Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supplementary Information

Synthesis of Alk-2-ynl Weinreb Amide via Pd/Cu-Catalysed Oxidative Carbonylation of Terminal Alkynes

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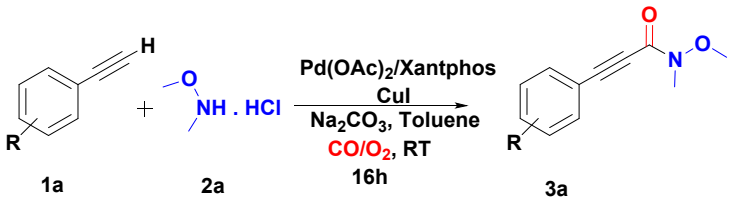
i. General Information

Materials, Solvents and Techniques:

All chemicals and solvents were purchased from commercial suppliers, i.e., Sigma Aldrich, Thermofischer Scientific, etc and used without further purification. The reaction progress was monitored using thin-layer chromatography, GC and GC-MS analysis. Gas chromatograms and mass spectra were obtained on the Shimadzu QP 2010 instrument. The obtained crude products were purified by column chromatography through 100-200 mesh silica gel. The ^{1}H and ^{13}C NMR spectra of purified products were obtained on an Agilent 400, 500 MHz and 101,126 MHz NMR, respectively, in $CDCl_3$ using TMS as an internal standard. The chemical shift values are shown in ppm (δ). ^{19}F NMR spectra of the purified compound were obtained on Agilent 470 MHz in CDCl3, using TMS as an internal standard with chemical shift values in ppm (δ). The products were confirmed by GC-MS, FTIR, ^{1}H and ^{13}C NMR spectroscopy techniques. The IR spectra of the products were obtained on the PerkinElmer UATR 2 and Bruker-Alpha II ATR FTIR Instruments. HRMS of products were recorded on ESI QTOF and maXis impact (Bruker Compass) instruments.

ii. General Experimental Procedure for the Synthesis of Alk-2-ynl Weinreb Amides:

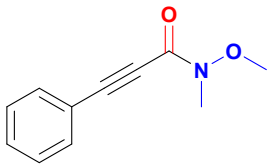


Alkyne **1a** (1mmol, 1equiv), *N, O*-dimethylhydroxylamine hydrochloride **2a** (2 mmol, 2equiv), $Pd(OAc)_2$ catalyst (2mol%), Xantphos (2mol%), Na_2CO_3 (4 mmol, 4equiv), CuI (10 mol%) in 10 mL toluene were charged in 100 mL stainless steel reactor, and the reactor was closed and pressurized with oxygen (1 atm) and CO (5 atm). Then, the reaction mixture was stirred at room temperature for 16 hours. After the completion of the reaction, the pressure was released carefully, and the reactor was opened. Then, the reaction mixture was diluted with ethyl acetate (10mL) and washed with brine solution and extracted with ethyl acetate (3×10ml). The combined organic layer dried over Na_2SO_4, and then the solvent was evaporated using rotary evaporation. The crude residue was then purified by column chromatography on silica gel using petroleum ether/ethyl acetate as an eluent system to afford the corresponding pure alkynyl weinreb amide and its derivatives. Finally, the pure

compound was confirmed by GC-MS, FT-IR, and NMR. All the new compounds were confirmed by GC-MS, FT-IR, NMR, and HR-MS techniques.

iii. Spectroscopic Data of Products:

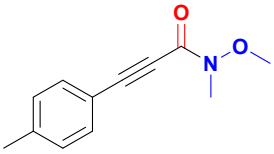
1. *N*-methoxy-*N*-methyl-3-phenylpropiolamide (3a)[2,3]:



The compound was prepared from phenylacetylene **(1a)** (1mmol,1eq) and *N,O*-dimethylhydroxylamine hydrochloride **2a** (2 mmol, 2equiv). The crude residue obtained was purified by column chromatography using petroleum ether/ethyl acetate to afford the pure product in 93% yield as a light brown solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (d, J = 7.4 Hz, 2H), 7.49 – 7.40 (m, 1H), 7.40 – 7.28 (m, 2H), 3.84 (s, 3H), 3.28 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 154.61 (s) (C=O), 132.55 (s) (CH), 130.24 (s) (CH), 128.51 (s) (CH), 120.35 (s) (C), 90.33 (s) (C≡C), 80.76 (s) (C≡C), 62.19 (s) (O-CH_3), 32.46 (s) (N-CH_3).
GC-MS (EI, 70 eV)- m/z (in % relative intensity): 189 (3, M^+), 159 (3), 129 (100), 101 (8), 75 (15), 51 (6).
FTIR (ν, (cm^{-1})): 2938 ν, 2217 ν (C≡C), 1636 ν (amide), 1489 ν, 1183 ν, 759 ν.

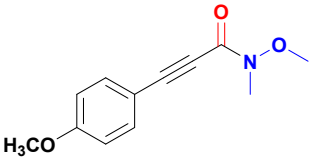
2. *N*-methoxy-*N*-methyl-3-(*p*-tolyl) propiolamide (3aa')



The compound was prepared from 1-ethynyl-4-methylbenzene **(1aa')** (1mmol,1eq) and *N,O*-dimethylhydroxylamine hydrochloride **2a** (2 mmol, 2equiv). The crude residue obtained was purified by column chromatography using petroleum ether/ethyl acetate to afford the pure product in 88% yield as a brown solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.9 Hz, 2H), 7.19 – 7.09 (m, 2H), 3.81 (s, 3H), 3.26 (s, 3H), 2.35 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 154.71 (s) (C=O), 140.73 (s) (C), 132.48 (s) (CH), 129.24 (s) (CH), 117.24 (s) (C), 90.78 (s) (C≡C), 80.40 (s) (C≡C), 61.97 (s) (O-CH_3), 32.49 (s) (N-CH_3), 21.55 (s) (CH_3).
GC-MS (EI, 70 eV)- m/z (in % relative intensity): 203(5, M^+), 172 (1), 173 (2), 143(100), 115 (9), 89 (8), 63(6).
FTIR (ν, (cm^{-1})): 2923 ν, 2213 ν (C≡C), 1622 ν (amide), 1410 ν, 1183 ν, 759 ν
HRMS (ESI) m/z found for $C_{12}H_{13}NO_2$ $[M+H]^+$, **204.1028**, calculated for $C_{12}H_{13}NO_2$ $[M+H]^+$, **204.1024**.

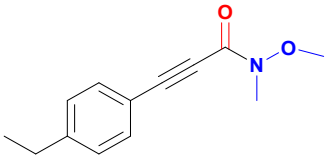
3. *N*-methoxy-3-(4-methoxyphenyl)-*N*-methylpropiolamide (3ab):[3]



The compound was prepared from 1-ethynyl-4-methoxybenzene (**1ab**) (1mmol,1eq) and *N,O*-dimethylhydroxylamine hydrochloride **2a** (2 mmol, 2equiv).The crude residue obtained was purified by column chromatography using petroleum ether/ethyl acetate to afford the pure product in 83 % yield as a brown solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.9 Hz, 2H), 3.78 (d, *J* = 3.5 Hz, 6H), 3.24 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.15 (s) (C), 155.01 (s) (C=O), 134.37 (s) (CH), 114.19 (s) (C), 112.15 (s) (CH), 91.07 (s) (C≡C), 80.10 (s) (C≡C), 61.95 (s) (O-CH_3), 55.32 (s) (O-CH_3), 32.51 (s) (N-CH_3).
GC-MS (EI, 70 eV)- m/z (in % relative intensity): 219 (6, M^+), 189 (3), 159 (100), 116 (14), 88 (12), 62 (7).
FTIR (ν, (cm^{-1})): 2923 ν, 2218 ν (C≡C), 1617 ν (amide), 1449 ν, 1252 ν, 1178 ν, 764 ν

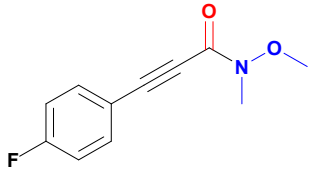
4. 3-(4-ethylphenyl)-*N*-methoxy-*N*-methylpropiolamide (3ac)



The compound was prepared from 1-ethyl-4-ethynylbenzen (**1ac**) (1mmol,1eq) and *N,O*-dimethylhydroxylamine hydrochloride **2a** (2 mmol, 2equiv).The crude residue obtained was purified by column chromatography using petroleum ether/ethyl acetate to afford the pure product in 85 % yield as a brownish liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.9 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 3.76 (s, 3H), 3.21 (s, 3H), 2.59 (q, *J* = 7.6 Hz, 2H), 1.15 (t, *J* = 7.6 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 155.04 (s) (C=O), 146.97 (s) (C), 132.60 (s) (CH), 128.06 (s) (CH), 117.43 (s) (C), 90.84 (s) (C≡C), 80.37 (s) (C≡C), 62.01 (s) (O-CH3), 32.47 (s) (N-CH3), 28.86 (s) (CH2), 15.10 (s) (CH3).
GC-MS (EI, 70 eV)- m/z (in % relative intensity): 217 (3, M^+), 187 (2), 157 (100), 114 (12), 88 (3), 63 (4).
FTIR (ν, (cm^{-1})): 2963 ν, 2933 ν, 2218 ν (C≡C), 1641ν (amide), 1410 ν, 1183 ν, 754 ν
HRMS (ESI) m/z found for $C_{13}H_{15}NO_2$ $[M+H]^+$, **218.1189**, calculated for $C_{13}H_{15}NO_2$ $[M+H]^+$, **218.1181**.

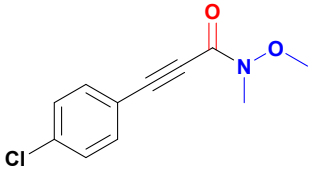
5. 3-(4-fluorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ad):



The compound was prepared from 1-ethynyl-4-fluorobenzene (**1ad**) (1mmol,1eq) and *N,O*-dimethylhydroxylamine hydrochloride **2a** (2 mmol, 2equiv).The crude residue obtained was purified by column chromatography using petroleum ether/ethyl acetate to afford the pure product in 78 % yield as a light brown solid .

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 8.4, 5.4 Hz, 2H), 7.03 (t, *J* = 8.7 Hz, 2H), 3.80 (s, 3H), 3.25 (s,3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.86 (s) (C), 162.34 (s), 154.54 (s) (C=O), 134.72 (d, *J* = 8.5 Hz) (CH), 116.49 (s) (CH), 116.07 (s), 115.85 (s) (C), 89.11 (s) (C≡C), 80.66 (s) (C≡C), 62.05 (s) (O-CH_3), 32.47 (s) (N-CH3).
^{19}F NMR (470 MHz, CDCl3) δ -107.29 (s).
GC-MS (EI, 70 eV)- m/z (in % relative intensity): 207 (3, M^+), 176 (1), 177 (2), 147 (100),119 (9), 74 (4), 57 (1).
FTIR (ν, (cm^{-1})): 2933 ν, 2218 ν (C≡C), 1636 ν (amide), 1415 ν, 1154 ν, 833 ν, 769 ν.
HRMS (ESI) m/z found for $C_{11}H_{10}FNO_2[M+H]^+$, **208.0771**, calculated for $C_{11}H_{10}FNO_2$ $[M+H]^+$, **208.0774.**

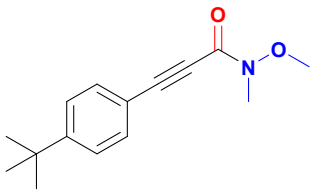
6. 3-(4-chlorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ae):



The compound was prepared from 1-chloro-4-ethynylbenzene (**1ae**) (1mmol,1eq) and *N,O*-dimethylhydroxylamine hydrochloride **2a** (2 mmol, 2equiv).The crude residue obtained was purified by column chromatography using petroleum ether/ethyl acetate to afford the pure product in 80 % yield as a brown solid .

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.6 Hz, 2H), 3.80 (s,3H), 3.25 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 154.27 (s) (C=O), 136.49 (s) (C), 133.73 (s) (CH), 128.92 (s) (CH), 118.82 (s) (C), 89.00 (s) (C≡C), 81.59 (s) (C≡C), 62.15 (s) (O-CH_3), 32.46 (s) (N-CH_3).
GC-MS (EI, 70 eV)- m/z (in % relative intensity): 223 (4, M^+), 192 (1), 193 (2), 163 (100), 135 (6), 74 (10), 50 (3).
FTIR (ν, (cm^{-1})): 2928 ν, 2213 ν (C≡C), 1636 ν (amide), 1410 ν, 1183 ν, 828 ν, 715 ν.
HRMS (ESI) m/z found for $C_{11}H_{10}ClNO_2[M+H]^+$, **224.0475**, calculated for $C_{11}H_{10}ClNO_2$ $[M+H]^+$, **224.0478**.

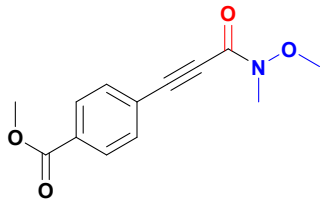
7. 3-(4-(tert-butyl)phenyl)-*N*-methoxy-*N*-methylpropiolamide (3af):



The compound was prepared from 1-(tert-butyl)-4-ethynylbenzene (**1af**) (1mmol,1eq) and *N,O*-dimethylhydroxylamine hydrochloride **2a** (2 mmol, 2equiv).The crude residue obtained was purified by column chromatography using petroleum ether/ethyl acetate to afford the pure product in 84 % yield as a brown solid .

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 3.25 (s, 3H), 1.27 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 154.77 (s) (C=O), 153.80 (s) (C), 132.39 (s) (CH), 125.52 (s) (CH), 117.26 (s) (C), 90.77 (s) (C≡C), 80.37 (s) (C≡C), 62.05 (s) (O-CH_3), 34.93 (s) (N-CH_3), 32.45 (s) ($C(CH_3)_3$), 31.00 (s) (CH_3).
GC-MS (EI, 70 eV)- m/z (in % relative intensity): 245 (3, M^+), 215 (1), 185 (100),155 (20), 115 (9), 71 (4), 51(1).
FTIR (ν, (cm^{-1})): 2958 ν, 2213 ν (C≡C), 1641 ν (amide), 1415 ν, 1183 ν, 833 ν.
HRMS (ESI) m/z found for $C_{15}H_{19}NO_2$ $[M+H]^+$, **246.1510**, calculated for $C_{15}H_{19}NO_2$ $[M+H]^+$, **246.1494**.

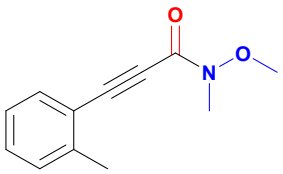
8. methyl 4-(3-(methoxy(methyl)amino)-3-oxoprop-1-yn-1-yl)benzoate (3ag):



The compound was prepared from methyl 4-ethynylbenzoate (**1ag**) (1mmol,1eq) and *N,O* -dimethylhydroxylamine hydrochloride **2a** (2 mmol, 2equiv).The crude residue obtained was purified by column chromatography using petroleum ether/ethyl acetate to afford the pure product in 72 % yield as a brown solid .

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 3.88 (s, 3H), 3.80 (s, 3H), 3.24 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.03 (s) (Ester C=O), 154.13 (s) (C=O), 132.37 (s) (CH), 131.27 (s) (CH), 129.52 (s) (C), 124.85 (s) (C), 88.83 (s) (C≡C), 82.90 (s) (C≡C), 62.21 (s) (O-CH_3), 52.32 (s) (ester O-CH_3), 32.43 (s) (N-CH_3).
GC-MS (EI, 70 eV)- m/z (in % relative intensity): 247 (2, M^+), 216 (4), 187 (100), 159 (6), 116 (1), 74 (10), 50 (2).
FTIR (ν, (cm^{-1})): 2919 ν, 2845 ν, 2218 ν (C≡C), 1715 ν (ester), 1632 ν (amide), 1415 ν, 1174 ν, 769 ν.
HRMS (ESI) m/z found for $C_{13}H_{13}NO_4$ $[M+H]^+$, **248.0917**, calculated for $C_{13}H_{13}NO_4$ $[M+H]^+$, **248.0923** .

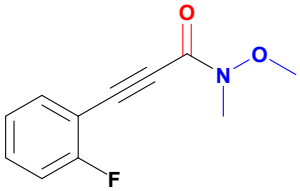
9. *N*-methoxy-*N*-methyl-3-(*o*-tolyl)propiolamide (3ah):



The compound was prepared from 1-ethynyl-2-methylbenzene (**1ah**) (1mmol,1eq) and *N,O*-dimethylhydroxylamine hydrochloride **2a** (2 mmol, 2equiv).The crude residue obtained was purified by column chromatography using petroleum ether/ethyl acetate to afford the pure product in 86 % yield as a brownish liquid .

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.6 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.26 – 7.21 (m, 1H), 7.18 (dd, *J* = 11.5, 4.0 Hz, 1H), 3.84 (s, 3H), 3.29 (s, 3H), 2.50 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 154.79 (s) (C=O), 141.57 (s) (C), 133.18 (s) (CH), 130.26 (s) (CH), 129.67 (s) (CH), 125.77 (s) (CH), 120.21 (s) (C), 89.35 (s) (C≡C), 84.55 (s) (C≡C), 62.19 (s) (O-CH_3), 32.44 (s) (N-CH_3), 20.55 (s) (CH_3).
GC-MS (EI, 70 eV)- m/z (in % relative intensity): 203 (5, M^+), 172 (1), 143 (100), 115 (52), 63 (8), 51 (3).
FTIR (ν, (cm^{-1})): 2933 ν, 2213 ν (C≡C), 1636 ν (amide), 1410 ν, 1183 ν, 759 ν.
HRMS (ESI) m/z found for $C_{12}H_{13}NO_2$ $[M+H]^+$, **204.1030**, calculated for $C_{12}H_{13}NO_2$ $[M+H]^+$, **204.1024**.

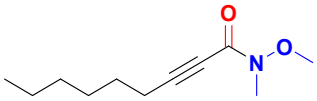
10. 3-(2-fluorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ai):



The compound was prepared from 1-ethynyl-2-fluorobenzene (**1ai**) (1mmol,1eq) and *N,O*-dimethylhydroxylamine hydrochloride **2a** (2 mmol, 2equiv).The crude residue obtained was purified by column chromatography using petroleum ether/ethyl acetate to afford the pure product in 77 % yield as a light brownish liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (t, *J* = 7.2 Hz, 1H), 7.43 (td, *J* = 7.5, 1.3 Hz, 1H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.12 (t, *J* = 8.9 Hz, 1H), 3.86 (s, 3H), 3.29 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 164.38 (s), 162.36 (s) (C), 154.28 (s) (C=O), 134.35 (s) (CH), 132.21 (s) (CH), 124.25 (s) (CH), 115.80 (s) (CH), 115.64 (s) (C), 109.23 (s) (C≡C), 85.49 (s) (C≡C), 62.32 (s) (O-CH_3), 32.47 (s) (N-CH_3).
^{19}F NMR (470 MHz, $CDCl_3$) δ -108.03 (s).
GC-MS (EI, 70 eV)- m/z (in % relative intensity): 207 (3, M^+), 176 (1), 177 (2), 147 (100), 119 (8), 74 (3), 57(1)
FTIR (ν, (cm^{-1})): 2938 ν, 2223 ν (C≡C), 1641 ν (amide), 1415 ν, 1183 ν, 754 ν.
HRMS (ESI) m/z found for $C_{11}H_{10}FNO_2$ $[M+H]^+$, **208.0776**, calculated for $C_{11}H_{10}FNO_2$ $[M+H]^+$, **208.0774**.

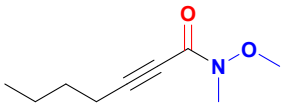
11. *N*-methoxy-*N*-methylnon-2-ynamide(3aj)[1]:



The compound was prepared from oct-1-yne (**1aj**) (1mmol,1eq) and *N,O*-dimethylhydroxylamine hydrochloride **2a** (2 mmol, 2equiv).The crude residue obtained was purified by column chromatography using petroleum ether/ethyl acetate to afford the pure product in 91 % yield as a brownish liquid .

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.77 (s, 3H), 3.22 (s, 3H), 2.38 (t, *J* = 7.1 Hz, 2H), 1.66 – 1.53 (m, 2H), 1.42 (dt, *J* = 14.6, 7.3 Hz, 2H), 1.35 – 1.21 (m, 4H), 0.89 (t, *J* = 6.9 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 154.69 (s) (C=O), 93.61 (s) (C≡C), 73.07 (s) (C≡C), 61.94 (s) (O-CH_3), 32.27 (s) (N-CH_3), 31.14 (s) (CH_2), 28.42 (s) (CH_2), 27.62 (s) (CH_2), 22.42 (s) (CH_2), 18.90 (s) (CH_2), 13.94 (s) (CH_3).
GC-MS (EI, 70 eV)- m/z (in % relative intensity): 197 (3, M^+), 137 (100), 107 (3), 81 (29), 55 (45).
FTIR (ν, (cm^{-1})): 2933 ν, 2864 ν, 2233 ν (C≡C), 1641 ν (amide), 1415 ν, 1188 ν, 725 ν.

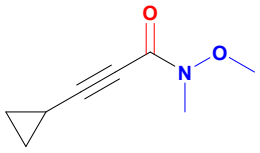
12. *N*-methoxy-*N*-methylhept-2-ynamide (3ak):[2]



The compound was prepared from hex-1-yne (**1ak**) (1mmol,1eq) and *N,O*-dimethylhydroxylamine hydrochloride **2a** (2 mmol, 2equiv).The crude residue obtained was purified by column chromatography using petroleum ether/ethyl acetate to afford the pure product in 94 % yield as a brownish liquid .

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.72 (s, 3H), 3.18 (s, 3H), 2.34 (t, *J* = 7.0 Hz, 2H), 1.61 – 1.48 (m, 2H), 1.41 (dq, *J* = 14.4, 7.3 Hz, 2H), 0.89 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 154.71 (s) (C=O), 93.63 (s) (C≡C), 73.09 (s) (C≡C), 61.94 (s) (O-CH_3), 32.30 (s) (N-CH_3), 29.70 (s) (CH_2), 21.86 (s) (CH_2), 18.61 (s) (CH_2), 13.44 (s) (CH_3).
GC-MS (EI, 70 eV)- m/z (in % relative intensity): 169 (3, M^+), 138 (1), 109 (100), 81 (13), 53 (33).
FTIR (ν, (cm^{-1})): 2933 ν, 2874 ν, 2238 ν (C≡C), 1641 ν (amide), 1415 ν, 1193 ν, 725 ν.

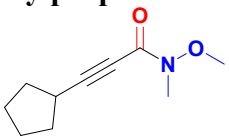
13. 3-cyclopropyl-*N*-methoxy-*N*-methylpropiolamide (3al):



The compound was prepared from ethynylcyclopropane (**1al)** (1mmol,1eq) and *N,O*-dimethylhydroxylamine hydrochloride **2a** (2 mmol, 2equiv).The crude residue obtained was purified by column chromatography using petroleum ether/ethyl acetate to afford the pure product in 92 % yield as a light brownish liquid .

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.76 (s, 3H), 3.21 (s, 3H), 1.50 – 1.32 (m, 1H), 0.98 – 0.85 (m, 4H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 155.06 (s) (C=O), 97.57 (s) (C≡C), 68.68 (s) (C≡C), 62.27 (s) ($O-CH_3$), 32.72 (s) ($N-CH_3$), 9.48 (s) (CH_2), -0.01 (s) (CH).
GC-MS (EI, 70 eV)- m/z (in % relative intensity): 153 (3, M^+), 122 (1), 93 (100), 65 (52), 53 (15).
FTIR (ν, (cm^{-1})): 2938 ν, 2218 ν (C≡C) , 1632 ν (amide), 1415 ν, 1174 ν, 729 ν.
HRMS (ESI) m/z found for $C_8H_{11}NO_2$ $[M+H]^+$, **154.0868**, calculated for $C_8H_{11}NO_2$ $[M+H]^+$, **154.0868**

14. 3-cyclopentyl-*N*-methoxy-*N*-methylpropiolamide (3am)



The compound was prepared from ethynylcyclopentane (**1am)** (1mmol,1eq) and *N,O*-dimethylhydroxylamine hydrochloride **2a** (2 mmol, 2equiv).The crude residue obtained was purified by column chromatography using petroleum ether/ethyl acetate to afford the pure product in 89 % yield as a light brownish liquid .

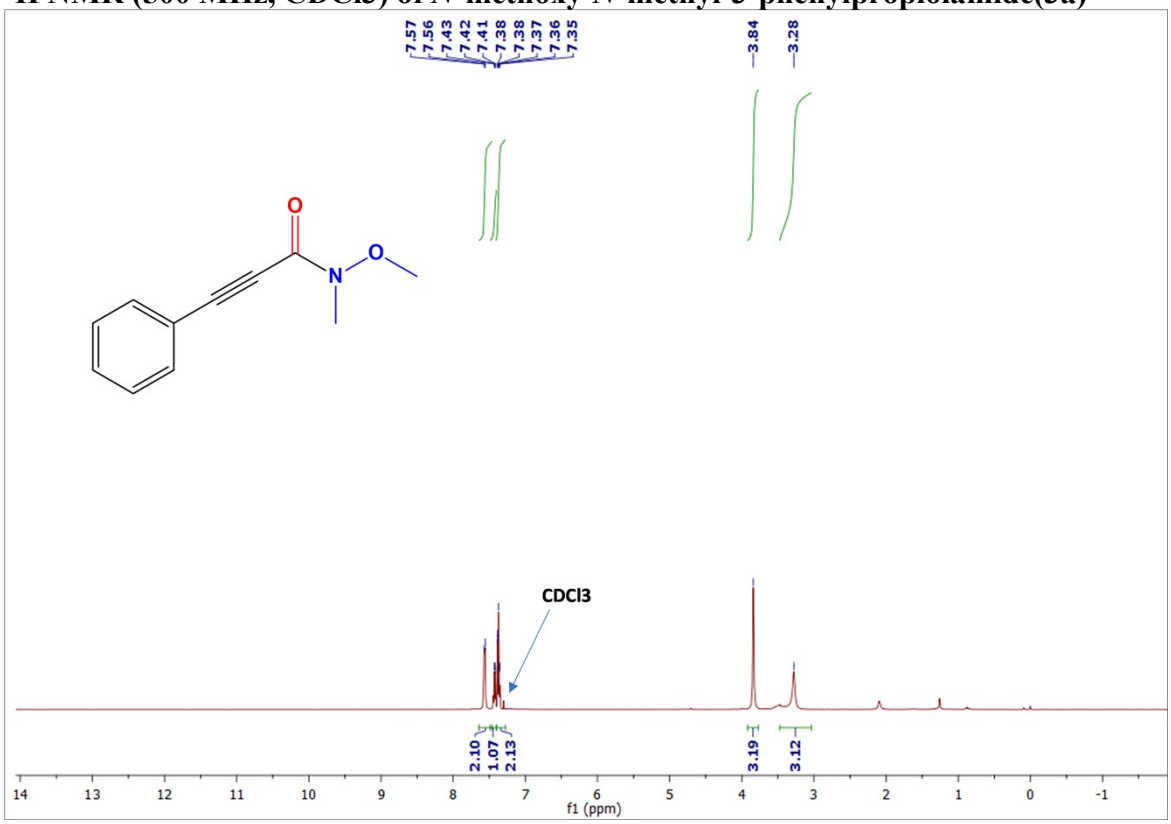
1H NMR (400 MHz, $CDCl_3$) δ 3.73 (s, 3H), 3.20 (s, 3H), 2.87 – 2.67 (m, 1H), 2.01 – 1.51 (m, 8H).
13C NMR (101 MHz, $CDCl_3$) δ 154.74 (s) (C=O), 97.63 (s) (C≡C), 72.63 (s) (C≡C), 61.80 (s) ($O-CH_3$), 33.15 (s) ($N-CH_3$), 30.04 (s) (CH_2), 29.64 (s) (CH), 25.07 (s) (CH_2).
GC-MS (EI, 70 eV)- m/z (in % relative intensity): 181 (2, M^+), 150 (1), 121 (100), 93 (8), 77 (43), 55 (25).
FTIR (ν, (cm^{-1})): 2953 ν, 2869 ν, 2224 ν (C≡C), 1640 ν (amide), 1449 ν, 1191ν, 719 ν.
HRMS (ESI) m/z found for $C_{10}H_{15}NO_2$ $[M+H]^+$, **182.1176**, calculated for $C_{10}H_{15}NO_2$ $[M+H]^+$, **182.1181**.

iv. References

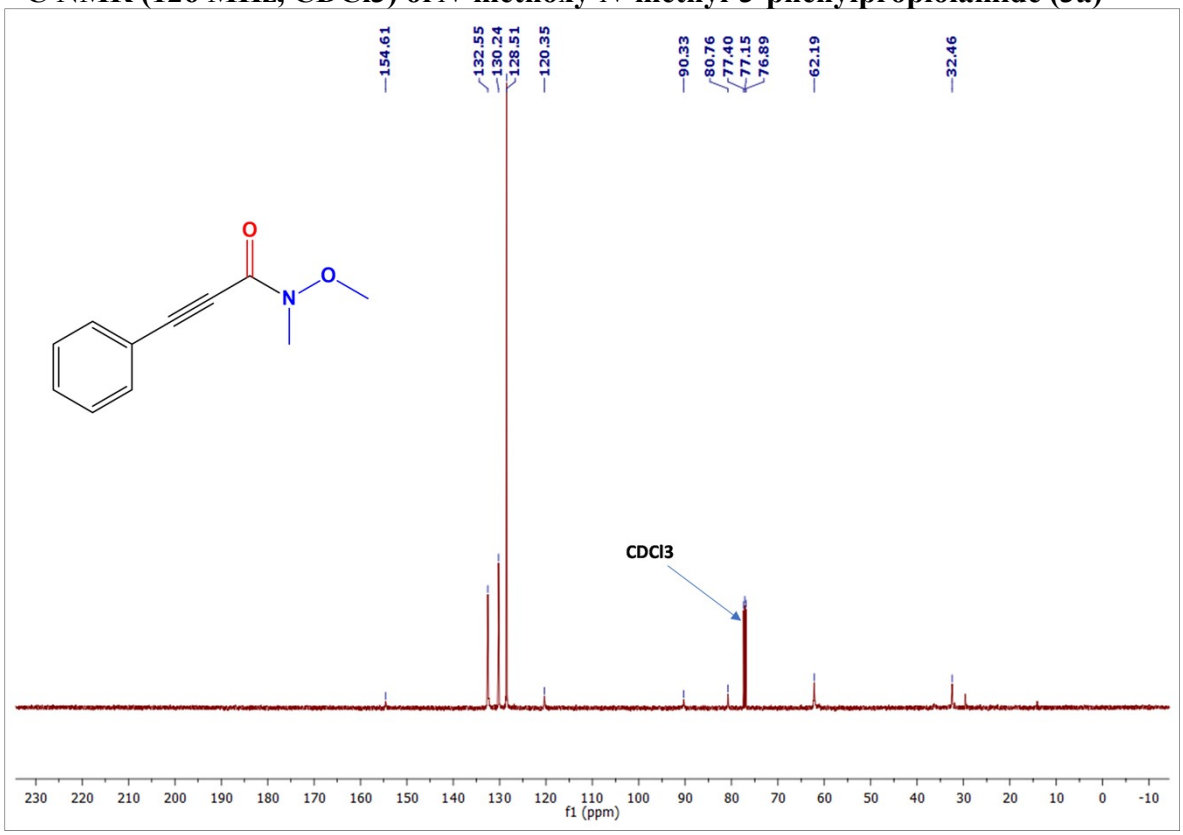
1. M. Murakami, Y. Hoshino, H. Ito and Y.Ito. *Chemistry letters*., 1998, 163-164.
2. P. Szuroczki , B. Boros and L. Kollar, T*etrahedron*., 2018,**74**, 6129-6136.
3. I. Iriarte, O. Olaizola, Dr. S. Vera, Prof. I. Gamboa, Prof. M. Oiarbide and Prof. C. Palomo, *Angew. Chem., Int. Ed*., 2017. **56**, 8860-8864.

v. ^{1}H and ^{13}C NMR spectra of 3a and it's derivatives:

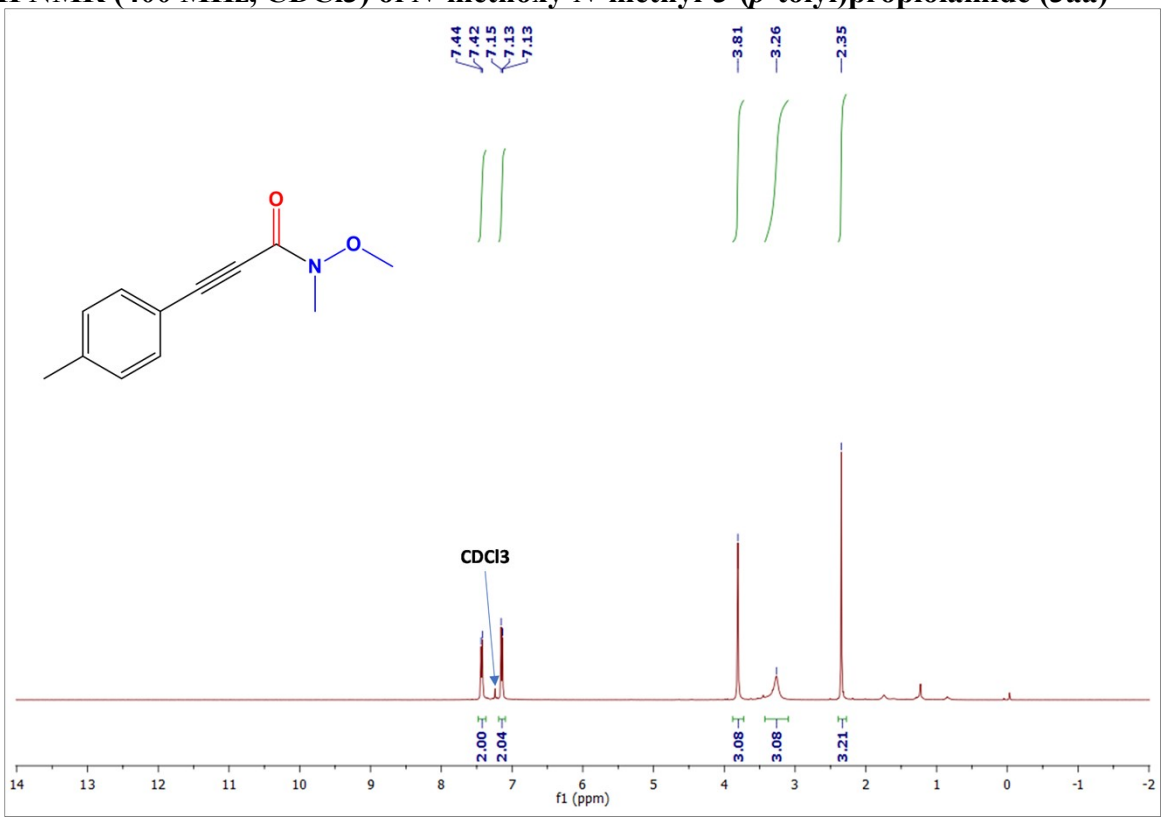
^{1}H NMR (500 MHz, CDCl3) of *N*-methoxy-*N*-methyl-3-phenylpropiolamide(3a)



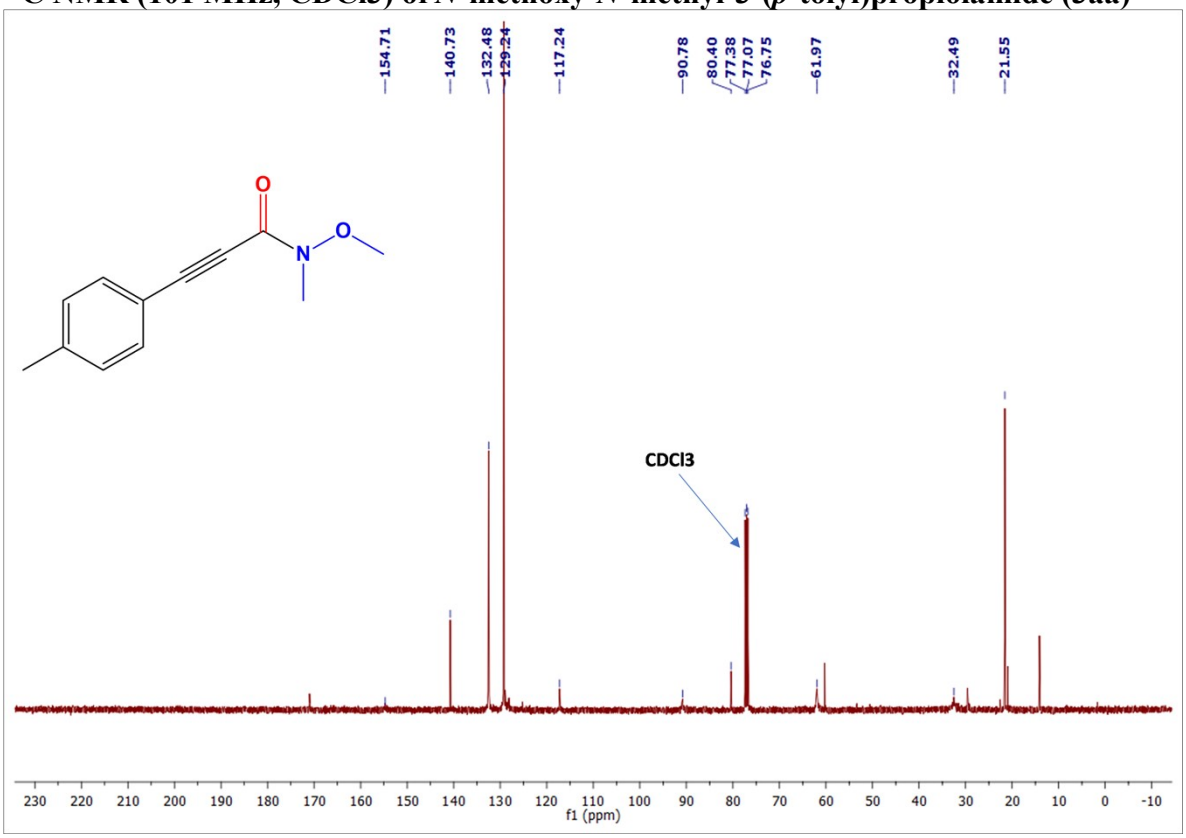
^{13}C NMR (126 MHz, CDCl3) of *N*-methoxy-*N*-methyl-3-phenylpropiolamide (3a)



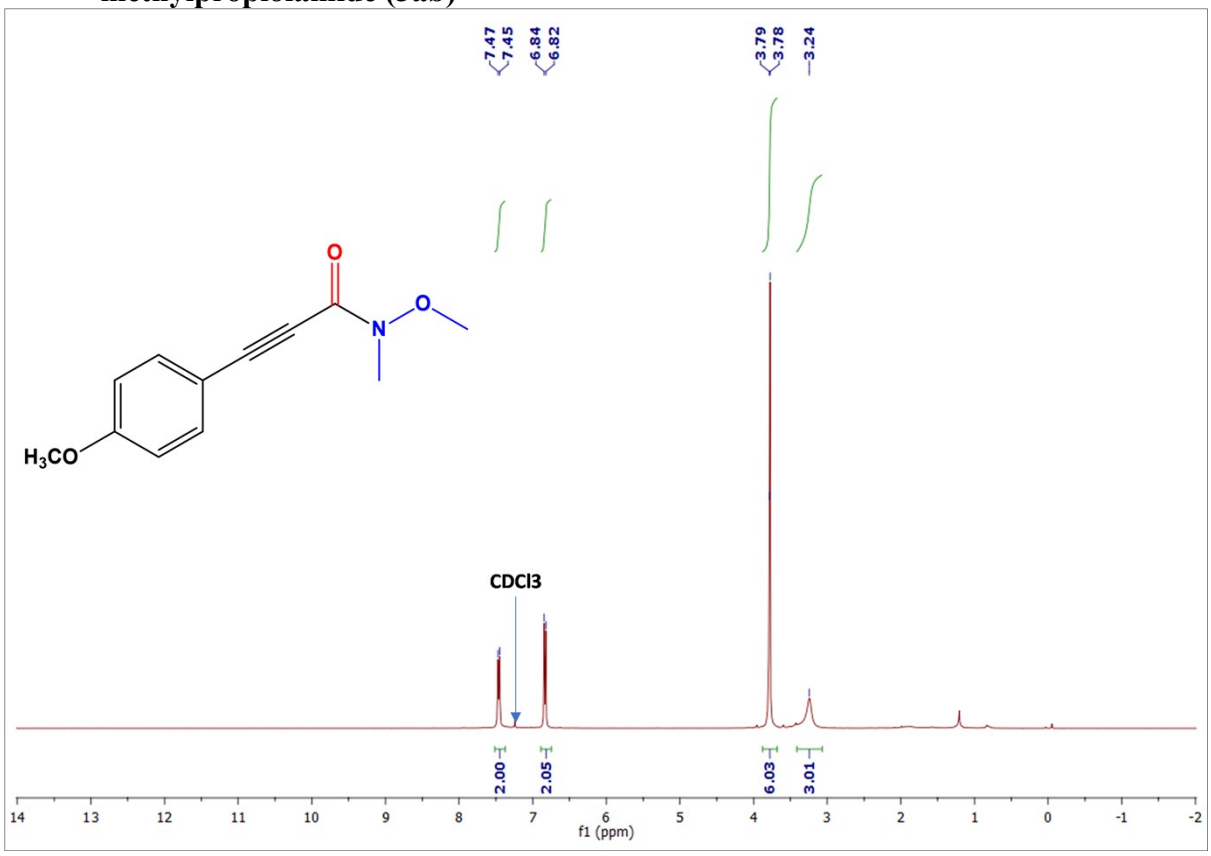
^{1}H NMR (400 MHz, CDCl3) of *N*-methoxy-*N*-methyl-3-(*p*-tolyl)propiolamide (3aa)



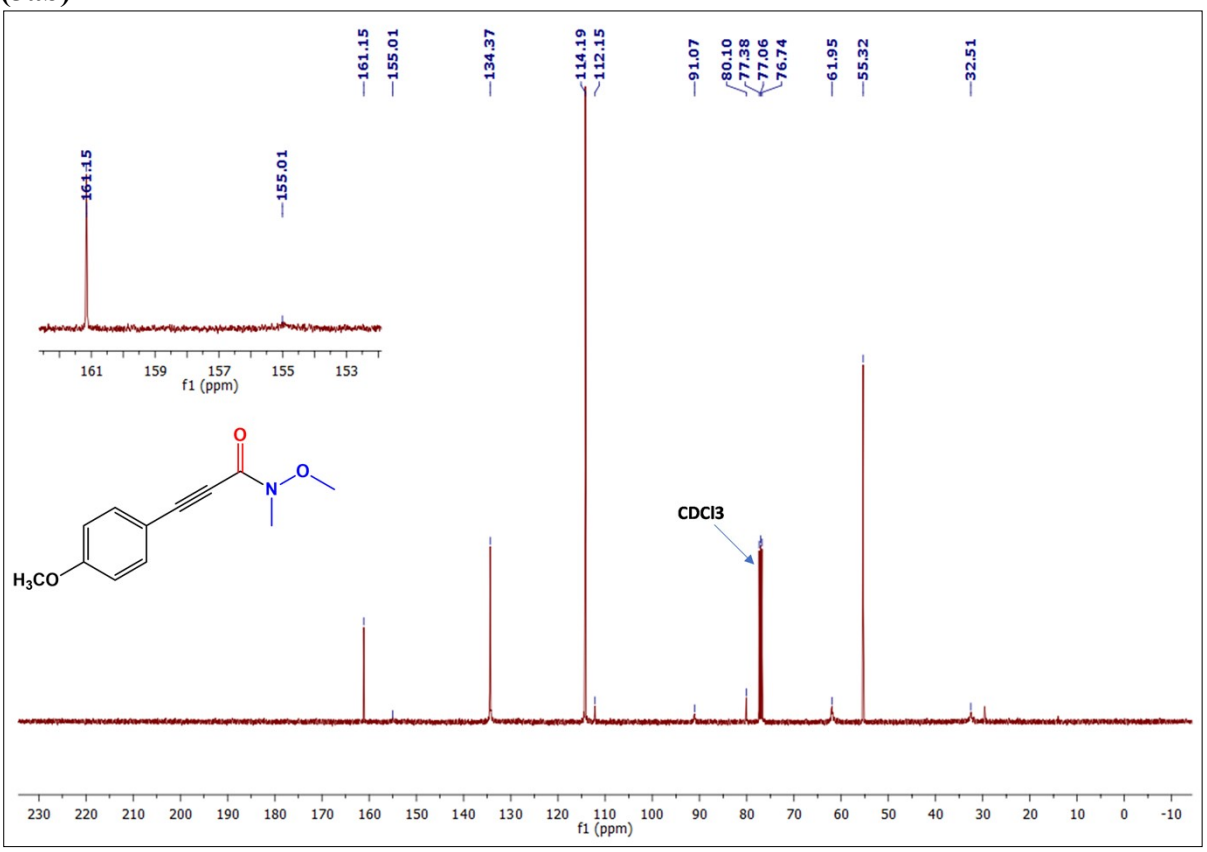
^{13}C NMR (101 MHz, CDCl3) of *N*-methoxy-*N*-methyl-3-(*p*-tolyl)propiolamide (3aa)



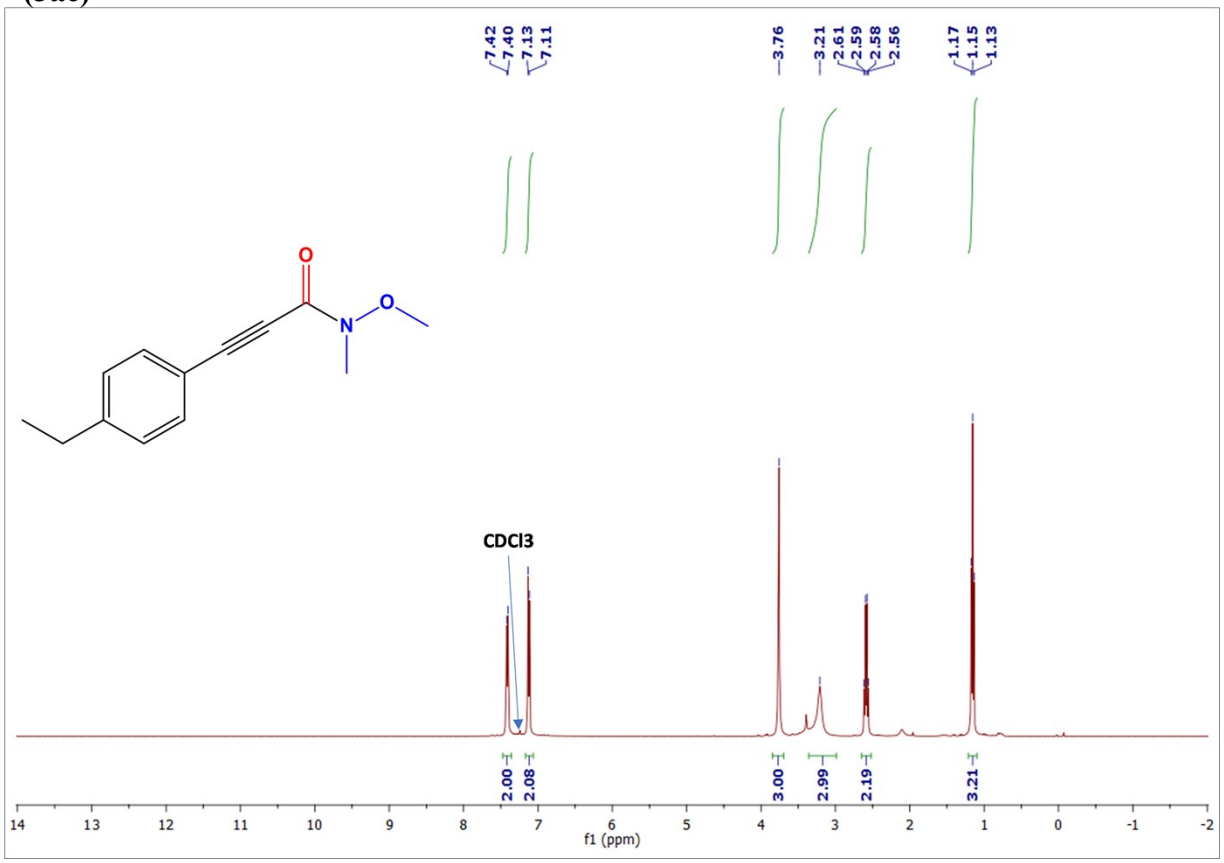
1H NMR (400 MHz, CDCl3) of *N*-methoxy-3-(4-methoxyphenyl)-*N*-methylpropiolamide (3ab)



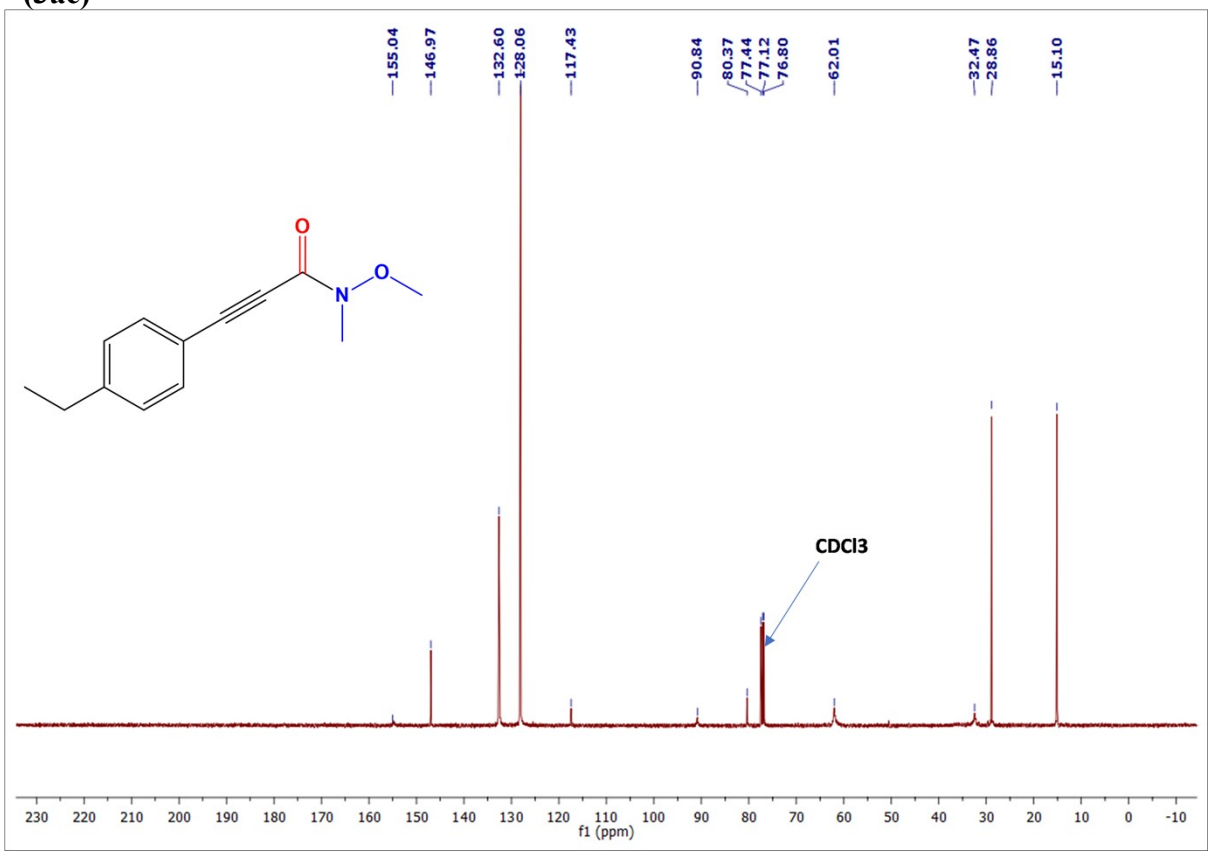
^{13}C NMR (101 MHz, CDCl3) of *N*-methoxy-3-(4-methoxyphenyl)-*N*-methylpropiolamide (3ab)



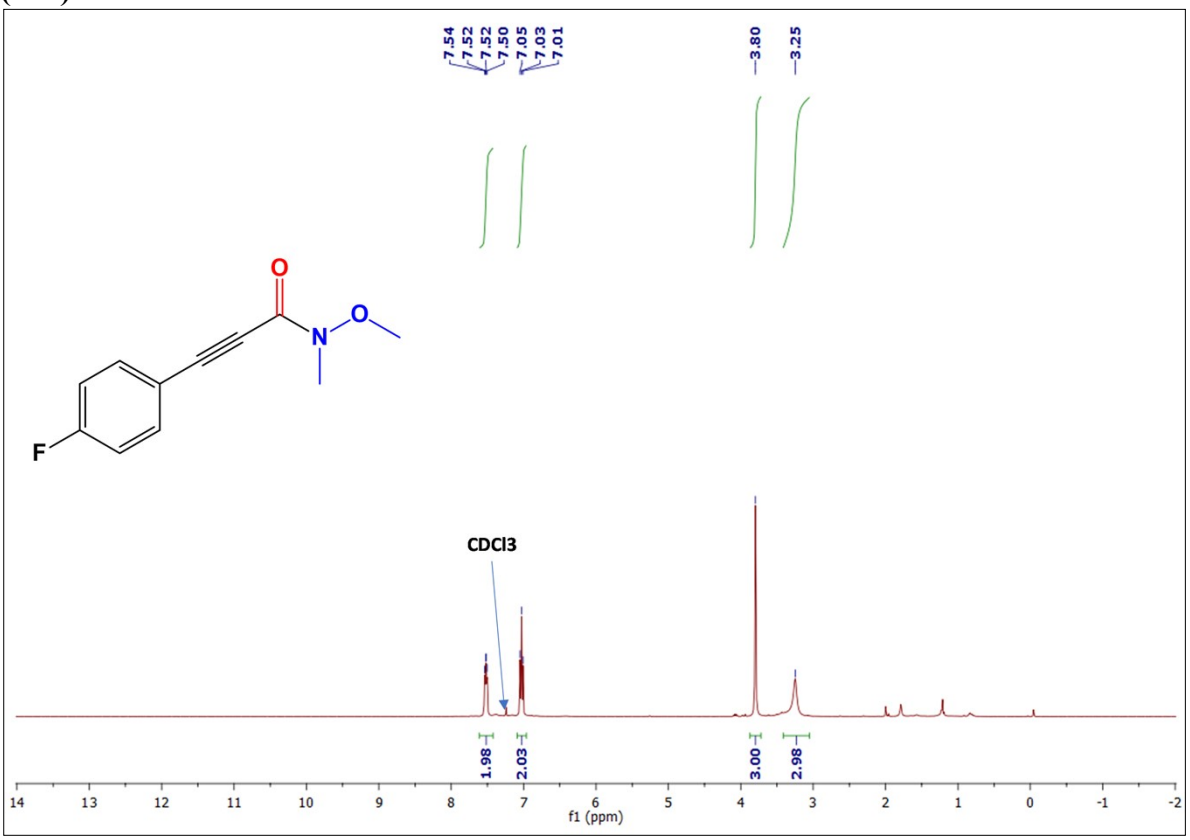
^{1}H NMR (400 MHz, CDCl3) of 3-(4-ethylphenyl)-*N*-methoxy-*N*-methylpropiolamide (3ac)



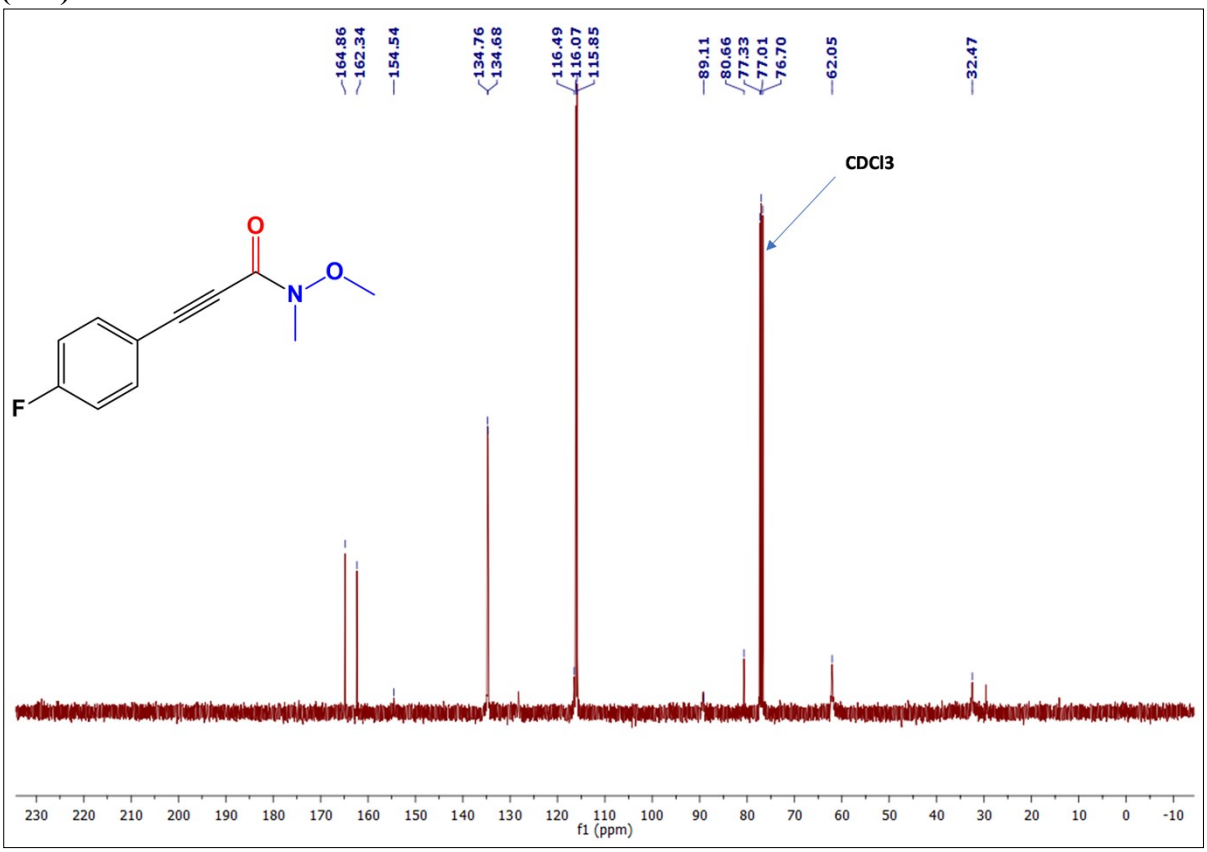
^{13}C NMR (101 MHz, CDCl3) of 3-(4-ethylphenyl)-*N*-methoxy-*N*-methylpropiolamide (3ac)



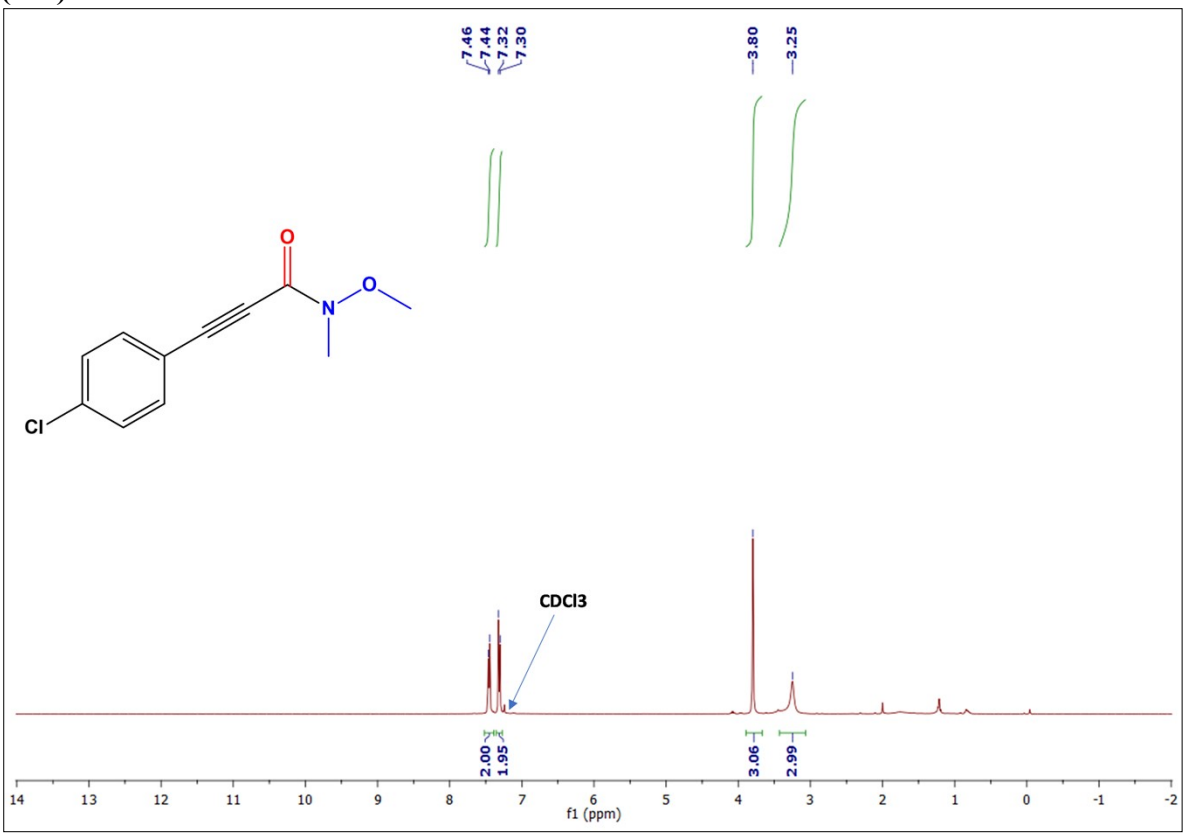
^{1}H NMR (400 MHz, CDCl3) of 3-(4-fluorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ad)



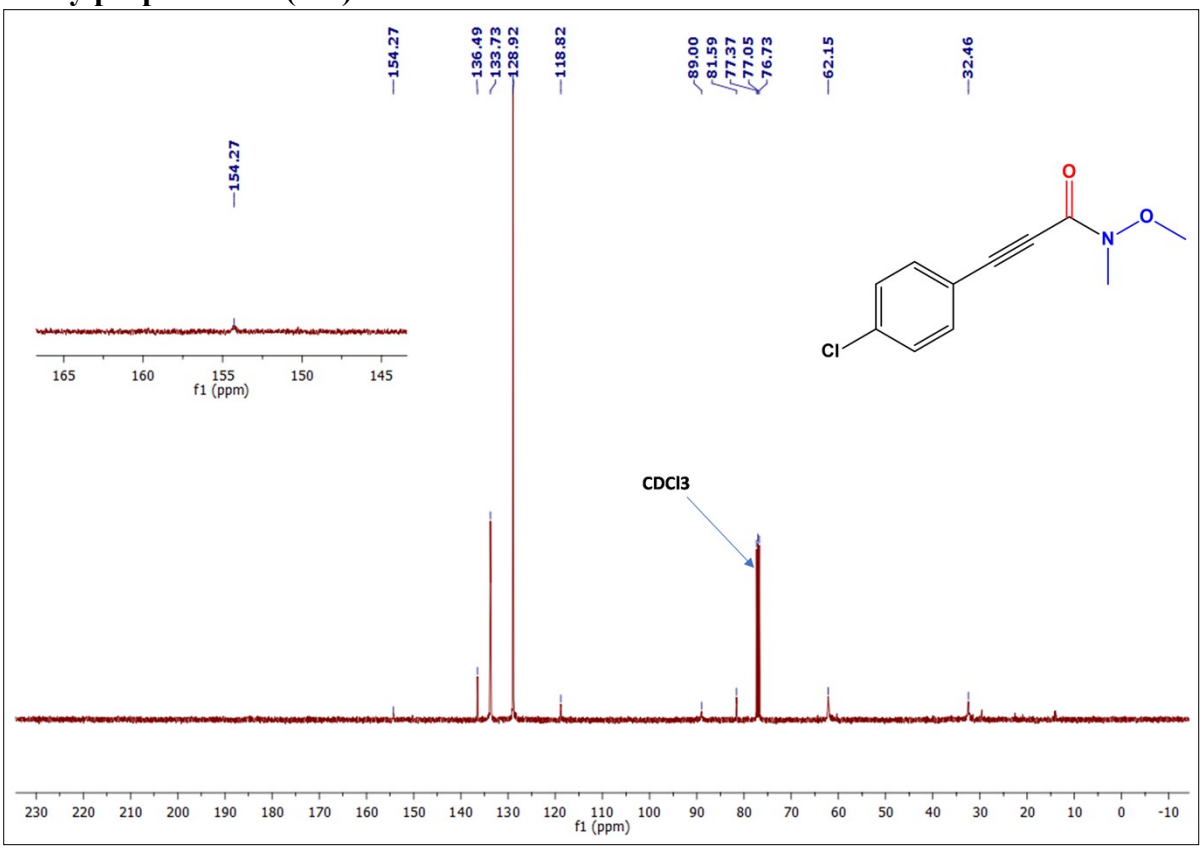
^{13}C NMR (101 MHz, CDCl3) of 3-(4-fluorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ad)



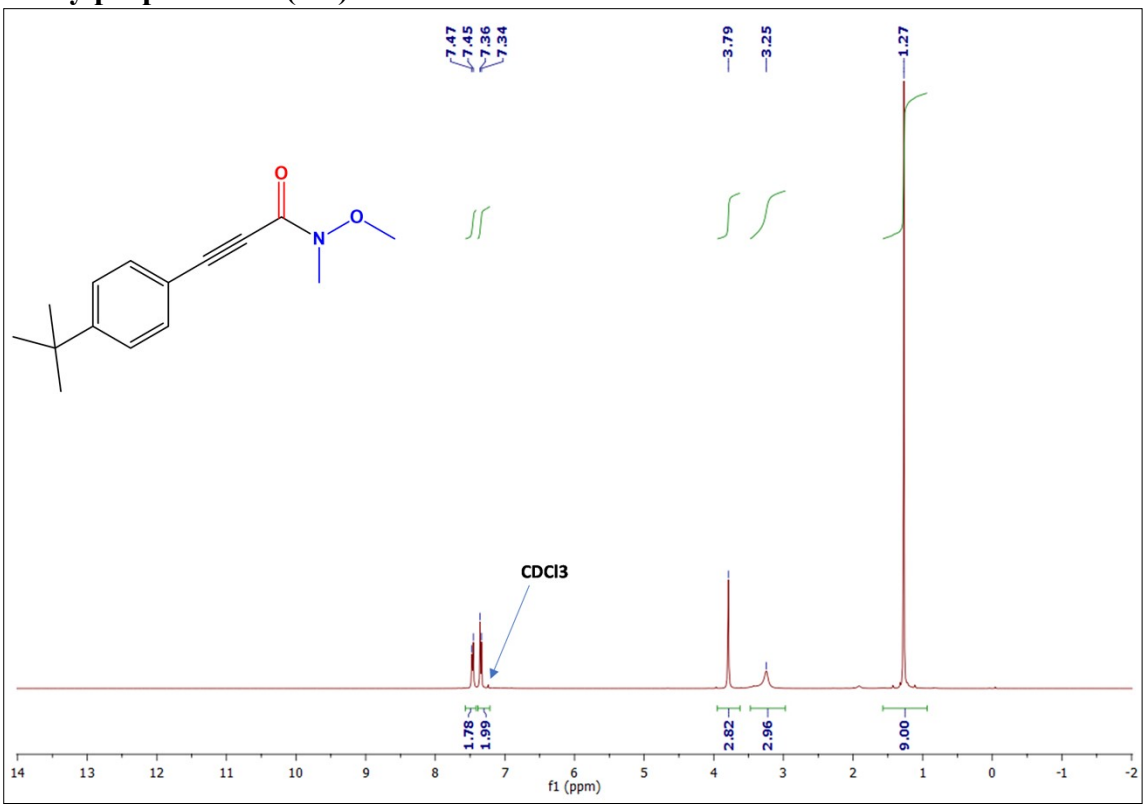
^{1}H NMR (400 MHz, CDCl3) of 3-(4-chlorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ae)



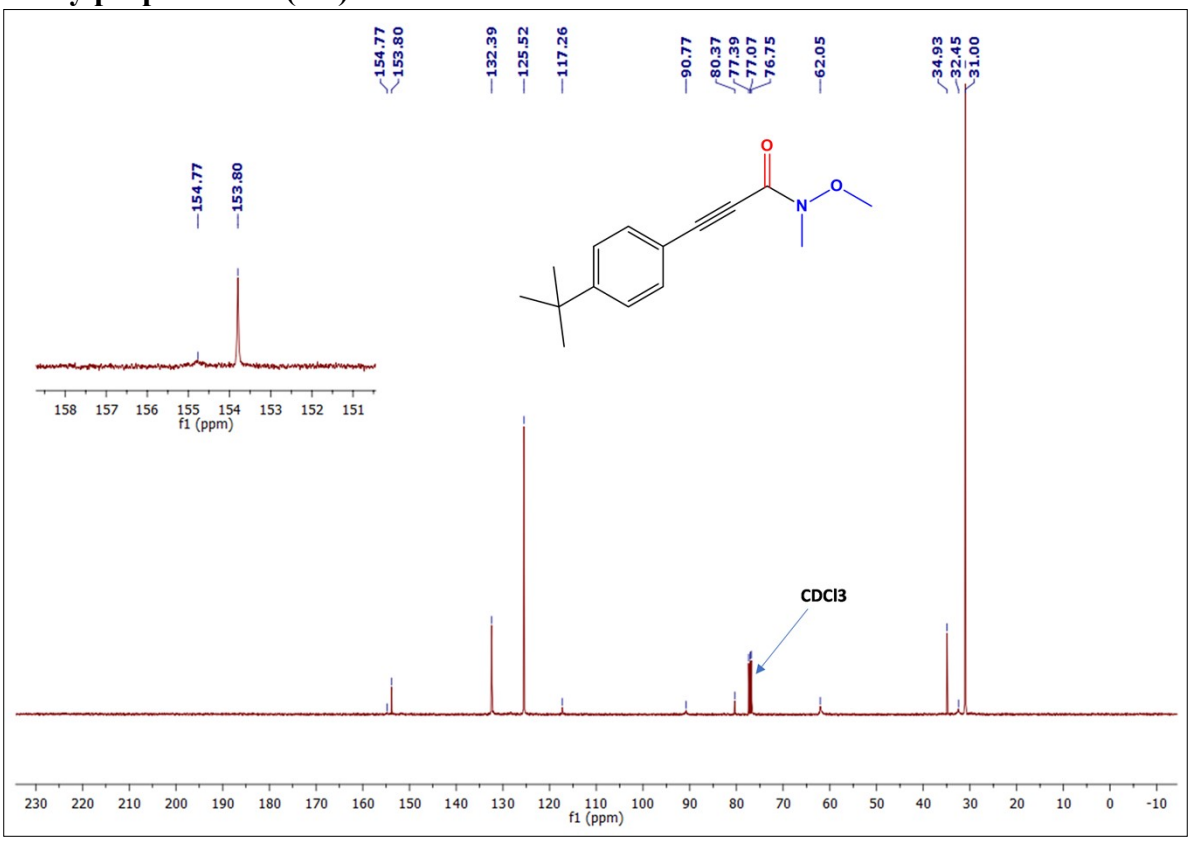
^{13}C NMR (101 MHz, CDCl3) of 3-(4-chlorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ae)



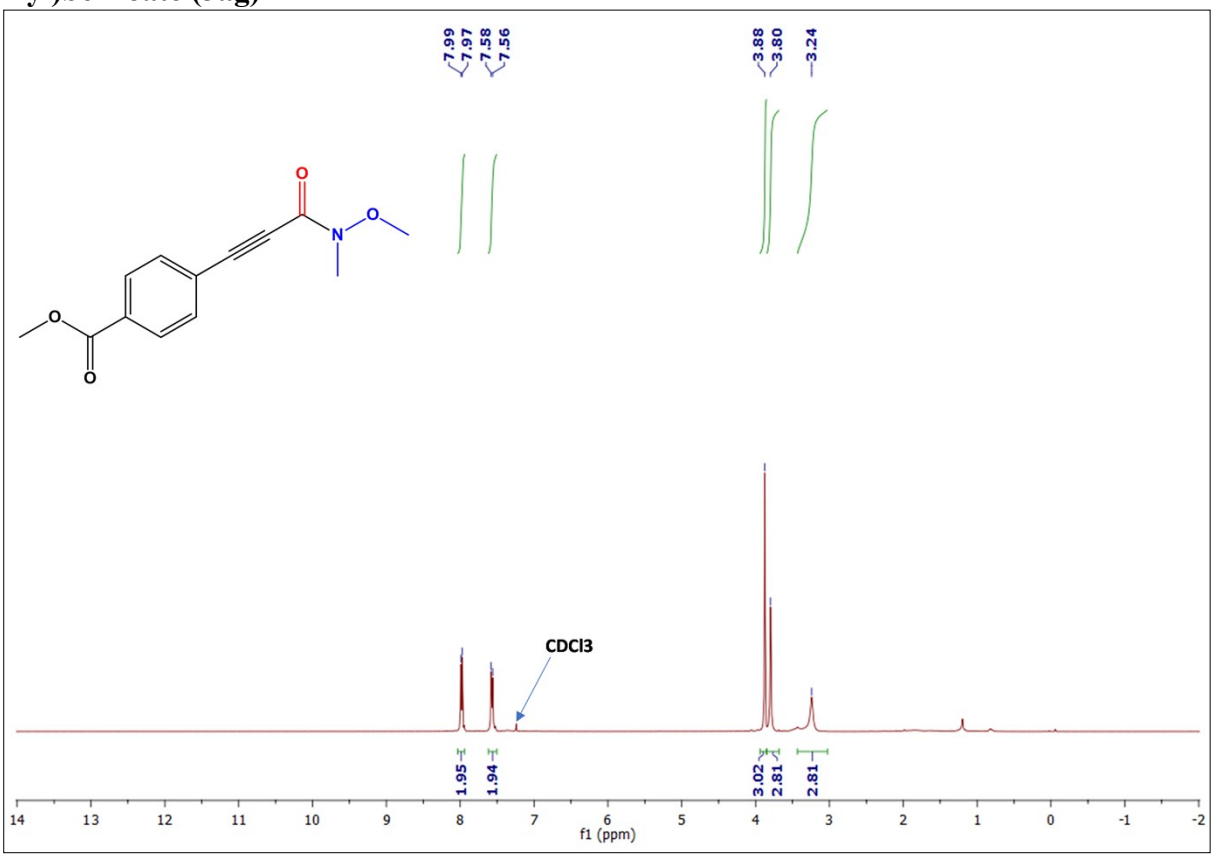
^{1}H NMR (400 MHz, CDCl3) of 3-(4-(tert-butyl)phenyl)-*N*-methoxy-*N*-methylpropiolamide (3af)



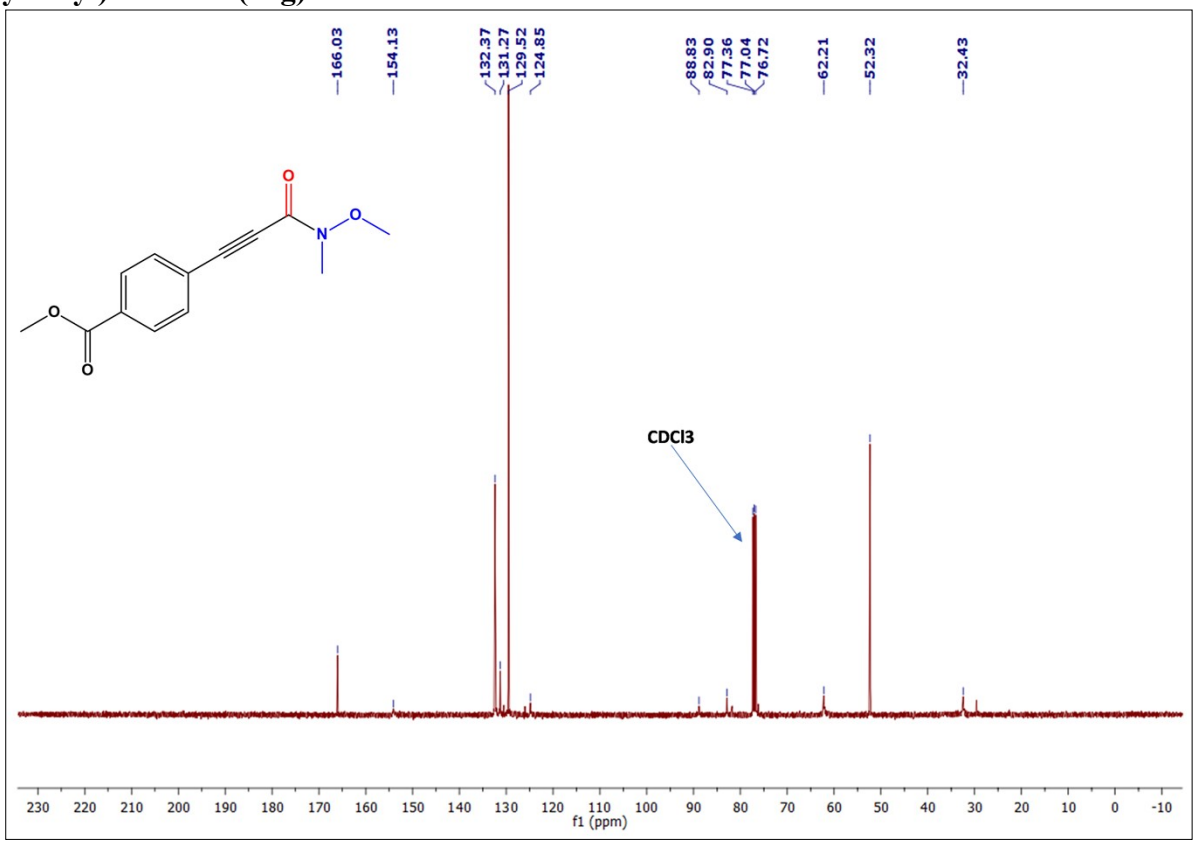
^{13}C NMR (101 MHz, CDCl3) of 3-(4-(tert-butyl)phenyl)-*N*-methoxy-*N*-methylpropiolamide (3af)



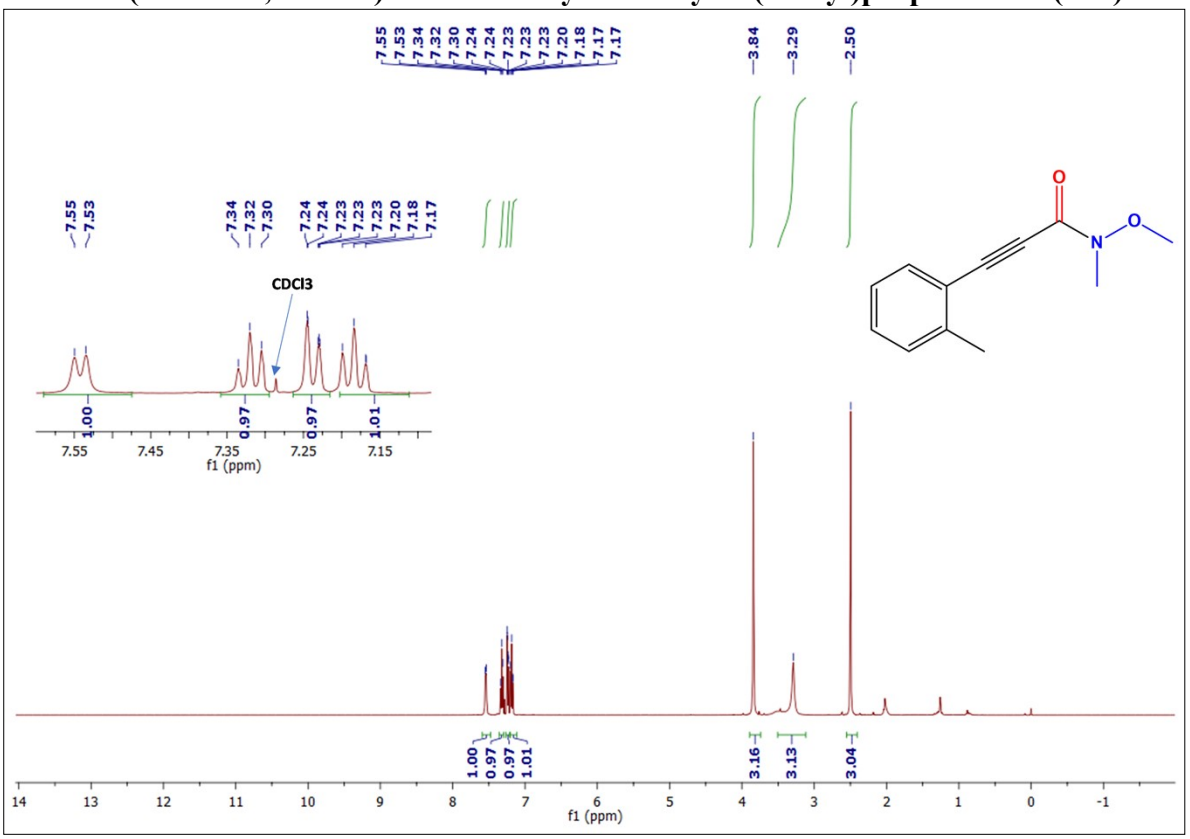
^{1}H NMR (400 MHz, CDCl3) of methyl 4-(3-(methoxy(methyl)amino)-3-oxoprop-1-yn-1-yl)benzoate (3ag)



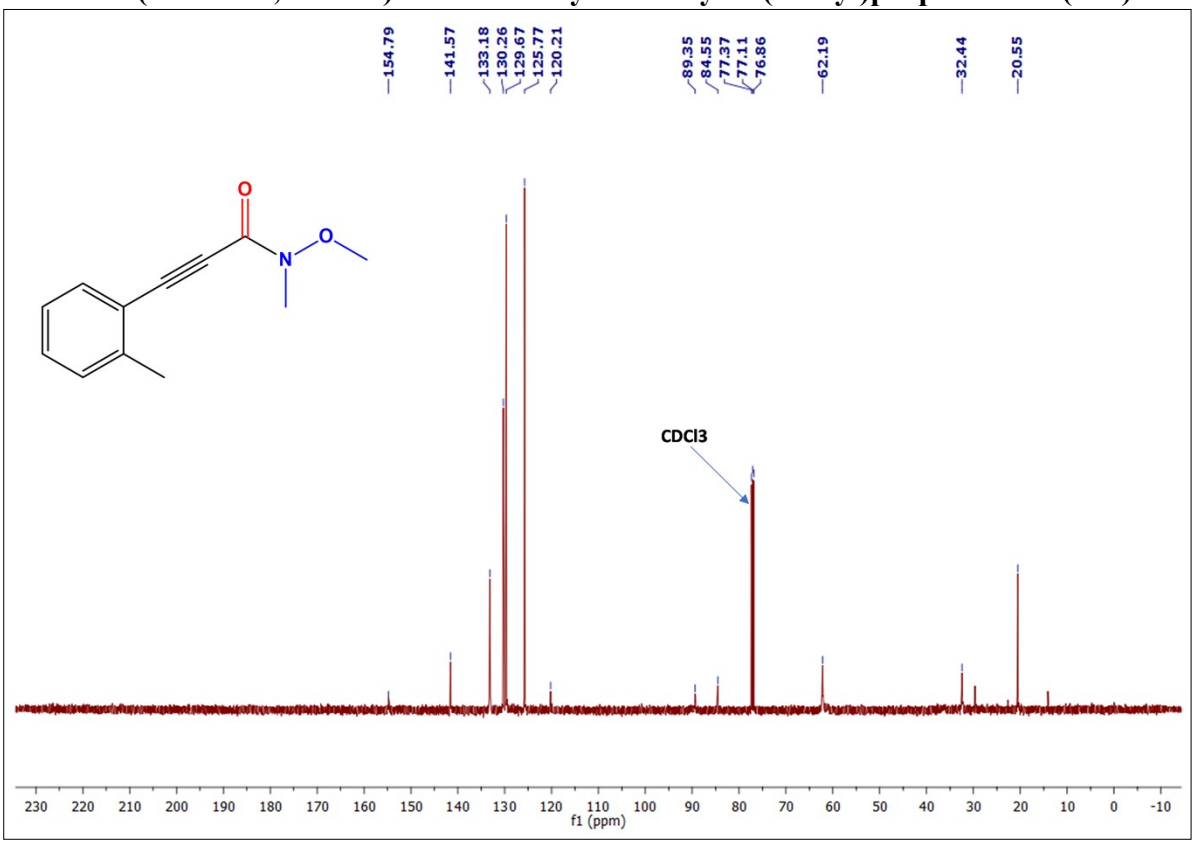
^{13}C NMR (101 MHz, CDCl3) of methyl 4-(3-(methoxy(methyl)amino)-3-oxoprop-1-yn-1-yl)benzoate (3ag)



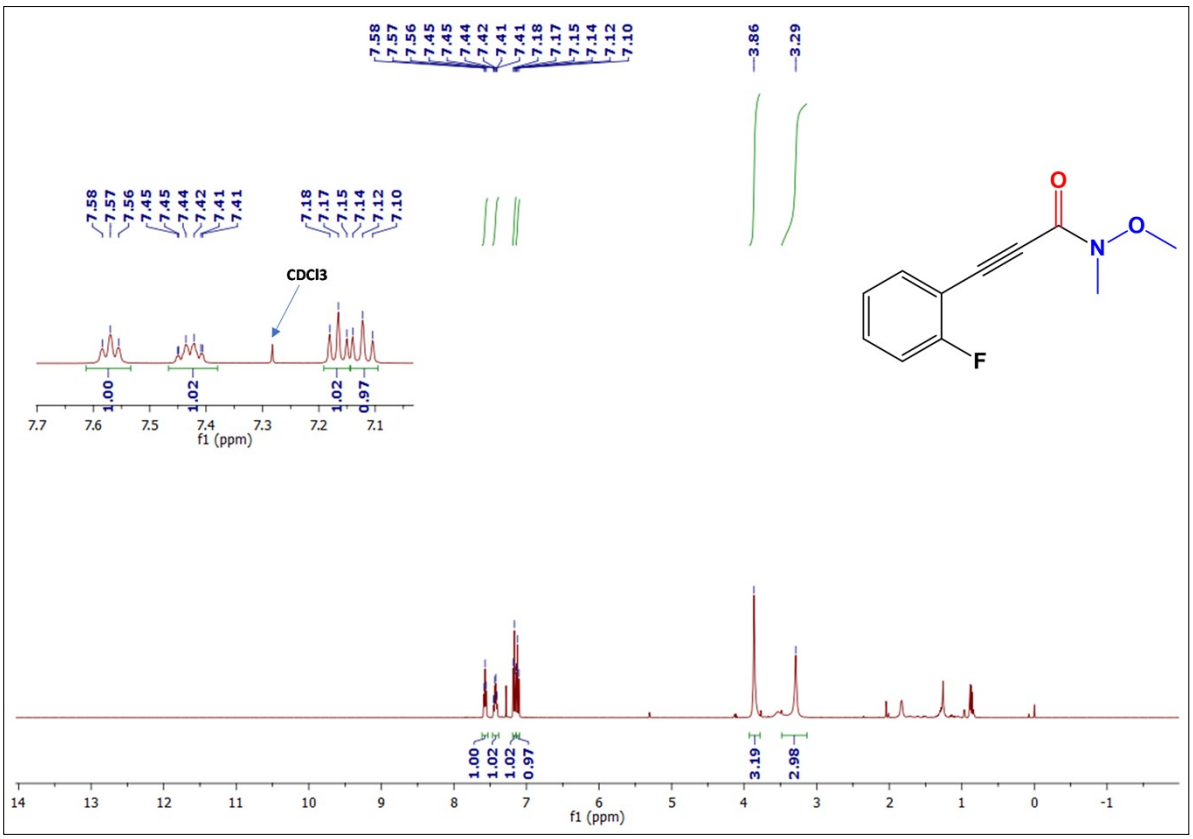
^{1}H NMR (500 MHz, CDCl3) of *N*-methoxy-*N*-methyl-3-(*o*-tolyl)propiolamide (3ah)



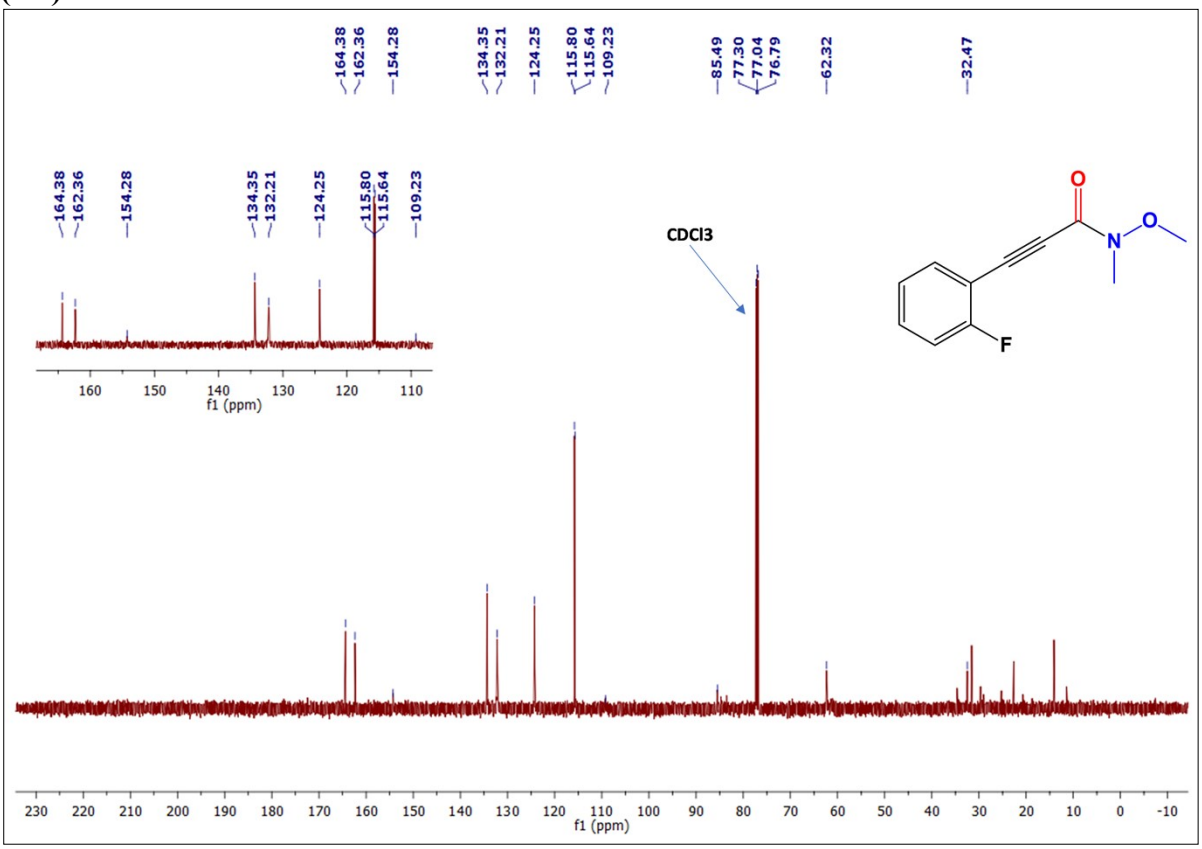
^{13}C NMR (126 MHz, CDCl3) of *N*-methoxy-*N*-methyl-3-(*o*-tolyl)propiolamide (3ah)



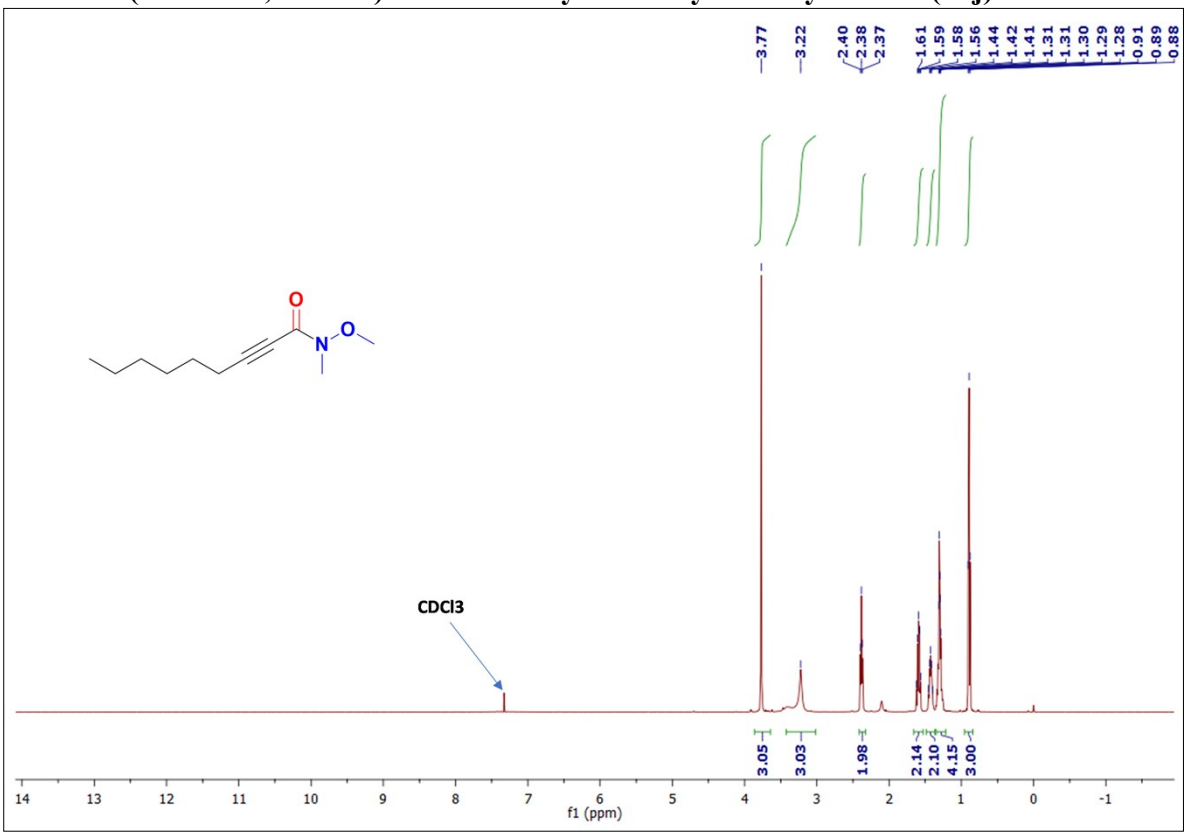
^{1}H NMR (500 MHz, CDCl3) of 3-(2-fluorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ai)



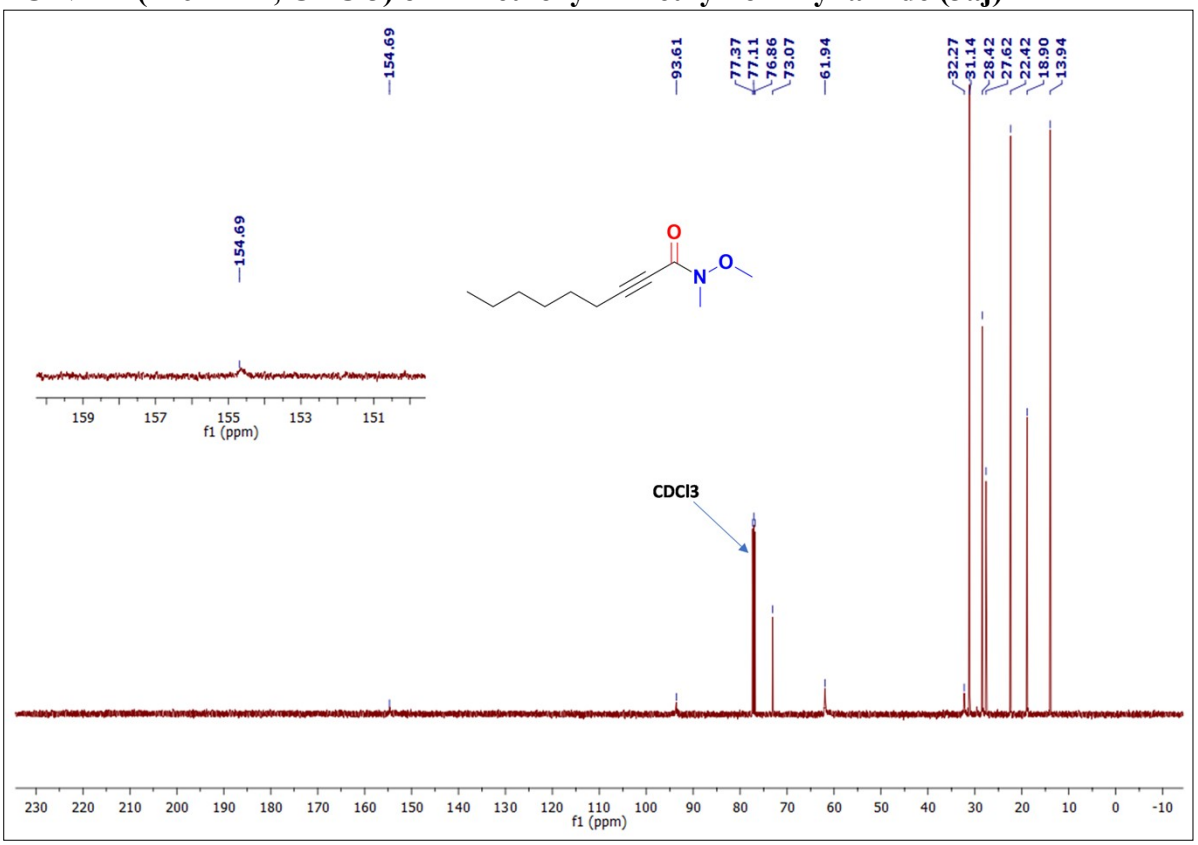
^{13}C NMR (126 MHz, CDCl3) of 3-(2-fluorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ai)



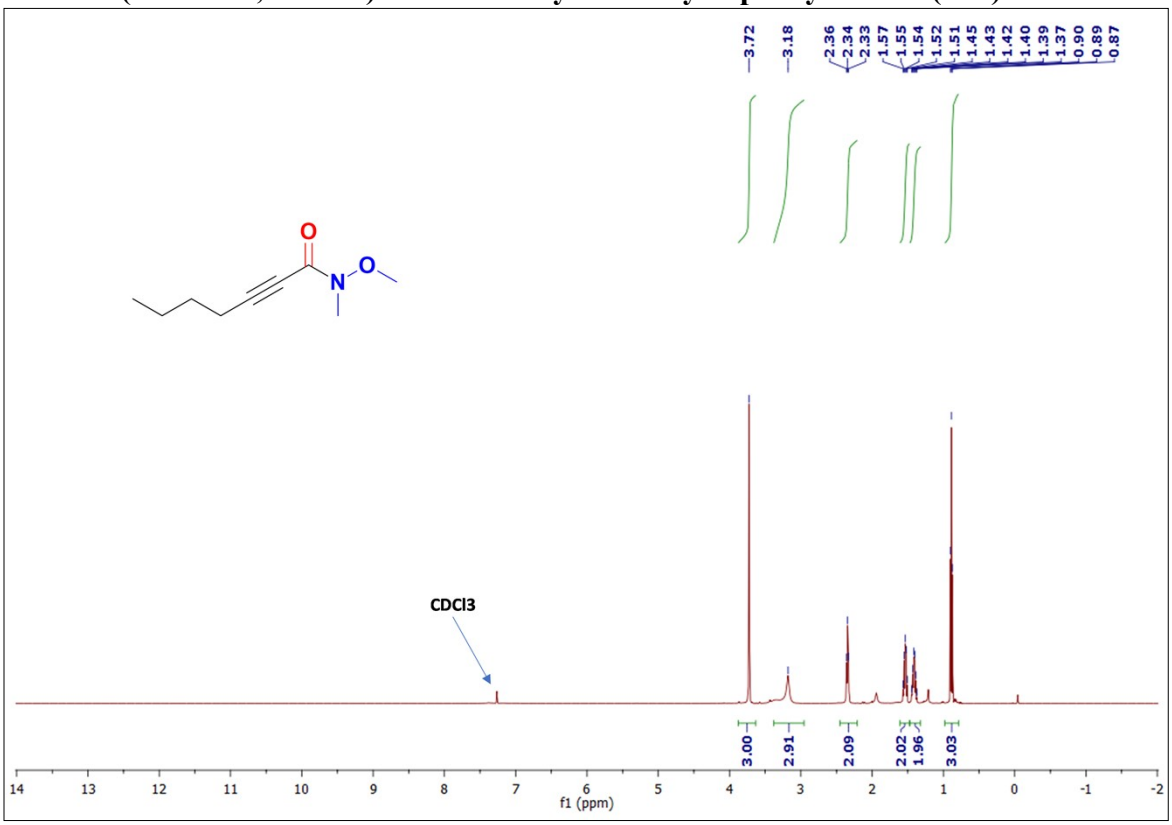
^{1}H NMR (500 MHz, CDCl3) of *N*-methoxy-*N*-methylnon-2-ynamide (3aj)



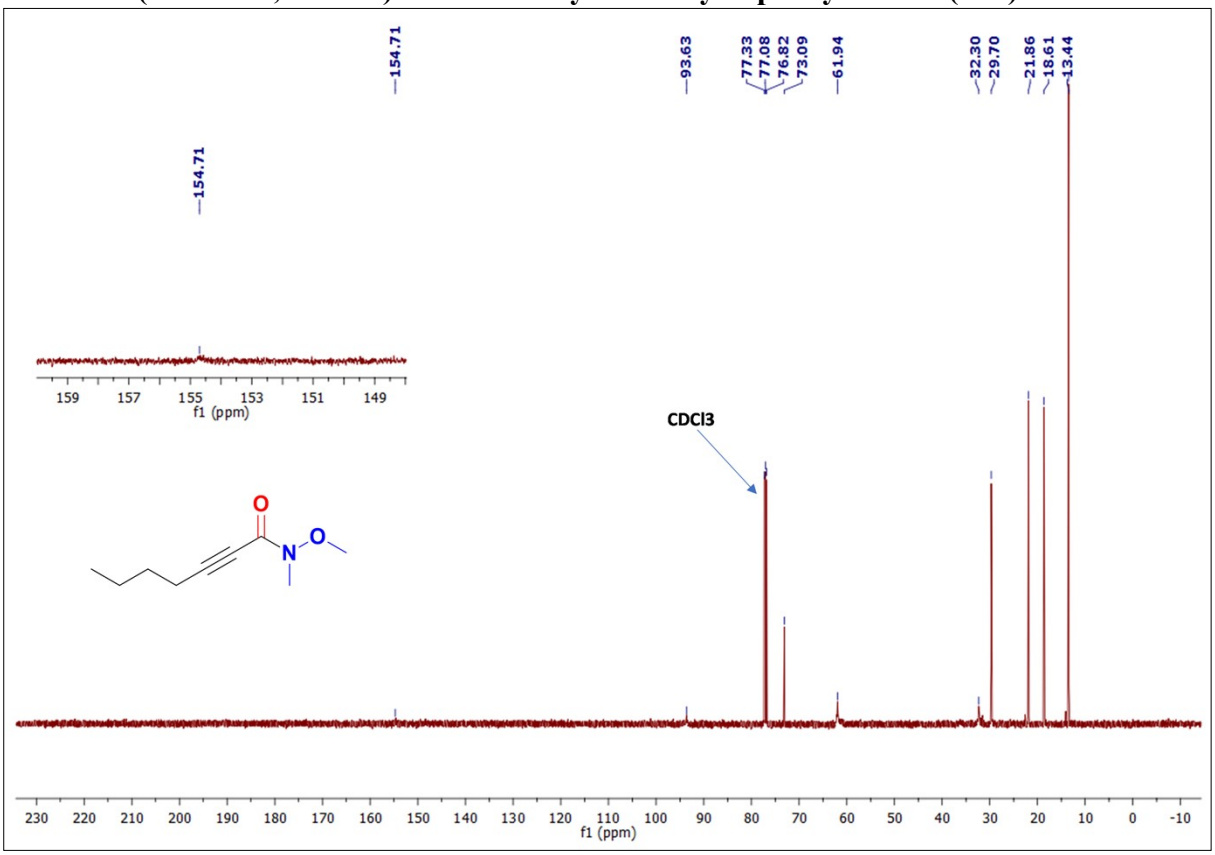
^{13}C NMR (126 MHz, CDCl3) of *N*-methoxy-*N*-methylnon-2-ynamide (3aj)



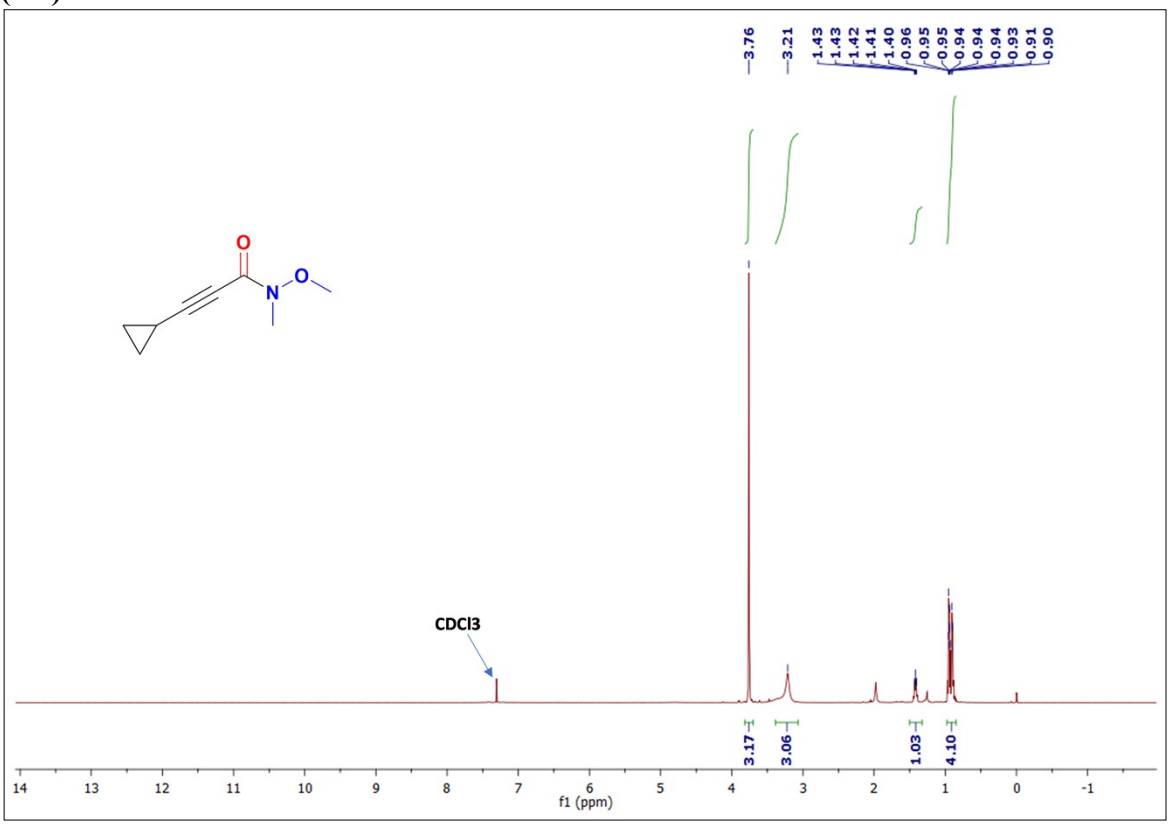
^{1}H NMR (500 MHz, CDCl3) of *N*-methoxy-*N*-methylhept-2-ynamide (3ak)



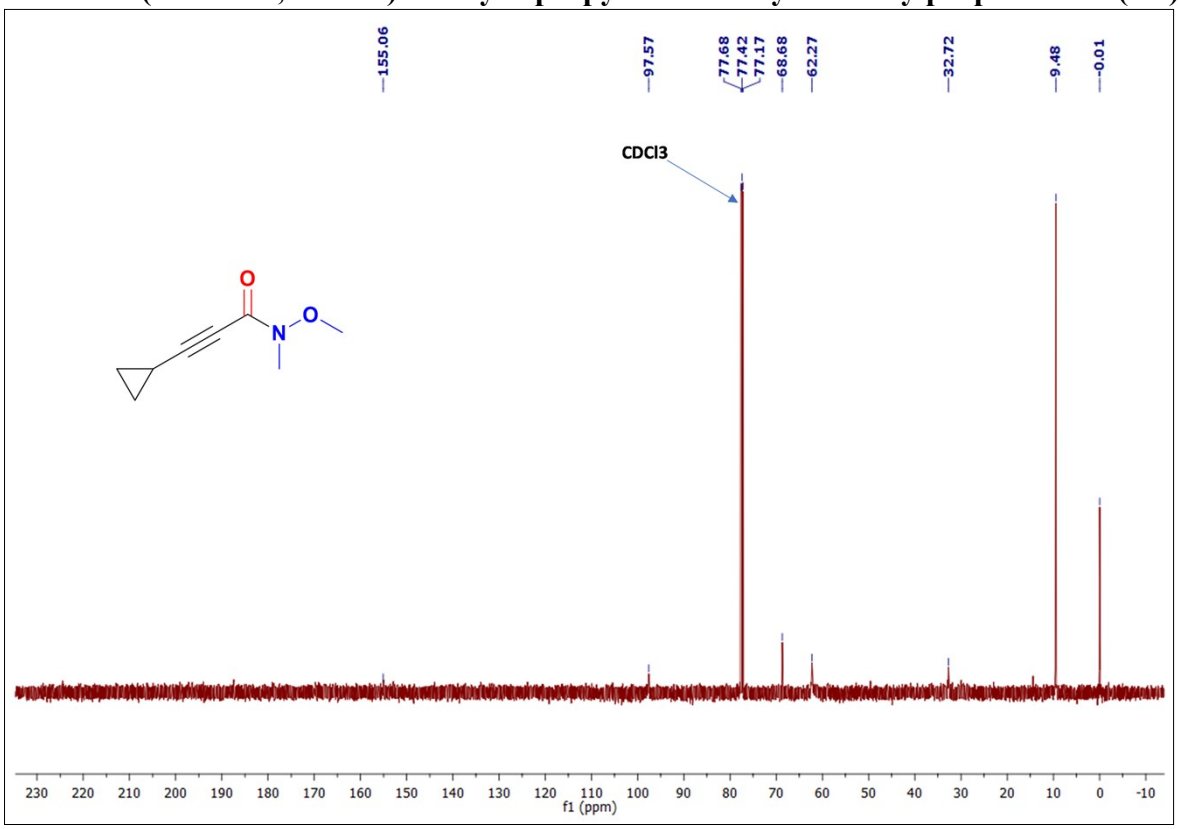
^{13}C NMR (126 MHz, CDCl3) of *N*-methoxy-*N*-methylhept-2-ynamide (3ak)



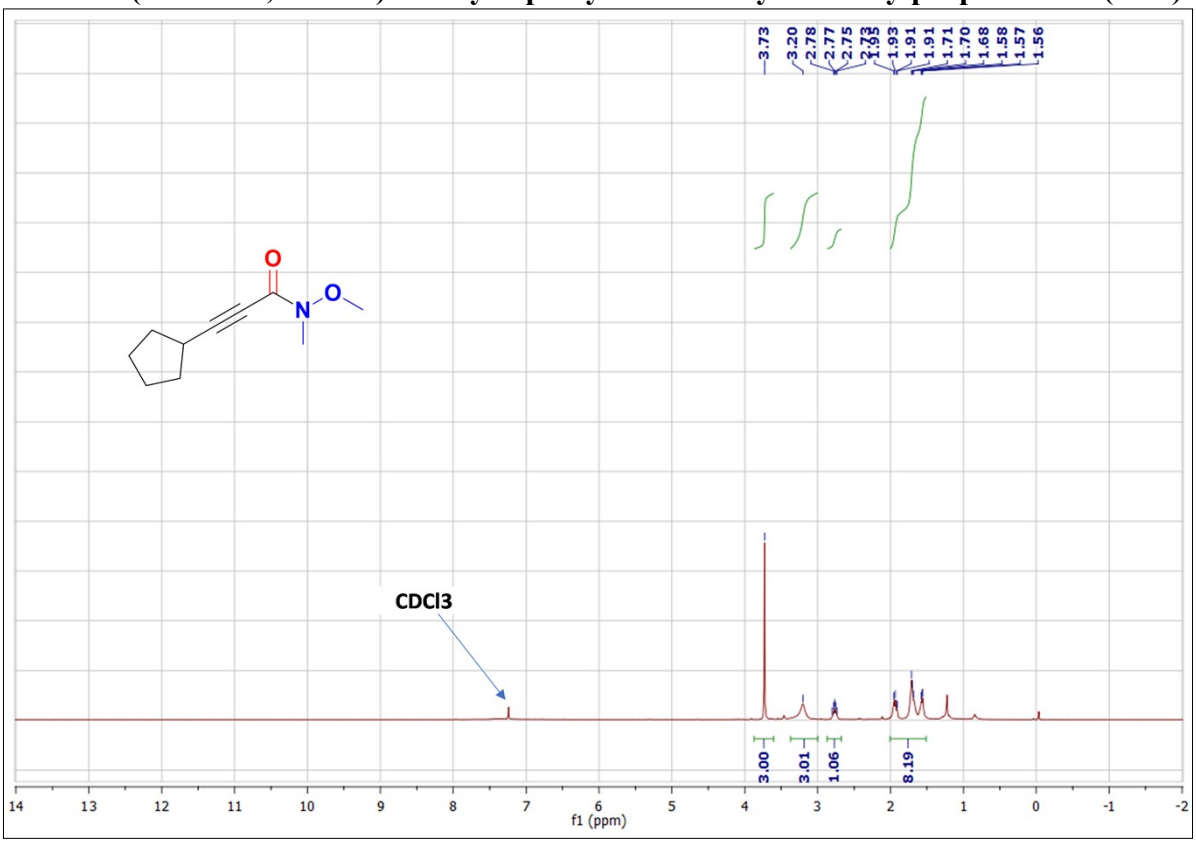
^{1}H NMR (500 MHz, CDCl3) of 3-cyclopropyl-*N*-methoxy-*N*-methylpropiolamide (3al)



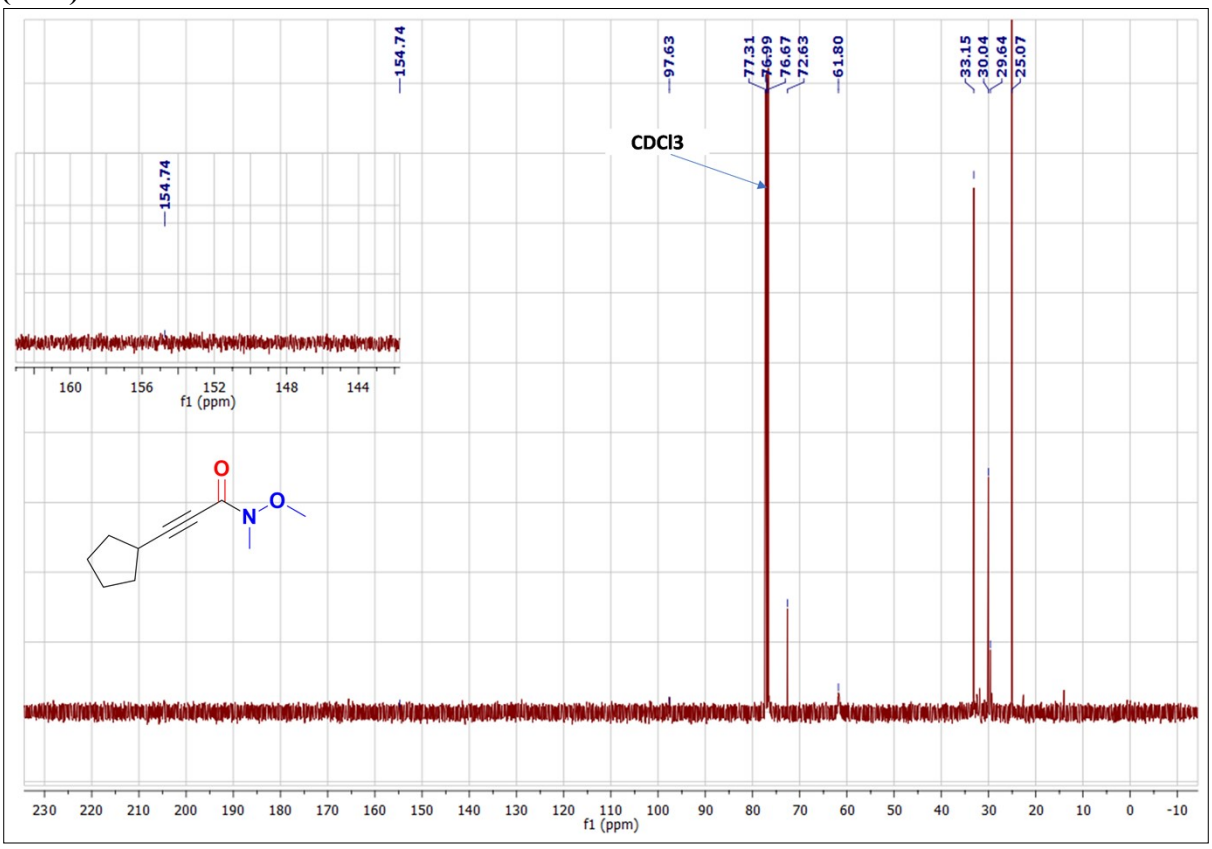
^{13}C NMR (126 MHz, CDCl3) of 3-cyclopropyl-*N*-methoxy-*N*-methylpropiolamide (3al)



^{1}H NMR (400 MHz, CDCl3) of 3-cyclopentyl-*N*-methoxy-*N*-methylpropiolamide (3am)

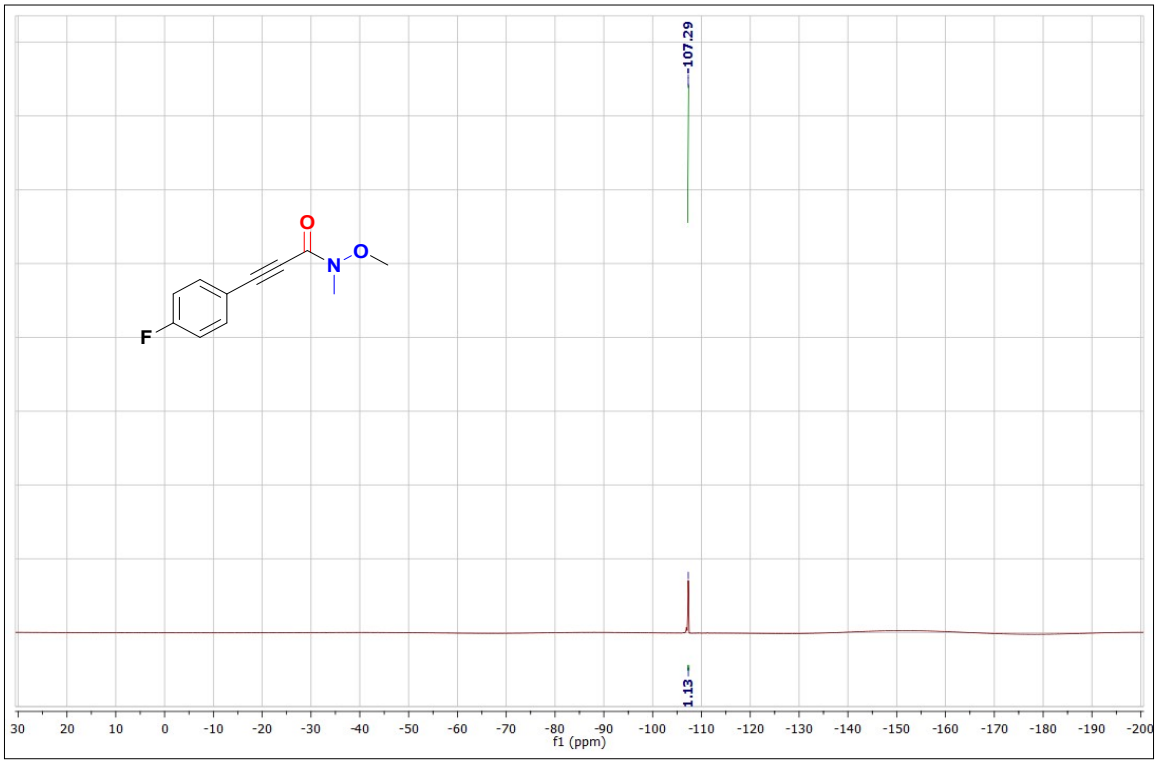


^{13}C NMR (101 MHz, CDCl3) of 3-cyclopentyl-*N*-methoxy-*N*-methylpropiolamide (3am)

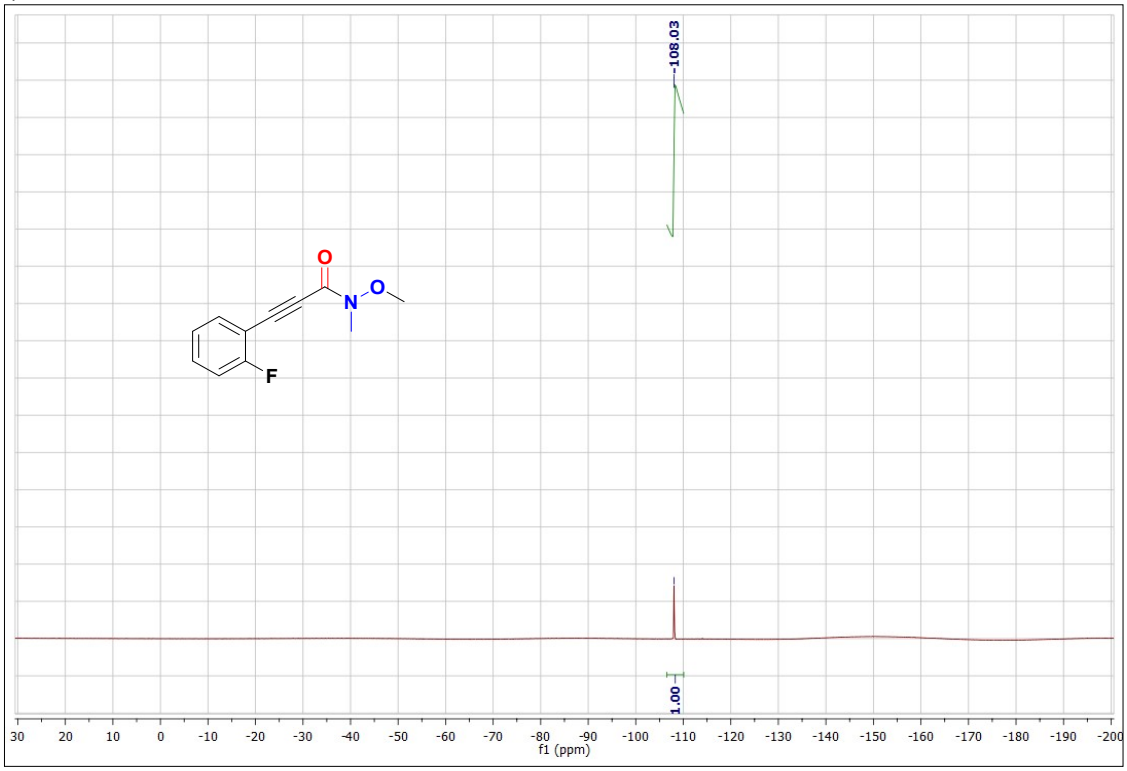


vi. ^{19}F NMR

^{19}F NMR (470 MHz, CDCl3) of 3-(4-fluorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ad)

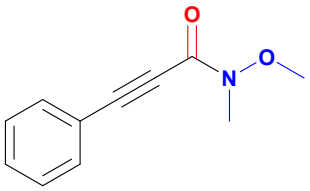


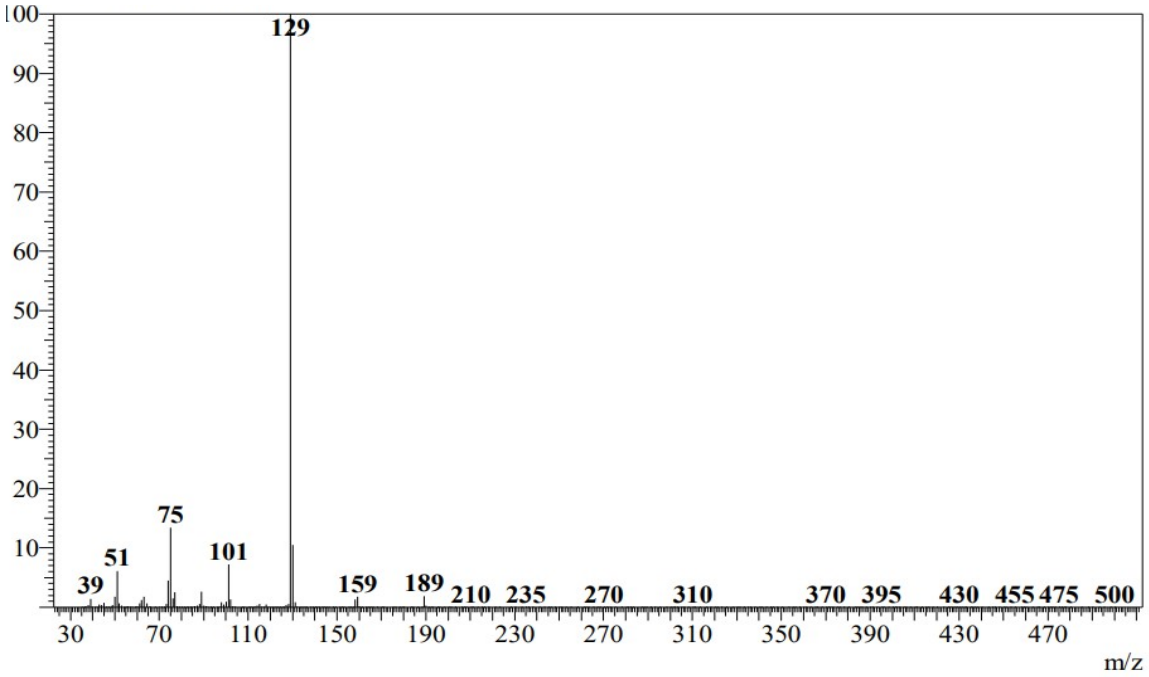
^{19}F NMR (470 MHz, $CDCl_3$) of 3-(2-fluorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ai)



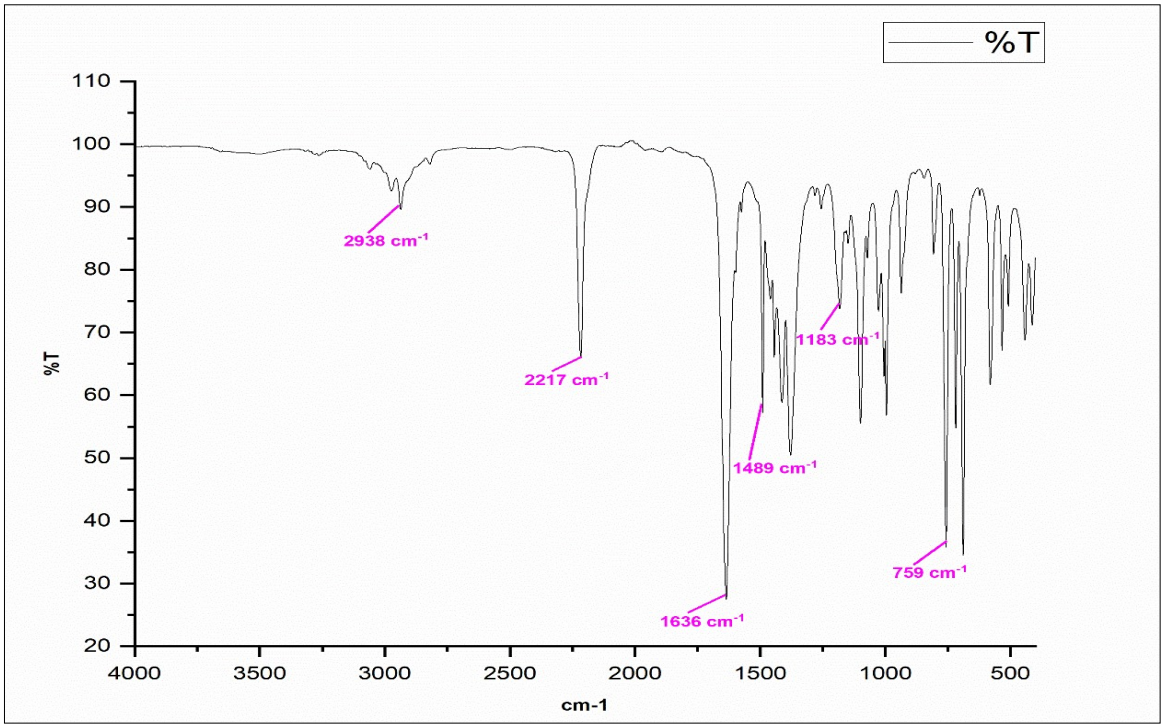
vii. GCMS and FTIR data of 3a and It's derivatives

a. GCMS spectra of *N*-methoxy-*N*-methyl-3-phenylpropiolamide(3a)

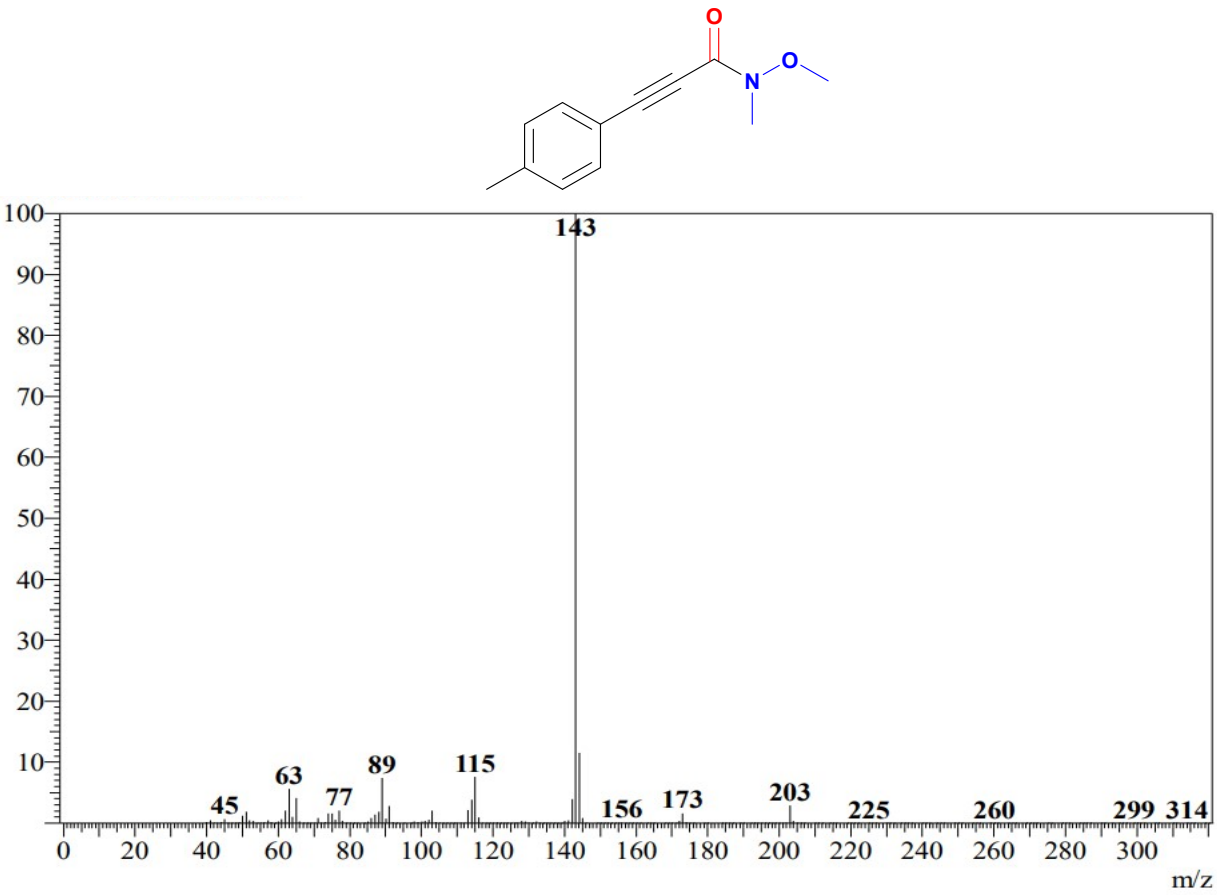




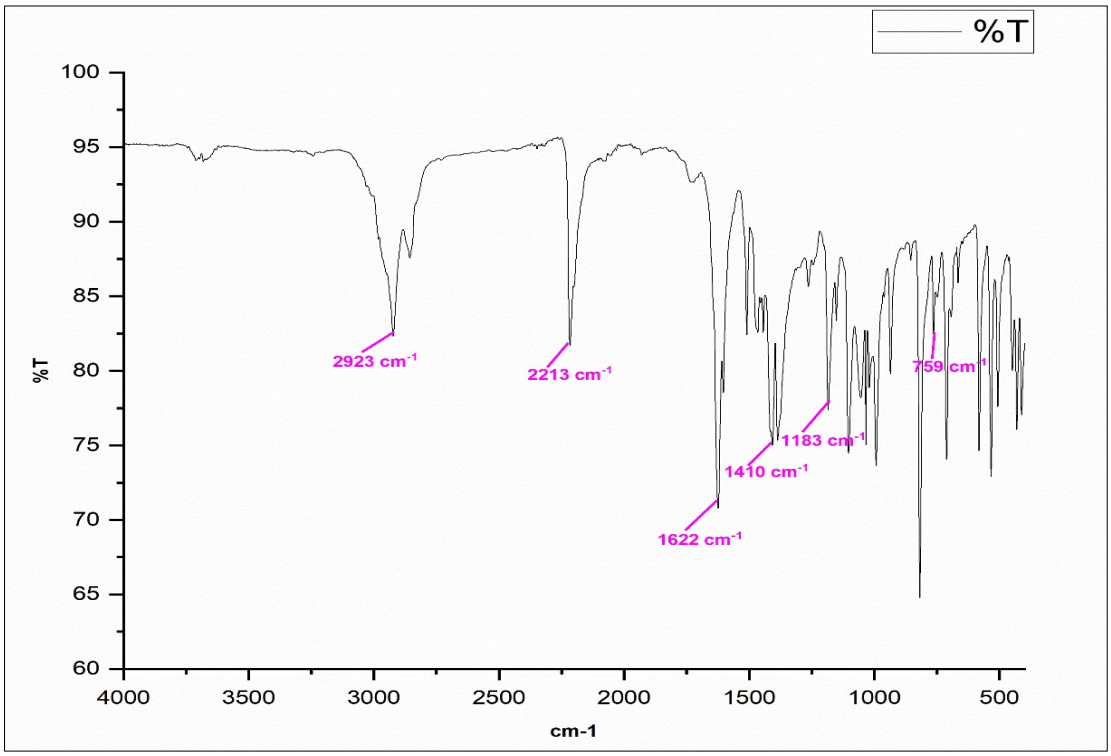
a. FTIR spectra of *N*-methoxy-*N*-methyl-3-phenylpropiolamide(3a)



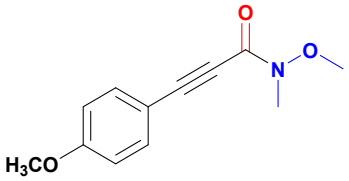
b. GCMS spectra of *N*-methoxy-*N*-methyl-3-(*p*-tolyl)propiolamide (3aa')

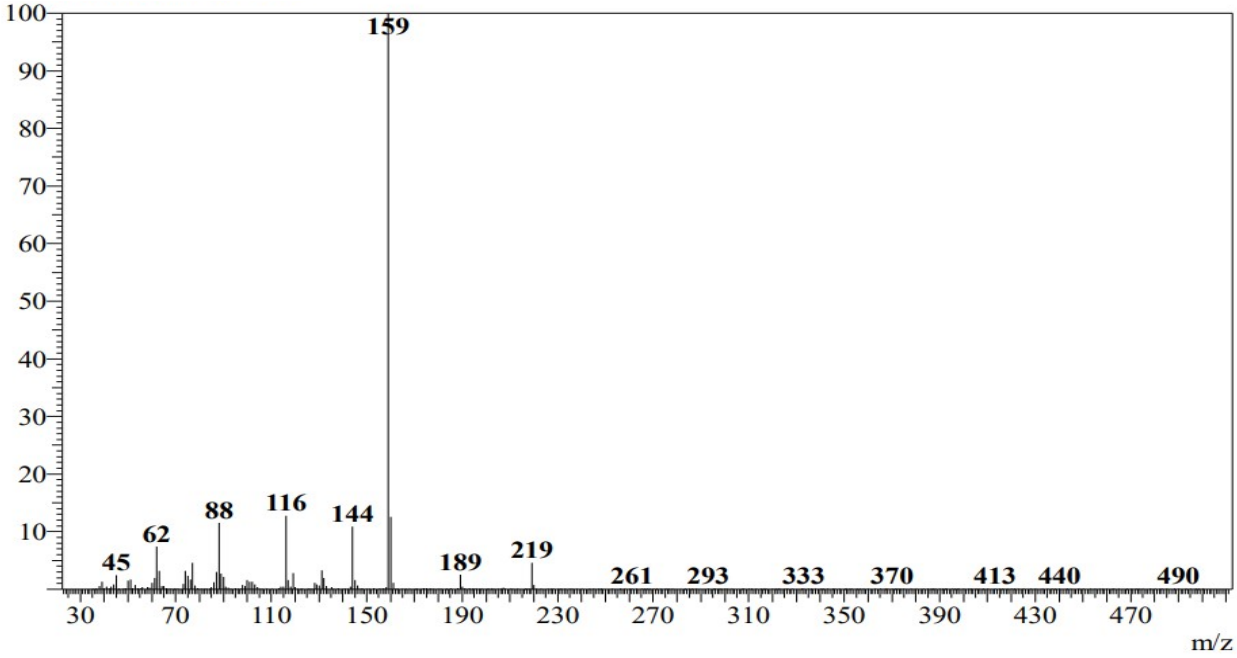


b. FTIR spectra of *N*-methoxy-*N*-methyl-3-(*p*-tolyl)propiolamide (3aa')

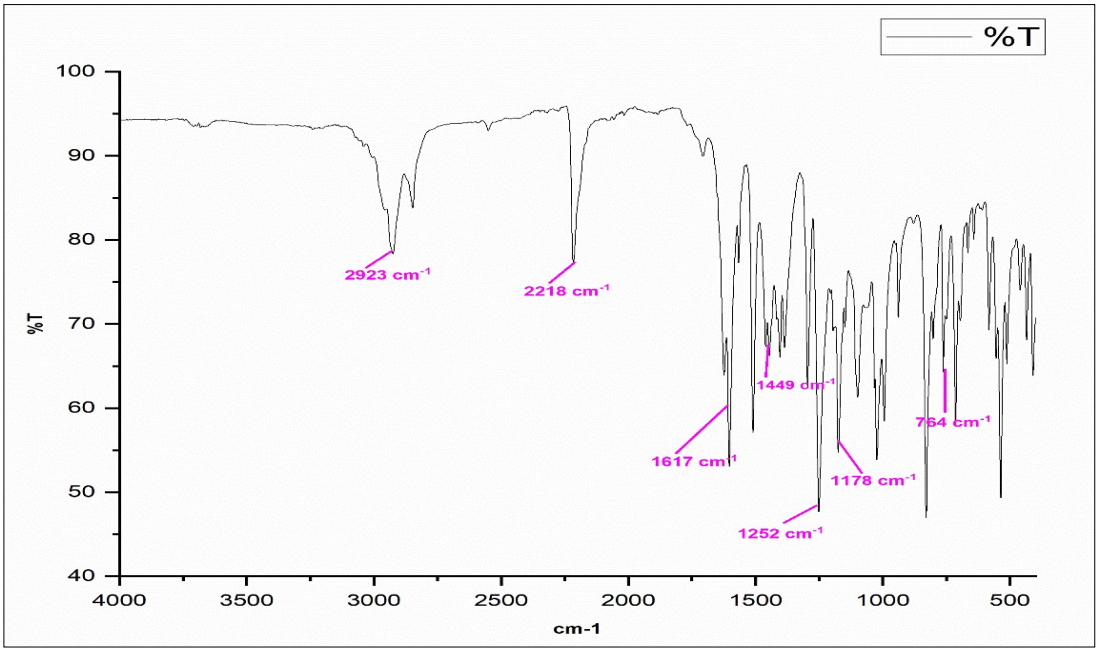


c. GCMS spectra of *N*-methoxy-3-(4-methoxyphenyl)-*N*-methylpropiolamide (3ab)

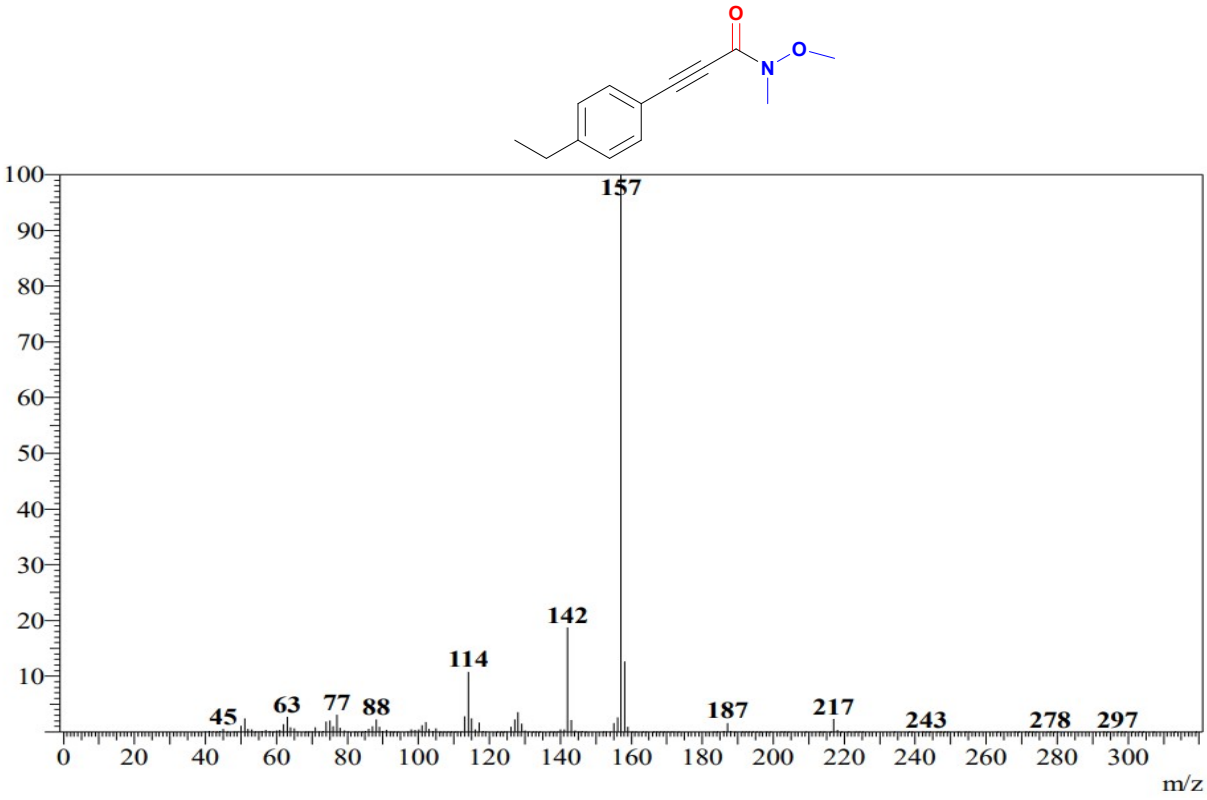




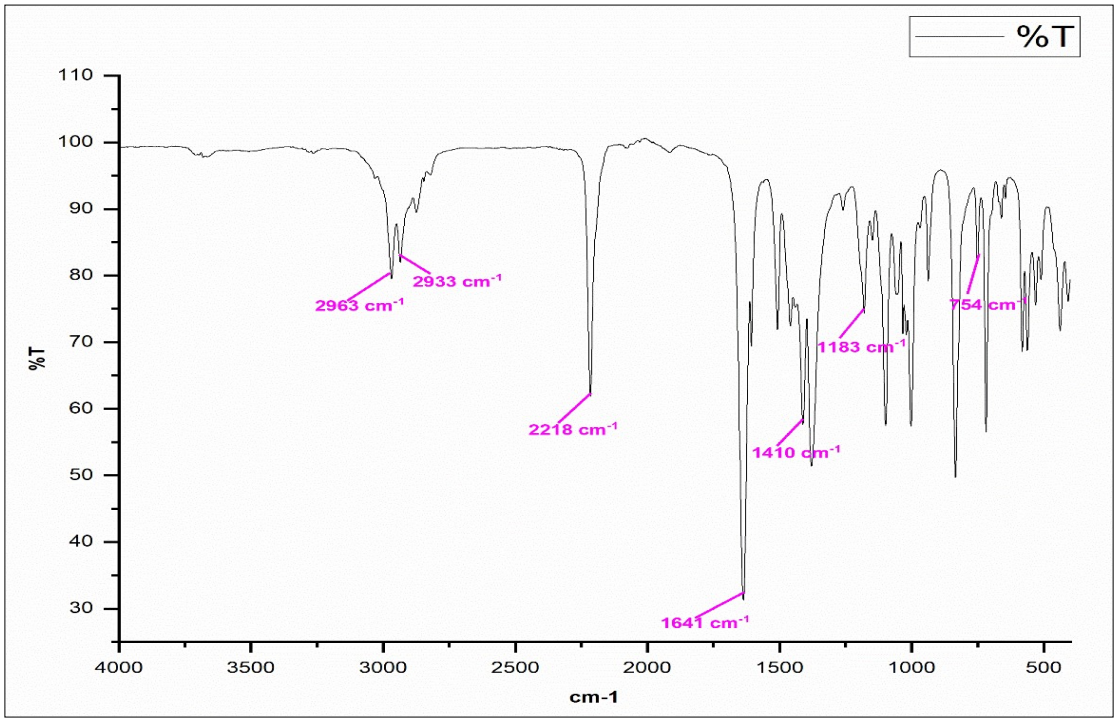
c. FTIR spectra of *N*-methoxy-3-(4-methoxyphenyl)-*N*-methylpropiolamide (3ab)



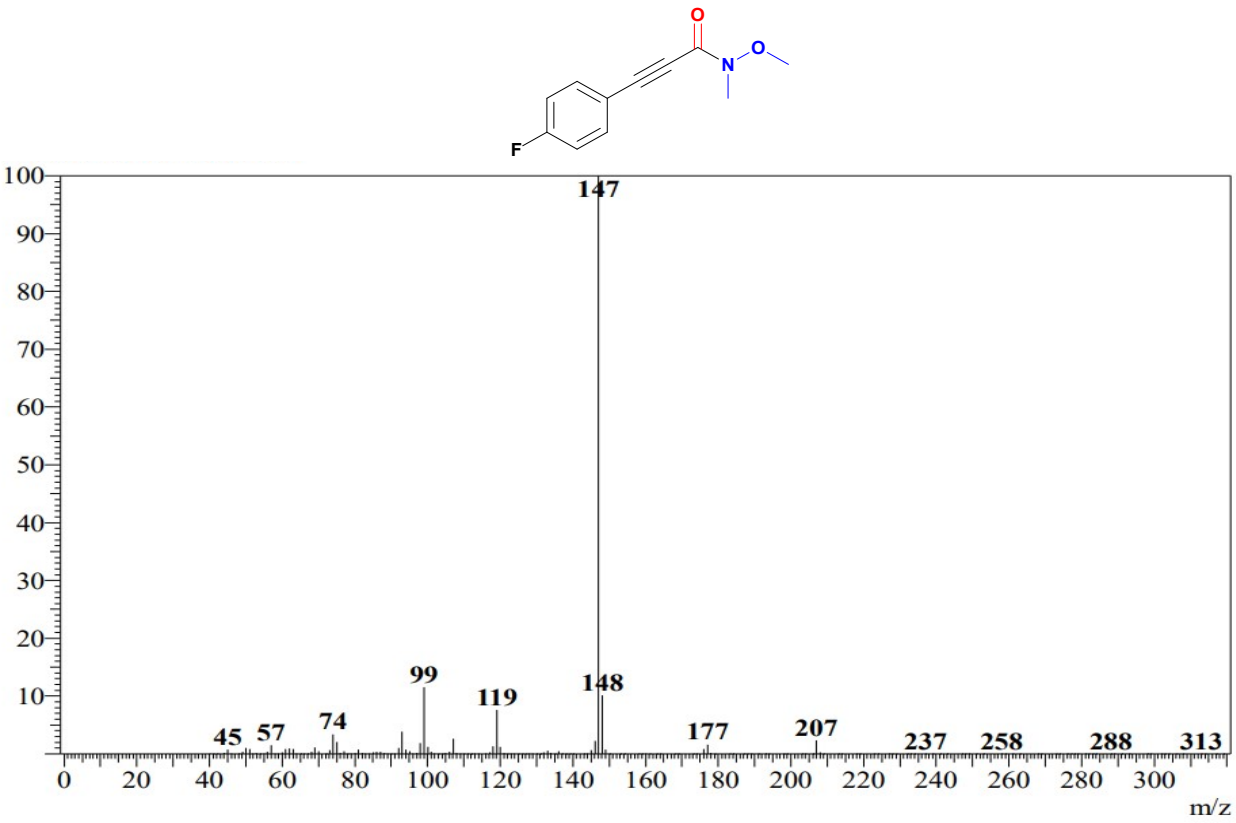
d. GCMS spectra of 3-(4-ethylphenyl)-*N*-methoxy-*N*-methylpropiolamide (3ac)



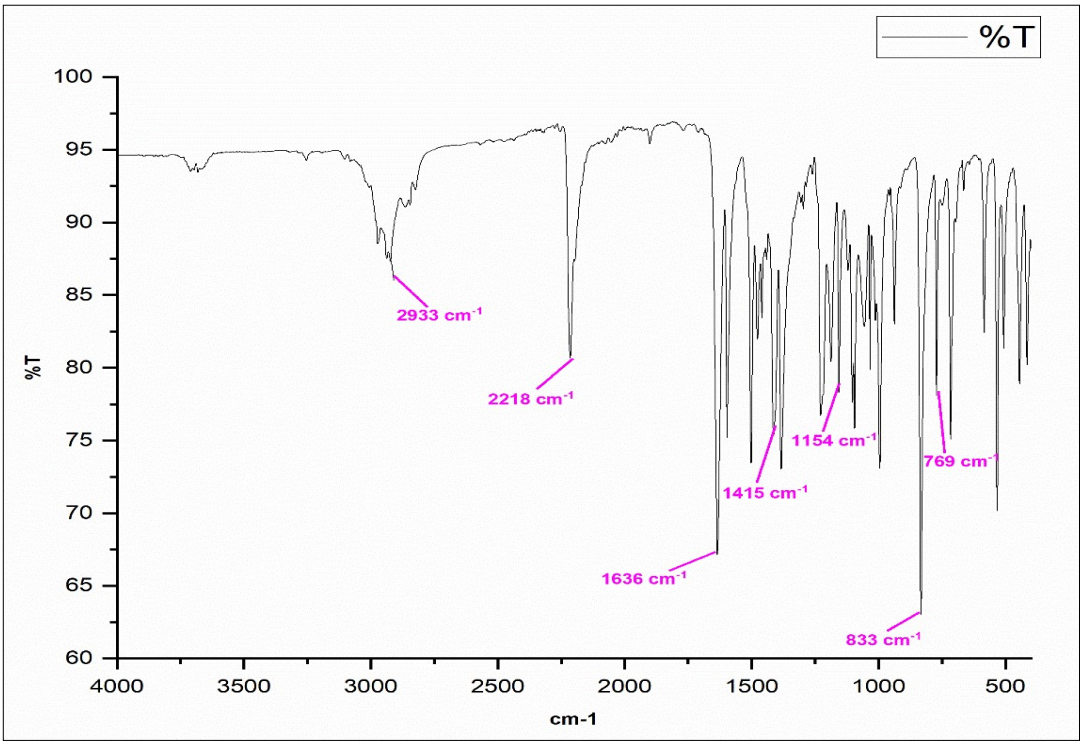
d. FTIR spectra of 3-(4-ethylphenyl)-*N*-methoxy-*N*-methylpropiolamide (3ac)



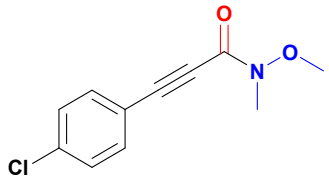
e. **GCMS spectra of 3-(4-fluorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ad)**

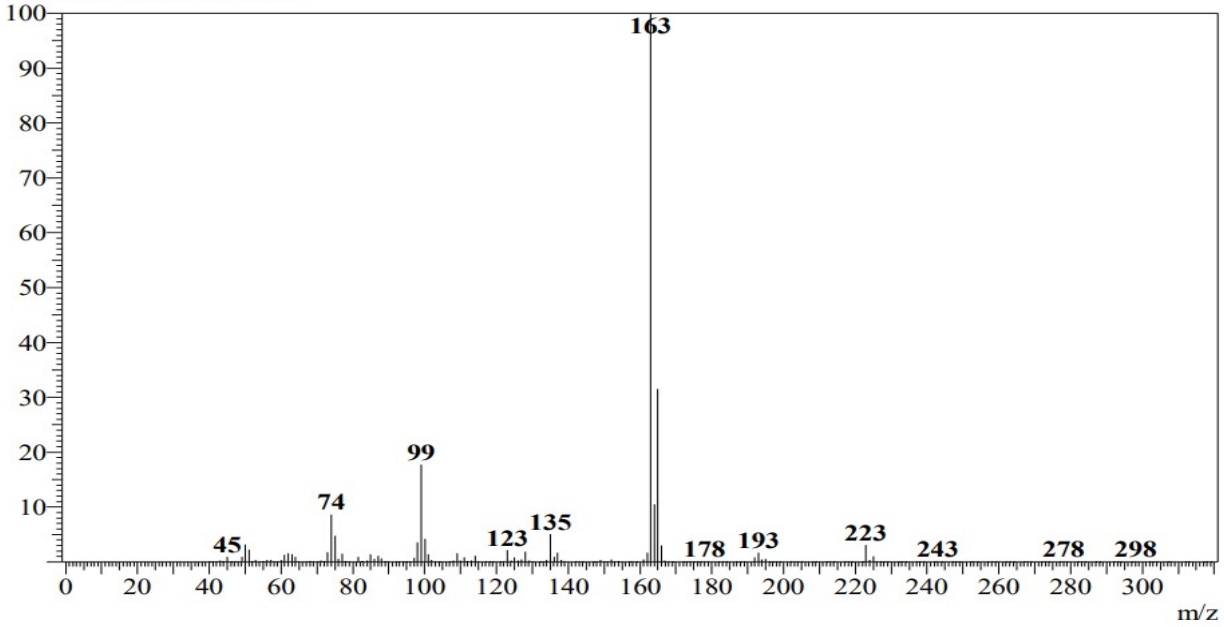


e. **FTIR spectra of 3-(4-fluorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ad)**

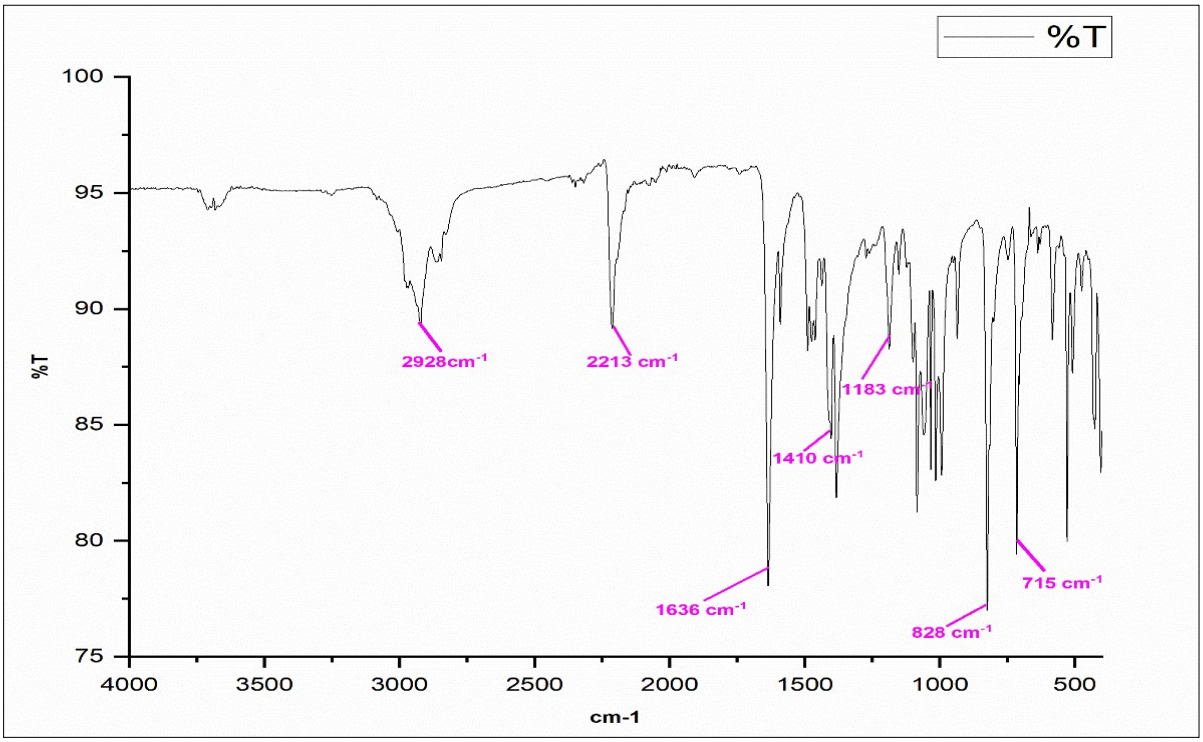


f. GCMS spectra of 3-(4-chlorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ae)

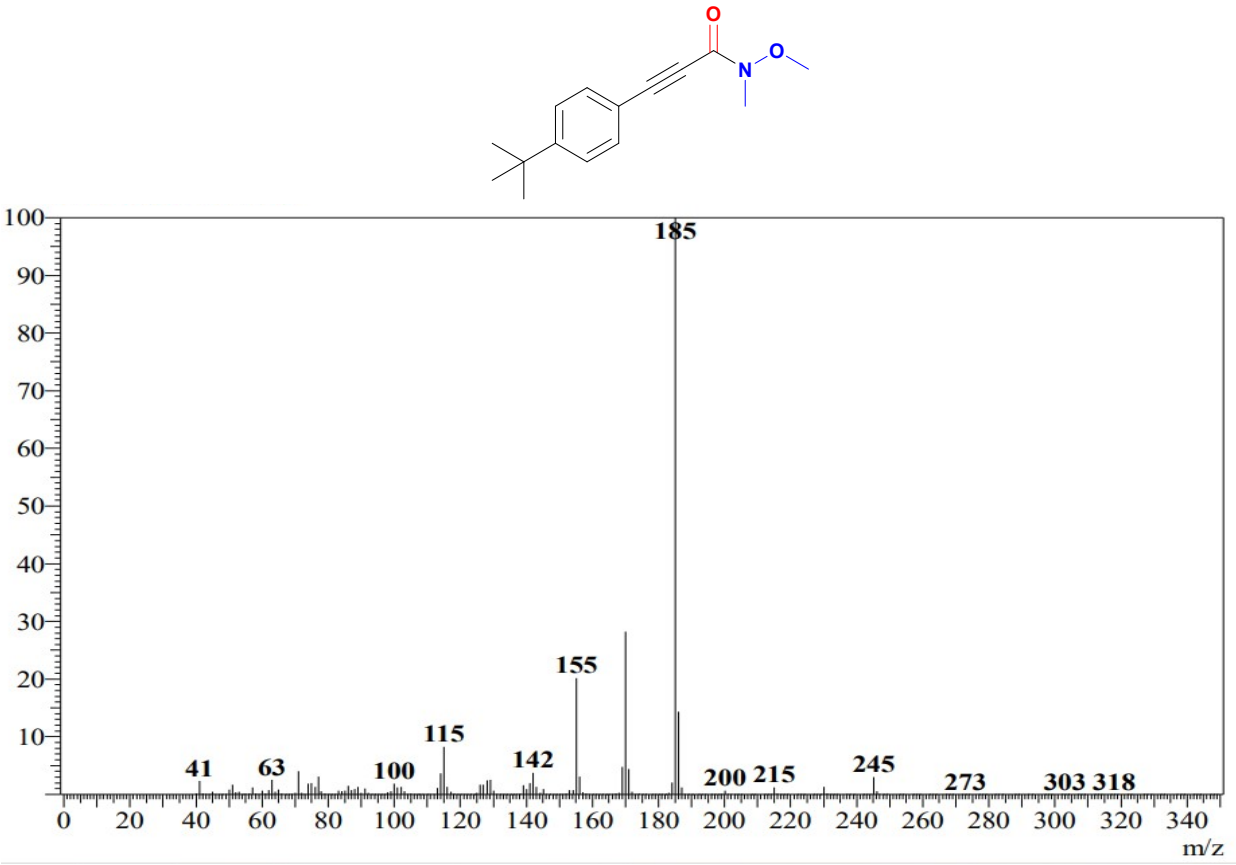




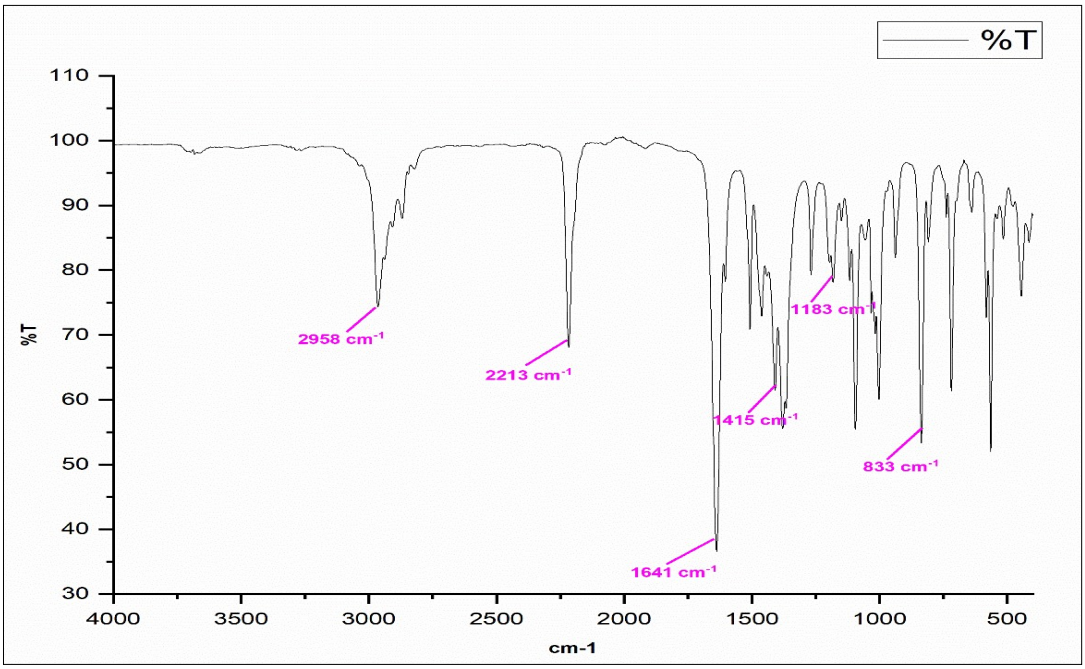
f. FTIR spectra of 3-(4-chlorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ae)



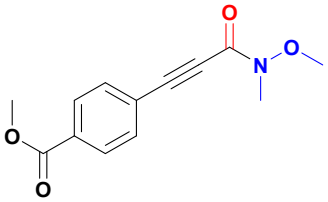
g. GCMS spectra of 3-(4-(tert-butyl)phenyl)-*N*-methoxy-*N*-methylpropiolamide (3af)

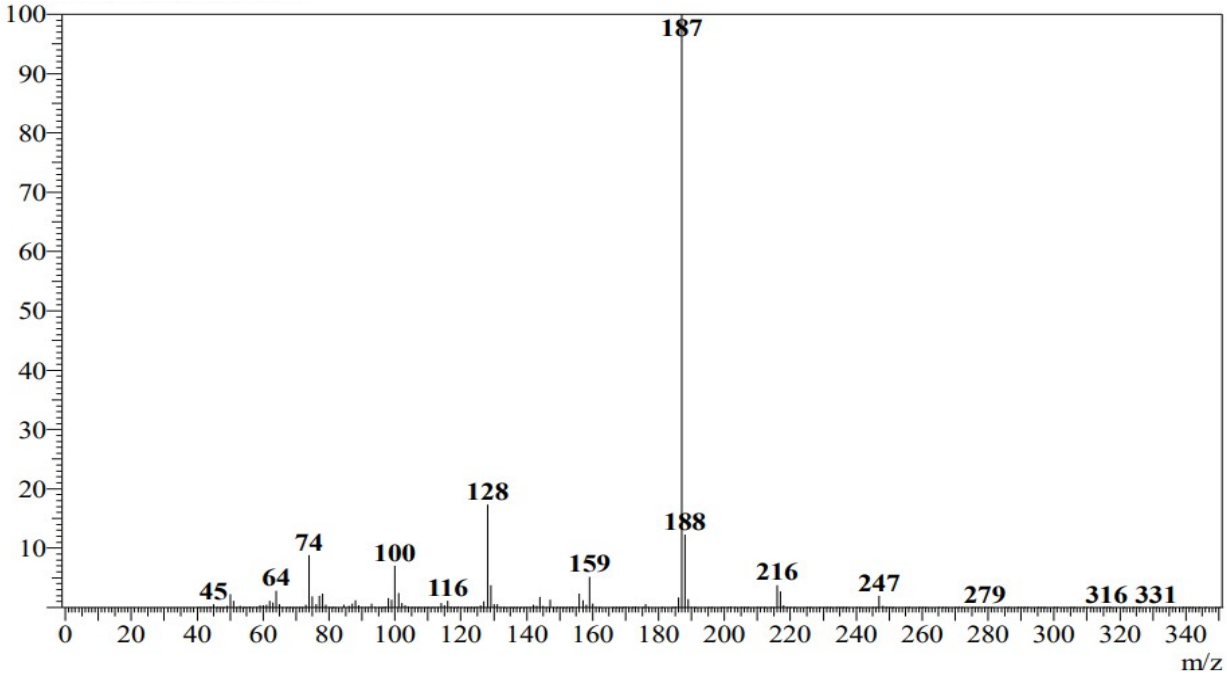


g. FTIR spectra of 3-(4-(tert-butyl)phenyl)-*N*-methoxy-*N*-methylpropiolamide (3af)

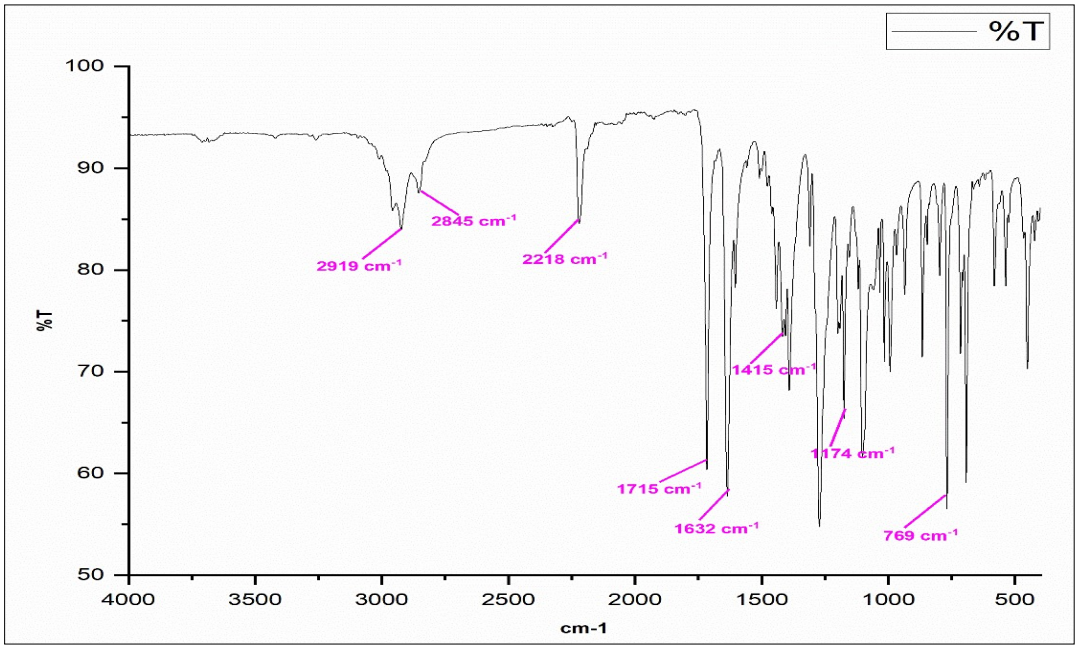


h. GCMS spectra of methyl 4-(3-(methoxy(methyl)amino)-3-oxoprop-1-yn-1-yl)benzoate (3ag)

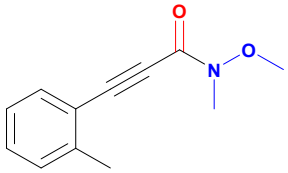


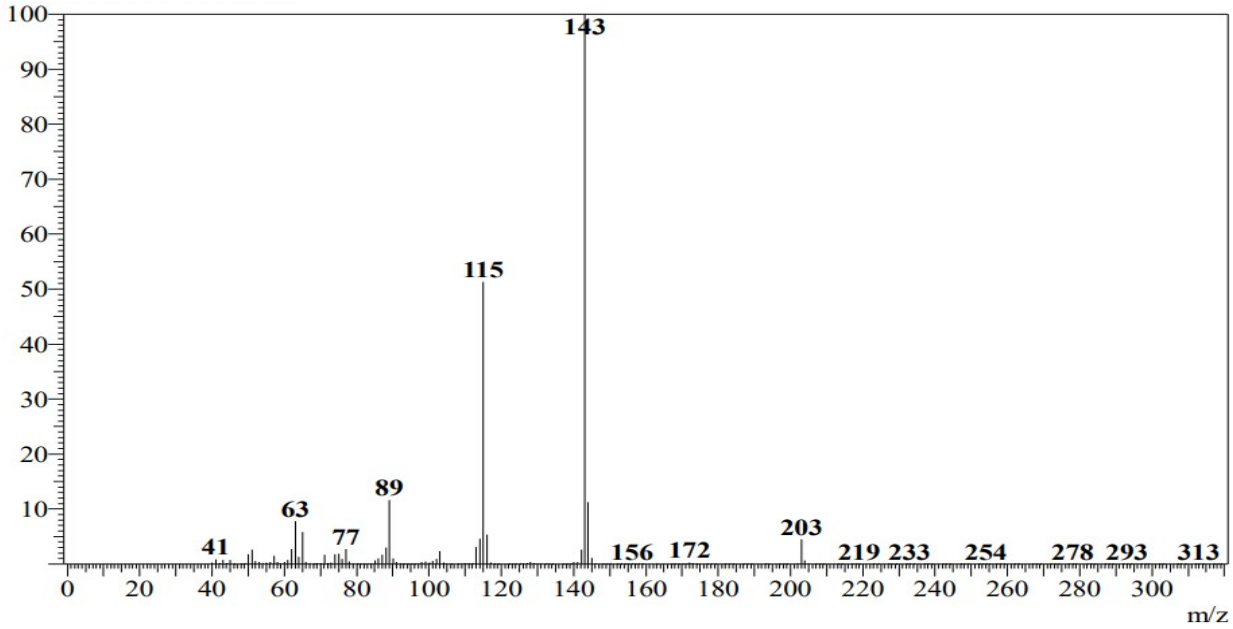


h. FTIR spectra of methyl 4-(3-(methoxy(methyl)amino)-3-oxoprop-1-yn-1-yl) benzoate (3ag)

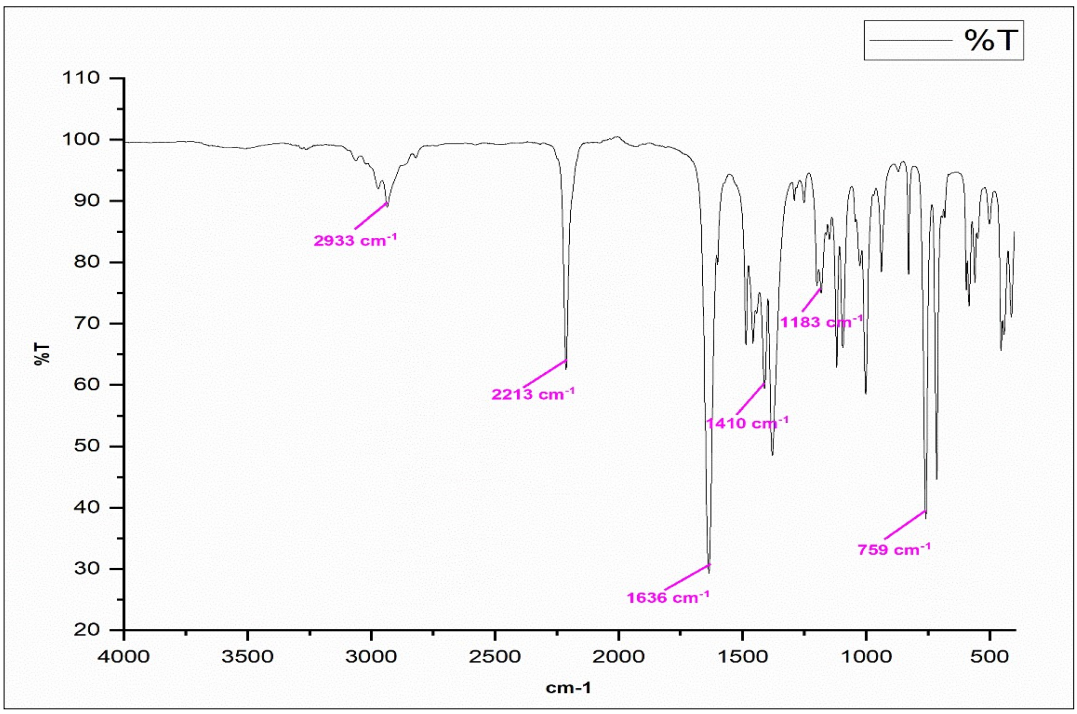


i. **GCMS spectra of *N*-methoxy-*N*-methyl-3-(*o*-tolyl)propiolamide (3ah)**

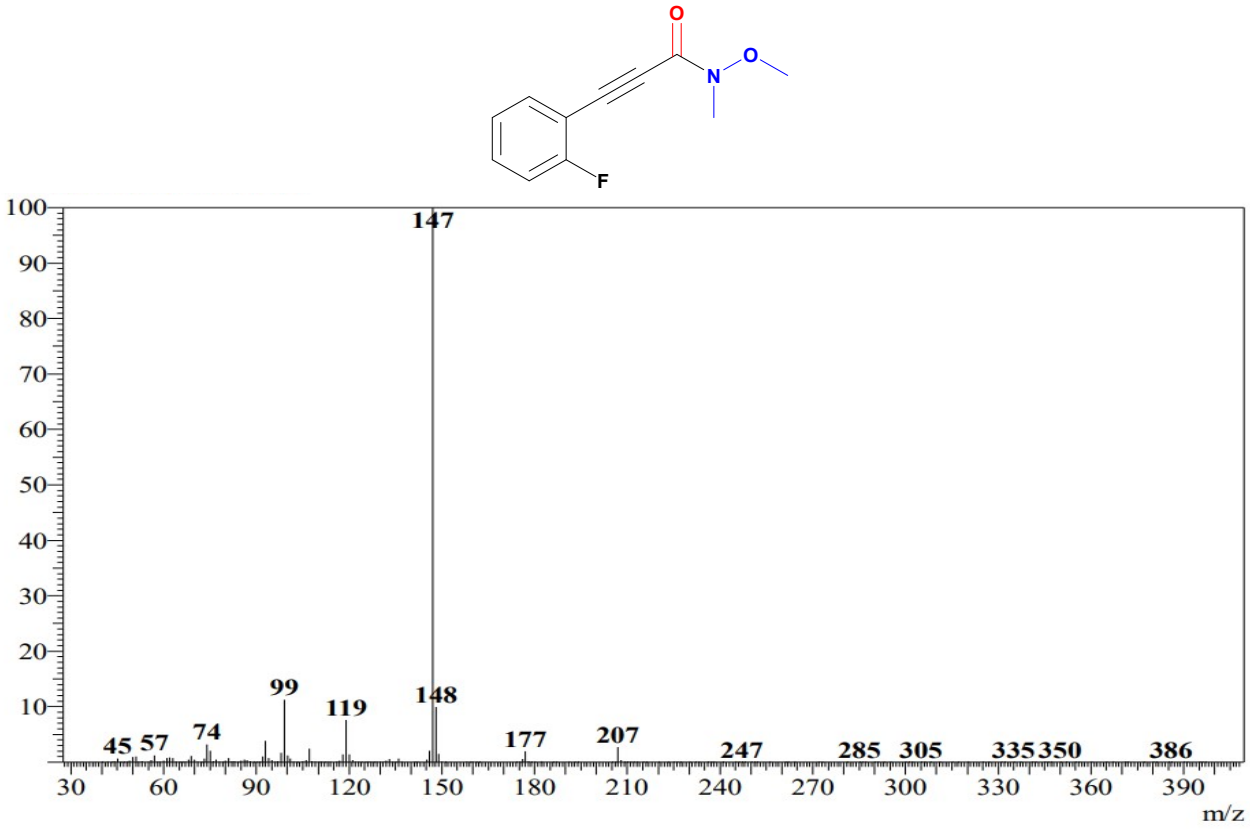




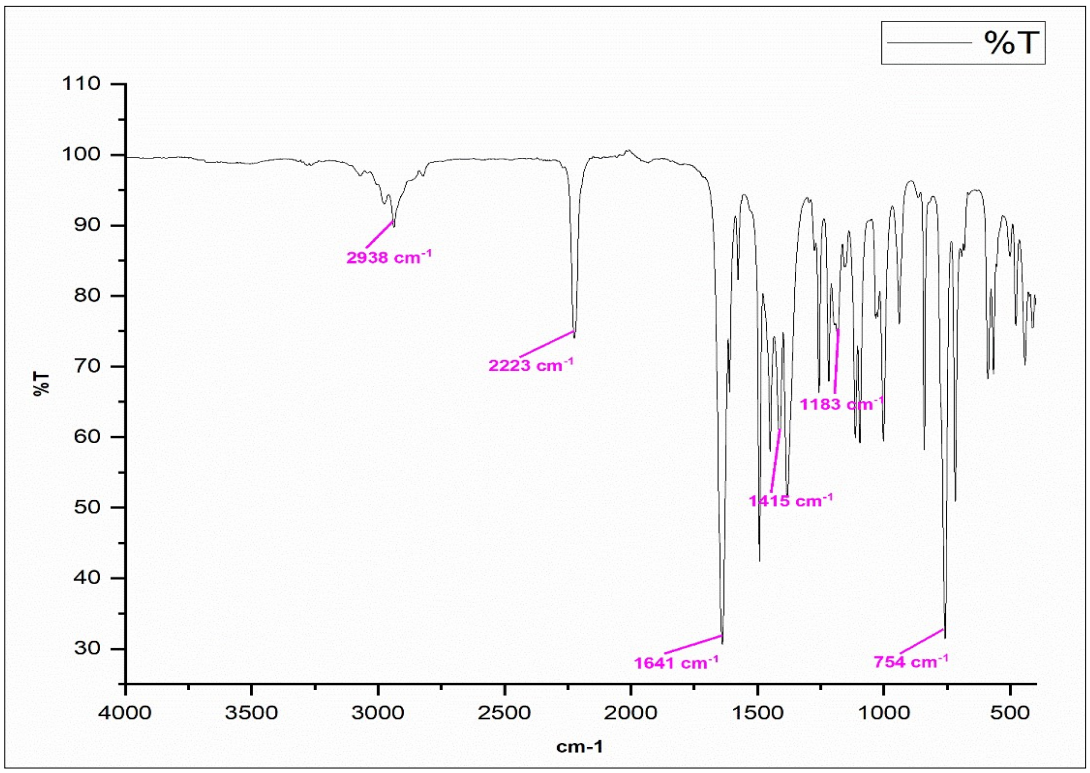
i. **FTIR spectra of *N*-methoxy-*N*-methyl-3-(*o*-tolyl)propiolamide (3ah)**



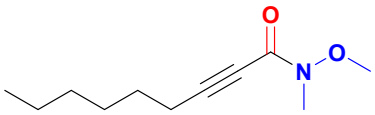
j. GCMS spectra of 3-(2-fluorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ai)

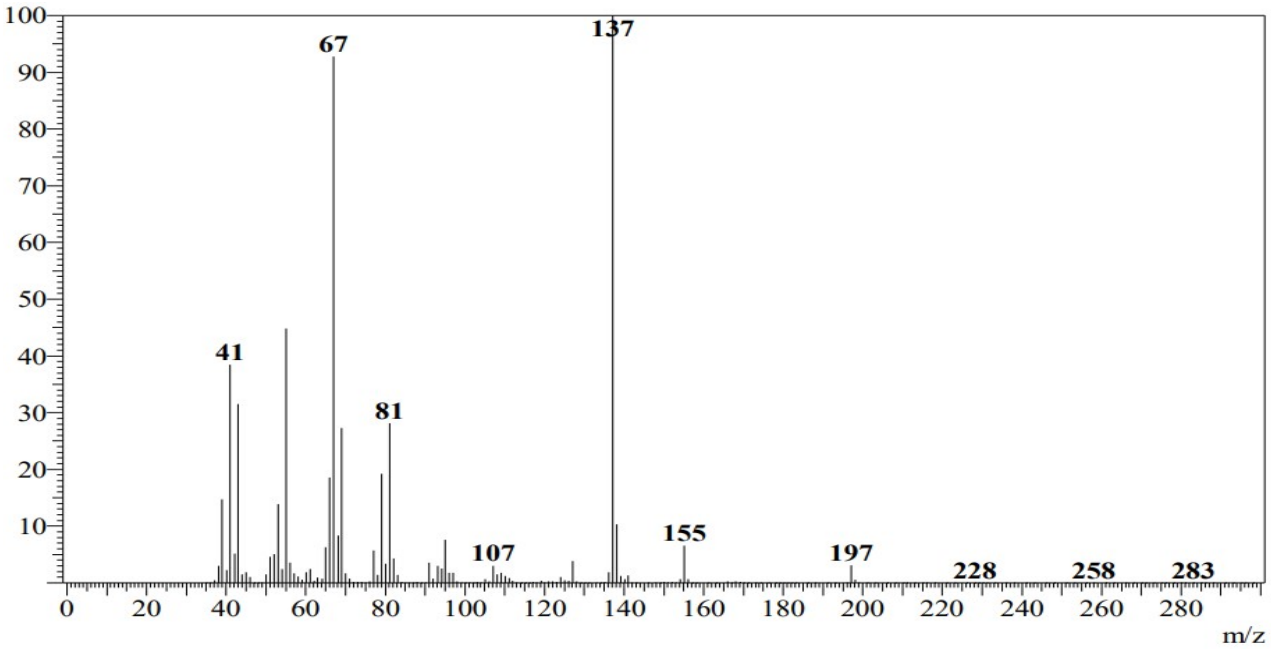


j. FTIR spectra of 3-(2-fluorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ai)

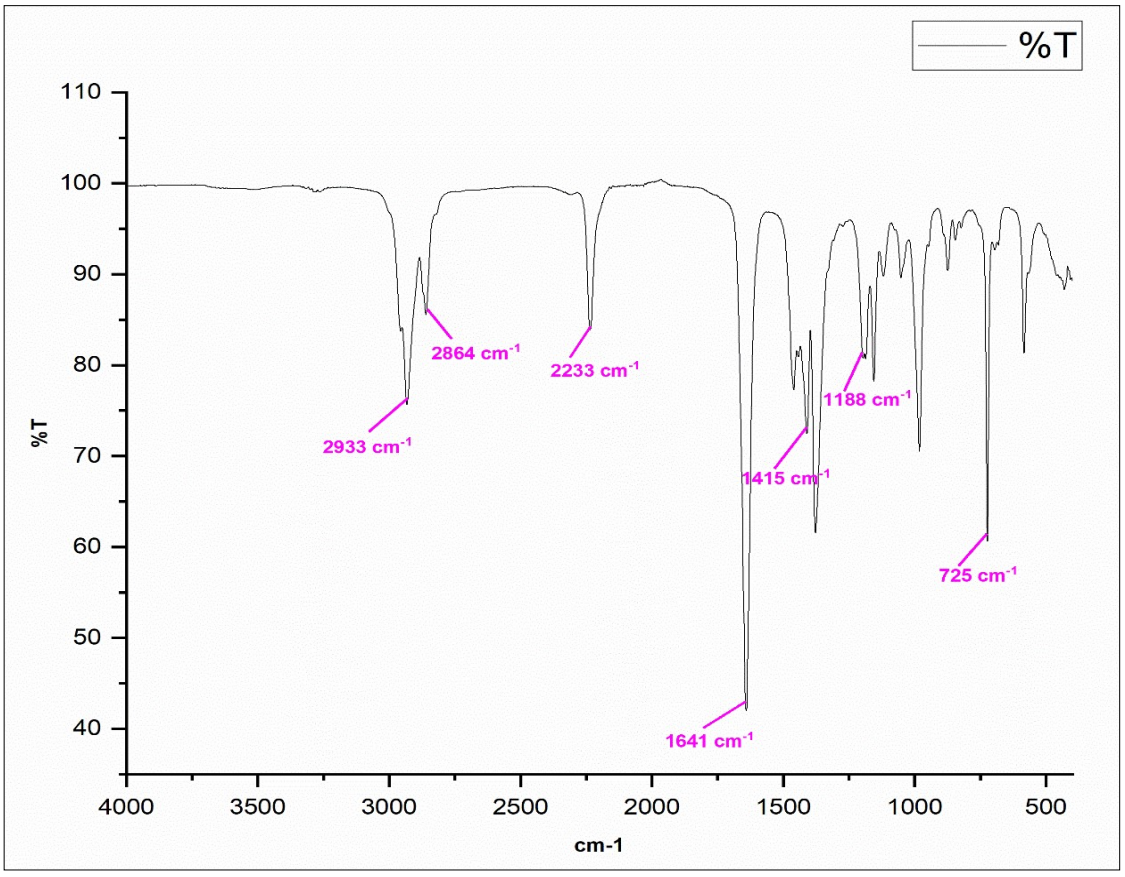


k. GCMS spectra of *N*-methoxy-*N*-methylnon-2-ynamide (3aj)

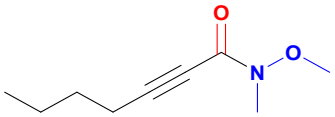


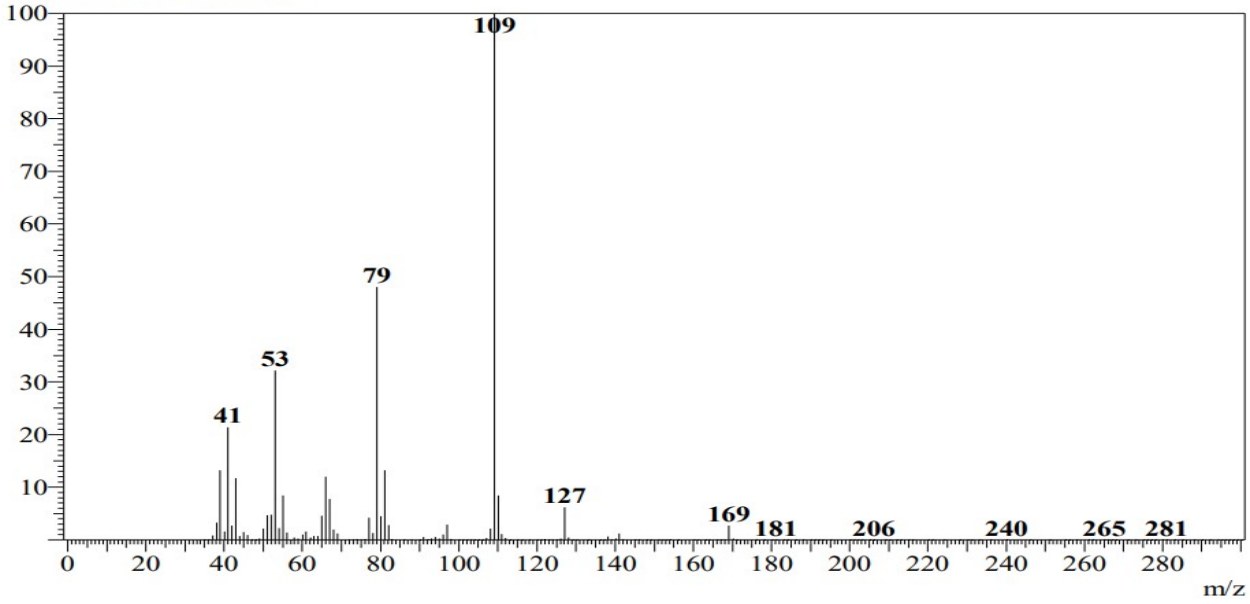


k. FTIR spectra of *N*-methoxy-*N*-methylnon-2-ynamide (3aj)

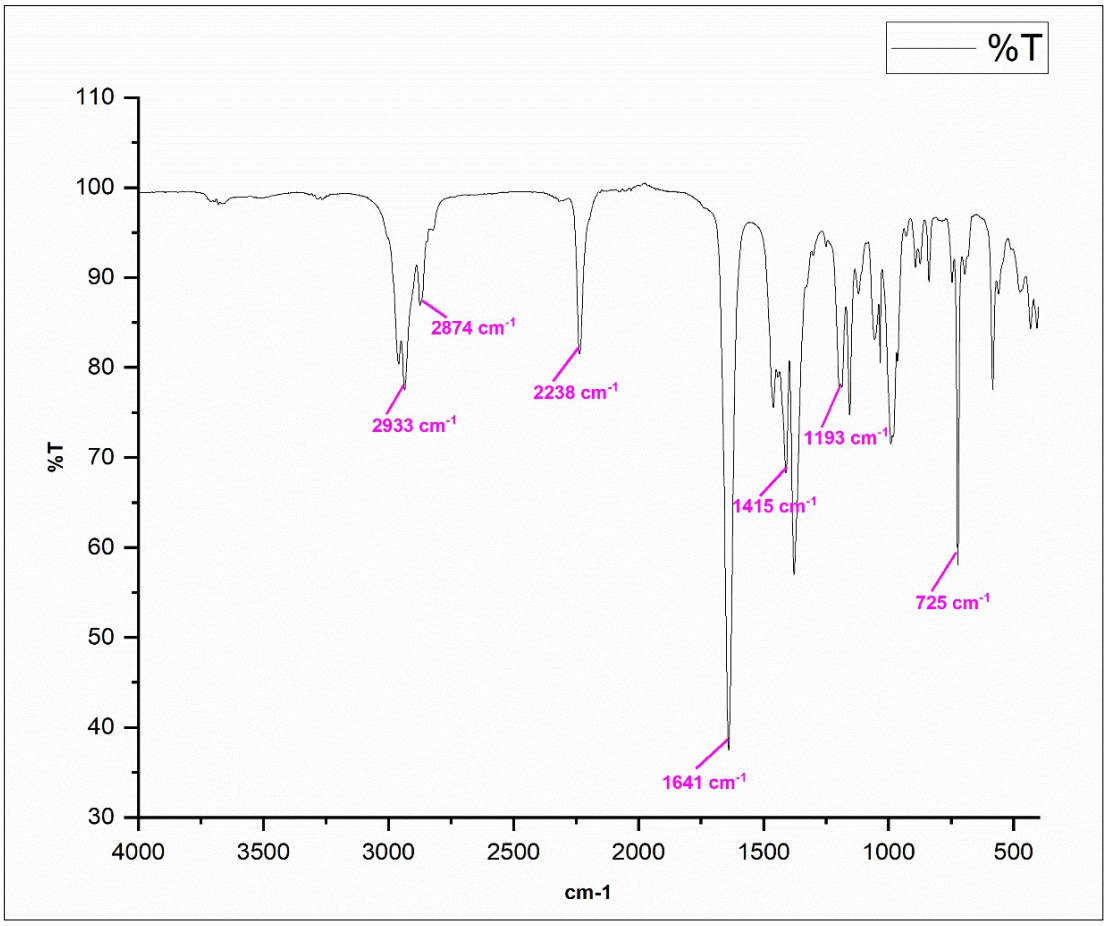


l. GCMS spectra of *N*-methoxy-*N*-methylhept-2-ynamide (3ak)

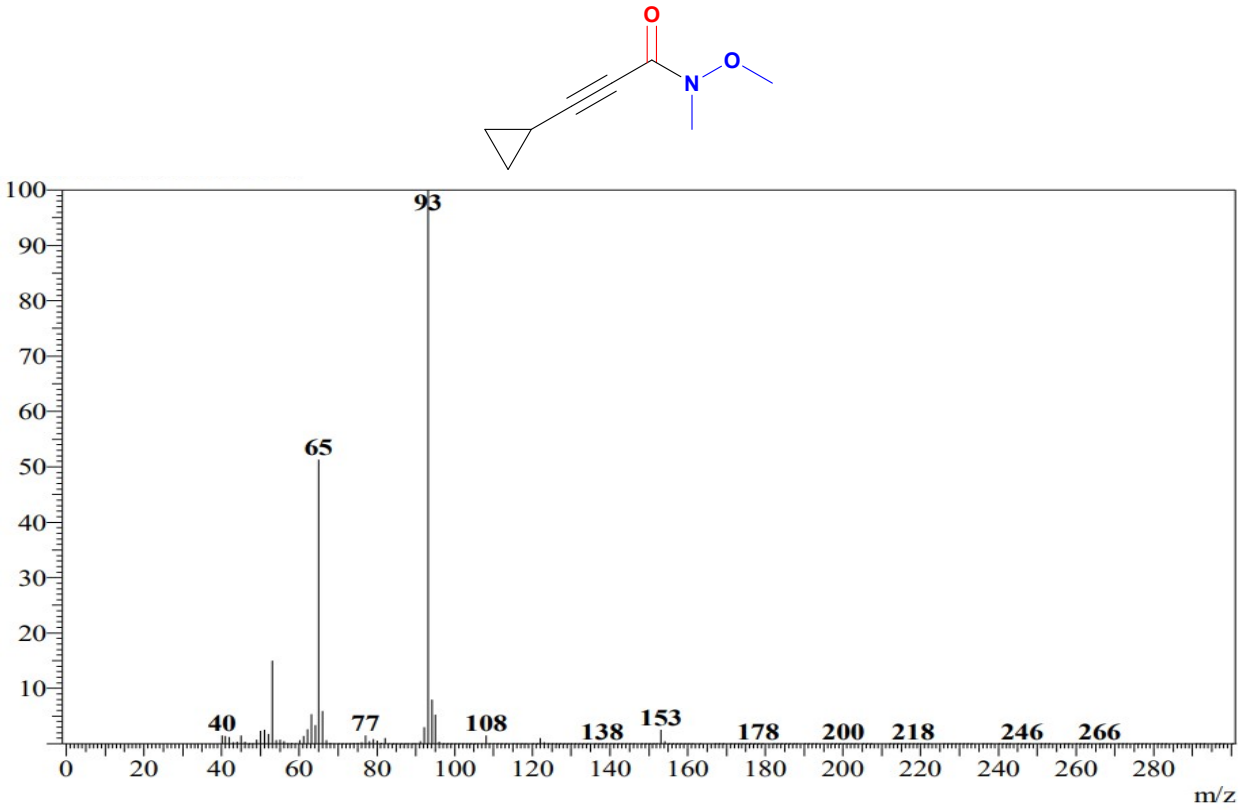




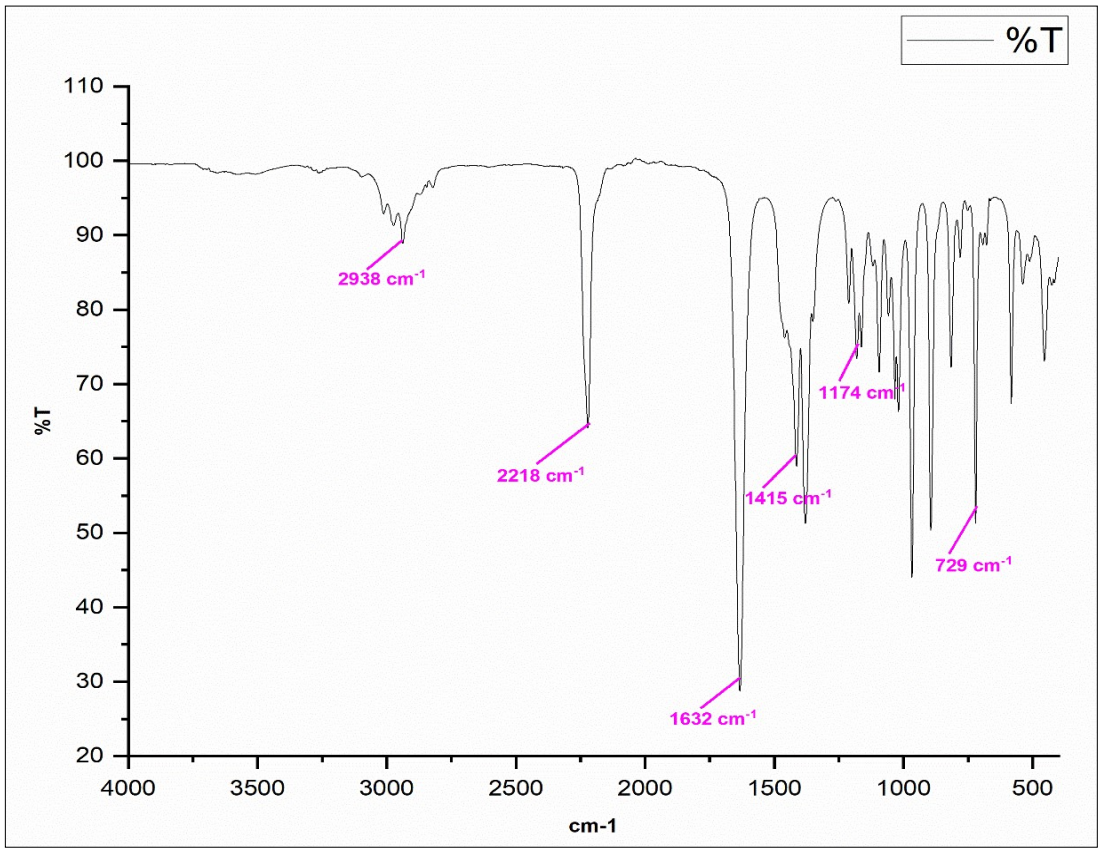
l. FTIR spectra of *N*-methoxy-*N*-methylhept-2-ynamide (3ak)



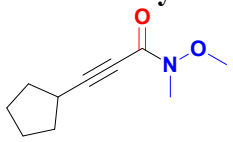
m. GCMS spectra of 3-cyclopropyl-*N*-methoxy-*N*-methylpropiolamide (3al)

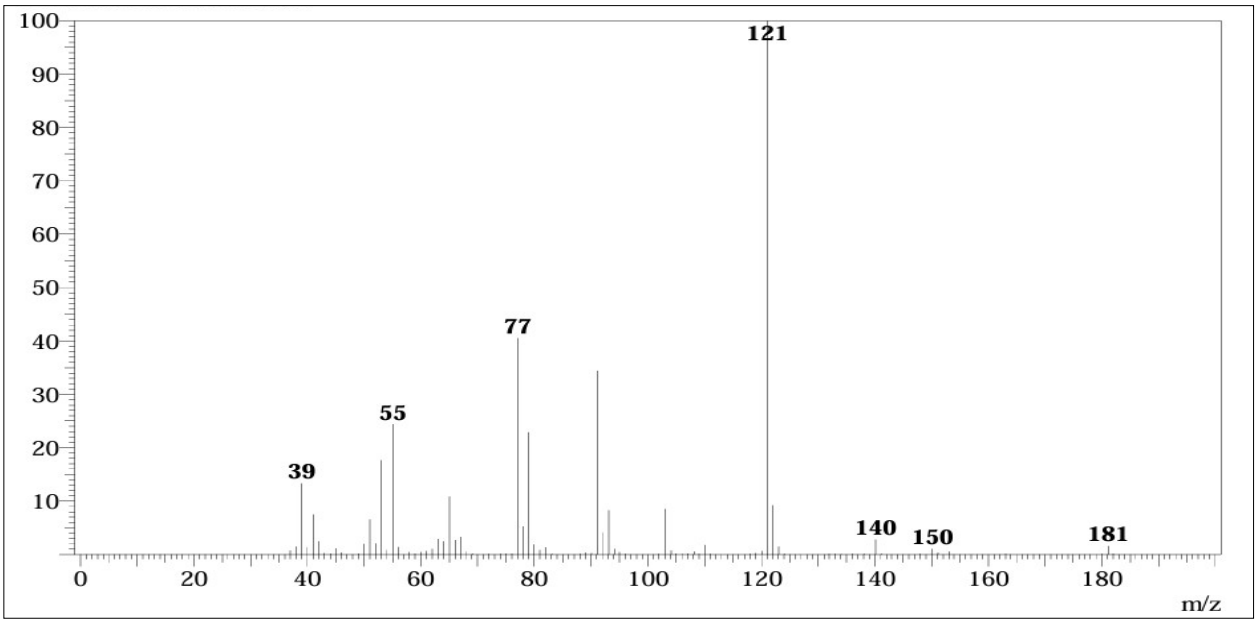


m. FTIR spectra of 3-cyclopropyl-*N*-methoxy-*N*-methylpropiolamide (3al)

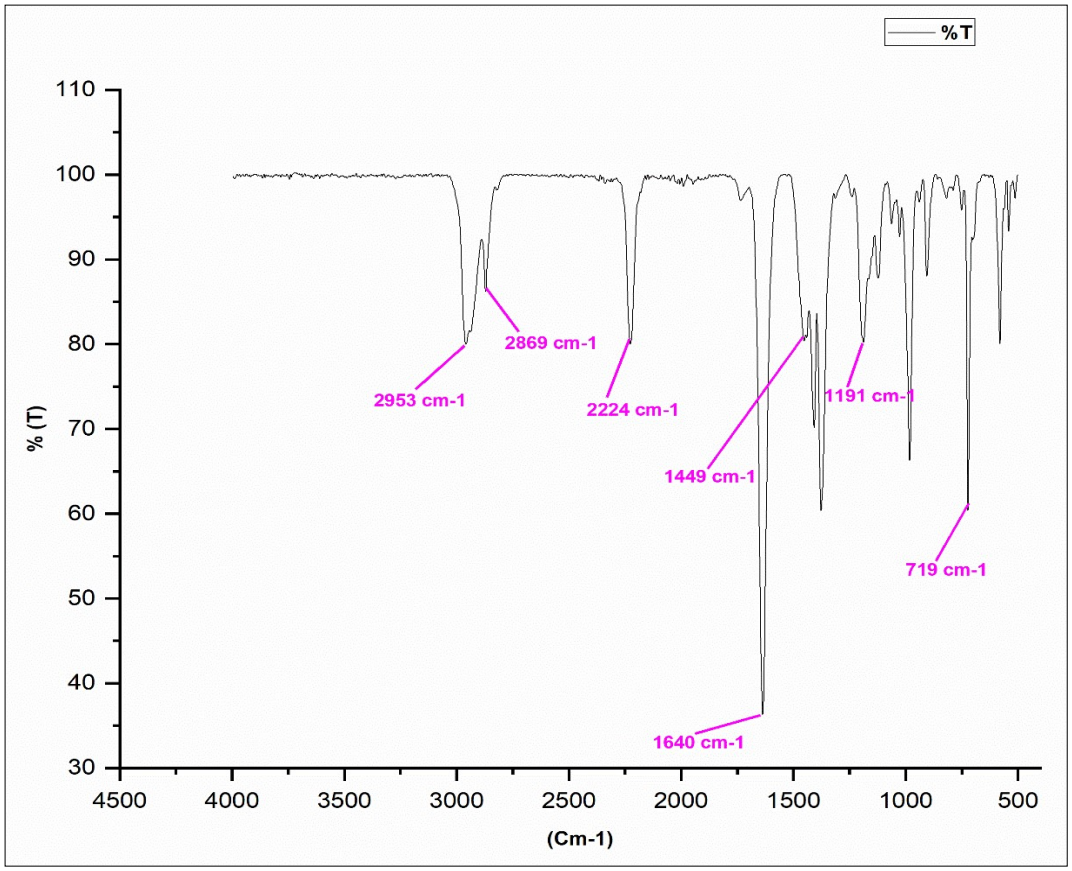


n. GCMS Spectra of 3-cyclopentyl-*N*-methoxy-*N*-methylpropiolamide (3am)



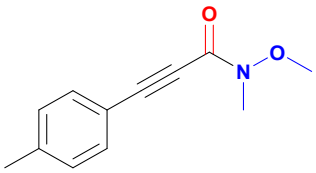


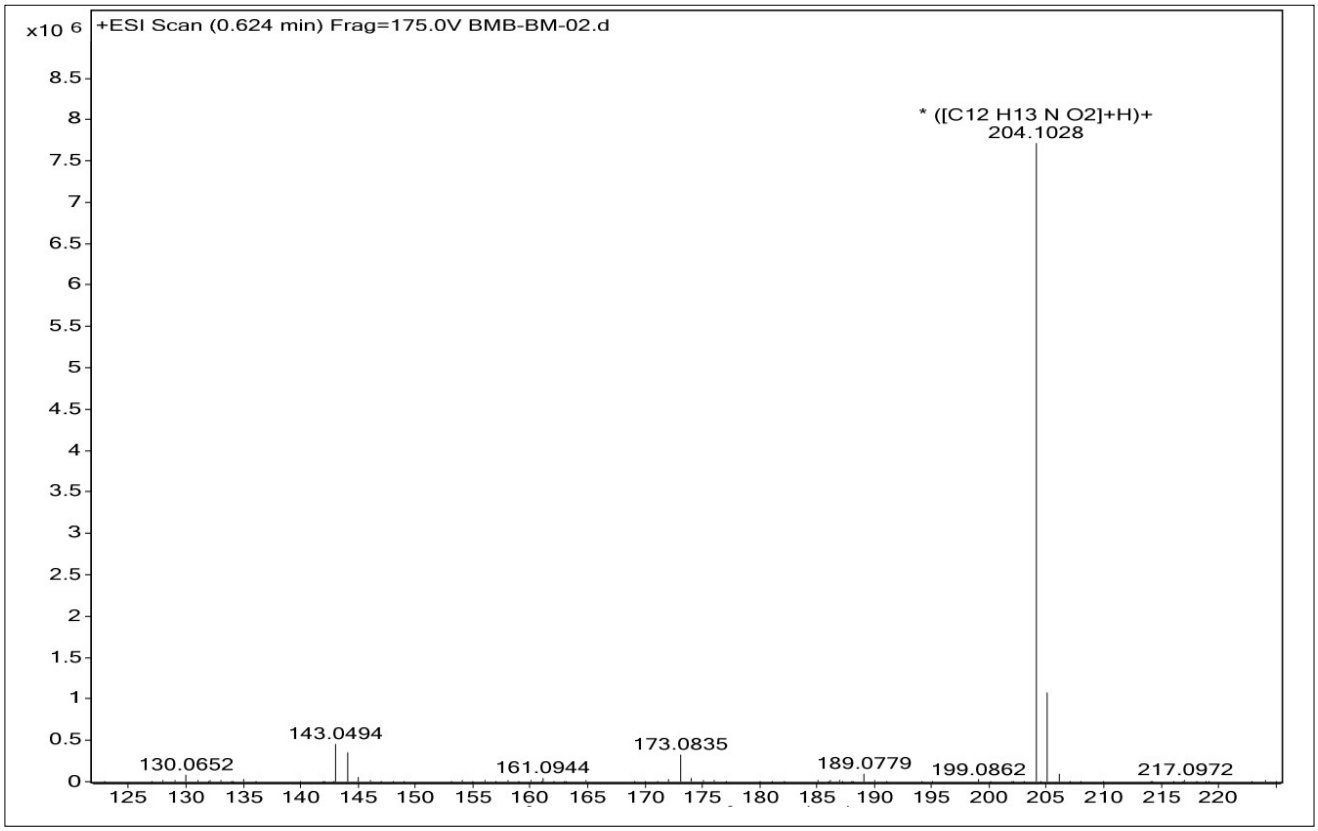
n. FTIR Spectra of 3-cyclopentyl-*N*-methoxy-*N*-methylpropiolamide (3am)



viii. HRMS Data of 3a derivatives:

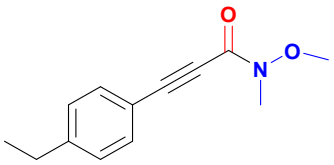
I. HRMS spectra of *N*-methoxy-*N*-methyl-3-(*p*-tolyl)propiolamide (3aa')

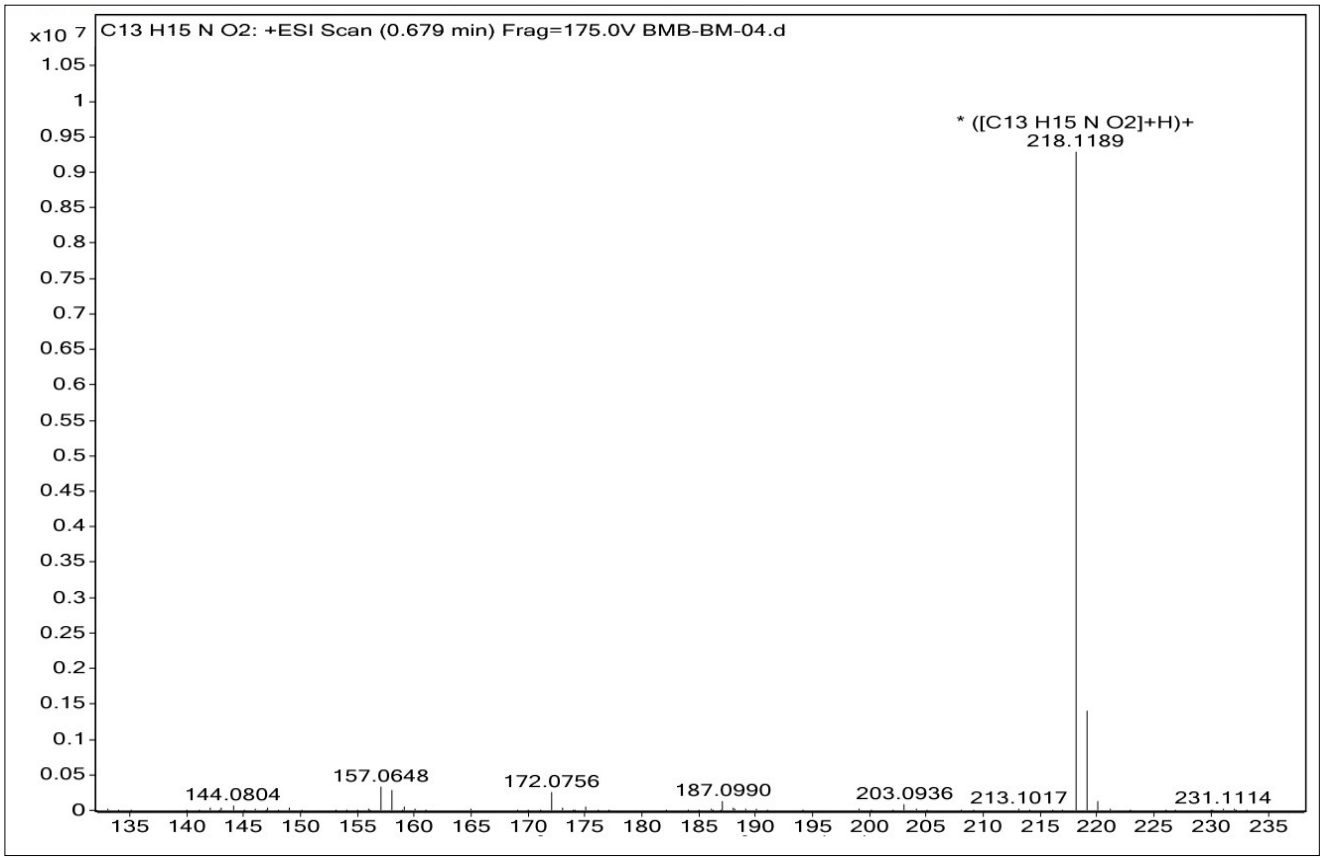




HRMS (ESI) of (3aa') : m/z found for $C_{12}H_{13}NO_2$ $[M+H]^+$, **204.1028**, calculated for $C_{12}H_{13}NO_2$ $[M+H]^+$, **204.1024**.

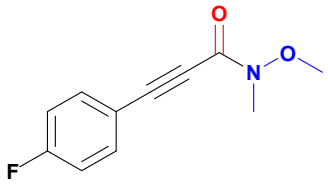
II. HRMS spectra of 3-(4-ethylphenyl)-*N*-methoxy-*N*-methylpropiolamide (3ac)

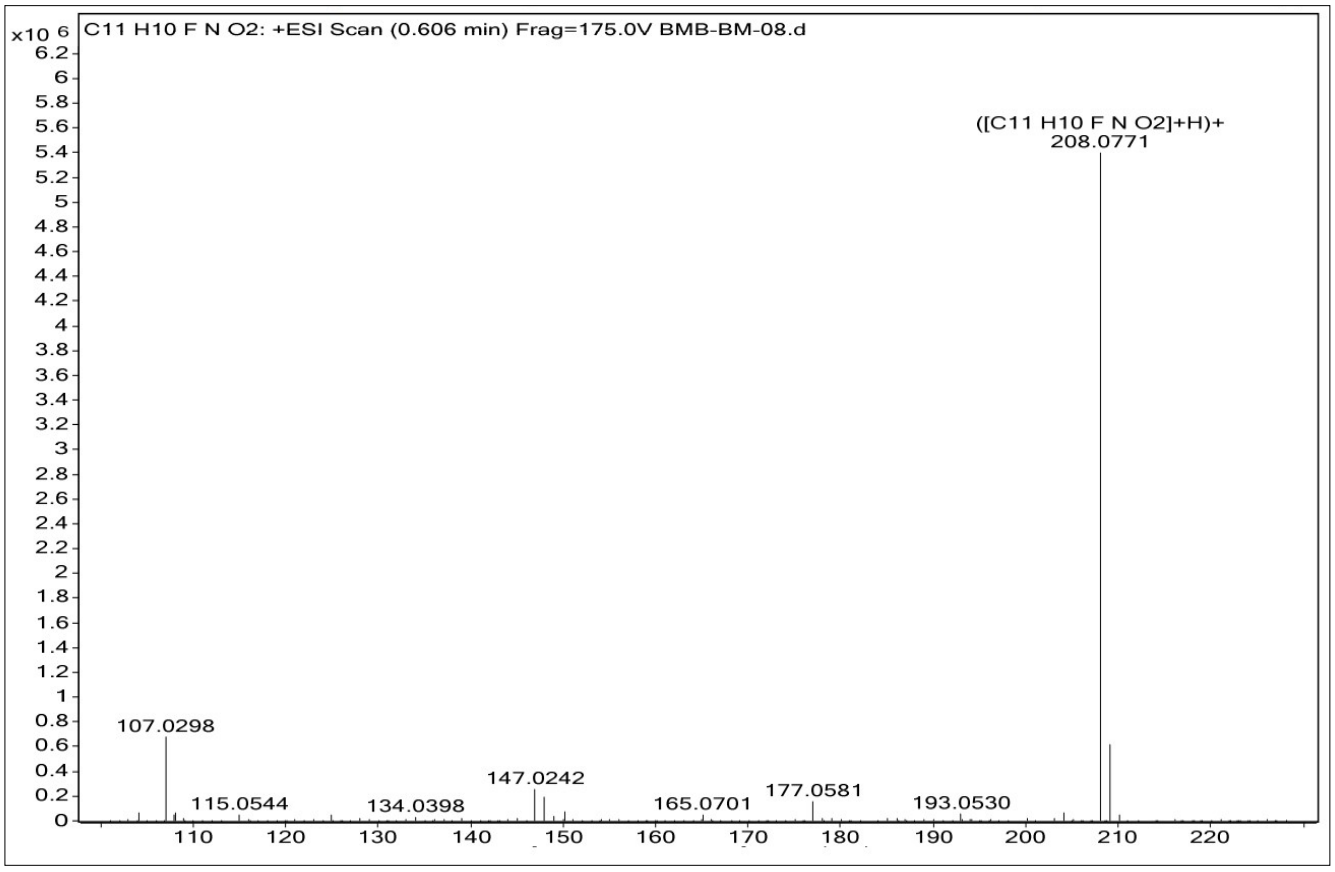




HRMS (ESI) of (3ac): m/z found for $C_{13}H_{15}NO_2$ $[M+H]^+$, **218.1189**, calculated for $C_{13}H_{15}NO_2$ $[M+H]^+$, **218.1181**.

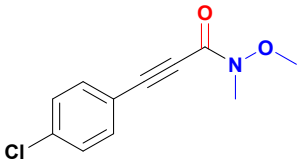
III. HRMS spectra of 3-(4-fluorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ad)

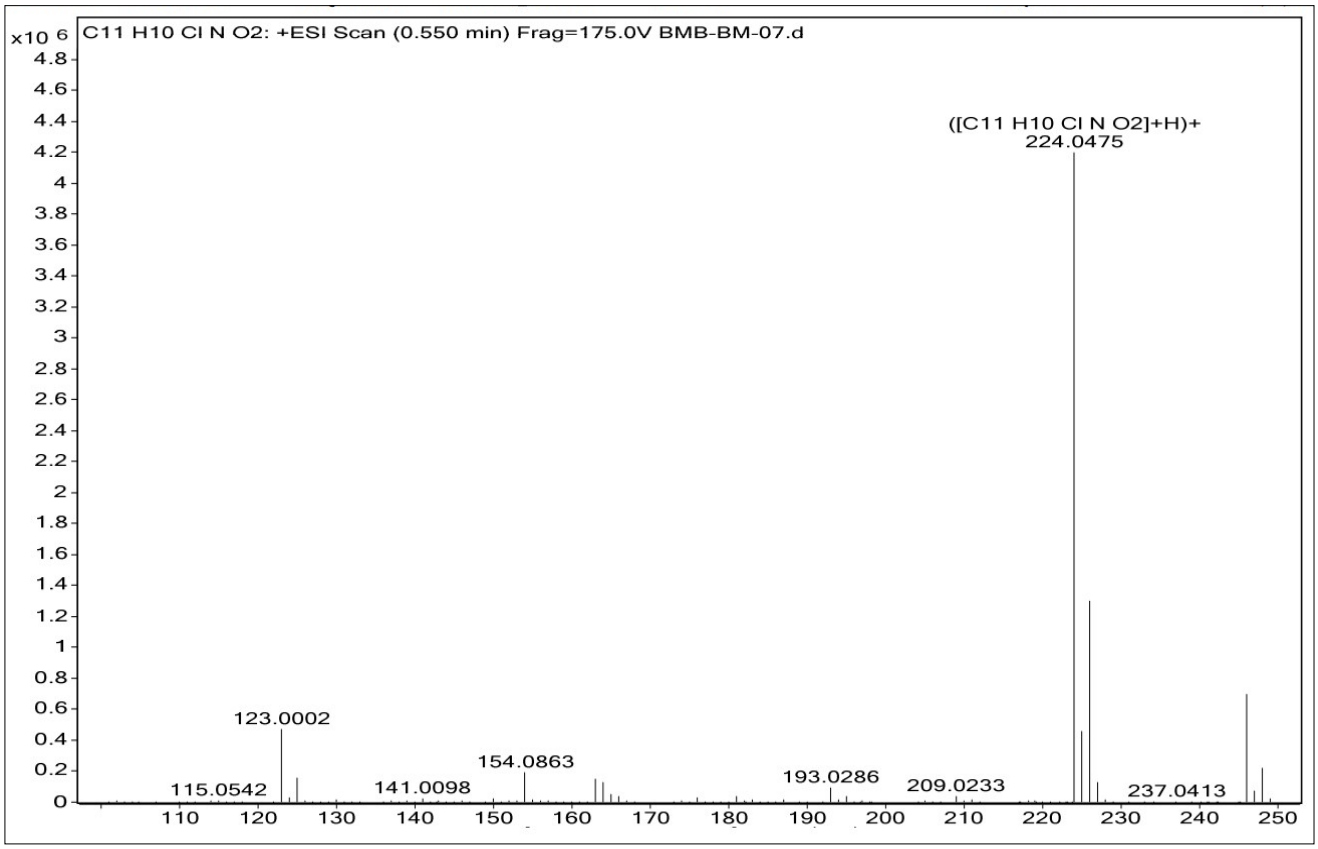




HRMS (ESI) of (3ad) : m/z found for $C_{11}H_{10}FNO_2[M+H]^+$, **208.0771**, calculated for $C_{11}H_{10}FNO_2$ $[M+H]^+$, **208.0774**

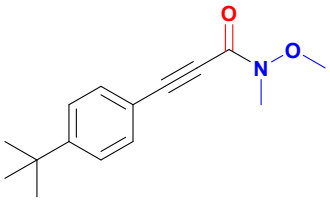
IV. HRMS spectra of 3-(4-chlorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ae)

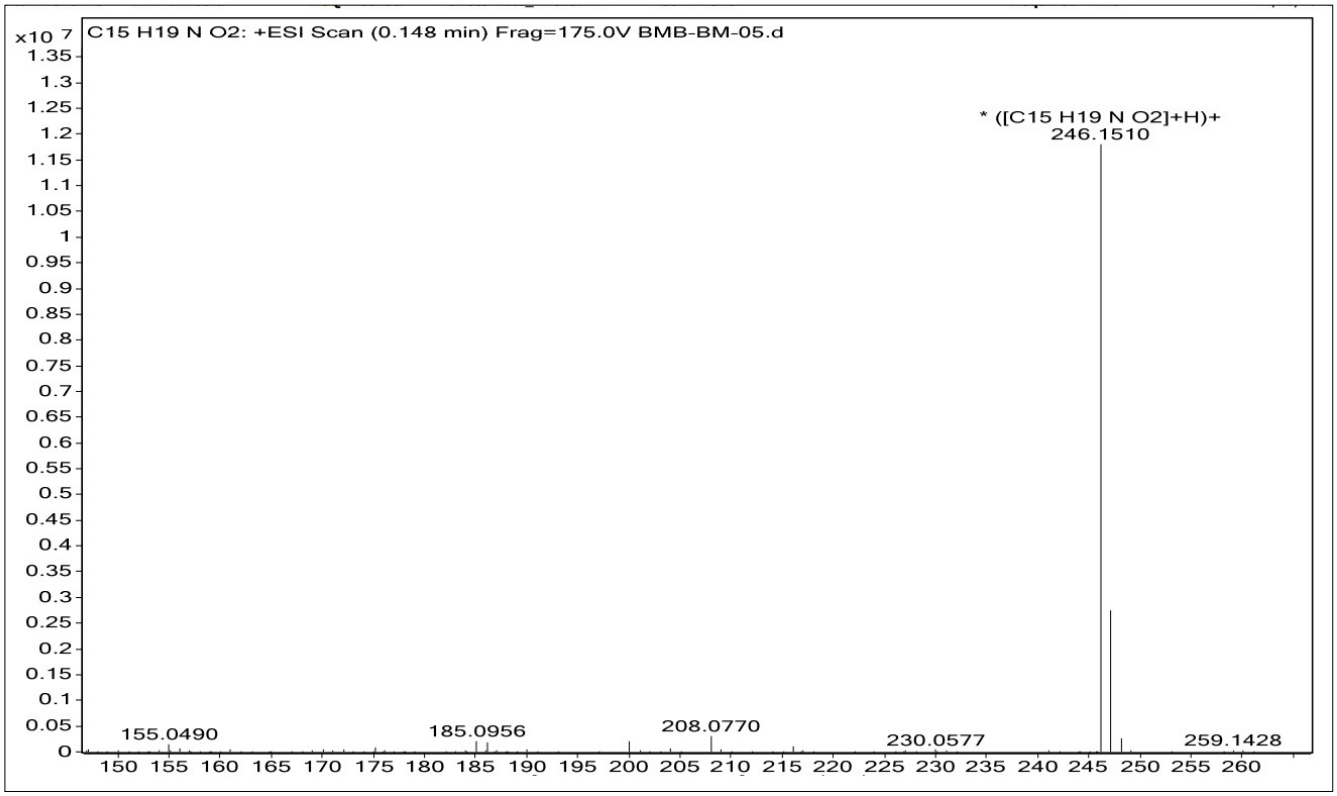




HRMS (ESI) of **(3ae) :** m/z found for $C_{11}H_{10}ClNO_2[M+H]^+$, **224.0475**, calculated for $C_{11}H_{10}ClNO_2$ $[M+H]^+$, **224.0478**

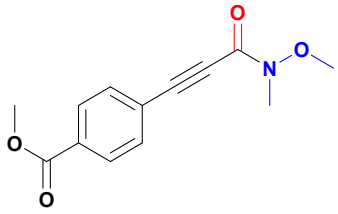
V. HRMS spectra of 3-(4-(tert-butyl)phenyl)-*N*-methoxy-*N*-methylpropiolamide (3af)

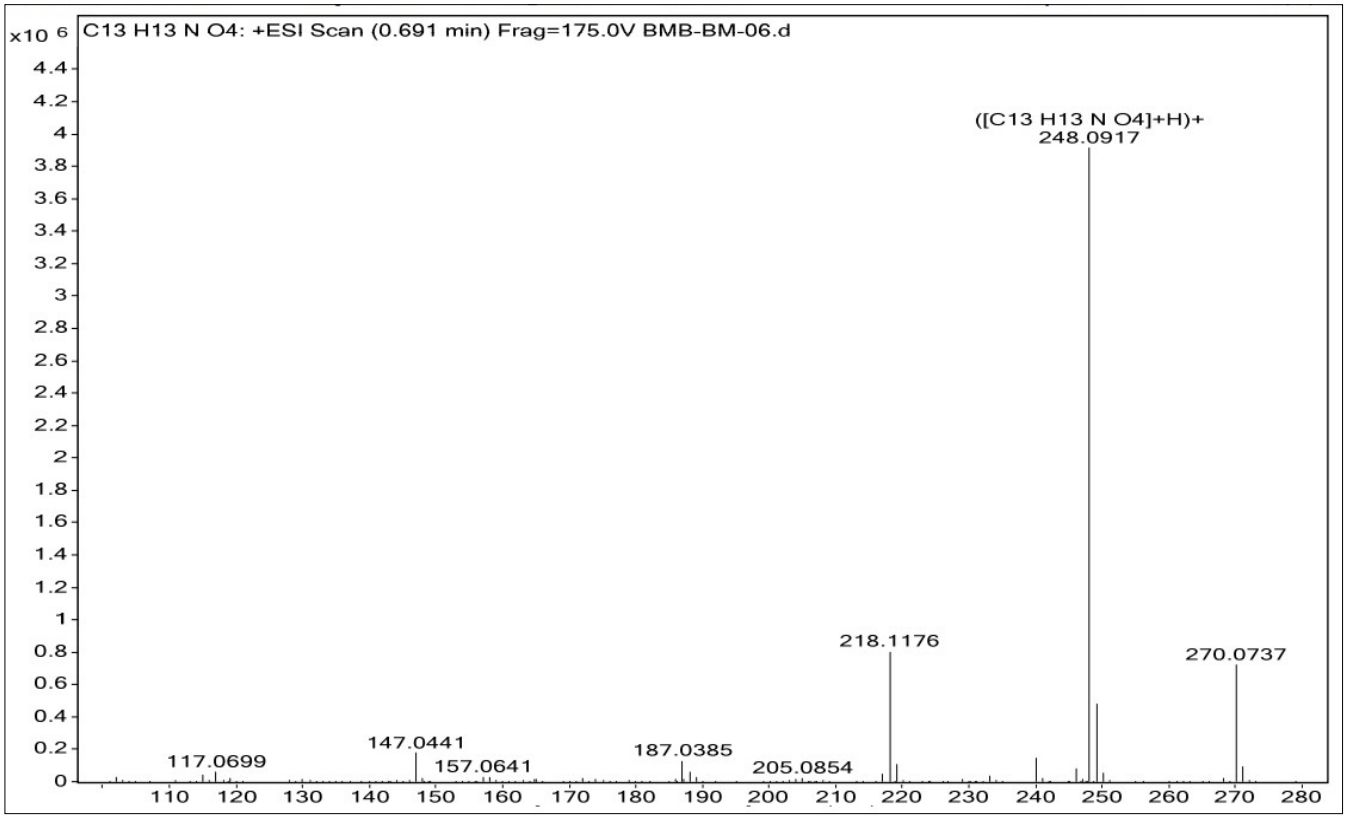




HRMS (ESI) of **(3af) :** m/z found for $C_{15}H_{19}NO_2$ $[M+H]^+$, **246.1510**, calculated for $C_{15}H_{19}NO_2$ $[M+H]^+$, **246.1494**.

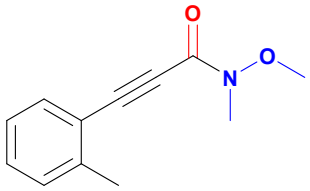
VI. HRMS spectra of methyl 4-(3-(methoxy(methyl)amino)-3-oxoprop-1-yn-1-yl) benzoate (3ag)

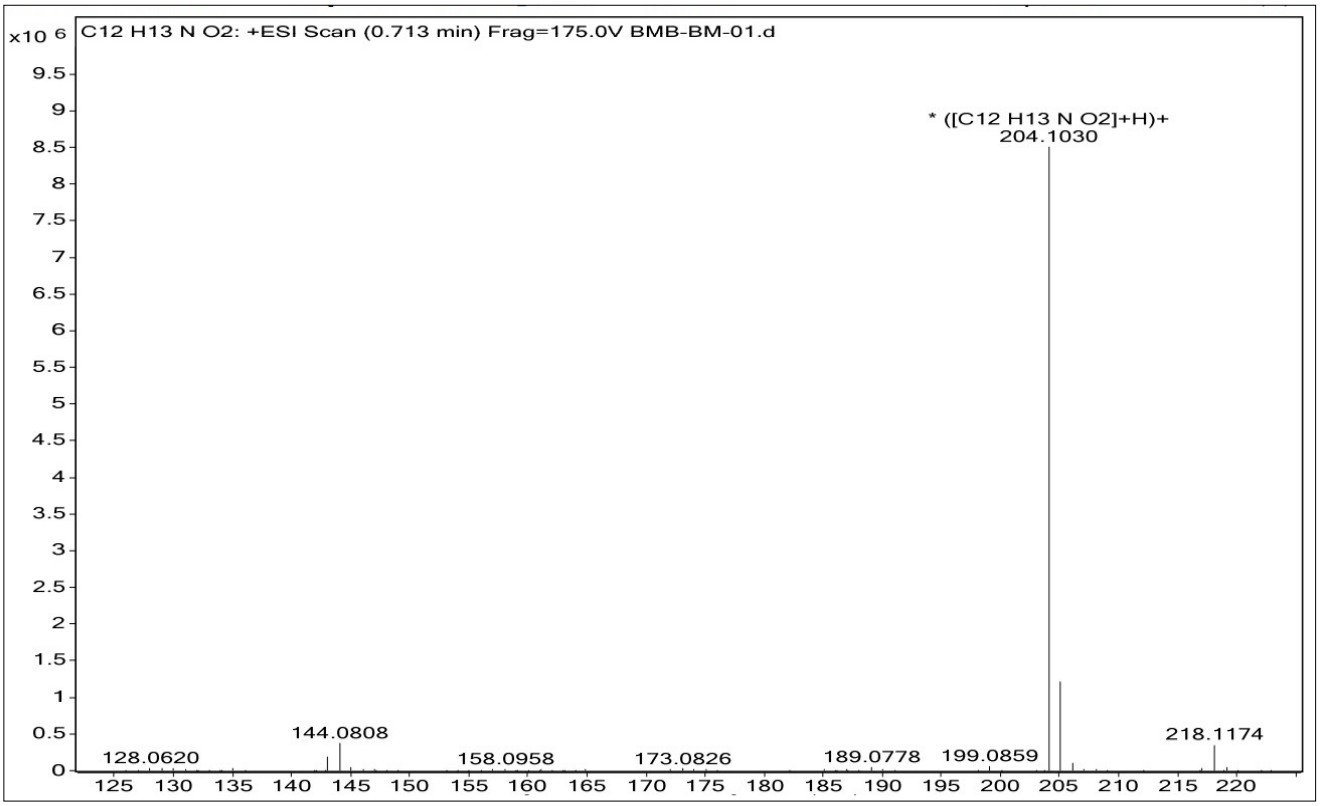




HRMS (ESI) of (3ag) : m/z found for $C_{13}H_{13}NO_4$ $[M+H]^+$, **248.0917**, calculated for $C_{13}H_{13}NO_4$ $[M+H]^+$, **248.0923**

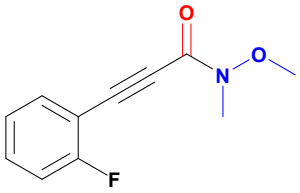
VII. HRMS spectra of *N*-methoxy-*N*-methyl-3-(*o*-tolyl) propiolamide (3ah)

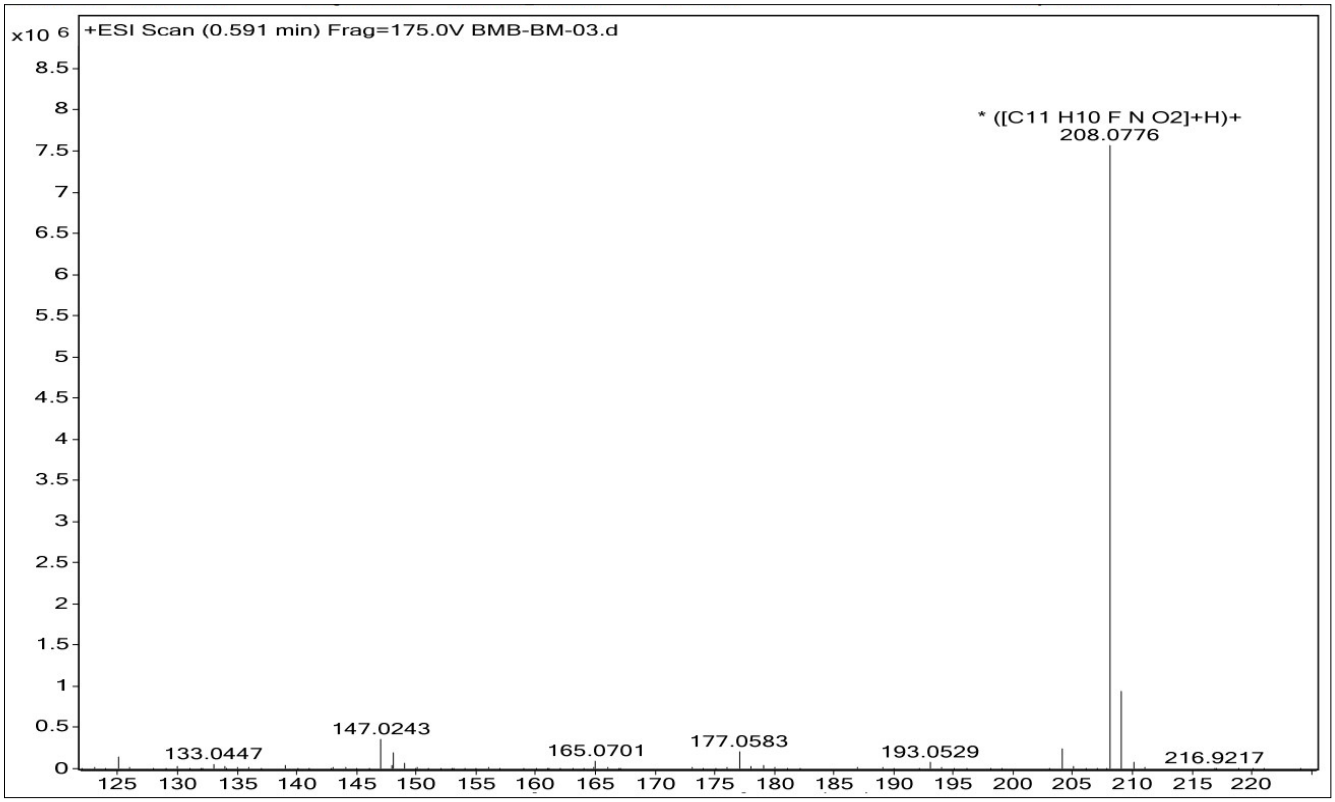




HRMS (ESI) of **(3ah) :** m/z found for $C_{12}H_{13}NO_2$ $[M+H]^+$, **204.1030**, calculated for $C_{12}H_{13}NO_2$ $[M+H]^+$, **204.1024**.

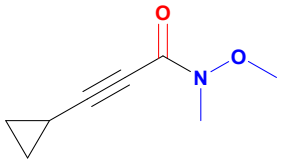
VIII. HRMS spectra of 3-(2-fluorophenyl)-*N*-methoxy-*N*-methylpropiolamide (3ai)

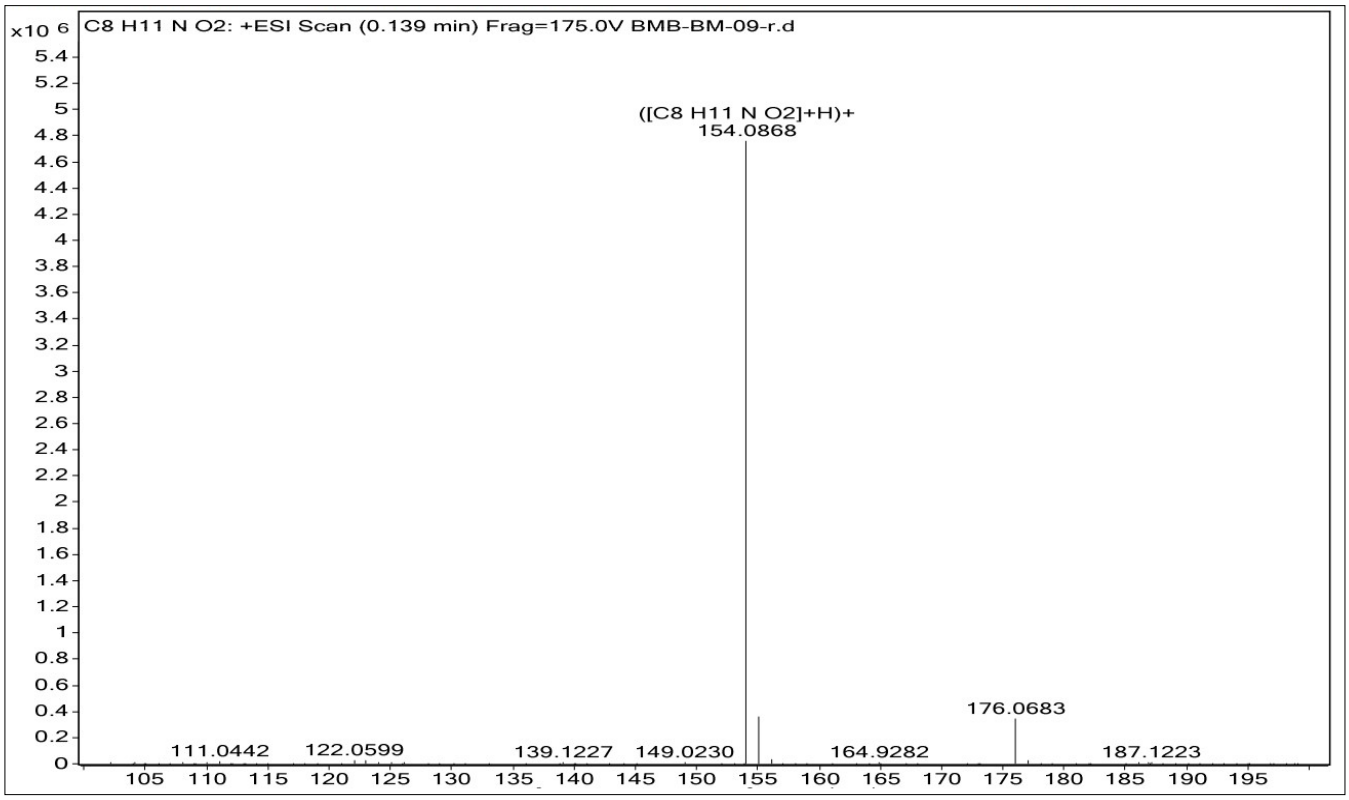




HRMS (ESI) of **(3ai) :** m/z found for $C_{11}H_{10}FNO_2$ $[M+H]^+$, **208.0776**, calculated for $C_{11}H_{10}FNO_2$ $[M+H]^+$, **208.0774**.

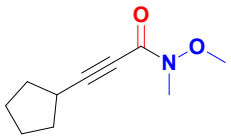
IX. HRMS spectra of 3-cyclopropyl-*N*-methoxy-*N*-methylpropiolamide (3al)



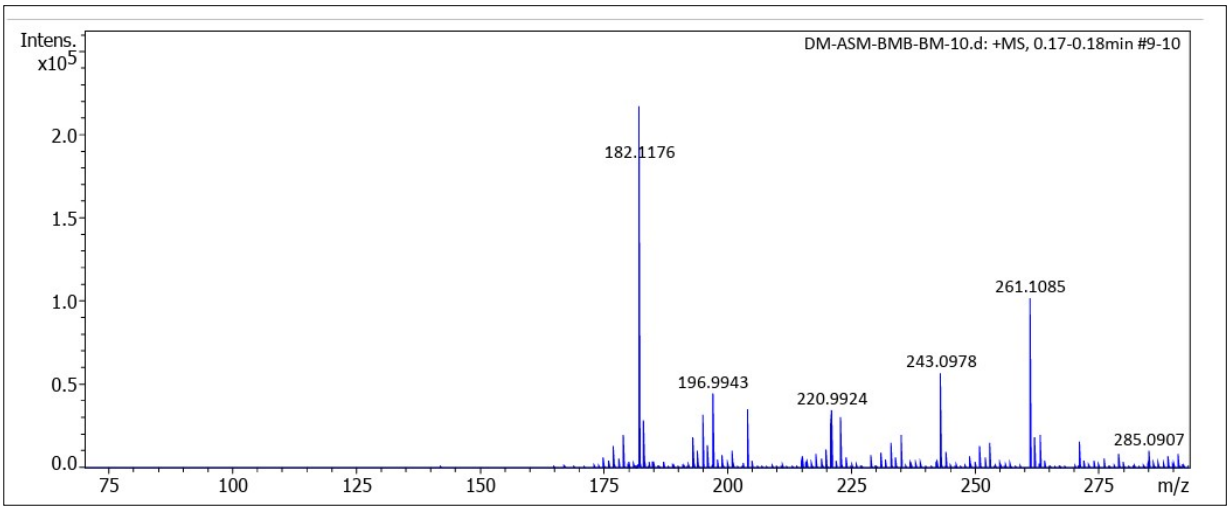


HRMS (ESI) of (3al): m/z found for $C_8H_{11}NO_2$ $[M+H]^+$, **154.0868**, calculated for $C_8H_{11}NO_2$ $[M+H]^+$, **154.0868**

X. HRMS Spectra of 3-cyclopentyl-*N*-methoxy-*N*-methylpropiolamide (3am)



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e¯ Conf	N-Rule
182.1176	1	C10H16NO2	182.1176	-0.5	12.3	1	100.00	4.0	even	ok



HRMS (ESI) m/z found for $C_{10}H_{15}NO_2$ $[M+H]^+$, **182.1176** , calculated for $C_{10}H_{15}NO_2$ $[M+H]^+$, **182.1181**.