Supporting Information For:

A convergent synthetic platform for single-nanoparticle combination cancer therapy: ratiometric loading and controlled release of cisplatin, doxorubicin, and camptothecin

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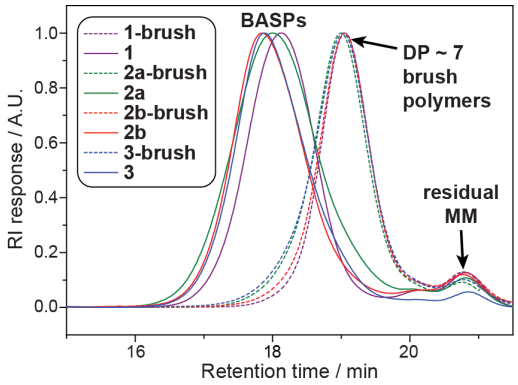


Figure S1. GPC traces of drug-loaded BASPs and their parent bottlebrush polymers (the latter are the brush polymers obtained after graft-through MM polymerization and before addition of platinum crosslinker). DP = average degree of polymerization.

Sample	M_w / kDa[a]	$Đ$[b]	% $Pt_{theo.}$[c]	% Pt[d]	% $DOX_{theo.}$[e]	% DOX[f]	% $CPT_{theo.}$[g]	% CPT[h]	Cu / ppm[i]	Ru / ppm[j]
1	142	1.2	2.2	n.d.	-	n.d.	-	n.d.	n.d.	n.d.
2a	182	1.4	2.2	n.d.	-	n.d.	2.7	n.d.	n.d.	n.d.
2b	103	1.7	2.2	n.d.	1.7	n.d.	-	n.d.	n.d.	n.d.
3	144	1.5	2.2	2.3	1.7	1.4	2.7	2.5	none detected	800

Table S1. Characterization data for multi-drug-loaded BASPs. *Note:* See Figure S29 for NMR integration data, which provides estimated molar ratio of CPT and DOX.
[a] weight-average molecular weight (M_w) from GPC. *Note:* M_w values were obtained by comparison to PEG standards.
[b] dispersity index from GPC (M_w/M_n).
[c] theoretical weight fraction of cisplatin based on brush-first ROMP stoichiometry.
[d] weight fraction of cisplatin as determined by inductively-coupled plasma mass spectrometry (ICP-MS)
[e] theoretical weight fraction of DOX based on brush-first ROMP stoichiometry.
[f] weight fraction of DOX as determined by UV-Vis.
[g] theoretical weight fraction of CPT based on brush-first ROMP stoichiometry.
[h] weight fraction of CPT as determined by UV-Vis.

[i] ppm of residual Cu in BASP after dialysis against water for 1 h (external solution exchanged after 30 min) and acetone for 1 h (external solution exchanged after 30 min) as determined by ICP-MS.
[j] ppm of residual Ru in BASP after dialysis against water for 1 h (external solution exchanged after 30 min) and acetone for 1 h (external solution exchanged after 30 min) as determined by ICP-MS.

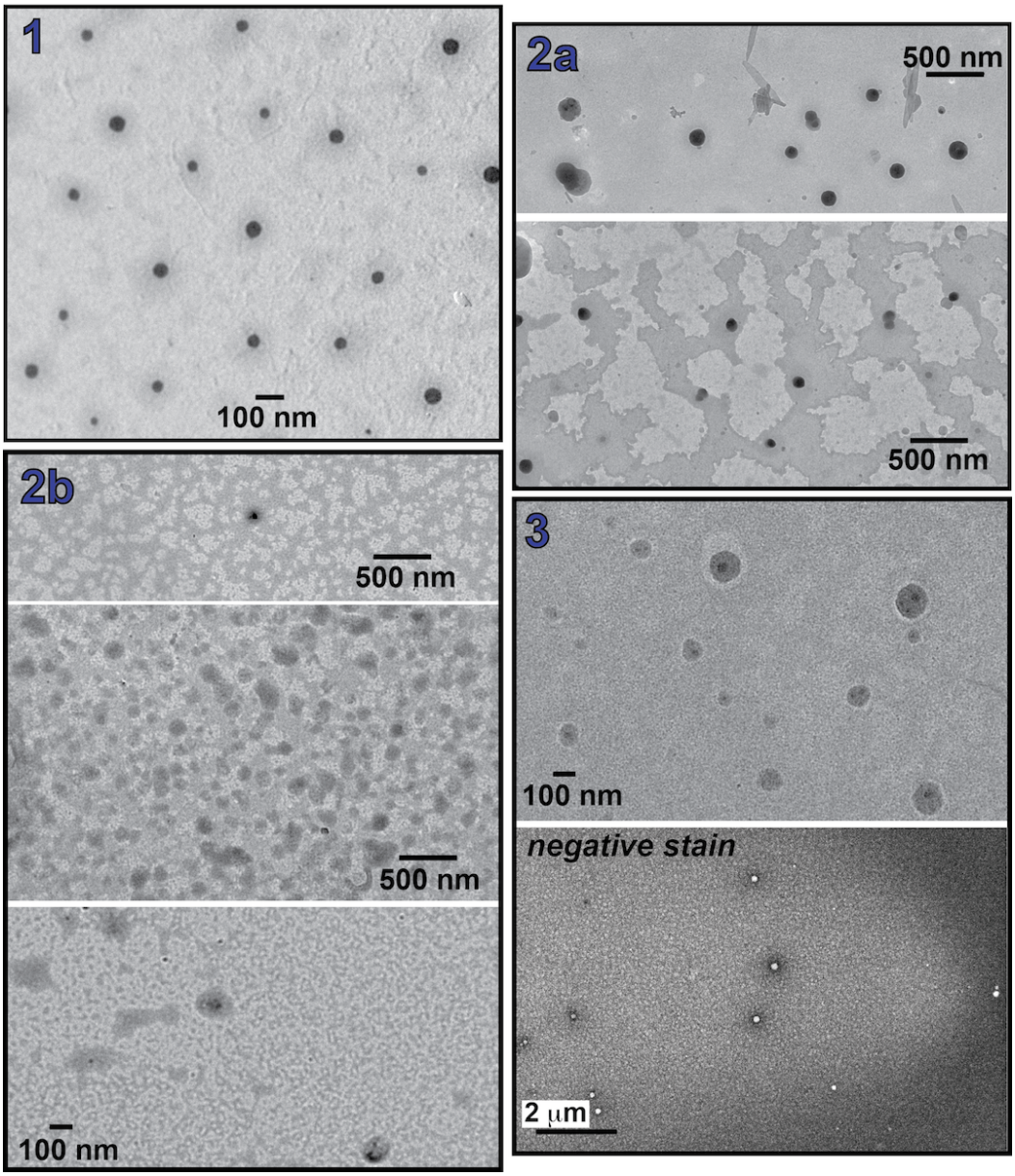


Figure S2. TEM images of the BASPs in the dry state (cast from aqueous solutions). BASP **1** was imaged without staining (upper left panel). BASPs **2a** and **2b** were imaged after staining with RuO_4. BASP **3** was imaged after staining with RuO_4 (top image of bottom right panel) and uranyl acetate (bottom image of bottom right panel) to provide positive and negative contrast, respectively.

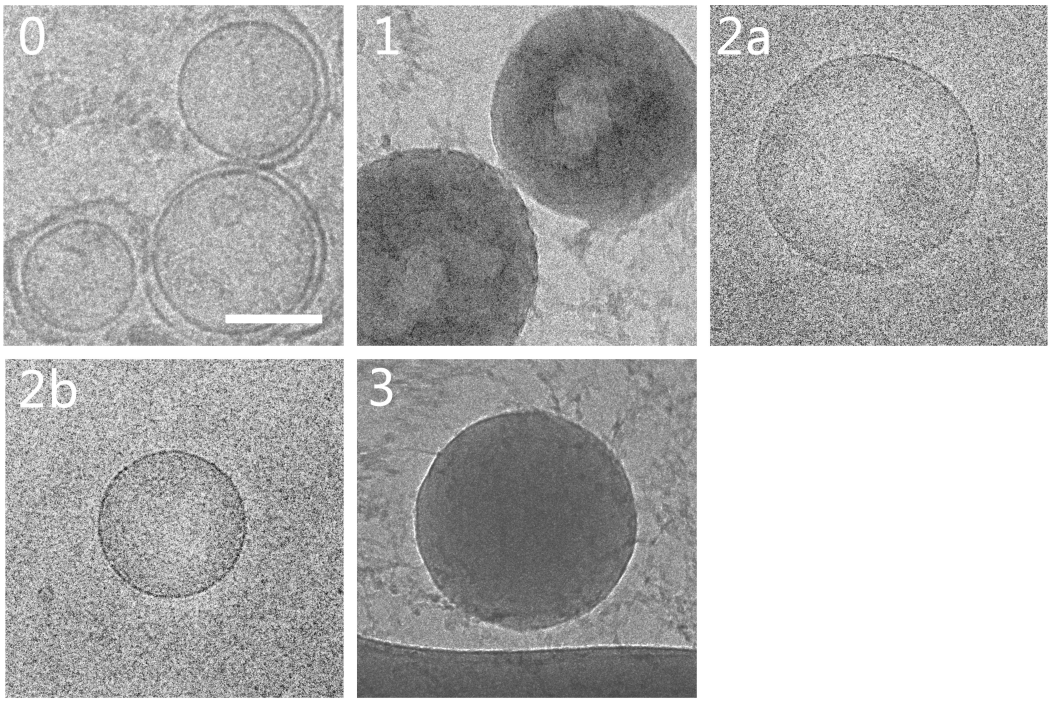


Figure S3. CryoTEM images of the BASPs in aqueous solution. The scale bar is 100 nm.

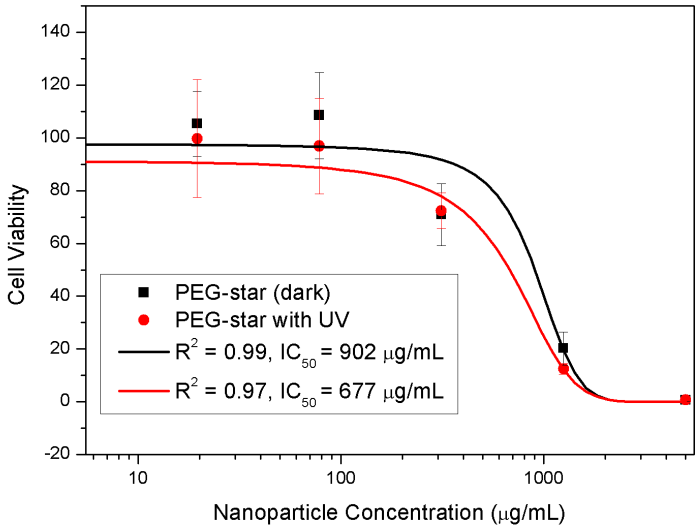


Figure S4. OVCAR3 cell viability data after 72 h of treatment with non-drug-loaded photo-cleavable BASP from our previous report.[1]

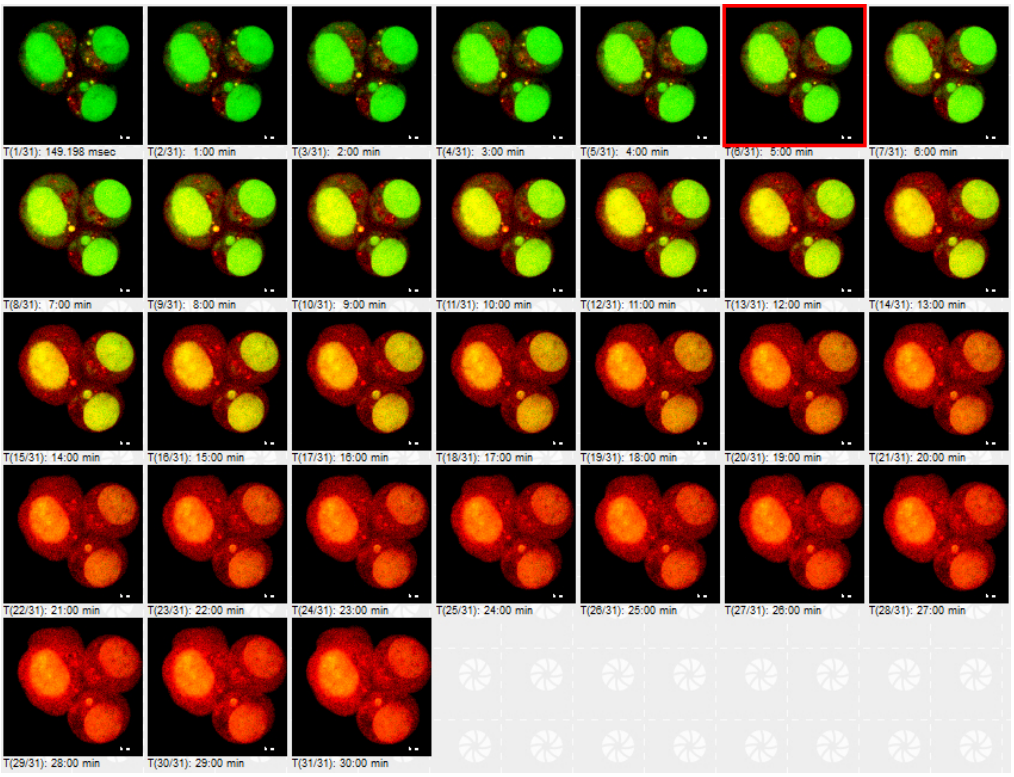


Figure S5. Live cell imaging: full image series.

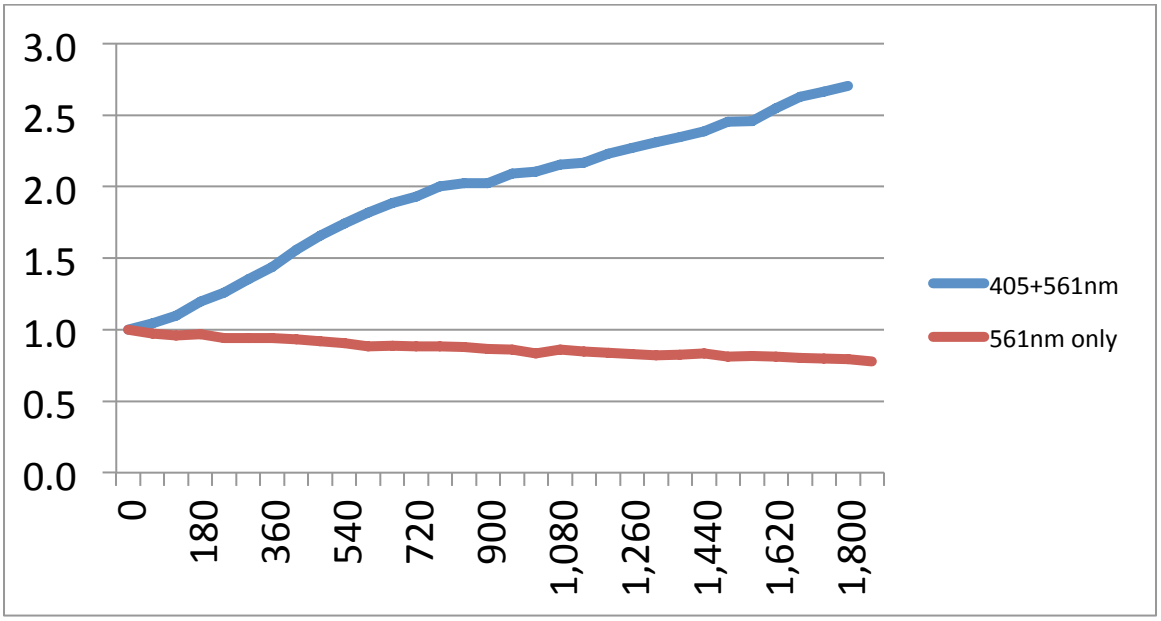


Figure S6. Mean DOX fluorescence intensity (fold versus time 0) as a function of irradiation time (seconds).

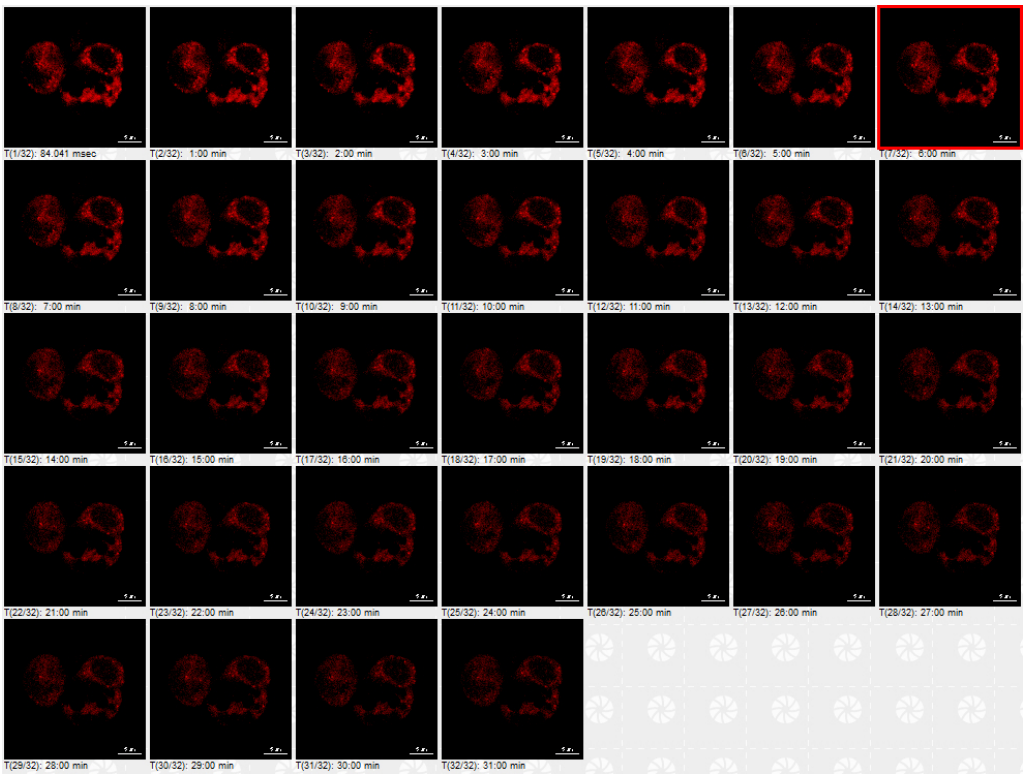


Figure S7. Live cell imaging control experiment: no irradiation.

General Considerations

All reagents and solvents were purchased from Aldrich or VWR and used as supplied unless otherwise noted. Platinum complexes **a3**[2], ruthenium metathesis catalyst (**cat**)[3], *N*-(glycine)-*cis*-5-norbornene-*exo*-dicarboximide **a1**[4], **PEG-MM**[1] and **PEG-Alkyne-MM**[5] were prepared according to literature procedures. Degassed dichloromethane (DCM) and tetrahydrofuran (THF) were passed through solvent purification columns prior to use.

Liquid chromatography–mass spectrometry (LC/MS) and preparative HPLC were performed on an Agilent 1260 LC system equipped with a Zorbax SB-C18 rapid resolution HT column and a Zorbax SB-C18 semi-preparative column. Solvent gradients consisted of mixtures of nano-pure water with 0.1% acetic acid (AcOH) and HPLC-grade acetonitrile. Mass spectra were obtained using an Agilent 6130 single quadrupole mass spectrometer.

Dynamic light scattering (DLS) measurements were made at room temperature using a Wyatt Technology DynaPro Titan 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 (Dynamics V6 software package from DynaPro Wyatt Technology)

^{1}H nuclear magnetic resonance (^{1}H-NMR), ^{13}C nuclear magnetic resonance (^{13}C-NMR) and ^{195}Pt nuclear magnetic resonance (^{195}Pt-NMR) spectra were recorded on Bruker AVANCE-400 NMR spectrometer, Mercury 300 MHz spectrometer, or INOVA 500 MHz spectrometer. Chemical shifts are reported in ppm and referenced to the $CHCl_3$ singlet at 7.26 ppm, DMSO at

2.50 ppm or CH_2Cl_2 at 5.30 ppm. ^{13}C-NMR spectra were referenced to the center line of the $CDCl_3$ triplet at 77.0 ppm, DMSO septet at 39.5 ppm or CD_2Cl_2 quintet at 54.0 ppm. ^{195}Pt-NMR spectra were referenced using an external K_2PtCl_6 in D_2O at -1628 ppm. Chemical shifts are expressed in parts per million (ppm), and splitting patterns are designated as s (singlet), d (doublet), t (triplet), m (multiplet) and br (broad). Coupling constants *J* are reported in Hertz (Hz). MestReNova NMR 7.0.1 software was used to analyze the NMR spectra.

Gel permeation chromatography (GPC) measurements were performed on an Agilent 1260 LC system with two Shodex KD-806M GPC columns in series at 60 °C and a flow rate of 1 mL / min. *N*,*N*-Dimethylformamide (DMF) with 0.2M LiBr was used as the eluent. A T-rEX refractive index detector (Wyatt) and a DAWN EOS 18-angle laser light scattering (MALLS) detector (Wyatt) were used for polymer analysis.

High-resolution mass spectrometry (HRMS) was obtained using a Bruker Daltonics APEXIV 4.7 Tesla Fourier Transform Ion Cyclotron Resonance Mass Spectrometer (FT-ICR-MS).

TEM images were obtained at the MIT Center for Materials Science and Engineering on a JEOL 2011 High Contrast Digital TEM. The samples were prepared as follows: 5.0 μL of a 0.050 mg/mL solution of 20xL (or 15 xL) BASP polymer was deposited via pipet on top of a carbon film-coated 200-mesh copper grid (purchased from Electron Microscopy Sciences) placed on a piece of parafilm carbon-coated side up. The sample was allowed to dry at room temperature and then ready for TEM imaging. For positive stain, the sample was further placed carbon-coated side up on top of a LC/MS vial covered with foil. The LC/MS vial was placed inside a 20mL scintillation vial and to the scintillation vial was added ~0.30 mL of a 0.5 wt% RuO_4 aqueous solution; the scintillation vial was capped and allowed to stand for 30 min. For negative stain, the sample was further stained with 2 wt% uranyl acetate aqueous solution. After 1 min, the excess staining solution was quickly wicked away by a piece of filter paper and the samples were left to dry under ambient conditions overnight.

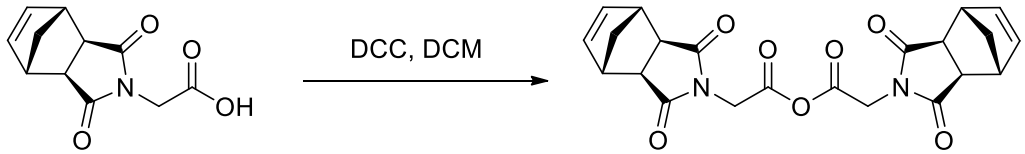
Photolysis experiments were performed using a Multiple Ray Lamp (UVP) fitted with an 8 W, longwave, filtered blacklight bulb (365 nm).

Cell Culture and Live Cell Imaging

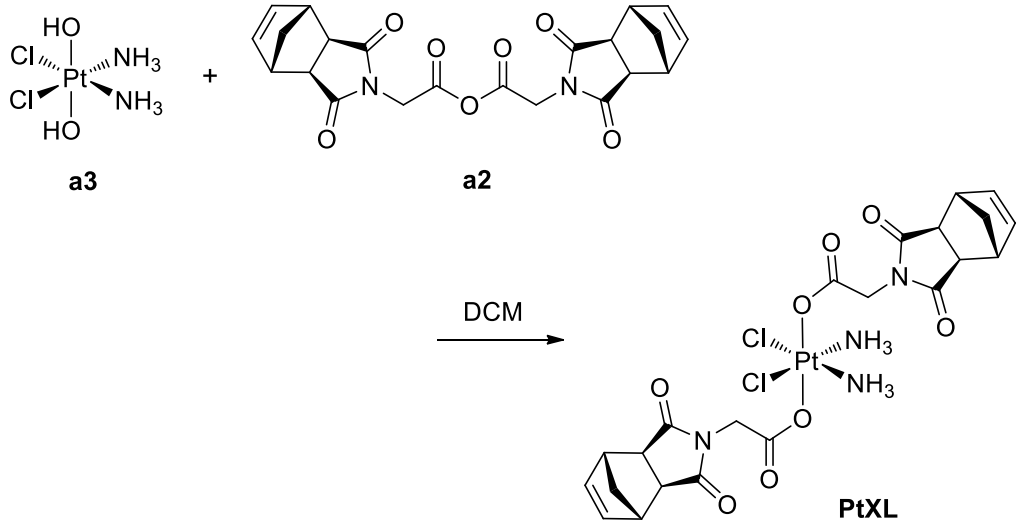
OVCAR3 cells (ATCC) were maintained in RPMI-1640 media supplemented with 0.01 mg/mL recombinant human insulin (Gibco), 20% fetal bovine serum, and penicillin/streptomycin in a 5% CO_2 humidified atmosphere (37 °C). Assays and imaging were performed on cells passaged 12-24 h prior. Dose-response curves were fit using a four-parameter logistic regression analysis and statistical significance was assessed by two-tailed t-test (95% CI) for *P<0.01, **P<0.05, and ***P<0.001. BASP drug conjugates were reconstituted in ultrapure water (18 MΩ) containing 5% D-glucose and stored at 4 °C in dark prior to use. Viability was assessed by CellTiter-Glo assay (Promega) following 72 h total incubation time with MDLP-spiked OPTIMEM medium. 90 min after nanoparticle introduction, assay plates were exposed for 10 min with a portable UV lamp (UVP Inc; 2.0±0.3 mW/cm^2 @ 365 nm) and returned to the incubator. Confocal fluorescence measurements were performed following incubation with 133 uM acridine orange (Sigma) and 66.6 μg/mL BASP drug conjugate in complete basal medium. After 30 min, cell growth media were replaced with 10 mM HEPES (pH 7.4) containing 10% FBS and imaging (1 exposure min^{-1}) was performed using the 405, 488, and/or 561 nm laser lines of a Nikon 1AR ultra-fast spectral scanning confocal microscope (λ_{em}: 525/50, 595/50 nm) fitted with a temperature-controlled environment chamber and 60x oil immersion objective.

Synthetic Procedures

Synthesis of Pt-XL

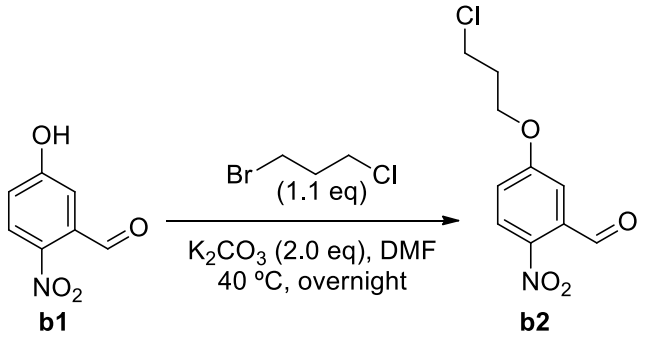


Norbornene anhydride a2. *N*-(glycine)-*cis*-5-norbornene-*exo*-dicarboximide (760 mg, 3.4 mmol) and *N*,*N*'-Dicyclohexylcarbodiimide (DCC) (360 mg, 1.7 mmol) were dissolved in anhydrous DCM (60 mL) and the resulting solution was stirred at room temperature overnight. The reaction mixture was then filtered and the filtrate was concentrated via rotary evaporator to give **3** as white solid (583 mg, 80% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.31 (t, J = 1.8 Hz, 2H), 4.38 (s, 2H), 3.35 – 3.31 (m, 2H), 2.78 (d, J = 1.4 Hz, 2H), 1.65 (d, J = 10.1 Hz, 1H), 1.54 (dt, J = 10.1, 1.4 Hz, 1H). ^{13}C NMR (101 MHz, CDCl3) δ 176.6, 161.6, 138.0, 48.1, 45.4, 42.9, 39.9. IR(neat): 1701, 1709, 1411, 1079 cm^{-1}. MS (ESI) m/z $(M+Li)^+$ calcd. for $C_{22}H_{20}N_2O_7Li$: 431.1 obsd.: 431.1.

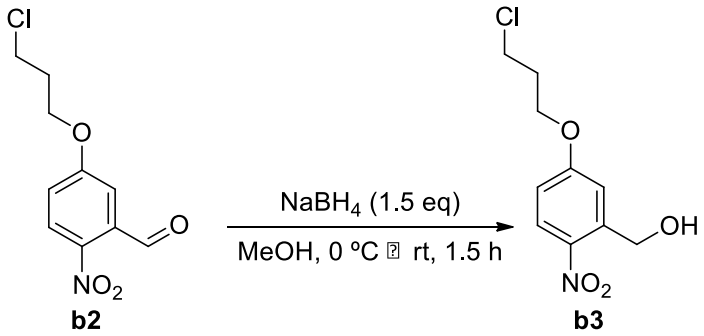


Synthesis of PtXL. Norbornene anhydride **a2** (550 mg, 1.3 mmol) and platinum complex **a3** (100 mg, 0.30 mmol) were dissolved in anhydrous DCM (10 mL) and the resulting solution was stirred at room temperature for 2 weeks. The reaction mixture was then filtered and the residual solid was washed with DCM (20 mL x 3). The solid was collected and dried under vacuum to give **PtXL** (white solid, 199 mg, 90% yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 6.50 (s, br, 6H), 6.31 (s, 4H), 4.13 (s, 4H), 3.10 (s, 4H), 2.70 (s, 4H), 1.66 (d, J = 9.0 Hz, 2H), 1.32 (d, J = 9.0 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 176.8, 174.0, 137.8, 47.2, 44.6, 42.6. (NOTE: one peak for the compound is buried under the solvent picks.) ^{195}Pt NMR (86 MHz, DMSO-d_6) δ 1234.3. IR(neat): 1712, 1682, 1246, 1178 cm^{-1}. MS (ESI) m/z $(M+H)^+$ calcd. for $C_{22}H_{27}Cl_2N_4O_8Pt$: 741.0837 obsd.: 741.0837.

Synthesis of DOX-MM

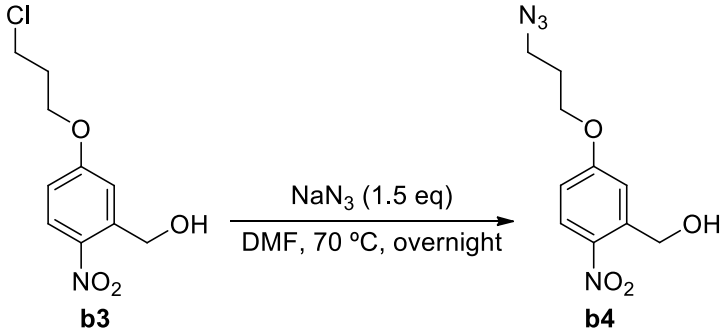


Synthesis of 5-(3-chloropropoxy)-2-nitrobenzaldehyde b2.[6] 1-bromo-3-chloropropane (0.650 mL, 0.00658 moles) was added to a solution of 5-hydroxy-2-nitrobenzaldehyde (1.0g, 0.00598 moles) and potassium carbonate (1.66g, 0.0120 moles) in anhydrous DMF (6 mL). The solution was stirred at 40 °C for 24 hours. The reaction was diluted with ethyl acetate (75 mL) and washed with saturated sodium bicarbonate solution (75 mL), water (75 mL), and brine (75 mL). The organic layer was dried with anhydrous magnesium sulfate, which was removed by filtration. The solution was concentrated and silica gel chromatography was performed using a gradient of 100% hexanes to 50% ethyl acetate in hexanes. The fractions containing product were collected, then solvent was removed by rotary evaporation, and dried overnight to yield 5-(3-chloropropoxy)-2-nitrobenzaldehyde as a bright-green yellow solid (yield 87%*). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 10.42 (s, 1H), 8.15 (d, J = 9.1 Hz, 1H), 7.32 (d, J = 2.9 Hz, 1H), 7.18 (dd, J = 9.0, 2.9 Hz, 1H), 4.27 (t, J = 5.9 Hz, 2H), 3.76 (t, J = 6.3 Hz, 2H), 2.35 – 2.24 (m, 2H). ^{13}C-NMR (100 MHz, CD_2Cl_2) δ 189.05, 163.84, 135.04, 127.84, 119.16, 114.57, 66.28, 41.74, 32.35 HRMS: calcd. for $C_{10}H_{10}ClNO_4$ $[M+H]^+$, 244.0371; found, 244.0366.
*Observed extra peaks, but does not interfere with next step: ^{1}H NMR (400 MHz, CD_2Cl_2) δ 4.27 (t, *J* = 5.9 Hz, 0.16), 3.62 (t, *J* = 6.4 Hz, 0.15H), 2.39-2.36 (m, 0.14H)



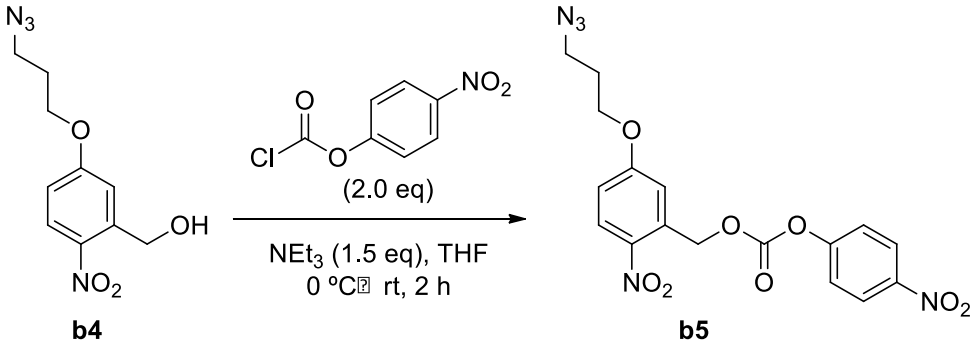
Synthesis of (5-(3-chloropropoxy)-2-nitrophenyl)methanol b3. Sodium borohydride (133 mg, 0.00351 moles) was added to 5-(3-chloropropoxy)-2-nitrobenzaldehyde (570 mg, 0.00234 moles) in anhydrous methanol (12 mL) at 0 °C under nitrogen. The reaction was stirred for 1.5 hours, then concentrated with a rotary evaporator. The mixture was diluted with ethyl acetate (75 mL), and washed with 30mL each of saturated sodium bicarbonate solution, water, and brine. The organic layer was dried with anhydrous magnesium sulfate, which was removed by filtration. The solution was concentrated and silica gel chromatography was performed using a gradient of 100% hexanes to 60% ethyl acetate in hexanes. The fractions containing product were collected, then solvent was removed by rotary evaporation, and dried overnight to yield (5-

(3-chloropropoxy)-2-nitrophenyl)methanol as a pale yellow solid (yield 69%*). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.16 (d, J = 9.1 Hz, 1H), 7.27 (d, J = 2.7 Hz, 1H), 6.92 (dd, J = 9.1, 2.8 Hz, 1H), 4.98 (s, 2H), 4.24 (t, J = 5.9 Hz, 2H), 3.77 (t, J = 6.3 Hz, 2H), 2.28 (p**, J = 6.1 Hz, 2H). ^{13}C-NMR (100 MHz, CD_2Cl_2) δ 163.99, 141.21, 128.42, 114.95, 113.90, 65.80, 63.24, 41.91, 32.52 HRMS: calcd. for $C_{10}H_{12}ClNO_4$ $[M+H]^+$, 246.0528; found, 246.0529.
*Observed extra NMR peaks, but does not interfere with next step: 1H NMR (400 MHz, Methylene Chloride-d2) δ 3.63 (t, *J* = 6.3 Hz, 0.14H), 2.39-2.31 (m, 0.24H)
** pseudo pentet



b3 **b4**

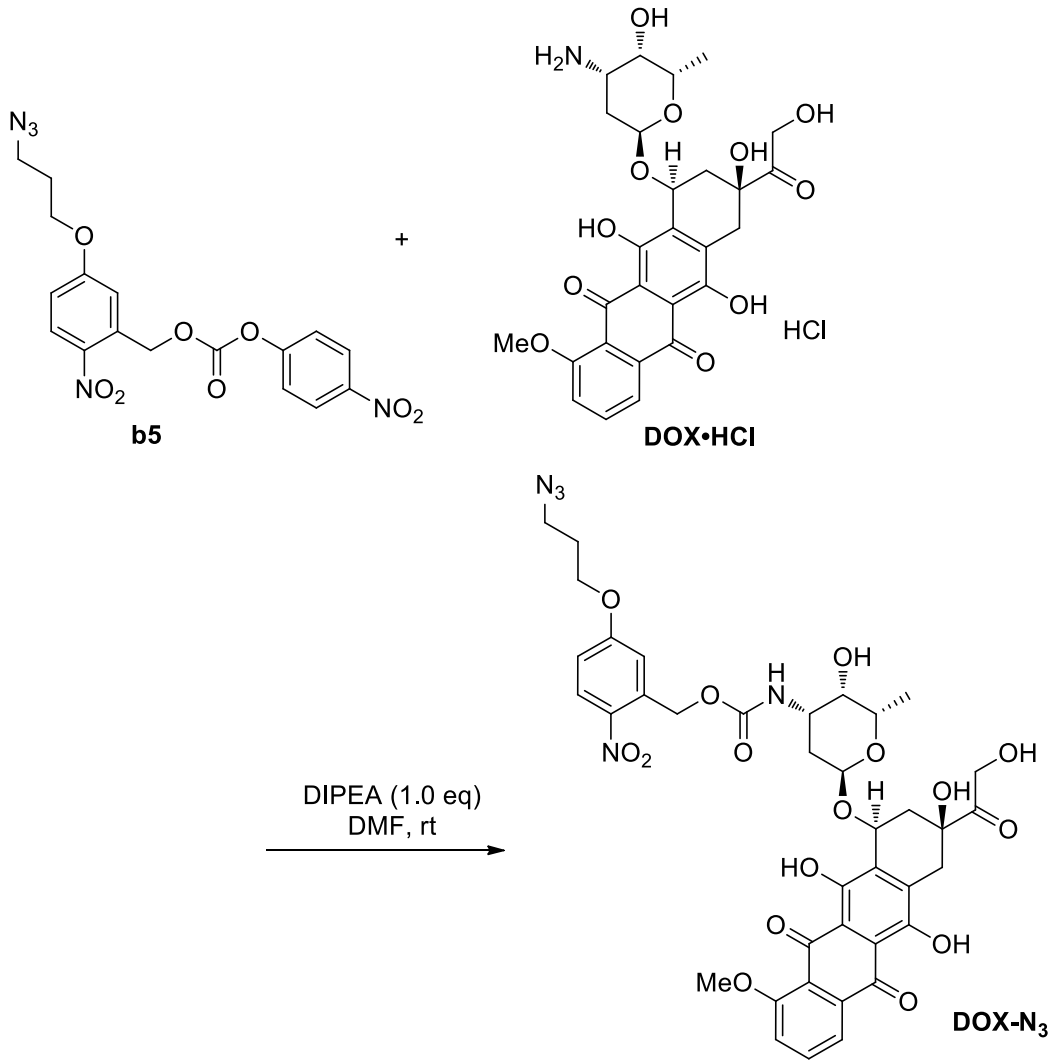
Synthesis of (5-(3-azidopropoxy)-2-nitrophenyl)methanol b4. DMF (7.5 mL) was added to (5-(3-chloropropoxy)-2-nitrophenyl)methanol (635 mg, 0.00258 moles) and sodium azide (252 mg, 0.00387 moles) in a flask, which was heated to 70 °C and stirred overnight. The reaction was diluted in ethyl acetate (100 mL), and washed twice with water (75 mL each) and once with brine (75 mL). The organic layer was dried with anhydrous magnesium sulfate, which was filtered out. The solution was concentrated on a rotary evaporator and dried on vacuum overnight to yield (5-(3-azidopropoxy)-2-nitrophenyl)methanol as a yellow solid (yield 88%).^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.16 (d, J = 9.1 Hz, 1H), 7.27 (d, J = 2.8 Hz, 1H), 6.91 (dd, J = 9.1, 2.8 Hz, 1H), 4.98 (s, 2H), 4.18 (t, J = 6.0 Hz, 2H), 3.53 (t, J = 6.6 Hz, 2H), 2.12-2.06 (m, 2H). ^{13}C-NMR (100 MHz, CD_2Cl_2) δ 163.99, 141.22, 128.43, 114.97, 113.93, 66.15, 63.26, 48.68, 29.13 HRMS: calcd. for $C_{10}H_{12}N_4O_4$ $[M+H]^+$, 253.0931; found, 253.0939.



b4 **b5**

Synthesis of compound b5.(A modified procedure was used referencing a previously reported reaction[5]) A solution of (5-(3-azidopropoxy)-2-nitrophenyl)methanol (250 mg, 0.00099 moles) and triethylamine (0.21 mL, 0.0015 moles) in tetrahydrofuran (5 mL) was added dropwise to a flask of 4-nitrophenyl chloroformate (423mg, 0.0021 moles) in tetrahydrofuran (15 mL) at 0 °C under nitrogen. The ice-bath was removed and the reaction was left to stir for one hour. The mixture was concentrated on a rotary evaporator and purified by silica gel chromatography from 100% hexanes to 100% ethyl acetate. The fractions containing product was concentrated on a

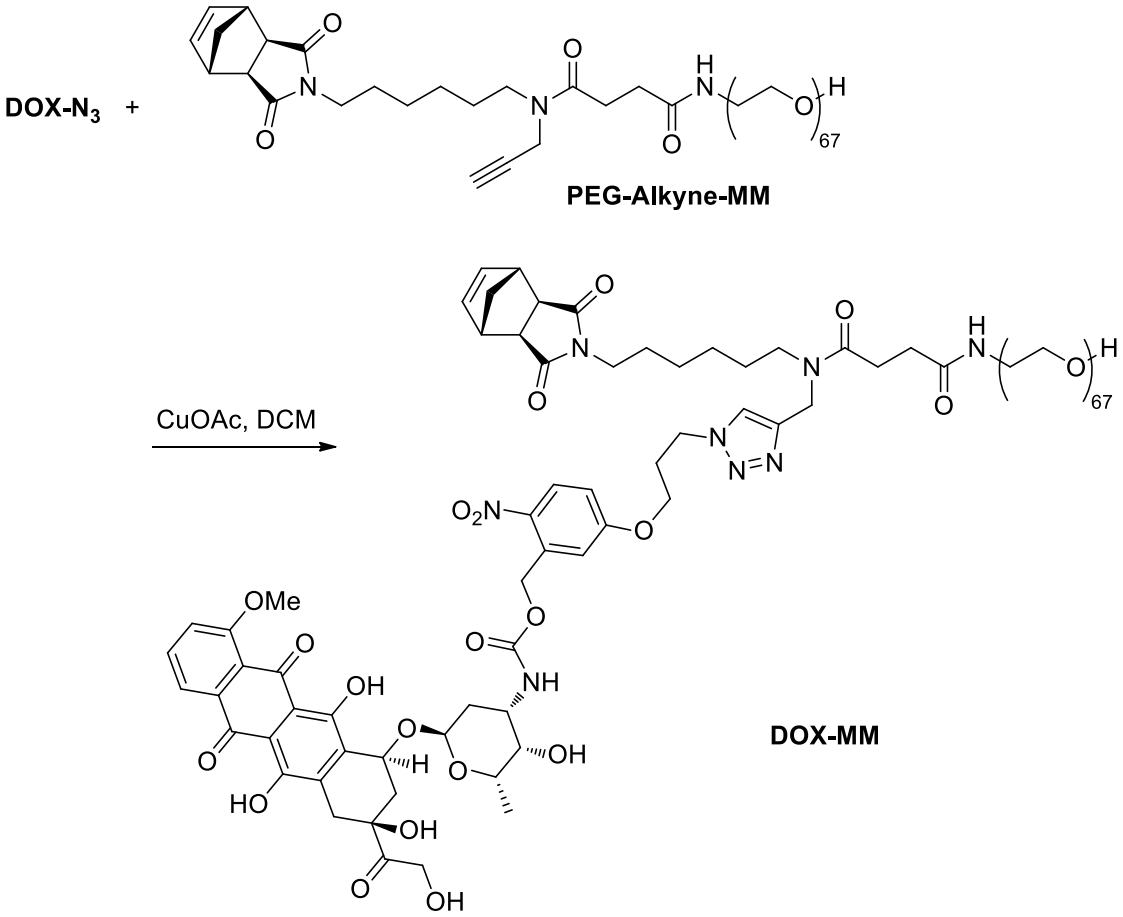
rotary evaporator and dried on vacuum overnight to yield **b5** as a yellow solid (yield 65%*). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.31 – 8.25 (m, 2H), 8.23 (d, J = 9.2 Hz, 1H), 7.49 – 7.40 (m, 2H), 7.20 (d, J = 2.7 Hz, 1H), 6.99 (dd, J = 9.2, 2.8 Hz, 1H), 5.72 (s, 2H), 4.19 (t, J = 6.0 Hz, 2H), 3.55 (t, J = 6.5 Hz, 2H), 2.16 – 2.05 (m, 2H). *Observed impurity peaks, but does not interfere with next step: ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.12-8.08 (m), 6.92-6.88 (m). ^{13}C-NMR (100 MHz, CD_2Cl_2) δ 163.88, 156.02, 152.65, 146.13, 140.66, 134.37, 128.73, 126.5, 125.81, 122.35, 116.1 , 115.11, 114.15, 68.12, 66.33, 48.58, 29.02 HRMS: calcd. for $C_{17}H_{15}N_5O_8$ $[M+NH_4]^+$, 435.1259; found, 435.1251.



Synthesis of compound DOX-N_3. Doxorubicin hydrochloride (70.6 mg, 0.000122 moles) was dissolved DMF (1.5mL), followed by addition of DIPEA (0.021 mL, 0.000122 moles) and **b5** (48 mg, 0.000116 moles). The solution was stirred at room temperature overnight, then diluted in ethyl acetate (75 mL), washed twice with water (50 mL each) and brine (50 mL). The organic layer was dried with anhydrous magnesium sulfate, which was removed by filtration. The solution was concentrated and silica gel chromatography was performed using a gradient of 100% dichloromethane to 10% methanol in dichloromethane. The fractions containing product were collected, then solvent was removed by rotary evaporation, and dried overnight to yield **DOX-N_3** as a red solid (yield 92%*). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 13.94 (s, 1H), 13.10 (s,

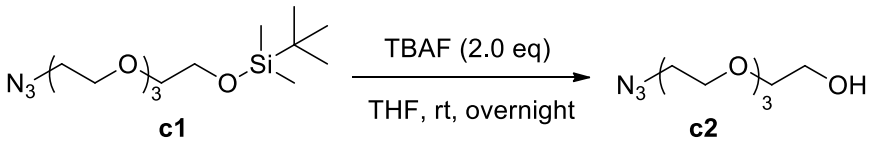
1H), 8.09 (d, J = 9.1 Hz, 1H), 7.91 (dd, J = 7.7, 1.1 Hz, 2H), 7.74 (t, J = 8.1 Hz, 1H), 7.35 (dd, J = 8.5, 1.1 Hz, 1H), 7.03 – 6.97 (m, 1H), 6.86 – 6.81 (m, 1H), 5.54 (d, J = 8.6 Hz, 1H), 5.51-5.47 (m, 1H), 5.40 (dd, 24.6, 15.7, 1H), 5.24-5.19 (m, 1H), 4.74 (s, 2H), 4.60 (s, 1H), 4.19-4.11 (m, 1H), 4.09 (t, J = 6.0 Hz, 2H) 3.99 (s, 3H), 3.89-3.82 (m, 1H), 3.68 (s, 1H), 3.48 (t, J = 6.5 Hz, 2H), 3.22 – 3.12 (m, 1H), 2.94-2.87(m, 1H), 2.50 (s, 1H), 2.34 (d, J = 14.7 Hz, 1H), 2.13 (dd, J = 14.6, 4.1 Hz, 1H), 2.02 (p**, J = 6.3 Hz, 2H), 1.91-1.80 (m, 2H), 1.29 (d, J = 6.5 Hz, 3H). ^{13}C-NMR (100 MHz, CD_2Cl_2) δ 214.52, 187.20, 163.64, 161.60, 156.56, 155.90, 155.49, 140.54, 136.24, 135.77, 134.17, 133.96, 128.32, 120.00, 119.21, 114.20, 113.48, 112.02, 111.87, 101.11, 77.18, 69.96, 67.96, 66.08, 66.03, 63.99, 57.03, 48.57, 47.48, 36.09, 34.40, 30.61, 28.97, 17.15 HRMS: calcd. for $C_{38}H_{39}N_5O_{16}$ $[M+Na]^+$, 844.2284; found, 844.2271. *Observed DMF, but does not interfere with the next step: 1H NMR (400 MHz, CD_2Cl_2) δ 7.96 (s), 2.91 (s), 2.82 (s); 13C-NMR (100 MHz, CD_2Cl_2) δ 162.89, 36.79, 31.61

**pseudo-pentet

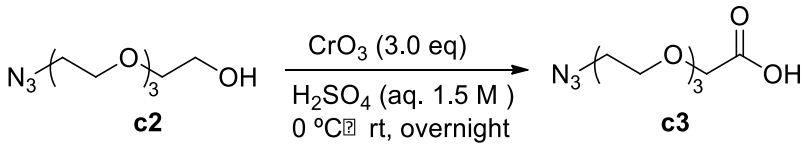


Synthesis of DOX-MM To a solution of **DOX-N_3** (49 mg, 0.060 mmol) and **PEG-Alkyne-MM** (300 mg, 0.060 mmol) in 10 ml DCM, was added CuOAc (0.6 mg, 4.8 μmmol) under N_2. The reaction was allowed to stir at room temperature and monitored by LC-MS until the complete consumption of **PEG-Alkyne-MM**. Then the solvent was removed under vacuum and the residue was purified by HPLC diluting with water (containing 0.1% acetic acid) and acetonitrile. The desired **DOX-MM** was obtained as light yellow powder (174 mg, 70% yield). ^{1}H NMR and MALDI were provided at the end of the SI.

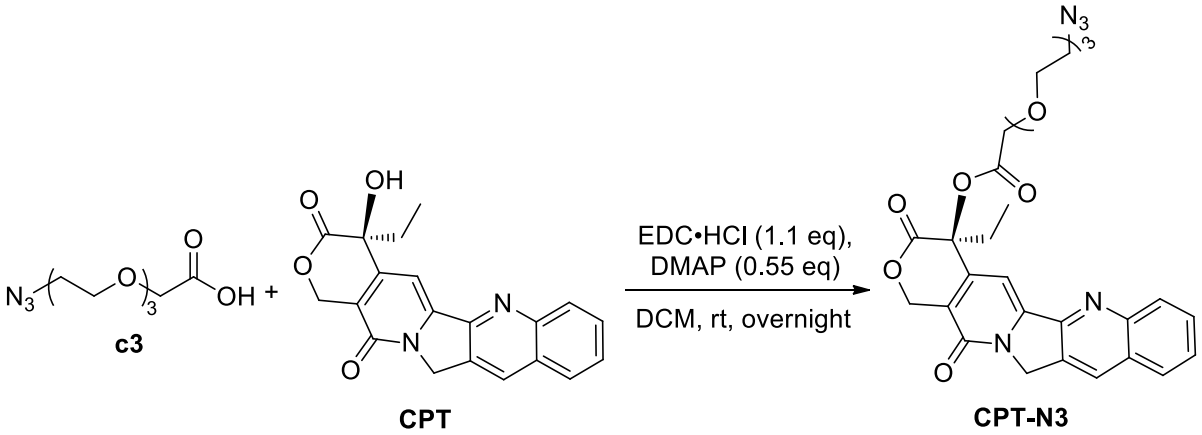
Synthesis of CPT-MM



Synthesis of c2 The THF (35 mL) solution of the silyl ether **c1**[7] (3.5 g, 10.5 mmol) and TBAF (5.5 g, 21 mmol) was allowed to stir under N_2 at room temperature overnight. Then the reaction mixture was concentrated under vacuum and the residue was purified by flash chromatography diluting with hexanes and ethyl acetate to give **c2** (colorless oil, 2.3 g, 99% yield). The characterization was compared with previously reported data.[8]

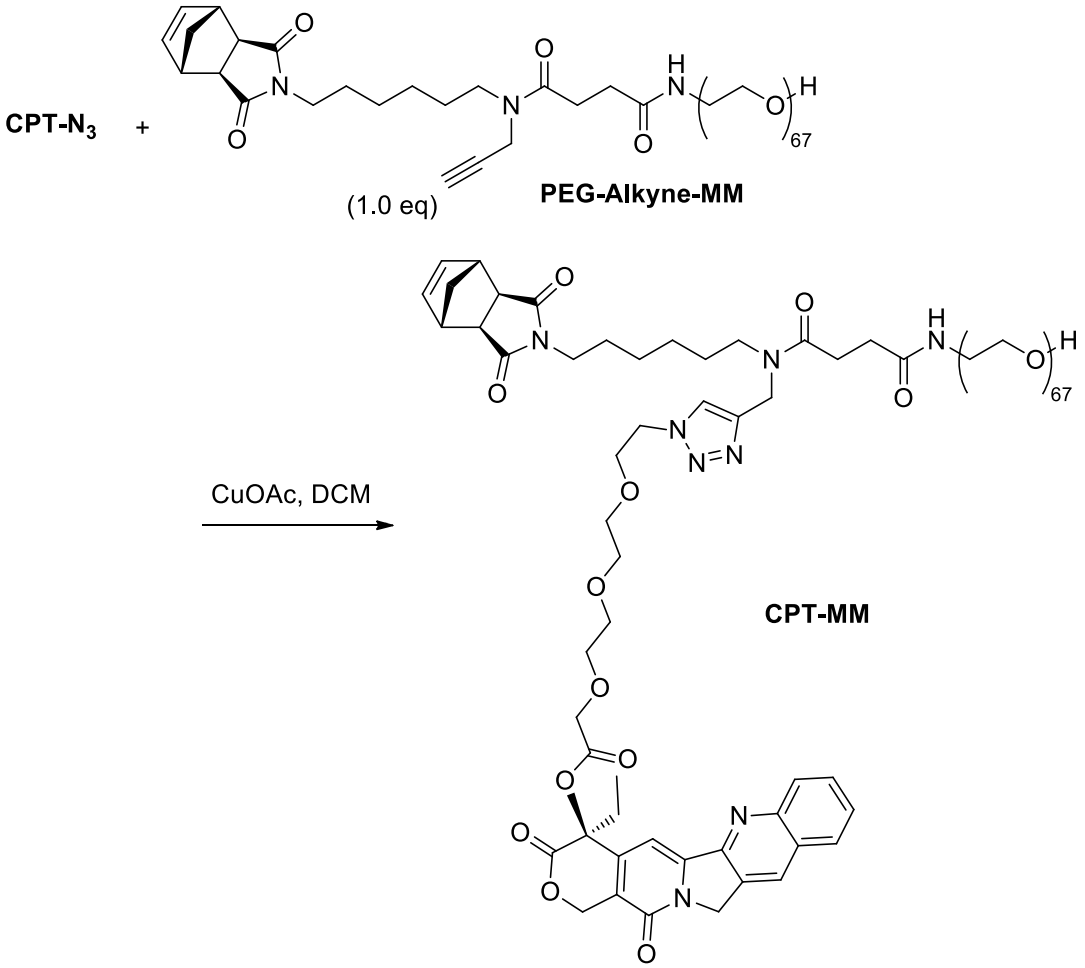


Synthesis of c3 To a solution of **c2** (1.1 g, 5.0 mmol) in acetone (55 mL) at 0 ˚C, was added a solution of CrO_3 (1.5 g, 15 mmol) in 1.5 M H_2SO_4 in water (31 mL) dropwise by an additional funnel. After addition, the reaction was allowed to stir at room temperature overnight. The reaction was then quenched by addition of isopropanol (30 mL) and concentrated under vacuum. The aqueous residue was extracted by DCM (50 mL × 4). The organic layer was combined, dried over Na_2SO_4 and concentrated under vacuum. The product was purified by silica flash chromatography diluting with hexanes and ethyl acetate to give colorless oil (1.2 g, 99% yield). The characterization was compared with previously reported data.[9]



Synthesis of CPT-N_3 The mixture of CPT (64 mg, 0.18 mmol), **c3** (86 mg, 0.37 mmol), *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDC·HCl, 71 mg, 0.37 mmol) and 4-dimethylaminopyridine (DMAP, 45 mg, 0.37 mmol) in DCM (10 mL) was allowed to stir under N_2 at room temperature overnight. The reaction was then concentrated under vacuum and the product was purified by flash chromatography diluting with 5% MeOH in DCM to give yellow solid (81 mg, 78% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (s, 1H), 8.22 (d, J = 8.4 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.84 (dd, J = 8.0, 6.9, 1H), 7.68 (dd, J = 8.4, 6.9, 1H), 7.21 (s, 1H), 5.70 (d, J = 17.2 Hz, 1H), 5.42 (d, J = 17.2 Hz, 1H), 5.29 (s, 2H), 4.36 (d, J = 5.5 Hz, 1H), 3.78 – 3.62 (m, 10H), 3.36 (t, J = 7.5 Hz, 2H), 2.35 – 2.11 (m, 2H), 0.98 (t, J = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 167.1, 157.1, 152.1, 148.7, 146.3, 145.2, 131.1, 130.5, 129.4, 128.3, 128.1, 128.0, 127.9, 120.1, 95.7, 76.2, 70. 9, 70.5, 70.5, 70.4, 69.8, 68.0, 67.0, 50.5, 49.8, 31.6, 7.4. MS (ESI) m/z $(M+Li)^+$ calcd. for $C_{28}H_{29}N_5O_8Li$: 564.2089 obsd.: 564.2098.



Synthesis of CPT-MM To a solution of **CPT-N_3** (50 mg, 0.089 mmol) and **PEG-Alkyne-MM** (300 mg, 0.089 mmol) in 10 ml DCM, was added CuOAc (0.6 mg, 4.8 μmmol) under N_2. The reaction was allowed to stir at room temperature and monitored by LC-MS until the complete consumption of **PEG-Alkyne-MM**. Then the solvent was removed under vacuum and the residue was purified by HPLC diluting with water (containing 0.1% acetic acid) and acetonitrile. The desired **CPT-MM** was obtained as light yellow powder (140 mg, 40% yield). ^{1}H NMR and MALDI are provided at the end of the SI.

General Procedure for BASP Synthesis

Note: All BASP syntheses were performed in a glovebox under N_2 atmosphere though similar results may be expected under ambient conditions.

Synthesis of 1. PEG-MM (70.0 mg) was added to a 4 mL vial containing a stir bar. **PtXL** (6.4 mg) was added to separate 4 mL vials containing a stir bar. THF (273 μL) was added to the vial with **PEG-MM** followed by a freshly prepared solution of catalyst **cat** in THF (0.02 mmol/mL, 152 μL) to give desired **PEG-MM**:**cat = 7**. Note that the total concentration of MM **PEG-MM** was 0.05 M. After 20 minutes of stirring at 25 °C, 406 μL of the polymerization mixture were transferred to the vials containing **PtXL**. The resulting mixtures were stirred at 25 °C for 6 hrs, at which point 1 drop of ethyl vinyl ether was added to quench the polymerization. The THF and excess ethyl vinyl ether were removed under vacuum.

Synthesis of 2a. PEG-MM (48.4 mg) and **CPT-MM** (23.1 mg) were added to a 4 mL vial containing a stir bar. **PtXL** (6.4 mg) was added to separate 4 mL vials containing a stir bar. THF (268 μL) was added to the vial with **PEG-MM** followed by a freshly prepared solution of catalyst **cat** in THF (0.02 mmol/mL, 149 μL) to give desired **PEG-MM**:**cat = 7**. Note that the total concentration of MM **PEG-MM** was 0.05 M. After 20 minutes of stirring at 25 °C, 406 μL of the polymerization mixture were transferred to the vials containing **PtXL**. The resulting mixtures were stirred at 25 °C for 6 hrs, at which point 1 drop of ethyl vinyl ether was added to quench the polymerization. The THF and excess ethyl vinyl ether were removed under vacuum.

Synthesis of 2b. PEG-MM (60.0 mg) and **DOX-MM** (9.7 mg) were added to a 4 mL vial containing a stir bar. **PtXL** (6.4 mg) was added to separate 4 mL vials containing a stir bar. THF (265 μL) was added to the vial with **PEG-MM** followed by a freshly prepared solution of catalyst **cat** in THF (0.02 mmol/mL, 147 μL) to give desired **PEG-MM**:**cat = 7**. Note that the total concentration of MM **PEG-MM** was 0.05 M. After 20 minutes of stirring at 25 °C, 397 μL of the polymerization mixture were transferred to the vials containing **PtXL**. The resulting mixtures were stirred at 25 °C for 6 hrs, at which point 1 drop of ethyl vinyl ether was added to quench the polymerization. The THF and excess ethyl vinyl ether were removed under vacuum.

Synthesis of 3. PEG-MM (38.8 mg), **CPT-MM** (22.3 mg) and **DOX-MM** (9.4 mg) were added to a 4 mL vial containing a stir bar. **PtXL** (6.4 mg) was added to separate 4 mL vials containing a stir bar. THF (258 μL) was added to the vial with **PEG-MM** followed by a freshly prepared solution of catalyst **cat** in THF (0.02 mmol/mL, 144 μL) to give desired **PEG-MM**:**cat = 7**. Note that the total concentration of MM **PEG-MM** was 0.05 M. After 20 minutes of stirring at 25 °C, 382 μL of the polymerization mixture were transferred to the vials containing **PtXL**. The resulting mixtures were stirred at 25 °C for 6 hrs, at which point 1 drop of ethyl vinyl ether was added to quench the polymerization. The THF and excess ethyl vinyl ether were removed under vacuum.

Spectral Data

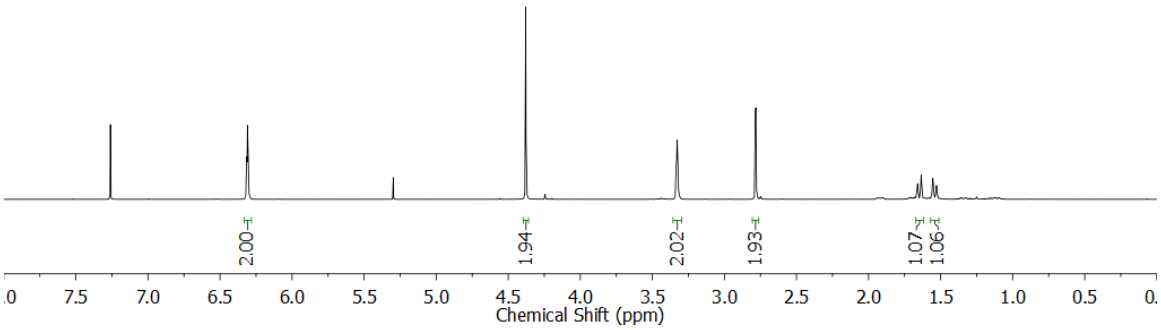


Figure S8. ^{1}H NMR spectrum of **a2** in $CDCl_3$.

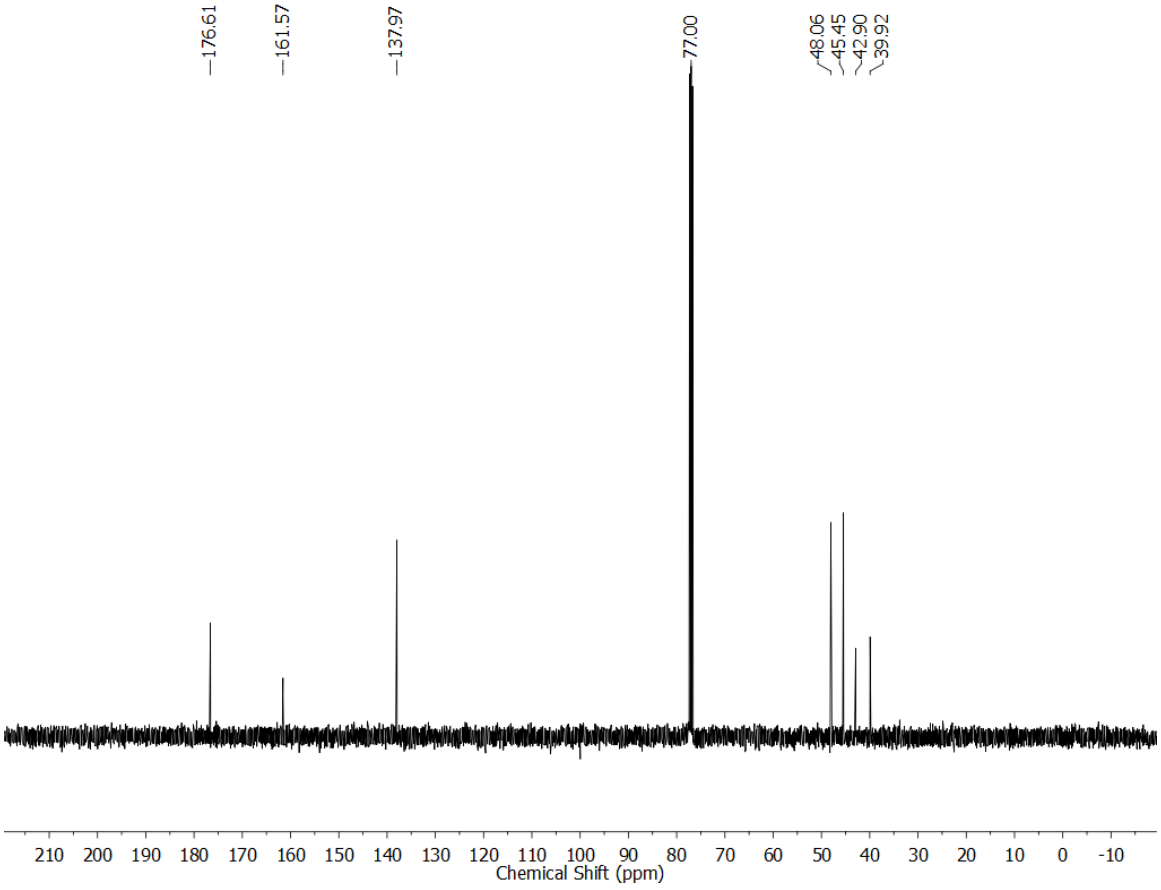


Figure S9. ^{13}C NMR spectrum of **a2** in $CDCl_3$.

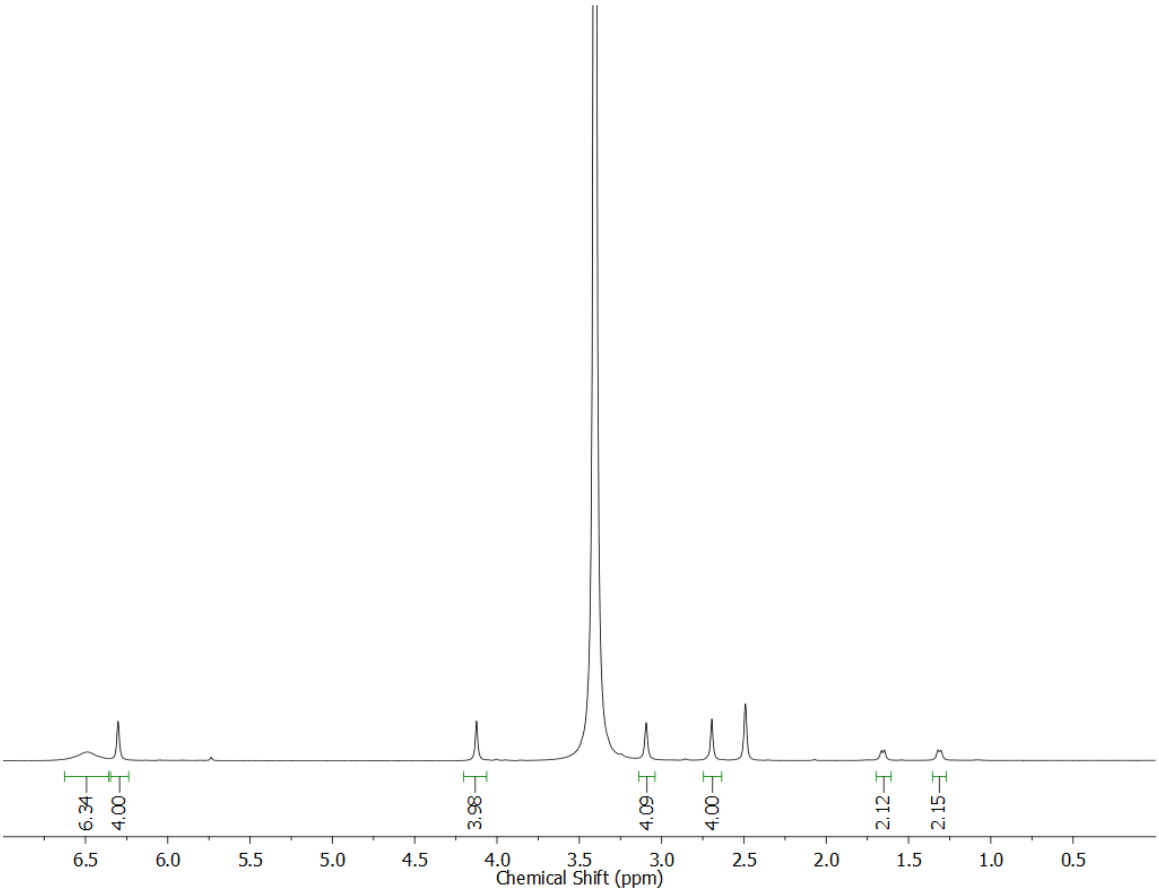


Figure S10. ^{1}H NMR spectrum of **Pt-XL** in DMSO-d_6.

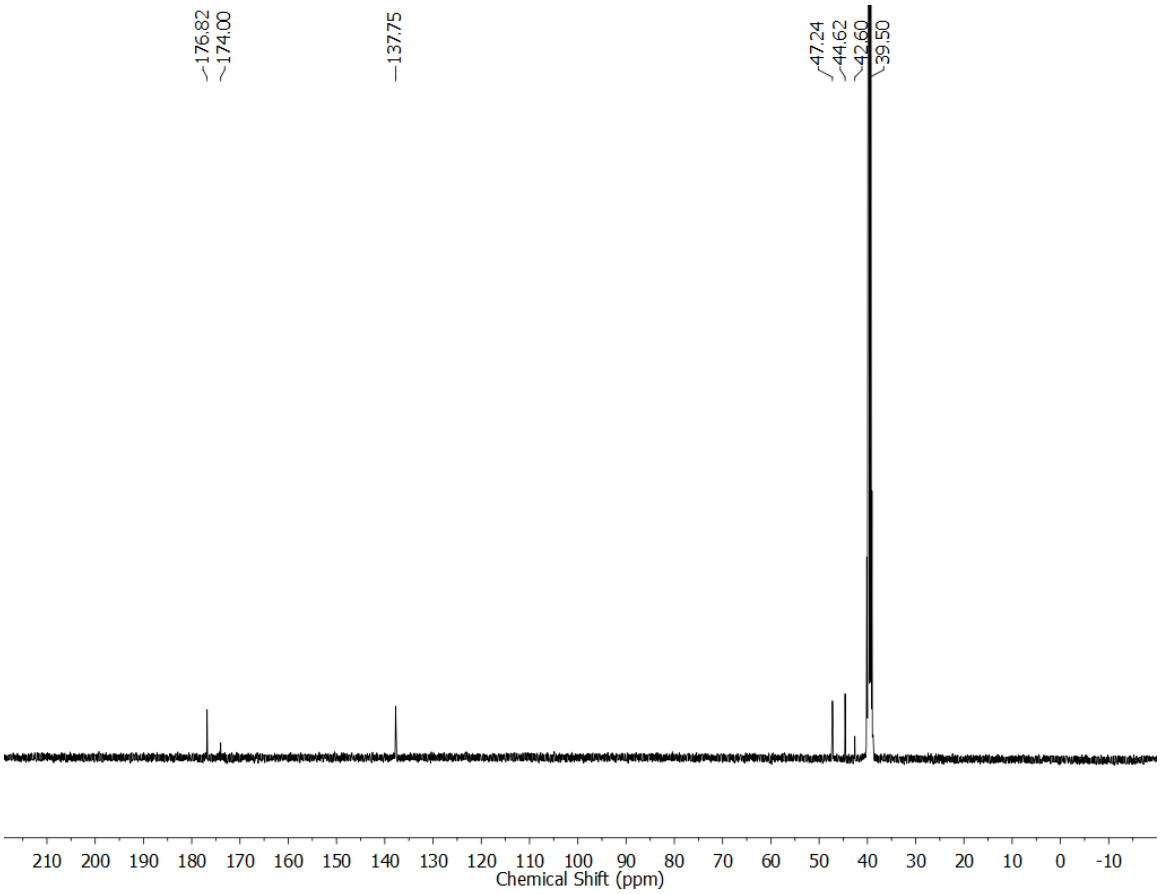


Figure S11. ^{13}C NMR spectrum of **Pt-XL** in DMSO-d_6.

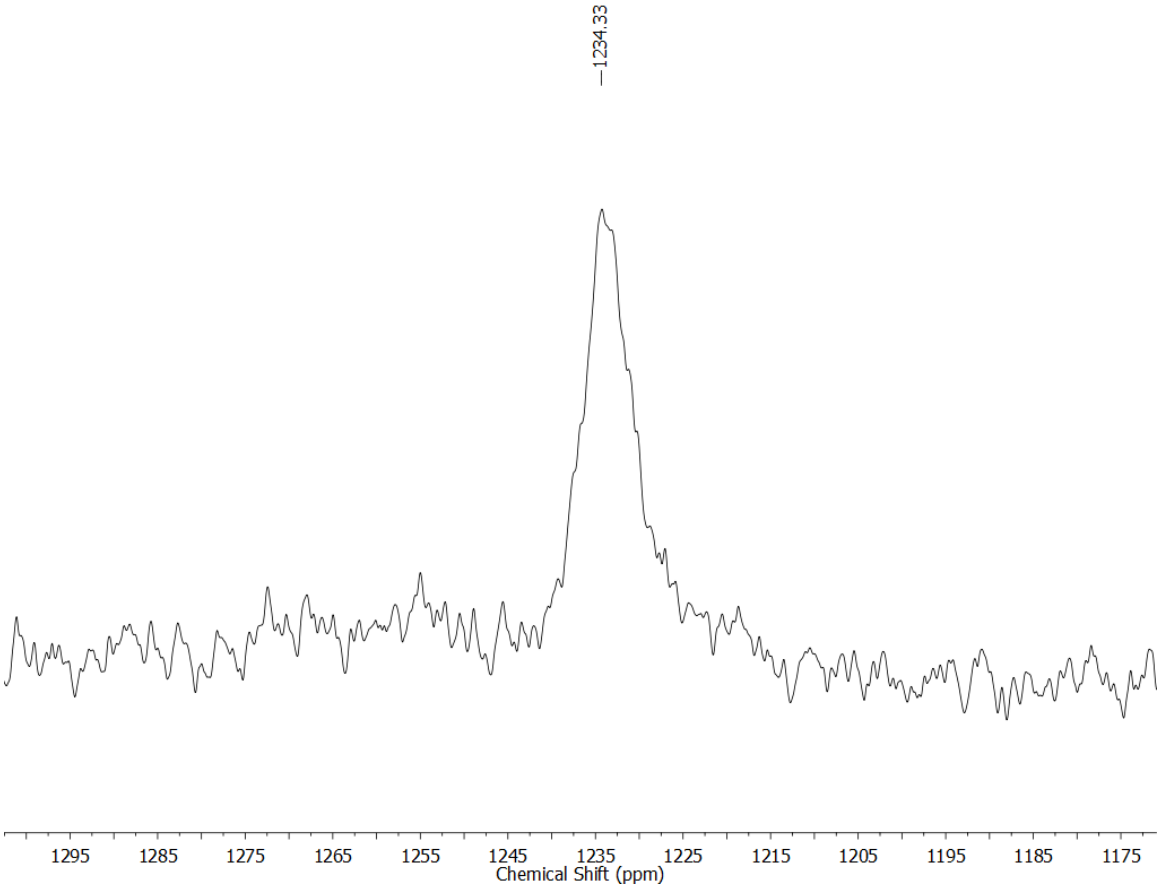


Figure S12. ^{195}Pt NMR spectrum of **Pt-XL** in DMSO-d_6.

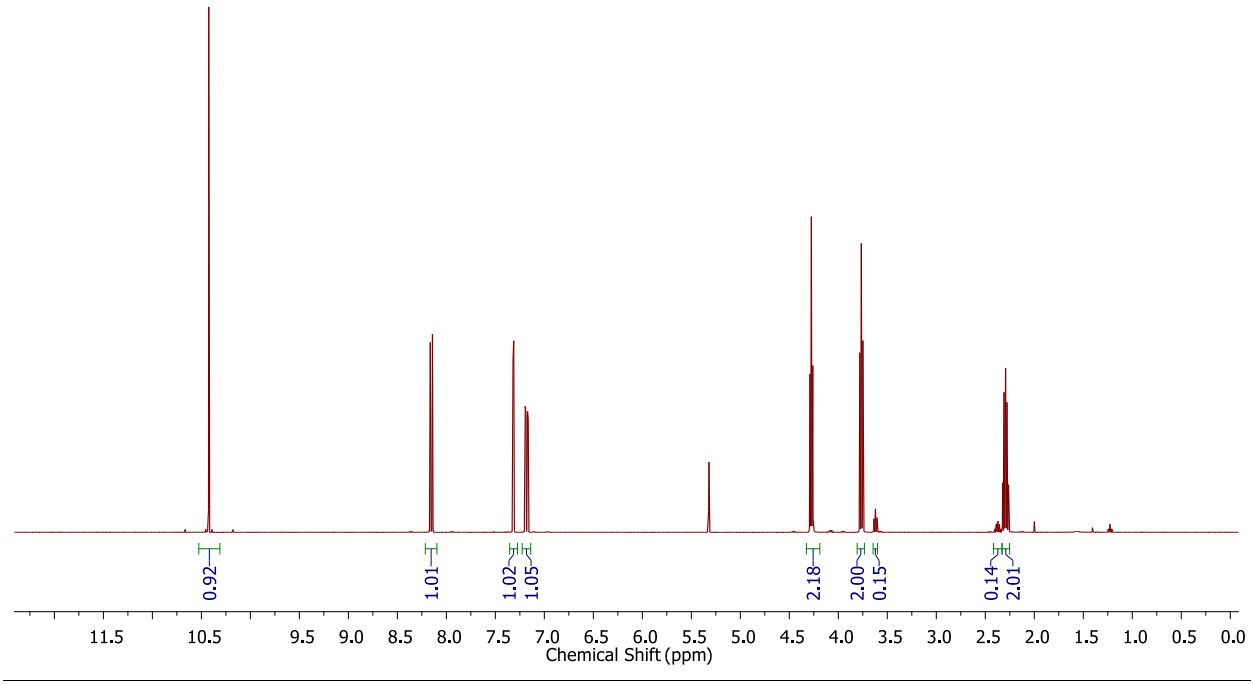


Figure S13. ^{1}H-NMR spectrum of **5-(3-chloropropoxy)-2-nitrobenzaldehyde b2** in CD_2Cl_2.

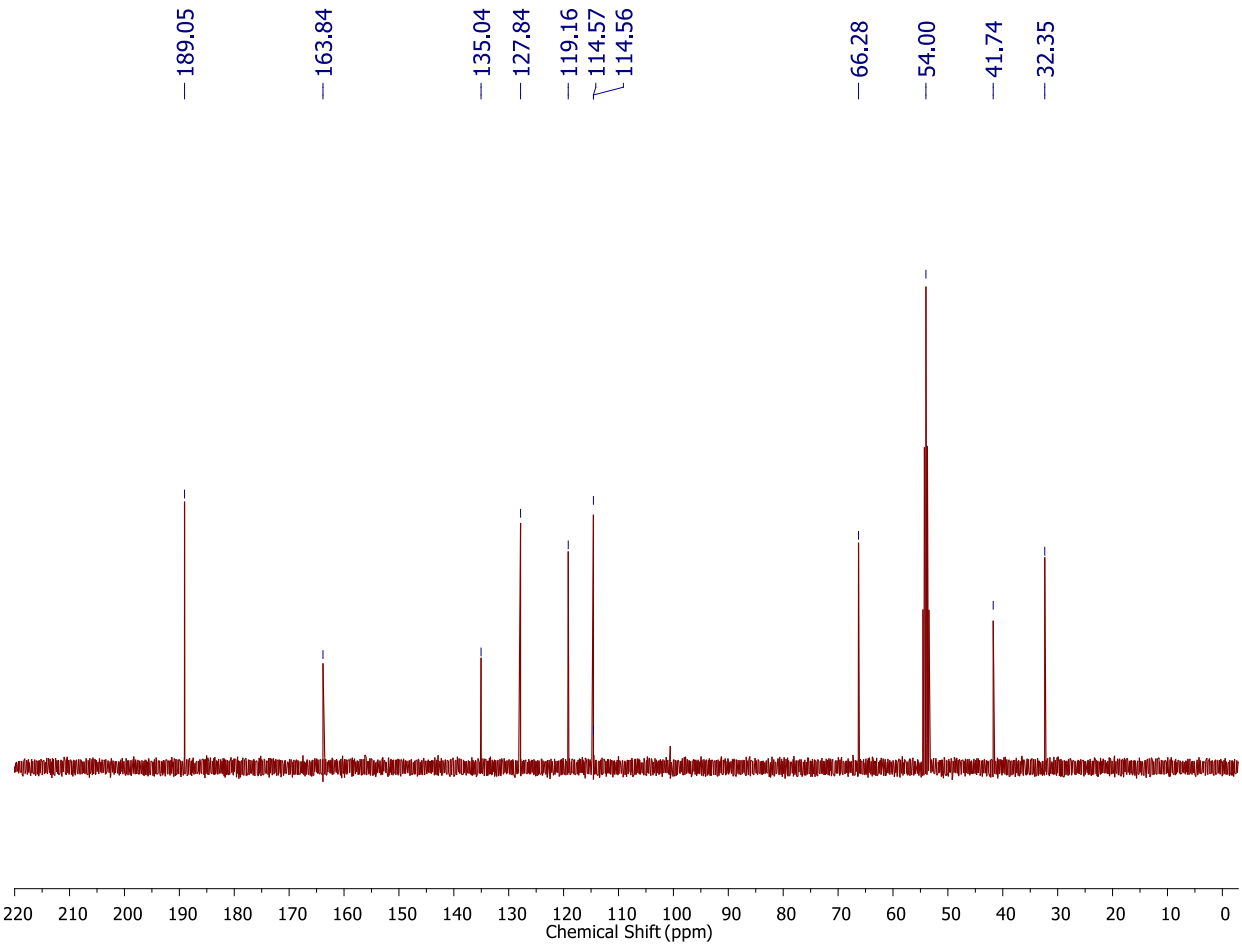


Figure S14. ^{13}C NMR spectrum of **5-(3-chloropropoxy)-2-nitrobenzaldehyde b2** in CD_2Cl_2.

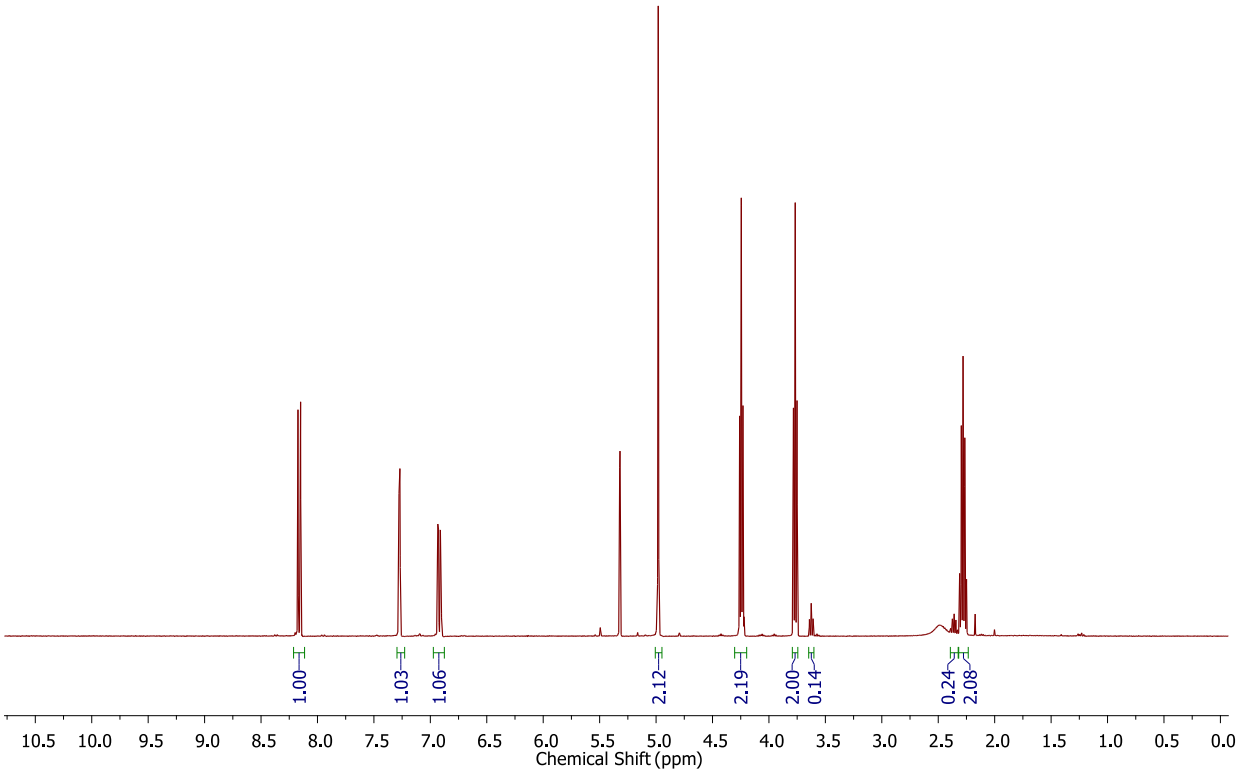


Figure S15. ^{1}H-NMR spectrum of **(5-(3-chloropropoxy)-2-nitrophenyl)methanol b3** in CD_2Cl_2.

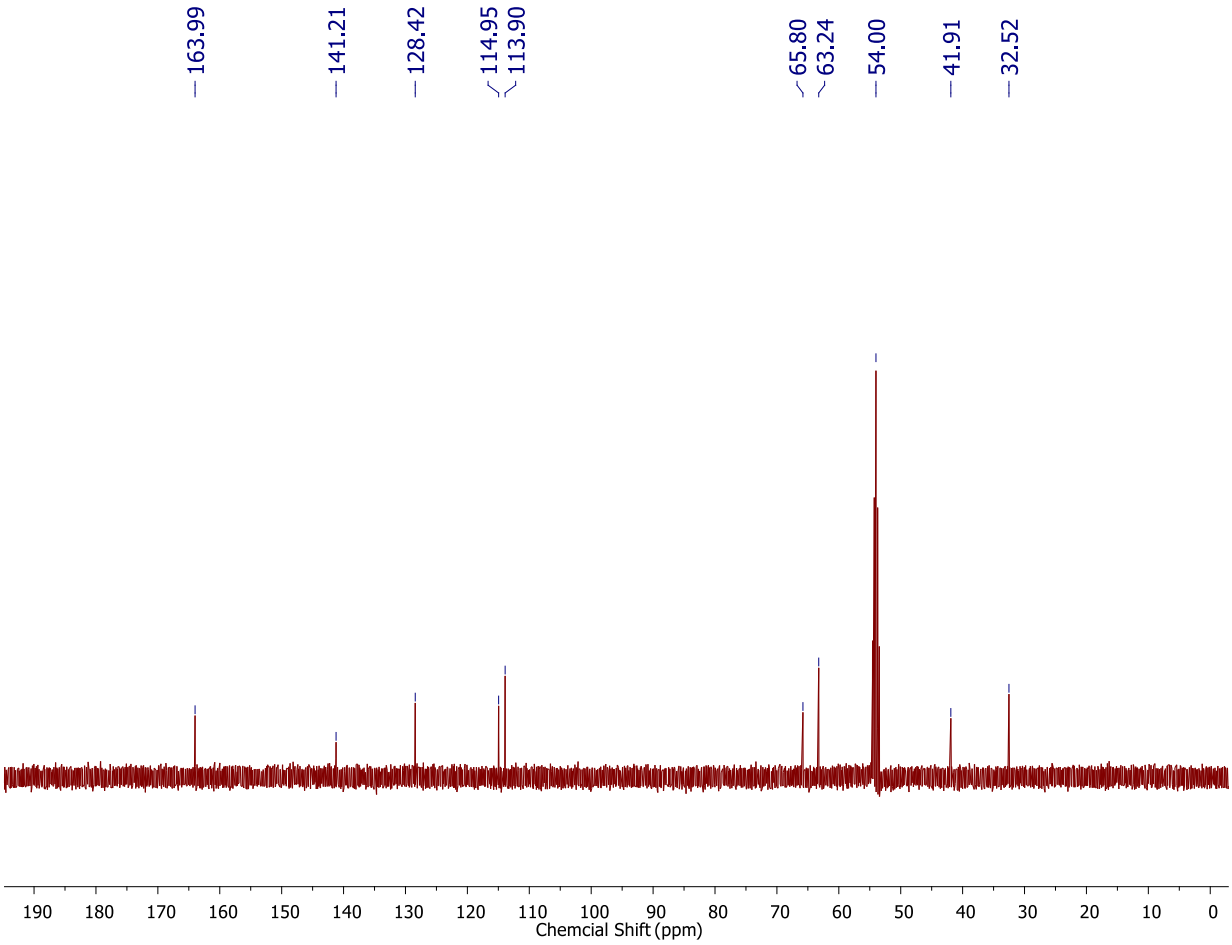


Figure S16. ^{13}C NMR spectrum of **(5-(3-chloropropoxy)-2-nitrophenyl)methanol b3** in CD_2Cl_2.

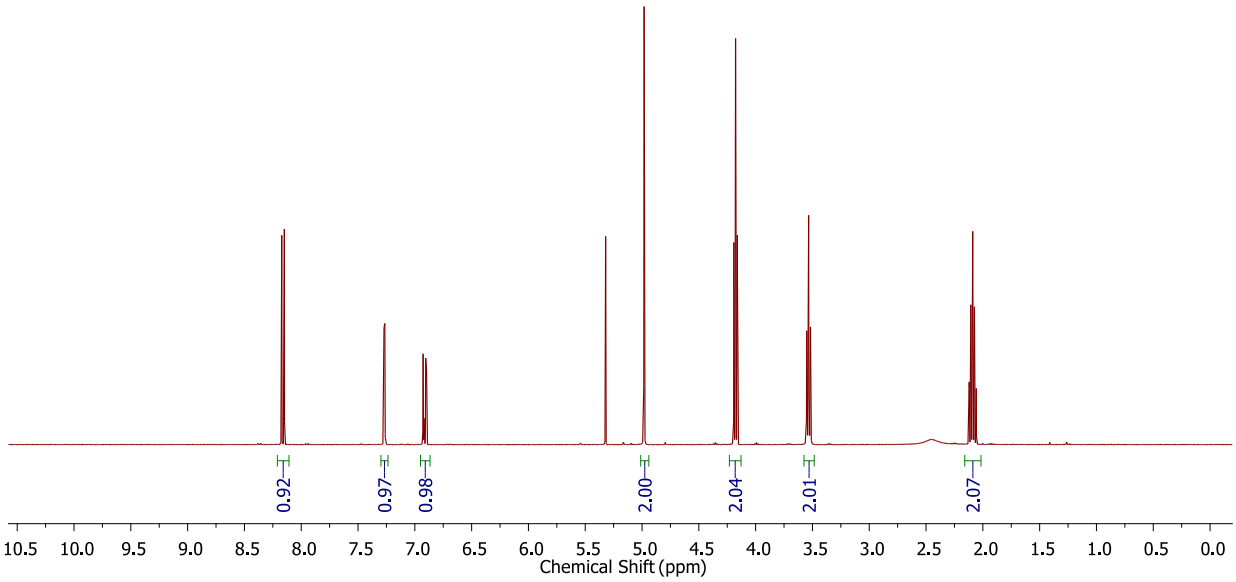


Figure S17. ^{1}H-NMR spectrum of **(5-(3-azidopropoxy)-2-nitrophenyl)methanol b4** in CD_2Cl_2.

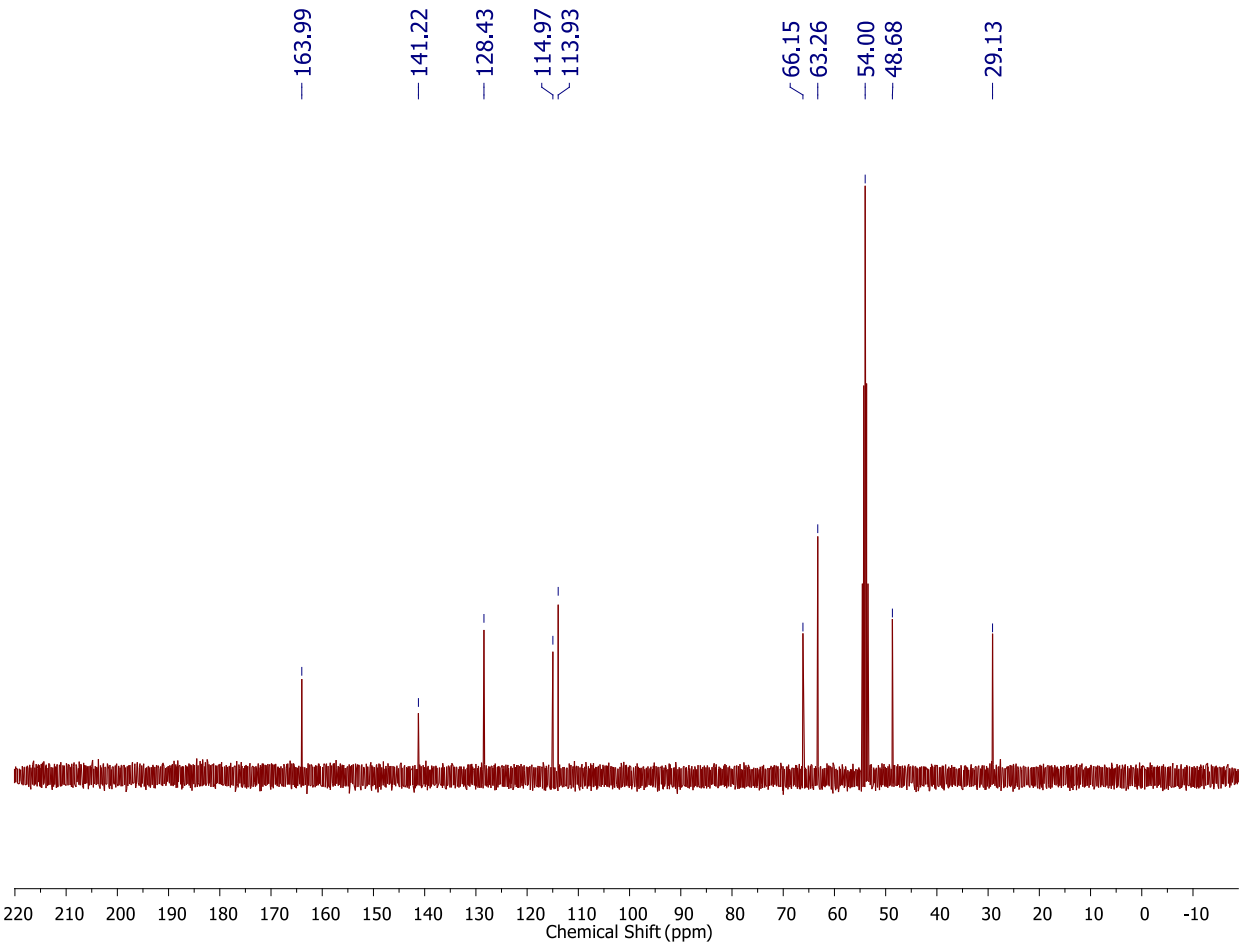


Figure S18. ^{13}C NMR spectrum of **(5-(3-azidopropoxy)-2-nitrophenyl)methanol b4** in CD_2Cl_2.

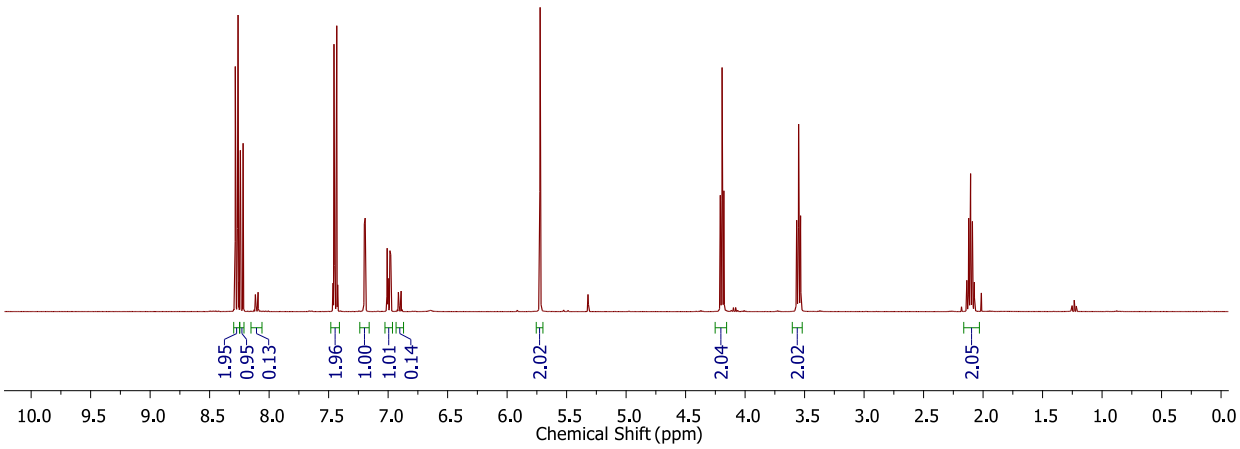


Figure S19. ^{1}H-NMR spectrum of compound **b5** in CD_2Cl_2.

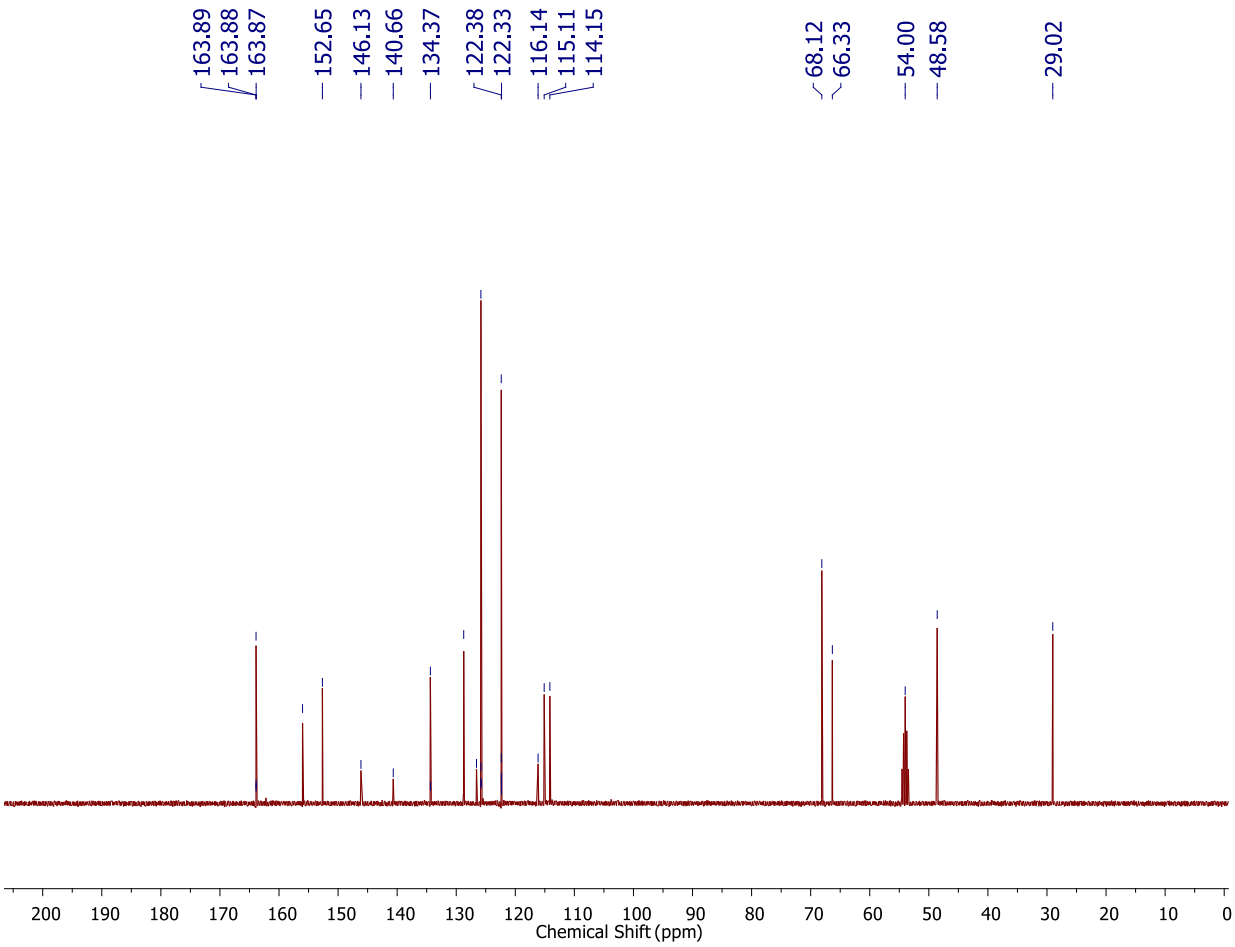


Figure S20. ^{13}C NMR spectrum of compound **b5** in CD_2Cl_2.

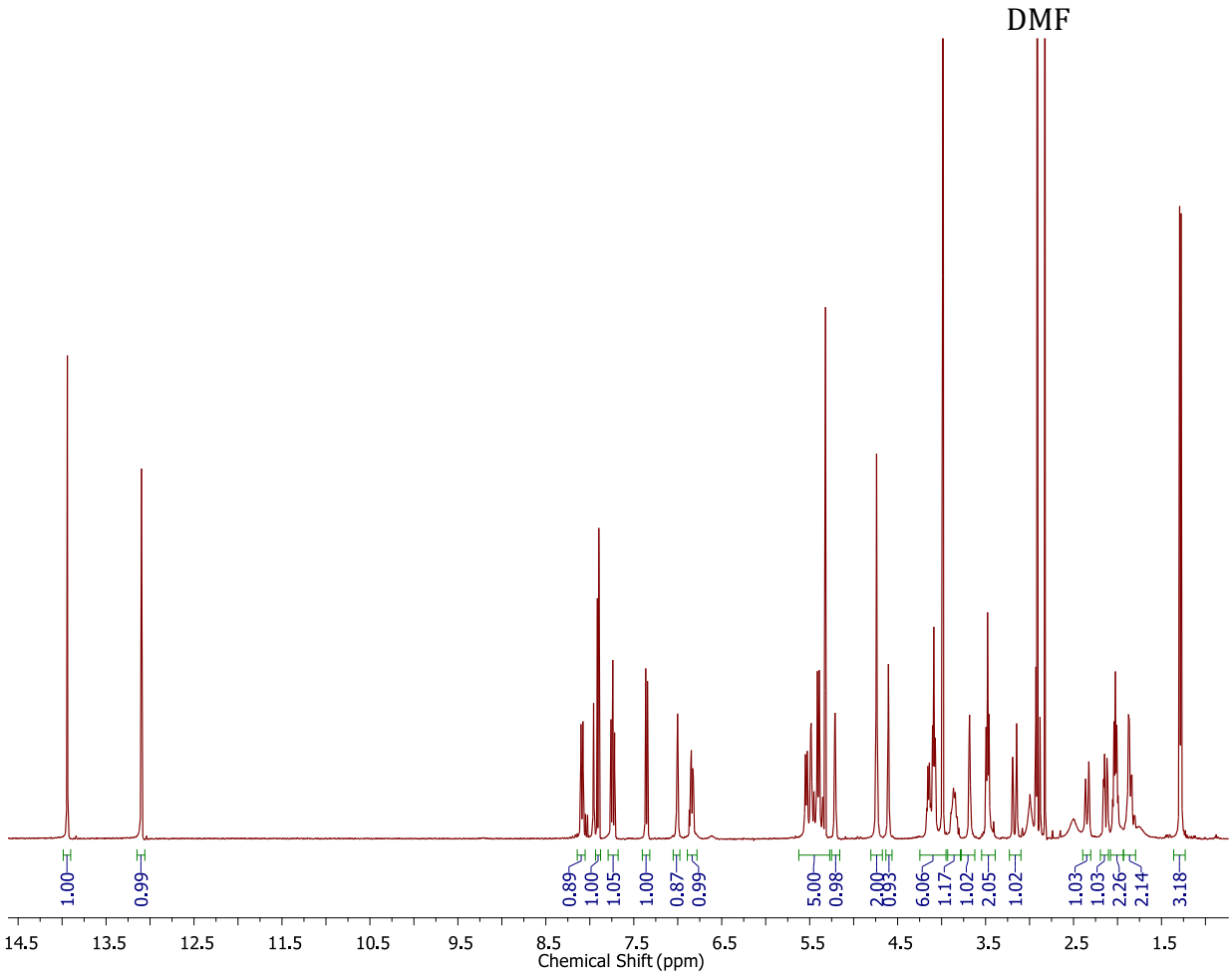


Figure S21. ^{1}H-NMR spectrum of **DOX-N$_3$** in CD_2Cl_2.

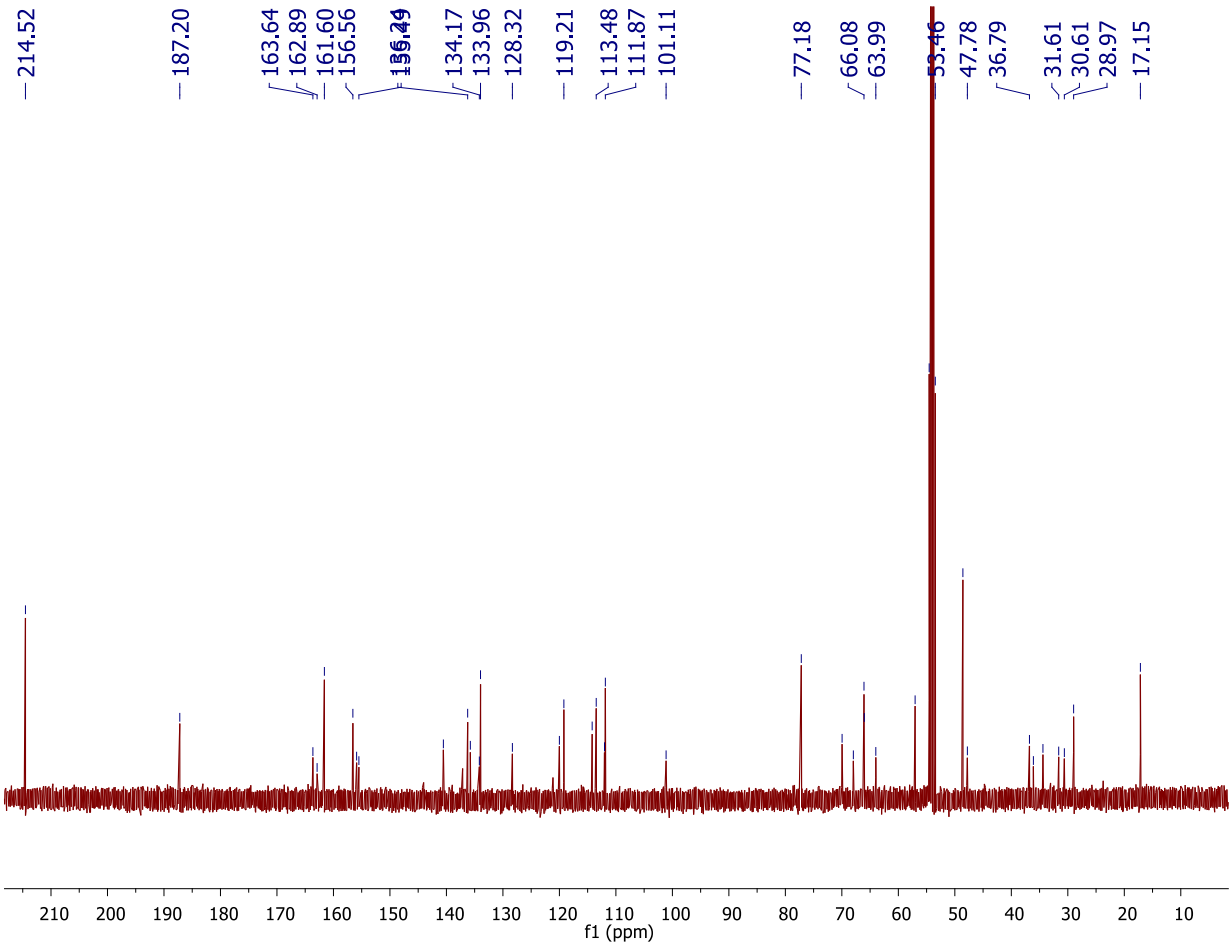


Figure S22. ^{13}C NMR spectrum of **DOX-N$_3$** in CD_2Cl_2.

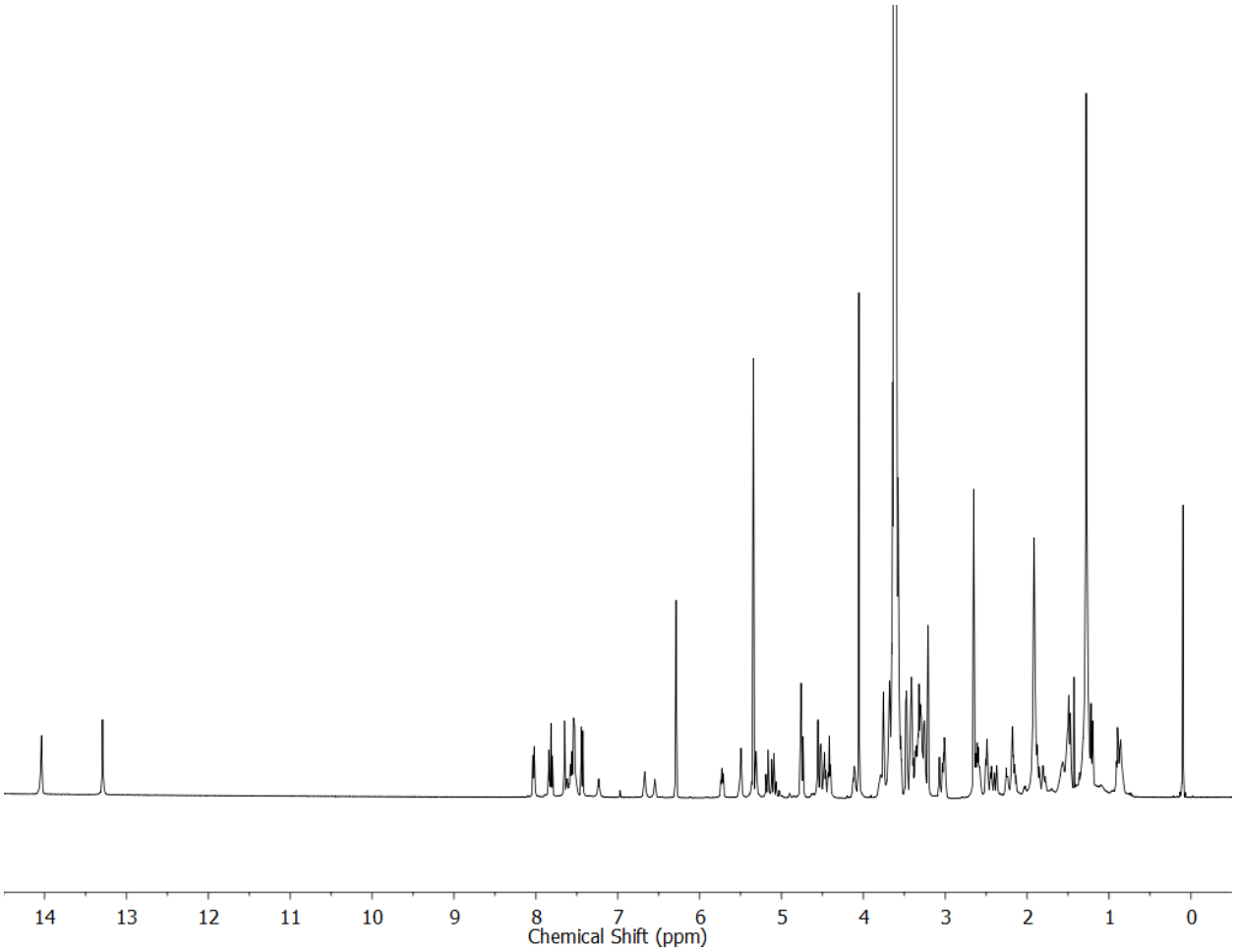


Figure S23. ^{1}H NMR spectrum of **DOX-MM** in CD_2Cl_2.

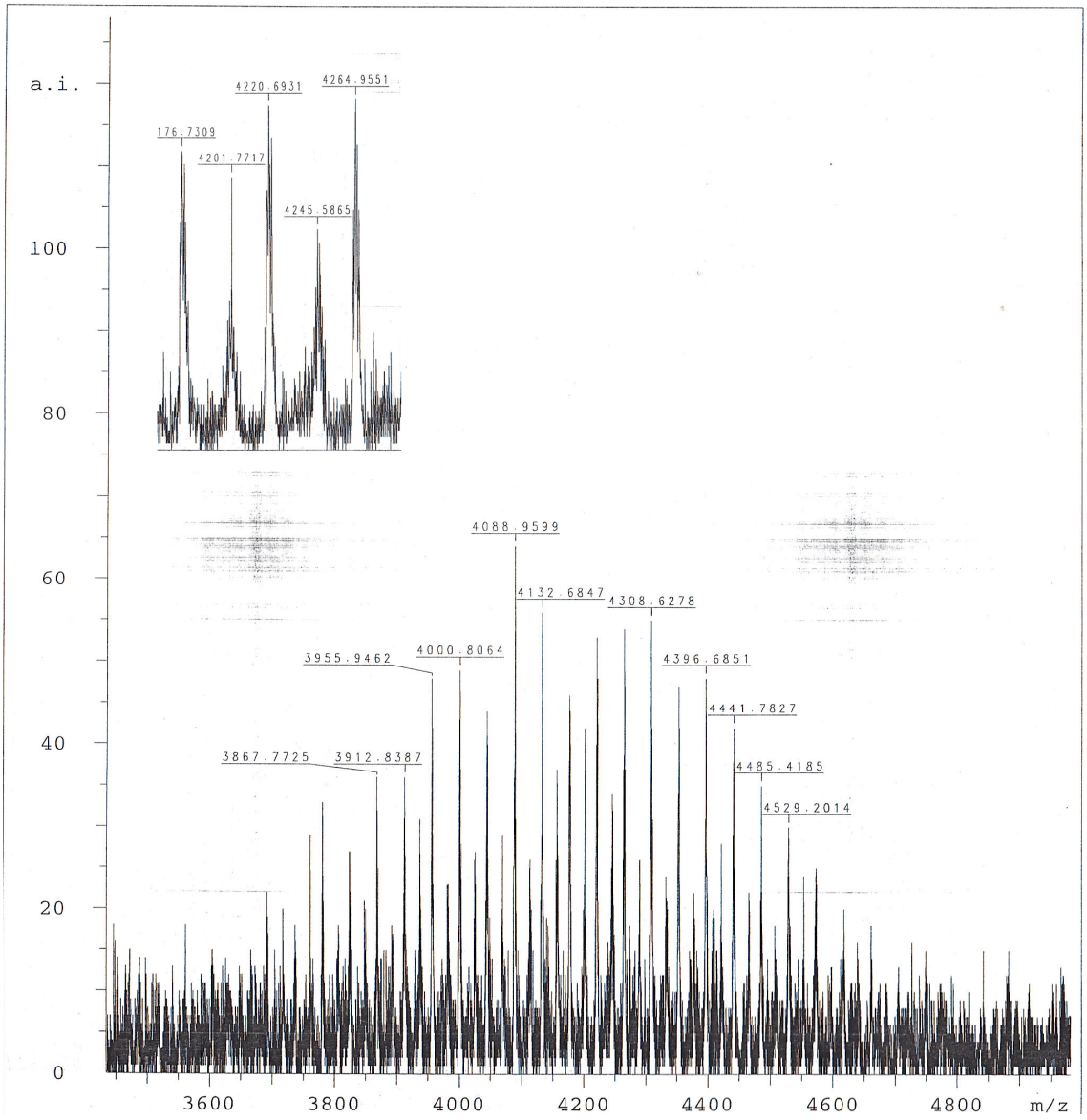


Figure S24. MALDI spectrum of **DOX-MM**. ($(M+Li)^+$ calcd. for $C_{194}H_{336}N_8O_{87}Li$: 4177.23 obsd.: 4176.73; $(M+MeOH+H)^+$ calcd. for $C_{195}H_{341}N_8O_{88}$: 4203.25 obsd.: 4201.77)

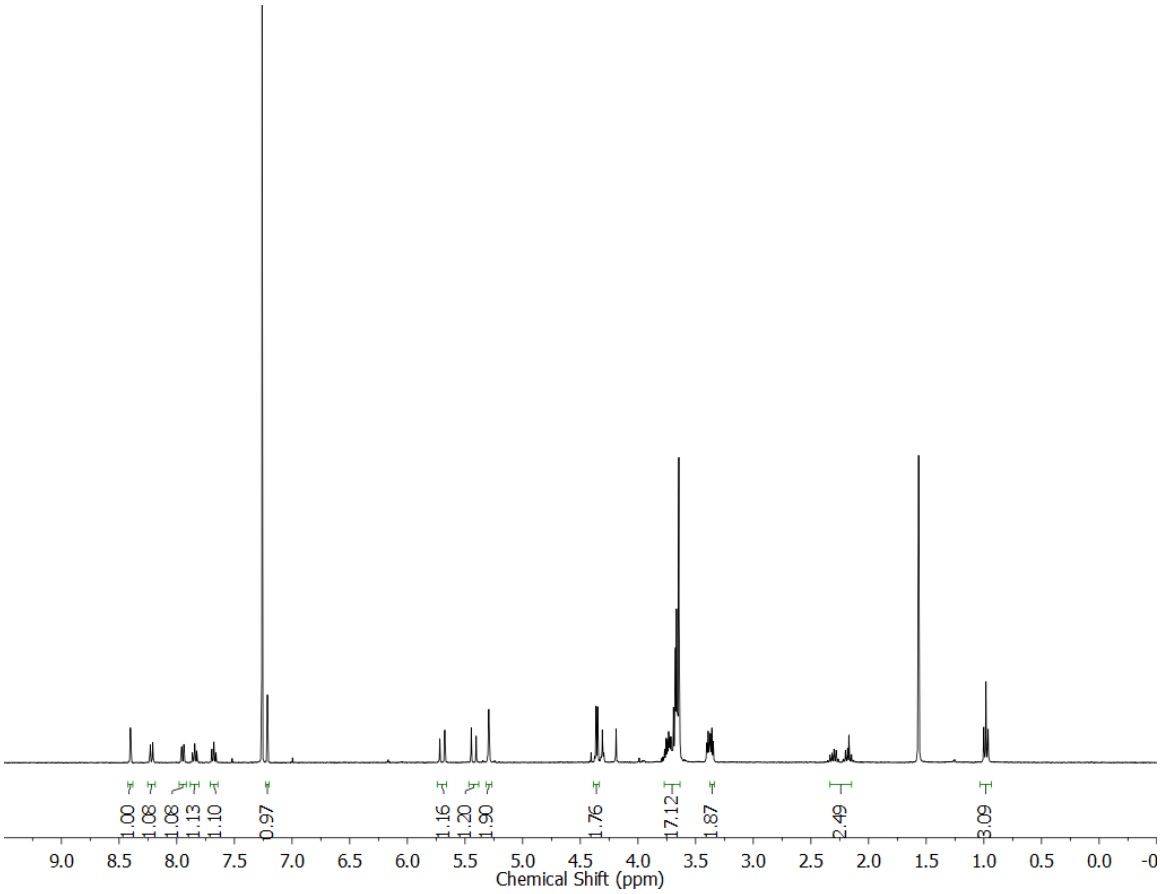


Figure S25. ^{1}H NMR spectrum of **CPT-N_3** in $CDCl_3$.

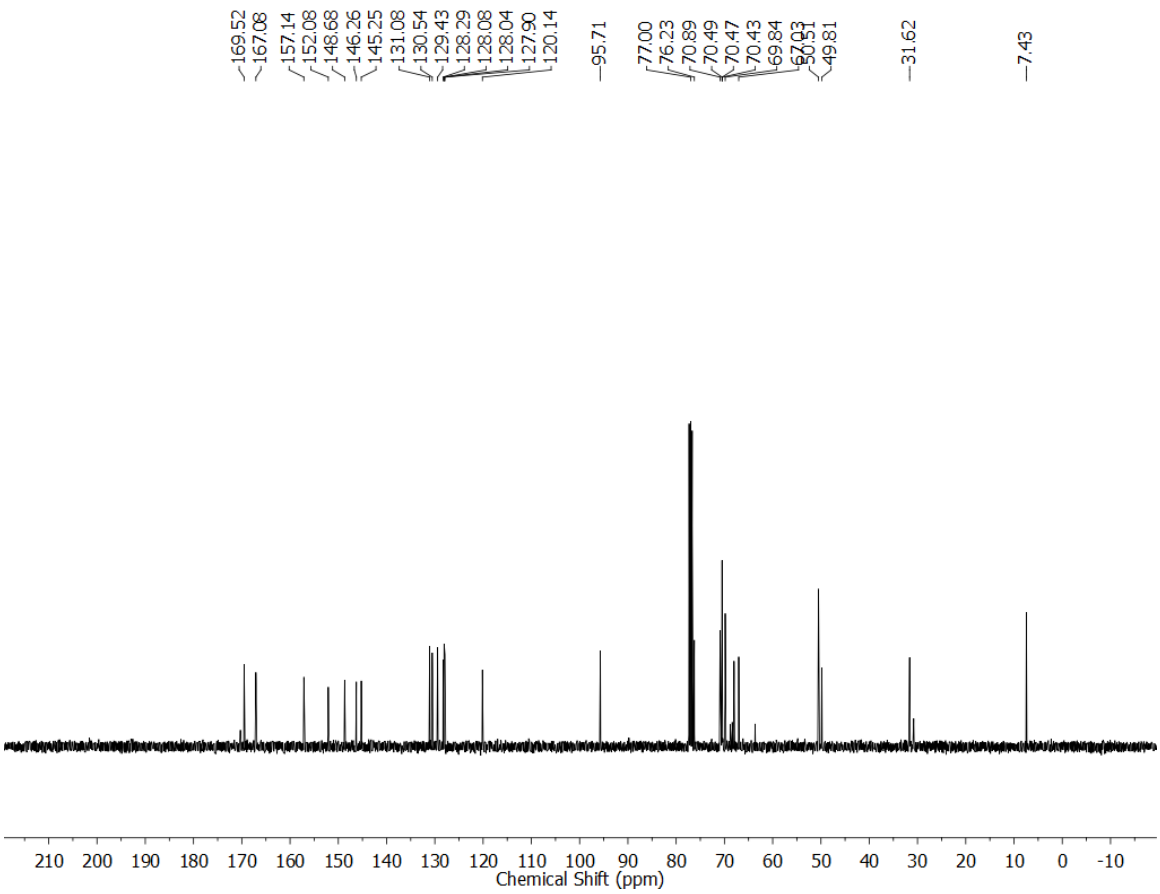


Figure S26. ^{13}C NMR spectrum of **CPT-N_3** in $CDCl_3$.

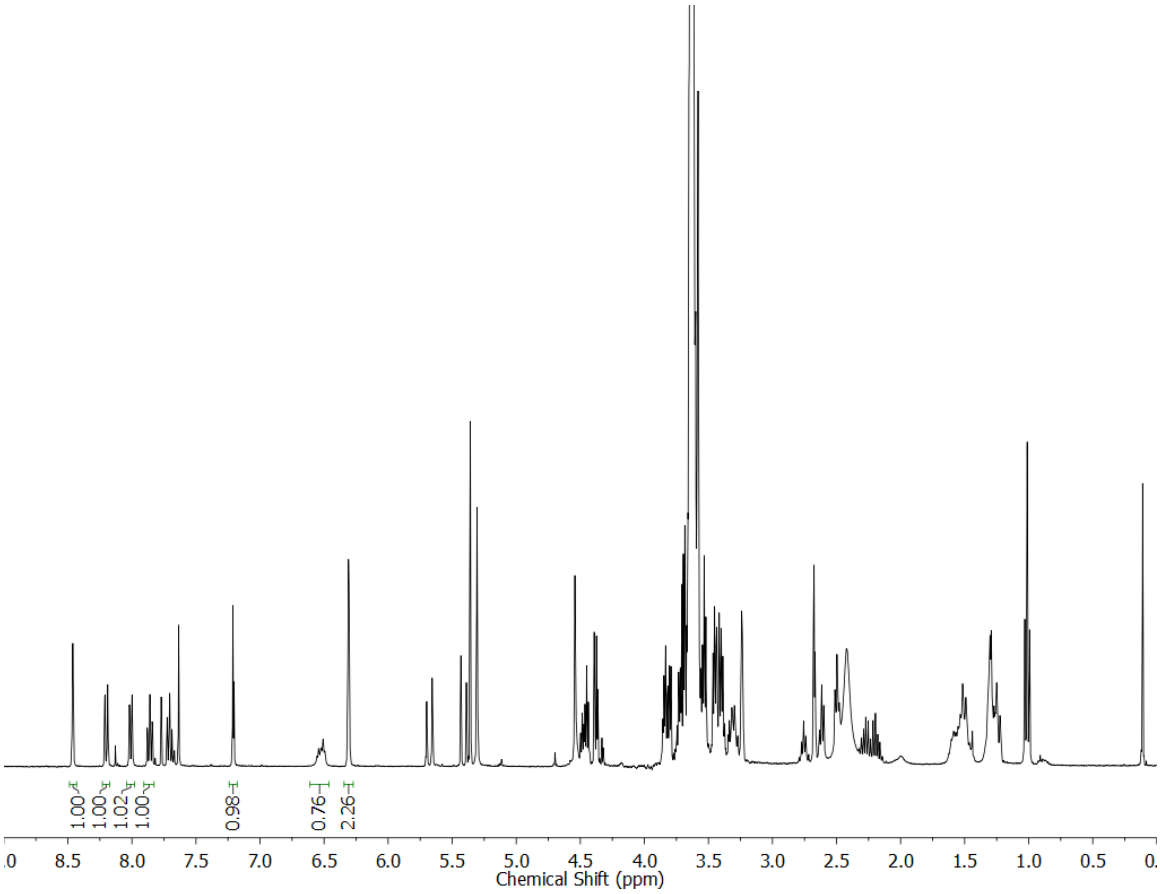


Figure S27. ^{1}H NMR spectrum of **CPT-MM** in CD_2Cl_2.

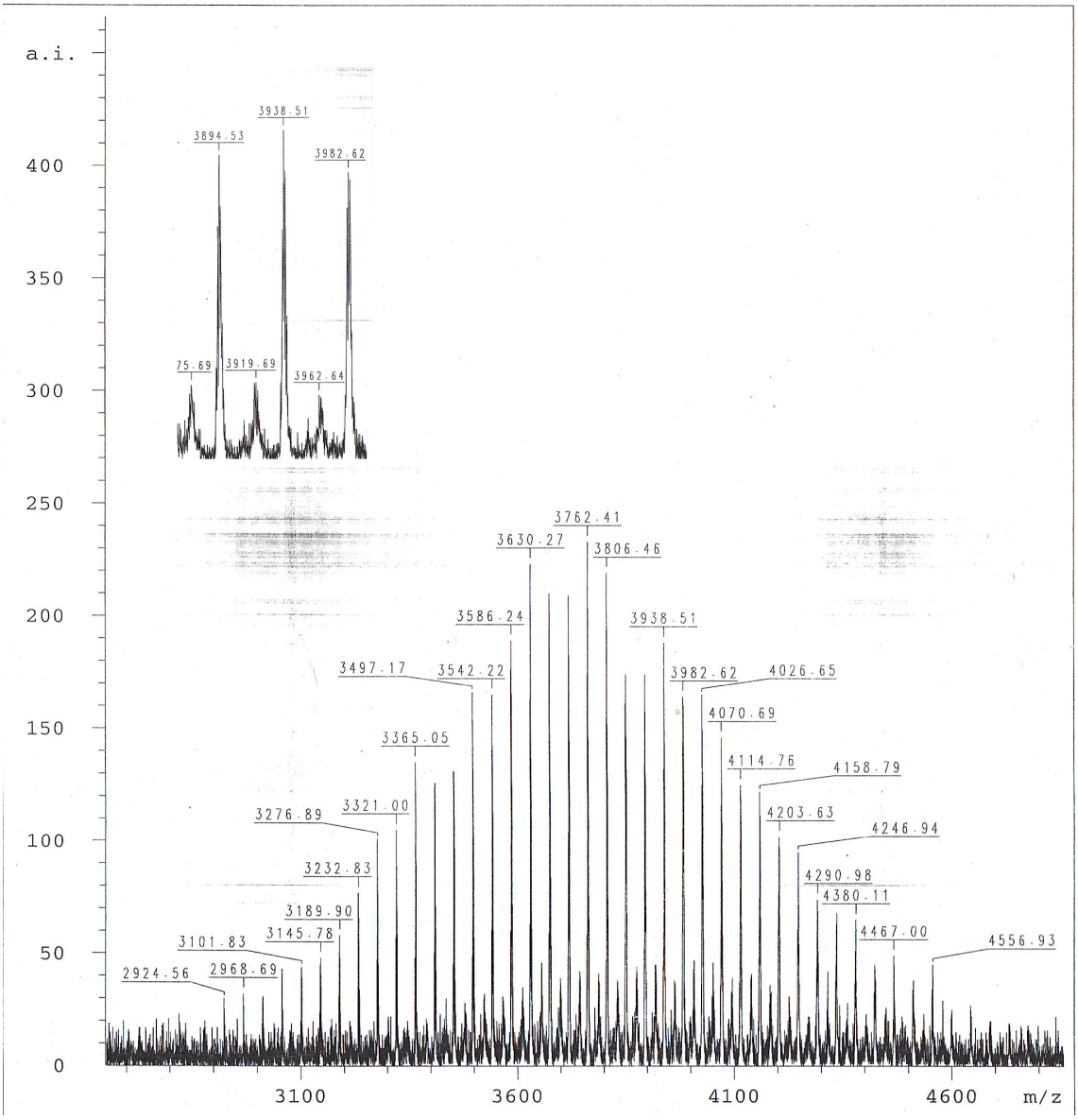


Figure S28. MALDI spectrum of **CPT-MM** ($(M+H_2O+Li)^+$ calcd. for $C_{184}H_{328}N_8O_{80}Li$: 3939.52 obsd.: 3938.51; $(M+Li)^+$ calcd. for $C_{184}H_{326}N_8O_{79}Li$: 3919.19 obsd.: 3919.69)

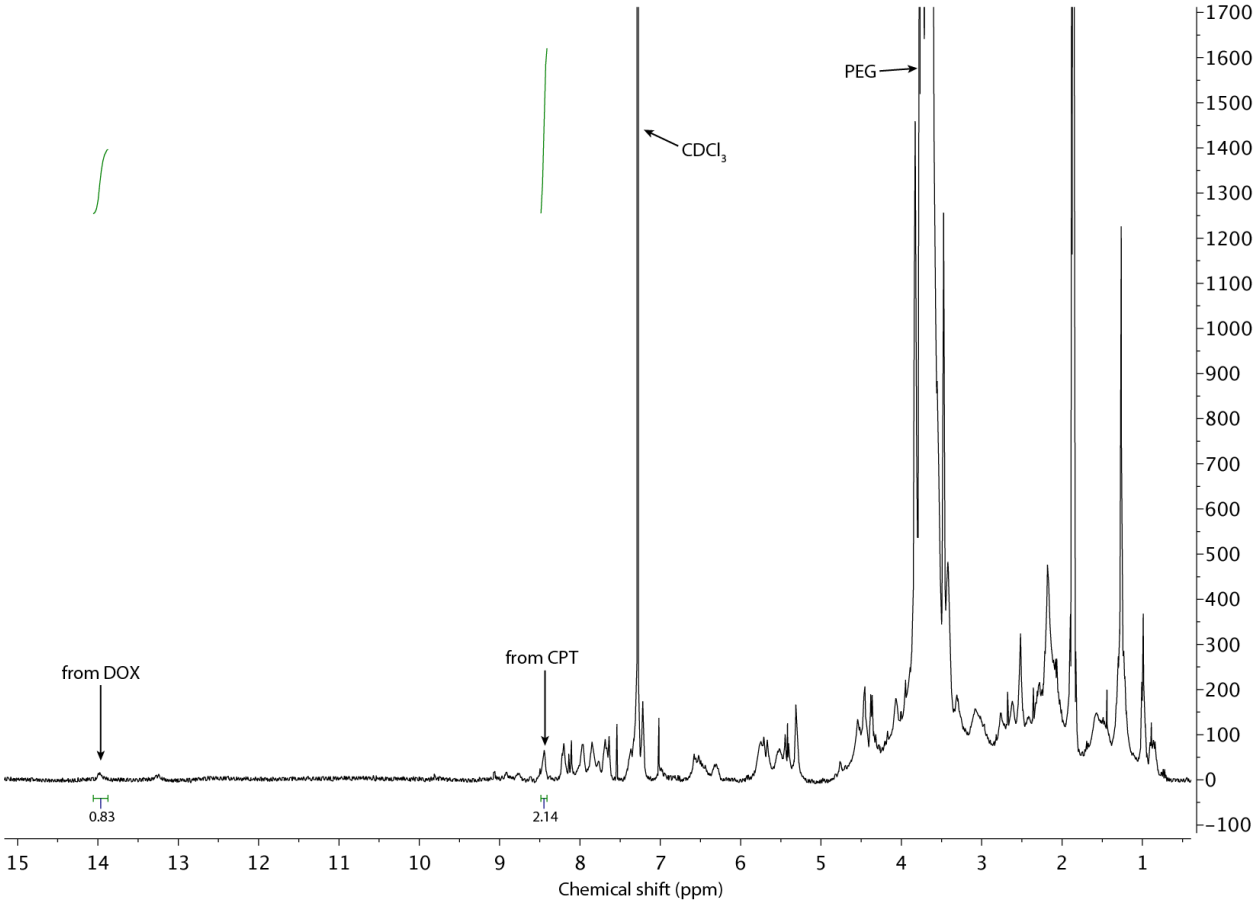


Figure S29. ^{1}H NMR spectrum of BASP **3** in $CDCl_3$. Specific resonances corresponding to DOX and CPT enable estimation of the CPT:DOX ratio.

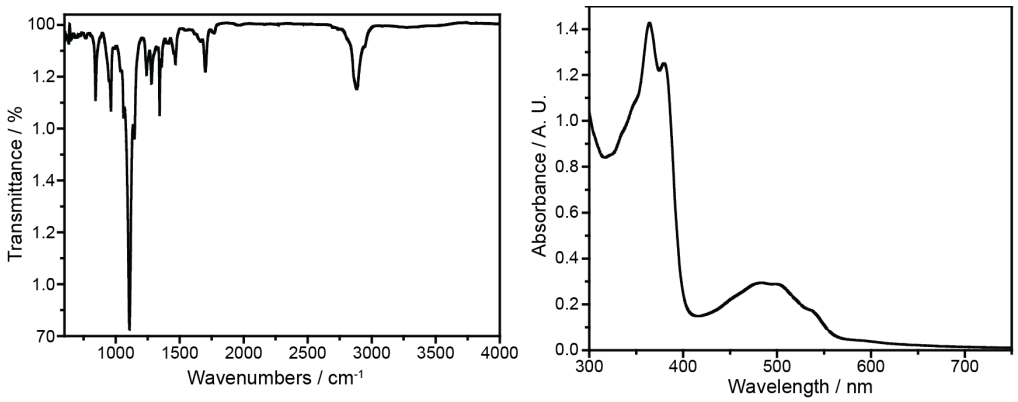


Figure S30. FTIR (left) and UV/Vis (right) spectra for BASP **3**. UV/Vis was used to estimate the DOX:CPT ratio given in Table S1.

Supporting References

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(3) Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H. A Practical and Highly Active Ruthenium-Based Catalyst that Effects the Cross Metathesis of Acrylonitrile. *Angew. Chem. Int. Ed.* **2002**, *41*, 4035-4037.
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