

Supporting Information

Influence of Polymer Structure and Architecture on Drug Loading and Redox-triggered Release

Peidong Wu,¹ Jingjing Gao,^{1,2} Priyaa Prasad,¹ Kingshuk Dutta,¹ Pintu Kanjilal,¹ S.

*Thayumanavan^{*1,3,4}*

¹Department of Chemistry, University of Massachusetts, Amherst, Massachusetts 01003,
USA

²Current address: Center for Nanomedicine, Department of Anesthesiology,
Perioperative and Pain Medicine, Brigham and Women's Hospital, Boston, MA 02115

³Department of Biomedical Engineering, University of Massachusetts Amherst, Amherst,
Massachusetts, USA

⁴Center for Bioactive Delivery, The Institute for Applied Life Sciences, University of
Massachusetts Amherst, Amherst, Massachusetts, USA

* Email: thai@chem.umass.edu (S.T.)

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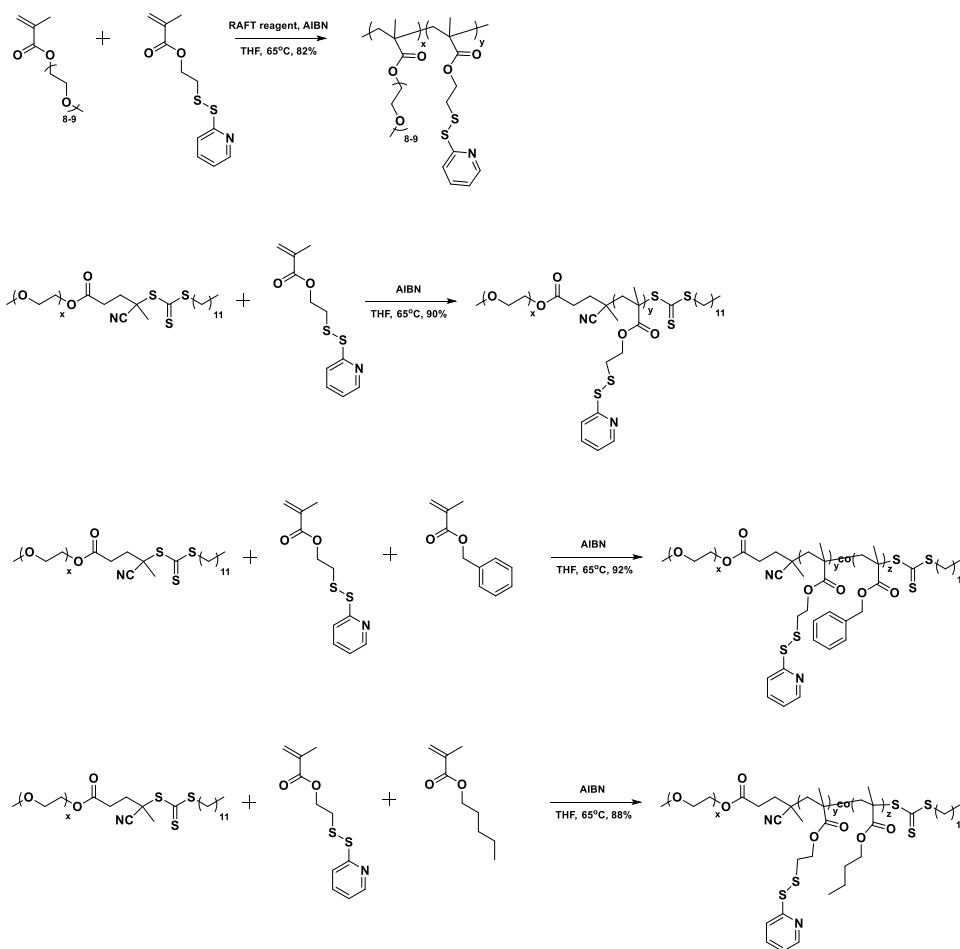


Figure S1. Synthesis route for random copolymers and block copolymers

Table S1. Feed ratio of polymer synthesis

Polymer	Raft (mg)	PDSMA (mg)	PEGMA (mg)	BnMA (mg)	BuMA (mg)	AIBN (mg)	Yield(%)
BCP ₁₀₀₀	100 (1 eq)	182.4 (10 eq)	-	-	-	2.35 (0.2 eq)	77
BCP ₅₀₀₀	200 (1 eq)	94.58 (10 eq)	-	-	-	1.22 (0.2 eq)	82
BCP ₁₀₀₀₀	200 (1 eq)	51.07 (10 eq)	-	-	-	0.66 (0.2 eq)	70
RCP	13.46 (2 eq)	297.92 (70 eq)	250 (30 eq)	-	-	1.09 (0.4 eq)	92
PBn ₁₀	200 (1 eq)	82.12 (9 eq)	-	6.53 (1 eq)	-	1.22 (0.2 eq)	87
PBn ₆₀	200 (1 eq)	37.83 (4 eq)	-	39.16 (6 eq)	-	1.22 (0.2 eq)	85
PBn ₈₀	200 (1 eq)	18.92 (2 eq)	-	52.21 (8 eq)	-	1.22 (0.2 eq)	83
PBU ₁₀	200 (1 eq)	82.12 (9 eq)	-	-	5.27 (1 eq)	1.22 (0.2 eq)	88
PBU ₆₀	200 (1 eq)	37.83 (4 eq)	-	-	31.60 (6 eq)	1.22 (0.2 eq)	81
PBU ₈₀	200 (1 eq)	18.92 (2 eq)	-	-	31.60 (8 eq)	1.22 (0.2 eq)	92

Table S2. Amount of TCEP for targeted crosslinking density

5mg Polymer	n (PDS) (mmol)	TCEP(25%) (mg)	TCEP(50%) (mg)	TCEP(100%) (mg)
BCP ₅₀₀₀	0.00628 ^a	0.225	0.451	0.901
RCP	0.01065 ^b	0.381	0.763	1.526
PBn ₁₀	0.00572	0.205	0.410	0.820
PBn ₆₀	0.00268	0.096	0.192	0.384
PBn ₈₀	0.00136	0.049	0.098	0.196
PBu ₁₀	0.00572	0.205	0.410	0.820
PBu ₆₀	0.00268	0.096	0.192	0.384
PBu ₈₀	0.00136	0.049	0.098	0.196

- The amount of PDS moieties for block copolymers were calculated based on wt % that converted from the ratio between each monomer.
- The amount of PDS moieties for random copolymers were calculated following previous report¹.

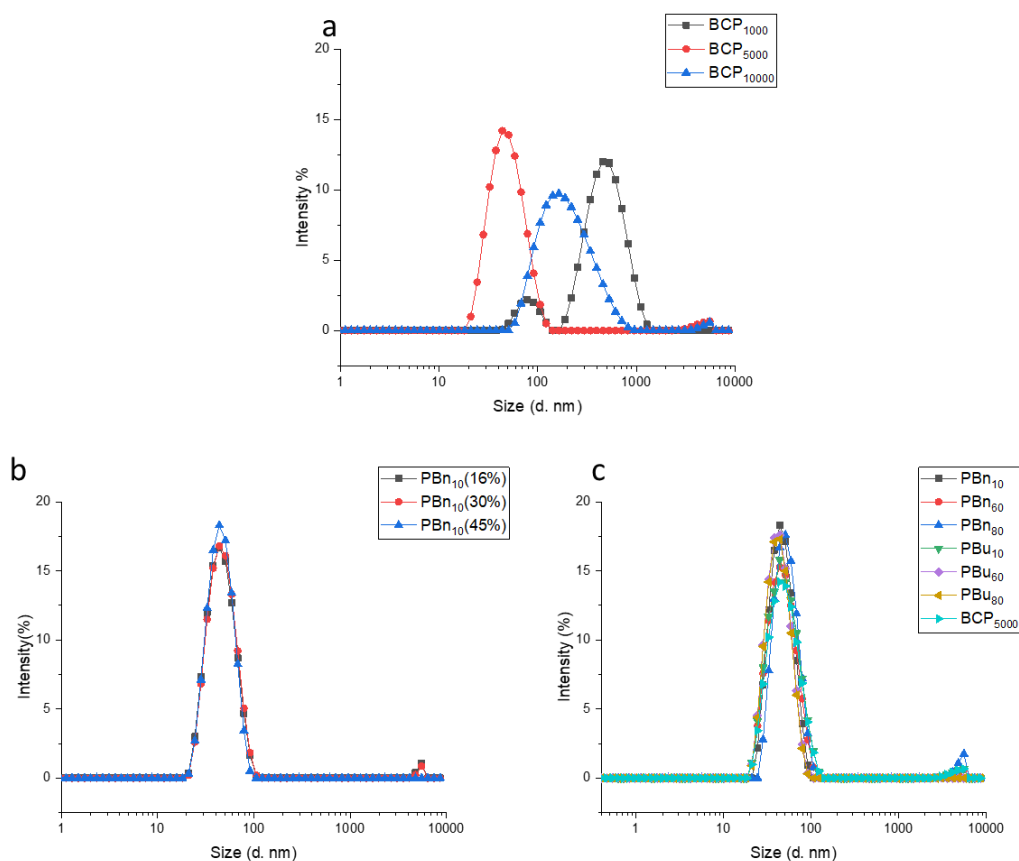


Figure S2. (a) The size distribution of BCP₁₀₀₀, BCP₅₀₀₀, BCP₁₀₀₀₀ micelles; (b) The size distribution of PBn₁₀ control nanogels with 25%, 50%, and 100% crosslinking; (c) The size distribution of PBn₁₀, PBn₆₀, PBn₈₀, PBu₆₀, and BCP₅₀₀₀ control nanogels at 25% crosslinking.

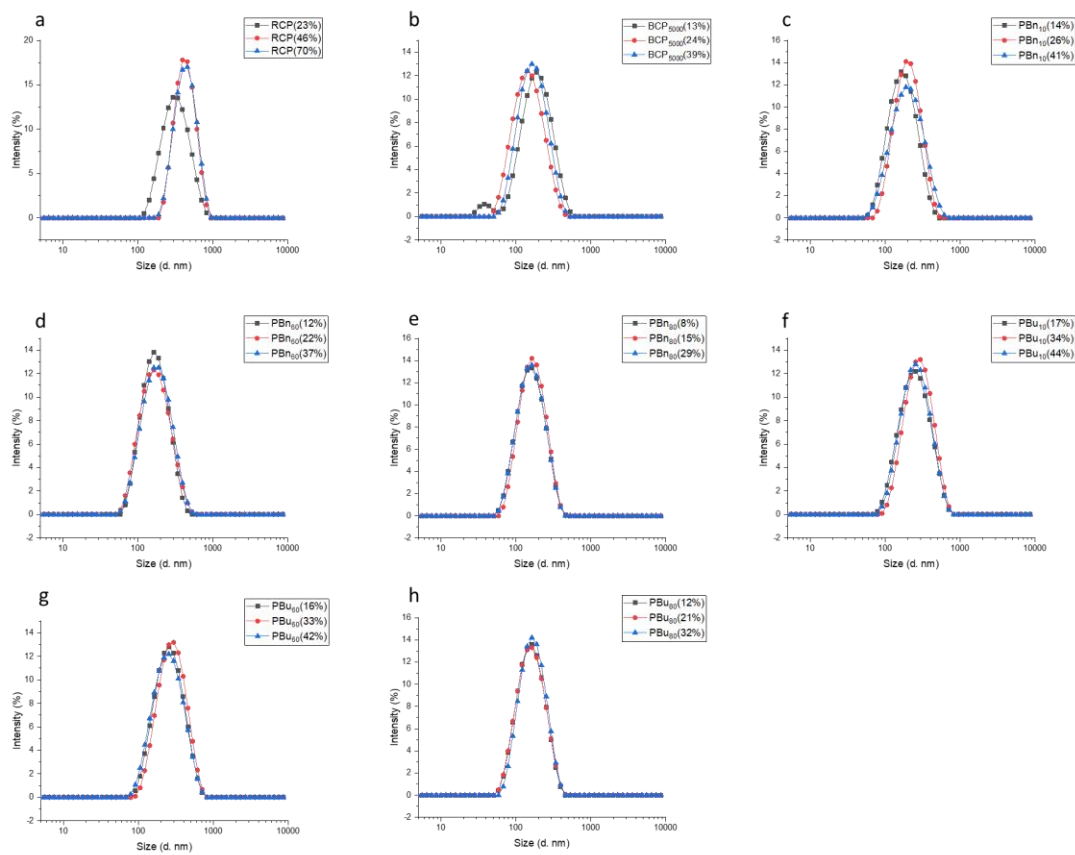


Figure S3. The size distribution of drug encapsulated nanogels with varied crosslinking density. (a)-(h): RCP, BCP₅₀₀₀, PBN₁₀, PBN₆₀, PBN₈₀, PBU₁₀, PBU₆₀, PBU₈₀.

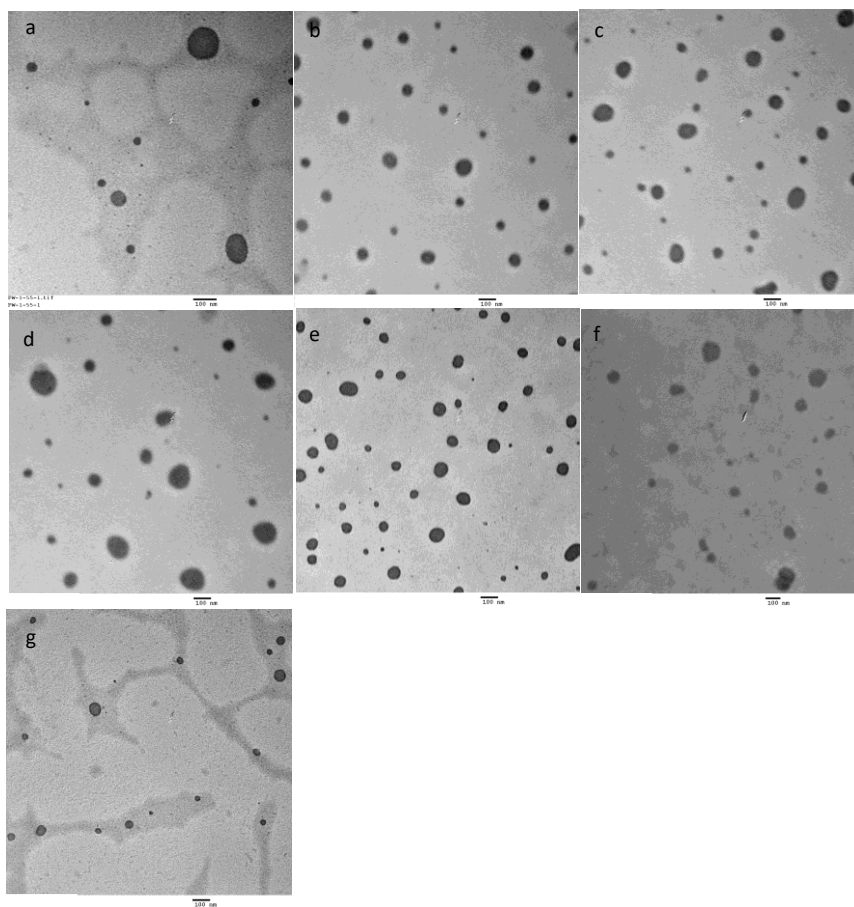


Figure S4. TEM images of drug encapsulated nanogels (a) BCP₅₀₀₀(24%); (b) PBn₁₀(26%); (c) PBn₆₀(22%); (d) PBn₈₀(15%); (e) PBu₁₀(34%); (f) PBu₆₀(33%); (g) PBu₈₀(21%). Scale bar 100 nm.

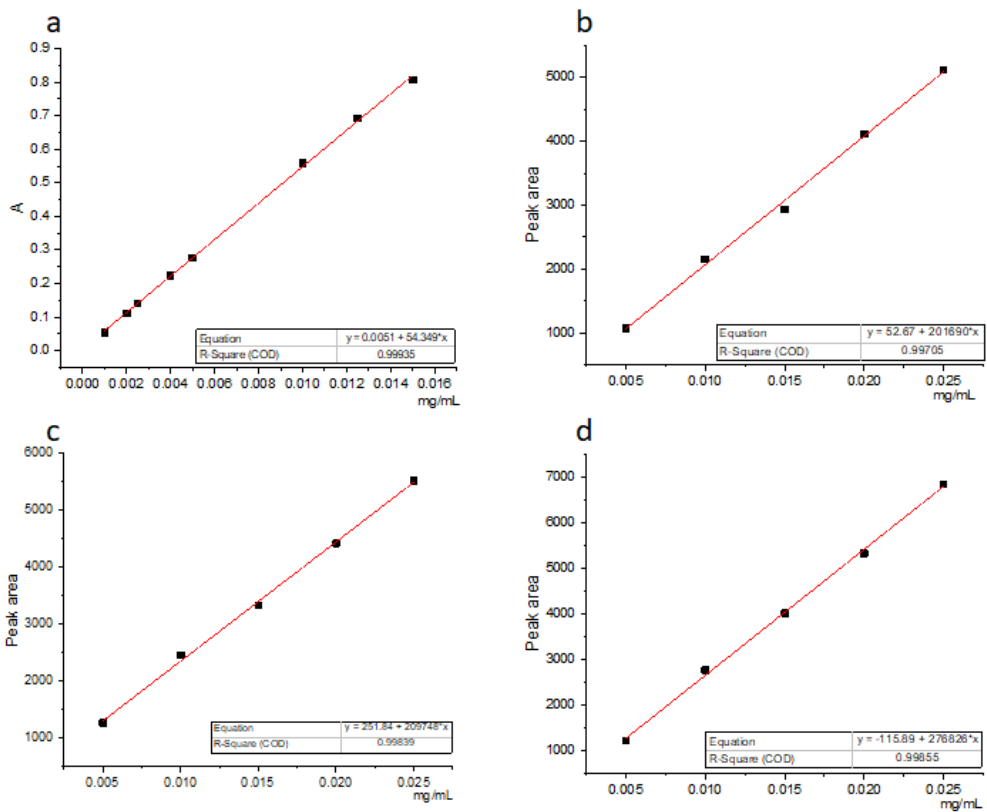


Figure S5. (a) Camptothecin standard plot at 365 nm in 90% (v/v) DMSO/water. (b) Paclitaxel standard plot using HPLC; (c) Docetaxel standard plot using HPLC; (d) Rapamycin standard plot using HPLC.

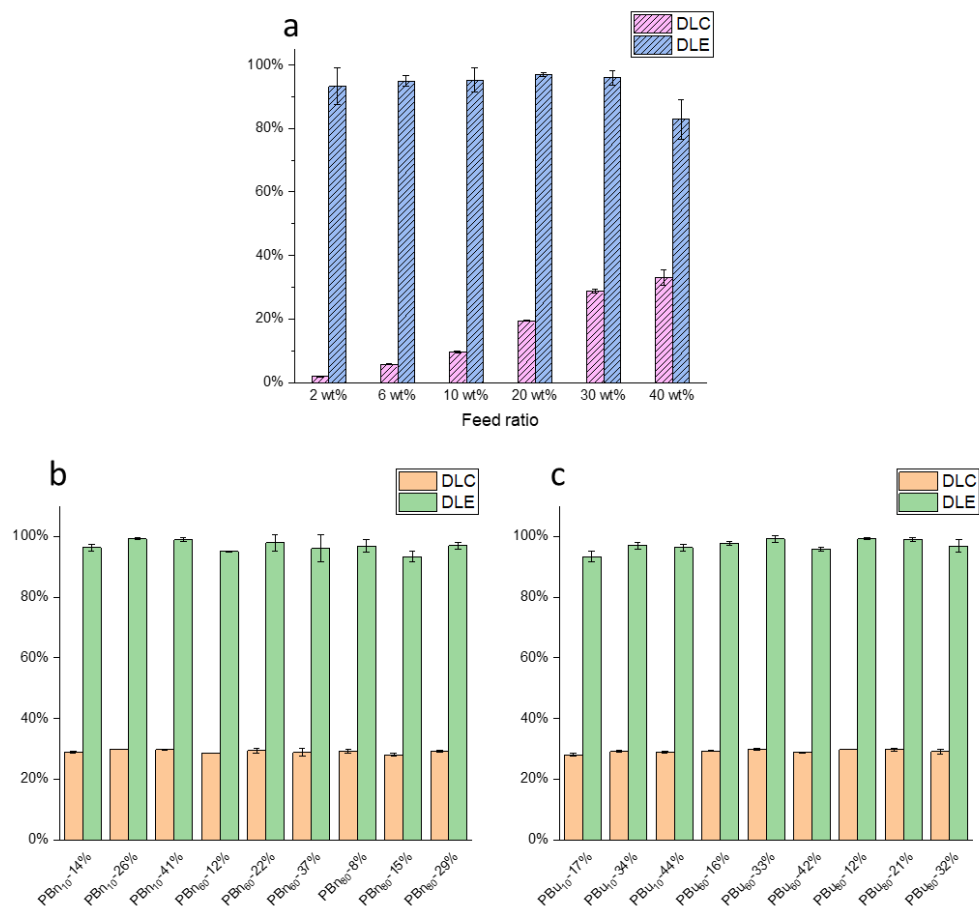


Figure S6. (a) Relationship between feed ratio and DLC/DLE; (b) DLC and DLE of PBn nanogels; (c) DLC and DLE of PBU nanogels.

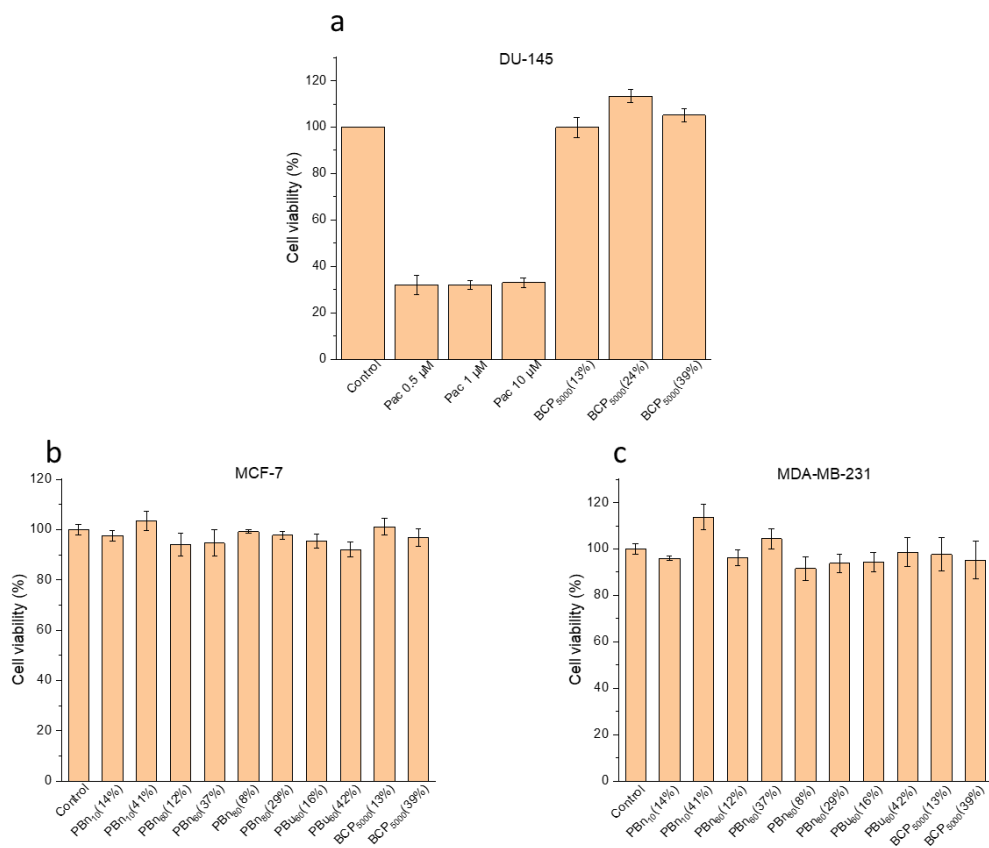


Figure S7. (a) DU-145 cell viability study with 0.5 μ M, 1 μ M, and 10 μ M paclitaxel and 0.1 mg/mL control nanogels. (b) MCF-7 cell viability study with 0.1 mg/mL control nanogels. (c) MDA-MB-231 cell viability study with 0.1 mg/mL control nanogels.

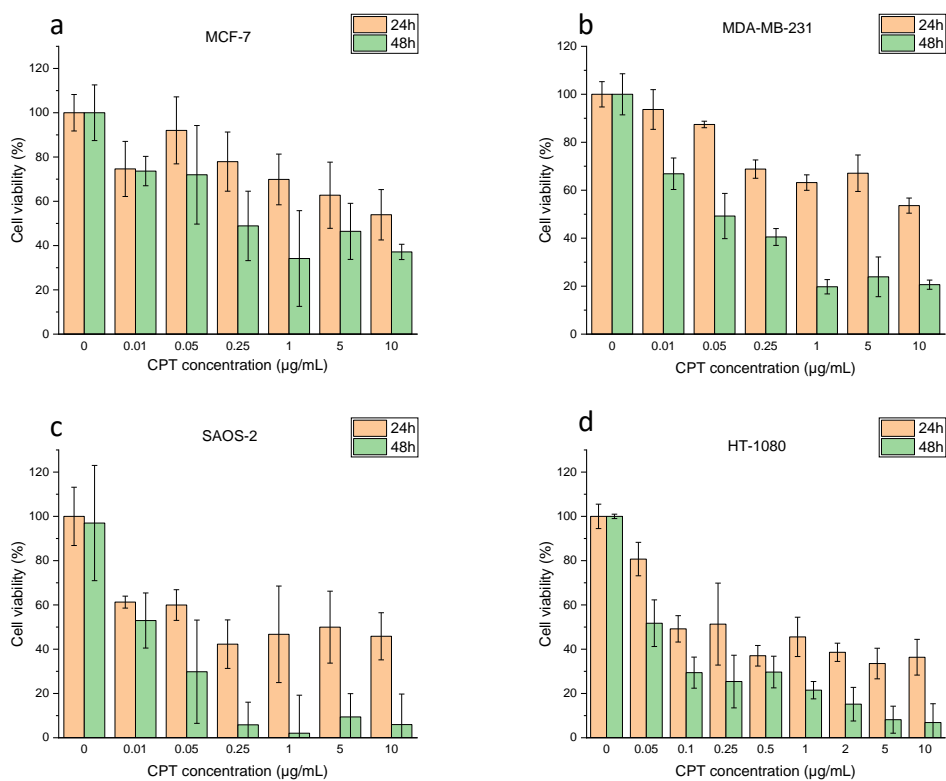


Figure S8. Free CPT cytotoxicity study in MCF-7 (a), MDA-MB-231 (b), SAOS-2 (c), and HT-1080 (d).

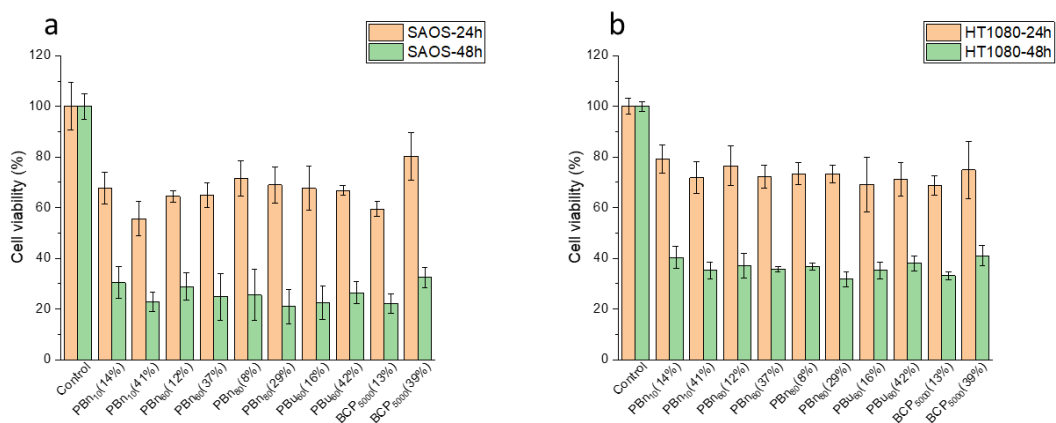


Figure S9. Cytotoxicity study of structural variant nanogels in SAOS-2 and HT-1080 cell lines (CPT concentration 0.05 µg/mL).

¹H NMR and ¹³C NMR of synthesized polymers

BCP₁₀₀₀ : ¹H NMR: (400 MHz, CDCl₃), δ (ppm): 8.43, 7.62, 7.06, 4.19, 3.78-3.43, 3.35, 3.00, 2.14-1.7, 1.22, 1.03, 0.86. Integration of the methoxy proton (in PEG unit at 3.35 ppm) and the aromatic proton (in pyridine unit at 8.43 ppm) provided the molar ratio of two monomers to be 1:10 (PEG/PDS). ¹³C NMR (101 MHz, CDCl₃), δ(ppm): 159.6, 149.5, 137.4, 121.1, 119.9, 71.9, 70.0, 61.7, 58.7, 44.5, 36.6, 31.6, 29.4, 22.3, 14.1.

BCP₅₀₀₀ : ¹H NMR (400 MHz, CDCl₃) δ (ppm): 8.43, 7.63, 7.06, 4.20, 3.80-3.43, 3.36, 3.00, 2.99-1.83, 1.24, 1.22, 1.05, 0.86. Integration of the methoxy proton (in PEG unit at 3.35 ppm) and the aromatic proton (in pyridine unit at 8.43 ppm) provided the molar ratio of two monomers to be 1:10 (PEG/PDS). ¹³C NMR (101 MHz, CDCl₃), δ(ppm): 159.6, 149.8, 137.2, 121.0, 119.9, 72.6, 70.6, 61.7, 59.0, 44.8, 37.0, 31.6, 29.4, 22.7, 14.1.

BCP₁₀₀₀₀ : ¹H NMR: (400 MHz, CDCl₃), δ (ppm): 8.43, 7.62, 7.06, 4.19, 3.78-3.43, 3.35, 3.00, 2.14-1.7, 1.03, 0.86. Integration of the methoxy proton (in PEG unit at 3.35 ppm) and the aromatic proton (in pyridine unit at 8.43 ppm) provided the molar ratio of two monomers to be 1:10 (PEG/PDS). ¹³C NMR (101 MHz, CDCl₃), δ(ppm): 159.6, 149.5, 137.4, 121.1, 119.9, 71.9, 70.0, 61.7, 58.7, 44.5, 36.6, 31.6, 29.4, 22.3, 14.1.

RCP : ¹H NMR: (400 MHz, CDCl₃), δ (ppm): 8.45, 7.66, 7.09, 4.21, 4.07, 3.63, 3.54, 3.37, 3.01, 1.83, 1.84, 1.05, 0.87. Integration of the methoxy proton (in PEG unit at 3.37 ppm) and the aromatic proton (in pyridine unit at 8.45 ppm) provided the molar ratio of two monomers to be 31:69 (PEG/PDS). ¹³C NMR (101 MHz, CDCl₃), δ(ppm): 159.4, 149.9, 137.1, 121.0, 119.9, 71.9, 70.7, 68.5, 62.7, 58.9, 44.8, 36.9, 31.8, 29.6, 22.8.

PBn₁₀ : Integration of the methoxy proton (in PEG unit at 3.38 ppm), the aromatic proton (in pyridine unit at 8.47 ppm), and the aromatic proton (in benzyl unit at 7.29) provided the molar ratio of three monomers to be 1: 9: 1 (PEG: PDS: Bn). ¹³C NMR (101 MHz, CDCl₃), δ(ppm): 159.60, 159.45, 149.77, 137.18, 128.60, 120.96, 119.92, 72.53, 71.95, 70.58, 69.00, 59.05, 44.84, 31.91, 29.62, 29.46, 29.34, 22.69, 14.15.

PBn₆₀ : ¹H NMR: (400 MHz, CDCl₃), δ (ppm): 8.44, 7.62, 7.29, 7.26, 7.05, 4.91, 4.22, 3.78-3.49, 3.38, 2.96-1.76, 1.25, 1.25, 0.88, 0.73. Integration of the methoxy proton (in PEG unit at 3.38 ppm), the aromatic proton (in pyridine unit at 8.47 ppm), and the aromatic proton (in benzyl unit at 7.29) provided the molar ratio of three monomers to be 1: 4: 6 (PEG: PDS: Bn). ¹³C NMR (101 MHz, CDCl₃), δ(ppm): 149.78, 137.15, 135.08, 128.56, 71.95, 70.58, 66.82, 59.05, 44.76, 31.91, 29.62, 29.34, 22.69, 14.13.

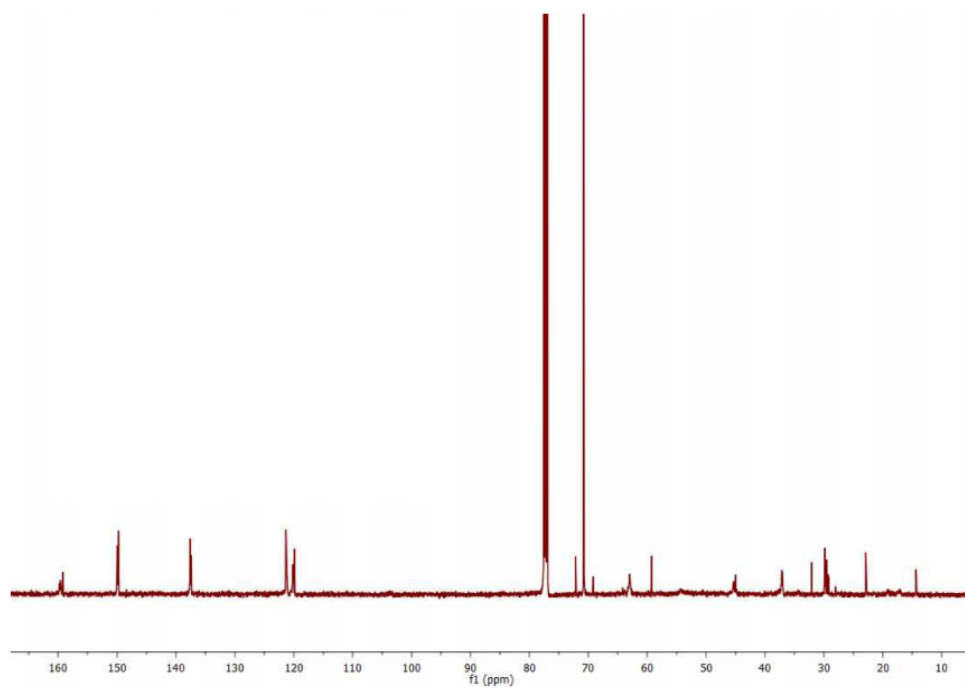
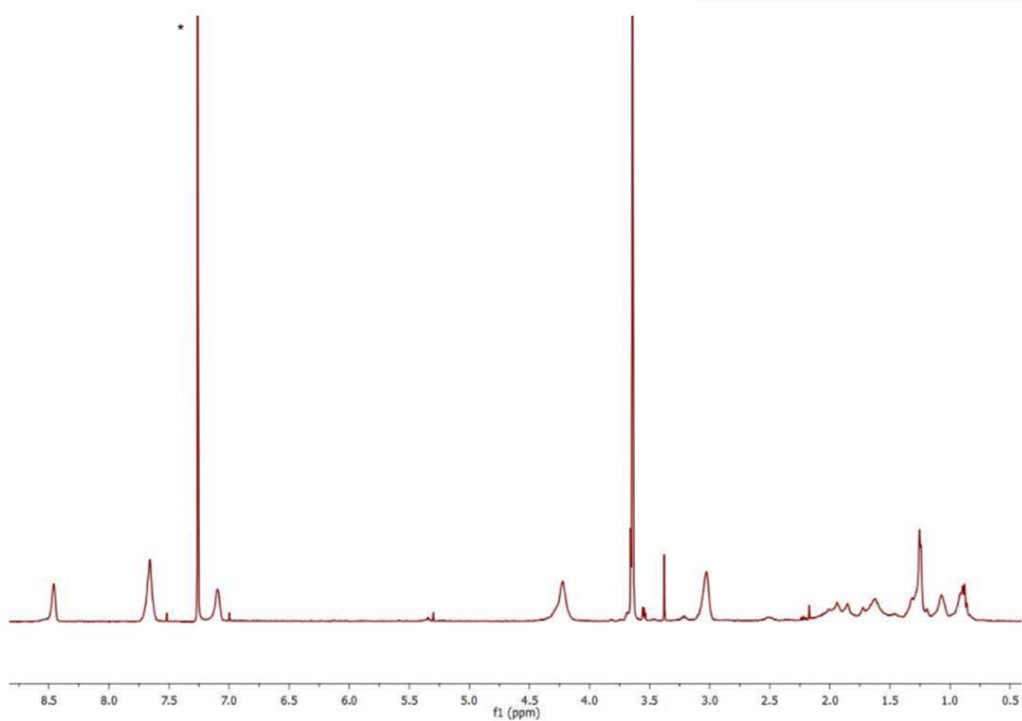
PBn₈₀ : ¹H NMR (400 MHz, CDCl₃) δ (ppm): 8.44, 7.61, 7.28, 7.05, 4.90, 4.87, 4.22, 4.21, 3.78, 3.64, 3.50, 3.38, 1.74, 1.25, 1.25, 1.24, 0.91, 0.89, 0.88, 0.72. Integration of the methoxy proton (in PEG unit at 3.38 ppm), the aromatic proton (in pyridine unit at 8.47 ppm), and the aromatic proton (in benzyl unit at 7.29) provided the molar ratio of three monomers to be 1: 2: 8 (PEG: PDS: Bn). ¹³C NMR (101 MHz, CDCl₃), δ(ppm): 137.10, 135.39, 135.09, 128.53, 128.40, 72.53, 71.95, 70.58, 59.05, 45.09, 31.91, 29.62, 29.45, 29.34, 22.69, 14.14.

PBu₁₀: ¹H NMR (400 MHz, CDCl₃) (ppm): δ 8.47, 7.67, 7.10, 4.23, 4.22, 3.93, 3.81, 3.64, 3.56, 3.47, 3.46, 3.38, 3.03, 1.91, 1.82, 1.71, 1.62, 1.38, 1.25, 1.04, 0.93, 0.88. Integration of the methoxy proton (in PEG unit at 3.38 ppm), the aromatic proton (in pyridine unit at 8.47 ppm), and the methylene proton next to ester group (in butyl unit at 3.93) provided the molar ratio of two monomers to be 1: 9 : 1 (PEG: PDS : Bu). ¹³C NMR (101 MHz, CDCl₃), δ(ppm): 149.79, 137.15, 72.58, 71.94, 70.57, 61.72, 59.04, 31.91, 30.20, 29.63, 29.34, 22.69, 19.34, 14.13.

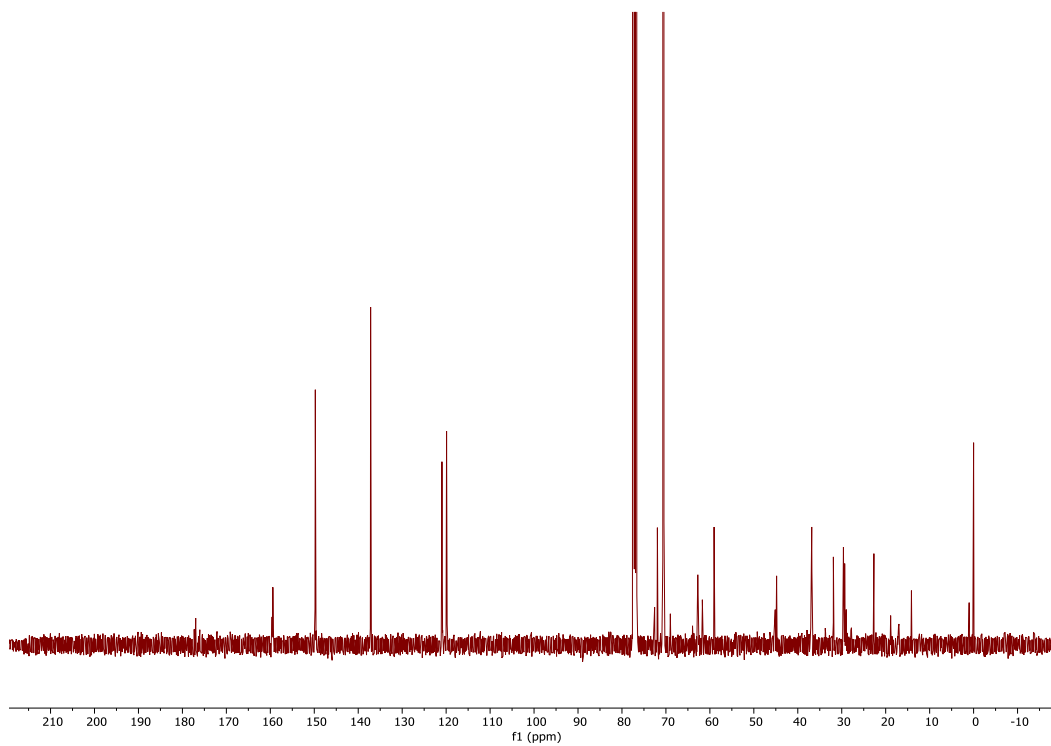
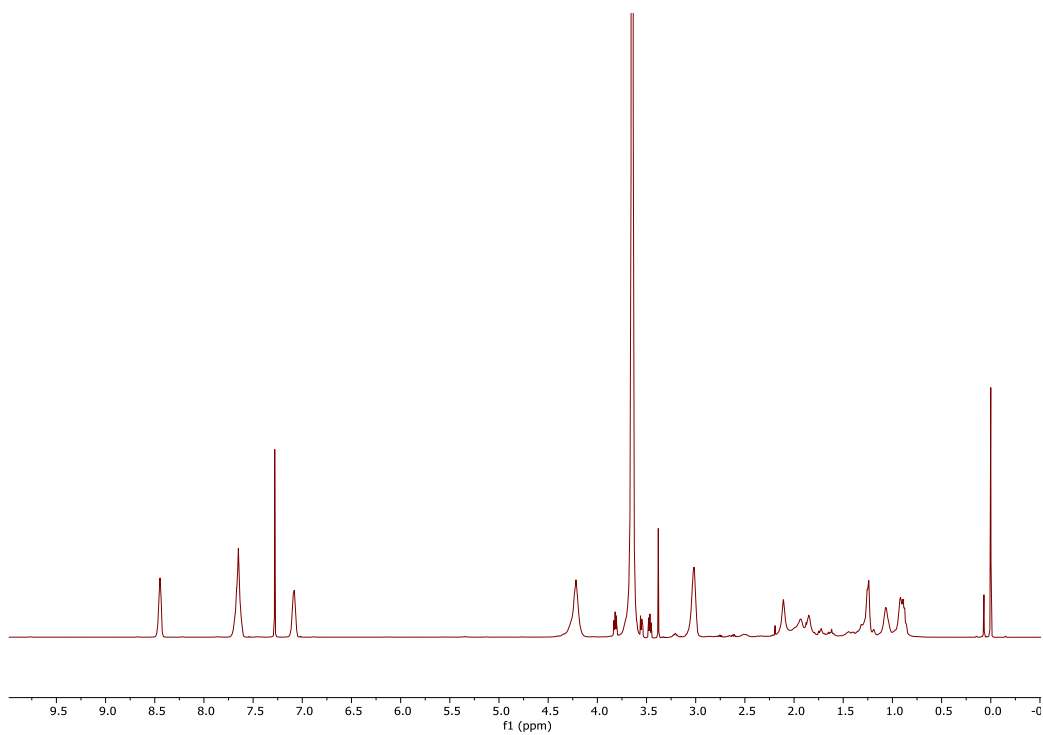
PBu₆₀: ¹H NMR (400 MHz, CDCl₃) (ppm): δ 8.47, 7.67, 7.10, 4.23, 4.22, 3.93, 3.81, 3.64, 3.56, 3.47, 3.46, 3.38, 3.03, 1.91, 1.82, 1.71, 1.62, 1.38, 1.25, 1.04, 0.93, 0.88. Integration of the methoxy proton (in PEG unit at 3.38 ppm), the aromatic proton (in pyridine unit at 8.47 ppm), and the methylene proton next to ester group (in butyl unit at 3.93) provided the molar ratio of two monomers to be 1: 4 : 6 (PEG: PDS : Bu). ¹³C NMR (101 MHz, CDCl₃), δ(ppm): 149.79, 137.15, 72.58, 71.94, 70.57, 61.72, 59.04, 31.91, 30.20, 29.63, 29.34, 22.69, 19.34, 14.13.

PBu₈₀: ¹H NMR (400 MHz, CDCl₃) (ppm): δ 8.47, 7.67, 7.10, 4.23, 4.22, 3.93, 3.81, 3.64, 3.56, 3.47, 3.46, 3.38, 3.03, 1.91, 1.82, 1.71, 1.62, 1.38, 1.25, 1.04, 0.93, 0.88. Integration of the methoxy proton (in PEG unit at 3.38 ppm), the aromatic proton (in pyridine unit at 8.47 ppm), and the methylene proton next to ester group (in butyl unit at 3.93) provided the molar ratio of two monomers to be 1: 2 : 8 (PEG: PDS : Bu). ¹³C NMR (101 MHz, CDCl₃), δ(ppm): 149.79, 137.15, 72.58, 71.94, 70.57, 61.72, 59.04, 31.91, 30.20, 29.63, 29.34, 22.69, 19.34, 14.13.

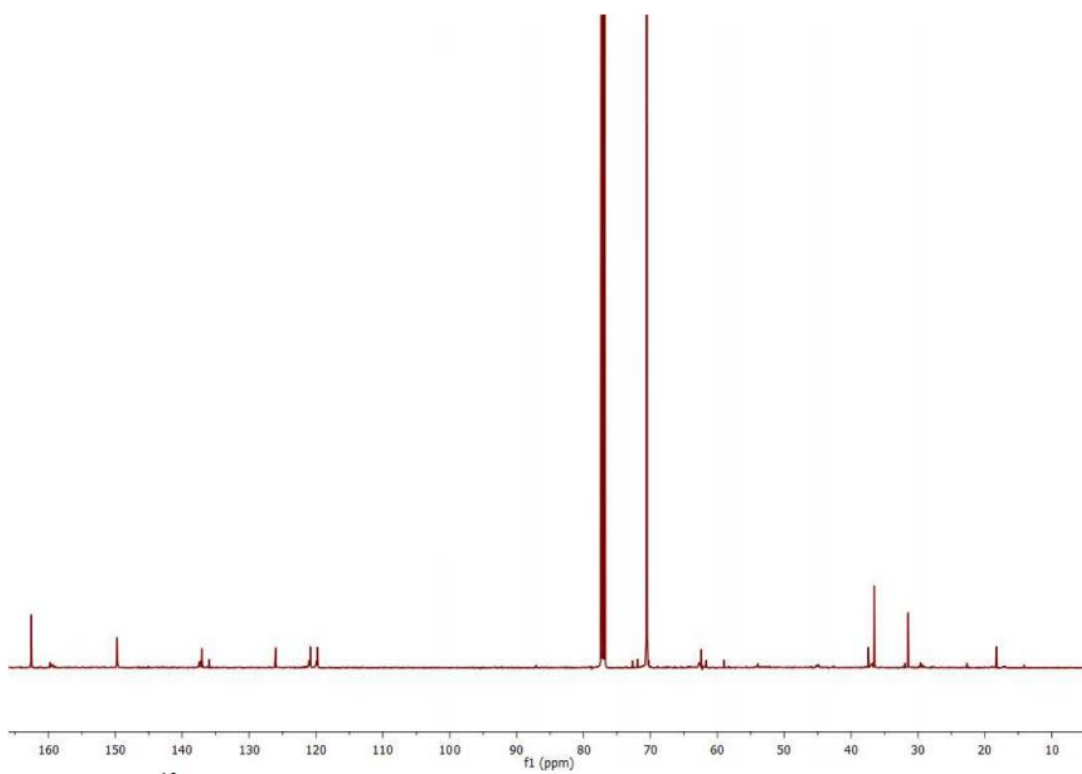
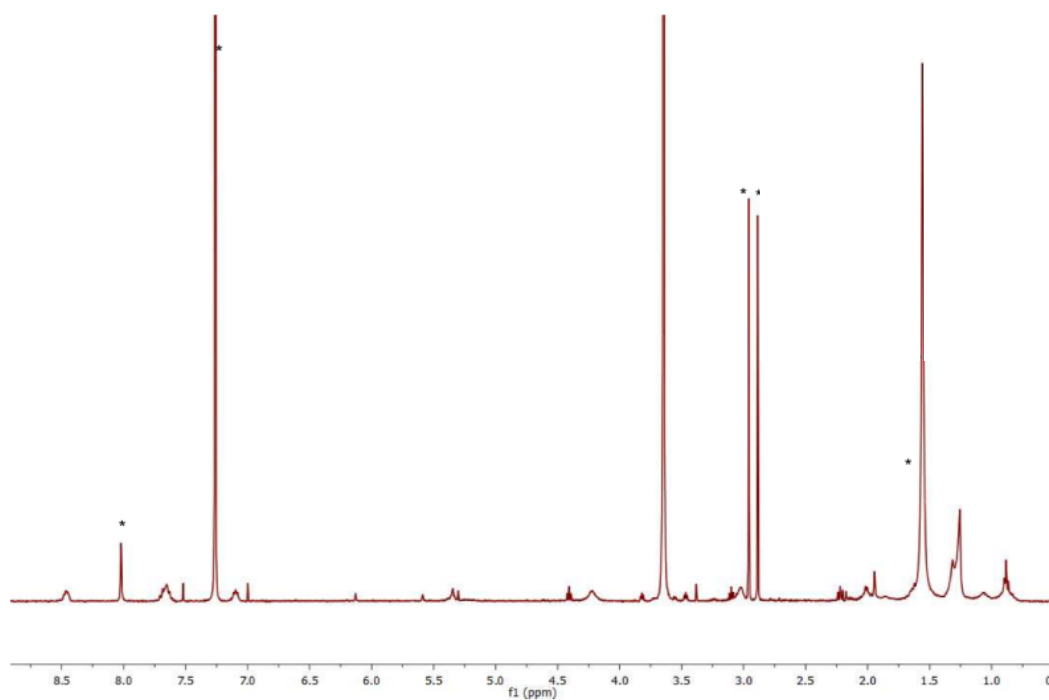
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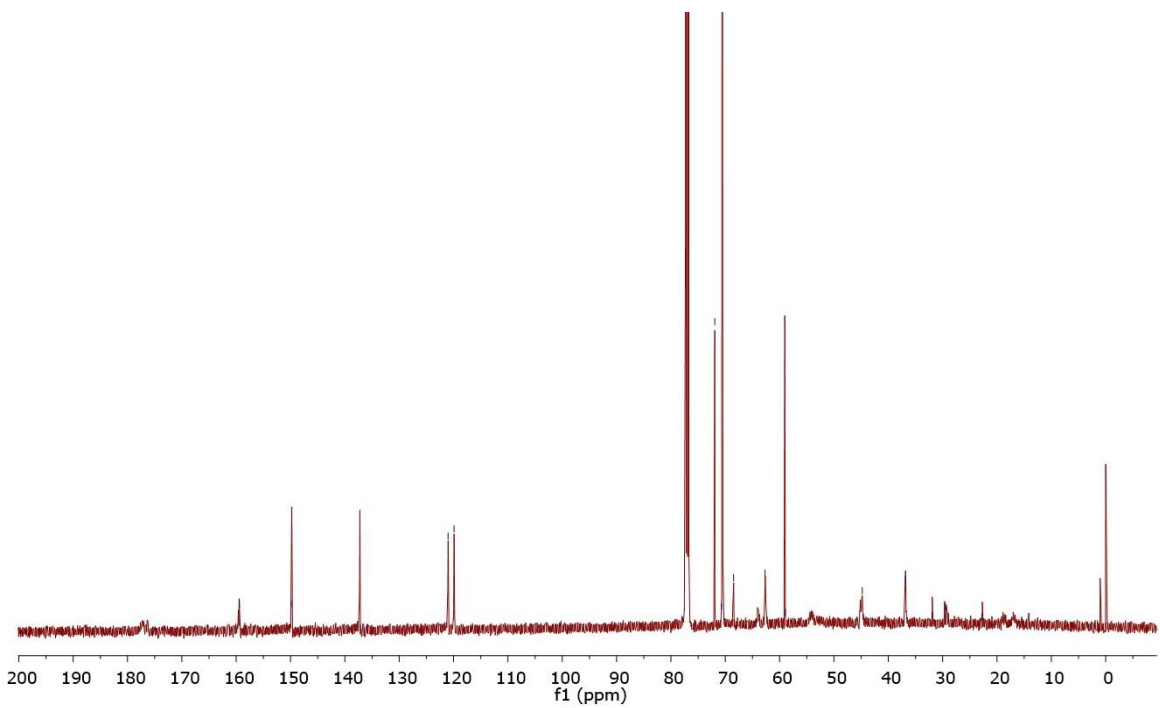
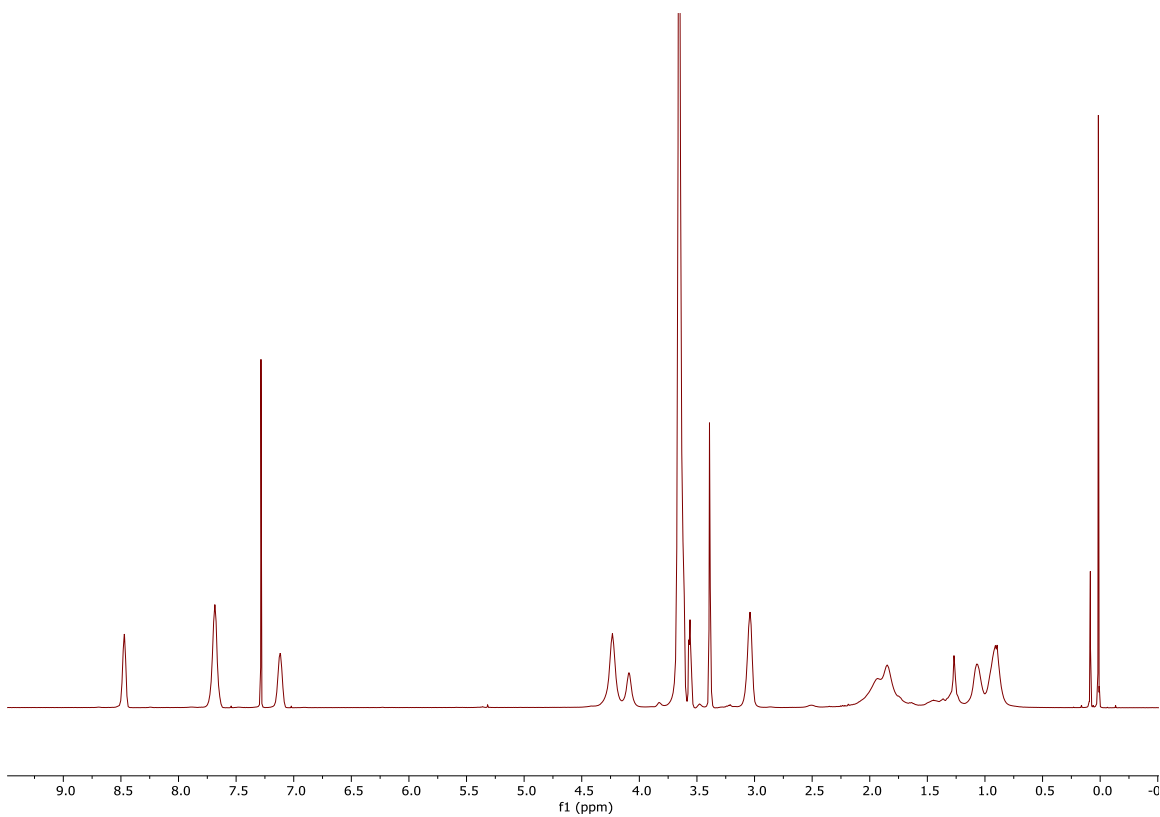
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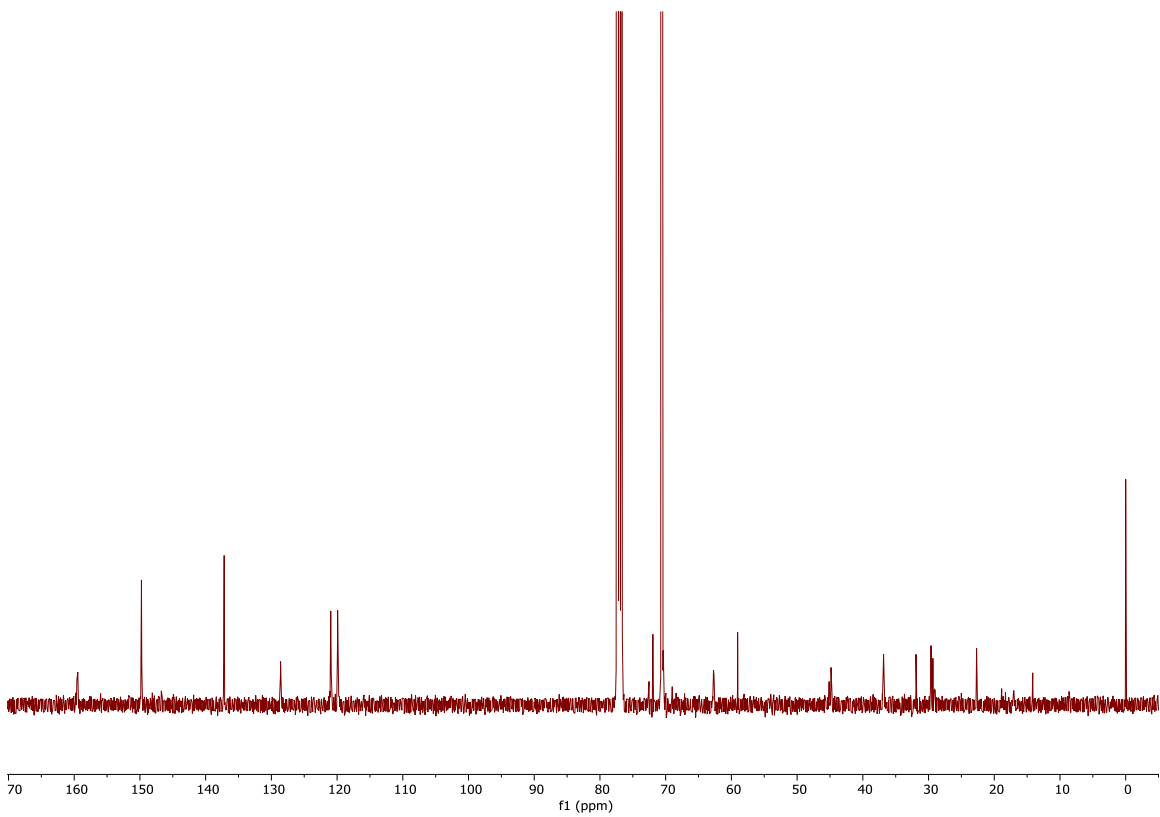
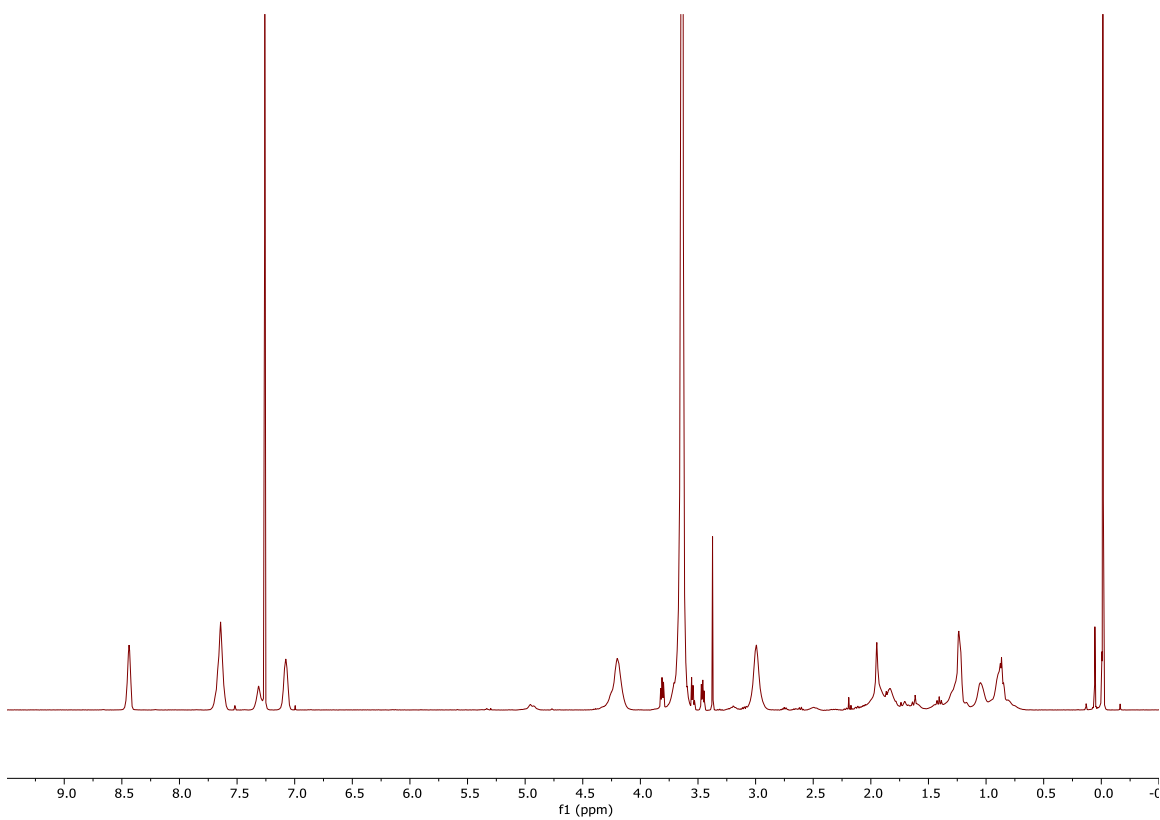
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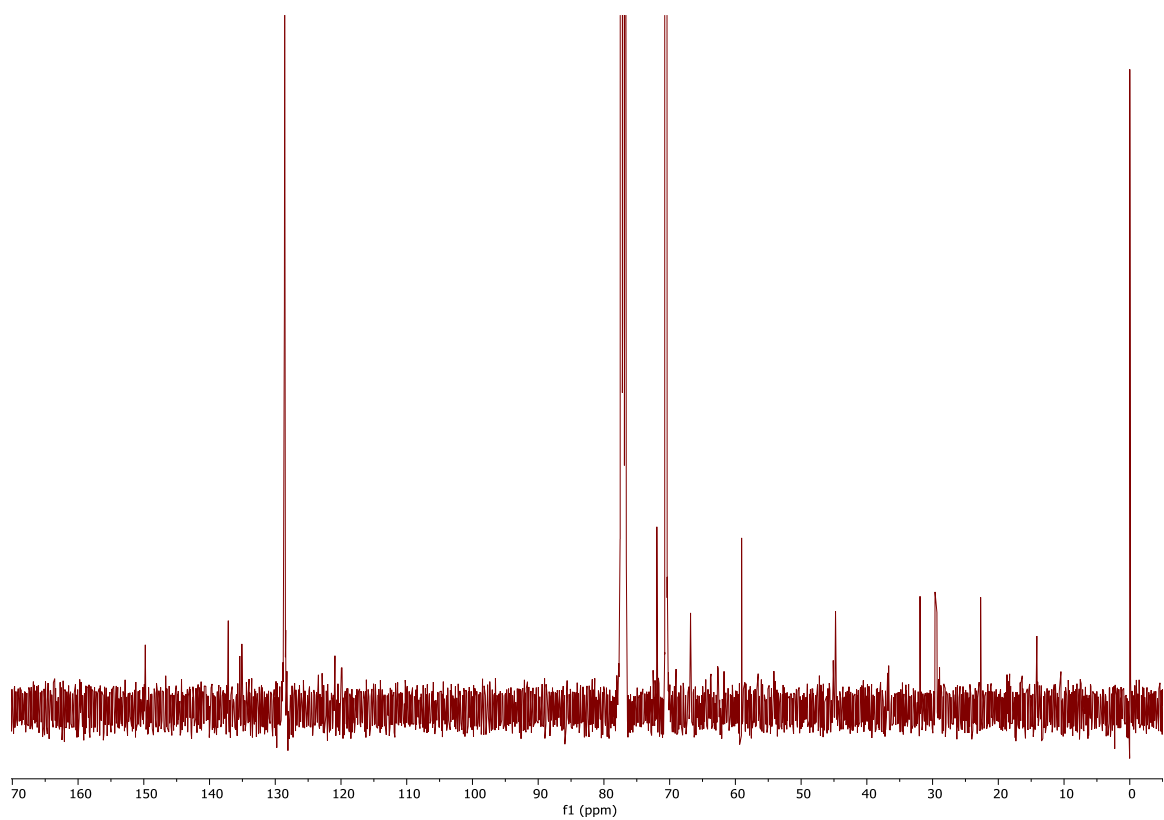
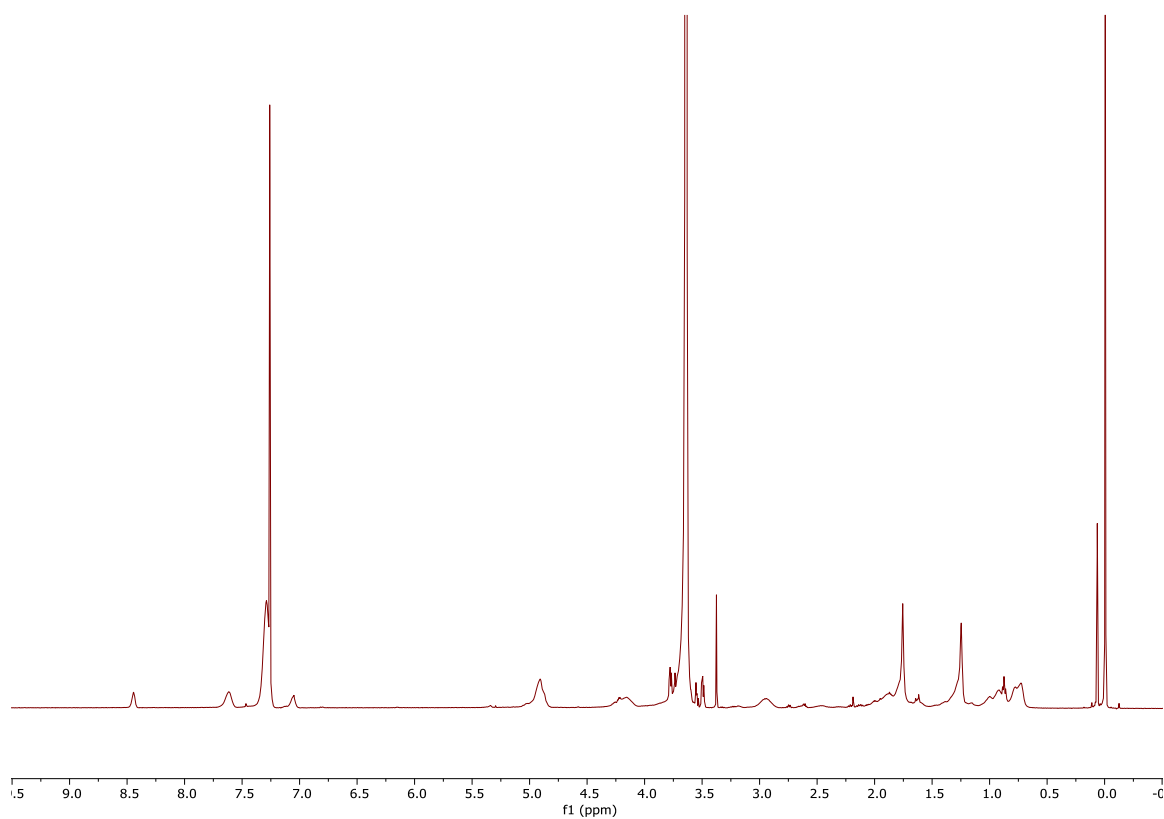
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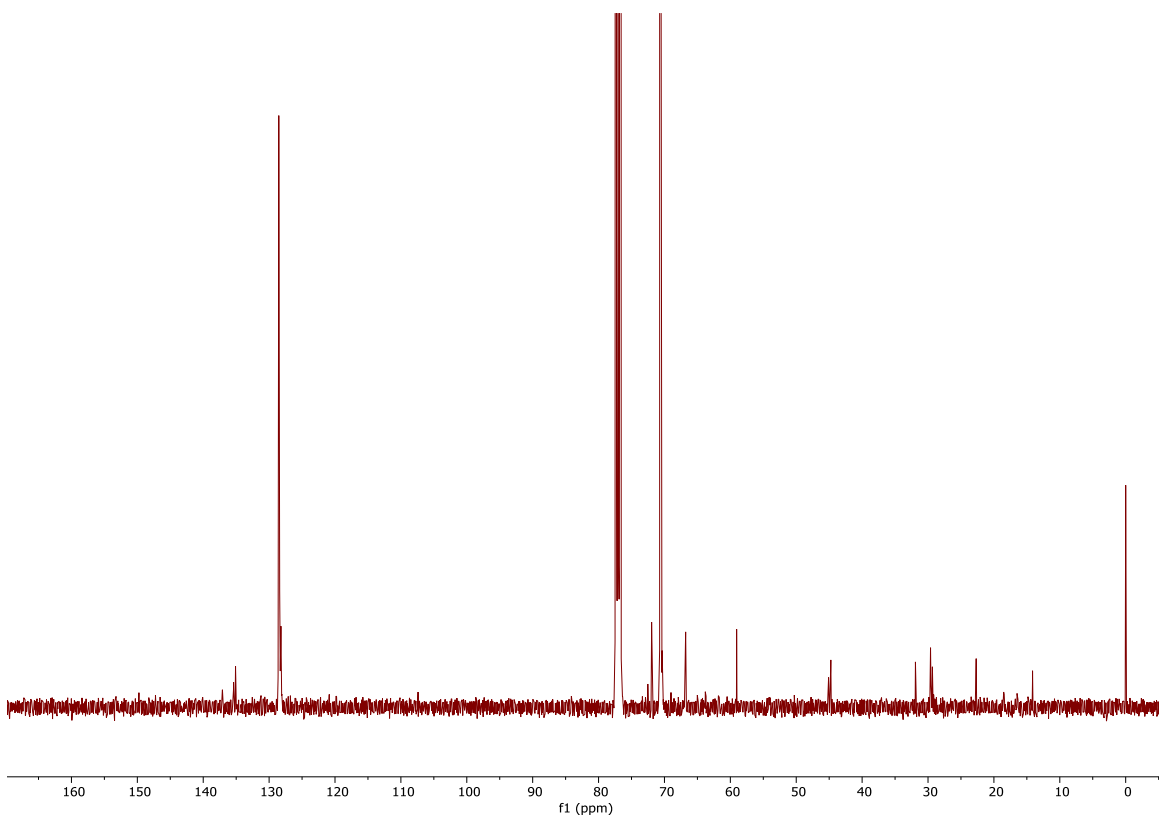
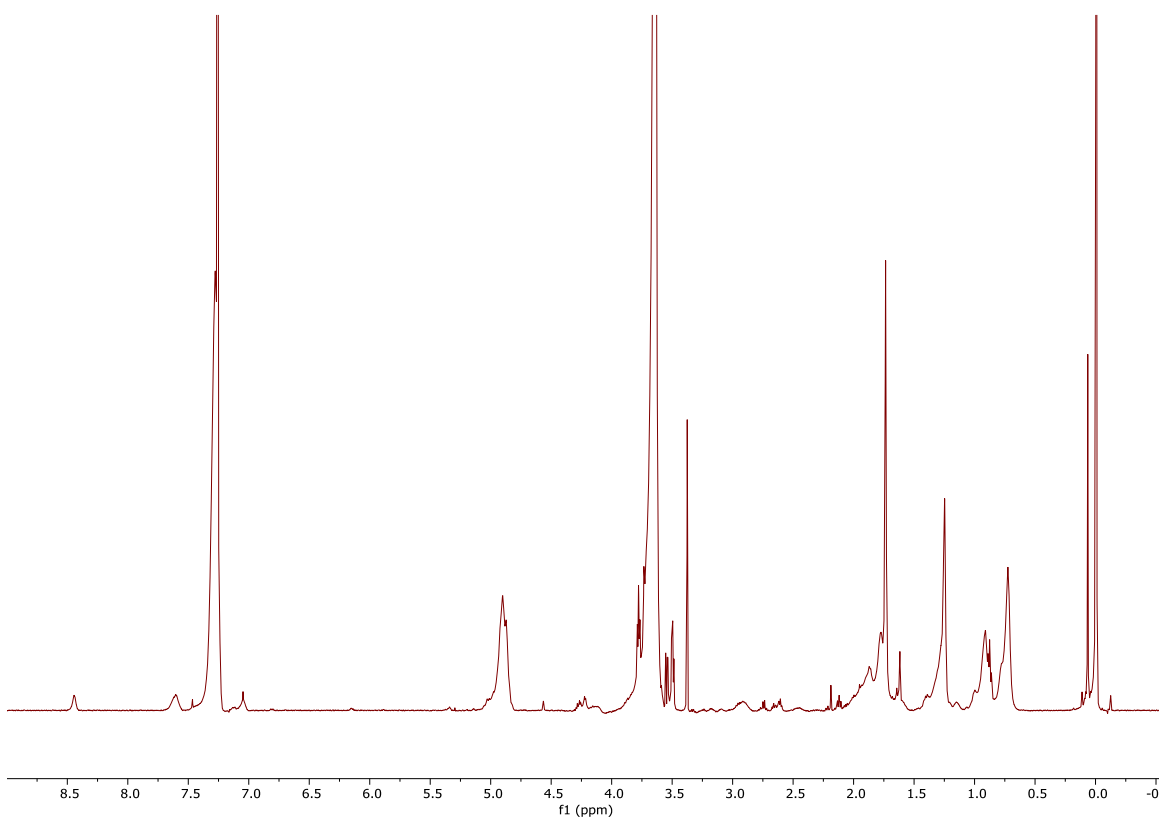
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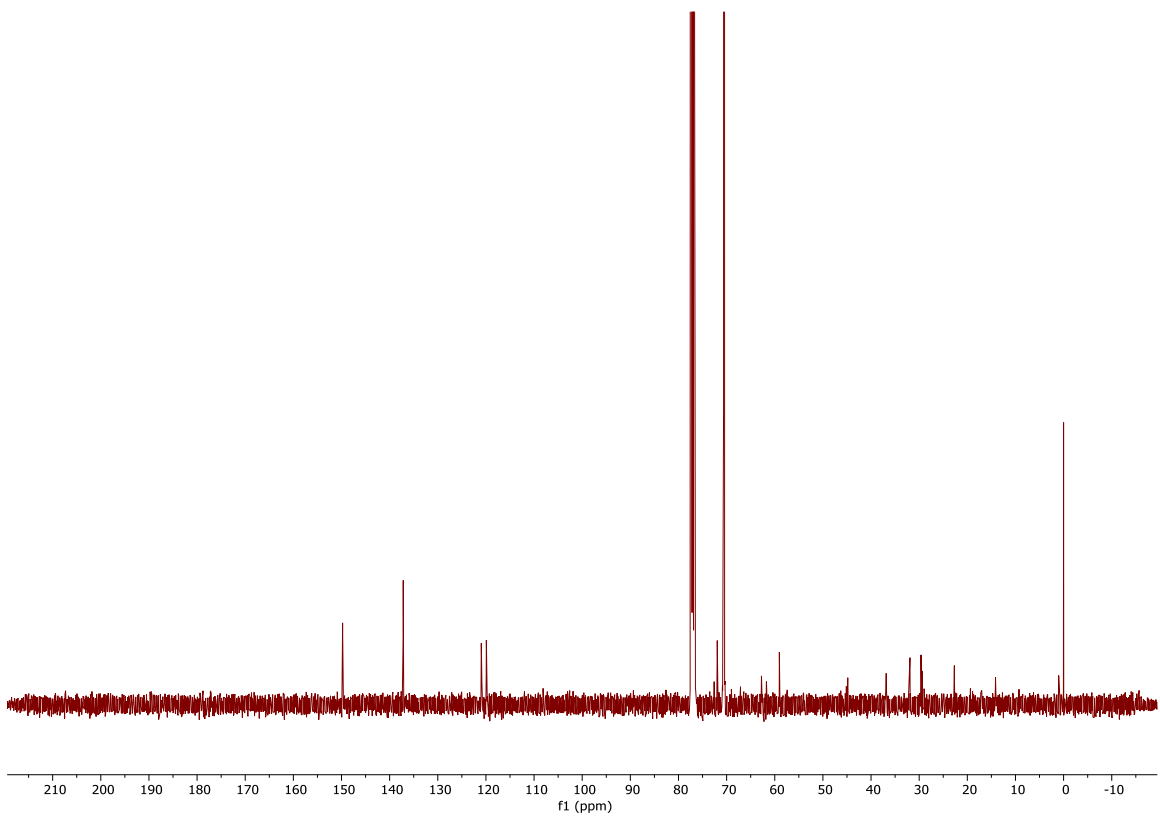
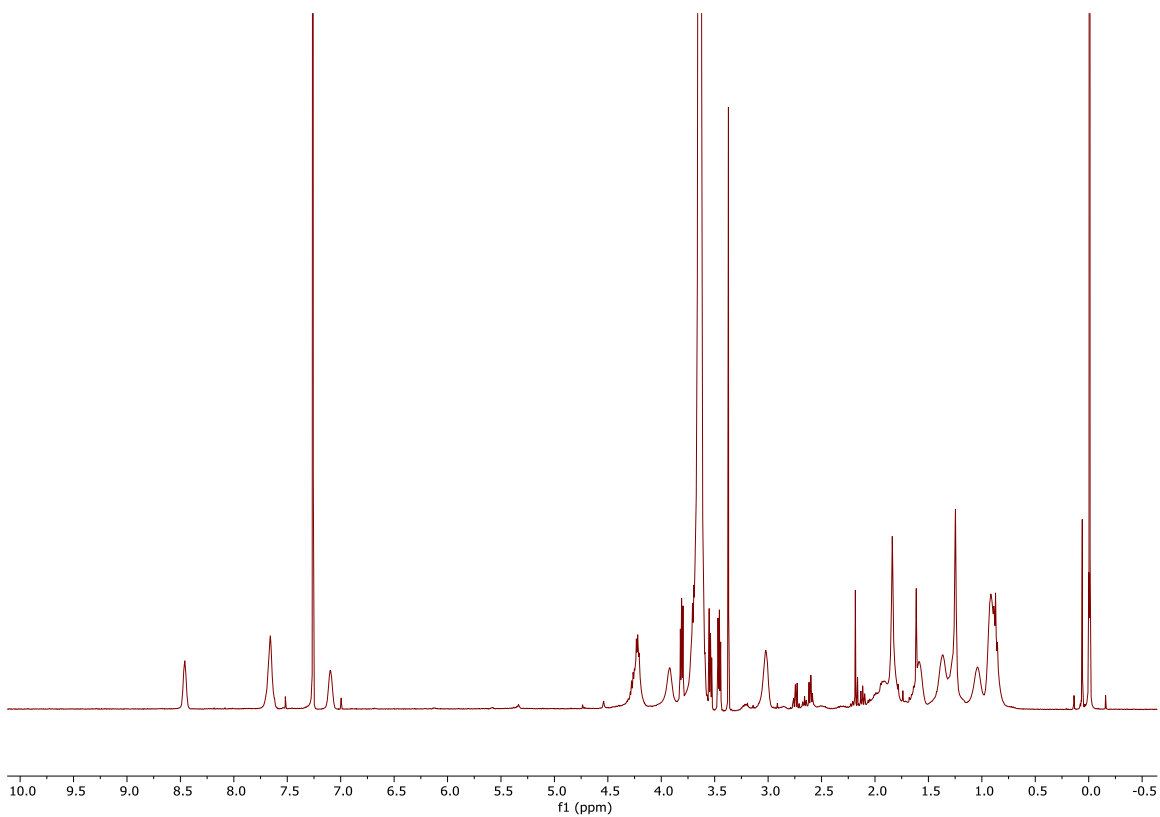
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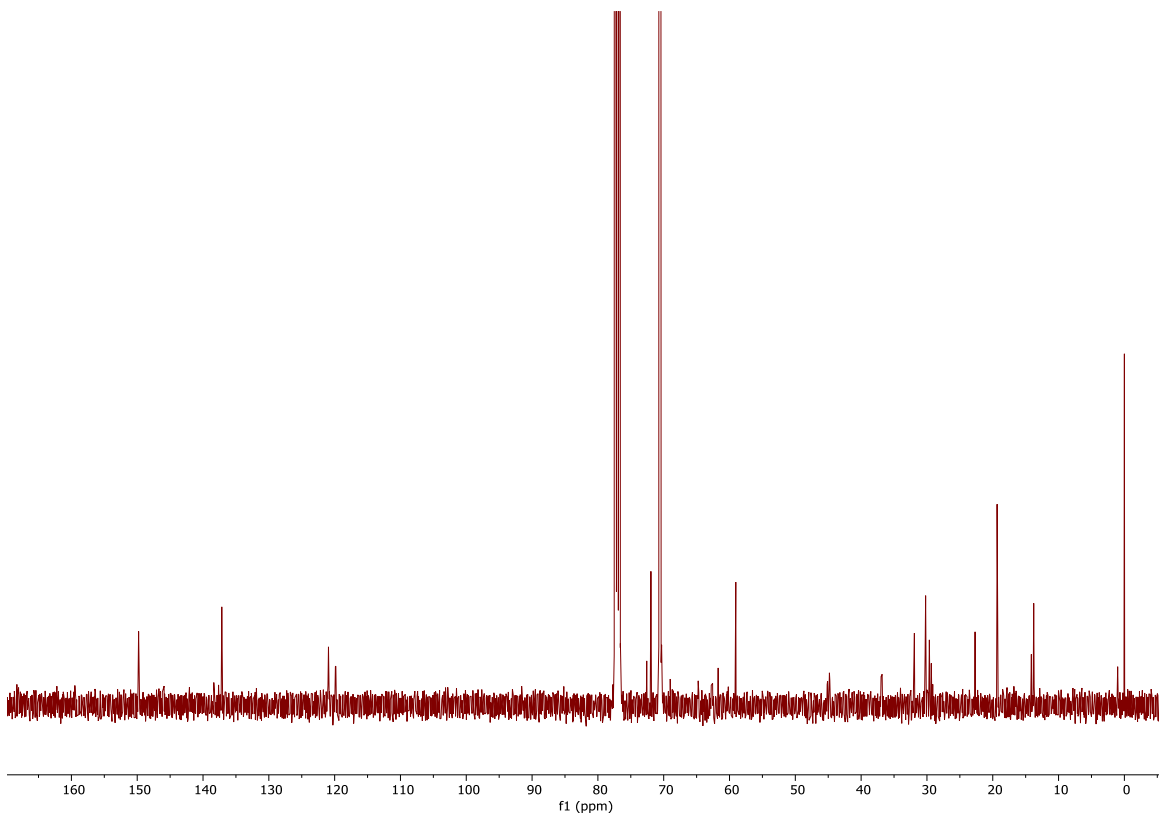
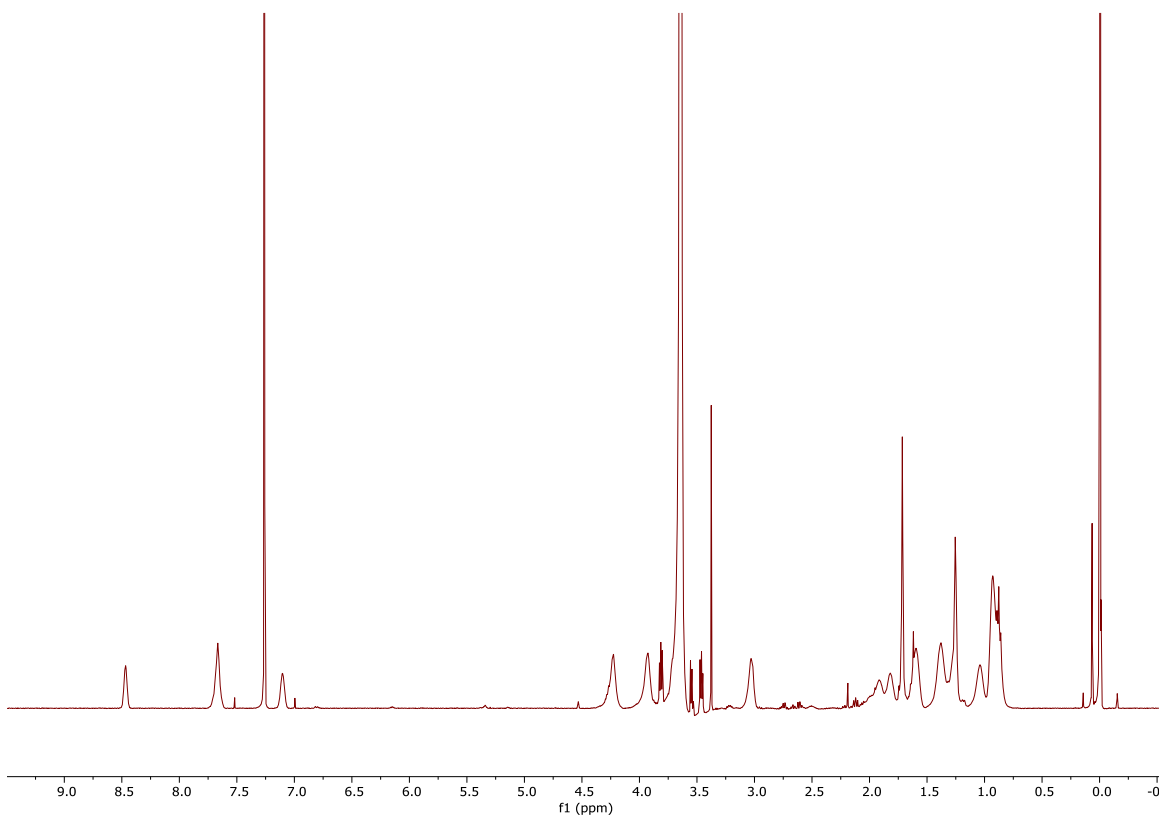
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PBu₁₀ ¹H NMR and ¹³C NMR



PBu₆₀ ¹H NMR and ¹³C NMR



PBu₈₀ ¹H NMR and ¹³C NMR

