Supporting Information

Reactive Block Copolymer Scaffolds

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Experimental Section

General Information. 2,2'-Azobisisobutyronitrile (AIBN) was recrystallized from methanol twice. Cumyl dithiobenzoate (CDB),[1] *p*-nitrophenyl methacrylate (NPMA),[2] and 3,3'-diethoxypropyl methacrylate (DEPMA)[3] were prepared according to literature procedures. Otherwise, chemicals were purchased from Aldrich and used as received. ^{1}H NMR spectra were recorded on a Bruker ARX 500 MHz, AVANCE 500 MHz, or ARX 600 MHz spectrometer. GPC data were obtained using a Shimadzu LC-10ATvp pump equipped with RID-10A detectors using HPLC grade 0.1 M LiBr in DMF or THF at 40 or 25 ºC, respectively, as the mobile phase with two 300 mm Polymer Laboratories 5μm mixed beads columns. A constant flow rate of 0.8 mL/min was maintained, and the instrument was calibrated using poly(methyl methacrylate) standards. UV-Vis spectra were recorded on a ThermoSpectronic Biomate 5 spectrometer (polymer) or Agilent 8453

UV-Vis Spectrophotometer (CDB). Infrared spectra were recorded on a Perkin-Elmer Spectrum One FT-IR spectrophotometer fit with an ATR assessor.

Poly(*p*-nitrophenyl methacrylate), 1. In a 25 mL Schlenk flask, NPMA (300 mg, 1.5 mmol), AIBN (5 mg, 0.03 mmol), and CDB (39 mg, 0.15 mmol) were degassed by three freeze-pump-thaw cycles and degassed DMSO (50 % w/v) was added. The mixture was then immersed in an oil bath at 70 °C and stirred for 3 h. The polymers were diluted in acetone and precipitated in diethyl ether (25 mL), filtered, and dried under vacuum to yield a light pink colored solid.

Kinetic study of NPMA. Using DMSO-d_6 as the solvent, the same polymerization conditions to form **1** above were employed for the kinetic study. The reaction was periodically sampled for ^{1}H NMR analysis. These same samples were used for GPC after removal of the solvent and redissolution in DMF. Conversions were determined by comparison of integrations of the vinylic peaks of the monomer at 5.96 and 6.33 with the aromatic proton peaks at 7.31 and 8.16 ppm

Chain extension of 1. Polymer **1** was prepared as described above with a M_n (DMF) = 7,400 and PDI = 1.21. A Schlenk flask was then charged with this polymer (140 mg, 0.018 mmol), AIBN (0.6 mg, 0.0038 mmol), and NPMA (700 mg, 3.4 mmol), dissolved in DMSO (33 % w/v) and degassed by three freeze-pump-thaw cycles. The mixture was then immersed in an oil bath at 70 °C and stirred for 20 h. The polymer was diluted with

acetone and then precipitated in diethyl ether (25 mL), filtered, and dried under vacuum to yield a light pink colored solid of pNPMA (M_n (DMF) = 29,000 and PDI = 1.19).

Kinetic study of poly(3,3'-diethoxypropyl methacrylate). In a 25 mL Schlenk flask, DEPMA (336 mg, 1.55 mmol), AIBN (2.4 mg, 0.015 mmol), and CDB (16 mg, 0.072 mol) were dissolved in DMF (50% v/v) and degassed by three freeze-pump-thaw cycles. The mixture was then immersed in an oil bath at 70 °C and periodically sampled and diluted with CD_3OD for ^1H NMR analysis. Conversion was calculated by comparison of the integration of the peaks corresponding to the methylene protons of the acetal (3.56 and 3.40 ppm) with the monomer alkene peaks (5.45 and 5.98 ppm). The solvent was removed from these same samples and diluted in THF for analysis by GPC. The results of the polymerization are depicted in Figure S1.

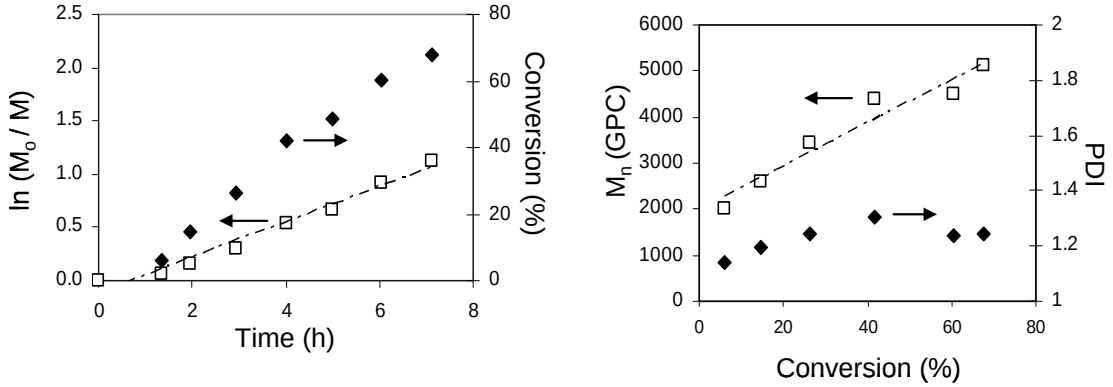

Figure S1. (a) Kinetic plot and (b) M_n and PDI with respect conversion for RAFT polymerization of DEPMA (100:5:1 of DEPMA:CDB:AIBN) at 70 °C in DMF.

Block copolymer synthesis, 2. In a 25 mL Schlenk flask, **1** (200 mg, 0.028 mmol, M_n (GPC (DMF) = 7000 and PDI = 1.22), AIBN (1 mg, 0.006 mmol) and DEPMA (246 mg, 1.14 mmol) were dissolved in DMF (50% w/v) and degassed by three freeze-pump-thaw

cycles. The mixture was then immersed in an oil bath at 70 °C and stirred for 15 h. The polymer was precipitated into hexanes and extensively dialyzed in methanol prior to drying *in vacuo* to obtain **2** (100 mg, 86%), M_n (GPC, THF) = 12000, PDI = 1.24. The GPC trace is provided as Figure S2. ^{1}H NMR (CD_3CN): δ 8.10 ($C_6H_4NO_2$), 7.24 ($C_6H_4NO_2$), 4.57 (CH), 3.95 ($COOCH_2$), 3.62, 3.47 ($OC\underline{H}_2CH_3$), 1.85-1.77 ($\underline{H}_2CC(CH_3)$ and $COOCH_2C\underline{H}_2CH$), 1.59-0.81 ($H_2CC(C\underline{H}_3)$ and $OCH_2C\underline{H}_3$). Composition was determined by comparison of the integrals of the aromatic proton peaks at 8.10 and 7.24 ppm with the CH peak of the acetal at 4.57 ppm. FT-IR: 2976, 2931, 1753, 1726, 1615, 1591, 1523, 1489, 1445, 1374, 1347, 1202, 1160, 1111, 1087, 1053, 970, 951, 887, 862, 745, 687 cm^{-1}.

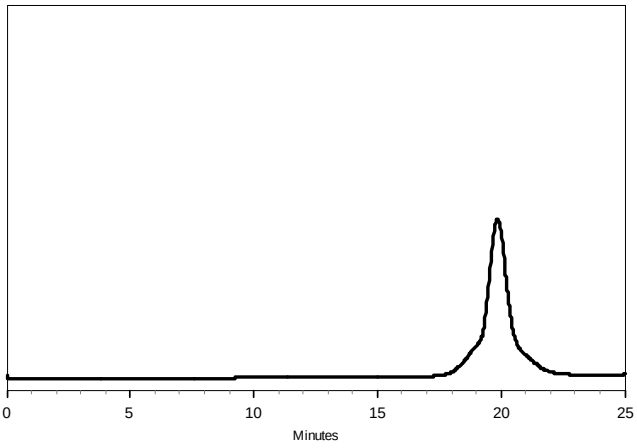

Figure S2. GPC trace of block copolymer **2**, THF as the eluent.

Block Functionalization, 3. Block copolymer **2** (33 mg, 0.063 mmol of NPMA repeat unit) was dissolved in DMSO (200 μL). Allylamine (49 mg, 0.86 mmol) and triethylamine (87 mg, 0.86 mmol) were added the reaction stirred at 50 °C for 3 h. The reaction was then cooled and the reaction dialyzed against MeOH. The polymer was then isolated by drying under vacuum to yield **3** (26 mg, 95%). Yield was based upon the

substitution calculated by ^{1}H NMR. ^{1}H NMR (CD_3CN): δ 5.82, 5.70 ($NCH_2C\underline{H}CH_2$), 5.17-5.06 ($NCH_2CHC\underline{H}_2$), 4.59 (CH), 4.15 ($NC\underline{H}_2CHCH_2$), 3.96 ($COOCH_2$), 3.63, 3.48 ($OC\underline{H}_2CH_3$), 1.86-1.79 (($\underline{H}_2CC(CH_3)$ and ($COOCH_2C\underline{H}_2CH$), 1.44-0.82 ($H_2CC(C\underline{H}_3)$ and $OCH_2C\underline{H}_3$). Substitution was calculated by comparison of the integrals of the vinylic proton peaks at 5.82-5.06 ppm with the CH acetal peak at 4.59 ppm. FT-IR: 3407, 2975, 2930, 2900, 1727, 1667, 1523, 1481, 1445, 1375, 1347, 1327, 1269, 1241, 1124, 1081, 1059, 976, 848, 750 cm^{-1}.

Block Functionalization, 4. Block copolymer **3** (26 mg, 0.092 mmol of DEPMA repeat unit) was dissolved in DMSO (200 μL) followed by TFA (200 μL). After 20 min, *O*-benzylhydroxylamine hydrochloride (105 mg, 0.66 mmol) and sodium acetate (54 mg, 0.66 mmol) were added and stirred at 50 °C. After 3 h, the reaction was cooled, diluted with MeOH, and dialyzed against methanol to yield **4** a white solid (27 mg, 98%). Yield was based upon the substitution calculated by ^{1}H NMR. M_n (GPC, THF) = 11,200, PDI = 1.22. A high molecular weight shoulder was observed in the GPC trace (Figure S3). Aminolysis of CTA end groups by alkyl amines is well known, and it is reported that oxidation of the remaining thiol to the disulfide readily occurs.[4] It is likely that the allylamine utilized in the first step of block copolymer modification converted the dithioester end of the block copolymer to a thiol group via aminolysis. The slight shoulder observed in the GPC could be due to the oxidized product. ^{1}H NMR (DMSO-d_6): δ 7.71, 6.74 (CHCNO), 7.41 ($C_6\underline{H}_5$)), 5.75, 5.64 ($NCH_2C\underline{H}CH_2$), 5.01-4.96 ($NCH_2CHC\underline{H}_2$ and CH_2Ph), 3.98 ($NC\underline{H}_2CHCH_2$ and $COOCH_2$), 2.56-2.38 ($OCH_2C\underline{H}_2$), 1.78-1.65 ($\underline{H}_2CC(CH_3)$), 1.22-0.72 ($H_2CC(C\underline{H}_3)$). Substitution was calculated by

comparison of the integrals of the oxime and benzyl aromatic peaks at 7.71-6.74 ppm with the CH_2 of the polymer backbone at 1.78-1.65 ppm. FT-IR: 3416, 3086, 3064, 3031, 2957, 2929, 1726, 1666, 1523, 1470, 1454, 1388, 1366, 1329, 1262, 1238, 1176, 1150, 1080, 1042, 1014, 985, 918, 841, 802, 749, 699 cm^{-1}.

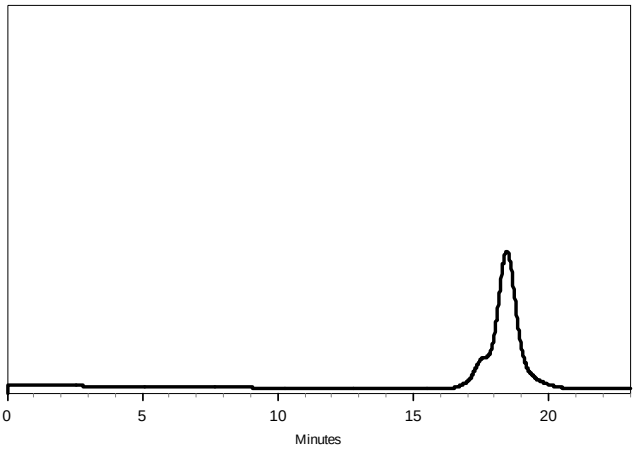

Figure S3. GPC trace of block copolymer **4**, THF as the eluent.

References

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2. Kiser, P. F.; Wilson, G.; Needham, D. *J. Control. Release* 2000, **68**, 9-22.
3. Zábranský, J.; Houska, M.; Kálal, J. *Makromol. Chem.* 1985, **186**, 215-222.
4. For example see: Qiu, X. P.; Winnik, F. M. *Macromolecules* 2007, **40**, 872-878.