

Supporting Information

for

CO₂/pH-responsive nanogels with built-in fluorescence read-out

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1. Materials

Dry solvents were obtained by passing over a column of activated alumina using an Innovative Technologies solvent purification system. Water for spectroscopy was purified to a resistivity of 18.2 M Ω -cm using a Millipore Simplicity Ultrapure water system. DEAEMA was filtered through a plug of alumina prior to use and stored at 4 °C. All other chemicals were purchased from Aldrich, Fluka or Acros and used as received.

2. Apparatus

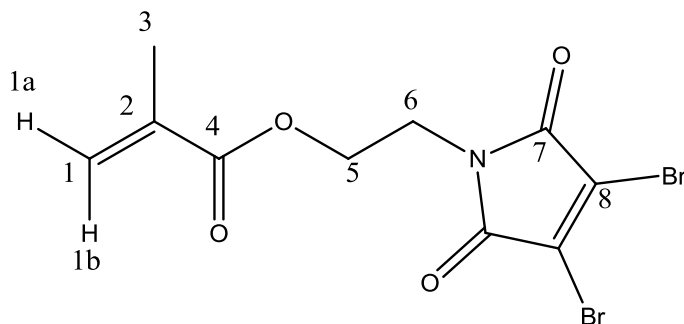
¹H and ¹³C NMR spectra were recorded on a Bruker DPX-400, or AV500 spectrometer at room temperature unless otherwise stated. Chemical shifts are given in ppm downfield from the internal standard tetramethylsilane (TMS). Infrared spectra were recorded (neat) on a PerkinElmer, Spectrum 100 FT-IR Spectrometer. High Resolution Mass Spectrometry (HR-MS) was conducted on a Bruker UHR-Q-ToF MaXis with electrospray ionization. Fluorescence spectra were recorded using an Agilent Cary Eclipse Fluorescence spectrophotometer. UV-vis spectroscopy was carried out on a Perkin Elmer Lambda 35 UV/vis spectrometer or an Agilent Cary 60 UV-Vis Spectrophotometer. Quartz cells with screw caps and four polished sides (Starna) were used for fluorescence and UV-vis measurements. Synchrotron small-angle X-ray scattering (SAXS) measurements were carried on the SAXS/WAXS beamline at the Australian Synchrotron facility at a photon energy of 11 keV. The samples in solution were run by using a 1.5 mm diameter quartz capillary. Temperature was held at 25 °C and controlled *via* a water bath connected to a brass block which is part of the sample holder. The measurements were collected at a sample-to-detector distance of 7.323 m to give a q range of 0.02 to 0.14 Å⁻¹, where q is the scattering vector and is related to the scattering angle (2θ) and the photon wavelength (λ) by the following equation:

$$q = \frac{4\pi \sin(\theta)}{\lambda}$$

All patterns were normalized to fixed transmitted flux using a quantitative beamstop detector. The scattering from a blank was measured in the same capillary and was subtracted for each measurement. The two-dimensional SAXS images were converted in one-dimensional SAXS profile ($I(q)$ versus q) by circular averaging, where $I(q)$ is the scattering intensity. The functions used for the fitting from the NIST SANS analysis package were “Guinier-Porod”,^{1,2} “Debye”,³ “PolyCoreForm”⁴ and “Debye”.³ ScatterBrain⁵ and Igor⁶ were used to plot and analyse the data. The scattering length density of the solvent and the monomers were calculated using the “Scattering Length Density Calculator” provided by NIST Center for Neutron Research. Limits for q range were applied for the fittings from 0.002 to 0.1 Å⁻¹. The stained transmission electron microscopy (TEM) images were obtained using a JEOL 2000FX or a JEOL 2100 LaB6 instrument operated at 200 kV. TEM samples were negatively stained by uranyl acetate (UA, 2.5 wt%) on formvar/carbon grids (300 Mesh, Cu, Elektron Technology UK LTD). Typically, formvar/carbon grids were cleaned by air plasma from a glow-discharge system (2 min, 20 mA) which also improved the hydrophobicity of the grids. 5 µL of particle solution was added onto the grid and the solution was left to air-dry for 3 h. 5 µL of a 2.5 wt% UA solution was then added onto the grid to stain the particles and was blotted away after 15 s before air-drying.

3. Monomers

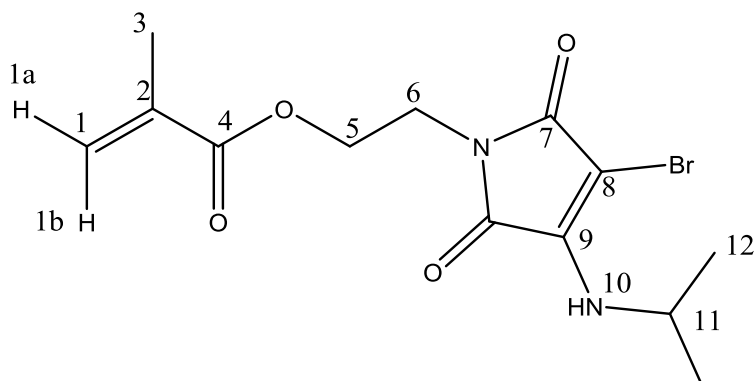
2-(3,4-dibromo-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)ethyl methacrylate (DBMMA, 1)



Synthetic procedure detailed in the main text. ¹H NMR (300 MHz, CDCl₃) δ 6.08 (1H, br s, H1b), 5.59 (1H, br s, H1a), 4.30 (2H, t, ³J_{H-H} = 6.0 Hz, H5), 3.95 (2H, t, ³J_{H-H} = 5.5 Hz, H6), 1.90 (3H, s, H3); ¹³C NMR (75 MHz, CDCl₃) δ 163.1 (C7), 136.2 (C8), 135.2 (C2), 128.9 (C4), 126.0 (C1), 61.0 (C5), 38.0 (C6), 17.6 (C3); FTIR (neat) ν_{max} / cm⁻¹ 1720 (C=O of ester), 1633 (C=O of maleimide), 1595 (C=C aromatic), 1170 (C-O of ester); HR-MS (MaXis) m/z found 389.8770, calc. 389.8770 ([M+Na]⁺, 100 %);

2-(3-bromo-4-(isopropylamino)-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)ethyl methacrylate

(ABMMA, 2)



Synthetic procedure detailed in the main text. ^1H NMR (300 MHz, CDCl_3) δ 6.09 (1H, br s, H1b), 5.58 (1H, br, H1a), 5.28 (1H, br, H10), 4.42 (1H, m, H11), 4.27 (2H, t, $^3J_{\text{H-H}} = 5.0$ Hz, H5), 3.84 (2H, t, $^3J_{\text{H-H}} = 6.0$ Hz, H6), 1.91 (3H, s, H3), 1.30 (6H, d, $^3J_{\text{H-H}} = 6.5$ Hz, H12); ^{13}C NMR (75 MHz, CDCl_3) δ 166.8 & 166.4 (C4, C8), 165.4 (C7), 141.7 (C9), 135.2 (C2), 125.7 (C1), 61.3 (C5), 44.2 (C11), 36.8 (C6), 23.1 (C12), 17.6 (C3); FTIR (neat) $\nu_{\text{max}} / \text{cm}^{-1}$ 3284 (H-N of isopropylamine), 1710 and 1657 (C=O of maleimide), 1181 (C-O of ester); HR-MS (MaXis) m/z found 367.0267, calc. 367.0264 ($[\text{M}+\text{Na}]^+$, 100%); $\lambda_{\text{ex,max}}$ (10^{-5} M in 1,4-dioxane at r.t.) 247 nm and 372 nm, $\lambda_{\text{em,max}}$ (10^{-5} M in 1,4-dioxane at r.t.) 482 nm.

4. Particles

Particles were synthesized following the general procedure detailed in the main text.

DEAEMA particles with OEGMA360 (3)

Synthetic procedure is detailed in the main text. In this case, oligoethylene glycol methacrylate (OEGMA), MW = 360 Da, Ω -end: OH (0.04 g), *N,N*-(diethylaminoethyl methacrylate) (DEAEMA) (2.5 g), ethylene glycol dimethacrylate (EGDMA) (0.025 g) and potassium persulfate (KPS) (0.025 g) were used in the general procedure.

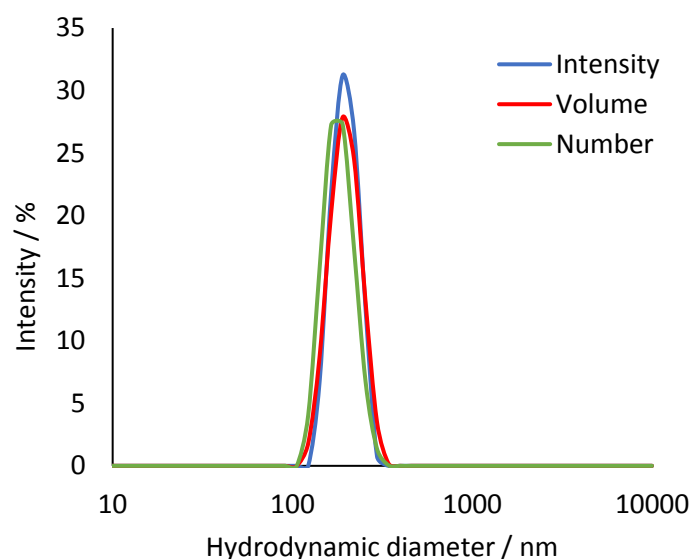


Figure S1. Intensity, volume and number-weighted particles size distribution obtained by DLS for **3**

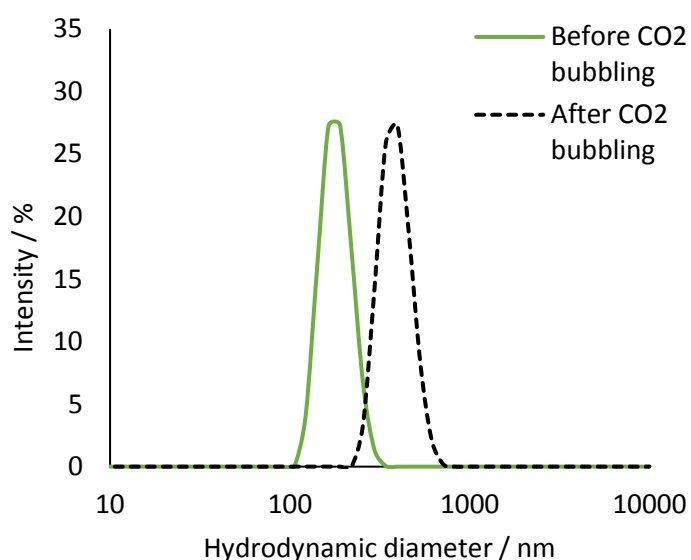


Figure S2. Number-weighted particles size distribution obtained by DLS before and after CO₂ bubbling for **3**

Fluorescent DEAEMA particles with OEGMA360 (**4**)

Synthetic procedure is detailed in the main text. Two batches of particles **4** were synthesized. A first one (**4a**) was synthesized using OEGMA, MW = 360 Da, Ω -end: OH (0.04 g), DEAEMA (2.5 g), EGDMA (0.025 g), KPS (0.025 g) and aminobromomaleimide methacrylate (ABMMA, **2**) (0.261 mmol, 0.09 g) following the general procedure. A second one (**4b**) was synthesized using OEGMA, MW = 360 Da, Ω -end: OH (0.04 g), DEAEMA (2.5 g), EGDMA (0.025 g), KPS (0.025 g) and aminobromomaleimide methacrylate (ABMMA, **2**) (0.145 mmol, 0.05 g) according to the general procedure. As demonstrated in the main text, the fluorescent monomer does not affect the size of the particles, see below the DLS of both **4a** and **4b**. Results (DLS and TEM) mentioned in the main text correspond to particles **4a**. The particles **4b** were utilized in the video showing the fluorescence intensity decrease during 10 min of CO₂ bubbling observed under a UV lamp at 345 nm (video available as supplementary data). Figure S5 is a picture of particles **4b** in solution before and after CO₂ bubbling.

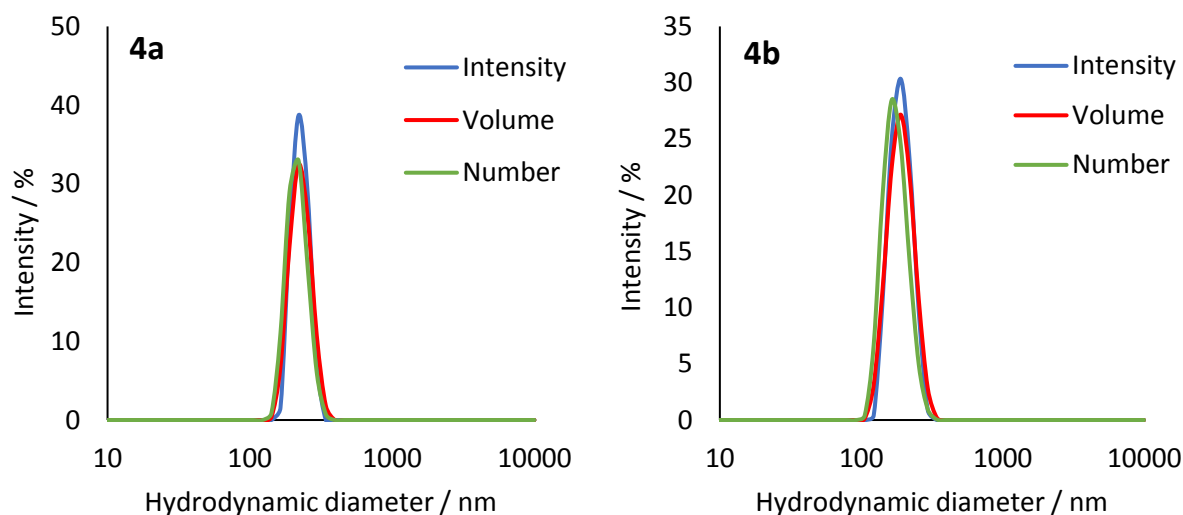


Figure S3. Intensity, volume and number-weighted particles size distribution obtained by DLS for **4a** and **4b**

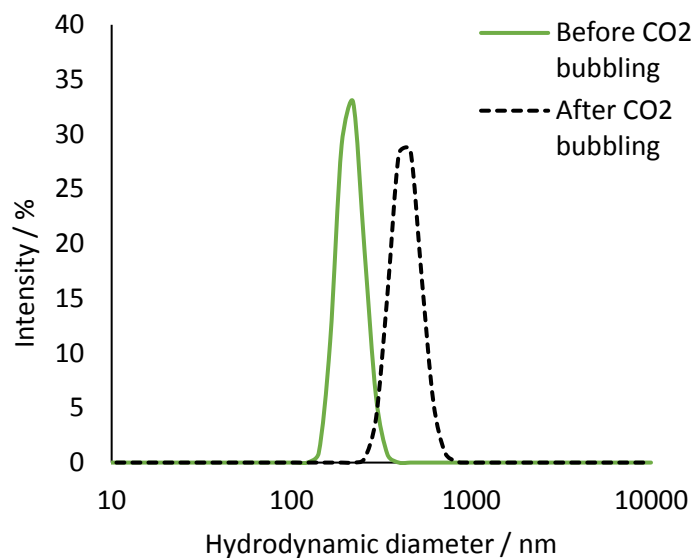


Figure S4. Number-weighted particles size distribution obtained by DLS before and after CO₂ bubbling for **4a**

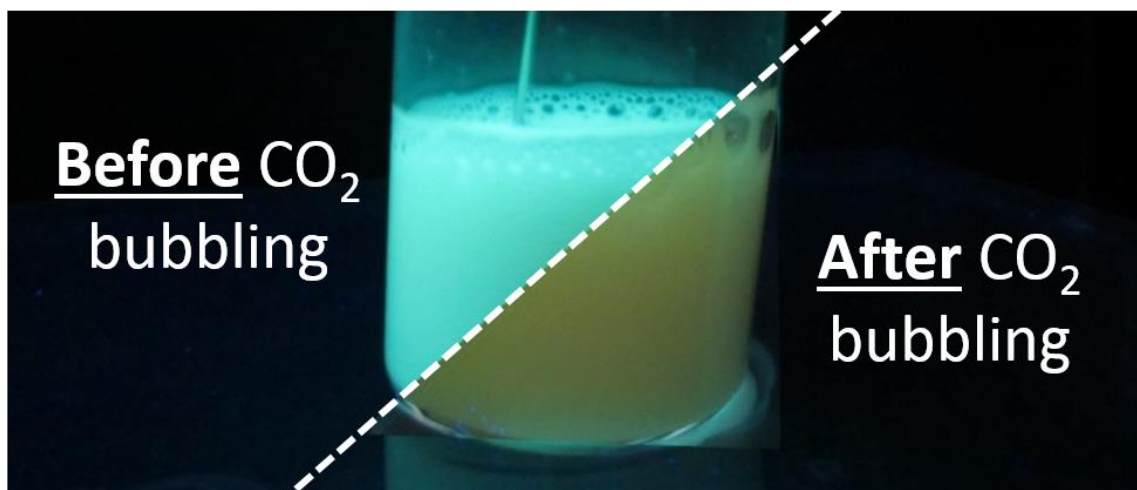


Figure S5. Pictures of particles **4b** before and after CO₂ bubbling observed under a UV lamp at 345 nm (see video)

DEAEMA particles with OEGMA500 (5)

Synthetic procedure is detailed in the main text. In this case, OEGMA, MW = 500 Da, Ω -end: CH₃ (0.055 g), DEAEMA (2.5 g), EGDMA (0.025 g) and KPS (0.025 g) were used in the general procedure.

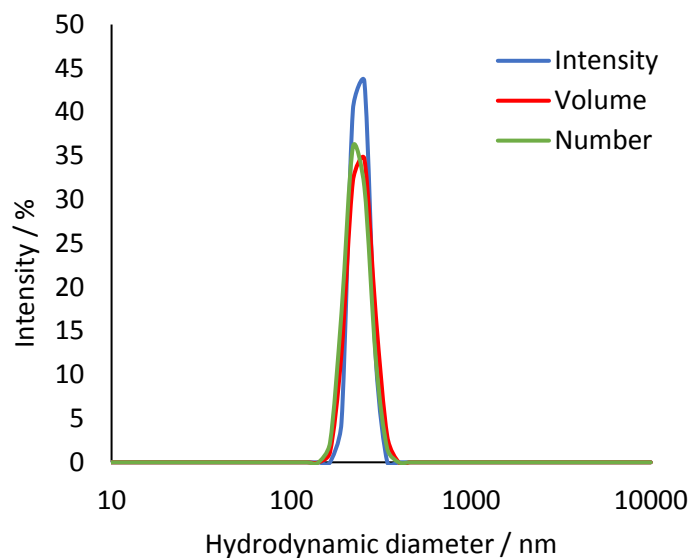


Figure S6. Intensity, volume and number-weighted particles size distribution obtained by DLS for 5

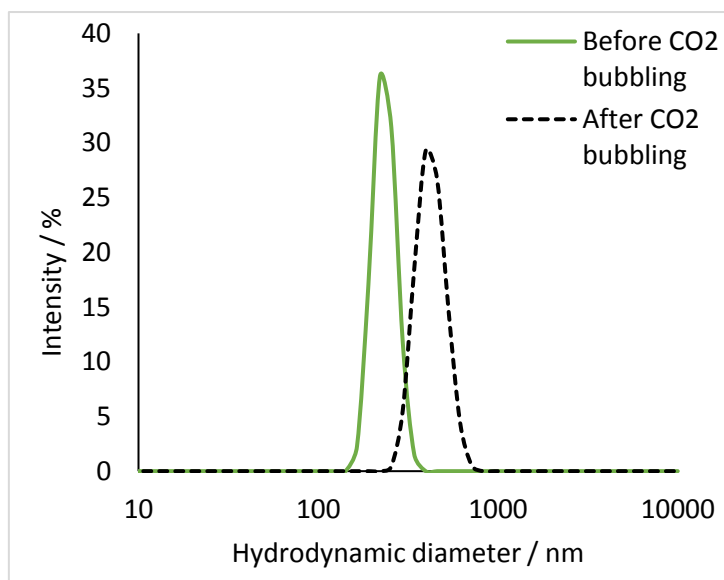


Figure S7. Number-weighted particles size distribution obtained by DLS before and after CO₂ bubbling for 5

DEAEMA particles with OEGMA950 (6)

Synthetic procedure is detailed in the main text. In this case, OEGMA, MW = 950 Da, Ω -end: CH₃ (0.105 g), DEAEMA (2.5 g), EGDMA (0.025 g) and KPS (0.025 g) were used in the general procedure.

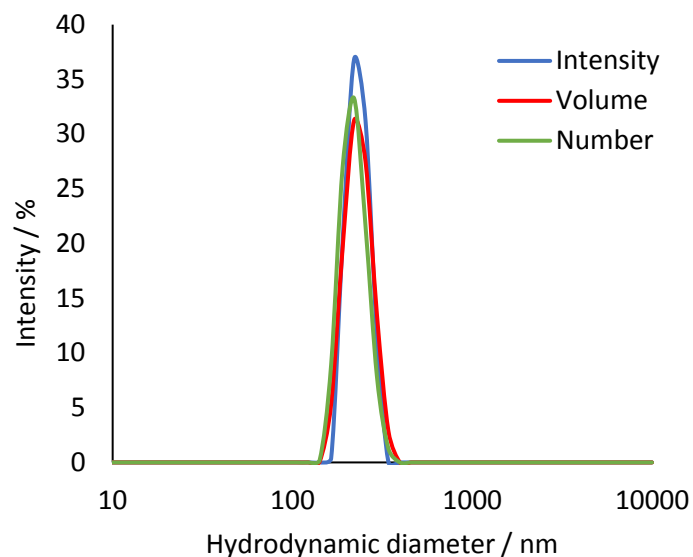


Figure S8. Intensity, volume and number-weighted particles size distribution obtained by DLS for **6**

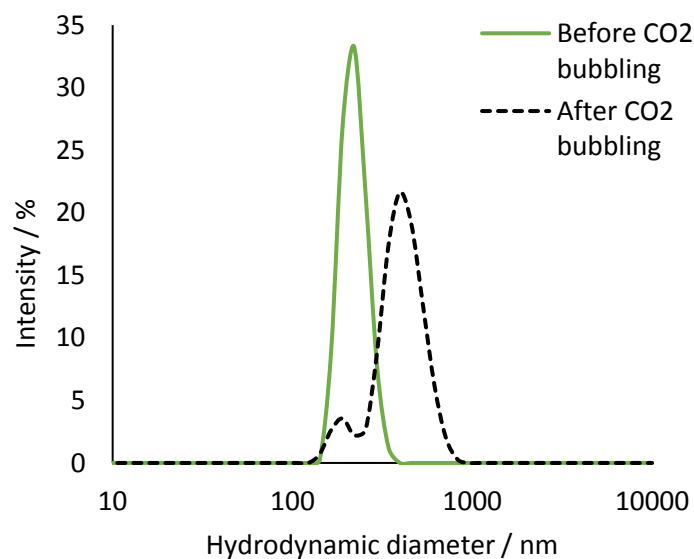


Figure S9. Number-weighted particles size distribution obtained by DLS before and after CO₂ bubbling for **6**

DEAEMA particles with OEGMA2000 (7)

Synthetic procedure is detailed in the main text. In this case, OEGMA, MW = 2000 Da, Ω -end: CH₃, 50 wt% solution in water (0.442 g), DEAEMA (2.5 g), EGDMA (0.025 g) and KPS (0.025 g) were used in the general procedure.

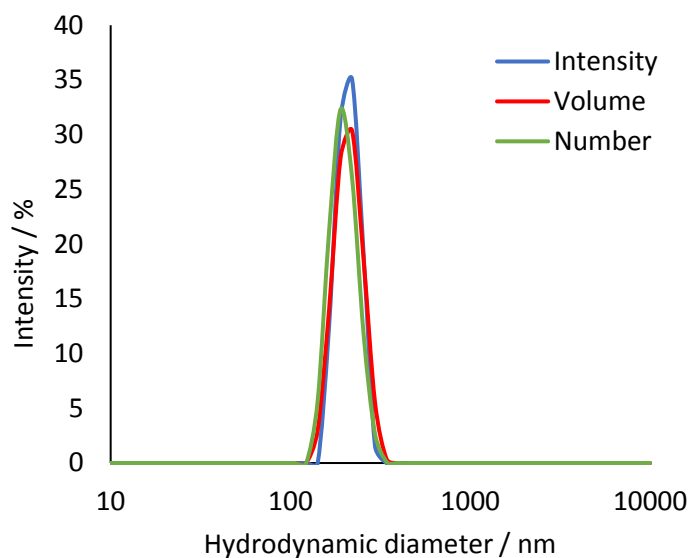


Figure S10. Intensity, volume and number-weighted particles size distribution obtained by DLS for **7**

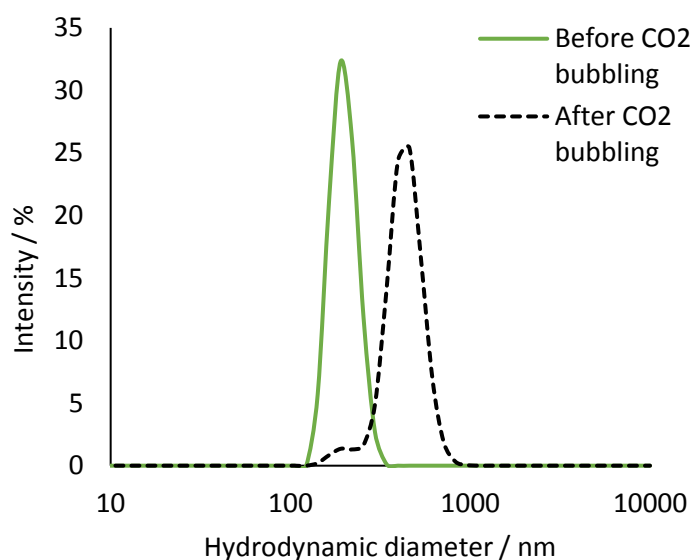


Figure S11. Number-weighted particles size distribution obtained by DLS before and after CO₂ bubbling for **7**

Fluorescent DEAEMA particles with OEGMA2000 (**8**)

Synthetic procedure is detailed in the main text. In this case, OEGMA, MW = 2000 Da, Ω -end: CH₃, received as 50 wt% solution in water (0.442 g), DEAEMA (2.5 g), EGDMA (0.025 g), KPS (0.025 g) and ABMMA, **2** (0.05 g) were used in the general procedure.

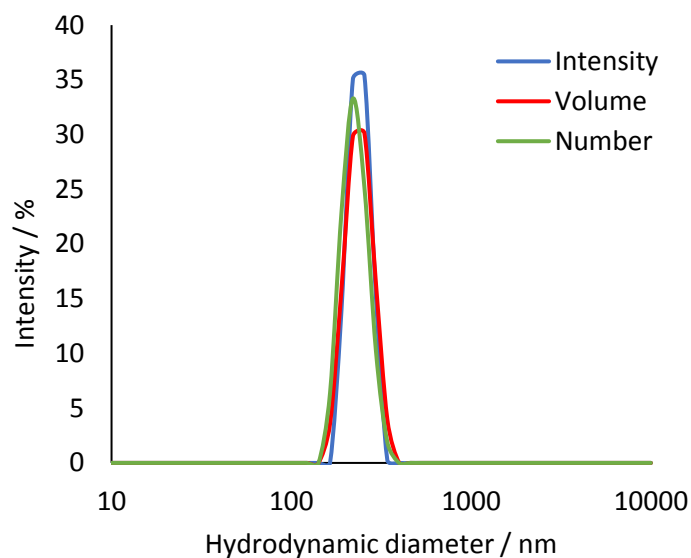


Figure S12. Intensity, volume and number-weighted particles size distribution obtained by DLS for **8**

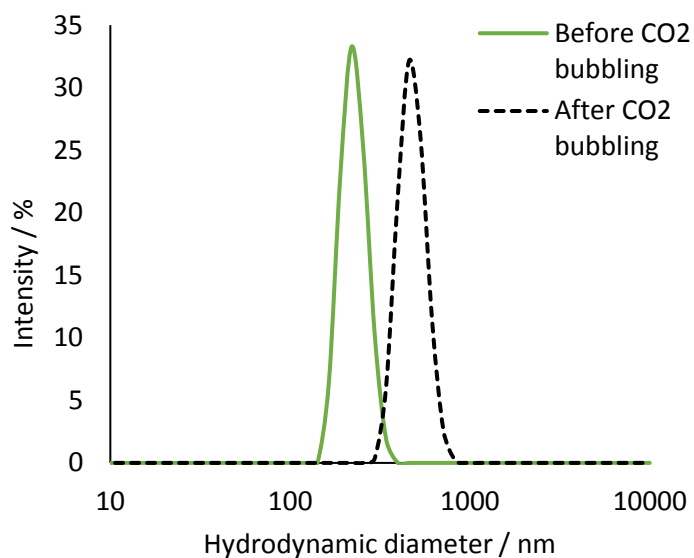


Figure S13. Number-weighted particles size distribution obtained by DLS before and after CO₂ bubbling for **8**

5. References

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