Supporting information

Click Chemistry route to tricyclic monosaccharide triazole hybrids: Design & Synthesis of Substituted Hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepines

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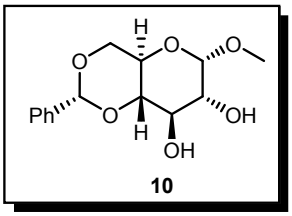
General Information

All reactions were performed using commercially available compounds without further purification. All reactions were carried out under nitrogen atmosphere and monitored by thin-layer chromatography using Merck 60 F_{254} pre coated silica gel plates (0.25 mm thickness). All solvents were purified according to the standard methods. Column chromatography was performed on 230-400 mesh silica gel using hexane and ethylacetate as eluent. Crude reaction mixtures and pure products were analyzed by mass spectrometry. Mass spectra were recorded on a mass spectrometer by the electrospray ionization method (ESI) and the data was acquired in positive ionization mode. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian (400 MHz) spectrometer using $CDCl_3$ as solvent. Chemical shifts (δ) were recorded in ppm with respect to TMS as an internal standard and coupling constants are quoted in Hertz (Hz).

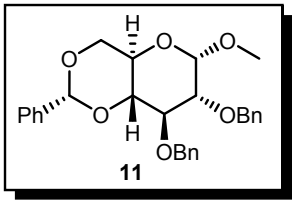
Experimental procedures



10

(4aR,6S,7R,8R,8aS)-6-methoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxine-7,8-diol (10). To a solution of **9** (10 g, 51.54 mmol) in anhydrous DMF, iodine (1.29 g, 5.15 mmol), benzaldehyde dimethyl acetal (8.4 ml, 56.70 mmol) were added and the reaction mixture was stirred at ambient temperature for 12h. The reaction was quenched with aqueous sodium thiosulphate solution and extracted with ethylacetate (3 × 100 mL) and washed with brine and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to obtain the crude product which was purified by flash column chromatography (EtOAc) to provide **10** (10.5 g, 75%) as a white solid.

R_f: 0.5 (8:2 DCM/MeOH); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.50-7.48 (m, 2H), 7.38-7.36 (m, 3H), 5.54 (s, 1H), 4.80 (d, *J* = 4.0 Hz, 1H), 4.30 (dd, *J* = 9.64, 4.4 Hz, 1H), 3.93 (t, *J* = 9.6 Hz, 1H), 3.86-3.71 (m, 2H), 3.68-3.59 (m, 1H), 3.54-3.44 (m, 4H), 2.81 (s, 1H), 2.33 (d, *J* = 8.78 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 136.9, 129.2, 128.3, 126.2, 101.9, 99.7, 80.9, 72.8, 71.7, 68.9, 62.3, 55.5; MS (ESI): 282.7



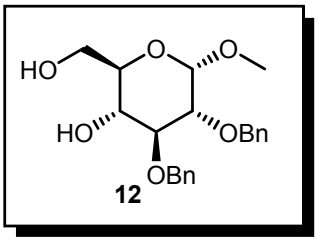
11

(4aR,6S,7R,8S,8aR)-7,8-bis(benzyloxy)-6-methoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxine (11).

To a solution (DMF) of **10** (1.0 equiv, 5.5 g, 19.51 mmol) was added NaH (3.0 equiv, 1.4 g, 58.51 mmol), benzyl bromide (1.0 equiv, 6.95 ml, 58.51 mmol) at 0 °C and the reaction was stirred at ambient temperature. After 24 h, the reaction mixture was quenched with water and extracted with ethylacetate (3 × 100 mL). Combined organic phases were dried over Na_2SO_4,

filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (9:1 hexanes/EtOAc) to provide **11** (9.0 g, 99%) as a white solid.

R_f: 0.6 (1:9 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.49-7.47 (m, 2H), 7.39-7.25 (m, 13H), 5.55 (s, 1H), 4.91 (d, *J* = 11.25 Hz, 1H), 4.85 (dd, *J* = 11.69, 7.45 Hz, 2H), 4.70 (d, *J* = 12.15 Hz, 1H), 4.59 (d, *J* = 3.60 Hz, 1H), 4.27 (dd, *J* = 10.04, 4.71 Hz, 1H), 4.05 (t, *J* = 9.29 Hz, 1H), 3.79-3.87 (m, 1H), 3.71 (t, *J* = 10.27 Hz, 1H), 3.63-3.60 (m, 1H), 3.57-3.54 (m, 1H), 3.40 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 138.7, 138.1, 137.4, 128.9, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.6, 126.0, 101.2, 99.2, 82.1, 79.2, 78.6, 75.3, 73.7, 69.0, 62.3, 55.3; MS (ESI): 462.9

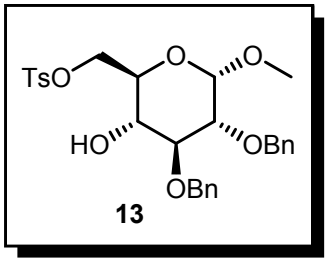


12

(2R,3R,4S,5R,6S)-4,5-bis(benzyloxy)-2-(hydroxymethyl)-6-methoxytetrahydro-2H-pyran-3-ol (12).

To a solution (MeOH) of **11** (1.0 equiv, 8.0 g, 17.31 mmol) was added pTSA (1.0 equiv, 3.2 g, 17.31 mmol) and the reaction was stirred at ambient temperature. The reaction mixture was quenched after 24h with water and extracted with ethylacetate (3 × 50 mL). Combined organic extract was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (1:1 hexanes/EtOAc) to provide **12** (6.0 g, 90%) as a pale yellow solid.

R_f: 0.2 (1:1 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40-7.28 (m, 10H), 5.03 (d, *J* = 11.22 Hz, 1H), 4.78-4.59 (m, 4H), 3.81-3.72 (m, 3H), 3.63-3.60 (m, 1H), 3.55-3.47 (m, 2H), 3.38 (s, 3H), 2.38-2.31 (s, 1H), 2.04-1.88 (s, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 138.6, 137.9, 128.5, 128.4, 128.0, 127.9, 127.9, 127.8, 98.1, 81.3, 79.7, 75.3, 73.1, 70.7, 70.2, 62.2, 55.2; MS (ESI): 375.5

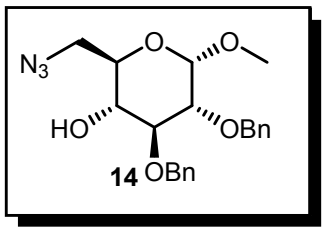


13

((2R,3R,4S,5R,6S)-4,5-bis(benzyloxy)-3-hydroxy-6-methoxytetrahydro-2H-pyran-2-yl)methyl 4-methylbenzenesulfonate (13).

To a solution (DCM) of **12** (1.0 equiv, 6.0 g, 16.04 mmol) was added pyridine (5.0 equiv, 6.4 mL, 80.21 mmol) at 0 ^{o}C and the reaction was stirred for 10 min. Tosyl chloride (2.0 equiv, 6.09 g, 32.08 mmol) was added and the reaction was stirred at ambient temperature. After 24 h, the reaction mixture was quenched with 1N HCl solution and extracted with DCM (3 × 50 mL). Combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced presssure. The crude residue was purified by column chromatography (8:2 hexanes/EtOAc) to provide **13** (7.4 g, 90%) as a gummy liquid.

R_f: 0.7 (1:1 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.77 (d, *J* = 8.29 Hz, 2H), 7.38-7.28 (m, 12H), 4.99 (d, *J* = 11.50 Hz, 1H), 4.75-4.61 (m, 3H), 4.55 (d, *J* = 3.2 Hz, 1H), 4.22 (d, *J* = 3.54 Hz, 2H), 3.76-3.67 (m, 2H), 3.48-3.39 (m, 2H), 3.32 (s, 3H), 2.43 (s, 3H), 2.27 (s, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 144.7, 138.5, 137.8, 132.9, 129.7, 128.6, 128.5, 128.0, 128.0, 127.9, 127.9, 98.0, 81.0, 79.4, 75.4, 73.1, 69.4, 68.9, 68.8, 55.3, 21.6; MS (M+17) (ESI): 545.5



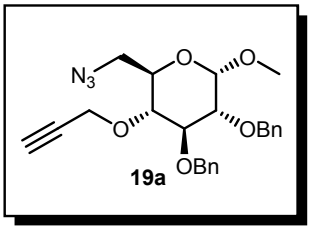
14

(2R,3R,4S,5R,6S)-2-(azidomethyl)-4,5-bis(benzyloxy)-6-methoxytetrahydro-2H-pyran-3-ol (14).

To a solution of **13** (1.0 equiv, 7.0 g, 13.25 mmol) in DMF was added NaN_3 (exess) and the reaction was refluxed at 80 ^{o}C. After 24 h, the reaction mixture was filtered through celite and

extracted with ethylacetate (3 × 50 mL). Combined organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude residue was purified by column chromatography (9:1 hexanes/EtOAc) to provide **14** (5 g, 92%) as a pale yellow oil.

R_f: 0.5 (3:7 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40-7.28 (m, 10H), 5.03 (d, *J* = 11.56 Hz, 1H), 4.76 (d, *J* = 12.06 Hz, 1H), 4.71-4.63 (m, 3H), 3.78-3.69 (m, 2H), 3.53 (dd, *J* = 9.54, 3.54 Hz, 1H), 3.48 (dd, *J* = 13.12, 2.43 Hz, 1H), 3.45-3.36 (m, 6H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 138.5, 137.8, 128.6, 128.5, 128.0, 128.0, 128.0, 127.9, 98.0, 81.0, 79.7, 75.3, 73.1, 70.6, 70.2, 55.3, 51.5; MS (M+17) (ESI): 416.5



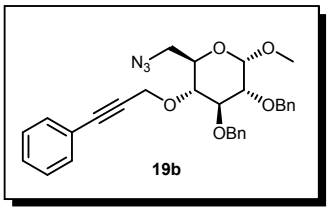
19a

General procedure for alkylation

Compound 19:

To a solution (DMF) of **14** (1.0 equiv, 0.225 mmol) was added NaH (1.5 equiv, 0.338 mmol), **18a-g** (2.0 equiv, 0.45 mmol) at 0 °C and the reaction was stirred at ambient temperature. After 2 h, the reaction mixture was quenched with water and extracted with ethylacetate (3 × 30 mL). Combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced presssure. The crude residue was purified by column chromatography (9:1 hexanes/EtOAc) to provide **19a-g** (90%).

R_f: 0.6 (2:8 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37-7.27 (m, 10H), 4.97 (d, *J* = 10.88 Hz, 1H), 4.76 (dd, *J* = 11.47, 5.39 Hz, 2H), 4.64 (d, *J* = 12.08 Hz, 1H), 4.60 (d, *J* = 3.52 Hz, 1H), 4.38 (dd, *J* = 15.68, 2.37 Hz, 1H), 4.33 (dd, *J* = 15.66, 2.34 Hz, 1H), 3.92 (t, *J* = 9.25 Hz, 1H), 3.75-3.69 (m, 1H), 3.58 (dd, *J* = 13.08, 2.32 Hz, 1H), 3.50 (dd, *J* = 9.64, 3.55 Hz, 1H), 3.45 (dd, *J* = 13.09, 6.24 Hz, 1H), 3.42-3.36 (m, 5H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 138.3, 137.8, 128.4, 128.3, 128.0, 127.9, 127.6, 97.8, 81.6, 79.8, 79.7, 75.6, 74.6, 73.2, 69.5, 59.8, 55.3, 51.3; MS (ESI): 437.5; **M.P:** 146-148 °C

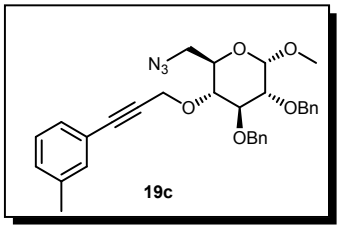


19b

(2R,3R,4S,5R,6S)-2-(azidomethyl)-4,5-bis(benzyloxy)-6-methoxy-3-(3-phenylprop-2-ynyloxy)tetrahydro-2H-pyran (19b).

Pale yellow solid.

R_f: 0.6 (2:8 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.47-7.30 (m, 15H), 5.02 (d, *J* = 10.84 Hz, 1H), 4.82 (t, J = 10.00, 2H), 4.70-3.69 (m, 1H), 4.66-4.56 (m, 3H), 4.00 (t, *J* = 9.26 Hz, 1H), 3.82-3.78 (m, 1H), 3.65 (dd, *J* = 13.04, 2.06 Hz, 1H), 3.56 (dd, *J* = 9.64, 3.53 Hz, 1H), 3.53-3.46 (m, 2H), 3.44 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 138.4, 137.9, 131.7, 128.6, 128.5, 128.4, 128.3, 128.1, 128.0, 127.7, 122.3, 97.9, 86.5, 85.1, 81.7, 79.8, 75.8, 73.3, 69.8, 60.7, 55.4, 51.5; MS (ESI): 513.5; **M.P:** 152-154 ^{o}C



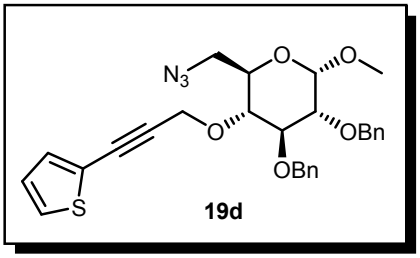
19c

(2R,3R,4S,5R,6S)-2-(azidomethyl)-4,5-bis(benzyloxy)-6-methoxy-3-(3-m-tolylprop-2-ynyloxy)tetrahydro-2H-pyran (19c).

Pale yellow liquid.

R_f: 0.6 (2:8 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.41-7.11 (m, 14H), 4.99 (d, *J* = 11.21, Hz, 1H), 4.79 (dd, *J* = 11.41, 8.22 Hz, 2H), 4.68-4.55 (m, 4H), 3.96 (t, *J* = 9.25 Hz, 1H), 3.80-3.74 (m, 1H), 3.62 (dd, *J* = 13.08, 2.18 Hz, 1H), 3.52 (dd, *J* = 9.66, 3.55 Hz, 1H), 3.49-3.42 (m, 2H), 3.41 (s, 3H), 2.31 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 138.4, 138.0, 137.9, 132.2,

129.4, 128.7, 128.4, 128.4, 128.2, 128.1, 128.0, 128.0, 127.7, 122.1, 97.9, 86.7, 84.7, 81.7, 79.8, 75.7, 73.3, 69.8, 60.7, 55.3, 51.5, 21.2; MS (ESI): 527.5;

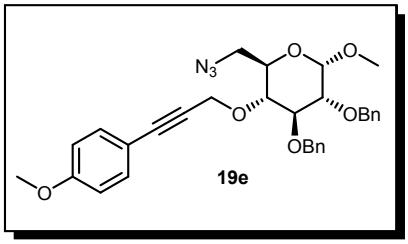


19d

(2R,3R,4S,5R,6S)-2-(azidomethyl)-4,5-bis(benzyloxy)-6-methoxy-3-(3-(thiophen-2-yl)prop-2-ynyloxy)tetrahydro-2H-pyran (19d).

Reddish brown liquid:

R_f: 0.6 (2:8 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40-7.29 (m, 10H), 7.26 (s, 1H), 7.20 (d, *J* = 3.54 Hz, 1H), 6.97 (dd, *J* = 5.05, 3.74 Hz, 1H), 4.99 (d, *J* = 10.88 Hz, 1H), 4.81-4.76 (m, 2H), 4.66 (d, *J* = 12.08 Hz, 1H), 4.59 (dd, *J* = 9.97, 3.92 Hz, 3H), 3.96 (t, *J* = 9.25 Hz, 1H), 3.78-3.72 (m, 1H), 3.60 (dd, *J* = 13.04, 2.21 Hz, 1H), 3.52 (dd, *J* = 9.65, 3.51 Hz, 1H), 3.49-3.43 (m, 2H), 3.42 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 138.3, 137.8, 132.4, 128.4, 128.4, 128.0, 127.9, 127.7, 127.5, 126.9, 97.8, 89.0, 81.7, 79.8, 75.7, 73.3, 69.7, 60.7, 55.3, 51.4; MS (ESI): 519.5



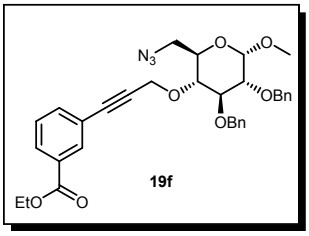
19e

(2R,3R,4S,5R,6S)-2-(azidomethyl)-4,5-bis(benzyloxy)-6-methoxy-3-(3-(4-methoxyphenyl)prop-2-ynyloxy)tetrahydro-2H-pyran (19e).

White solid:

R_f: 0.6 (2:8 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43-7.29 (m, 12H), 6.84 (d, *J* = 8.30 Hz, 2H), 4.98 (d, *J* = 10.80 Hz, 1H), 4.84-4.76 (m, 2H), 4.69-4.52 (m, 4H), 3.97 (t, *J* = 9.20 Hz, 1H), 3.81 (s, 3H), 3.79-3.74 (m, 1H), 3.63-3.60 (m, 1H), 3.56-3.50 (m, 1H), 3.47-3.41 (m,

5H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 159.7, 138.4, 137.9, 133.1, 128.4, 128.4, 128.0, 128.0, 127.9, 127.7, 114.3, 113.9, 97.9, 86.4, 83.6, 81.7, 79.8, 75.7, 73.3, 69.8, 60.8, 55.3, 55.2, 51.5; MS (ESI): 543.5; **M.P:** 140-143 °C

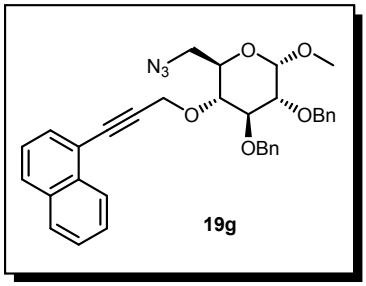


19f

ethyl 3-(3-((2R,3R,4S,5R,6S)-2-(azidomethyl)-4,5-bis(benzyloxy)-6-methoxytetrahydro-2H-pyran-3-yloxy)prop-1-ynyl)benzoate (19f).

Pale yellow solid:

R_f: 0.6 (2:8 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.11 (s, 1H), 8.00 (d, *J* = 7.86 Hz, 1H), 7.58 (d, *J* = 7.73 Hz, 1H), 7.42-7.27 (m, 11H), 5.00 (d, *J* = 10.86 Hz, 1H), 4.80 (dd, *J* = 11.47, 5.00 Hz, 2H), 4.67-4.54 (m, 4H), 4.38 (q, *J* = 7.13 Hz, 2H), 3.97 (t, *J* = 9.24 Hz, 1H), 3.81-3.74 (m, 1H), 3.61 (dd, *J* = 13.10, 2.17 Hz, 1H), 3.53 (dd, *J* = 9.67, 3.52 Hz, 1H), 3.50-3.43 (m, 2H), 3.40 (s, 3H), 1.39 (t, *J* = 7.13 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.7, 138.3, 137.8, 135.7, 132.7, 130.7, 129.5, 128.5, 128.4, 128.0, 128.0, 128.0, 127.7, 122.7, 97.9, 85.9, 85.5, 81.7, 79.8, 75.7, 73.3, 69.7, 61.2, 60.5, 55.4, 51.4, 14.2; MS(M+17) (ESI): 602.4; **M.P:** 147-150 °C



19g

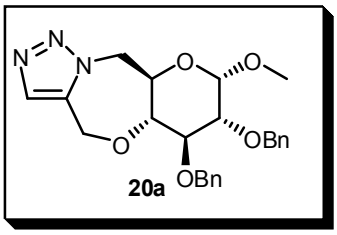
(2R,3R,4S,5R,6S)-2-(azidomethyl)-4,5-bis(benzyloxy)-6-methoxy-3-(3-(naphthalen-1-yl)prop-2-ynyloxy)tetrahydro-2H-pyran (19g).

Pale yellow solid:

R_f: 0.6 (2:8 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.29 (d, *J* = 8.08 Hz, 1H), 7.88-7.82 (m, 2H), 7.67 (d, *J* = 7.08 Hz, 1H), 7.59-7.48 (m, 2H), 7.45-7.28 (m, 11H), 5.02 (d, *J* = 10.80, 1H), 4.88-4.72 (m, 4H), 4.70-4.60 (m, 3H), 4.01 (t, *J* = 9.22 Hz, 1H), 3.83-3.78 (m, 1H), 3.66 (dd, *J* = 13.07, 2.03 Hz, 1H), 3.59-3.45 (m, 4H), 3.42-3.40 (m, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 138.3, 137.8, 133.1, 132.9, 130.6, 128.9, 128.3, 128.3, 128.1, 127.9, 127.8, 127.6, 126.6, 126.2, 125.8, 125.0, 119.8, 97.8, 89.7, 84.4, 81.6, 79.7, 75.6, 73.2, 69.7, 60.7, 55.2, 51.4; MS (ESI): 563.5; **M.P:** 174-176 °C

General procedure for click reaction:

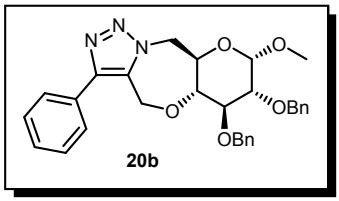
The solution (DMF) of **19a-g** (1.0 equiv, 0.183 mmol) was refluxed at 140 °C. After 24 h, the reaction mixture was filtered through celite and extracted with ethylacetate (3 × 30 mL). Combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced presssure. The crude residue was purified by column chromatography (8:2 hexanes/EtOAc) to provide **20a-g** (99%):



20a

Compound 20a: White solid

R_f: 0.3 (1: 1 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.57 (s, 1H), 7.40-7.28 (m, 10H) 5.10-5.03 (m, 2H), 4.84-4.81 (m, 3H), 4.67 (d, *J* = 12.15 Hz, 1H), 4.58 (d, *J* = 3.55 Hz, 1H), 4.47 (d, *J* = 14.88 Hz, 1H), 4.23 (dd, *J* = 14.07, 10.63 Hz, 1H), 3.86 (t, *J* = 9.18 Hz, 1H), 3.75 (dt, *J* = 10.46, 2.98 Hz, 1H), 3.56-3.50 (m, 2H), 3.40 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 138.7, 137.9, 136.4, 132.7, 128.4, 128.3, 128.0, 127.9, 127.9, 127.6, 98.4, 88.4, 79.4, 78.6, 76.2, 73.6, 65.9, 62.0, 55.8, 52.9; MS (ESI): 438.1; **M.P:** 148-150 °C; HRMS calc for $C_{24}H_{27}N_3O_5$ $[M+H]^+$: 438.2023; found 438.1988.

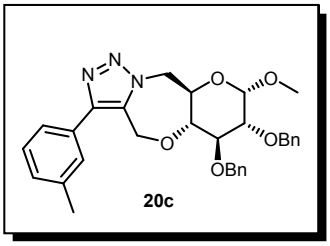


20b

(5aR,6S,7R,8S,9aR)-6,7-bis(benzyloxy)-8-methoxy-3-phenyl-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine (20b).

White solid.

R_f: 0.3 (1: 1 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.56-7.54 (m, 2H), 7.47 (t, 2H), 7.43-7.26 (m, 11H), 5.27 (s, 1H), 5.08 (dd, *J* = 14.04, 2.99 Hz, 1H), 4.83 (t, 3H), 4.67 (d, *J* = 12.15 Hz, 1H), 4.60-4.54 (m, 2H), 4.29 (dd, *J* = 14.01, 10.68 Hz, 1H), 3.89-3.76 (m, 2H), 3.61-3.50 (m, 2H), 3.41 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 145.8, 138.7, 137.9, 133.0, 130.3, 128.8, 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.6, 98.5, 88.5, 79.3, 78.6, 76.2, 73.6, 65.8, 62.1, 55.8, 53.3; MS (ESI): 513.5; **M.P:** 158-161 °C; HRMS calc for $C_{30}H_{31}N_3O_5$ $[M+H]^+$: 514.2336; found 514.2307.

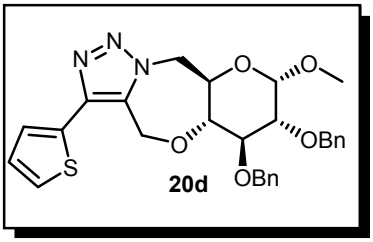


20c

(5aR,6S,7R,8S,9aR)-6,7-bis(benzyloxy)-8-methoxy-3-m-tolyl-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine (20c).

Pale yellow solid.

R_f: 0.3 (1: 1 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43-7.20 (m, 14H), 5.28 (d, *J* = 8.00, 1H), 5.08 (dd, *J* = 14.04, 3.03 Hz, 1H), 4.84-4.81 (m, 3H), 4.67 (d, *J* = 12.16 Hz, 1H), 4.58-4.54 (m, 2H), 4.29 (dd, *J* = 14.01, 10.66 Hz, 1H), 3.90-3.76 (m, 2H), 3.60-3.49 (m, 2H), 3.40 (s, 3H), 2.42 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 138.7, 138.6, 137.9, 132.8, 130.2, 129.1, 128.7, 128.6, 128.4, 128.3, 128.0, 127.9, 127.9, 127.6, 124.9, 98.4, 88.5, 79.3, 78.5, 76.1, 73.6, 65.8, 62.1, 55.7, 53.3, 21.4; MS (ESI): 527.5; **M.P:** 156-158 °C; HRMS calc for $C_{31}H_{33}N_3O_5$ $[M+H]^+$: 528.2493; found 528.2431.

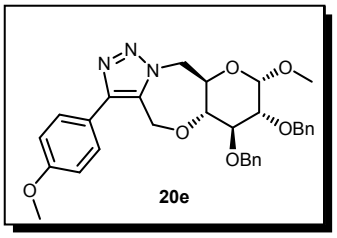


20d

(5aR,6S,7R,8S,9aR)-6,7-bis(benzyloxy)-8-methoxy-3-(thiophen-2-yl)-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine (20d).

Pale yellow solid:

R_f: 0.3 (1: 1 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.42-7.26 (m, 12H), 7.13 (dd, *J* = 4.91, 3.71 Hz, 1H), 5.35 (d, *J* = 15.09 Hz, 1H), 5.06 (dd, *J* = 14.07, 2.97 Hz, 1H), 4.84-4.82 (m, 3H), 4.67 (d, *J* = 12.13 Hz, 1H), 4.58-4.53 (m, 2H), 4.27 (dd, *J* = 14.02, 10.69 Hz, 1H), 3.86 (t, *J* = 9.20 Hz, 1H), 3.79 (dt, *J* = 10.60, 2.88 Hz, 1H), 3.60-3.50 (m, 2H), 3.40 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 140.3, 138.6, 137.9, 132.4, 131.7, 128.4, 128.3, 128.0, 128.0, 127.9, 127.6, 126.1, 125.6, 98.4, 88.5, 79.3, 78.5, 76.1, 73.6, 65.7, 61.9, 55.8, 53.3; MS (ESI): 519.4; **M.P:** 172-174 °C; HRMS calc for $C_{28}H_{29}N_3O_5S$ $[M+H]^+$: 520.1901; found 520.1865.



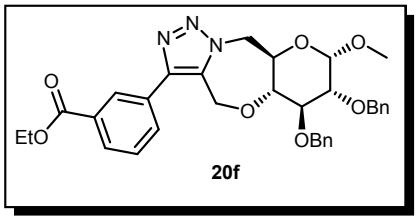
20e

(5aR,6S,7R,8S,9aR)-6,7-bis(benzyloxy)-8-methoxy-3-(4-methoxyphenyl)-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine (20e).

Colourless solid:

R_f: 0.3 (1: 1 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.49 (d, *J* = 8.61 Hz, 2H), 7.39-7.29 (m, 10H), 7.01 (d, *J* = 8.61 Hz, 2H), 5.23 (d, *J* = 14.96 Hz, 1H), 5.07 (dd, *J* = 14.04, 3.02 Hz, 1H), 4.85-4.82 (m, 3H), 4.67 (d, *J* = 12.15 Hz, 1H), 4.60-4.54 (m, 2H), 4.28 (dd, *J* = 14.02, 10.65 Hz, 1H), 3.89-3.76 (m, 5H), 3.58 (d, *J* = 9.04 Hz, 1H), 3.53 (dd, *J* = 9.49, 3.51 Hz, 1H), 3.41 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 159.7, 138.6, 137.9, 129.1, 128.4, 128.3, 128.0, 127.9, 127.9, 127.6, 122.8, 114.2, 98.4, 88.5, 79.3, 78.5, 76.1, 73.6, 65.8, 62.1, 55.7, 55.3, 53.3;

MS (ESI): 543.5; **M.P:** 137-139 ^{o}C;

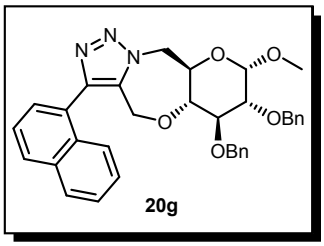


20f

ethyl 3-((5aR,6S,7R,8S,9aR)-6,7-bis(benzyloxy)-8-methoxy-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepin-3-yl)benzoate (20f).

White solid.

R_f: 0.3 (1: 1 EtOAc/hexanes); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.19 (s, 1H), 8.09 (d, *J* = 7.83 Hz, 1H), 7.81 (d, *J* = 7.76 Hz, 1H), 7.56 (t, *J* = 7.76 Hz, 1H), 7.41-7.28 (m, 10H), 5.26 (d, *J* = 15.05 Hz, 1H), 5.10 (dd, *J* = 14.06, 3.03 Hz, 1H), 4.85-4.82 (m, 3H), 4.68.4.58 (m, 3H), 4.41 (q, *J* = 7.11 Hz, 2H), 4.31 (dd, *J* = 14.07, 10.66 Hz, 1H), 3.88-3.77 (m, 2H), 3.62-3.51 (m, 2H), 3.42 (s, 3H), 1.41 (t, *J* = 7.13 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.1, 145.0, 138.6, 137.9, 133.3, 132.2, 131.1, 130.6, 129.4, 129.0, 128.8, 128.4, 128.3, 128.1, 128.0, 127.9, 127.6, 98.5, 88.6, 79.3, 78.5, 76.2, 73.6, 65.7, 62.0, 61.2, 55.8, 53.3, 14.3; MS+18 (ESI): 602.4; **M.P:** 144-146 ^{o}C; HRMS calc for $C_{33}H_{35}N_3O_7$ $[M+H]^+$: 586.2548; found 586.2443.



20g

(5aR,6S,7R,8S,9aR)-6,7-bis(benzyloxy)-8-methoxy-3-(naphthalen-1-yl)-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine (20g).

White solid:

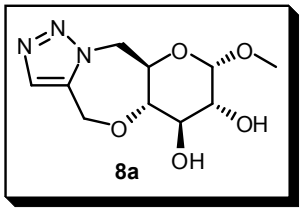
R_f: 0.3 (1: 1 EtOAc/hexanes);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99-7.91 (m, 3H), 7.58-7.50 (m, 3H), 7.46 (d, *J* = 6.88 Hz, 1H), 7.36-7.25 (m, 10H), 5.17 (dd, *J* = 14.11, 2.99 Hz, 1H), 4.95 (d, *J* = 14.97 Hz, 1H), 4.83-

4.79 (m, 3H), 4.68 (d, J = 12.14 Hz, 1H), 4.61 (d, J = 3.42 Hz, 1H), 4.54 (d, J = 14.96 Hz, 1H), 4.39 (dd, J = 13.95, 10.78 Hz, 1H), 3.89 (t, J = 9.29 Hz, 2H), 3.63-3.51 (m, 2H), 3.44 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 144.7, 138.5, 137.9, 134.6, 133.8, 131.8, 129.3, 128.4, 128.3, 128.3, 128.0, 128.0, 127.9, 127.6, 127.2, 126.7, 126.1, 125.4, 125.2, 98.5, 88.7, 79.3, 78.5, 76.2, 73.6, 65.9, 62.2, 55.8, 53.4; MS (ESI): 563.5; **M.P:** 168-170 ^{o}C; HRMS calc for $C_{34}H_{33}N_3O_5$ $[M+H]^+$: 564.2493; found 564.2434.

General procedure for OBn deprotection:

To a solution of **20a-g** (1.0 equiv, 0.183 mmol) in MeOH was added 10% Pd/C (70 mg) and the reaction was stirred at ambient temperature under hydrogen atmosphere. After 24 h, the reaction mixture was filtered through silica gel and concentrated under reduced presssure. The crude residue was purified by column chromatography (EtOAc) to provide **8a-g** (95%);

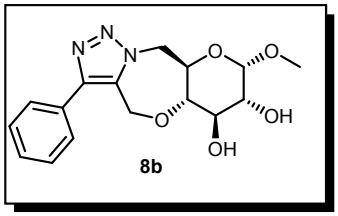


8a

(5aS,6R,7R,8S,9aR)-8-methoxy-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine-6,7-diol (8a).

White solid.

R_f: 0.2 (EtOAc); $[\alpha]_D^{20}$ = +113.31 (c = 0.25, CH_3OH), **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.60 (s, 1H), 5.13-5.09 (m, 2H), 4.82 (d, J = 3.75 Hz, 1H), 4.53 (d, J = 14.93 Hz, 1H), 4.31 (dd, 1H), 3.82-3.71 (m, 2H), 3.49-3.43 (m, 5H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 136.1, 132.9, 99.1, 87.0, 72.1, 71.9, 65.8, 62.0, 56.0, 52.5, 29.6; IR(KBr): υ 765, 1078, 2138, 3501 cm^{-1}; MS (ESI): 258.0 **M.P:** 147-150 ^{o}C; HRMS calc for $C_{10}H_{15}N_3O_5$ $[M+H]^+$: 258.1084; found 258.1068.

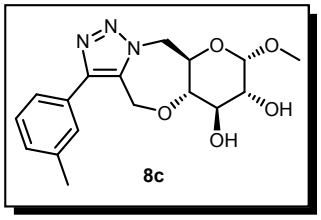


8b

(5aS,6R,7R,8S,9aR)-8-methoxy-3-phenyl-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine-6,7-diol (8b).

Pale red solid.

R_f: 0.2 (EtOAc); $[\alpha]_D^{20}$ = +182.73 (c = 0.25, CH_3OH), **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.58-7.54 (m, 2H), 7.50-7.47 (m, 2H), 7.44-7.40 (m, 1H), 5.23 (d, *J* = 15.06 Hz, 1H), 5.00 (dd, *J* = 13.93, 3.03 Hz, 1H), 4.80-4.75 (m, 2H), 4.60 (dd, *J* = 13.91, 10.70 Hz, 1H), 3.73-3.64 (m, 2H), 3.55-3.49 (m, 2H), 3.45 (s, 3H), 1.30-1.28 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 129.9, 128.5, 128.2, 127.5, 100.0, 87.3, 71.7, 70.9, 65.8, 61.3, 54.6, 52.6; IR(KBr): υ 1070, 2075, 3512 cm^{-1}; MS (ESI): 334.1; **M.P:** 150-154 ^oC; HRMS calc for $C_{16}H_{19}N_3O_5$ $[M+H]^+$: 334.1397; found 334.1377.

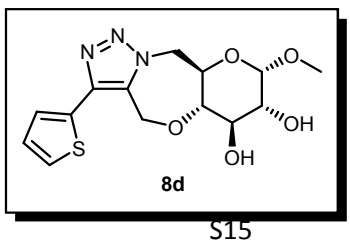


8c

(5aS,6R,7R,8S,9aR)-8-methoxy-3-m-tolyl-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine-6,7-diol (8c).

White solid:

R_f: 0.2 (EtOAc); $[\alpha]_D^{20}$ = +158.37 (c = 0.25, CH_3OH), **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.53-7.30 (m, 3H), 7.21 (d, *J* = 6.19 Hz, 1H), 5.33 (d, *J* = 13.73 Hz, 1H), 5.20-5.06 (m, 1H), 4.80-4.79 (m, 1H), 4.74-4.62 (m, 1H), 4.37-4.31 (m, 1H), 3.84-3.72 (m, 2H), 3.68-3.61 (m, 1H), 3.50-3.46 (m, 1H), 3.44 (s, 3H), 2.40 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 138.6, 129.2, 128.7, 124.7, 99.3, 87.1, 71.8, 65.7, 55.9, 36.6, 31.5, 29.6, 21.4; IR(KBr): υ 1073, 2240, 3415 cm^{-1};
MS (ESI): 348.1; **M.P:** 130-134 ^oC; HRMS calc for $C_{17}H_{21}N_3O_5$ $[M+H]^+$: 348.1554; found 348.1527.



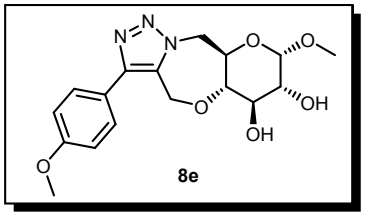
8d

(5aS,6R,7R,8S,9aR)-8-methoxy-3-(thiophen-2-yl)-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine-6,7-diol (8d).

White solid.

R_f: 0.2 (EtOAc); $[\alpha]_D^{20}$ = +106.84 (c = 0.25, CH_3OH), **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.11 (dd, *J* = 4.91, 3.71 Hz, 1H), 7.23 (dd, *J* = 13.47, 8.07 Hz, 2H), 5.32 (d, *J* = 15.09 Hz, 1H), 5.03-5.01 (m, 1H), 4.53 (dd, *J* = 12.32, 9.40 Hz, 2H), 4.30-4.27 (m, 1H), 3.81 (t, *J* = 9.20 Hz, 1H), 3.72-3.70 (m, 1H), 3.58-3.47 (m, 2H), 3.38 (d, *J* = 4.85 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 140.3, 138.6, 137.9, 132.4, 131.7, 125.6, 98.4, 88.5, 76.1, 73.6, 65.7, 61.9, 55.8, 53.3;

IR(KBr): υ 1055, 2093, 2951 cm^{-1}; MS(M+23) (ESI): 362.5; **M.P:** 145-150 °C; HRMS calc for $C_{17}H_{21}N_3O_6$ $[M+H]^+$: 364.1503; found 364.1482.

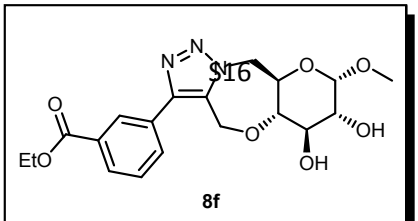


8e

(5aS,6R,7R,8S,9aR)-8-methoxy-3-(4-methoxyphenyl)-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine-6,7-diol (8e).

White solid.

R_f: 0.2 (EtOAc); $[\alpha]_D^{20}$ = +165.40 (c = 0.25, CH_3OH), **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.48 (d, *J* = 8.40 Hz, 2H), 6.97 (d, *J* = 8.41 Hz, 2H), 5.27 (d, *J* = 14.93 Hz, 1H), 5.10 (dd, *J* = 14.06, 2.77 Hz, 1H), 4.81 (d, *J* = 3.57 Hz, 1H), 4.59 (d, *J* = 14.93 Hz, 1H), 4.34 (dd, *J* = 13.91, 10.83 Hz, 1H), 3.86-3.73 (m, 5H), 3.65 (dd, *J* = 9.38, 3.67 Hz, 1H), 3.50-3.44 (m, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 159.8, 145.7, 132.0, 129.1, 122.5, 114.3, 99.2, 87.0, 72.0, 71.9, 65.8, 62.0, 55.9, 55.3, 52.8; IR(KBr): υ 1058, 2057, 3508 cm^{-1}; MS (ESI): 364.1; **M.P:** 230-234 °C; HRMS calc for $C_{16}H_{19}N_3O_5$ $[M+H]^+$: 334.1397; found 334.1377.



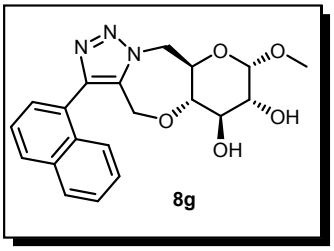
8f

ethyl3-((5aS,6R,7R,8S,9aR)-6,7-dihydroxy-8-methoxy-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepin-3-yl)benzoate (8f).

White solid:

R_f: 0.2 (EtOAc); $[\alpha]_D^{20}$ = +86.21 (c = 0.25, CH_3OH), **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.20 (s, 1H), 8.09 (d, *J* = 7.82 Hz, 1H), 7.83 (d, *J* = 7.70 Hz, 1H), 7.55 (t, *J* = 7.77 Hz, 1H), 5.35 (d, *J* = 14.99 Hz, 1H), 5.16 (dd, *J* = 14.11, 3.13 Hz, 1H), 4.84 (d, *J* = 3.81 Hz, 1H), 4.67 (d, *J* = 15.02 Hz, 1H), 4.44-4.35 (m, 3H), 3.85-3.77 (m, 2H), 3.68 (dd, *J* = 9.48, 3.83 Hz, 1H), 3.56-3.47 (m, 4H), 1.41 (t, *J* = 7.13 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.1, 145.1, 132.9, 132.1, 131.1, 130.5, 129.5, 129.0, 128.6, 99.2, 87.1, 72.1, 71.9, 65.7, 61.9, 61.2, 56.0, 52.9, 14.3;

IR(KBr): υ 1082, 1715, 2077, 3398 cm^{-1}; MS (ESI): 405.5; **M.P:** 131-134 ^oC; HRMS calc for $C_{19}H_{23}N_3O_7$ $[M+H]^+$: 406.1609; found 406.1582.



8g

(5aS,6R,7R,8S,9aR)-8-methoxy-3-(naphthalen-1-yl)-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine-6,7-diol (8g).

White solid:

R_f: 0.2 (EtOAc); $[\alpha]_D^{20}$ = +29.05 (*c* = 0.25, CH_3OH), **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.00-7.89 (m, 1H), 7.55-7.44 (m, 2H), 7.40-7.30 (m, 1H), 7.14 (d, *J* = 4.62 Hz, 2H), 6.98 (t, *J* = 4.41 Hz, 1H), 5.13 (dd, *J* = 14.08, 3.13 Hz, 1H), 4.50 (d, *J* = 14.83 Hz, 1H), 4.37 (dd, *J* = 14.07, 10.68 Hz, 1H), 4.12 (d, *J* = 7.14 Hz, 1H), 3.82-3.79 (m, 2H), 3.68 (d, *J* = 3.74 Hz, 2H), 3.53-3.45 (m,

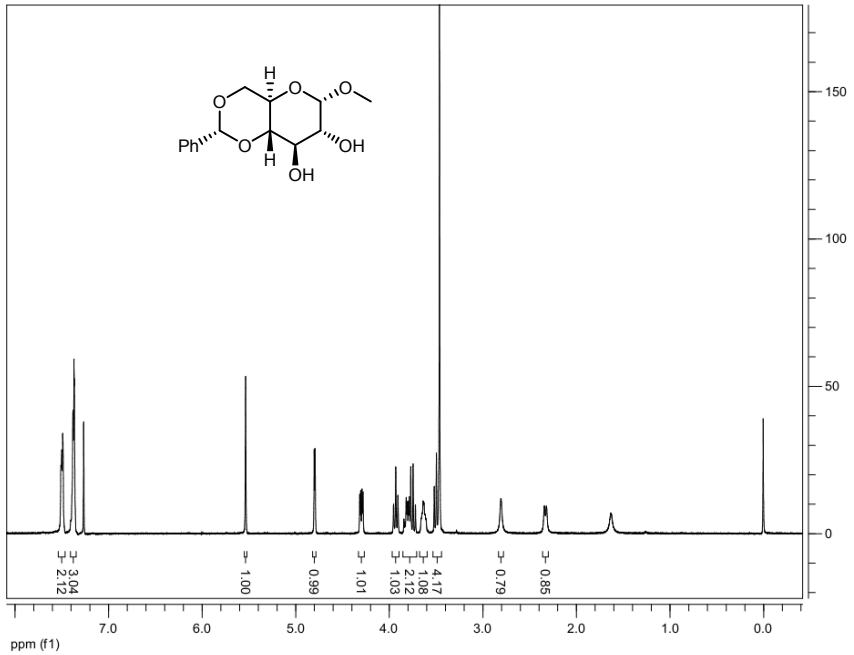
5H); **^{13}C NMR (100 MHz, $CDCl_3$) δ** 146.0, 138.1, 136.8, 133.4, 130.0, 127.8, 125.3, 125.2, 99.1, 87.1, 72.1, 71.9, 65.9, 62.0, 56.0, 52.7; IR(KBr): υ 1054, 2083, 3368 cm^{-1}; MS (ESI): 383.6; **M.P:** 183-187 ^oC; HRMS calc for $C_{20}H_{21}N_3O_5$ $[M+H]^+$: 384.1554; found 384.1526.

General procedure for synthesis of compound 17b-g: To a solution (DMF) of **15 (**1.0 equiv, 8.928 mmol) was added $Pd(PPh_3)_4$ (0.05 equiv, 0.44 mmol,) **Ar-Br** (1.0 equiv, 8.928 mmol), K_2CO_3 (10.0 equiv, 89.28 mmol), CuI (0.1 equiv, 0.892 mmol) was added and the reaction was stirred at 80 ^oC. After 24 h, the reaction mixture was filtered in celite and extracted with ethylacetate (3 × 30 mL). Combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (8:2 hexanes/EtOAc) to provide **17b-g** (80%): R_f: 0.3 (2:8 EtOAc/hexanes).

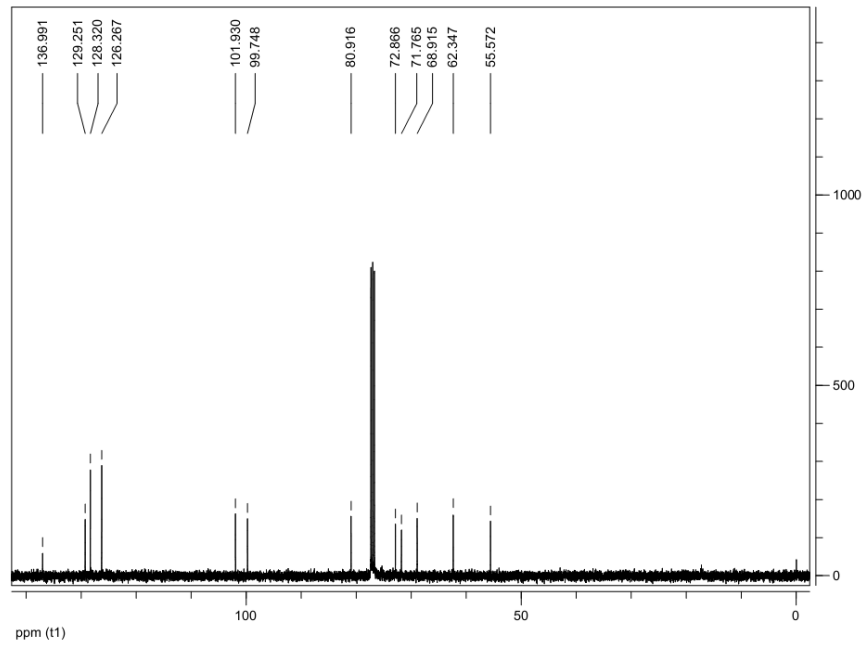
General procedure for synthesis of compound 18a-g: To a solution (DCM) of **15 &17b-g (**1.0 equiv, 2.89 mmol) was added TsCl (1.2 equiv, 3.47 mmol) then KOH powder (2.5 equiv, 3.62 mmol) was added portion wise about 30 min at 0 ^oC and the reaction was stirred at 0 ^oC. After 1 h, the reaction mixture was quenched with water and extracted with DCM (3×10 ml). Combined organic phases were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude residue was purified by column chromatography (9:1 hexanes/EtOAc) to provide **18a-g** (90%): R_f: 0.6 (2:8 EtOAc/hexanes);

(4aR,6S,7R,8R,8aS)-6-methoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxine-7,8-diol (10).

^{1}H NMR (400 MHz, $CDCl_3$)

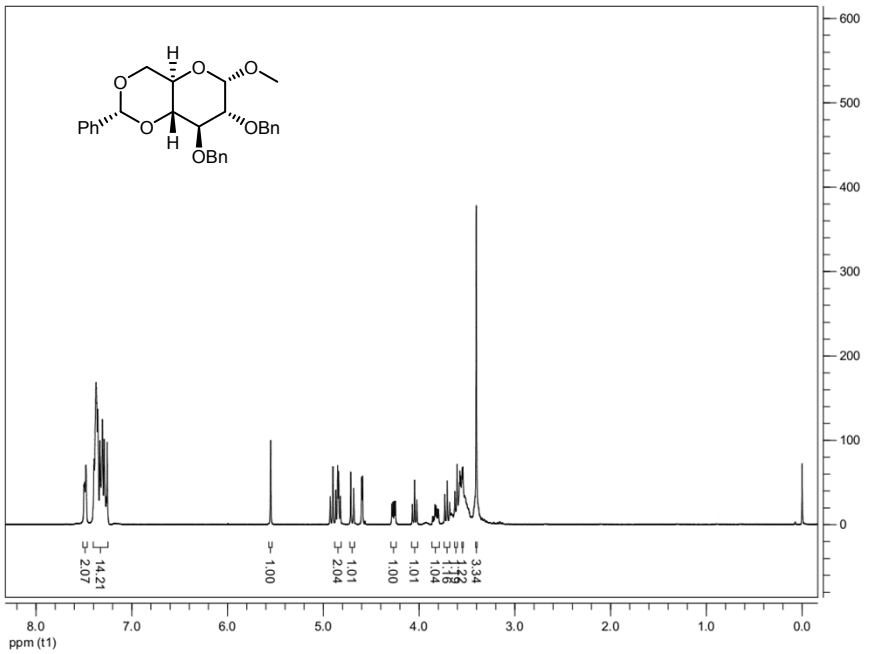


^{13}C NMR (400 MHz, $CDCl_3$)

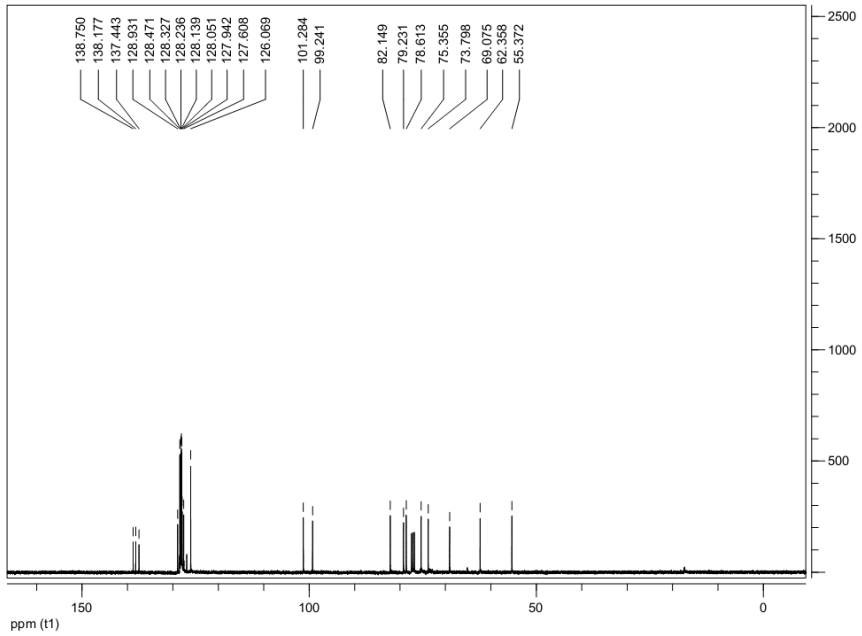


(4aR,6S,7R,8S,8aR)-7,8-bis(benzyloxy)-6-methoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxine (11).

^{1}H NMR (400 MHz, $CDCl_3$)

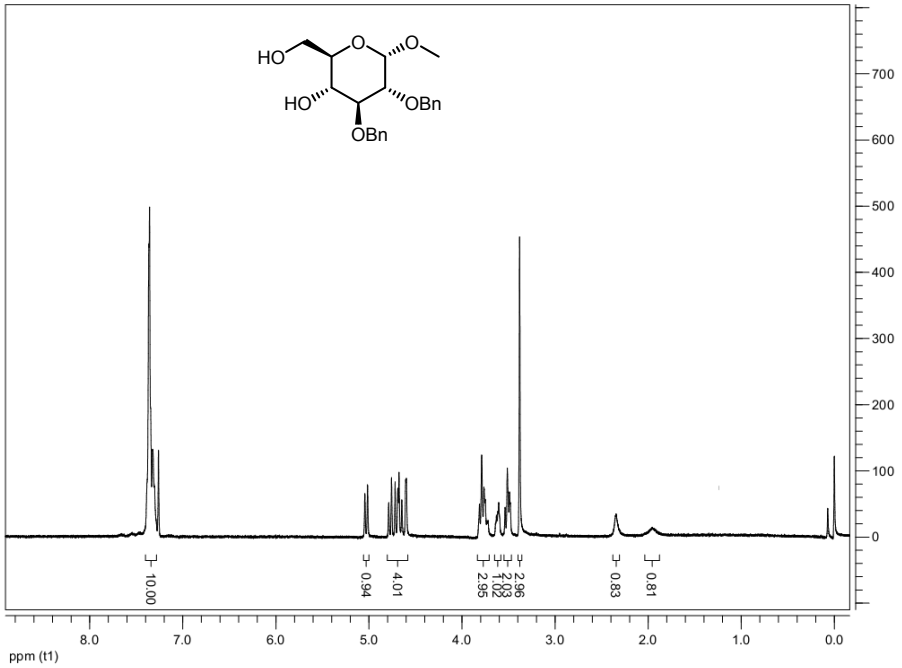


^{13}C NMR (400 MHz, $CDCl_3$)

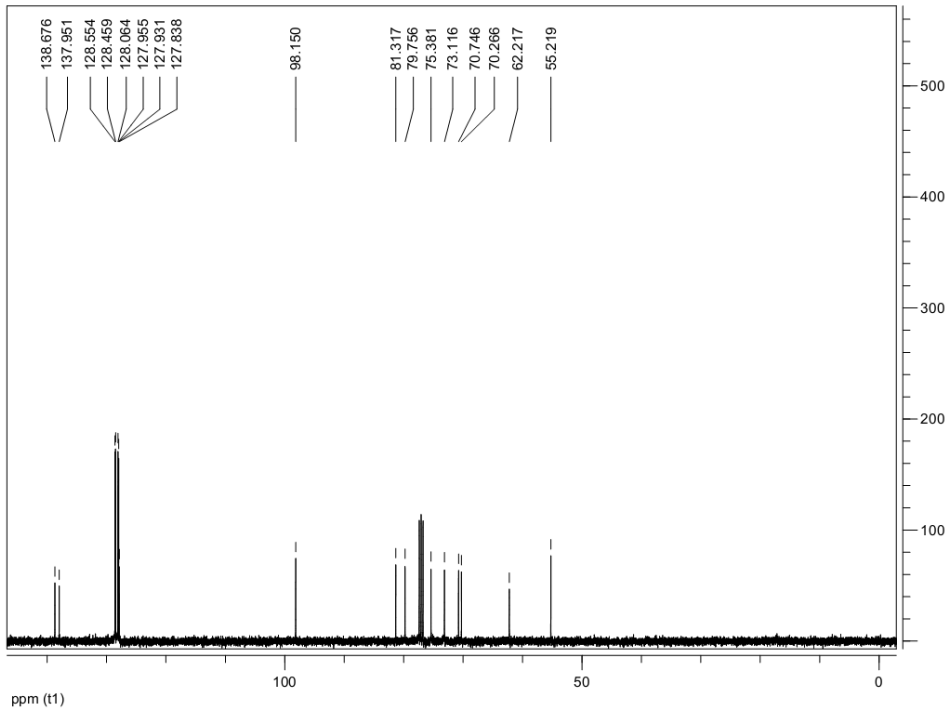


(2R,3R,4S,5R,6S)-4,5-bis(benzyloxy)-2-(hydroxymethyl)-6-methoxytetrahydro-2H-pyran-3-ol (12).

^{1}H NMR (400 MHz, $CDCl_3$)

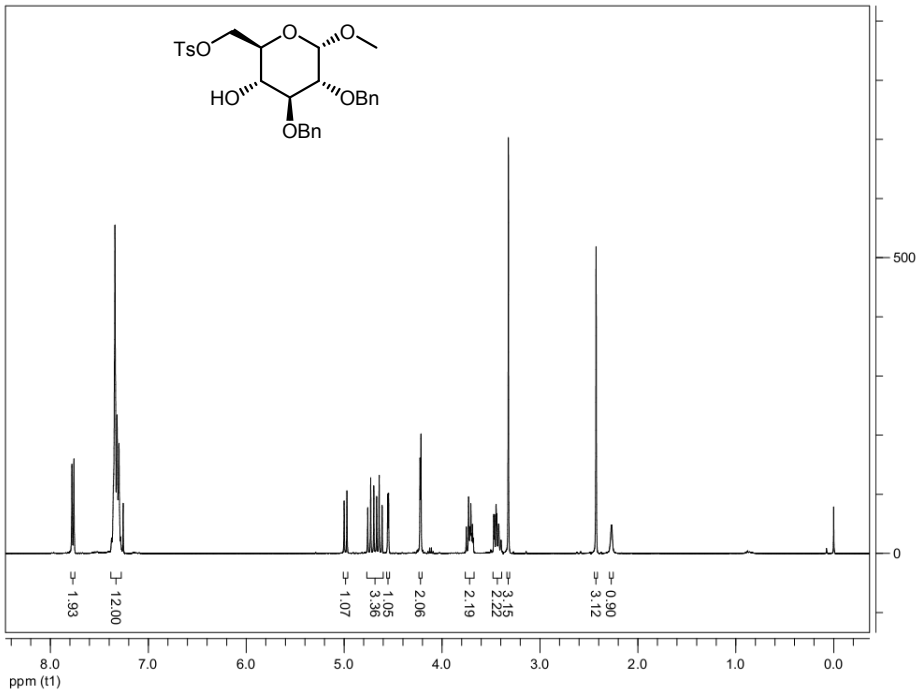


^{13}C NMR (400 MHz, $CDCl_3$)

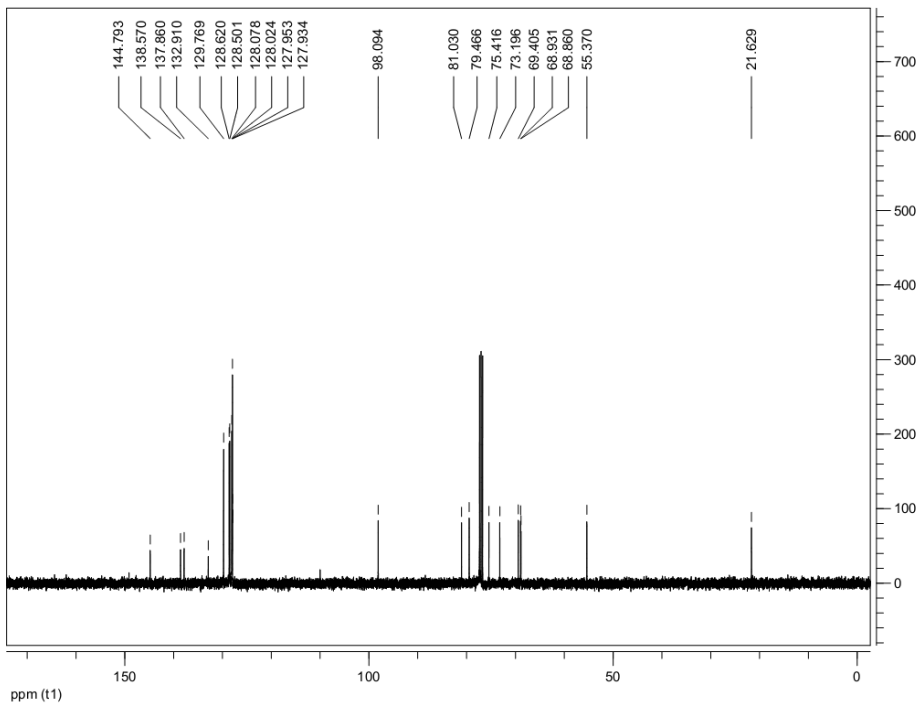


((2R,3R,4S,5R,6S)-4,5-bis(benzyloxy)-3-hydroxy-6-methoxytetrahydro-2H-pyran-2-yl)methyl 4-methylbenzenesulfonate (13).

^{1}H NMR (400 MHz, $CDCl_3$)

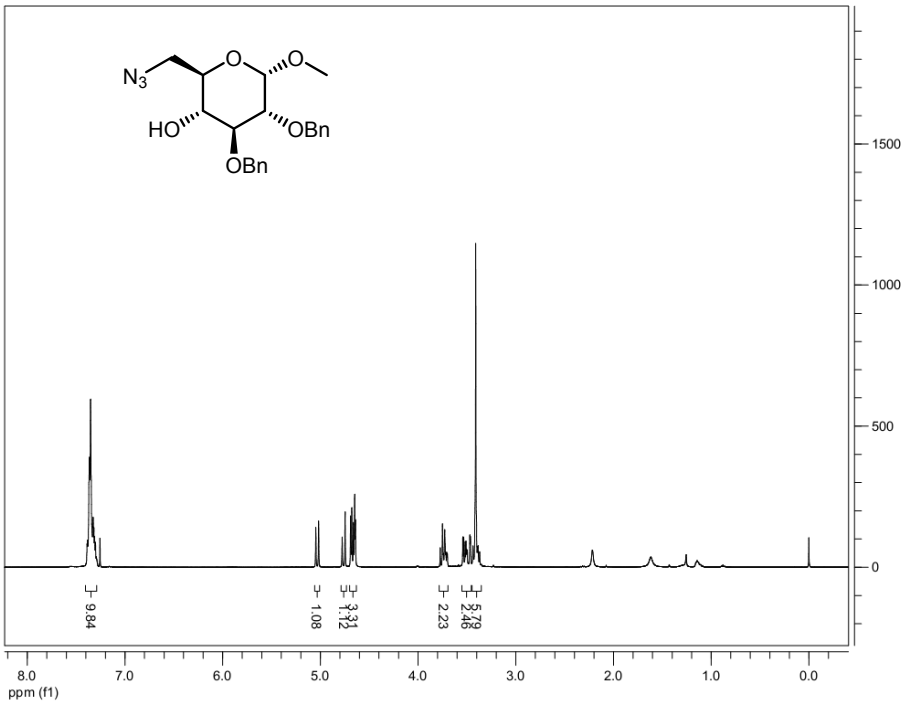


^{13}C NMR (400 MHz, $CDCl_3$)

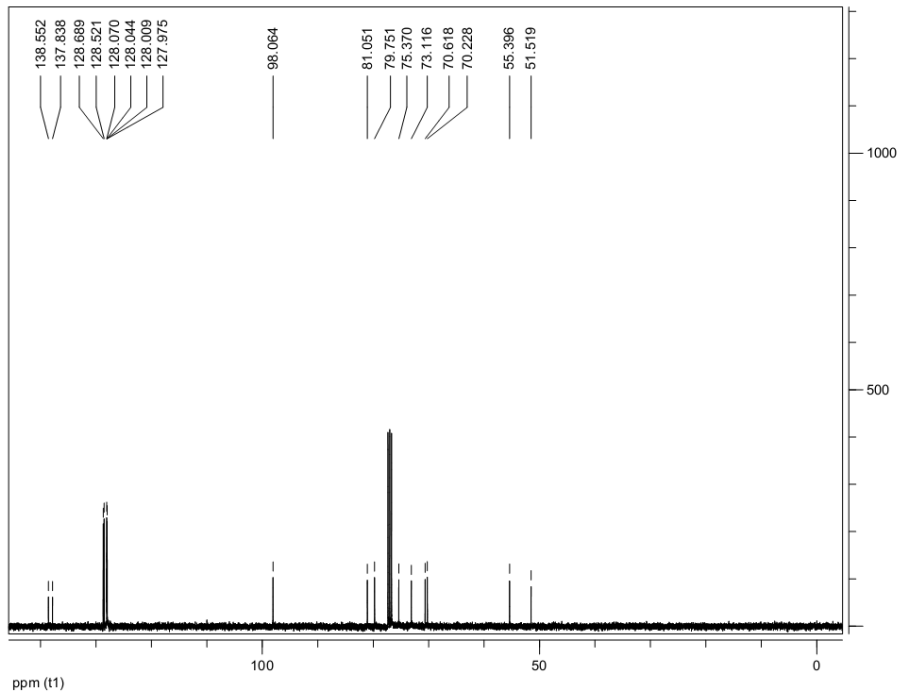


(2R,3R,4S,5R,6S)-2-(azidomethyl)-4,5-bis(benzyloxy)-6-methoxytetrahydro-2H-pyran-3-ol (14).

^{1}H NMR (400 MHz, $CDCl_3$)

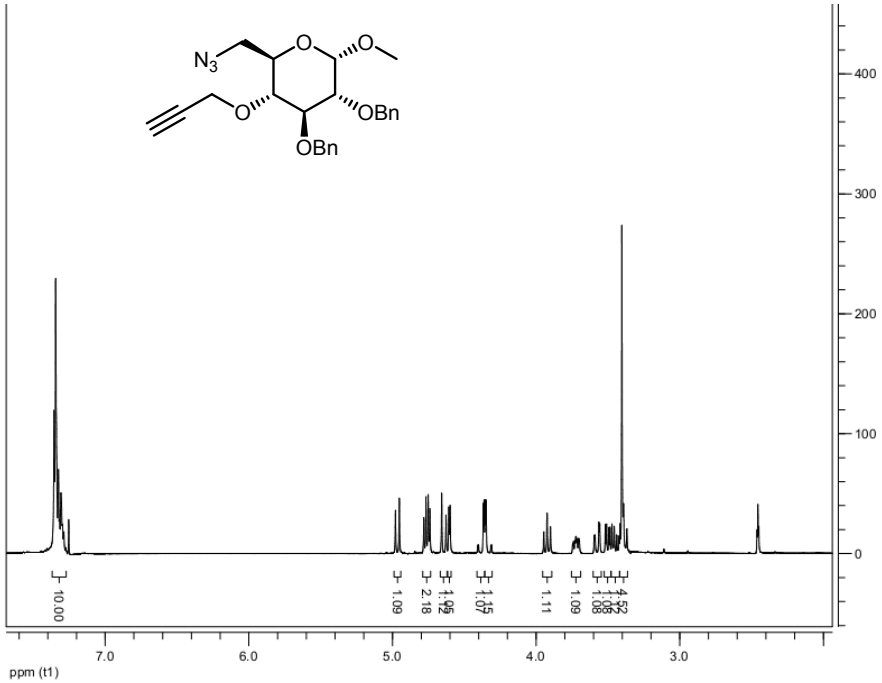


^{13}C NMR (400 MHz, $CDCl_3$)

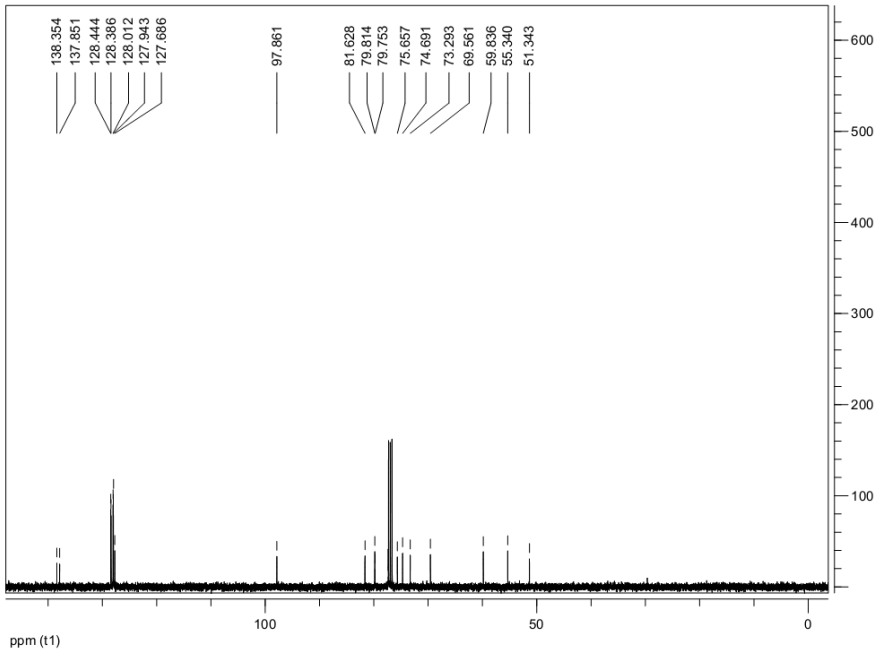


(2R,3R,4S,5R,6S)-2-(azidomethyl)-4,5-bis(benzyloxy)-6-methoxy-3-(prop-2-ynyloxy)tetrahydro-2H-pyran (19a).

^{1}H NMR (400 MHz, $CDCl_3$)

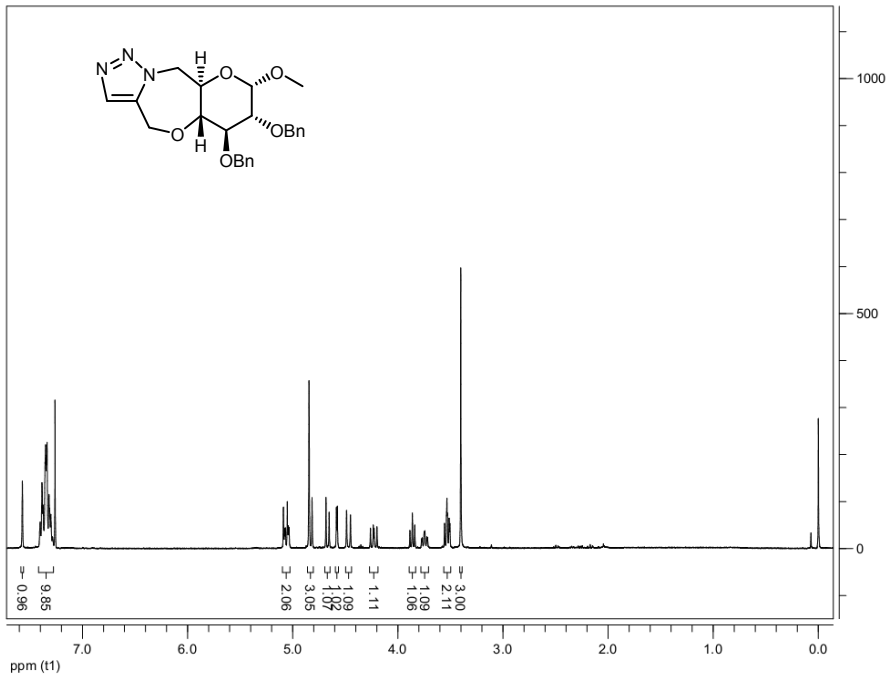


^{13}C NMR (400 MHz, $CDCl_3$)

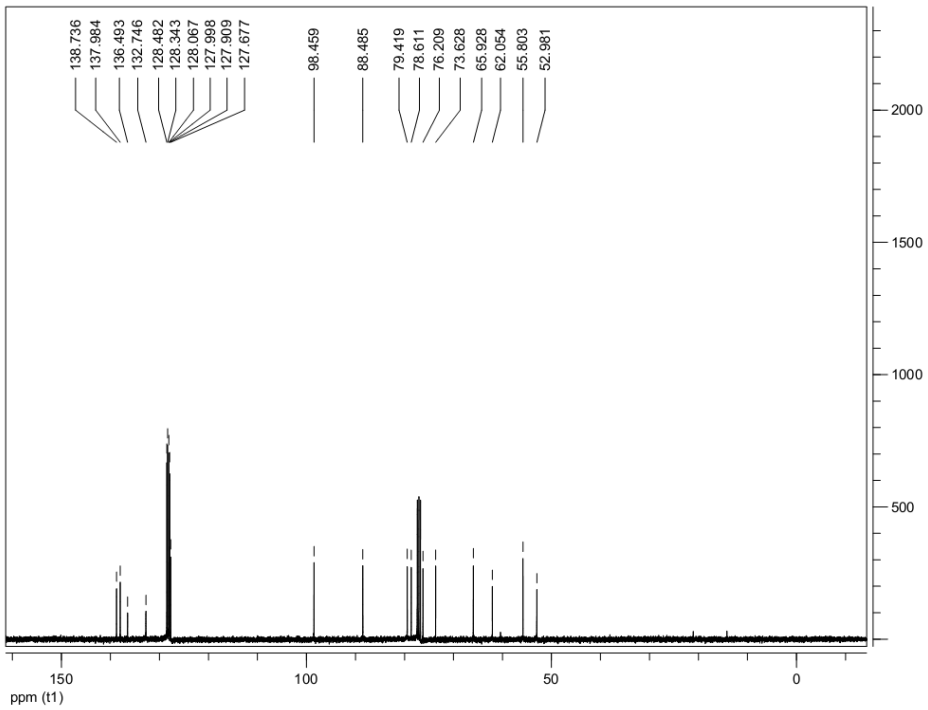


(5aR,6S,7R,8S,9aR)-6,7-bis(benzyloxy)-8-methoxy-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine (20a).

^{1}H NMR (400 MHz, $CDCl_3$)

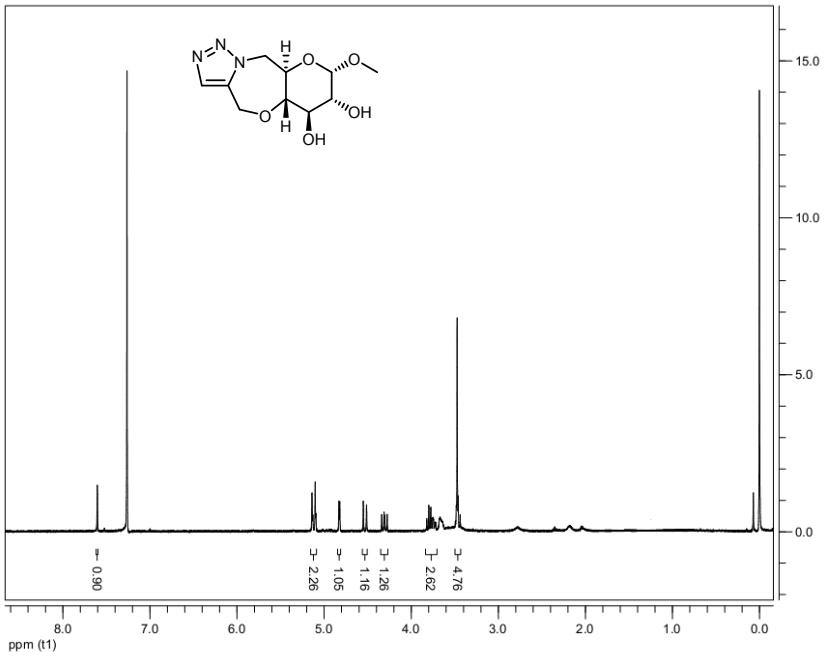


^{13}C NMR (400 MHz, $CDCl_3$)

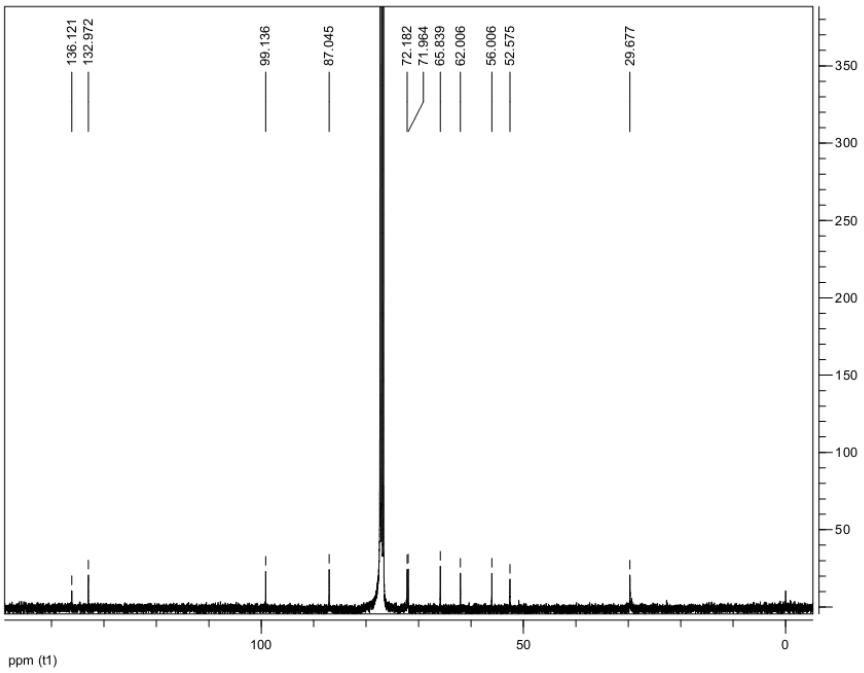


(5aS,6R,7R,8S,9aR)-8-methoxy-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine-6,7-diol (8a).

^{1}H NMR (400 MHz, $CDCl_3$)

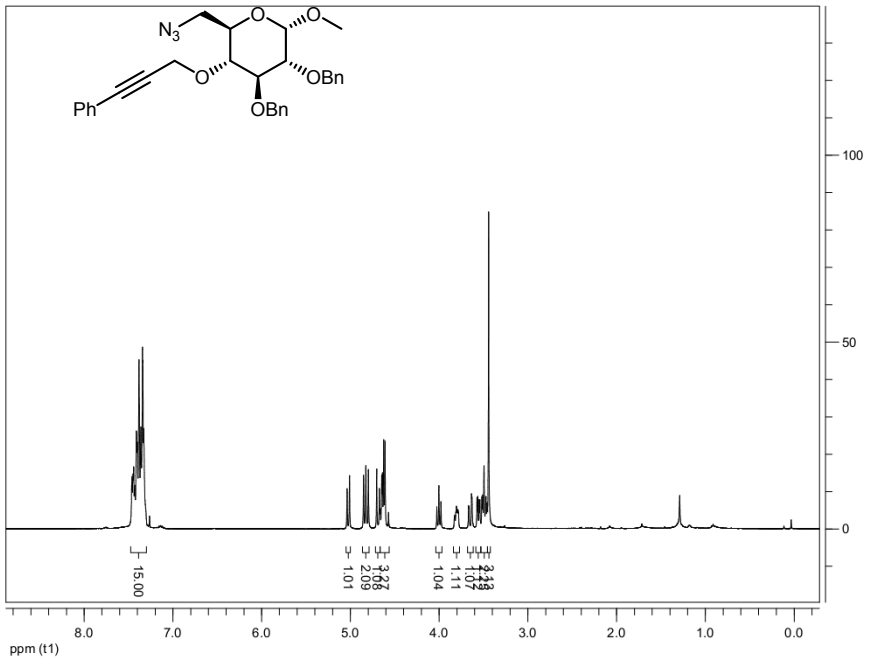


^{13}C NMR (400 MHz, $CDCl_3$)

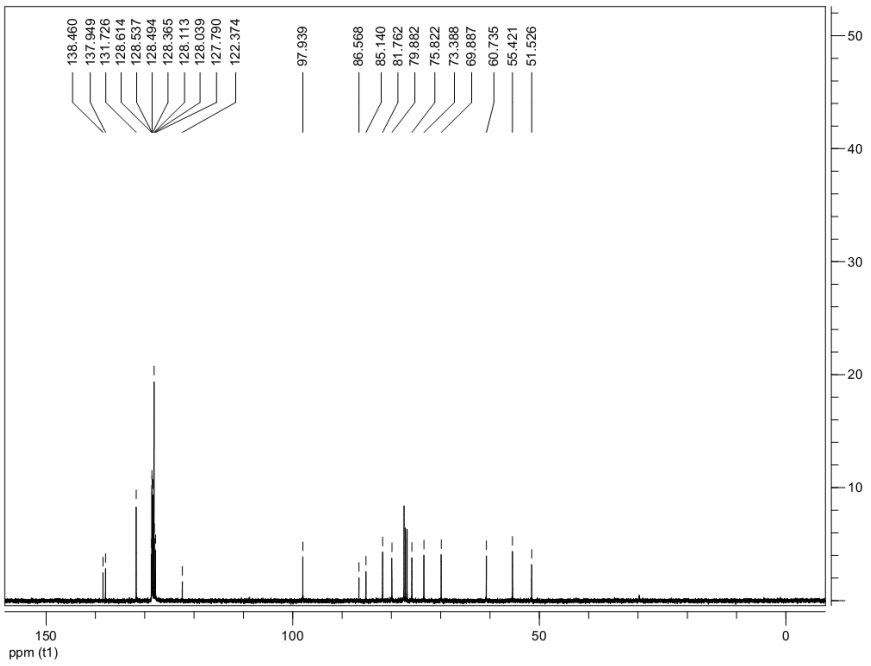


(2R,3R,4S,5R,6S)-2-(azidomethyl)-4,5-bis(benzyloxy)-6-methoxy-3-(3-phenylprop-2-ynyloxy)tetrahydro-2H-pyran (19b).

^{1}H NMR (400 MHz, $CDCl_3$)

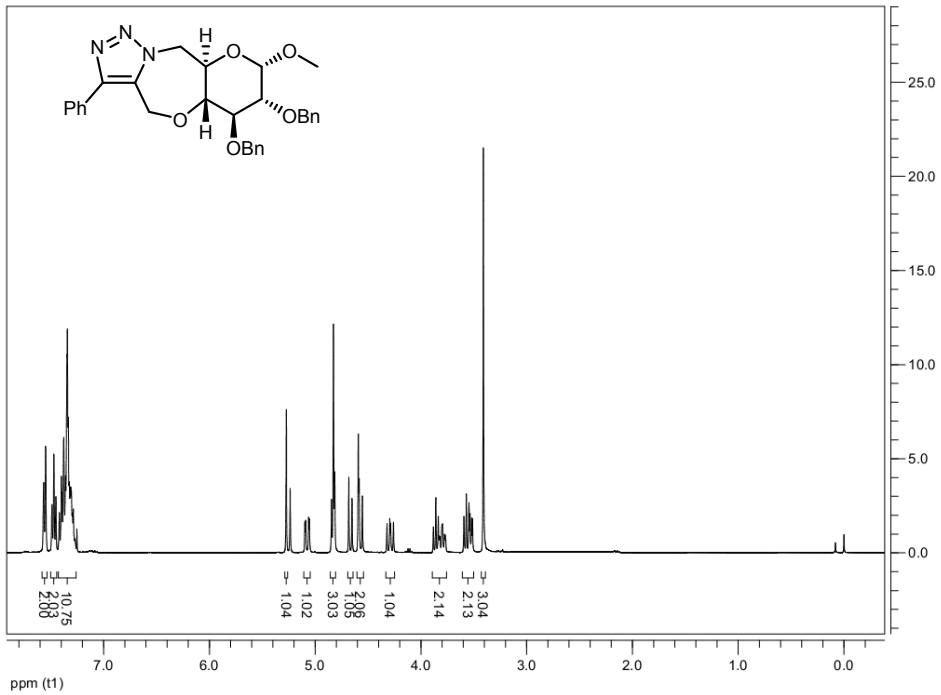


^{13}C NMR (400 MHz, $CDCl_3$)

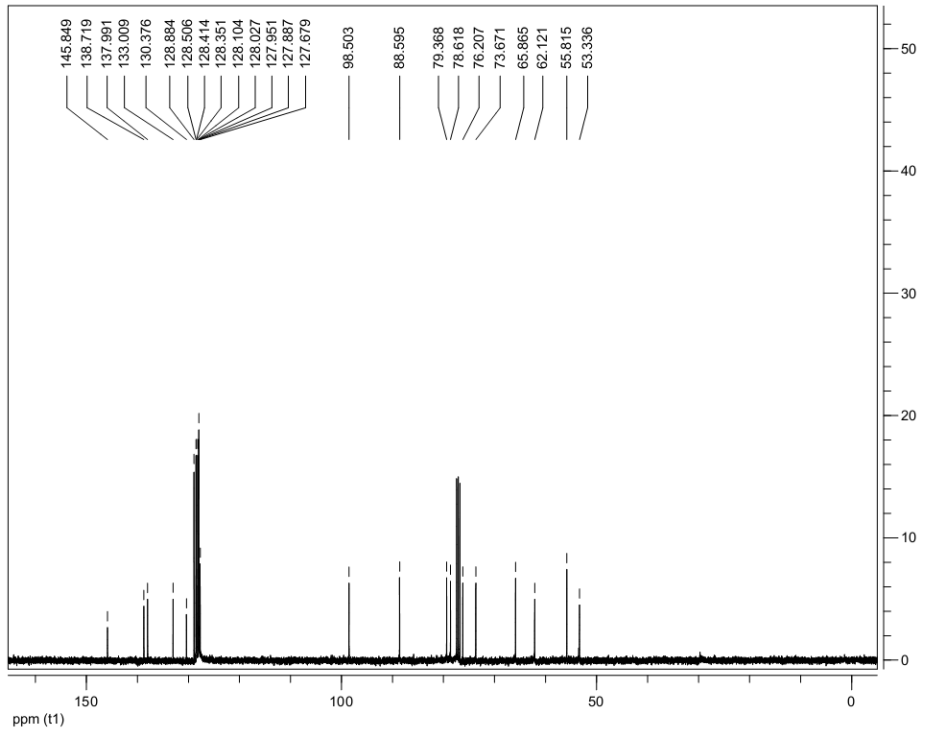


(5aR,6S,7R,8S,9aR)-6,7-bis(benzyloxy)-8-methoxy-3-phenyl-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine (20b).

^{1}H NMR (400 MHz, $CDCl_3$)

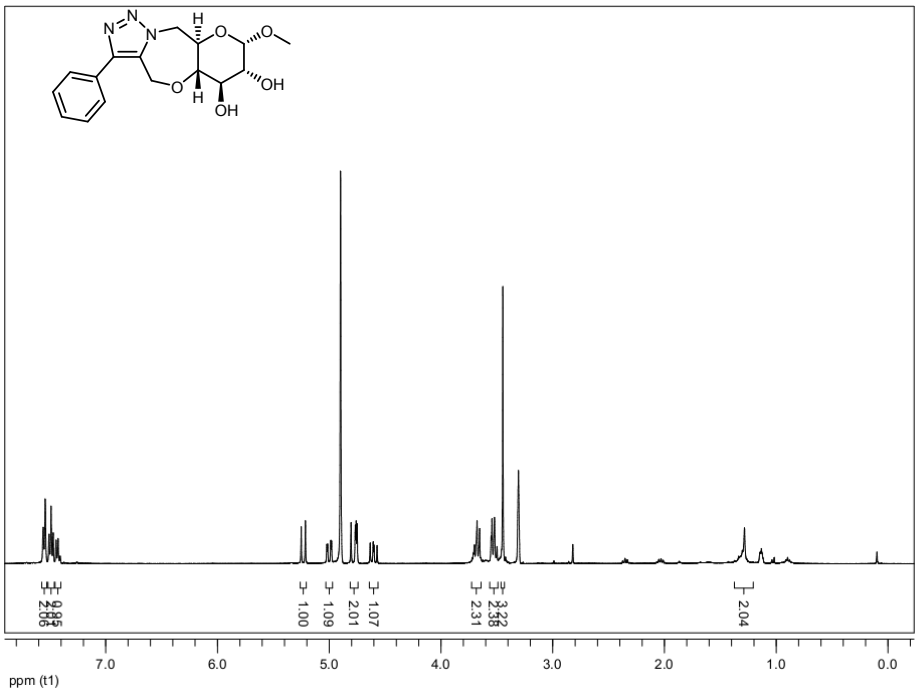


^{13}C NMR (400 MHz, $CDCl_3$)

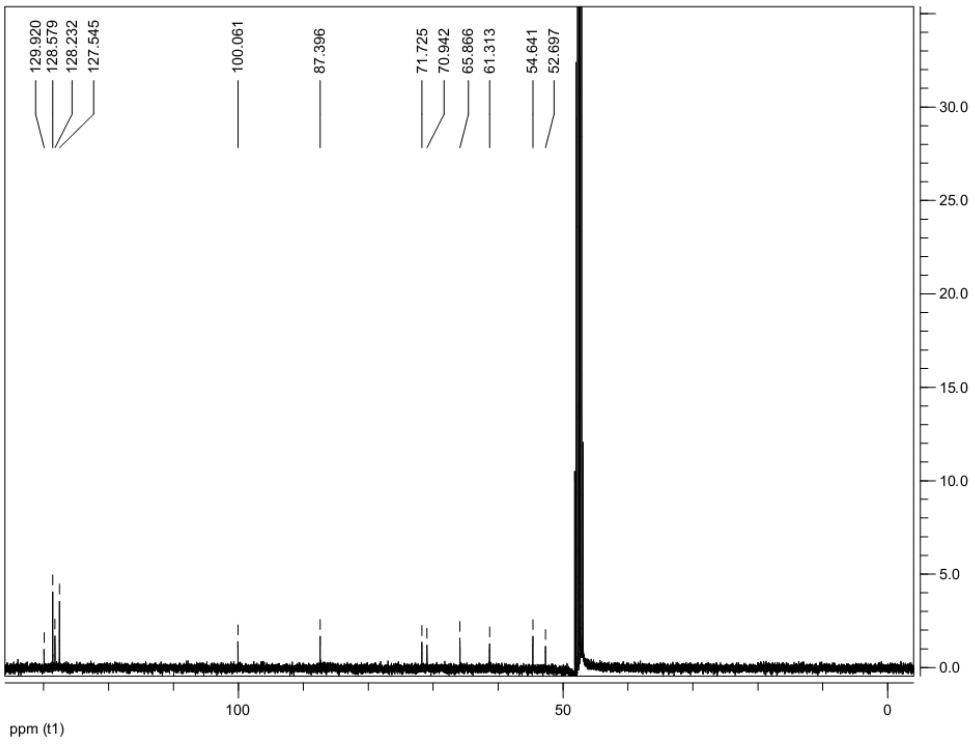


(5aS,6R,7R,8S,9aR)-8-methoxy-3-phenyl-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine-6,7-diol (8b).

^{1}H NMR (400 MHz, $CDCl_3$)

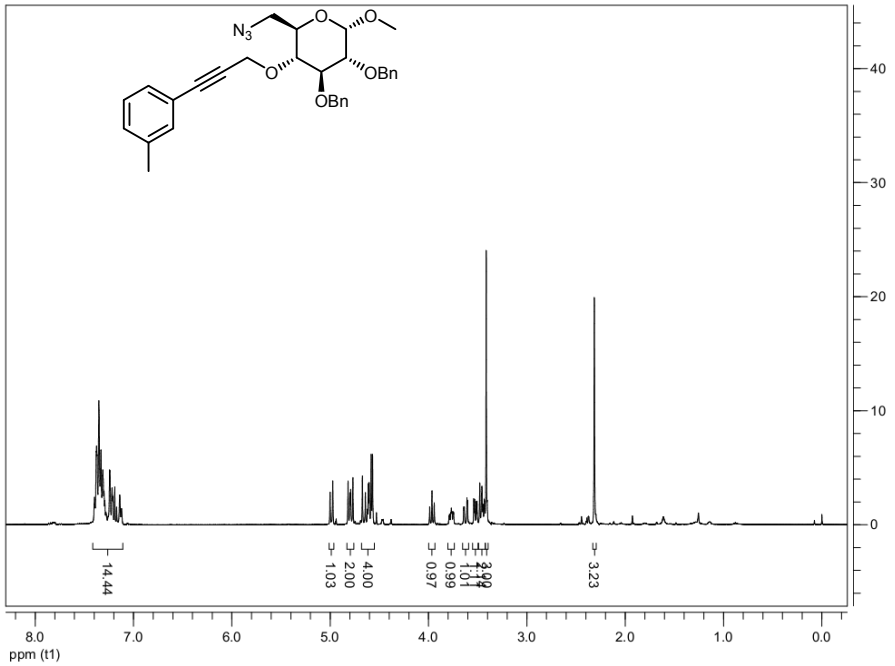


^{13}C NMR (400 MHz, $CDCl_3$)

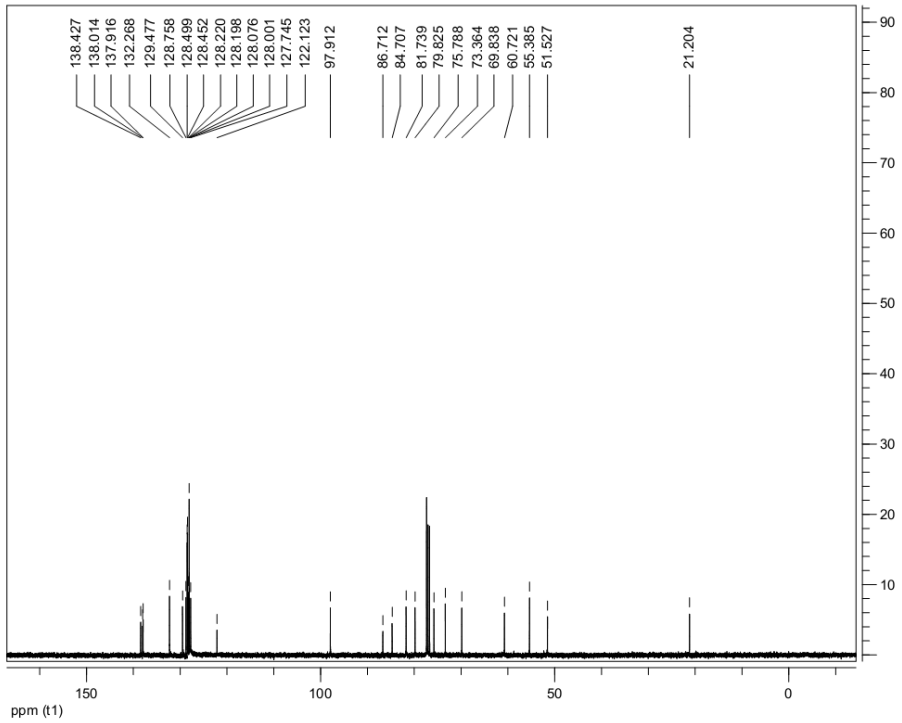


(2R,3R,4S,5R,6S)-2-(azidomethyl)-4,5-bis(benzyloxy)-6-methoxy-3-(3-m-tolylprop-2-ynyloxy)tetrahydro-2H-pyran (19c).

^{1}H NMR (400 MHz, $CDCl_3$)

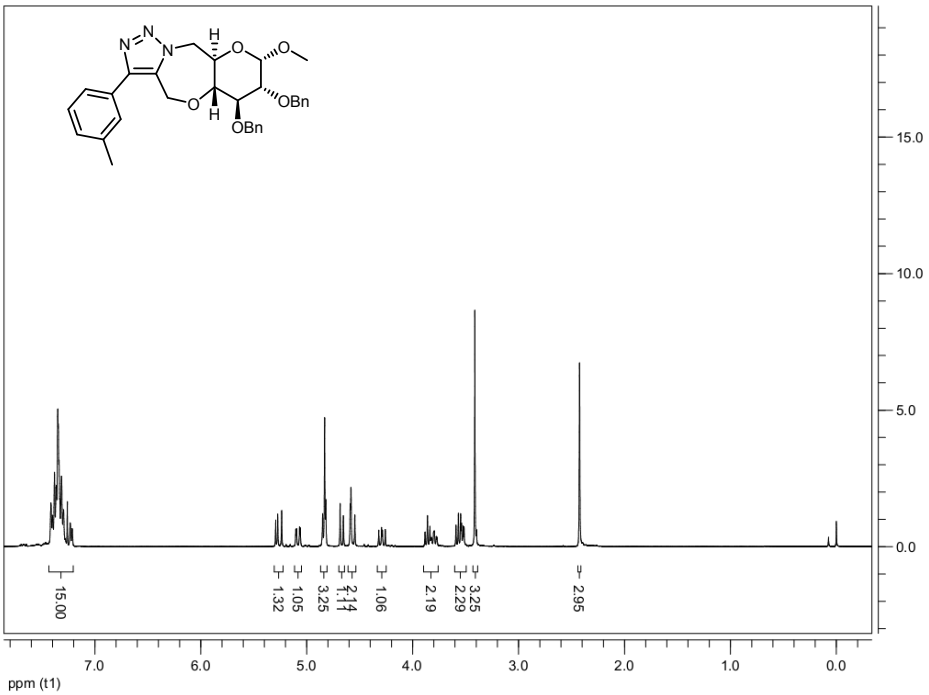


^{13}C NMR (400 MHz, $CDCl_3$)

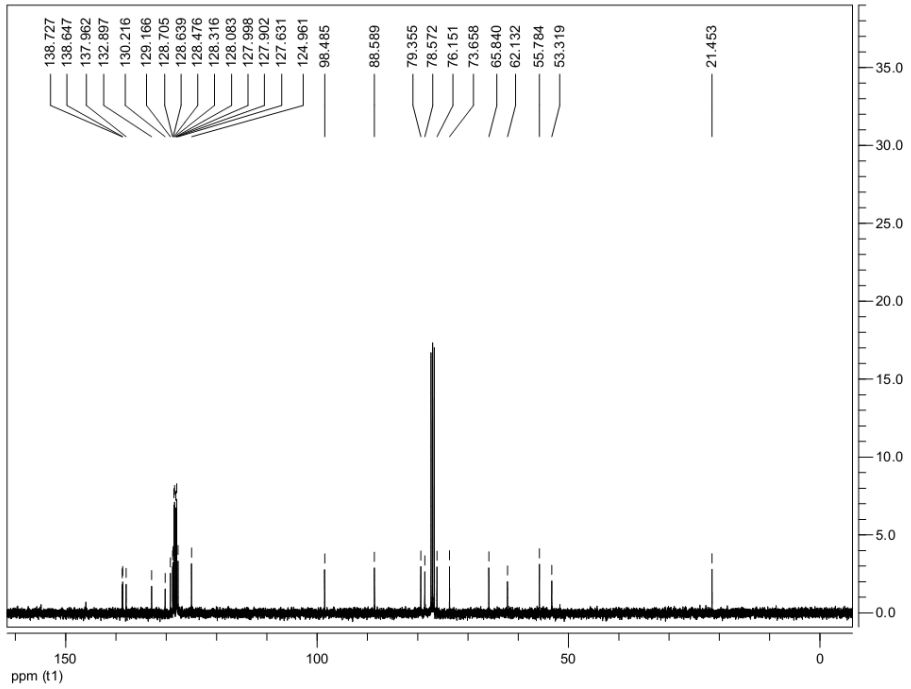


(5aR,6S,7R,8S,9aR)-6,7-bis(benzyloxy)-8-methoxy-3-m-tolyl-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine (20c).

^{1}H NMR (400 MHz, $CDCl_3$)

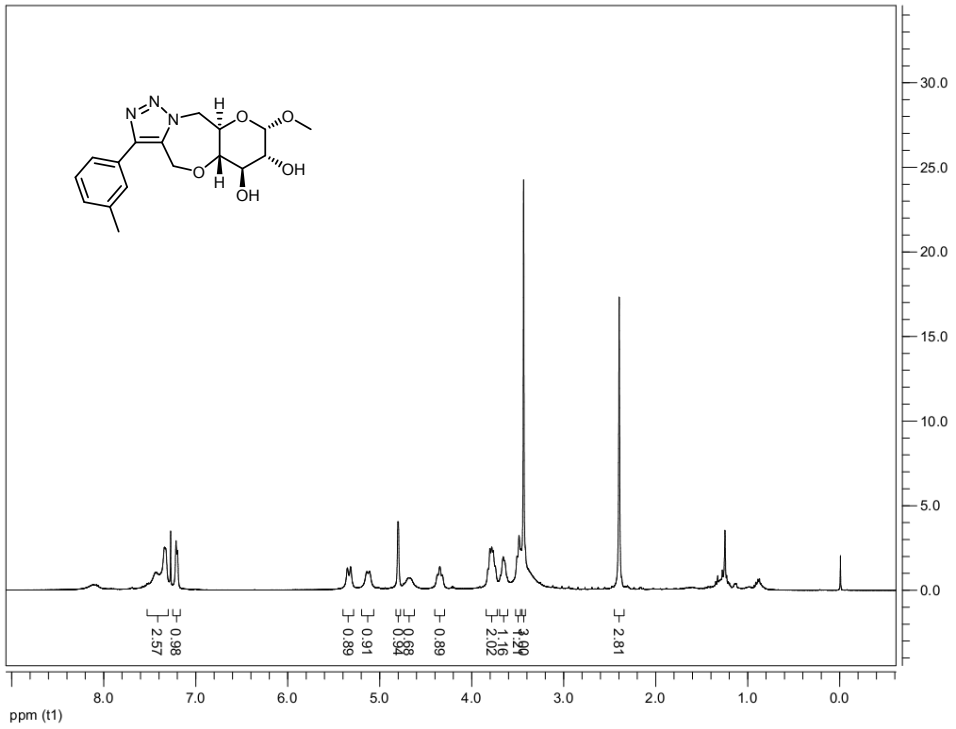


^{13}C NMR (400 MHz, $CDCl_3$)

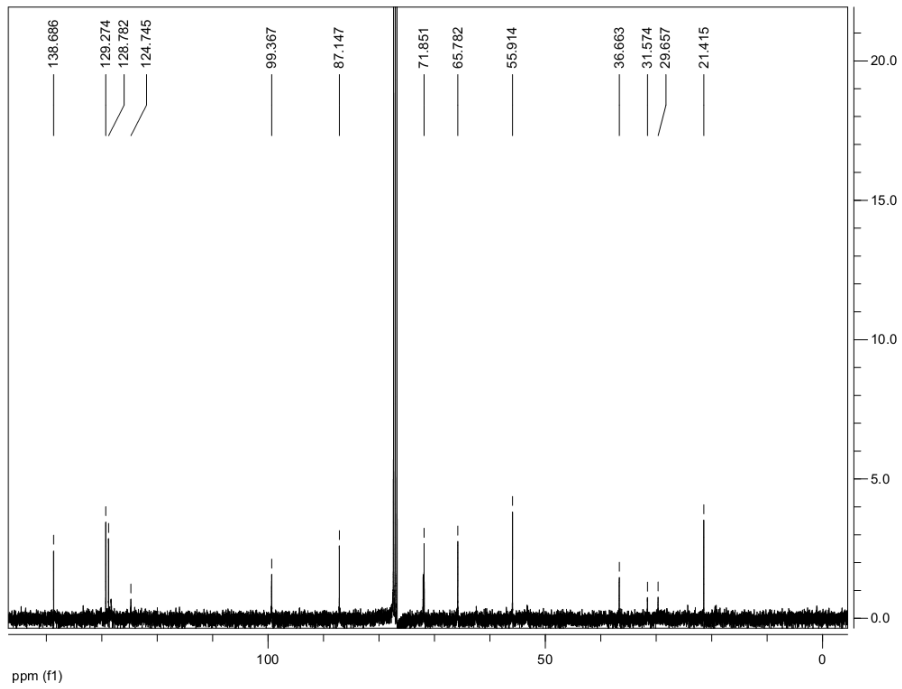


(5aS,6R,7R,8S,9aR)-8-methoxy-3-m-tolyl-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine-6,7-diol (8c).

^{1}H NMR (400 MHz, $CDCl_3$)

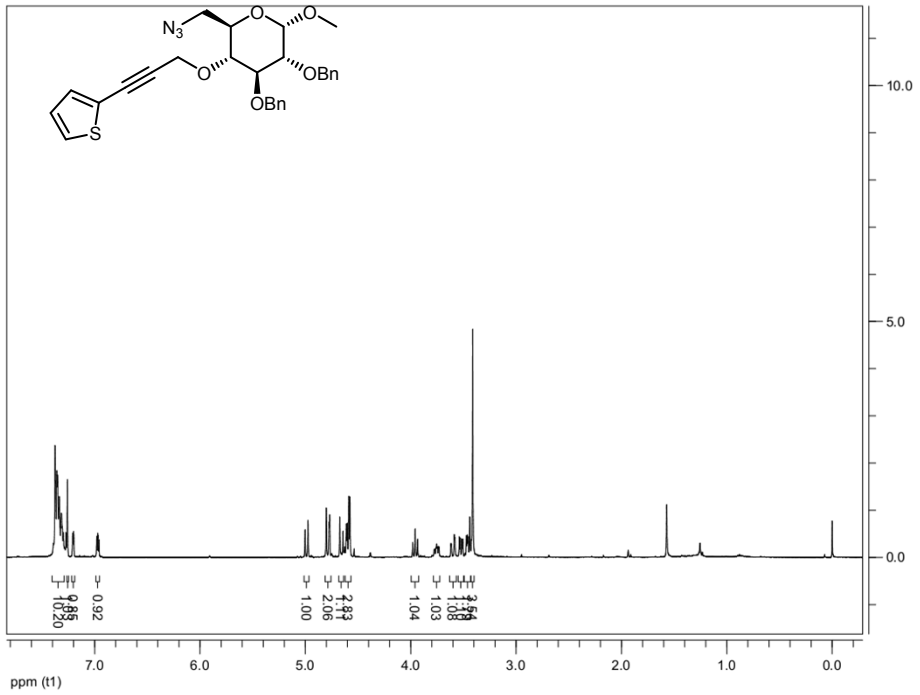


^{13}C NMR (400 MHz, $CDCl_3$)

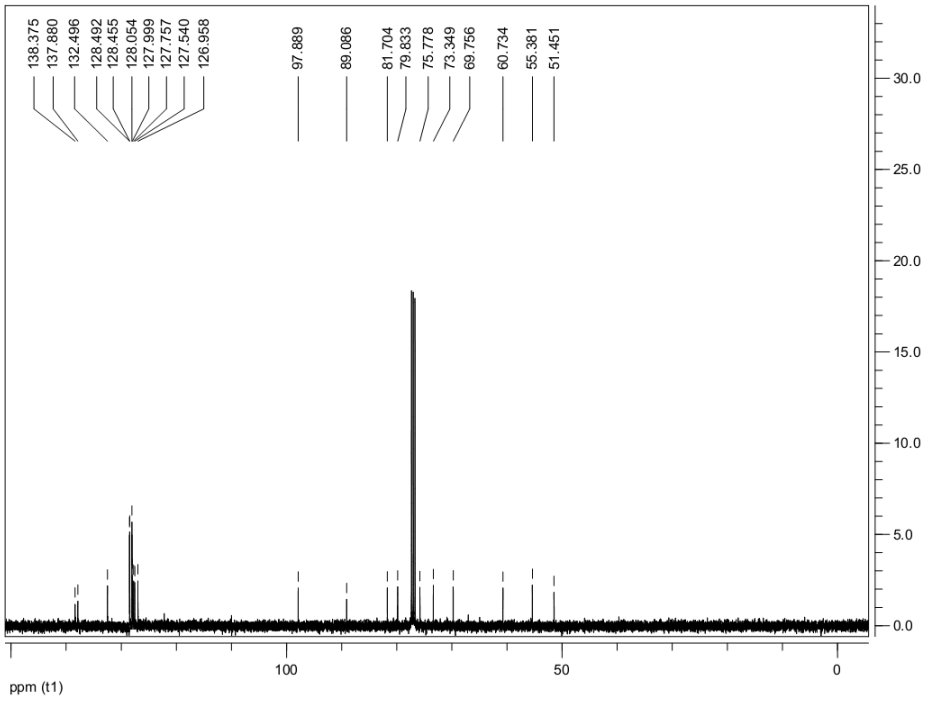


(2R,3R,4S,5R,6S)-2-(azidomethyl)-4,5-bis(benzyloxy)-6-methoxy-3-(3-(thiophen-2-yl)prop-2-ynyloxy)tetrahydro-2H-pyran (19d).

^{1}H NMR (400 MHz, $CDCl_3$)

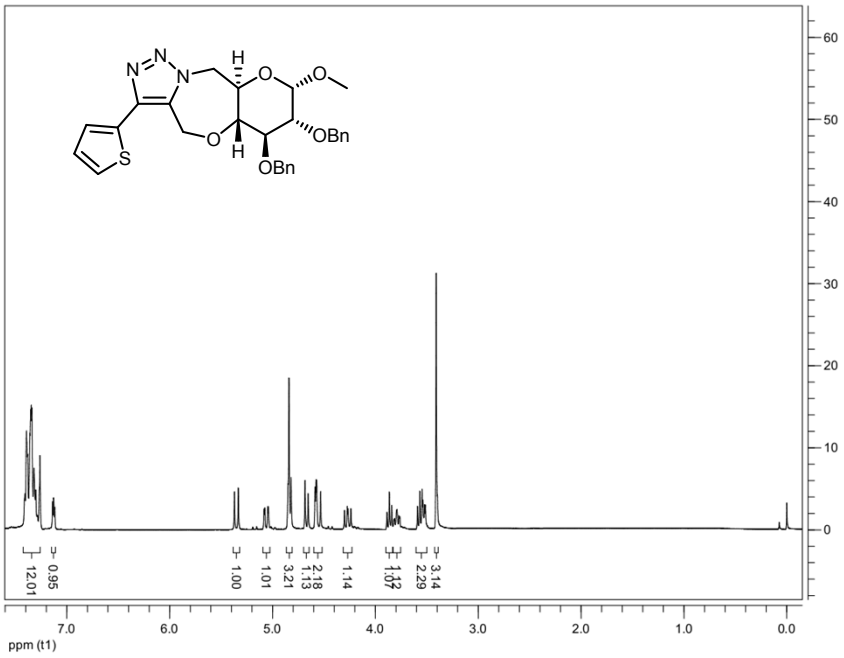


^{13}C NMR (400 MHz, $CDCl_3$)

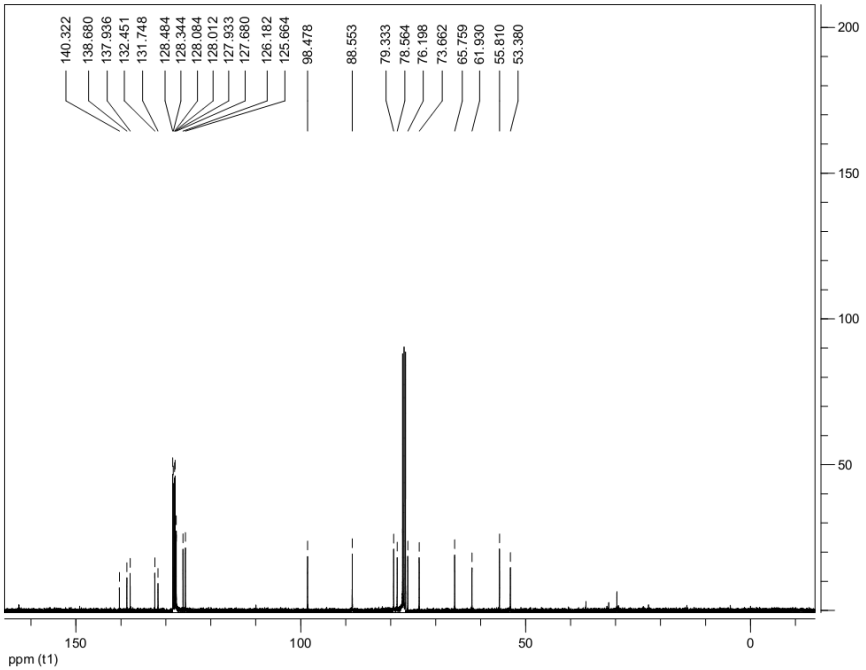


(5aR,6S,7R,8S,9aR)-6,7-bis(benzyloxy)-8-methoxy-3-(thiophen-2-yl)-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine (20d).

^{1}H NMR (400 MHz, $CDCl_3$)

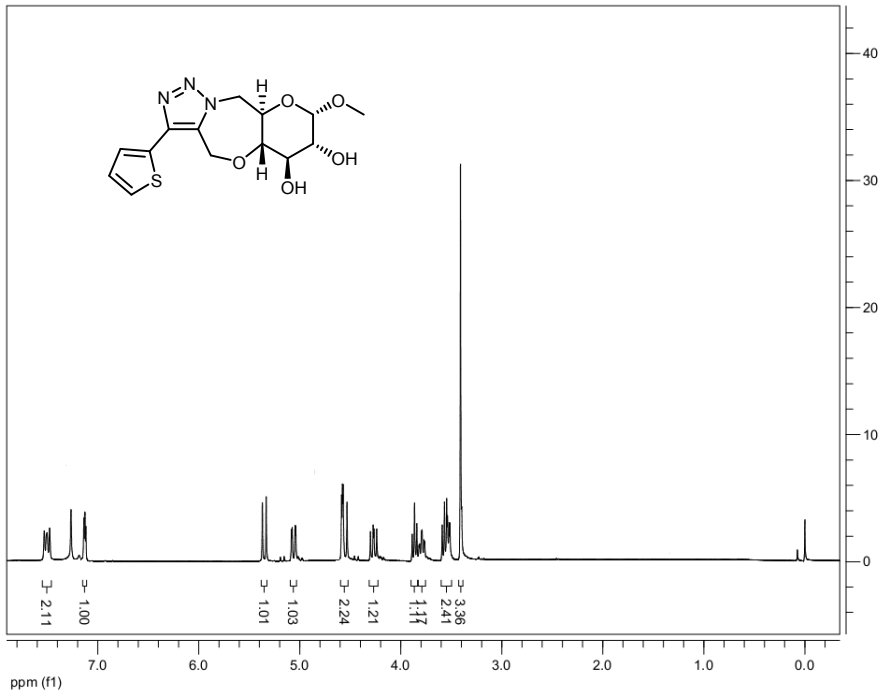


^{13}C NMR (400 MHz, $CDCl_3$)

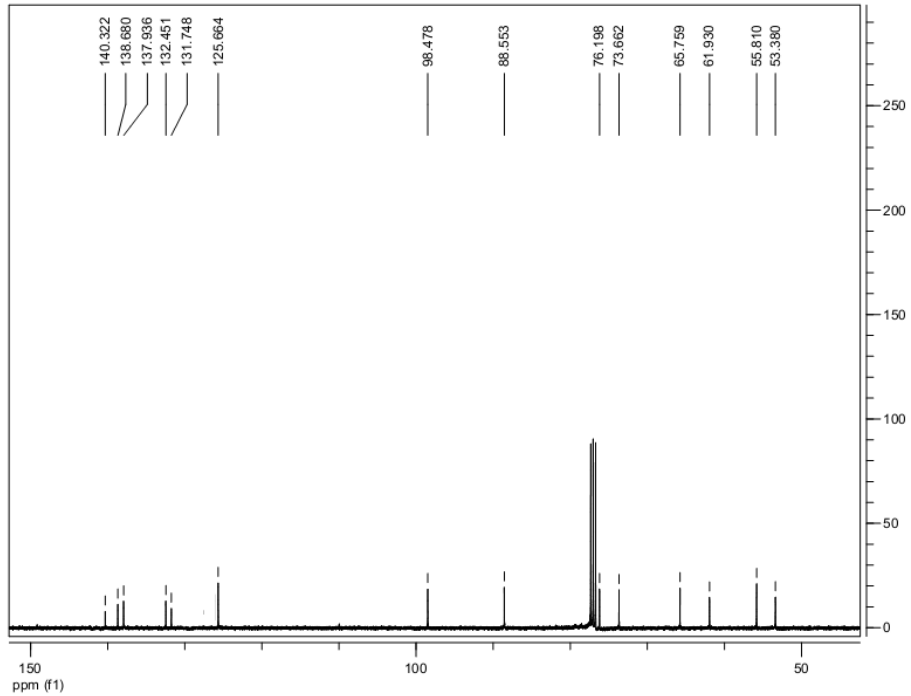


(5aS,6R,7R,8S,9aR)-8-methoxy-3-(thiophen-2-yl)-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine-6,7-diol (8d).

^{1}H NMR (400 MHz, $CDCl_3$)

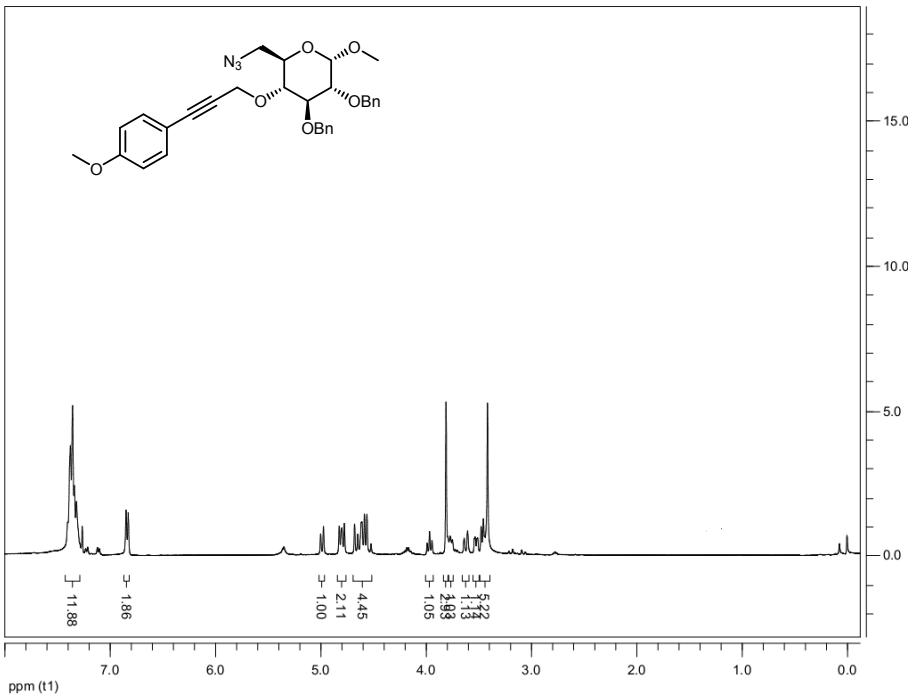


^{13}C NMR (400 MHz, $CDCl_3$)

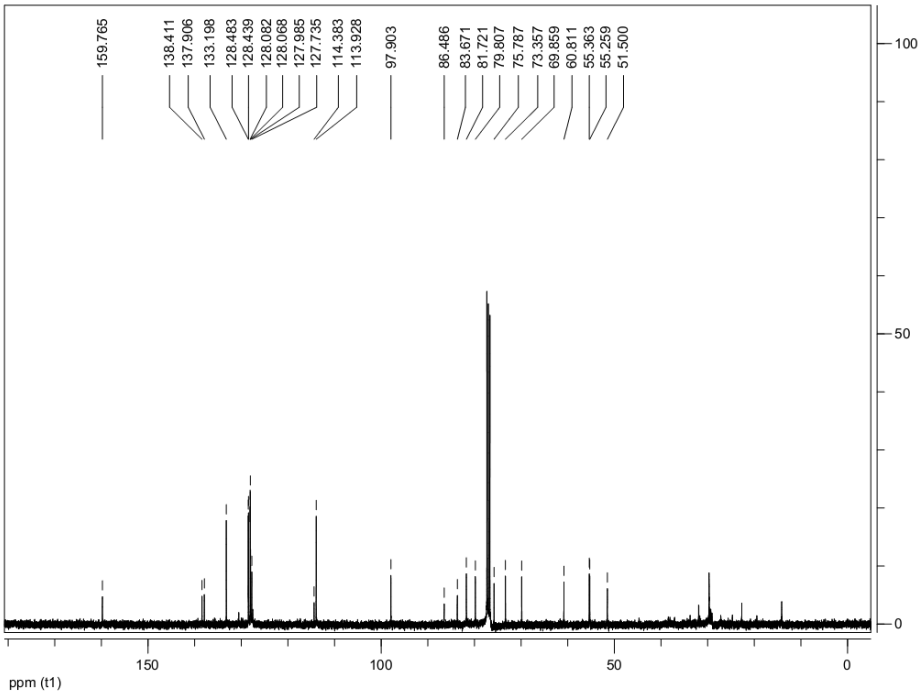


(2R,3R,4S,5R,6S)-2-(azidomethyl)-4,5-bis(benzyloxy)-6-methoxy-3-(3-(4-methoxyphenyl)prop-2-ynyloxy)tetrahydro-2H-pyran (19e).

^{1}H NMR (400 MHz, $CDCl_3$)

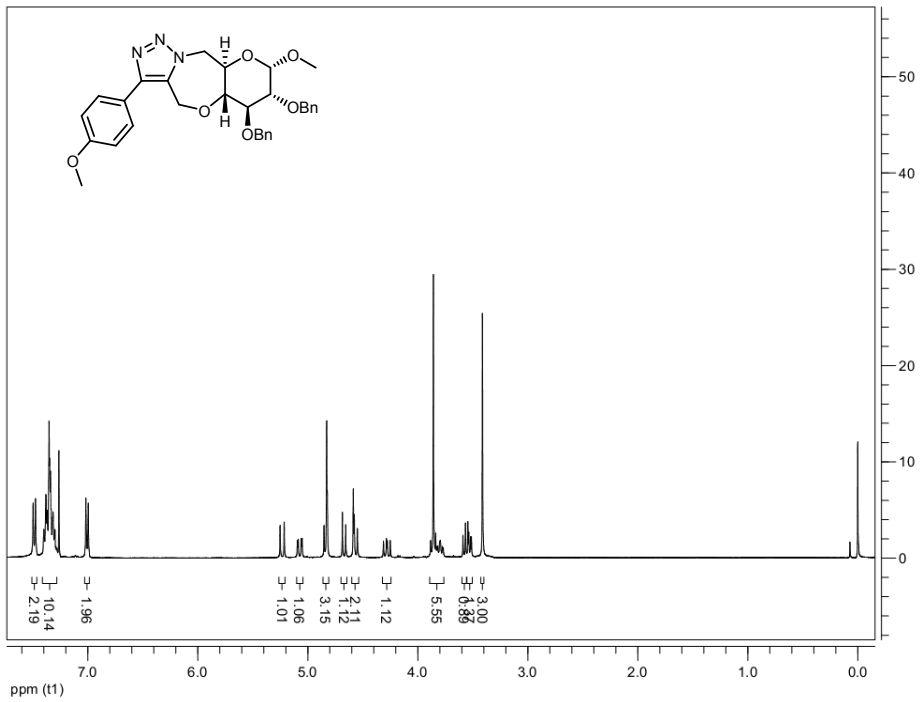


^{13}C NMR (400 MHz, $CDCl_3$)

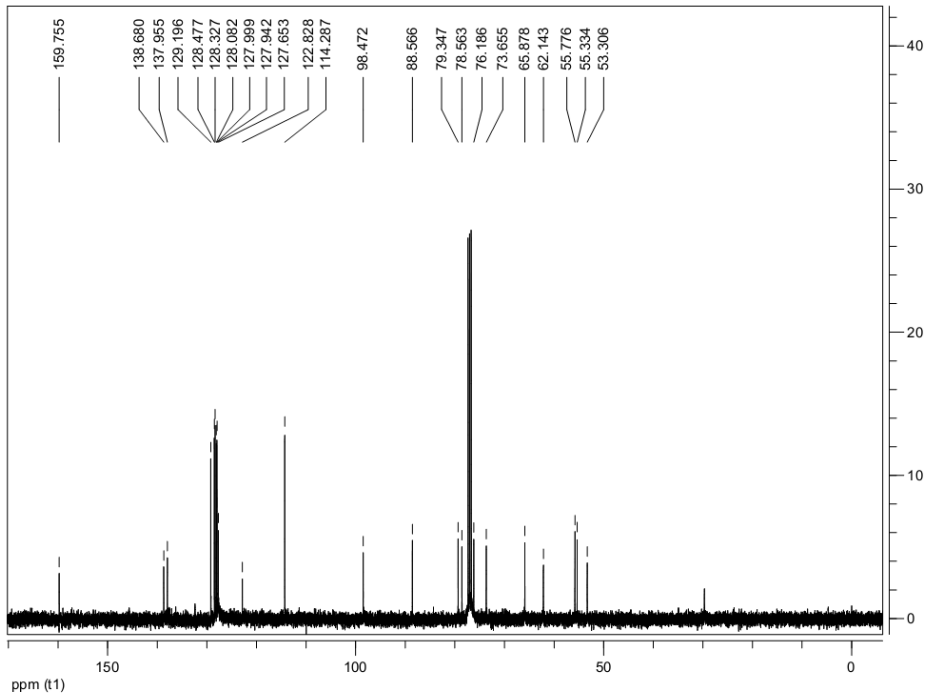


(5aR,6S,7R,8S,9aR)-6,7-bis(benzyloxy)-8-methoxy-3-(4-methoxyphenyl)-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine (20e).

^{1}H NMR (400 MHz, $CDCl_3$)

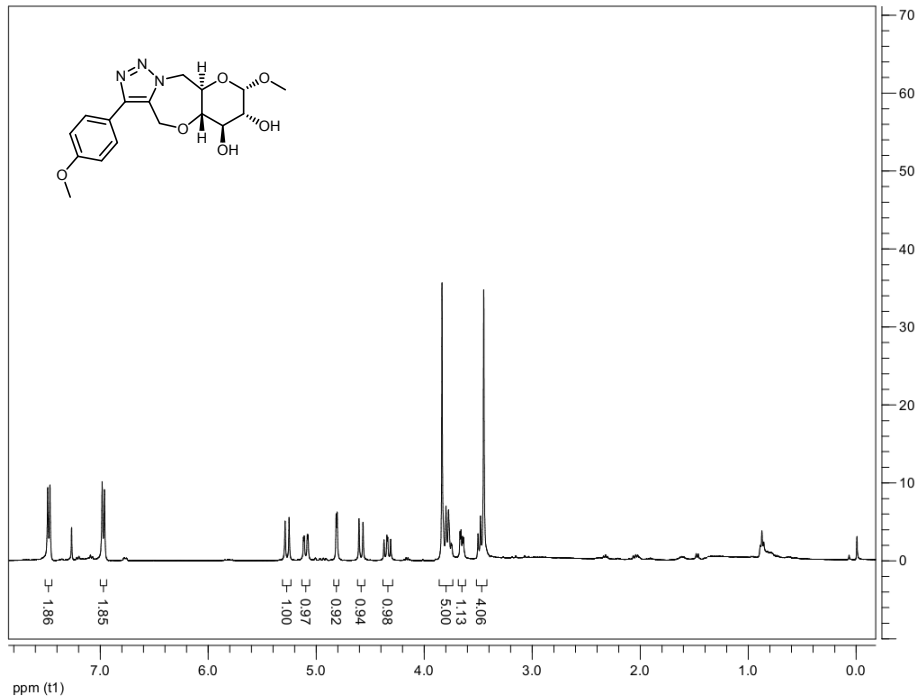


^{13}C NMR (400 MHz, $CDCl_3$)

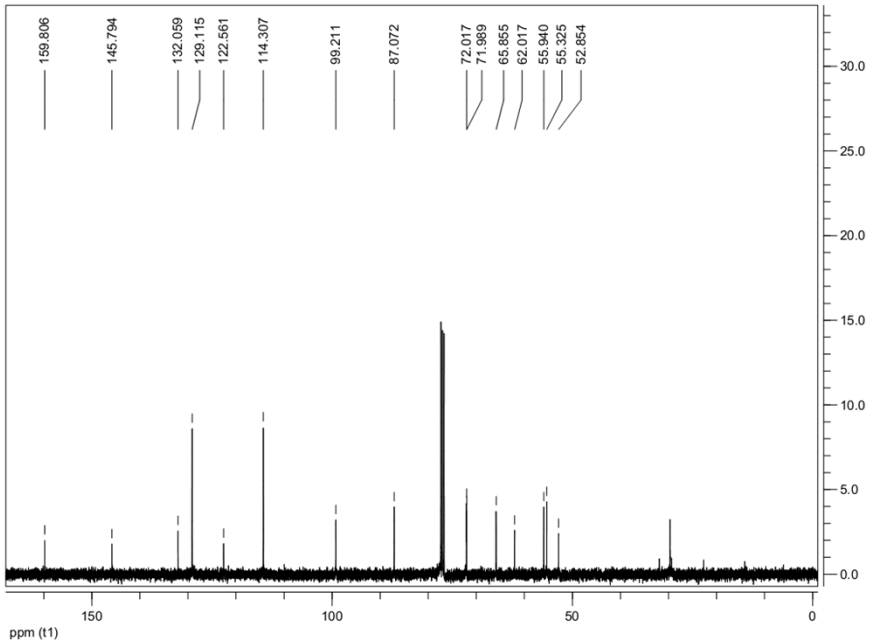


(5aS,6R,7R,8S,9aR)-8-methoxy-3-(4-methoxyphenyl)-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine-6,7-diol (8e).

^{1}H NMR (400 MHz, $CDCl_3$)

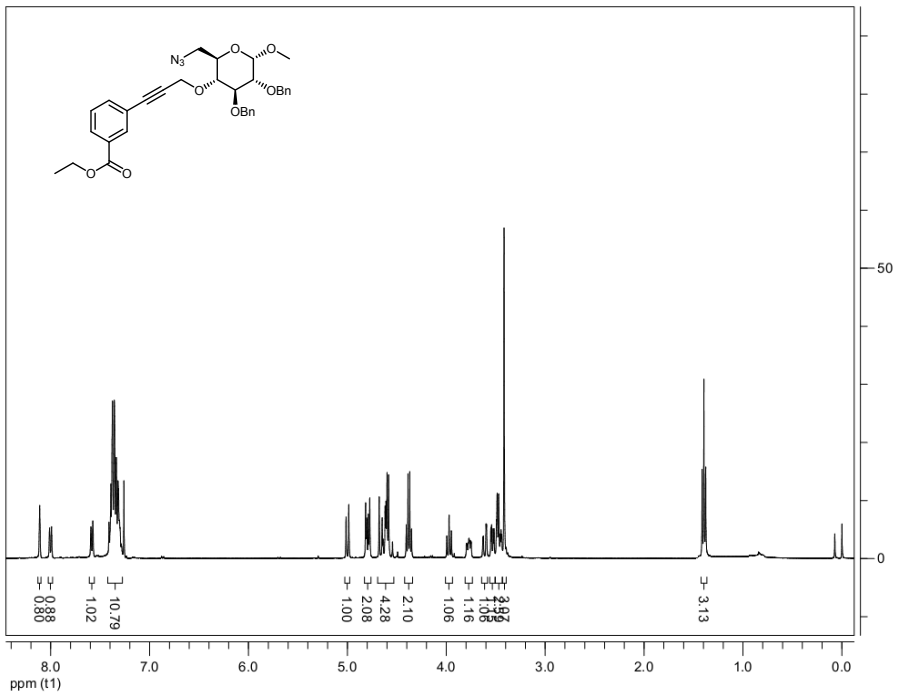


^{13}C NMR (400 MHz, $CDCl_3$)

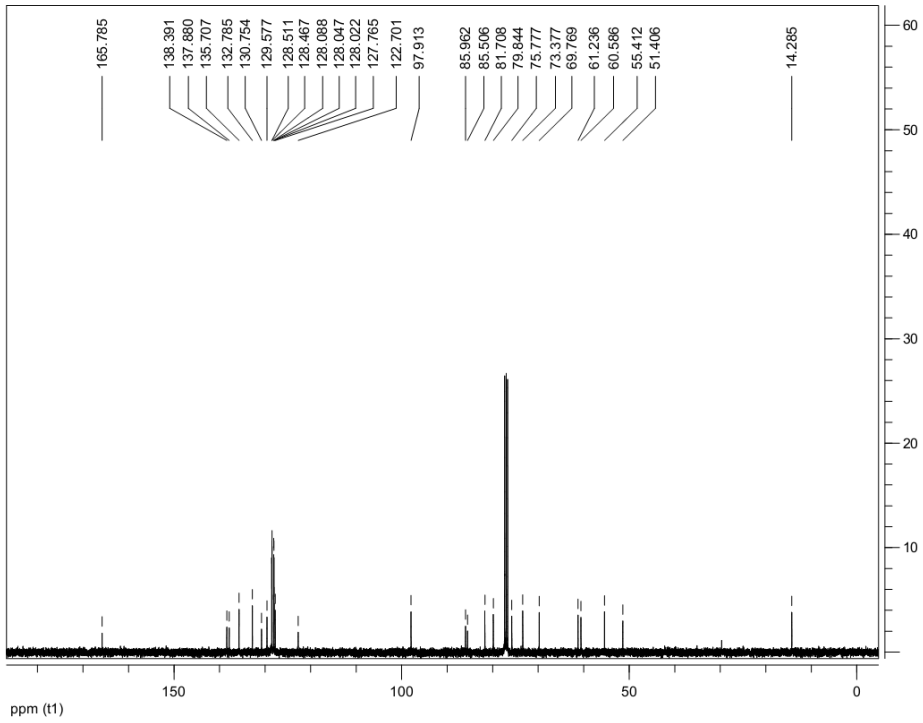


ethyl 3-(3-((2R,3R,4S,5R,6S)-2-(azidomethyl)-4,5-bis(benzyloxy)-6-methoxytetrahydro-2H-pyran-3-yloxy)prop-1-ynyl)benzoate (19f).

^{1}H NMR (400 MHz, $CDCl_3$)

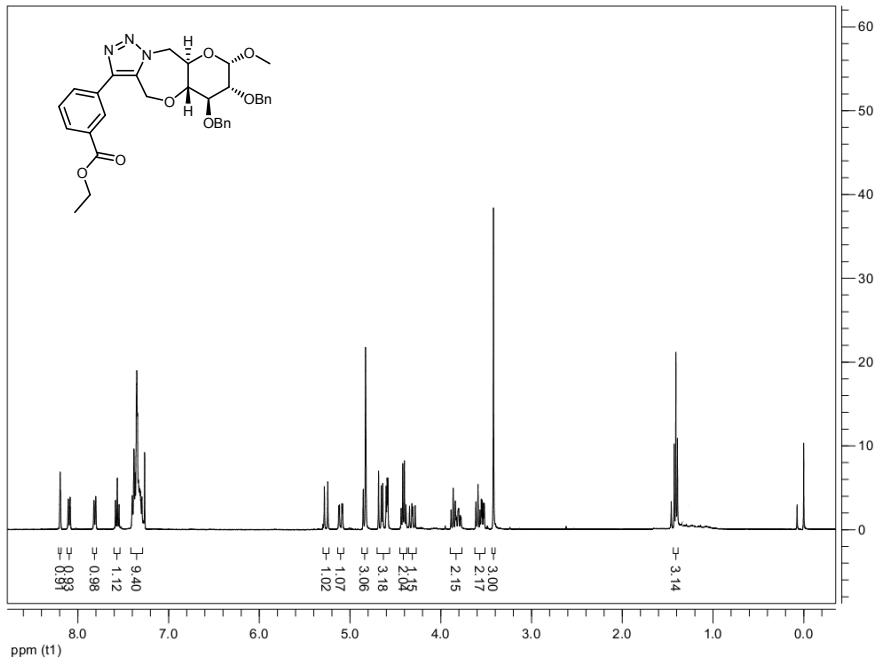


^{13}C NMR (400 MHz, $CDCl_3$)

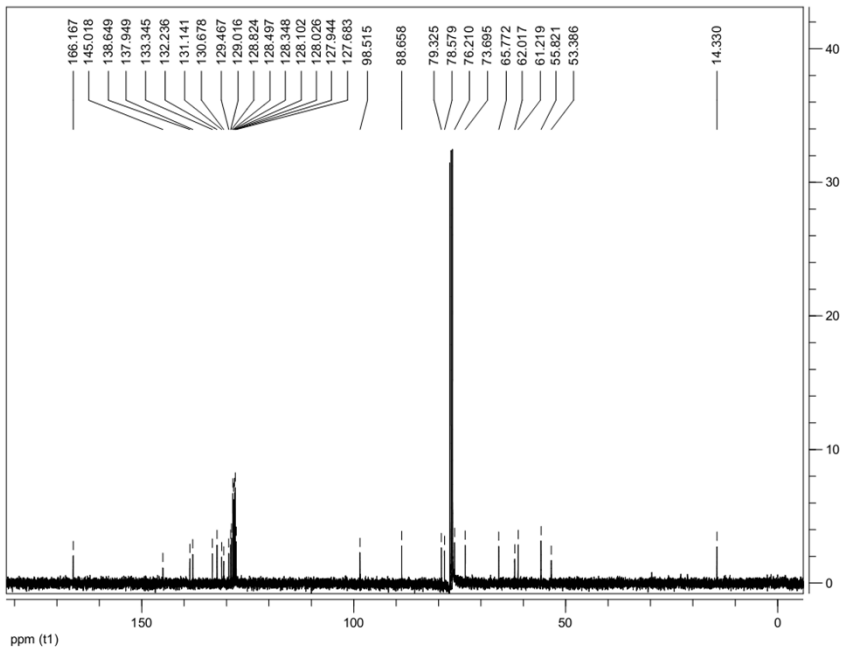


ethyl 3-((5aR,6S,7R,8S,9aR)-6,7-bis(benzyloxy)-8-methoxy-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepin-3-yl)benzoate (20f).

^{1}H NMR (400 MHz, $CDCl_3$)

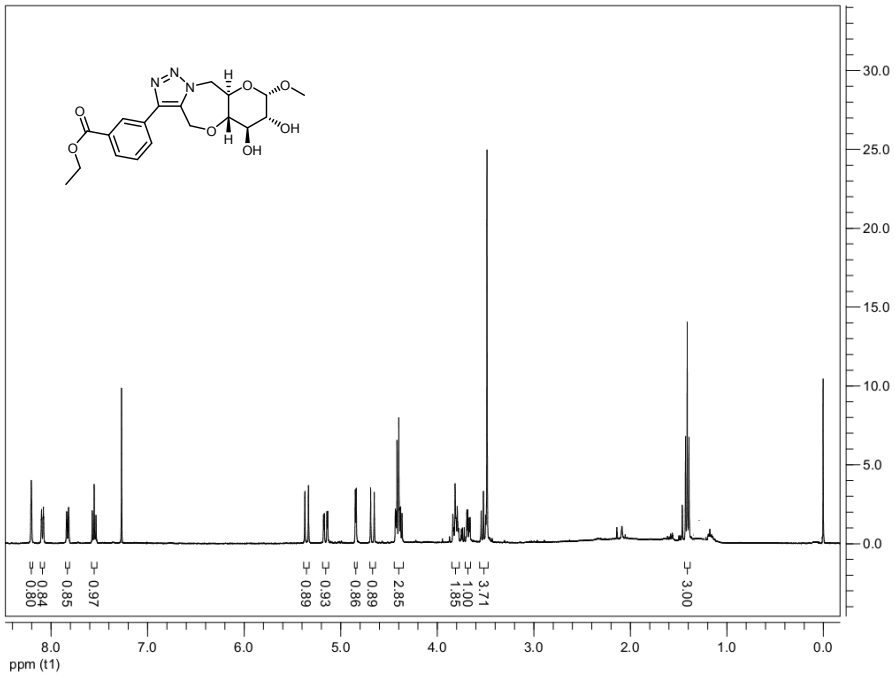


^{13}C NMR (400 MHz, $CDCl_3$)

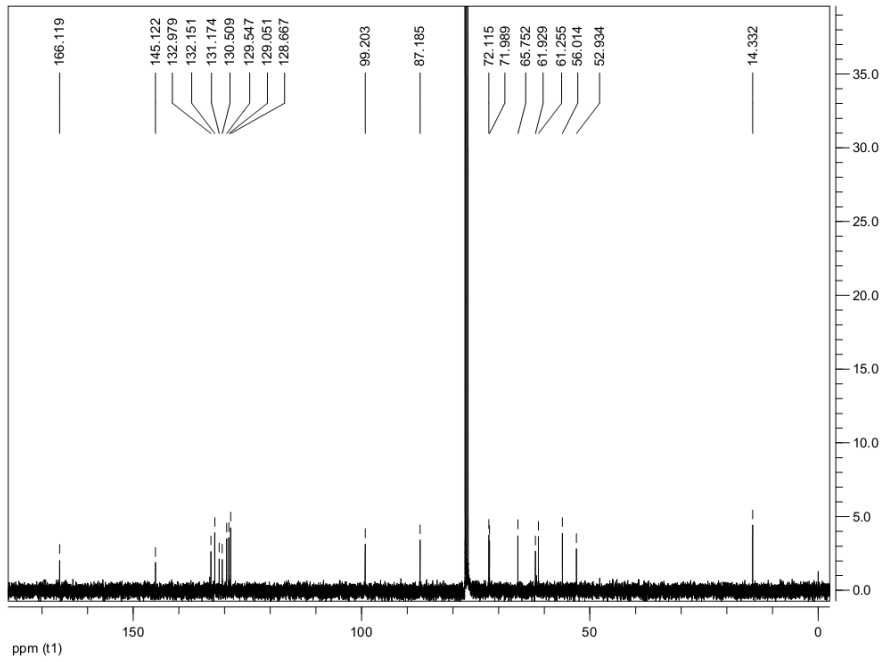


ethyl 3-((5aS,6R,7R,8S,9aR)-6,7-dihydroxy-8-methoxy-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepin-3-yl)benzoate (8f).

^{1}H NMR (400 MHz, $CDCl_3$)

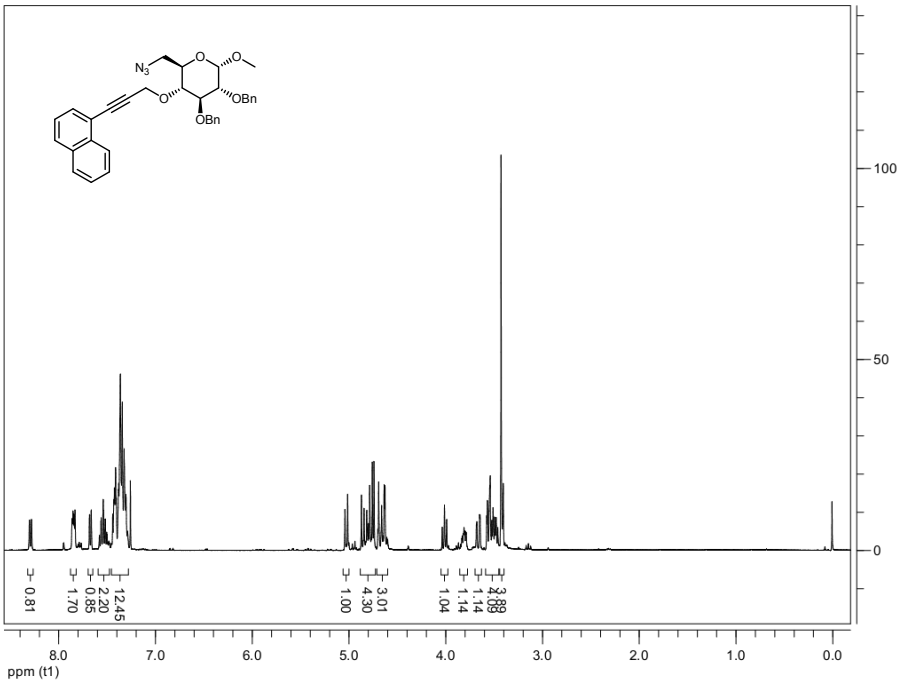


^{13}C NMR (400 MHz, $CDCl_3$)

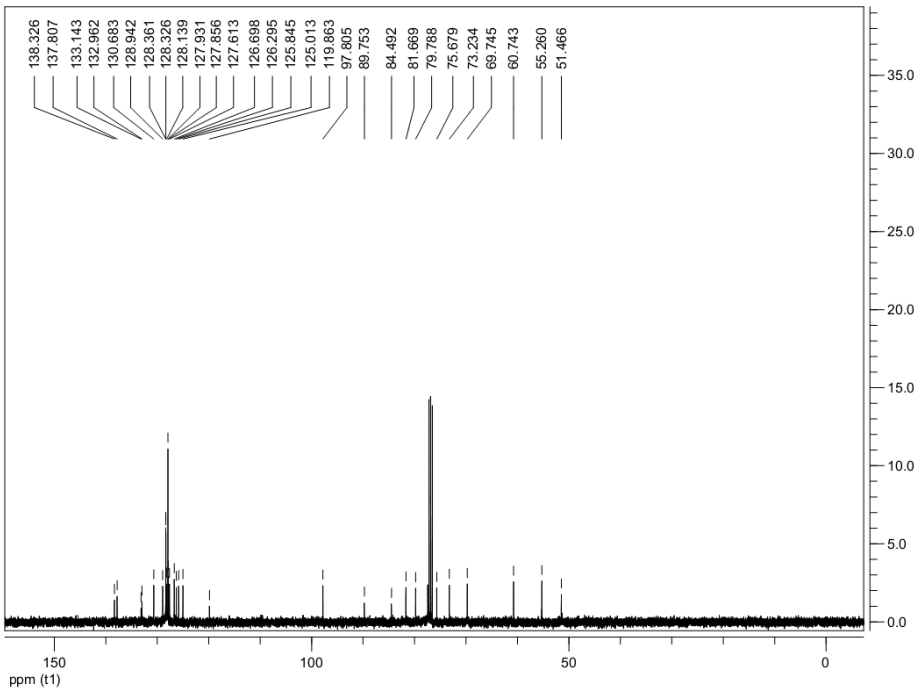


(2R,3R,4S,5R,6S)-2-(azidomethyl)-4,5-bis(benzyloxy)-6-methoxy-3-(3-(naphthalen-1-yl)prop-2-ynyloxy)tetrahydro-2H-pyran (19g).

^{1}H NMR (400 MHz, $CDCl_3$)

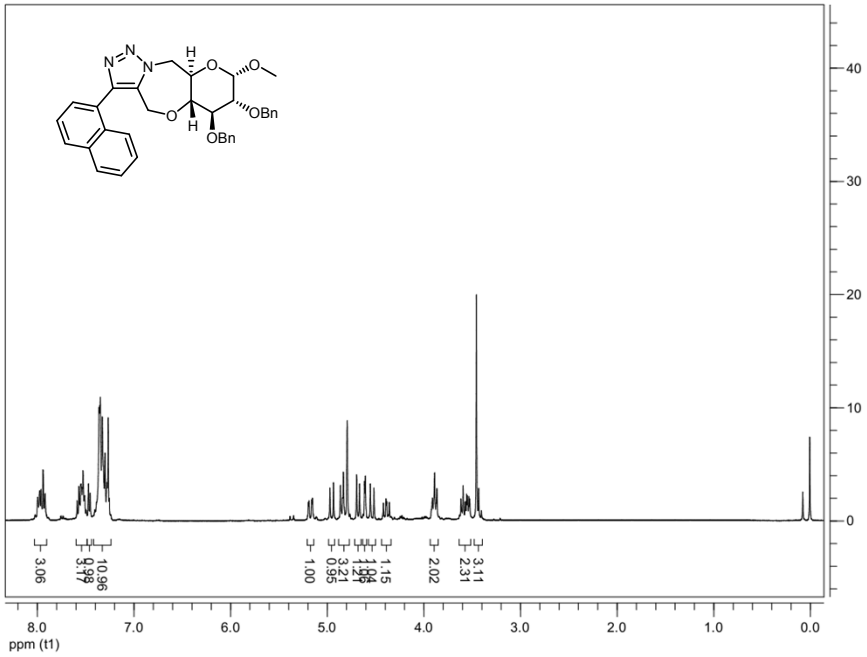


^{13}C NMR (400 MHz, $CDCl_3$)

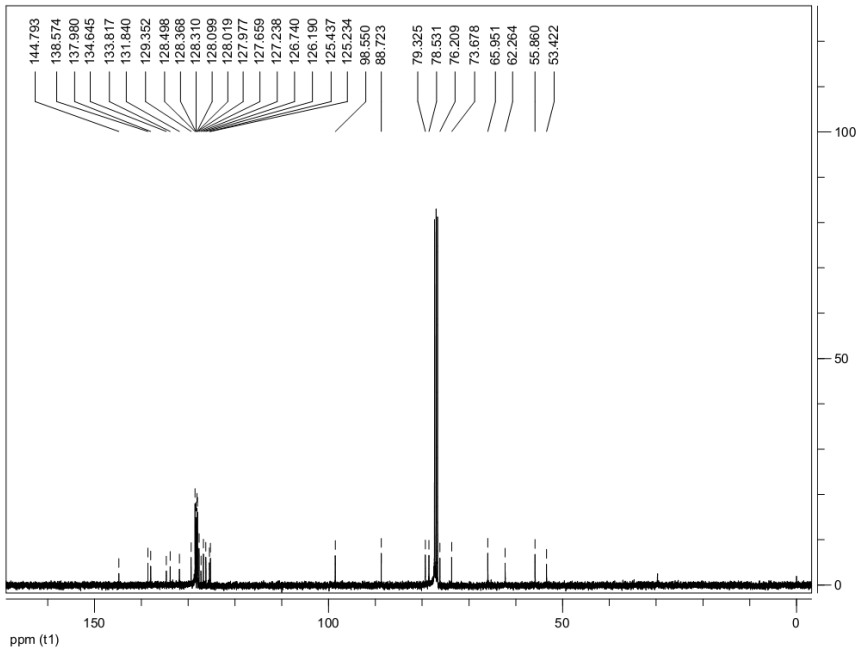


(5aR,6S,7R,8S,9aR)-6,7-bis(benzyloxy)-8-methoxy-3-(naphthalen-1-yl)-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine (20g).

^{1}H NMR (400 MHz, $CDCl_3$)

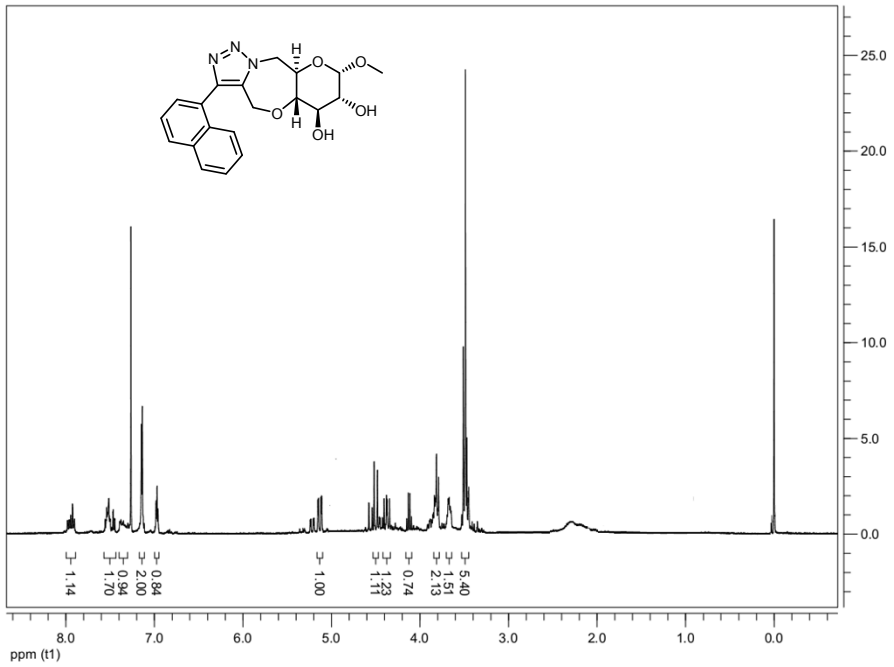


^{13}C NMR (400 MHz, $CDCl_3$)



(5aS,6R,7R,8S,9aR)-8-methoxy-3-(naphthalen-1-yl)-5a,6,7,8,9a,10-hexahydro-4H-pyrano[2,3-f][1,2,3]triazolo[5,1-c][1,4]oxazepine-6,7-diol (8g).

^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (400 MHz, $CDCl_3$)