

Dual pH- and ultrasound responsive nanoparticles with pH-triggered surface charge conversional properties

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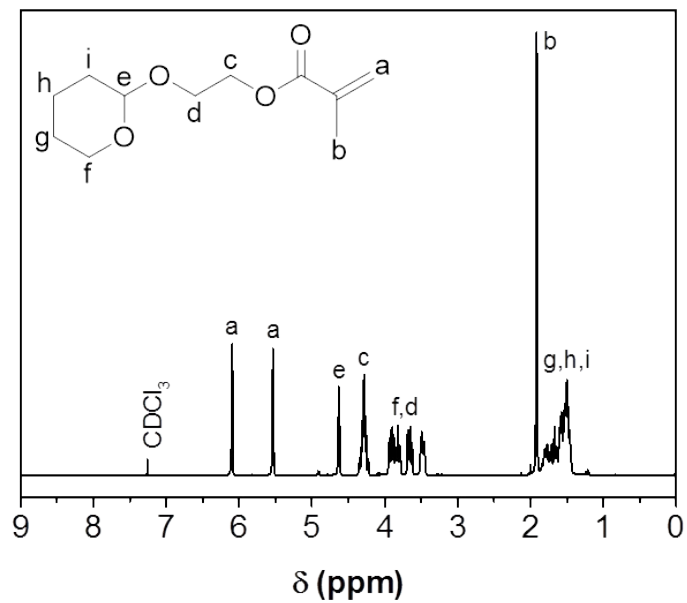


Figure S1. ¹H NMR spectrum (300 MHz, CDCl₃) of monomer THP protected HEMA (THP-HEMA) and assignment of the signals.

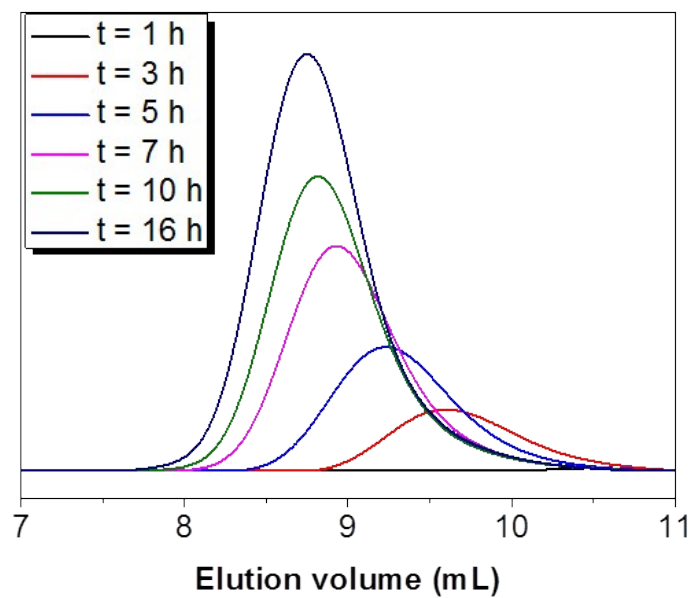


Figure S2. Overlay of the SEC traces (CHCl₃) from kinetic studies of the RAFT copolymerization of P5.

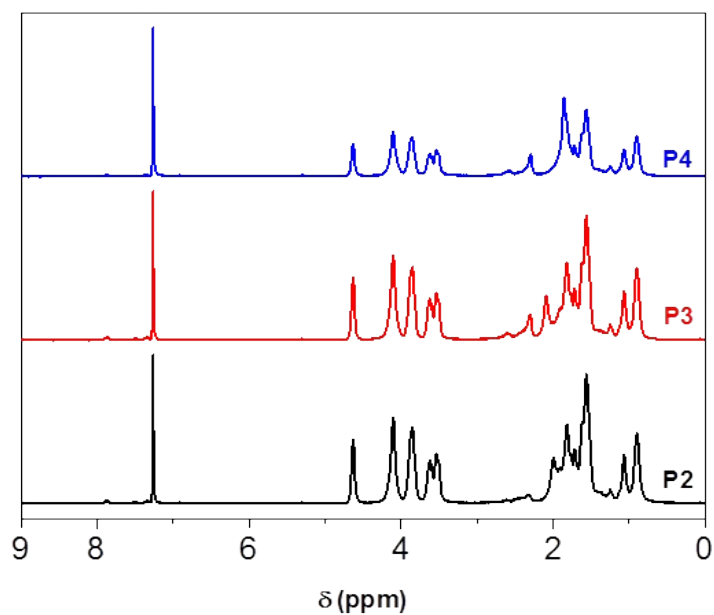
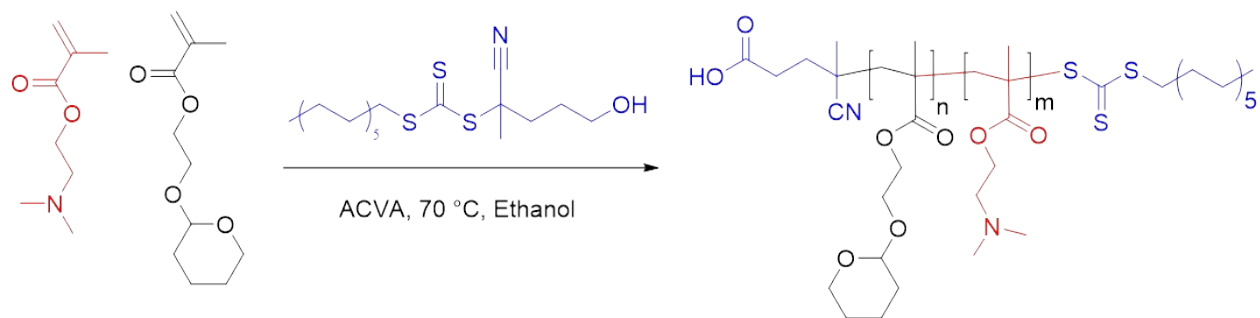


Figure S3. ^1H NMR spectra (300 MHz, CDCl_3) of **P2**, **P3** and **P4**.



Scheme S1. Schematic representation of the RAFT copolymerization of THP-HEMA and DMAEMA by using CDB as CTA.

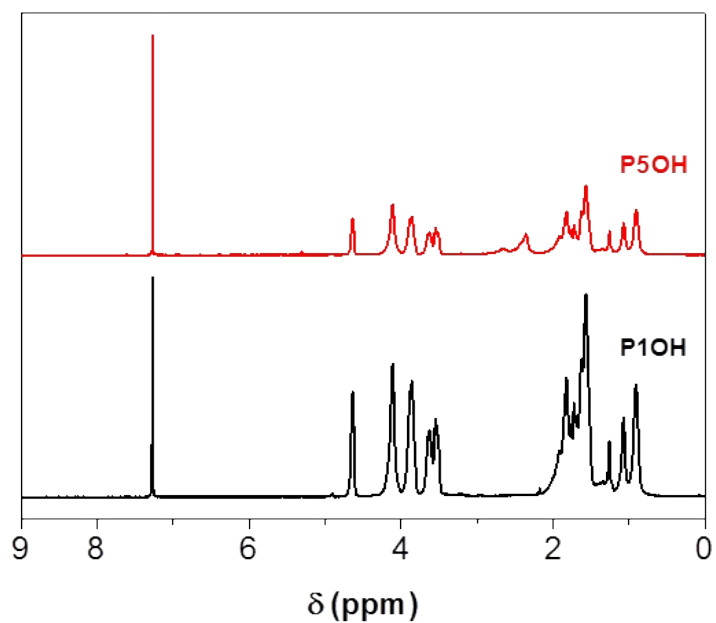


Figure S4. ¹H NMR spectra (300 MHz, CDCl₃) of **P1OH** and **P5OH**.

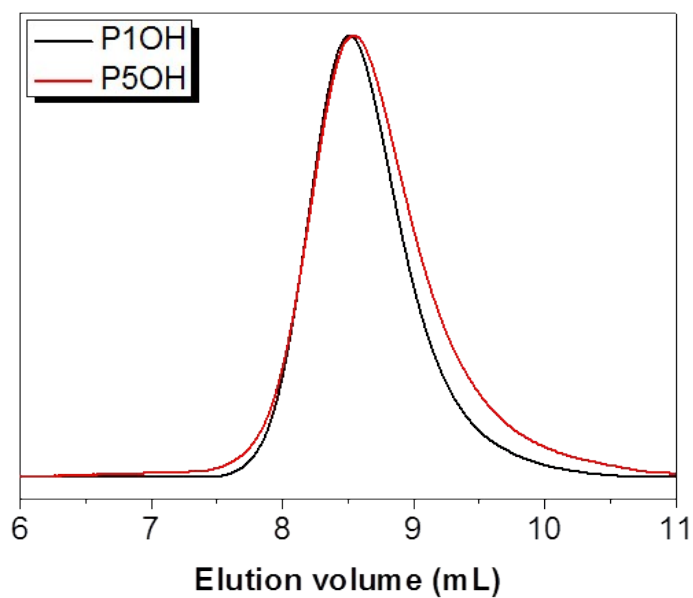
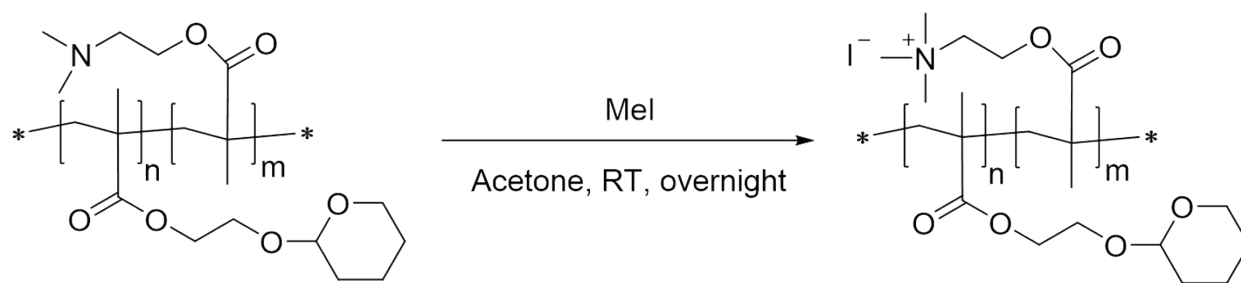


Figure S5. Normalized SEC traces (CHCl₃) of the isolated copolymers **P1OH** and **P5OH**.



Scheme S2. Schematic representation of the quaternization of the synthesized copolymers (**P2** to **P5**).

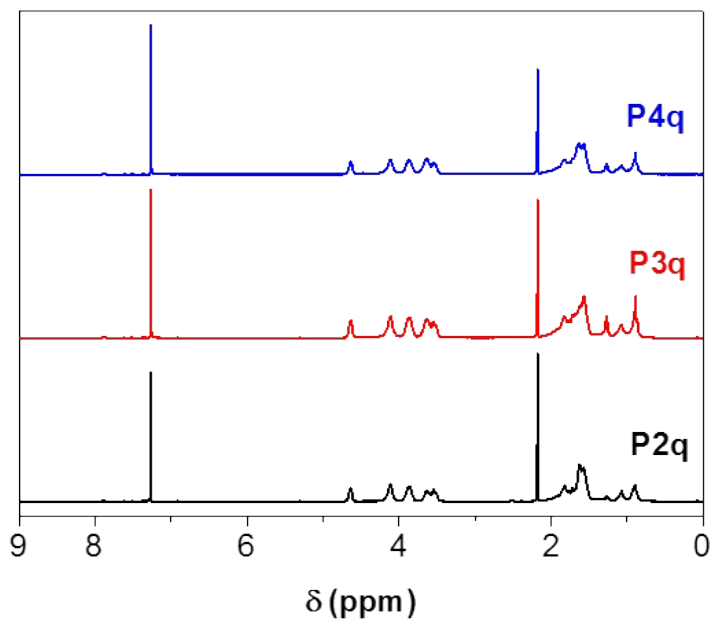


Figure S6. ¹H NMR spectra (300 MHz, CDCl₃) of **P2q** to **P4q**.

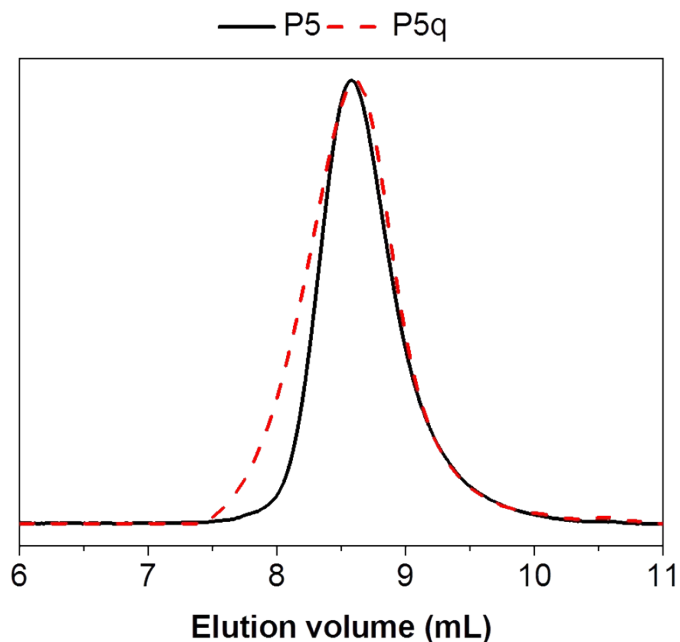


Figure S7. Normalized SEC traces (CHCl_3) of the isolated copolymers **P5** and **P5q**.

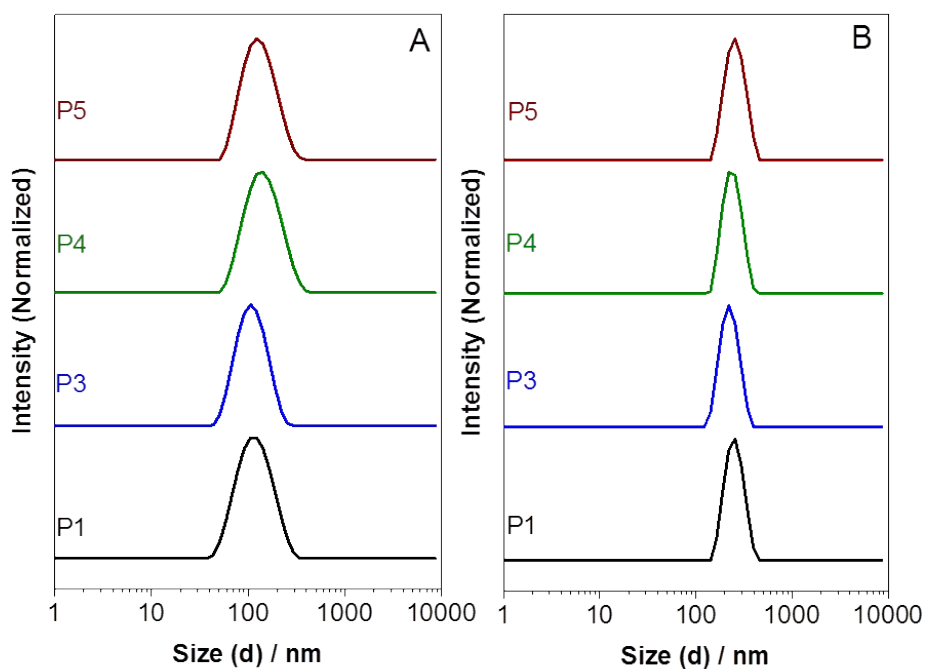


Figure S8. Normalized intensity size distributions of nanoparticles in water (**P1**, **P3**, **P4**, and **P5**) with an initial acetone-polymer concentration of 1 mg mL^{-1} , (A) prepared by dropping acetone-polymer solution to water (AW), (B) dropping water to acetone-polymer solution (WA).

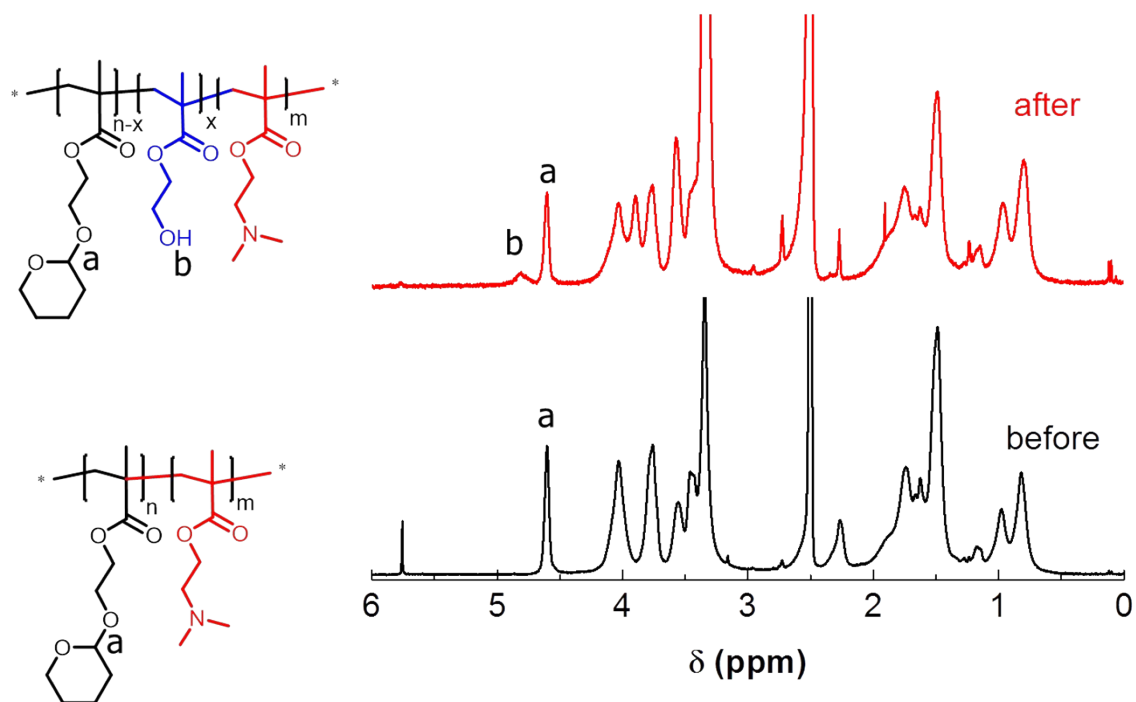


Figure S9. ^1H NMR spectrum (300 MHz, DMSO-d_6) of **P3** nanoparticles before and after treatment with 0.1 M acetic acid (pH = 3.1, stored at 37 °C for 24 h).

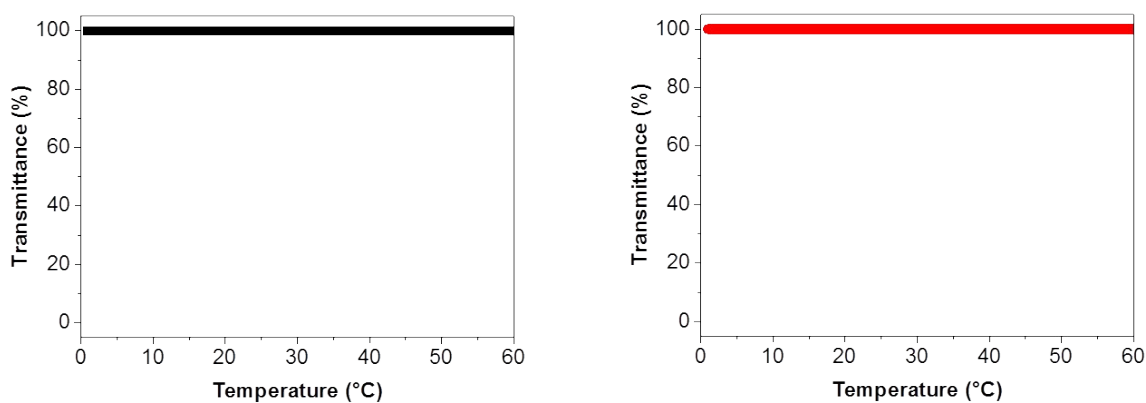


Figure S10. (Left) Transmittance curve of **P4** solution at pH 4.0 during heating from 0 to 60 °C ($c = 1 \text{ mg mL}^{-1}$, heating rate 1 K min^{-1}). (Right) Transmittance curve of **P5** solution at pH 5.0 during heating from 0 to 60 °C ($c = 1 \text{ mg mL}^{-1}$, heating rate 1 K min^{-1}).

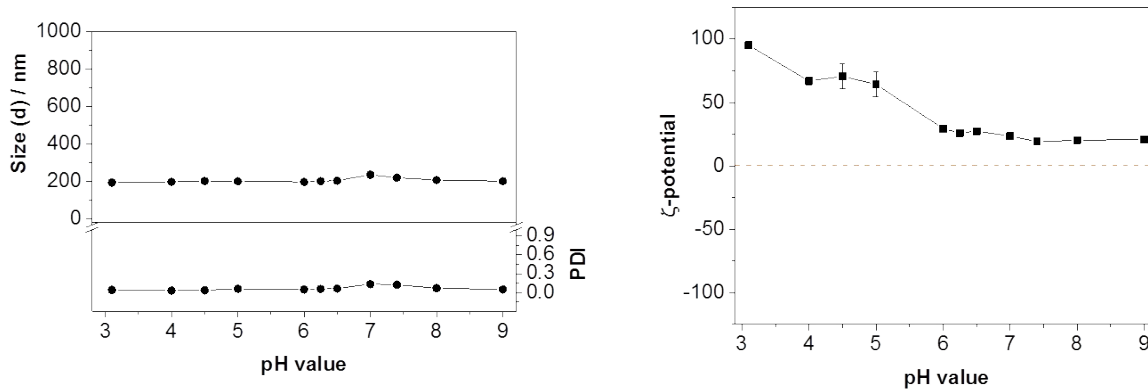


Figure S11. (Left) Intensity weighted diameters and PDI values of **P2q** nanoparticles as a function of the pH value. (Right) ζ -Potentials of the **P2q** nanoparticles as a function of the pH value.

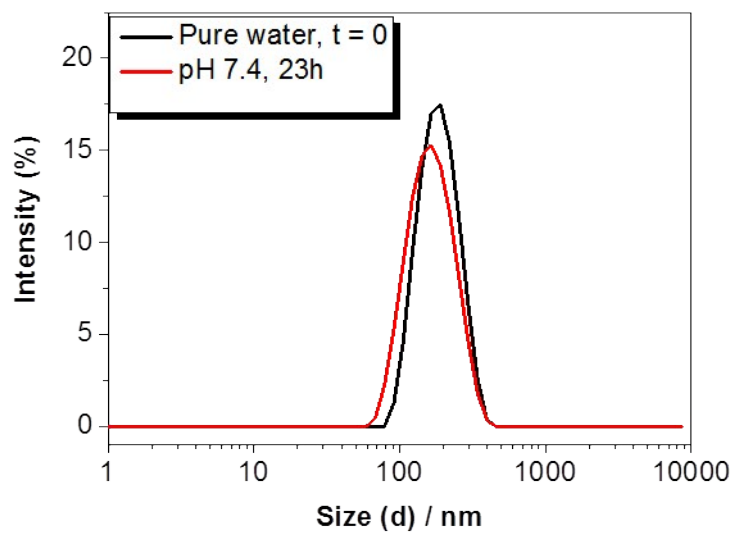


Figure S12. Intensity weighted size distributions of **P3q** nanoparticles in water before and after storage at pH value of 7.4 for 23 h at 37 °C.

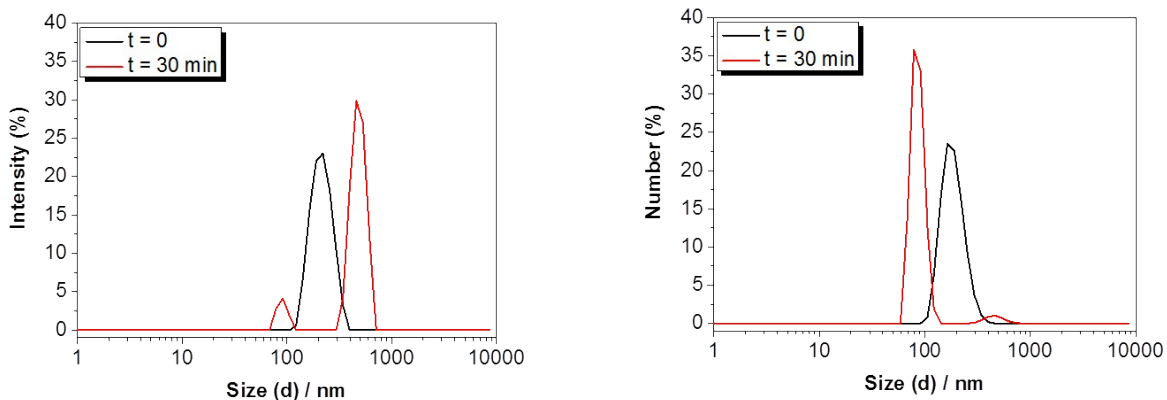


Figure S13. (Left) Intensity weighted size distributions of **P1** nanoparticles in water before and after 30 min. ultrasound treatment (20 W). (Right) Number % size distributions of **P1** nanoparticles in water before and after 30 min. ultrasound treatment (20 W).

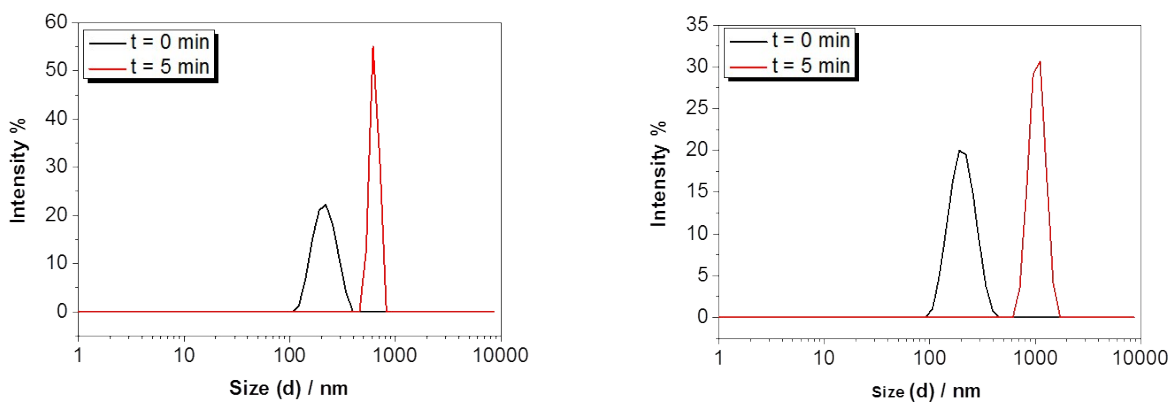


Figure S14. (Left) Intensity weighted size distributions of **P1** nanoparticles in water before and after 5 min. ultrasound treatment (40 W). (Right) Intensity weighted size distributions of **P5** nanoparticles in water before and after 5 min. ultrasound treatment (40 W).

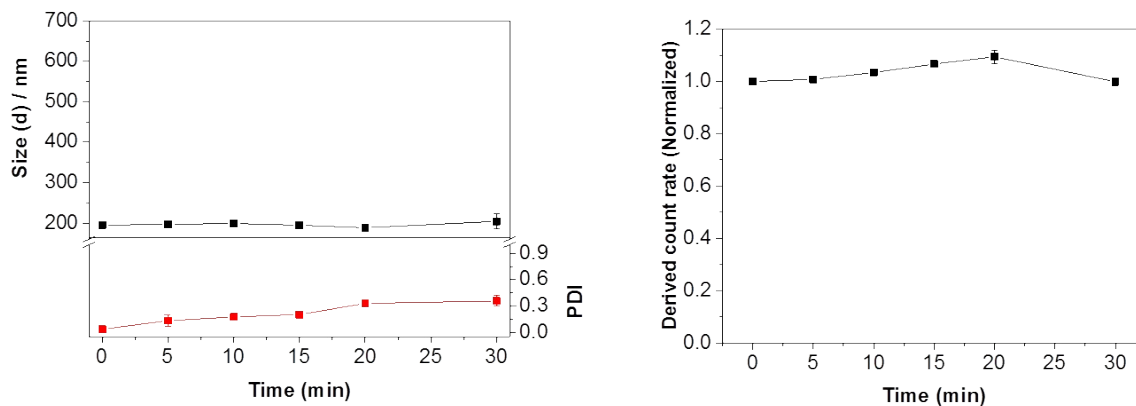


Figure S15. (Left) Intensity weighted size and PDI values of **PMMA** nanoparticles as a function of the ultrasound irradiation time (20 W). (Right) Normalized count rate of the **PMMA** nanoparticles as a function of the ultrasound irradiation time (20 W).

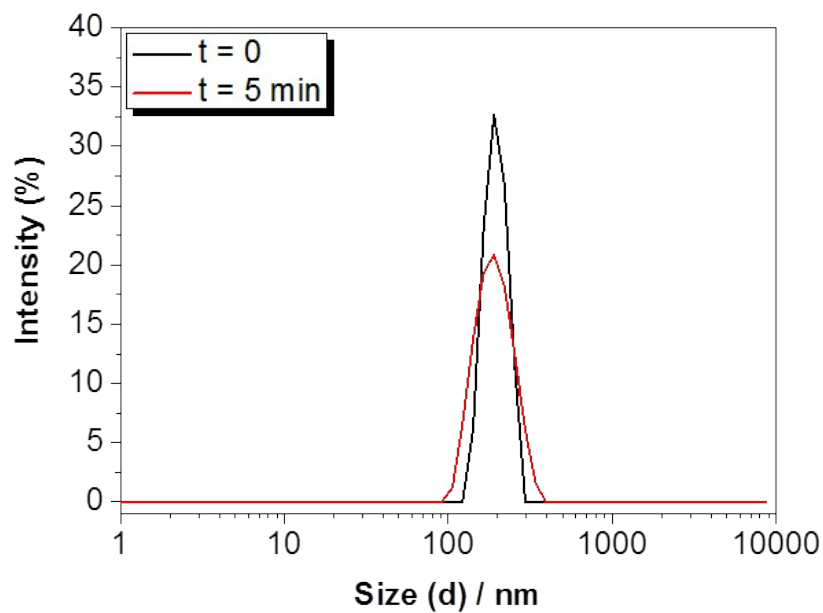


Figure S16. Intensity weighted size distribution of **PMMA** nanoparticles in water before and after 5 min. ultrasound treatment (40 W).

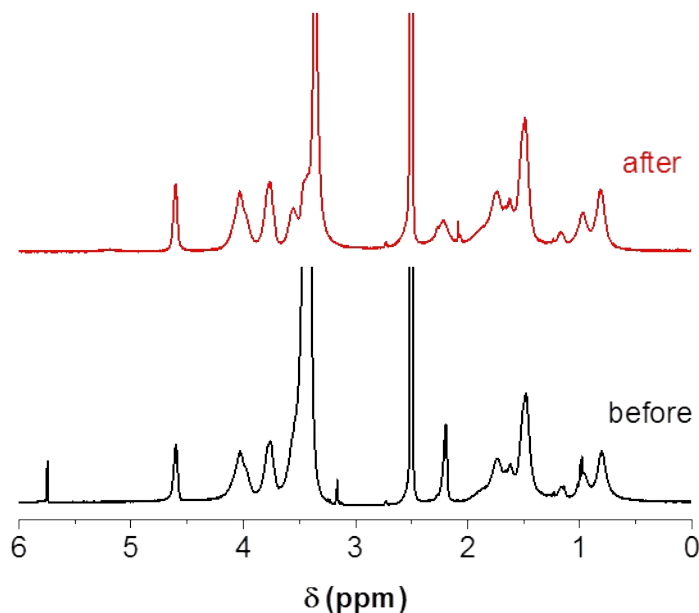


Figure S17. ^1H NMR spectrum (300 MHz, DMSO- d_6) of **P5** nanoparticles before and after ultrasound treatment (5 min, 40 W).

Synthesis of poly(methyl acrylate) (PMA) and synthesis of PMA nanoparticles:

400 mg methyl acrylate (4.646 mmol), 11.5 mg CPADB (0.041 mmol) and 2.88 mg ACVA (0.010 mmol) were dissolved in DMF in a Biotage microwave reaction vial (5 mL) equipped with a magnetic stir bar. The total volume of the reaction mixture was 4.65 mL. After the reaction was degassed for 40 min by argon purging, the t_0 sample for ^1H NMR was taken, and the flask was immersed in a preheated oil bath under stirring at 70 °C. After 16 h, the polymerization was stopped by cooling to room temperature and exposing to air. Monomer conversion was determined via ^1H NMR as 38%. The polymer was purified by precipitating in cold diethyl ether (2 times). The resulting polymer was dried under high vacuum at room temperature until constant weight. The number average molar mass (M_n) and dispersity (D_M) were determined SEC in CHCl_3 by using PMMA standards. SEC in CHCl_3 : $M_n = 3,200 \text{ g mol}^{-1}$ and $D_M = 1.26$ (Figure S17). The number average molar mass (M_n) was calculated as $3,700 \text{ g mol}^{-1}$ via ^1H NMR by comparing the ω -RAFT end groups signals and the methyl proton signal of **PMA** (Figure S17). **PMA** nanoparticles were prepared by nanoprecipitation method by dropping water into acetone-polymer solution.

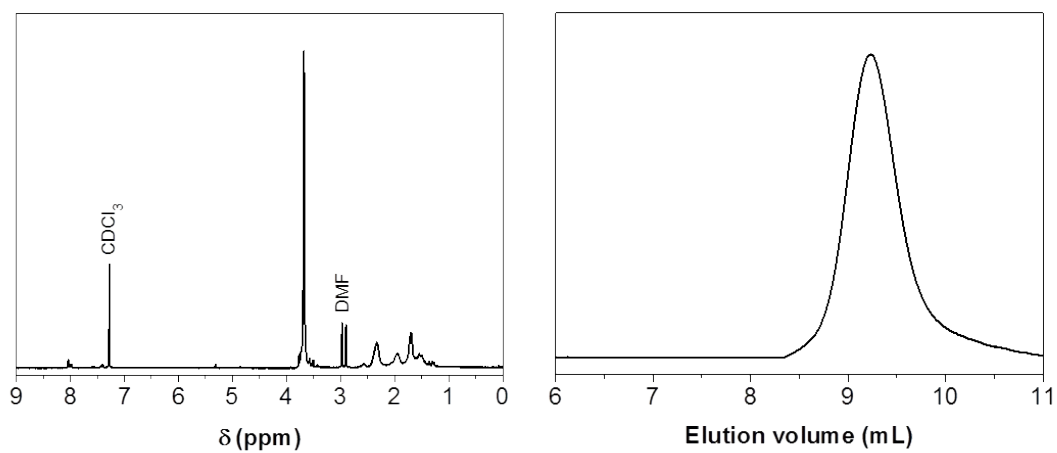


Figure S18. (Left) ^1H NMR spectrum (300 MHz, CDCl_3) of **PMA**. (Right) SEC trace (CHCl_3) of the isolated **PMA**.

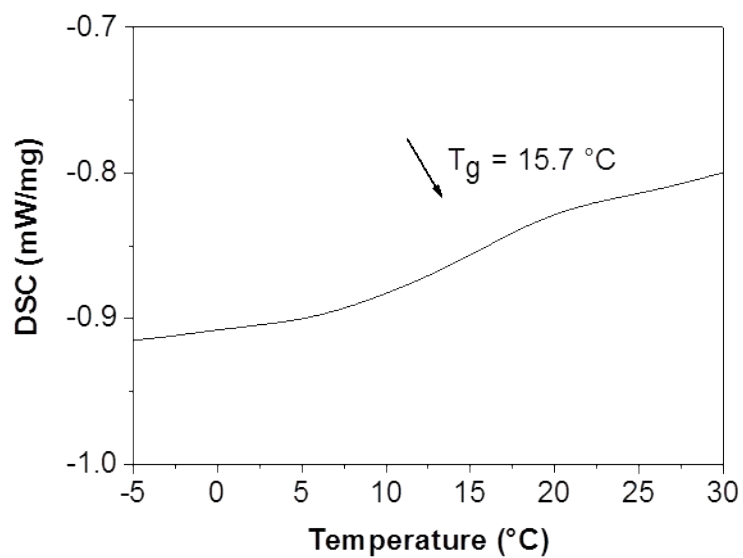


Figure S19. DSC heating run of **PMA** (heating rate 20 K min^{-1}).

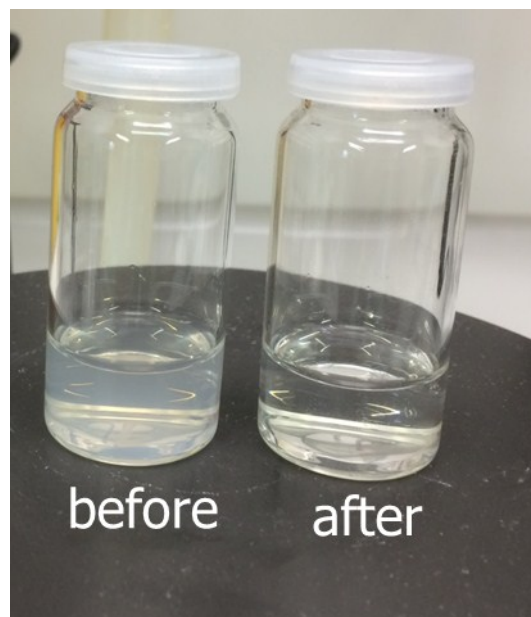


Figure S20. Photograph of PMA nanoparticle suspension before and after 2 min. ultrasound treatment (40 W).

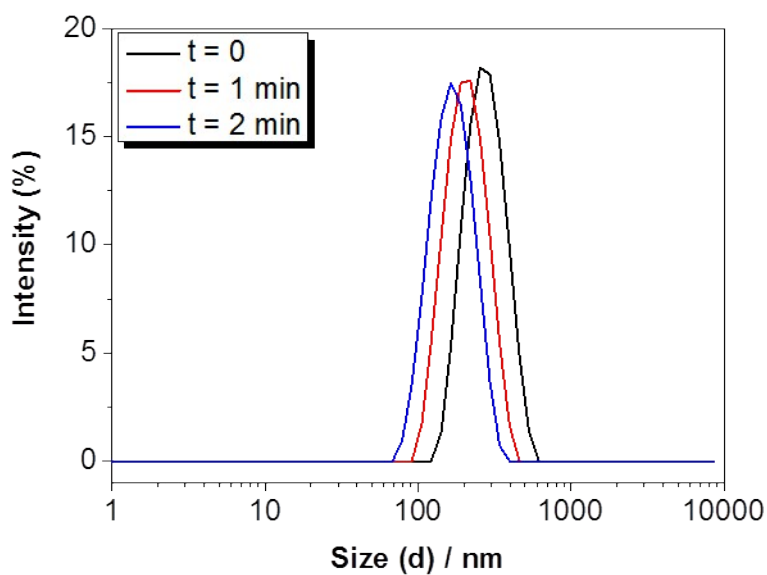


Figure S21. Intensity weighted size distribution of PMA nanoparticles in water before and after 1 and 2 min. ultrasound treatment (40 W).

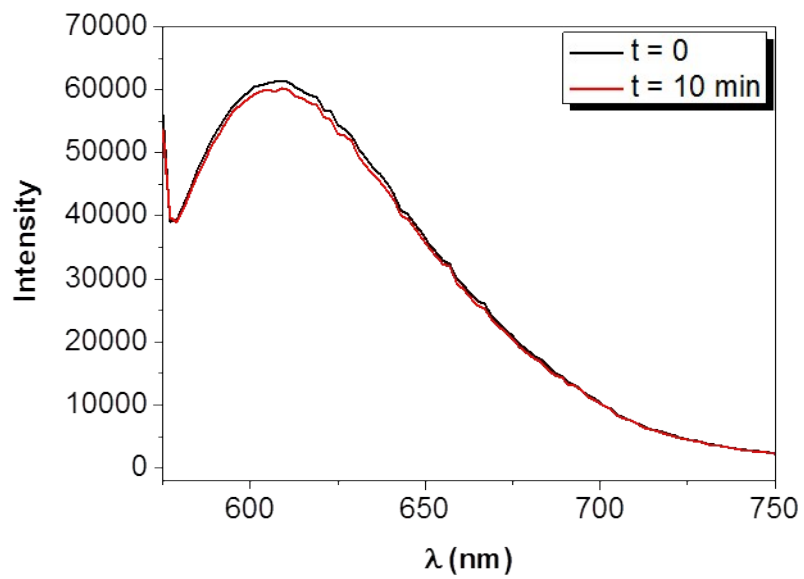


Figure S22. Fluorescence emission spectra of Nile Red encapsulated **P4** nanoparticles (0.5 mg mL^{-1}) before and after storage at $37 \text{ }^\circ\text{C}$ for 10 min. in pure water.