Supporting information for:

Clickable PEG-*branch*-azide bivalent-bottle-brush polymers by ROMP: grafting-through and -to

Jeremiah A. Johnson,[†] Ying Y. Lu,[†] Alan O. Burts,[†] Yeon-Hee Lim,[‡] M.G. Finn,[‡] Jeffrey T. Koberstein, Nicholas J. Turro,[#] David A. Tirrell, [†,] Robert H. Grubbs[†,]**

Division of Chemistry and Chemical Engineering, California Institute of Technology, 1200 E. California Blvd., Pasadena, California 91125, Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92037, Department of Chemical Engineering, Columbia University, 500 West 120th Street, New York, New York, 10027, and Department of Chemistry, Columbia University, 3000 Broadway, New York, New York 10027

Materials and methods

All reagents and solvents were purchased from Aldrich or VWR and used as supplied unless otherwise noted. Ruthenium catalyst **1**[1] and 3-(*tert*-butyldimethylsilyloxymethyl)-2-nitrobenzoic acid **8**[2] were prepared according to literature procedures. Degassed dichloromethane (DCM), tetrahydrofuran (THF), and dimethyl sulfoxide (DMSO) were passed through solvent purification columns prior to use.[3] Doxorubicin hydrochloride (**DOX**-HCl) was purchased from Axxora LLC.

Gel permeation chromatography (GPC) was performed using two I-series Mixed Bed Low MW ViscoGel columns (Viscotek) connected in series with a DAWN EOS multiangle laser light scattering (MALLS) detector (Wyatt Technology) and an Optilab DSP differential refractometer (Wyatt Technology). Experiments were performed at room temperature using 0.2 M LiBr in *N,N*-dimethylformamide (DMF) eluant at a flow rate of 1 mL / min. Molecular weights were calculated from *dn/dc* values that were obtained assuming 100% mass elution from the columns. Dynamic light scattering (DLS) measurements were made at room temperature using a Brookhaven ZetaPALS DLS instrument. Samples were dissolved in nanopure water at a concentration of ~1 mg / mL. A fresh, clean, polystyrene cuvette was washed with compressed air to remove dust. The sample solution was passed through a 0.4 μm Teflon syringe filter directly into the cuvette; the cuvette was capped and placed in the DLS instrument for particle sizing. At least 3 measurements were made per sample and average hydrodynamic diameters were calculated by fitting the DLS correlation function using the CONTIN routine (ISDA software package from Brookhaven instruments). Nuclear magnetic resonance (NMR) experiments were performed on either a Mercury 300 MHz spectrometer, an INOVA 500 MHz spectrometer, or an INOVA 600 MHz spectrometer. Varian VNMRJ and MestReNove NMR 5.3.2 software were used to obtain and analyze the NMR spectra, respectively. Analytical high-performance liquid chromatography mass spectrometry (HPLC-MS or LC-MS) data were obtained using an Agilent 1100 series HPLC system equipped with a variable wavelength ultraviolet-visible (UV-Vis) detector and an Agilent 1100 VL LC/MSD mass spectrometer. Separation was achieved using a 9.4 X 50 mm Agilent Zorbax XDB-C18 column with mobile phase gradients of 0.1% acetic acid in water and acetonitrile. Experiments were performed at room temperature with a flow rate of 1.0 mL / min. Preparatory HPLC (prep-HPLC) was performed on an Agilent 1100 series HPLC system with an Agilent 1200 series automated fraction collector and an 1100 series variable wavelength detector. Separation was achieved using a 9.4 X 250 mm Agilent Eclipse XDB-C18 column with 0.05% acetic acid in water and acetonitrile mobile phase (solvent gradient detailes below). Experiments were performed at room temperature with a flow rate of 5 mL / min. High-resolution mass spectrometry data were obtained on an Agilent 6200 series accurate-mass time-of-flight (TOF) LC/MS. Matrix assisted laser desorption ionization mass spectrometry (MALDI) measurements were performed by the California Institute of Technology mass spectrometry facility using a Voyager De_Pro TOF mass spectrometer (Applied Biosystems) outfitted with a 355 nm YAG laser from Blue Ion Technologies. In a typical experiment, 1.0 mg of polymer sample was dissolved in 100 μL of THF and diluted 10-fold with the MALDI matrix, dithranol (10 mg / mL in THF). To each sample was added 0.1 μL of saturated NaI in ethanol and 0.35 μL of the sample-matrix mixture

was spotted on a MALDI plate for analysis. The Voyager De_Pro was operated in linear mode with an accelerating voltage of 20,000 V, grid voltage of 95.2%, guide wire 0.03%, extraction delay time 250 ns, acquisition mass range 800-5000 Da, and laser rep rate 20 Hz. The instrument was calibrated externally using a Sequazyme Mass Standard Kit supplied by Applied Biosystems. Photolysis experiments were performed using a Multiple Ray Lamp (UVP) fitted with an 8 W, longwave, filtered blacklight bulb (365 nm). Sample vials were placed as close as possible to the light source and irradiated for the desired time before analysis by LC-MS. Spectra/Por 7 dialysis membranes (Spectrum Labs) were used for macromonomer purification. Fourier-transform infrared spectroscopy (FTIR) experiments were performed on a Nicolet 6700 FTIR spectrometer (Thermo Scientific) under a scrubbed-air atmosphere in transmission/absorbance mode. A solution of polymer (~10 μL, ~1 mg / mL) in dichloromethane (DCM) was drop-deposited onto a KBr plate using a Pasteur pipette. After DCM evaporation to give a thin polymer film, the plate was inserted into the spectrometer and 8 scans were taken at 1 cm^{-1} resolution from 4000 cm^{-1} to 700 cm^{-1}.

***Exo-N*-(6-hydroxyhexyl)-5-norbornene-2,3-dicarboximide (norb-C6OH).** A solution of 6-amino-1-hexanol (3.0 g, 25.6 mmol) and *cis*-5-norbornene-*exo*-2,3,-dicarboxylic anhydride (4.0 g, 24.4 mmol) in toluene (50 mL) was added to a dried, 150 mL round-bottom flask fitted with a Dean-Stark trap and placed in an oil bath preset to 140 ºC for 24 h while stirring. The reaction mixture was transferred to a silica gel column primed using 10% ethyl acetate in hexanes (10% EtOAc/hexane). A 300 mL portion of 10% EtOAc/hexanes was flushed through the column before elution of the product using 50% EtOAc/hexanes (TLC R_f = 0.3, 50% EtOAc/hexanes, $KMnO_4$ stain). Removal of solvent by rotary evaporation yielded 6.0 g of **norb-C6OH** as a colorless oil (94%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.00 (s, 2H), 3.26 (t, J = 6.4 Hz, 2H), 3.13 (t, J = 7.3, 2H), 2.93 (s, 2 H), 2.38 (s, 2H), 1.31 – 1.15 (m, 5H), 1.14 – 0.95 (m, 4H), 0.92 (t, J = 7.4 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$): δ 177.9, 137.5, 61.8, 47.5, 44.8, 42.4, 38.3, 32.2, 27.4, 26.4, 25.0; TOF HRMS calcd. for $C_{15}H_{22}NO_3$ $[M+H]^+$ 264.1600, found 264.1612.

Norbornene aldehyde (2). A three-neck round bottom flask containing a stir bar was equipped with a vacuum adaptor and two 150 mL addition funnels each capped with a rubber septum. The flask was flame dried under vacuum, cooled to room temperature, and backfilled with argon. A positive argon pressure (using a mercury bubbler) was maintained through the course of the reaction. DCM (58 mL) was added to the flask via cannula followed by oxalyl chloride (3.21 mL, 37.36 mmol). The solution was cooled to -76 ºC using an acetone/dry ice bath. One of the addition funnels was charged with DCM (7.3 mL) and DMSO (5.31 mL, 74.72 mmol) while **norb-C6OH** (6.60 g, 24.90 mmol) dissolved in DCM (43 mL) was added to the other. The DMSO/DCM solution was added dropwise to the flask containing oxalyl chloride over 15 min while stirring. After the addition, the solution was stirred for 15 min at -76 ºC. The solution of **norb-C6OH** in DCM was then added dropwise over 20 min while stirring. The addition funnel was washed twice with 5 mL of DCM and the reaction mixture was stirred for 30 min at -76 ºC. Triethylamine (20.83 mL, 149.4 mmol) and DCM (3.7 mL) were combined in the washed addition funnel that previously held **norb-C6OH** and this solution was added dropwise over 15 min to the flask during which time a thick white precipitate formed. After the addition the mixture was stirred for 10 min before warming to room temperature and transferring to a separatory funnel.

The mixture was washed twice with 50 mL of 1 M HCl and once with brine, dried over Na_2SO_4 and concentrated on a rotary evaporator. The crude product was purified by silica gel column chromatography (30% EtOAc/hexanes, TLC R_f = 0.25, stain with anisaldehyde solution) to yield **3** (5.83 g, 89%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.52 (s, 1H), 6.08 (s, 2H) 3.23 (t, *J* = 7.3 Hz, 2H), 3.02 (s, 2H), 2.46 (s, 2H), 2.22 (td, *J* = 7.2, 1.4 Hz, 2H), 1.52 – 1.22 (m, 5H), 1.21 – 1.05 (m, 2H), 0.99 (d, *J* = 9.8 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$): δ 202.0, 177.7, 137.6, 47.6, 44.9, 43.3, 42.5, 38.1, 27.3, 26.2, 21.3; TOF HRMS calcd. for $C_{15}H_{19}NO_3$ $[M+H]^+$ 262.1443, found 262.1438.

Norbornene amine (3). Aldehyde **2** (1.0 g, 3.83 mmol), 3-chloropropylamine hydrochloride (523 mg, 4.0 mmol), and sodium carbonate (426 mg, 1.05 mmol) were dissolved in methanol (10 mL) in a round-bottom flask. The mixture was stirred at room temperature under argon atmosphere for 30 min to form an imine intermediate (reaction monitored by TOF-LC/MS, calcd. for imine $C_{18}H_{26}ClN_2O_2$ $[M+H]^+$: 337.1683, found: 337.1614). The reaction mixture was cooled to 0 ºC using an ice bath; $NaBH_4$ (232 mg, 6.13 mmol) was carefully added. The ice bath was removed and the mixture was stirred for 3 min before quenching with 100 mL of saturated $NaHCO_{3(aq.)}$. The mixture was transferred to a separatory funnel and washed five times with DCM (100 mL). The organic fractions were combined and dried over Na_2SO_4, filtered, and concentrated on a rotary evaporator. The resulting oil was purified by silica gel chromatography (2% MeOH/CH_2Cl_2, TLC R_f = 0.2, stain with ninhydrin solution) to yield **3** as a colorless oil (1.01 g, 78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.13 (s, 2H), 3.46 (t, *J* = 6.4 Hz, 2H), 3.29 (t, *J* = 7.3 Hz, 2H), 3.10 (s, 2H), 2.60 (t, *J* = 6.8 Hz, 2H), 2.51 (s, 2H), 2.44 (t, *J* = 7.1 Hz, 2H), 1.83 – 1.75 (m, 2H), 1.40 (m, 2H), 1.37 – 1.29 (m, 3H), 1.23 – 1.12 (m, 4H), 1.06 (d, *J* = 9.7 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$): δ 177.78, 137.63, 49.49, 47.59, 46.64, 44.96, 42.95, 42.54, 38.36, 32.56, 29.55, 27.49, 26.60, 26.58; TOF HRMS calcd. for $C_{18}H_{28}ClN_2O_2$ $[M+H]^+$ 339.1839, 341.1801, found 339.1879, 341.1834.

Norbornene carboxylic acid (4). Succinic anhydride (134 mg, 1.34 mmol) was combined with amine **3** (434 mg, 1.28 mmol) in DCM (13 mL) and the resulting solution was stirred for 1 h at room temperature before transfer to a silica gel column. Elution with 60% EtOAc/hexanes (TLC R_f = 0.2, stain with bromocresol green solution) gave the purified acid **4** (394 mg, 71%) as a mixture of amide rotamers after concentration on a rotary evaporator. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.71 – 9.86 (br, 1H), 6.18 (s, 2H), 3.49 (t, *J* = 5.7 Hz, 0.85H), 3.43 (t, *J* = 6.2 Hz, 1.15H), 3.40 – 3.29 (m, 4H), 3.24 – 3.16 (m, 2H), 3.15 (s, 2H), 2.55 (m, 6H), 2.00 – 1.85 (m, 2H), 1.55 – 1.36 (m, 5H), 1.21 (m, 4H), 1.10 (d, *J* = 9.7 Hz, 1H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 178.09, 178.07, 176.32, 171.70, 171.54, 137.70, 64.25, 48.45, 47.69, 45.95, 45.05, 44.80, 44.15, 42.66, 42.63, 41.86, 38.42, 38.27, 31.24, 30.61, 30.51, 29.37, 29.33, 28.57, 28.46, 27.78, 27.46, 27.43, 27.26, 26.47, 26.44, 26.21, 26.13; TOF HRMS calcd. for $C_{22}H_{32}ClN_2O_5$ $[M+H]^+$ 439.2000, 441.19705, found 439.2077, 441.2026.

Norbornene *N*-hydroxysuccinimidyl ester (5). DCM (10 mL) was added to a flask containing *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (EDC, 262 mg, 1.37 mmol), *N*-hydroxysuccinimide (157 mg, 1.37 mmol), 4-(dimethylamino)pyridine (DMAP, 11.1 mg, 0.091 mmol), and **4** (400 mg, 0.91 mmol). The resulting solution was

stirred under argon at room temperature for 20 h. The mixture was transferred to a silica gel column. Elution with 70% EtOAc/hexanes (TLC R_f = 0.2, stain with anisaldehyde solution and/or visualize under UV light) gave **5** (391 mg, 75%) after concentration on a rotary evaporator. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.22 (s, 2H), 3.52 (t, *J* = 5.5 Hz, 0.86H), 3.47 (t, *J* = 6.1 Hz, 1.14H), 3.42 – 3.33 (m, 4H), 3.28 – 3.15 (m, 4H), 2.91 (t, *J* = 6.1 Hz, 2H), 2.77 (s, 4H), 2.67 (m, 2H), 2.61 (s, 2H), 2.00 – 1.91 (m, 2H), 1.56 – 1.40 (m, 5H), 1.25 (m, 4H), 1.14 (d, *J* = 9.7 Hz, 1H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 178.06, 169.74, 169.55, 169.16, 168.53, 168.47, 137.80, 64.30, 48.36, 47.78, 45.93, 45.14, 44.64, 44.13, 42.83, 42.73, 41.89, 38.51, 38.35, 31.34, 30.70, 30.62, 28.74, 27.74, 27.59, 27.53, 27.39, 26.71, 26.64, 26.55, 26.37, 26.23, 25.62, 25.50; TOF HRMS calcd. for $C_{26}H_{35}ClN_3O_7$ $[M+H]^+$ 536.2164, 538.2134, found 536.2167, 538.2155.

Norbornene PEG (6). *O*-(2-Aminoethyl)polyethylene glycol 3000 (100 mg, 33.3 μmol) and **5** (18.8 mg, 35 μmol) were dissolved in anhydrous DMF (1 mL). The resulting solution was stirred at room temperature for 4 h. The reaction mixture was added dropwise to diethyl ether (20 mL) to precipitate **6** as a white solid which was collected by centrifugation and decanting of the ether before redissolving in DCM (1 mL). This process of precipitation, centrifugation, and re-dissolving was repeated five times. On the fifth iteration, the precipitate was dried under vacuum to afford macromonomer **6** as a white powder (112 mg, 95%). GPC (0.2 M LiBr in DMF) 3,300 Da, PDI 1.10. MALDI mass spectrum and NMR are shown in supporting information (Figures S1-S3).

Synthesis of azido-bivalent-brush polymer library by ROMP and chloride/azide exchange. MM **6** (30 mg, ~9.1 μmol) was placed in 8 separate 2 mL gas chromatography (GC) vials with stir bars. The vials were capped with screw caps outfitted with septa. DCM (~91 μL, 0.1 M **6**) was added to each vial and the solutions were stirred until all of **6** dissolved. In a separate vial, a stock solution of catalyst **1** in DCM was prepared (20 mg **1** / mL DCM). Aliquots of this solution were then added via syringe to each vial containing MM **6** such that the **6**:**1** ratios were those listed in Table I. During the additions a needle connected to an argon line was quickly inserted through the septa of the vials to alleviate pressure from adding the catalyst solution. Each of the vials was stirred at room temperature for 60 min. The viscosity of the polymerization mixture noticeably increased within 10 min, especially for those with the highest ratios of **6** to **1**, which suggested the formation of high molecular weight species. After 10 min, one drop of ethyl vinyl ether was added to quench the polymerization. Then, a needle connected to vacuum was introduced and the DCM was removed rapidly *in vacuo*. After ~30 min of drying under vacuum, the vials were backfilled with argon and solid NaN_3 was added (2.8 mg, 27 μmol) followed by anhydrous DMF (1 mL). The vials were placed in an oil bath preset to 40 °C and stirred for 48 h to convert the alkyl chloride sidechains of **6** to azides. Finally, the reaction mixtures were diluted with 2 mL of water, transferred to pre-wetted dialysis bags (8 kDa MWCO), and stirred against deionized water overnight to remove excess sodium azide and DMF. Lyophilization gave ***n*N$_3$** bivalent brush polymers as white, fluffy powders. GPC and DLS characterization data are provided in Table I and Figure 2. FTIR spectra are shown in Figure 3. A representative ^{1}H NMR spectrum is given in the supporting information (Figure S4).

DOX-NBOC-alkyne (9). A suspension of **7** (9 mg, 39 μmol) in THF (1 mL) and triethylamine (6.5 μL, 47 μmol) was treated with 4-nitrophenyl chloroformate (9 mg, 47 μmol). TLC and ^{1}H NMR confirmed complete conversion to carbonate **8** within 15 min. The reaction mixture was transferred to a short silica gel column and eluted with 80% EtOAc. UV active fractions with R_f = 0.4 were combined and dried on a rotary evaporator. The resulting white solid, **8**, was immediately dissolved in anhydrous DMF (1 mL). **DOX**-HCl (20 mg, 37 μmol) and anhydrous *N*,*N*-diisopropylethylamine (DIPEA, 9.8 μL, 56 μmol) were added and the resulting solution was stirred overnight at room temperature. The reaction mixture was diluted with 20 mL EtOAc and washed twice with 0.1 M HCl (10 mL), once with H_2O (10 mL), and once with brine (10 mL) before drying over magnesium sulfate, filtration, and concentration on a rotary evaporator. The resulting red solid was purified by column chromatography. The column was eluted first with 3% MeOH/CH_2Cl_2 and then with 5% MeOH/CH_2Cl_2 to give **9** as a red solid (21 mg, 71%). ^{1}H NMR (500 MHz, acetone) δ 8.25 (t, *J* = 5.5 Hz, 1H), 7.75 – 7.68 (m, 2H), 7.65 (d, *J* = 7.5 Hz, 1H), 7.61 – 7.58 (m, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.45 – 7.40 (m, 1H), 6.26 (d, *J* = 8.3 Hz, 1H), 5.40 (d, *J* = 3.3 Hz, 1H), 5.15 – 5.02 (m, 3H), 4.80 (s, 1H), 4.74 (s, 2H), 4.24 (q, *J* = 6.3 Hz, 1H), 4.15 – 4.08 (m, 2H), 3.94 (s, 3H), 3.90 – 3.81 (m, 1H), 3.66 (s, 1H), 3.04 (d, *J* = 18.1 Hz, 1H), 2.81 (d, *J* = 18.3 Hz, 1H), 2.69 (t, *J* = 2.5 Hz, 1H), 2.43 (d, *J* = 14.5 Hz, 1H), 2.16 (dd, *J* = 14.5, 4.3 Hz, 1H), 2.00 (td, *J* = 13.2, 4.0 Hz, 1H), 1.27 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (500 MHz, acetone) δ 214.57, 187.28, 187.12, 165.39, 161.95, 157.07, 155.82, 148.77, 136.75, 135.67, 135.40, 134.52, 132.64, 132.44, 132.01, 131.80, 131.46, 128.94, 121.62, 121.01, 120.03, 118.35, 111.79, 101.87, 80.64, 77.20, 72.61, 70.60, 69.69, 68.48, 65.82, 62.24, 56.99, 48.48, 36.59, 34.03, 30.78, 29.68, 17.45; TOF HRMS calcd. for $C_{39}H_{36}N_3O_{16}$ $[M-H]^-$ 802.2101, found 802.2081.

Coupling of 9 to brush polymers via CuAAC. Each azido-bivalent-brush polymer ***n*N$_3$** (10 mg, ~3 μmol of azide) was placed in a vial followed by 1.21 mL of a 50 nM aqueous solution of THPTA, 69.7 μL of a 36.8 mg / mL solution of **9** in DMSO, and 50 μL of a 1.0 M aqueous solution of sodium ascorbate. The vial was sealed, evacuated for 20 s, and backfilled with argon. A 10 μL aliquot of a 1.0 M solution of $CuSO_4$•$5H_2O$ in water was added via a gastight syringe and the vial was placed in a preheated oil bath and stirred at 40 °C. After 12 h, another aliquot of 1.0 M aqueous sodium ascorbate (50 μL) followed by $CuSO_4$•$5H_2O$ (10 μL) was added. Finally, after 36 h, aliquots of sodium ascorbate and supper sulfate were added to yield mixtures containing 10 equivalents (30.3 μL) of copper and 50 equivalents (151.5 μL) of sodium ascorbate with respect to azide. The reaction progress was followed by LC-MS (Figure 4); upon completion the vial contents were directly subjected to prep-HPLC purification (see **LC methods** below). The purified ***n*DOX** bivalent-brush polymer solutions were concentrated on a rotary evaporator to remove MeCN. Then, the polymer solutions were transferred to centrifuge filters (30 kDa MWCO) and spun at 3000 rpm for 45 min to concentrate the polymer. The concentrated polymer was rediluted with water (15 mL) and centrifuged. This process was repeated five times. The resulting solution was then either lyophilized to dryness or used directly in cell viability assays. A representative FTIR spectrum after click chemistry is given in Figure 4; the ^{1}H NMR spectrum is shown in the supporting information (Figure S5).

LC methods. For analytical LC-MS studies a general method was used; the percentage of acetonitrile (MeCN) in water was varied linearly from 5% to 95% over 5 min followed by a 2 min hold at 95%. This method was used to generate the data shown in Figure 4 (inset) and Figure 5A. Prep-HPLC was performed using an optimized gradient to achieve maximum separation between ***n*DOX**-loaded polymers and free **DOX**-alkyne **9**. A mixed solvent system of 0.05% acetic acid in nanopure water (solvent A) and MeCN (solvent B) was used. Before sample injection, the column was equilibrated for 3 min with 100% solvent A at a 5 mL / min flow rate. Upon injection of 100 μL of sample solvent B was varied from 10% to 78% over 8.5 min at a flow rate of 5 mL / min. At least two runs were performed with manual fraction collection to determine the elution time of the ***n*DOX**-polymer; an automatic fraction collector was set to collect over this retention time for ~13 more injections. The typical elution time for ***n*DOX** polymers was between ~5.7 and ~6.5 min with higher ***n*** samples eluting at slightly longer times (Figure 4).

Cell culture. Human breast cancer cell line MCF-7 (ATCC, HTB-22) was cultured at 37 °C under a humidified atmosphere of 5% CO_2 / 95% air. The cells were grown in Eagle's Minimum Essential Medium (EMEM, ATCC, 30-2003) supplemented with 10% fetal bovine serum (Gibco, 10437028), 1% penicillin/streptomycin (Gibco, 105140122), and 10 μg/mL bovine insulin (Sigma, I0516). The cells were continuously maintained in the culture medium and subcultured every 3-4 days.

Drug treatment and cell viability assay. MCF-7 cells were seeded at 10,000 cells/well in a 96-well plate and allowed to attach for 20 h before drug treatment. Prior to drug exposure, the culture medium was removed and the cells were washed once with warm phosphate-buffered saline (PBS). Then, fresh media with drug concentrations ranging from 0 to 100 μM (based on integrated LC-MS absorbance at 500 nm) were added to the appropriate wells. After 10 min at 37 °C, one plate of cells was exposed to UV light (Multiple Ray Lamp with filtered blacklight bulb, 365 nm) for 10 min while the control plate was kept in the dark. The cells were subsequently incubated at 37 °C under a humidified atmosphere of 5% CO_2 / 95% air for 24 h. The medium was removed and the cells were washed twice with warm PBS before fresh drug-free medium was added to each well. The cells were incubated for another 24 h before analysis by the MTT cell proliferation assay (ATCC, 30-1010K). Cells were washed once with warm PBS and incubated with fresh medium containing MTT reagent for 3 h at 37 °C. Detergent was added to solubilize the purple formazan crystals formed by proliferating cells. Absorbance at 570 nm was measured on a Safire II (Tecan) plate reader. Data were fit to a sigmoidal function to determine the half-maximum inhibitory concentration (IC_{50}).

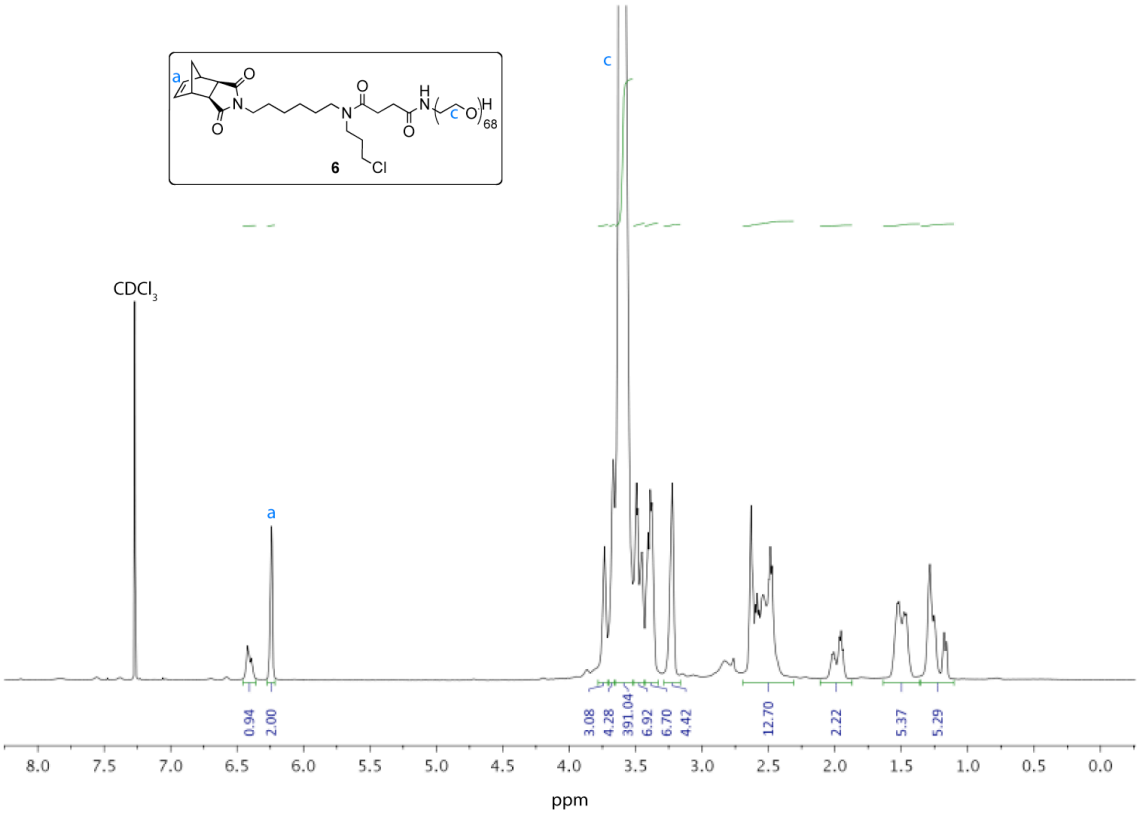

Figure S1. 500 MHz ^{1}H NMR spectrum of MM **6** in $CDCl_3$.

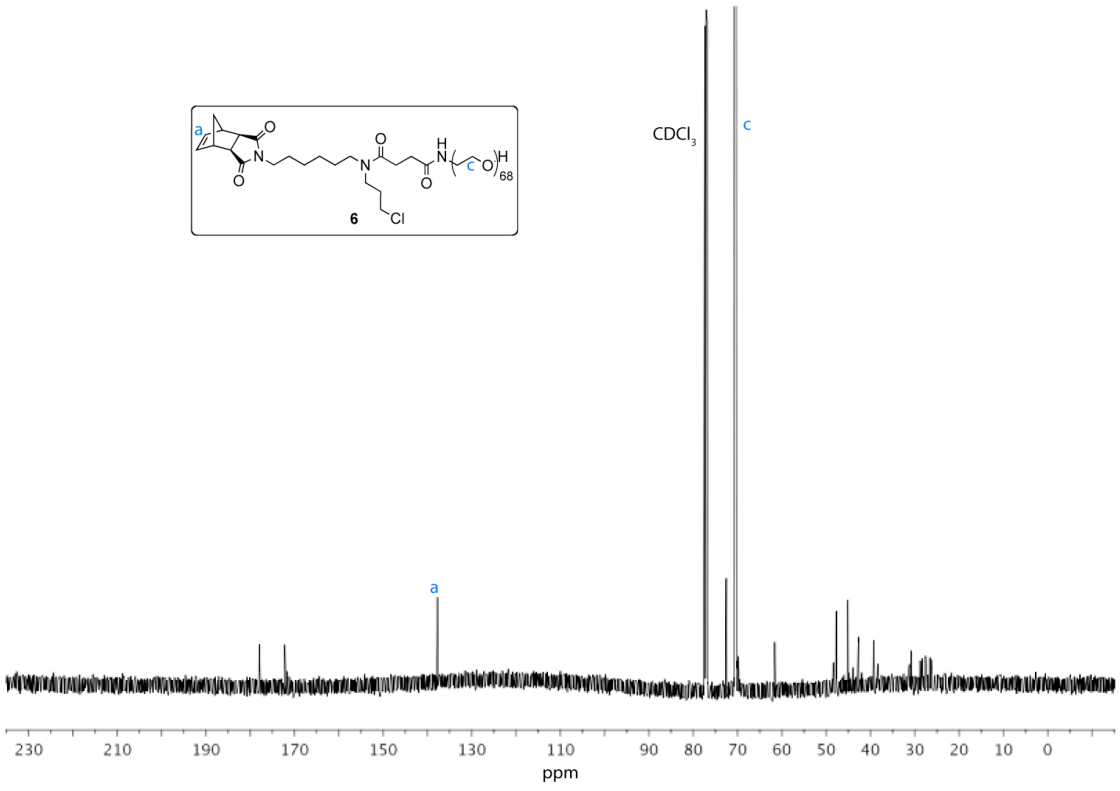

Figure S2. 500 MHz ^{13}C NMR spectrum of MM **6** in $CDCl_3$.

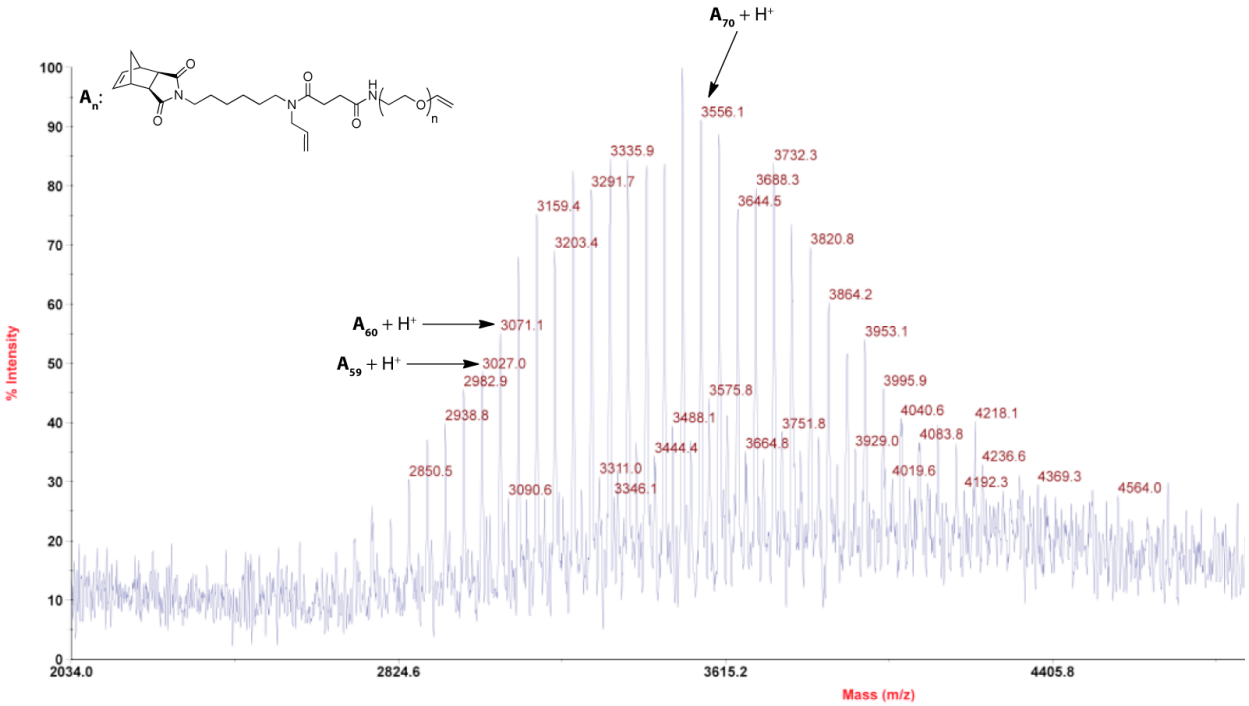

Figure S3. MALDI spectrum of MM **6**.

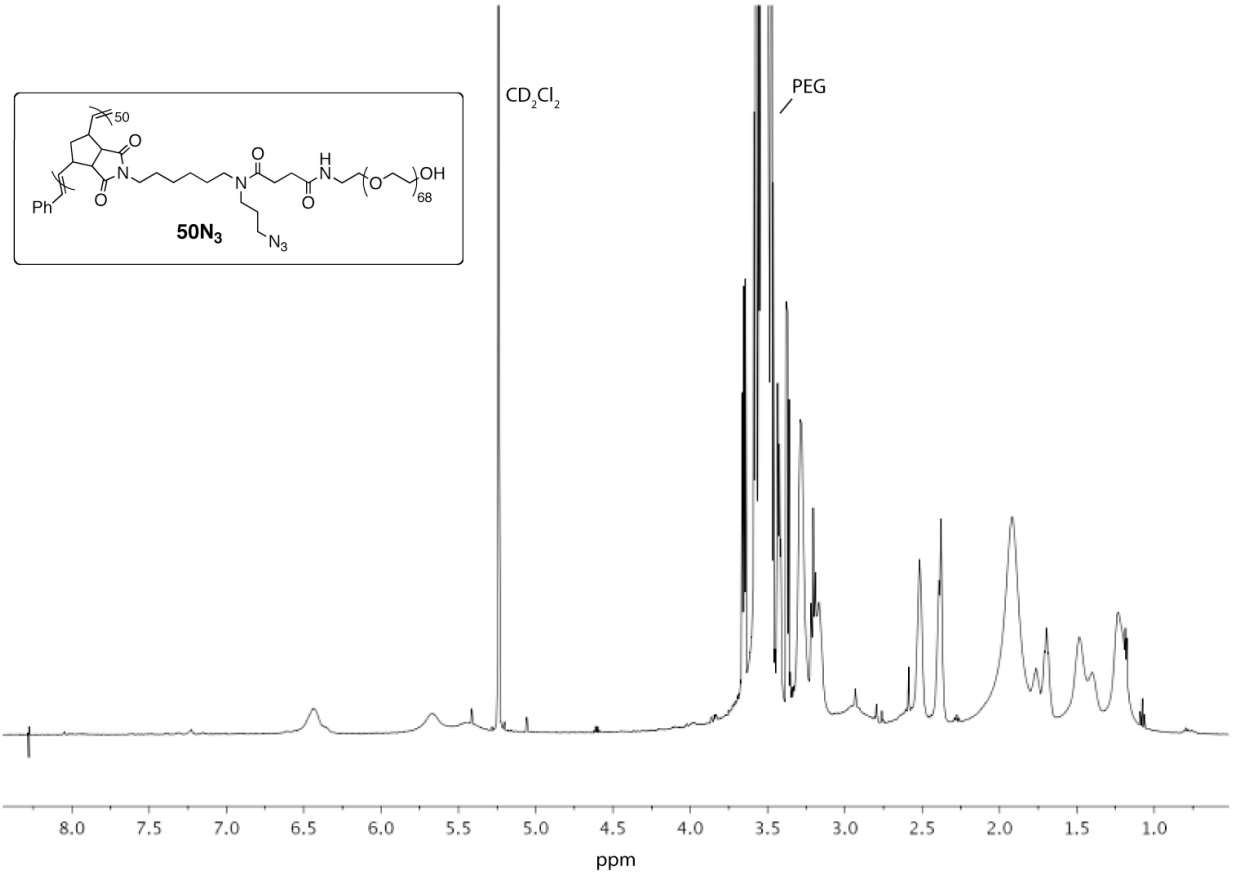

Figure S4. 500 MHz ^{1}H NMR spectrum of **$50N_3$** in CD_2Cl_2.

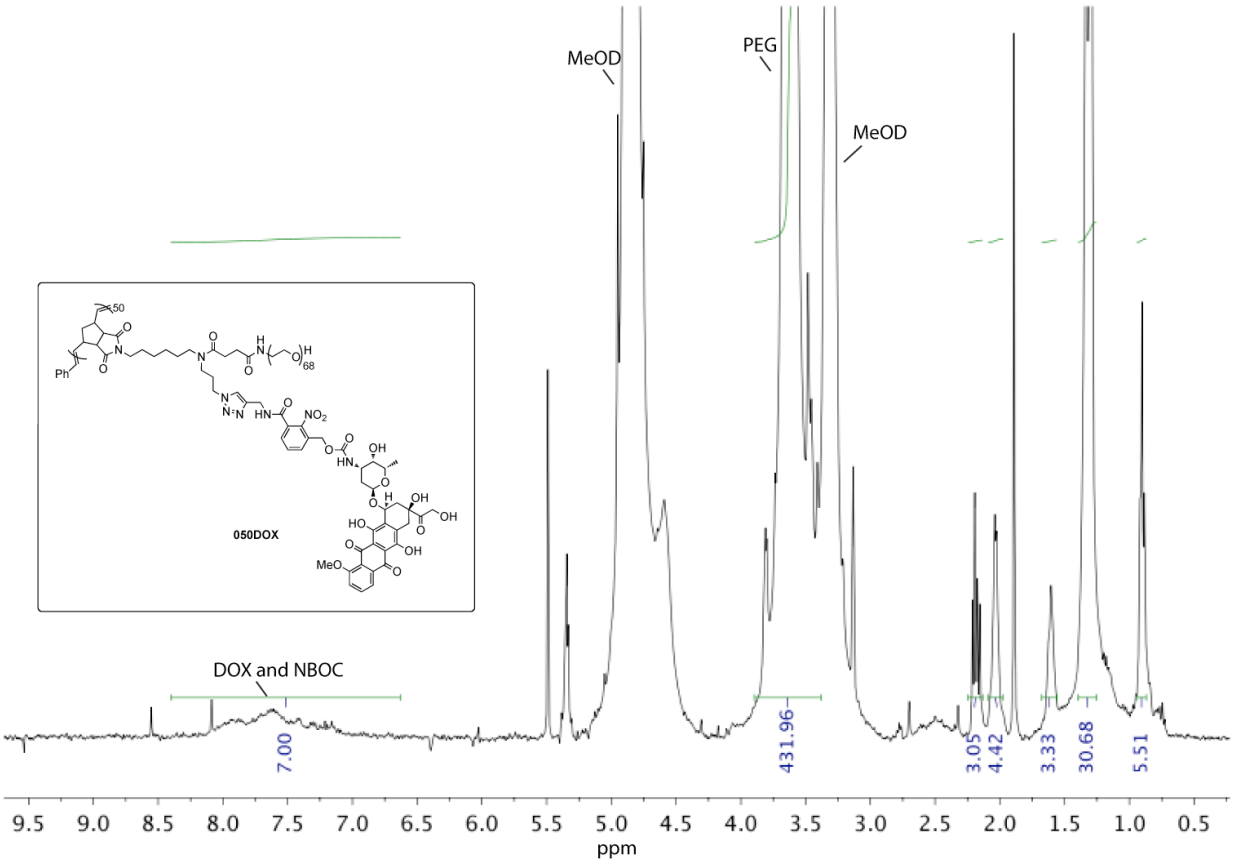

Figure S5. 600 MHz ^{1}H NMR spectrum of **050DOX** in MeOD.

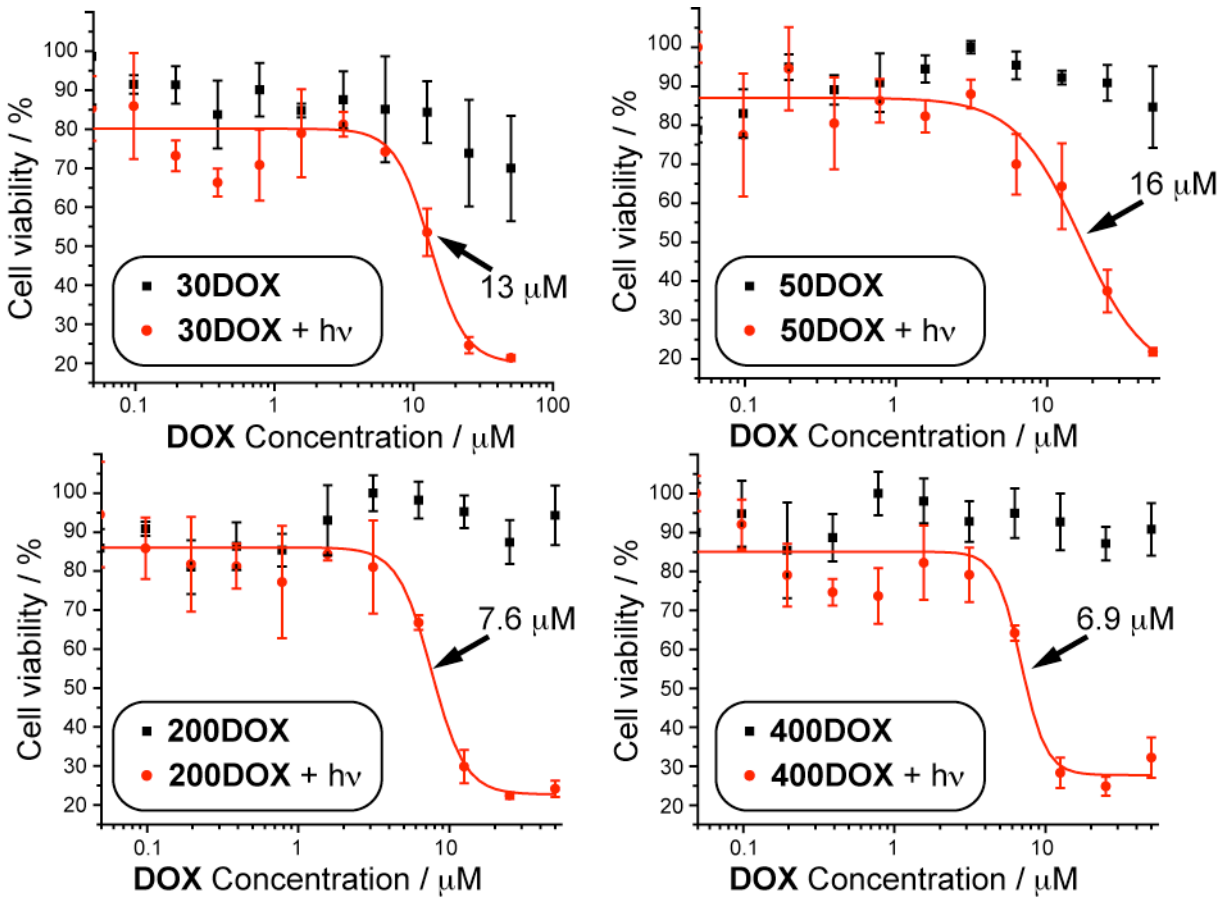

Figure S6. Cell viability for various ***n*DOX** polymers before and after UV irradiation.

(1) Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2002**, *41*, 4035-4037.

(2) Johnson, J. A.; Finn, M. G.; Koberstein, J. T.; Turro, N. J. *Macromolecules (Washington, DC, U. S.)* **2007**, *40*, 3589-3598.

(3) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518-1520.