Electronic Supporting Information for:

The effects of cononsolvents on the synthesis of responsive particles via polymerisation-induced thermal self-assembly.

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Characterisation of poly(acrylic acid) macroCTAs

SEC Chromatograms

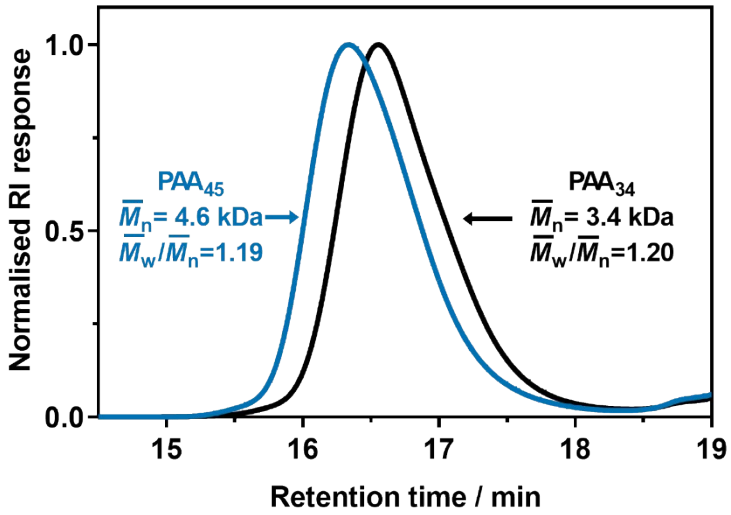

Figure S1. SEC chromatograms for poly(acrylic acid) macroCTAs synthesised by RAFT-mediated polymerisation in ethanol. SEC conditions: THF containing 4% w/v AcOH and 0.025% w/v BHT, calibrated with narrow PMMA standards. Samples were methylated with trimethylsilyl diazomethane before analysis.

^{1}H NMR Spectra

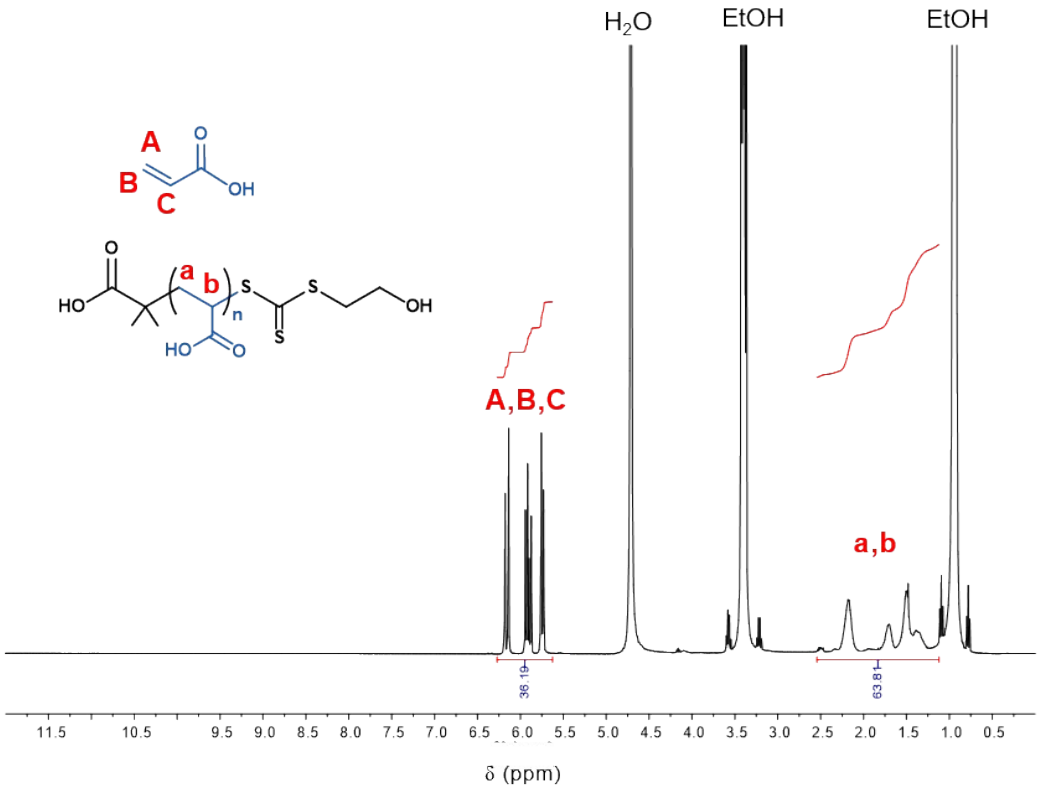

Figure S2. ^{1}H NMR spectrum of pAA_{34} macro-CTA before purification for determination of monomer conversion.

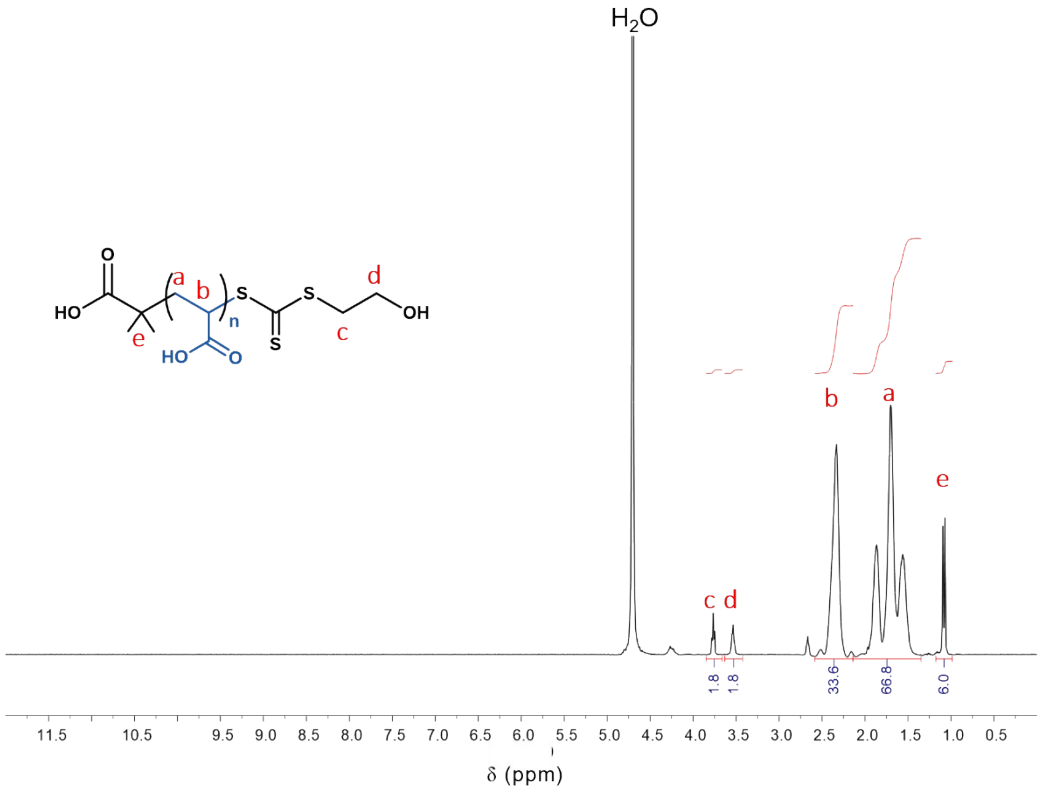

Figure S3. ^{1}H NMR spectrum of pAA_{34} macro-CTA after purification for determination of DP_n.

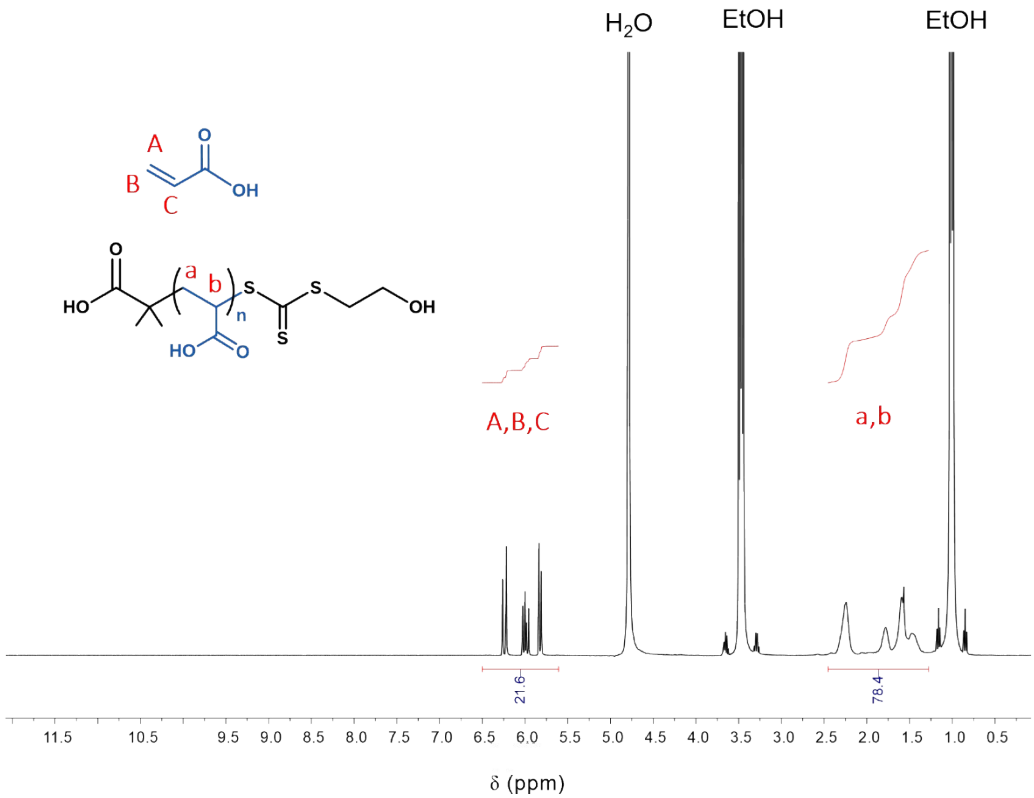

Figure S4. ^{1}H NMR spectrum of pAA_{45} macro-CTA before purification for determination of monomer conversion.

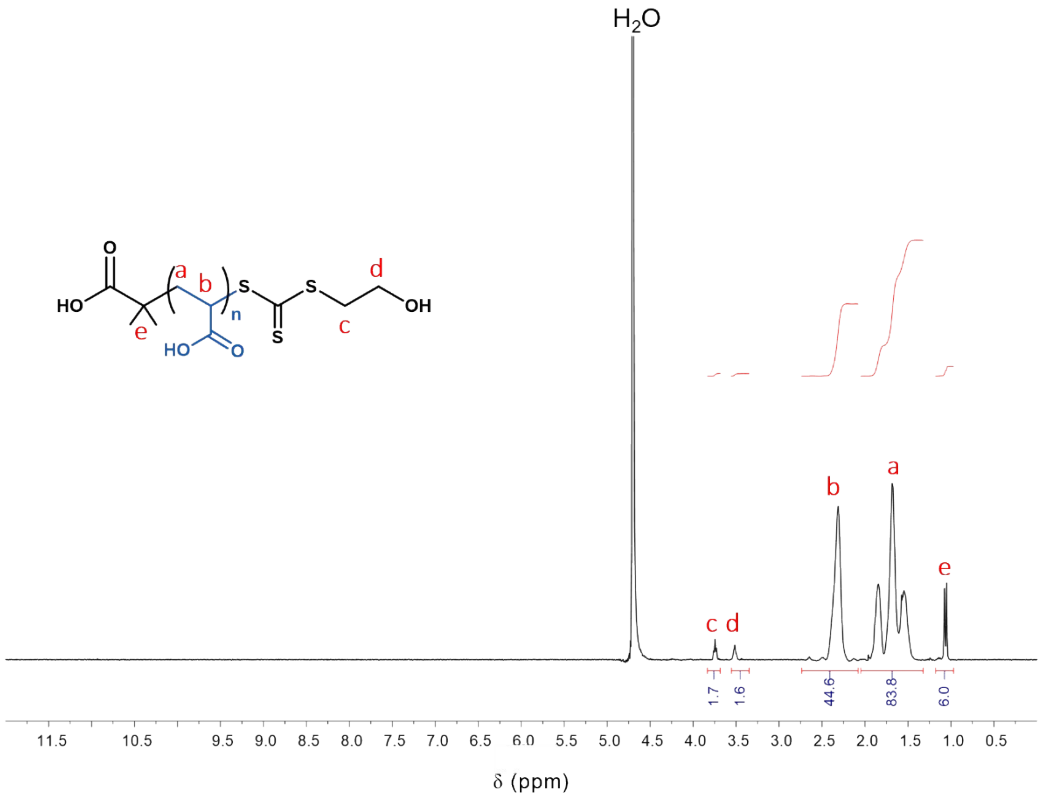

Figure S5. ^{1}H NMR spectrum of pAA_{45} macro-CTA after purification for determination of DP_n.

Summary of characterisation data for poly(acrylic acid) macroCTAs

Table S1. Summary of the data for pAA macroCTAs.

[AA]/[HEMP][a]	[HEMP]/[AIBN][a]	Conversion[b] / %	$DP_{n,theo}$[c]	$DP_{n,NMR}$[d]	$M_{n,theo}$[e] / kDa	$M_{n,SEC}$[f] / kDa	M_w/M_n[f]
61	10	64	39	34	3.2	3.4	1.20
60	5	78	47	45	4.1	4.6	1.19

[a]General reaction conditions: solids content 25% w/w in EtOH and 70 °C. [b] Determined by ^{1}H NMR spectroscopy using the ratio of the sum of vinyl proton integrals and the repeating monomer units. [c]Calculated using $DP_{n,theo}$ = [AA]/[HEMP] × conversion. [d] Calculated from the end-group analysis using the proton signals corresponding only to the R-group of the CTA (2 × CH_3) and the protons from the polymer backbone by ^{1}H NMR spectroscopy. [e]Calculated using $M_{n,\,theo} = M_e + (DP_n \times M_{MA})$ where M_e is the molecular weight of the end groups and M_{MA} is the molecular weight of the esterified AA repeating unit. [f] Determined by SEC after methylation of the purified pAA macro-CTAs. (GPC: THF 4% acetic acid, 0.025% BHT, calibrated with near-monodisperse pMMA standards).

DLS correlation functions for pAA-*b*-pNIPAM/BIS nanogels

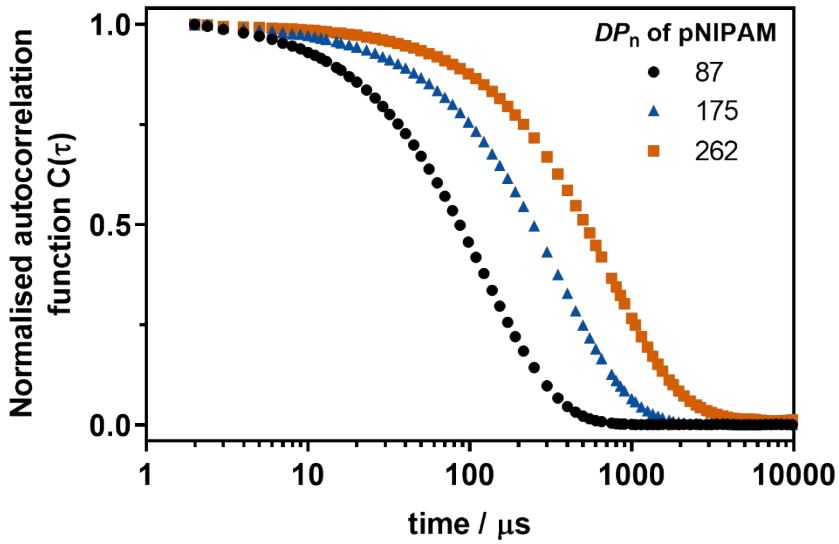

Figure S6. DLS Correlation functions for pAA_{45}-*b*-$pNIPAM_x/BIS_3$ nanogels synthesised in water, where x= 87, 175 and 262.

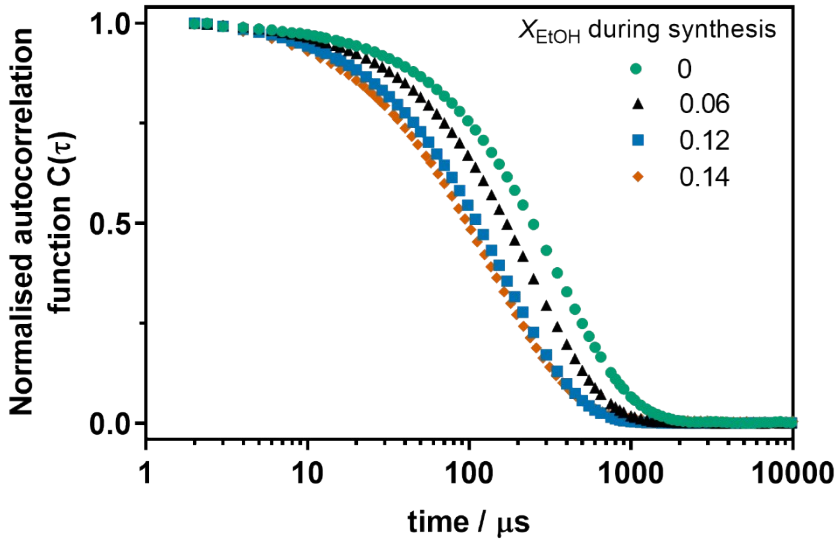

Figure S7. DLS Correlation functions for pAA_{45}-*b*-$pNIPAM_{175}/BIS_3$ nanogels synthesised in water/EtOH mixtures.

Summary of characterisation data for pAA-*b*-pNIPAM/BIS nanogels

Table S2. Data for the synthesis of pAA_{45}-*b*-$pNIPAM_x/BIS_3$ nanogels by RAFT dispersion polymerisation in water/ethanol mixtures

Target composition $[pAA_{45}]$:[NIPAM]:[BIS][a]	X_{EtOH} [b]	Conversion[c] / %	$DP_{n,theo}$ [d]	$M_{n,theo}$ [e] / kg mol^{-1}	D_h ± S.D. / nm [f] (PDI)	ζ-potential ± S.D. [g] / mV
[1]:[87]:[3]	0.06	99	87	13.8	56 ± 19 (0.11)	-29.7 ± 3.9
[1]:[87]:[3]	0.12	79	69	11.8	55 ± 25 (0.21)	-32.6 ± 5.5
[1]:[87]:[3]	0.14	100	87	13.8	67 ± 34 (0.25)	-29.4 ± 5.3
[1]:[262]:[3]	0.12	86	226	29.5	203 ± 67 (0.11)	-17.6 ± 1.4

[a]General reaction conditions: Targeted $[pAA_{45}]$/[ACVA]=5, solids content 10% w/w, 70 °C for 18 h. [b]Mole fraction of ethanol used during nanogel synthesis. [c]Gravimetric determination by moisture analysis of solids content against predicted solids content. [d]For an equivalent diblock synthesised without crosslinker, estimated from [NIPAM/$[pAA_{45}]$×conversion. [e]Calculated using $M_{n,\,theo} = M_e + nM_{AA} + xM_{NIPAM} + yM_{BIS}$, where M_e is the molecular weight of the CTA end groups, n, x and y are the DP_n of pAA, pNIPAM, and BIS respectively. [f]DLS data obtained from 0.1% w/v nanogels dispersions in DI water at pH 7 and 25 °C. [g]Average zeta-potential and the standard deviation of five run measurements for 0.1% w/v nanogels dispersions in DI water with 1 mM KCl at pH 7 and 25 °C.

Number particle size distribution of pAA_{45}-*b*-$pNIPAM_{175}/BIS_3$ nanogels

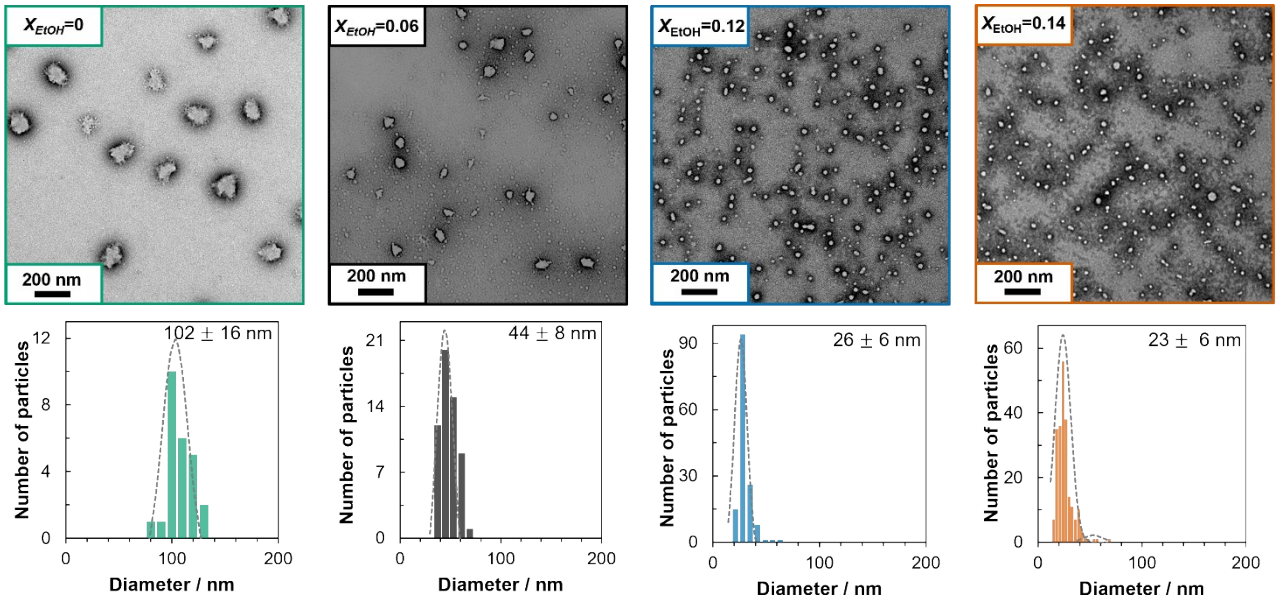

Figure S8. Transmission electron micrographs with their number particle size distributions of pAA_{45}-*b*-$pNIPAM_{87}/BIS_3$ nanogels synthesised in water/EtOH mixtures

Characterisation of pAA_{45}-*b*-$pNIPAM_{87}/BIS_3$ nanogels

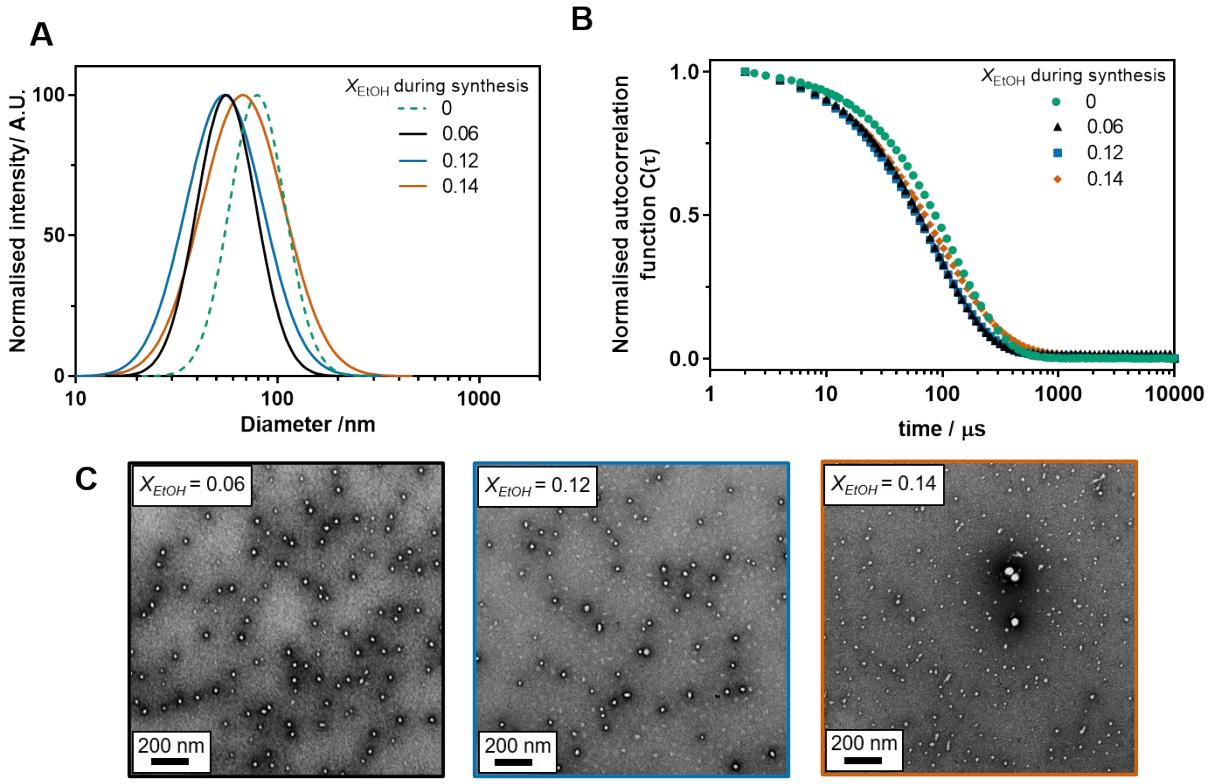

Figure S9. Characterisation of pAA_{45}-*b*-$pNIPAM_{87}/BIS_3$ nanogels synthesised in water/EtOH mixtures (a) Intensity average lognormal size distribution curves and (b) their respective autocorrelation functions with time from dynamic light scattering. (c) Transmission electron micrographs. DLS and TEM samples were prepared from 0.1% w/v nanogel dispersions in water at pH 7 at 25 °C. TEM samples were stained with phosphotungstic acid (0.75% w/v, pH 7).

Characterisation of pAA_{45}-*b*-$pNIPAM_{262}/BIS_3$ nanogels

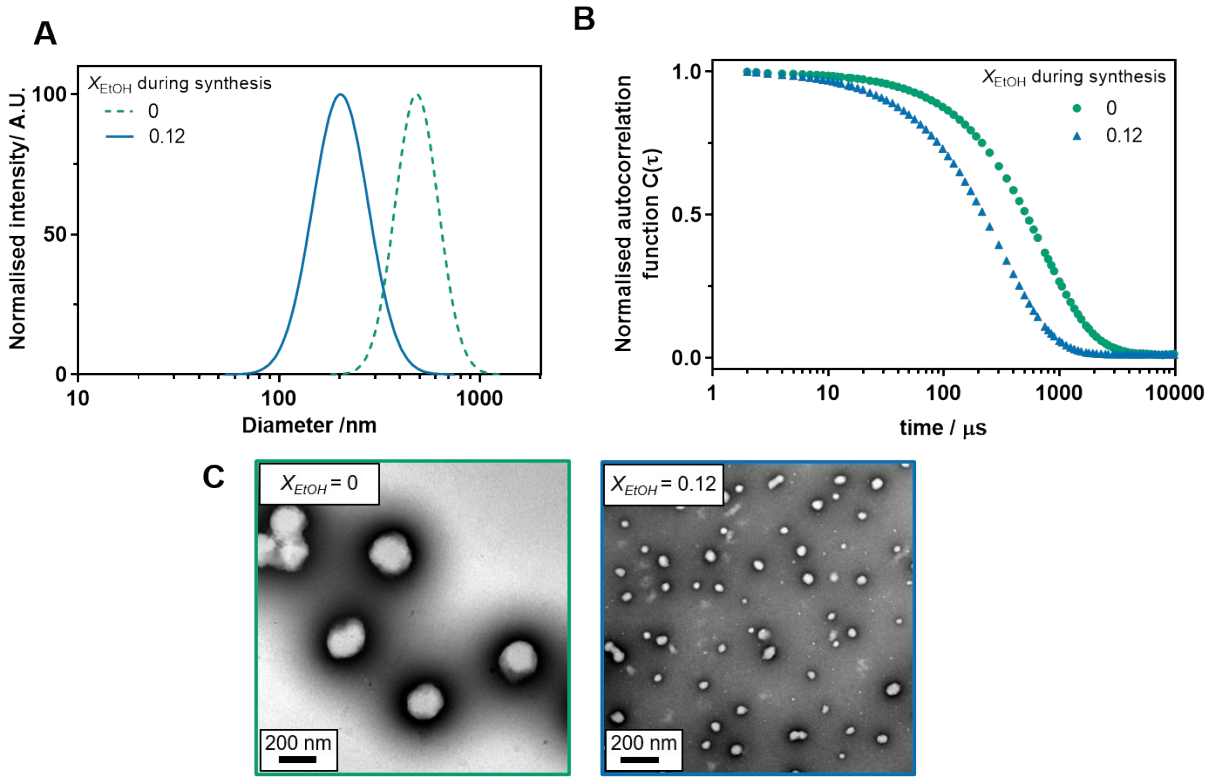

Figure S10. Characterisation of pAA_{45}-*b*-$pNIPAM_{262}/BIS_3$ nanogels synthesised in water/EtOH mixtures (a) Intensity average lognormal size distribution curves and (b) their respective autocorrelation functions with time from dynamic light scattering. (c) Transmission electron micrographs. DLS and TEM samples were prepared from 0.1% w/v nanogel dispersions in water at pH 7 at 25 °C. TEM samples were stained with phosphotungstic acid (0.75% w/v, pH 7).

Synthesis of pNIPAM *via* ethanolic RAFT solution polymerisation.

A mixture of NIPAM (3.01 g, 26.59 mmol), HEMP (0.06 g, 0.27 mmol), AIBN (0.008 g, 0.08 mmol) and ethanol (to give a 25% w/w solids solution) was purged thoroughly with N_2 for 30 minutes. The flask was then placed onto a DrySyn® heating block preheated to 70 °C and left to react for 240 minutes. The reaction was quenched by removing the flask from the heat source and opened to air. NIPAM conversion (98%) was calculated by ^{1}H NMR spectroscopy. The product was recovered by precipitation into hexane (400 mL). The product was then dissolved in water and purified by dialysis against water and freeze-drying to give a pale-yellow solid. PNIPAM$_{98}$ $\bar{M}_n$= 9.0 kDa, $\bar{M}_w/\bar{M}_n$ = 1.31. PNIPAM$_{190}$: conversion (95%) $\bar{M}_n$= 19.6 kDa, $\bar{M}_w/\bar{M}_n$ = 1.35; δH (400 MHz; $CDCl_3$, 25 °C) (ppm): 3.42 (br. s, H, -NC*H*), 2.67 (s, 2H, -CH_2SC), 2.48-1.95(br. d, 1H,-C*H*-), 1.95-1.46 (br. t, 2H, -CH_2-), 1.11 (br. s, 6H, -CH(CH_3)$_2$).

Cloud point measurements of linear pNIPAM in water/EtOH mixtures

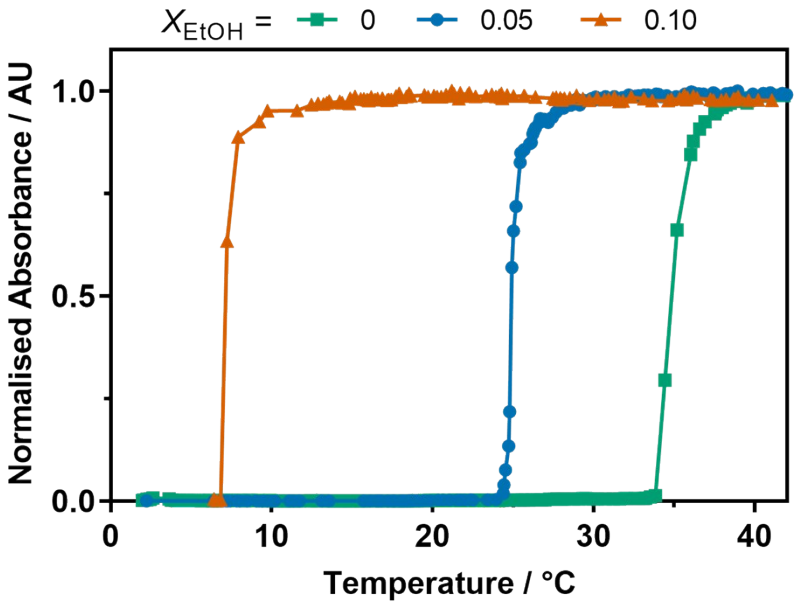

Figure S11. Cloud point curves of pNIPAM$_{98}$ in different X_{EtOH} fractions. Polymers were synthesised *via* RAFT ethanolic polymerisation. The cloud points were determined from the inflection point of the normalised absorbance curve at 550 nm at a heating rate of 0.12 °C min^{-1}

Synthesis of pNIPAM *via* free radical precipitation polymerisation.

NIPAM (0.5 g, 4.4 mmol) was dissolved in the corresponding water-ethanol cononsolvent mixture and degassed with N_2 for 30 minutes. Ammonium persulfate (0.32 mL, 69.3 mM) in water previously degassed was added *via* syringe into each of the NIPAM solutions to give a 10% w/w solids solution. The target mole fractions of ethanol and water were X_e=0, X_e=0.05, X_e=0.10 and X_e=0.15. Solutions were immersed into an oil bath preheated to 70 °C and left to react overnight. NIPAM monomer conversion (100 %) was estimated by ^{1}H NMR spectroscopy. The crude product was dialysed against DI water to exchange ethanol to water. For further characterisation, the polymers were freeze-dried to give white solids. δH (400 MHz, D_2O, 25 °C): 3.81 (br. d, H, -NC*H*), 2.30-1.79(br. d, 1H,-C*H*-), 1.79-1.27 (br. t, 2H, -CH_2-), 1.27-0.24 (br. s, 6H, -CH(CH_3)$_2$).

SEC of pNIPAM homopolymers synthesised in cononsolvents

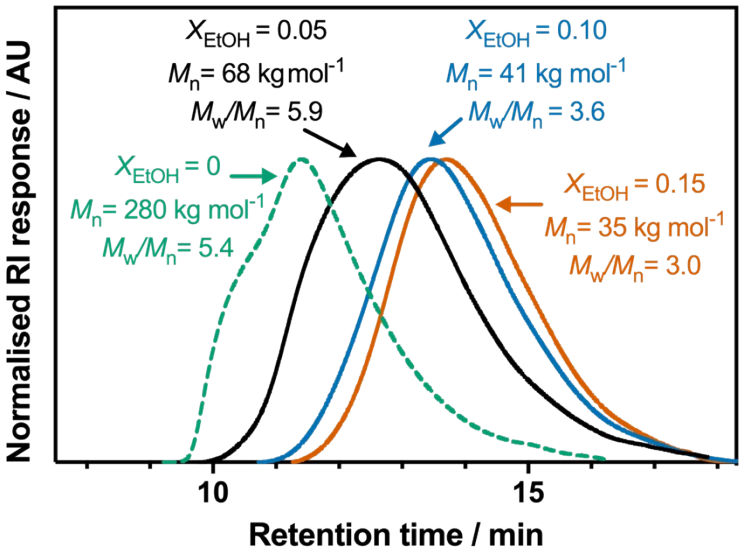

Figure S12. SEC chromatograms of pNIPAM homopolymers synthesised by precipitation polymerisation in different water and water/EtOH mixtures. SEC was performed in DMF (0.1% w/v LiBr) against pMMA standards.

Determination of the volume phase transition temperature (VPTT) of nanogels

The experimental D_h data was fitted with a Boltzmann sigmoidal model using a least squares regression to assist in the determination of the VPTT of the aqueous nanogel dispersions. The fit using sigmoidal models have previously been reported to determine the VPTT indicating a good approximation to experimental data.[1,2] Herein, Equation S1 relates the hydrodynamic size (D_h) at a specific temperature (T), where D_t and D_b are respectively the swollen ("top" temperature at 12.5 °C) and shrunken ("bottom" temperature 60 °C) hydrodynamic diameters, ω is the halfway point between the swollen and shrunk state (i.e. VPTT) and σ is the steepness of the curve (i.e. the sharpness around the phase transition).

$$D_h = D_t + \frac{D_t - D_b}{1 + e^{\left(\frac{\omega - T}{\sigma}\right)}} \qquad \text{Equation S1}$$

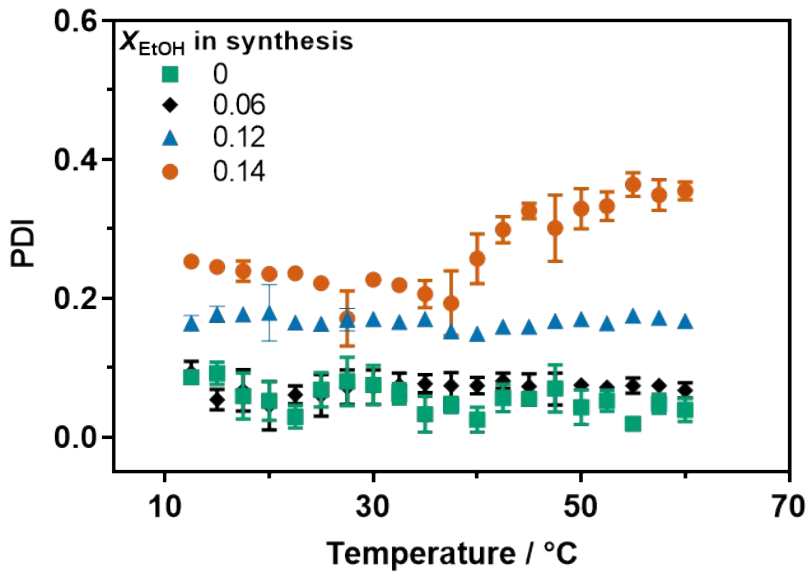

Figure S13. Variable temperature PDI data for pAA_{45}-*b*-($pNIPAM_{175}/BIS_3$) nanogels synthesised in water and water/EtOH mixtures as obtained by DLS.

Summary of data for pAA_{34}-*b*-$pNIPAM_x$ block copolymers

Table S3. Summary of data for pAA_{37}-*b*-$pNIPAM_x$ block copolymers

Targeted pNIPAM DP_n (x)[a]	X_{EtOH} [b]	Conversion[c] / %	$DP_{n,theo}$ [d]	Cloud point (T_c)[e] / °C	D_h ± S.D. / nm [f] (PDI)
92	0	>99	92	43	ill-defined
92	0.06	99	92	43	139 ± 57 (0.17)
92	0.11	99	91	45	178 ± 50 (0.08)
92	0.14	>99	92	47	153 ± 55 (0.13)
184	0	>99	184	34	49 ± 12 (0.06)
184	0.06	>99	184	36	63 ± 13 (0.04)
184	0.12	>99	184	39	93 ± 44 (0.22)
184	0.15	99	182	39	140 ± 56 (0.16)
280	0	>99	280	34	60 ± 12 (0.04)
280	0.06	99	277	34	63 ± 19 (0.09)
280	0.12	99	277	35	92 ± 36 (0.15)
280	0.15	99	277	36	141 ± 56 (0.16)

[a]General reaction conditions: Targeted [pAA_{34}]/[ACVA]=5, solids content 10% w/w,70 °C for 18 h. [b]Mole fraction of ethanol used during nanogel synthesis. [c]Gravimetric determination by moisture analysis of solids content against predicted solids content. [d]Estimated from [NIPAM/[pAA_{34}]×conversion. [e]Cloud points were estimated from the inflection point of the normalised absorbance curve of 1% w/v dispersions in water at 550 nm at a heating rate of 0.12 °C min^{-1}. [f]DLS data obtained from 0.1% w/v dispersions in DI water at pH 7 and 50 °C.

Cloud point measurements of pAA_{34}-*b*-$pNIPAM_{184}$ diblock copolymers synthesised in water and water/EtOH mixtures

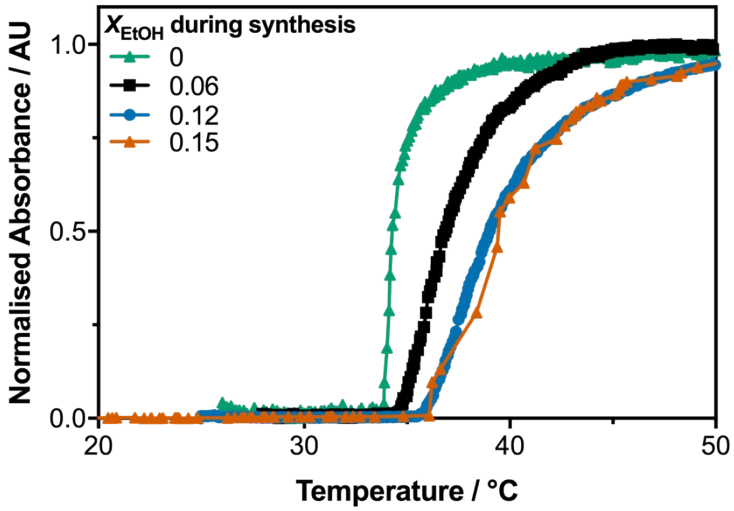

Figure S14. Turbidimetry experiments of purified pAA_{34}-*b*-$pNIPAM_{184}$ diblock copolymers at pH 7 in water.

^{1}H NMR spectra of pNIPAM homopolymers synthesised in cononsolvents

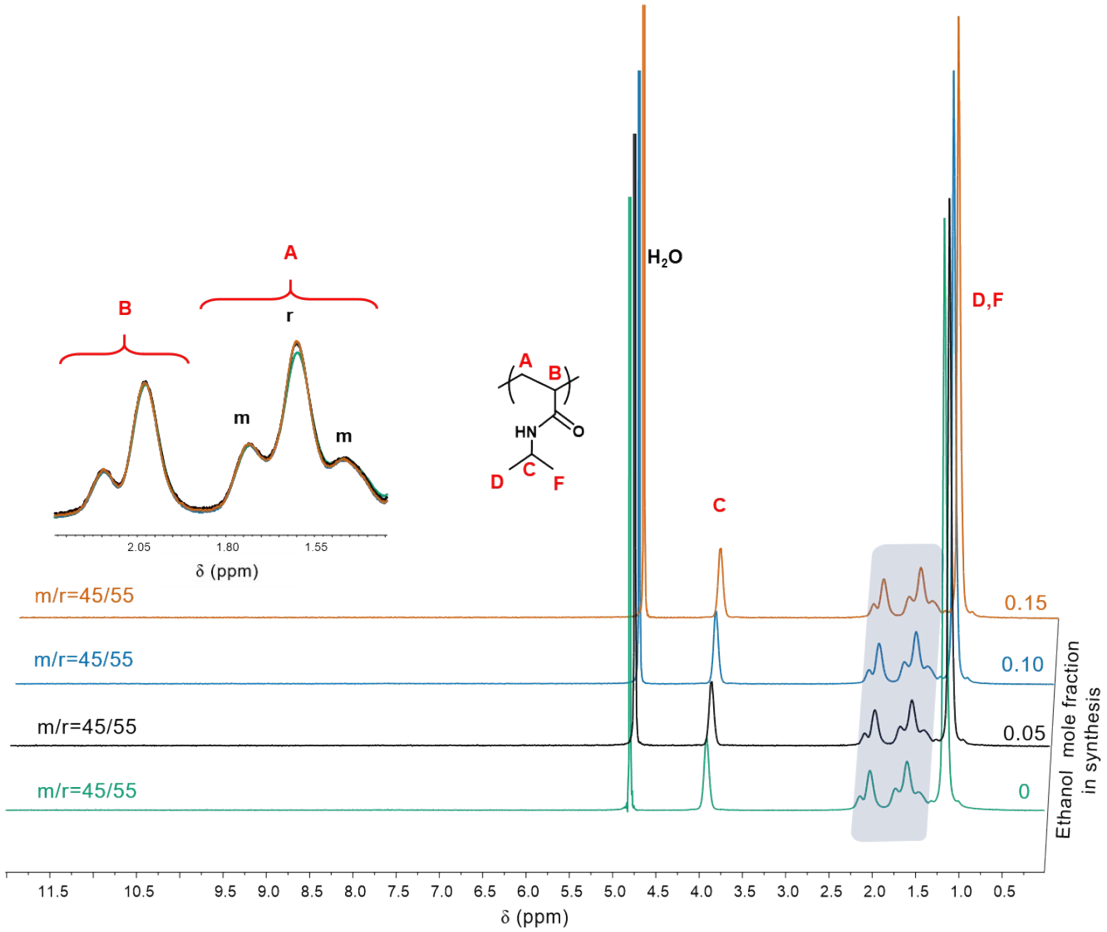

Figure S15. ^{1}H NMR spectra pNIPAM homopolymers synthesised by precipitation polymerisation in different water and water/EtOH mixtures. Spectra were recorded in D_2O.

Notes and references

1. A. L. Navarro-Verdugo, F. M. Goycoolea, G. Romero-Meléndez, I. Higuera-Ciapara and W. Argüelles-Monal, *Soft Matter*, 2011, **7**, 5847-5853.
2. S. Bandyopadhyay, A. Sharma, M. A. Ashfaq Alvi, R. Raju and W. R. Glomm, *RSC Advances*, 2017, **7**, 53192-53202.