

SUPPORTING INFORMATION

Synthetic details for the preparation of the PEO-PSAGMA-PDEA triblock copolymer

Synthesis of PEO₄₅-Br macro-initiator

Monohydroxy-capped PEO (PEO₄₅-OH; mean degree of polymerization = 45 and $M_w/M_n = 1.07$) was purchased from Aldrich. The PEO-based macro-initiator (PEO₄₅-Br) was synthesized by esterification of the hydroxy end-group of PEO₄₅-OH using 2-bromoisobutyric acid in the presence of 1,3-dicyclohexyl carbodiimide (DCC) and 4-(dimethylamino)pyridine (4-DMAP) as described in the literature (see Lee, S. B.; Russell, A. J.; Matyjaszewski, K. *Biomacromolecules* **2003**, 4, 1386). ¹H NMR studies [CDCl₃: δ 4.3 (2H, COOCH₂), δ 3.1-3.8 (183H, OCH₂CH₂O), δ 1.9 (6H, C(CH₃)₂Br)] indicated that the degree of esterification of the PEO₄₅-OH precursor was essentially 100 %.

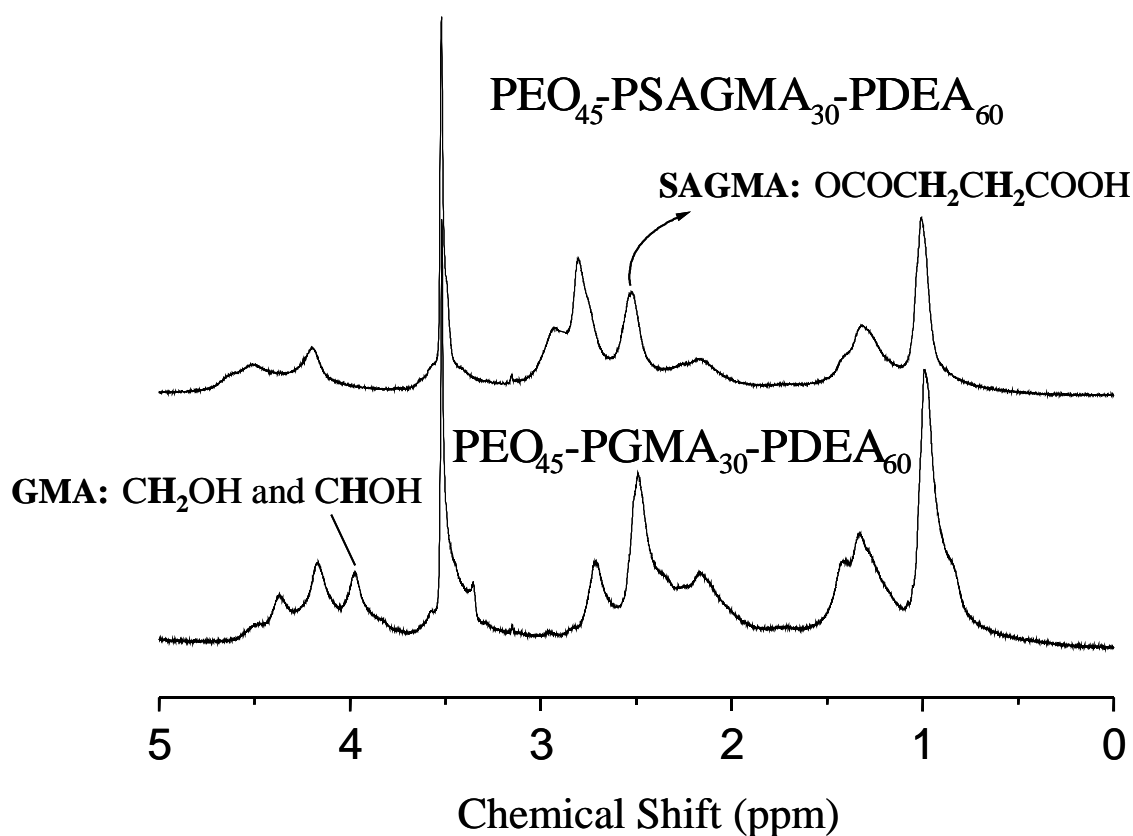
ATRP protocol

PEO₄₅-Br (2.00 g, 0.93 mmol) and GMA (4.47 g, 27.9 mmol, target DP = 30) were dissolved in methanol (6 ml). After purging with nitrogen for 30 min., Cu(I)Br (66.0 mg, 0.46 mmol) and bpy (147.0 mg, 0.94 mmol) were added. The reaction mixture immediately became dark brown and progressively more viscous, indicating the onset of polymerization. After 4 h, ¹H NMR analysis indicated that 96 % GMA had been polymerized. A 50 w/v % methanolic solution of DEA monomer (10.32 g, 55.8 mmol, target DP = 60; previously purged with nitrogen gas for 30 min.) was then added to this reaction solution. The reaction mixture was maintained under dry nitrogen for the duration of the second-stage polymerization. After 15 h, the vinyl double bonds at δ 5.5-6.0 were no longer detected by ¹H NMR, indicating very high conversion (> 99 %). The reaction solution turned blue on exposure to air, indicating aerial oxidation of the Cu(I) catalyst. The resulting copolymer was diluted with methanol and passed through a silica column to remove the spent ATRP catalyst. The final PEO₄₅-PGMA₃₀-PDEA₆₀ triblock copolymer precursor was dried under vacuum overnight to obtain a white product. The

number-average molecular weight (M_n) of the copolymer obtained by ^1H NMR studies was 18,700. DMF GPC studies [vs. poly(methyl methacrylate) standards] indicated a M_n of 21,200 g mol^{-1} and a M_w/M_n of 1.34.

Esterification of the GMA block

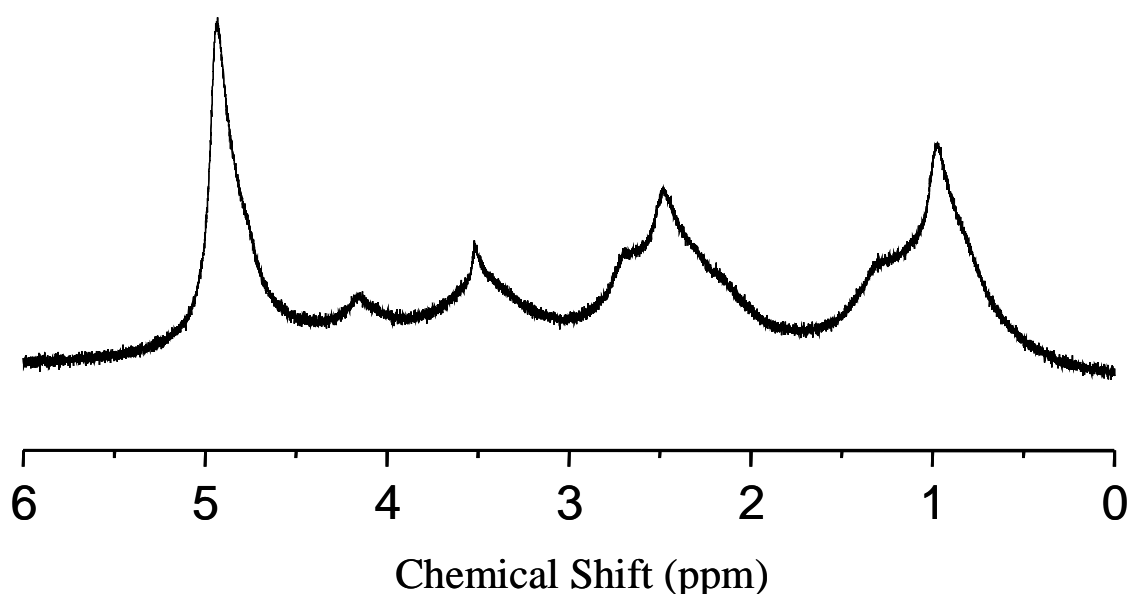
The hydroxy groups of the GMA residues of the triblock copolymer were reacted with excess succinic anhydride (SA; SA/GMA molar ratio = 4.0) in anhydrous pyridine at a triblock copolymer concentration of 25 w/v %. ^1H NMR studies indicated that complete esterification was achieved within 24 h at 20 °C. A five-fold molar excess of methanol (relative to the unreacted SA) was added to consume the unreacted SA, followed by precipitation into excess 2:1 diethyl ether/*n*-hexane to remove the small molecule by-products. The final zwitterionic $\text{PEO}_{45}\text{-PSAGMA}_{30}\text{-PDEA}_{60}$ triblock copolymer was dried under vacuum overnight to obtain a white product. No GMA signals were observed from ^1H NMR spectrum (see Supporting Figure 1), indicating at least 95 % esterification was achieved under these mild conditions.



Supporting Figure 1. ^1H NMR spectra of the $\text{PEO}_{45}\text{-PGMA}_{30}\text{-PDEA}_{60}$ triblock precursor (lower spectrum) and the S2 corresponding zwitterionic $\text{PEO}_{45}\text{-PSAGMA}_{30}\text{-PDEA}_{60}$ triblock copolymer (upper spectrum) recorded in d_5 -pyridine.

The PEO₄₅-PSAGMA₃₀-PDEA₆₀ triblock copolymer (5.00 g, 6.25 mmol SAGMA units) was added in 40 mL double-distilled water and the solution was adjusted to pH 9.0. After the copolymer was dissolved, the solution was stirred for another 2 h to make sure that micellization reached equilibrium. The cross-linking reagent, 2,2'-(ethylenedioxy)bis(ethylamine) (0.926 g, 6.25 mmol, 100 mol % relative to SAGMA units) was added at 20 °C under stirring. The solution was re-adjusted to pH 9.0 and stirred for 30 min at 20 °C. 1-(3-(Dimethylamino)propyl)-3-ethylcarbodiimide methiodide [3.71 g, 12.5 mmol, two equivalents of 2,2'-(ethylenedioxy)bis(ethylamine)] was added to the reaction solution. The reaction mixture was stirred at 20 °C for a further 3 h, and thereafter the solution was dialyzed against distilled water for three days using dialysis membrane (20 kDa cut-off molecular weight) to remove small molecule by-products. A solid sample was obtained by lyophilization for ¹H NMR measurement.

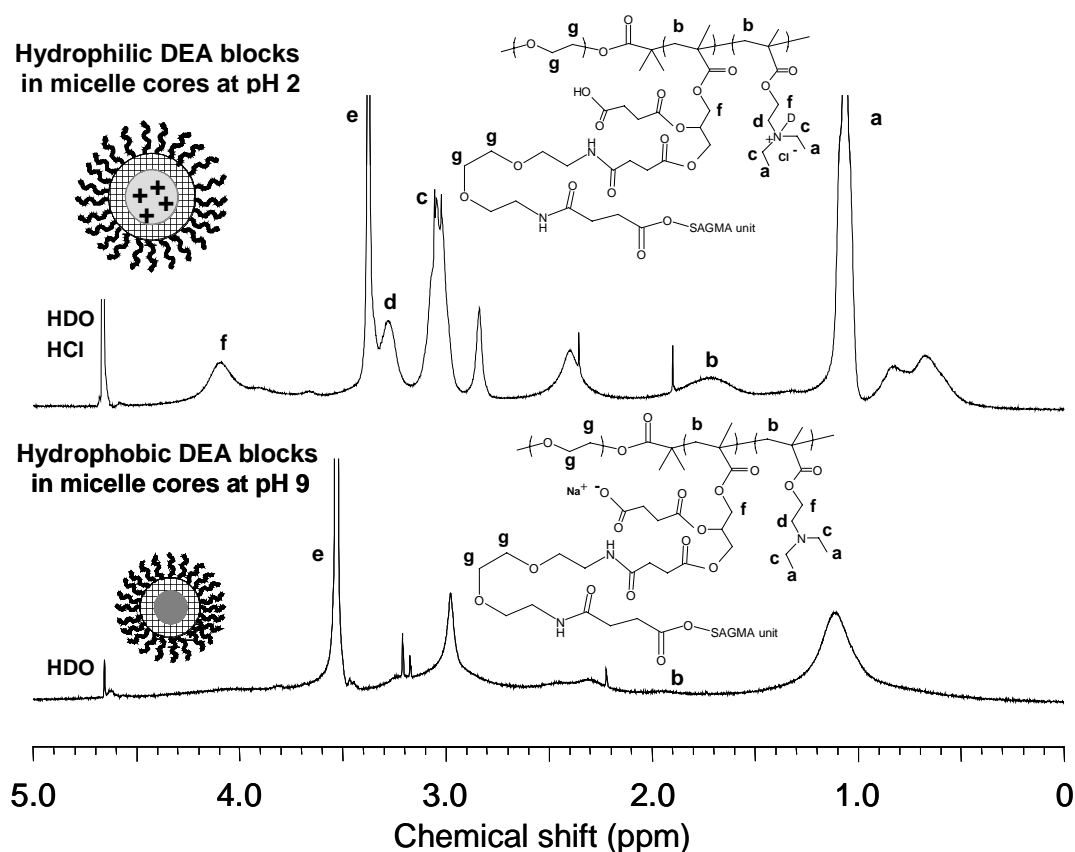
Supporting Figure 2 shows the ¹H NMR spectra of the shell cross-linked micelles redispersed in d₅-pyridine after freeze-drying from water. The signals are significantly broadened due to the solid-like nature of the shell cross-linked micelles. The incorporation efficiency of cross-linking agent was estimated by ¹H NMR studies based on the increase of the integrated signals at δ 3.1-3.8 (due to the



Supporting Figure 2. ¹H NMR spectrum (d₅-pyridine) of the shell cross-linked micelles prepared from the PEO₄₅-PSAGMA₃₀-PDEA₆₀ triblock copolymer. The target degree of cross-linking was 100 %.

OCH₂CH₂O of PEO and CONHCH₂CH₂OCH₂CH₂OCH₂CH₂NHCO of the cross-linked residues), relative to the backbone methacrylate [CH₂CH(CH₃)] and DEA residue [N(CH₂CH₃)₂] signals at δ 0.6 - 1.6. The incorporation efficiency of the cross-linking agent, which is not necessarily the same as the degree of cross-linking, is estimated to be around 40 %.

Supporting Fig. 3 shows ¹H NMR spectra of the shell cross-linked micelles recorded at pH 2 (DCI/D₂O) and pH 9 (NaOD/D₂O). These results indicate that the hydrophobic PDEA micellar core is highly solvated at pH 2 due to protonation, which leads to cationic nanogel character. In contrast, the PDEA chains are largely deprotonated (and hence dehydrated) at pH 9, since the PDEA signals that were originally prominent at 1.1, 3.1, 3.3-3.4 and 4.2 ppm are now substantially attenuated.



Supporting Figure 3. ¹H NMR spectrum (D₂O) of the shell cross-linked micelles prepared from the PEO₄₅-PSAGMA₃₀-PDEA₆₀ triblock copolymer at pH 2 and pH 9. The target degree of cross-linking was 100 %.

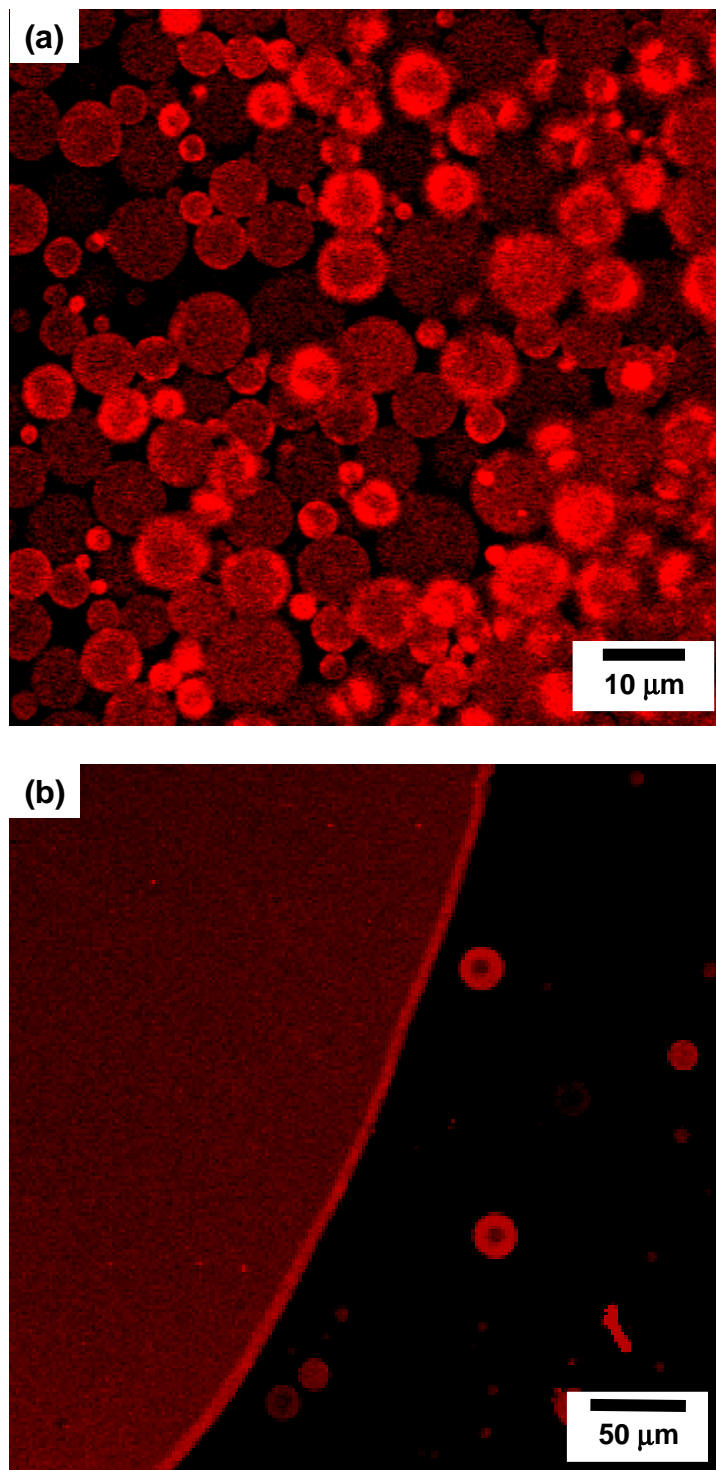
Synthesis of Fluorescent Shell Cross-linked Micelles

To the 5 mL shell cross-linked micelles (5 wt.% solid content, approximately 0.38 mmol carboxylic acid group) aqueous solution, Rhodamine B [0.18 g, 0.38 mmol, one equivalent based on carboxylic acid groups] and 1-(3-(dimethylamino)propyl)-3-ethylcarbodiimide methiodide [0.22 g, 0.75 mmol, two equivalents based on carboxylic acid groups] was added and the solution was adjusted to pH 9. After stirring for 1 h at 20 °C, the cross-linking reagent, 2,2'-(ethylenedioxy)bis(ethylamine) (56 mg, 0.38 mmol, 100 mol % relative to carboxylic acid group) was added at 20 °C under stirring. The reaction mixture was stirred at 20 °C for a further 24 h, and thereafter the solution was dialyzed against distilled water for one week using dialysis membrane (20 kDa cut-off molecular weight) to remove small molecule by-products.

The 1-undecanol-in-water emulsion droplets stabilized with fluorescent shell cross-linked micelles were observed with a confocal laser scanning microscope (Zeiss LSM 510 Meta on a Axiovert 200M microscope). This was equipped with a He-Ne laser, operating at 543 nm and 1 mW. The diluted emulsion was placed on the glass slide and a cover glass was placed over it. The confocal laser scanning image was produced using an emission wavelength between 550 and 600 nm.

Confocal laser microscopy studies of the 1-undecanol-in-water emulsion (see Supporting Figure 4a) confirmed the presence of a red halo surrounding the emulsion droplets. This indicates that the shell cross-linked micelles were adsorbed at the oil-water interface, as expected. After lowering the solution pH to pH 2 by adding HCl, almost all of the emulsion droplets coalesced to form giant millimeter-sized 1-undecanol droplets within a few minutes. In Supporting Figure 4b, part of one of these millimeter-sized 1-undecanol droplets, and also a few remaining emulsion droplets of 15-20 μm diameter, were imaged approximately 1 h after the addition of HCl.

Supporting Figure 4. Confocal laser scanning images of 1-undecanol-in-water emulsion droplets prepared at pH 8 using Rhodamine B-labeled fluorescent shell cross-linked micelles (a) before demulsification and (b) after demulsification at pH 2. The red halo in image (a) indicates that the shell cross-linked micelles were adsorbed around the micrometer-sized emulsion droplets, as expected. There is also some evidence for the presence of the shell cross-linked micelles at the surface of the millimeter-sized macroscopic droplets at pH 2.

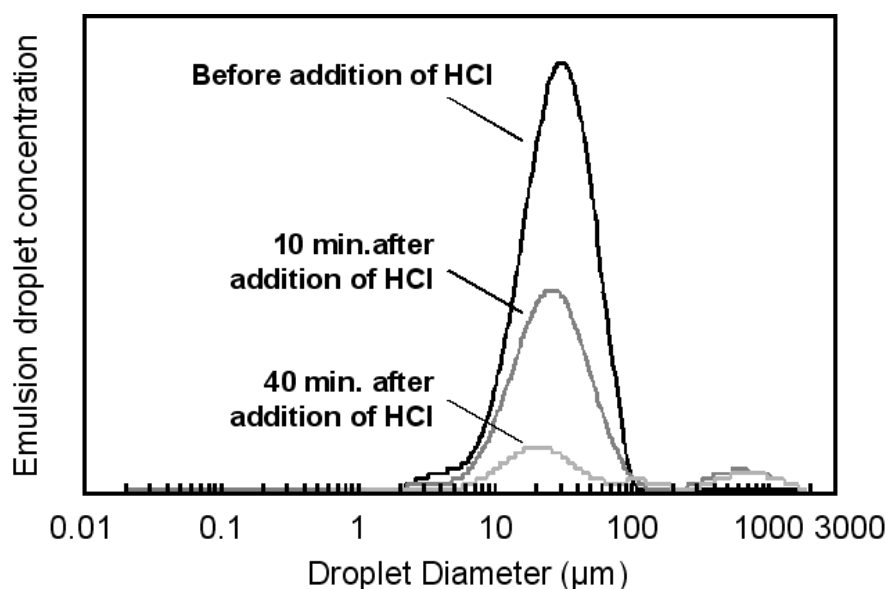


Supporting Table 1. Summary of the properties of the 1-undecanol-in-water emulsions stabilized with shell cross-linked micelles.

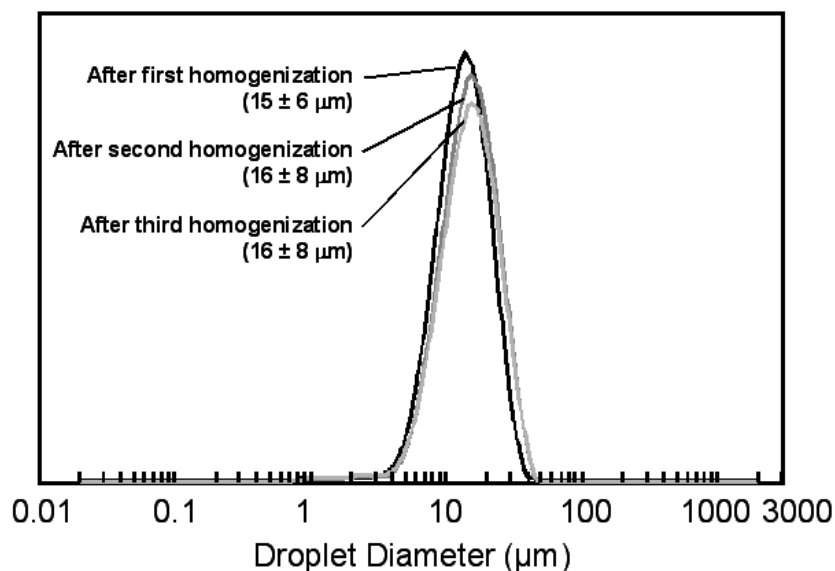
Target Degree of Cross-linking	pH	Conductivity of Shell Cross-linked Micelle Solution / μScm^{-1}	Conductivity of Emulsion / μScm^{-1}	Type of Emulsion	% Emulsion @ 24 hours ¹	% Emulsion @ 3 months ¹	Oil Droplet Diameter ² / μm	Droplet Diameter Range ³ / μm
100 %	2.2	1830	1750	Oil/water	5	~ 0 ⁴	-	-
	8.5	110	60	Oil/water	59	53	18 \pm 15	2-80
0 %	2.4	> 1999	620	Oil/water	60	35	69 \pm 64	2-155
	8.3	1034	330	Oil/water	68	66	45 \pm 19	5-75

1. Calculated as follows: % emulsion = (volume of emulsion/initial volume of oil + volume of aqueous SCL micelle solution prior to emulsification) x 100 %
2. As measured using a Malvern MasterSizer 2000 instrument.
3. As estimated by optical microscopy.
4. A small number of droplets remained on the glass wall between the oil and water phases.

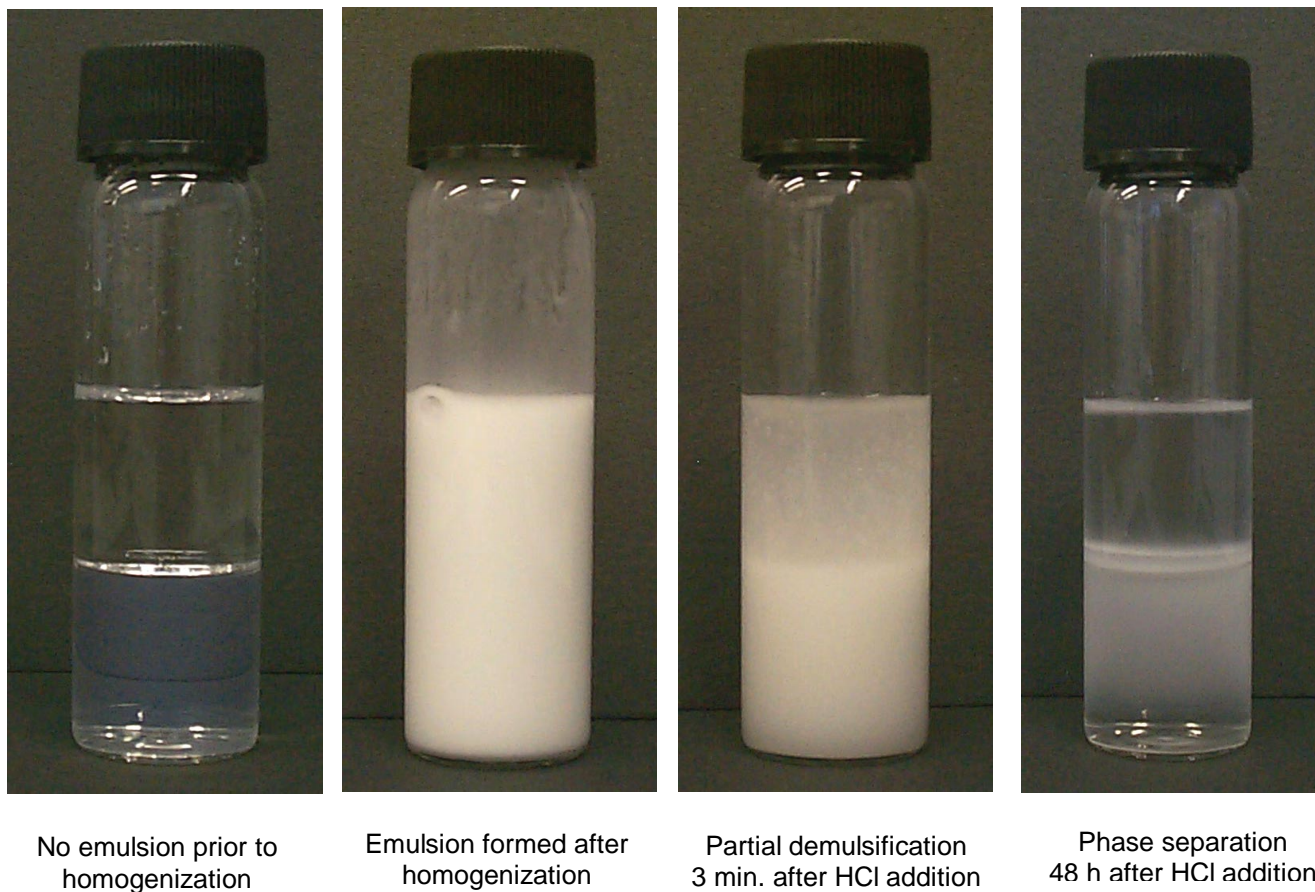
Supporting Figure 5. Change in the droplet size distribution of a 1-undecanol-in-water emulsion prepared at pH 9 using shell cross-linked micelles (target degree of cross-linking = 100 %) during pH-induced demulsification as measured using a Malvern MasterSizer 2000 instrument. The solution pH was changed from 8.5 to 2.8. This illustrates the rapid reduction in droplet concentration at low pH.



Supporting Figure 6. Droplet size distributions of a 1-undecanol-in-water emulsion after three (re)homogenization cycles at pH 9 using shell cross-linked micelles (target degree of cross-linking = 100 %) as measured using a Malvern MasterSizer 2000 instrument.



Supporting Figure 7. A series of digital photographs illustrating the rapid macroscopic phase separation of the 1-undecanol-in-water emulsion prepared using SCL micelles with a target degree of cross-linking of 100 %.



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