Supporting Information for: Temperature Responsive Poly(phosphonate) copolymers: from single chains to macroscopic coacervates

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Materials

Solvents and chemicals were purchased from Acros Organics, Sigma Aldrich or Fluka and used as received, unless otherwise stated. All chemicals were purchased in highest purities, dry and stored over molecular sieve (4Å), if possible. 2-(Benzyloxy)ethanol and DBU were distilled from calcium hydride and stored over molecular sieve (4Å) under argon prior to use. Deuterated solvents were purchased from Deutero GmbH (Kastellaun, Germany) and used as received. Ultrapure water with a resistivity of 18.2 MΩ cm^{-1} (Milli-Q, Millipore®) was used to prepare buffers. Dulbecco's Modified Eagle Medium (DMEM), fetal bovine albumin (FBS penicillin and streptomycin were purchased from Invitrogen, Germany. RAW264.7 cells were purchased from the American Type Culture Collection (ATCC) and cultivated in DMEM supplemented with 10% FBS, 100 units of penicillin, and 100 mg mL^{-1} streptomycin.

Instrumentation and Characterization Techniques

Size exclusion chromatography (SEC) measurements were performed in DMF (1 g L^{-1} LiBr added) at 60°C and a flow rate of 1 mL min^{-1} with an PSS SECcurity as an integrated instrument, including a PSS GRAM 100-1000 column and a refractive index (RI) detector. Calibration was carried out using poly(ethylene glycol) standards provided by Polymer Standards Service. All NMR experiments were acquired on a Bruker 500 AMX system. The temperature was kept at

298.3 K and calibrated with a standard ^{1}H methanol NMR sample using the topspin 3.0 software (Bruker). $^{13}C\{H\}$ NMR spectra were referenced internally to solvent signals. $^{31}P\{H\}$ NMR spectra were referenced externally to phosphoric acid. The $^{13}C\{H\}$ NMR (125 MHz) and $^{31}P\{H\}$ NMR (201 MHz) measurements were obtained with a 1H powergate decoupling method using 30 ° degree flip angle. 1D NMR spectra were processed with the MestReNova 9.0.1-13254 software whereas ^{1}H DOSY (diffusion orientated spectroscopy) NMR spectra were processed with the TopSpin 3.0 software. Differential Scanning Calorimetry (DSC) measurements were performed using a Mettler-Toledo DSC823 thermal analysis system in the temperature range from -100 to 100 °C under nitrogen with a heating rate of 10 °C min^{-1}. Cloud points were determined either in ultrapure water with a resistivity of 18.2 MΩ cm^{-1} (Milli-Q, Millipore®) or in otherwise stated salt solutions and detected by optical transmittance of a light beam (λ = 500 nm) through a 1 cm sample cell. The measurements were performed in a Jasco V-630 photo spectrometer with a Jasco ETC-717 Peltier element. The intensity of the transmitted light was recorded versus the temperature of the sample cell. The temperature ramp was 1 °C min^{-1} and values were recorded every 0.1 °C. Murine macrophage-like cells (RAW 264.7) were cultivated in DMEM supplemented with 10% FBS, 100 units of penicillin, and 100 mg mL^{-1} streptomycin. Cells were grown in humidified incubator at 37°C and 5% CO_2. The effect of **P(1_x-*co*-2_y)** and **P(1_x-*co*-2_y)** on cell viability of RAW 264.7 cells was measured by CellTiter-Glo Luminescent Cell Viability Assay (Promega) according to manufacturer. Briefly, RAW 264.7 cells were seeded at a density of 15,000 cells cm-2 in 96-well plates (5,000 cells per well in 100 µL volume) and kept at 37°C for 12 h. The cell culture medium was removed from the wells, the polymer solution was added to the indicated concentrations (50 µL per well) and incubated with cells for 48 h. CellTiter-Glo Buffer (10 mL) was transferred to a bottle containing CellTiter-Glo Substrate forming the CellTiter-Glo Reagent. To each well the CellTiter-Glo Reagent (100 µL) was added and the plate was shaken for 2 minutes on an orbital shaker. The luminescent signals were measured with a Tecan infinite M1000.

For CW-EPR spectroscopy, about 15–20 µL of the final sample (15 mg mL^{-1} polymer solution with 0.2 mM TEMPO in DPBS buffer) were filled into micropipettes (BLAUBRAND® intraMARK, Wertheim, Germany) and capped with capillary tube sealant (CRITOSEAL® Leica). The filled micropipettes were then introduced into the X-band ($\nu \approx 9.4$ GHz) benchtop EPR spectrometer MiniScope MS400 (Magnettech, Berlin, Germany) via a guide tube.

The EPR measurements were performed with a magnetic field sweep of 10 mT centered around 336 mT with a scan time of 100 s. The microwave power was set to 8 mW and the modulation amplitude to 0.02 mT. The exact microwave frequencies were recorded with the frequency counter RACAL DANA (model 2101, Neu-Isenburg, Germany). Temperatures were adjusted with the Temperature Controller H03 (Magnettech) with an accuracy of ± 0.25 °C. A temperature control time of at least 2 min was maintained after each temperature change.

Experimental

***O,O*-diethyl *n*-hexyl phosphonic acid diester:** Triethylphosphite (198.00 g, 1.19 mol) and *n*-hexyl bromide (106.00 g, 0.64 mol) were heated at 150 °C for 17 h in a round-bottom flask equipped with a dean-stark receiver to collect the formed bromoethane. Fractionated distillation of the mixture yielded the desired phosphonic acid diester as a colorless liquid. (126.53 g, 0.63 mol, yield: 99 %, bp 72-80 °C / 4 mbar). ^{1}H NMR ($CDCl_3$, 500 MHz, 298K, ppm): δ = 4.12 - 4.00 (m, 4H, -O-O-C**H$_2$**-), 1.74 - 1.66 (m, 2H, -P-C**H$_2$**-), 1.60 - 1.52 (m, 2H, -P-CH2-C**H$_2$**-), 1.38 - 1.21 (m, 6H, -P-CH_2-CH_2-C**H$_2$**-C**H$_2$**-C**H$_2$**-), 0.86 (t, 3H, -C**H$_3$**, $^{3}J_{CH}$ = 6.9 Hz). ^{13}C{H} NMR ($CDCl_3$, 125 MHz, 298K, ppm): δ = 61.44 (d, -P-O-**C**-, $^{2}J_{CP}$ = 6.5 Hz), 31.38 (s, P-**C**-), 30.38 (d, -P-C-**C**-, $^{2}J_{CP}$ = 16.9 Hz), 25.81 (d, -P-C-C-**C**-, $^{3}J_{CP}$ = 140.4 Hz), 22.50 (d, -P-C-C-C-**C**-, $^{4}J_{CP}$ = 2 Hz), 22.45 (s, -P-C-C-C-C-**C**-), 16.58 (d, -**C**, $^{5}J_{CP}$ = 2 Hz), 14.11 (s, -P-O-C-**C**). ^{31}P{H} NMR ($CDCl_3$, 201 MHz, 298K, ppm): δ = 32.61

***N*-hexyl phosphonic acid dichloride**: *O,O*-Diethyl *n*-hexyl phosphonic acid diester (100.00 g, 0.49 mol) and DMF (0.70 mL) was added drop wise to refluxing thionylchloride (139.00 g, 1.17 mol). Strong gas evolution of methylene chloride and sulfur dioxide indicated the progress of the reaction. After 24 h the gas evolution declined. Fractionated distillation of the raw product yielded the desired dichloride as a colorless liquid (69.61 g, yield: 36 %, b.p. 130-135°C / 60 mbar). ^{1}H NMR ($CDCl_3$, 500 MHz, 298K, ppm): δ = 2.61 - 2.50 (m, 2H, -P-C**H$_2$**-), 1.87 - 1.76 (m, H, -P-CH_2-C**H$_2$**-), 1.50 - 1.42 (m, 2H, -P-CH_2-CH_2-C**H$_2$**-), 1.33 - 1.27 (m, 4H, -P-CH_2-CH_2-CH_2-C**H$_2$**-C**H$_2$**-), 0.88 (t, 3H, -CH3, $^{3}J_{HH}$ = 10 Hz). ^{13}C{H} NMR ($CDCl_3$, 125 MHz, 298K, ppm): δ = 42.98 (d, -P-**C**-, $^{1}J_{CP}$ = 96.3 Hz), 31.04 (d, -P-C-**C**-, $^{2}J_{CP}$ = 1.6 Hz), 29.24 (d, -P-C-C-**C**-, $^{3}J_{CP}$

= 21.5 Hz), 22.87 (d, -P-C-C-C-**C**-, $^4J_{CP}$ = 6.5 Hz), 22.25 (s, -P-C-C-C-C-**C**-), 13.91 (s, -**C**). $^{31}P\{H\}$ NMR ($CDCl_3$, 201 MHz, 298K, ppm): δ = 51.27

2-*n*-Hexyl-2-oxo-1,3,2-dioxaphospholane (3): A flame-dried three-necked round-bottom flask, equipped with a magnetic stirring bar and two dropping funnels, was charged with 250 mL dry THF and cooled to -21°C. *N*-hexyl phosphonic acid dichloride (30.18 g, 0.15 mol) was dissolved in dry THF (250 mL) and transferred into one dropping funnel via a flame-dried stainless steel capillary. A solution of dry ethylene glycol (19.33 g, 0.15 mol) and dry pyridine (23.51 g, 0.30 mol) in THF (250 mL) was transferred into the second dropping funnel via a flame-dried stainless steel capillary. Dropping speed was adjusted to be approximately equal for both mixtures. After complete addition the solution was stirred for 3 hours and kept over-night at 4 °C to facilitate the precipitation of the pyridinium hydrochloride byproduct. The precipitate was removed by filtration via a flame-dried Schlenk funnel and the solvent was removed at reduced pressure. Fractionated distillation yielded the desired product as colorless oil (13.61 g, yield: 48 %, b.p. 90 °C / 4x10^{-2} mbar). ^1H NMR ($CDCl_3$, 500 MHz, 298K, ppm): δ = 4.46 - 4.36 (m, 2H, -P-O-C**H$_2$**-), 4.35 – 4.14 (m, 4H, -P-O-C**H$_2$**-), 1.88 (dt, 2H, -P-C**H$_2$**-, $^2J_{HP}$ = 17.1 Hz, $^3J_{HH}$ = 8.0 Hz), 1.56 (dp, 2H, -P-CH_2-C**H$_2$**-, $^3J_{HP}$ = 20.8 Hz, $^3J_{HHb}$ = 7.9 Hz, $^3J_{HHc}$ = 6.6 Hz), 1.33 (p, 2H, -P-CH_2-CH_2-C**H$_2$**-, $^3J_{HH}$ = 7.4 Hz), 1.27 – 1.17 (m, 4H, -P-CH_2-CH_2-CH_2-C**H$_2$**-C**H$_2$**-), 0.81 (t, 3H, -C**H$_3$**, $^3J_{HH}$ = 6.6 Hz). $^{13}C\{H\}$ NMR ($CDCl_3$, 125 MHz, 298K, ppm): δ = 66.15 (s, -P-O-**C**-), 31.15 (s, -P-**C**-), 30.03 (d, -P-C-**C**-), $^2J_{CP}$ = 16.4 Hz), 25.61 (d, -P-C-C-**C**-, $^3J_{CP}$ = 130.4 Hz), 22.54 (d, -P-C-C-C-**C**-, $^4J_{CP}$ = 5.4 Hz), 22.28 (s, -P-C-C-C-C-**C**-), 13.91 (s, -**C**). $^{31}P\{H\}$ NMR ($CDCl_3$, 201 MHz, 298K, ppm): δ = 51.42

Representative procedure for the (co-)polymerization of (1) with (2) or (3): The respective monomers were weighed into a flame-dried Schlenk-tube, dissolved in dry benzene and dried by repeated lyophilization. The monomers were dissolved in dry dichloromethane at a total concentration of 4 mol L^{-1}. A stock solution of initiator 2-(benzyloxy)ethanol in dry dichloromethane was prepared with a concentration 0.2 mol L^{-1} and the calculated amount was

added to the monomer solution via gas tight syringe (Hamilton®). A stock solution of DBU in dry dichloromethane was prepared with a concentration of 0.2 mol L^{-1}. The monomer solution and the catalyst solution were adjusted to 30 °C. The polymerization was initiated by the addition of the calculated volume of catalyst solution containing 3.0 equivalents of DBU in respect to the initiator. Polymerization was terminated after 16 h by the rapid addition of an excess of formic acid dissolved in dichloromethane with a concentration of 20 mg mL^{-1}. The colorless, amorphous polymers were purified by precipitation in cold diethyl ether or petrol ether (for **(2)** content above 70% and **(3)** content above 50 %), dialyzed against Milli-Q (Millipore®) water and dried at reduced pressure.

Representative NMR data of $P(3)_{120}$: ^{1}H NMR (DMSO-d_6, 500 MHz, 298K, ppm): δ = 7.37 - 7.29 (m, aromatic C**H**), 4.85 (t, terminal -O-**H**), 4.53 (s, aryl-C$\mathbf{H_2}$-), 4.22 - 4.01 (m, backbone -C$\mathbf{H_2}$-C$\mathbf{H_2}$-), 3.63 (t, backbone terminal -C$\mathbf{H_2}$-OH), 1.80 - 1.71 (m, side-chain -P-C$\mathbf{H_2}$-), 1.53 - 1.43 (m, side-chain -P-CH_2-C$\mathbf{H_2}$-), 1.37 - 1.30 (m, side-chain -P-CH_2-CH_2-C$\mathbf{H_2}$-), 1.29 - 1.19 (m, side-chain -P-CH_2-CH_2-CH_2-C$\mathbf{H_2}$-C$\mathbf{H_2}$-), 0.88 - 0.82 (m, side-chain -C$\mathbf{H_3}$). ^{13}C{H} NMR (DMSO-d_6, 125 MHz, 298K, ppm): δ 133.78, 128.80, 127.97 (s, aromatic **C**), 64.56 (s, broad, backbone -**C**H_2-), 60.85 (s, aryl-**C**-), 31.29 (s, -P-**C**-), 30.06 (d, -P-C-**C**-, $^{2}J_{CP}$ = 16.7 Hz), 25.03 (d, -P-C-C-**C**-, 3JCP = 140.0 Hz), 22.41 (d, -P-C-C-C-**C**-, $^{4}J_{CP}$ = 3.7 Hz), 22.35 (s, -P-C-C-C-C-**C**-), 14.17 (s, -**C**). ^{31}P{H} NMR (DMSO-d_6, 201 MHz, 298K, ppm): δ 33.51 (backbone), 32.95 (terminal).

Representative NMR data of $P(\mathbf{1}_{15}$-*co*-$\mathbf{2}_{118})$: ^{1}H NMR (DMSO-d_6, 500 MHz, 298K, ppm): δ = 7.37 - 7.29 (m, aromatic C**H**), 4.85 (t, terminal -O-**H**), 4.53 (s, aryl-C$\mathbf{H_2}$-), 4.22 - 4.01 (m, backbone -C$\mathbf{H_2}$-C$\mathbf{H_2}$-), 3.63 (t, backbone terminal -C$\mathbf{H_2}$-OH), 1.84 - 1.70 (m, side-chain -P-C$\mathbf{H_2}$-), 1.63 - 1.56 (m, side-chain -P-C$\mathbf{H_2}$-), 1.54 - 1.41 (m, side-chain -P-CH_2-C$\mathbf{H_2}$-), 1.40 - 1.29 (m, side-chain -P-CH_2-CH_2-C$\mathbf{H_2}$-), 1.05 (dt, side-chain -P-CH_2-C$\mathbf{H_3}$, $^{3}J_{HP}$ = 20.1 Hz, $^{3}J_{HH}$ = 7.6 Hz), 0.86 (t, side-chain -P-CH_2-CH_2-CH_2-C$\mathbf{H_3}$, $^{3}J_{HH}$ = 7.3 Hz). ^{13}C{H} NMR (DMSO-d_6, 125 MHz, 298K, ppm): δ

133.78, 128.80, 127.97 (s, aromatic **C**), 64.56 (s, broad, backbone -**C**H_2-), 60.85 (s, aryl-**C**-), 24.66 (d, side-chain -P-**C**-, $^1J_{CP}$ = 145.0 Hz), 24.42 (d, side-chain –P-C-**C**-, $^2J_{CP}$ = 5 Hz), 23.41 (d, side-chain -P-C-C-**C**-, $^3J_{CP}$ = 16.3 Hz), 18.06 (d, side-chain -P-**C**-, $^1J_{CP}$ = 138.8 Hz), 13.90 (s, side-chain -P-C-C-C-**C**), 6.68 (d, side-chain -P-C-**C**, $^2J_{CH}$ = 6.3 Hz). ^{31}P{H} NMR (DMSO-d_6, 201 MHz, 298K, ppm): δ = 34.43 (backbone), 34.18 (terminal), 33.28 (backbone), 33.04 (terminal).

Representative NMR data of P($\mathbf{1_{32}}$-*co*-$\mathbf{3_{30}}$): ^{1}H NMR (DMSO-d_6, 500 MHz, 298K, ppm): δ = 7.37 - 7.29 (m, aromatic C**H**), 4.85 (t, terminal -O-**H**), 4.53 (s, aryl-C$\mathbf{H_2}$-), 4.22 - 4.01 (m, backbone -C$\mathbf{H_2}$-C$\mathbf{H_2}$-), 3.63 (t, backbone terminal -C$\mathbf{H_2}$-OH), 1.83 - 1.69 (m, side-chain -P-C$\mathbf{H_2}$-), 1.55 - 1.41 (m, side-chain -P-CH_2-C$\mathbf{H_2}$-), 1.38 - 1.31 (m, side-chain, -P-CH_2-CH_2-C$\mathbf{H_2}$-), 1.30 - 1.1.19 (m, side-chain -P-CH_2-CH_2-CH_2-C$\mathbf{H_2}$-C$\mathbf{H_2}$-), 1.05 (dt, side-chain -P-CH_2-C$\mathbf{H_3}$, $^2J_{HP}$ = 20.1 Hz, $^3J_{HH}$ = 7.6 Hz), 0.86 (t, side-chain -P-CH_2-CH_2-CH_2-CH_2-CH_2-C$\mathbf{H_3}$, $^3J_{HH}$ = 6.8 Hz). ^{13}C{H} NMR (DMSO-d_6, 125 MHz, 298K, ppm): δ 133.78, 128.80, 127.97 (s, aromatic **C**), 64.56 (s, broad, backbone -**C**H_2-), 60.85 (s, aryl-**C**-), 31.29 (s, -P-**C**-), 30.06 (d, -P-C-**C**-, $^2J_{CP}$ = 16.7 Hz), 25.03 (d, -P-C-C-**C**-, 3JCP = 140.0 Hz), 22.41 (d, -P-C-C-C-**C**-, $^4J_{CP}$ = 3.7 Hz), 22.35 (s, -P-C-C-C-C-**C**-), 18.06 (d, side-chain -P-**C**-, $^1J_{CP}$ = 138.8 Hz), 14.17 (s, -**C**), 6.68 (d, side-chain -P-C-**C**, $^2J_{CH}$ = 6.3 Hz). ^{31}P{H} NMR (DMSO-d_6, 201 MHz, 298K, ppm): δ = 34.44 (backbone), 34.20 (terminal), 33.21 (backbone), 33.01 (terminal).

Supporting tables

Table S1: Characterization data of the copolymers of **(1)** and **(2)**.

polymer [a]	**monomer feed** [b]	**copolymer composition** [c]	M_n / g mol^{-1} [c]	**conversion / %**	$Đ$ [d]	T_g / °C [e]	T_{cp} / °C [f]
P($\mathbf{1_{113}}$-*co*-$\mathbf{2_{47}}$)	0.70 / 0.30	0.70 / 0.30	23,000	89	1.18	-55	> 100

P(1_{51}-*co*-2_{51})	0.50 / 0.50	0.50 / 0.50	15,000	83	1.30	-55	50
P(1_{24}-*co*-2_{27})	0.46 / 0.54	0.47 / 0.53	7,700	79	1.29	-42	51
P(1_{33}-*co*-2_{76})	0.29 / 0.71	0.30 / 0.71	17,000	82	1.30	-44	26
P(1_{24}-*co*-2_{99})	0.19 / 0.81	0.19 / 0.81	19,500	72	1.26	-46	16
P(1_{15}-*co*-2_{118})	0.12 / 0.88	0.11 / 0.89	21,000	74	1.21	-45	8

a: Type of polymer and degree of polymerization as determined by ^{1}H NMR spectroscopy. b: Monomer feed ratio. c: Determined via ^{1}H NMR spectroscopy. d: Determined via SEC in DMF at 333 K (vs. PEG standard). e: Determined via DSC measurements. f: Determined via UV Vis spectroscopy.

Table S2: Characterization data of the copolymers of **(1)** and **(3)**.

polymer [a]	**monomer feed** [b]	**copolymer composition** [c]	M_n / g mol^{-1} [c]	**conversion / %**	$Đ$ [d]	T_g / °C [e]	T_{cp} / °C [f]
P(3)$_{120}$	-	-	23,000	74	1.20	-46	-
P(3)$_{46}$	-	-	8,800	86	1.30	-40	-

P(1_{41}-*co*-3_{16})	0.71 / 0.29	0.71 / 0.29	8,600	93	1.19	-43	55
P(1_{62}-*co*-3_{56})	0.52 / 0.48	0.52 / 0.48	19,000	68	1.20	-50	56
P(1_{32}-*co*-3_{30})	0.49 / 0.51	0.52 / 0.48	10,000	80	1.28	-54	26
P(1_{40}-*co*-3_{80})	0.30 / 0.70	0.33 / 0.67	21,000	70	1.30	-53	-
P(1_{18}-*co*-3_{43})	0.29 / 0.71	0.29 / 0.71	10,000	75	1.25	-54	-

a: Type of polymer and degree of polymerization as determined by 1H NMR spectroscopy. b: Monomer feed ratio. c: Determined via 1H NMR spectroscopy. d: Determined via SEC in DMF at 333 K (vs. PEG standard). e: Determined via DSC measurements. f: Determined via UV Vis spectroscopy.

Supporting figures

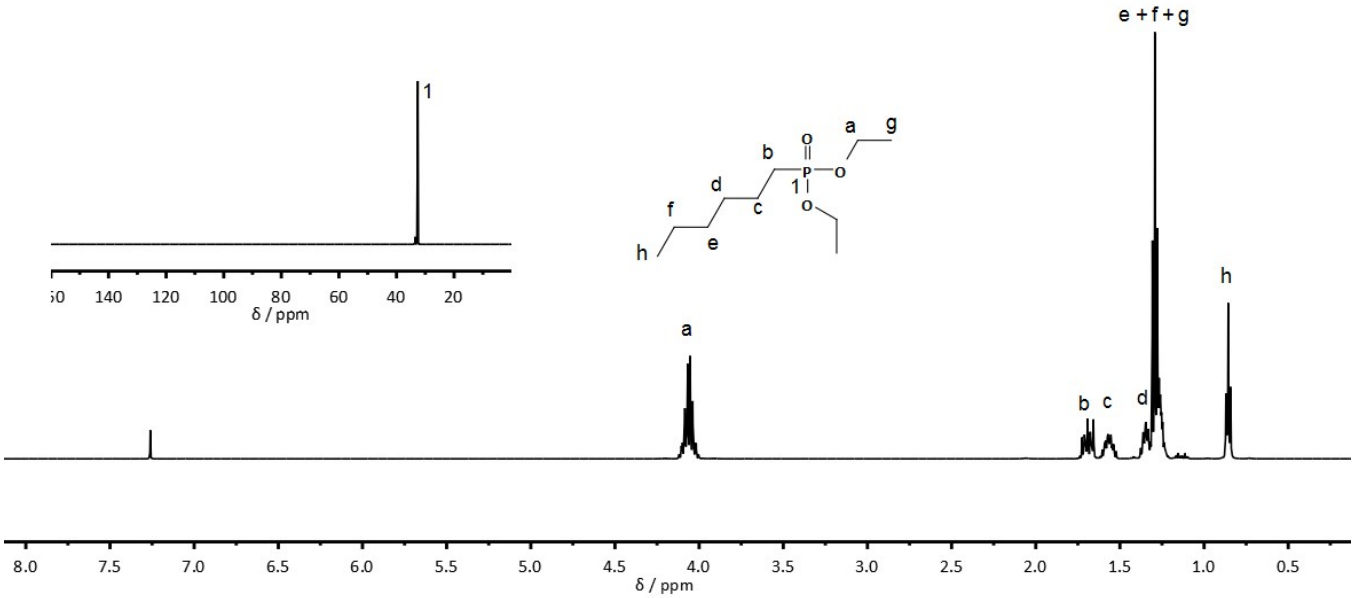

Figure S1: ^{1}H (500 MHz) and $^{31}P\{H\}$ (201 MHz) NMR spectra of O,O-diethyl *n*-hexyl phosphonic acid diester in $CDCl_3$ at 298K.

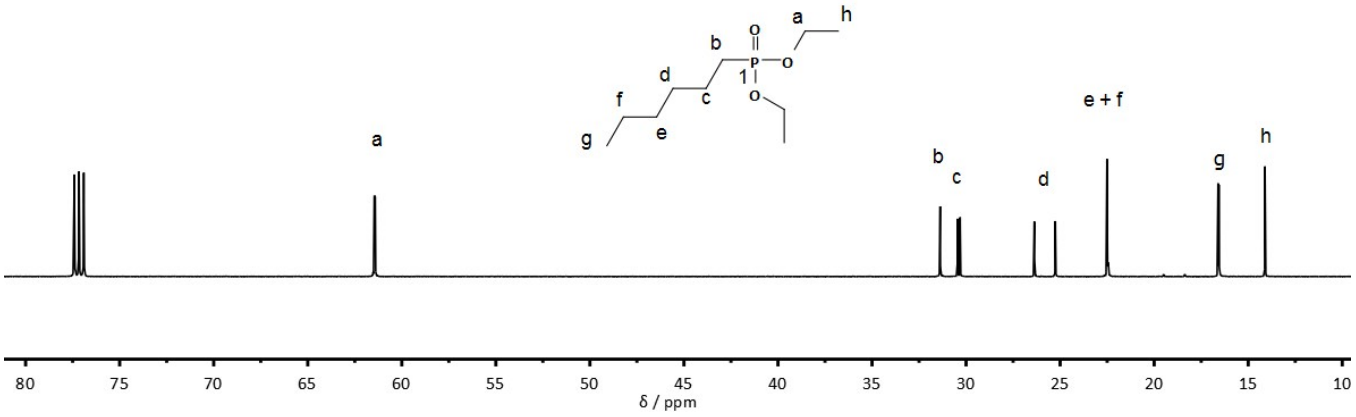

Figure S2: ^{13}C (125 MHz) NMR spectrum of O,O-diethyl *n*-hexyl phosphonic acid diester in $CDCl_3$ at 298K.

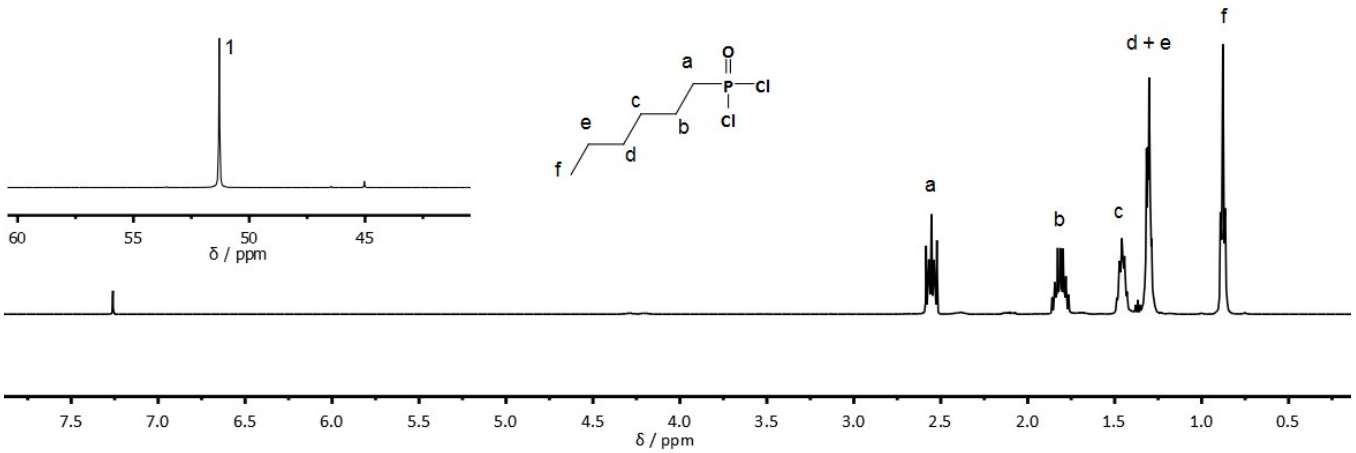

Figure S3: ^{1}H (500 MHz) and $^{31}P\{H\}$ (201 MHz) NMR spectra of *n*-hexyl phosphonic acid dichloride in $CDCl_3$ at 298K.

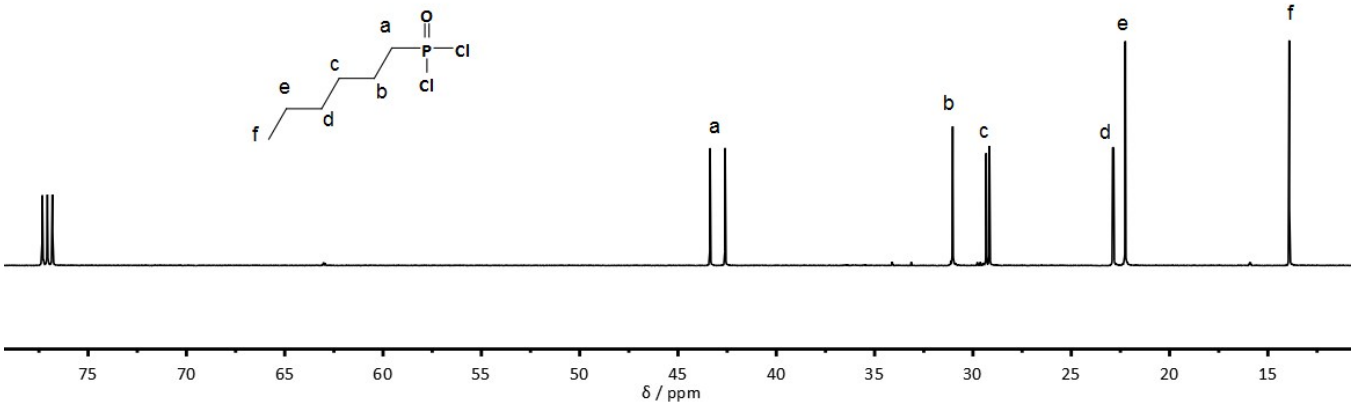

Figure S4: ^{13}C (125 MHz) NMR spectrum of *n*-hexyl phosphonic acid dichloride in $CDCl_3$ at 298K.

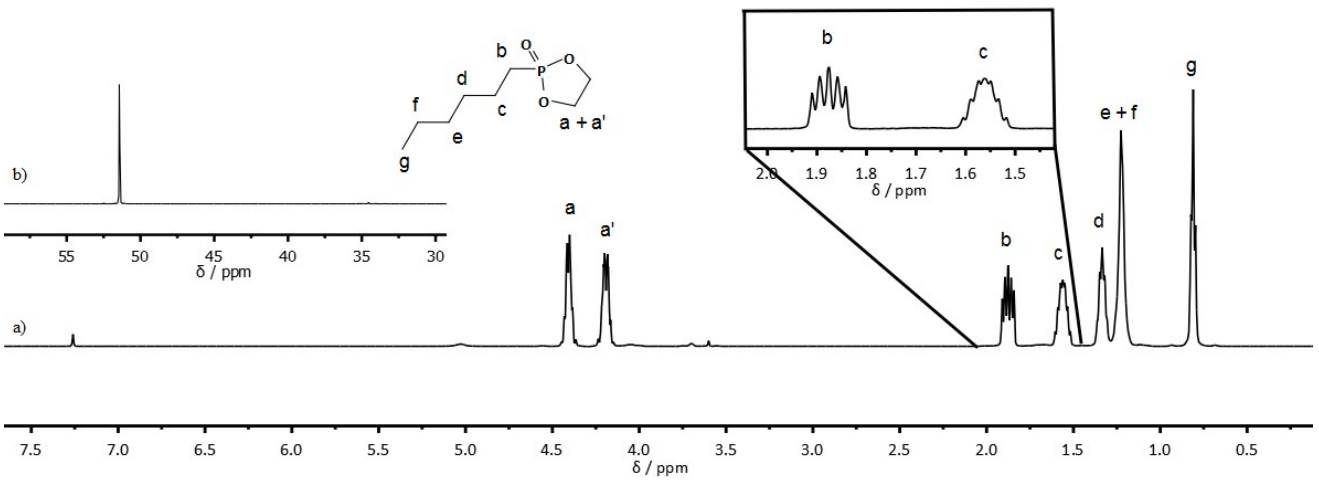

Figure S5: a) ^{1}H NMR (500 MHz) and b) $^{31}P\{H\}$ NMR (201 MHz) spectra of **(3)** in $CDCl_3$ at 298 K. Region from 2.05 - 1.42 ppm magnified for clarification of J_{HP} coupling.

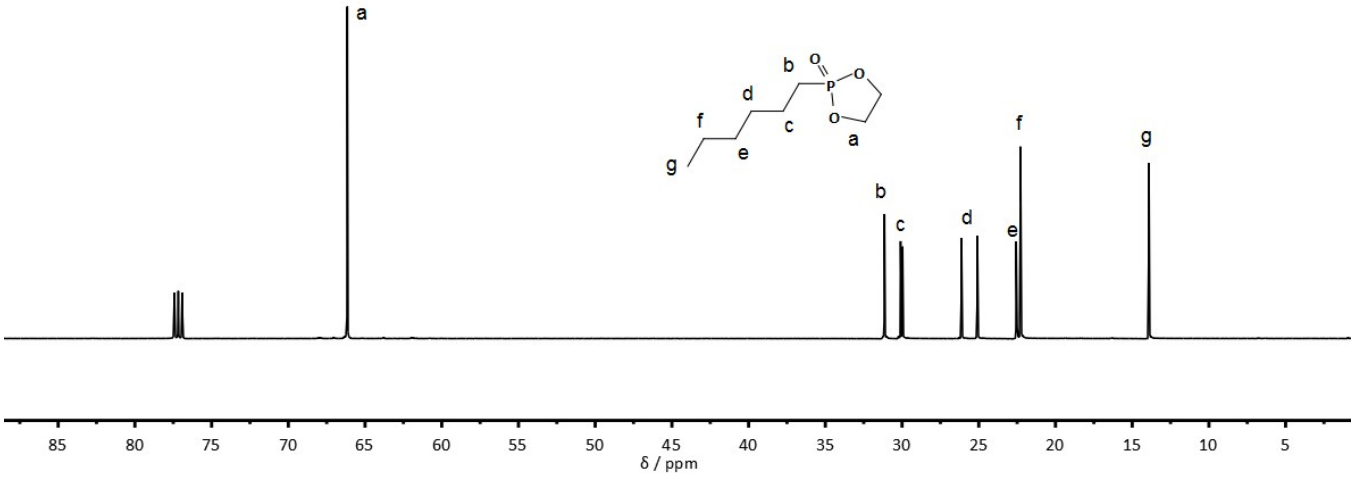

Figure S6: ^{13}C (125 MHz) NMR spectrum of 2-*n*-hexyl-2-oxo-1,3,2-dioxaphospholane (^{n}HexPPn, **(3)**) in $CDCl_3$ at 298K.

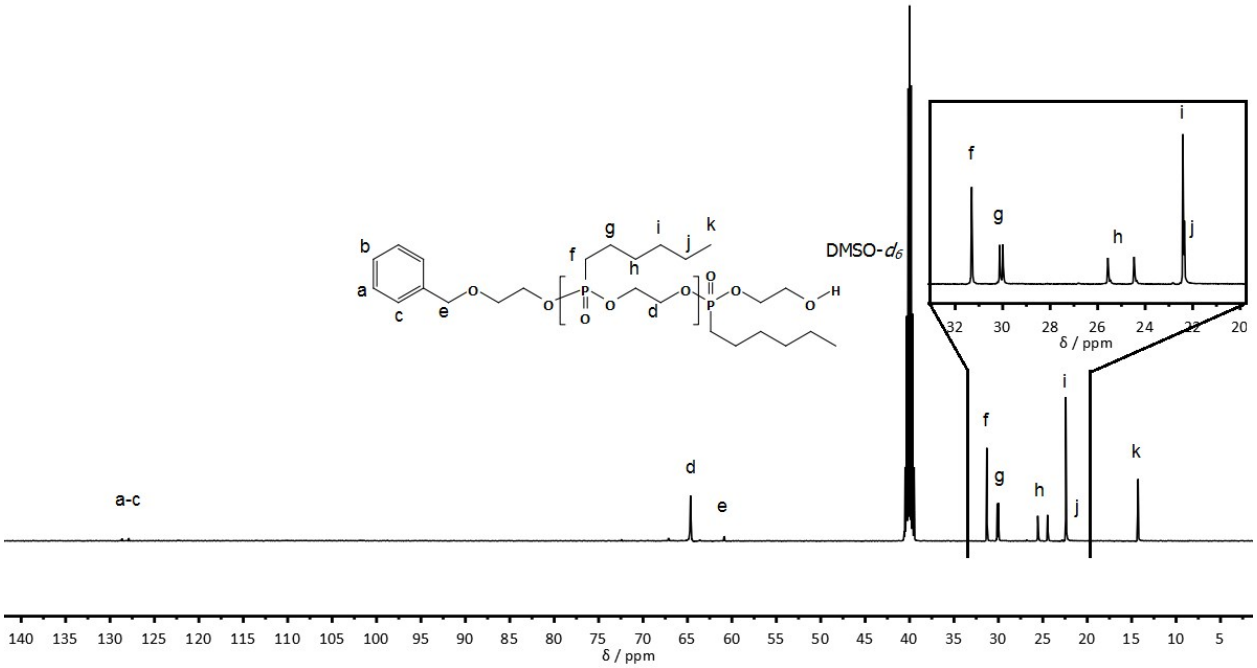

Figure S7: ^{13}C (125 MHz) NMR spectrum of **P(3)$_{120}$** in DMSO-d_6 at 298K. Region from 32 to 20 ppm magnified for clarification.

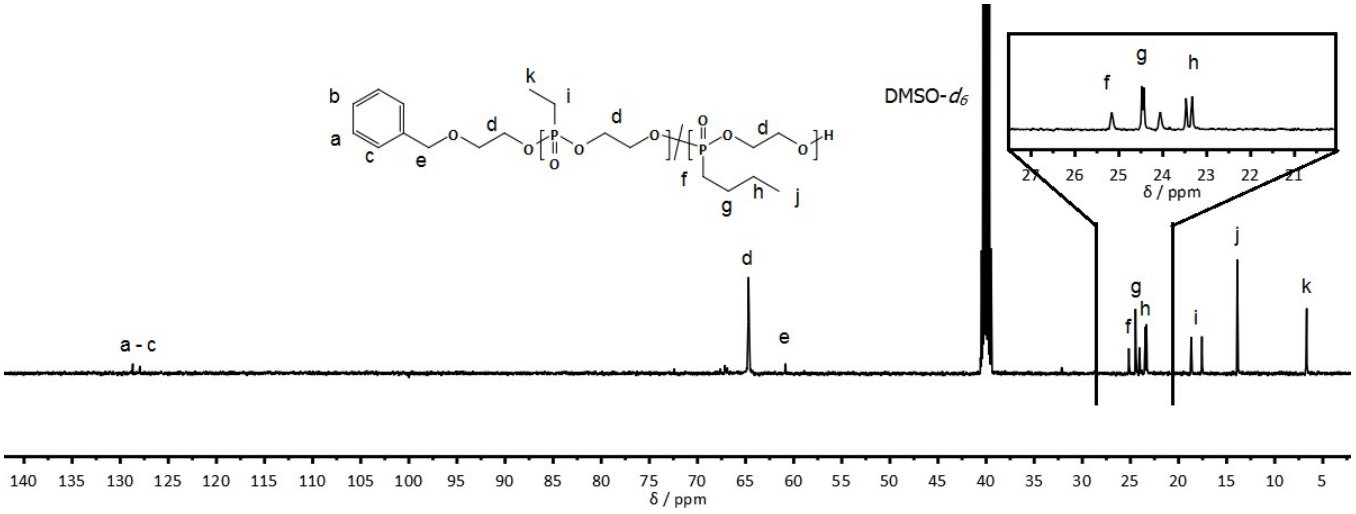

Figure S8: ^{13}C (125 MHz) NMR spectrum of **P(1$_{15}$-*co*-2$_{118}$)** in DMSO-d_6 at 298K. Region from 27 to 20 ppm magnified for clarification.

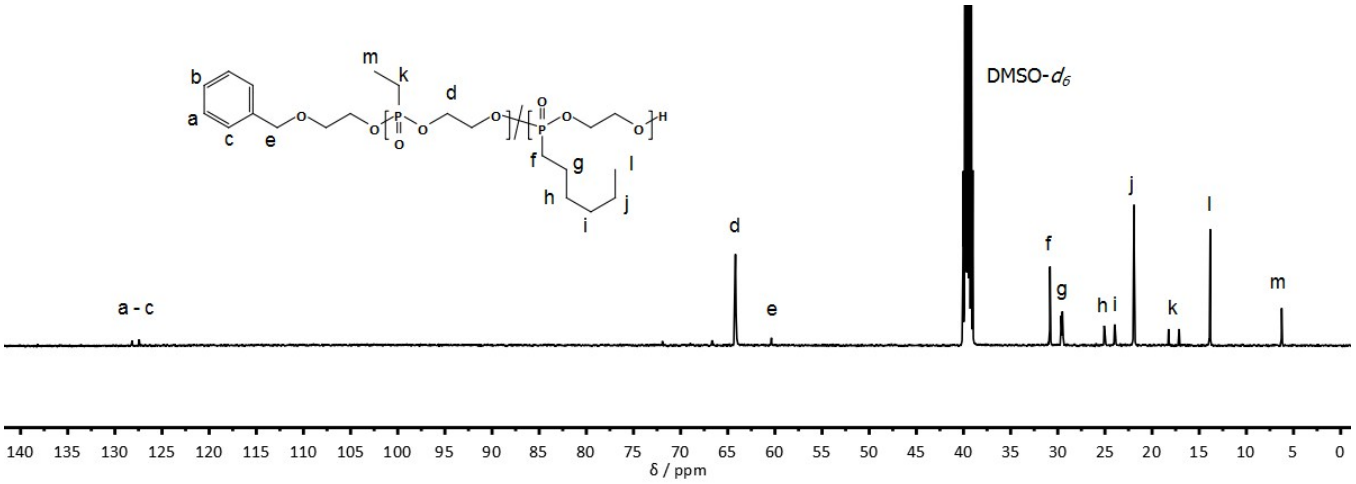

Figure S9: ^{13}C (125 MHz) NMR spectrum of **P($\mathbf{1}_{62}$-*co*-$\mathbf{3}_{56}$)** in DMSO-d_6 at 298K.

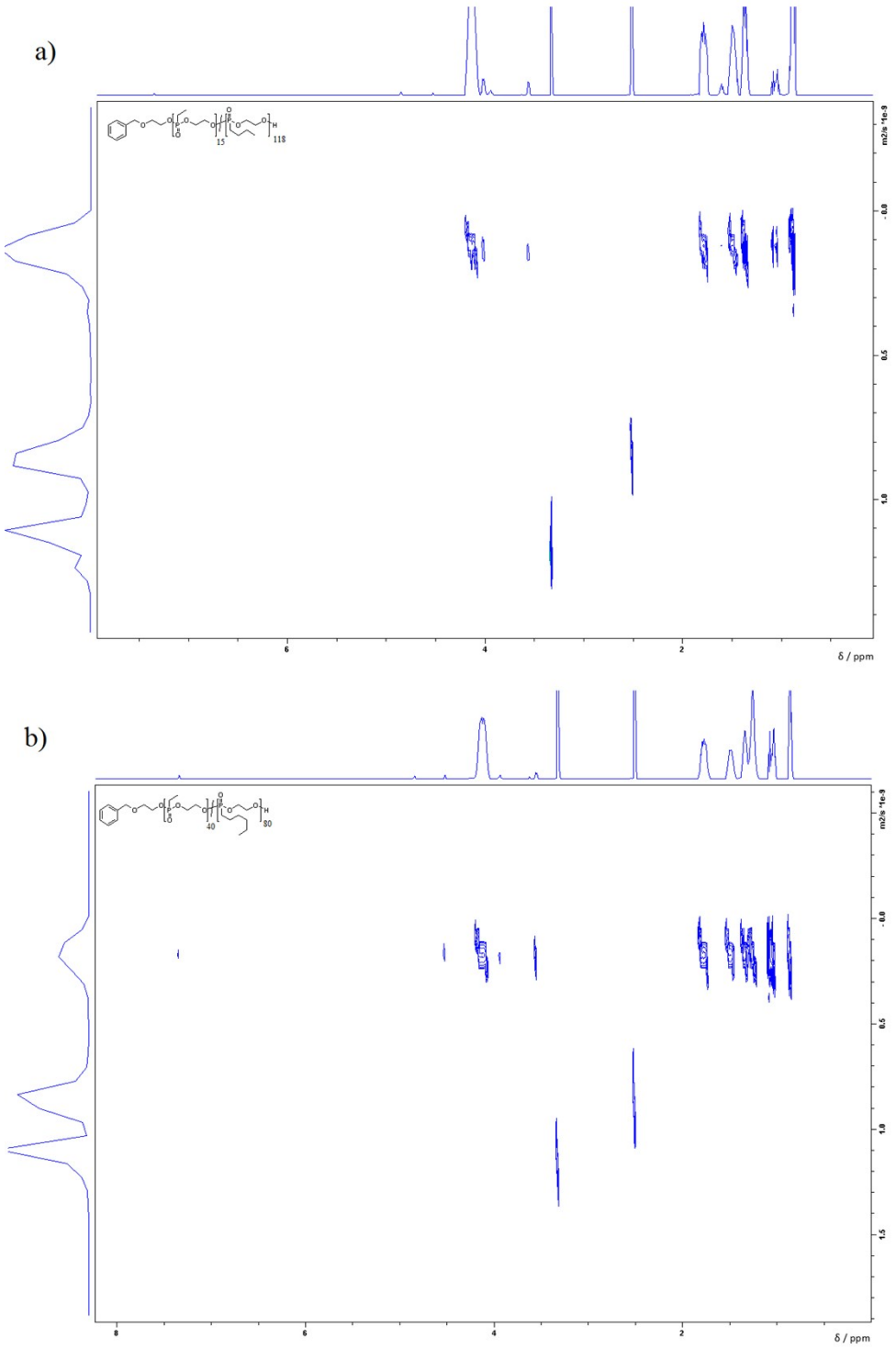

Figure S10: ^{1}H DOSY NMR (500 MHz) spectra of a) **P($\mathbf{1}_{15}$-*co*-$\mathbf{2}_{118}$)** and b) **P($\mathbf{1}_{40}$-*co*-$\mathbf{3}_{80}$)** in DMSO-d_6 at 298K.

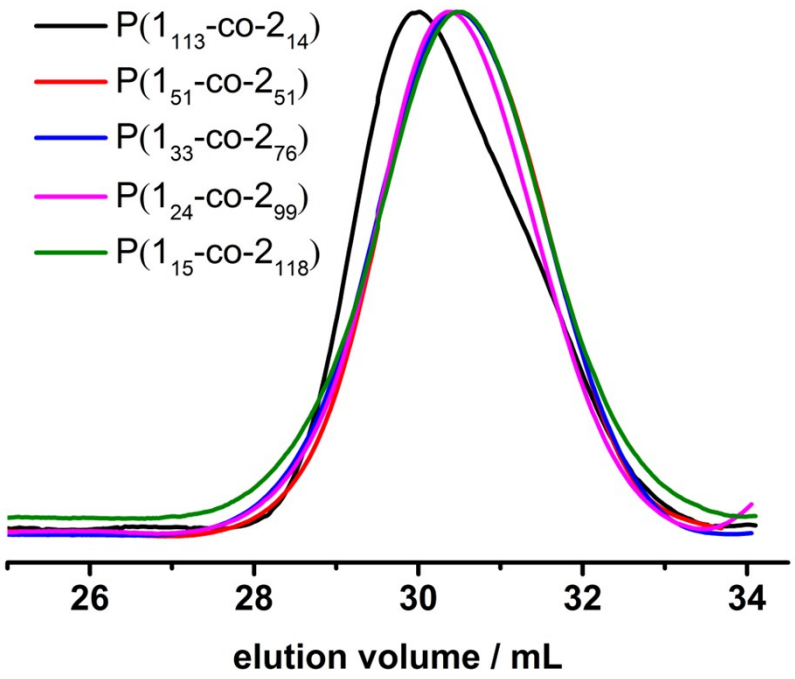

Figure S11: SEC traces (RI detection) of **P($\mathbf{1}_x$-*co*-$\mathbf{2}_y$)** with different copolymer compositions measured in DMF at 333 K (RI detection).

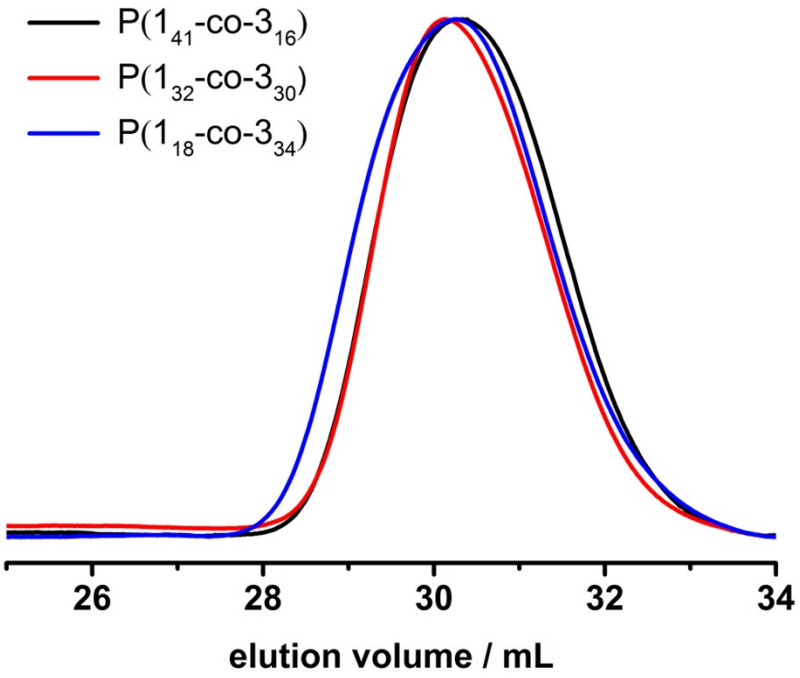

Figure S12: SEC traces (RI detection) of **P($\mathbf{1}_x$-*co*-$\mathbf{3}_y$)** with different copolymer compositions measured in DMF at 333 K (RI detection).

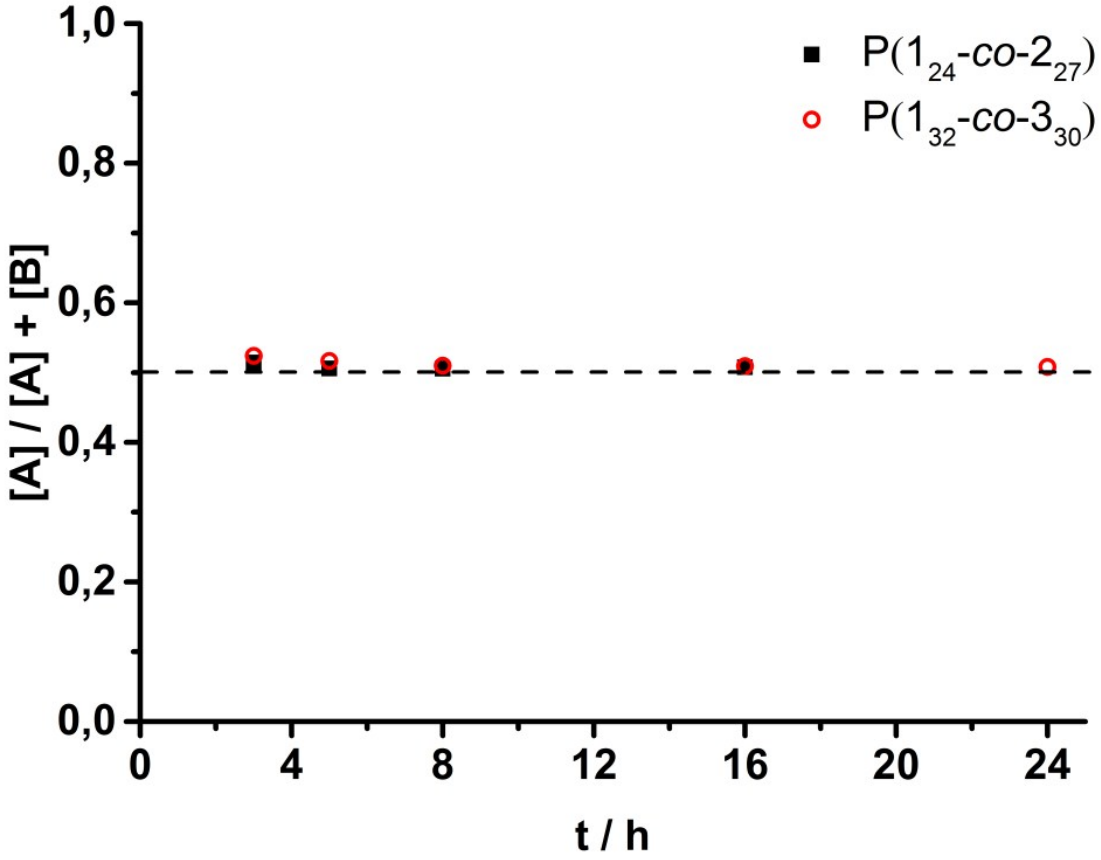

Figure S13: The molar fraction of **(1)** plotted against the reaction time: copolymerization of **(1)** and **(2)** (black squares) and copolymerization of **(1)** and **(3)** (red circle).

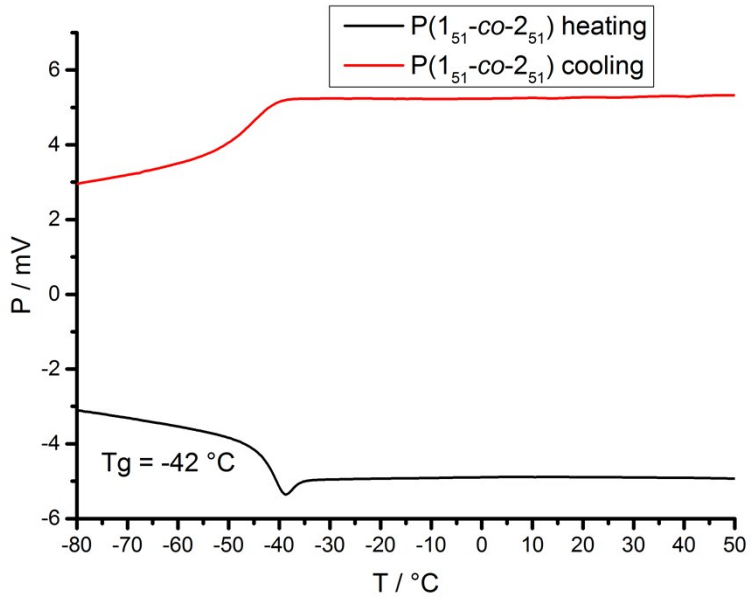

Figure S14: DSC measurement of **P(1$_{51}$-*co*-2$_{51}$)** at a heating rate of 10 °C min^{-1} in the temperature range from -80 °C to 50 °C.

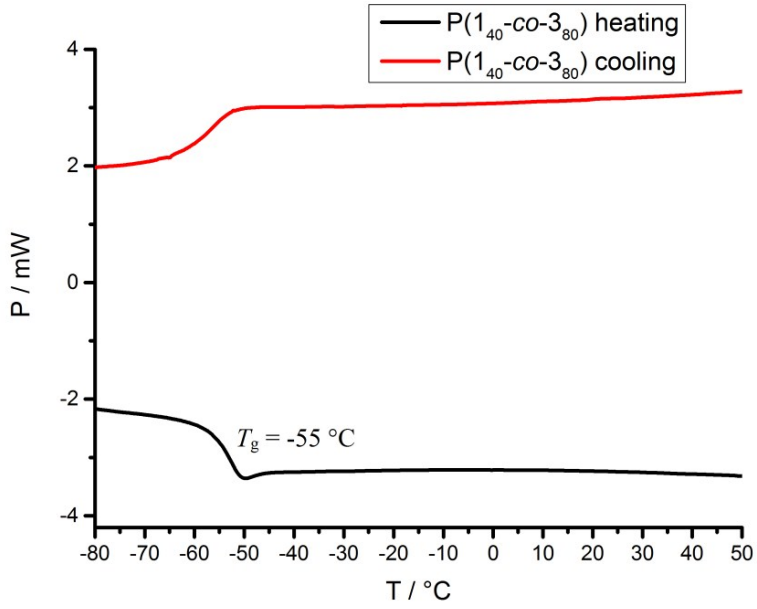

Figure S15: DSC measurement of **P(1$_{40}$-*co*-3$_{80}$)** at a heating rate of 10 °C min^{-1} in the temperature range from -80 °C to 50 °C.

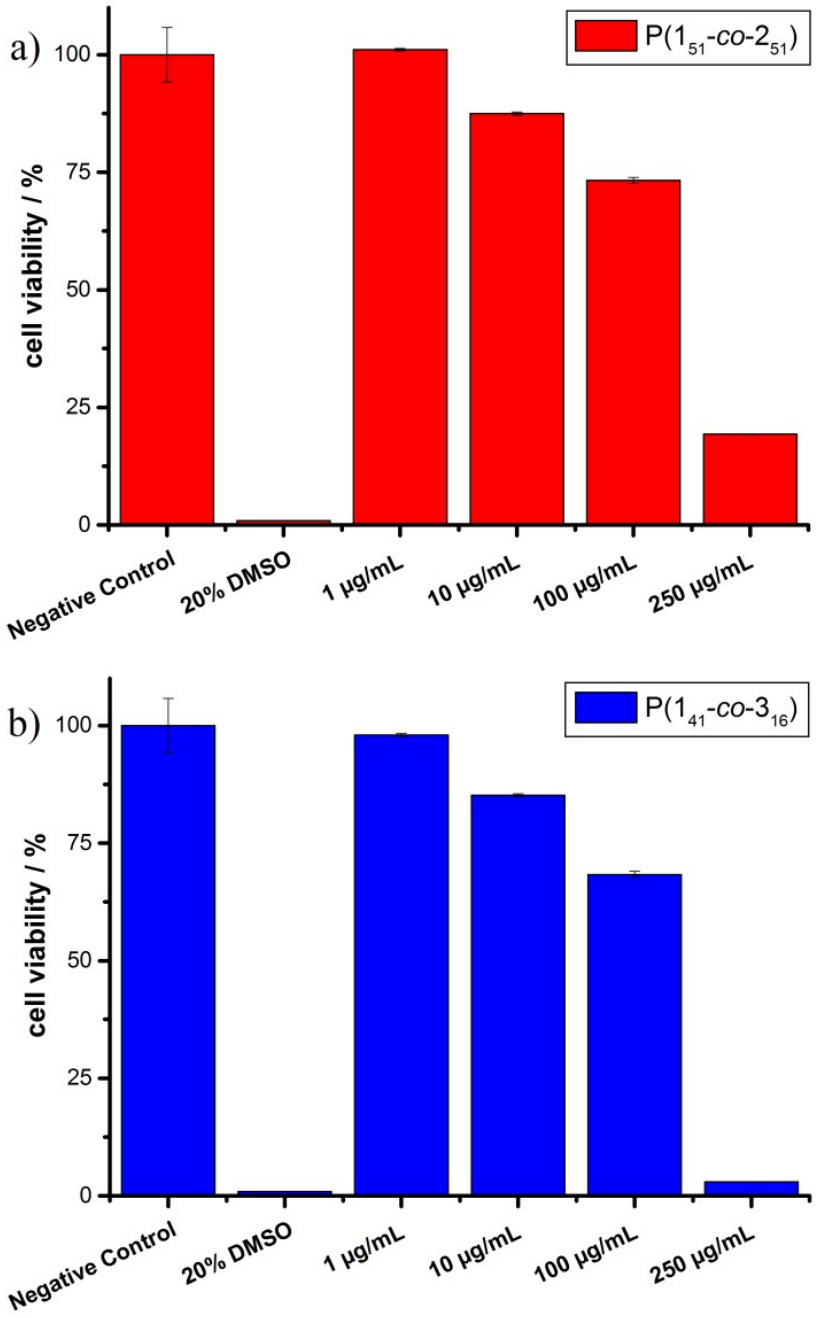

Figure S16: *In vitro* cell-viability assay of RAW264.7 cell-line treated with a) **P($\mathbf{1_{51}}$-*co*-$\mathbf{2_{51}}$)** and b) **P($\mathbf{1_{41}}$-*co*-$\mathbf{3_{16}}$)** after 48 h of incubation. The experiments were carried out as three independent replicates.

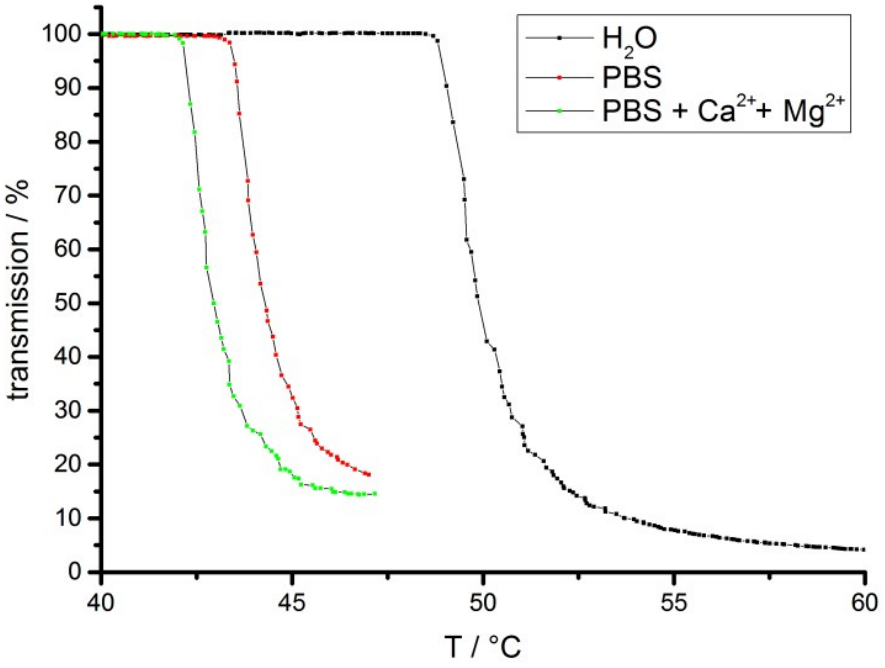

Figure S17: Turbidity measurements of **P($\mathbf{1_{51}}$-*co*-$\mathbf{2_{51}}$)** in ultrapure water (black), in the presence of monovalent ions (red) and divalent ions (green), respectively. Measurements were performed at a concentration of 10 g L^{-1} and a heating rate of 1 °C min^{-1}. Transmission was measured at 500 nm. Cloud point temperature (T_{cp}) was measured at the inflection of the heating curve.

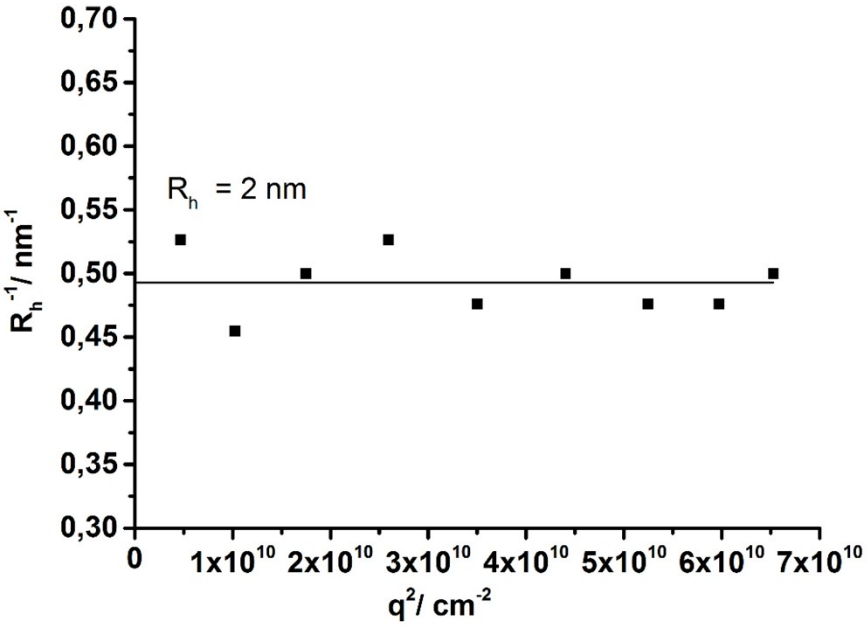

Figure S18: Dynamic light scattering results of **P(1$_{33}$-*co*-2$_{76}$)** at 15 mg mL^{-1} in DPBS at 20°C.

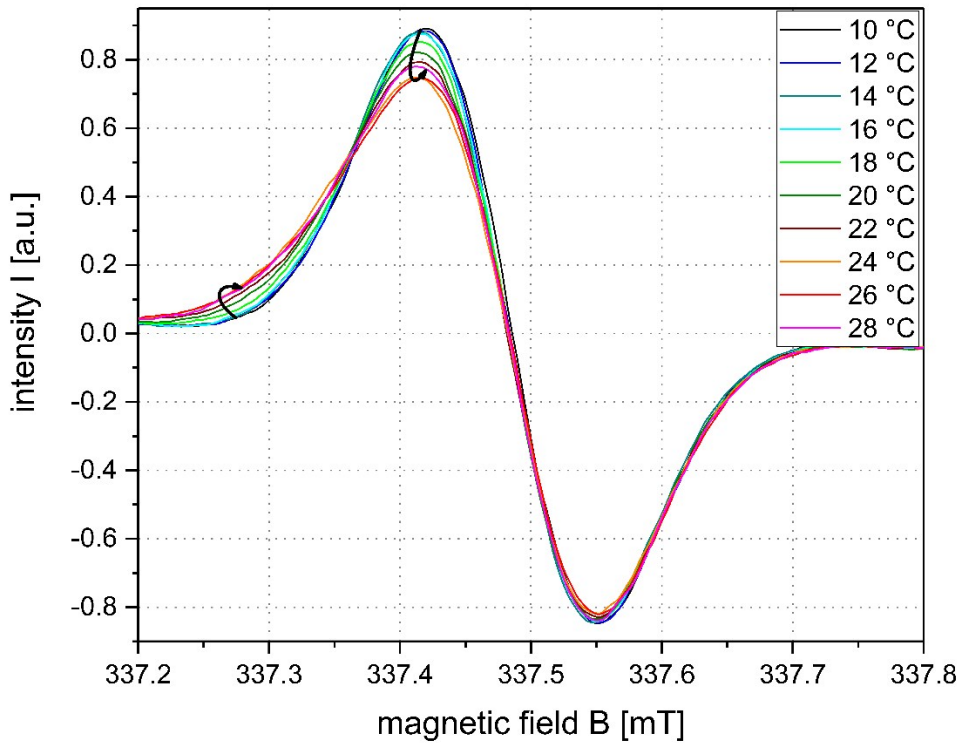

Figure S19: Full high-field peak of CW EPR spectra of an aqueous solution of 15 mg mL^{-1} **P(1$_{33}$-*co*-2$_{76}$)** with 0.2 mM TEMPO in DPBS buffer.