# *Combining Ring-Opening Multibranching and RAFT Polymerization: Multifunctional Linear-Hyperbranched Block Copolymers via Hyperbranched Macro Chain Transfer Agents*

*Supporting Information*

Lutz Nuhn[†], Christoph Schüll[†§], Holger Frey[†], and Rudolf Zentel[†*]

[†] Institute of Organic Chemistry, Johannes Gutenberg-University Mainz, Duesbergweg 10-14, D-55128 Mainz, Germany

[§] Graduate School Materials Science in Mainz (MAINZ), Staudingerweg 9, D-55128 Mainz, Germany

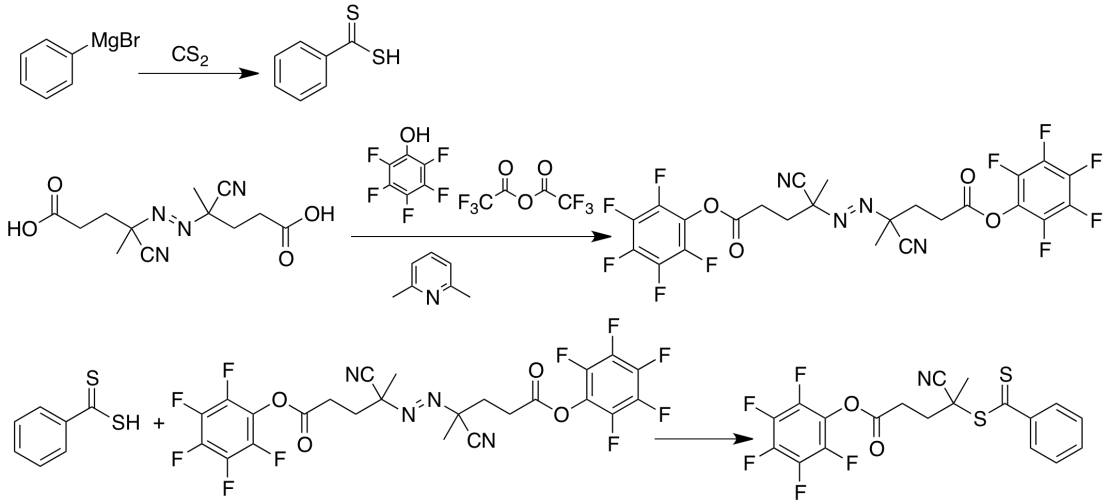
E-mail (*= corresponding authors): zentel@uni-mainz.de

# Content:

# Syntheses

## 1. Synthesis of Pentafluorophenyl 4-cyano-4-((phenylcarbonothioyl)thio)pentanoate PFP-CTA

The following procedure was slightly modified from a literature procedure[1]:



**Scheme S1: Synthesis of Pentafluorophenyl 4-cyano-4-((phenylcarbonothioyl)thio)pentanoate**

**Dithiobenzoic Acid**

In a two-necked round bottom flask equipped with a reflux condenser, a dropping funnel and a magnetic stir bar 1M phenylmagnesium bromide (15 mL; 0.015 mol) was dissolved in anhydrous THF (75 mL) under nitrogen atmosphere. The dropping funnel was filled with carbon disulfide (1.64 mL; 0.027 mol) under nitrogen atmosphere and this component was then dropped slowly to the reaction mixture while stirring vigorously. The reaction mixture turned red brown and was stirred for another two hours at 45°C after complete addition of carbon disulfide, before it was pored on ice (110 g) with conc. HCl (50mL). The suspension changed its color to purple and was extracted with diethyl ether (100 mL) three times. All organic phases were combined, dried over $MgSO_4$ and concentrated by rotary evaporation affording dithiobenzoic acid (2.36 g; 0.015 mol; quantitative) as a violet liquid of characteristic odor.

$^1$H-NMR (dioxane-d$^8$, 300 MHz): δ [ppm] = 8.07 (d, *J* = 6 Hz, 2H, o-Ar*H*); 7.61 (t, *J* = 6 Hz, 1H, p-Ar*H*); 7.41 (t, *J* = 6 Hz, 2H, m-Ar*H*).

**Bis(pentafluorophenyl) 4,4'-(diazene-1,2-diyl)bis(4-cyanopentanoate)**

In a two-necked round bottom flask equipped with septums and a magnetic stir bar pentafluorophenol (17.2 g; 0.093 mol), azobis(4-cyanovaleric acid) (10.9 g; 0.039 mol) and 2,6-lutidine (34.4 mL; 0.295 mol) were dissolved in anhydrous dichloromethane (225 mL) under nitrogen atmosphere. While cooling with an ice bath and stirring vigorously trifluoroacetic anhydride (16.2 mL; 0.116 mol) was added slowly via syringe through the septum. After

complete addition the mixture was allowed to warm to room temperature within 12 h while stirring. It was subsequently extracted three times with water (100 mL) and the organic phase dried over $MgSO_4$ and concentrated by rotary evaporation at 25°C. The raw product was dissolved in dichloromethane and precipitated in cold n-hexane to remove remaining lutidine. This process had to be repeated six times affording bis(pentafluorophenyl) 4,4'-(diazene-1,2-diyl)bis(4-cyanopentanoate) (7.85 g; 0.013 mol; 33%) as a colorless powder.

$^1$H-NMR ($CDCl_3$, 300 MHz): δ [ppm] = 2.96-2.54 (m, 8H, C*H*$_2$); 1.80 (s, 6H, C*H*$_3$).

$^{19}$F-NMR ($CDCl_3$, 376 MHz): δ [ppm] = -152.85 (d, *J* = 15 Hz, 2F, o-Ar*F*); -157.54 (t, *J* = 22 Hz, 1F, p-Ar*F*); -162.19 (t, *J* = 19 Hz, 2F, m-Ar*F*).

**Pentafluorophenyl 4-cyano-4-((phenylcarbonothioyl)thio)pentanoate PFP-CTA**

In a two-necked round bottom flask equipped with a reflux condenser, a septum and a magnetic stir bar dithiobenzoic acid (2.20 g; 0.014 mol) and bis(pentafluorophenyl) 4,4'-(diazene-1,2-diyl)bis(4-cyanopentanoate) (7.10 g; 0.011 mol) were dissolved in ethyl acetate (120 mL) under nitrogen atmosphere. The solution was bubbled with argon for one hour to deoxygenate the reaction, before it was refluxed for 12 h under nitrogen atmosphere. The reaction mixture was then concentrated by rotary evaporation and purified by column chromatography (elution chloroform: cyclohexane = 3:1) affording pentafluorophenyl 4-cyano-4-((phenylcarbonothioyl)thio)pentanoate **PFP-CTA** as a purple solid (1.69 g; 0.004 mol; 72%).

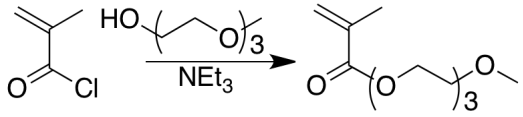
$^1$H-NMR ($CDCl_3$, 300 MHz): δ [ppm] = 7.93 (d, *J* = 6 Hz, 2H, o-Ar*H*); 7.59 (t, *J* = 7.5 Hz, 1H, p-Ar*H*); 7.42 (t, *J* = 7.5 Hz, 2H, m-Ar*H*), 3.10-3.03 (m, 2H, -$CH_2$-C*H*$_2$-CO-); 2.82-3.72 (m, 1H, -C*H*$_2$-$CH_2$-CO-); 2.61-2.51 (m, 1H, -C*H*$_2$-$CH_2$-CO-); 1.99 (s, 3H, -C*H*$_3$).

$^{13}$C-NMR (CDCl3, 75 MHz): δ [ppm] = 219.91 (-*C*$S_2$-); 167.92 (-*C*OO-); 144.47 ($H_5$Ar*C*-O); 142.96-142.81 (m-$F_5$Ar*C*, multiplet); 141.70-140.34 ($F_5$Ar*C*-O, multiplet); 139.74-139.47 (p-$F_5$Ar*C*, multiplet); 136.38-136.22 and 134.16-133.37 (o-$F_5$ArC, multiplet); 133.37 (p-$H_5$Ar*C*); 128.80 (m-$H_5$Ar*C*); 126.86 (o-$H_5$Ar*C*); 118.38 (-*C*N); 45.64 ($C_{quat}$); 33.15 (-$CH_2$-*C*$H_2$-CO-); 29.24 (-*C*$H_2$-$CH_2$-CO-); 24.44(-*C*$H_3$).

$^{19}$F-NMR ($CDCl_3$, 376 MHz): δ [ppm] = -152.85 (d, *J* = 19 Hz, 2F, o-Ar*F*); -157.59 (t, *J* = 21 Hz, 1F, p-Ar*F*); -162.20 (t, *J* = 19 Hz, 2F, m-Ar*F*).

## 2. Synthesis of Tri(ethylene glycol) methyl ether methacrylate $MEO_3MA$

The following procedure was slightly modified from a literature procedure[2]:




**Scheme S2: Synthesis of Tri(ethylene glycol) methyl ether methacrylate**

**Tri(ethylene glycol) methyl ether methacrylate $MEO_3MA$**

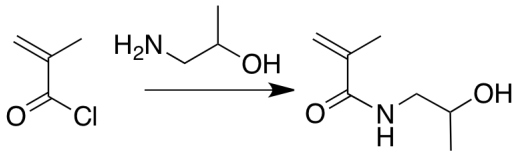
In a round bottom flask equipped with a dropping funnel and a magnetic stir bar tri(ethylene glycol) monomethyl ether (29.4 mL; 0.188 mol) was dissolved in anhydrous dichloromethane (90 mL) under nitrogen atmosphere. Triethylamine (50.5 mL; 0.363 mol) was added via syringe through a septum. The dropping funnel was filled with methacryloyl chloride (10.6 mL; 0.125 mol) under nitrogen atmosphere and this component was then dropped slowly to the reaction mixture while stirring vigorously and cooling with an ice bath. After complete addition the reaction mixture was cooled for further 15 min and then slowly warmed to room temperature for about 12 h. It was filtered through filter paper to remove precipitated salts and then concentrated by rotary evaporation. The crude mixture was purified by column chromatography (gradient elution cyclohexane : ethyl acetate from 6:1 to 5:1 ) affording tri(ethylene glycol) methyl ether methacrylate **$MEO_3MA$** as a colorless liquid (11.0 g; 0.047 mol; 38%). Due to educt contamination di(ethylene glycol) methyl ether methacrylate could by isolated as a byproduct (2.0 g; 0.011; 9%).

$^1$H-NMR ($CDCl_3$, 300 MHz): δ [ppm] = 6.08 (m, 1H, C=C$H_2$-*cis*); 5.52 (m, 1H, C=C$H_2$ *trans*); 4.25 (t, $J$ = 5 Hz, 2H, COO-C$H_2$-$CH_2$-); 3.70 (t, $J$ = 5 Hz, 2H, COO-$CH_2$-C$H_2$-); 3.63 -3.58 (m, 6H, O-C$H_2$-C$H_2$-O-C$H_2$-$CH_2$-O-CH3); 3.49 (t, $J$ = 6 Hz, 2H, $CH_2$-C$H_2$-O-$CH_3$); 3.32 (s, 3H, O-C$H_3$); 1.89 (s, 3H, =C-C$H_3$).

$^{13}$C-NMR ($CDCl_3$, 75 MHz): δ [ppm] = 167.32 (-$C$O$_2$-); 136.17 ($C$=$CH_2$); 125.70 (C=$C$H$_2$); 71.93 ($CH_2$-$C$H$_2$-O-$CH_3$); 70.65 (O-$C$H$_2$-$CH_2$-O-$CH_2$-$CH_2$-O-$CH_3$); 70.63 (O-$CH_2$-$CH_2$-O-$C$H$_2$-$CH_2$-O-$CH_3$); 70.59 (O-$CH_2$-$C$H$_2$-O-$CH_2$-$CH_2$-O-$CH_3$); 69.14 (COO-$CH_2$-$C$H$_2$-); 63.88 (COO-$C$H$_2$-$CH_2$-); 59.02 (O-$C$H$_3$); 18.30 (=C-$C$H$_3$).

## 3. Synthesis of 2-Hydroxypropyl methacrylamide HPMA

The following procedure was slightly modified from a literature procedure[3]:




**Scheme S3: Synthesis of 2-Hydroxypropyl methacrylamide**

**2-Hydroxypropyl methacrylamide HPMA**

In a round bottom flask equipped with a dropping funnel and a magnetic stir bar 1-aminopropan-2-ol (10.0 mL; 0.129 mol) was dissolved in anhydrous dichloromethane (100 mL) under nitrogen atmosphere. The dropping funnel was filled with methacryloyl chloride (5.8 mL; 0.059 mol) under nitrogen atmosphere and this component was then dropped slowly to the reaction mixture while stirring vigorously and cooling with an ice bath. After complete addition the reaction mixture was slowly warmed to room temperature for about 12 h. It was then filtered through filter paper to remove precipitated salts and then concentrated by rotary evaporation. The crude mixture was purified by column chromatography (elution chloroform : methanol = 10:1) affording 2-hydroxypropyl methacrylamide **HPMA** (7.0 g; 0.049 mol; 83%) as colorless powder.

$^{1}$H-NMR ($CDCl_3$, 300 MHz): δ [ppm] = 6.43 (br, 1H, -CO-N*H*-); 5.72 (m, 1H, C=C*H*$_2$ *trans*); 5.34 (m, 1H, C=C*H*$_2$ *trans*); 3.94 (dqd, *J* = 7.6, 6.3, 3.0 Hz, 1H, -C*H*(OH)-); 3.49 (ddd, *J* = 13.9, 6.5, 3.0 Hz, 1H, -CO-NH-C*H*$_2$-); 3.16 (ddd, *J* = 13.9, 7.6, 5.1 Hz, 1H, -CO-NH-C*H*$_2$-); 3.04 (br, 1H, -O*H*); 1.96 (s, 3H, =C-C*H*$_3$); 1.19 (d, J = 6.3 Hz, 1H, CH(OH)-C*H*$_3$).

$^{13}$C-NMR ($CDCl_3$, 75 MHz): δ [ppm] = 169.60 (-*C*O$_2$-); 139.72 (*C*=CH$_2$); 120.27 (C=*C*H$_2$); 67.56 (*C*H(OH)); 47.30 (-CO-NH-*C*H$_2$-); 21.12 (CH(OH)-*C*H$_3$); 18.78 (=C-*C*H$_3$).

# Characterization Data

## 1. Spectroscopic Data of Pentafluorophenyl 4-cyano-4-((phenylcarbonothioyl)thio)pentanoate PFP-CTA

**$^1$H-NMR PFP-CTA**

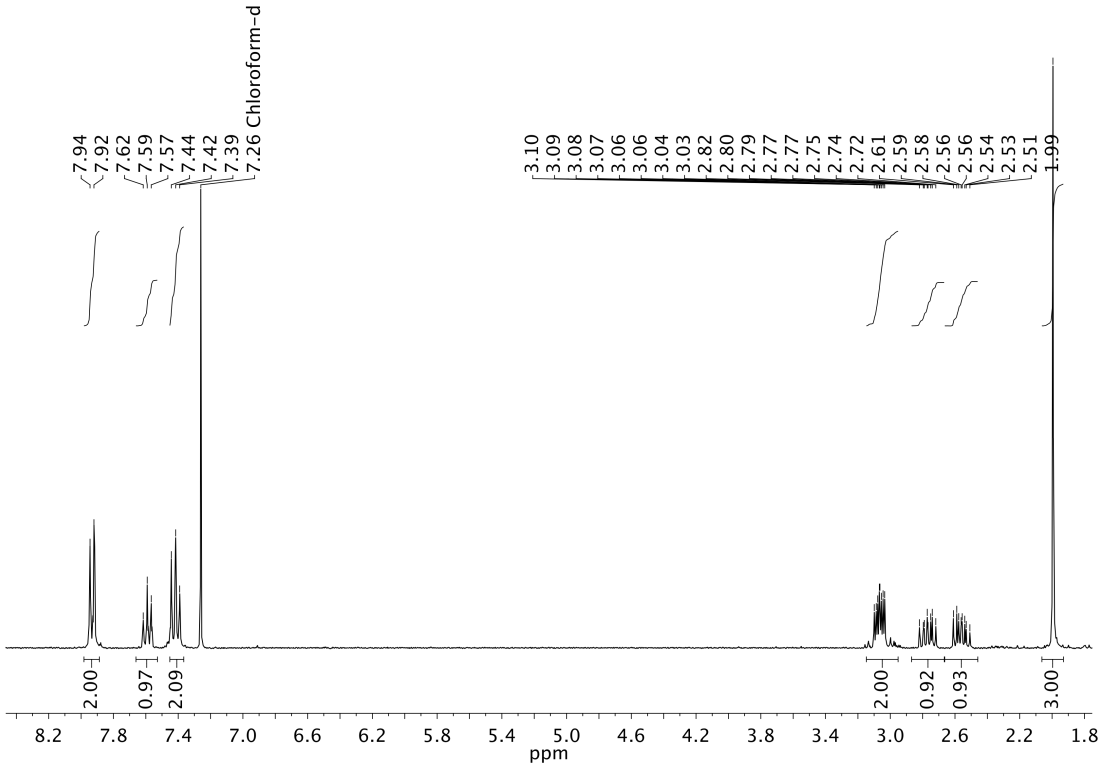



**Figure S1: 1H-NMR ($CDCl_3$, 300 MHz) Pentafluorophenyl 4-cyano-4-((phenylcarbonothioyl)thio)pentanoate**

**$^{13}$C-NMR PFP-CTA**

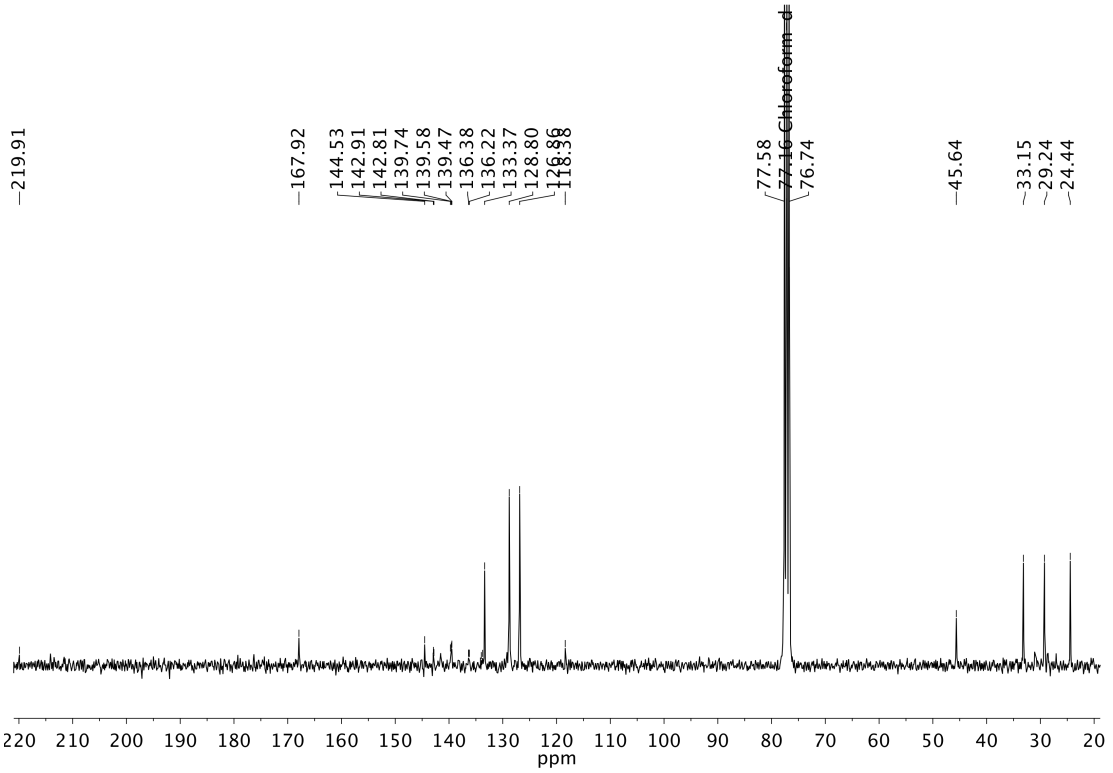



**Figure S2: $^{13}$C-NMR ($CDCl_3$, 75 MHz) Pentafluorophenyl 4-cyano-4-((phenylcarbonothioyl)thio)pentanoate**

**$^{19}$F-NMR PFP-CTA**

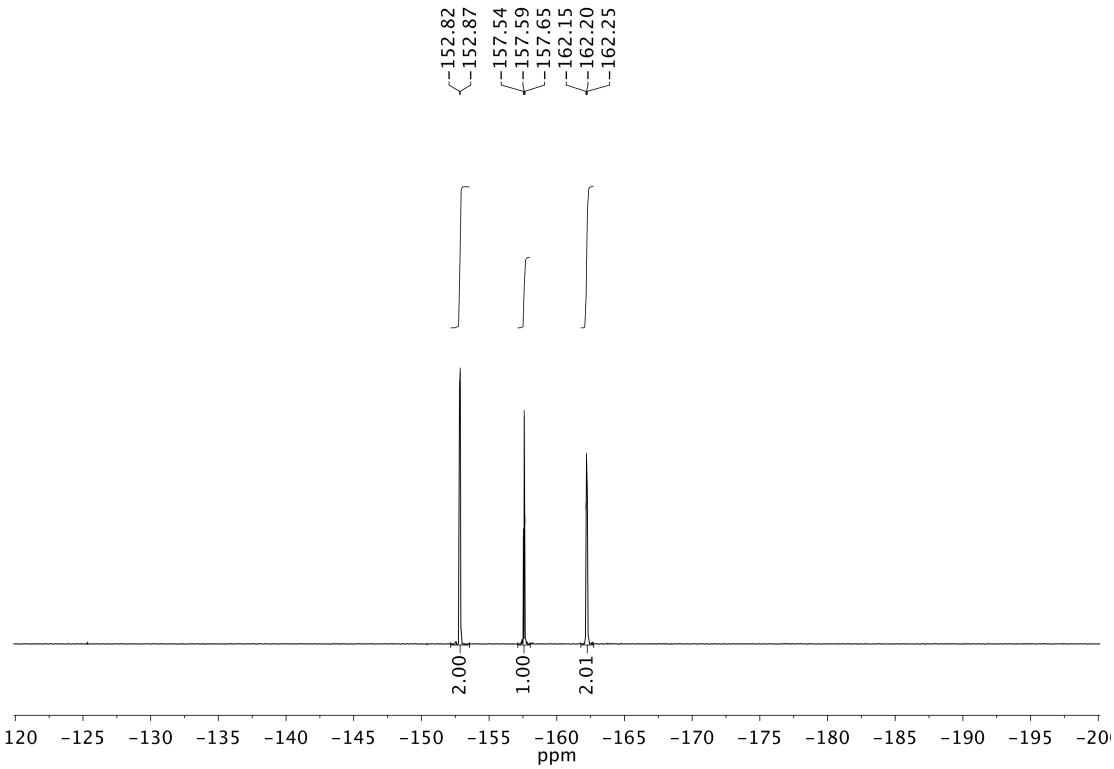



**Figure S3: $^{19}$F-NMR ($CDCl_3$, 376 MHz) Pentafluorophenyl 4-cyano-4-((phenylcarbonothioyl)thio)pentanoate**

## 2. Spectroscopic Data of Tri(ethylene glycol) methyl ether methacrylate $MEO_3MA$

**$^1$H-NMR $MEO_3MA$**

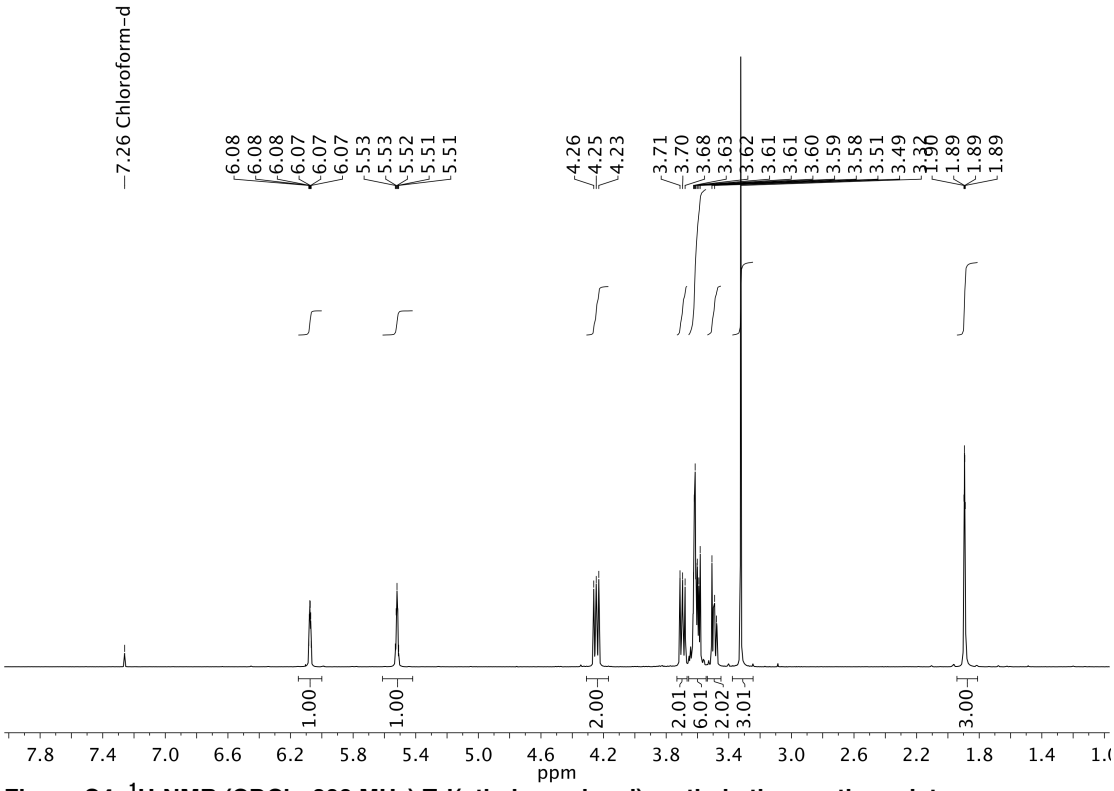



**Figure S4: $^1$H-NMR ($CDCl_3$, 300 MHz) Tri(ethylene glycol) methyl ether methacrylate**

**$^{13}$C-NMR $MEO_3MA$**

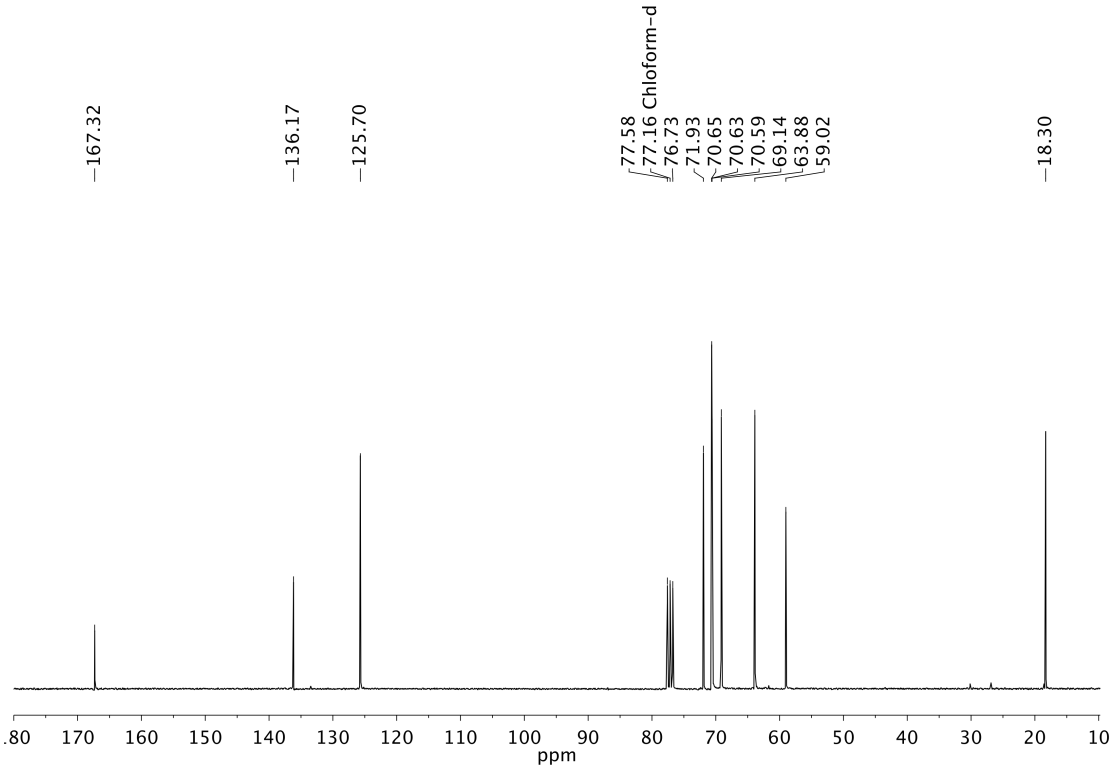



**Figure S5: $^{13}$C-NMR ($CDCl_3$, 75 MHz) Tri(ethylene glycol) methyl ether methacrylate**

## 3. Spectroscopic Data of 2-Hydroxypropyl methacrylamide HPMA

**$^{1}$H-NMR HPMA**

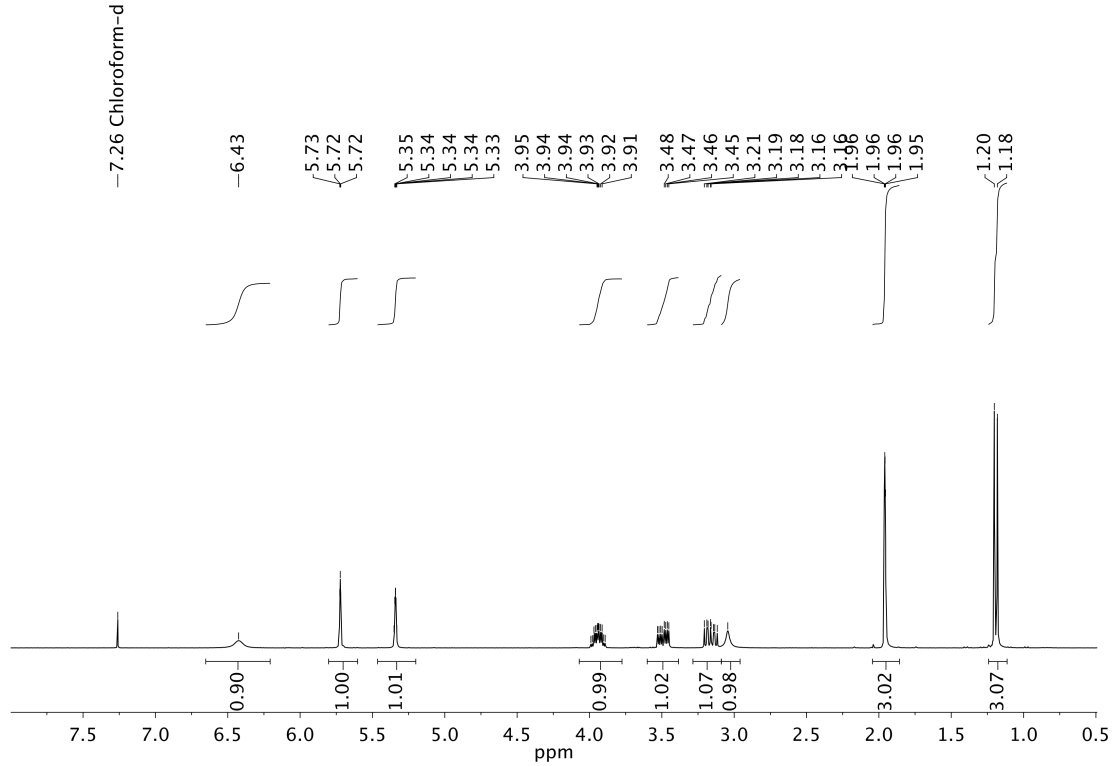



**Figure S6: $^{1}$H-NMR ($CDCl_3$, 300 MHz) 2-Hydroxypropyl methacrylamide**

**$^{13}$C-NMR HPMA**

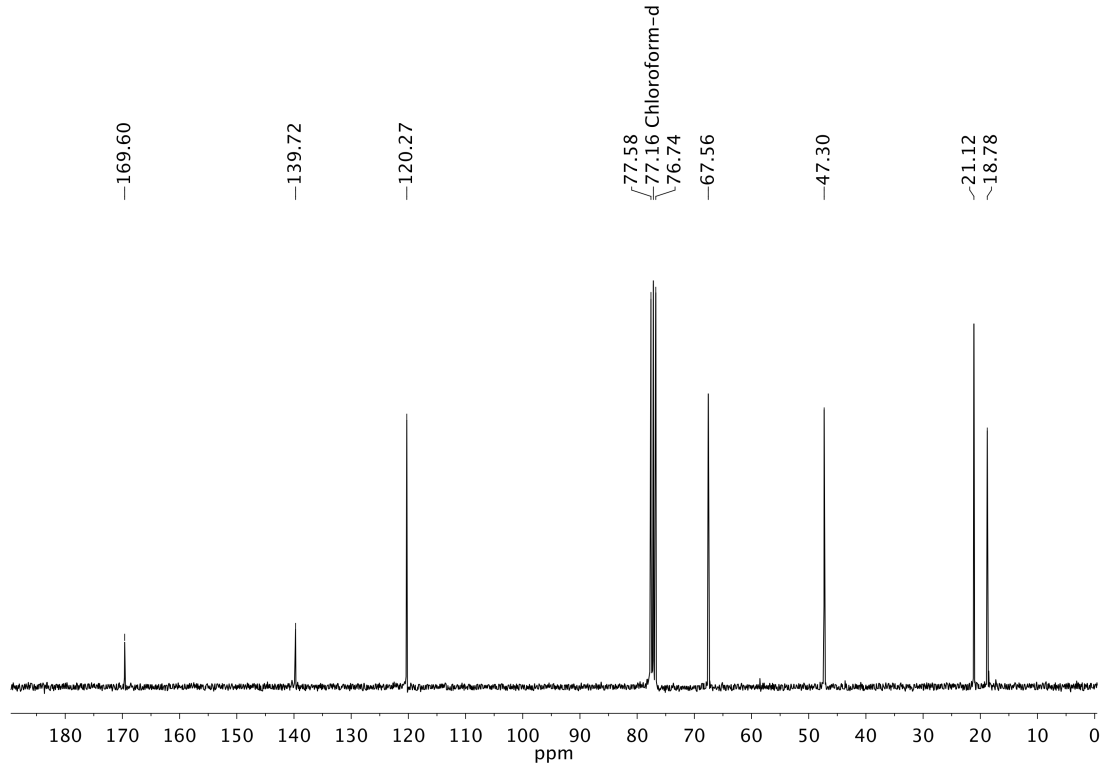



**Figure S7: $^{13}$C-NMR ($CDCl_3$, 75 MHz) 2-Hydroxypropyl methacrylamide**

## 4. Spectroscopic Data of Hyperbranched Polyglycerol Dendrons

**$^{1}$H-NMR hbPG-NBn$_2$**

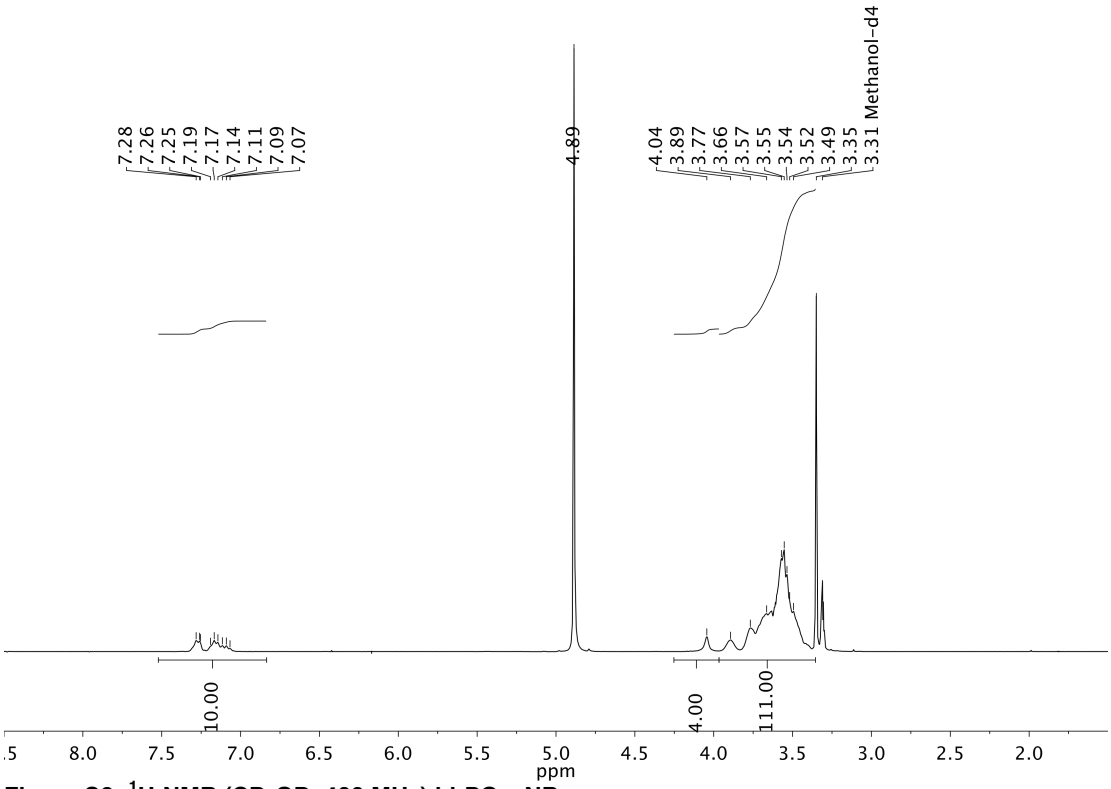



**Figure S8: $^{1}$H-NMR ($CD_3OD$, 400 MHz) hbPG$_{21}$-NBn$_2$**

**Inverse Gated $^{13}$C-NMR hbPG-NBn$_2$**

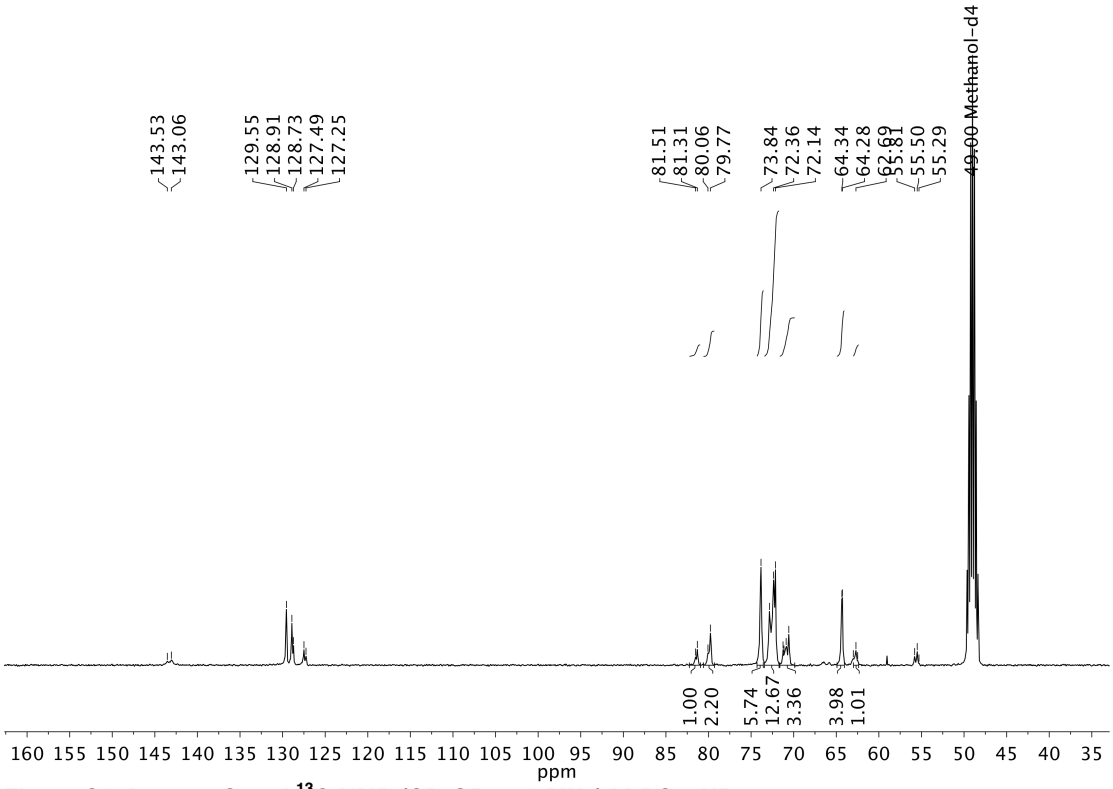



**Figure S9: Inverse Gated $^{13}$C-NMR ($CD_3OD$, 100 MHz) hbPG$_{21}$-NBn$_2$**

**Degree of Branching by Inverse Gated $^{13}$C-NMR of hbPG-NBn$_2$**

| Polymer | $L_{13}$ | $L_{14}$ | D | T | DB* |
|---|---|---|---|---|---|
| $Bn_2$TRIS-hbPG$_{21}$ | 0.10 | 0.29 | 0.22 | 0.39 | 0.53 |
| $Bn_2$TRIS-hbPG$_{32}$ | 0.10 | 0.28 | 0.27 | 0.35 | 0.59 |
| $Bn_2$TRIS-hbPG$_{91}$ | 0.10 | 0.28 | 0.26 | 0.36 | 0.58 |

**Table S1: Inverse Gated $^{13}$C NMR (100MHz, $CD_3OD$) characterization data of benzyl protected hyperbranched polyglycerol dendron analogues – Repeat Units: $L_{13}$=linear-1,3, $L_{14}$: linear-1,4, D: dendritic, T: terminal.[4] *: Degree of branching (DB) determined using the established equation $DB=2D/(2D+L_{13}+L_{14})$.[5]**

**$^1$H-NMR hbPG-NH$_2$**

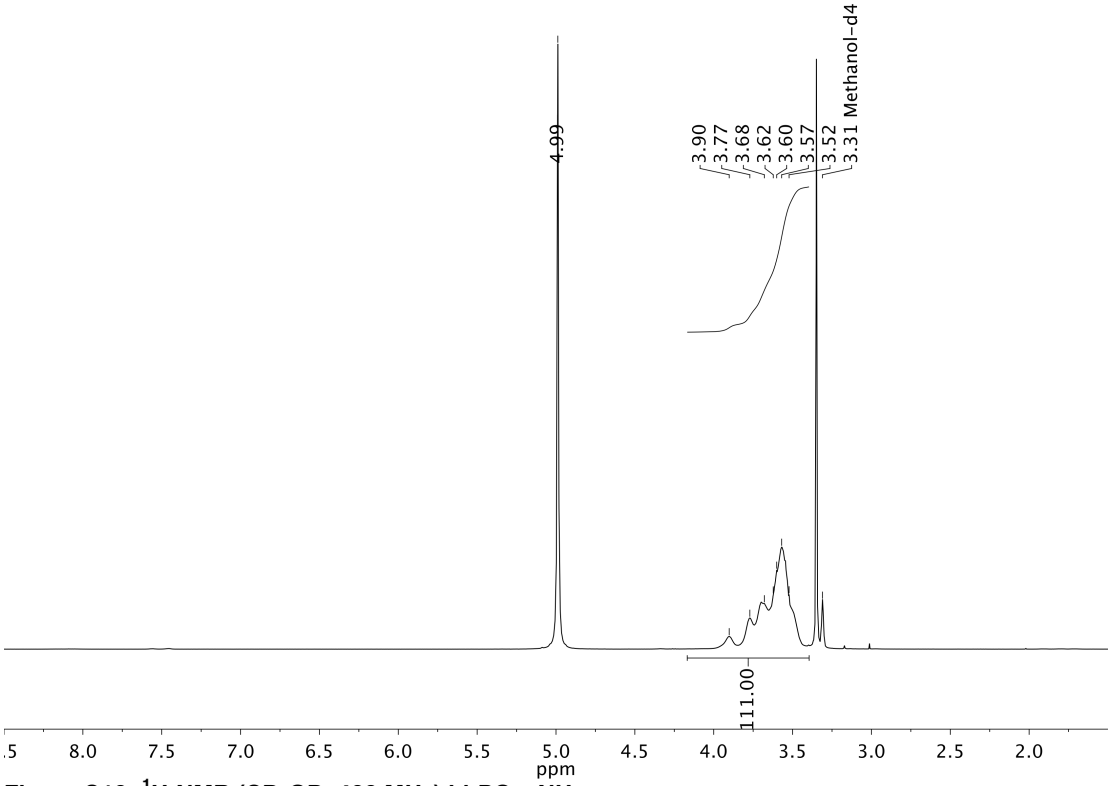



**Figure S10: $^1$H-NMR ($CD_3OD$, 400 MHz) hbPG$_{21}$-NH$_2$**

**$^1$H-NMR hbPG-CTA**

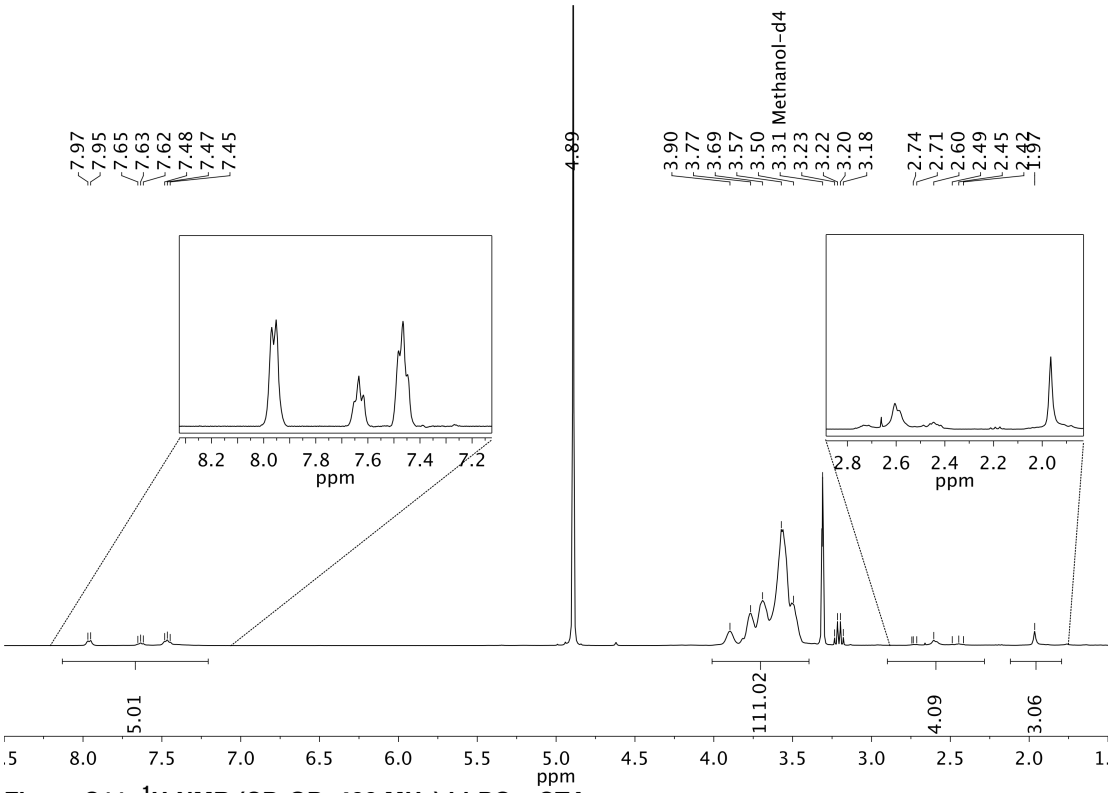



**Figure S11: $^1$H-NMR ($CD_3OD$, 400 MHz) hbPG$_{21}$-CTA**

## 5. Chromatographic and Spectroscopic Data of Linear-Hyperbranched Polyglycerol Block Copolymers

**$^1$H-NMR hbPG-*b*-P(MEO$_3$MA)**

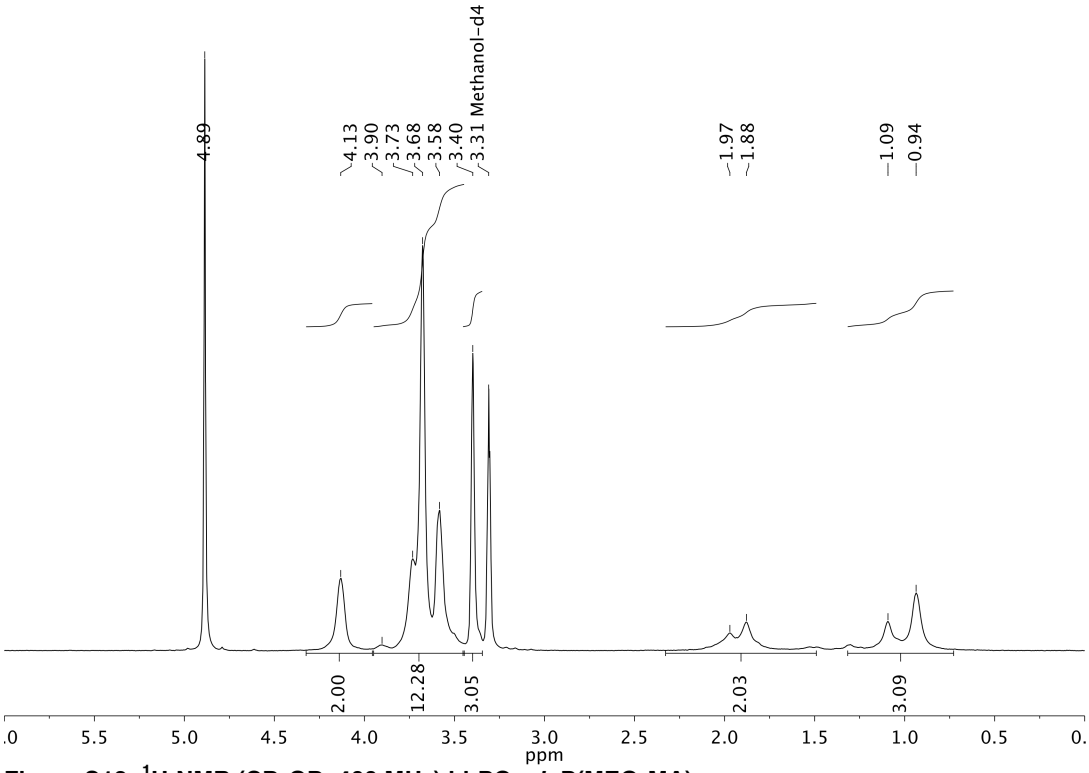



**Figure S12: $^1$H-NMR (CD$_3$OD, 400 MHz) hbPG$_{21}$-*b*-P(MEO$_3$MA)$_{46}$**

**$^1$H-NMR hbPG-*b*-P(HPMA)**

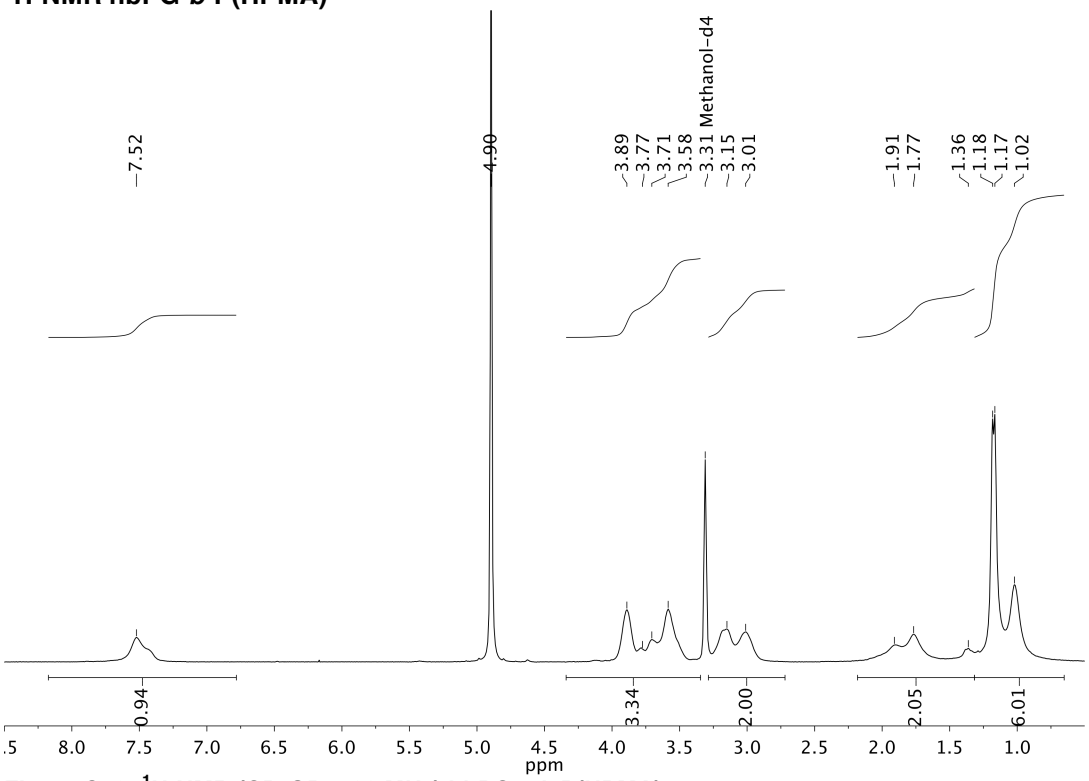



**Figure S13: $^1$H-NMR (CD$_3$OD, 400 MHz) hbPG$_{91}$-*b*-P(HPMA)$_{194}$**

**$^1$H-NMR hbPG-*b*-P(HPMA)-Biotin**

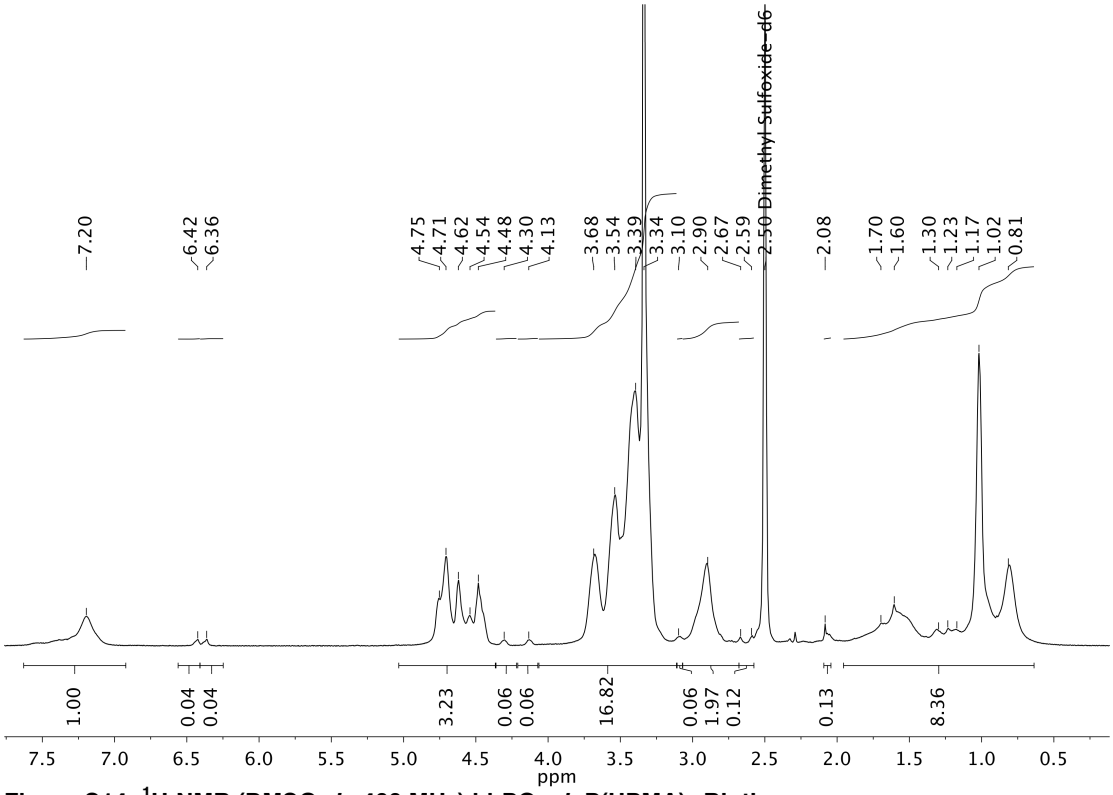



**Figure S14: $^1$H-NMR (DMSO-*d*$_6$, 400 MHz) hbPG$_{21}$-*b*-P(HPMA)$_9$-Biotin**

**Size Exclusion Chromatography of hbPG-*b*-P(HPMA)-Biotin**

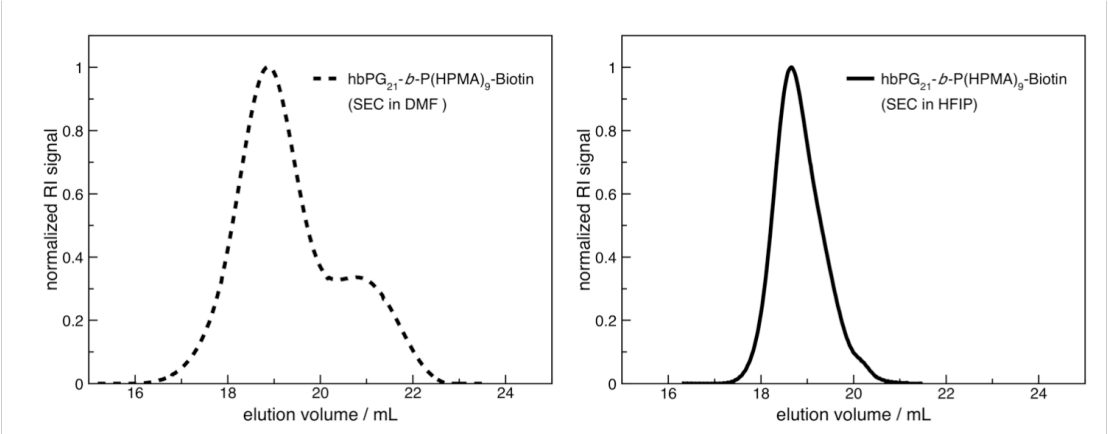



**Figure S15: Elugram size exclusion chromatography of hbPG$_{21}$-*b*-P(HPMA)$_9$-Biotin in DMF (left) and HFIP (right).**

**$^1$H-NMR hbPG-*b*-P(HPMA)-TxRed**

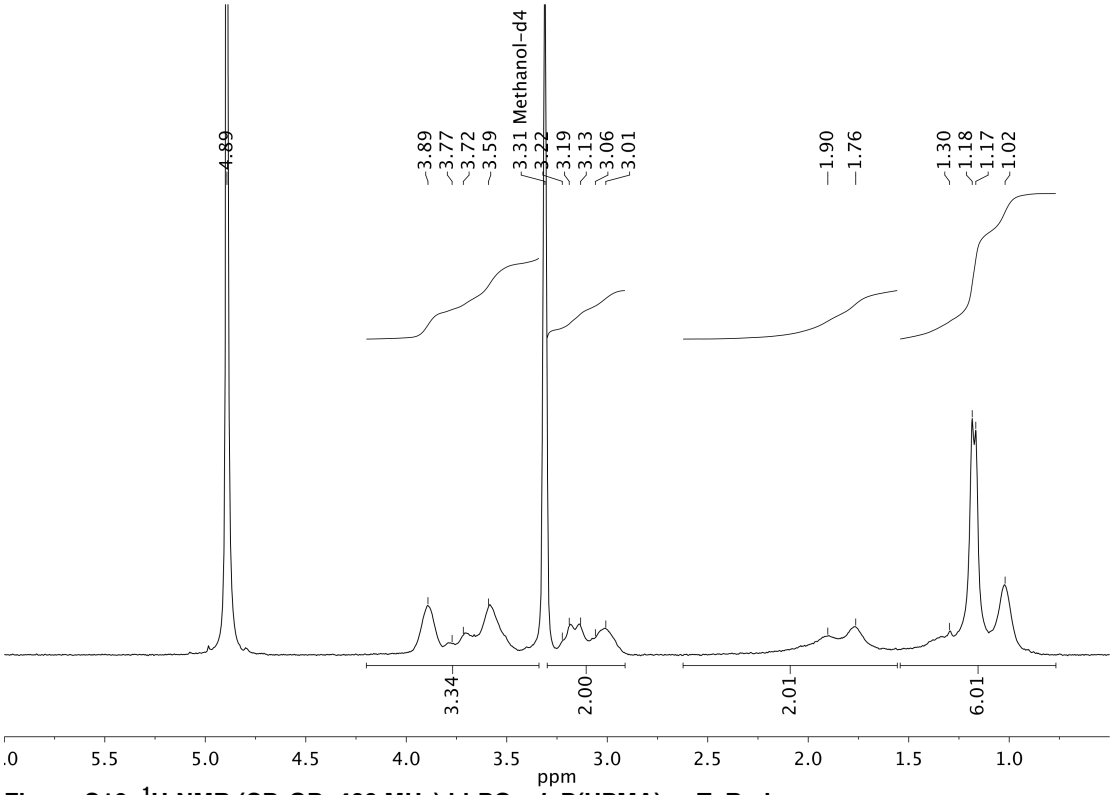



**Figure S16: $^1$H-NMR ($CD_3OD$, 400 MHz) $hbPG_{91}$-*b*-$P(HPMA)_{194}$-TxRed**

**Size Exclusion Chromatography of hbPG-*b*-P(HPMA)-TxRed**

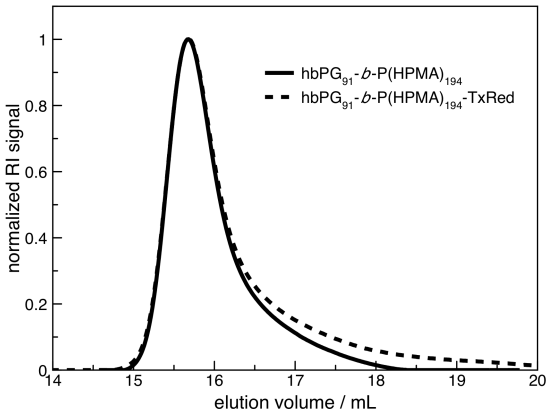



**Figure S17: Elugram size exclusion chromatography of $hbPG_{91}$-*b*-$P(HPMA)_{194}$ and $hbPG_{91}$-*b*-$P(HPMA)_{194}$-TxRed in DMF.**

## References


(1) Roth, P. J.; Wiss, K. T.; Zentel, R.; Theato, P. *Macromolecules* **2008**, *41*, 8513-8519.

(2) Han, S.; Hagiwara, M.; Ishizone, T. *Macromolecules* **2003**, *36*, 8312-8319.

(3) Renner, C.; Piehler, J.; Schrader, T. *Journal of the American Chemical Society* **2005**, *128*, 620-628.

(4) Sunder, A.; Hanselmann, R.; Frey, H.; Mülhaupt, R. *Macromolecules* **1999**, *32*, 4240-4246.

(5) Hölter, D.; Burgath, A.; Frey, H. *Acta Polymerica* **1997**, *48*, 30-35.