Electronic Supplementary Material (ESI) for Polymer Chemistry

Synthesis of thermoresponsive oxazolone end-functional polymers for reactions with amines using thiol-Michael addition "click" chemistry

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Electronic Supporting Information

1.0 General

1.1 Reagents

Dimethylphenyl phosphine (DMPP) 99%, triethylamine (TEA) > 99%, and *n*-hexylamine > 99% were all purchased from Aldrich and used without further purification. *N*-isopropylacrylamide (97%) was purchased from Aldrich and recrystallized from petroleum ether prior to use. RAFT agent methyl-2-(*n*-butyltrithiocarbonyl) propanoate (MBTCCP) was synthesized and purified according to a literature procedure before use.[1] Azobisisobutyronitrile (AIBN) was purchased from Aldrich and recrystallized from methanol before use. 1,4-dioxane (>99%) was purchased from Janssen Chimica and distilled before use. Anhydrous tetrahydrofuran (THF) >99.9%, *N,N*-dimethylformamide (DMF, HPLC grade), and diethyl ether (technical grade) were obtained from Aldrich and used without additional prior distillation. 4,4 dimethyl-2-vinyl oxazolone was a gift and distilled under vacuum prior to use.

1.2 Analyses

Nuclear Magnetic Resonance (NMR)

NMR spectra were recorded on a Bruker AC-400 Spectrometer for ^{1}H NMR (400 MHz) and ^{13}C (100 MHz). Chemical shifts are reported in ppm relative to deuterated solvent resonances.

Size Exclusion Chromatography (SEC)

Polymers were characterized on a Polymer Laboratories SEC system operating in DMF eluent at 60^{o}C fitted with a guard column (PL Gel 5μm) and two Polymer Laboratories PL Mixed D columns, a Waters 410 differential refractometer (DRI) and a Waters 481 UV detector operating at 309 nm or 263 nm as appropriate. The instrument operated at a flow rate of 1.0 mL min^{-1} and was calibrated with narrow linear polystyrene (PS) standards ranging in molecular weight from 460,000 g mol^{-1} to 580 g mol^{-1}. Molecular weights and polydispersity indices (PDI) were calculated using Waters EMPOWER software.

MALDI-TOF mass spectrometry

MALDI-TOF (Matrix-Assisted Laser Desorption and Ionization Time Of Flight) mass spectrometry analysis was performed on a Bruker Biflex III MALDI-TOF instrument equipped with nitrogen laser operating at 337 nm, a 2GHz sampling rate digitiser, pulsed ion extraction source and reflectron. The laser pulse width is 3ns and maximum power is 200 mJ. Spectra were recorded in the linear mode with an acceleration voltage of 19 kV and delay of 200 ns. 100 single shot aquisitions were summed to give the spectra and the data were analyzed using Bruker XTOF software.

Samples of PNIPAM were prepared by dissolving the matrix (*trans*-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene]malononitrile, DCTB) in the solvent (dichloromethane, 30 mg mL^{-1}) and mixing with the polymer (PNIPAM, 2 mg mL^{-1}) in the ratio 1:50 (v/v). 1 μL was spotted directly onto

[1] Pascual, S.; Monteiro, M. J. *Eur. Polym. J.* **2009**, *45*, 2513-2519.

a thin layer of sodium trifluoroacetate in acetone (concentration 19 mg mL^{-1}) that had been deposited to act as a cationizing agent.

2.0 Synthesis and characterization of PNIPAM-CTA

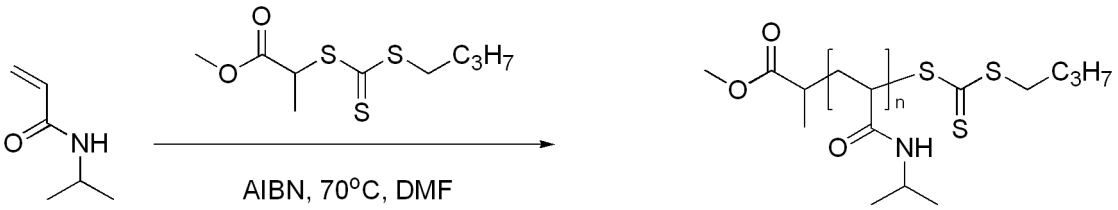

Figure SS1: Polymerization of NIPAM mediated by MBTCCP.

Method: A magnetic stir bar was charged to a Schlenk tube along with *N*-isopropylacrylamide, MBTCCP, AIBN and DMF solvent and the mixture was deoxygenated by a series of freeze-pump thaw cycles. When no further bubbles were observed the reaction mixture was switched to an argon atmosphere and the Schlenk tube immersed in a thermostated oil bath operating at 70°C and left for a period of five hours. After this time had elapsed the polymerization reaction was stopped by opening the reaction to air, and the polymer was purified by precipitation in diethyl ether, separated using Buchner filtration and drying under vacuum at 30°C overnight. The polymer was analyzed by ^{1}H NMR spectroscopy, SEC, and MALDI-TOF mass spectrometry.

SEC analysis (relative to PS calibration; Fig. SS3): M_n = 7850 g.mol^{-1}; M_w = 8300 g.mol^{-1}; PDI = 1.05.

^{1}H NMR analysis (Fig. SS2): DP_n = 26 (determined from the ratio of the triplet at 3.7 ppm, labeled B, to that of the broad resonance at 4.1 ppm, labeled A); M_n^{NMR} = 3200 g mol^{-1} (= 87 + (26 x 113.16) +165).

MALDI-TOF analysis: see Fig. SS8 and Table SS1 below.

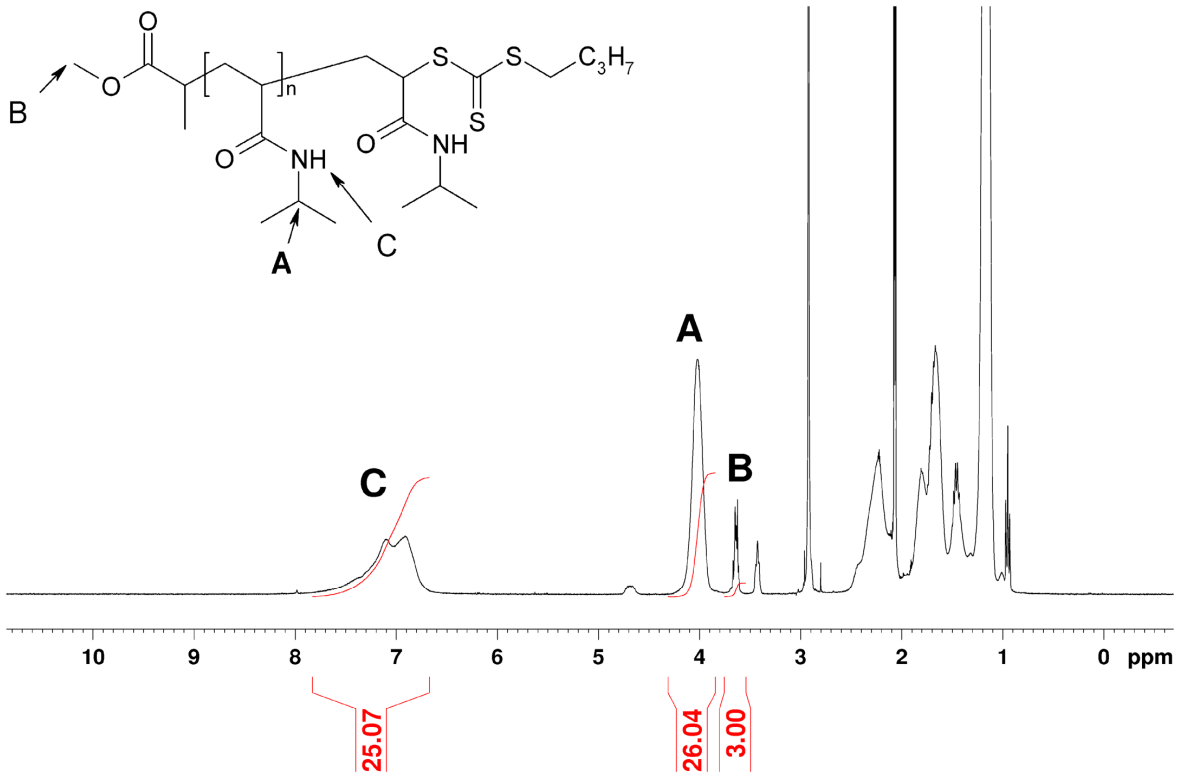

Figure SS2: ^{1}H NMR spectrum of PNIPAM-CTA.

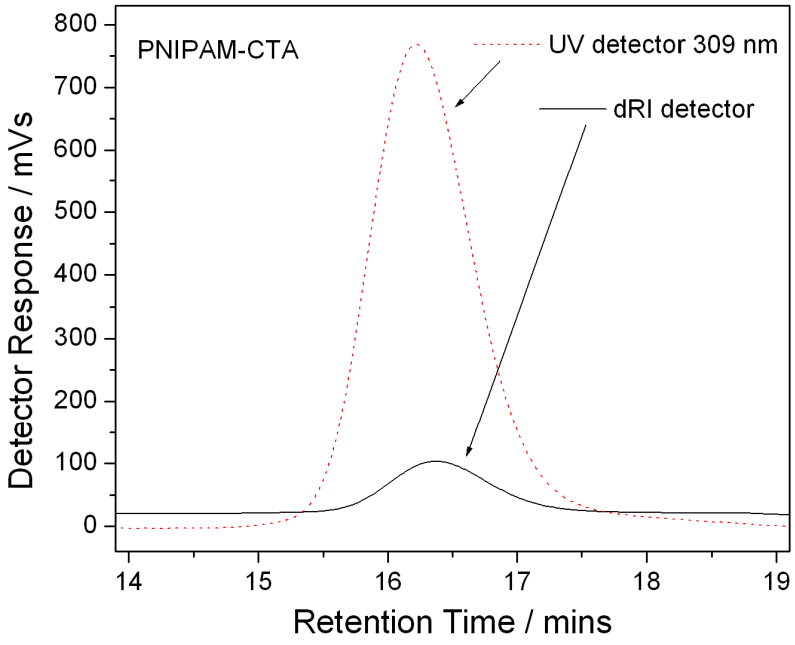

Figure SS3: Overlaid SEC chromatograms from dRI and UV detector for PNIPAM-CTA.

3.0 Aminolysis of PNIPAM-CTA in the presence of DMPP

Figure SS4: Aminolysis of PNIPAM-CTA to PNIPAM-SH in the presence of DMPP.

Method: A magnetic stir bar was charged to a Schlenk tube along with PNIPAM-CTA (1.0 g, 2.9 x10^{-4} mol), DMPP (60 µL, 4.16 x 10^{-4} mol), *n*-hexylamine (0.3mL, 0.23 g, 2.2 x 10^{-3} mol) and THF (3 mL, solvent) and the reaction mixture was deoxygenated by a series of freeze-pump thaw cycles. When no further bubbles were observed the mixture was stirred at ambient temperature for two hours. When this time had elapsed the product was precipitated into diethyl ether, filtered using Buchner apparatus and dried under vacuum at 30°C. A white powder was obtained and analyzed by SEC (Fig. SS5-6).

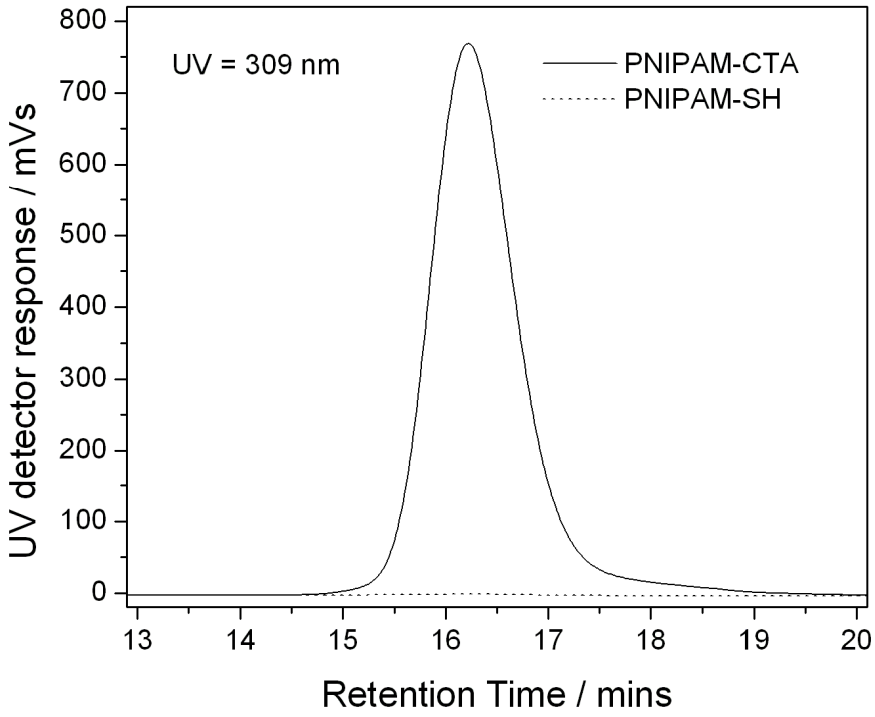

Figure SS5: Overlaid raw SEC chromatograms from the UV detector operating at 309 nm of PNIPAM-CTA before aminolysis (solid line) and PNIPAM-CTA after aminolysis (dotted line).

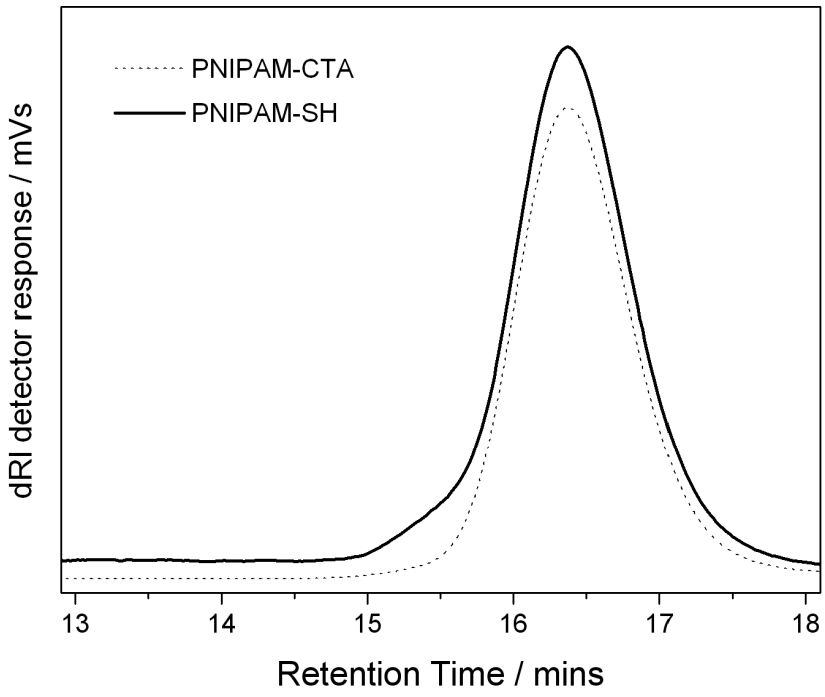

Figure SS6: Overlaid raw SEC chromatograms from the dRI detector corresponding to PNIPAM-CTA before aminolysis (dotted line) and PNIPAM-SH after aminolysis (solid line) by *n*-hexylamine in the presence of DMPP.

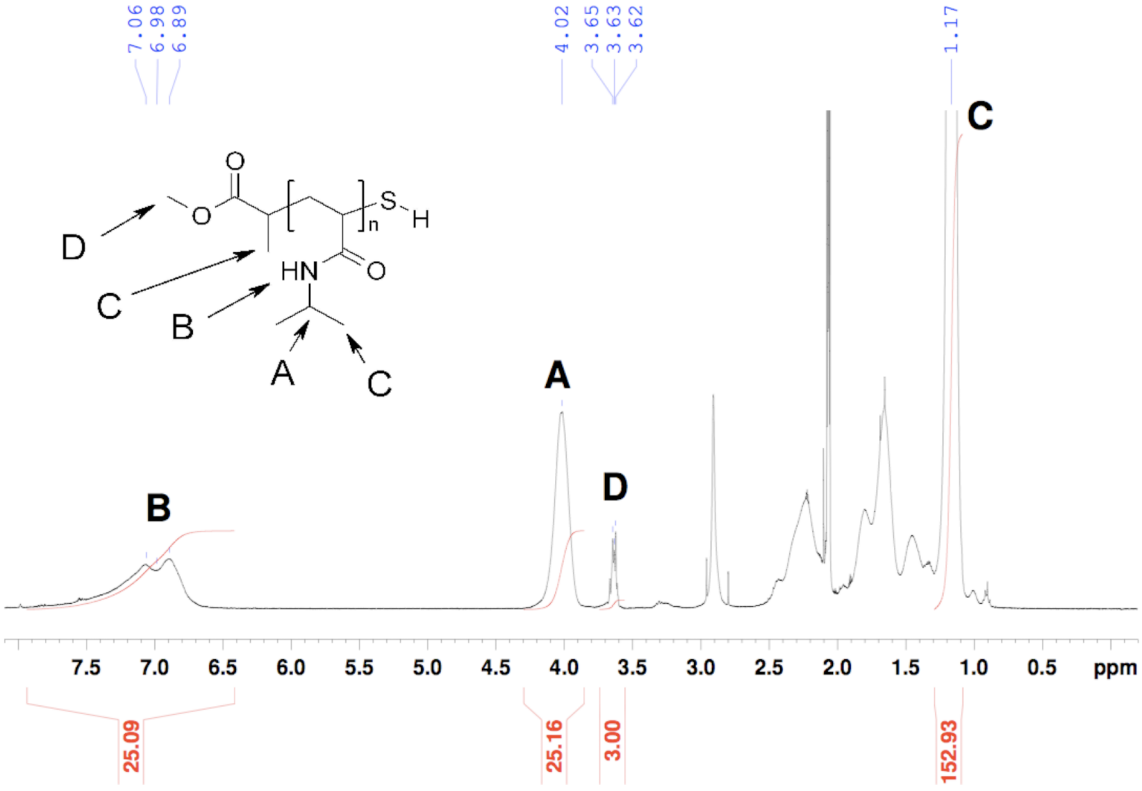

Figure SS7: ^{1}H NMR spectrum of PNIPAM-SH.

NMR analysis: Fig. SS7 shows the absence of a signal at 0.95 ppm compared with Fig. SS2, corresponding to the loss of aliphatic protons as the $-S(C=S)C_4H_9$ group is cleaved by aminolysis. The DP_n is calculated to be 25 in this spectrum: integral D corresponds to the 3 protons of chain end and integral A corresponds to the proton of the PNIPAM repeating units.

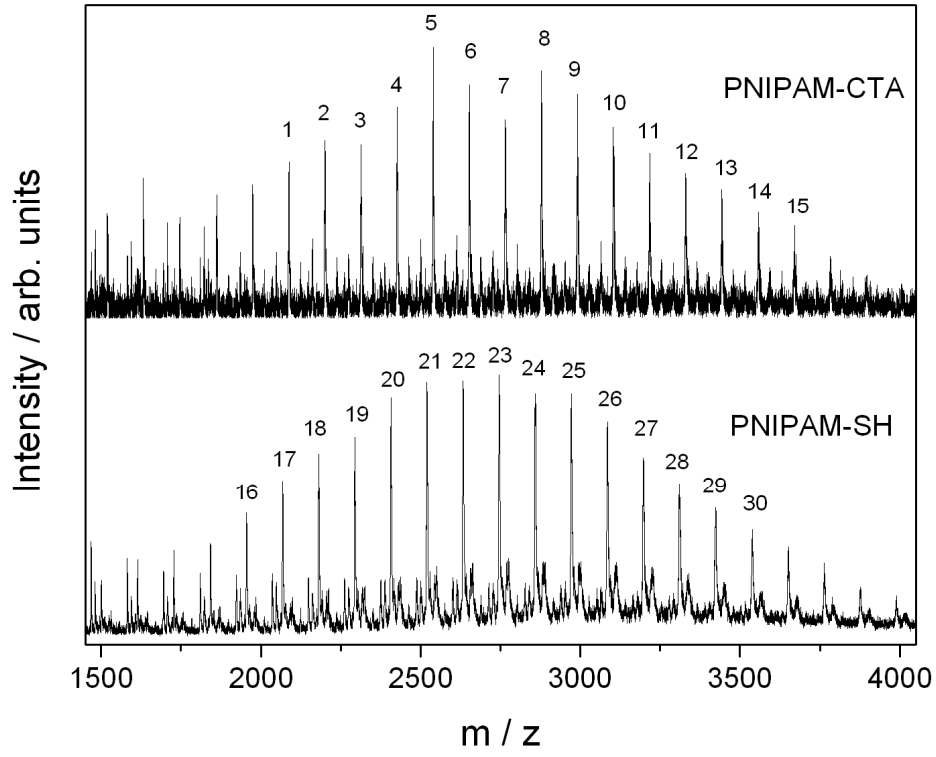

Figure SS8: MALDI-TOF spectra for PNIPAM-CTA (top) and PNIPAM-SH (bottom).

Table SS1: Analysis of MALDI-TOF spectra of PNIPAM-CTA and PNIPAM-SH (Figure SS8).

DPn (PNIPAM)	Label[a]	PNIPAM-CTA m/z (exp.)	Label[a]	PNIPAM-SH m /z (exp.)
16	*1*	2087.04	*16*	1953.89
17	*2*	2199.20	*17*	2066.82
18	*3*	2311.84	*18*	2179.94
19	*4*	2425.99	*19*	2293.35
20	*5*	2538.69	*20*	2406.47
21	*6*	2652.50	*21*	2519.38
22	*7*	2765.20	*22*	2632.61
23	*8*	2878.46	*23*	2745.72
24	*9*	2991.14	*24*	2858.62
25	*10*	3103.24	*25*	2971.73
26	*11*	3217.81	*26*	3084.82
27	*12*	3329.44	*27*	3197.73
28	*13*	3442.78	*28*	3310.57
29	*14*	3556.05	*29*	3424.06
30	*15*	3669.61	*30*	3536.77

[a] label in Fig. SS8.

4.0 Optimized thiol-Michael addition reaction between PNIPAM-SH and VDM

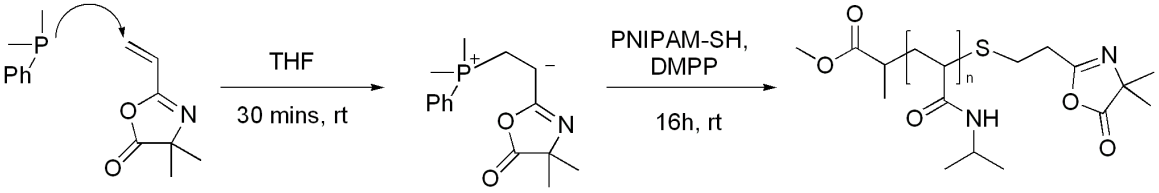

Figure SS9: Thiol-Michael addition reaction between PNIPAM-SH and VDM.

Method: A magnetic stir bar was charged to a Schlenk tube along with VDM (15 µL, 1.08 x 10^{-4} mol), DMPP (25 µL, 1.73 x 10^{-4} mol), and THF (1 mL, solvent) and stirred at room temperature for 30 minutes. The reaction media increased in viscosity and a yellow color was observed. After this time had elapsed, PNIPAM-SH (0.1 g, 3.1 x 10^{-5} mol) and an additional quantity of DMPP (15 µL, 1.04 x 10^{-4} mol) were added to the reaction mixture and the solution was left to react for 16 hours. It should be noted that the viscosity decreased upon addition of PNIPAM and the yellow color diminished. When this time had elapsed the polymer was precipitated into diethyl ether, filtered using Buchner apparatus and dried under vacuum at room temperature.

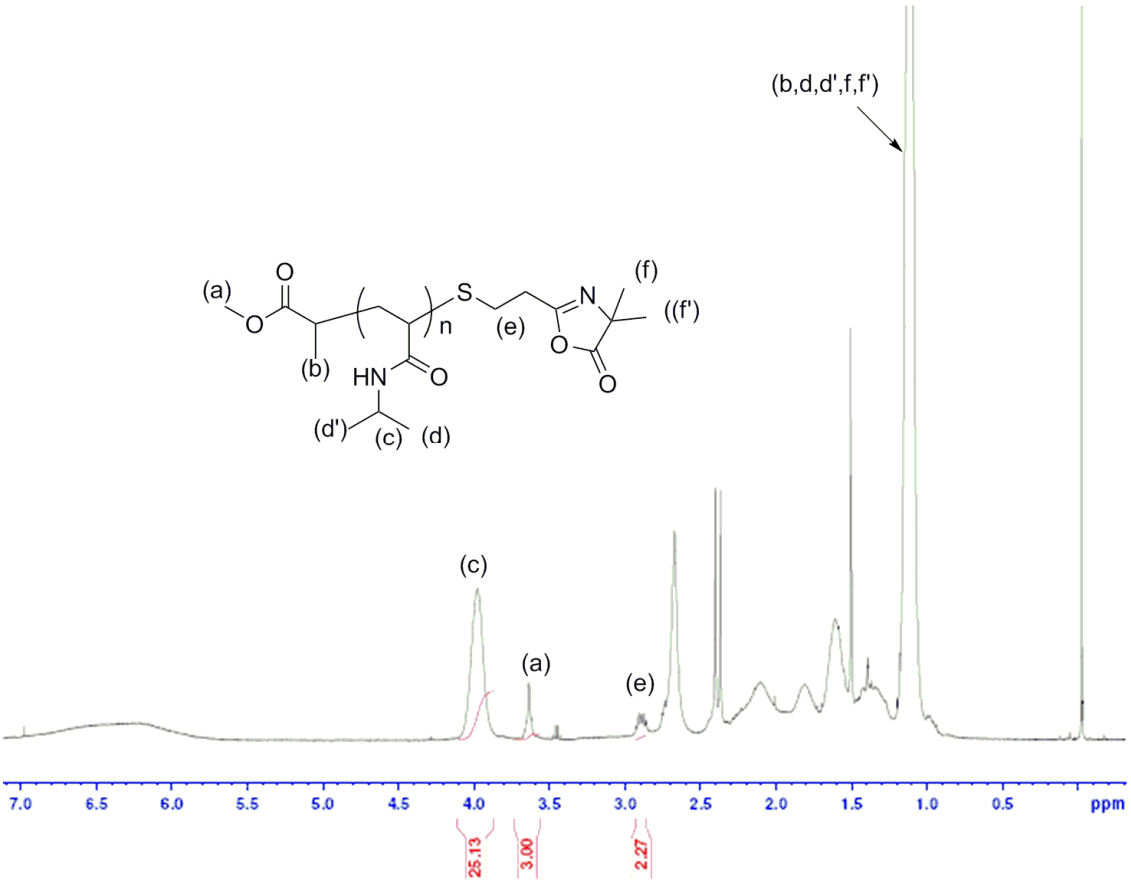

Figure SS10: ^{1}H NMR spectrum PNIPAM-VDM after thiol-Michael addition "click" reaction.

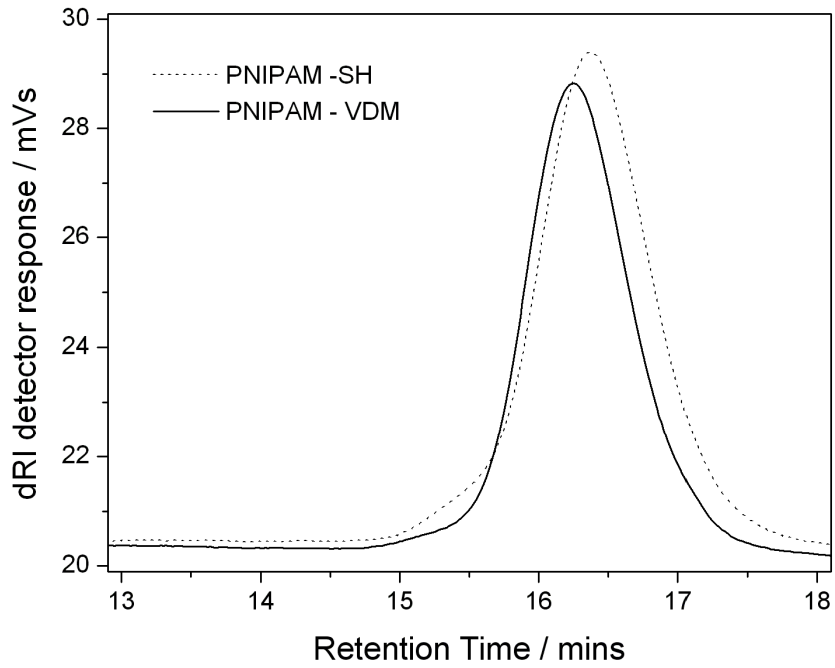

Figure SS11: Overlaid raw SEC chromatograms from the dRI detector corresponding to PNIPAM-SH (dotted trace) and the product of the optimized thiol-Michael addition reaction between PNIPAM-SH and VDM (PNIPAM-VDM, solid line) in the presence of DMPP; ratio $[VDM]_0$ / $[DMPP]_0$ = 1 / 2.6.

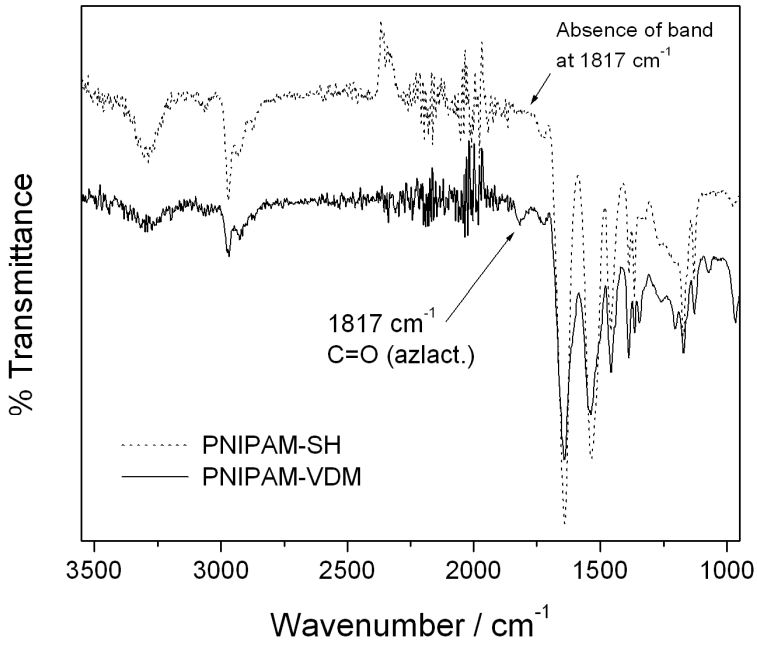

Figure SS12: Overlaid Infra-Red spectra of PNIPAM-SH before thiol-Michael addition reaction with VDM (dotted line), and after the thiol-Michael addition reaction between PNIPAM-SH and VDM, titled PNIPAM-VDM (solid line). The appearance of the peak corresponding to the azlactone ring is labeled.

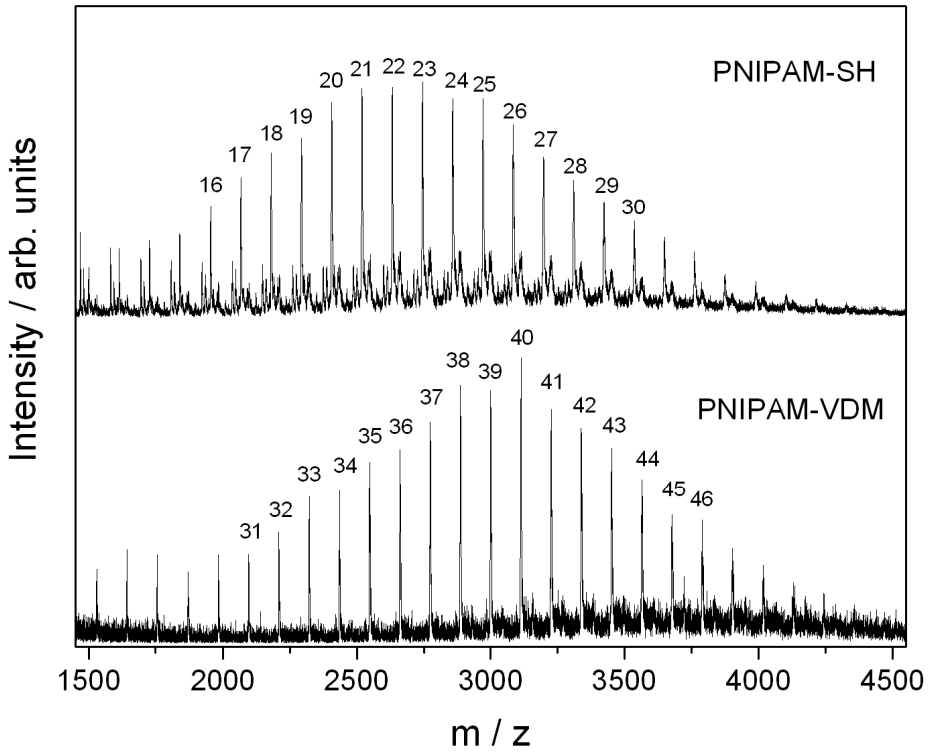

Figure SS13: MALDI-TOF spectra for PNIPAM-SH (top) and PNIPAM-VDM (bottom).

Table SS2: Analysis of MALDI-TOF spectra before (PNIPAM-SH) and after (PNIPAM-VDM) thiol-Michael addition "click" reaction of VDM to PNIPAM (Figure SS13).

DP_n (PNIPAM)	Label[a]	PNIPAM-SH m /z (exp.)	Label[a]	PNIPAM-VDM m /z (exp.)
16	*16*	1953.89	*31*	2093.05
17	*17*	2066.82	*32*	2204.39
18	*18*	2179.94	*33*	2319.51
19	*19*	2293.35	*34*	2432.49
20	*20*	2406.47	*35*	2545.62
21	*21*	2519.38	*36*	2658.67
22	*22*	2632.61	*37*	2771.79
23	*23*	2745.72	*38*	2884.82
24	*24*	2858.62	*39*	2997.59
25	*25*	2971.73	*40*	3110.90
26	*26*	3084.82	*41*	3223.92
27	*27*	3197.73	*42*	3337.13
28	*28*	3310.57	*43*	3450.04
28	*29*	3424.06	*44*	3563.24
30	*30*	3536.77	*45*	3676.16

[a] label in Fig. SS13.

5.0 Determination of the optimum conditions for the thiol-Michael addition of PNIPAM-SH to VDM

Online ^{1}H NMR was used to analyze a mixture of DMPP and VDM. DMPP (20 µL, 0.14 mmol) and VDM (17 µL, 0.12 mmol) were dissolved in $CDCl_3$ and placed in an NMR tube. The sample was analyzed by ^{1}H NMR (200 MHz, 32 scans) at t = 0, t = 1 hour and t = 4 hours (Fig. SS14).

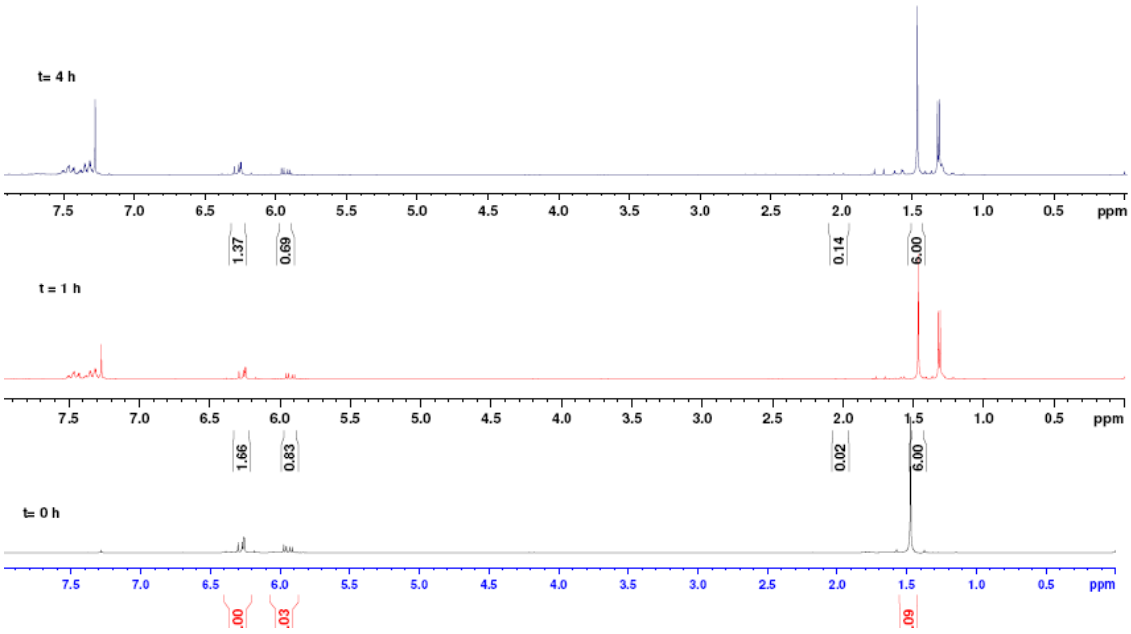

Figure SS14: Stacked online ^{1}H NMR spectra at t = 0, t = 1 hour and t = 4 hours for the reaction between dimethylphenyl phosphine (DMPP) and VDM in $CDCl_3$, ratio [DMPP] / [VDM] = 1.15 / 1.

6.0 Reaction between PNIPAM-VDM and 4-fluorobenzylamine

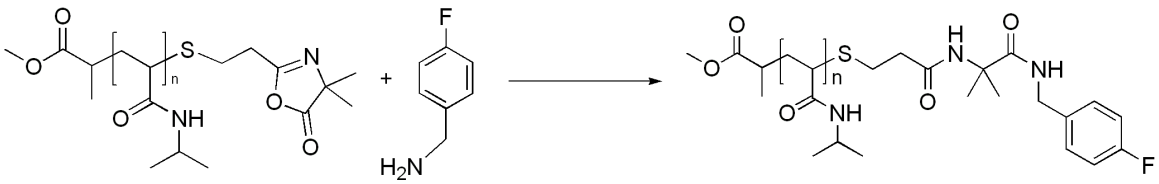

Figure SS15: Reaction between PNIPAM-VDM and 4-fluorobenzylamine.

Method: A magnetic stir bar was charged to a small round bottomed flask along with PNIPAM-VDM and anhydrous THF solvent. Once the polymer had dissolved, 4-fluorobenzylamine was added and the mixture left to stir for four hours. When this time had elapsed, the polymer was precipitated into diethyl ether, separated using Buchner filtration and dried under vacuum at room temperature. The ^{1}H NMR spectrum (Fig. SS17) shows the appearance of new signals at 7.0 ppm and 7.4 ppm that correspond to the aromatic protons of 4-fluorobenzylamine. Integrations of protons (g) (2H) and protons (a) (3H) show that the reaction is quantitative (see Fig. SS17).

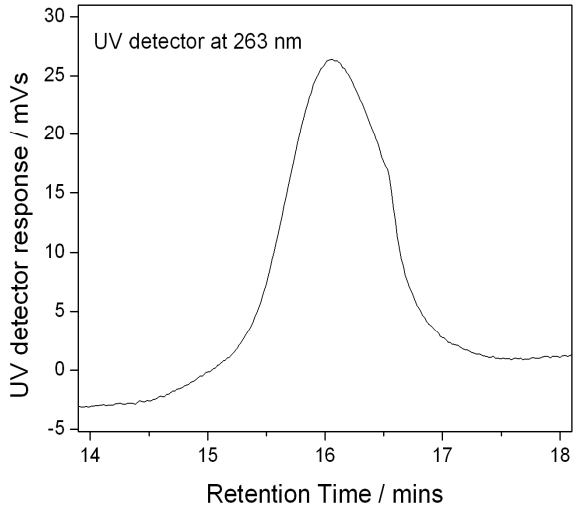

Figure SS16: Raw SEC chromatogram from the UV detector at 263 nm for the product of the reaction with PNIPAM-VDM and 4-fluorobenzylamine.

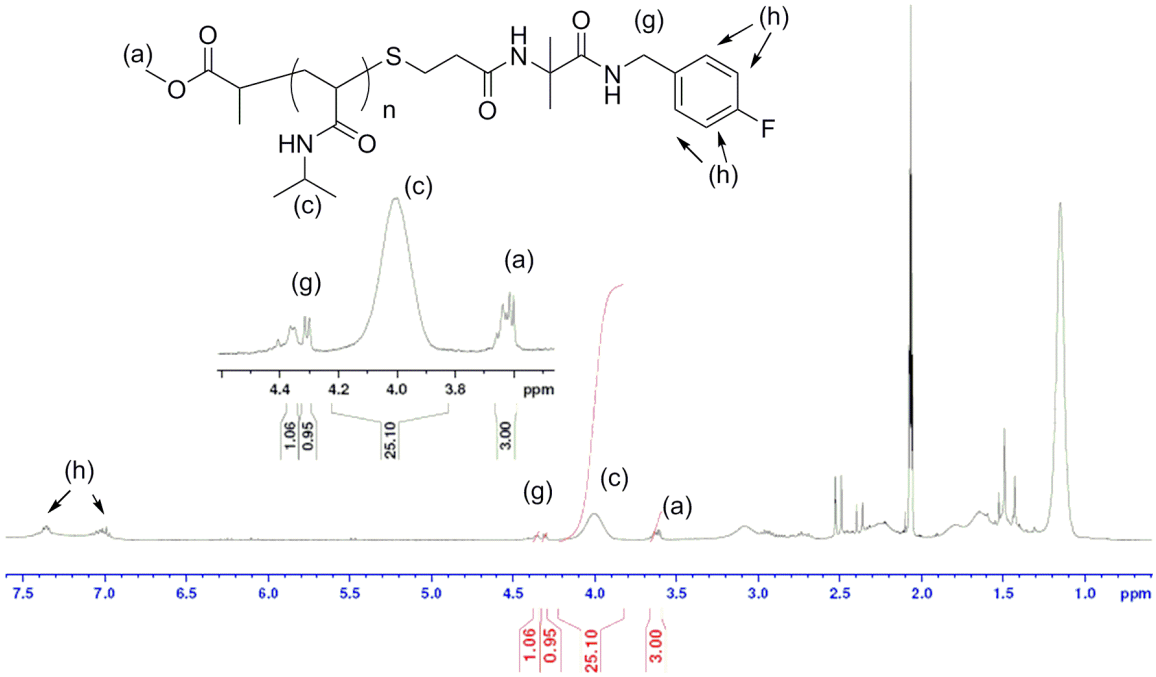

Figure SS17: ^{1}H NMR spectrum of PNIPAM-VDM after reaction with 4-fluorobenzylamine.