

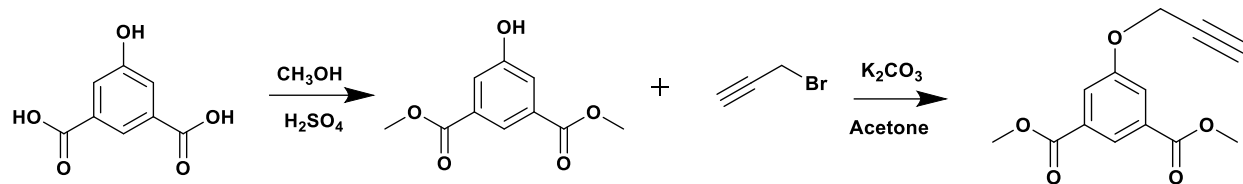
## Supporting Information

### **Tracking solvent-induced conformational collapse of periodically grafted amphiphilic polymers using PFG NMR diffusometry**

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**Scheme S1:** Synthesis of dimethyl 5-(prop-2yn-1-yloxy) isophthalate as a monomer.

**Synthesis of dimethyl, 5-dihydroxyisophthalate:** 15 g of 3,5-dihydroxyisophthalic acid was dissolved in 300 mL of methanol (MeOH) along with a catalytic amount of sulfuric acid ( $\text{H}_2\text{SO}_4$ ). The mixture was refluxed for 12 hours after the addition was complete. The resulting reaction mixture was then extracted with chloroform ( $\text{CHCl}_3$ ) ( $3 \times 75$  mL) after addition of water. The organic layer was subsequently dried over sodium sulfate ( $\text{Na}_2\text{SO}_4$ ), concentrated under reduced pressure, and dried to yield the desired product. Yield-90%

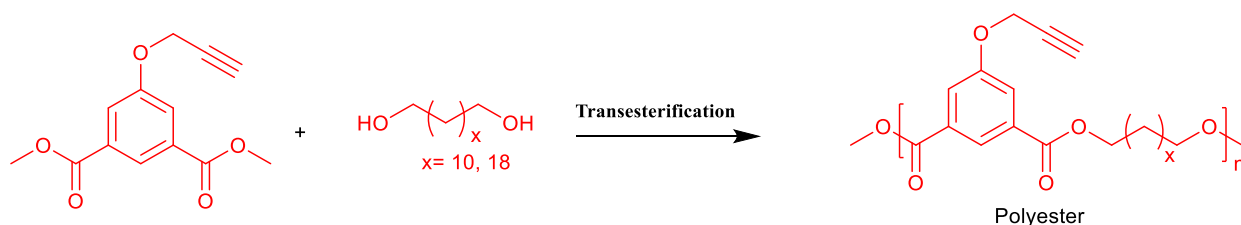
**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):** 8.26 (1H,t,ArCH), 7.74 (2H,d,ArCH), 3.94(6H,s,ArCOOCH<sub>3</sub>)

**Synthesis of propargyl bromide:** 50 ml of propargyl alcohol and 10 ml of pyridine were combined in a 250 ml round bottom flask. Using a dropping funnel, 30 ml of phosphorus tribromide ( $\text{PBr}_3$ ) was added dropwise to the mixture. The reaction mixture was stirred at room temperature for 12 hours. Subsequently, the product was distilled at  $70^\circ\text{C}$  to yield a clear solution of propargyl bromide. Yield-85%

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):** 3.683(2H,d,CHCCH<sub>2</sub>Br), 2.240(1H,t, CHCCH<sub>2</sub>Br)

**Synthesis of dimethyl 5-(prop-2yn-1-yloxy) isophthalate (1):** 10 gm of dimethyl, 5-dihydroxyisophthalate, 8 ml of propargyl bromide and 20 gm of potassium carbonate ( $\text{K}_2\text{CO}_3$ ) were combined in 150 ml of acetone. The mixture was refluxed under a nitrogen atmosphere for 24 hours. After concentration, the solution was subjected to recrystallization, yielding transparent crystals. Yield = 72 %

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):** 8.32 (s, 1H, ArCH); 7.82 (d, 2H, ArCH); 4.78 (d, 2H, ArOCH<sub>2</sub>CCH); 3.940 (s, 6H, ArCOCH<sub>3</sub>); 2.548 (t, 1H, ArOCH<sub>2</sub>CCH)

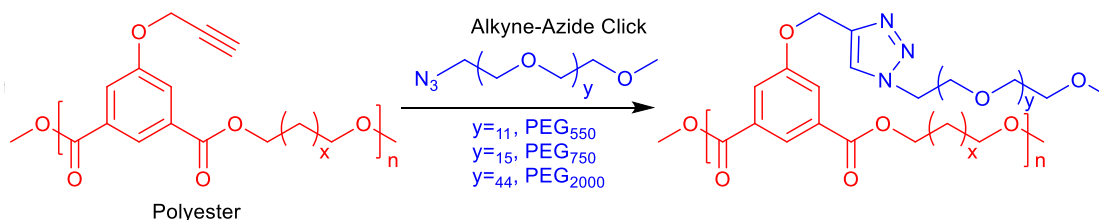


**Scheme S2:** Synthesis of parent polymer of PE<sub>12</sub> and PE<sub>20</sub> by melt transesterification polymerization using 1,12 dodecanediol or 1,20 docosanediol, respectively.

**Synthesis of parent polymer with the polymer backbone of C<sub>12</sub> (PE<sub>12</sub>):** 5 gm of **1** (20 mmol), 4.075 gm (20 mmol) of 1,12 dodecanediol, 238  $\mu$ l (2 mmol) of DBTDL (dibutyltin dilaurate) were added under a nitrogen atmosphere. The polymerization proceeded under dry nitrogen purge for 5 hours at 120°C and then in kugelrohr at 160°C under reduced pressure (<1 torr) for 8 hrs. The polymer was obtained as a white solid with a yield of 77% after precipitation using chloroform as a solvent and methanol as a non-solvent.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** 8.32 (s, 1H, ArCH); 7.82 (d, 2H, ArCH); 4.78 (d, 2H, ArOCH<sub>2</sub>CCH); 4.32 (t, 4H, ArCOOCH<sub>2</sub>); 2.548 (t, 1H, ArOCH<sub>2</sub>CCH), 1.78 (q, 4H, ArCOOCH<sub>2</sub>CH<sub>2</sub>); 0.8-1.6 (CH<sub>2</sub> of aliphatic chain)

The polyester, PE<sub>20</sub>, was synthesized using the same procedure with a yield of 80%.



**Scheme S3:** Synthesis of PGAP through the reaction of parent polymers (PE<sub>12</sub> and PE<sub>20</sub>) with various PEG azides (PEG-550 azide, PEG-750 azide and PEG-2k azide).

**Synthesis of polymers (PE<sub>12</sub>PEG<sub>550</sub>):** 2 gm (5 mmol) of the parent polyester, 4.43 gm (7.5 mmol) of PEG-550 monomethyl ether azide were dissolved in 15 ml of chloroform and purged with N<sub>2</sub> gas. To this solution, 98 mg (0.5 mmol) of CuI and 900  $\mu$ l (5 mmol) of DIPEA were added under a nitrogen atmosphere. After degassing, the reaction mixture was stirred at 60°C for 3 days. The solution was concentrated and precipitated into

methanol; the isolated sample was redissolved in chloroform and reprecipitated once more in methanol. The resulting polymer was light brown in color, with a yield of 80%.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** 8.29 (s, 1H, ArCH); 7.9 (s, 1H, triazole ring) 7.82 (d, 2H, ArCH); 5.28 (d, 2H, ArOCH<sub>2</sub>triazole); 4.57 (t, 2H, ArCH<sub>2</sub>PEG); 4.32 (t, 4H, ArCOOCH<sub>2</sub>); 3.9 (t, 2H, CH<sub>2</sub>PEG); 3.5-3.7 (PEG protons); 3.3 (terminal OCH<sub>3</sub>); 1.78 (q, 4H, ArCOOCH<sub>2</sub>CH<sub>2</sub>); 0.8-1.6 (CH<sub>2</sub> of aliphatic chain)

Using the above procedures, three other amphiphilic polymers, namely PE<sub>12</sub>-g-PEG<sub>750</sub> (yield 76 %), PE<sub>20</sub>-g-PEG<sub>550</sub> (yield 80 %), PE<sub>20</sub>-g-PEG<sub>750</sub> (yield 75%), were prepared and purified. In the case of PE<sub>12</sub>-g-PEG<sub>2000</sub> (yield 78 %) and PE<sub>20</sub>-g-PEG<sub>2000</sub> (yield 82%), the reprecipitation was done in Pet. Ether.

**Synthesis of PEG-550 tosylate:** 10 gm (14.3 mmol) of PEG-550 monomethyl ether was dissolved in THF, followed by addition of 1.7 grams (28 mmol) of NaOH dissolved in 20 ml of water. The mixture was cooled in an ice-water bath. Subsequently, tosyl chloride in THF was added dropwise to the cooled solution. After stirring overnight, the organic layer was separated, concentrated using a rotary evaporator, and dried under vacuum to yield a light-yellow liquid (yield=85%).

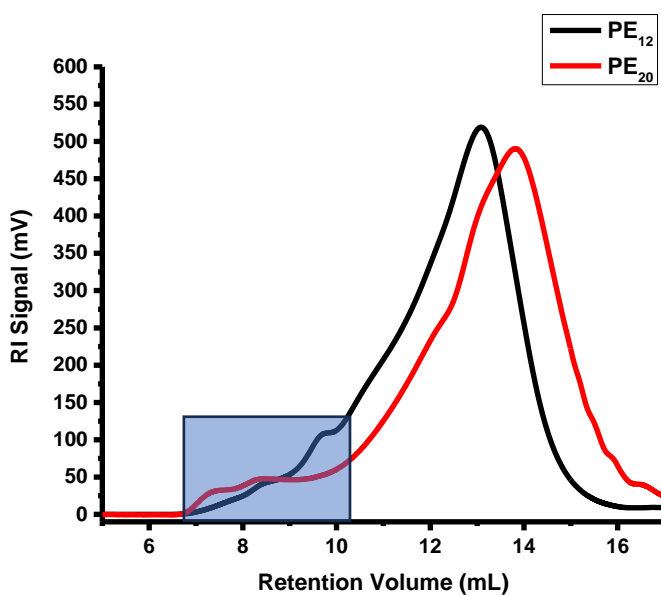
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** 2.45 (s, 3H, ArCHCH<sub>3</sub>); 3.38 (s, 3H, OCH<sub>3</sub>); 3.54-3.70 (CH<sub>2</sub> s of PEG skeleton); 4.16 (t, 2H, OCH<sub>2</sub>); 7.34 (d, 2H, ArCH); 7.79 (d, 2H, ArCH).

Using the above procedure, PEG-750 tosylate and PEG-2k tosylate were prepared with yields of 70% and 80%, respectively.

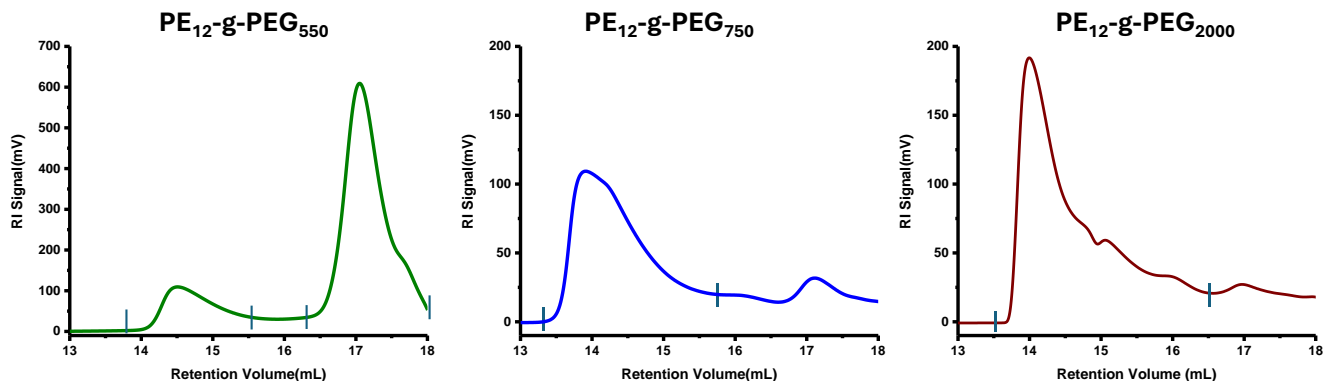
**Synthesis of PEG-550 azide:** 5 gm of the PEG-550 tosylate and 2 gm of sodium azide were dissolved in DMF. The mixture was heated overnight at 60°C with constant stirring. After completion of the reaction, DMF was removed under vacuum to obtain a yellow liquid, which was then poured into the water and extracted with diethyl ether. The organic layer was washed with water once, and the solvent was evaporated under reduced pressure to yield the product (80% yield). **<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** 3.34 (t, 2H, CH<sub>2</sub>N<sub>3</sub>); 3.36-3.65 (aliphatic chain CH<sub>2</sub> and terminal CH<sub>3</sub>). Using the above procedure, PEG-750 azide and PEG-2k azide were prepared with yields of 75% and 78%, respectively.

**Table S1:** Summary of molecular weights for parent and grafted polymers, including Mark-Houwink constant and radius, determined using GPC instrument with a viscometer detector.

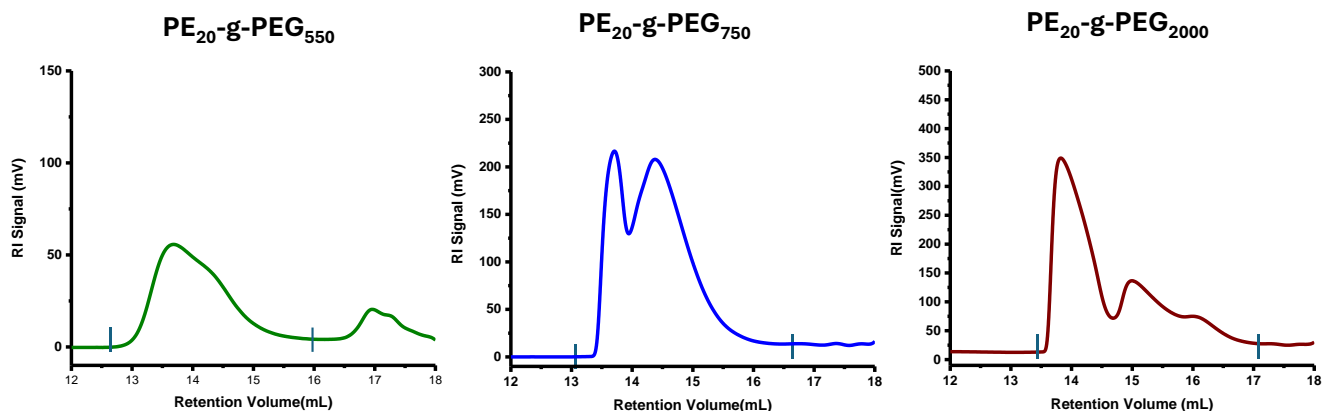
| Polymers                                | $M_n$ (g/mol)<br>(Da)    | $M_w$ (g/mol)<br>(Da)    | PDI                  | M-H <sub>a</sub>     | $R_h$ (nm) |
|---|--------------------------|--------------------------|----------------------|----------------------|------------|
| PE <sub>12</sub>                        | 36,000                   | 1,62,000                 | 4.5                  | 0.5                  | 7          |
| PE <sub>20</sub>                        | 22,000                   | 66,000                   | 3                    | 0.5                  | 4          |
| PE <sub>12</sub> -g-PEG <sub>550</sub>  | P <sub>1</sub> =1,80,000 | P <sub>1</sub> =2,16,000 | P <sub>1</sub> =1.2  | P <sub>1</sub> =0.7  | 5          |
|   | P <sub>2</sub> = 9,800   | P <sub>2</sub> = 11,760  | P <sub>2</sub> = 1.2 | P <sub>2</sub> = 0.5 | 2          |
| PE <sub>12</sub> -g-PEG <sub>750</sub>  | 1,46,300                 | 1,90,200                 | 1.3                  | 0.8                  | 7          |
| PE <sub>12</sub> -g-PEG <sub>2000</sub> | 1,56,000                 | 2,02,800                 | 1.5                  | 0.8                  | 7          |
| PE <sub>20</sub> -g-PEG <sub>550</sub>  | 98,000                   | 1,27,400                 | 1.3                  | 0.7                  | 5          |
| PE <sub>20</sub> -g-PEG <sub>750</sub>  | 58,000                   | 75,400                   | 1.3                  | 0.5                  | 7          |
| PE <sub>20</sub> -g-PEG <sub>2000</sub> | 1,13,200                 | 2,60,300                 | 2                    | 0.7                  | 7          |



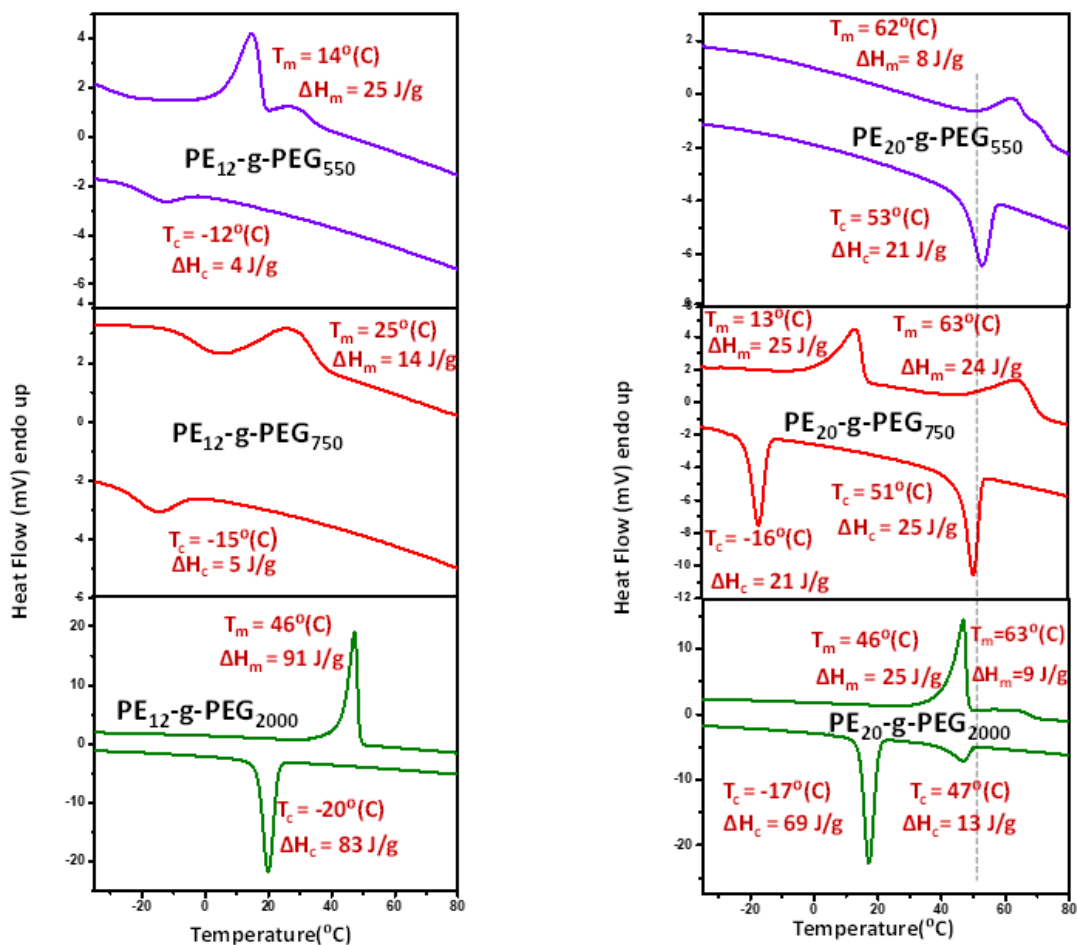
**Figure S1:** RI signals for parent polymers: The black curve represents the parent polymer with a C<sub>12</sub> hydrocarbon segment (P<sub>12</sub>), while the red curve represents the RI signal of a parent polymer with a C<sub>20</sub> hydrocarbon segment (P<sub>20</sub>). The shaded region reflects the presence of some multi-chain species with significantly higher molecular weight.



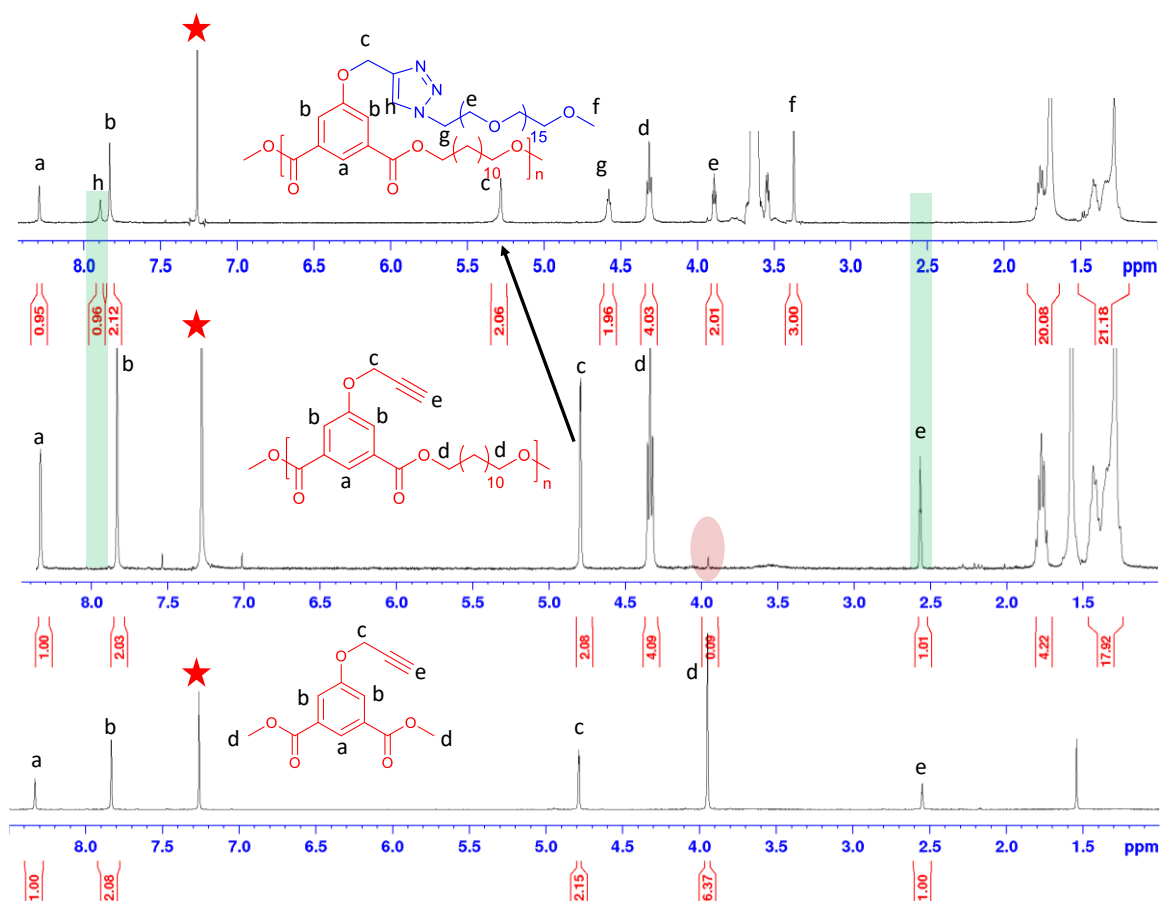
**Figure S2:** RI signals of PGAPs: The green color represents the polymer with a C<sub>12</sub> backbone and PEG side chain of 550 (PE<sub>12</sub>-g-PEG<sub>550</sub>); the blue color represents the polymer with C<sub>12</sub> backbone and a PEG side chain of 750 (PE<sub>12</sub>-g-PEG<sub>750</sub>); and the wine color represents the polymer with C<sub>12</sub> backbone and a PEG side chain of 2000 (PE<sub>12</sub>-g-PEG<sub>2000</sub>). Here, in the case of PEG550 clicked polymer, the lower molecular weight peak is prominent, but as the longer PEG segments are installed, the relative contribution from the lower molecular weight peak diminishes. It appears to suggest that as the size of the installed PEG segments increases, the difference in hydrodynamic sizes between the two species diminishes and they appear to elute at closer time intervals. The region of the chromatogram utilized to estimate the molecular weights and dispersity are marked directly on the curves.



**Figure S3:** RI signals of PGAPs: The green color represents the polymer with a C<sub>20</sub> backbone and PEG side chain of 550 (PE<sub>20</sub>-g-PEG<sub>550</sub>); the blue color represents the polymer with C<sub>20</sub> backbone and a PEG side chain of 750 (PE<sub>20</sub>-g-PEG<sub>750</sub>); and the wine color represents the polymer with C<sub>20</sub> backbone and a PEG side chain of 2000 (PE<sub>20</sub>-g-PEG<sub>2000</sub>). The multi-modal distribution is evident in all the chromatograms, although as the clicked PEG length increases, the relative intensity of the low molecular weight shoulder becomes relatively weak. This reflects the fact that longer the size of the PEG segment installed in each repeat unit the smaller becomes the difference in the hydrodynamic size between the two species. The region of the chromatogram utilized to estimate the molecular weights and dispersity are marked directly on the curves.



**Figure S4:** DSC thermograms of different PGAPs; the left panel shows thermograms of PE<sub>12</sub>-g-PEG<sub>550</sub>, PE<sub>12</sub>-g-PEG<sub>750</sub>, and PE<sub>12</sub>-g-PEG<sub>2000</sub> and the right panel shows those of PE<sub>20</sub>-g-PEG<sub>550</sub>, PE<sub>20</sub>-g-PEG<sub>750</sub>, and PE<sub>20</sub>-g-PEG<sub>2000</sub>. In the case of PE<sub>12</sub>-g-PEG<sub>y</sub>, the melting/crystallization peaks are due to the PEG segments, as the C12 chains do not crystallize; on the other hand, in the case of PE<sub>20</sub>-g-PEG<sub>y</sub>, samples both the C20 and the pendant PEG segments crystallize independently, except in the case of PE<sub>12</sub>-g-PEG<sub>550</sub>, where melting due to only C20 segments is seen; it appears that the crystallization of the C20 segments impedes the crystallization of the PGG550 segments, which was seen in the case of PE<sub>12</sub>-g-PEG<sub>550</sub>.



**Figure S5:** Stack plot of the <sup>1</sup>H NMR spectra of dimethyl, 5-propargyloxy isophthalate, the parent clickable polyester (PE<sub>12</sub>), and the polymer after clicking with MPEG750 azide, namely PE<sub>12</sub>-g-PEG<sub>750</sub>. The relative intensity of the residual methyl ester peak (3.96 ppm) in the polymer was used to estimate the degree of polymerization (DP) (as shown below), assuming that both ends are terminated by the isophthalate unit; this represents the upper limit of M<sub>n</sub>. Disappearance of the propargyl proton peaks (highlighted) and appearance of the triazole ring proton (highlighted) after click reaction confirms complete transformation.

### Calculation of Degree of Polymerization

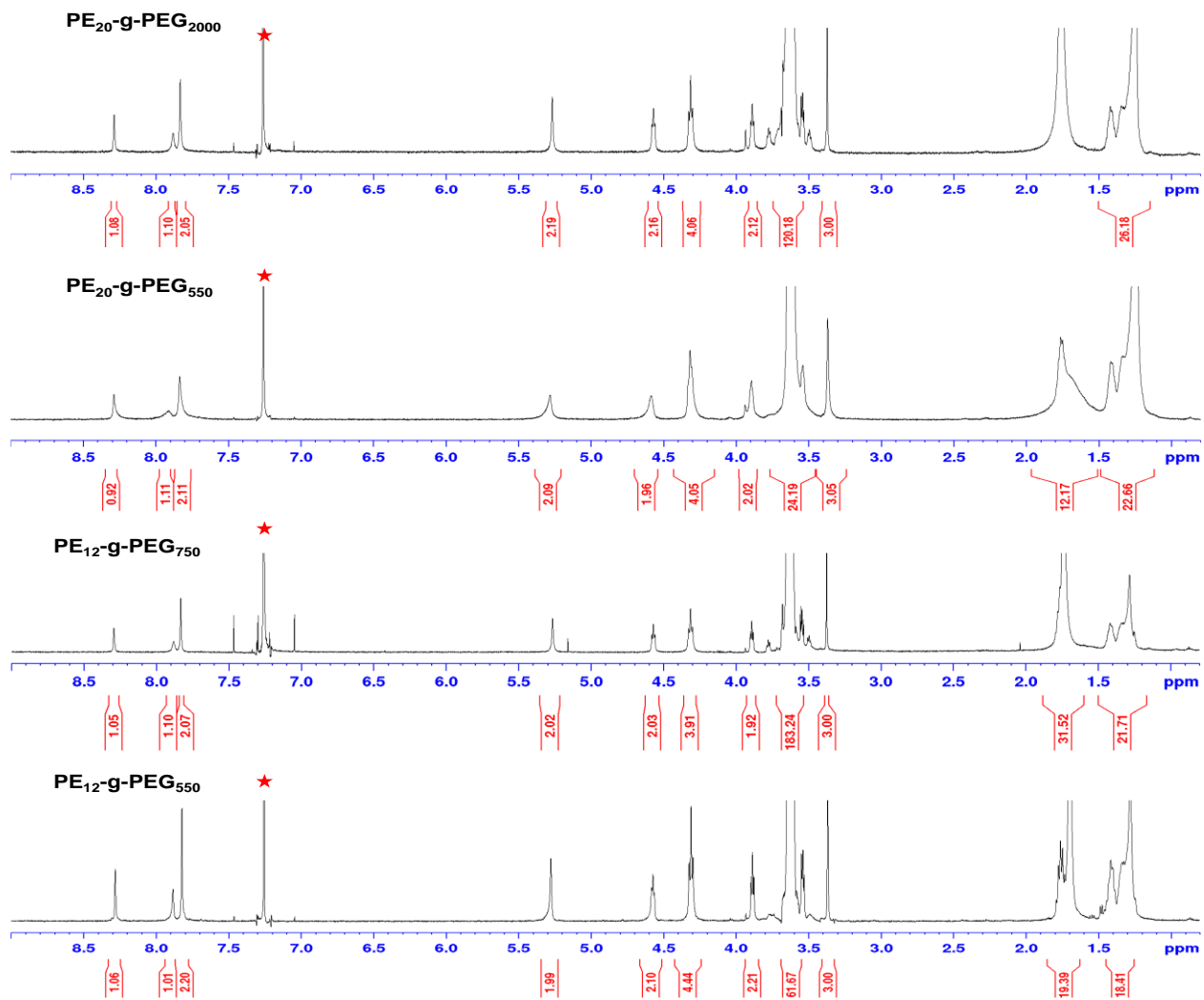
If one assumes that both ends of the polymer are capped with methyl ester end groups, then the degree of polymerization (DP) is calculated as:

$$DP = \frac{\frac{I_a}{1}}{\frac{I_{OCH_3}}{6}} = \frac{\frac{1}{0.09}}{\frac{1}{6}} = 66$$

If one assumes that only one end of the polymer is capped with methyl ester end group, then the degree of polymerization (DP) is calculated as:

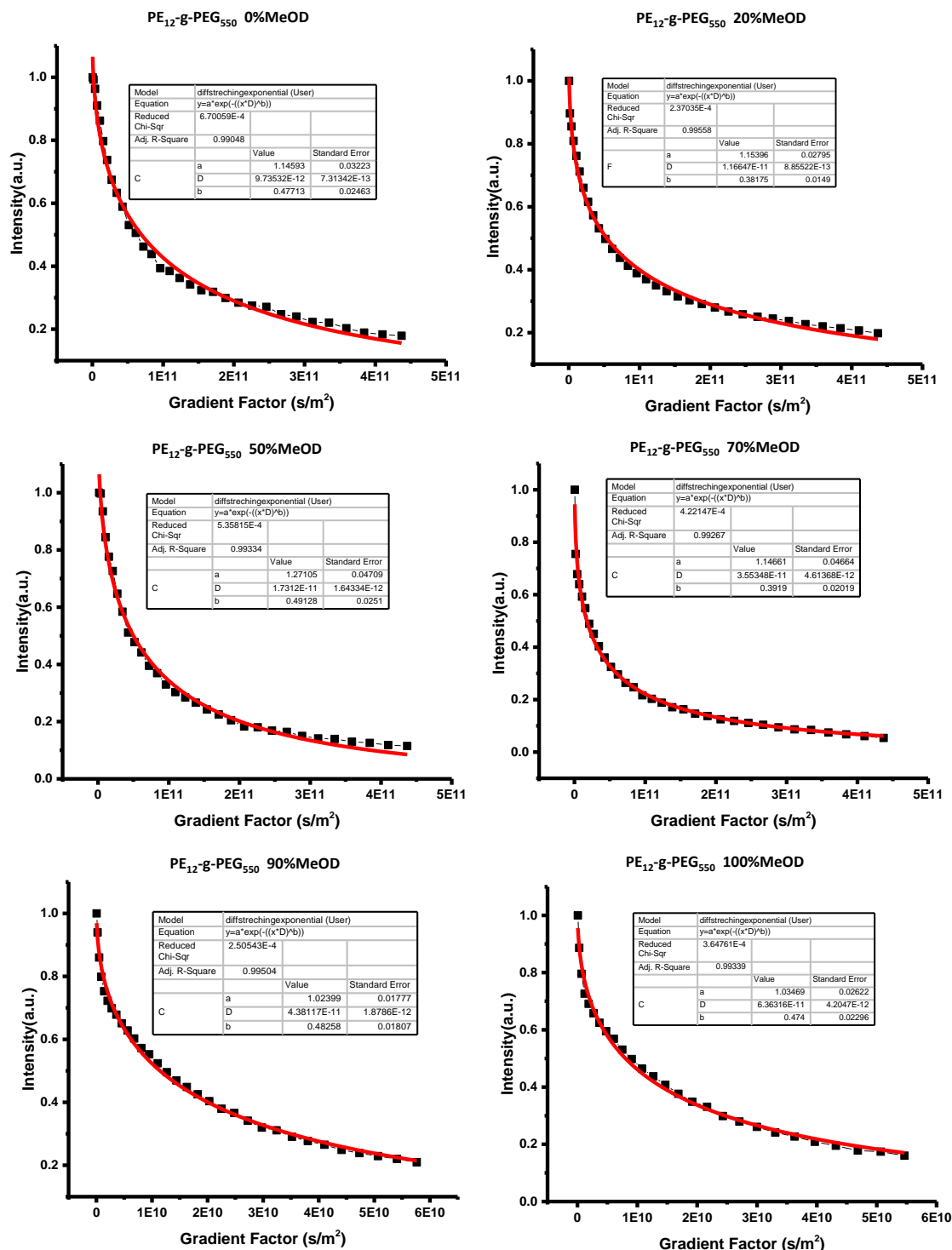
$$DP = \frac{\frac{I_a}{1}}{\frac{I_{end\ group}}{3}} = \frac{\frac{1}{0.09}}{\frac{1}{3}} = 33$$





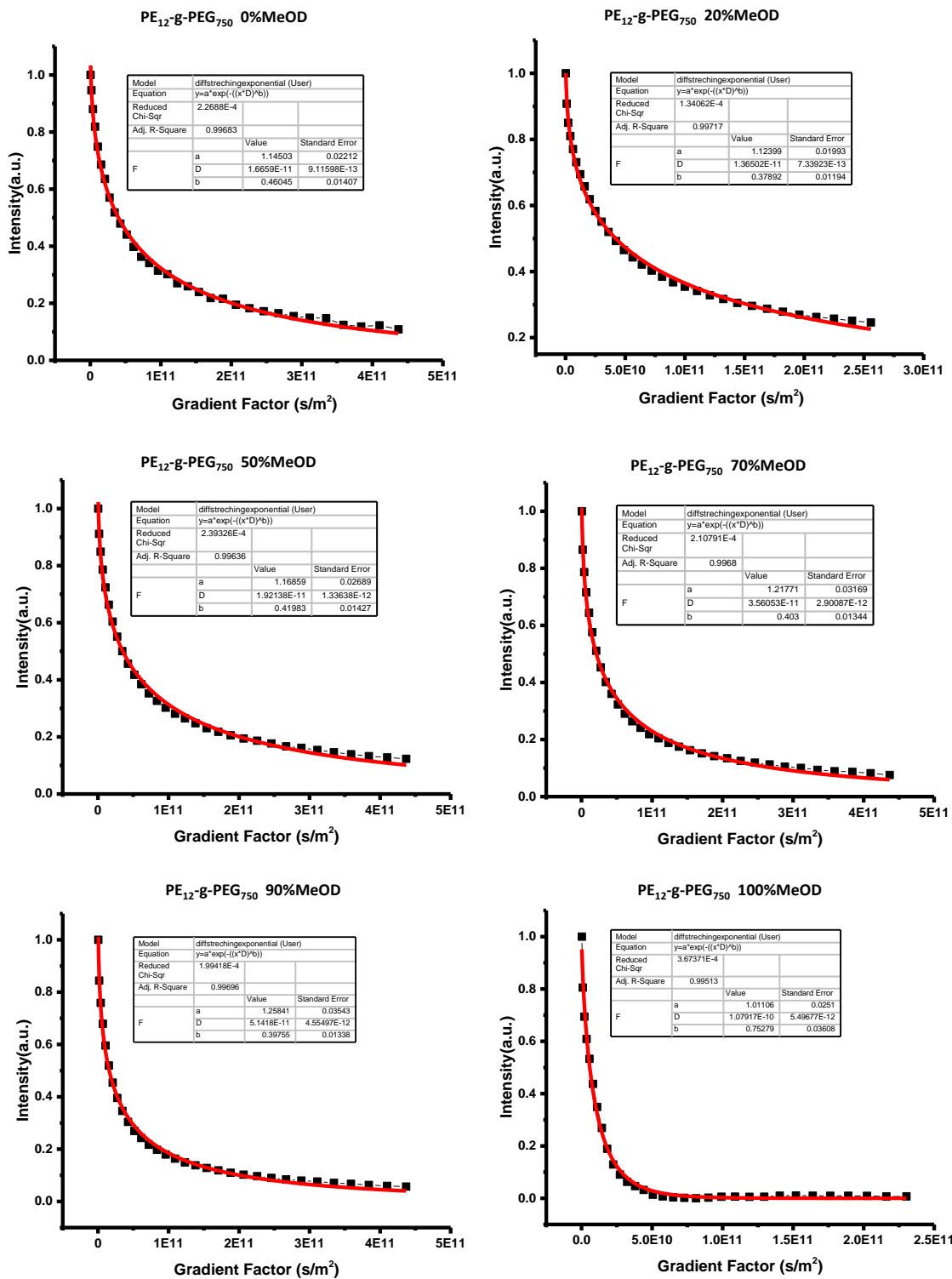
**Figure S6:** Stack plot of the  $^1\text{H}$  NMR spectra of the different PGAPs revealing the complete disappearance of the propargyl peaks after clicking and the appearance of the triazole ring protons.

PE<sub>12</sub>-g-PEG<sub>550</sub>



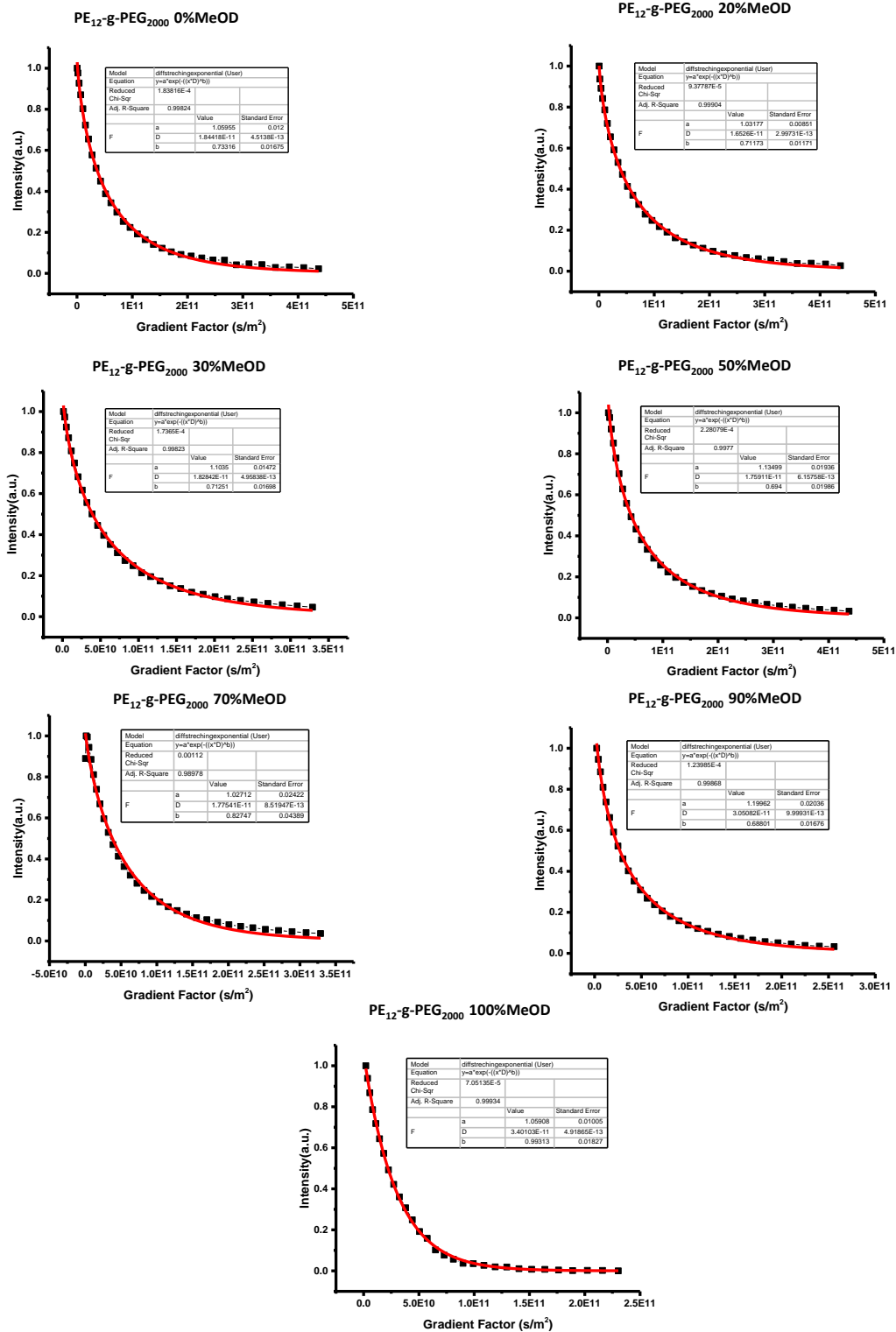
**Figure S7:** Plots of NMR spin echo attenuation intensity against gradient factor for PE<sub>12</sub>-g-PEG<sub>550</sub> were generated using equation 2, across various CDCl<sub>3</sub>-MeOD compositions, and modeled using a stretched exponential behavior.

PE<sub>12</sub>-g-PEG<sub>750</sub>



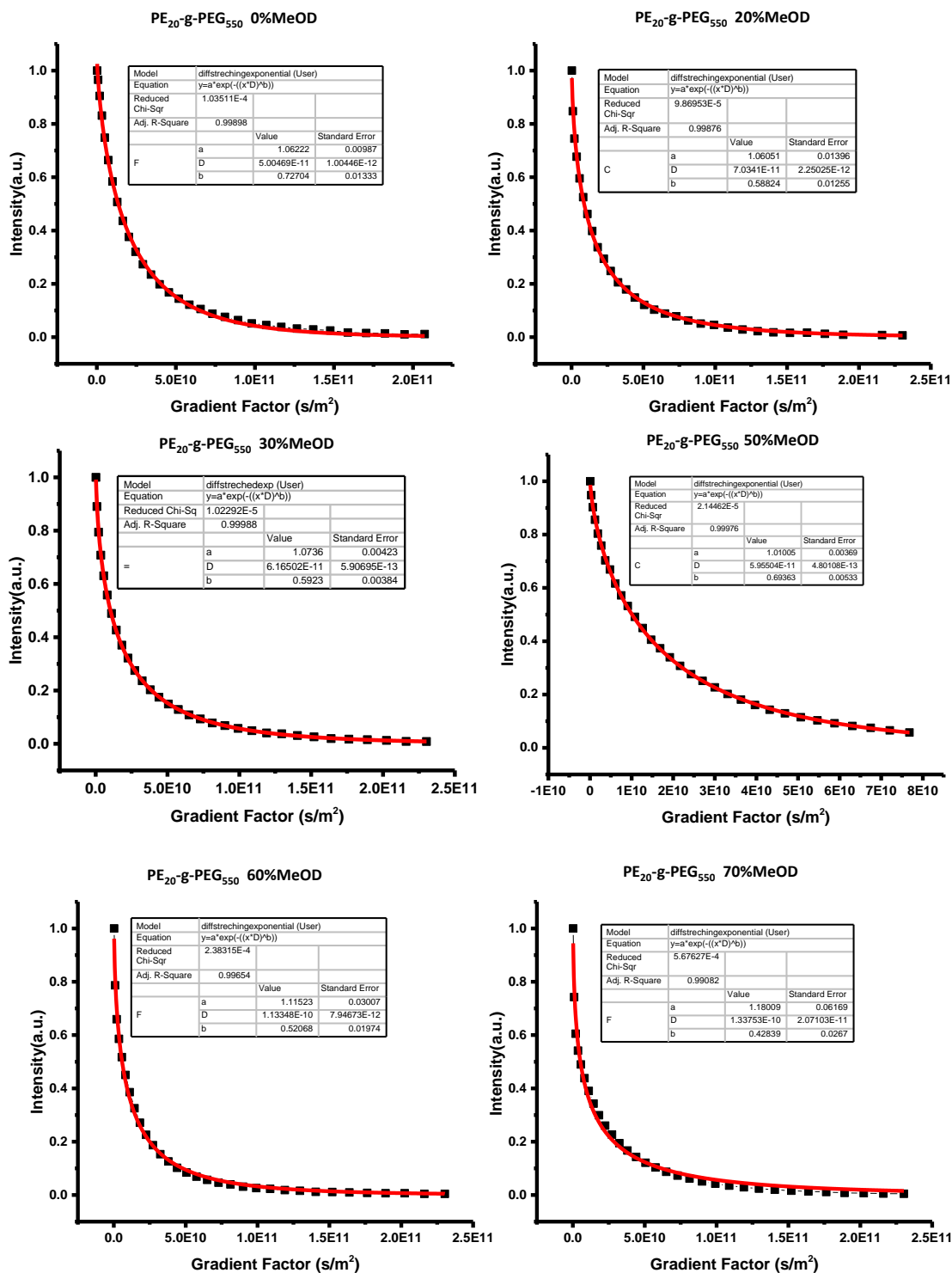
**Figure S8:** Plots of NMR spin echo attenuation intensity against gradient factor for PE<sub>12</sub>-g-PEG<sub>750</sub> were generated using equation 2, across various CDCl<sub>3</sub>-MeOD compositions, and modeled using a stretched exponential behavior.

PE<sub>12</sub>-g-PEG<sub>2000</sub>



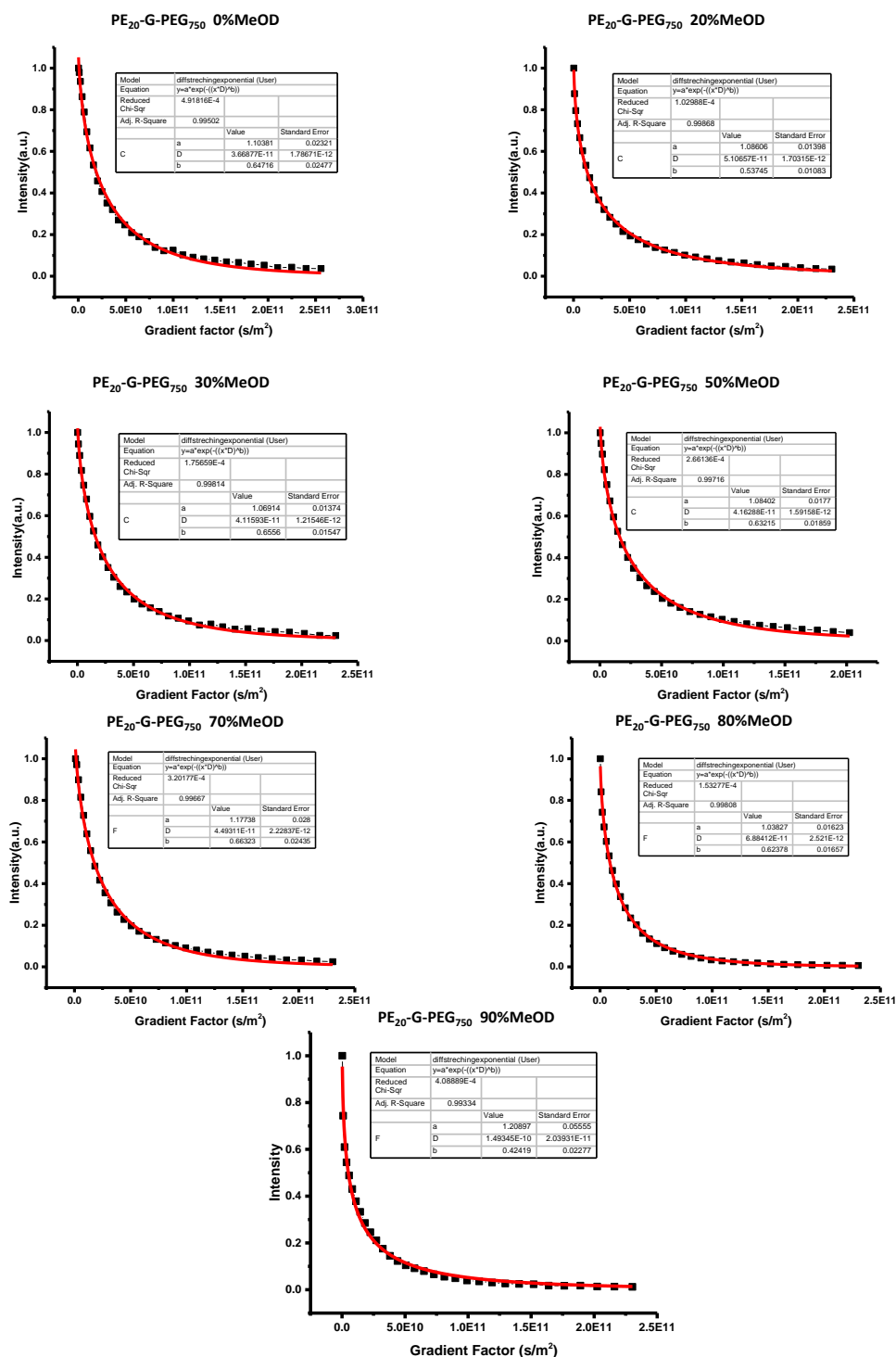
**Figure S9:** Plots of NMR spin echo attenuation intensity against gradient factor for PE<sub>12</sub>-g-PEG<sub>2000</sub> were generated using equation 2, across various CDCl<sub>3</sub>-MeOD compositions, and modeled using a stretched exponential behavior.

PE<sub>20</sub>-g-PEG<sub>550</sub>



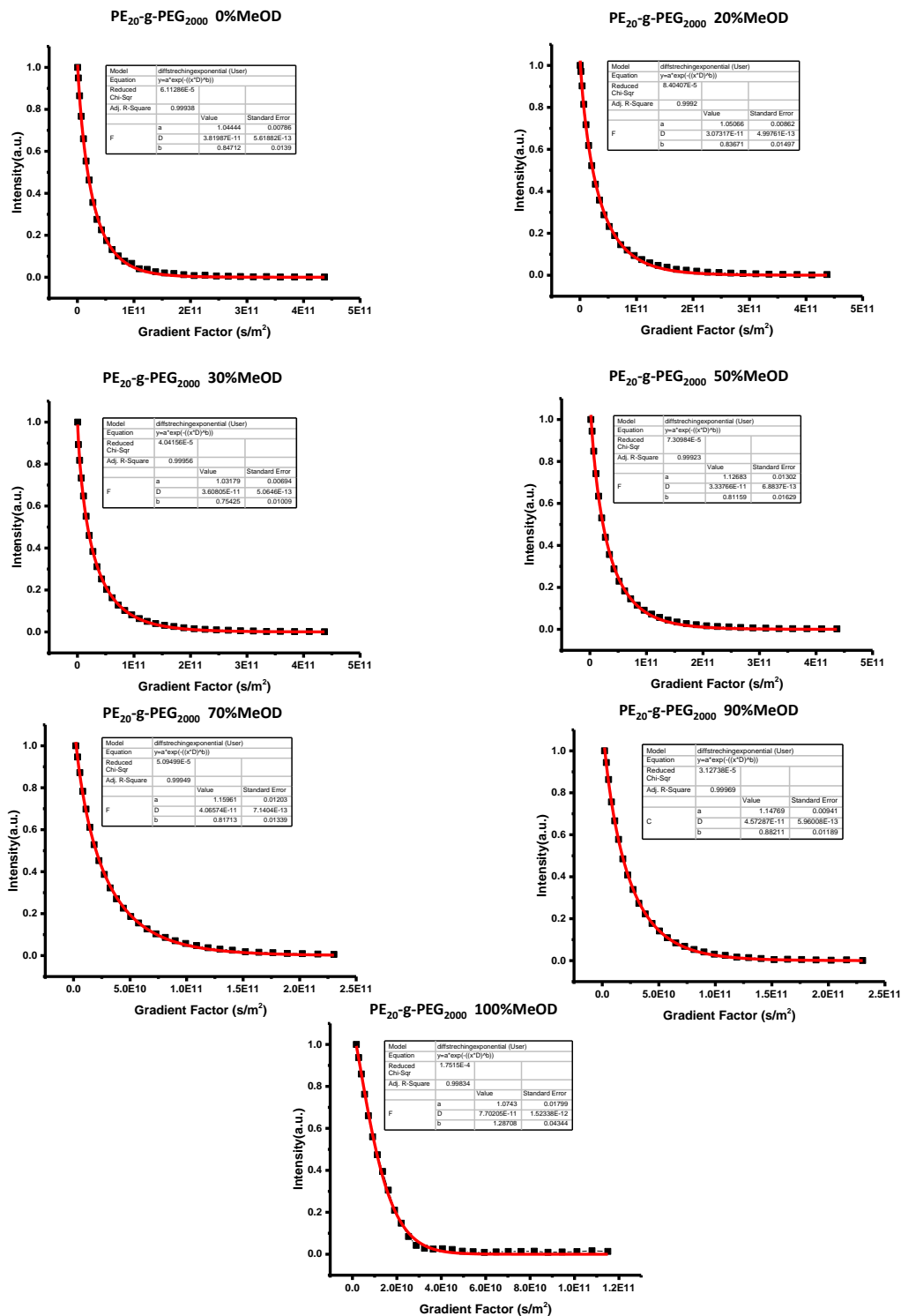
**Figure S10:** Plots of NMR spin echo attenuation intensity against gradient factor for PE<sub>20</sub>-g-PEG<sub>550</sub> were generated using equation 2, across various CDCl<sub>3</sub>-MeOD compositions, and modeled using a stretched exponential behavior.

PE<sub>20</sub>-g-PEG<sub>750</sub>



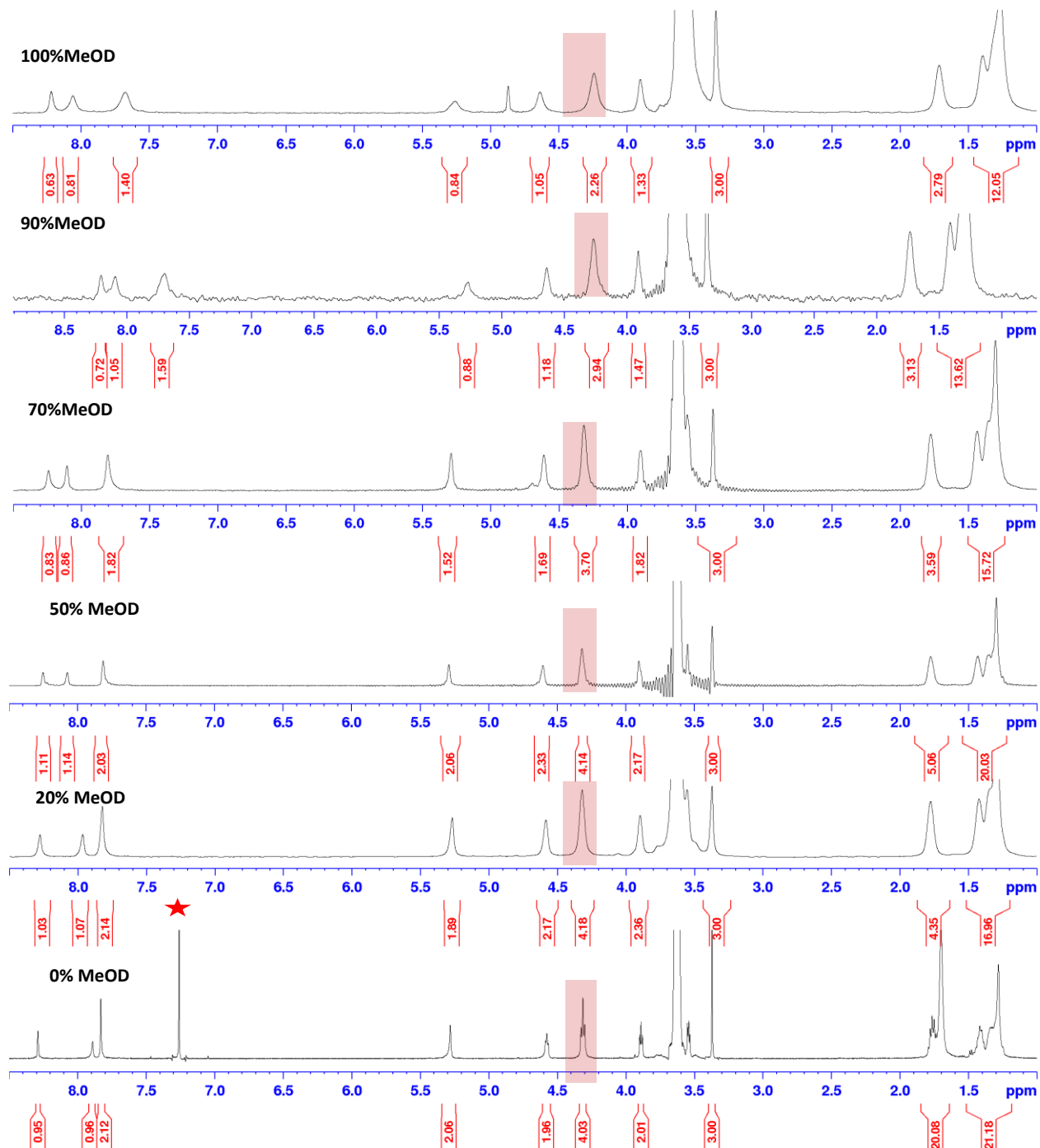
**Figure S11:** Plots of NMR spin echo attenuation intensity against gradient factor for PE<sub>20</sub>-g-PEG<sub>750</sub> were generated using equation 2, across various CDCl<sub>3</sub>-MeOD compositions, and modeled using a stretched exponential behavior.

PE<sub>20</sub>-g-PEG<sub>2000</sub>



**Figure S12:** Plots of NMR spin echo attenuation intensity against gradient factor for PE<sub>20</sub>-g-PEG<sub>2000</sub> were generated using equation 2, across various CDCl<sub>3</sub>-MeOD compositions, and modeled using a stretched exponential behavior.

# PE<sub>12</sub>-g-PEG<sub>550</sub>



**Figure S13:** Stack plot of <sup>1</sup>H NMR spectra of PE<sub>12</sub>-g-PEG<sub>550</sub> in different CDCl<sub>3</sub>-MeOD compositions. Spectra where the solvent peaks are not visible (all, except 0 % MeOD) were recorded using the PFG self-diffusion sequence, which suppresses the solvent peaks. ★ represents the CHCl<sub>3</sub> peak in the spectra.

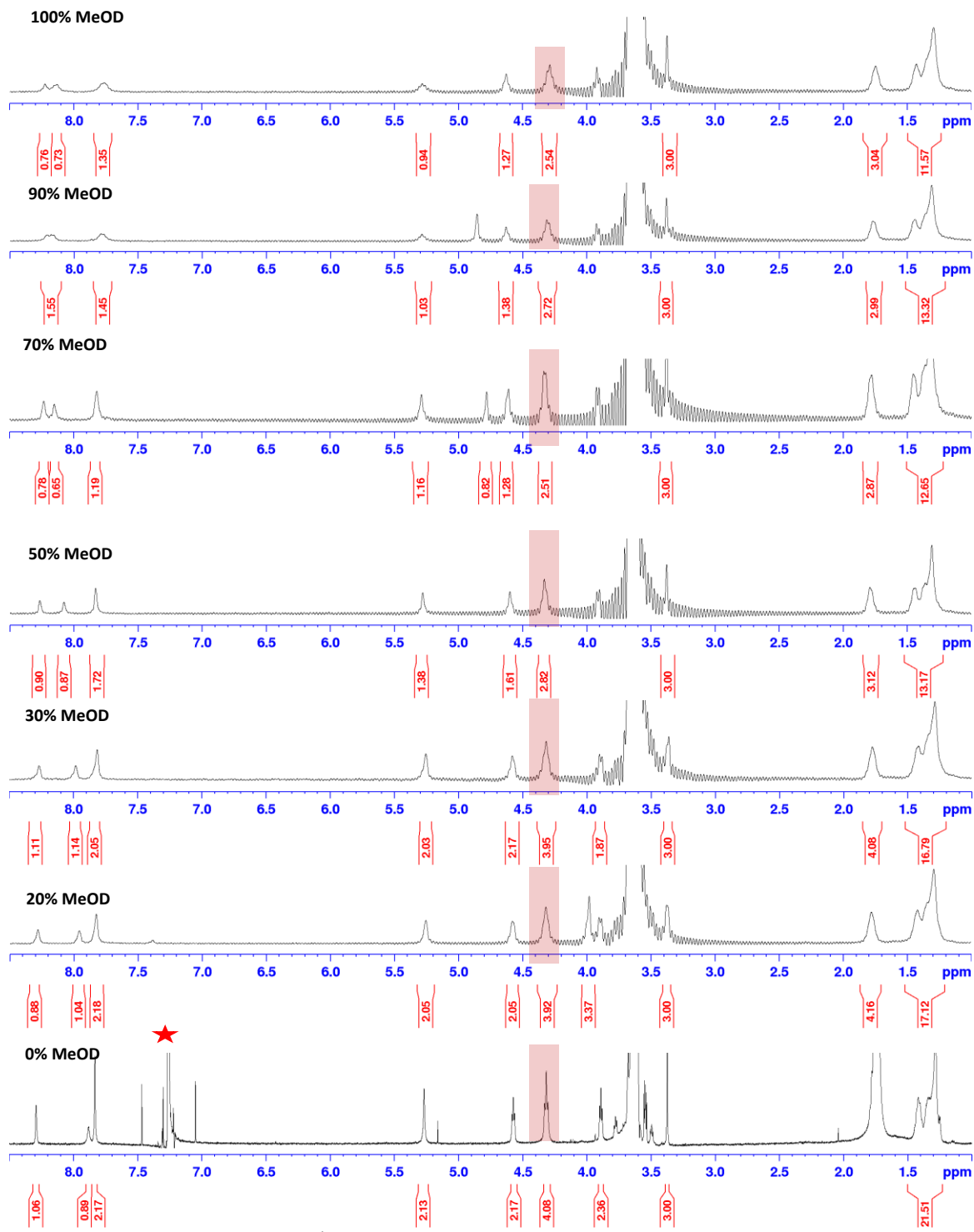


# PE<sub>12</sub>-g-PEG<sub>750</sub>



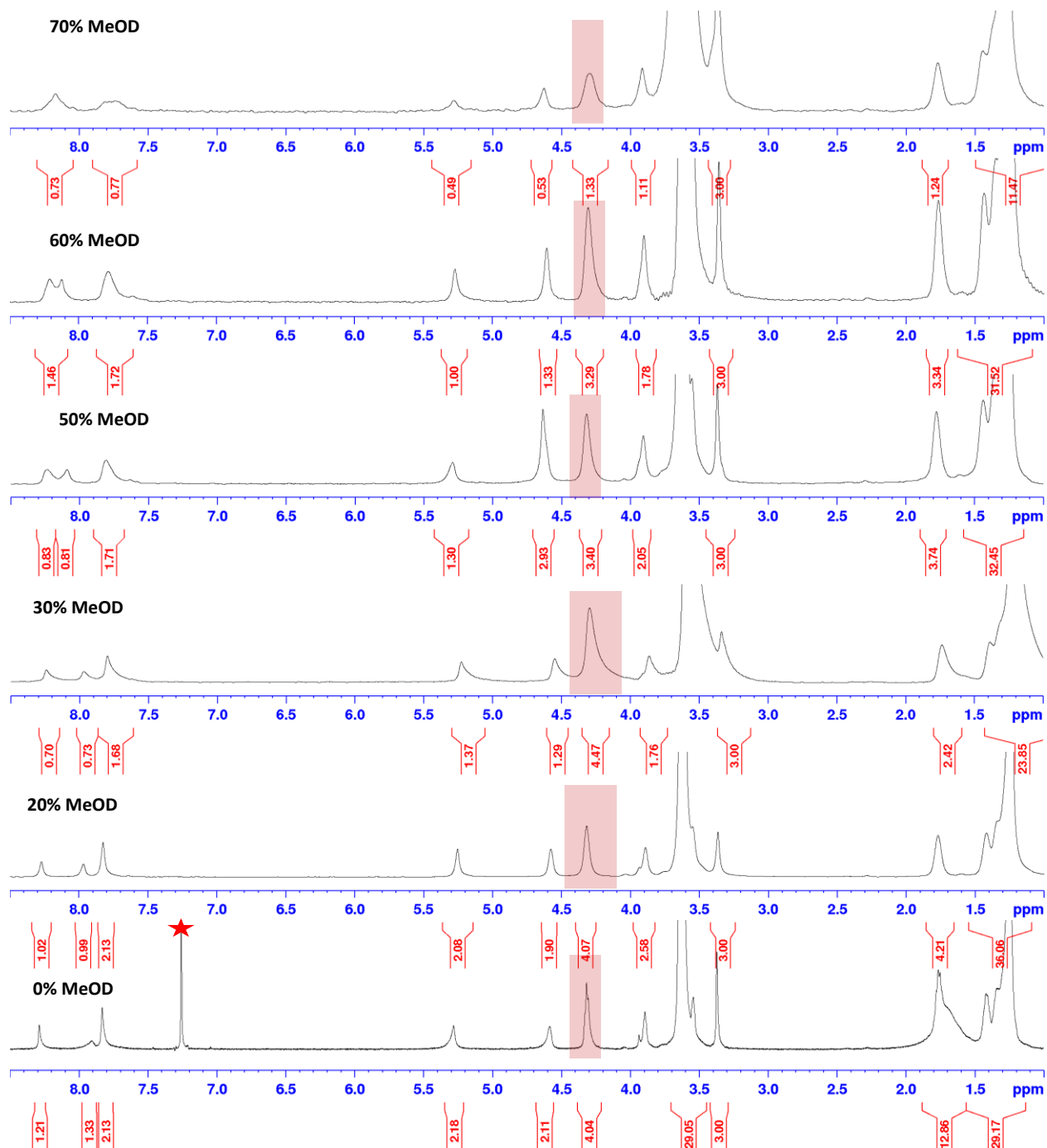
**Figure S14:** Stack plot of <sup>1</sup>H NMR spectra of PE<sub>12</sub>-g-PEG<sub>750</sub> in different CDCl<sub>3</sub>-MeOD compositions. Spectra where the solvent peaks are not visible (all, except 0 % MeOD) were recorded using the PFG self-diffusion sequence, which suppresses the solvent peaks. ★ represents the CHCl<sub>3</sub> peak in the spectra.

# PE<sub>12</sub>-g-PEG<sub>2000</sub>



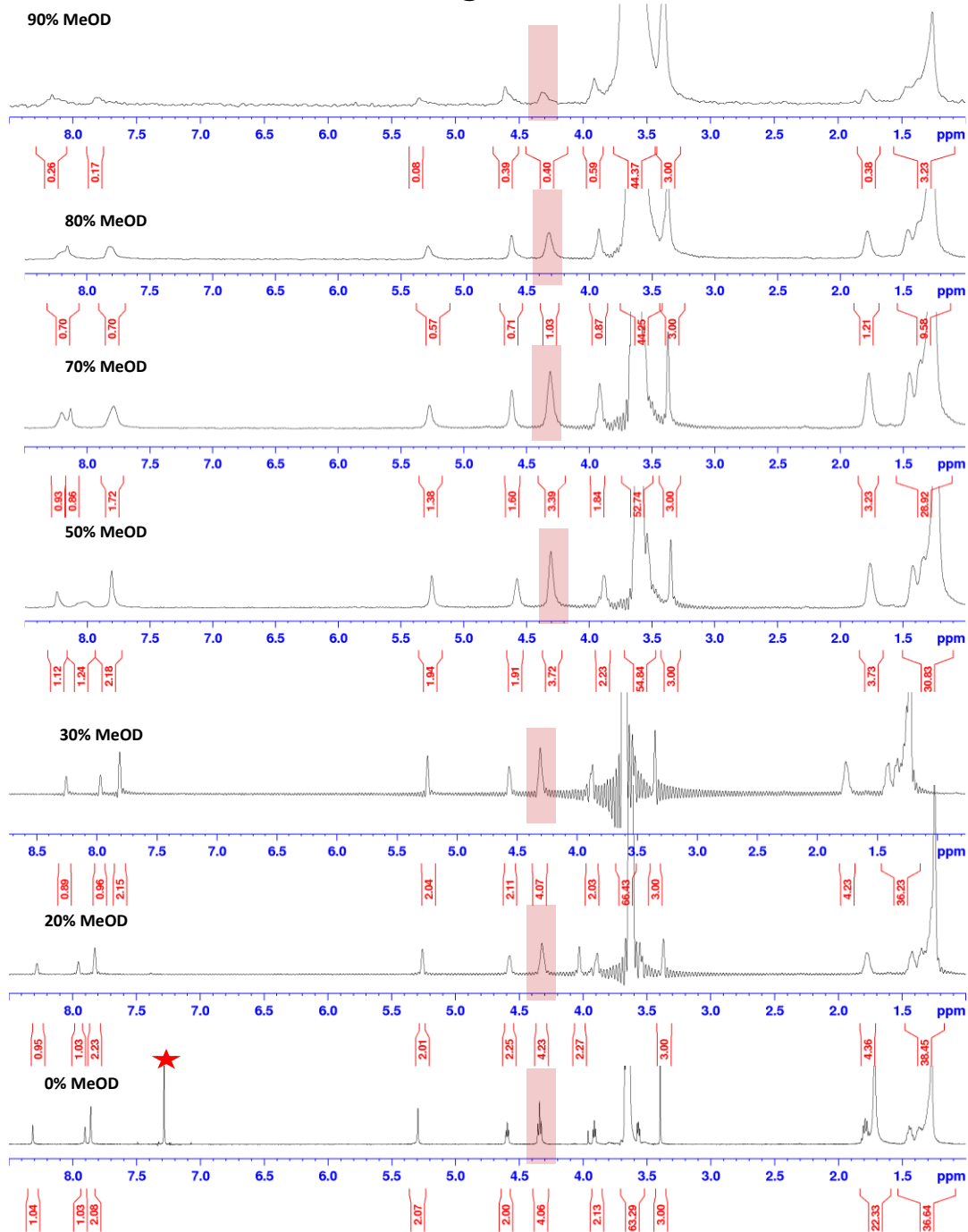
**Figure S15:** Stack plot of <sup>1</sup>H NMR spectra of PE<sub>12</sub>-g-PEG<sub>2000</sub> in different CDCl<sub>3</sub>-MeOD compositions. Spectra where the solvent peaks are not visible (all, except 0 % MeOD) were recorded using the PFG self-diffusion sequence, which suppresses the solvent peaks. ★ represents the CHCl<sub>3</sub> peak in the spectra.

# PE<sub>20</sub>-g-PEG<sub>550</sub>



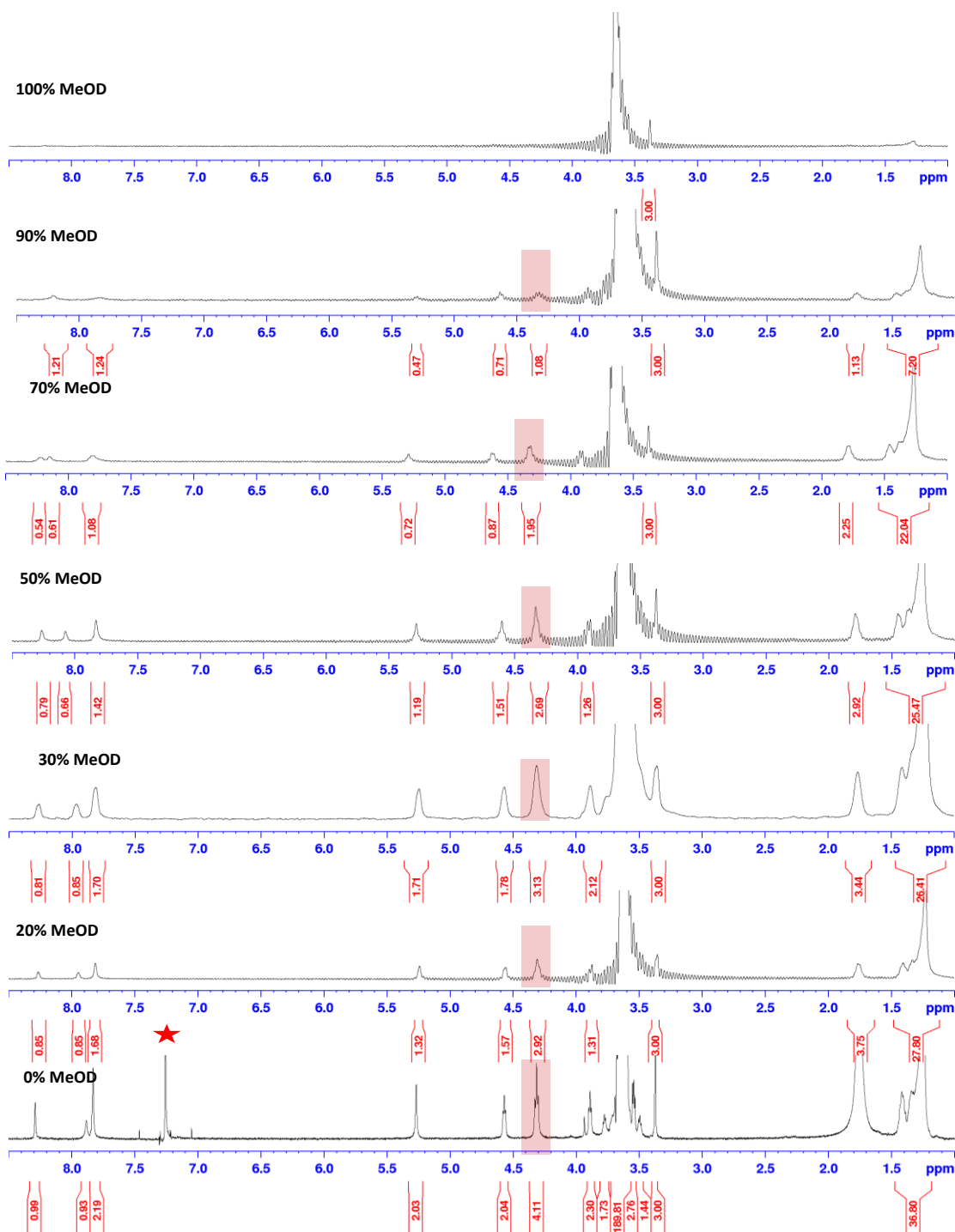
**Figure S16:** Stack plot of <sup>1</sup>H NMR spectra of PE<sub>20</sub>-g-PEG<sub>550</sub> in different CDCl<sub>3</sub>-MeOD compositions. Spectra where the solvent peaks are not visible (all, except 0 % MeOD) were recorded using the PFG self-diffusion sequence, which suppresses the solvent peaks. ★ represents the CHCl<sub>3</sub> peak in the spectra.

# PE<sub>20</sub>-g-PEG<sub>750</sub>

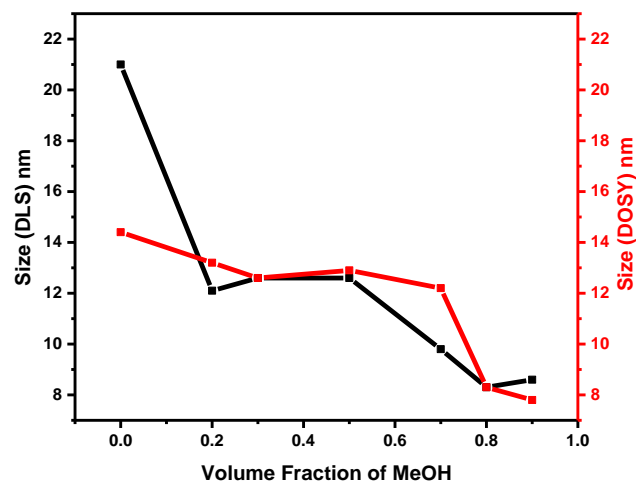


**Figure S17:** Stack plot of <sup>1</sup>H NMR spectra of PE<sub>20</sub>-g-PEG<sub>750</sub> in different CDCl<sub>3</sub>-MeOD compositions. Spectra where the solvent peaks are not visible (all, except 0, 20 and 30 % MeOD) were recorded using the PFG self-diffusion sequence, which suppresses the solvent peaks. ★ represents the CHCl<sub>3</sub> peak in the spectra.

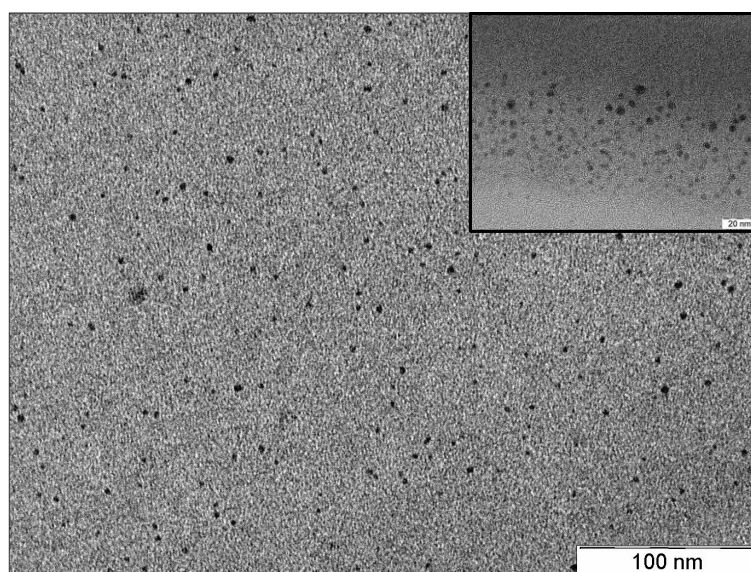
# PE<sub>20</sub>-g-PEG<sub>2000</sub>



**Figure S18:** Stack plot of <sup>1</sup>H NMR spectra of PE<sub>20</sub>-g-PEG<sub>2000</sub> in different CDCl<sub>3</sub>-MeOD compositions. Spectra where the solvent peaks are not visible (all, except 0% MeOD) were recorded using the PFG self-diffusion sequence, which suppresses the solvent peaks. ★ represents the CHCl<sub>3</sub> peak in the spectra.



**Figure S19:** Comparison of Size from DLS Data with DOSY Data for PE<sub>20</sub>-g-PEG<sub>750</sub> at various volume fractions of MeOH.



**Figure S20:** TEM image of PE<sub>20</sub>-g-PEG<sub>750</sub> taken in a solution of chloroform-methanol (10:90, v/v) at a concentration of 1 mg/mL; it shows fairly uniform SCNPs. Inset shows an image at higher magnification which shows the size distribution more clearly; the average size of the particle was estimated using Image-J and was found to be ~5 nm.