Supporting Information for:

Iridium-catalyzed α-alkynylation of cyclic nonaromatic eneformamides: Application to the synthesis of azapolycyclic architectures

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Contents:

1. Experimental Section

All experiments involving air- and moisture-sensitive reagents were carried out under an inert atmosphere of nitrogen and using freshly distilled solvents. All alkynes, secondary amines, and electrophiles such as allyltrimethylsilane were newly purchased and used without further purification Column chromatography was performed on silica gel (230-400 mesh). Thin-layer chromatography (TLC) was performed using Silicycle SiliaplateTM glass backed plates (250 µm thickness, 60 Å porosity, F-254 indicator) and visualized using UV (254 nm) or CAM, *p*-anisaldehyde, or $KMnO_4$ stain. All reported temperatures were internal to the reaction vessel. Unless otherwise indicated, ^1H, ^{13}C, and DEPT-135, COSY 45, and HMQC (or HSQC) spectra were acquired using C_6D_6 or $CDCl_3$ as solvent at room temperature. Chemical shifts are quoted in parts per million (ppm). HRMS-EI^+ data were obtained using either electron spray ionization (ESI) or electron impact (EI) techniques. High-resolution ESI was obtained on an LTQ-FT (ion trap; analyzed using Excalibur). High resolution EI was obtained on an Autospec (magnetic sector; analyzed using MassLynx).

General Procedure A: Ir-catalyzed alkynylation

To an oven-dried tube equipped with a stir bar was sequentially added the eneformamide (1 mmol), $[IrCp^*Cl_2]_2$ (2 mol%), $AgNTf_2$ (10 mol%), NaOAc (20 mol%), Cs_2CO_3 (50 mol%), and AgOAc (2 mmol, 2 equiv). The terminal alkyne (2 mmol, 2 equiv), dissolved in 2-MeTHF/HFIP (4 mL/1 mL) was then introduced by means of a syringe. The resulting reaction mixture was stirred at 90 ºC for the desired length of time (GC-MS and TLC monitoring). Upon completion, the contents were diluted with CH_2Cl_2 and filtered through Celite. The solvents were removed *in vacuo* and the crude product was directly subjected to flash chromatography on silica pretreated with trimethylamine.

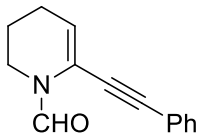
General Procedure B: Catalytic hydrogenation

EtOAc (8 mL) was added to a flask containing 10% Pd/C (200 mg) at room temperature. The flask was degassed and placed under an inert atmosphere of nitrogen. A solution of the alkynyl enamide (0.5 mmol) in EtOAc (2 mL) was added. After complete addition, the nitrogen line was cut off and then replaced with a balloon of hydrogen. After complete consumption of the enamide (based on LC-MS and TLC monitoring), the mixture was filtered through a plug of Celite and concentrated under reduced pressure.

General Procedure C:

Chemoselective reduction to alkenyl eneformamides: To an oven-dried 8 mL reaction vial was added PPh_3 (1.5 equiv), the alkynyl eneformamide (0.5 mmol, 1.0 equiv) dissolved in 2-MeTHF (4 mL) and water (1 mL)). The solution was heated to 65 °C and stirred for 22 h. The solvents were removed under reduced pressure, toluene (10 mL) was added, and the solution dried over $MgSO_4$. The toluene was removed under reduced pressure, and cold Et_2O was added and the solution was filtered over silica. The Et_2O solvent was removed under reduced pressure, and the crude product was advanced to the next step without further purification.

Hexannulation: A vial was flame-dried, evacuated and flushed with nitrogen. A solution of tetracyanoethylene (128 mg, 1.0 mmol, 2 equiv) in 2-MeTHF (2 mL) was added to the vial followed by a solution of crude amino diene (0.5 mmol) in toluene (2 mL). The mixture was stirred for 12 h at room temperature. The crude mixture was concentrated under reduced pressure and purified by flash chromatography on silica (pretreated with 1% Et_3N), eluting with hexane/EtOAc.

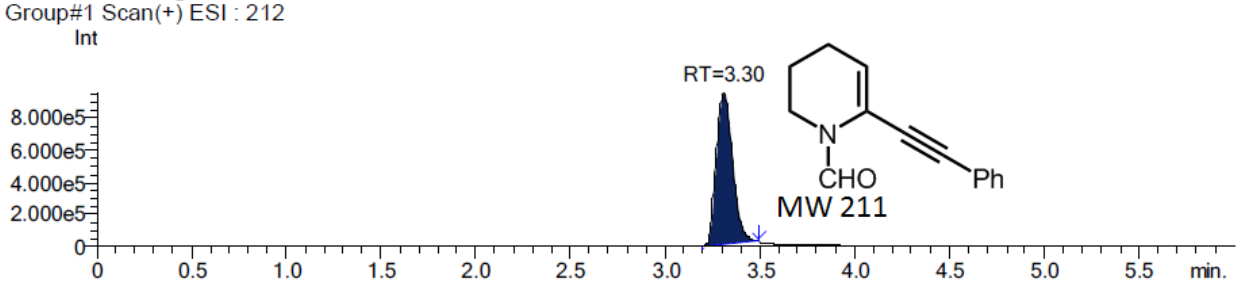


2a

Prepared from **3a** (1.0 mmol) and phenylacetylene using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (70:30). Yield = 171 mg, 81%. ^{1}H NMR (400 MHz, C_6D_6) δ 9.35 (1H), 7.28 to 7.21 (2H), 7.00 to 6.93 (3H), 5.28 to 5.25 (1H), 3.46 to 3.43 (2H), 1.60 to 1.52 (2H), 1.20 to 1.14 (2H). ^{13}C NMR (101 MHz, C_6D_6) δ 160.5, 132.0, 129.3, 129.0, 122.7, 121.5, 118.0, 93.39, 83.0, 39.3, 23.5, 20.8. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{14}H_{13}NO$ 211.0997; found 211.0993.

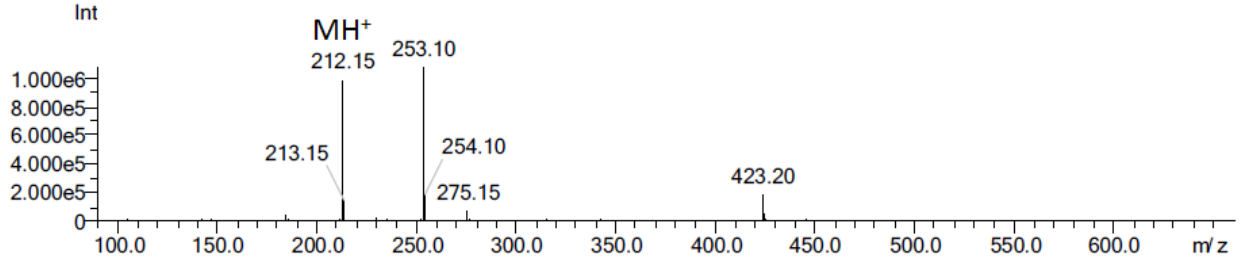
MS Chromatogram

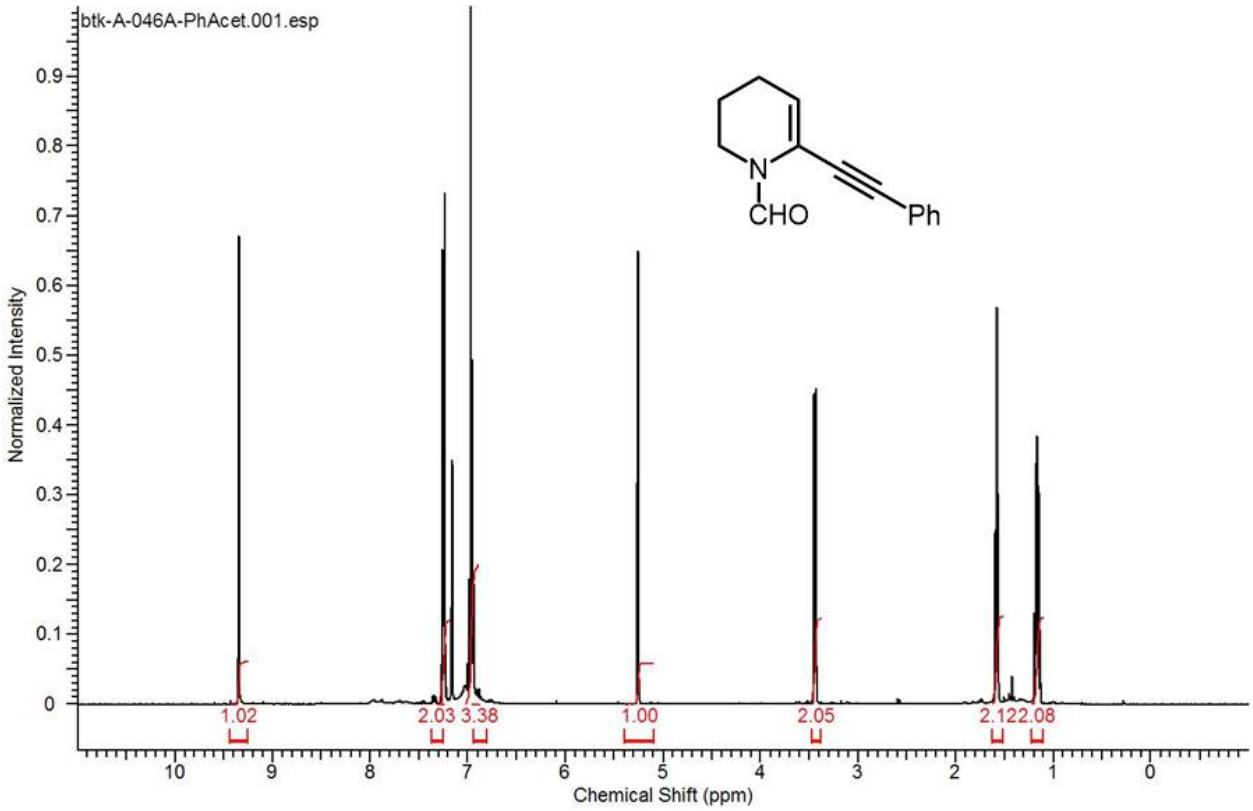
Group#1 Scan(+) ESI : 212

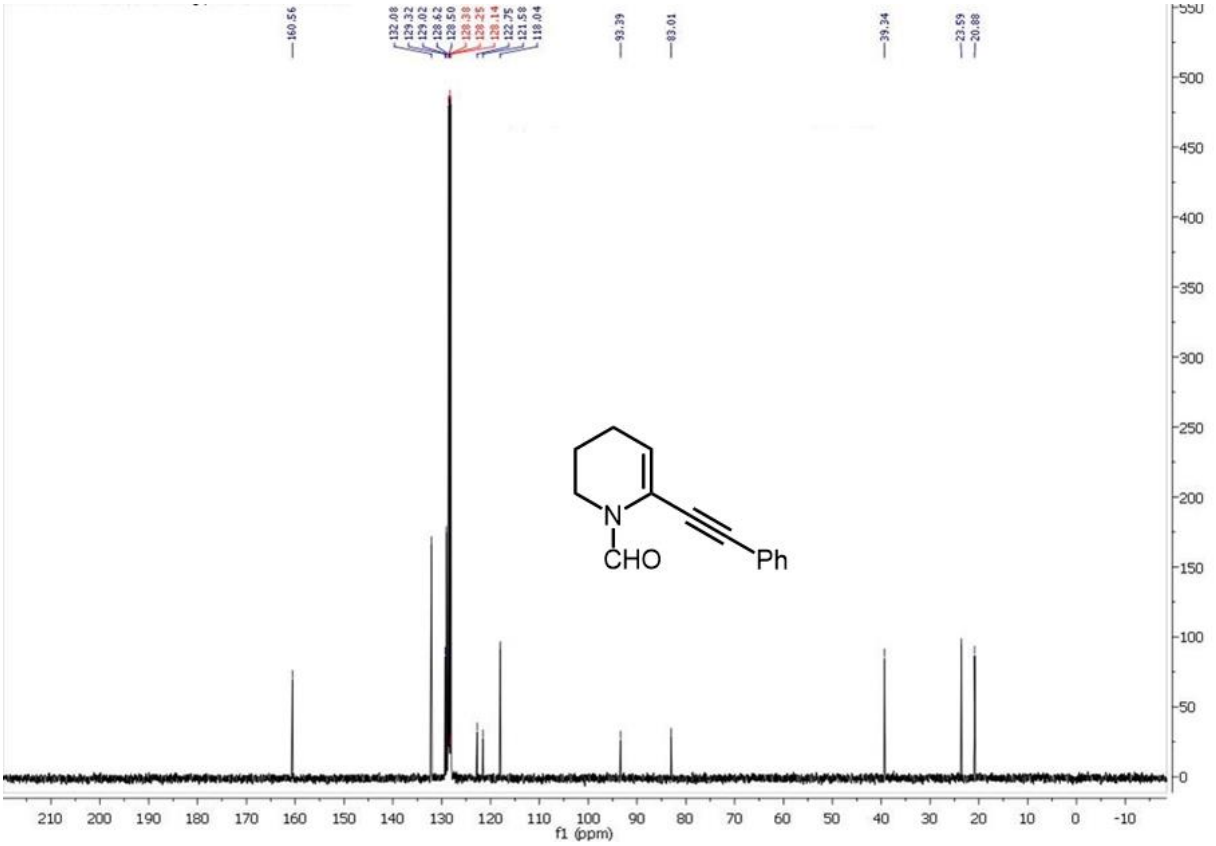


MS Spectrum

Group#1 - MS Mass(212) Peak: 17, RT: 3.19 to 3.47 min



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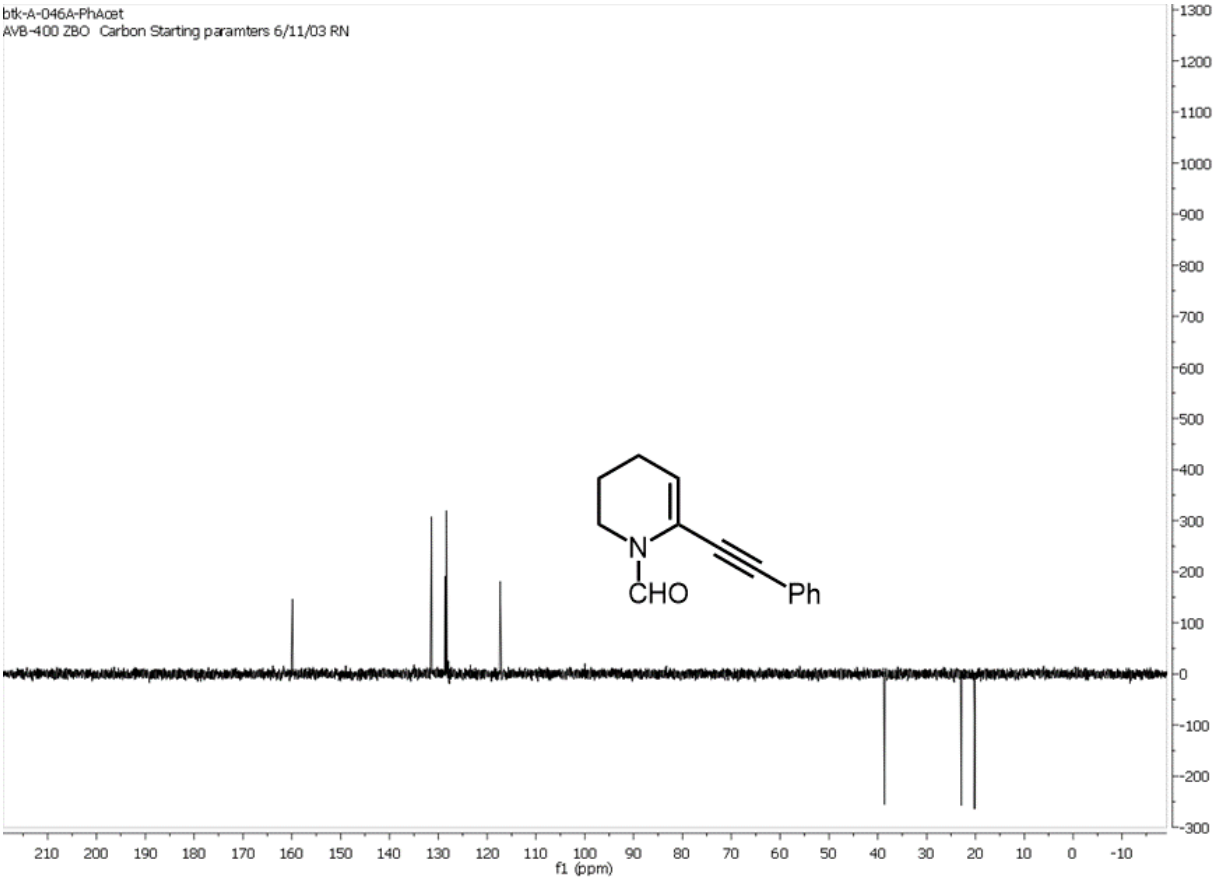
Ph
f1 (ppm)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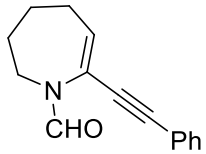
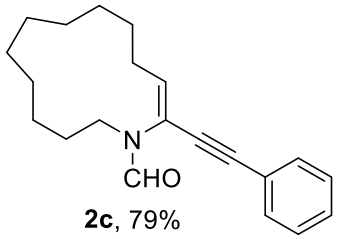
f1 (ppm)



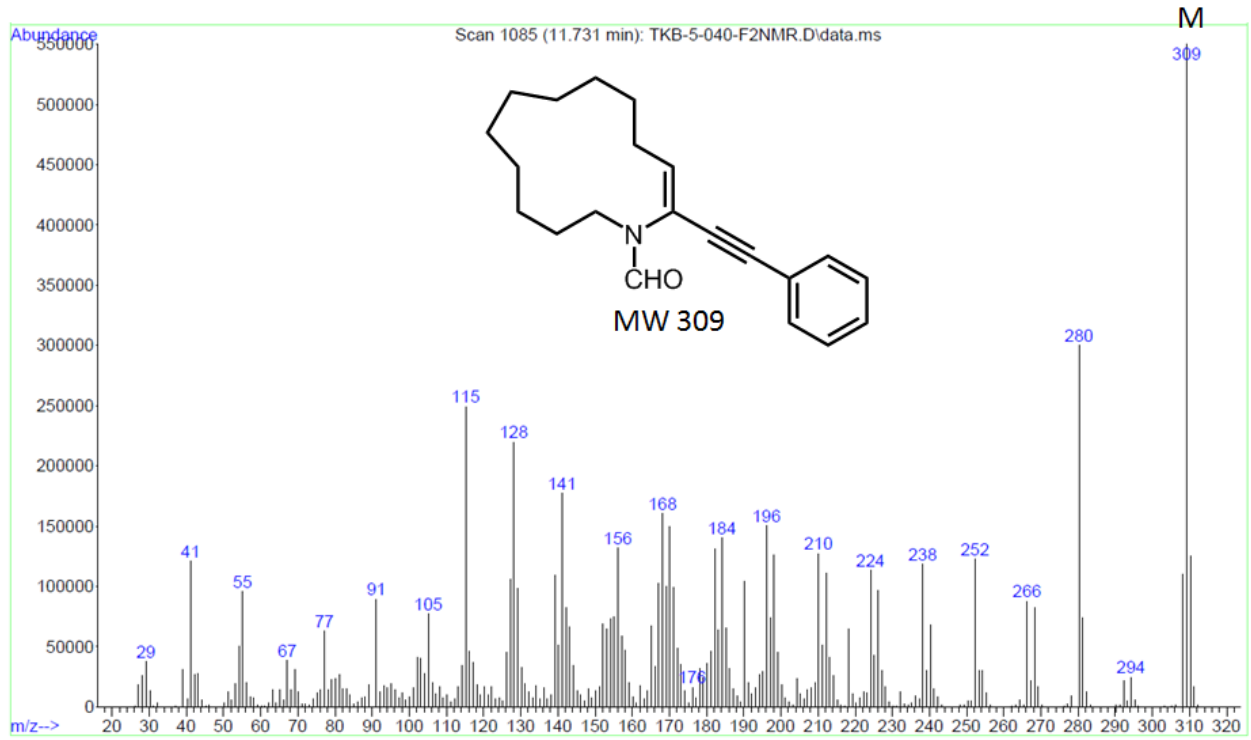
2b, 94%

Prepared from **1b** (1.0 mmol) and phenylacetylene using **General Procedure A**. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (70:30). Yield = 189.5 mg, 84%. Data as previously reported by us.[1]



2c, 79%

Prepared from **3c** (1.0 mmol) and phenylacetylene using **General Procedure A**. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (90:10). Yield = 244 mg, 79%. ^{1}H NMR (400 MHz, $CDCl_3$, mixture of rotamers) δ 8.29 & 8.15 (1H, s,s), 7.72 to 7.12 (5H, m), 5.88 to 5.72 (1H, m), 3.76 to 3.65 (2H, t), 2.60 to 2.14 (2H, m), 1.73 to1.04 (16H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 162.5, 136.9, 135.68, 135.6, 135.3, 135.2, 135.2, 134.0, 133.1, 132.5, 132.2, 132.1, 132.0, 131.9, 131.7, 131.6, 131.59, 130.3, 129.6, 129.1, 128.8, 128.6, 128.5, 128.4, 128.3, 128.1, 127.9, 127.7, 122.3, 121.8, 95.3, 88.9, 85.4, 85.2, 42.8, 41.3, 36.5, 34.6, 31.4, 29.7, 29.2, 28.6, 28.5, 28.4, 28.2, 28.1, 28.0, 27.9, 27.6, 26.9, 26.8, 26.7, 26.5, 26.4, 26.2, 26.0, 25.9, 25.8, 25.6, 25.5, 25.5, 25.3, 25.0, 24.9, 24.8, 24.7, 24.5, 23.7, 23.6, 23.6, 23.4. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{21}H_{27}NO$ 309.2093; found 309.2096.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41
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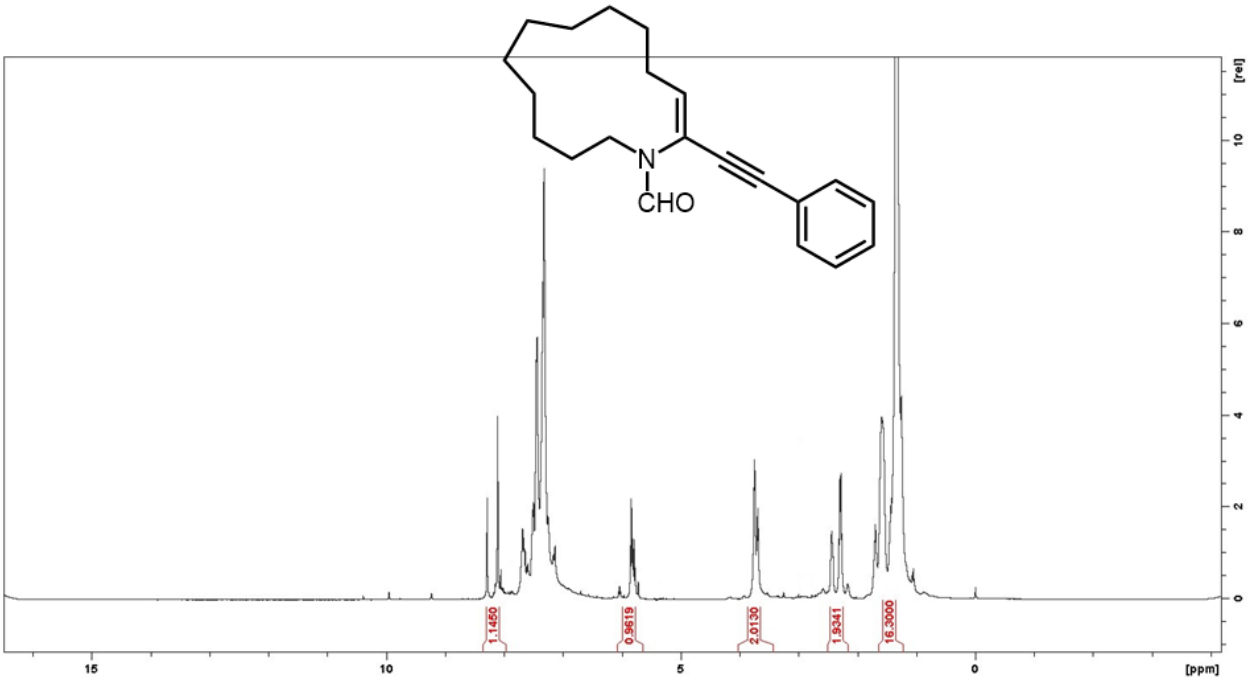
m/z-->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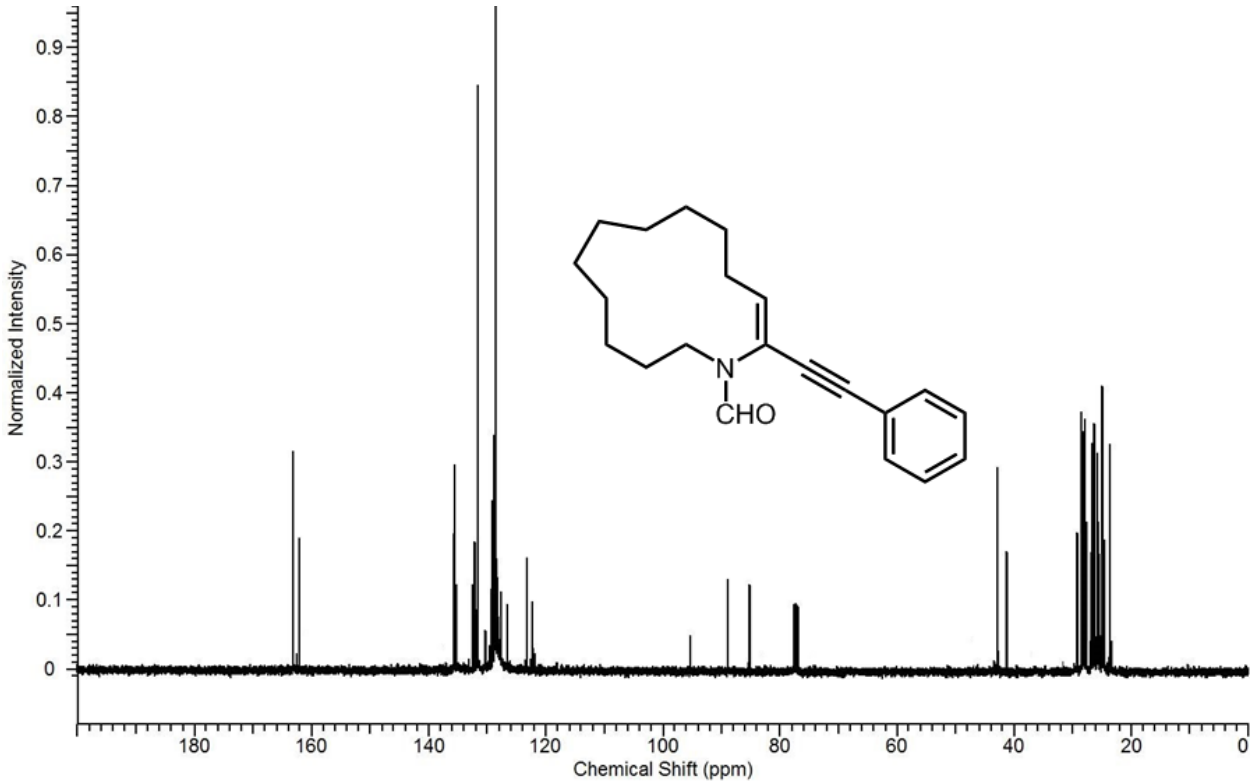
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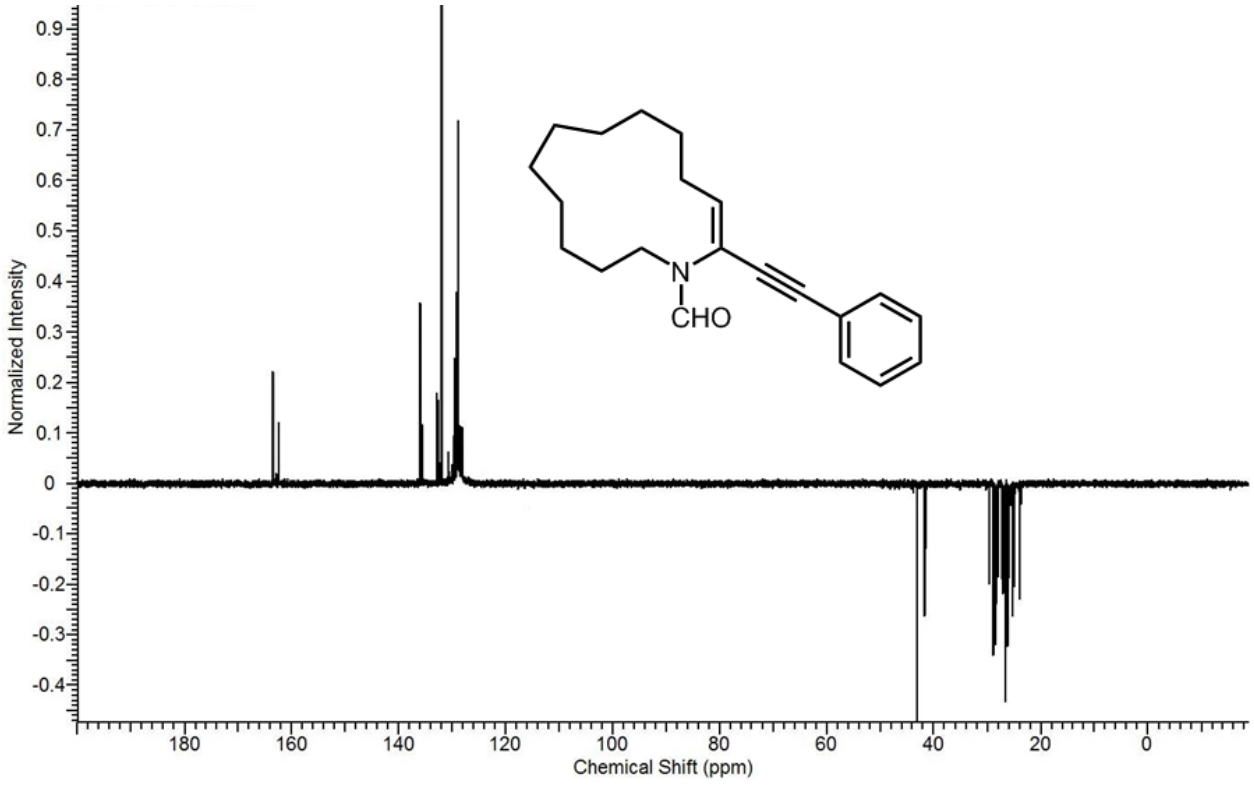
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20
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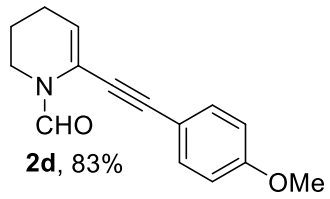
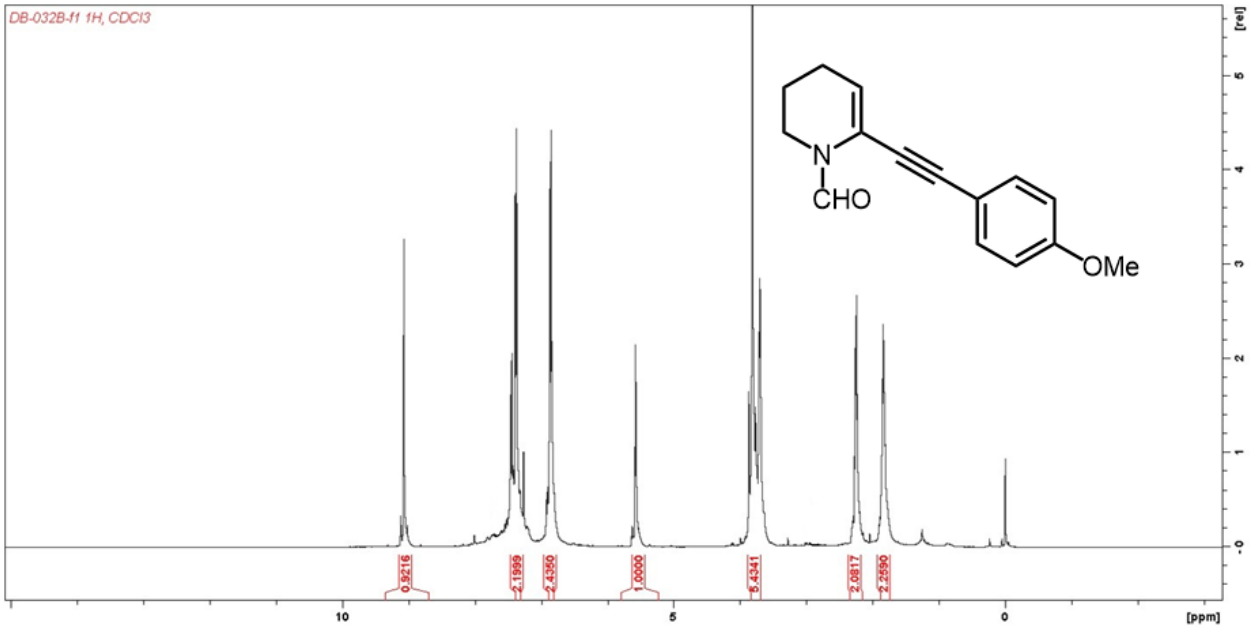
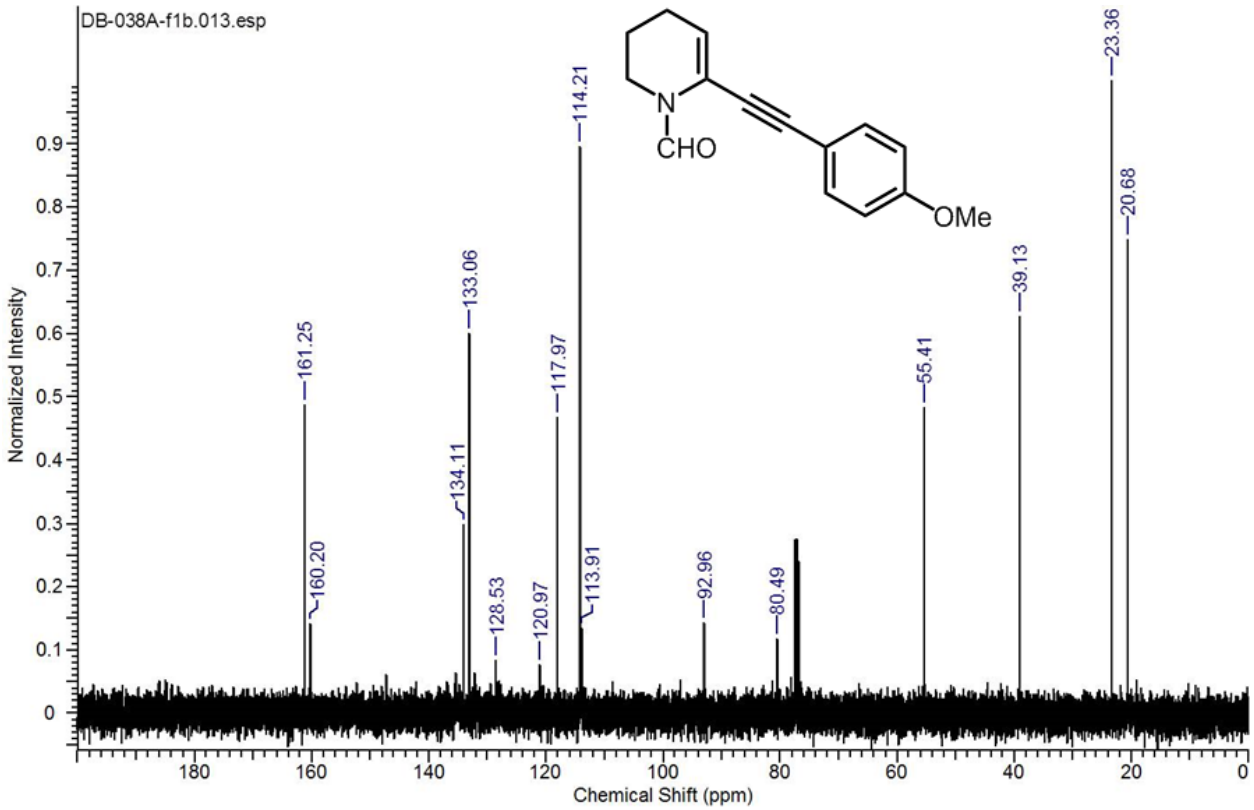
Chemical Shift (ppm)



2d, 83%

Prepared from **3a** (1.0 mmol) and *p*-methoxyphenylacetylene using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (50:50). Yield = 200 mg, 83%. ^{1}H NMR (400 MHz, Chloroform-d, mixture of rotamers) δ 9.06 (1H, s), 7.32 (2H, d), 6.75 (2H, d), 5.59 to 5.57 (1H, t), 3.71 to 3.52 (5H, m), 2.27 to 2.18 (2H, m), 1.88 to 1.73 (2H, m). ^{13}C NMR (101 MHz, Chloroform-d) δ 161.3, 160.2, 134.1, 133.1, 128.5, 121.0, 118.0, 114.2, 113.9, 93.0, 80.5, 55.4, 39.1, 23.4, 20.7. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{15}H_{15}NO_2$ 241.1103; found 241.1107.

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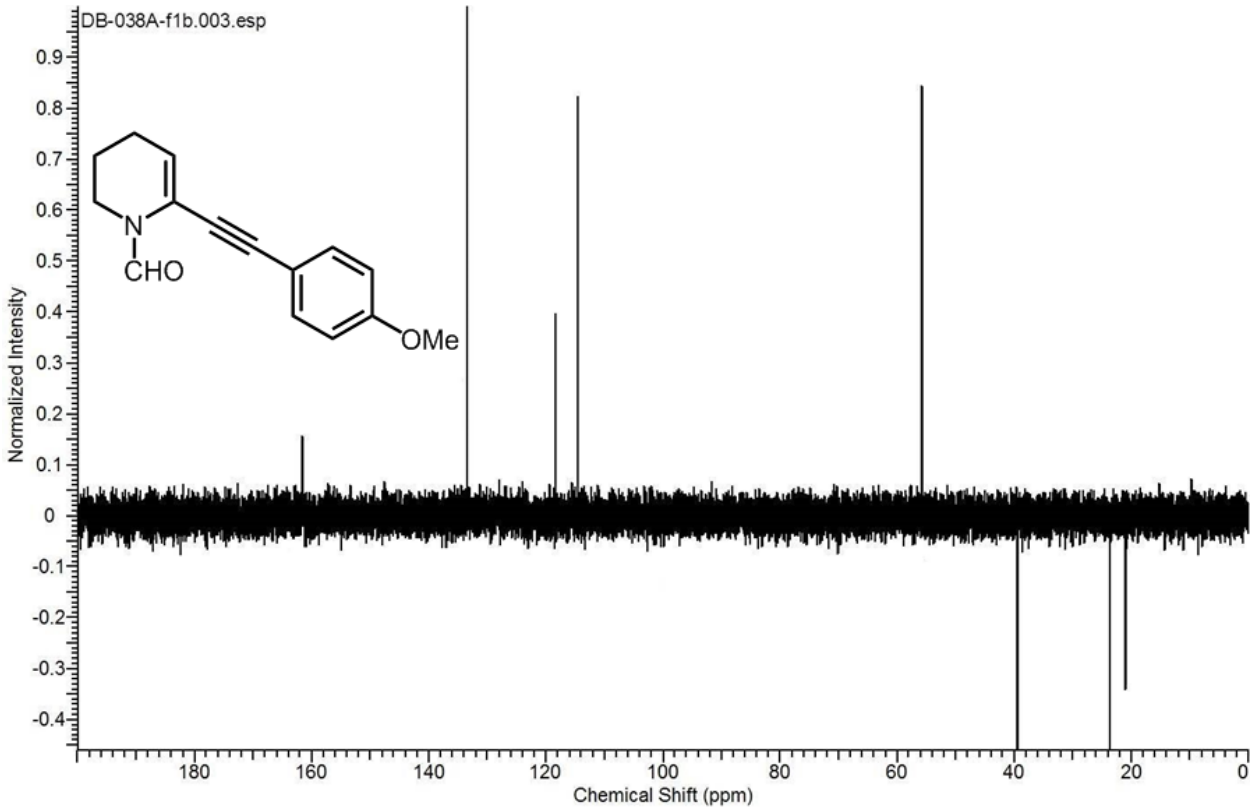
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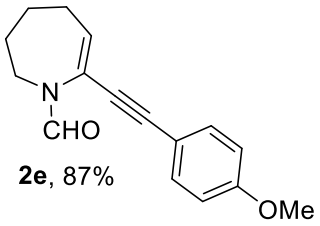
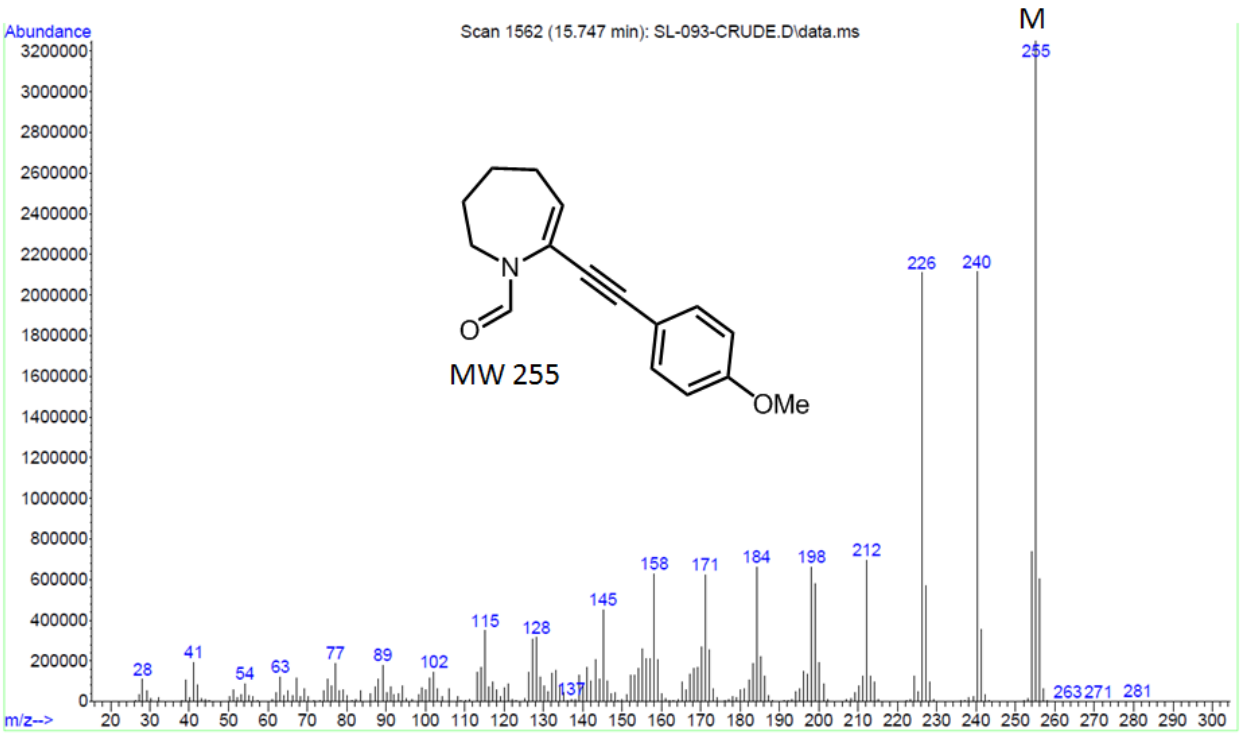
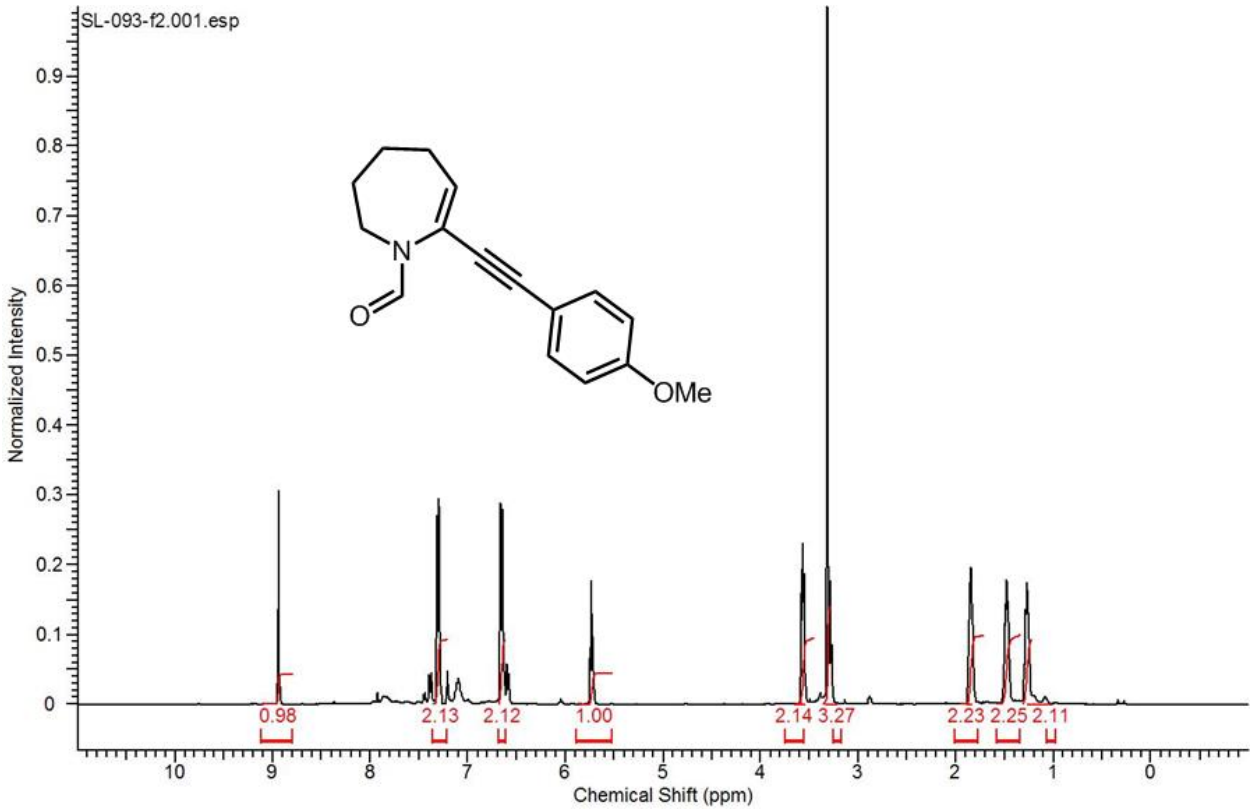


2e, 87%

Prepared from **3b** (1.0 mmol) and *p*-methoxyphenylacetylene using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (50:50). Yield = 247 mg, 97%. ^{1}H NMR (400 MHz, Benzene-d_6, rotamers) δ 8.94 to 8.37 (1H, s), 7.46 to 7.00 (2H, m), 6.67 to 6.58 (2H, m), 6.06 to 5.72 (1H, t), 3.58 to 3.55 (3H, s), 1.87 to 1.83 (2H, m), 1.51 to 1.38 (2H, m), 1.30 to 1.07 (2H, m). ^{13}C NMR (101 MHz, Benzene-d6) δ 161.4, 160.2, 135.4, 128.8, 125.9, 114.4, 89.9, 85.3, 54.6, 43.9, 28.0, 27.4, 24.1. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{16}H_{17}NO_2$ 255.1259; found 255.1263.

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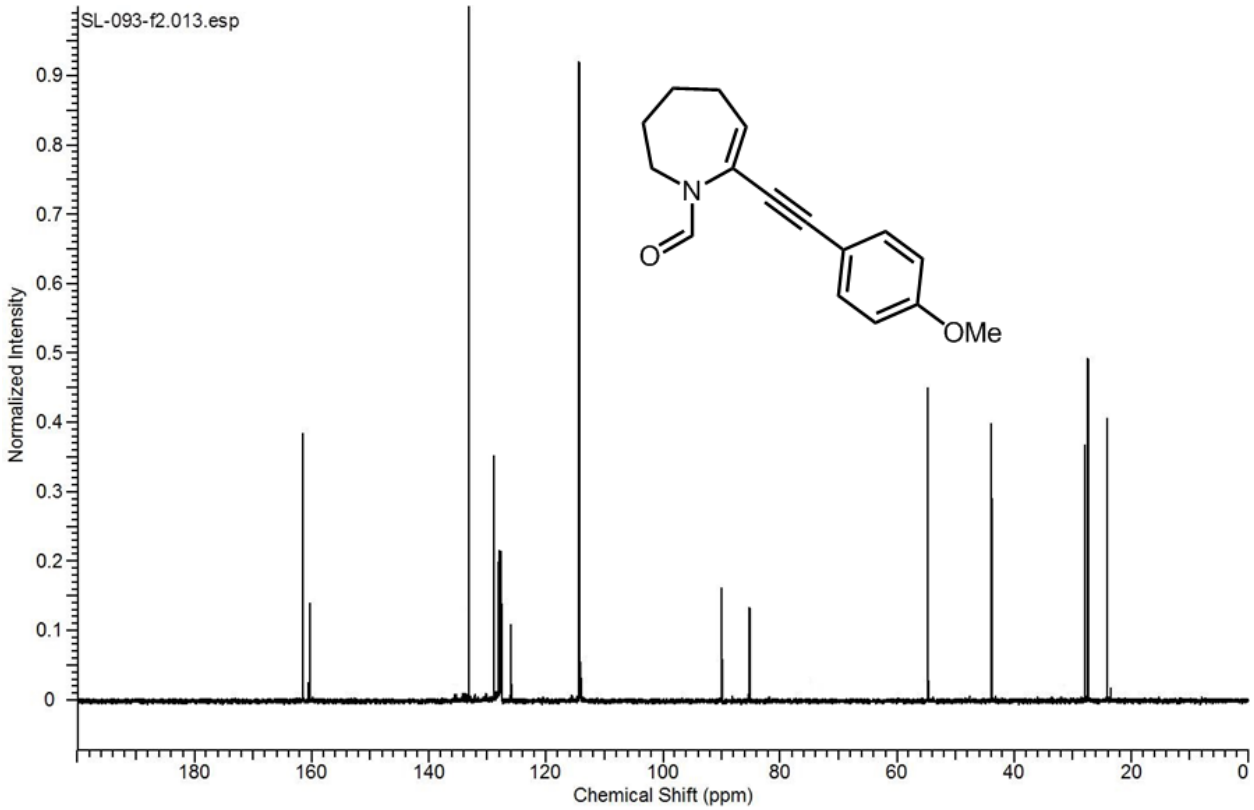
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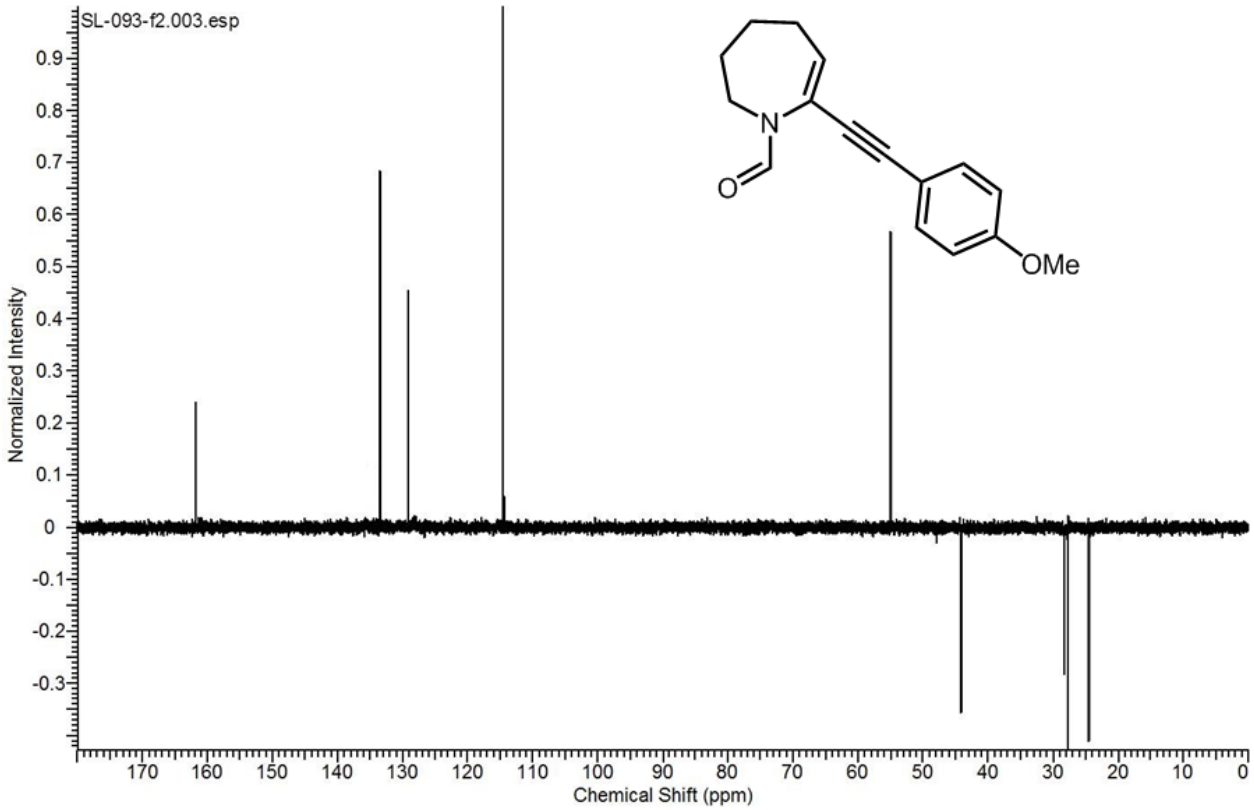
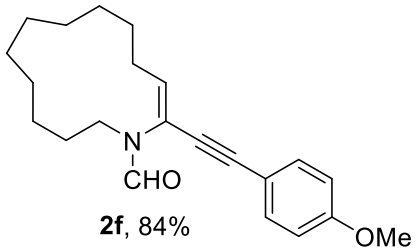
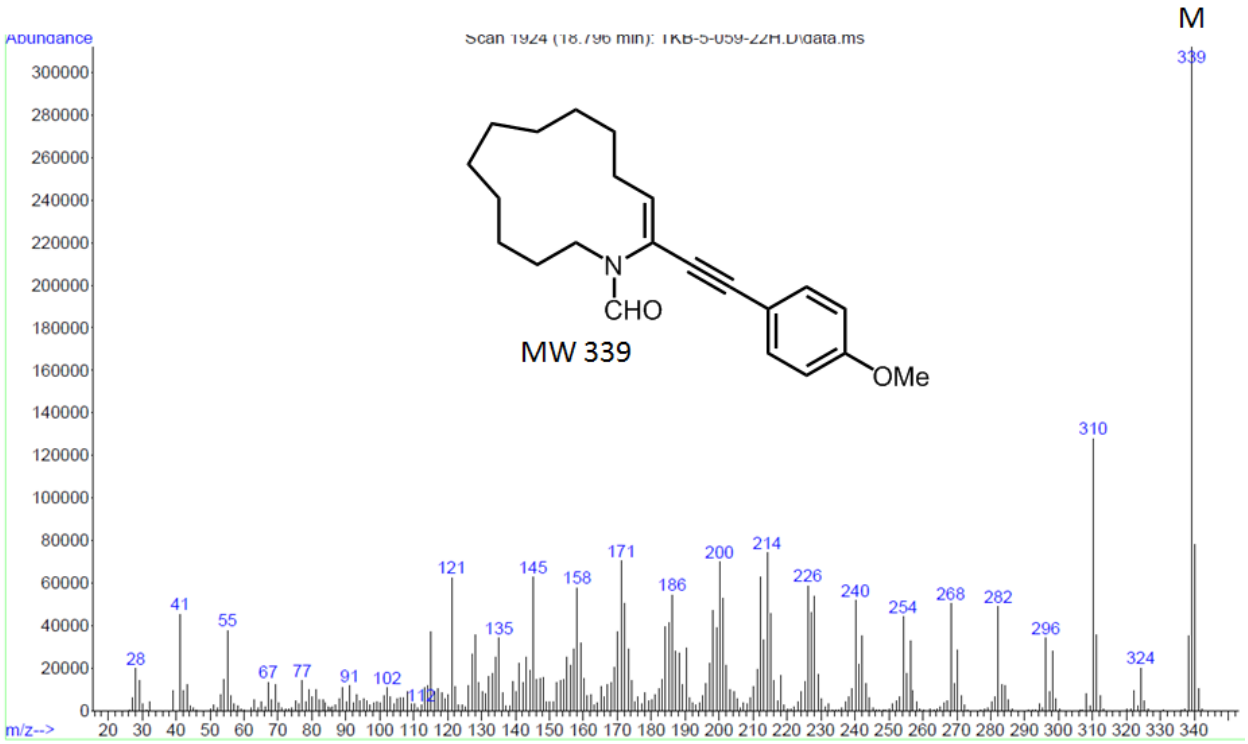




2f, 84%

Prepared from **3c** (1.0 mmol) and *p*-methoxyphenylacetylene using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (50:50). Yield = 285 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$, mixture of rotamers) δ 8.31 & 8.13 (1H, s,s), 7.48 to 7.26 (2H, dd), 6.97 to 6.82 (2H, dd), 5.89 to 5.73 (1H, t), 3.86 to 3.66 (5H, m), 2.30 to 2.14 (2H, m), 1.73 to1.22 (16H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 162.1, 160.9, 160.2, 160.1, 159.9, 139.7, 134.9, 134.8, 134.0, 133.2, 133.1, 133.1, 133.0, 132.9, 123.3, 123.3, 119.6, 114.2, 114.2, 114.1, 114.1, 114.0, 113.9, 113.8, 113.2, 95.3, 88.9, 87.9, 83.9, 81.3, 81.2, 77.5, 77.1, 76.8, 73.0, 60.4, 55.4, 55.3, 47.7, 42.7, 41.2, 29.2, 28.5, 28.5, 28.4, 28.3, 28.2, 28.1, 27.9, 27.6, 26.8, 26.8, 26.7, 26.5, 26.2, 26.0, 25.7, 25.6, 25.5, 25.2, 24.9, 24.8, 24.4, 23.7, 23.6, 23.5, 23.3, 21.1. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{22}H_{29}NO_2$ 339.2198; found 339.2193.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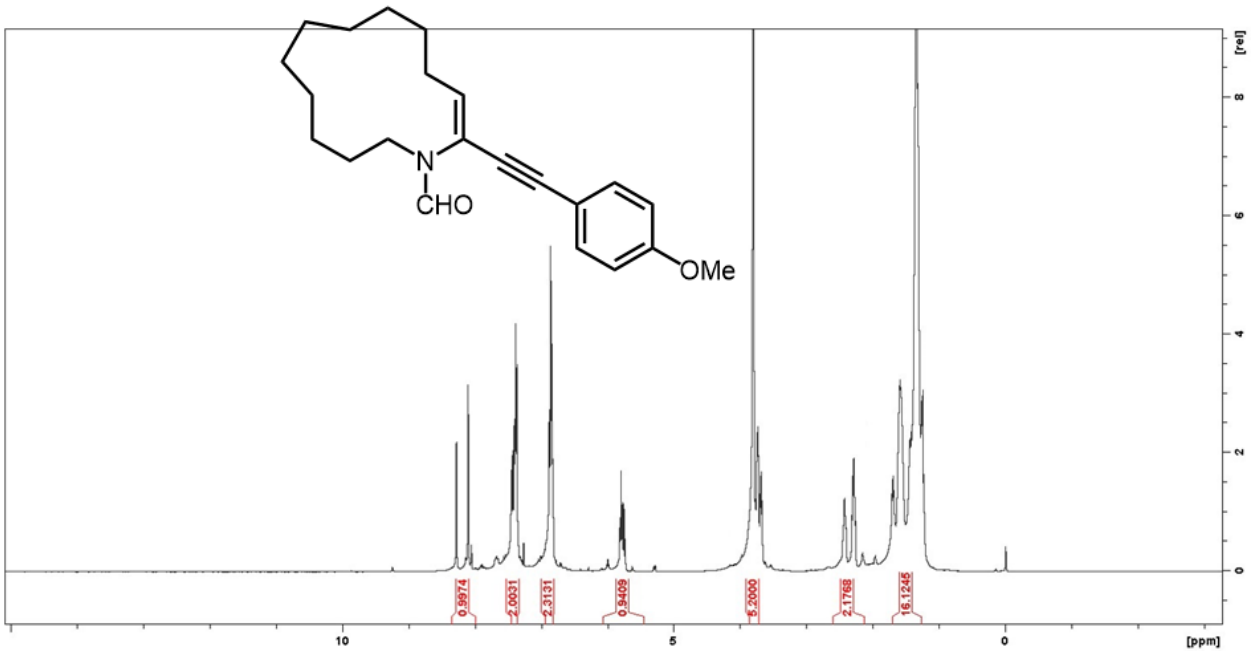
OMe
m/z-->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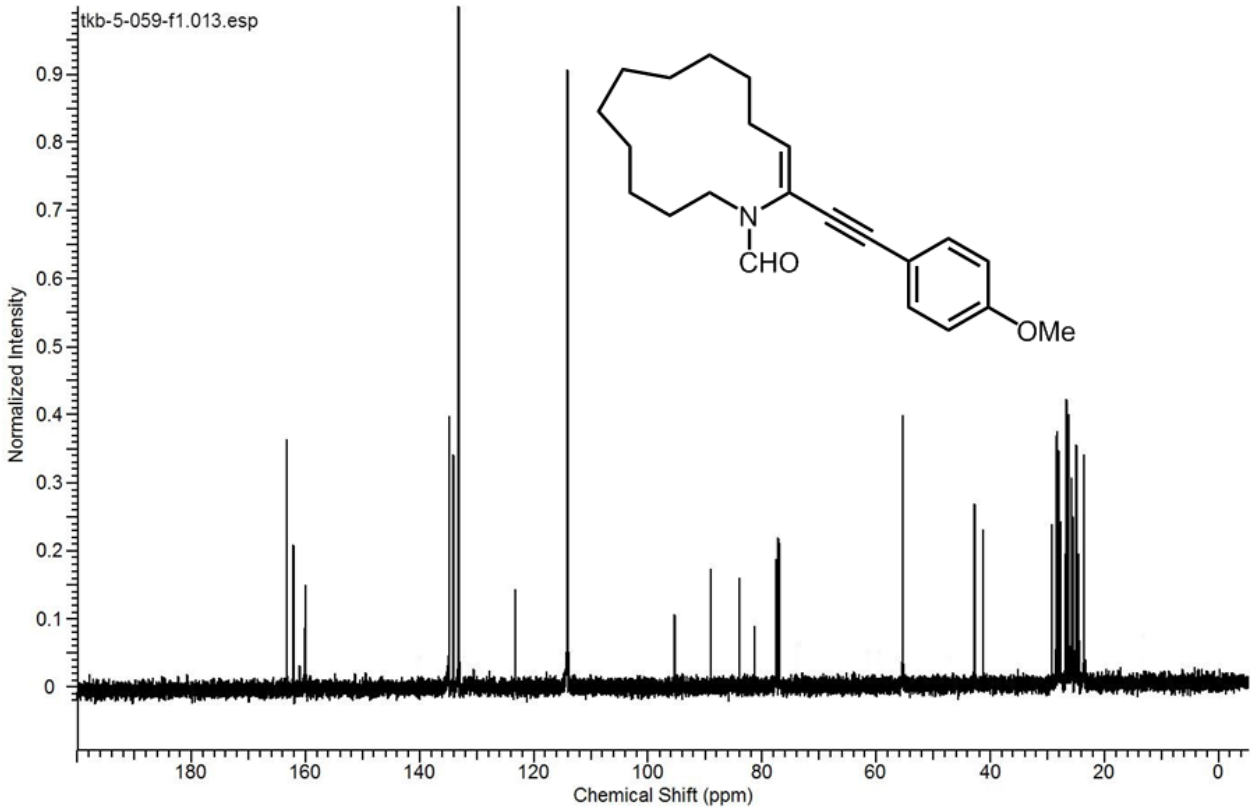
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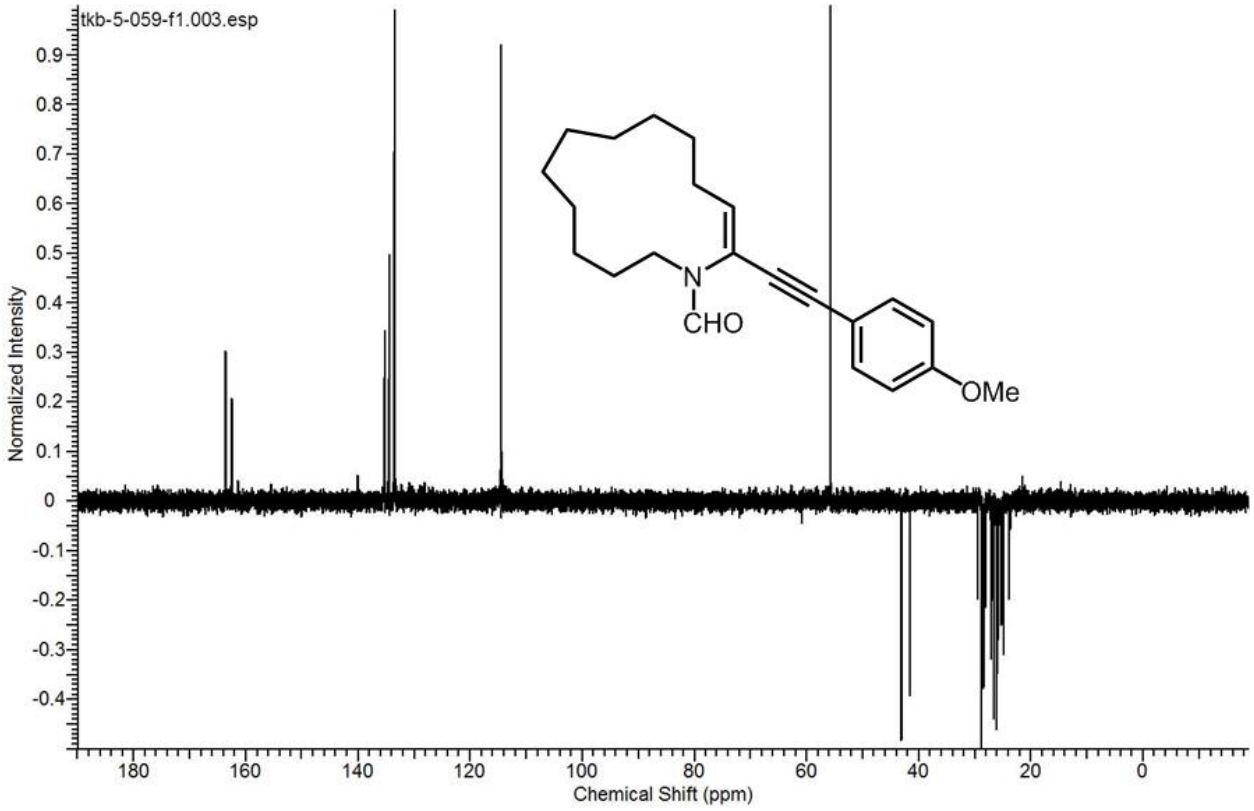
OMe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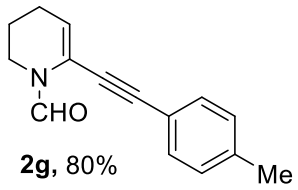
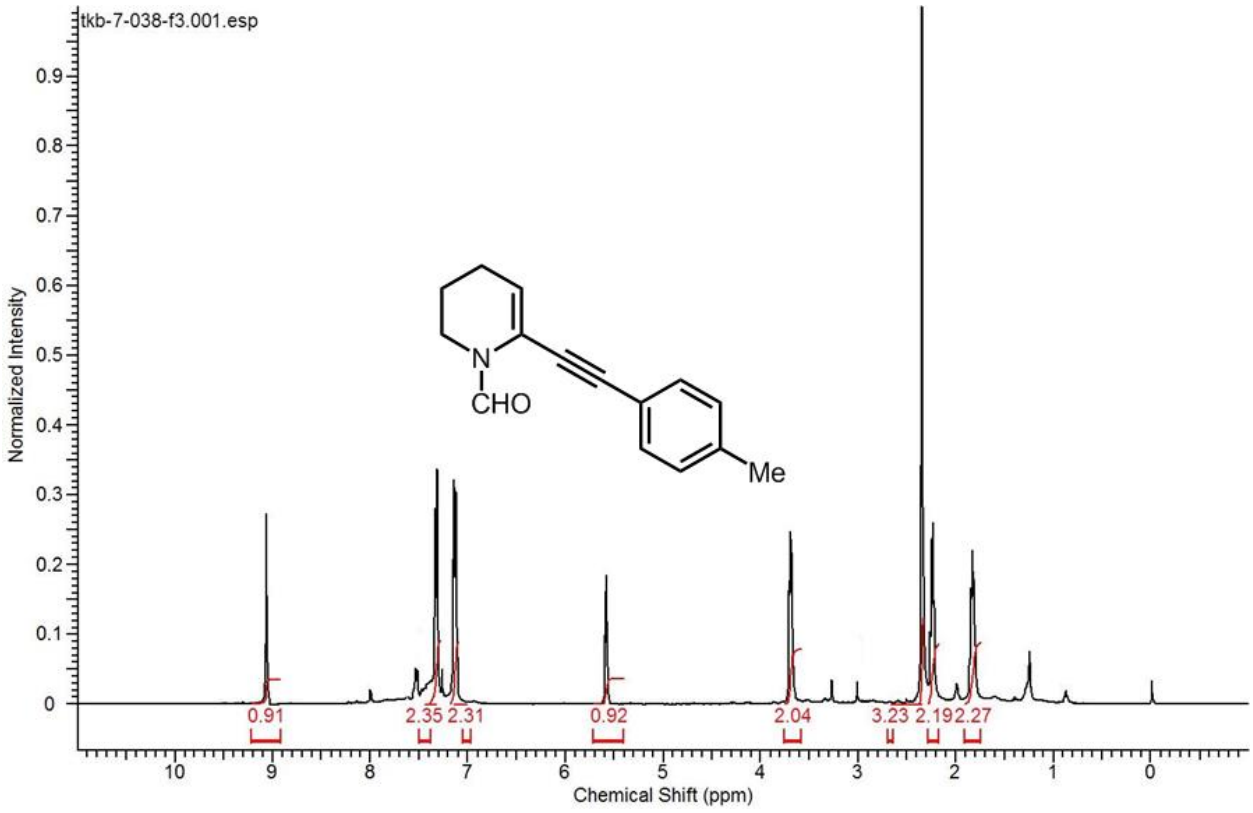
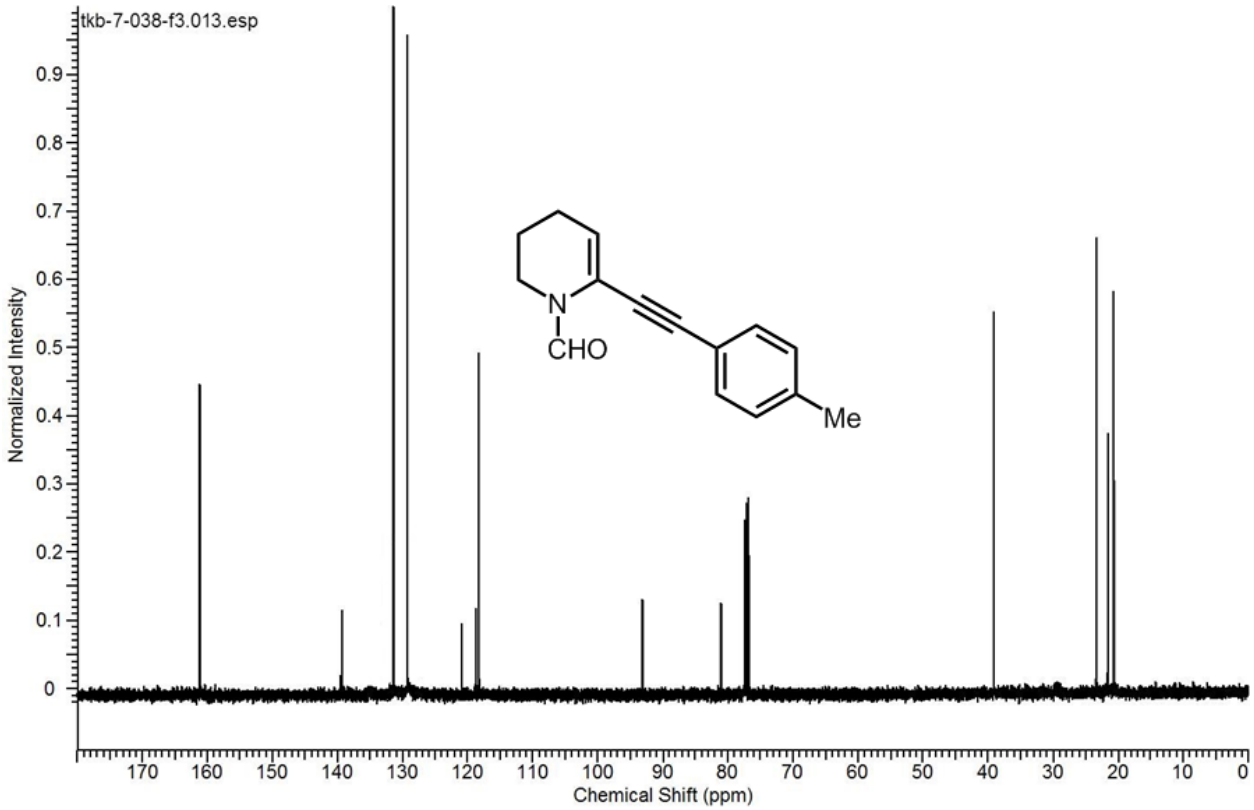
CHO
OMe



2g, 80%

Prepared from **3a** (1.0 mmol) and *p*-methylphenylacetylene using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (50:50). Yield = 203 mg, 80%. ^{1}H NMR (400 MHz, Chloroform-d) δ 9.06 (1H, s), 7.32 (2H, d), 7.26 (2H, d), 5.59 to 5.57 (1H, t), 3.71 to 3.52 (2H, t), 2.34 to 2.18 (5H, m), 1.81 to 1.76 (2H, m). ^{13}C NMR (101 MHz, Chloroform-d) δ 161.2, 139.6, 133.1, 132.2, 128.6, 120.9, 118.8, 93.1, 81.1, 39.1, 23.4, 21.6, 20.7. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{15}H_{15}NO$ 225.1154; found 225.1159.

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Normalized Intensity
Chemical Shift (ppm)
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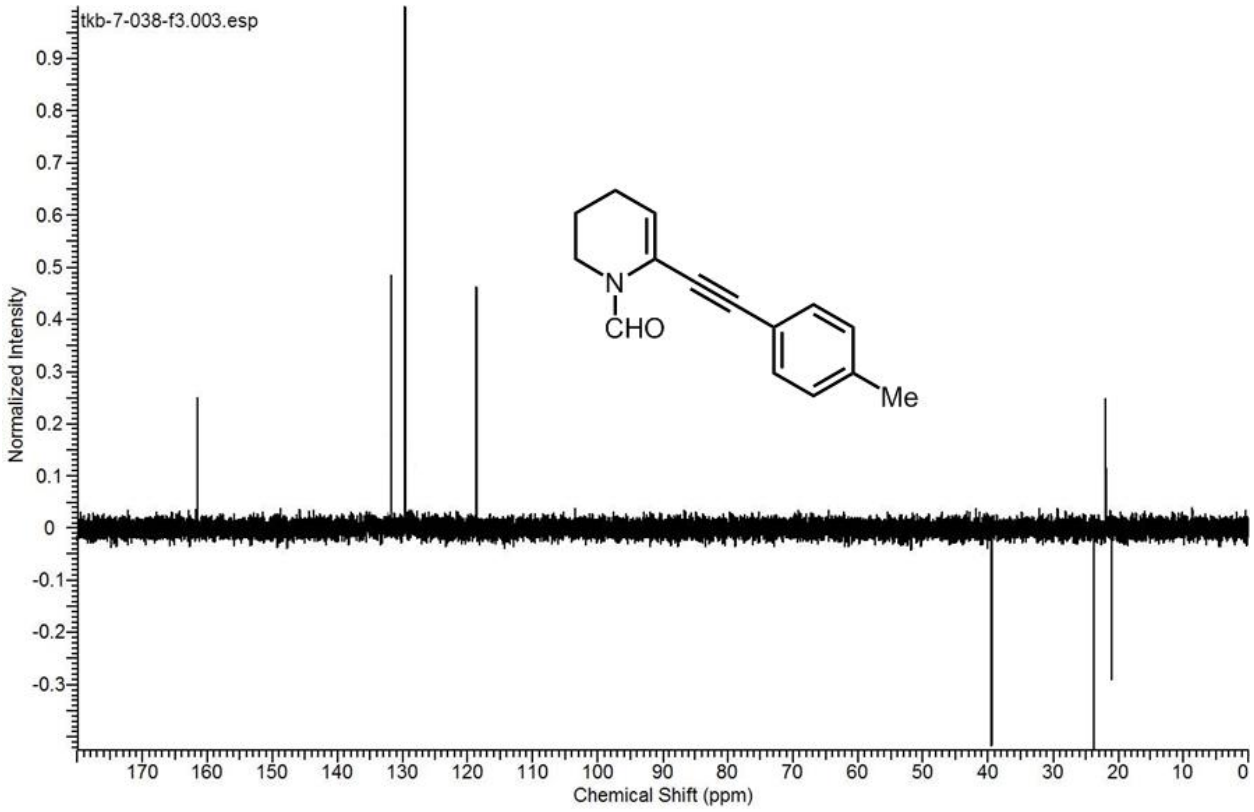
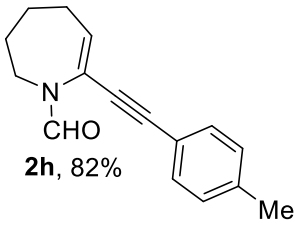
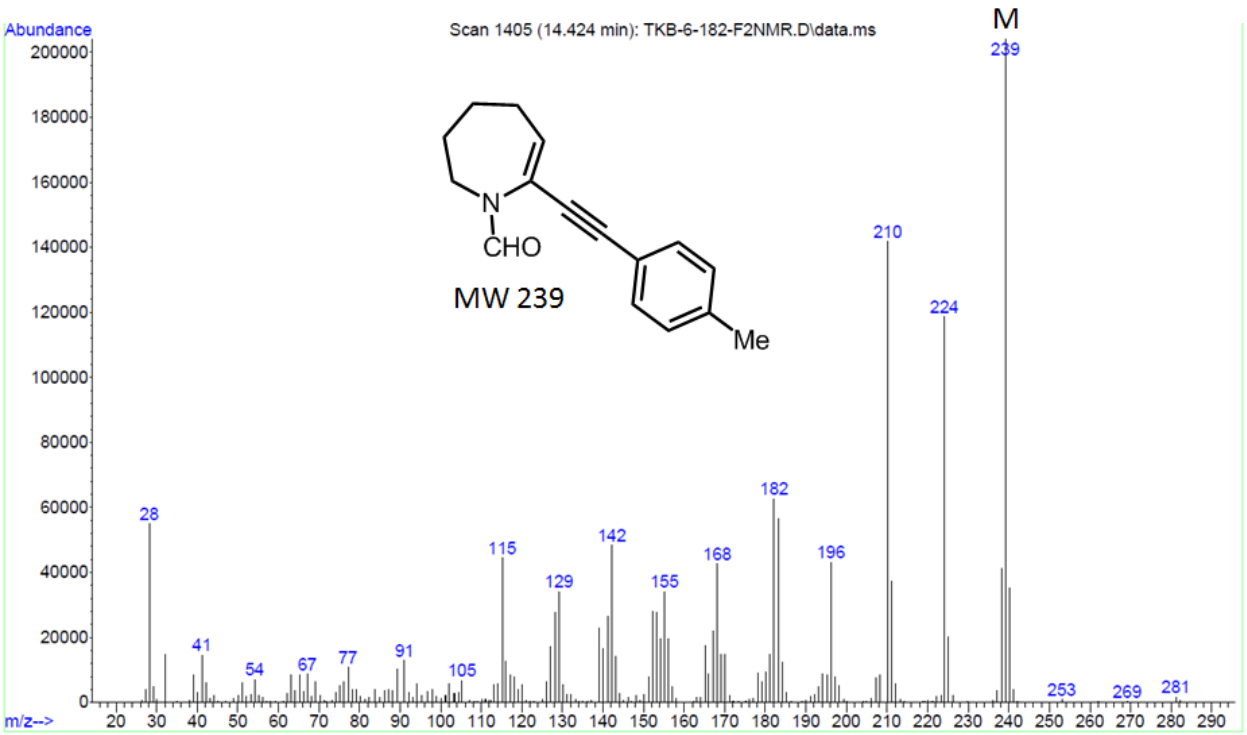
CHO
Me

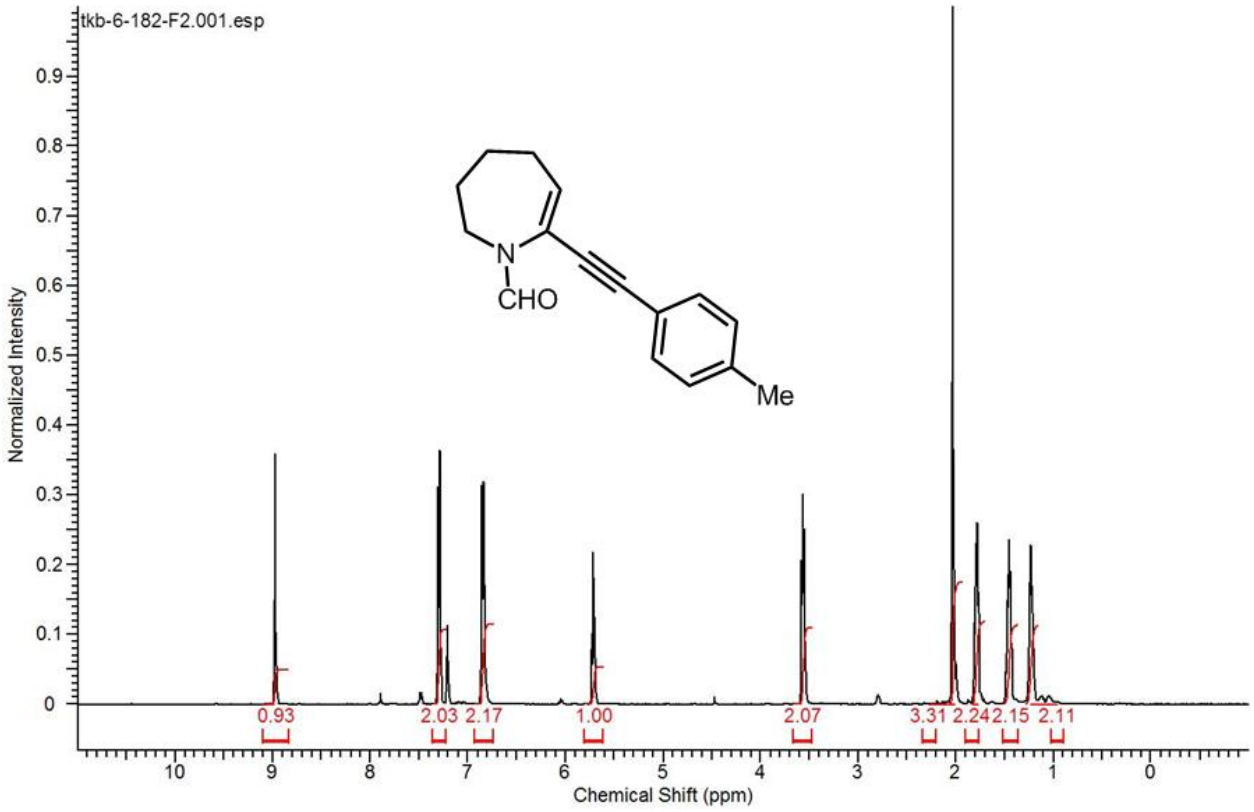

tkb-7-038-f3.003.esp
Normalized Intensity
Chemical Shift (ppm)
N
CHO
Me



2h, 82%

Prepared from **3b** (1.0 mmol) and *p*-methylphenylacetylene using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (50:50). Yield = 220 mg, 82%. ^1H NMR (400 MHz, Benzene-d6) δ 8.98 (1H, s), 7.89 to 7.21 (2H, d) 6.86 to 6.04 (2H, d), 5.73 to 5.70 (1H, s), 3.58 to 3.55 (2H, t), 2.03 to 1.99 (3H, s), 1.81 to 1.62 (2H, m), 1.49 to 1.37 (2H, t), 1.26 to 1.03 (2H, t). 13C NMR (101 MHz, Benzene-d6) δ 161.4, 138.8, 133.9, 129.3, 126.9, 119.5, 90.0, 86.0, 43.8, 27.9, 27.4, 24.1, 21.1. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{16}H_{17}NO$ 239.1310; found 239.1314.




tkb-6-182-F2.001.esp
Normalized Intensity
Chemical Shift (ppm)
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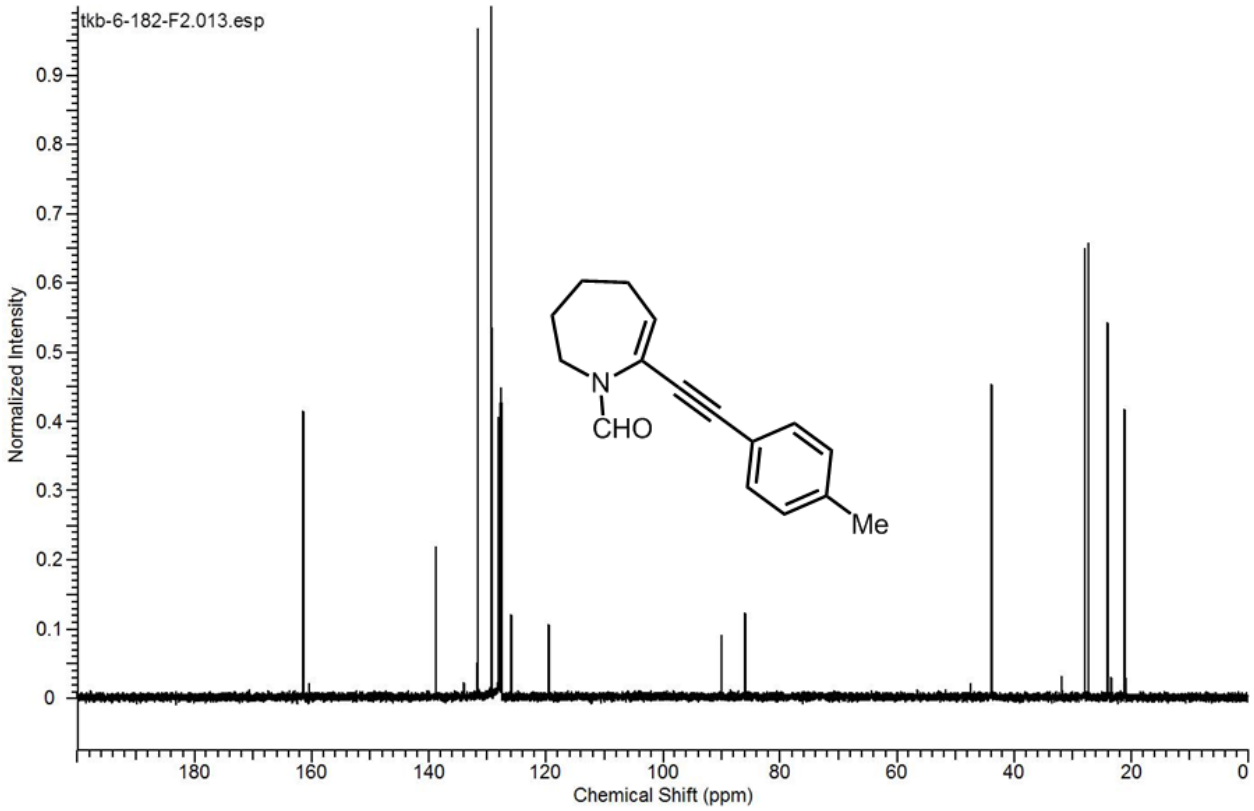
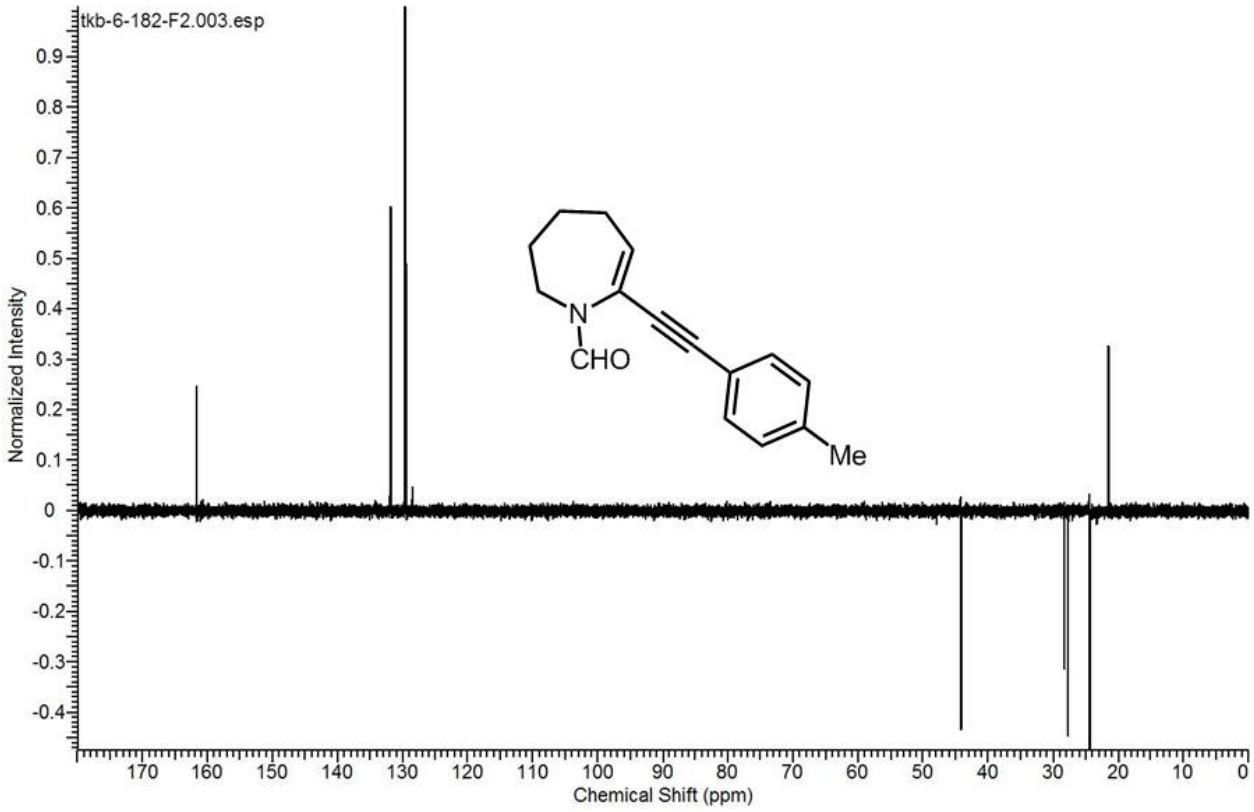
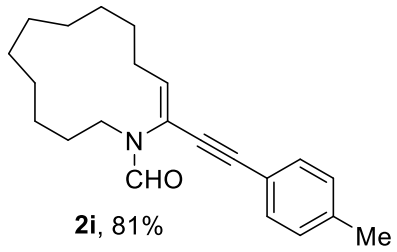
2.17
1.00
2.07
3.31
2.24
2.15
2.11
N
CHO
Me


tkb-6-182-F2.013.esp
Normalized Intensity
Chemical Shift (ppm)
N
CHO
Me

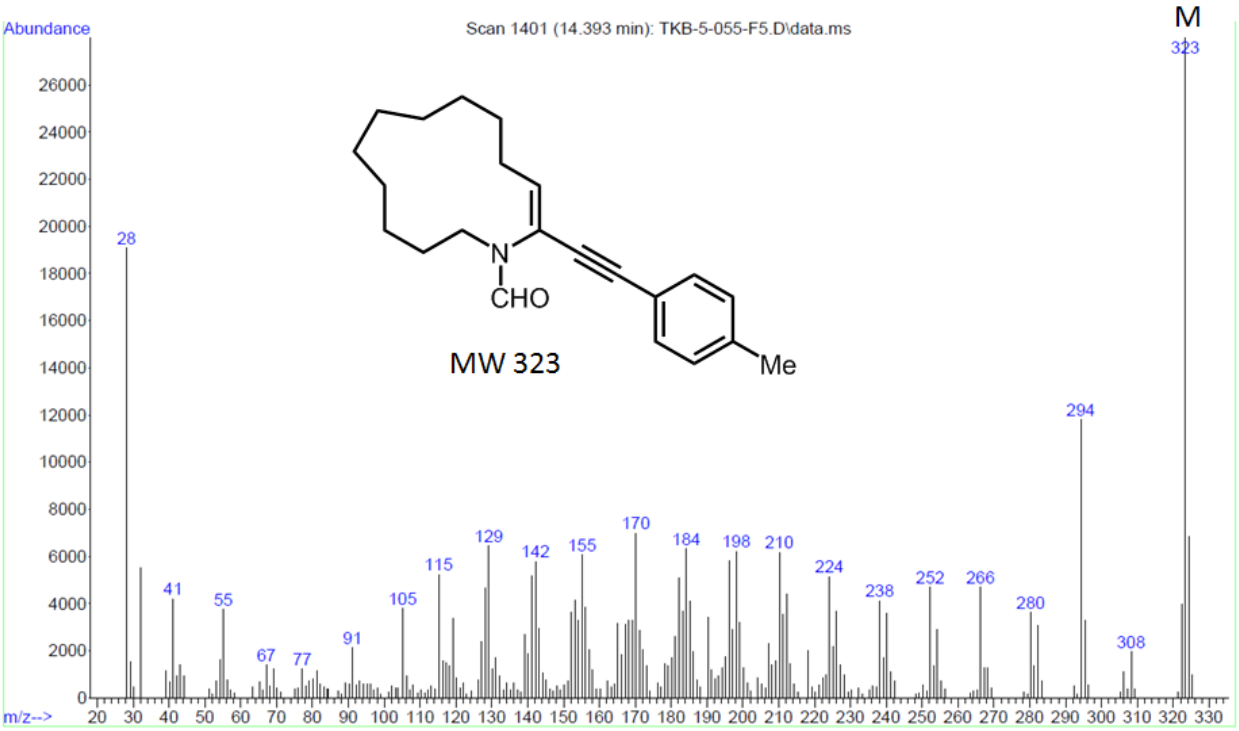


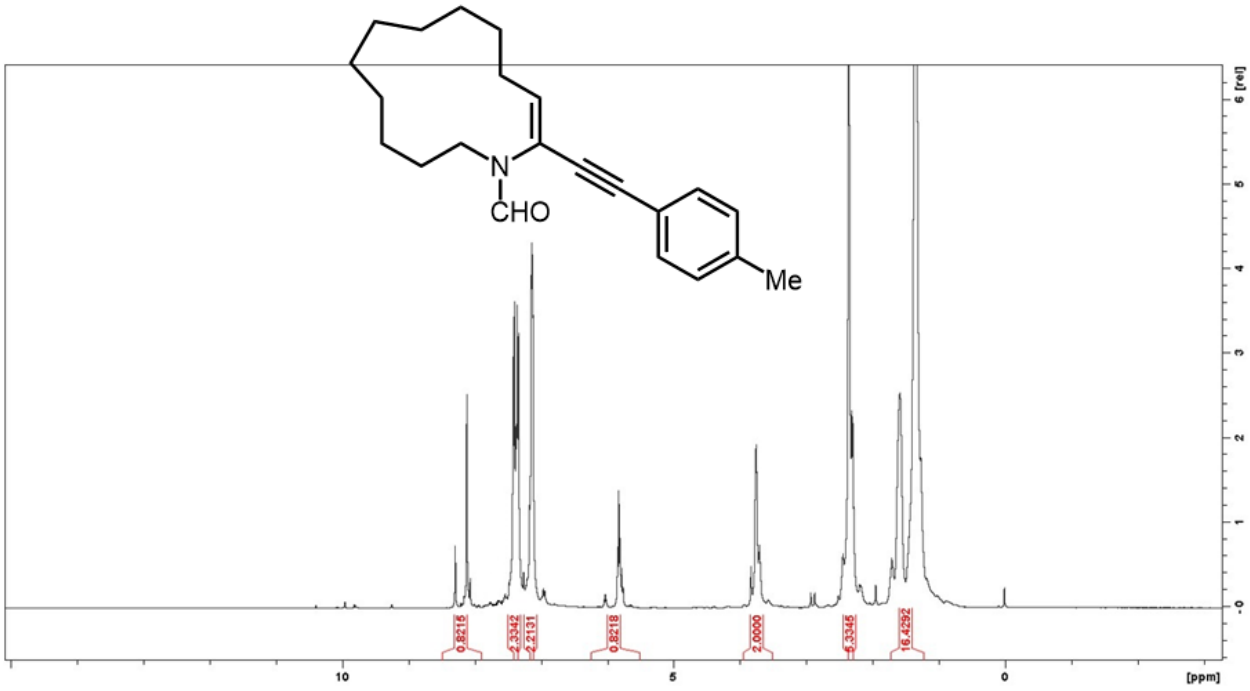


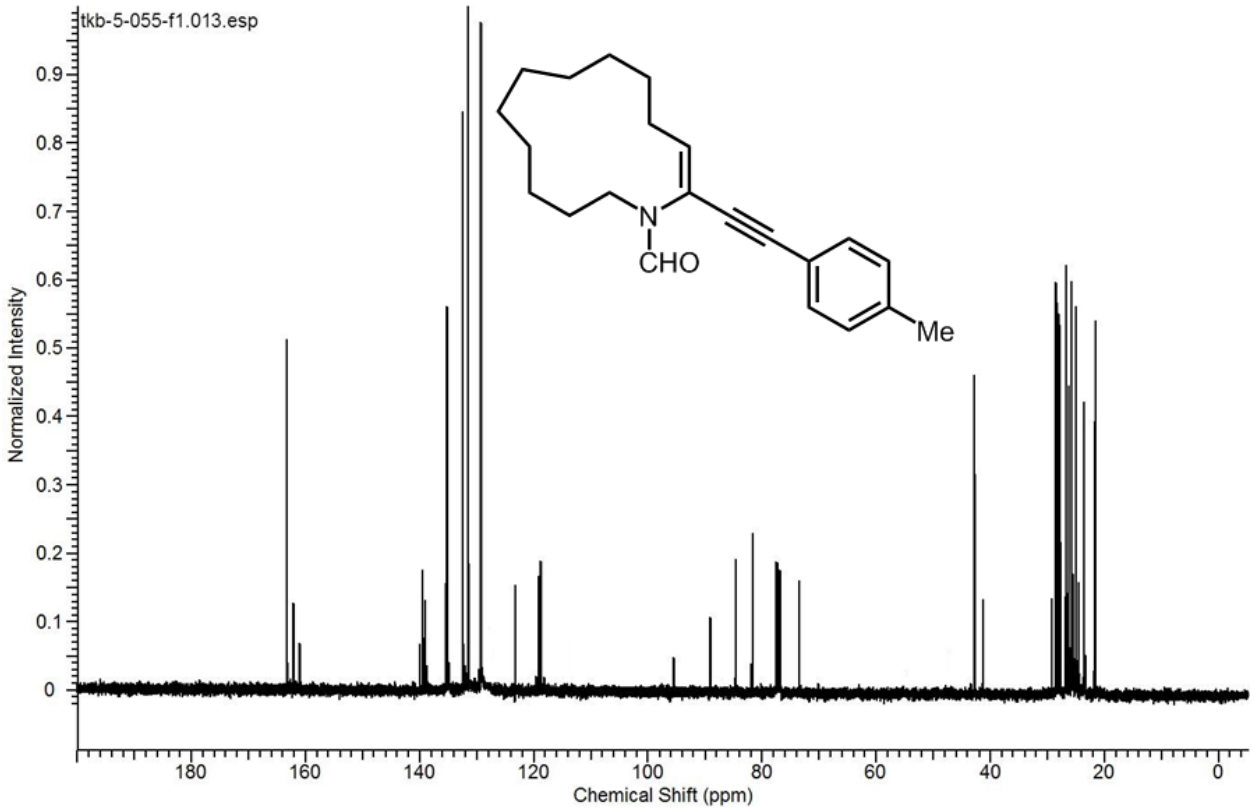
2i, 81%

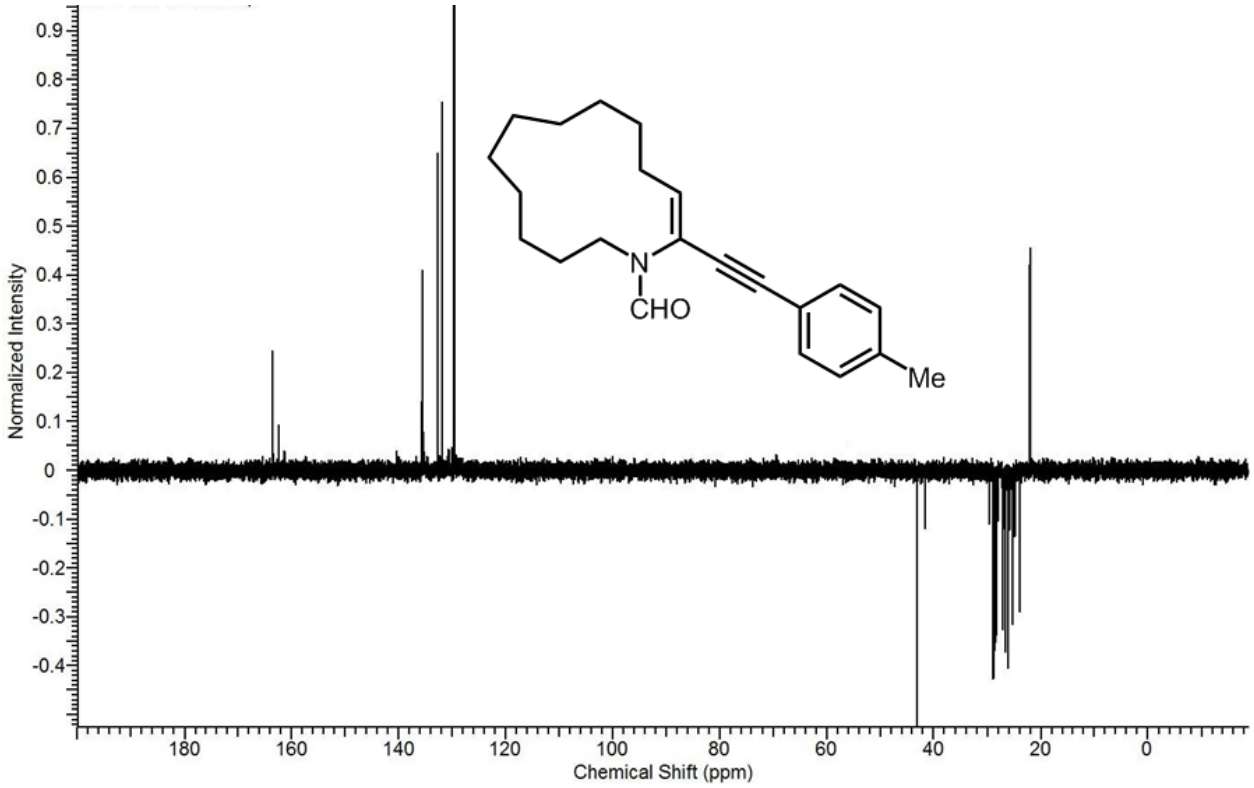
Prepared from **3c** (1.0 mmol) and *p*-methylphenylacetylene using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (50:50). Yield = 294 mg, 81%. ^{1}H NMR (400 MHz, $CDCl_3$, mixture of rotamers) δ 8.29 & 8.05, 7.74 to 7.26 (4H, m), 5.84 to 5.76 (1H, m), 3.84 to 3.66 (2H, m), 2.47 to 2.15 (5H, m), 1.73 to 1.17 (16H, m). ^{13}C NMR (101 MHz, $CDCl_3$, mixture of rotamers) δ 163.2, 162.6, 162.1, 160.9, 140.0, 139.5, 139.3, 139.0, 138.7, 135.3, 135.2, 135.2, 134.9, 134.9, 132.4, 132.2, 132.1, 131.9, 131.8, 131.5, 131.5, 131.5, 130.5, 130.3, 129.6, 129.3, 129.3, 129.2, 129.1, 128.9, 128.6, 128.5, 128.2, 128.2, 128.0, 127.7, 127.7, 127.6, 123.2, 119.1, 119.1, 118.8, 114.2, 95.4, 89.1, 88.2, 84.7, 84.6, 81.9, 81.6, 77.5, 77.2, 76.8, 73.5, 55.3, 47.8, 43.3, 42.8, 41.2, 29.8, 29.2, 28.6, 28.5,

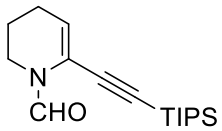
28.5, 28.4, 28.3, 28.1, 27.9, 27.7, 26.9, 26.8, 26.7, 26.5, 26.2, 26.0, 25.8, 25.6, 25.5, 25.2, 24.9, 24.8, 24.6, 24.4, 23.7, 23.6, 23.5, 23.3, 21.7, 21.6, 21.6, 21.6. **HRMS-EI**$^{+}$ (*m/z*): calc'd for $C_{22}H_{29}NO$ 323.2249; found 323.2252.





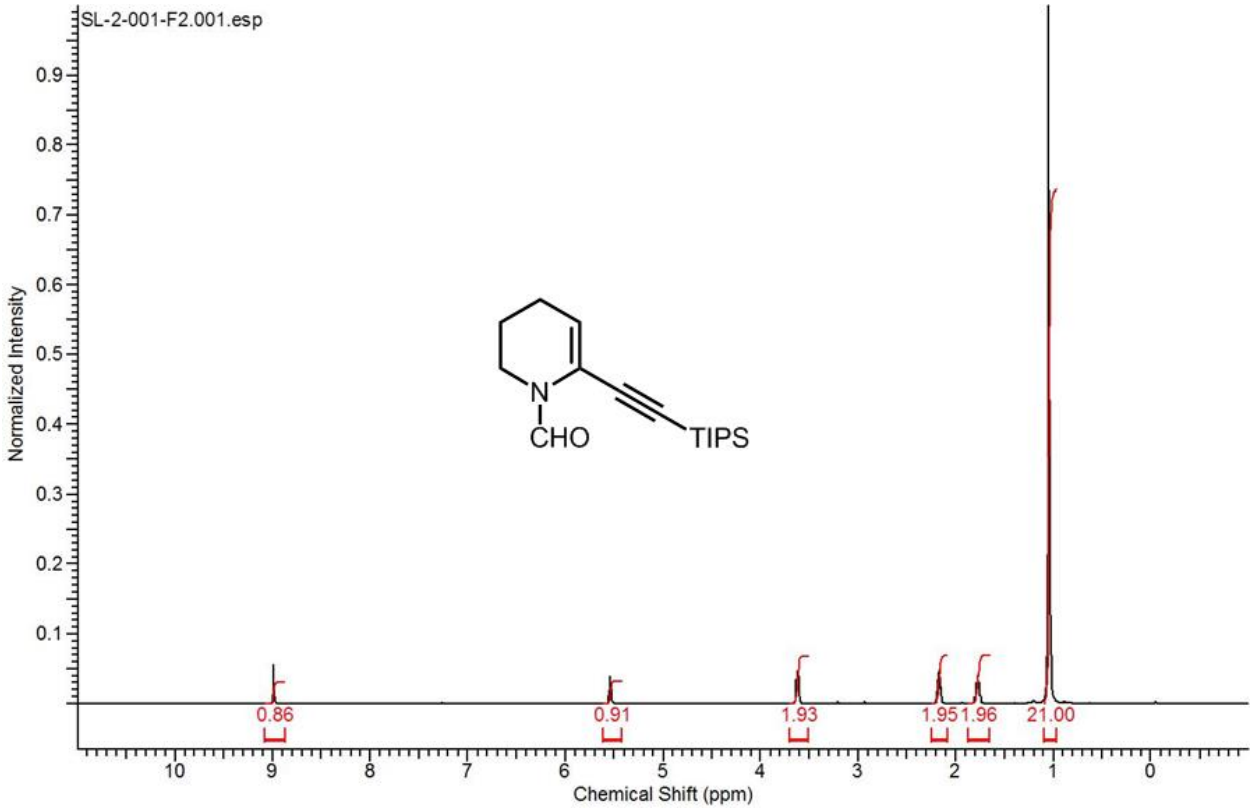

tkb-5-055-f1.013.esp
Normalized Intensity
Chemical Shift (ppm)
N
CHO
Me

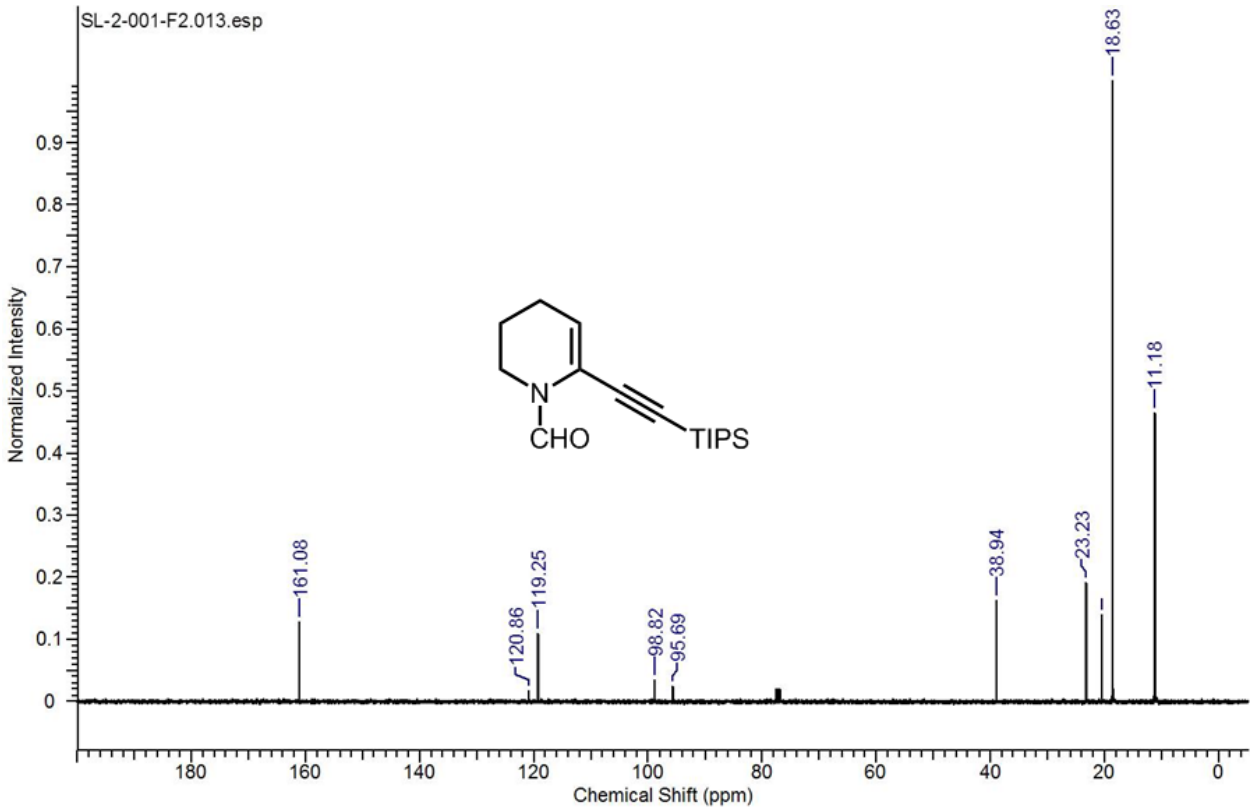

Normalized Intensity
Chemical Shift (ppm)
N
CHO
Me



2j, 82%

Prepared from **3a** (1.00 mmol) and triisopropylsilylacetylene using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (90:10). Yield = 239 mg, 82%. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.99 (s, 1H), 5.54 (t, *J* = 4.4 Hz, 1H), 3.66 – 3.58 (m, 2H), 2.17 (td, *J* = 6.3, 4.1 Hz, 2H), 1.78 (m, 4H), 1.05 (m, 21H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 120.8, 119.2, 98.8, 95.6, 38.9, 23.2, 20.5, 18.6, 11.4, 11.1, 10.8. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{17}H_{29}NOSi$ 291.2018; found 291.2022.




SL-2-001-F2.013.esp
Normalized Intensity
Chemical Shift (ppm)
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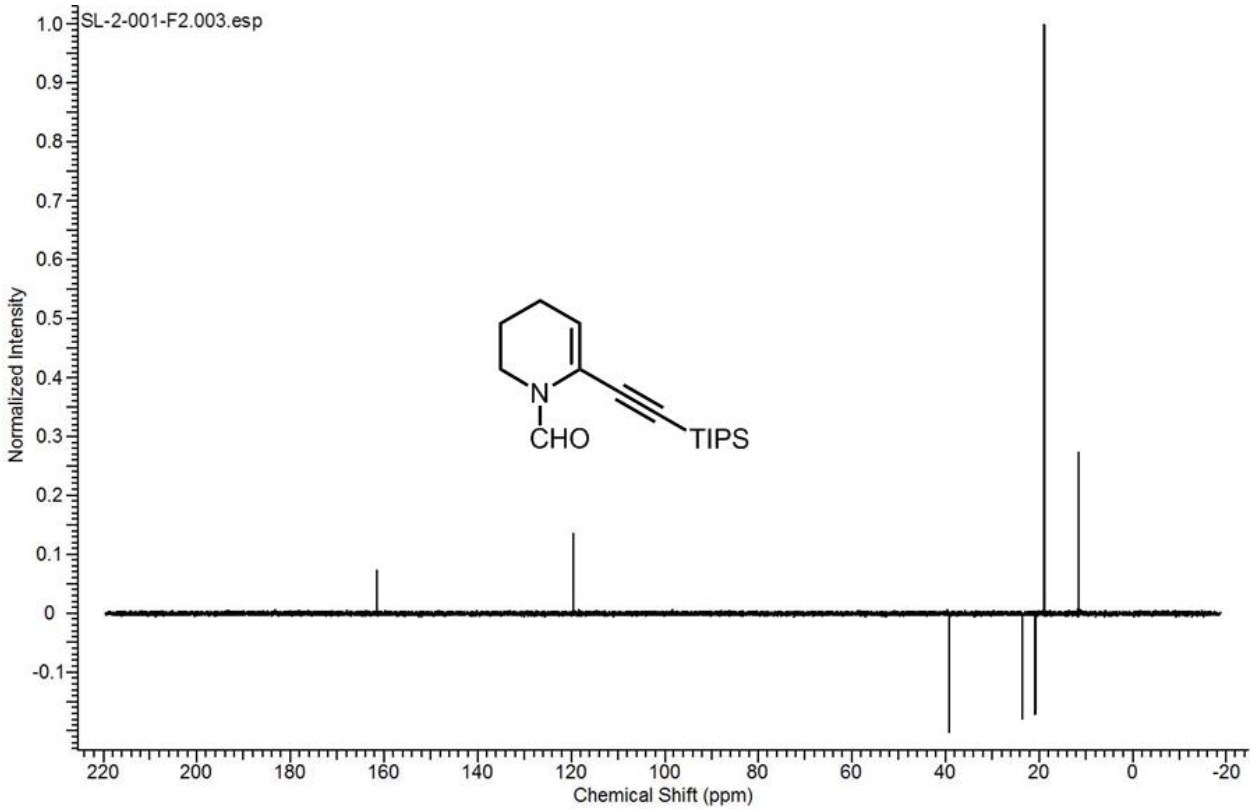
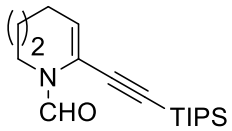
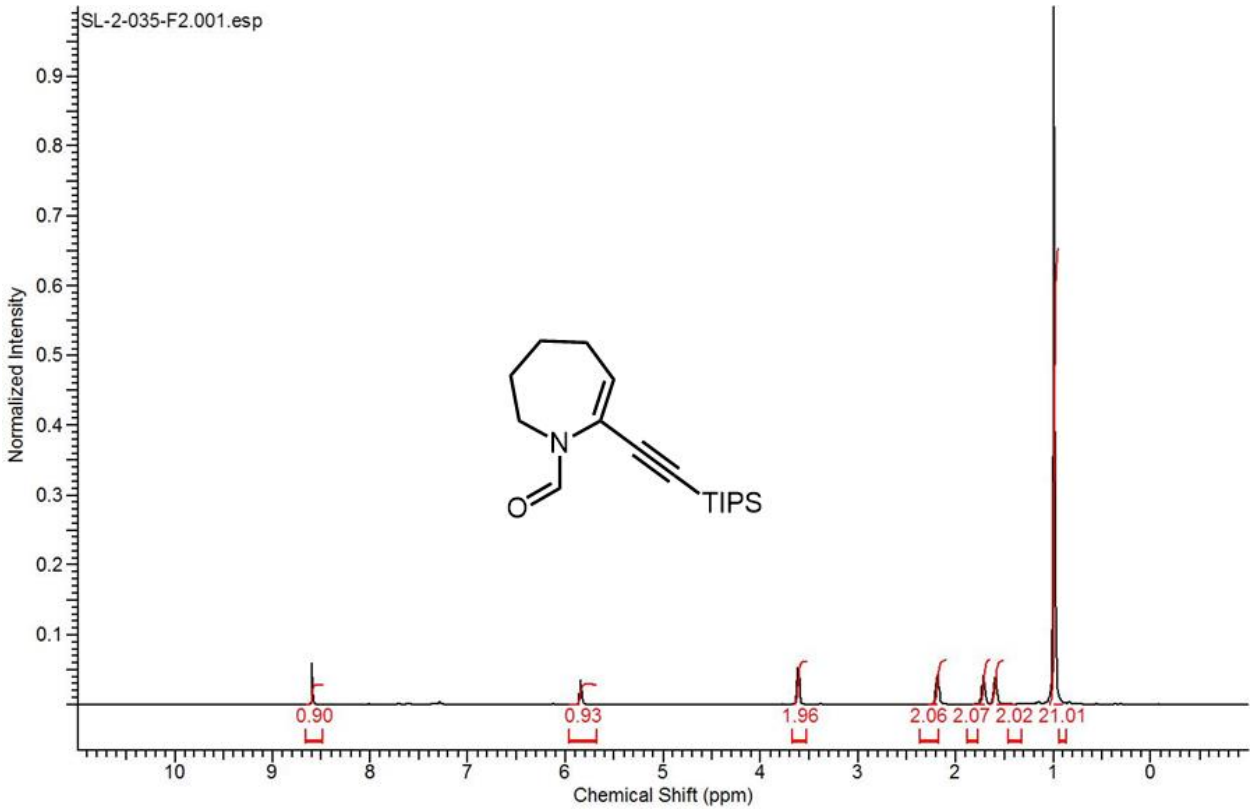
11.18
161.08
120.86
119.25
98.82
95.69
38.94
23.23
N
CHO
TIPS

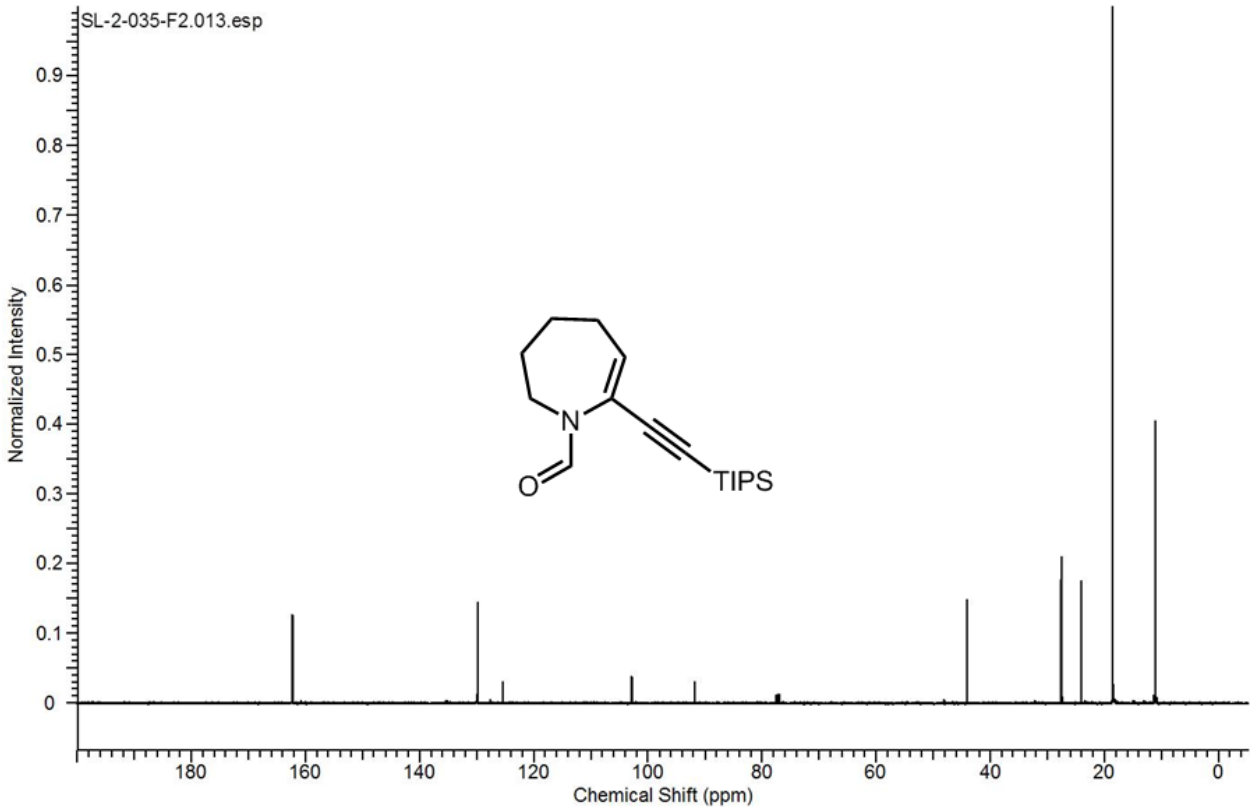

SL-2-001-F2.003.esp
Normalized Intensity
Chemical Shift (ppm)
N
CHO
TIPS

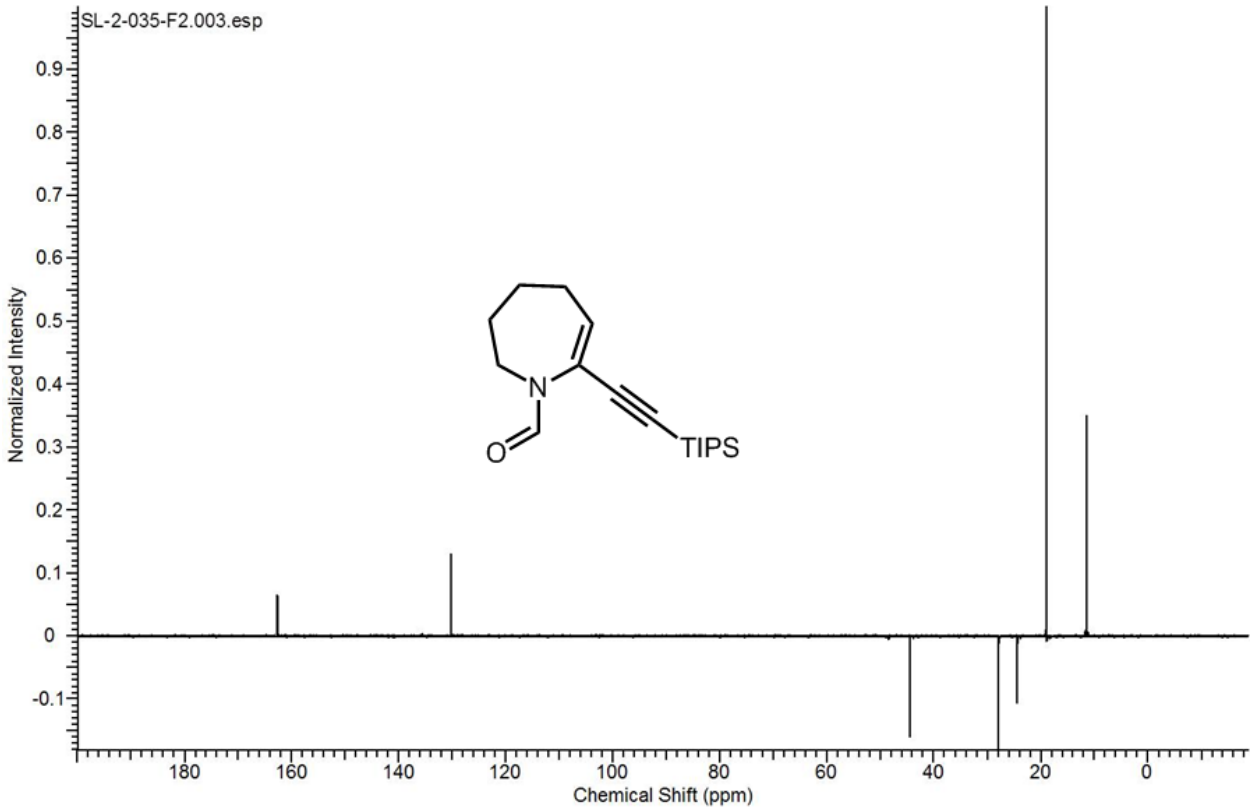


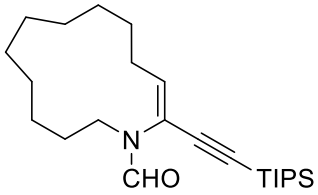
2k, 86%

Prepared from **3b** (1.00 mmol) and triisopropylsilylacetylene using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (90:10). Yield = 262 mg, 86%. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.59 (s, 1H), 5.84 (t, *J* = 6.1 Hz, 1H), 3.62 (t, *J* = 5.9 Hz, 2H), 2.19 (q, *J* = 5.9 Hz, 2H), 1.72 (p, *J* = 6.1 Hz, 2H), 1.58 (q, *J* = 6.1 Hz, 2H), 0.99 (s, 21H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.25, 129.90, 125.42, 102.79, 91.85, 44.10, 27.67, 27.50, 24.08, 18.59, 10.87. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{18}H_{31}NOSi$ 305.5370; found 305.5373.



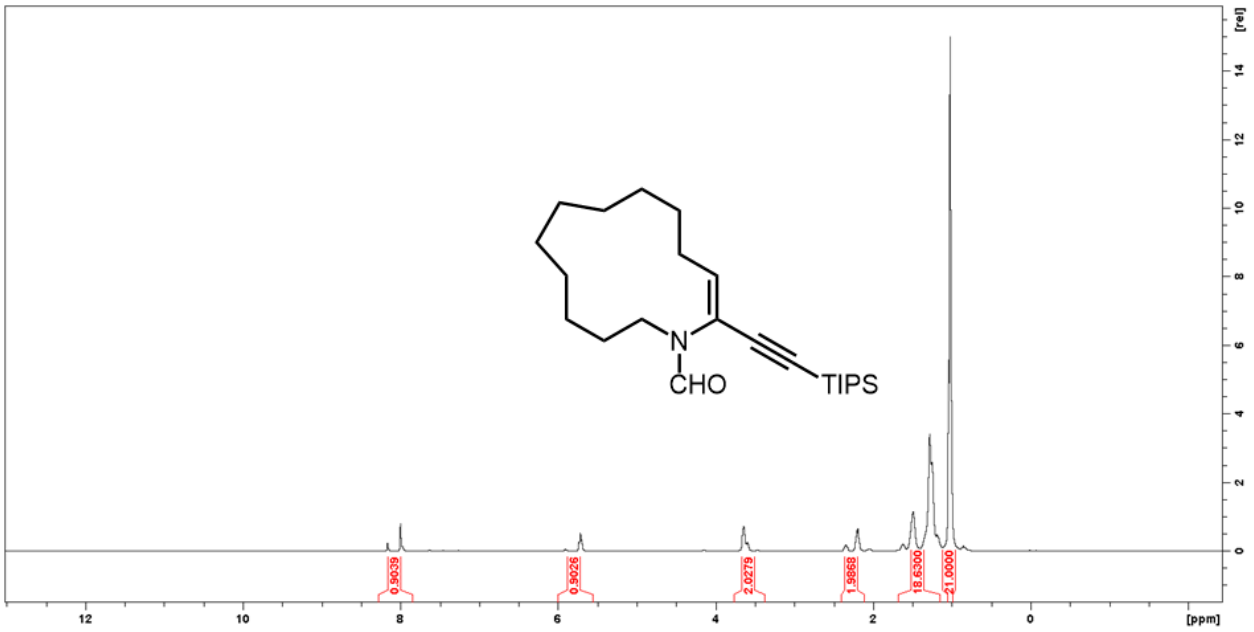

SL-2-035-F2.013.esp
Normalized Intensity
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
N
O
TIPS
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

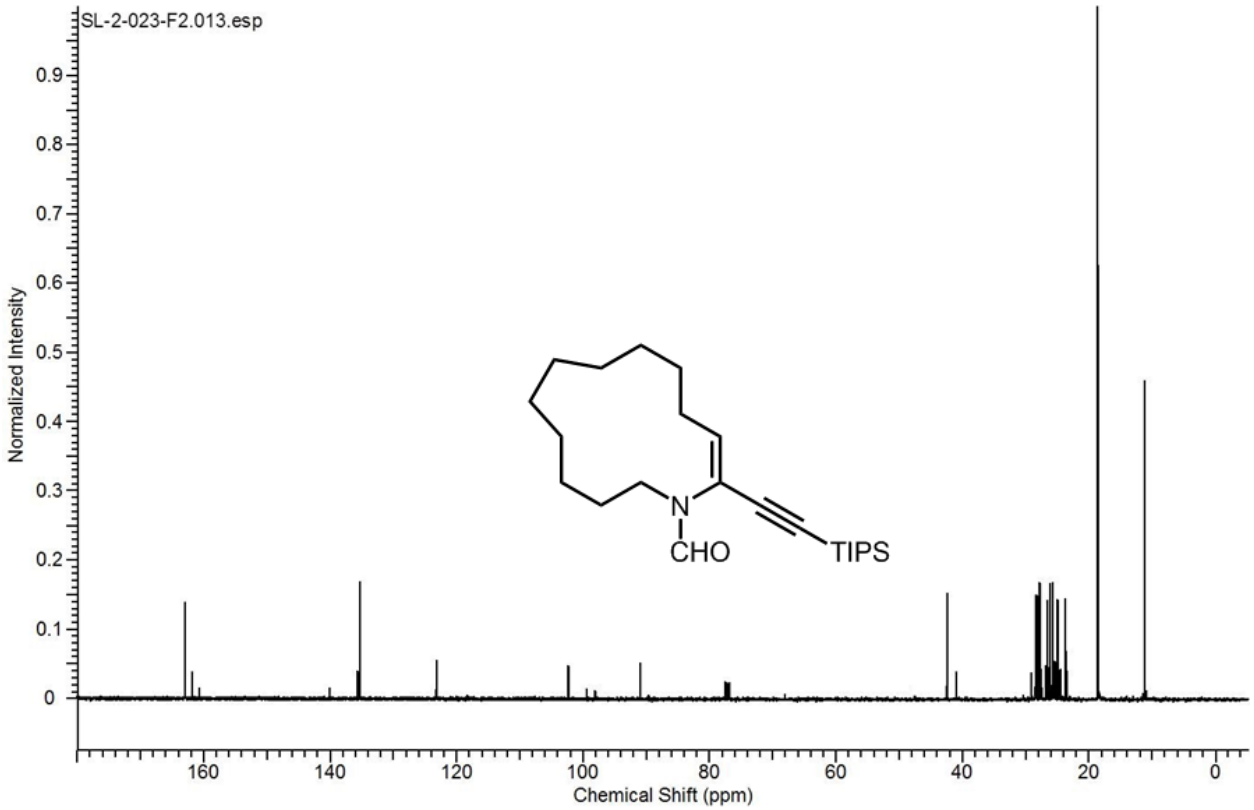

SL-2-035-F2.003.esp
Normalized Intensity
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
N
O
TIPS
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

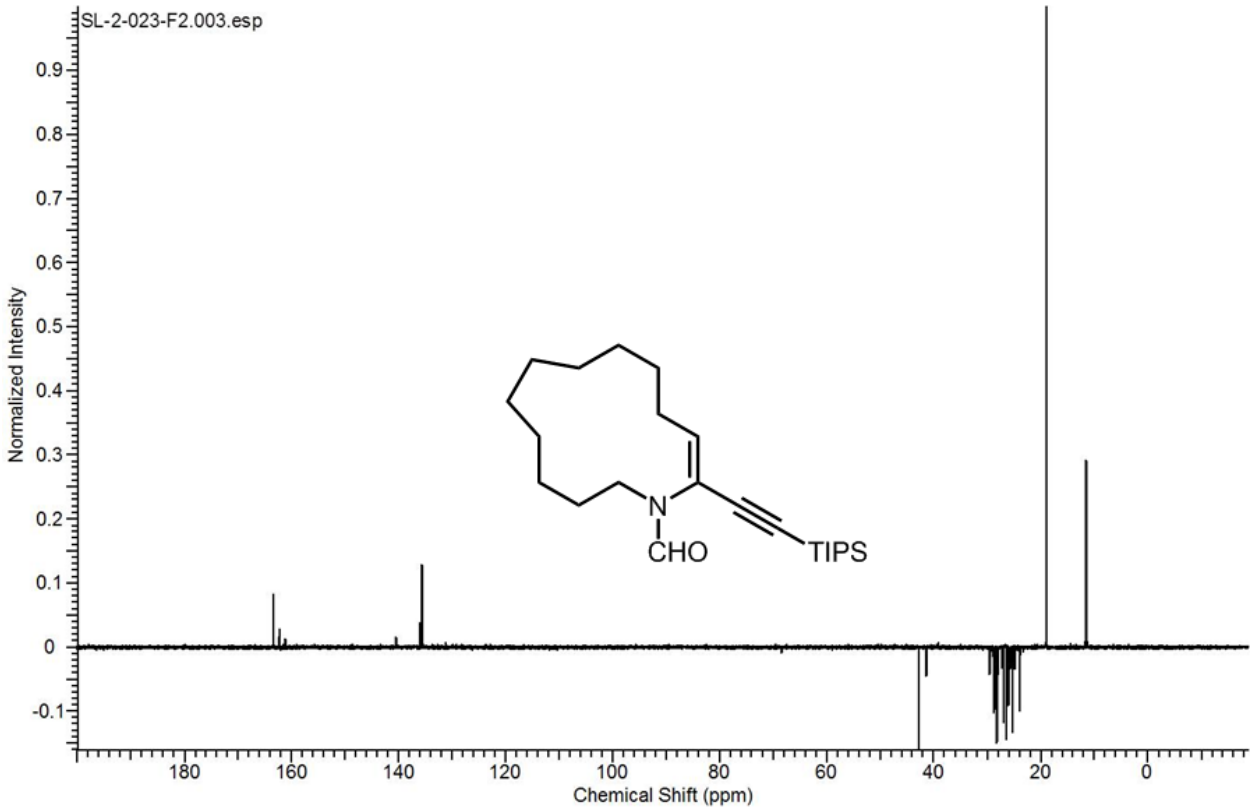


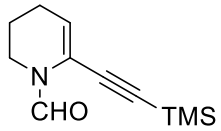
2l, 81%

Prepared from **3c** (1.00 mmol) and triisopropylsilylacetylene using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (90:10). Yield = 316 mg, 81%.^{1}H NMR (400 MHz, Chloroform-*d, mixture of rotamers*) δ 7.99 (s, 1H), 5.72 (t, *J* = 7.2 Hz, 1H), 3.62 (dt, *J* = 20.1, 5.6 Hz, 2H), 2.20 (q, *J* = 6.7 Hz, 2H), 1.49-1.26 (m, 16H), 1.03 (s, 21H). ^{13}C NMR (101 MHz, $CDCl_3$, rotamers) δ 163.00, 161.91, 160.70, 140.10, 135.70, 135.30, 130.83, 128.77, 123.38, 123.19, 118.27, 102.45, 102.30, 99.47, 98.14, 90.93, 89.72, 77.50, 77.18, 76.87, 68.05, 47.59, 42.46, 40.99, 38.75, 30.38, 29.16, 28.94, 28.56, 28.53, 28.43, 28.33, 28.26, 27.84, 27.79, 27.72, 27.66, 27.52, 26.82, 26.79, 26.62, 26.53, 26.13, 26.02, 25.76, 25.46, 25.44, 25.32, 24.99, 24.74, 24.41, 23.76, 23.67, 23.57, 23.45, 23.00, 18.60, 18.59, 14.06, 11.49, 11.21, 11.19, 10.93. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{24}H_{43}NOSi$ 389.3114; found 389.3110.



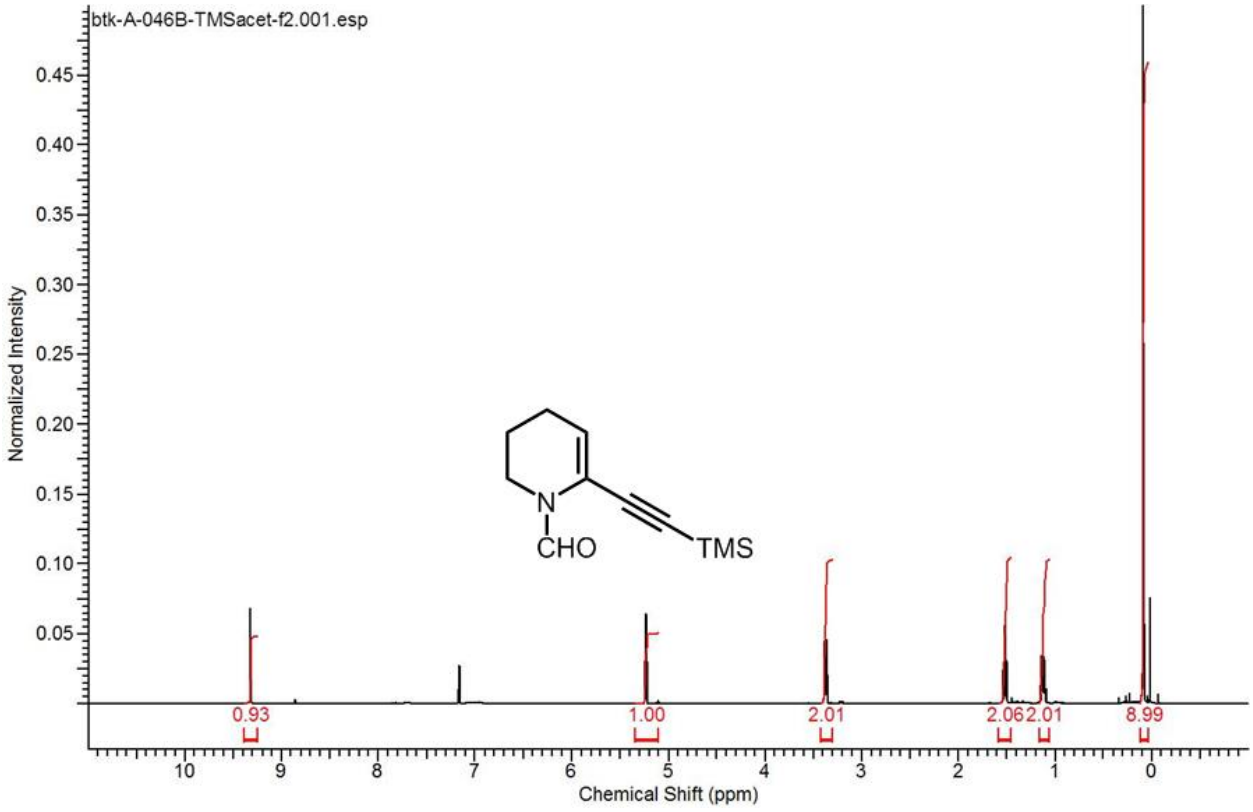

SL-2-023-F2.013.esp
Normalized Intensity
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
N
CHO
TIPS
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

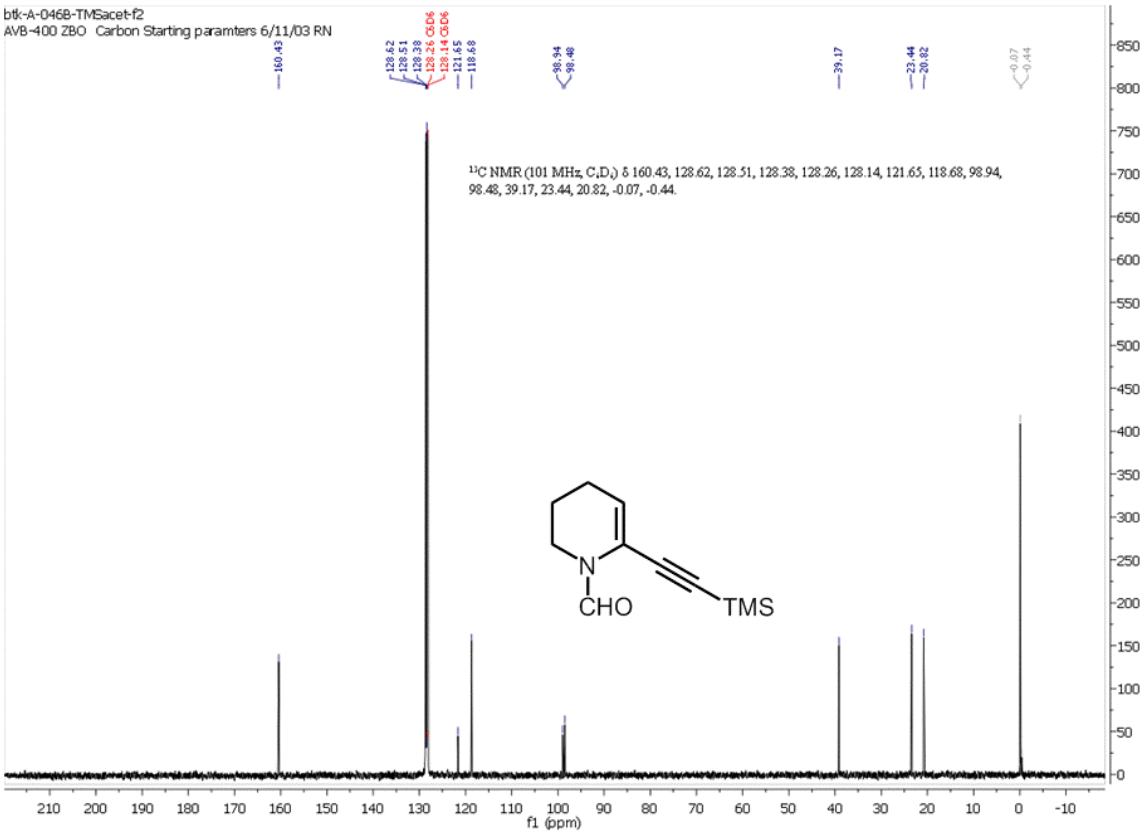

SL-2-023-F2.003.esp
Normalized Intensity
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
N
CHO
TIPS
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

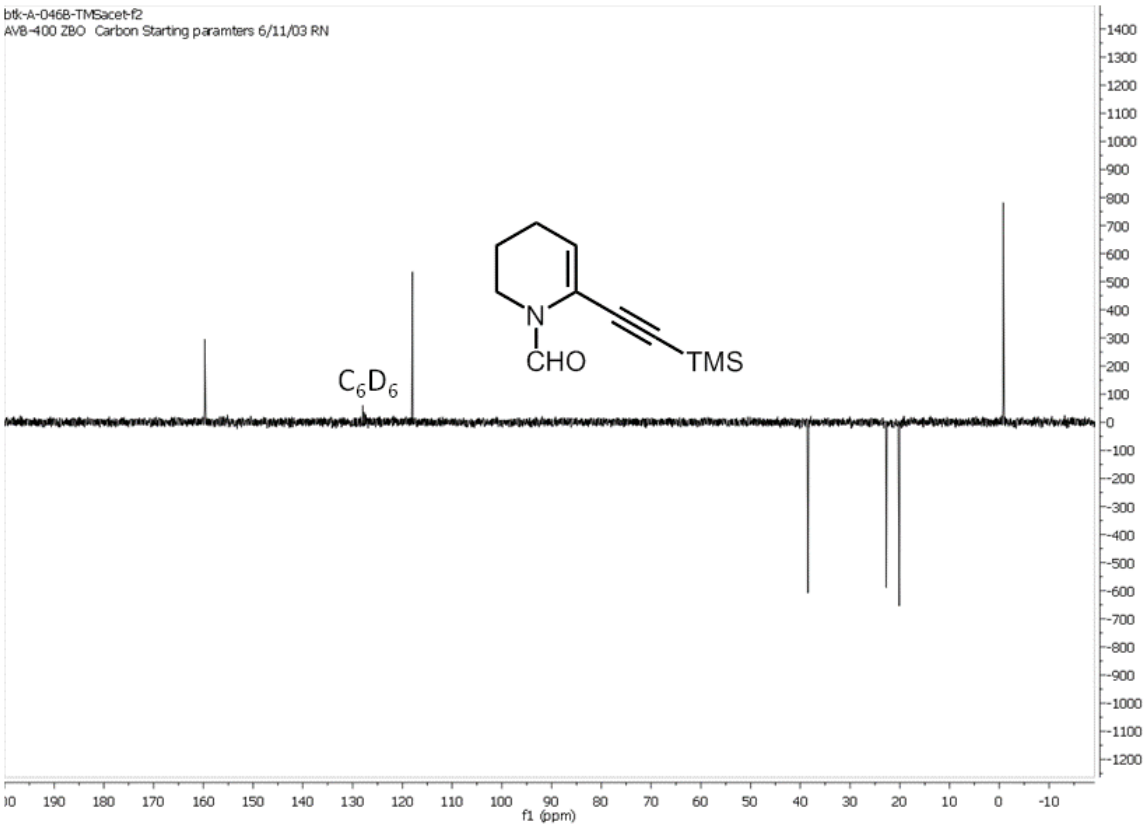


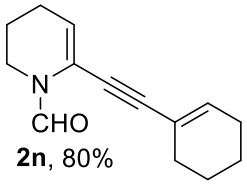
2m, 86%

Prepared from **3a** (1.00 mmol) and trimethylsilylacetylene (2 mmol, 2 equiv) using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (90:10). Yield = 178 mg, 86%. ^{1}H NMR (400 MHz, C_6D_6) δ 9.32 (s, 1H), 5.24 to 5.22 (t, 1H), 3.39 to 3.36 (t, 2H), 1.54 to 1.47 (m, 2H), 1.15 to 1.09 (m, 2H), 0.09 (s, 9H). ^{13}C NMR (101 MHz, C_6D_6) δ 160.4, 121.6, 118.6, 98.9, 98.4, 39.2, 23.4, 20.8, 0.1. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{11}H_{17}NOSi$ 207.1079; found 207.1083.



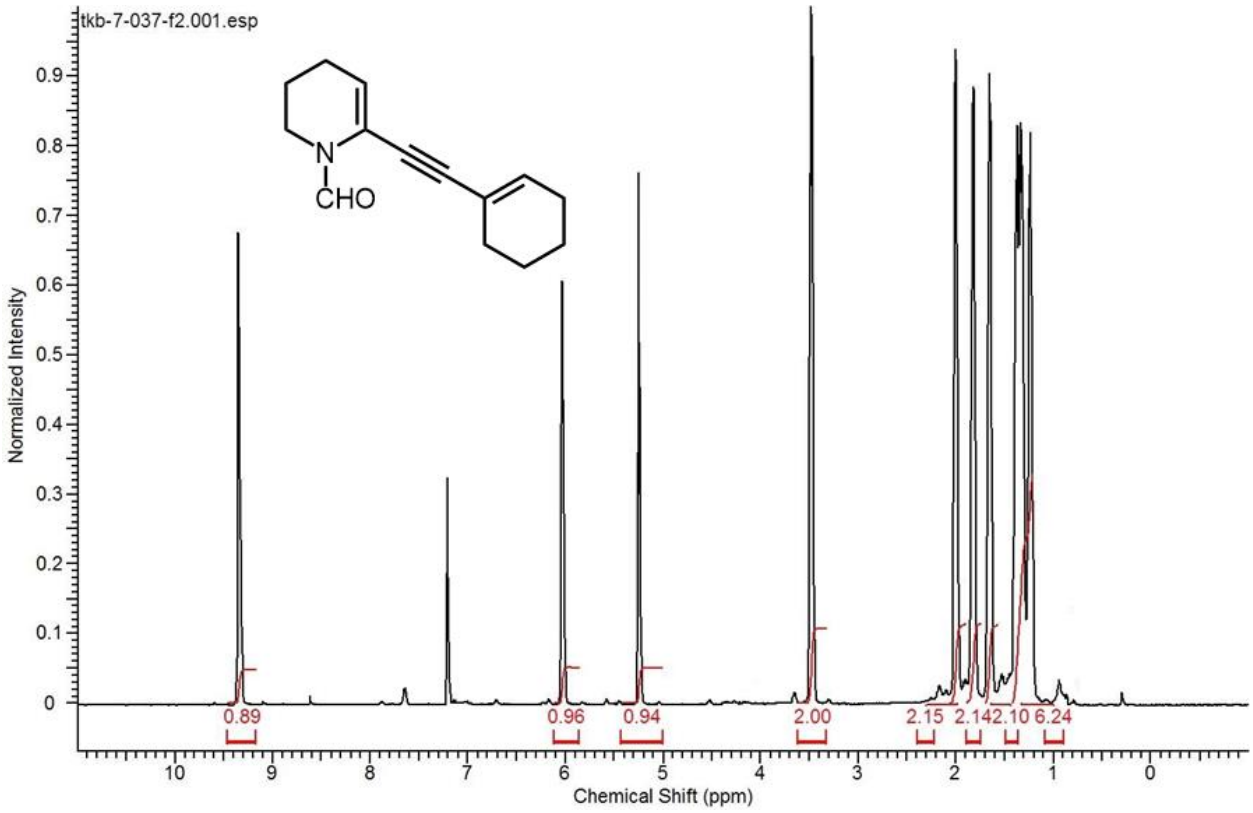

btk-A-046B-TMSacet-f2
AVB-400 ZBO Carbon Starting paramters 6/11/03 RN
160.43
128.62
128.51
128.38
128.26 C6D6
128.14 C6D6
121.65
118.68
98.94
98.48
39.17
23.44
20.82
-0.07
-0.44
^{13}C NMR (101 MHz, C$_6$D$_6$) δ 160.43, 128.62, 128.51, 128.38, 128.26, 128.14, 121.65, 118.68, 98.94, 98.48, 39.17, 23.44, 20.82, -0.07, -0.44.
N
CHO
TMS
f1 (ppm)

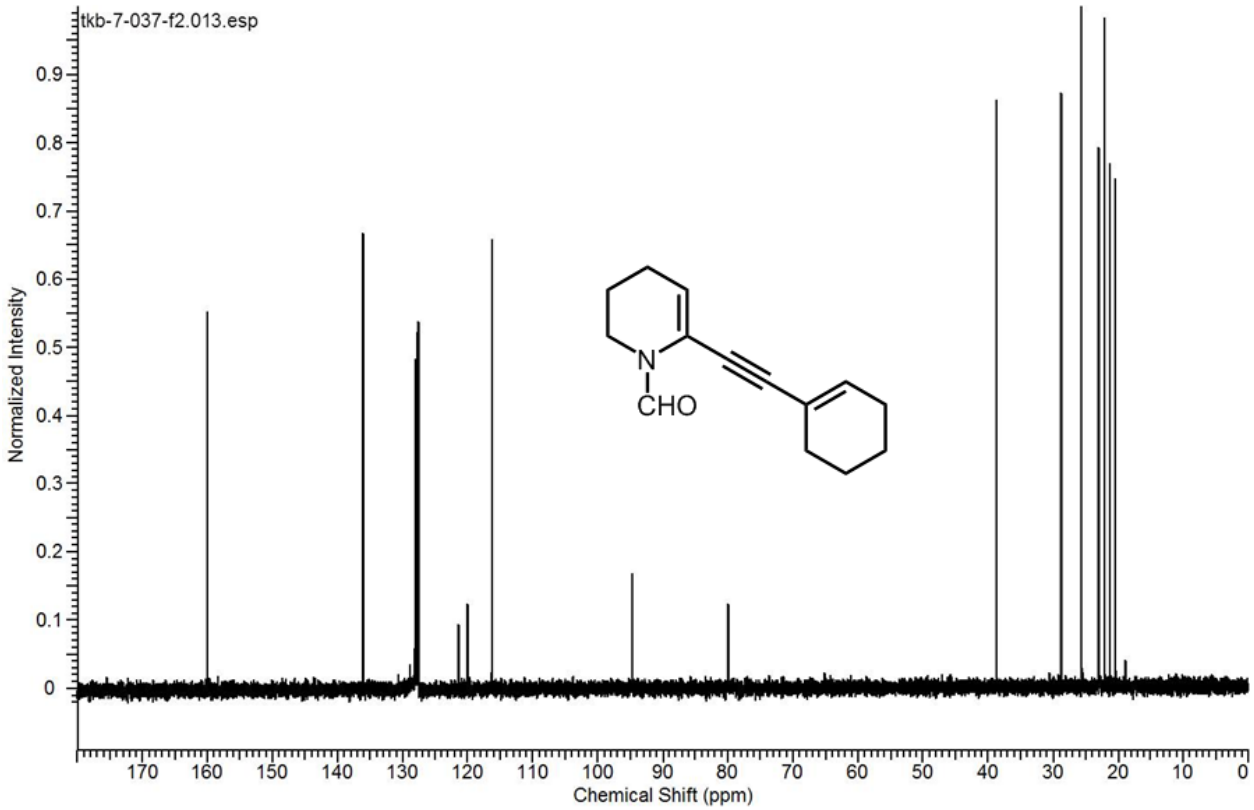

btk-A-046B-TMSacet-f2
AVB-400 ZBO Carbon Starting paramters 6/11/03 RN
N
CHO
TMS
C_6D_6
f1 (ppm)

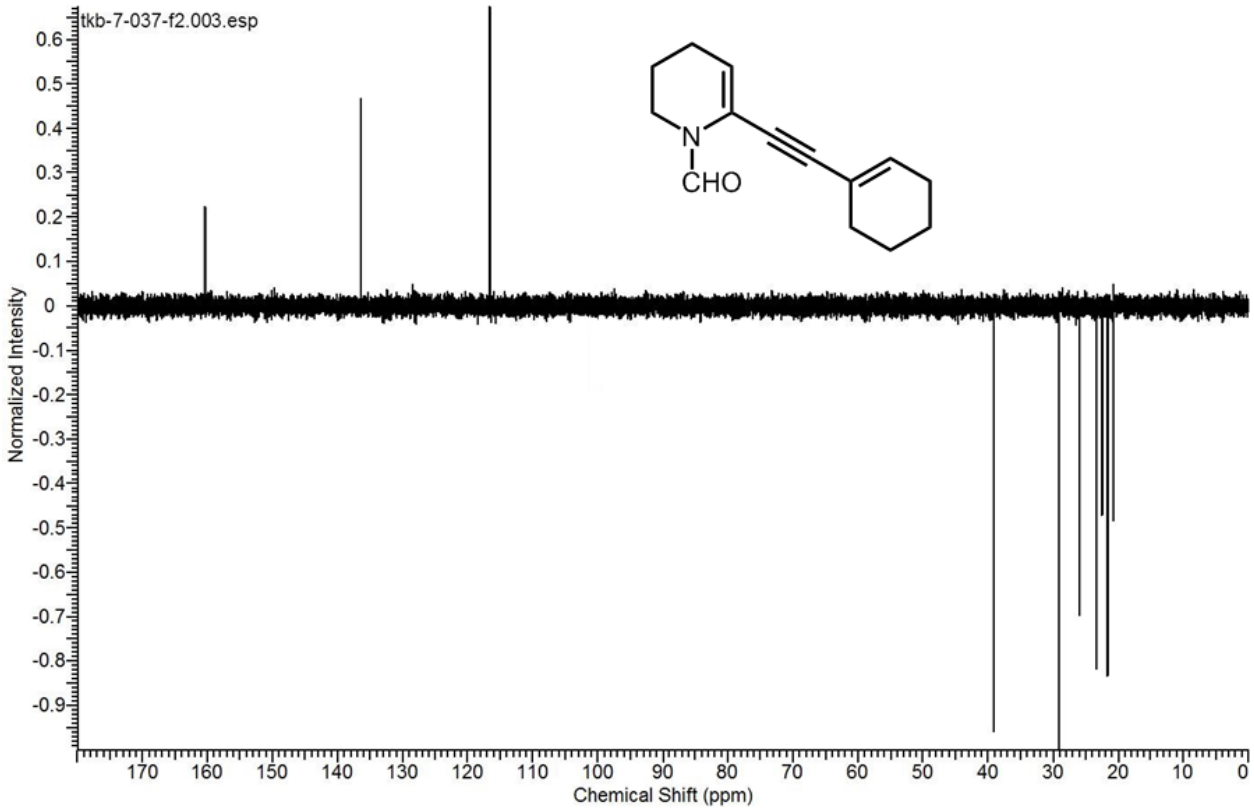


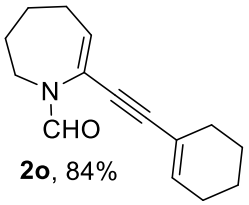
2n, 80%

Prepared from **3a** and 1-ethynylcyclohexene (0.24 mL, 2 mmol, 2 equiv) using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (80:20). Yield = 172 mg, 80%. ^{1}H NMR (400 MHz, C_6D_6) δ 9.39 (1H, s), 6.01 to 5.96 (1H, t), 5.22 to 5.20 (1H, t), 3.46 to 3.43 (2H, t), 1.99 to 1.94 (2H, m), 1.78 to 1.73 (2H, m), 1.57 to 1.46 (2H, q), 1.35 to 1.22 (4H, m), 1.17 to 1.11 (2H, m). ^{13}C NMR (101 MHz, C_6D_6) δ 160.6, 136.6, 121.9, 120.6, 116.8, 95.3, 80.6, 39.3, 29.3, 26.2, 23.5, 22.7, 21.9, 20.9. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{14}H_{17}NO$ 215.1310; found 215.1313.



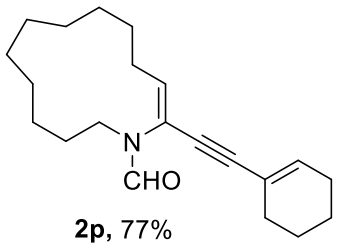

tkb-7-037-f2.013.esp
Normalized Intensity
Chemical Shift (ppm)
N
CHO


tkb-7-037-f2.003.esp
Normalized Intensity
Chemical Shift (ppm)
N
CHO



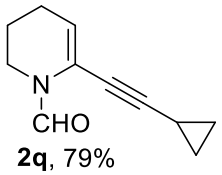
2o, 84%

Prepared from **3b** and 1-ethynylcyclohexene (0.24 mL, 2 mmol, 2 equiv) using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (80:20). Yield = 208 mg, 84%. Data as previously reported by us.[1]



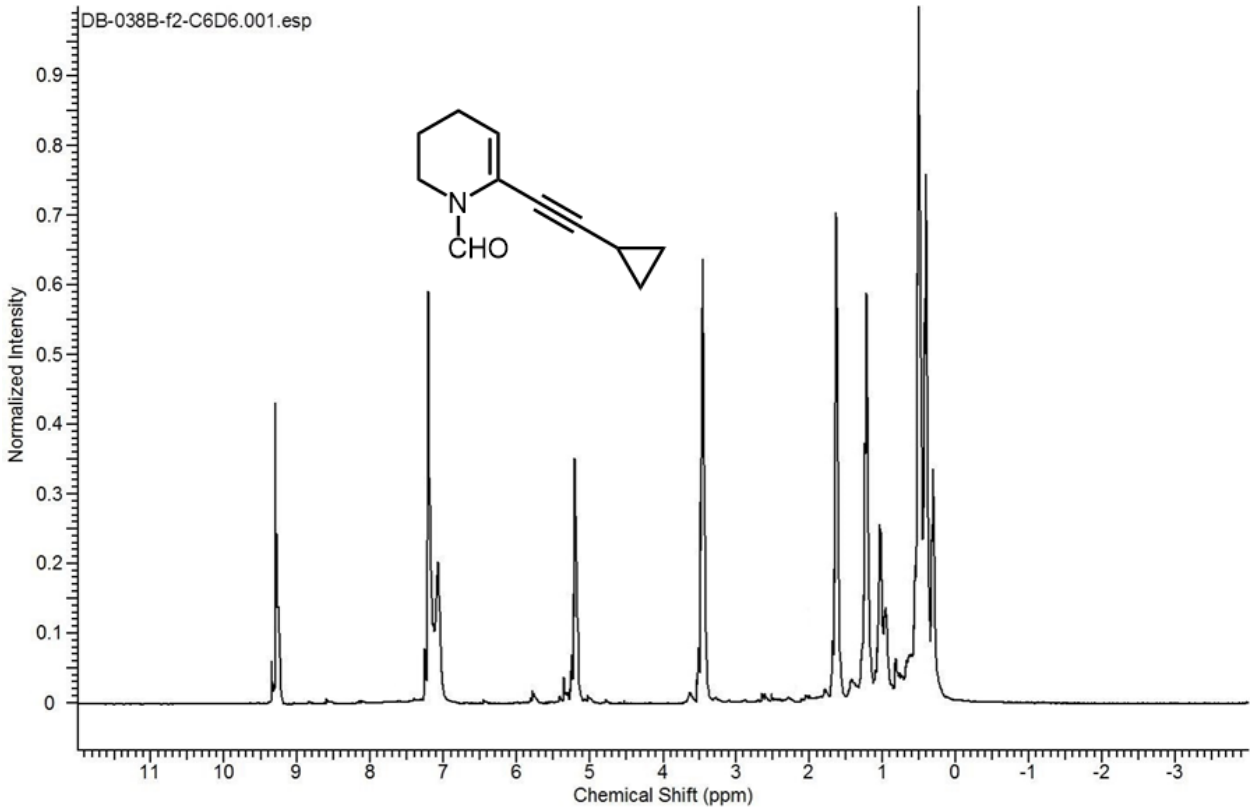
2p, 77%

Prepared from **3c** (1 mmol) and 1-ethynylcyclohexene (0.24 mL, 2 mmol, 2 equiv) using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (80:20). Yield = 241 mg, 77%. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{21}H_{31}NO$ 313.2406; found 313.2410.



2q, 79%

Prepared from **3a** (1.0 mmol) and 1-ethynylcyclopropane (2 mmol, 2 equiv) using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (80:20). Yield = 156 mg, 79%. 1H NMR (400 MHz, Benzene-d6) δ 9.45 to 9.12 (1H, s), 5.42 to 5.03 (1H, t), 3.64 to 3. 43 (2H, t), 1. 77 to 1.52 (2H, m), 1. 48 to 0.22 (7H, m). 13C NMR (101 MHz, Chloroform-d) δ 161.6, 121.2, 117.6, 97.8, 68.7, 39.4, 23.5, 21.1, 9.1, 0.3. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{11}H_{13}NO$ 175.0997; found 175.0993.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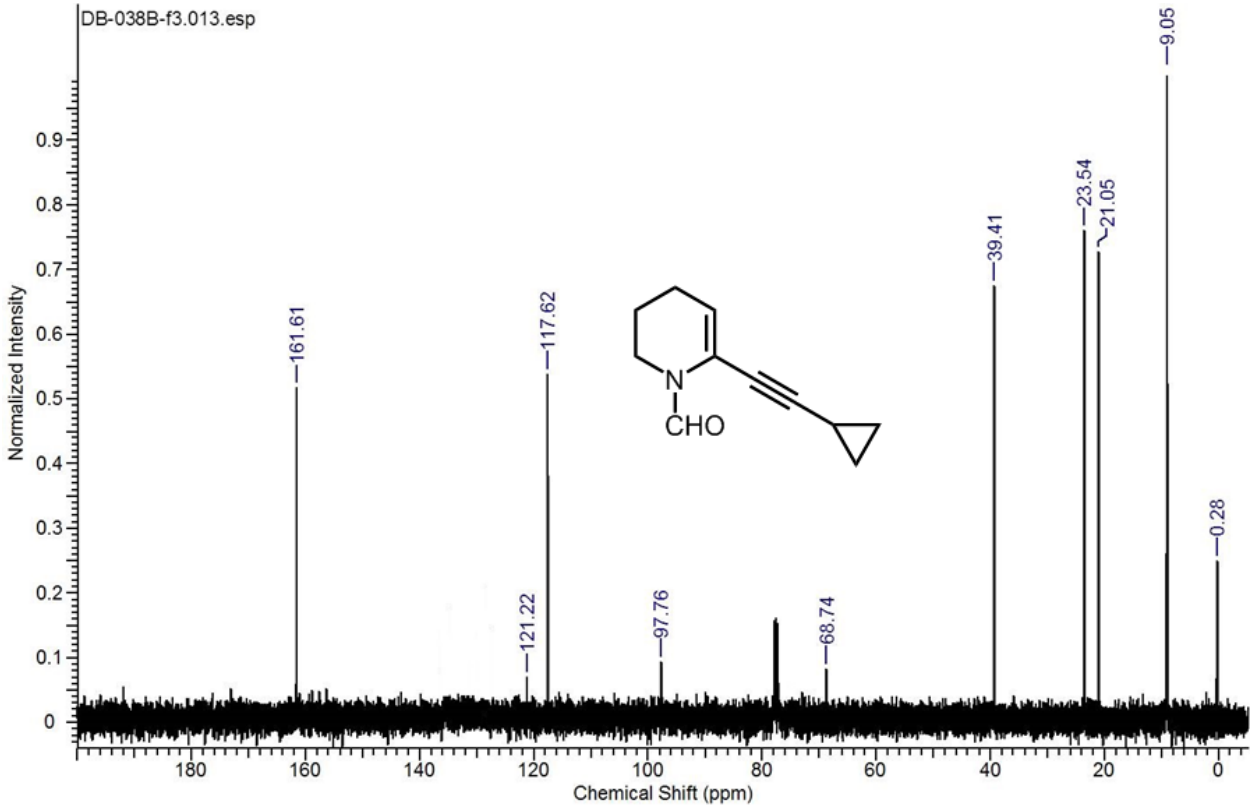
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Chemical Shift (ppm)
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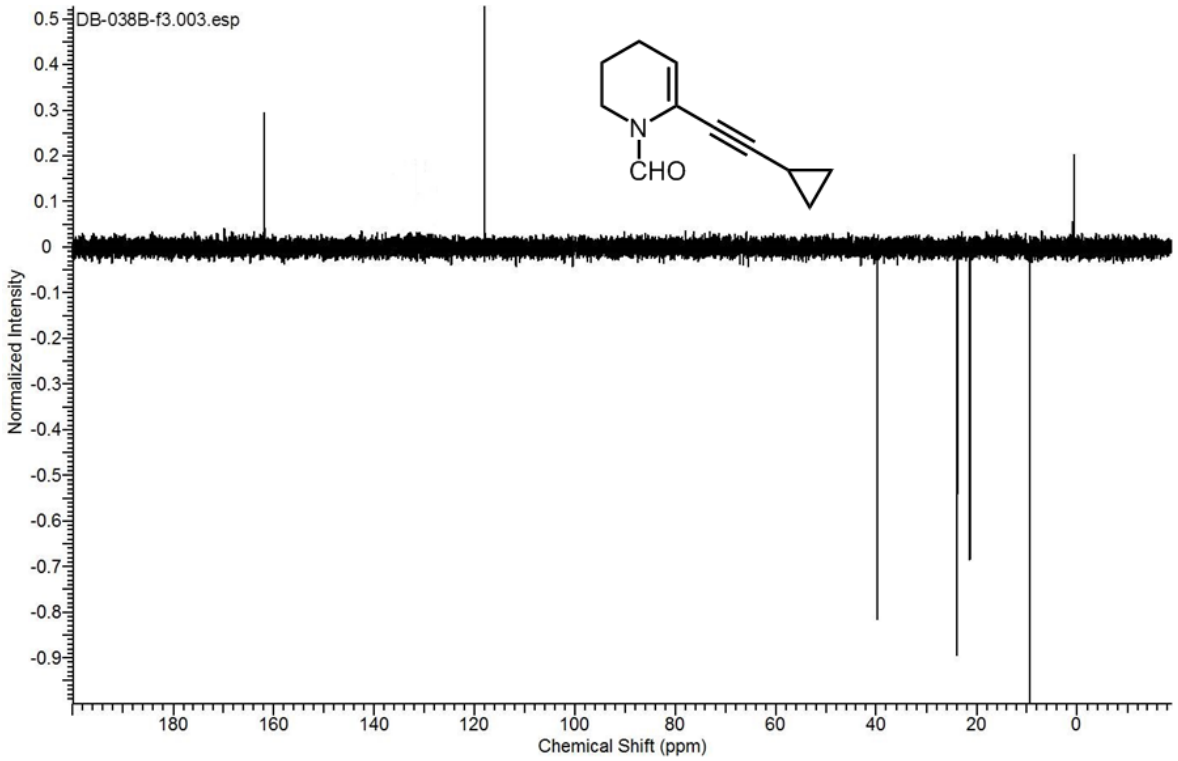
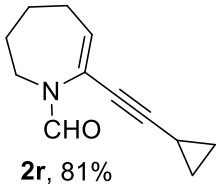
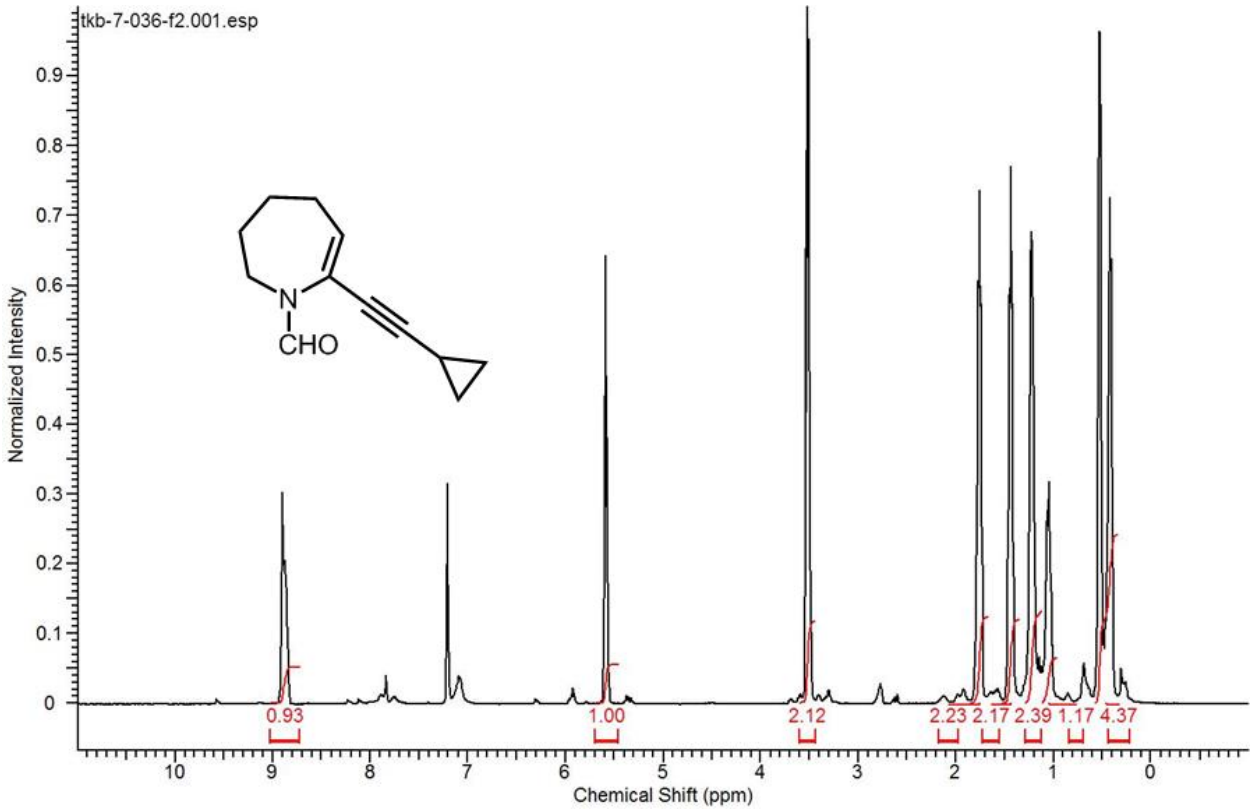




2r, 81%

Prepared from **3b** (1.0 mmol) and 1-ethynylcyclopropane (2 mmol, 2 equiv) using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (80:20). Yield = 153 mg, 81%. 1H NMR (400 MHz, Benzene-d_6) δ 8.90 to 8.85 (1H, s), 5.60 to 5.37 (1H, t), 3.54 to 3.29 (2H, t), 2.13 to 1.92 (2H, m), 1.77 to 1.41 (2H, m), 1.24 to 1.18 (2H, m), 1.08 to 1.01 (2H, m), 0.85 to 0.26 (4H, m). 13C NMR (101 MHz, Benzene-d_6) δ 161.69, 93.78, 73.06, 43.73, 27.87, 27.13, 23.50, 8.43. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{12}H_{15}NO$ 189.1154; found 189.1151.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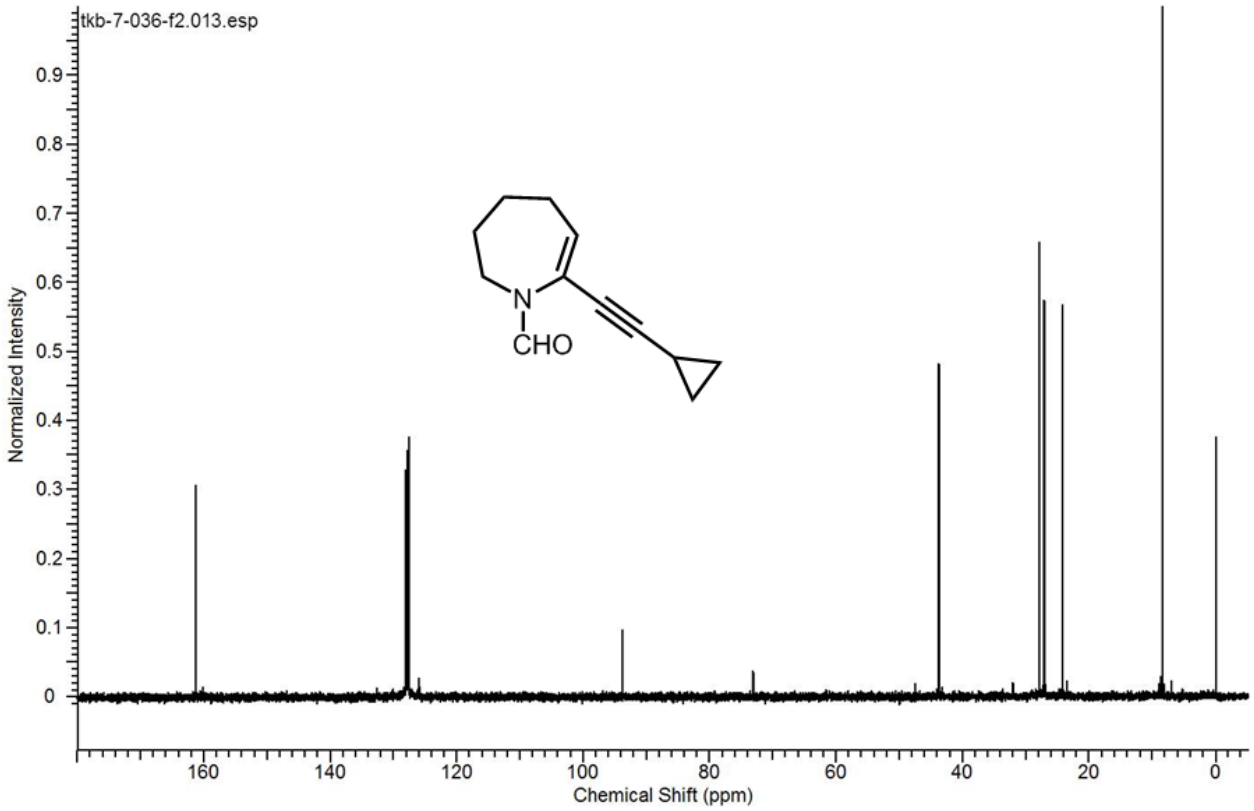
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Chemical Shift (ppm)
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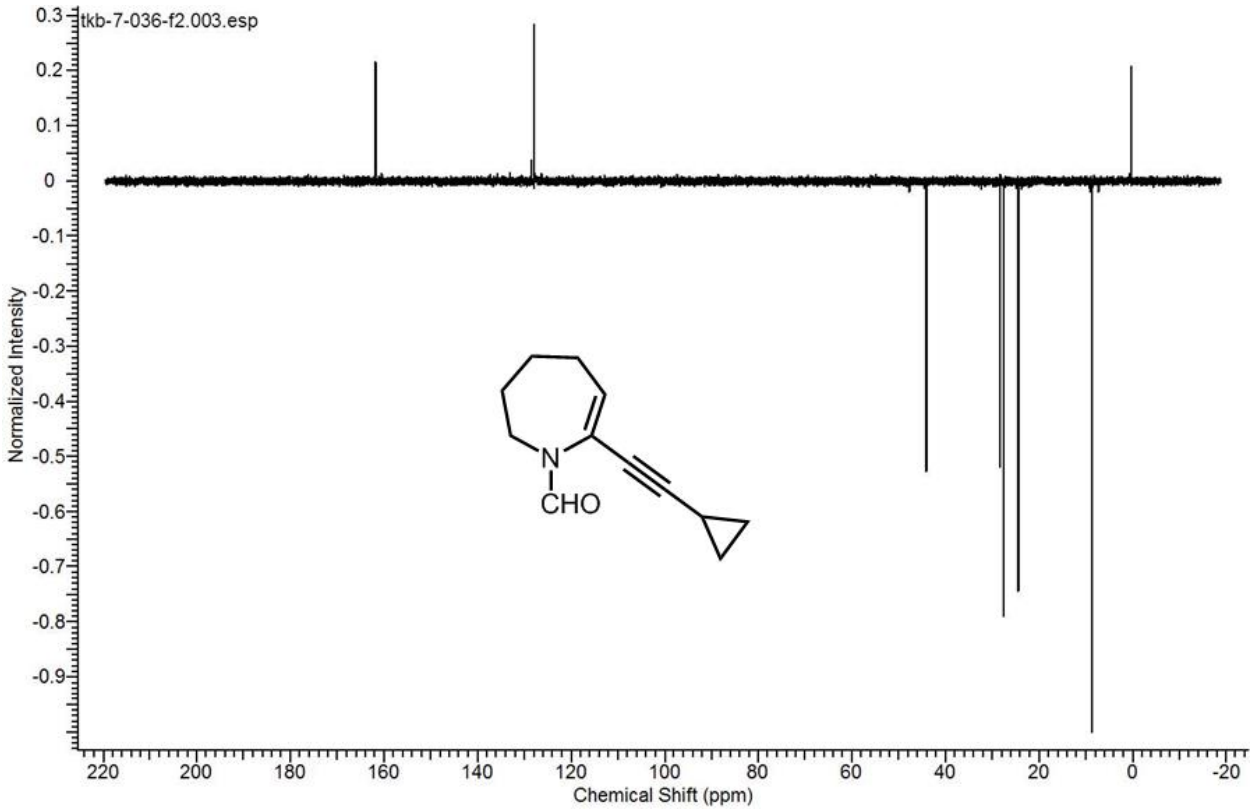
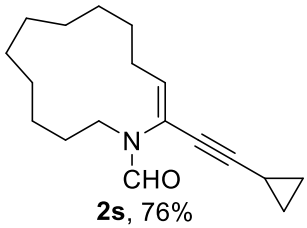
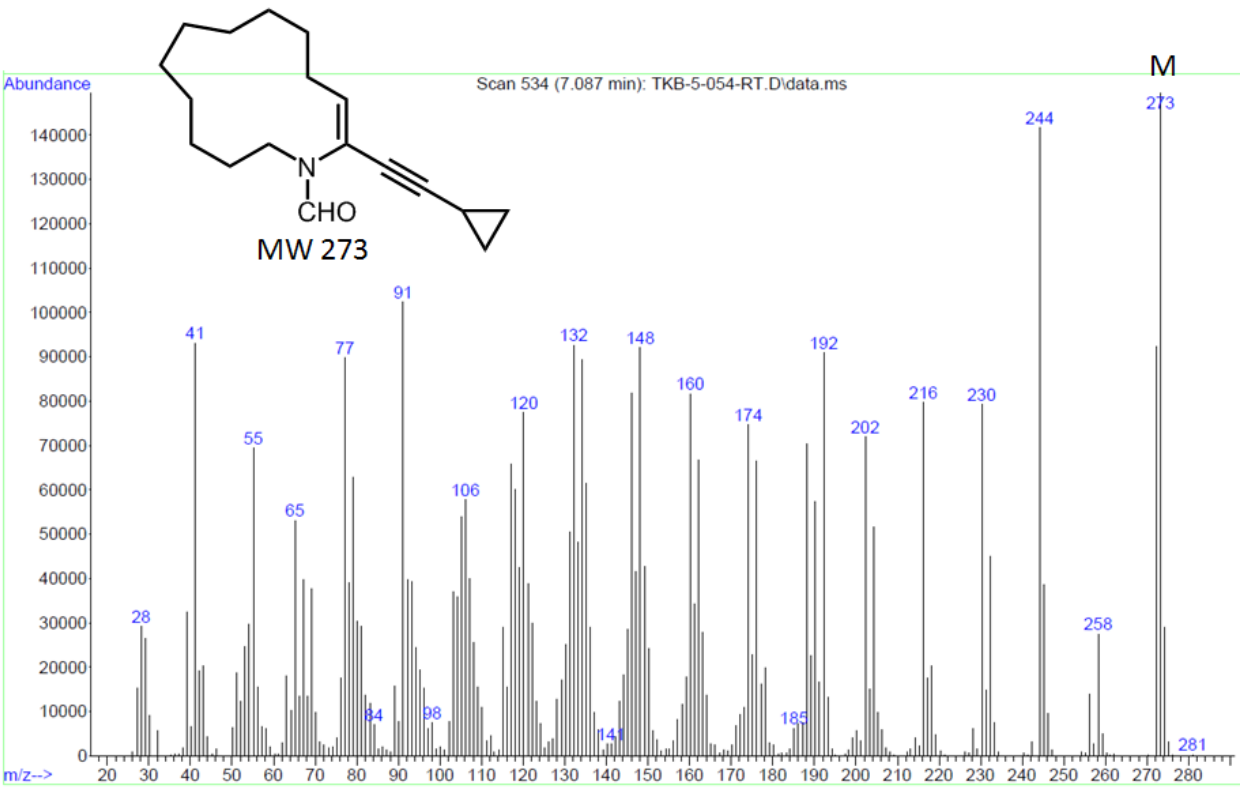




2s, 76%

Prepared from **3c** (1 mmol) and 1-ethynylcyclopropane (2 mmol, 2 equiv) using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (80:20). Yield = 208 mg, 76%. ^{1}H NMR (400 MHz, $CDCl_3$, mixture of rotamers) δ 8.16 & 7.96 (1H, s,s), 5.80 to 5.57 (1H, t), 3.66 to 3.41 (2H, t), 2.36 to 2.02 (2H, m), 1.73 to 0.98 (17H, m), 0.93 to 0.68 (4H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 162.0, 138.8, 134.0, 123.2, 123.1, 99.9, 93.0, 77.4, 77.1, 76.8, 71.7, 68.9, 47.5, 43.1, 42.5, 40.9, 28.8, 28.5, 28.4, 28.4, 28.2, 28.0, 28.0, 27.9, 27.7, 27.6, 27.5, 26.8, 26.6, 26.6, 26.4, 26.1, 26.0, 25.9, 25.8, 25.7, 25.6, 25.4, 25.1, 24.9, 24.8, 24.6, 24.4, 23.7, 23.6, 23.5, 23.3, 9.8, 9.6, 9.3, 9.0, 8.7, 8.6, 8.5. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{18}H_{27}NO$ 273.2093; found 273.2090.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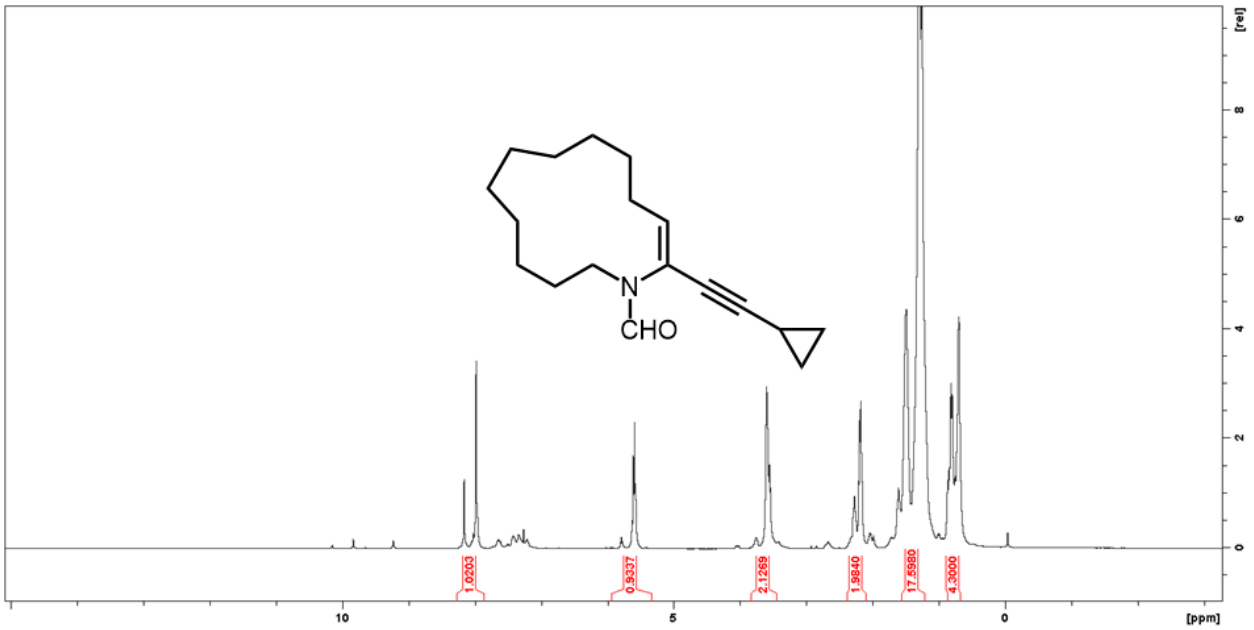
281
m/z-->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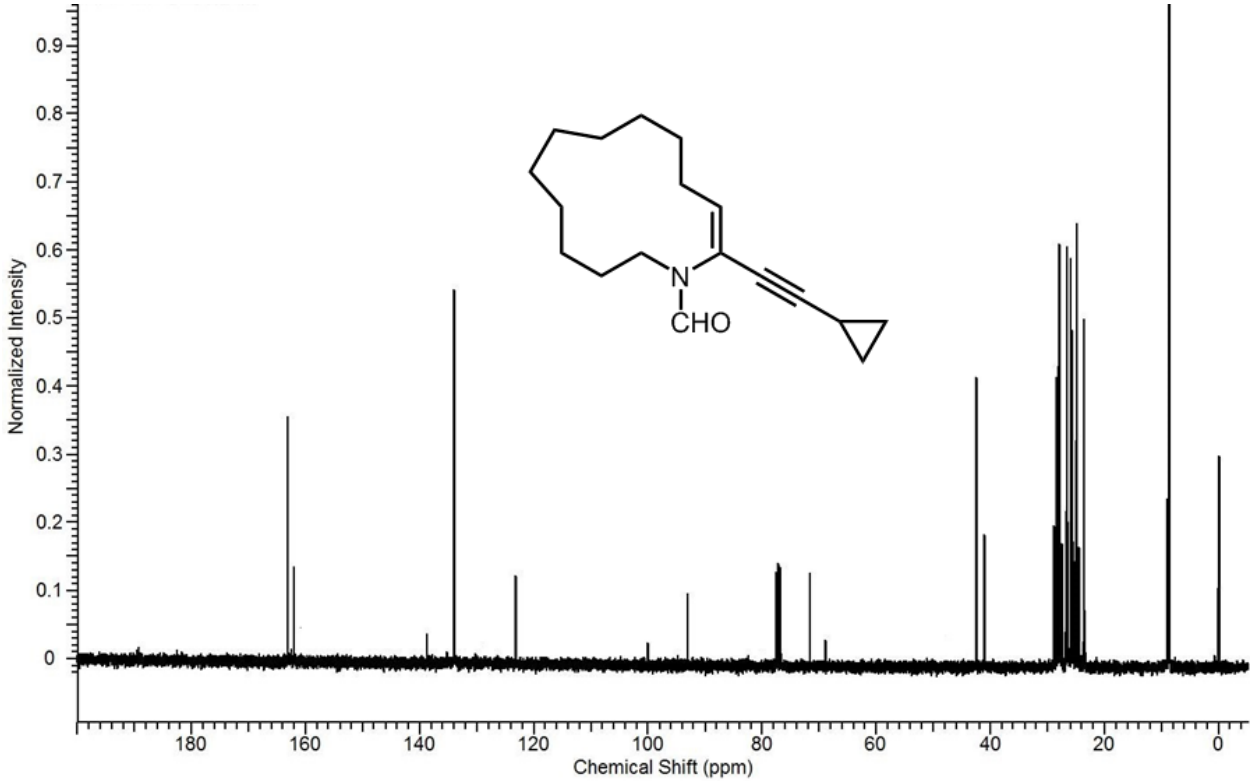
[ppm]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20
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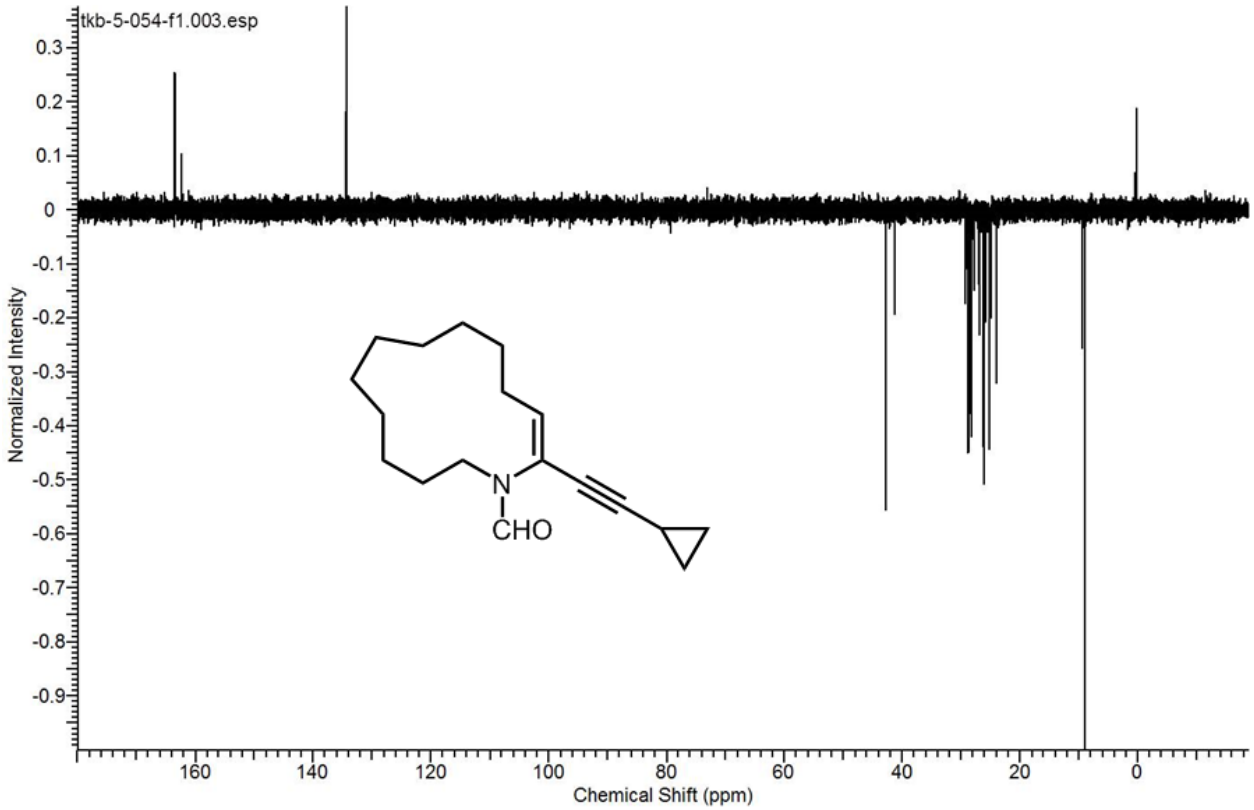
Chemical Shift (ppm)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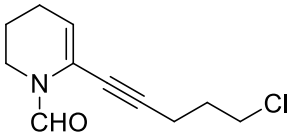
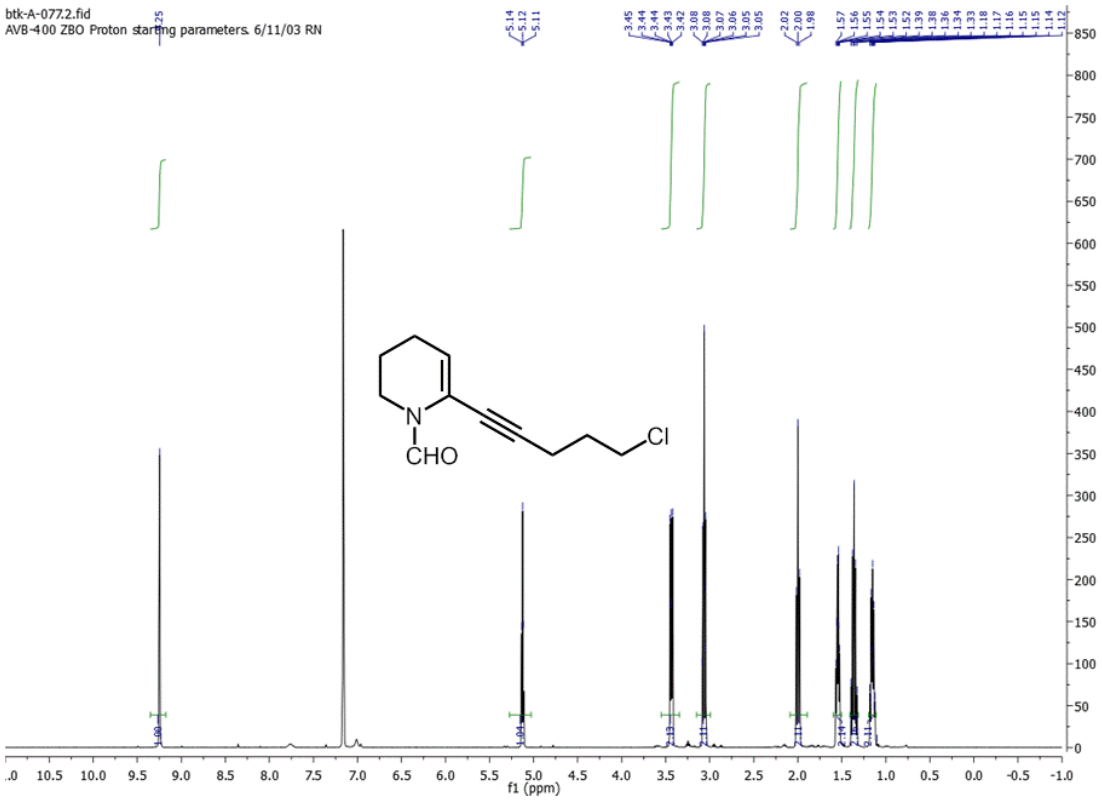
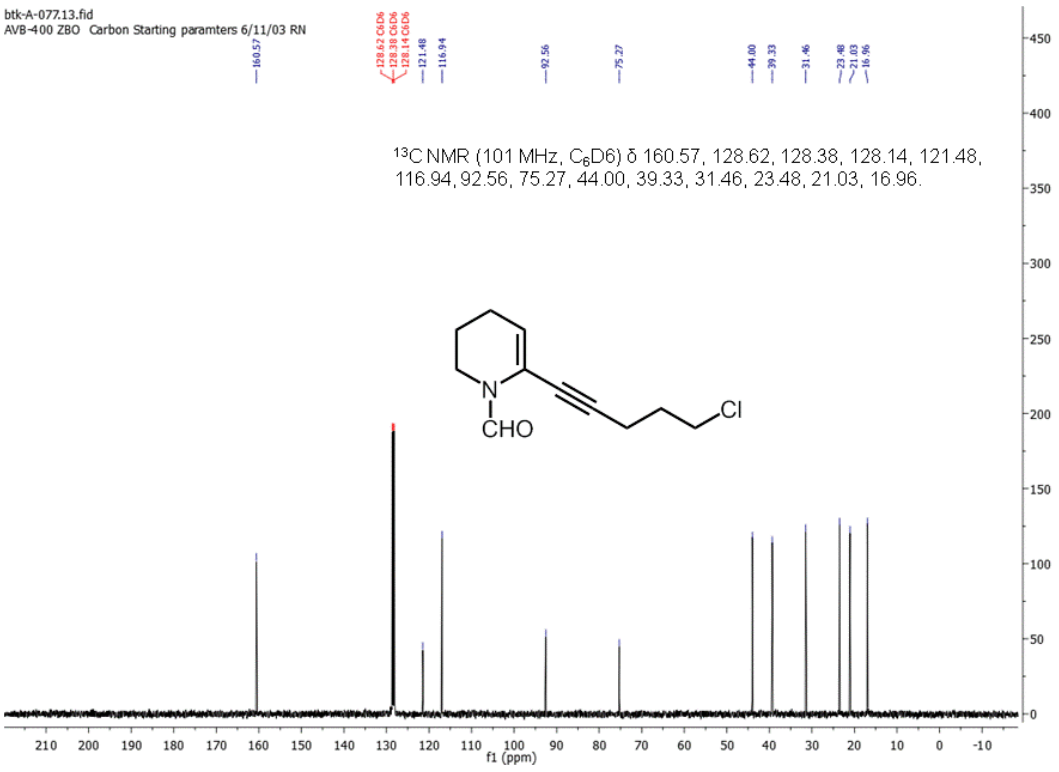
Chemical Shift (ppm)



2t, 95%

Prepared from **3a** (1.0 mmol) and 5-chloro-1-pentyne (0.21 mL, 2.0 mmol, 2 equiv) using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (70:30). Yield = 200 mg, 95%. ^{1}H NMR (400 MHz, C_6D_6) δ 9.25 (1H, s), 5.14 to 5.11 (1H, t), 3.45 to 3.42 (2H, t), 3.08 to 3.05 (2H, t), 2.02 to 1.98 (2H, t), 1.57 to 1.33 (4H, m), 1.18 to 1.12 (2H, m). ^{13}C NMR (101 MHz, C_6D_6) δ 160.5, 121.5, 116.9, 92.5, 75.2, 44.0, 39.3, 31.4, 23.4, 21.0, 16.9. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{11}H_{14}ClNO$ 211.0764; found 211.0769.

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121.48
116.94
92.56
75.27
44.00
39.33
31.46
23.48
21.03
16.96
^{13}C NMR (101 MHz, C_6D6) δ 160.57, 128.62, 128.38, 128.14, 121.48, 116.94, 92.56, 75.27, 44.00, 39.33, 31.46, 23.48, 21.03, 16.96.
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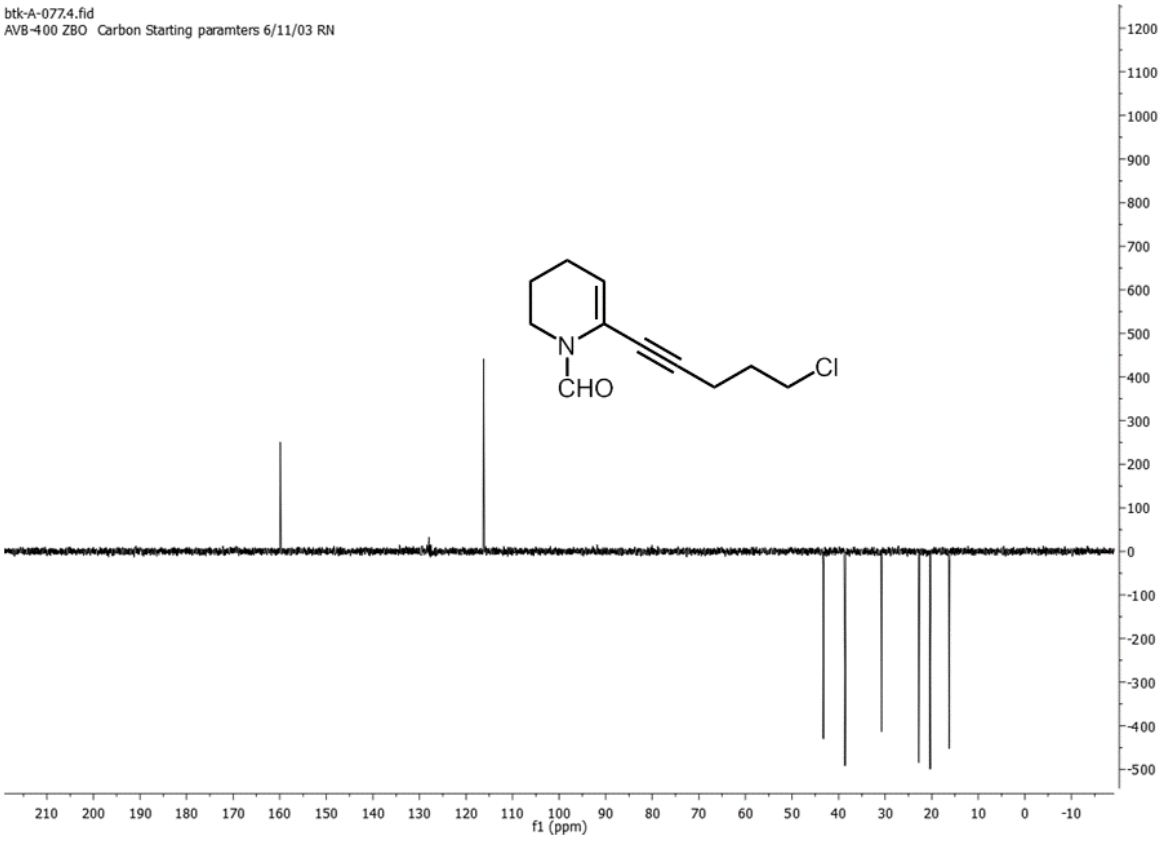
CHO
Cl
f1 (ppm)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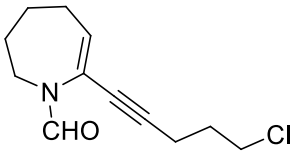
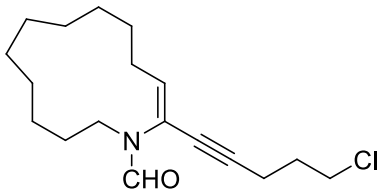
CHO
Cl
f1 (ppm)



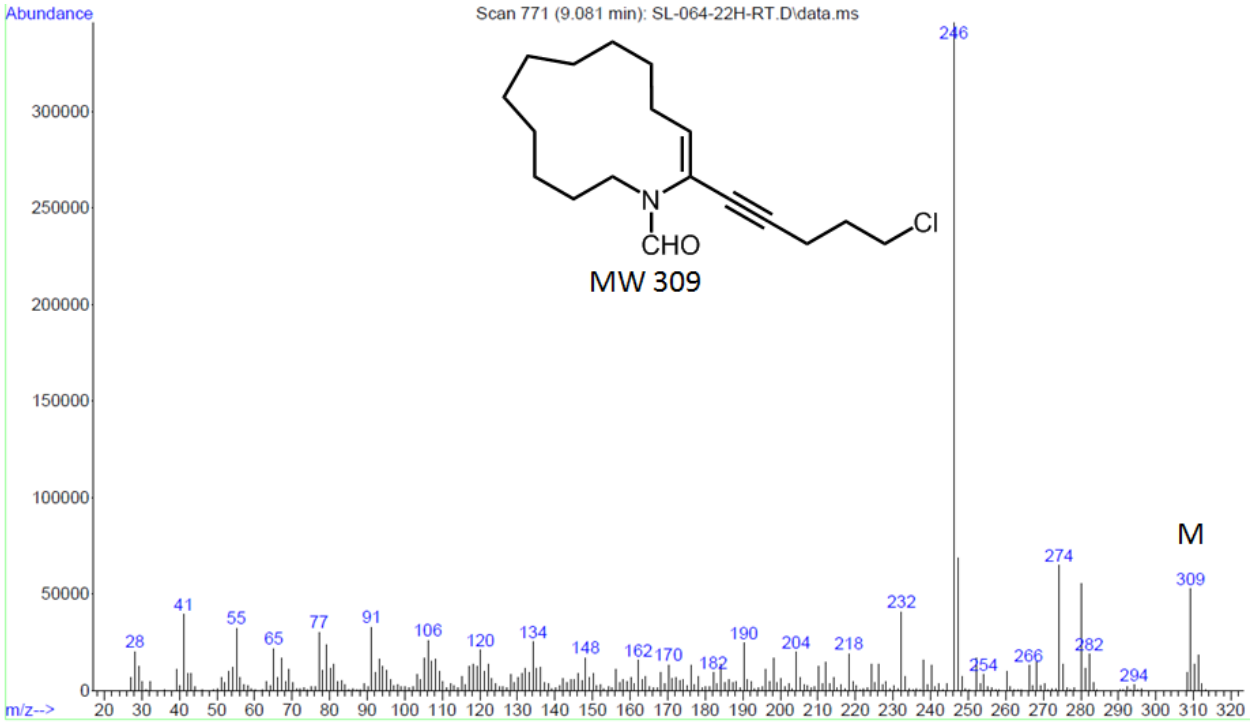
2u, 90%

Prepared from **3b** (1.0 mmol) and 5-chloro-1-pentyne (0.21 mL, 2.0 mmol) using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (90:10). Yield = 203 mg, 90%. Data as previously reported by us.[1]



2v, 91%

Prepared from **3c** (1.0 mmol) and 5-chloro-1-pentyne (0.21 mL, 2.0 mmol) using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (90:10). Yield = 281 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$, mixture of rotamers) δ 8.18 & 7.96 (1H, s,s), 5.85 to 5.77 (1H, t), 3.77 to 3.55 (4H, m), 2.68 to 1.18 (22H, m). ^{13}C NMR (101 MHz, $CDCl_3$, mixture of rotamers) δ 163.1, 162.0, 160.8, 139.2, 135.2, 122.9, 122.6, 94.4, 87.8, 86.8, 77.5, 77.5, 77.4, 77.1, 76.8, 75.0, 47.6, 43.6, 43.6, 43.4, 42.5, 41.0, 31.2, 31.1, 31.0, 28.9, 28.5, 28.4, 28.4, 28.2, 28.1, 28.0, 27.8, 27.6, 27.5, 26.8, 26.7, 26.6, 26.4, 26.3, 26.0, 25.9, 25.7, 25.5, 25.4, 25.2, 24.8, 24.8, 24.6, 24.4, 23.7, 23.6, 23.5, 23.3, 16.8, 16.6, 16.6. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{18}H_{28}ClNO$ 309.1859; found 309.1862.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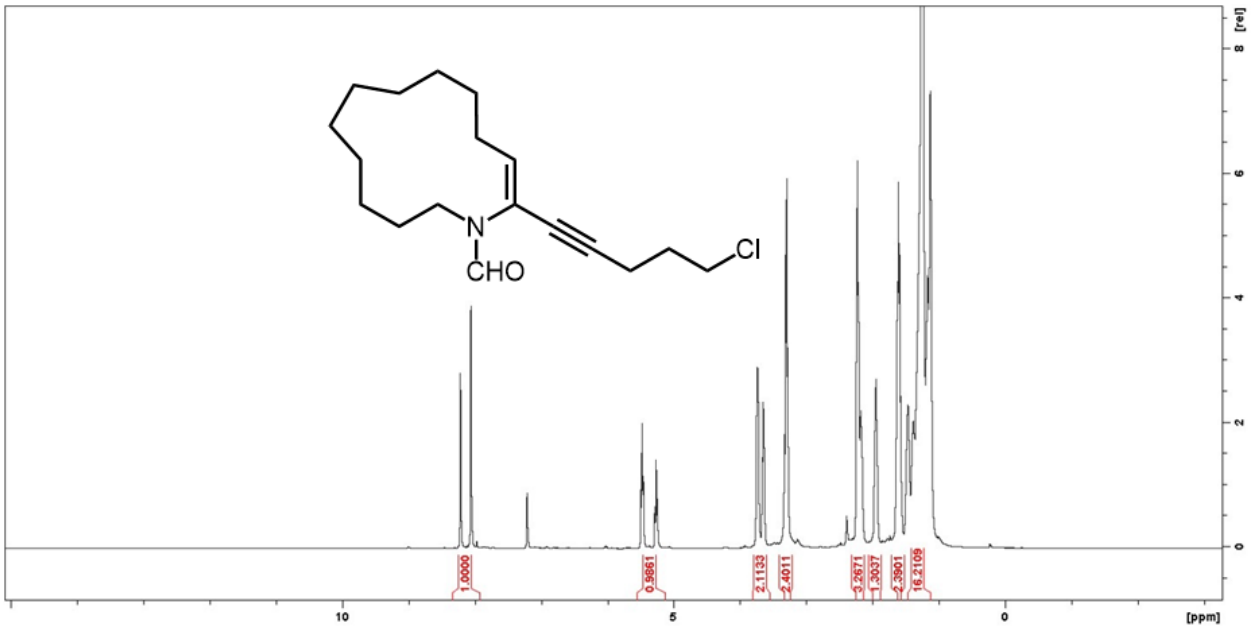
m/z-->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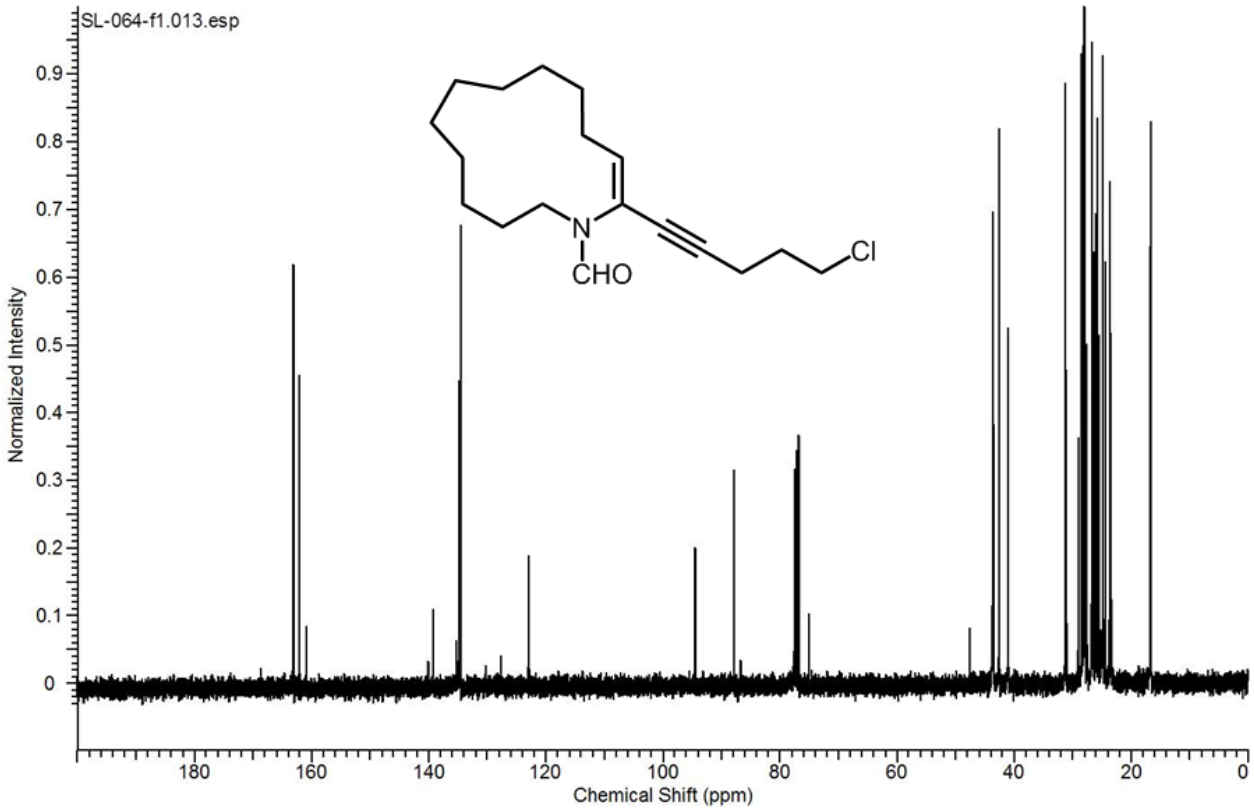
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Normalized Intensity
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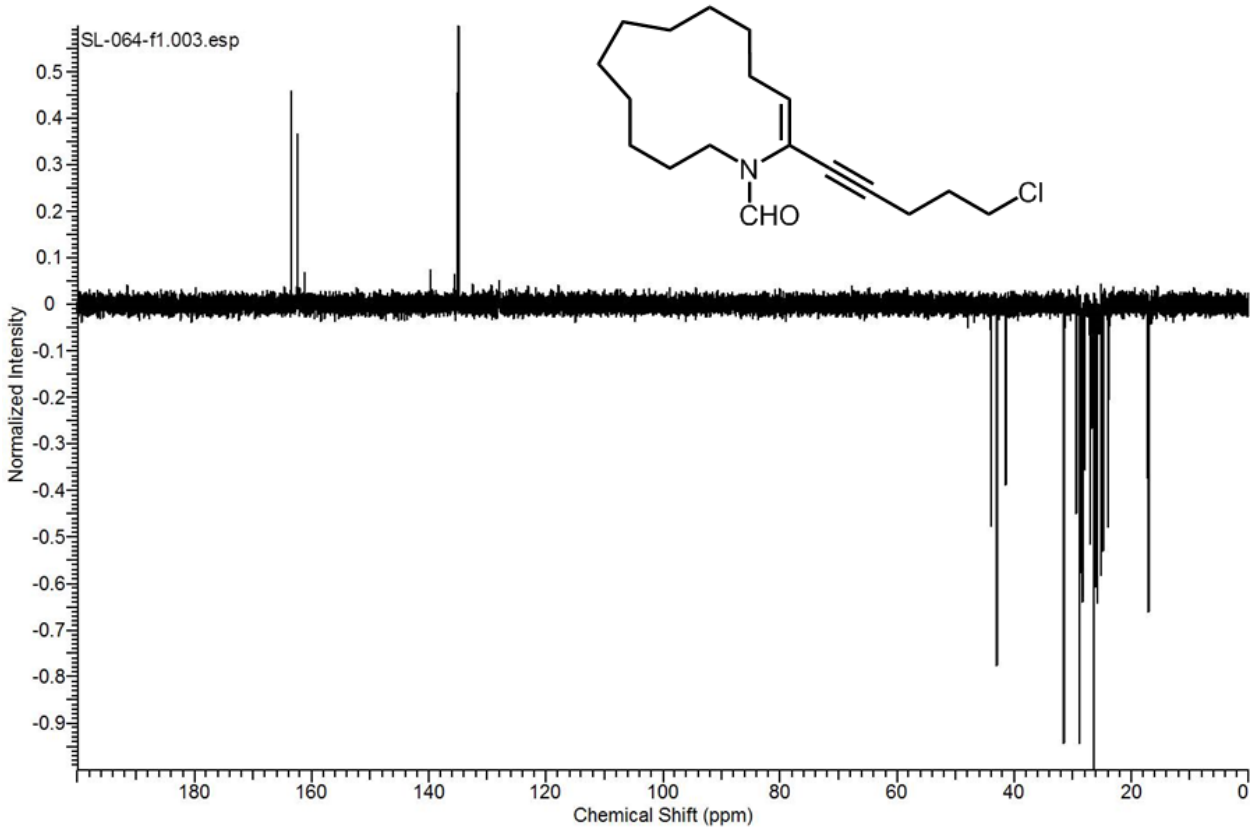
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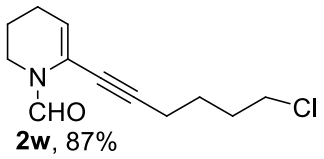
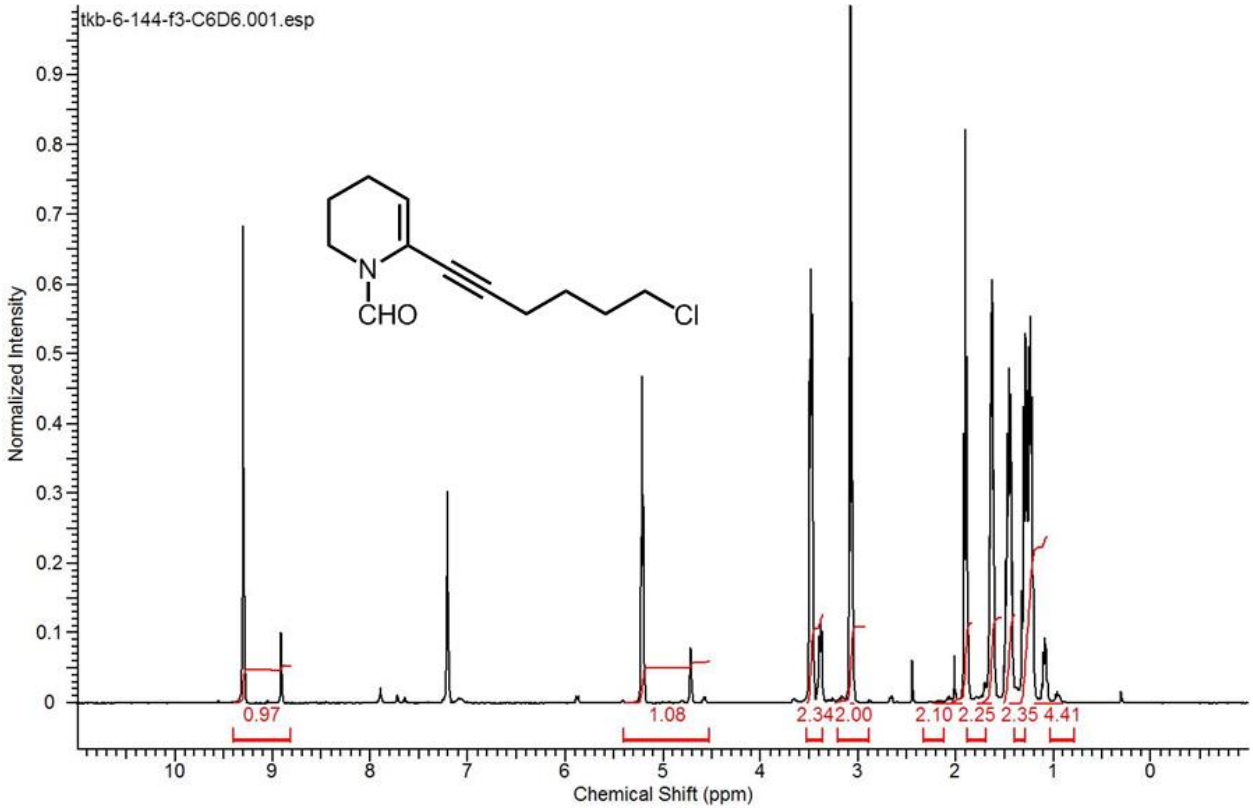
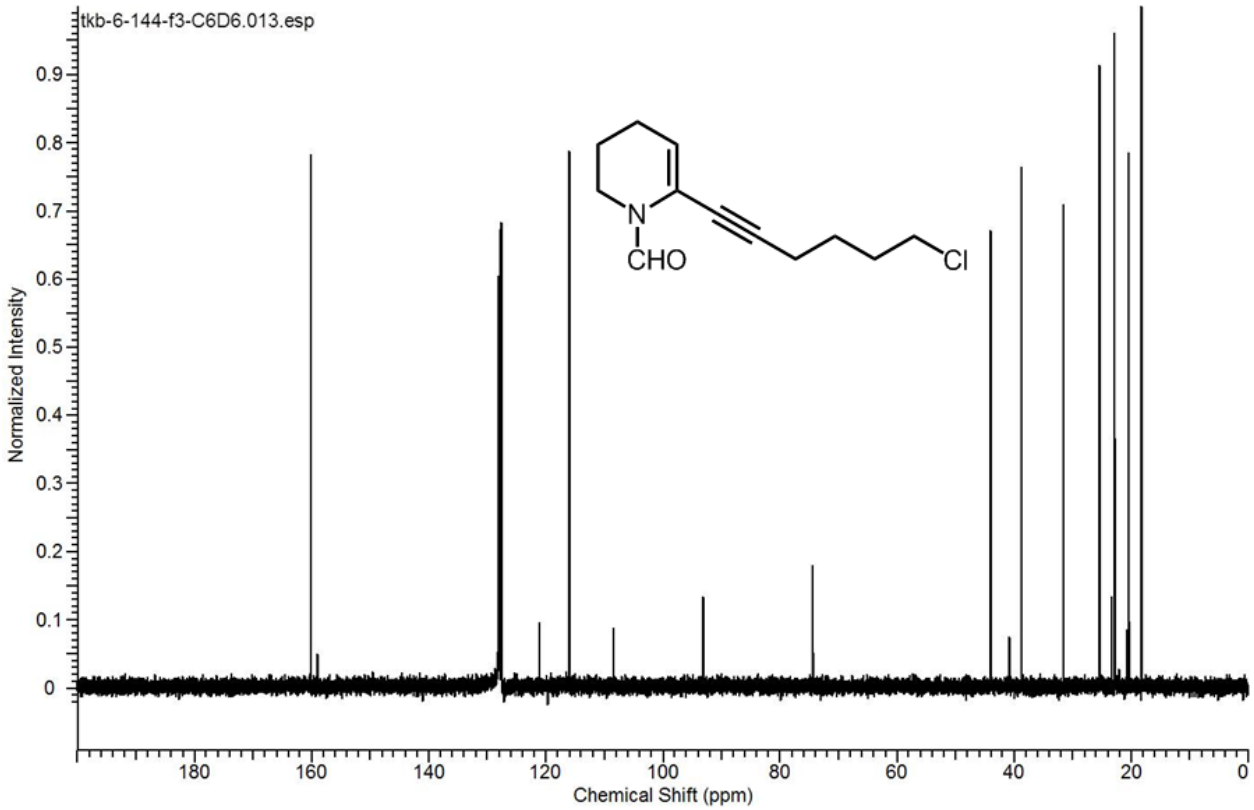


2w, 87%

Prepared from **3a** (1.0 mmol) and 6-chloro-1-hexyne (2.0 mmol, 2 equiv) using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (90:10). Yield = 196 mg, 87%. ^1H NMR (400 MHz, Benzene-d6) δ 9.30 to 8.91 (1H, s), 5.22 to 4.71 (1H, t), 3.50 to 3.37 (2H, t), 3.09 to 3.06 (2H, t), 2.01 to 1.88 (2H, m), 1.70 to 1.61 (2H, m), 1.51 to 1.42 (2H, m), 1.32 to 1.20 (2H, m), 1.12 to 0.94 (4H, m). 13C NMR (101 MHz, Benzene-d6) δ 160.1, 121.1, 116.0, 108.3, 93.1, 74.4, 44.0, 38.8, 31.5, 25.4, 23.4, 20.8, 18.2. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{12}H_{16}ClNO$ 225.0920; found 225.0923.

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0
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CHO
Cl
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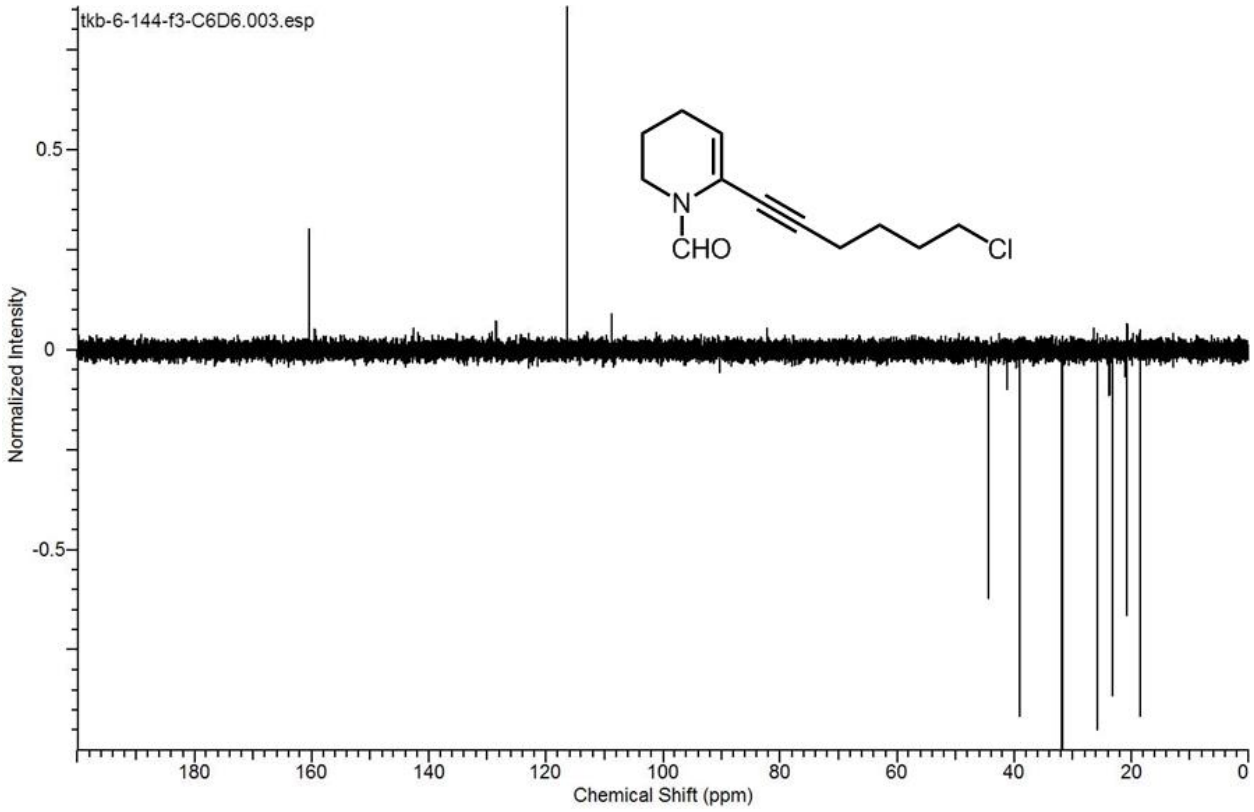
140
120
100
80
60
40
20
0
Chemical Shift (ppm)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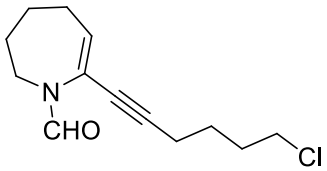
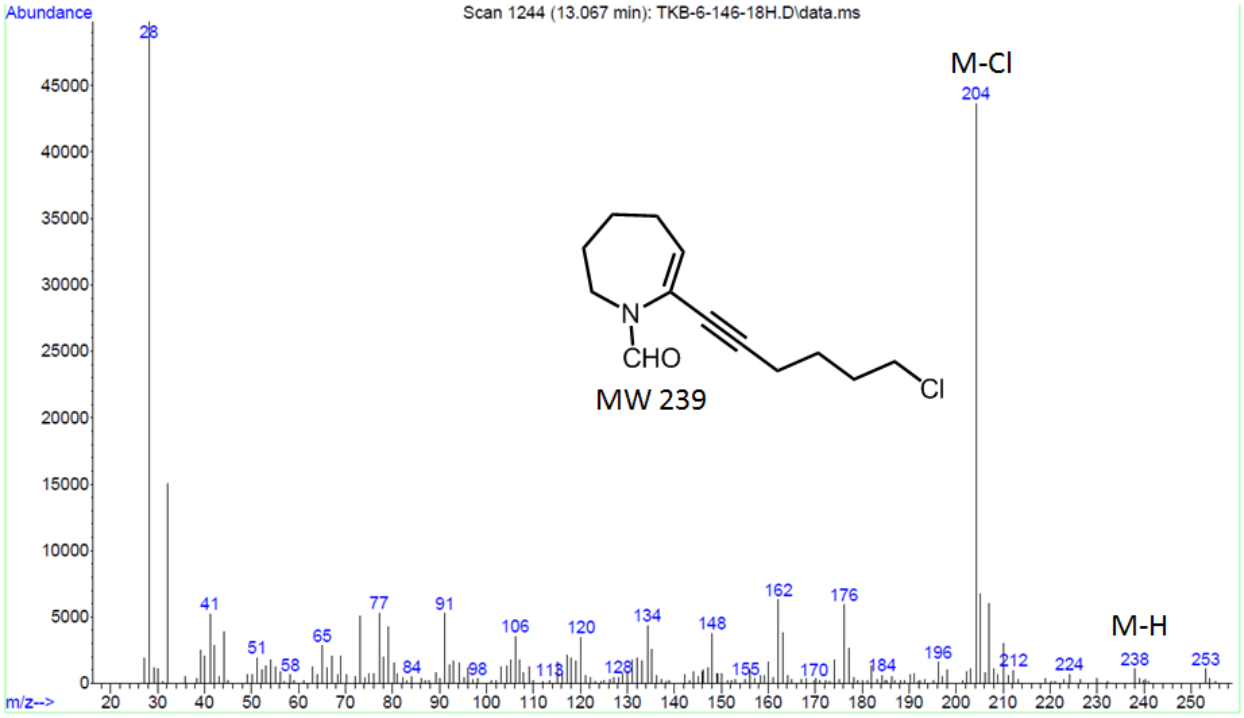
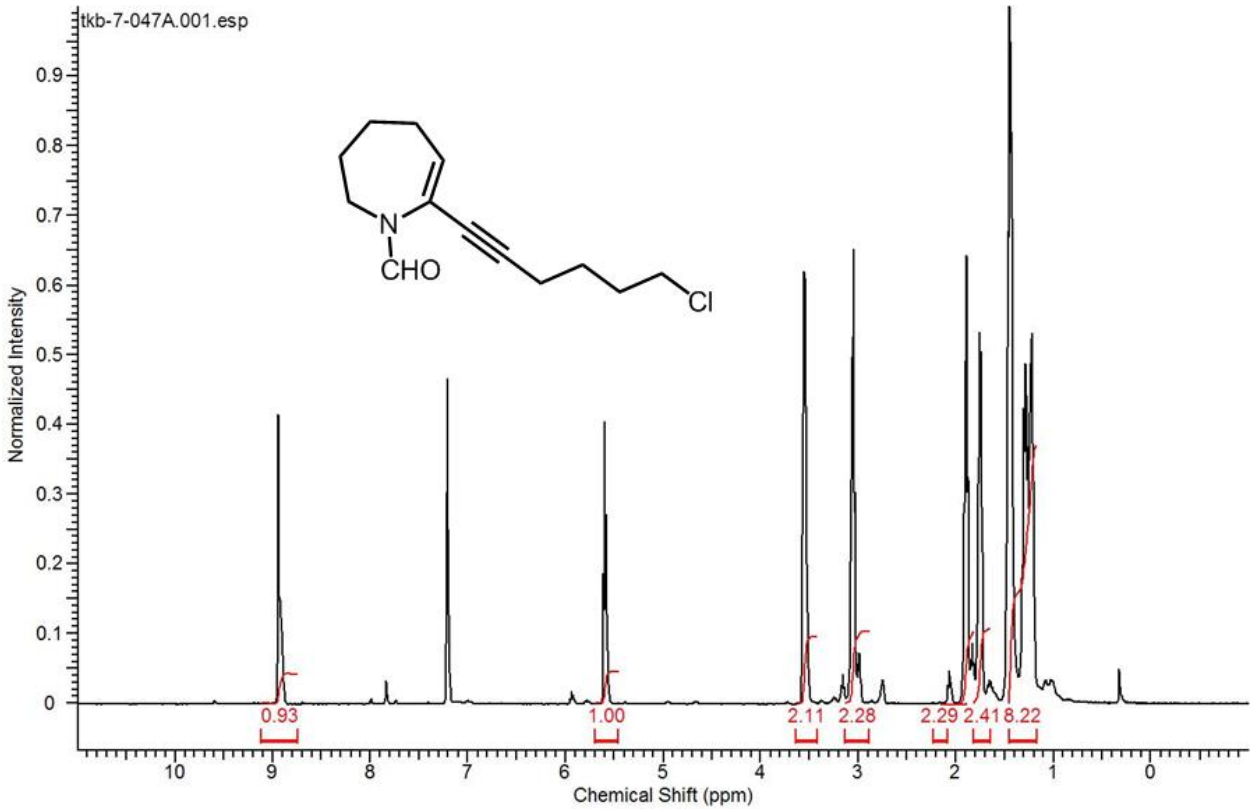
Chemical Shift (ppm)



2x, 92%

Prepared from **3b** (160 mg, 1.0 mmol) and 6-chloro-1-hexyne (2.0 mmol, 2 equiv) using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (90:10). Yield = 220 mg, 92%. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.56 to 8.07 (1H, s), 5.80 to 5.77 (1H, t), 3.80 to 3.41 (2H, t), 2.68 to 2.19 (4H, m), 1.93 to 1.50 (10H, m). ^{13}C NMR (101 MHz, Chloroform-d) δ 162.5, 128.8, 125.4, 89.9, 8.1, 44.5, 31.6, 28.7, 27.8, 25.6, 23.6, 18.6. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{13}H_{18}ClNO$ 239.1077; found 239.1074.

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CHO
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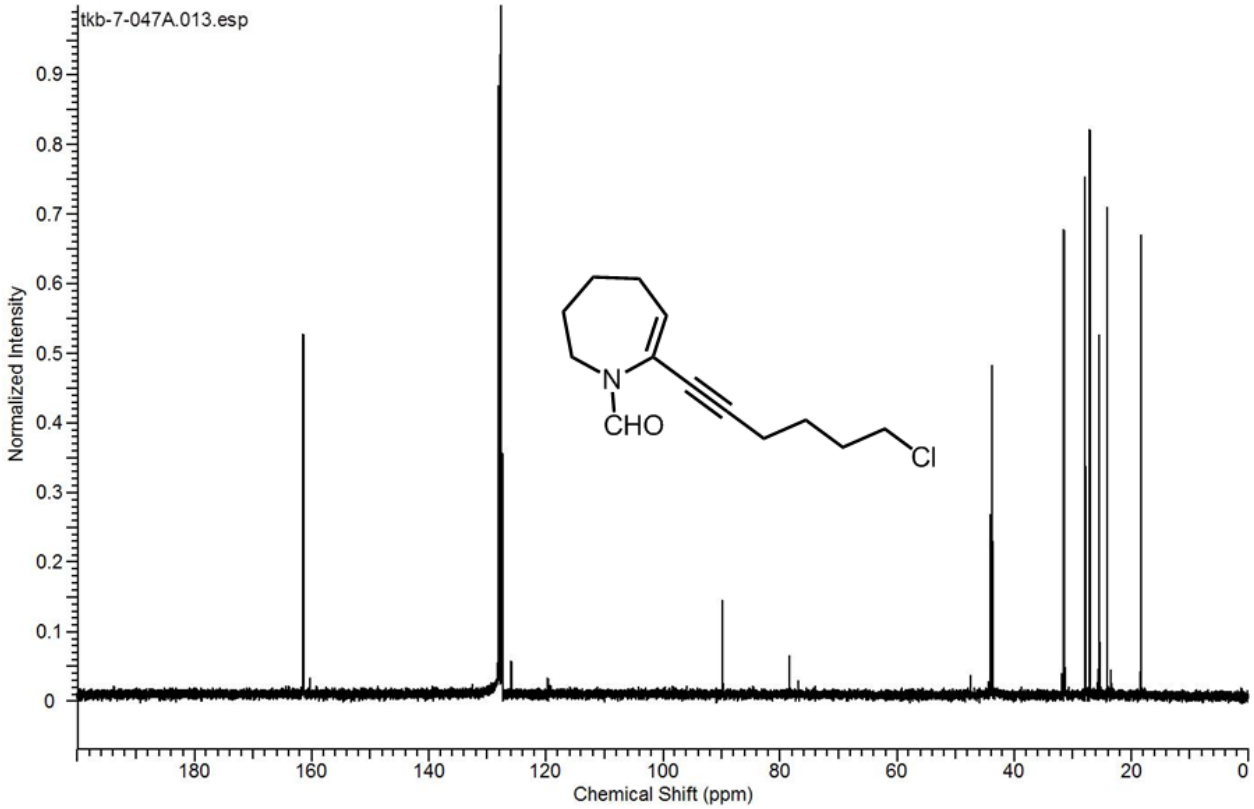
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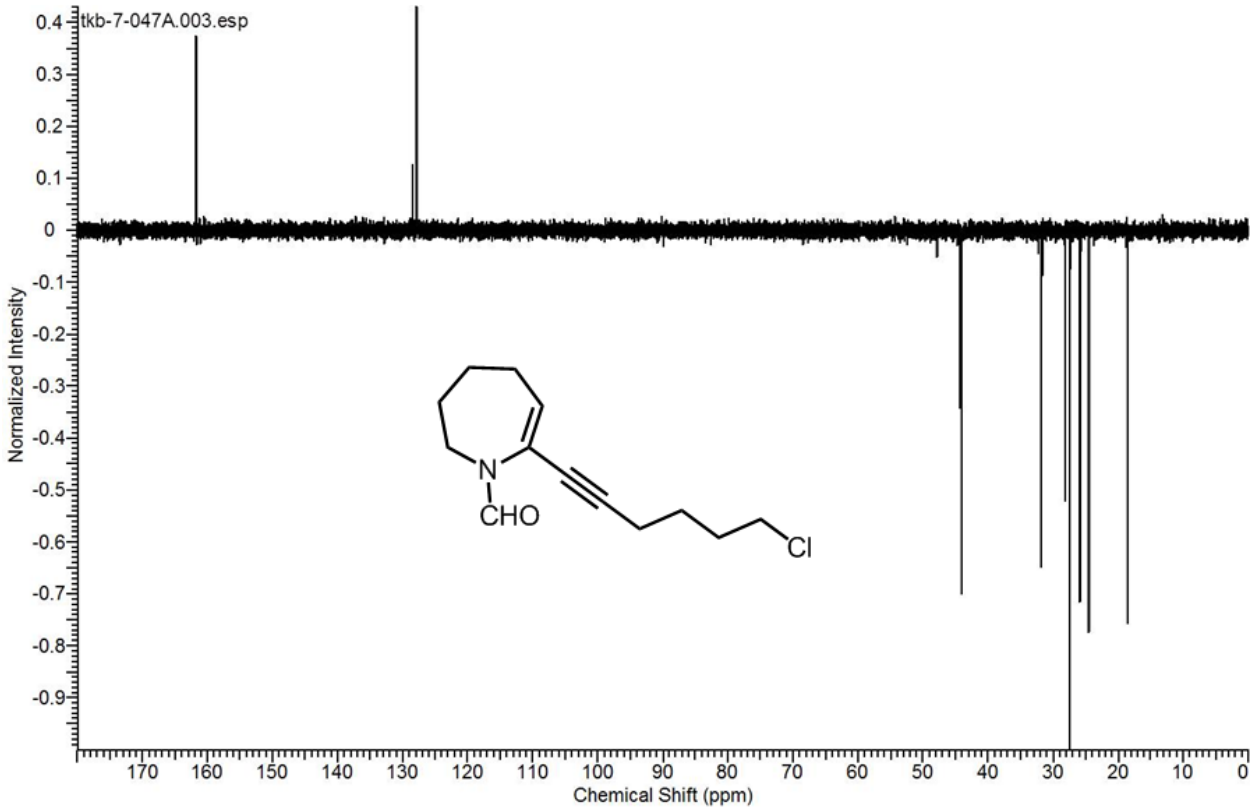
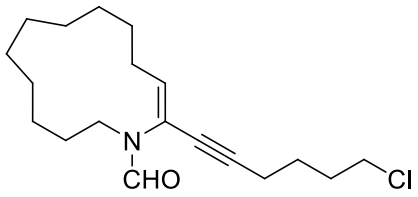
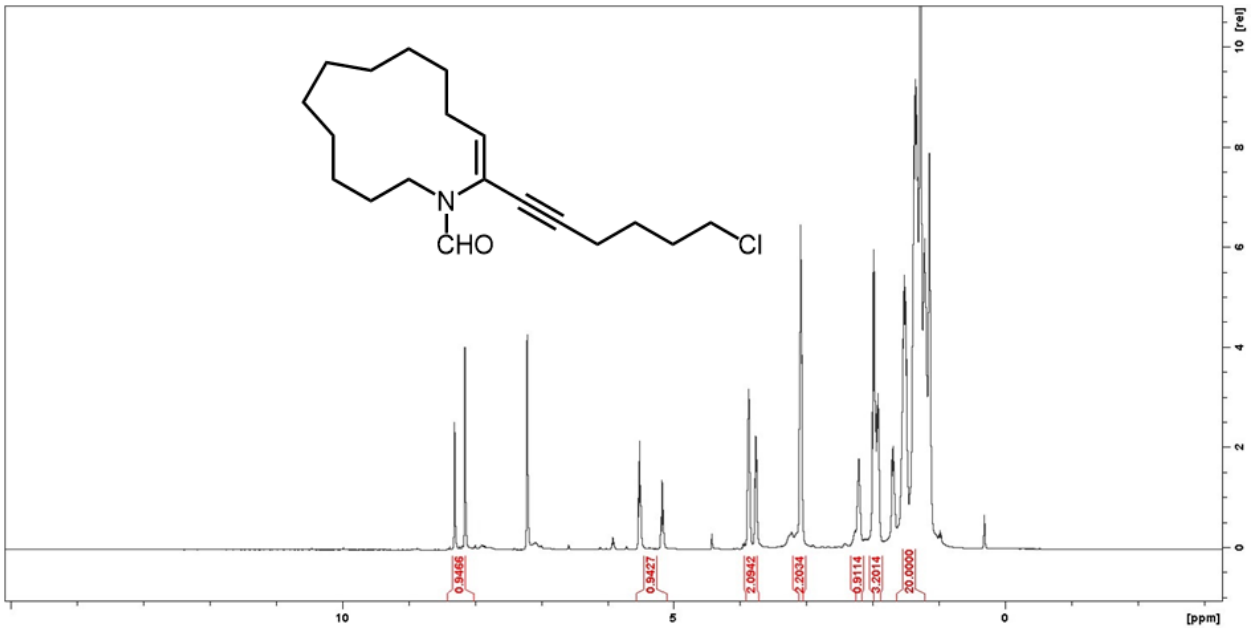
Normalized Intensity
Chemical Shift (ppm)
N
CHO
Cl





2y, 93%

Prepared from **3c** (243 mg, 1.0 mmol) and 6-chloro-1-hexyne (2.0 mmol, 2 equiv) using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (90:10). Yield = 300 mg, 93%. ^{1}H NMR (400 MHz, Benzene-d_6, mixture of rotamers) δ 8.30 to 7.87 (1H, s), 5.53 to 5.15 (1H, t), 3.88 to 3.74 (2H, t), 3.24 to 3.06 (2H, m), 2.29 to 0.97 (24H, m). 13C NMR (101 MHz, Benzene-d6) δ 162.2, 161.1, 138.6, 138.2, 133.4, 123.5, 123.3, 95.3, 88.7, 77.7, 75.2, 44.1, 44.0, 42.3, 31.6, 28.5, 27.7, 26.7, 25.8, 25.6, 24.8, 24.5, 23.7, 23.6, 23.4, 18.4. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{19}H_{30}ClNO$ 323.2016; found 323.2020.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20.0000
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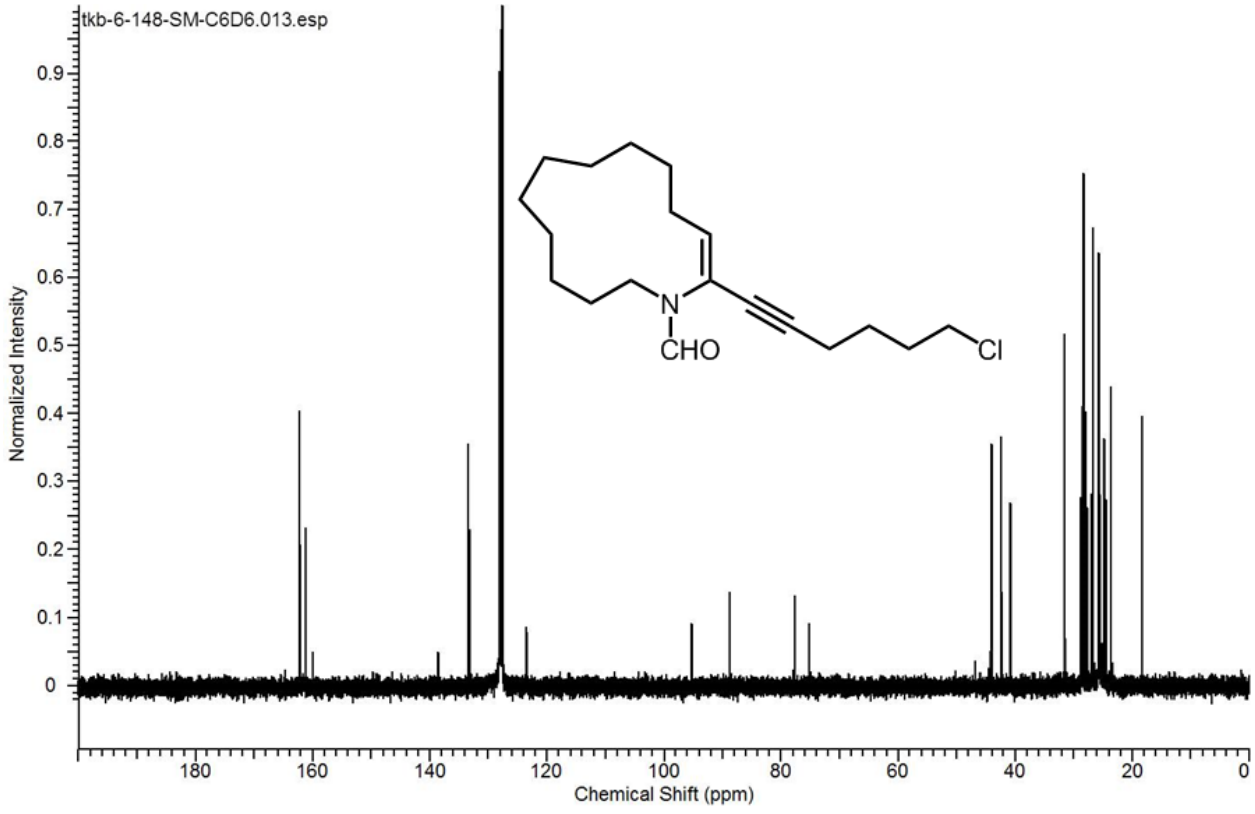
0
[ppm]
10 [rel]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CHO
Cl
Normalized Intensity
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80
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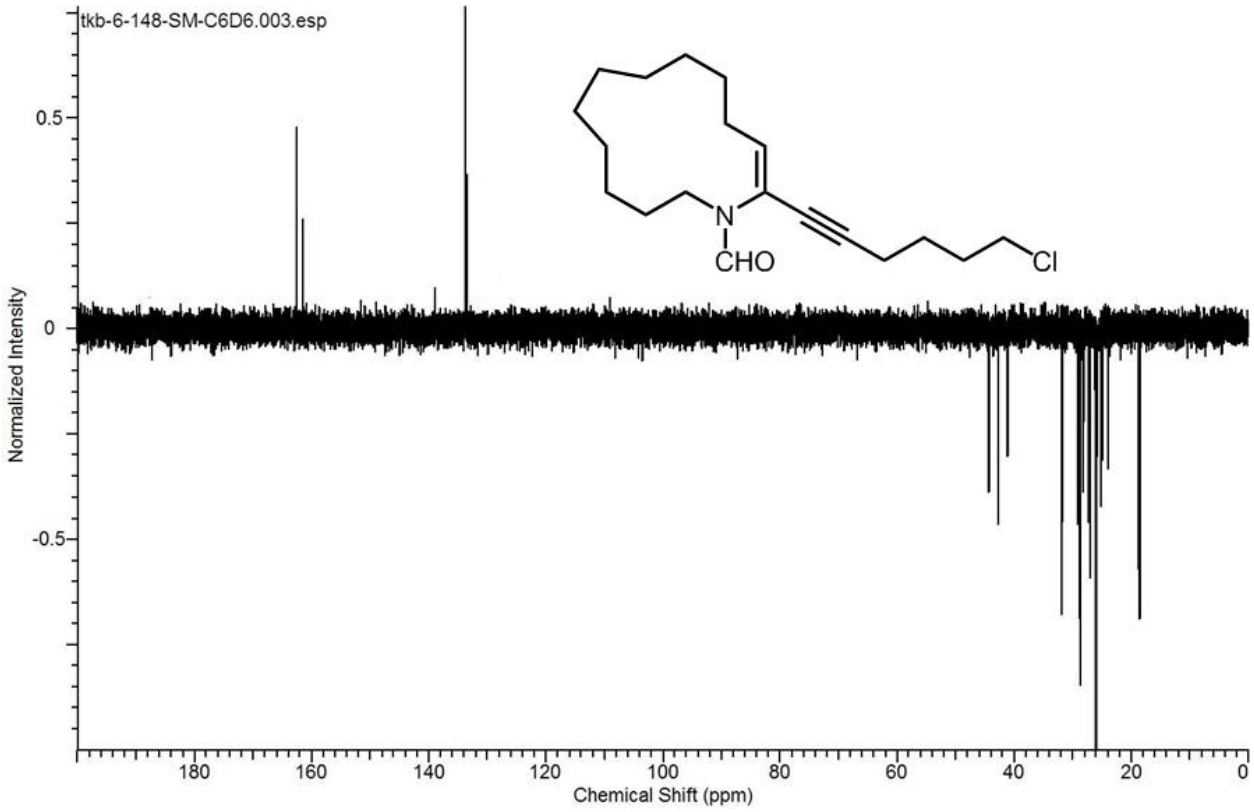
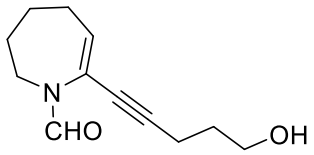
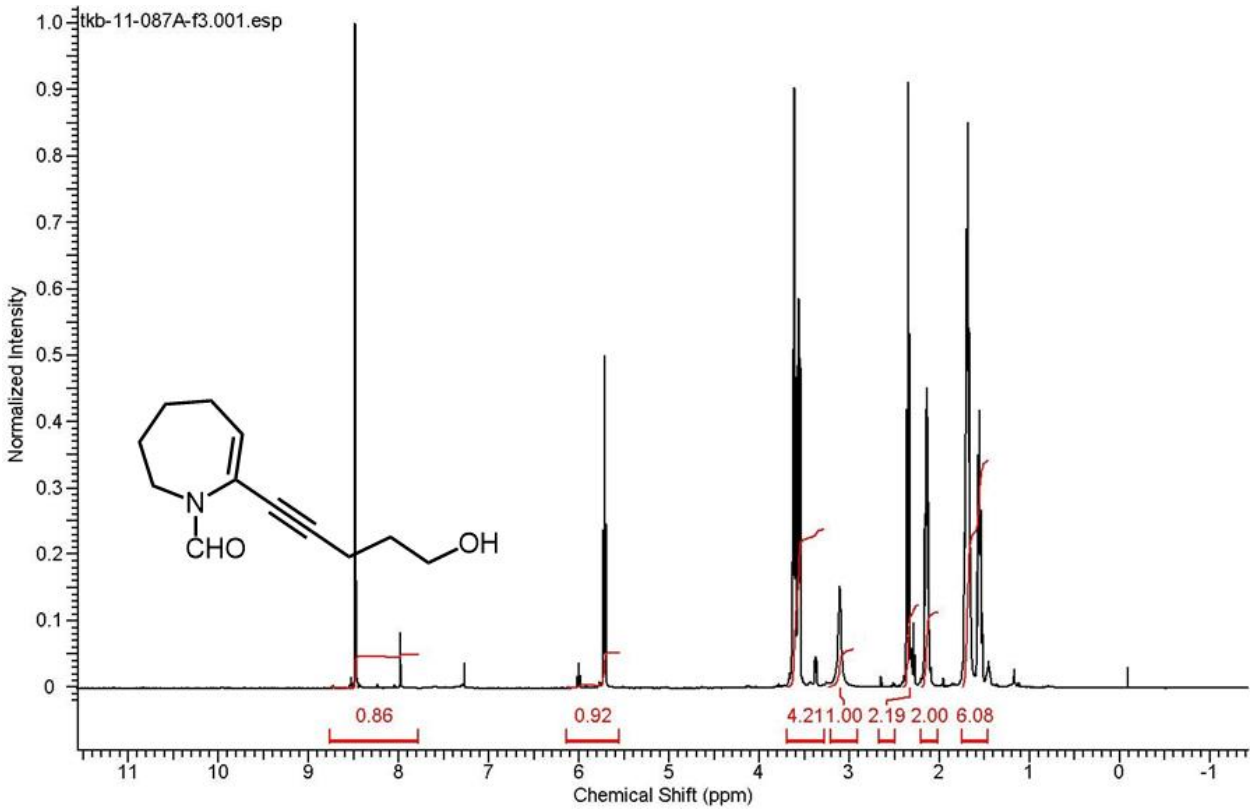
40
20
0
Chemical Shift (ppm)





2z, 86%

Prepared from **3b** (1.0 mmol) and 4-pentyn-1-ol (2.0 mmol, 2 equiv) using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (20:80). Yield = 178 mg, 86%. ^{1}H NMR (400 MHz, Chloroform-*d, rotamers*) δ 8.33 (s, 1H), 5.76 (t, *J* = 6.1 Hz, 1H), 3.58 – 3.49 (m, 4H), 3.15 (s, 1H), 2.30 (t, *J* = 7.0 Hz, 2H), 2.09 (p, *J* = 6.8, 6.4 Hz, 2H), 1.58 – 1.49 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.61, 134.11, 128.65, 125.42, 90.46, 77.52, 61.08, 48.49, 44.22, 32.18, 31.17, 31.14, 30.96, 27.74, 27.32, 24.15, 23.52, 15.90, 15.76, 15.73. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{12}H_{17}NO_2$ 207.1259; found 207.1263.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Normalized Intensity
Chemical Shift (ppm)
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2.00
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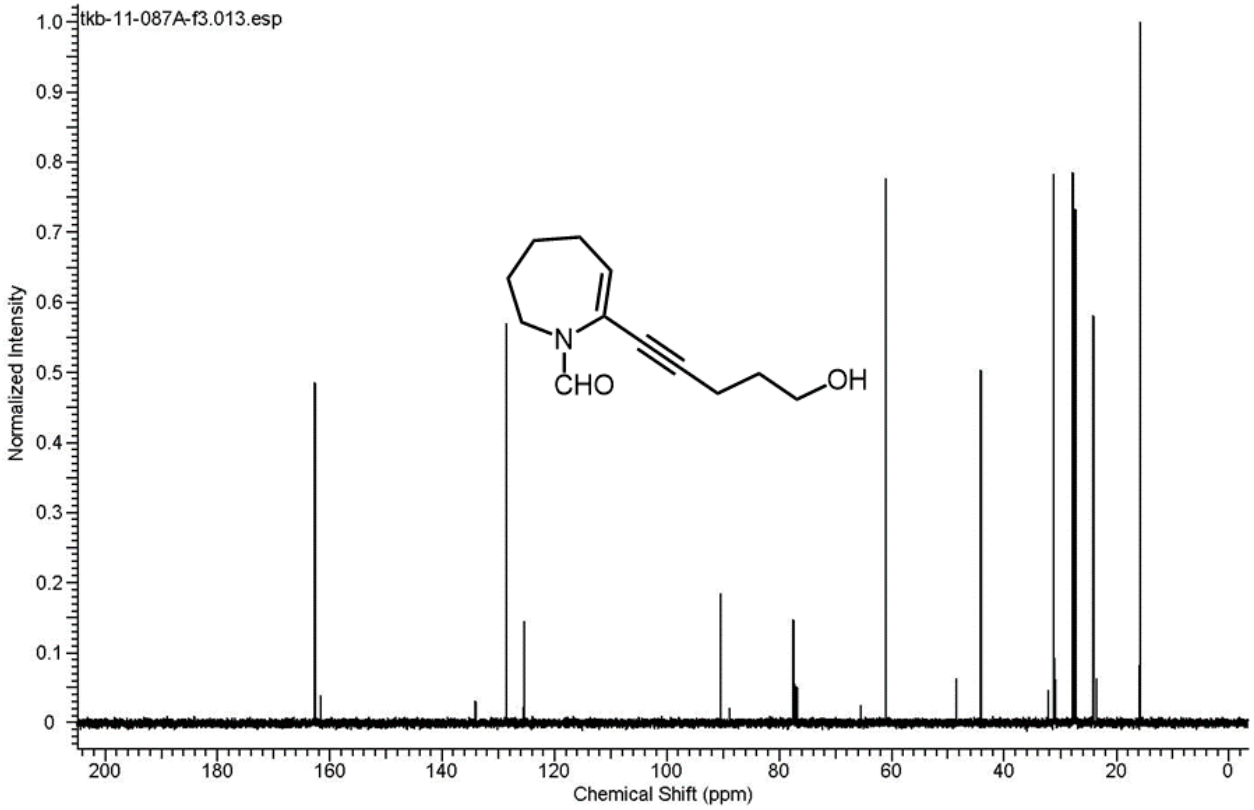
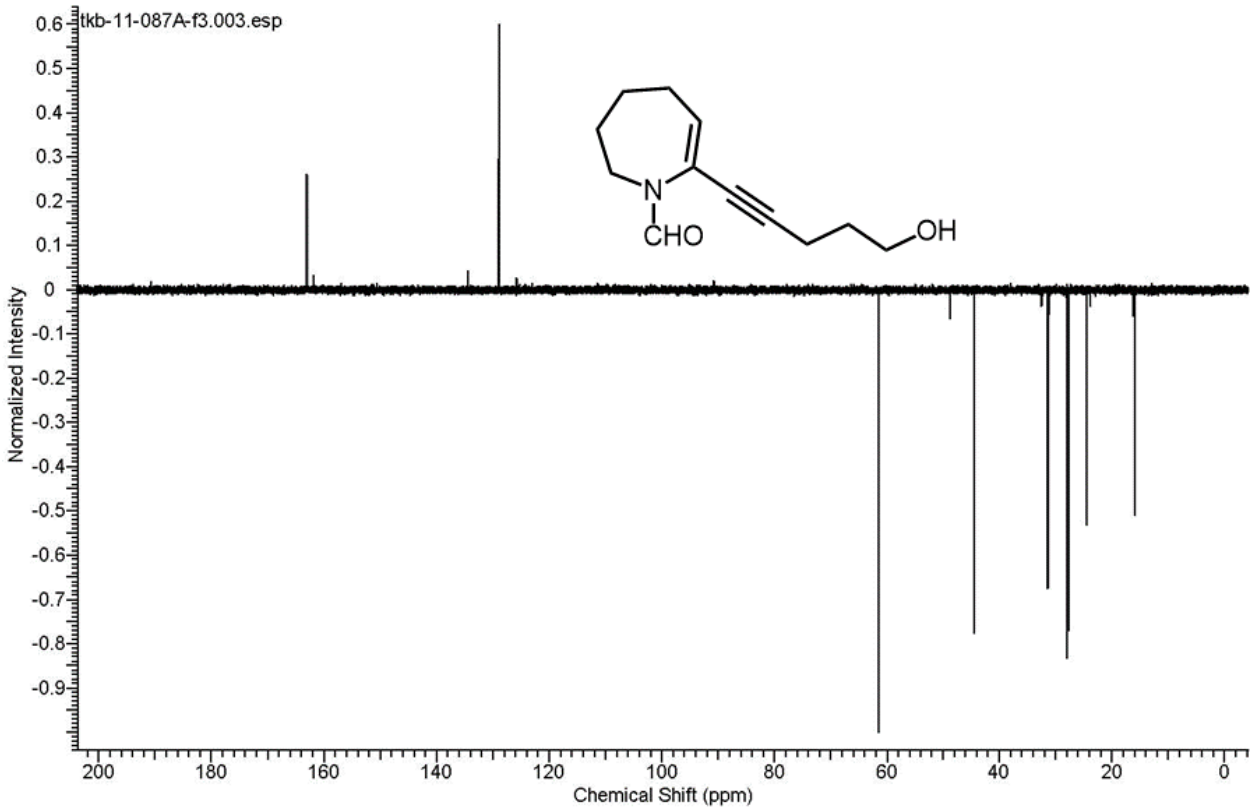
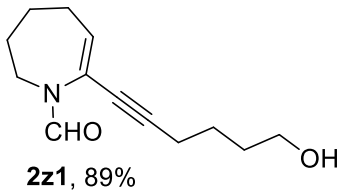
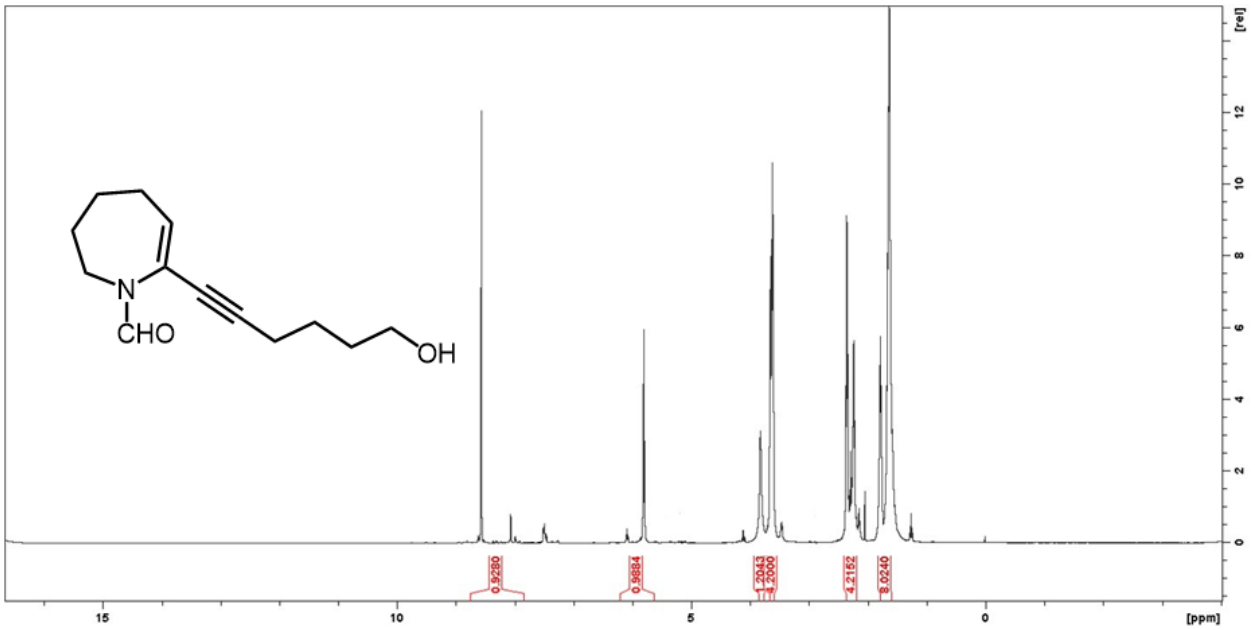

tkb-11-087A-f3.013.esp
Normalized Intensity
Chemical Shift (ppm)
N
CHO
OH





2z1, 89%

Prepared from **3b** (1.0 mmol) and 5-hexyn-1-ol (2.0 mmol, 2 equiv) using **General Procedure A.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (20:80). Yield = 197 mg, 89%. ^{1}H NMR (400 MHz, Chloroform-*d, mixture of rotamers*) δ 8.22 (s, 1H), 5.56 (t, *J* = 6.1 Hz, 1H), 3.58 (s, 1H), 3.44 – 3.33 (m, 4H), 2.15 – 1.95 (m, 4H), 1.42 – 1.26 (m, 8H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.63, 161.50, 128.64, 128.51, 128.45, 125.33, 119.61, 90.80, 77.42, 65.56, 62.12, 61.76, 61.72, 61.57, 61.55, 44.14, 31.74, 31.62, 27.63, 27.22, 24.75, 24.69, 24.07, 18.90. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{13}H_{19}NO_2$ 221.1416; found 221.1419.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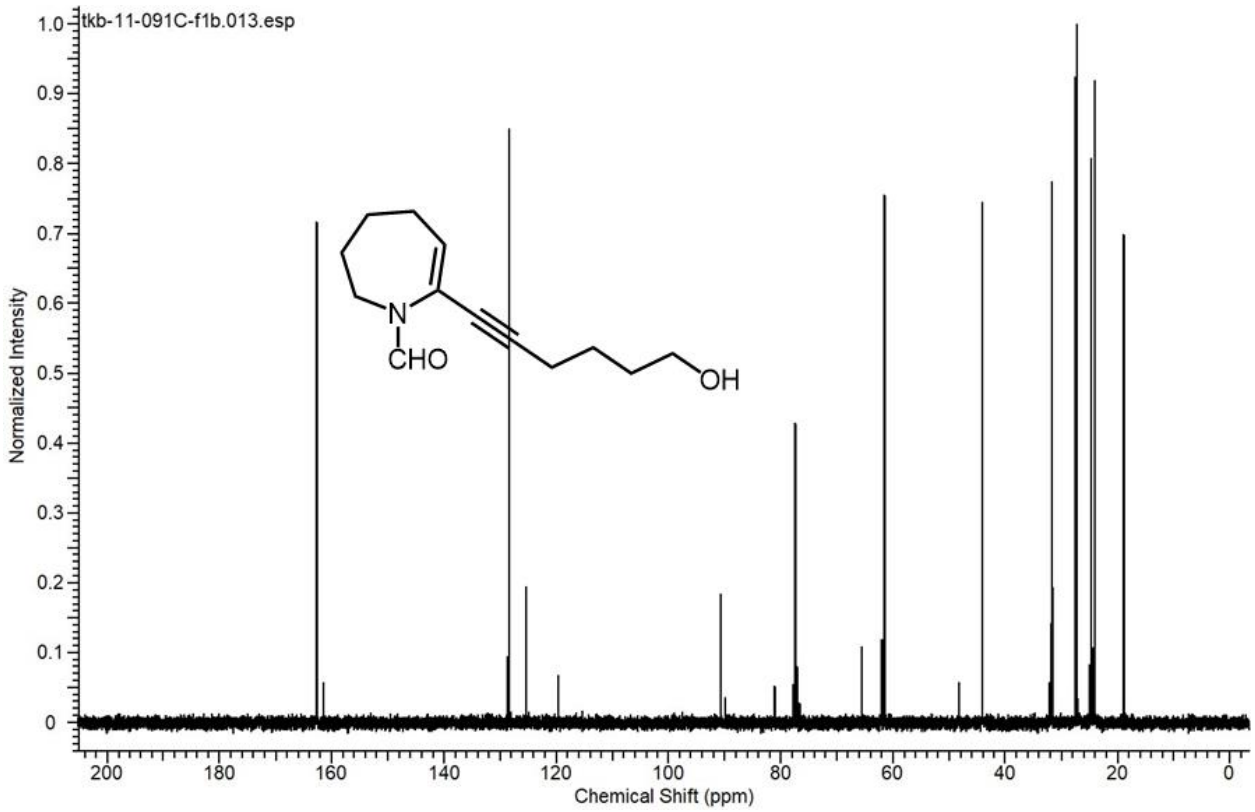
5
0
[ppm]
[rel]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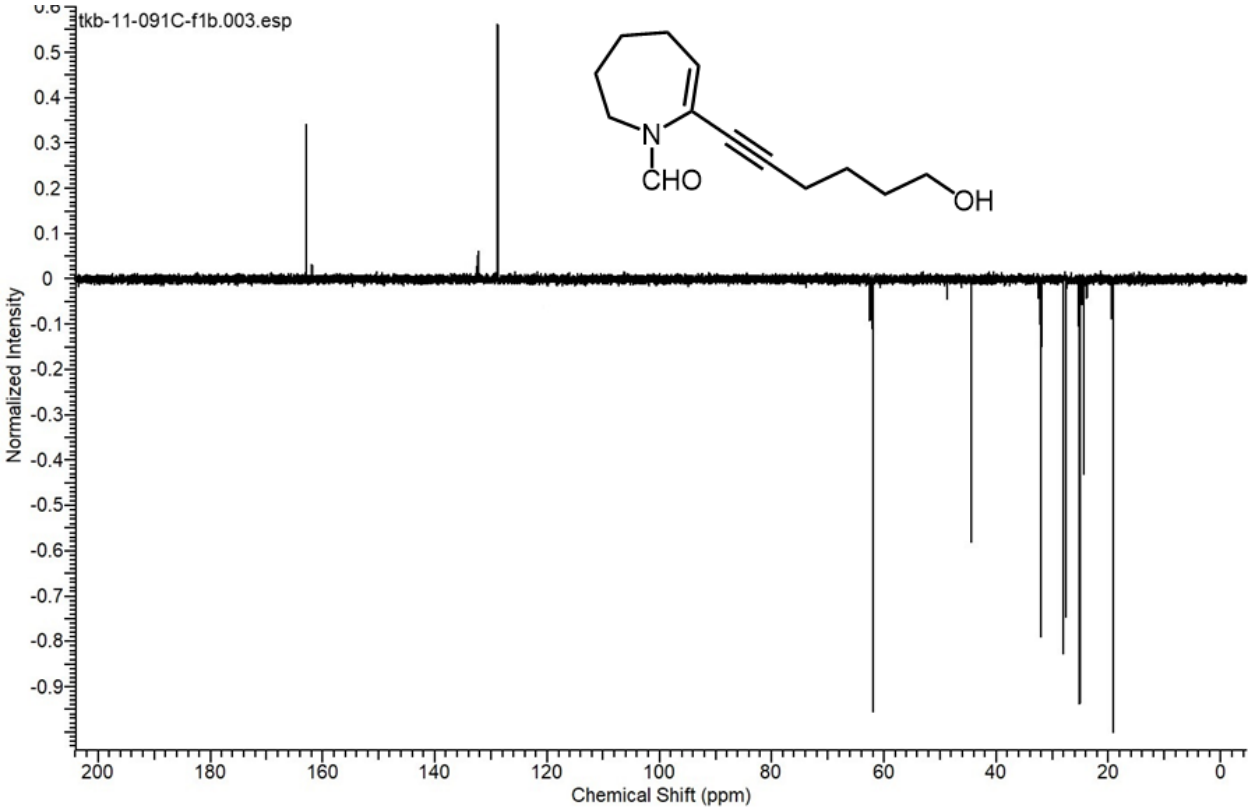
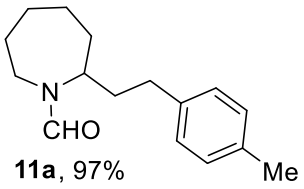
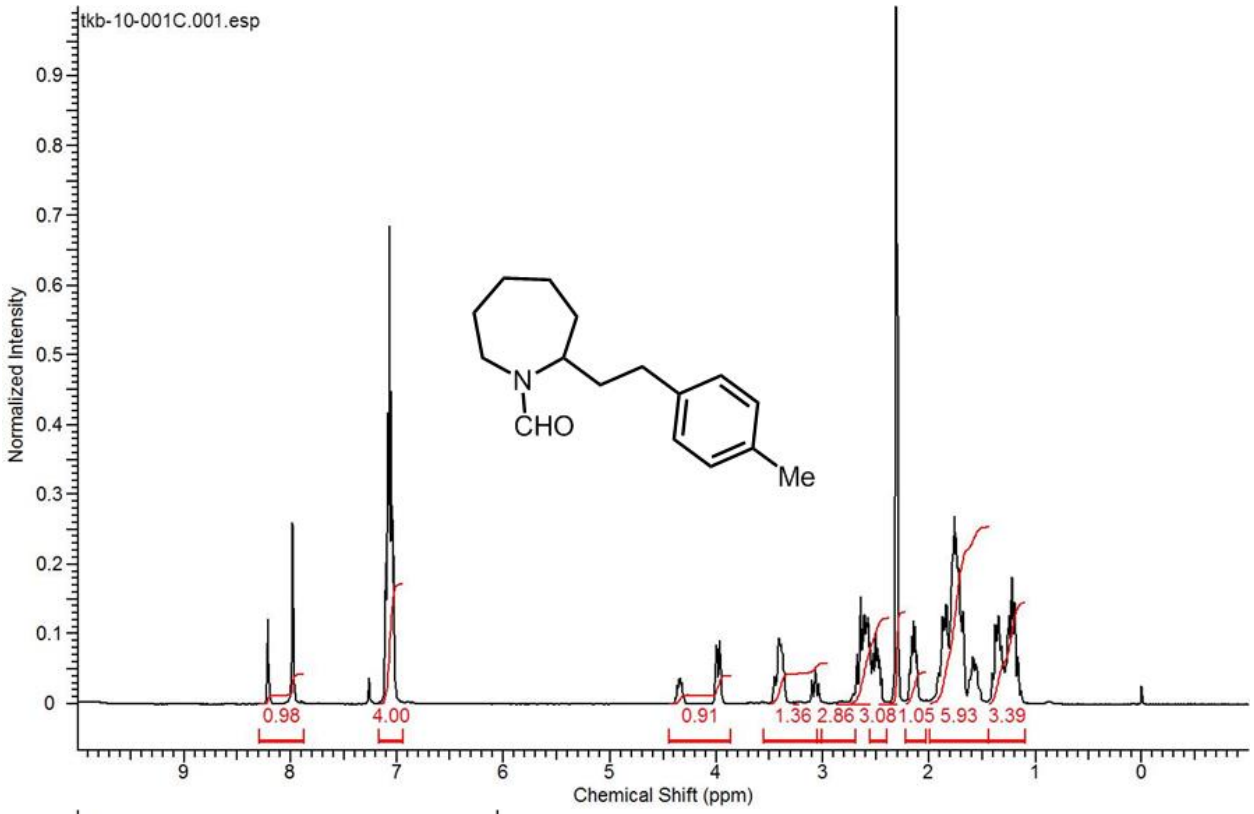
CHO
OH
Normalized Intensity
Chemical Shift (ppm)





11a, 97%

Prepared using **General Procedure B.** Yield = 119 mg, 97%. ^{1}H NMR (400 MHz, Chloroform-*d*, *mixture of rotamers*) δ 8.20 & 7.98 (s, 1H), 7.17 – 7.01 (m, 4H), 4.36 – 3.98 (m, 1H), 3.47 – 3.34 (m, 1H), 2.72 – 2.43 (m, 3H), 2.31 (s, 3H), 2.15 (dt, *J* = 14.7, 7.4 Hz, 1H), 1.85 – 1.66 (m, 6H), 1.30 – 1.11 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 163.6, 138.8, 137.7, 135.7, 135.3, 129.3, 129.1, 128.2, 57.6, 52.3, 44.0, 39.6, 36.7, 36.6, 34.8, 33.3, 32.3, 32.1, 31.8, 30.2, 29.5, 27.6, 24.9, 24.6, 21.0. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{19}H_{23}NO$ 245.1780; found 245.1782.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Normalized Intensity
Chemical Shift (ppm)
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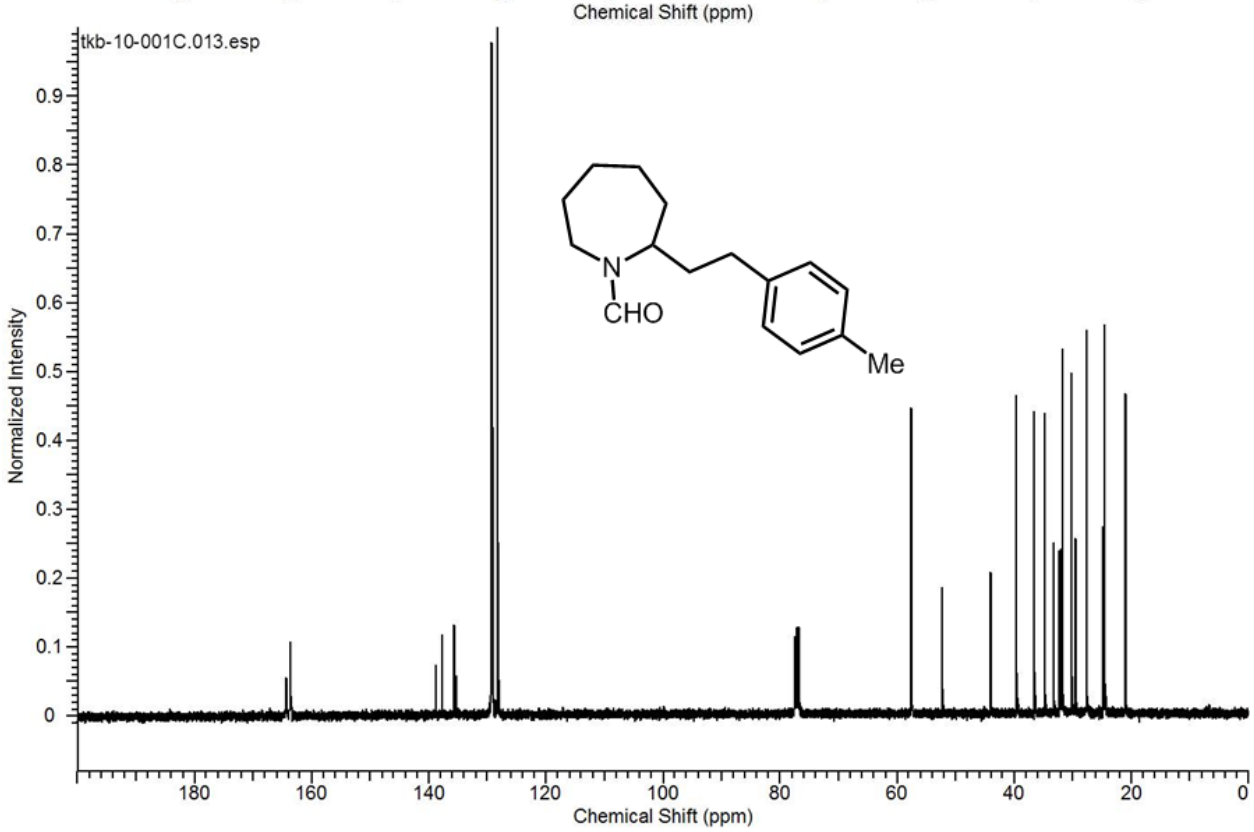
CHO
Me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Normalized Intensity
Chemical Shift (ppm)
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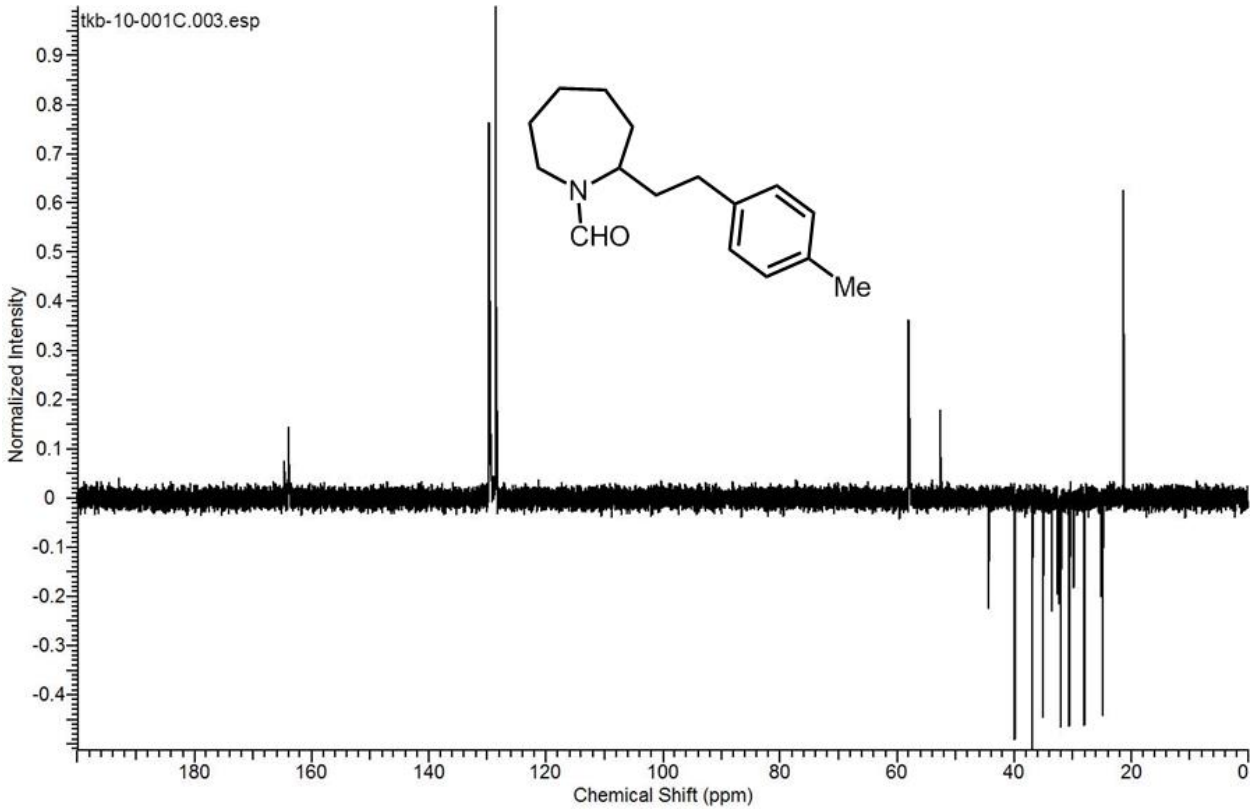
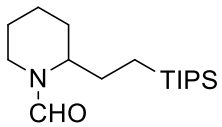
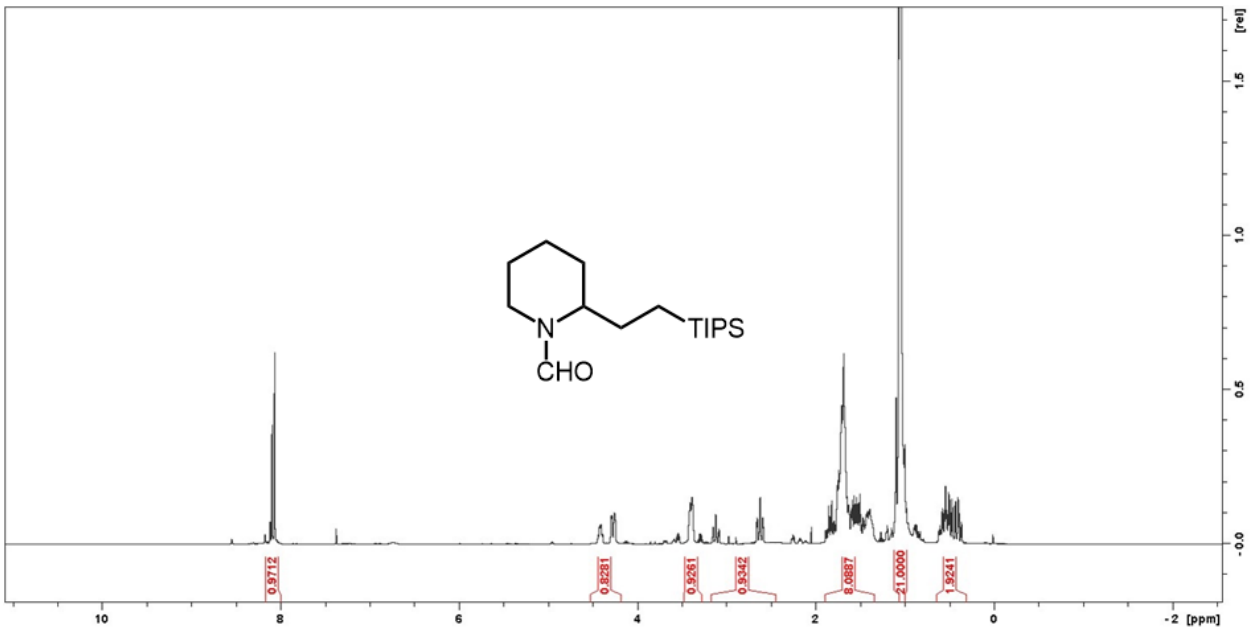
CHO
Me





11b, 93%

Prepared using **General Procedure B.** Yield = 138 mg, 93%. ^{1}H NMR (400 MHz, Chloroform-*d*, *mixture of rotamers*) δ 7.82 & 7.80 (s, 1H), 4.11 & 3.94 (dt, *J* = 13.7, 3.2 Hz, 1H), 3.18 – 3.09 (m, 1H), 2.86 – 2.13 (m, 1H), 1.49 – 1.38 (m, 8H), 0.87 – 0.72 (m, 21H), 0.38 – 0.08 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4, 161.3, 58.0, 50.4, 42.6, 36.1, 29.7, 27.4, 26.7, 25.2, 24.9, 23.9, 20.1, 19.7, 18.9, 18.8, 18.7, 18.6, 11.0, 10.9, 10.8, 10.7, 5.9, 5.5. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{17}H_{35}NOSi$ 297.2488; found 297.2491.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1.9241
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2
0
-2 [ppm]
[rel]
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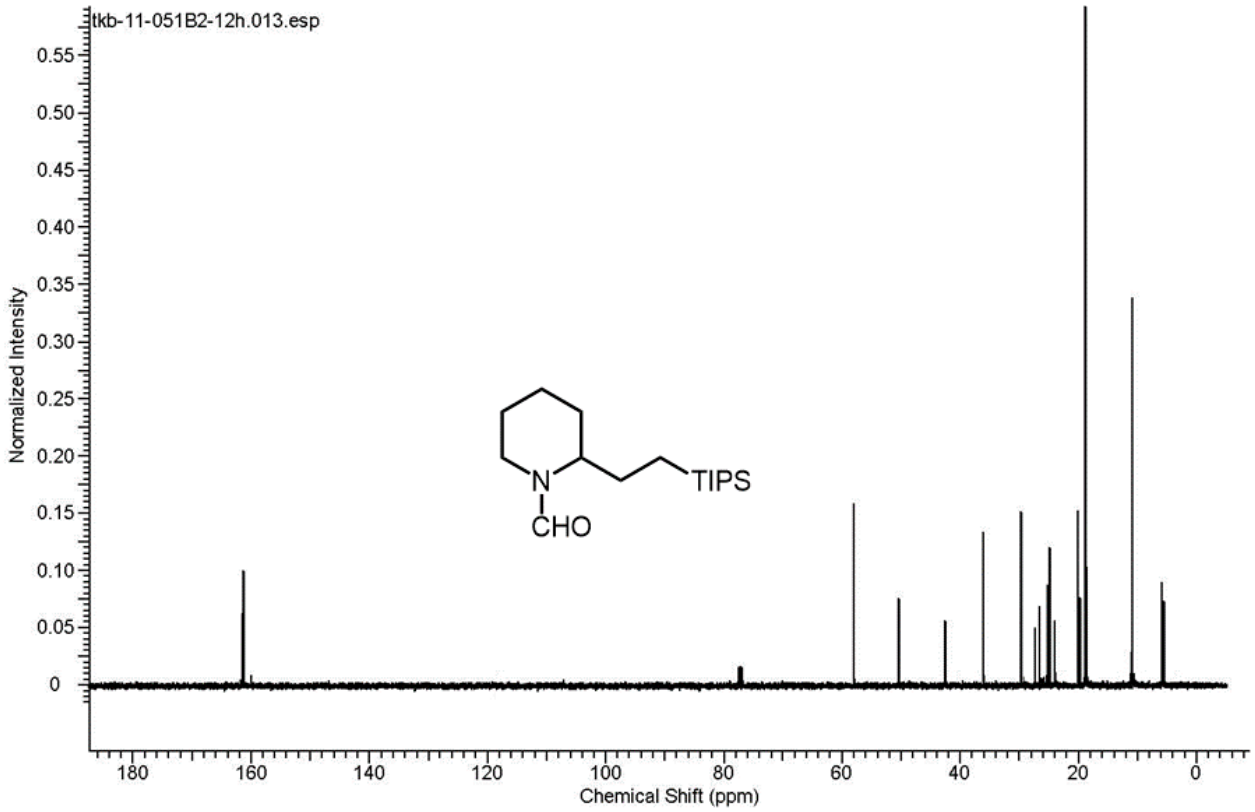
1.0
0.5
-0.0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0.15
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TIPS
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CHO
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80
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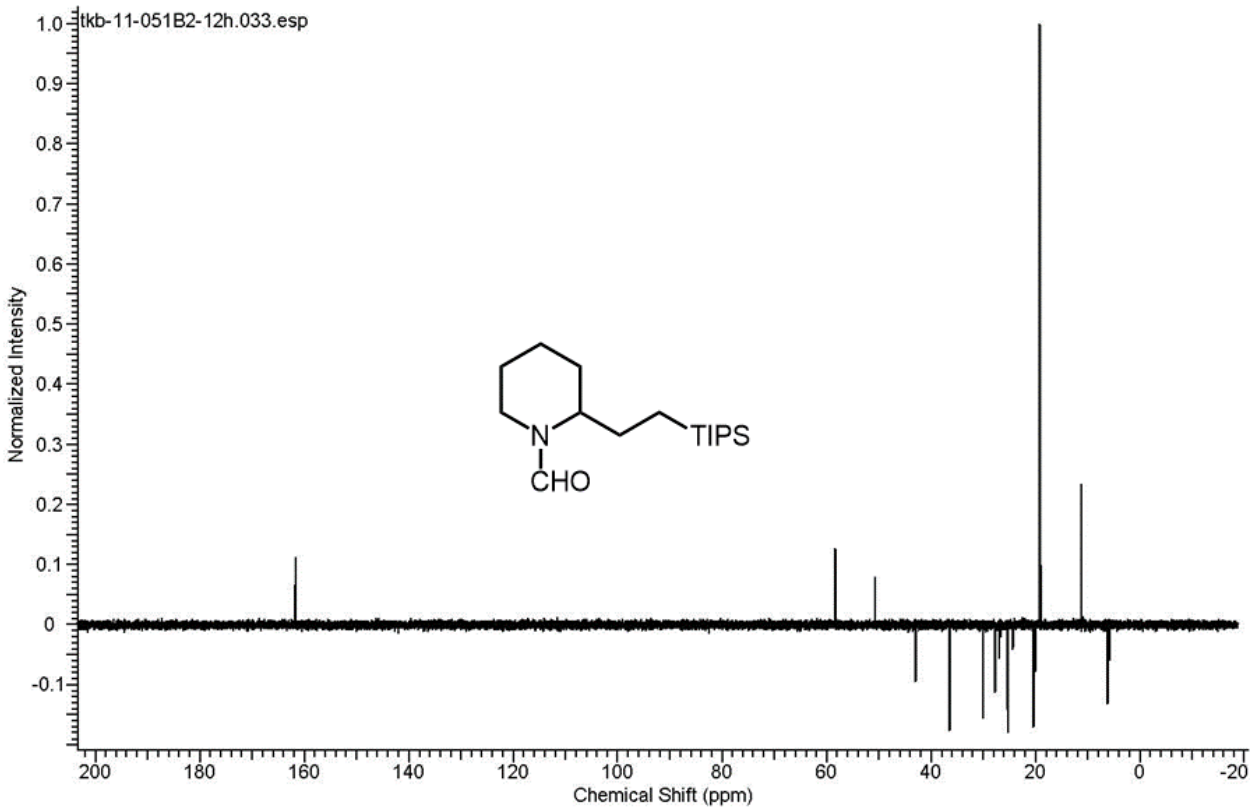
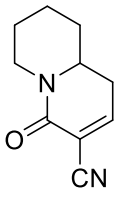
Chemical Shift (ppm)





4, 67%

***N*-formyl reduction of 2j:** To **2j** (291 mg, 1.0 mmol) dissolved in freshly distilled CH_2Cl_2 (10 mL) was added $NaBH_3CN$ (315 mg, 5 mmol, 5 equiv) slowly under nitrogen at 0 °C. TFA (1.14 g, 10 mmol, 10 equiv) was added slowly and the mixture was stirred for 10 min at 0 °C, then for ~12 h at room temperature (monitoring by LCMS and TLC; the reduced compound is significantly more polar). Upon completion, the reaction was quenched with *sat*. $NaHCO_3$. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered and evaporated to obtain the crude product, which were purified by flash chromatography on silica eluting with hexane/EtOAc.

Desilylation: To all of reduced **2j** in THF (10.0 mL) were added CF_3CO_2H (310 mg, 2.7 mmol) and a 1.0 M solution of TBAF (4.0 mL, 4.0 mmol) in THF successively at 0 °C. The resulting reaction mixture was stirred at 0 °C for 3 h. The reaction was quenched with water, and the aqueous layer was extracted with diethyl ether. The combined organic layers were washed with water and

brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give corresponding desilylated products.

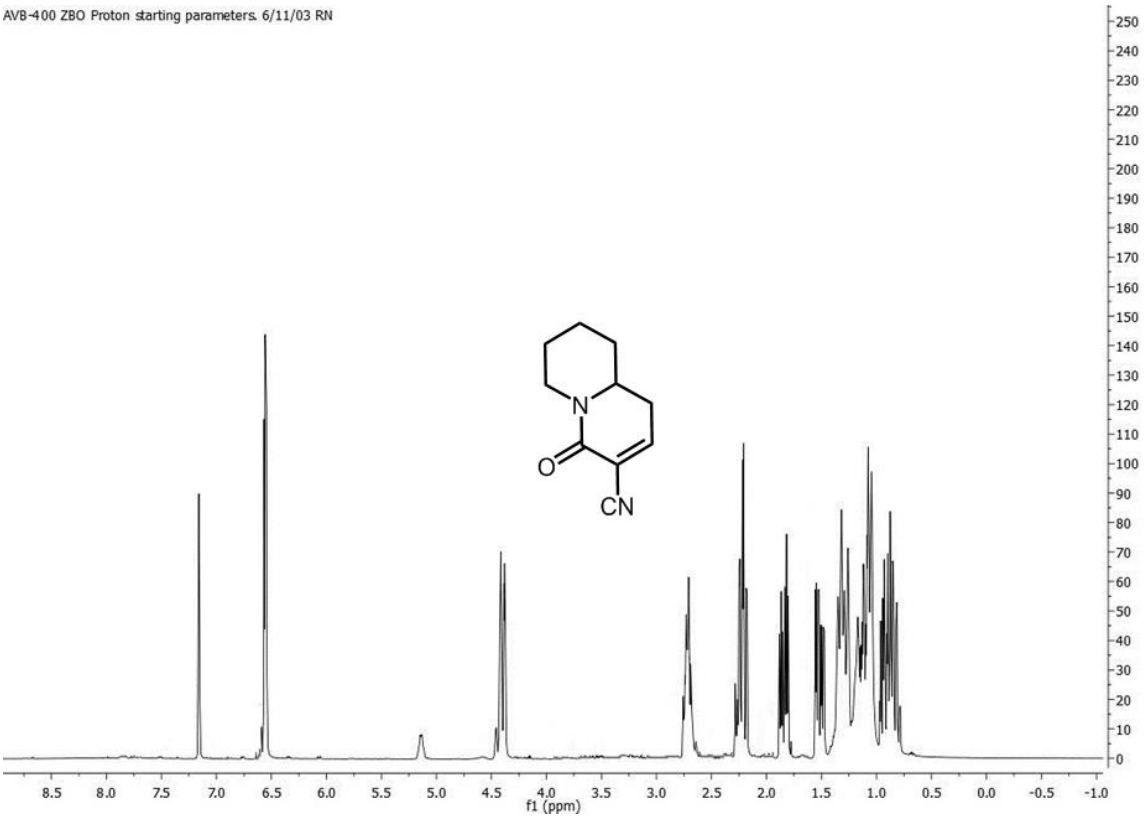
Hydroboration-oxidation[2]: To a solution of the crude alkynyl piperidine (1.0 equiv) in freshly distilled CH_2Cl_2 (4 mL) at –78 °C was added dropwise a 2 M solution of $BH_3{\cdot}SMe_2$ in THF (500 μL, 1 equiv). After a few minutes, the mixture was warmed to room temperature and stirring was continued for 6 h. It was then cooled to 0 °C and a few drops of 10% NaOH (aq) were added slowly followed by 0.5 mL of 30% H_2O_2. The mixture was returned to room temperature and stirred for 3 h. Water was added and the mixture was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford crude aldehyde as an oil.

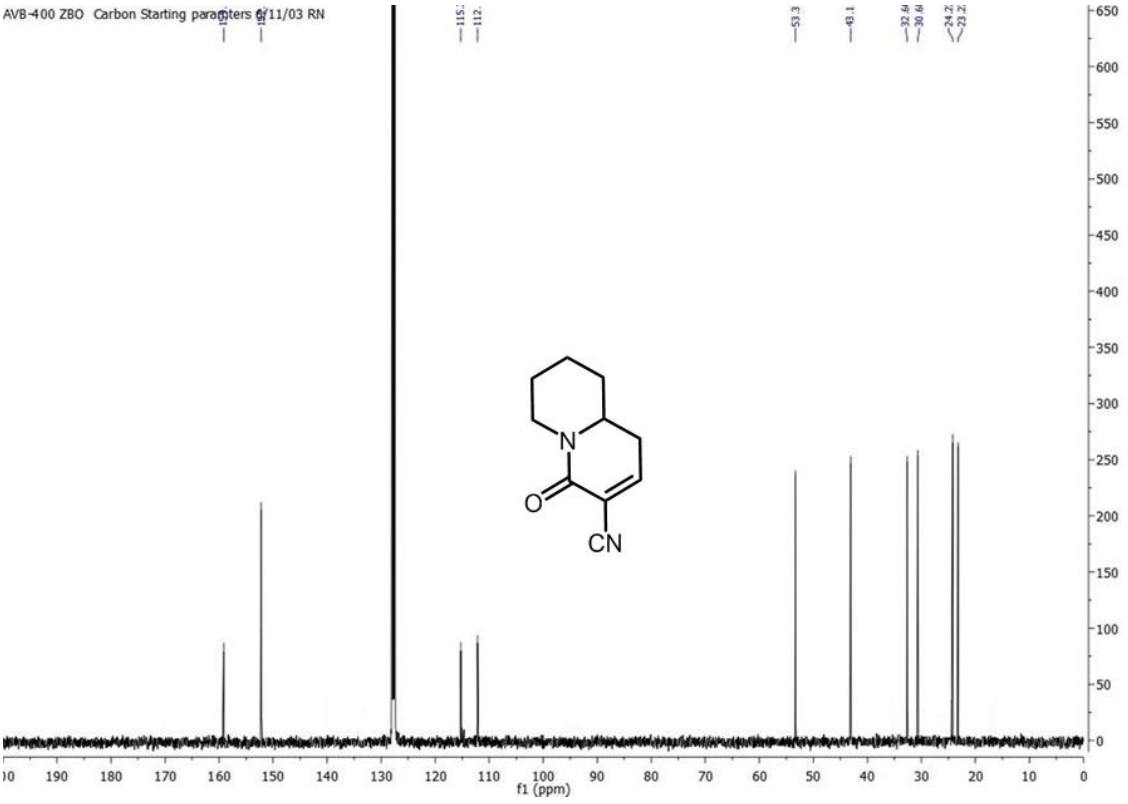
Deformylation: 6% HCl (1.5 mL) was added to the solution of *N*-formylated aldehyde (50 mg, 0.18 mmol) in MeOH (10 mL) and the resulting mixture was stirred at room temperature for 18 h. After completion of reaction (monitored by TLC), H_2O was added and the whole mixture was neutralized with aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic phase was washed with brine, dried over Na_2SO_4 and evaporated under reduce pressure to give the free piperidinal as an oil.

Acylation: The piperidinal was dissolved in dichloromethane (5 mL) and triethylamine (1.0 mL, 7.10 mmol) was added drop-wise at 0 °C, followed by the drop-wise addition of cyanoacetylchloride (727 mg, 7.10 mmol) as a solution in dichloromethane (2 mL). The resulting red solution was stirred at the same temperature for 2 h and then warmed to room temperature for 3 h, at which time saturated aqueous $NaHCO_3$ (10 mL) was added and volatiles removed *in vacuo*. The resulting aqueous solution was extracted with ethyl acetate (3 x 10 mL) and the combined organic extracts were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting acylated piperidinal was obtained as a red oil.

Knoevenagel condensation: To the acylated piperidinal was added a 20 mM solution of HCl/CH_2Cl_2 (prepared from AcCl/MeOH) and stirring was continued for 12 h at room temperature (TLC monitoring). The solution was diluted with DCM and transferred to a separatory funnel. Sat. aqueous NH_4Cl was added and the layers were separated. The aqueous layer was extracted with DCM and the combined layers were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo to obtain the bicycle as an oil. ^1H NMR (400 MHz, C_6D_6) δ 6.57 to 6.54 (t, 1H), 4.42 to 4.38 (m, 1H), 2.76 to 2.67 (m, 1H), 2.28 to 2.18 (m, 2H), 1.88, to 1.80 (m, 2H), 1.55

to 0.78 (m, 5H). ^{13}C NMR (101 MHz, C_6D6) δ 159.15, 152.19, 115.27, 112.15, 53.31, 43.11, 32.60, 30.68, 24.22, 23.22. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{10}H_{12}N_2O$ 176.0950; found 176.0955.

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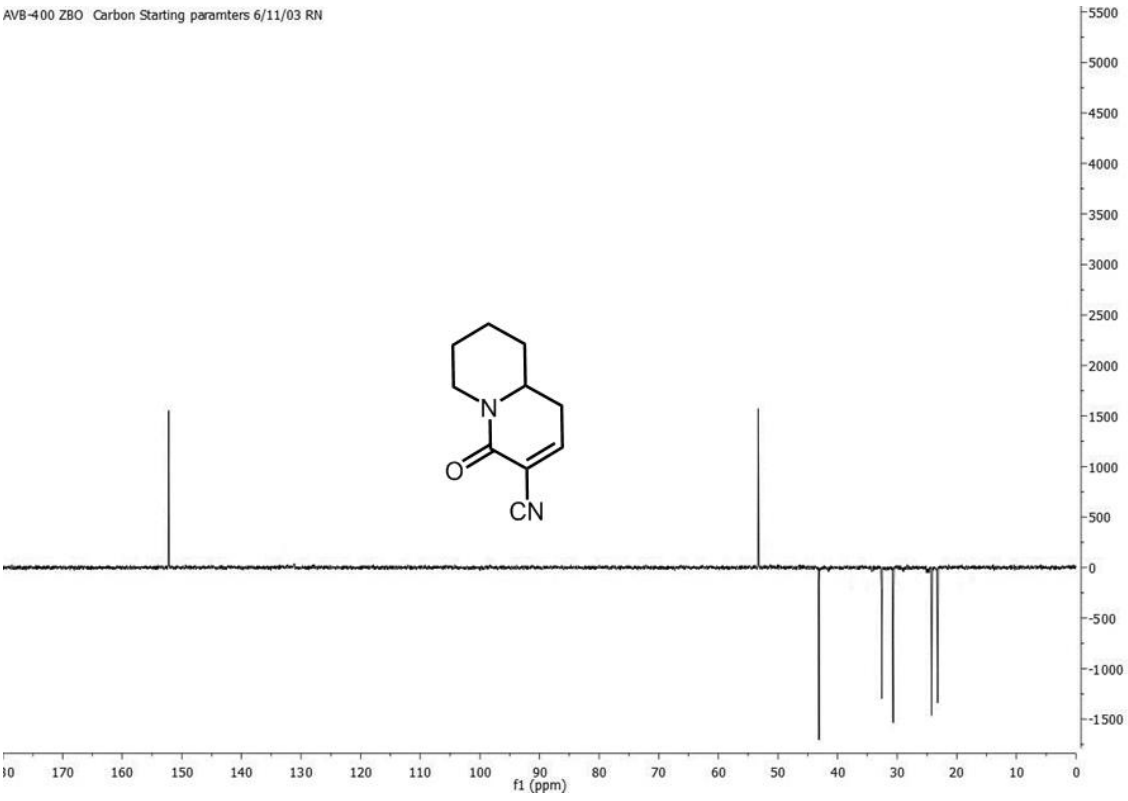
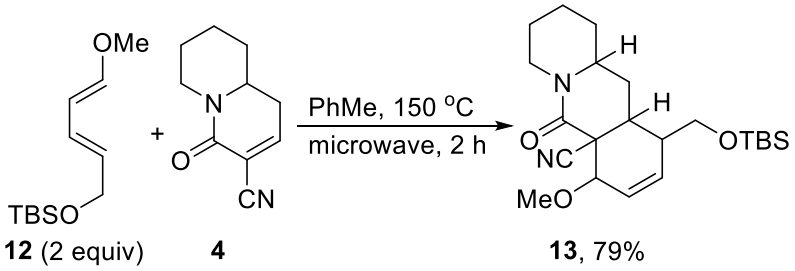
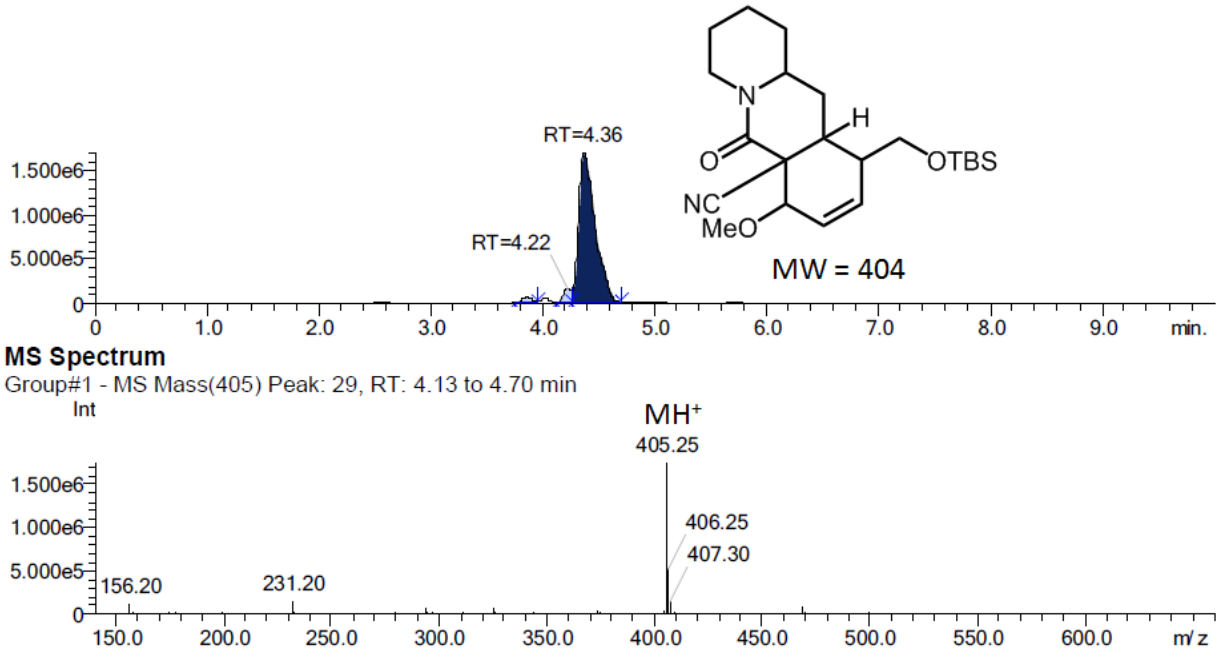
f1 (ppm)

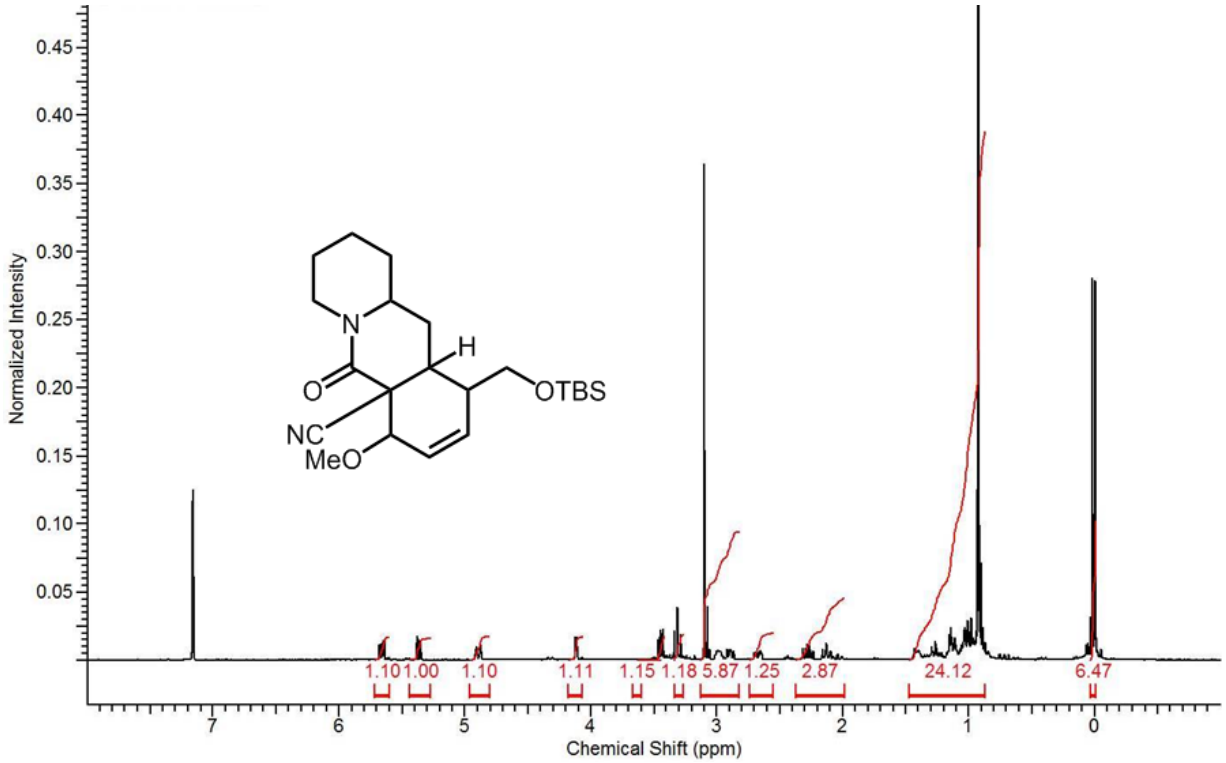

AVB-400 ZBO Carbon Starting paramters 6/11/03 RN
f1 (ppm)



A 10 mL microwave vial was flame-dried, evacuated and flushed with nitrogen. A solution of dienophile **4** (176 mg, 1.0 mmol) in toluene (2 mL) was added to the vial under a nitrogen atmosphere followed by a solution of diene **12**[3] (456 mg, 2 mmol) in toluene (2 mL). The mixture was heated to 150 °C under microwave irradiation for 2 h. It was then cooled to room temperature and the toluene was azeotroped off. Purification by flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (80:20) afforded tricycle **13** in 79% yield and >95:5 dr.

Note: It is critical to have absolutely pure starting materials as any minor impurities simply lead to decomposition of the diene. ^{1}H NMR (400 MHz, Benzene-d_6) δ 5.66 (ddd, J = 10.4, 4.3, 2.9 Hz, 1H), 5.37 (ddt, J = 10.4, 2.0, 1.0 Hz, 1H), 4.89 (dp, J = 13.1, 1.9 Hz, 1H), 4.12 (ddt, J = 4.1, 1.9, 0.9 Hz, 1H), 3.45 (dd, J = 9.9, 6.3 Hz, 1H), 3.31 (t, J = 9.8 Hz, 1H), 3.09 – 2.84 (m, 5H), 2.78 – 2.62 (m, 1H), 2.29 – 2.04 (m, 3H), 1.45 – 0.87 (m, 24H), 0.02 (s,s, 6H). ^{13}C NMR (101 MHz, C_6D_6) δ 161.9, 127.4, 123.7, 118.9, 76.7, 62.9, 59.1, 55.3, 49.1, 43.9, 38.0, 33.05, 31.0, 25.6, 25.3, 24.9, 23.3, 17.9, -5.7. **HRMS-EI**$^+$ (*m/z*): calc'd for $C_{22}H_{36}N_2O_3Si$ 404.2495; found 404.2491.




Normalized Intensity
Chemical Shift (ppm)
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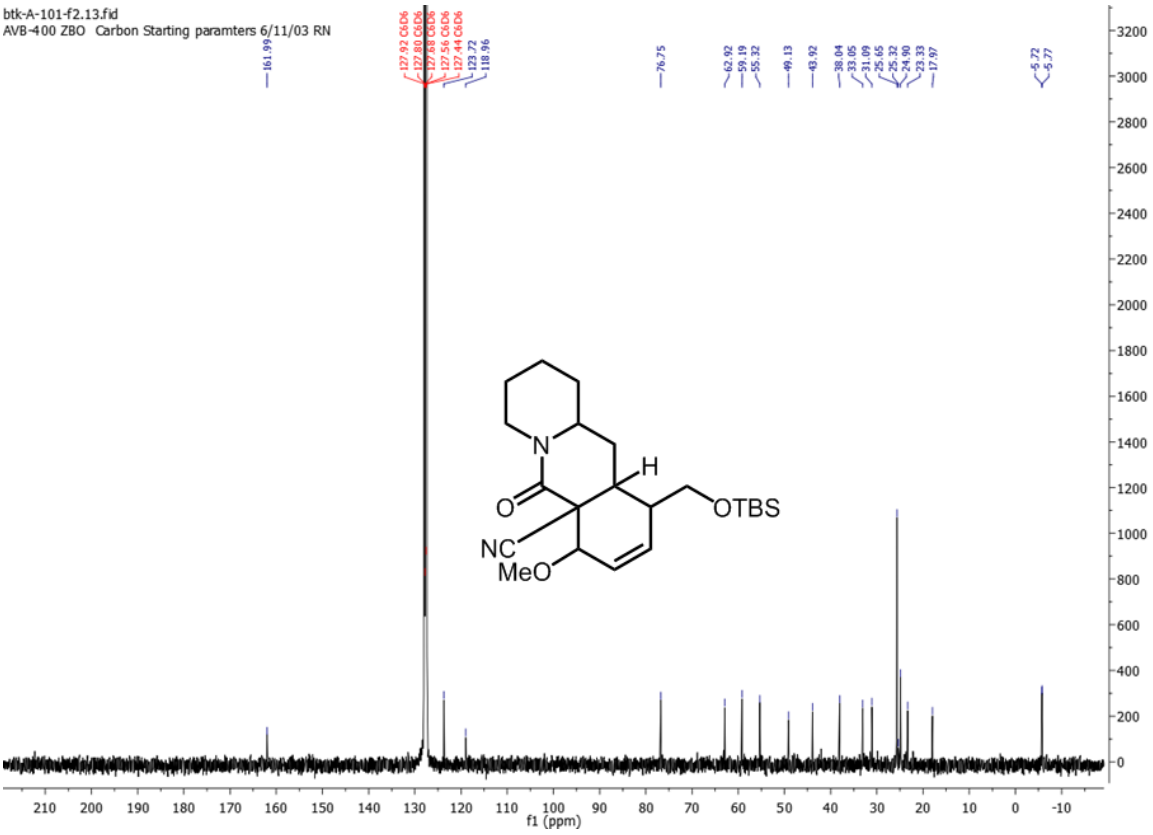
OTBS
NC
MeO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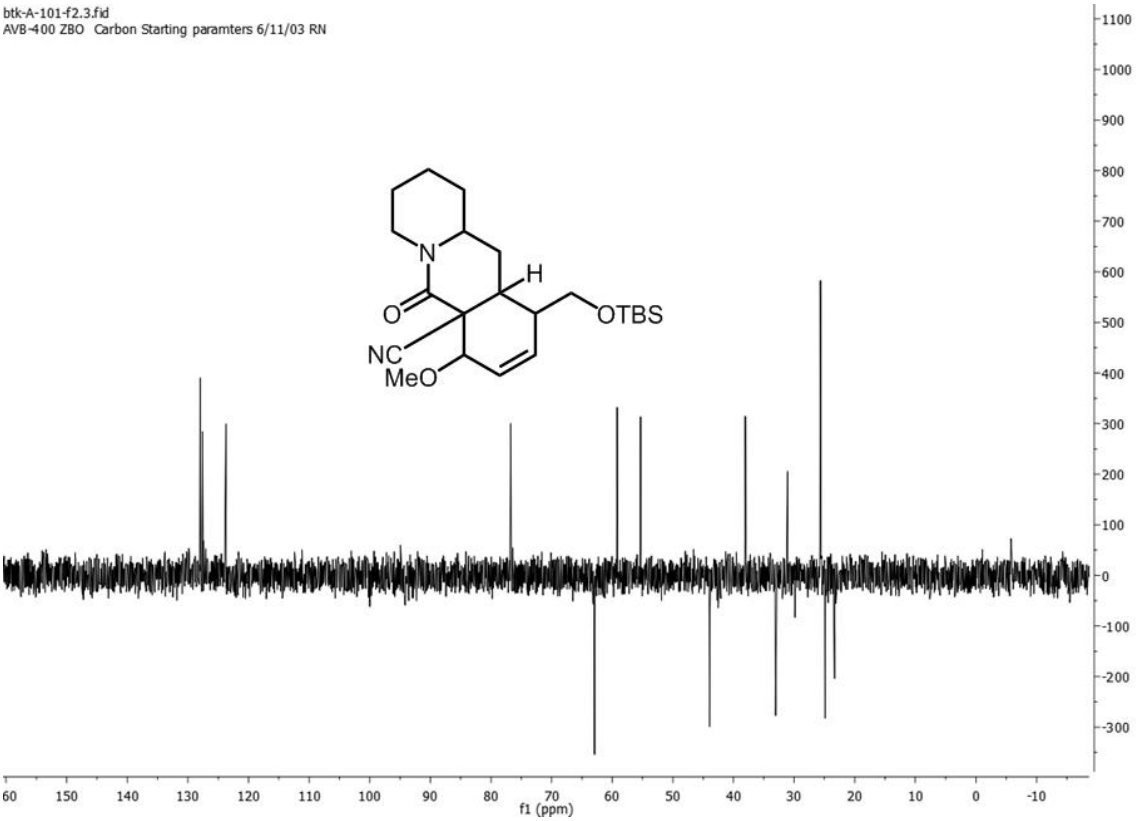
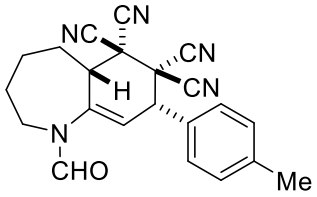
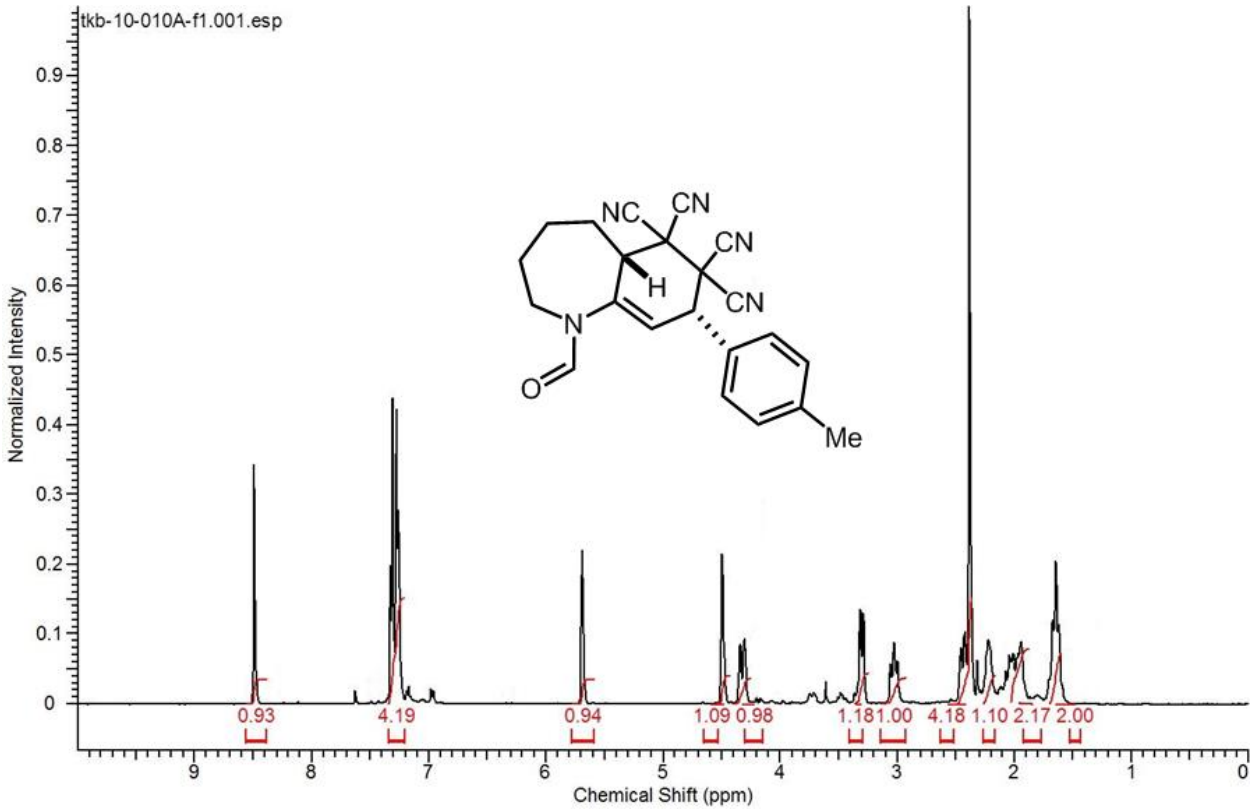
AVB-400 ZBO Carbon Starting paramters 6/11/03 RN
f1 (ppm)
N
H
O
OTBS
NC
MeO





14a; 95%, 95:5 dr

Prepared using **General Procedure C.** Yield = 176 mg, 95%. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.49 (s, 1H), 7.35 – 7.25 (m, 4H), 5.69 (d, *J* = 3.3 Hz, 1H), 4.49 (d, *J* = 3.3 Hz, 1H), 4.32 (dd, *J* = 15.1, 4.2 Hz, 1H), 3.30 (d, *J* = 10.5 Hz, 1H), 3.03 (t, *J* = 12.5 Hz, 1H), 2.44 (dd, *J* = 13.9, 4.8 Hz, 1H), 2.38 (s, 3H), 2.21 (q, *J* = 6.3 Hz, 1H), 1.98 (d, *J* = 33.5 Hz, 2H), 1.66 (q, *J* = 11.5, 11.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.7, 140.9, 137.6, 130.1, 129.9, 129.3, 113.2, 113.1, 111.5, 111.3, 109.7, 109.4, 46.9, 44.7, 43.9, 31.1, 28.6, 26.7, 21.3. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{22}H_{19}N_5O$ 369.1590; found 369.1593.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Normalized Intensity
Chemical Shift (ppm)
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0.98
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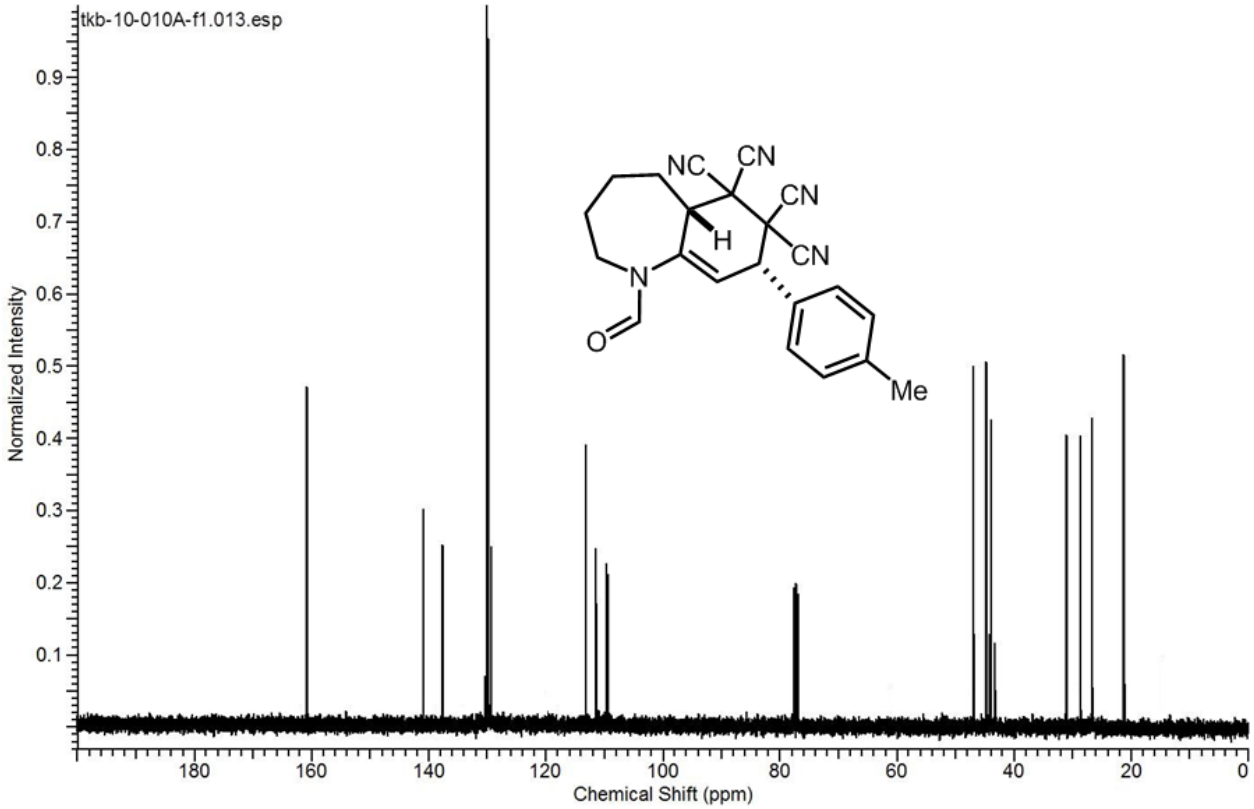
4.18
1.10
2.17
2.00
NC
CN
CN
CN
H
N
O
Me


tkb-10-010A-f1.013.esp
Normalized Intensity
Chemical Shift (ppm)
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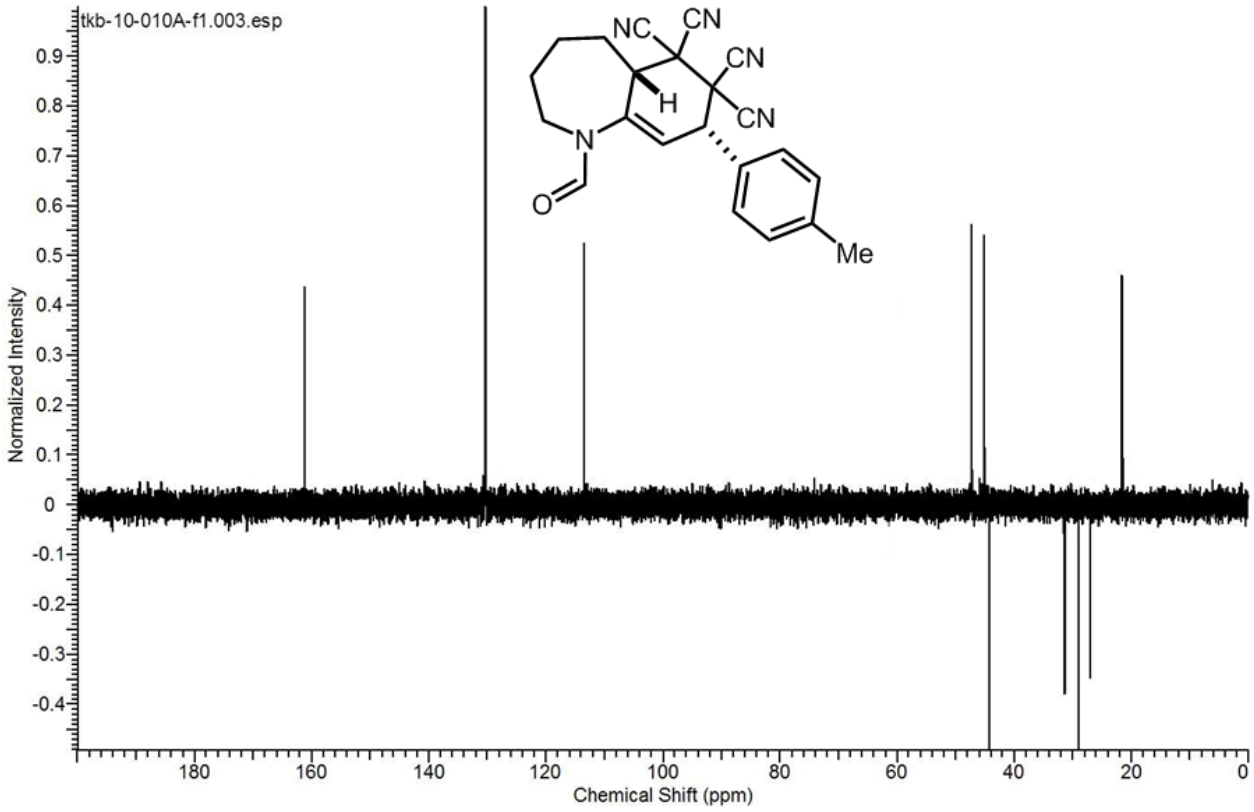
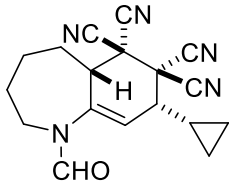
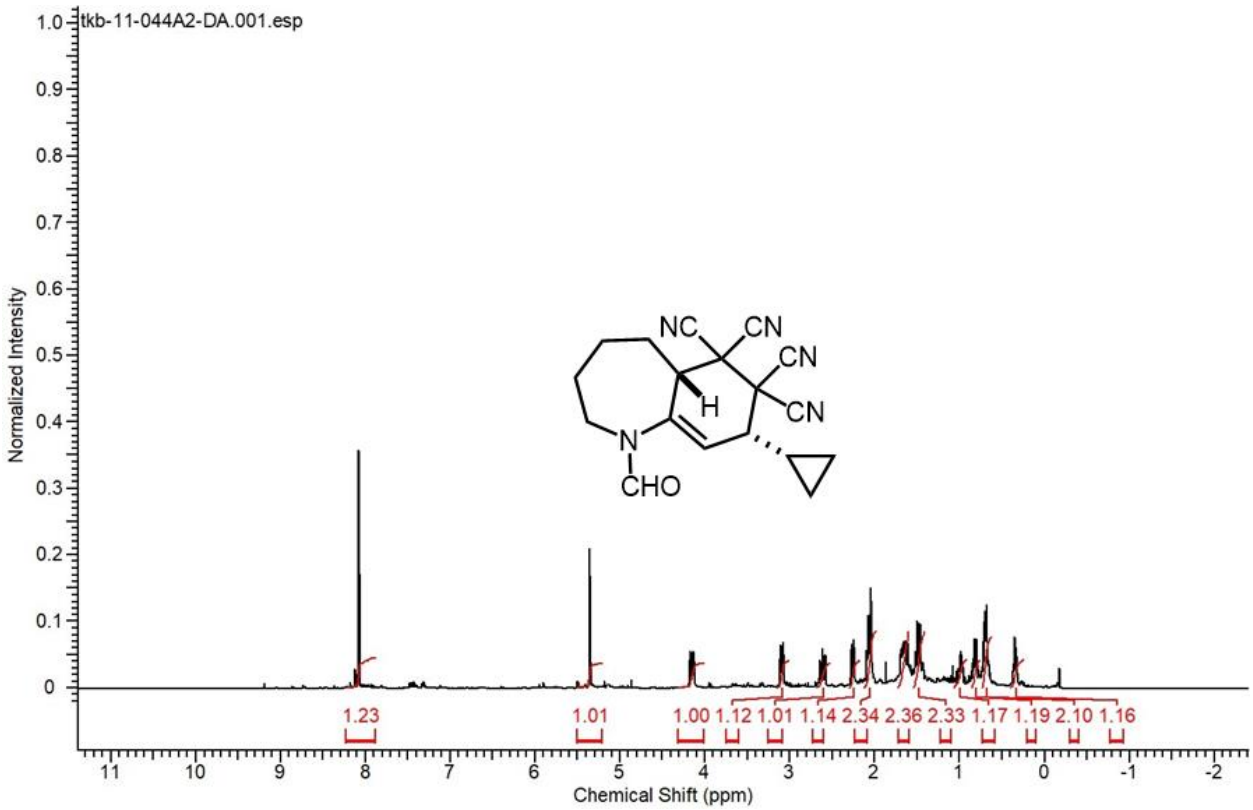
CN
CN
CN
H
N
O
Me





14b; 87%, 95:5 dr

Prepared using **General Procedure C.** Yield = 139 mg, 87%. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.18 (s, 1H), 5.35 (d, *J* = 2.2 Hz, 1H), 4.15 (dd, *J* = 14.6, 3.8 Hz, 1H), 3.14 – 3.04 (m, 1H), 2.62 – 2.55 (m, 1H), 2.25 (ddd, *J* = 10.1, 3.6, 2.1 Hz, 1H), 2.24 – 2.02 (m, 2H), 1.71 – 1.45 (m, 4H), 0.98 (dddd, *J* = 10.3, 7.7, 4.9, 2.7 Hz, 1H), 0.92 – 0.80 (m, 1H), 0.80 – 0.65 (m, 2H), 0.41 – 0.20 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.6, 136.3, 114.8, 111.2, 111.1, 109.3, 108.8, 46.4, 45.9, 44.6, 44.2, 30.4, 29.7, 28.9, 26.9, 13.3, 5.6, 3.5. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{18}H_{17}N_5O$ 319.1433; found 319.1437.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Chemical Shift (ppm)
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1.00 1.12 1.01 1.14 2.34 2.36 2.33 1.17 1.19 2.10 1.16
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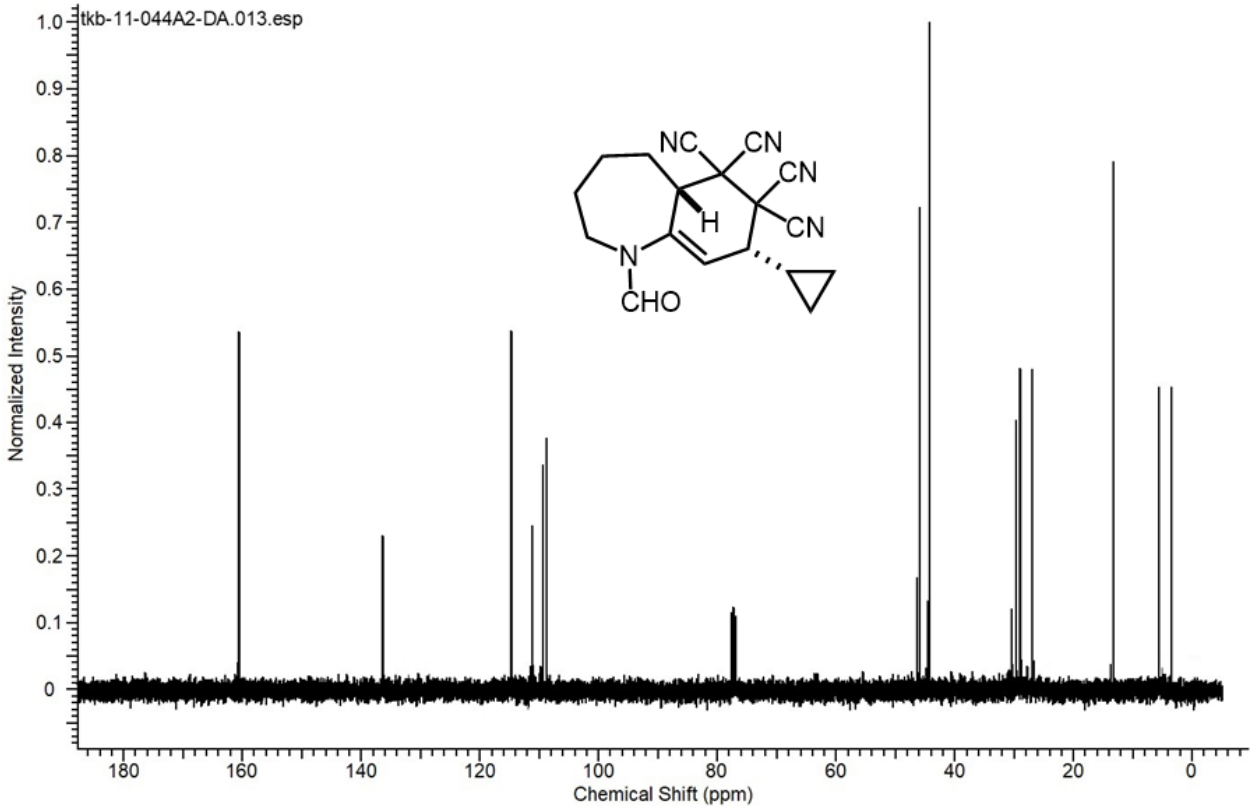
CN
CN
CN
H
N
CHO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Normalized Intensity
Chemical Shift (ppm)
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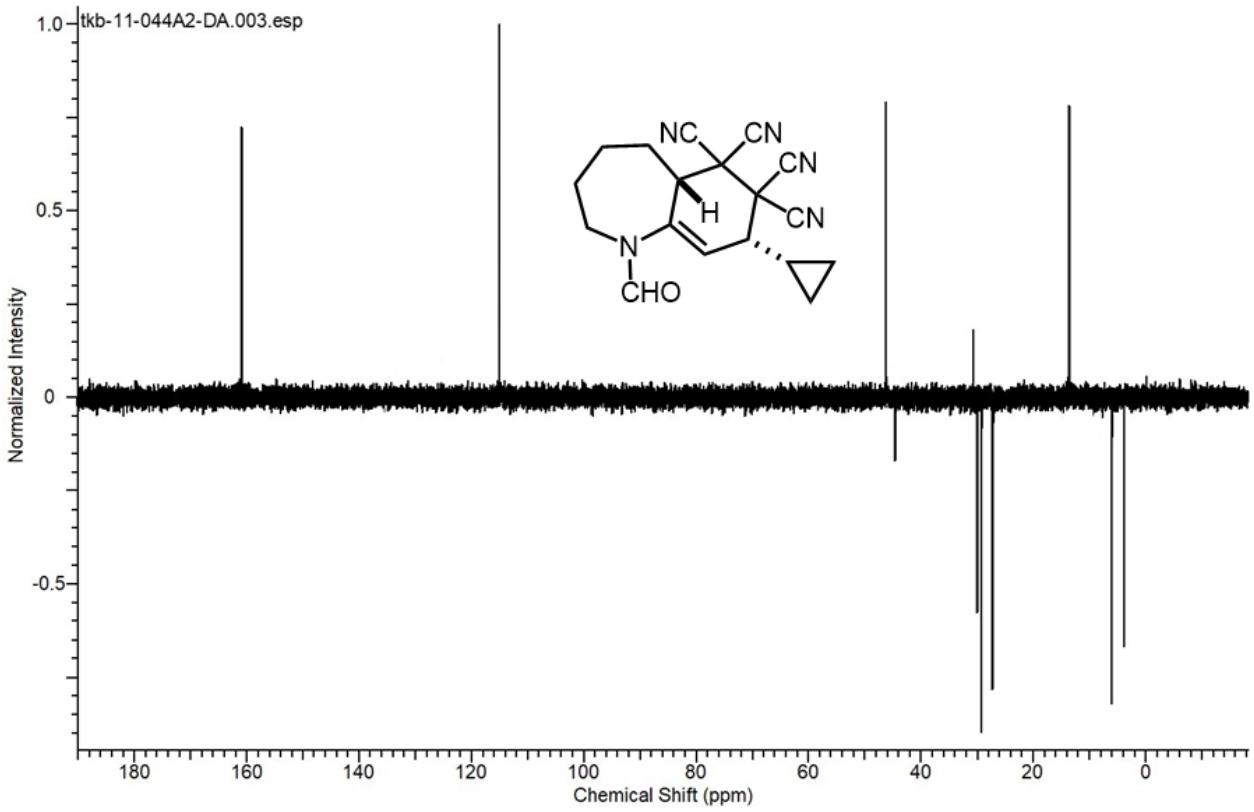
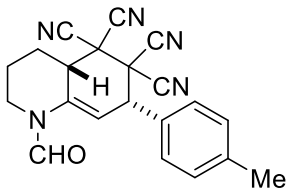
CN
CN
CN
H
N
CHO





14c; 92%, 95:5 dr

Prepared using **General Procedure C.** Yield = 164 mg, 92%. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.11 (s, 1H), 7.42 – 7.25 (m, 4H), 5.58 (d, *J* = 2.5 Hz, 1H), 4.46 – 4.36 (m, 1H), 4.32 – 4.24 (m, 1H), 3.00 (ddt, *J* = 12.8, 4.7, 2.3 Hz, 1H), 2.83 – 2.64 (m, 1H), 2.38 (dt, *J* = 12.4, 4.2 Hz, 1H), 2.31 – 2.07 (m, 4H), 1.99 (dp, *J* = 13.6, 3.4 Hz, 1H), 1.68 (ddt, *J* = 17.1, 12.8, 6.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7, 141.0, 136.3, 130.2, 130.1, 130.0, 129.2, 114.4, 111.3, 110.9, 109.8, 108.9, 46.0, 43.7, 43.5, 41.5, 41.4, 41.3, 40.7, 29.4, 24.1, 21.4. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{21}H_{17}N_5O$ 355.1433; found 355.1430.

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Acquired   : 25 Oct 2018  18:21     using AcqMethod 150-250_new.M
Instrument :    Instrument #1
Sample Name:
Misc Info  :
Vial Number: 1
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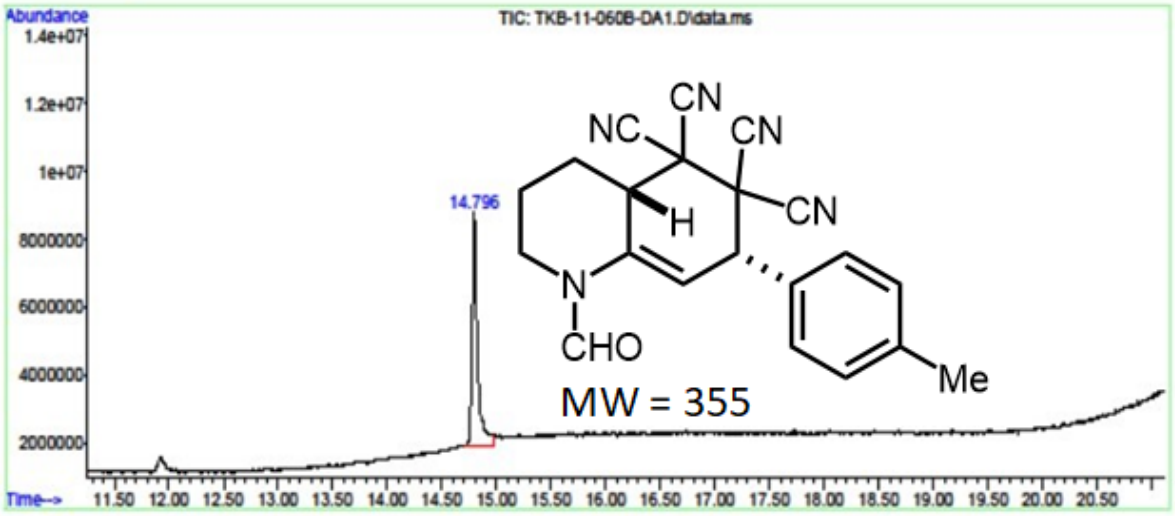

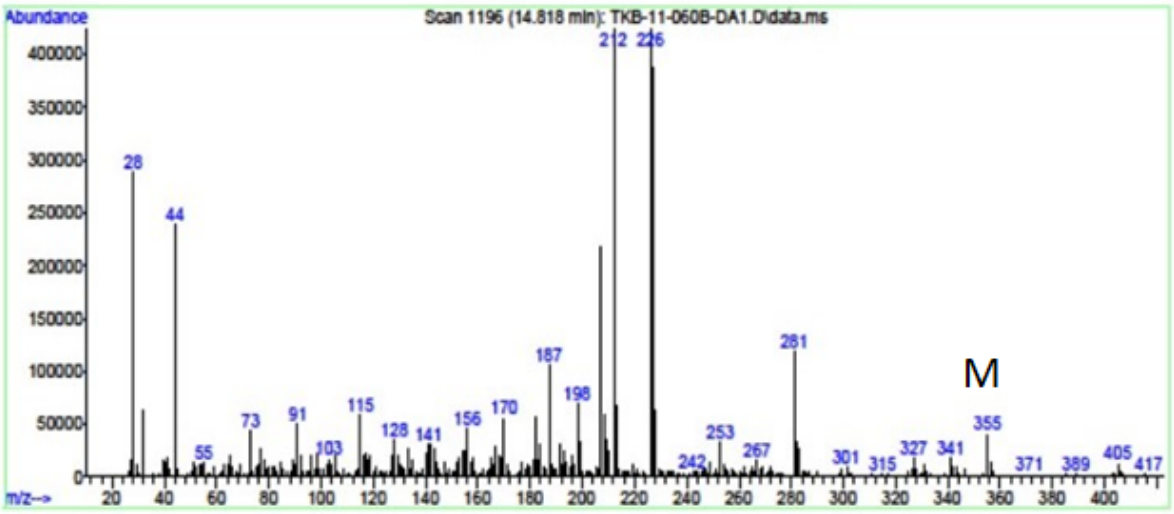

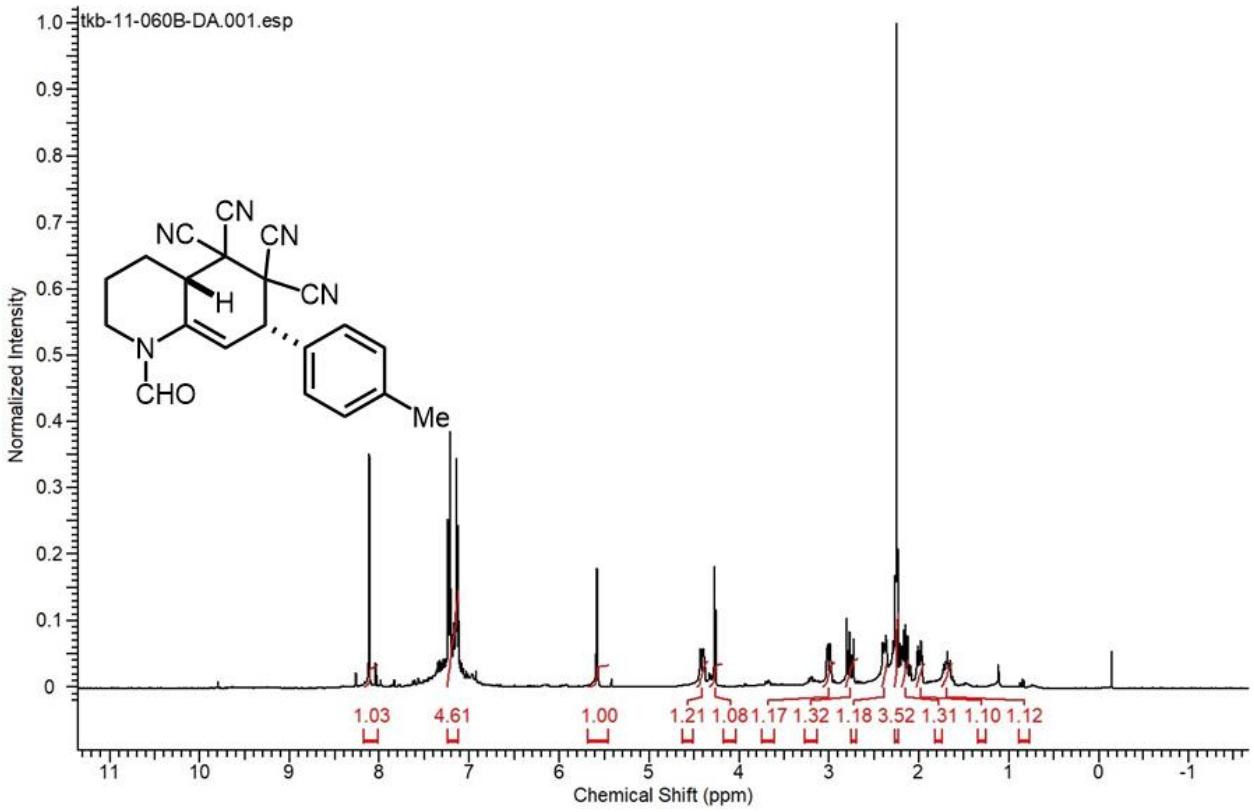
tkb-11-060B-DA.001.esp
Normalized Intensity
Chemical Shift (ppm)
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1.00
1.21
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1.17
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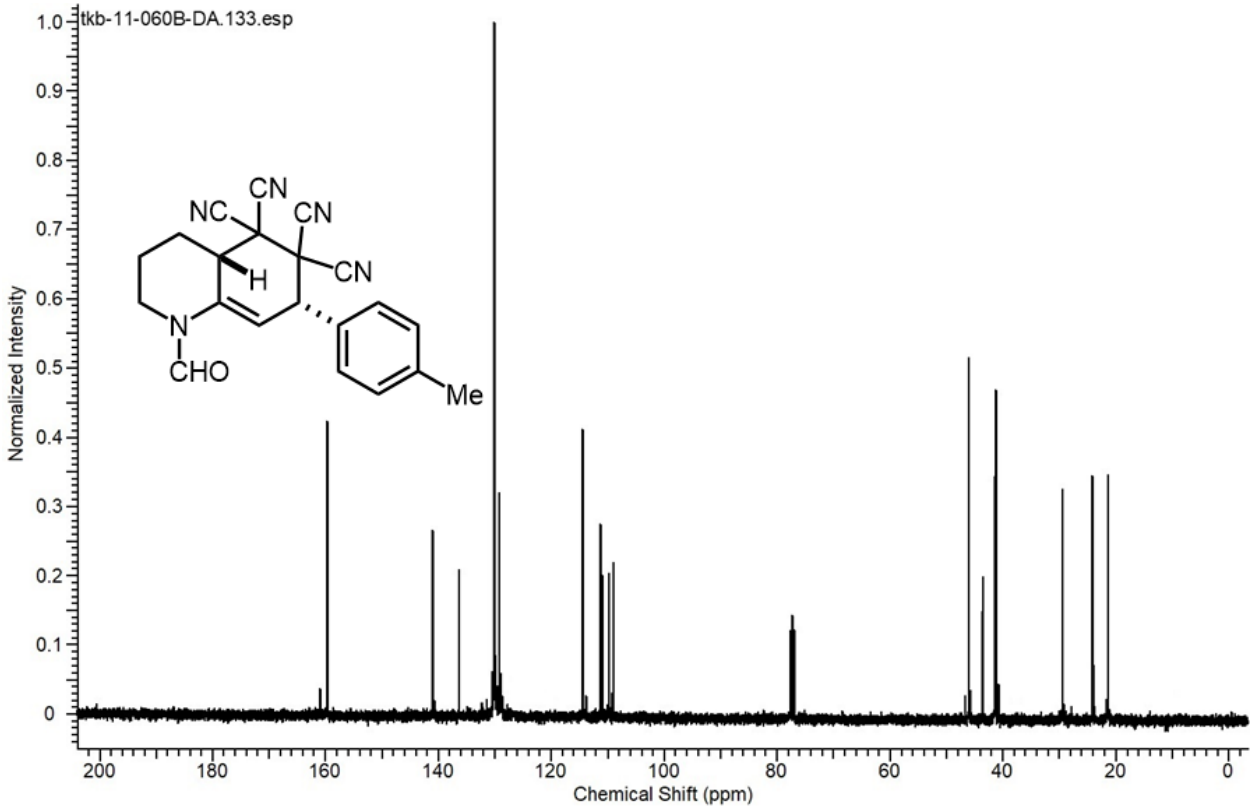
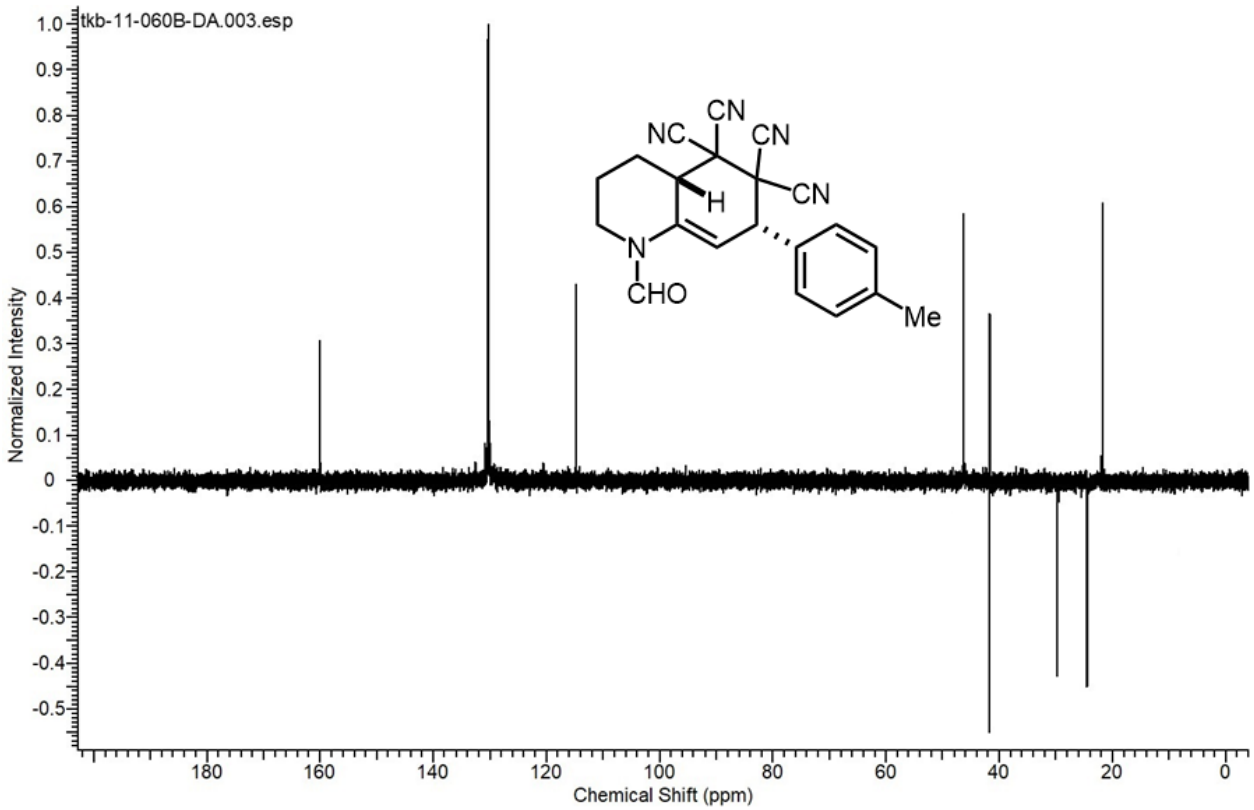
1.18
3.52
1.31
1.10
1.12
CN
NC
CN
CN
H
N
CHO
Me


tkb-11-060B-DA.133.esp
Normalized Intensity
Chemical Shift (ppm)
CN
NC
CN
CN
H
N
CHO
Me


tkb-11-060B-DA.003.esp
Normalized Intensity
Chemical Shift (ppm)
CN
NC
CN
CN
H
N
CHO
Me

References

(1) Beng, T. K.; Wilkerson-Hill, S. M.; Sarpong, R. *Org. Lett.* **2014**, *16*, 916.

(2) Bassler, D. P.; Alwali, A.; Spence, L.; Beale, O.; Beng, T. K. *J. Organomet. Chem.* **2015**, *780*, 6.

(3) Marth, C. J.; Gallego, G. M.; Lee, J. C.; Lebold, T. P.; Kulyk, S.; Kou, K. G. M.; Qin, J.; Lilien, R.; Sarpong, R. *Nature (London, U. K.)* **2015**, *528*, 493.