Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting Information

Orthogonally Clickable Hyperbranched Polymers: Effect of Reactant Size and Polarity on Core-Functionalization of Peripherally *Jacketed* HBPs

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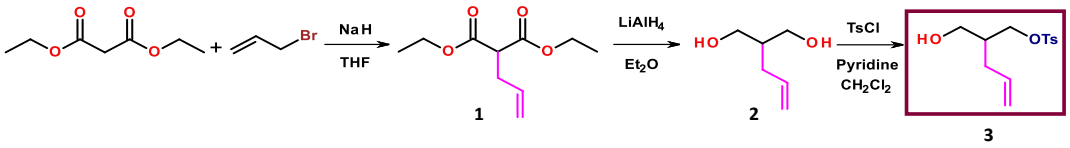
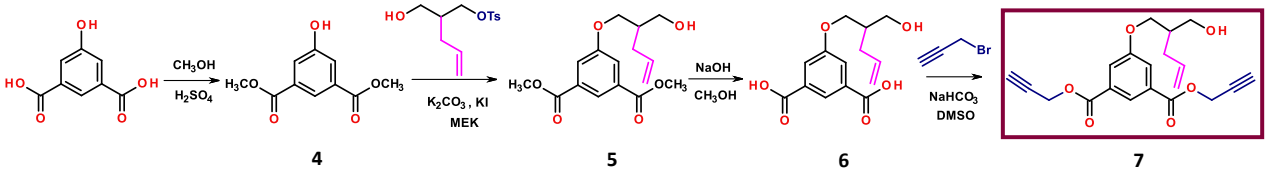
Experimental Section

Synthesis



Scheme S1. *Preparation of clickable allyl group bearing spacer which is used to prepare the monomer.*



Scheme S2. *Preparation of allyl and propargyl groups bearing AB_2 monomer.*

Diethyl 2-allylmalonate (1)

NaH (5 g, 60 wt. % in mineral oil, 125 mmol) was taken in 100 mL of dry THF and diethylmalonate (DEM) (40g, 250 mmol) was added drop wise to it at 0 ^{o}C. The reaction mixture was stirred for 1 h at 0 ^{o}C. To this reaction mixture, allyl bromide (15.1 g, 125 mmol) was added drop wise at 0 ^{o}C and the reaction mixture was stirred for 36 h at room temperature. The reaction mixture was quenched with aq. NH_4Cl and the solvent was removed using rotary evaporator. To this residue, 60 mL of water was added; it was then extracted with ethyl acetate and the combined organic extract was concentrated under reduced pressure. The obtained crude mixture had both DEM and mono-allyl DEM. The mono-allyl DEM was separated from DEM by fractional distillation under reduced pressure. The mono-allyl DEM was a colorless viscous liquid, and was obtained in 52 % yield with respect to allyl bromide.

^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 1.25 (t, 6H, -OCH_2**CH_3**); 2.61-2.65 (m, 2H, CH_2CH**CH_2**CH-); 3.41 (t, 1H, CH_2CHCH_2**CH**-); 4.16-4.21 (q, -O**CH_2**CH_3); 5.03-5.13 (m, 2H, **CH_2**$CHCH_2CH$-); 5.72-5.82 (m, 1H, CH_2**CH**CH_2CH-).

2-Allylpropane-1, 3-diol (2)

Lithium aluminium hydride (3.8 g, 100 mmol) was added to dry diethyl ether under ice-cold condition. Diethyl 2-allylmalonate (10 g, 50 mmol) was taken in dry diethyl ether and it was added to the reaction mixture in drop wise manner with continuous stirring and it was continued for 24 h at room temperature. The unreacted $LiAlH_4$ was quenched with 10 % NaOH solution; once quenching was complete (hydrogen evolution ceased), the white viscous solution was filtered and the residue was washed with diethyl ether. The obtained filtrate was concentrated under reduced pressure and distilled in Kugelrohr at 125 ^oC under high vacuum. The product was a colorless viscous liquid. Yield = 65 %.

^1H NMR (400 MHz, $CDCl_3$, δ ppm): 1.78-1.87 (m, 1H, CH_2CHCH_2**CH**-); 2.02-2.06 (m, 2H, CH_2CH**CH_2**CH-); 3.12 (t (broad), 2H, **HO**CH_2CH-); 3.60-3.81 (m, 4H, HO**CH_2**CH-); 5.0-5.08 (m, 2H, **CH_2**$CHCH_2CH$-); 5.72-5.82 (m, 1H, CH_2**CH**CH_2CH-).

2-(Hydroxymethyl) pent-4-en-1-yl 4-methylbenzenesulfonate (3)

2-Allylpropane-1,3-diol (4 g, 34.48 mmol), pyridine (2.99g, 37.92 mmol) were taken in dry DCM (10 mL) and the solution was cooled to 0 ^oC. Tosyl chloride (6.57 g, 34.48 mmol) was dissolved in dry DCM (10 mL) and it was added drop wise to the ice-cold solution. The reaction mixture was allowed to come to room temperature and the stirring was continued for 72 h. The reaction mixture was diluted with DCM (40 mL), it was washed with 0.1M aq. HCl (50 mL). The resultant DCM layer was separated, passed through anhydrous Na_2SO_4 and it was concentrated under reduced pressure. The obtained crude product had the mixture of mono and di tosylated products. Finally, the required mono tosylated product was obtained by column chromatography where pet ether and ethyl acetate (75:25) was used as the eluent. Yield = 30 % (pure mono tosylated product).

^1H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.71 (s, 1H, **HO**CH_2CH-); 1.90-1.94 (m, 1H, CH_2CHCH_2**CH**-); 2.04-2.10 (m, 2H, CH_2CH**CH_2**CH-); 2.45 (s, 3H, -Ar**CH_3**); 3.55-3.66 (m, 2H, HO**CH_2**CH-); 4.01-4.12 (m, 2H, HO**CH_2**CH-); 4.98-5.03 (m, 2H, **CH_2**$CHCH_2CH$-); 5.62-5.72 (m, 1H, CH_2**CH**CH_2CH-); 7.34-7.36 (d, 2H, -**Ar**CH_3); 7.78-7.80 (d, 2H, -O_2S**Ar**CH_3).

Dimethyl 5-hydroxyisophthalate (4)

5-Hydroxyisophthalic acid (20 g, 109.9 mmol) was taken in 250 mL dry methanol and the conc. H_2SO_4 (10 mL) was added to it. The solution was refluxed for 12 h and the solvent was removed under reduced pressure. Water was added to the obtained residue and it was extracted with ethyl acetate. The organic layer was washed with 10% aq. $NaHCO_3$, water, brine, and dried over anhydrous Na_2SO_4. It was concentrated under reduced pressure to get the product as a white solid. Yield = 96 %, m.p. 161-164^oC.

^1H NMR (400 MHz, $CDCl_3$, δ ppm): 3.95 (s, 6H, -COO**CH_3**); 6.52 (s, 1H, -Ar**OH)**; 7.78 (d, 2H, **ArH**); 8.25 (s, 1H, **ArH**).

Dimethyl 5-((2-(hydroxymethyl) pent-4-en-1-yl) oxy) isopthalate (5)

The compound **(3)** (2 g, 7.41 mmol), K_2CO_3 (3.7 g, 26.94 mmol) and catalytic amount of KI were taken in 50 mL of dry acetonitrile. The mixture was degassed for 10 min. Dimethyl 5-hydroxyisophthalate (1.4 g, 6.73 mmol) was added to the reaction mixture. The reaction mixture was refluxed for 72 h under nitrogen atmosphere. Then the solvent was removed under reduced pressure; water was added to the obtained residue and it was extracted with $CHCl_3$ and extract was washed with brine solution. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to yield the product as brownish ash color solid. Without further purification, we proceeded to next step. Yield = 80 %.

^1H NMR (400 MHz, $CDCl_3$, δ ppm): 2.12-2.20 (m, 1H, CH_2CHCH_2**CH**-); 2.28-2.31 (t, 2H, CH_2CH**CH_2**CH-); 3.77-3.86 (m, 2H, HO**CH_2**CH-); 3.97 (s, 6H, -COO**CH_3**); 4.12 (d, 2H, ArO**CH_2**CH-); 5.10-5.16 (m, 2H, **CH_2**$CHCH_2CH$-); 5.82-5.92 (m, 1H, CH_2**CH**CH_2CH-); 7.78-7.79 (d, 2H, -**ArH**); 8.30 (s, 1H, -**ArH**).

5-((2-(hydroxymethyl) pent-4-en-1-yl) oxy) isophthalic acid (6)

Compound **(5)** (1.5 g, 4.88 mmol), NaOH (0.78 g, 19.54 mmol) were taken in methanol (20 mL) and stirred for 48 h at 60 ^oC. Then, the methanol was removed under reduced pressure, the obtained residue was dissolved in small amount of water and acidified with dil. HCl to get a white precipitate. The precipitate was filtered and dried to get the product as a white crystalline solid. Without further purification, we proceeded to next step. Yield = 75 %.

^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 1.93-1.99 (m, 1H, CH_2CHCH_2**CH**-); 2.16-2.20 (t, 2H, CH_2CH**CH_2**CH-); 3.15-3.20 (m, 2H, HO**CH_2**CH-); 3.97-4.07 (m, 2H, -ArO**CH_2**CH-); 4.68 (s, 1H, **HO**CH_2CH-); 5.00-5.08 (m, 2H, **CH_2**$CHCH_2CH$-); 5.80-5.91 (m, 1H, CH_2**CH**CH_2CH-); 7.64 (d, 2H, -**ArH**); 8.06 (s, 1H, -**ArH**).

PEG 350 monomethyl ether tosylate (8)

PEG 350 monomethyl ether (15 g, 42.8 mmol) was taken in THF. NaOH (5.1 g, 128.57 mmol) in water (7 mL) was added to it and the solution was cooled to 0 ^oC. Tosyl chloride (12.2 g, 64.28 mmol) in THF was added dropwise to the ice-cold solution and stirred for 12 h. Then the organic layer was separated and the water layer was extracted with DCM. The combined organic layers were washed with brine and passed through Na_2SO_4. The solvent was evaporated under reduced pressure to yield the product as a light yellow viscous liquid. Yield = 85 %.

^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 2.42 (s, 3H, -Ar**CH_3**); 3.34 (s, 3H, -O**CH_3**); 3.50-3.71 (CH_2 s of PEG skeleton); 4.11-4.14 (t, 2H, -**CH_2**OSO_2ArCH_3); 7.30 (d, 2H, -OSO_2**ArH**CH_3); 7.75(t, 2H, -OSO_2**ArH**CH_3).

TEG monomethyl ether tosylate (9) was prepared via the same procedure as compound 8.

PEG 350 monomethyl ether azide (10)

PEG 350 monomethyl ether mono tosylate (3 g, 5.95 mmol), NaN_3 (1.54 g, 23.8 mmol) were dissolved in acetonitrile and heated at 65 ^oC for 2 days with stirring under nitrogen atmosphere. The solvent was evaporated under reduced pressure and water was added to it. The water layer was extracted with DCM and it was concentrated under reduced pressure to yield the product as a light yellow viscous liquid. Yield = 88%.

^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 3.34 (t, 3H, -CH_2O**CH_3**); 3.52-3.67 (-CH_2**CH_2**N_3 and CH_2 s of PEG skeleton).

PEG 350 monomethyl ether thiol (11)

PEG 350 monomethyl ether mono tosylate (6 g, 11.88 mmol), thiourea (2.7 g, 35.64 mmol) were dissolved in absolute ethanol and refluxed for 24 h. Then the reaction mixture was cooled to room temperature and NaOH (2N) solution was added to it until the solution become basic. The reaction mixture was refluxed for 36 h under nitrogen atmosphere and then acidified with dil. HCl

(2N). The solvent was evaporated using pump at room temperature. Water (10 mL) was added to it and extracted with EtOAc. Then the solvent was removed under reduced pressure, it was again extracted with diethyl ether and filtered to remove the sodium tosylate. Then, it was washed with brine solution, passed through Na_2SO_4 and concentrated under reduced pressure to get the product as a light yellow viscous liquid. Yield = 56%.

^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 1.57 (t, 1H, -CH_2CH_2**SH**); 2.67(q, 2H, -CH_2**CH_2**SH); 3.34 (s, 3H, -CH_2CH_2O**CH_3**); 3.51-3.71 (CH_2 s of PEG skeleton).

The other thiols like **TEG monomethyl ether thiol (12)** (55 %), **Docosyl thiol (13)** (61 %) were prepared via the same procedure as compound 11.

Docosyl tosylate (14), Docosyl azide (15) were prepared as shown in reference R1.

Reference R1: Samuel, A. Z.; Ramakrishnan. S. *Macromolecules* **2012**, *45*, 2348.

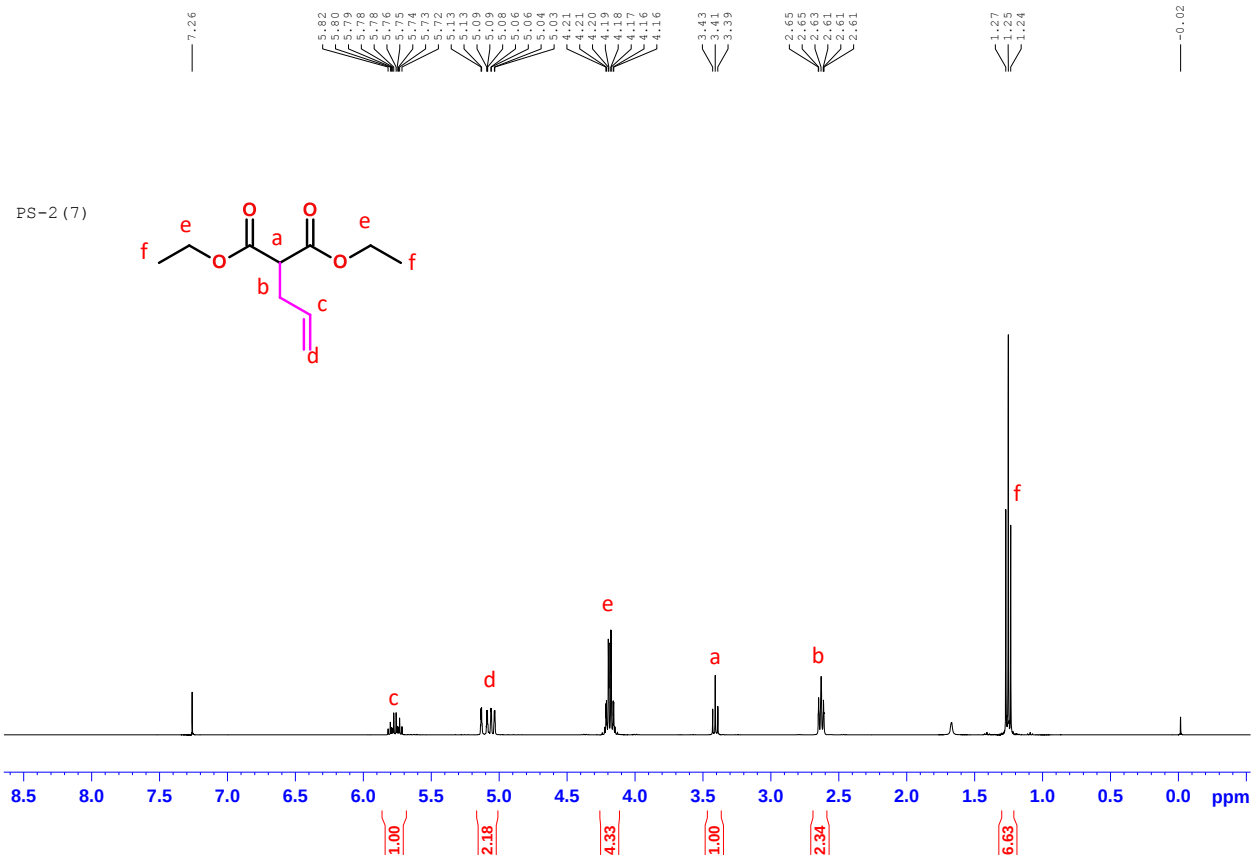


Figure S1: ^{1}H-NMR spectrum (in $CDCl_3$) of diethyl 2-allylmalonate.

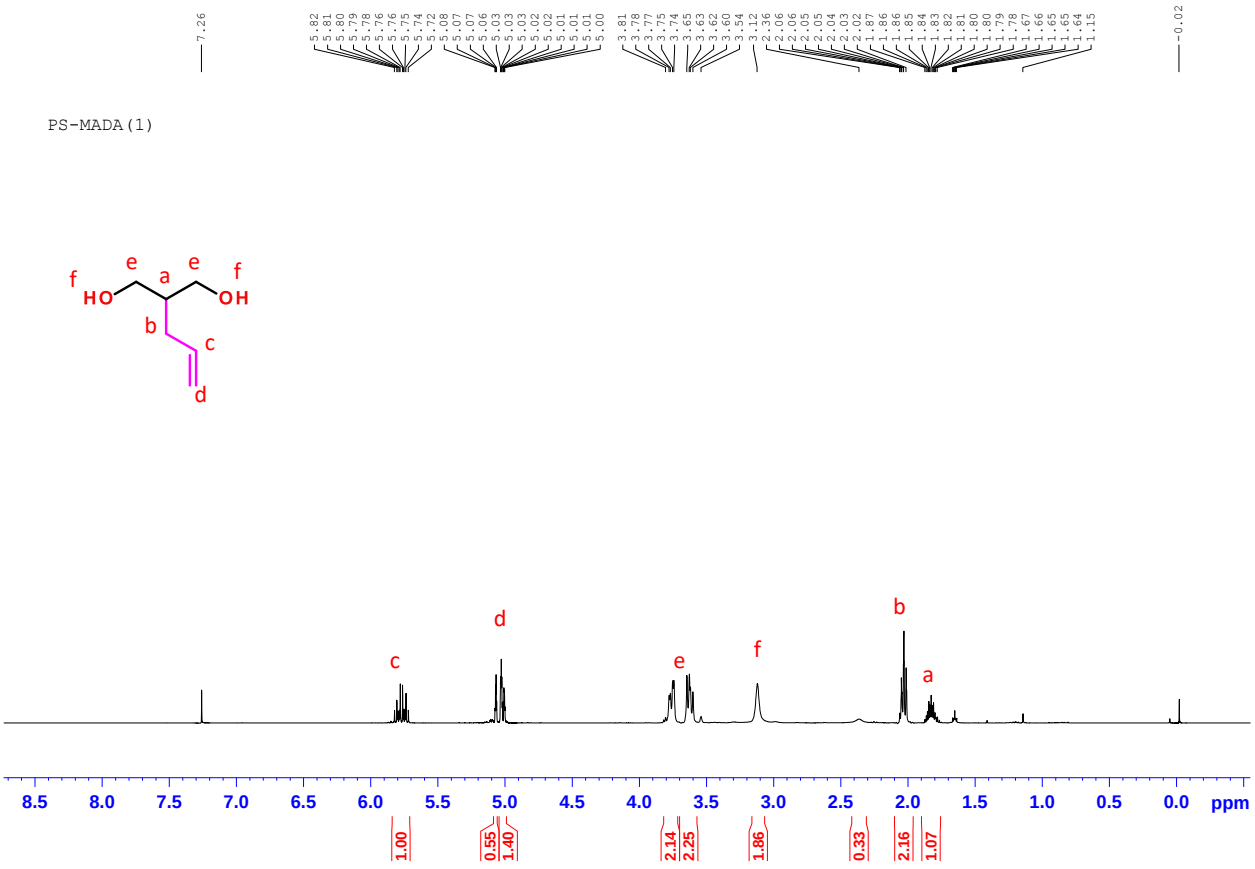


Figure S2: ^{1}H-NMR spectrum (in $CDCl_3$) of 2-allylpropane-1,3-diol.

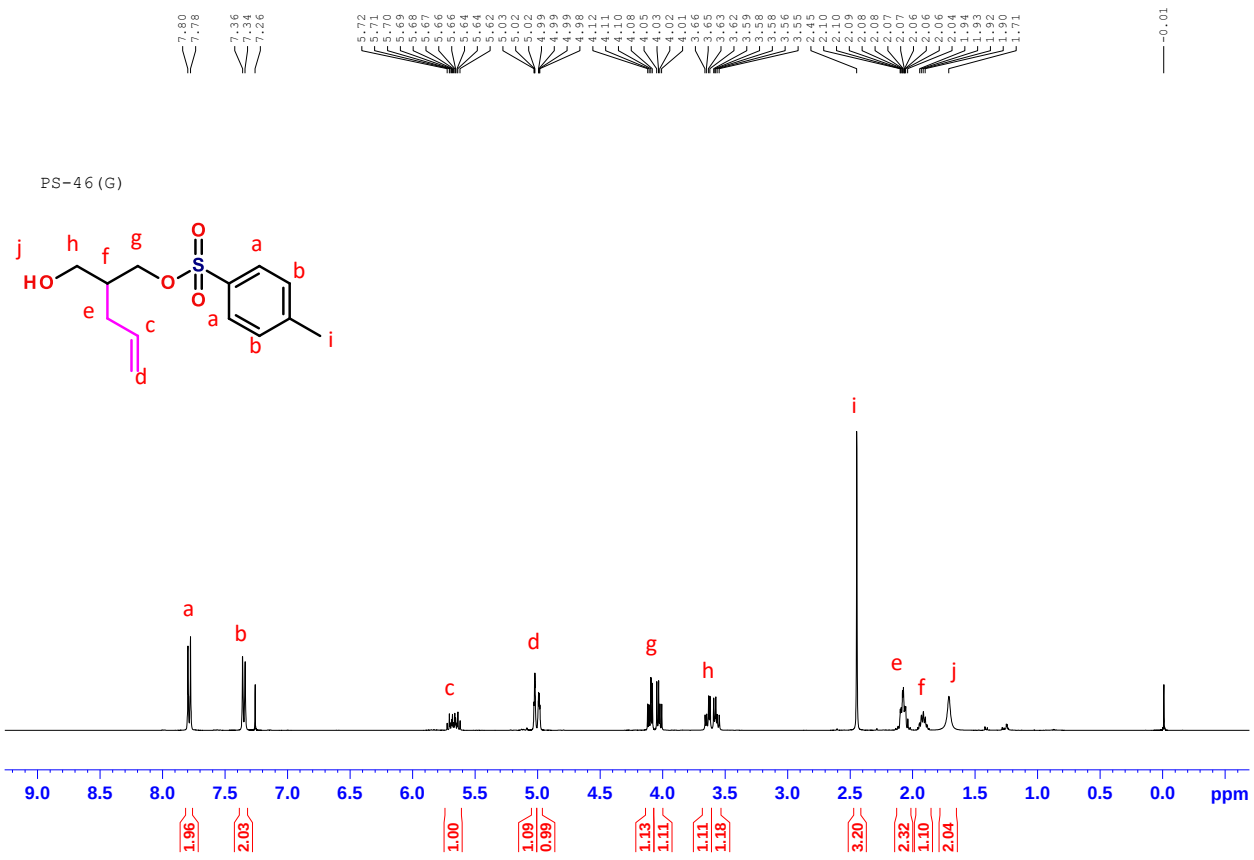


Figure S3: ^{1}H-NMR spectrum (in $CDCl_3$) of 2-(hydroxymethyl) pent-4-en-1-yl 4-methylbenzenesulfonate.

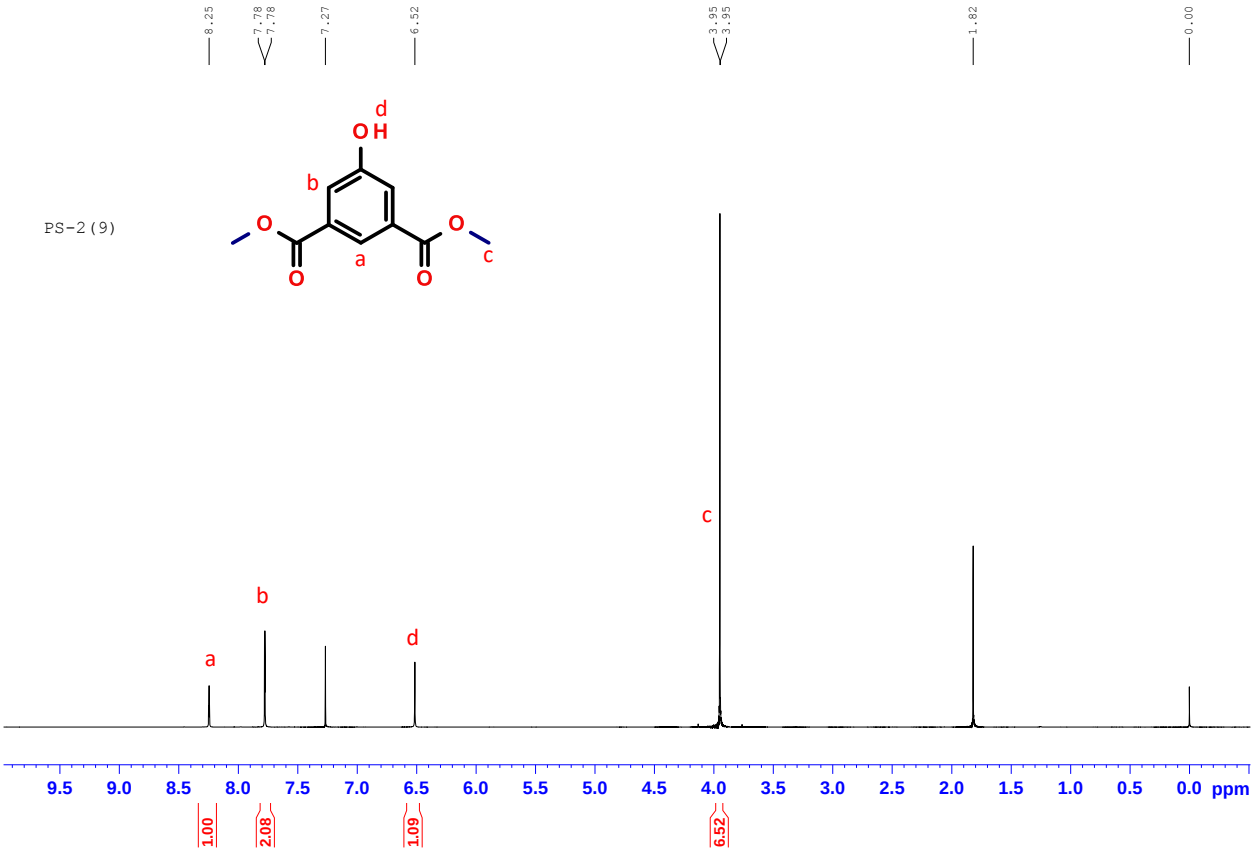


Figure S4: ^{1}H-NMR spectrum (in $CDCl_3$) of dimethyl 5-hydroxyisophthalate.

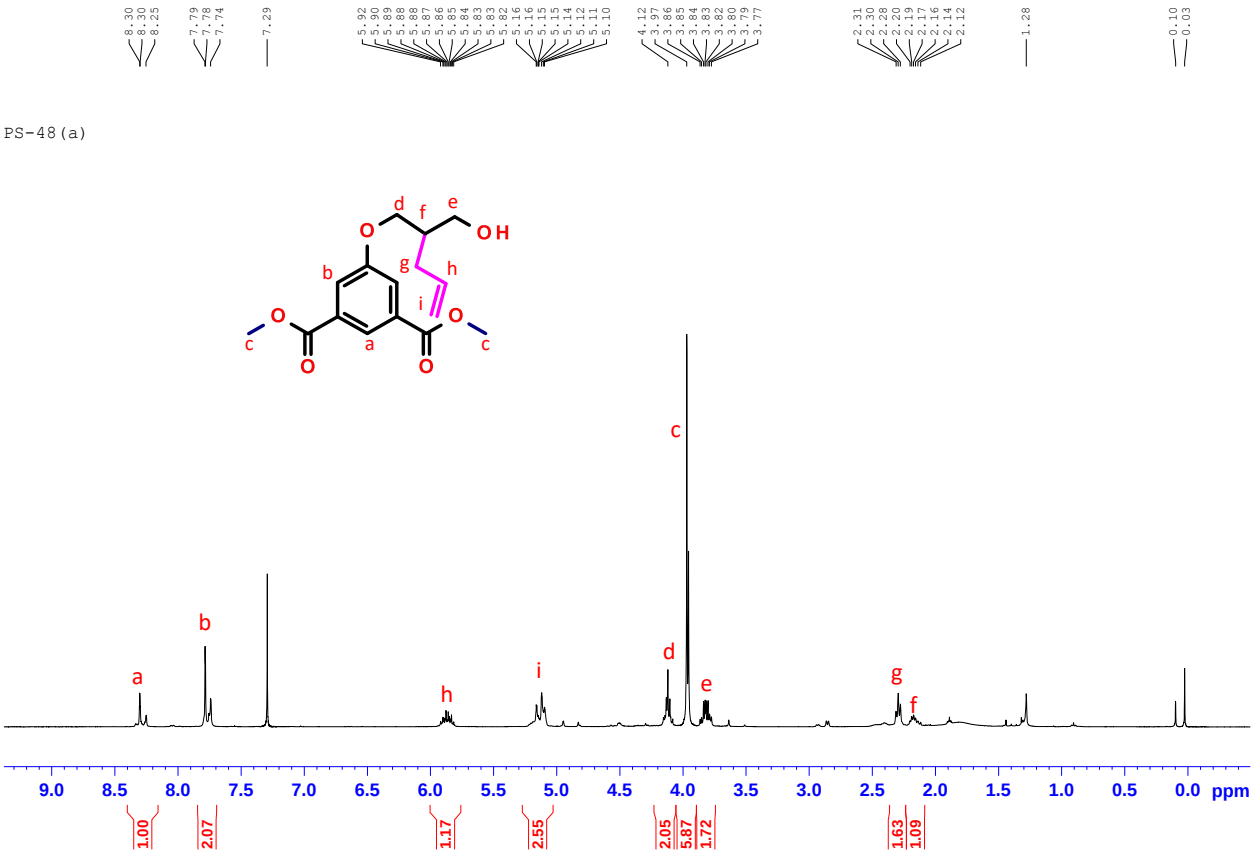


Figure S5: ^{1}H-NMR spectrum of (in $CDCl_3$) dimethyl 5-((2-(hydroxymethyl)pent-4-en-1-yl)oxy) isopthalate.

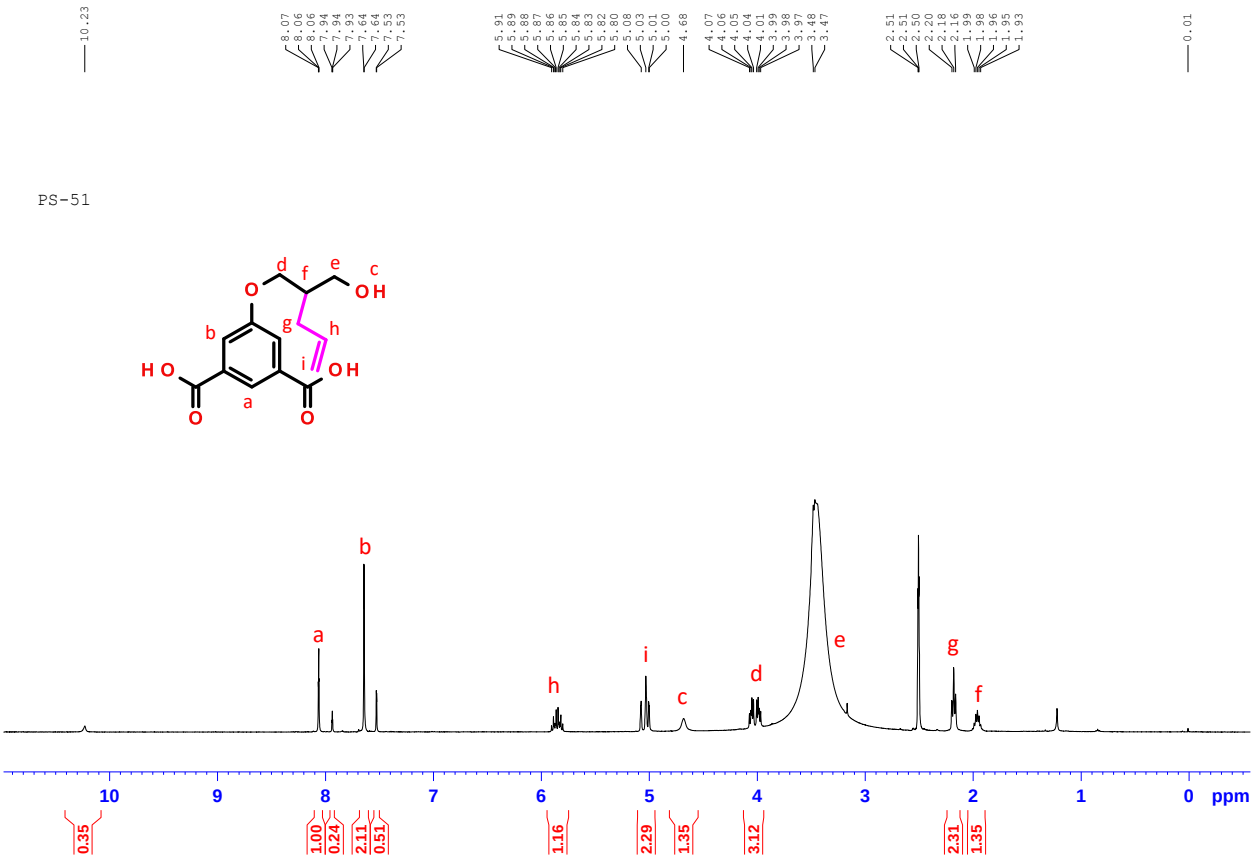


Figure S6: ^{1}H-NMR spectrum (in DMSO-d_6) of 5-((2-(hydroxymethyl) pent-4-en-1-yl) oxy) isophthalic acid.

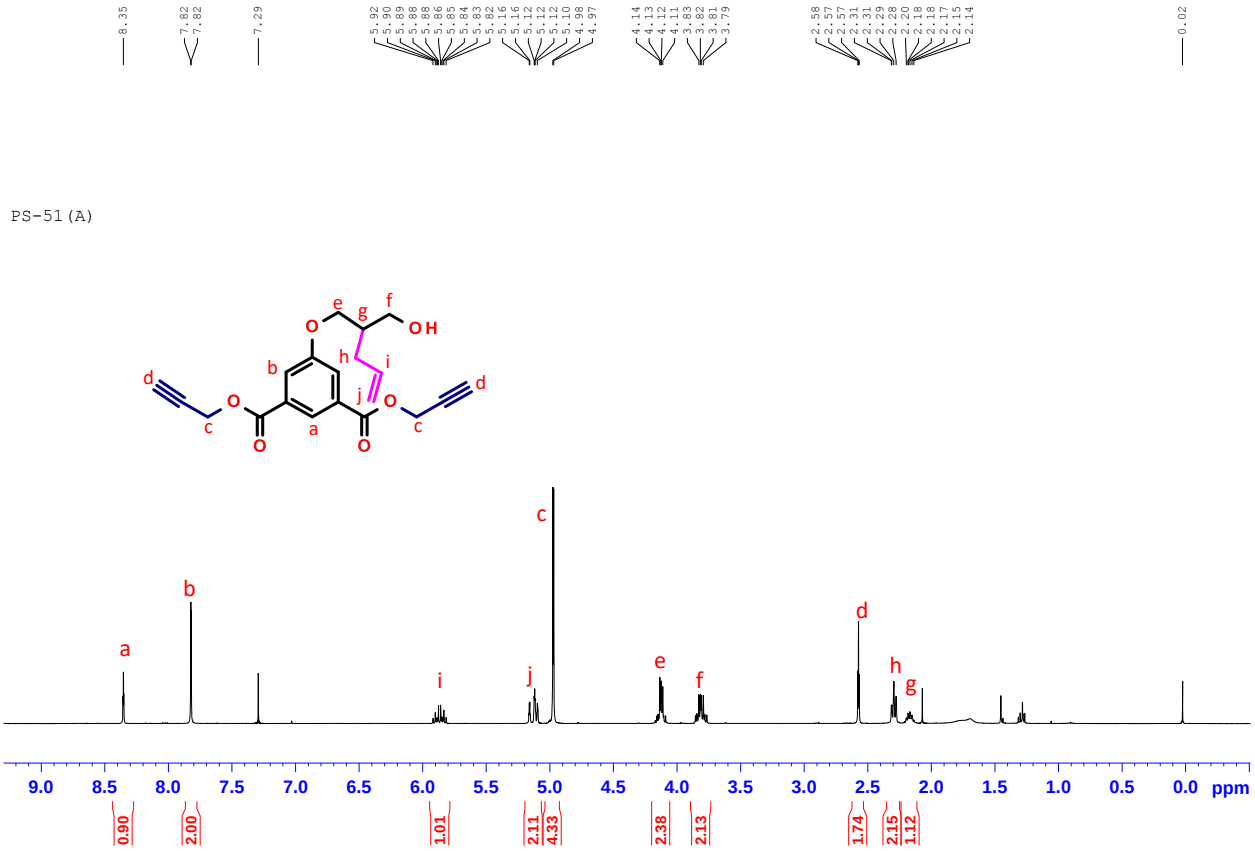


Figure S7: ^{1}H-NMR spectrum (in $CDCl_3$) of di(prop-2-yn-1-yl) 5-((2-(hydroxymethyl)pent-4-en-1-yl)oxy) isophthalate (AB_2 type monomer).

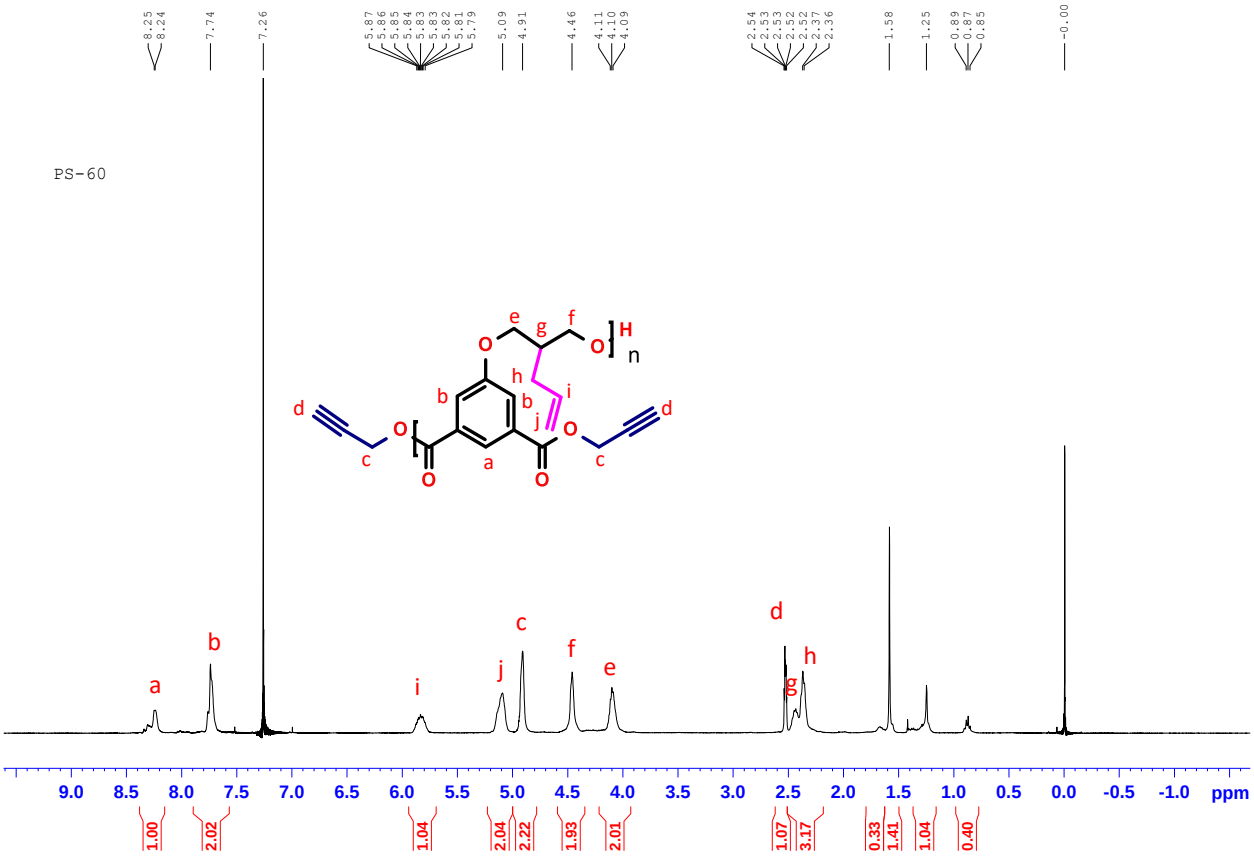


Figure S8: ^{1}H-NMR spectrum (in $CDCl_3$) of the parent HBP.

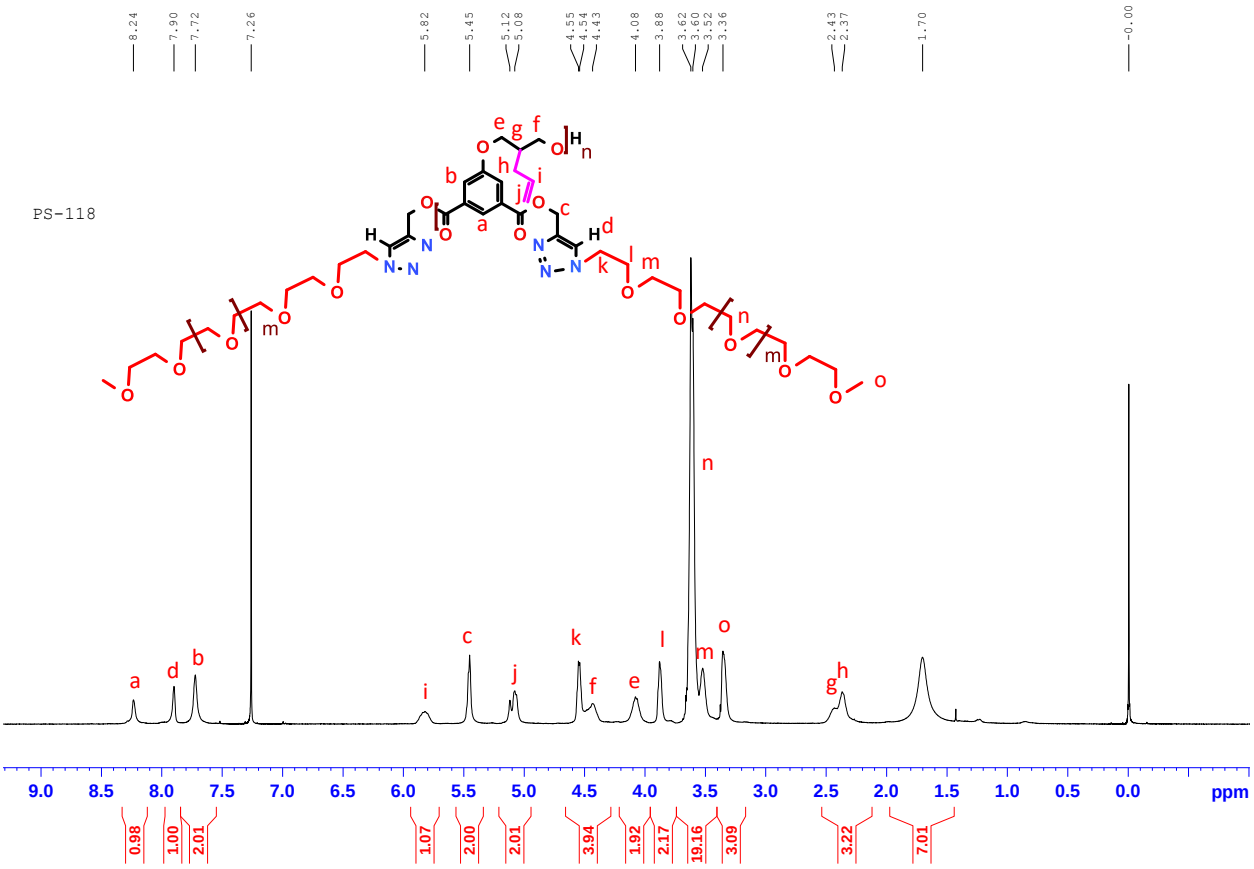


Figure S9: ^{1}H-NMR spectrum (in $CDCl_3$) of HBP-PEG350.

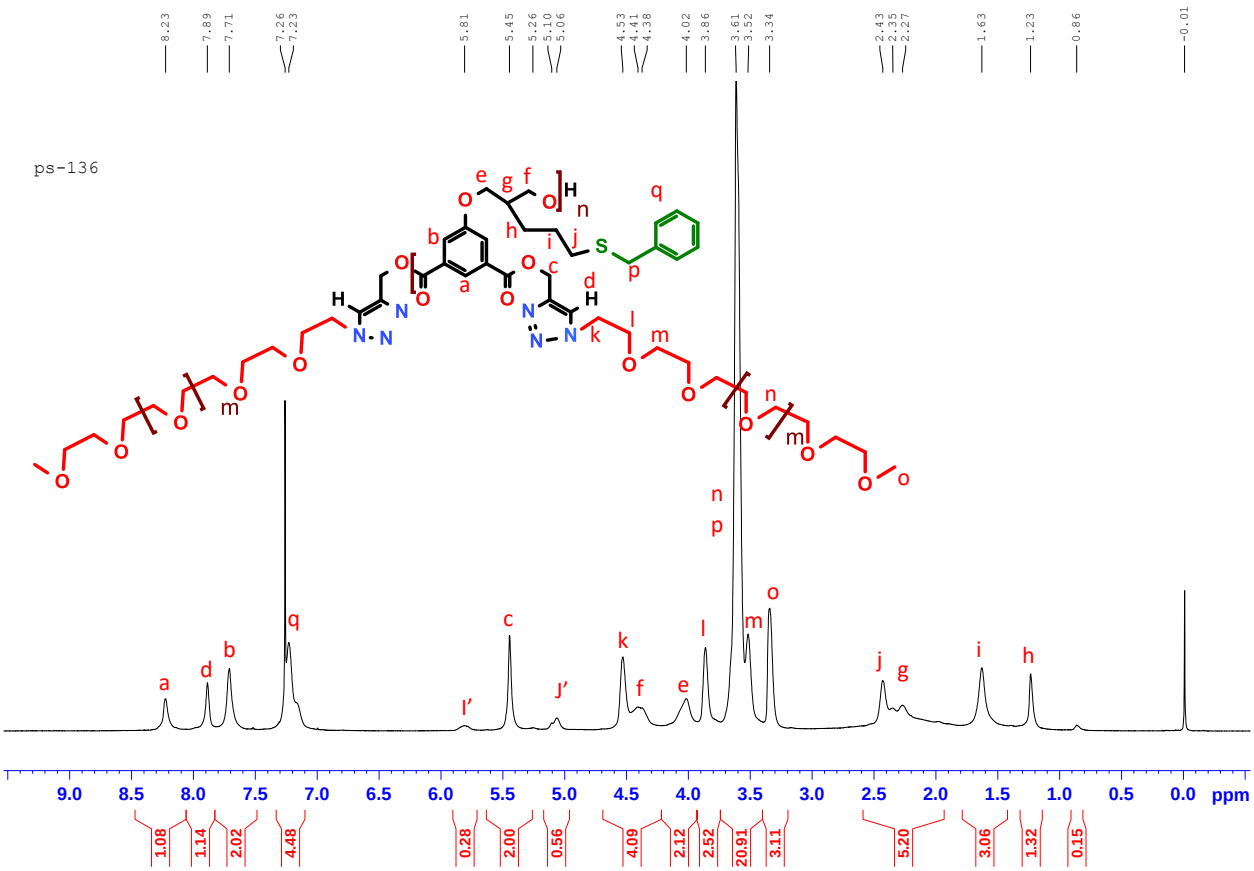


Figure S10: ^{1}H-NMR spectrum (in $CDCl_3$) of HBP-PEG350-BT.

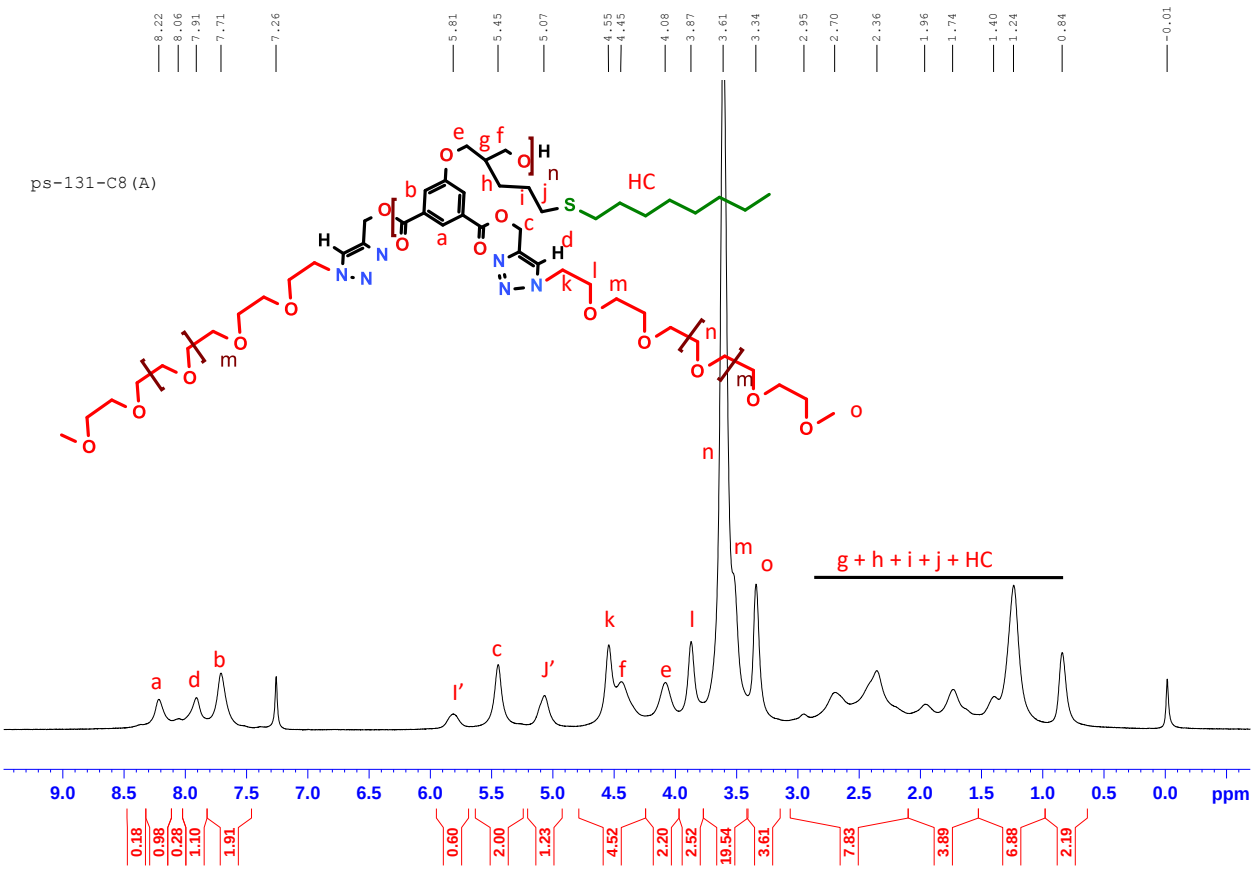


Figure S11: ^{1}H-NMR spectrum (in $CDCl_3$) of HBP-PEG350-C8.

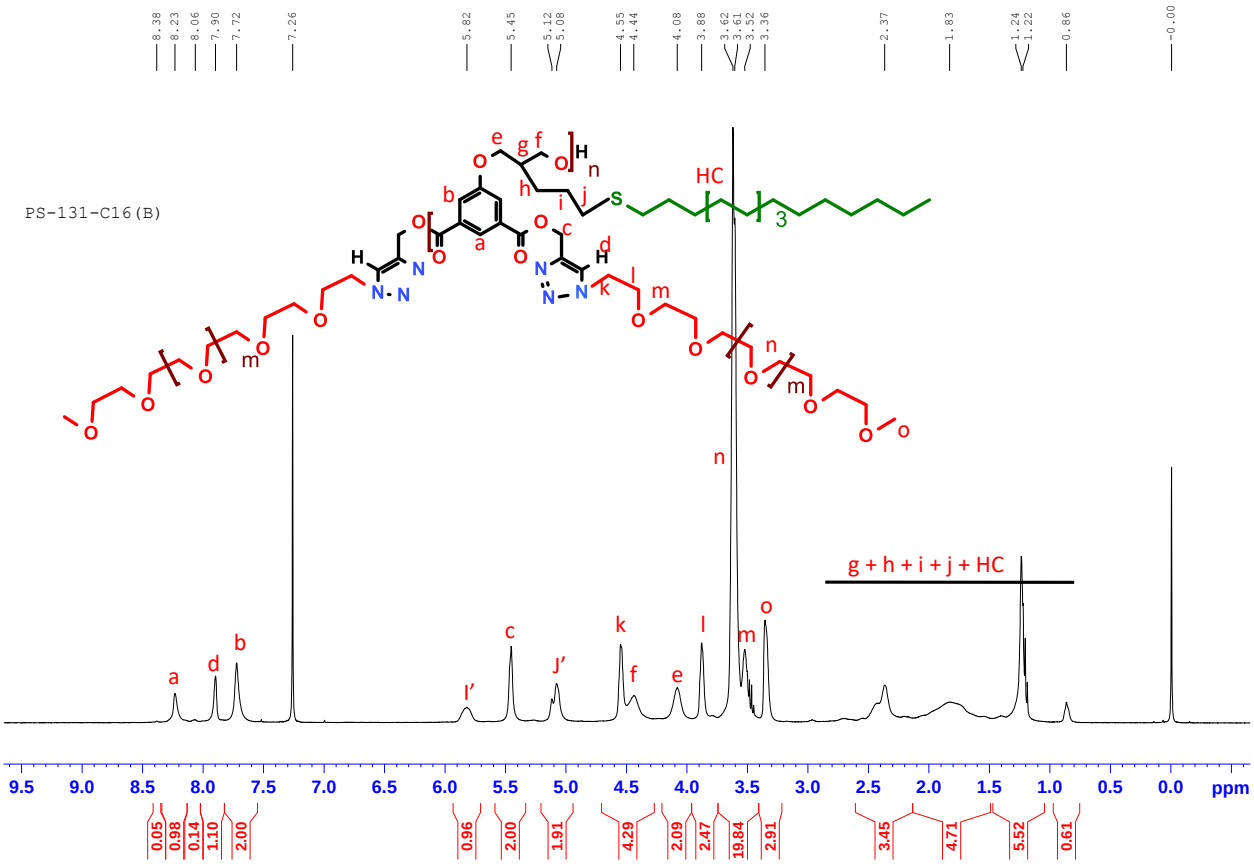


Figure S12: ^{1}H-NMR spectrum (in $CDCl_3$) of HBP-PEG350-C16.

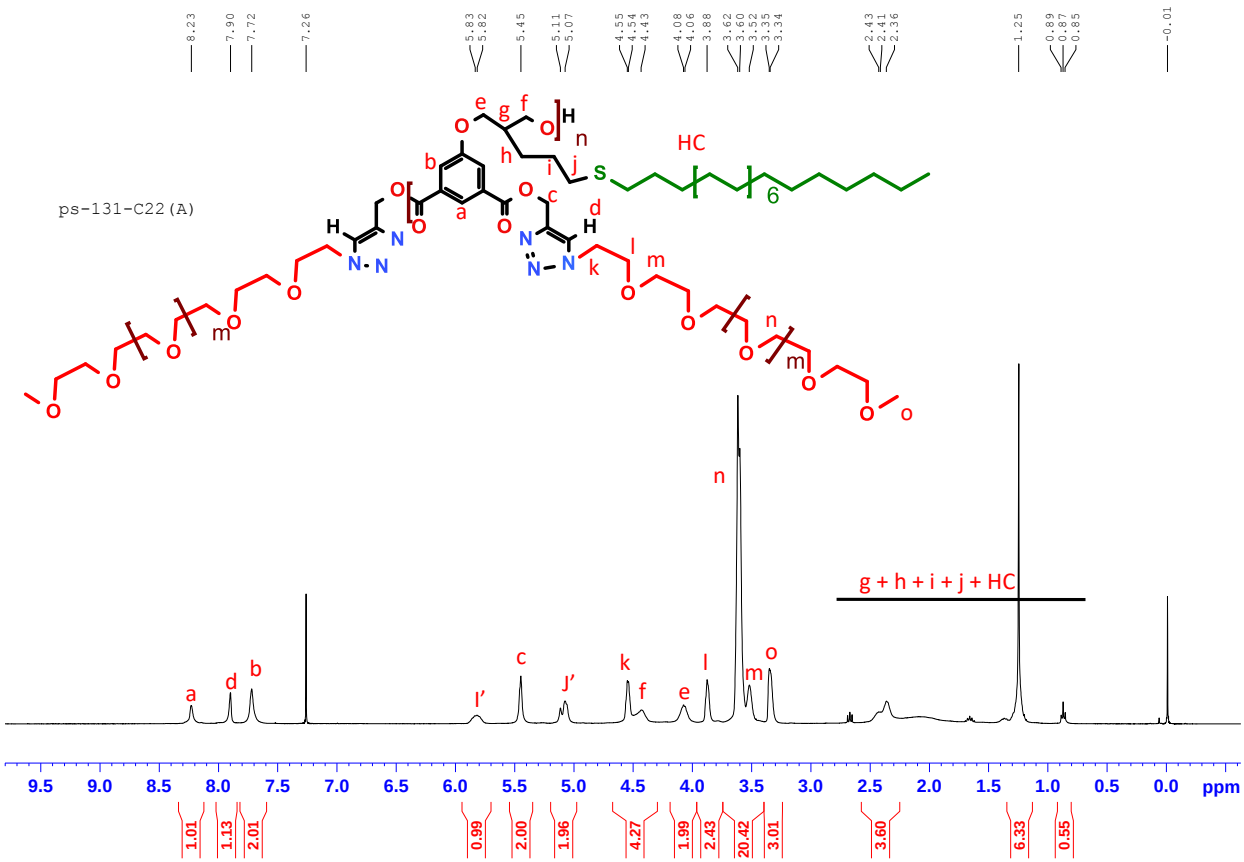


Figure S13: ^{1}H-NMR spectrum (in $CDCl_3$) of HBP-PEG350-C22.

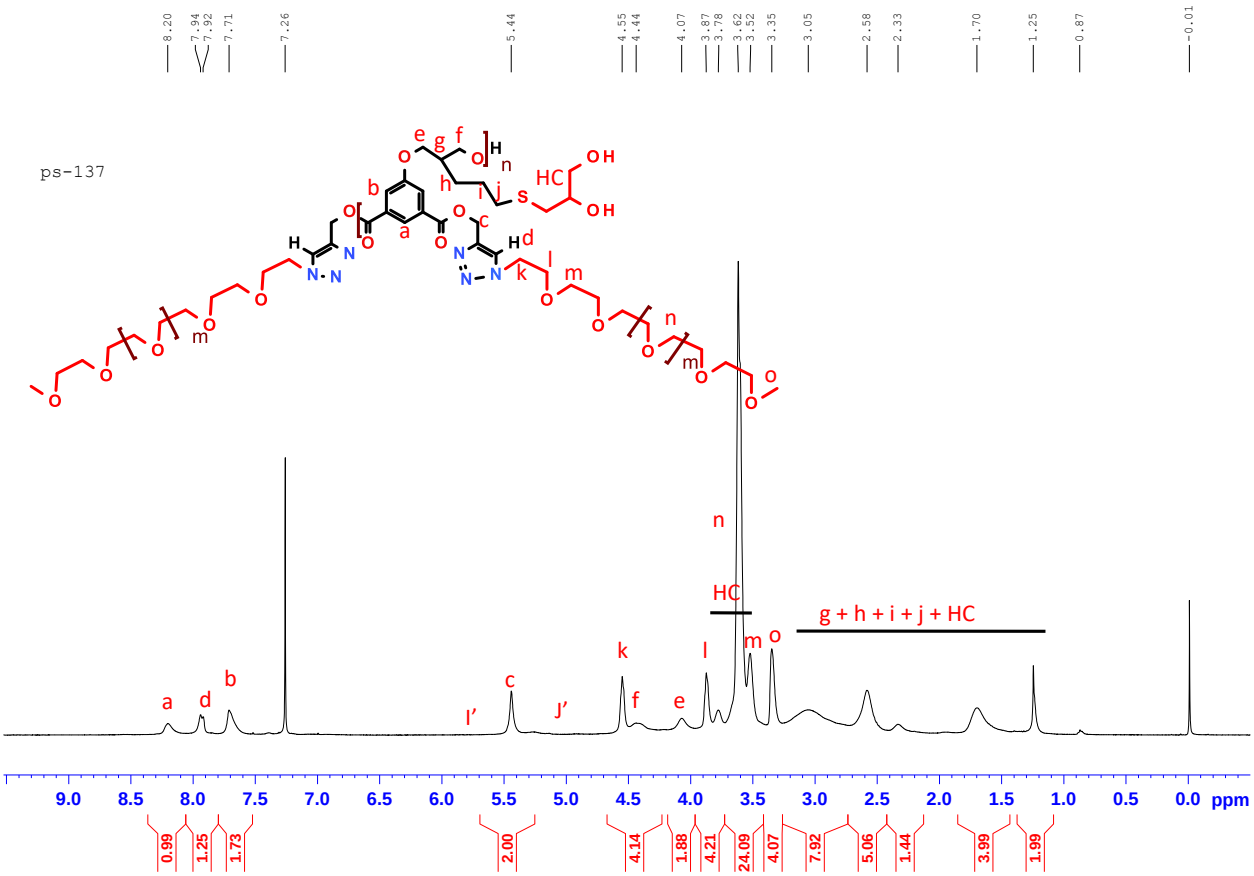


Figure S14: ^{1}H-NMR spectrum (in $CDCl_3$) of HBP-PEG350-TG.

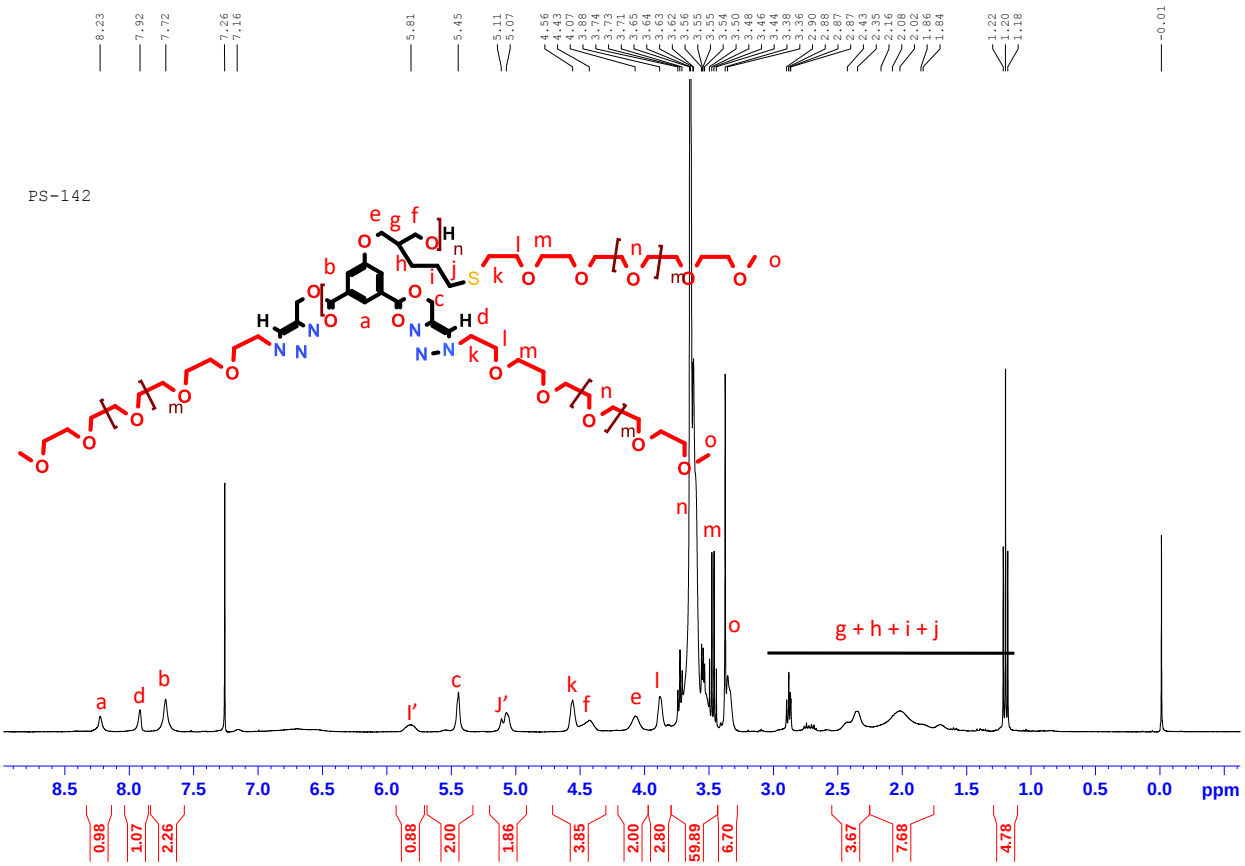


Figure S15: ^{1}H-NMR spectrum (in $CDCl_3$) of HBP-PEG350-PEG350.

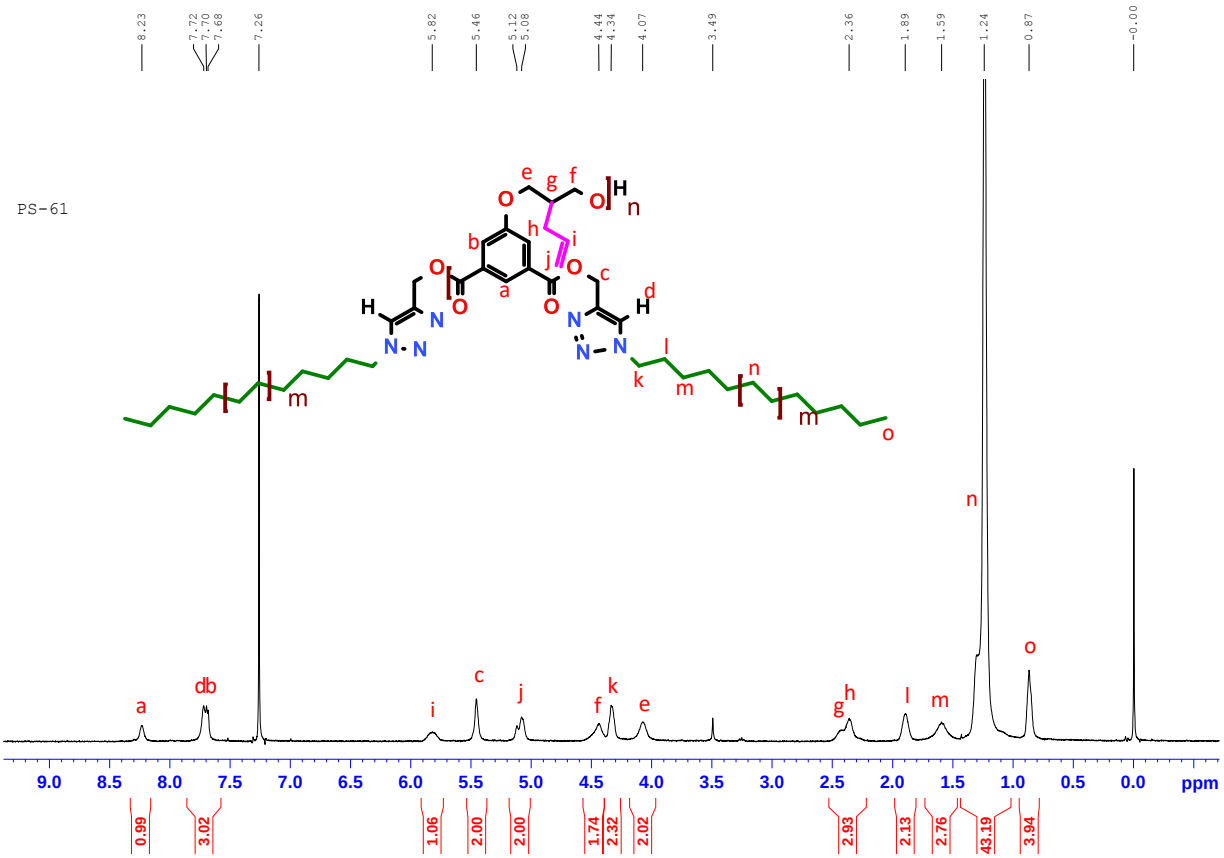


Figure S16: ^{1}H-NMR spectrum (in $CDCl_3$) of HBP-DOCO.

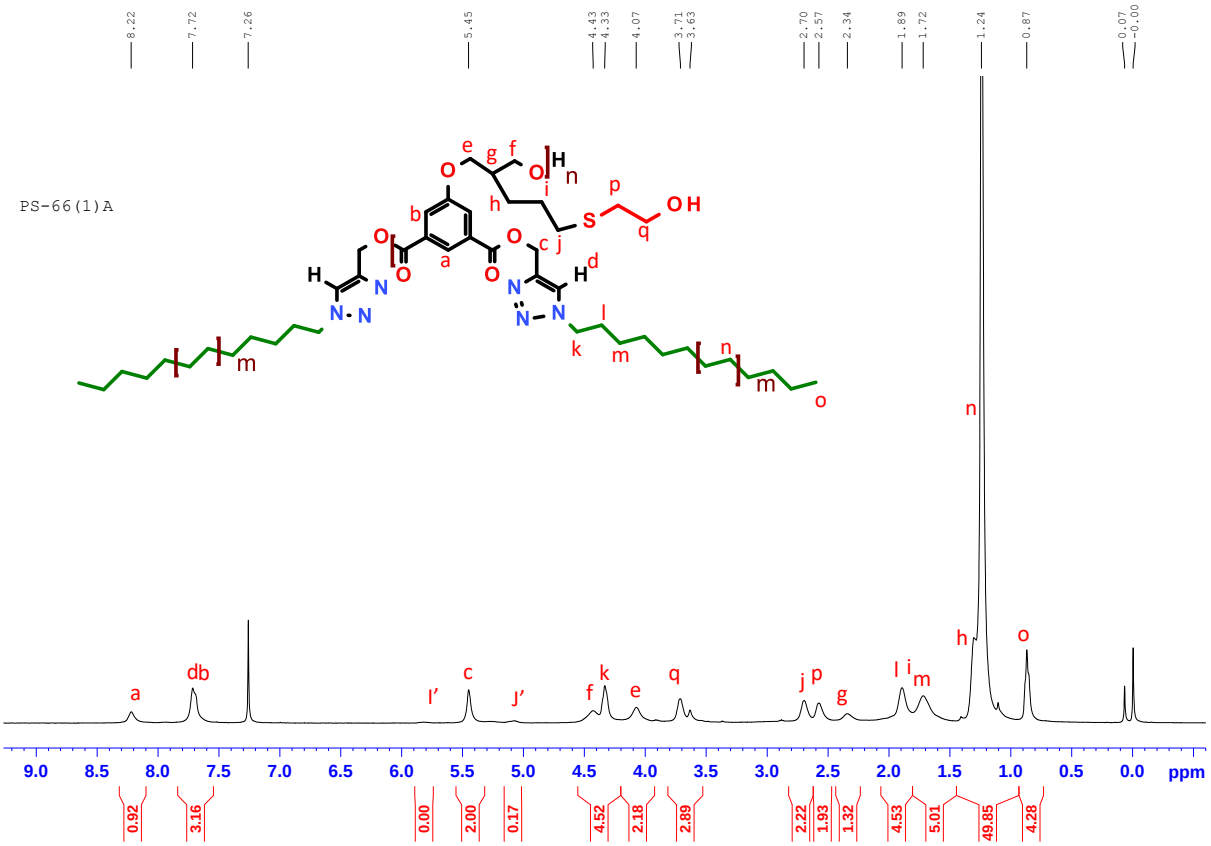


Figure S17: ^{1}H-NMR spectrum (in $CDCl_3$) of HBP-DOCO-ME.

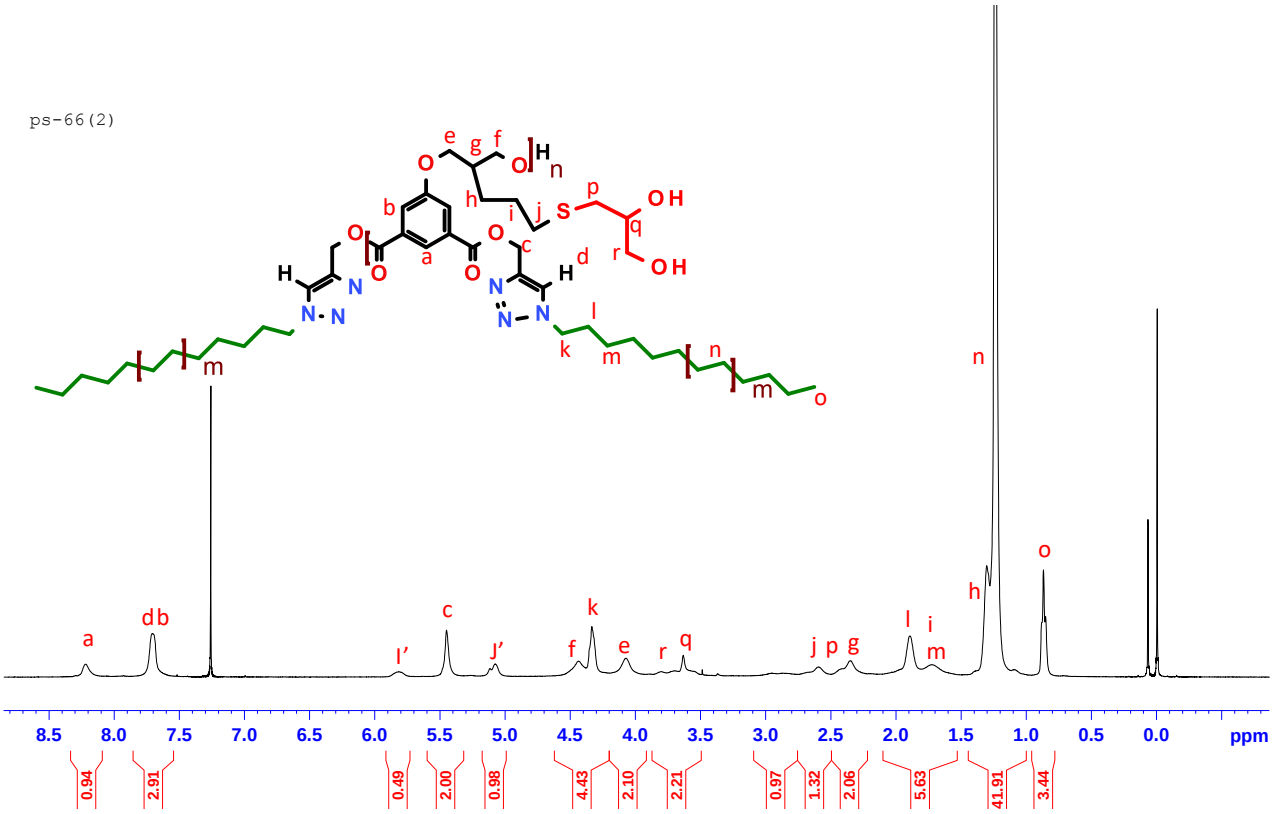


Figure S18: ^{1}H-NMR spectrum (in $CDCl_3$) of HBP-DOCO-TG.

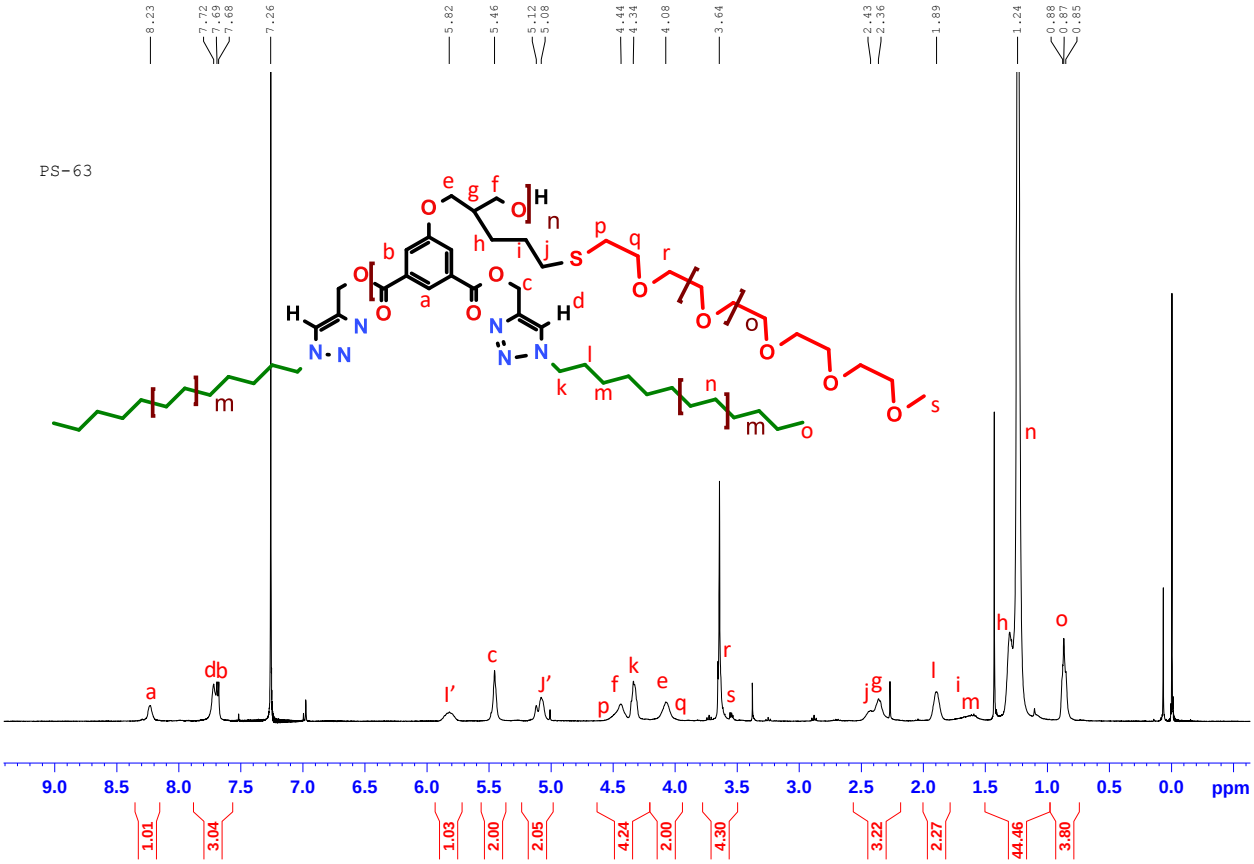


Figure S19: ^{1}H-NMR spectrum (in $CDCl_3$) of HBP-DOCO-PEG350.

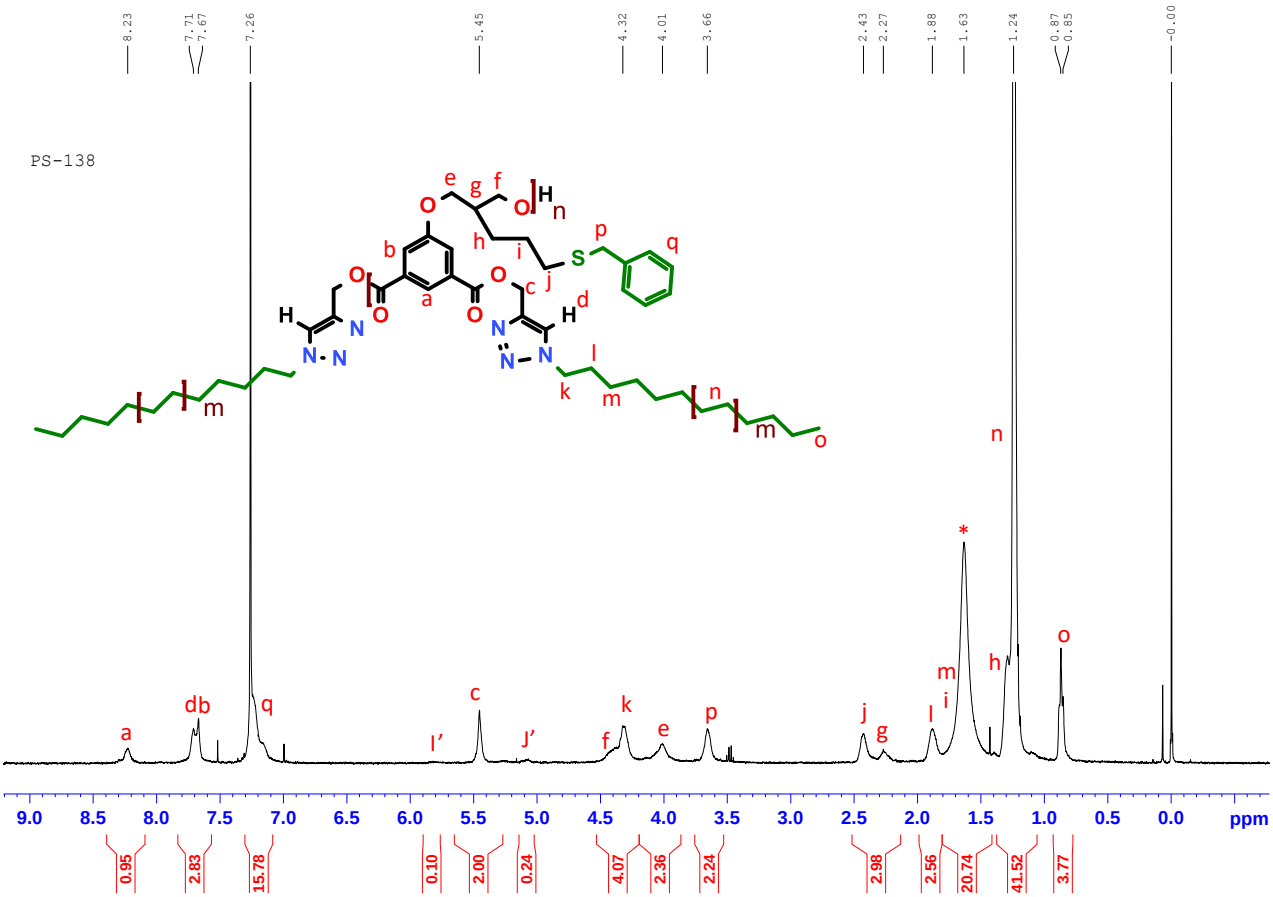


Figure S20: ^{1}H-NMR spectrum (in $CDCl_3$) of HBP-DOCO-BT.

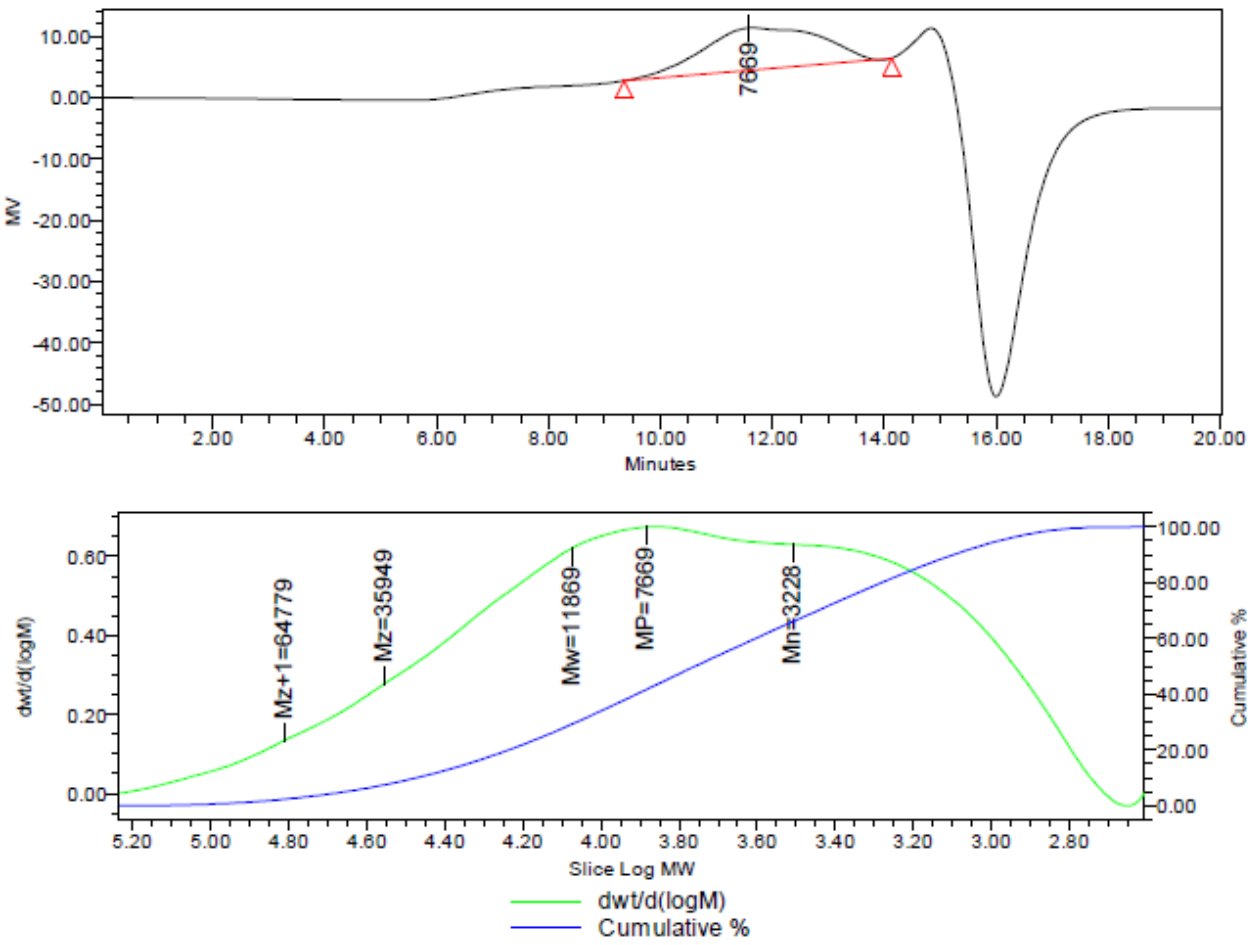


Figure S21: GPC curve (R. I.) of the parent HBP. M_n and PDI of the HBP were found to be 3200 g/mol and 3.7, respectively. A broad shoulder at low elution times may indicate some level of aggregation; as this is not evident after the clicking of the propargyl end groups either with PEG or Docosyl azide.

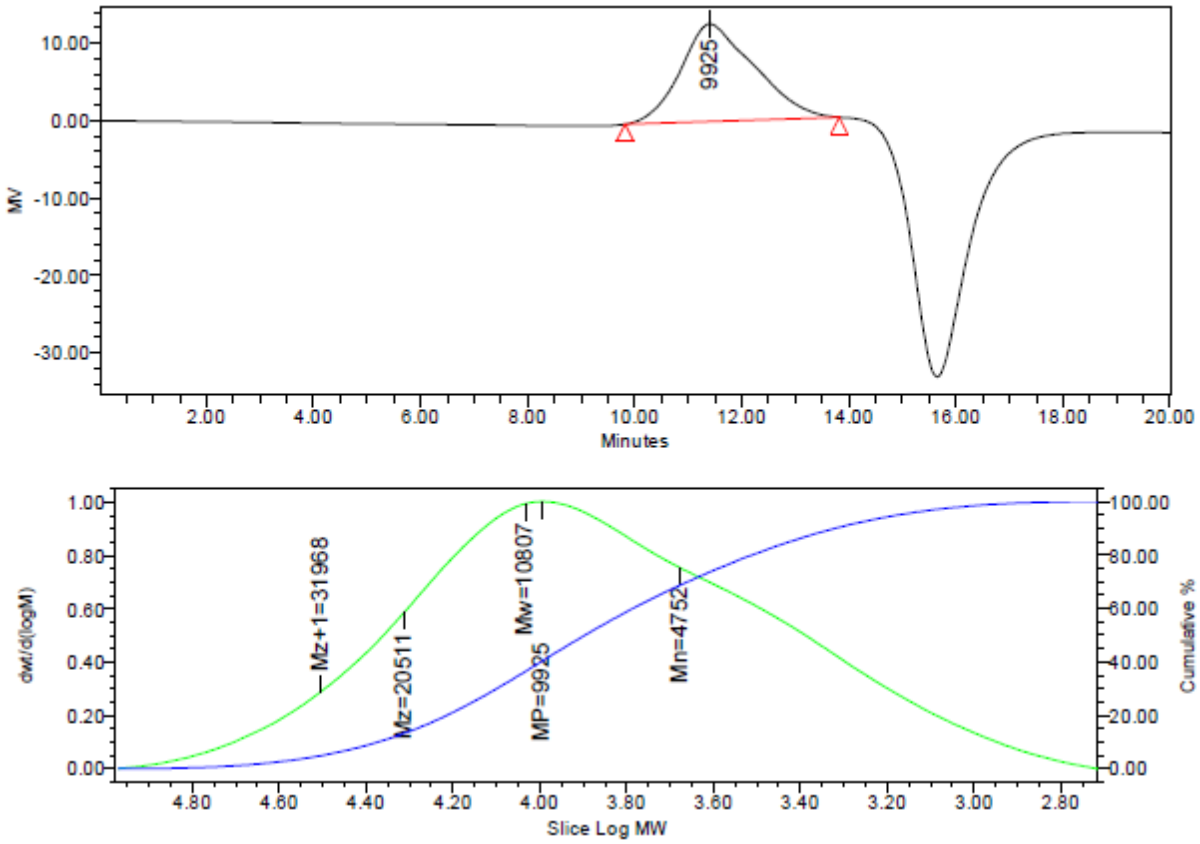


Figure S22: GPC curve (R. I.) of the parent HBP-PEG350. M_n and PDI of the HBP were found to be ~ 4800 g/mol and 2.3, respectively

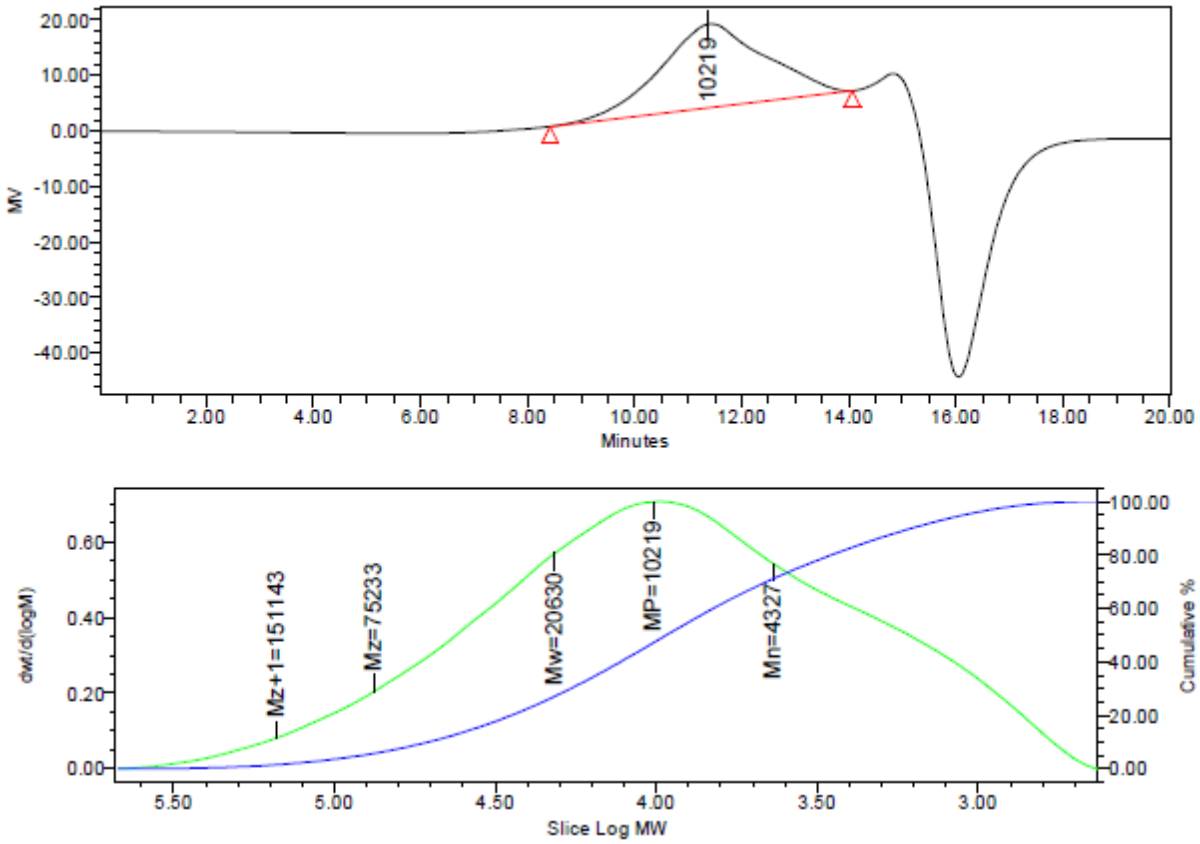


Figure S23: GPC curve (R. I.) of the parent HBP-DOCO. M_n and PDI of the HBP were found to be ~ 4300 g/mol and 4.8, respectively.

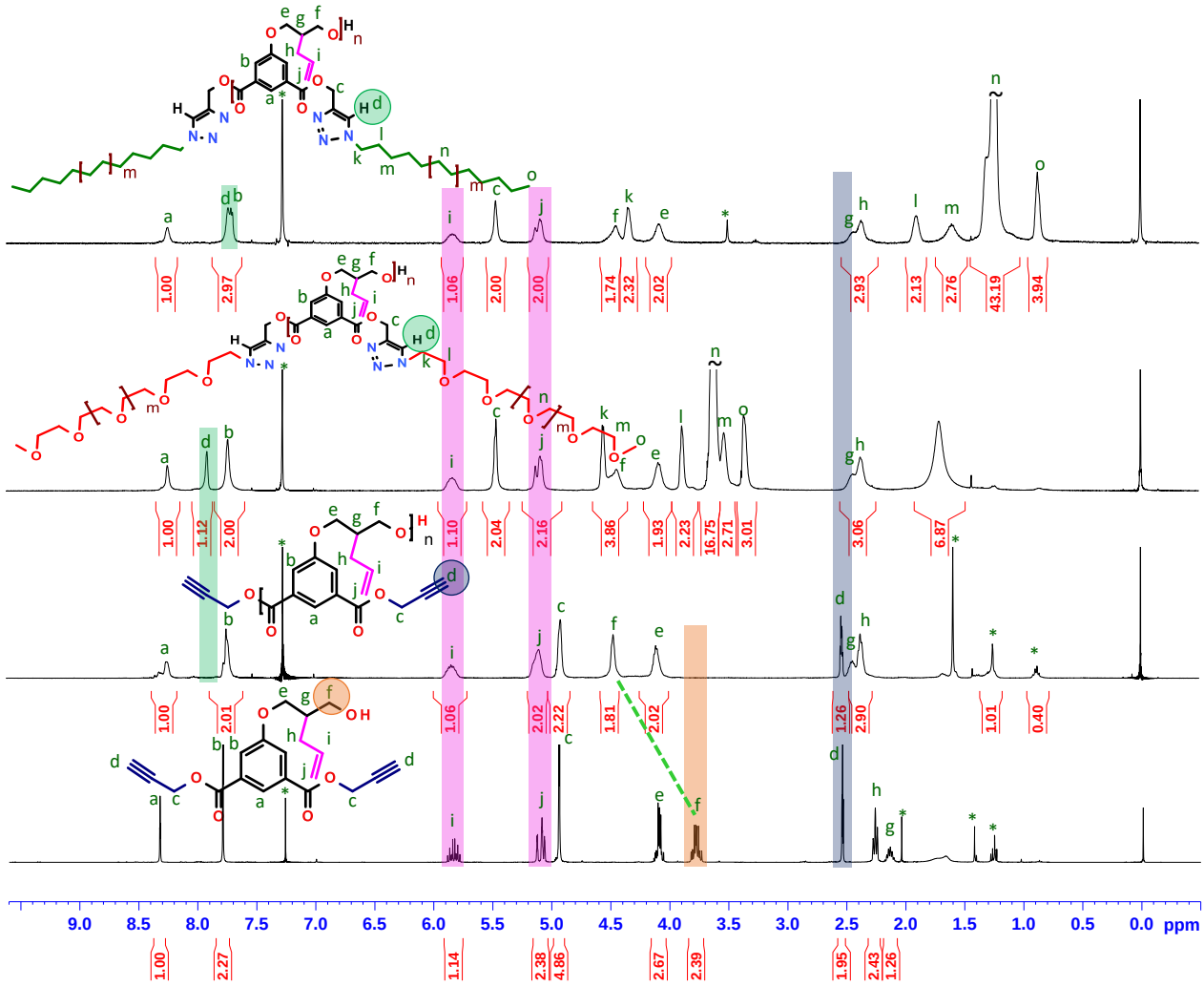


Figure S24: ^{1}H-NMR spectra (in $CDCl_3$) of the monomer, parent HBP, and those peripherally clicked with either PEG350-azide or docosyl azide, along with the peak assignments. The grey band reveals the disappearance of the propargyl peak and the green band reveals the appearance of the triazole peaks. The peaks marked by an asterisk (*) are due to solvents or DBTDL catalyst.

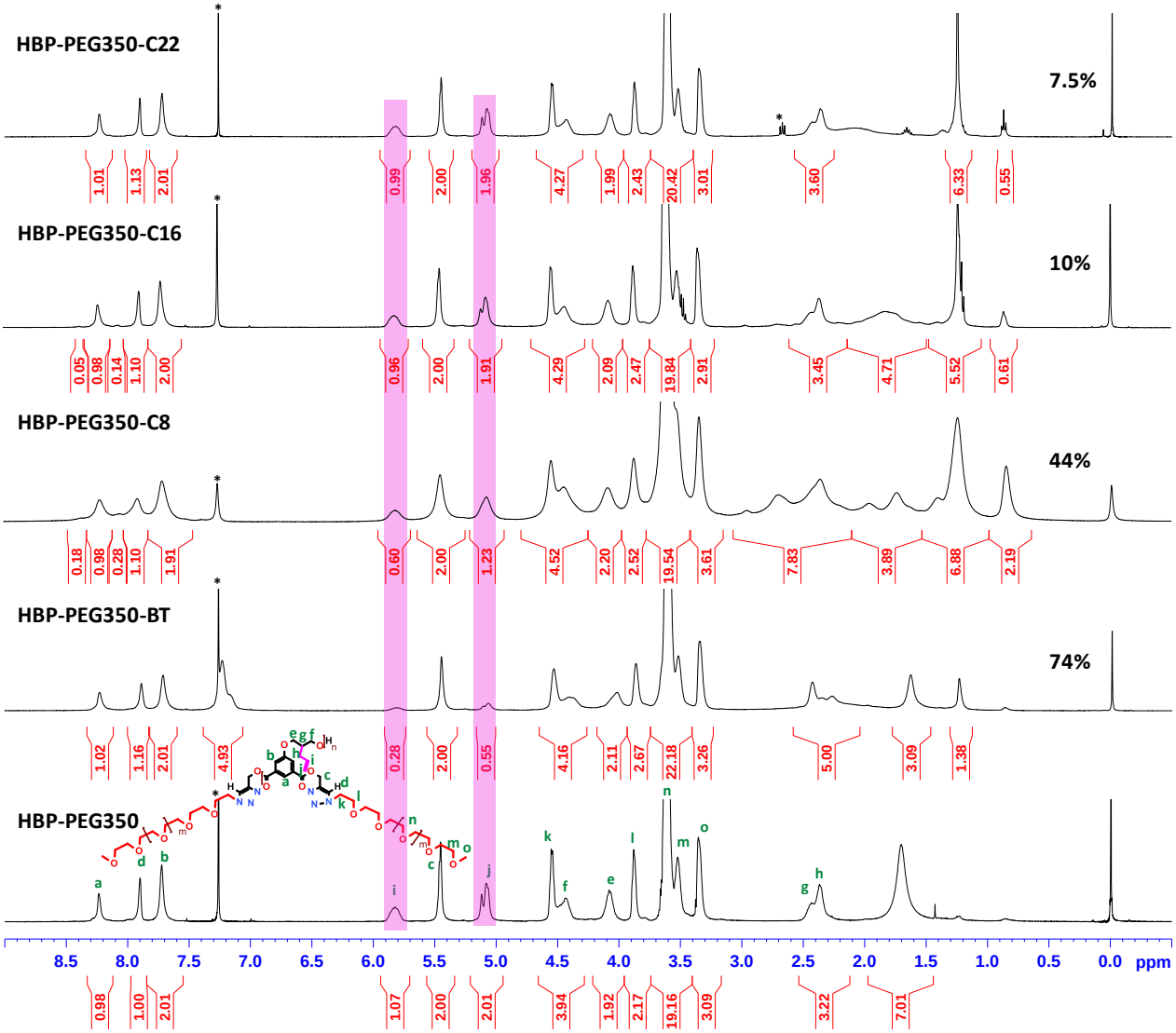


Figure S25: ^{1}H-NMR spectra (in $CDCl_3$) of the core functionalization of peripherally PEGylated HBP, along with the peak assignments. The intensity of the residual allyl peaks reveals the extent of reaction; the intensity of the peak at ~5.5 ppm, due to the methylene protons adjacent to the triazole ring, was set to value of 2 and the relative intensity of the peak at ~5.8 ppm due to a single allyl proton was used to estimate the extent of reaction. The peaks marked by an asterisk (*) are due to solvents.

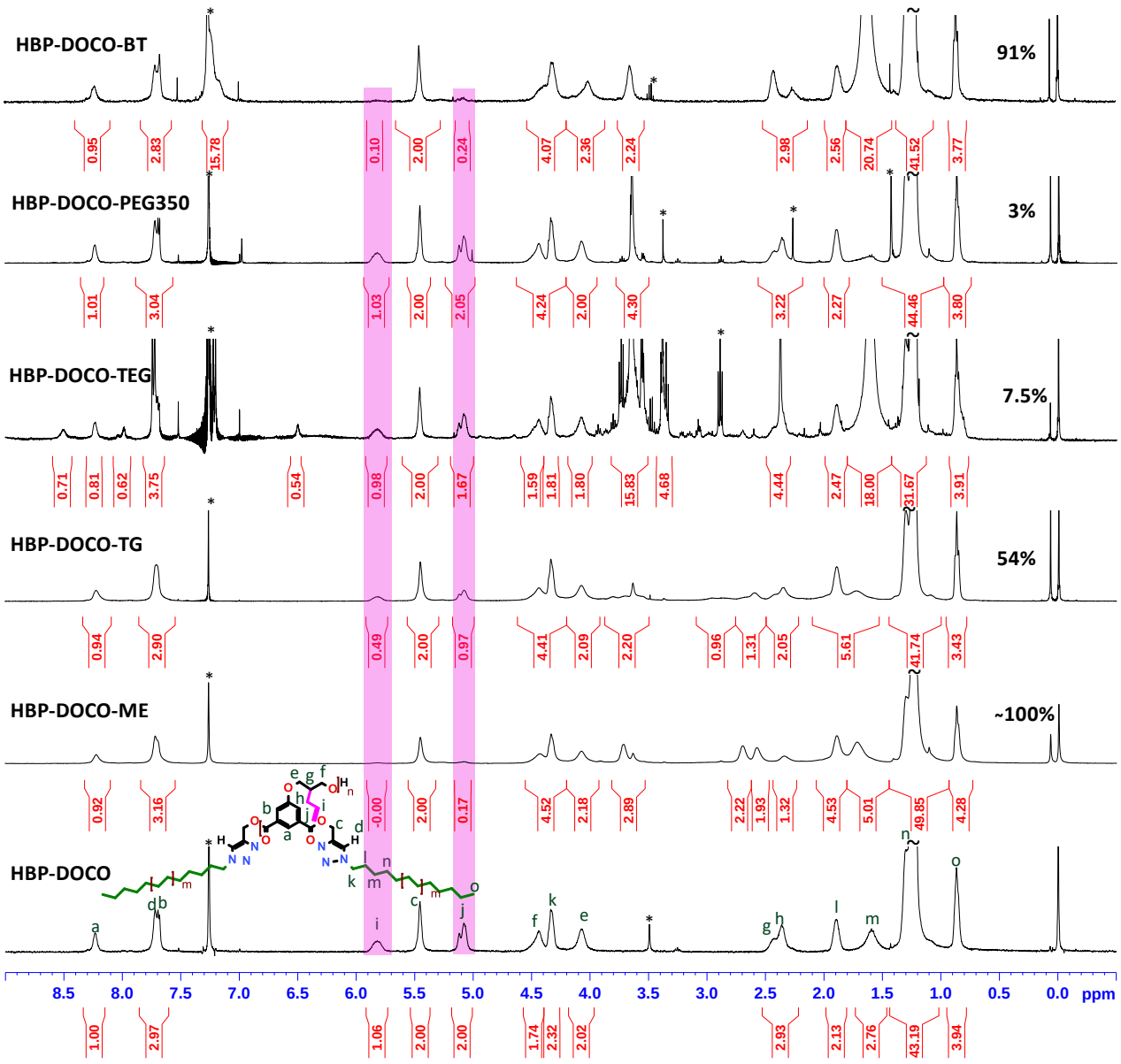


Figure S26: ^{1}H-NMR spectra (in $CDCl_3$) of the core functionalization of peripherally hydrophobically *jacketed* DOCO-HBPs, along with the peak assignments. The intensity of the residual allyl peaks reveals the extent of reaction; the intensity of the peak at ~5.5 ppm, due to the methylene protons adjacent to the triazole ring, was set to value of 2 and the relative intensity of the peak at ~5.8 ppm due to a single allyl proton was used to estimate the extent of reaction. The peaks marked by an asterisk (*) are due to solvents.

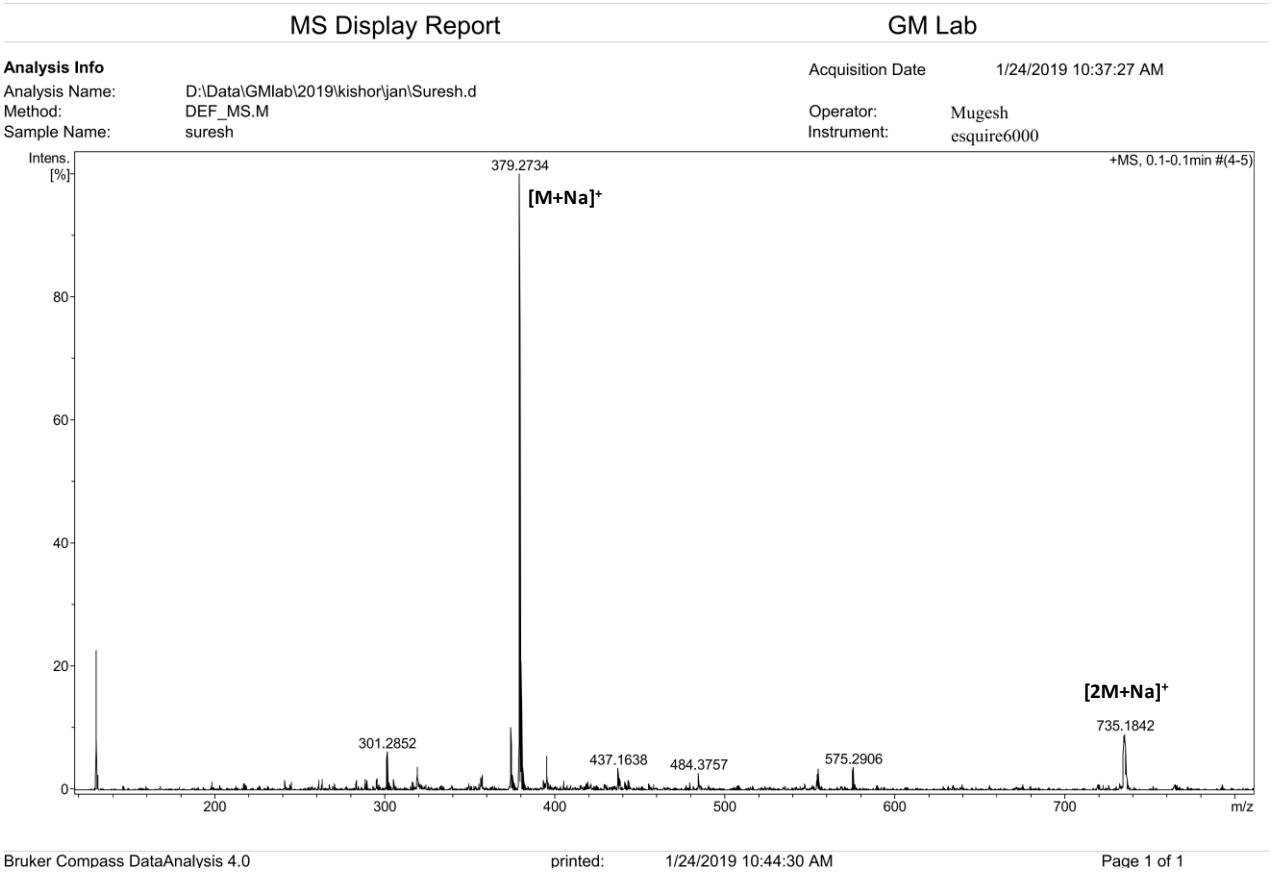


Figure S27: Mass spectrum (ESI-MS) of AB_2 monomer. The molecular weight of the monomer is 356.37 and the peak at 379.2734 is belongs to $[M+Na]^+$.