Supporting Information

Elucidation of the Properties of Discrete Oligo(meth)acrylates

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Content

A. Experimental procedures

1. Materials

The monomers methyl methacrylate (MMA, Merck, ≥ 99%) and di(ethylene glycol) ethyl ether acrylate (DEGEEA, Sigma-Aldrich, ≥ 90%) were deinhibited over a column of activated basic alumina prior to use. 2-2'-azoisobutyronitrile (AIBN, Sigma-Aldrich, 12 wt.% in acetone) was recrystallized twice from methanol prior to use. Tetrahydrofuran (RCI Labscan, 99.9%), dichloromethane (Merck, ≥ 99%), methanol (Scharlau chemicals, 99.9%), *N*,*N*-dimethylformamide (Merck, ≥ 99%), acetone (Chem-Supply, 99.8%), chloroform-d (Cambridge isotope Laboratories, 99.8%), petroleum spirit (Boiling range 40-60 °C, Chem-Supply, ≥ 99%), *n*-butyl acetate (chem-supply, ≥ 99%) and ethyl acetate (Ajax Finechem, ≥ 99%) were used without further purification. The RAFT agents 2-cyano-2-propyl dodecyl trithiocarbonate (CPD-TTC) and 2-cyano-2-propyl ethyl trithiocarbonate (CPE-TTC) were synthesized according to literature procedures.[1] The reagents and chemicals used for the synthesis of CPD-TTC and CPE-TTC RAFT agents were purchased from Sigma-Aldrich or VWR and used as received.

2. Analytical methods

I. Automated Flash Column Chromatography (AFCC)

Purification of oligomers was performed via Automated Flash Column Chromatography (AFCC) on a Puriflash® XS420+ (Interchim®) equipped with Puriflash® Intersoft V5.0 software. Separation were monitored via a diode array detector (range 200-400 nm) at lambda 305 nm (RAFT trithiocarbonate endgroup) and 254 nm. The oligomers were embedded on celite and dry loaded on a pre-column cartridge (Interchim puriflash® F0012). The pre-column was subsequently wetted with eluent and attached to the pre-wetted normal phase silica cartridge (Interchim puriflash® F0040) on the integrated column holder. Oligomer separation was performed with an optimized mobile phase (eluent) gradient mixture and a flow rate of 25 mL/min. For the separation of oligo(MMA), an ethyl acetate:petroleum spirit gradient (30:70 to 90:10 v/v%) was applied. For the separation of oligo(DEGEEA), an acetone:petroleum spirit gradient (15:85 to 95:5 v/v%) was applied. Fractions were automatically collected by a fraction collector in racks with 18 x 150 mm glass tubes.

II. Size-exclusion chromatography (SEC)

Analysis of the di(ethylene glycol) ethyl ether acrylate (DEGEEA) oligomers was performed on a PSS SECcurity^2 GPC system operated by PSS WinGPC software, equipped with a SDV 5.0 µm guard column (50 x 8 mm), followed by three SDV analytical 5.0 µm columns with varying porosity (1000 Å, 100000 Å and 1000000 Å) (50 x 8 mm) and a differential refractive index detector using tetrahydrofuran (THF, RCI Labscan, 99.9%) as the eluent at 40 °C with a flow rate of 1 mL·min^{-1}. Analysis of the methyl methacrylate (MMA) oligomers was performed on Tosoh EcosHLC-8320 Gel Permeation Chomatography apparatus equipped with both refractive index (RI) and ultraviolet (UV) detectors (UV detection, λ = 280 nm) using Tosoh alpha 4000 and 2500 columns. *N*,*N*-dimethylformamide (DMF, Merck, ≥ 99%) with 10 mM LiBr was used as mobile phase with flow rate of 1 mL·min^{-1}.

III. Nuclear magnetic resonance (NMR) spectroscopy

1D proton (1H) NMR and 2D diffusion-ordered NMR spectroscopy (DOSY NMR) were recorded in deuterated chloroform on a Bruker DRX600 NMR spectrometer (14.1 Tesla magnet). NMR spectra were collected and analyzed in MestReNova and Bruker's TopSpin™ software packages. DOSY NMR measurements were performed at 25 °C with a Bruker multinuclear z-gradient inverse probe head capable of producing gradients in the z direction with a strength of 55 G cm-1. Typically, 1 mg of oligomer was dissolved in 1 mL of $CDCl_3$. All spectra were acquired in 5 mm NMR tubes. Sample spinning was deactivated during the measurements to avoid convection. The standard Bruker pulse program ledbpgp2s1d from Bruker's TopSpin™ software package was selected and the gradient strength was exponentially incremented in 12 gradient steps from 2 % up to 95 % of the maximum gradient strength. For each DOSY NMR experiment a series of 16 spectra on a 32 K data points were collected. All oligomer experiments were consistently performed with a diffusion delay of 100 ms to keep the relaxation contribution constant for all samples. A gradient pulse length of 2.2 ms was applied in order to ensure full signal attenuation. Diffusion coefficients of a chosen narrow chemical shift range were extracted from T1/T2 analysis module of Bruker's TopSpin™ software package.

IV. Differential scanning calorimetry (DSC)

Oligomers of MMA and DEGEEA were analyzed via Differential Scanning Calorimetry (DSC) on a PerkinElmer Instrument model DSC8000 under nitrogen flow and cooled with a PerkinElmer intracooler 2 to determine the glass transition temperatures (T_g) and melting points (T_m). Oligomers were prepared in aluminum pans (7-10 mg/oligomer) and covers (PerkinElmer®).

The oligo(DEGEEA) samples were first heated to 100 °C at 50 °C/min, equilibrated at this temperature for 1 min, and subsequently cooled to -80 °C at 150 °C/min. Secondly, the samples were held at -80 °C for 5 min and the then reheated to -20 °C at 10 °C/min, equilibrated at this temperature for 1 min, and subsequently cooled to -80 °C at 150 °C/min. this second cycle was repeated to confirm the thermal transitions of the DEGEEA oligomers.

The oligo(MMA) samples were first heated to 100 °C at 50 °C/min, equilibrated at this temperature for 1 min, and subsequently cooled to -80 °C at 150 °C/min. Secondly, the samples were held at -80 °C for 5 min and the then reheated to 30 °C at 10 °C/min, equilibrated at this temperature for 1 min, and subsequently cooled to -80 °C at 150 °C/min. this second cycle was repeated to confirm the thermal transitions of the MMA oligomers.

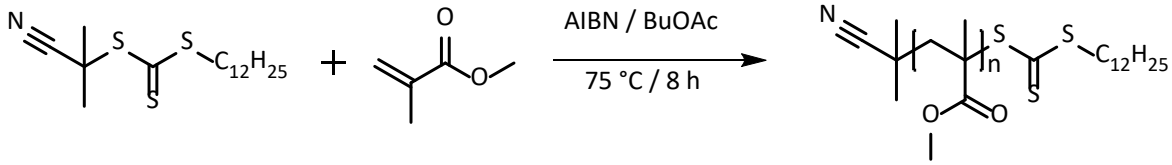
V. Electrospray ionisation mass spectrometry (ESI-MS)

Analysis was carried out at the Monash Analytical Platform, Australia (School of Chemistry, Monash University). From each sample 1 mg was dissolved in 1 mL dichloromethane (DCM, HPLC grade). The DCM solution was diluted (±100 times) by adding 1 drop to a 1 mL mixture of DCM:methanol (MeOH) (DCM:MeOH = 3:1 v/v). This mixture was infused directly into the MS via a Kd Scientific infusion pump at a static flow rate of 647 µL/h. The MS setup was as follows: Agilent 6220 time-of-flight mass spectrometry (TOF MS) system (Santa Clara, CA, USA) with a multimode dual nebuliser ESI/APCI source working in dedicated ESI mode. The MS was operated in positive mode using the following conditions: nebulizer pressure 35 psi, gas flow-rate 8 L·min-1, gas temperature 300 °C, capillary voltage 2500 V and skimmer 65 V. Instrument was operated in the extended dynamic range mode with data collected in m/z range 200–3000. Spectra were recorded over a 1 minute time period with 1 scan/s and subsequently averaged out before analysis. Spectra were analyzed with Agilent Masshunter Qualitative Analysis B.07.00.

3. Synthetic procedures

Additional information. The choice of RAFT agent (different Z-group) influences the separation resolution in flash column chromatography. It is generally observed that a shorter alkyl Z-group like e.g. the ethyl-S is more suitable for bulky monomers (e.g. di(ethylene glycol) ethyl ether acrylate) whereas a dodecyl-S Z-group proofed very efficient for less bulky monomers (e.g. methyl methacrylate).

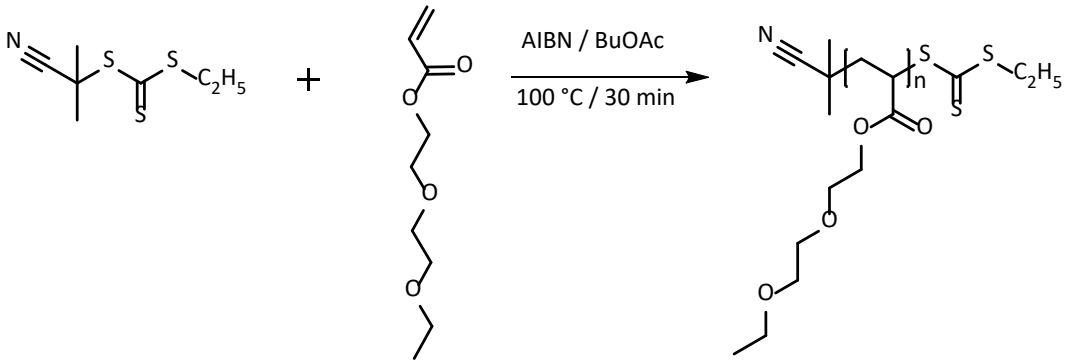
I. Synthesis of discrete oligo(methyl methacrylate)s



Scheme S1. Reaction scheme for the synthesis of oligo(methyl methacrylate)

General procedure for the synthesis of oligo(methyl methacrylate). 0.05 equivalents of recrystallized 2-2'-azoisobutyronitrile (AIBN), 1 equivalent of 2-cyano-2-propyl dodecyl trithiocarbonate (CPD-TTC) RAFT agent, X equivalents of deinhibited methyl methacrylate (MMA) monomer (with X = 1, 3 or 5, different chain lengths were targeted to construct the discrete oligomer library) and 50 vol.% of *n*-butyl acetate as reaction solvent were added into a glass vial with a magnetic stirrer. The glass vial was sealed by a rubber septum. The solution was degassed for 10 min by N_2 purging and the mixture was subsequently reacted in a preheated oil bath for 8 hours at 75 °C. The polymerization was quenched by submerging the glass vial in liquid N2 and exposure to ambient atmosphere. The oligo(MMA) mixture was dried, redissolved in dichloromethane, embedded on celite and dry loaded on a pre-column cartridge (Interchim puriflash® F0012). The pre-column was subsequently wetted with eluent (mobile phase) and attached to a pre-wetted normal phase silica cartridge (Interchim puriflash® F0040). Separation was performed with an optimized mobile phase (eluent) gradient mixture of ethyl acetate:petroleum spirit (30:70 to 90:10 v/v%) to obtain discrete MMA oligomers with degree of polymerization (DP) 1 to 7. All discrete oligomers were analyzed by ESI-MS, SEC, DOSY-NMR and DSC as shown and discussed throughout the manuscript.

II. Synthesis of discrete oligo(di(ethylene glycol) ethyl ether acrylate)s



Scheme S2. Reaction scheme for the synthesis of oligo(di(ethylene glycol) ethyl ether acrylate)

General procedure for the synthesis of oligo(di(ethylene glycol) ethyl ether acrylate). 0.05 equivalents of recrystallized 2-2'-azoisobutyronitrile (AIBN), 1 equivalent of 2-cyano-2-propyl ethyl trithiocarbonate (CPE-TTC) RAFT agent, X equivalents of deinhibited di(ethylene glycol) ethyl ether acrylate (DEGEEA) monomer (with X = 2, 6 or 8, different chain lengths were targeted to construct the discrete oligomer library) and 50 vol.% of *n*-butyl acetate as reaction solvent were added into a glass vial with a magnetic stirrer. The glass vial was sealed by a rubber septum. The solution was degassed for 10 min by N_2 purging and the mixture was subsequently reacted in a preheated oil bath for 30 minutes at 100 °C. The polymerization was quenched by submerging the glass vial in liquid N2 and exposure to ambient atmosphere. The oligo(DEGEEA) mixture was dried, redissolved in dichloromethane, embedded on celite and dry loaded on a pre-column cartridge (Interchim puriflash® F0012). The pre-column was subsequently wetted with eluent (mobile phase) and attached to a pre-wetted normal phase silica cartridge (Interchim puriflash® F0040). Separation was performed with an optimized mobile phase (eluent) gradient mixture of acetone:petroleum spirit (15:85 to 95:5 v/v%) to obtain discrete DEGEEA oligomers with degree of polymerization (DP) 1 to 10. All discrete oligomers were analyzed by ESI-MS, SEC, DOSY-NMR and DSC as shown and discussed throughout the manuscript.

B. Supplementary results

1. Thermal analysis of discrete oligomers via DSC

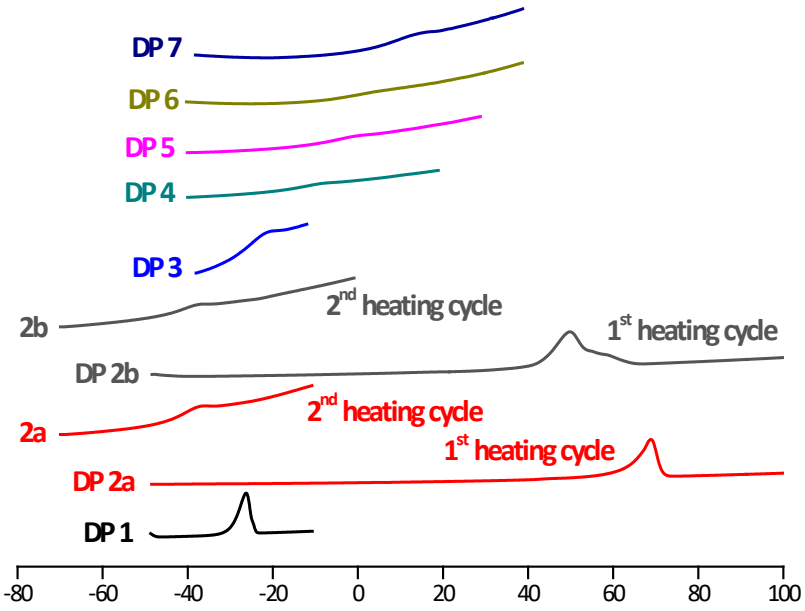


Figure S1. Differential scanning calorimetry (DSC) analysis of the individual discrete (dispersity ($Đ$) = 1) oligo(methyl methacrylates)s (oligo(MMA)s) with degree of polymerization (DP) 1 to 7. All results for the discrete oligo(MMA)s are summarized in Table S1. DP 2a and 2b were obtained after stereoselective separation on the silica cartridge via automated column chromatography, both a glass transition (T_g) and melting point (T_m) were observed during slow heating (10 °C/min) depending on the rate of cooling in the previous cycle (T_g observed upon fast cooling with 150 °C/min).

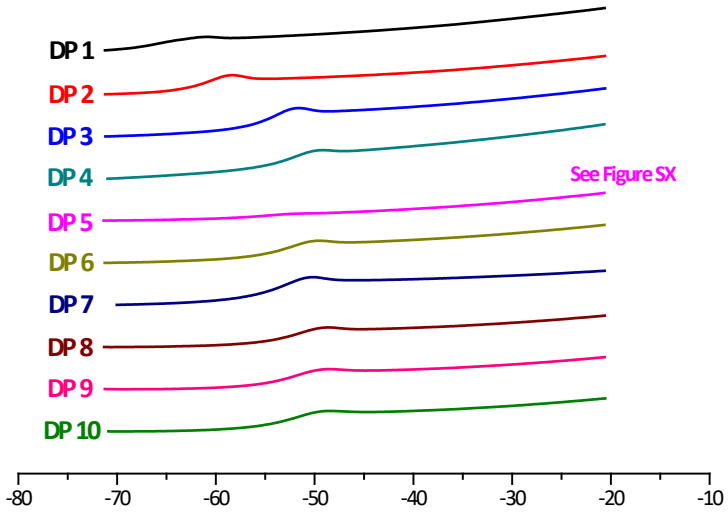


Figure S2. Differential scanning calorimetry (DSC) analysis of the individual discrete (dispersity (*Đ*) = 1) oligo(di(ethylene glycol) ethyl ether acrylate)s (oligo(DEGEEA)s) with degree of polymerization (DP) 1 to 10. All results for the discrete oligo(DEGEEA)s are summarized in Table S2.

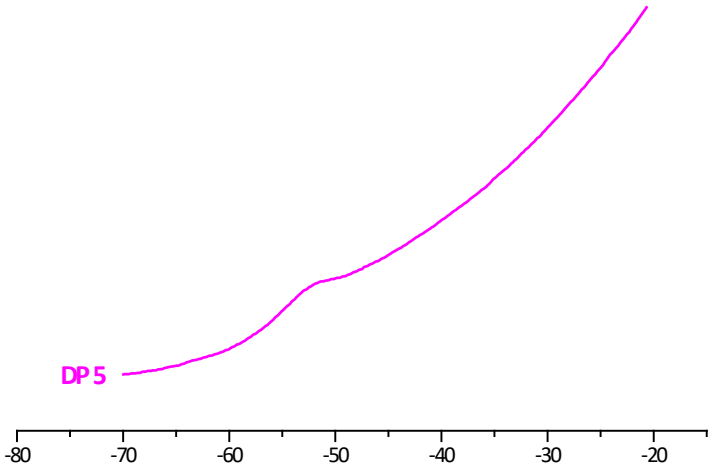


Figure S3. Zoom of differential scanning calorimetry (DSC) analysis of the individual discrete (dispersity (*Đ*) = 1) oligo(di(ethylene glycol) ethyl ether acrylate) (oligo(DEGEEA)) with degree of polymerization (DP) 5.

2. Stereoselective oligomers

Oligo(MMA) DP 1 to 7

Phases: Liquid (L) – SOLID (S) – oily/viscous (V)

Chain length 1 (L) 2a (S) 2b (S) 3 (V) 4 (V) 5 (V) 6 (V) 7 (V)

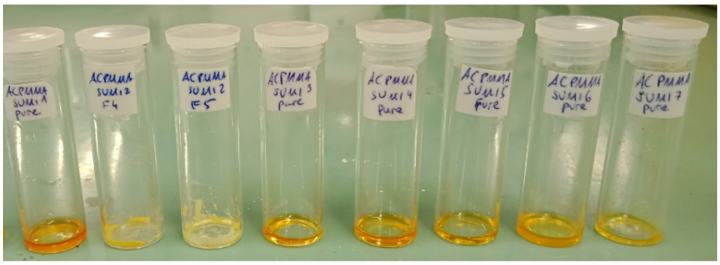
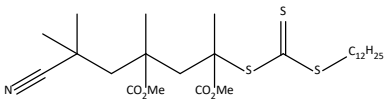
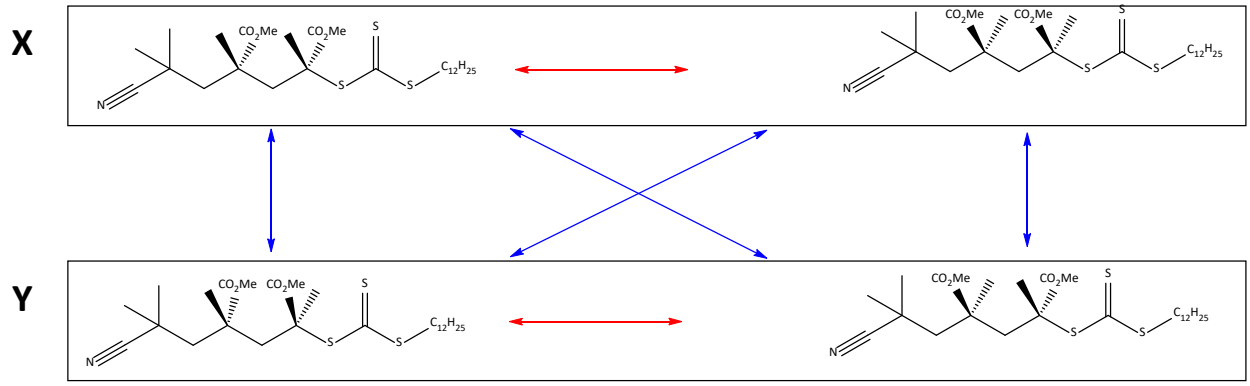


Figure S4. Oligo(MMA) DP 1 to 7. DP 1 appears as a liquid and only a melting point transition was observed. DP 3 to 7 appear oily/viscous and only a glass transition was observed. DP 2a and 2b both represent chain length (DP) = 2 and appear as a solid. 2 discrete fractions were collected from the automated flash column which both have a preferred stereochemistry (either enantiomers RR/SS or SR/RS are preferred, however still observed a mixture as discussed below). Analysis of both fractions is discussed in the main manuscript. Both fractions have a glass transition and melting point depending on the cooling rate for crystallization (glass transition only upon fast cooling (150 °C/min)).



PMMA - Chain Length 2



Scheme S3. Chemical structure for the stereoisomers of oligo(MMA) DP = 2. In total 4 stereoisomers can be obtained being SS-RR-SR-RS of which 2 pairs are enantiomerically related SS/RR and SR/RS. All other pairs are diastereomerically related. Mixtures of enantiomerically related pairs (referred to as mixtures X and Y in Scheme S3) were isolated by flash chromatography into fractions DP 2a and 2b. DP 2a and DP 2b thus represent mixtures of enantiomeric pairs X and Y with a diastereomeric excess of 35:65 (DP 2a) and 82:18 (DP 2b). See NMR analysis of both DP 2a and 2b in Figure S5, S6 and S7.

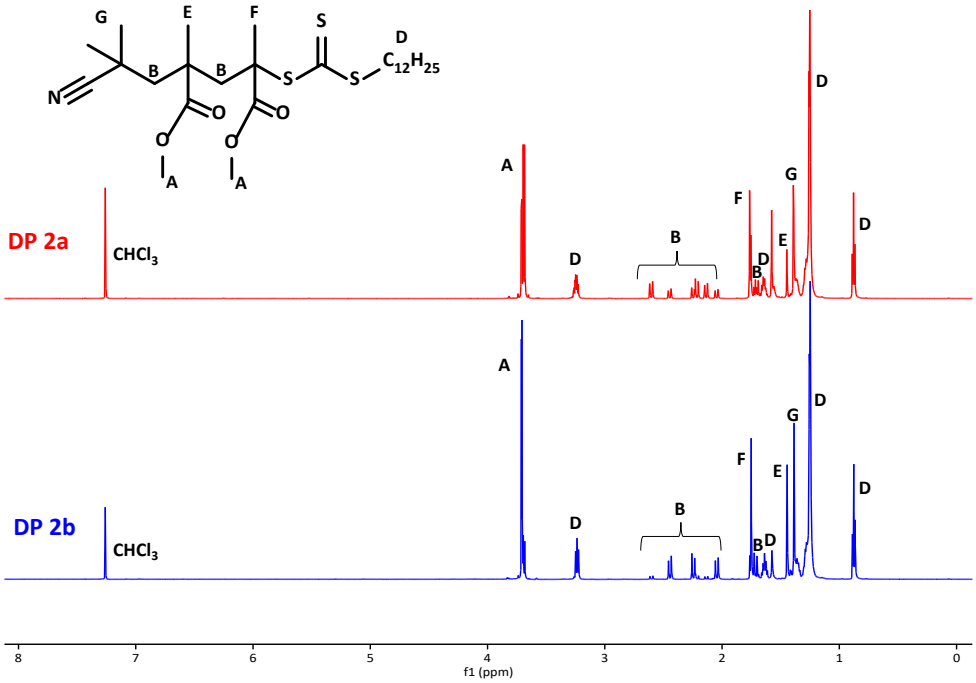


Figure S5. ^{1}H NMR analysis for DP 2a and 2b of oligo(MMA) dimers.

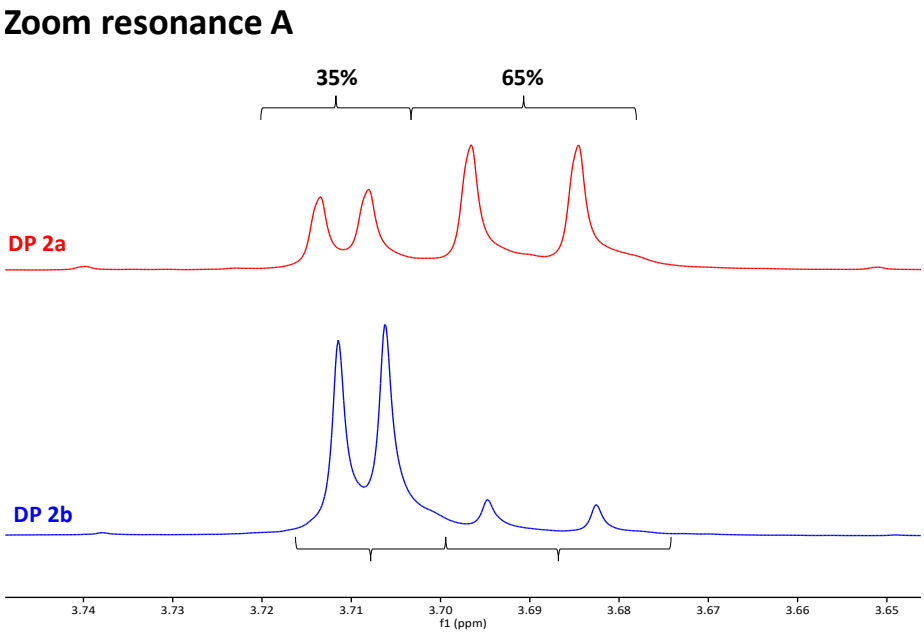


Figure S6. Zoom of ^{1}H NMR analysis resonance A. DP 2a and DP 2b thus represent mixtures of enantiomeric pairs X and Y with a diastereomeric excess of 35:65 (DP 2a) and 82:18 (DP 2b) determined upon integration of the selected resonance peaks of A.

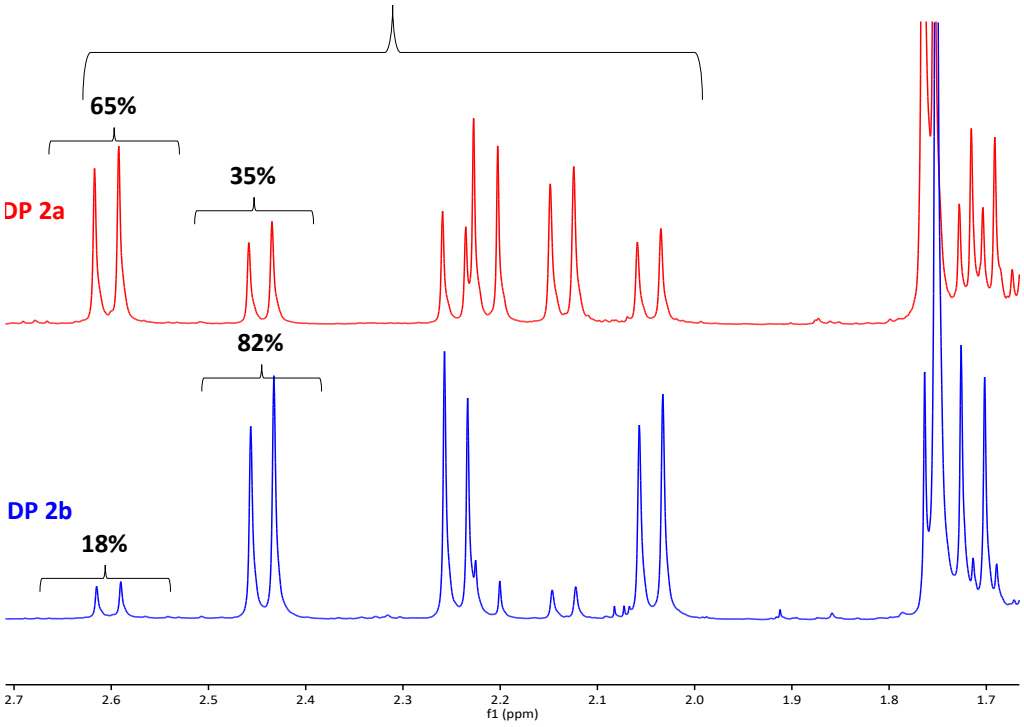


Figure S7. Zoom of ^{1}H NMR analysis resonance B. A diastereomeric excess of 35:65 (DP 2a) and 82:18 (DP 2b) was calculated upon integration of selected resonance peaks of B.

3. Summarized results of discrete oligomer properties

Table S1. Overview of the raw data resulting from analysis of all 8 PMMA separated oligomers *via* electrospray ionization mass spectrometry (ESI-MS), diffusion-ordered nuclear magnetic resonance (DOSY-NMR) spectroscopy and differential scanning calorimetry (DSC).

CL	$Mass_{[th]}^{Na+}$ (Da)	$Mass_{[exp]}$ (Da)	Mass Accuracy (ppm)	D (10^{-10} $m^2 \cdot s^{-1}$)	T_g (°C)	T_m (°C)	[a]Amount (mg)	[a]Isolated Yield (mol%)
1	446.22157*	446.21969	4.2	11.170 ± 0.281	-	-26.3 (-34.0 - -24.0)	114	11
2a	568.25594	568.25208	6.8	9.197 ± 0.146	43.0 ± 0.5	49.8 (31.0 – 67.0)	61	5
2b	568.25594	568.25265	5.8	9.154 ± 0.006	42.4 ± 0.6	68.9 (41.0 – 74.0)	31	3
3	668.30837	668.30604	3.5	7.853 ± 0.008	26.3 ± 0.9	-	108	7
4	768.36080	768.35675	5.3	7.282 ± 0.041	13.9 ± 0.2	-	119	7
5	868.41323	868.40926	4.6	6.864 ± 0.101	-7.3 ± 0.8	-	85	4
6	968.46566	968.46370	2.0	6.513 ± 0.162	-1.7 ± 0.4	-	66	3
7	1068.51809	1068.51563	2.3	6.198 ± 0.030	3.4 ± 0.7	-	47	2

[a]Actual amounts and isolated yields represent the combined results after separation and multiple polymerization reactions where different chain lengths were targeted to construct a final discrete oligomer library. CL = Chain Length, $Mass_{[th]}^{Na}$ = theoretically expected single sodium-charged monoisotopioc mass, $MW_{[exp]}$ = experimentally obtained single sodium-charged monoisotopioc mass from ESI-MS, Mass accuracy = difference between theoretically expected and experimentally obtained single sodium-charged monoisotopioc mass. D = diffusion coefficient from DOSY-NMR spectroscopy, T_g = glass transition temperature from DSC, * = single hydrogen-charged instead of sodium-charged.

Table S2. Overview of the raw data resulting from analysis of all 10 PDEGEEA separated oligomers *via* electrospray ionization mass spectrometry (ESI-MS), diffusion-ordered nuclear magnetic resonance (DOSY-NMR) spectroscopy and differential scanning calorimetry (DSC).

CL	$Mass_{[th]}^{Na}$ (Da)	$Mass_{[exp]}$ (Da)	Mass Accuracy (ppm)	D (10^{-10} $m^2 \cdot s^{-1}$)	T_g (°C)	T_m (°C)	[a]Amount (mg)	[a]Isolated Yield (mol%)
1	394.11750*	394.11991	6.1	9.635 ± 0.090	-67.3 ± 0.6	-	21	6
2	604.20430	604.20324	1.8	7.998 ± 0.038	-61.8 ± 0.2	-	125	22
3	792.30916	792.30520	5.0	6.968 ± 0.051	-56.1 ± 0.6	-	80	11
4	980.41402	980.41205	2.0	6.305 ± 0.063	-54.4 ± 0.4	-	34	4
5	1168.51888	1168.51271	5.3	5.711 ± 0.012	-54.7 ± 0.4	-	24	2
6	1356.62374	1356.62249	0.9	5.389 ± 0.097	-54.2 ± 0.1	-	62	5
7	1544.72860	1544.72824	0.2	5.095 ± 0.032	-54.1 ± 0.4	-	68	5
8	1732.83346	1732.83041	1.8	4.839 ± 0.014	-53.5 ± 0.2	-	60	4
9	1920.93832	1920.93681	0.8	4.649 ± 0.045	-53.2 ± 0.3	-	52	3
10	2109.04318	2109.04226	0.4	4.482 ± 0.004	-53.2 ± 0.2	-	44	2

[a]Actual amounts and isolated yields represent the combined results after separation and multiple polymerization reactions where different chain lengths were targeted to construct a final discrete oligomer library. CL = Chain Length, $Mass_{[th]}^{Na}$ = theoretically expected single sodium-charged monoisotopioc mass, $MW_{[exp]}$ = experimentally obtained single sodium-charged monoisotopioc mass from ESI-MS, Mass accuracy = difference between theoretically expected and experimentally obtained single sodium-charged monoisotopioc mass. D = diffusion coefficient from DOSY-NMR spectroscopy, T_g = glass transition temperature from DSC, * = single hydrogen-charged instead of sodium-charged.

4. Diffusion-ordered NMR spectroscopy (DOSY-NMR)

I. 2D DOSY-NMR spectra of MMA oligomers

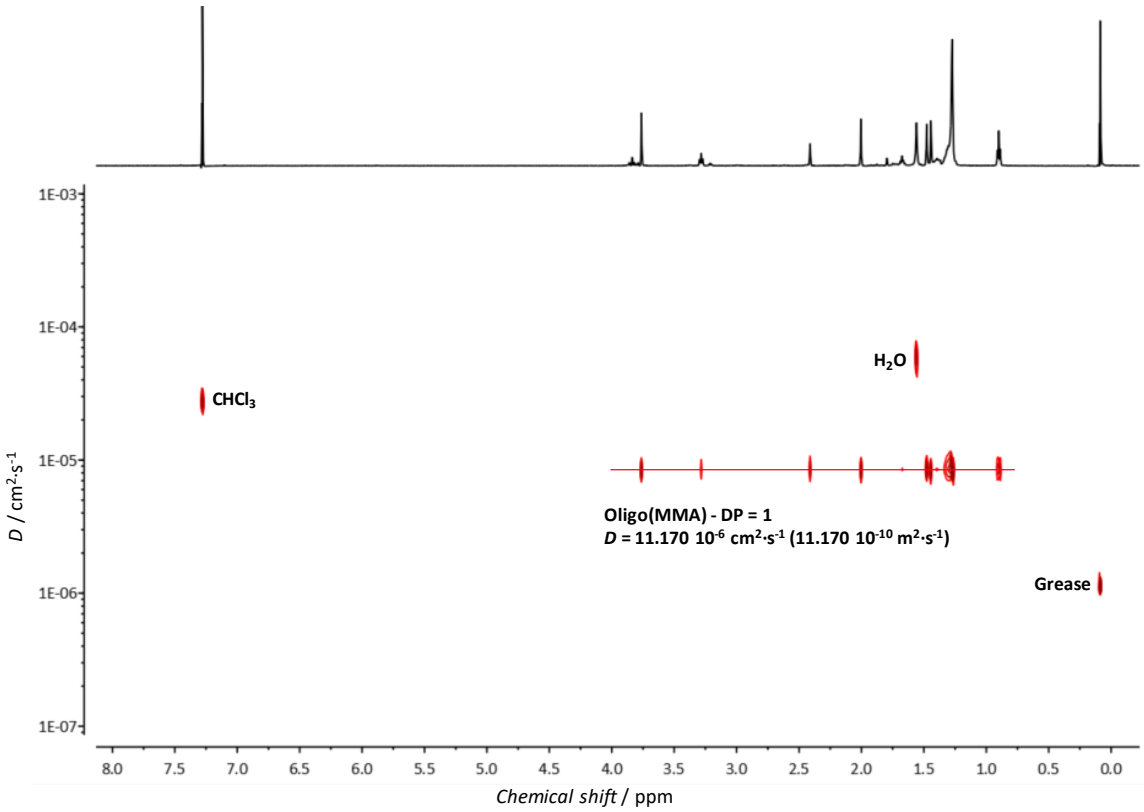


Figure S8. 2D DOSY-NMR analysis of oligo(MMA) DP = 1.

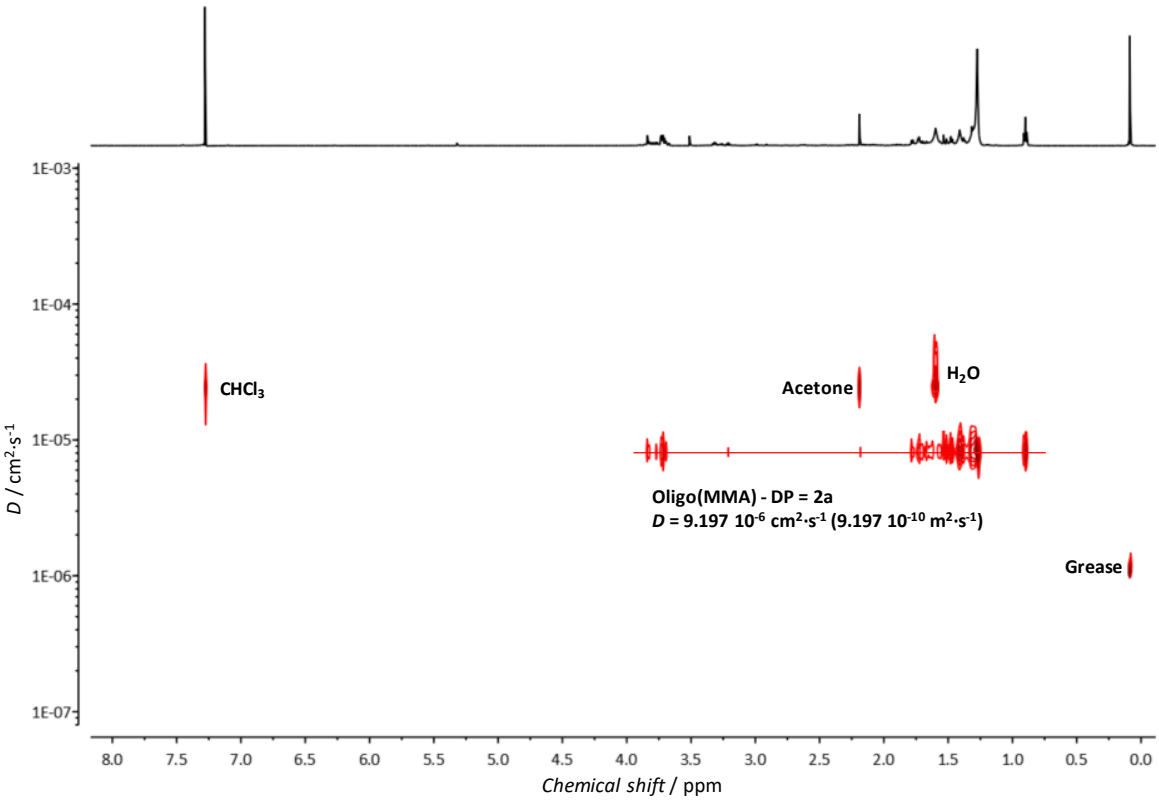


Figure S9. 2D DOSY-NMR analysis of oligo(MMA) DP = 2a.

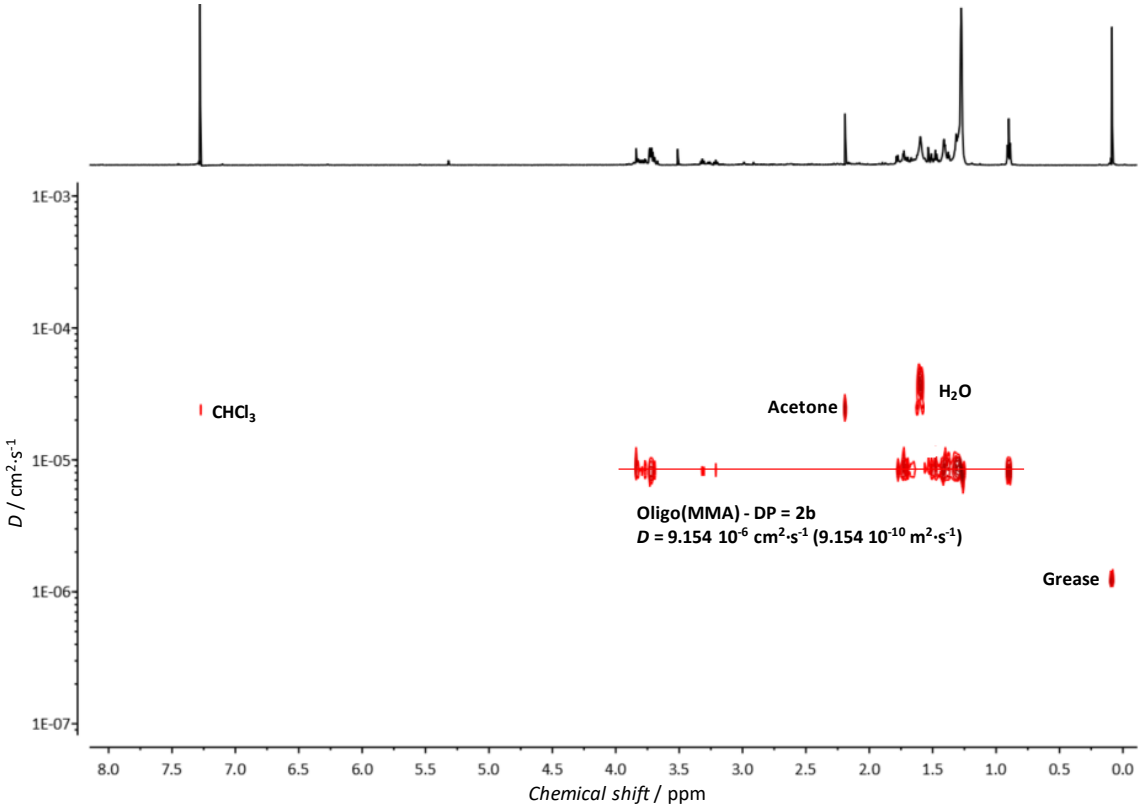


Figure S10. 2D DOSY-NMR analysis of oligo(MMA) DP = 2b.

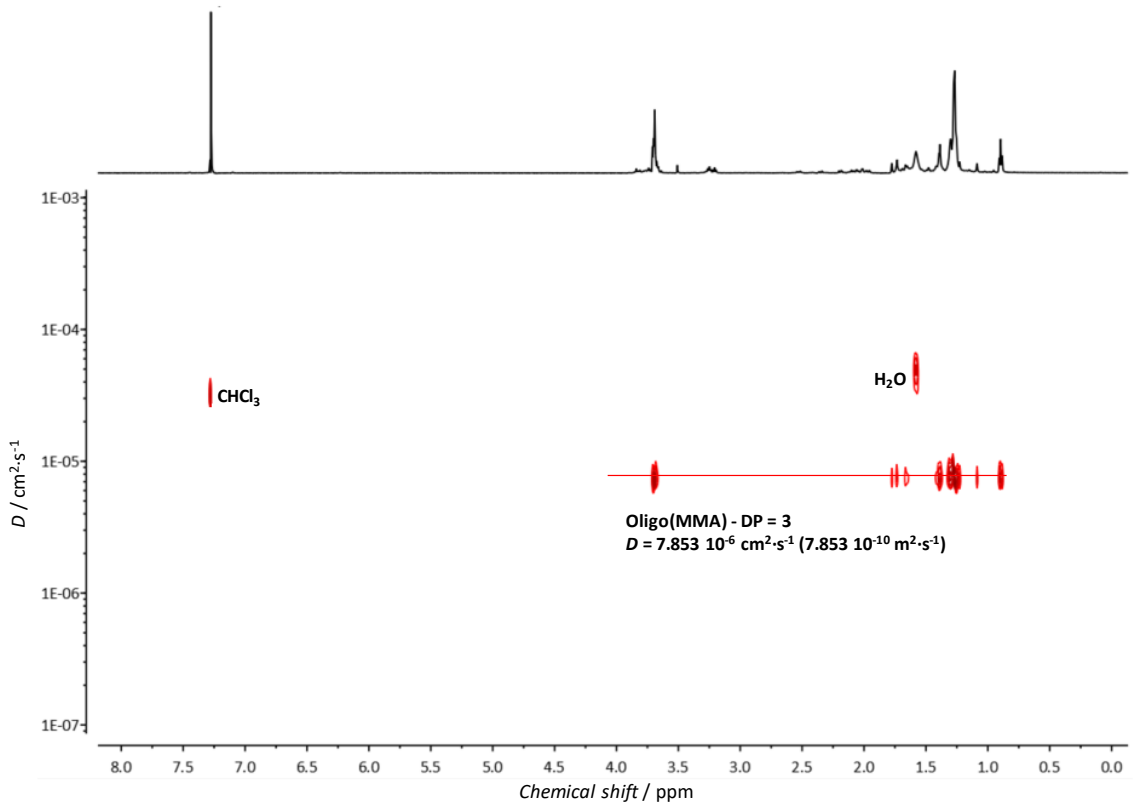


Figure S11. 2D DOSY-NMR analysis of oligo(MMA) DP = 3.

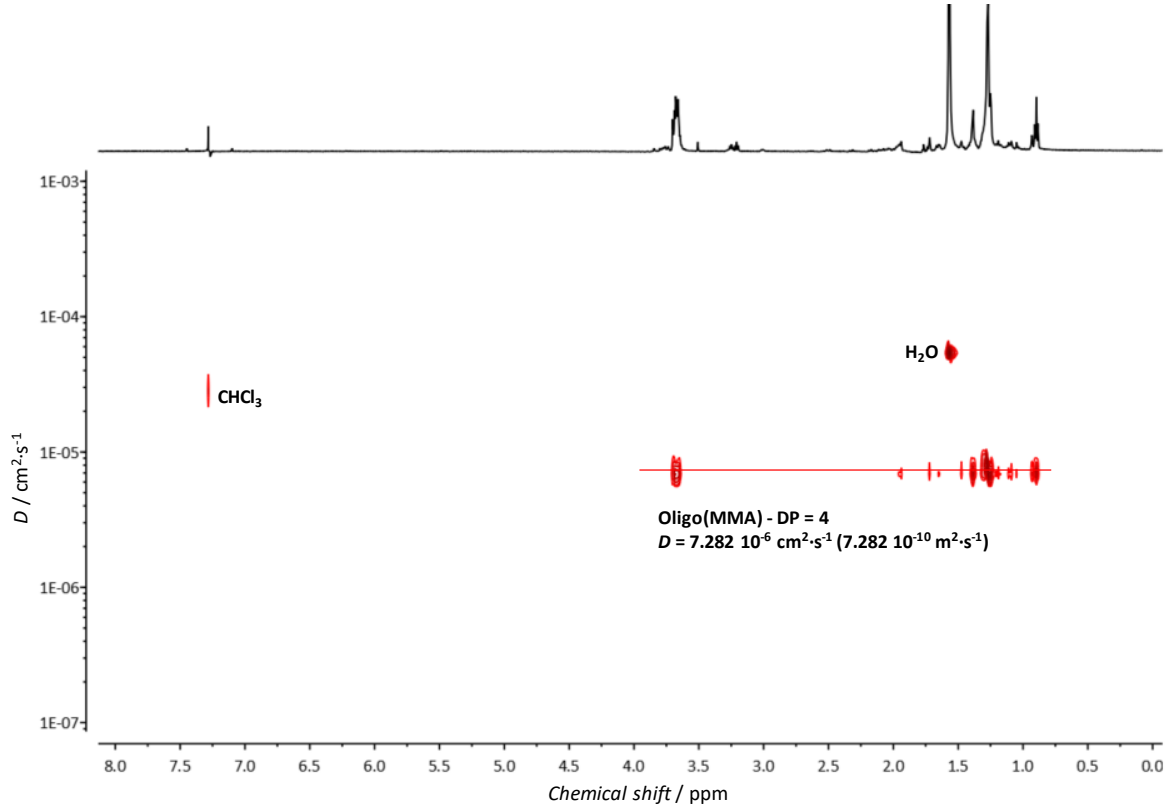


Figure S12. 2D DOSY-NMR analysis of oligo(MMA) DP = 4.

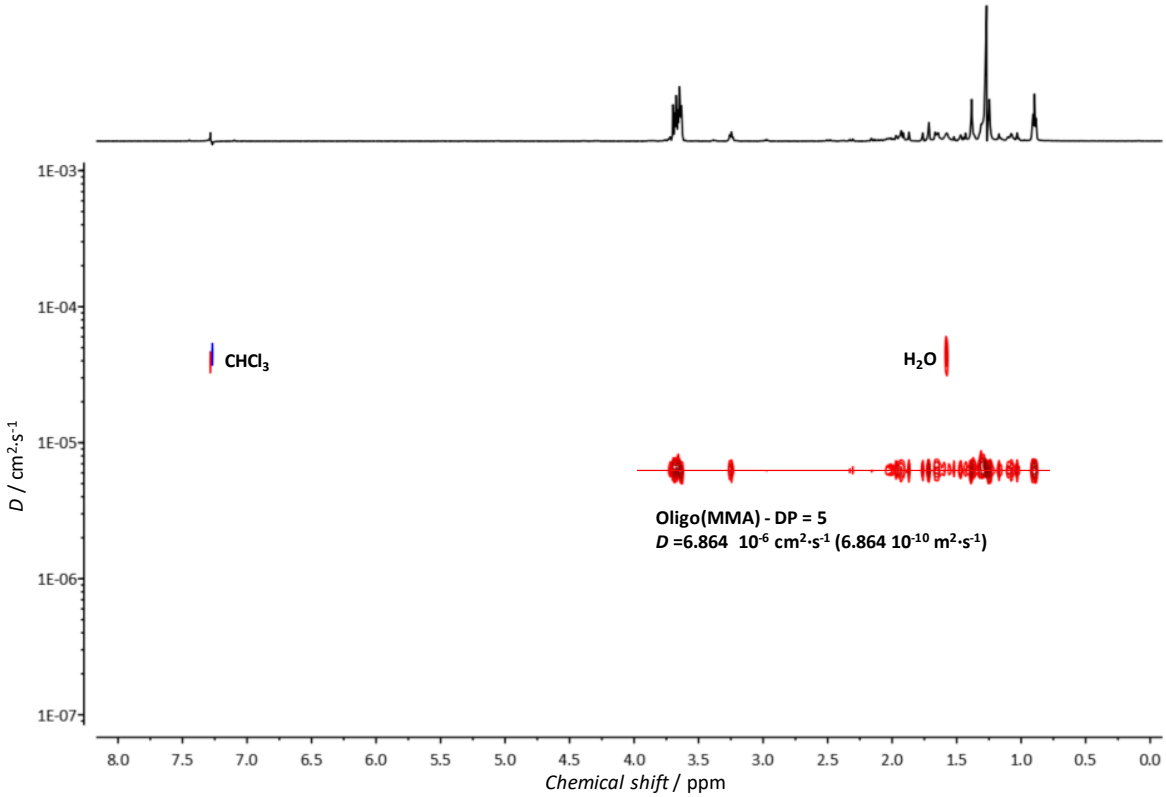


Figure S13. 2D DOSY-NMR analysis of oligo(MMA) DP = 5.

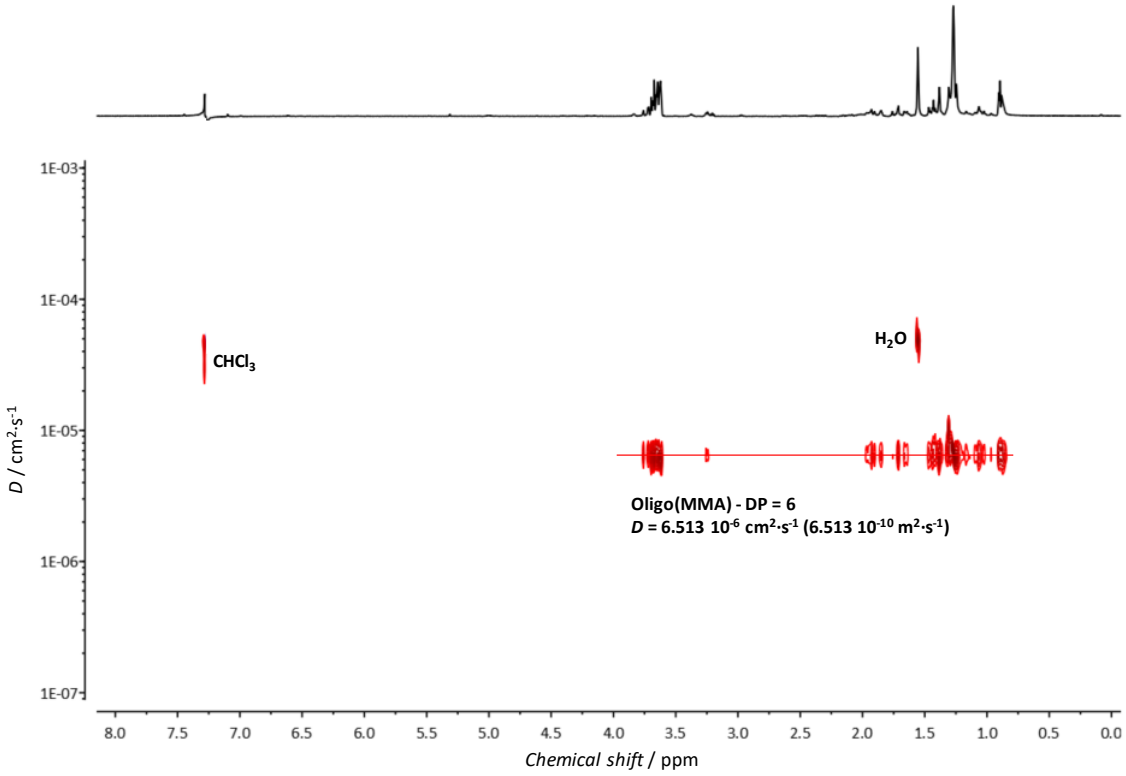


Figure S14. 2D DOSY-NMR analysis of oligo(MMA) DP = 6.

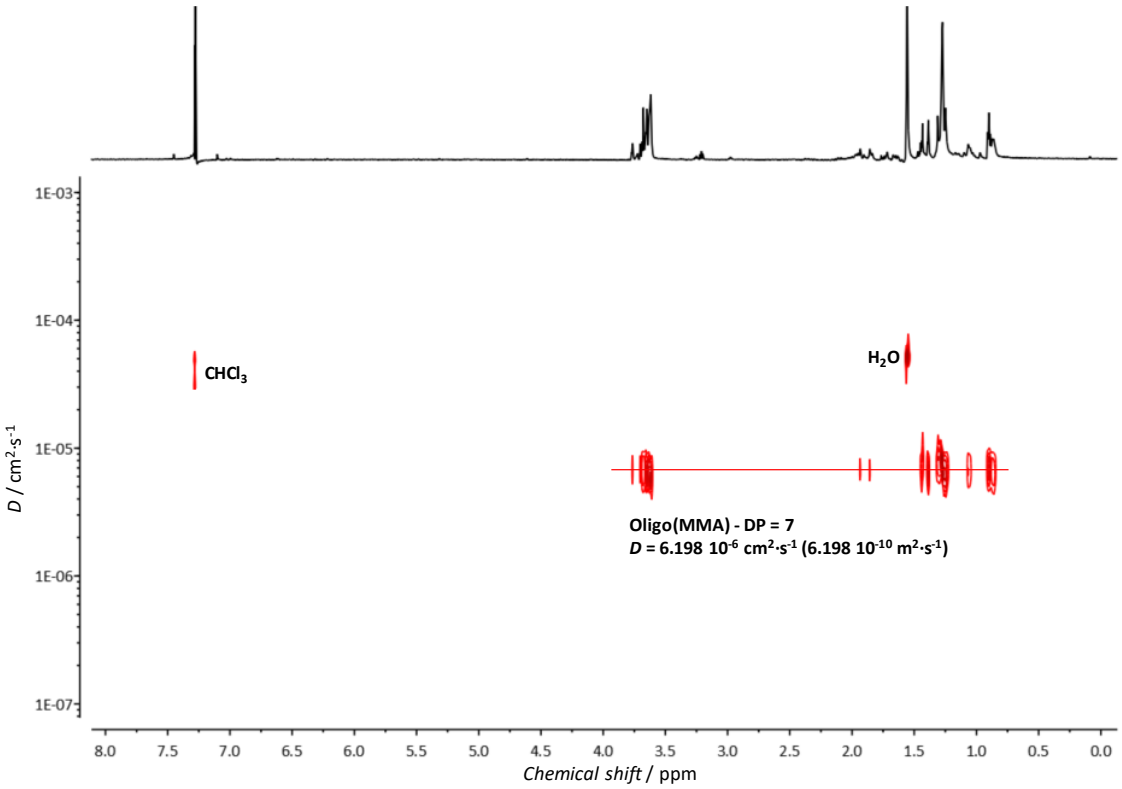


Figure S15. 2D DOSY-NMR analysis of oligo(MMA) DP = 7.

II. 2D DOSY-NMR spectra of DEGEEA oligomers

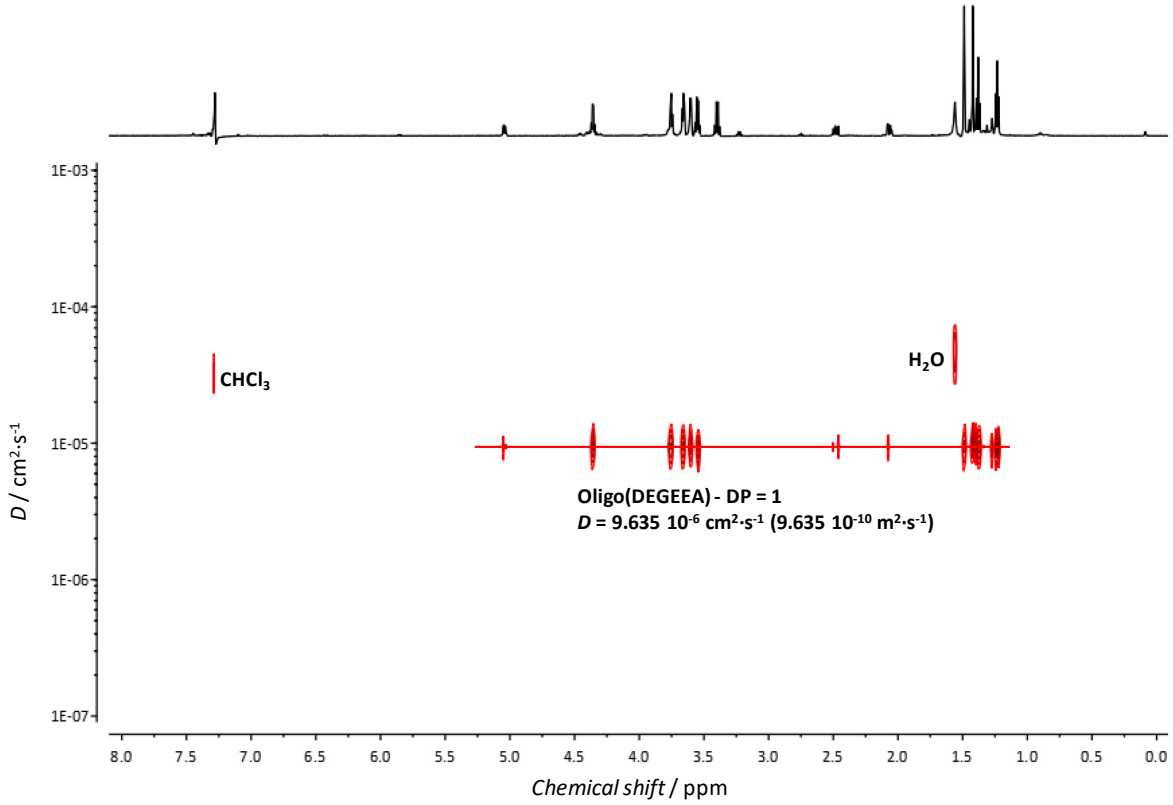


Figure S16. 2D DOSY-NMR analysis of oligo(DEGEEA) DP = 1.

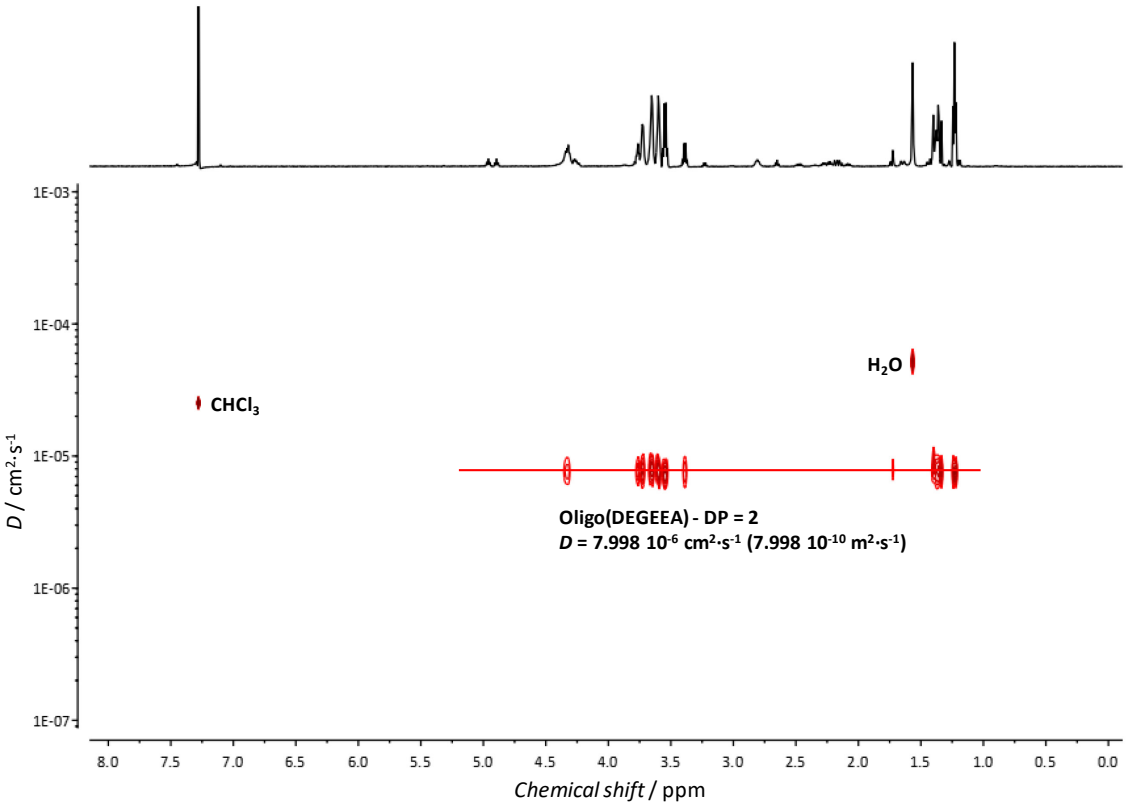


Figure S17. 2D DOSY-NMR analysis of oligo(DEGEEA) DP = 2.

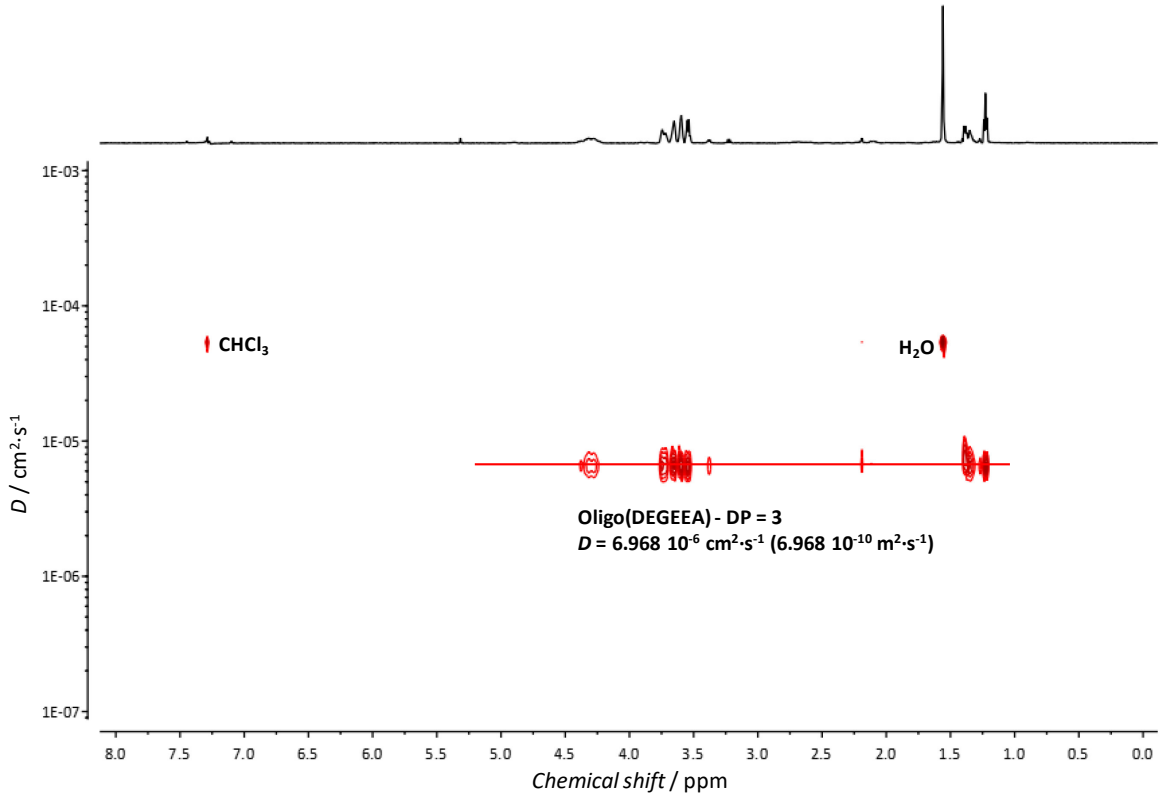


Figure S18. 2D DOSY-NMR analysis of oligo(DEGEEA) DP = 3.

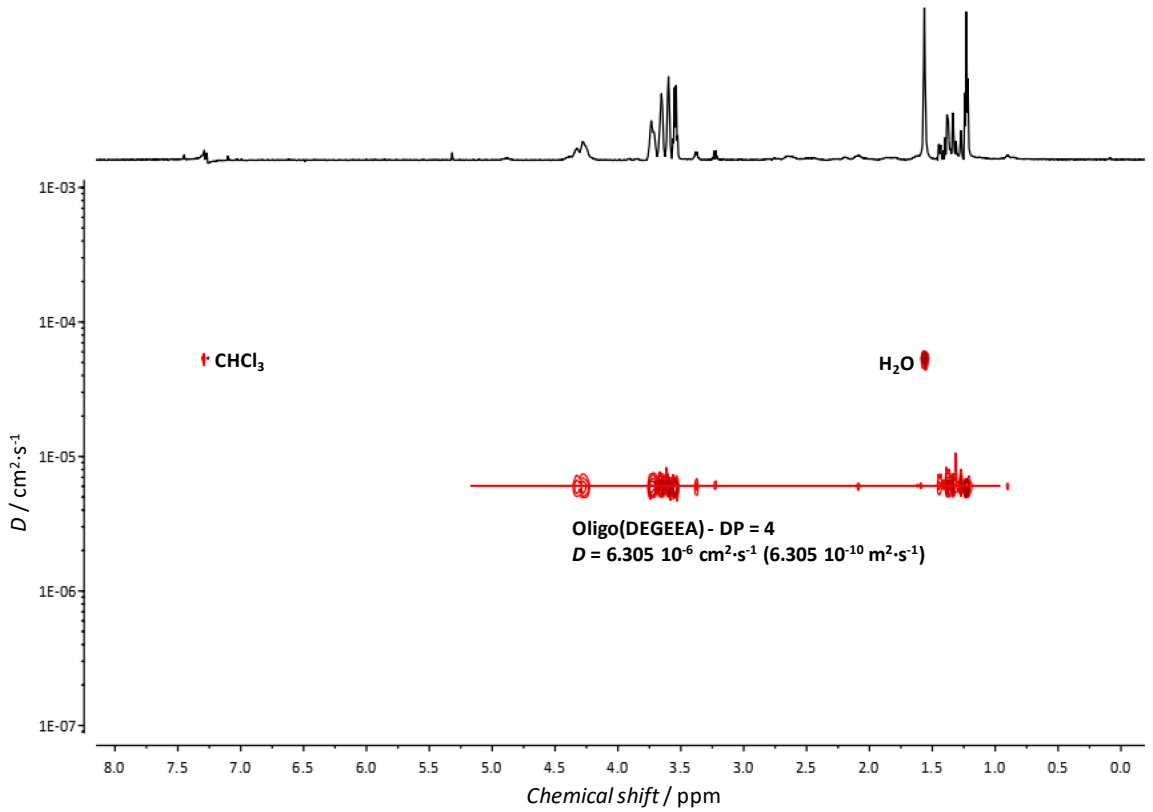


Figure S19. 2D DOSY-NMR analysis of oligo(DEGEEA) DP = 4.

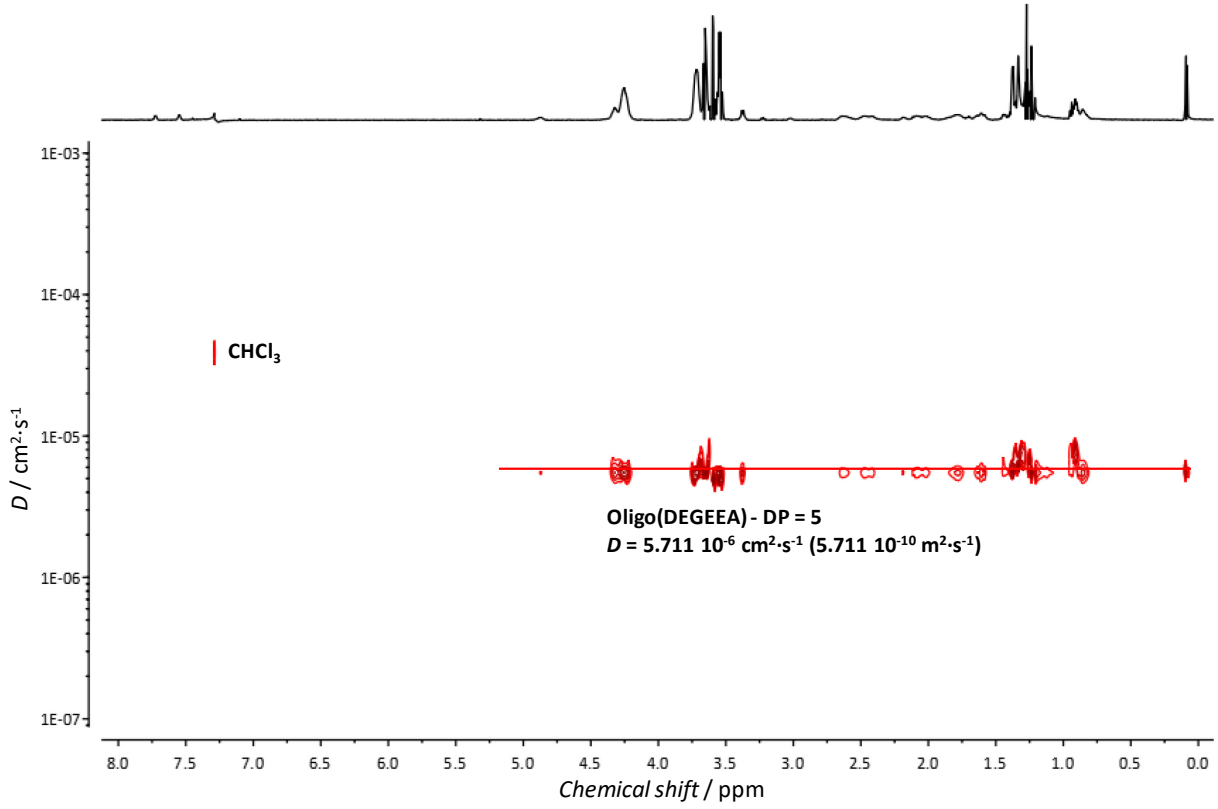


Figure S20. 2D DOSY-NMR analysis of oligo(DEGEEA) DP = 5.

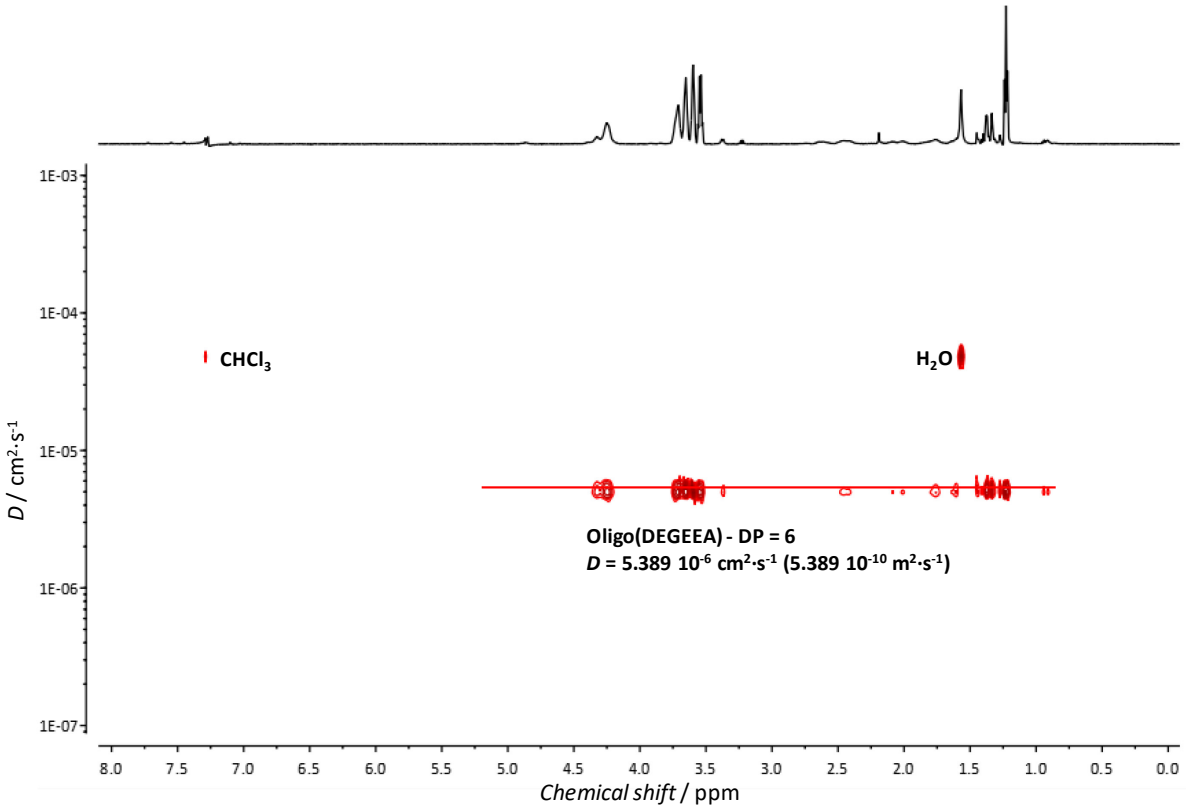


Figure S21. 2D DOSY-NMR analysis of oligo(DEGEEA) DP = 6.

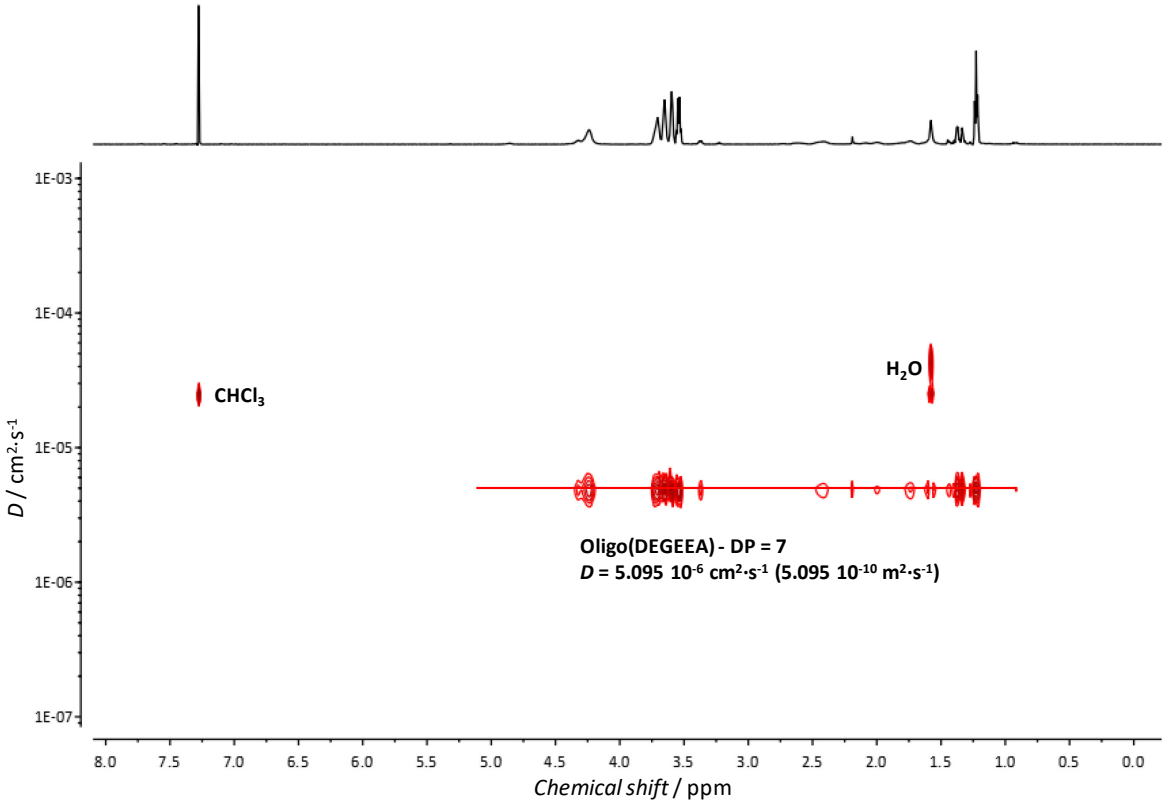


Figure S22. 2D DOSY-NMR analysis of oligo(DEGEEA) DP = 7.

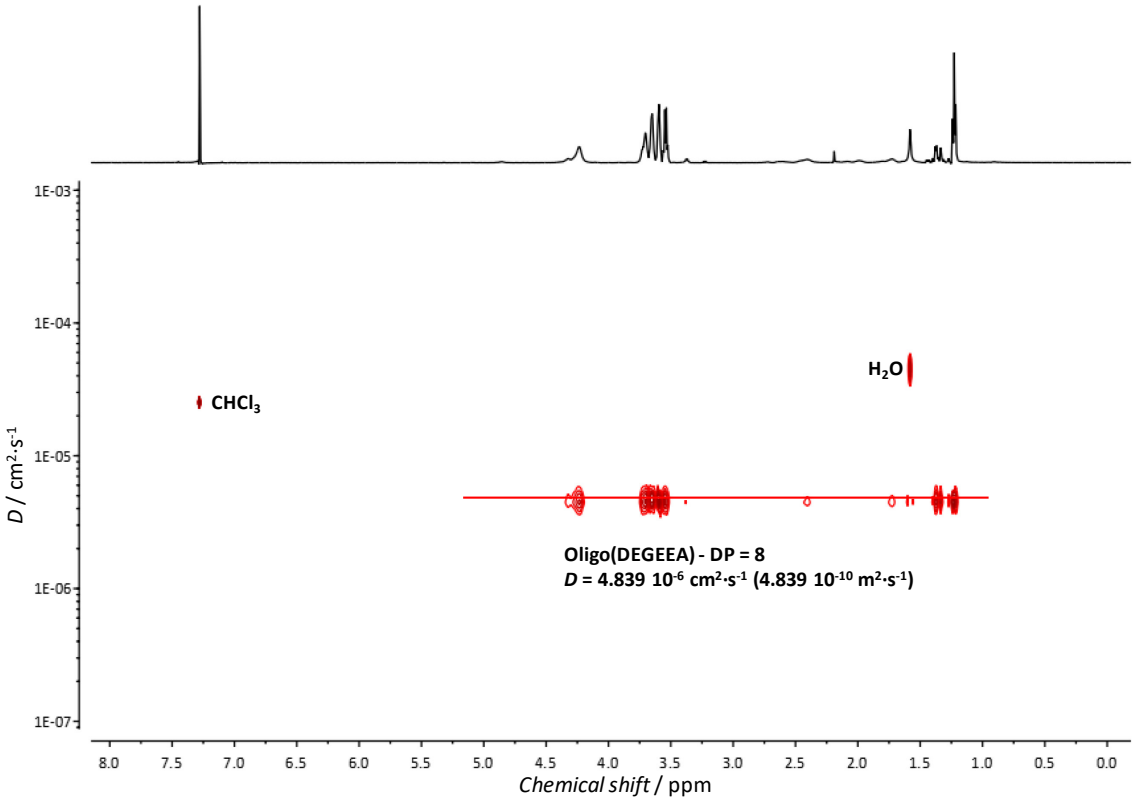


Figure S23. 2D DOSY-NMR analysis of oligo(DEGEEA) DP = 8.

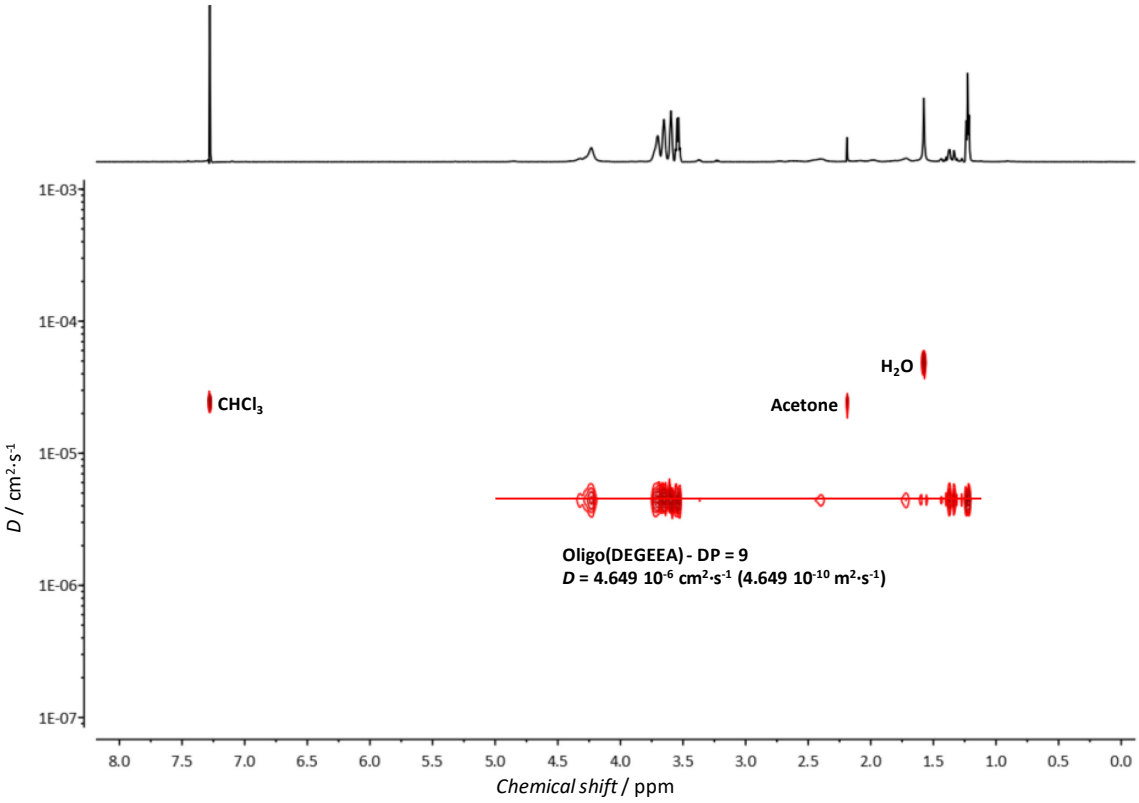


Figure S24. 2D DOSY-NMR analysis of oligo(DEGEEA) DP = 9.

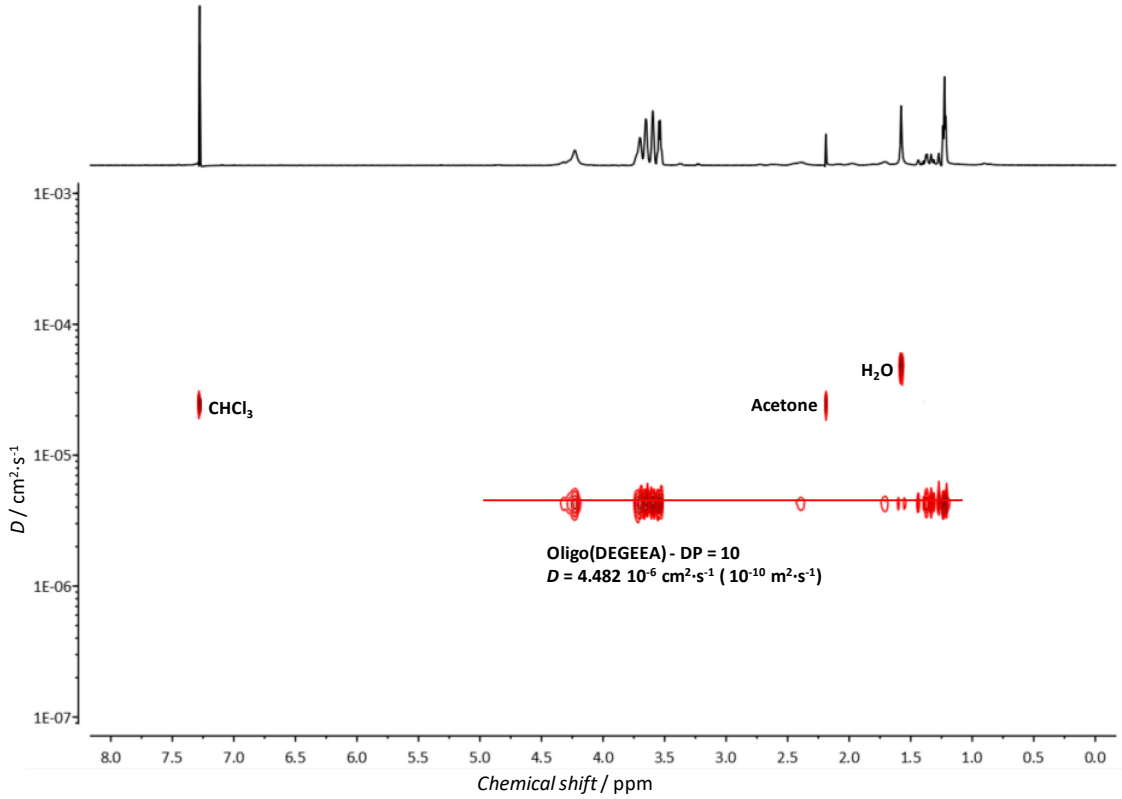


Figure S25. 2D DOSY-NMR analysis of oligo(DEGEEA) DP = 10.

C. References

1. Y. K. Chong, G. Moad, E. Rizzardo and S. H. Thang, *Macromolecules*, 2007, **40**, 4446-4455.