Electronic Supplementary Material (ESI) for Chemical Communications

Efficient Synthesis of Multifunctional Polymers via Thiol-epoxy "Click" Chemistry

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General Methods and Materials

Glycidyl methacrylate, 2,2′-azobis(2-methylpropionitril) (AIBN), Lithum hydroxide (LiOH), thiophenol, benzyl mercaptan, triethylene glycol monomethyl ether, 1-naphthylacetic acid, and 1-palmitoyl chloride were purchased from commercial sources. NMR spectra were recorded on Bruker AV500 MHz spectrometers, using $CDCl_3$, CD_2Cl_2, and CH_3OD as the solvent. UV-visible spectroscopic analysis was performed on JASCO V-670 UV-Vis-NIR spectrophotometer using 2.0 mm path length and 0.3 mL volume quartz cuvette. Infrared spectroscopic analyses were carried out using attenuated total reflection (ATR)-Fourier transform infrared (FTIR) spectrometer with OPUS 6 as software (Bruker Optics Alpha system with a built-in diamond ATR). Elemental analyses were performed by the Micro-Laboratory at ETH Zurich using LECO CHN-900.

Synthesis

Poly(glycidyl methacrylate) 1: Glycidyl methacrylate (6 g, 42 mmol) and AIBN (30 mg, 0.18 mmol) were taken in a schlenk tube and purged with N_2 gas for 40 min. The polymerization was carried out at 50 °C for 20 min. The polymerization mixture was cooled to room temperature, diluted with CH_2Cl_2, and precipitated into methanol 3 times and dried under vacuum to give 0.7 g of the polymer. ^{1}H-NMR (δ, ppm, 500 MHz, CD_2Cl_2): 0.60-1.20 (m, 3H), 1.85-1.96 (m, 2H, $\mathbf{CH_2}CCH_3$), 2.60 (s, 1H, $COOCH_2CH\mathbf{CH_2}O$), 2.80 (s, 1H, $COOCH_2CH\mathbf{CH_2}O$), 3.20 (s, 1H, $CH_2\mathbf{CH}CH_2O$), 3.75 (bs, 1H, $COO\mathbf{CH_2}$), 4.28 (bs, 1H, $COO\mathbf{CH_2}$); ^{13}C-NMR (δ, ppm, 125 MHz, CD_2Cl_2): 18.8, 29.8, 44.5-45.2, 48.9-49.1, 65.8-66.1, 176.4-177.4; Elemental analysis (%) calcd: C 59.14, H 7.09, O 33.76; found: C 58.91, H 6.99, O 33.77; IR (cm^{-1}): 756, 843, 905, 990, 1139, 1254, 1726; GPC ($CHCl_3$): M_n = 1.8×10^6, M_w = 3.2×10^6, PDI (M_w/M_n) = 1.8 (Figure S1).

Polymer 2 (Solvent-free protocol): To an ice cold solution of 0.3 g poly(glycidyl methacrylate), **1**, and thiophenol (0.47 g, 4.3 mmol), LiOH (44 mg, 1.1 mmol) was added slowly, the cooling was removed and the resulting reaction mixture was stirred at room temperature for 3 h. Then, water (5 mL) was added, and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The CH_2Cl_2 solution was then concentrated and precipitated into methanol 3 times and dried. Yield = 0.43 g (80%). ^{1}H-NMR (δ, ppm, 500 MHz, CD_2Cl_2): 0.60-1.24 (m, 3H), 1.80-1.96 (m, 2H, $\mathbf{CH_2}CCH_3$), 3.02 (s, 2H, $\mathbf{CH_2}S$), 3.62 (bs, 1H, $CH(\mathbf{OH})CH_2S$), 3.93 (s, 2H, $COO\mathbf{CH_2}$), 4.08 (s, 1H, $\mathbf{CH}(OH)CH_2S$), 7.16-7.34 (m, 5H, -S**Ph**); ^{13}C-NMR (δ, ppm, 125 MHz, CD_2Cl_2): 18.0, 37.6, 45.2, 67.7, 68.0, 126.8,129.3-129.9,

135.5,177.0-177.5; IR (cm^{-1}): 690, 745, 1146, 1238, 1580, 1726 ; GPC ($CHCl_3$): M_n = 2.4×10^6, $M_w = 5.3\times10^6$, PDI (M_w/M_n) = 2.2.

Polymer 2 (in-solvent protocol): To an ice cold solution of 20 mg of poly(glycidyl methacrylate), **1**, and thiophenol (15.5 mg, 0.14 mmol) in 1 mL THF, LiOH (2.95 mg, 0.07 mmol) was added slowly, the cooling was removed and the resulting mixture was stirred at room temperature for 12 h. Then, water (2 mL) was added, and the aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL). The CH_2Cl_2 solution was then concentrated and precipitated into methanol and dried. Yield = 28 mg (78%).

Polymer 3: 0.1 g of Polymer **2** was taken in dry THF (5 mL) and stirred at 0 °C for 5 min. Then, Et_3N (0.12 g, 1.2 mmol) and catalytic amount of DMAP was added. After 10 min, 1-naphthylacetyl chloride[1] (0.24 g, 1.2 mmol) in dry THF (5 mL) was added dropwise. The cooling was removed and the resulting reaction mixture was stirred at room temperature for 12 h. After which time, the contents were poured into acidic ice-cold water and extracted with CH_2Cl_2. The resulting solution was then concentrated and precipitated into methanol 3 times to give 0.16 g of polymer **3**. (yield = 94 %). ^{1}H-NMR (δ, ppm, 500 MHz, CD_2Cl_2): 0.55-1.20 (bm, 3H), 1.70-1.99 (m, 2H, **CH$_2$**CCH$_3$), 2.60-3.14 (bs, 2H, **CH$_2$**S), 3.60-4.21 (bm, 4H, COO**CH$_2$**CH(OCO**CH$_2$**Nap)CH$_2$S), 5.07 (bs, 1H, **CH**(OCOCH$_2$Nap)CH$_2$S), 6.58-8.12 (m, 12H, CH(OCOCH$_2$**Nap**)CH$_2$S **Ph**); ^{13}C-NMR (δ, ppm, 125 MHz, CD_2Cl_2): 18.0, 34.4, 37.4, 38.6, 45.0, 67.9, 70.5, 124.0-135.6, 177.0-177.5; IR (cm^{-1}): 690, 745, 1146, 1238, 1580, 1726. GPC ($CHCl_3$): $M_n = 6.1\times10^6$, $M_w = 1.0\times10^7$, PDI (M_w/M_n) = 1.7.

Polymer 6: 2-(2-(2-Methoxyethoxy)ethoxy)ethanethiol, **4**, was prepared according to the literature procedure.[2] Reaction of **4** with polymer **1**, according to the procedure described above (solvent-free protocol, precipitation from ether), gave polymer **6**. ^{1}H-NMR (δ, ppm, 500 MHz, $CDCl_3$): 0.60-1.24 (m, 3H), 1.80-2.18 (bs, 2H, **CH$_2$**CCH$_3$), 2.60-2.99 (m, 4H, **CH$_2$SCH$_2$**), 3.40 (s, 3H, **CH$_3$**OCH$_2$), 3.50-4.46 (m, 14H, **CH$_2$CH**(**OH**)CH$_2$SCH$_2$**CH$_2$**(O**CH$_2$CH$_2$**)$_2$OCH$_3$) (Figure S4).

Polymer 7: Reaction of benzylmercaptan, **5**, with polymer **1**, according to the procedure described above (solvent-free protocol, precipitation from methanol), gave polymer **7**. ^{1}H-NMR (δ, ppm, 500 MHz, $CDCl_3$): 0.60-1.24 (m, 3H), 1.80-1.96 (m, 2H, **CH$_2$**CCH$_3$), 2.52 (s, 1H, **CH$_2$**SCH(OH)), 3.50 (bs, 1H, CH(**OH**)CH$_2$S), 3.71 (s, 2H, S**CH$_2$**Ph), 3.87 (s, 2H, COO**CH$_2$**), 4.03 (s, 1H, **CH**(OH)CH$_2$S), 7.16-7.34 (m, 5H, - SCH$_2$**Ph**) (Figure S5).

Polymer 8: 50 mg of Polymer **6** and DMAP (5.0 mg, 0.04 mmol) was taken in dry THF (3 mL) and stirred in ice-water bath for 5 min. Then, Et_3N (60 mg, 0.60 mmol) was added dropwise. After 10 min, 1-palmitoyl chloride (164 mg, 0.60 mmol) in dry THF (3 mL) was added dropwise. The cooling was removed and the reaction mixture was stirred at room temperature for 12 h. After which time, the contents were poured into acidic ice-cold water and extracted with CH_2Cl_2. The resulting solution was then concentrated and precipitated into methanol to give 88 mg of compound **8** (yield = 79 %). ^{1}H-NMR (δ, ppm, 500 MHz, $CDCl_3$): 0.88 (t, 6H), 1.26 (bs, 26H), 1.62 (bs, 4H), 2.32 (bs, 2H), 2.77 (bs, 4H), 3.38 (s, 3H), 3.54-3.64 (bs, 8H), 4.10 (bs, 2H), 5.15 (bs, 1H) (Figure S4).

Polymer 9: Reaction of 2-mercaptoethanol, with polymer **1**, according to the procedure described above (solvent-free protocol, precipitation from acetonitrile), gave polymer **9**. ^{1}H-NMR (δ, ppm, 500 MHz, MeOD): 0.60-1.24 (m, 3H), 1.80-2.05 (m, 2H, **CH_2**CCH_3), 2.79 (bs, 4H, **CH_2SCH_2**), 3.77 (bs, 2H, SCH_2**CH_2**), 4.01 (bs, 3H, O **CH_2CH**(OH)) (Figure S6).

Polymer 10: Reaction of 2-mercaptoacetic acid methyl ester, with polymer **1**, according to the procedure described above (solvent-free protocol), gave polymer **10**. ^{1}H-NMR (δ, ppm, 500 MHz, MeOD): 0.60-1.24 (m, 3H), 1.80-2.05 (m, 2H, **CH_2**CCH_3), 2.79 (bs, 2H, **CH_2**SCH_2CO), 3.13 (s, 2H, S**CH_2**CO), 3.27 (s, 1H, SCH_2CH(**OH**)), 3.37 (s, 3H, O**CH_3**), 4.01 (bs, 3H, O **CH_2CH**(OH)) (Figure S7).

Thiol end-functional PEG 12: To a solution of poly(ethylene glycol) diglycidyl ether (M_n = 500, M_w = 800, PDI (M_w/M_n) = 1.6), **11**, (2 g, 4 mmol) and 4-methoxybenzyl mercaptan (2.4 g, 16 mmol), LiOH (168 mg, 4 mmol) was added at 0 °C. After the addition, cooling was removed and the reaction mixture was stirred at room temperature for 3 h. Then water (20 mL) was added, and the crude product was extracted with CH_2Cl_2 (2 × 20 mL) and purified by column chromatography (DCM/MeOH; 9.5:0.5) to yield 3.0 g of polymer **12** (Yield = 94%). ^{1}H-NMR (δ, ppm, 500 MHz, $CDCl_3$): 2.53-2.60 (m, 4H, CH(OH)**CH_2**S), 3.46-3.79 (bs, 44H, O**CH_2CH_2**O and **CH_2**$CH(OH)CH_2S$**CH_2**), 3.85 (s, 6H, Ph**CH_3**), 3.93 (s, 2H, **CH**$(OH)CH_2S$), 6.86 (d, 4H, SCH_2**Ph**), 7.24 (d, 4H, SCH_2**Ph**); ^{13}C-NMR (δ, ppm, 125 MHz, $CDCl_3$): 34.5, 36.2, 55.5, 69.2-70.5, 73.2-73.6, 74.5, 114.2, 130.2, 130.4, 158.8; GPC ($CHCl_3$): M_n = 800, M_w = 1000, PDI (M_w/M_n) = 1.2 (Figure S9); End group claculations were performed on the MALDI-TOF-MS data using Polytools 2.0 software from Bruker Daltonics; repeat unit: 44, end group 1: 227, end group 2: 211.

Thiol and Naphthalene end-functional PEG 13: Polymer **12** (1 g, 1.2 mmol) was taken in dry THF (5 mL) and stirred in ice-water bath for 5 min. Then, Et_3N (0.726 g, 7.2 mmol) was added dropwise. After 10 min, 1-naphthylacetyl chloride (1.46 g, 7.2 mmol) in dry THF (5 mL) was added dropwise. The reaction mixture was stirred at room temperature for 12 h. After which time, contents were poured into acidic ice-cold water and extracted with CH_2Cl_2. The resulting solution was then concentrated and the product was purified by column chromatography (DCM/MeOH; 9.5:0.5) to yield 1.2 g of polymer **13** (Yield = 86%). ^{1}H-NMR (δ, ppm, 500 MHz, $CDCl_3$): 2.52-2.60 (m, 4H, CH(OH)**CH_2**S), 3.41-3.69 (bm, 44H, O**CH_2CH_2**O and **CH_2**CH(OH)CH_2S**CH_2**), 3.77 (s, 6H, Ph**CH_3**), 4.10 (s, 4H, **CH_2**Nap), 5.12 (m, 2H, **CH**($OCOCH_2$Nap), 6.78 (d, 4H, SCH_2**Ph**), 7.13 (d, 4H, SCH_2**Ph**), 7.41-7.53 (m, 8H, **Nap**), 7.76-7.98 (m, 4H, **Nap**), 8.01 (m, 2H, **Nap**); ^{13}C-NMR (δ, ppm, 125 MHz, $CDCl_3$): 34.9, 36.9, 39.4, 55.5, 70.1-71.1, 72.5, 114.2, 124.1-134.0, 158.8, 171.2; GPC ($CHCl_3$): M_n = 1200, M_w = 1500, PDI (M_w/M_n) = 1.2 (Figure S9); End group claculations were performed on the MALDI-TOF-MS data using Polytools 2.0 software from Bruker Daltonics; repeat unit: 44, end group 1: 395, end group 2: 379.

Table 1. Solubility behavior of the polymers (++ = high solubility, + = good solubility, - = insoluble).

Polymer	Heptane	Toluene	$CHCl_3$	CH_2Cl_2	CH_3CN	CH_3OH	H_2O
1	-	-	++	++	++	-	-
2	-	-	++	++	+	-	-
3	-	-	++	++	+	-	-
6	-	-	+	+	++	++	-
7	-	-	++	++	+	-	-
8	++	++	++	++	-	-	-
9	-	-	-	-	-	++	++

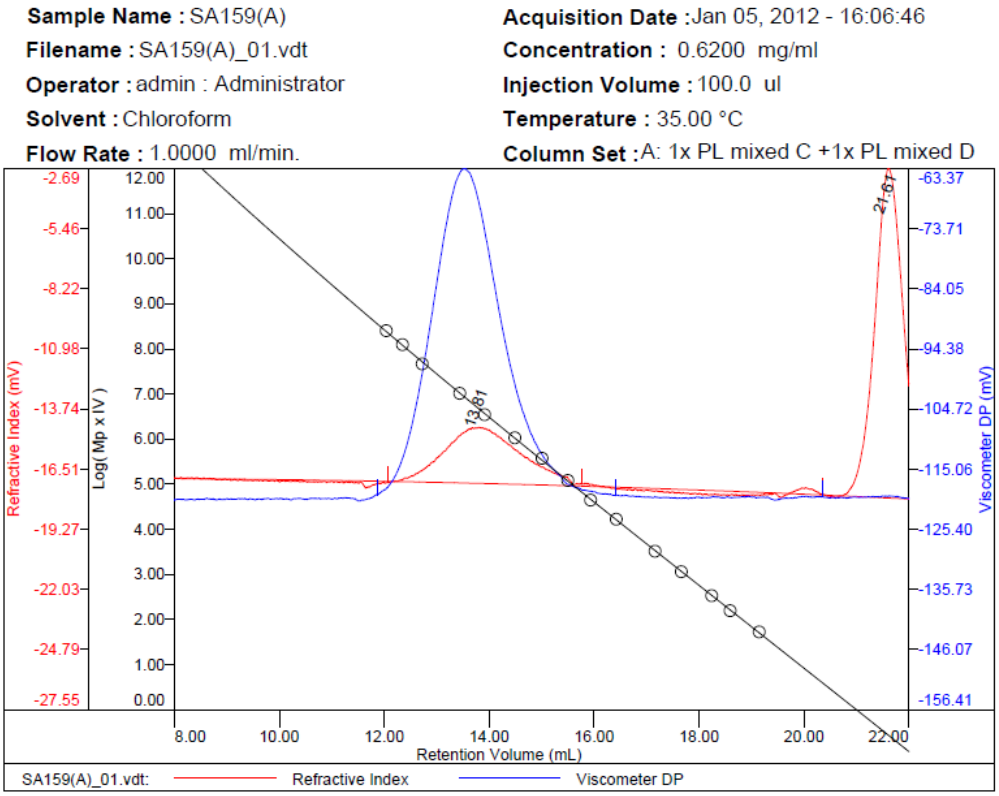

Figure S1. GPC profile of polymer **1** ($CHCl_3$). PS calibration curve can also be seen.

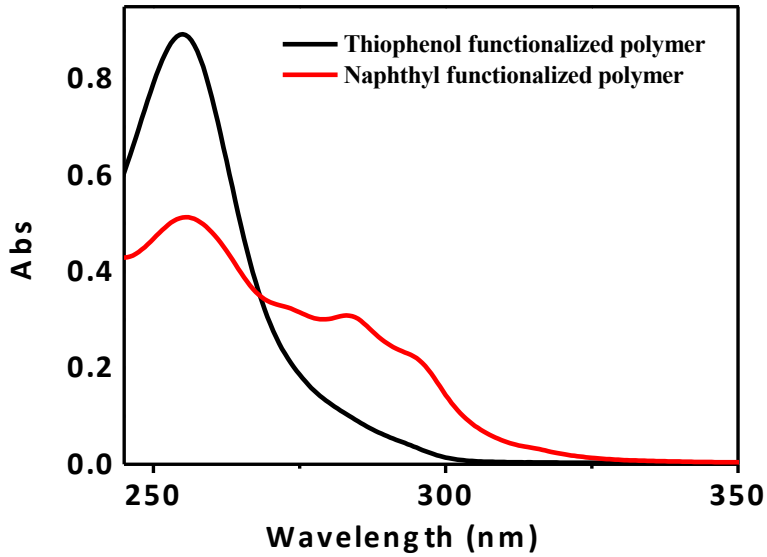

Figure S2. UV-Vis spectra of thiophenol functionalized polymethacrylate, **2**, (black-0.3mg/mL) and naphthyl functionalized polymethacrylate, **3**, (red-0.1mg/mL) in Chloroform.

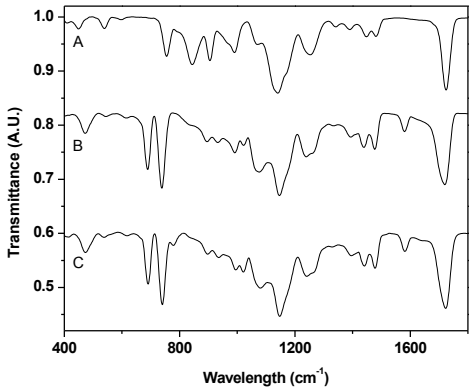

Figure S3. IR spectra of polymer **1** (A), polymer **2** (B), and polymer **3** (C).

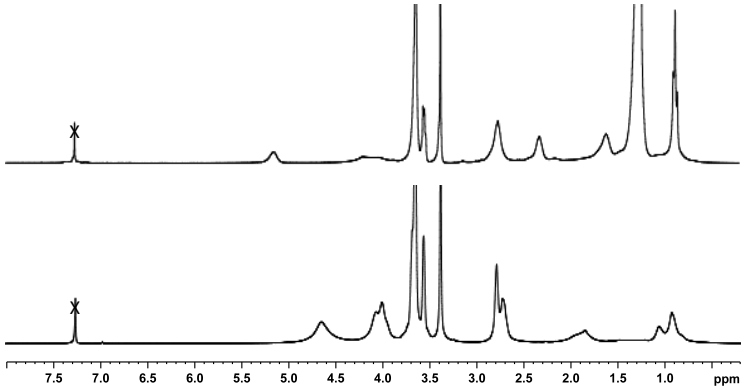

Figure S4. ^{1}H-NMR of polymer **6** (bottom) and **8** (top) in $CDCl_3$. Solvent peak are shown with a cross sign.

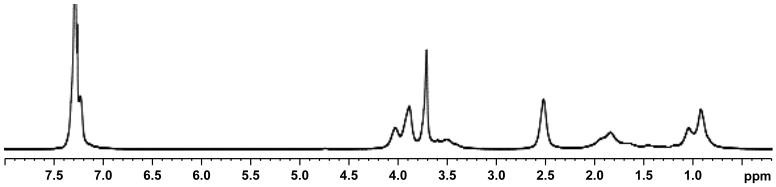

Figure S5. ^{1}H-NMR of polymer **7** in $CDCl_3$.

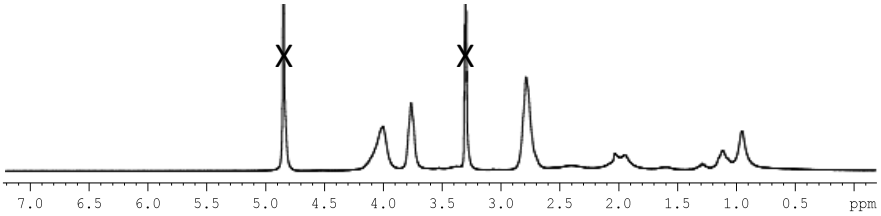

Figure S6. ^{1}H-NMR of polymer **9** in MeOD. Solvent peaks are shown with a cross sign.

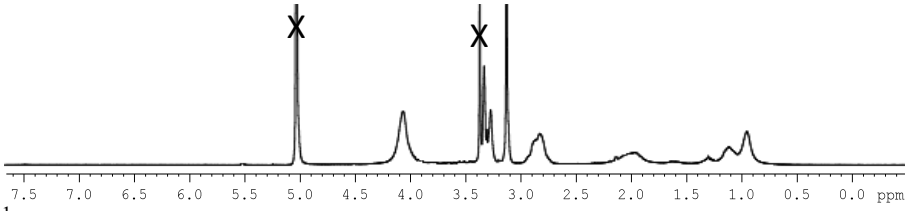

Figure S7. ^{1}H-NMR of polymer **10** in MeOD. Solvent peaks are shown with a cross sign.

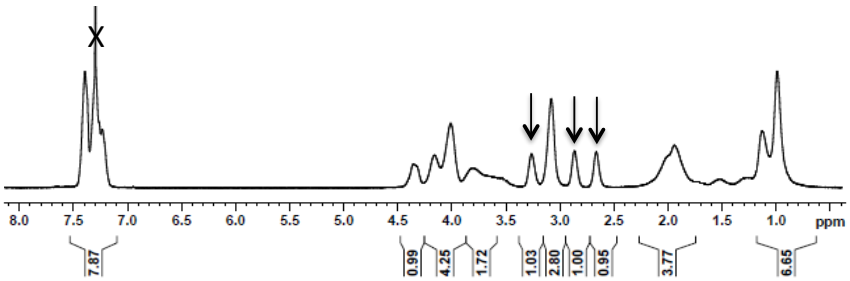

Figure S8. ^{1}H-NMR of polymer **1** after modification with 0.6 equiv. of thio-phenol (using 'in-solvent' protocol). The unreacted epoxy proton resonances are shown with arrows.

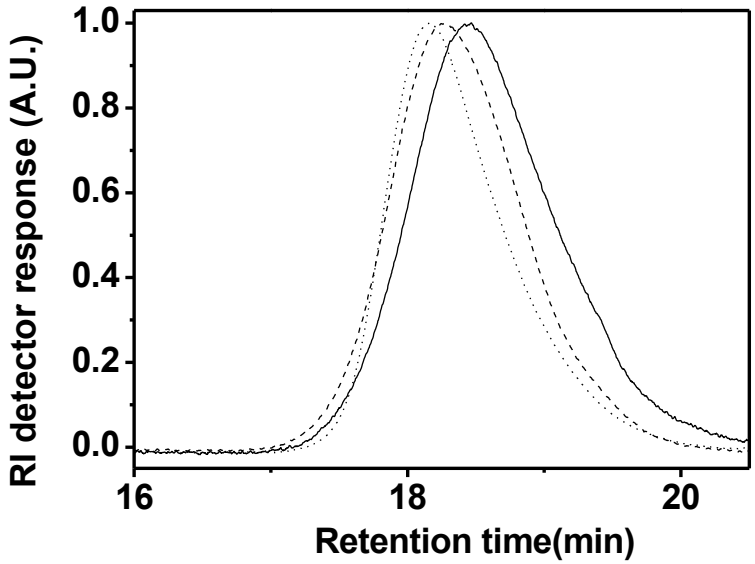

Figure S9. GPC profiles of poly(ethylene glycol) diglycidyl ether, **11** (solid line), modified with 4-methoxybenzyl mercaptan to give **12** (dash line), and after second modification with naphthylacetyl chloride to give **13** (dot line), in $CHCl_3$ against PS standards.

References:

1. C. Hass, B. Kirste, H. Kurreck, and G. Schloemp. *J. Am. Chem. Soc.*, 1983, **105**, 7375-7383.

2. (*a*) C.Wendeln, S. Rinnen, C. Schulz, H. F. Arlinghaus, and B. J. Ravoo, *Langmuir*, 2010, **26**, 15966-15971; (*b*) S. S. Erdem, I. V. Nesterova, S. A. Soper, and R. P. Hammer, *J. Org. Chem.*, 2009, *74*, 9280-9286.