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Supporting Information

Synthesis of novel imidazole-based triheterocycles *via* a domino Ugi/Michael reaction and silver-catalyzed heteroannulation

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General Experimental Methods

All the reagents were purchased from commercial sources and used without further purification. The ^{1}H and ^{13}C NMR spectrums were recorded on a Bruker Avance 300 spectrometer (300 MHz) or a Bruker Avance 2+ 600 MHz NMR spectrometer using $CDCl_3$ and DMSO-d_6 as solvents unless otherwise noted and tetramethylsilane (TMS) as internal standard. Resonance patterns are reported with the notations s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). The notation bs is used to indicate a broad signal. Coupling constants (J) are reported in hertz (Hz). For the Mass spectrometry, ion source temperature was 150-250 °C, as required. High-resolution ESI-mass spectra were performed with a resolution of 10,000. Thin layer chromatography was carried out using plates coated with 70-230 mesh silica gels. The melting points were determined on a digital apparatus and are uncorrected. All the microwave-assisted experiments were performed on a monomode CEM-Discover microwave reactor (CEM Corporation P.O. Box 200 Matthews, NC 28106) in the standard configuration as delivered, including proprietary software.

Table S1. Starting materials for domino Ugi/Michael reaction.

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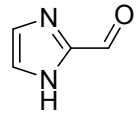
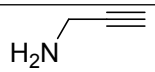
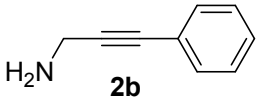
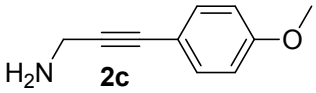
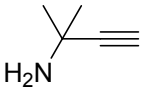
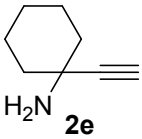
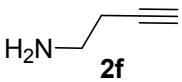
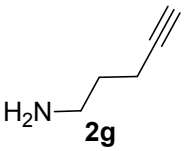
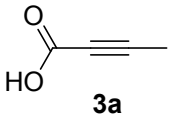
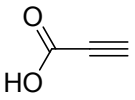
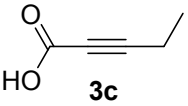
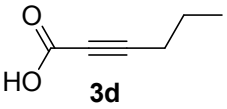
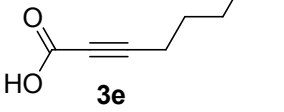
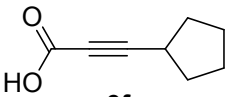
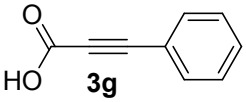
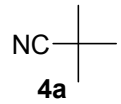
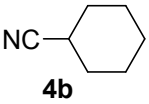
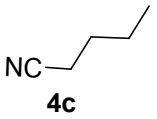
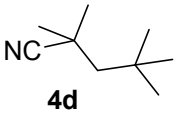
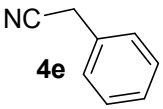
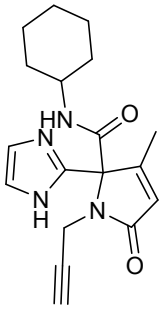
 **1a**	 **2a**  **2b**  **2c**  **2d**  **2e**  **2f**  **2g**	 **3a**  **3b**  **3c**  **3d**  **3e**  **3f**  **3g**	 **4a**  **4b**  **4c**  **4d**  **4e**

General procedure for synthesis of Ugi/Michael products 5a-u

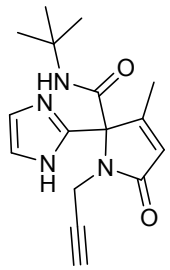
To a solution of imidazole-2-carbaldehyde **1a** (100mg, 1 equiv) in methanol (3 mL) were added successively Na_2SO_4, propargyl amines **2a-g** (1.2 equiv), 2-alkynoic acids **3a-g** (1.2 equiv) and isonitriles **4a-e** (1.2 equiv) in a screw capped vial equipped with a magnetic stir bar. The reaction mixture was stirred at room temperature for 24-48 h and 50 ^oC for 24 h in closed vial. After completion of the reaction, the mixture was diluted with EtOAc (50 mL) and was extracted with water (50 mL). Organic layer was washed with brine (50 mL), dried over magnesium sulfate and evaporated under reduced pressure to obtained residue which was subjected to silica gel column chromatography (1-5 % MeOH in DCM) to afford the desired product **5a-u** as solid.

***N*-cyclohexyl-2-(1*H*-imidazol-2-yl)-3-methyl-5-oxo-1-(prop-2-yn-1-yl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5a)**



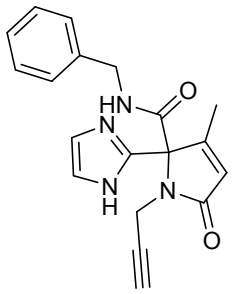
Offwhite solid, Yield 72%, Melting point: 180-182 ^oC. **^{1}H NMR (300 MHz, DMSO-d_6)** δ 12.17 (s, 1H), 10.23 (d, *J*= 7.92Hz, 1H), 7.13-6.99 (m, 2H), 6.00-5.99 (m, 1H), 4.23-4.16 (m, 1H), 3.80-3.73 (m, 1H), 3.71-3.68 (m, 1H), 2.83 (t, *J*= 2.64Hz, 1H), 1.80-1.74 (m, 2H), 1.71 (d, *J*= 1.32Hz, 3H), 1.69-1.52 (m, 3H), 1.37-1.22 (m, 5H). **^{13}C NMR (75 MHz, DMSO-d_6)** δ 171.6, 163.0, 158.7, 141.7, 127.0, 121.7, 117.9, 74.4, 73.4, 48.1, 31.9, 31.8, 30.0, 25.1, 24.1, 12.7. **HRMS** (ESI) calculated for $C_{18}H_{23}N_4O_2$ ($[M+H]^+$) 327.1815, found 327.1818.

***N*-(*tert*-butyl)-2-(1*H*-imidazol-2-yl)-3-methyl-5-oxo-1-(prop-2-yn-1-yl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5b)**



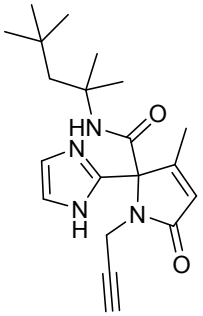
Offwhite solid, Yield 46%, Melting point: 185-187 ^oC. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 11.07 (s, 1H), 9.23 (s, 1H), 7.05-7.05 (m, 2H), 5.90 (s, 1H), 4.24-4.06 (m, 2H), 2.08 (t, *J*= 2.64Hz, 1H)，1.87 (s, 3H), 1.42 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.3, 163.3, 160.5, 141.6, 127.9, 121.2, 117.1, 77.5, 74.6, 72.7, 52.1, 31.0, 28.4, 13.2. **HRMS** (ESI) calculated for $C_{16}H_{21}N_4O_2$ ($[M+H]^+$) 301.1659, found 301.1659.

***N*-benzyl-2-(1*H*-imidazol-2-yl)-3-methyl-5-oxo-1-(prop-2-yn-1-yl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5c)**



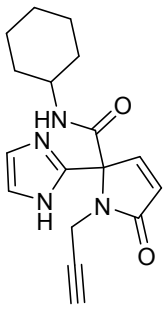
Offwhite solid, Yield 35%, Melting point: 160-162 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 11.13 (s, 1H), 10.07-10.03 (m, 1H), 7.35-7.29 (m, 5H), 7.06-7.05 (m, 2H), 5.91-5.90 (m, 1H), 4.64-4.50 (m, 2H), 4.32-4.26 (m, 1H), 4.10-4.03 (m, 1H), 1.93 (t, *J*= 2.64Hz, 1H)，1.84 (s, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.2, 164.9, 160.4, 141.3, 137.9, 128.6, 127.8, 127.4, 121.3, 117.4, 76.9, 74.2, 72.8, 44.2, 30.8, 13.2. **HRMS** (ESI) calculated for $C_{19}H_{19}N_4O_2$ ($[M+H]^+$) 335.15024, found 334.1504.

2-(1*H*-imidazol-2-yl)-3-methyl-5-oxo-1-(prop-2-yn-1-yl)-*N*-(2,4,4-trimethylpentan-2-yl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5d)



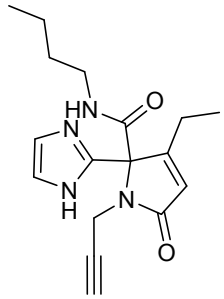
Offwhite solid, Yield 52%, Melting point: 168-170 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 11.07 (s, 1H), 9.31 (s, 1H), 7.06-7.04 (m, 2H), 5.91-5.90 (m, 1H), 4.31-4.25 (m, 1H), 4.09-4.02 (m, 1H), 2.07 (t, *J*= 2.64Hz, 1H)，1.92-1.87 (m, 4H), 1.65 (d, *J*= 14.88Hz, 1H), 1.50 (s, 3H), 1.48 (s, 3H), 1.02 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.2, 163.4, 160.4, 141.4, 128.2, 121.2, 116.8, 77.9, 74.8, 72.7, 56.3, 52.5, 31.6, 31.5, 31.1, 28.4, 28.3, 13.4. **HRMS** (ESI) calculated for $C_{20}H_{29}N_4O_2$ ($[M+H]^+$) 357.2285, found 357.2269.

***N*-cyclohexyl-2-(1*H*-imidazol-2-yl)-3-methyl-5-oxo-1-(prop-2-yn-1-yl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5e)**



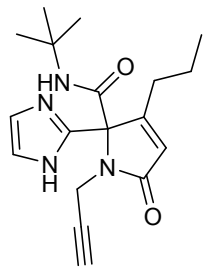
Light yellow solid, Yield 27%, Melting point: 62-64 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 10.61 (s, 1H), 8.39 (d, *J*= 6.96Hz, 1H), 7.09-7.04 (m, 4H), 6.22 (d, *J*= 5.85Hz, 1H), 4.26-4.25 (m, 2H), 3.85-3.75 (m, 1H), 2.20 (t, *J*= 2.64Hz, 1H)，1.96-1.72 (m, 5H), 1.35-1.25 (m, 5H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 172.8, 164.2, 149.3, 140.8, 128.7, 125.6, 116.9, 77.9, 73.1, 49.5, 32.5, 32.4, 31.4, 25.5, 24.7, 24.6. **HRMS** (ESI) calculated for $C_{17}H_{21}N_4O_2$ ($[M+H]^+$) 313.1659, found 313.1658.

***N*-butyl-3-ethyl-2-(1*H*-imidazol-2-yl)-5-oxo-1-(prop-2-yn-1-yl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5f)**



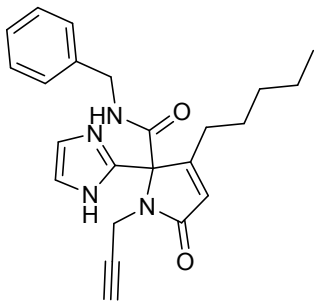
Offwhite solid, Yield 51%, Melting point: 130-131 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 11.17 (s, 1H), 9.54 (s, 1H), 7.06 (s, 2H), 5.92-5.91 (m, 1H), 4.33-4.01 (m, 2H), 3.40-3.33 (m, 2H), 2.31-2.20 (m, 1H), 2.09-1.95 (m, 2H), 1.62-1.57 (m, 2H), 1.44-1.36 (m, 2H), 1.03 (t, *J*= 7.26Hz, 3H), 0.95 (t, *J*= 7.35Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.3, 166.4, 164.8, 141.7, 127.8, 119.4, 117.3, 77.2, 73.9, 72.5, 40.0, 31.3, 30.9, 20.3, 20.2, 13.7, 10.9. **HRMS** (ESI) calculated for $C_{17}H_{23}N_4O_2$ ($[M+H]^+$) 315.1815, found 315.1825.

***N*-(*tert*-butyl)-2-(1*H*-imidazol-2-yl)-5-oxo-1-(prop-2-yn-1-yl)-3-propyl-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5g)**



Offwhite solid, Yield 63%, Melting point: 149-150 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 11.49 (s, 1H), 9.81 (s, 1H), 7.06-7.04 (m, 2H), 5.88-5.87 (m, 1H), 4.32-4.36 (m, 1H), 4.03-3.96 (m, 1H), 2.24-2.13 (m, 1H), 2.03 (t, *J*= 2.64Hz, 1H), 1.98-1.94 (m, 1H), 1.43 (s, 9H), 0.91-0.82 (m, 5H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.4, 165.0, 163.2, 141.8, 127.6, 119.8, 117.2, 77.4, 74.3, 72.5, 52.1, 30.8, 28.8, 28.4, 19.9, 13.6. **HRMS** (ESI) calculated for $C_{18}H_{25}N_4O_2$ ($[M+H]^+$) 329.1972, found 329.1976.

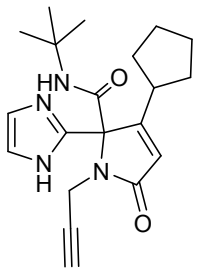
***N*-benzyl-2-(1*H*-imidazol-2-yl)-5-oxo-3-pentyl-1-(prop-2-yn-1-yl)-2,5-dihydro-1H-pyrrole-2-carboxamide (5h)**



Offwhite solid, Yield 45%, Melting point: 115-116 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 11.52 (s, 1H), 10.49 (s, 1H), 7.37-7.29 (m, 5H), 7.07 (s, 1H), 7.03 (s, 1H), 5.88-5.87 (m, 1H), 4.65-4.49 (m, 2H), 4.35-4.28 (m, 1H), 4.04-3.98 (m, 1H), 2.16-2.10 (m, 1H), 2.00-1.95 (m, 1H), 1.91 (t, *J*= 2.55Hz, 1H), 1.38-1.14(m, 4H), 0.81 (t, *J*= 6.69Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.3, 165.1, 165.0, 141.4, 137.8,

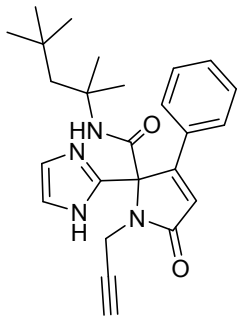
128.6, 127.9, 127.8, 127.4, 119.8, 117.3, 77.5, 74.0, 72.3, 44.2, 31.0, 30.7, 26.8, 26.2, 22.2, 13.9. **HRMS** (ESI) calculated for $C_{23}H_{27}N_4O_2$ ([M+H]$^+$) 391.2134, found 391.2128.

***N*-(*tert*-butyl)-3-cyclopentyl-2-(1*H*-imidazol-2-yl)-5-oxo-1-(prop-2-yn-1-yl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5i)**



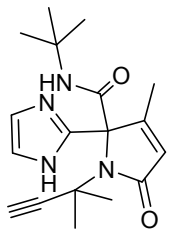
Offwhite solid, Yield 54%, Melting point: 140-142 ^{o}C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 11.4 (s, 1H), 9.54 (s, 1H), 7.05-7.04 (m, 1H), 5.90 (s, 1H), 4.26-3.97 (m, 2H), 2.58-2.48 (m, 1H), 2.03 (t, *J*= 2.64Hz, 1H), 1.97-1.48 (m, 8H), 1.43 (s, 9H), 1.38-0.97 (m, 2H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.5, 170.1, 163.5, 141.7, 127.8, 118.5, 116.9, 77.6, 74.4, 72.4, 52.2, 38.0, 33.1, 30.7, 28.5, 25.2. **HRMS** (ESI) calculated for $C_{20}H_{27}N_4O_2$ ([M+H]$^+$) 355.2128, found 355.2133.

2-(1*H*-imidazol-2-yl)-5-oxo-3-phenyl-1-(prop-2-yn-1-yl)-*N*-(2,4,4-trimethylpentan-2-yl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5j)



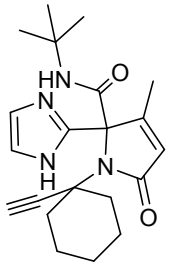
Offwhite solid, Yield 52%, Melting point: 186-187 ^{o}C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 11.4 (s, 1H), 9.86 (s, 1H), 7.33-7.26 (m, 5H), 7.07 (m, 2H), 6.53 (s, 1H), 4.29-3.95 (m, 2H), 2.00 (t, *J*= 2.45Hz, 1H), 1.79-1.60 (m, 2H), 1.40 (s, 3H), 1.38 (s, 3H), 0.98 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 172.0, 162.6, 159.5, 141.4, 130.4, 130.2, 127.3, 127.0, 121.2, 117.9, 104.0, 77.3, 72.4, 71.4, 56.3, 53.0, 31.5, 29.7, 28.0. **HRMS** (ESI) calculated for $C_{25}H_{31}N_4O_2$ ([M+H]$^+$) 419.2441, found 419.2441.

***N*-(*tert*-butyl)-2-(1*H*-imidazol-2-yl)-3-methyl-1-(2-methylbut-3-yn-2-yl)-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5k)**



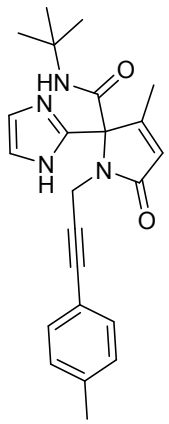
White solid, Yield 57%, Melting point: 207-208 ^{o}C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 10.81 (s, 1H), 8.46 (bs, 1H), 7.06-7.01 (m, 2H), 5.77-5.76 (m, 1H), 2.31 (s, 1H), 1.79 (s, 3H), 1.76 (d, *J*= 1.50Hz, 3H), 1.71 (s, 3H), 1.41 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 172.5, 165.8, 158.7, 142.7, 128.1, 122.2, 116.1, 86.0, 75.8, 71.9, 52.3, 51.9, 28.3, 27.7, 27.5, 12.7. **HRMS** (ESI) calculated for $C_{18}H_{25}N_4O_2$ ([M+H]$^+$) 329.1972, found 329.1978.

***N*-(*tert*-butyl)-1-(1-ethynylcyclohexyl)-2-(1*H*-imidazol-2-yl)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5l)**



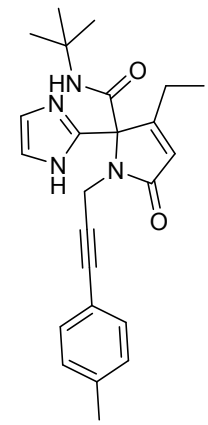
Offwhite solid, Yield 62%, Melting point: 249-251 ^{o}C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 10.86 (s, 1H), 8.76 (bs, 1H), 7.03-7.02 (m, 2H), 5.71-5.70 (m, 1H), 2.54-2.45 (m, 1H), 2.40 (s, 1H), 2.35-2.01(m, 4H), 1.73 (s, 3H), 1.66-1.53 (m, 5H), 1.41 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 172.6, 165.6, 158.6, 143.1, 127.8, 122.3, 116.1, 83.0, 75.9, 75.6, 58.4, 51.8, 33.9, 33.6, 28.3, 24.9, 23.3, 12.6. **HRMS** (ESI) calculated for $C_{21}H_{29}N_4O_2$ ([M+H]$^+$) 369.2285, found 369.2279.

***N*-(*tert*-butyl)-2-(1*H*-imidazol-2-yl)-3-methyl-5-oxo-1-(3-(*p*-tolyl)prop-2-yn-1-yl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5m)**



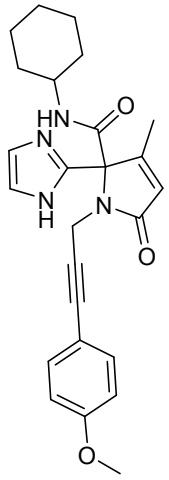
White solid, Yield 42%, Melting point: 189-190 ^{o}C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 11.40 (s, 1H), 9.83 (s, 1H), 7.10-7.05 (m, 6H), 5.90-5.89 (m, 1H), 4.63-4.20 (m, 2H), 2.32 (s, 3H), 1.86 (d, *J*= 1.32Hz, 3H), 1.36 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.6, 163.4, 160.5, 142.2, 138.4, 131.6, 128.9, 128.0, 121.3, 119.3, 117.2, 85.2, 81.9, 74.8, 52.0, 32.3, 28.4, 21.5, 13.2. **HRMS** (ESI) calculated for $C_{23}H_{27}N_4O_2$ ([M+H]$^+$) 391.2128, found 391.2126.

***N*-(*tert*-butyl)-3-ethyl-2-(1*H*-imidazol-2-yl)-5-oxo-1-(3-(*p*-tolyl)prop-2-yn-1-yl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5n)**



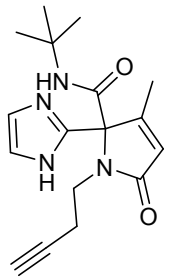
Offwhite solid, Yield 48%, Melting point: 171-173 ^{o}C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 11.36 (s, 1H), 9.77 (s, 1H), 7.10-7.03(m, 6H), 5.90-5.89 (m, 1H), 4.68 (d, *J*= 17.70Hz, 1H), 4.22 (d, *J*= 17.88Hz, 1H), 2.31 (s, 3H), 2.28-1.99 (m, 2H), 1.35 (s, 9H), 1.01 (t, *J*= 7.35Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.6, 166.5, 163.5, 142.4, 138.4, 131.5, 128.8, 127.9, 119.4, 119.3, 117.1, 85.1, 81.9, 74.5, 52.0, 32.2, 28.4, 21.5, 20.3, 11.0. **HRMS** (ESI) calculated for $C_{24}H_{29}N_4O_2$ ([M+H]$^+$) 405.2285, found 405.2285.

***N*-cyclohexyl-3-ethyl-2-(1*H*-imidazol-2-yl)-1-(3-(4-methoxyphenyl)prop-2-yn-1-yl)-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5o)**



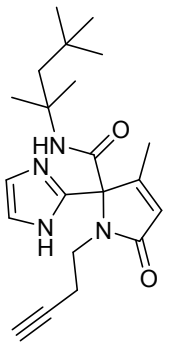
Offwhite solid, Yield 21%, Melting point: 179-181 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 11.19 (s, 1H), 9.47 (*d*, *J*= 7.32Hz, 1H), 7.16-7.13 (m, 2H), 7.08-7.06 (m, 2H), 6.79-6.77 (m, 2H), 5.92-5.91 (m, 1H), 4.56-4.29 (m, 2H), 3.83-3.81 (m, 1H), 3.80 (s, 3H), 1.88 (d, *J*= 1.14Hz, 3H), 1.71-1.55 (m, 5H), 1.34-1.30 (m, 5H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.4, 164.1, 160.3, 159.6, 141.9, 133.2, 128.3, 121.4, 117.0, 114.4, 113.7, 85.1, 81.2, 74.4, 55.3, 49.1, 32.5, 32.3, 25.5, 24.6, 13.2. **HRMS** (ESI) calculated for $C_{25}H_{29}N_4O_3$ ($[M+H]^+$) 433.2234, found 433.2237.

1-(but-3-yn-1-yl)-*N*-(*tert*-butyl)-2-(1*H*-imidazol-2-yl)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5p)



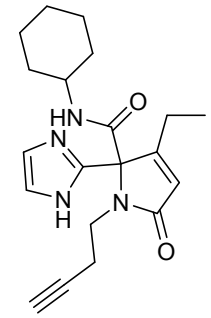
White solid, Yield 51%, Melting point: 185-186 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 11.70 (s, 1H), 10.17, 7.08-7.06 (m, 2H), 5.76-5.75 (m, 1H), 3.54-3.28 (m, 2H), 2.58-2.39 (m, 2H), 1.93 (t, *J*= 2.45Hz, 1H), 1.79 (d, *J*= 1.50Hz, 3H), 1.44 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.9, 163.1, 160.0, 141.6, 127.9, 121.8, 117.8, 81.7, 75.2, 69.8, 52.1, 41.1, 28.4, 17.4, 13.1. **HRMS** (ESI) calculated for $C_{17}H_{23}N_4O_2$ ($[M+H]^+$) 315.1815, found 315.1814.

1-(but-3-yn-1-yl)-2-(1*H*-imidazol-2-yl)-3-methyl-5-oxo-N-(2,4,4-trimethylpentan-2-yl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5q)



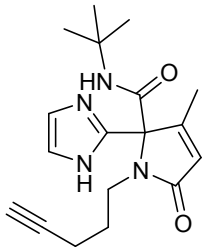
White solid, Yield 71%, Melting point: 167-169 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 11.31 (s, 1H), 9.84 (s, 1H), 7.07 (S, 2H), 5.80 (s, 1H), 3.44-3.37 (m, 2H), 2.60-32.40 (m, 2H), 1.95 (t, *J*= 2.55Hz, 1H), 1.81 (d, *J*= 1.20Hz, 3H), 1.67-1.62 (m, 2H), 1.50 (s, 3H), 1.02 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.8, 162.6, 160.0, 141.5, 127.7, 121.8, 117.9, 81.5, 75.5, 69.7, 56.1, 52.3, 41.3, 31.5, 28.6, 28.3, 17.2, 13.2. **HRMS** (ESI) calculated for $C_{21}H_{31}N_4O_2$ ($[M+H]^+$) 371.2441, found 371.2453.

1-(but-3-yn-1-yl)-*N*-cyclohexyl-3-ethyl-2-(1*H*-imidazol-2-yl)-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5r)



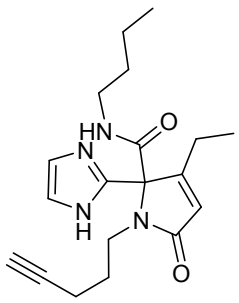
White solid, Yield 73%, Melting point: 201-202 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 11.97 (s, 1H), 10.40 (d, *J*= 7.14Hz, 1H), 7.11 (s, 1H), 7.06 (s, 1H), 5.71 (s, 1H), 3.90-3.80 (m, 1H), 3.54-3.29 (m, 2H), 2.50-2.44 (m, 2H), 2.23-2.11(m, 1H), 2.01-1.23 (m, 12H), 0.99 (t, *J*= 7.34Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.8, 166.0, 163.6, 141.7, 127.8, 119.8, 117.9, 81.5, 74.7, 69.7, 49.2, 41.1, 32.5(2), 25.6, 24.7, 24.6, 20.2, 17.4, 11.0. **HRMS** (ESI) calculated for $C_{20}H_{27}N_4O_2$ ($[M+H]^+$) 355.2128, found 355.2126.

***N*-(*tert*-butyl)-2-(1H-imidazol-2-yl)-3-methyl-5-oxo-1-(pent-4-yn-1-yl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5s)**



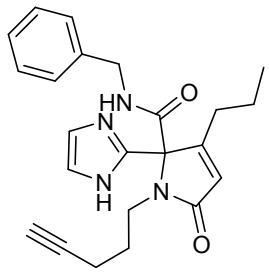
White solid, Yield 34%, Melting point: 191-192 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** *δ* 11.97 (s, 1H), 10.33 (s, 1H), 7.10-7.04 (m, 2H), 5.74-5.73 (m, 1H), 3.50-3.39 (m, 1H), 3.22-3.12 (m, 1H), 2.14-2.12 (m, 2H), 1.83 (t, *J*= 2.64Hz, 1H), 1.78 (d, *J*= 1.32Hz, 3H), 1.69-1.66 (m, 2H), 1.44 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** *δ* 173.9, 163.2, 159.7, 141.9, 127.5, 121.9, 118.0, 83.4, 75.0, 68.7, 52.0, 41.3, 28.4, 26.4, 16.4, 13.0. **HRMS** (ESI) calculated for $C_{18}H_{25}N_4O_2$ ($[M+H]^+$) 329.1972, found 329.1975.

***N*-butyl-3-ethyl-2-(1*H*-imidazol-2-yl)-5-oxo-1-(pent-4-yn-1-yl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5t)**



White solid, Yield 46%, Melting point: 167-169 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** *δ* 12.12 (s, 0.55H), 11.87 (s, 0.45H), 10.43-10.39 (m, 1H), 7.12-7.02 (m, 2H), 5.72-5.69 (m, 1H), 3.92-3.84 (m, 1H), 3.45-3.18 (m, 2H), 2.19-1.62 (m, 12H), 1.48-1.38 (m, 5H), 1.02-0.97 (m, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** *δ* 173.8, 173.1, 165.6, 164.6, 164.3, 163.8, 142.6, 142.0, 127.6, 127.1, 121.2, 120.1, 118.0, 117.7, 83.4, 74.5, 73.8, 68.7, 55.1, 49.0, 48.9, 41.3, 32.5, 30.1, 29.6, 26.3, 26.1, 25.6, 25.4, 24.6, 20.2, 16.4, 11.0, 10.9. **HRMS** (ESI) calculated for $C_{21}H_{29}N_4O_2$ ($[M+H]^+$) 369.2285, found 369.2280.

***N*-benzyl-2-(1*H*-imidazol-2-yl)-5-oxo-1-(pent-4-yn-1-yl)-3-propyl-2,5-dihydro-1*H*-pyrrole-2-carboxamide (5u)**

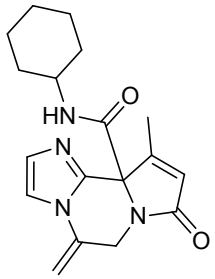


White solid, Yield 55%, Melting point: 201-202 ^{o}C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 12.00 (s, 0.50H), 11.20 (s, 0.50H), 10.93 (s, 0.50H), 10.14 (s, 0.50H), 7.36-6.91(m, 7H), 5.77-5.69 (m, 1H), 4.59 (t, *J*= 4.80Hz, 1H), 4.44 (s, 1H), 4.33 (d, *J*= 5.40Hz, 1H), 3.43-3.17 (m, 1H), 2.09-2.04 (m, 1H), 1.82-1.26 (m, 7H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.7, 165.1, 165.0, 159.7, 159.5, 141.6, 141.3, 138.1, 137.9, 135.7, 129.3, 128.7, 127.8, 127.7, 127.6, 127.5, 127.4, 122.2, 122.1, 118.1, 117.6, 83.3, 74.8, 74.4, 68.8, 46.0, 44.2, 44.0, 41.4, 26.2, 16.3, 13.1. **HRMS** (ESI) calculated for $C_{21}H_{23}N_4O_2$ ($[M+H]^+$) 363.1815, found 363.1818.

General procedure for synthesis of triheterocycles 6a-u under microwave irritation

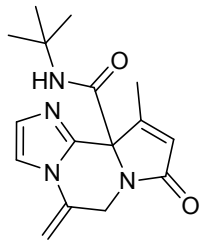
To a sealed large (10 mL) microwave process vial, $AgSbF_6$ (5 mol%) were loaded along with water (2 mL). Ugi/Michael products **5a-u** (0.1 mmol) was added. The reaction vial was evacuated, backfilled with nitrogen (5 cycles) and was stirred at 120 °C for 0.5 h under microwave irritation. After completion, the reaction mixture was cooled to ambient temperature and the reaction mixture was extracted three times with ethyl acetate (20 mL×3). The combined organic phase was washed with brine solution, dried with MgSO4 and concentrated. The residue was subjected to silica gel column chromatography (1-3 % MeOH in DCM) to afford the desired triheterocycles **6a-u** as solid. In the case of synthesis of **6m**, **6n** and **6o**, the reactions were run at 70 °C for 12 h using $CHCl_3$ (2 mL) as solvent in oil bath.

***N*-cyclohexyl-10-methyl-5-methylene-8-oxo-5,6,8,10a-tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine-10a-carboxamide (6a)**



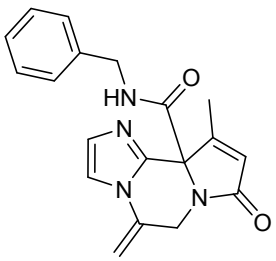
White solid, Yield 98%, Melting point: 147-148 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.42 (d, *J*= 7.53Hz, 1H), 7.28 (d, *J*= 1.50Hz, 1H), 7.137.42 (d, *J*= 1.53Hz, 1H), 5.98-5.96 (m, 1H), 5.08 (s, 1H), 5.03 (d, *J*= 15.63Hz, 1H), 4.86 (s, 1H), 3.84 (d, *J*= 15.63Hz, 1H), 3.79-3.73 (m, 1H), 2.37 (d, *J*= 1.50Hz, 3H), 1.97-1.61 (m, 5H), 1.42-1.12 (m, 5H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.0, 162.6, 158.2, 140.0, 134.6, 129.8, 123.7, 115.4, 97.8, 71.6, 49.1, 39.5, 32.7, 32.6, 25.4, 24.5, 14.4. **HRMS** (ESI) calculated for $C_{18}H_{23}N_4O_2$ ($[M+H]^+$) 327.1815, found 327.1817.

***N*-(*tert*-butyl)-10-methyl-5-methylene-8-oxo-5,6,8,10a-tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine-10a-carboxamide (6b)**



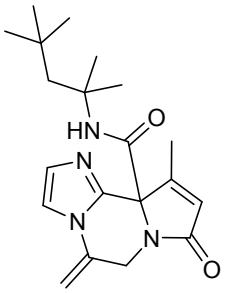
White solid, Yield 91%, Melting point: 218-219 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.35 (s, 1H), 7.29 (s, 1H), 7.13 (s, 1H), 5.97 (s, 1H), 5.08 (s, 1H), 5.02 (d, *J*= 15.63Hz, 1H), 4.86 (s, 1H), 3.82 (d, *J*= 15.63Hz, 1H), 2.38 (s, 3H), 1.34 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.1, 162.5, 158.4, 140.2, 134.6, 129.8, 123.6, 115.3, 97.7, 72.0, 52.2, 39.6, 28.4, 14.4. **HRMS** (ESI) calculated for $C_{16}H_{21}N_4O_2$ ($[M+H]^+$) 301.1659, found 301.1656.

***N*-benzyl-10-methyl-5-methylene-8-oxo-5,6,8,10a-tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine-10a-carboxamide (6c)**



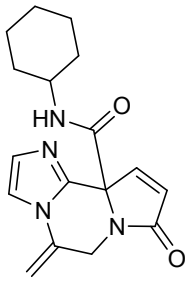
White solid, Yield 90%, Melting point: 51-52 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.84 (s, 1H), 7.37-7.23 (m, 6H), 7.11-7.10 (m, 1H), 5.97-5.96 (m, 1H), 5.09-5.00 (m, 2H), 4.87-4.86 (m, 1H), 4.61-4.54 (m, 1H), 4.37-4.31 (m, 1H), 3.89-3.83 (m, 1H), 2.31 (s, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 170.0, 163.9, 158.2, 139.7, 137.4, 134.5, 129.9, 128.8, 127.8, 123.7, 115.4, 98.0, 71.6, 44.4, 39.6, 14.4. **HRMS** (ESI) calculated for $C_{19}H_{19}N_4O_2$ ($[M+H]^+$) 335.15024, found 334.1500.

10-methyl-5-methylene-8-oxo-*N*-(2,4,4-trimethylpentan-2-yl)-5,6,8,10a-tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine-10a-carboxamide (6d)



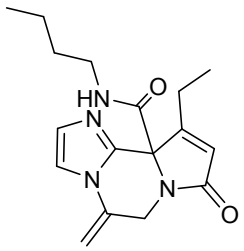
White solid, Yield 89%, Melting point: 189-190 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.33 (s, 1H), 7.27 (d, *J*= 1.50Hz, 1H), 1.34 (d, *J*= 1.50Hz, 1H), 5.98-5.97 (m, 1H), 5.08-5.06 (m, 2H), 5.03 (d, *J*= 15.81Hz, 1H), 4.86-4.84 (m, 1H), 3.84 (d, *J*= 16.20Hz, 1H), 2.39 (s, 3H), 1.96 (d, *J*= 14.88Hz, 1H), 1.44 (s, 3H), 1.38 (d, *J*= 14.48Hz, 1H), 1.36 (s, 3H), 0.84 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 170.8, 162.1, 158.0, 140.2, 134.5, 129.7, 123.7, 115.2, 97.7, 72.1, 56.0, 51.7, 39.4, 31.5, 31.2, 28.8, 28.7, 14.5. **HRMS** (ESI) calculated for $C_{20}H_{29}N_4O_2$ ($[M+H]^+$) 357.2285, found 357.2280.

***N*-cyclohexyl-5-methylene-8-oxo-5,6,8,10a-tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine-10a-carboxamide (6e)**



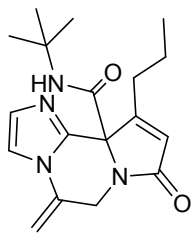
White solid, Yield 87%, Melting point: 136-138 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.38 (d, *J*= 5.85Hz, 1H), 7.34 (s, 1H), 7.28 (d, *J*= 1.14Hz, 1H), 7.12 (d, *J*= 1.11Hz, 1H), 6.29 (d, *J*= 5.82Hz, 1H), 5.09 (s, 1H), 5.05 (d, *J*= 16.38Hz, 1H), 4.87 (s, 1H), 4.05 (d, *J*= 16.02Hz, 1H), 3.76-3.68 (m, 1H), 1.94-1.61 (m, 5H), 1.40-1.12 (m, 5H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 170.0, 162.6, 146.3, 140.4, 134.7, 129.9, 128.2, 115.0, 98.0, 70.3, 49.3, 39.4, 32.6, 32.5, 25.4, 24.5. **HRMS** (ESI) calculated for $C_{17}H_{21}N_4O_2$ ($[M+H]^+$) 313.1659, found 313.1665.

***N*-butyl-10-ethyl-5-methylene-8-oxo-5,6,8,10a-tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine-10a-carboxamide (6f)**



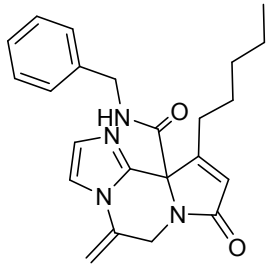
White solid, Yield 97%, Melting point: 108-110 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.47-7.43 (m, 1H), 7.29 (d, *J*= 1.32Hz, 1H), 7.13 (d, *J*= 1.32Hz, 1H), 5.97 (s, 1H), 5.08 (s, 1H), 5.03 (d, *J*= 15.63Hz, 1H), 4.86 (s, 1H), 3.83 (d, *J*= 15.60Hz, 1H), 3.38-3.05 (m, 3H), 2.56-2.46 (m, 1H), 1.55-1.46 (m, 2H), 1.38-1.26 (m, 2H), 1.20 (t, *J*= 7.25Hz, 3H), 0.92 (t, *J*= 7.25Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.0, 164.2, 163.9, 140.1, 134.5, 129.8, 121.4, 115.5, 97.9, 71.6, 40.2, 39.5, 31.3, 21.2, 20.0, 13.7, 10.9. **HRMS** (ESI) calculated for $C_{17}H_{23}N_4O_2$ ($[M+H]^+$) 315.1815, found 315.1820.

***N*-(*tert*-butyl)-5-methylene-8-oxo-10-propyl-5,6,8,10a-tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine-10a-carboxamide (6g)**



White solid, Yield 94%, Melting point: 218 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.29-7.26 (m, 2H), 7.13 (d, *J*= 1.29Hz, 1H), 5.96 (s, 1H), 5.08 (s, 1H), 5.02 (d, *J*= 15.63Hz, 1H), 4.86 (s, 1H), 3.81 (d, *J*= 15.63Hz, 1H), 3.06-2.94 (m, 1H), 2.53-2.43 (m, 1H), 1.71-1.57 (m, 2H), 1.34 (s, 9H), 1.02 (d, *J*= 7.34Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.2, 163.0, 162.6, 140.2, 134.6, 129.7, 121.6, 115.4, 97.7, 72.0, 52.2, 39.5, 29.7, 28.4, 20.0, 13.8. **HRMS** (ESI) calculated for $C_{18}H_{25}N_4O_2$ ($[M+H]^+$) 329.1972, found 329.1973.

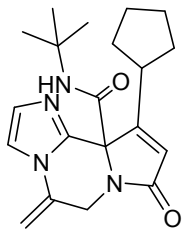
***N*-benzyl-5-methylene-8-oxo-10-pentyl-5,6,8,10a-tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine-10a-carboxamide (6h)**



White solid, Yield 88%, Melting point: 139-140 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.85-7.82 (m, 1H), 7.37-7.24 (m, 6H), 7.12-7.11 (m, 1H), 5.95-5.94 (m, 1H), 5.08 (s, 1H), 5.03 (d, *J*= 15.81Hz, 1H), 4.86 (s, 1H), 4.61-4.54 (m, 1H), 4.36-4.30 (m, 1H), 3.85 (d, *J*= 15.81Hz, 1H), 3.00-2.89 (m, 1H), 2.45-2.34 (m, 1H), 1.57-1.47 (m, 2H), 1.32-1.25 (m, 2H), 0.90-0.86 (m, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.2, 164.1, 163.2, 139.8, 137.4, 134.4, 129.9, 128.8, 127.8, 127.7, 121.6, 115.4, 98.0, 71.6, 44.4, 39.6, 31.2,

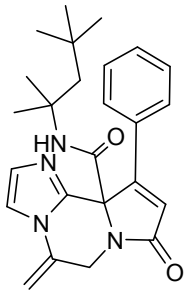
27.7, 26.2, 22.3, 14.0. **HRMS** (ESI) calculated for $C_{23}H_{27}N_4O_2$ ($[M+H]^+$) 391.2134, found 391.2128.

***N*-(*tert*-butyl)-10-cyclopentyl-5-methylene-8-oxo-5,6,8,10a-tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine-10a-carboxamide (6i)**



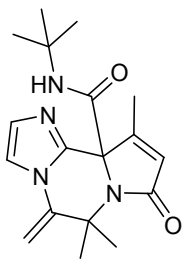
Offwhite solid, Yield 86%, Melting point: 182-183 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.28 (s, 1H), 7.14 (s, 1H), 7.10 (s, 1H), 5.99 (s, 1H), 5.07 (s, 1H), 4.99 (d, *J*= 15.63Hz, 1H), 4.84 (s, 1H), 3.78 (d, *J*= 15.63Hz, 1H), 3.55-3.44(m, 1H), 2.15-2.00 (m, 2H), 1.81-1.64 (m, 4H), 1.55-1.42 (m, 2H), 1.33 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.4, 169.0, 162.5, 140.2, 134.7, 129.8, 120.7, 115.3, 97.6, 72.1, 52.3, 39.4, 38.3, 35.1, 34.4, 28.5, 25.8, 25.3. **HRMS** (ESI) calculated for $C_{20}H_{27}N_4O_2$ ($[M+H]^+$) 355.2128, found 355.2128.

5-methylene-8-oxo-10-phenyl-*N*-(2,4,4-trimethylpentan-2-yl)-5,6,8,10a-tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine-10a-carboxamide (6j)



White solid, Yield 60%, Melting point: 137-139 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.95-7.91 (m, 2H), 7.47-7.44 (m, 3H), 7.29-7.28 (m, 1H), 7.14-7.13 (m, 1H), 6.56 (s, 1H), 6.49-6.48 (m, 1H), 5.13-5.08 (m, 2H), 4.87 (s, 1H), 3.98-3.92 (m, 1H), 1.68-1.62 (m, 1H), 1.35-1.30 (m, 1H), 1.24 (s, 3H), 1.18 (s, 3H), 0.78 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 169.7, 162.9, 159.2, 140.0, 134.6, 131.2, 130.3, 129.8, 129.4, 128.3, 123.9, 115.2, 97.4, 72.5, 56.2, 52.5, 39.3, 31.4, 31.1, 28.3, 27.7. **HRMS** (ESI) calculated for $C_{25}H_{31}N_4O_2$ ($[M+H]^+$) 419.2441, found 419.2438.

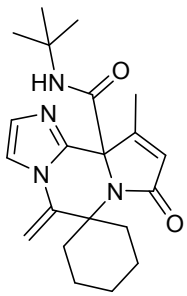
***N*-(*tert*-butyl)-6,6,10-trimethyl-5-methylene-8-oxo-5,6,8,10a-tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine-10a-carboxamide (6k)**



White solid, Yield 85%, Melting point: 186-188 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.29 (s, 1H), 7.19 (d, *J*= 1.14Hz, 1H), 7.14 (d, *J*= 1.32Hz, 1H), 5.86-5.85(m, 1H), 5.07 (d, *J*= 2.28Hz, 1H), 4.97 (d, *J*= 2.46Hz, 1H), 2.30 (d, *J*= 1.32Hz, 1H), 1.99 (s, 3H), 1.50 (s, 3H), 1.31 (s, 9H). **^{13}C NMR (75 MHz,**

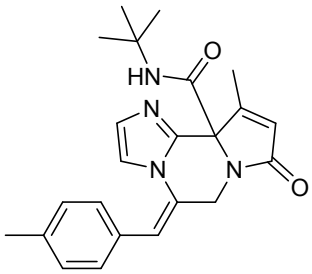
$CDCl_3$) δ 172.7, 164.0, 156.6, 144.5, 140.9, 129.5, 125.3, 116.8, 97.7, 73.4, 57.7, 51.8, 28.2, 26.7, 24.6, 14.1. **HRMS** (ESI) calculated for $C_{18}H_{25}N_4O_2$ ($[M+H]^+$) 329.1972, found 329.1964.

***N*-(*tert*-butyl)-10'-methyl-5'-methylene-8'-oxo-8',10a'-dihydro-5'*H*-spiro[cyclohexane-1,6'-imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine]-10a'-carboxamide (6l)**



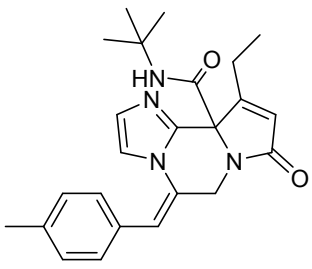
White solid, Yield 55%, Melting point: 202-203 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 8.22 (s, 1H), 7.16-7.13 (m, 2H), 5.83-5.81 (m, 1H), 5.04 (d, *J*= 2.28Hz, 1H), 4.94 (d, *J*= 2.46Hz, 1H), 3.46-3.38 (m, 1H), 2.18 (d, *J*= 1.32Hz, 3H), 1.96-1.71 (m, 6H), 1.35 (s, 9H), 1.31-1.21 (m, 4H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 174.3, 163.8, 157.9, 144.0, 140.4, 129.4, 125.3, 116.7, 97.2, 73.6, 60.6, 51.7, 36.0, 31.7, 28.2, 25.8, 22.7, 22.2, 13.5. **HRMS** (ESI) calculated for $C_{21}H_{29}N_4O_2$ ($[M+H]^+$) 369.2285, found 369.2286.

(*Z*)-*N*-(*tert*-butyl)-10-methyl-5-(4-methylbenzylidene)-8-oxo-5,6,8,10a-tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine-10a-carboxamide (6m) ZL-1275



White solid, Yield 92%, Melting point: 175-176 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.78 (s, 1H), 7.15-7.04 (m, 1H), 6.91 (d, *J*= 1.32Hz, 1H), 6.78 (d, *J*= 1.14Hz, 1H), 6.28 (s, 1H), 6.02 (s, 1H), 4.93 (d, *J*= 14.88Hz, 1H), 3.85 (d, *J*= 14.49Hz, 1H), 2.35 (s, 6H), 1.34(s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.8, 162.7, 158.6, 140.9, 138.1, 130.4, 129.5, 128.5, 126.8, 123.9, 118.8, 116.1, 72.6, 52.1, 42.7, 28.4, 21.3, 14.3. **HRMS** (ESI) calculated for $C_{23}H_{27}N_4O_2$ ($[M+H]^+$) 391.2128, found 391.2122.

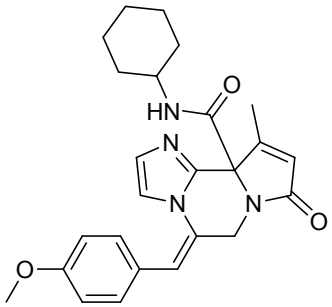
(*Z*)-*N*-(*tert*-butyl)-10-ethyl-5-(4-methylbenzylidene)-8-oxo-5,6,8,10a-tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine-10a-carboxamide (6n)



White solid, Yield 83%, Melting point: 158-159 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.73 (s, 1H), 7.14-7.04 (m, 1H), 6.91 (s, 1H), 6.79 (s, 1H), 6.28 (s, 1H), 6.02 (s, 1H), 4.93 (d, *J*= 14.67Hz, 1H), 3.84 (d, *J*= 14.70Hz, 1H), 3.00-2.96 (m, 1H), 2.58-2.45 (m, 1H), 2.35(s, 3H), 1.33 (s, 9H), 1.23(t, *J*= 7.25Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.8,

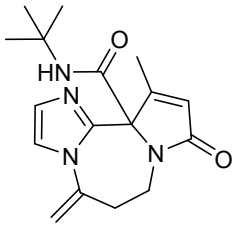
164.6, 162.9, 141.0, 138.1, 130.4, 129.5, 128.5, 128.4, 126.8, 121.5, 118.8, 116.2, 72.6, 52.1, 42.6, 28.4, 21.3, 21.1, 10.9. **HRMS** (ESI) calculated for $C_{24}H_{29}N_4O_2$ ($[M+H]^+$) 405.2285, found 405.2276.

(*Z*)-*N*-cyclohexyl-5-(4-methoxybenzylidene)-10-methyl-8-oxo-5,6,8,10a-tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine-10a-carboxamide (6o)



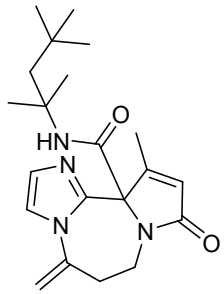
Offwhite solid, Yield 63%, Melting point: 158-160 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.87 (d, *J*= 7.92Hz, 1H), 7.10-7.08 (m, 2H), 6.93-6.82 (m, 4H), 6.26 (s, 1H), 6.02-6.01 (m, 1H), 4.93 (d, *J*= 14.88Hz, 1H), 3.84 (d, *J*= 14.88Hz, 1H), 3.82 (s, 3H), 3.77-3.72 (m, 1H), 2.36 (d, *J*= 1.32Hz, 1H), 1.77-1.61 (m, 5H), 1.41-1.17 (m, 5H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.7, 162.8, 159.3, 158.5, 140.7, 130.0, 128.6, 126.4, 125.5, 123.9, 118.7, 115.9, 114.2, 72.3, 55.3, 49.0, 42.7, 32.6(2), 25.4, 24.4, 14.3. **HRMS** (ESI) calculated for $C_{25}H_{29}N_4O_3$ ($[M+H]^+$) 433.2234, found 433.2232.

***N*-(*tert*-butyl)-11-methyl-5-methylene-9-oxo-6,7,9,11a-tetrahydro-5*H*-imidazo[1,2-*a*]pyrrolo[2,1-*c*][1,4]diazepine-11a-carboxamide (6p)**



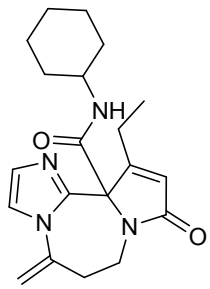
White solid, Yield 95%, Melting point: 167-168 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.50 (s, 1H), 7.03-7.02 (m, 1H), 7.00-6.98 (m, 1H), 5.94-5.93 (m, 1H), 5.10 (s, 1H), 5.03 (s, 1H), 4.39-4.30 (m, 1H), 3.36-3.27 (m, 1H), 2.93-2.84 (m, 1H), 2.59-2.49 (m, 1H), 2.33 (s, 3H), 1.33 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.8, 163.1, 158.3, 142.0, 141.7, 128.0, 123.6, 121.5, 109.7, 75.2, 52.1, 39.0, 33.3, 28.4, 15.0. **HRMS** (ESI) calculated for $C_{17}H_{23}N_4O_2$ ($[M+H]^+$) 315.1815, found 315.1812.

11-methyl-5-methylene-9-oxo-*N*-(2,4,4-trimethylpentan-2-yl)-6,7,9,11a-tetrahydro-5*H*-imidazo[1,2-*a*]pyrrolo[2,1-*c*][1,4]diazepine-11a-carboxamide (6q)



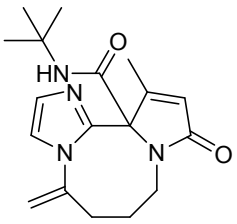
White solid, Yield 76%, Melting point: 113-115 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.56 (s, 1H), 7.04 (d, *J*= 1.32Hz, 1H), 6.98 (d, *J*= 1.32Hz, 1H), 5.95 (d, *J*= 1.50Hz, 1H), 5.10 (s, 1H), 5.02 (s, 1H), 4.42-4.32 (m, 1H), 3.38-3.29 (m, 1H), 2.92-2.83 (m, 1H), 2.58-2.48 (m, 1H), 2.36 (d, *J*= 1.50Hz, 3H), 1.79 (d, *J*= 14.88Hz, 1H), 1.46 (d, *J*= 14.88Hz, 1H), 1.44 (s, 3H), 1.41 (s, 3H), 0.90 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.8, 162.7, 158.3, 141.9, 141.7, 127.9, 123.6, 121.5, 109.3, 75.3, 56.1, 53.0, 39.0, 33.2, 31.5, 31.4, 28.4, 28.0, 15.2. **HRMS** (ESI) calculated for $C_{21}H_{31}N_4O_2$ ($[M+H]^+$) 371.2441, found 371.2442.

***N*-cyclohexyl-11-ethyl-5-methylene-9-oxo-6,7,9,11a-tetrahydro-5*H*-imidazo[1,2-*a*]pyrrolo[2,1-*c*][1,4]diazepine-11a-carboxamide (6r)**



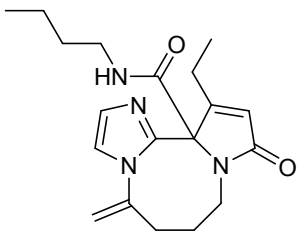
White solid, Yield 93%, Melting point: 152-153 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.69 (d, *J*= 8.10Hz, 1H), 7.04-6.98 (m, 2H), 5.97-5.96 (m, 1H), 5.11(s, 1H), 5.05 (s, 1H), 4.39-4.35 (m, 1H), 3.83-3.75 (m, 1H), 3.33-3.75(m, 1H), 3.12-2.89 (m, 2H), 2.56-2.39 (m, 2H), 1.94-1.22 (m, 10H), 1.16 (t, *J*= 7.25Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.9, 164.2, 163.4, 141.9, 141.6, 128.0, 121.7, 121.3, 110.0, 74.9, 49.0, 38.6, 33.3, 32.7, 32.6, 25.4, 24.5, 21.5, 11.3. **HRMS** (ESI) calculated for $C_{20}H_{27}N_4O_2$ ($[M+H]^+$) 355.2128, found 355.2122.

***N*-(*tert*-butyl)-12-methyl-5-methylene-10-oxo-5,6,7,8,10,12a-hexahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*][1,4]diazocine-12a-carboxamide (6s)**



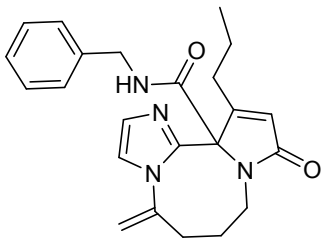
White solid, Yield 52%, Melting point: 163-164 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 10.29 (s, 1H), 7.06 (s, 1H), 6.77 (s, 1H), 5.78-5.77 (m, 1H), 5.08 (d, *J*= 2.25Hz, 1H), 4.81 (d, *J*= 2.28Hz, 1H), 4.27-4.16 (m, 1H), 3.07-3.03 (m, 1H), 2.67-2.57 (m, 1H), 2.45-2.40 (m, 1H), 1.90 (s, 3H), 1.74-1.66 (m, 2H), 1.43 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.3, 162.1, 157.9, 144.4, 142.1, 127.6, 122.2, 122.1, 110.8, 74.2, 51.9, 39.6, 33.2, 28.5, 22.8, 13.0. **HRMS** (ESI) calculated for $C_{18}H_{25}N_4O_2$ ($[M+H]^+$) 329.1972, found 329.1967.

***N*-butyl-12-ethyl-5-methylene-10-oxo-5,6,7,8,10,12a-hexahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*][1,4]diazocine-12a-carboxamide (6t)**



White solid, Yield 41%, Melting point: 169-171 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 10.38 (d, *J*= 7.14Hz, 1H), 7.06 (d, *J*= 1.14Hz, 1H), 6.77 (d, *J*= 1.14Hz, 1H), 5.80-5.78 (m, 1H), 5.08 (d, *J*= 2.18Hz, 1H), 4.80 (d, *J*= 2.18Hz, 1H), 4.27-4.17 (m, 1H), 3.91-3.82 (m, 1H), 3.09-3.02 (m, 1H), 2.66-2.57 (m, 1H), 2.44-2.39 (m, 1H), 2.44-2.10 (m, 2H), 1.98-1.70 (m, 2H), 1.78-1.25 (m, 10H), 0.99 (t, *J*= 7.22Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.4, 164.0, 162.7, 144.4, 142.1, 127.7, 122.1, 120.3, 110.7, 73.7, 49.0, 39.5, 33.2, 32.8, 32.6, 25.6, 24.5, 22.9, 19.9, 11.3. **HRMS** (ESI) calculated for $C_{21}H_{29}N_4O_2$ ($[M+H]^+$) 369.2285, found 369.2278.

***N*-benzyl-5-methylene-10-oxo-12-propyl-5,6,7,8,10,12a-hexahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*][1,4]diazocine-12a-carboxamide (6u)**



White solid, Yield 44%, Melting point: 184 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 10.85-10.81 (m, 1H), 7.37-7.27 (m, 5H), 7.04 (d, *J*= 1.14Hz, 1H), 6.78 (d, *J*= 1.14Hz, 1H), 5.80-5.79 (m, 1H), 5.10 (d, *J*= 2.25Hz, 1H), 4.82 (d, *J*= 2.25Hz, 1H), 4.70-4.48 (m, 2H), 4.30-4.20 (m, 1H), 3.13-3.06 (m, 1H), 2.64-2.57 (m, 1H), 2.45-2.40 (m, 1H), 1.85 (d, *J*= 1.53Hz, 3H), 1.74-1.68 (m, 1H), 1.30-1.26 (m, 1H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.2, 164.0, 157.8, 144.3, 141.6, 138.2, 128.7, 127.8, 127.7, 122.4, 122.3, 111.0, 74.0, 44.5, 44.3, 39.6, 33.2, 22.8, 13.0. **HRMS** (ESI) calculated for $C_{21}H_{23}N_4O_2$ ($[M+H]^+$) 363.1815, found 363.1807.

Crystallographic data for compound 6a

Single crystals of **6a,** suitable for X-ray diffraction were obtained by slow evaporation from MeOH at room temperature. X-ray intensity data were collected at 100K on an Agilent Supernova diffractometer, equipped with an Atlas CCD detector, using Mo Kα radiation (λ = 0.71073 Å). The images were interpreted and integrated with the CrysAlisPro software from Rigaku Oxford Diffraction.[1] Using Olex2,[2] the structures were solved with the ShelxS[3] structure solution program using Direct Methods and refined with the ShelxL[3] refinement package using full-matrix least squares minimization on F^2. Non-hydrogen atoms were anisotropically refined and the hydrogen atoms in the riding mode with isotropic temperature factors were fixed at 1.2 times U_{eq} of the parent atoms (1.5 for methyl groups). Respectively, CCDC 1500316 contains the supplementary crystallographic data for this paper and can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033; or deposit@ccdc.cam.ac.uk).

Crystallographic data

6a, $C_{18}H_{22}N_4O_2$, M =326.39 gmol^{-1}, monoclinic, space group $C2/c$, a = 14.5377(9) Å, b = 14.3910(8) Å, c = 17.5761(15) Å, β = 106.774(8)°, V = 3520.7(5) Å^3, Z = 8, T = 100.00(10) K, μ(MoKα) = 0.083 mm^{-1}, *Dcalc* = 1.232 g/cm^3, 10995 reflections measured (5.15° ≤ 2Θ ≤ 52.744°), 3595 unique (R_{int} = 0.0193, R_{sigma} = 0.0205) which were used in all calculations. The final R_1 was 0.0396 (I > 2σ(I)) and wR_2 was 0.0978 (all data).

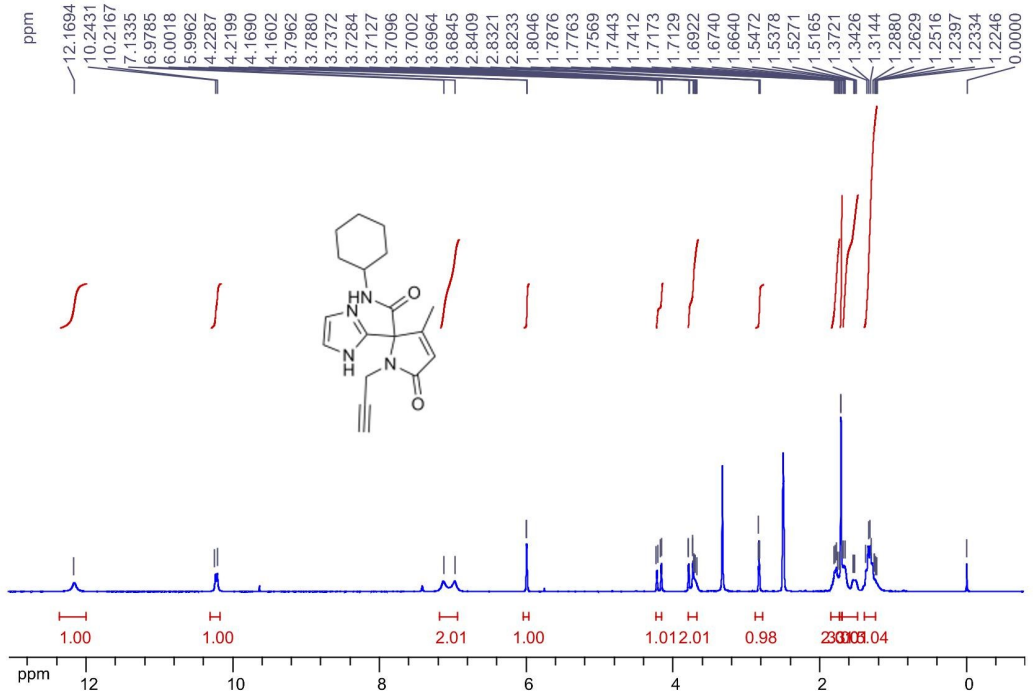
References:

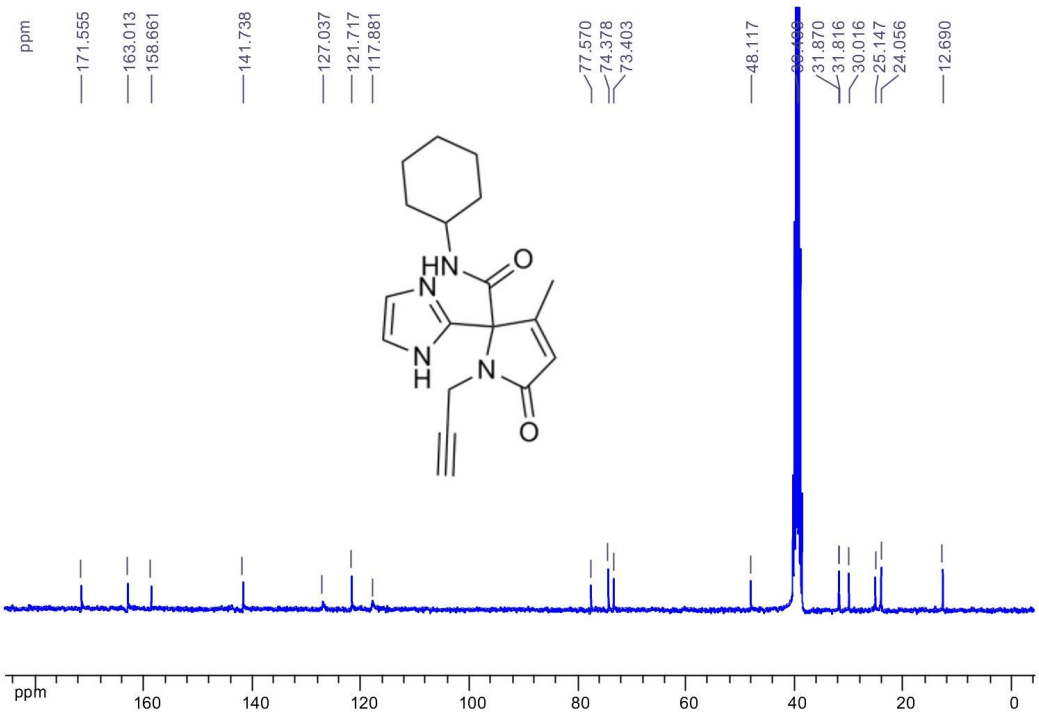
[1] CrysAlis PRO (**2012**). Agilent Technologies UK Ltd, Yarnton, Oxfordshire, England.

[2] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, OLEX2: a complete structure solution, refinement and analysis program. *J. Appl. Cryst.* (**2009**). 42, 339-341.

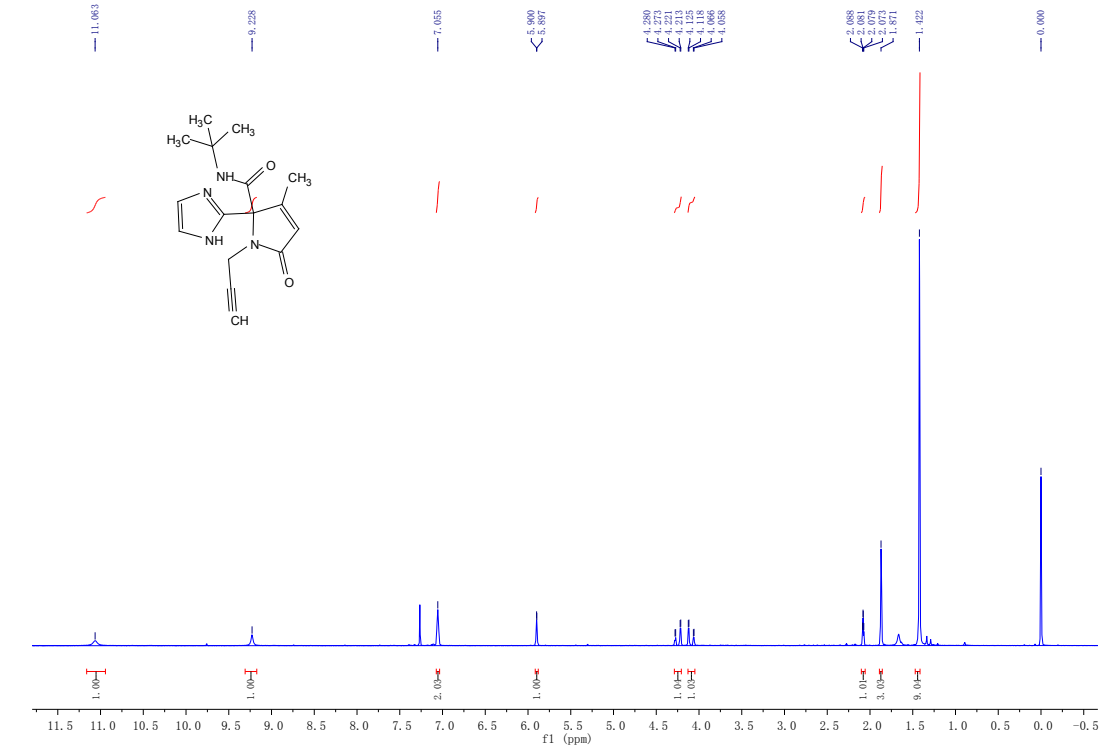
[3] G.M. Sheldrick, *Acta Cryst*. (**2008**). 64, 112-122

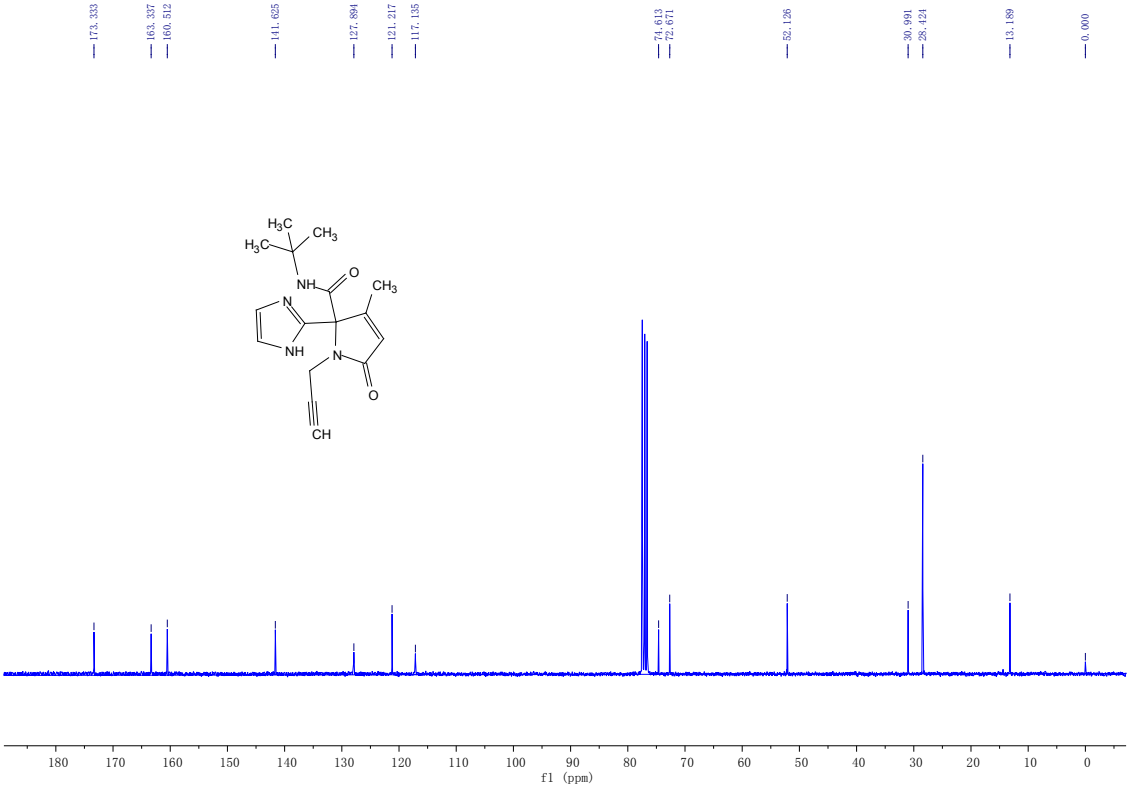
^{1}H and ^{13}C NMR spectra of compound **5a** (300 MHz, DMSO-d_6)



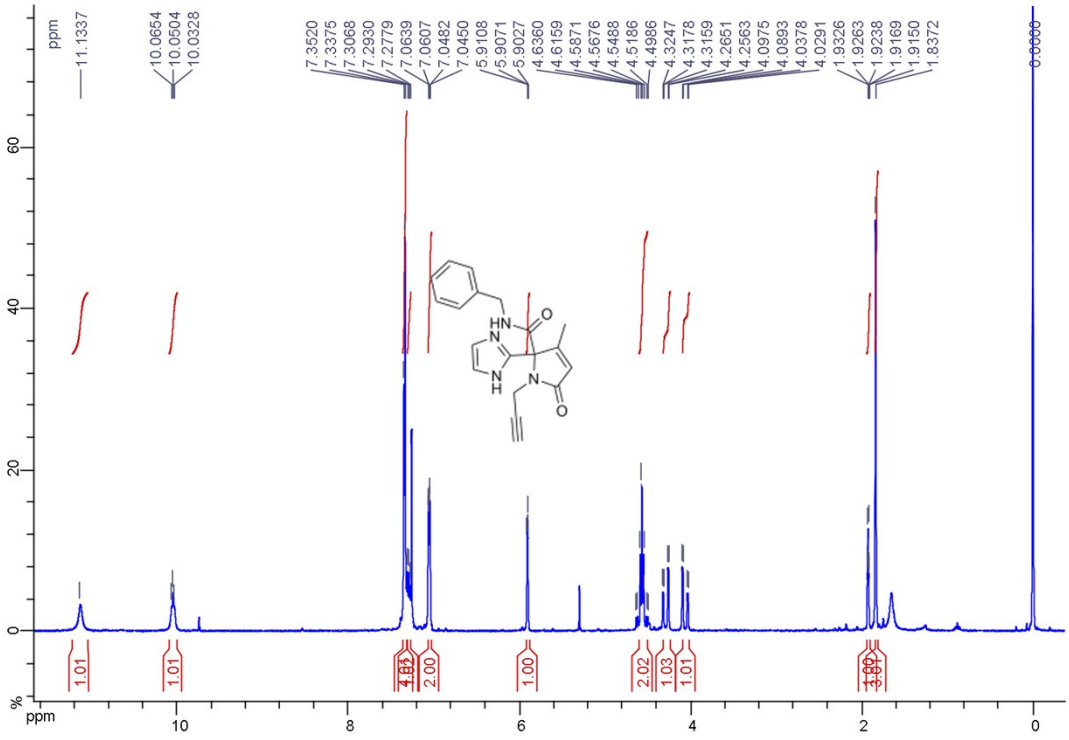


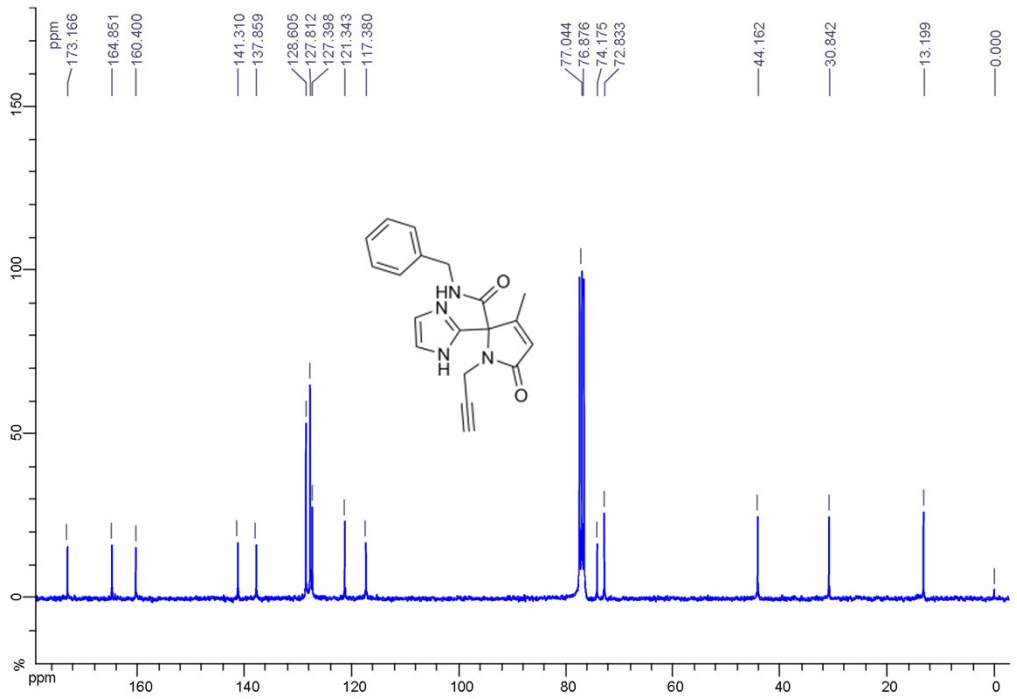
^{1}H and ^{13}C NMR spectra of compound **5b** (300 MHz, $CDCl_3$)



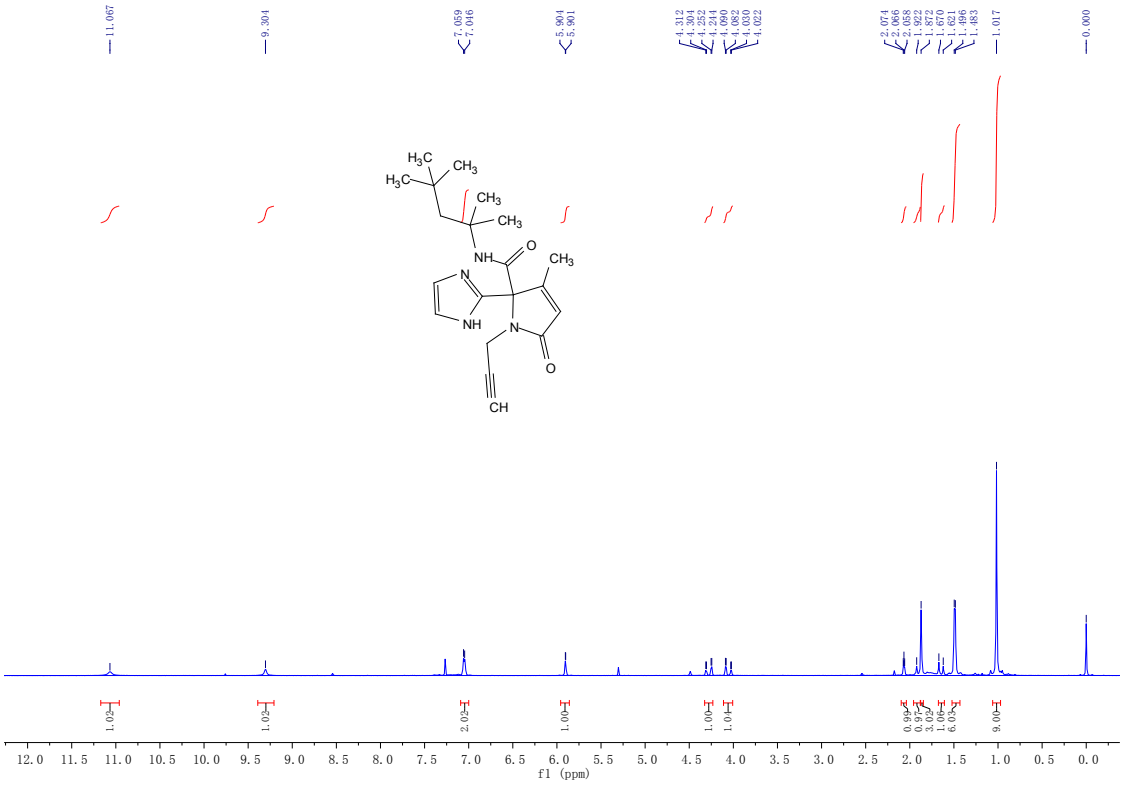


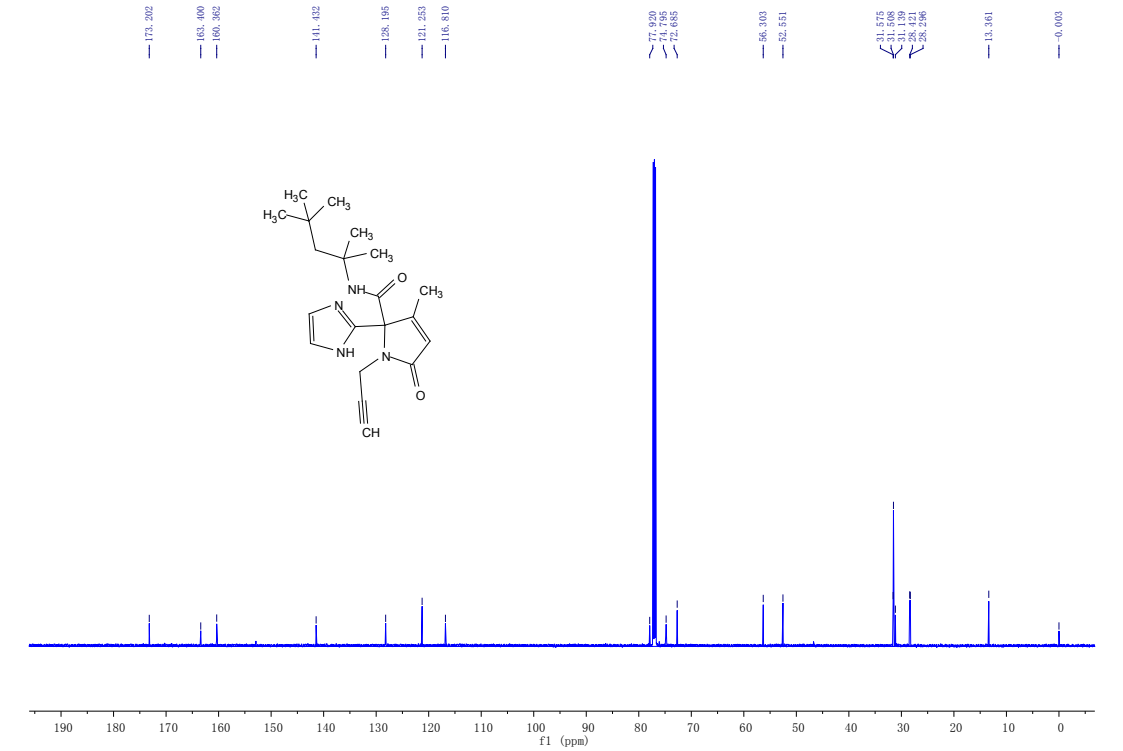
^{1}H and ^{13}C NMR spectra of compound **5c** (300 MHz, $CDCl_3$)



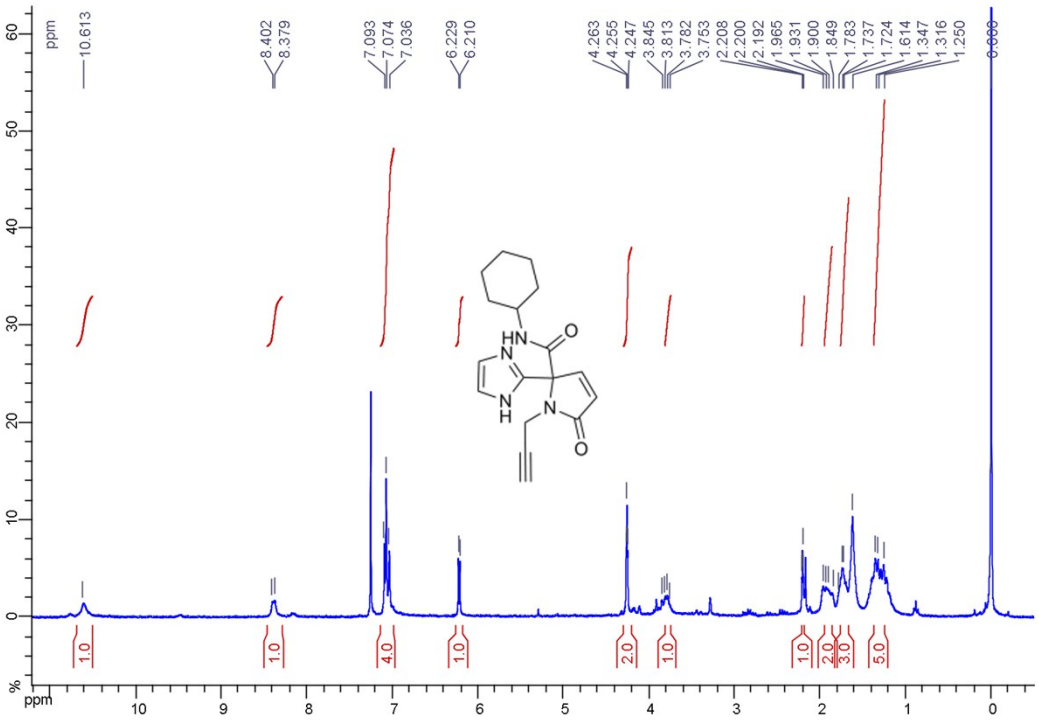


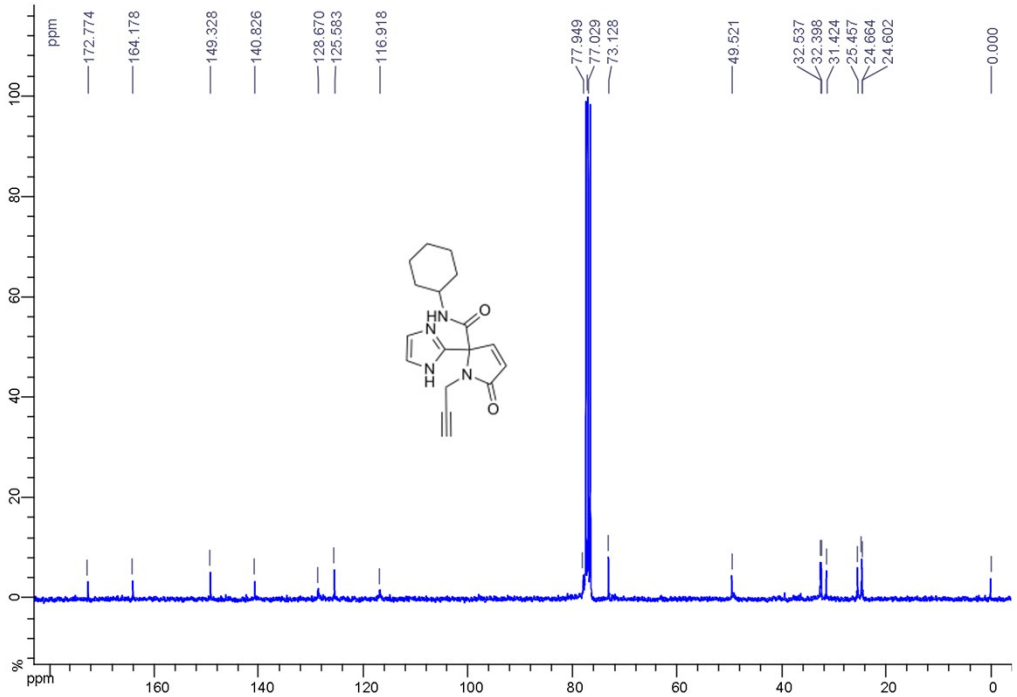
^{1}H and ^{13}C NMR spectra of compound **5d** (300 MHz, $CDCl_3$)



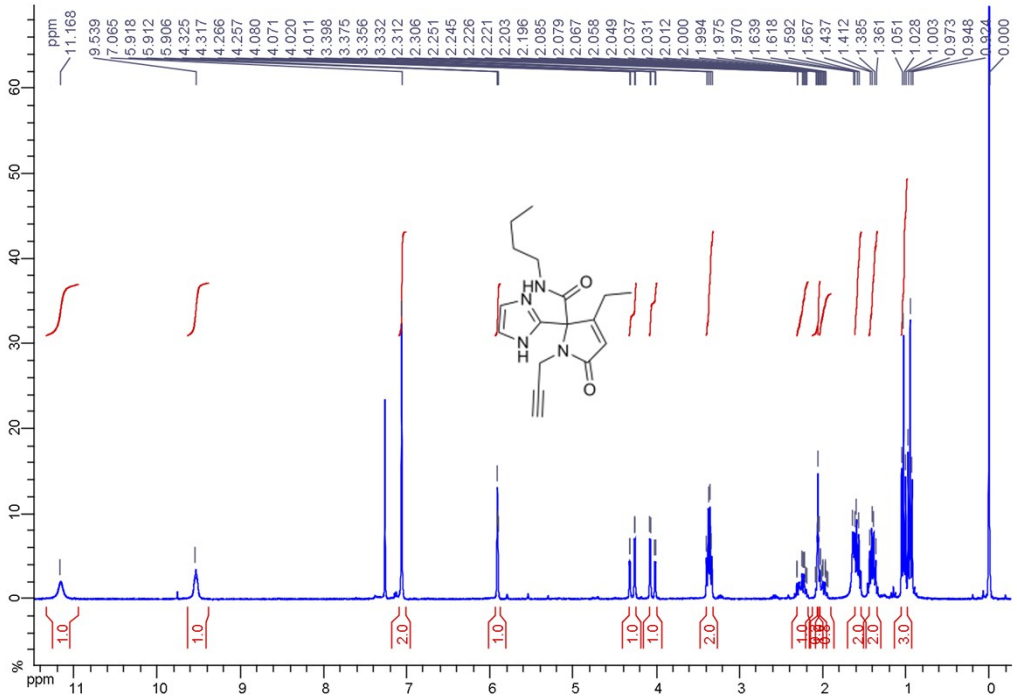


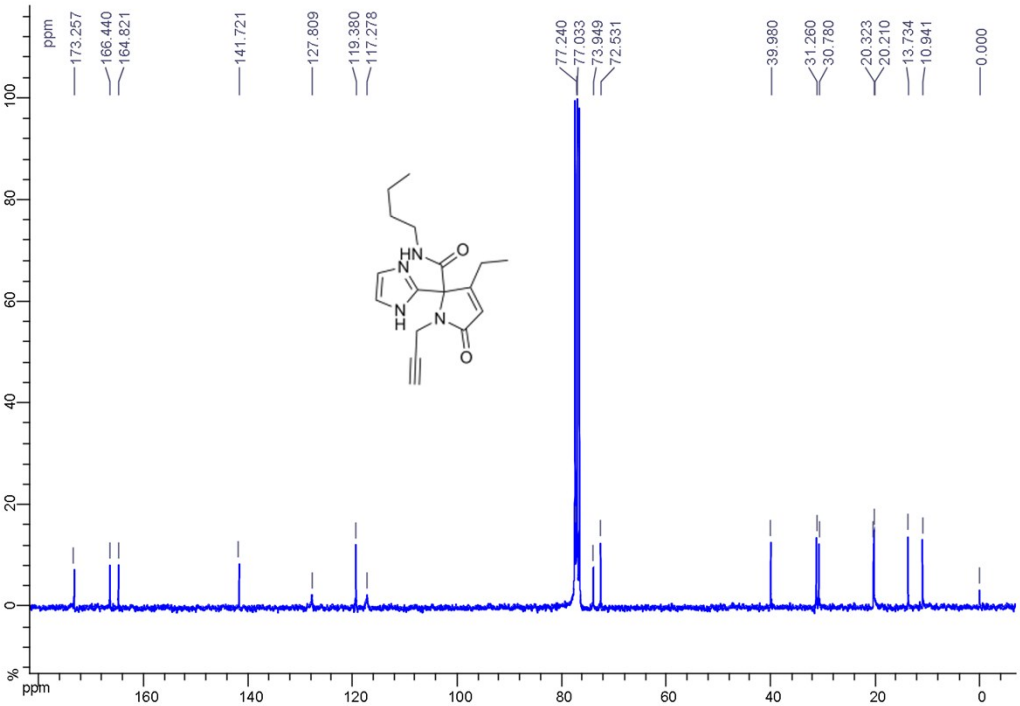
^{1}H and ^{13}C NMR spectra of compound **5e** (300 MHz, $CDCl_3$)



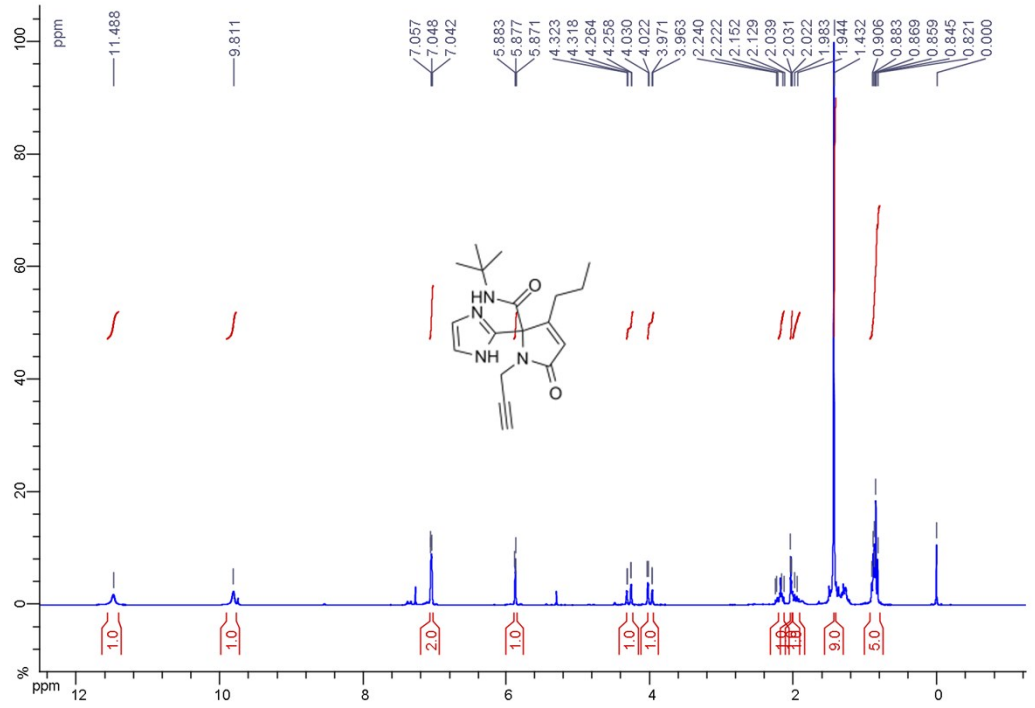


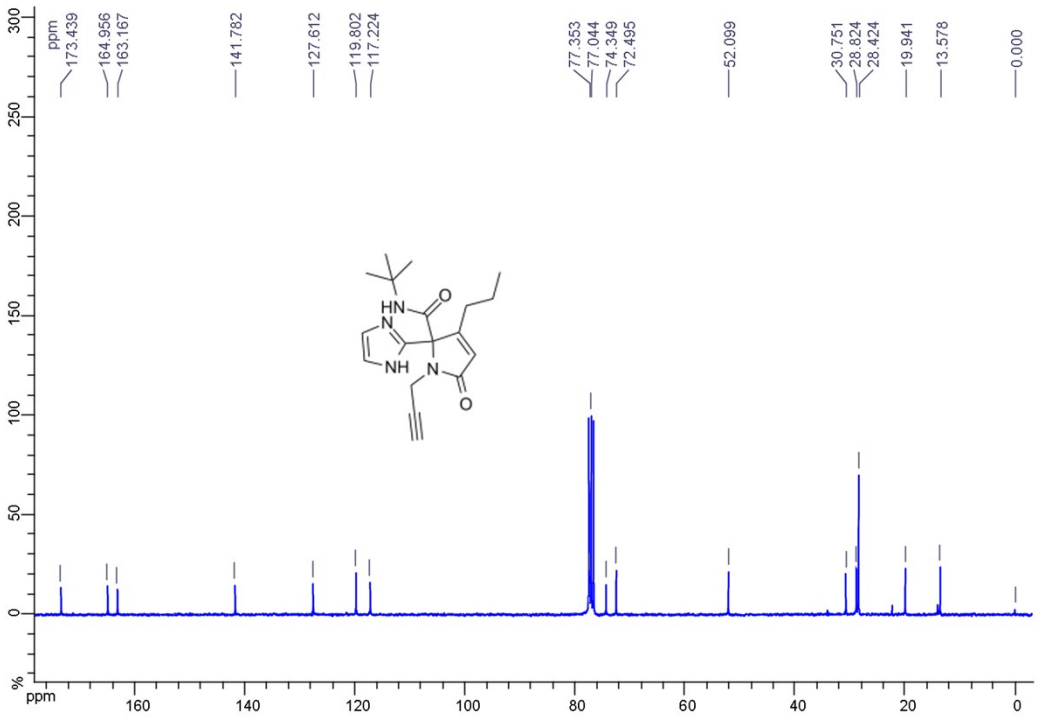
^{1}H and ^{13}C NMR spectra of compound **5f** (300 MHz, $CDCl_3$)



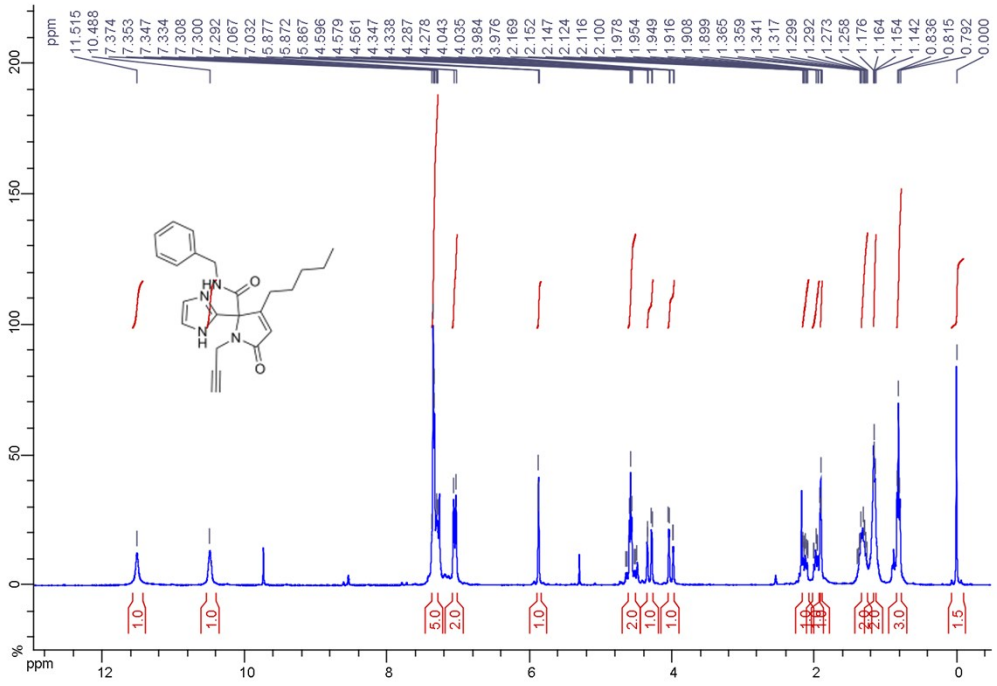


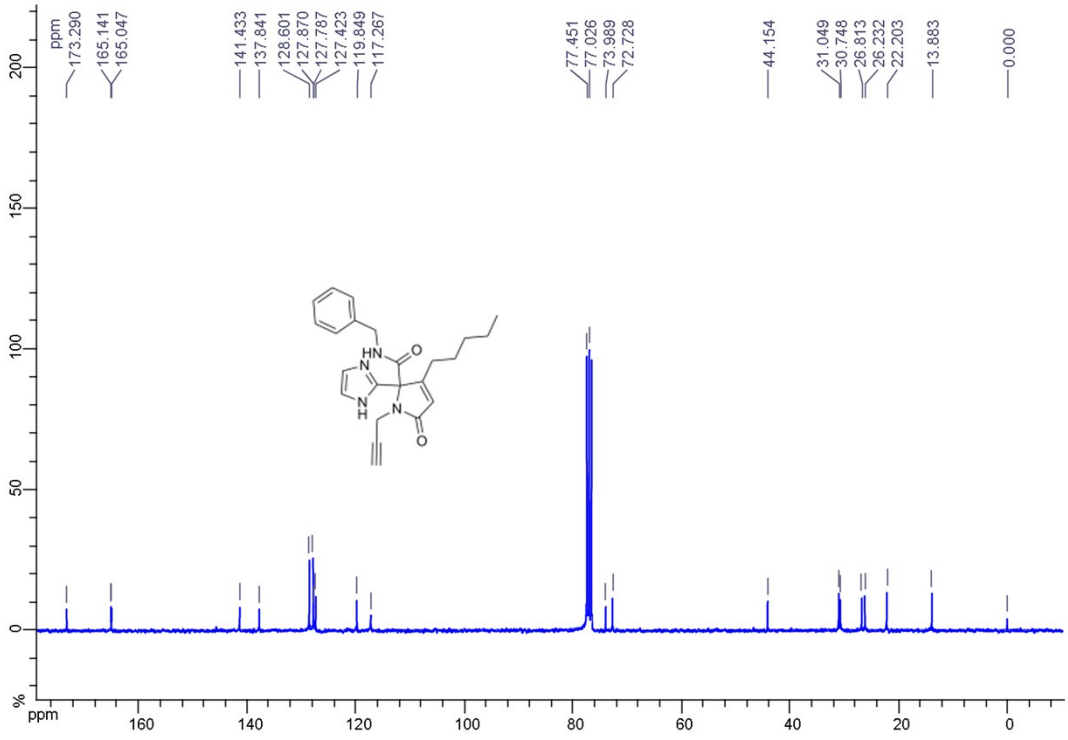
^{1}H and ^{13}C NMR spectra of compound **5g** (300 MHz, $CDCl_3$)



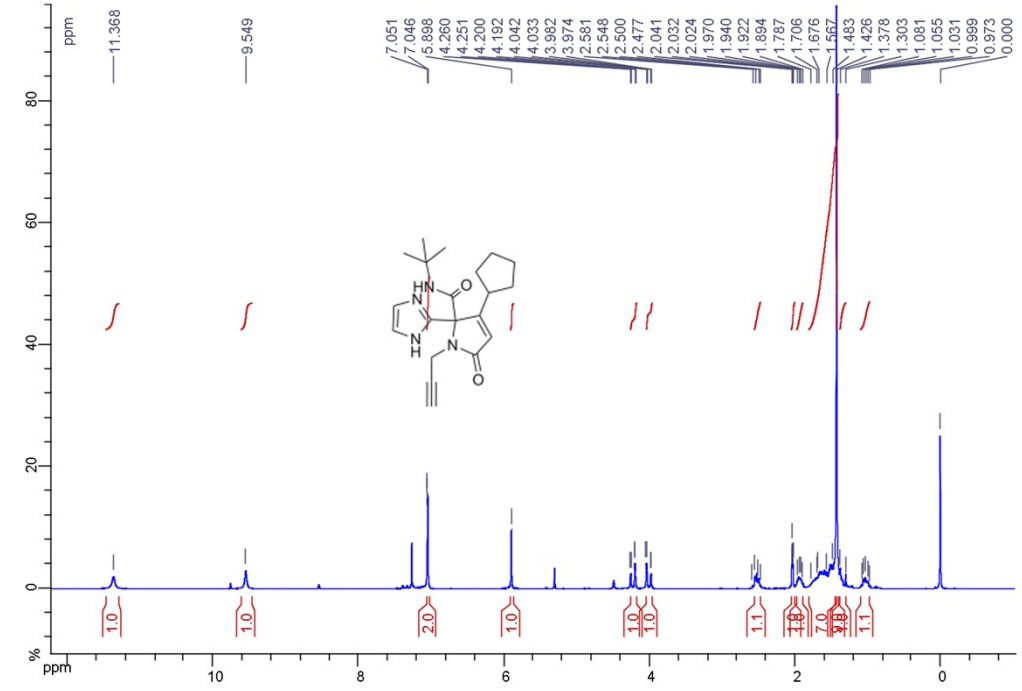


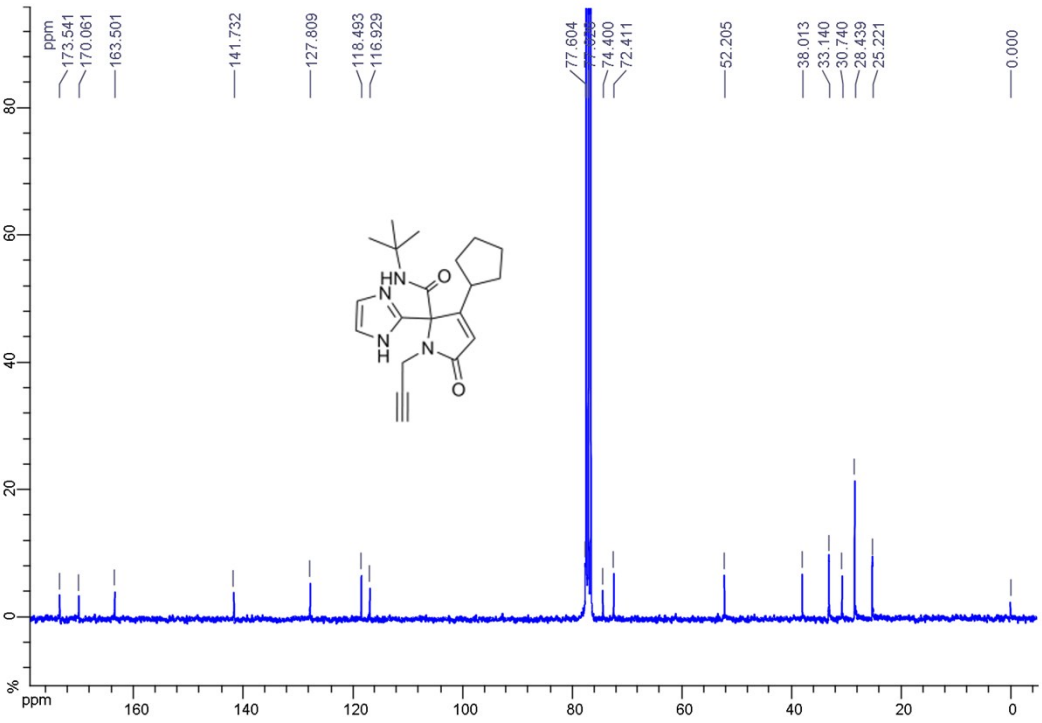
^{1}H and ^{13}C NMR spectra of compound **5h** (300 MHz, $CDCl_3$)



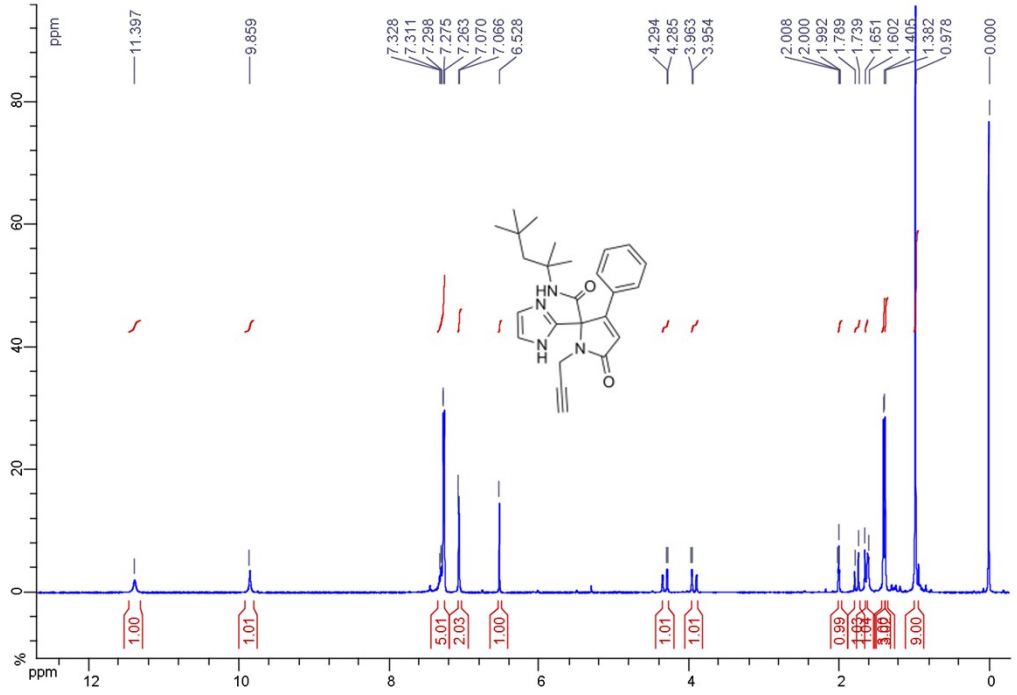


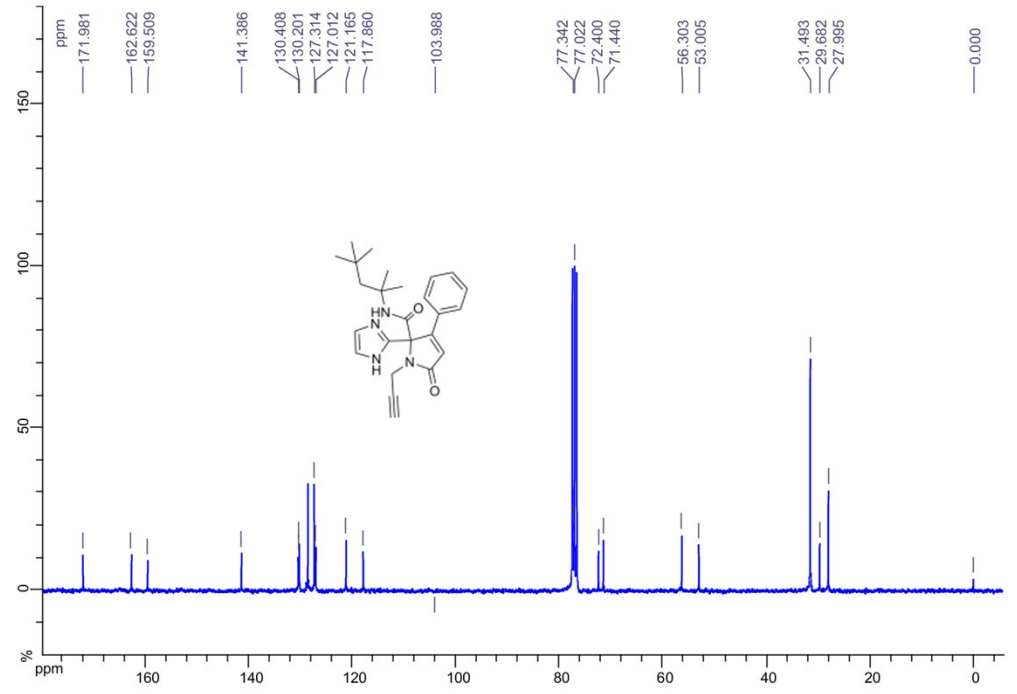
^{1}H and ^{13}C NMR spectra of compound **5i** (300 MHz, $CDCl_3$)



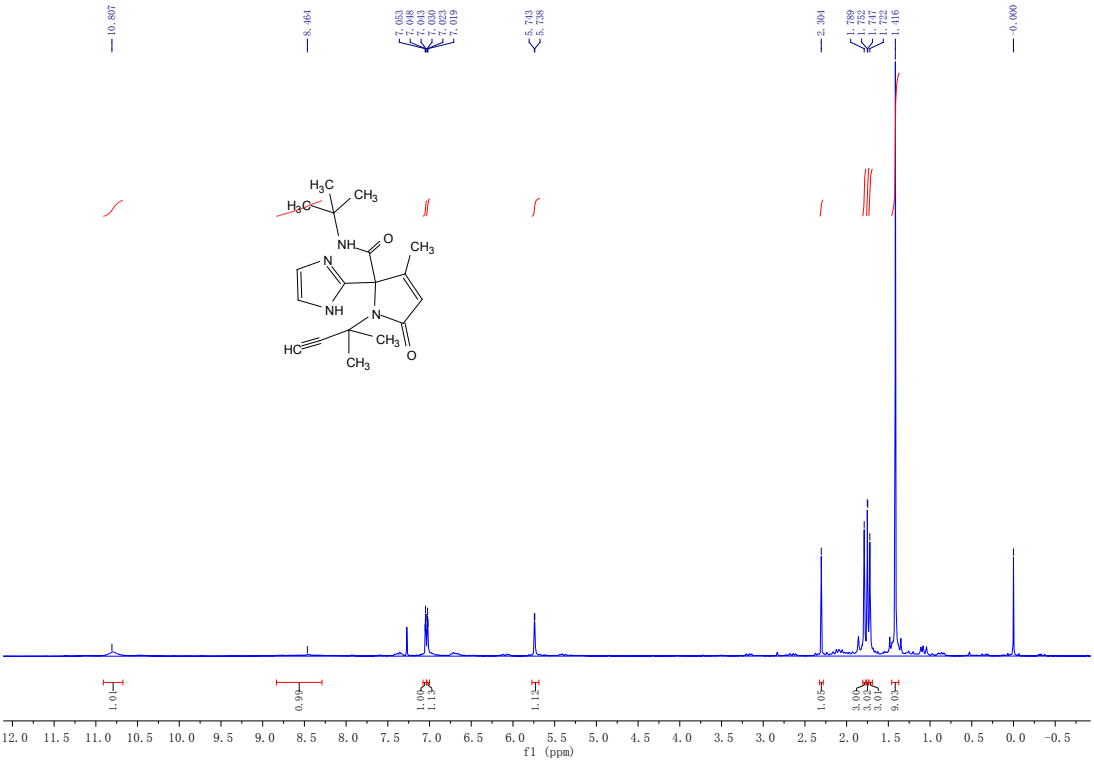


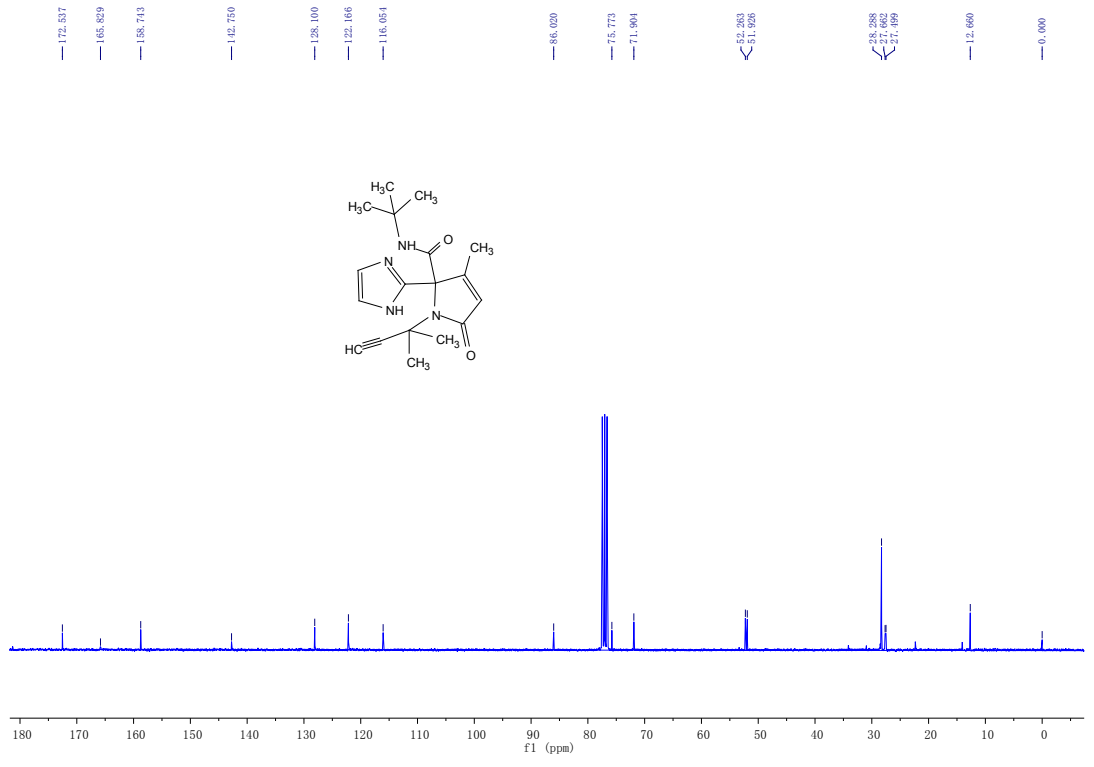
^{1}H and ^{13}C NMR spectra of compound **5j** (300 MHz, $CDCl_3$)



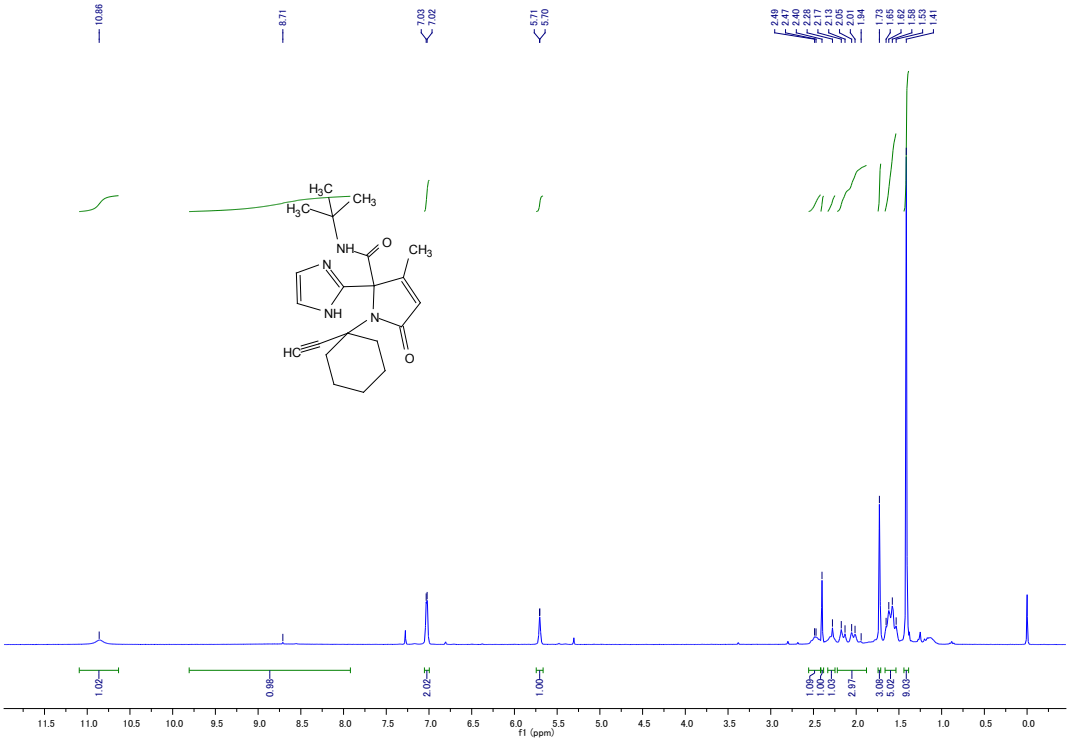


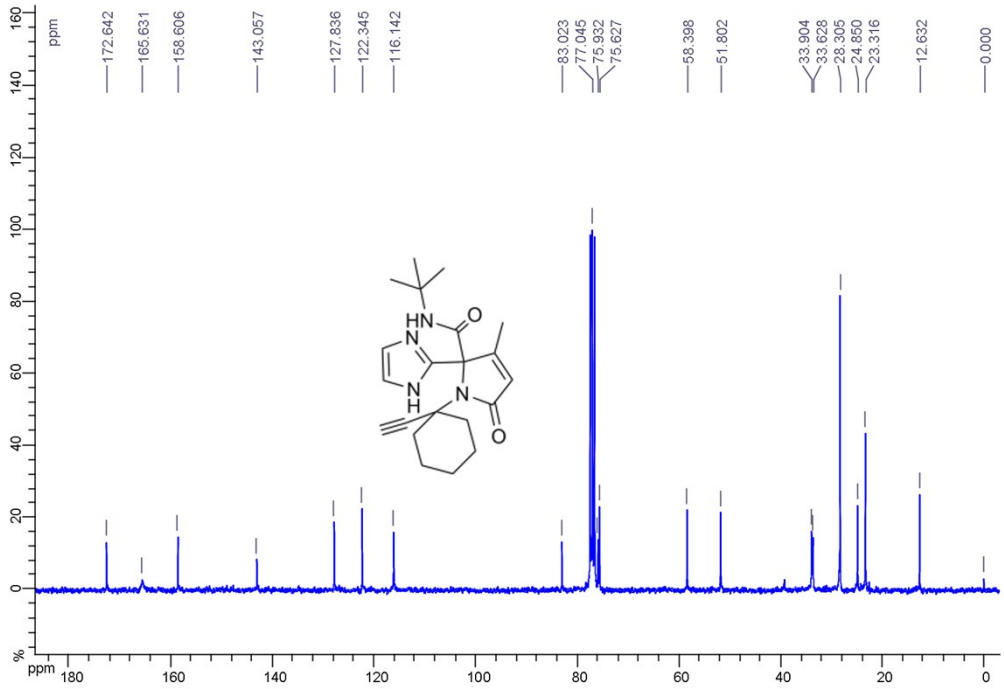
^{1}H and ^{13}C NMR spectra of compound **5k** (300 MHz, $CDCl_3$)



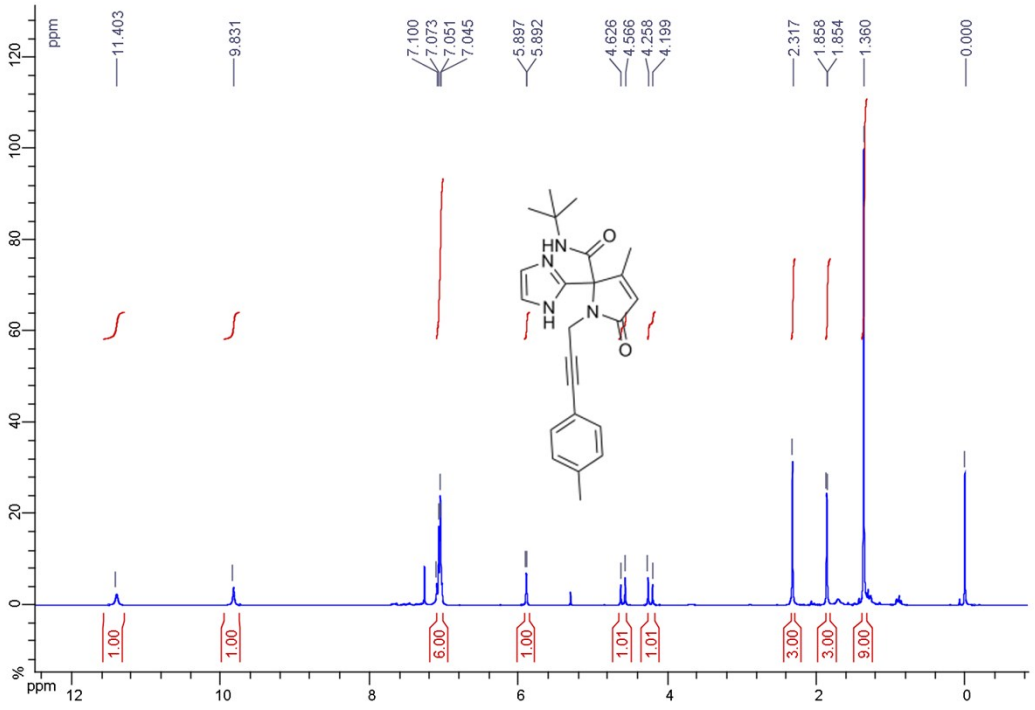


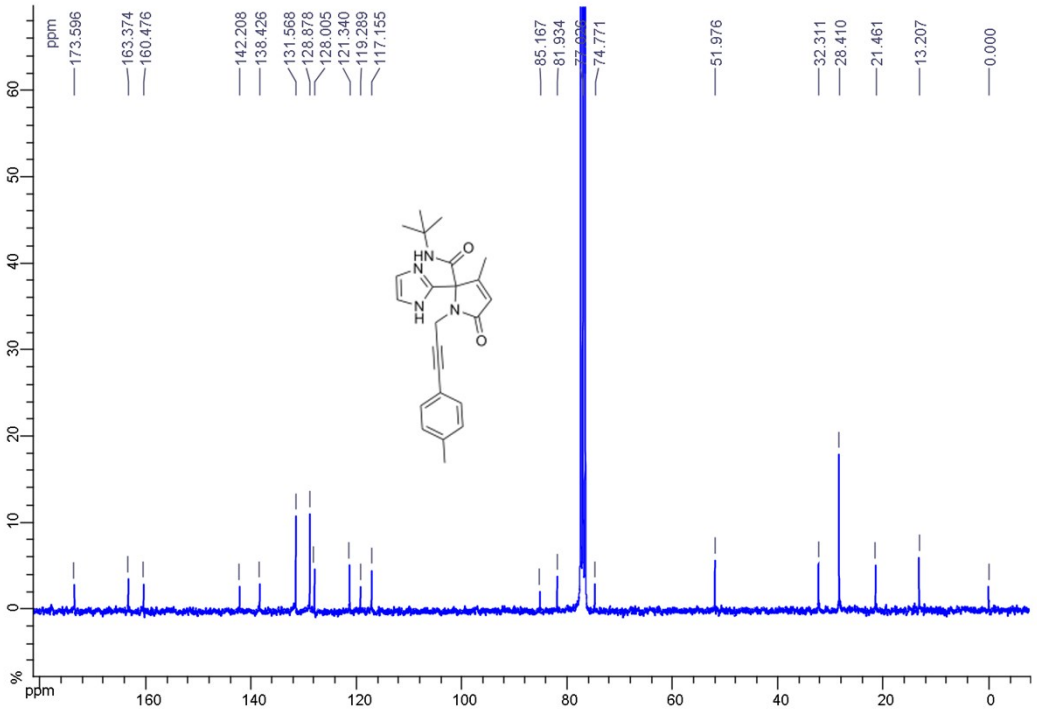
^{1}H and ^{13}C NMR spectra of compound **5l** (300 MHz, $CDCl_3$)



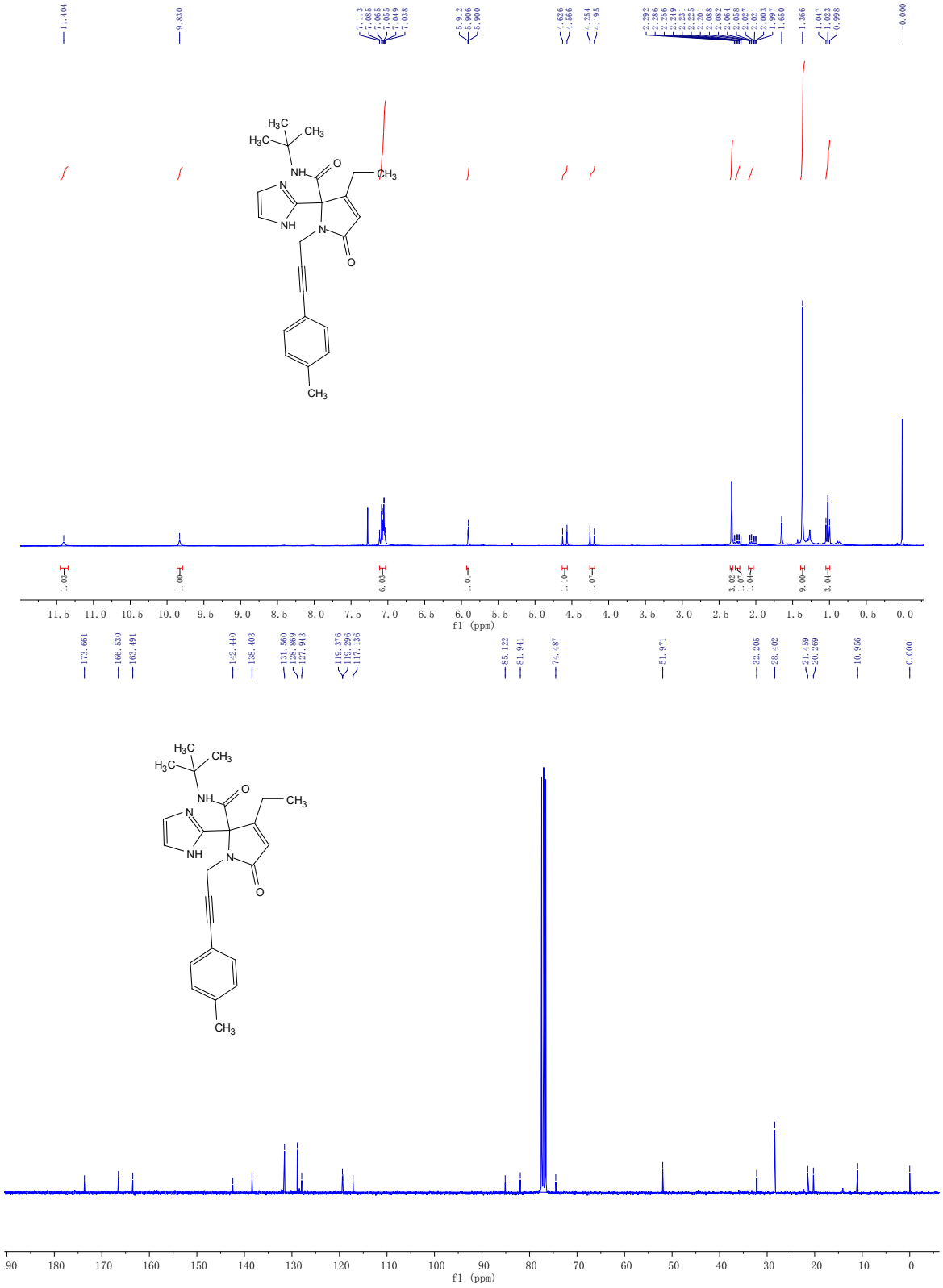


^{1}H and ^{13}C NMR spectra of compound **5m** (300 MHz, $CDCl_3$)

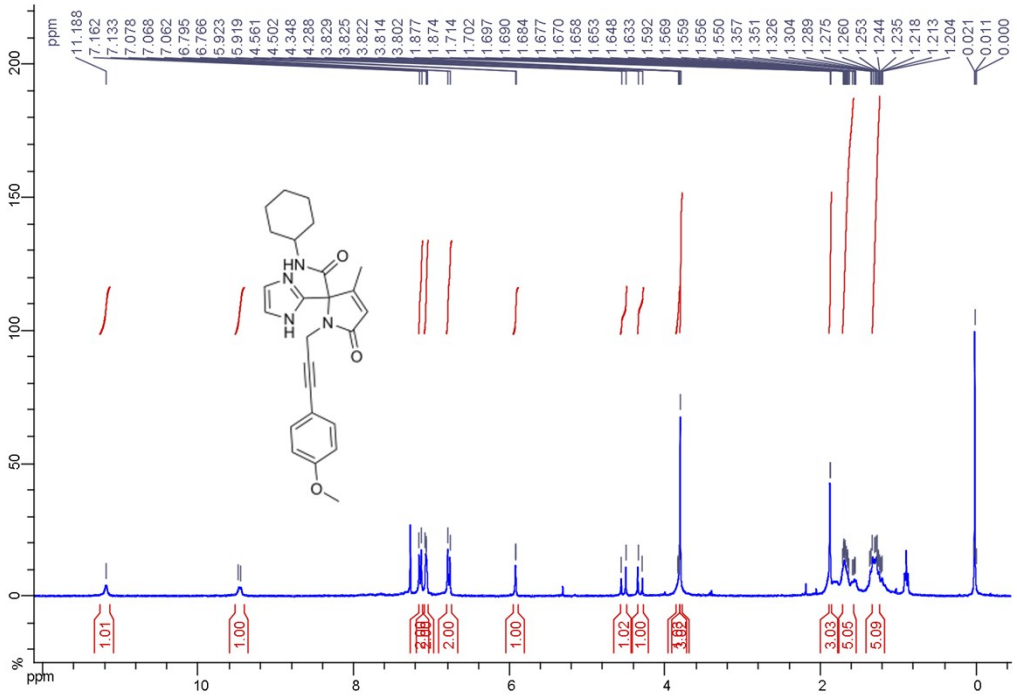


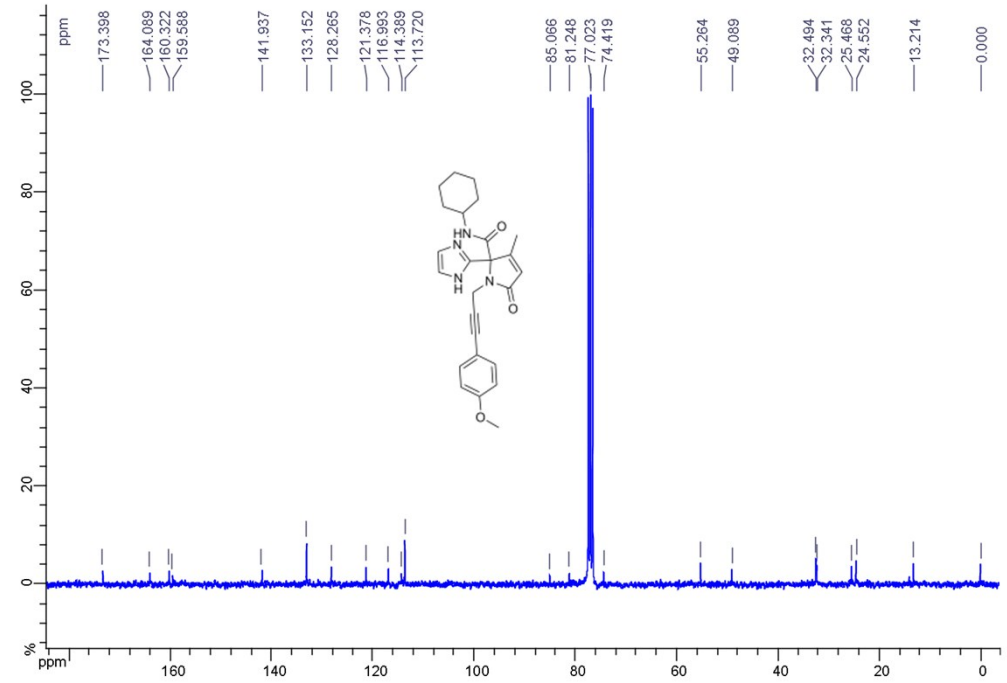


^{1}H and ^{13}C NMR spectra of compound **5n** (300 MHz, $CDCl_3$)

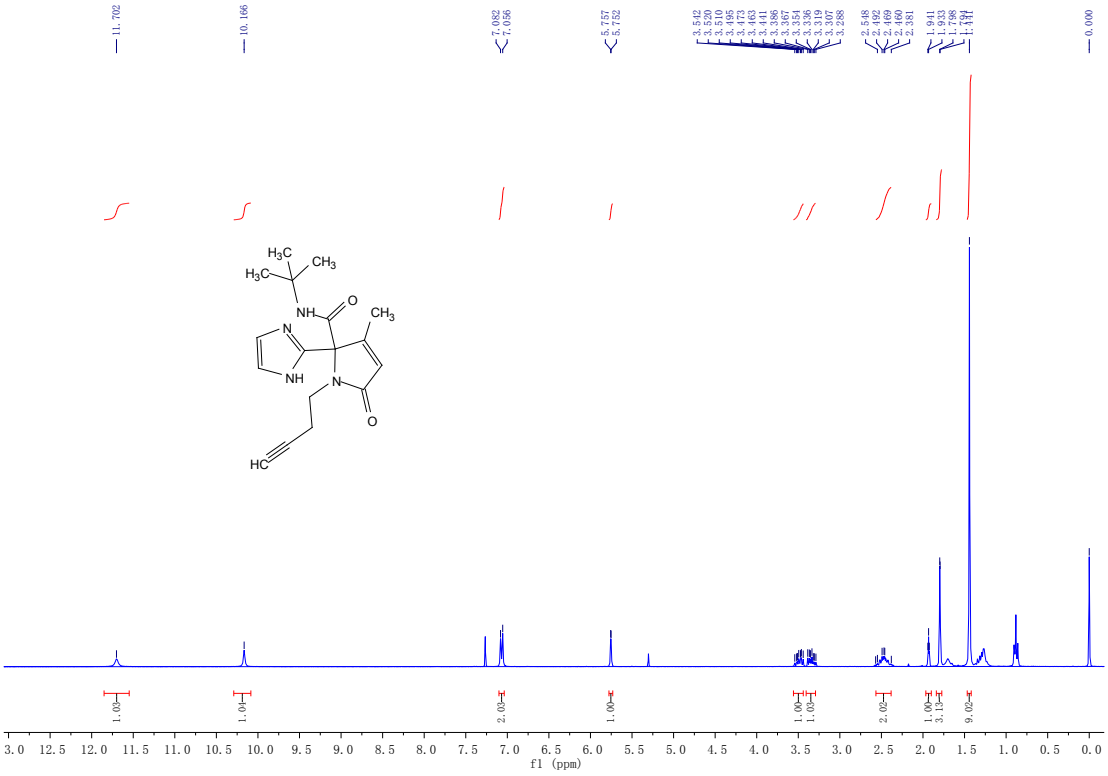


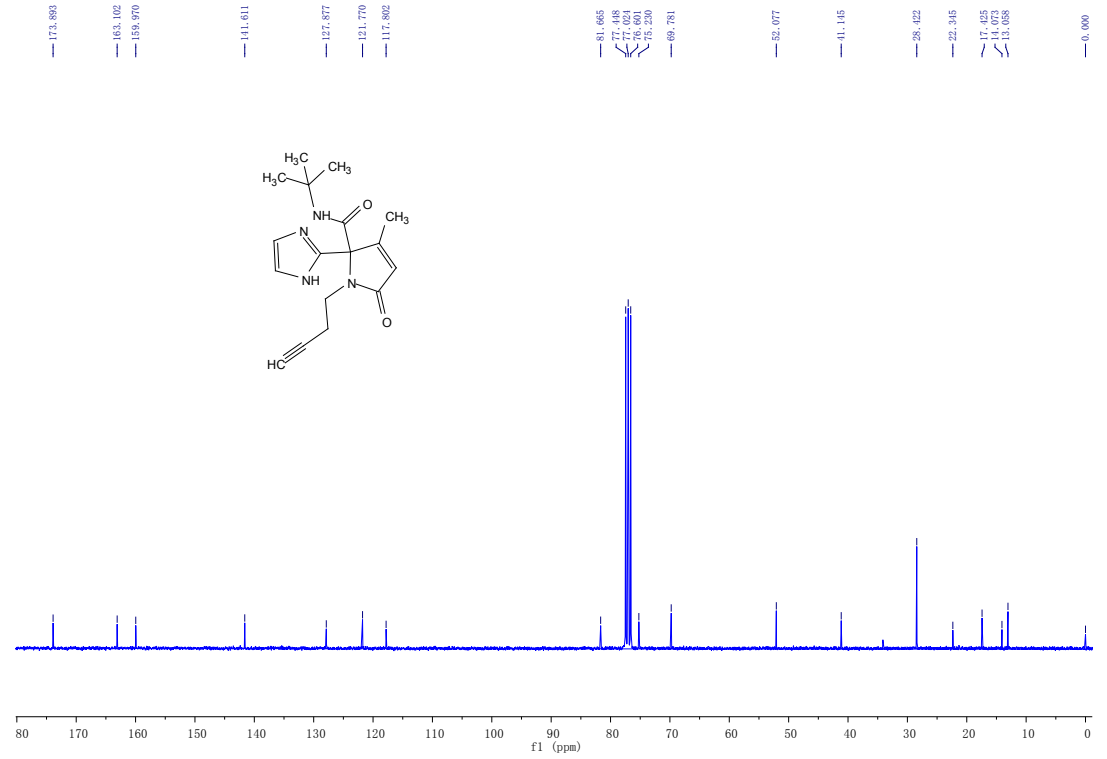
^{1}H and ^{13}C NMR spectra of compound **5o** (300 MHz, $CDCl_3$)



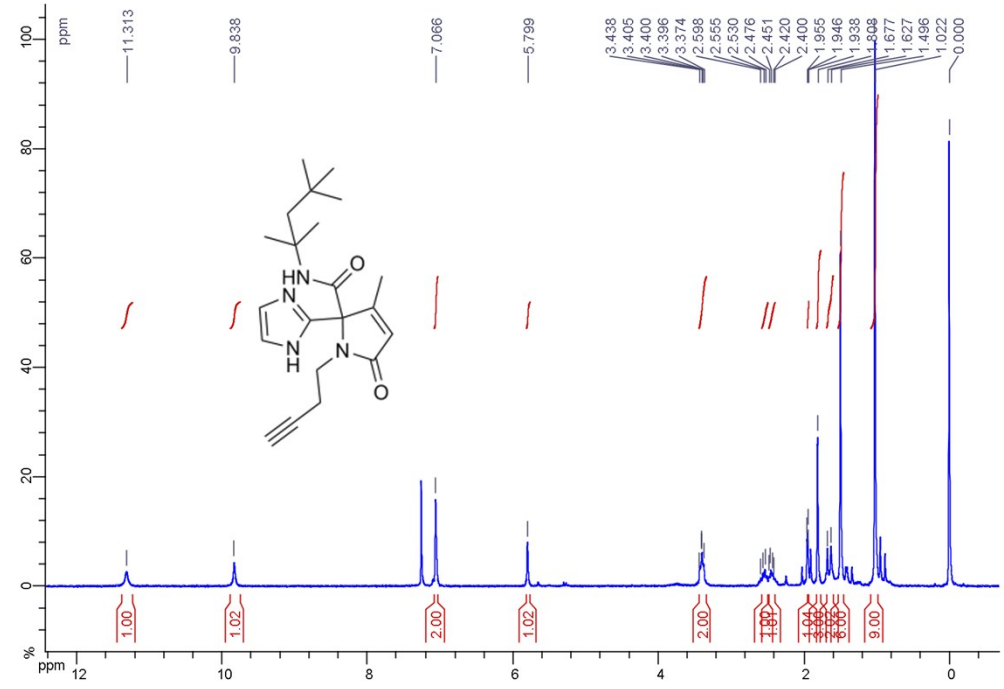


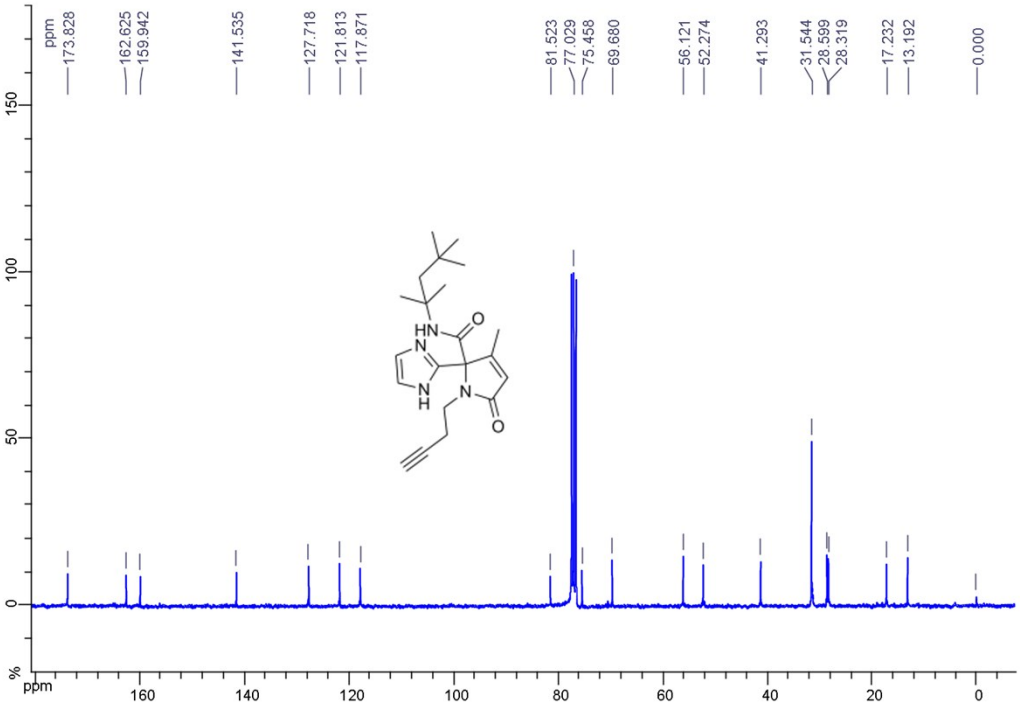
^{1}H and ^{13}C NMR spectra of compound **5p** (300 MHz, $CDCl_3$)



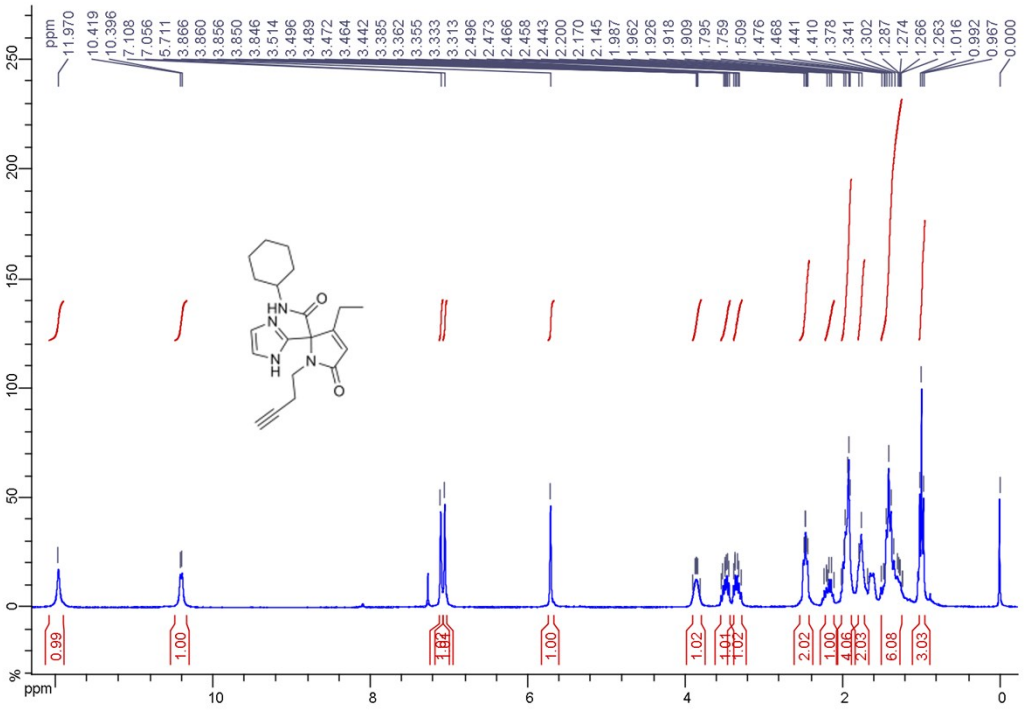


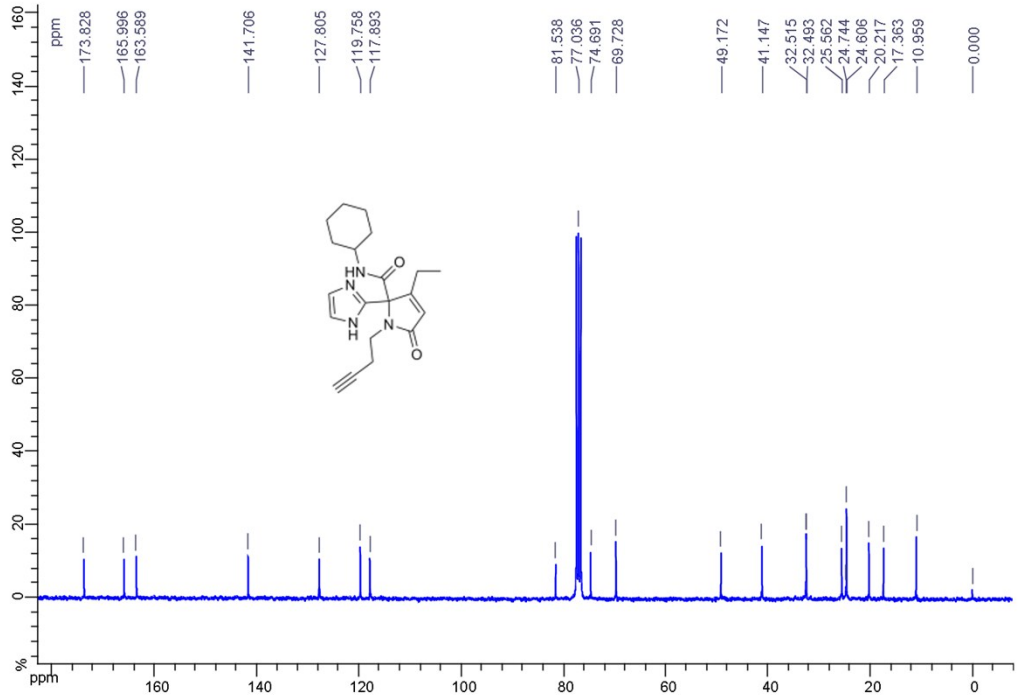
^{1}H and ^{13}C NMR spectra of compound **5q** (300 MHz, $CDCl_3$)



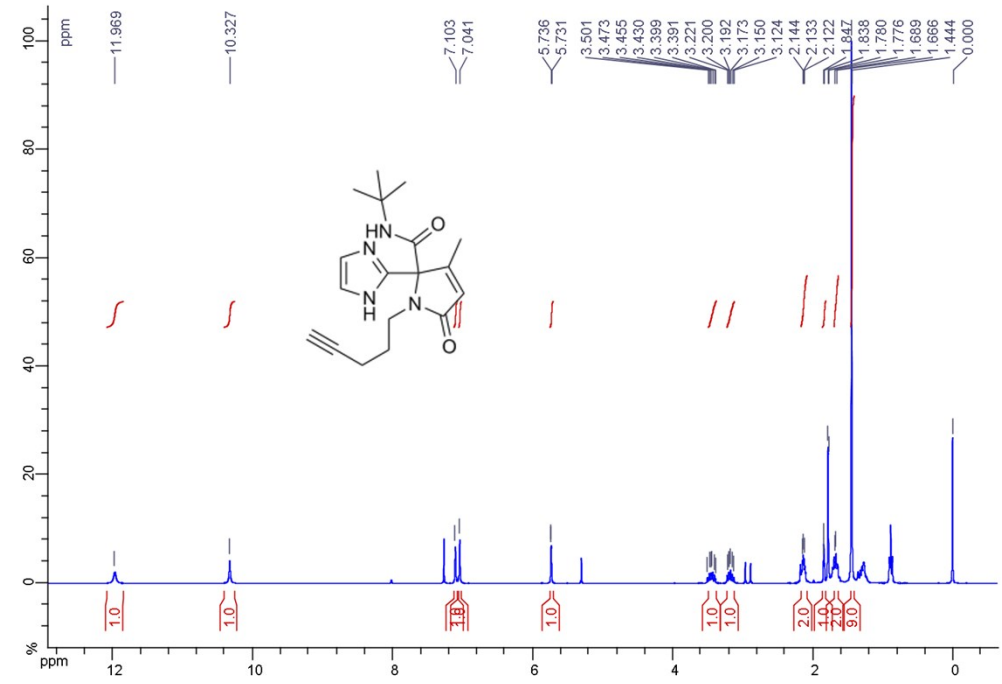


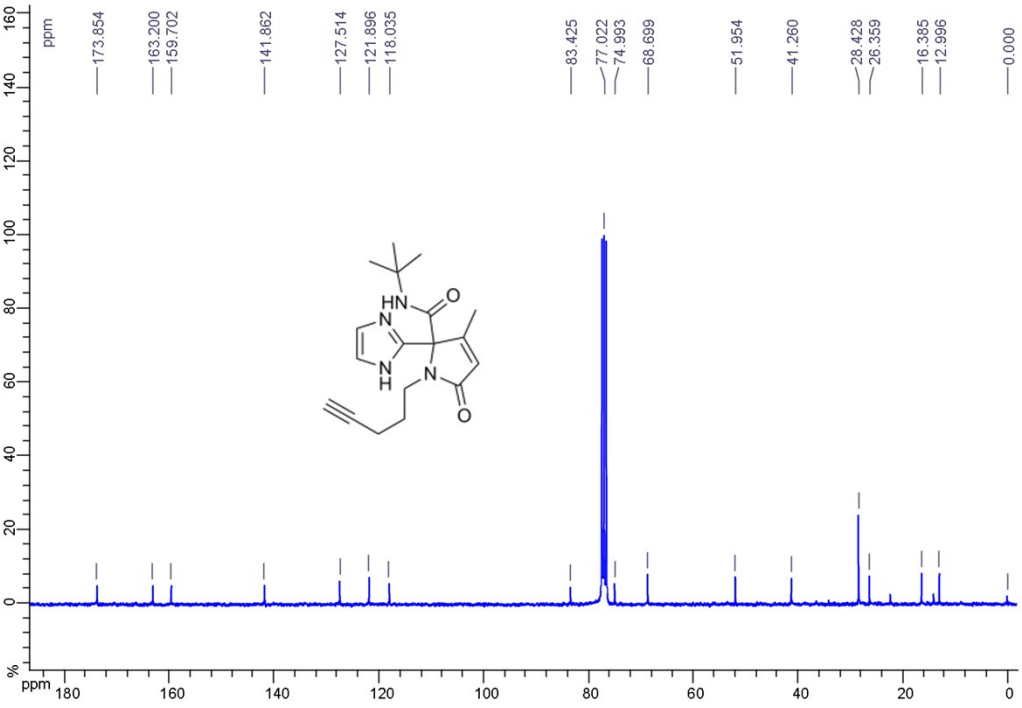
^{1}H and ^{13}C NMR spectra of compound **5r** (300 MHz, $CDCl_3$)



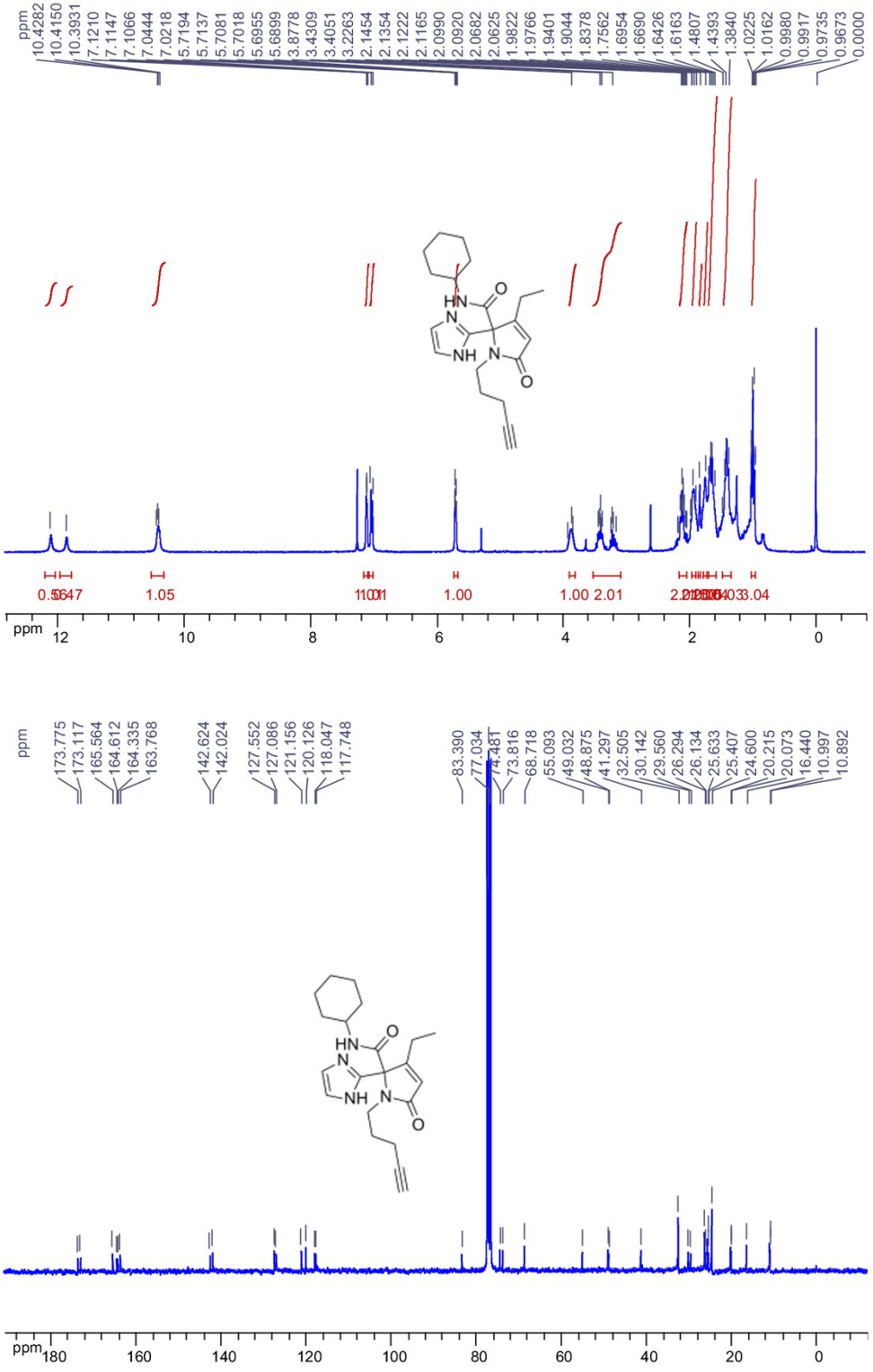


^{1}H and ^{13}C NMR spectra of compound **5s** (300 MHz, $CDCl_3$)

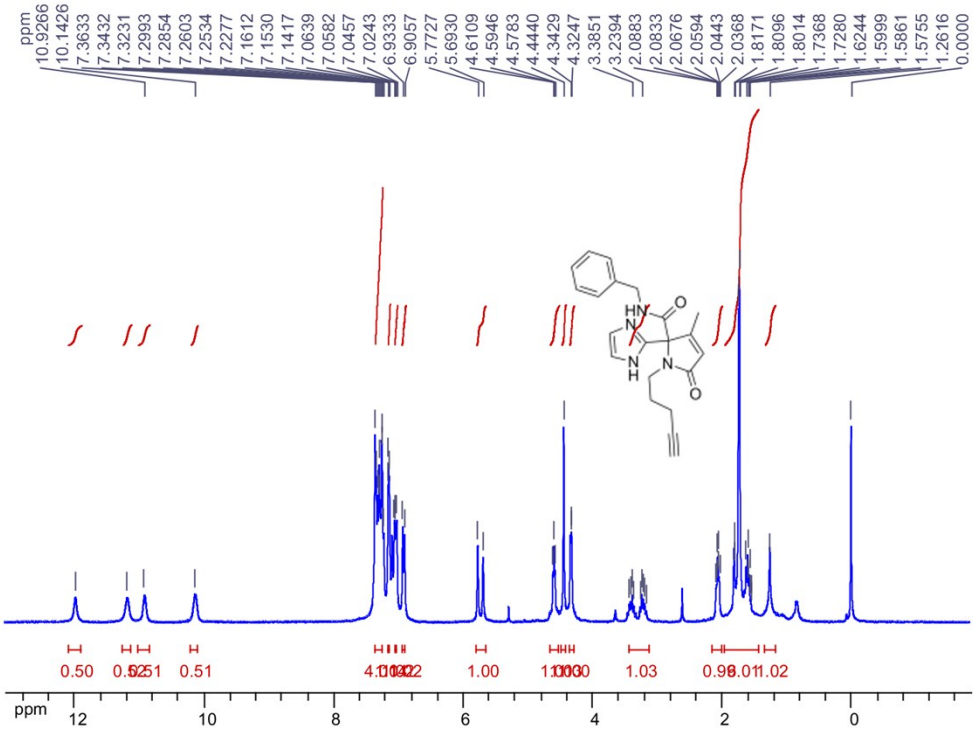


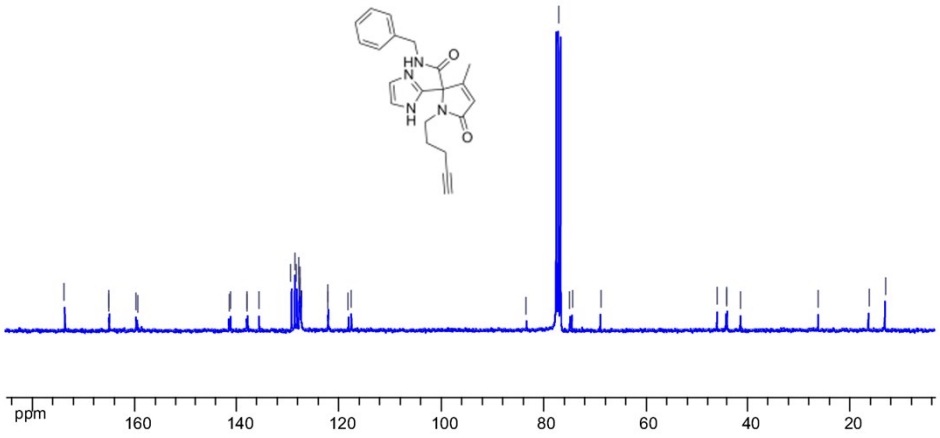


^{1}H and ^{13}C NMR spectra of compound **5t** (300 MHz, $CDCl_3$)

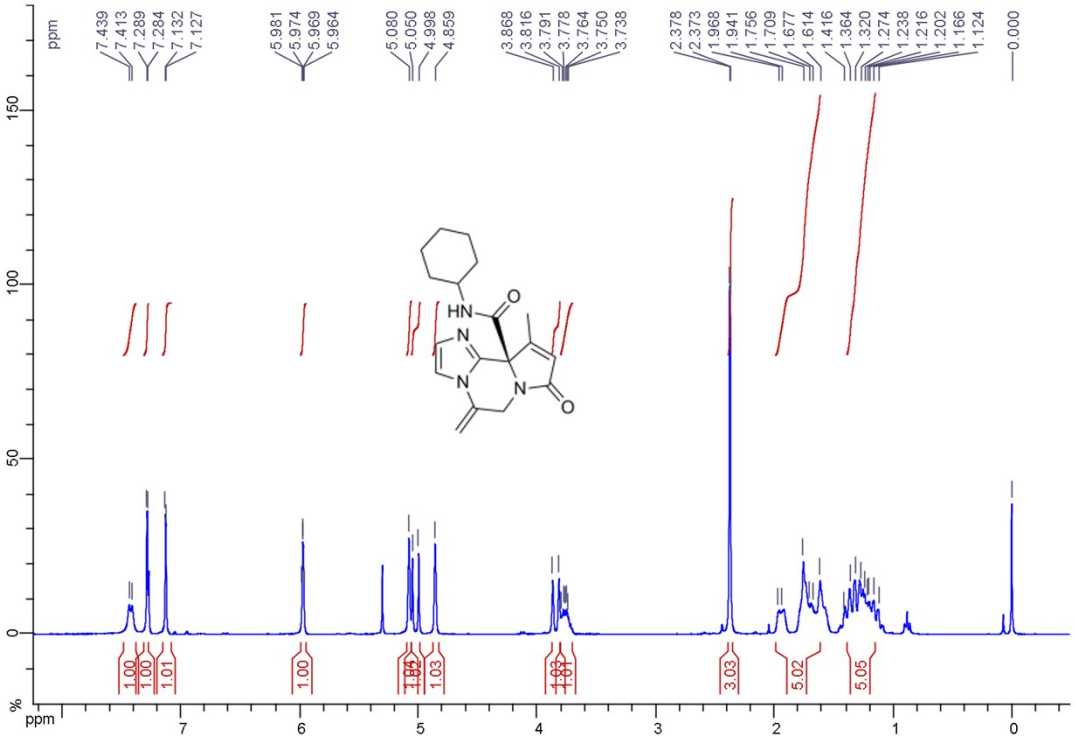


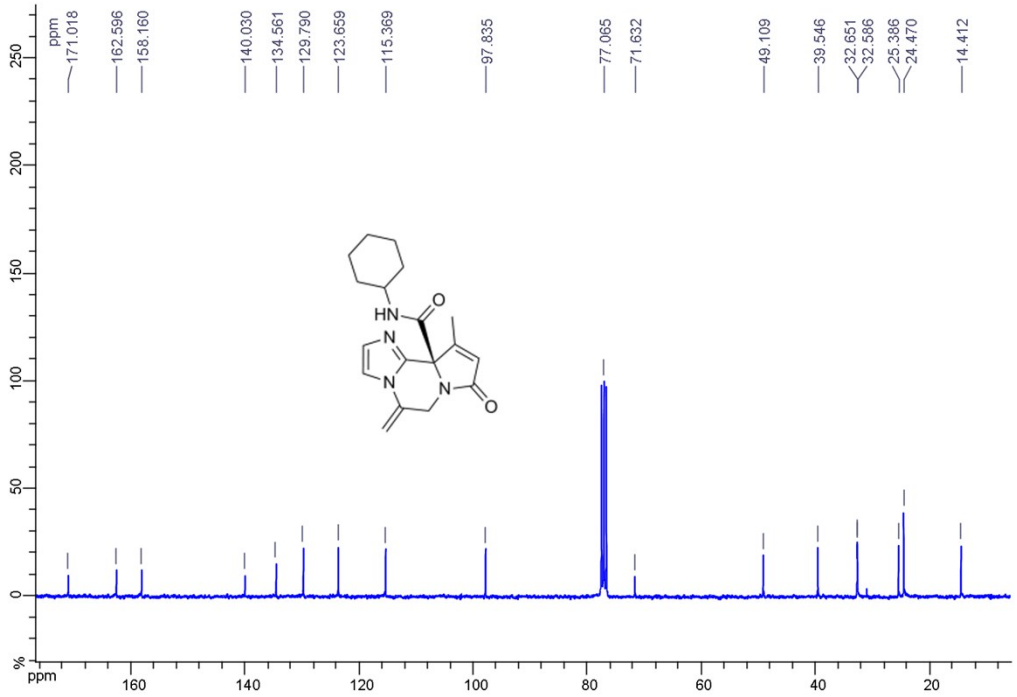
^{1}H and ^{13}C NMR spectra of compound **5r** (300 MHz, $CDCl_3$)



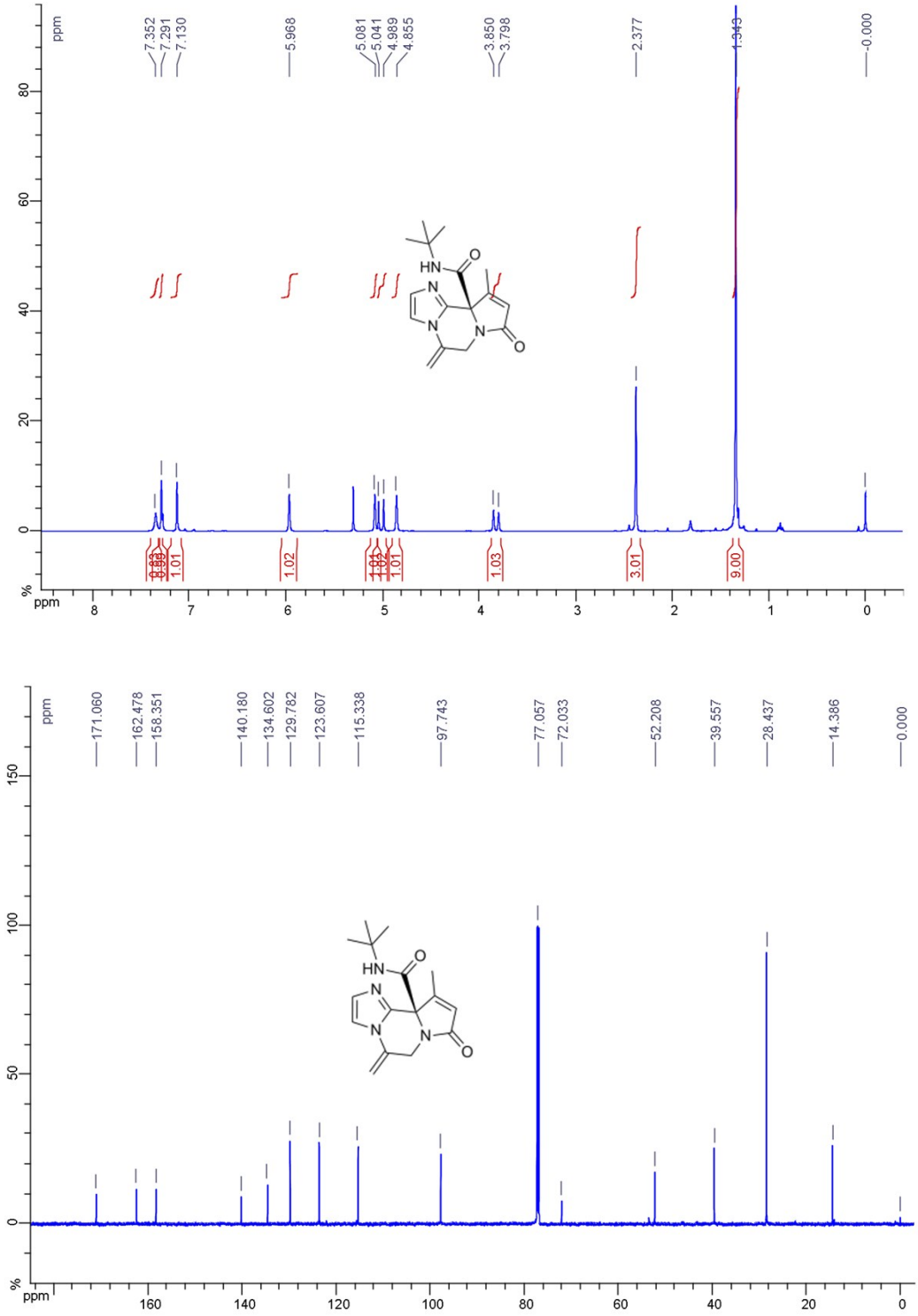


^{1}H and ^{13}C NMR spectra of compound **6a** (300 MHz, $CDCl_3$)

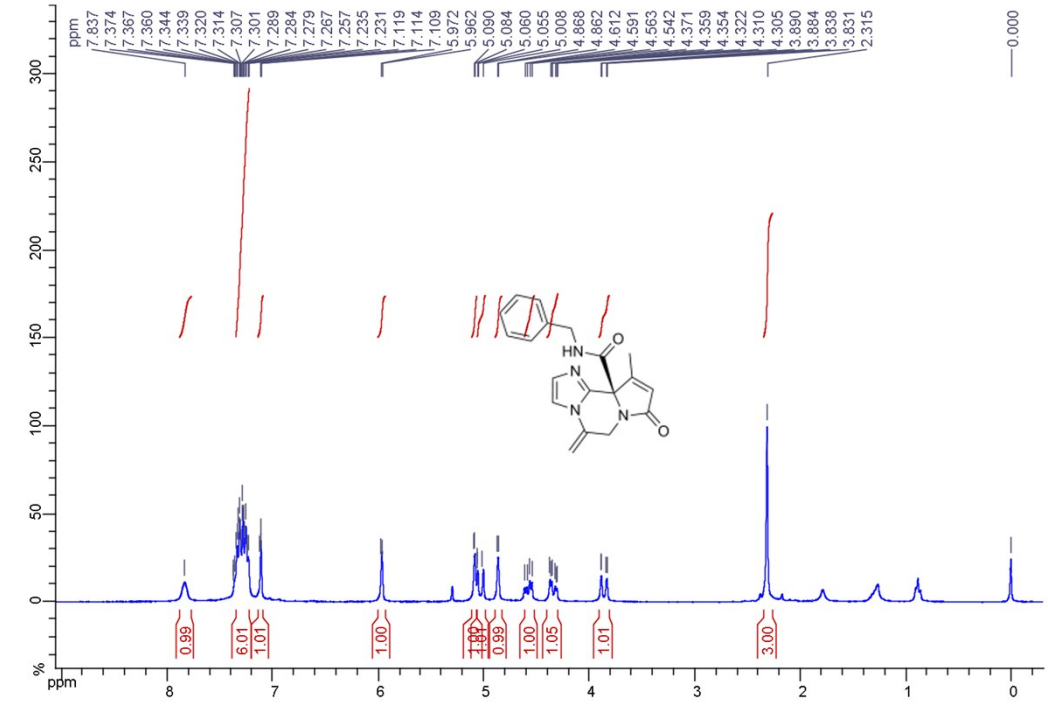


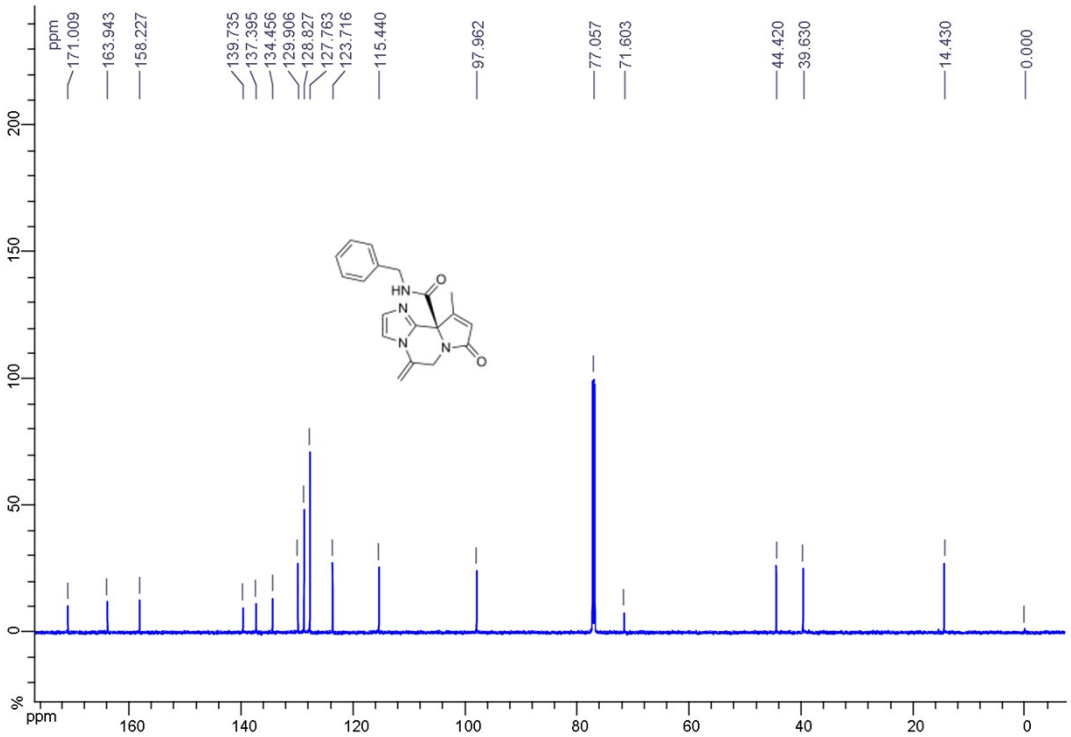


^{1}H and ^{13}C NMR spectra of compound **6b** (300 MHz, $CDCl_3$)

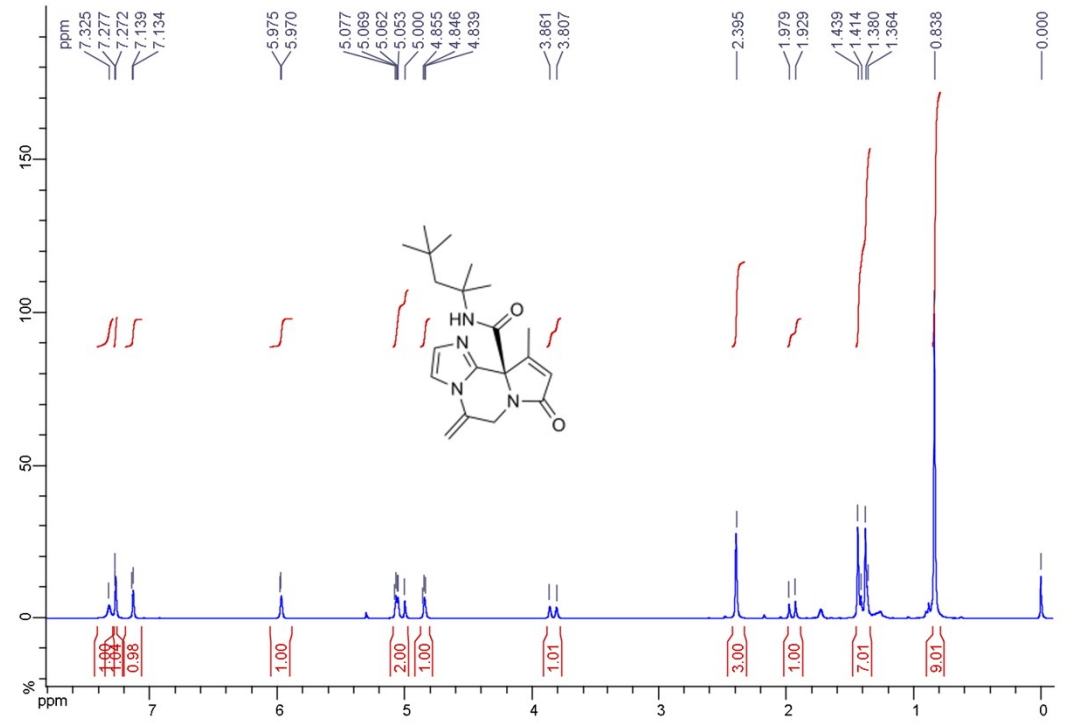


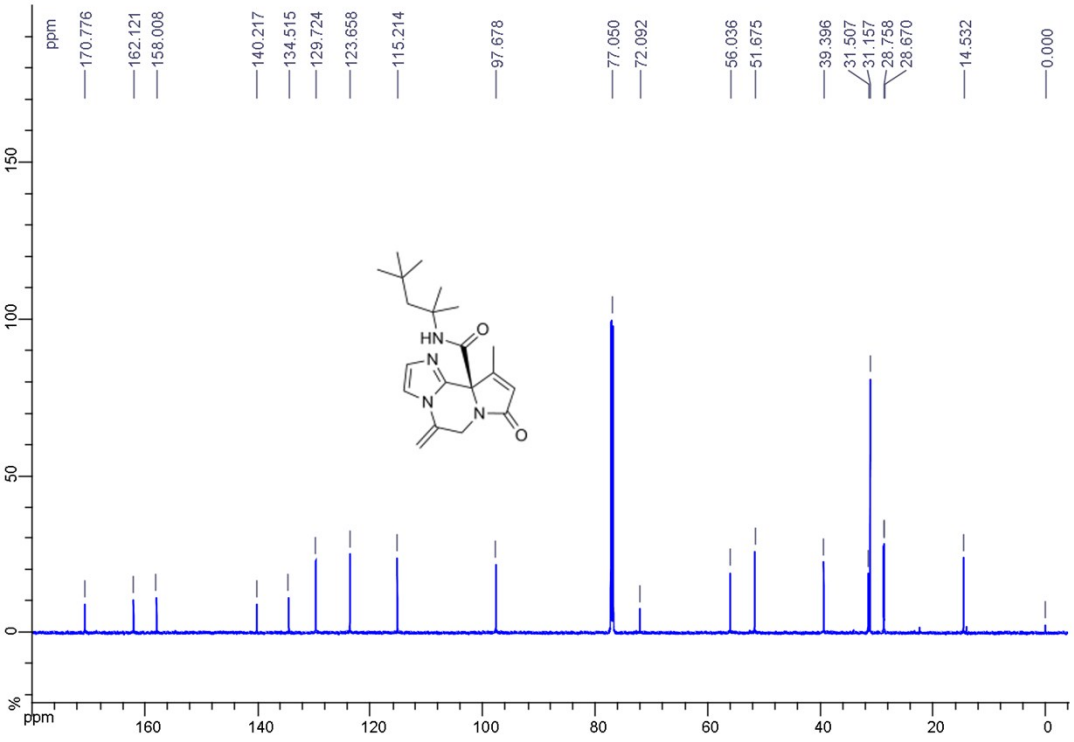
^{1}H and ^{13}C NMR spectra of compound **6c** (300 MHz, $CDCl_3$)



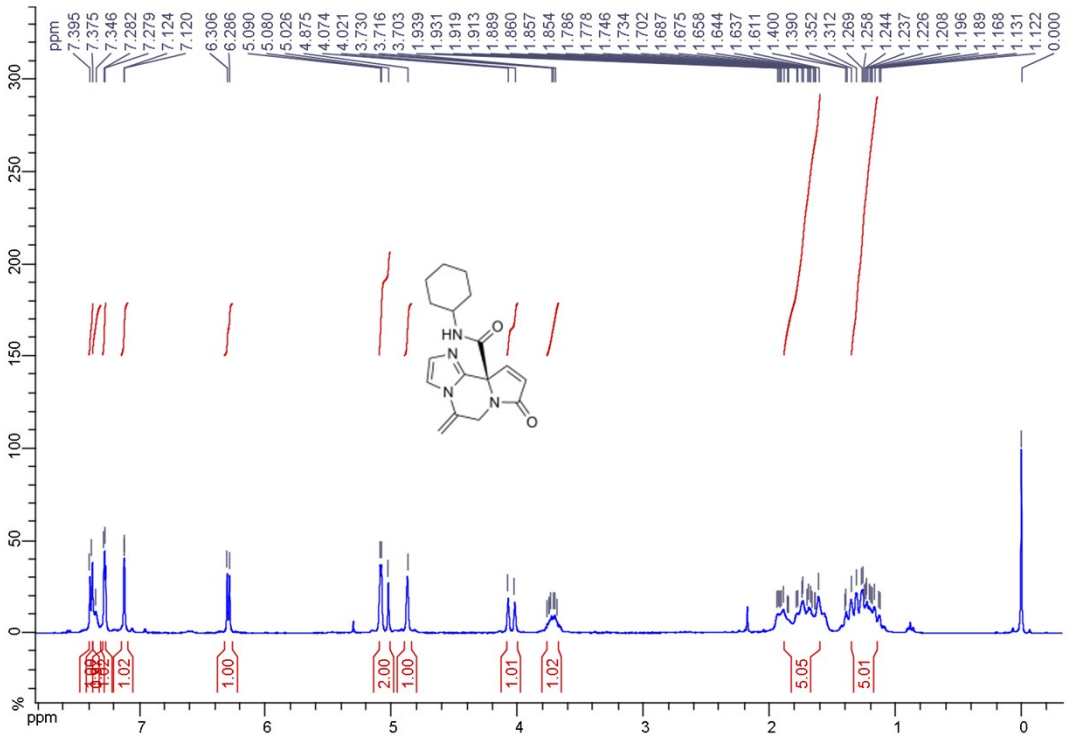


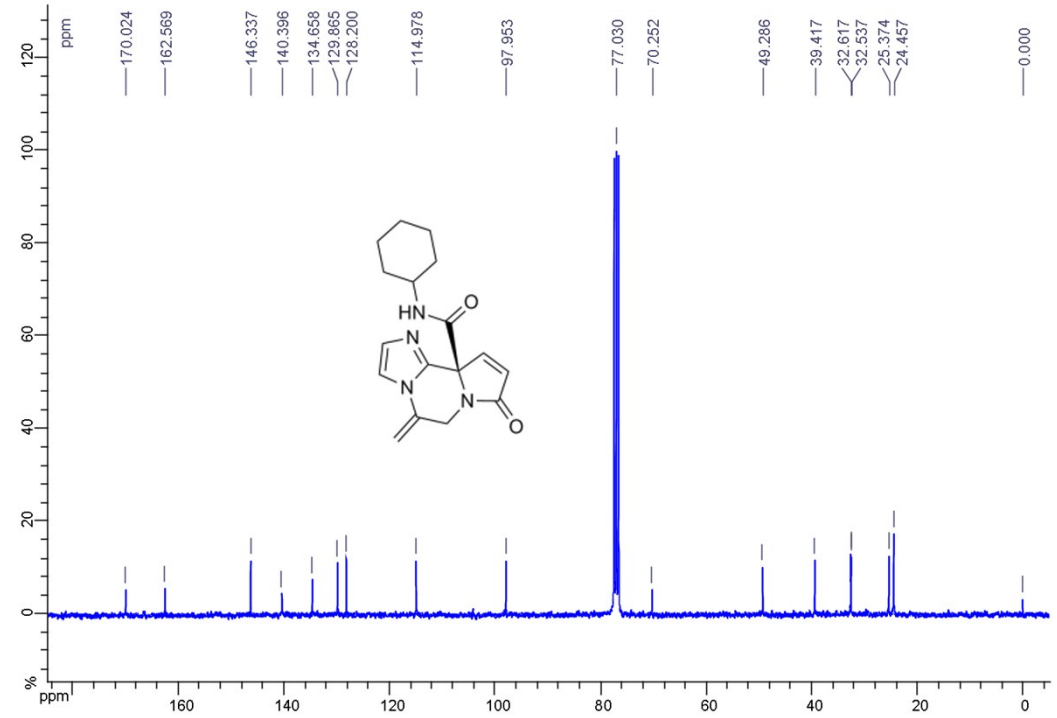
^{1}H and ^{13}C NMR spectra of compound **6d** (300 MHz, $CDCl_3$)



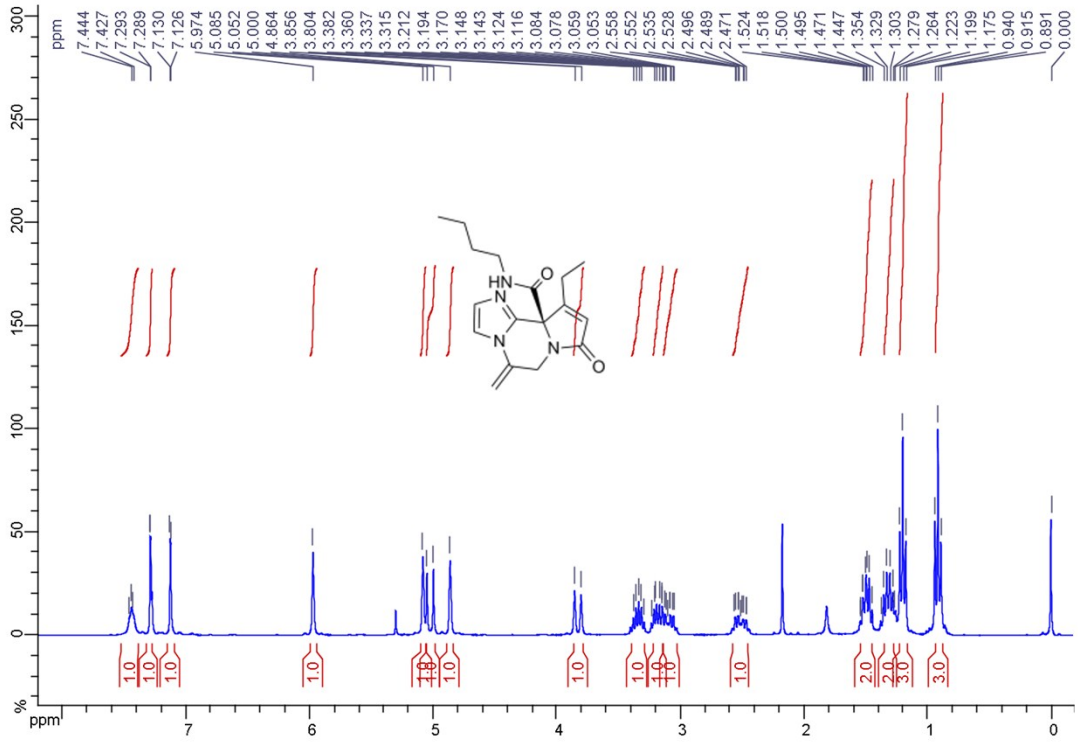


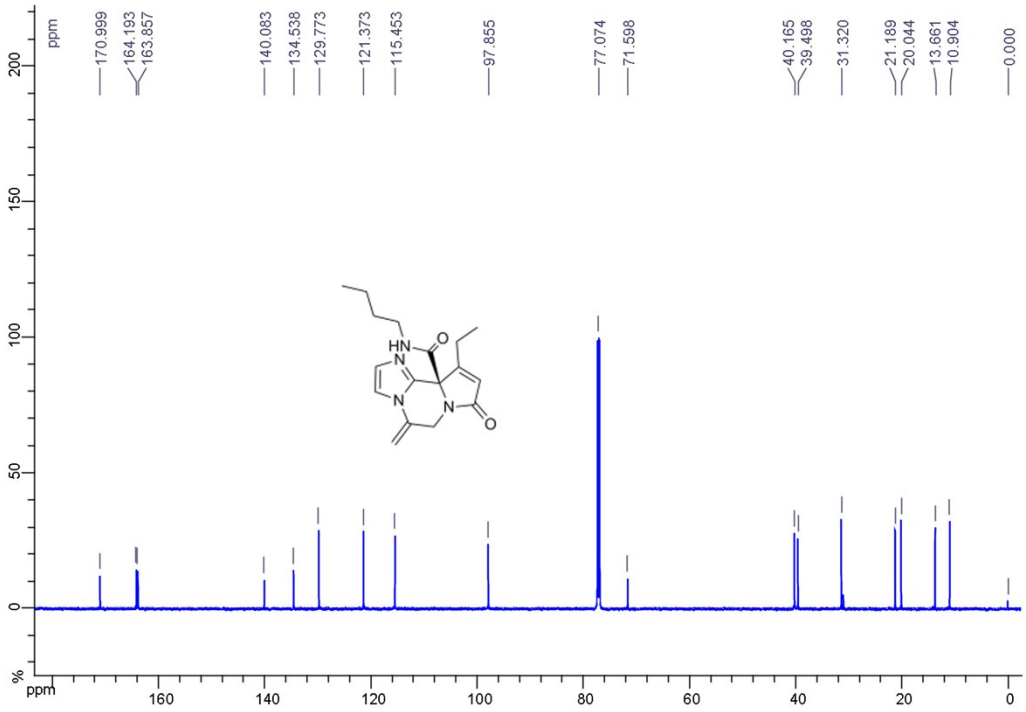
^{1}H and ^{13}C NMR spectra of compound **6e** (300 MHz, $CDCl_3$)



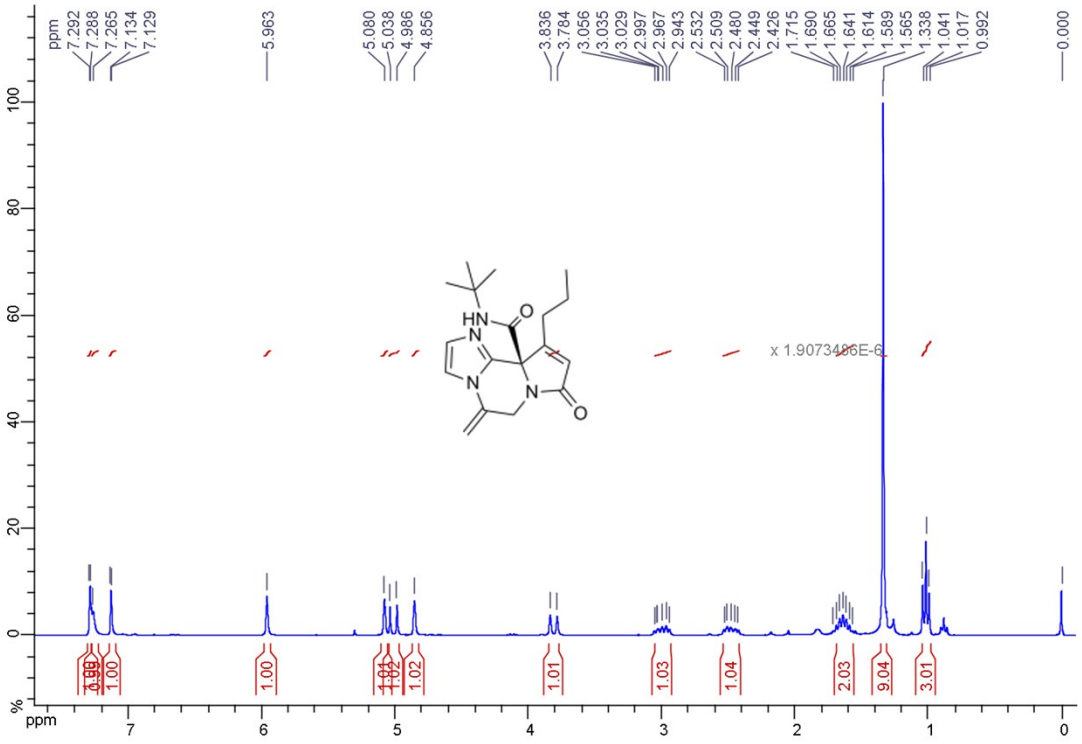


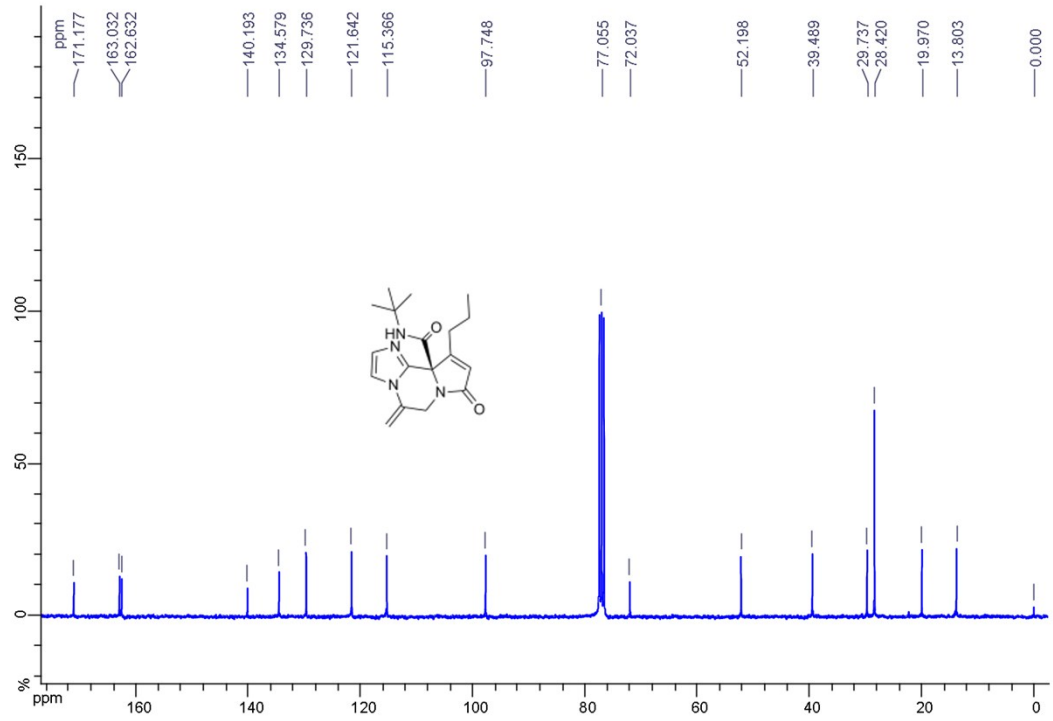
^{1}H and ^{13}C NMR spectra of compound **6f** (300 MHz, $CDCl_3$)



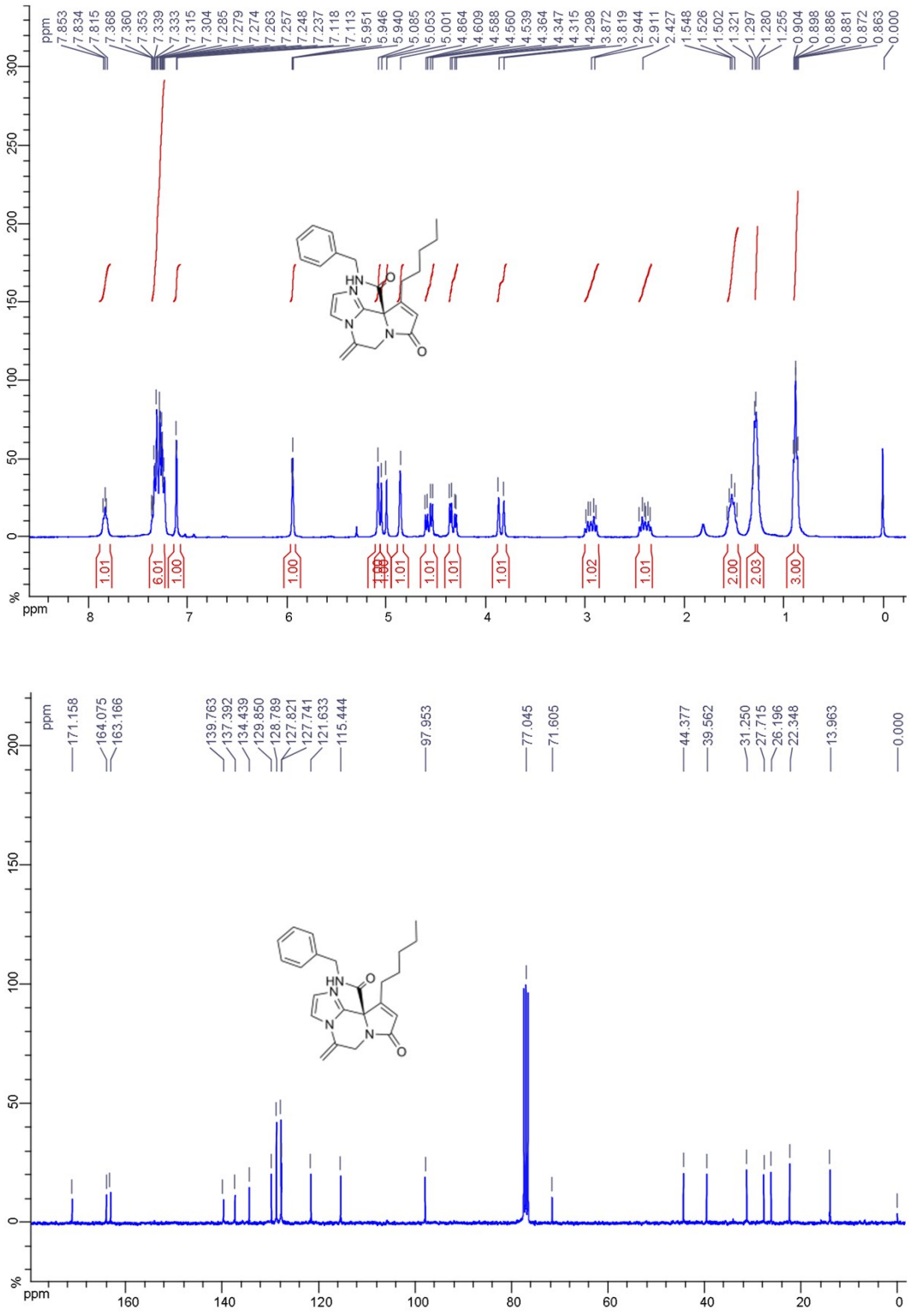


^{1}H and ^{13}C NMR spectra of compound **6g** (300 MHz, $CDCl_3$)

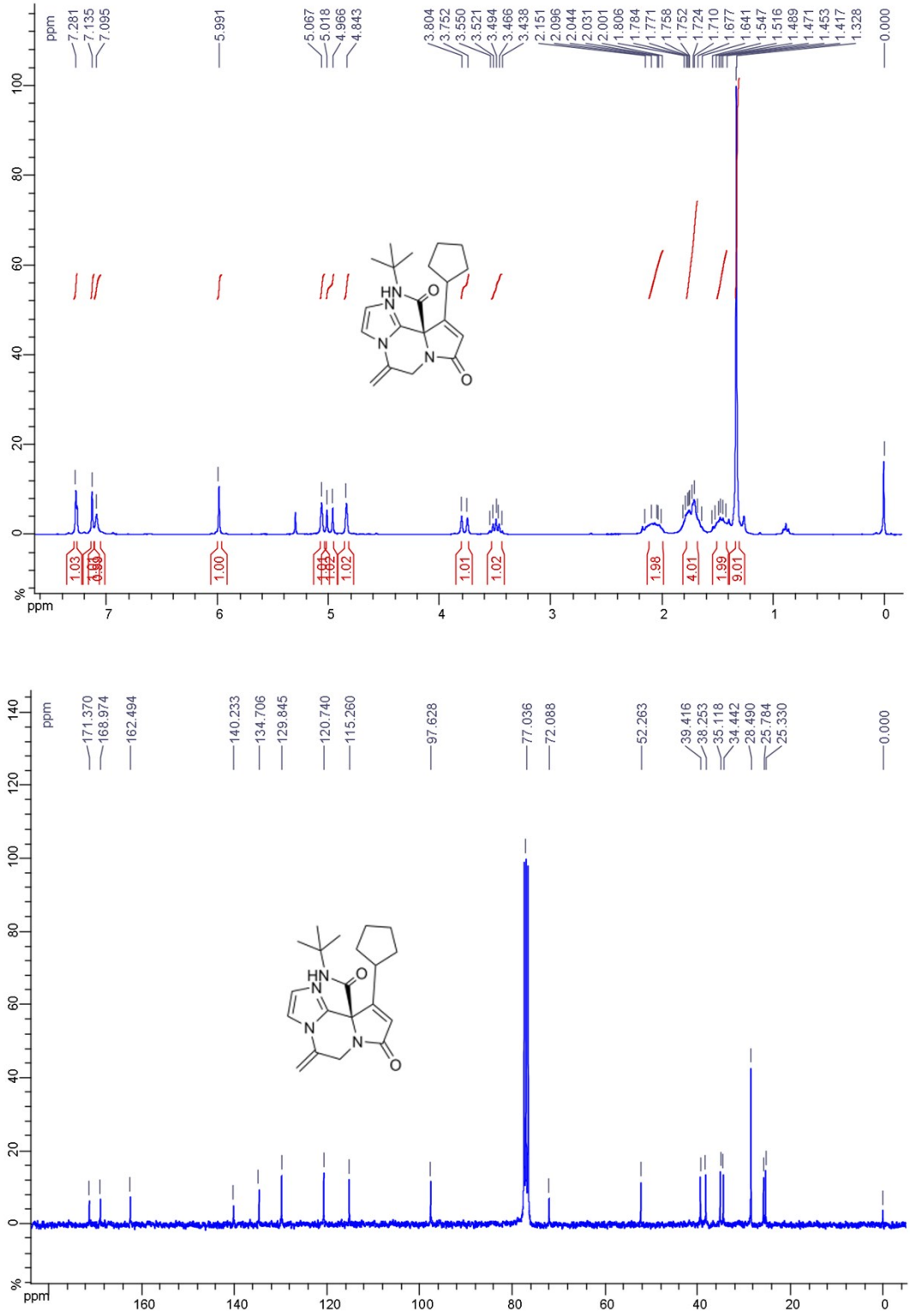




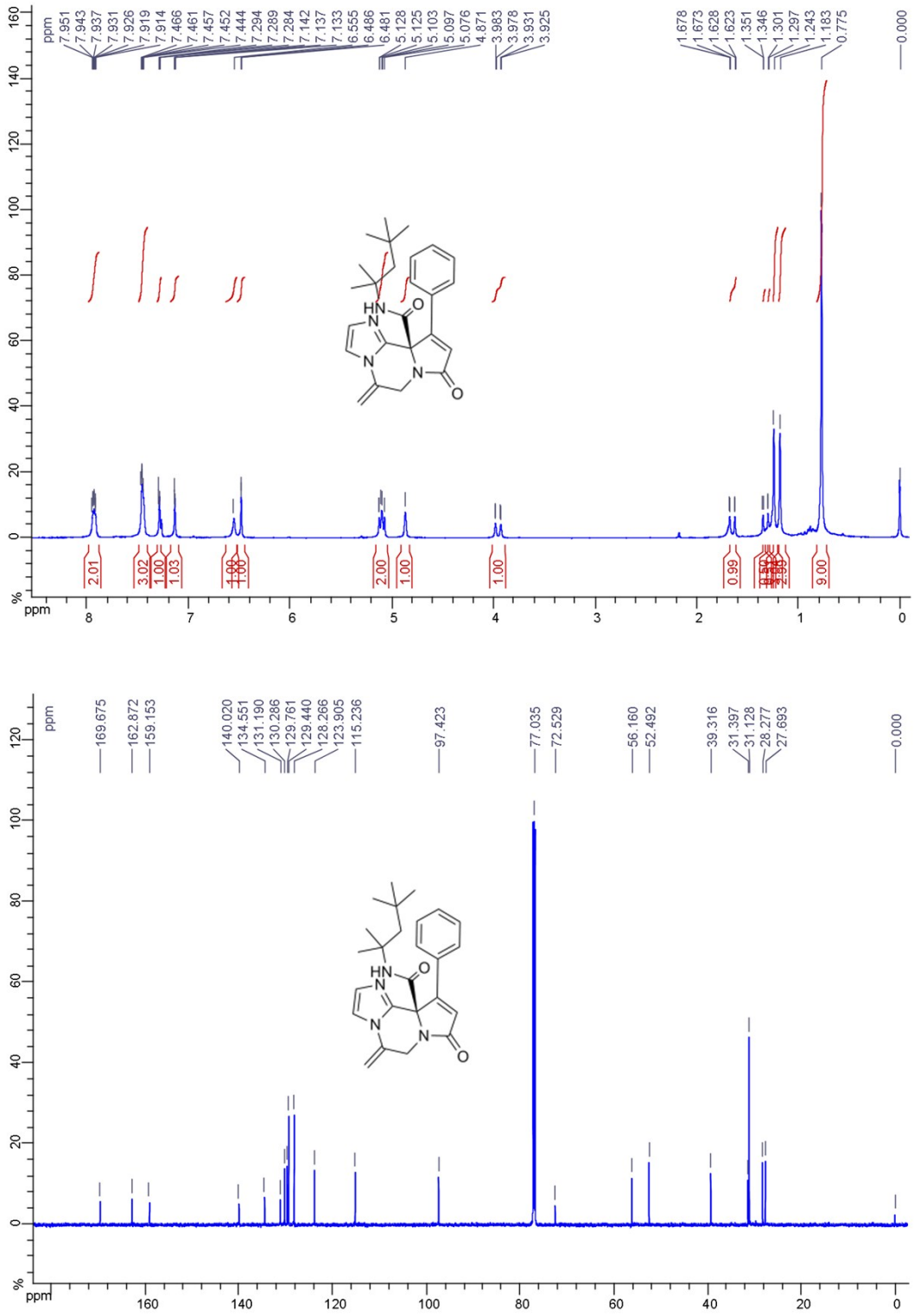
^{1}H and ^{13}C NMR spectra of compound **6h** (300 MHz, $CDCl_3$)



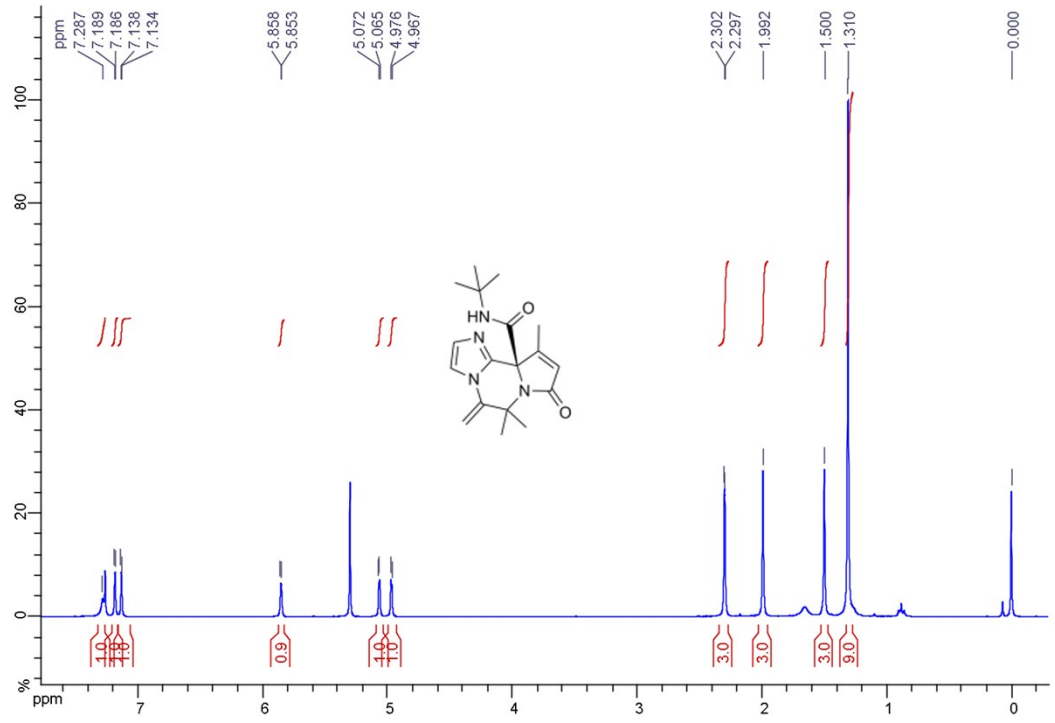
^{1}H and ^{13}C NMR spectra of compound **6i** (300 MHz, $CDCl_3$)

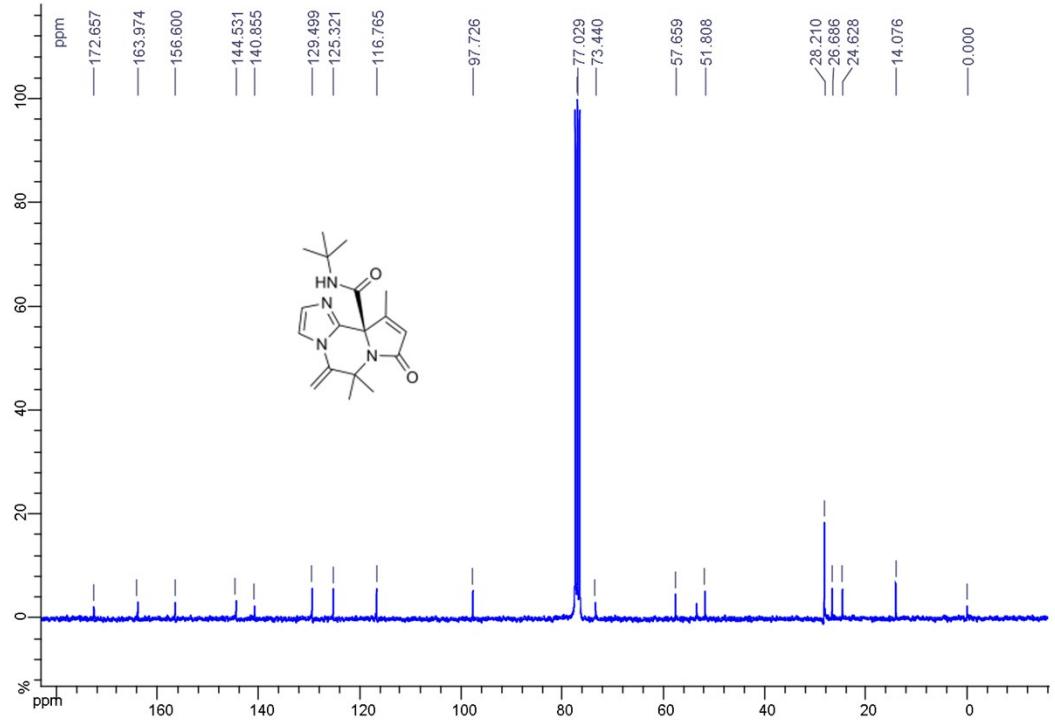


^{1}H and ^{13}C NMR spectra of compound **6j** (300 MHz, $CDCl_3$)

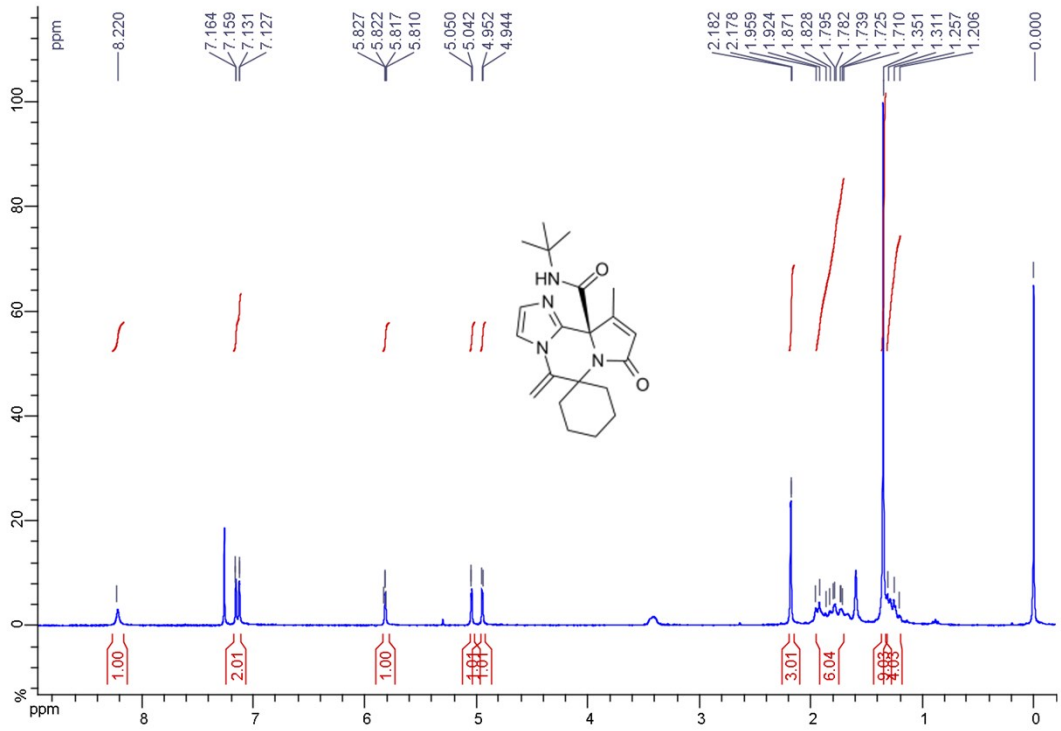


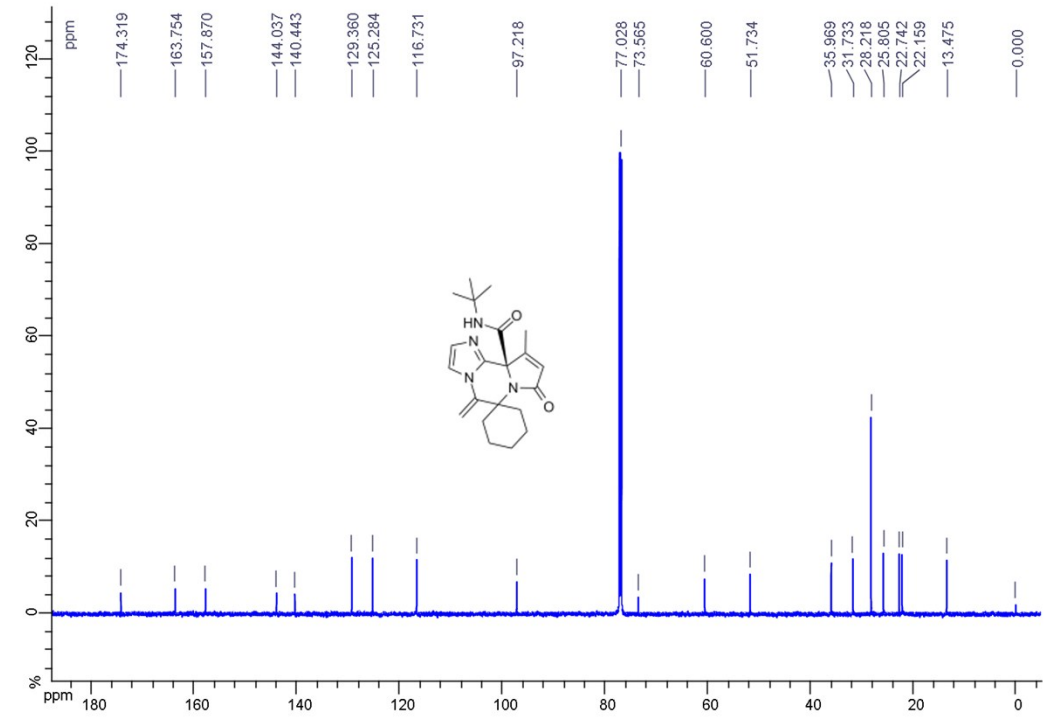
^{1}H and ^{13}C NMR spectra of compound **6k** (300 MHz, $CDCl_3$)



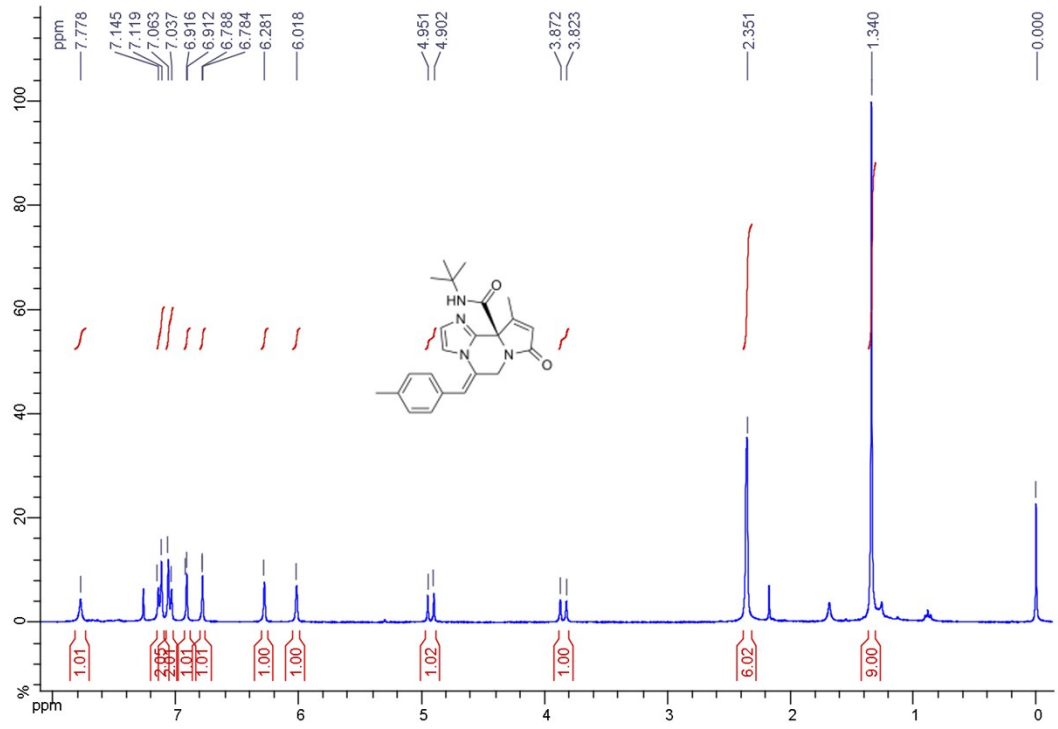


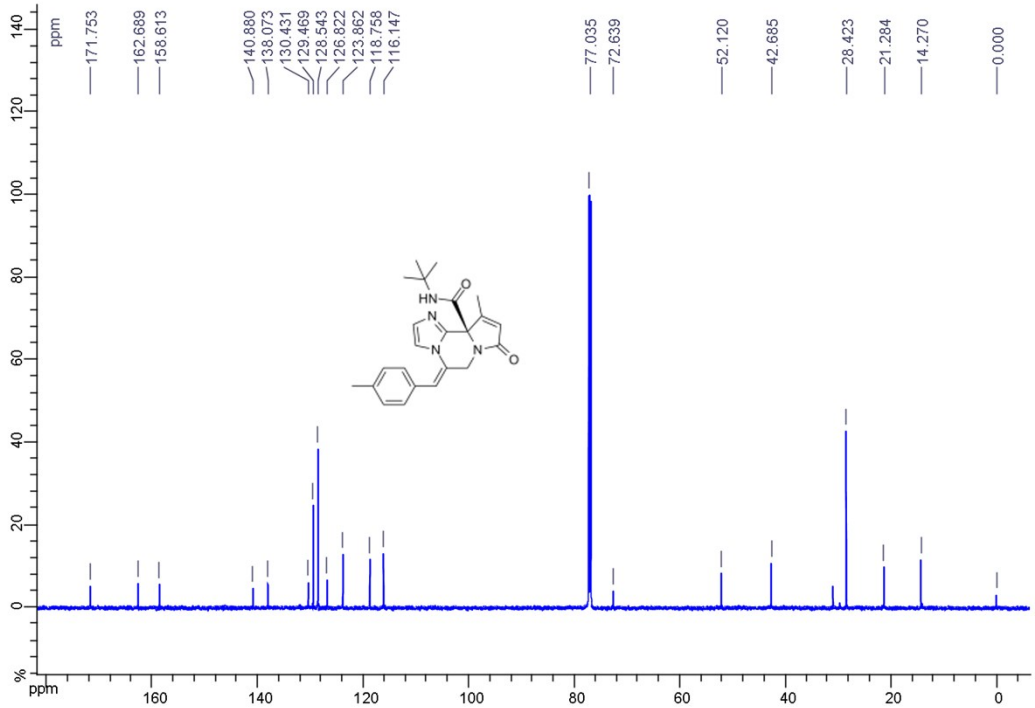
^{1}H and ^{13}C NMR spectra of compound **6l** (300 MHz, $CDCl_3$)



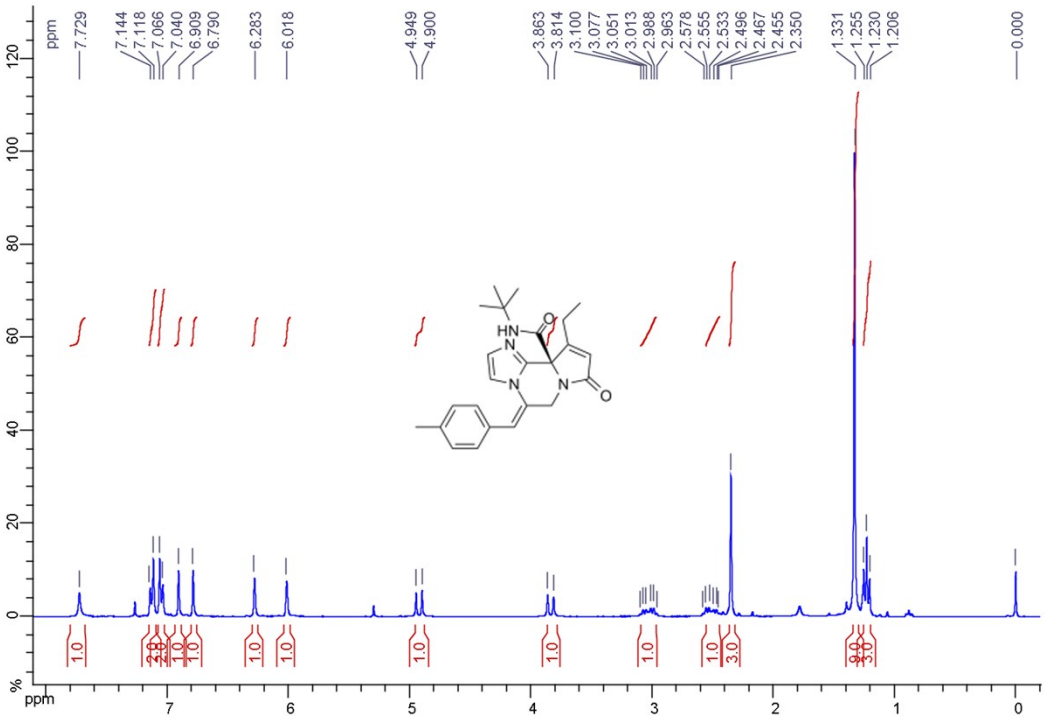


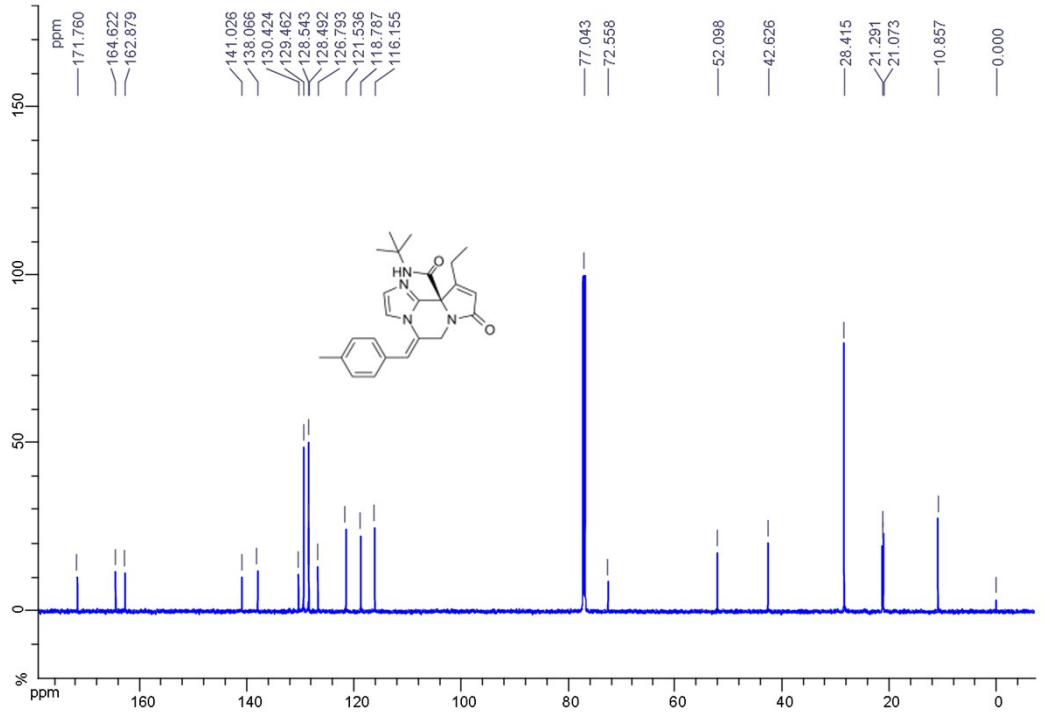
^{1}H and ^{13}C NMR spectra of compound **6m** (300 MHz, $CDCl_3$)



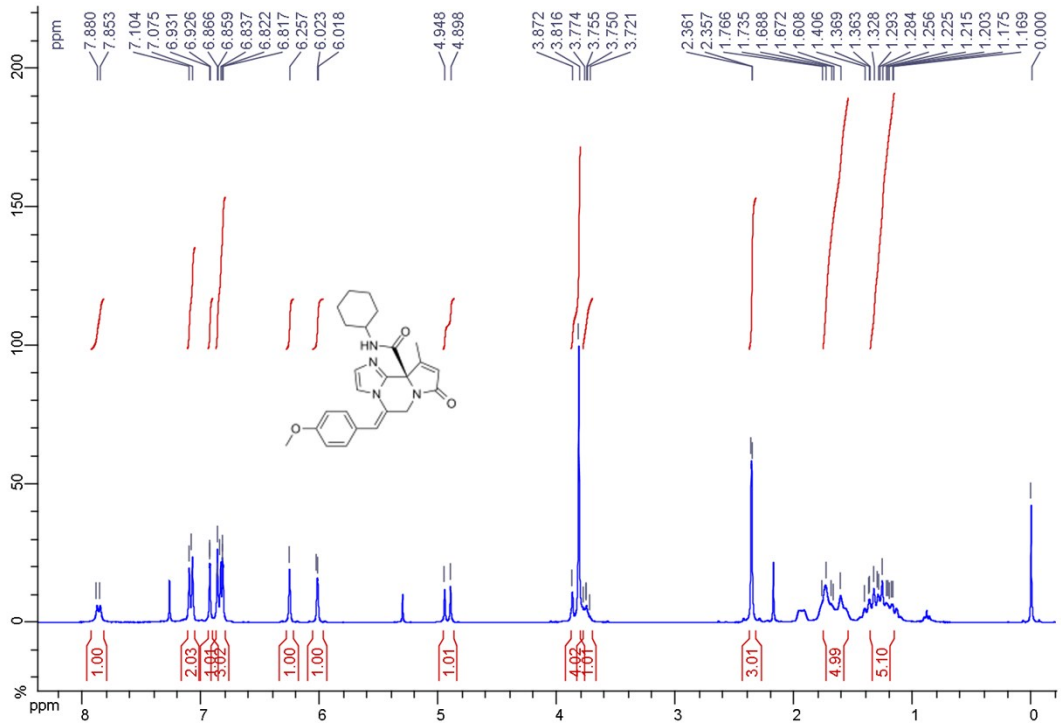


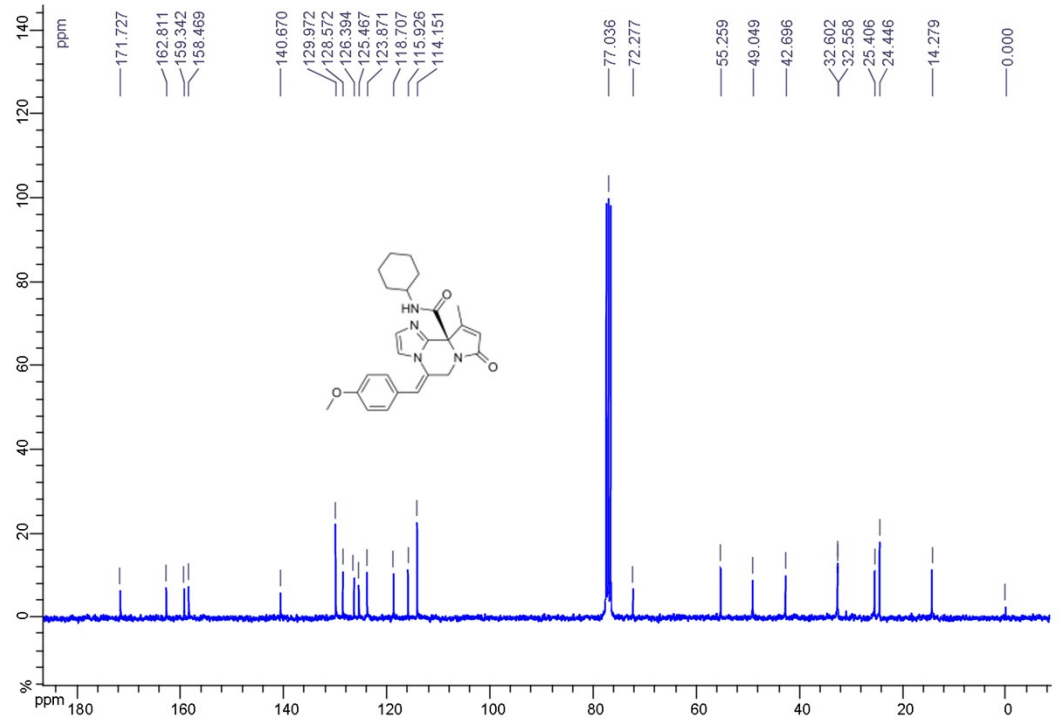
^{1}H and ^{13}C NMR spectra of compound **6n** (300 MHz, $CDCl_3$)



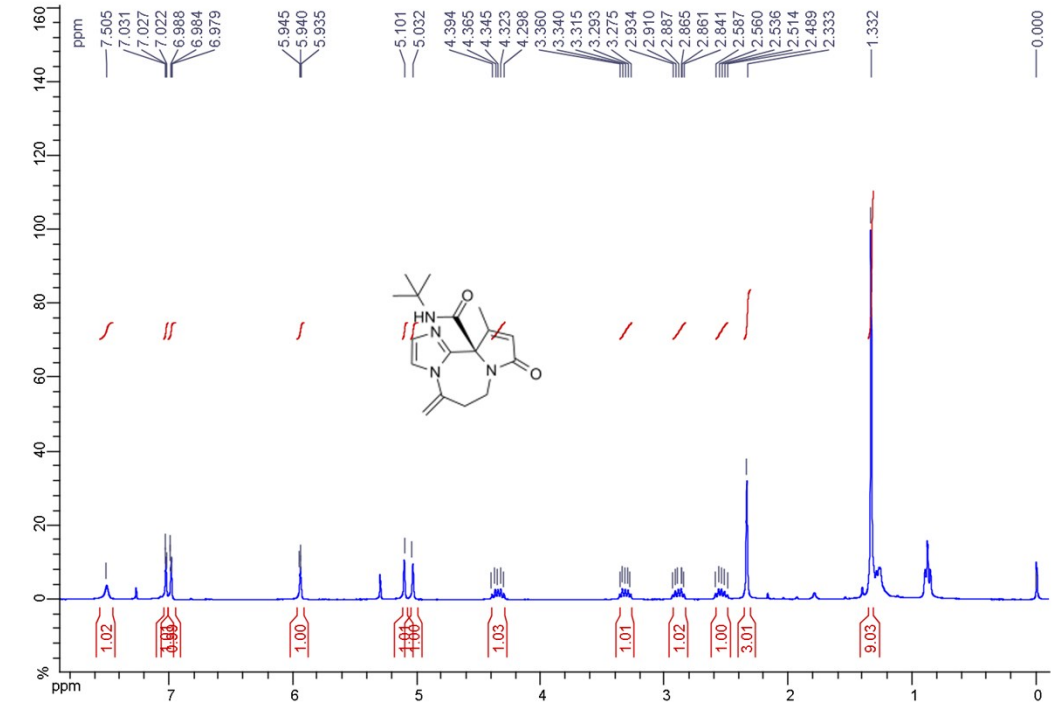


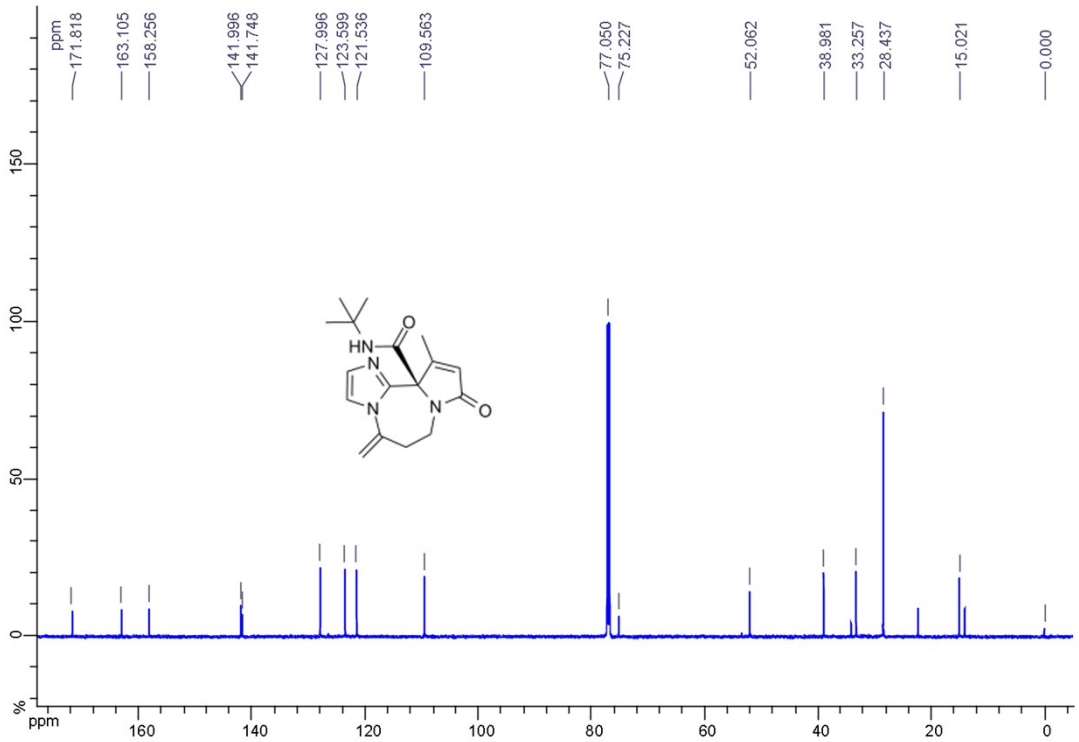
^{1}H and ^{13}C NMR spectra of compound **6o** (300 MHz, $CDCl_3$)



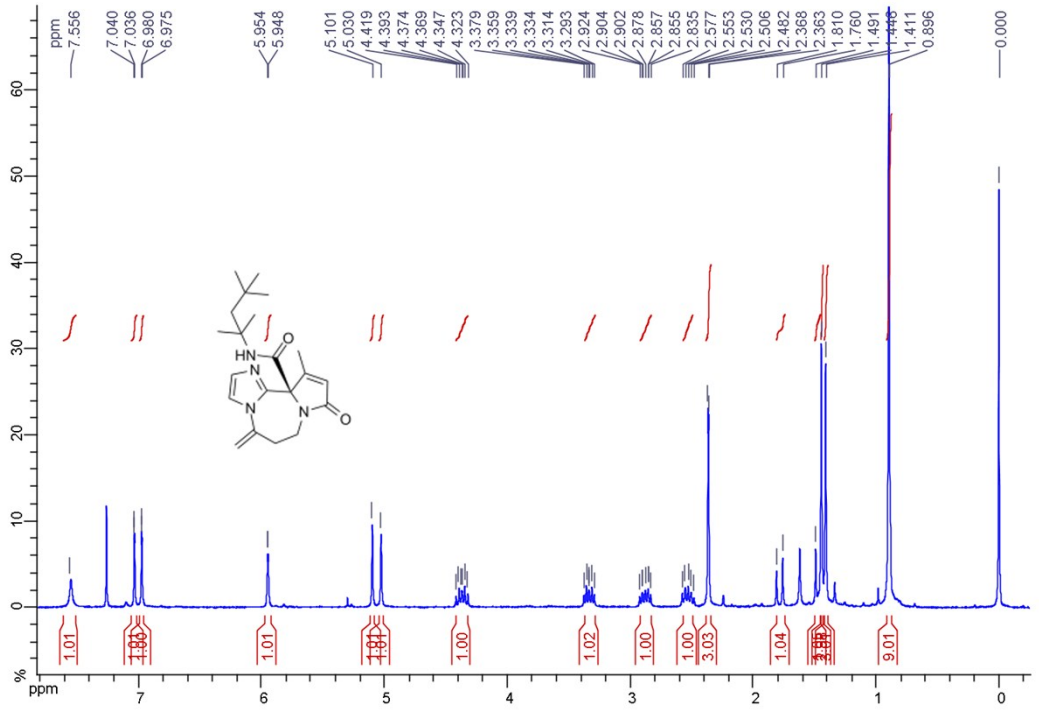


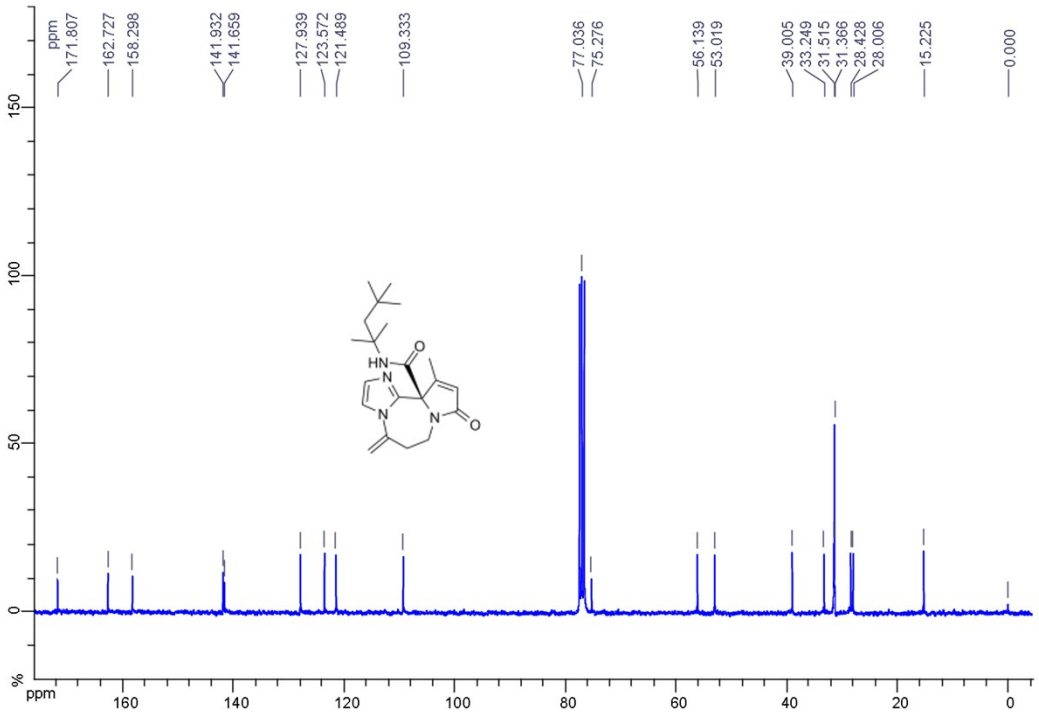
^{1}H and ^{13}C NMR spectra of compound **6p** (300 MHz, $CDCl_3$)



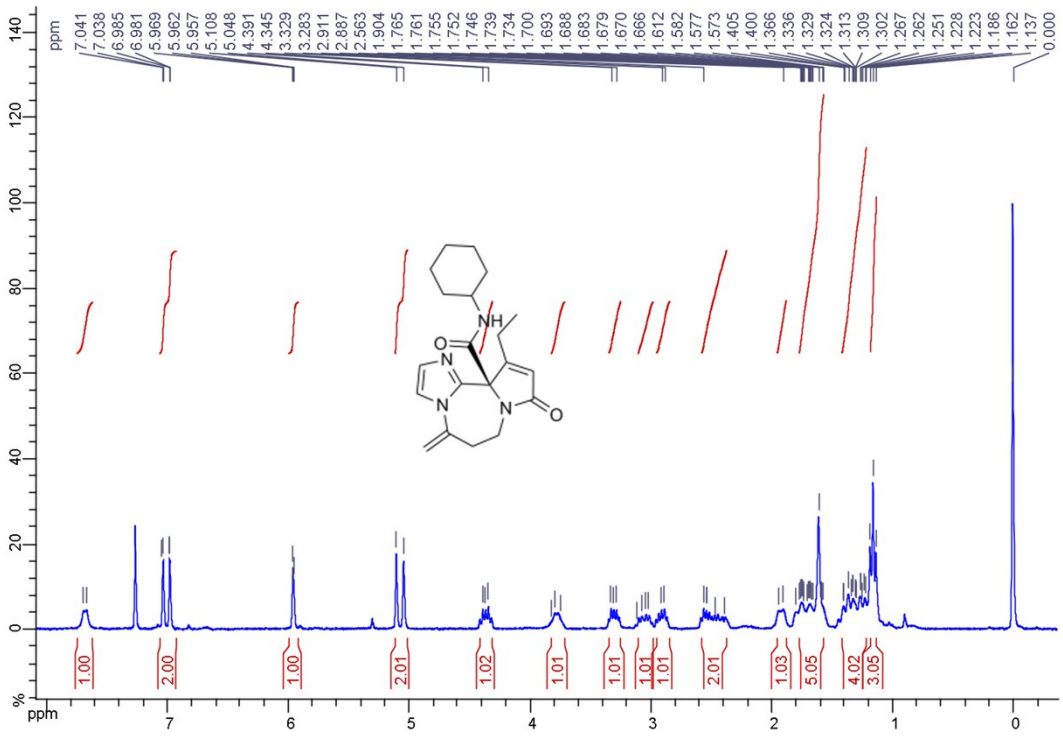


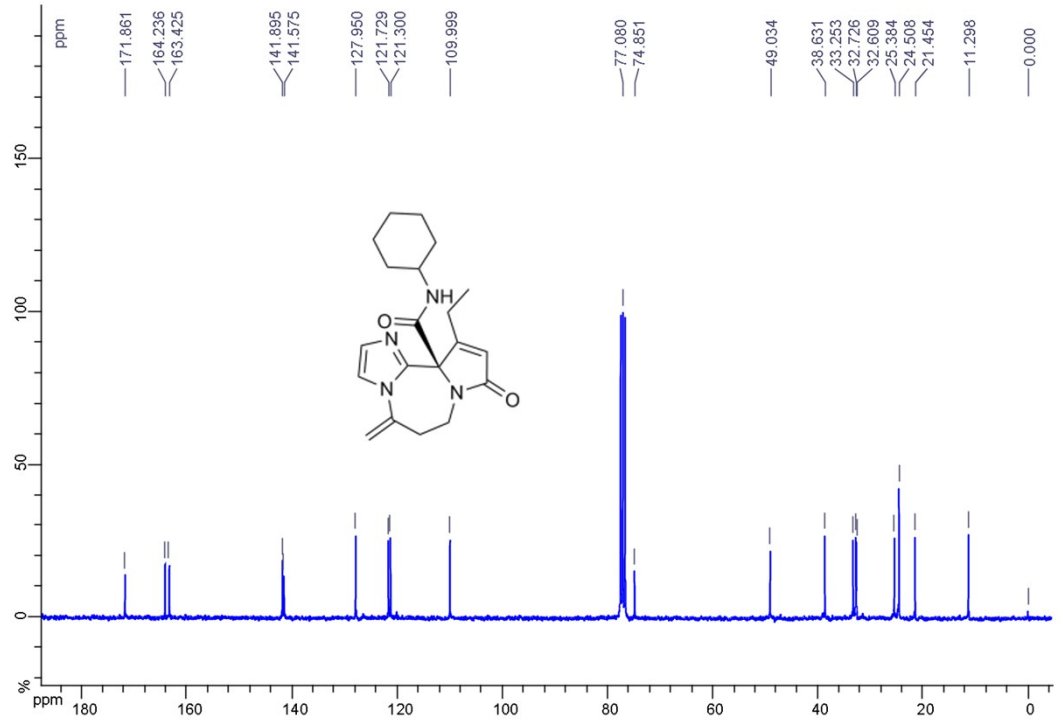
^{1}H and ^{13}C NMR spectra of compound **6q** (300 MHz, $CDCl_3$)



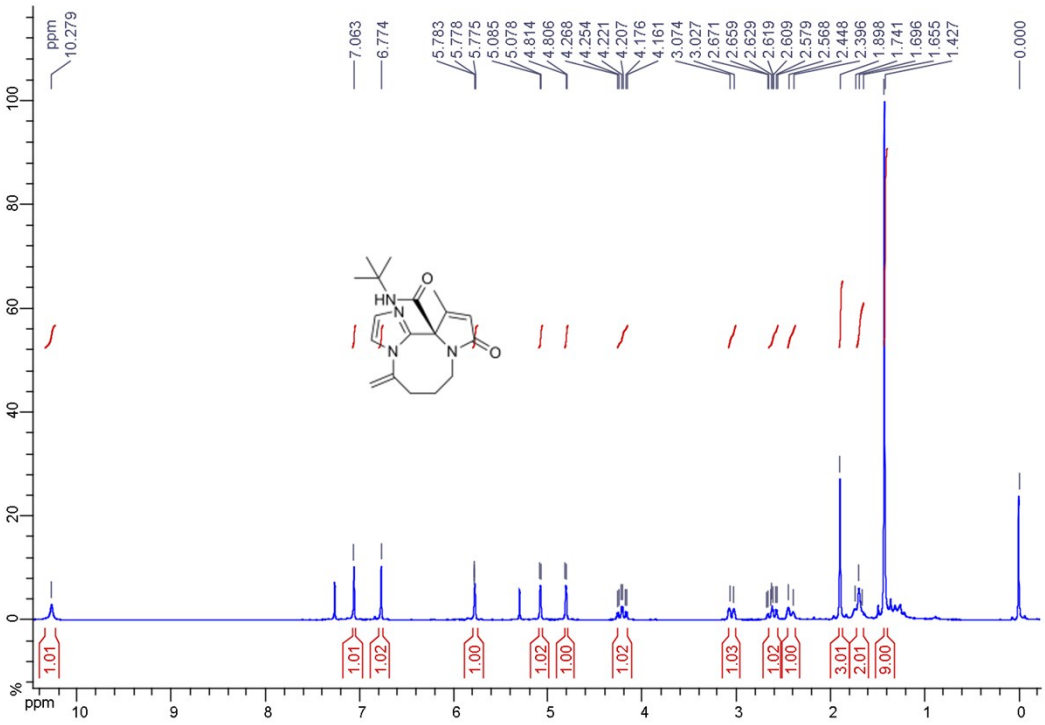


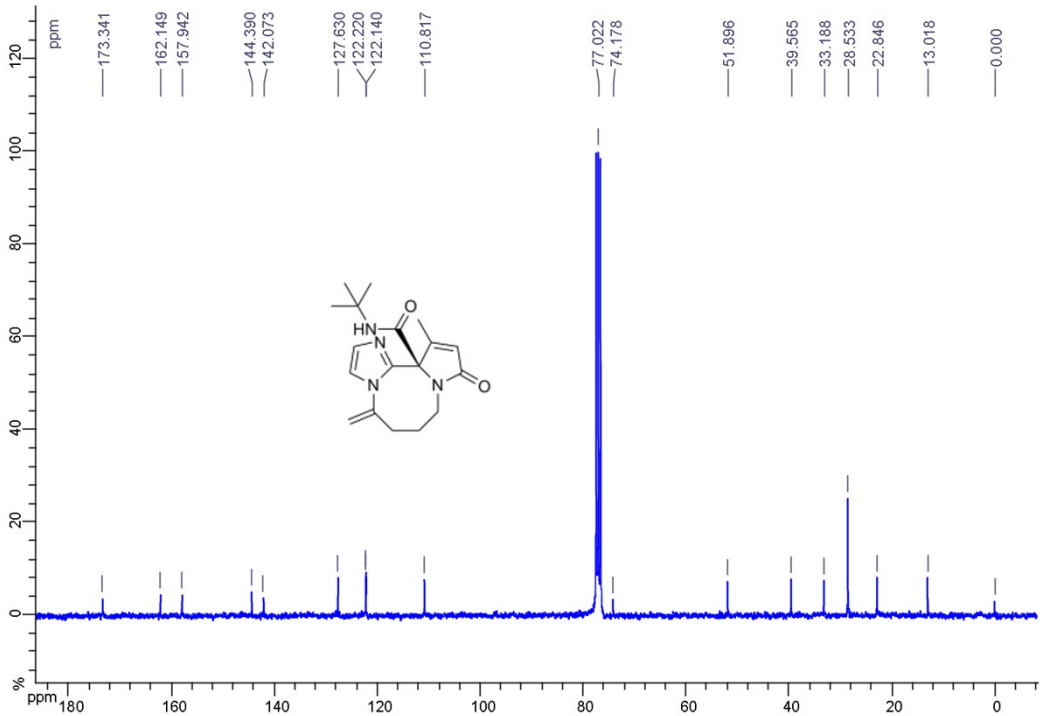
^{1}H and ^{13}C NMR spectra of compound **6r** (300 MHz, $CDCl_3$)



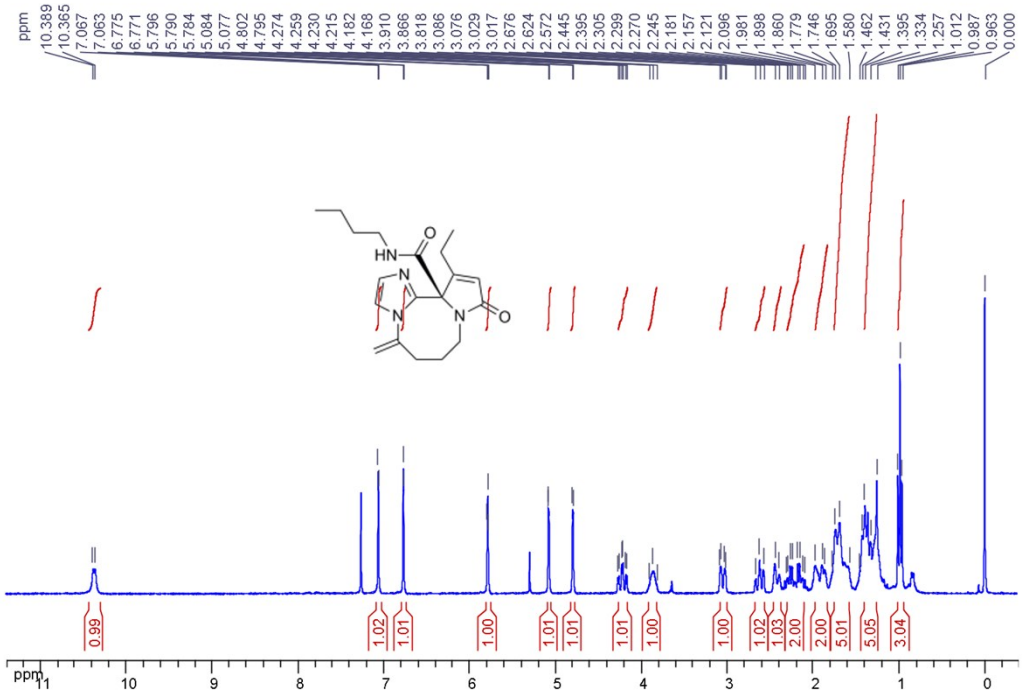


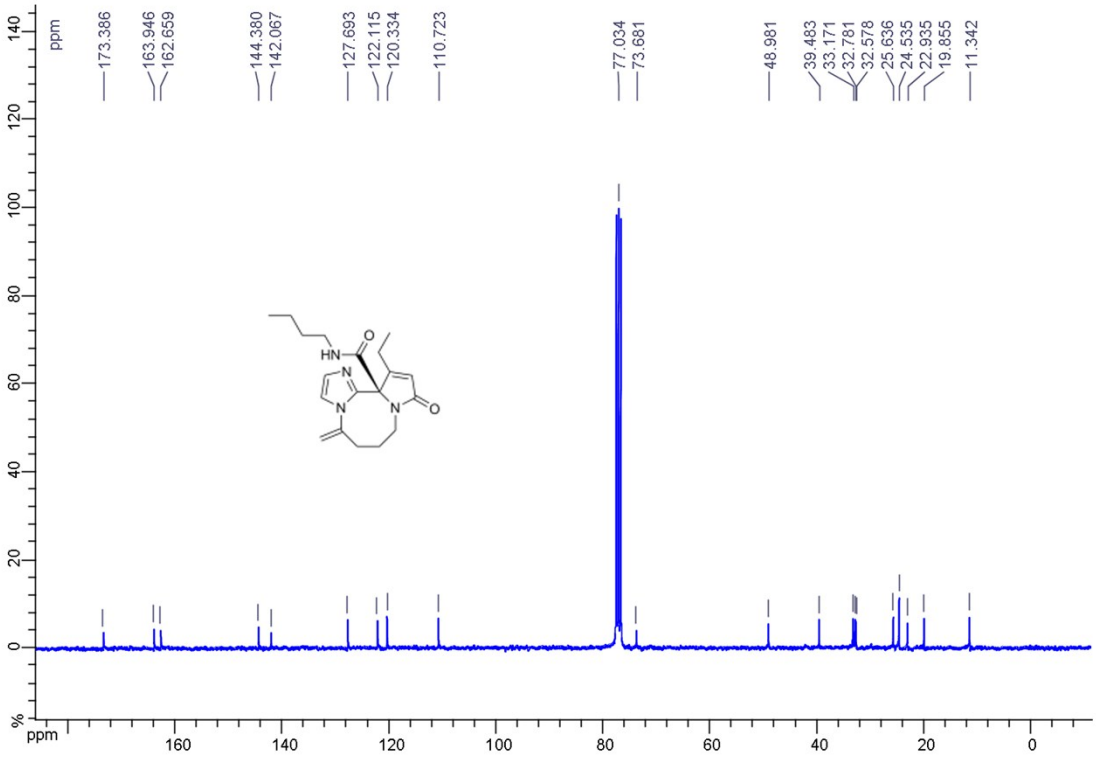
^{1}H and ^{13}C NMR spectra of compound **6s** (300 MHz, $CDCl_3$)





^{1}H and ^{13}C NMR spectra of compound **6t** (300 MHz, $CDCl_3$)





^{1}H and ^{13}C NMR spectra of compound **6u** (300 MHz, $CDCl_3$)