SUPPORTING INFORMATION

Study and Application of Non-catalyzed Conjugation Reactions of Azides and Cycloocta-1,2,3-selenadiazoles

Petra Jedináková†, Peter Šebej‡,§, Tomáš Slanina‡, Petr Klán‡ and Jan Hlaváč†,*

†*Institute of Molecular and Translation Medicine, Hnevotinska 5, 779 00 Olomouc, Czech Republic.*

‡*Department of Chemistry and RECETOX, Faculty of Science, Masaryk University, Kamenice 5, 625 00 Brno, Czech Republic*

hlavac@orgchem.upol.cz

Experimental procedures

1.1. Instrumentation

LC/MS analyses were performed using UHPLC/MS with an UHPLC chromatograph Acquity with a PDA detector and a single quadrupole mass spectrometer (Waters) with an X-Select C18 column at 30 °C and a flow rate of 600 μL/min. The mobile phase consisted of (A) 0.01 mol dm^{-3} ammonium acetate in water and (B) acetonitrile; a linearly programmed gradient was used over the course of 2.5 min and then maintained the corresponding concentrations for 1.5 min. Four methods with various solvent gradients were used for the measurements (change of % of A): method 1 (from 50 to 20%), method 2 (from 80 to 20%), method 3 (from 95 to 40%), method 4 (from 100 to 50%). The column was re-equilibrated at 10% B for 1 min. The APCI ionization operated at a discharge current of 5 μA, vaporizer temperature of 350 °C and capillary temperature of 200 °C.

Purity of the compounds was determined as a ratio of the given peak area to of the total area of all peaks of the mixture.

Purification was performed using semipreparative HPLC with a Waters 1500 series HPLC instrument equipped with an Autosampler 2707, a Binary HPLC pump 1525, a Waters Photodiode Array Detector 2998 and a Waters Fraction Collector III with a YMC C18 reverse phase column, 20 × 100 mm, with 5 μm particles. The mobile phase consisted of acetonitrile and 10 mmol dm^{-3} aqueous ammonium acetate gradient over 6 min.

NMR spectra were measured in DMSO-d_6, methanol-d_4 and D_2O using a Jeol ECX-500 (500 MHz) spectrometer and a Bruker Avance 300 MHz instrument, with operating frequencies of 300.13 MHz for ^{1}H, 75.48 MHz for ^{13}C and 282.42 MHz for ^{19}F equipped with a BBFO probe with *z*-gradients and a Bruker Avance 500 MHz instrument with operating frequencies of 500.13 MHz for ^{1}H, 125.77 MHz for ^{13}C and 470.53 MHz for ^{19}F equipped with BBFO probe with *z*-gradients. The chemical shifts (δ) are reported in parts per million (ppm), and coupling constants

(*J*) are reported in Hertz (Hz). Acetate salts exhibited a singlet at 1.7–1.9 ppm in the ^{1}H NMR spectrum and two resonances at 173 and 23 ppm in ^{13}C NMR spectrum.

HRMS analysis was performed using an Orbitrap Elite high-resolution mass spectrometer (Thermo Fischer Scientific, MA, USA) operating at a positive full scan mode (120 000 FWMH) in the range of 200–900 m/z. The settings for electrospray ionization were as follows: oven temperature of 300 °C, sheath gas of 8 arb. units and a voltage source of 1.5 kV. The acquired data were internally calibrated with diisooctyl phthalate in methanol (m/z 391.2843). Samples were diluted to a final concentration of 20 μmol L^{-1} with 0.1% formic acid in water and methanol (50:50, v/v). The samples were injected by direct infusion into the mass spectrometer.

The MALDI/TOF spectra were recorded on Bruker Ultraflextreme MALDI-TOF instrument using sinapinic acid matrix prepared according to published procedure.[1] Samples were mixed with sinapinic acid solution in 1:1 ratio, spotted on MALDI target (Bruker Anchorchip) and analyzed in the range of 30-210 kDa, and the detector voltage of 2855 V. From each spot, 2000 representative shots were collected. The mass spectra were exported to text files, normalized using Microsoft Excel and visualized with mMass 5.5.0.[2]

The mass spectra were recorded on a GC-coupled (with a 60 m J&W DB-5MS (ID 0.25 mm, film 0.25 μm) column) HP 6890/5972 mass spectrometer in a positive mode with EI (70 eV) detector. The UV-vis spectra were obtained with matched 1.0 cm quartz cells on an Agilent 8453 diode-array spectrophotometer against air as a background reference.

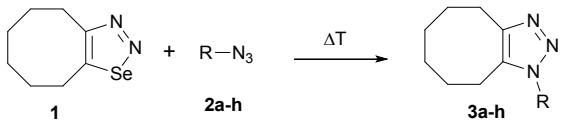
The UV/VIS spectra were obtained from PDA detector during UHPLC/PDA/MS analysis.

The solid-phase syntheses were performed in plastic reaction vessels (syringes equipped with one porous disk each) using a manually operated synthesizer.[3] The volume of the wash solvent was 10 mL per gram of the resin. For washing, the resin slurry was shaken with fresh solvent for at least 1 min before the solvent was replaced. The yields of the crude products were calculated with respect to the loading of the first building block.

1.2. Experimental procedures for synthesis of individual compounds

1.2.1. Synthesis of triazoles 3a-h via thermal heating

Derivatives **3a-3h** were synthesized according to the following scheme:



General procedure:

Corresponding azide **2** (50 mg) was dissolved in DMSO (4 mL) and cycloocta-1,2,3-selenadiazole **1** (1.5 equivalent) was added. The reaction mixture was stirred at 110 °C overnight. DMSO was removed using a freeze dryer. Resultant solid was suspended in methanol, insoluble selenium was filtered off and crude product as methanolic solution was purified using semipreparative HPLC. Solvents were removed using a freeze dryer and all products were obtained as white or yellowish amorphous solid.

1-Phenyl-4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazole (3a)

Derivative **3a** was prepared from cyclooctaselenadiazole **1**[4] and azide **2a**.[5]

Crude product was purified using semipreparative HPLC. The mobile phase consisted of (A) 0.01 mol dm^{-3} ammonium acetate in water and (B) acetonitrile, with B linearly programmed to shift from 40% to 70% over the course of 6 min. White solid, 24 mg (26%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 1.42–1.51 (m, 4 H), 1.64–1.77 (m, 4 H), 2.68–2.76 (m, 2 H), 2.84–2.90 (m, 2 H), 7.49–7.53 (m, 2 H), 7.55–7.63 (m, 3 H); ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ ppm 21.39, 23.74, 24.52, 25.27, 26.48, 27.95, 125.21, 129.36, 129.57, 133.96, 136.27, 143.92. HRMS m/z calculated for $C_{14}H_{18}N_3$ $[M+H]^+$ 228.1495, found 228.1496.

1-(4-Methoxyphenyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazole (3b)

Derivative **3a** was prepared from cyclooctaselenadiazole **1**[4] and azide **2b**.[5]

Crude product was purified using semipreparative HPLC. The mobile phase consisted of (A) 0.01 mol dm^{-3} ammonium acetate in water and (B) acetonitrile, with B linearly programmed to shift from 40% to 70% over the course of 6 min. White solid, 49 mg (48%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 1.42–1.49 (m, 4 H), 1.65–1.73 (m, 4 H), 2.65–2.69 (m, 2 H), 2.83–2.88 (m, 2 H), 3.84 (s, 3 H), 7.10–7.15 (m, 2 H), 7.40–7.43 (m, 2 H); ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ ppm 21.35, 23.77, 24.52, 25.27, 26.46, 27.96, 55.52, 114.58, 126.74, 129.12, 134.07, 143.58, 159.73. HRMS m/z calculated for $C_{15}H_{20}N_3O$ $[M+H]^+$ 258.1601, found 258.1602.

1-(4-Nitrophenyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazole (3c)

Derivative **3a** was prepared from cyclooctaselenadiazole **1**[4] and azide **2c**.[5]

Crude product was purified using semipreparative HPLC. The mobile phase consisted of (A) 0.01 mol dm^{-3} ammonium acetate in water and (B) acetonitrile, with B linearly programmed to shift from 40% to 70% over the course of 6 min. Yellow solid, 43 mg (52%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 1.44–1.52 (m, 4 H), 1.68–1.79 (m, 4 H), 2.80–2.84 (m, 2 H), 2.87–2.92 (m, 2 H), 7.85–7.89 (m, 2 H), 8.41–8.46 (m, 2 H); ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ ppm 21.49, 23.71, 24.37, 25.33, 26.32, 27.91, 125.06, 125.91, 134.36, 141.08, 144.76, 147.34. HRMS m/z calculated for $C_{14}H_{17}N_4O_2$ $[M+H]^+$ 273.1346, found 273.1347.

3-(4,5,6,7,8,9-Hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-2*H*-chromen-2-one (3d)

Derivative **3a** was prepared from cyclooctaselenadiazole **1**[4] and azide **2d**.[6]

Crude product was purified using semipreparative HPLC. The mobile phase consisted of (A) 0.01 mol dm^{-3} ammonium acetate in water and (B) acetonitrile, with B linearly programmed to shift from 40% to 70% over the course of 6 min. Yellow solid, 13 mg (17%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 1.42–1.52 (m, 4 H), 1.72 (dq, J = 12.06, 6.10 Hz, 4 H), 2.75 (t, J = 6.30 Hz, 2 H), 2.88 (t, J = 6.30 Hz, 2 H), 7.46–7.51 (m, 1 H), 7.56 (d, J = 8.30 Hz, 1 H), 7.75–7.80 (m, 1 H), 7.87 (dd, J = 7.70, 1.40 Hz, 1 H), 8.56 (s, 1 H); ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ ppm 20.97, 23.55, 24.39, 25.35, 25.77, 27.64, 116.48, 118.08, 122.57, 125.26,

129.67, 133.60, 135.85, 142.37, 143.44, 153.35, 156.89. HRMS m/z calculated for $C_{17}H_{18}N_3O_2$ $[M+H]^+$ 296.1394, found 296.1393.

1-Benzyl-4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazole (3e)

Derivative **3a** was prepared from cyclooctaselenadiazole **1**[4] and azide **2e**.[7]

Crude product was purified using semipreparative HPLC. The mobile phase consisted of (A) 0.01 mol dm^{-3} ammonium acetate in water and (B) acetonitrile, with B linearly programmed to shift from 40% to 70% over the course of 6 min. White solid, 47 mg (49%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 1.27–1.34 (m, 4 H), 1.41–1.47 (m, 2 H), 1.59–1.64 (m, 2 H), 2.67–2.70 (m, 2 H), 2.76–2.79 (m, 2 H), 5.52 (s, 2 H), 7.13–7.16 (m, 2 H), 7.27–7.31 (m, 1 H), 7.33–7.37 (m, 2 H); ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ ppm 20.67, 23.84, 24.30, 25.38, 25.52, 28.11, 50.44, 126.98, 127.74, 128.66, 133.14, 136.34, 143.95. HRMS m/z calculated for $C_{15}H_{20}N_3$ $[M+H]^+$ 242.1652, found 242.1653.

1-((2*R*,3*R*,4*S*,5*R*)-5-((4,5,6,7,8,9-Hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)methyl)-3,4-dihydroxytetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (3f)

Derivative **3a** was prepared from cyclooctaselenadiazole **1**[4] and azide **2f**.[8]

Crude product was purified using semipreparative HPLC. The mobile phase consisted of (A) 0.01 mol dm^{-3} ammonium acetate in water and (B) acetonitrile, with B linearly programmed to shift from 20% to 50% over the course of 6 min. White solid, 40 mg (57%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 1.29–1.39 (m, 4 H), 1.61 (quint, J = 5.70 Hz, 2 H), 1.64–1.70 (m, 2 H), 1.76 (d, J = 1.15 Hz, 3 H), 2.72–2.79 (m, 4 H), 4.03–4.11 (m, 3 H), 4.49 (dd, J = 14.70, 6.30 Hz, 1 H), 4.60 (dd, J = 14.70, 4.20 Hz, 1 H), 5.74 (d, J = 4.87 Hz, 1 H), 7.20 (d, J = 1.15 Hz, 1 H); ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ ppm 11.95, 20.75, 23.87, 24.31, 25.47, 25.85, 28.09, 48.33, 70.46, 71.81, 81.79, 88.42, 109.76, 134.20, 136.38, 143.27, 150.69, 163.61. HRMS m/z calculated for $C_{18}H_{26}N_5O_5$ $[M+H]^+$ 392.1928, found 392.1926.

1-((3a*R*,4*R*,6*R*,6a*R*)-6-((4,5,6,7,8,9-Hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)methyl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (3g)

Derivative **3a** was prepared from cyclooctaselenadiazole **1**[4] and azide **2g**.[8]

Crude product was purified using semipreparative HPLC. The mobile phase consisted of (A) 0.01 mol dm^{-3} ammonium acetate in water and (B) acetonitrile, with B linearly programmed to shift from 30% to 60% over the course of 6 min. White solid, 31 mg (48%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 1.28–1.30 (m, 3 H), 1.31–1.36 (m, 4 H), 1.47 (s, 3 H), 1.56–1.64 (m, 4 H), 1.75 (d, J = 1.15 Hz, 3 H), 2.66 (q, J = 5.60 Hz, 2 H), 2.75 (td, J = 6.50, 2.60 Hz, 2 H), 4.28–4.32 (m, 1 H), 4.50 (dd, J = 14.30, 7.70 Hz, 1 H), 4.62 (dd, J = 14.30, 4.30 Hz, 1 H), 4.93 (dd, J = 6.59, 4.30 Hz, 1 H), 5.10 (dd, J = 6.44, 1.86 Hz, 1 H), 5.74 (d, J = 1.72 Hz, 1 H), 7.46 (d, J = 1.15 Hz, 1 H), 11.49 (s, 1 H); ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ ppm 11.85, 20.70, 23.77, 24.22, 25.12, 25.45, 25.85, 26.86, 28.09, 48.49, 81.20, 83.49, 85.55, 92.66, 109.61, 113.44, 133.96, 138.93, 143.21, 150.40, 163.81. HRMS m/z calculated for $C_{21}H_{30}N_5O_5$ $[M+H]^+$ 432.2241, found 432.2240.

(2*R*,3*R*,4*R*,5*R*)-2-((Benzoyloxy)methyl)-5-(5-((4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)methyl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)tetrahydrofuran-3,4-diyl dibenzoate (3h)

Derivative **3a** was prepared from cyclooctaselenadiazole **1**[4] and azide **2h**.[8]

Crude product was purified using semipreparative HPLC. The mobile phase consisted of (A) 0.01 mol dm^{-3} ammonium acetate in water and (B) acetonitrile, with B linearly programmed to shift from 50% to 80% over the course of 6 min. White solid, 25 mg (43%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 1.29–1.42 (m, 4 H), 1.55–1.62 (m, 2 H), 1.67–1.75 (m, 2 H), 2.75 (t, J = 6.40 Hz, 2 H), 2.82 (t, J = 6.20 Hz, 2 H), 4.63 (dd, J = 12.10, 5.70 Hz, 1 H), 4.70 (dd, J = 12.10, 3.70 Hz, 1 H), 4.75 (td, J = 5.73, 4.12 Hz, 1 H), 4.94 (d, J = 15.00 Hz, 1 H), 5.01 (d, J = 15.00 Hz, 1 H), 5.93 (t, J = 6.40 Hz, 1 H), 5.95–5.99 (m, 1 H), 6.20 (d, J = 3.97 Hz, 1 H),

7.41–7.47 (m, 4 H), 7.49 (t, J = 7.88 Hz, 2 H), 7.62–7.67 (m, 3 H), 7.86–7.91 (m, 4 H), 7.99–8.02 (m, 3 H), 11.74 (br s, 1 H); $^{13}C\{^{1}H\}$ NMR (126 MHz, DMSO-d_6) δ ppm 20.81, 23.91, 24.12, 25.44, 25.69, 28.16, 43.24, 63.63, 70.41, 73.20, 78.72, 89.91, 109.14, 128.43, 128.51, 128.68, 128.71, 128.72, 129.20, 129.30, 129.31, 129.33, 133.40, 133.47, 133.82, 133.93, 141.97, 143.22, 149.96, 162.28, 164.59, 164.61, 165.46.

1.2.2. Study of photochemical reaction of cyclooctaselenadiazole 1 and azide 2

1.2.2.1. Reaction with UV/VIS and GC/MS monitoring

A solution of selenadiazole **1** (1.8×10^{-3} mmol, 0.38 mg) and benzyl azide **2e** (1.8×10^{-3} mmol, 0.24 mg) in methanol (3 mL) was irradiated of using light from a medium-pressure mercury arc filtered through a 313 nm filter (λ_{irr} = 313.5 ± 1.5 nm). The reaction was monitored with time (before the irradiation started and then after 5, 10, 20, 30, 50, 70, 90, 150 min and after 16 h) using UV/VIS spectrophotometer. GC/MS analysis of the reaction mixture was performed after 16 hours of irradiation.

1.2.2.2. Reaction with NMR monitoring

^{1}H NMR of a solution of selenadiazole **1** (0.018 mmol, 3.8 mg) and benzyl azide **2e** (0.018 mmol, 2.4 mg) in methanol-d_4 (0.6 mL) was measured and the reaction mixture was then irradiated using light from a medium-pressure mercury arc (Figure S2) effectively filtered through the Pyrex glass of the NMR tube (transparent at λ > 280 nm, Figure S3) for 2 hours. After irradiation, ^{1}H NMR of the reaction mixture was measured again.

1.2.2.3 Determination of reactive excited state multiplicity

Oxygenated (bubbled with oxygen for 10 min), aerated (bubbled with air for 10 min) and degassed (bubbled with dry nitrogen for 10 min) solutions of selenadiazole **1** (c = 3.1 × 10^{-3} mmol, 0.67 mg), benzyl azide **2e** (c = 3.1 × 10^{-3} mmol, 0.4 mg) and TMS as internal standard in methanol-d_4 (0.7 mL) were irradiated of using light from a medium-pressure mercury arc filtered through the Pyrex glass of the NMR tube (Figures S2 and S3). The reaction was monitored with time using ^{1}H NMR (before the irradiation started and then after 5, 10, 20, 30, 50, 70 min and after 16 h keeping in dark).

The decrease in concentration of selenadiazole **1** with time as a function of concentration of oxygen determined by ^{1}H NMR is summarized in Table S1 for comparison.

Table S1: Decrease in concentration of cycloocta-1,2,3-selenadiazole **1** after irradiation with different concentration of oxygen.

	CONCENTRATION OF SELENADIAZOLE 1 (× 10^{-3} mol dm^{-3})		
REACTION TIME	**OXYGEN**	**AIR**	**DEGASS**
Before irradiation	4.4	4.4	4.4
5 min	3.5	3.1	3.3
10 min	3.4	2.7	3.0
20 min	2.6	2.1	2.0
30 min	2.2	2.1	1.9
50 min	1.9	1.4	0.8
70 min	1.6	1.3	0.66
After 16 h keeping in dark	1.4	1.3	0.81

1.2.2.4 Reactions with sensitizer

^{1}H NMR of a solution of selenadiazole **1** (0.018 mmol, 4 mg), benzyl azide **2e** (0.018 mmol, 2.4 mg) and benzophenone (1, 10 or 50 equivalent) in methanol-d_4 (0.6 mL) was measured and the reaction mixture was then irradiated using light from a medium-pressure mercury arc (Figure S2)

effectively filtered through a 365 ± 15 nm filter. The output consists of only λ_{irr} = 366 ± 1 nm. The reaction was monitored after 2 hours and 16 hours of irradiation.

Reaction with sensitizer – effect of oxygen

Oxygenated (bubbled with oxygen for 10 min) and degassed (bubbled with nitogen for 10 min) solutions of selenadiazole **1** (0.018 mmol, 4 mg), benzyl azide **2e** (0.018 mmol, 2.4 mg) and benzophenone (10 equivalent) in methanol-d_4 (0.7 mL) were irradiated of using light from a medium-pressure mercury arc (Figure S2) filtered through a 365 ± 15 nm filter. The reaction was monitored using ^{1}H NMR after 2 hours and 16 hours of irradiation.

1.2.3. Photochemical transformation of cycloocta-1,2,3-selenadiazole 1

^{1}H NMR of a solution of selenadiazole **1** (0.024 mmol, 5.2 mg) in methanol-d_4 (0.6 mL) was measured and the solution was irradiated using light from a medium-pressure mercury arc (Figure S2) effectively filtered through the Pyrex glass of the NMR tube (transparent at λ > 280 nm, Figure S3) for 1 hour. After irradiation, ^{1}H and ^{13}C NMR spectra of the reaction mixture were measured again.

1.2.4. Synthesis of triazoles 3a-d and 3f- 3h via photochemical reaction

1.2.4.1. Irradiation of mixture of derivative 1 and azide 2 (Method I)

General procedure: ^{1}H NMR spectrum of a solution of equimolar amounts of selenadiazole **1** and azide (**2a-d** and **2f-2h**) in methanol-d_4 (c = 0.03 mol dm^{-3}) was measured and the was then irradiated using light from a medium-pressure mercury arc (Figure S2) effectively filtered through a Pyrex glass of the NMR tube (transparent at λ > 280 nm, Figure S3) for 1 hour. After irradiation, ^{1}H NMR of reaction mixture was measured again. The reaction mixture was then kept in dark and ^{1}H NMR spectra were measured after 2 and 16 hours of standing.

1.2.4.2. Irradiation of derivative 1 followed by addition of azide 2 (Method II)

General procedure: A solution of selenadiazole **1** in methanol-d_4 (c = 0.03 mol dm^{-3}) in NMR tube was irradiated using light from a medium-pressure mercury arc (Figure S2) effectively filtered through a Pyrex glass of the NMR tube (transparent at $\lambda > 280$ nm, Figure S3) for 1 hour. After irradiation, equimolar amount of azide (**2a-d, 2f** and **2h**) was added to reaction mixture and ^{1}H NMR of the reaction mixture was measured. The reaction mixture was then kept in dark and ^{1}H NMR spectra were measured again after 2 and 16 hours of standing.

The reaction conversions determined by ^{1}H NMR in the reaction mixtures following Method I and Method II are summarized in Table S2 for comparison.

Table S2: Conversions of cycloocta-1,2,3-selenadiazole **1** after irradiation with azides **2a-d**, **2f** and **2h**

	CONVERSION (%)					
	METHOD I			**METHOD II**		
Azide	**A***	**B***	**C***	**D***	**E***	**F***
2a	11	11	11	15	17	17
2b	22	24	24	17	28	28
2c	30	31	32	12	14	14
2d	6	8	8	18	23	23
2f	32	35	37	12	22	24
2g	23	28	39	-	-	-
2h	6	22	32	7	12	17

*A Conversion was measured directly after 1 h irradiation of a mixture of **1** and azide **2**

*B Conversion was measured after 1 h of irradiation of a mixture of **1** and azide **2** and subsequent 2 h keeping in dark

*C Conversion was measured after 1 h of irradiation of **1** and azide **2** and subsequent 16 h keeping in dark

*D Conversion was measured directly after 1 h of irradiation of **1** and subsequent addition of azide **2**

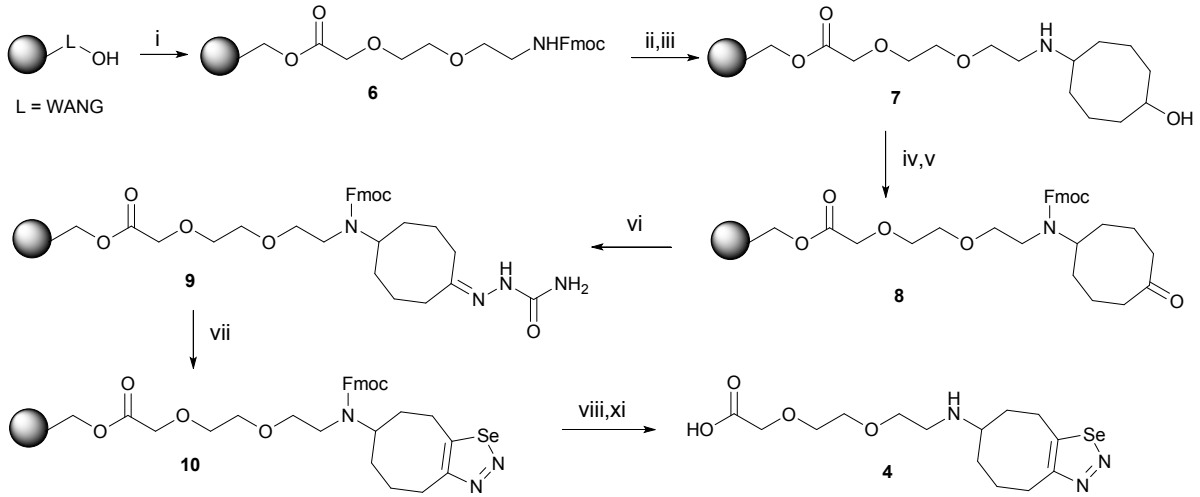
*E Conversion was measured after 1 h of irradiation of **1**, subsequent addition of azide **2** and keeping the mixture in dark for 2 h

*F Conversion was measured after 1 h of irradiation of **1**, subsequent addition of azide **2** and keeping the mixture in dark for 16h

Solid-phase synthesis of derivatives 4 and 5

2-(2-(2-((4,5,6,7,8,9-Hexahydrocycloocta[*d*][1,2,3]selenadiazol-7-yl)amino)ethoxy)ethoxy)acetic acid (4)

Derivative **4** was prepared according to the following reaction sequence:



(i) FAEEAA, HOBt, DIC, DIEA, DCM/DMF 1:1, rt, overnight; (ii) 50% piperidine/DMF, rt, 15 min; (iii) 5-hydroxycyclooctanone, 20% AcOH/DMF, rt, overnight; $NaBH(OAc)_3$, rt, 6h; (iv) Fmoc-OSu, DCM, rt, 30 min; (v) Dess-Martin periodinane, DCM, rt, 30min; (vi) Semicarbazide hydrochloride, 20% AcOH/DMF, rt, overnight; (vii) Selenium dioxide, 20% AcOH/DMF, rt, overnight; (viii) 50%TFA/DCM, rt, 1h; (xi) 20% piperidine/MeOH, rt, 30 min.

Resin 6

Wang Resin (1 g) was washed with DCM and a solution of FAEEAA (3.0 mmol, 1.16 g), HOBt (3.0 mmol, 405 mg), DIEA (0.4 mmol, 68 μL) and DIC (3.0 mmol, 464 μL) in 10 mL DCM/DMF (1:1, v/v) was added. The resin was shaken overnight, washed five times with DMF and five times with DCM. LC/MS analysis of cleaved product: MS (ESI) exact mass calcd. for $C_{21}H_{24}NO_6$ $[M+H]^+$ 386.14; found 386.36, t_R = 1.85 min, purity: 93%.

Resin 7

Resin **6** (1 g) was washed three times with DMF. A solution of 10 mL of 50% piperidine in DMF was added to the resin and the slurry was shaken for 15 minutes. The resin was washed three times with DMF, three times with DCM and three times with anhydrous DMF. A solution of 5-hydroxycylooctanone[9] (5 mmol, 710 mg) in 10 mL 20% AcOH/anhydrous DMF was added and the slurry was shaken overnight. The next day, $NaBH(OAc)_3$ (5.0 mmol, 1.1 g) was added in three portions and the syringe was punctured with a needle just below the plunger to enable hydrogen

gas evolve. The slurry was shaken for two hours after each portion. The resin was washed three times with 5% AcOH/DMF (v/v), three times with DMF, neutralized with 20% (v/v) piperidine/DMF for five minutes, washed three times with DMF and three times with DCM. For identification, Fmoc-OSu (0.5 mmol, 170 mg) in DCM (1 mL) was added to resin **7** (20 mg). The slurry was shaken for 30 min. The resin was washed three times with DCM. LC/MS analysis of cleaved product: MS (ESI) exact mass calcd. for $C_{29}H_{38}NO_7$ $[M+H]^+$ 512.26; found 512.42, t_R = 1.92 min, purity: 42%.

Resin 8

Resin **7** (1 g) was washed three times with DCM. A solution of Fmoc-OSu (5.0 mmol, 1.7 g) in DCM (10 mL) was added to the resin and the slurry was shaken for 30 minutes. The resin was washed three times with DCM. A solution of 0.2 mol dm^{-3} Dess-Martin periodinane in DCM (10 mL) was added to the resin and the slurry was shaken for 30 minutes. The resin was washed five times with DCM. LC/MS analysis of cleaved product: MS (ESI) exact mass calcd. for $C_{29}H_{36}NO_7$ $[M+H]^+$ 510.24; found 510.40, t_R = 2.04 min, purity: 40%.

Resin 9

Resin **8** (1 g) was washed three times with DMF. A solution of semicarbazide hydrochloride (5.0 mmol, 558 mg) in 20% (v/v) AcOH/DMF (10 mL) was added to the resin and the slurry was shaken overnight. The resin was washed three times with 5% (v/v) AcOH/DMF, three times with DMF and three times with DCM. LC/MS analysis of cleaved product: MS (ESI) exact mass calcd. for $C_{30}H_{39}N_4O_7$ $[M+H]^+$ 567.27; found 567.48, t_R = 1.95 min, purity: 40%.

Resin 10

Resin **9** (1 g) was washed three times with DMF. A solution of selenium dioxide (5 mmol, 550 mg) in 20% (v/v) AcOH/DMF (10 mL) was added to the resin and the slurry was shaken overnight. The resin was washed three times with 5% (v/v) AcOH/DMF, three times with DMF and three times with DCM.

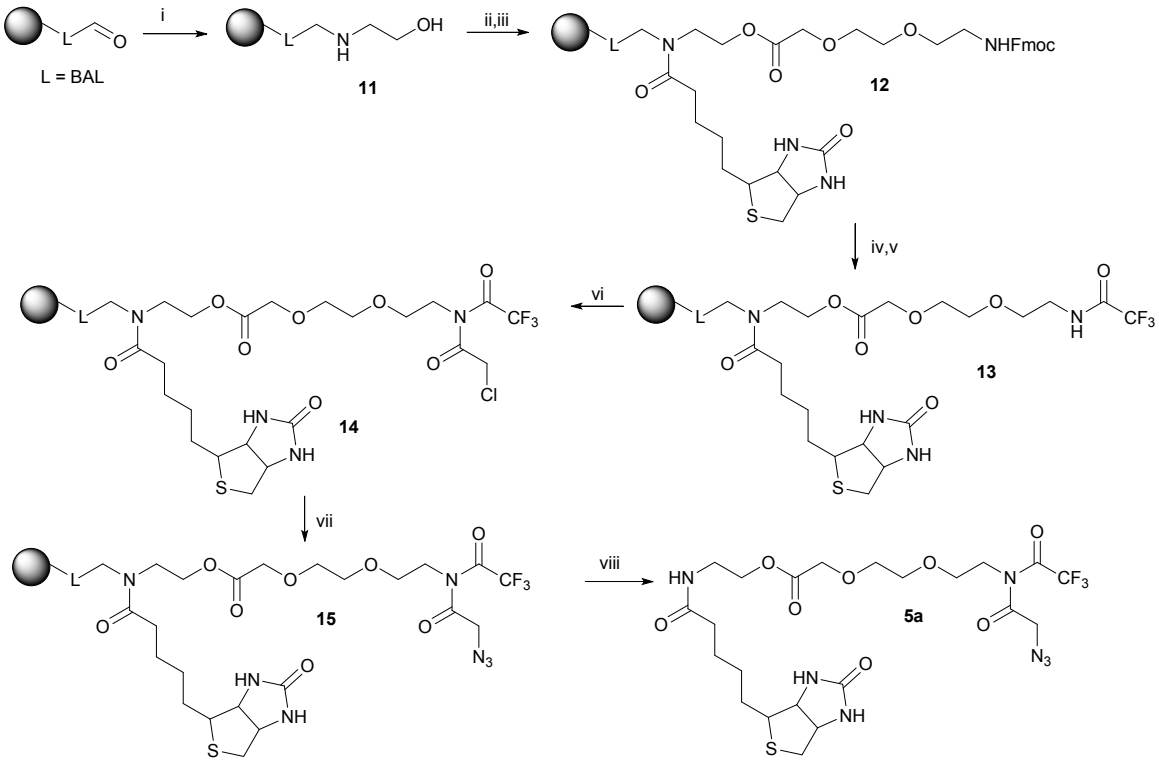
2-(2-(2-((4,5,6,7,8,9-Hexahydrocycloocta[*d*][1,2,3]selenadiazol-6-yl)amino)ethoxy)ethoxy)acetic acid (4)

Resin **10** (1 g) was treated by TFA in DCM (1:1) at room temperature for 1 hour. The cleavage cocktail was evaporated by a stream of nitrogen. 20% piperidine in methanol (5 mL) was added, solution was stirred for 30 min. Solution containing crude product was purified using semipreparative HPLC. The mobile phase consisted of (A) 0.01 mol dm^{-3} ammonium acetate in water and (B) acetonitrile, with B linearly programmed to shift from 10% to 40% over the course of 6 min. Colourless oil, 31 mg (25%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 1.33–1.42 (m, 1 H), 1.59–1.71 (m, 3 H), 1.89–1.97 (m, 1 H), 1.99–2.07 (m, 1 H), 2.31–2.37 (m, 1 H), 2.62–2.69 (m, 1 H), 2.70–2.75 (m, 1 H), 3.04–3.11 (m, 1 H), 3.16–3.25 (m, 1 H), 3.28–3.38 (m, 2 H), 3.43–3.52 (m, 6 H), 3.62 (s, 2 H), 5.27 (br s, 1 H); ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ ppm 23.18, 26.02, 27.63, 31.84, 35.35, 45.17, 56.88, 68.72, 69.13, 69.43, 70.38, 159.53, 160.78, 173.19. HRMS m/z calculated for $C_{14}H_{24}N_3O_4Se$ $[M+H]^+$ 378.0927, found 378.0926.

2-(5-(2-Oxohexahydro-1*H*-thieno[3,4-d]imidazol-4-yl)pentanamido)ethyl 2-(2-(2-(*N*-(2-azidoacetyl)-2,2,2-trifluoroacetamido)ethoxy)ethoxy)acetate (5a)

Derivative **5a** was prepared according to the following reaction sequence:



(i) aminoethanole, 20% AcOH/DMF, rt, overnight, $NaBH(OAc)_3$, rt, on; (ii) Biotin, HOBt, DIC, DMF, rt, overnight; (iii) FAEEAA, HOBt, DIC, DIEA, DCM/DMF 1:1, rt, overnight; (iv) 50% piperidine/DMF, rt, 15 min; (v) Ethyl trifluoracetate, DBU, DMF, rt, overnight; (vi) Chloroacetylchloride, pyridine, DCM, rt, 2h; (vii) Sodium azide, DMF, 80 °C, 2h; (viii) 50%TFA/DCM, rt, 1h.

Resin 11

Aminomethyl resin with BAL linker[10] (1 g) was washed three times with DCM and three times with dry DMF. A solution of 2-aminoethanol (5.0 mmol, 302 µL) in 10 mL 20% (v/v) AcOH/anhydrous DMF was added and the slurry was shaken overnight. The next day, $NaBH(OAc)_3$ (5.0 mmol, 1.1 g) was added in three portions and the syringe was punctured with a needle just below the plunger to enable hydrogen gas evolve. The slurry was shaken for two hours after each portion. The resin was washed three times with DMF, neutralized with 20% (v/v) piperidine/DMF for ten minutes, washed three times with DMF and three times with DCM. For identification, Fmoc-OSu (0.5 mmol, 170 mg) in DCM (1 mL) was added to resin 11 (20 mg). The slurry was shaken for 30 min. The resin was washed three times with DCM. LC/MS analysis of

cleaved product: MS (ESI) exact mass calcd. for $C_{17}H_{18}NO_3$ $[M+H]^+$ 284.12; found 284.47, t_R = 2.55 min, purity: 88%.

Resin 12

Resin **11** (1 g) was washed three times with DMF. Biotin (2.0 mmol, 489 mg) was dissolved in DMF (10 mL) at higher temperature (~80°C). The solution was cooled to room temperature, HOBt (2.0 mmol, 270 mg) and DIC (2.0 mmol, 310 µL) was added, the resulting solution was added to the resin and the slurry was shaken overnight. The resin was washed five times with DMF and five times with DCM. Solution of FAEEAA (3.0 mmol, 1.16 g), HOBt (3.0 mmol, 405 mg), DIEA (0.4 mmol, 68 µL) and DIC (3.0 mmol, 464 µL) in 10 mL DCM/DMF (1:1, v/v) was added. The resin was shaken overnight, washed five times with DMF and five times with DCM. LC/MS analysis of cleaved product: MS (ESI) exact mass calcd. for $C_{33}H_{43}N_4O_8S$ $[M+H]^+$ 655.27; found 655.34, t_R = 2.35 min, purity: 86%.

Resin 13

Resin **12** (1 g) was washed three times with DMF. A solution of 10 mL of 50% piperidine in DMF was added to the resin and the slurry was shaken for 15 minutes. The resin was washed five times with DMF. A solution of ETFA (1.0 mmol, 120 µL), DBU (1.2 mmol. 180 µL), in DMF (10 mL) was added. The resin was shaken overnight, washed five times with DMF and five times with DCM. LC/MS analysis of cleaved product: MS (ESI) exact mass calcd. for $C_{20}H_{32}F_3N_4O_7S$ $[M+H]^+$ 529.18; found 529.32, t_R = 3.75 min, purity: 86%.

Resin 14

Resin **13** (1 g) was washed three times with anhydrous DCM. A solution of chloracetylchloride (170 µL, 2 mmol), pyridine (320 µL, 4 mmol), in anhydrous DCM (10 mL) was added. The resin was shaken for 2 hours and washed five times with DCM. MS (ESI) exact mass calcd. for $C_{22}H_{33}ClF_3N_4O_8S$ $[M+H]^+$ 604.15; found 604.84, t_R = 4.52 min, purity: 79%.

Resin 15

Resin **14** (1 g) was washed three times with DMF. A solution of sodium azide (300 mg, 5 mmol), in DMF (10 mL) was added. The resin was shaken at 80 °C for 2 hours and washed three times with DMF and three times with DCM. MS (ESI) exact mass calcd. for $C_{22}H_{33}F_3N_7O_8S$ $[M+H]^+$ 612.20; found 611.98, t_R = 4.60 min, purity: 73%.

2-(5-(2-oxohexahydro-1*H*-thieno[3,4-d]imidazol-4-yl)pentanamido)ethyl 2-(2-(2-(*N*-(2-azidoacetyl)-2,2,2-trifluoroacetamido)ethoxy)ethoxy)acetate (5a)

Resin **15** (1 g) was treated by TFA in DCM (1:1, v/v) at room temperature for 1 hour. The cleavage cocktail was evaporated by a stream of nitrogen. Oily product was dissolved in methanol (5 mL) and purified by semipreparative HPLC with light scattering detector. The mobile phase consisted of (A) 0.01 mol dm^{-3} ammonium acetate in water and (B) acetonitrile, with B linearly programmed to shift from 35% to 50% over the course of 6 min. White solid, 57 mg (25%).

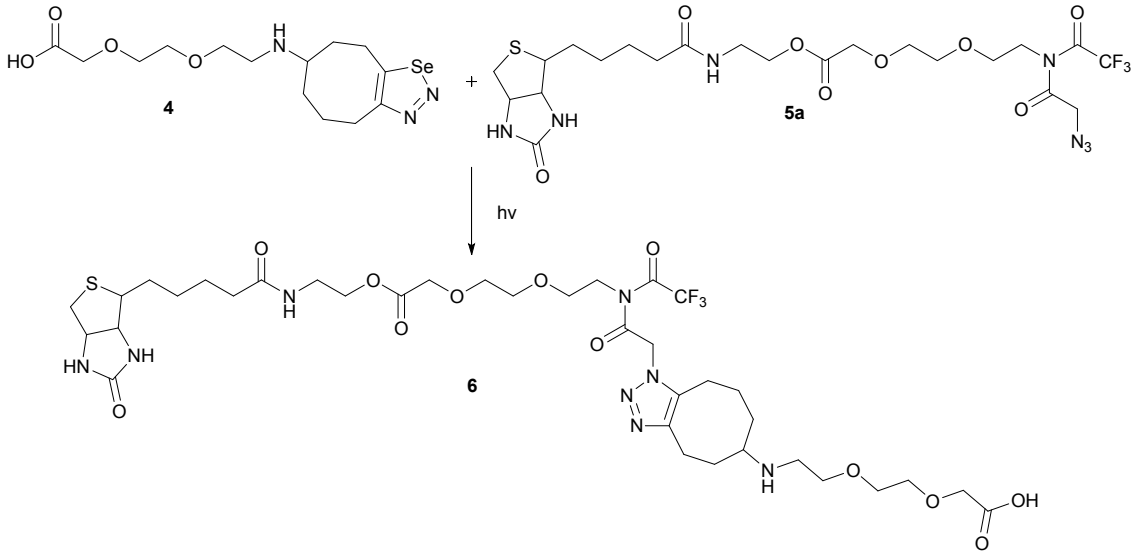
^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.25–1.39 (m, 2 H), 1.43–1.56 (m, 3 H), 1.59–1.69 (m, 1 H), 2.07 (t, J = 7.33 Hz, 2 H), 2.89 (d, J = 13.30 Hz, 1 H), 3.00 (dd, J = 13.20, 5.60 Hz, 1 H), 3.21 (ddd, J = 8.64, 6.01, 4.35 Hz, 1 H), 3.25–3.32 (m, 3 H), 3.34 (t, J = 5.72 Hz, 2 H), 3.51 (t, J = 5.80 Hz, 2 H), 3.54–3.56 (m, 2 H), 3.58–3.60 (m, 1 H), 4.07 (t, J = 5.72 Hz, 2 H), 4.11 (s, 2 H), 4.20 (dd, J = 7.67, 4.24 Hz, 1 H), 4.44 (d, J = 17.90 Hz, 1 H), 4.53 (d, J = 17.90 Hz, 1 H), 4.78–4.83 (m, 1 H), 7.92 (t, J = 5.61 Hz, 1 H), 8.02–8.08 (m, 1 H), 9.45 (br s, 1 H); ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ ppm 25.04, 27.76, 28.13, 35.02, 37.19, 37.44, 51.81, 54.60, 58.17, 61.06, 62.78, 67.55, 67.78, 69.45, 69.91, 117.33, 155.87, 156.57, 167.71, 168.65, 170.10, 172.30. HRMS m/z calculated for $C_{22}H_{33}F_3N_7O_8S$ $[M+H]^+$ 612.2058, found 612.2068.

1.3. Experimental procedures for conjugation reactions of derivative 4 and 5a resp.5b

Synthesis of 2-(2-(2-((1-(2,11,16-trioxo-20-(2-oxohexahydro-1*H*-thieno[3,4-d]imidazol-4-yl)-3-(2,2,2-trifluoroacetyl)-6,9,12-trioxa-3,15-diazaicosyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta[d][1,2,3]triazol-6-yl)amino)ethoxy)ethoxy)acetic acid (6):

1.3.1. Reaction without presence of avidin

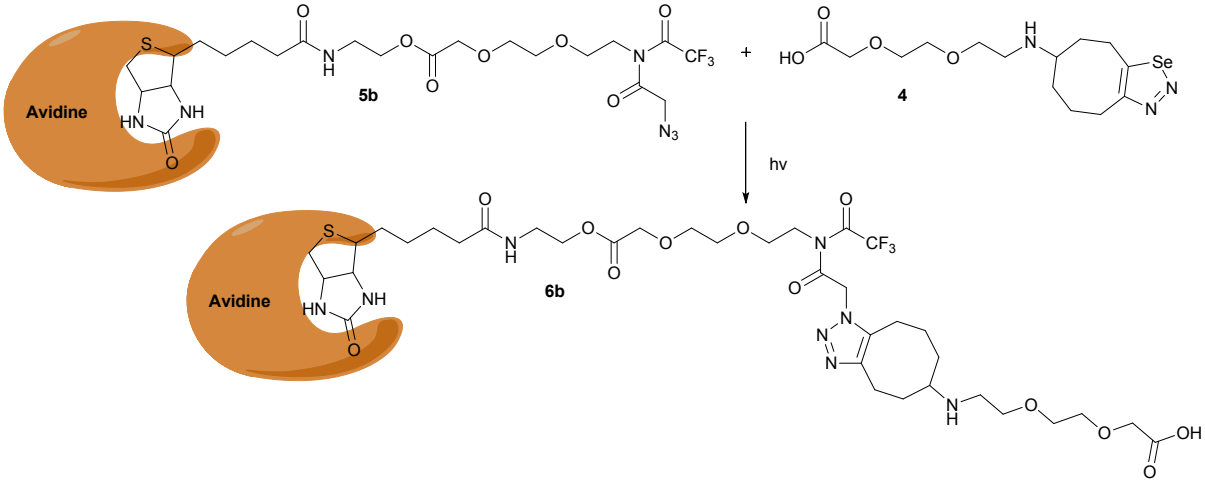
Reaction between derivatives **4** and **5a** was performed according to the following scheme to afford 2-(2-(2-((1-(2,11,16-trioxo-20-(2-oxohexahydro-1*H*-thieno[3,4-d]imidazol-4-yl)-3-(2,2,2-trifluoroacetyl)-6,9,12-trioxa-3,15-diazaicosyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta[d][1,2,3]triazol-6-yl)amino)ethoxy)ethoxy)acetic acid **(6a)**:



^{1}H and ^{19}F NMR spectra of a solution of PEG-selenadiazole **4** (0.008 mmol, 3 mg) and azide **5a** (0.008 mmol, 5 mg) in D_2O (0.6 mL) were measured and the reaction mixture was then irradiated using light from a medium-pressure mercury arc (Figure S2) effectively filtered through a Pyrex glass of the NMR tube (transparent at $\lambda > 280$ nm, Figure S3) for 1 hour. After irradiation, ^{1}H and ^{19}F NMR spectra of the reaction mixture were measured. The reaction mixture was then irradiated for another 1 hour and the ^{1}H and ^{19}F NMR spectra of the reaction mixture were measured again.

NMR: For ^{1}H NMR see Figure S49.

1.3.2. Reaction in presence of avidin



To a solution of **5a** (8 mg, 0.013 mmol) in D_2O (0.6 mL) in an NMR tube was mixed with commercially available avidin (20 mg; 65 kDa) to form conjugate **5b**. Subsequently PEG-selenadiazole **4** (5 mg, 0.013 mmol) was added. The reaction mixture was then irradiated with a medium-pressure mercury arc (Figure S2) filtered through a Pyrex glass of the NMR tube (transparent at $\lambda > 280$ nm, Figure S3) for 1 hour. After irradiation, ^{1}H and ^{19}F NMR spectra of reaction mixture were measured. The reaction mixture was then irradiated for another 1 hour and the ^{1}H and ^{19}F NMR spectra of the reaction mixture were measured again.

NMR: For ^{1}H NMR see Figure S48.

1.4. Kinetic study of a reaction between cyclooctyne and 2e

A solution of **1** (c = 23 mmol dm^{-3}) in methanol-d_4 (0.6 mL) was irradiated with a medium-pressure mercury arc (Figure S2) filtered through a Pyrex glass of the NMR tube (transparent at $\lambda > 280$ nm, Figure S3) until no starting material was observable by ^{1}H NMR (ca. 2 h). Benzylazide (**2e**, 5 μL) was then added to the reaction mixture, agitated and the following reaction was monitored by ^{1}H NMR spectroscopy. The change of the relative concentration of cyclooctyne as reactant and triazole **3e** as product (calculated from the ratio of the integrals of the characteristic peaks of cyclooctyne and **3e** against the integral of the peak of non-deuterated methanol as an impurity) was plot (Figure S1) and the data were fit with pseudo-first order kinetic equation which

allowed to calculate observed rate constant of the cyclooctyne disappearance to be $k_{obs} = 4.4 \times 10^{-3}$ s^{-1} and estimate the half-life to be $\tau_{1/2} \sim 38$ min under the experimental conditions.

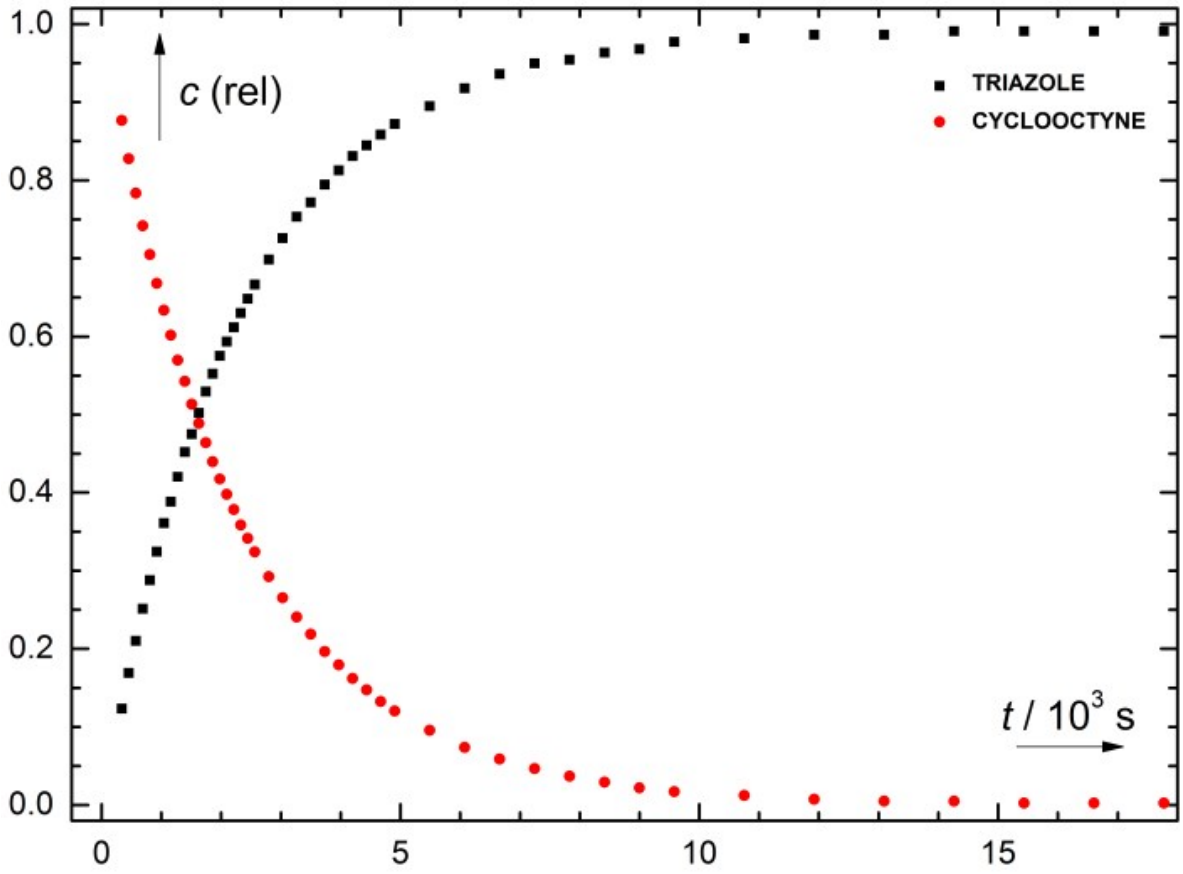


Figure S1. The kinetics of the cycloaddition reaction of cyclooctyne with benzyl azide ($c = 80 \times 10^{-3}$ mol dm^{-3}).

1.5. Determination of quantum yield of triazole 3e appearence

Samples of methanolic solution ($A \sim 1.1$ at $\lambda_{irr} = 313$ nm) of cycloocta-1,2,3-selenadiazole **1** ($c = 1.9 \times 10^{-3}$ mol.dm^{-3}) and benzylazide **2e** ($c = 6.1 \times 10^{-3}$ mol.dm^{-3}) were prepared by dilution of stock solutions and irradiated using a 40 W medium pressure mercury arc (Figure S2) equipped with a 313 nm band-pass filter ($\lambda_{em} = 313.5 \pm 1.5$ nm; Figure S27 in ref.[11]) in matched 1.000 cm quartz cells. Appearance of acetophenone ($\Phi_{app} = 0.30$) upon irradiation of valerophenone solution ($c = 1.9 \times 10^{-3}$ mol.dm^{-3}; $A \sim 0.3$ at $\lambda_{irr} = 313$ nm) was used as an actinometer.[12] All samples (both **1** and benzylazide **2e**, and valerophenone, respectively) were bubbled with dry nitrogen 10

minutes prior to irradiation and the concentration of both triazole **3e** and acetophenone was followed by gas chromatography.

Both valerophenone and cycloocta-1,2,3-selenadiazole **1** and benzylazide **2e** samples, respectively, were irradiated as at least three independently prepared samples and each sample was analyzed at least five times. Hexadecane (c = 1.1 × 10^{-3} mol.dm^{-3}) was used as an internal standard in all samples and concentrations of analytes (acetophenone and triazole **3e**) were calculated from calibration curves (all of them consists of at least five concentration points and were linear in the range c = 0.1–5.0 × 10^{-3} mol.dm^{-3} with $R^2 > 0.99$ for linear fit to data). The samples of triazole **3e** were kept at least six hours in dark after irradiation and prior to determination of concentration of triazole **3e** to allow high conversion of cyclooctyne to the triazole **3e** (six hours equals to about 10 half-lives – for more details see text above and Figure S1).

The conversion was kept below 25% for **2e** and below 10% for valerophenone to avoid the interference of photoproducts. The relative standard deviation of the mean for the acetophenone concentrations was found to be below 10%. Higher standard deviations of the mean of concentration of triazole **3e** in the samples were mainly caused by non-uniform adsorption of elementary selenium on the cuvette surfaces acting as an effective light filter in all UV and visible range of light (see Figure S21).

All stock solutions (with 10-fold higher concentration than used in the experiments) were prepared by direct weighting of the respective compounds into a volumetric flasks and filling with a solvent. The stock solutions were kept in fridge and used within a week from preparation.

Spectral data

1.6. Spectral characteristic of medium-pressure mercury arc and Pyrex glass NMR tube

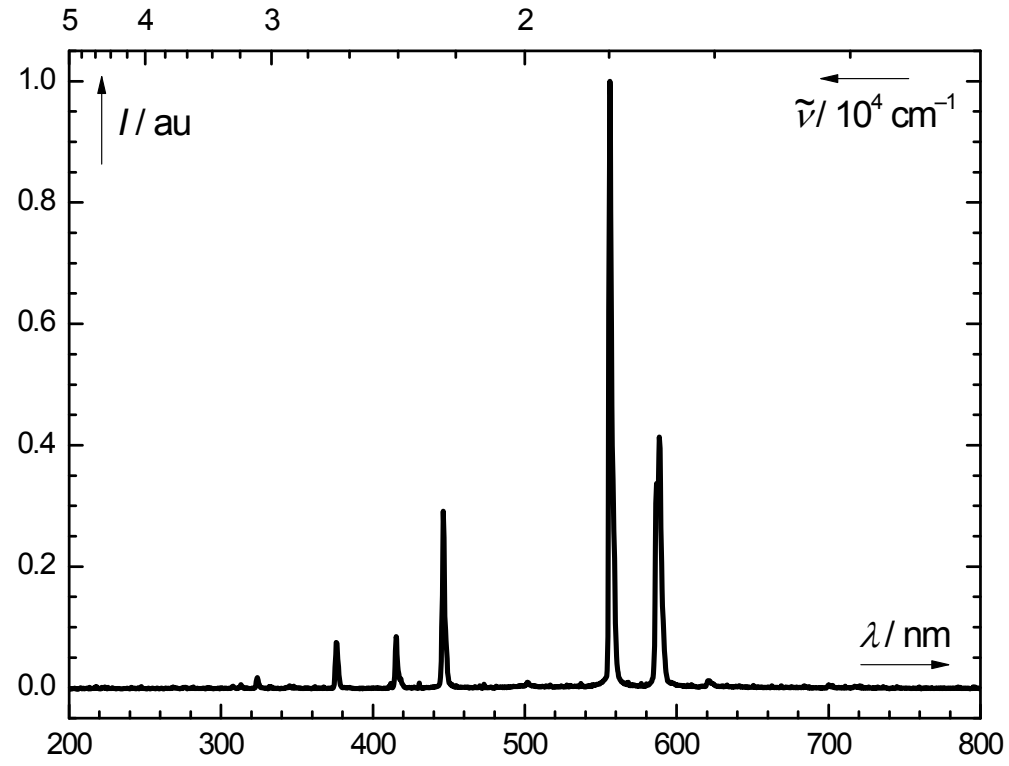


Figure S2. Normalized output spectrum of 40 W medium-pressure Hg discharged lamp.

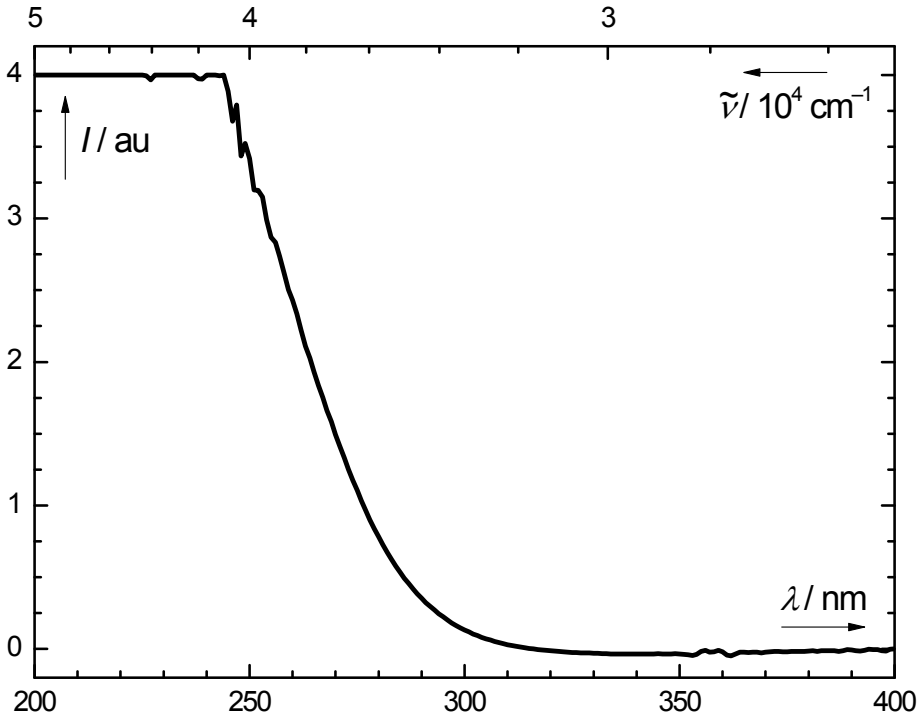


Figure S3. Absorption spectrum of a typical Pyrex glass NMR tube used in the irradiation experiments.

1.7. UV/VIS spectra of starting compounds and products

1.7.1. UV/VIS Spectra of starting compounds 1; 2a-2h

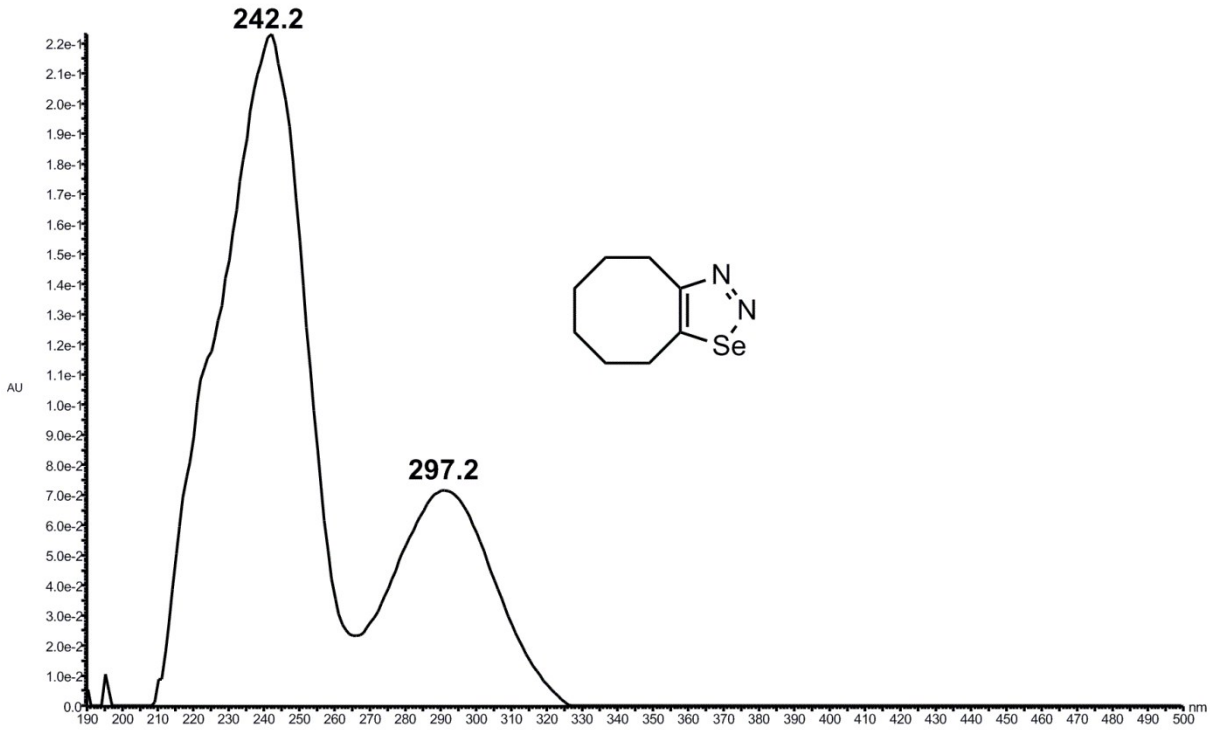


Figure S4. Absorption spectra of 1,2,3-selenadiazole **1** in methanol/H_2O 1:1 (v/v).

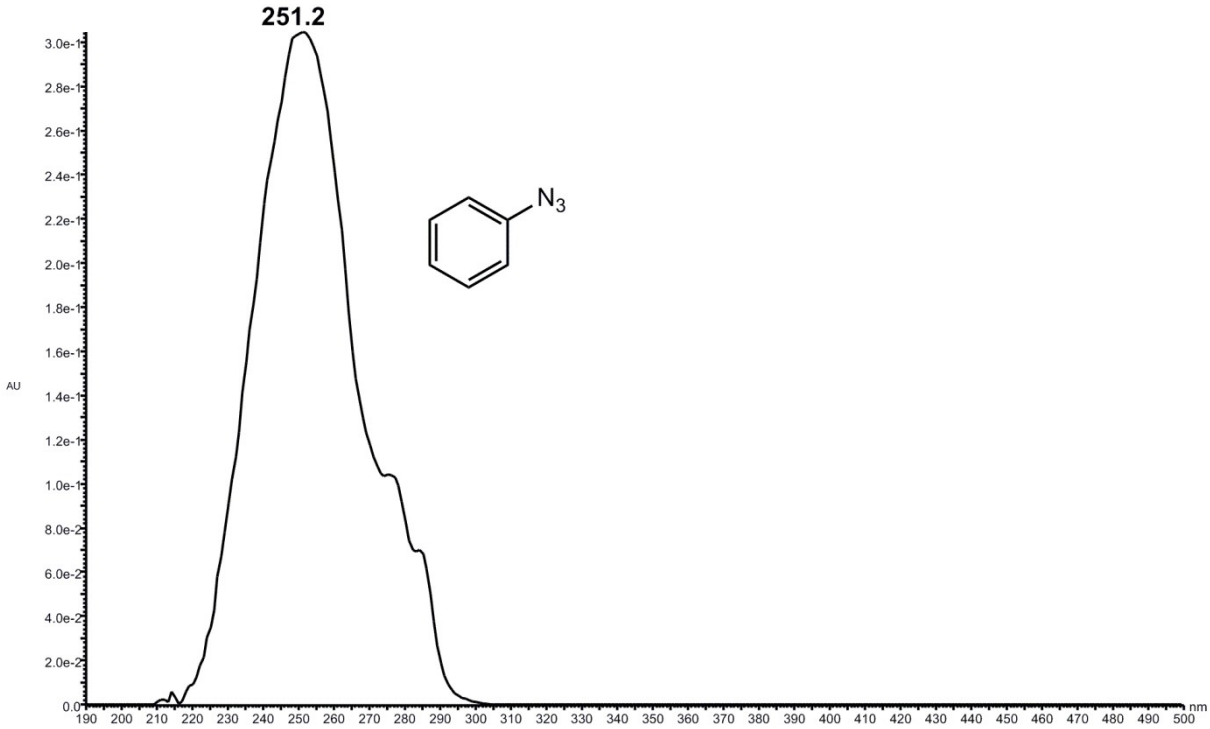


Figure S5. Absorption spectra of azide **2a** in methanol/H_2O 1:1 (v/v).

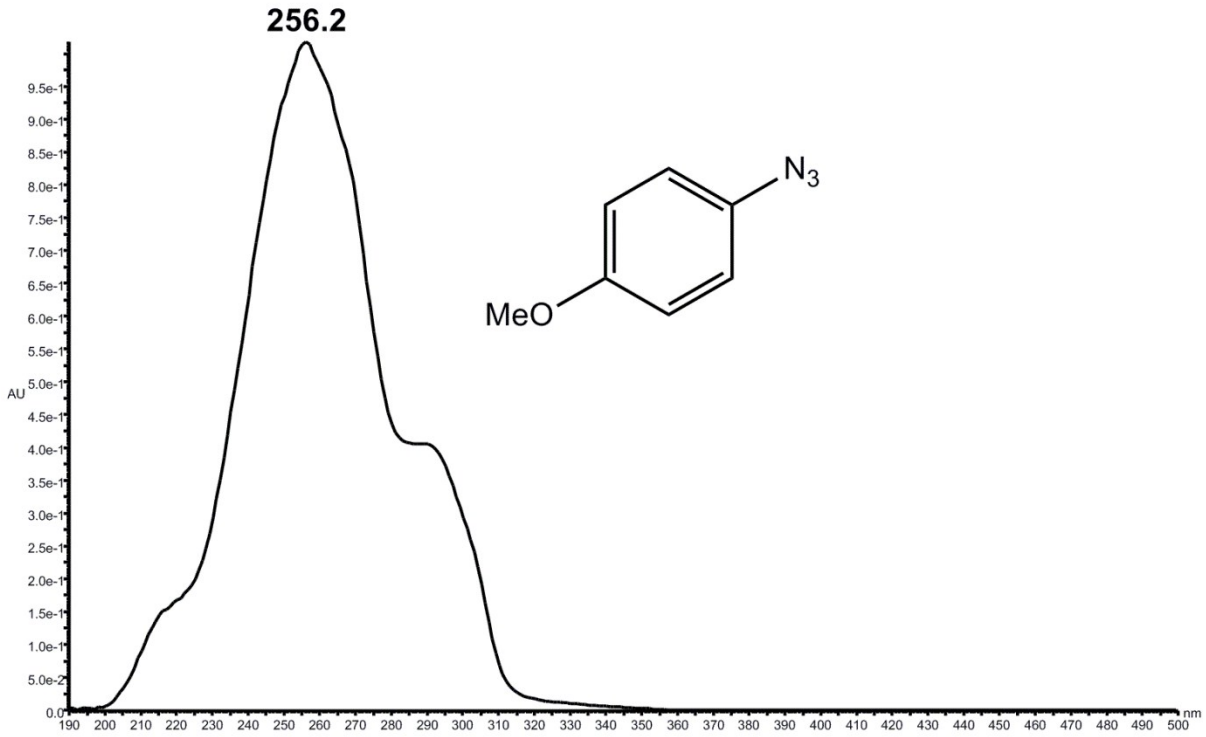


Figure S6. Absorption spectra of azide **2b** in methanol/H_2O 1:1 (v/v).

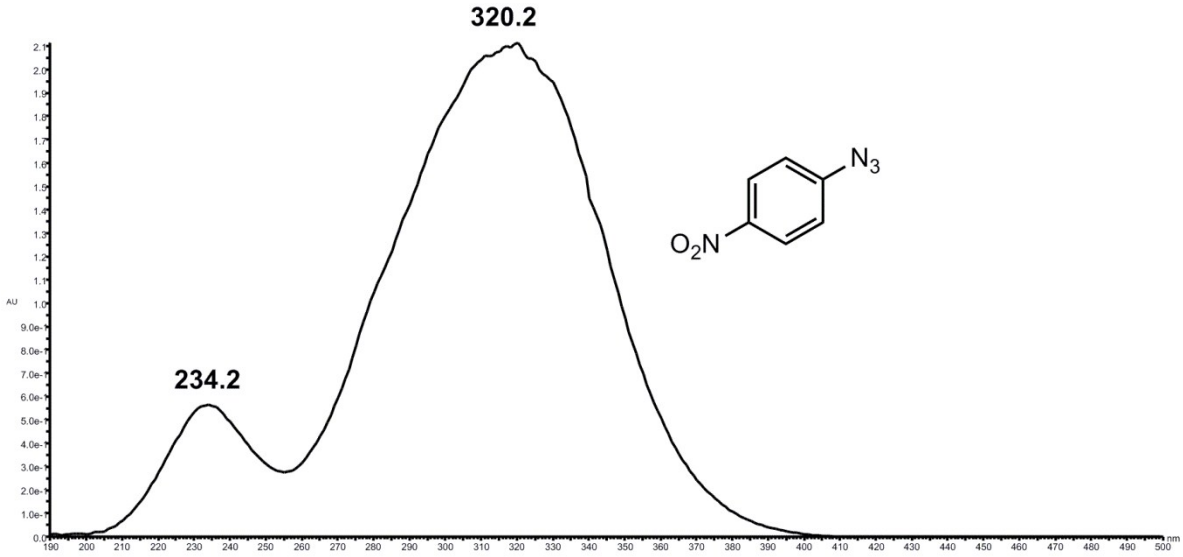


Figure S7. Absorption spectra of azide **2c** in methanol/H_2O 1:1 (v/v).

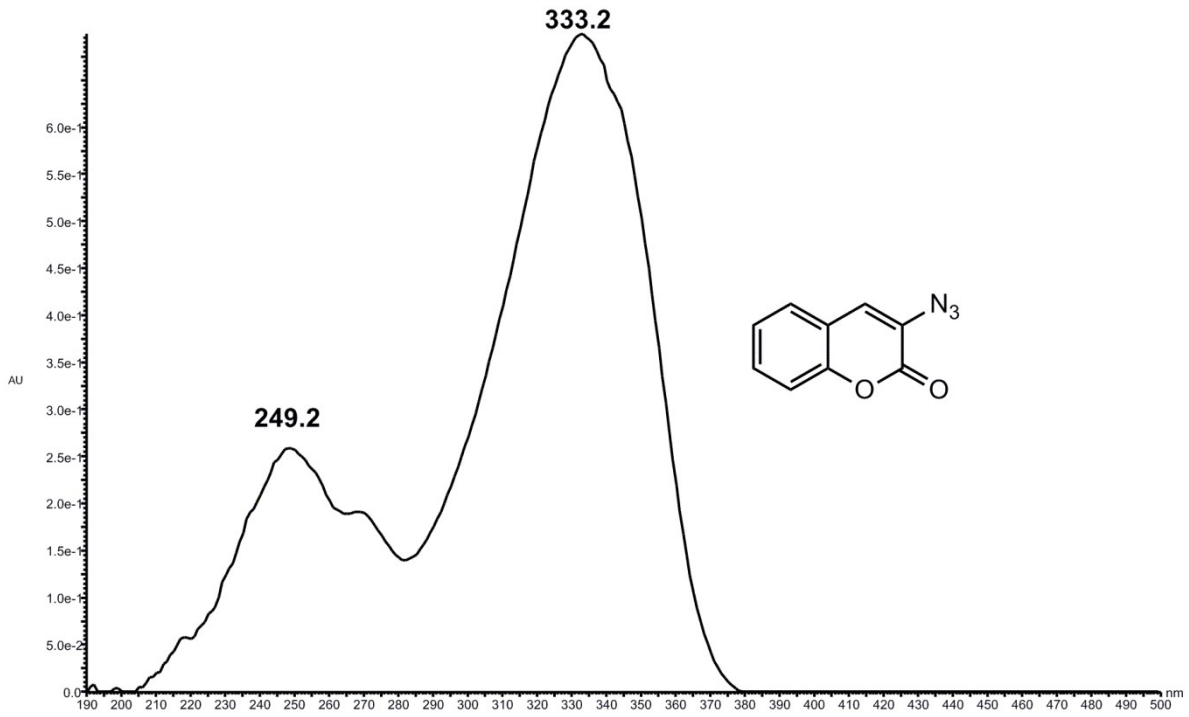


Figure S8. Absorption spectra of azide **2d** in methanol/H_2O 1:1 (v/v).

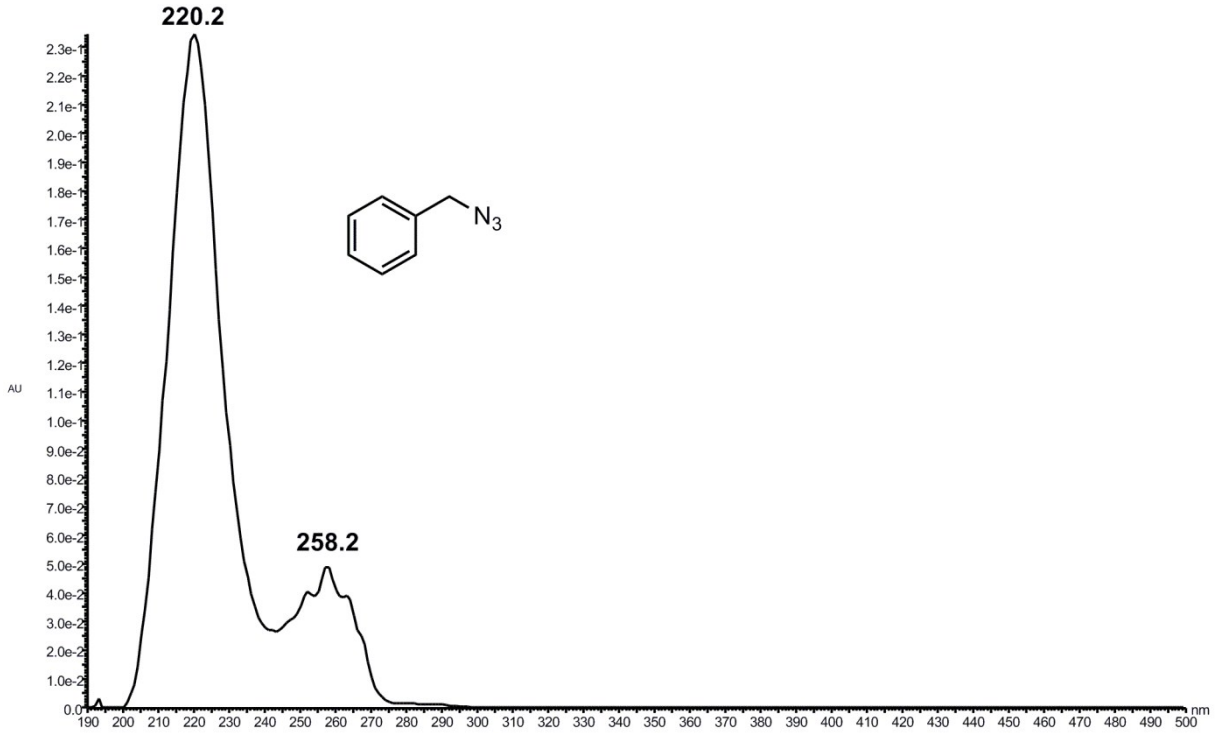


Figure S9. Absorption spectra of azide **2e** in methanol/H_2O 1:1 (v/v).

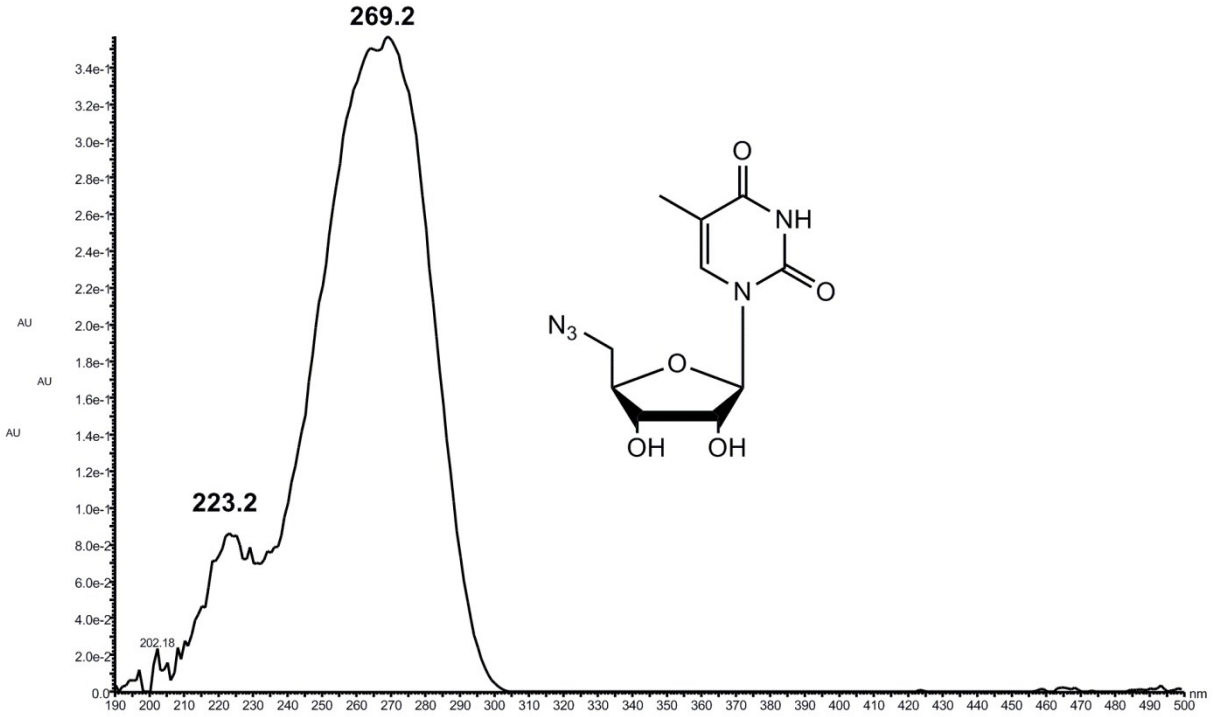


Figure S10. Absorption spectra of azide **2f** in methanol/H_2O 1:1 (v/v).

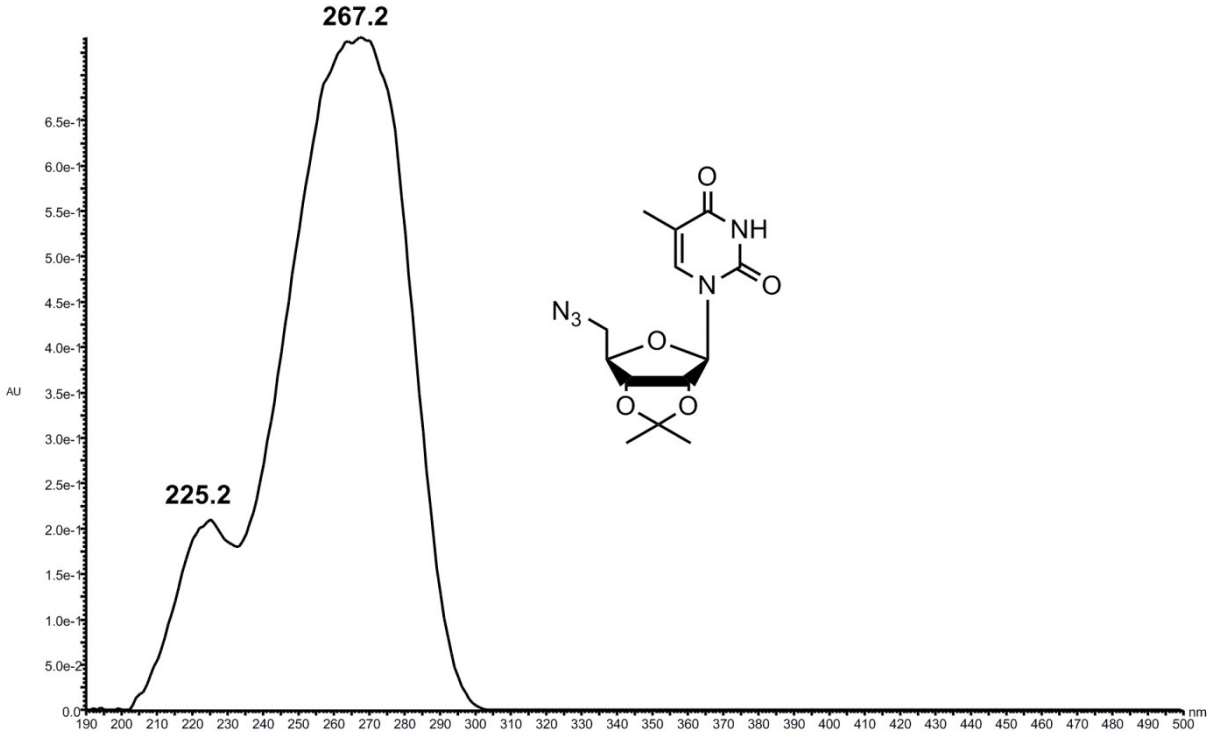


Figure S11. Absorption spectra of azide **2g** in methanol/H_2O 1:1 (v/v).

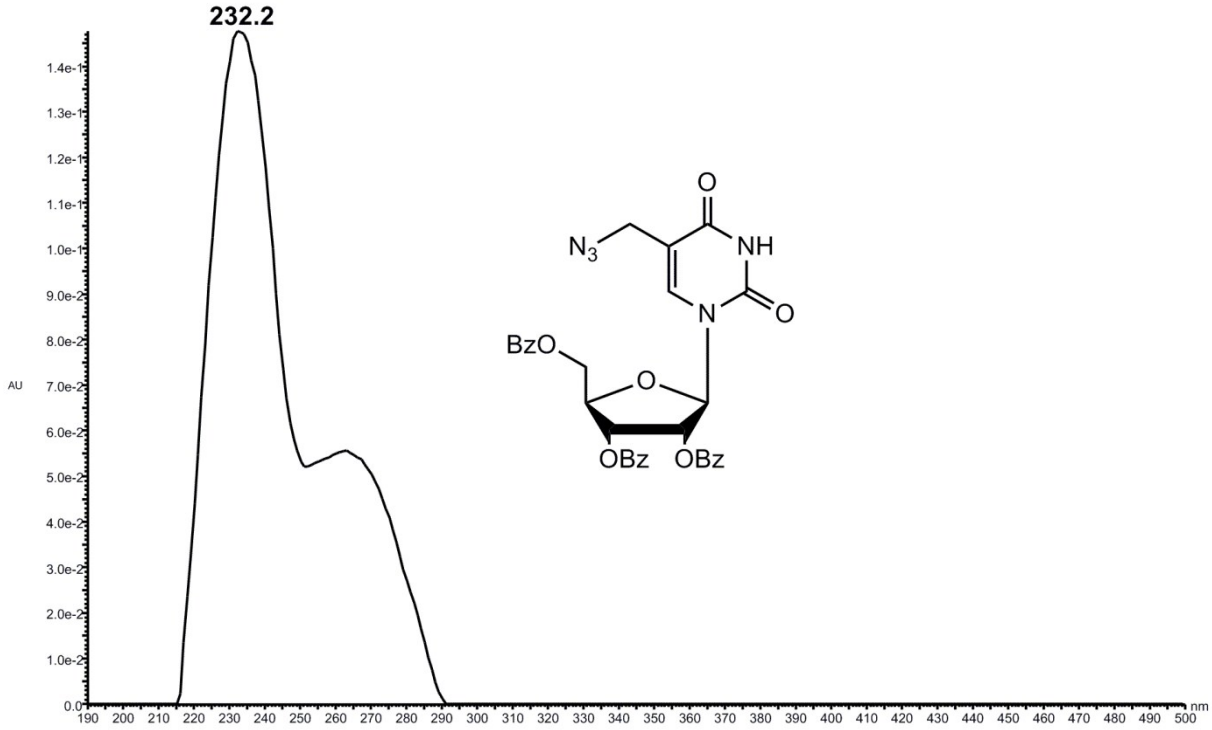


Figure S12. Absorption spectra of azide **2h** in methanol/H_2O 1:1 (v/v).

1.7.2. UV/VIS spectra of triazole products 3a-3e

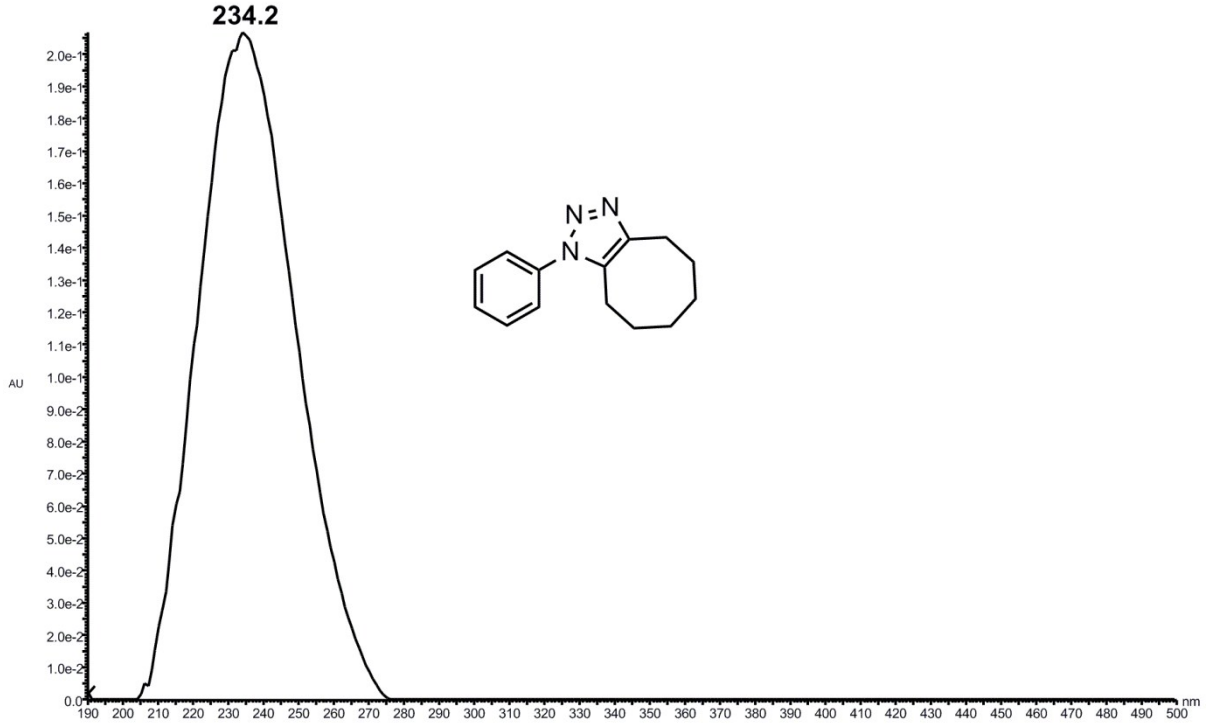


Figure S13. Absorption spectra of triazole **3a** in methanol/H_2O 1:1 (v/v).

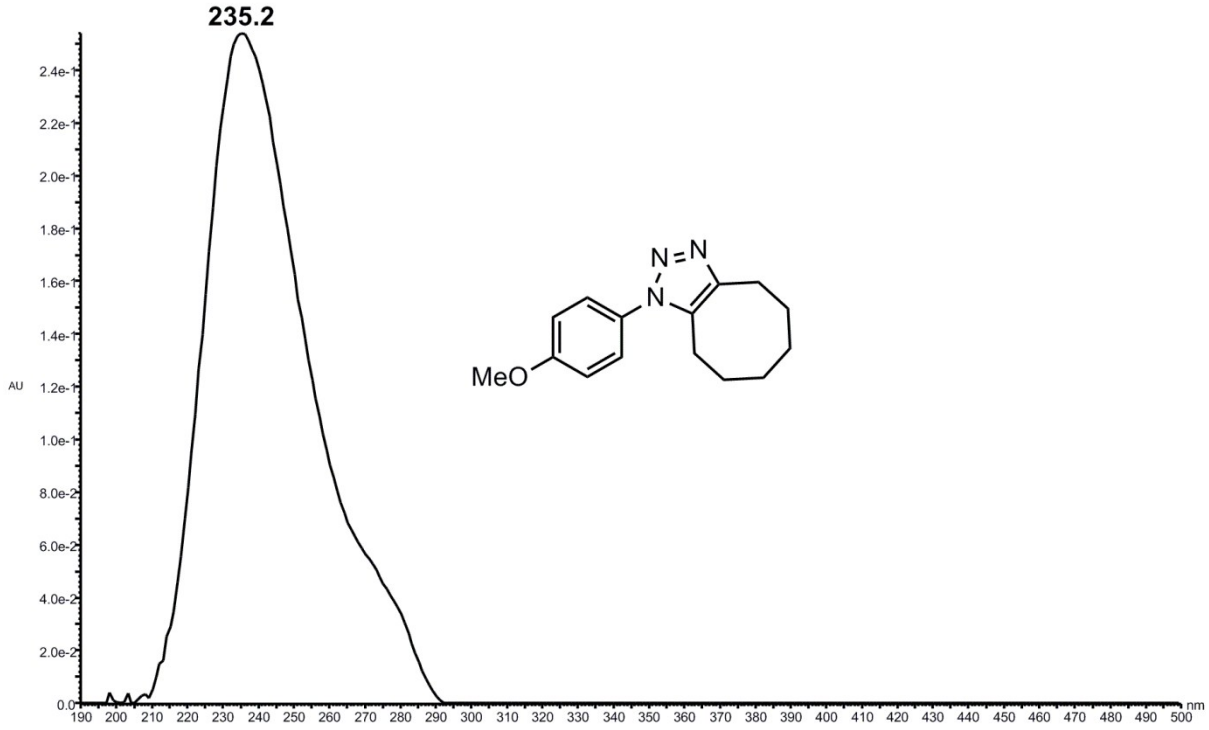


Figure S14. Absorption spectra of triazole **32** in methanol/H_2O 1:1 (v/v).

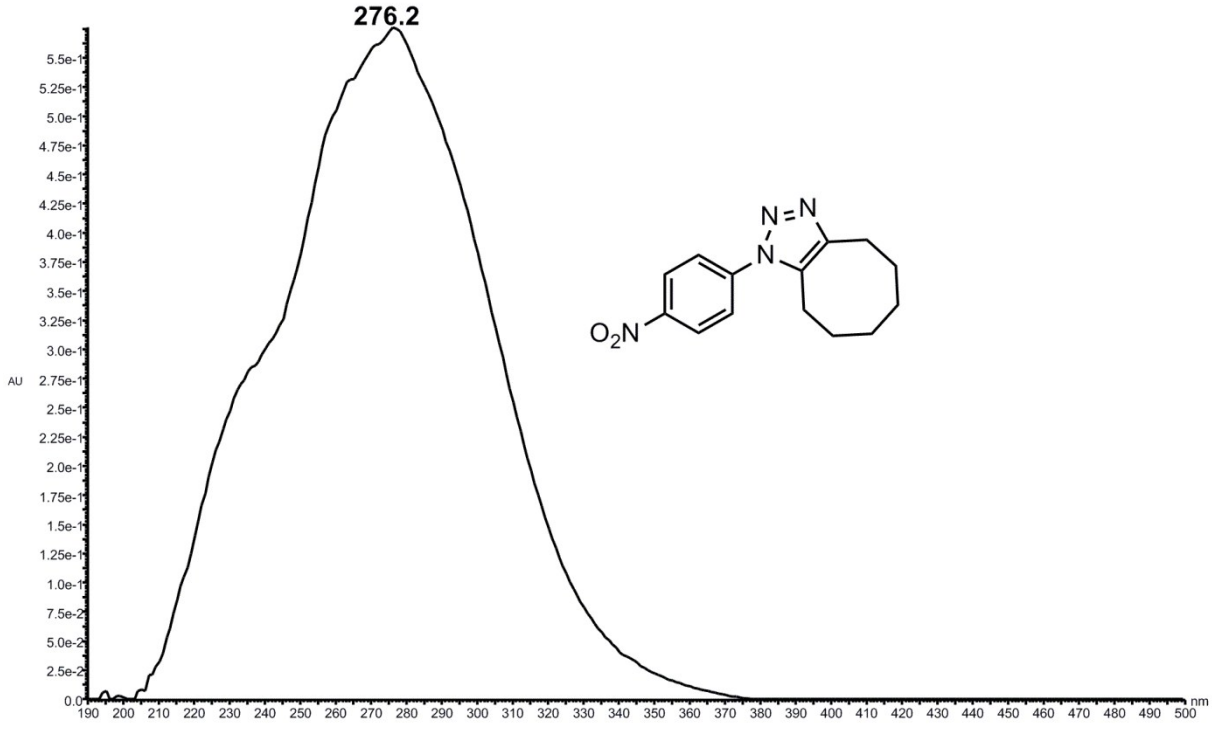


Figure S15. Absorption spectra of triazole **3c** in methanol/H_2O 1:1 (v/v).

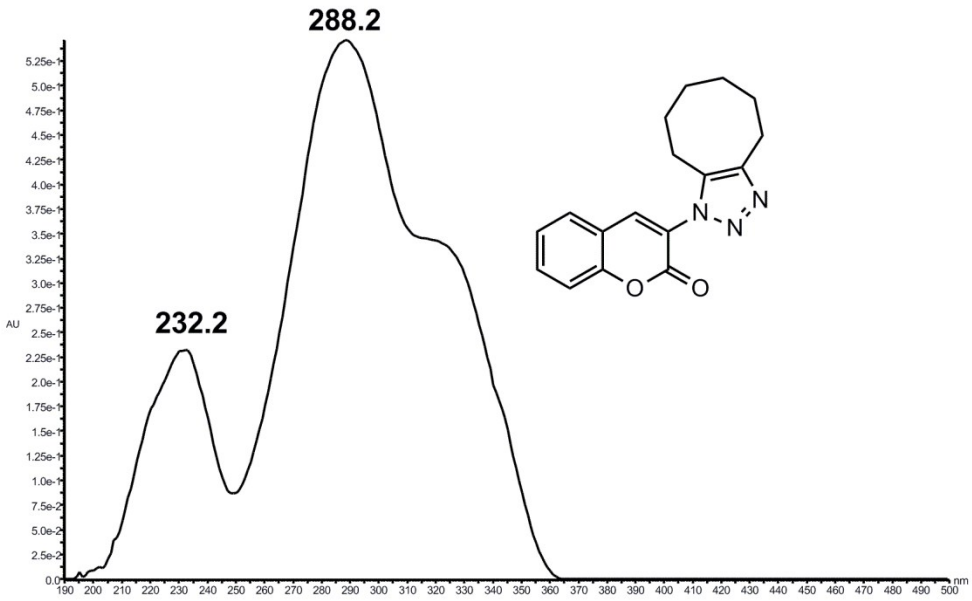


Figure S16. Absorption spectra of triazole **3d** in methanol/H_2O 1:1 (v/v).

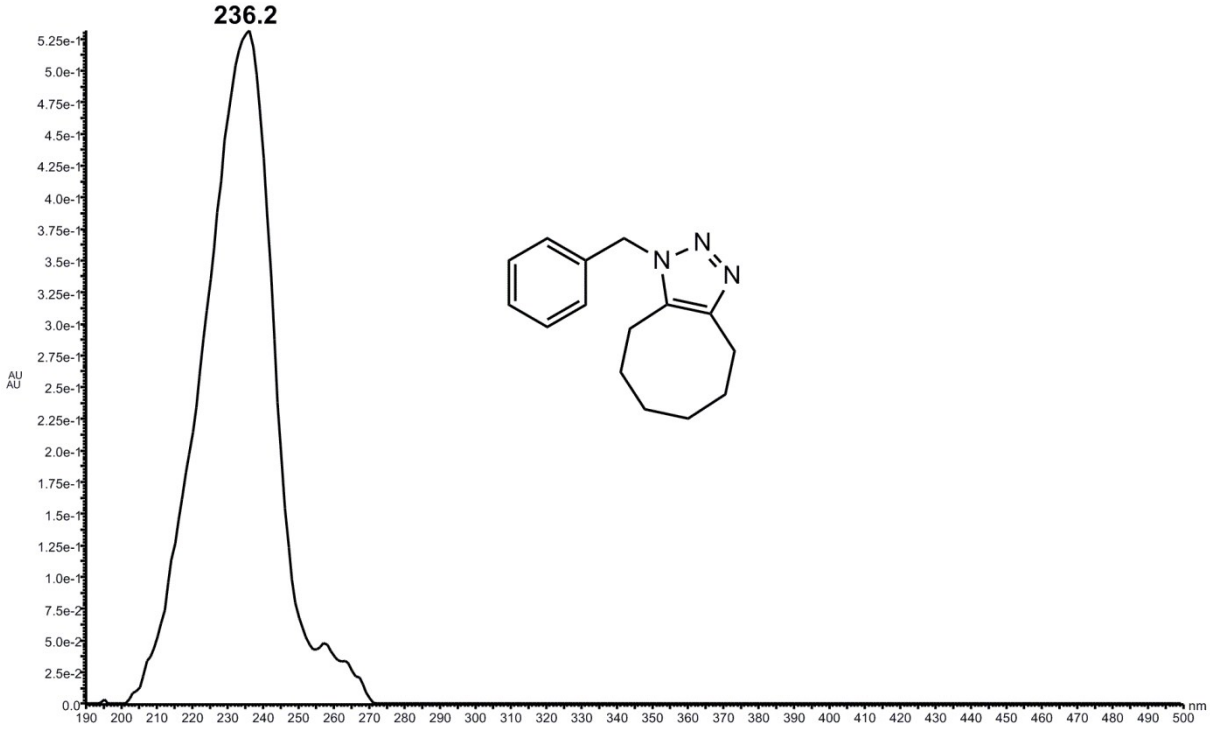


Figure S17. Absorption spectra of triazole **3e** in methanol/H_2O 1:1 (v/v).

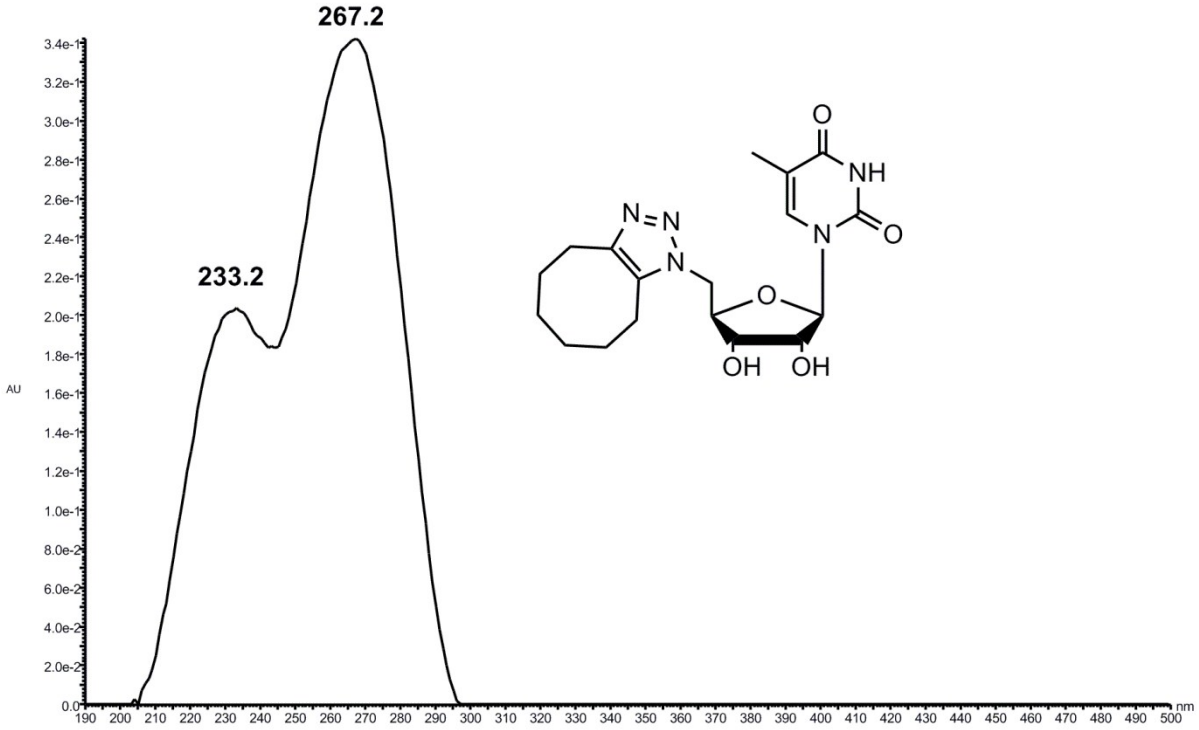


Figure S18. Absorption spectra of triazole **3f** in methanol/H_2O 1:1 (v/v).

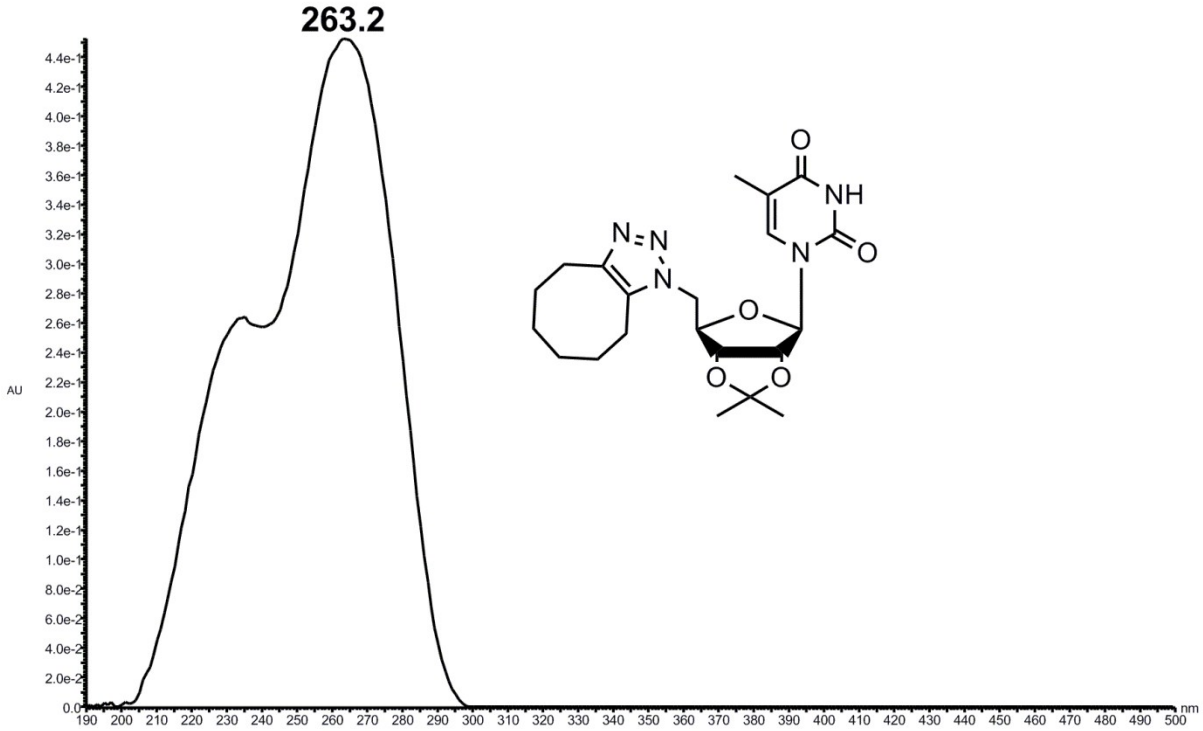


Figure S19. Absorption spectra of triazole **3g** in methanol/H_2O 1:1 (v/v).

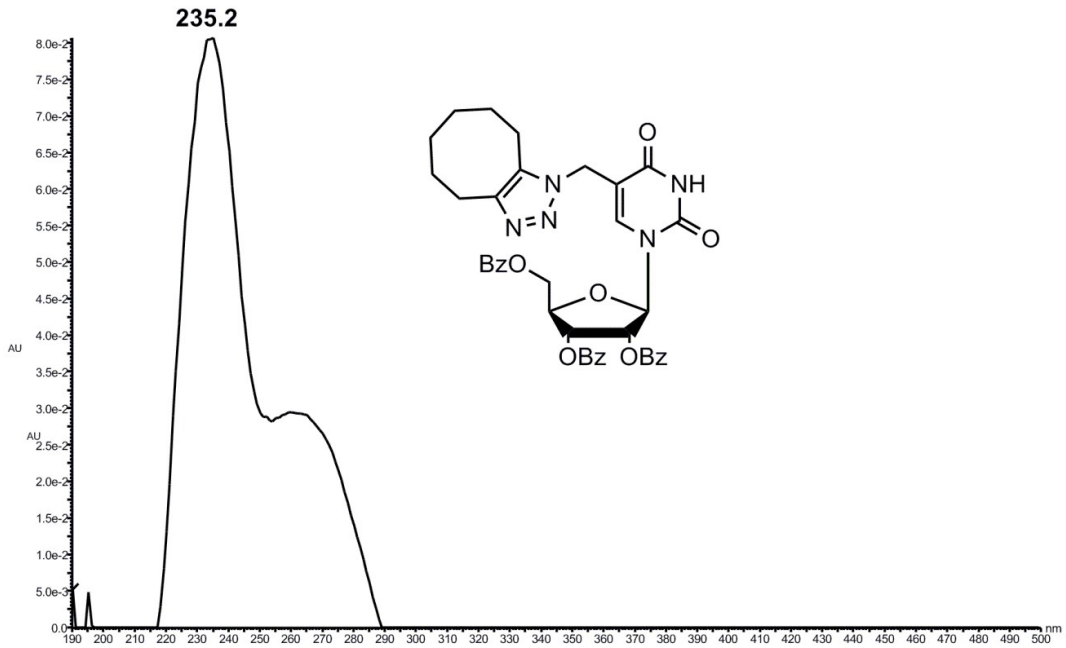


Figure S20. Absorption spectra of triazole **3h** in methanol/H_2O 1:1 (v/v).

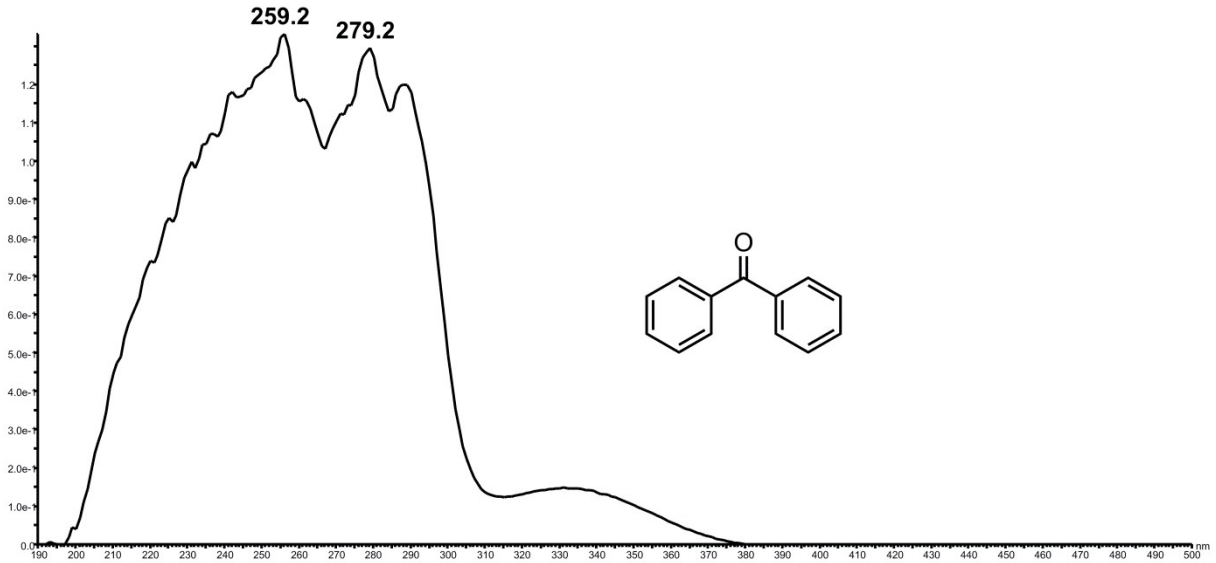


Figure S21. Absorption spectra of benzophenone in methanol.

1.7.3. UV/VIS monitoring of reaction between derivatives 1 and 2e

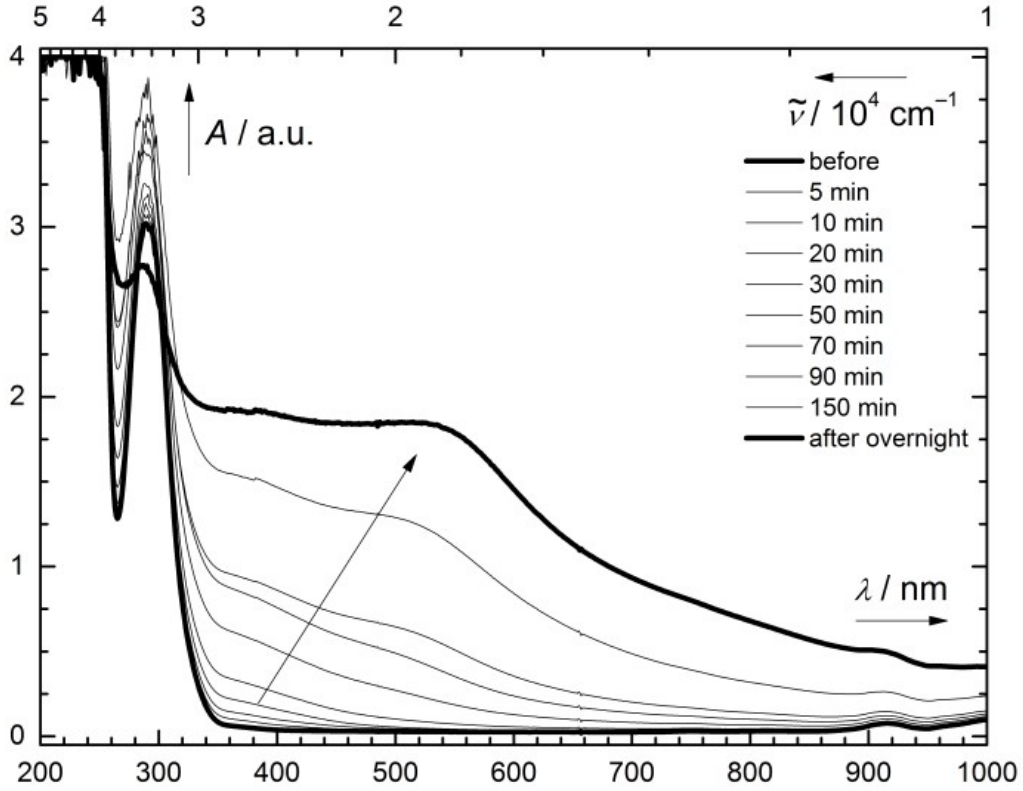


Figure S22. Change of absorption spectra of cycloocta-1,2,3-selenadiazole **1** (c = 3 × 10^{-3} mol dm^{-3}) and benzylazide **2e** (c = 2.8 × 10^{-3} mol dm^{-3}) in methanol upon irradiation with medium-pressure mercury arc (Figure S2) filtered through a 313 nm filter (λ_{irr} = 313.5 ± 1.5 nm). Broad peak at about 500 nm corresponds to elementary selenium releasing from cycloocta-1,2,3-selenadiazole 1 in form of nanoparticles with diameter approximately 180 nm.[13]

1.8. GC/MS spectra

1.8.1. GC spectrum of reaction mixture after irradiation of derivatives 1 and 2e

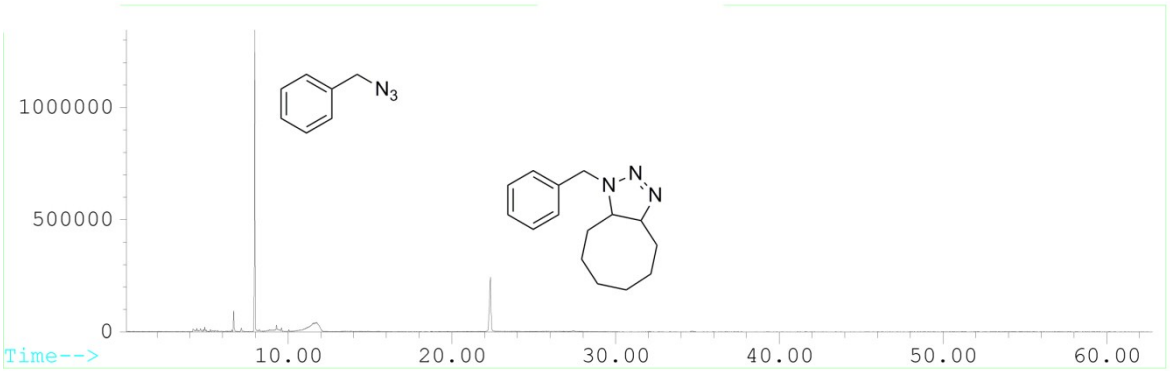


Figure S23. GC chromatogram obtained from reaction mixture after irradiation of equimolar amounts of cycloocta-1,2,3-selenadiazole **1** and benzylazide in methanol (c = 0.003 mol dm^{-3}).

1.8.2. GC/MS spectrum of reaction mixture after irradiation of derivative 1

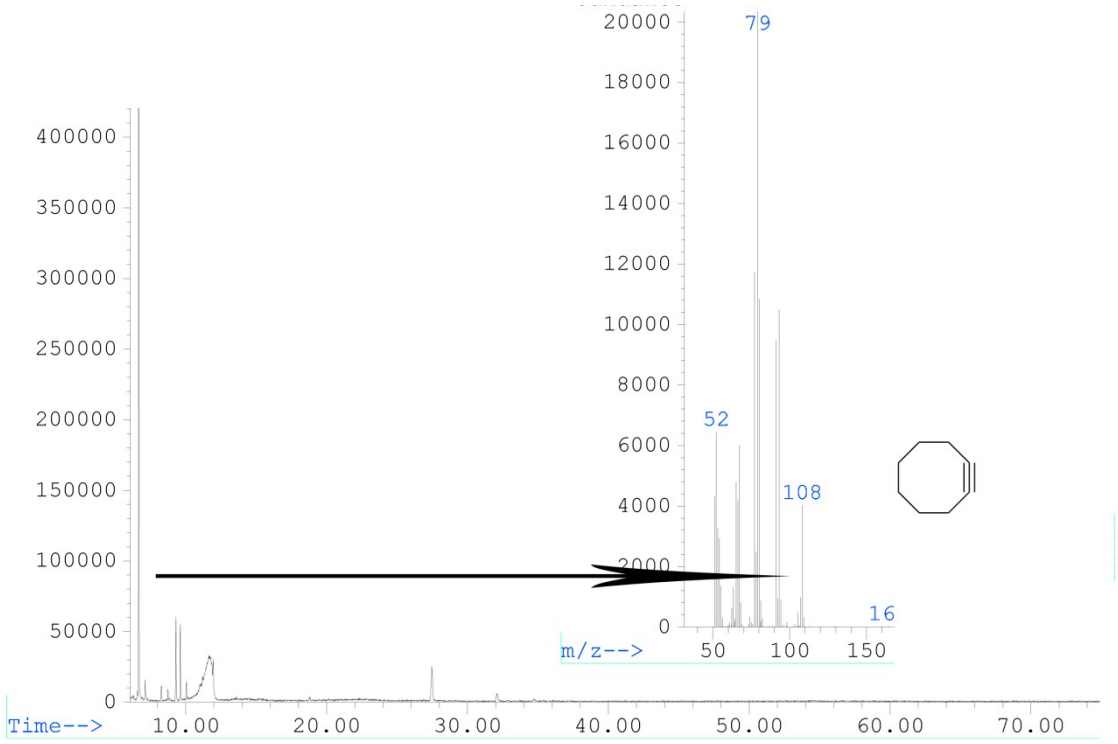


Figure S24. GC/MS spectrum after irradiation of cycloocta-1,2,3-selenadiazole **1** ($c \sim 0.03$ mol dm^{-3}) in methanol-d_4.

1.9. NMR spectra

1.9.1. NMR spectra of triazoles 3

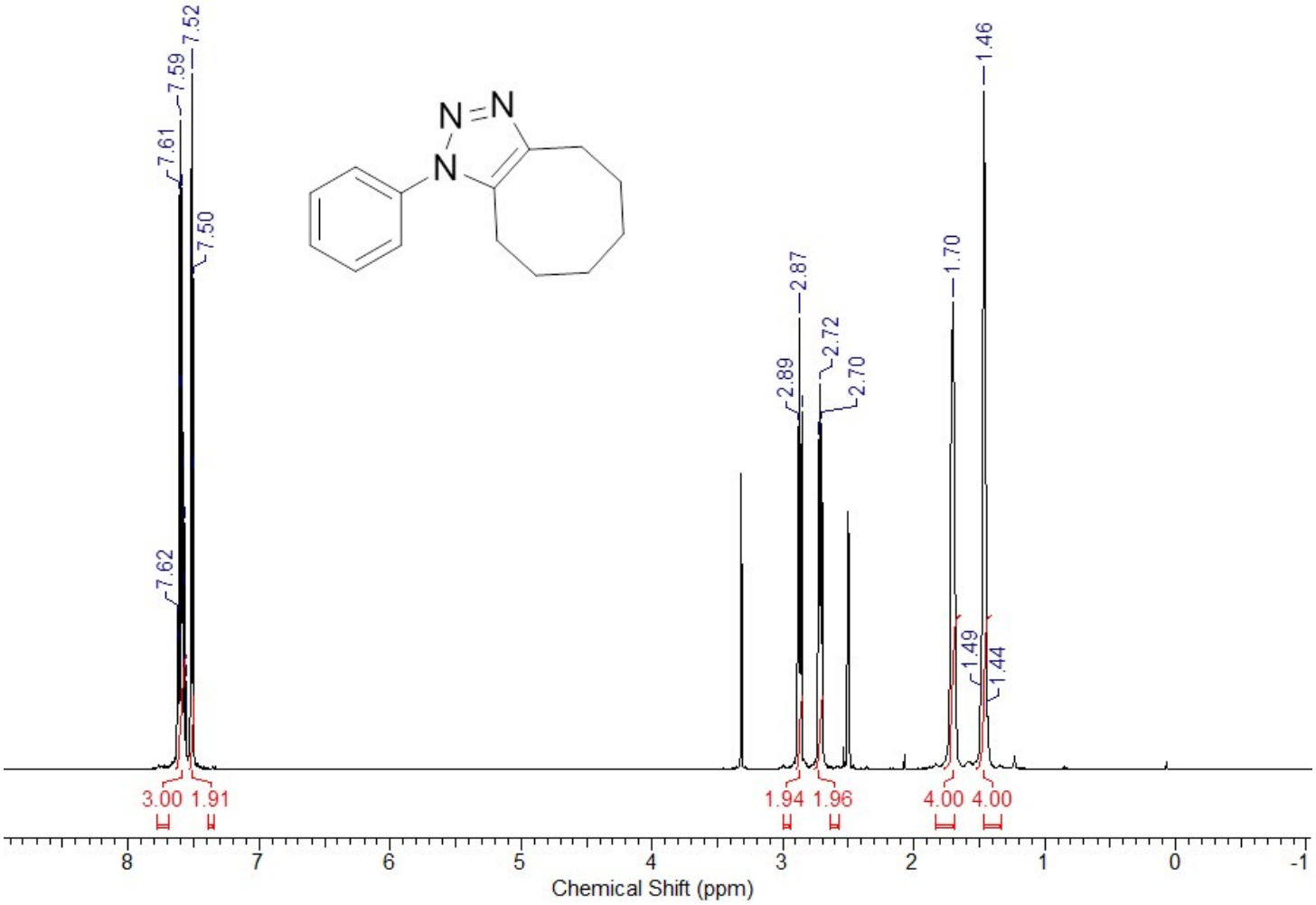


Figure S25. ^{1}H NMR (DMSO-d_6, 500 MHz): 1-phenyl-4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazole (**3a**).

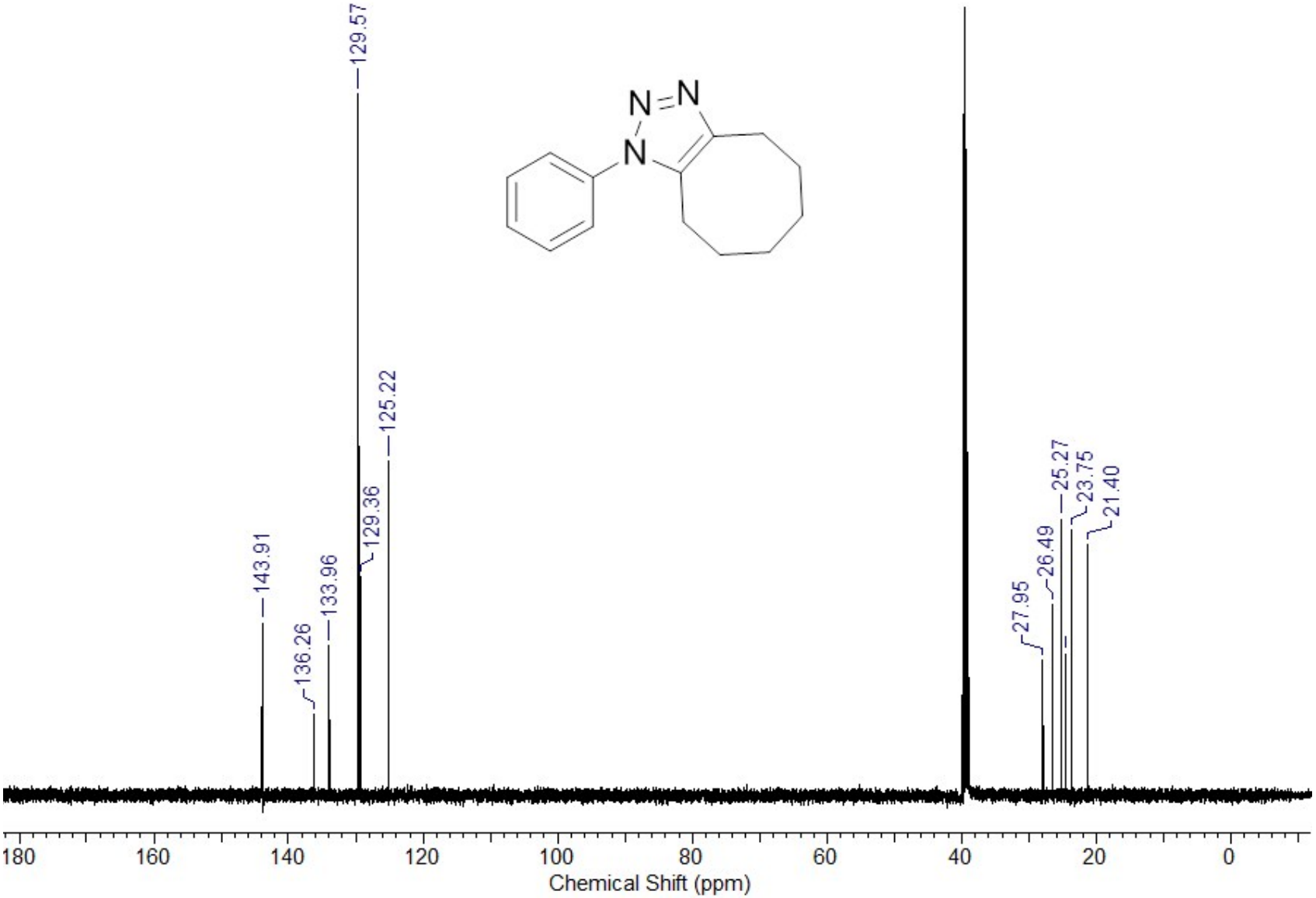


Figure S26. $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz): 1-phenyl-4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazole (**3a**).

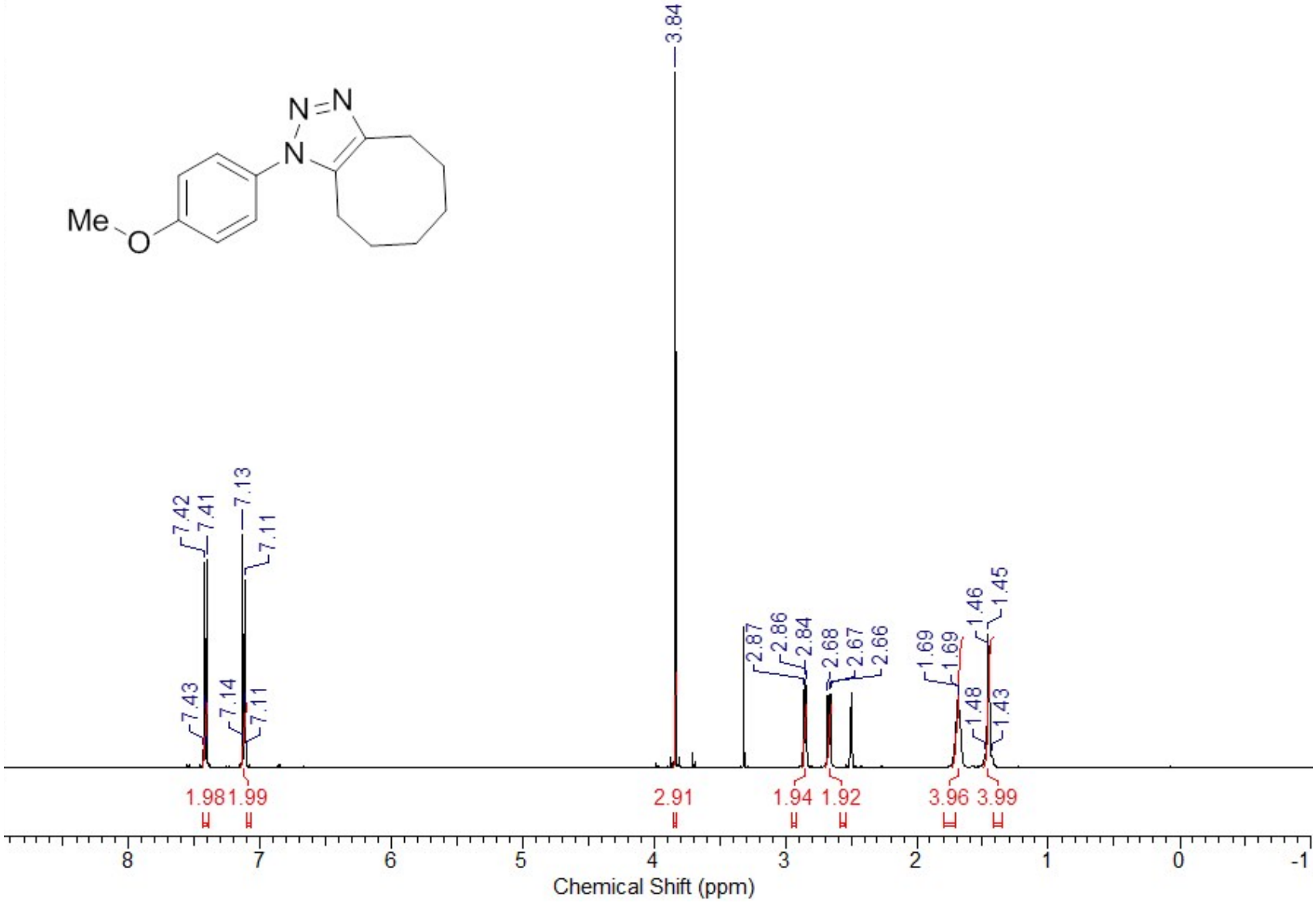


Figure S27. ^{1}H NMR (DMSO-d_6, 500 MHz): 1-(4-methoxyphenyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazole (**3b**).

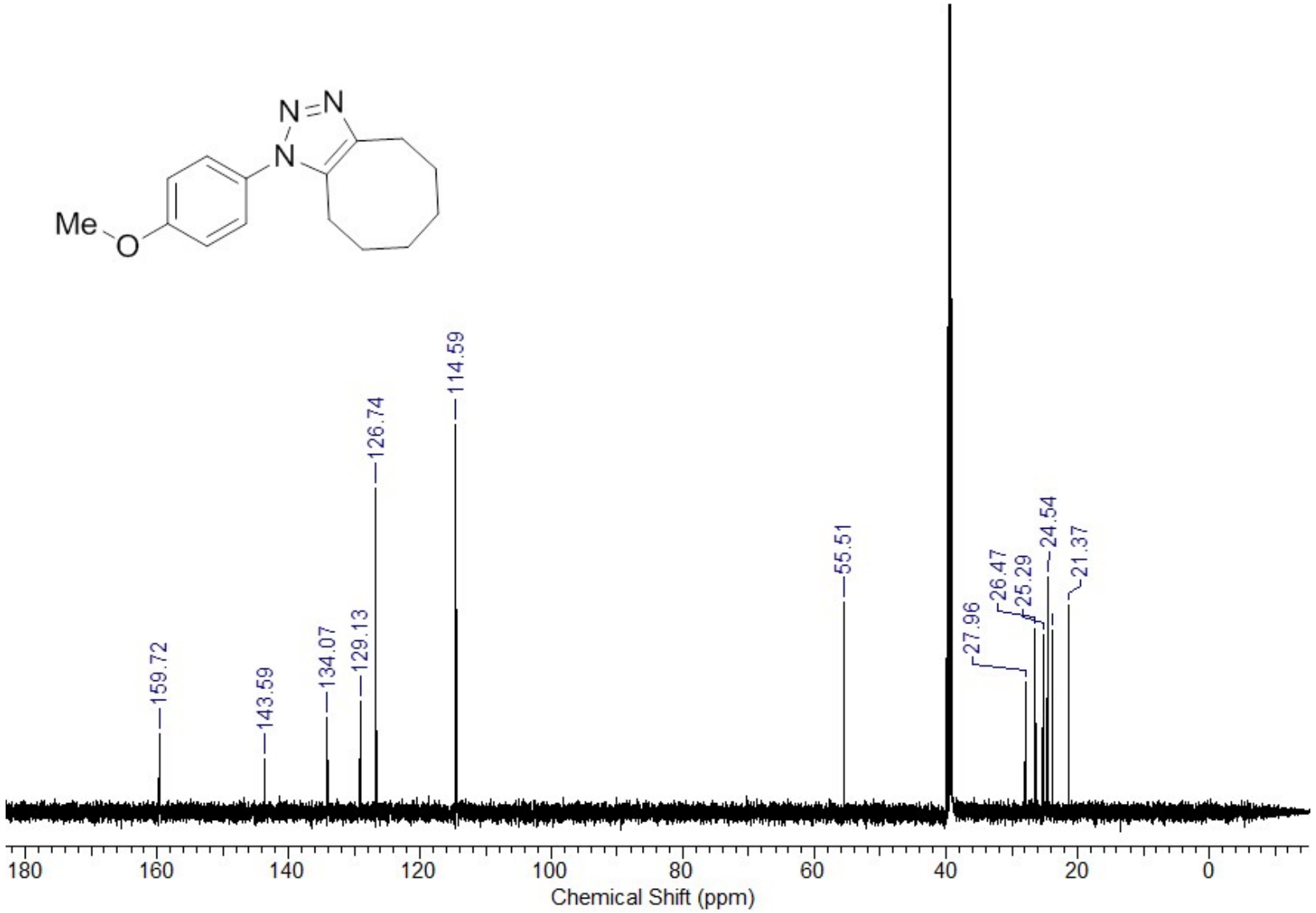


Figure S28. $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz): 1-(4-methoxyphenyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazole (**3b**).

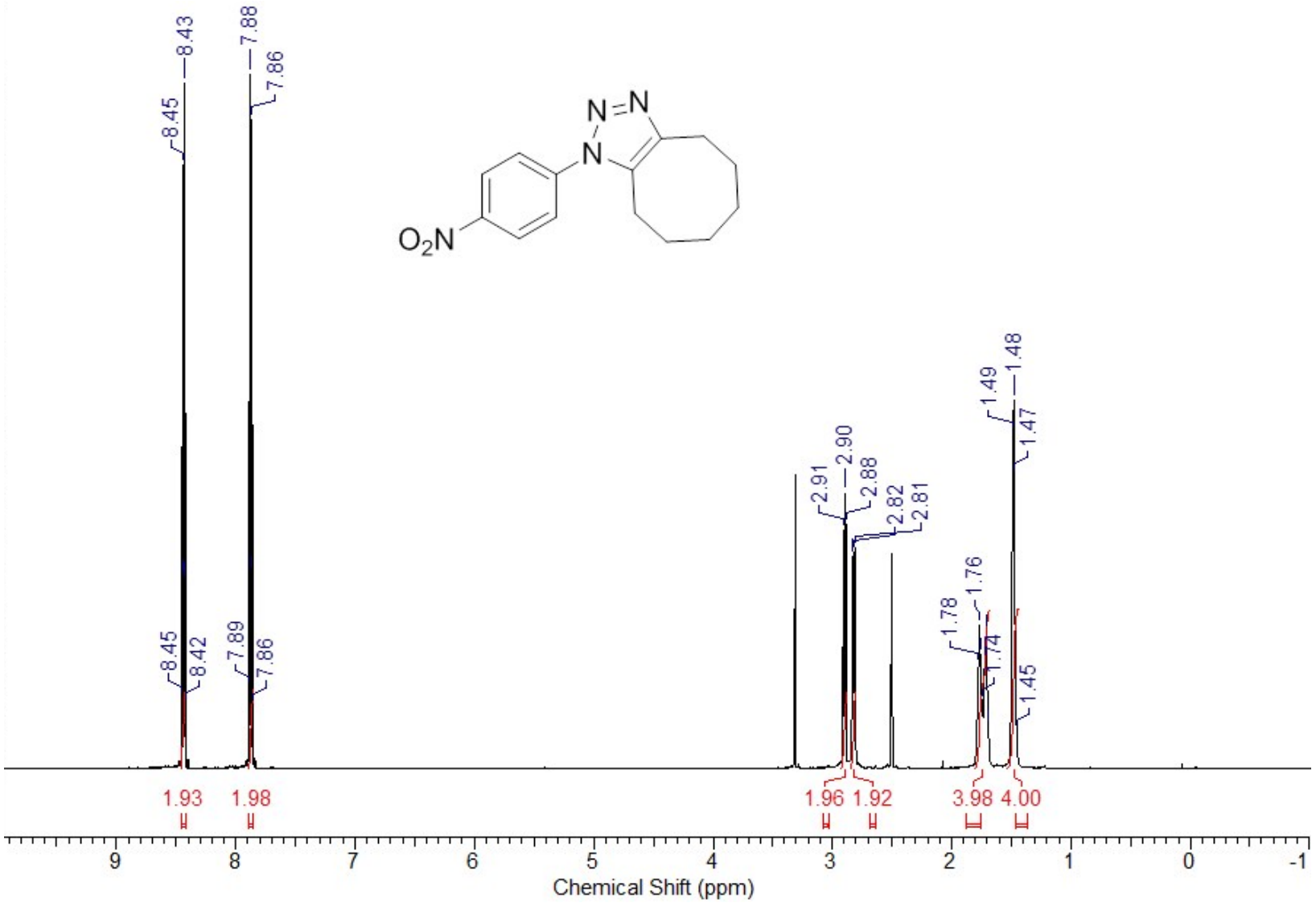


Figure S29. ^{1}H NMR (DMSO-d_6, 500 MHz): 1-(4-nitrophenyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazole (**3c**).

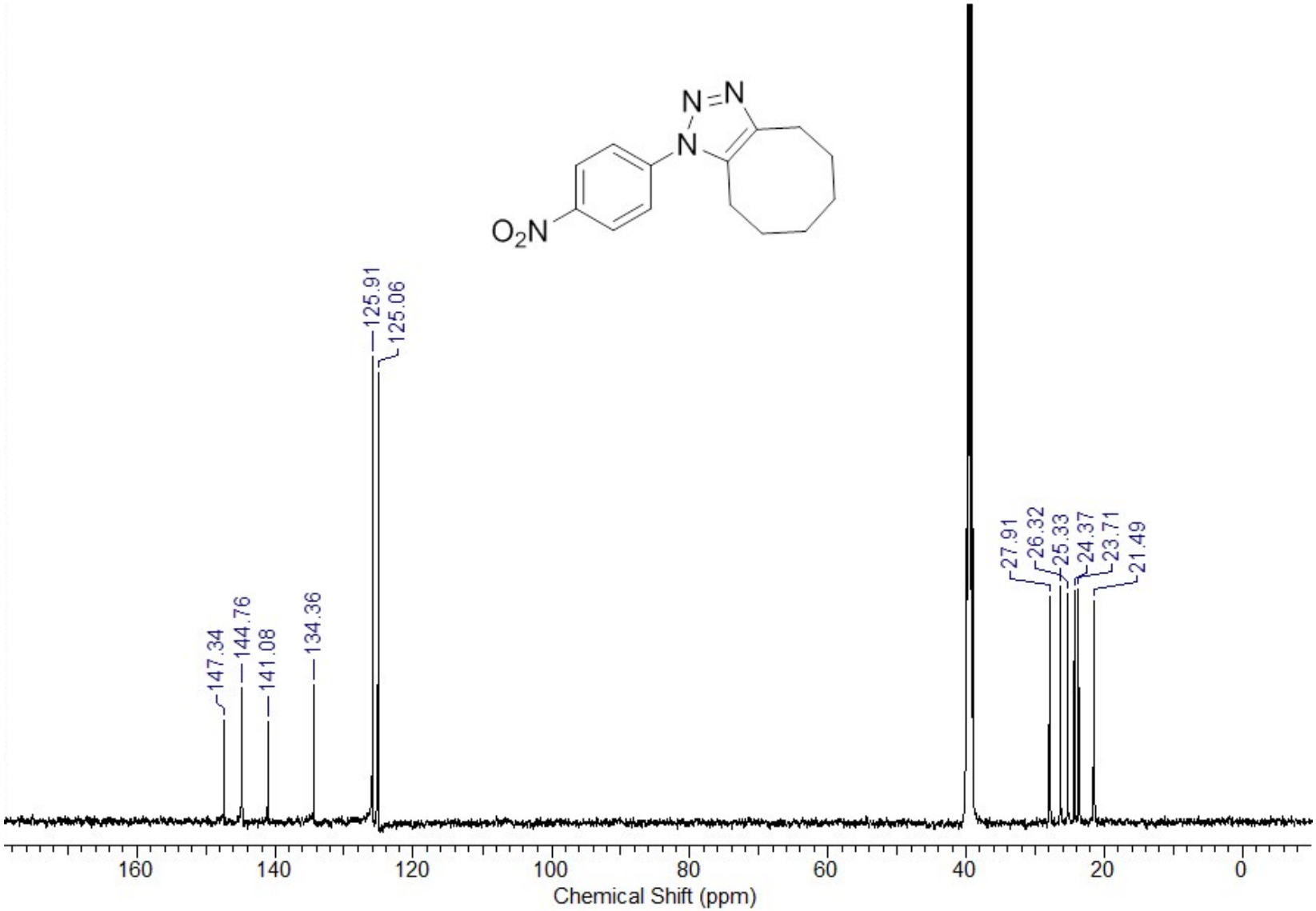


Figure S30. $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz): 1-(4-nitrophenyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazole (**3c**).

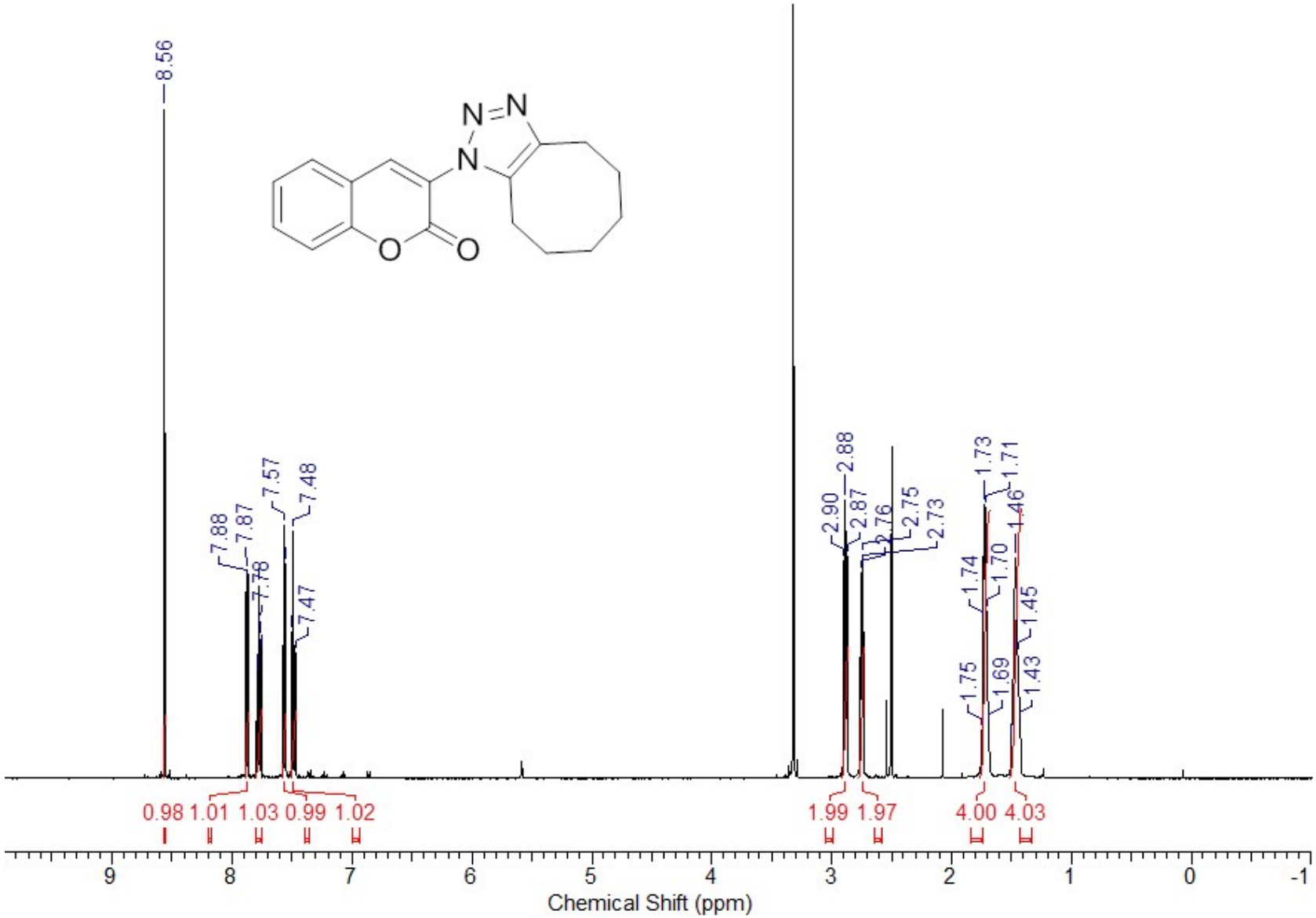


Figure S31. ^{1}H NMR (DMSO-d_6, 500 MHz): 3-(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-2*H*-chromen-2-one (**3d**).

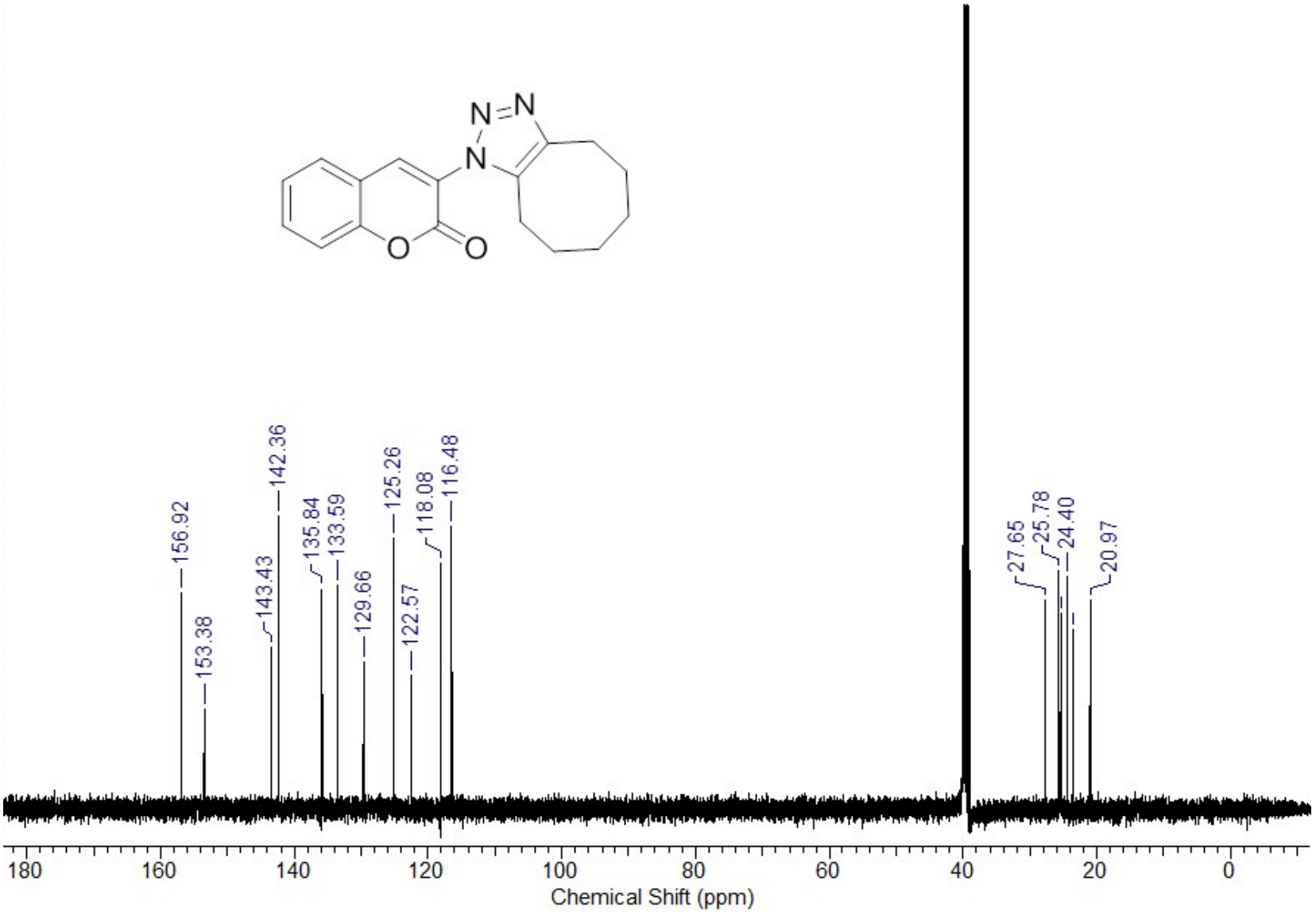


Figure S32. $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz): 3-(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-2*H*-chromen-2-one (**3d**).

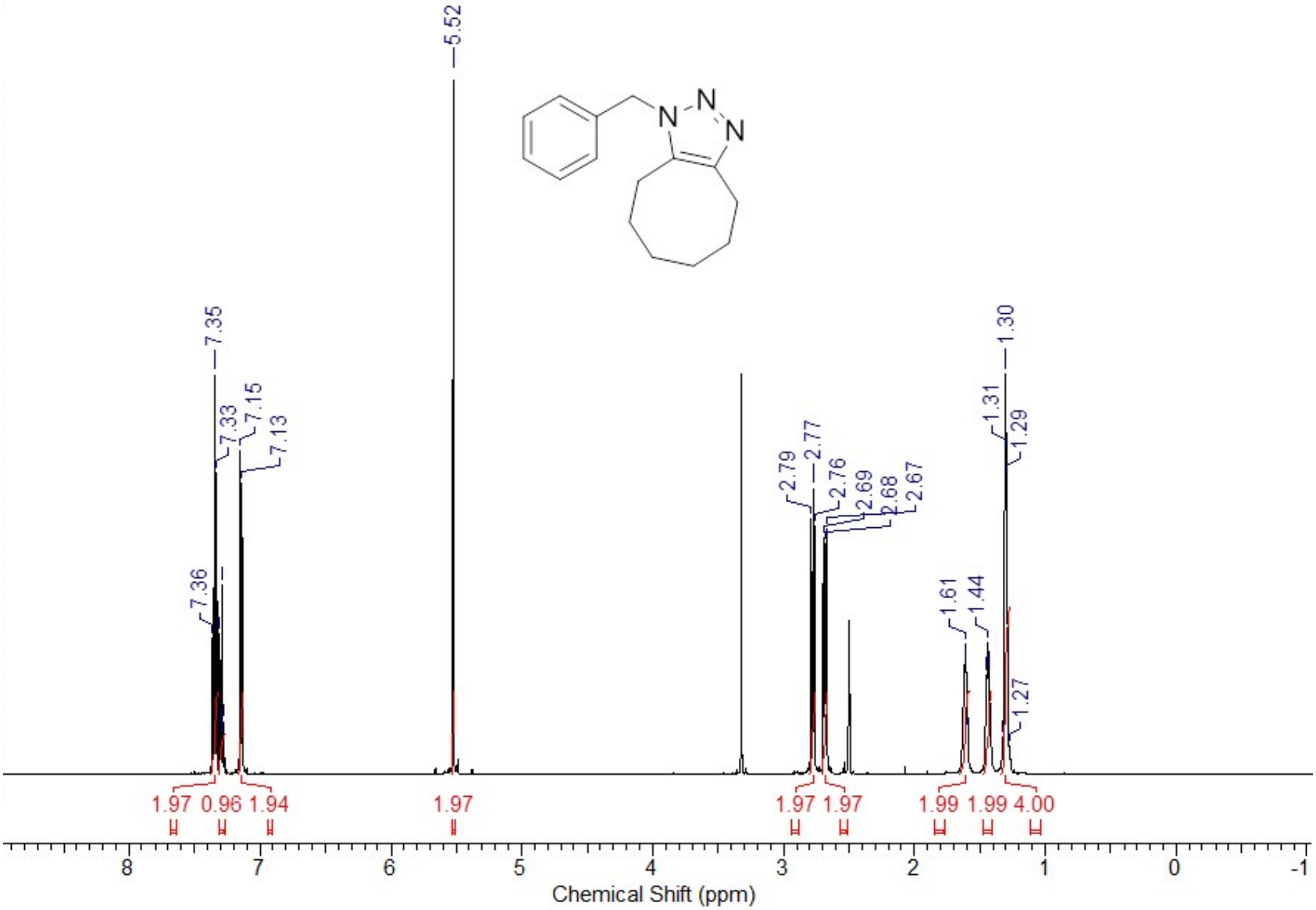


Figure S33. ^{1}H NMR (DMSO-d_6, 500 MHz): 1-benzyl-4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazole (**3e**).

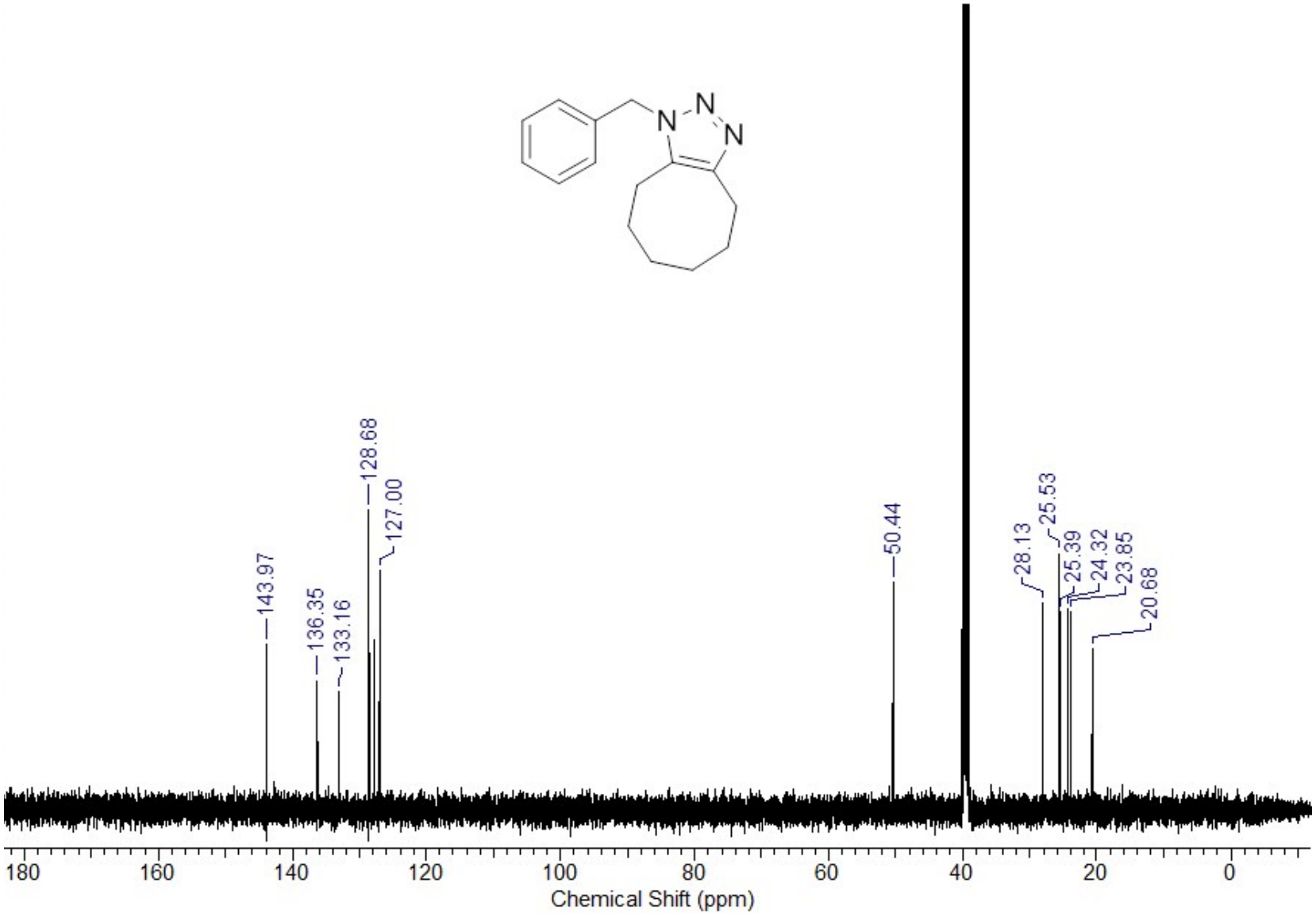


Figure S34. $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz): 1-benzyl-4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazole (**3e**).

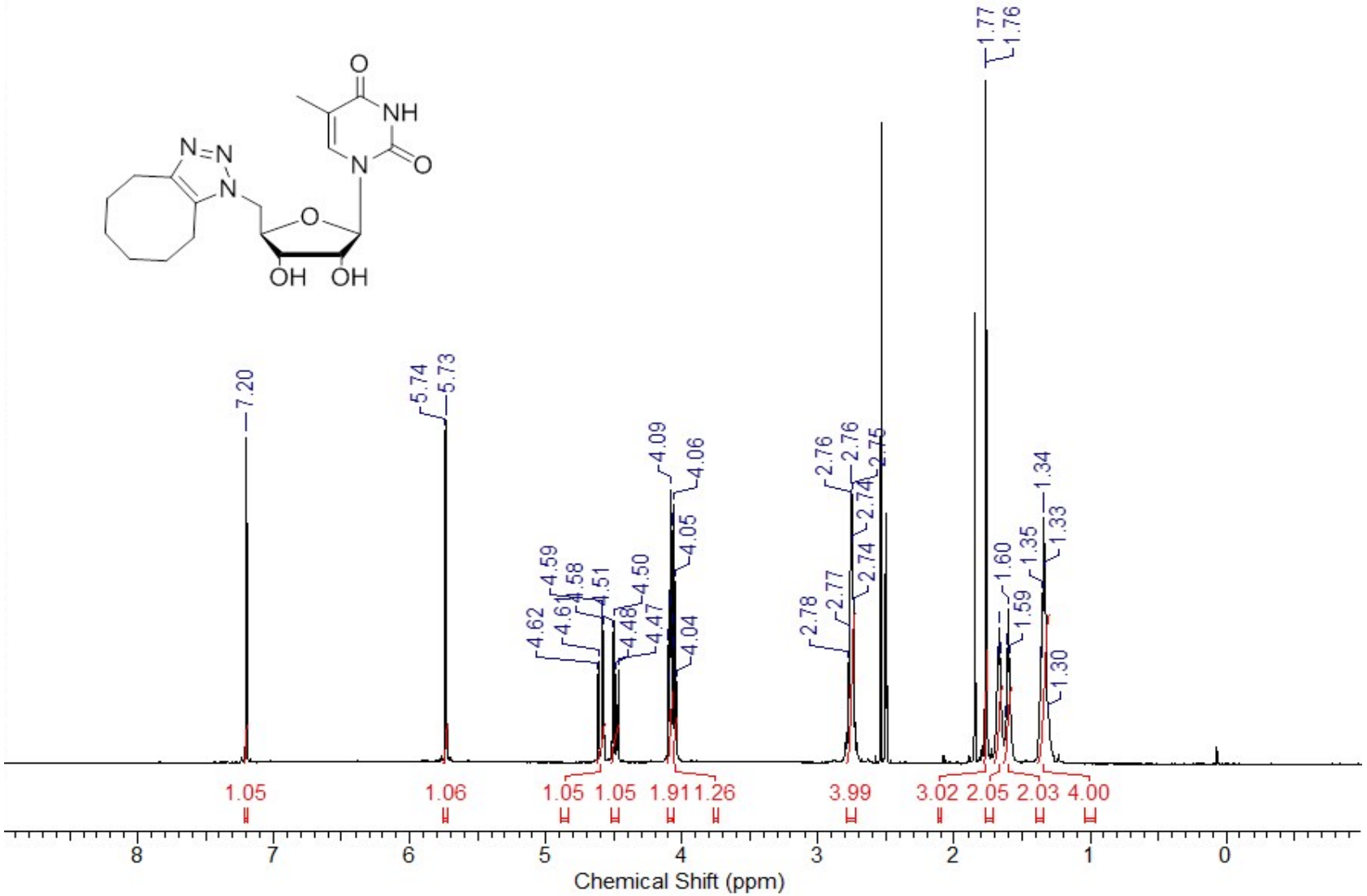


Figure S35. ^{1}H NMR (DMSO-d_6, 500 MHz): 1-((2*R*,3*R*,4*S*,5*R*)-5-((4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)methyl)-3,4-dihydroxytetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (**3f**).

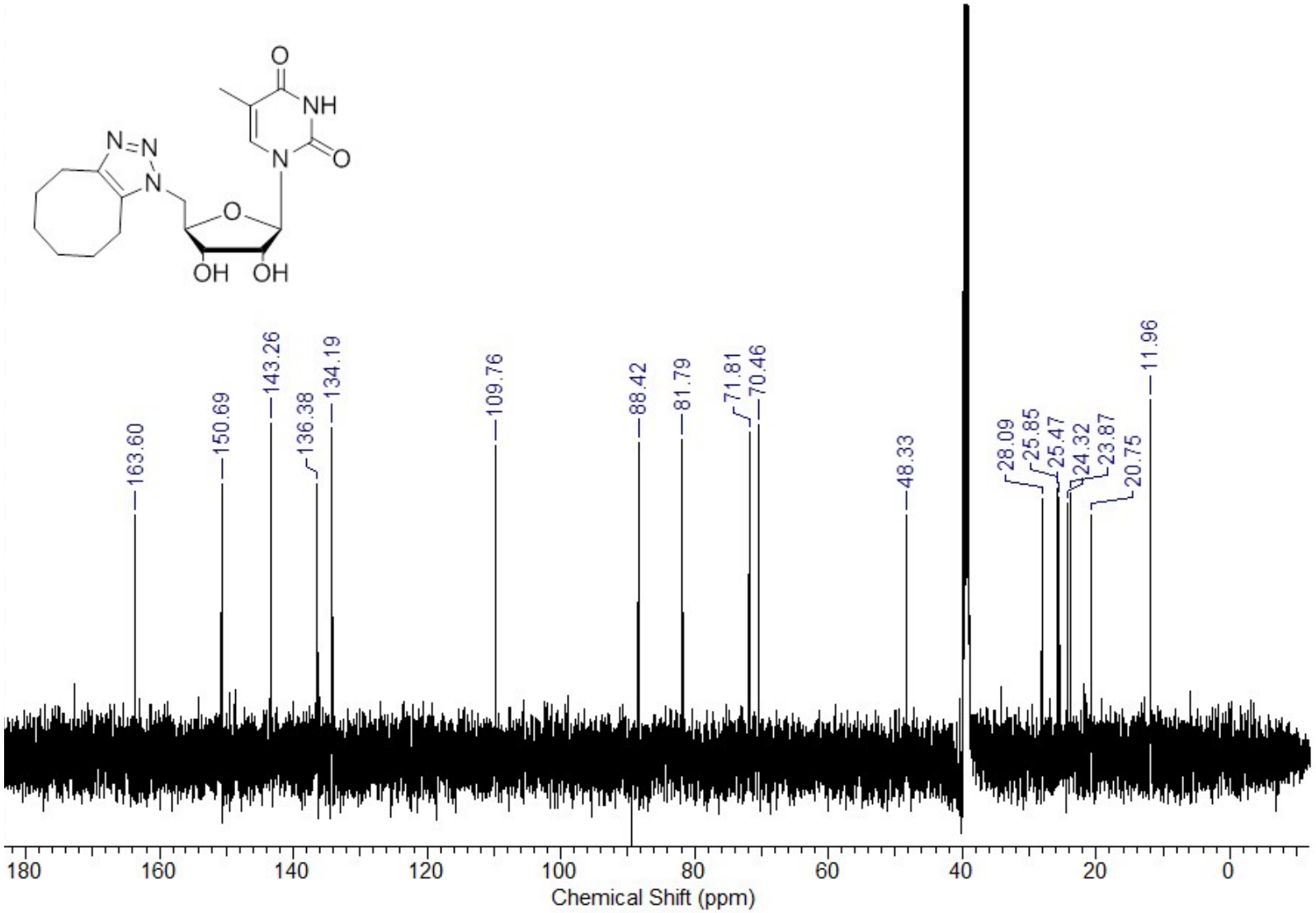


Figure S36. $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz): 1-((2*R*,3*R*,4*S*,5*R*)-5-((4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)methyl)-3,4-dihydroxytetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (**3f**).

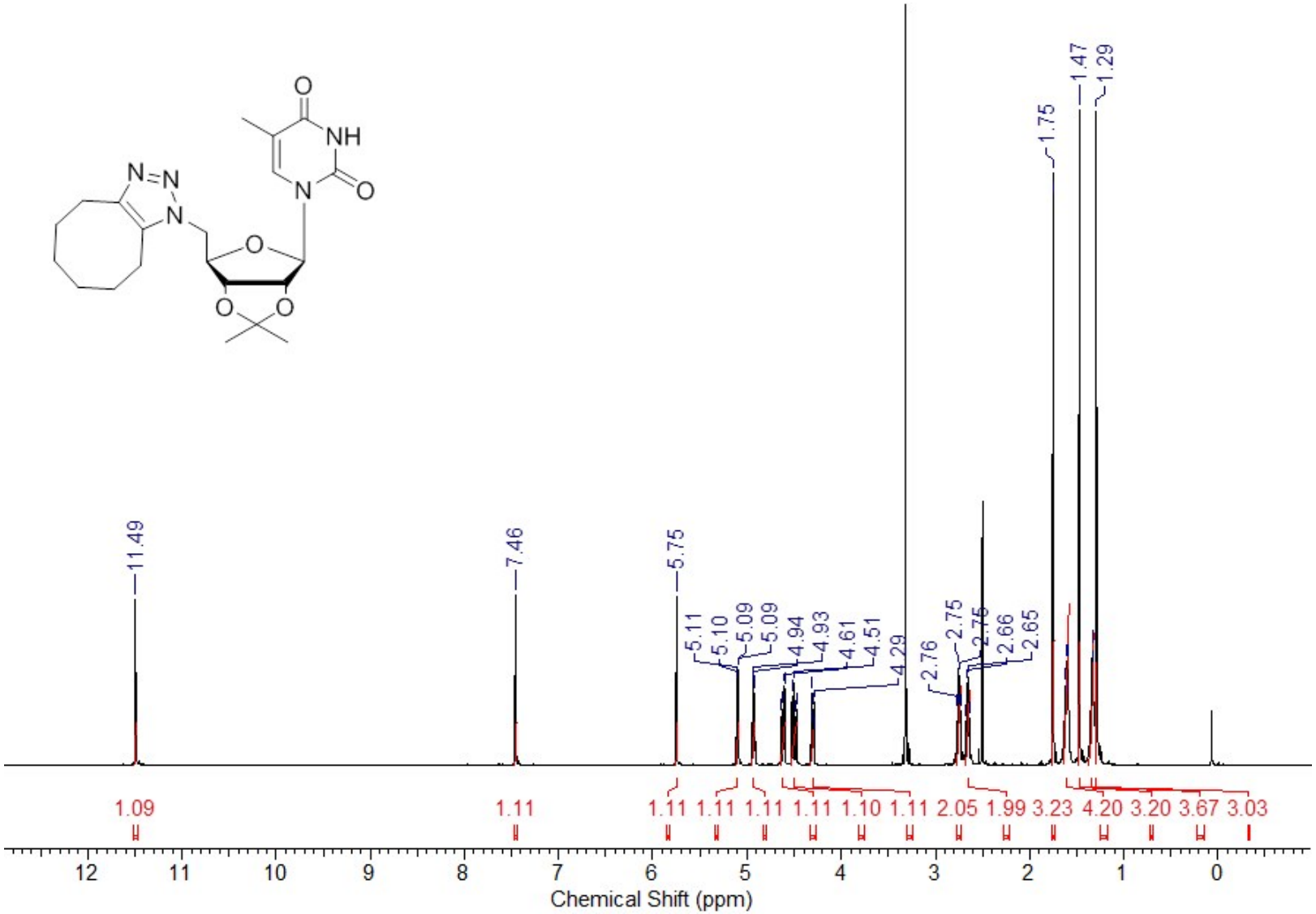


Figure S37. [1]H NMR (DMSO-d_6, 500 MHz): 1-((3a*R*,4*R*,6*R*,6a*R*)-6-((4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)methyl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (**3g**).

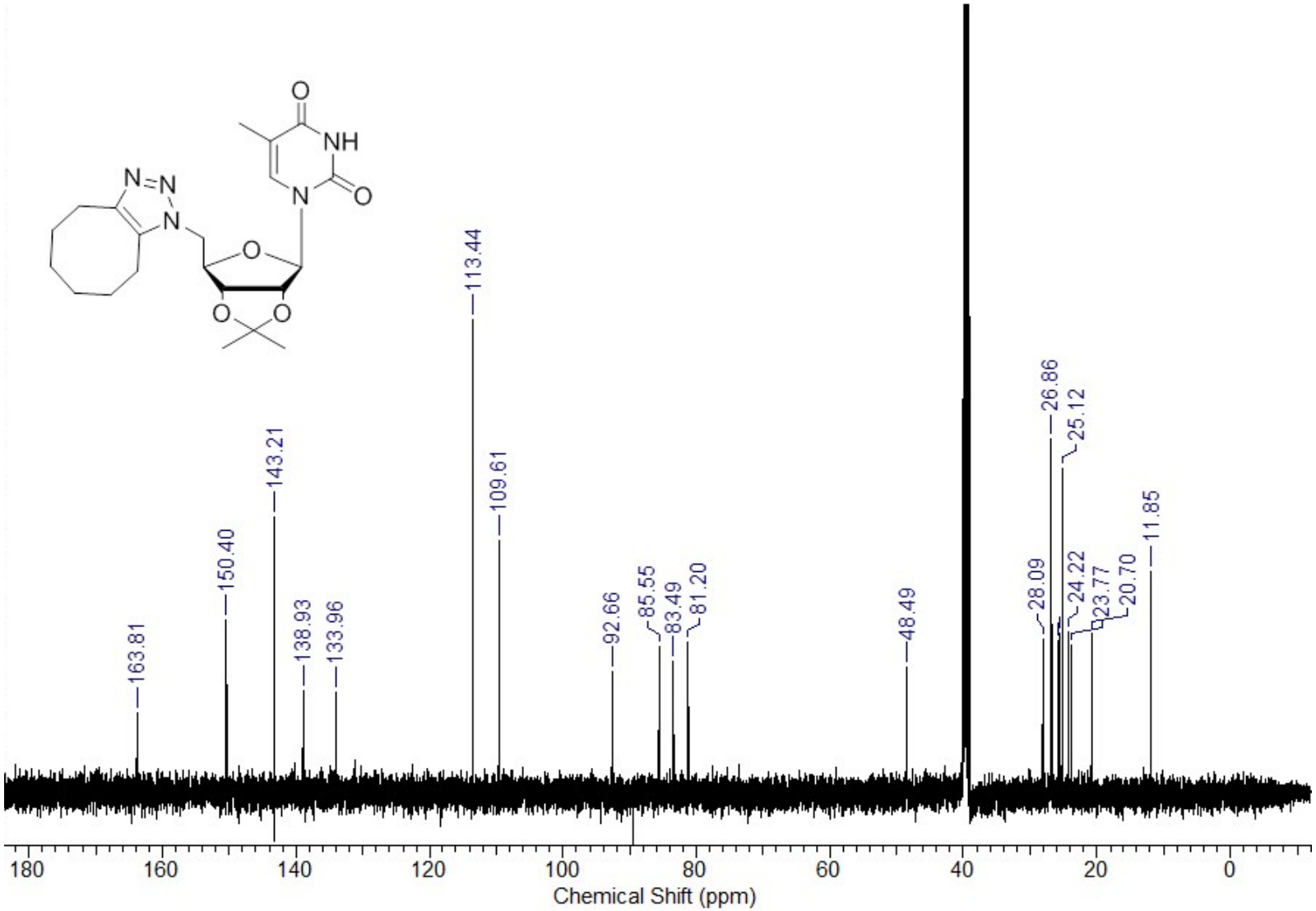


Figure S38. $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz): 1-((3a*R*,4*R*,6*R*,6a*R*)-6-((4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)methyl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (**3g**).

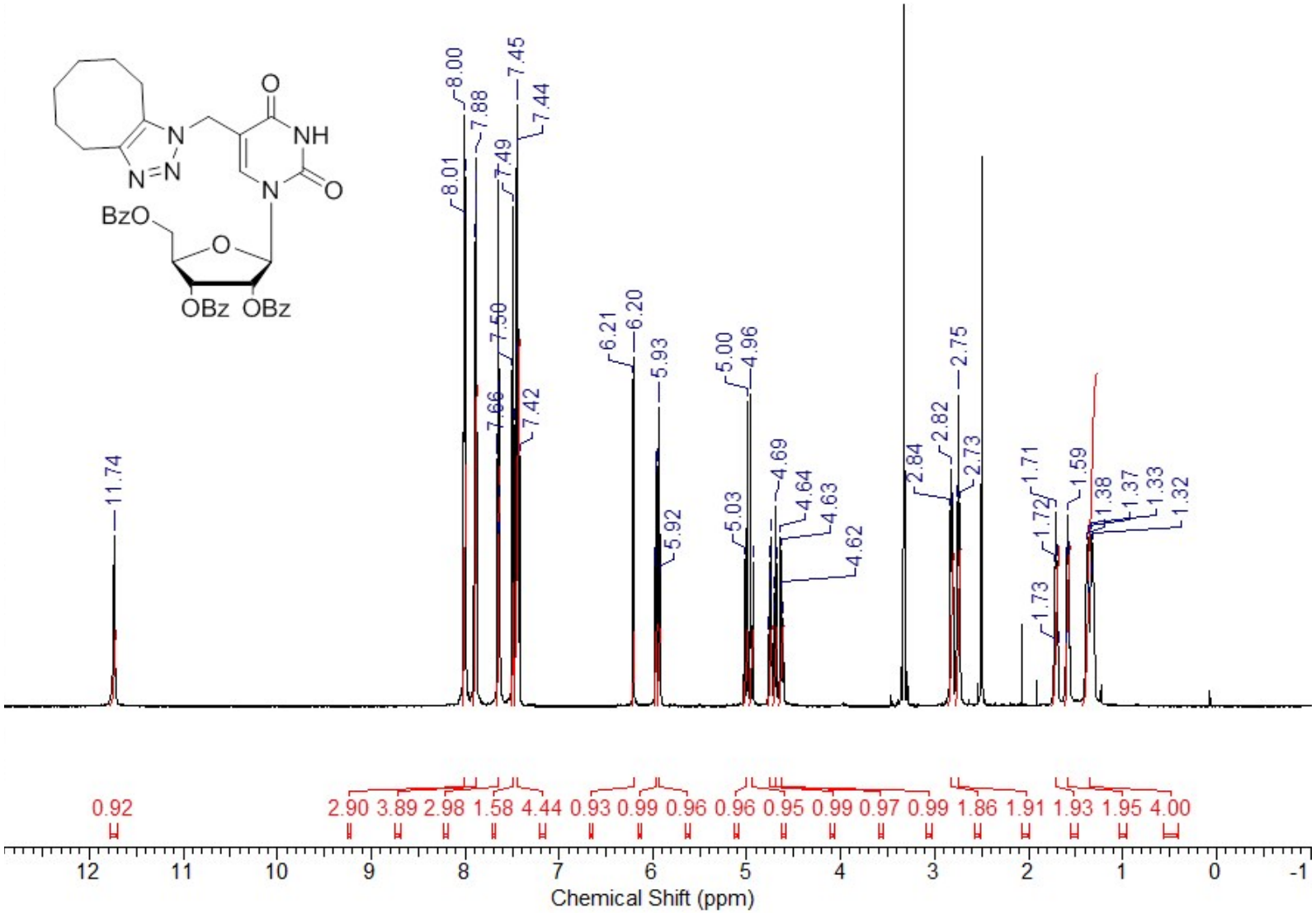


Figure S39. ^{1}H NMR (DMSO-d_6, 126 MHz): (2*R*,3*R*,4*R*,5*R*)-2-((benzoyloxy)methyl)-5-(5-((4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)methyl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)tetrahydrofuran-3,4-diyl dibenzoate (**3h**).

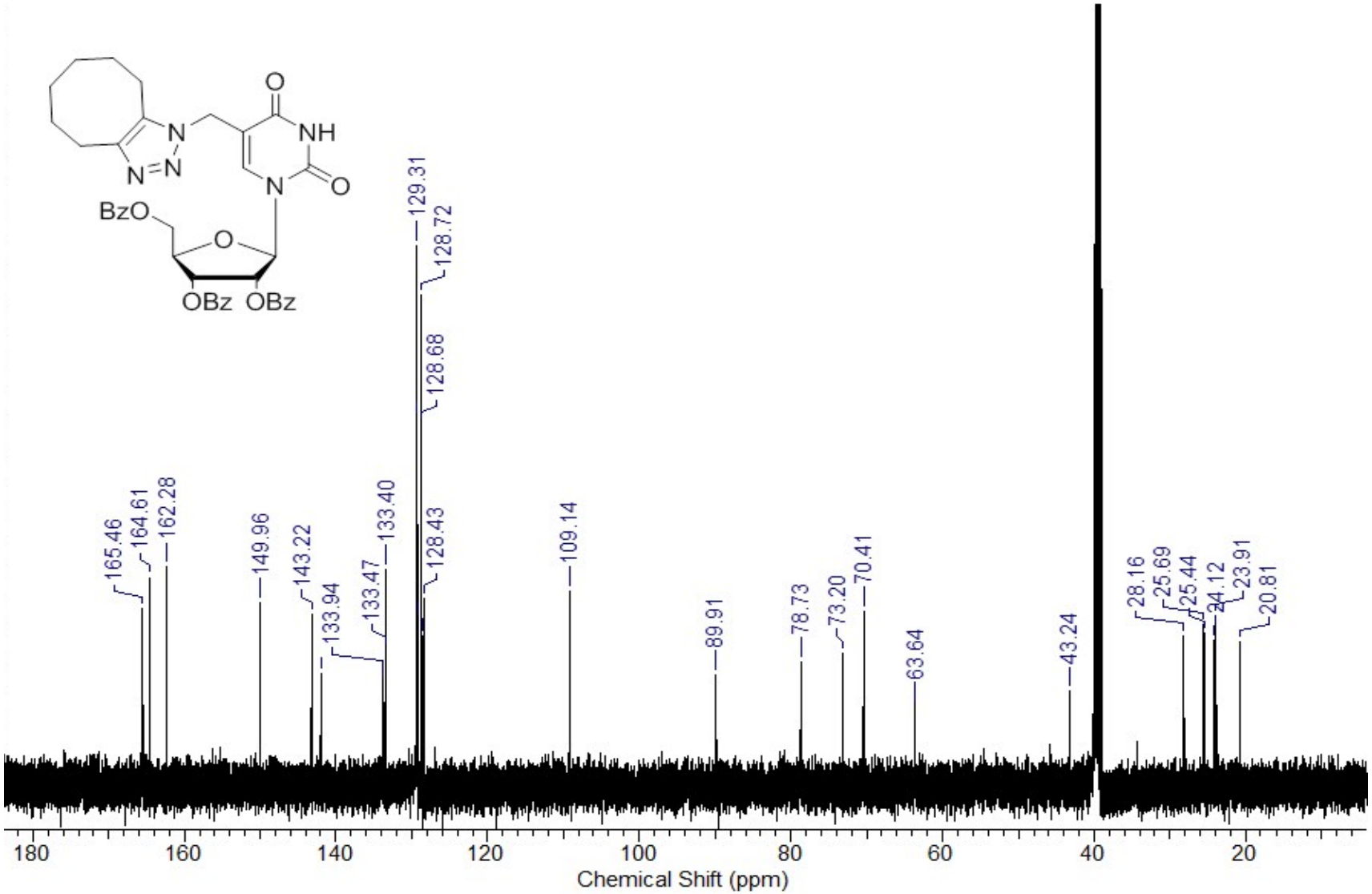


Figure S40. $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz): (2*R*,3*R*,4*R*,5*R*)-2-((benzoyloxy)methyl)-5-(5-((4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)methyl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)tetrahydrofuran-3,4-diyl dibenzoate (**3h**).

1.9.2. NMR spectra of derivatives 4 and 5

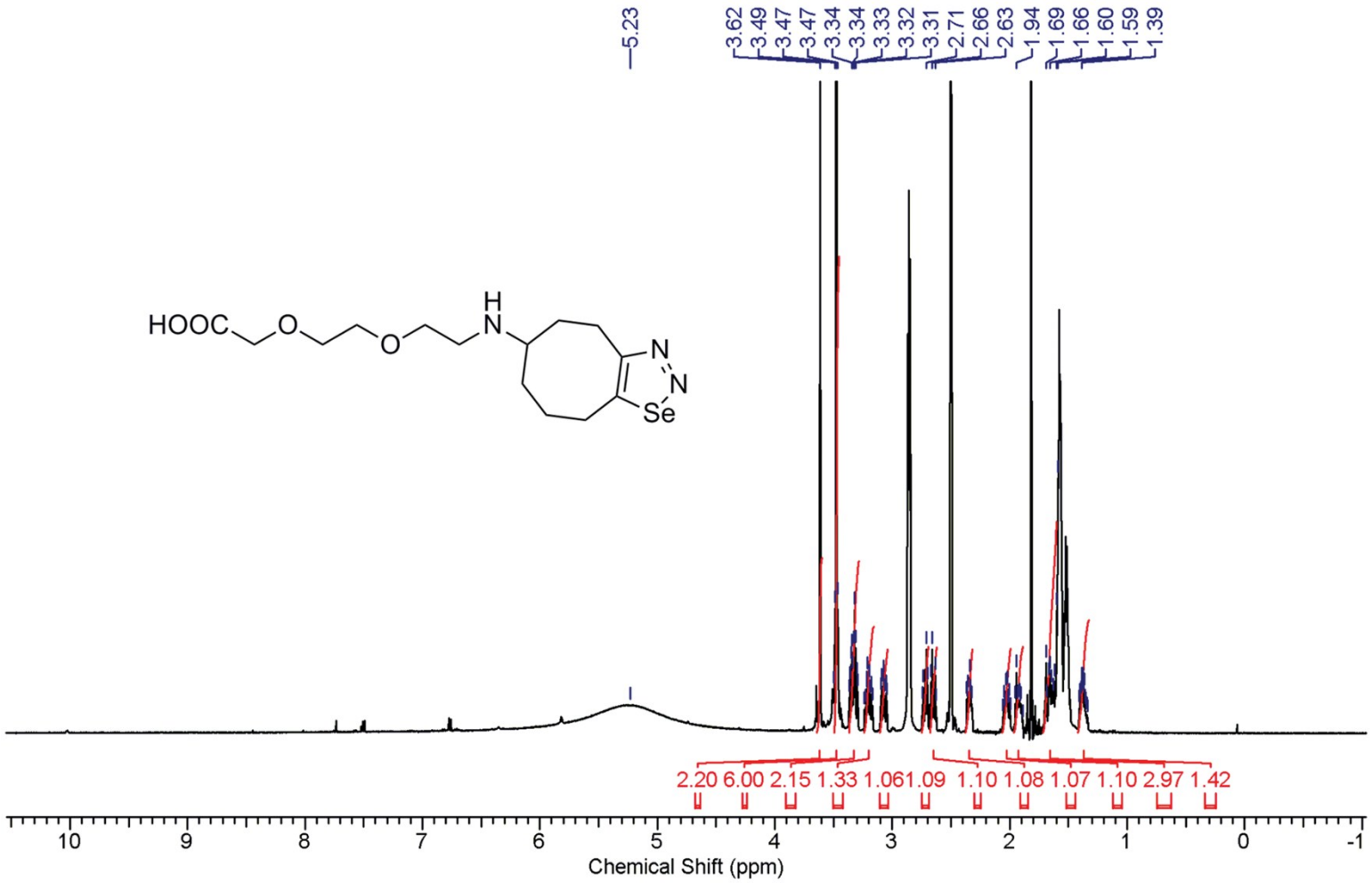


Figure S41. ^{1}H NMR (DMSO-d_6, 500 MHz): 2-(2-(2-((4,5,6,7,8,9-hexahydrocycloocta[d][1,2,3]selenadiazol-6-yl)amino)ethoxy)ethoxy)acetic acid **(4)**. Signals at ppm 1.49–1.54 (m, 2 H), 1.55–1.59 (m, 4 H), 2.83–2.89 (m, 4 H) corresponds to residual piperidine.

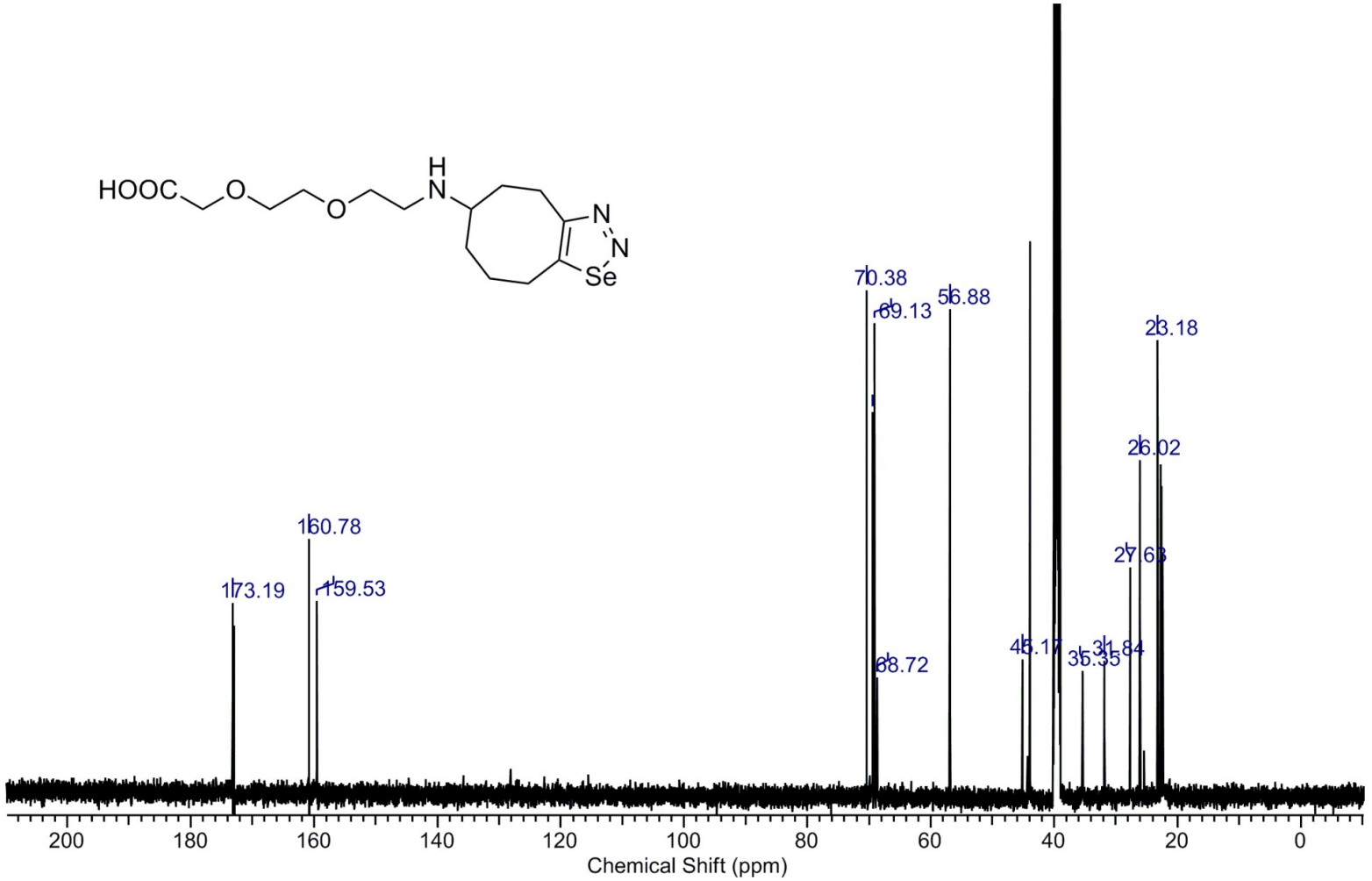


Figure S42. $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz): 2-(2-(2-((4,5,6,7,8,9-hexahydrocycloocta[*d*][1,2,3]selenadiazol-6-yl)amino)ethoxy)ethoxy)acetic acid **(4)**. Signals at ppm 22.36, 22.39, 22.58, 22.70, 43.90 corresponds to residual piperidine.

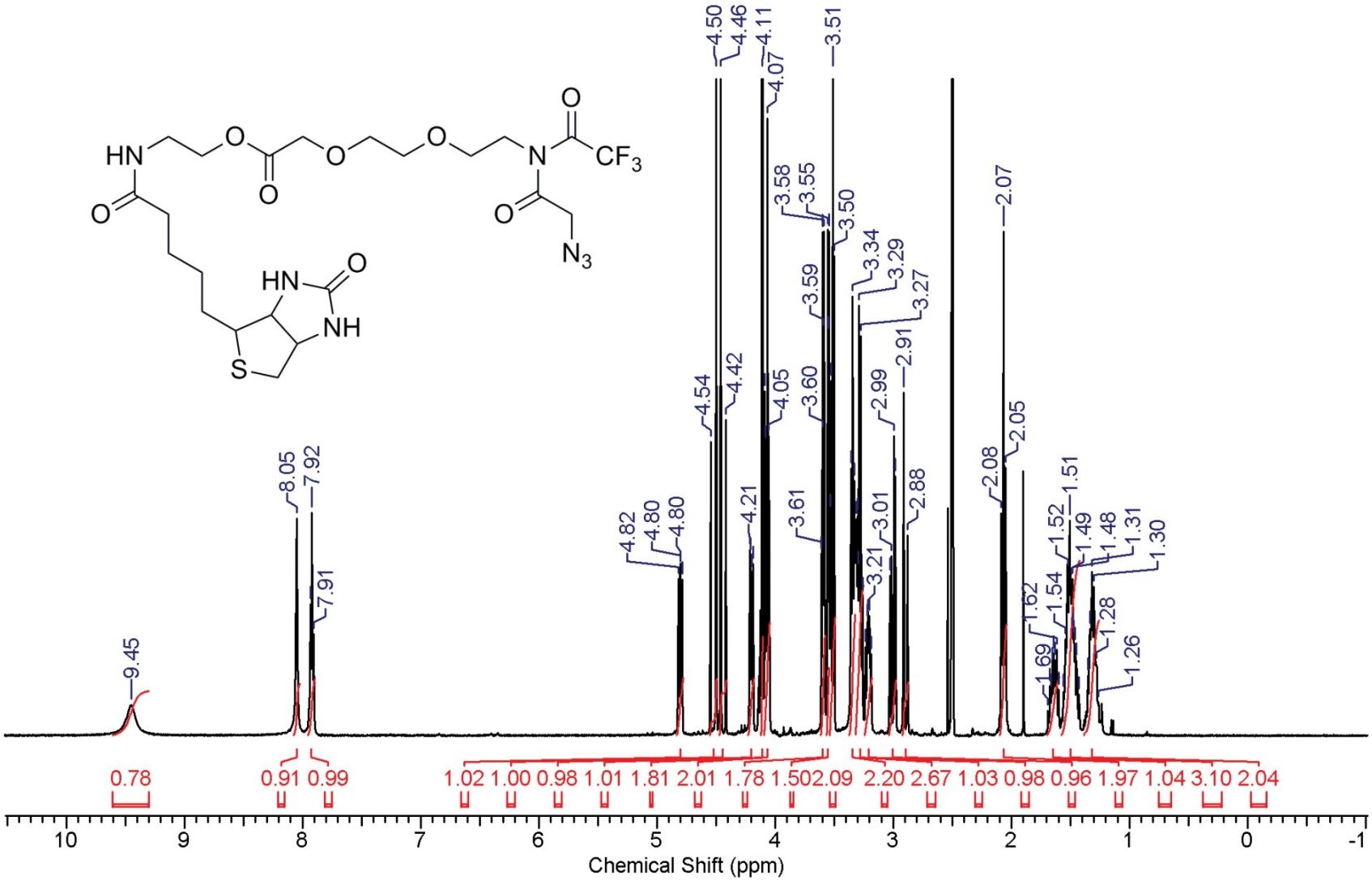


Figure S43. ^{1}H NMR (DMSO-d_6, 500 MHz): (2-(5-(2-oxohexahydro-1*H*-thieno[3,4-d]imidazol-4-yl)pentanamido)ethyl 2-(2-(2-(*N*-(2-azidoacetyl)-2,2,2-trifluoroacetamido)ethoxy)ethoxy)acetate **(5a).**

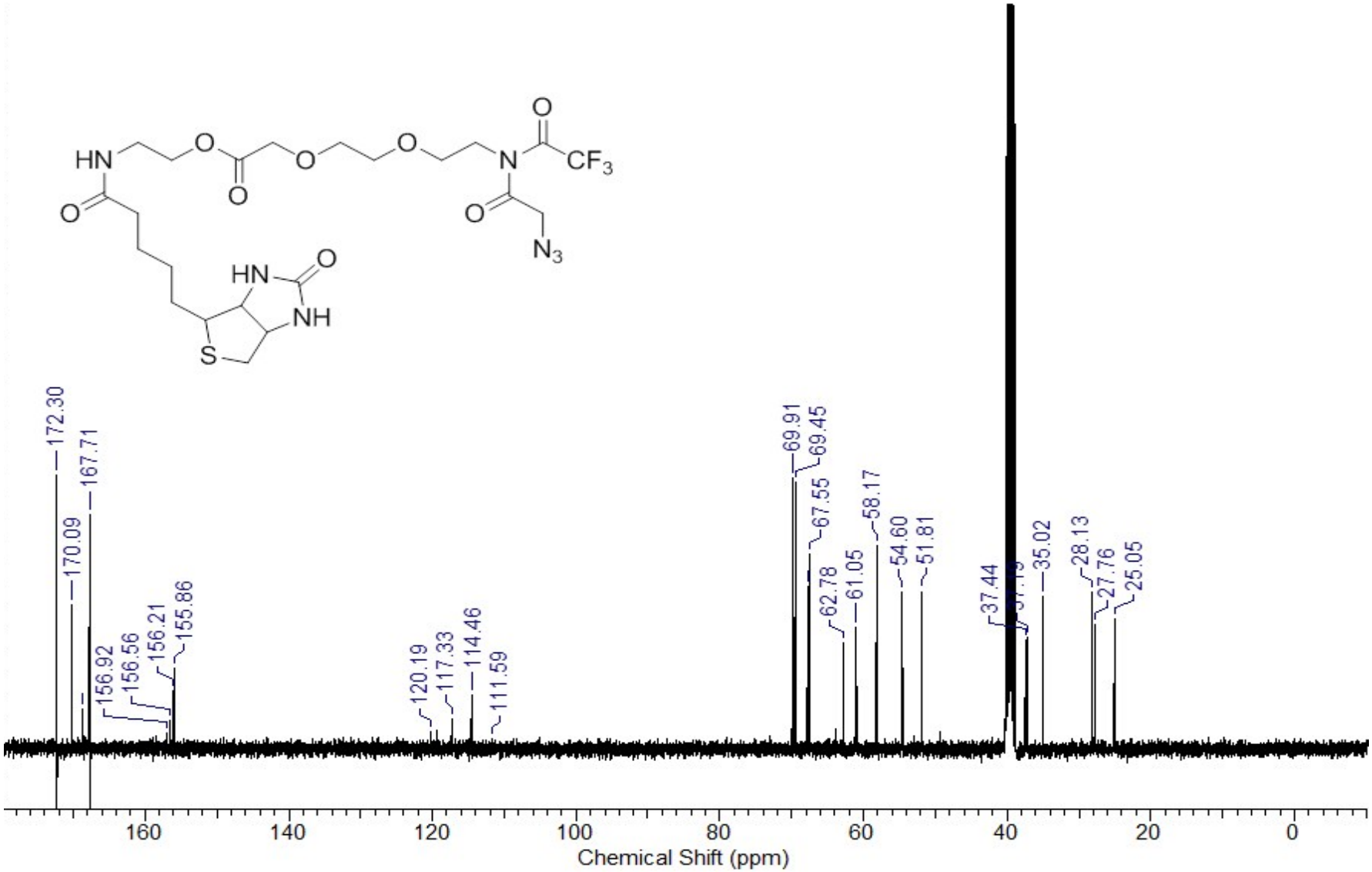


Figure S44. $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz): (2-(5-(2-oxohexahydro-1*H*-thieno[3,4-d]imidazol-4-yl)pentanamido)ethyl 2-(2-(2-(*N*-(2-azidoacetyl)-2,2,2-trifluoroacetamido)ethoxy)ethoxy)acetate **(5a).**

1.9.3. NMR spectra from photoreaction monitoring

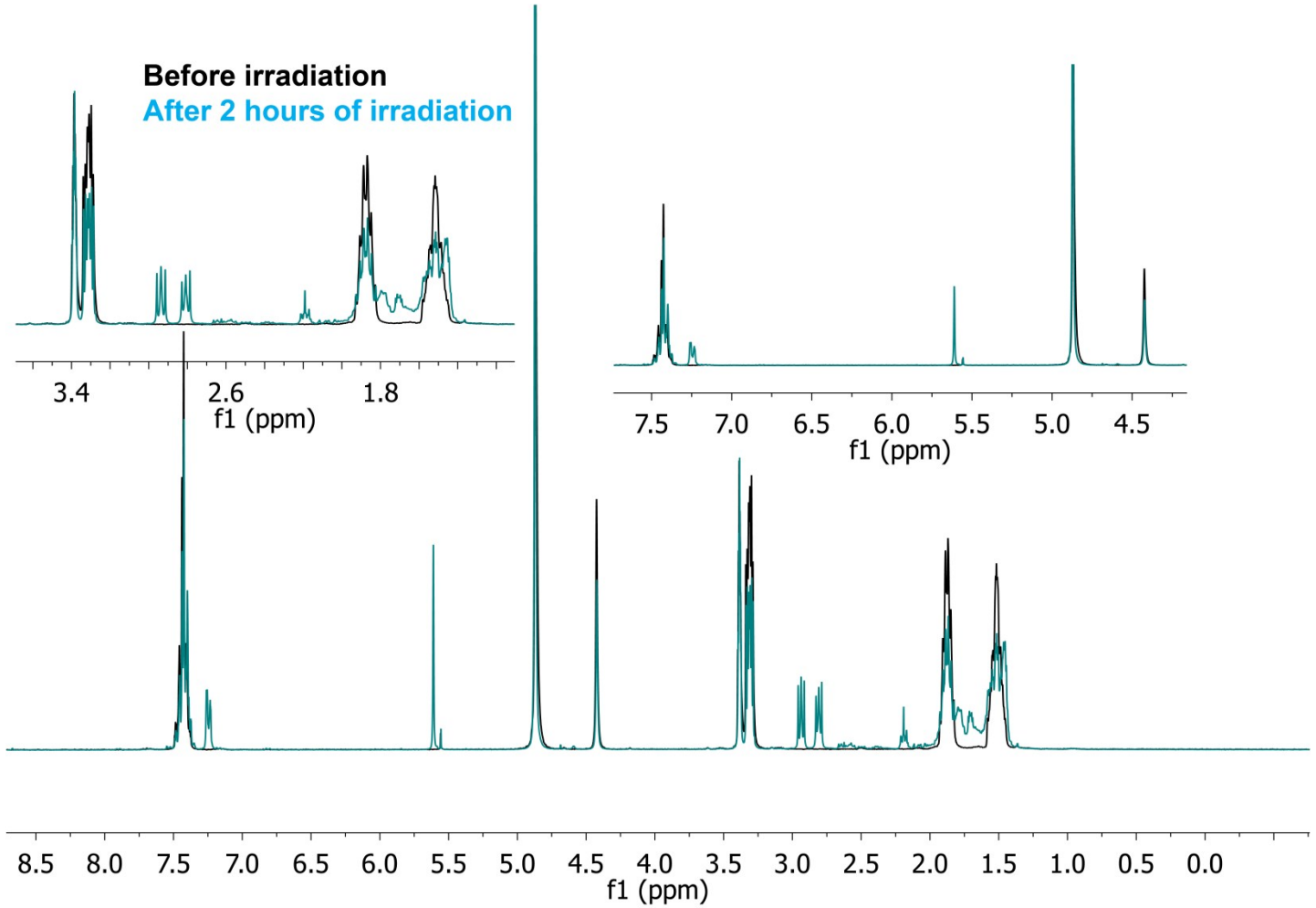


Figure S45. ^{1}H NMR (methanol-d_4, 400 MHz) spectra of mixture of 1,2,3-selenadiazole **1** (c ~ 0.03 mol dm^{-3}) and benzylazide **2e** (c ~ 0.03 mol dm^{-3}) upon irradiation with a medium-pressure mercury arc (Figure S2) filtered through a Pyrex glass of the NMR tube (transparent at λ > 280 nm, Figure S3). Insets shown expanded regions.

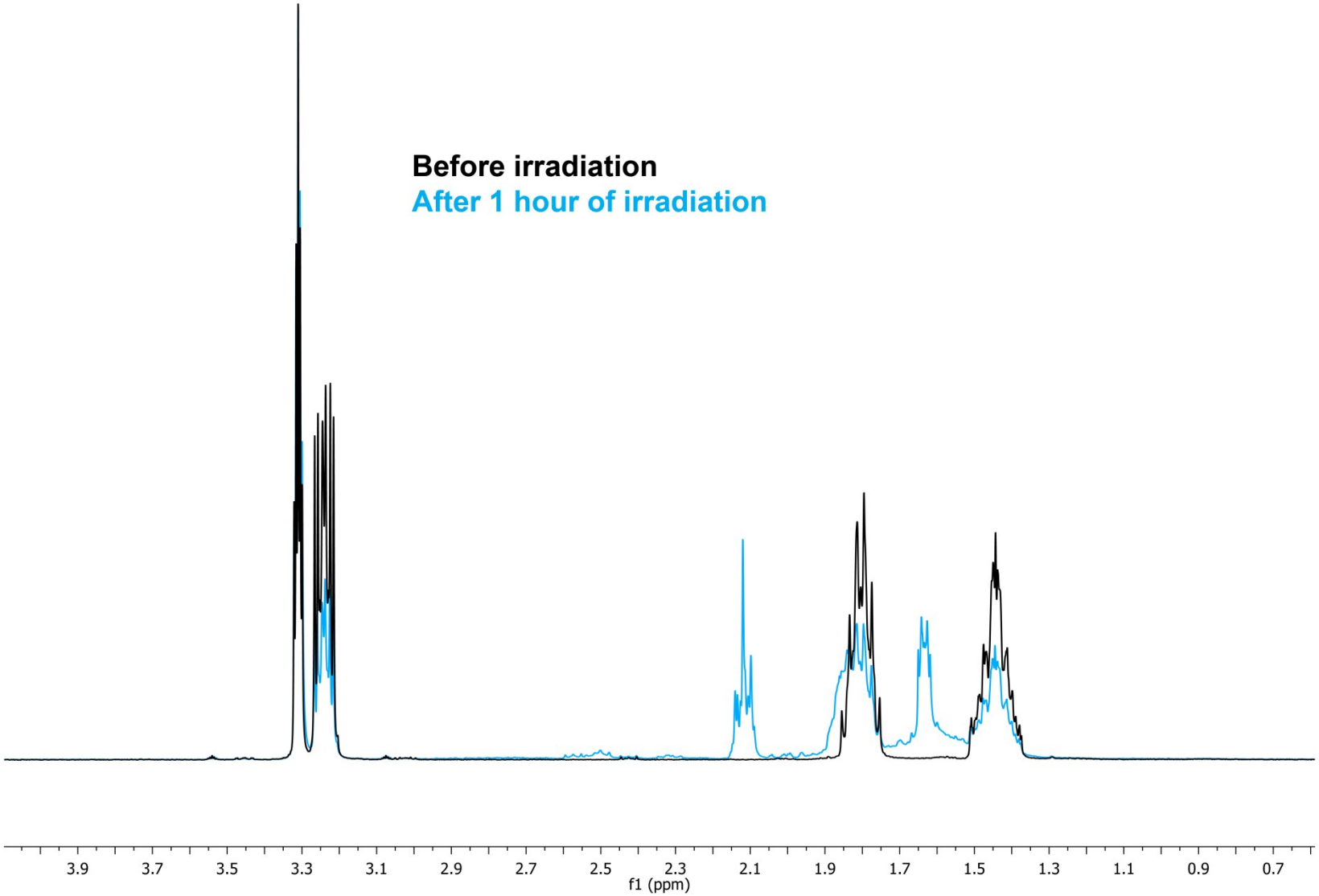


Figure S46. ^{1}H NMR (methanol-d_4, 400 MHz) spectra of cycloocta-1,2,3-selenadiazole **1** ($c \sim 0.4$ mol dm^{-3}) before and after irradiation with a medium-pressure mercury arc (Figure S2) filtered through a Pyrex glass of the NMR tube (transparent at $\lambda > 280$ nm, Figure S3).

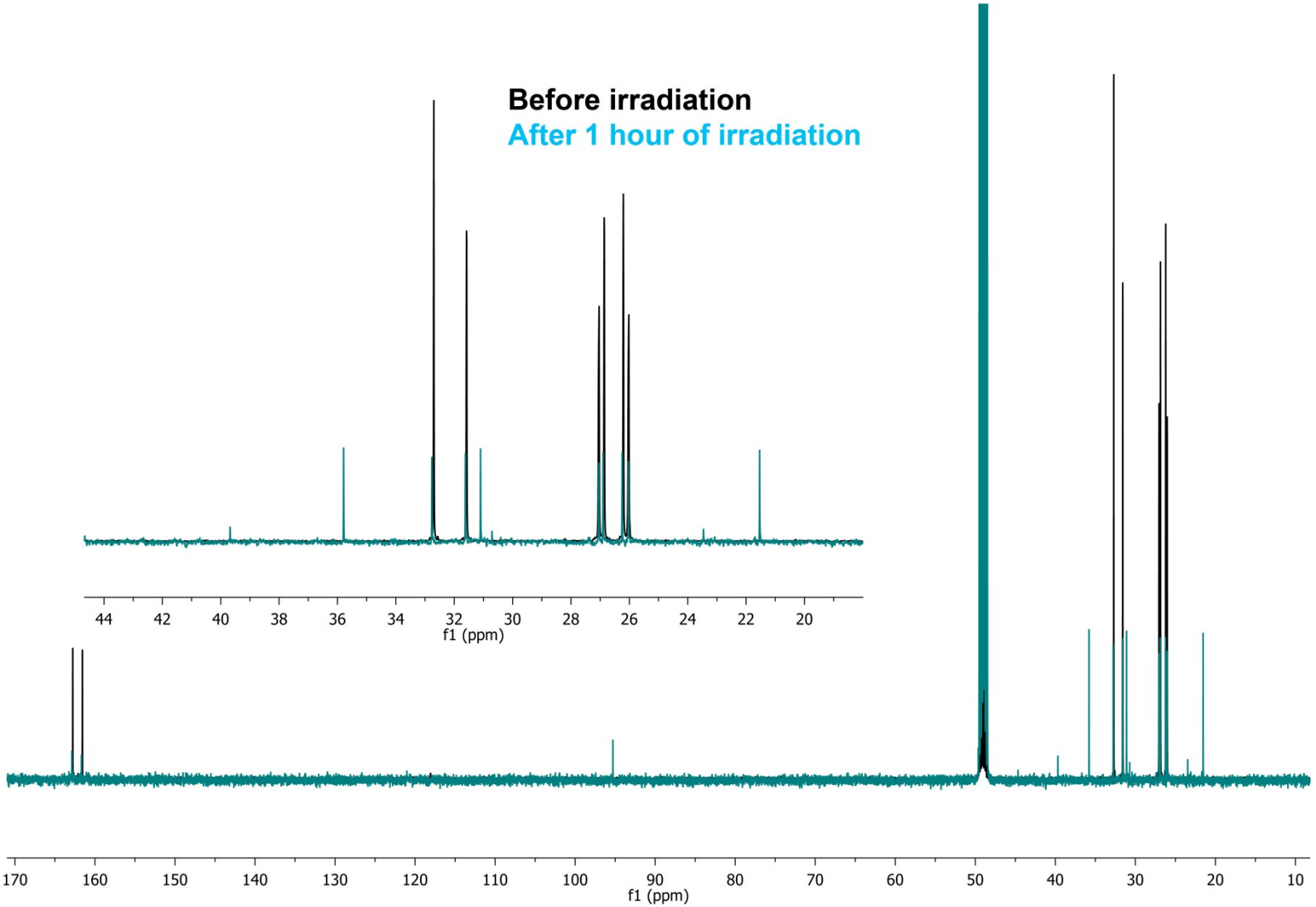


Figure S47. $^{13}C\{^{1}H\}$ NMR spectra (methanol-d_4, 100 MHz) of cycloocta-1,2,3-selenadiazole **1** ($c \sim 0.04$ mol dm^{-3}) before and after irradiation with a medium-pressure mercury arc (Figure S2) filtered through a Pyrex glass of the NMR tube (transparent at $\lambda > 280$ nm, Figure S3).

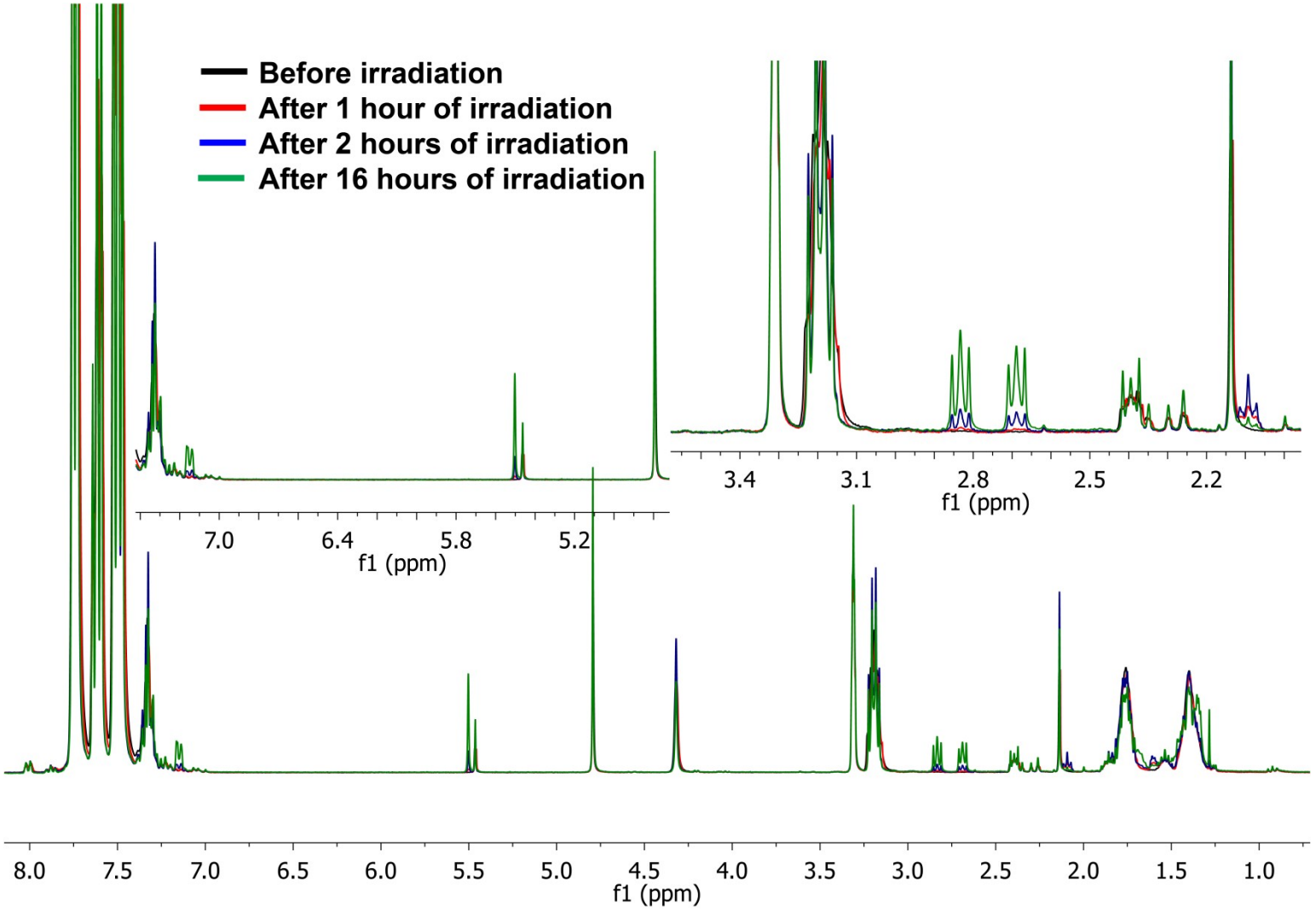


Figure S48. ^{1}H NMR (methanol-d_4, 400 MHz) spectra of mixture of 1,2,3-selenadiazole **1** ($c \sim 0.03$ mol dm^{-3}), benzylazide **2e** ($c \sim 0.03$ mol dm^{-3}) and benzophenone ($c \sim 0.3$ mol dm^{-3}) before and after irradiation with a medium-pressure mercury arc (Figure S2) filtered through a 365 nm filter.

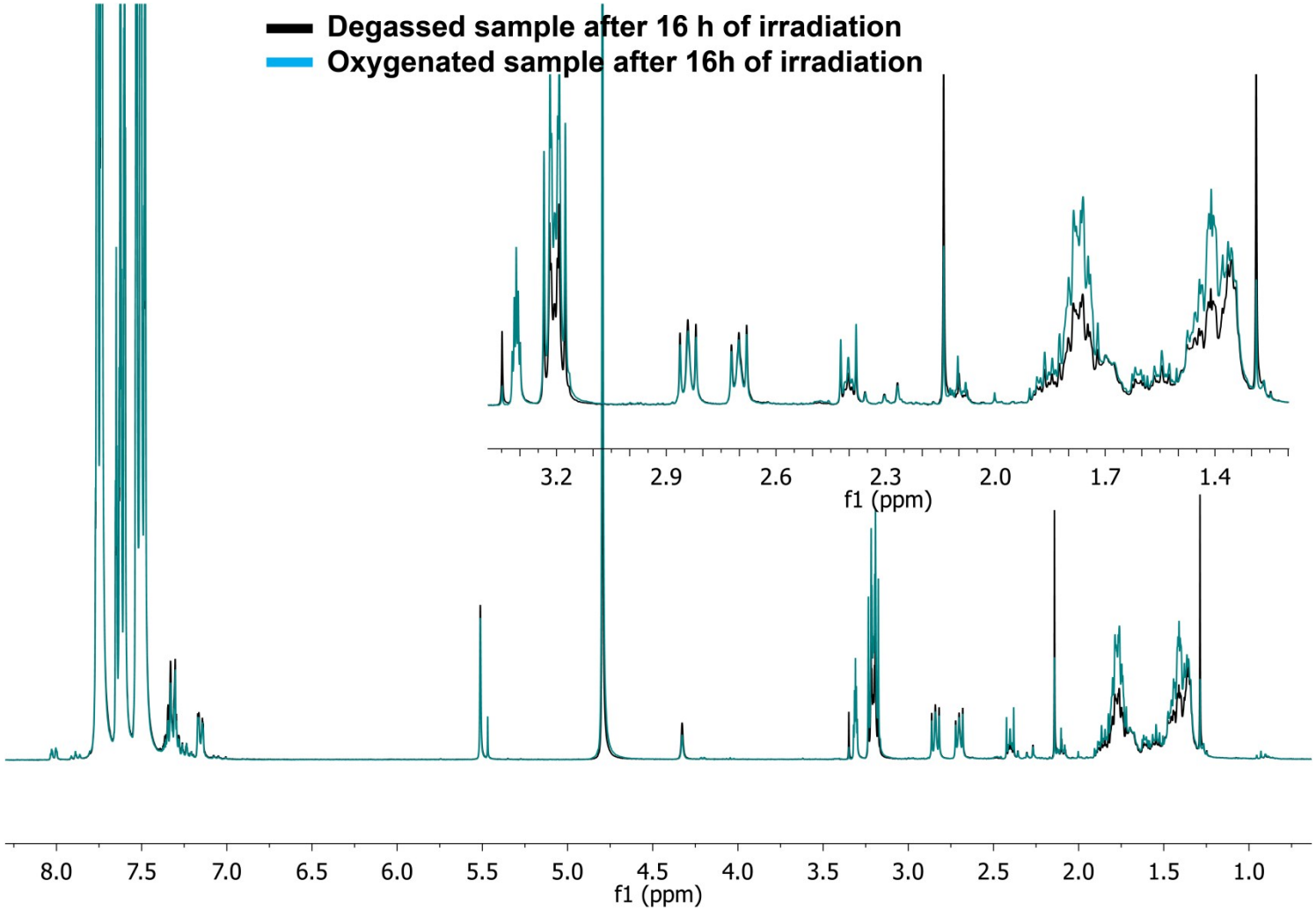


Figure S49. ^{1}H NMR (methanol-d_4, 400 MHz) spectra of mixture of 1,2,3-selenadiazole **1** (c ~ 0.03 mol dm^{-3}), benzylazide **2e** (c ~ 0.03 mol dm^{-3}) and benzophenone (c ~ 0.3 mol dm^{-3}) in degassed and oxygenated samples after 16 hours of irradiation with a medium-pressure mercury arc (Figure S2) filtered through a 365 nm filter.

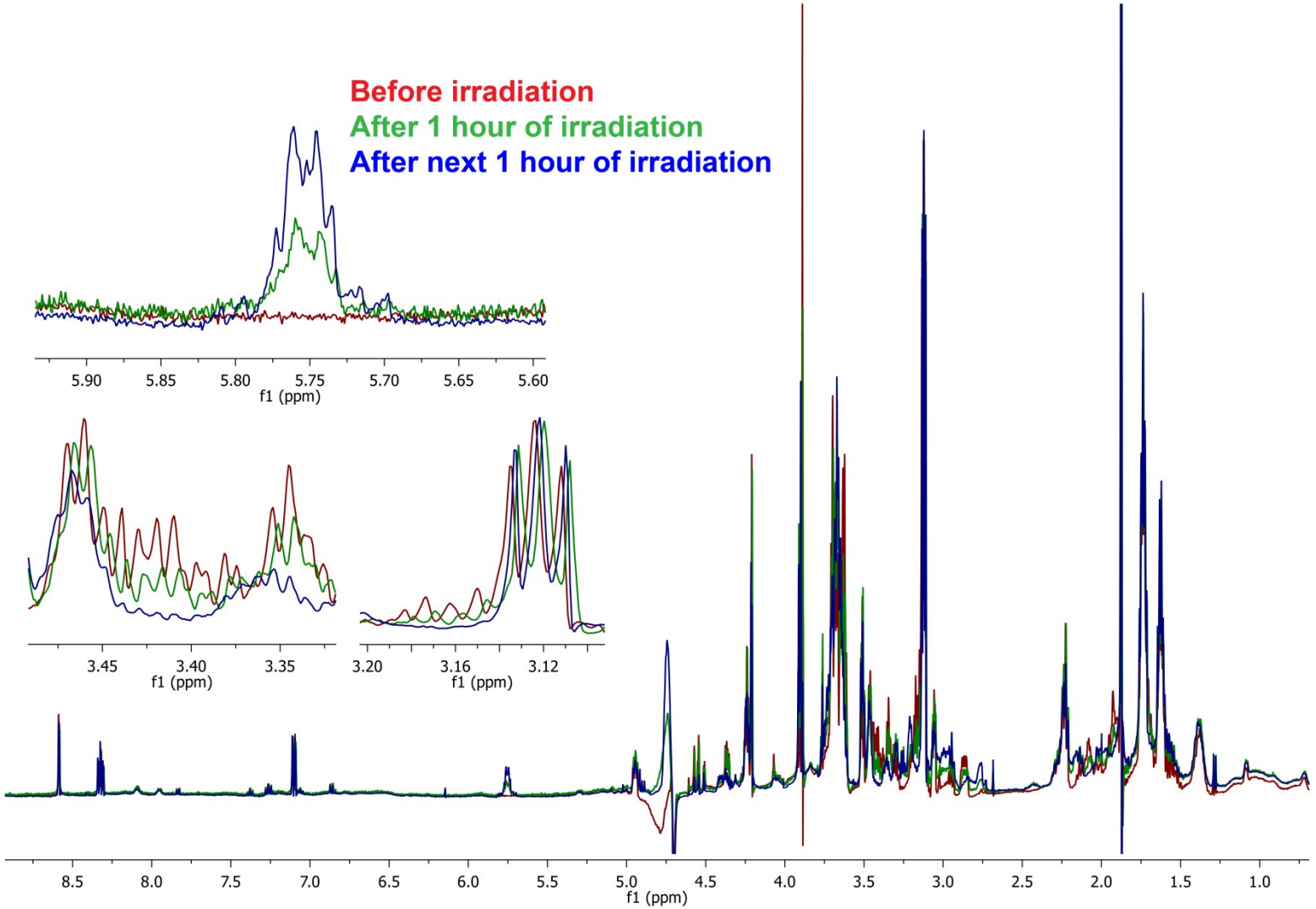


Figure S50. ^{1}H NMR (methanol-d_4, 400 MHz) spectra of reaction between modified biotin **5a** ($c \sim 0.01$ mol dm^{-3}) and cycloocta-1,2,3-selenadiazole **4** ($c \sim 0.01$ mol dm^{-3}) with a medium-pressure mercury arc (Figure S2) filtered through a Pyrex glass of the NMR tube (transparent at $\lambda > 280$ nm, Figure S3).

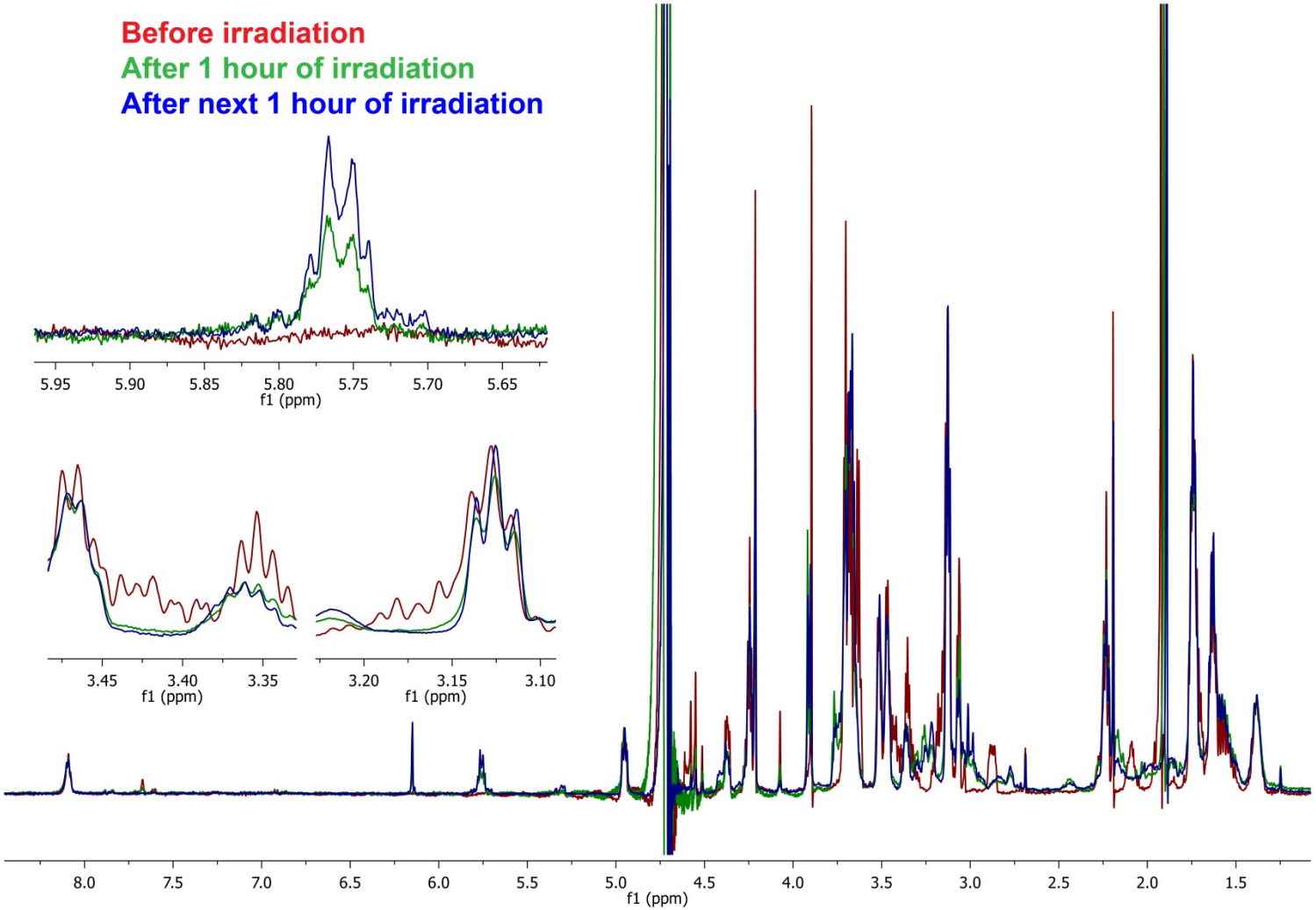


Figure S51. ^{1}H NMR (D_2O, 500 MHz) spectra of reaction between modified biotin **5a** ($c \sim 0.01$ mol dm^{-3}) and cycloocta-1,2,3-selenadiazole **4** ($c \sim 0.01$ mol dm^{-3}) with a medium-pressure mercury arc (Figure S2) filtered through a Pyrex glass of the NMR tube (transparent at $\lambda > 280$ nm, Figure S3).

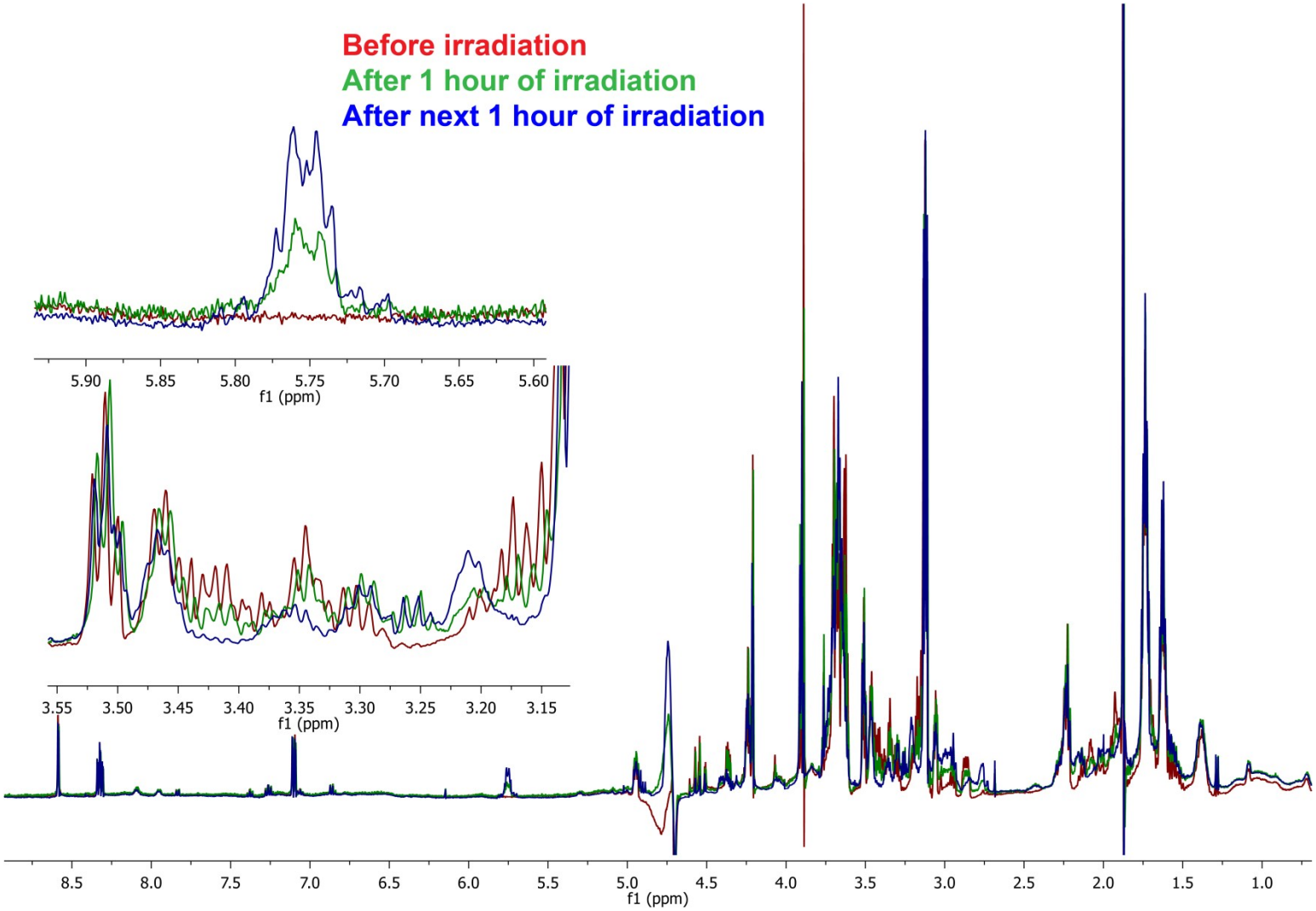


Figure S52. ^{1}H NMR (D_2O, 500 MHz) spectra of reaction between avidin complex **5b** ($c \sim 0.02$ mol dm^{-3}) and cycloocta-1,2,3-selenadiazole **4** ($c \sim 0.02$ mol dm^{-3}) with a medium-pressure mercury arc (Figure S2) filtered through a Pyrex glass of the NMR tube (transparent at $\lambda > 280$ nm, Figure S3).

1.10. LC/MS analysis of reaction between derivatives 4 and 5a.

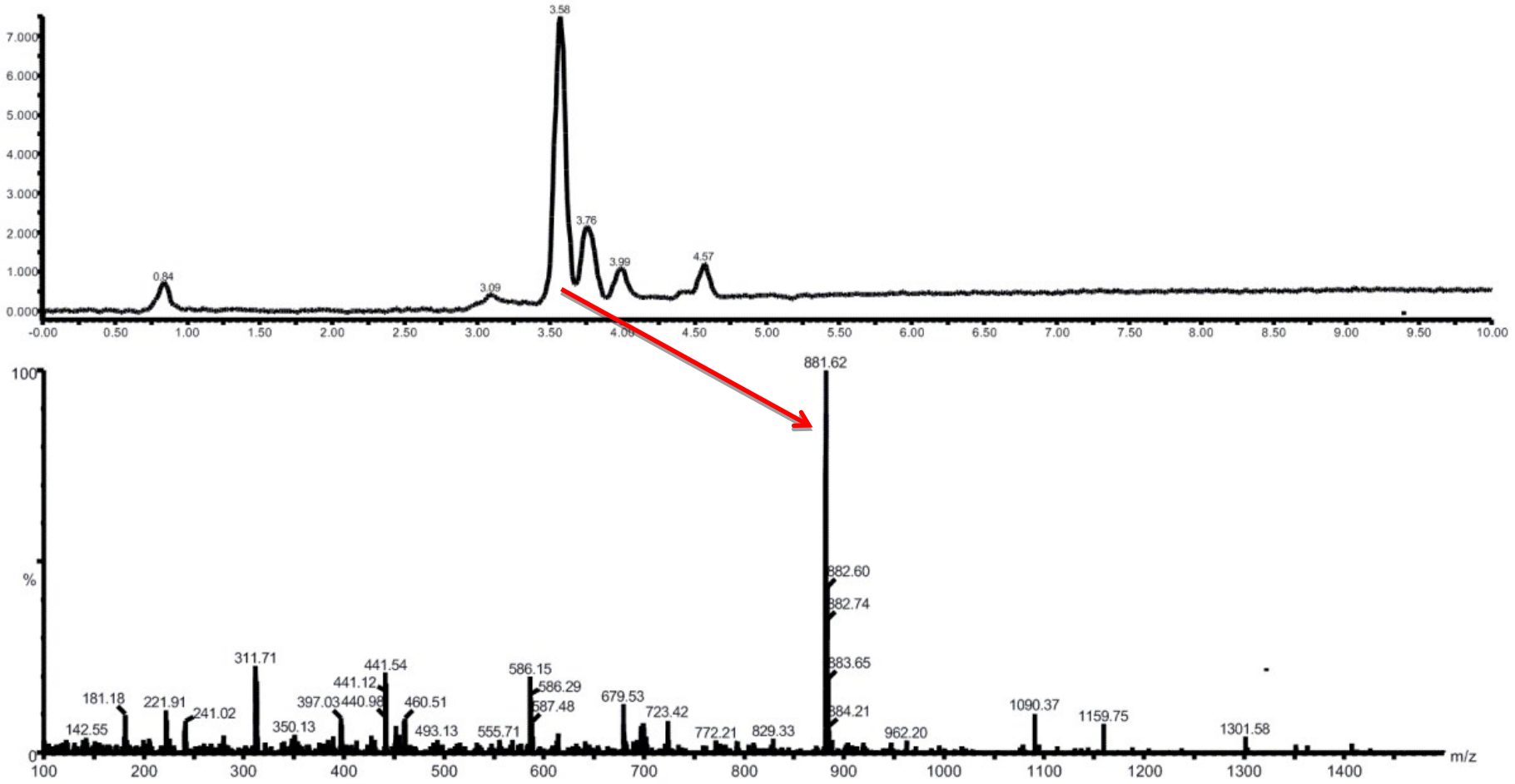


Figure S53. HPLC chromatogram and mass spectrum of products formed by reaction of modified biotin **5a** and cycloocta-1,2,3-selenadiazole **4**.

1.11. MALDI-TOF monitoring of reaction between derivatives 4 and 5b.

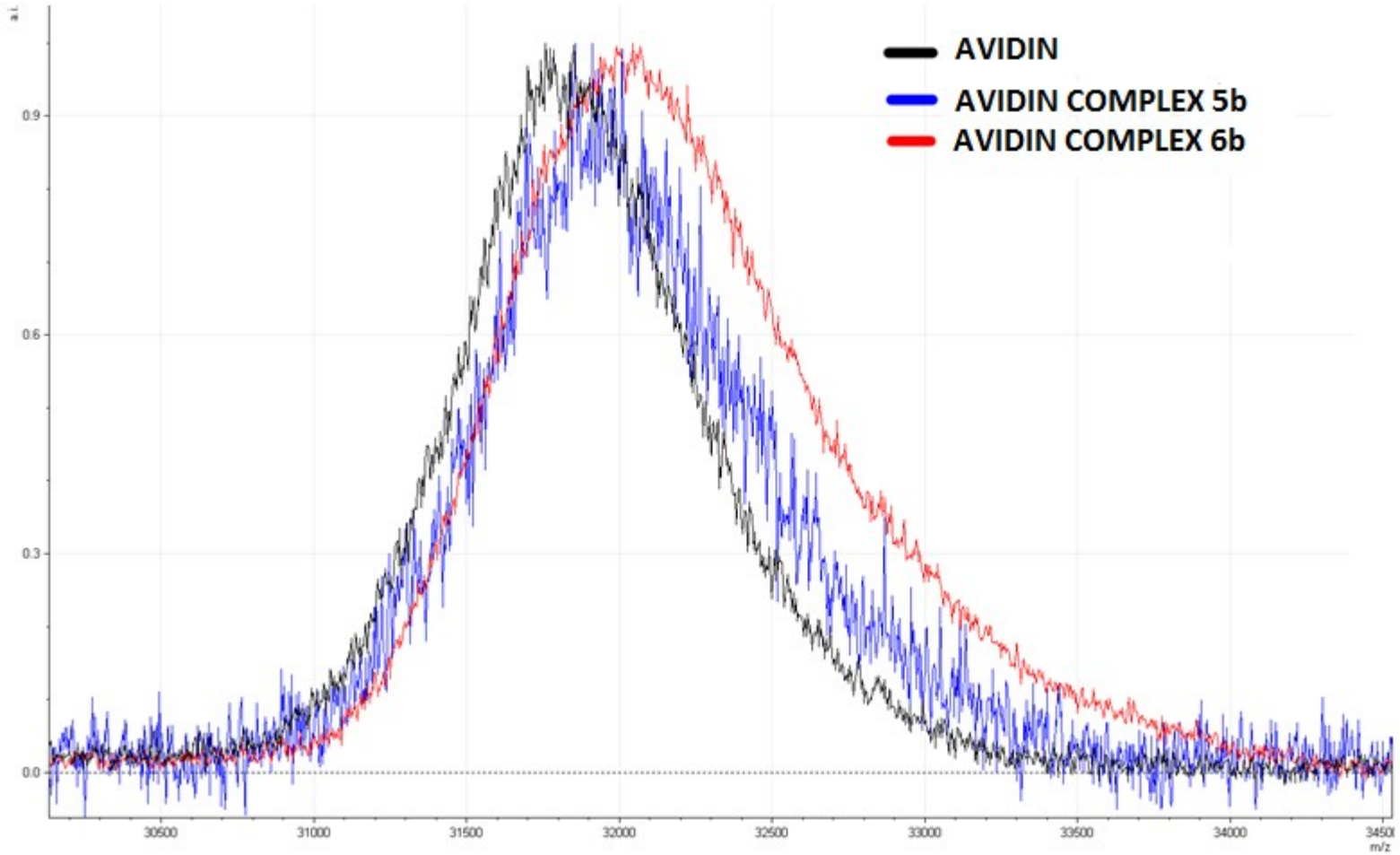


Figure S54. MALDI analysis of avidin, avidin – biotin complex **5b** and product **6b**.

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