Supporting Information

Reactive Polyphosphoester Triblocks as Stabilizers and Modifiers of Emulsion Templated Degradable Scaffolds.

Pascal Boucq[a], Louise Seronvalle[a], Anne des Rieux[b], Christine Jérôme*[a], Antoine Debuigne*[a]

[a] Center for Education and Research on Macromolecules (CERM), CESAM Research Unit, Chemistry Department, University of Liège (ULiege), Quartier Agora, 13 Allée du Six Août, Sart-Tilman, B-4000 Liège, Belgium.

[b] Advanced Drug Delivery and Biomaterials UCLouvain, Université Catholique de Louvain, Louvain Drug Research Institute, 1200, Bruxelles, Belgium.

*Corresponding authors: Antoine Debuigne adebuigne@uliege.be; Christine Jérôme C.Jerome@uliege.be

Synthesis of 2-methoxy-2-oxo-1,3,2-dioxaphospholane (MEP)

A flame-dried 500 mL two-necked flask was charged with dry THF (175 mL), dry MeOH (7.6 mL, 175 mmol), and dry TEA (25 mL, 180 mmol) under argon. A solution of COP (25 g, 175 mmol) in dry THF (25 mL) was added dropwise at 0 °C via an addition funnel. The reaction mixture was stirred overnight under argon. The resulting triethylammonium salt was removed by filtration, and the solvent was evaporated. The residue was purified by fractional distillation (80–90 °C, reduced pressure), yielding MEP as a colorless liquid (17.58 g, 127 mmol, 76.4%). The monomer was characterized by ^{1}H and ^{31}P NMR spectroscopy (Bruker 400 MHz, 25 °C, TMS reference), and spectra were analyzed with MestReNova (14.1.0) (Figure S1). The

chemical shifts for the ^{1}H spectrum are referenced relative to $CDCl_3$ at 7.26 ppm. ^{1}H NMR: δ = 4.61-4.31 (m, 4H), 3.87 (d, 3H) ppm. ^{31}P NMR: δ = 18.85-18.20 ppm.

Synthesis of 2-butoxy-2-oxo-1,3,2-dioxaphospholane (BEP)

A flame-dried 500 mL two-necked flask was charged with dry THF (175 mL), dry butanol (16.01 mL, 175 mmol), and dry TEA (25 mL, 180 mmol) under argon. A solution of COP (25 g, 175 mmol) in dry THF (25 mL) was added dropwise at 0 °C via an addition funnel. The reaction mixture was stirred overnight under argon. The resulting triethylammonium salt was removed by filtration, and the solvent was evaporated. The residue was purified by fractional distillation (90-100 °C, reduced pressure), yielding BEP as a colorless liquid (24.6 g, 136 mmol, 78%). The monomer was characterized by ^{1}H and ^{31}P NMR spectroscopy (Bruker 400 MHz, 25 °C, TMS reference), and spectra were analyzed with MestReNova (14.1.0) (Figure S2). The chemical shifts for the ^{1}H spectrum are referenced relative to $CDCl_3$ at 7.26 ppm. ^{1}H NMR: δ = 4.5-4.25 (m, 4H), 4.2-4.05 (dt, 2H), 1.75-1.60 (p, 2H), 1.5-1.3 (sx, 2H), 1.05-0.85 (t, 3H) ppm. ^{31}P NMR: δ = 17.85-17.30 ppm.

Synthesis of 2-heptoxy-2-oxo-1,3,2-dioxaphospholane (HEP)

A flame-dried 500 mL two-necked flask was charged with dry THF (175 mL), dry 1-heptanol (24.73 mL, 175 mmol), and dry TEA (25 mL, 180 mmol) under argon. A solution of COP (25 g, 175 mmol) in dry THF (25 mL) was added dropwise at 0 °C via an addition funnel. The reaction mixture was stirred overnight under argon. The resulting triethylammonium salt was removed by filtration, and the solvent was evaporated. The residue was purified by fractional distillation (90-100 °C, reduced pressure), yielding BEP as a colorless liquid (28.7 g, 129 mmol, 74%). The monomer was characterized by ^{1}H and ^{31}P NMR spectroscopy (Bruker 400 MHz, 25 °C, TMS reference), and spectra were analyzed with MestReNova (14.1.0) (Figure S3). The chemical shifts for the ^{1}H spectrum are referenced relative to $CDCl_3$ at 7.26 ppm. ^{1}H NMR: δ

= 4.5-4.25 (m, 4H), 4.2-4.05 (dt, 2H), 1.75-1.60 (p, 2H), 1.45-1.2 (m, 8H), 0.95-0.8 (t, 3H) ppm. ^{31}P NMR: δ = 17.85-17.25 ppm.

Synthesis of dimethacrylated poly(2-methoxy-2-oxo-1,3,2-dioxaphospholane) (PM-DMA)

Tetraethylene glycol (0.53 g, 2.7 mmol) and TU (1.33 g, 3.6 mmol) were introduced into a 100 mL flame-dried flask and dehydrated by three cycles of azeotropic distillation with toluene. MEP (3 g, 21.6 mmol) was then added, and the mixture was placed under vacuum for 15 min. Subsequently, dry dichloromethane (10 mL) was introduced under an argon atmosphere. Polymerization was initiated by the addition of dry DBU (1.8 mL, 12 mmol) at 0 °C and allowed to proceed for 45 min under stirring. The reaction was terminated by adding an excess of 2-isocyanatoethyl methacrylate (1.5 mL, 10.6 mmol), followed by stirring for 30 min at 25 °C. The resulting polymer was precipitated twice in ice-cold diethyl ether, collected with methanol, and stabilized by addition of hydroquinone (0.7 mol%). The product was dried under vacuum for 24 h, yielding a viscous polymer. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, Figure S4): δ = 6.2-6.05 (s, 2H), 5.65-5.5 (s, 2H), 4.4-4.1 (m, 50H), 3.9-3.75 (m, 30H), 3.75-3.65 (m, 4H), 3.65-3.60 (m, 8H), 2.0-1.9 (s, 6H) ppm. ^{31}P NMR ($CDCl_3$, 25 °C): δ = 1.08, -0.17, -1.46 ppm.

The resulting polymer was analyzed by size exclusion chromatography (SEC, Waters) in DMF containing 0.025 M of LiBr at 55°C with a PS calibration (PSS GRAM 100 Å) giving the following features : Mn = 1090, Mw = 1830, Mz = 3360, with a dispersity of 1.67.

Table S1. PolyHIPE formulation

Samples	PM-DMA (mg)	PMBM-DMA (mg)	PMHM-DMA (mg)	LAP (mg)	Water (mg)	Internal Phase	Internal Phase (g)
PH_0	150	-	-	1	150	Mineral Oil	1.416
PH_1	150	30	-	1	150	Cyclohexane	1.309
PH_2	150	30	-	1	150	Mineral Oil	1.416
PH_3	150	-	30	1	150	Cyclohexane	1.309
PH_4	150	-	30	1	150	Mineral Oil	1.416
PH_5	75	75	-	1	150	Cyclohexane	1.309
PH_6	75	75	-	1	150	Mineral Oil	1.416
PH_7	75	-	75	1	150	Cyclohexane	1.309
PH_8	75	-	75	1	150	Mineral Oil	1.416
PH_9	-	150	-	1	150	Cyclohexane	1.309
PH_{10}	-	150	-	1	150	Mineral Oil	1.416
PH_{11}	-	-	150	1	150	Cyclohexane	1.309
PH_{12}	-	-	150	1	150	Mineral Oil	1.416

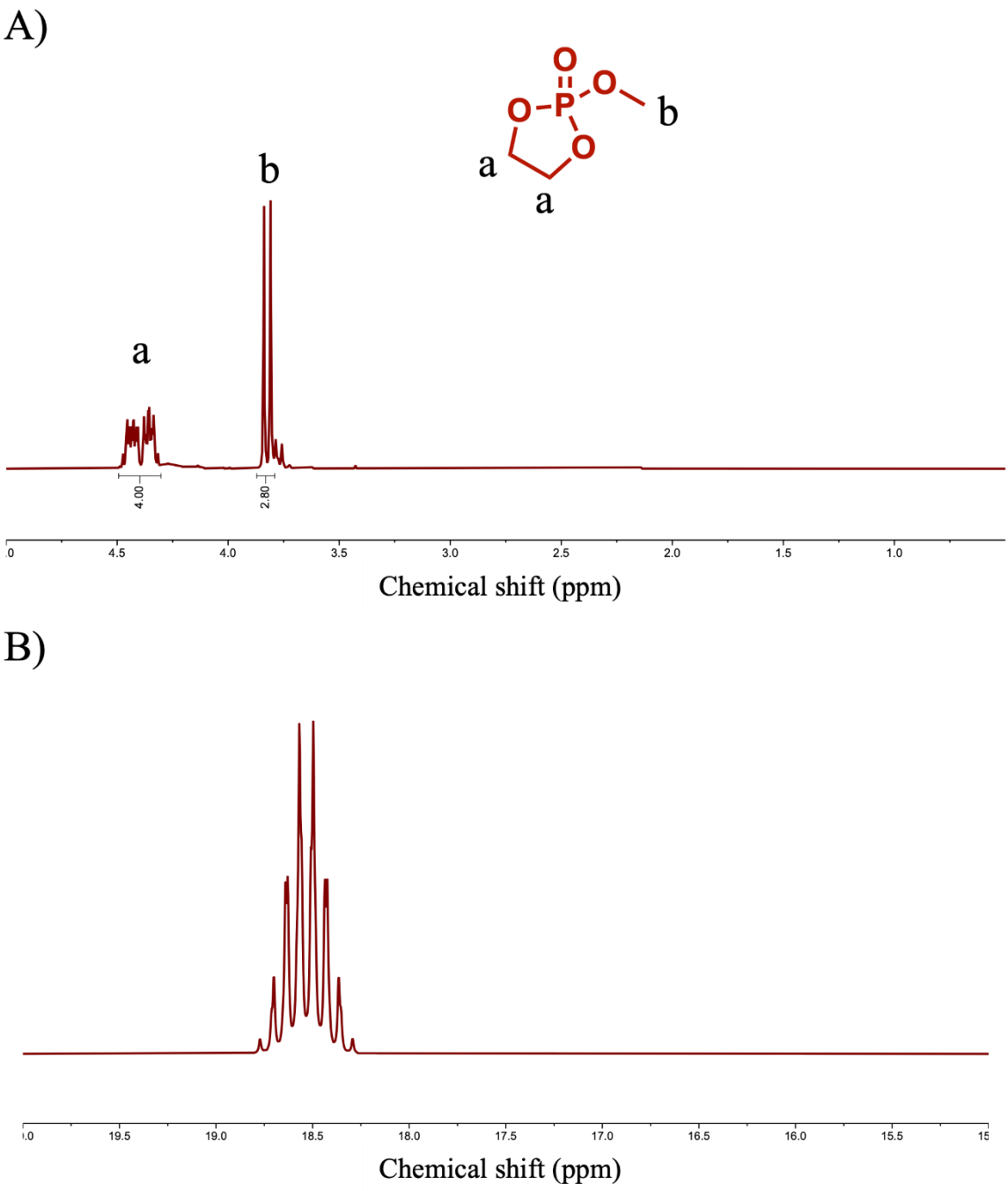


Figure S1. (A) ^{1}H NMR and (B) ^{31}P NMR spectra of MEP.

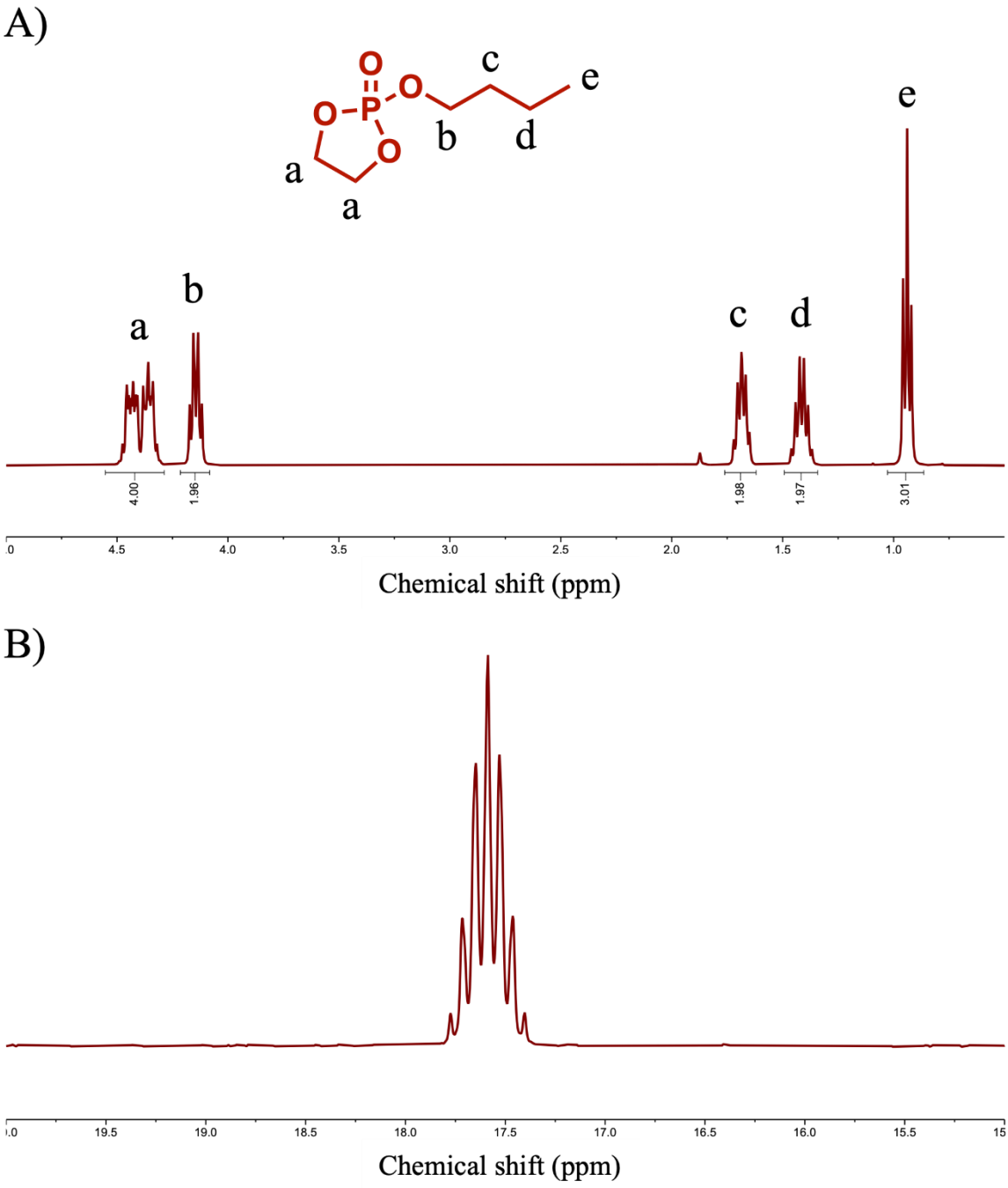


Figure S2. (A) ^{1}H NMR and (B) ^{31}P NMR spectra of BEP.

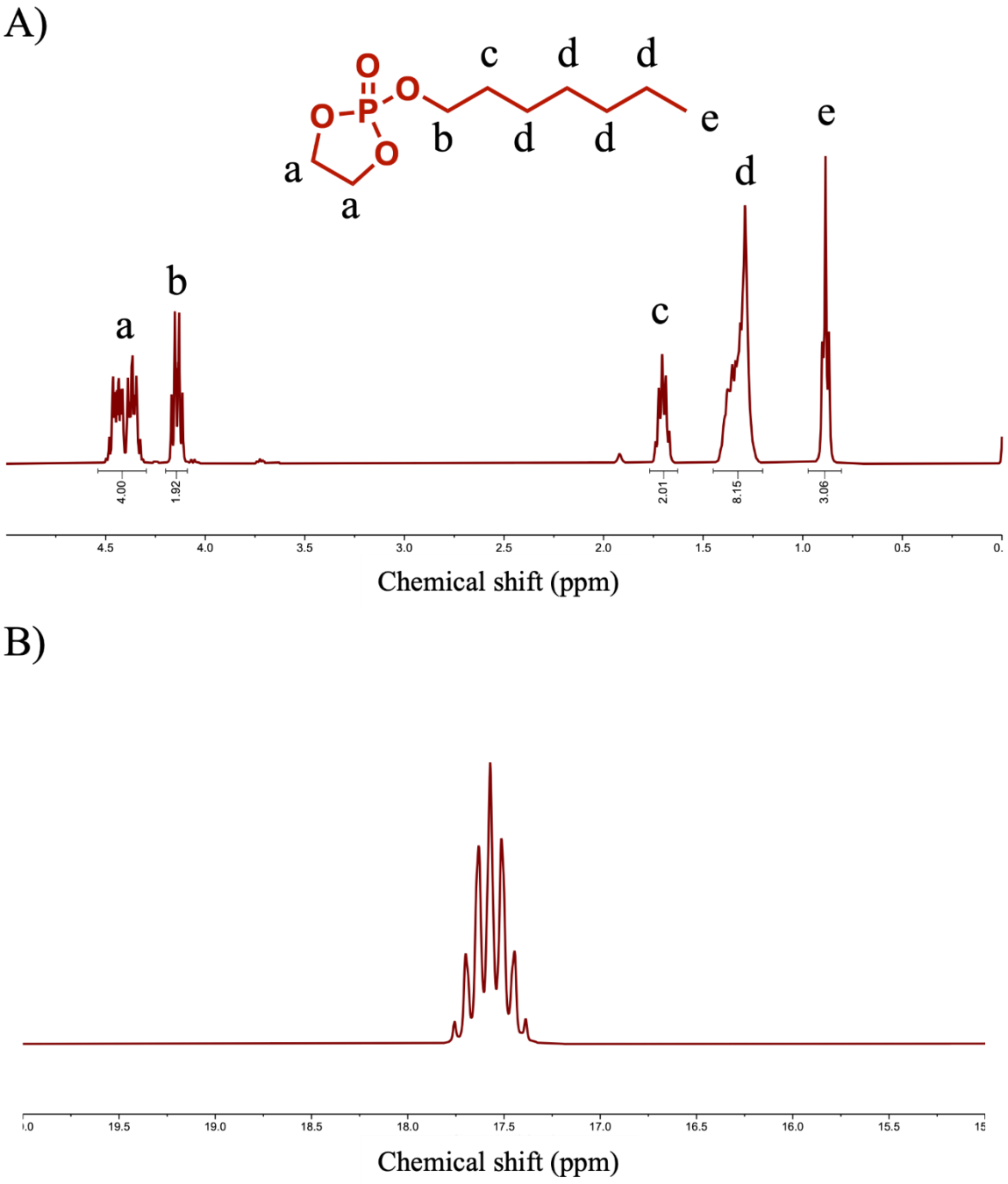


Figure S3. (A) ^{1}H NMR and (B) ^{31}P NMR spectra of HEP.

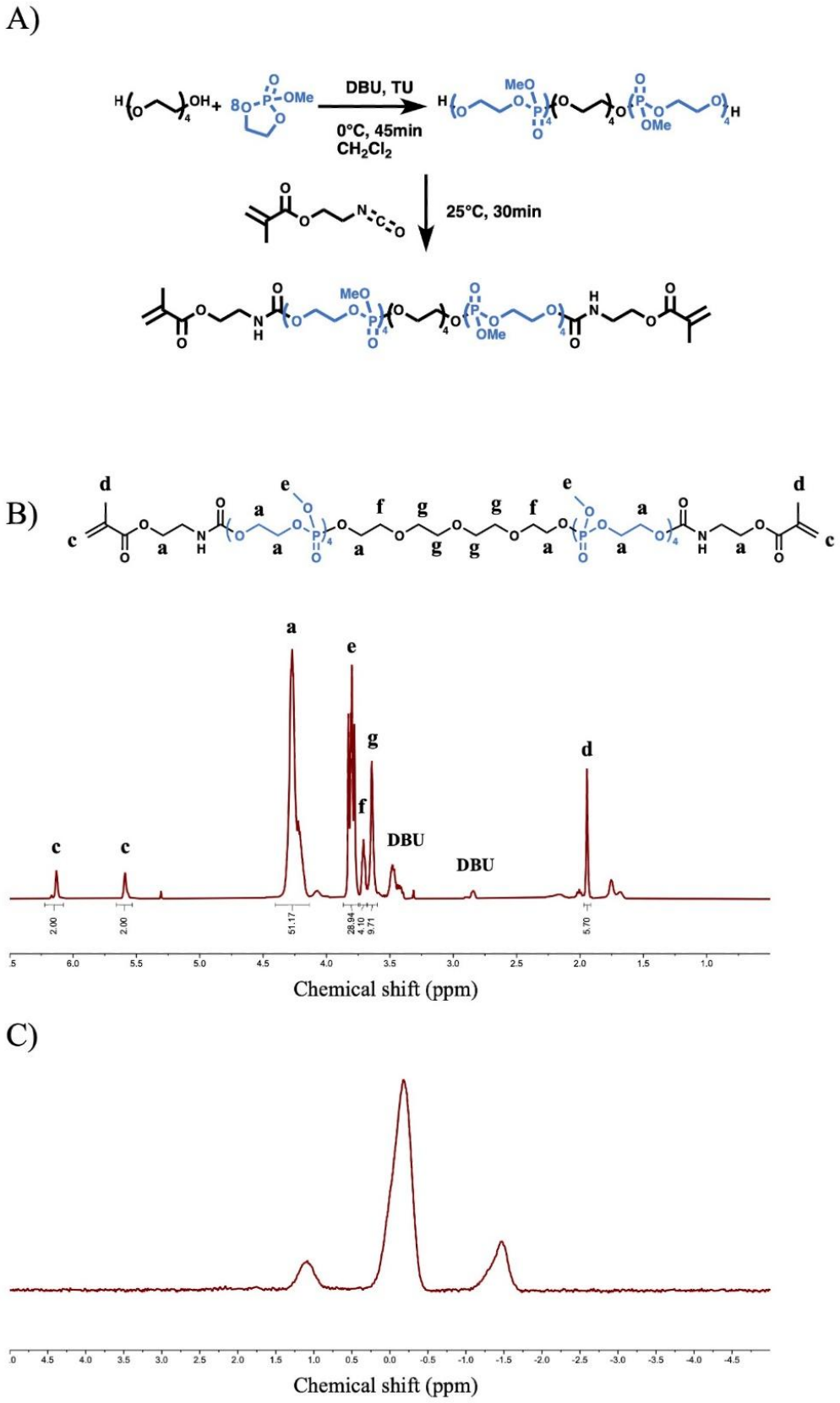


Figure S4. PM-DMA (A) synthesis, (B) ^{1}H NMR, and (C) ^{31}P NMR spectra.

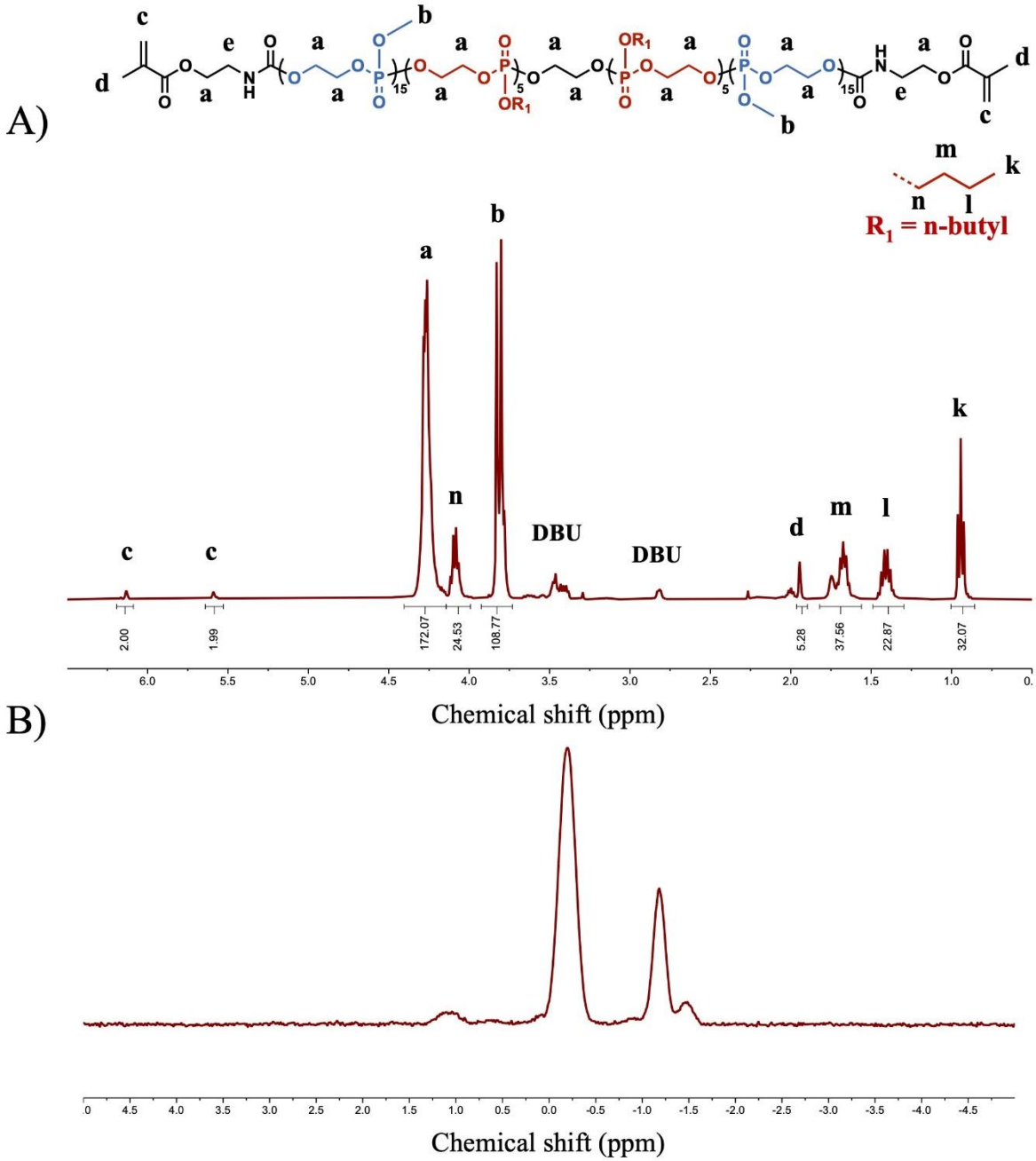


Figure S5. (A) ^{1}H NMR and (B) ^{31}P NMR spectra of PMBM-DMA.

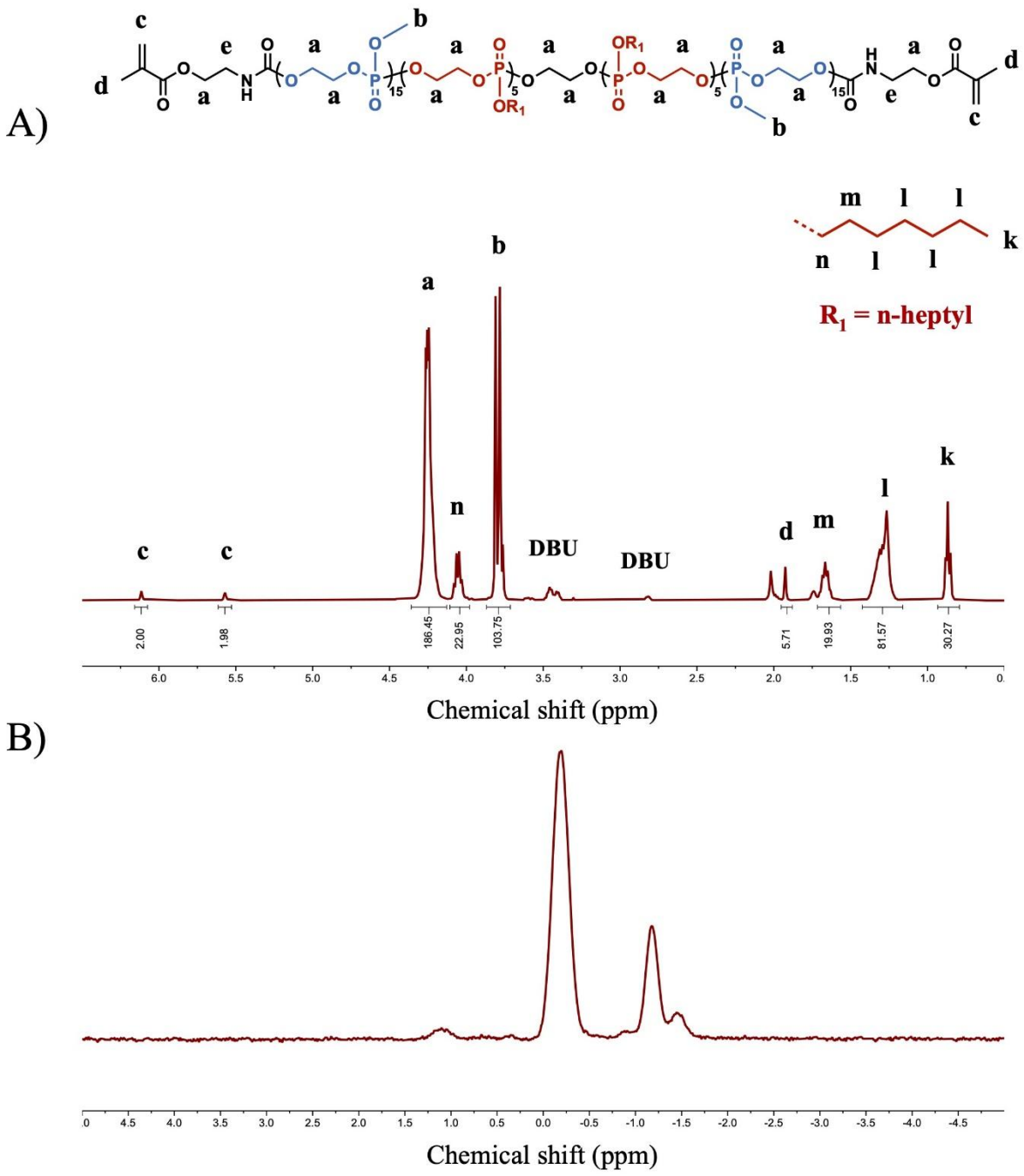
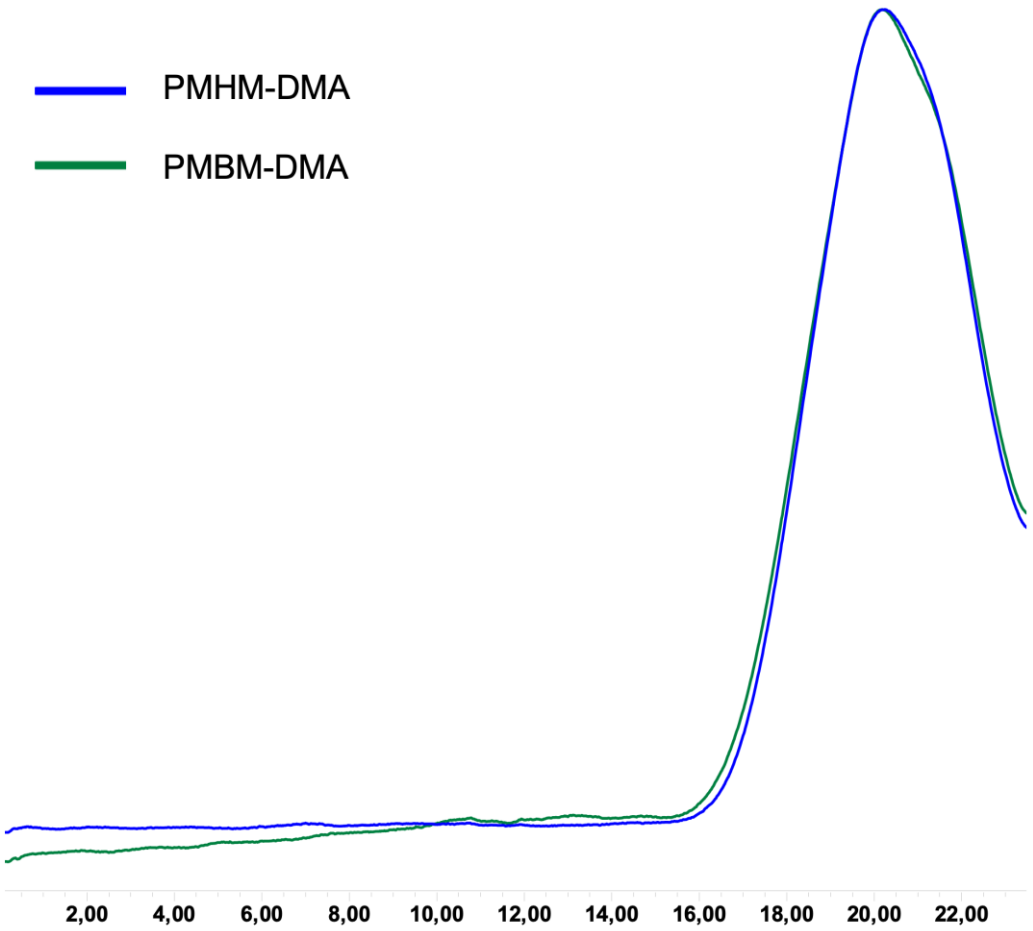


Figure S6. (A) ^{1}H NMR and (B) ^{31}P NMR spectra of PMHM-DMA.

A)



B)

Surfactant	RT	Mp (Da)	Mn (Da)	Mw (Da)	Dispersity
PMHM-DMA	20.08	6700	4900	7600	1.55
PMBM-DMA	20.08	6700	4900	7800	1.59

Figure S7. A) SEC curves in DMF of the triblock PMHM-DMA and PMBM-DMA. B) Summary of SEC characteristics.

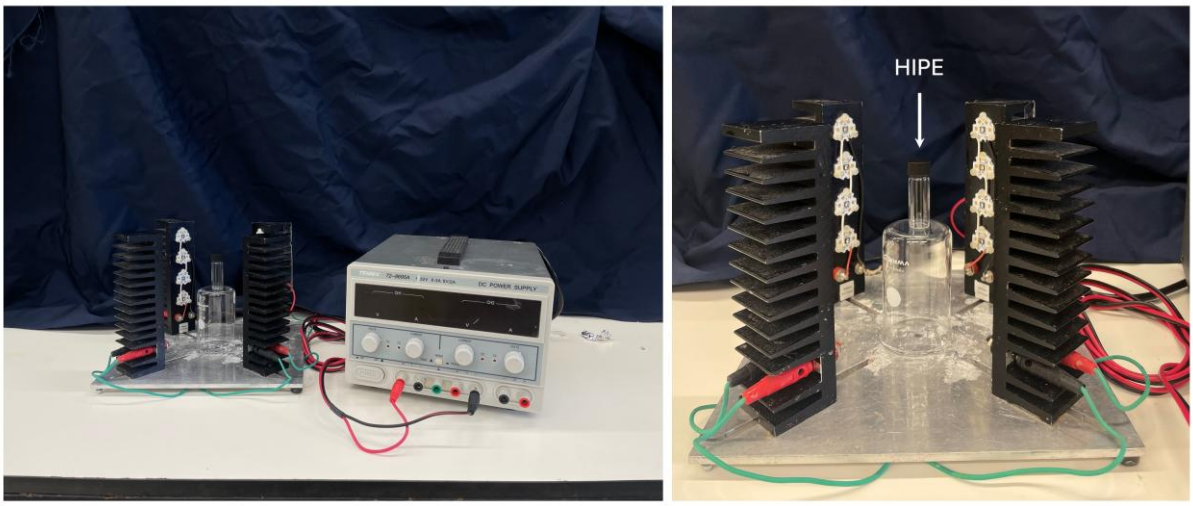


Figure S8. Photoirradiation setup to cure the emulsion.

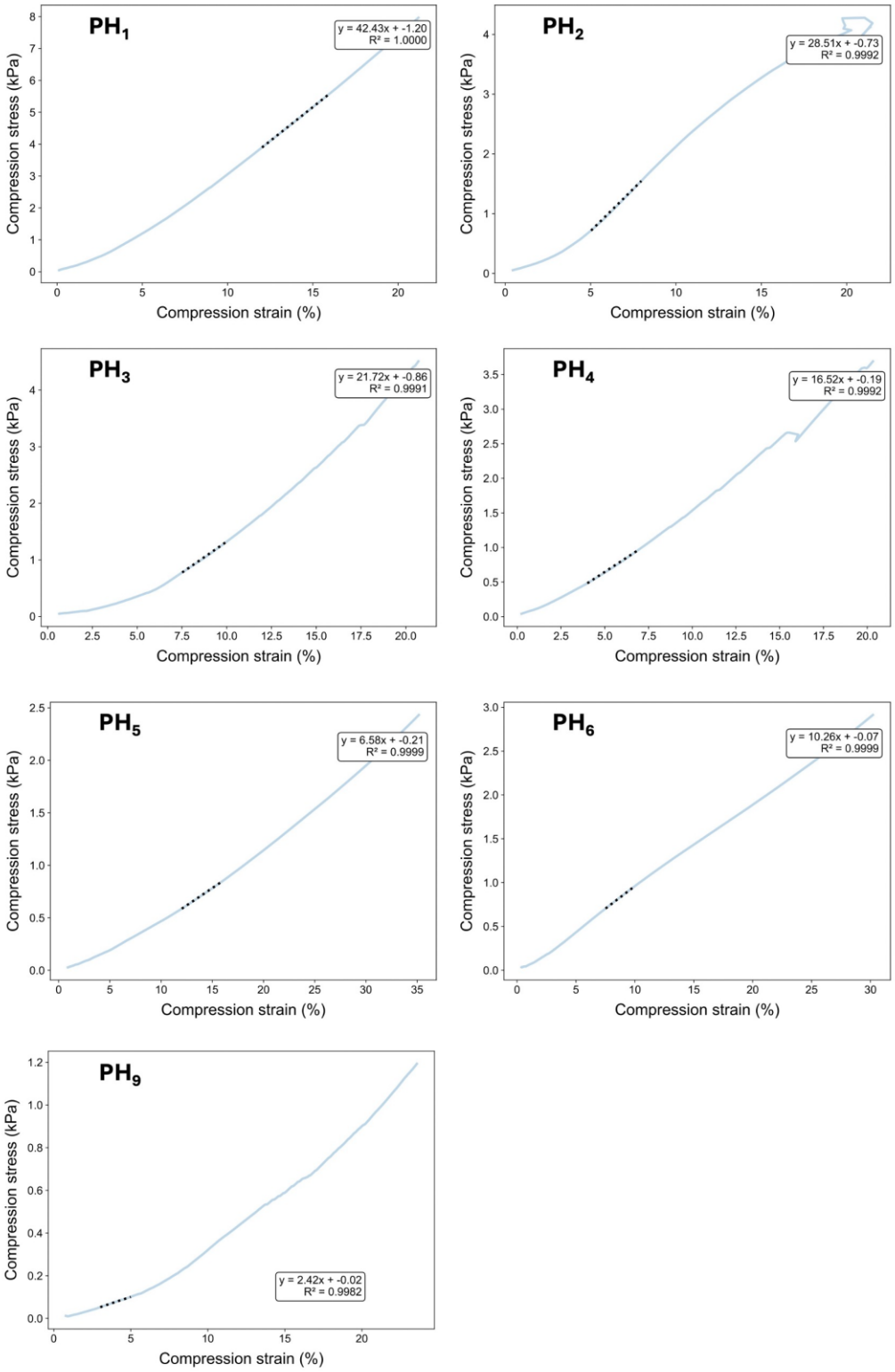


Figure S9. Representative compression test curves for all tested polyHIPE formulations, including determination of the Young's modulus.

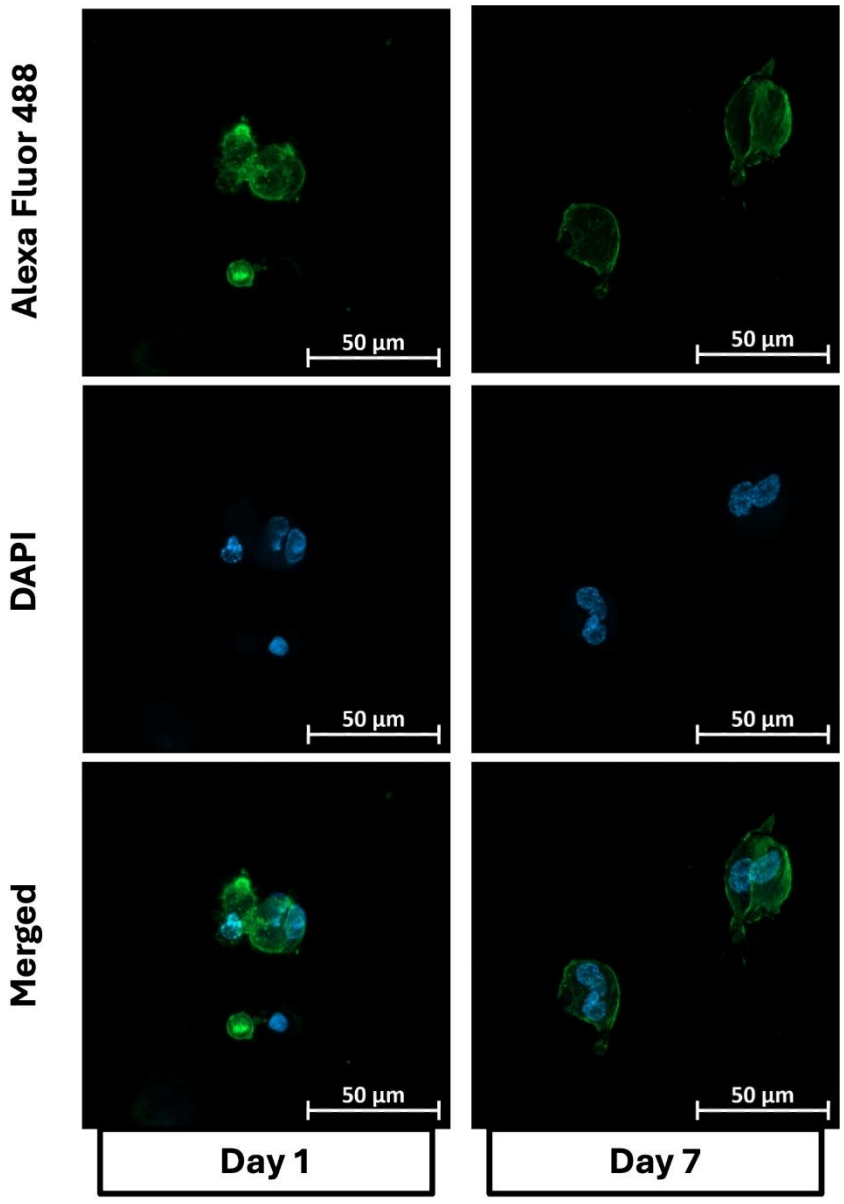


Figure S10. CLSM images of cell morphology after 1 and 7 days of culture on a PPE scaffold made with 40 wt% of PMHM-DMA and 60 wt% PM-DMA in the external phase.