM F200 at 200 kV. Firstly, the grid were droped 10 μL of sample for 1 min without any staining. The sample were dried under high vacuum for 30 min before TEM test.

Gel permeation chromatography (GPC). Molecular weights and polydispersity indexes were estimated by a Waters gel permeation chromatography (GPC) system, which was performed at 40 ^{o}C in DMF at a flow rate of 1.0 mL·min $^{-1}$ (Isocratic HPLC pump Waters 1515 and detecter Waters 2414).

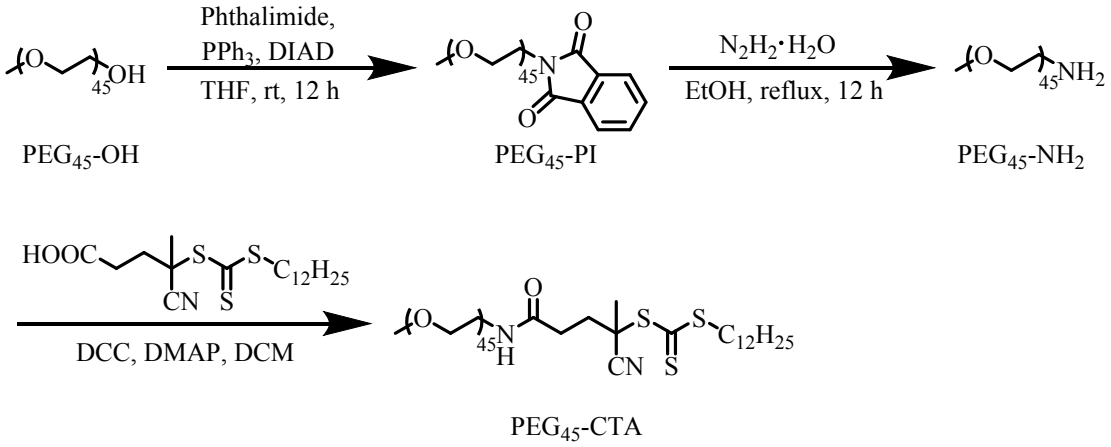
All tests were performed at 25 ^{o}C except GPC. In order to investigated the lifetime of transient micelles at different pH, we used buffers of pH 6.0 to 6.5 with MES buffer (100 mM) and from pH 7.0 to 7.5 with MOPS buffer (100 mM).

Procedures.

Synthesis of macromolecular chain transfer agent (PEG_{45}-CTA).

PEG_{45}-CTA was prepared according to Scheme S1. Detailed synthetic procedures for preparation of PEG_{45}-CTA are following.

Scheme 1



Synthesis of PEG_{45}-PI.

In a 500 mL round-bottom flask, PEG_{45}-OH (10 g, 5 mmol), Phthalimide (7.35g, 50 mmol) and triphenylphosphane (13.2g, 50 mmol) were dissolved in 100 mL of THF. After stirring for 15 min at ambient temperature, DIAD (10 g, 50 mmol) was added dropwise to above mixture within 30 min. The mixture was stirred at rt for 12 h and ethanol (200 mL) was added. After removing all the solvent by evaporation, pure PEG_{45}-PI was obtained as a yellow solid by repeated (three times) precipitated of the crude product into cold diethyl ether and subsequent dissolution into THF, and dried in a vacuum oven at 40 ^{o}C for 48 h (9.64 g, 89.2% yield). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.85 (dd, J = 5.4, 3.1 Hz, 2H), 7.72 (dd, J = 5.5, 3.0 Hz, 2H), 3.90 (t, J = 5.9 Hz, 2H), 3.74 (t, J = 5.8 Hz, 2H), 3.65 (d, J = 5.6 Hz, 176H), 3.38 (s, 3H).

Synthesis of PEG_{45}-NH_2.

In a 500 mL round-bottom flask, PEG_{45}-PI (8.5 g, 4 mmol) was dissolved in 200 mL of ethanol, then hydrazine monohydrate (80%, 24 mmol) was added, and the solution was refluxed for 12 h under stirring. After removing white precipitate by filtration, the solution was basified with NaOH aqueous (1M) and the solution was evaporated. The crude product was purified by three cycles of precipitation into large amount of cold diethyl ether followed by dissolution in THF. The pure PEG_{45}-NH_2 was obtained as a white solid by dried in

a vacuum oven at 40 °C for 48 h (7.6 g, 95% yield). ^{1}H-NMR (400 MHz, DMSO): δ 3.52 (s, 178H), 3.25 (s, 2H), 2.69 (t, J = 5.6 Hz, 3H).

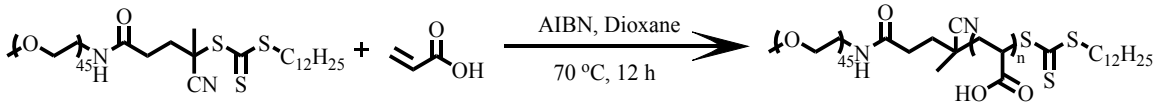
Synthesis of PEG_{45}-CTA.

In a 500 mL round-bottom flask, PEG_{45}-NH_2 (6 g, 3 mmol), CTA (3.6 g, 9 mmol) and DMAP (0.12 g, 1 mmol) were dissolved in 200 mL of anhydrous dichloromethane. After stirring for 15 min, DCC (6.18 g, 30 mmol) dissolved in 20 mL anhydrous CH_2Cl_2 was added dropwise into the above solution within 30 min at 0 °C. And then the mixture was stirred at room temperature for 72 h. The generated white precipitate was removed by filtration, and the solvent was evaporated. The impurities were taken away by repeated (at least three times) precipitated of the crude product into cold diethyl ether and subsequent dissolution into THF. The pure PEG_{45}-CTA was obtained as a yellow solid by using vacuum drying at rt for 48 h (8.5 g, 85% yield). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 3.69 – 3.62 (m, 180H), 3.51 – 3.42 (m, 2H), 3.38 (s, 3H), 3.37 – 3.29 (m, 2H), 2.56 – 2.46 (m, 2H), 2.42 – 2.23 (m, 3H), 1.89 (d, J = 7.4 Hz, 2H), 1.73 – 1.61 (m, 2H), 1.33 – 1.21 (m, 18H), 0.88 (t, J = 6.8 Hz, 3H).

RAFT Polymerization of PEG_{45} -b-PAA.

PEG_{45}-b-PAA were synthesis by reversible addition‐fragmentation chain‐transfer (RAFT) polymerization. The following is an example of detailed experiment procedures for preparing PEG_{45} -b-PAA_{78} are abstracted.

Scheme S2



Synthesis of PEG_{45}-b-PAA_{78}.

Acrylic acid (2 g, 27.8 mmol), PEG_{45}-CTA (0.667 g, 0.278 mmol), AIBN (4.6 mg, 0.0278 mmol) and dry 1,4-dioxane were loaded into a polymer pipe, and the reaction system removed air by blowing nitrogen for at least 30 min. Then, the mixture was stirred in a preheated oil bath at 75 °C for 24 h. After precipitation three times in cold ethyl acetate, the yellow solid (2.16 g, 81% yield) was dried at 40 °C for 48 h in vacuum. ^{1}H-NMR (400 MHz, DMSO-D): 12.2 (s, 1H, -COO**H**), 3.79 ppm (s, 180H, -(C**H**$_2$C**H**$_2$)$_{44}$-), 2.2 ppm (s, 1H, -C**H**- in the backbone) and 1.3-1.8 ppm (m, 2H, -C**H**$_2$- in the backbone). M_n = 8016 g/mol, based on ^{1}H-NMR.

PEG_{45}-b-PAA_{110} was synthesis by the similar polymer procedures. A yellow solid of PEG_{45}-b-PAA_{110} was obtained in 79% yield. ^{1}H-NMR (400 MHz, DMSO-D): 12.2 (s, 1H, -COO**H**), 3.79 ppm (s, 180H, -(C**H**$_2$C**H**$_2$)$_{45}$-), 2.2 ppm (s, 1H, -C**H**- in the backbone) and 1.3-1.8 ppm (m, 2H, -C**H**$_2$- in the backbone). M_n = 10320 g/mol, based on ^{1}H-NMR.

Results and Discussion

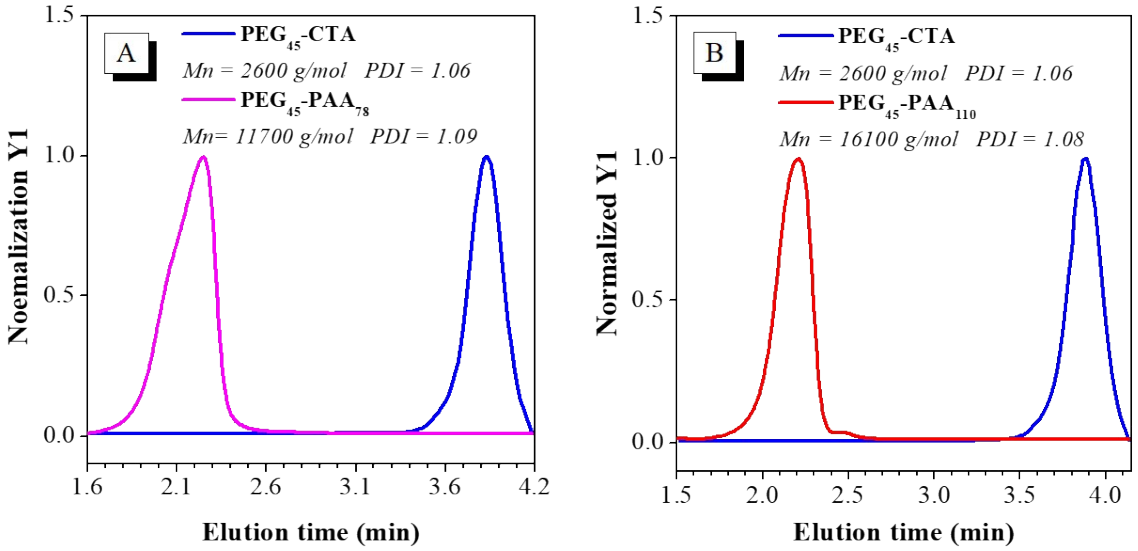


Figure S1. The GPC curves of PEG-CTA, PEG-b-PAA_{78} and PEG-b-PAA_{110} in DMF.

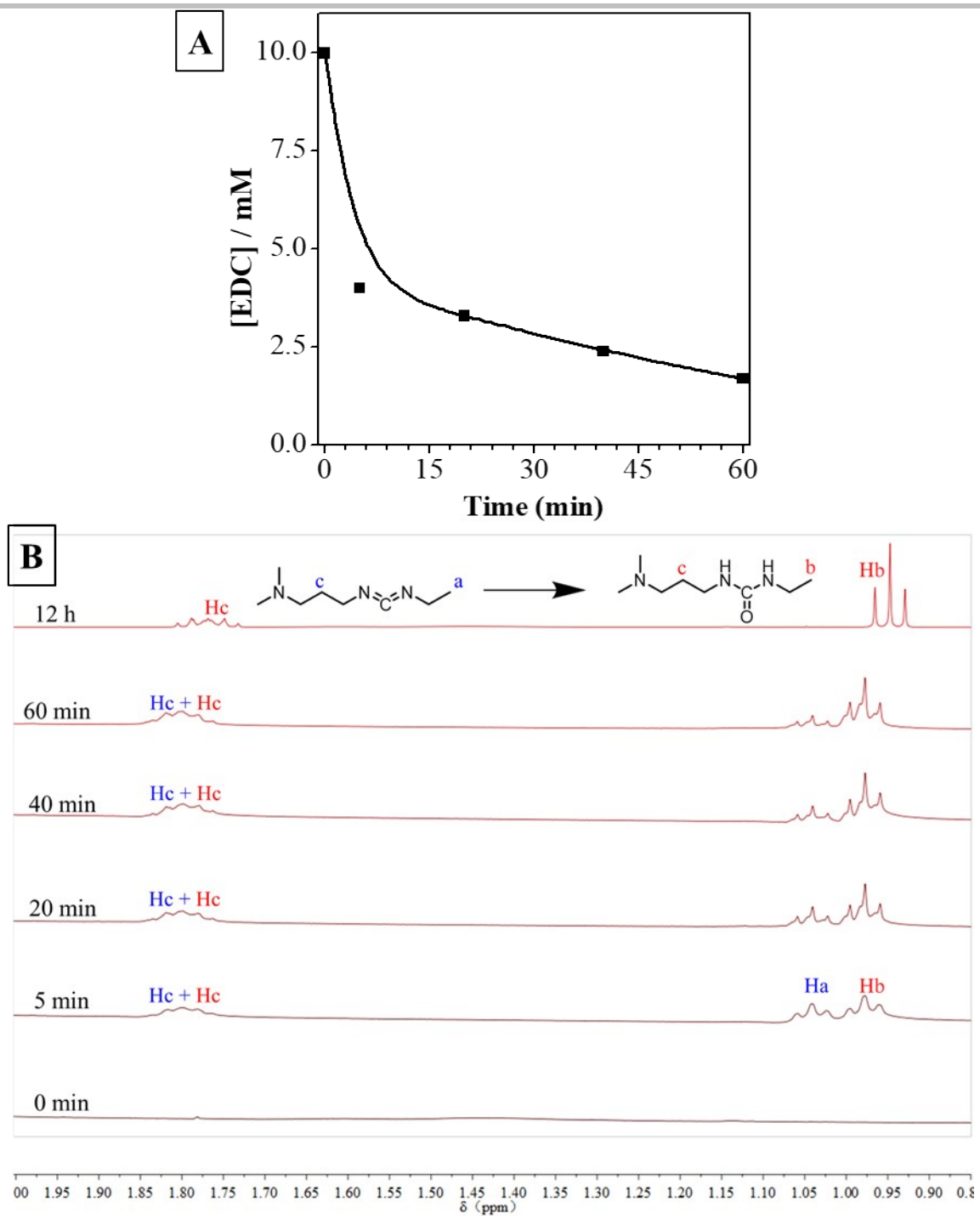


Figure S2. (A) EDC concentrations as a function of time based on ^{1}H NMR spectra. (B) Time-dependent NMR spectra of PEG_{45}-PAA_{78} (10 mM acid groups) with NHS (10 mM) and EDC (10 mM).

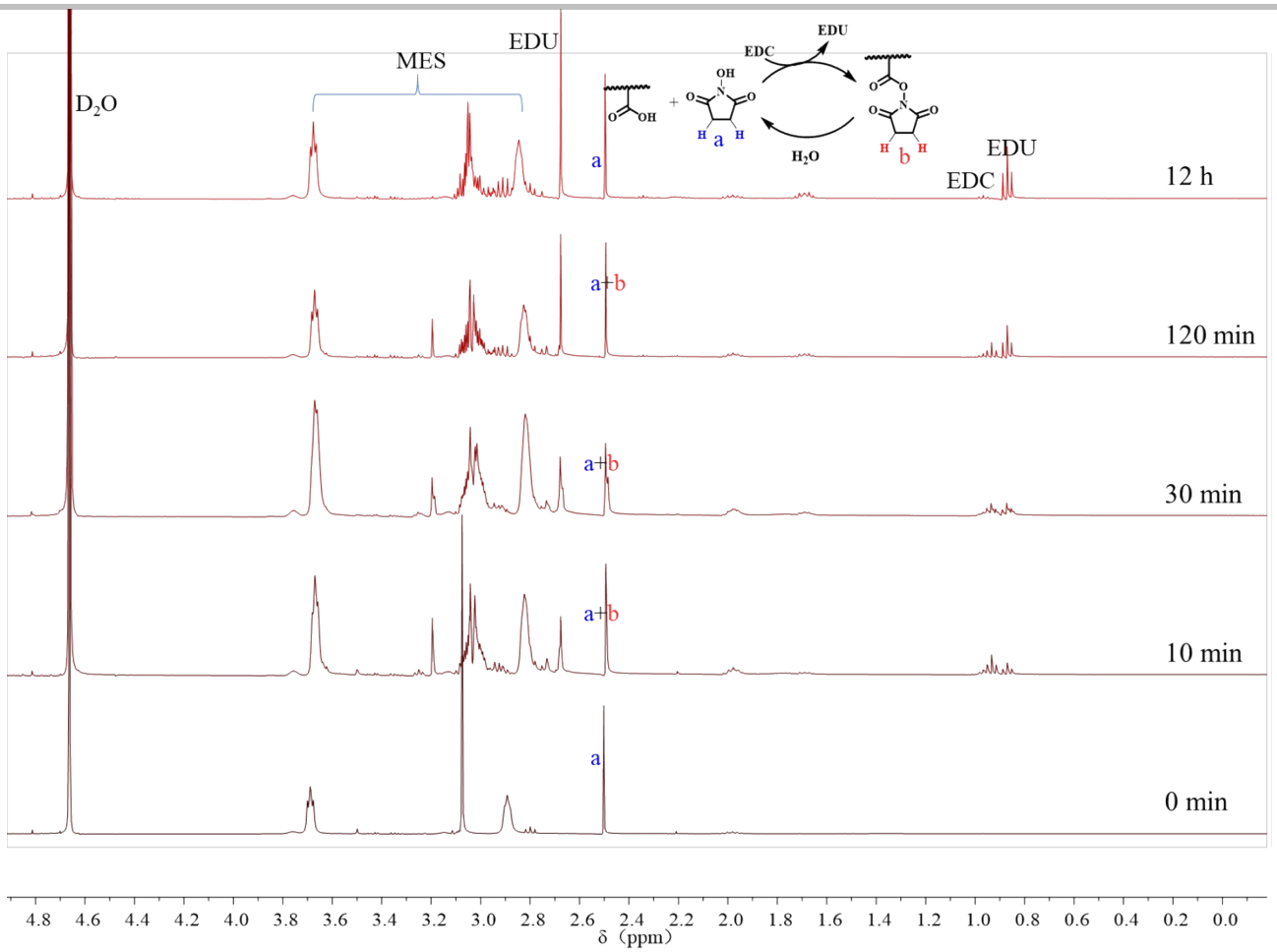


Figure S3. Time-dependent ^{1}H-NMR spectra of PEG_{45}-PAA_{78} (6 mM) and NHS (20 mM) after the addition of EDC (3eq). Experimental conditions: pH 6.5, 100 mM MES.

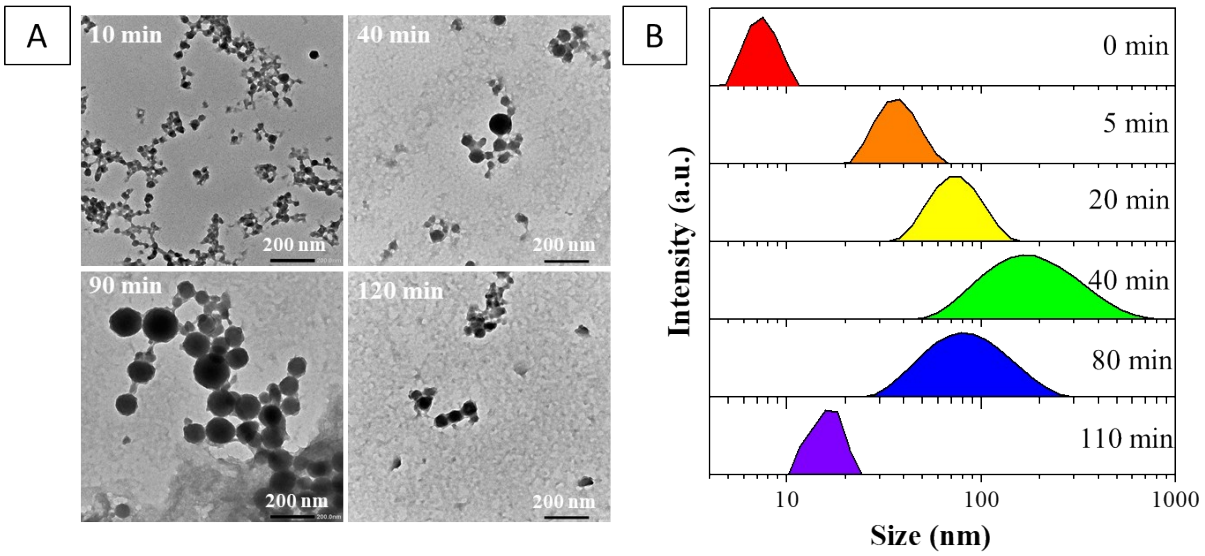


Figure S4. (A) Time-dependent TEM images of PEG_{45}-PAA_{78} and NHS in the presence of EDC. (B) Time-dependent DLs show the change of the diameter of transient micelles. Experimental conditions: NHS (20 mM), PEG_{45}-PAA_{78} (6 mM acid groups), EDC (18 mM) and pH6.5 (100 mM MES buffer).

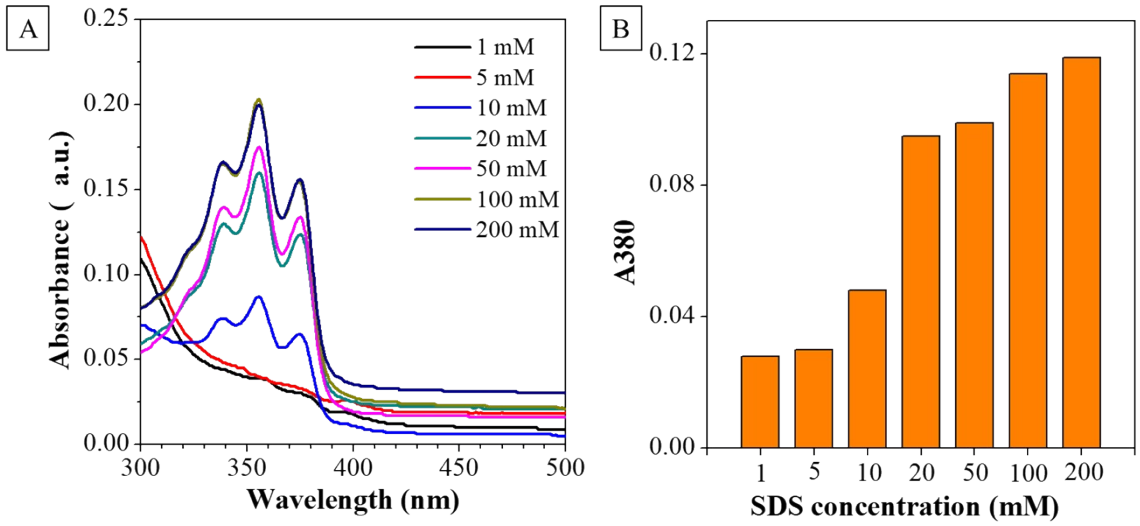


Figure S5. Solubilization of DPH by sodium dodecyl sulfate (SDS, CMC: 8 mM) micelles by UV-vis spectroscopy. a) UV-vis spectra of DPH (2.5uM) as the SDS concentration in aqueous solution. B) the absorbance intensity of DPH as the SDS concentration at 380 nm. The DPH was dissolved in THF to make a 1 mM solution. Experiment condition: pH 6.5, 100 mM MES.

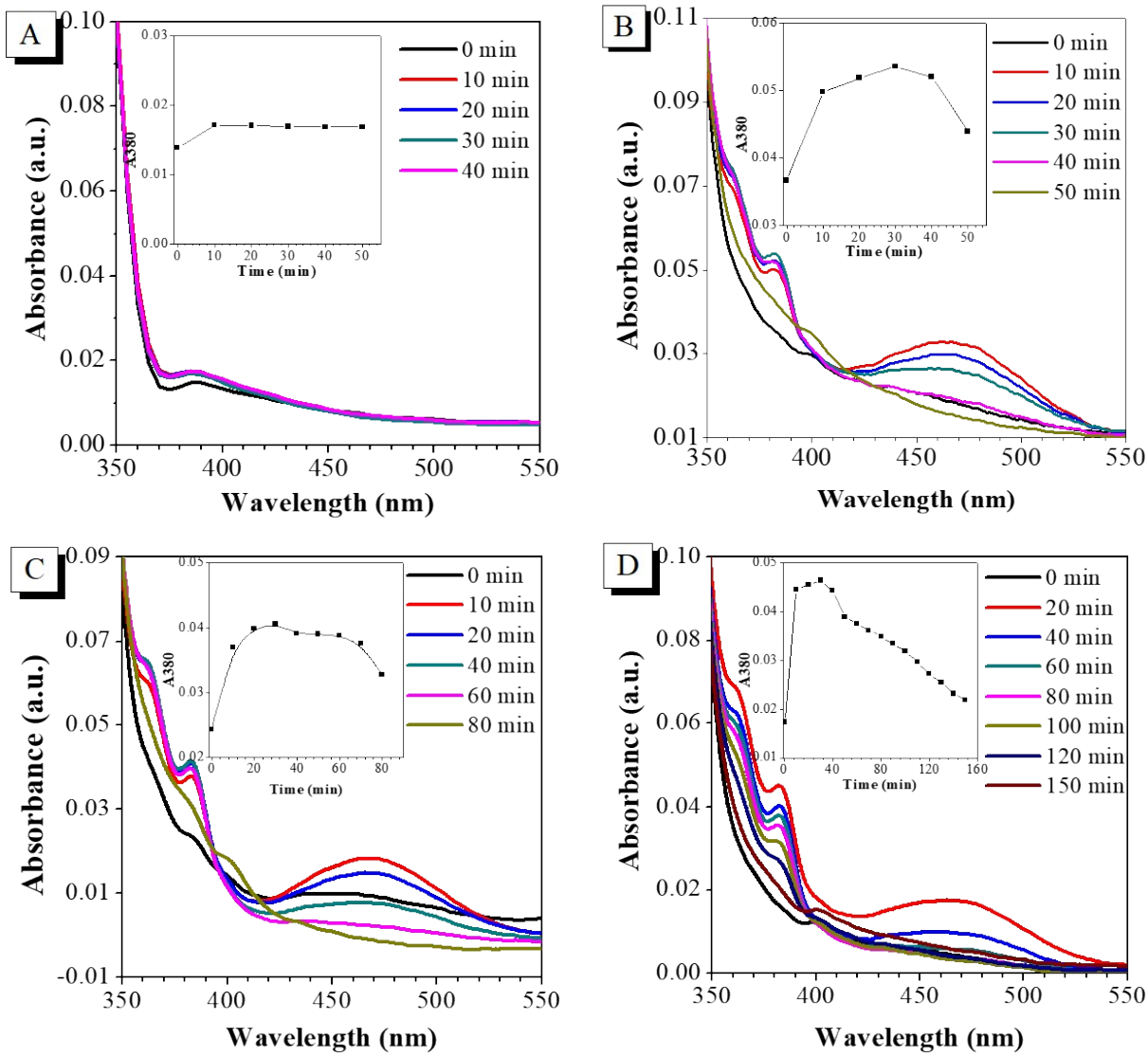


Figure S6. UV-vis spectra over time following addition of different concentrations of EDC to PEG_{45}-PAA_{78} (6 mM) and DPH (2.5 μM). (A) 1 eq EDC. (B) 6 eq EDC. (C) 10 eq EDC. Experimental conditions: 100 mM MES, pH 6.5.

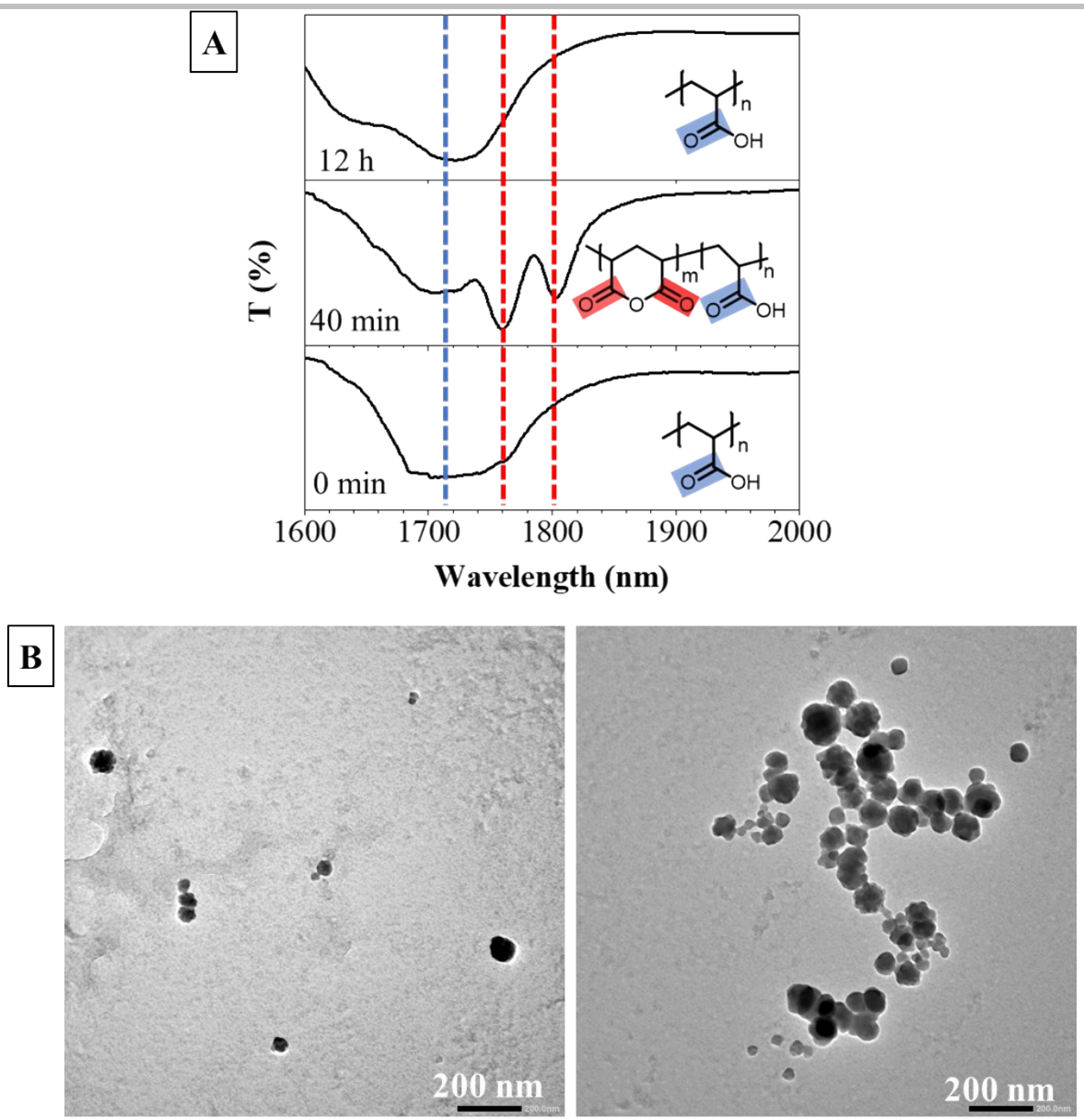


Figure S7. (A) FTIR spectra of the PEG45-PAA78 (6 Mm acid groups) before and after the addition of EDC (3eq). (B) TEM images of PEG45-PAA78 (6 mM acid groups) in the presence of EDC (3 eq) at 40 min. Experimental conditions: EDC (18 mM) and pH 6.5 (100 mM MES).

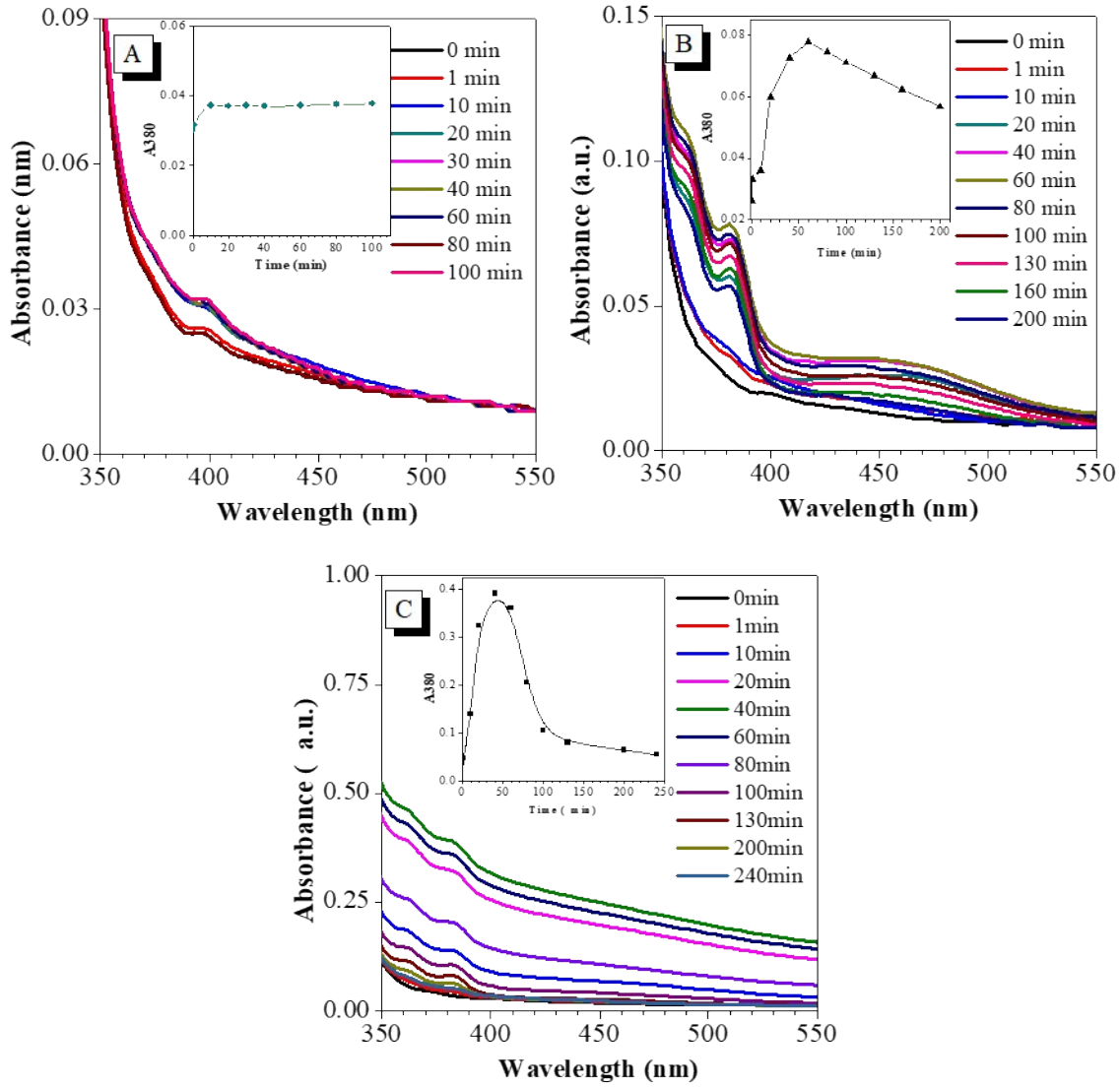


Figure S8. UV-vis spectra over time following addition of different concentrations of EDC to PEG_{45}-PAA_{78} (6 mM), NHS (20 mM) and DPH (2.5 μM). (A) 1 eq EDC. (B) 6 eq EDC. (C) 10 eq EDC. Experimental conditions: 100 mM MES, pH 6.5.

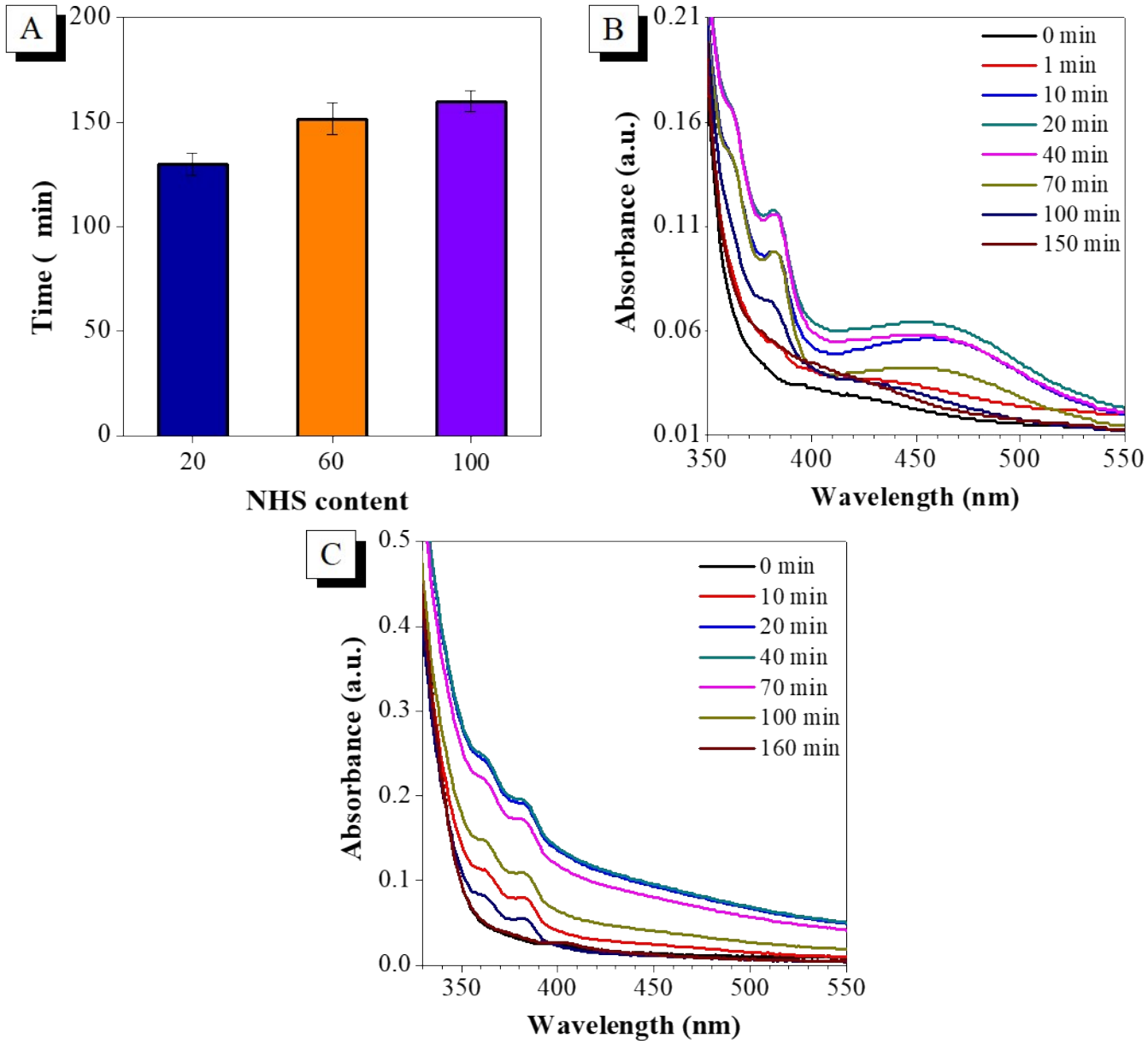


Figure S9. (A) Lifetime of transient micelles with varying concentration of NHS (C). UV-vis spectra over time following addition of NHS to mixture. (B) 60 mM NHS. (C) 100 mM NHS. Experimental conditions: PEG_{45}-PAA_{78} (6 Mm), EDC (20 mM), DPH (2.5 μM) and pH 6.5 (100 mM MES).

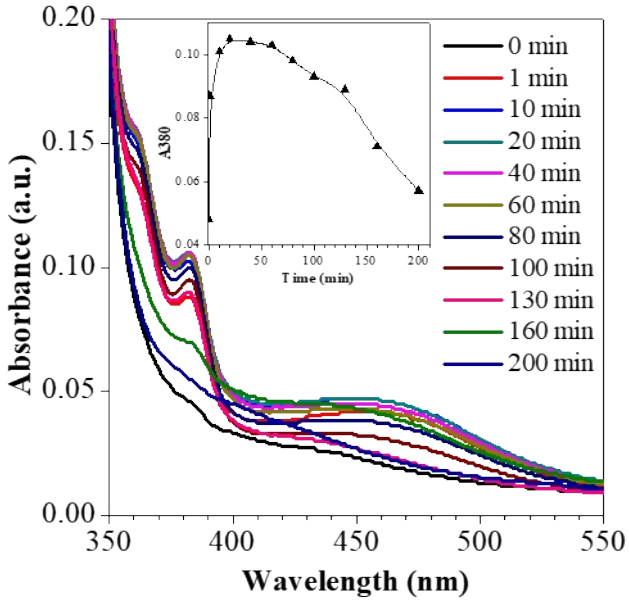


Figure S10. UV-vis spectra as time following addition of 6 eq EDC to PEG_{45}-PAA_{110} (6 Mm), NHS (20 mM) and DPH (2.5 μM). The inset shows a change of the absorbance intensity at 380 nm over time. Experimental conditions: pH 6.5.

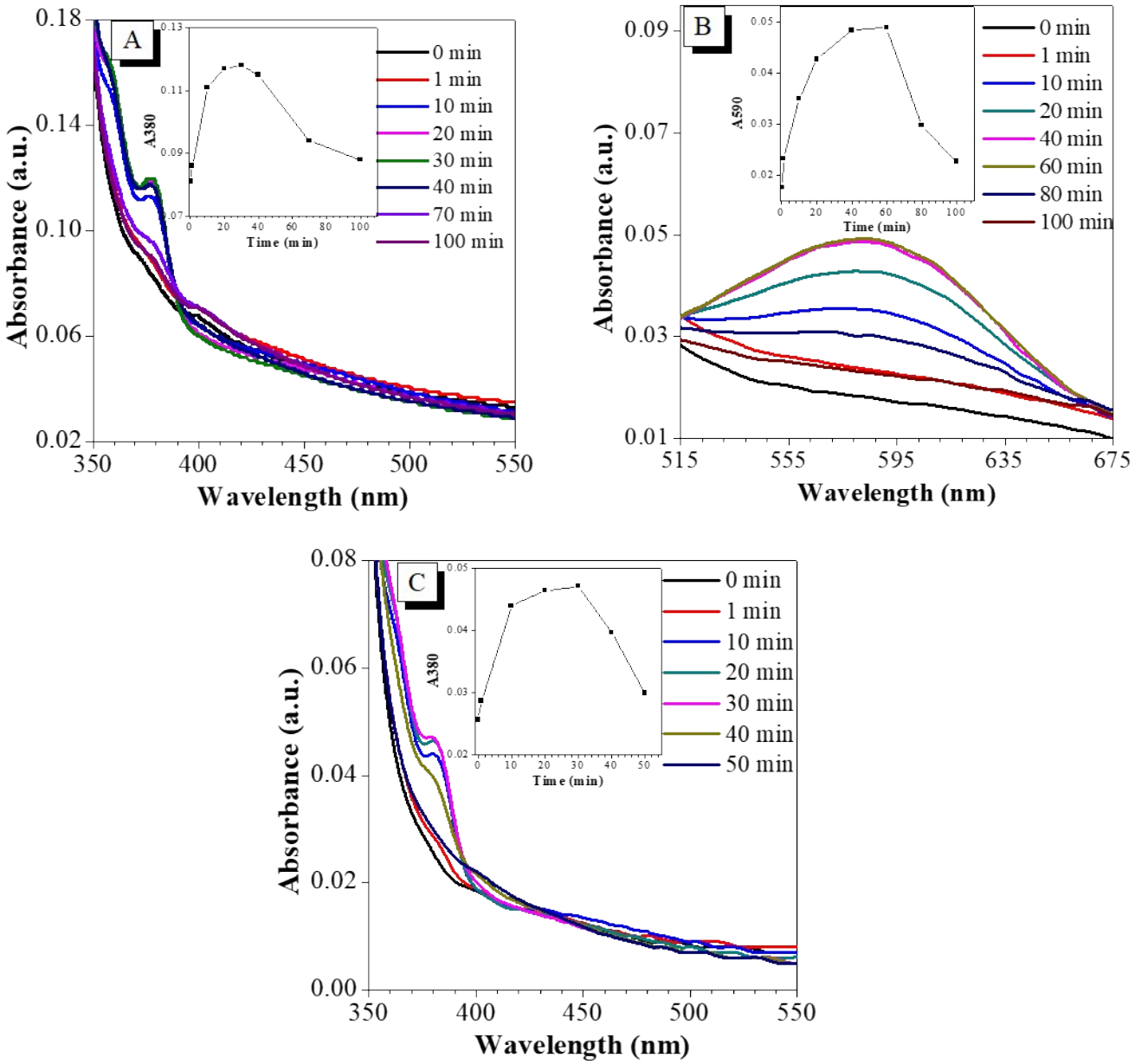


Figure S11. UV-vis spectra as time following addition of 1 eq EDC to PEG_{45}-PAA_{78} (6 Mm) in the presence of different nucleophile (20 mM). (A) PFP (20 mM), DPH (2.5 uM). (B) PNP (20 mM), Nile red (2.5 uM). (C) HONB (20 mM), and DPH (2.5 uM). The inset shows a change of the absorbance intensity at 380 nm over time. Experimental conditions: pH 6.5.

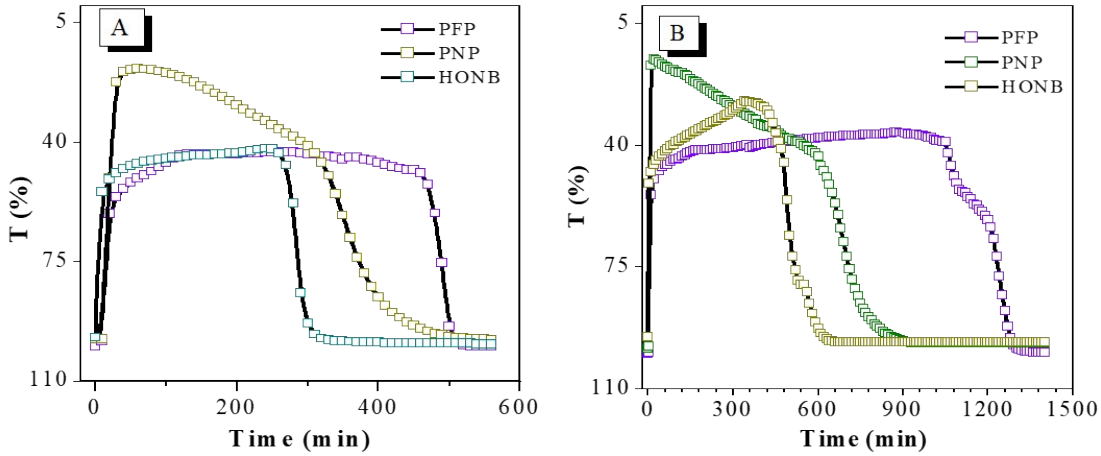


Figure S12. The turbidity (at 600 nm) as time upon addition of EDC to PEG_{45}-PAA_{78} (6 mM) in the presence of different nucleophile (20 mM). (A) 3 eq EDC. (B) 6 eq EDC. Experiment condition: pH 6.5.

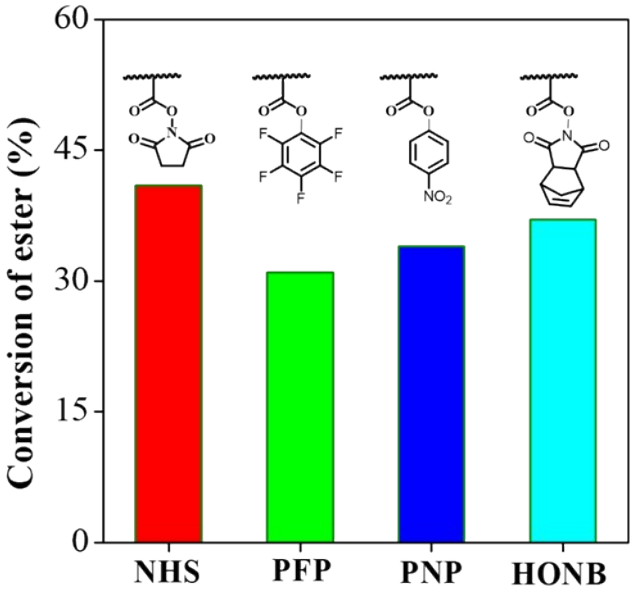


Figure S13. Maximum ester conversion rates for different nucleophiles (NHS, PFP, PNP and HONB) based on time-dependent NMR data. Experimental conditions: PEG_{45}-PAA_{78} (10 mM acid groups), nucleophile (10 mM), EDC (10 mM) and pH 6.5 (100 mM MES).

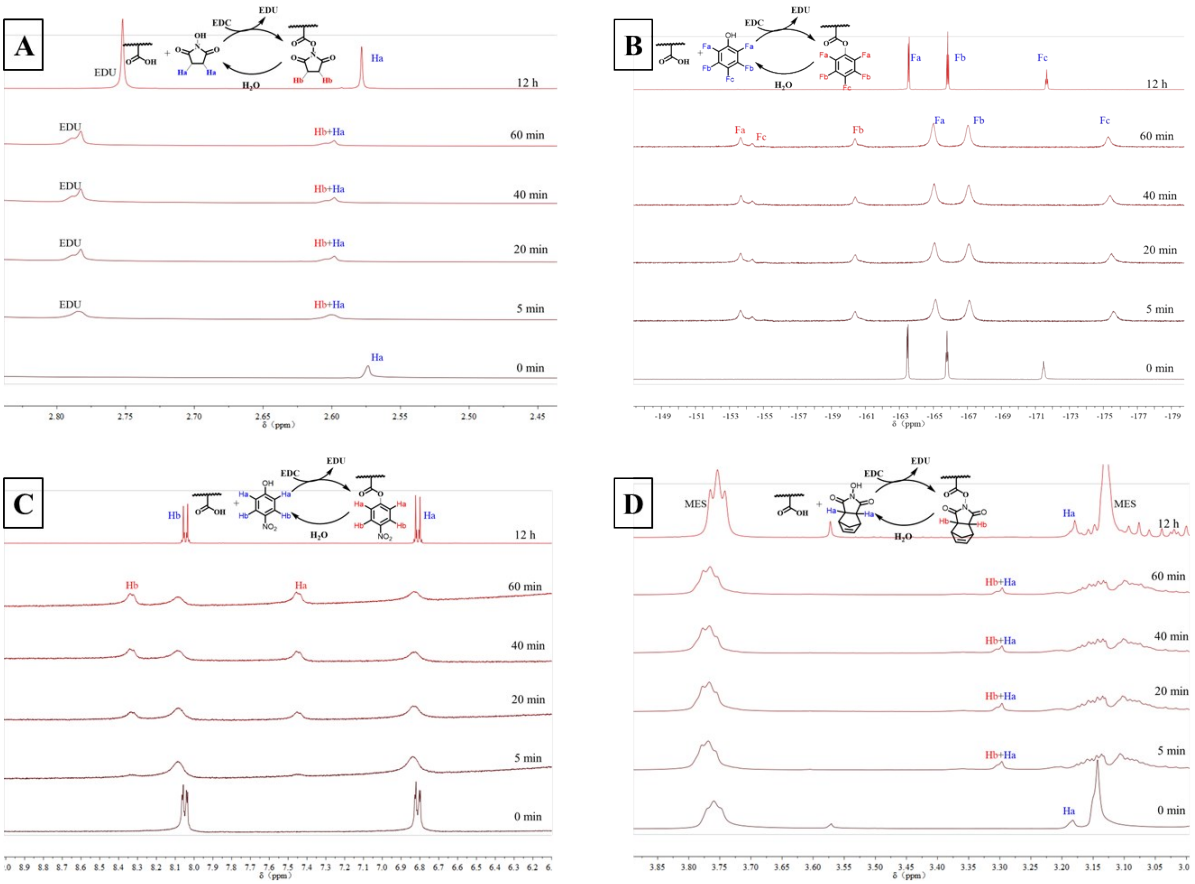


Figure S14. Time-dependent NMR spectra of PEG_{45}-PAA_{78} (10 mM acid groups) with different nucleophile (10 mM) and EDC (10 mM). (A) NHS. (B) PFP. (C) PNP. (D) HONB. Experimental conditions: pH 6.5.

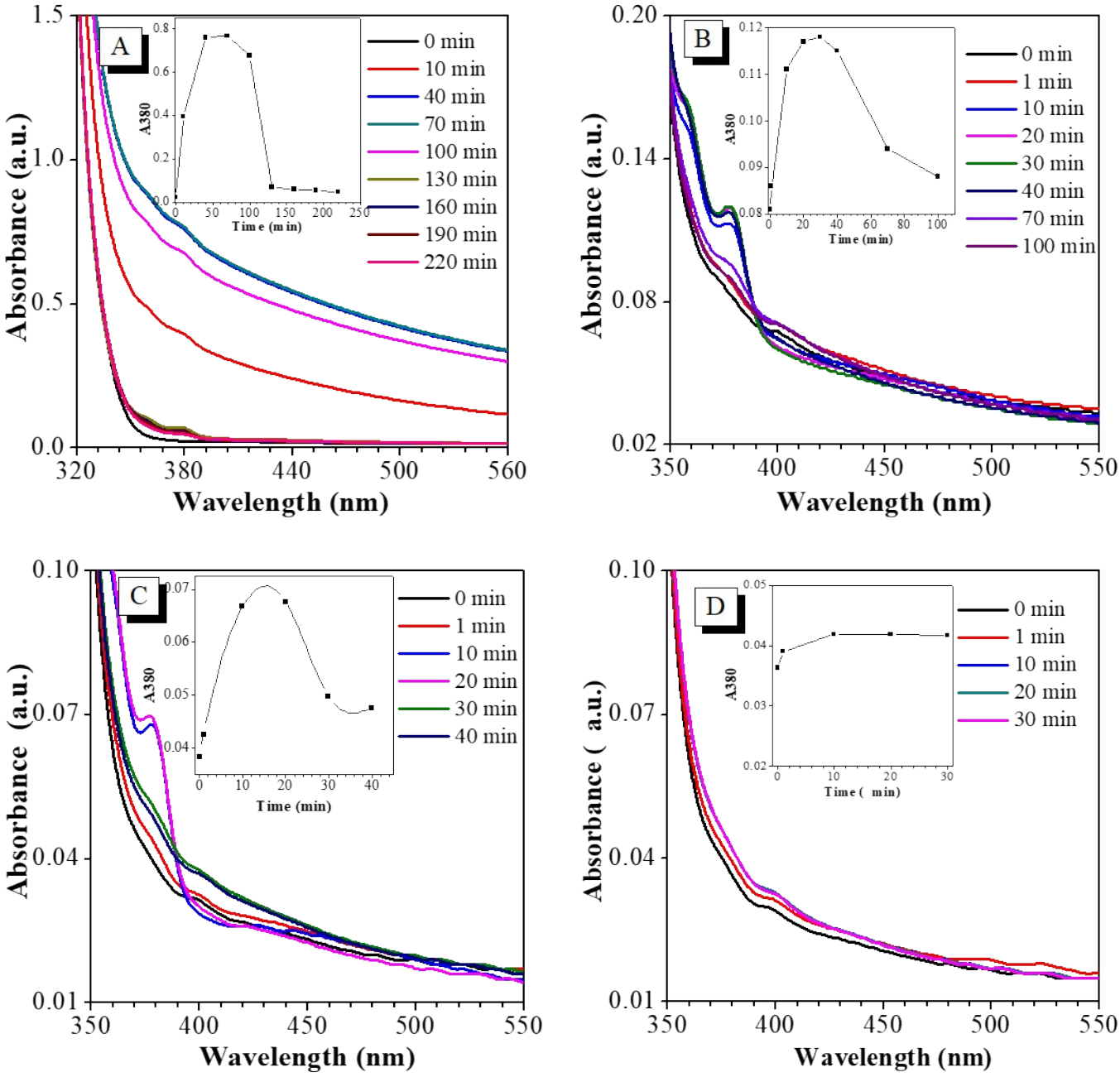


Figure S15. UV-vis spectra as time following addition of 1 eq EDC to PEG_{45}-PAA_{78}(6 mM), PFP (20 mM) and DPH (2.5 μM) under different pH. The inset shows a change of the absorbance intensity at 380 nm over time. (A) pH 6.0. (B) pH 6.5. (C) pH 7.0. (D) pH 7.5.

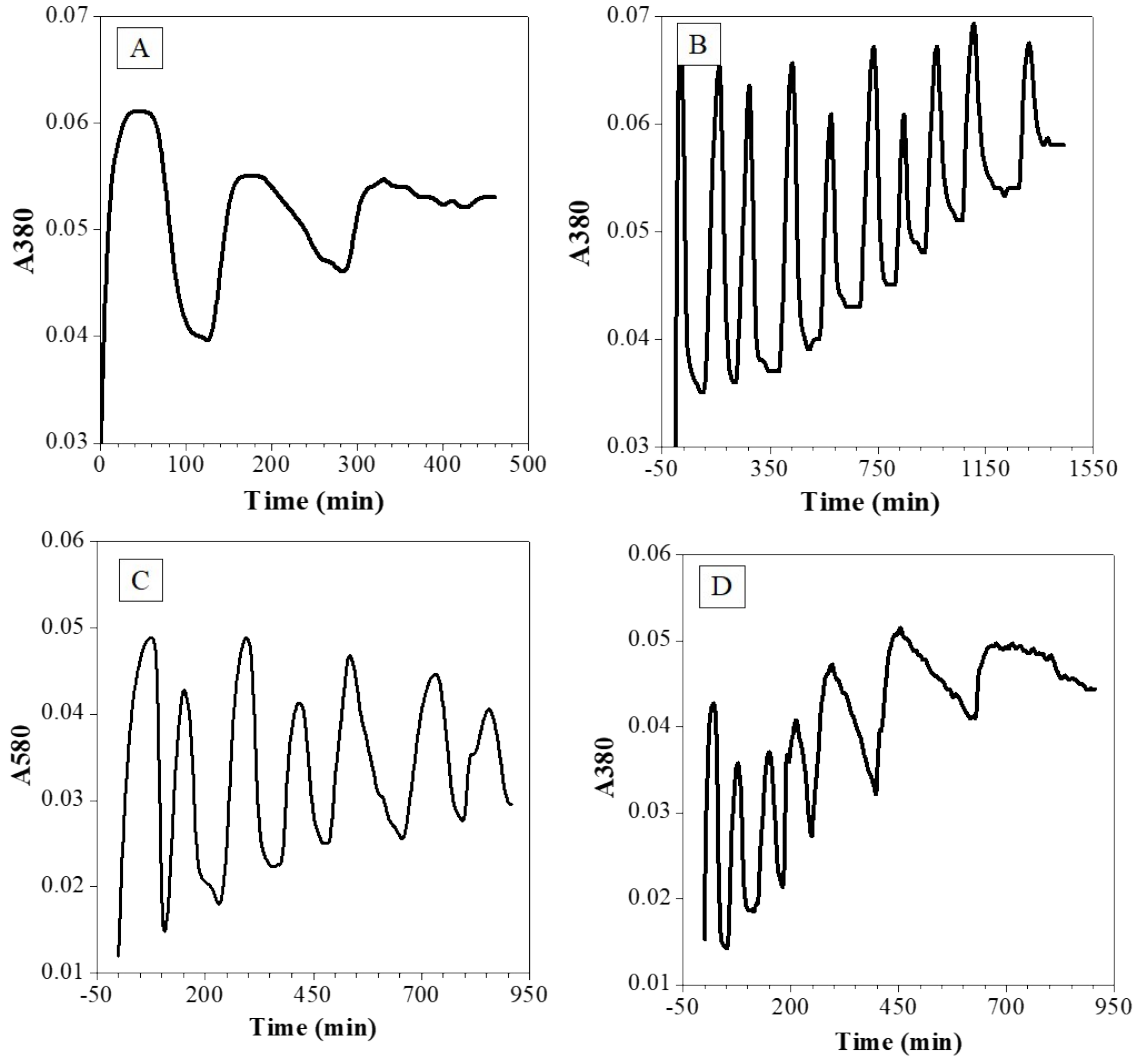


Figure S16. Reversible trapping cycles of transient micelles fueled by repeatedly adding EDC. Experiment condition: PEG_{45}-PAA_{78} (6 mM), (A) NHS (20 mM), DPH (2.5 μM) and EDC (3 eq). (B) PFP (20 mM), DPH (2.5 μM) and EDC (1 eq). (C) PNP (20 mM), Nile Red (2.5 μM) and EDC (1 eq). (D) HONB (20 mM), DPH (2.5 μM) and EDC (1 eq). Experimental condition: pH 6.5.

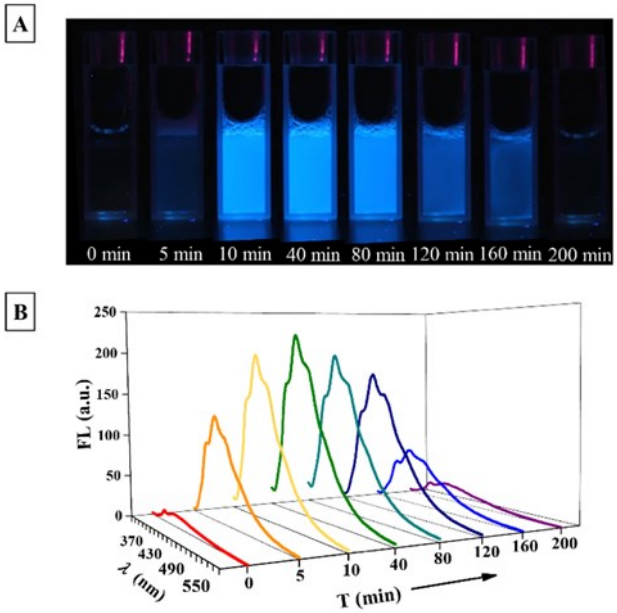


Figure S17. (A) Time-dependent fluorescence images of PEG_{45}-PAA_{78} (6 mM acid groups), NHS (20 mM) and DPH (2.5 μM) after adding EDC under 365 nm. (B) Time-dependent fluorescence spectra of DPH resulting from A. Experimental conditions: pH6.5, 100 mM MES buffer.

Monitoring reaction acceleration

We used anthracene dimerization as a model reaction to study the transient micelle catalytic property in a deoxygenated solution. The dimerization reaction was irradiated with near-UV (λ = 365 nm; ~0.7 mW·cm $^{-2}$).

In order to verify that the decrease in UV absorption is caused by the formation of dimerization products, we used anthracene (10 mM) dimerization was performed in a deoxygenated acetonitrile solution under UV light, and the extent of conversion of dimer was calculated by the change in UV-Vis spectra and ^{1}H NMR, respectively.

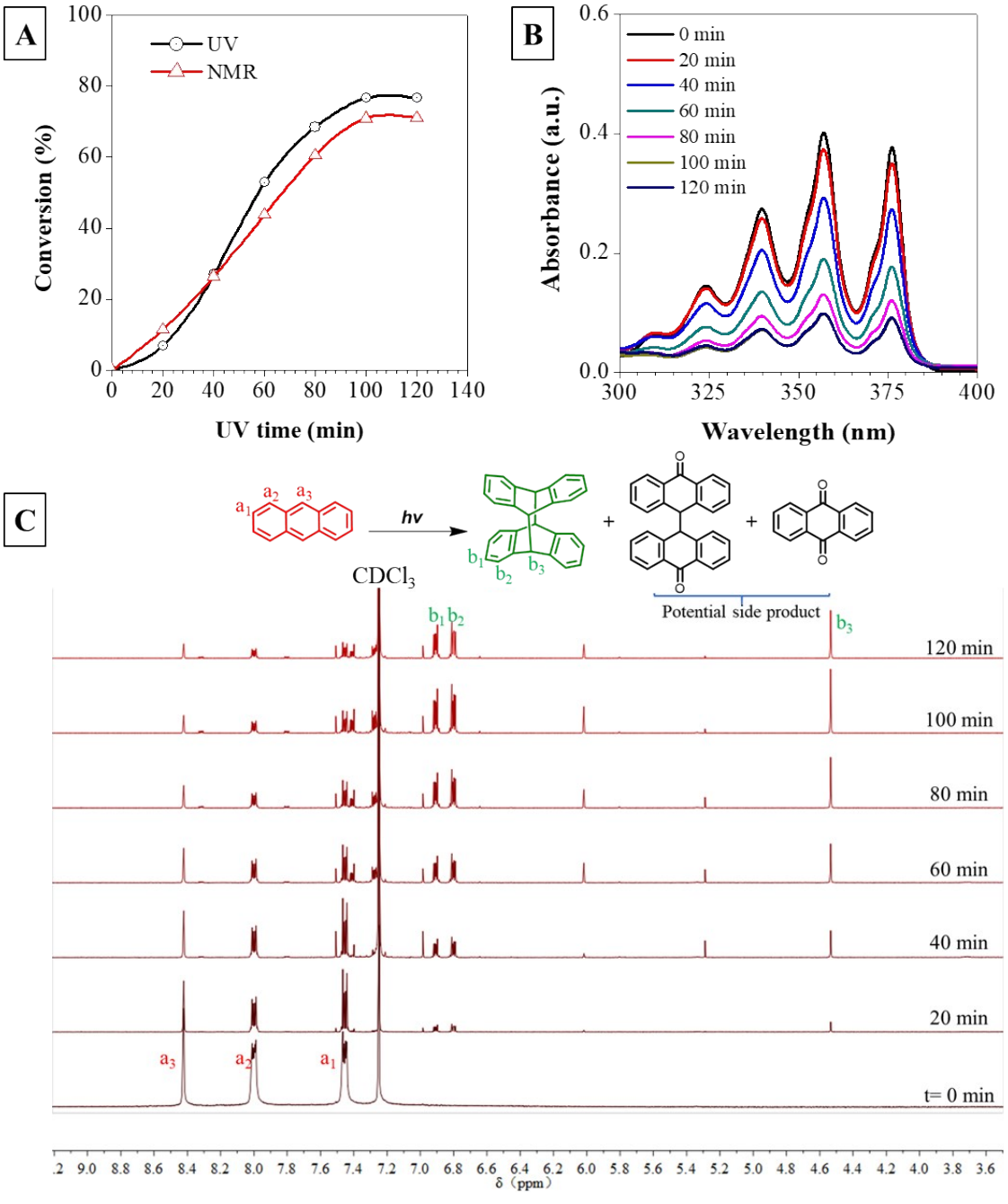


Figure S18. (A) Conversion (%) of the dimer as a function of time under UV light in a deoxygenated acetonitrile solution. (B) Time-dependent UV-Vis spectra of anthracene after exposure to UV light in the acetonitrile solution (0.1 mM). (C) Changes in ^{1}H NMR spectra (400 MHz, $CDCl_3$) of anthracene (1 mM) as a function of UV-induced dimerization.

Anthracene was dissolved in tetrahydrofuran to prepare a 2 mM solution. In a typical catalytic process, 3.3 μL of above solution were added into the deoxygenated buffer solution (100 mM MES, pH 6.5) containing PEG_{45}-b-PAA_{78} (6 mM acid groups), NHS (20 mM) and EDC under UV light. And then, situ UV-vis absorption spectroscopy was used to follow the progress of anthracene dimerization.

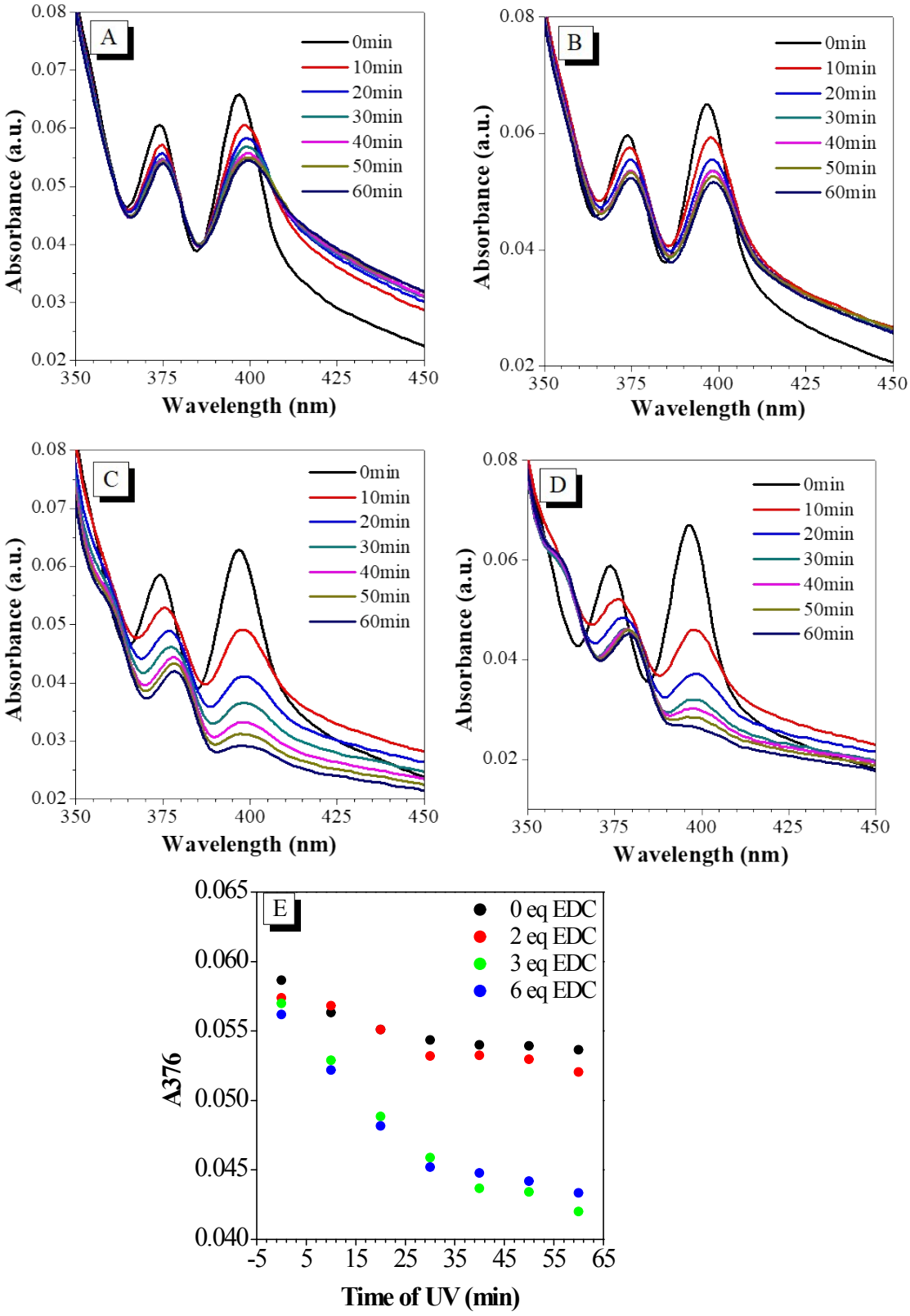


Figure S19. The UV-vis spectra as time upon different content of EDC to PEG_{45}-PAA_{78} (6mM), NHS (20 mM) and anthracene (6 μM) under 365 nm. (A) 0 eq EDC. (B) 2 eq EDC. (C) 3 eq EDC. (D) 6 eq EDC. (E) Absorbance intensity changes at 376 nm over time, compiled from results reported in Figures S18A–D. Experimental condition: pH 6.5.

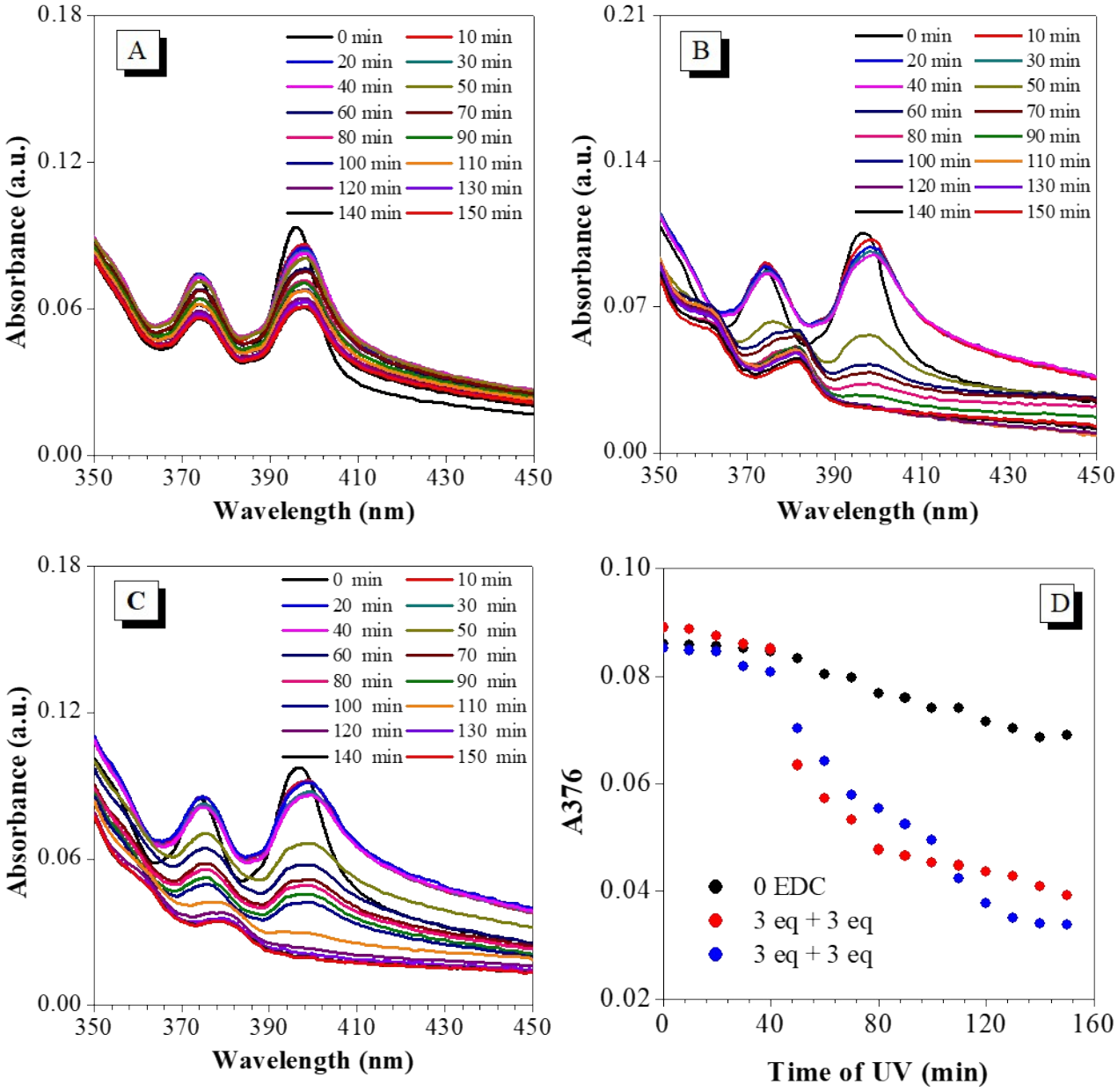


Figure S20. The UV-vis spectra of PEG_{45}-PAA_{78} (6 mM), anthracene (10 μM) and NHS (20 mM) under UV light after repeated addition of 3 eq EDC at 375 nm. (A) 0 eq EDC. (B) EDC were added at 40 min and then re-added at 80 min. (C) EDC were added at 40 min and then re-added after completing the first cycle. (D) Absorbance intensity changes at 376 nm over time compiled from results reported in Figures S19A–C. Experimental condition: pH 6.5.

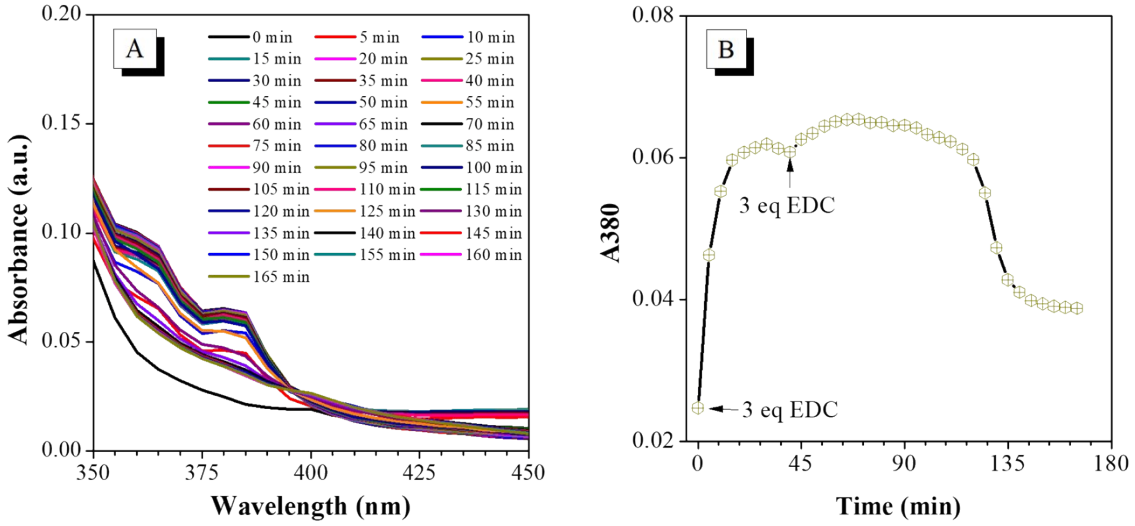
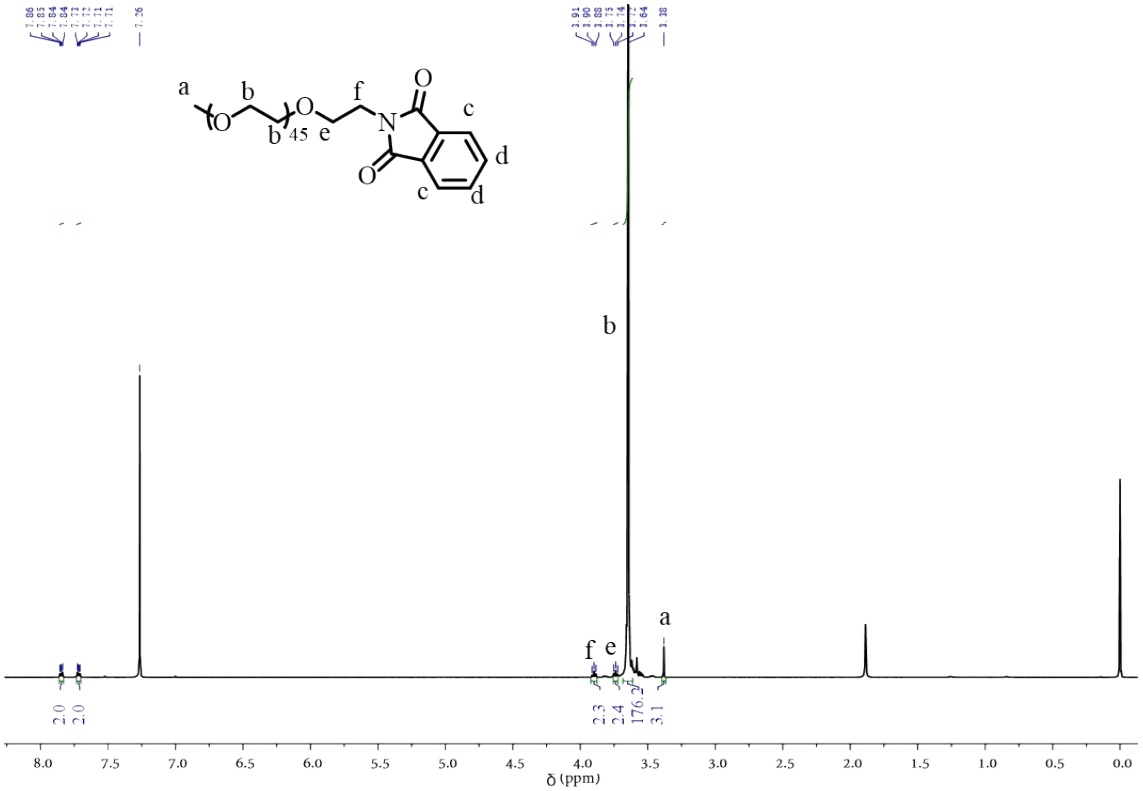


Figure S21. (A) The UV-vis spectra of PEG_{45}-PAA_{78} (6 mM), DPH (2.5 μM) and NHS (20 mM) under UV light after repeated addition of 3 eq EDC at 40 min. (B) Time-dependent fluorescence intensity of DPH resulting from A at 380 nm. Experimental condition: pH 6.5.

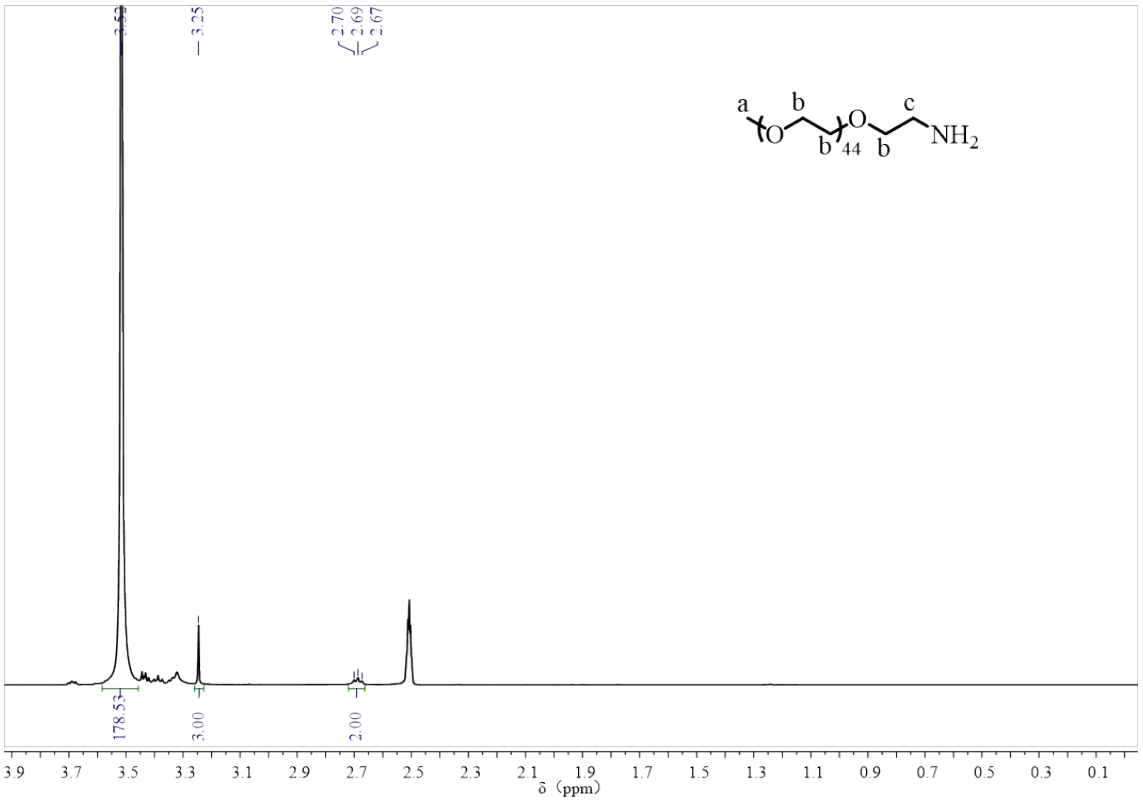
References

[1] L. Yuan, L. He, Y. Wang, X. Lang, F. Yang, Y. Zhao, H. Zhao, *Macromolecules* **2020**, *53*, 3175-3181.

Spectroscopic Characterization.

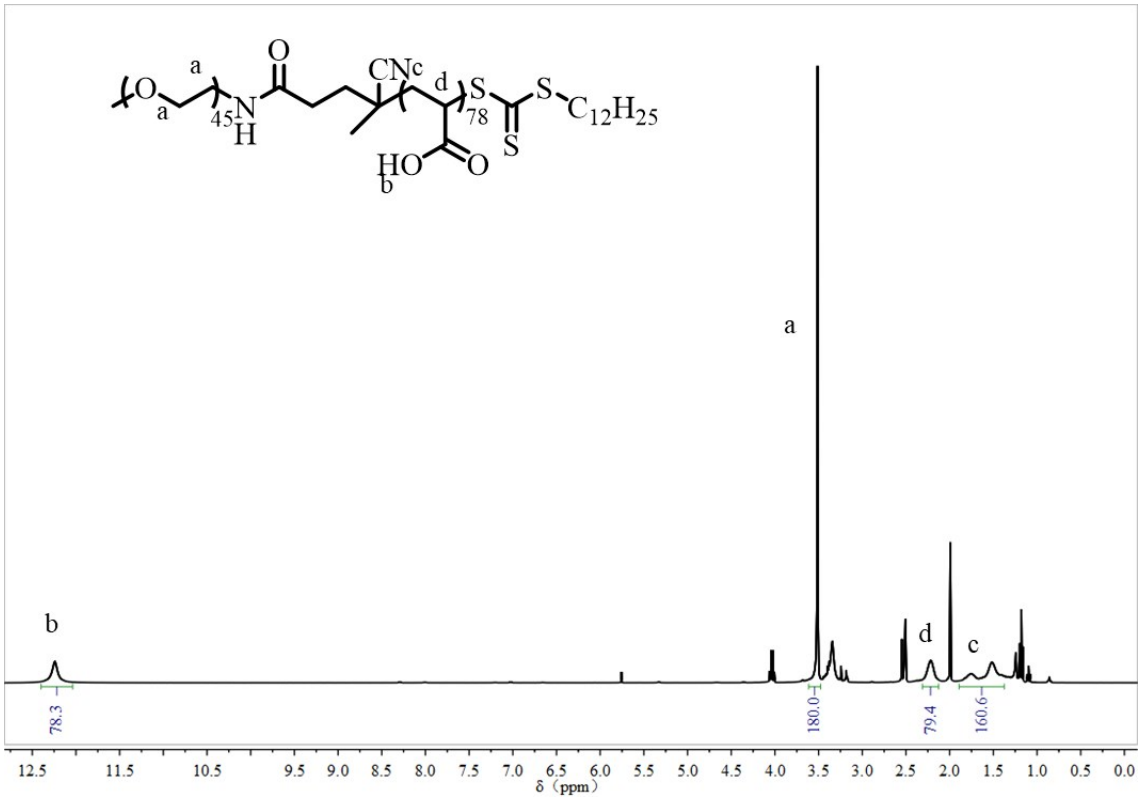


^{1}H NMR spectrum of PEG_{45}-PI (400 MHz, $CDCl_3$).

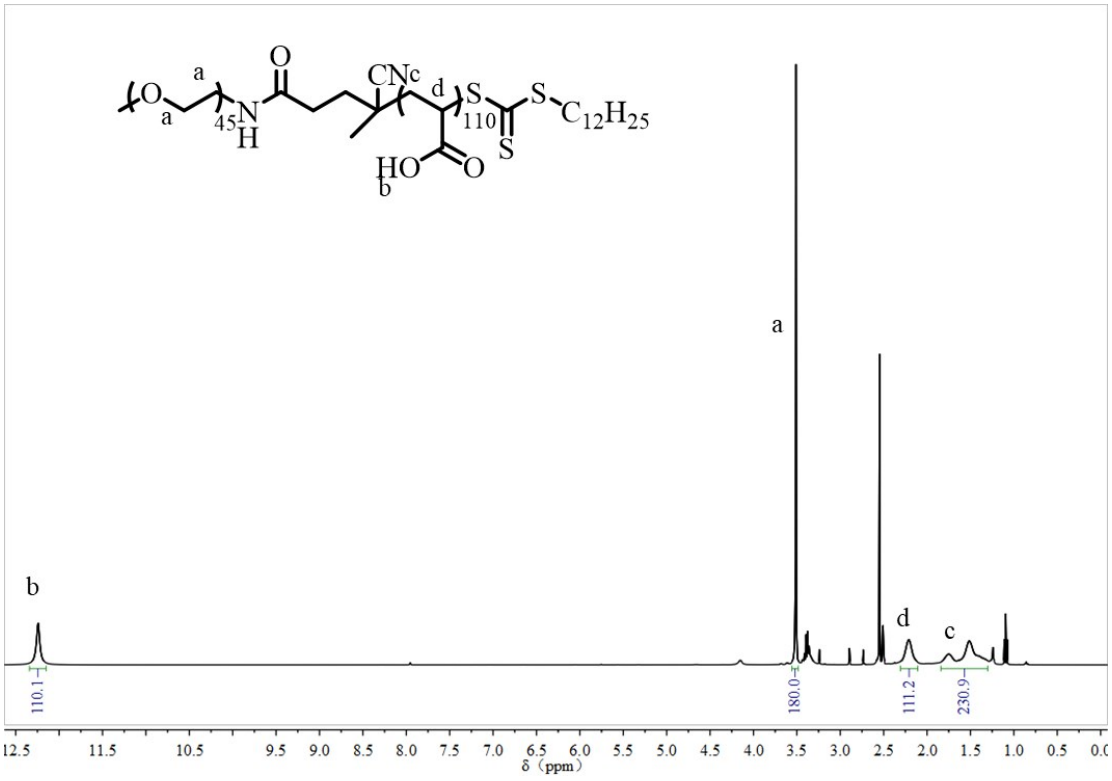


^{1}H NMR spectrum of PEG_{45}-NH_2 (400 MHz, DMSO-D_6).

^{1}H NMR spectrum of PEG_{45}-CTA (400 MHz, $CDCl_3$).



^{1}H NMR spectrum of PEG_{45}-b-PAA_{78} (400 MHz, DMSO-D_6).



^{1}H NMR spectrum of PEG$_{45}$-b-PAA$_{110}$ (400 MHz, DMSO-D$_6$).