Supporting Information

PDMAEMA from α to ω Chain Ends: Tools for Elucidating the Structure of Poly(2-(dimethylamino)ethyl methacrylate)

Maria Rosella Telaretti Leggieri,[a] Tahani Kaldéus,[a,b] Mats Johansson,[a,b] and Eva Malmström*[a,b]

[a] Division of Coating Technology, Department of Fibre and Polymer Technology, School of Engineering Science in Chemistry, Biotechnology and Health, KTH Royal Institute of Technology, Teknikringen 56–58, SE-100 44 Stockholm, Sweden.
[b] Wallenberg Wood Science Center, Department of Fibre and Polymer Technology, KTH Royal Institute of Technology, Teknikringen 56--58, SE-100 44 Stockholm, Sweden.
*Email: mavem@kth.se.

1. Experimental

Materials

2-(Dimethylamino)ethyl methacrylate (DMAEMA, 98%) and methyl methacrylate (MMA, 99%) were purchased from Merck and passed through a column of activated basic aluminium oxide prior to use, to remove the inhibitor. Aluminium oxide (90 active basic), copper(I) bromide (CuBr, 99.9%), copper(II) bromide ($CuBr_2$, 99%), copper(I) chloride (CuCl, ≥99%), copper(II) chloride ($CuCl_2$, 99%), 2,5-dihydroxybenzoic acid (DHB, 98%), *N,N*-dimethylacetamide (99.8%), ethyl α-bromoisobutyrate (EBiB, 98%), ethyl α-bromophenylacetate (EBPA, 97%), 1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTETA, 97%), 10-phenylphenothiazine (PTH, ≥95%), sodium trifluoroacetate (NaTFA, 98%) were purchased from Merck and used as received. Acetone (98%), deuterated acetone (acetone-d_6, 99.8%), deuterated chloroform ($CDCl_3$, 99.8%), deuterium oxide (D_2O, 99.96%), *N,N*-dimethylformamide (DMF, >99.9%), methanol (MeOH, >99.9%) and tetrahydrofuran (THF, ≥99%) were purchased from VWR Chemicals and used as received.

Synthesis of PDMAEMA by ATRP

A round-bottom flask was charged with EBiB (954 mg, 4.89 mmol), DMAEMA (50.0 g, 318 mmol), DMF as the internal standard (1.79 g, 24.5 mmol) and placed in ice bath under magnetic stirring. The flask was sealed with a rubber septum and degassed by purging argon in the solution for 15 min. CuBr (702 mg, 4.89 mmol) and HMTETA (2.26 g, 9.79 mmol) were dissolved in acetone (50.0 g, 861 mmol) in a conical flask. The flask was sealed with a rubber septum and degassed by purging argon in the solution for 10 min. The CuBr solution was transferred into the flask under argon flow, which was stopped after an additional 5 min. The reaction was allowed to start by placing the flask in an oil bath pre-heated to 30 °C. Small aliquots were withdrawn from the solution under argon flow, purified and used for NMR, SEC and MALDI-TOF MS analyses. At 52% monomer conversion (t = 135 min), argon was purged in the solution and a degassed 10 g/L acetone solution of $CuBr_2$ (1.09 g, 4.89 mmol) was added and stirred in for 1 min. Finally, the reaction mixture was quenched by placing the flask in an ice bath and exposing it to air. The copper complexes were removed by passing the mixture through a column of basic aluminium oxide. The polymer, dissolved in acetone, was precipitated twice in 100 mL/$g_{polymer}$ ice-cold heptane. The recovered PDMAEMA (82% yield) was stored in acetone solution at 4 °C. PDMAEMA was dried under vacuum at room temperature prior to use.

Synthesis of $PDMAEMA_{Cl}$ by ATRP

The polymerization was carried out with the same experimental conditions and reagent molar ratios described above for the synthesis of PDMAEMA. The reagent amounts were as follows: EBiB (191 mg, 979 µmol), DMAEMA (10.0 g, 63.6 mmol), CuCl (96.9 mg, 979 µmol), HMTETA (451 mg, 1.96 mmol), acetone (10.0 g), $CuCl_2$ (132 mg, 979 µmol). $PDMAEMA_{Cl}$ was recovered at 48% conversion and purified according to the procedure above described.

Synthesis of $PDMAEMA_{UV,EBiB}$ and $PDMAEMA_{UV,EBPA}$ by photomediated ATRP

For the synthesis of $PDMAEMA_{UV,EBiB}$, a glass vial initially covered with aluminum foil was charged with *N,N*-dimethylacetamide (4.00 g), DMAEMA (4.00 g, 25.4 mmol), EBiB (76.3 mg, 391 µmol) and PTH (10.77 mg, 39.1 µmol),

and equipped with a magnetic stir bar. For the synthesis of $PDMAEMA_{UV,EBPA}$, EBPA (95.1 mg, 391 µmol) replaced EBiB. The vial was sealed with a rubber septum and degassed by purging argon in the solution for 10 min. After that, the vial was placed on the plate of a Phoseon FireJet FJ800 UV LED light source (wavelength: 365 nm), which was placed on top of a stirring plate (Figure S26). Under magnetic stirring, the solution was exposed to UV light, with a light intensity of 1.5 mW/cm^2, for 20 min. Then, the polymer was precipitated twice in 100 mL/$g_{polymer}$ ice-cold heptane and then stored at 4 °C.

Chain Extension of PDMAEMA by ATRP

PDMAEMA was chain extended with MMA, producing a PDMAEMA-*b*-PMMA block copolymer. A round-bottom flask was charged with PDMAEMA, previously synthesized (6.87 g, 1.17 mmol), MMA (50.0 g, 499 mmol) and DMF as the internal standard (4.56 g, 62.4 mmol) and placed in ice bath under magnetic stirring. A solution of CuCl (124 mg, 1.25 mmol) and HMTETA (575 mg, 2.50 mmol) in acetone (25.0 g, 172 mmol) was added. The flask was sealed with a rubber septum and degassed by purging argon in the solution for 15 min. The reaction was allowed to start by placing the flask in an oil bath pre-heated to 50 °C. Small aliquots were withdrawn from the solution under argon flow, purified and used for NMR and SEC analyses. At 55% conversion (t = 280 minutes), the reaction was stopped by placing the flask in an ice bath and exposing the mixture to air. The copper complexes were removed by passing the mixture through a column of with basic aluminium oxide. PDMAEMA-*b*-PMMA, dissolved in THF, was precipitated three times in 100 mL/$g_{polymer}$ ice-cold methanol and dried under vacuum at room temperature. The copolymer was recovered with 42% yield and stored at 4 °C.

Characterization Techniques

Nuclear Magnetic Resonance (NMR) Spectroscopy. One- and two-dimensional NMR experiments were conducted with a Bruker Avance spectrometer (400 MHz), at room temperature, using acetone-d_6, $CDCl_3$ and D_2O as solvents. One bond proton–proton correlations were investigated by correlation spectroscopy (COSY); one bond carbon–proton correlations by heteronuclear single quantum coherence (HSQC); two and three bond carbon–proton correlations by heteronuclear multiple bond correlation (HMBC); the multiplicity of carbon atoms was determined with distortionless enhancement by polarization transfer (DEPT); diffusion-ordered spectroscopy (DOSY) was used to separate the signals of molecules of different sizes on the basis of the signal decay related to their diffusion. ^{1}H-NMR spectra were acquired with 64 scans, 1 s relaxation delay; ^{13}C-NMR spectra with 4096 scans, 10 s relaxation delay; DEPT spectra with 3072 scans, 10 s relaxation delay; COSY spectra with 4 scans, 1.5 s relaxation delay, 512 increments; HSQC and HMBC spectra with 10 scans, 4 s relaxation delay, 512 increments. Samples for ^{1}H-NMR were prepared at a concentration of 10–20 mg/mL, while samples for ^{13}C-NMR at 90 mg/mL. In ^{1}H-NMR and ^{13}C-NMR spectra, the following signals of the solvents were used as reference: $CDCl_3$, 7.26 and 77.16 ppm; acetone-d_6, 2.05 and 29.84 ppm respectively. In ^{1}H-NMR spectra in D_2O, the solvent signal at 4.79 ppm was used as reference. During polymerization reactions, DMF was used as internal standard. The conversion was determined by the ratio between the integrated monomer signals $H_{b'}$ and $H_{b''}$ at end of reaction and at t = 0, while the integral of a selected signal of the internal standard was set to 1 (Figure S1). Nearly identical values of conversion were obtained from the ratio between the integrated polymer and monomer signals denoted H_e and $H_{e'}$.

Size-Exclusion Chromatography (SEC). A Tosoh EcoSEC HLC-8320GPC system was used to determine the molecular weight distribution (MWD), number average molecular weight ($\bar{M}_n$) and dispersity ($Đ = \bar{M}_w/\bar{M}_n$) of the polymers. The instrument was equipped with an EcoSEC RI detector and three PSS PFG 5 µm micro columns (MicroGuard, 100 Å, and 300 Å), with a resolving range between 300 and 100 000 g/mol. SEC was performed with DMF as eluent (0.2 mL/min), containing 0.01 M LiBr, and toluene as the internal standard, at 50 °C. The calibration was created using PSS poly(methyl methacrylate) standards. The samples were purified by filtering through basic aluminium oxide, dissolved in 3 g/L DMF containing toluene and filtered through Thermo Fisher Scientific Fisherbrand PTFE membrane filters with 0.45 µm pore size prior analysis.

Matrix-Assisted Laser Desorption Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS). Mass spectra were generated using a Bruker UltraFlex MALDI-TOF mass spectrometer equipped with a Bruker Scout-MTP ion source, a N_2 laser operating at 337 nm and a reflector. The instrument was used in positive ion mode and calibrated using Polymer Factory SpheriCal monodisperse dendrimer standards. The samples were prepared by mixing 5 µL of a 1 g/L polymer solution in THF with 5 µL of a 2 g/L NaTFA solution in THF and 40 µL of a 10 g/L DHB solution in THF, and applying approximately 1 µL of this mixture to a Bruker MPT 284 target plate. The spectra were acquired by screening the sample spot surface in the range of *m/z* 1000–8000, with laser power set to 20–25% (the lowest intensity allowing for the acquisition of high-resolution spectra of the analyzed samples). Simulated isotope distributions were produced using the EnviPat Web 2.4 software developed by Loos et al.[1].

Elemental Analysis (EA). Total nitrogen analysis by means of a PAC Antek MultiTek elemental analyzer was used to determine the molar ratio between the two polymer blocks in the copolymer and back-calculate the copolymer's average molecular weight ($\bar{M}_{n,EA}$), by detecting the nitrogen in the PDMAEMA block. A calibration curve (Figure S25) was made by injecting 1–15 µL samples of PDMAEMA macroinitiator (the same polymer batch used for chain extension) dissolved in acetone (10 g/L). Each datapoint of the calibration curve resulted from the average of six measurements. Thereafter, PDMAEMA-*b*-PMMA was dissolved in acetone and analyzed similarly. The moles of DMAEMA per gram of copolymer were determined, from which the moles of MMA per gram of copolymer were back-calculated. From this ratio and on the basis of the known DP of PDMAEMA, the DP_{EA} of PMMA was estimated. $\bar{M}_{n,EA}$ of PDMAEMA-*b*-PMMA was calculated as the sum of the molecular weight of PMMA based on DP_{EA} and $\bar{M}_{n,NMR}$ of PDMAEMA.

2. Supplementary Characterization

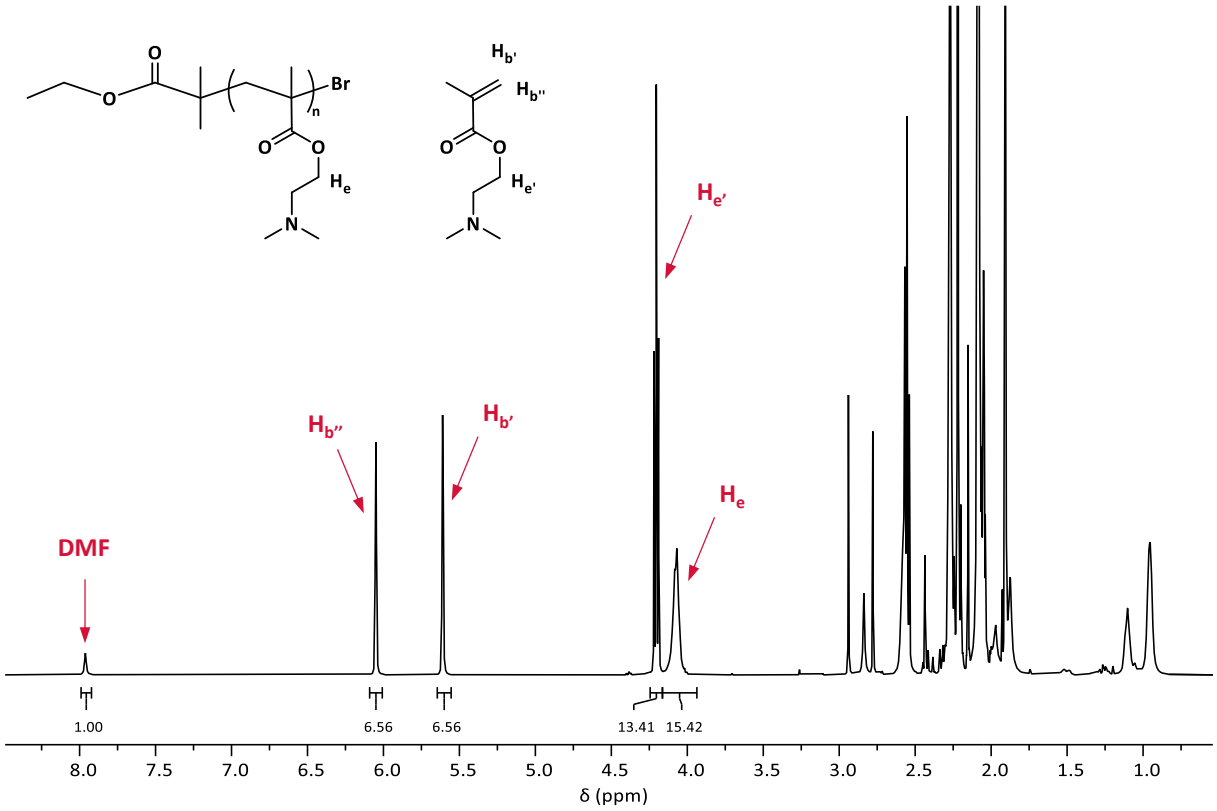


*Figure S1. ^{1}H-NMR spectrum of PDMAEMA polymerization mixture at t = 135 min (end of reaction), in $CDCl_3$. The singlet arising from the internal standard's proton –NC**H**O is labelled as "DMF".*

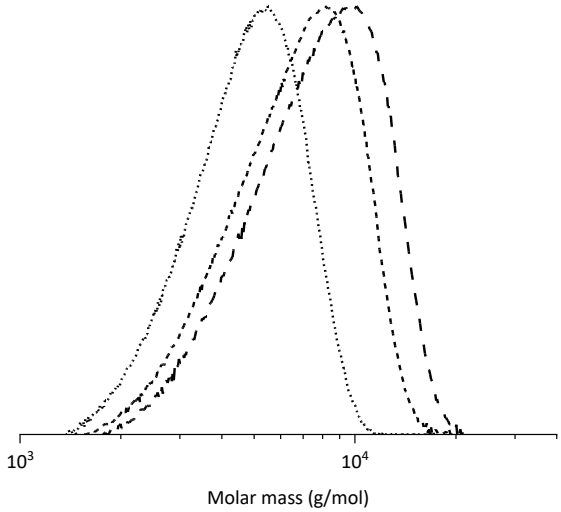


Figure S2. Overlay of molecular weight distributions of PDMAEMA isolated at progressive monomer conversion: 20% conversion (dots); 35% conversion (small dashes); 48% conversion (long dashes).

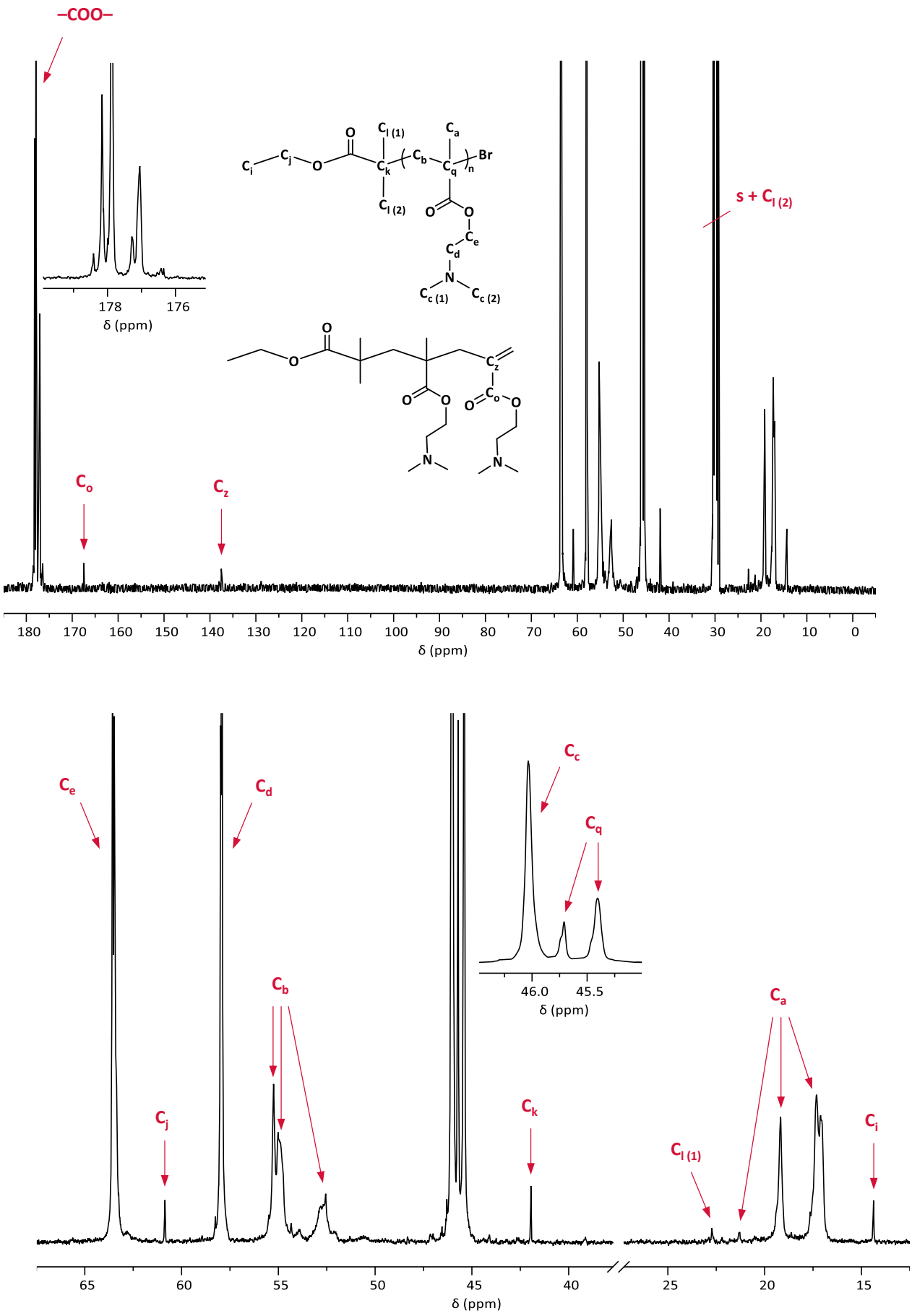


Figure S3. ^{13}C-NMR of PDMAEMA in acetone-d_6 (top) and enlargement (bottom). The deuterated solvent's peak is marked with an "s" notation.

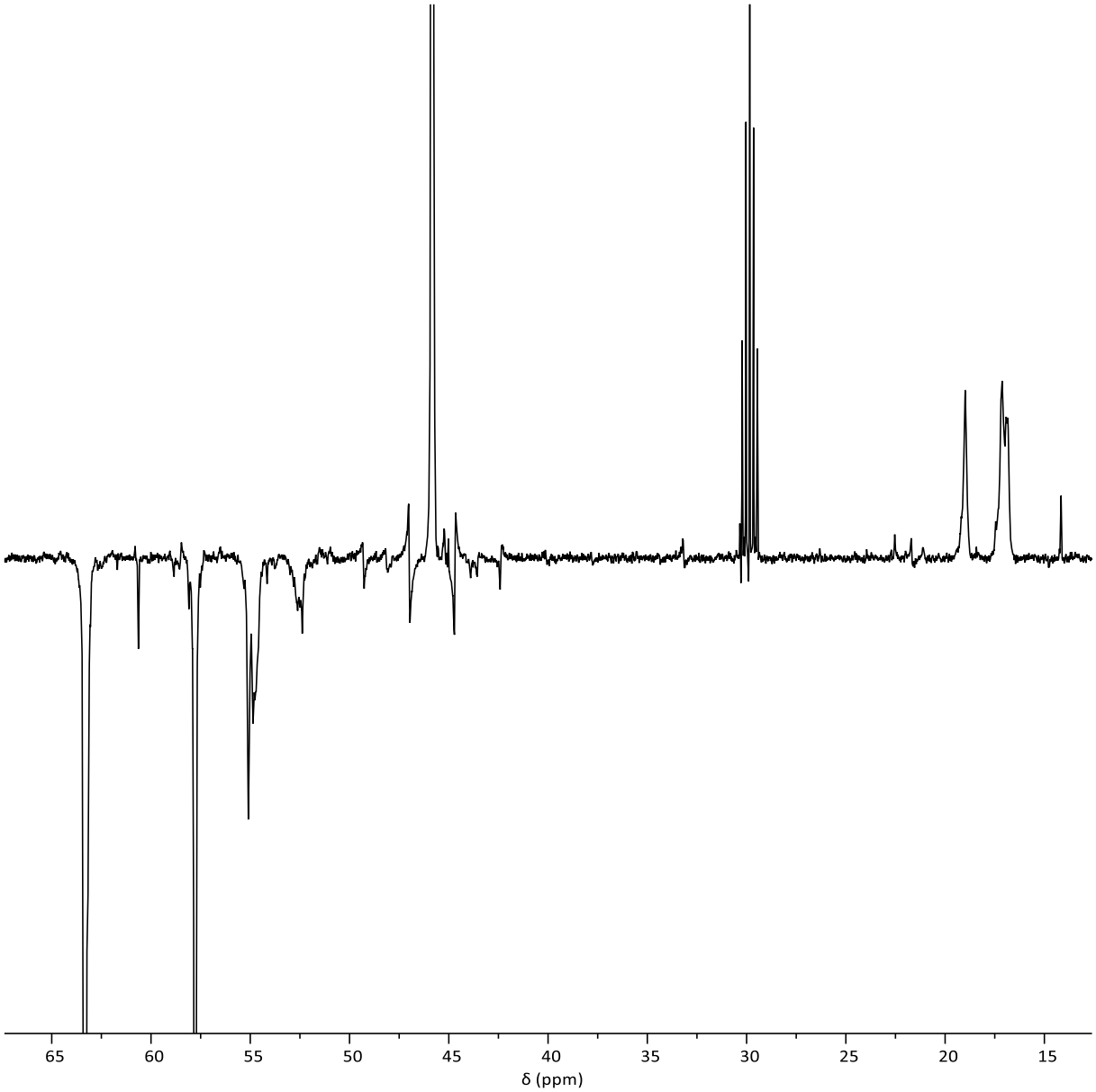
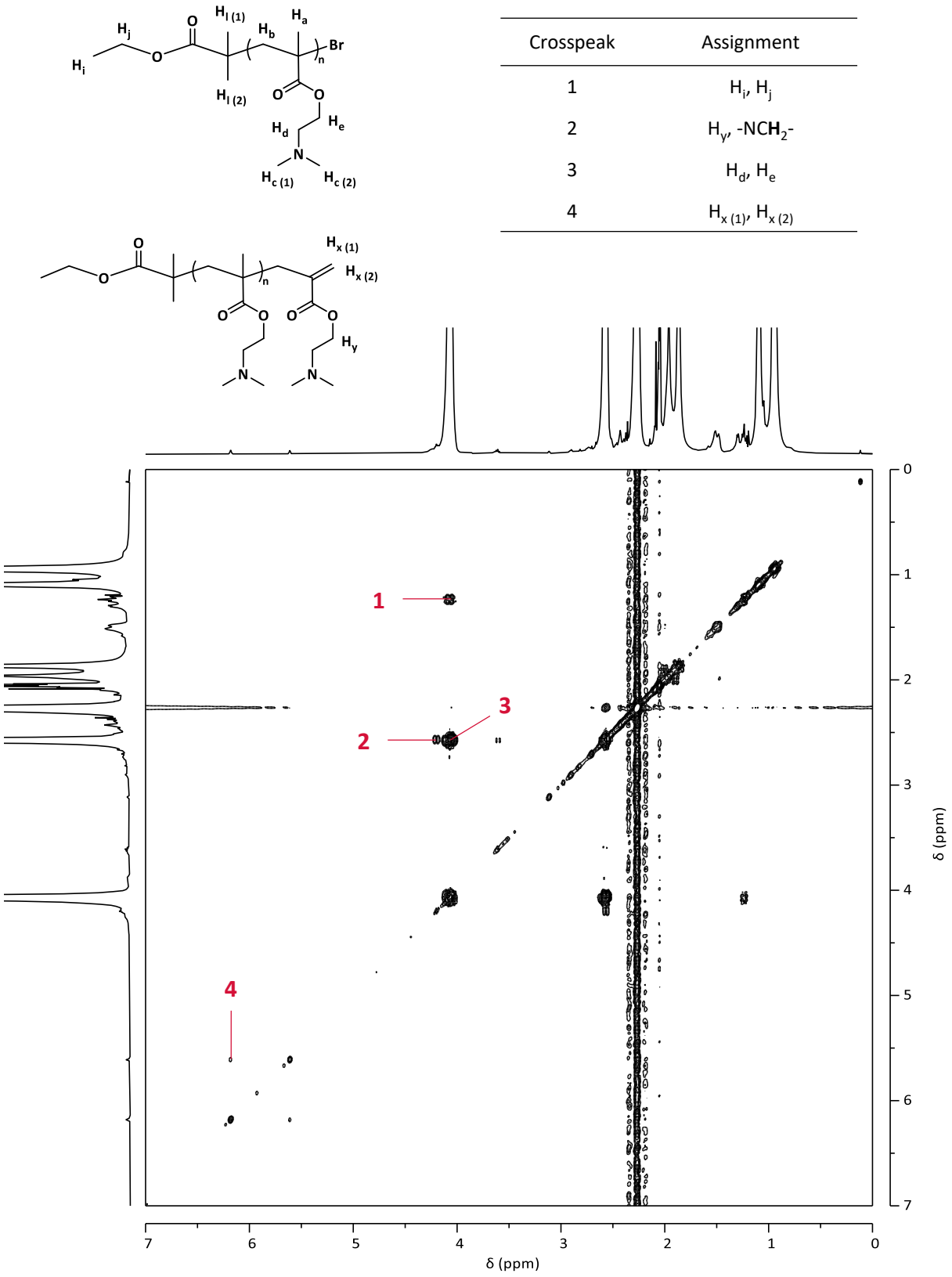
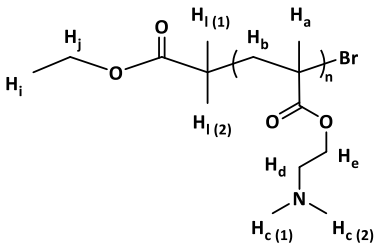


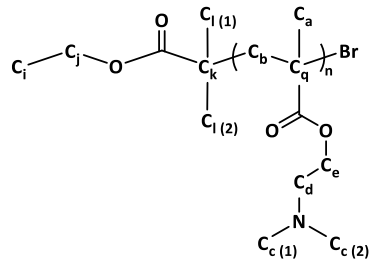
Figure S4. DEPT spectrum of PDMAEMA in acetone-d_6.



Crosspeak	Assignment
1	H_i, H_j
2	H_y, -NC**H**$_2$-
3	H_d, H_e
4	$H_{x\,(1)}$, $H_{x\,(2)}$

Figure S5. COSY spectrum of PDMAEMA in acetone-d_6 and relative assignments.





Crosspeak	Assignment
1	C_i, H_i
2	C_a, H_a
3	$C_{l\,(1)}$, $H_{l\,(1)}$
4	$C_{l\,(2)}$, $H_{l\,(2)}$
5	C_c, H_c
6	C_b, H_b
7	C_d, H_d
8	C_j, H_j
9	C_e, H_e

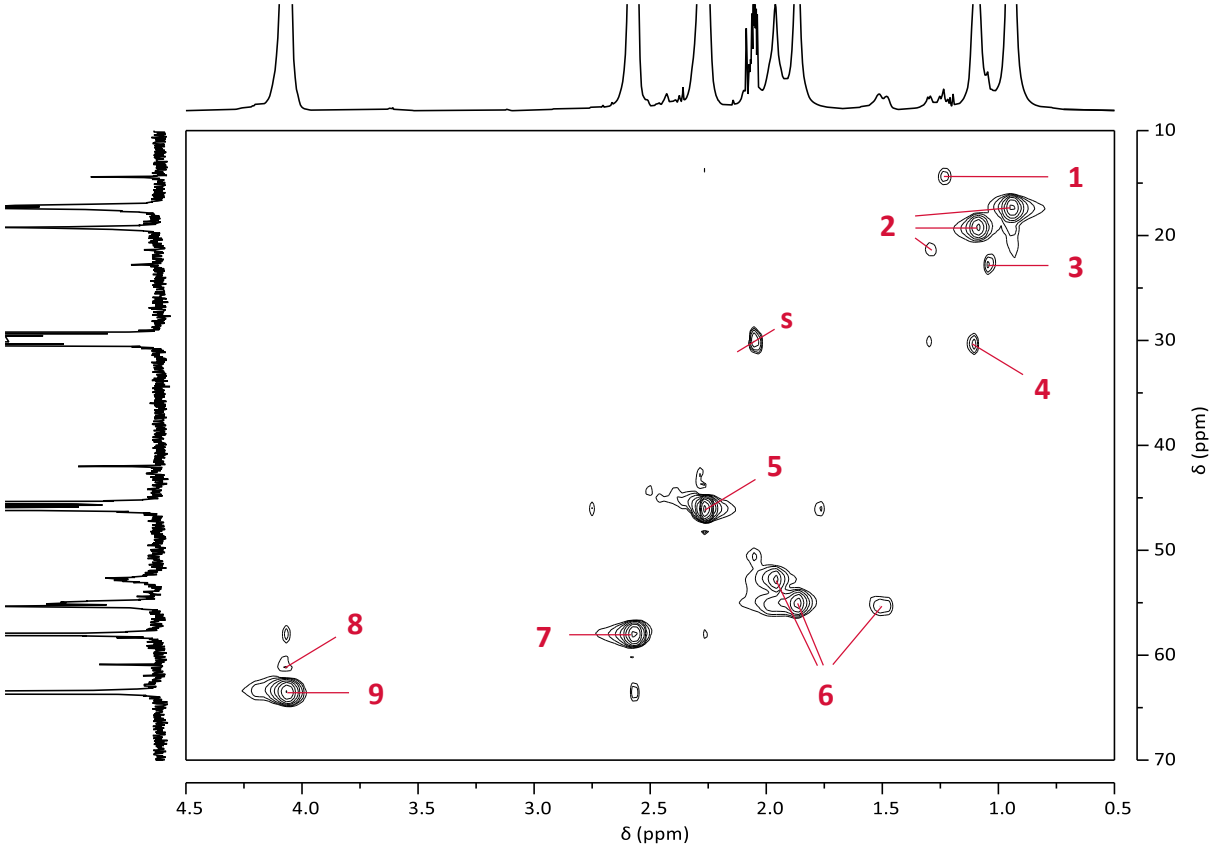


Figure S6. HSQC spectrum of PDMAEMA in acetone-d_6 and relative assignments. The solvent's crosspeak is marked with an "s" notation.

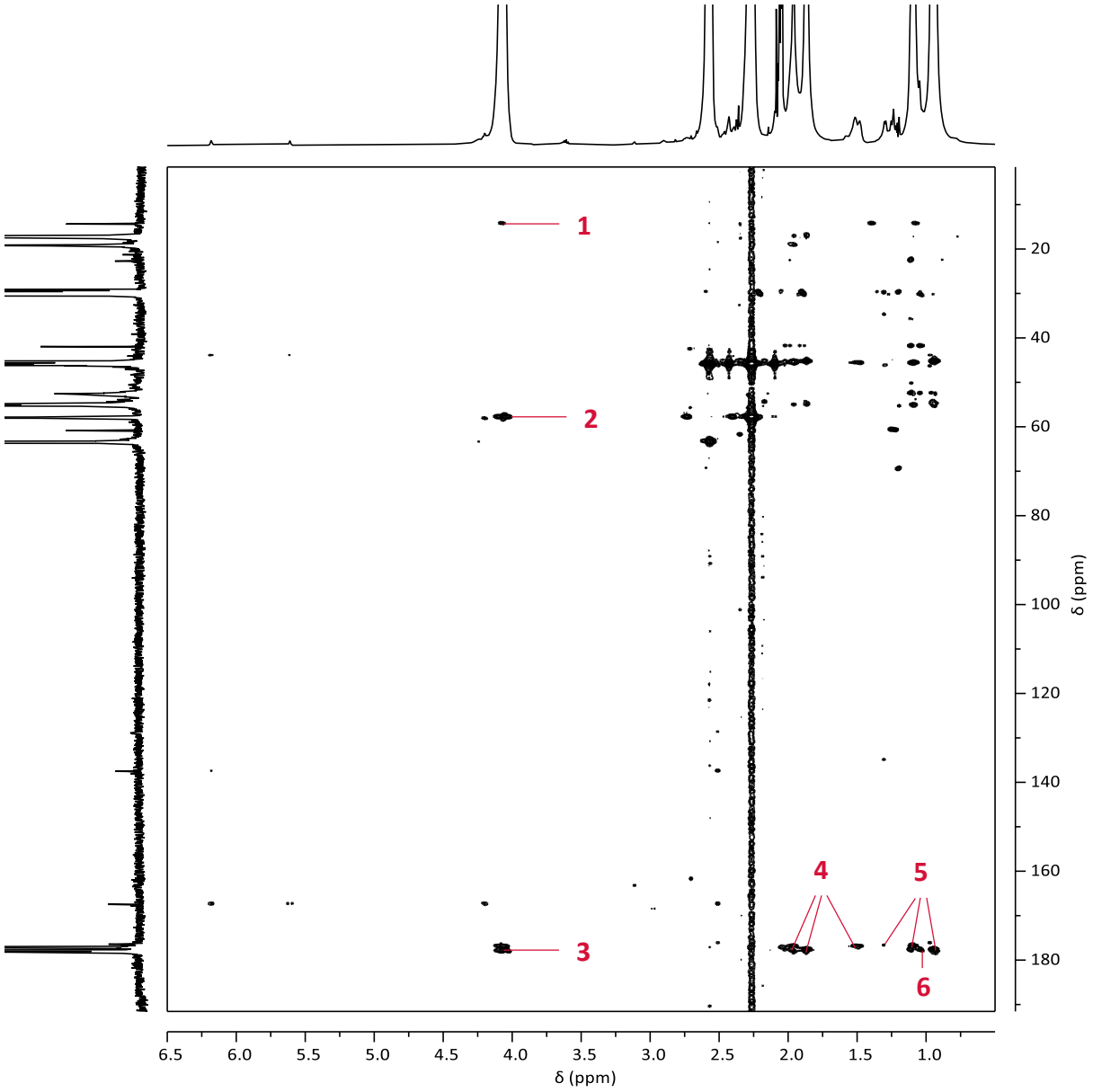


Figure S7. HMBC spectrum of PDMAEMA in acetone-d_6. An enlargement of the top right area and of the bottom left area are shown in Figure S8. All assignments are reported in Figure S9.

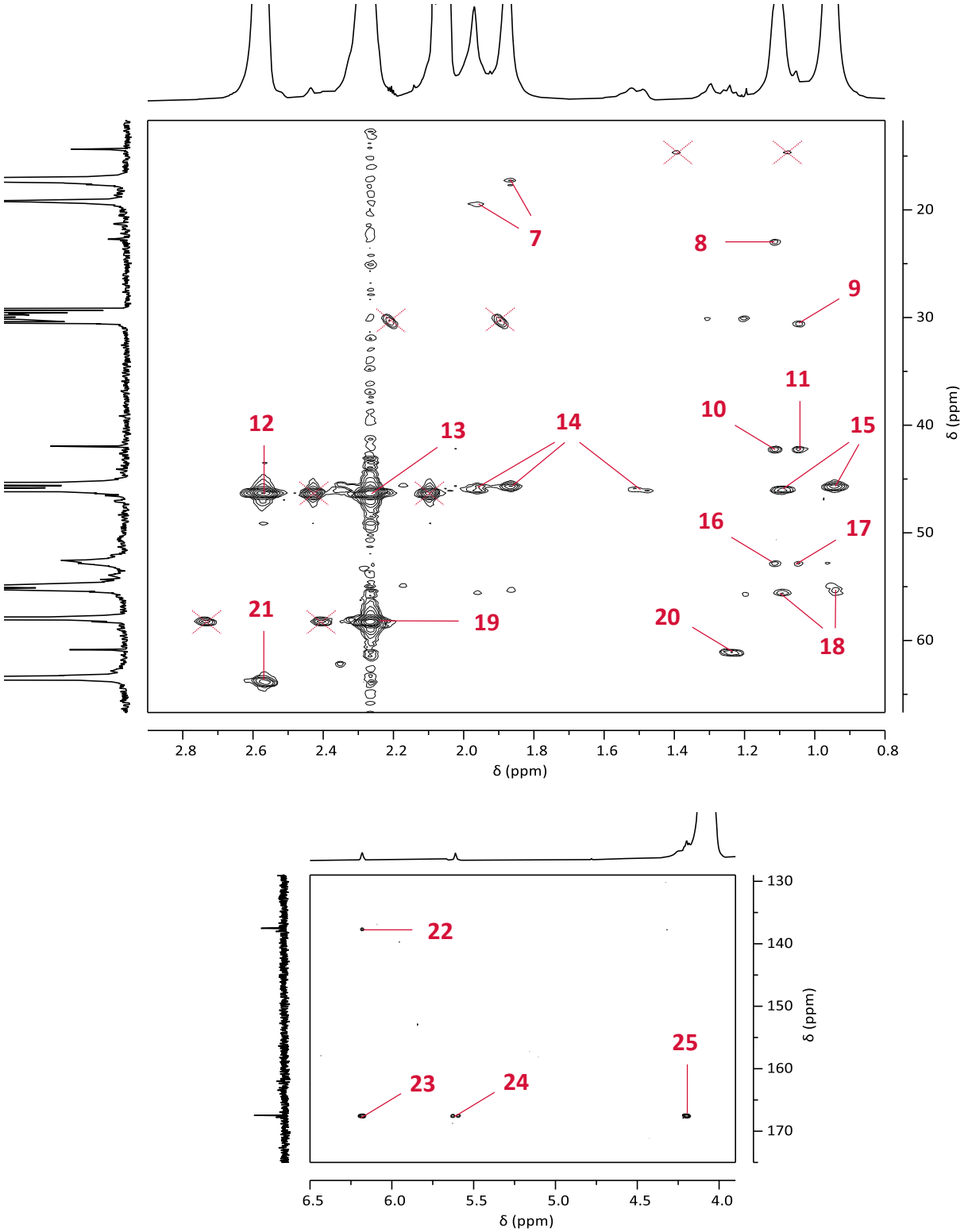


Figure S8. Enlargements of the HMBC spectrum of PDMAEMA in acetone-d_6. The full spectrum is reported in Figure S7 and the assignments in Figure S9. The signals arising from one bond C–H correlations are marked with a dotted cross.

Crosspeak	Assignment
1	C_i, H_j
2	C_d, H_e
3	–**C**OO–, H_e
4	–**C**OO–, H_b
5	–**C**OO–, H_a
6	–**C**OO–, H_l
7	C_a, H_b
8	$C_{l\,(1)}$, $H_{l\,(2)}$
9	$C_{l\,(2)}$, $H_{l\,(1)}$
10	C_k, $H_{l\,(2)}$
11	C_k, $H_{l\,(1)}$
12	C_c, H_d
13	$C_{c\,(2)}$, $H_{c\,(1)}$ + $C_{c\,(1)}$, $H_{c\,(2)}$
14	C_q, H_b
15	C_q, H_a
16	C_b, $H_{l\,(2)}$
17	C_b, $H_{l\,(1)}$
18	C_b, H_a
19	C_d, H_c
20	C_j, H_i
21	C_e, H_d
22	C_z, $H_{x\,(2)}$
23	C_o, $H_{x\,(2)}$
24	C_o, $H_{x\,(1)}$
25	C_o, H_y

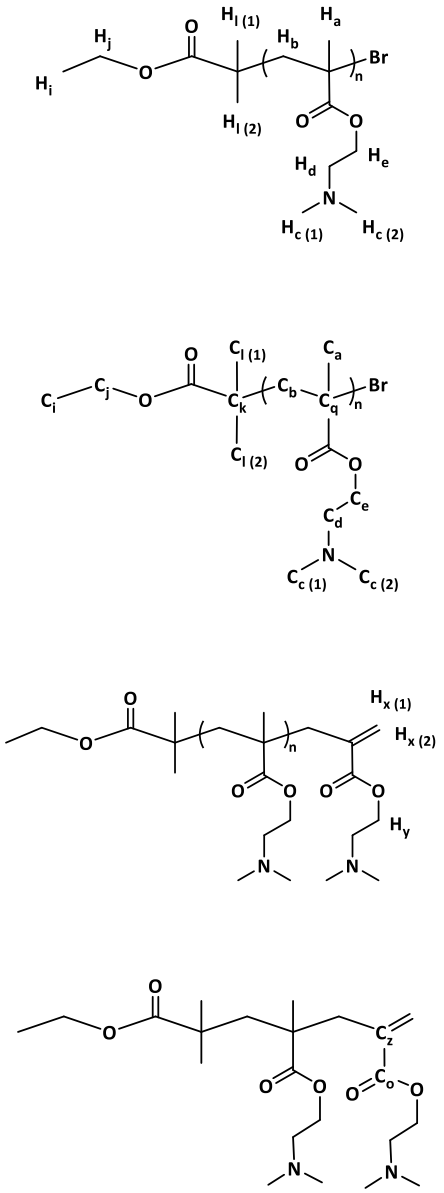


Figure S9. Assignments for the HMBC spectrum of PDMAEMA in acetone-d_6.

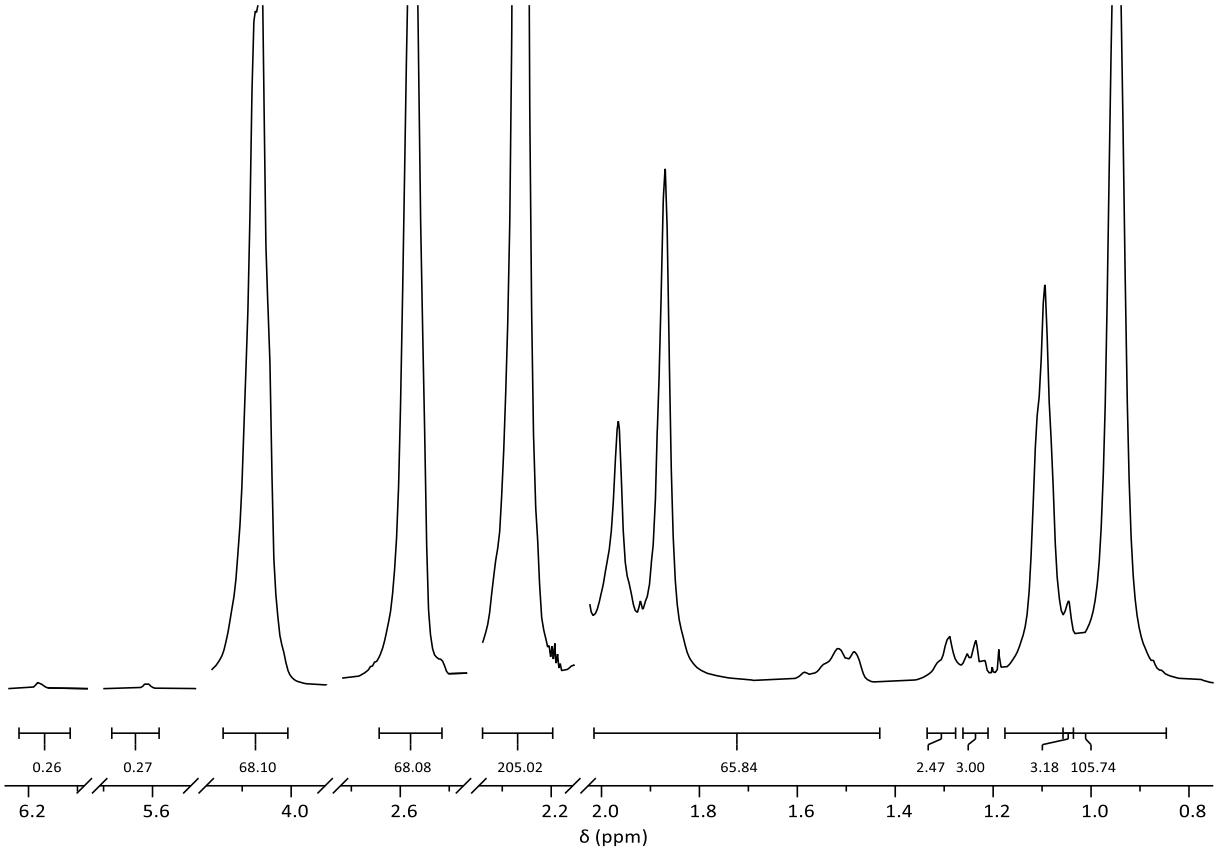


Figure S10. Integrated signals in the ^{1}H-NMR spectrum of purified PDMAEMA in acetone-d_6.

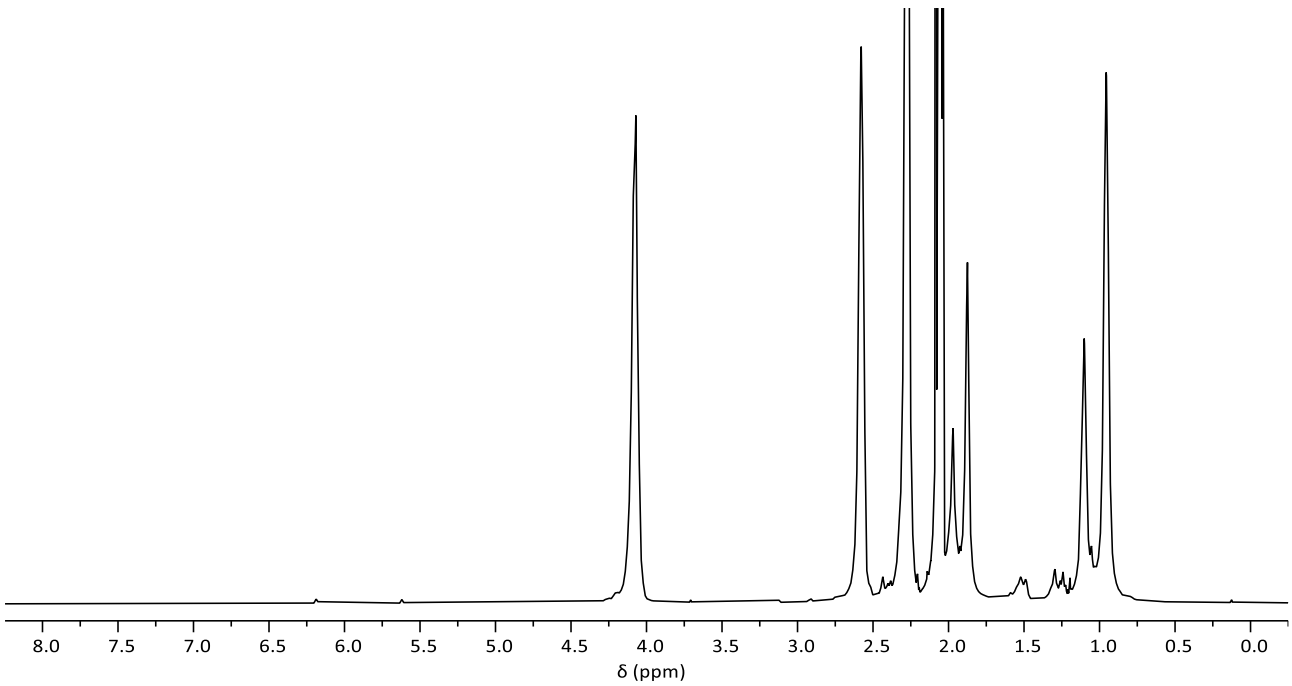


Figure S11. ^{1}H-NMR spectrum of purified PDMAEMA in acetone-d_6.

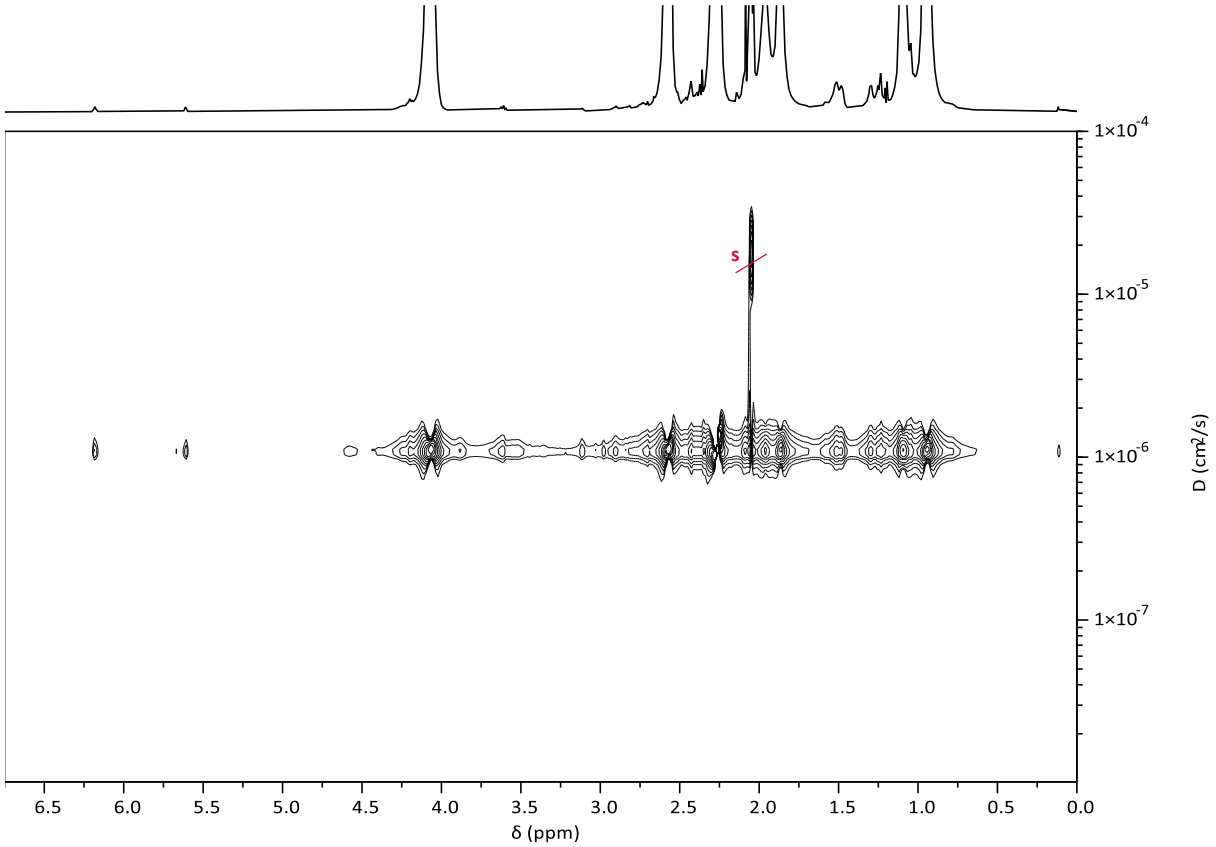


Figure S12. DOSY spectrum of PDMAEMA in acetone-d_6. The solvent's signal is marked with an "s" notation.

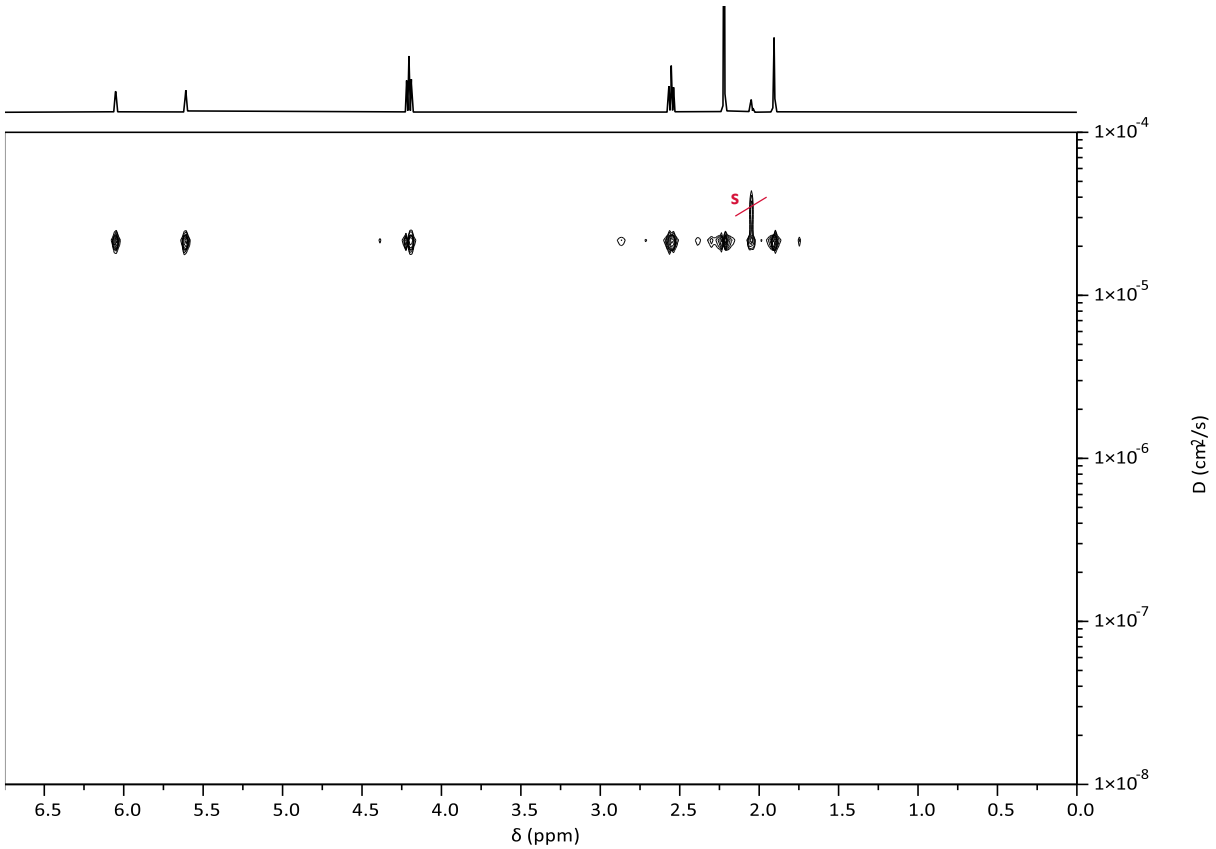


Figure S13. DOSY spectrum of DMAEMA in acetone-d_6. The solvent's signal is marked with an "s" notation.

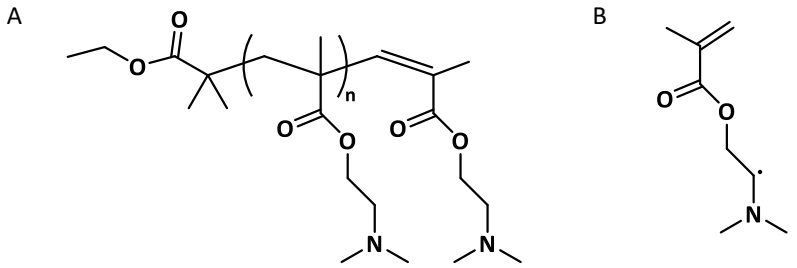


Figure S14. (A) Structure III-A. (B) Proposed structure of DMAEMA radical, competing in initiating the polymerization.

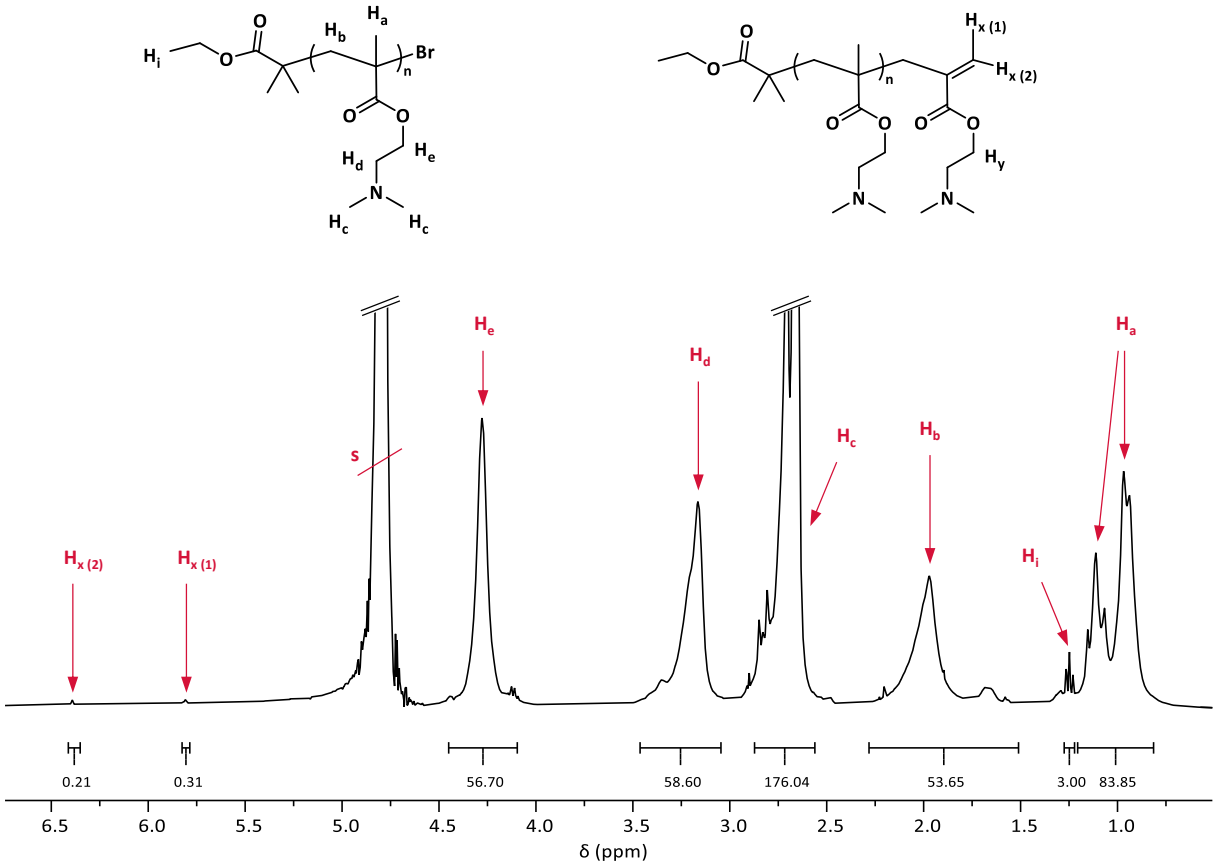


Figure S15. Integrated signals in the ^{1}H-NMR spectrum of purified PDMAEMA in D_2O.

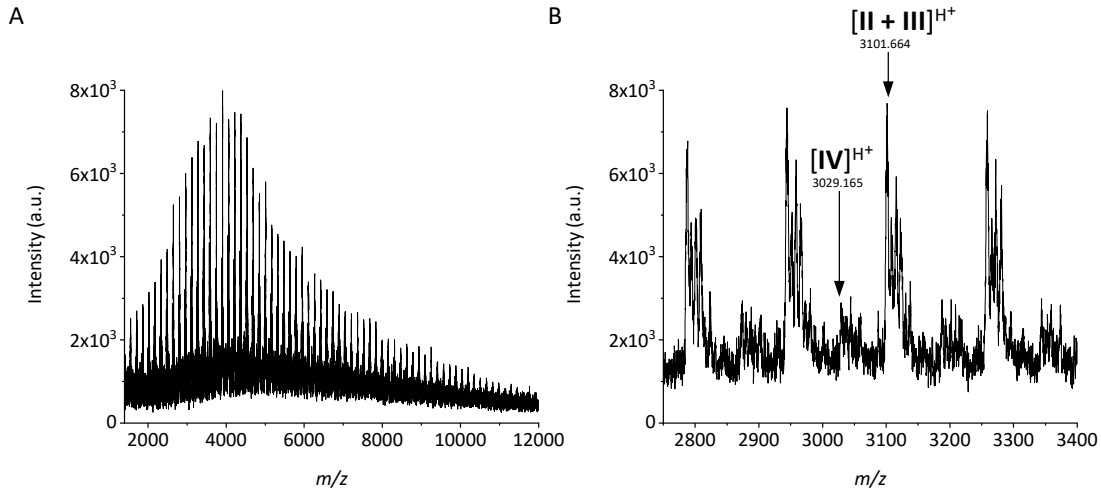


Figure S16. (A) MALDI-TOF MS spectrum of PDMAEMA acquired in linear mode. (B) Enlargement.

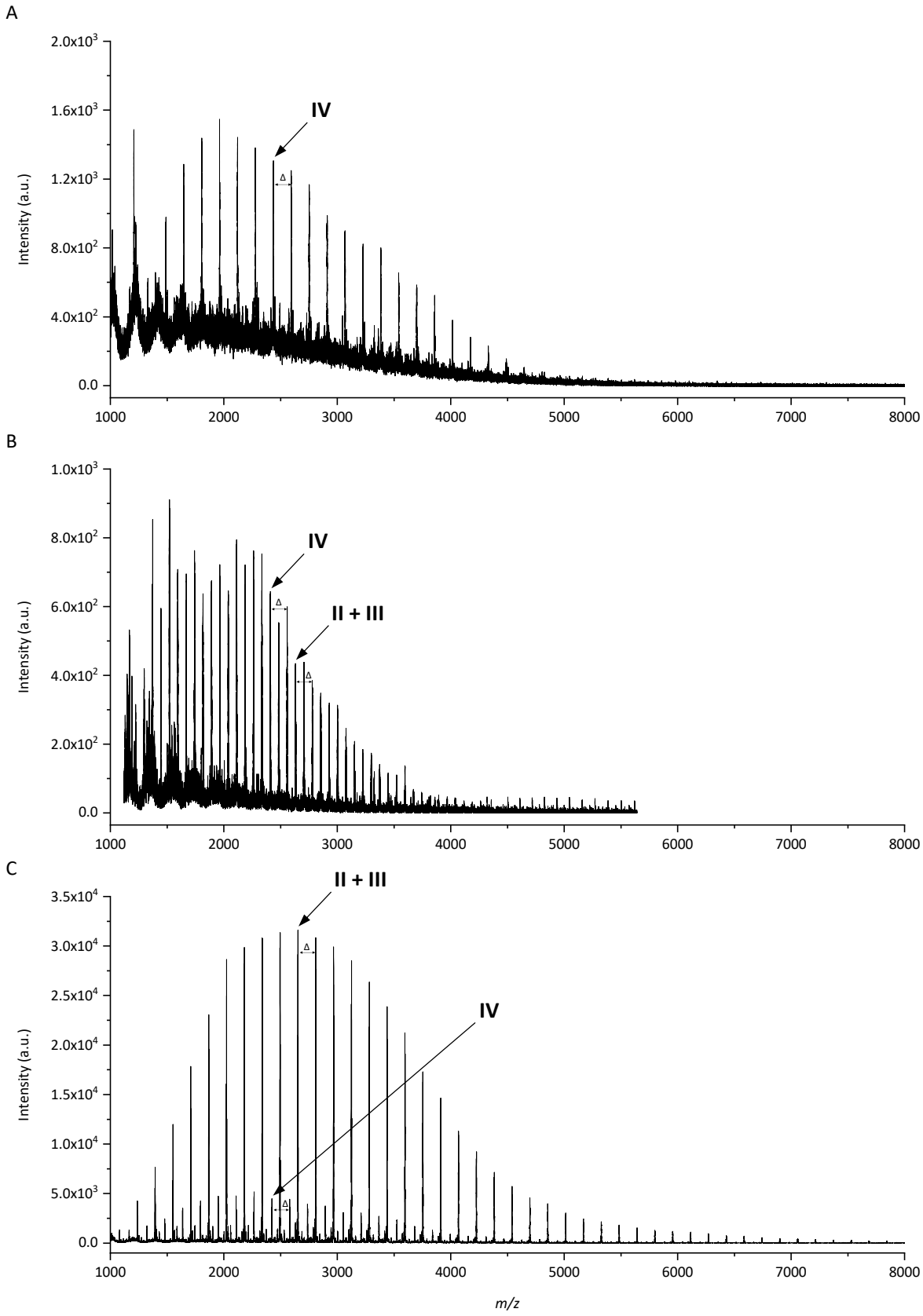


Figure S17. MALDI-TOF MS spectra of PDMAEMA in reflector mode isolated at increasing conversion: (A) 14% conversion, (B) 35% conversion and (C) 52% conversion.

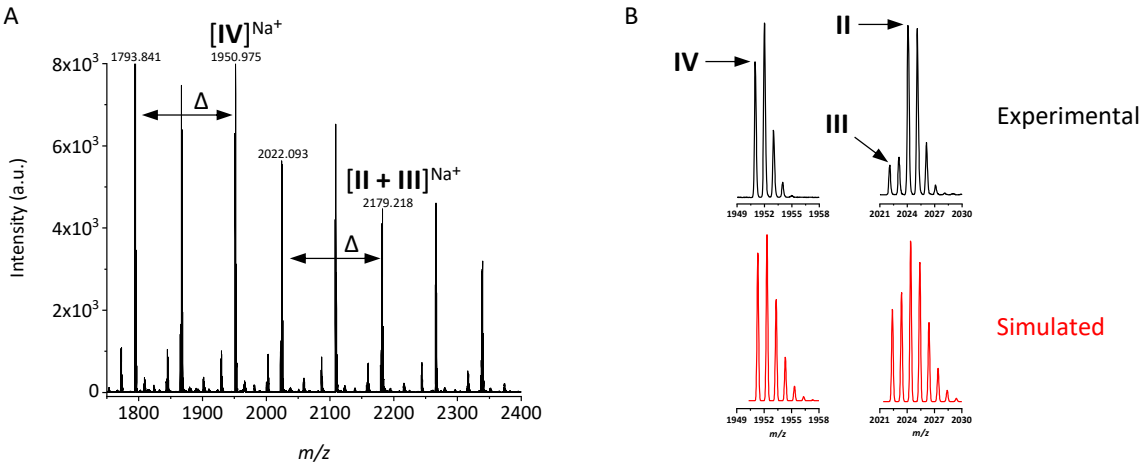


Figure S18. (A) Enlargement of the MALDI-TOF MS spectrum in reflector mode of PDMAEMA$_{Cl}$ synthesized by CuCl-mediated ATRP, where monoisotopic masses of different populations are reported. In the case of populations II and III, whose signals overlap, the monoisotopic mass of population III is reported. (B) Comparison between experimental and simulated isotope distributions, with arrows pointing at the monoisotopic masses of different populations for DP = 12. The simulated isotope distribution arising from populations II+III is based on a 1:1 intensity ratio between populations II and III (in this case, not reflecting the experimental distribution).

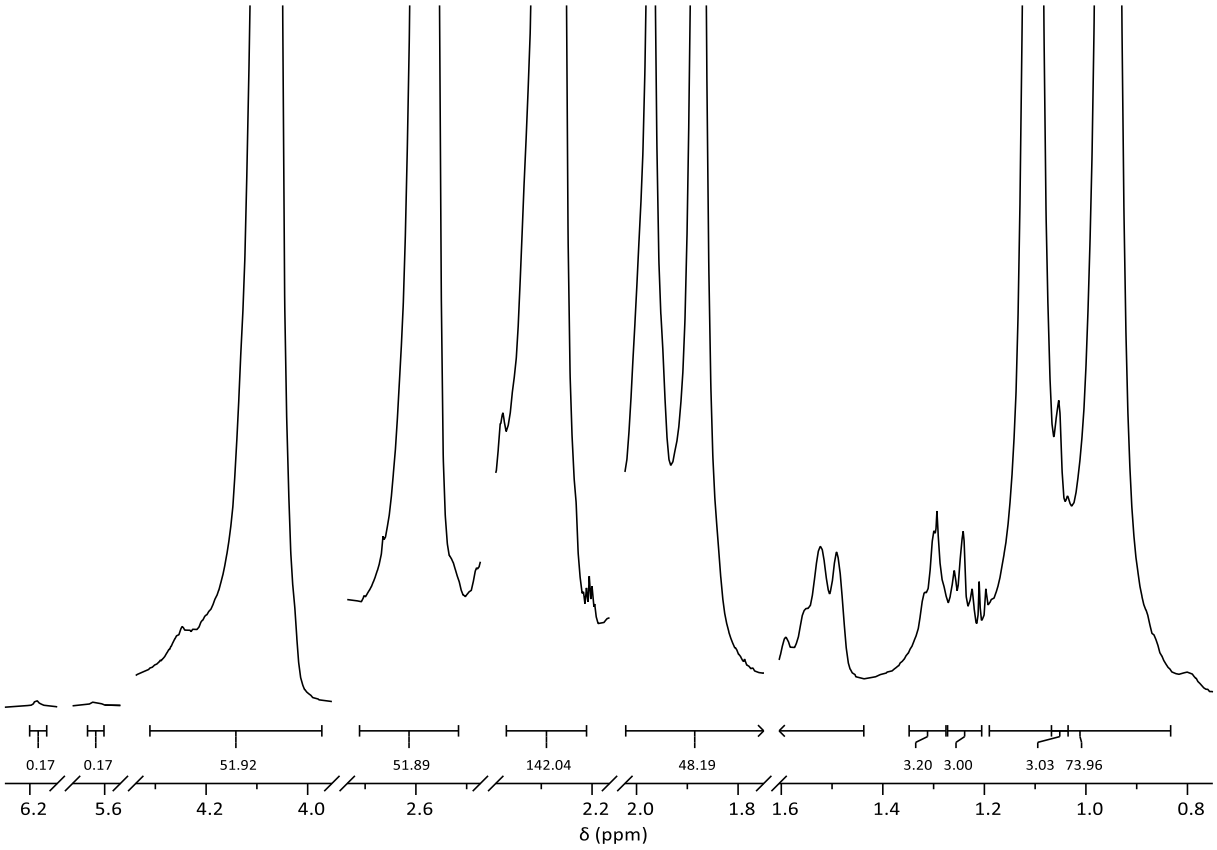


Figure S19. Integrated signals in the ^{1}H-NMR spectrum of PDMAEMA$_{Cl}$ in acetone-d$_6$.

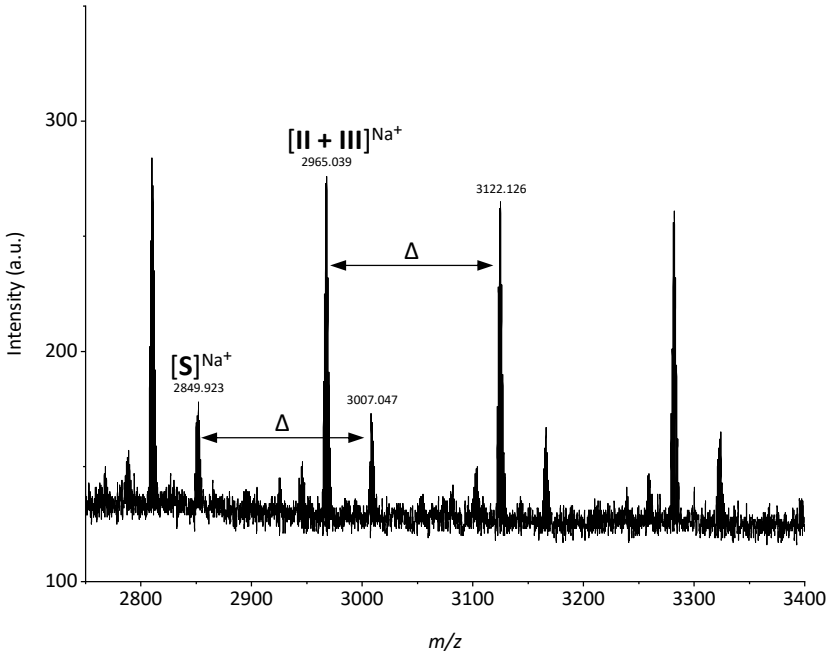


Figure S20. Enlargement of the MALDI-TOF MS spectrum in reflector mode of PDMAEMA$_{UV,EBiB}$, where monoisotopic masses of different populations are reported. The "S" label refers to a population of self-initiated PDMAEMA chains, whose masses correspond to those of terminated chains with repeating units of DMAEMA, not including the mass of the initiator EBiB. Signals of low intensity originating from adducts with H^+ are present in the spectrum. The range of m/z, different from that of the mass spectra reported in Figures 3, S18 and S21, was selected due to higher noise at m/z < 2750.

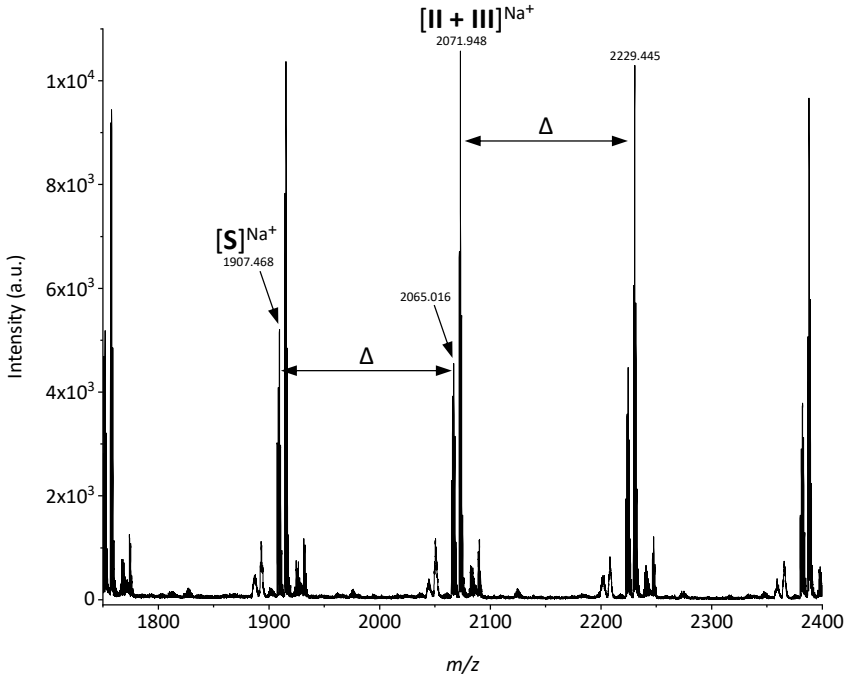


Figure S21. Enlargement of the MALDI-TOF MS spectrum in reflector mode of PDMAEMA$_{UV,EBPA}$, where monoisotopic masses of different populations are reported. The "S" label refers to a population of self-initiated PDMAEMA chains, whose masses correspond to those of terminated chains with repeating units of DMAEMA, not including the mass of the initiator EBPA. For both the populations identified and labelled, signals of lower intensity originating from adducts with H^+ as well as with K^+ are present in the spectrum.

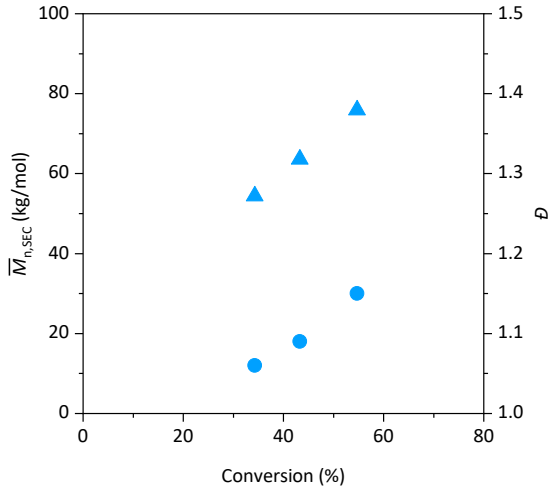


Figure S22. $\overline{M}_n$ (▲) and Đ (●) determined by SEC as a function of degree of conversion for PDMAEMA-b-PMMA.

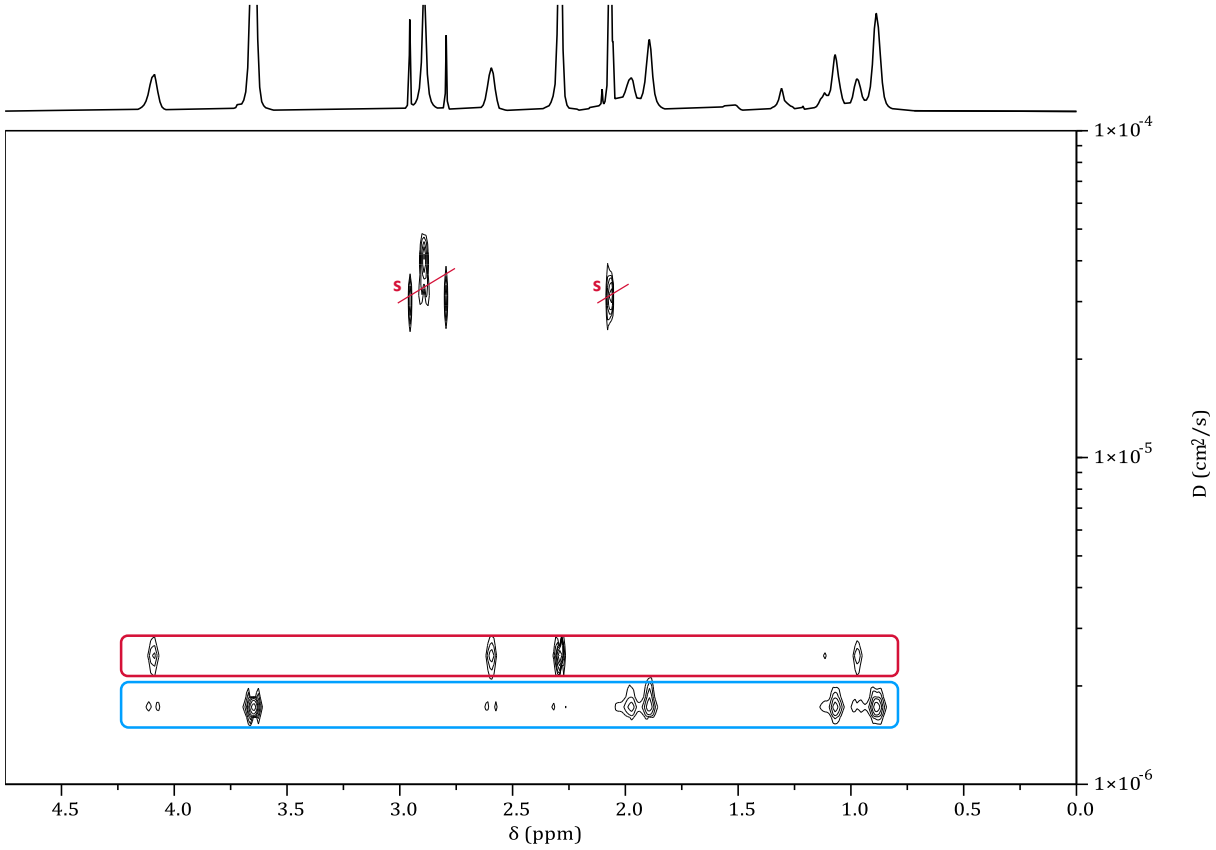


Figure S23. DOSY spectrum in acetone-d_6 of aliquot from PDMAEMA-b-PMMA reaction mixture at t = 150 min, 34% conversion. The signals of PDMAEMA homopolymer are highlighted in the red rectangle. The signals of PDMAEMA-b-PMMA copolymer are highlighted in the blue rectangle. Solvent signals are marked with an "s" notation.

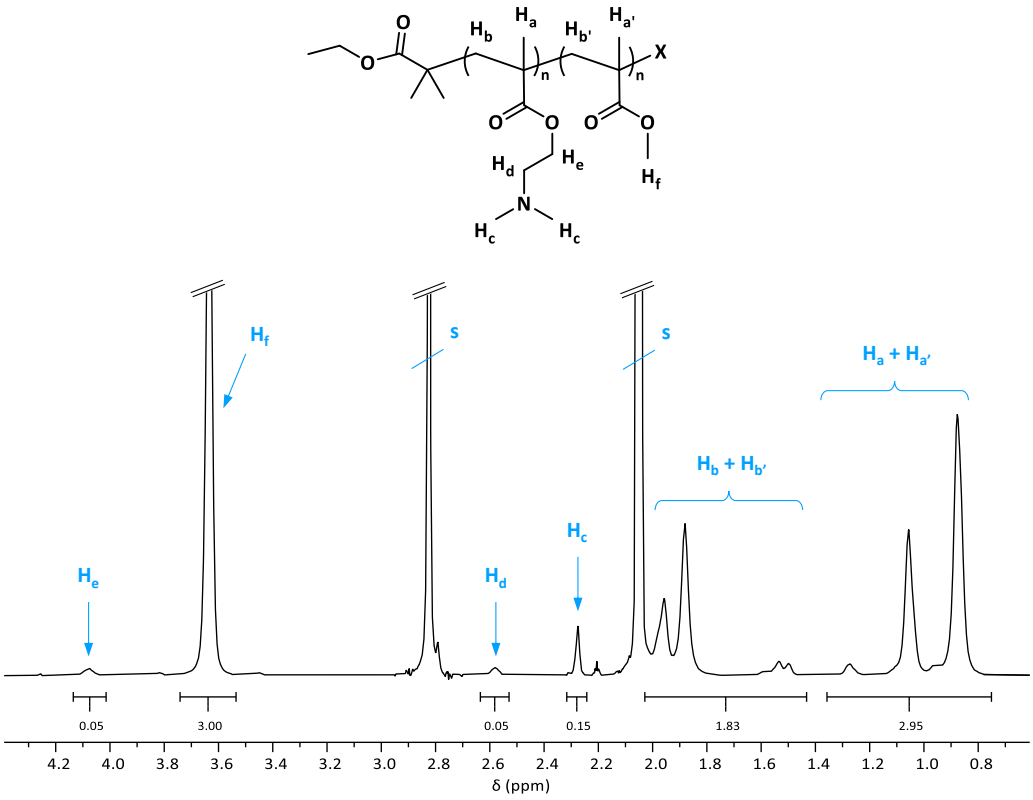


Figure S24. Integrated signals in the ^{1}H-NMR spectrum of purified PDMAEMA-b-PMMA in acetone-d_6. Solvent peaks are marked with an "s" notation: acetone-d_6 (2.05 ppm) and water (2.84 ppm).

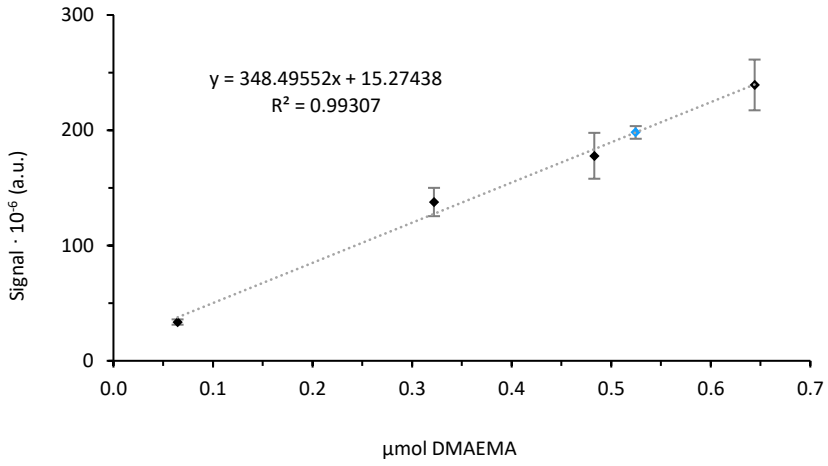


Figure S25. Plot of total nitrogen analysis of PDMAEMA-b-PMMA (◆). The dotted line is the trendline obtained by plotting the calibration dataset of PDMAEMA samples (◆). The error bars show the deviation from the mean, based on a set of six measurements for each point.

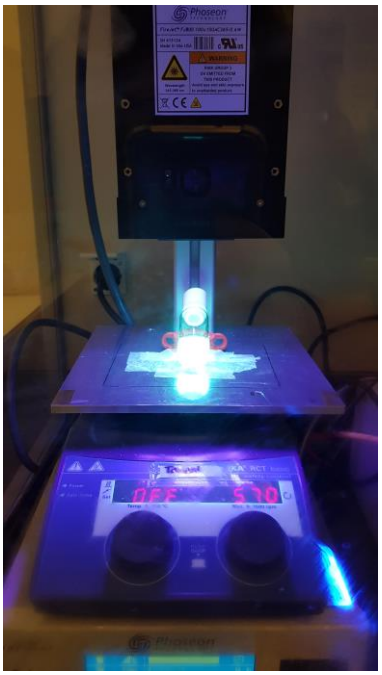


Figure S26. Experimental set-up for the photomediated ATRP of DMAEMA.

References

(1) Loos, M.; Gerber, C.; Corona, F.; Hollender, J.; Singer, H. Accelerated isotope fine structure calculation using pruned transition trees. *Anal. Chem.* **2015**, *87* (11), 5738-5744, DOI: 10.1021/acs.analchem.5b00941.