Supporting Information

'Click' Reaction in Conjunction with Diazeniumdiolate Chemistry: Developing High-Load Nitric Oxide Donors

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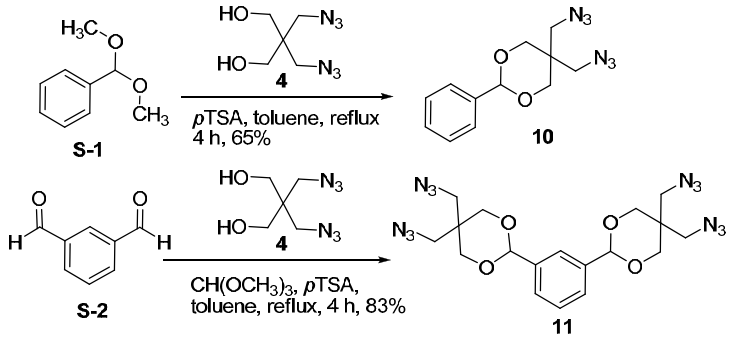
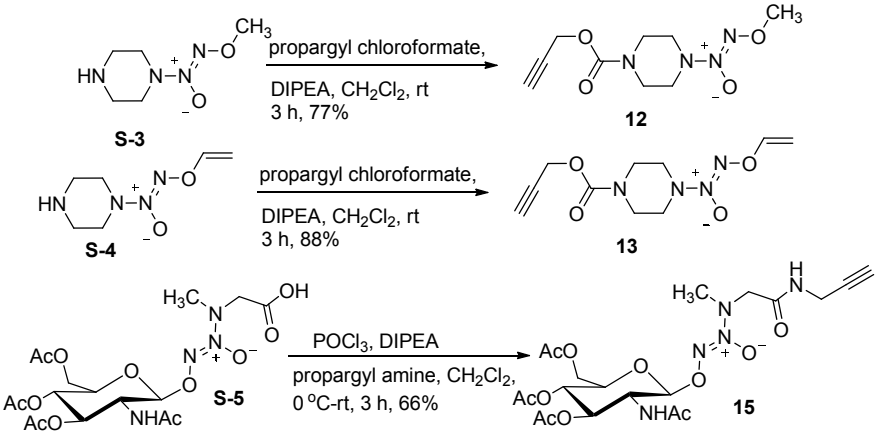
Table of Contents

Synthesis of bis-azide (10) and tetrakis-azide (11).



Scheme S1. Synthesis of bis-azide **10** and tetrakis-azide **11**.

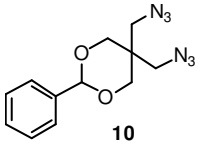
Synthesis of alkynes (12), (13), and (15).



Scheme S2. Synthesis of alkynes **12**, **13**, and **15**.

General. Starting materials were purchased from Aldrich Chemical Co. (Milwaukee, WI) unless otherwise indicated. NMR spectra were recorded on a 400 MHz Varian UNITY INOVA spectrometer; chemical shifts (δ) are reported in parts per million (ppm) downfield from tetramethylsilane. Ultraviolet (UV) spectra were recorded on an Agilent Model 8453 or a Hewlett-Packard model 8451A diode array spectrophotometer. Elemental analyses were performed by Midwest Microlab (Indianapolis, IN). IR spectra were acquired by using a Buck Scientific M-500 spectrometer. High resolution mass spectra (HRMS) were recorded on Agilent 6250 series Accurate-Mass Q-TOF LC/MS by electrospray ionization (ESI). Chromatography was performed on a Biotage SP1 Flash Purification System. Prepacked silica gel flash chromatography columns were purchased from Silicycle (Quebec City, Canada). Compounds **4**[1], **14**[2], **S-3**[3], **S-4**[3], and **S-5**[4] were prepared by using the reported procedures.

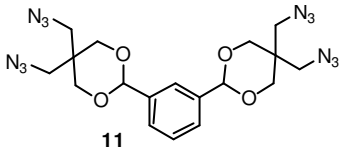
5,5-Di(azidomethyl)-2-phenyl-1,3-dioxane (10) [OA-1-107]. To a solution of benzaldehyde dimethyl acetal **S-1** (1.04 g, 6.98 mmol), and 2,2-di(azidomethyl)propane-1,3-diol **4** (1.69 g, 9.07 mmol) in dry toluene (15 mL) was added *para*-toluene sulfonic acid (*p*TSA) (100 mg). The reaction mixture was refluxed for 4 h, then cooled to rt, and diluted with ethyl acetate. The combined organic layer was washed with 5% $NaHCO_3$, then brine, dried over anhydrous Na_2SO_4 and evaporated. The crude product was purified by flash column chromatography (4:1 hexane/ethyl acetate) to give compound **10** as a white solid (1.0 g, 65%). UV (ethanol) λ_{max} (ε) 237 nm (3.98 $mM^{-1}cm^{-1}$); IR (neat) 3020, 2978, 2909, 2125, 1590, 1428, 1290, 1078 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.25 (s, 2H), 3.75 (d, J = 10.5 Hz, 2H), 3.84 (s, 2H), 4.05 (d, J = 10.5 Hz, 2H), 5.41 (s, 1H), 7.36-7.41 (m, 3H), 7.45-7.48 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 134.87, 126.58, 125.75, 123.36, 99.46, 67.86, 49.67, 48.96, 35.47.



10

Anal. Calcd for $C_{12}H_{14}N_6O_2$: C, 52.55; H, 5.14; N, 30.64, Found: C, 52.68; H, 5.25; N, 30.31.

1,3-*Bis*-[5,5-di(azidomethyl)-1,3-dioxan-2-yl]benzene (11) [RN-2-151]. To a solution of isophthalaldehyde **S-2** (358 mg, 2.67 mmol), 2,2-di(azidomethyl)propane-1,3-diol **4** (1.50 g, 8.05 mmol), and trimethyl orthoformate (1.2 mL, 10.68 mmol) in dry toluene (13 mL) was added *p*TSA (102 mg, 0.53 mmol). The reaction mixture was refluxed for 4 h, then cooled to RT, and diluted with ethyl acetate. The combined organic layer was washed with 5% $NaHCO_3$, then brine, dried over anhydrous Na_2SO_4 and evaporated. The crude product was purified by flash column chromatography (4:1 hexane/ethyl acetate) to give compound **11** as a white solid (1.04 g, 83%). UV (ethanol) λ_{max} (ε) 237 nm (4.59 $mM^{-1}cm^{-1}$); IR (neat) 3149, 3052, 2909, 2134, 1590, 1392, 1340, 1092 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.25 (s, 4H), 3.75 (d, J = 11.9 Hz, 4H), 3.83 (s, 4H), 4.05 (d, J = 11.9 Hz, 4H), 5.42 (s, 2H), 7.38-7.48 (m, 3H), 7.56 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.67, 128.36, 126.66, 123.60, 101.63, 70.40, 52.22, 51.51, 38.03.



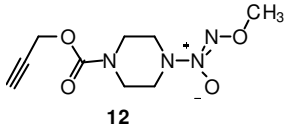
11

Anal. Calcd for $C_{18}H_{22}N_{12}O_4$: C, 45.95; H, 4.71; N, 35.73, Found: C, 45.93; H, 4.73; N, 35.48.

General procedure for synthesis of compounds (12) and (13).

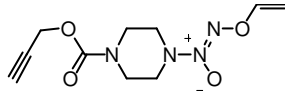
Propargyl chloroformate (1.5 equiv) was added to a solution of amine **S-3** or **S-4** (1 equiv) and diisopropylethylamine (DIPEA) (3 equiv) in CH_2Cl_2 (3 mL per mmol of diazeniumdiolate). The reaction mixture was stirred at rt for 3 h. Solvent was evaporated and crude mass was purified by flash column chromatography.

***O*^{2}-Methyl 1-[4-(Propargyloxycarbonyl)piperazin-1-yl]diazen-1-ium-1,2-diolate (12)** [RN-2-103]. Starting from **S-3** (600 mg, 3.75 mmol), DIPEA (960 µL, 5.63 mmol), and propargyl chloroformate (556 µL, 5.63 mmol), **12** was isolated as a white solid (695 mg, 77%). UV (ethanol) λ_{max} (ε) 247 nm (6.5 $mM^{-1}cm^{-1}$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.49 (t, *J* = 2.5 Hz, 1H), 3.39-3.42 (m, 4H), 3.68-3.71 (m, 4H), 4.03 (s, 3H), 4.73 (d, *J* = 2.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.96, 77.97, 74.81, 61.11, 53.28, 51.02, 42.56.


12

Anal. Calcd for $C_9H_{14}N_4O_4$: C, 44.63; H, 5.83; N, 23.13, Found: C, 44.60; H, 5.85; N, 22.90.

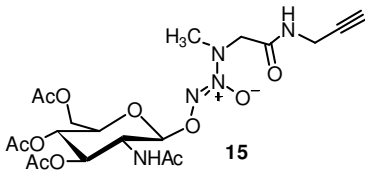
***O*^{2}-Vinyl 1-[4-(Propargyloxycarbonyl)piperazin-1-yl]diazen-1-ium-1,2-diolate (13)** [RN-2-146]. Starting from **S-4** (500 mg, 2.90 mmol), DIPEA (803 µL, 4.35 mmol), and propargyl chloroformate (426 µL, 4.35 mmol), **13** was isolated as a white solid (647 mg, 88%). UV (ethanol) λ_{max} (ε) 259 nm (7.8 $mM^{-1}cm^{-1}$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.49 (t, *J* = 2.4 Hz, 1H), 3.49 (d, *J* = 5.2 Hz, 4H), 3.71 (d, *J* = 5.2 Hz, 4H), 4.44 (dd, *J* = 6.7, 2.6 Hz, 1H), 4.73 (d, *J* = 2.4 Hz, 2H), 4.87 (dd, *J* = 14.1, 2.6 Hz, 1H), 6.81 (dd, *J* = 14.1, 6.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.95, 148.42, 92.71, 77.92, 74.86, 53.33, 50.76, 42.48.


13

Anal. Calcd for $C_{10}H_{14}N_4O_4$: C, 47.24; H, 5.55; N, 22.04, Found: C, 47.30; H, 5.55; N, 21.93.

***O*^{2}-(3,4,6-Tri-*O*-acetyl-β-D-*N*-acetylglucosaminyl) 1-[*N*-(Propargylaminocarbonylmethyl)-*N*-methylamino]diazen-1-ium-1,2-diolate (15)** [OA-1-63]. Under nitrogen, a solution of $POCl_3$ (0.12 mL, 1.88 mmol) in dry CH_2Cl_2 (3 mL) was added to an ice-cold mixture of carboxylic acid **S-5**, and DIPEA (0.32 mL, 1.88

mmol) in dry CH_2Cl_2 (10 mL). After 10 min, propargyl amine (0.16 mL) was added to the reaction mixture and allowed to stir at rt for 3 h. Then the reaction was diluted with



15

CH_2Cl_2, and the organic layer was washed with 5% $NaHCO_3$, 3 M HCl, then brine, dried over anhydrous Na_2SO_4 and evaporated. The crude product was purified by flash column chromatography (19:1 CH_2Cl_2/ CH_3OH) to give compound **15** as white solid (425 mg, 66%). UV (ethanol) λ_{max} (ε) 244 nm (7.6 $mM^{-1}cm^{-1}$); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.95 (s, 3H), 2.04 (s, 3H), 2.05 (s, 3H), 2.09 (s, 3H), 2.31 (t, *J* = 2.6 Hz, 1H), 3.27 (s, 3H), 3.87 (ddd, *J* = 10.0, 4.8, 2.4 Hz, 1H), 4.02-4.16 (m, 5H), 4.18-4.20 (m, 1H), 4.27 (dd, *J* = 12.4, 4.8 Hz, 1H), 5.09 (t, *J* = 9.4 Hz, 1H), 5.44 (dd, *J* = 10.5, 9.3 Hz, 1H), 5.49 (t, *J* = 8.8 Hz, 1H), 6.34 (d, *J* = 8.8 Hz, 1H), 7.11 (t, *J* = 5.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.94, 170.67, 170.63, 169.36, 100.09, 72.64, 71.91, 68.15, 61.84, 59.21, 56.40, 52.66, 41.23, 23.19, 20.68, 20.56; HRMS (ESI) *m/z* calculated for $C_{20}H_{30}N_5O_{11}$ $[M+H]^+$ 516.19363, found 516.19352.

General procedures for the 'Click' reaction.

***Method A*: $CuSO_4$/Na-ascorbate**

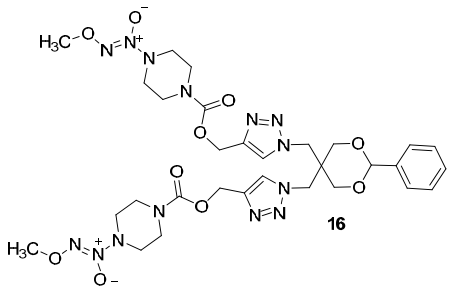
To a solution of azide **10** or **11** (1.0 equiv), alkyne **12**-**14** (1.1 equiv per azido group), and Na-ascorbate (40 mol% per azido group), in THF (7.5 mL per mmol of azide) was added a solution of $CuSO_4 \cdot 5H_2O$ (20 mol% per azido group) in water (2.5 mL per mmol of azide). The reaction was stirred at rt for 15-45 min (TLC monitoring). The reaction was extracted ethyl acetate three times. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 and evaporated. The crude mass was purified by flash column chromatography.

***Method B*: CuI/DIPEA**

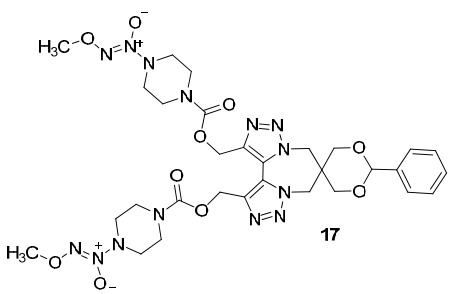
To a solution of azide **10** (1.0 equiv), alkyne **12**-**14** (2.2 equiv), and CuI (2.0 equiv) in acetonitrile (20 mL per mmol of azide) was added DIPEA dropwise. The reaction was stirred at rt for 15-45 min (TLC monitoring). The solvent was removed under vacuum; ethyl acetate was added to the residual solid and filtered. The filtrate was evaporated. The crude mass was purified by flash column chromatography.

Compound (16) [OA-1-112]. Using *Method A*, starting from **10** (50 mg, 0.18 mmol), alkyne **12** (100 mg, 0.4 mmol), $CuSO_4 \cdot 5H_2O$ (18 mg, 0.07 mmol), and Na-

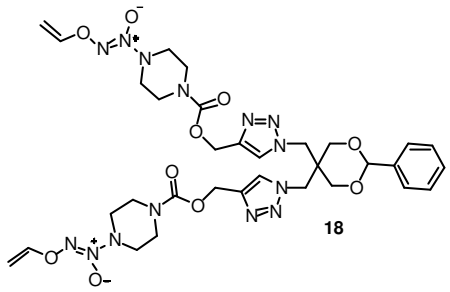
ascorbate (29 mg, 0.14 mmol), compound **16** was isolated as a white solid (81 mg, 60%). UV (ethanol) λ_{max} (ε) 247 nm (15.9 $mM^{-1}cm^{-1}$); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.37 (*broad*, 8H), 3.64-3.70 (m, 8H), 3.77 (d, *J* = 12.2 Hz, 2H), 4.00 (d, *J* = 12.2 Hz, 2H), 4.02 (s, 6H), 4.36 (s, 2H), 4.61 (s, 2H), 5.27 (d, *J* = 5.0 Hz, 4H), 5.54 (s, 1H), 7.41-7.50 (m, 5H), 7.80 (s, 1H), 8.24 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.52, 143.05, 143.04, 136.89, 129.40, 128.42, 126.51, 126.44, 125.84, 102.23, 70.38, 61.11, 58.60, 58.41, 51.04, 50.16, 48.45, 42.53, 39.34; HRMS (ESI) *m/z* calculated for $C_{30}H_{43}N_{14}O_{10}$ $[M+H]^+$ 759.32811, found 759.32858.



Compound (17) [OA-1-120]. Using *Method B*, starting from **10** (50 mg, 0.18 mmol), alkyne **12** (102 mg, 0.41 mmol), CuI (69 mg, 0.36 mmol), and DIPEA (62 μL, mmol), compound **17** was isolated as a white solid (102 mg, 74%). UV (ethanol) λ_{max} (ε) 247 nm (14.1 $mM^{-1}cm^{-1}$); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.38 (*broad*, 8H), 3.62 (*broad*, 8H), 3.98 (d, *J* = 11.5 Hz, 2H), 4.02 (s, 6H), 4.06 (*broad*, 2H), 4.19 (d, *J* = 11.5 Hz, 2H), 4.77 (*broad*, 2H), 5.26 (d, *J* = 6.5 Hz, 4H), 5.57 (s, 1H), 7.40-7.54 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.00, 153.95, 142.06, 142.00, 136.55, 129.48, 128.41, 125.95, 124.16, 102.25, 71.61, 61.11, 57.55, 51.12, 50.82, 50.10, 42.42; HRMS (ESI) *m/z* calculated for $C_{30}H_{41}N_{14}O_{10}$ $[M+H]^+$ 757.31246, found 757.31386.



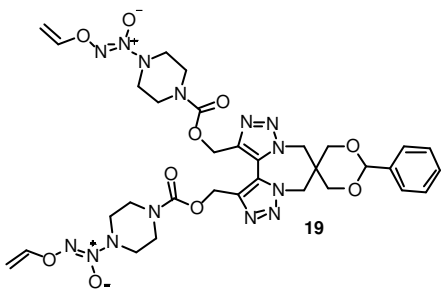
Compound (18) [OA-1-117]. Using *Method A,* starting from **10** (50 mg, 0.18 mmol), alkyne **13** (93 mg, 0.36 mmol), $CuSO_4 \cdot 5H_2O$ (18 mg, 0.07 mmol), and Na-ascorbate (29 mg, 0.14 mmol), compound **18** was isolated as a white solid (96 mg, 67%). UV (ethanol) λ_{max} (ε) 259 nm (14.9 $mM^{-1}cm^{-1}$); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.45 (*broad*, 8H), 3.65-3.70 (m, 8H), 3.77 (d, *J* = 12.3 Hz, 2H), 4.01 (d, *J* = 12.3 Hz, 2H), 4.36 (s, 2H), 4.43 (ddd, *J* = 6.6, 2.6, 1.2, 2H), 4.60 (s, 2H), 4.86 (dd, *J* = 14.1, 2.6 Hz, 2H), 5.28 (d, *J* = 5.9 Hz,



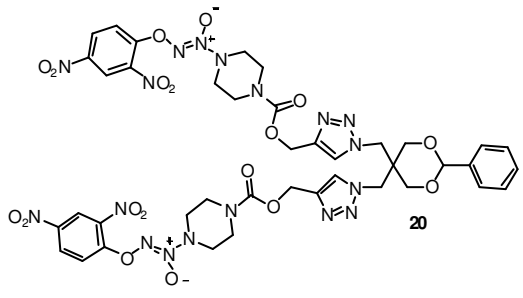
4H), 5.54 (s, 1H), 6.78-6.83 (m, 2H), 7.41-7.50 (m, 5H), 7.79 (s, 1H), 8.24 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.50, 148.42, 143.04, 143.02, 136.88, 129.42, 128.43, 126.50, 126.44, 125.84, 109.99, 102.24, 92.72, 92.68, 70.38, 58.64, 58.45, 50.76, 50.16, 48.44, 42.43, 39.35, 30.87; HRMS (ESI) *m/z* calculated for $C_{32}H_{43}N_{14}O_{10}$ $[M+H]^+$ 783.32811, found 783.32926.

Anal. Calcd for $C_{32}H_{42}N_{14}O_{10}\cdot H_2O$: C, 48.00; H, 5.54; N, 24.49, Found: C, 48.08; H, 5.15; N, 24.22.

Compound (19) [OA-1-121]. Using *Method B*, starting from **10** (50 mg, 0.18 mmol), alkyne **13** (106 mg, 0.41 mmol), CuI (69 mg, 0.36 mmol), and DIPEA (62 μL, 0.36 mmol), compound **19** was isolated as a white solid (63 mg, 44%). UV (ethanol) λ_{max} (ε) 252 nm (16.5 $mM^{-1}cm^{-1}$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.46 (*broad*, 8H), 3.63 (*broad*, 8H), 3.99 (d, *J* = 11.5 Hz, 2H), 4.07 (*broad* s, 2H), 4.19 (d, *J* = 11.5 Hz, 2H), 4.43 (d, *J* = 5.3 Hz, 2H), 4.78 (*broad* s, 2H), 4.86 (d, *J* = 14.0 Hz, 2H), 5.24 (d, *J* = 6.3 Hz, 4H), 5.57 (s, 1H), 6.80 (dd, *J* = 14.0, 6.6 Hz, 2H), 7.41-7.52 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.96, 153.92, 148.42, 141.95, 141.88, 136.56, 129.49, 128.41, 125.95, 124.17, 102.24, 92.68, 71.60, 57.57, 51.14, 50.52, 50.12, 42.41; HRMS (ESI) *m/z* calculated for $C_{32}H_{41}N_{14}O_{10}$ $[M+H]^+$ 781.31246, found 781.31333.

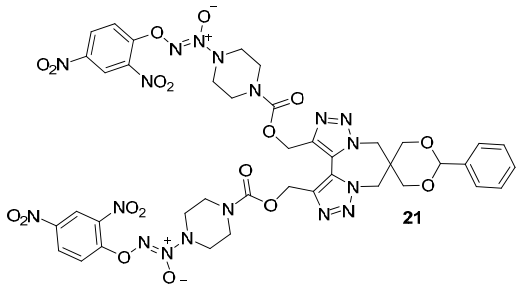


Compound (20) [OA-1-110]. Using *Method A,* starting from **10** (39 mg, 0.14 mmol), alkyne **14** (113 mg, 0.29 mmol), $CuSO_4\cdot 5H_2O$ (13 mg, 0.06 mmol), and Na-ascorbate (23 mg, 0.11 mmol), compound **20** was isolated as a yellow solid (113 mg, 75%). UV (ethanol) λ_{max} (ε) 249 nm (14.6 $mM^{-1}cm^{-1}$), λ_{max} (ε) 302 nm (16.1 $mM^{-1}cm^{-1}$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.62 (*broad*, 8H), 3.73 (*broad*, 10H), 4.02 (d, *J* = 12.0 Hz, 2H), 4.36 (s, 2H), 4.61 (s, 2H), 5.29 (d, *J* = 9.6 Hz, 4H), 5.55 (s, 1H), 7.40-7.49 (m, 5H), 7.64-7.68 (m, 2H), 7.81 (s, 1H), 8.25 (s, 1H), 8.46 (d, J = 9.1 Hz, 2H), 8.87 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.42, 153.58, 153.53, 142.95, 142.91, 142.45, 137.35, 136.84,

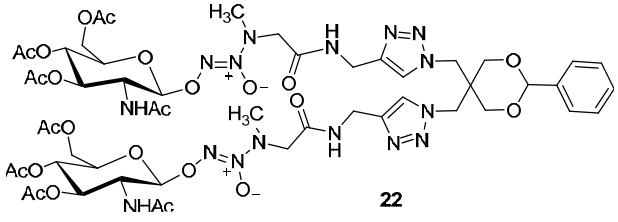


129.45, 129.08, 129.05, 128.44, 126.50, 125.82, 122.12, 117.72, 117.67, 102.26, 70.38, 58.77, 58.53, 50.39, 50.16, 48.46, 42.29, 39.35; HRMS (ESI) *m/z* calculated for $C_{40}H_{43}N_{18}O_{18}$ $[M+H]^+$ 1063.29972, found 1063.30243.

Compound (21) [OA-1-136]. Using *Method B*, starting from **10** (50 mg, 0.18 mmol), alkyne **14** (165 mg, 0.42 mmol), CuI (69 mg, 0.36 mmol), and DIPEA (62 μL, 0.36 mmol), compound **21** was isolated as a yellow solid (109 mg, 72%). UV (ethanol) λ_{max} (ε) 251 nm (13.2 $mM^{-1}cm^{-1}$), λ_{max} (ε) 302 nm (12.4 $mM^{-1}cm^{-1}$); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.69 (*broad*, 16H), 4.00 (d, *J* = 11.6 Hz, 2H), 4.09 (*broad*, 2H), 4.20 (d, *J* = 11.6 Hz, 2H), 4.79 (*broad*, 2H), 5.25 (d, *J* = 7.4 Hz, 2H), 5.58 (s, 1H), 7.41-7.52 (m, 5H), 7.67 (d, *J* = 9.2 Hz, 2H), 8.46 (dd, *J* = 9.2, 1.7 Hz, 2H), 8.87 (d, *J* = 1.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.94, 153.89, 153.55, 142.47, 141.75, 141.68, 137.38, 136.47, 129.54, 129.08, 128.43, 125.92, 124.18, 122.11, 117.79, 102.27, 71.60, 57.71, 51.20, 50.16, 42.43; HRMS (ESI) *m/z* calculated for $C_{40}H_{41}N_{18}O_{18}$ $[M+H]^+$ 1061.28407, found 1061.28523.

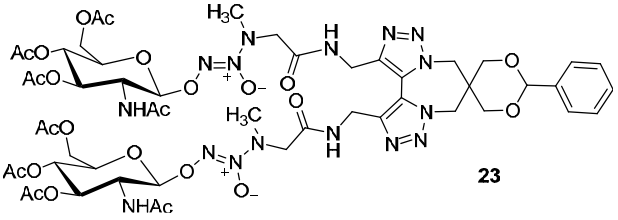


Compound (22) [OA-1-154]. Using *Method A,* starting from **10** (50 mg, 0.18 mmol), alkyne **15** (216 mg, 0.42 mmol), $CuSO_4 \cdot 5H_2O$ (18 mg, 0.07 mmol), and Na-ascorbate (29 mg, 0.14 mmol), compound **22** was isolated as a white solid (152 mg, 63%). UV (ethanol) λ_{max} (ε) 250 nm (14.8 $mM^{-1}cm^{-1}$); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.84 (s, 3H), 1.88 (s, 3H), 2.02 (s, 9H), 2.03 (s, 3H), 2.07 (s, 6H), 3.25 (s, 3H), 3.26 (s, 3H), 3.81-3.88 (m, 4H), 3.95-4.28 (m, 14H), 4.31 (s, 2H), 4.52-4.65 (m, 4H), 4.71 (s, 2H), 5.08 (t, *J* = 9.2 Hz, 2H), 5.36-5.45 (m, 4H), 5.52 (s, 1H), 6.54 (d, *J* = 8.9 Hz, 1H), 6.68 (d, *J* = 8.8 Hz, 1H), 7.36-7.51 (m, 5H), 7.70 (s, 1H), 7.95 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.44, 170.82, 170.66, 170.53, 169.37, 167.73, 167.66, 144.62, 144.28, 137.10, 129.35, 128.41, 125.98, 124.91, 124.83, 102.14, 100.40, 100.30, 72.50, 72.03, 71.86, 70.45, 68.29, 68.20, 61.81, 56.75, 56.65, 52.80, 52.49, 50.35, 41.61, 39.02, 34.95, 34.68, 23.15,

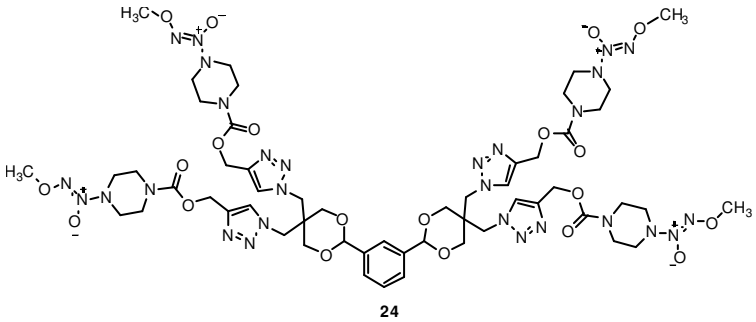


23.12, 20.68, 20.61, 20.56; HRMS (ESI) *m/z* calculated for $C_{52}H_{73}N_{16}O_{24}$ $[M+H]^+$ 1305.49781, found 1305.49776.

Compound (23) [OA-1-149]. Using *Method B*, starting from **10** (38 mg, 0.14 mmol), alkyne **15** (mg, mmol), CuI (53 mg, 0.28 mmol), and DIPEA (47 μL, 0.28 mmol), compound **23** was isolated as a white solid (100 mg, 56%). UV (ethanol) λ_{max} (ε) 250 nm (13.4 $mM^{-1}cm^{-1}$); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.86 (s, 3H), 1.95 (s, 3H), 2.01 (s, 3H), 2.02 (s, 6H), 2.03 (s, 3H), 2.07 (s, 6H), 3.17 (s, 3H), 3.19 (s, 3H), 3.79-3.85 (m, 3H), 3.88 (s, 2H), 3.95 (s, 2H), 3.99-4.19 (m, 11H), 4.23-4.29 (m, 2H), 4.58-4.67 (m, 4H), 5.05-5.14 (m, 2H), 5.38-5.45 (m, 4H), 5.58 (s, 1H), 6.40 (d, *J* = 8.5 Hz, 1H), 6.49 (d, *J* = 8.8 Hz, 1H), 7.40-7.43 (m, 3H), 7.52-7.54 (m, 2H), 7.68 (*broad* t, 1H), 7.75 (*broad* t, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 170.90, 170.77, 170.64, 170.53, 169.38, 168.11, 143.27, 136.89, 129.47, 128.43, 126.03, 123.05, 122.93, 102.14, 100.34, 100.19, 72.40, 71.99, 71.90, 68.19, 61.78, 56.42, 56.15, 52.92, 50.81, 42.31, 41.63, 41.53, 34.64, 23.27, 23.15, 20.70, 20.63, 20.60, 20.56; HRMS (ESI) *m/z* calculated for $C_{52}H_{71}N_{16}O_{24}$ $[M+H]^+$ 1303.48216, found 1303.48232.

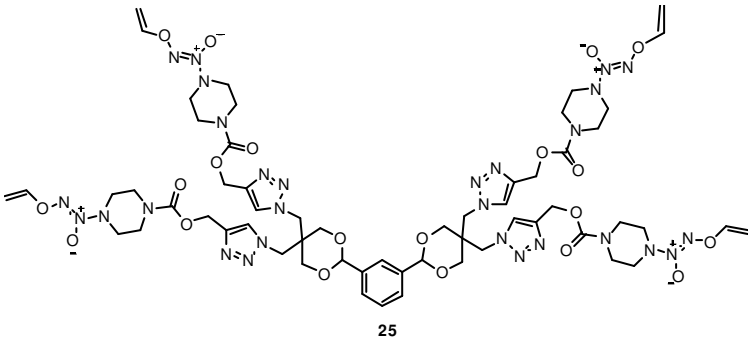


Compound (24) [OA-1-128]. Under N_2 using *Method A*, starting from **11** (50 mg, 0.11 mmol), alkyne **12** (103 mg, 0.43 mmol), $CuSO_4 \cdot 5H_2O$ (21 mg, 0.09 mmol), and Na-ascorbate (34 mg, 0.17 mmol), compound **24** was isolated as a white solid (83 mg, 54 %). UV (ethanol) λ_{max} (ε) 246 nm (23.9 $mM^{-1}cm^{-1}$); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.37 (*broad*, 16H), 3.66 (*broad*, 16H), 3.80 (d, *J* =10.9 Hz, 4H), 4.02 (s, 16H), 4.36 (s, 4H), 4.60 (s, 4H), 5.27 (s, 8H), 5.57 (s, 2H), 7.45-7.60 (m, 4H), 7.79 (s, 2H), 8.23 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.52, 143.04, 143.00, 137.22, 128.57, 126.73, 126.53, 126.47,



123.61, 101.72, 70.37, 61.10, 58.56, 58.35, 51.00, 50.11, 48.46, 42.50, 39.28; HRMS (ESI) *m/z* calculated for $C_{54}H_{79}N_{28}O_{20}$ $[M+H]^+$ 1439.60199, found 1439.60359.

Compound (25) [RN-2-152]. Under N_2 using *Method A*, starting from **11** (71 mg, 0.15 mmol), alkyne **12** (173 mg, 0.68 mmol), $CuSO_4 \cdot 5H_2O$ (30 mg, 0.12 mmol), and Na-ascorbate (71 mg, 0.36 mmol), compound **24** was isolated as a white solid (103 mg, 46%). UV (ethanol) λ_{max} (ε) 259 nm (23.8 $mM^{-1}cm^{-1}$); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.45 (*broad*, 16H), 3.65-3.70 (m, 16H), 3.80 (d, *J* = 12.1 Hz, 4H), 4.02 (d, *J* = 12.1 Hz, 4H), 4.35 (s, 4H), 4.44 (dd, *J* = 6.6, 2.6 Hz, 4H), 4.60 (s, 4H), 4.86 (td, *J* = 14.1, 2.1 Hz, 4H), 5.27 (d, *J* = 7.7 Hz, 8H), 5.57 (s, 2H), 6.81 (ddd, *J* = 14.1, 6.6, 1.8 Hz, 4H), 7.45-7.58 (m, 4H), 7.79 (s, 2H), 8.22 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.58, 148.48, 143.12, 143.08, 137.28, 128.67, 126.81, 126.57, 126.53, 123.67, 101.82, 92.80, 92.75, 70.47, 58.68, 58.46, 50.81, 50.19, 48.51, 42.47, 39.38; HRMS (ESI) *m/z* calculated for $C_{58}H_{79}N_{28}O_{20}$ $[M+H]^+$ 1487.60199, found 1487.60508.



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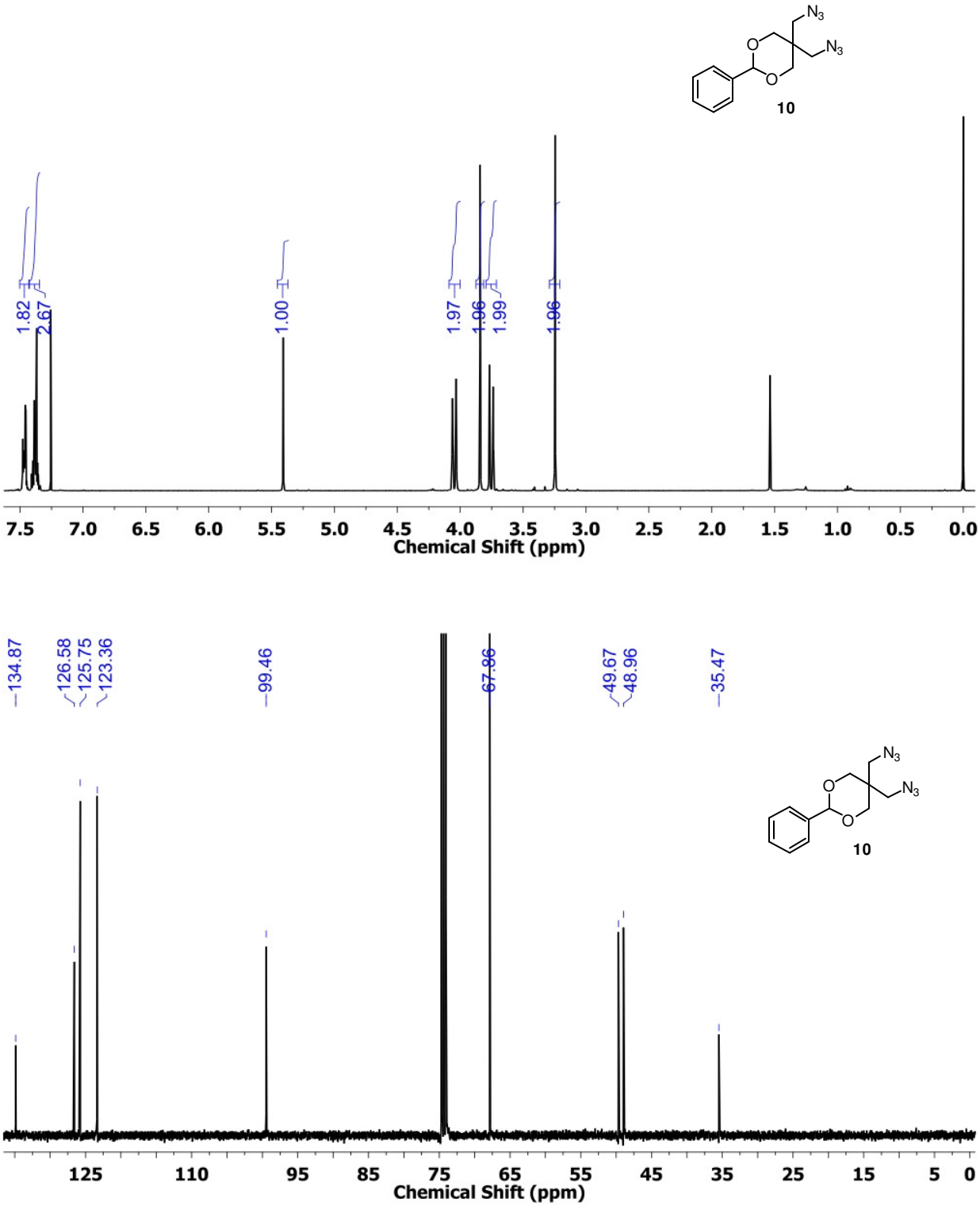

Figure S1. ^{1}H NMR and ^{13}C NMR spectra of compound **10**.

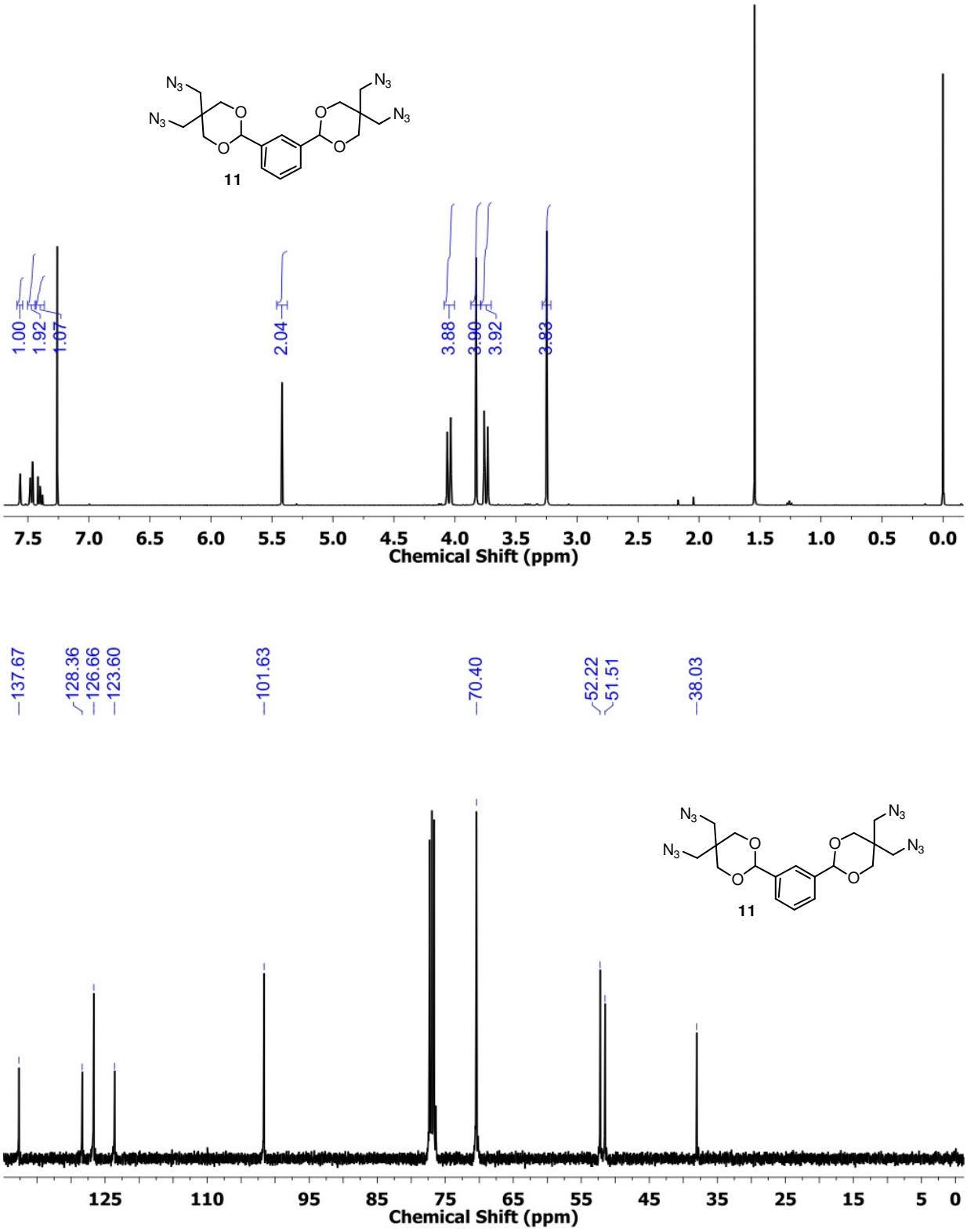

Figure S2. ^{1}H NMR and ^{13}C NMR spectra of compound **11**.

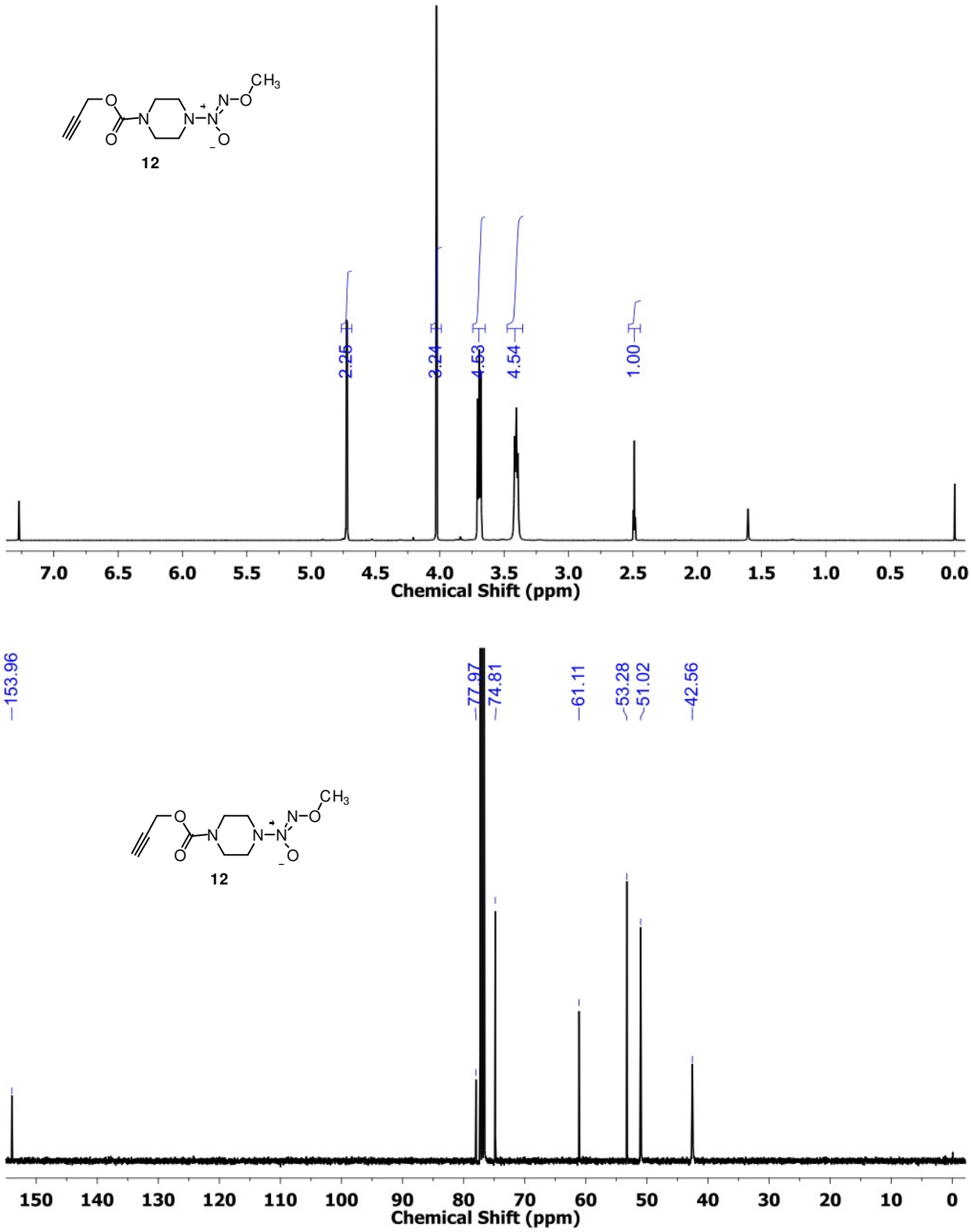

Figure S3. ^{1}H NMR and ^{13}C NMR spectra of compound **12**.

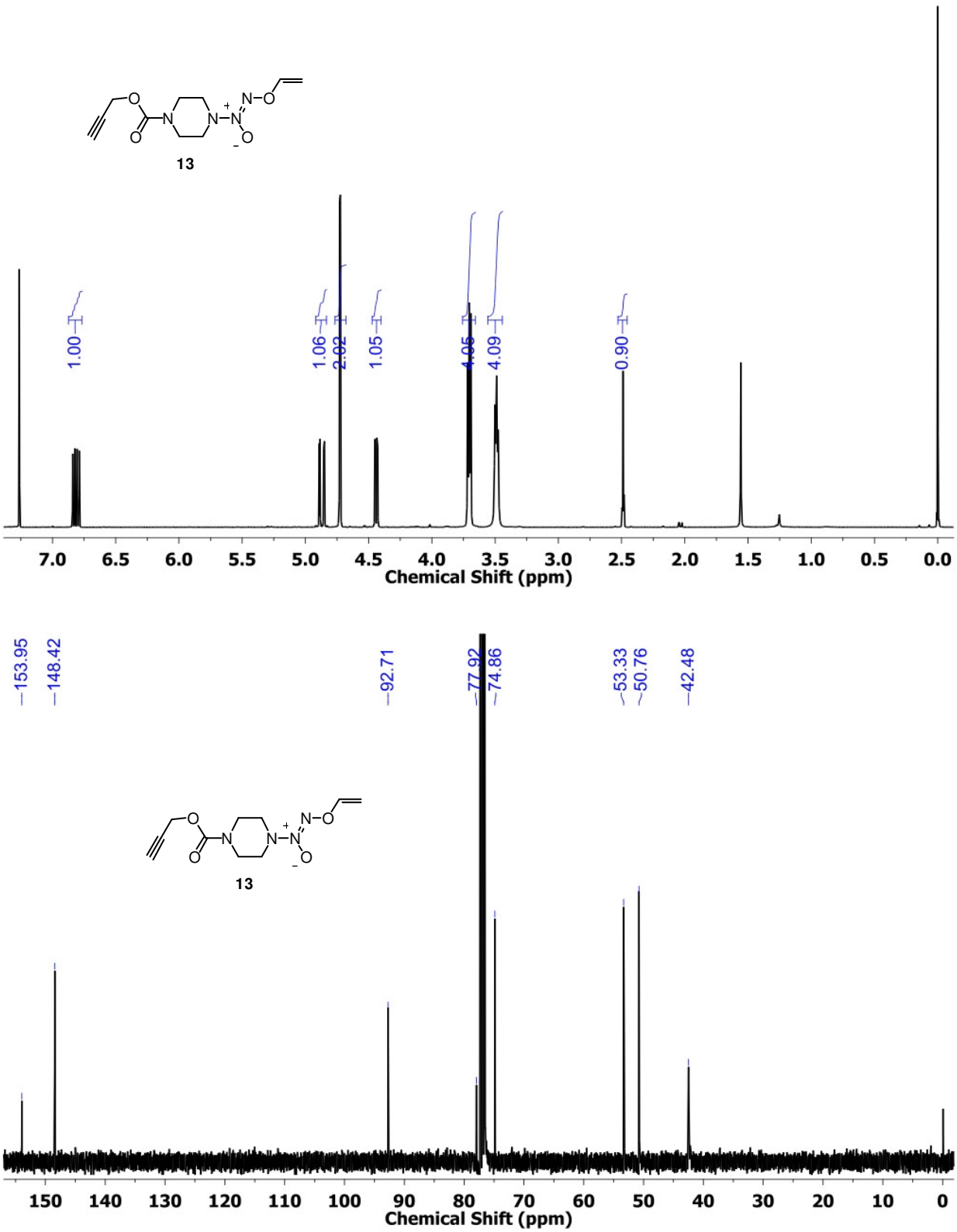

Figure S4. ^{1}H NMR and ^{13}C NMR spectra of compound **13**.

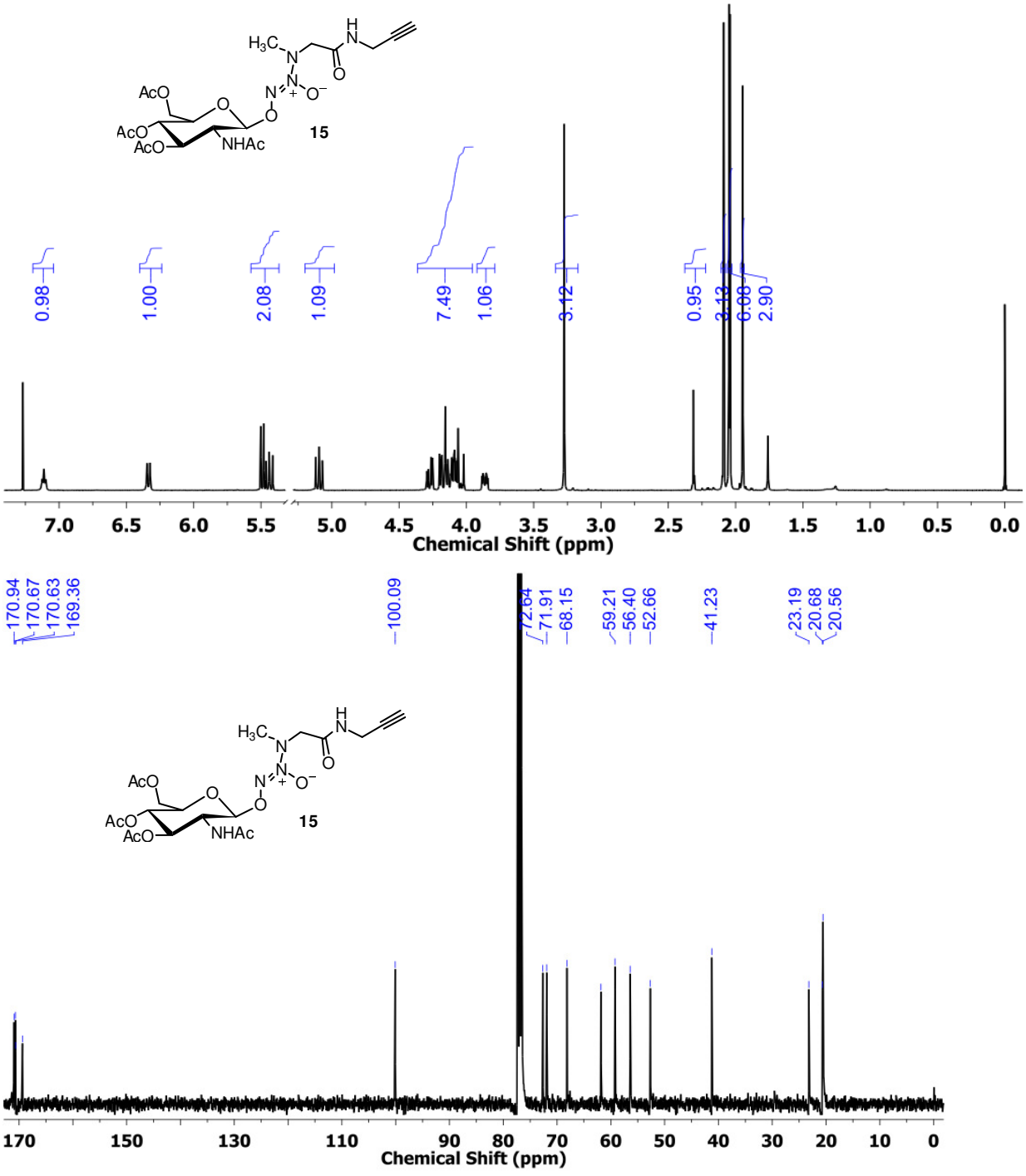

Figure S5. ^{1}H NMR and ^{13}C NMR spectra of compound **15**.

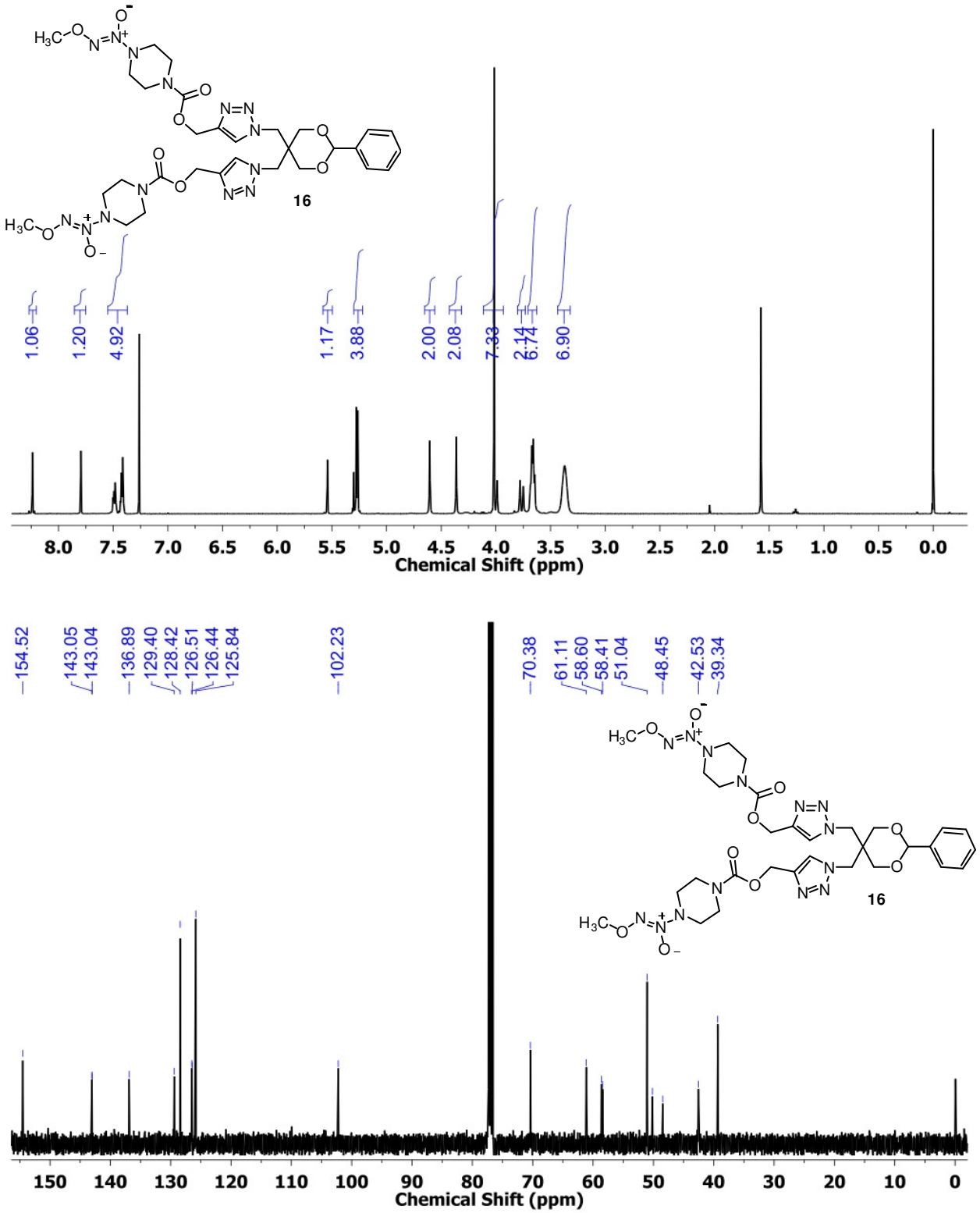

Figure S6. ^{1}H NMR and ^{13}C NMR spectra of compound **16**.

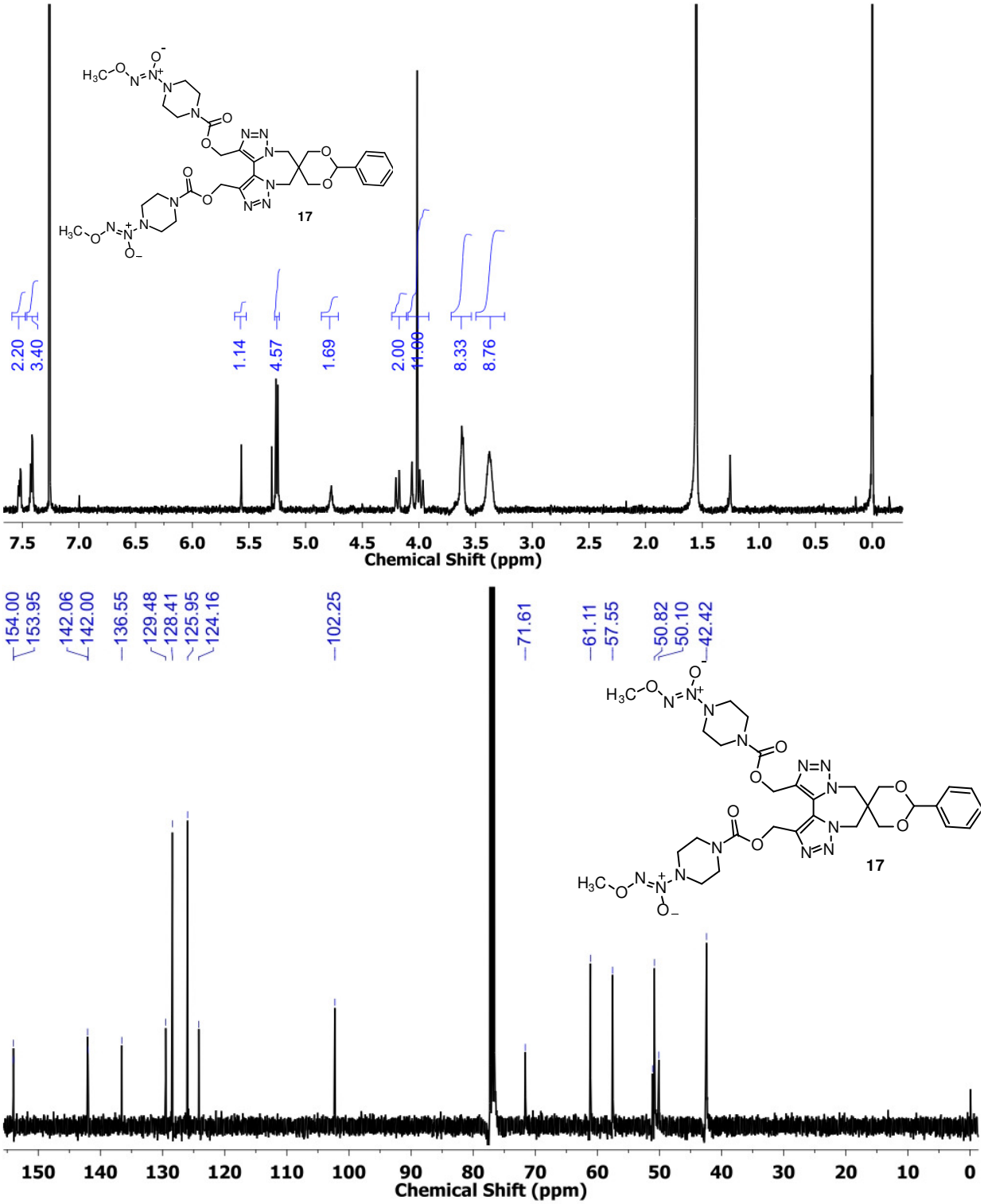

Figure S7. ^{1}H NMR and ^{13}C NMR spectra of compound **17**.

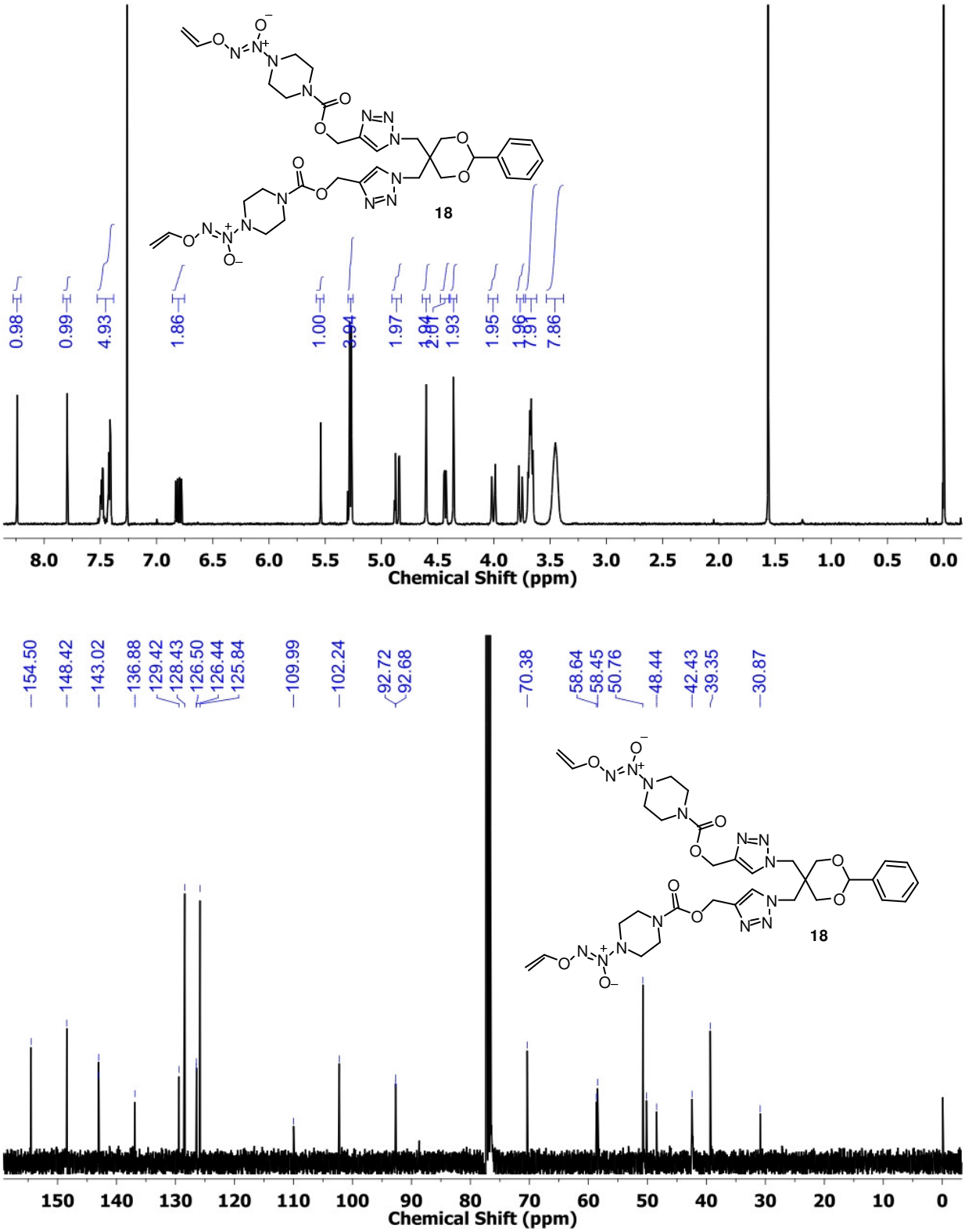

Figure S8. ^{1}H NMR and ^{13}C NMR spectra of compound **18**.

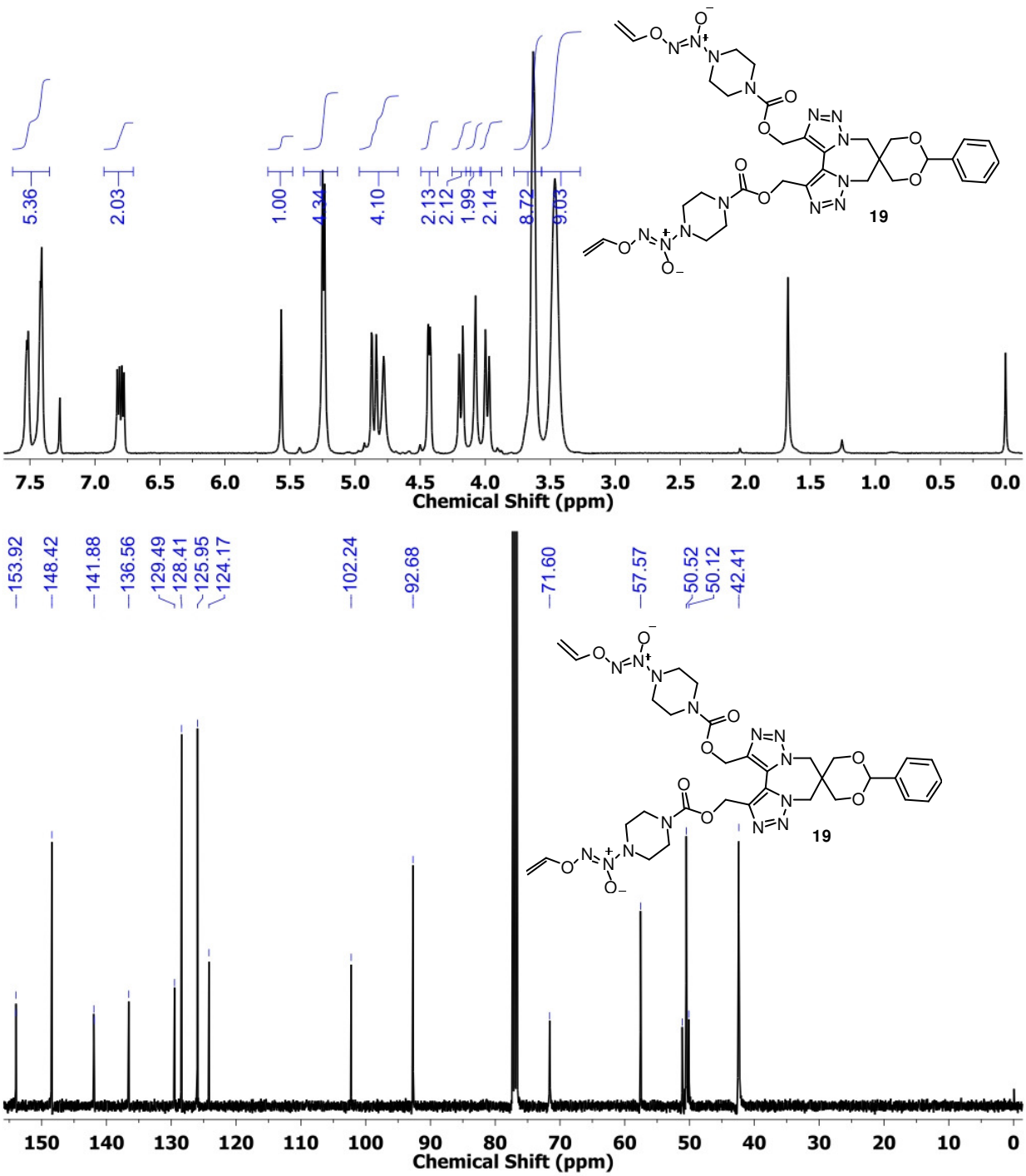

Figure S9. ^{1}H NMR and ^{13}C NMR spectra of compound **19**.

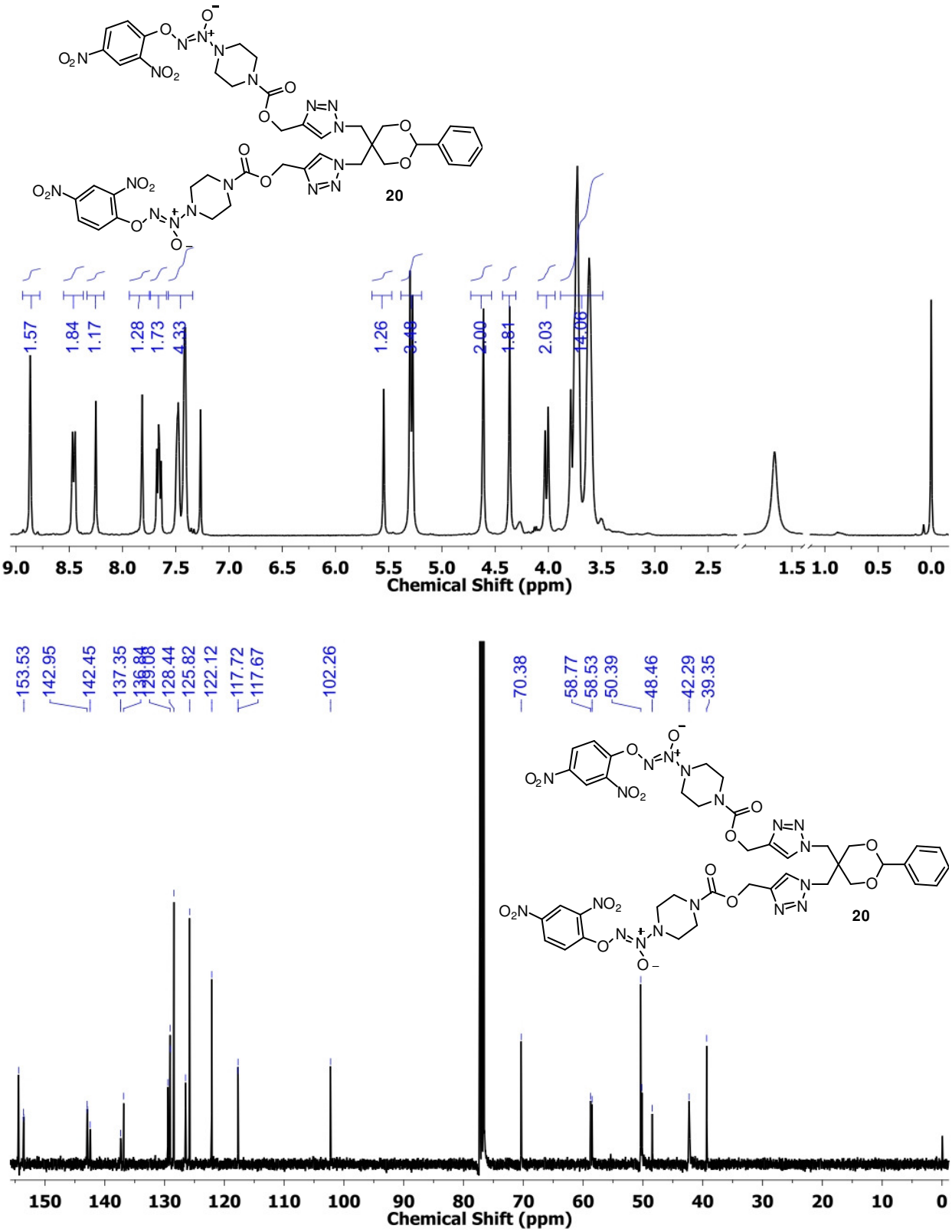

Figure S10. ^{1}H NMR and ^{13}C NMR spectra of compound **20**.

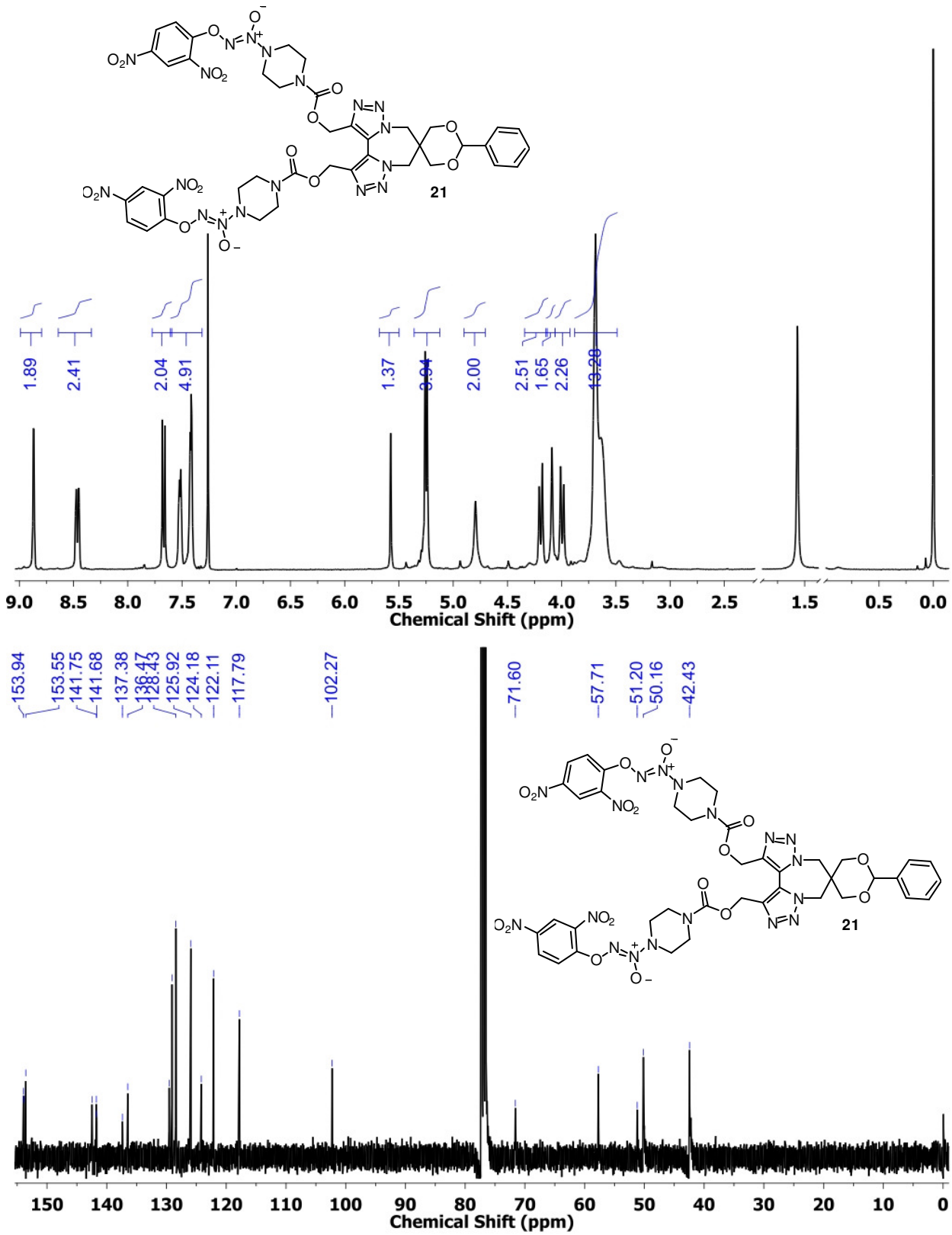

Figure S11. ^{1}H NMR and ^{13}C NMR spectra of compound **21**.

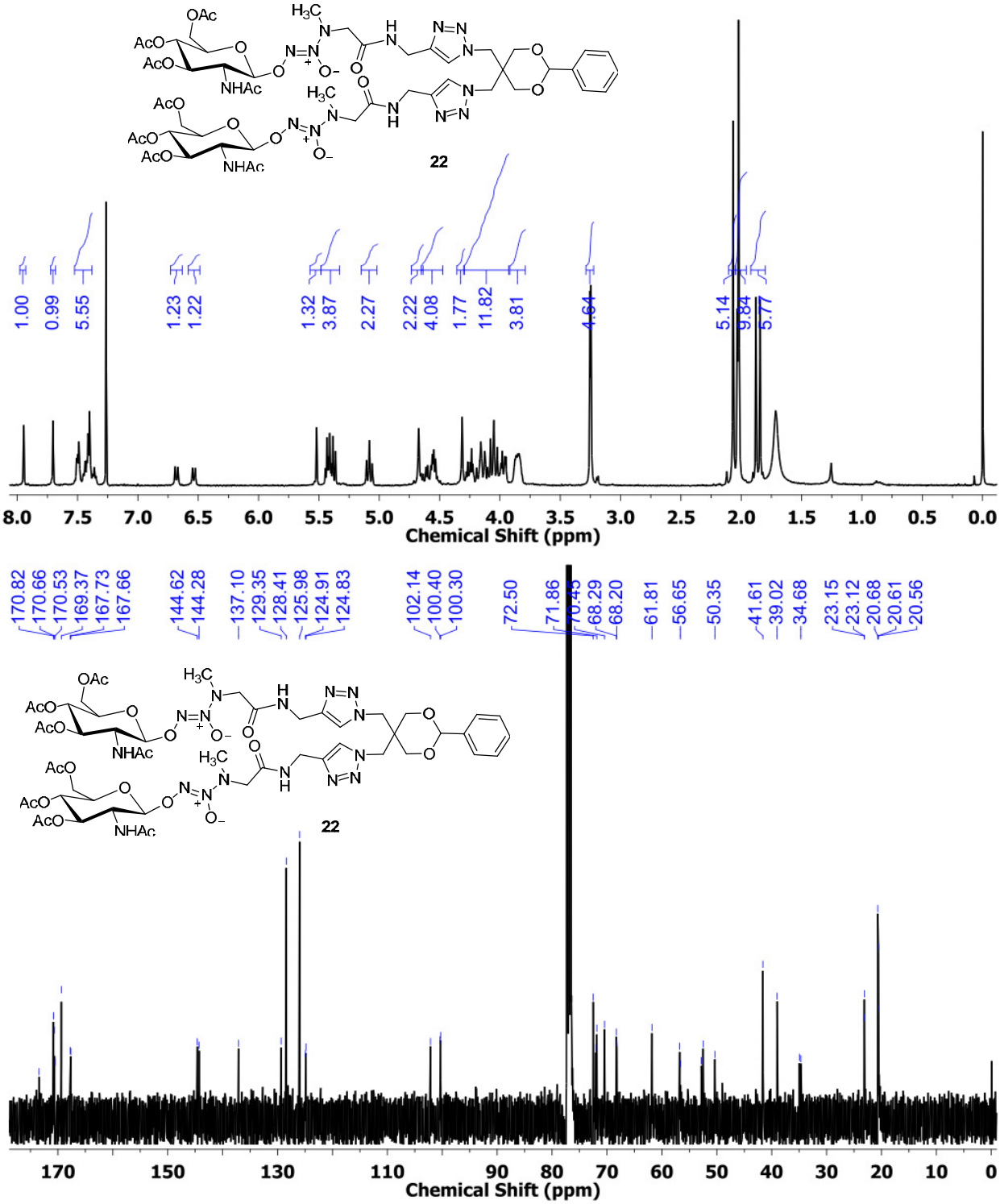

Figure S12. ^{1}H NMR and ^{13}C NMR spectra of compound **22**.

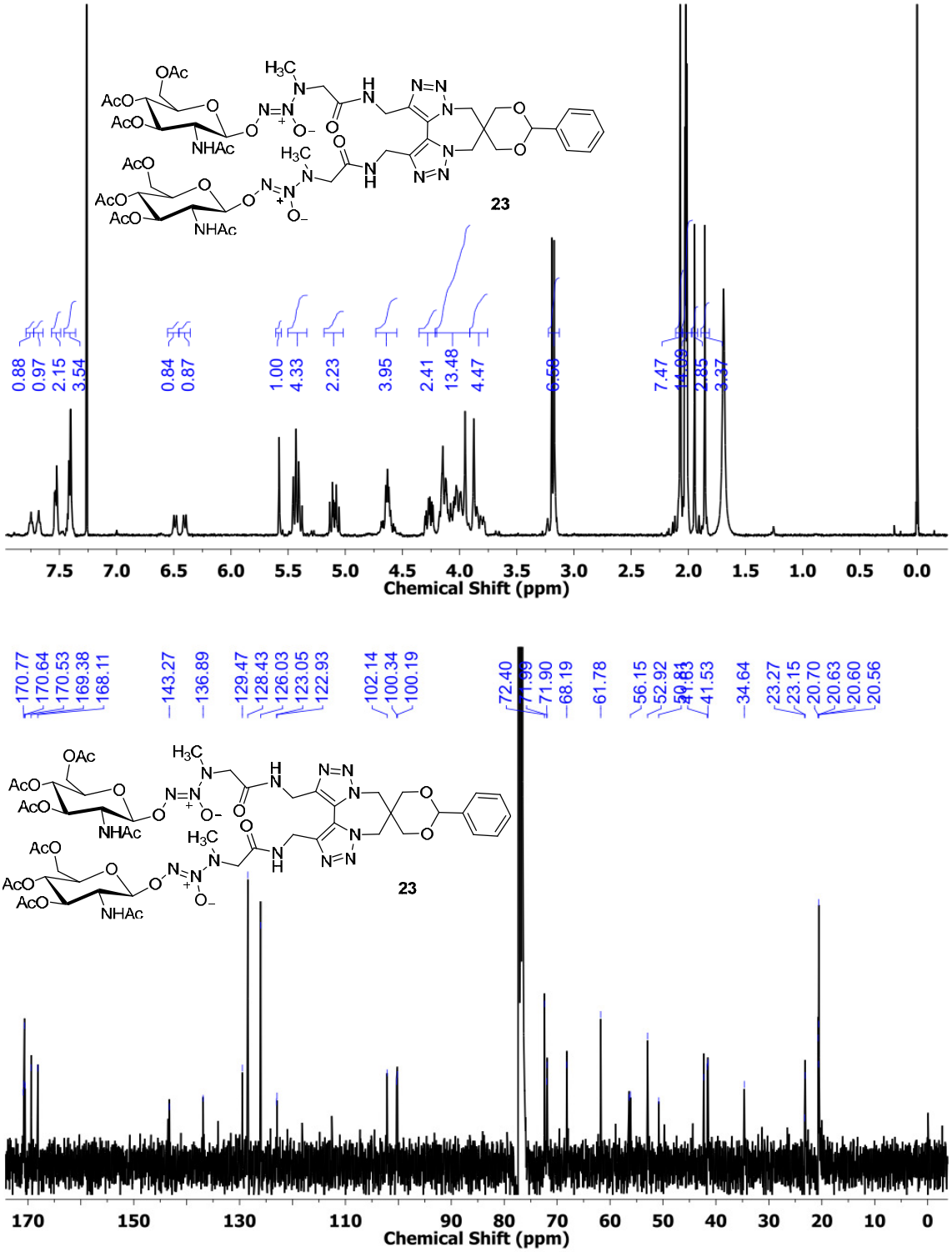

Figure S13. ^{1}H NMR and ^{13}C NMR spectra of compound **23**.

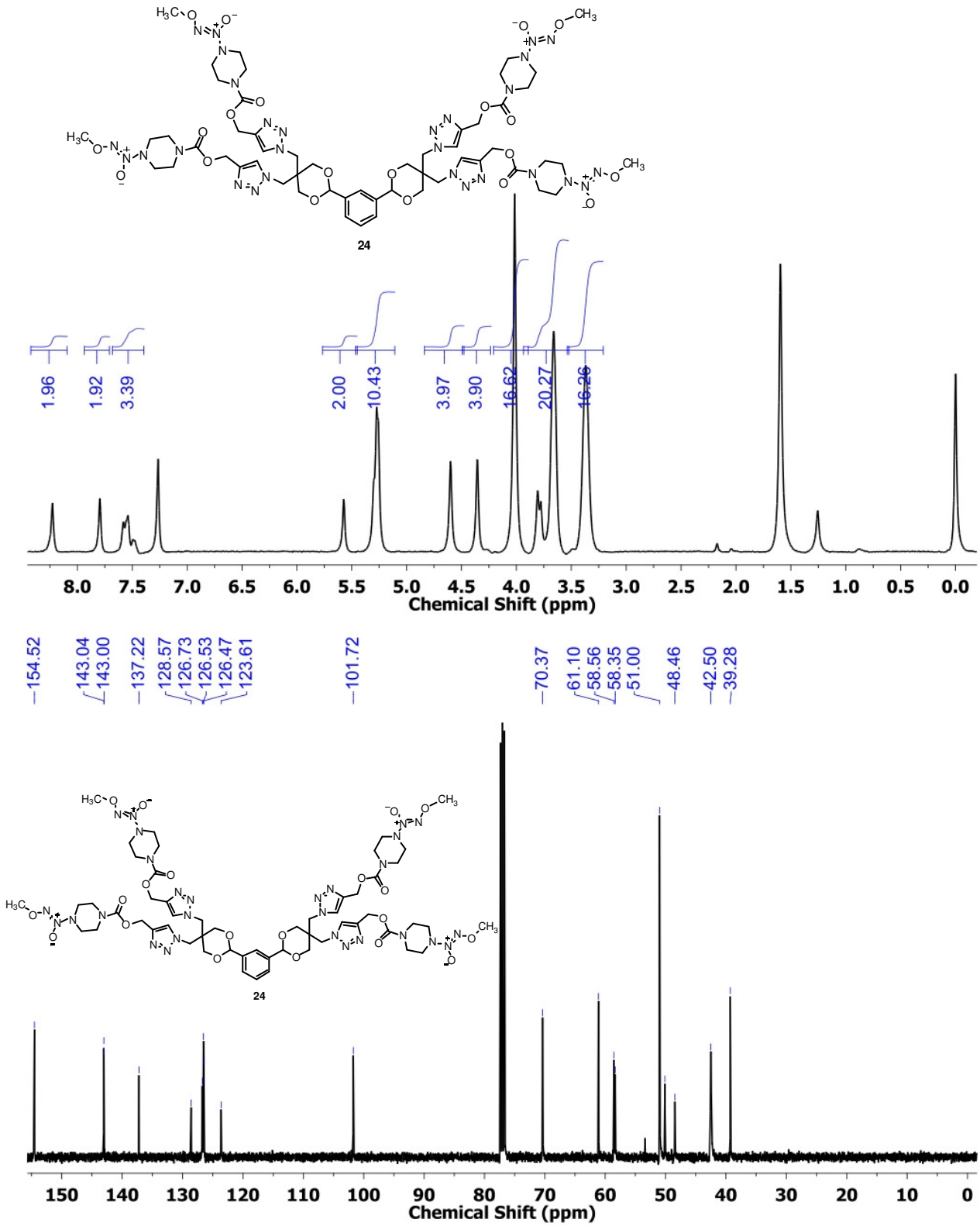

Figure S14. ^{1}H NMR and ^{13}C NMR spectra of compound **24**.

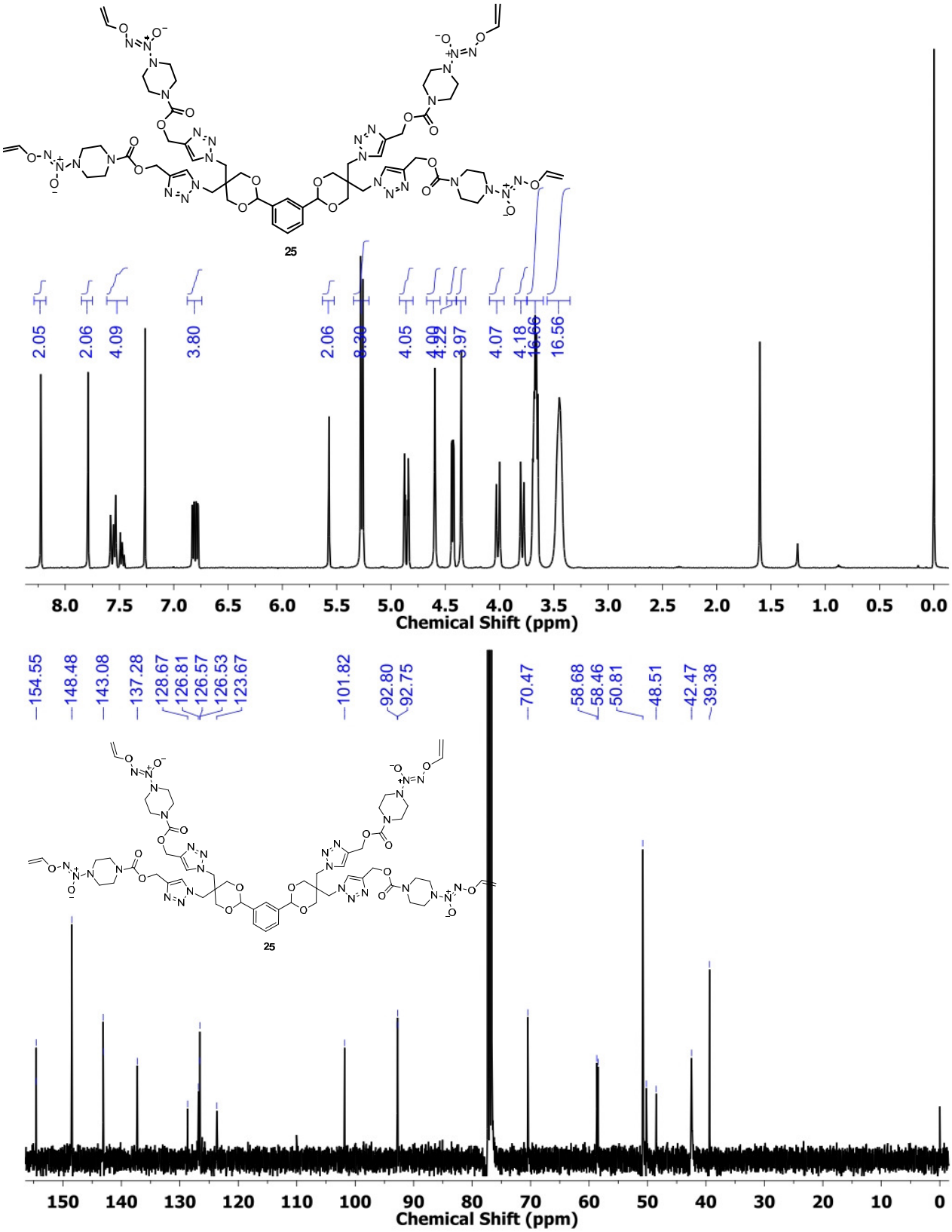

Figure S15. ^{1}H NMR and ^{13}C NMR spectra of compound **25**.

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1) Grassing, C. R.; Bitha, P.; Hlavka, J. J.; Lin, Y. I. Eur. Patent 0 231 847 A2, 1987.
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3) Saavedra, J. E.; Booth, M. N.; Hrabie, J. A.; Davies, K. M.; Keefer, L. K. *J. Org. Chem.* **1999**, *64*, 5124-5131.
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