

A GENERAL A<sup>3</sup>-COUPLING REACTION BASED ON FUNCTIONALIZED ALKYNES

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CONTENTS

General Information .....	S1
Procedure for the synthesis of (but-3-yn-1-yloxy)trimethylsilane (3b) .....	S1
Spectroscopic data for compound 3b .....	S1
Procedure for the synthesis of 2-(but-3-yn-1-yloxy)tetrahydro-2H-pyran (3c) .....	S1
Spectroscopic data for compound 3c .....	S2
Procedure for the synthesis of ((but-3-yn-1-yloxy)methyl)benzene (3d) .....	S2
Spectroscopic data for compound 3d .....	S2
Procedure for the synthesis of but-3-yn-1-yl 4-methylbenzenesulfonate (3e) .....	S2
Spectroscopic data for compound 3e .....	S2
General procedure for the synthesis of hydroxypropargylamine derivatives .....	S2
Spectroscopic data for compounds 4a-v .....	S2
<sup>1</sup> H NMR and <sup>13</sup> C NMR spectra for compounds 3b-e and 4a-v .....	S6

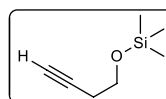
General information

All reagents were purchased from Aldrich. Thin layer chromatography (TLC) was performed using silica gel 60 F<sub>254</sub> pre-coated plates, and the chemicals were made visible using vanillin as a coloring reagent (using 1.0 g vanillin in a 99:1 CH<sub>3</sub>CO<sub>2</sub>H / H<sub>2</sub>SO<sub>4</sub> solution). Gas chromatography was performed using a Shimadzu® GC2014 instrument equipped with a DB-5 column (30 m length, 0.25 mm id, 0.25 μm film) and a flame ionization detector (FID). All new compounds were characterized by NMR, IR, EI-MS, and HRMS spectroscopy. The <sup>1</sup>H NMR (400 MHz) and <sup>13</sup>C NMR (100 MHz) spectra were recorded on a Bruker® DRX 400 spectrometer using tetramethylsilane (TMS) as the internal standard. Chemical shifts are reported in parts per million (ppm, δ) downfield of TMS. The IR spectra were recorded using a Bomen Hartmann & Braun® MB-Series Model Arid-Zone® instrument. Low-resolution mass spectra were recorded using a Shimadzu® QP 5000 MS after gas chromatographic separation using an HP-5MS GC column (30 m length, 0.25 mm id, 0.25 μm film). High-resolution mass spectra were recorded using a Bruker® Daltonics MicroTOF Ic LC/MS instrument from direct injections of the pure samples.

Procedure for the synthesis of (but-3-yn-1-yloxy)trimethylsilane (3b)

Imidazole (1.8 g, 26 mmol) and chlorotrimethylsilane (2.8 g, 3.3 mL, 26 mmol) were added to a stirred solution of 3-butyn-1-ol (1.4 g, 1.5 mL, 20 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (15 mL) at 0 °C. The reaction was warmed to room temperature and quenched with water (20 mL). The aqueous phase was then extracted with EtOAc (3 × 15 mL). The extracts were combined, washed with brine (15 mL), dried over MgSO<sub>4</sub>, and concentrated under reduced pressure. The crude product was purified using a Kugelrohr distillation apparatus (100 °C, 760 mm Hg), giving (but-3-yn-1-yloxy)trimethylsilane (3b) (2.3 g, 80%).

Spectroscopic data for compound 3b



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.67 (t, 2H, *J* 7.1 Hz), 2.37 (td, 2H, *J* 7.1, 2.7 Hz), 1.93 (t, 1H, *J* 2.7 Hz), 0.09 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 81.1, 69.3, 61.1, 22.7, -0.5; CAS 17869-75-9.

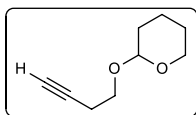
Procedure for the synthesis of 2-(but-3-yn-1-yloxy)tetrahydro-2H-pyran (3c)

3,4-Dihydropyran (2.5 g, 2.7 mL, 30 mmol) was added to a stirred

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solution of 3-butyn-1-ol (1.4 g, 1.5 mL, 20 mmol) and Amberlyst 15<sup>®</sup> at 0 °C, and the resulting mixture was stirred overnight. The reaction was diluted with EtOAc (15 mL) and quenched with NaHCO<sub>3</sub> (20 mL, saturated aqueous solution). The aqueous phase was extracted with EtOAc (2 × 15 mL) and the extracts were combined, washed with brine (15 mL), dried over MgSO<sub>4</sub>, and concentrated under reduced pressure. The crude product was purified using a Kugelrohr distillation apparatus (140 °C, 760 mm Hg), giving 2-(but-3-yn-1-yloxy) tetrahydro-2H-pyran (**3c**) (2.7 g, 89%).

#### Spectroscopic data for compound 3c

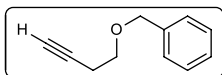


<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.65 (t, 1H, *J* 3.3 Hz), 3.88 (ddd, 1H, *J* 11.3, 8.3, 3.3 Hz), 3.83 (dt, 1H, *J* 9.7, 7.0 Hz), 3.57 (dt, 1H, *J* 9.7, 7.0 Hz), 2.49 (td, 2H, *J* 7.0, 2.7 Hz), 3.54-3.48 (m, 1H), 1.90-1.47 (m, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 98.8, 81.4, 69.1, 65.5, 62.2, 30.5, 25.4, 19.9, 19.4; CAS 40365-61-5.

#### Procedure for the synthesis of ((but-3-yn-1-yloxy)methyl)benzene (**3d**)

NaH (0.9 g, 60% in mineral oil, 22 mmol) was added to a stirred solution of 3-butyn-1-ol (1.4 g, 1.5 mL, 20 mmol) in dry THF (20 mL) at 0 °C. Benzyl chloride (2.5 g, 2.3 mL, 20 mmol) was added after 10 min, and the resulting mixture was stirred for 1 h. The reaction was quenched with NH<sub>4</sub>Cl (20 mL, saturated aqueous solution). The aqueous phase was extracted with EtOAc (3 × 15 mL), and the extracts were combined, dried over MgSO<sub>4</sub>, and concentrated under reduced pressure. The crude product was purified using a Kugelrohr distillation apparatus (110 °C, 1 mm Hg), giving ((but-3-yn-1-yloxy)methyl)benzene (**3d**) (2.9 g, 90%).

#### Spectroscopic data for compound 3d

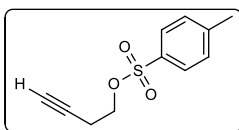


<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.39-7.24 (m, 5H), 3.59 (t, 2H, *J* 6.9 Hz), 4.55 (s, 2H), 2.49 (td, 2H, *J* 6.9, 2.7 Hz), 1.97 (t, 1H, *J* 2.7 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 138.1, 128.4, 127.8, 127.7, 81.3, 73.0, 69.3, 68.2, 19.9; CAS 22273-77-4.

#### Procedure for the synthesis of but-3-yn-1-yl 4-methylbenzenesulfonate (**3e**)

*p*-Toluenesulfonyl chloride (3.8 g, 20 mmol) was added to a stirred solution of 3-butyn-1-ol (1.4 g, 1.5 mL, 20 mmol), triethylamine (2.2 g, 3.0 mL, 22 mmol), and 4-dimethylaminopyridine (2.5 mg, 0.02 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (15 mL) at 0 °C, and the resulting mixture was stirred for 3 h. The reaction was quenched with water (20 mL), and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 15 mL); the extracts were then dried over MgSO<sub>4</sub> and concentrated under reduced pressure. The crude product was purified using a Kugelrohr distillation apparatus (150 °C, 1 mm Hg), giving but-3-yn-1-yl 4-methylbenzenesulfonate (**3e**) (4.4 g, 99%).

#### Spectroscopic data for compound 3e



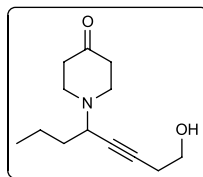
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.80 (d, 2H, *J* 8.3 Hz), 7.35 (d, 2H, *J* 8.3 Hz), 4.11 (t, 2H, *J* 7.0 Hz), 2.55 (td, 2H, *J* 7.0, 2.7 Hz), 1.97 (t, 1H, *J* 2.7 Hz), 2.45 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 144.9, 132.9, 129.9, 127.9, 78.4, 70.7, 67.4, 21.6, 19.4; CAS 23418-85-1.

#### General procedure for the synthesis of hydroxypropargylamine derivatives

CuCl (9 mg, 0.1 mmol), 4 Å molecular sieves (300 mg), 4-piperidone hydrochloride monohydrate (169 mg, 1.1 mmol), and EtOAc (2 mL) were added, in that order, to a 10-mL round-bottomed flask. The mixture was stirred at 70 °C and then triethylamine (110 mg, 150 μL, 1.1 mmol), alkynol (2.0 mmol), and the appropriated aldehyde (1.0 mmol) were added. The reaction mixture was stirred, and the progress of the reaction was monitored by GC-FID or TLC. The reaction mixture was filtered through a short Celite<sup>®</sup> pad in a column, which was eluted with EtOAc (3 × 5 mL). A saturated NH<sub>4</sub>Cl solution (10 mL) was added to the organic phase, and the mixture was stirred vigorously for 20 min, separated, and the organic phase was treated with HCl (15 mL, 10% v/v) in a separatory funnel. The aqueous phase was washed with EtOAc (10 mL) to remove any homocoupling products, neutralized with a saturated NaHCO<sub>3</sub> solution (3 × 10 mL), and extracted with EtOAc (4 × 10 mL). The organic extracts were combined, dried over MgSO<sub>4</sub>, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using the appropriate eluent.

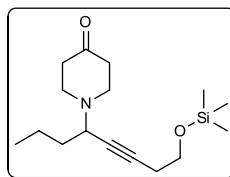
#### Spectroscopic data for compounds 4a-v

##### 1-(8-Hydroxyoct-5-yn-4-yl)piperidin-4-one (**4a**)



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.69 (t, 2H, *J* 6.4 Hz), 3.47 (tt, 1H, *J* 7.0, 2.0 Hz), 2.95-2.86 (m, 2H), 2.76-2.67 (m, 2H), 2.48 (td, 2H, *J* 6.4, 2.0 Hz), 2.54-2.39 (m, 4H), 1.88 (OH), 1.67-1.59 (m, 2H), 1.59-1.36 (m, 2H), 0.95 (t, 3H, *J* 7.3 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 209.1, 82.3, 79.1, 61.3, 56.6, 49.2, 41.5, 36.0, 23.0, 19.9, 13.8; IR (film) ν<sub>max</sub>/cm<sup>-1</sup>: 3427, 2958, 2931, 2869, 2817, 1714, 1461, 1412, 1376, 1337, 1205, 1126, 1048, 759; EI-MS *m/z* 180 (M<sup>+</sup>, 100), 162 (13), 148 (3), 136 (<1), 120 (4), 108 (24), 92 (9), 80 (13), 65 (11), 55 (25); ESI-HRMS calcd. for C<sub>13</sub>H<sub>21</sub>NO<sub>2</sub> [M+H] 224.1651, found 224.1656. Eluent: hexane/EtOAc (1:1), *R<sub>f</sub>* 0.4.

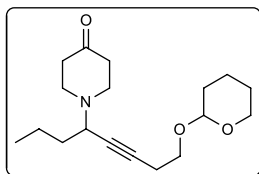
##### 1-(8-((Trimethylsilyl)oxy)oct-5-yn-4-yl)piperidin-4-one (**4b**)



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.65 (t, 2H, *J* 7.2 Hz), 3.44 (ddt, 1H, *J* 7.6, 7.5, 2.0 Hz), 2.95-2.86 (m, 2H), 2.76-2.67 (m, 2H), 2.42 (td, 2H, *J* 7.1, 2.0 Hz), 2.53-2.43 (m, 4H), 1.62 (q, 2H, *J* 7.3 Hz), 1.58-1.38 (m, 2H), 0.95 (t, 3H, *J* 7.3 Hz), 0.12 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 209.2, 82.7, 78.2, 61.5, 56.6, 49.2, 41.5, 36.0, 22.9, 19.9, 13.8, -0.5; IR (film) ν<sub>max</sub>/cm<sup>-1</sup>: 2957, 2934, 2871, 2814, 2749, 1719, 1470, 1415, 1382, 1339, 1250, 1206, 1101, 1057, 1001, 921, 874, 842, 755; EI-MS *m/z* 280 (M<sup>+</sup>, <1), 252 (84), 210 (2), 183 (1), 162 (23), 154 (18), 148 (3), 140 (1), 120 (9), 119 (15), 103 (25), 73 (100), 68 (10), 59 (8), 55 (12); ESI-HRMS calcd. for C<sub>16</sub>H<sub>29</sub>NO<sub>2</sub>Si [M+H] 296.2046, found 296.2038. Eluent: hexane/EtOAc (1:1), *R<sub>f</sub>* 0.8.

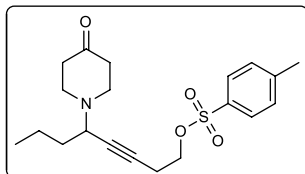
##### 1-(8-((Tetrahydro-2H-pyran-2-yl)oxy)oct-5-yn-4-yl)piperidin-4-one (**4c**)

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.65 (t, 1H, *J* 3.3 Hz), 3.87 (ddd, 1H, *J* 11.3, 8.5, 3.1 Hz), 3.79 (dt, 1H, *J* 9.5, 7.1 Hz), 3.50 (dt, 2H, *J* 9.5, 7.0 Hz), 3.44 (ddt, 1H, *J* 7.6, 7.5, 2.0 Hz), 2.96-2.86 (m, 2H), 2.77-2.67 (m, 2H), 2.50 (td, 2H, *J* 7.0, 2.0 Hz), 2.55-2.38 (m, 4H), 1.88-1.37



(m, 10H), 0.94 (t, 3H, *J* 7.3 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 209.2, 98.7, 82.8, 77.9, 66.1, 62.1, 56.6, 49.2, 41.5, 36.0, 30.6, 25.4, 20.1, 19.9, 19.3, 13.8; IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 2955, 2939, 2871, 2816, 2749, 2226, 1719, 1466, 1455, 1441, 1382, 1340, 1285, 1205, 1136, 1123, 1071, 1033, 969, 905, 869, 813, 761; EI-MS *m/z* 264 (M<sup>-43</sup>, 48), 234 (3), 206 (2), 180 (3), 164 (41), 162 (100), 148 (3), 136 (34), 122 (68), 107 (9), 98 (6), 92 (14), 85 (75), 67 (51), 55 (40); ESI-HRMS calcd. for C<sub>18</sub>H<sub>29</sub>NO<sub>3</sub> [M+H] 308.2226, found 308.2223. Eluent: hexane/EtOAc (1:1), *R<sub>f</sub>* 0.6.

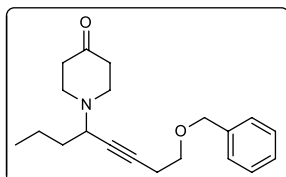
#### 5-(4-Oxopiperidin-1-yl)oct-3-yn-1-yl 4-methylbenzenesulfonate (4d)



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.79 (d, 2H, *J* 8.0 Hz), 7.36 (d, 2H, *J* 8.0 Hz), 4.08 (t, 2H, *J* 7.0 Hz), 3.40 (ddt, 1H, *J* 6.7, 6.6, 2.0 Hz), 2.89-2.79 (m, 2H), 2.69-2.61 (m, 2H), 2.58 (td, 2H, *J* 7.0, 2.0 Hz),

2.46 (s, 3H), 2.51-2.36 (m, 4H), 1.65-1.53 (m, 2H), 1.53-1.34 (m, 2H), 0.93 (t, 3H, *J* 7.3 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 208.9, 144.9, 133.1, 129.9, 127.9, 79.8, 79.7, 67.9, 56.5, 49.1, 41.4, 35.8, 21.6, 19.8, 19.7, 13.7; IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 2959, 2933, 2871, 2814, 2751, 2269, 1715, 1597, 1495, 1468, 1416, 1361, 1340, 1291, 1208, 1189, 1177, 1127, 1096, 1073, 983, 903, 816, 765, 664; EI-MS *m/z* 334 (M<sup>-43</sup>, 27), 162 (100), 160 (3), 125 (4), 108 (4), 98 (4), 92 (22), 91 (37), 79 (16), 77 (11), 65 (25), 55 (32); ESI-HRMS calcd. for C<sub>20</sub>H<sub>27</sub>NO<sub>4</sub>S [M+H] 378.1739, found 378.1739. Eluent: hexane/EtOAc (1:1), *R<sub>f</sub>* 0.7.

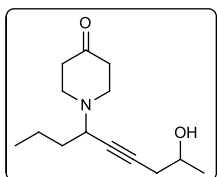
#### 1-(8-(Benzyloxy)oct-5-yn-4-yl)piperidin-4-one (4e)



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.38-7.26 (m, 5H), 4.54 (s, 3H), 3.57 (t, 2H, *J* 7.0 Hz), 3.44 (ddt, 1H, *J* 7.7, 7.6, 2.0 Hz), 2.93-2.85 (m, 2H), 2.76-2.66 (m, 2H), 2.52 (td, 2H, *J* 7.0, 2.0 Hz), 2.49-2.37 (m, 4H), 1.62 (q, 2H, *J* 7.5 Hz), 1.57-1.36 (m, 2H),

0.94 (t, 3H, *J* 7.3 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 209.2, 138.1, 128.4, 127.6, 82.6, 78.1, 72.9, 68.9, 56.6, 49.2, 41.5, 36.0, 20.1, 19.9, 13.8; IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 3029, 2957, 2932, 2869, 2814, 2749, 1717, 1496, 1454, 1412, 1381, 1362, 1339, 1206, 1102, 1075, 1028, 1002, 737, 697, 606; EI-MS *m/z* 270 (M<sup>-43</sup>, 54), 240 (39), 228 (2), 206 (<1), 198 (6), 178 (<1), 162 (4), 148 (6), 136 (10), 122 (9), 106 (7), 92 (15), 91 (100), 79 (13), 77 (10), 65 (26), 55 (24); ESI-HRMS calcd. for C<sub>20</sub>H<sub>27</sub>NO<sub>2</sub> [M+H] 314.2120, found 314.2113. Eluent: hexane/EtOAc (2:1), *R<sub>f</sub>* 0.7.

#### 1-(8-Hydroxynon-5-yn-4-yl)piperidin-4-one (4f)

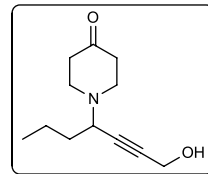


<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.92 (sext, 1H, *J* 6.2 Hz), 3.47 (ddt, 1H, *J* 7.5, 7.4, 1.9 Hz), 2.95-2.87 (m, 2H), 2.76-2.68 (m, 2H), 2.54-2.30 (m, 6H), 1.98 (OH), 1.70-1.59 (m, 2H), 1.59-1.37 (m, 2H), 1.25 (d, 3H, *J* 6.2 Hz), 0.95 (t, 3H, *J* 7.3 Hz); <sup>13</sup>C NMR

(100 MHz, CDCl<sub>3</sub>) δ 209.1, 82.0, 79.8, 66.5, 56.6, 49.2, 41.5, 36.1, 29.2, 22.4, 19.9, 13.8; IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 3416, 2961, 2932, 2872, 2816, 2229, 1715, 1460, 1416, 1380, 1340, 1207, 1125, 1073, 939, 762; EI-MS *m/z* 194 (M<sup>-43</sup>, 100), 176 (3), 150 (25), 138 (2), 120 (3), 108 (74), 94 (10), 80 (40), 67 (20), 55 (53); ESI-HRMS calcd.

for C<sub>14</sub>H<sub>23</sub>NO<sub>2</sub> [M+H] 238.1807, found 238.1798. Eluent: hexane/EtOAc (1:1), *R<sub>f</sub>* 0.6.

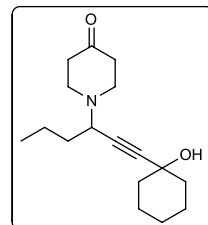
#### 1-(1-Hydroxyhept-2-yn-4-yl)piperidin-4-one (4g)



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.29 (d, 2H, *J* 1.8 Hz), 3.51 (ddt, 1H, *J* 7.6, 7.4, 1.8 Hz), 2.97-2.88 (m, 2H), 2.77-2.69 (m, 2H), 2.54-2.39 (m, 4H), 1.90 (OH), 1.70-1.61 (m, 2H), 1.61-1.37 (m, 2H), 0.96 (t, 3H, *J* 7.3 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 209.0, 84.1,

82.8, 56.5, 50.9, 49.2, 41.4, 35.7, 19.8, 13.7; IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 3416, 2959, 2934, 2871, 2818, 1715, 1461, 1415, 1382, 1340, 1207, 1137, 1072, 972, 762, 623; EI-MS *m/z* 166 (M<sup>-43</sup>, 100), 154 (1), 136 (1), 124 (5), 106 (2), 96 (49), 94 (12), 81 (6), 68 (11), 55 (24); ESI-HRMS calcd. for C<sub>12</sub>H<sub>19</sub>NO<sub>2</sub> [M+H] 210.1494, found 210.1505. Eluent: hexane/EtOAc (1:1), *R<sub>f</sub>* 0.4.

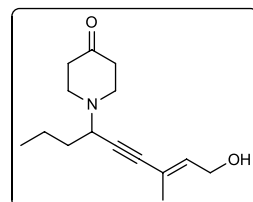
#### 1-(1-(1-Hydroxycyclohexyl)hex-1-yn-3-yl)piperidin-4-one (4h)



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.52 (t, 1H, *J* 7.5 Hz), 2.96-2.88 (m, 2H), 2.77-2.67 (m, 2H), 2.55-2.39 (m, 4H), 1.74-1.61 (m, 4H), 1.60-1.35 (m, 11H), 0.96 (t, 3H, *J* 7.3 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 209.1, 89.7, 81.0, 68.8, 56.4, 49.2, 41.5, 40.3, 36.0, 25.2, 23.5, 19.8, 13.7; IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 3419, 2833, 2857, 2814, 2750, 1715, 1449, 1384,

1339, 1207, 1170, 1132, 1073, 965, 903, 749; EI-MS *m/z* 234 (M<sup>-43</sup>, 100), 206 (10), 192 (<1), 178 (2), 164 (3), 154 (2), 136 (39), 119 (4), 108 (10), 98 (10), 91 (11), 81 (13), 79 (14), 67 (16), 66 (30), 55 (43); ESI-HRMS calcd. for C<sub>17</sub>H<sub>27</sub>NO<sub>2</sub> [M+H] 278.2120, found 278.2122. Eluent: hexane/EtOAc (1:1), *R<sub>f</sub>* 0.7.

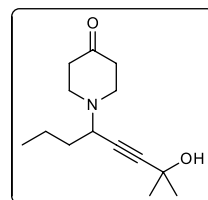
#### (E)-1-(9-Hydroxy-7-methylnon-7-en-5-yn-4-yl)piperidin-4-one (4i)



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.95 (tq, 1H, *J* 6.8, 1.4 Hz), 4.21 (d, 2H, *J* 6.8 Hz), 3.58 (t, 1H, *J* 7.5 Hz), 2.98-2.88 (m, 2H), 2.78-2.68 (m, 2H), 2.59-2.39 (m, 4H), 1.82 (dt, 3H, *J* 1.4, 0.7 Hz), 1.73 (OH), 1.67 (q, 2H, *J* 7.5 Hz), 1.60-1.39 (m, 2H), 0.96 (t, 3H, *J* 7.3 Hz); <sup>13</sup>C NMR

(100 MHz, CDCl<sub>3</sub>) δ 209.1, 135.1, 120.5, 88.2, 84.9, 59.0, 56.9, 49.3, 41.5, 35.9, 19.9, 17.9, 13.8; IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 3416, 3028, 2958, 2932, 2871, 2815, 2749, 2204, 1716, 1633, 1467, 1459, 1414, 1380, 1339, 1207, 1131, 1072, 1003, 971, 917, 757, 621; EI-MS *m/z* 206 (M<sup>-43</sup>, 100), 202 (<1), 188 (1), 164 (2), 148 (1), 136 (17), 120 (5), 107 (10), 98 (6), 91 (12), 81 (14), 79 (17), 77 (19), 67 (10), 65 (12), 55 (27); ESI-HRMS calcd. for C<sub>15</sub>H<sub>24</sub>NO<sub>2</sub> [M+H] 250.1807, found 250.1802. Eluent: hexane/EtOAc (2:1), *R<sub>f</sub>* 0.5.

#### 1-(7-Hydroxy-7-methyloct-5-yn-4-yl)piperidin-4-one (4j)

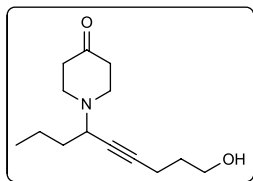


<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.48 (t, 1H, *J* 7.6 Hz), 2.94-2.86 (m, 2H), 2.74-2.67 (m, 2H), 2.54-2.39 (m, 4H), 1.68-1.60 (m, 2H), 1.51 (s, 6H), 1.56-1.37 (m, 2H), 0.95 (t, 3H, *J* 7.3 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 209.1, 90.9, 78.9, 65.2, 56.3, 49.2, 41.4, 35.8, 31.9, 19.8, 13.7; IR (film)  $\nu_{\max}/\text{cm}^{-1}$ :

3420, 2960, 2934, 2872, 2816, 2751, 1715, 1460, 1378, 1361, 1339, 1229, 1208, 1169, 1134, 1073, 951, 752, 610, 552; EI-MS *m/z* 222

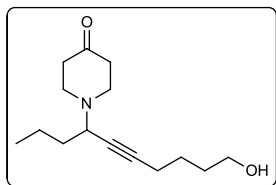
( $M^{-15}$ , 1), 194 (100), 178 (2), 166 (<1), 152 (3), 136 (43), 124 (6), 108 (10), 97 (12), 94 (11), 82 (6), 66 (34), 55 (18); ESI-HRMS calcd. for  $C_{14}H_{23}NO_2$  [ $M+H$ ] 238.1807, found 238.1804. Eluent: hexane/EtOAc (2:1),  $R_f$  0.4.

**1-(9-Hydroxynon-5-yn-4-yl)piperidin-4-one (4k)**



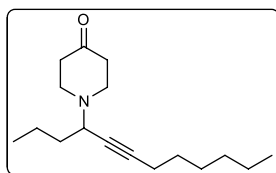
$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  3.73 (t, 2H,  $J$  6.2 Hz), 3.43 (ddt, 1H,  $J$  7.6, 7.5, 2.1 Hz), 2.94-2.86 (m, 2H), 2.75-2.66 (m, 2H), 2.54-2.38 (m, 4H), 2.32 (td, 2H,  $J$  6.9, 2.1 Hz), 1.83 (OH), 1.74 (qt, 2H,  $J$  6.3 Hz), 1.66-1.57 (m, 2H), 1.56-1.34 (m, 2H), 0.94 (t, 3H,  $J$  7.3 Hz);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  209.3, 85.2, 77.6, 61.8, 56.6, 49.2, 41.5, 36.1, 31.7, 19.9, 15.2, 13.8; IR (film)  $\nu_{max}/cm^{-1}$ : 3418, 2957, 2934, 2871, 2815, 2750, 2226, 1714, 1470, 1433, 1416, 1381, 1340, 1207, 1139, 1126, 1071, 1001, 930, 805, 759; EI-MS  $m/z$  194 ( $M^{-43}$ , 100), 176 (1), 166 (10), 150 (4), 134 (6), 124 (16), 106 (8), 95 (37), 79 (15), 77 (16), 67 (18), 65 (12), 55 (28); ESI-HRMS calcd. for  $C_{14}H_{23}NO_2$  [ $M+H$ ] 238.1807, found 238.1804. Eluent: hexane/EtOAc (2:1),  $R_f$  0.4.

**1-(10-Hydroxydec-5-yn-4-yl)piperidin-4-one (4l)**



$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  3.66 (t, 2H,  $J$  6.4 Hz), 3.44 (ddt, 1H,  $J$  7.3, 7.2, 2.0 Hz), 2.94-2.86 (m, 2H), 2.75-2.68 (m, 2H), 2.54-2.39 (m, 4H), 2.24 (td, 2H,  $J$  6.9, 2.0 Hz), 1.71-1.31 (m, 9H), 0.95 (t, 3H,  $J$  7.3 Hz);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  209.4, 85.6, 77.3, 62.3, 56.6, 49.2, 41.5, 36.1, 31.9, 25.4, 19.9, 18.4, 13.8; IR (film)  $\nu_{max}/cm^{-1}$ : 3415, 2956, 2935, 2870, 2815, 2749, 2223, 1715, 1458, 1380, 1339, 1207, 1126, 1071, 971, 803, 760; EI-MS  $m/z$  208 ( $M^{-43}$ , 100), 190 (1), 180 (1), 164 (5), 148 (11), 138 (4), 122 (7), 109 (10), 93 (9), 91 (12), 79 (18), 77 (14), 67 (15), 65 (11), 55 (35); ESI-HRMS calcd. for  $C_{15}H_{25}NO_2$  [ $M+H$ ] 252.1964, found 252.1954. Eluent: hexane/EtOAc (1:1),  $R_f$  0.3.

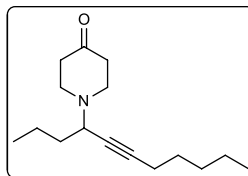
**1-(Dodec-5-yn-4-yl)piperidin-4-one (4m)**



$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  3.44 (ddt, 1H,  $J$  7.5, 7.4, 2.0 Hz), 2.95-2.87 (m, 2H), 2.76-2.68 (m, 2H), 2.54-2.39 (m, 4H), 2.18 (td, 2H,  $J$  7.0, 2.0 Hz), 1.66-1.22 (m, 12H), 0.95 (t, 3H,  $J$  7.3 Hz), 0.88 (t, 3H,  $J$  7.0 Hz);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  209.3, 86.1, 76.9, 56.7, 49.2, 41.5, 36.2, 31.3, 29.0, 28.5, 22.5, 19.9, 19.6, 13.9, 13.8; IR (film)  $\nu_{max}/cm^{-1}$ : 2957, 2931, 2870, 2859, 2814, 2749, 2224, 1721, 1466, 1380, 1339, 1206, 1139, 1127, 1073, 1001, 971, 801, 758, 727, 612; EI-MS  $m/z$  220 ( $M^{-43}$ , 100), 206 (<1), 178 (2), 162 (2), 148 (5), 136 (7), 120 (5), 108 (5), 93 (7), 81 (11), 79 (11), 67 (15), 55 (24); ESI-HRMS calcd. for  $C_{17}H_{29}NO$  [ $M+H$ ] 264.2327, found 264.2317. Eluent: hexane/EtOAc (3:1),  $R_f$  0.6.

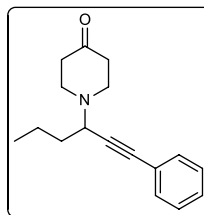
**1-(Undec-5-yn-4-yl)piperidin-4-one (4n)**

$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  3.44 (ddt, 1H,  $J$  7.5, 7.4, 2.0 Hz), 2.95-2.86 (m, 2H), 2.76-2.65 (m, 2H), 2.54-2.38 (m, 4H), 2.18 (td, 2H,  $J$  7.0, 2.0 Hz), 1.66-1.26 (m, 10H), 0.95 (t, 3H,  $J$  7.2 Hz), 0.89 (t, 3H,  $J$  7.0 Hz);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  209.3, 86.1, 76.9,



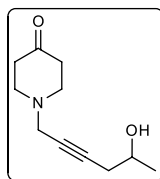
56.6, 49.2, 41.5, 36.2, 31.0, 28.7, 22.1, 19.9, 18.5, 13.9, 13.8; IR (film)  $\nu_{max}/cm^{-1}$ : 2957, 2932, 2871, 2861, 2814, 2748, 2225, 1721, 1466, 1380, 1339, 1206, 1127, 1073, 1001, 972, 802, 760, 731, 610; EI-MS  $m/z$  206 ( $M^{-43}$ , 100), 178 (<1), 162 (2), 148 (3), 136 (8), 120 (3), 108 (4), 93 (4), 81 (9), 79 (10), 67 (15), 55 (19); ESI-HRMS calcd. for  $C_{16}H_{27}NO$  [ $M+H$ ] 250.2171, found 250.2168. Eluent: hexane/EtOAc (3:1),  $R_f$  0.6.

**1-(1-Phenylhex-1-yn-3-yl)piperidin-4-one (4o)**



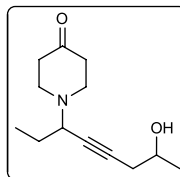
$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.44-7.36 (m, 2H), 7.32-7.24 (m, 3H), 3.70 (t, 1H,  $J$  7.5 Hz), 3.05-2.96 (m, 2H), 2.87-2.77 (m, 2H), 2.57-2.41 (m, 4H), 1.80-1.71 (m, 2H), 1.67-1.46 (m, 2H), 0.99 (t, 3H,  $J$  7.3 Hz);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  209.0, 131.7, 128.3, 128.0, 123.1, 86.7, 86.0, 57.1, 49.4, 41.5, 35.9, 19.9, 13.8; IR (film)  $\nu_{max}/cm^{-1}$ : 3079, 3055, 2958, 2932, 2871, 2813, 2749, 2204, 1717, 1597, 1489, 1442, 1381, 1338, 1206, 1132, 1071, 1027, 1003, 972, 927, 914, 756, 691, 617; EI-MS  $m/z$  212 ( $M^{-43}$ , 100), 182 (<1), 170 (<1), 156 (1), 142 (24), 128 (11), 115 (51), 102 (6), 84 (6), 77 (6), 70 (5), 55 (8); ESI-HRMS calcd. for  $C_{17}H_{21}NO$  [ $M+H$ ] 256.1701, found 256.1706. Eluent: hexane/EtOAc (10:1),  $R_f$  0.3.

**1-(5-Hydroxyhex-2-yn-1-yl)piperidin-4-one (4p)**



$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  3.95 (sext, 1H,  $J$  6.2 Hz), 3.41 (t, 1H,  $J$  2.2 Hz), 2.86 (t, 4H,  $J$  6.2 Hz), 2.50 (t, 4H,  $J$  6.2 Hz), 2.39 (ddt, 2H,  $J$  6.4, 6.3, 2.2 Hz), 1.26 (d, 3H,  $J$  6.2 Hz);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  208.4, 82.3, 76.9, 66.4, 52.1, 46.8, 41.0, 29.3, 22.5; IR (film)  $\nu_{max}/cm^{-1}$ : 3412, 2968, 2910, 2816, 2767, 2712, 2232, 1715, 1419, 1378, 1346, 1324, 1289, 1193, 1115, 1083, 1011, 976, 940, 834, 808, 757, 617; EI-MS  $m/z$  195 ( $M^+$ , 36), 178 (11), 162 (2), 150 (64), 136 (13), 122 (11), 112 (43), 108 (100), 98 (25), 94 (31), 80 (53), 65 (20), 56 (68), 55 (67), 53 (73); ESI-HRMS calcd. for  $C_{11}H_{17}NO_2$  [ $M+H$ ] 196.1338, found 196.1333. Eluent: hexane/EtOAc (1:1),  $R_f$  0.2.

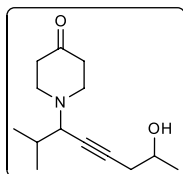
**1-(7-Hydroxyoct-4-yn-3-yl)piperidin-4-one (4q)**



$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  3.93 (sext, 1H,  $J$  6.1 Hz), 3.37 (ddt, 1H,  $J$  6.5, 6.4, 1.9 Hz), 2.96-2.86 (m, 2H), 2.78-2.68 (m, 2H), 2.54-2.40 (m, 5H), 2.36 (ddd, 1H,  $J$  16.4, 5.9, 1.9 Hz), 2.21 (OH), 1.75-1.61 (m, 2H), 1.26 (d, 3H,  $J$  6.1 Hz), 1.03 (t, 3H,  $J$  7.4 Hz);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  209.2, 82.1, 79.5, 66.4, 58.5, 49.1, 41.3, 29.1, 27.0, 22.3, 11.2; IR (film)  $\nu_{max}/cm^{-1}$ : 3422, 2967, 2932, 2909, 2875, 2815, 2749, 1714, 1461, 1416, 1379, 1339, 1211, 1126, 1079, 1007, 970, 940, 841, 764, 621; EI-MS  $m/z$  208 ( $M^{-15}$ , 1), 194 (100), 176 (5), 150 (35), 140 (9), 136 (4), 120 (5), 108 (75), 93 (7), 91 (10), 80 (50), 79 (30), 77 (16), 65 (11), 55 (32); ESI-HRMS calcd. for  $C_{13}H_{21}NO_2$  [ $M+H$ ] 224.1651, found 224.1639. Eluent: hexane/EtOAc (1:1),  $R_f$  0.4.

**1-(7-Hydroxy-2-methyloct-4-yn-3-yl)piperidin-4-one (4r)**

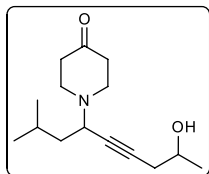
$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  3.92 (sext, 1H,  $J$  6.2 Hz), 2.97 (dt, 1H,  $J$  9.9, 1.9 Hz), 2.93-2.84 (m, 2H), 2.71-2.62 (m, 2H), 2.54-2.33 (m, 6H), 1.86-1.75 (m, 1H), 1.26 (d, 3H,  $J$  6.2 Hz), 1.06 (d, 3H,  $J$



6.6 Hz), 1.02 (d, 3H, *J* 6.6 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 209.6, 82.5, 79.0, 66.6, 64.0, 49.4, 41.5, 31.1, 29.2, 22.4, 20.5, 19.8; IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 3417, 2967, 2909, 2870, 2815, 2750, 1714, 1468, 1416, 1380, 1337, 1280, 1262, 1214, 1113, 1075, 988, 940, 831, 764, 627;

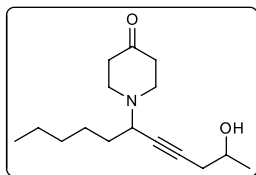
EI-MS *m/z* 222 (M<sup>-15</sup>, 2), 194 (100), 176 (5), 150 (36), 136 (1), 132 (3), 120 (6), 108 (72), 93 (8), 91 (10), 80 (47), 79 (19), 77 (16), 67 (11), 55 (34); ESI-HRMS calcd. for C<sub>14</sub>H<sub>23</sub>NO<sub>2</sub> [M+H] 238.1807, found 238.1797. Eluent: hexane/EtOAc (1:1), *R<sub>f</sub>* 0.6.

*1-(8-Hydroxy-2-methylnon-5-yn-4-yl)piperidin-4-one (4s)*



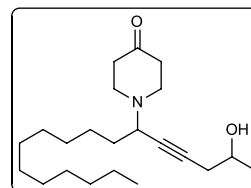
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.92 (sext, 1H, *J* 6.1 Hz), 3.55 (t, 1H, *J* 7.6 Hz), 2.96-2.87 (m, 2H), 2.76-2.67 (m, 2H), 2.54-2.41 (m, 6H), 2.41 (ddd, 1H, *J* 16.5, 5.4, 0.9 Hz), 2.35 (ddd, 1H, *J* 16.5, 6.3, 2.0 Hz), 1.94 (OH), 1.84 (non, 1H, *J* 6.5 Hz), 1.54 (ddd, 2H, *J* 8.3, 6.5, 2.6 Hz), 1.25 (d, 3H, *J* 6.1 Hz), 0.98 (t, 6H, *J* 7.0 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 209.2, 82.0, 79.7, 66.5, 55.0, 49.2, 42.8, 41.5, 29.2, 22.7, 22.4, 22.2; IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 3425, 2957, 2930, 2868, 2815, 2749, 1716, 1469, 1416, 1383, 1340, 1207, 1119, 1075, 1004, 975, 940, 762, 622; EI-MS *m/z* 236 (M<sup>-15</sup>, 2), 194 (100), 176 (5), 168 (6), 150 (42), 136 (2), 120 (7), 108 (66), 93 (13), 91 (14), 80 (44), 79 (15), 77 (13), 67 (13), 65 (12), 55 (34); ESI-HRMS calcd. for C<sub>15</sub>H<sub>25</sub>NO<sub>2</sub> [M+H] 252.1964, found 252.1973. Eluent: hexane/EtOAc (1:1), *R<sub>f</sub>* 0.4.

*1-(2-Hydroxyundec-4-yn-6-yl)piperidin-4-one (4t)*



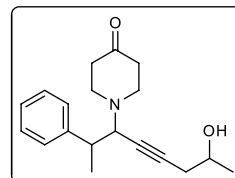
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.92 (sext, 1H, *J* 6.2 Hz), 3.45 (ddt, 1H, *J* 6.8, 6.7, 1.9 Hz), 2.96-2.86 (m, 2H), 2.77-2.67 (m, 2H), 2.54-2.39 (m, 5H), 2.38 (td, 1H, *J* 6.4, 6.2, 2.0 Hz), 2.18 (OH), 1.69-1.60 (m, 2H), 1.55-1.38 (m, 2H), 1.38-1.28 (m, 4H), 1.25 (d, 3H, *J* 6.2 Hz), 0.90 (t, 3H, *J* 7.0 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 209.2, 82.1, 79.7, 66.5, 56.9, 49.2, 41.4, 33.9, 31.4, 29.2, 26.3, 22.5, 22.3, 13.9; IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 3428, 2958, 2930, 2859, 2815, 2749, 1717, 1458, 1416, 1379, 1339, 1206, 1123, 1075, 1005, 983, 939, 763, 621; EI-MS *m/z* 250 (M<sup>-15</sup>, 1), 206 (<1), 194 (100), 182 (6), 176 (5), 164 (<1), 150 (35), 138 (2), 120 (6), 108 (64), 98 (12), 93 (9), 91 (10), 80 (40), 79 (17), 77 (12), 67 (12), 65 (10), 55 (35); ESI-HRMS calcd. for C<sub>16</sub>H<sub>27</sub>NO<sub>2</sub> [M+H] 266.2120, found 266.2113. Eluent: hexane/EtOAc (1:1), *R<sub>f</sub>* 0.4.

*1-(2-Hydroxyheptadec-4-yn-6-yl)piperidin-4-one (4u)*



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.92 (sext, 1H, *J* 6.1 Hz), 3.45 (ddt, 1H, *J* 6.7, 6.4, 2.0 Hz), 2.96-2.86 (m, 2H), 2.76-2.67 (m, 2H), 2.55-2.41 (m, 4H), 2.41 (ddd, 1H, *J* 16.5, 5.4, 1.0 Hz), 2.35 (ddd, 1H, *J* 16.5, 6.3, 0.6 Hz), 1.94 (OH), 1.69-1.58 (m, 2H), 1.54-1.36 (m, 2H), 1.33-1.23 (m, 16H), 1.25 (d, 3H, *J* 6.2 Hz), 0.88 (t, 3H, *J* 7.0 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 209.2, 82.1, 79.9, 66.5, 57.0, 49.2, 41.5, 34.0, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 26.7, 22.7, 22.4, 14.1; IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 3428, 2953, 2924, 2853, 2816, 2749, 1715, 1466, 1416, 1378, 1339, 1208, 1118, 1081, 1003, 971, 940, 832, 721, 622; EI-MS *m/z* 334 (M<sup>-15</sup>, 1), 304 (<1), 292 (<1), 266 (3), 237 (<1), 194 (100), 176 (5), 164 (<1), 150 (22), 138 (4), 120 (5), 108 (40), 98 (10), 93 (8), 91 (8), 80 (28), 79 (14), 77 (8), 67 (12), 55 (35); ESI-HRMS calcd. for C<sub>22</sub>H<sub>39</sub>NO<sub>2</sub> [M+Na] 372.2878, found 372.2875. Eluent: hexane/EtOAc (3:1), *R<sub>f</sub>* 0.4.

*1-(7-Hydroxy-2-phenyloct-4-yn-3-yl)piperidin-4-one (4v) (diastereoisomeric mixture)*



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.94 (sext, 1H, *J* 6.0 Hz), 3.73 (t, 1H, *J* 6.6 Hz), 3.68-3.48 (m, 2H), 3.01-2.83 (m, 5H), 2.78-2.68 (m, 1H), 2.66-2.58 (m, 2H), 2.57-2.45 (m, 2H), 2.45-2.39 (m, 2H), 2.31-2.01 (m, 8H), 1.87-1.81 (m, 1H), 1.40 (d, 3H, *J* 6.9 Hz), 1.38 (d, 2H, *J* 7.0 Hz), 1.27 (d, 4H, *J* 6.1 Hz), 1.02 (d, 1H, *J* 6.2 Hz), 0.99 (d, 1H, *J* 6.2 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 209.3, 209.2, 144.6, 144.5, 144.4, 128.3, 128.0, 127.7, 127.6, 127.1, 126.7, 126.6, 126.1, 83.5, 83.4, 83.2, 78.5, 78.4, 78.3, 67.8, 66.4, 66.1, 66.0, 63.2, 63.1, 53.3, 42.9, 41.4, 41.2, 29.1, 28.9, 25.5, 22.3, 21.9, 21.8, 20.1, 19.2, 19.1; IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 3421, 3084, 3060, 3027, 2967, 2927, 2907, 2874, 2813, 2749, 1713, 1603, 1494, 1453, 1416, 1375, 1337, 1216, 1125, 1075, 939, 843, 757, 700, 554; EI-MS *m/z* 194 (M<sup>-105</sup>, 100), 176 (2), 150 (14), 141 (3), 120 (2), 108 (38), 105 (8), 91 (7), 80 (26), 77 (9), 65 (4), 53 (11); ESI-HRMS calcd. for C<sub>19</sub>H<sub>23</sub>NO<sub>2</sub> [M+H] 300.1964, found 300.1957. Eluent: hexane/EtOAc (1:1), *R<sub>f</sub>* 0.4.

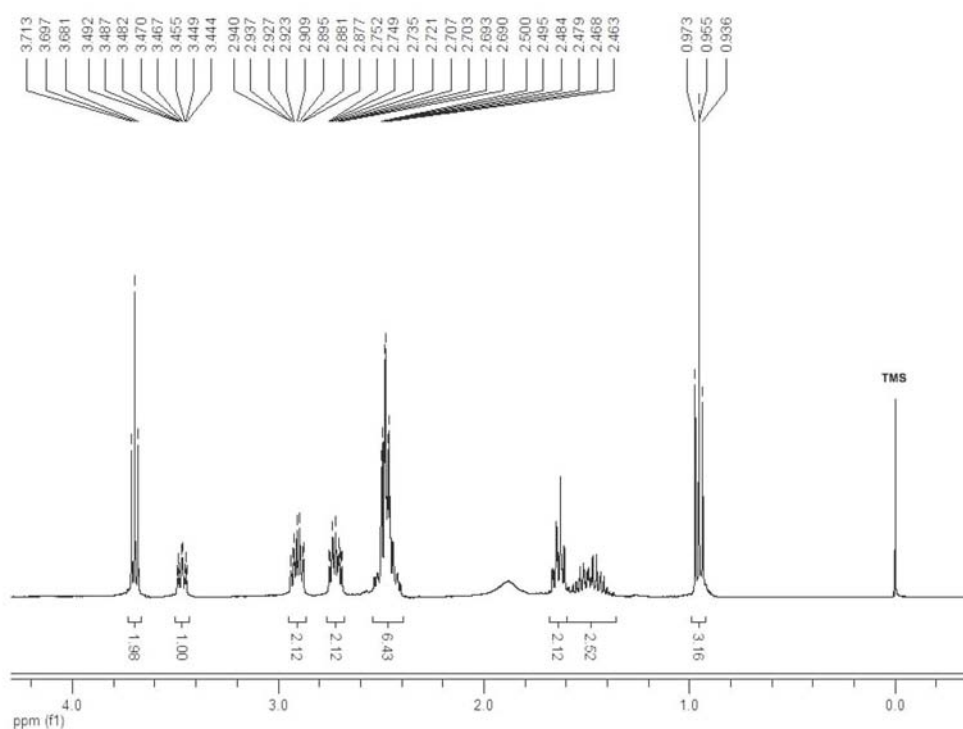
**<sup>1</sup>H NMR and <sup>13</sup>C NMR spectra for compounds 3b-e and 4a-v**

Figure 1S. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(8-hydroxyoct-5-yn-4-yl)piperidin-4-one (4a)

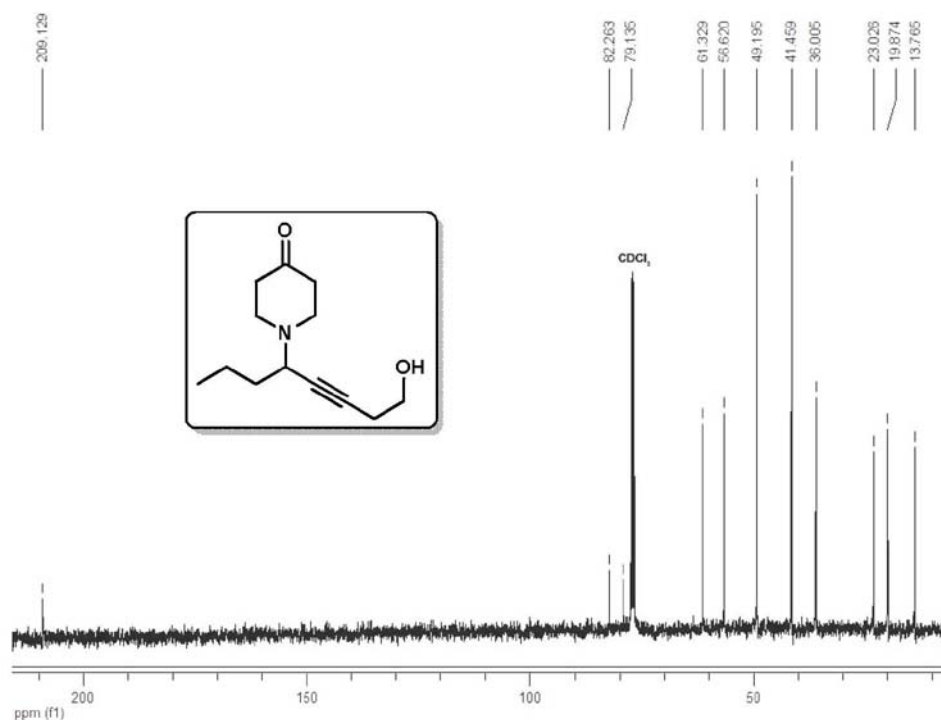


Figure 2S. <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(8-hydroxyoct-5-yn-4-yl)piperidin-4-one (4a)

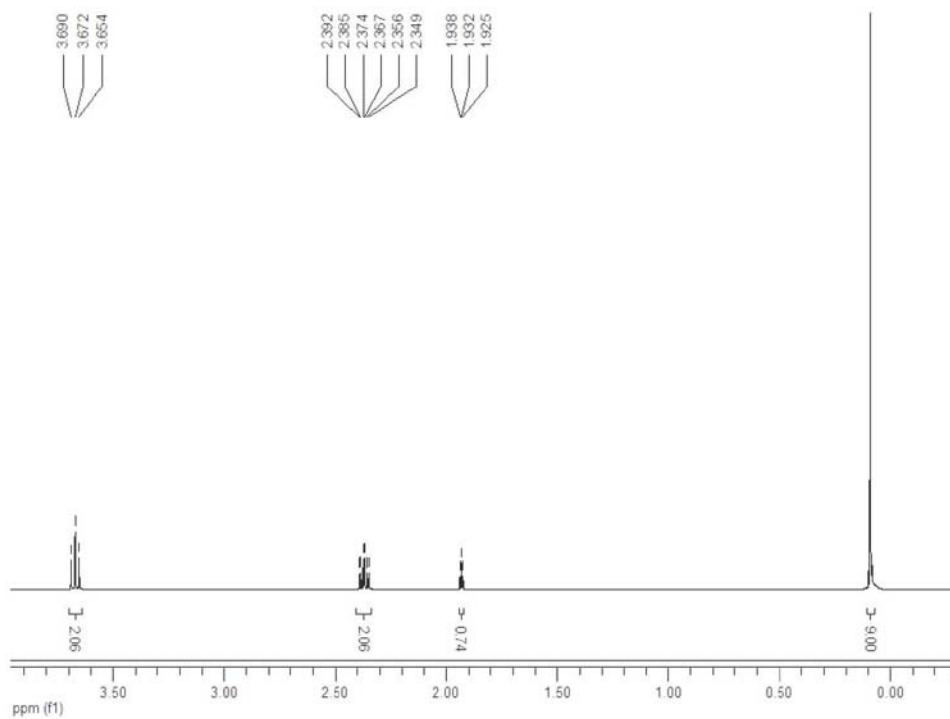


Figure 3S. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of (but-3-yn-1-yloxy)trimethylsilane (3b)

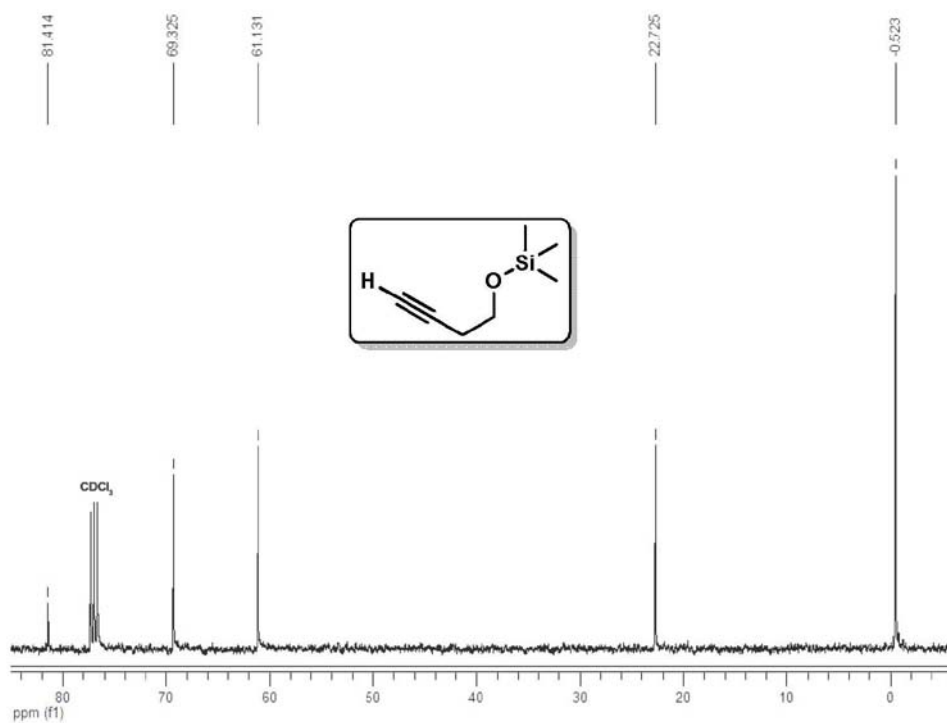


Figure 4S. <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of (but-3-yn-1-yloxy)trimethylsilane (3b)

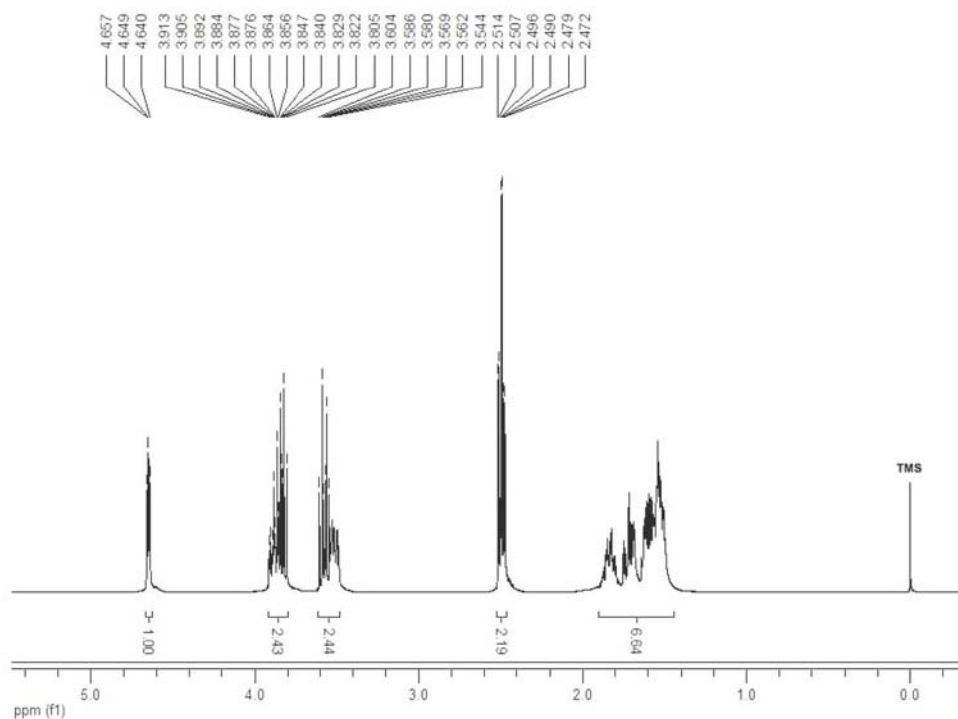


Figure 5S.  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of 2-(but-3-yn-1-yloxy)tetrahydro-2H-pyran (**3c**)

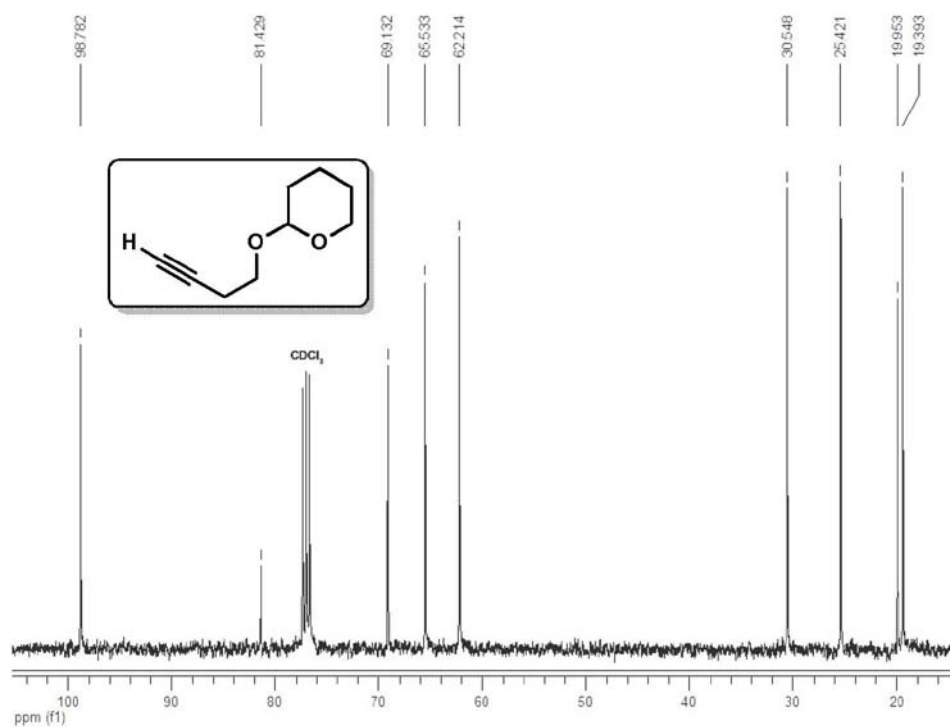


Figure 6S.  $^{13}\text{C}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of 2-(but-3-yn-1-yloxy)tetrahydro-2H-pyran (**3c**)



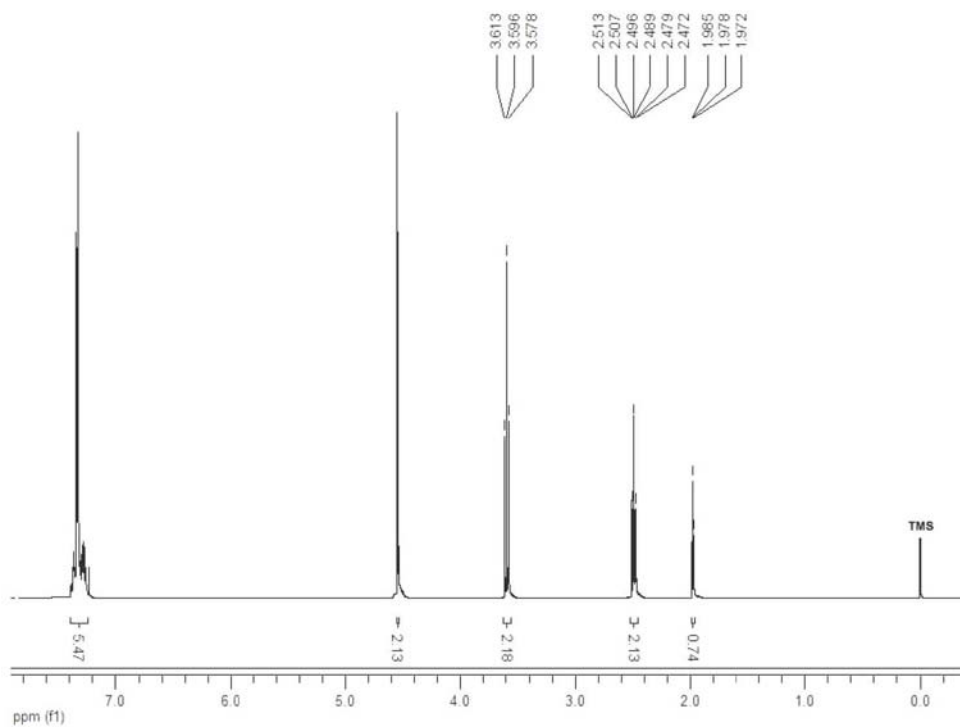


Figure 7S. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of ((but-3-yn-1-yloxy)methyl)benzene (3d)

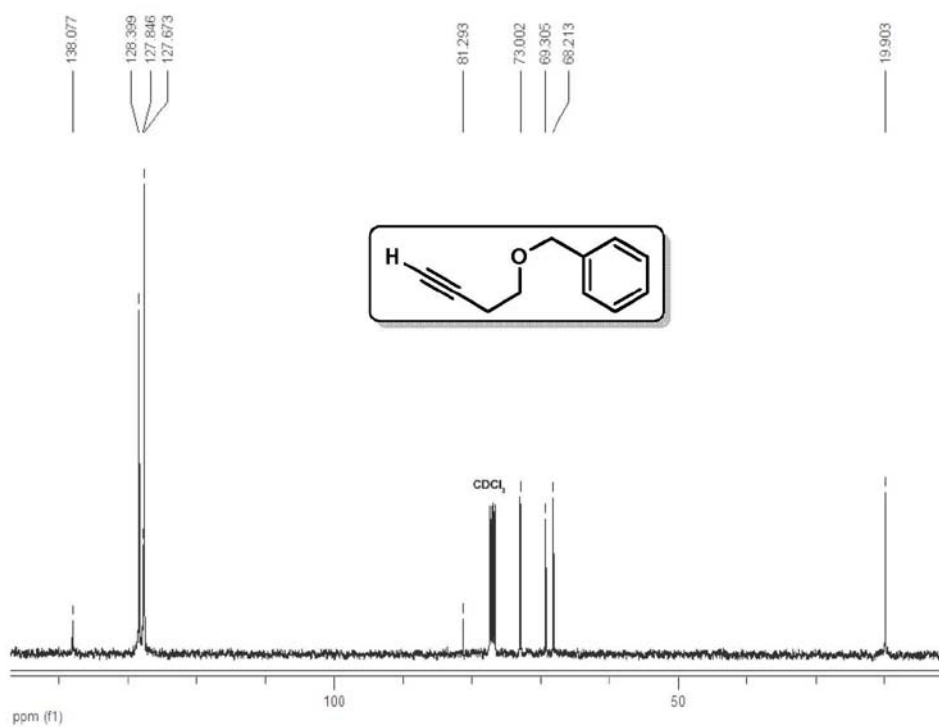


Figure 8S. <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of ((but-3-yn-1-yloxy)methyl)benzene (3d)

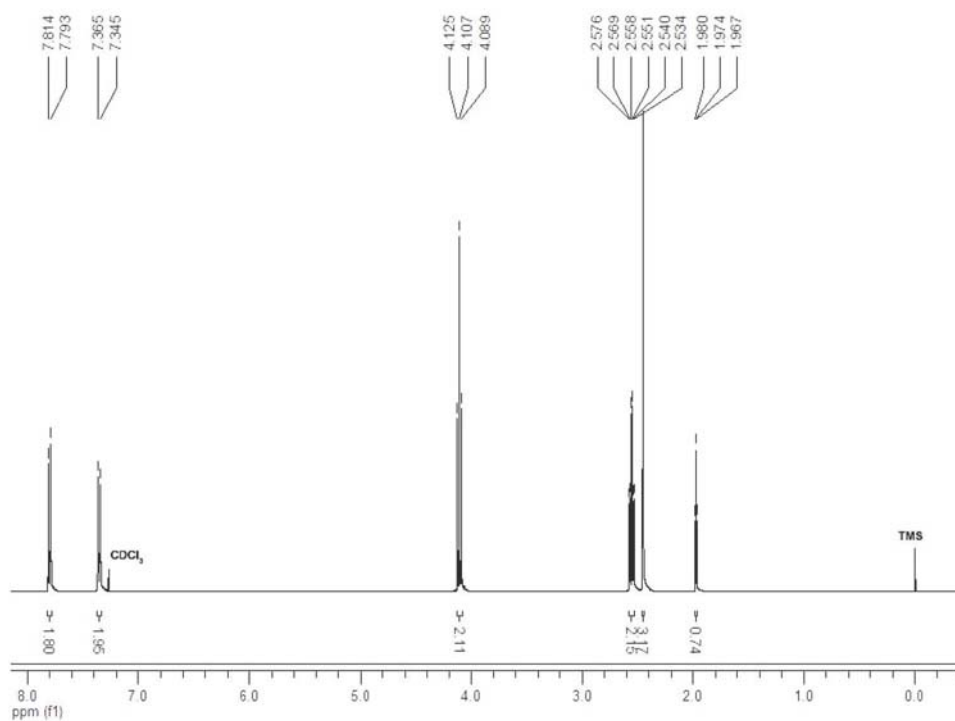


Figure 9S. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of but-3-yn-1-yl 4-methylbenzenesulfonate (3e)

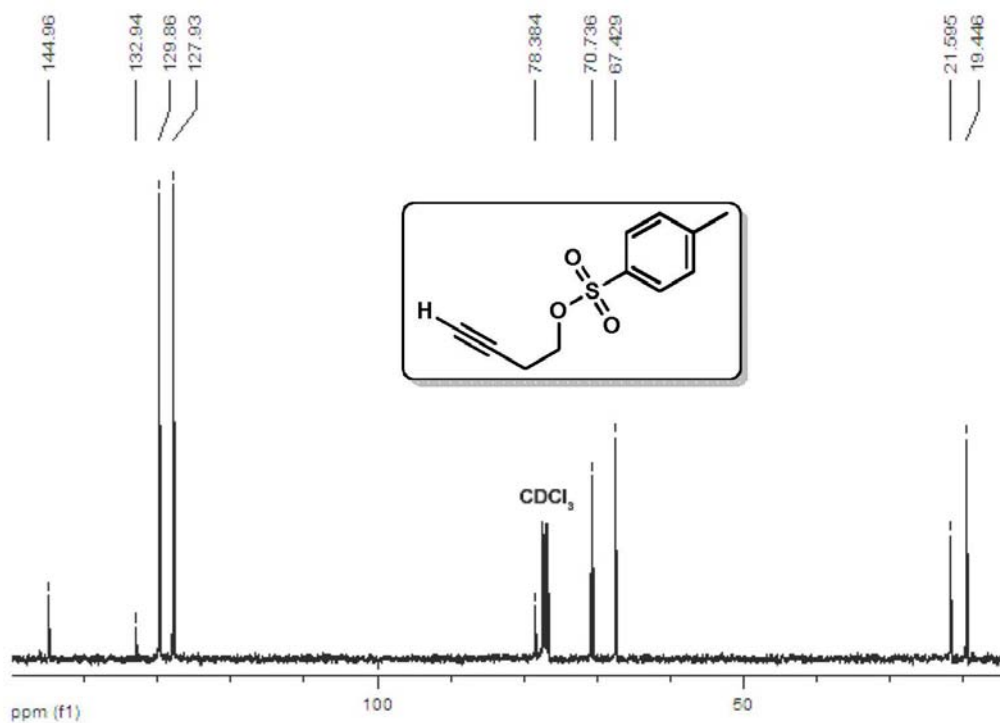


Figure 10S. <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of but-3-yn-1-yl 4-methylbenzenesulfonate (3e)

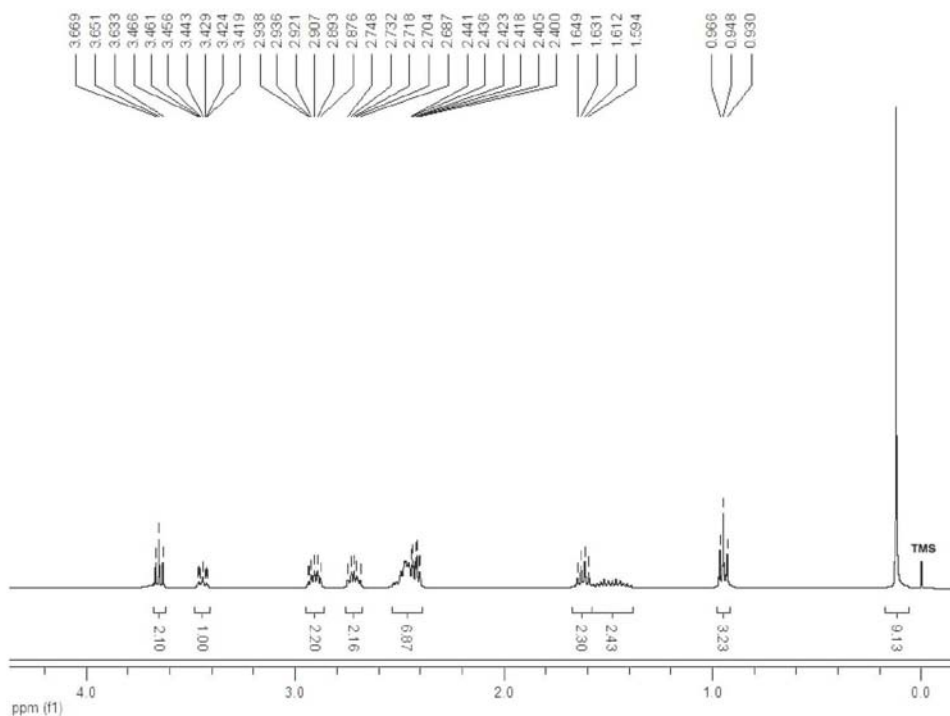


Figure 11S. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(8-((trimethylsilyl)oxy)oct-5-yn-4-yl)piperidin-4-one (**4b**)

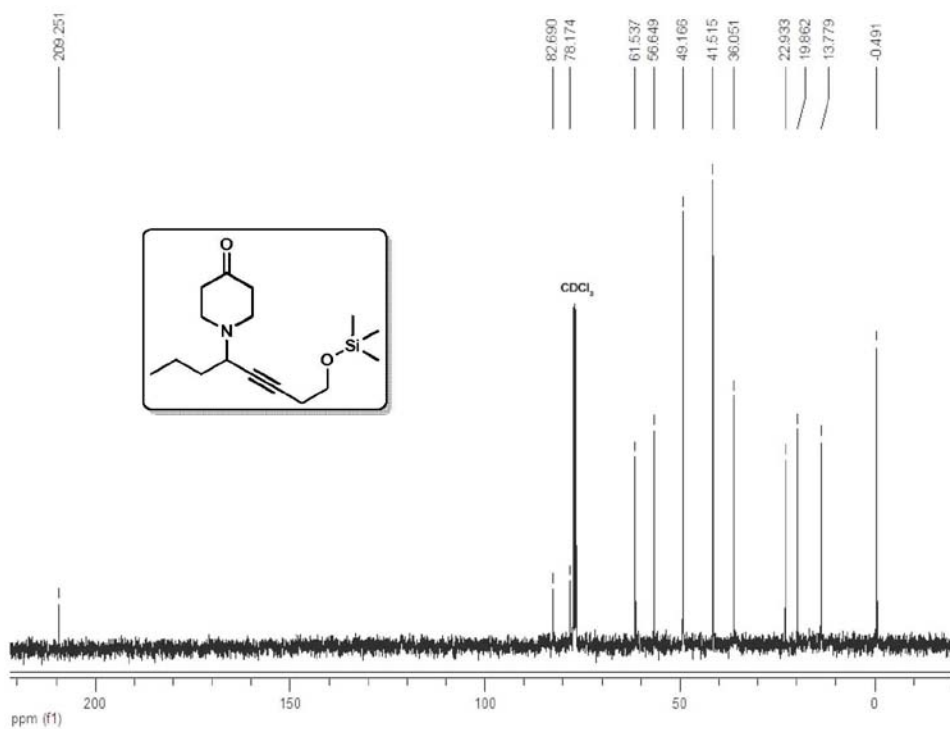


Figure 12S. <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(8-((trimethylsilyl)oxy)oct-5-yn-4-yl)piperidin-4-one (**4b**)

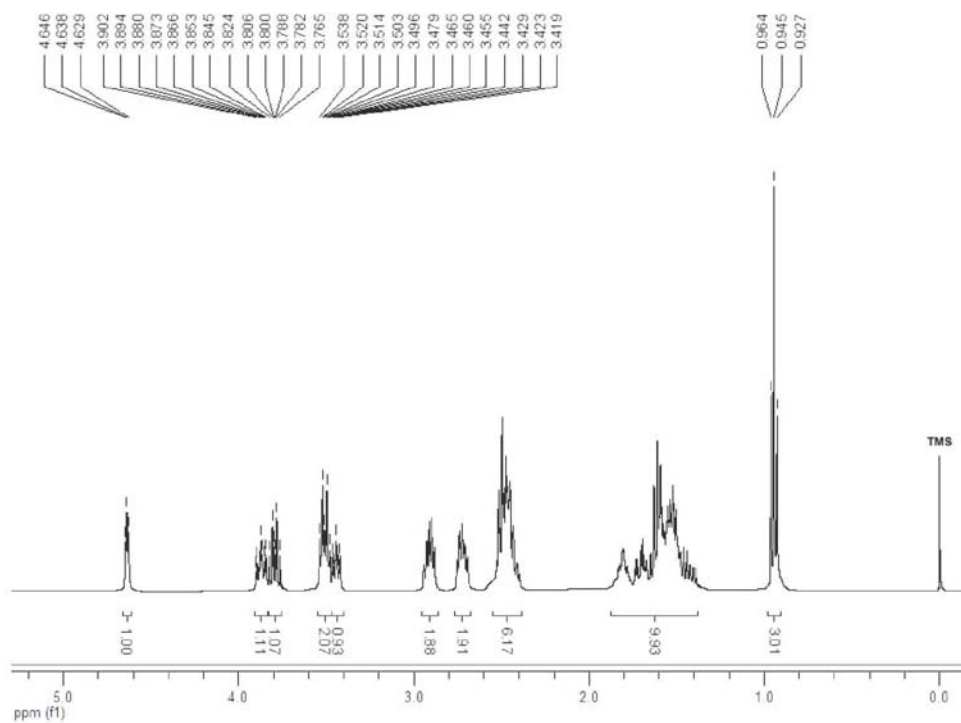


Figure 13S.  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of 1-(8-((tetrahydro-2H-pyran-2-yl)oxy)oct-5-yn-4-yl)piperidin-4-one (**4c**)

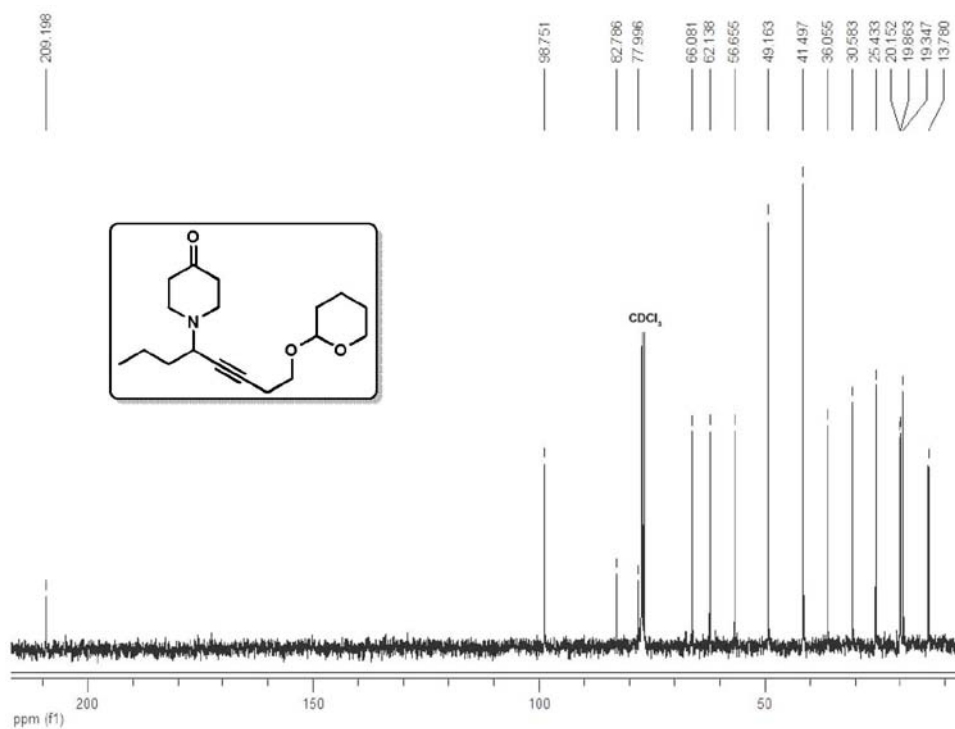
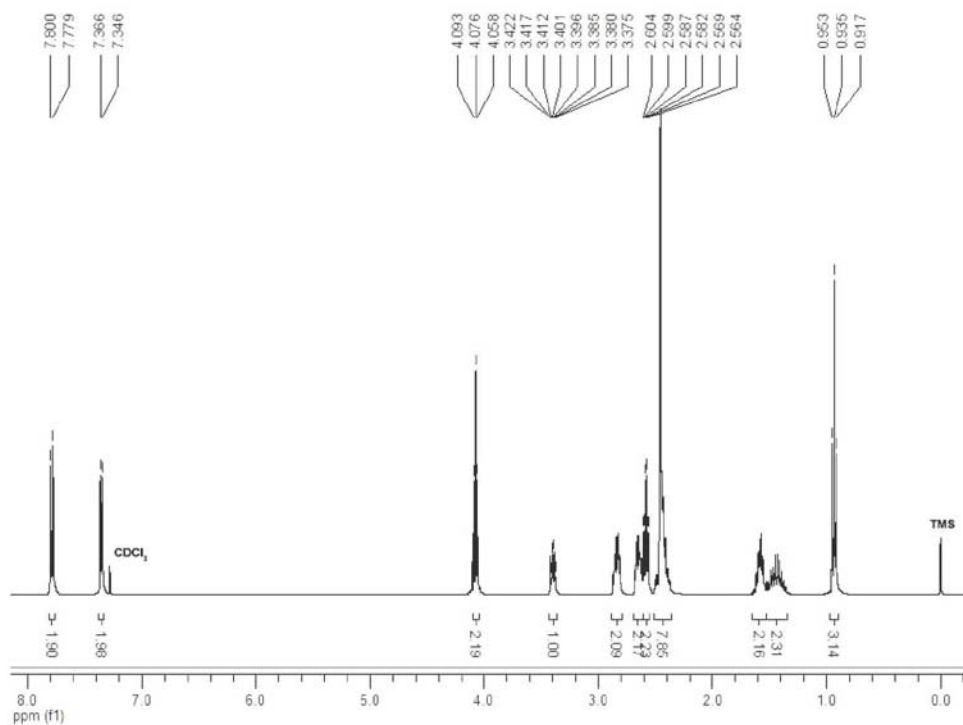
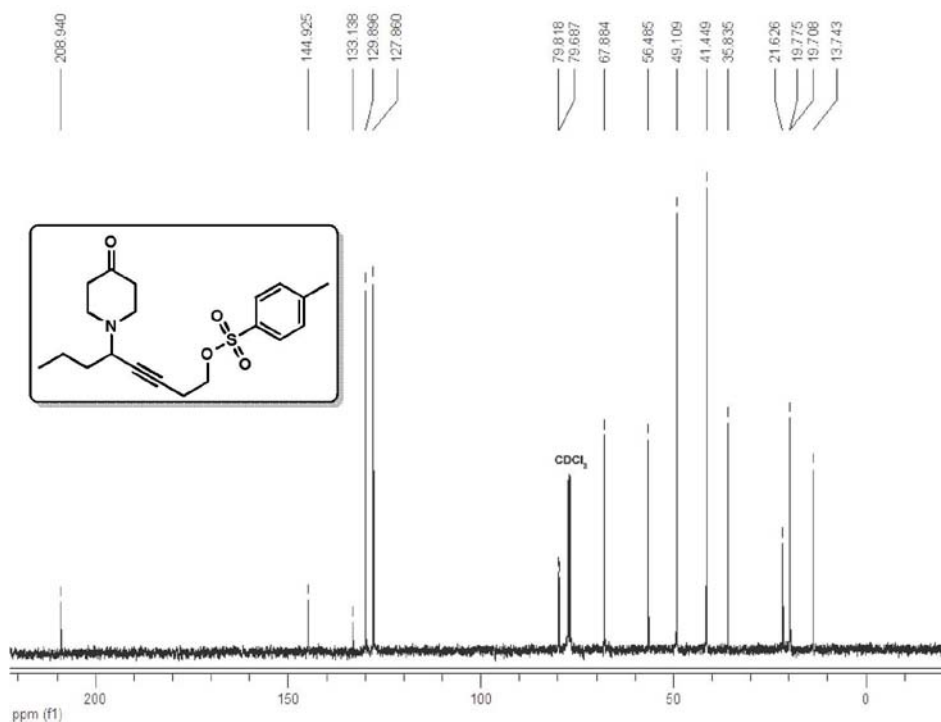


Figure 14S.  $^{13}\text{C}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of 1-(8-((tetrahydro-2H-pyran-2-yl)oxy)oct-5-yn-4-yl)piperidin-4-one (**4c**)



**Figure 15S.** <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 5-(4-oxopiperidin-1-yl)oct-3-yn-1-yl 4-methylbenzenesulfonate (**4d**)



**Figure 16S.** <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 5-(4-oxopiperidin-1-yl)oct-3-yn-1-yl 4-methylbenzenesulfonate (**4d**)

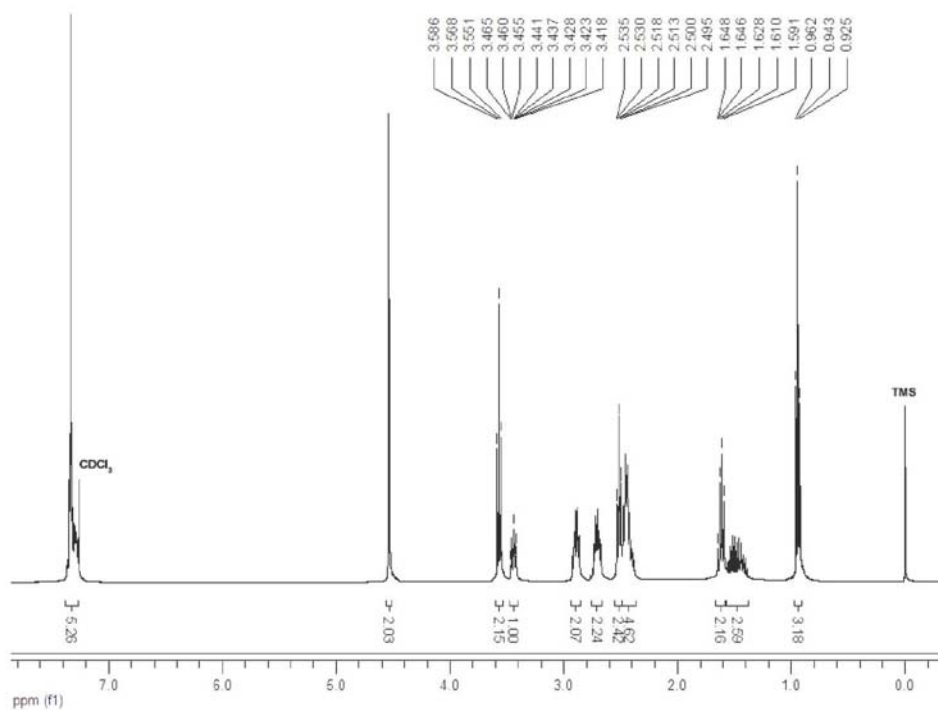


Figure 17S.  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of 1-(8-(benzyloxy)oct-5-yn-4-yl)piperidin-4-one (**4e**)

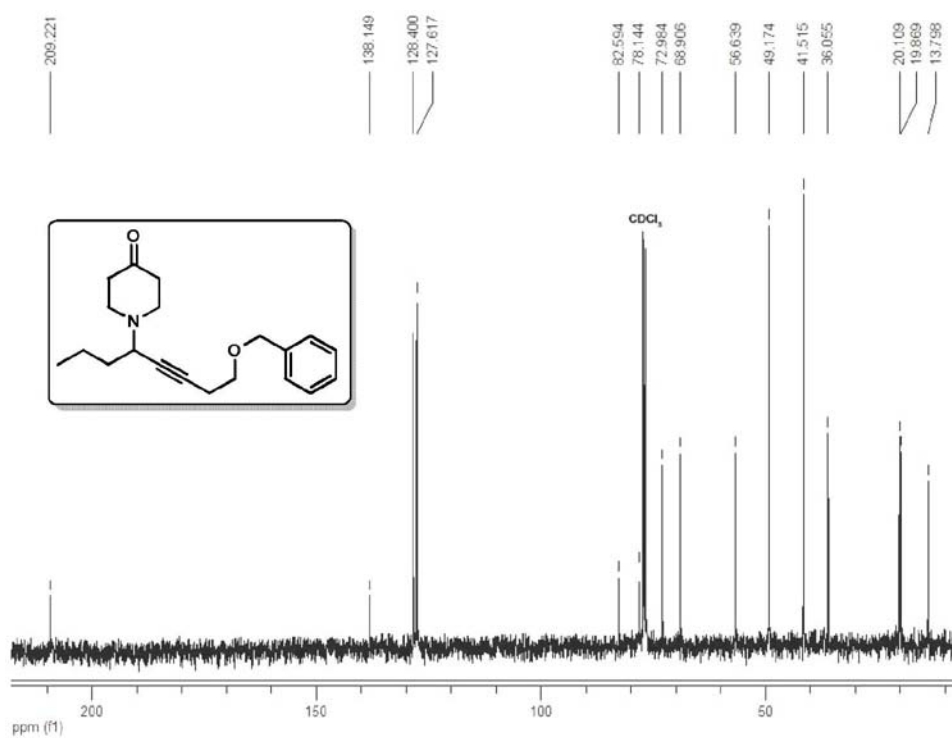


Figure 18S.  $^{13}\text{C}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of 1-(8-(benzyloxy)oct-5-yn-4-yl)piperidin-4-one (**4e**)

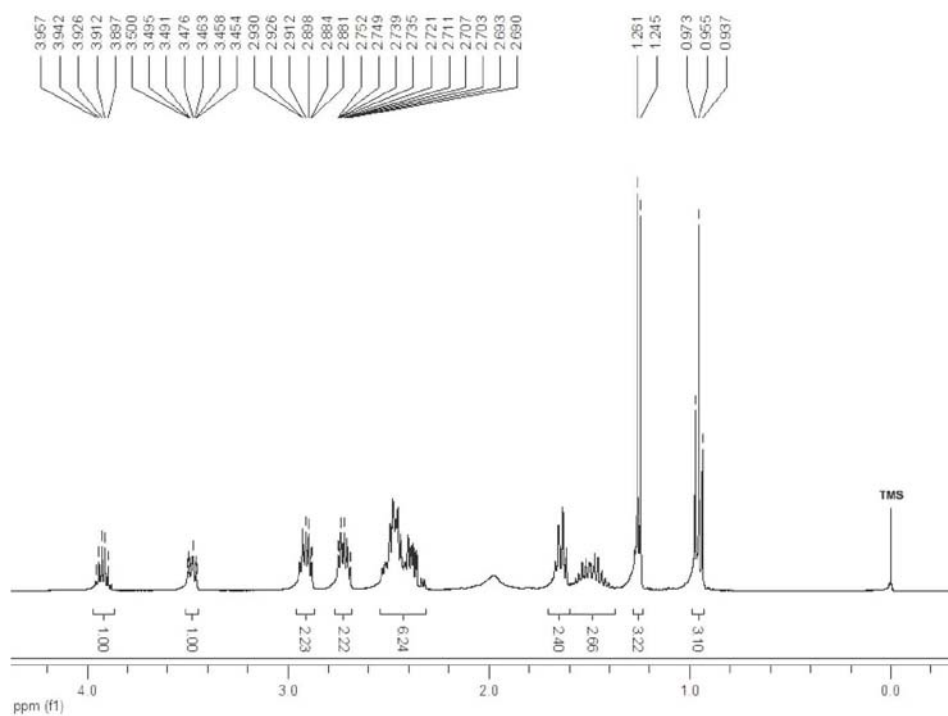


Figure 19S. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(8-hydroxynon-5-yn-4-yl)piperidin-4-one (**4f**)

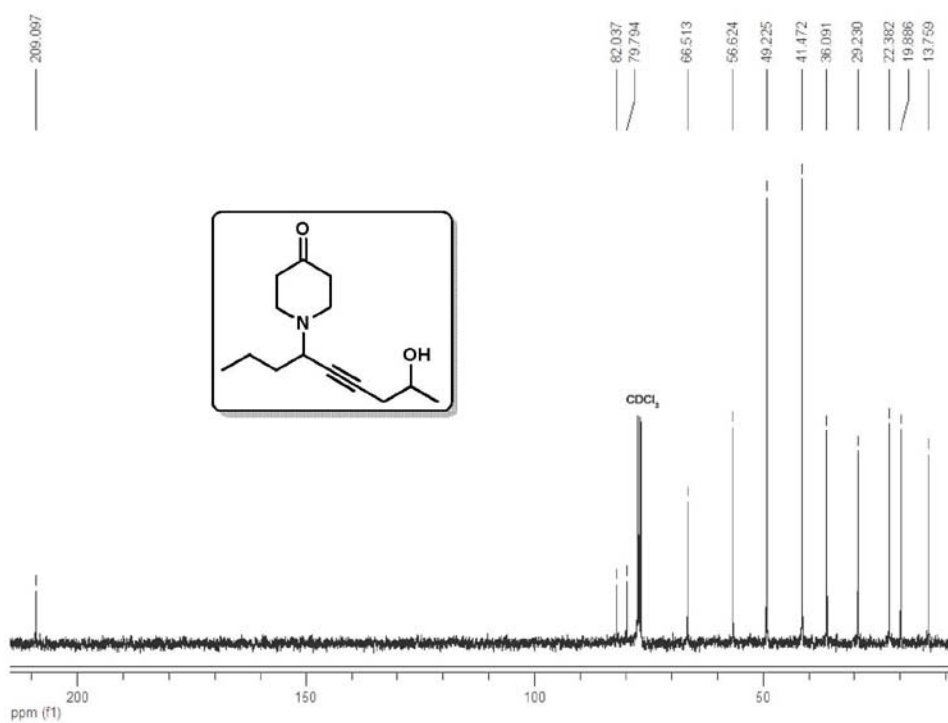


Figure 20S. <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(8-hydroxynon-5-yn-4-yl)piperidin-4-one (**4f**)

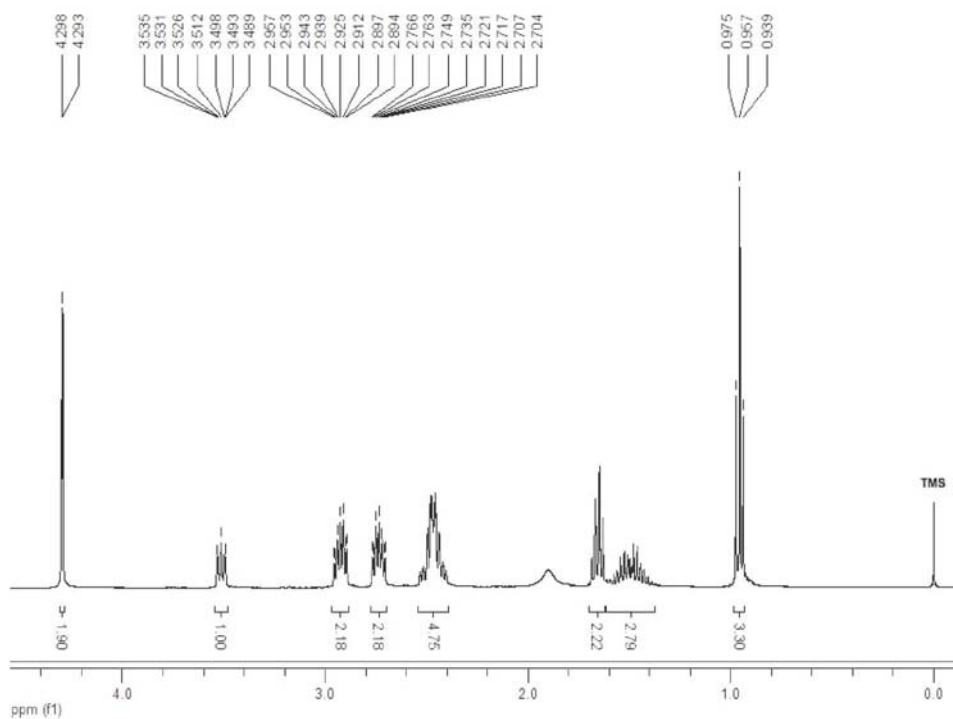


Figure 21S. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(1-hydroxyhept-2-yn-4-yl)piperidin-4-one (**4g**)

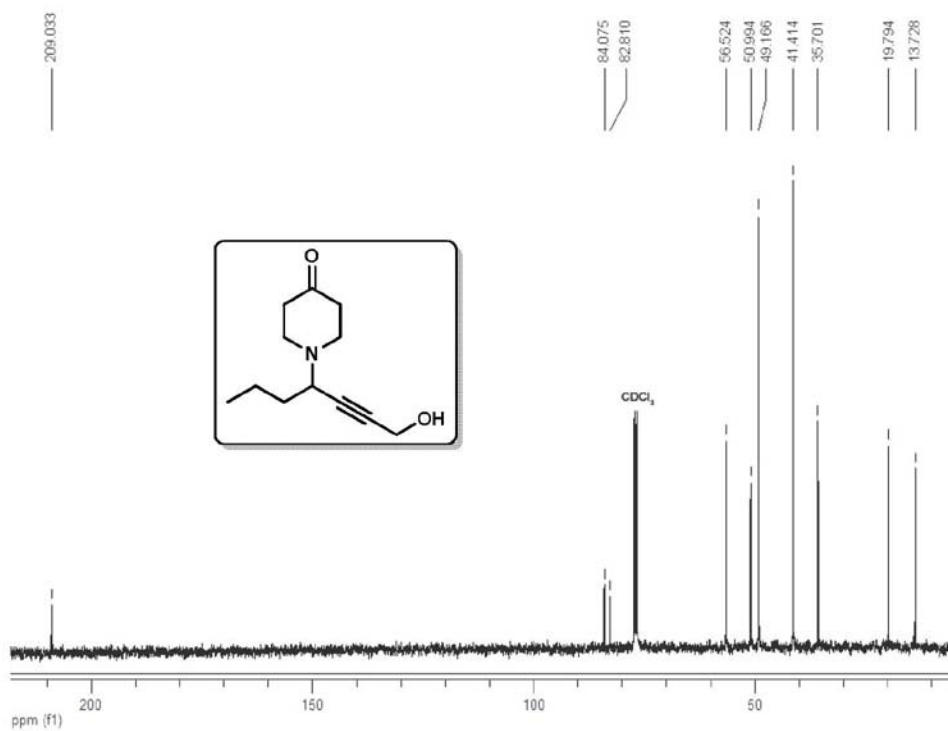
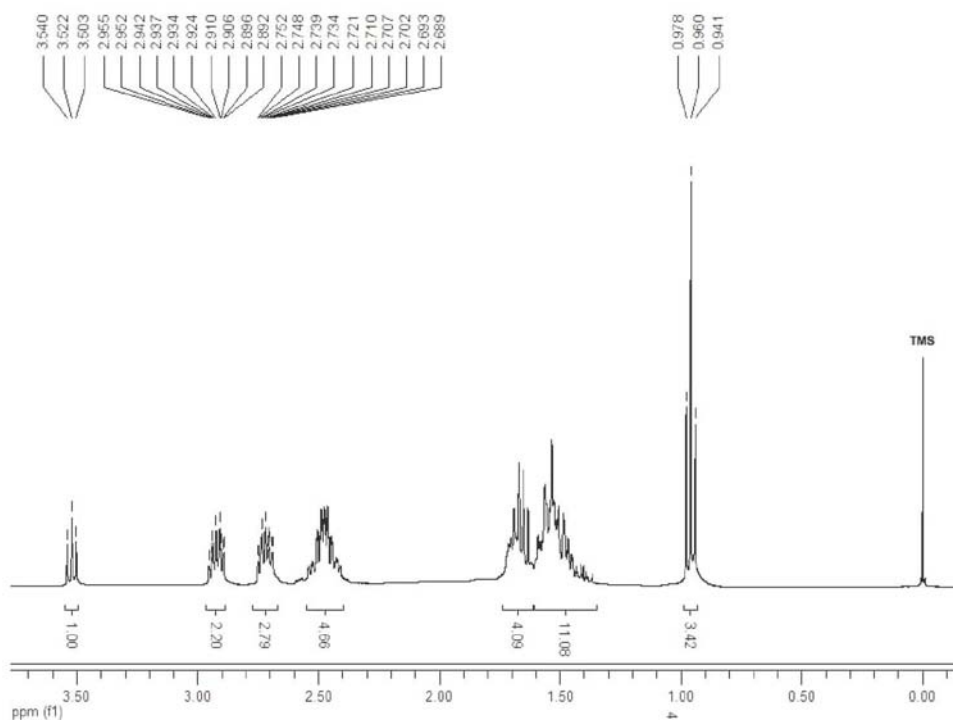
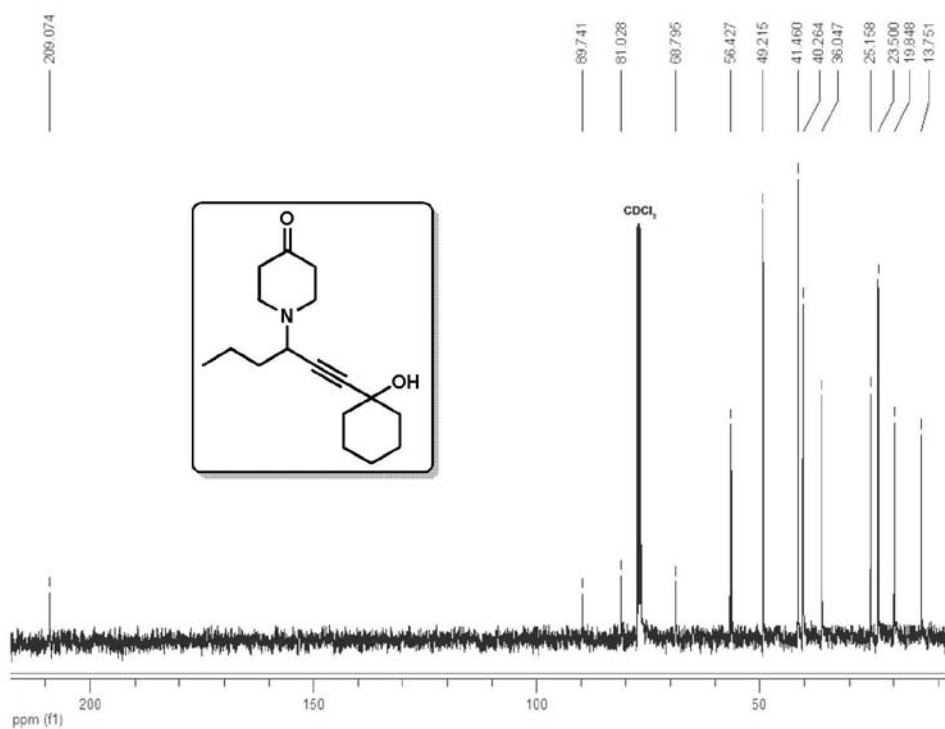


Figure 22S. <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(1-hydroxyhept-2-yn-4-yl)piperidin-4-one (**4g**)





**Figure 23S.** <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(1-(1-hydroxycyclohexyl)hex-1-yn-3-yl)piperidin-4-one (**4h**)



**Figure 24S.** <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(1-(1-hydroxycyclohexyl)hex-1-yn-3-yl)piperidin-4-one (**4h**)



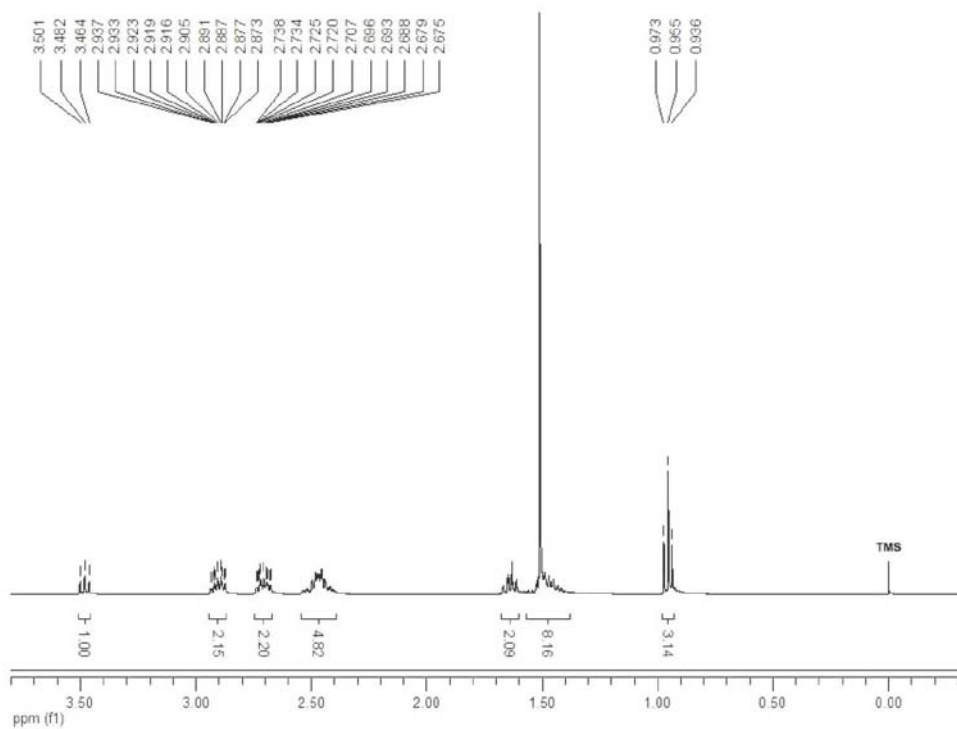


Figure 27S. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(7-hydroxy-7-methyloct-5-yn-4-yl)piperidin-4-one (4j)

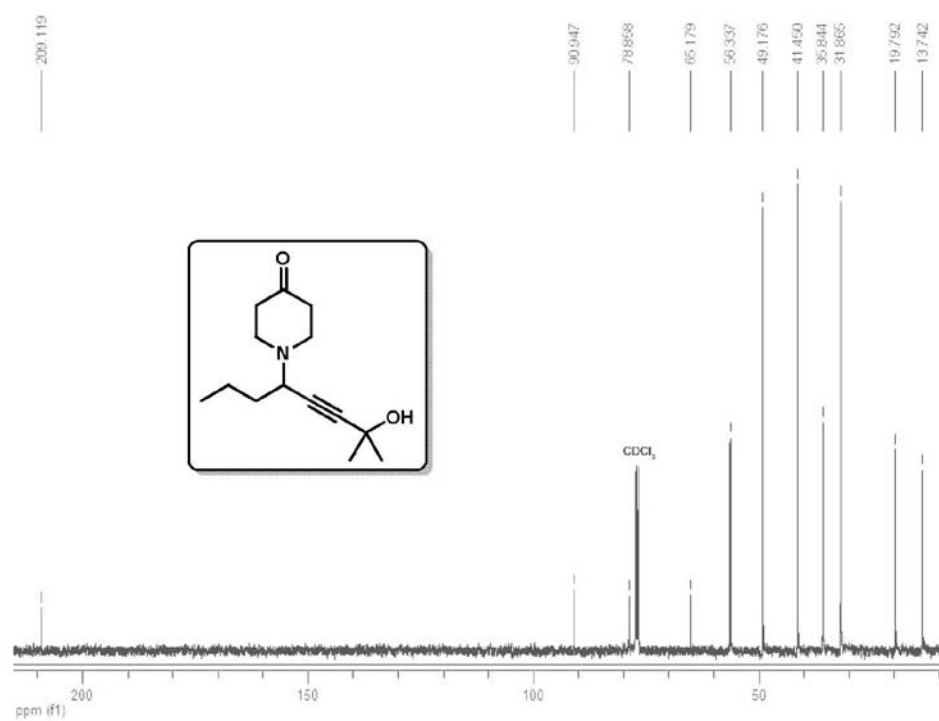


Figure 28S. <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(7-hydroxy-7-methyloct-5-yn-4-yl)piperidin-4-one (4j)

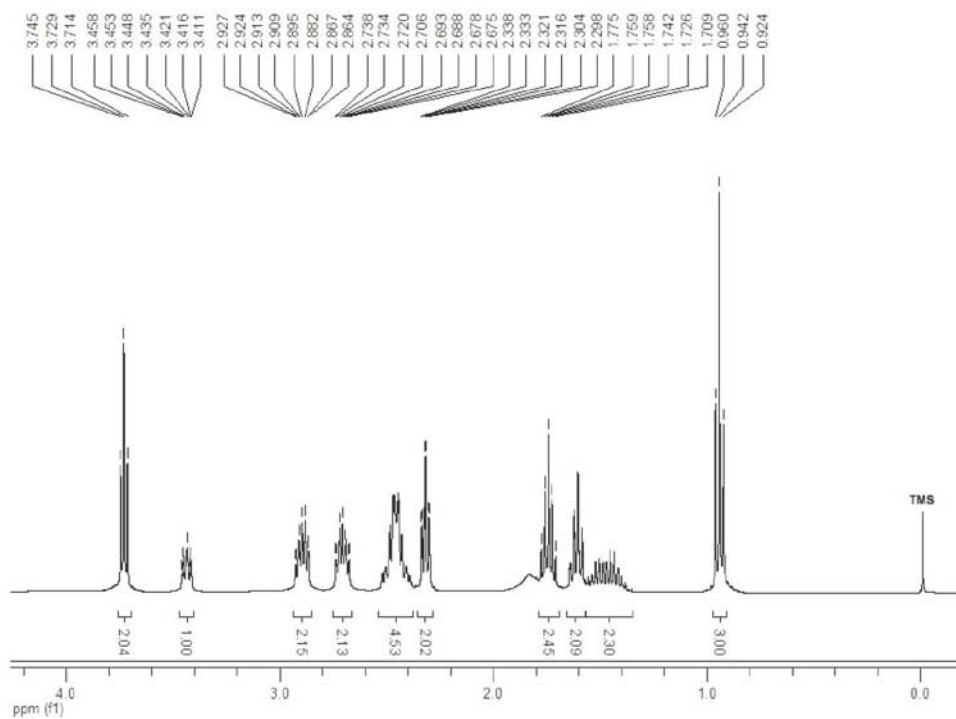


Figure 29S. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(9-hydroxynon-5-yn-4-yl)piperidin-4-one (4k)

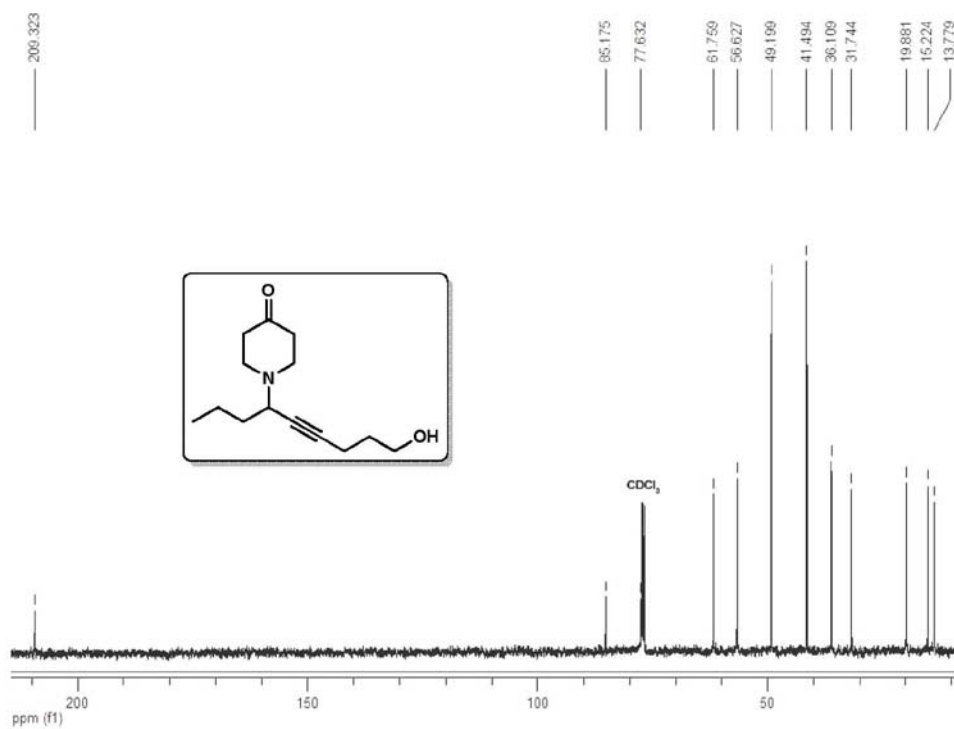


Figure 30S. <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(9-hydroxynon-5-yn-4-yl)piperidin-4-one (4k)

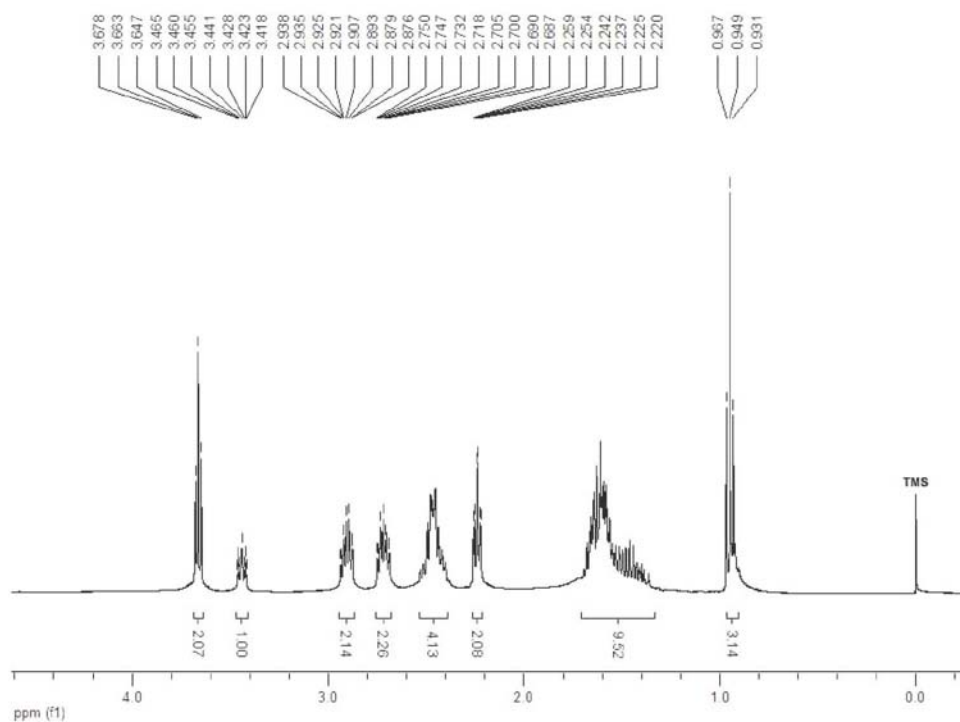


Figure 31S. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(10-hydroxydec-5-yn-4-yl)piperidin-4-one (4l)

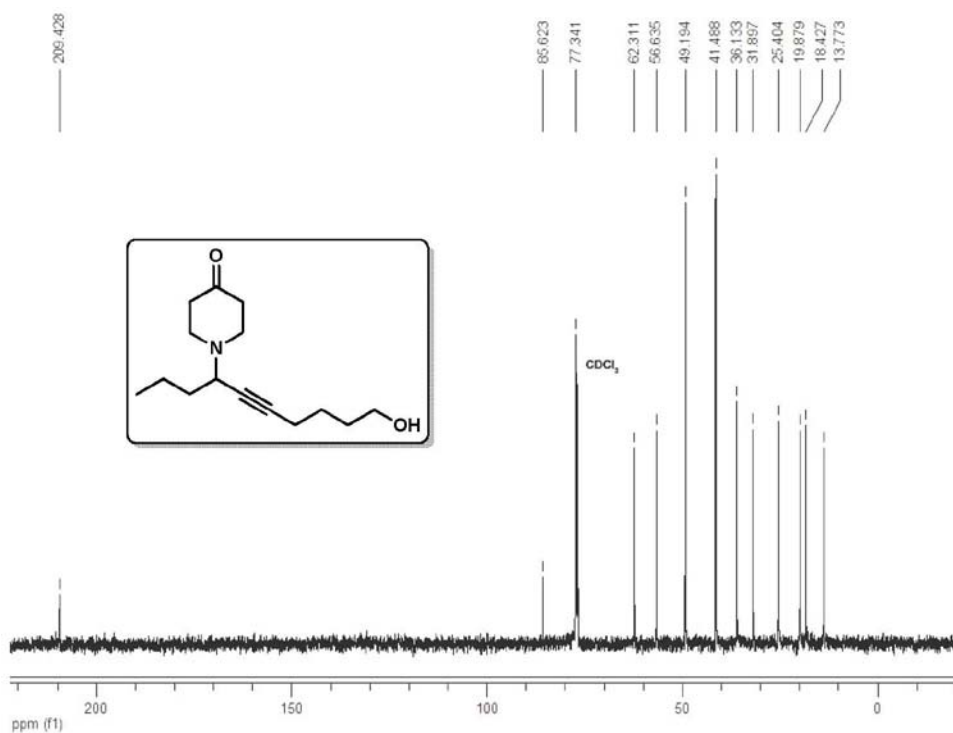


Figure 32S. <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(10-hydroxydec-5-yn-4-yl)piperidin-4-one (4l)

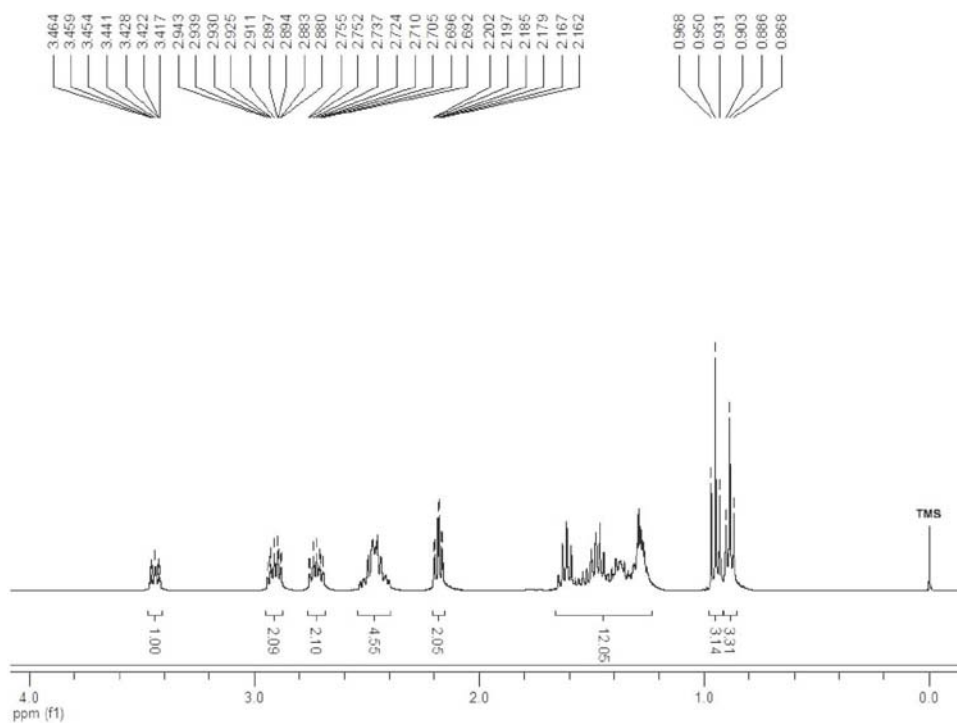


Figure 33S.  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of 1-(dodec-5-yn-4-yl)piperidin-4-one (**4m**)

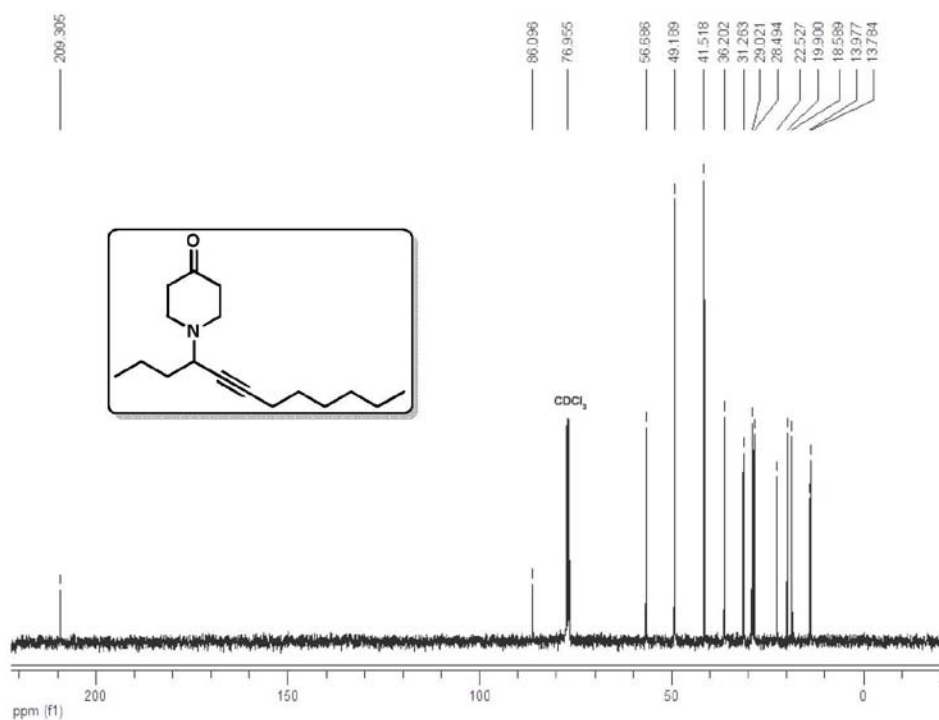


Figure 34S.  $^{13}\text{C}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of 1-(dodec-5-yn-4-yl)piperidin-4-one (**4m**)

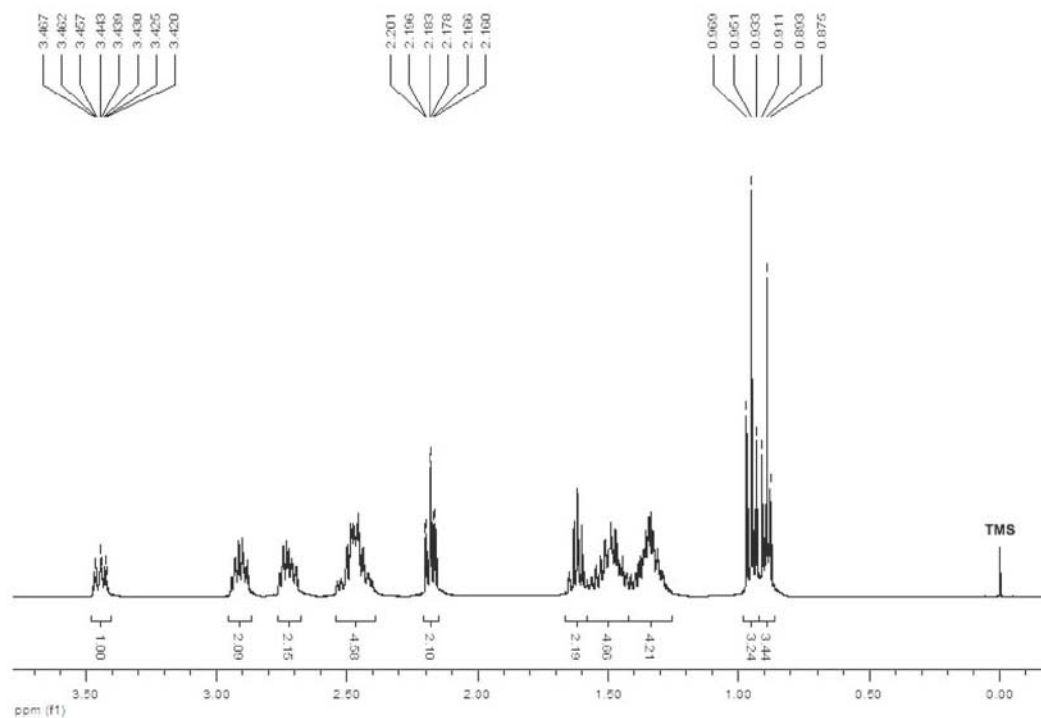


Figure 35S. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(undec-5-yn-4-yl)piperidin-4-one (4n)

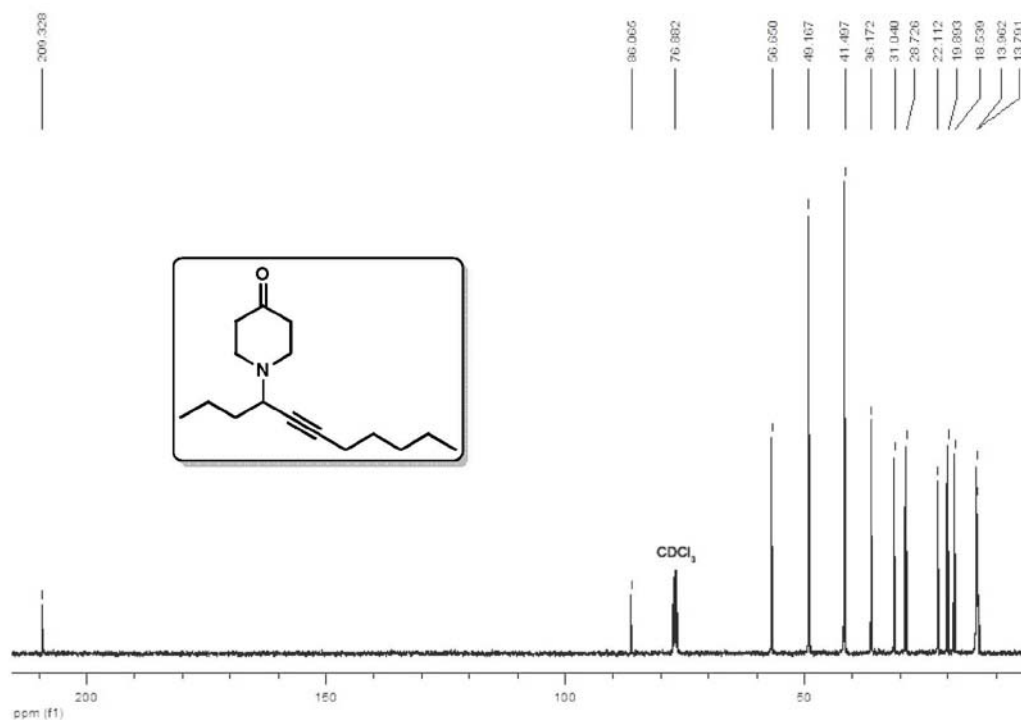


Figure 36S. <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(undec-5-yn-4-yl)piperidin-4-one (4n)

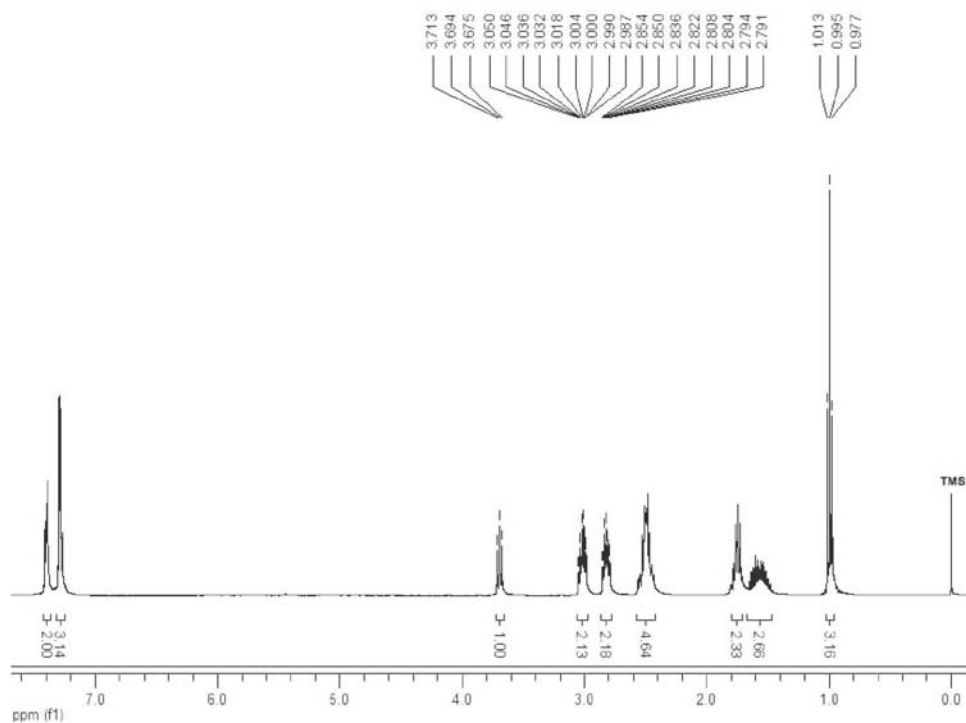


Figure 37S. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(1-phenylhex-1-yn-3-yl)piperidin-4-one (4o)

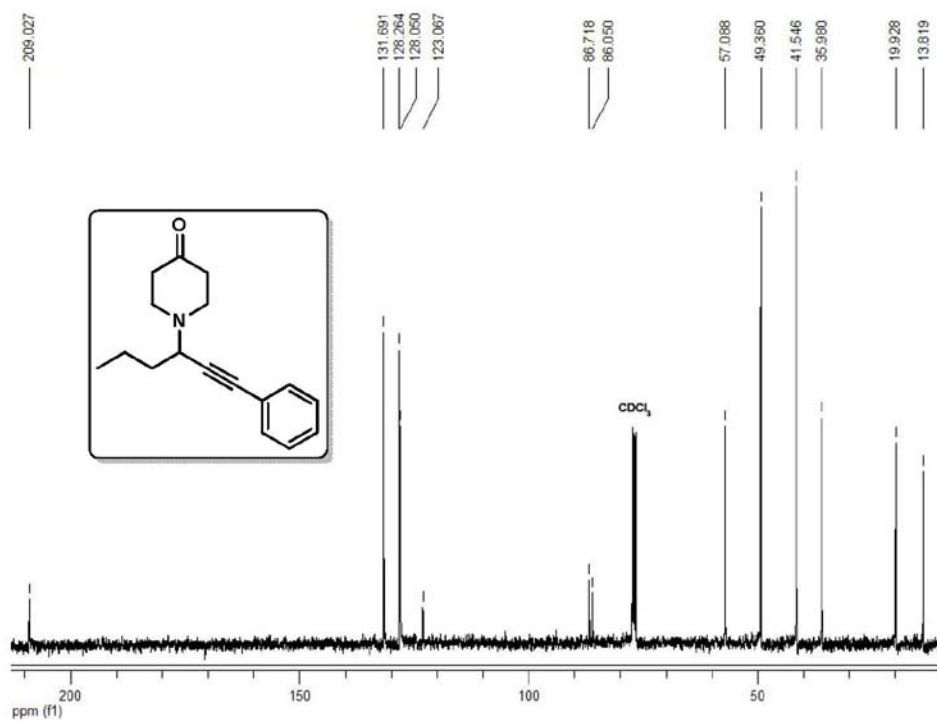


Figure 38S. <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(1-phenylhex-1-yn-3-yl)piperidin-4-one (4o)



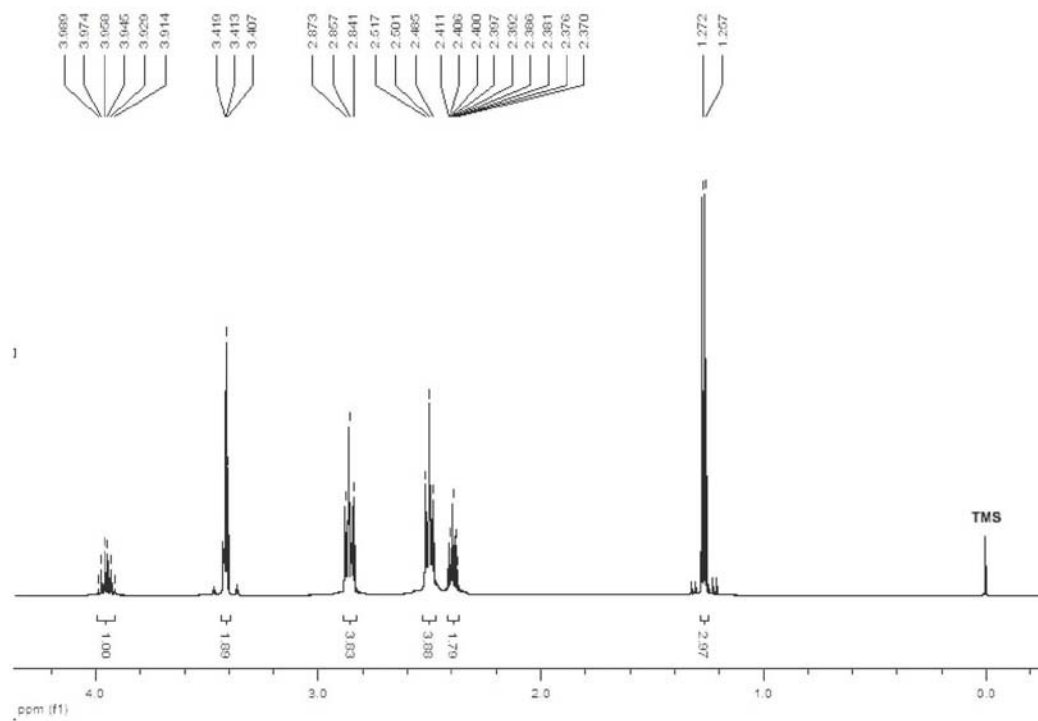


Figure 39S. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(5-hydroxyhex-2-yn-1-yl)piperidin-4-one (**4p**)

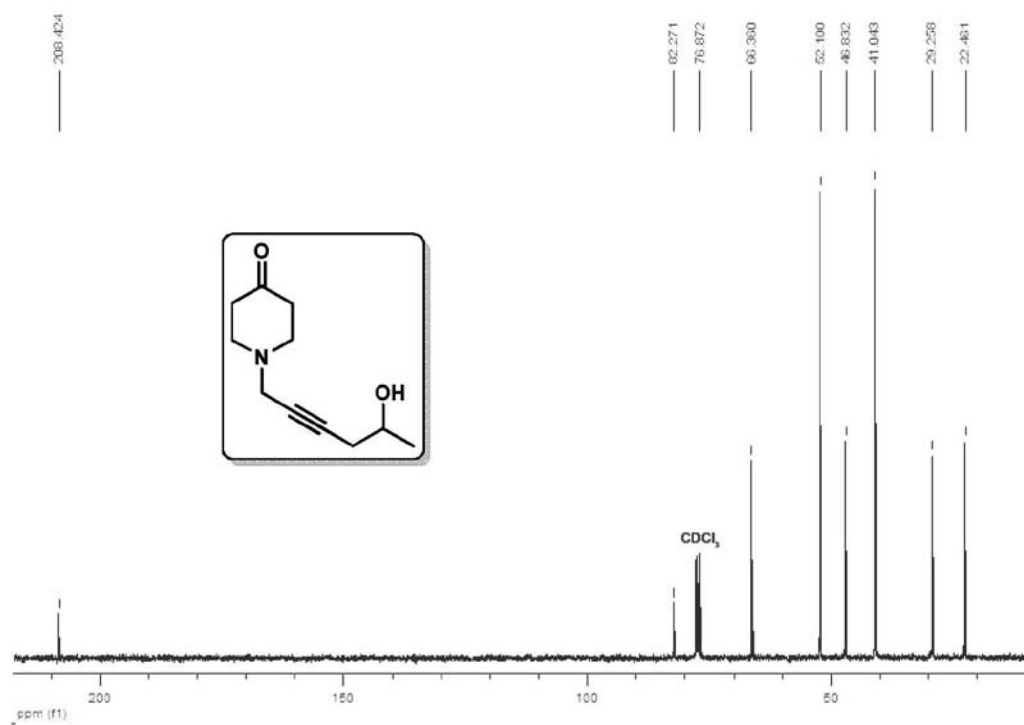


Figure 40S. <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(5-hydroxyhex-2-yn-1-yl)piperidin-4-one (**4p**)

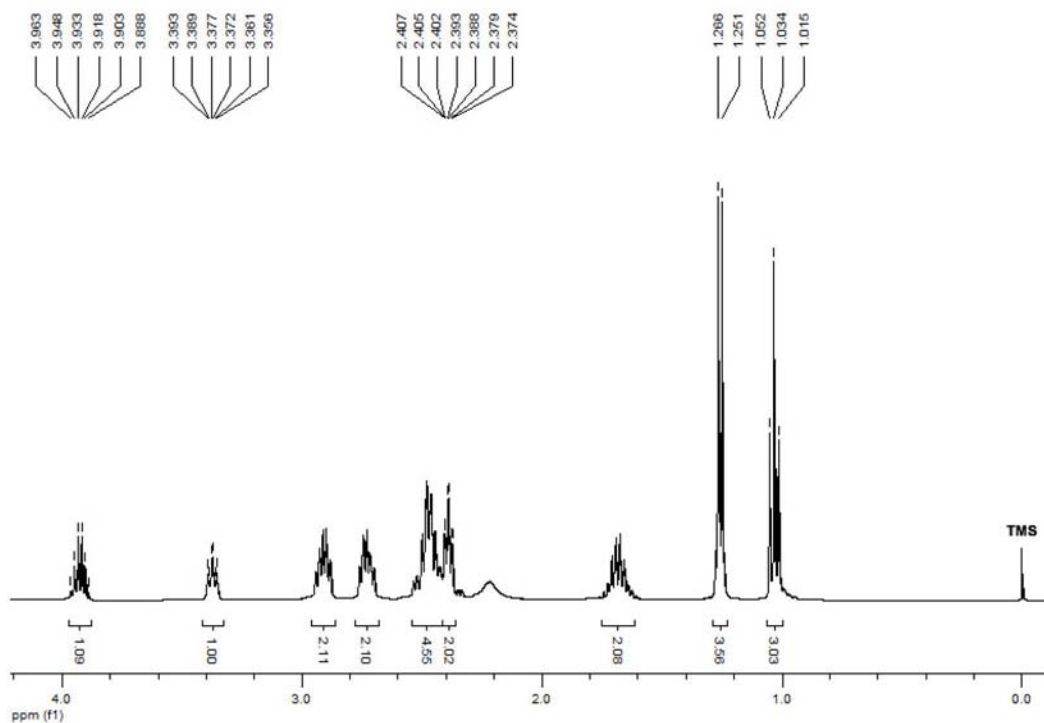


Figure 41S.  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of 1-(7-hydroxyoct-4-yn-3-yl)piperidin-4-one (4q)

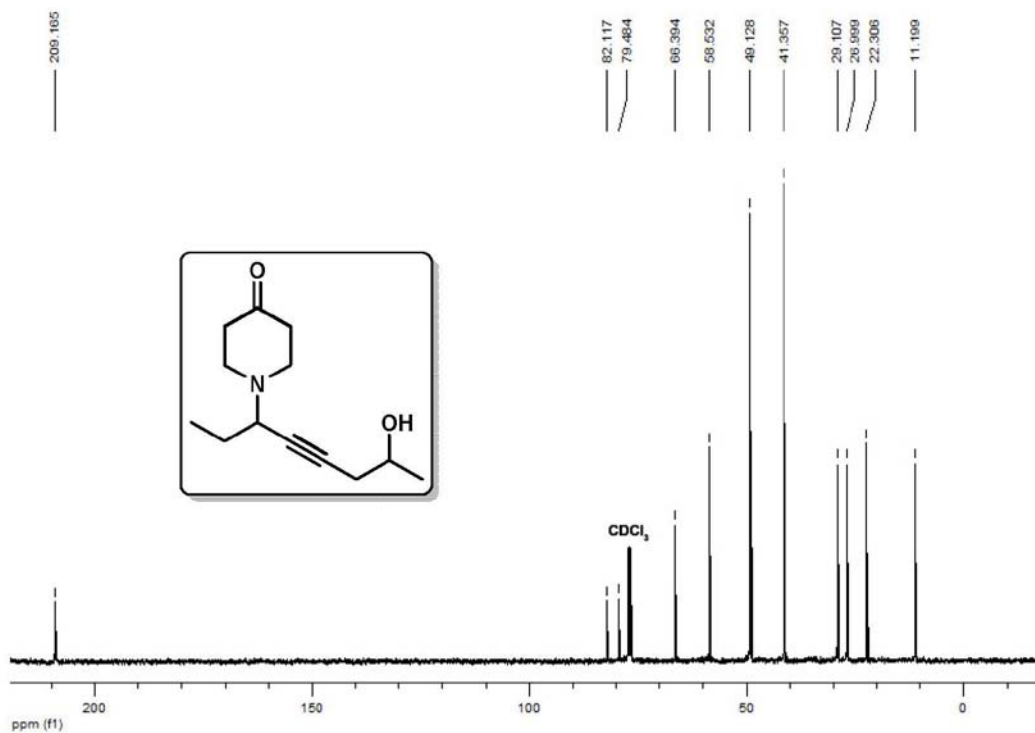


Figure 42S.  $^{13}\text{C}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of 1-(7-hydroxyoct-4-yn-3-yl)piperidin-4-one (4q)

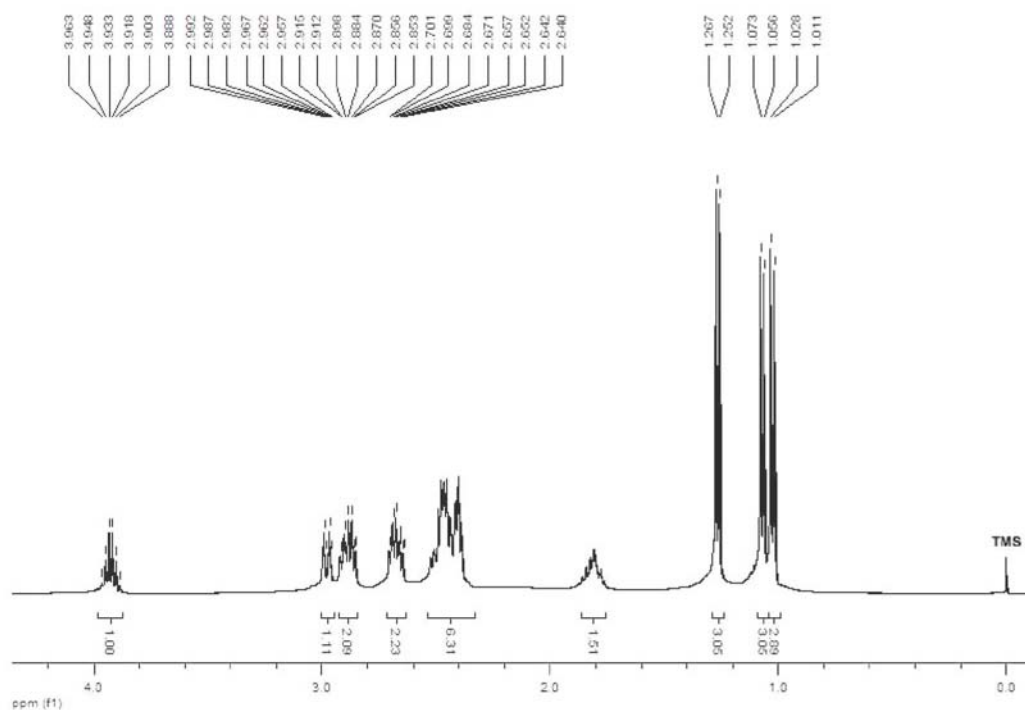


Figure 43S. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(7-hydroxy-2-methyloct-4-yn-3-yl)piperidin-4-one (4r)

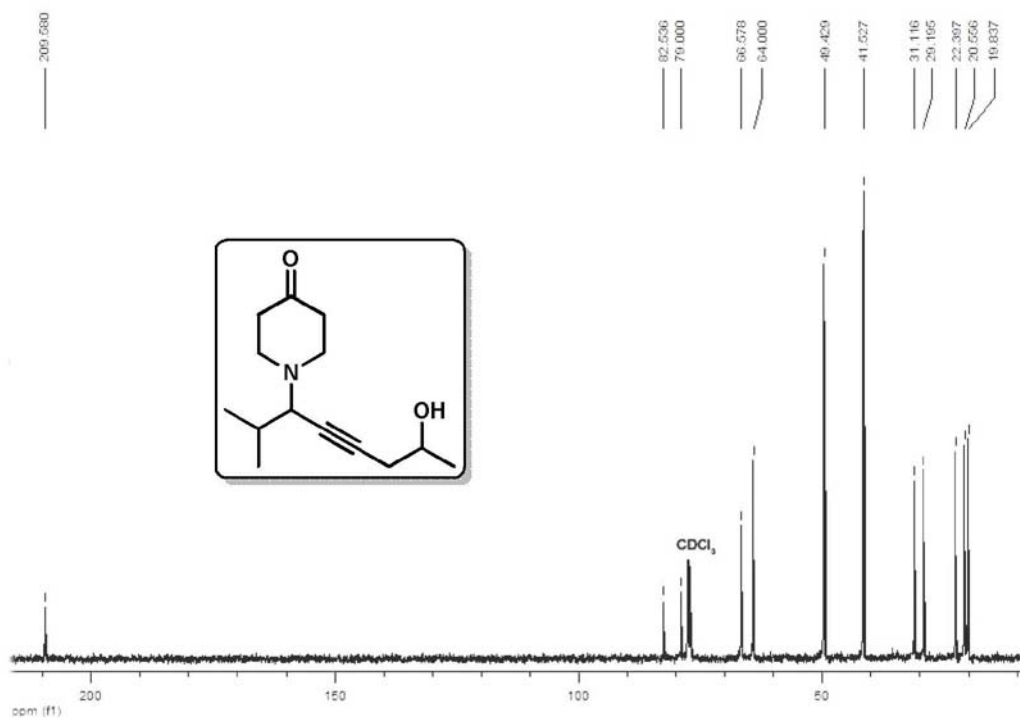


Figure 44S. <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(7-hydroxy-2-methyloct-4-yn-3-yl)piperidin-4-one (4r)

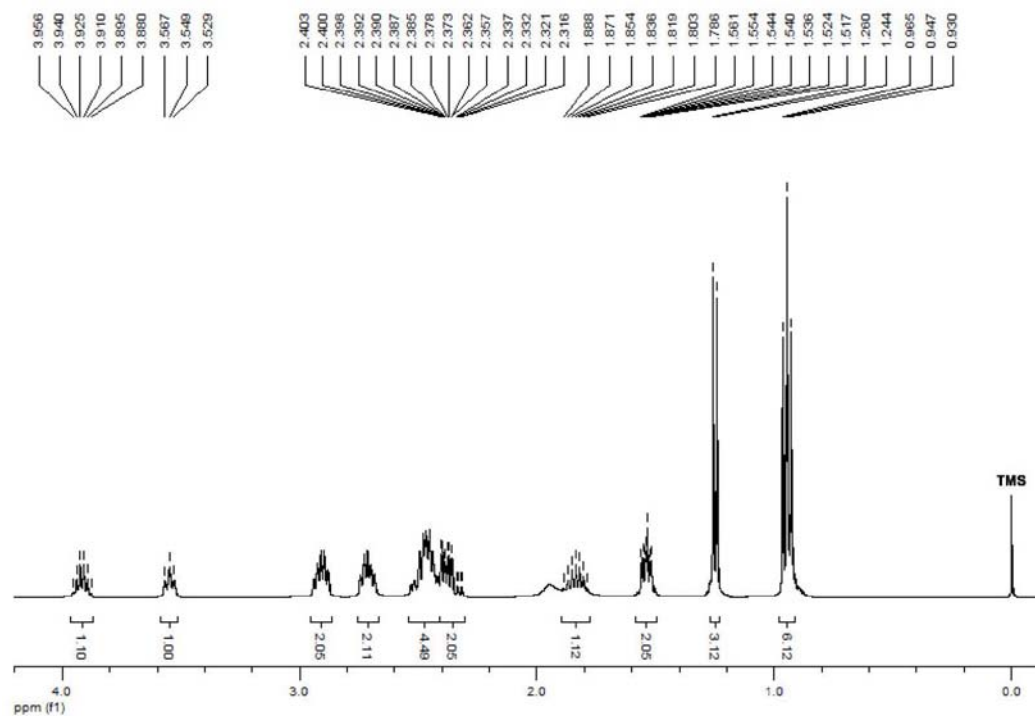


Figure 45S.  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of 1-(8-hydroxy-2-methylnon-5-yn-4-yl)piperidin-4-one (4s)

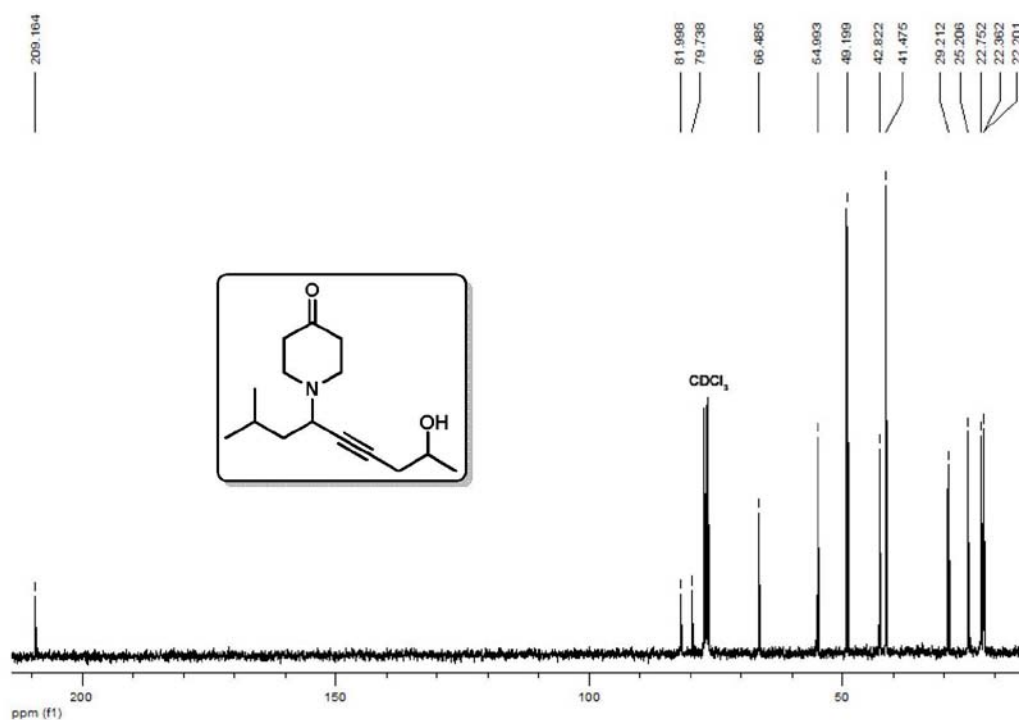


Figure 46S.  $^{13}\text{C}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of 1-(8-hydroxy-2-methylnon-5-yn-4-yl)piperidin-4-one (4s)

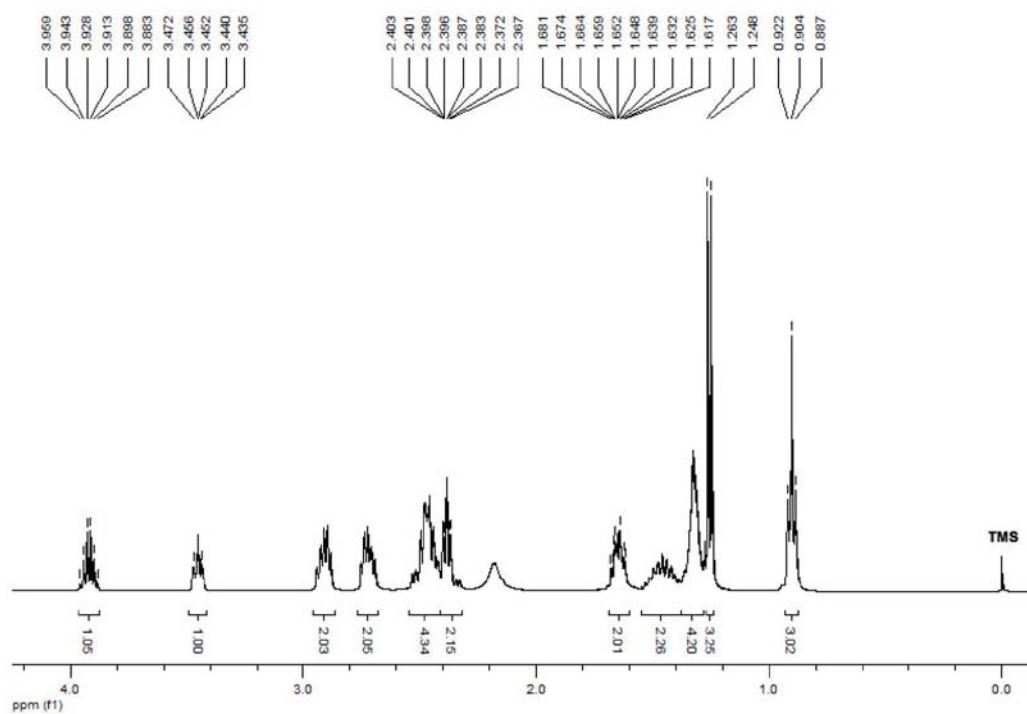


Figure 47S. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(2-hydroxyundec-4-yn-6-yl)piperidin-4-one (4t)

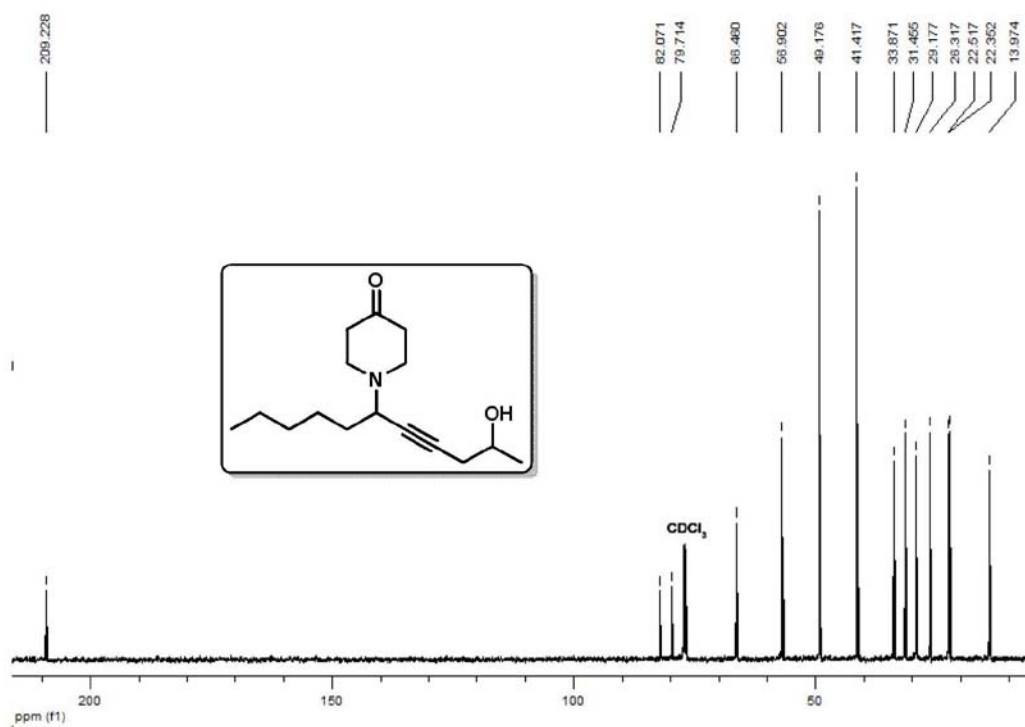


Figure 48S. <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(2-hydroxyundec-4-yn-6-yl)piperidin-4-one (4t)

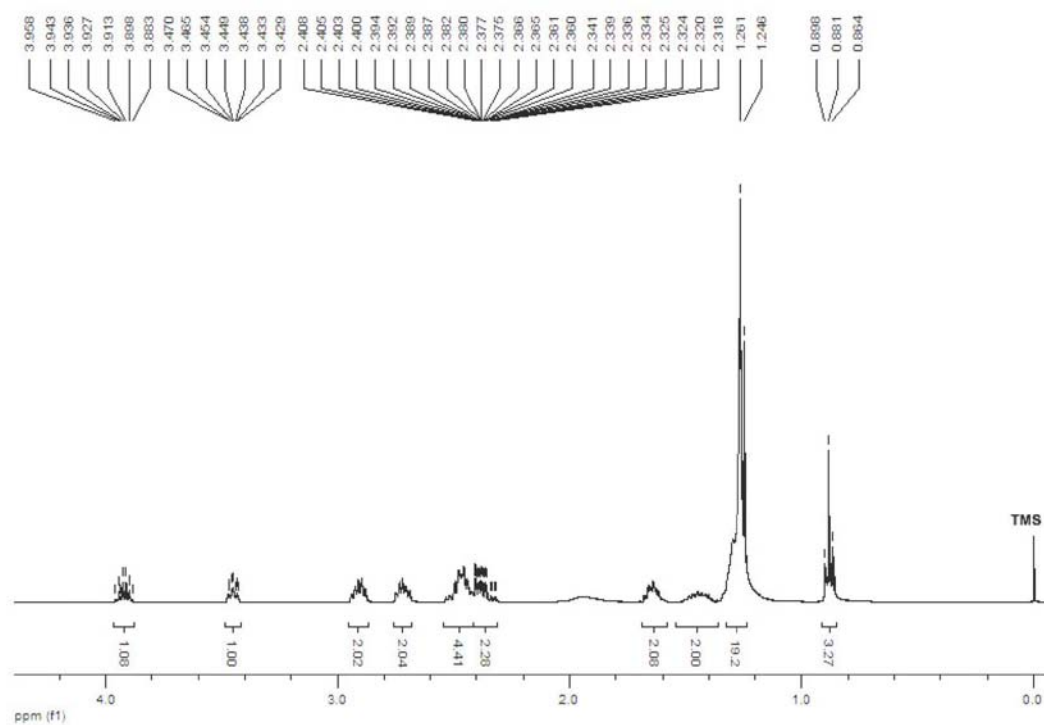


Figure 49S.  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of 1-(2-hydroxyheptadec-4-yn-6-yl)piperidin-4-one (**4u**)

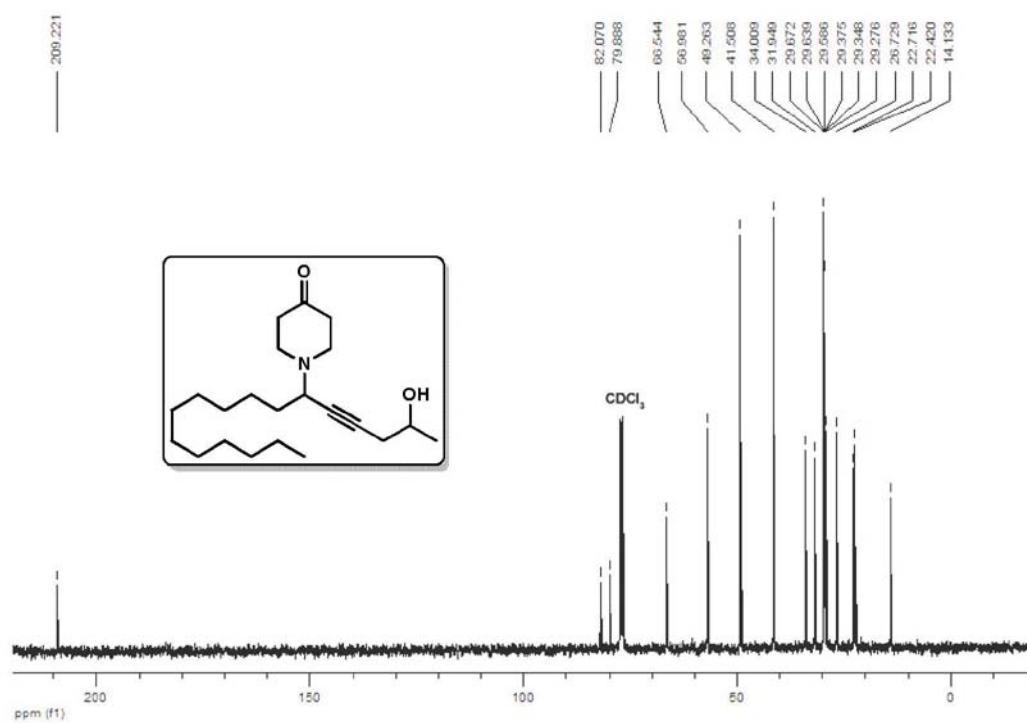


Figure 50S.  $^{13}\text{C}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of 1-(2-hydroxyheptadec-4-yn-6-yl)piperidin-4-one (**4u**)

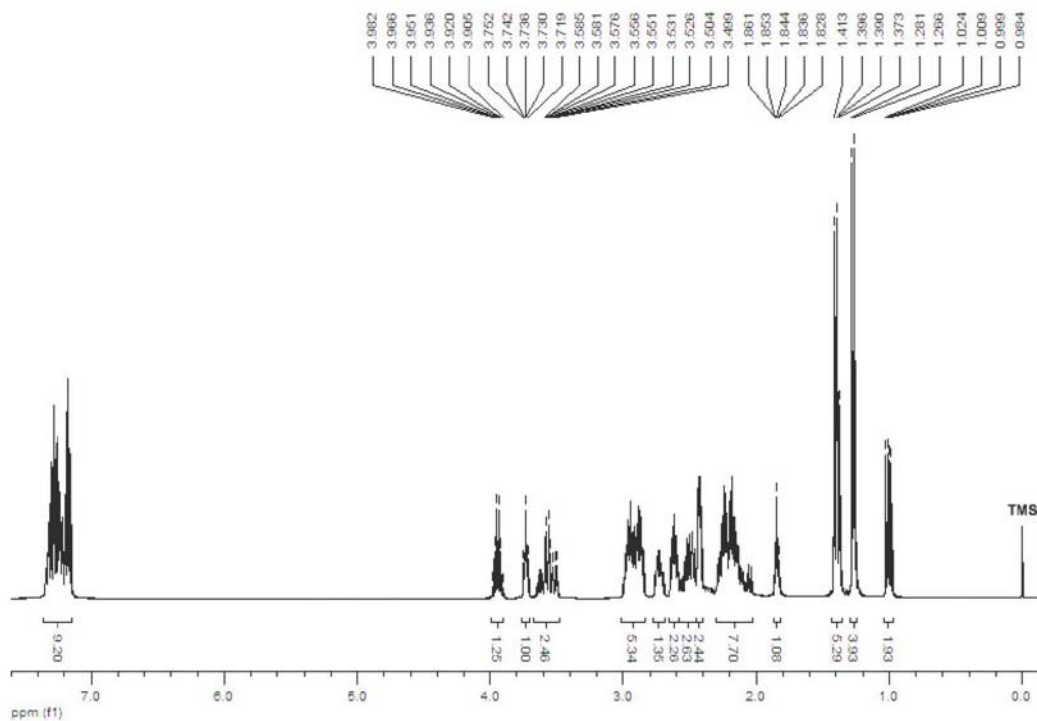


Figure 51S. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(7-hydroxy-2-phenyloct-4-yn-3-yl)piperidin-4-one (4v)

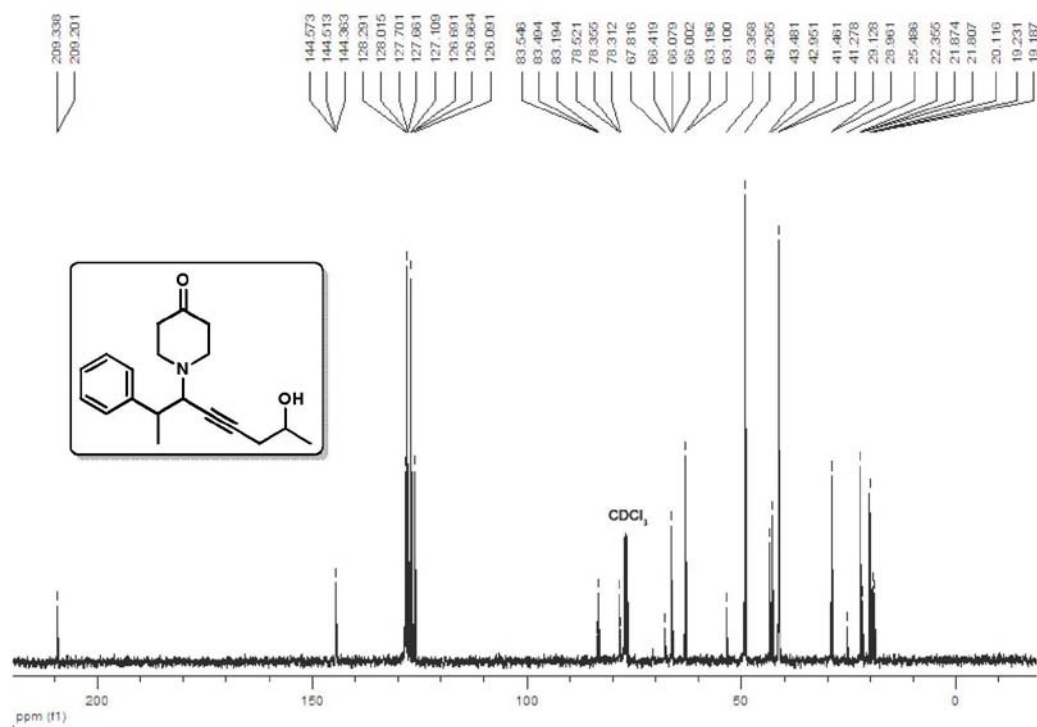


Figure 52S. <sup>13</sup>C NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(7-hydroxy-2-phenyloct-4-yn-3-yl)piperidin-4-one (4v)