# Supporting Information

## Solvent Directed Base-Enabled Diastereodivergent Domino Cycloaddition of Isoxazole–Oxindole Styrenes and Michael Additions of Isoxazole–Styrenes with Vinyl Malononitriles

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# Contents

**1. General information**

All the solvents and required chemicals were procured from SD-Fine, Sigma–Aldrich, and Spectrochem, and used without purification and distillation. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethyl silane on a δ scale. $^{1}$H NMR and $^{13}$C NMR spectra were recorded in $CDCl_3$ on a Bruker Avance 400 or 500 MHz spectrometers respectively. All chemical shift values are quoted in ppm and coupling constants in Hz. The solvent peak was used as a reference value for $^{1}$H NMR: TMS = 0.00 ppm, $CDCl_3$ = 7.26 or DMSO-$d_6$ = 2.50 ppm; for $^{13}$C NMR: $CDCl_3$ = 77.00 ppm or DMSO-$d_6$ = 39.52 ppm. The following was used to explain multiplicities: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, td = triplet of doublet, q = quartet, m = multiplet, and br = broad. Mass spectra of all the compounds were record with an Agilent Technologies-6530 spectrometer.

**2. Synthesis of Starting Materials**:

3-methyl-4-nitro-5-isatylidenyl-isoxazole **1a-1l**[1], vinyl malononitrile **2a-2b**[2]**,** with 3-methyl-4-nitro-5-styryl-isoxazole **4a-4h**[3] were synthesized according to the procedures reported in the literature.

**3. General procedure for synthesis of for spirooxindoles (3 or 3):**

To a stirred solution of isoxazole-oxindole styrene (0.1 mmol, 1.0 equiv.) and vinyl malononitrile (0.1 mmol, 1.0 equiv.) in EtOH/THF (3 mL) was added $K_2CO_3$ (10 mol%). The reaction mixture was stirred at room temperature and monitored by TLC. Upon completion, the solvent was evaporated *in vacuo*. The resulting crude product was purified by silica gel column chromatography using Hexane/EtOAc (25-30%) as the eluent to afford the desired products, **3a-n** or **3a'-h'**.

**4. General procedure for synthesis of Michael adducts (5f–5h):**

To a stirred solution of isoxazole-styrene (0.1 mmol, 1.0 equiv) and vinyl malononitrile (0.1 mmol, 1.0 equiv) in EtOH (3 mL), $K_2CO_3$ (10 mol%) was added. The reaction mixture was stirred at room temperature and monitored by TLC until completion. The solvent was then evaporated, and the resulting crude product was purified by silica gel column chromatography. Elution with a 5-10% Hexane/EtOAc mixture gave the desired products, **5f-5h**.

**5. Gram-scale reaction for spirooxindoles (3n or 3j):**

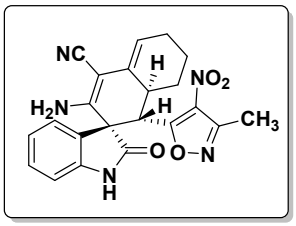
To a stirred solution of isoxazole-oxindole styrene (2.53 mmol, 1.0 equiv.) and vinyl malononitrile (2.53mmol, 1.0 equiv.) in EtOH/THF (10 mL) was added $K_2CO_3$ (10 mol%). The reaction mixture was stirred at room temperature and monitored by TLC. Upon completion, the solvent was evaporated *in vacuo*. The resulting crude product was purified by silica gel column chromatography using Hexane/EtOAc (25-30%) as the eluent to afford the desired products, **3j** or **3f'**.

**6. Gram-scale reaction for Michael adducts (5c):**

To a stirred solution of isoxazole-styrene (3.63 mmol, 1.0 equiv) and vinyl malononitrile (3.63 mmol, 1.0 equiv) in EtOH (10 mL), $K_2CO_3$ (10 mol%) was added. The reaction mixture was stirred at room temperature and monitored by TLC until completion. The solvent was then evaporated, and the resulting crude product was purified by silica gel column chromatography. Elution with a 5-10% Hexane/EtOAc mixture gave the desired products, **5c**.

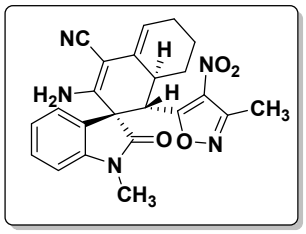
**7. Characterization of the compounds 3a-3r:**

***(1'S,3R,8a'S)-3'-amino-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3a):***




Yield = 35 mg (85%) Yellow solid; M.P: 252-254 °C; **$^1$H NMR (400 MHz, $CDCl_3$+DMSO-$d_6$) δ** 10.77 (s, 1H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.11 (d, *J* = 7.6 Hz, 1H), 6.89 (t, *J* = 7.6 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 5.80 (s, 2H), 5.66 (s, 1H), 4.35 (d, *J* = 12.8 Hz, 1H), 3.61 – 3.50 (m, 1H), 2.27 (s, 3H), 2.20 – 2.15 (m, 2H), 1.74 (d, *J* = 14.4 Hz, 1H), 1.50 – 1.42 (m, 1H), 1.25 – 1.23 (m, 1H), 1.07 (dd, *J* = 23.6, 11.2 Hz, 1H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ** 175.2, 170.5, 155.5, 153.3, 142.9, 132.0, 130.7, 130.4, 127.0, 124.4, 122.5, 118.0, 117.7, 110.5, 81.3, 55.3, 45.7, 32.1, 27.1, 25.1, 21.7, 11.3. **Mass (ESI-MS):** m/z Calculated $C_{22}H_{19}N_5O_4$ for: 417.1437; Observed: 418.1524 (M+1).

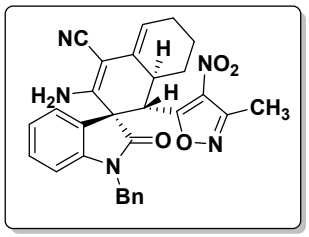
***(1'S,3R,8a'S)-3'-amino-1-methyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3b):***




Yield = 37 mg (88%) Yellow solid; M.P: 246-248 °C; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ** 7.27 (t, *J* = 7.6 Hz, 1H), 7.16 (d, *J* = 7.2 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 5.86 (s, 2H), 5.67 (s,

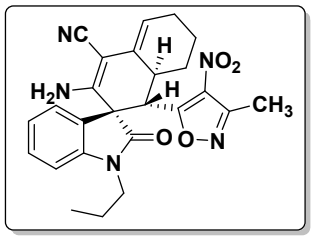
1H), 4.35 (d, *J* = 12.4 Hz, 1H), 3.57 – 3. 46 (m, 1H), 3.02 (s, 3H), 2.24 (s, 3H), 2.22 – 2.12 (m, 2H), 1.74 (d, *J* = 13.2 Hz, 1H), 1.51 – 1.38 (m, 1H), 1.24 (d, *J* = 12.4 Hz, 1H), 1.11 – 1.00 (m, 1H). **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 173.3, 170.7, 155.0, 149.5, 143.8, 131.5, 130.8, 128.8, 125.1, 124.3, 123.6, 122.0, 116.7, 108.7, 86.9, 54.5, 45.6, 32.2, 29.6, 26.8, 25.2, 21.4, 11.4. **Mass (ESI-MS):** m/z Calculated $C_{23}H_{21}N_5O_4$ for: 431.1594; Observed: 432.1673 (M+1).

***(1'S,3R,8a'S)-3'-amino-1-benzyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3c):***



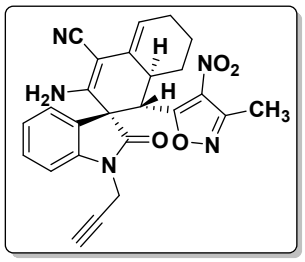

Yield = 41 mg (80%) White solid; M.P: 142-146 °C; **$^{1}$H NMR (400 MHz, $CDCl_3$) δ** 7.36 – 7.30 (m, 5H), 7.25 – 7.21 (m, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.02 (t, *J* = 7.2 Hz, 1H), 6.64 (d, *J* = 7.6 Hz, 1H), 6.03 (s, 1H), 5.10 (d, *J* = 14.8 Hz, 1H), 4.65 (dd, *J* = 28.4, 15.6 Hz, 2H), 4.08 (s, 2H), 3.96 – 3.85 (m, 1H), 2.37 (s, 3H), 2.31 – 2.32 (m, 2H), 1.84 (d, *J* = 12.8 Hz, 1H), 1.69 – 1.63 (m, 1H), 1.33 (dd, *J* = 12.0, 3.6 Hz, 1H), 1.20 (dd, *J* = 25.2, 13.2 Hz, 1H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ** 172.6, 169.8, 155.1, 152.7, 142.5, 132.0, 130.4, 126.3, 124.4, 123.6, 118.1, 117.9, 110.2, 81.7, 55.1, 45.8, 32.3, 29.9, 27.0, 25.1, 21.6, 11.3. **Mass (ESI-MS):** m/z Calculated $C_{29}H_{25}N_5O_4$ for: 507.1907; Observed: 508.1976 (M+1).

***(1'S,3R,8a'S)-3'-amino-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-1-propyl-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3d):***



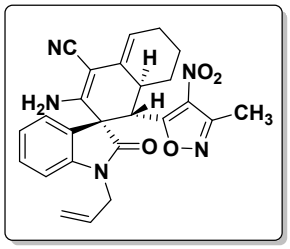

Yield = 41 mg (90%) Light Yellow Solid; M.P: 215-217 °C; **$^{1}$H NMR (400 MHz, DMSO-$d_6$) δ** 7.26 (t, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 6.97 – 6.92 (m, 2H), 5.81 (s, 2H), 5.67 (s, 1H), 4.37 (d, *J* = 12.4 Hz, 1H), 3.64 – 3.50 (m, 2H), 3.45 – 3.40 (m, 1H), 2.25 (s, 3H), 2.22 – 2.08 (m, 2H), 1.75 (d, *J* = 12.4 Hz, 1H), 1.54 – 1.43 (m, 3H), 1.24 (d, *J* = 10.4 Hz, 1H), 1.07 – 1.042 (m, 1H), 0.86 (t, *J* = 7.6 Hz, 3H). **Mass (ESI-MS):** m/z Calculated $C_{25}H_{25}N_5O_4$ for: 459.1907; Observed: 458.1842 (M-1).

***(1'S,3R,8a'S)-3'-amino-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-1-(prop-2-yn-1-yl)-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3e):***



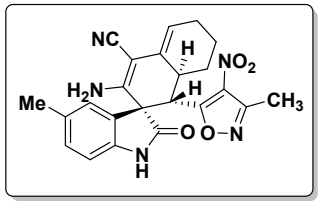
Yield = 42 mg (92%) White solid; M.P: 216-218 °C; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ** 7.31 (t, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 7.01 (t, *J* = 7.6 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 5.82 (s, 2H), 5.69 (s, 1H), 4.55 (dd, *J* = 17.6, 2.0 Hz, 1H), 4.37 (d, *J* = 12.4 Hz, 1H), 4.24 (dd, *J* = 18.0, 2.0 Hz, 1H), 3.57 – 3.41 (m, 1H), 3.21 (s, 1H), 2.24 (s, 3H), 2.25 - 2.10 (m, 2H), 1.83 – 1.69 (m, 1H), 1.56 – 1.46 (m, 1H), 1.34 – 1.20 (m, 1H), 1.16 – 1.00 (m, 1H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ** 172.6, 169.8, 155.1, 152.7, 142.5, 132.0, 130.4, 126.3, 124.4, 123.6, 118.2, 117.9, 110.2, 81.7, 77.2, 75.2, 55.1, 45.8, 32.3, 29.9, 27.0, 25.1, 21.7, 11.3. **Mass (ESI-MS):** m/z Calculated $C_{25}H_{21}N_5O_4$ for: 455.16; Observed: 456.1680 (M+1).

***(1'S,3R,8a'S)-1-allyl-3'-amino-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3f):***



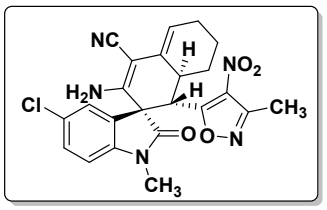

Yield = 43 mg (95%) Yellow solid; M.P: 230-232 °C; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ** 7.26 (t, *J* = 7.6 Hz, 1H), 7.20 (d, *J* = 7.2 Hz, 1H), 6.98 (t, *J* = 7.2 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 5.85 (s, 2H), 5.75 – 5.63 (m, 2H), 5.23 – 5.15 (m, 2H), 4.39 (d, *J* = 12.4 Hz, 1H), 4.30 (dd, *J* = 16.4, 4.8 Hz, 1H), 4.11 (dd, *J* = 16.0, 6.0 Hz, 1H), 3.59 – 3.48 (m, 1H), 2.26 (s, 3H), 2.21 – 2.15 (m, 2H), 1.75 (d, *J* = 14.4 Hz, 1H), 1.54 – 1.39 (m, 1H), 1.29 – 1.20 (m, 1H), 1.15 – 1.01 (m, 1H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ** 173.2, 170.2, 155.6, 153.0, 143.5, 132.0, 131.7, 130.5, 130.4, 126.4, 124.3, 123.3, 118.3, 118.0, 117.9, 110.2, 81.5, 54.2, 45.7, 42.8, 32.3, 27.0, 25.1, 21.6, 11.3. **Mass (ESI-MS):** m/z Calculated $C_{25}H_{23}N_5O_4$ for: 457.1750; Observed: 458.1836 (M+1).

***(1'S,3R,8a'S)-3'-amino-5-methyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3g):***



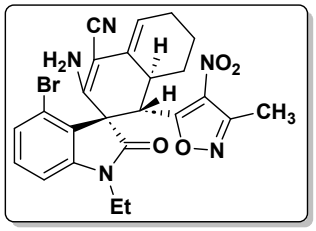

Yield = 34 mg (80%) Yellow solid; M.P: 260-262 °C; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ** 10.65 (s, 1H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.90 (s, 1H), 6.56 (d, *J* = 7.6 Hz, 1H), 5.79 (s, 2H), 5.66 (s, 1H), 4.28 (d, *J* = 12.4 Hz, 1H), 3.60 – 3.48 (m, 1H), 2.26 (s, 3H), 2.24 – 2.16 (m, 2H), 2.15 (s, 3H), 1.80 – 1.70 (m, 1H), 1.54 – 1.40 (m, 1H), 1.31 – 1.23 (m, 1H), 1.06 (dd, *J* = 24.0, 11.6 Hz, 1H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ** 175.1, 170.4, 155.5, 153.3, 140.3, 132.1, 131.5, 130.7, 130.6, 127.1, 124.9, 118.0, 117.7, 110.2, 81.3, 55.4, 45.8, 32.0, 27.1, 25.1, 21.7, 20.8, 11.2. **Mass (ESI-MS):** m/z Calculated $C_{23}H_{21}N_5O_4$ for: 431.16; Observed: 432.1681 (M+1).

***(1'S,3R,8a'S)-3'-amino-5-chloro-1-methyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3h):***



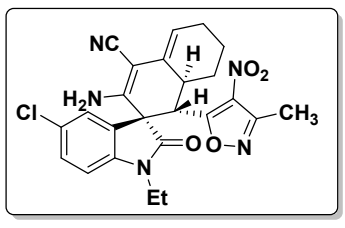

Yield = 46 mg (98%) White solid; M.P: 265-267 °C; **$^1$H NMR (400 MHz, $CDCl_3$+DMSO-$d_6$) δ** 7.35 – 7.30 (m, 2H), 6.93 – 6.88 (m, 1H), 6.00 (s, 2H), 5.68 (s, 1H), 4.36 (d, *J* = 12.4 Hz, 1H), 3.53 – 3.41 (m, 1H), 3.01 (s, 3H), 2.27 (s, 3H), 2.24 - 2.12 (m, 2H), 1.78 – 1.67 (m, 1H), 1.54 - 1.37 (m, 1H), 1.28 – 1.18 (m, 1H), 1.13 – 1.01 (m, 1H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ** 173.2, 169.8, 155.6, 152.4, 143.2, 132.2, 130.5, 130.2, 128.5, 127.3, 124.7, 118.0, 117.9, 111.0, 81.6, 55.0, 45.9, 32.2, 27.1, 27.0, 25.1, 21.6, 11.3. **Mass (ESI-MS):** m/z Calculated $C_{23}H_{20}ClN_5O_4$ for: 465.12; Observed: 466.1284 (M+1).

***(1'S,3R,8a'S)-3'-amino-4-bromo-1-ethyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3i):***




Yield = 49 mg (94%) Yellow solid; M.P: 273-274 °C; **$^1$H NMR (400 MHz, DMSO-$d_6$)** δ 8.26 (s, 1H), 7.20 (s, 1H), 7.13 (d, J = 7.2 Hz, 1H), 6.90 (dd, J = 7.8, 1.0 Hz, 1H), 6.04 (s, 2H), 4.70 (d, J = 12.5 Hz, 1H), 3.73 – 3.66 (m, 2H), 3.40 (d, J = 7.0 Hz, 1H), 2.26 (s, 3H), 2.15 (dd, J = 14.2, 3.7 Hz, 2H), 1.73 (d, J = 12.2 Hz, 1H), 1.46 – 1.41 (m, 1H), 1.22 (s, 1H), 1.09 (d, J = 6.2 Hz, 1H), 1.01 (t, J = 7.2 Hz, 3H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$)** δ 172.4, 169.3, 155.7, 151.5, 145.6, 132.3, 130.2, 126.8, 125.1, 119.7, 118.1, 108.9, 81.5, 79.5, 56.4, 42.4, 35.4, 32.0, 27.2, 25.1, 21.7, 12.1, 11.2.

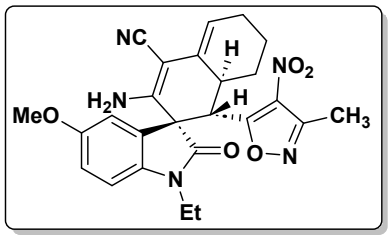
***(1'S,3R,8a'S)-3'-amino-5-chloro-1-ethyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3j):***




Yield = 45 mg (94%) Yellow solid; M.P: 273-275 °C; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ** 7.35 – 7.29 (m, 2H), 6.94 (d, *J* = 8.8 Hz, 1H),

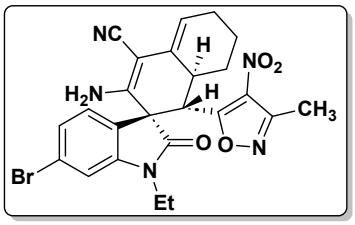
5.96 (s, 2H), 5.67 (s, 1H), 4.37 (d, *J* = 12.4 Hz, 1H), 3.77 3.66 (m, 1H), 3.53 – 3.42 (m, 2H), 2.28 (s, 3H), 2.20 - 2.10 (m, 2H), 1.80 – 1.68 (m, 1H), 1.55 - 1.37 (m, 1H), 1.30 – 1.19 (m, 1H), 1.14 – 1.06 (m, 1H), 1.03 (t, *J* = 7.2 Hz, 3H). **$^{13}$C NMR (100 MHz, DMSO-*d*$_6$) δ** 172.7, 169.9, 155.6, 152.4, 142.4, 132.2, 130.5, 130.2, 128.6, 127.1, 124.9, 118.0, 117.9, 111.1, 81.5, 55.1, 45.6, 35.3, 32.2, 27.0, 25.1, 21.6, 12.1, 11.3. **Mass (ESI-MS):** m/z Calculated $C_{24}H_{22}ClN_5O_4$ for: 479.1360; Observed: 480.1452 (M+1).

***(1'S,3R,8a'S)-3'-amino-1-ethyl-5-methoxy-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3k):***



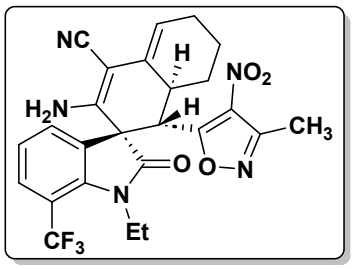

Yield = 45 mg (94%) Brown solid; M.P: 263-265 °C; **$^{1}$H NMR (400 MHz, DMSO-*d*$_6$) δ** $^{1}$H NMR (400 MHz, DMSO) δ 6.87 (d, *J* = 1.6 Hz, 1H), 6.83 (d, *J* = 1.6 Hz, 2H), 5.75 (s, 2H), 5.69 – 5.64 (m, 1H), 4.37 (d, *J* = 12.4 Hz, 1H), 3.65 (s, 3H), 2.25 (s, 3H), 2.21 – 2.12 (m, 2H), 1.97 (d, *J* = 7.7 Hz, 1H), 1.76 (s, 1H), 1.44 (s, 1H), 1.34 (d, *J* = 5.5 Hz, 1H), 1.23 (s, 2H), 1.08 (s, 1H), 1.02 (t, *J* = 7.2 Hz, 3H). **$^{13}$C NMR (100 MHz, DMSO-*d*$_6$) δ** 172.7, 170.2, 155.8, 155.5, 153.1, 136.5, 132.0, 130.6, 127.5, 117.9, 116.4, 110.4, 81.5, 79.54, 56.02, 55.3, 45.6, 35.2, 32.2, 27.1, 25.1, 21.7, 12.1, 11.2.

***(1'S,3R,8a'S)-3'-amino-6-bromo-1-ethyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3l):***



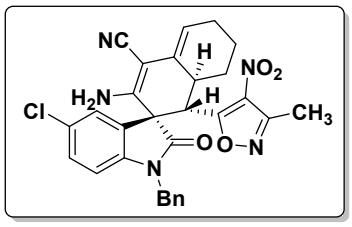

Yield = 49 mg (93%) Yellow solid; M.P: 273-275 °C; **$^{1}$H NMR (400 MHz, DMSO-*d*$_6$) δ** 7.25 – 7.16 (m, 2H), 7.13 (dd, J = 8.2, 1.0 Hz, 2H), 6.90 (dd, J = 7.8, 1.0 Hz, 1H), 6.04 (s, 2H), 4.70 (d, J = 12.5 Hz, -1H), 2.50 – 2.49 (m, 2H), 2.26 (s, 2H), 2.17 (d, J = 4.9 Hz, 1H), 1.75 (s, 1H), 1.45 – 1.41 (m, 1H), 1.27 (d, J = 7.0 Hz, 1H), 1.11 – 1.08 (m, 3H), 1.06 (d, J = 4.3 Hz, 1H), 1.01 (s, 3H). **$^{13}$C NMR (100 MHz, DMSO-*d*$_6$) δ** 169.3, 155.7, 151.5, 145.69, 132.3, 132.2, 130.2, 126.8, 125.1, 119.7, 118.1, 108.9, 81.5, 79.5, 56.4, 42.4, 35.4, 32.0, 27.20, 25.1, 21.7, 12.1, 11.2.

***(1'S,3R,8a'S)-3'-amino-1-ethyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-7-(trifluoromethyl)-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3m):***



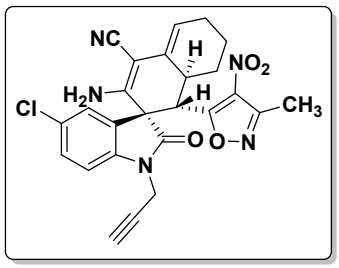
Yield = 44 mg (80%) White solid; M.P: 270-271 °C; **$^1$H NMR (400 MHz, DMSO-*d*$_6$)** δ 8.27 (s, 1H), 7.21 (s, 1H), 7.14 (d, J = 7.5 Hz, 1H), 6.91 (d, J = 7.7 Hz, 1H), 6.05 (s, 2H), 4.71 (d, J = 12.4 Hz, 1H), 2.27 (s, 3H), 2.18 (d, J = 4.2 Hz, 2H), 1.73 (s, 1H), 1.45 (d, J = 9.3 Hz, 1H), 1.34 (d, J = 5.6 Hz, 1H), 1.22 (d, J = 3.4 Hz, 2H), 1.11 (d, J = 6.0 Hz, 2H), 1.07 (d, J = 5.6 Hz, 1H), 1.02 (s, 3H). **$^{13}$C NMR (100 MHz, DMSO-*d*$_6$) δ** $^{13}$C NMR (101 MHz, DMSO) δ 178.7, 174.6, 166.3, 164.9, 130.7, 128.5, 127.8, 127.4, 126.9, 122., 121.6, 113.1, 112.9, 112.7, 105.2, 104.0, 85.6, 79.5, 66.4, 46.9, 44.2, 36.3, 29.4, 27.5, 26.8, 21.2, 21.0, 13.1. $^{19}$F NMR (376 MHz, **DMSO-*d*$_6$**) δ −54.67.

***(1'S,3R,8a'S)-3'-amino-1-benzyl-5-chloro-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3n):***



Yield = 52 mg (97%) Light Yellow solid; M.P: 148-150 °C; **$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.29 – 7.21 (m, 3H), 7.19 – 7.14 (m, 3H), 7.08 (d, *J* = 8.5 Hz, 1H), 6.47 (d, *J* = 8.4 Hz, 1H), 5.95 (s, 1H), 4.99 (d, *J* = 15.6 Hz, 1H), 4.59 (d, *J* = 15.6 Hz, 1H), 4.48 (d, *J* = 12.4 Hz, 1H), 3.98 (s, 2H), 3.80 - 3.70 (m, 1H), 2.32 (s, 3H), 2.25 – 2.12 (m, 2H), 1.79 – 1.67 (m, 1H), 1.29 – 1.10 (m, 4H). **$^{13}$C NMR (100 MHz, DMSO-*d*$_6$) δ** 173.5, 169.8, 155.6, 152.3, 142.5, 135.7, 132.2, 130.4, 130.3, 129.0, 128.2, 127.9, 127.6, 125.1, 118.1, 117.9, 111.7, 81.8, 55.1, 45.3, 44.3, 32.4, 27.0, 25.1, 21.7, 11.3. **Mass (ESI-MS):** m/z Calculated $C_{29}H_{24}ClN_5O_4$ for: 541.15; Observed: 542.1608 (M+1).

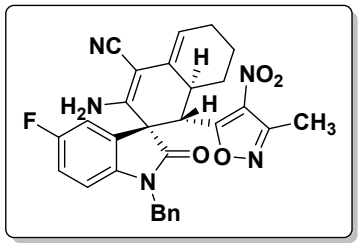
***(1'S,3R,8a'S)-3'-amino-5-chloro-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-1-(prop-2-yn-1-yl)-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3o):***



Yield = 43 mg (87%) White solid; M.P: 177-179 °C; **$^1$H NMR (400 MHz, DMSO-*d*$_6$) δ** 7.41 - 7.35 (m, 2H), 6.96 (d, *J* = 8.0 Hz, 1H), 5.95 (s, 2H), 5.69 (s, 1H), 4.55 (dd, *J* = 18.0, 2.4 Hz, 1H), 4.38 (d, *J* = 12.8 Hz, 1H), 4.23 (dd, *J* = 17.6, 2.0 Hz, 1H), 3.52 – 3.39 (m, 1H), 3.23 (s, 1H), 2.26 (s, 3H), 2.24 – 2.11 (m, 2Hs 1.81 – 1.70 (m, 1H), 1.55 – 1.38 (m, 1H), 1.30 – 1.20 (m, 1H), 1.13 – 1.00 (m, 1H). **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 171.9, 169.9, 155.0, 148.2, 140.4, 131.7, 130.8, 129.5, 128.4, 126.7,

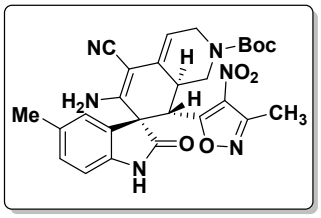
124.9, 122.8, 116.4, 110.9, 87.4, 75.2, 73.4, 54.7, 45.4, 32.3, 30.0, 26.7, 25.1, 21.3, 11.4. **Mass (ESI-MS):** m/z Calculated $C_{25}H_{20}ClN_5O_4$ for: 489.1204; Observed: 490.1284 (M+1).

***(1'S,3R,8a'S)-3'-amino-1-benzyl-5-fluoro-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3p):***



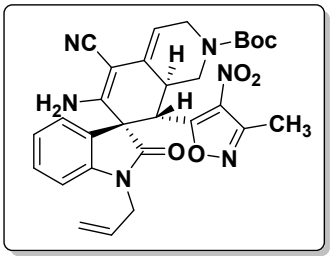

Yield = 44 mg (84%) White solid; M.P: 179-181 °C; **$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.29 – 7.19 (m, 4H), 7.17 (s, 1H), 6.94 (dd, *J* = 7.6, 2.4 Hz, 1H), 6.82 (td, *J* = 8.4, 2.0 Hz, 1H), 6.49 (dd, *J* = 8.4, 4.0 Hz, 1H), 5.95 (s, 1H), 5.00 (d, *J* = 15.6 Hz, 1H), 4.54 (dd, *J* = 46.0, 15.6 Hz, 2H), 3.98 (s, 2H), 3.86 – 3.72 (m, 1H), 2.32 (s, 3H), 2.30 – 2.13 (m, 2H), 1.80 – 1.68 (m, 1H), 1.20 – 1.04 (m, 3H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ** 173.7, 169.9, 160.1 (d, *J* = 239.5 Hz), 157.8, 155.6, 152.5, 139.9, 135.9, 132.2, 130.4 (d, *J* = 8.3 Hz), 129.0, 128.0, 127.9 (d, *J* = 19.4 Hz), 127.8, 127.6, 118.1, 117.9, 117.1, 116.8 (d, *J* = 23.4 Hz), 112.9 (d, *J* = 25.4 Hz), 112.7, 111.3, 111.2 (d, *J* = 8.0 Hz), 81.8, 55.2, 45.3, 44.3, 32.4, 27.0, 25.1, 21.7, 11.3. **Mass (ESI-MS):** m/z Calculated $C_{29}H_{24}FN_5O_4$ for: 525.1812; Observed: 526.1905 (M+1).

***tert-butyl (3R,8'S,8a'S)-6'-amino-5'-cyano-5-methyl-8'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-8',8a'-dihydro-1'H-spiro[indoline-3,7'-isoquinoline]-2'(3'H)-carboxylate (3q):***




Yield = 46 mg (87%) Light Yellow solid; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ** 10.71 (s, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.92 (s, 1H), 6.57 (d, *J* = 8.0 Hz, 1H), 6.06 (s, 2H), 5.59 – 5.55 (m, 1H), 4.33 (d, *J* = 12.6 Hz, 2H), 3.83 – 3.43 (m, 3H), 2.27 (s, 3H), 2.15 (s, 3H), 1.38 (s, 9H). **$^{13}$C NMR (100 MHz, DMSO) δ** 174.7, 168.9, 155.6, 154.3, 154.0, 140.4, 132.1, 131.6, 130.8, 126.5, 125.3, 117.6, 110.3, 80.2, 79.7, 55.3, 43.9, 42.7, 31.4, 31.1, 28.4, 20.9, 11.2. **Mass (ESI-MS):** m/z Calculated $C_{27}H_{28}N_6O_6$ for: 532.2070; Observed: 555.1993 (M+Na).

***tert-butyl (3R,8'S,8a'S)-1-allyl-6'-amino-5'-cyano-8'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-8',8a'-dihydro-1'H-spiro[indoline-3,7'-isoquinoline]-2'(3'H)-carboxylate (3r):***

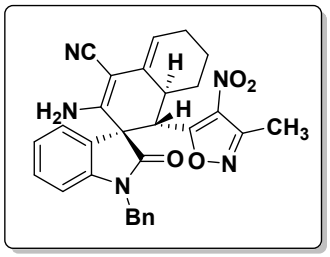



Yield = 42 mg (75%) White solid; M.P: 174-176 °C; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ** 7.31 – 7.21 (m, 2H), 6.99 (t, *J* = 7.6 Hz, 1H),

6.83 (d, *J* = 7.6 Hz, 1H), 6.10 (s, 2H), 5.75 - 5.63 (m, 1H), 5.61 (s, 1H), 5.26 – 5.13 (m, 2H), 4.44 (d, *J* = 12.8 Hz, 1H), 4.30 (dd, *J* = 16.4, 4.8 Hz, 2H), 4.11 (dd, *J* = 16.4, 6.0 Hz, 1H), 3.86 – 3.43 (m, 4H), 2.27 (s, 3H), 1.38 (s, 9H). **$^{13}$C NMR (100 MHz, DMSO-*d*$_6$) δ** 172.8, 168.7, 155.7, 154.0, 143.6, 132.0, 131.6, 130.6, 125.8, 124.6, 124.5, 123.3, 118.3, 117.6, 113.8, 110.3, 79.9, 79.7, 60.2, 54.7, 42.8, 42.6, 31.7, 31.1, 28.3, 11.2. **Mass (ESI-MS):** m/z Calculated $C_{29}H_{30}N_6O_6$ for: 558.2227; Observed: 581.2145 (M+Na).

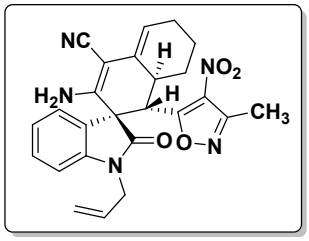
**8. Characterization of the compounds *3a-3l*:**

***(1'S,3S,8a'S)-3'-amino-1-benzyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3a)***



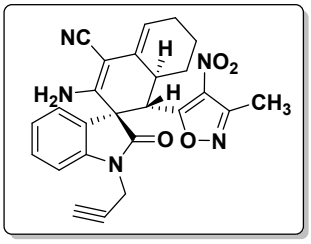

Yield = 41 mg (80%) White solid; M.P: 302-304 °C; **$^{1}$H NMR (400 MHz, DMSO-*d*$_6$) δ** 7.58 (d, *J* = 2.0 Hz, 1H), 7.40 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.32 – 7.19 (m, 4H), 7.05 – 6.98 (m, 1H), 6.97 – 6.94 (m, 2H), 6.36 (s, 2H), 5.71 (s, 1H), 4.95 (d, *J* = 15.6 Hz, 1H), 4.38 (dd, *J* = 23.6, 12.8 Hz, 2H), 3.22 – 3.03 (m, 1H), 2.21 (s, 3H), 2.21 – 2.14 (m, 2H), 1.76 - 1.63 (m, 1H), 1.63 – 1.48 (m, 1H), 1.15 – 1.00 (m, 2H). **$^{13}$C NMR (100 MHz, DMSO-*d*$_6$) δ** 173.7, 168.9, 155.4, 152.8, 142.6, 136.0, 132.0, 130.7, 130.1, 129.7, 129.0, 128.0, 127.7, 127.4, 125.2, 118.2, 117.8, 111.7, 80.4, 55.7, 44.6, 34.1, 27.0, 25.1, 21.2, 11.5. **Mass (ESI-MS):** m/z Calculated $C_{29}H_{25}N_5O_4$ for: 507.1907; Observed: 508.1976 (M+1).

***(1'S,3S,8a'S)-1-allyl-3'-amino-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3b):***



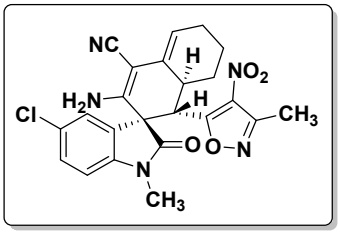

Yield = 36 mg (79%) White solid; M.P: 247-249 °C; **$^{1}$H NMR (400 MHz, DMSO-*d*$_6$) δ** 7.48 (d, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 6.28 (s, 2H), 5.69 (s, 1H), 5.51 - 5.36 (m, 1H), 5.02 (dd, *J* = 10.4, 1.2 Hz, 1H), 4.72 (dd, *J* = 17.2, 1.6 Hz, 1H), 4.36 (d, *J* = 12.8 Hz, 1H), 4.33 – 4.26 (m, 1H), 3.81 (dd, J = 16.4, 6.0 Hz 1H), 3.20 – 3.40 (m, 1H), 2.32 (s, 3H), 2.25 – 2.15 (m, 2H), 1.73 (d, *J* = 10.8 Hz, 1H), 1.61 – 1.45 (m, 1H), 1.27 – 1.06 (m, 2H). **$^{13}$C NMR (100 MHz, DMSO-*d*$_6$) δ** 173.4, 169.0, 155.6, 153.7, 143.4, 132.3, 131.5, 130.0, 129.9, 128.6, 125.2, 123.1, 117.9, 117.7, 117.4, 110.1, 79.9, 56.0, 44.9, 42.8, 33.8, 27.2, 25.1, 21.5, 11.26, 0.6. **Mass (ESI-MS):** m/z Calculated $C_{25}H_{23}N_5O_4$ for: 457.1750; Observed: 458.1836 (M+1).

***(1'S,3S,8a'S)-3'-amino-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-1-(prop-2-yn-1-yl)-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3c):***



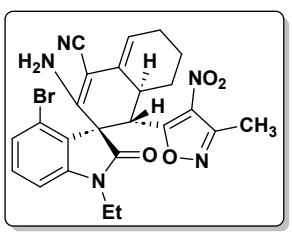

Yield = 33 mg (72%) White solid; M.P: 239-241 °C; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ** 7.47 (d, *J* = 7.2 Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.29 (s, 2H), 5.69 (s, 1H), 4.48 (dd, *J* = 18.0, 2.4 Hz, 1H), 4.36 (d, *J* = 12.8 Hz, 1H), 3.98 (dd, *J* = 18.0, 2.4 Hz, 1H), 3.15 (t, *J* = 2.4 Hz, 1H), 3.13 – 3.01 (m, 1H), 2.31 (s, 3H), 2.26 – 2.13 (m, 2H), 1.79 – 1.66 (m, 1H), 1.61 – 1.46 (m, 1H), 1.27 – 1.18 (m, 1H), 1.11 (dd, *J* = 24.6, 12.0 Hz, 1H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ** 172.5, 168.3, 155.6, 152.2, 141.4, 132.2, 130.4, 130.1, 129.7, 127.5, 125.1, 118.3, 117.8, 111.4, 80.6, 77.1, 74.2, 56.0, 45.2, 33.5, 29.8, 27.2, 25.1, 21.2, 11.5. **Mass (ESI-MS):** m/z Calculated $C_{25}H_{21}N_5O_4$ for: 455.16; Observed: 456.1680 (M+1).

***(1'S,3S,8a'S)-3'-amino-5-chloro-1-methyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3d):***




Yield = 37 mg (80%) White solid; M.P: 248-250 °C; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ** 7.53 (s, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.31 (s, 2H), 5.70 (s, 1H), 4.29 (d, *J* = 12.8 Hz, 1H), 3.19 - 3.02 (m, 1H), 2.86 (s, 3H), 2.34 (s, 3H), 2.24 – 2.15 (m, 2H), 1.78 – 1. 66 (m, 1H), 1.66 – 1.50 (m, 1H), 1.29 – 1.20 (m, 1H), 1.17 – 1.02 (m, 1H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ** 173.5, 168.6, 155.5, 152.6, 143.3, 132.1, 130.4, 130.1, 129.7, 127.2, 124.9, 118.3, 117.8, 111.1, 80.5, 56.2, 45.1, 33.5, 27.3, 27.0, 25.1, 21.3, 11.3. **Mass (ESI-MS):** m/z Calculated $C_{23}H_{20}ClN_5O_4$ for: 465.12; Observed: 466.1284 (M+1).

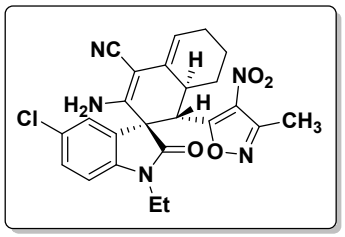
***(1'S,3S,8a'S)-3'-amino-4-bromo-1-ethyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3e):***




Yield = 44 mg (85%) Light yellow solid; M.P: 234-235 °C; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ** ) δ 8.27 (s, -1H), 7.21 (s, 1H), 7.14 (d, J = 7.6 Hz, 1H), 6.91 (d, J = 7.6 Hz, 1H), 6.05 (s, -2H), 4.71 (d, J = 12.4 Hz, -

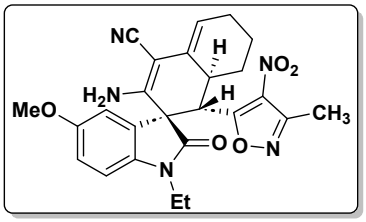
1H), 2.27 (s, 3H), 2.18 (d, J = 4.2 Hz, 1H), 1.74 (d, J = 12.0 Hz, 2H), 1.34 (d, J = 5.6 Hz, 1H), 1.23 (m, 2H), 1.11 (m, 2H), 1.07 (d, J = 5.6 Hz, 1H), 1.02 (m, 3H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$)** δ 172.4, 169.3, 155.7, 151.5, 145.6, 132.3, 130.2, 126.8, 125.1, 119.7, 118.1, 108.9, 81.5, 79.5, 56.4, 42.4, 35.4, 32.0, 25.1, 21.7, 12.1, 11.24.

***(1'S,3S,8a'S)-3'-amino-5-chloro-1-ethyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3f):***



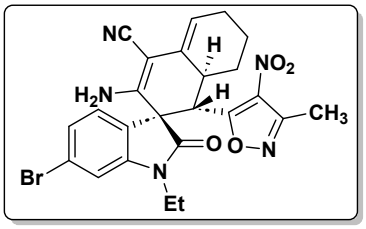

Yield = 41 mg (85%) White solid; M.P: 232-234 °C; **$^{1}$H NMR (400 MHz, DMSO-$d_6$) δ** 7.52 (d, *J* = 2.0 Hz, 1H), 7.45 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.29 (s, 2H), 5.70 (s, 1H), 4.30 (d, *J* = 12.9 Hz, 1H), 3.74 – 3.62 (m, 1H), 3.23 (dt, *J* = 13.9, 7.0 Hz, 1H), 3.10 (t, *J* = 11.8 Hz, 1H), 2.32 (s, 3H), 2.26 – 2.15 (m, 2H), 1.78 – 1.66 (m, 1H), 1.65 – 1.52 (m, 7.9 Hz, 1H), 1.32 - 1.23 (m, 1H), 1.22 – 1.05 (m, 1H), 0.70 (t, *J* = 7.2 Hz, 3H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ** 173.1, 168.7, 155.5, 152.6, 142.4, 132.3, 130.7, 130.1, 129.8, 127.1, 125.1, 118.2, 117.8, 111.0, 80.4, 56.1, 45.1, 35.2, 33.5, 27.3, 25.1, 21.2, 11.8, 11.2. **Mass (ESI-MS):** m/z Calculated $C_{24}H_{22}ClN_5O_4$ for: 479.1360; Observed: 480.1452 (M+1).

***(1'S,3S,8a'S)-3'-amino-1-ethyl-5-methoxy-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3g):***



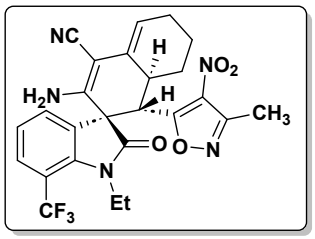

Yield = 39 mg (80%) White solid; M.P: 214-215 °C; **$^{1}$H NMR (400 MHz, DMSO-$d_6$) δ** 1H NMR (400 MHz, DMSO) δ 6.96 – 6.92 (m, 2H), 6.89 – 6.85 (m, 1H), 6.19 (s, 2H), 5.67 (p, J = 2.8 Hz, 1H), 4.29 (d, J = 12.8 Hz, 1H), 3.76 (s, 3H), 3.21 – 3.16 (m, 1H), 3.11 – 3.05 (m, 1H), 2.50 (p, J = 1.9 Hz, 2H), 2.29 (s, 3H), 2.19 (d, J = 4.9 Hz, 1H), 1.72 (d, J = 9.8 Hz, 1H), 1.55 (s, 1H), 1.18 – 1.07 (m, 2H), 0.69 (t, J = 7.2 Hz, 3H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ** 172.8, 169.0, 155.7, 155.4, 153.5, 136.6, 132.2, 130.0, 129.8, 118.0, 114.1, 112.5, 110.0, 80.0, 79.5, 56.3, 56.1, 45.0, 35.0, 33.4, 27.3, 25.1, 21.4, 11.8, 11.2.

***(1'S,3S,8a'S)-3'-amino-6-bromo-1-ethyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3h):***



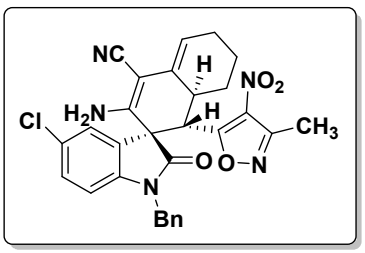
Yield = 44 mg (84%) Yellow solid; M.P: 238-240 °C; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ** 7.20 (d, J = 7.9 Hz, 1H), 7.14 (d, J = 7.5 Hz, 1H), 6.91 (d, J = 7.2 Hz, 1H), 6.05 (s, 2H), 5.81 – 5.53 (m, 1H), 4.71 (d, J = 12.5 Hz, 1H), 2.51 (p, J = 1.8 Hz, 2H), 2.27 (s, 3H), 2.18 (d, J = 4.2 Hz, 2H), 1.74 (d, J = 12.1 Hz, 1H), 1.45 (d, J = 9.3 Hz, 1H), 1.36 – 1.29 (m, 1H), 1.22 (d, J = 3.4 Hz, 2H), 1.11 (s, 1H), 1.02 (s, 2H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ** 172.8, 169.0, 155.7, 155.4, 153.5, 136.6, 132.2, 130.0, 129.8, 118.0, 114.1, 112.5, 110.0, 79.5, 56.1, 45.0, 35.0, 33.4, 29.4, 27.3, 25.1, 21.4, 11.8.

***(1'S,3S,8a'S)-3'-amino-1-ethyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-7-(trifluoromethyl)-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3i):***




Yield = 37 mg (72%) White solid; M.P: 215-216 °C; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ** 8.26 (s, 1H), 7.20 (s, 1H), 7.13 (dd, J = 8.2, 1.0 Hz, 1H), 6.90 (dd, J = 7.8, 1.0 Hz, 1H), 6.04 (s, 2H), 4.70 (d, J = 12.5 Hz, 1H), 3.70 (d, J = 7.0 Hz, 1H), 3.40 (d, J = 7.0 Hz, 1H), 2.26 (s, 3H), 2.19 – 2.11 (m, 2H), 1.71 (s, 1H), 1.44 (d, J = 9.0 Hz, 1H), 1.21 (d, J = 3.4 Hz, 1H), 1.16 (d, J = 4.3 Hz, 1H), 1.08 (s, 1H), 1.01 (t, J = 7.2 Hz, 3H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ $^{13}$C NMR (100 MHz, DMSO-$d_6$)** δ 178.7, 174.7, 174.6, 164.9, 130.7, 128.5, 127.8, 127.4, 126.9, 122.3, 121.6, 113.1, 112.9, 112.7, 104.0, 85.6, 79.5, 66.6, 66.4, 46.9, 44.2, 29.4, 27.5, 26.8, 21.2, 21.0, 20.8, 13.1. $^{19}$F NMR (376 MHz, **DMSO-$d_6$**) δ −54.45.

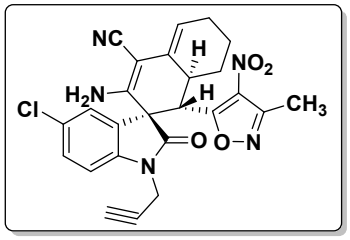
***(1'S,3S,8a'S)-3'-amino-1-benzyl-5-chloro-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3j):***




Yield = 42 mg (78%) White solid; M.P: 234-236 °C; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ** 7.60 (d, *J* = 2.0 Hz, 1H), 7.43 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.30 – 7.20 (m, 3H), 7.05 (d, *J* = 8.4 Hz, 1H),

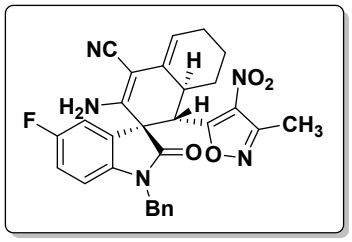
6.94 (d, *J* = 6.8 Hz, 2H), 6.36 (s, 2H), 5.70 (s, 1H), 4.95 (d, *J* = 10.8 Hz, 1H), 4.39 (dd, *J* = 19.4, 14.2 Hz, 2H), 3.18 – 3.00 (m, 1H), 2.21 (s, 3H), 2.20 – 2.11 (m, 2H), 1.76 – 1.48 (m, 2H), 1.13 - 1.00 (m, 2H). **$^{13}$C NMR (100 MHz, DMSO-*d*$_6$) δ** 173.7, 168.9, 155.4, 152.8, 142.6, 136.0, 132.0, 130.7, 130.1, 129.7, 129.0, 128.0, 127.7, 127.4, 125.2, 118.2, 117.8, 111.7, 80.4, 55.7, 44.6, 34.1, 27.0, 25.1, 21.2, 11.5. **Mass (ESI-MS):** m/z Calculated $C_{29}H_{24}ClN_5O_4$ for: 541.15; Observed: 542.1608 (M+1).

***(1'S,3S,8a'S)-3'-amino-5-chloro-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-1-(prop-2-yn-1-yl)-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3k):***




Yield = 35 mg (72%) White solid; M.P: 216-218 °C; **$^{1}$H NMR (400 MHz, DMSO-*d*$_6$) δ** 7.57 (d, *J* = 2.0 Hz, 1H), 7.48 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.32 (s, 2H), 5.70 (s, 1H), 4.48 (dd, *J* = 18.0, 2.4 Hz, 1H), 4.35 (d, *J* = 12.8 Hz, 1H), 4.03- 3.95 (m, 1H), 3.19 (t, *J* = 2.4 Hz, 1H), 3.16 – 3. 04 (m, 1H), 2.32 (s, 3H), 2.23 – 2.11 (m, 2H), 1.74 – 1.53 (m, 2H), 1.27 - 1.19 (m, 1H), 1.09 (dd, *J* = 23.6, 10.8 Hz, 1H). **$^{13}$C NMR (100 MHz, DMSO-*d*$_6$) δ** 172.5, 168.3, 155.6, 152.2, 141.4, 132.2, 130.4, 130.1, 129.7, 127.5, 125.1, 118.3, 117.8, 111.4, 80.6, 77.1, 74.2, 56.0, 45.2, 33.5, 29.8, 27.2, 25.1, 21.2, 11.5. **Mass (ESI-MS):** m/z Calculated $C_{25}H_{20}ClN_5O_4$ for: 489.1204; Observed: 490.1284 (M+1).

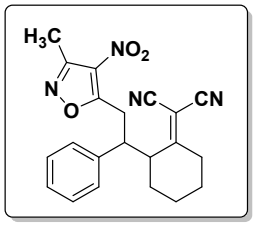
***(1'S,3S,8a'S)-3'-amino-1-benzyl-5-fluoro-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3l'):***




Yield = 44 mg (84%) White solid; M.P: 152-154 °C; **$^{1}$H NMR (400 MHz, DMSO-*d*$_6$) δ** 7.50 (dd, *J* = 8.0, 2.4 Hz, 1H), 7.31 – 7.18 (m, 4H), 7.06 – 6.99 (m, 1H), 6.98 – 6.92 (m, 2H), 6.35 (s, 2H), 5.70 (s, 1H), 4.96 (d, *J* = 15.6 Hz, 1H), 4.39 (dd, *J* = 23.6, 12.8 Hz, 2H), 3.21 – 3.04 (m, 1H), 2.22 (s, 3H), 2.20 – 2.13 (m, 2H), 1.75 - 1.63 (m, 1H), 1.64 – 1.48 (m, 1H), 1.15 – 1.01 (m, 2H). **$^{13}$C NMR (100 MHz, DMSO-*d*$_6$) δ** 173.8, 169.0, 158.9 (d, *J* = 239.5 Hz), 155.4, 153.0, 140.0, 136.1, 132.0, 130.5(d, *J* = 8.3 Hz), 129.9, 128.9, 127.9 (d, *J* = 19.4 Hz), 118.1, 117.8, 116.5 (d, *J* = 23.4 Hz), 113.4 (d, *J* = 25.4 Hz), 111.1 (d, *J* = 8.0 Hz), 80.4, 55.8, 44.6, 34.0, 27.0, 25.1, 21.2, 21.2, 11.5. **Mass (ESI-MS):** m/z Calculated $C_{29}H_{24}FN_5O_4$ for: 626.23; Observed: 649.2216 (M+Na).

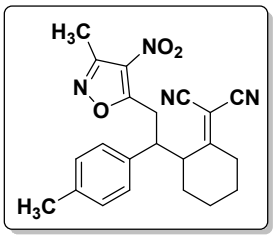
**9. Characterization of the compounds 5a-5h:**

***2-(2-(2-(3-methyl-4-nitroisoxazol-5-yl)-1-phenylethyl)cyclohexylidene)malononitrile (5a):***



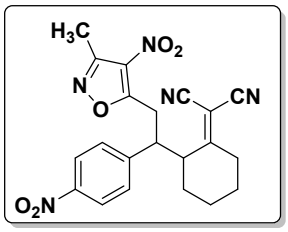
Yield = 30 mg (80%) White semi solid; **$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.32 (m, 3H), 7.16 (d, *J* = 5.6 Hz, 2H), 3.64 (td, *J* = 11.6, 4.0 Hz, 1H), 3.51 – 3.45 (m, 2H), 3.22 (dd, *J* = 14.0, 4.0 Hz, 1H), 3.15 (d, *J* = 13.2 Hz, 1H), 2.75 (td, *J* = 13.2, 5.6 Hz, 1H), 2.45 (s, 3H), 2.29 – 2.20 (m, 1H), 1.70 – 1.49 (m, 5H). **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 186.2, 172.3, 155.3, 137.8, 129.3, 128.3, 127.6, 111.6, 111.2, 84.8, 48.5, 44.2, 32.5, 31.3, 30.4, 28.7, 19.6, 11.5. **Mass (ESI-MS):** m/z Calculated $C_{21}H_{20}N_4O_3$ for: 376.1535; Observed: 377.1601 (M+1).

***2-(2-(2-(3-methyl-4-nitroisoxazol-5-yl)-1-(p-tolyl)ethyl)cyclohexylidene)malononitrile (5b):***



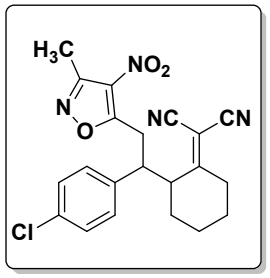
Yield = 30 mg (77%) Light yellow semi solid; **$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.09 (d, *J* = 7.6 Hz, 2H), 7.01 (d, *J* = 6.4 Hz, 2H), 3.57 (td, *J* = 11.6, 4.0 Hz, 1H), 3.45 – 3.39 (m, 2H), 3.18 (dd, *J* = 13.6, 3.6 Hz, 1H), 3.11 (d, *J* = 13.2 Hz, 1H), 2.73 (td, *J* = 13.2, 5.6 Hz, 1H), 2.44 (s, 3H), 2.29 (s, 3H), 2.25 – 2.16 (m, 1H), 1.68 – 1.39 (m, 5H). **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 186.6, 172.5, 155.3, 138.0, 134.7, 130.1, 129.9, 127.5, 111.7, 111.3, 84.6, 48.7, 43.8, 32.6, 31.3, 30.4, 28.8, 21.1, 19.6, 11.5. **Mass (ESI-MS):** m/z Calculated $C_{22}H_{22}N_4O_3$ for: 390.1692; Observed: 413.1576 (M+Na).

***2-(2-(2-(3-methyl-4-nitroisoxazol-5-yl)-1-(3-nitrophenyl)ethyl)cyclohexylidene)malononitrile (5c):***



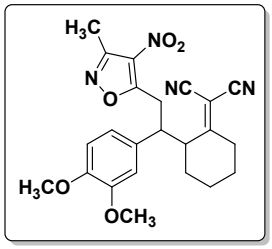
Yield = 33 mg (79%) White solid; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ** 8.24 (s, 1H), 8.14 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.66 (t, *J* = 8.0 Hz, 1H), 3.99 (td, *J* = 10.8, 4.0 Hz, 1H), 3.55 – 3.43 (m, 2H), 3.42 – 3.37 (m, 1H), 2.91 – 2.85 (m, 2H), 2.37 (s, 3H), 2.09 (d, *J* = 10.8 Hz, 1H), 1.79 – 1.68 (m, 1H), 1.59 – 1.45 (m, 2H), 1.31 (t, *J* = 11.2 Hz, 2H). **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 186.2, 172.3, 155.3, 137.8, 129.3, 128.3, 127.6, 111.6, 111.3, 84.8, 48.5, 44.2, 32.5, 31.3, 30.4, 28.7, 19.6, 11.5. **Mass (ESI-MS):** m/z Calculated $C_{21}H_{19}N_5O_5$ for: 421.14; Observed: 444.1271 (M+Na).

***2-(2-(1-(4-chlorophenyl)-2-(3-methyl-4-nitroisoxazol-5-yl)ethyl)cyclohexylidene)malononitrile (5d):***



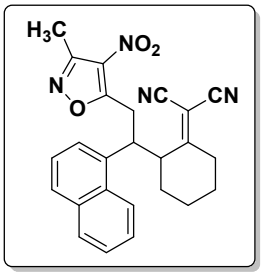
Yield = 33 mg (82%) White solid; M.P: 184-186 °C; **$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.29 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 7.2 Hz, 2H), 3.61 (td, *J* = 11.6, 3.6 Hz, 1H), 3.45 – 3.37 (m, 2H), 3.20 (dd, *J* = 13.6, 3.6 Hz, 1H), 3.13 (d, *J* = 14.0 Hz, 1H), 2.74 – 2.66 (m, 1H), 2.46 (s, 3H), 2.23 – 2.19 (m, 1H), 1.63 – 1.45 (m, 5H). **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 185.6, 171.9, 155.4, 136.3, 134.2, 130.2, 129.6, 129.0, 111.6, 111.1, 85.0, 48.4, 43.5, 32.4, 31.3, 30.3, 28.6, 19.5, 11.5. **Mass (ESI-MS):** m/z Calculated $C_{21}H_{19}ClN_4O_3$ for: 410.11; Observed: 433.1027 (M+Na).

***2-(2-(1-(3,4-dimethoxyphenyl)-2-(3-methyl-4-nitroisoxazol-5-yl)ethyl)cyclohexylidene)malononitrile (5e):***



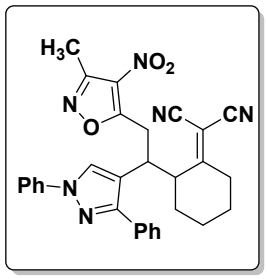
Yield = 30 mg (70%) Light yellow solid; M.P: 183-185 °C; **$^1$H NMR (400 MHz, $CDCl_3$) δ** 6.78 – 6.60 (m, 3H), 3.85 (s, 3H), 3.83 (s, 3H), 3.61 – 3.44 (m, 2H), 3.38 (dd, *J* = 10.0, 3.2 Hz, 1H), 3.15 – 3.11 (m, 2H), 2.70 (td, *J* = 13.6, 5.6 Hz, 1H), 2.44 (s, 3H), 2.23 – 2.19 (m, 1H), 1.77 – 1.60 (m, 3H), 1.47 (m, 2H). **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 186.4, 172.3, 155.3, 149.5, 148.9, 130.2, 130.0, 111.7, 111.2, 84.7, 56.0, 55.8, 48.8, 43.9, 32.4, 31.4, 30.4, 28.7, 19.7, 11.5. **Mass (ESI-MS):** m/z Calculated $C_{23}H_{24}N_4O_5$ for: 436.1747; Observed: 459.1634 (M+Na).

***2-(2-(2-(3-methyl-4-nitroisoxazol-5-yl)-1-(naphthalen-2yl)ethyl)cyclohexylidene)malononitrile (5f):***



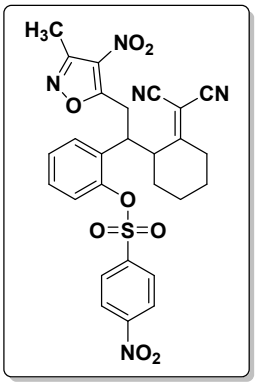
Yield = 33 mg (78%) White solid; M.P: 128-130 °C**; $^1$H NMR (400 MHz, $CDCl_3$) δ** 7.85 – 7.80 (m, 2H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.46 – 7.40 (m, 2H), 4.76 (td, *J* = 11.2, 4.4 Hz, 1H), 3.70 (d, *J* = 12.4 Hz, 1H), 3.53 – 3.45 (m, 1H), 3.38 (dd, *J* = 13.6, 4.4 Hz, 1H), 3.21 (d, *J* = 14.0 Hz, 1H), 2.91 (td, *J* = 13.2, 5.2 Hz, 1H), 2.27 – 2.24 (m, 1H), 2.22 (s, 3H), 1.73 – 1.46 (m, 5H). **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 186.3, 172.1, 155.0, 134.8, 133.7, 132.2, 129.4, 128.5, 126.6, 125.9, 125.8, 124.6, 120.8, 111.8, 111.2, 84.9, 49.2, 36.3, 33.7, 31.6, 30.5, 28.9, 20.6, 11.2. **Mass (ESI-MS):** m/z Calculated $C_{25}H_{22}N_4O_3$ for: 426.17; Observed: 449.1571 (M+1).

***2-(2-(1-(1,3-diphenyl-1H-pyrazol-4-yl)-2-(3-methyl-4-nitroisoxazol-5-yl)ethyl)cyclohexylidene)malononitrile (5g):***




Yield = 38 mg (74%) White solid; M.P: 178-180 °C; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ** 8.85 (s, 1H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.43 – 7.40 (m, 3H), 7.35 – 7.32 (m, 3H), 3.95 (td, *J* = 11.2, 4.0 Hz, 1H), 3.46 – 3.36 (m, 2H), 3.24 – 3.15 (m, 1H), 2.86 (d, *J* = 13.2 Hz, 1H), 2.65 – 2.57 (m, 1H), 2.30 (s, 3H), 2.03 (d, *J* = 15.6 Hz, 1H), 1.85 (d, *J* = 14.4 Hz, 1H), 1.60 – 1.43 (m, 3H), 1.323 – 1.30 (m, 1H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ** 186.7, 173.1, 155.7, 152.3, 139.7, 130.6, 130.0, 129.4, 129.0, 128.7, 128.4, 127.9, 126.9, 118.6, 112.5, 112.4, 84.5, 48.9, 34.0, 33.8, 31.6, 30.6, 28.6, 20.0, 11.4. **Mass (ESI-MS):** m/z Calculated $C_{30}H_{26}N_6O_3$ for: 518.21; Observed: 519.2139 (M+1).

***2-(1-(2-(dicyanomethylene)cyclohexyl)-2-(3-methyl-4-nitroisoxazol-5-yl)ethyl)phenyl 4-nitrobenzenesulfonate(5h):***




Yield = 43 mg (75%) White solid; M.P: 181-183 °C; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ** 8.41 (d, *J* = 9.2 Hz, 2H), 8.04 (d, *J* = 9.2 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 2H), 3.73 (td, *J* = 11.2, 3.6 Hz, 1H), 3.43 (dd, *J* = 14.4, 3.6 Hz, 1H), 3.28 – 3.19 (m, 2H), 2.91 – 2.75 (m, 2H), 2.38 (s, 3H), 1.77 – 1.57 (m, 2H), 1.55 – 1.41 (m, 2H), 1.29 (dd, *J* = 28.0, 13.2 Hz, 2H). **$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ** 186.7, 172.9, 155.6, 151.4, 148.3, 139.5, 130.5, 130.4, 130.2, 125.3, 122.9, 112.5, 112.4, 84.5, 48.3, 43.1, 32.5, 31.4, 30.2, 28.6, 19.1, 11.5. **Mass (ESI-MS):** m/z Calculated $C_{27}H_{23}N_5O_8S$ for: 577.1267; Observed: 578.1237 (M+1).

**10. References**

1. S. Nagaraju, K. Sathish, N. Satyanarayana, B. Paplal and D. Kashinath, *J. Heterocycl. Chem.*, 2020, **57**, 469–476.

2. Y.-Q. Yu, Z.-L. Wang, *J. Chin. Chem. Soc.,* 2013, **60**, 288–292.

3. M. F. A. Adamo, E. F. Duffy, V. R. Konda, F. Murphy, *Heterocycles* 2007, **71**, 5.

**11. Copies of 2D NMR (*NOESY spectrum)*:**

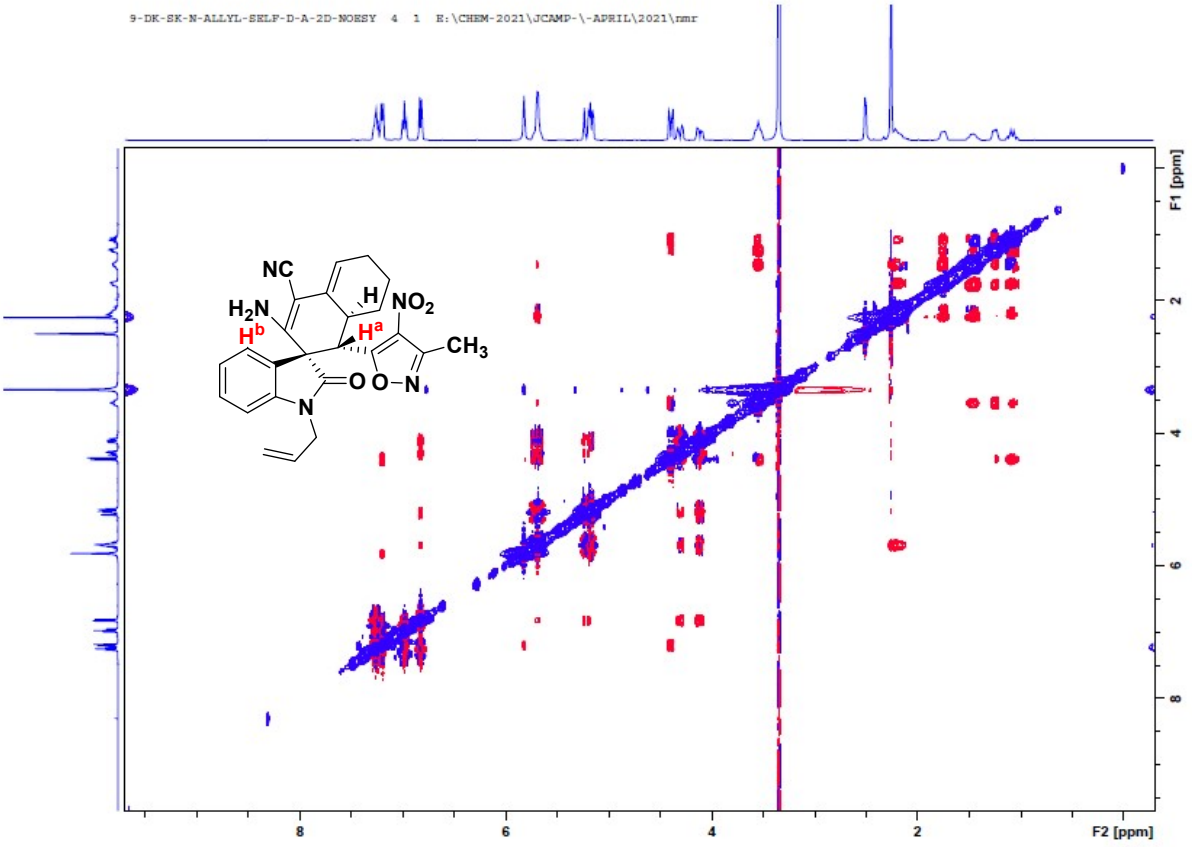



***Figure-1:*** *NOESY spectrum of the compound* ***3e***

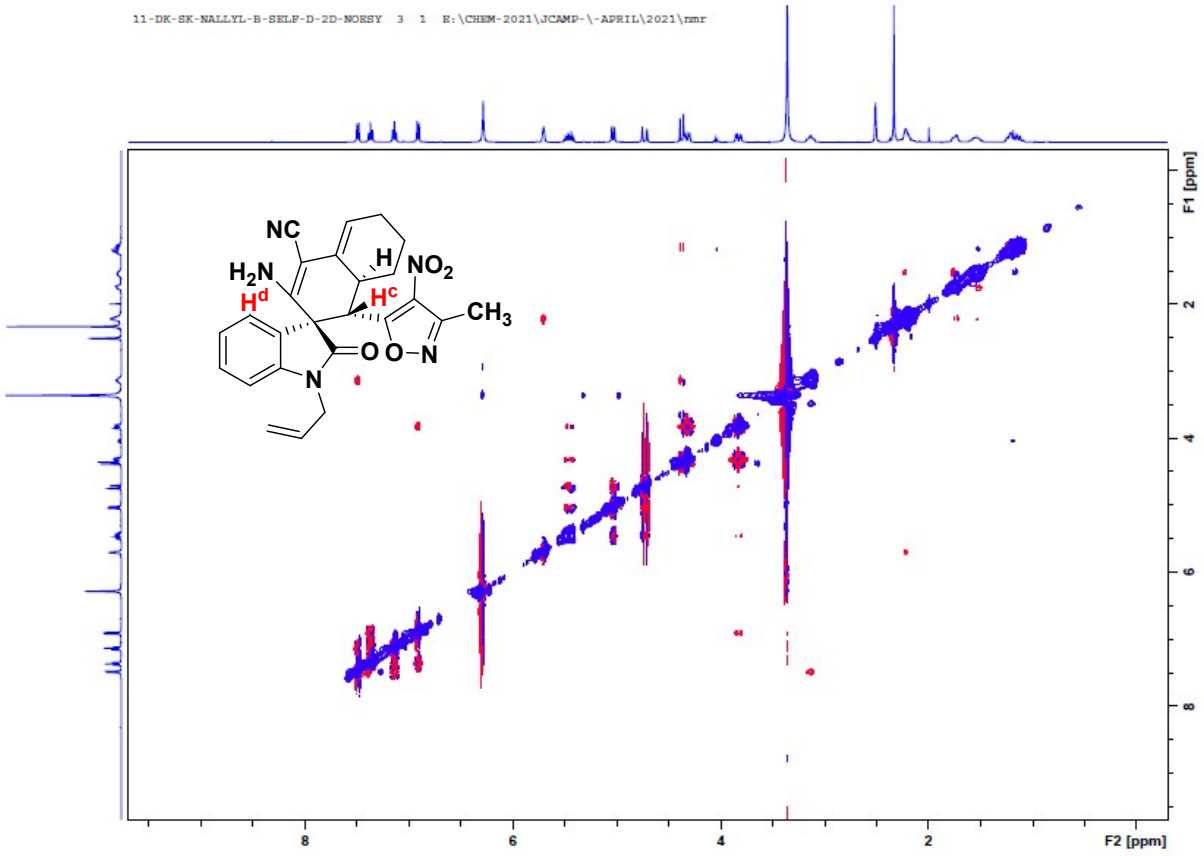
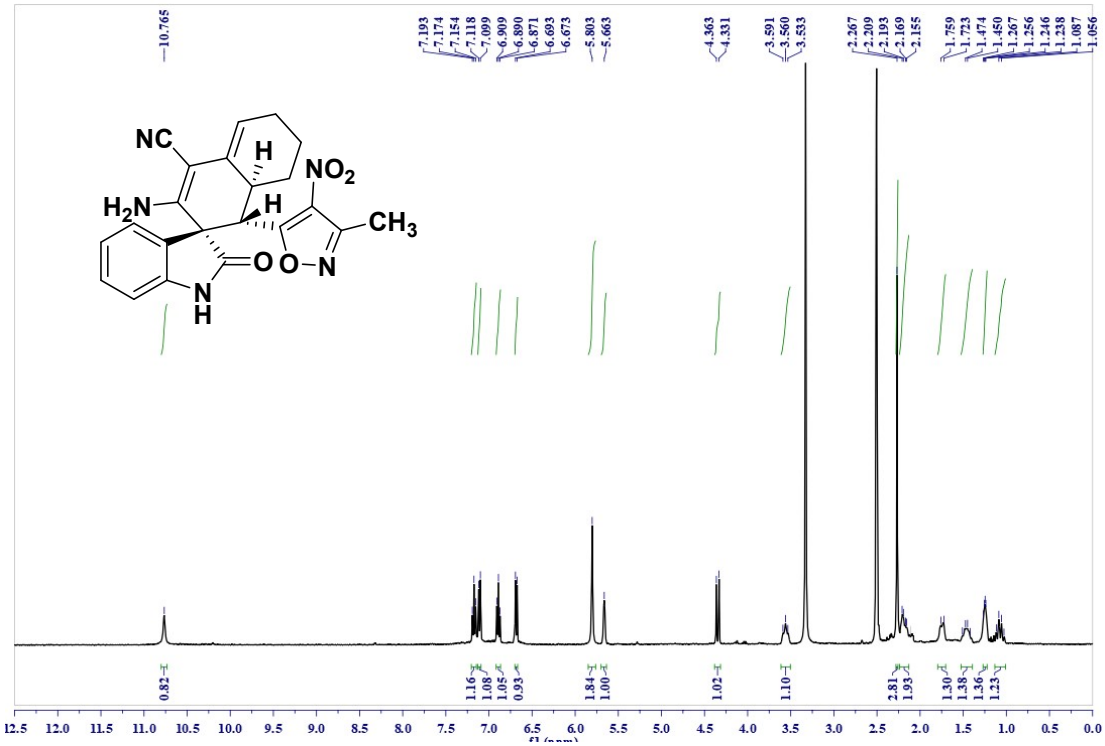
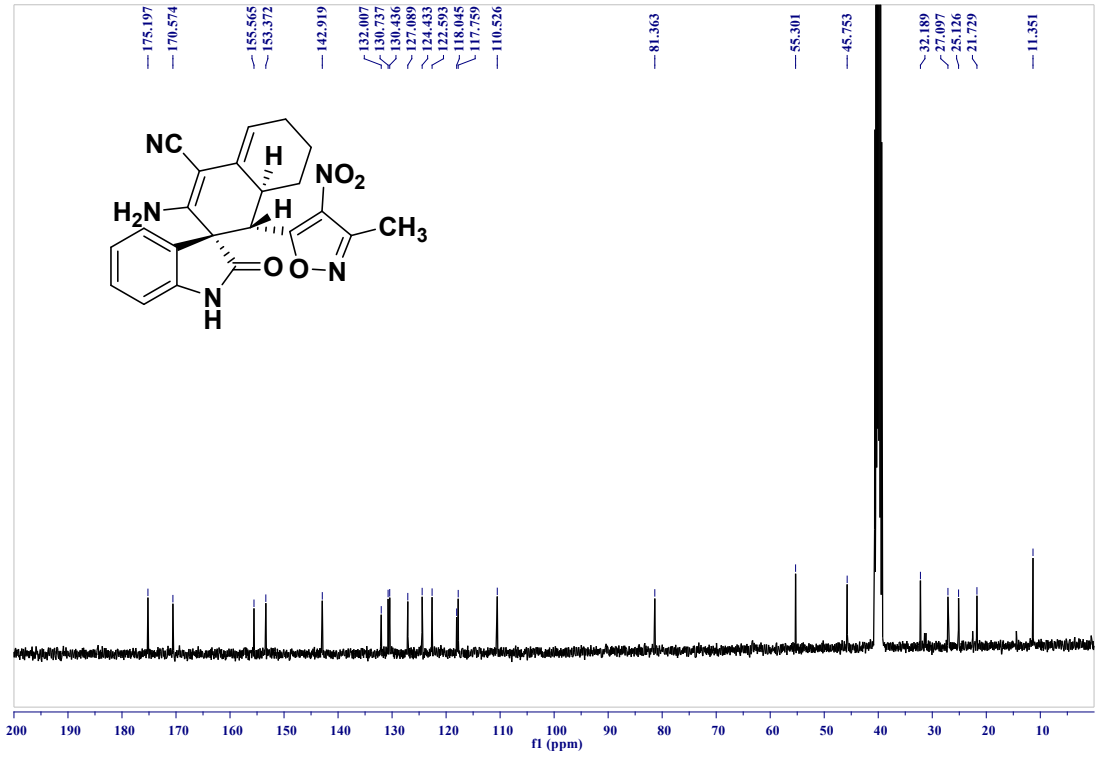


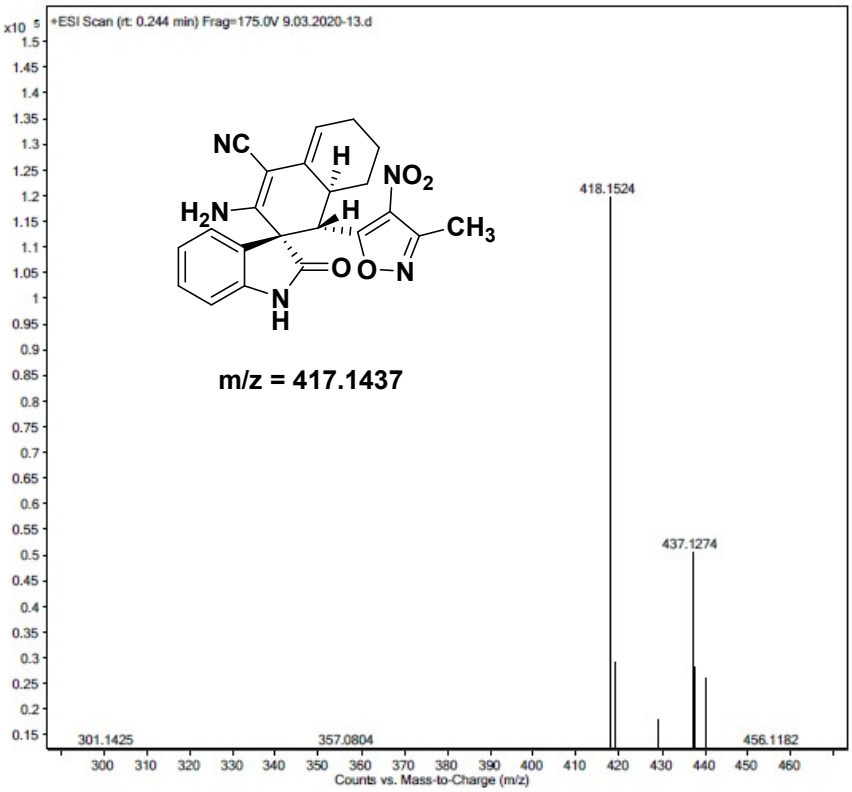

***Figure-2:*** *NOESY spectrum of the compound* ***3b***

## 12. Copies of $^{1}H$, $^{13}C\{^{1}H\}$ NMR and mass spectra:

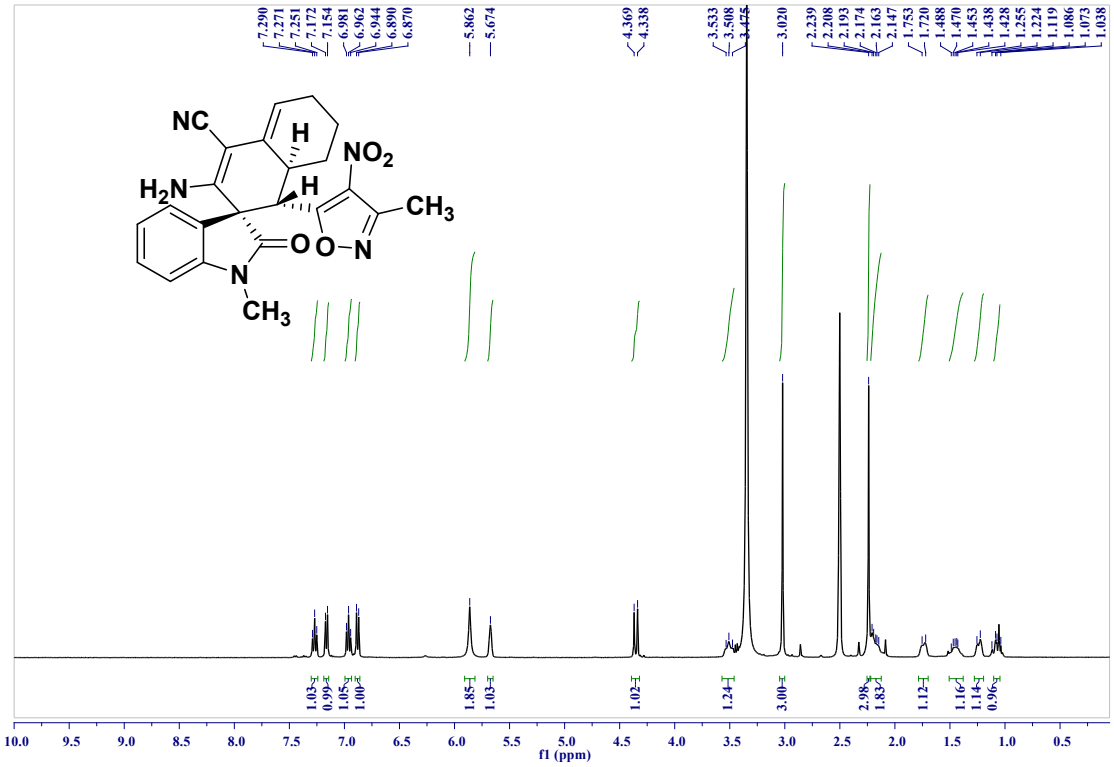
***(1'S,3R,8a'S)-3'-amino-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3a):***

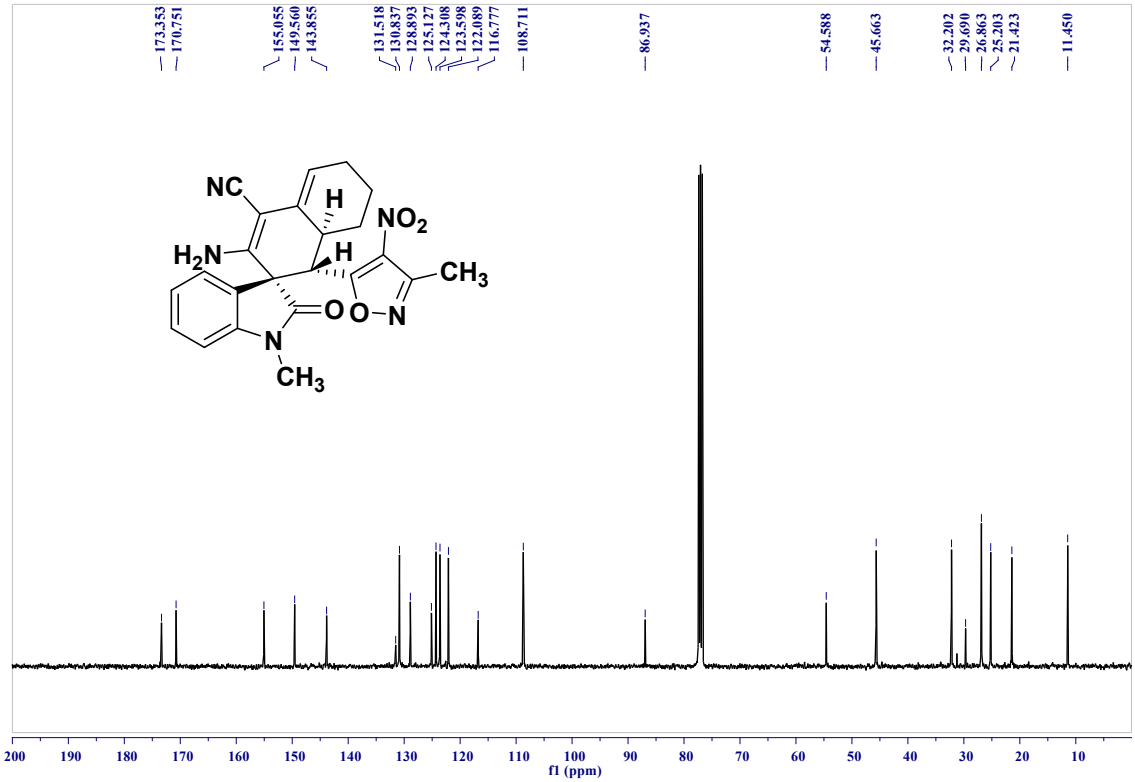





***(1'S,3R,8a'S)-3'-amino-1-methyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3b):***




173.353
170.751
155.055
149.560
143.855
131.518
130.837
128.893
125.127
124.308
123.598
122.089
116.777
108.711
86.937
54.588
45.663
32.202
29.690
26.863
25.203
21.423
11.450
NC
H
NO2
H2N
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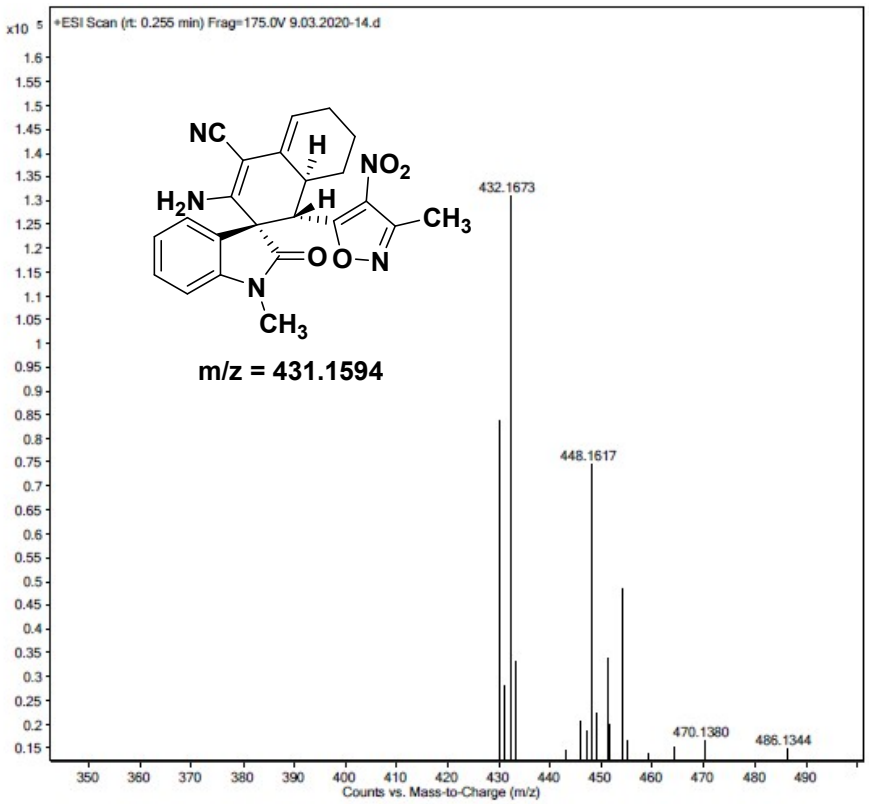
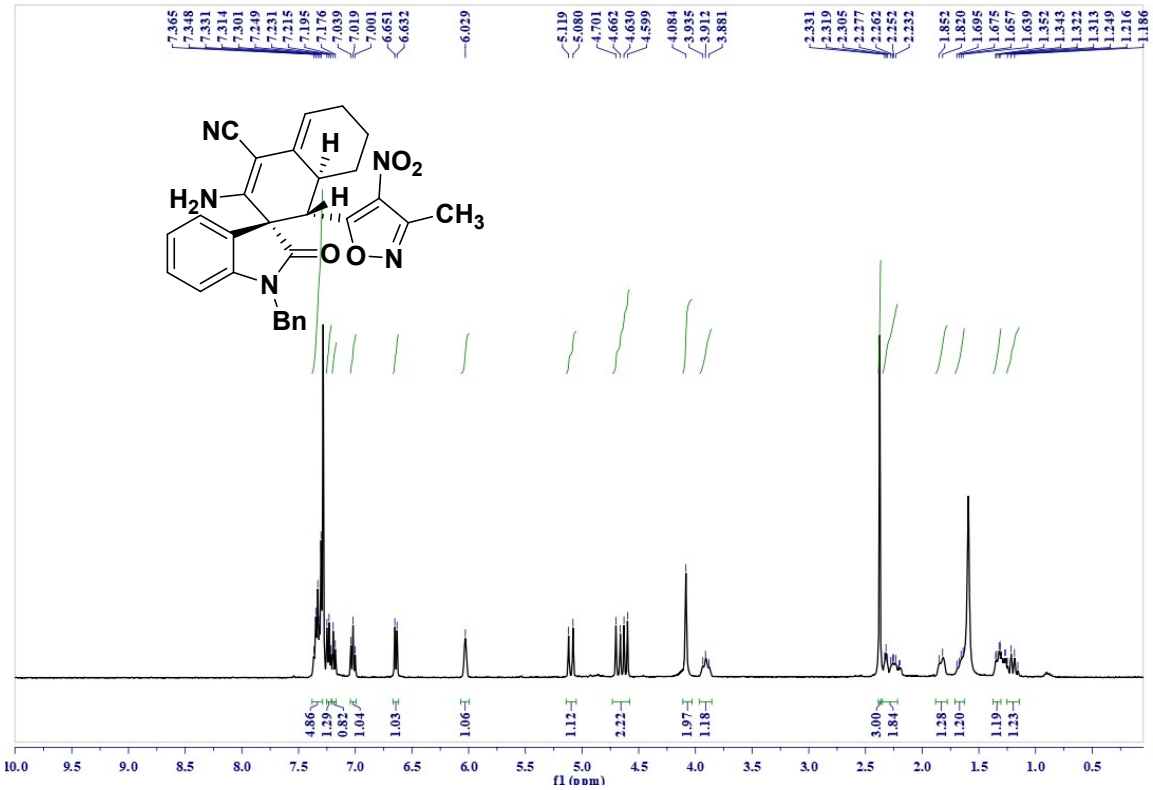
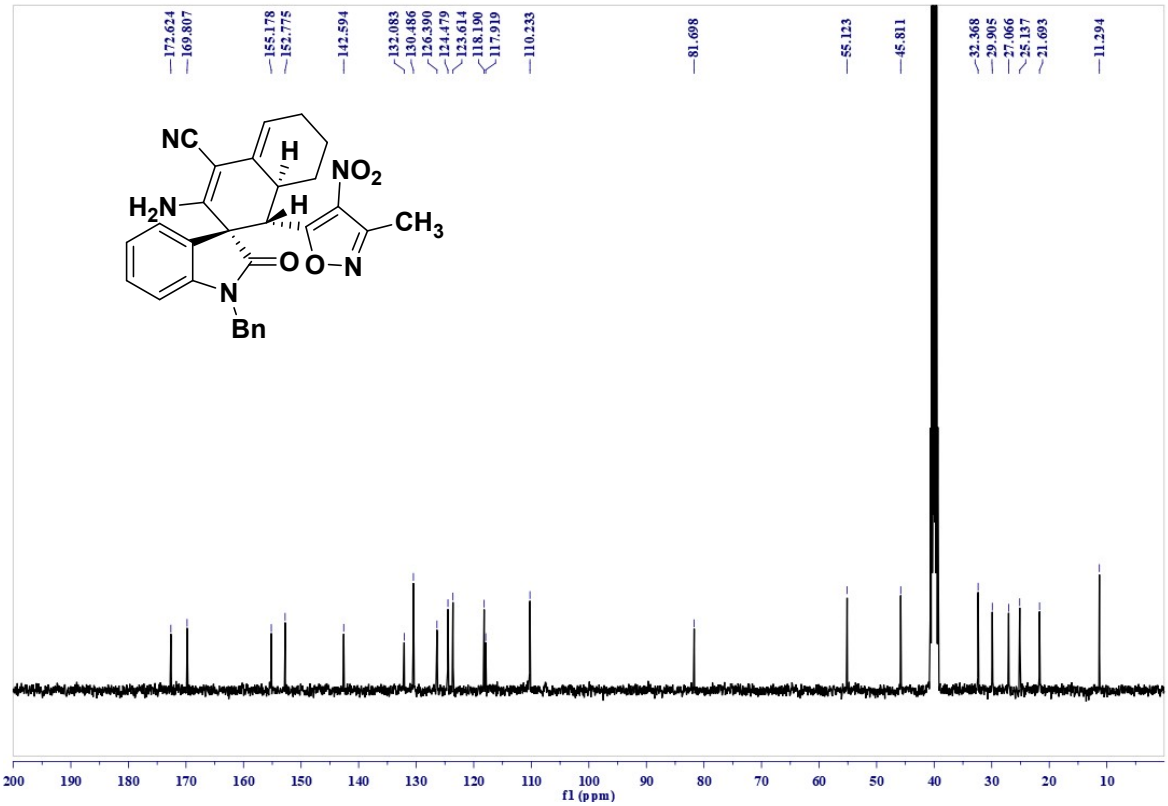
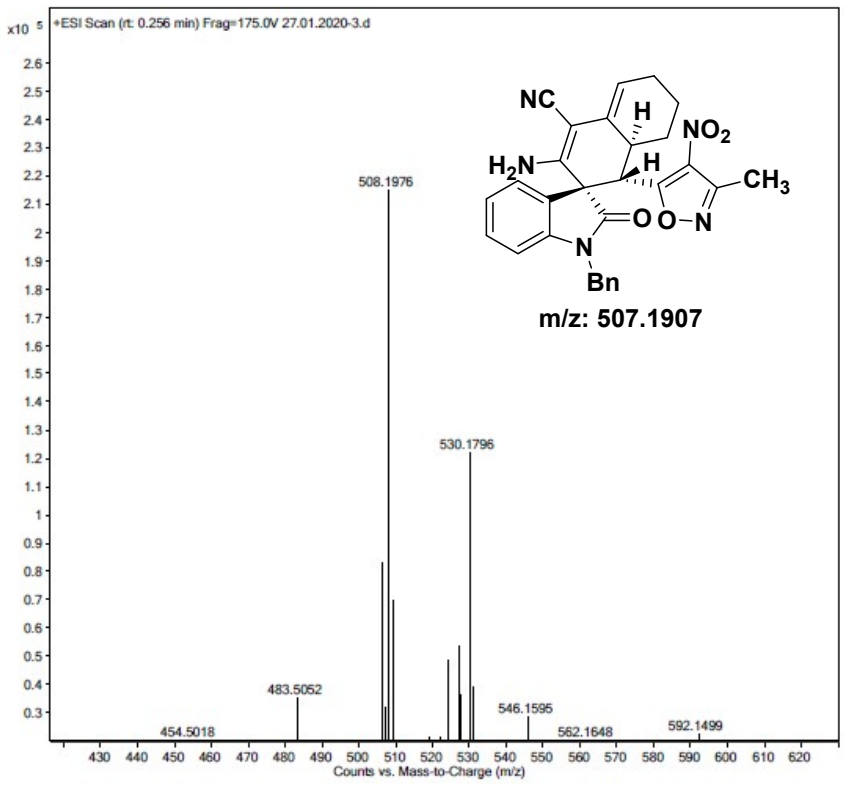
CH3
O
O
N
N
CH3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


x10 5
*ESI Scan (rt: 0.255 min) Frag=175.0V 9.03.2020-14.d
NC
H
NO2
H2N
H
CH3
O
O
N
N
CH3
m/z = 431.1594
432.1673
448.1617
470.1380
486.1344
Counts vs. Mass-to-Charge (m/z)

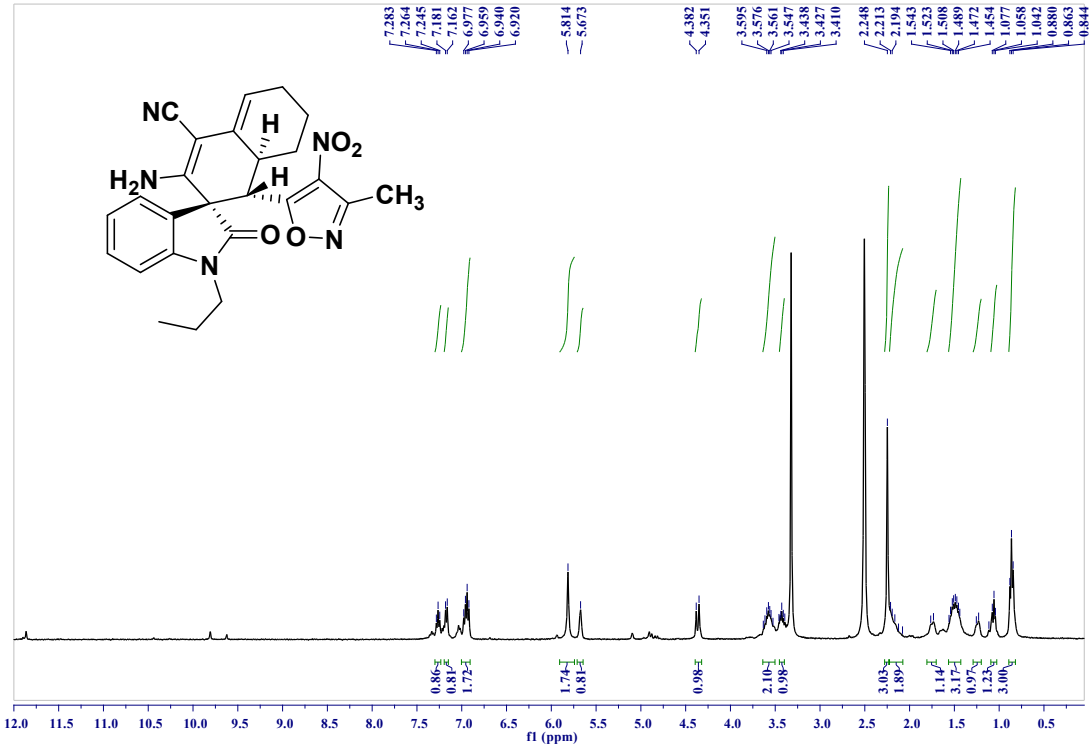
***(1'S,3R,8a'S)-3'-amino-1-benzyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3c):***

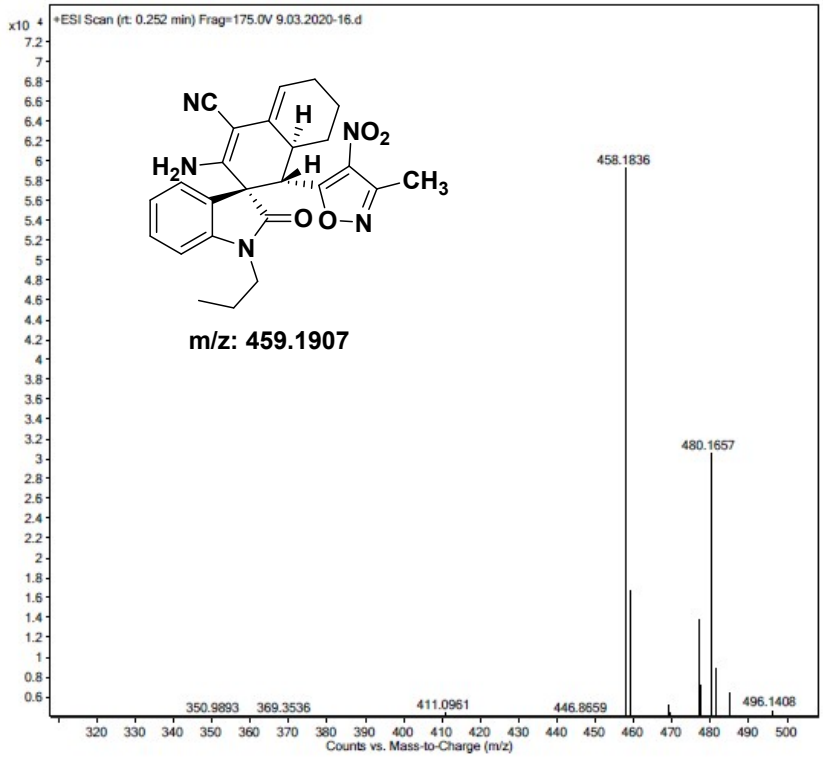


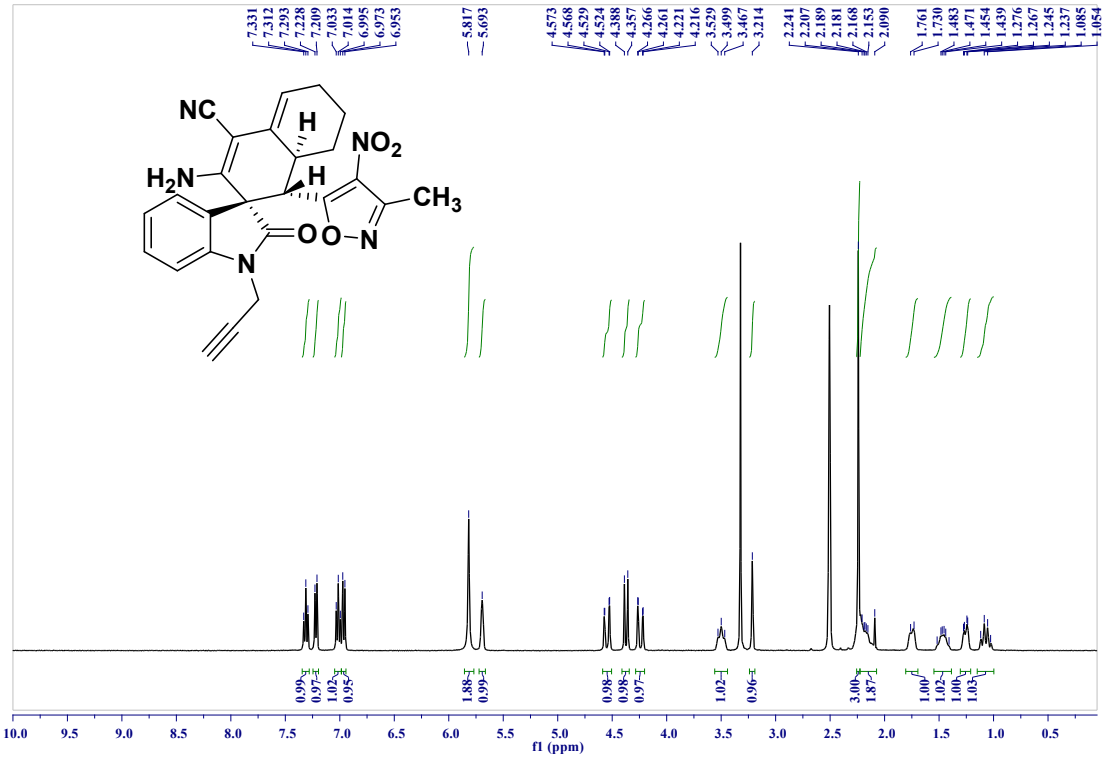


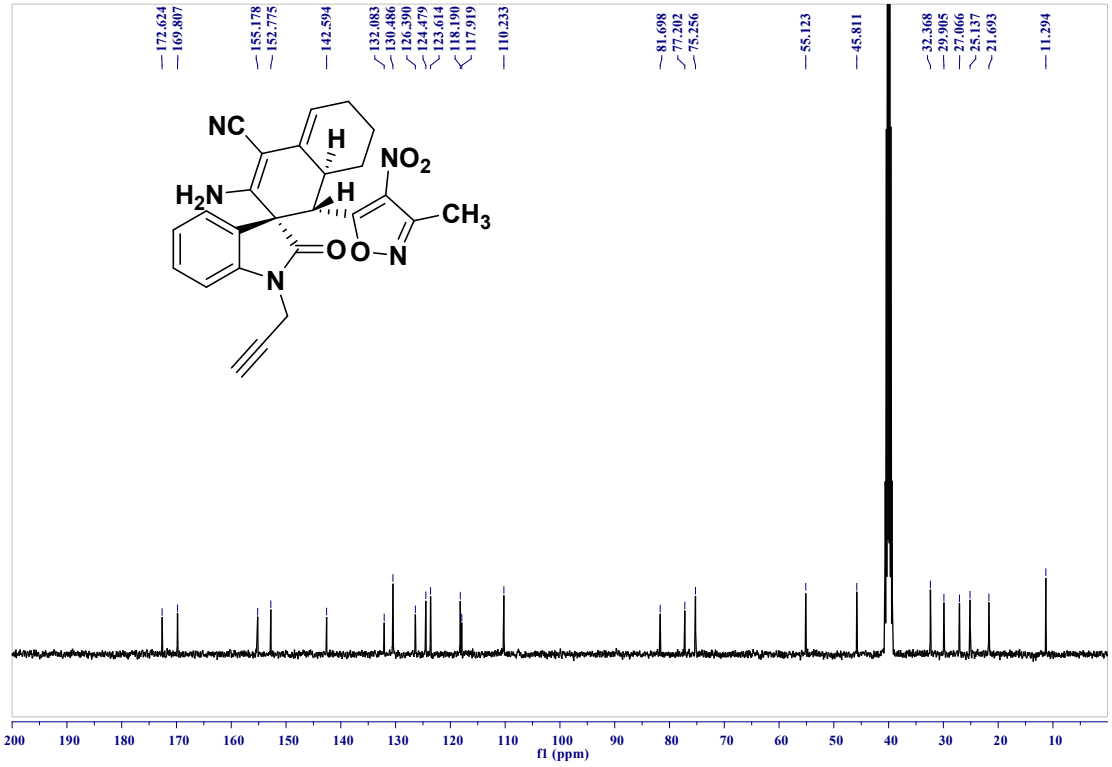

***(1'S,3R,8a'S)-3'-amino-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-1-propyl-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3d):***

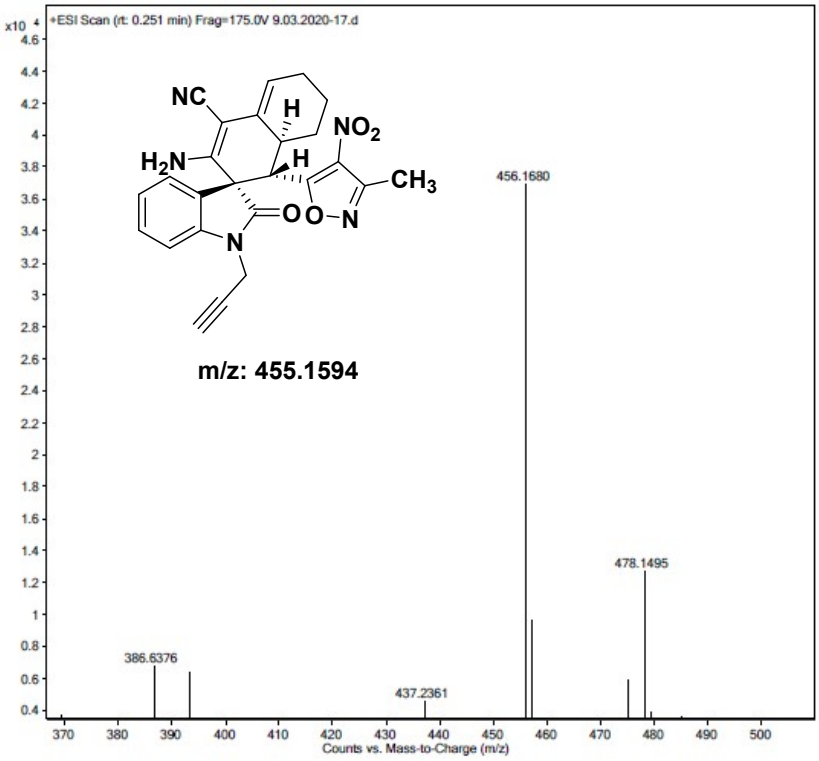




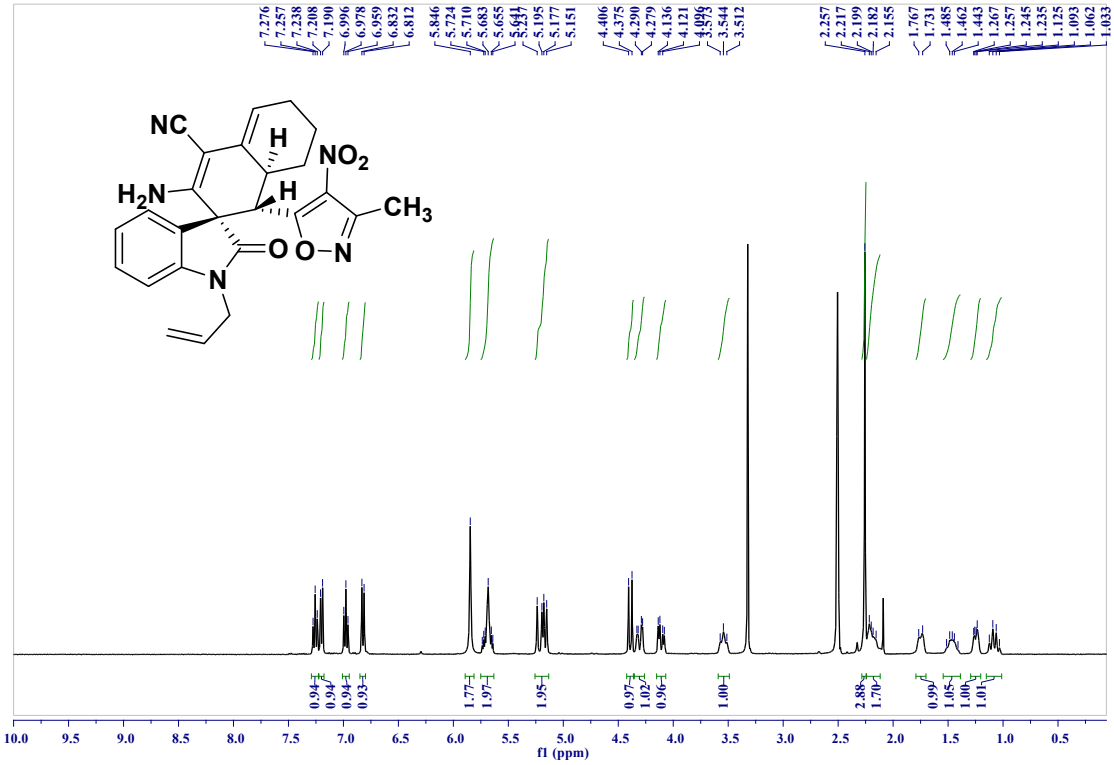

***(1'S,3R,8a'S)-3'-amino-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-1-(prop-2-yn-1-yl)-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3e):***

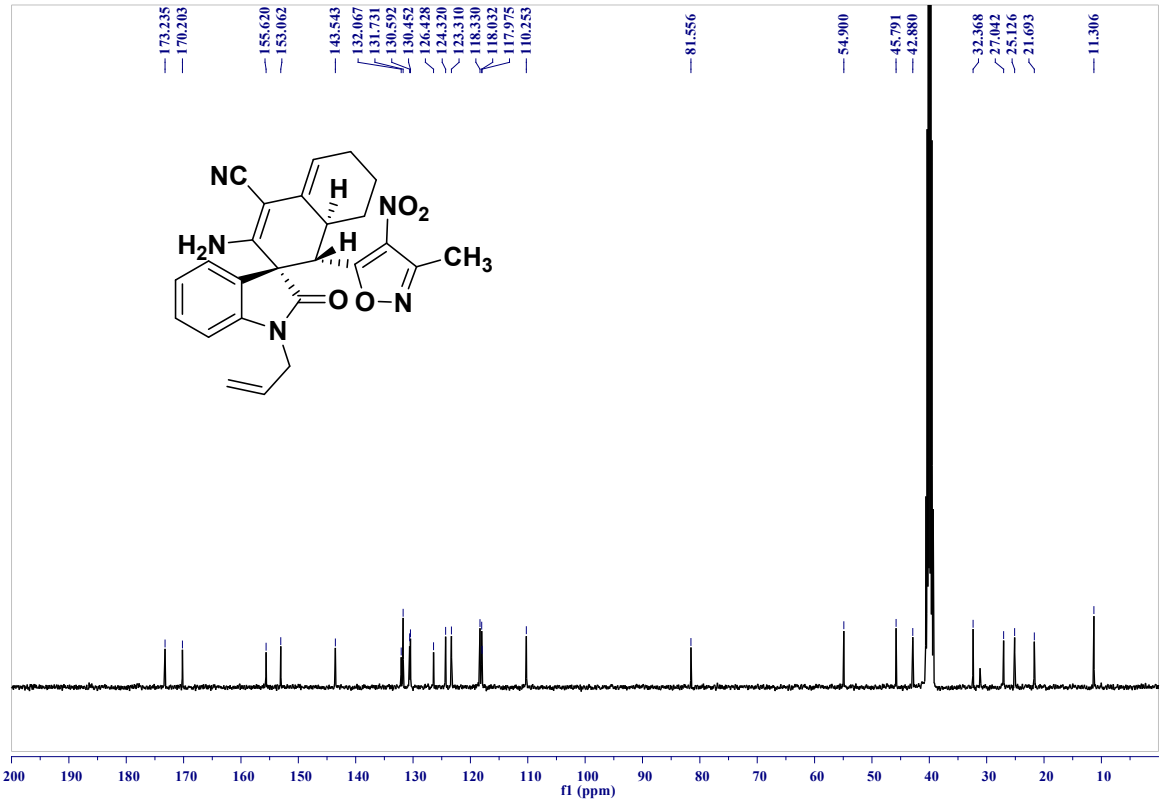


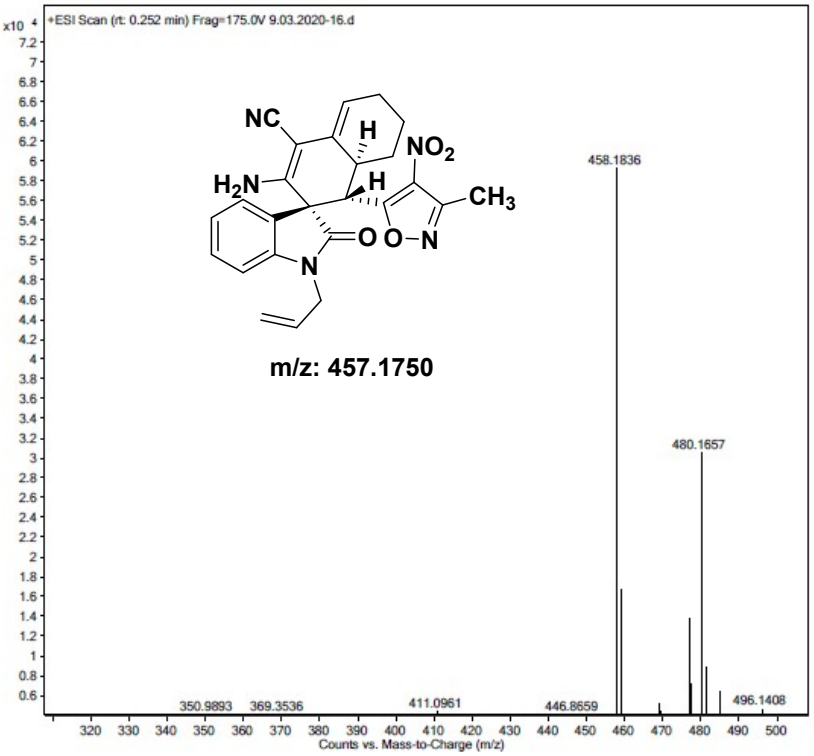


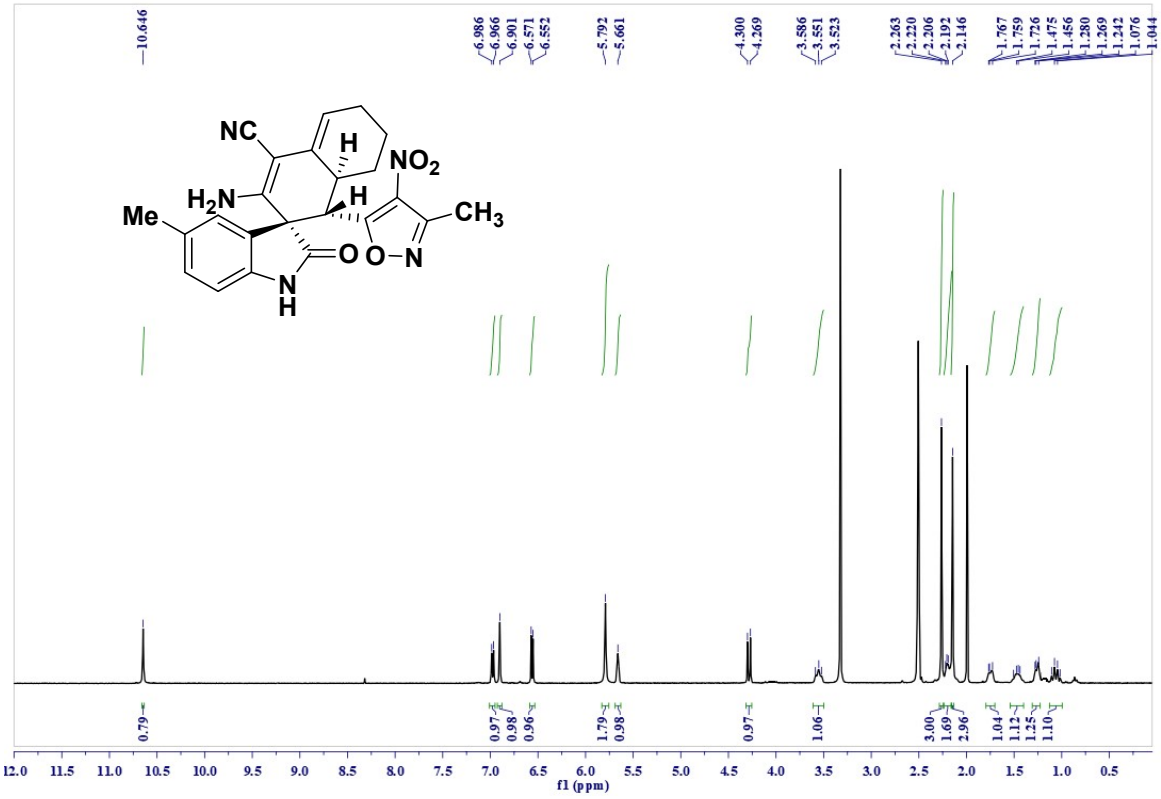

***(1'S,3R,8a'S)-1-allyl-3'-amino-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3f):***

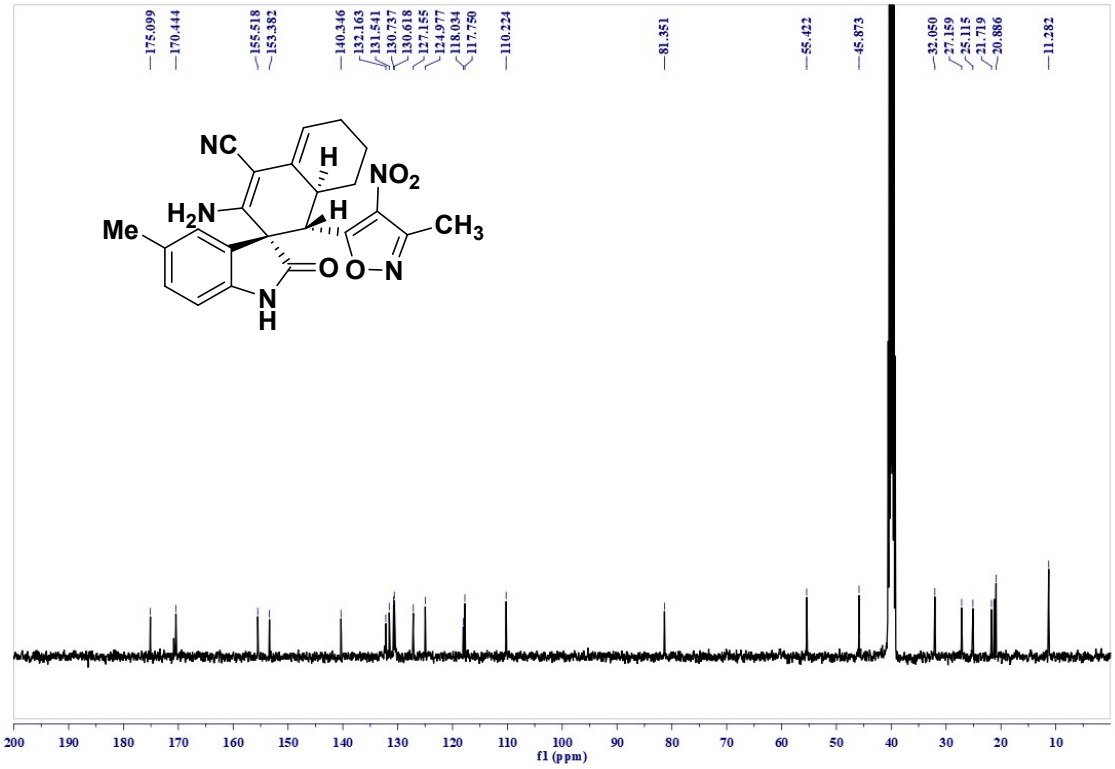

NC
H
NO2
H2N
H
CH3
O
O
N
N
f1 (ppm)


NC
H
NO2
H2N
H
CH3
O
O
N
N
f1 (ppm)




***(1'S,3R,8a'S)-3'-amino-5-methyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3g):***




175.099
170.444
155.518
153.382
140.346
132.163
131.541
130.737
130.618
127.155
124.977
118.034
117.750
110.324
81.351
55.422
45.873
32.050
27.159
25.115
21.719
20.886
11.282
NC
H
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H2N
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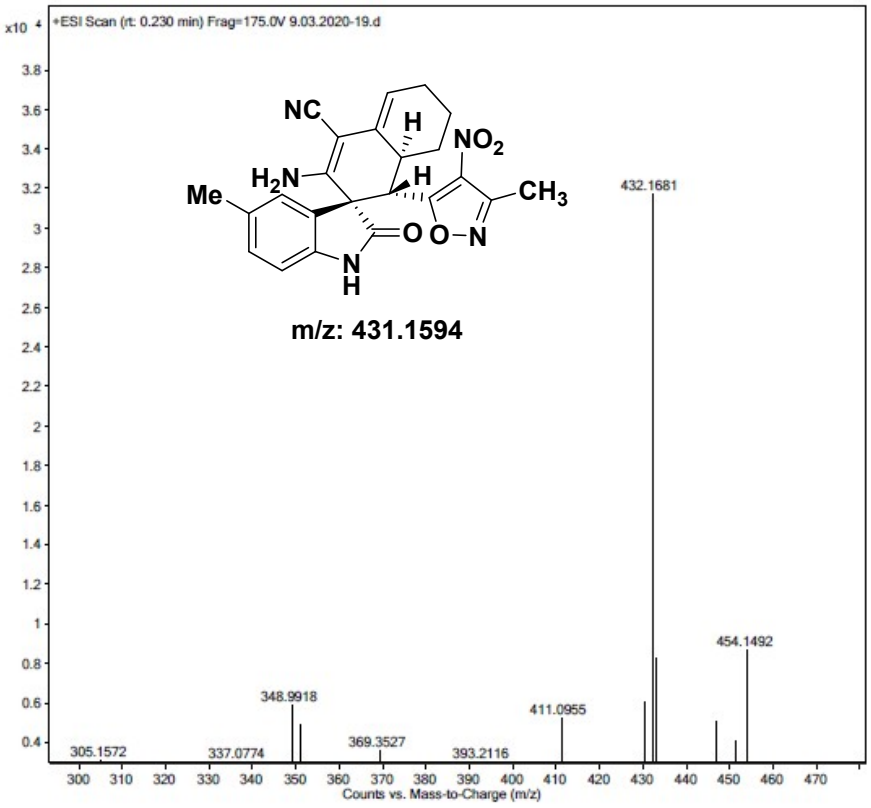
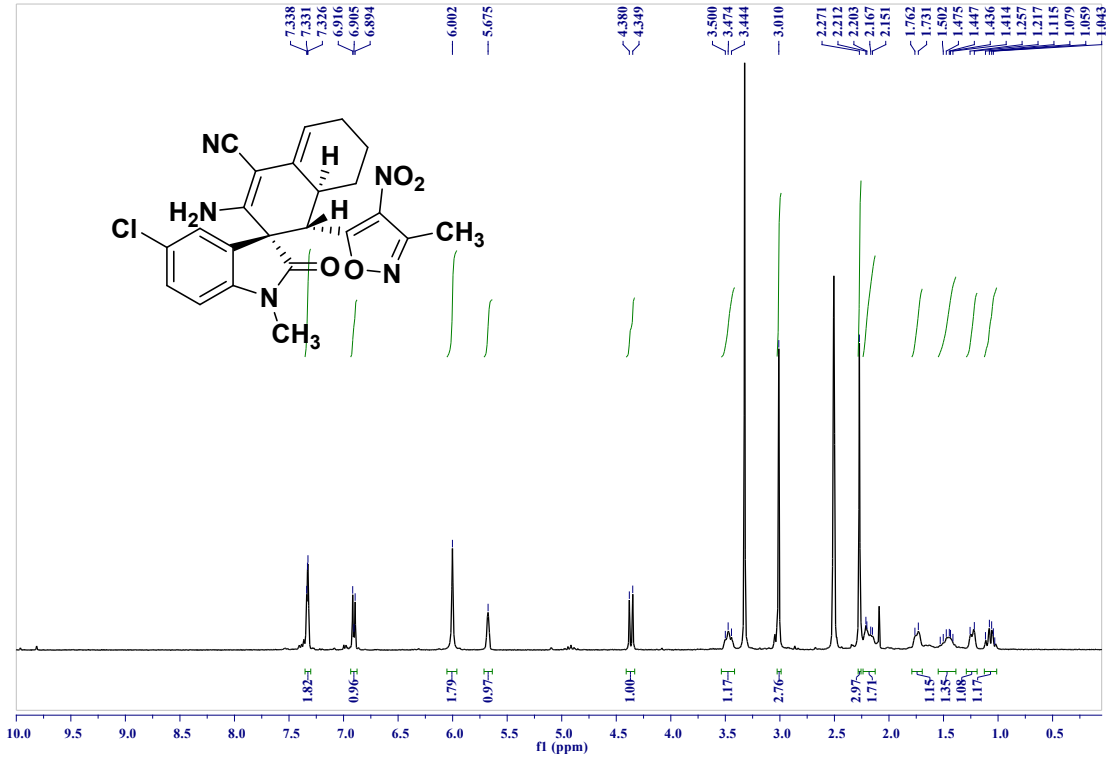
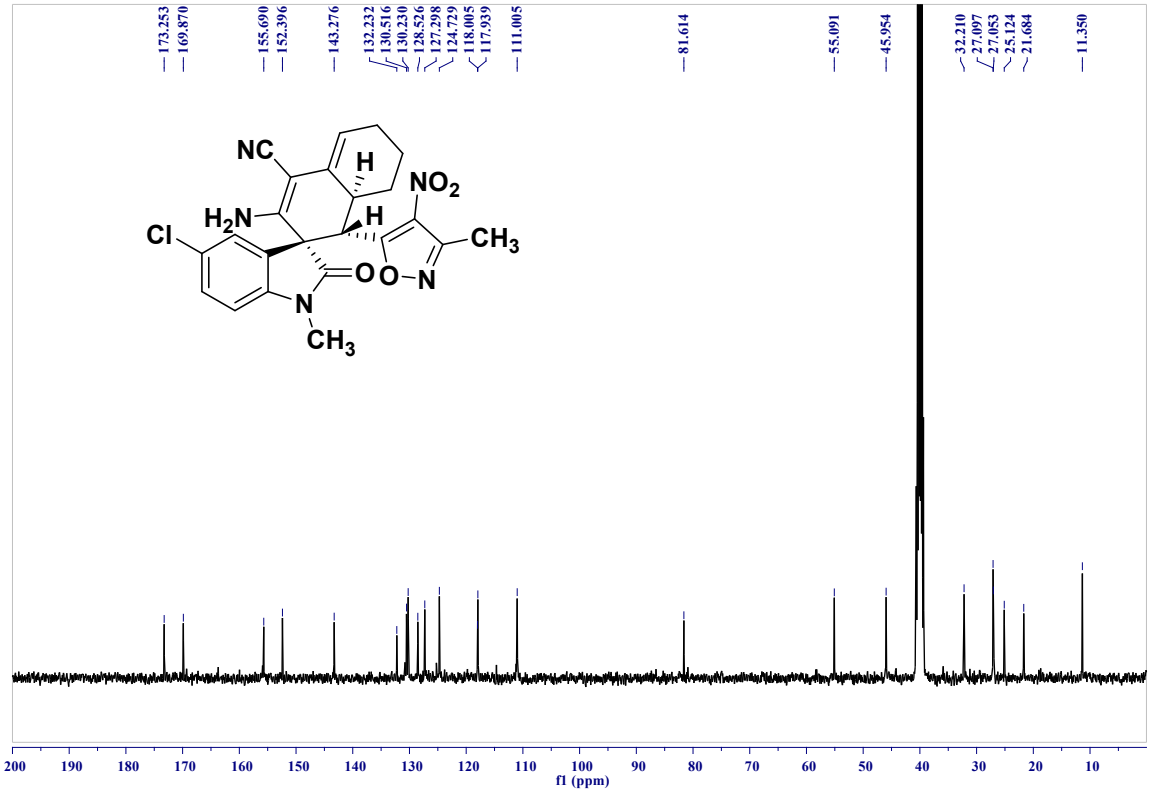
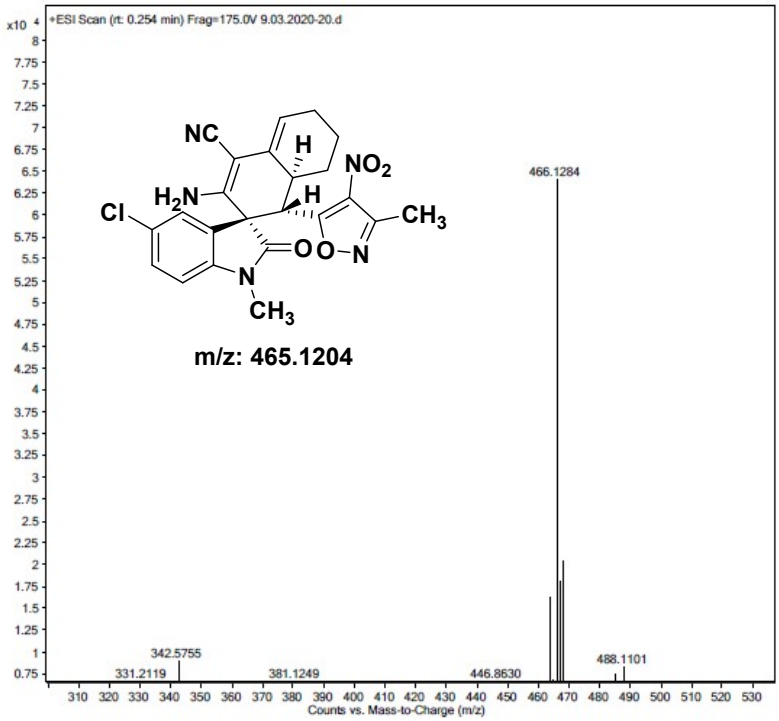
Me
CH3
O
O
N
N
H
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


x10 4
+ESI Scan (rt: 0.230 min) Frag=175.0V 9.03.2020-19.d
NC
H
NO2
H2N
H
Me
CH3
O
O
N
N
H
m/z: 431.1594
432.1681
454.1492
348.9918
411.0955
369.3527
305.1572
337.0774
393.2116
Counts vs. Mass-to-Charge (m/z)

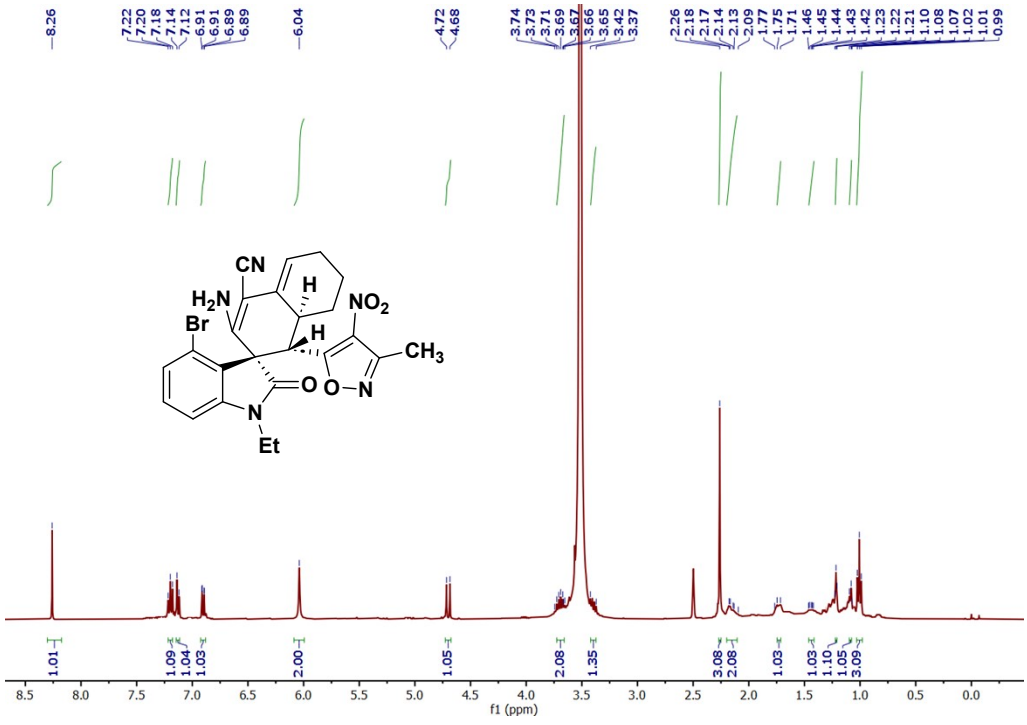
***(1'S,3R,8a'S)-3'-amino-5-chloro-1-methyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3h):***

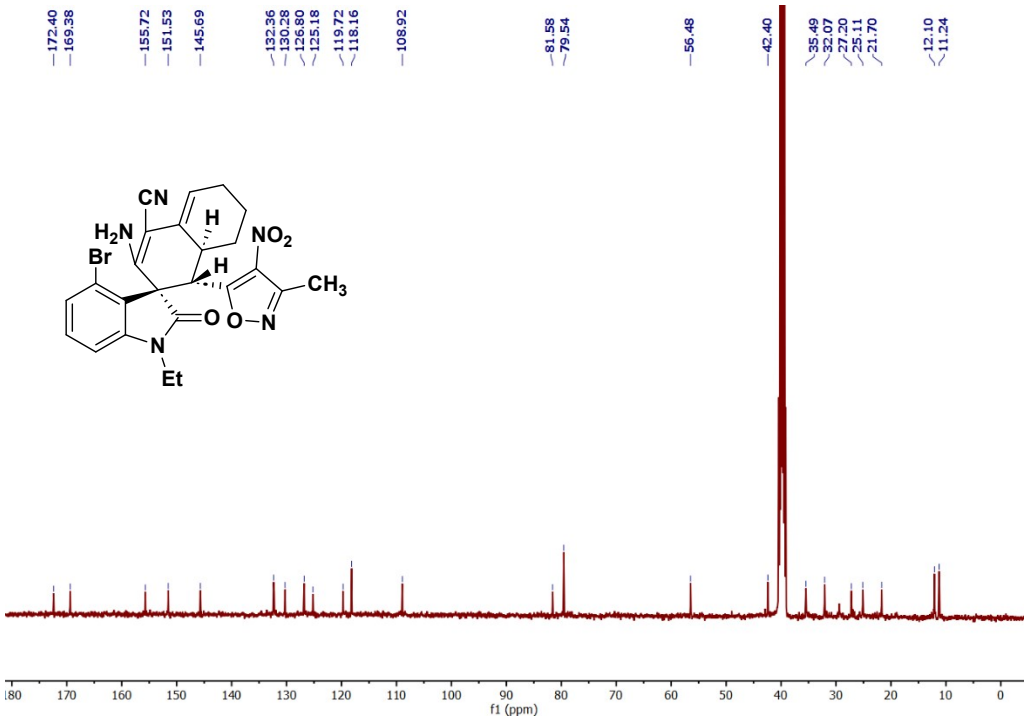


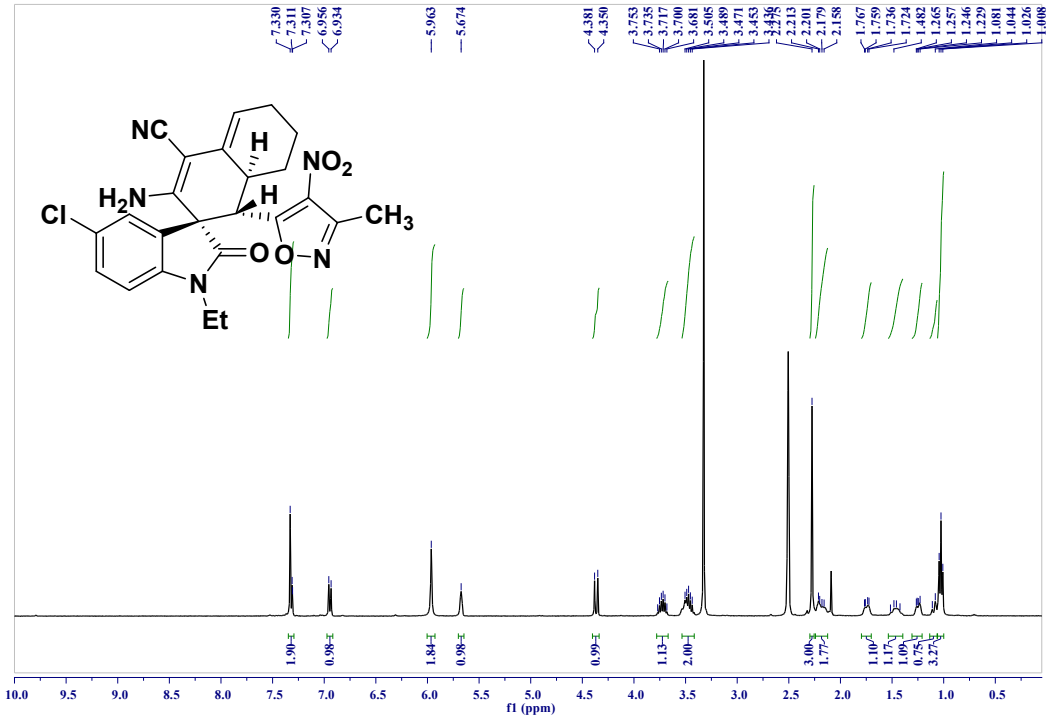


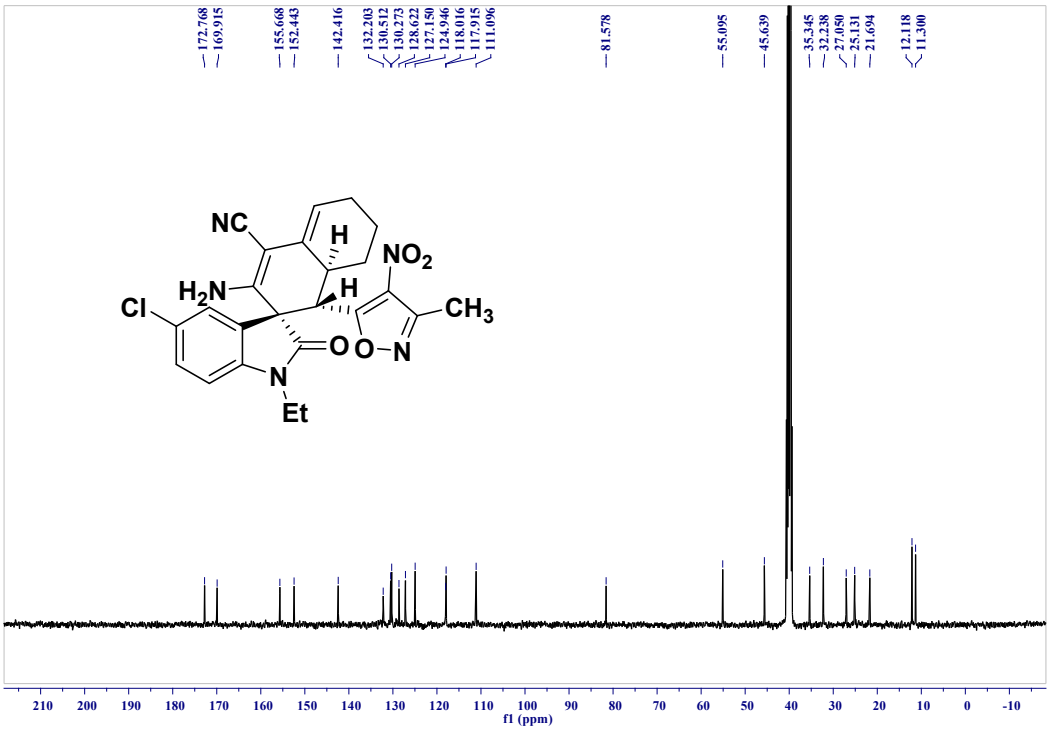

***(1'S,3R,8a'S)-3'-amino-4-bromo-1-ethyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3i):***

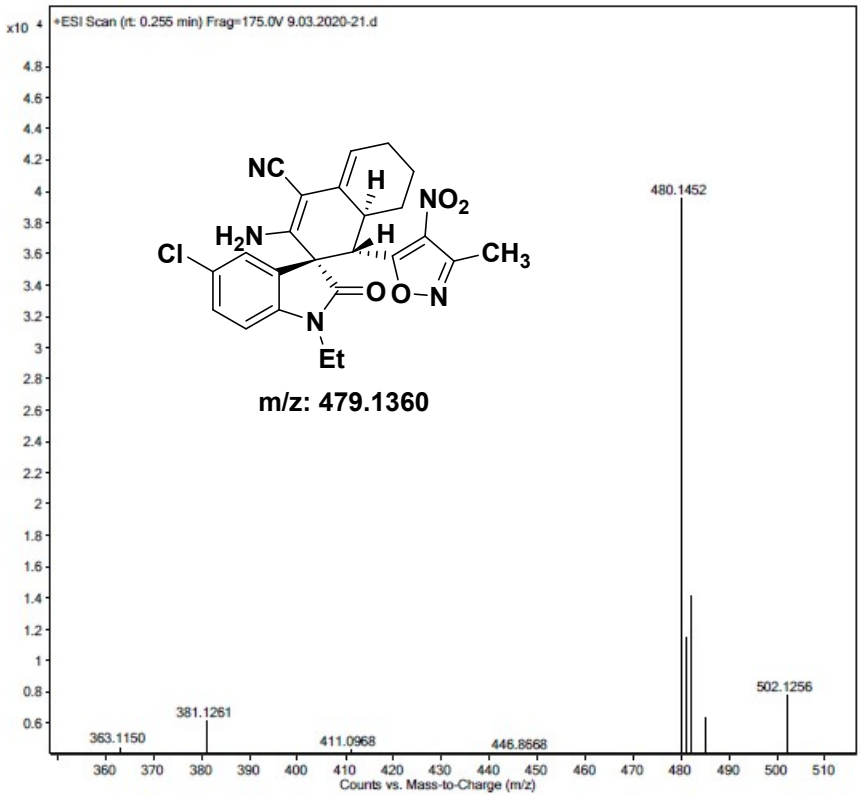




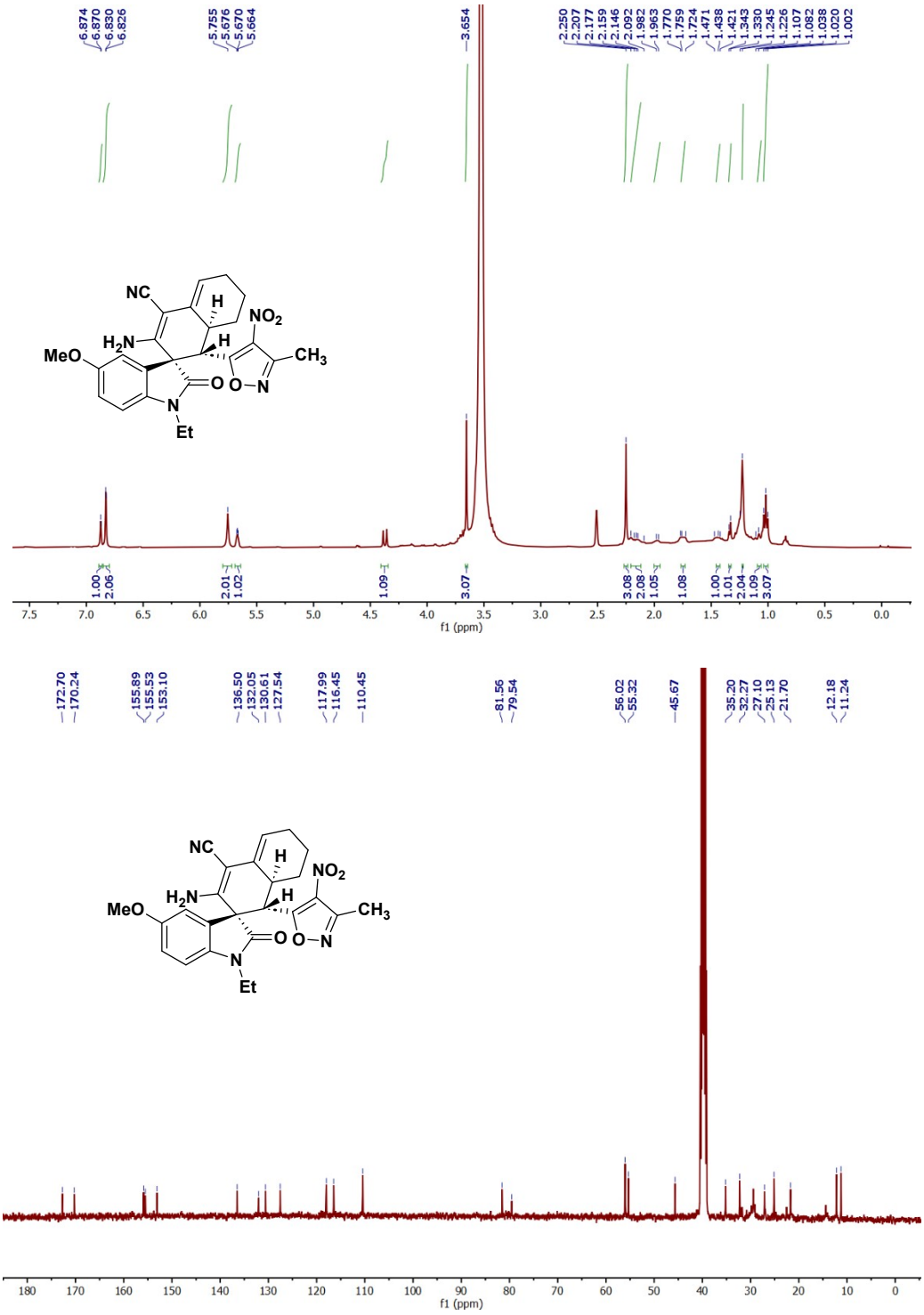

***(1'S,3R,8a'S)-3'-amino-5-chloro-1-ethyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3j):***



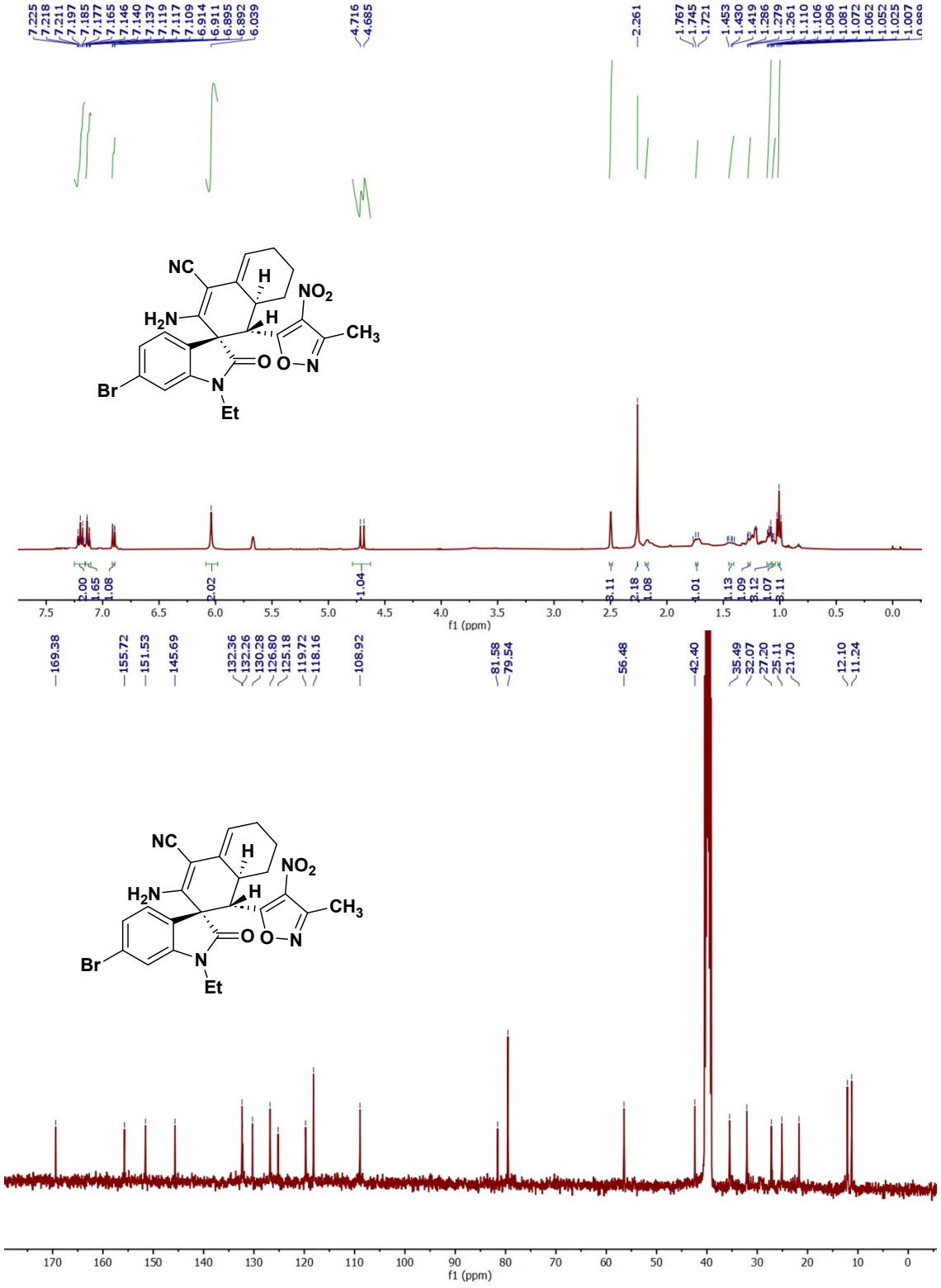

172.768
169.915
155.668
152.443
142.416
132.203
130.512
130.273
128.622
127.150
124.946
118.016
117.915
111.096
81.578
55.095
45.639
35.345
32.238
27.050
25.131
21.694
12.118
11.300
NC
H
NO2
H2N
H
Cl
CH3
O
O
N
N
Et
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


x10 4
*ESI Scan (rt: 0.255 min) Frag=175.0V 9.03.2020-21.d
NC
H
NO2
H2N
H
Cl
CH3
O
O
N
N
Et
m/z: 479.1360
480.1452
502.1256
381.1261
363.1150
411.0968
446.8868
Counts vs. Mass-to-Charge (m/z)

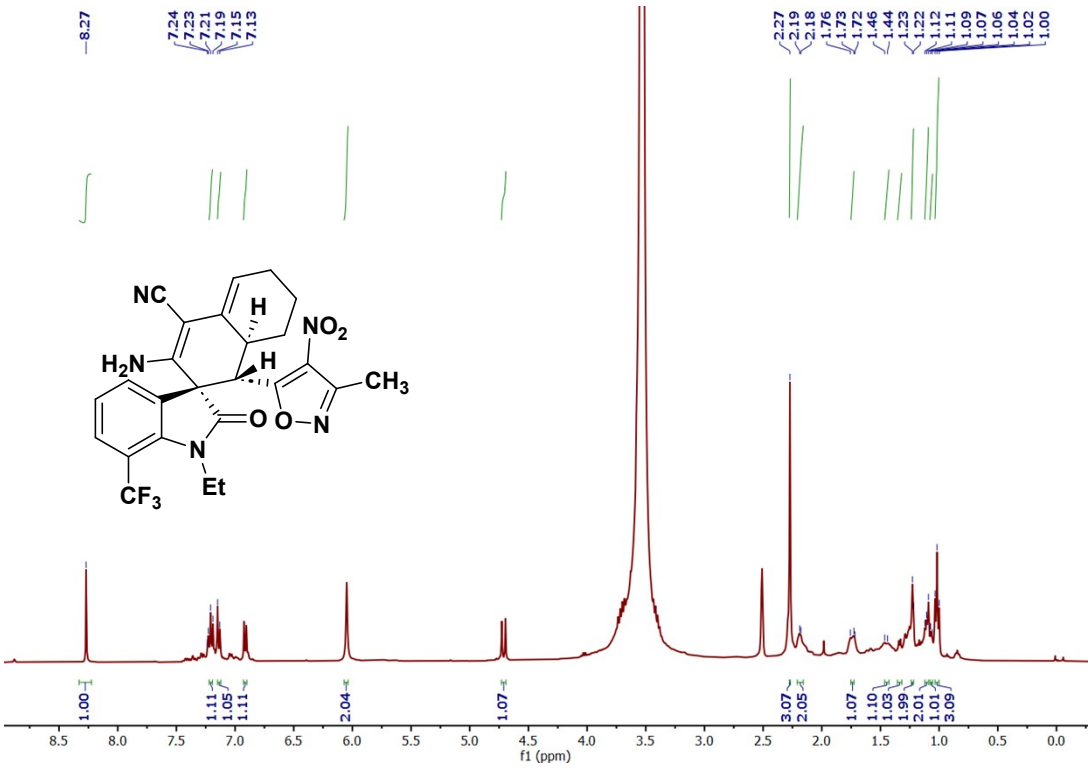
***(1'S,3R,8a'S)-3'-amino-1-ethyl-5-methoxy-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3k):***

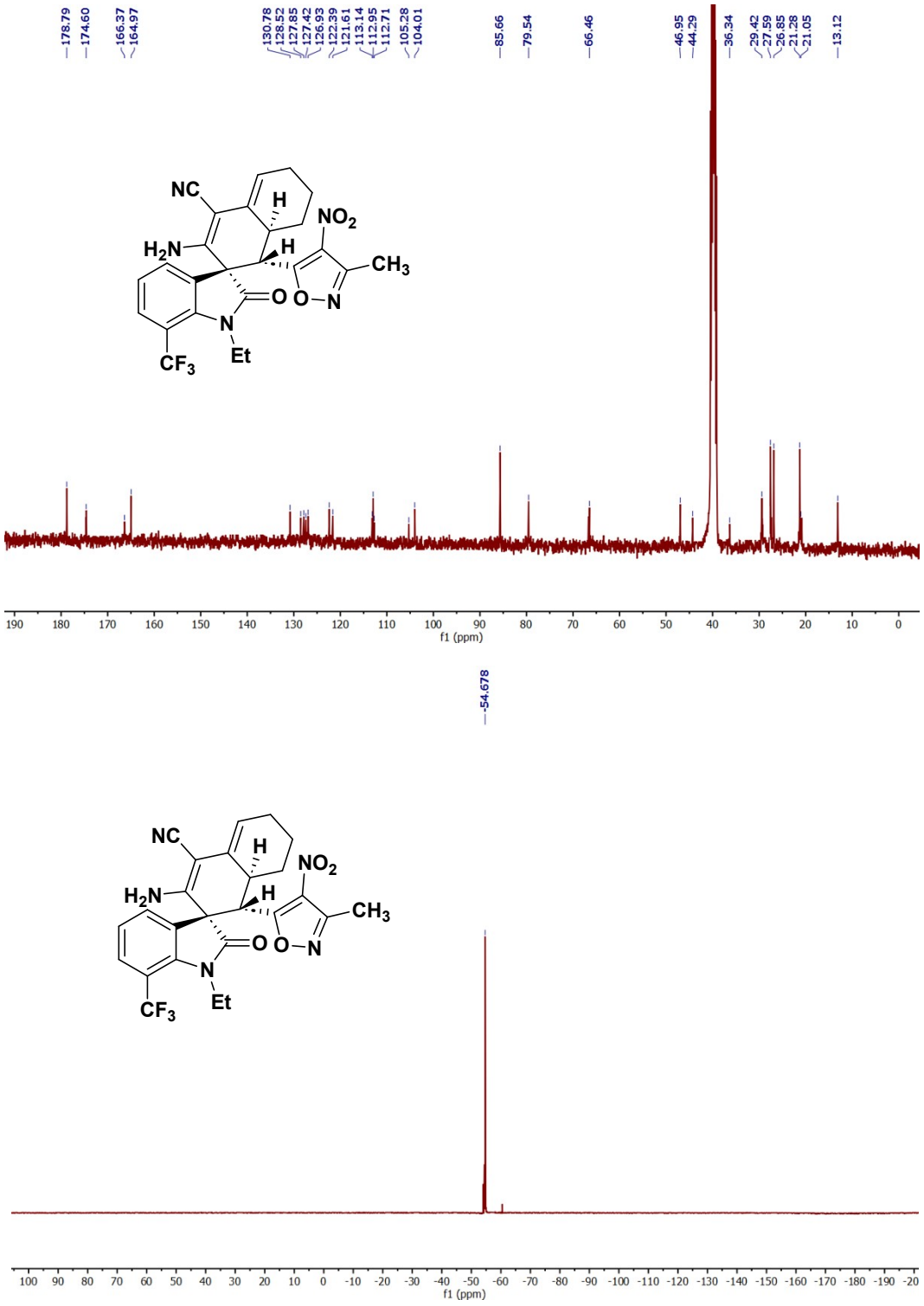


***(1'S,3R,8a'S)-3'-amino-6-bromo-1-ethyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3l):***

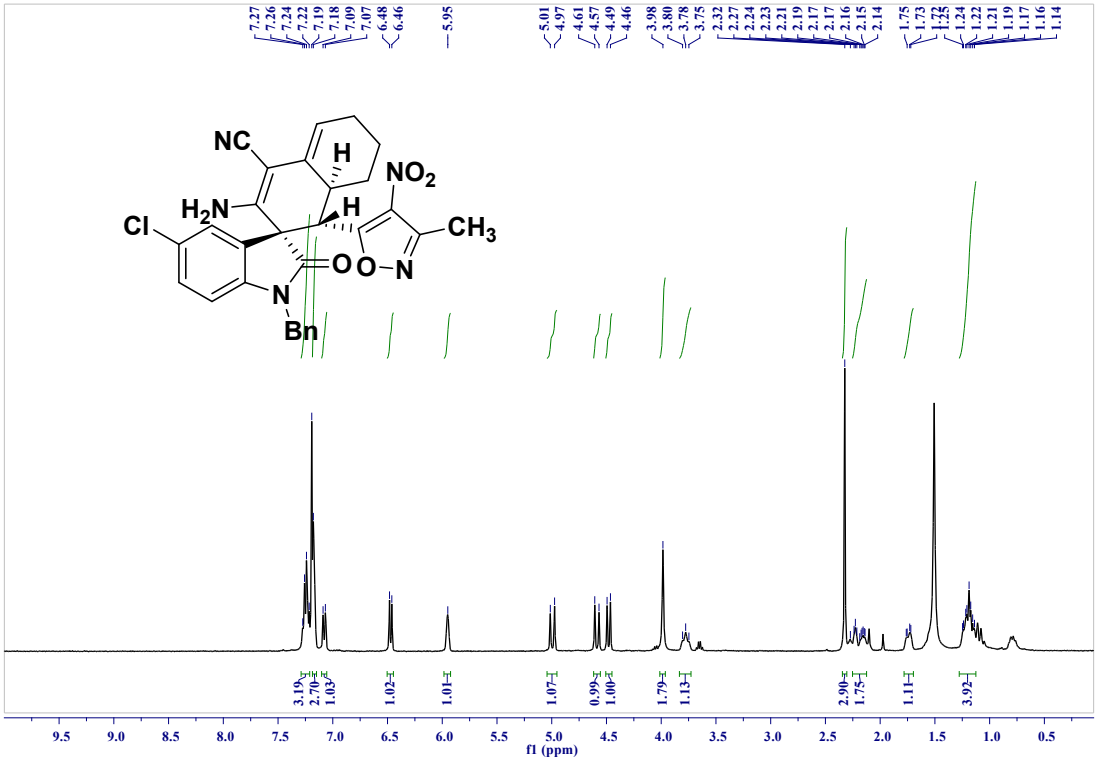


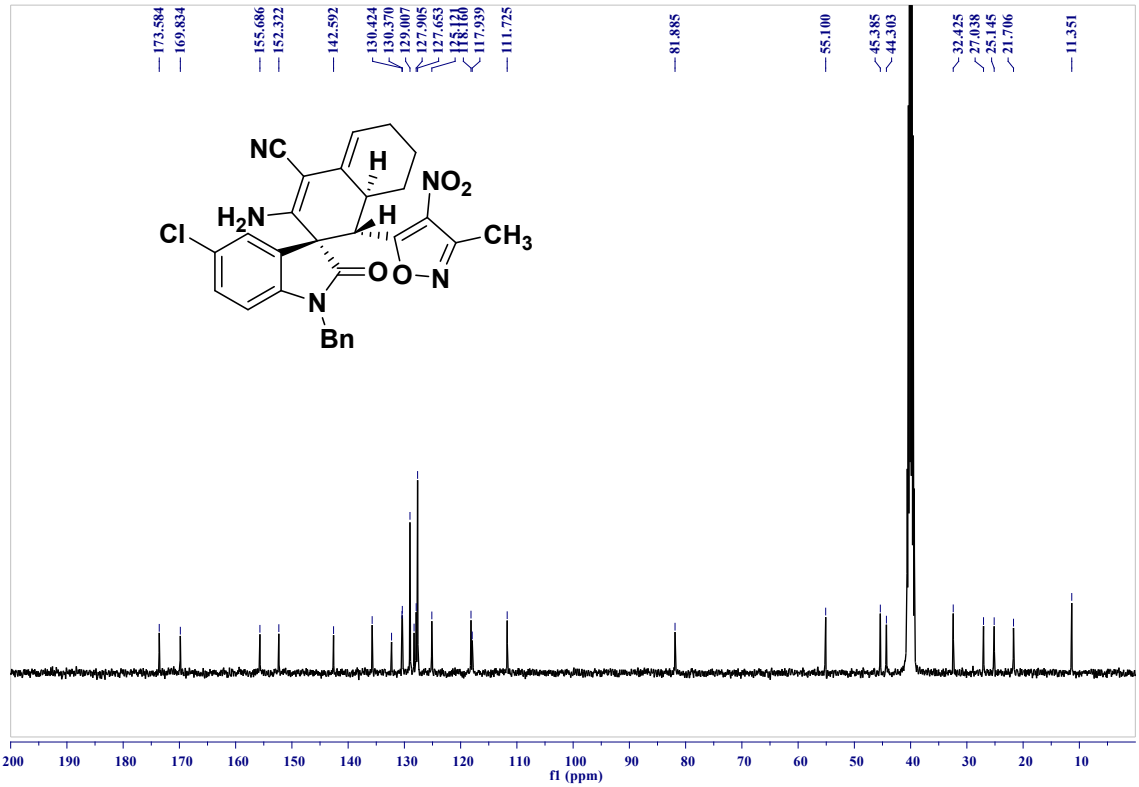
***(1'S,3R,8a'S)-3'-amino-1-ethyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-7-(trifluoromethyl)-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3m):***

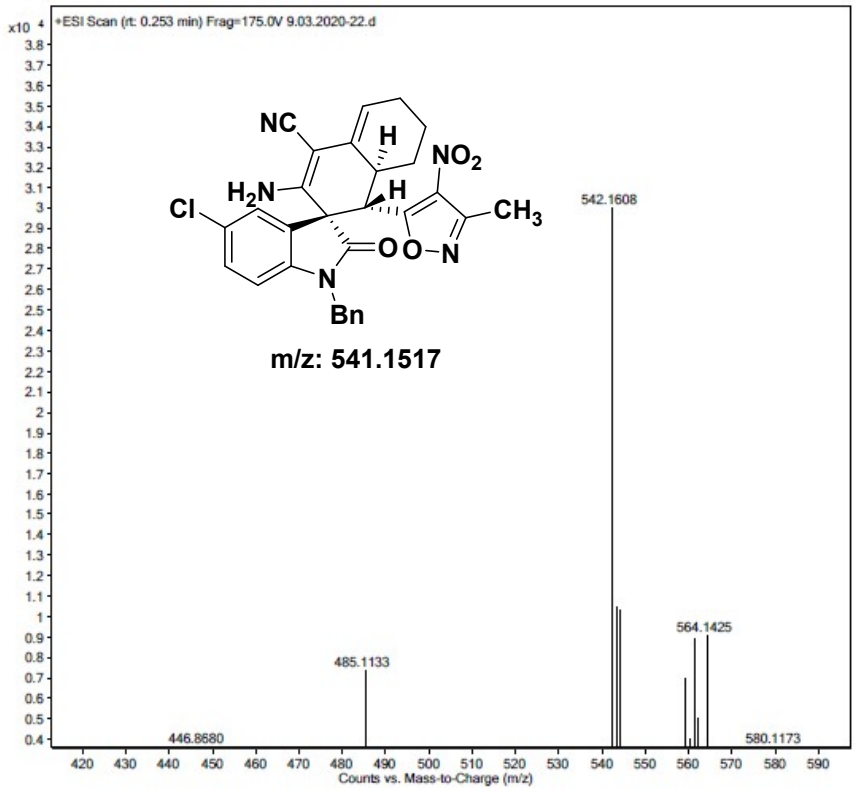




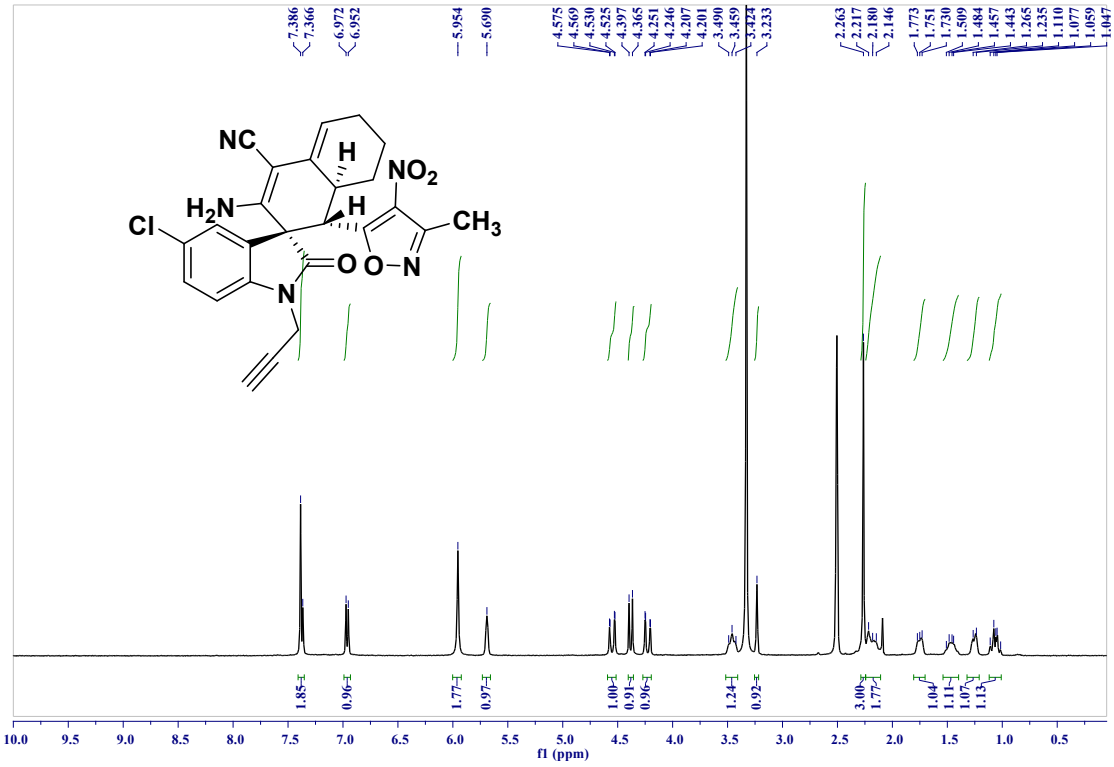

***(1'S,3R,8a'S)-3'-amino-1-benzyl-5-chloro-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3n):***

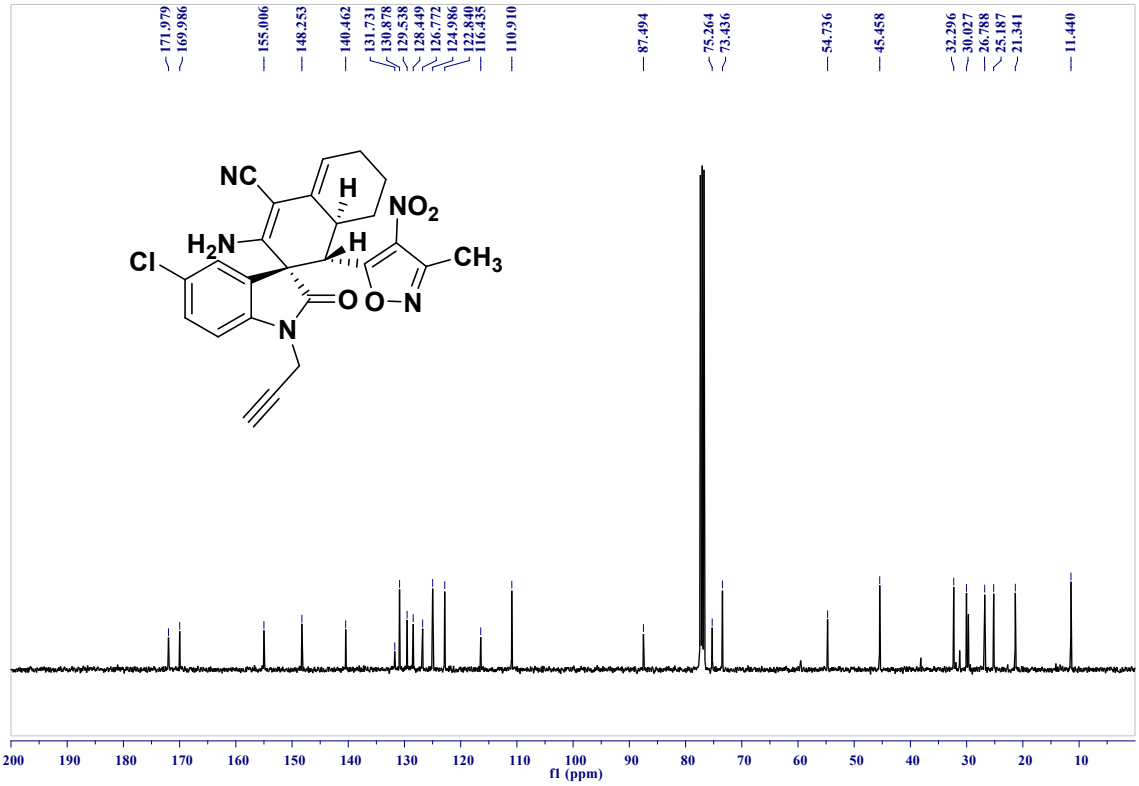

NC
H
NO2
H2N
H
Cl
CH3
O
O
N
N
Bn
f1 (ppm)

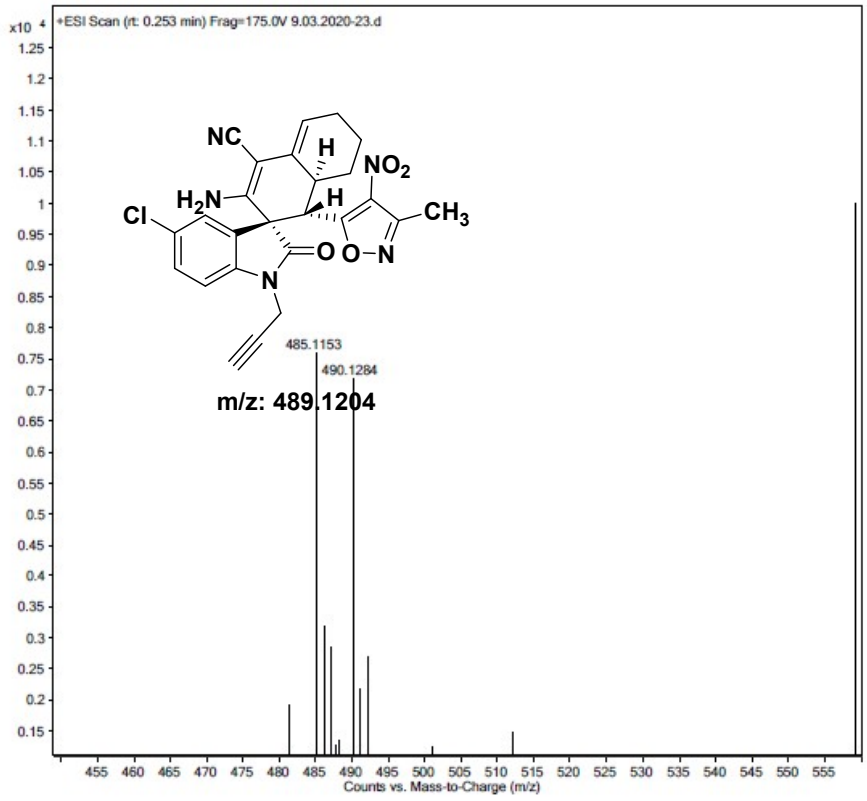

NC
H
NO2
H2N
H
Cl
CH3
O
O
N
N
Bn
f1 (ppm)



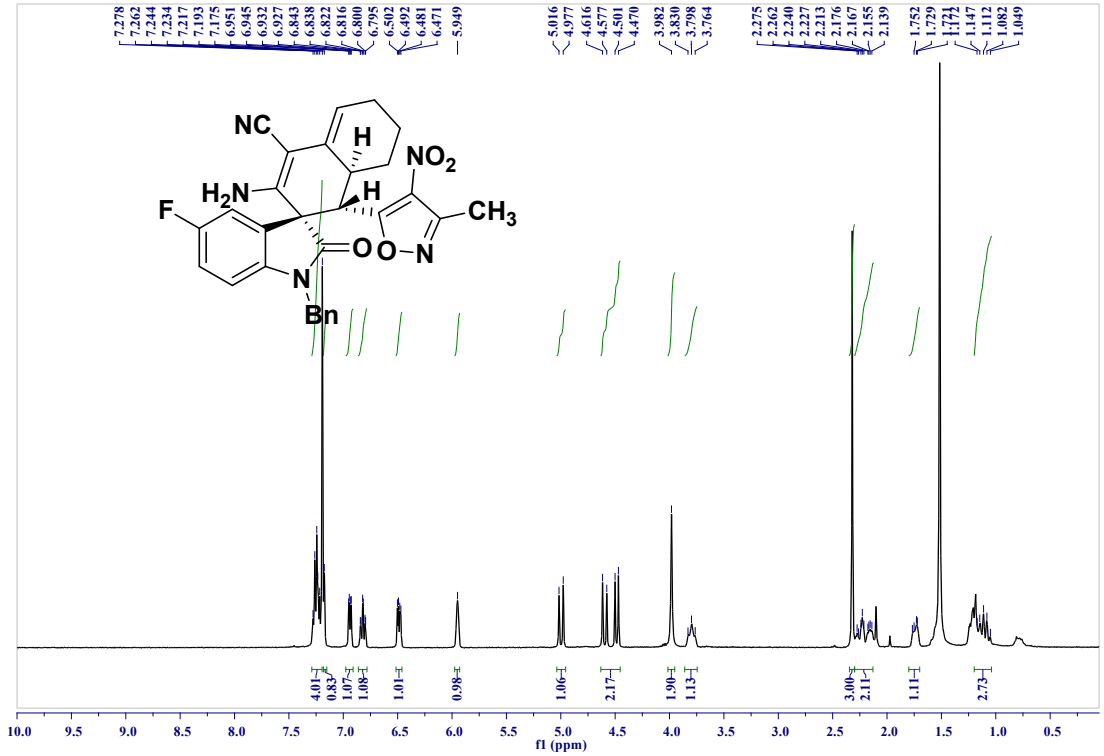

***(1'S,3R,8a'S)-3'-amino-5-chloro-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-1-(prop-2-yn-1-yl)-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3o):***

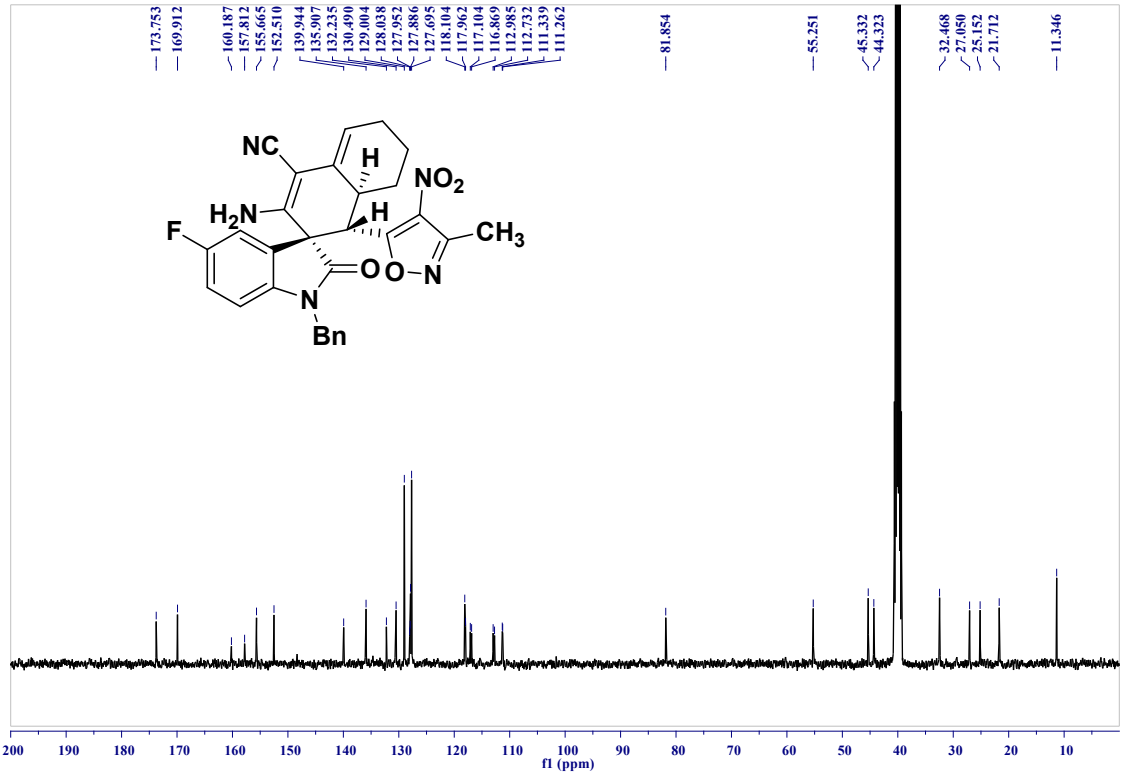


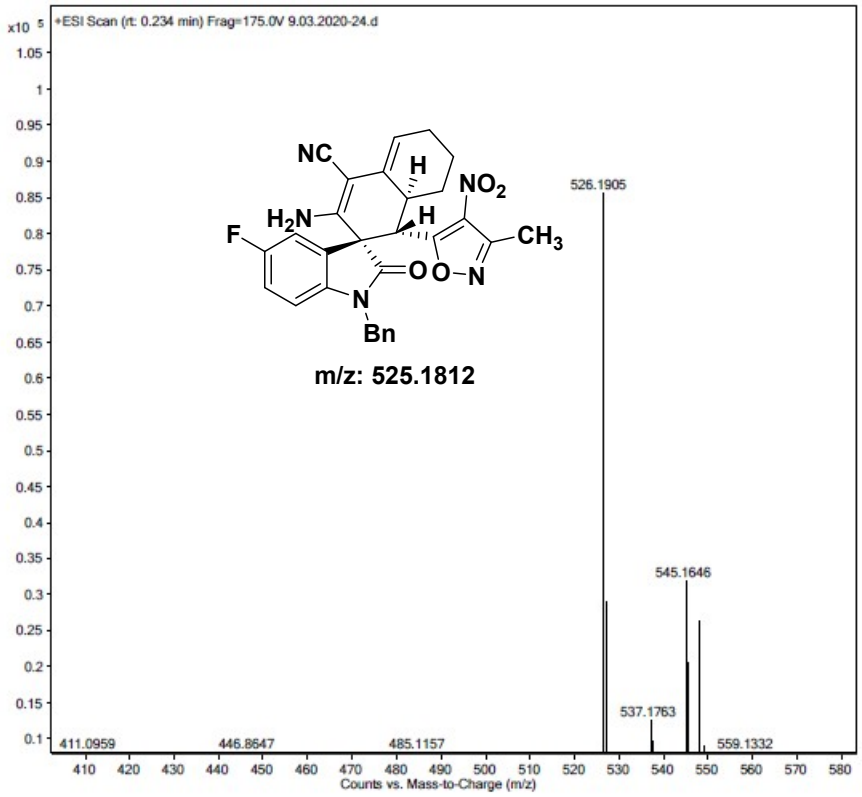

171.979
169.986
155.006
148.253
140.462
131.731
130.878
129.538
128.449
126.772
124.986
122.840
116.435
110.910
87.494
75.264
73.436
54.736
45.458
32.296
30.027
26.788
25.187
21.341
11.440
NC
H
NO2
H2N
H
Cl
CH3
O
O
N
N
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


x10 4
+ESI Scan (rt: 0.253 min) Frag=175.0V 9.03.2020-23.d
1.25
1.2
1.15
1.1
1.05
1
0.95
0.9
0.85
0.8
0.75
0.7
0.65
0.6
0.55
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
NC
H
NO2
H2N
H
Cl
CH3
O
O
N
N
485.1153
490.1284
m/z: 489.1204
455 460 465 470 475 480 485 490 495 500 505 510 515 520 525 530 535 540 545 550 555
Counts vs. Mass-to-Charge (m/z)

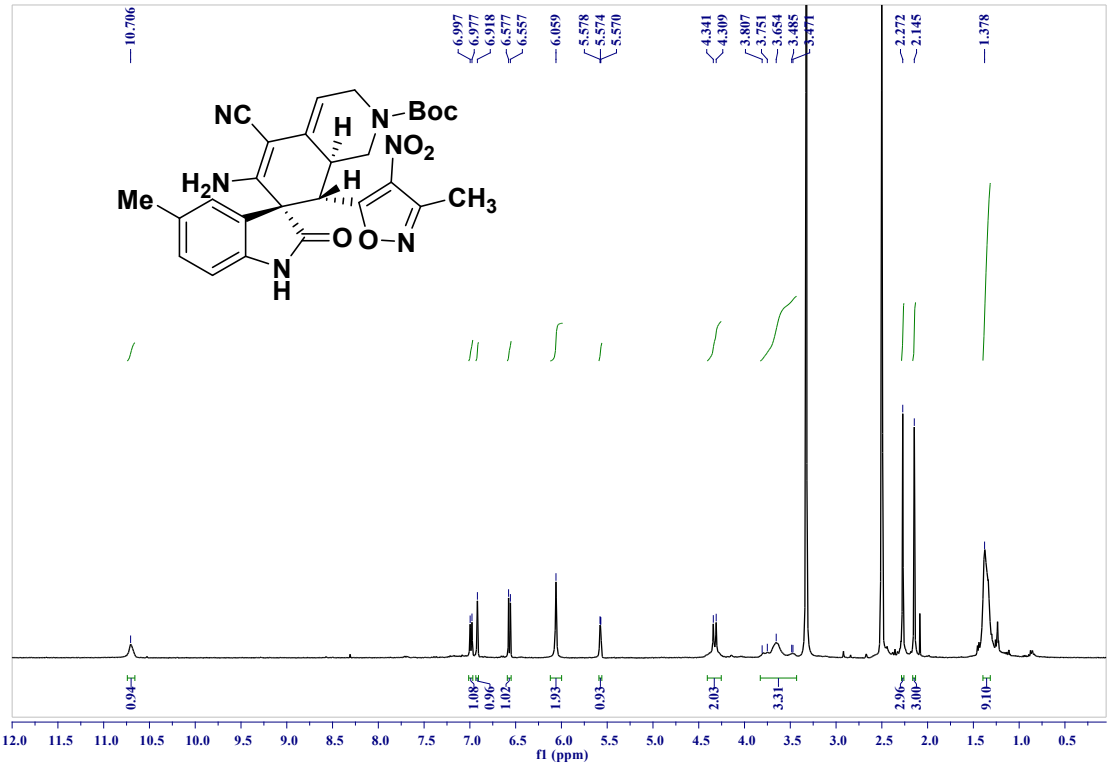
***(1'S,3R,8a'S)-3'-amino-1-benzyl-5-fluoro-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3p):***

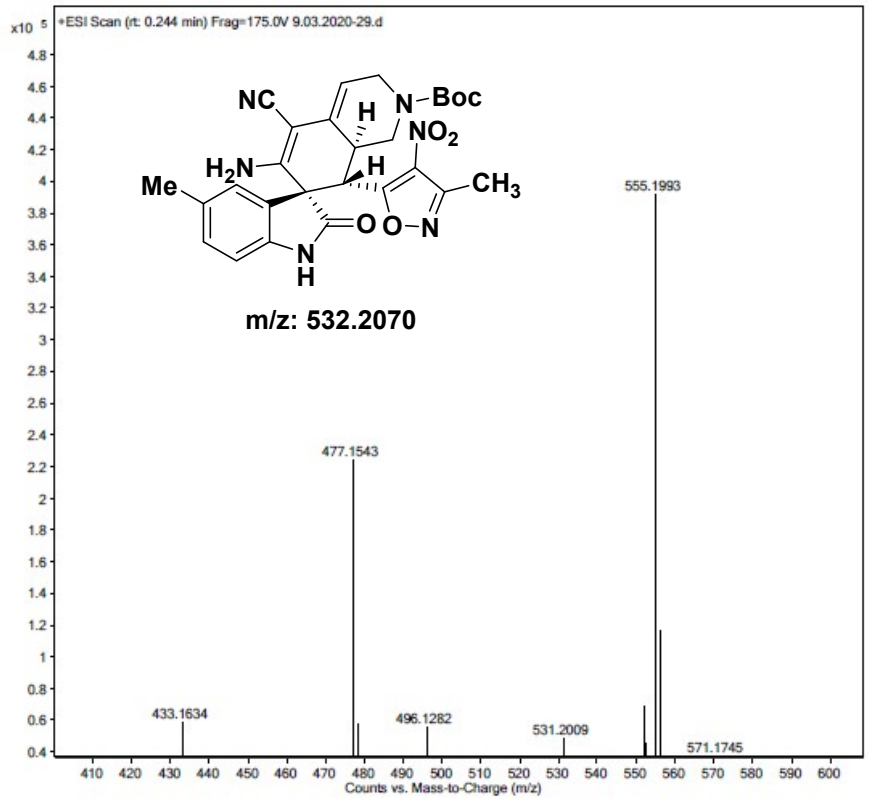


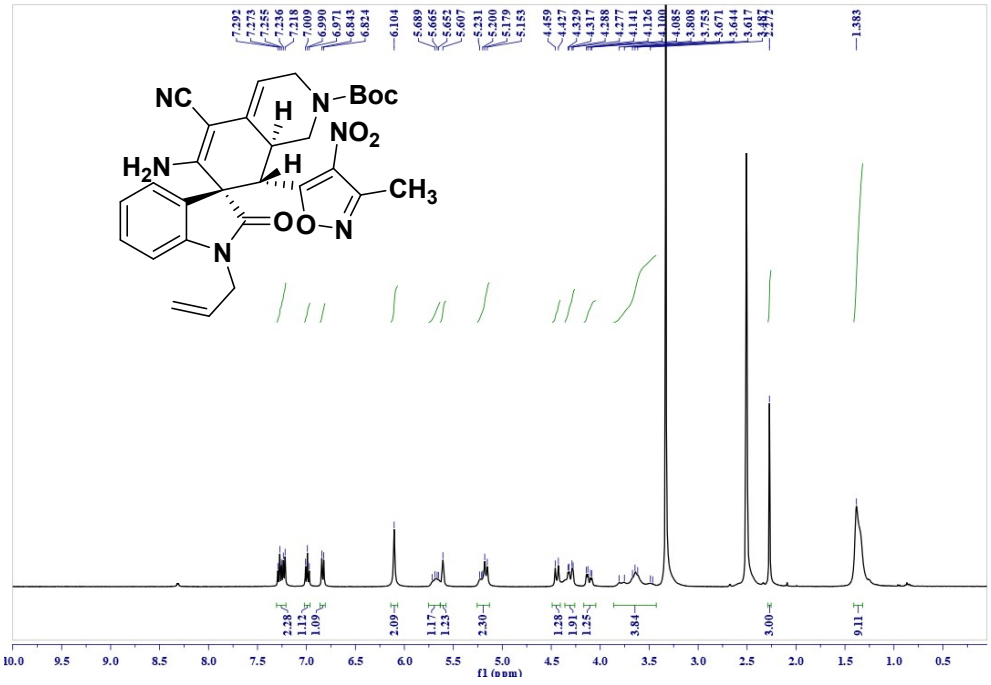


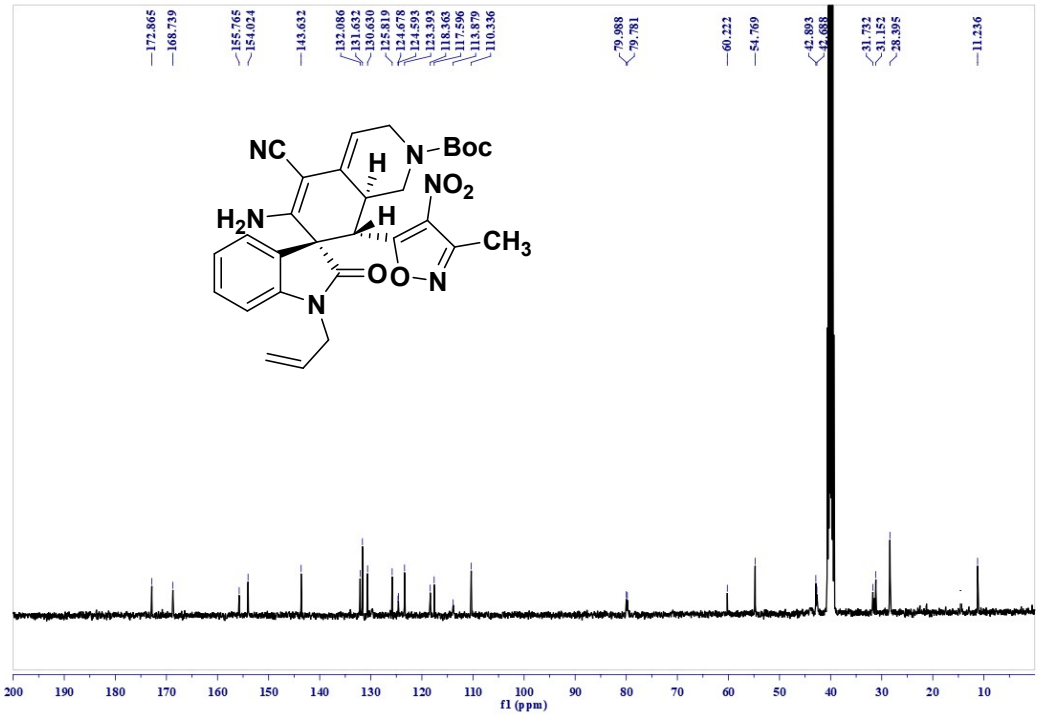

***tert-butyl (3R,8'S,8a'S)-6'-amino-5'-cyano-5-methyl-8'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-8',8a'-dihydro-1'H-spiro[indoline-3,7'-isoquinoline]-2'(3'H)-carboxylate (3q):***

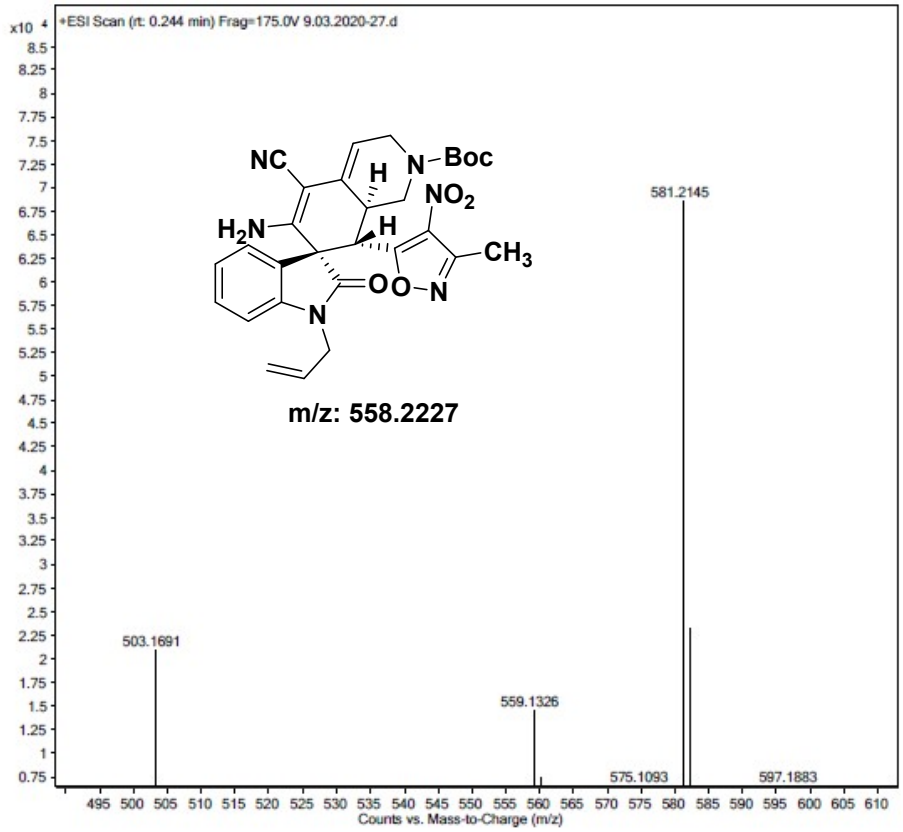




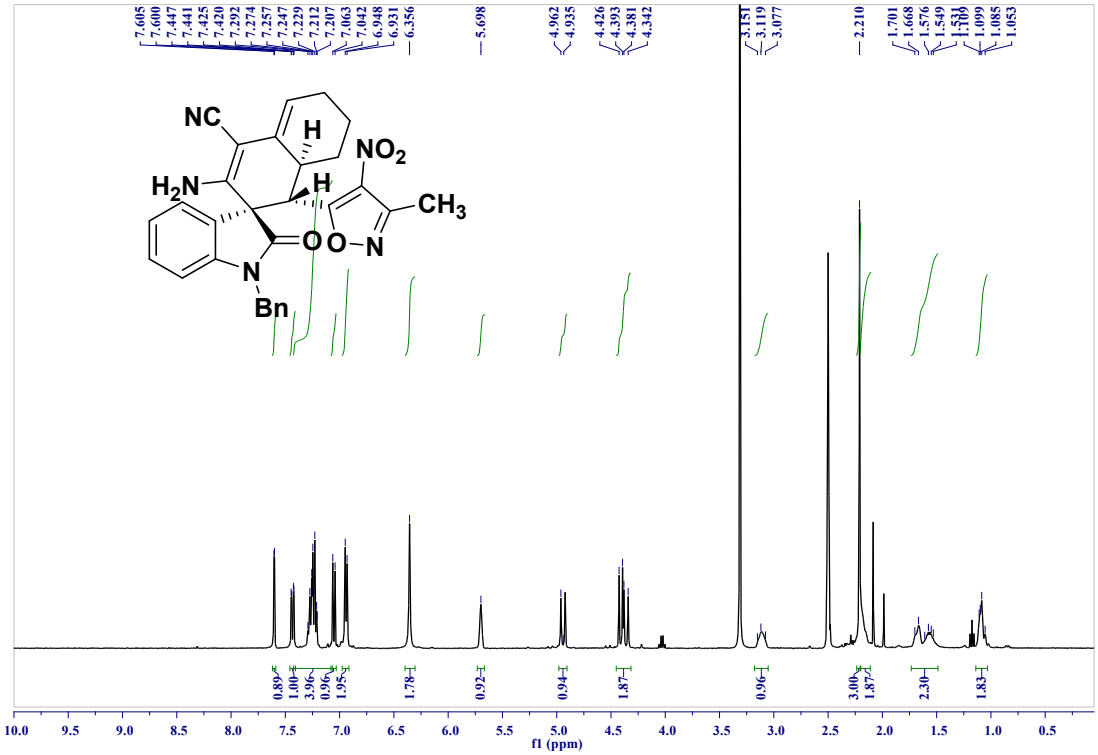

***tert-butyl (3R,8'S,8a'S)-1-allyl-6'-amino-5'-cyano-8'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-8',8a'-dihydro-1'H-spiro[indoline-3,7'-isoquinoline]-2'(3'H)-carboxylate (3r):***

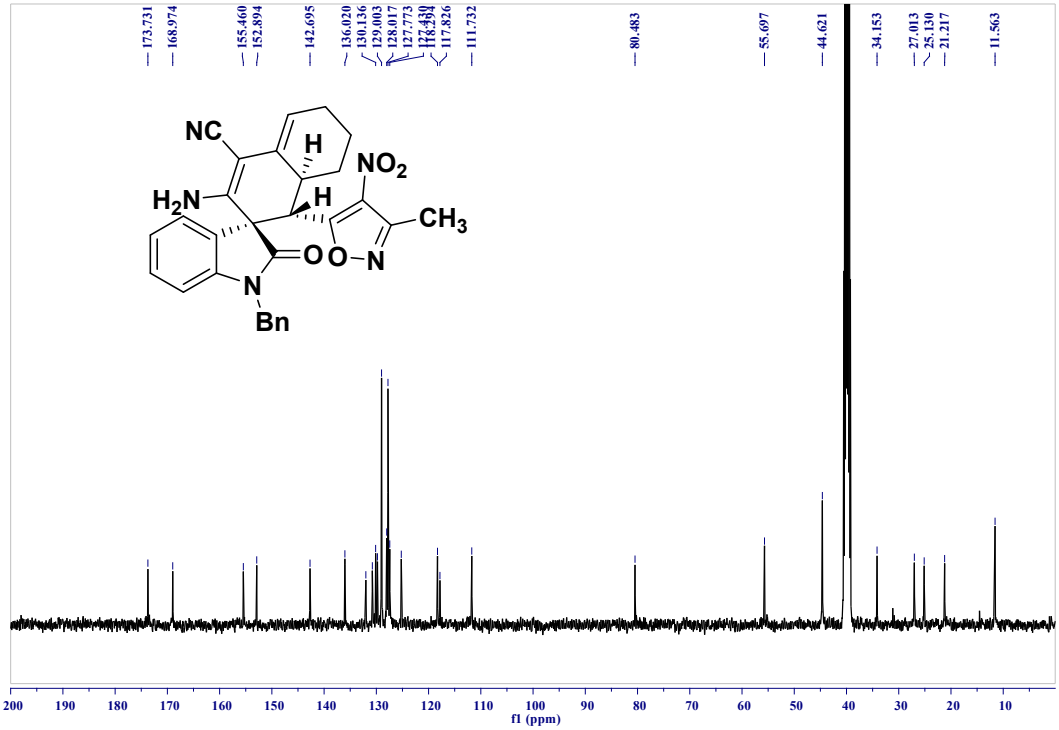


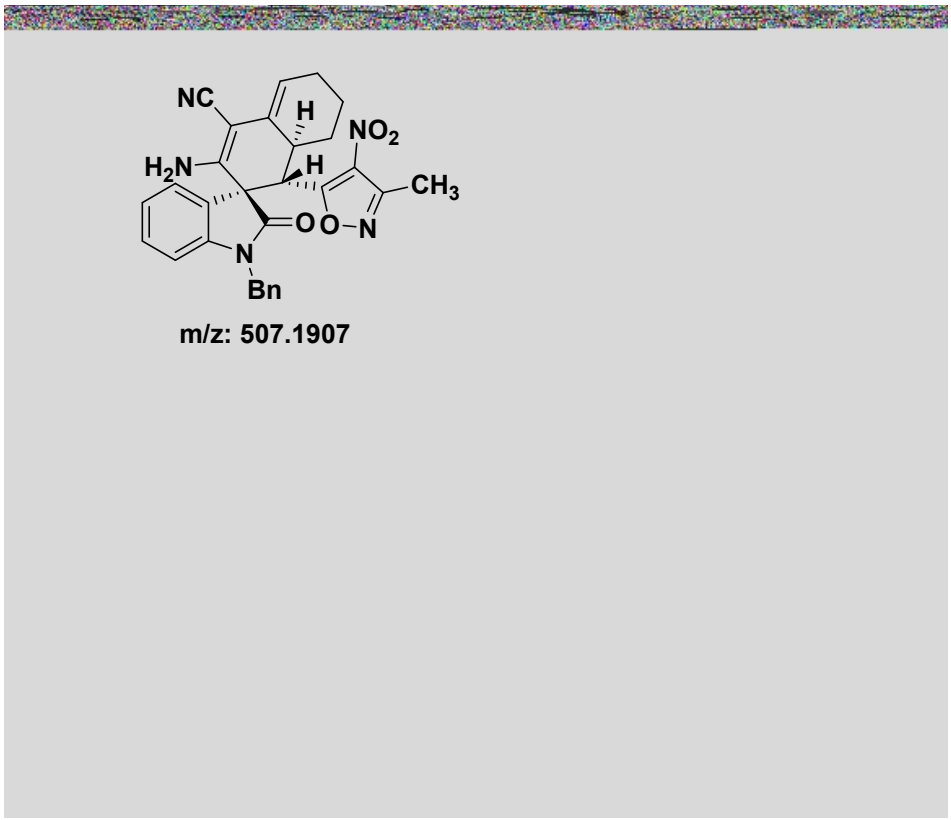

172.865
168.739
155.765
154.024
143.632
132.086
131.632
130.630
125.819
124.678
124.593
123.393
118.363
117.596
113.879
110.336
79.988
79.781
60.222
54.769
42.893
42.688
31.732
31.152
28.395
11.236
NC
H
N–Boc
NO2
H2N
H
CH3
O
O
N
N
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


x10 4
+ESI Scan (rt: 0.244 min) Frag=175.0V 9.03.2020-27.d
NC
H
N–Boc
NO2
H2N
H
CH3
O
O
N
N
m/z: 558.2227
581.2145
503.1691
559.1326
575.1093
597.1883
Counts vs. Mass-to-Charge (m/z)

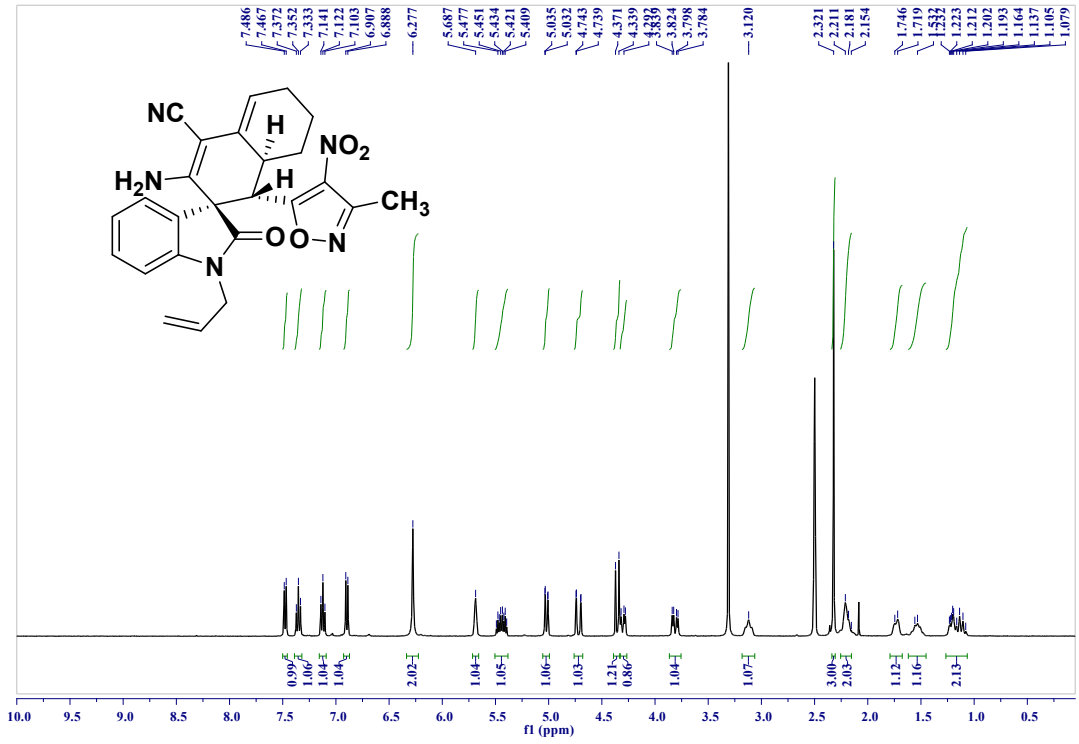
***(1'S,3S,8a'S)-3'-amino-1-benzyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3a)***

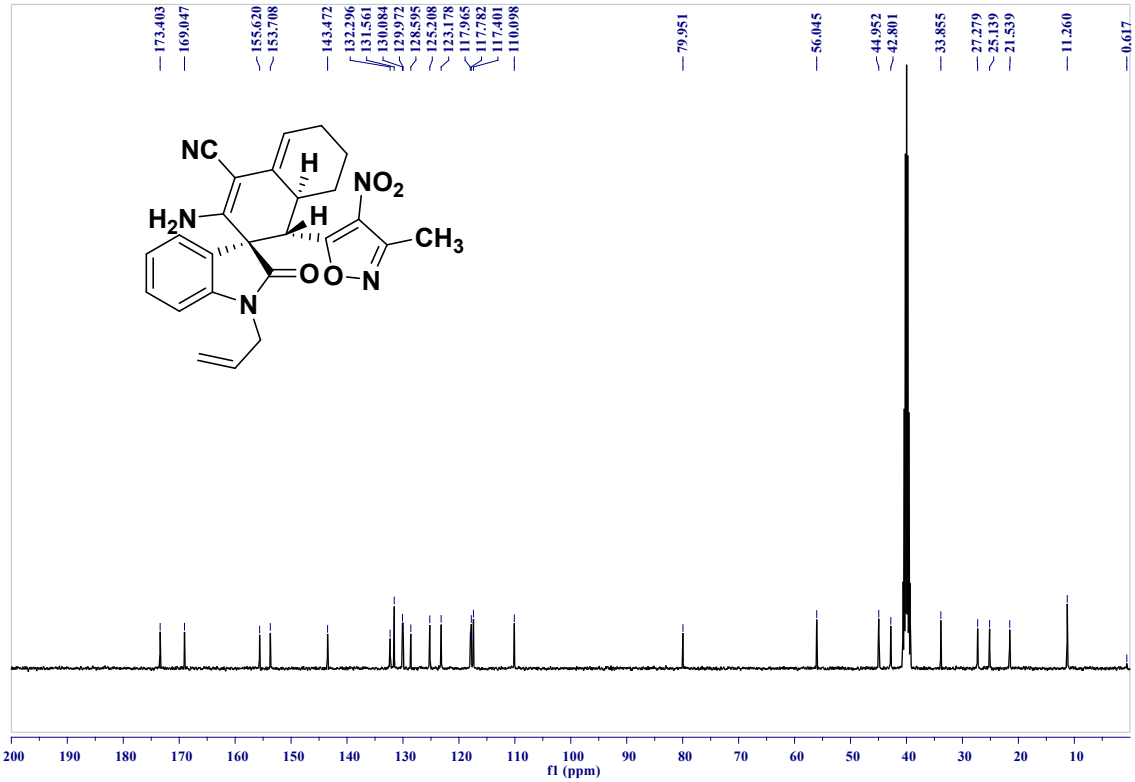


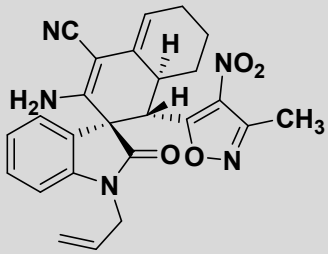






***(1'S,3S,8a'S)-1-allyl-3'-amino-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3b):***

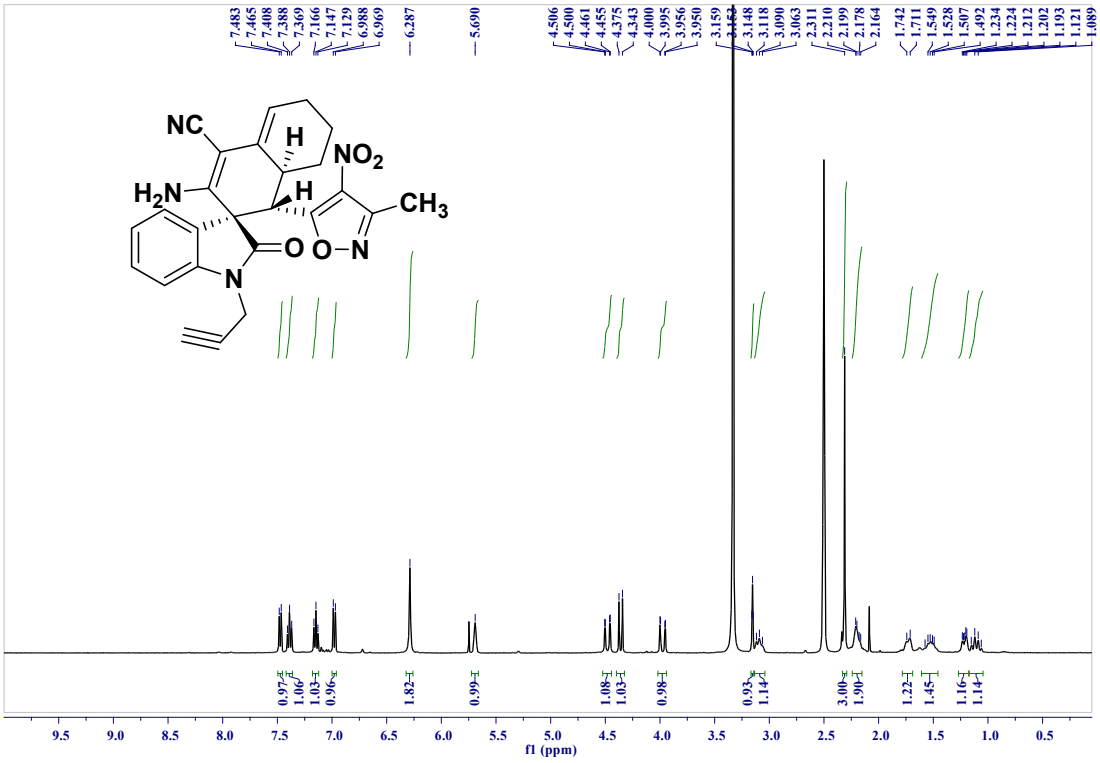


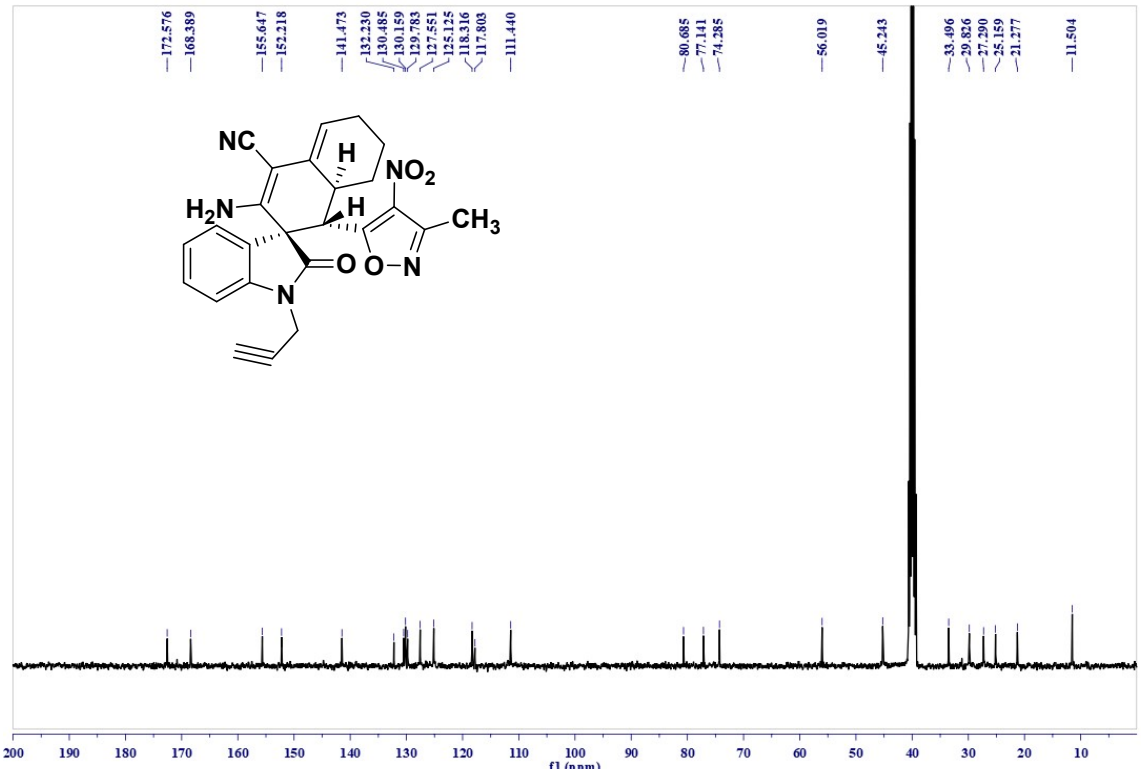

173.403
169.047
155.620
153.708
143.472
132.296
131.561
130.084
129.972
128.595
125.208
123.178
117.965
117.782
117.401
110.098
79.951
56.045
44.952
42.801
33.855
27.279
25.139
21.539
11.260
0.617
NC
H
NO2
H2N
H
CH3
O
O
N
N
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

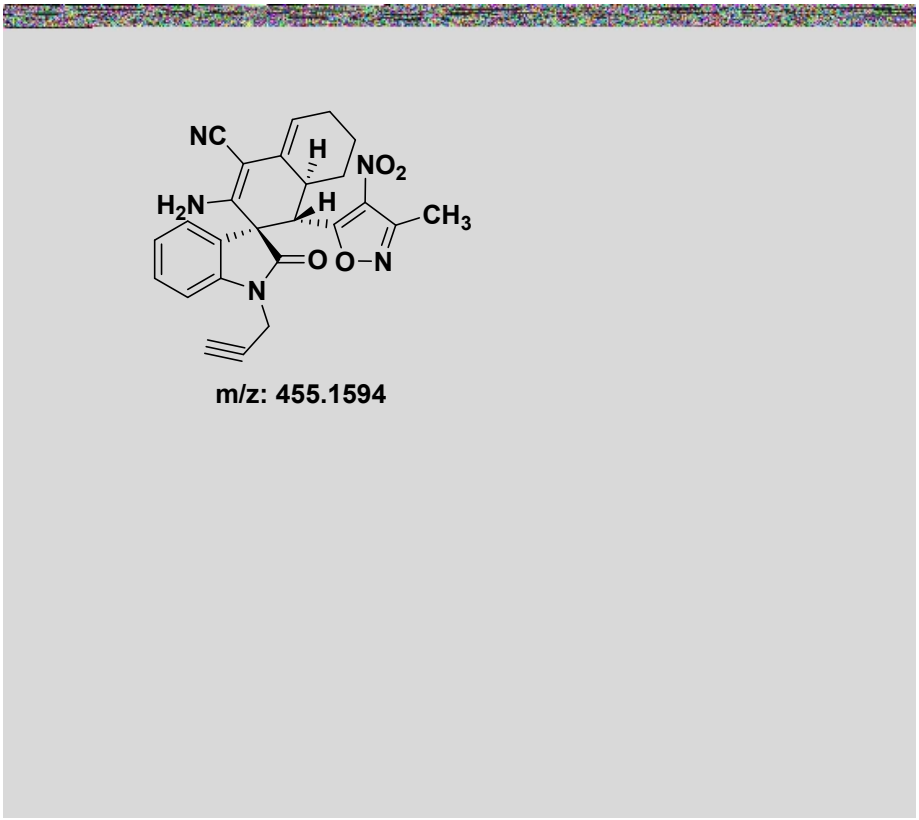

NC
H
NO2
H2N
H
CH3
O
O
N
N

**m/z: 457.1750**

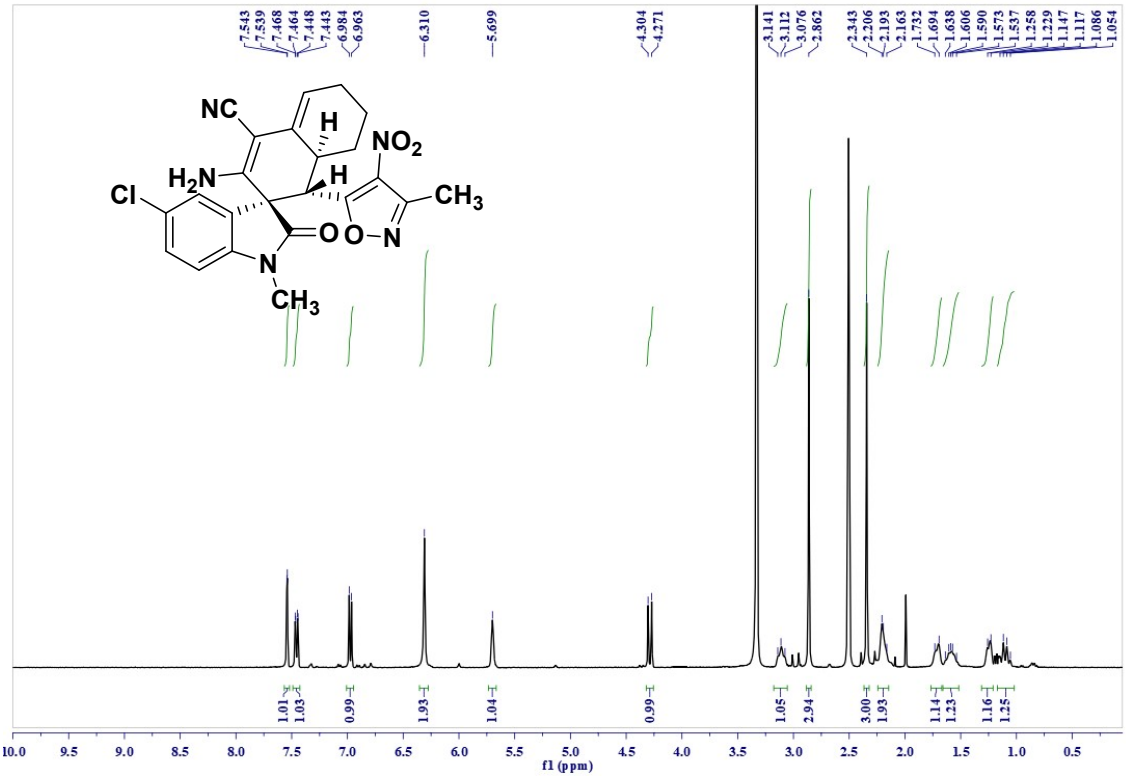
***(1'S,3S,8a'S)-3'-amino-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-1-(prop-2-yn-1-yl)-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3c):***

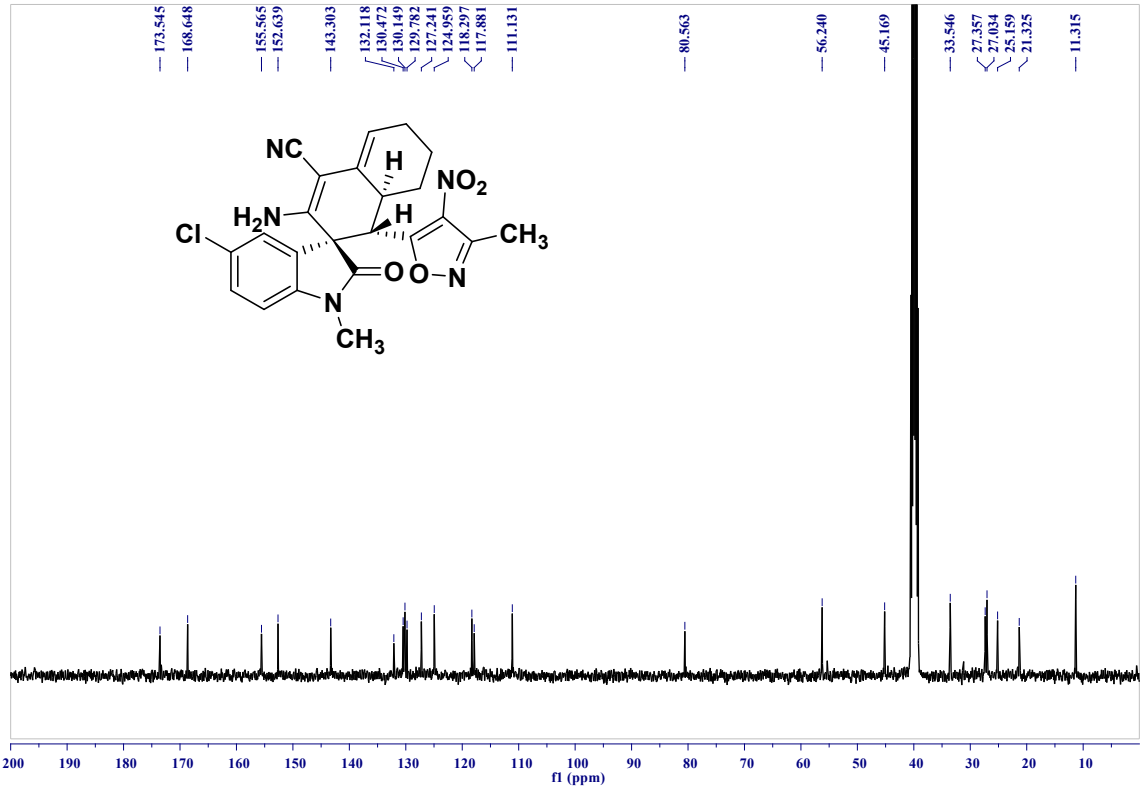


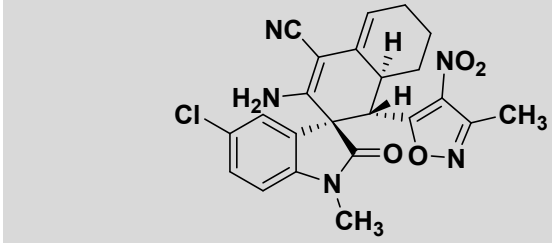






***(1'S,3S,8a'S)-3'-amino-5-chloro-1-methyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3d):***

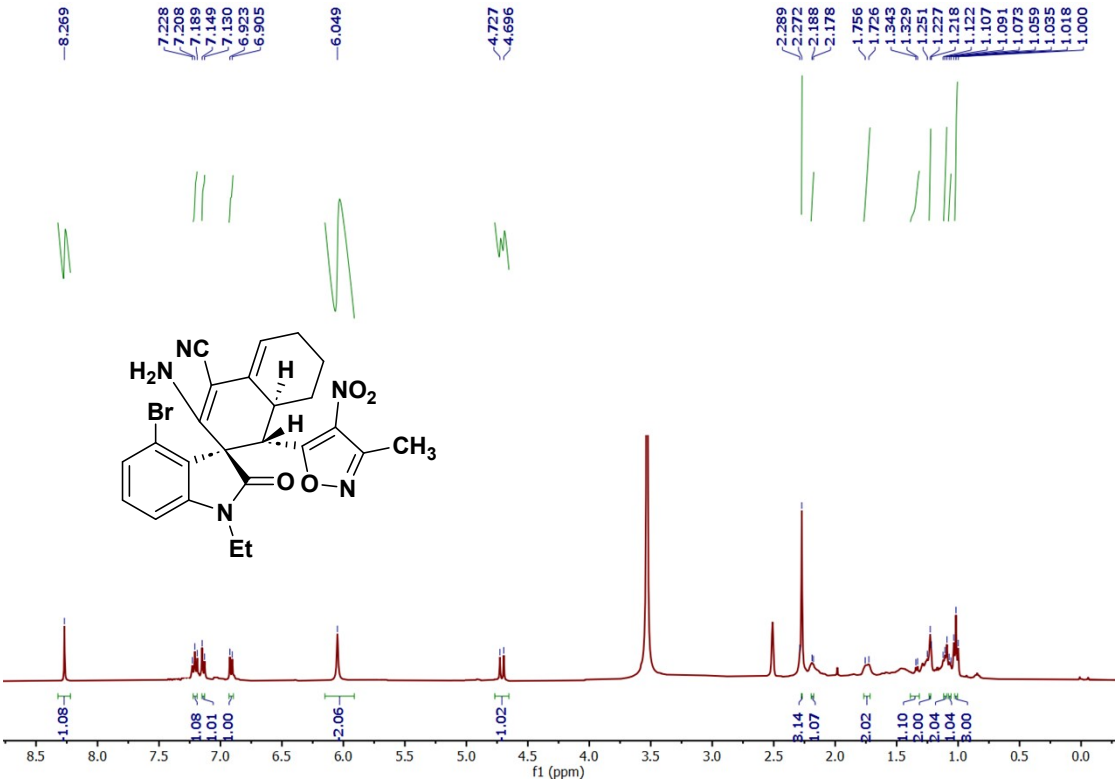


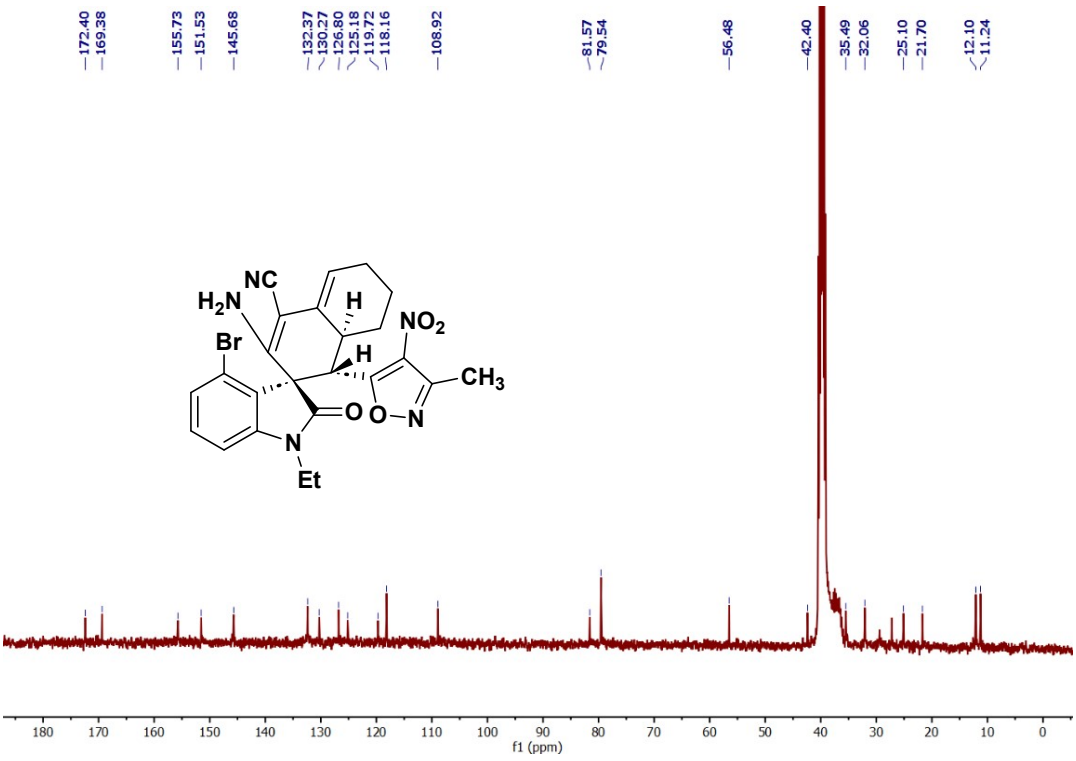

173.545
168.648
155.565
152.639
143.303
132.118
130.472
130.149
129.782
127.241
124.959
118.297
117.881
111.131
80.563
56.240
45.169
33.546
27.357
27.034
25.159
21.325
11.315
NC
H
NO2
H2N
H
Cl
CH3
O
O
N
N
CH3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


NC
H
NO2
H2N
H
Cl
CH3
O
O
N
N
CH3

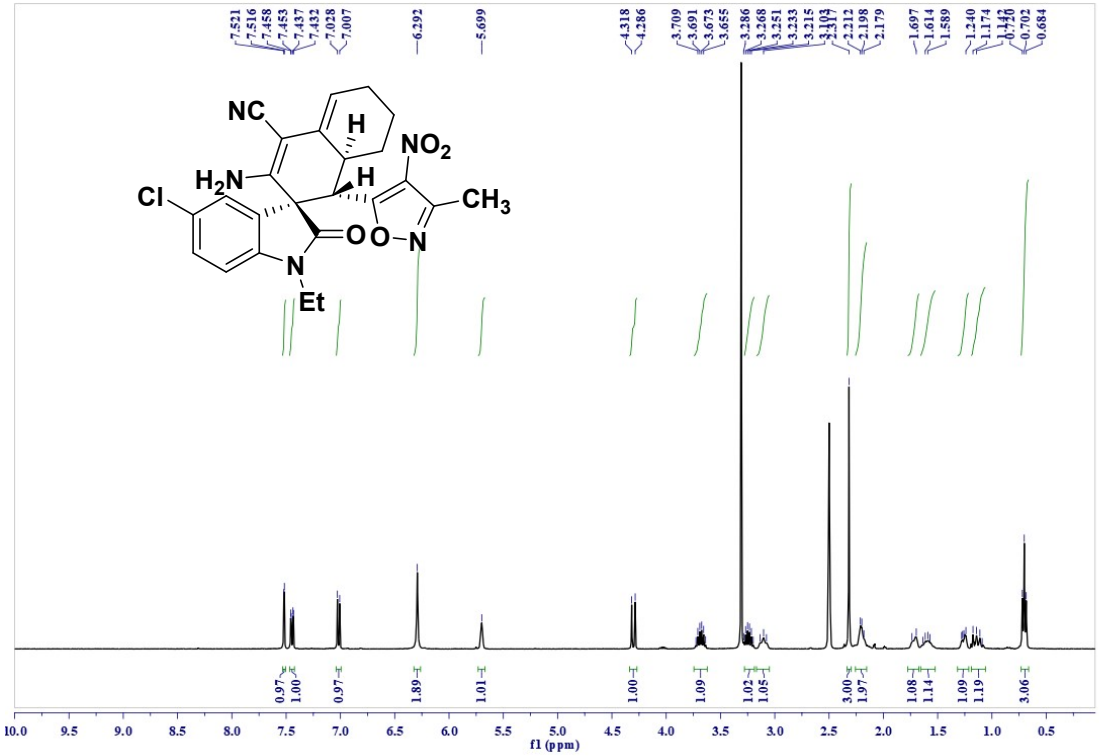
**m/z: 465.1204**

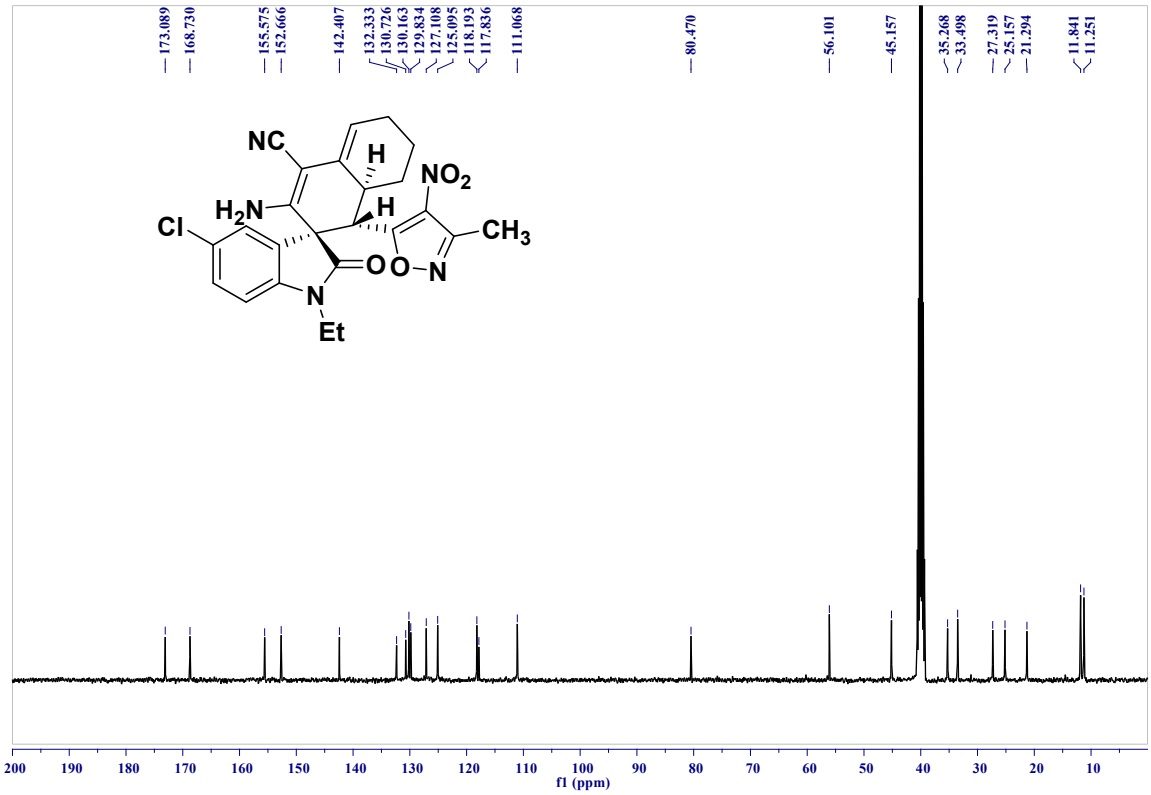
***(1'S,3S,8a'S)-3'-amino-4-bromo-1-ethyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3e):***

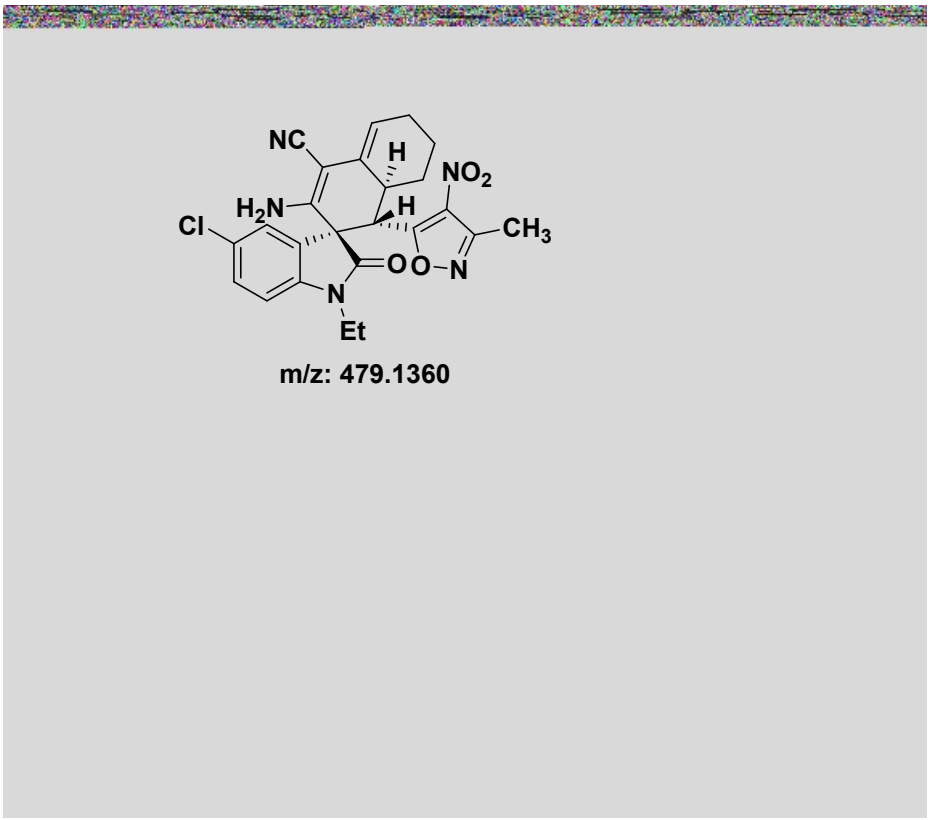


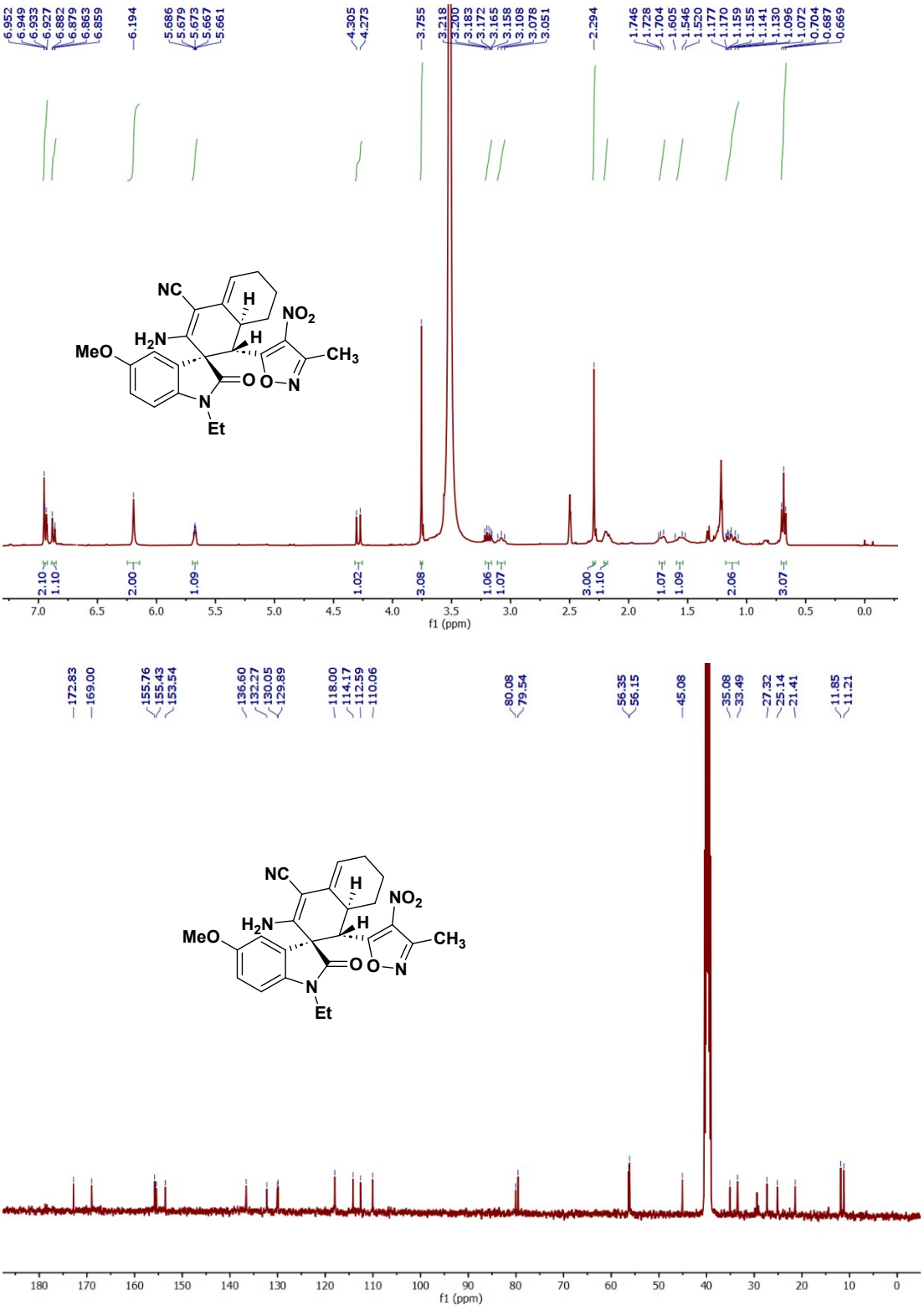
***(1'S,3S,8a'S)-3'-amino-5-chloro-1-ethyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3f):***



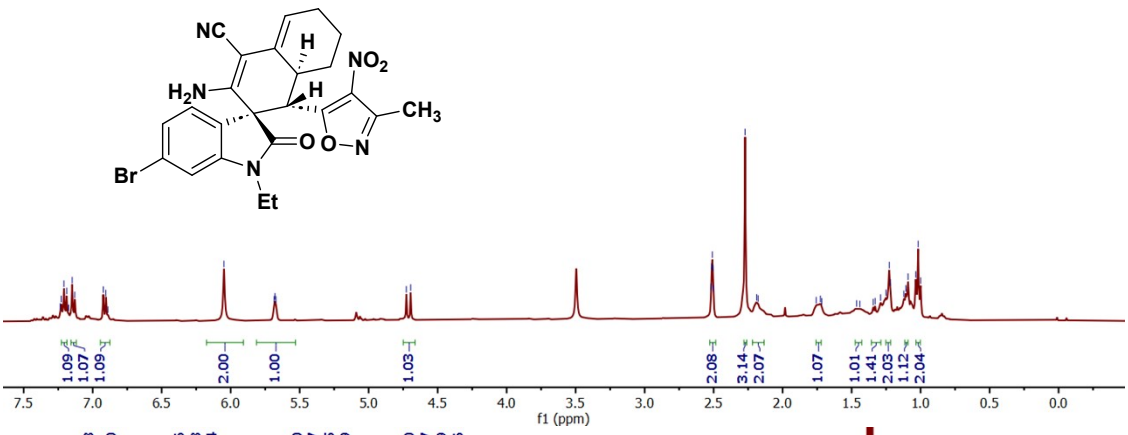


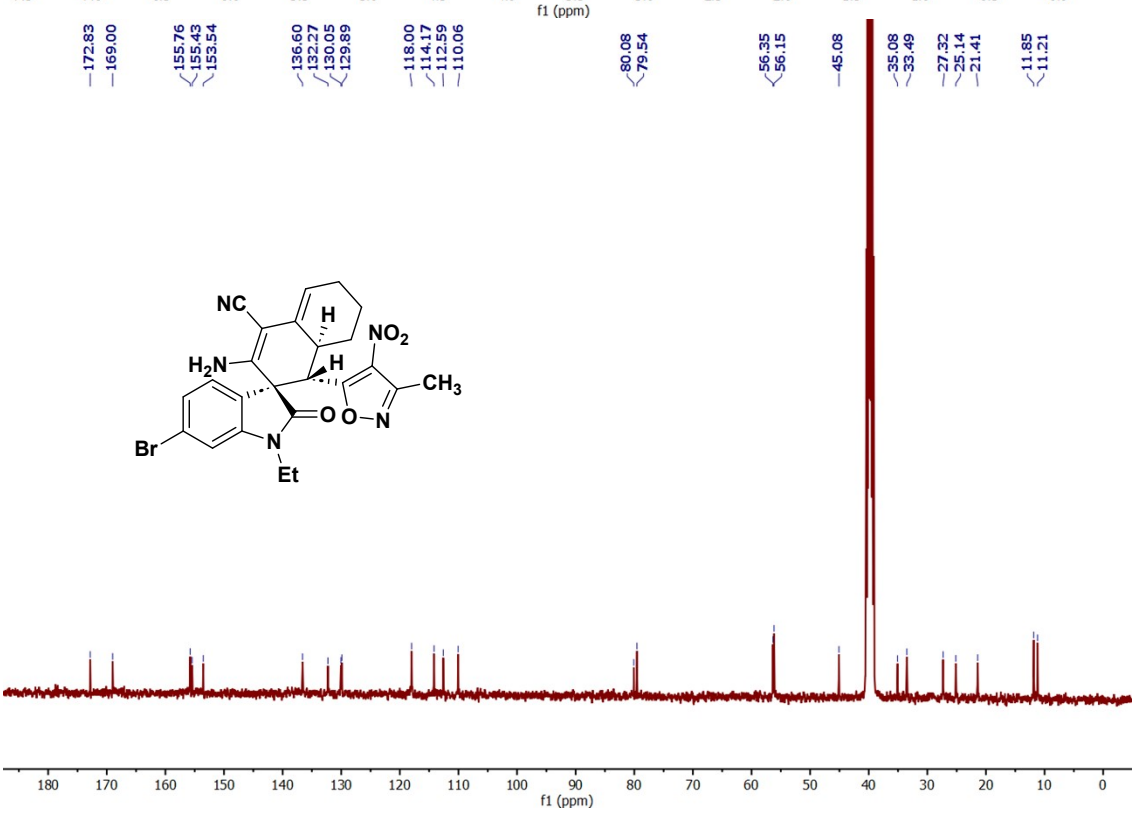

***(1'S,3S,8a'S)-3'-amino-1-ethyl-5-methoxy-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3g):***



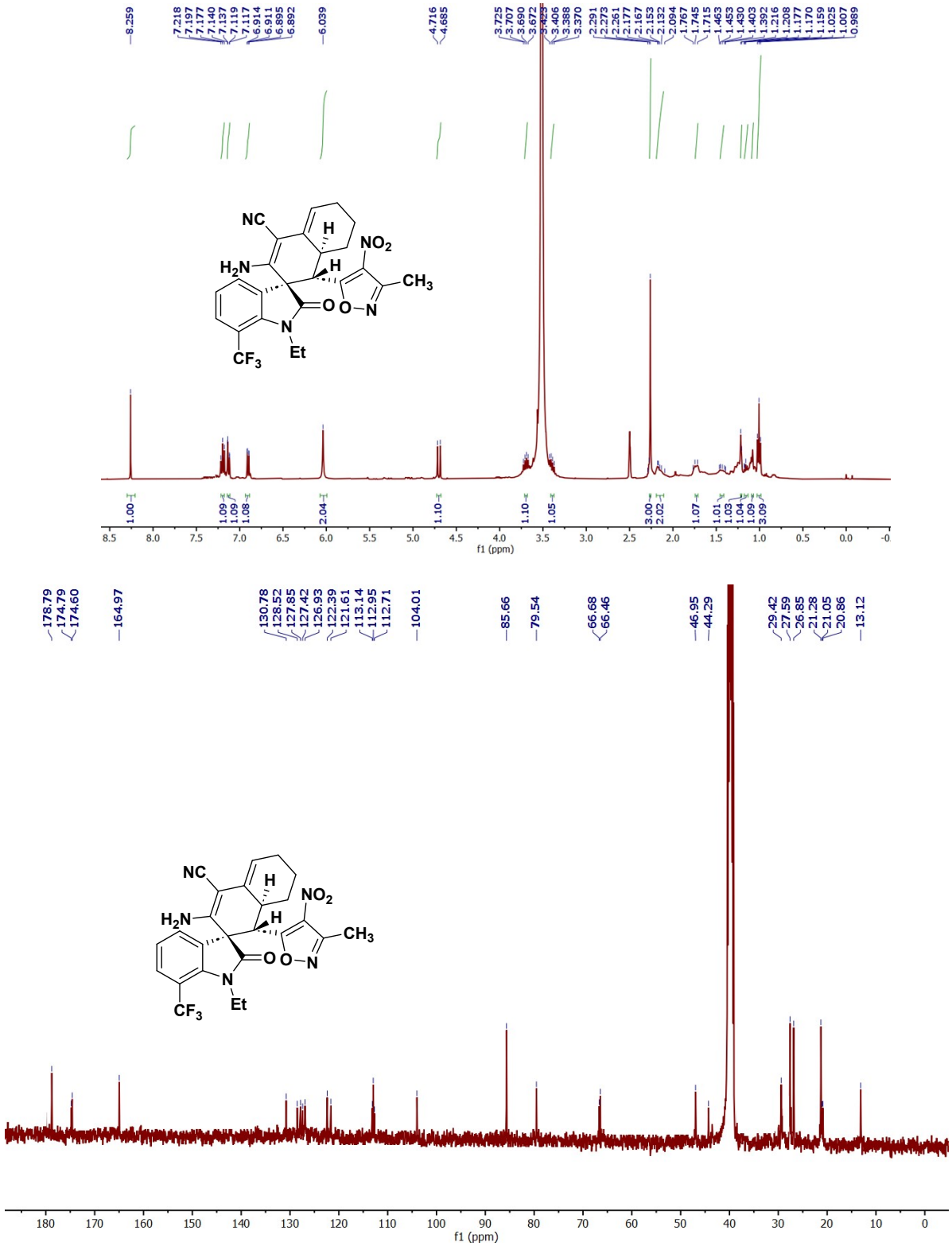

***(1'S,3S,8a'S)-3'-amino-6-bromo-1-ethyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3h):***

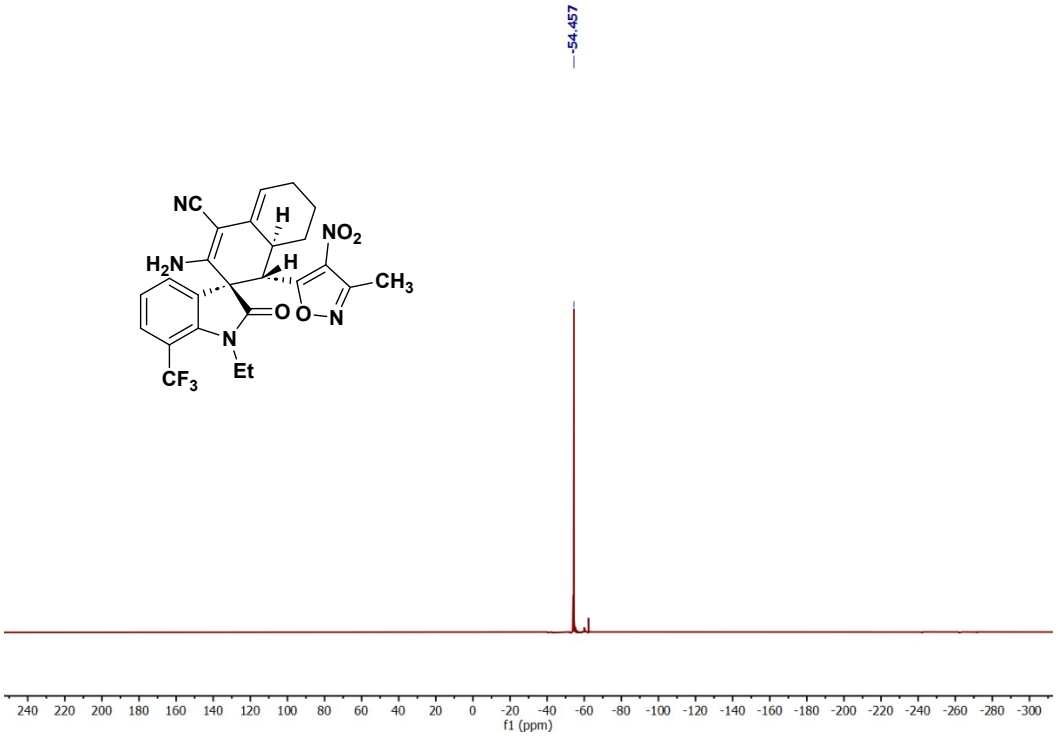

7.236
7.228
7.208
7.189
7.175
7.149
7.130
6.923
6.905
6.890
6.049
5.685
5.678
5.672
4.727
4.696
2.519
2.514
2.509
2.505
2.500
2.272
2.188
2.178
1.756
1.726
1.717
1.463
1.440
1.343
1.329
1.290
1.251
1.227
1.218
1.122
1.107
1.091
1.035
1.018
1.000


NC
H
NO2
H2N
H
CH3
O
O
N
Br
N
Et
1.09
1.07
1.09
2.00
1.00
1.03
2.08
3.14
2.07
1.07
1.01
1.41
2.03
1.12
2.04
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

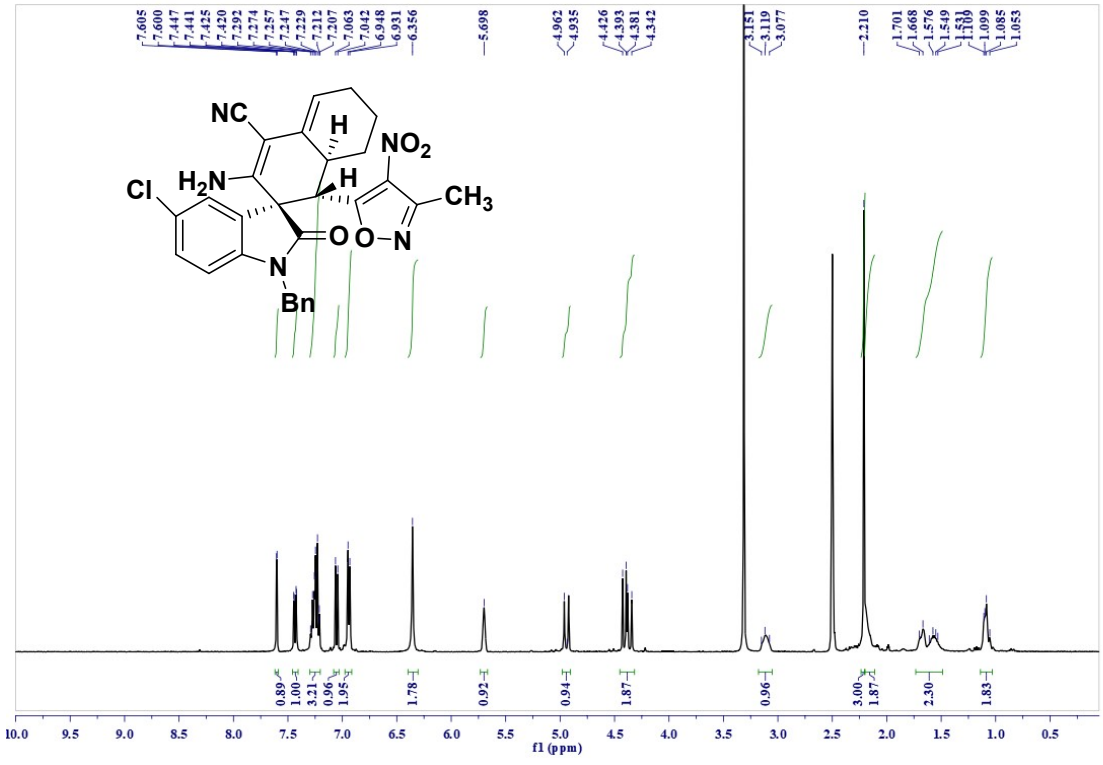

172.83
169.00
155.76
155.43
153.54
136.60
132.27
130.05
129.89
118.00
114.17
112.59
110.06
80.08
79.54
56.35
56.15
45.08
35.08
33.49
27.32
25.14
21.41
11.85
11.21
NC
H
NO2
H2N
H
CH3
O
O
N
Br
N
Et
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

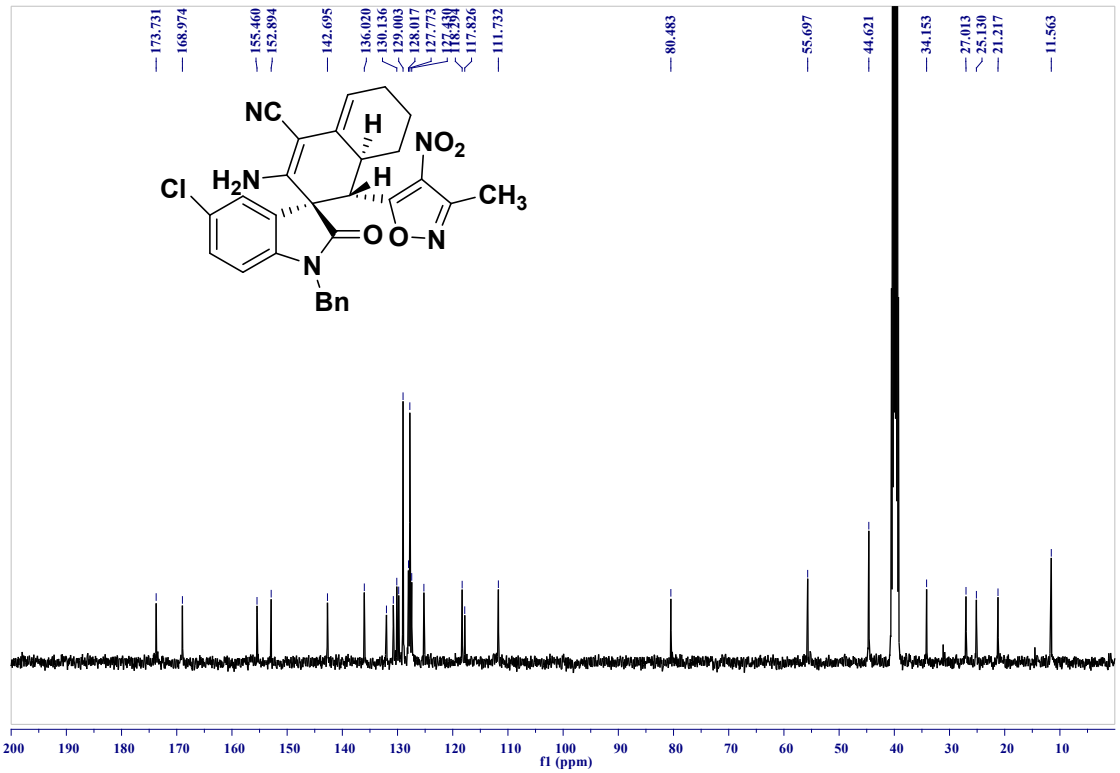
***(1'S,3S,8a'S)-3'-amino-1-ethyl-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-7-(trifluoromethyl)-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3i):***

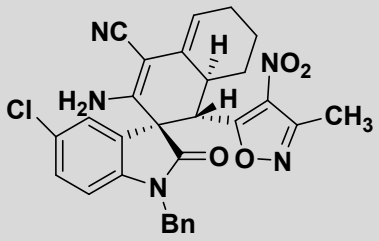





***(1'S,3S,8a'S)-3'-amino-1-benzyl-5-chloro-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3j):***

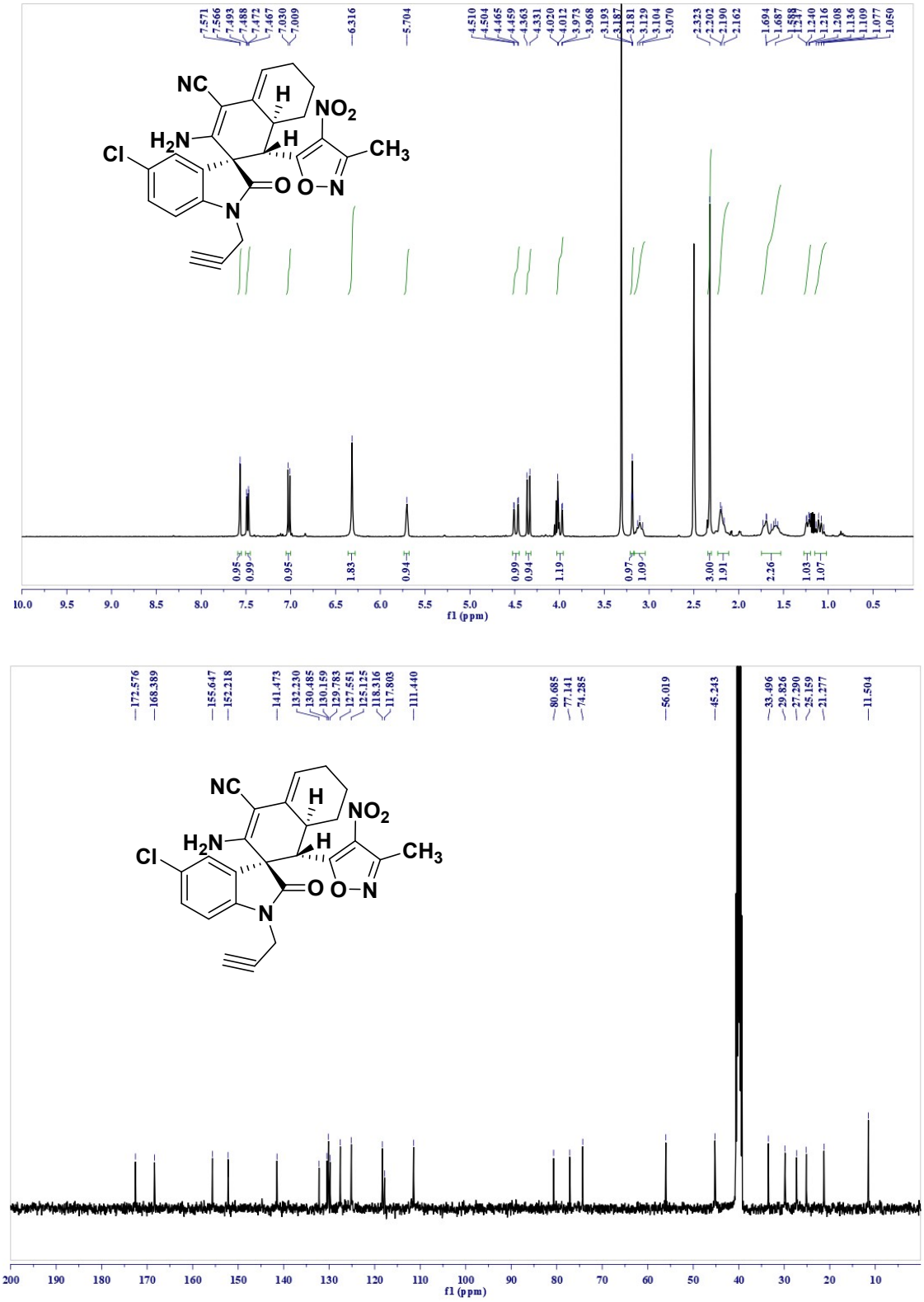


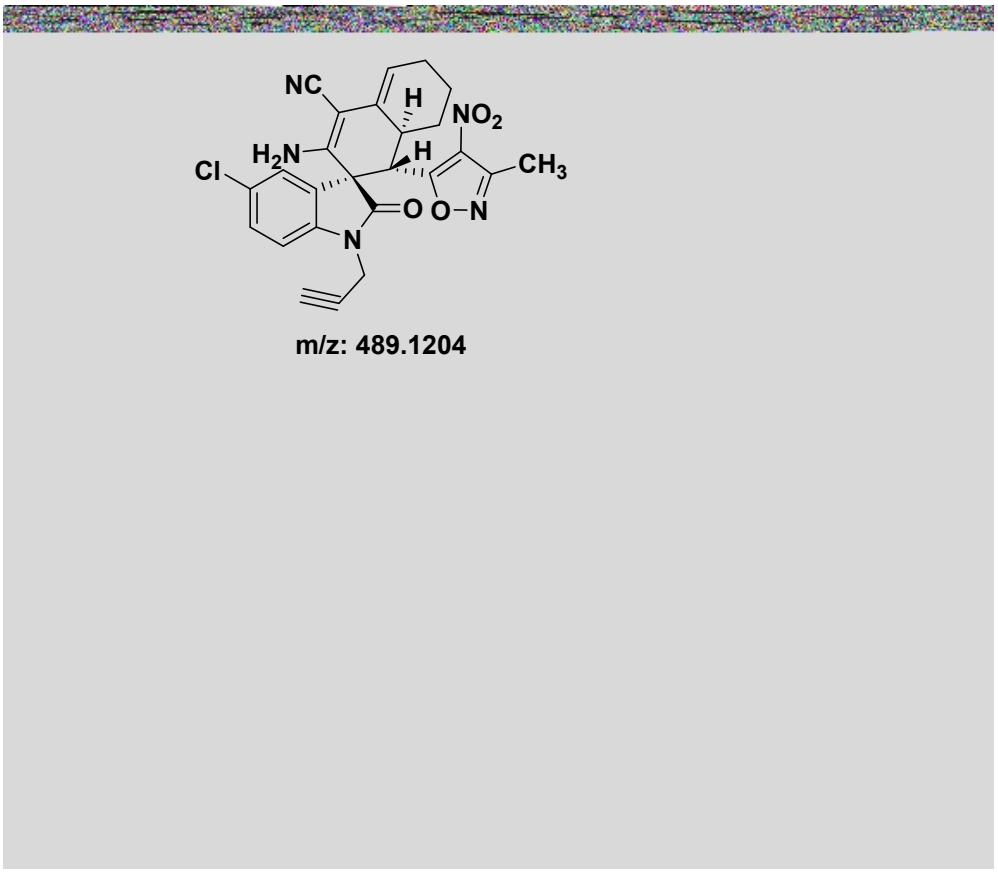

173.731
168.974
155.460
152.894
142.695
136.020
130.136
129.003
128.017
127.773
117.826
111.732
80.483
55.697
44.621
34.153
27.013
25.130
21.217
11.563
NC
H
NO2
Cl
H2N
H
CH3
O
O
N
N
Bn
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


NC
H
NO2
Cl
H2N
H
CH3
O
O
N
N
Bn

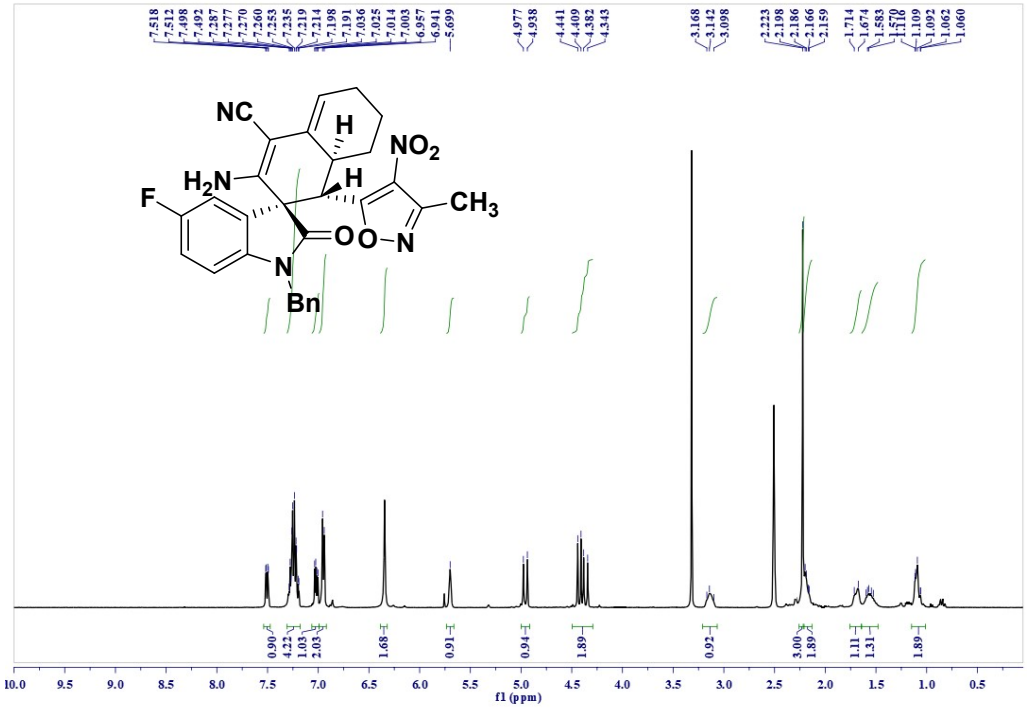
m/z: 541.1517

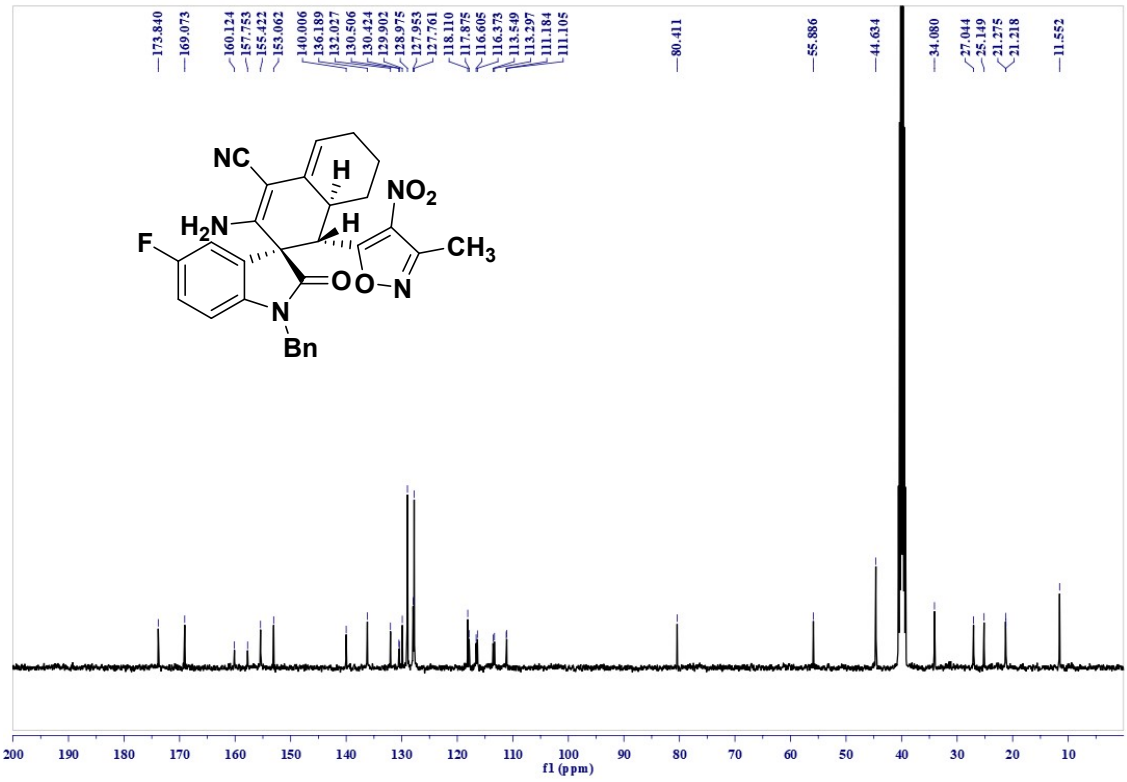
***(1'S,3S,8a'S)-3'-amino-5-chloro-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-1-(prop-2-yn-1-yl)-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3k):***

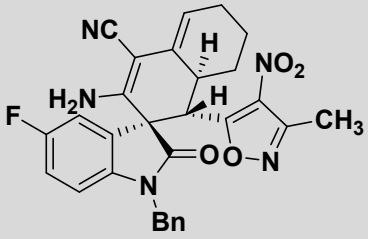





***(1'S,3S,8a'S)-3'-amino-1-benzyl-5-fluoro-1'-(3-methyl-4-nitroisoxazol-5-yl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile (3l'):***

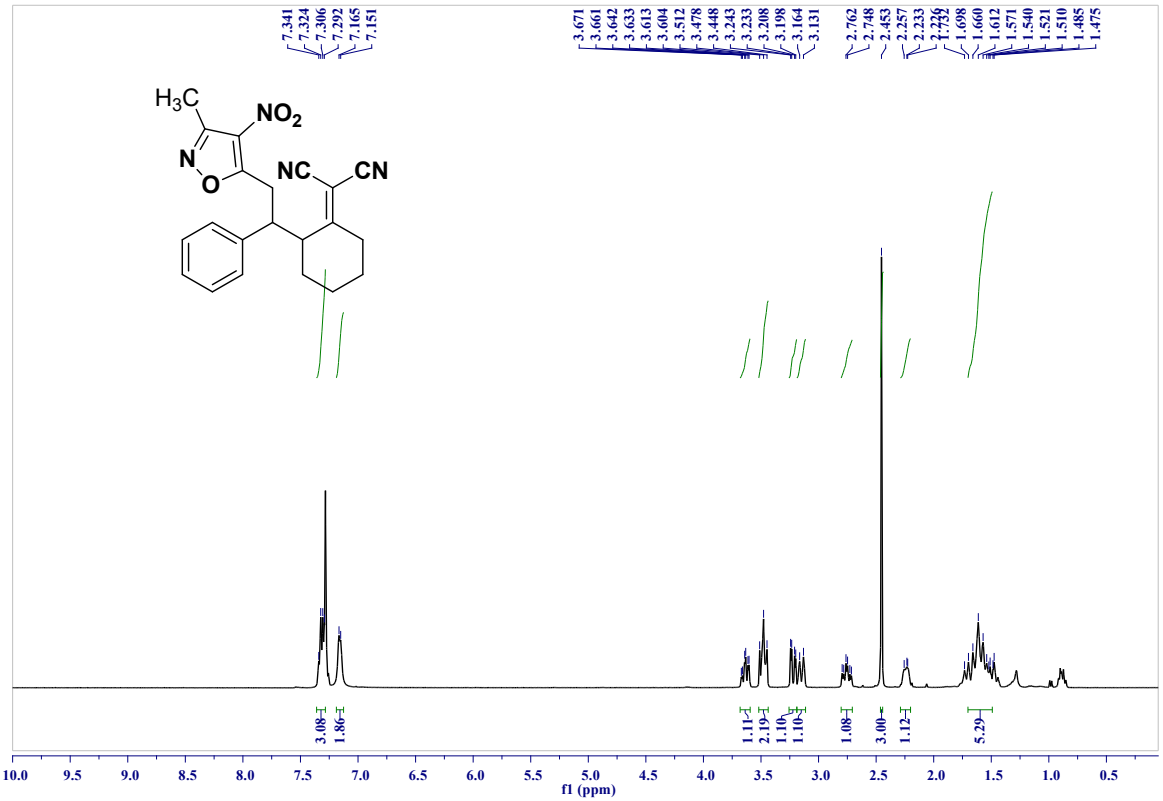


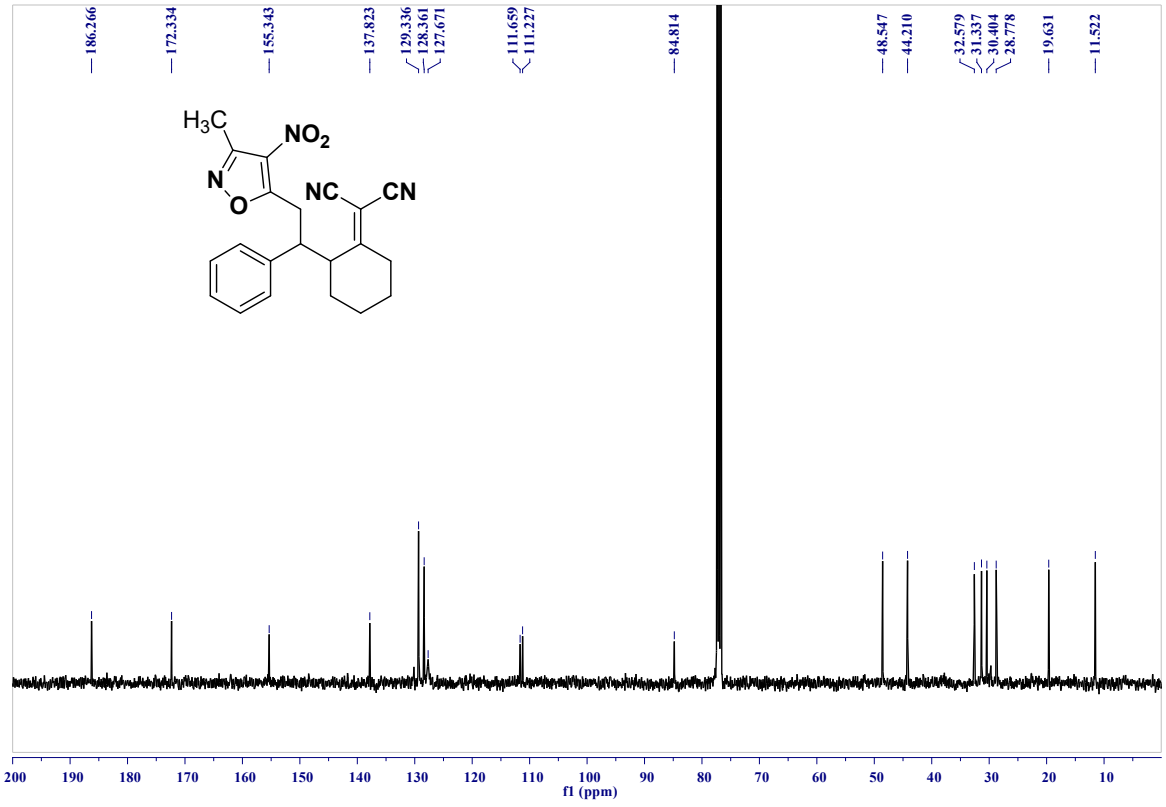

173.840
169.073
160.124
157.753
155.422
153.062
140.006
136.189
132.027
130.506
130.424
129.902
128.975
127.953
127.761
118.110
117.875
116.605
116.373
113.549
113.297
111.184
111.105
80.411
55.886
44.634
34.080
27.044
25.149
21.275
21.218
11.552
NC
H
NO2
H2N
H
F
CH3
O
O
N
N
Bn
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

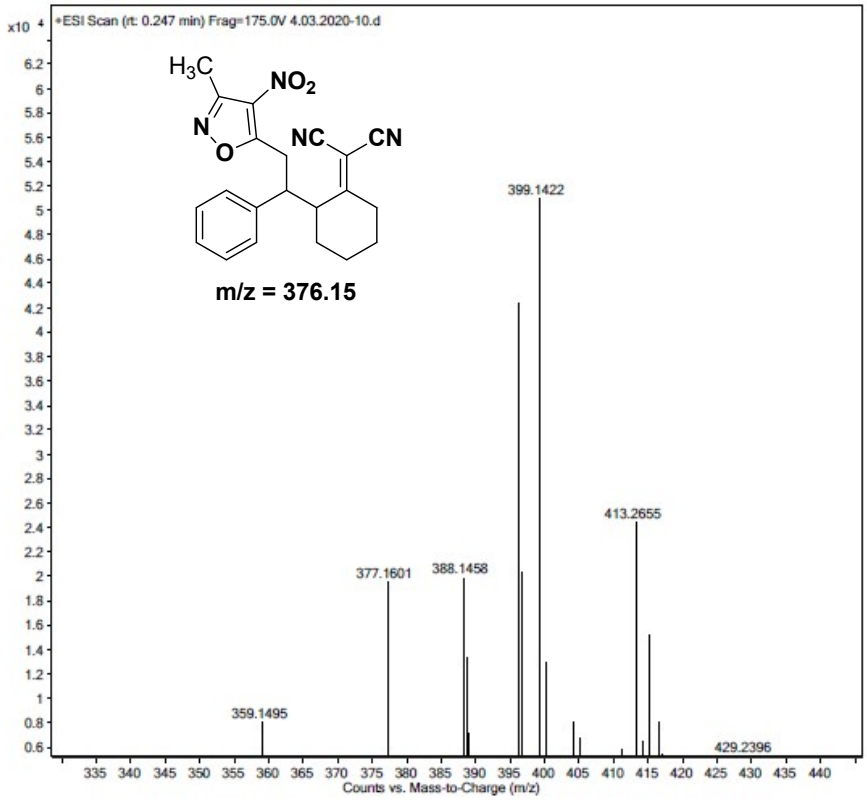

NC
H
NO2
H2N
H
F
CH3
O
O
N
N
Bn

**m/z: 525.1812**

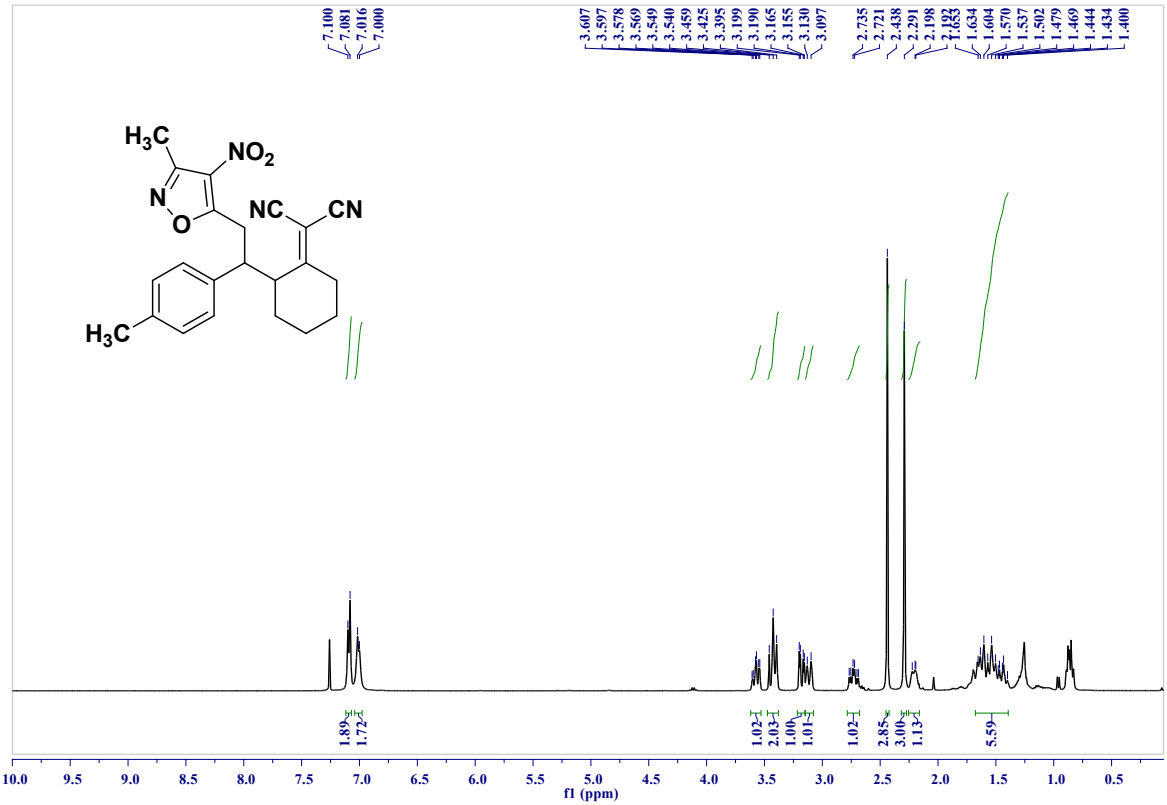
***2-(2-(2-(3-methyl-4-nitroisoxazol-5-yl)-1-phenylethyl)cyclohexylidene)malononitrile (5a):***

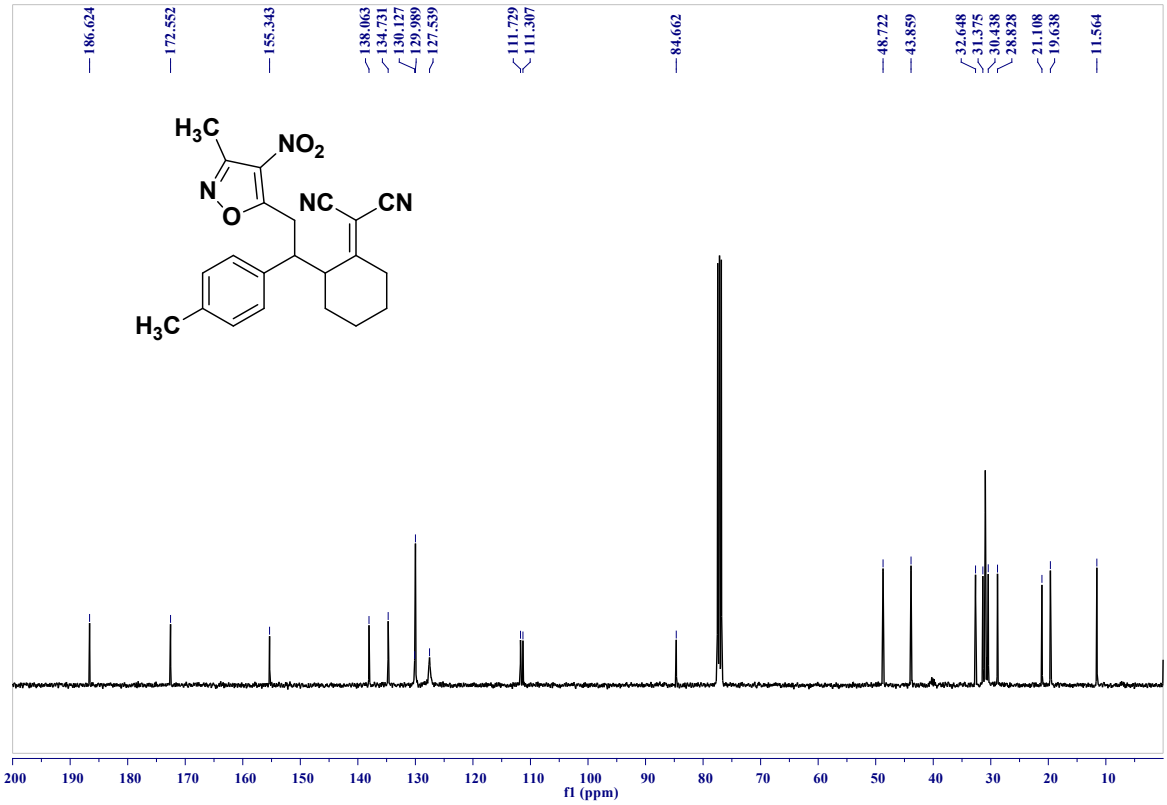


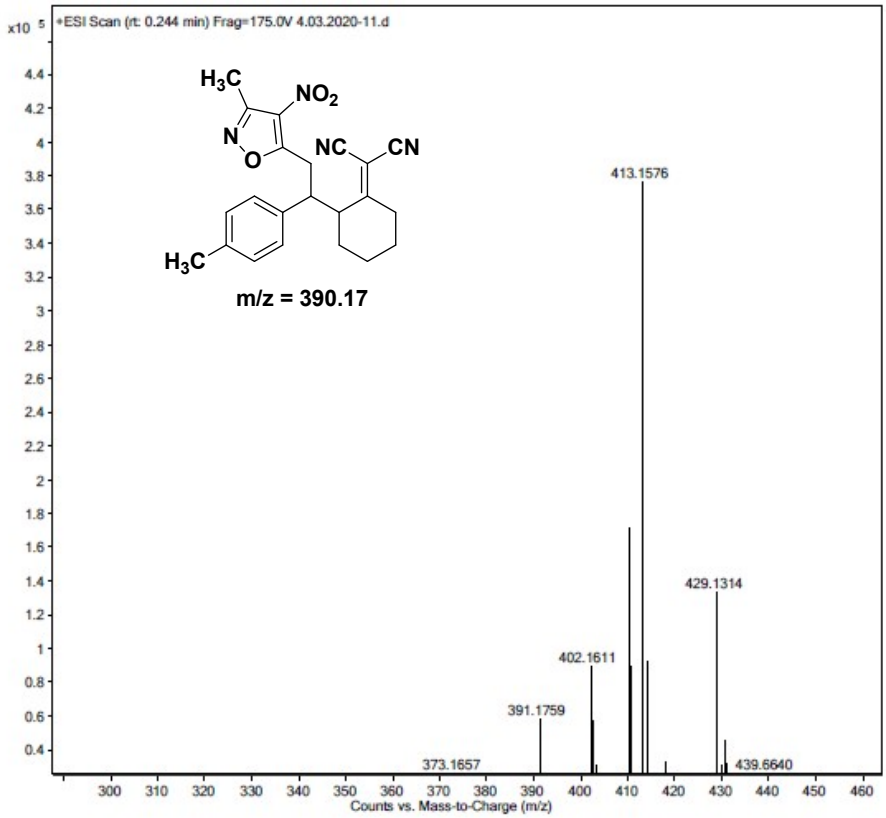





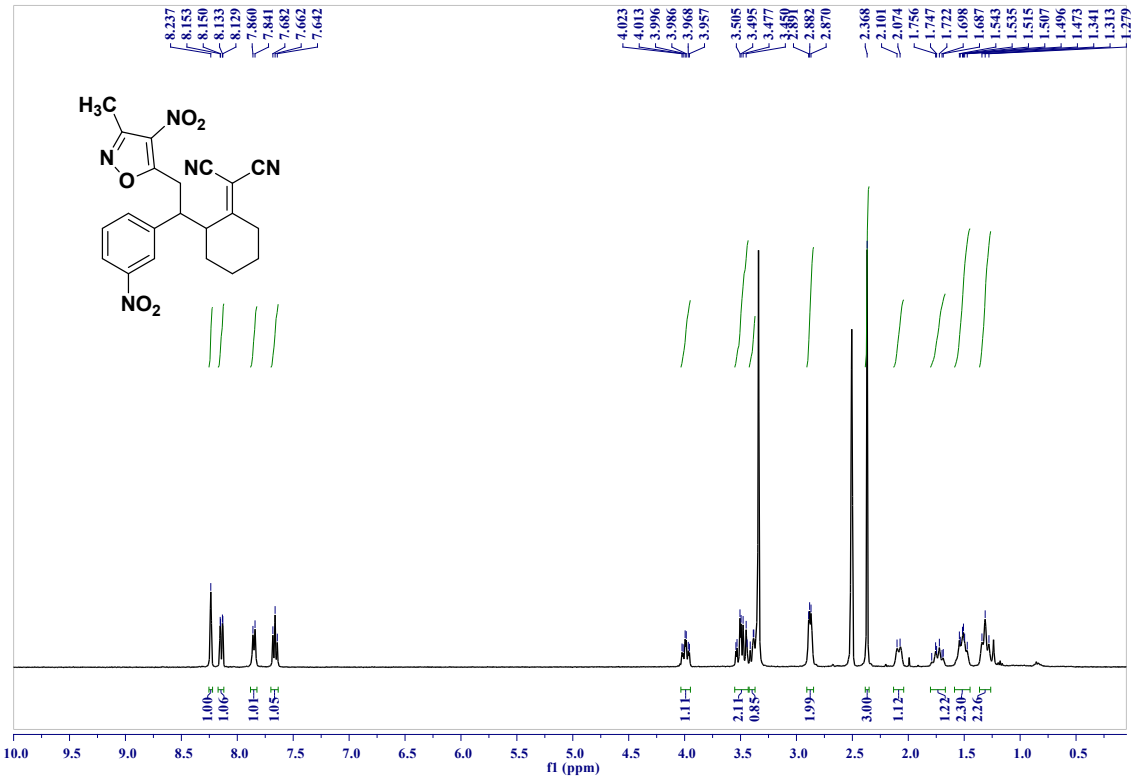

***2-(2-(2-(3-methyl-4-nitroisoxazol-5-yl)-1-(p-tolyl)ethyl)cyclohexylidene)malononitrile (5b):***

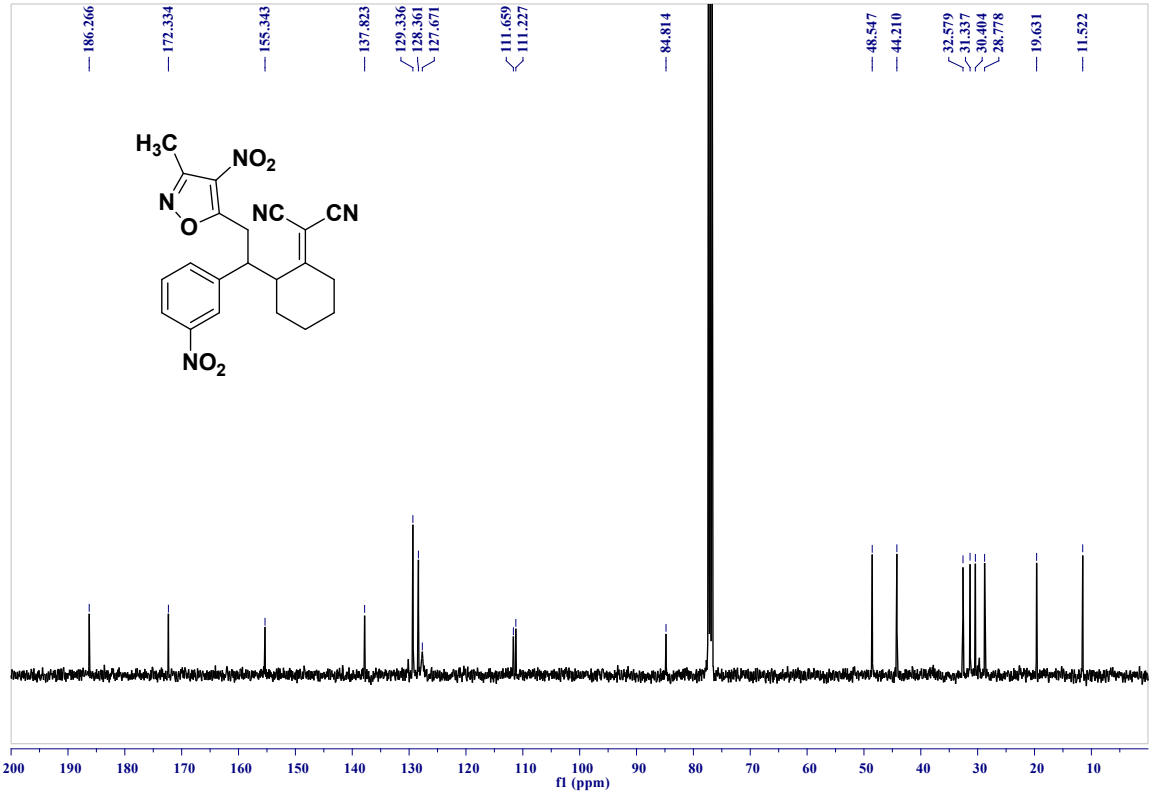


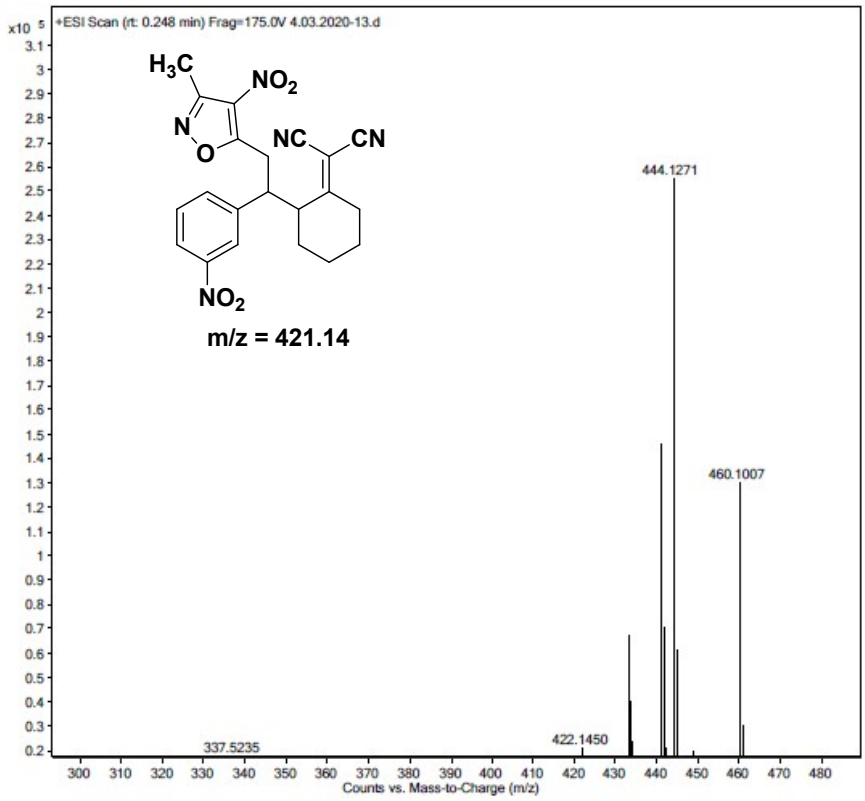

186.624
172.552
155.343
138.063
134.731
130.127
129.989
127.539
111.729
111.307
84.662
48.722
43.859
32.648
31.375
30.438
28.828
21.108
19.638
11.564
H3C
NO2
N
O
NC
CN
H3C
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


x10 5
+ESI Scan (rt: 0.244 min) Frag=175.0V 4.03.2020-11.d
H3C
NO2
N
O
NC
CN
H3C
m/z = 390.17
413.1576
429.1314
402.1611
391.1759
373.1657
439.6640
Counts vs. Mass-to-Charge (m/z)

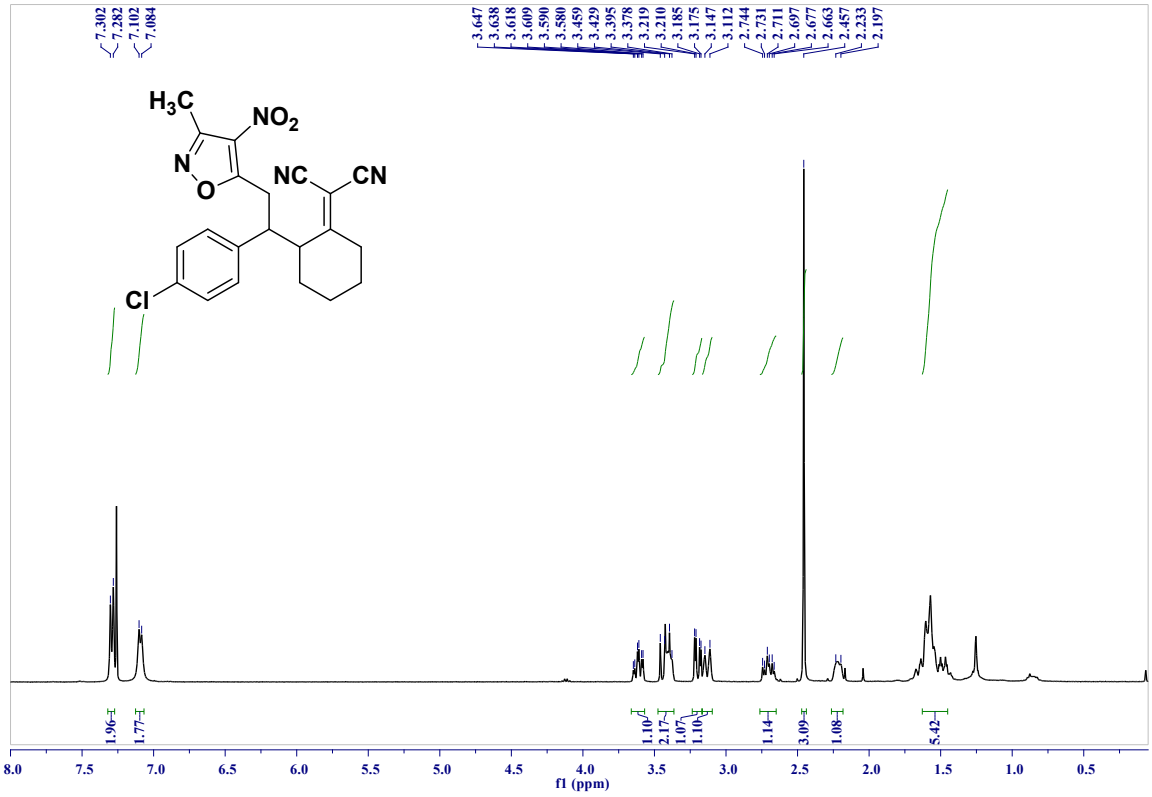
***2-(2-(2-(3-methyl-4-nitroisoxazol-5-yl)-1-(3-nitrophenyl)ethyl)cyclohexylidene)malononitrile (5c):***

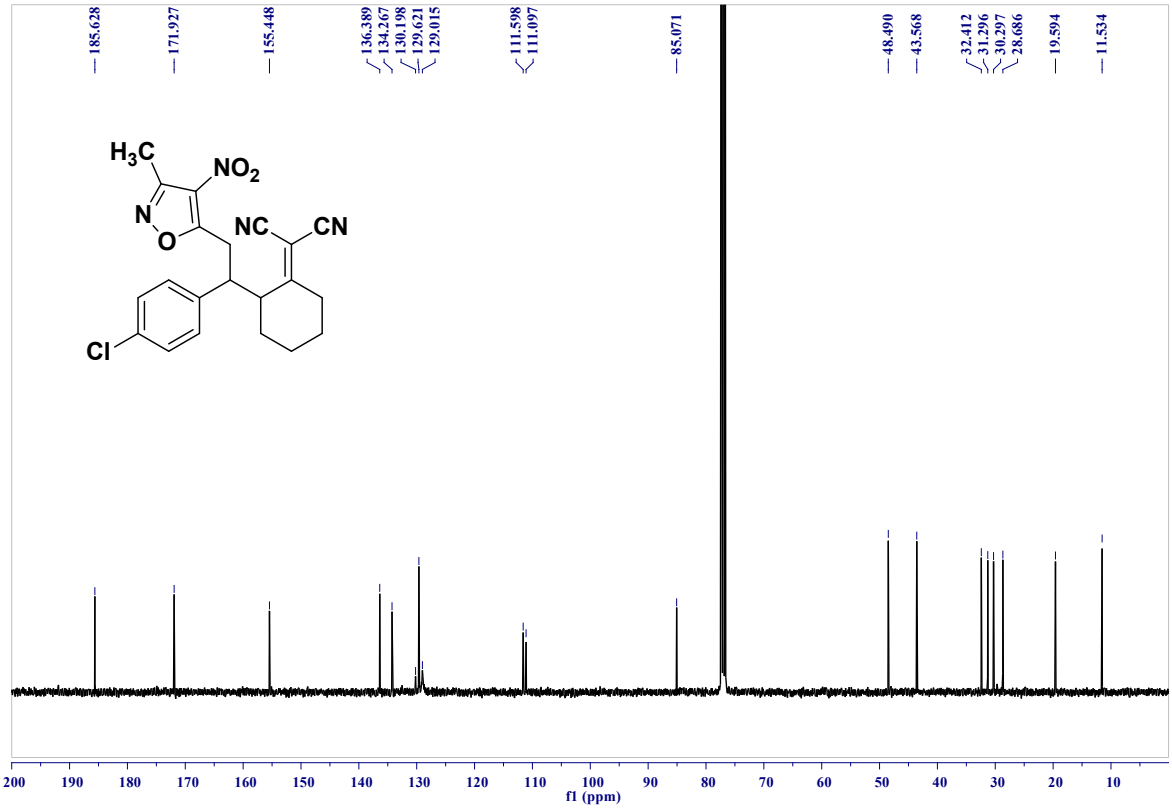


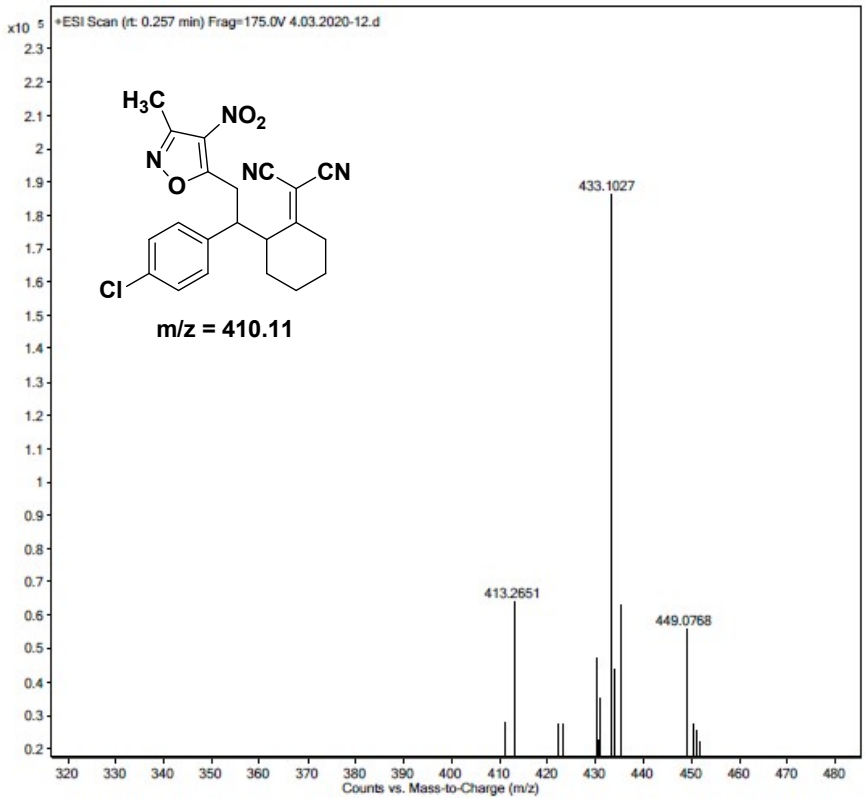





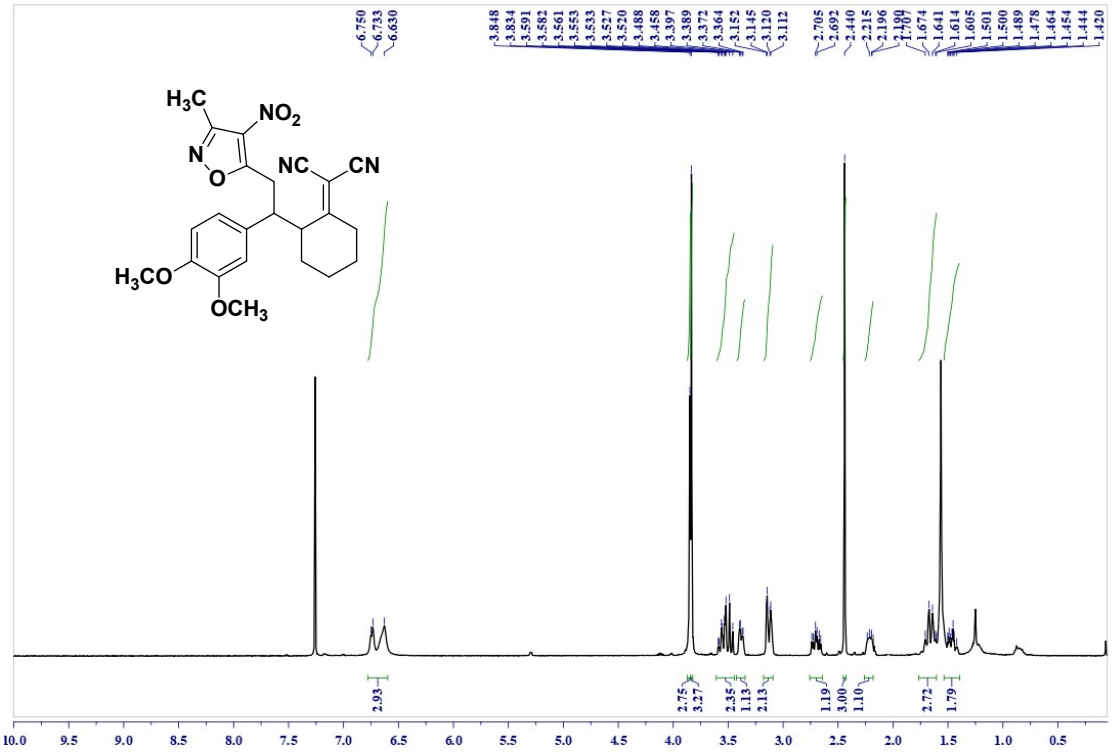

***2-(2-(1-(4-chlorophenyl)-2-(3-methyl-4-nitroisoxazol-5-yl)ethyl)cyclohexylidene)malononitrile (5d):***

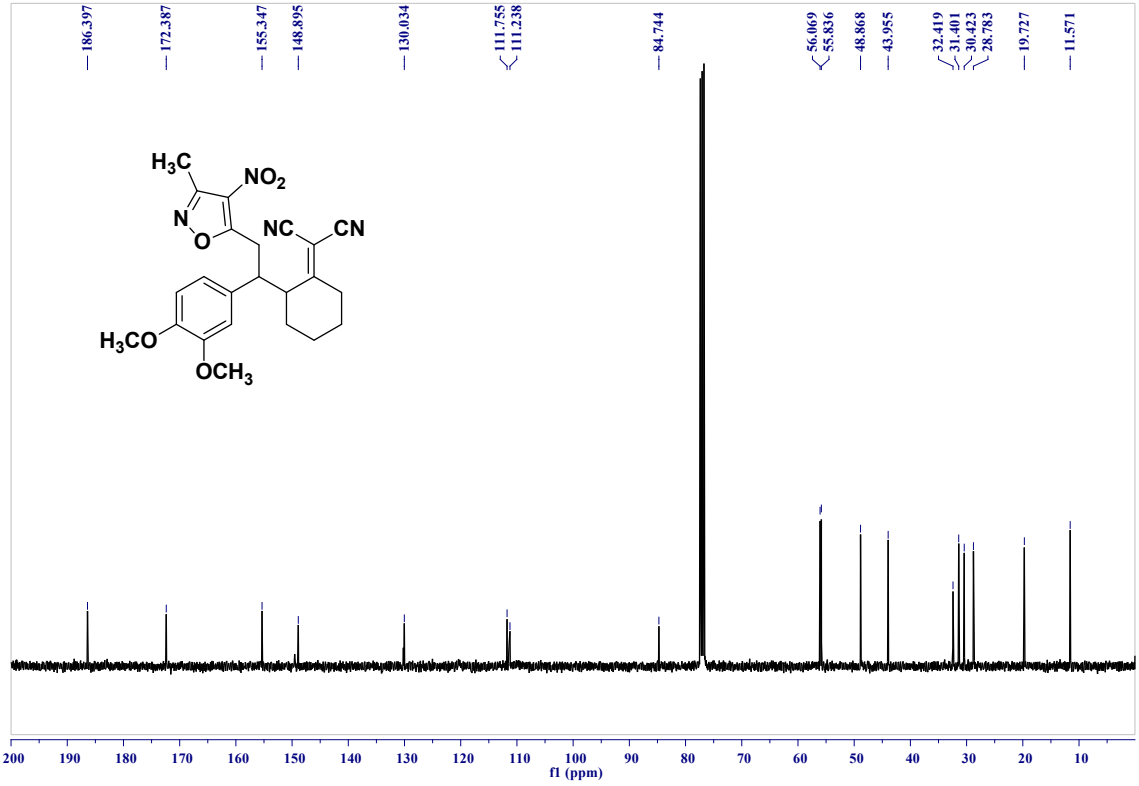


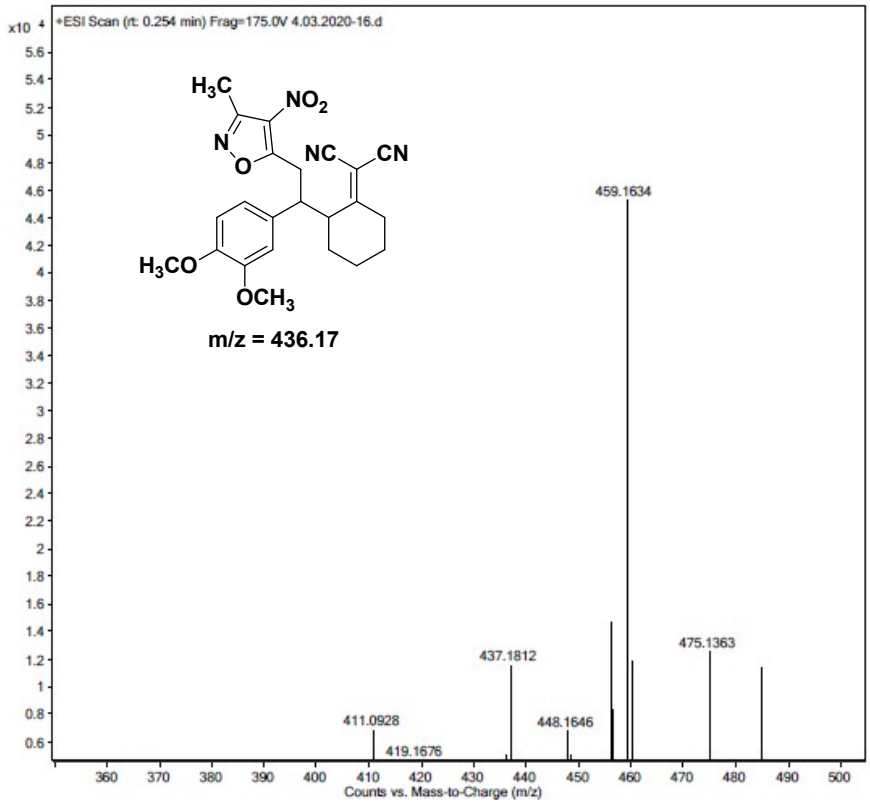

185.628
171.927
155.448
136.389
134.267
130.198
129.621
129.015
111.598
111.097
85.071
48.490
43.568
32.412
31.296
30.297
28.686
19.594
11.534
H3C
NO2
N
O
NC
CN
Cl
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


x10 5
+ESI Scan (rt: 0.257 min) Frag=175.0V 4.03.2020-12.d
H3C
NO2
N
O
NC
CN
Cl
m/z = 410.11
433.1027
413.2651
449.0768
Counts vs. Mass-to-Charge (m/z)

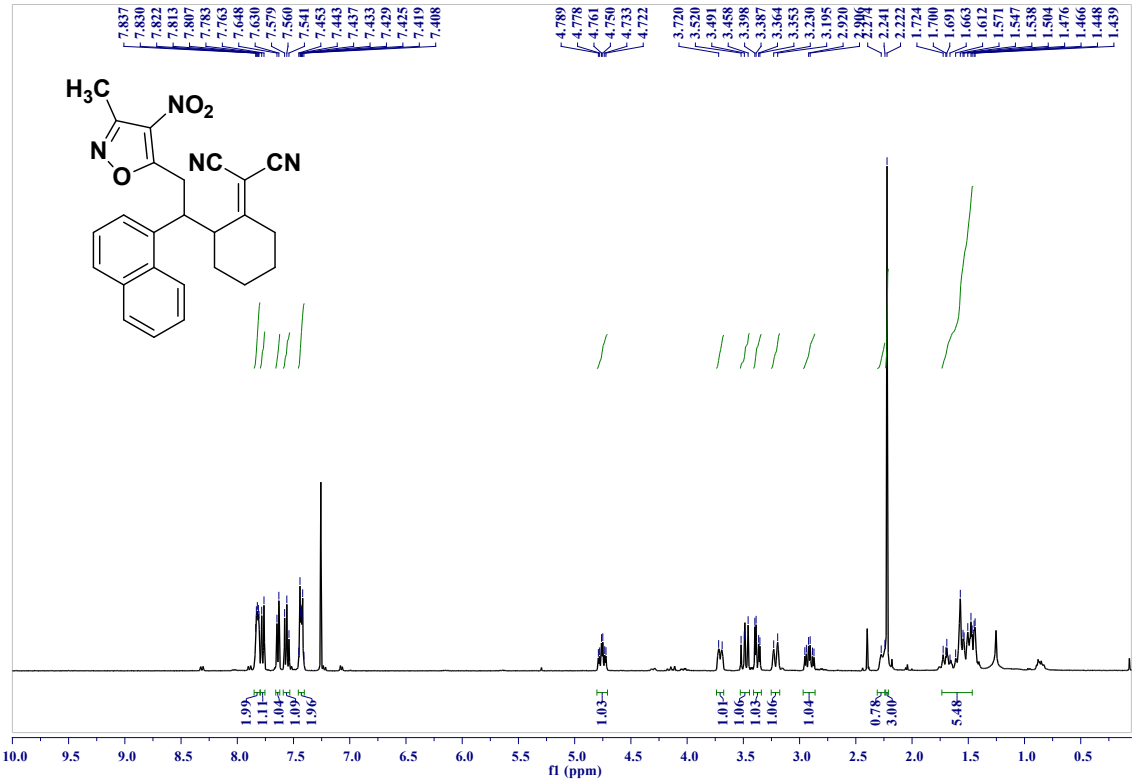
***2-(2-(1-(3,4-dimethoxyphenyl)-2-(3-methyl-4-nitroisoxazol-5-yl)ethyl)cyclohexylidene)malononitrile (5e):***

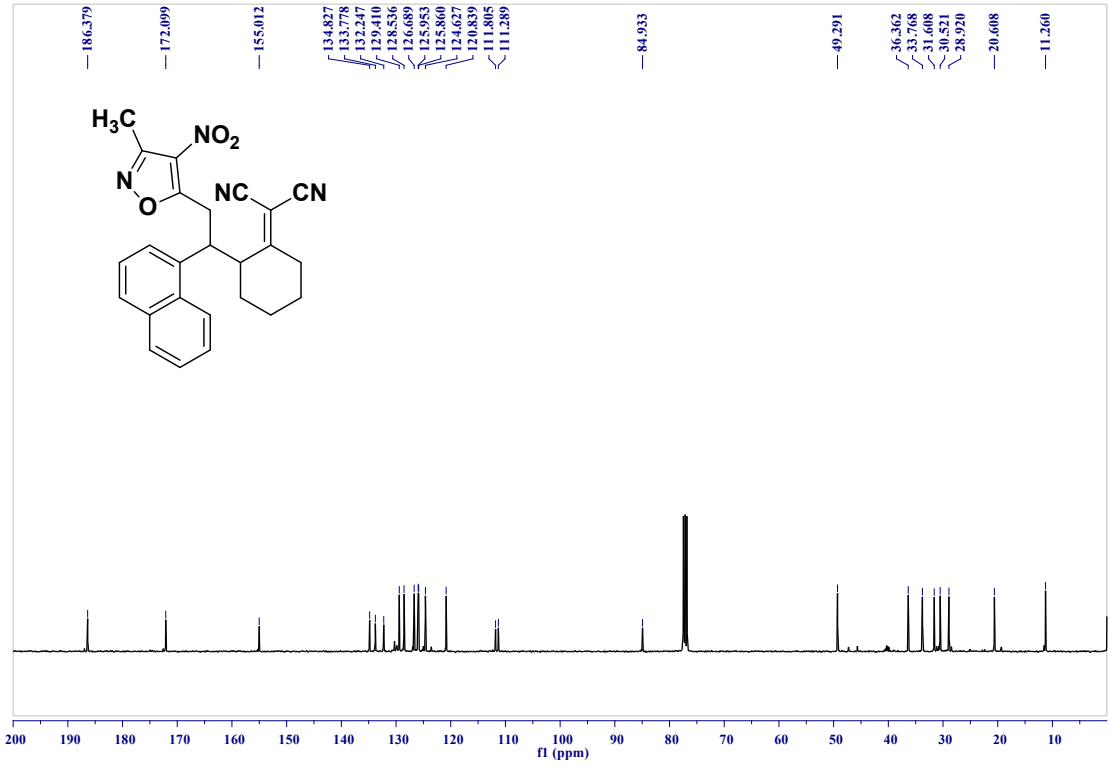


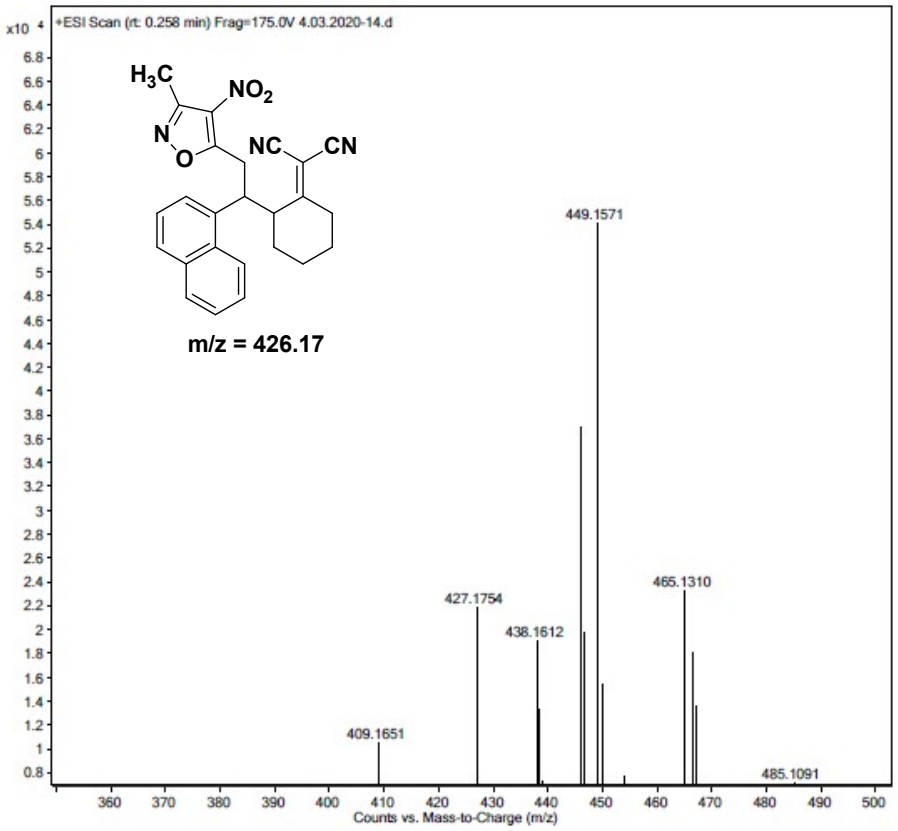





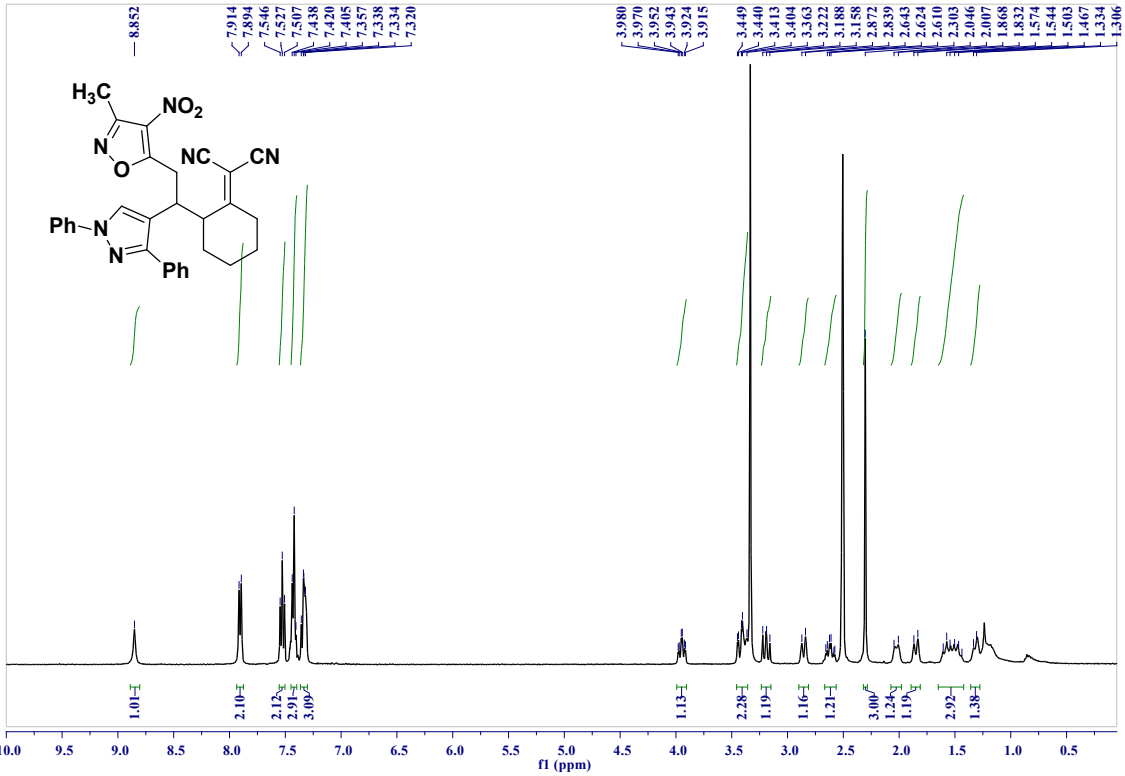

***2-(2-(2-(3-methyl-4-nitroisoxazol-5-yl)-1-(naphthalen-2-yl)ethyl)cyclohexylidene)malononitrile (5f):***

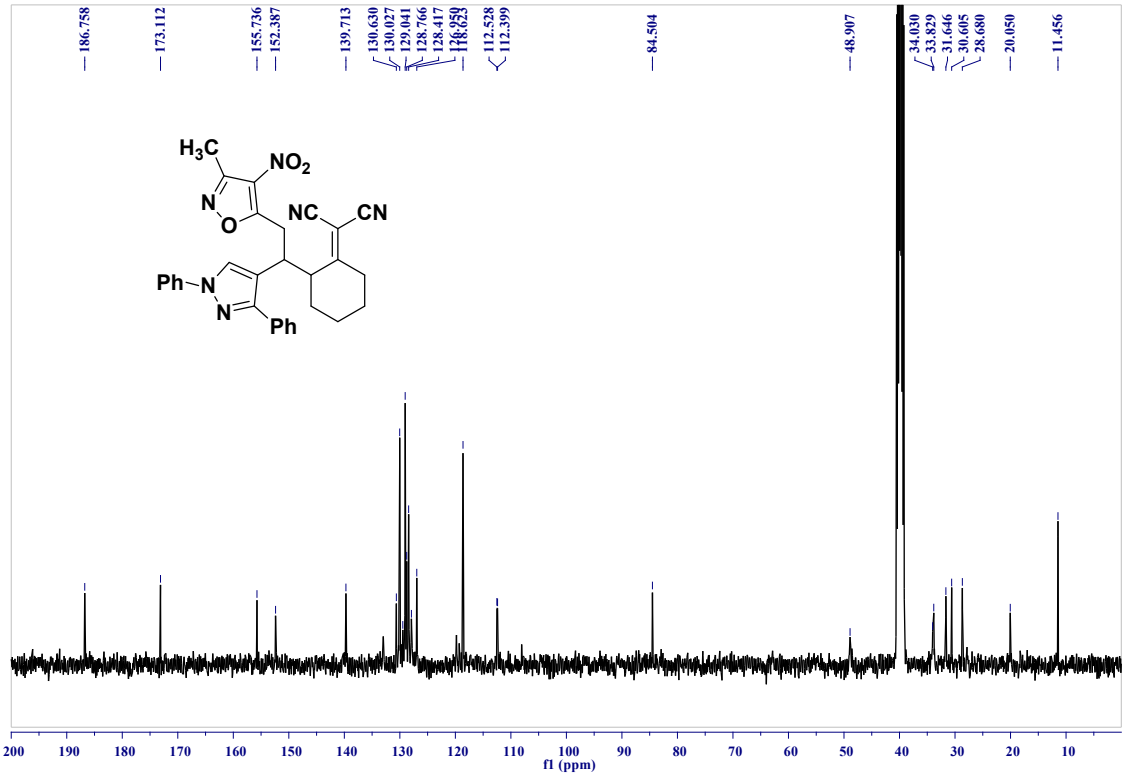


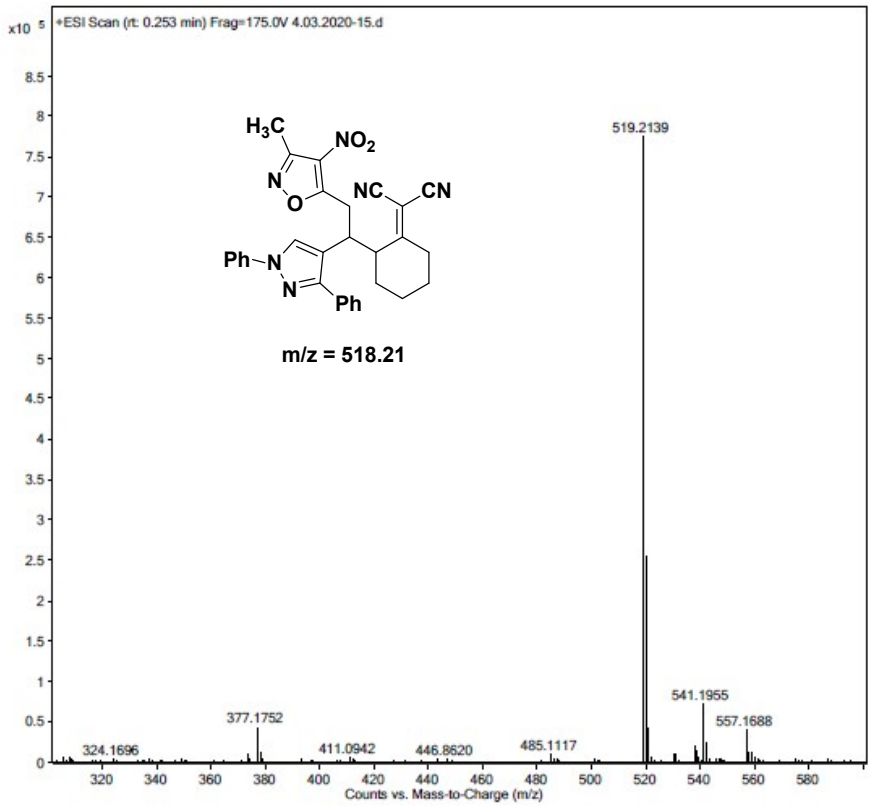

186.379
172.099
155.012
134.827
133.778
132.247
129.410
128.536
126.689
125.953
125.860
124.627
120.839
111.805
111.289
84.933
49.291
36.362
33.768
31.608
30.521
28.920
20.608
11.260
H3C
NO2
N
O
NC
CN
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


x10 4
+ESI Scan (rt: 0.258 min) Frag=175.0V 4.03.2020-14.d
H3C
NO2
N
O
NC
CN
m/z = 426.17
449.1571
427.1754
438.1612
465.1310
409.1651
485.1091
Counts vs. Mass-to-Charge (m/z)

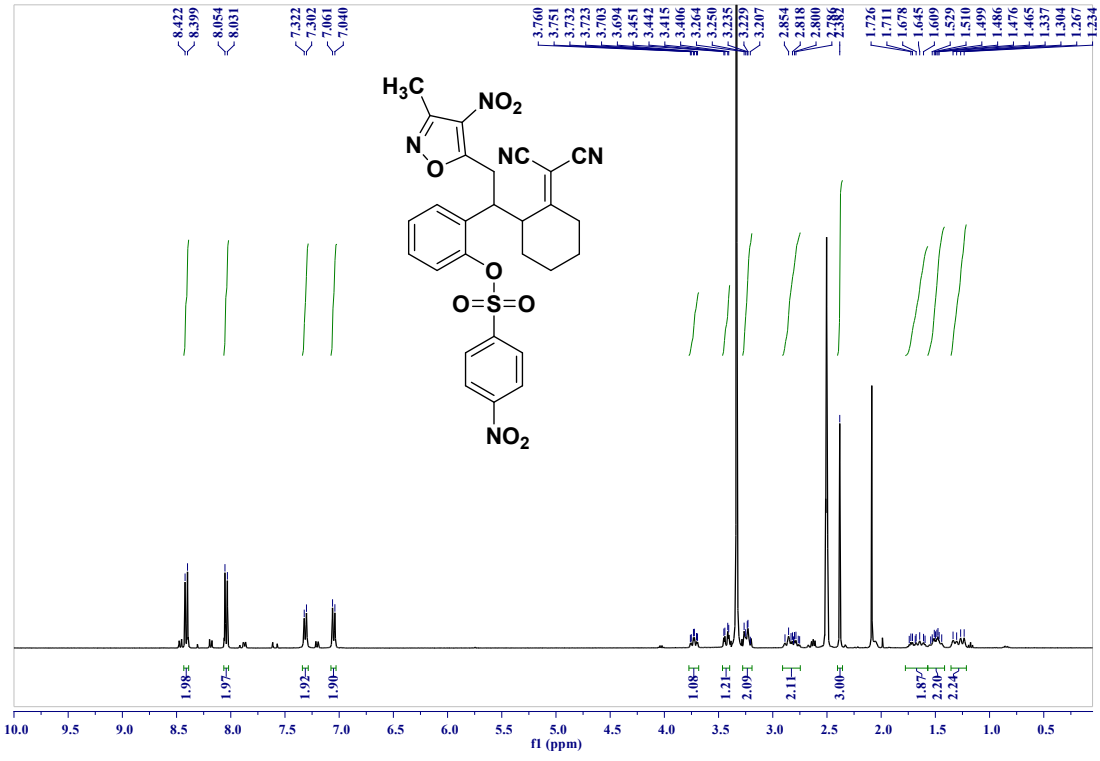
***2-(2-(1-(1,3-diphenyl-1H-pyrazol-4-yl)-2-(3-methyl-4-nitroisoxazol-5-yl)ethyl)cyclohexylidene)malononitrile (5g):***

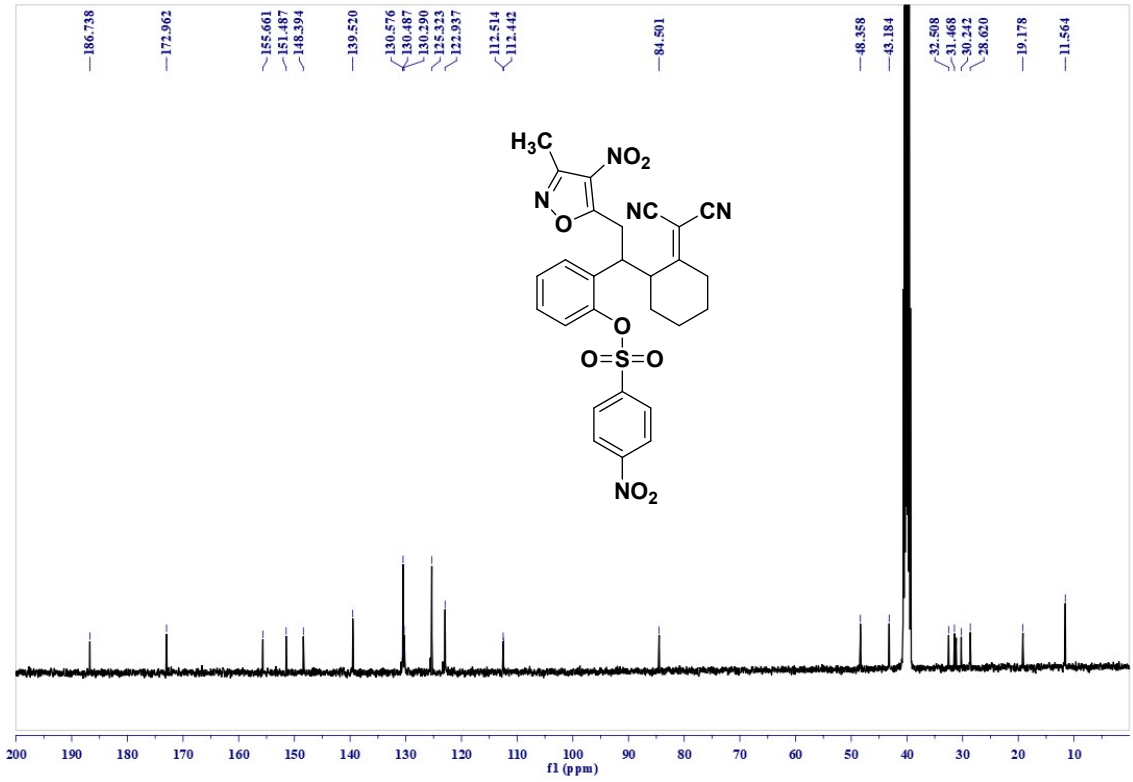





***2-(1-(2-(dicyanomethylene)cyclohexyl)-2-(3-methyl-4-nitroisoxazol-5-yl)ethyl)phenyl 4-nitrobenzenesulfonate (5h):***




186.738
172.962
155.661
151.487
148.394
139.520
130.576
130.487
130.290
125.323
122.937
112.514
112.442
84.501
48.358
43.184
32.508
31.468
30.242
28.620
19.178
11.564
H3C
NO2
N
O
NC
CN
O
O=S=O
NO2
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)