SUPPORTING INFORMATION

Synthesis of (spiro)cyclopentapyridinones via C_{sp3}-H functionalization: A post-Ugi gold-catalyzed regioselective tandem cyclization

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Experimental Section

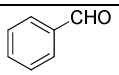
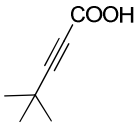
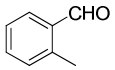
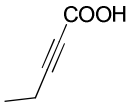
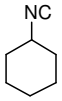
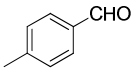
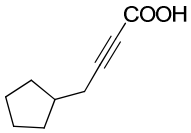
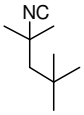
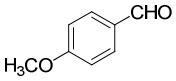
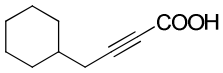
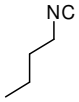
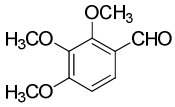
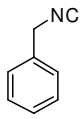
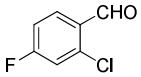
Materials:

All the starting materials, reagents and catalysts were purchased from Aldrich or Acros and used as such. For thin layer chromatography, analytical TLC plates (Alugram SIL G/UV254 and 70-230 mesh silica gel (E. M. Merck) were used). Column chromatography was performed using silica gel (Merck, 60-120 mesh size). Anhydrous solvents were purchased from Acros Organics and stored over molecular sieves. The chromatographic solvents used for isolation/purification of compounds were distilled prior to use. The chromatographic solvents are mentioned as volume:volume ratios. Reactions were typically run in oven-dried screw-cap vial under inert atmosphere.

Apparatus:

^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz & 300 MHz instrument using $CDCl_3$ and DMSO-d_6 as a solvent. The ^{1}H and ^{13}C chemical shifts are reported in parts per million relative to tetramethylsilane using the residual solvent signal as the internal reference. The following abbreviations were used to designate chemical shift multiplicities: s = singlet, bs = broad singlet, d = doublet, dd = double doublet, t = triplet, m = multiplet. The ^{13}C NMR spectra are proton decoupled. The melting points were determined on a digital Barnsted Electrothermal 9200 apparatus and are uncorrected. Mass spectra were recorded by using a Kratos MS50TC and a Kratos Mach III system. The ion source temperature was 150-250 ^{o}C, as required. High resolution EI-mass spectra were performed with a resolution of 10,000. The low-resolution spectra were obtained with a HP5989A MS instrument. The low resolution ESI-MS were obtained with a Thermo Scientific instrument.

Table 1. Starting materials.

Aldehyde	2-alkynoic acid	Isonitrile
 **1a**	 **3a**	 **4a**
 **1b**	 **3b**	 **4b**
 **1c**	 **3c**	 **4c**
 **1d**	 **3d**	 **4d**
 **1e**		 **4e**
 **1f**		
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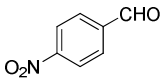
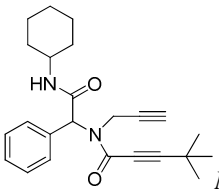
 **1h**		

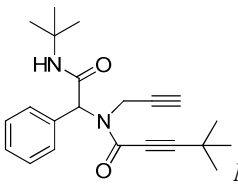
General procedure for synthesis of Ugi products.

To a solution of aldehyde **1a-i** (150 mg, 1 equiv) in methanol (10 mL) were added successively Na_2SO_4 (0.3g), propargylamine (1.1 equiv), alkynoic acid **3a-f** (1.1 equiv) and isonitrile **4a-e** (1.1 equiv) in a screw capped vial equipped with a magnetic stir bar. The reaction mixture was stirred at room temperature for 16-48 h in closed vial. After completion of the reaction, the mixture was diluted with EtOAc (100 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 obtain residue which was subjected to silica gel column chromatography (10% Diethyl ether in Dichloromethane) to afford the desired product **5a-t** as solid.



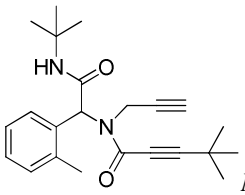
N-(2-(cyclohexylamino)-2-oxo-1-phenylethyl)-4,4-dimethyl-*N*-(prop-2-ynyl)pent-2-ynamide (**5a**).

White solid, Yield 90 % (mixture of rotamers ~ 1:2). Melting point: 135-137 ^{o}C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.46-7.29 (m, 5H), 6.35-6.26 (m, 0.32H), 6.09 (s, 1H), 5.87-5.74 (m, 0.64H), 4.35-4.19 (m, 1.70H), 3.99-3.75 (m, 1H), 3.64-3.52 (m, 0.34H), 2.22-1.86 (m, 3H), 1.79-1.53 (m, 4H), 1.42-1.01 (m, 14H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 167.7, 167.5, 155.5, 155.1, 134.3, 133.9, 129.5, 129.0, 128.7, 128.6, 103.1, 102.2, 79.4, 72.4, 72.1, 71.9, 71.2, 66.9, 60.3, 48.9, 48.6, 36.8, 32.9 (2), 32.7 (2), 32.2, 29.9, 27.8, 25.4, 24.7 (2). **HRMS** calculated for $C_{24}H_{30}N_2O_2$ 378.2307, found 378.2328.



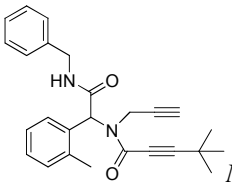
N-(2-(*tert*-butylamino)-2-oxo-1-phenylethyl)-4,4-dimethyl-*N*-(prop-2-ynyl)pent-2-ynamide (**5b**).

White solid, Yield 86 % (mixture of rotamers ~ 1:2). Melting point: 160-162 ^{o}C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.45-7.29 (m, 5H), 6.22 (bs, 0.30H), 6.04 (s, 0.66H), 5.98 (s, 0.32H), 5.71 (bs, 0.65H) 4.42-4.18 (m, 1.70H), 3.59 (d, *J* = 17.7 Hz, 0.31H), 2.16-2.12 (m, 0.28H), 1.98-1.93 (m, 0.62H), 1.44 (s, 3H), 1.36 (s, 6H), 1.29 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.1, 167.8, 155.5, 155.1, 134.5, 134.0, 129.5 (2), 129.0, 128.8, 128.7, 128.5, 102.9, 102.1, 79.5, 79.4, 72.5, 72.0, 70.9, 67.2, 60.4, 52.2, 51.8, 36.7, 32.2, 30.0, 29.8, 28.6, 28.5, 27.8 (2). **HRMS** calculated for $C_{22}H_{28}N_2O_2$ 352.2151, found 352.2134.



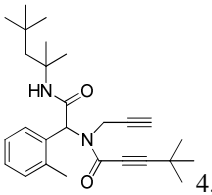
N-(2-(*tert*-butylamino)-2-oxo-1-*o*-tolylethyl)-4,4-dimethyl-*N*-(prop-2-ynyl)pent-2-ynamide (**5c**).

White solid, Yield 93 % (mixture of rotamers ~ 1:2). Melting point: 202-204 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.41-7.15 (m, 4H), 6.21 (bs, 0.31H), 6.12 (s, 0.65H), 6.04 (s, 0.34H), 5.57 (bs, 0.62H), 4.40 (bd, J = 18.3 Hz, 0.65H), 4.17 (t, *J* = 17.1 Hz, 1H), 3.55 (d, *J* = 17.4 Hz, 0.33H), 2.32-2.24 (m, 3H), 2.08 (bs, 0.32H), 1.83 (bs, 0.59H), 1.44 (s, 3H), 1.36 (s, 6H), 1.32-1.27 (m, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.9, 168.6, 155.3, 155.2, 139.5, 138.5, 132.6, 132.3, 130.9, 130.6, 129.2, 129.0 (2), 128.9, 126.7, 126.3, 102.7, 101.7, 79.3, 79.0, 72.4, 71.9, 71.7, 70.1, 64.9, 57.8, 52.2, 51.8, 36.4, 31.6, 30.0, 29.9, 28.6, 28.5, 27.8 (2), 19.4, 19.1. **HRMS** calculated for $C_{23}H_{30}N_2O_2$ 366.2307, found 366.2278.



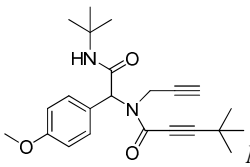
N-(2-(benzylamino)-2-oxo-1-*o*-tolylethyl)-4,4-dimethyl-*N*-(prop-2-ynyl)pent-2-ynamide (**5d**).

White solid, Yield 92% (mixture of rotamers ~ 1:2). Melting point: 188-190 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.41-7.15 (m, 9H), 6.80-6.72 (m, 0.29H), 6.25 (bs, 1H), 6.15-6.05 (m, 0.64H), 4.70-4.42 (m, 2H), 4.38-4.13 (m, 1.62H), 3.55 (dd, *J* = 17.4 Hz, J = 2.4 Hz, 0.33H), 2.29 (s, 3H), 1.82 (bs, 1H), 1.29 (s, 5.7H), 1.27 (s, 2.8H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 169.4, 155.3, 155.2, 139.2, 138.5, 137.6, 131.9 (2), 131.0, 130.7, 129.3, 129.2 (2), 129.1, 128.7, 128.6, 128.0, 127.8, 127.6, 127.4, 126.6, 126.3, 103.1, 102.0, 78.9, 78.8, 72.3, 71.8, 71.6, 70.6, 64.4, 57.9, 43.8, 43.7, 36.4, 31.7, 29.9 (2), 27.8 (2), 19.3, 19.2. **HRMS** calculated for $C_{26}H_{28}N_2O_2$ 400.2151, found 400.2139.



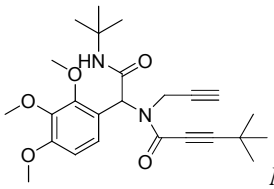
4,4-dimethyl-*N*-(2-oxo-1-*o*-tolyl-2-(2,4,4-trimethylpentan-2-ylamino)ethyl)-*N*-(prop-2-ynyl)pent-2-ynamide (**5e**).

White solid, Yield 96% (mixture of rotamers ~ 1:2). Melting point: 163-165°C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.43-7.16 (m, 4H), 6.15 (bs, 0.30H), 6.06 (s, 1H), 5.54 (bs, 0.58H), 4.39 (dd, *J* = 18.1 Hz, *J* = 2.7 Hz, 0.66H), 4.21-4.11 (m, 1H), 3.67 (dd, *J* = 16.8 Hz, *J* = 2.1 Hz, 0.31H), 2.31-2.28 (m, 3H), 2.06 (bt, 0.31H), 1.89-1.81 (m, 1H), 1.77 (bd, 0.60H), 1.61 (s, 0.60H), 1.59-1.52 (m, 0.35H), 1.56-1.39 (m, 6H), 1.34-1.26 (m, 9H), 1.02 (s, 3H), 0.95 (s, 6H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.5, 168.1, 155.3, 155.1, 139.3, 138.5, 132.5, 132.4, 130.9, 130.6, 129.2 (2), 129.1, 128.9, 126.5, 126.2, 102.6, 101.7, 79.2, 79.0, 72.4, 72.1, 71.6, 70.4, 64.7, 58.2, 56.4, 56.0, 53.4, 52.7, 52.4, 36.5, 31.8, 31.6 (2), 31.5, 31.4, 30.0, 29.9, 29.1, 28.9, 28.1, 27.8 (2), 19.3 (2). **HRMS** calculated for $C_{27}H_{38}N_2O_2$ 422.2933, found 422.2942.



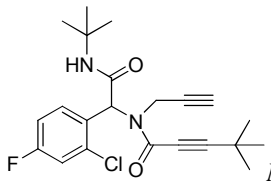
N-(2-(*tert*-butylamino)-1-(4-methoxyphenyl)-2-oxoethyl)-4,4-dimethyl-*N*-(prop-2-ynyl)pent-2-ynamide (**5f**).

White solid, Yield 83 % (mixture of rotamers ~ 1:2). Melting point: 147-149 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.38-7.20 (m, 2H), 6.96-6.84 (m, 2H), 6.19 (bs, 0.30H), 5.97 (s, 0.64H), 5.92 (s, 0.33), 5.64 (bs, 0.61H), 4.41 (m, 1.67H), 3.82 (s, 3H), 3.58 (d, *J* = 17.7 Hz, 0.33H), 2.14 (bs, 0.28H), 1.97 (bs, 0.60), 1.43 (s, 3H), 1.35 (s, 6H), 1.31-1.27 (m, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.3, 168.1, 159.9, 159.8, 155.4, 155.1, 131.0, 130.8, 126.4, 125.9, 114.4, 114.1, 102.8, 101.8, 79.7, 79.5, 72.5, 72.0, 71.9, 70.9, 66.8, 60.0, 55.3, 55.2, 52.1, 51.7, 36.5, 32.0, 30.0, 29.9, 28.6 (2), 27.8 (2). **HRMS** calculated for $C_{23}H_{30}N_2O_3$ 282.2256, found 282.2250.



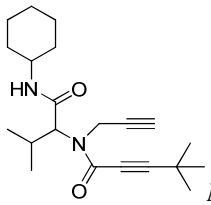
N-(2-(*tert*-butylamino)-2-oxo-1-(2,3,4-trimethoxyphenyl)ethyl)-4,4-dimethyl-*N*-(prop-2-yn-1-yl)pent-2-ynamide (**5g**).

White solid, Yield 91 % (mixture of rotamers ~ 1:1). Melting point: 62-64 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.14-6.99 (m, 1H), 6.71-6.64 (m, 1H), 6.24 (s, 1H), 6.07 (bs, 0.44H), 5.59 (bs, 0.53H), 4.48-4.16 (m, 1.59H), 3.93-3.83 (m, 9H), 3.76 (dd, *J* = 17.1 Hz, *J* = 2.7 Hz, 0.57H), 2.06 (bs, 0.43H), 1.92 (bt, 0.50H), 1.41 (s, 4H), 1.36-1.26 (m, 14H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.7, 168.5, 155.3, 155.1, 154.6, 154.5, 153.0, 152.8, 141.9, 141.8, 124.5, 124.4, 120.4, 119.9, 107.1, 106.8, 101.9, 101.4, 79.6 (2), 72.6, 72.0, 71.4, 70.7, 61.6, 60.8, 60.6, 60.5, 55.9 (2), 55.0, 52.0, 51.7, 36.5, 31.8, 30.0, 29.9, 28.6 (2), 27.8, 27.7. **HRMS** calculated for $C_{25}H_{34}N_2O_5$ 442.2468, found 442.2492.



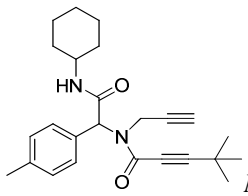
N-(2-(*tert*-butylamino)-1-(2-chloro-4-fluorophenyl)-2-oxoethyl)-4,4-dimethyl-*N*-(prop-2-yn-1-yl)pent-2-ynamide (**5h**).

White solid, Yield 89 % (mixture of rotamers ~ 1:2). Melting point: 171-173 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.63-7.38 (m, 1H), 7.22-6.99 (m, 2H), 6.27 (bs, 0.34H), 6.21 (s, 0.37H), 6.16 (s, 0.57H), 5.75 (bs, 0.55H), 4.44-4.21 (m, 1.60H), 3.47 (dd, *J* = 17.7 Hz, *J* = 2.1 Hz, 0.40H), 2.14 (bs, 0.34H), 1.95 (bs, 0.52H), 1.45-1.27 (m, 18H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 167.8, 167.3, 164.3 (2), 161.0, 160.9, 155.4, 155.0, 137.5, 137.3, 137.1, 137.0, 132.1, 131.9, 131.8, 128.5, 128.4, 128.2, 128.1, 117.6, 117.4, 117.3, 117.1, 114.7, 114.5, 114.4, 114.1, 102.9, 102.0, 79.0, 78.5, 72.3, 72.2, 71.7, 70.9, 64.1, 57.3, 52.4, 51.9, 36.7, 31.5, 29.9 (2), 28.5 (2), 27.8 (2). **HRMS** calculated for $C_{22}H_{26}ClFN_2O_2$ 404.1667, found 404.0869.



N-(1-(cyclohexylamino)-3-methyl-1-oxobutan-2-yl)-4,4-dimethyl-*N*-(prop-2-ynyl)pent-2-ynamide (**5i**).

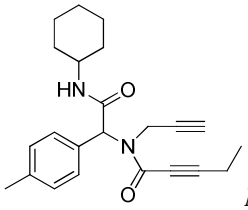
White solid, Yield 71 % (mixture of rotamers ~ 1:4). Melting point: 56-59 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 6.06-5.89 (m, 0.78H), 5.50-5.40 (m, 0.16H), 4.58 (dd, *J* = 18.0 Hz, *J* = 2.7 Hz, 0.88H), 4.41-4.12 (m, 2.27H), 3.85-3.60 (m, 1H), 2.48-2.29 (m, 1H), 2.24 (bt, 0.77H), 2.16 (bs, 0.19H), 1.99-1.78 (m, 2H), 1.76-1.50 (m, 4H), 1.44-1.24 (m, 11H), 1.24-1.03 (3H), 1.02-0.89 (m, 6H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.4, 167.7, 156.0, 154.5, 102.5, 79.4, 78.7, 72.4, 71.7, 71.1, 68.7, 63.2, 48.4, 48.2, 35.6, 33.0, 32.8, 32.7, 32.5, 30.1, 29.9, 27.9, 27.8, 27.5, 27.1, 25.4 (2), 24.7, 24.6 (2), 20.0, 19.4 (2). **HRMS** calculated for $C_{21}H_{32}N_2O_2$ 344.2464, found 344.2473.



N-(2-(cyclohexylamino)-2-oxo-1-*p*-tolylethyl)-4,4-dimethyl-*N*-(prop-2-ynyl)pent-2-ynamide (**5j**).

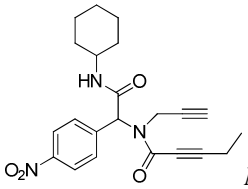
White solid, Yield 82 % (mixture of rotamers ~ 1:2). Melting point: 129-131 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.31-7.13 (m, 4H), 6.29 (bs, 0.31H), 6.04 (s, 1H), 5.76 (bs, 0.60H), 4.32-4.20 (m, 1.62H), 4.00-

3.73 (m, 1H), 3.55 (d, *J* = 17.7 Hz, 0.33H), 2.36 (s, 3H), 2.21-1.86 (m, 3H), 1.80-1.53 (m, 3H), 1.48-0.85 (m, 15H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 167.9, 167.8, 155.5, 155.1, 138.8, 138.4, 131.3, 130.8, 129.7, 129.4, 102.9, 102.0, 79.5, 72.5, 72.0 (2), 71.2, 66.7, 60.2, 48.8, 48.6, 36.7, 32.9, 32.7 (2), 32.1, 30.0, 29.9, 27.8 (2), 25.4, 24.8, 24.7, 21.1. **HRMS** calculated for $C_{25}H_{32}N_2O_2$ 392.2464, found 392.2450.



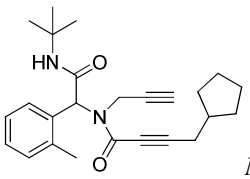
N-(2-(cyclohexylamino)-2-oxo-1-(*p*-tolyl)ethyl)-*N*-(prop-2-yn-1-yl)pent-2-ynamide (**5k**).

Pale yellow solid, Yield 92 % (mixture of rotamers ~ 1:2). Melting point: 100-102 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.31-7.14 (m, 4H), 6.30 (bd, 0.37H), 6.09 (s, 0.39H), 6.00 (s, 0.60H), 5.78 (bs, 0.59H), 4.34-4.29 (m, 1H), 4.23 (dd, *J* = 17.7 Hz, *J* = 2.1 Hz, 0.61H), 3.99-3.74 (m, 1H), 3.57 (dd, *J* = 17.7 Hz, *J* = 2.4 Hz, 0.39H), 2.40 (m, 2H), 2.36 (m, 3H), 2.18 (m, 0.36H), 2.04 (m, 0.65H), 2.01-1.86 (m, 2H), 1.80-1.54 (m, 4H), 1.47-1.27 (m, 2H), 1.22 (bt, 3H), 1.18-1.02 (m, 2H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 167.8, 155.4, 155.0, 138.9, 138.5, 131.1, 130.8, 129.7, 129.5, 129.4 (2), 97.0, 96.2, 79.5, 79.4, 73.2, 72.7, 72.0, 71.4, 66.6, 60.6, 48.9, 48.6, 36.8, 32.9, 32.8, 32.7 (2), 32.2, 25.4, 24.8, 24.7 (2), 21.1, 12.7 (2), 12.6. **HRMS** calculated for $C_{23}H_{28}N_2O_2$ 364.2151, found 364.2173.



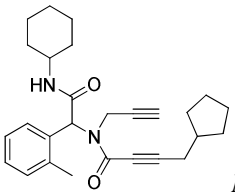
N-(2-(cyclohexylamino)-1-(4-nitrophenyl)-2-oxoethyl)-*N*-(prop-2-yn-1-yl)pent-2-ynamide (**5l**).

Pale yellow solid, Yield 91 % (mixture of rotamers ~ 1:3). Melting point: 69-71 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 8.29-8.17 (m, 2H), 7.65-7.54 (m, 2H), 6.34-6.25 (m, 0.22H), 6.21 (s, 0.24H), 6.14-6.00 (m, 1.45H), 4.50 (dd, *J* = 18.3 Hz, *J* = 2.7 Hz, 0.72H), 4.37 (dd, *J* = 18.3 Hz, *J* = 2.1 Hz, 0.77H), 4.26 (dd, *J* = 17.4 Hz, *J* = 2.7 Hz, 0.25H), 4.00-3.76 (m, 1H), 3.70 (dd, *J* = 17.7 Hz, *J* = 2.1 Hz, 0.25H), 2.48-2.35 (m, 2H), 2.22-2.18 (m, 0.22H), 2.12-2.07 (m, 0.68H), 2.06-1.87 (m, 2H), 1.82-1.62 (m, 3H), 1.46-1.08 (m, 8H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 166.6, 166.2, 155.4, 154.8, 147.8, 141.8, 141.2, 130.5, 130.1, 123.9, 123.7, 97.9, 97.5, 78.6, 78.5, 72.8, 72.7, 72.3, 65.4, 59.7, 49.2, 48.8, 37.3, 32.9, 32.8 (2), 32.6, 32.5, 25.4, 25.3, 24.8, 24.7 (2), 24.6, 12.7, 12.6, 12.5. **HRMS** calculated for $C_{22}H_{25}N_3O_4$ 395.1845, found 395.1847.



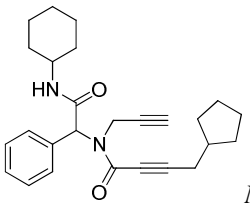
N-(2-(*tert*-butylamino)-2-oxo-1-(*o*-tolyl)ethyl)-4-cyclopentyl-*N*-(prop-2-yn-1-yl)but-2-ynamide (**5m**).

White solid, Yield 88% (mixture of rotamers ~ 1:2). Melting point: 173-175 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.45-7.14 (m, 4H), 6.23-6.03 (m, 1.30H), 5.54 (bs, 0.61H), 4.50-4.10 (m, 1.66H), 3.68-3.53 (m, 0.33H), 2.46-2.36 (m, 2H), 2.30 (bs, 3H), 2.20-2.03 (m, 1.35H), 1.92-1.74 (m, 2.65H), 1.71-1.49 (m, 4H), 1.48-1.18 (m, 11H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.8, 168.6, 155.2, 155.1, 139.5, 138.5, 132.5, 132.3, 130.9, 130.6, 129.2, 129.1, 128.9, 126.6, 126.3, 94.5, 79.3, 79.0, 73.8, 73.3, 71.6, 70.3, 64.7, 57.9, 52.2, 51.8, 38.3, 36.4, 32.2, 32.0, 31.8, 28.6, 25.1, 24.7, 19.4, 19.2. **HRMS** calculated for $C_{25}H_{32}N_2O_2$ 392.2464, found 392.2434.



N-(2-(cyclohexylamino)-2-oxo-1-(*o*-tolyl)ethyl)-4-cyclopentyl-*N*-(prop-2-yn-1-yl)but-2-ynamide (**5n**).

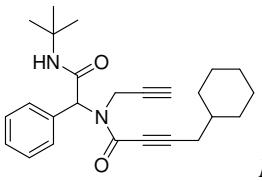
Pale yellow solid, Yield 84 % (mixture of rotamers ~ 1:2). Melting point: 100-102 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.40-7.16 (m, 4H), 6.32 (bd, 0.35H), 6.20-6.14 (m, 1H), 5.69-5.60 (m, 0.60H), 4.40-4.16 (m, 1.61H), 4.03-3.75 (m, 1H), 3.58-3.45 (m, 0.53H), 2.44-2.36 (m, 2H), 2.26-2.31 (m, 3H), 2.18-2.05 (m, 1H), 2.02-1.76 (m, 4H), 1.75-1.49 (m, 7H), 1.44-1.02 (m, 7H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.5, 168.4, 155.2, 155.1, 139.4, 138.5, 132.4, 132.1, 131.0, 130.6, 129.2 (2), 129.1, 128.9, 126.6, 126.3, 95.5, 94.5, 79.2, 79.0, 73.7, 73.2, 71.8, 70.5, 64.4, 57.7, 48.9, 48.7, 38.3 (2), 36.4, 32.9 (2), 32.7 (2), 32.1, 32.0, 31.7, 25.4 (2), 25.1, 24.8, 24.7 (2), 19.3, 19.2. **HRMS** calculated for $C_{27}H_{34}N_2O_2$ 418.2620, found 418.2620.



N-(2-(cyclohexylamino)-2-oxo-1-phenylethyl)-4-cyclopentyl-*N*-(prop-2-yn-1-yl)but-2-ynamide (**5o**).

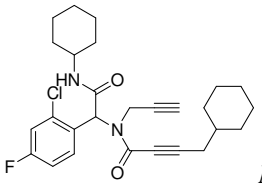
White solid, Yield 92 % (mixture of rotamers ~ 1:2). Melting point: 102-104 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.46-7.31 (m, 5H), 6.27 (bd, 0.35H), 6.18 (s, 0.37H), 6.07 (s, 0.63H), 5.80 (bs 0.60H), 4.43-4.18

(m, 1.62H), 4.00-4.75 (m, 1H), 3.67-3.57 (m, 0.39H), 2.44-2.36 (m, 2H), 2.20-2.06 (m, 1H), 2.05-1.51 (m, 12H), 1.45-1.03 (m, 8H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 167.7, 167.5, 155.4, 155.0, 134.2, 134.0, 129.6, 129.4, 129.0, 128.9, 128.8, 128.7, 95.7, 95.0, 79.3 (2), 73.7, 73.2, 72.1, 71.4, 66.7, 60.6, 49.0, 48.6, 38.3, 36.8, 32.9 (2), 32.8, 32.7, 32.3, 32.1, 32.0, 25.4, 25.1, 24.8, 24.7, 22.7. **HRMS** calculated for $C_{26}H_{32}N_2O_2$ 404.2464, found 404.2424.



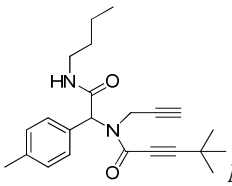
N-((tert-butylcarbamoyl)(phenyl)methyl)-4-cyclohexyl-*N*-(prop-2-ynyl)but-2-ynamide (**5p**).

White solid, Yield 86 % (mixture of rotamers ~ 1:2). Melting point: 120-122 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.44-7.30 (m, 5H), 6.1 (bs, 0.3H), 6.07 (s, 0.34H), 6.01 (s, 0.65H), 5.70 (bs, 0.62H), 4.43-4.27 (m, 1.33H), 4.26-4.15 (m, 0.34H), 3.71-3.59 (m, 0.34H), 2.33-2.22 (m, 2H), 2.15-2.09 (m, 0.3H), 1.98-1.91 (m, 0.61H), 1.87-1.51 (m, 5H), 1.42 (s, 3H), 1.36 (s, 6H), 1.29-0.94 (m, 5H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.0, 167.7, 155.4, 155.0, 134.4, 134.2, 129.6, 129.4, 129.0, 128.8, 128.7, 128.6, 95.0, 94.3, 79.4, 74.6, 74.2, 71.9, 71.1, 66.9, 60.6, 52.2, 51.8, 36.7(3), 32.7, 32.6, 32.4, 28.6, 28.5, 26.7, 25.9. **HRMS** calculated for $C_{25}H_{32}N_2O_2$ 392.2464, found 392.2492.



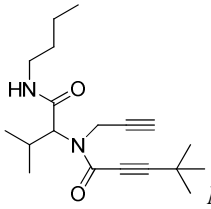
N-((cyclohexylcarbamoyl)(2-chloro-4-fluorophenyl)methyl)-4-cyclohexyl-*N*-(prop-2-ynyl)but-2-ynamide (**5q**).

White solid, Yield 87 % (mixture of rotamers ~ 1:2). Melting point: 68-70 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.66-7.54 (m, 0.55H), 7.47-7.33 (m, 0.43H), 7.23-7.10 (m, 1H), 7.10-6.95 (m, 1H), 6.44-6.27 (m, 0.83 H), 6.20 (s, 0.54H), 5.89 (d, *J* = 6.6 Hz, 0.51H), 4.44-4.27 (m, 1.57H), 3.99-3.71 (m, 1H), 3.53-3.37 (m, 0.32H), 2.33-2.22 (m, 2H), 2.19-1.50 (m, 13H), 1.46-0.93 (m, 11H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 167.4, 167.1, 164.3, 161.0, 155.3, 154.8, 137.3, 137.2, 137.1, 136.9, 132.3, 132.2, 132.1, 128.3, 128.2, 128.0, 127.9, 117.6, 117.3(2), 117.0, 114.7, 114.4(2), 114.1, 95.2, 94.3, 78.8, 78.5, 74.3, 73.9, 72.3, 71.3, 63.7, 57.2, 49.1, 48.7, 36.7, 32.8(2), 32.6(2), 31.6, 26.7(2), 25.9, 25.4, 25.3, 24.8, 24.7, 24.6. **HRMS** calculated for $C_{27}H_{32}ClFN_2O_2$ 470.2136, found 470.2147.



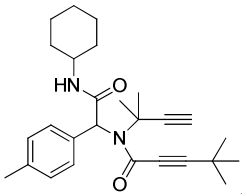
N-(2-(butylamino)-2-oxo-1-*p*-tolylethyl)-4,4-dimethyl-*N*-(prop-2-ynyl)pent-2-ynamide (**5r**).

White solid, Yield 80% (mixture of rotamers ~ 1:2). Melting point: 79-81 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.33-7.13 (m, 4H), 6.42-6.32 (m, 0.30H), 6.07 (m, 0.31H), 6.03 (s, 0.67H), 5.93-5.82 (m, 0.63H), 4.33-4.19 (m, 1.67H), 3.61 (d, *J* = 18 Hz, 0.31H), 3.38 (q, *J* = 6.0 Hz, 0.66H), 3.29 (q, *J* = 6.6 Hz, 1.33H), 2.36 (s, 3H), 2.20-2.15 (m, 0.30H), 2.06-2.01 (m, 0.60H), 1.62-1.21 (m, 13H), 1.00-0.84 (m, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.8, 168.7, 155.5, 155.1, 138.9, 138.5, 131.0, 130.8, 129.7, 129.5, 129.4 (2), 102.1, 79.4 (2), 72.4, 71.8, 71.3, 66.7, 60.5, 39.5, 39.4, 36.8, 32.2, 31.4, 31.3, 30.0, 29.9, 27.9, 27.8, 21.1, 20.0 (2), 13.7. **HRMS** calculated for $C_{23}H_{30}N_2O_2$ 366.2307, found 366.2308.



N-(1-(butylamino)-3-methyl-1-oxobutan-2-yl)-4,4-dimethyl-*N*-(prop-2-ynyl)pent-2-ynamide (**5s**).

White solid, Yield 95% (mixture of rotamers ~ 1:5). Melting point: 52-54 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 6.11-5.96 (m, 0.87H), 5.63-5.50 (m, 0.15H), 4.62-4.06 (m, 3H), 3.34-3.04 (m, 2H), 2.48-2.30 (m, 1H), 2.24 (bs, 0.82H), 2.17 (bs, 0.16H), 1.55-1.40 (m, 2H), 1.39-1.24 (m, 11H), 1.03-0.86 (m, 11H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 169.3, 168.6, 156.1, 154.6, 102.6 ,101.7, 79.3, 78.7 ,77.4, 77.0, 76.6, 72.4, 71.8, 71.0, 68.5, 63.3, 39.3, 39.0, 35.7, 34.1, 31.4, 31.3, 30.1, 29.9, 27.9, 27.8, 27.4, 26.9, 22.3, 20.1, 20.0 (2), 19.5, 19.4, 19.3, 14.0, 13.7. **HRMS** calculated for $C_{19}H_{30}N_2O_2$ 318.2307, found 318.2329.



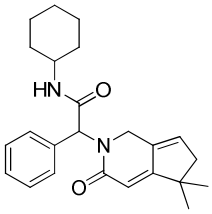
N-(2-(cyclohexylamino)-2-oxo-1-(*p*-tolyl)ethyl)-4,4-dimethyl-*N*-(2-methylbut-3-yn-2-yl)pent-2-ynamide (**5t**).

Pale yellow solid, Yield 75 % (mixture of rotamers ~ 1:2). Melting point: 106-108 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.41-7.27 (m, 2H), 7.18-7.09 (bs2H), 5.99-5.35 (m, 1H), 3.91-3.63 (m, 1H), 2.52 (s, 1H), 2.34 (s, 3H), 2.00-1.72 (m, 6H), 1.71-1.46 (m, 4H), 1.43-0.97 (m, 13H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.2,

155.3, 137.4, 133.3, 129.0, 128.5, 86.8, 74.0, 65.9, 56.0, 48.5, 32.7, 32.6, 30.1, 27.7, 25.5, 24.6 (2), 21.0. **HRMS** calculated for $C_{27}H_{36}N_2O_2$ 420.2777, found 420.2801.

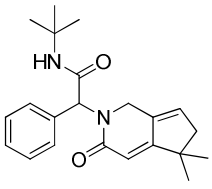
General procedure for gold-catalyzed tandem cyclization.

To a glass vial IPrAuCl (5 mol%) and AgOTf (5 mol%) were loaded along with DCE (2 mL). Ugi product **5a-s** (0.2 mmol) was added and reaction mixture was stirred at 120°C in a screw capped vial until completion. After completion, reaction mixture was purified by silica gel column chromatography (20% diethyl ether in dichloromethane) to afford compound **6a-s**.



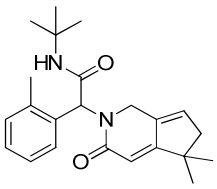
N-cyclohexyl-2-(5,5-dimethyl-3-oxo-5,6-dihydro-1*H*-cyclopenta[*c*]pyridin-2(3*H*)-yl)-2-phenylacetamide (**6a**).

White Solid, Yield 68 %, Melting point: 174-176 °C. **^{1}H NMR (400 MHz, DMSO)** δ 8.11 (d, 1H, *J* = 5.46 Hz), 7.46-7.30 (m, 3H), 7.26-7.17 (m, 2H), 6.19 (s, 1H), 5.91 (bs, 1H), 5.47 (s, 1H), 4.63 (d, 1H, J = 13.05 Hz), 3.70-3.55 (m, 2H), 2.35 (bs, 2H), 1.82-1.48 (m, 6H), 1.34-1.18 (m, 4H), 1.17-1.03 (m, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.9, 168.5, 165.3, 134.9, 133.6, 131.9, 129.3, 128.7, 128.1, 109.6, 59.3, 48.6, 48.4, 43.7, 40.8, 32.8 (2), 28.3, 28.2, 25.4, 24.7 (2). **HRMS** Calculated for $C_{24}H_{30}N_2O_2$ 378.2307, found 378.2310.



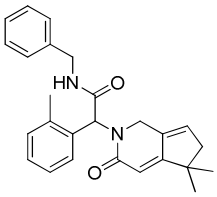
N-tert-butyl-2-(5,5-dimethyl-3-oxo-5,6-dihydro-1*H*-cyclopenta[*c*]pyridin-2(3*H*)-yl)-2-phenylacetamide (**6b**).

White Solid, Yield 78 %, Melting point: 184-186 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.42-7.33 (m, 5H), 6.24 (s, 1H), 5.77 (s, 1H), 5.66 (bs, 1H), 5.54 (s, 1H), 4.62 (d, 1H, *J* = 16.95 Hz), 3.80 (d, 1H, *J* = 16.95 Hz), 2.36 (bs, 2H), 1.36 (s, 9H), 1.18-1.14 (m, 6H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 169.0, 168.7, 165.2, 135.2, 133.7, 131.7, 129.4, 128.7, 128.1, 109.7, 59.6, 51.6, 48.6, 43.7, 40.8, 28.7, 28.3, 28.2. **HRMS** Calculated for $C_{22}H_{28}N_2O_2$ 352.2151, found 352.2150.



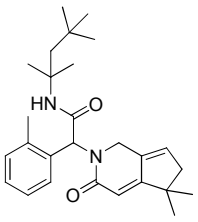
N-(*tert*-butyl)-2-(5,5-dimethyl-3-oxo-5,6-dihydro-1*H*-cyclopenta[*c*]pyridin-2(3*H*)-yl)-2-(*o*-tolyl)acetamide (**6c**).

White Solid, Yield 91%, Melting point: 229-231°C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.42 (d, 1H, J = 7.14 Hz), 7.31-7.16 (m, 3H), 6.25 (s, 1H), 5.71 (s, 1H), 5.52 (m, 2H), 4.59 (d, 1H, *J* = 17.1 Hz), 3.57 (d, 1H, *J* = 17.7 Hz), 2.34 (bs, 2H), 2.25 (s, 3H), 1.36 (s, 9H), 1.17-1.13 (m, 6H) . **^{13}C NMR (75 MHz, $CDCl_3$)** δ 169.9, 168.4, 164.8, 138.6, 133.7, 133.4, 131.4, 130.8, 129.5, 128.4, 126.0, 109.6, 57.6, 51.6, 48.5, 43.9, 40.7, 28.6, 28.3, 28.2, 19.3. **HRMS** Calculated for $C_{23}H_{30}N_2O_2$ 366.2307, found 366.2317.



N-benzyl-2-(5,5-dimethyl-3-oxo-5,6-dihydro-1*H*-cyclopenta[*c*]pyridin-2(3*H*)-yl)-2-(*o*-tolyl)acetamide **(6d**).

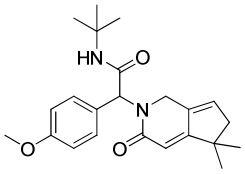
White Solid, Yield 59 %, Melting point: 193-195 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.45-7.38 (m, 1H), 7.34-7.17 (m, 8H), 6.41 (s, 1H), 6.10 (m, 1H), 5.77-5.71 (m, 1H), 5.52 (s, 1H), 4.63-4.40 (m, 3H), 3.65 (dd, 1H, J = 17.1 Hz, *J* = 2.4 Hz), 2.35 (bs, 2H), 2.25 (s, 3H), 1.17-1.13 (m, 6H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 170.4, 168.7, 164.9, 138.5, 137.9, 133.6, 132.7, 131.8, 130.8, 129.6, 128.6, 127.7, 127.3, 126.0, 109.4, 57.4, 48.5, 43.9, 43.5, 40.7, 28.2, 19.2. **HRMS** Calculated for $C_{26}H_{28}N_2O_2$ 400.2151, found 400.2141.



2-(5,5-dimethyl-3-oxo-5,6-dihydro-1*H*-cyclopenta[*c*]pyridin-2(3*H*)-yl)-2-(*o*-tolyl)-*N*-(2,4,4-trimethylpentan-2-yl)acetamide (**6e**).

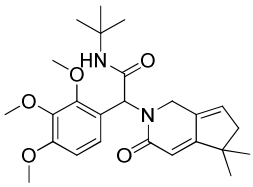
Pale yellow Solid, Yield 64 %, Melting point: 169-171 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.48-7.42 (m, 1H), 7.30-7.18 (m, 3H), 6.24 (s, 1H), 5.76-5.70 (m, 1H), 5.60-5.51 (m, 2H), 4.53 (dd, 1H, *J* = 16.8 Hz, *J* = 2.7 Hz), 3.61 (dd, 1H, *J* = 17.1 Hz, *J* = 2.4 Hz), 2.39-2.32 (m, 2H), 2.25 (s, 3H), 1.84 (d, 1H, *J* = 14.7 Hz), 1.54 (d, 1H, *J* = 15 Hz), 1.45 (m, 6H), 1.17-1.13 (m, 6H), 0.95 (s, 9H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ

169.2, 168.4, 164.7, 138.6, 133.7, 133.1, 131.5, 130.8, 129.7, 128.4, 125.9, 109.6, 57.8, 55.7, 52.8, 48.6, 43.9, 40.7, 31.5, 28.8, 28.3, 28.2, 19.3. **HRMS** Calculated for $C_{27}H_{38}N_2O_2$ 422.2933, found 422.2903.



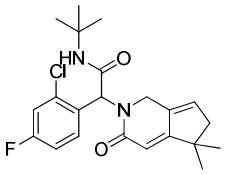
N-(*tert*-butyl)-2-(5,5-dimethyl-3-oxo-5,6-dihydro-1*H*-cyclopenta[*c*]pyridin-2(3*H*)-yl)-2-(4-methoxyphenyl)acetamide **(6f)**.

White Solid, Yield 70%, Melting point: 200-202 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.32 (d, 2H, *J* = 8.49 Hz), 6.90 (d, 2H, *J* = 8.49 Hz), 6.17 (s, 1H), 5.76 (s, 1H), 5.59 (bs, 1H), 5.53 (s, 1H), 4.59 (d, 1H, *J* = 18.0 Hz), 3.86-3.75 (m, 4H), 2.36 (bs, 2H), 1.35 (s, 9H), 1.1.17-1.13 (m, 6H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 169.3, 168.6, 165.2, 159.4, 133.7, 131.6, 130.8, 127.0, 114.1, 109.7, 59.1, 55.2, 51.6, 48.6, 43.5, 40.7, 28.7, 28.3, 28.2. **HRMS** Calculated for $C_{23}H_{30}N_2O_3$ 382.2256, found 382.2252.



N-(*tert*-butyl)-2-(5,5-dimethyl-3-oxo-5,6-dihydro-1*H*-cyclopenta[*c*]pyridin-2(3*H*)-yl)-2-(2,3,4-trimethoxyphenyl)acetamide **(6g)**.

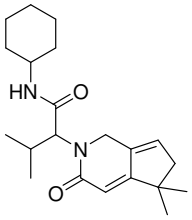
White Solid, Yield 67 %, Melting point: 174-176 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.14 (d, 1H, *J* = 8.67 Hz), 6.67 (d, 1H, *J* = 8.67 Hz), 6.32 (s, 1H), 5.77-5.76 (m, 1H), 5.59-5.54 (m, 2H), 4.56 (d, 1H, *J* = 14.52 Hz), 3.92-3.80 (m, 10H), 2.41-2.27 (m, 2H), 1.35 (s, 9H), 1.17-1.13 (m, 6H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 169.6, 168.4, 164.8, 154.1, 152.8, 142.2, 133.8, 131.4, 124.8, 121.0, 110.0, 106.7, 60.8, 60.7, 55.9, 55.3, 51.4, 48.6, 44.0, 40.7, 28.7, 28.4, 28.2. **HRMS** Calculated for $C_{25}H_{34}N_2O_5$ 442.2468, found 442.2431.



N-(*tert*-butyl)-2-(2-chloro-4-fluorophenyl)-2-(5,5-dimethyl-3-oxo-5,6-dihydro-1*H*-cyclopenta[*c*]pyridin-2(3*H*)-yl)acetamide **(6h)**.

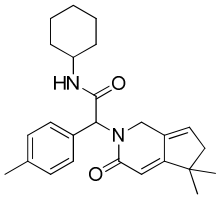
White Solid, Yield 90 %, Melting point: 213-215 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.65-7.56 (m, 1H), 7.22-7.14 (m, 1H), 7.09-7.98 (m, 1H), 6.26 (s, 1H), 5.85-5,72 (m, 2H), 5.53 (s, 1H), 4.50 (d, 1H, *J* = 17.4 Hz), 3.75 (d 1H, *J* = 16.2 Hz), 2.39 (bs 2H), 1.36 (s, 9H), 1.21-1.13 (m, 6H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ

168.7, 168.6, 164.8, 136.4, 136.2, 133.3, 132.0, 131.9, 128.9 (2), 117.6, 117.3, 114.2, 113.9, 109.5, 57.6, 51.7, 48.6, 44.2, 40.8, 28.5, 28.2. **HRMS** Calculated for $C_{22}H_{26}ClFN_2O_2$ 404.1667, found 404.1686.



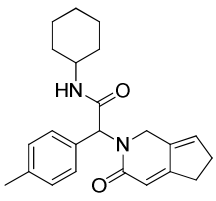
N-cyclohexyl-2-(5,6-dihydro-5,5-dimethyl-3-oxo-1*H*-cyclopenta[*c*]pyridin-2(3*H*)-yl)-3-methylbutanamide **(6i)**.

Pale yellow Solid, Yield 81 %, Melting point: 141-143 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 6.10 (m, 1H), 5.91 (s, 1H), 5.49 (s, 1H), 4.50 (d, *J* = 1.4 Hz, 1H), 4.44-4.16 (m, 2H), 3.77-3.62 (m, 1H), 2.46-2.30 (m, 3H), 1.91-1.54 (m, 5H), 1.37-1.07 (m, 11H), 0.97 (d, *J* = 6.4 Hz, 3H), 0.86 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.8, 168.6, 165.6, 133.3, 132.0, 109.6, 48.6, 47.9, 40.8, 32.9, 32.7, 28.4, 28.1, 25.4, 25.0, 24.7, 24.6, 19.7, 18.4. **HRMS** Calculated for $C_{21}H_{32}N_2O_2$ 344.2464, found 344.2470.



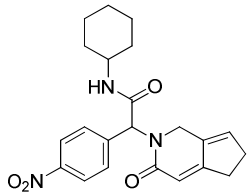
N-cyclohexyl-2-(5,5-dimethyl-3-oxo-5,6-dihydro-1*H*-cyclopenta[*c*]pyridin-2(3*H*)-yl)-2-(*p*-tolyl)acetamide **(6j)**.

White Solid, Yield 74%, Melting point: 160-162 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.28 (d, 2H, *J* = 7.98 Hz), 7.18 (d, 2H, *J* = 7.98 Hz), 6.26 (s, 1H), 5.81-5.67 (m, 2H), 5.53 (s, 1H), 4.58 (dd, 1H, *J* = 16.8 Hz, *J* = 2.46 Hz), 3.91-3.74 (m, 2H), 2.41-2.31 (m, 5H), 1.97-1.86 (m, 2H), 1.74-1.54 (m, 4H), 1.42-1.26 (m, 3H), 1.21-1.03 (m, 7H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.7 (2), 165.2, 138.0, 133.7, 131.8, 131.7, 129.4, 129.3, 109.7, 59.1, 48.6, 48.4, 43.6, 40.8, 32.8 (2), 28.3, 28.2, 25.4, 24.8, 24.7, 21.1. **HRMS** Calculated for $C_{25}H_{32}N_2O_2$ 392.2464, found 392.2446.



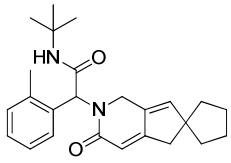
N-cyclohexyl-2-(3-oxo-5,6-dihydro-1*H*-cyclopenta[*c*]pyridin-2(3*H*)-yl)-2-(*p*-tolyl)acetamide **(6k)**.

White Solid, Yield 52 %, Melting point: 126-128 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.27 (d, 2H, *J* = 7.89 Hz), 7.17 (d, 2H, *J* = 7.71 Hz), 6.25 (s, 1H), 5.93 (bs, 1H), 5.75 (bd, 1H, *J* = 7.53 Hz), 5.66 (s, 1H), 4.55 (d, 1H, *J* = 14.67 Hz), 3.93-3.75 (m, 2H), 2.72-2.62 (m, 2H), 2.60-2.50 (m, 2H), 2.35 (s, 3H), 1.98-1.86 (m, 2H), 1.66-1.55 (m, 1H), 1.44-1.25 (m, 3H), 1.21-1.04 (m, 4H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.6, 164.9, 160.8, 137.9, 136.0, 135.2, 131.8, 129.3, 129.2, 111.0, 59.0, 48.4, 43.3, 32.8, 31.6, 27.8, 25.4, 24.8, 24.7, 21.1. **HRMS** Calculated for $C_{23}H_{28}N_2O_2$ 364.2151, found 364.2143.



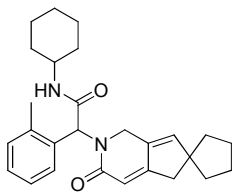
N-cyclohexyl-2-(4-nitrophenyl)-2-(3-oxo-5,6-dihydro-1*H*-cyclopenta[*c*]pyridin-2(3*H*)-yl)acetamide (**6l**)

White Solid, Yield 61 %, Melting point: 201-203 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 8.21 (d, 2H, *J* = 8.7 Hz), 7.58 (d, 2H, *J* = 8.4 Hz), 6.38 (s, 1H), 6.24-6.12 (m, 1H), 6.09-6.01 (m, 1H), 5.70 (s, 1H), 4.48 (d, 1H, *J* = 18,0 Hz), 4.01-3.75 (m, 2H), 2.76-2.54 (m, 4H), 2.01-1.05 (m, 12H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 167.3, 165.1, 162.0, 147.4, 142.8, 136.7, 135.3, 129.7, 123.6, 110.5, 58.4, 48.6, 43.6, 32.8, 31.8, 28.0, 25.4, 24.7. **HRMS** Calculated for $C_{22}H_{25}N_3O_4$ 395.1845, found 395.1845.



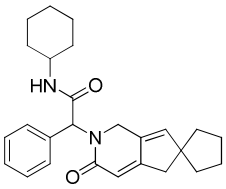
N-(*tert*-butyl)-2-(3-oxospiro[cyclopenta[*c*]pyridine-6,1'-cyclopentan]-2(1*H*,3*H*,5*H*)-yl)-2-(*o*-tolyl)acetamide **(6m**).

White Solid, Yield 62 %, Melting point: 103-105°C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.44-7.38 (m, 1H), 7.32-7.18 (m, 3H), 6.23 (s, 1H), 5.69 (s, 1H), 5.60 (bs, 1H), 5.50 (s, 1H), 4.55 (d, 1H, *J* = 17.7 Hz), 3.54 (d, 1H, *J* = 18.0 Hz), 2.50 (bs, 2H), 2.25 (s, 3H), 1.60-1.24 (m, 16H), 0.92-0.84 (m, 1H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 169.8, 164.4, 159.5, 142.7, 138.6, 133.3, 133.2, 130.8, 129.5, 128.4, 126.0, 111.1, 57.6, 56.3, 51.6, 43.6, 42.6, 39.3, 28.6, 24.3, 19.3. **HRMS** Calculated for $C_{25}H_{32}N_2O_2$ 392.2464, found 392.2484.



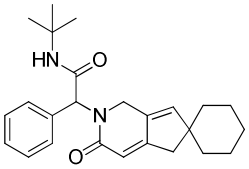
N-cyclohexyl-2-(3-oxospiro[cyclopenta[*c*]pyridine-6,1'-cyclopentan]-2(1*H*,3*H*,5*H*)-yl)-2-(*o*-tolyl)acetamide (**6n**)

White Solid, Yield 58 %, Melting point: 185-187 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.45-7.38 (m, 1H), 7.31-7.16 (m, 3H), 6.31 (s, 1H), 5.72 (bs, 1H), 5.64-5.53 (m, 2H), 4.53 (bd, 1H, *J* = 17.13 Hz), 3.92-3.76 (m, 1H), 3.58 (bd, 1H, *J* = 17.13 Hz), 2.50 (bs, 2H), 2.26 (s, 3H), 1.99-1.88 (m, 2H), 1.76-1.85 (m, 16H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 169.3, 164.4, 159.6, 142.9, 138.6, 133.1 (2), 130.8, 129.5, 128.5, 126.0, 111.0, 57.4, 56.3, 48.5, 43.5, 42.6, 39.3, 32.8 (2), 25.5, 24.8, 24.7, 24.3 (2), 19.3. **HRMS** Calculated for $C_{27}H_{34}N_2O_2$ 418.2620, found 418.2626.



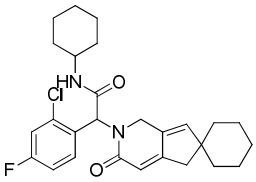
N-cyclohexyl-2-(3-oxospiro[cyclopenta[*c*]pyridine-6,1'-cyclopentan]-2(1*H*,3*H*,5*H*)-yl)-2-phenylacetamide (**6o**)

Off white Solid, Yield 62 %, Melting point: 98-100 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.44-7.30 (m, 5H), 6.30 (s, 1H), 5.87-5.73 (m, 2H), 5.62 (s, 1H), 4.56 (d, 1H, *J* = 17.13 Hz), 3.93-3.74 (m, 2H), 2.52 (bs, 2H), 2.00-1.85 (m, 2H), 1.75-1.04 (m, 15H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.5, 164.9, 160.0, 143.2, 134.9, 133.1, 129.3, 128.6, 128.1, 111.1, 59.2, 56.4, 48.4, 43.3, 42.7, 39.3 (2), 32.8 (2), 25.4, 24.7 (2), 24.3 . **HRMS** Calculated for $C_{26}H_{32}N_2O_2$ 404.2464, found 404.2438.



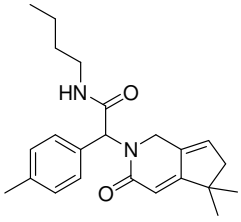
N-(*tert*-butyl)-2-(3'-oxospiro[cyclohexane-1,6'-cyclopenta[*c*]pyridin]-2'(1'*H*,3'*H*,5'*H*)-yl)-2-phenylacetamide (**6p**)

Off white Solid, Yield 65 %, Melting point: 105-107 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.45-7.30 (m, 5H), 6.23 (s, 1H), 5.82 (s, 1H), 5.69-5.55 (m, 2H), 4.57 (d, 1H, J = 16.8 Hz), 3.77 (d, 1H, *J* = 17.4 Hz), 2.45 (s, 2H), 1.46-1.20 (m, 19H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 169.0, 164.8, 159.5, 143.9, 135.2, 133.0, 129.4, 128.7, 128.1, 111.3, 59.5, 51.6, 49.4, 43.3, 40.5, 37.3, 37.2, 28.6, 25.5, 23.3. **HRMS** Calculated for $C_{25}H_{32}N_2O_2$ 392.2464, found 392.2434.



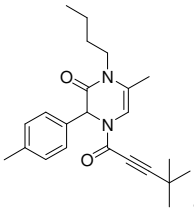
2-(2-chloro-4-fluorophenyl)-*N*-cyclohexyl-2-(3'-oxospiro[cyclohexane-1,6'-cyclopenta[*c*]pyridin]-2'(1'*H*,3'*H*,5'*H*)-yl)acetamide (**6q**)

Pale yellow Solid, Yield 67 %, Melting point: 125-127 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.71-7.63 (m, 1H), 7.21-7.14 (m, 1H), 7.08-6.96 (m, 1H), 6.29 (s, 1H), 5.97-5.81 (m, 2H), 5.62 (s, 1H), 4.44 (d, 1H, *J* = 16.8 Hz), 3.88-3.67 (m, 2H), 2.47 (s, 2H), 1.98-1.83 (m, 2H), 1.75-1.46 (m, 7H), 1.45-1.02 (m, 14H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.1, 164.3, 159.6, 144.3, 136.3, 136.2, 132.7, 132.2, 132.1, 128.7 (2), 117.6, 117.2, 114.1, 113.9, 111.3, 57.3, 49.5, 48.5, 43.8, 40.5, 37.2, 32.7, 25.5, 25.4, 24.7 (2), 23.3. **HRMS** Calculated for $C_{27}H_{32}ClFN_2O_2$ 470.2136, found 470.2120.



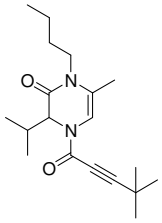
N-butyl-2-(5,6-dihydro-5,5-dimethyl-3-oxo-1H-cyclopenta[*c*]pyridin-2(3*H*)-yl)-2-p-tolylacetamide (**6r**)

White Solid, Yield 41 %. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.29 (d, *J* = 7.92 Hz, 2H), 7.18 (d, *J* = 7.53 Hz, 2H), 6.28 (s, 1H), 5.99 (m, 1H), 5.78 (bs, 1H), 5.52 (s, 1H), 4.57 (d, *J* = 17.13 Hz, 1H), 3.88 (d, *J* = 17.13 Hz, 1H), 3.36-3.18 (m, 2H), 2.43-2.25 (m, 5H), 1.54-1.40 (m, 2H), 1.36-1.25 (m, 2H), 1.19-1.11(m, 6H), 0.89 (t, *J* = 7.17 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 169.7, 168.8, 165.2, 138.0, 133.6, 131.8, 131.7, 129.3(2), 109.6, 59.1, 48.6, 43.7, 40.8, 39.2, 31.4, 28.3, 28.2, 21.4, 20.0, 13.7. **HRMS** Calculated for $C_{23}H_{30}N_2O_2$ 366.2307, found 366.2325.



4-(4,4-dimethylpent-2-ynoyl)-1-butyl-3,4-dihydro-6-methyl-3-*p*-tolylpyrazin-2(1H)-one (**7a**)

White Solid, Yield 25 %. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.08 (d, *J* = 7.89 Hz, 2H), 6.99 (d, *J* = 8.1 Hz, 2H), 6.05 (s, 1H), 5.87 (s, 1H), 4.00-3.86 (m, 1H), 3.59-3.46 (m, 1H), 2.47 (s, 3H), 2.27 (s, 3H), 1.54-1.28 (m, 13H), 0.92 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.1, 165.5, 159.7, 137.9, 133.4, 129.5, 125.7, 122.3, 121.8, 119.2, 57.1, 42.8, 32.6, 31.1, 31.0, 21.0, 20.0, 18.5, 13.7. **HRMS** Calculated for $C_{23}H_{30}N_2O_2$ 366.2307, found 366.2311.



4-(4,4-dimethylpent-2-ynoyl)-1-butyl-3,4-dihydro-3-isopropyl-6-methylpyrazin-2(1*H*)-one (**7b**)

White Solid, Yield 26 %. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.97 (s, 1H), 4.68 (d, *J* = 5.64 Hz, 1H), 3.95-3.81 (m, 1H), 3.69-3.56 (m, 1H), 2.45 (s, 3H), 2.25-2.13 (m, 1H), 1.60-1.49 (m, 2H), 1.41-1.33 (m, 11H), 1.00-0.92 (m, 6H), 0.85 (d, *J* = 6.96 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.2, 165.4, 158.9, 122.7, 122.0, 118.6, 59.0, 42.6, 32.7, 32.4, 31.3, 30.9, 20.1, 19.4, 18.5, 17.6, 13.7. **HRMS** Calculated for $C_{19}H_{30}N_2O_2$ 318.2307, found 318.2315.

Crystallography. Single crystals of **6f**, suitable for X-ray diffraction were obtained by slow evaporation from a ethylacetate solution 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 = 0.7107 Å). The images were interpreted and integrated with the CrysAlisPro software from Agilent Technologies[1]. Using Olex2[2], the structure was solved with the ShelxS[3] structure solution program using Direct Methods and refined with the ShelxL 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). Dichloromethane is disordered over two positions. CCDC 937689 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 $C_{23}H_{30}N_2O_3$, M =382.49 g mol^{-1}, triclinic, P-1 (no. 2), a =9.9200(14) Å, b = 10.6423(9) Å, c = 11.0407(14) Å, α = 95.237(8)°, β = 115.250(13)°, γ = 91.298(9)°, V = 1047.4(2) $Å^3$, T = 100.0(2) K, Z = 2, ρ_{calcd} = 1.213 g cm^{-3}, μ(Mo Kα) = 0.080 mm^{-1}, F(000) = 412, crystal size 0.2 x 0.2 x 0.2 mm^3, 4280 reflections measured, 3503 unique (R_{int} = 0.0266) which were used in all calculations. The final wR_2 was 0.1505 (all data) and R_1 was 0.0546 (>2sigma(I)).

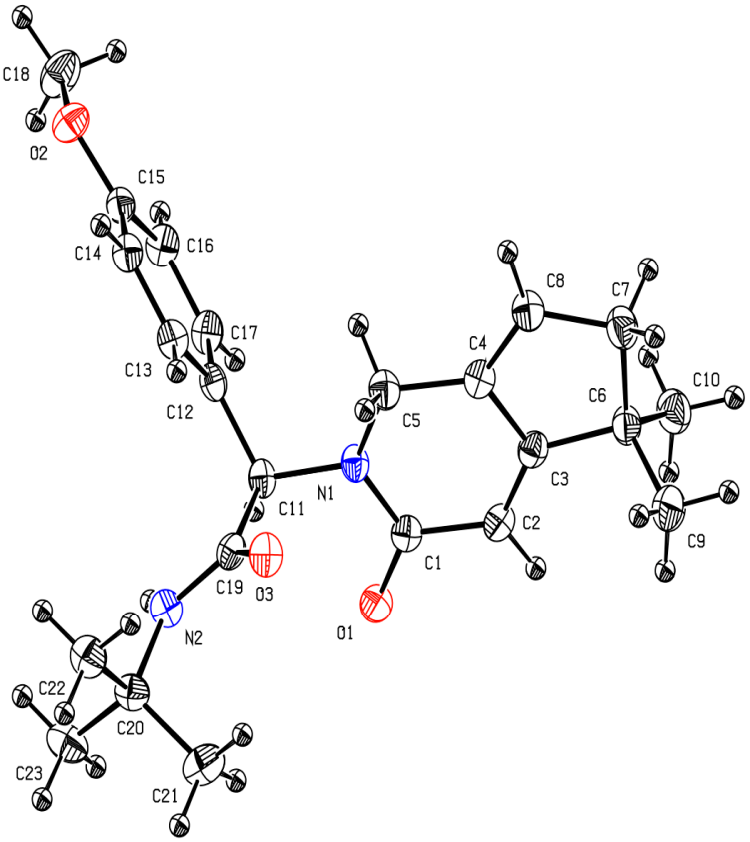
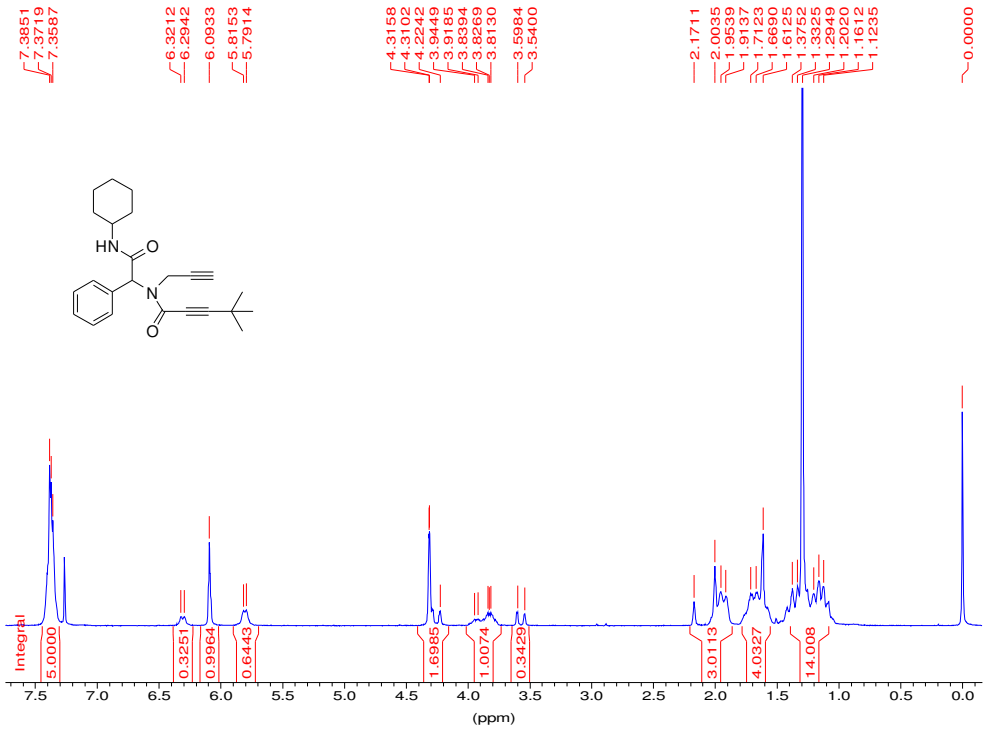


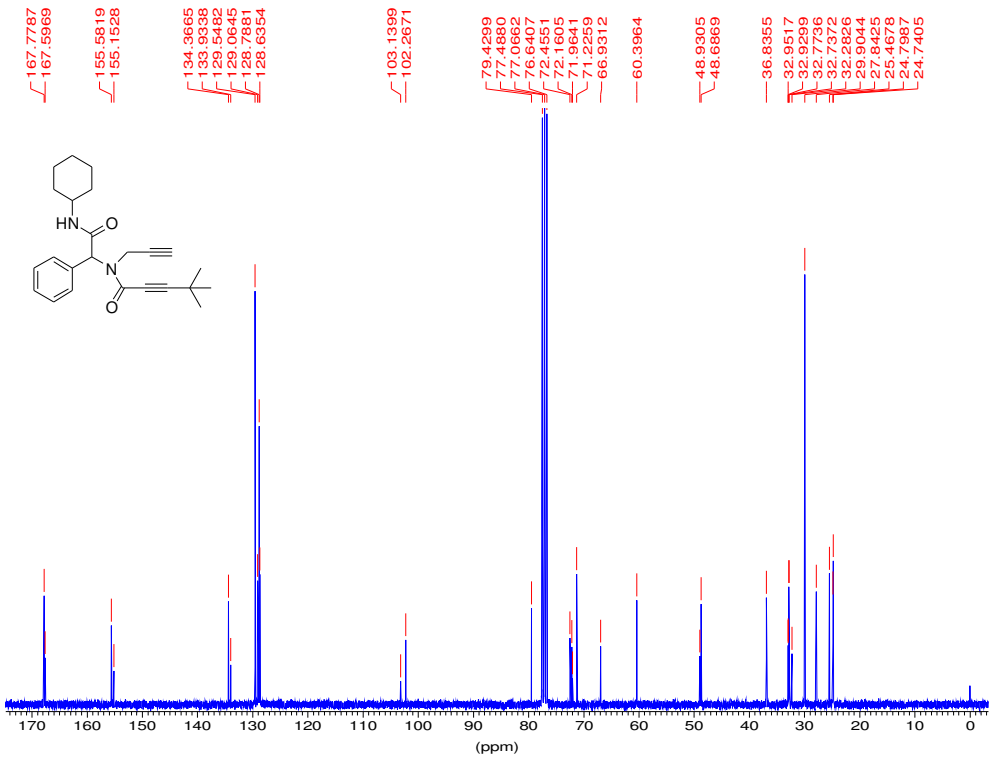
Figure 1: Crystal structure of compound **6f**. Thermal ellipsoid set at 50% probability.

References

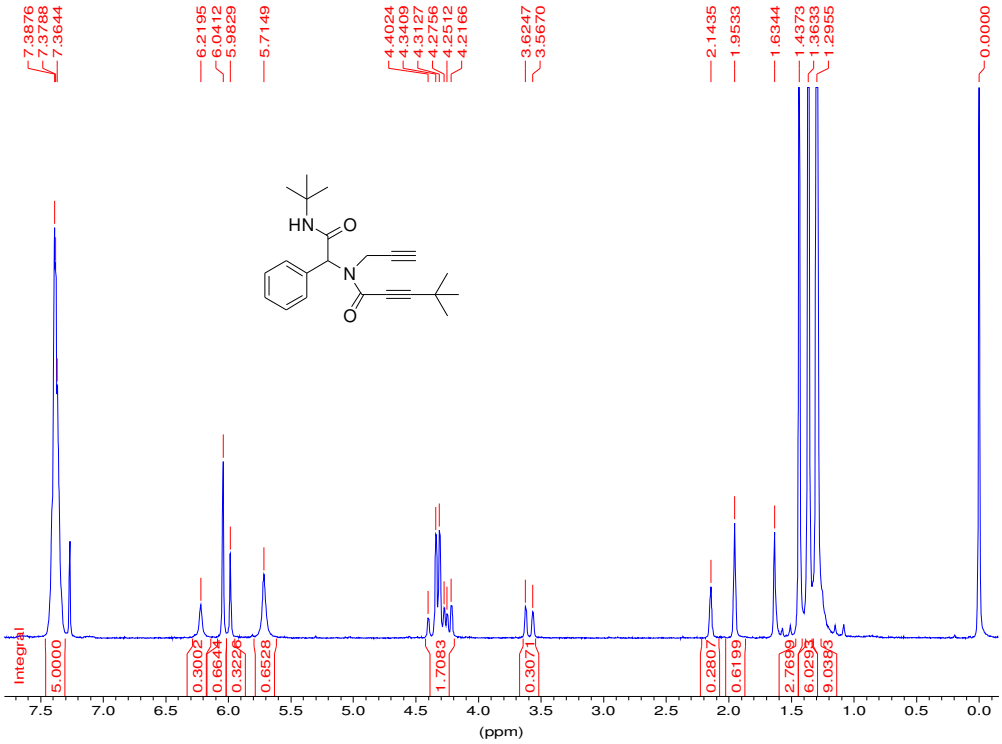
[1] CrysAlis PRO (2012). Agilent Technologies UK Ltd, Yarnton,Oxfordshire, England.
[2] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, OLEX2: a complete structure solution, refinement and analysis program. J. Appl. Cryst. (2009). 42, 339-341.
[3] G. M. Sheldrick, ActaCryst. (2008). A64, 112-122

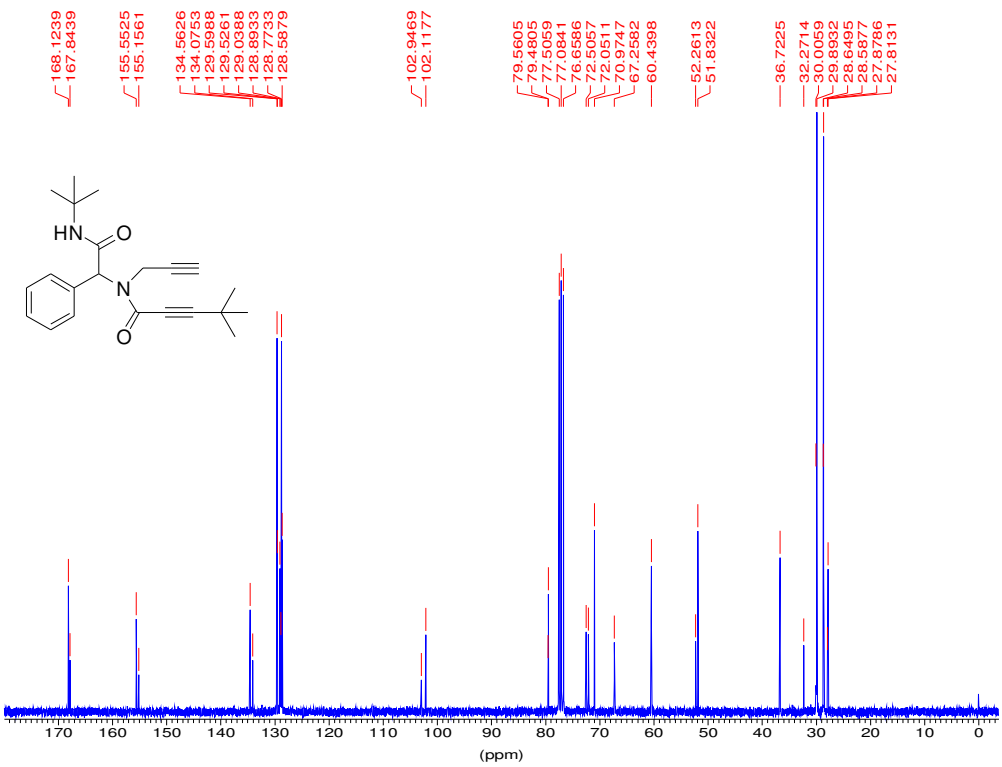
^{1}H and ^{13}C NMR spectra of compound **5a** (300 MHz, $CDCl_3$).



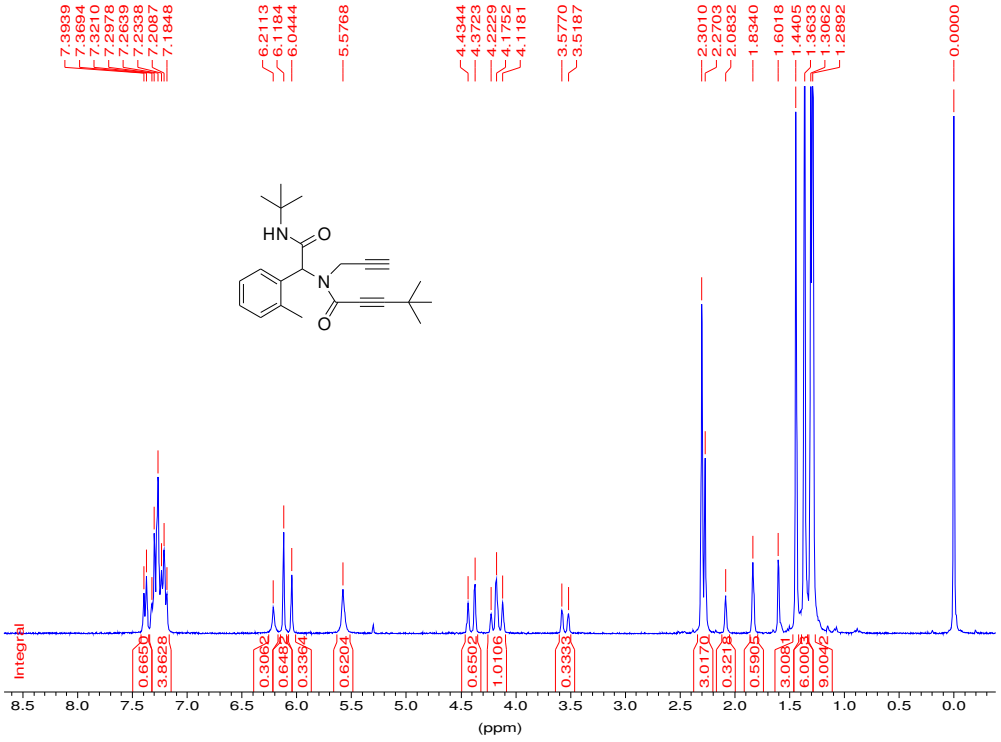


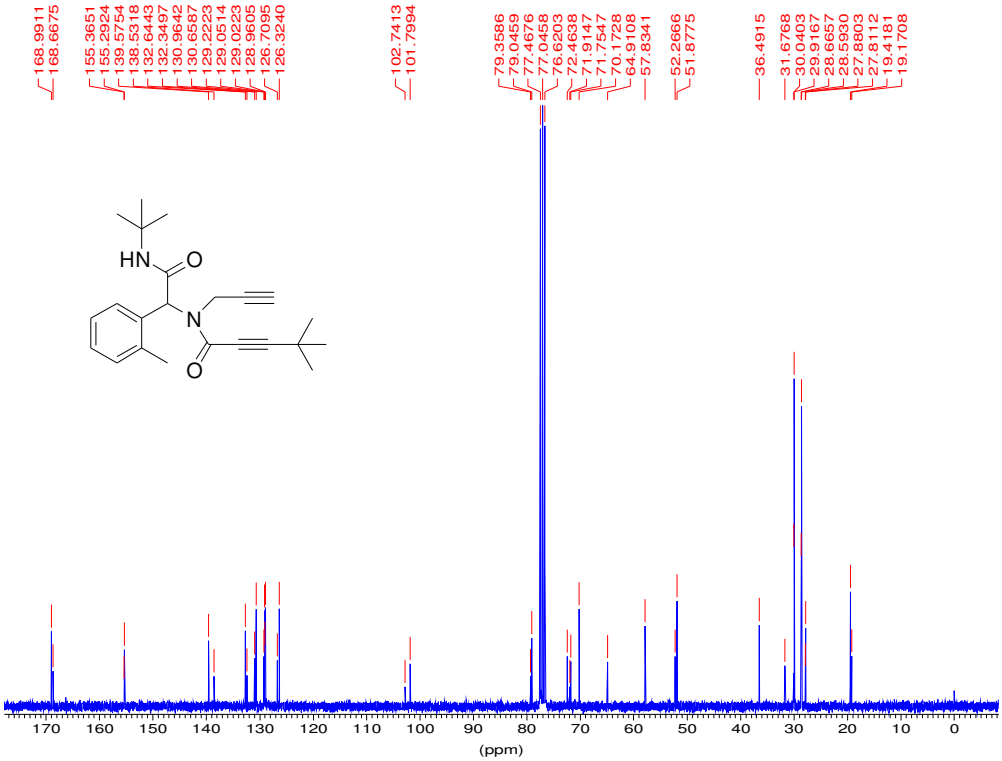
^{1}H and ^{13}C NMR spectra of compound **5b** (300 MHz, $CDCl_3$).



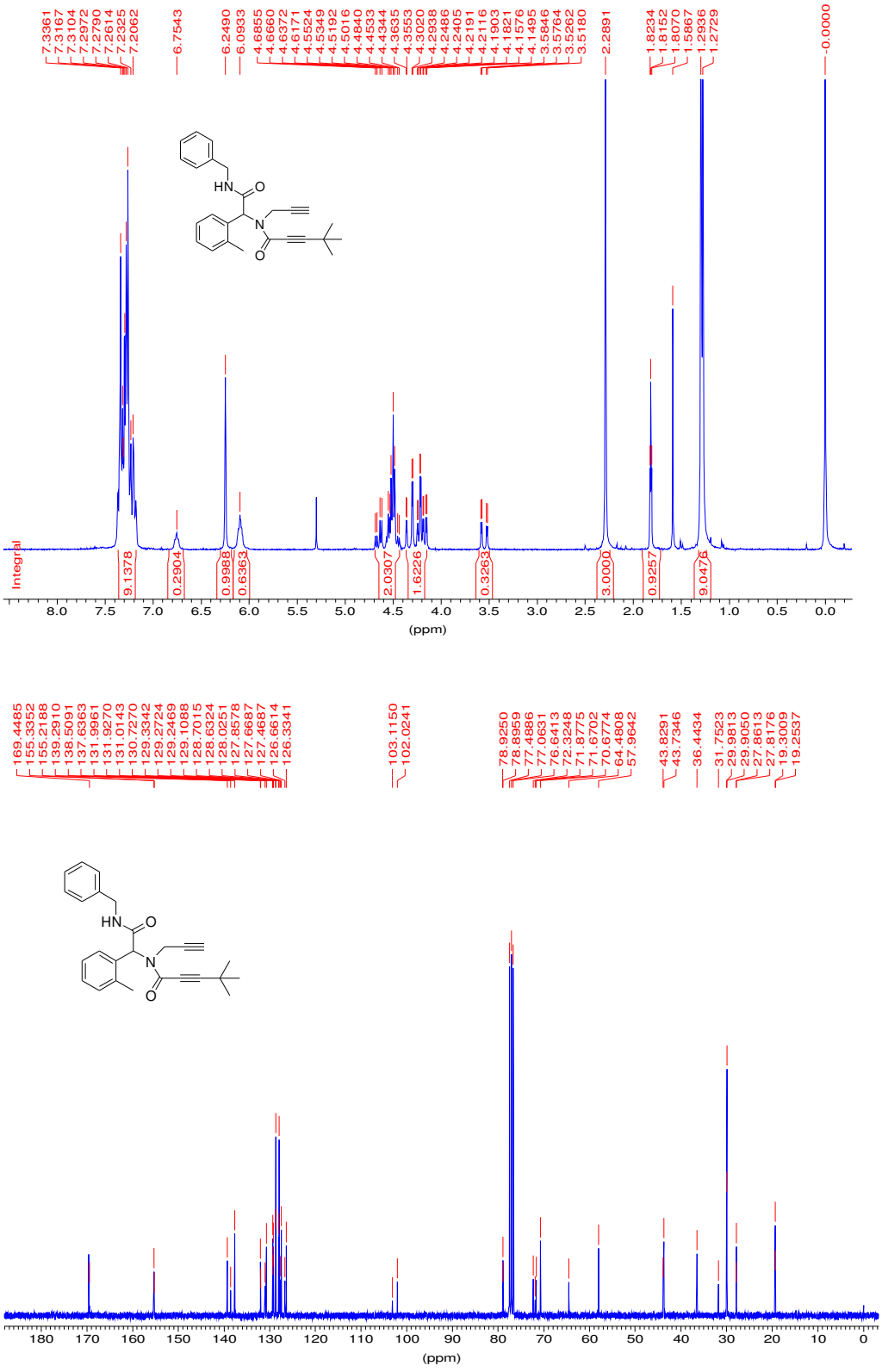


^{1}H and ^{13}C NMR spectra of compound **5c** (300 MHz, $CDCl_3$).

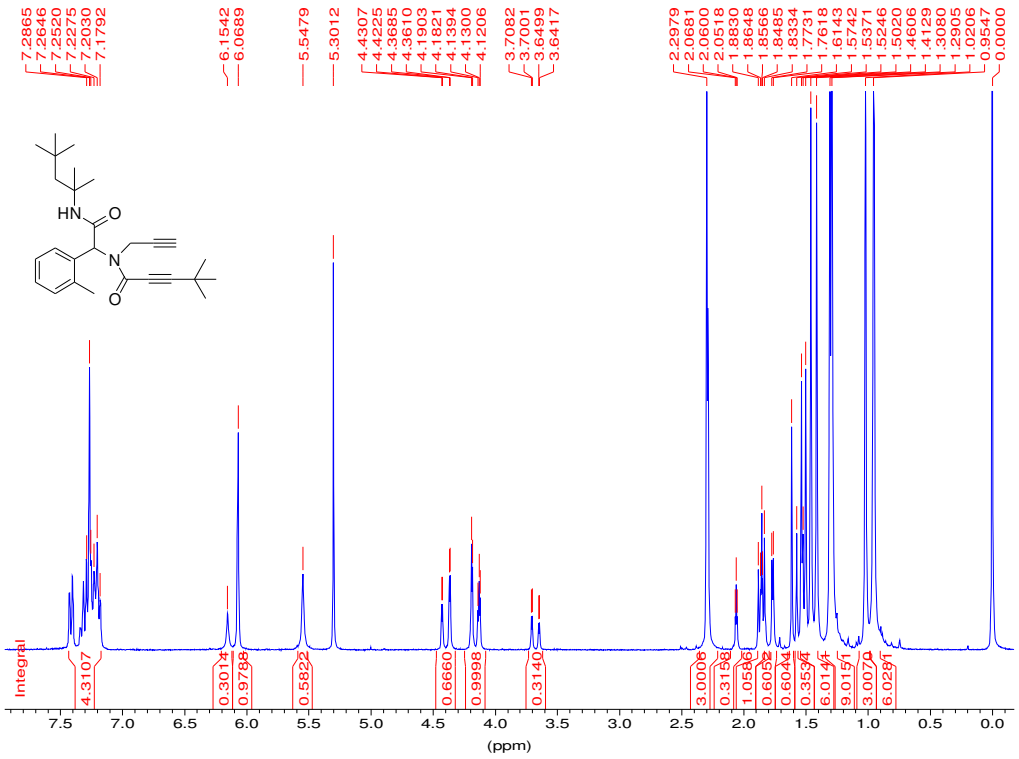


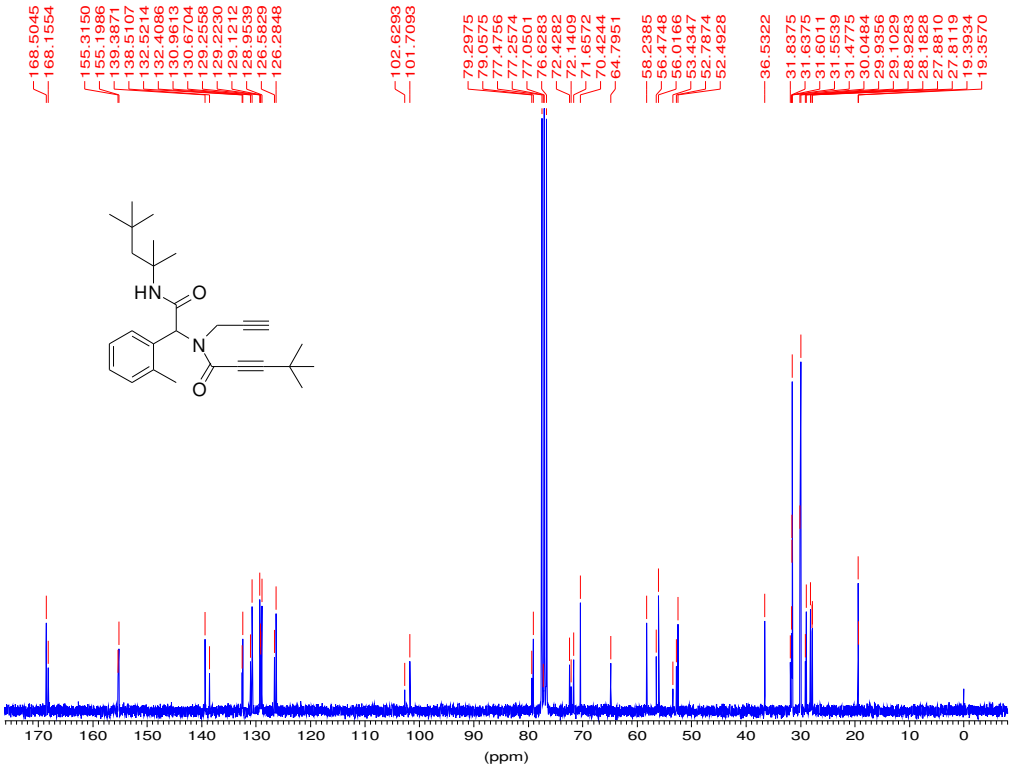


^{1}H and ^{13}C NMR spectra of compound **5d** (300 MHz, $CDCl_3$).

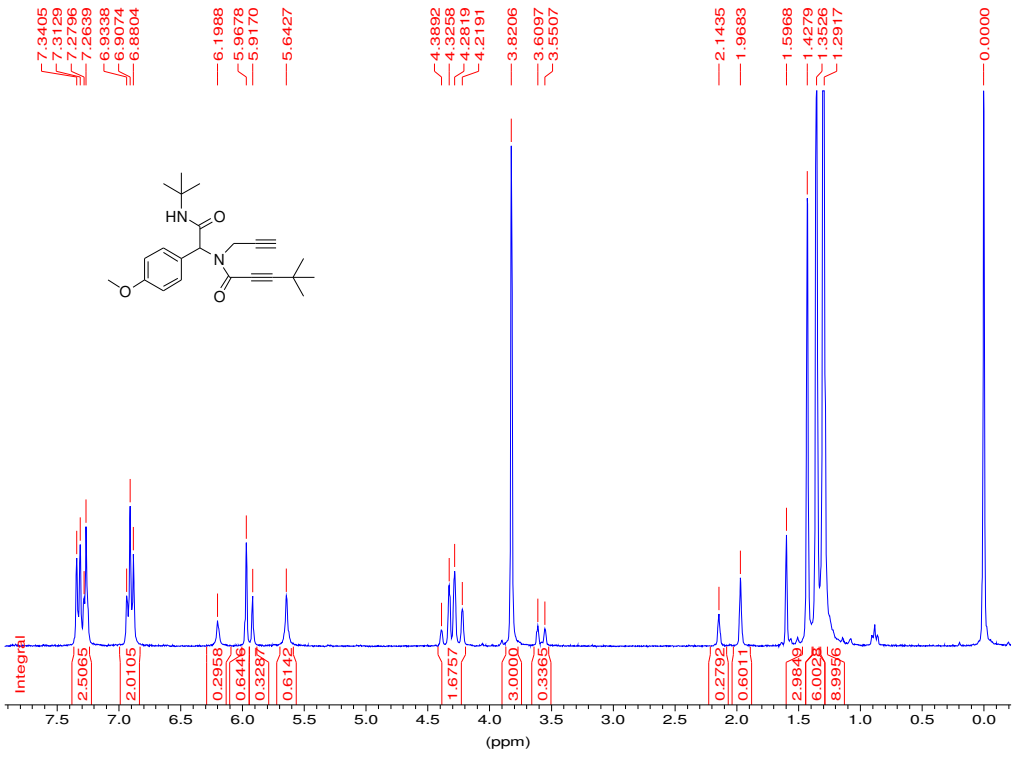


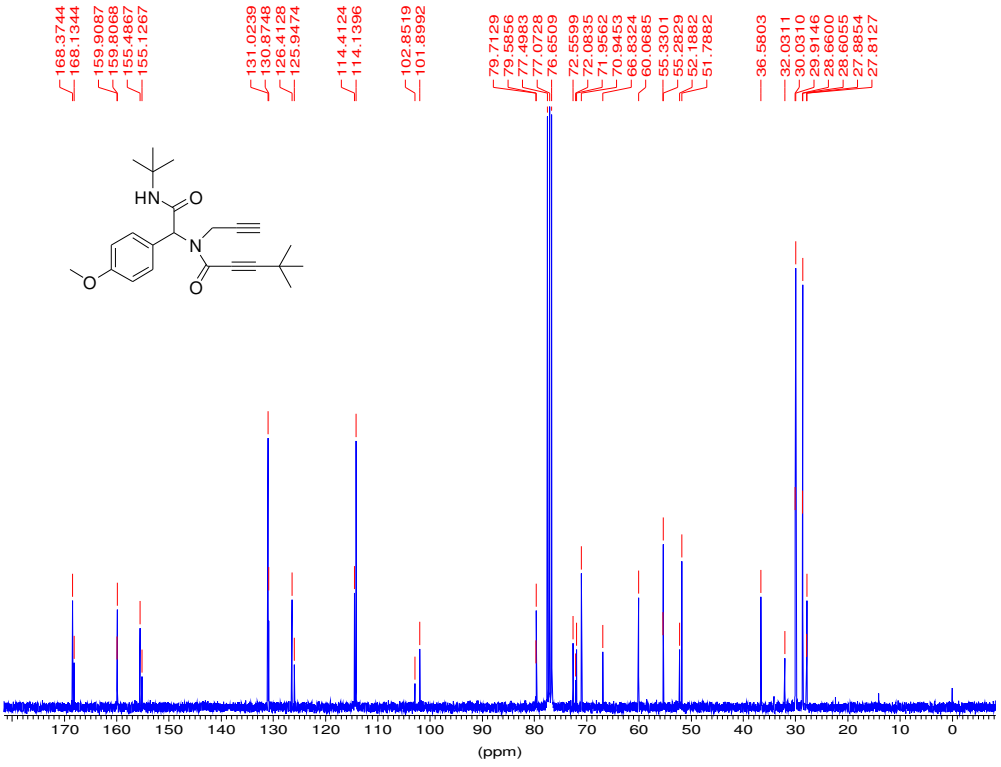
^{1}H and ^{13}C NMR spectra of compound **5e** (300 MHz, $CDCl_3$).



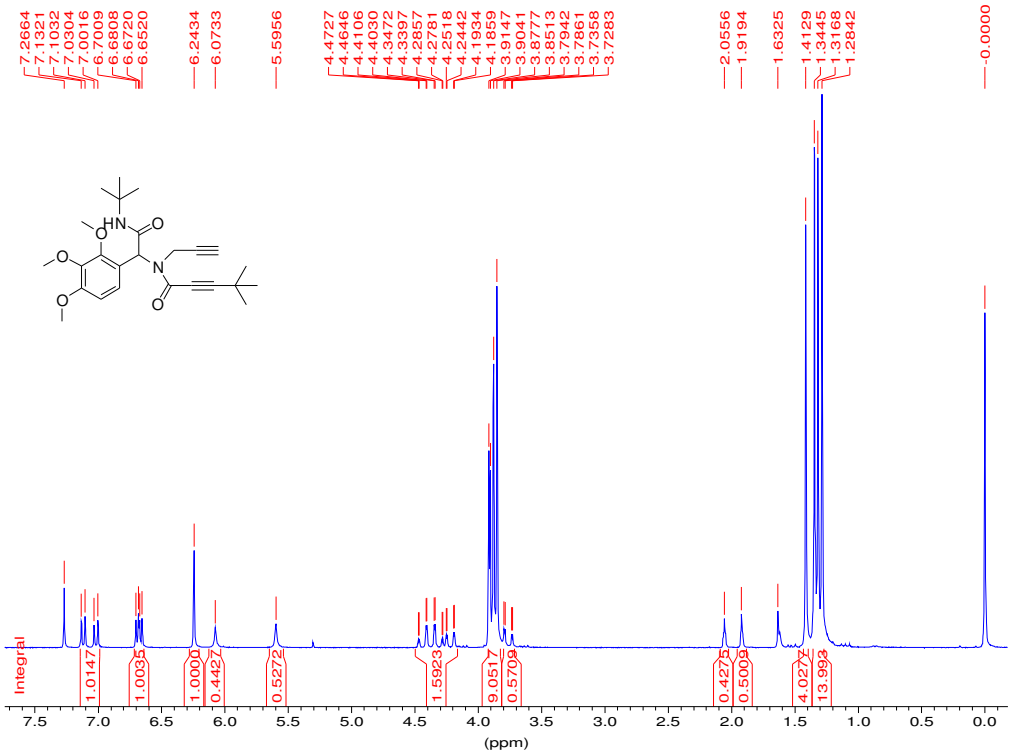


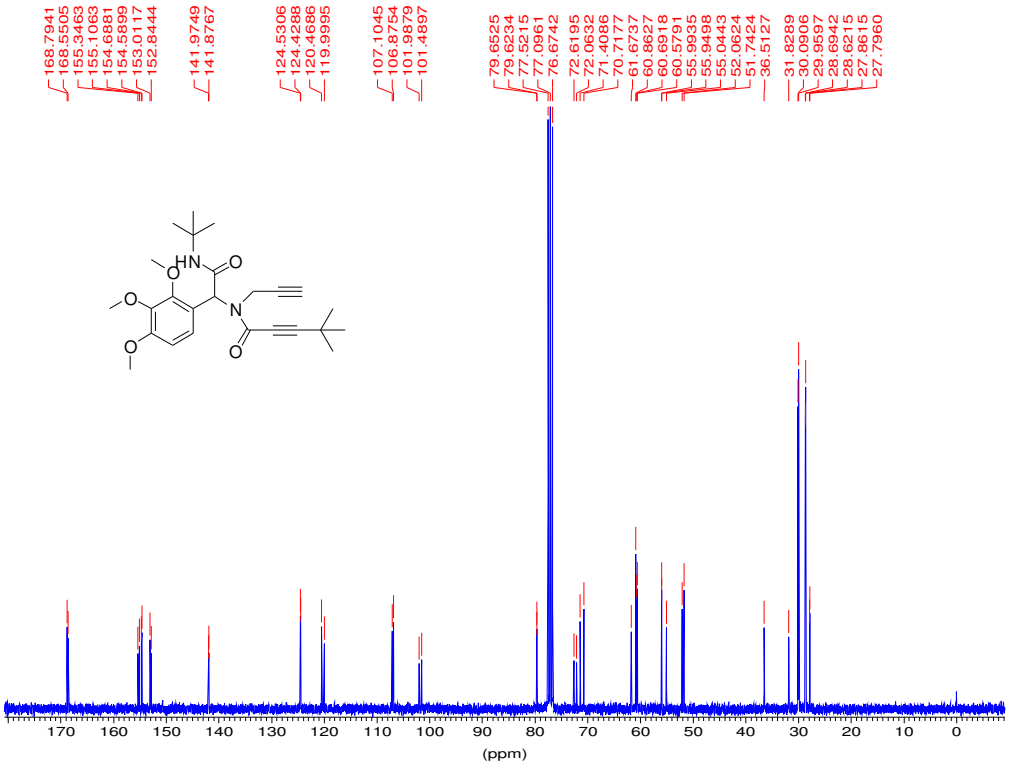
^{1}H and ^{13}C NMR spectra of compound **5f** (300 MHz, $CDCl_3$).



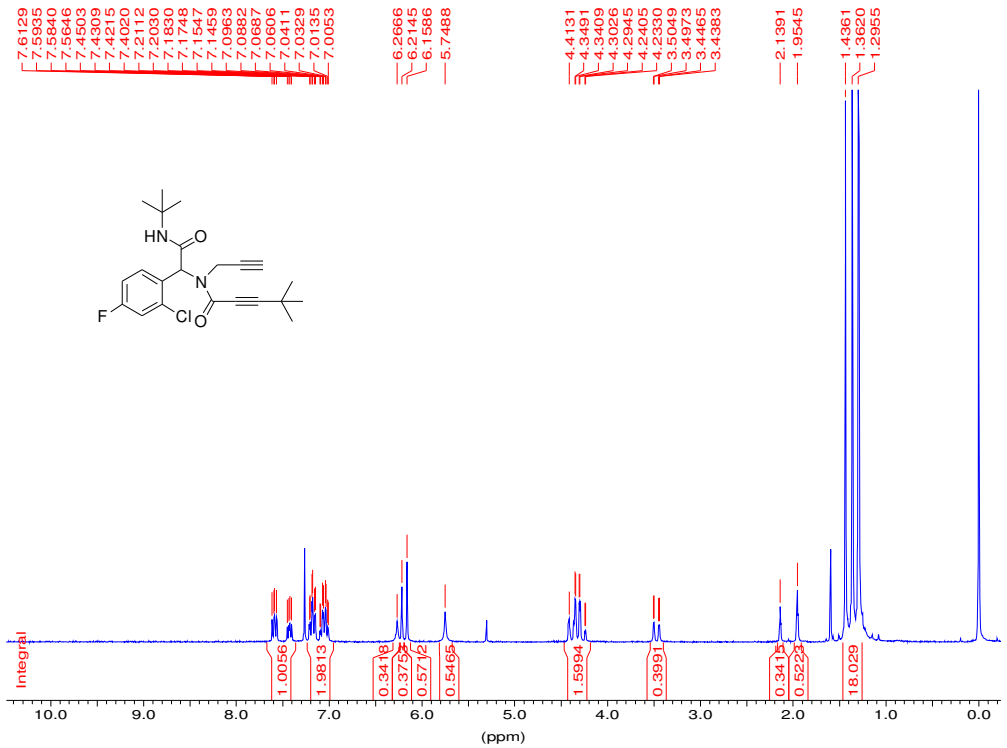


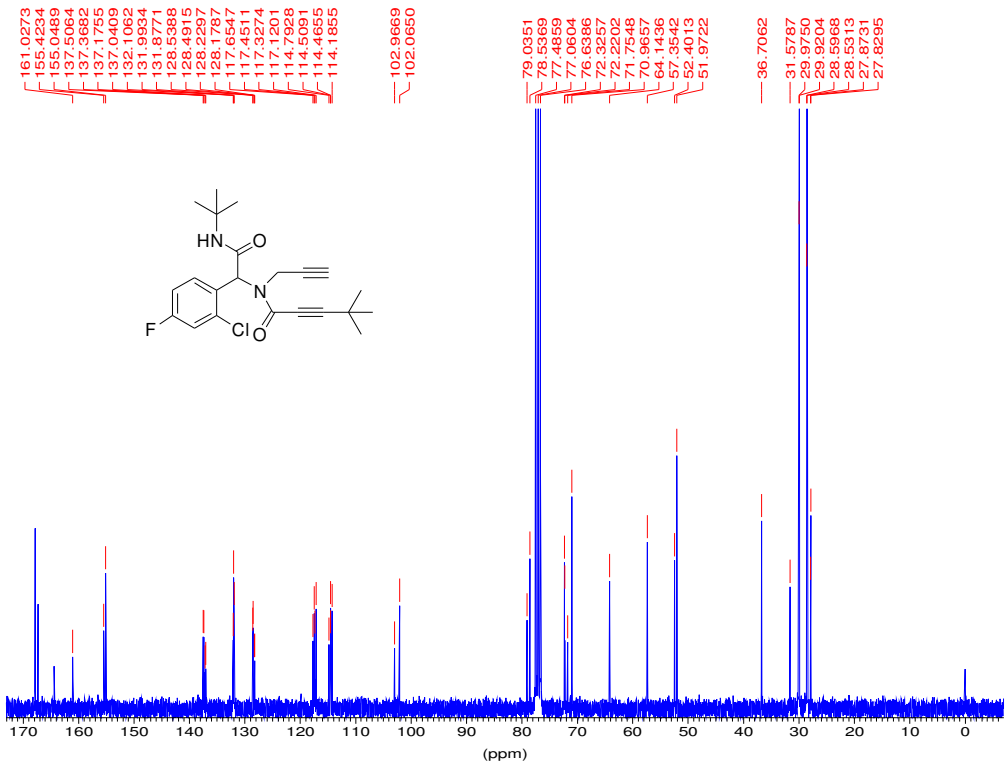
^{1}H and ^{13}C NMR spectra of compound **5g** (300 MHz, $CDCl_3$).



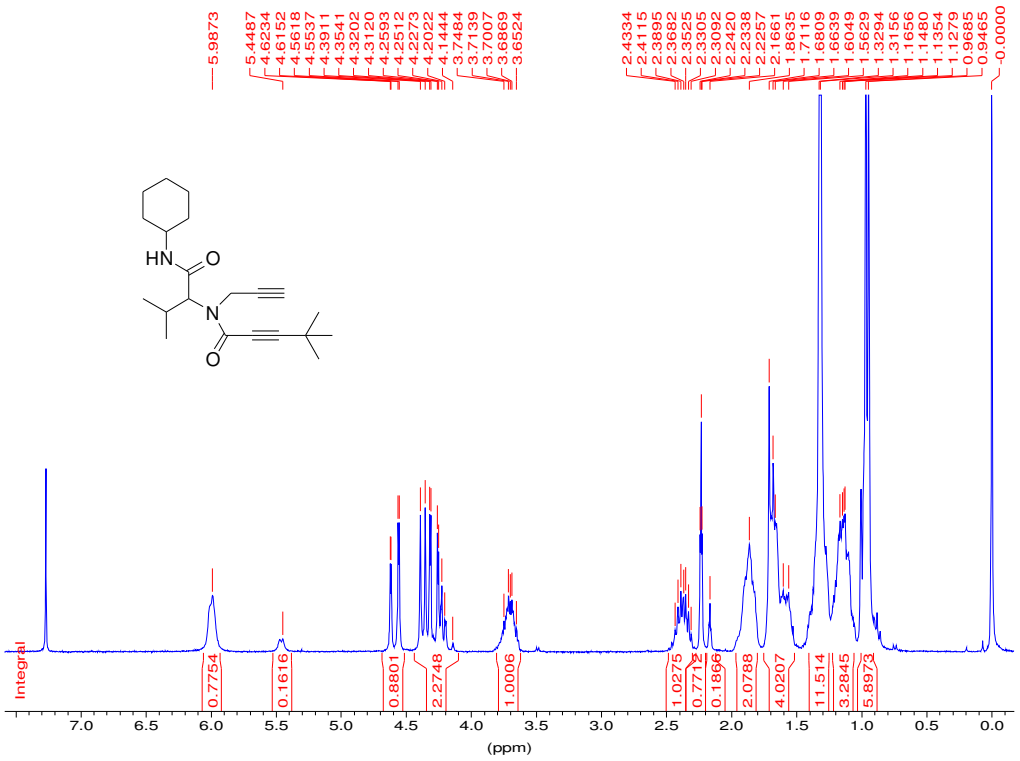


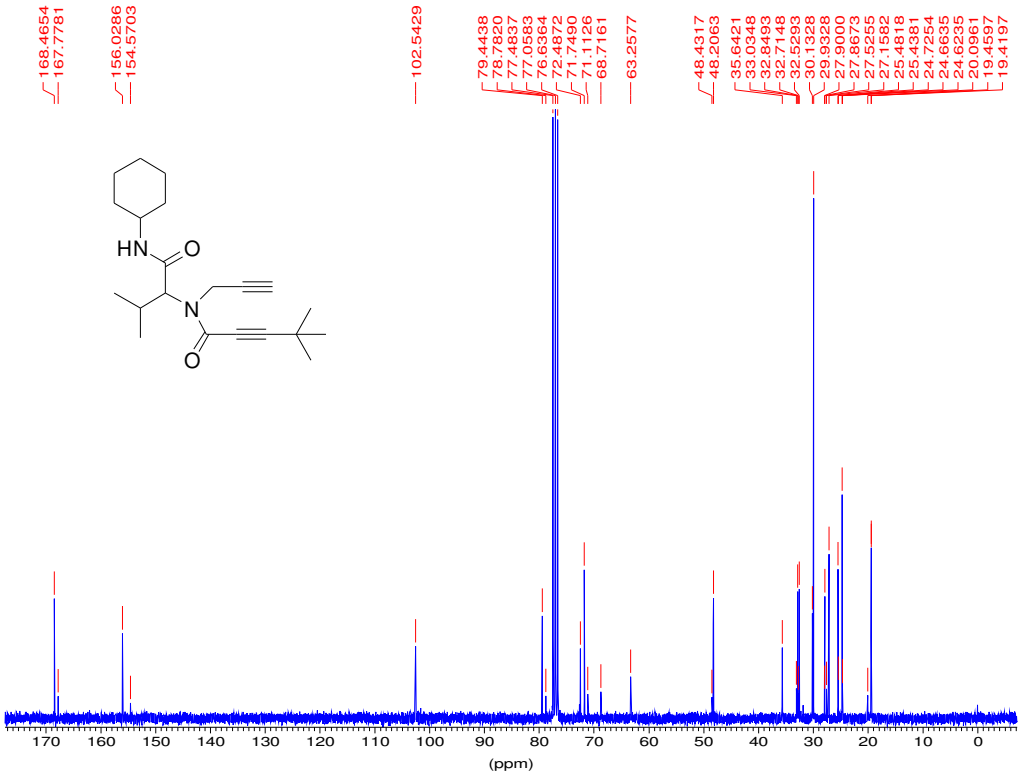
^{1}H and ^{13}C NMR spectra of compound **5h** (300 MHz, $CDCl_3$).



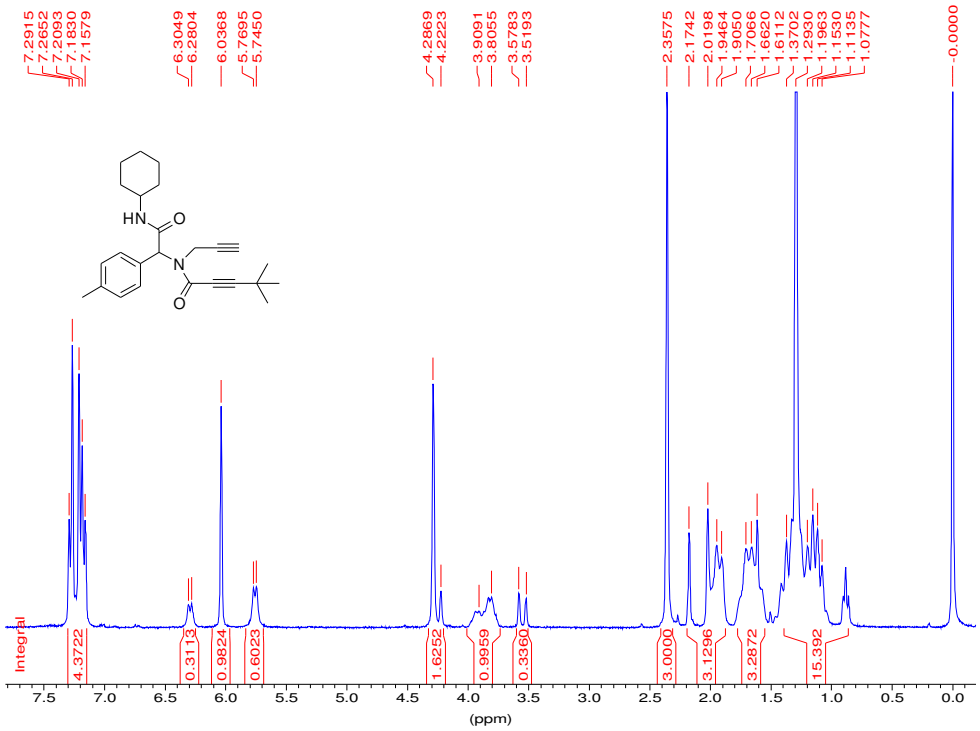


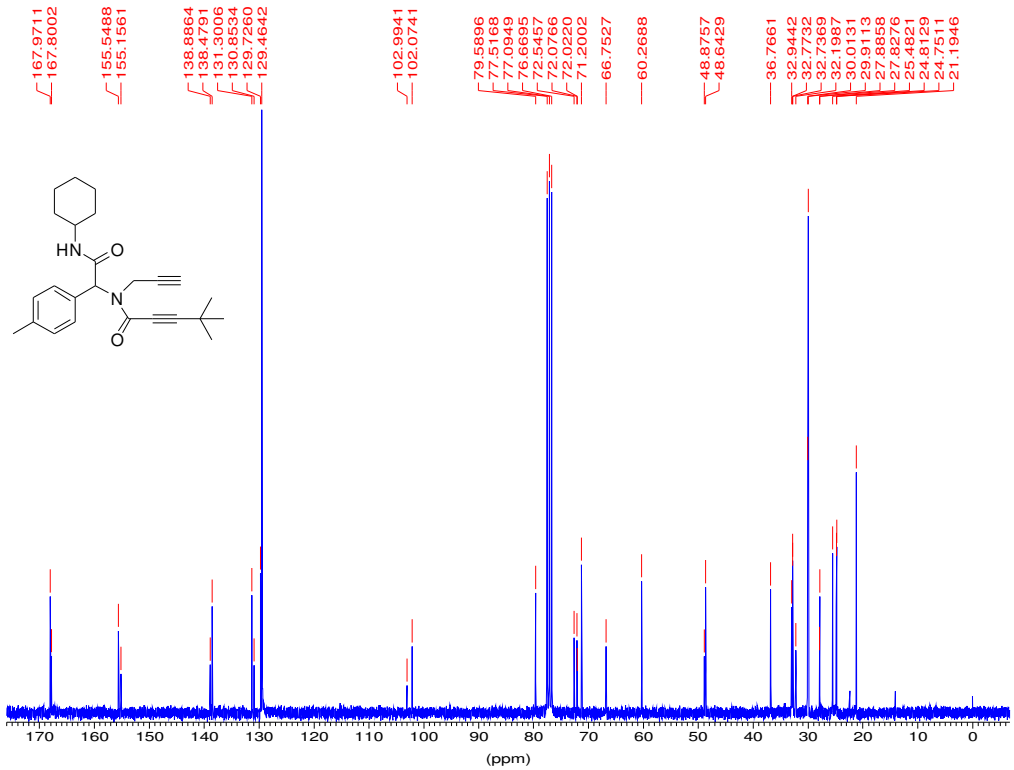
^{1}H and ^{13}C NMR spectra of compound **5i** (300 MHz, $CDCl_3$).



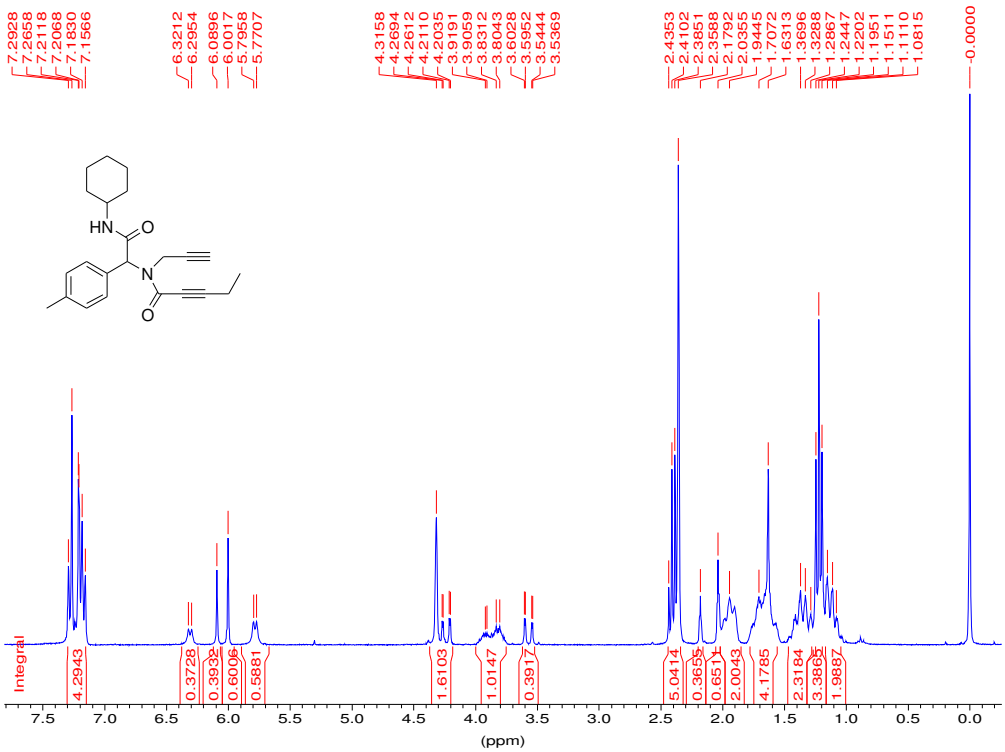


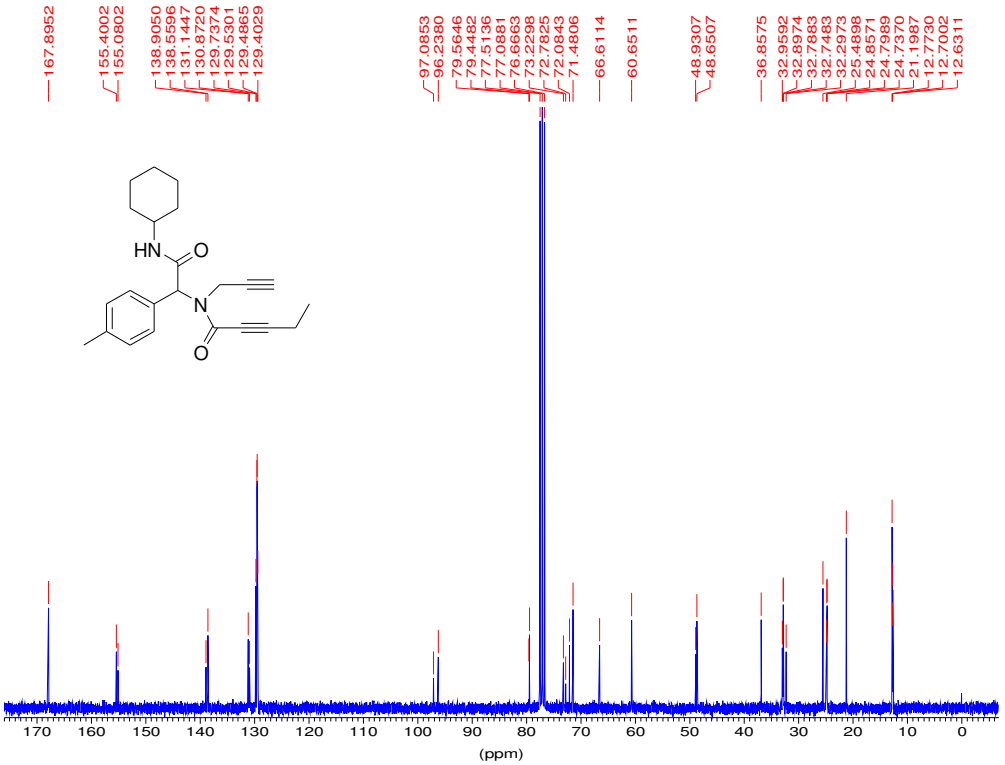
^{1}H and ^{13}C NMR spectra of compound **5j** (300 MHz, $CDCl_3$).



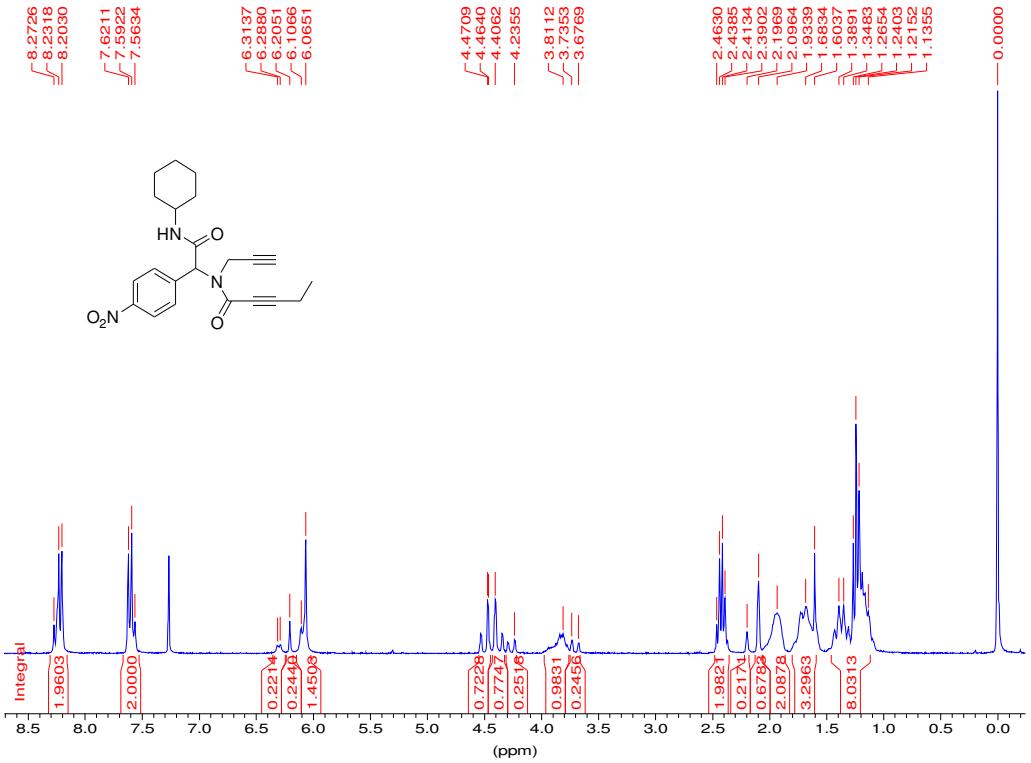


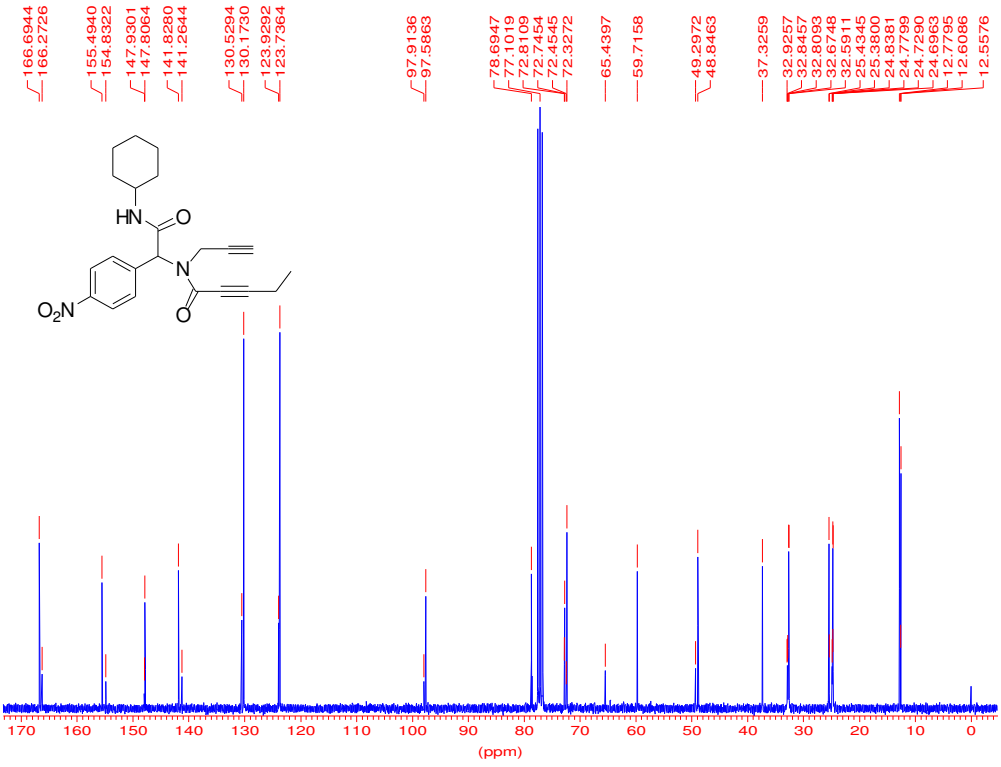
^{1}H and ^{13}C NMR spectra of compound **5k** (300 MHz, $CDCl_3$).



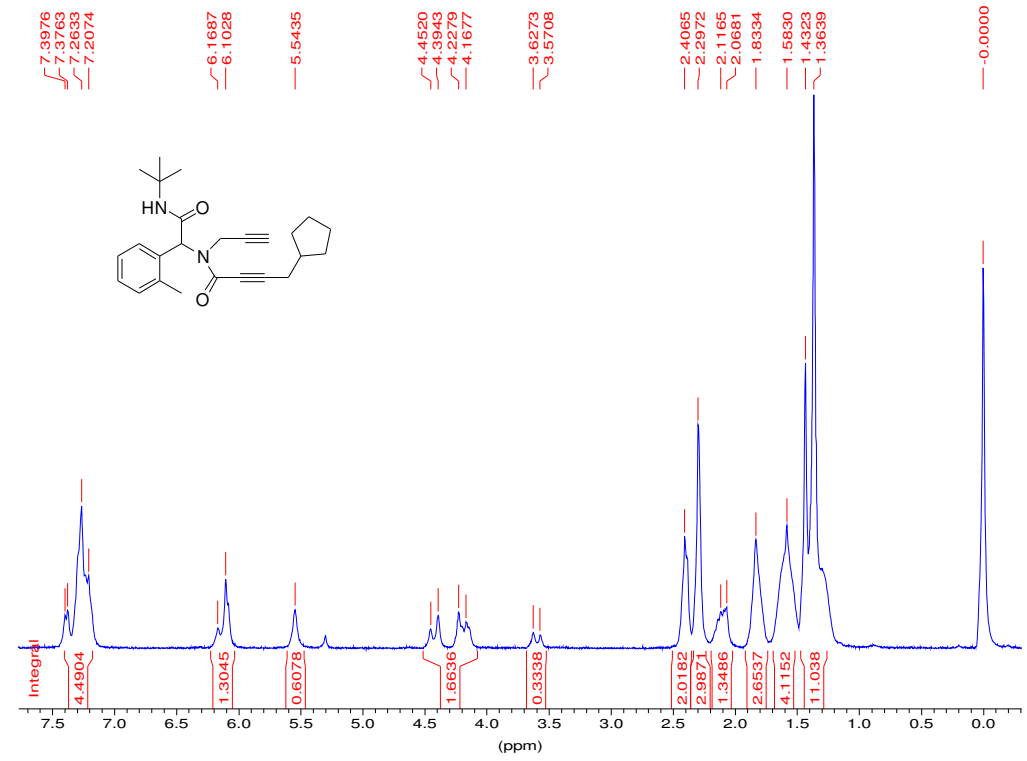


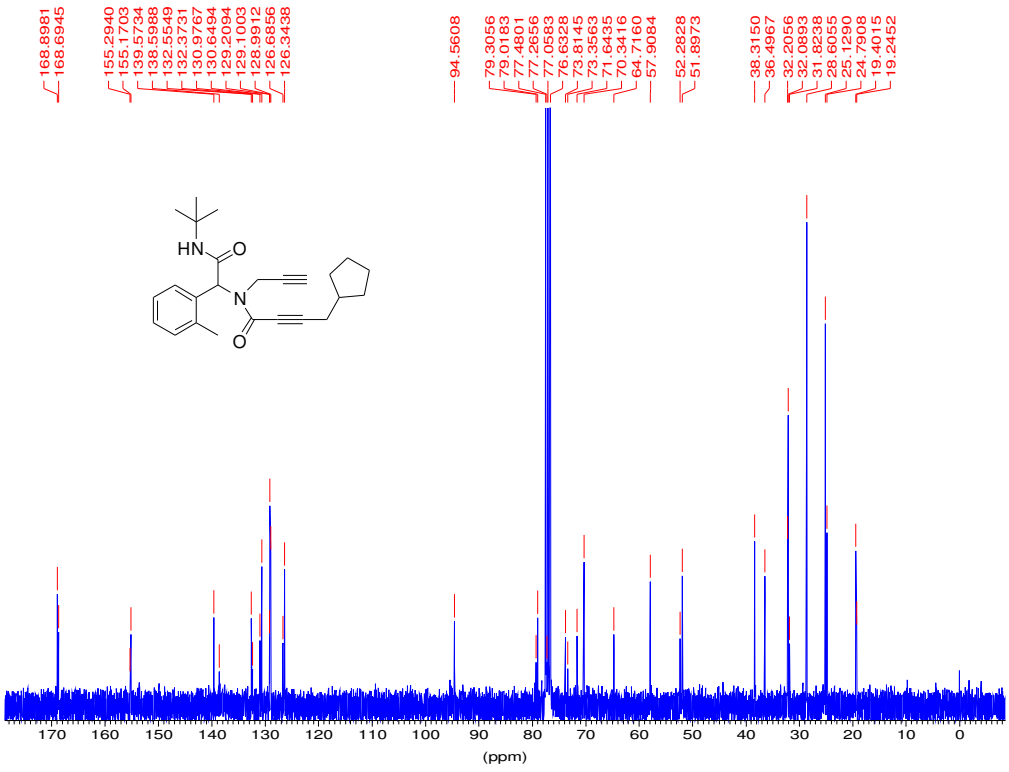
^{1}H and ^{13}C NMR spectra of compound **5l** (300 MHz, $CDCl_3$).



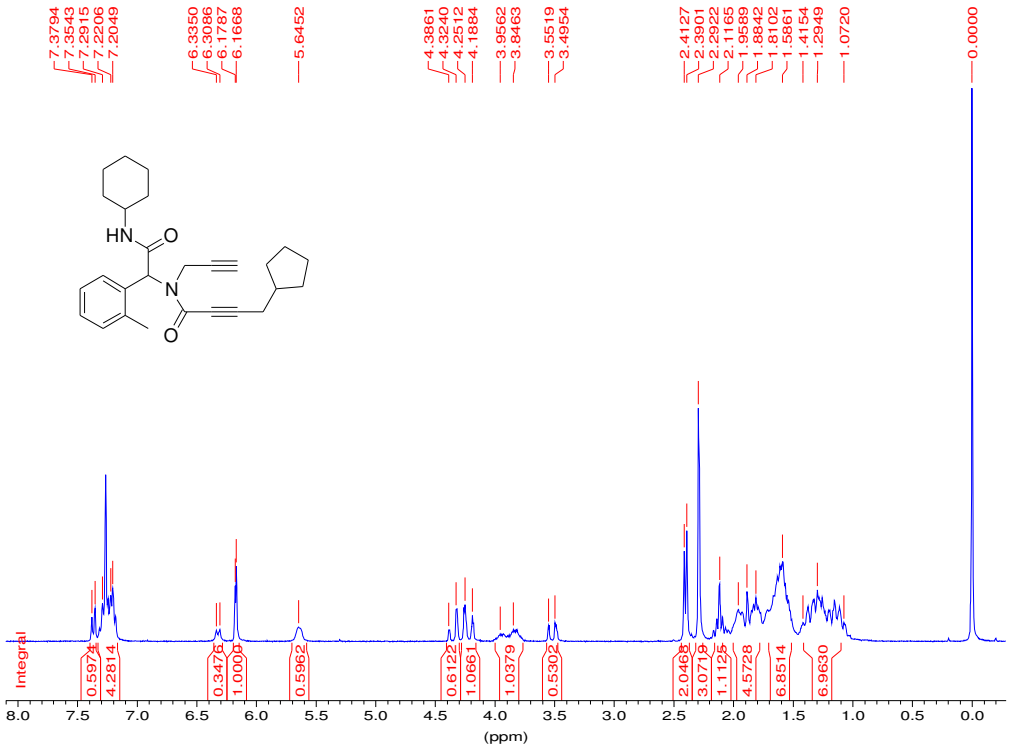


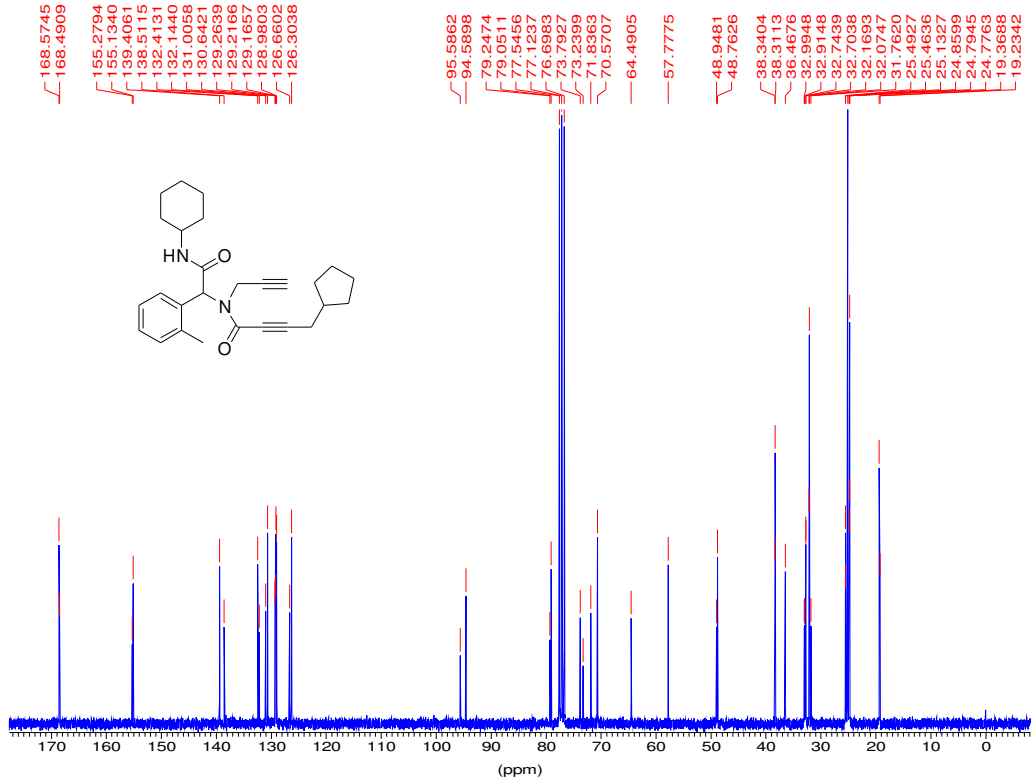
^{1}H and ^{13}C NMR spectra of compound **5m** (300 MHz, $CDCl_3$).



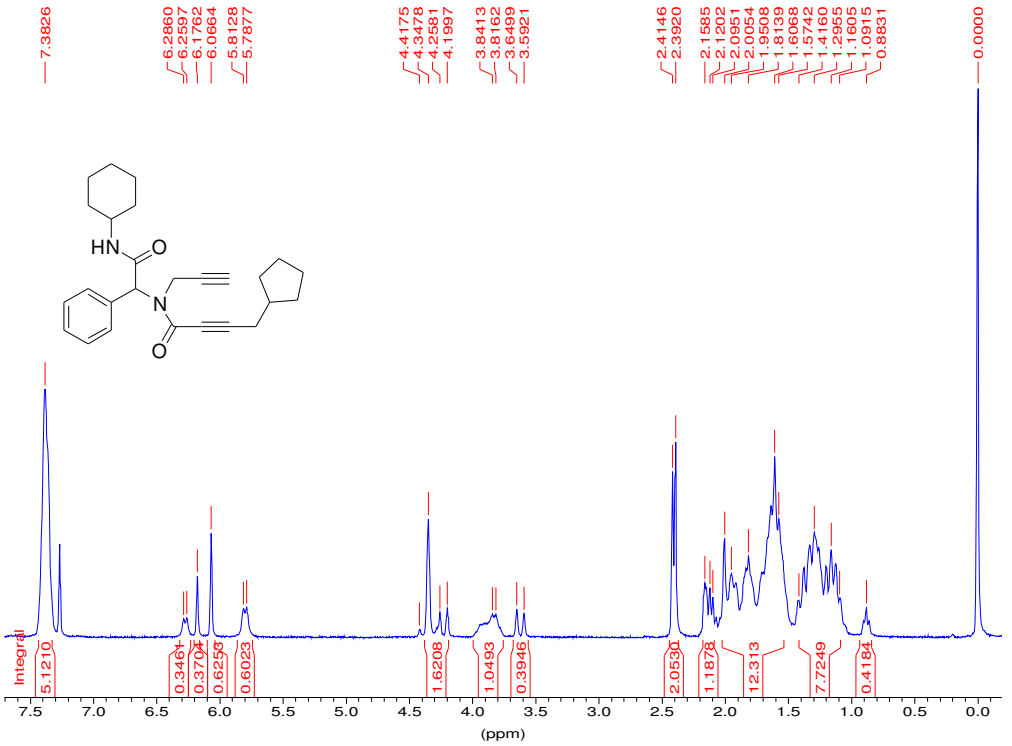


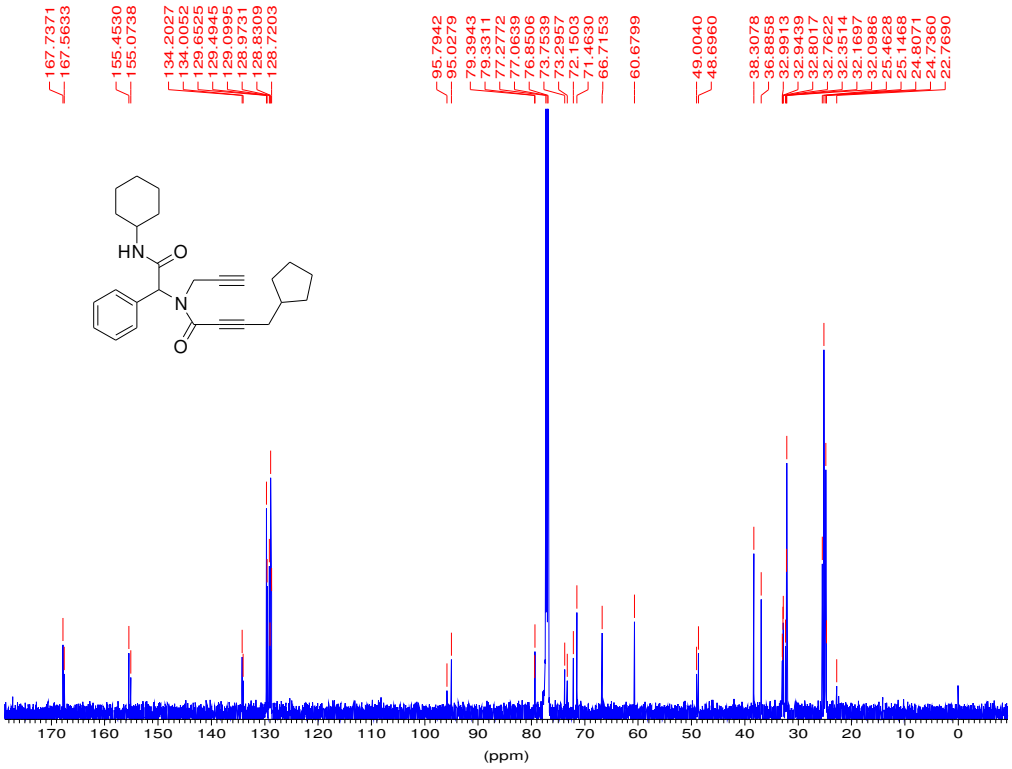
^{1}H and ^{13}C NMR spectra of compound **5n** (300 MHz, $CDCl_3$).



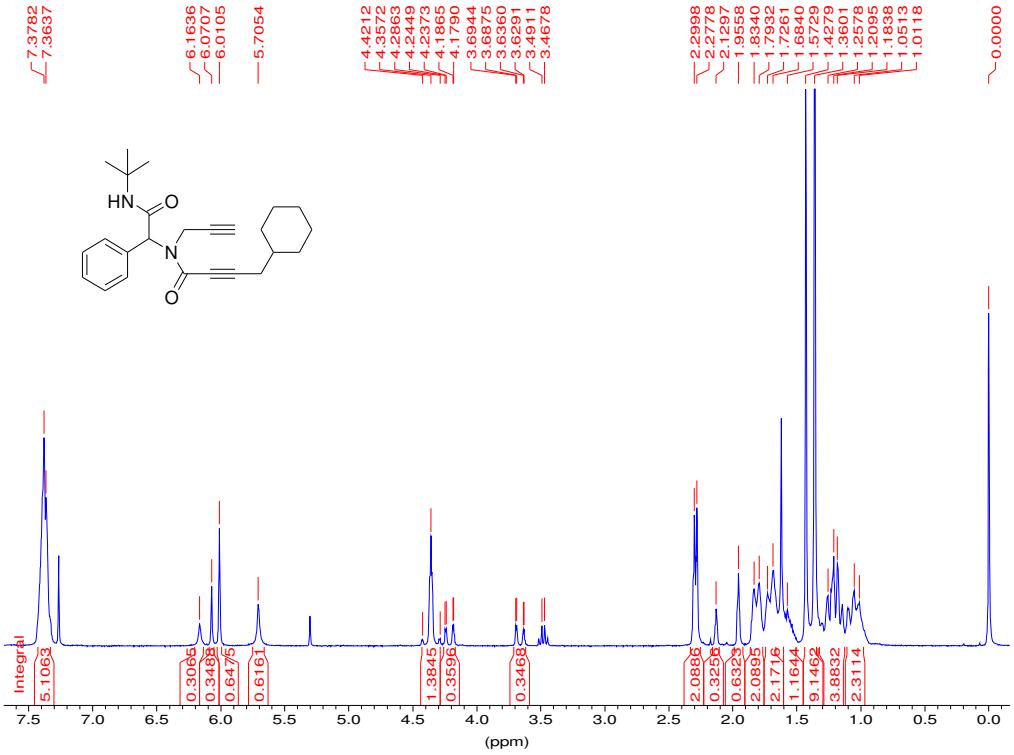


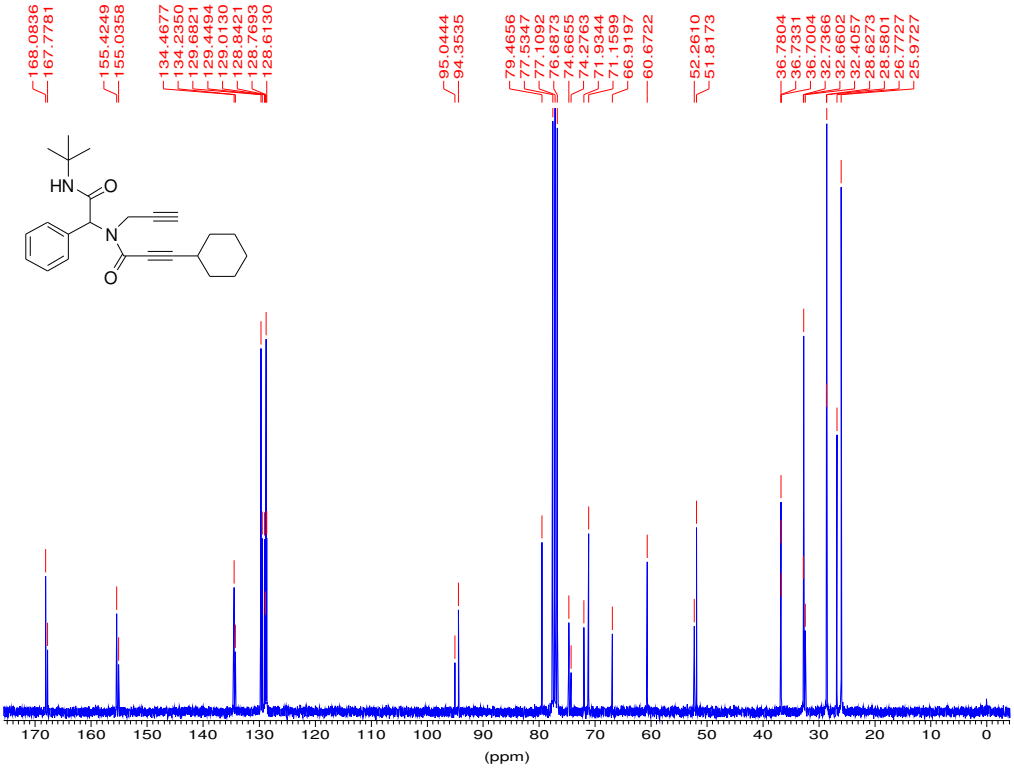
^{1}H and ^{13}C NMR spectra of compound **5o** (300 MHz, $CDCl_3$).



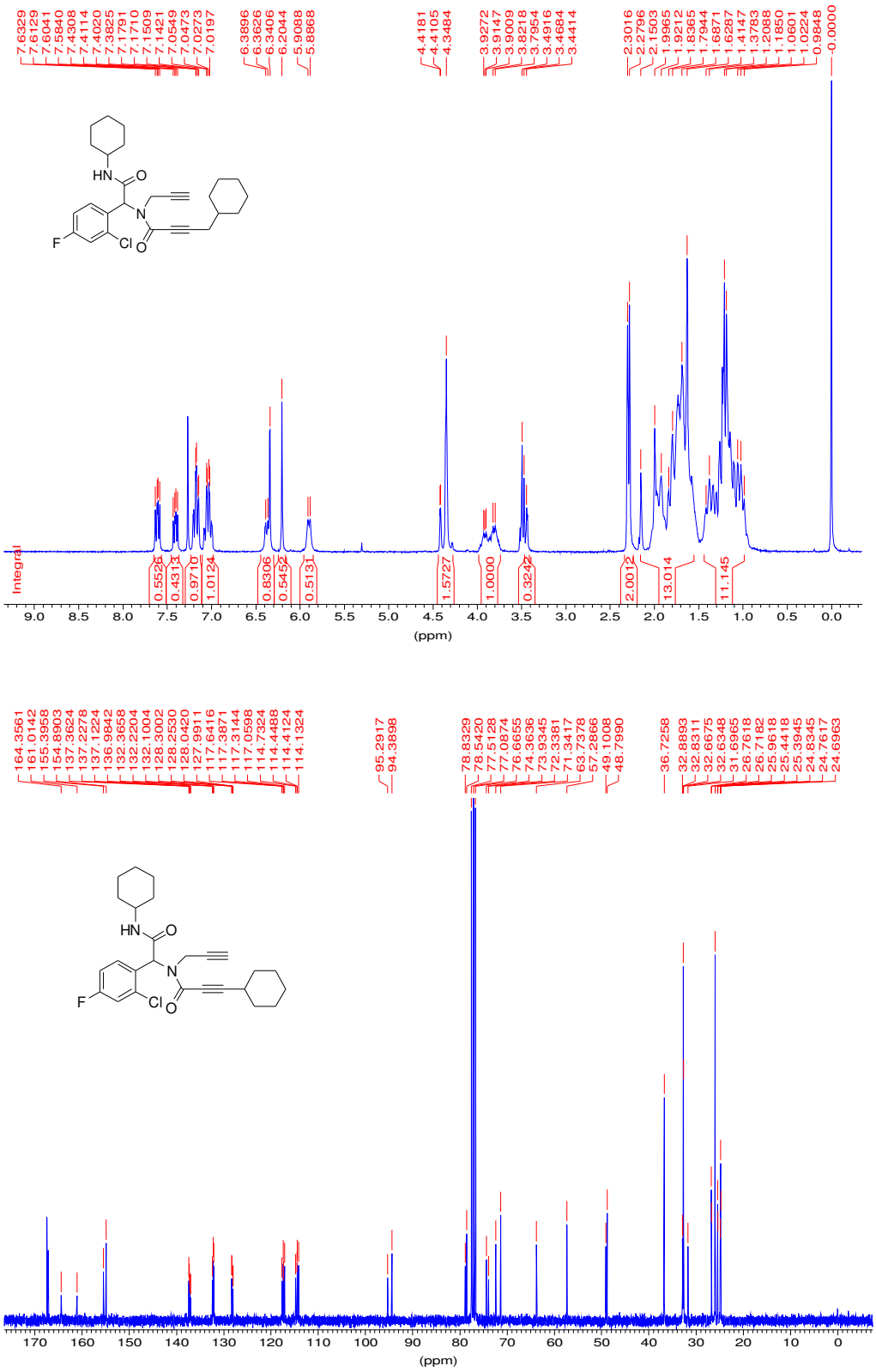


^{1}H and ^{13}C NMR spectra of compound **5p** (300 MHz, $CDCl_3$).

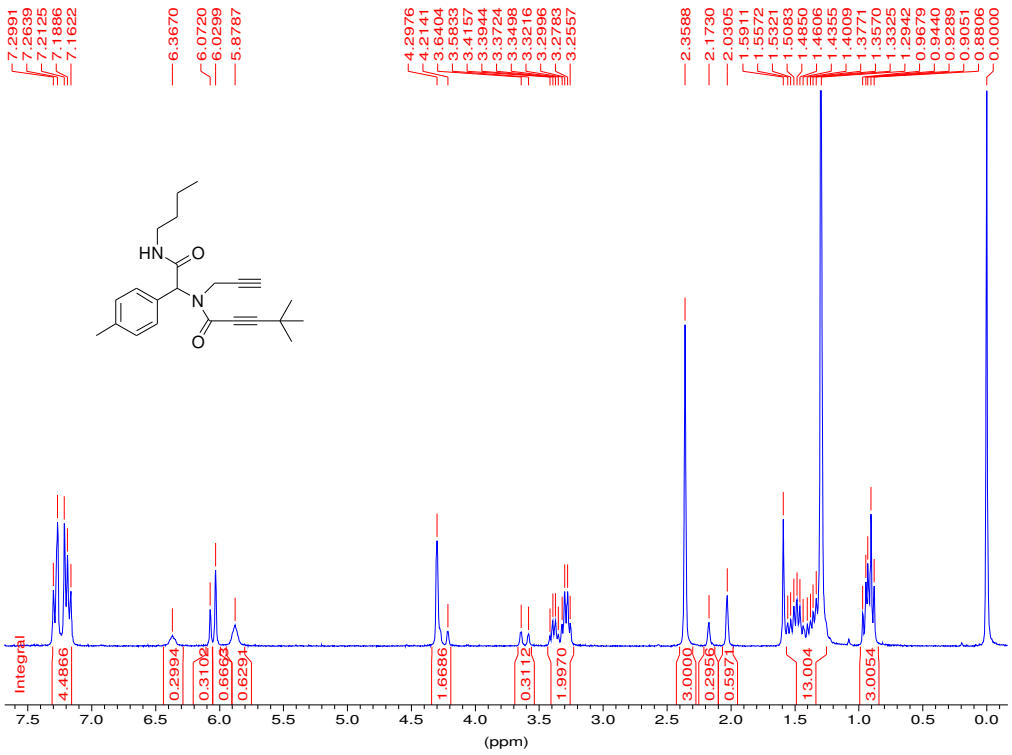


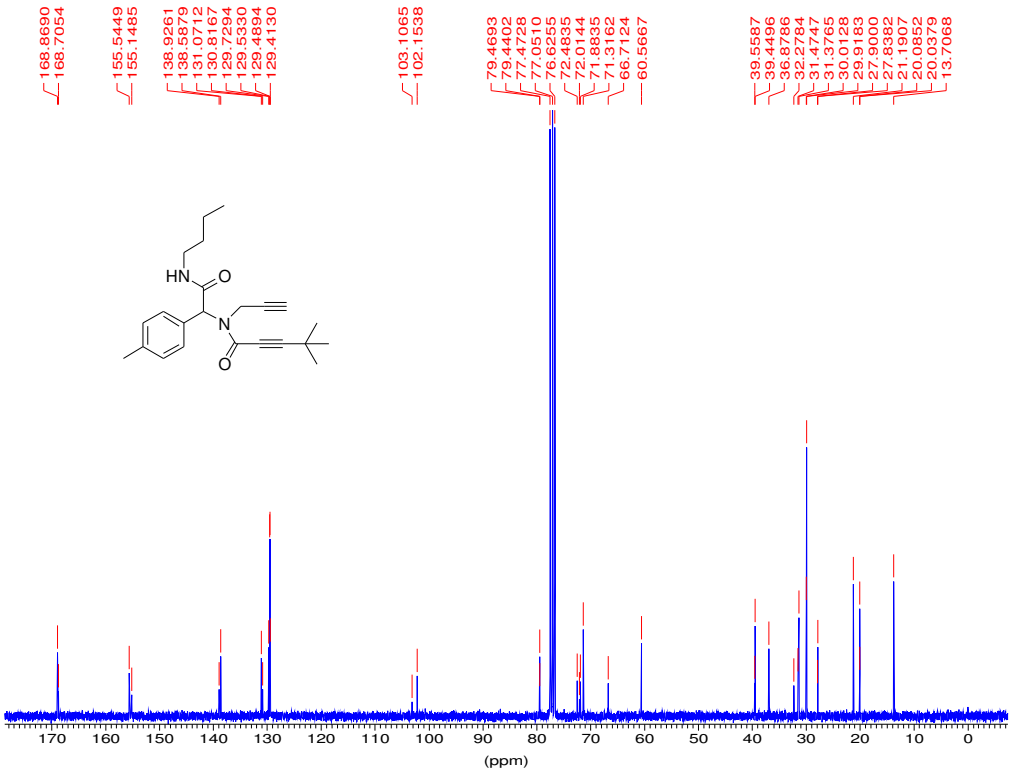


^{1}H and ^{13}C NMR spectra of compound **5q** (300 MHz, $CDCl_3$).

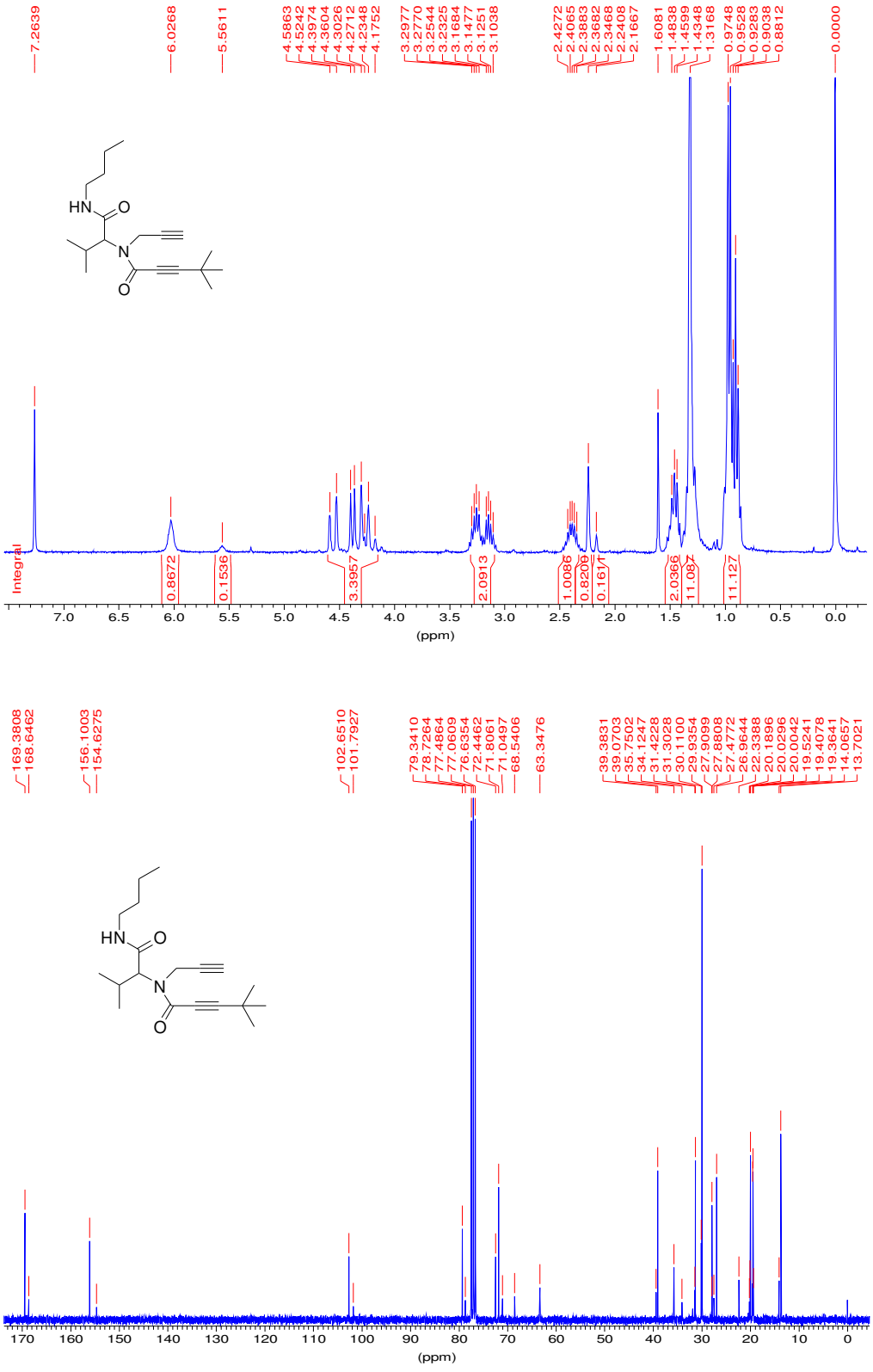


^{1}H and ^{13}C NMR spectra of compound **5r** (300 MHz, $CDCl_3$).

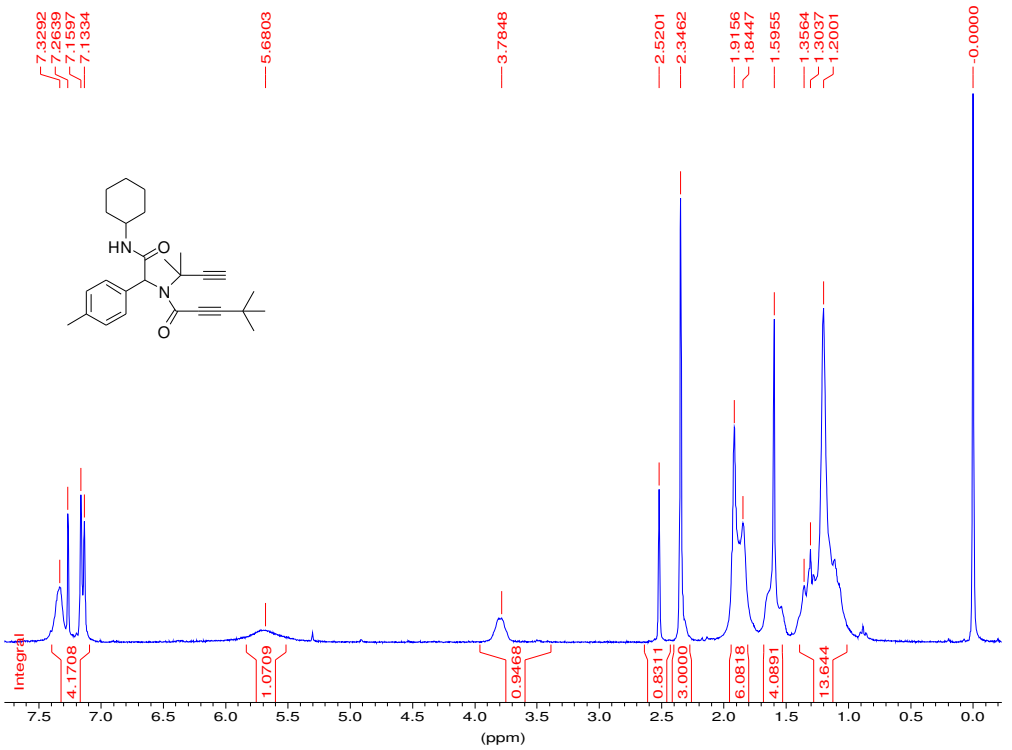


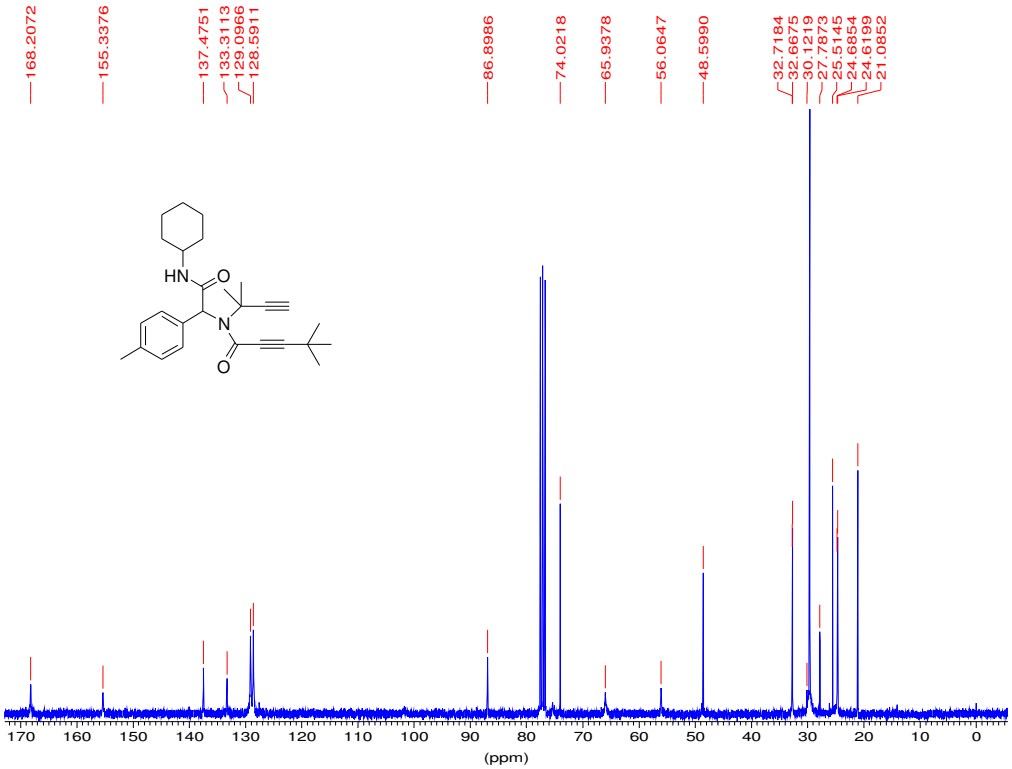


^{1}H and ^{13}C NMR spectra of compound **5s** (300 MHz, $CDCl_3$).

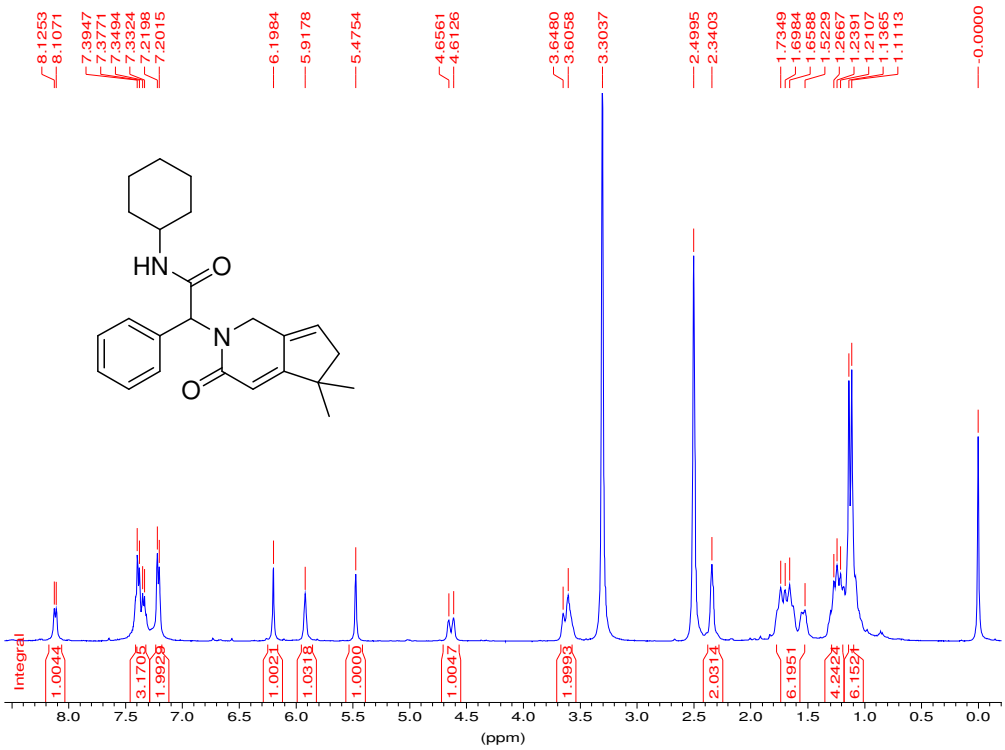


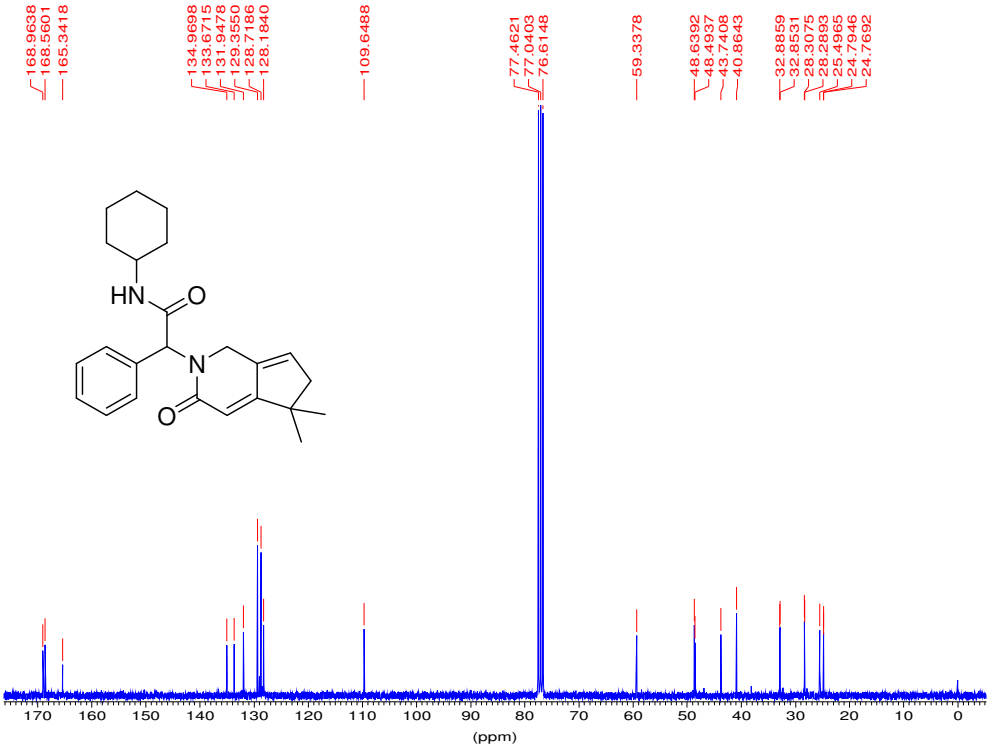
^{1}H and ^{13}C NMR spectra of compound **5t** (300 MHz, $CDCl_3$).



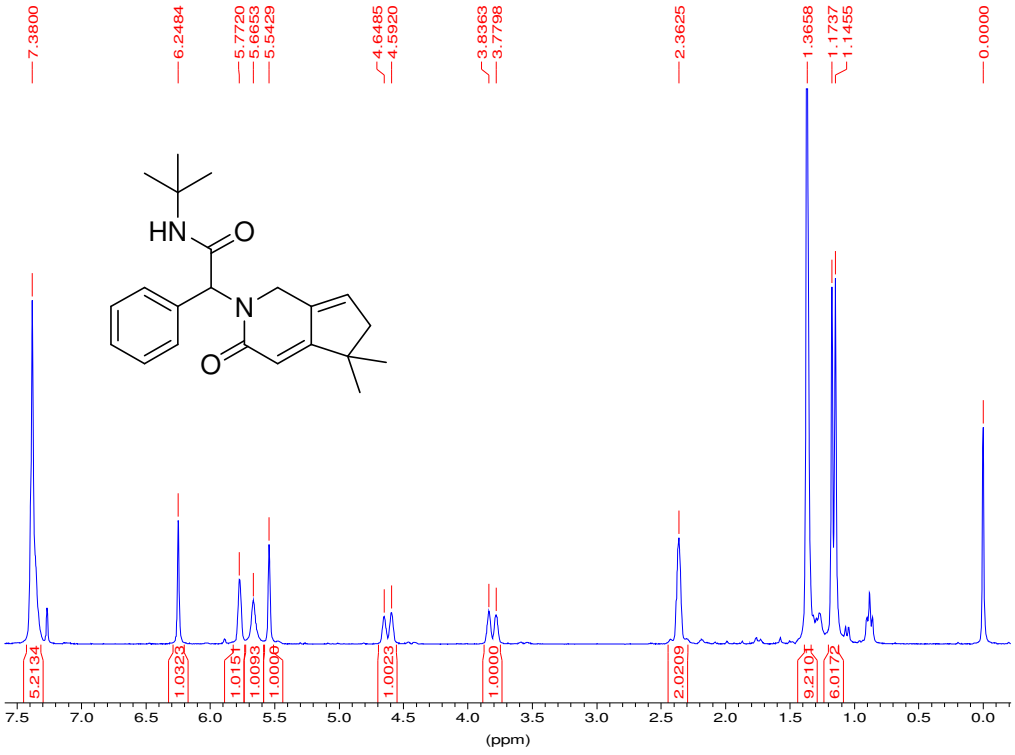


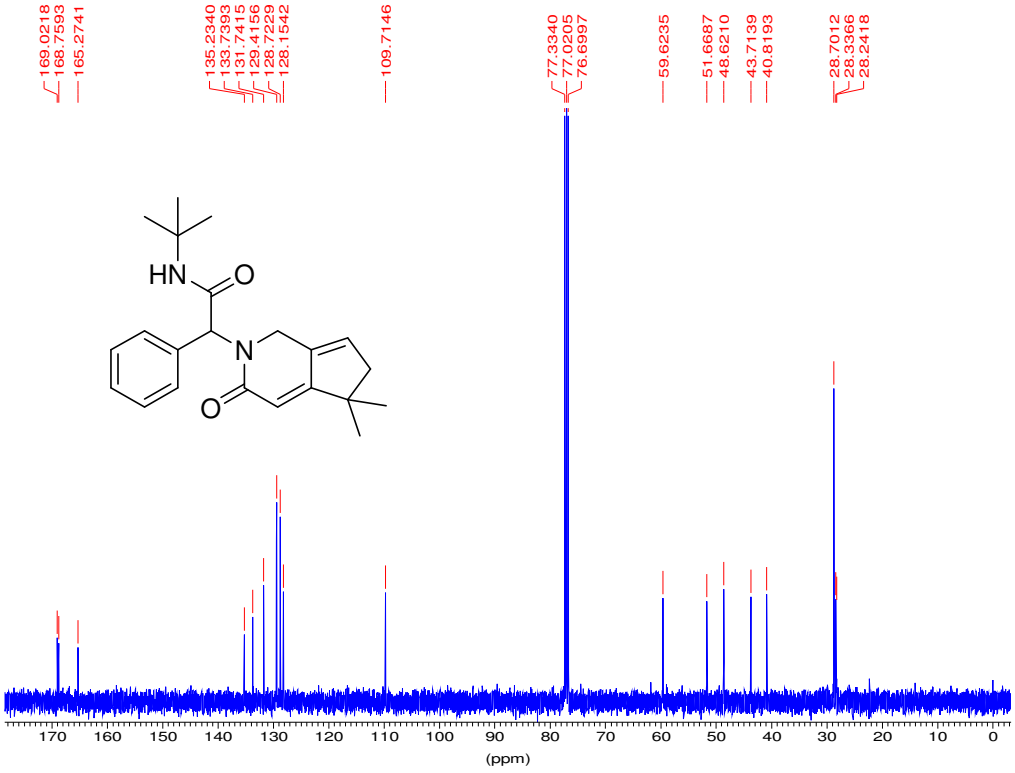
^{1}H and ^{13}C NMR spectra of compound **6a** (300 MHz, $CDCl_3$).



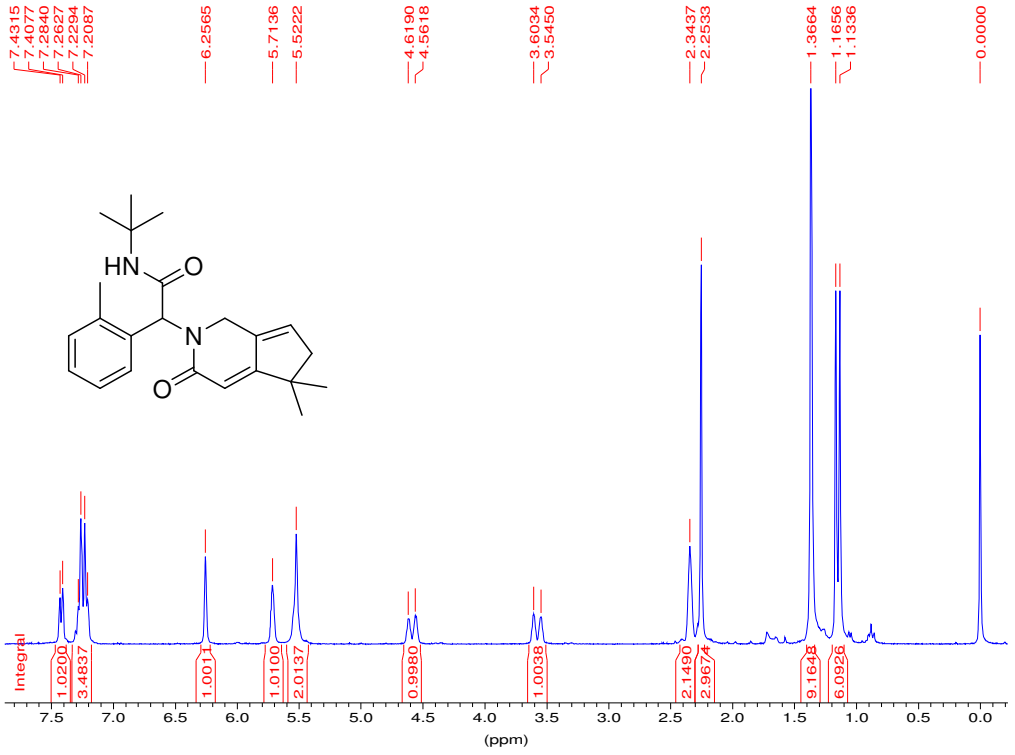


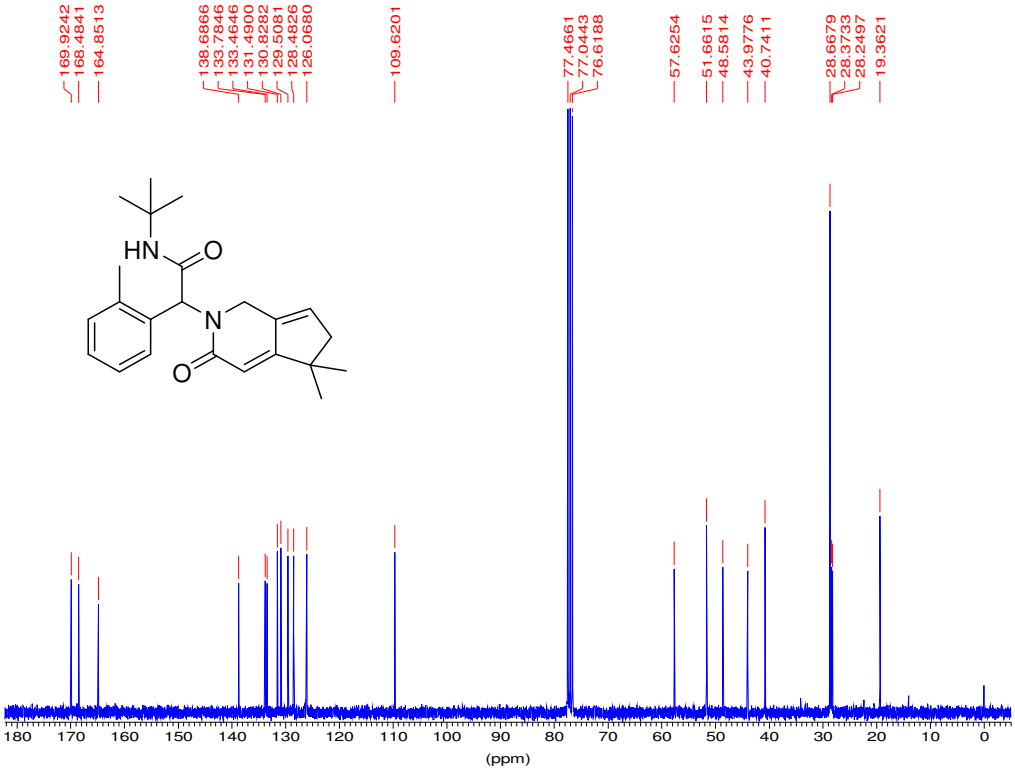
^{1}H and ^{13}C NMR spectra of compound **6b** (300 MHz, $CDCl_3$).



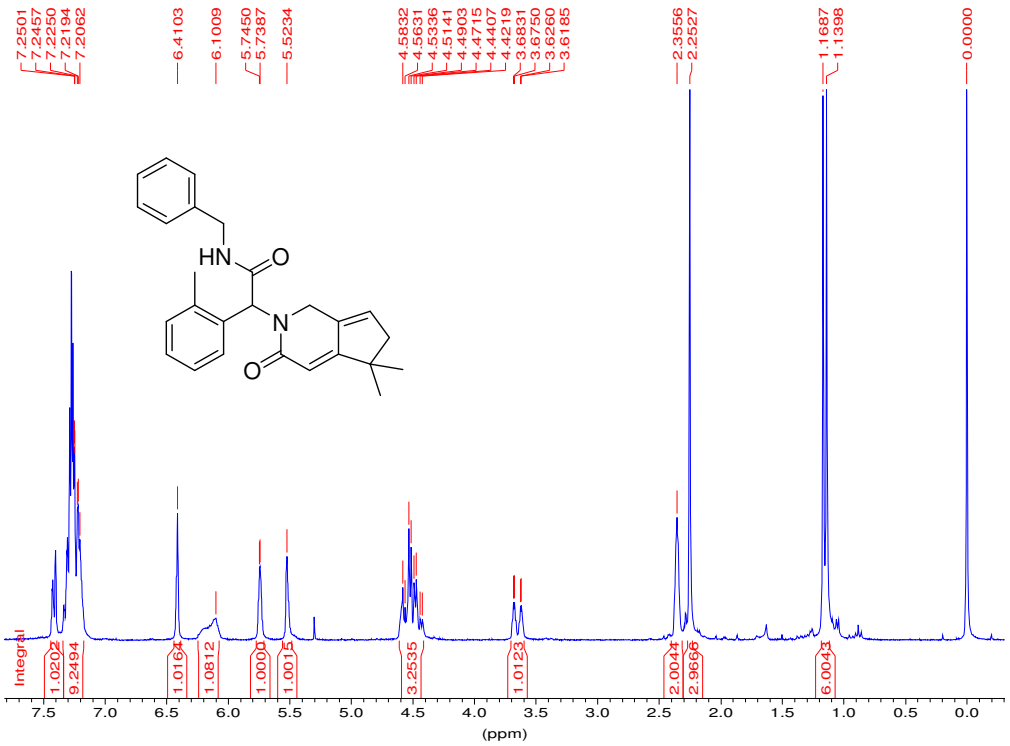


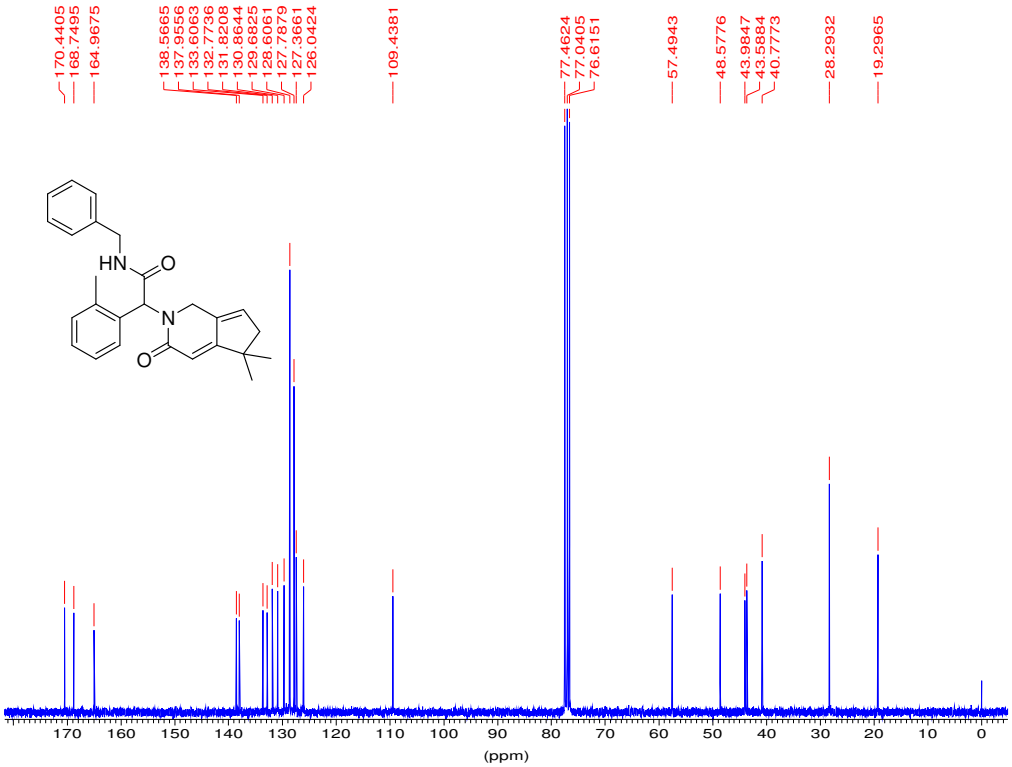
^{1}H and ^{13}C NMR spectra of compound **6c** (300 MHz, $CDCl_3$).



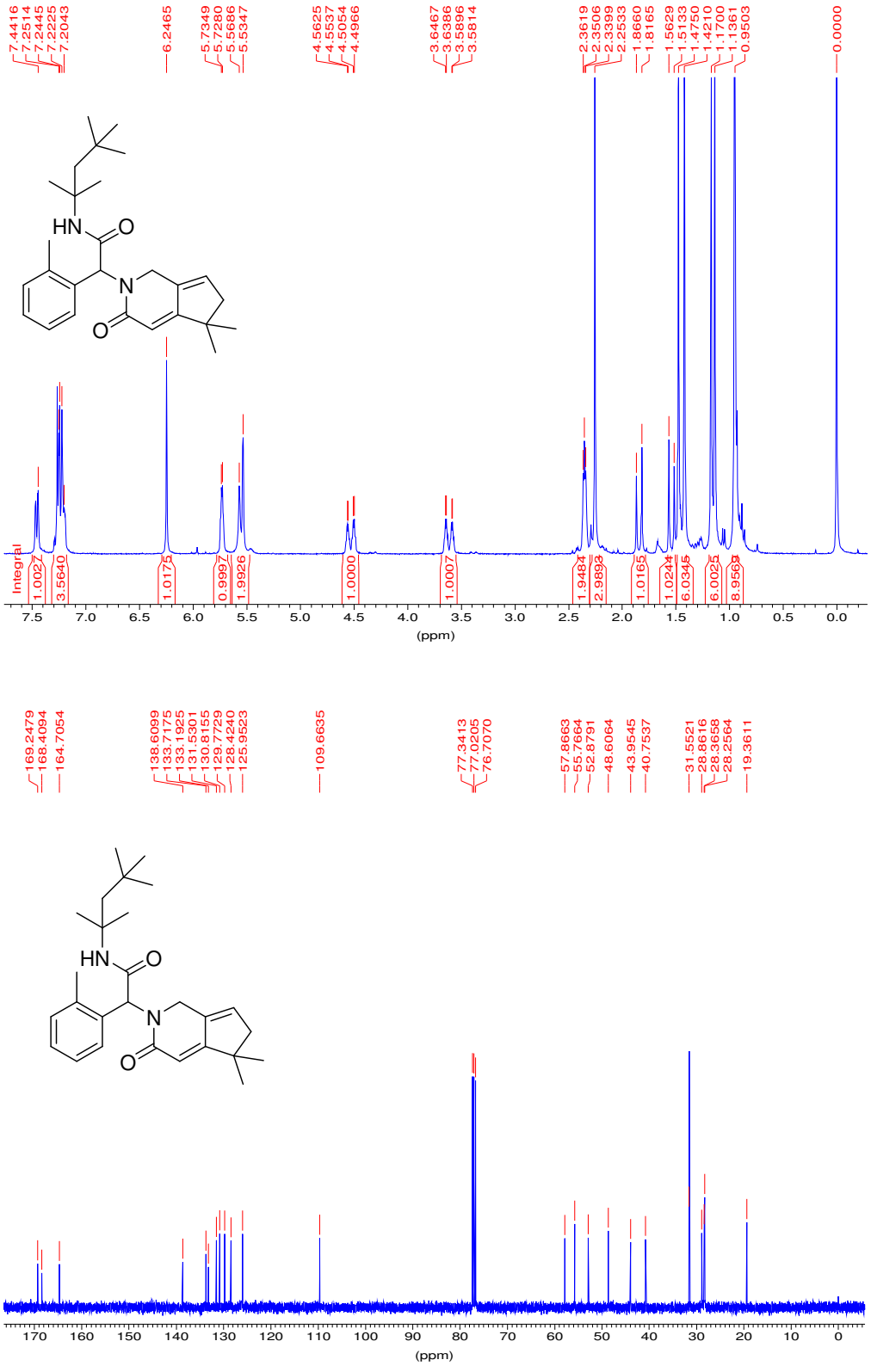


^{1}H and ^{13}C NMR spectra of compound **6d** (300 MHz, $CDCl_3$).

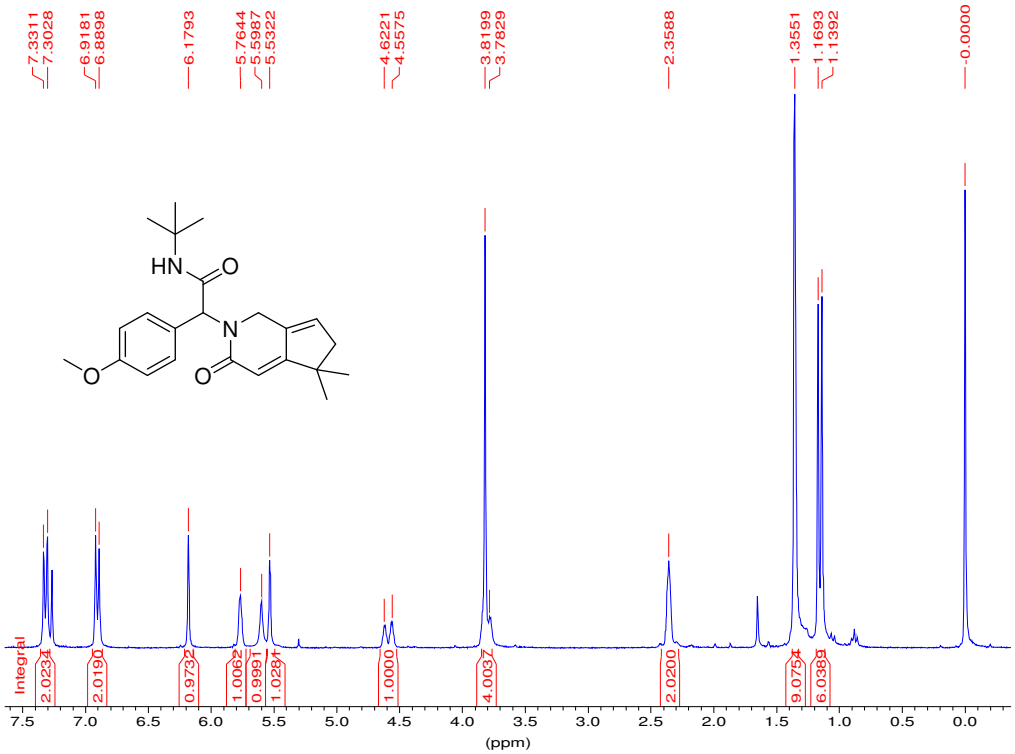


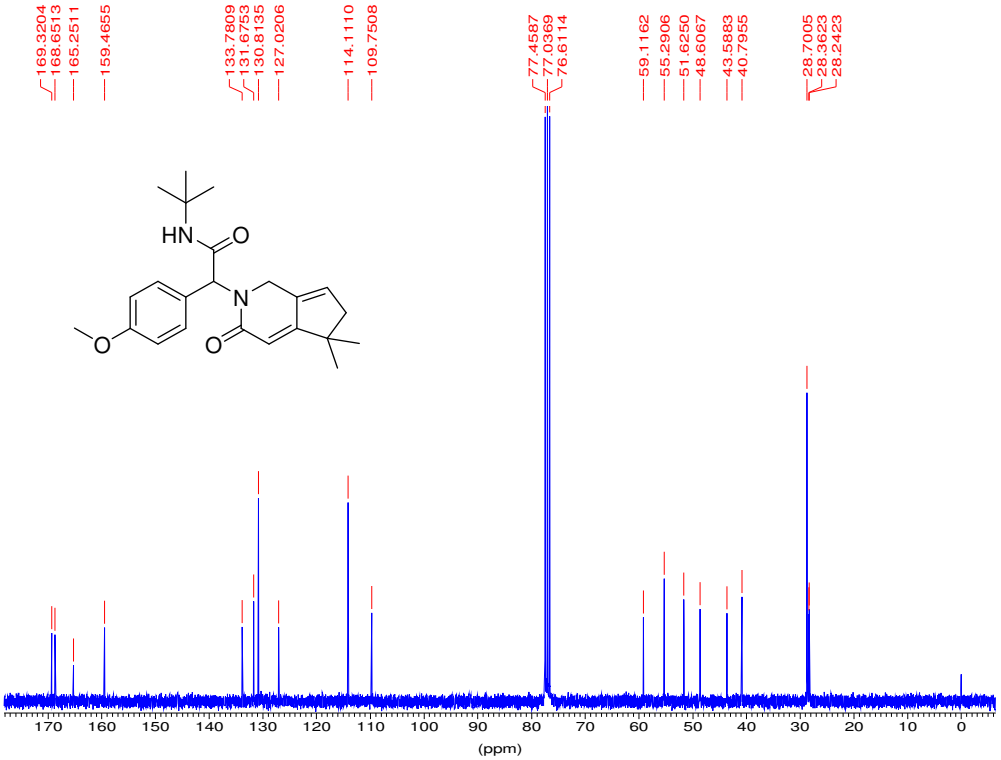


^{1}H and ^{13}C NMR spectra of compound **6e** (300 MHz, $CDCl_3$).

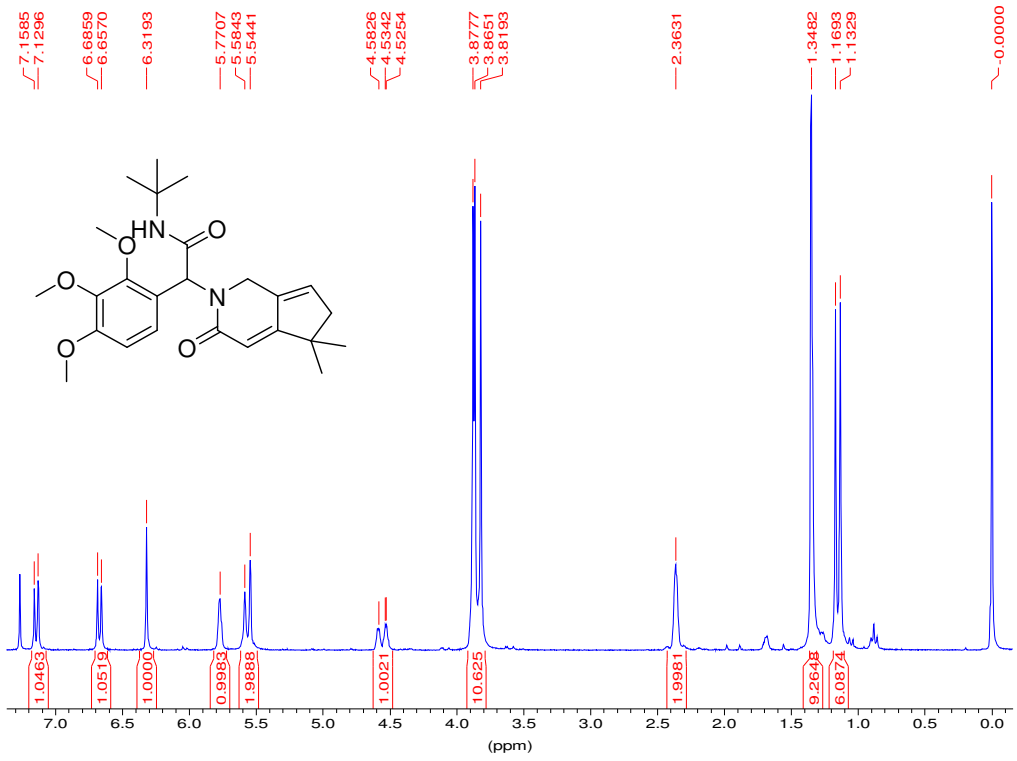


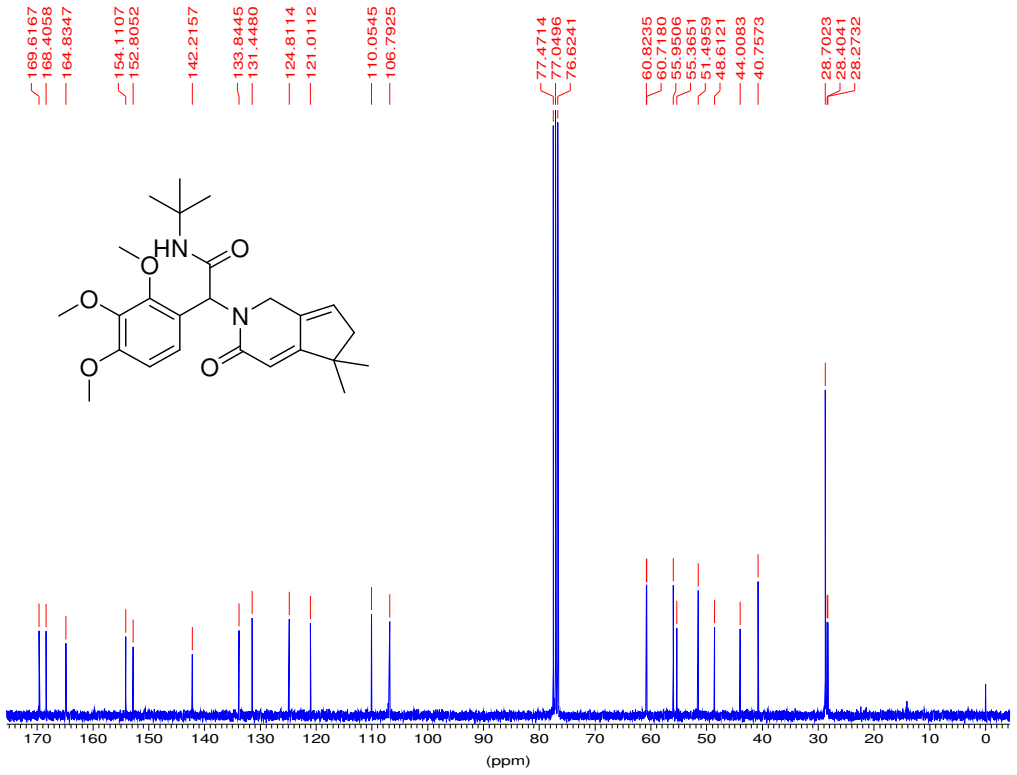
^{1}H and ^{13}C NMR spectra of compound **6f** (300 MHz, $CDCl_3$).



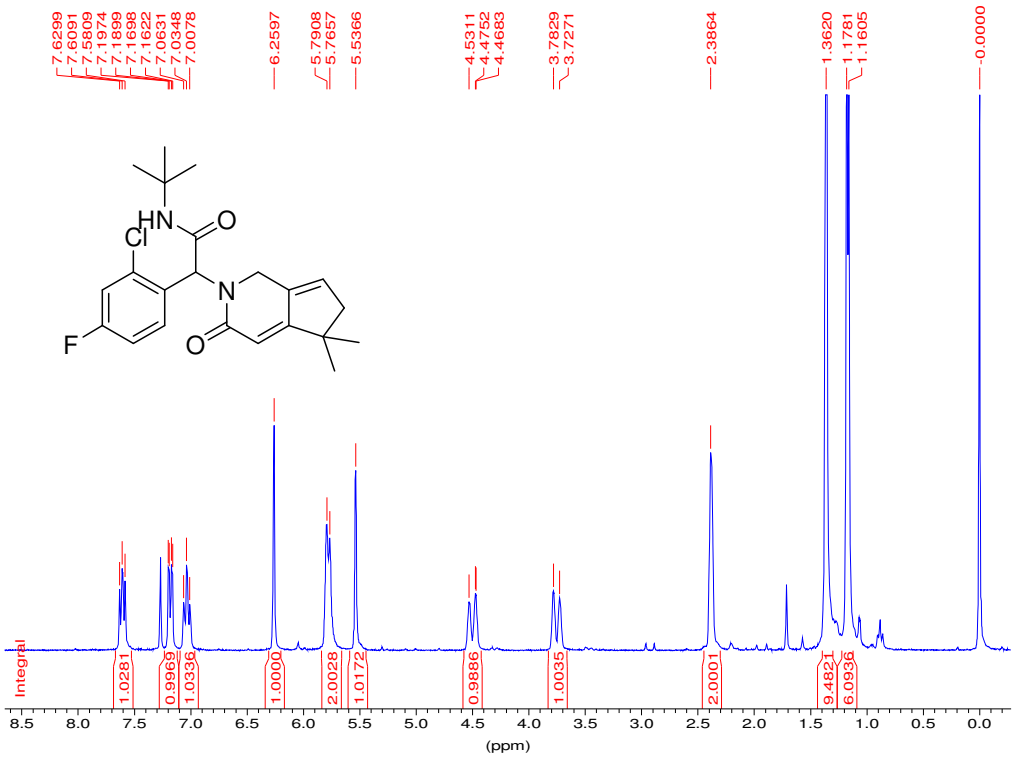


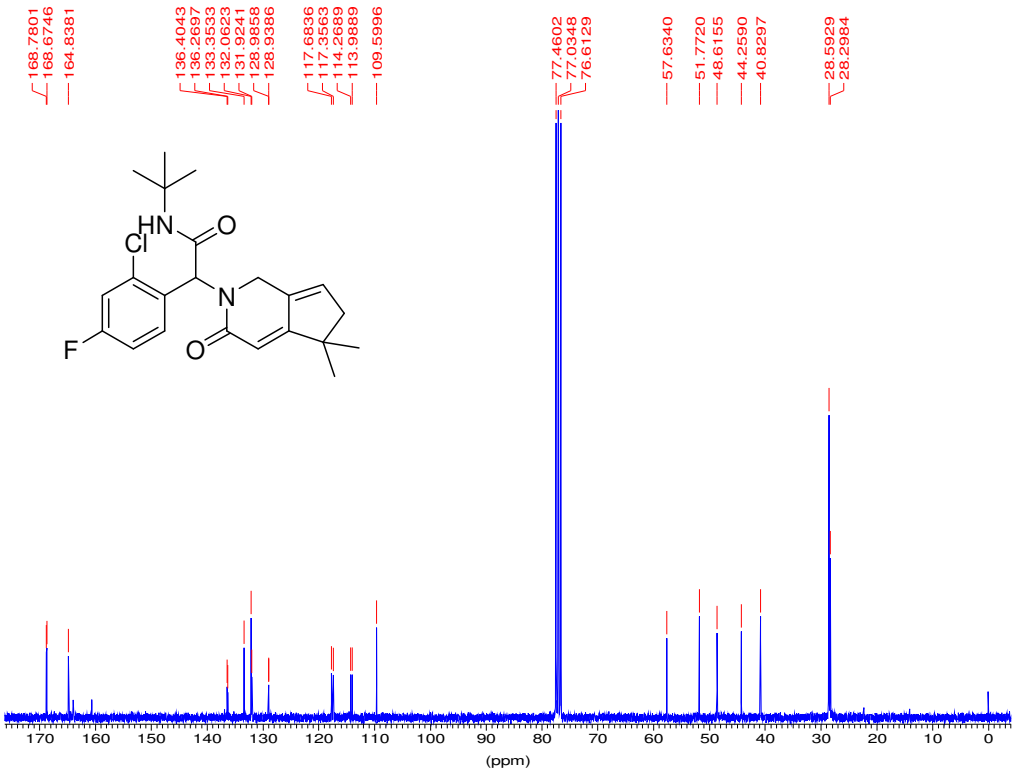
^{1}H and ^{13}C NMR spectra of compound **6g** (300 MHz, $CDCl_3$).



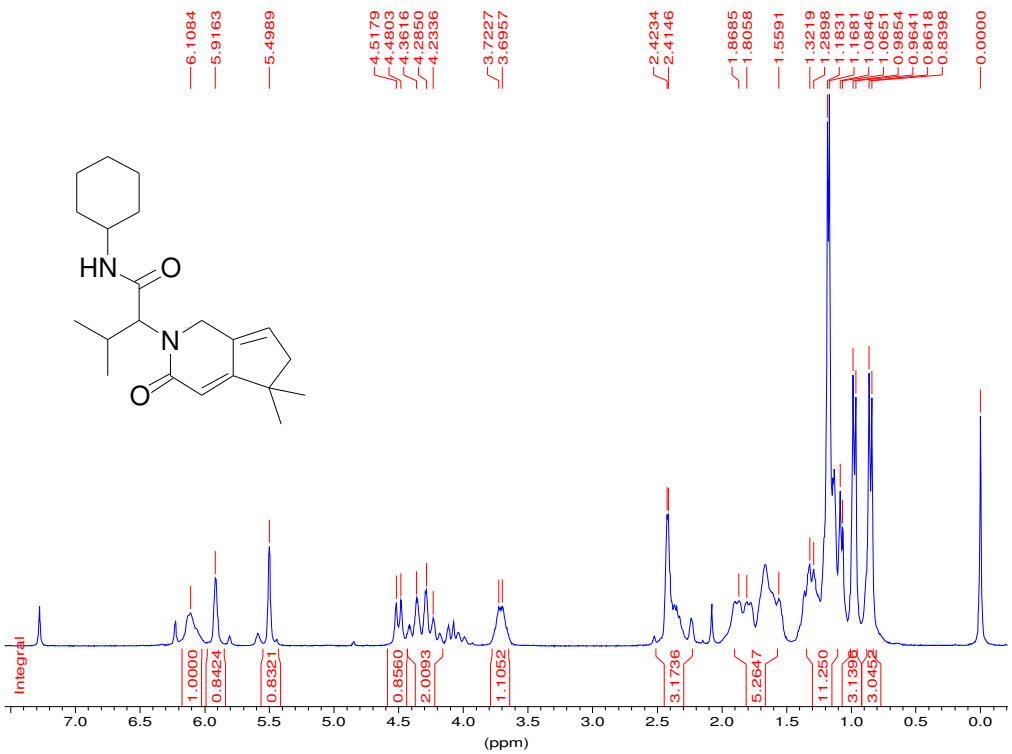


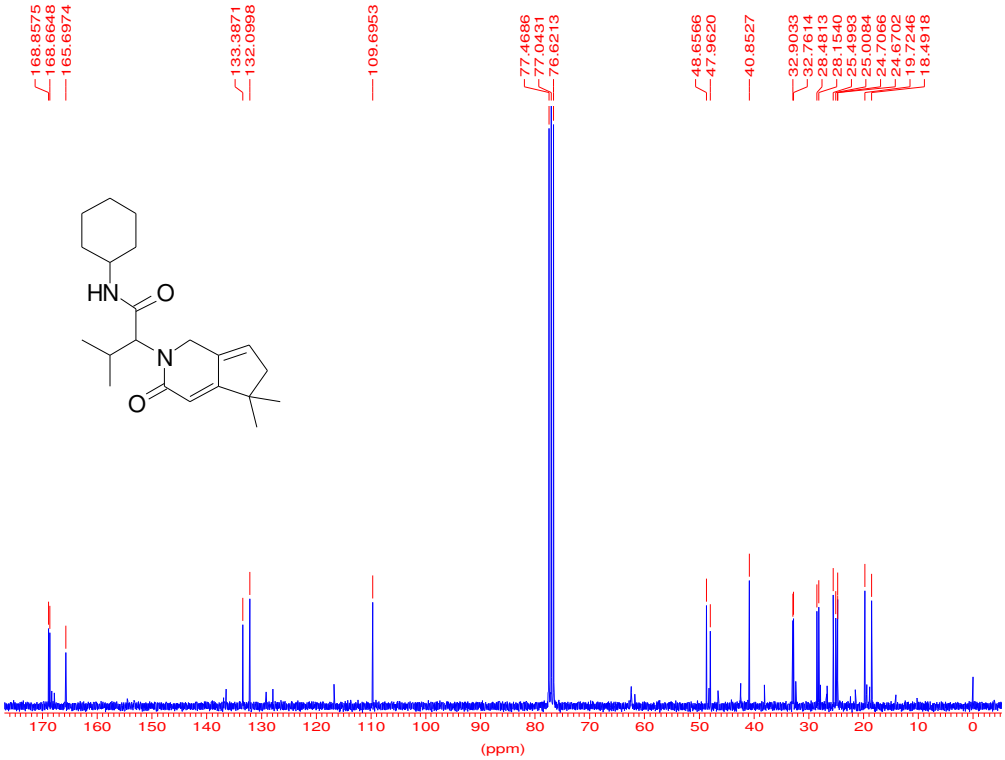
^{1}H and ^{13}C NMR spectra of compound **6h** (300 MHz, $CDCl_3$).



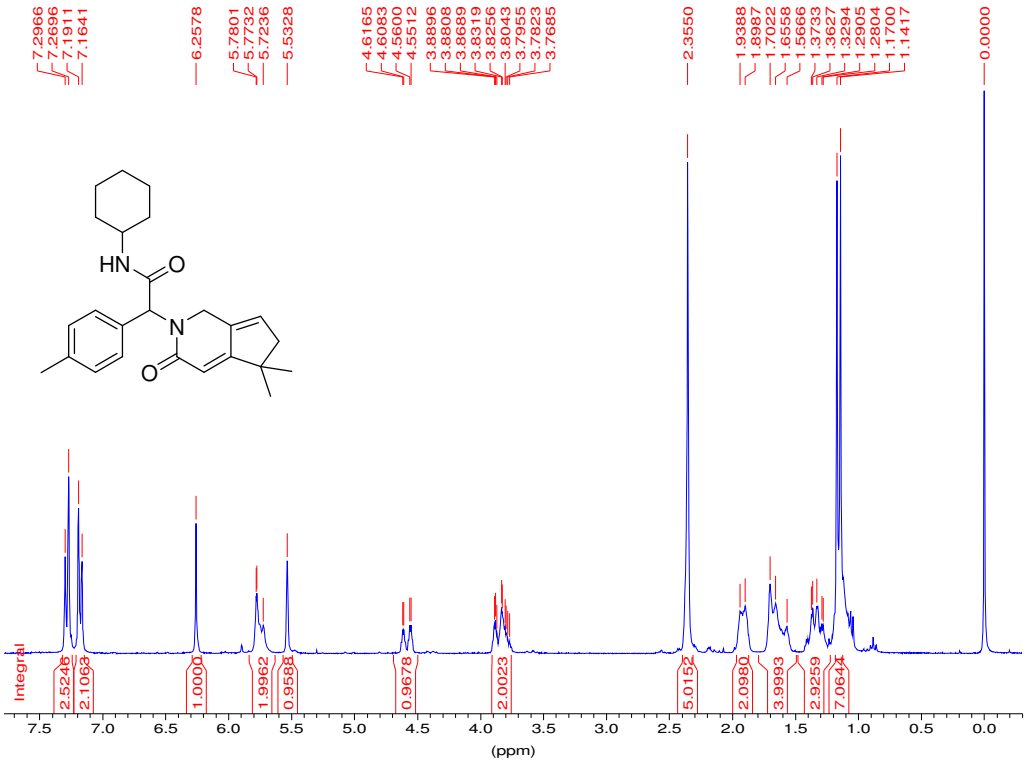


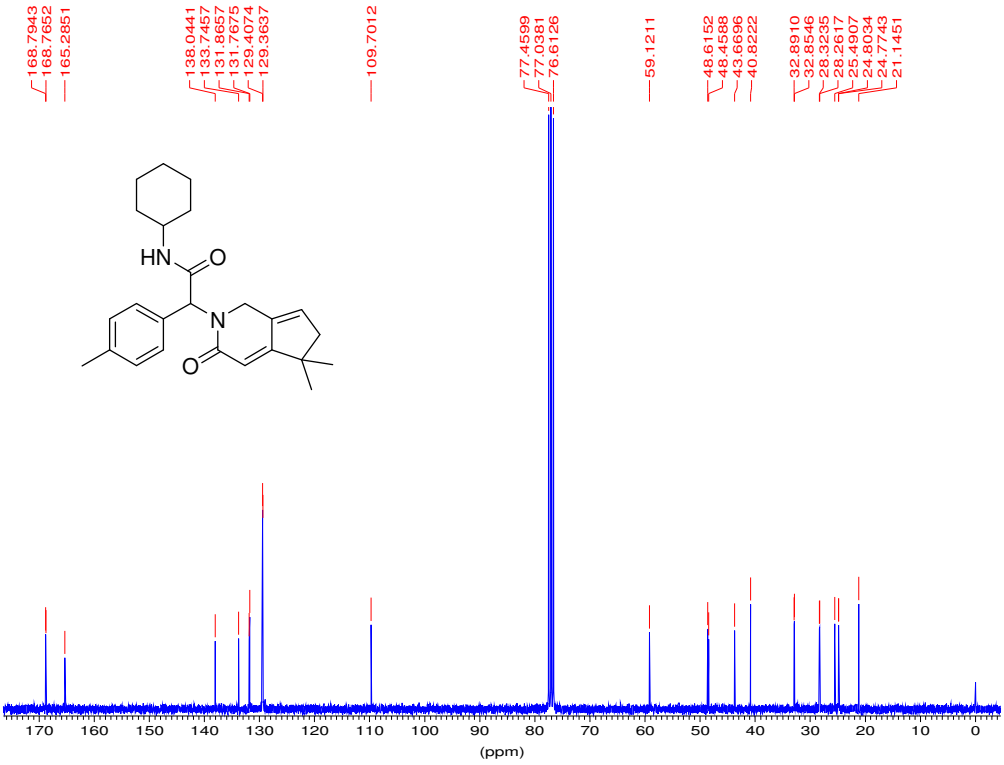
^{1}H and ^{13}C NMR spectra of compound **6i** (300 MHz, $CDCl_3$).



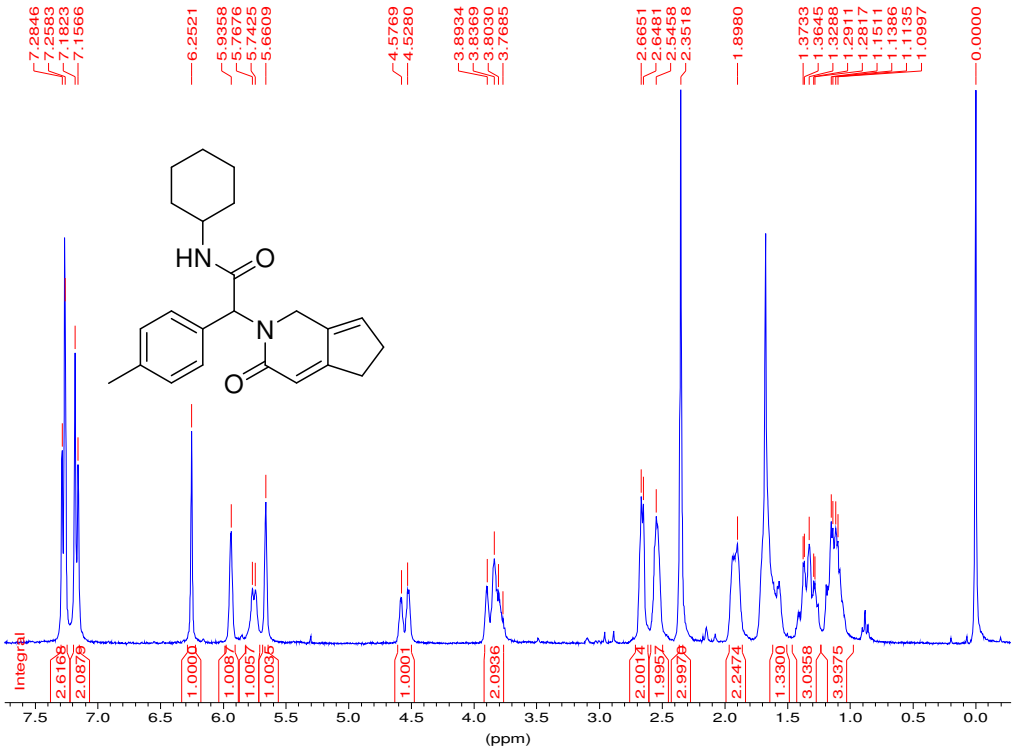


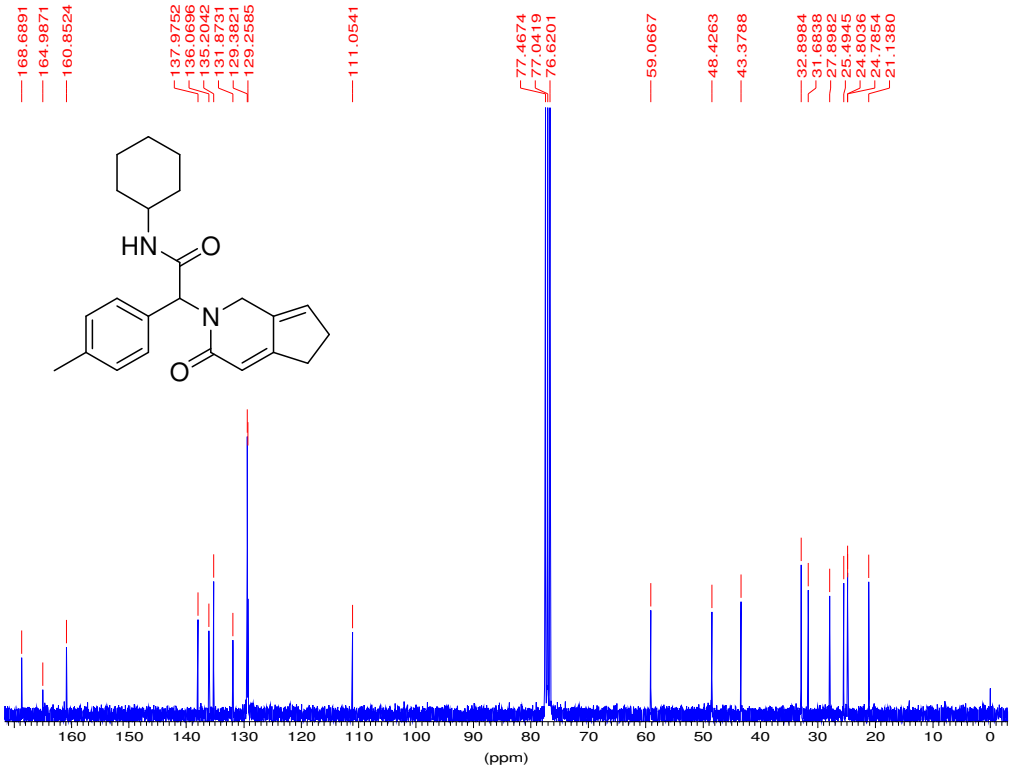
^{1}H and ^{13}C NMR spectra of compound **6j** (300 MHz, $CDCl_3$).



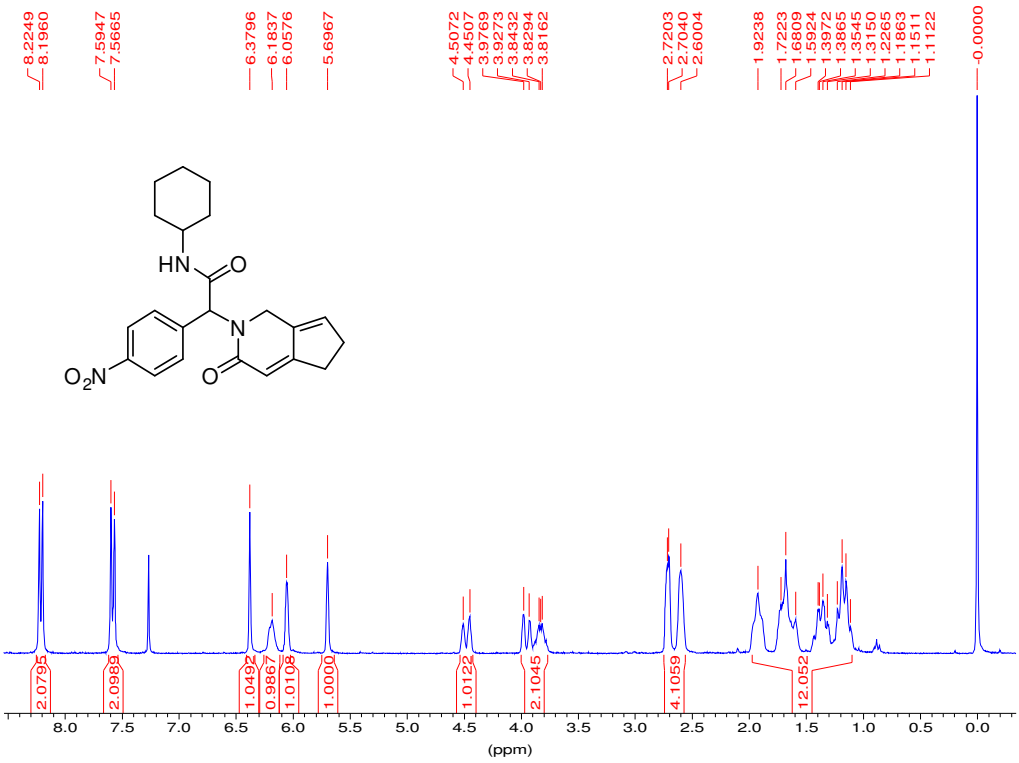


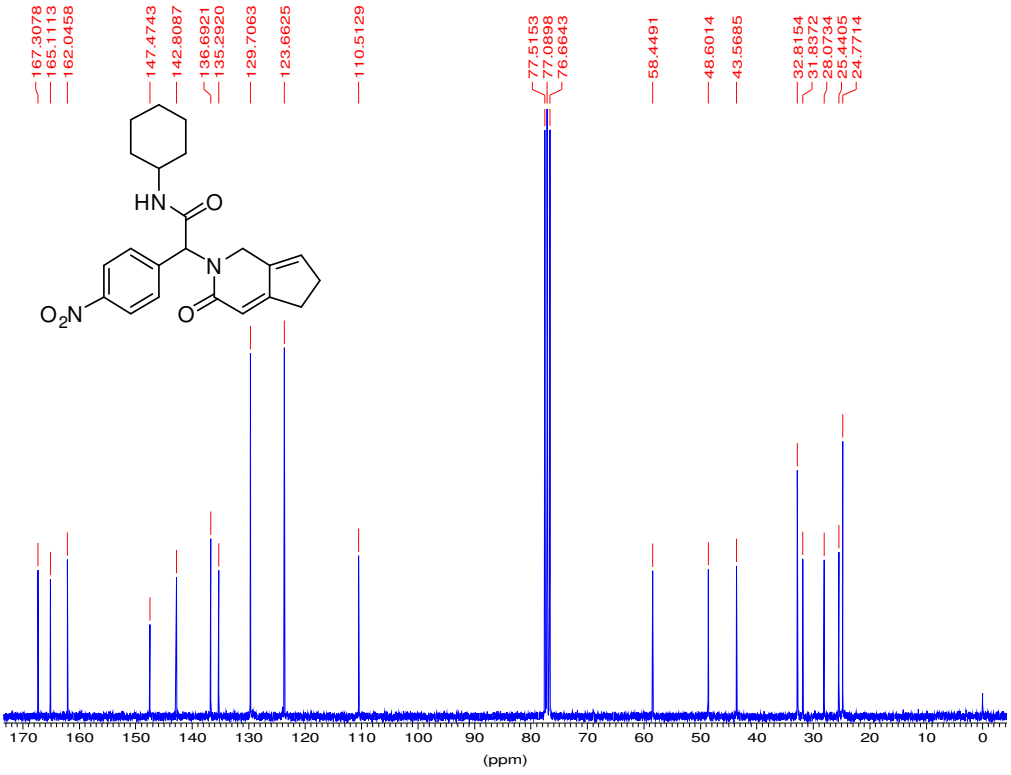
^{1}H and ^{13}C NMR spectra of compound **6k** (300 MHz, $CDCl_3$).



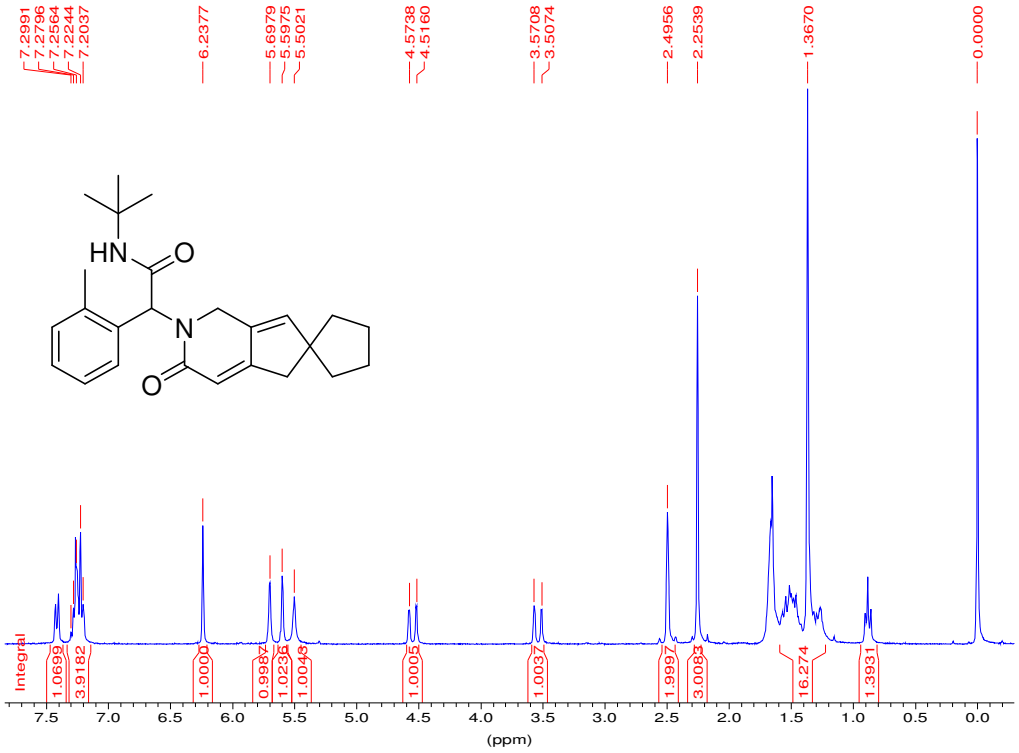


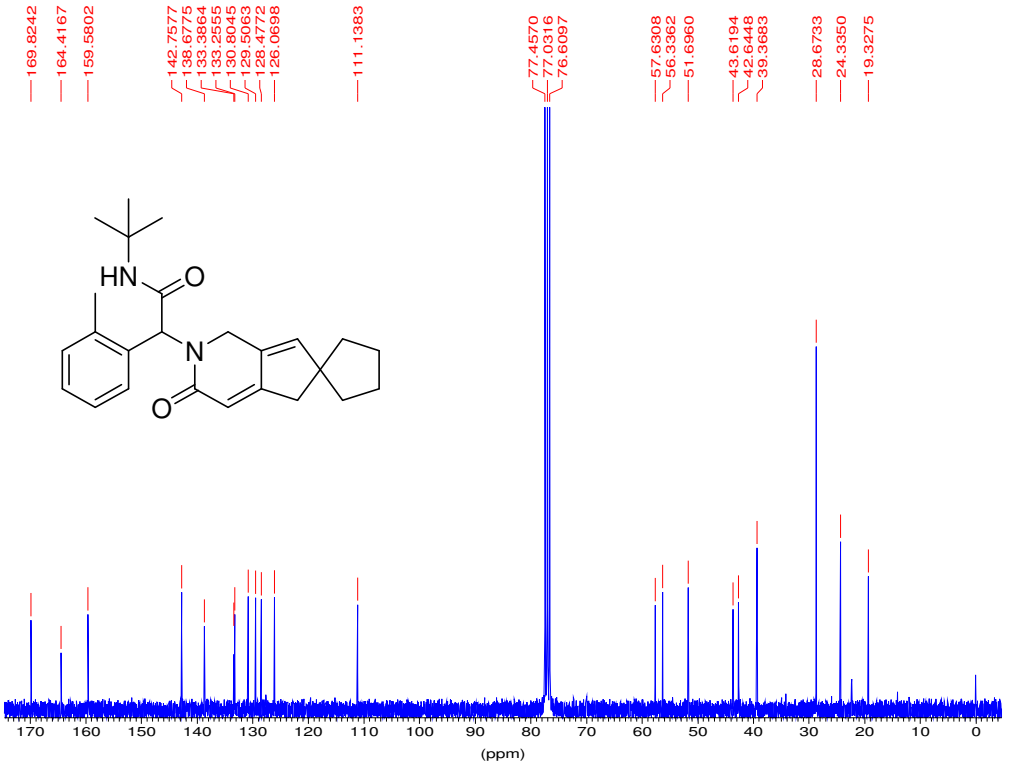
^{1}H and ^{13}C NMR spectra of compound **6l** (300 MHz, $CDCl_3$).



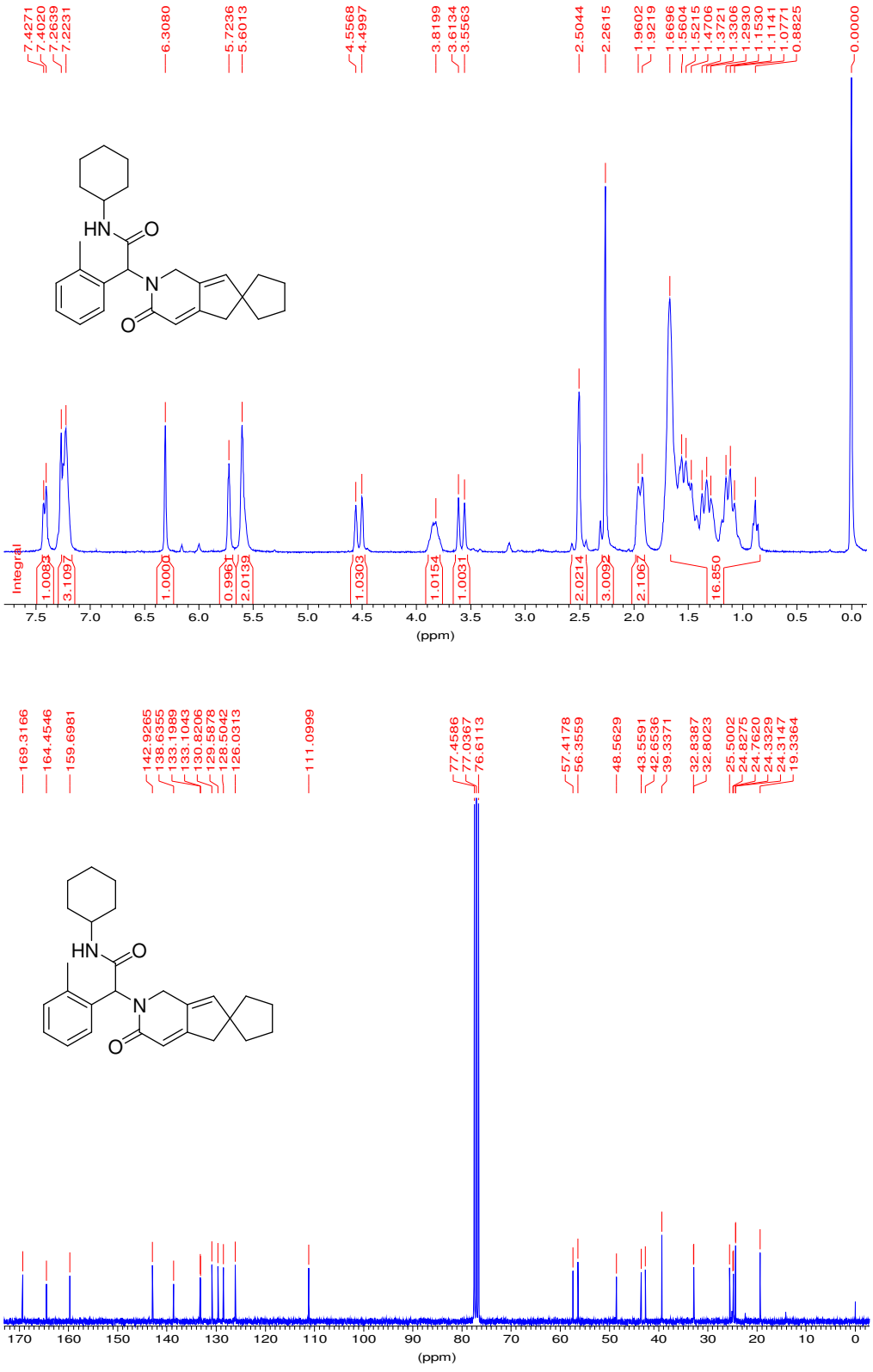


^{1}H and ^{13}C NMR spectra of compound **6m** (300 MHz, $CDCl_3$).

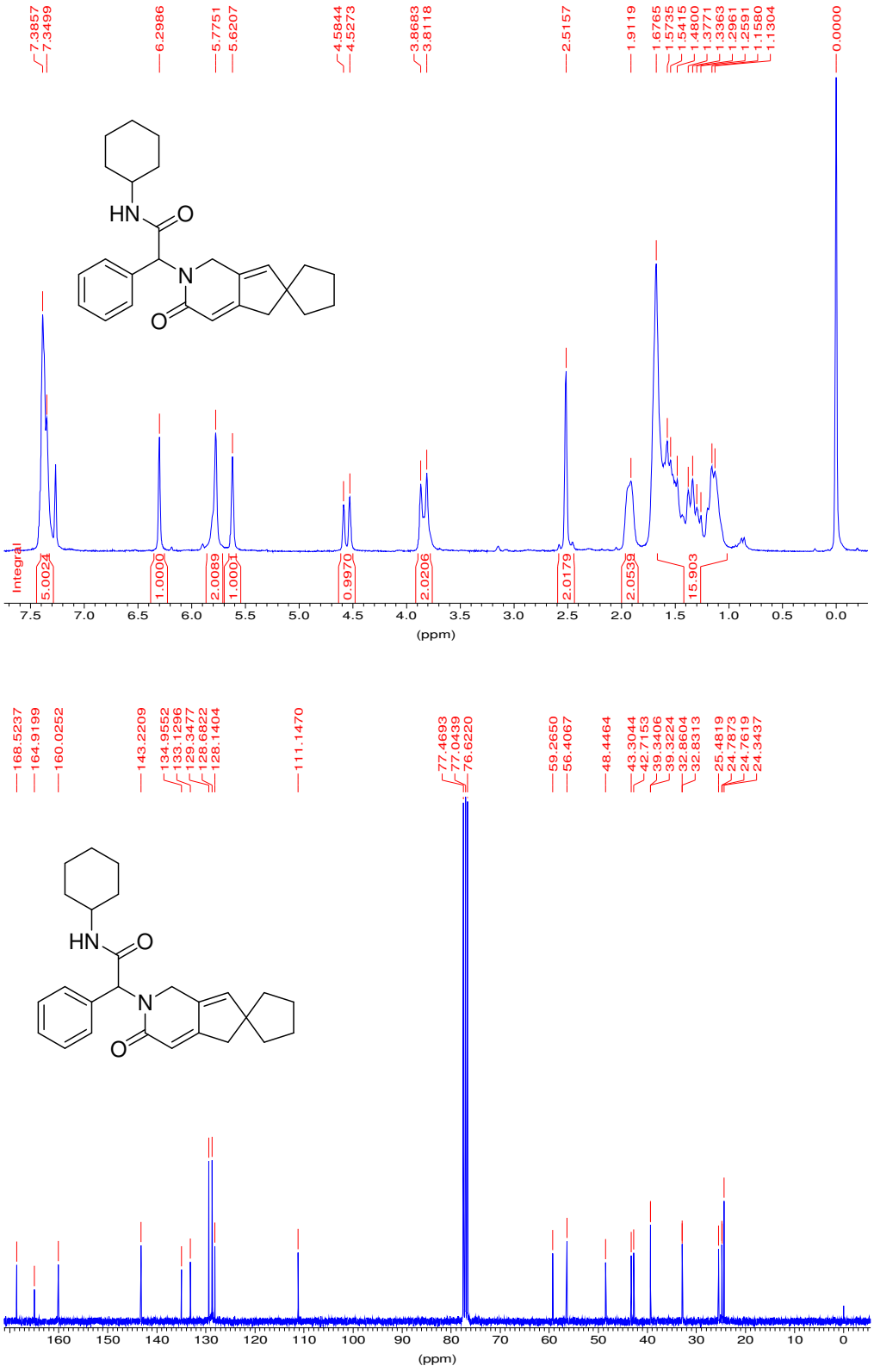




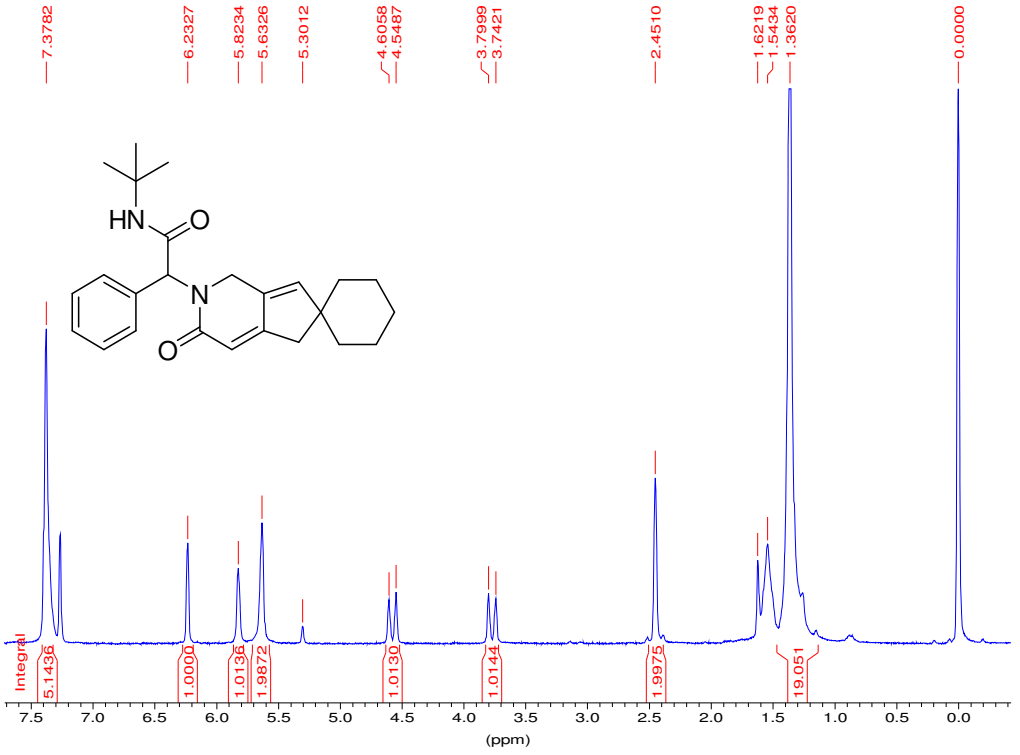
^{1}H and ^{13}C NMR spectra of compound **6n** (300 MHz, $CDCl_3$).

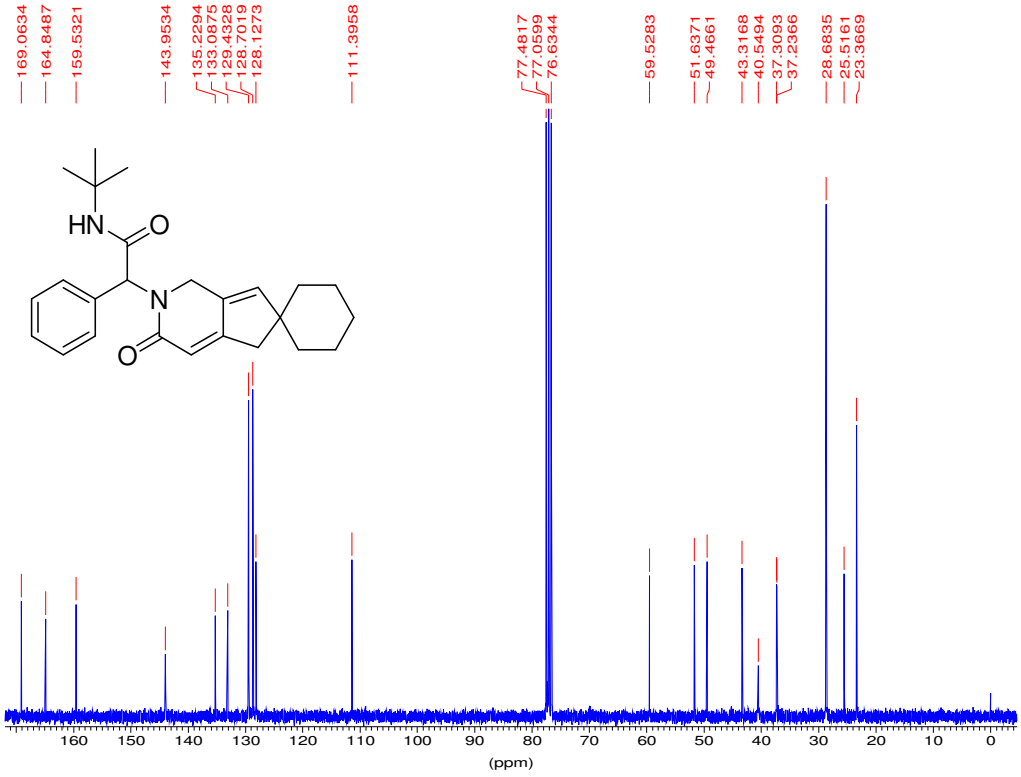


^{1}H and ^{13}C NMR spectra of compound **6o** (300 MHz, $CDCl_3$).

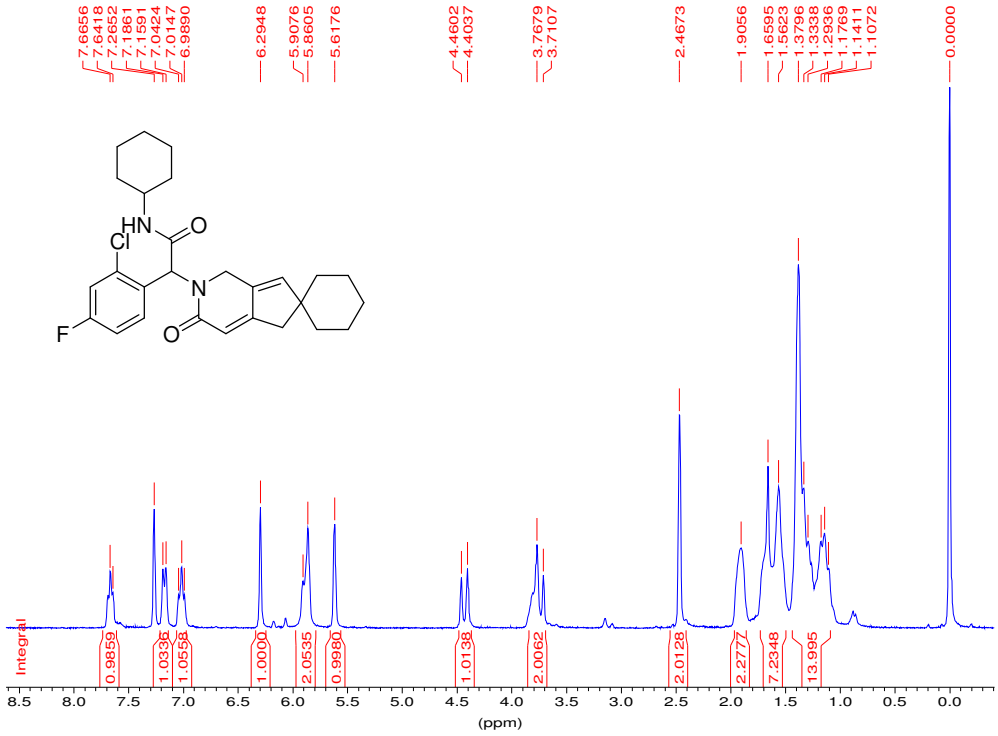


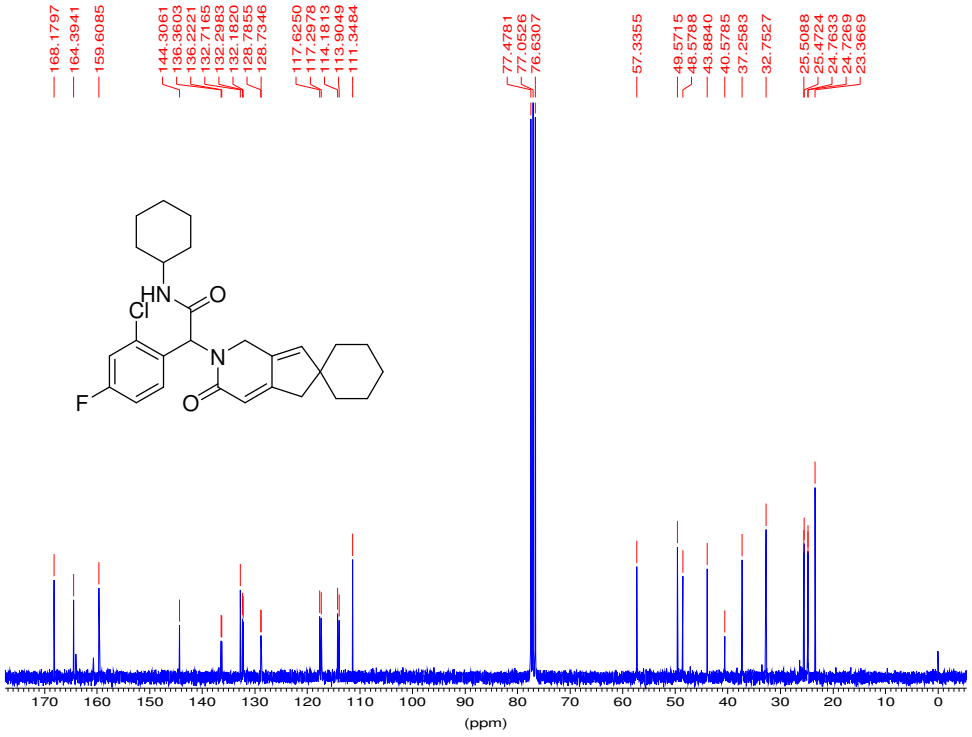
^{1}H and ^{13}C NMR spectra of compound **6p** (300 MHz, $CDCl_3$).



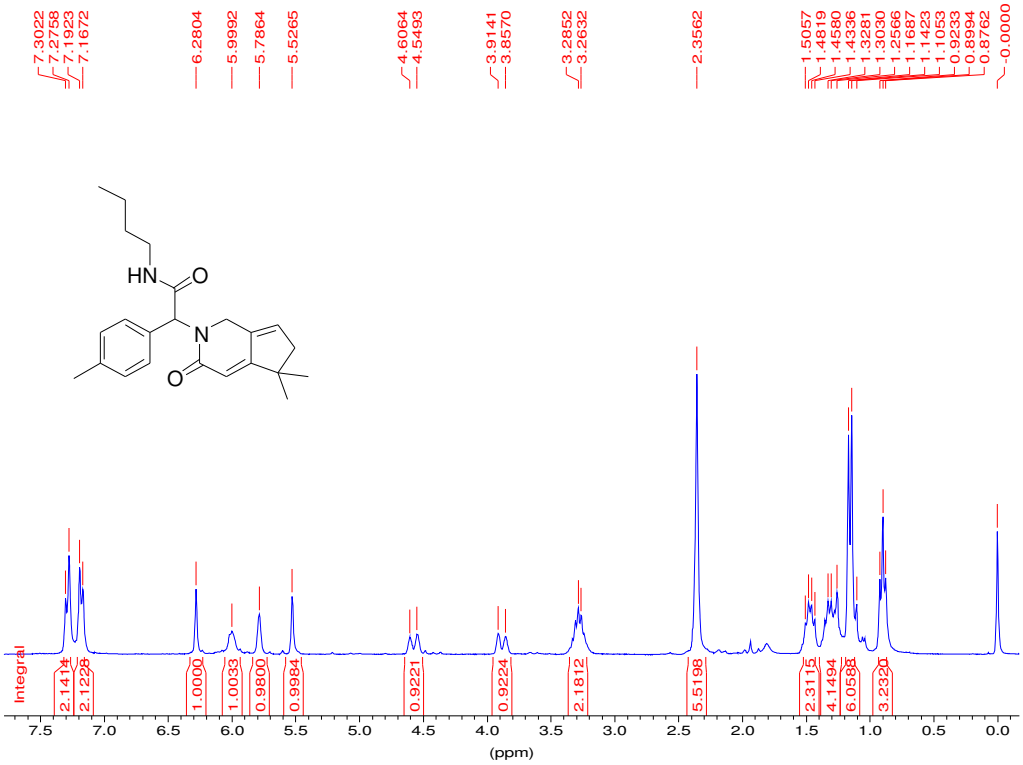


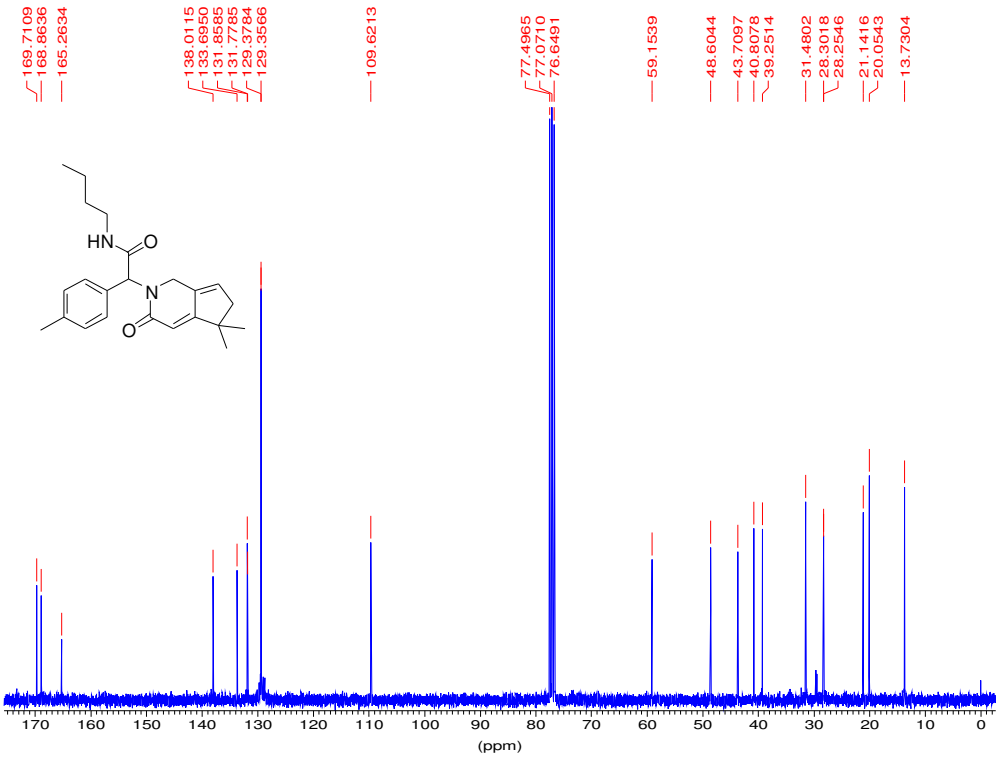
^{1}H and ^{13}C NMR spectra of compound **6q** (300 MHz, $CDCl_3$).



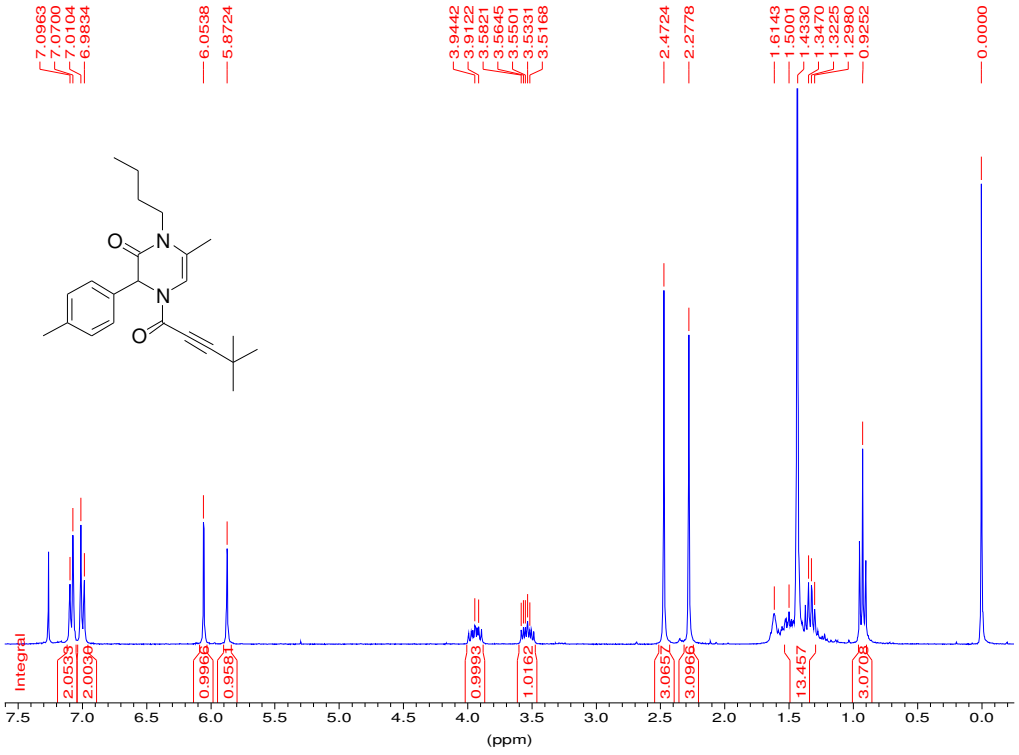


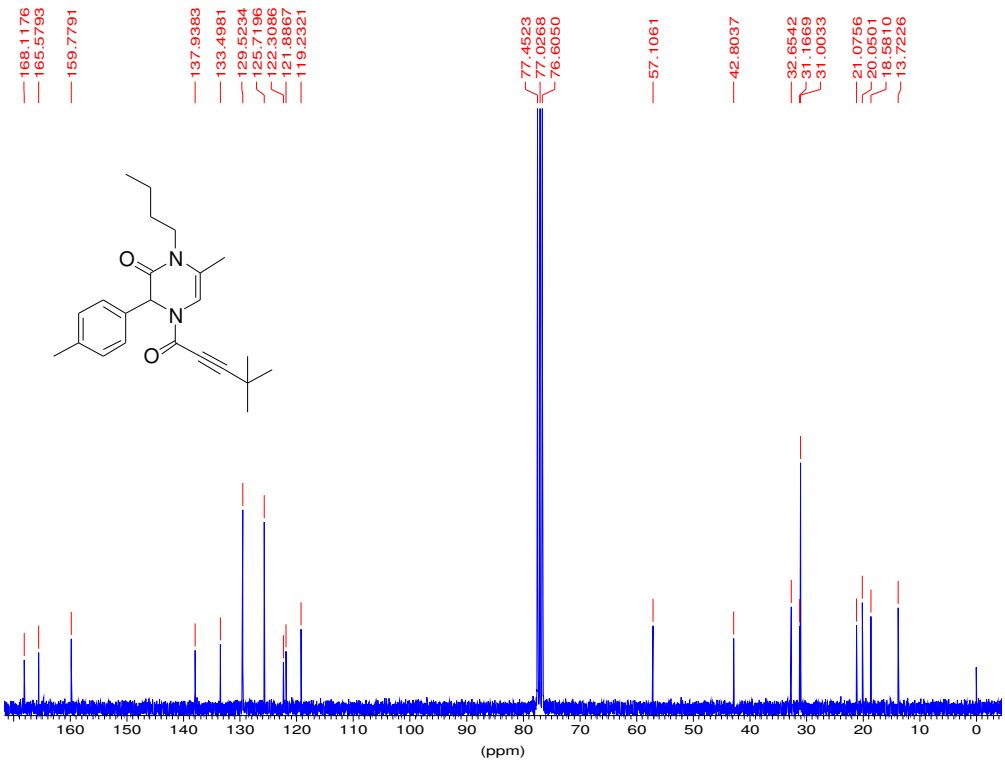
^{1}H and ^{13}C NMR spectra of compound **6r** (300 MHz, $CDCl_3$).





^{1}H and ^{13}C NMR spectra of compound **7a** (300 MHz, $CDCl_3$).





^{1}H and ^{13}C NMR spectra of compound **7b** (300 MHz, $CDCl_3$).