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SUPPORTING INFORMATION

Concise route to indoloazocines via a sequential Ugi / gold-catalyzed intramolecular hydroarylation

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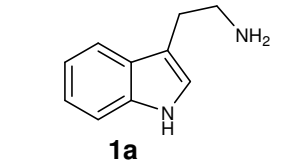
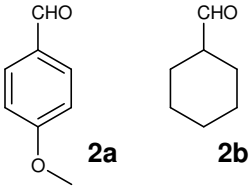
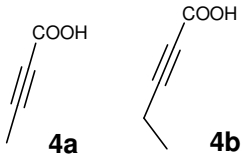
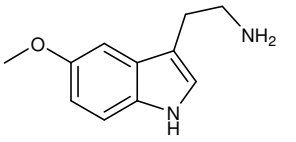
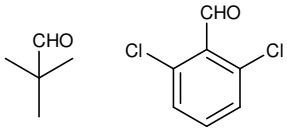
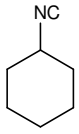
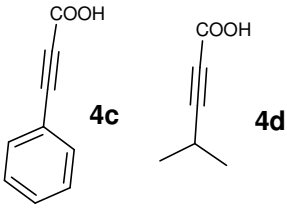
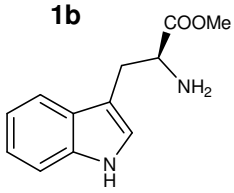
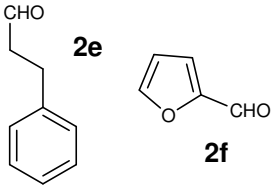
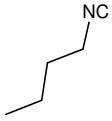
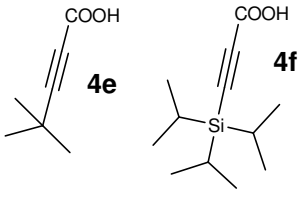
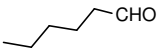
General Experimental Methods

NMR spectra were recorded on a 300 MHz instrument using $CDCl_3$ and DMSO d_6 as solvent unless and otherwise stated. The ^{1}H and ^{13}C chemical shifts are reported in parts per million relative to tetramethylsilane as an internal standard. For the Mass spectrometry, ion source temperature was 150-250 °C, as required. High-resolution EI-mass spectra were performed with a resolution of 10,000. For chromatography, analytical TLC plates and 70-230 mesh silica gel were used. All the solvents and chemicals were purchased and used as available. Optical rotations were measured using a PROPOL ® Automatic Process Polarimeter.

Table 1. Starting materials

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

General procedure for synthesis of Ugi products **5a-p**

To a solution of tryptamine **1a-b** (100mg, 1 equiv) in methanol (3 mL) were added successively Na_2SO_4 (0.3g), aldehyde **2a-g** (1 equiv), isonitrile **3a-c** (1 equiv) and 2-alkynoic acid **4a-e** (1 equiv) in a screw capped vial equipped with a magnetic stir bar.

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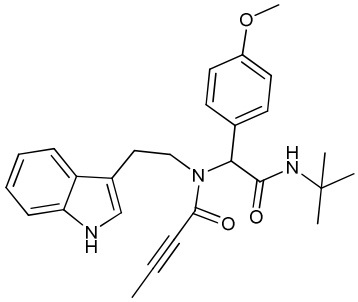
The reaction mixture was stirred at room temperature for 20-24h in closed vial. After completion of the reaction, the mixture was diluted with EtOAc (100 mL) and was extracted with water (50 mL). Organic layer was washed with brine (50 mL), dried over magnesium sulfate and evaporated under reduced pressure to obtained residue which was subjected to silica gel column chromatography (80 % EtOAc in Heptane) to afford the desired product **5a-p** as white solid.

Ugi products appear as mixture of two rotamers, so ^{1}H and ^{13}C NMR spectra are not very characteristic. Only representative data for one compound are given.



N-(2-(1*H*-indol-3-yl)ethyl)-*N*-(2-(*tert*-butylamino)-1-(4-methoxyphenyl)-2-oxoethyl)but-2-ynamide (**5a**)

White solid, Yield 82% (mixture of rotamers ~ 3/2).

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.7 (bs, 0.6H), 10.6 (bs, 0.4H), 7.90 (s, 0.4H), 7.77 (s, 0.6H), 7.37-7.23 (m, 3H), 7.13-6.95 (m, 4H), 6.94-6.79 (m, 2H), 6.02 (s, 0.4H), 5.93 (s, 0.6H), 3.79 (s, 3H), 3.66-3.44 (m, 2H), 2.85-2.71 (m, 1H), 2.24-2.14 (m, 1H), 2.06 (s, 1.2H), 2.01 (s, 1.8H), 1.28 (s, 3.1H), 1.24 (s, 5.9H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 169.1, 159.7, 154.7, 136.5, 131.2, 130.9, 128.4, 127.3, 123.0, 121.3, 121.2, 118.6, 118.4, 118.3, 114.5, 111.9, 111.8, 111.7, 111.4, 88.8, 74.5, 60.1, 55.7, 50.8 (x 2), 28.8, 26.5, 4.1, 3.7.

HRMS calculated for $C_{27}H_{31}N_3O_3$ 445.2365, found 445.2347.

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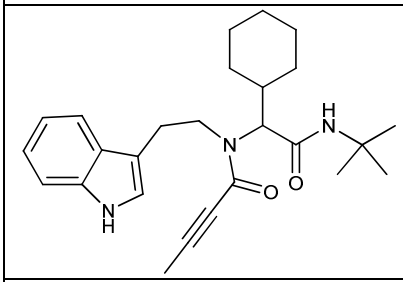
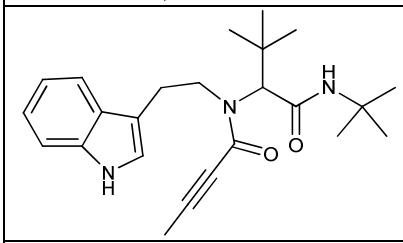
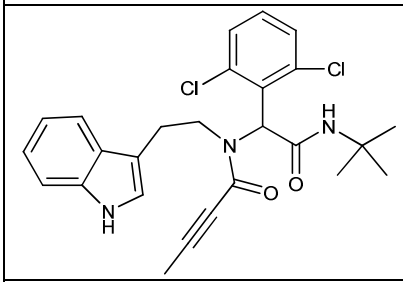
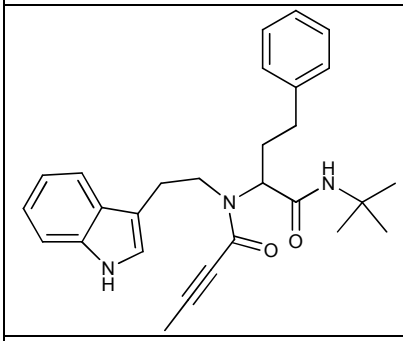
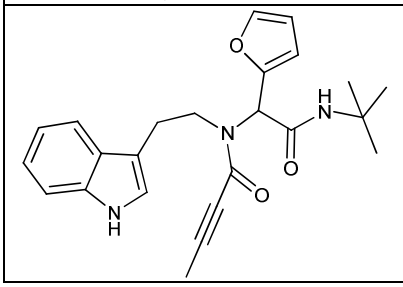
Table 2. Ugi products **5b-p**

Structure	Data
	*N*-(2-(1*H*-indol-3-yl)ethyl)-*N*-(2-(*tert*-butylamino)-1-cyclohexyl-2-oxoethyl)but-2-ynamide **(5b)** White solid, Yield 95% HRMS calculated for $C_{27}H_{31}N_3O_3$ 445.2365 found 445.2347
	*N*-(2-(1*H*-indol-3-yl)ethyl)-*N*-(1-(*tert*-butylamino)-3,3-dimethyl-1-oxobutan-2-yl)but-2-ynamide (**5c**) White solid, Yield 89%, HRMS calculated for $C_{26}H_{35}N_3O_2$ 421.2729 found 421.2754
	*N*-(2-(1*H*-indol-3-yl)ethyl)-*N*-(2-(*tert*-butylamino)-1-(2,6-dichlorophenyl)-2-oxoethyl)but-2-ynamide (**5d**) White solid, Yield 76%, HRMS calculated for $C_{26}H_{27}Cl_2N_3O_2$ 483.1480 found 483.1479
	*N*-(2-(1*H*-indol-3-yl)ethyl)-*N*-(1-(*tert*-butylamino)-1-oxo-4-phenylbutan-2-yl)but-2-ynamide (**5e**) White solid, Yield 75%, HRMS calculated for $C_{28}H_{33}N_3O_2$ 443.2573 found 443.2551
	*N*-(2-(1*H*-indol-3-yl)ethyl)-*N*-(2-(*tert*-butylamino)-1-(furan-2-yl)-2-oxoethyl)but-2-ynamide (**5f**) White solid, Yield 43%, HRMS calculated for $C_{24}H_{27}N_3O_3$ 405.2052 found 405.2031

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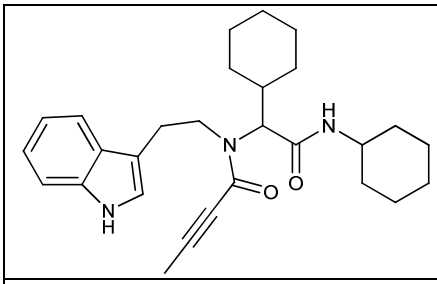
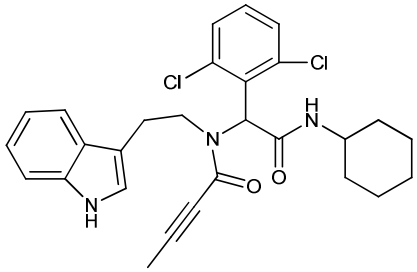
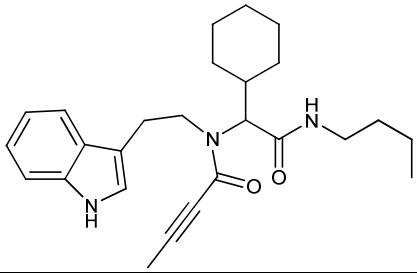
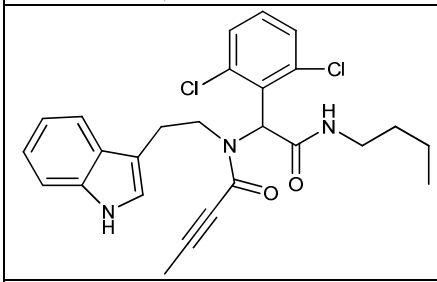
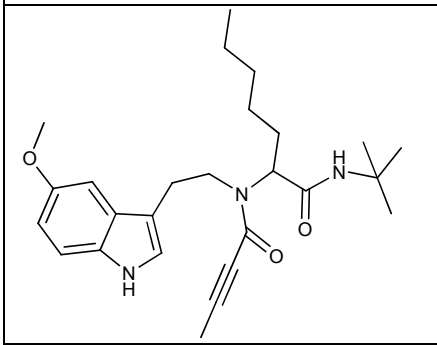
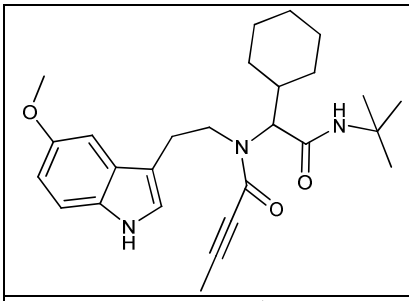
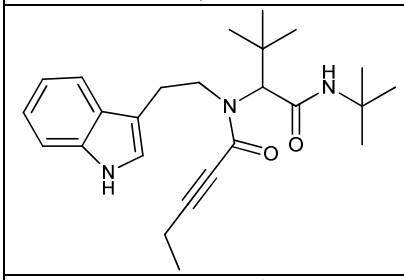
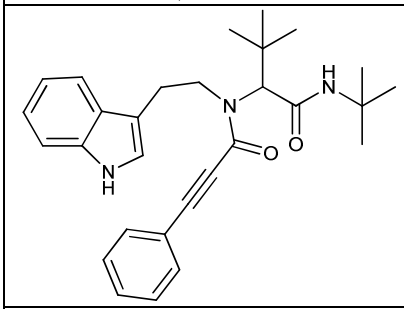
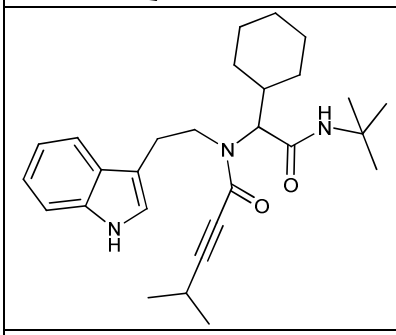
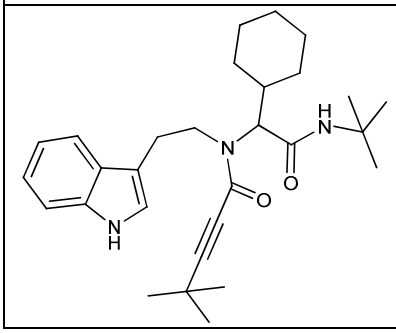
	*N*-(2-(1*H*-indol-3-yl)ethyl)-*N*-(1-cyclohexyl-2-(cyclohexylamino)-2-oxoethyl)but-2-ynamide (**5g)** White solid, Yield 84%, HRMS calculated for $C_{28}H_{37}N_3O_2$ 447.2886 found 447.2914
	*N*-(2-(1*H*-indol-3-yl)ethyl)-*N*-(2-(cyclohexylamino)-1-(2,6-dichlorophenyl)-2-oxoethyl)but-2-ynamide (**5h)** White solid, Yield 84%, HRMS calculated for $C_{28}H_{29}Cl_2N_3O_2$ 509.1637 found 509.1600
	*N*-(2-(1*H*-indol-3-yl)ethyl)-*N*-(2-(butylamino)-1-cyclohexyl-2-oxoethyl)but-2-ynamide (**5i)** White solid, Yield 88%, HRMS calculated for $C_{26}H_{35}N_3O_2$ 421.2729 found 421.2758
	*N*-(2-(1*H*-indol-3-yl)ethyl)-*N*-(2-(butylamino)-1-(2,6-dichlorophenyl)-2-oxoethyl)but-2-ynamide (**5j)** White solid, Yield 91%, HRMS calculated for $C_{26}H_{27}Cl_2N_3O_2$ 483.148 found 483.1451
	*N*-*tert*-butyl-2-(*N*-(2-(5-methoxy-1*H*-indol-3-yl)ethyl)but-2-ynamido)heptanamide (**5k**) White solid, Yield 34%, HRMS calculated for $C_{26}H_{37}N_3O_3$ 439.2835 found 439.2827

	*N*-(2-(*tert*-butylamino)-1-cyclohexyl-2-oxoethyl)-*N*-(2-(5-methoxy-1*H*-indol-3-yl)ethyl)but-2-ynamide (**5l)** White solid, Yield 48%, HRMS calculated for $C_{27}H_{37}N_3O_3$ 451.2835 found 451.2826
	*N*-(2-(1*H*-indol-3-yl)ethyl)-*N*-(1-(*tert*-butylamino)-3,3-dimethyl-1-oxobutan-2-yl)pent-2-ynamide (**5m)** White solid, Yield 82%, HRMS calculated for $C_{25}H_{35}N_3O_2$ 409.2729 found 409.2729
	2-(*N*-(2-(1*H*-indol-3-yl)ethyl)-3-phenylpropiolamido)-*N*-*tert*-butyl-3,3-dimethylbutanamide (**5n**) White solid, Yield 75%, HRMS calculated for $C_{29}H_{35}N_3O_2$ 457.2729 found 457.2725
	*N*-(2-(1*H*-indol-3-yl)ethyl)-*N*-(2-(*tert*-butylamino)-1-cyclohexyl-2-oxoethyl)-4-methylpent-2-ynamide (**5o**) White solid, Yield 86%, HRMS calculated for $C_{28}H_{39}N_3O_2$ 449.3042 found 449.3005
	*N*-(2-(1*H*-indol-3-yl)ethyl)-*N*-(2-(*tert*-butylamino)-1-cyclohexyl-2-oxoethyl)-4,4-dimethylpent-2-ynamide (**5p**) White solid, Yield 84%, HRMS calculated for $C_{29}H_{41}N_3O_2$ 463.3199 found 463.3212

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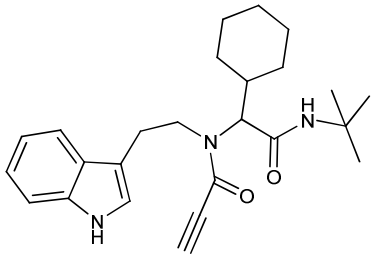
General procedure for synthesis of **5q**

To a solution of tryptamine **1a** (200mg, 1 equiv) in methanol (3 mL) were added successively Na_2SO_4 (0.5g), cyclohexylcarboxaldehyde **2b** (1 equiv), *tert*-butylisonitrile **3a** (1 equiv) and 3-(triisopropylsilyl)propiolic acid **4f** (1 equiv) in a screw capped vial equipped with a magnetic stir bar. The reaction mixture was stirred at room temperature for 24h 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 obtained residue which was used directly for the deprotection step without purification. Residue was dissolved in THF (3 mL) and solution of tetrabutylammonium fluoride, 1M in THF (560µL, 1 equiv) was added at 0 ^{o}C. Reaction was completed in 30 min. Reaction mixture was partitioned between diethyl (100 mL) ether and water (50 mL). Organic layer was separated, washed with brine, dried over magnesium sulfate and evaporated under reduced pressure to obtain residue. This residue was subjected to silica gel column chromatography (50 % EtOAc in Heptane) to afford the desired product **5q** as white solid in 92% yield.

Table 3. Ugi product **5q**

Structure	Data
	*N*-(2-(1*H*-indol-3-yl)ethyl)-*N*-(2-(*tert*-butylamino)-1-cyclohexyl-2-oxoethyl)propiolamide (**5q**) White solid, Yield 92%, HRMS calculated for $C_{25}H_{33}N_3O_2$ 407.2573 found 407.2569

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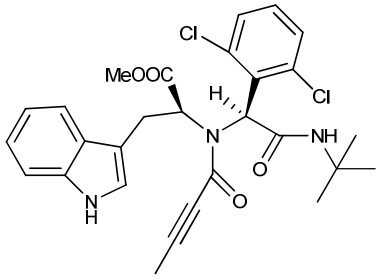
General procedure for synthesis of Ugi adducts **5r** & **5s**.

To a solution of L-tryptophan methylester **1c** (100mg, 1 equiv) in methanol (3 mL) were added successively Na_2SO_4 (0.3g), 2,6-dichlorobenzaldehyde **2d** (1 equiv), *tert*-butylisonitrile **3a** (1 equiv) and 2-butynoic acid **4a** (1 equiv) in a screw capped vial equipped with a magnetic stir bar. The reaction mixture was stirred at room temperature for 24h 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 obtained residue. The diastereoisomers formed during the reaction were separated by silica gel column chromatography (40-80 % EtOAc in Heptane) to afford pure diastereoisomers **5r** and **5s**. Isolated yield was 14% (**5r**) and 29% (**5s**) and also there were fractions were both of these were together so combined yield was 92%.



(*S*)-methyl 2-(*N*-((*S*)-2-(*tert*-butylamino)-1-(2,6-dichloro-phenyl)-2-oxoethyl)but-2-ynamido)-3-(1*H*-indol-3-yl)propanoate (**5r**)

White solid, Yield 14%, $[\alpha]_D = +7.23^o$ (c = 0.79, $CHCl_3$)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (bs, 1H), 7.78 (bs, 1H), 7.12 (d, J = 8.03 Hz 1H), 7.12-7.02 (m, 2H), 6.93-6.84 (m, 3H), 6.73 (t, J = 8.20 Hz, 1H), 6.59 (s, 1H), 6.53 (s, 1H), 4.30 (t, J = 6.55 Hz, 1H), 3.84 (s, 3H), 3.62 (dd, J = 5.96, 15.4 Hz, 1H), 3.03 (dd, J = 6.83, 15.5 Hz, 1H), 2.04 (s, 3H), 1.41 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 167.8, 155.8, 136.1, 130.6, 129.6, 129.2, 128.4, 126.8, 122.8, 121.5, 119.1, 118.0, 111.5, 110.8, 91.3, 72.8, 64.5, 59.7, 53.1, 51.6, 28.2, 25.2, 4.1.

HRMS calculated for $C_{28}H_{29}Cl_2N_3O_4$ 541.1535, found 541.1540.

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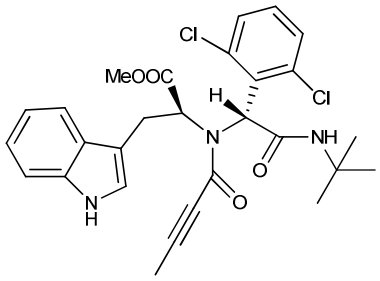

(*S*)-methyl 2-(*N*-((*R*)-2-(*tert*-butylamino)-1-(2,6-dichloro-phenyl)-2-oxoethyl)but-2-ynamido)-3-(1*H*-indol-3-yl)propanoate (**5s**)

White solid, Yield 29%, $[\alpha]_D = -40.7^o$ (*c* = 0.33, $CHCl_3$)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (bs, 1H), 7.78 (d, *J* = 7.92 Hz 1H), 7.37-7.27 (m, 3H), 7.25-7.08 (m, 4H), 6.66 (s, 1H), 5.65 (bs, 1H), 4.19 (t, *J* = 7.01 Hz, 1H), 3.86 (dd, *J* = 7.92, 14.6 Hz, 1H), 3.68 (dd, *J* = 6.02, 14.8 Hz, 1H), 3.39 (s, 3H), 2.03 (s, 3H), 1.17 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 166.9, 156.7, 136.0, 130.6, 129.1, 127.6, 124.4, 124.2, 122.0, 119.3, 112.1, 111.2, 90.6, 73.2, 64.7, 59.4, 51.7, 51.5, 28.1, 26.6, 4.1.

HRMS calculated for $C_{28}H_{29}Cl_2N_3O_4$ 541.1535, found 541.1505.

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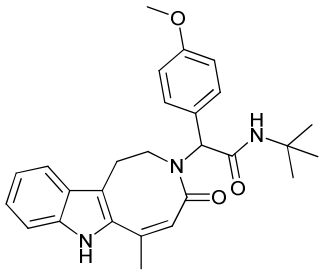
General procedure for $Au(PPh_3)OTf$ catalyzed cyclization

To a glass vial $Au(PPh_3)Cl$ (5 mol %) and AgOTf (5 mol %) were loaded along with chloroform (2 mL). Ugi product **5a-s** was added and reaction mixture was stirred at rt for 8-10h in screw capped vial. After completion, reaction mixture was partitioned between EtOAc (100 mL) and water (50 mL). Organic layer was washed with brine (50 mL), dried over magnesium sulfate and evaporated under reduced pressure. The residue obtained was purified by silica gel column chromatography (20% diethyl ether in dichloromethane) to afford compound **6a-s** as white solid.

In ^{1}H NMR spectra of indoloazocines **6a-s**, recorded at 298 K, signals of the 8-membered ring protons are often broadened due to the ring flipping.



(*Z*)-*N*-*tert*-butyl-2-(4-methoxyphenyl)-2-(6-methyl-4-oxo-1*H*-azocino[5,4-*b*]indol-3(2*H*,4*H*,7*H*)-yl)acetamide (**6a**)

White solid, Yield 85%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.29-7.23 (m, 4H), 7.17 (t, *J* = 7.00 Hz, 1H), 7.12-7.10 (m, 1H), 7.04 (t, *J* = 7.20 Hz, 1H), 6.83 (d, *J* = 8.60 Hz, 2H), 6.00 (d, *J* = 1.3 Hz, 1H), 5.84, (s, 1H), 5.64 (bs, 1H), 4.23-4.05 (m, 1H), 4.02-3.92 (m, 1H), 3.84 (s, 3H), 2.70-2.60 (m, 1H), 2.20-2.16 (m, 4H), 1.18 (s, 9H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 169.4, 169.0, 159.4, 136.2, 134.1, 132.5, 130.9, 128.7, 128.6, 123.0, 122.5, 118.9, 118.5, 114.3, 111.3, 109.2, 60.11, 55.6, 50.6, 44.5, 28.7, 25.5, 24.1.

HRMS calculated for $C_{27}H_{31}N_3O_3$ 445.2365, found 445.2371.

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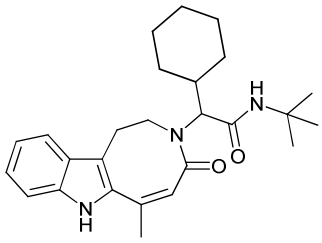


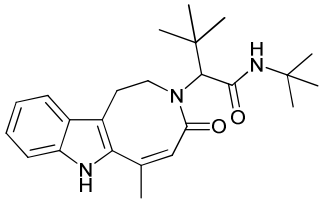
(*Z*)-*N*-*tert*-butyl-2-cyclohexyl-2-(6-methyl-4-oxo-1*H*-azocino[5,4-*b*]indol-3(2*H*,4*H*,7*H*)-yl)acetamide (**6b**)

White solid, Yield 84%.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.46 (d, *J* = 7.90 Hz, 1H), 7.28-7.26 (m, 1H), 7.17 (t, *J* = 7.10 Hz, 1H), 7.07 (t, *J* = 7.21 Hz, 1H), 5.94 (s, 1H), 4.54-4.04 (m, 2H), 4.03-3.80 (m, 1H), 3.30-3.20 (m, 1H), 3.16-2.98 (m, 1H), 2.25-2.17 (m, 4H), 1.83-1.69 (m, 3H), 1.53-1.08 (m, 5H), 1.05 (s, 9H), 0.94-0.70 (m, 3H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 170.9, 169.3, 135.9, 134.8, 131.4, 128.7, 123.0, 121.5, 119.4, 118.9, 110.5, 109.9, 51.0, 35.7, 30.2, 29.7, 29.2, 28.3, 26.3, 25.7, 25.6, 23.9.

HRMS calculated for $C_{26}H_{35}N_3O_2$ 421.2729, found 421.2736.



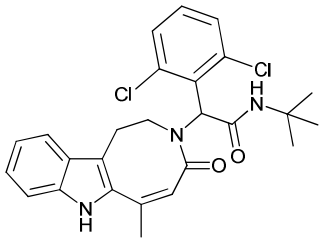
(*Z*)-*N*-*tert*-butyl-3,3-dimethyl-2-(6-methyl-4-oxo-1*H*-azocino[5,4-*b*]indol-3(2*H*,4*H*,7*H*)-yl)acetamide (**6c**)

White solid, Yield 90%

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.43 (d, *J* = 7.81 Hz, 1H), 7.29-7.26 (m, 1H), 7.17 (t, *J* = 7.56 Hz, 1H), 7.06 (t, *J* = 7.56 Hz, 1H), 5.94 (s, 1H), 5.79-5.5.50 (m, 1H), 4.92-4.60 (m, 1H), 4.55-4.16 (m, 2H), 3.43-3.12 (m, 1H), 3.16-2.88 (m, 1H), 2.21 (s, 3H), 1.28-1.00 (m, 18H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 168.5, 136.0, 132.9, 131.6, 129.0, 122.9, 121.6, 119.4, 118.9, 110.7, 109.4, 51.2, 36.8, 29.7, 28.8, 28.4, 28.2, 27.9, 23.3.

HRMS calculated for $C_{24}H_{33}N_3O_2$ 395.2573, found 395.2549.



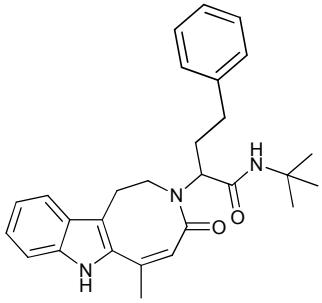
(*Z*)-*N*-*tert*-butyl-2-(2,6-dichlorophenyl)-2-(6-methyl-4-oxo-1*H*-azocino[5,4-*b*]indol-3(2*H*,4*H*,7*H*)-yl)acetamide (**6d**)

White solid, Yield 91%

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.37-7.19 (m, 6H), 7.14-7.06 (m, 1H), 6.79 (s, 1H), 6.08 (s, 1H), 5.60 (bs, 1H), 4.40-4.22 (m, 1H), 3.97-3.03 (m, 2H), 2.93-2.48 (m, 1H), 2.25 (s, 3H), 0.87 (bs, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 166.7, 138.1, 136.2, 135.7, 132.0, 131.5, 130.2, 129.4, 128.5, 123.3, 121.3, 119.6, 118.4, 111.1, 108.3, 65.8, 51.2, 43.9, 27.6, 24.3, 15.2.

HRMS calculated for $C_{26}H_{27}Cl_2N_3O_2$ 483.1480, found 483.1480.



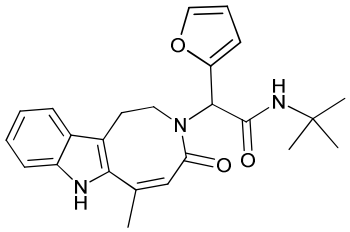
(*Z*)-*N*-*tert*-butyl-2-(6-methyl-4-oxo-1*H*-azocino[5,4-*b*]indol-3(2*H*,4*H*,7*H*)-yl)-4-phenylbutanamide (**6e**)

White solid, Yield 85%

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.44 (d, *J* = 7.96 Hz, 1H), 7.30-7.17 (m, 5H), 7.12-7.05 (m, 3H), 6.27 (s, 1H), 5.97 (s, 1H), 467-4.58 (m, 1H), 4.14-3.91 (m, 2H), 3.31-3.03 (m, 2H), 2.65-2.40 (m, 3H), 2.24 (s, 3H), 2.16-2.02 (m, 1H), 0.96 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 169.5, 140.9, 135.8, 134.7, 131.3, 128.7, 128.4, 128.3, 126.0, 123.3, 121.8, 119.7, 119.0, 110.5, 109.8, 50.8, 32.4, 29.6, 28.1, 25.8, 24.1.

HRMS calculated for $C_{28}H_{33}N_3O_2$ 443.2573, found 443.2548.



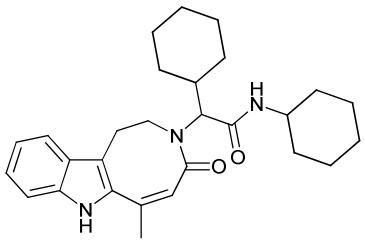
(*Z*)-*N*-*tert*-butyl-2-(furan-2-yl)-2-(6-methyl-4-oxo-1*H*-azocino[5,4-*b*]indol-3(2*H*,4*H*,7*H*)-yl)acetamide (**6f**).

White solid, Yield 72%

^{1}H NMR (300 MHz, DMSO-d$_6$) δ 10.83 (s, 1H), 7.69 (s, 1H), 7.59 (s, 1H), 7.29 (d, *J* = 8.30 Hz, 1H), 7.12-7.07 (m, 2H), 6.96 (t, *J* = 7.41 Hz, 1H), 6.56 (s, 1H), 6.39 (s, 1H), 5.94-5.93 (m, 2H), 4.20-4.03 (m, 1H), 3.93-3.82 (m, 1H), 2.60-2.42 (m, 1H), 2.23 (s, 3H), 1.98-1.92 (m, 1H), 1.19 (s, 9H).

^{13}C NMR (75 MHz, CDCl$_3$) δ 170.2, 166.4, 148.0, 143.0, 136.0, 135.7, 131.5, 128.7, 123.0, 121.2, 119.3, 118.7, 112.2, 110.9 (x 2), 109.7, 55.7, 51.4, 44.6, 28.2, 25.0, 24.2.

HRMS calculated for $C_{24}H_{27}Cl_2N_3O_3$ 405.2052, found 405.2050.



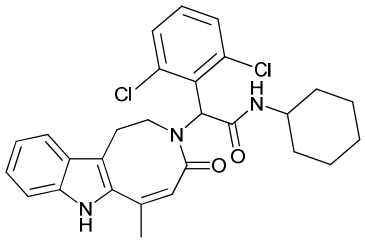
(*Z*)-*N*,2-dicyclohexyl-2-(6-methyl-4-oxo-1*H*-azocino[5,4-*b*]indol-3(2*H*,4*H*,7*H*)-yl)acetamide (**6g)**

White solid, Yield 88%

^{1}H NMR (300 MHz, CDCl$_3$) δ 7.99 (s, 1H), 7.47 (d, *J* = 7.82 Hz, 1H), 7.27-7.26 (m, 1H), 7.17 (t, *J* = 7.10 Hz, 1H), 7.08 (t, *J* = 7.40 Hz, 1H), 5.95 (s, 1H), 4.40-4.08 (m, 1H), 3.99-3.76 (m, 1H), 3.42-3.24 (m, 2H), 3.09-2.94 (m, 1H), 2.31-2.20 (m, 4H), 1.87-1.58 (m, 4H), 1.52-0.49 (m, 17H).

^{13}C NMR (75 MHz, CDCl$_3$) δ 170.9, 169.4, 135.8, 134.6, 131.4, 128.8, 123.1, 122.0, 119.6, 118.8, 110.4, 109.8, 47.9, 35.1, 32.6, 31.9, 30.3, 29.7, 29.1, 26.3, 25.7, 25.6, 25.4, 25.3, 24.4, 24.3, 23.8.

HRMS calculated for $C_{28}H_{37}N_3O_2$ 447.2886, found 447.2868.



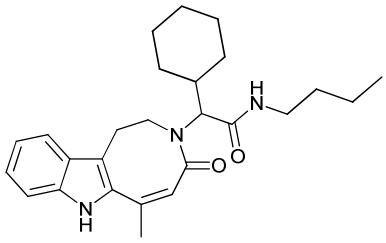
(*Z*)-*N*-cyclohexyl-2-(2,6-dichlorophenyl)-2-(6-methyl-4-oxo-1*H*-azocino[5,4-*b*]indol-3(2*H*,4*H*,7*H*)-yl)acetamide (**6h**)

White solid, Yield 89%

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.40-7.30 (m, 4H), 7.29-7.20 (m, 2H), 7.17-7.09 (m, 1H), 6.81 (s, 1H), 6.10 (s, 1H), 5.72-5.62 (m, 1H), 4.41-4.28 (m, 1H), 3.75-3.57 (m, 1H), 3.56-3.36 (m, 2H), 2.87-2.68 (m, 1H), 2.27 (s, 3H), 1.76-1.66 (m, 1H), 1.44-1.20 (m, 6H), 1.13-0.85 (m, 3H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 168.7, 166.1, 136.9, 135.8, 134.5, 132.1, 131.7, 130.6, 129.4, 128.0, 122.1, 121.9, 118.4, 118.1, 110.7, 107.8, 54.8, 48.0, 44.0, 31.7, 31.5, 24.9, 24.6, 23.7.

HRMS calculated for $C_{28}H_{29}Cl_2N_3O_2$ 509.1637, found 509.1634.



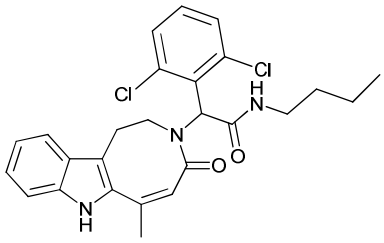
(*Z*)-*N*-butyl-2-cyclohexyl-2-(6-methyl-4-oxo-1*H*-azocino[5,4-*b*]indol-3(2*H*,4*H*,7*H*)-yl)acetamide (**6i**)

White solid, Yield 89%

^{1}H NMR (300 MHz, DMSO-d_6) δ 10.79 (s, 1H), 7.83 (bs, 1H), 7.36 (d, *J* = 7.72 Hz, 1H), 7.27 (d, *J* = 8.10 Hz, 1H), 7.09 (t, *J* = 7.26 Hz, 1H), 6.95 (t, *J* = 7.57 Hz, 1H), 5.91 (s, 1H), 4.57 (d, *J* = 11.0 Hz, 1H), 4.25-4.12 (m, 1H), 3.99-3.79 (m, 1H), 3.13-2.78 (m, 4H), 2.21 (s, 3H), 2.05-1.90 (m, 1H), 1.69-1.48 (m, 3H), 1.40-0.98 (m, 9H), 0.93-0.60 (m, 5H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 169.1, 169.0, 135.8, 133.1, 132.1, 128.3, 122.5, 122.0, 118.5, 118.1, 110.7, 108.4, 38.1, 36.2, 30.6, 29.7, 28.6, 25.9, 25.5, 25.3 (2), 23.4, 19.4, 13.5.

HRMS calculated for $C_{26}H_{35}N_3O_2$ 421.2729, found 421.2726.



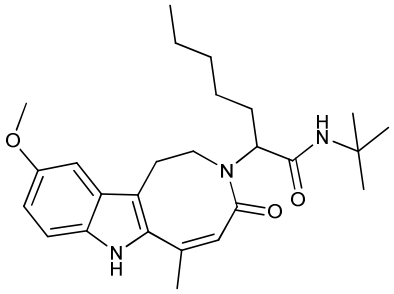
(*Z*)-*N*-butyl-2-(2,6-dichlorophenyl)-2-(6-methyl-4-oxo-1*H*-azocino[5,4-*b*]indol-3(2*H*,4*H*,7*H*)-yl)acetamide (**6j**)

White solid, Yield 80%

^{1}H NMR (300 MHz, DMSO-d$_6$) δ 10.8 (s, 1H), 7.96-7.67 (m, 1H), 7.49-7.30 (m, 3H), 7.25 (d, *J* = 8.22 Hz, 1H), 7.07 (t, *J* = 7.22 Hz, 1H), 6.88 (t, *J* = 7.45 Hz, 1H), 6.81-6.67 (m, 1H), 6.37 (s, 1H), 5.97 (s, 1H), 4.37-4.05 (m, 1H), 3.97-3.81 (m, 1H), 3.09-2.92 (m, 2H), 2.76-2.54 (m, 1H), 2.28 (s, 3H), 2.04-1.88 (m, 1H), 1.40-1.10 (m, 4H), 0.88-0.78 (m, 3H).

^{13}C NMR (75 MHz, DMSO-d$_6$) δ 168.7, 167.1, 135.7, 134.2, 132.0, 131.8, 130.6, 129.4, 128.0, 122.0, 121.9, 118.8, 117.8, 110.6, 107.7, 57.3, 44.2, 30.5, 24.8, 23.6, 19.5, 13.6.

HRMS calculated for $C_{26}H_{27}Cl_2N_3O_2$ 483.1480, found 483.1468.



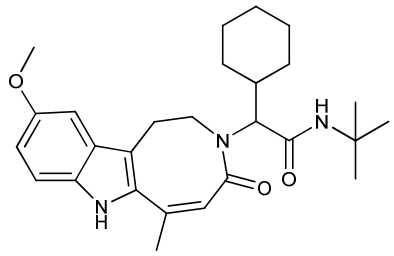
(*Z*)-*N*-*tert*-butyl-2-(10-methoxy-6-methyl-4-oxo-1*H*-azocino[5,4-*b*]indol-3(2*H*,4*H*,7*H*)-yl)heptanamide (**6k**)

White solid, Yield 85%

^{1}H NMR (300 MHz, DMSO-d$_6$) δ 10.68 (s, 1H), 7.17 (d, *J* = 8.65 Hz, 1H), 7.14-7.06 (m, 1H), 6.83 (s, 1H), 6.74 (d, *J* = 8.75 Hz, 1H), 5.89 (s, 1H), 4.60-4.51 (m, 1H), 4.17-3.83 (m, 2H), 3.73 (s, 3H), 3.09-2.89 (m, 2H), 2.20 (s, 3H), 1.86-1.83 (m, 1H), 1.66-1.53 (m, 1H), 1.22-0.98 (m, 15H), 0.75 (t, *J* = 7.19 Hz, 3H).

^{13}C NMR (75 MHz, CDCl$_3$) δ 170.6, 169.9, 154.1, 134.8, 132.1, 131.0, 129.1, 121.6, 113.8, 111.5, 109.6, 100.2, 55.8, 50.8, 31.6, 28.2, 27.8, 26.0, 25.9, 24.1, 22.4, 13.9.

HRMS calculated for $C_{26}H_{37}N_3O_3$ 439.2835, found 439.2842.



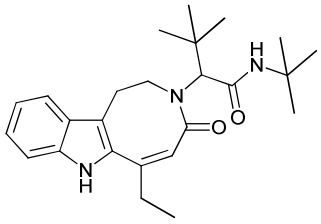
(*Z*)-*N*-*tert*-butyl-2-cyclohexyl-2-(10-methoxy-6-methyl-4-oxo-1*H*-azocino[5,4-*b*]indol-3(2*H*,4*H*,7*H*)-yl)acetamide (**6l**)

White solid, Yield 65%

^{1}H NMR (300 MHz, DMSO-d$_6$) δ 10.64 (s, 1H), 7.53 (bs, 1H), 7.16 (d, *J* = 8.69 Hz, 1H), 6.79 (s, 1H), 6.72 (dd, *J* = 1.70, 8.75 Hz, 1H), 5.88 (s, 1H), 4.61-4.48 (m, 1H), 4.22-4.09 (m, 1H), 3.98-3.84 (m, 1H), 3.71 (s, 3H), 3.14-2.80 (m, 2H), 2.20 (s, 3H), 2.02-1.88 (m, 1H), 1.72-1.50 (m, 3H), 1.49-1.17 (m, 3H), 1.12 (s, 9H), 1.09-0.79 (m, 3H).

^{13}C NMR (75 MHz, CDCl$_3$) δ 170.8, 169.4, 154.0, 134.5, 132.1, 131.0, 129.2, 121.4, 113.7, 111.4, 109.8, 100.2, 55.8, 51.0, 35.6, 30.2, 29.1, 28.3, 26.3, 25.7 (x 2), 23.9.

HRMS calculated for $C_{27}H_{37}N_3O_3$ 451.2835, found 451.2847.



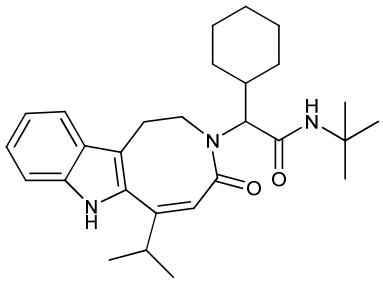
(*Z*)-*N*-*tert*-butyl-2-(6-ethyl-4-oxo-1*H*-azocino[5,4-*b*]indol-3(2*H*,4*H*,7*H*)-yl)-3,3-dimethylbutanamide (**6m**)

White solid, Yield 85%

^{1}H NMR (300 MHz, CDCl$_3$) δ 8.04-7.84 (m, 1H), 7.44 (d, *J* = 8.04 Hz, 1H), 7.29-7.24 (m, 1H), 7.17 (t, *J* = 7.08 Hz, 1H), 7.06 (t, *J* = 7.47 Hz, 1H), 5.94 (s, 1H), 5.79-5.47 (m, 1H), 4.93-4.59 (m, 1H), 4.53-4.16 (m, 2H), 3.42-3.20 (m, 1H), 3.15-2.86 (m, 1H), 2.53 (q, *J* = 7.17 Hz, 2H), 1.42-0.77 (m, 21H).

^{13}C NMR (75 MHz, CDCl$_3$) δ 171.4, 168.5, 138.9, 136.0, 131.0, 129.0, 122.8, 120.2, 119.3, 118.8, 110.6, 109.9, 65.8, 51.2, 29.9, 28.3, 27.8, 15.2, 14.0, 12.8.

HRMS calculated for $C_{25}H_{35}N_3O_2$ 409.2729, found 409.2723.



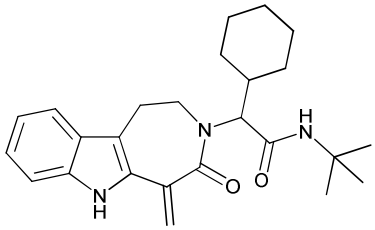
(*Z*)-*N*-*tert*-butyl-2-cyclohexyl-2-(6-isopropyl-4-oxo-1*H*-azocino[5,4-*b*]indol-3(2*H*,4*H*,7*H*)-yl)acetamide (**6o**)

White solid,Yield 81%

^{1}H NMR (300 MHz, DMSO-d$_6$) δ 10.75 (s, 1H), 7.52 (bs, 1H), 7.33 (bs, 1H), 7.25 (d, *J* = 8.20 Hz, 1H), 7.06 (t, *J* = 7.33 Hz, 1H), 6.94 (t, *J* = 7.48 Hz, 1H), 5.80 (s, 1H), 4.66-4.38 (m, 1H), 4.21-4.07 (m, 1H), 3.98-3.59 (m, 1H), 3.07-2.69 (m, 2H), 2.00-1.83 (m, 1H), 1.70-1.47 (m, 3H), 1.37-0.47 (m, 23H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 171.6, 169.2, 145.0, 135.9, 131.2, 128.8, 122.7, 119.3, 118.8, 110.4, 50.9, 34.1, 30.1, 28.3, 26.3, 25.7 (x 2), 25.3.

HRMS calculated for $C_{28}H_{39}N_3O_2$ 449.3042, found 449.3054.



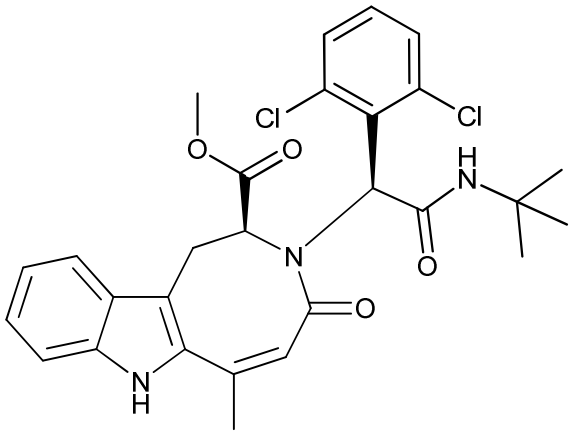
N-*tert*-butyl-2-cyclohexyl-2-(5-methylene-4-oxo-1,2,4,5-tetrahydroazepino[4,5-*b*]indol-3(6*H*)-yl)acetamide (**6q**)

White solid, Yield 56%

^{1}H NMR (300 MHz, CDCl$_3$) δ 8.12 (s, 1H), 7.47 (d, *J* = 8.10 Hz, 1H), 7.35 (d, *J* = 7.89 Hz, 1H), 7.26-7.20 (m, 1H), 7.11 (t, *J* = 7.68 Hz, 1H), 6.07-5.88 (m, 2H), 5.73 (s, 1H), 4.61-4.47 (m, 1H), 3.91-.82 (m, 2H), 2.99-2.91 (m, 2H), 2.18-2.02 (m, 1H), 1.86-1.53 (m, 4H), 1.40-1.11 (m, 13H), 1.06-0.91 (m, 2H).

^{13}C NMR (75 MHz, CDCl$_3$) δ 171.2, 169.3, 138.6, 136.2, 128.5, 128.4, 123.3, 120.2, 119.8, 118.9, 113.8, 111.0, 51.3, 35.8, 29.9, 29.0, 28.5, 26.3, 25.7, 25.6, 25.0.

HRMS calculated for $C_{25}H_{33}N_3O_2$ 407.2573, found 407.2573.



(*S*,*Z*)-methyl 3-((*S*)-2-(*tert*-butylamino)-1-(2,6-dichloro-phenyl)-2-oxoethyl)-6-methyl-4-oxo-2,3,4,7-tetrahydro-1*H*-azocino[5,4-*b*]indole-2-carboxylate (**6r**)

White solid, Yield 62%, $[\alpha]_D = +145.6^o$ (*c* = 0.15, $CHCl_3$)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.58 (s, 1H), 7.42-7.31 (m, 1H), 7.28-7.26 (m, 1H), 7.25-7.20 (m, 1H), 7.14 (t, *J* = 7.33 Hz, 1H), 6.93 (t, *J* = 7.71 Hz, 1H), 6.89-6.80 (m, 1H), 6.73 (s, 1H), 6.63 (d, *J* = 7.85 Hz, 1H), 5.81 (s, 1H), 5.29 (s, 1H), 4.97 (d, *J* = 8.35 Hz, 1H), 3.87 (s, 3H), 3.32 (d, *J* = 17.3 Hz, 1H), 2.13 (s, 3H), 1.44 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 172.0, 169.4, 166.7, 136.1, 135.6, 131.5, 131.2, 130.0, 129.5, 127.7, 122.7, 121.5, 118.9, 118.0, 111.2, 106.2, 59.4, 58.0, 53.3, 51.6, 28.4, 24.9, 23.5.

HRMS calculated for $C_{28}H_{29}Cl_2N_3O_4$ 541.1535, found 541.1535.

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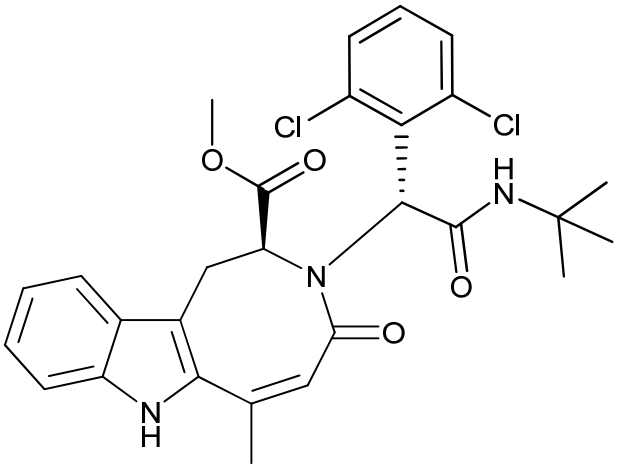

(*S*,*Z*)-methyl 3-((*R*)-2-(*tert*-butylamino)-1-(2,6-dichlorophenyl)-2-oxoethyl)-6-methyl-4-oxo-2,3,4,7-tetrahydro-1*H*-azocino[5,4-*b*]indole-2-carboxylate (**6s**)

White solid, Yield 49%, $[\alpha]_D = +161.7^o$ (*c* = 0.59, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.56 (d, *J* = 7.72 Hz, 1H), 7.45-7.40 (m, 2H), 7.36-7.15 (m, 4H), 7.00 (s, 1H), 5.86 (s, 1H), 5.59 (s, 1H), 4.20 (d, *J* = 6.22 Hz, 1H), 3.91 (dd, *J* = 7.72, 17.1 Hz, 1H), 3.72-3.65 (m, 1H), 3.61 (s, 3H), 2.14 (s, 3H), 0.68 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 169.7, 166.5, 136.4, 134.3, 132.2, 131.4, 130.6, 129.2, 128.4, 123.6, 122.3, 120.2, 118.4, 111.4, 106.4, 61.3, 56.5, 52.5, 51.1, 27.3, 26.8, 23.4.

HRMS calculated for $C_{28}H_{29}Cl_2N_3O_4$ 541.1535, found 541.1542.

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Crystallographic data for compound **6s**

Crystals of **6s**, suitable for X-ray diffraction were obtained by slow evaporation from Methanol at rt. A cubic shaped crystal with approximate dimensions 0.4 x 0.2 x 0.1 mm^2, was selected and mounted in a nylon loop for data collection. X-ray intensity data were collected on an Agilent Supernova diffractometer equipped with a CCD detector using Mo Kα radiation (λ = 0.7107Å). The images were interpreted and integrated with the CrysAlisPro software from Agilent. Using Olex2,[1] the structure was solved with the ShelxS[2] structure solution program using Direct Methods and refined with the ShelxL[2] 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). CCDC 873949 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).

Summarized crystallographic data for **6s**

$C_{28}H_{29}N_3O_4Cl_2$, M =542.44 g mol^{-1}, orthorhombic, $P2_12_12_1$ (no. 19), a = 11.4032(7) Å, b = 14.2768(8) Å, c = 16.2935(7) Å, V = 2652.6(2) $Å^3$, T = 293(2) K, Z = 4, ρ_{calcd} = 1.358 g cm^{-3}, μ(Mo Kα) = 0.284 mm^{-1}, F(000) = 1136, crystal size 0.4 x 0.2 x 0.1 mm^3, 12398 reflections measured, 6146 unique (R_{int} = 0.0337) which were used in all calculations. The final wR_2 was 0.1038 (all data) and R_1 was 0.0448 (>2sigma(I))

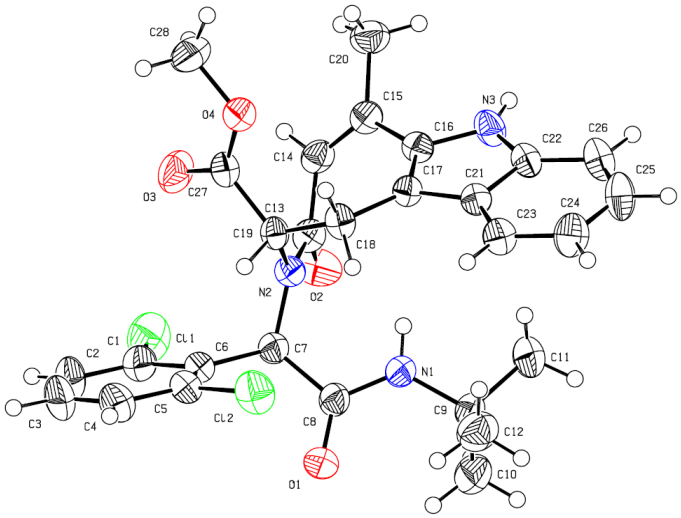


Figure 1. Single crystal X-ray molecular structure of **6s**, with atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. CCDC 873949

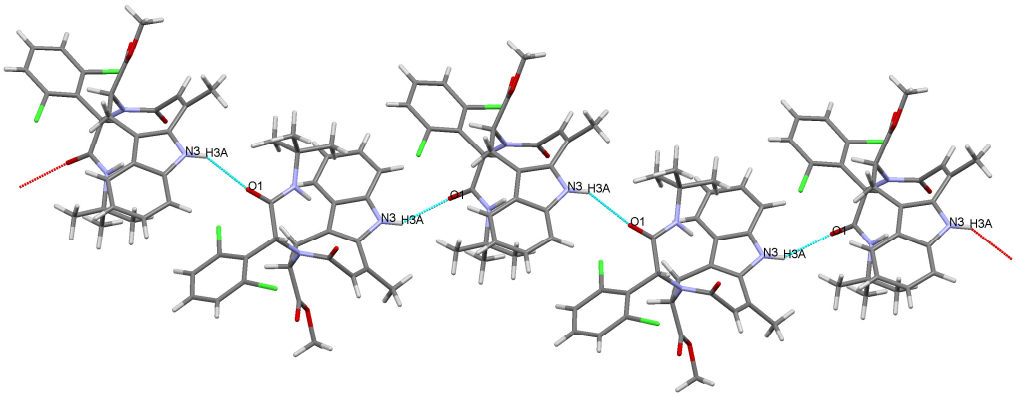


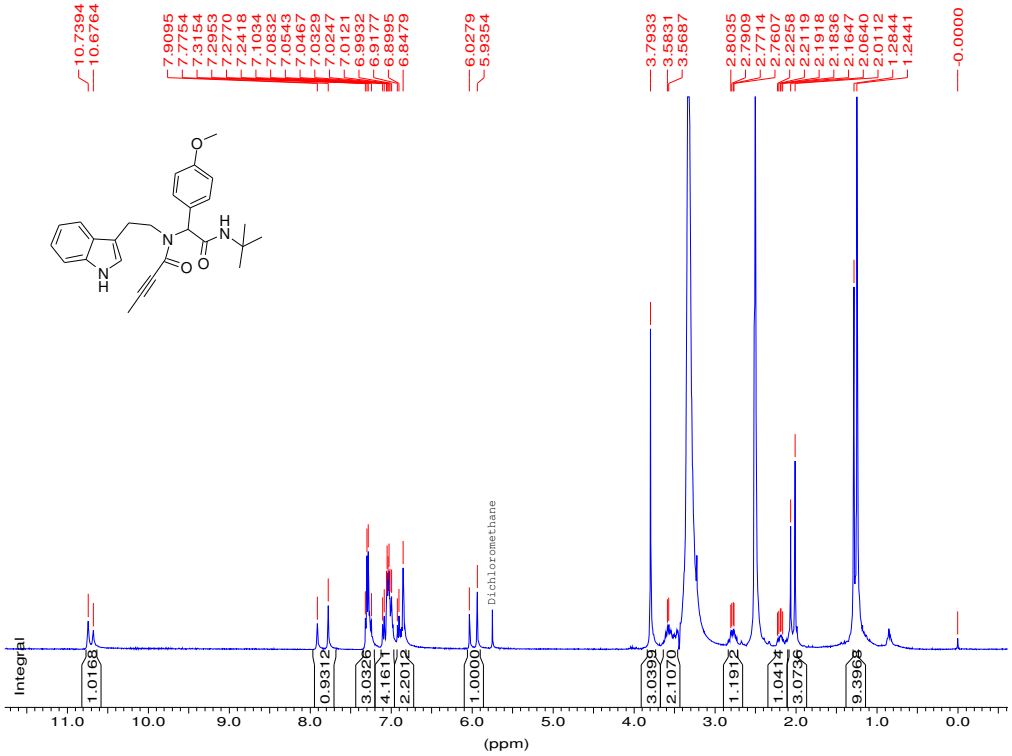
Figure 2. Depiction of intermolecular hydrogen bonds in the crystal packing of **6s**.

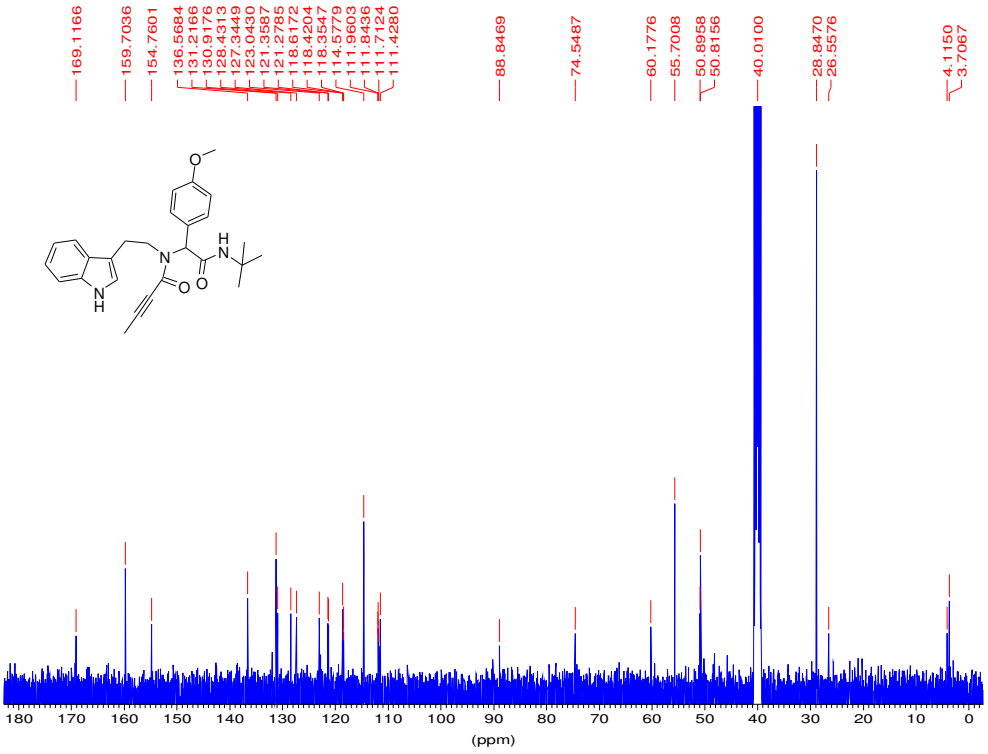
Intermolecular hydrogen bonding between indole nitrogen N3 and oxygen O1 from amide makes a chain like network in the crystal packing (Fig 2.). Amide oxygen O2 from the 8-membered ring and oxygen O3/O4 from ester group does not take part in any critical intermolecular hydrogen bonding.

References

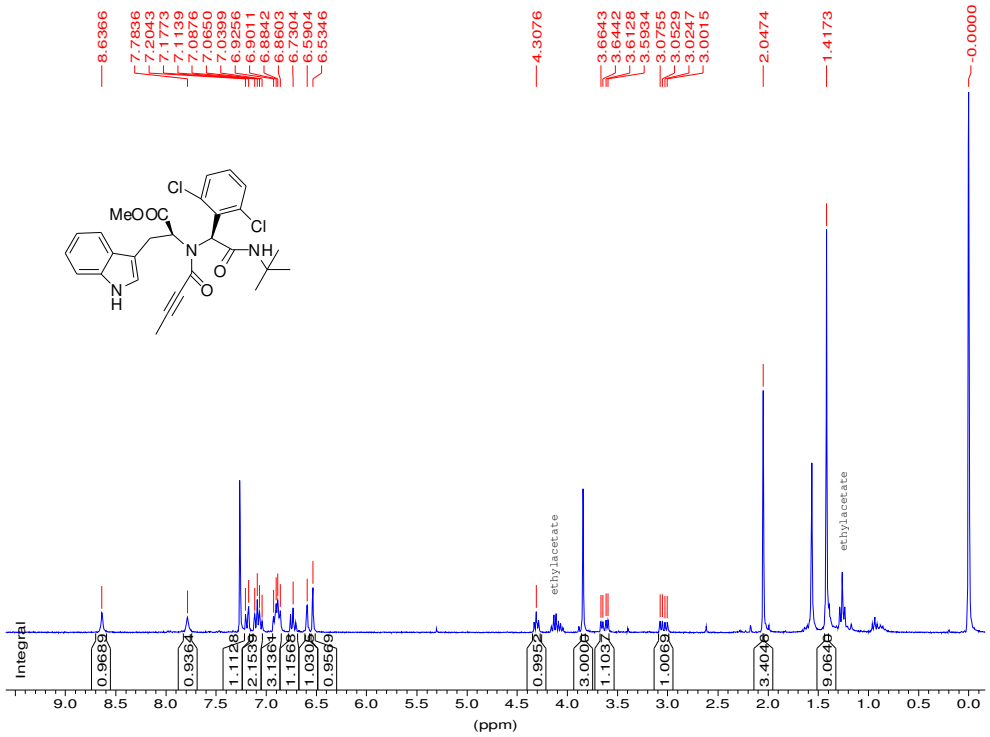
1. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, OLEX2: a complete structure solution, refinement and analysis program. *J. Appl. Cryst.* 2009, **42**, 339.
2. G.M. Sheldrick, *Acta Cryst.* 2008, **A64**, 112.

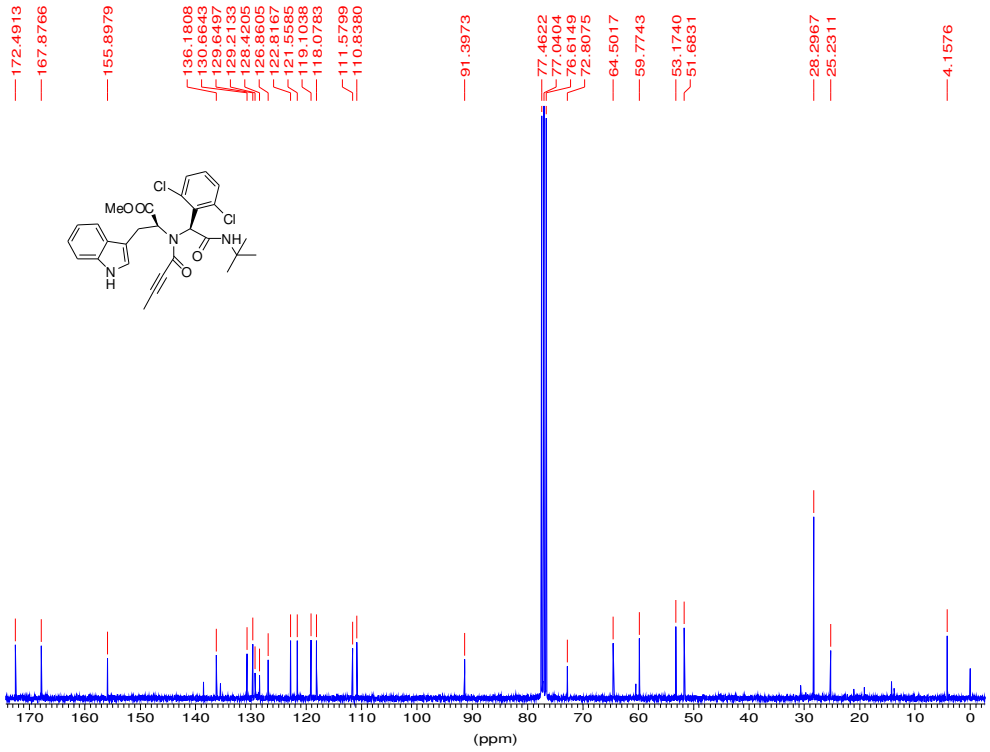
^{1}H and ^{13}C NMR spectra of compound **5a** (400 MHz, DMSO-d_6)



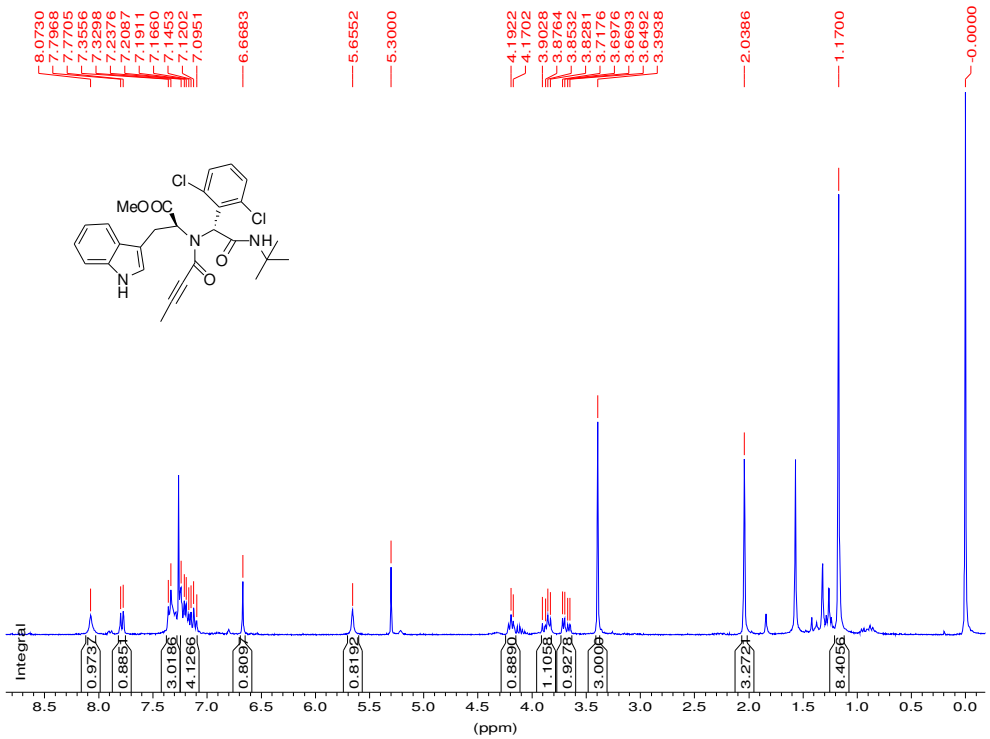


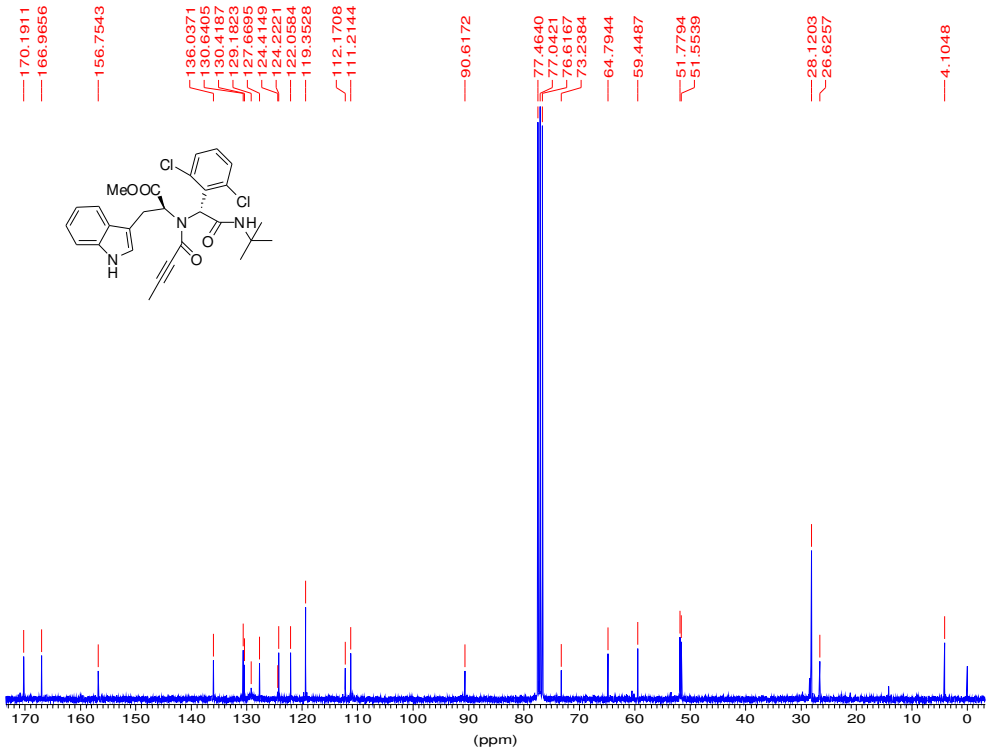
^{1}H and ^{13}C NMR spectra of compound **5r** (300 MHz, $CDCl_3$)



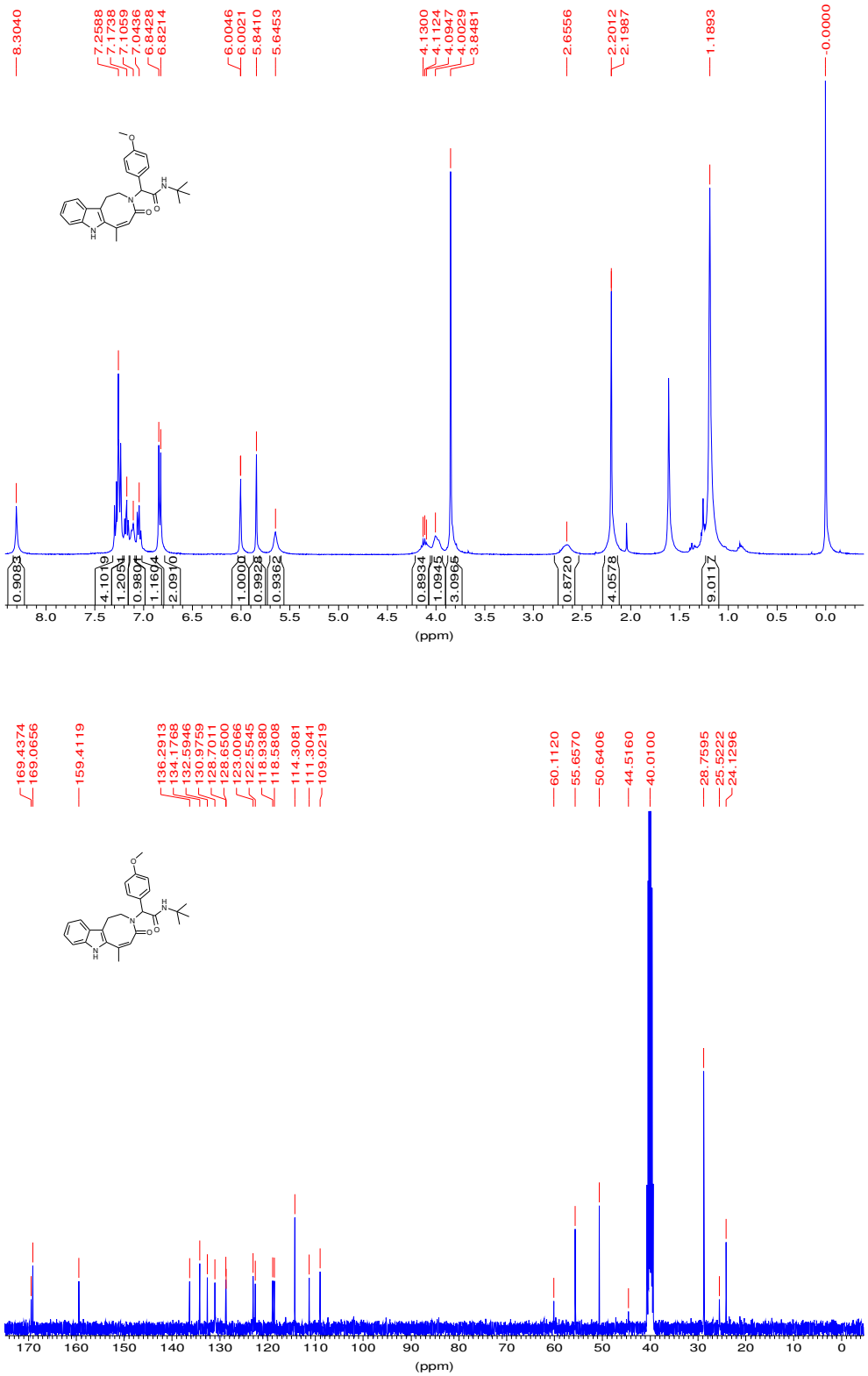


^{1}H and ^{13}C NMR spectra of compound **5s** (300 MHz, $CDCl_3$)

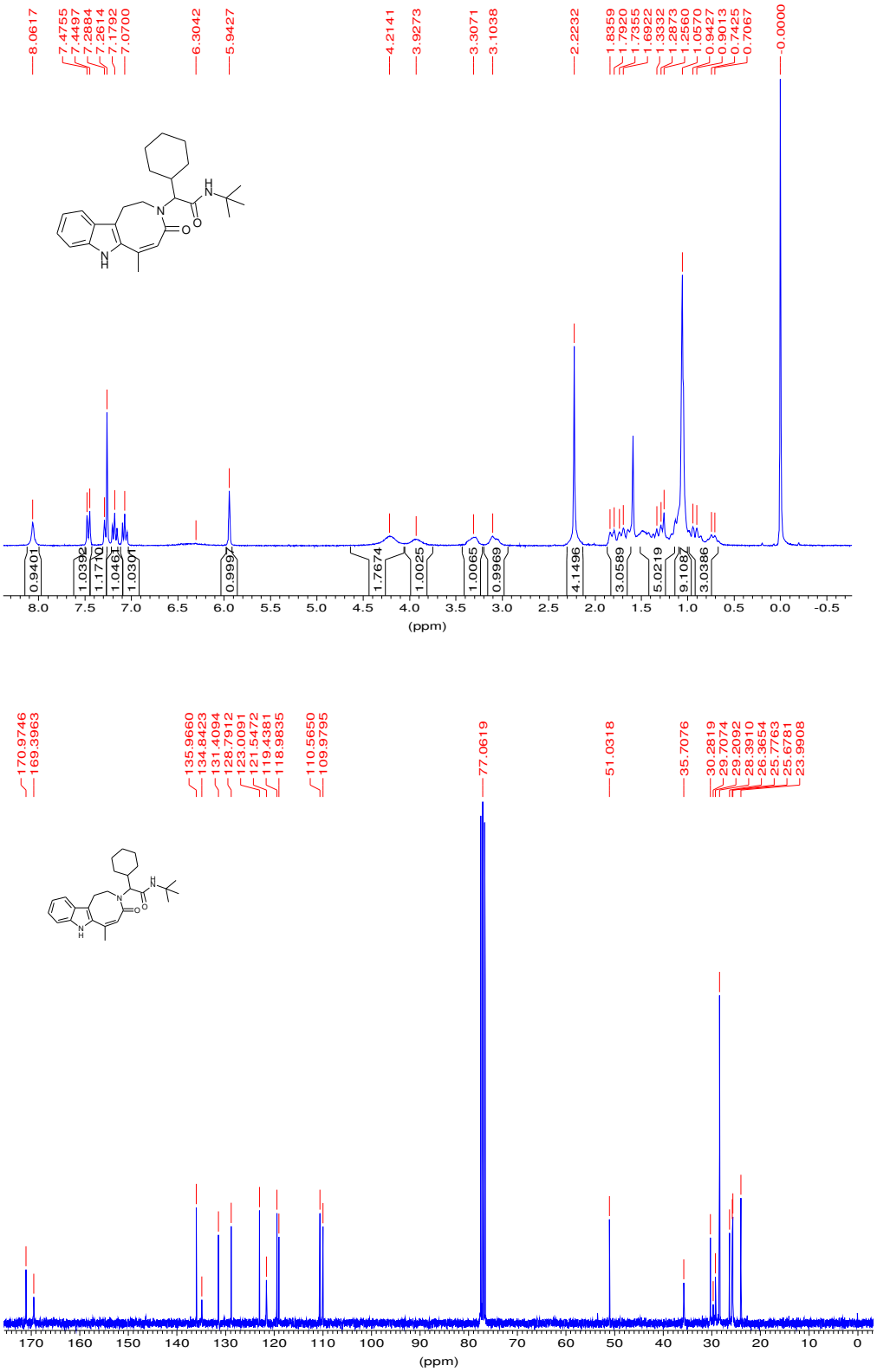




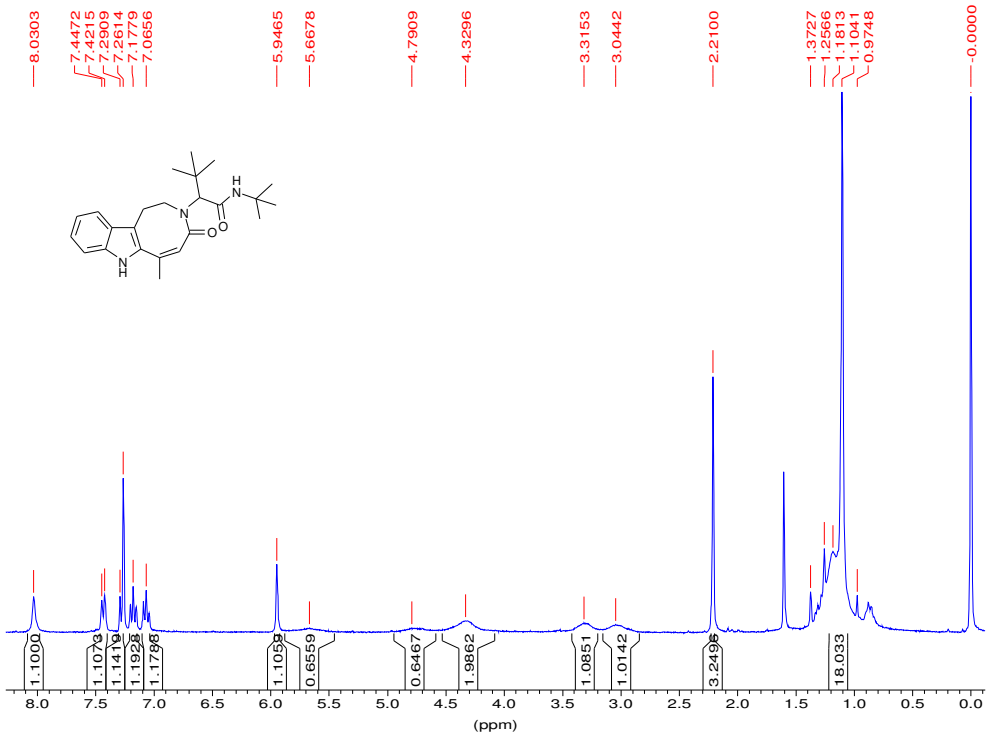
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, DMSO-d_6) of compound **6a**

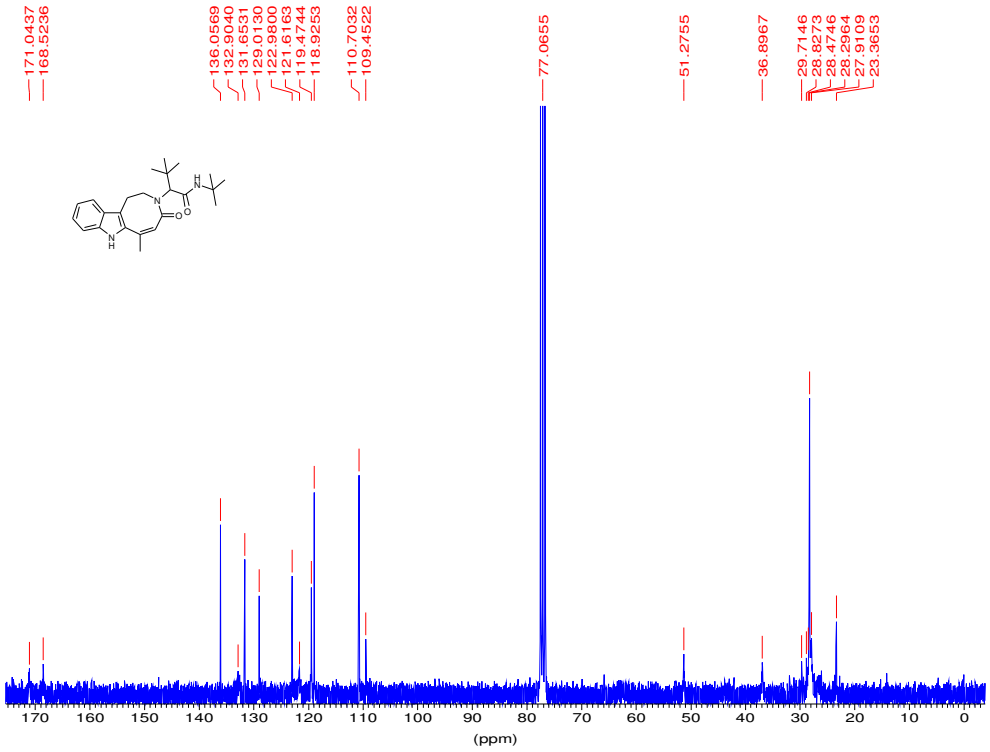


^{1}H NMR (300 MHz, $CDCl_3$) and ^{13}C NMR (75 MHz, DMSO-d_6) of compound **6b**

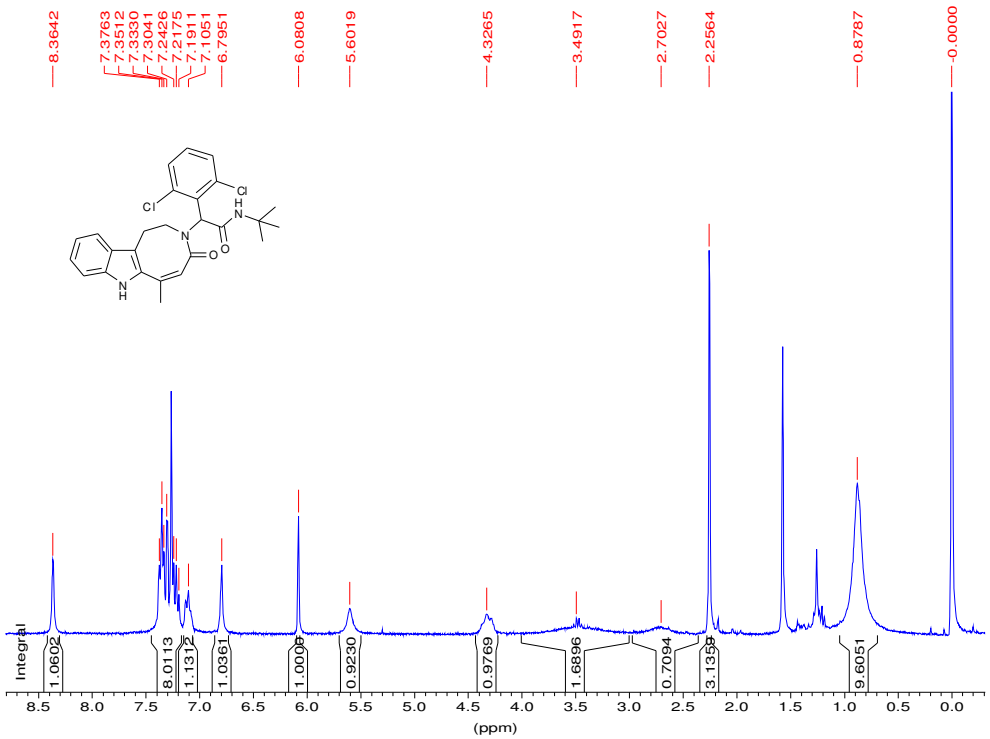


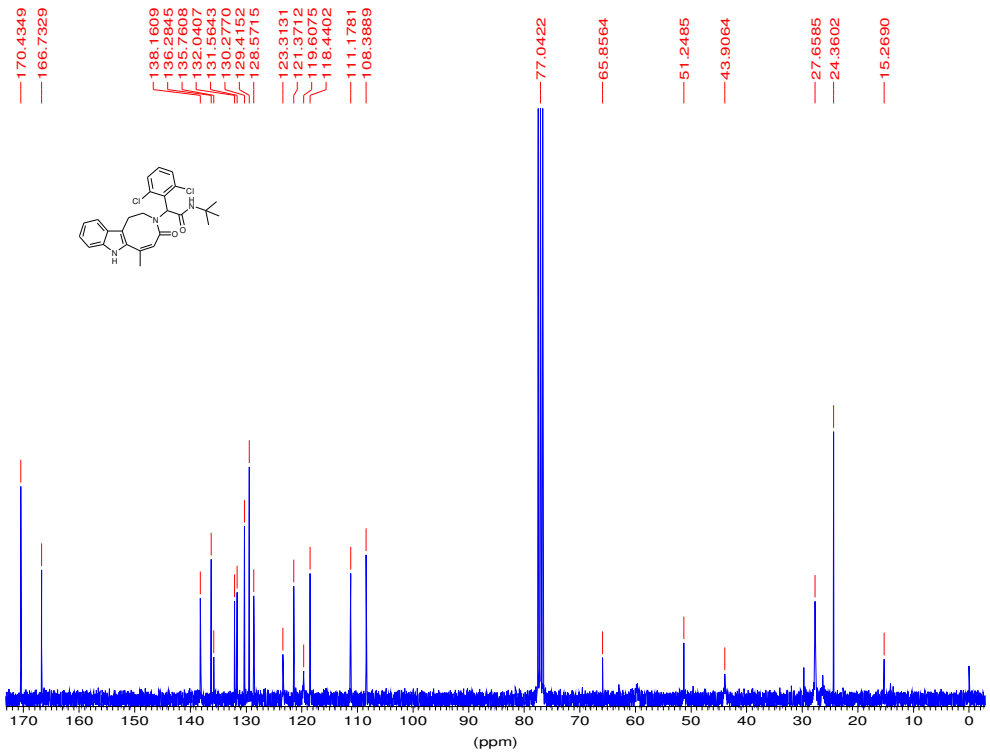
^{1}H and ^{13}C NMR of compound **6c** (300 MHz, $CDCl_3$)



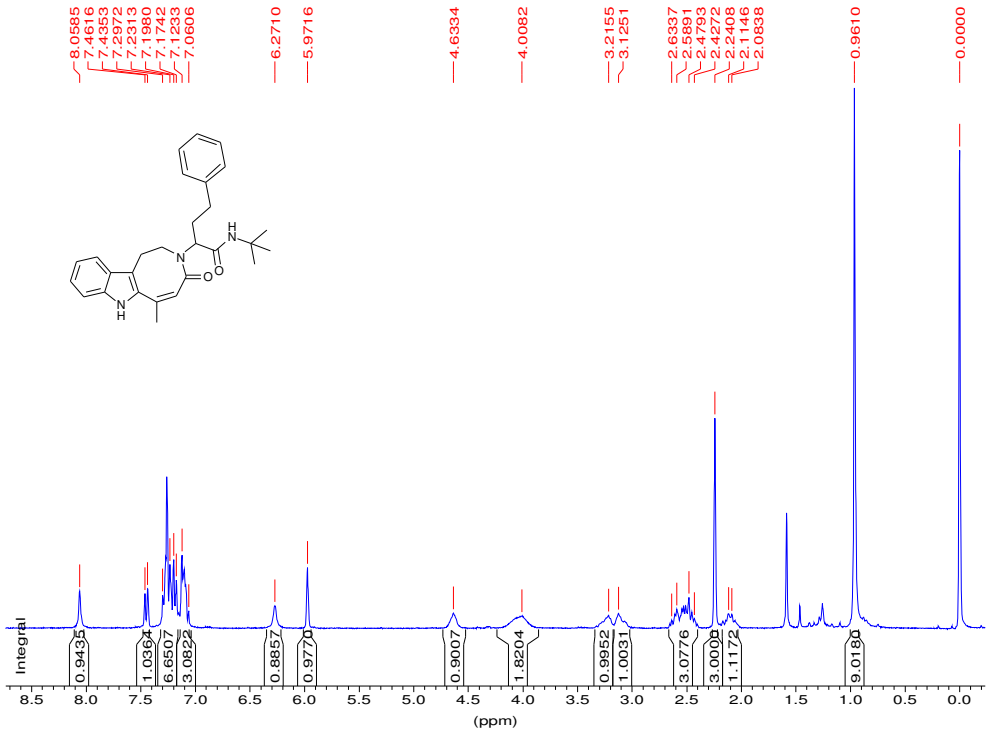


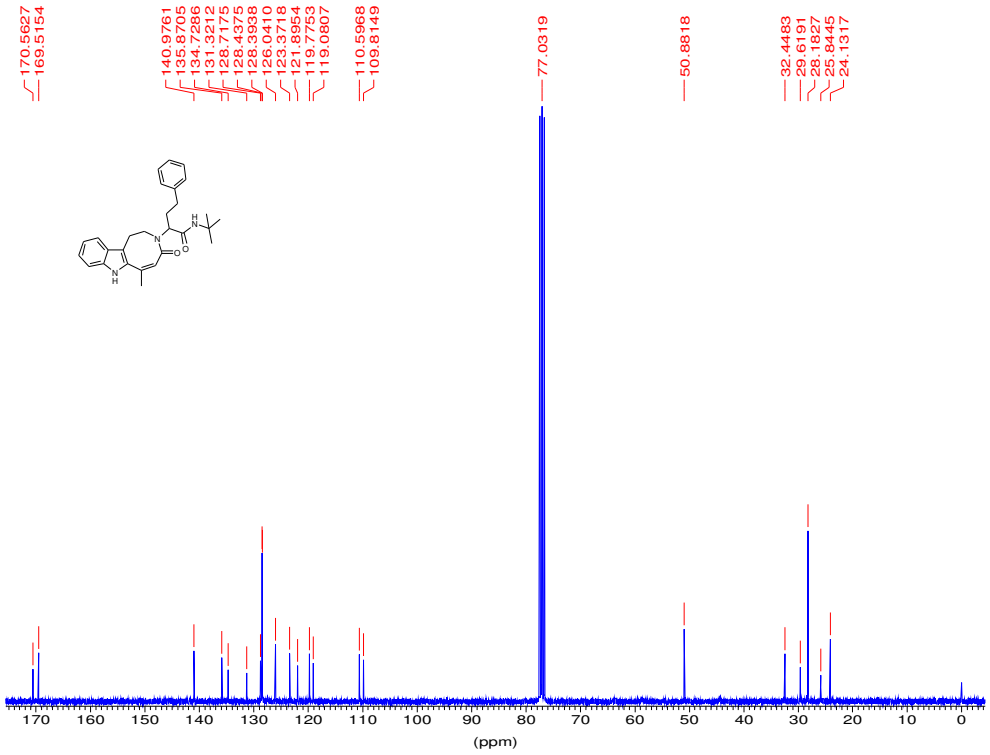
^{1}H and ^{13}C NMR of compound **6d** (300 MHz, $CDCl_3$)



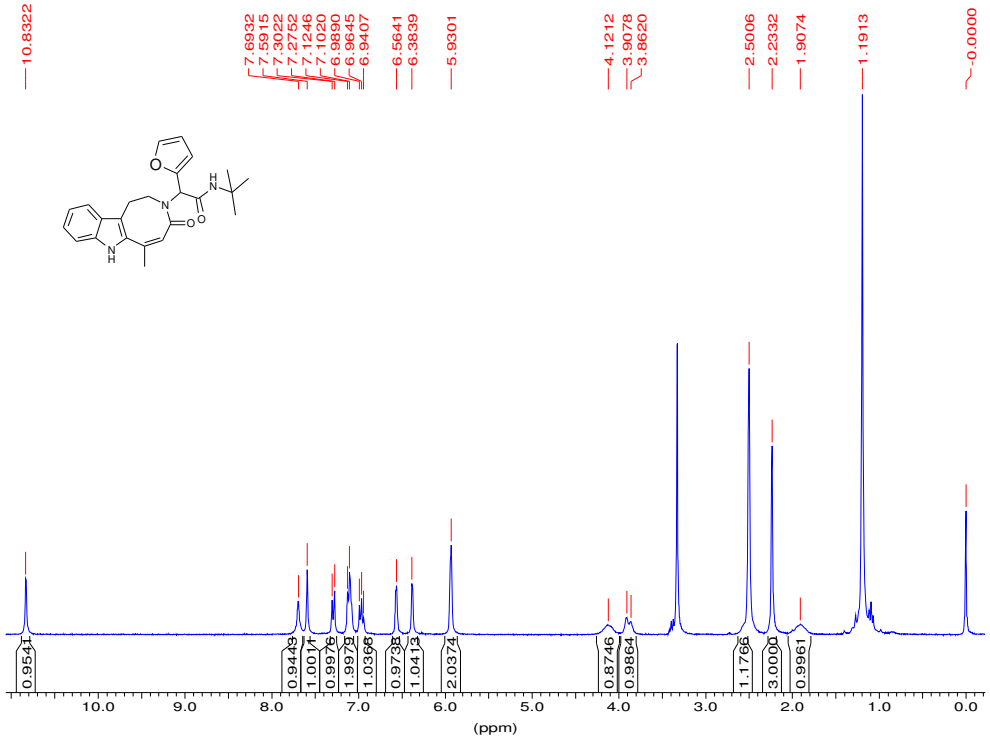


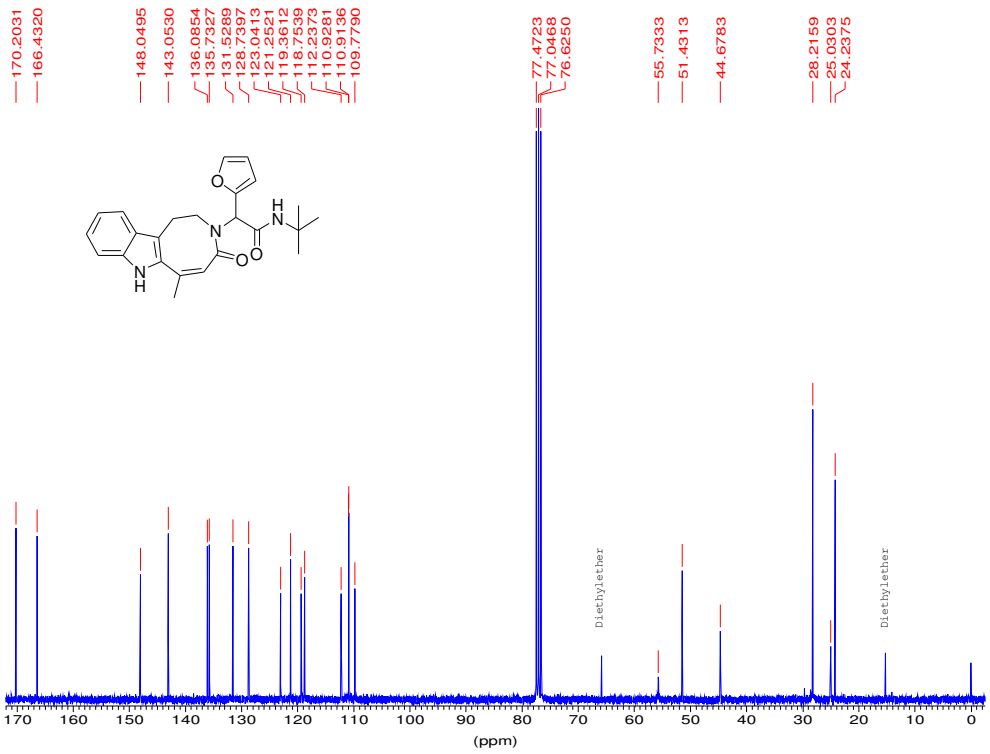
^{1}H and ^{13}C NMR of compound **6e** (300 MHz, $CDCl_3$)



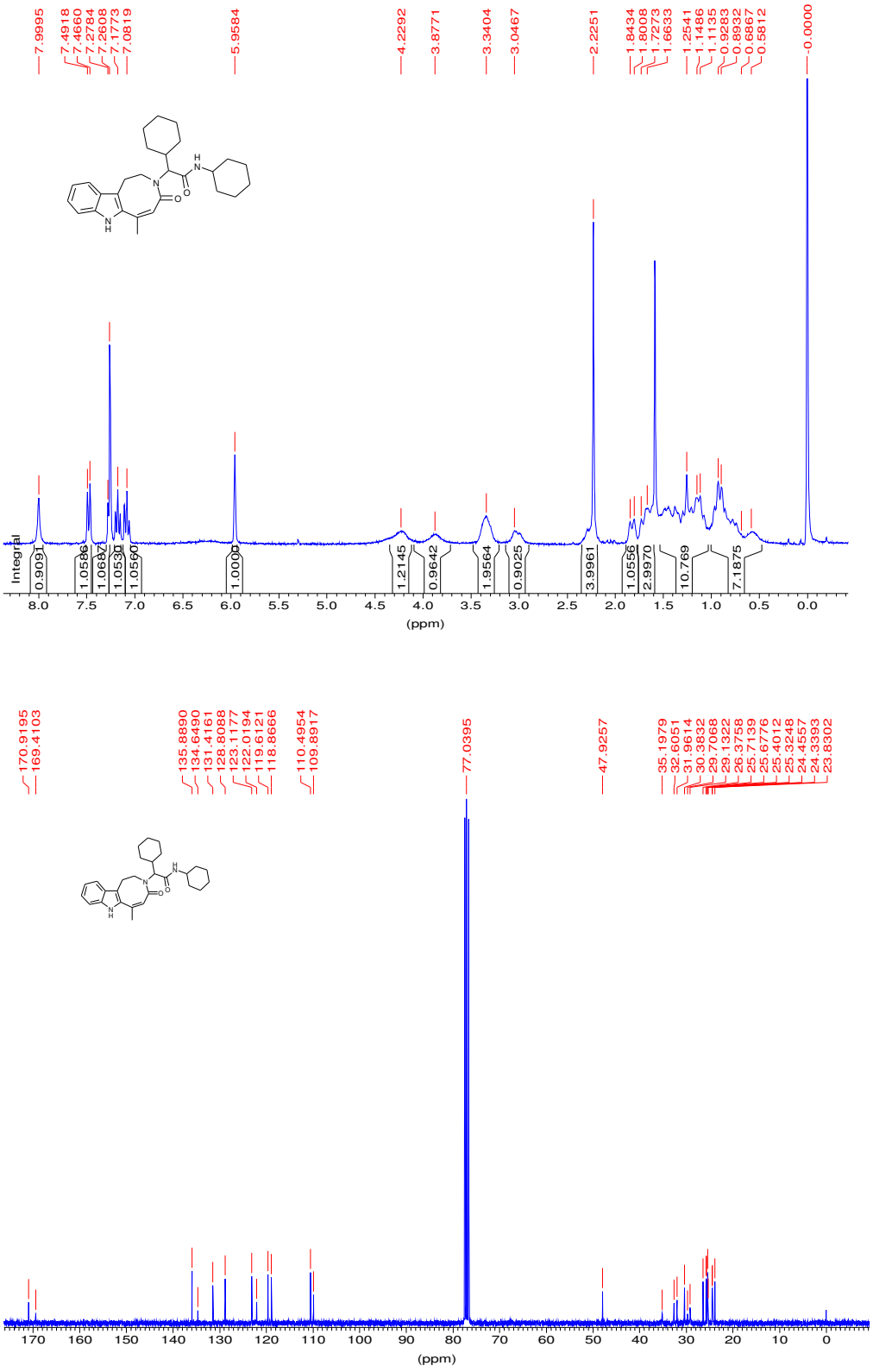


^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR (75 MHz, $CDCl_3$) of compound **6f**

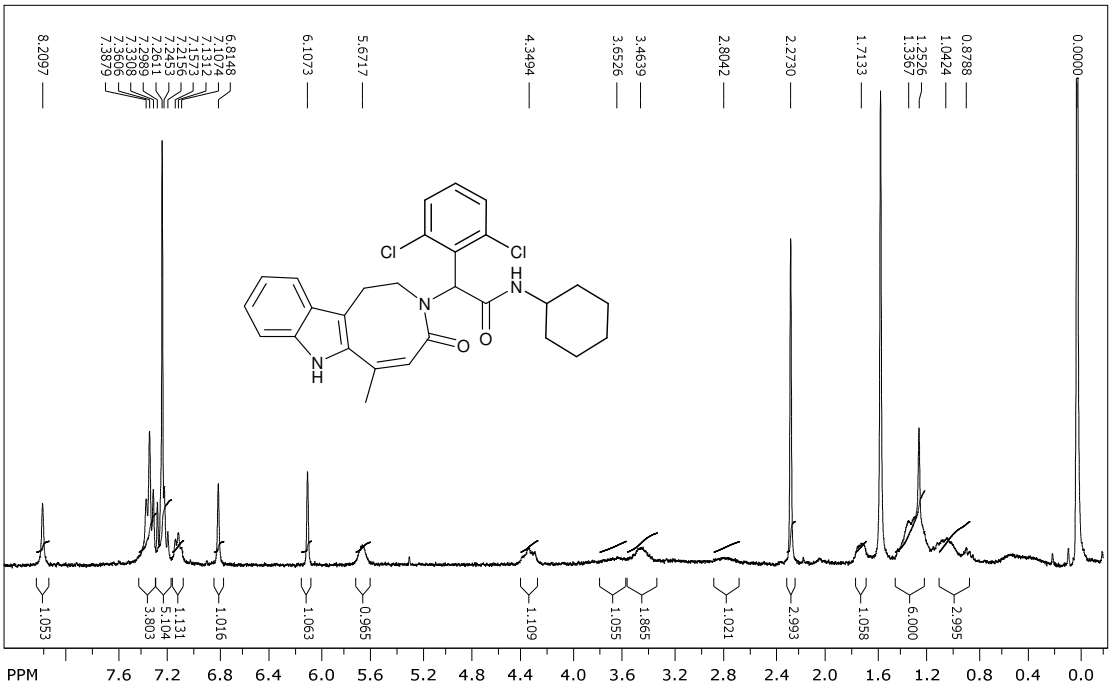


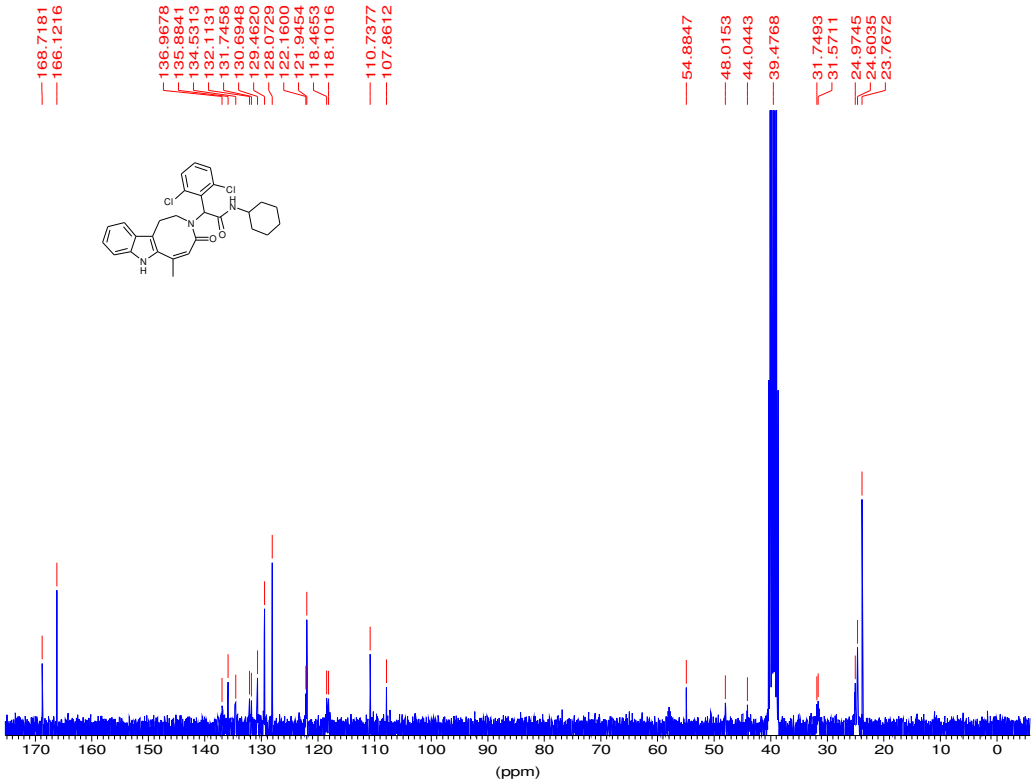


^{1}H and ^{13}C NMR of compound **6g** (300 MHz, $CDCl_3$)

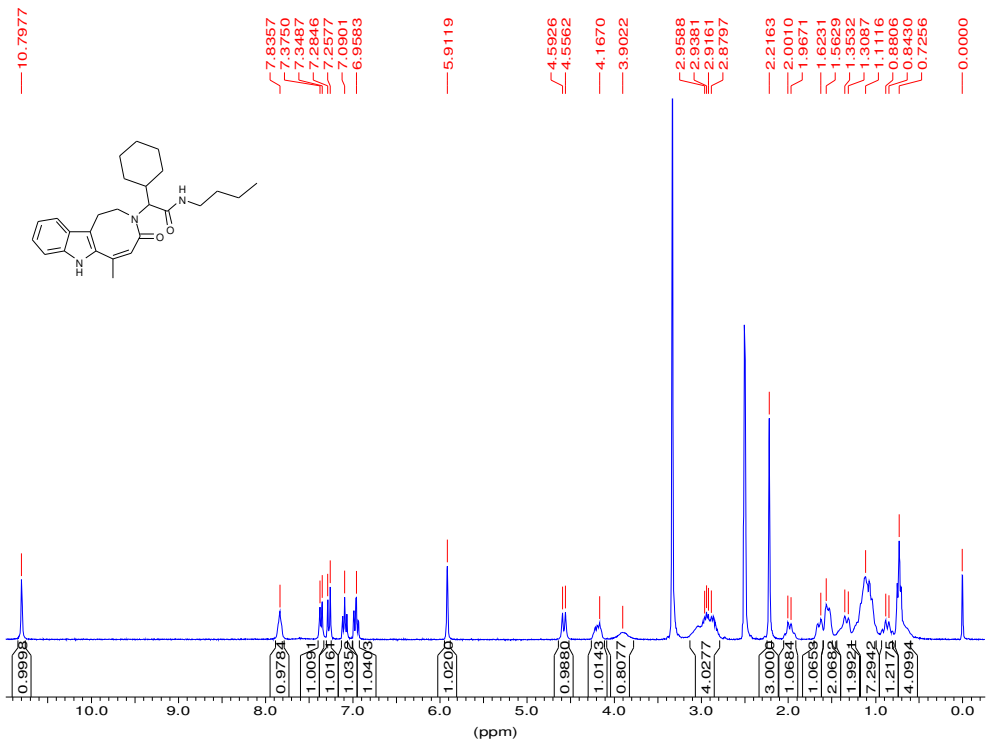


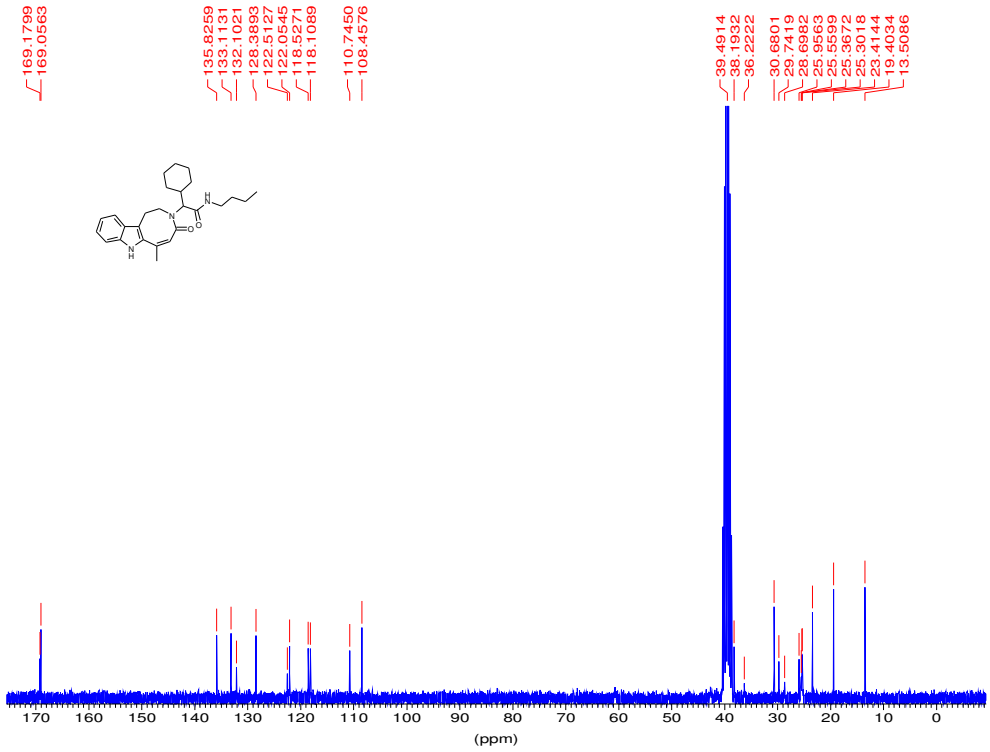
^{1}H NMR (300 MHz, $CDCl_3$) and ^{13}C NMR (75 MHz, DMSO-d_6) of compound **6h**



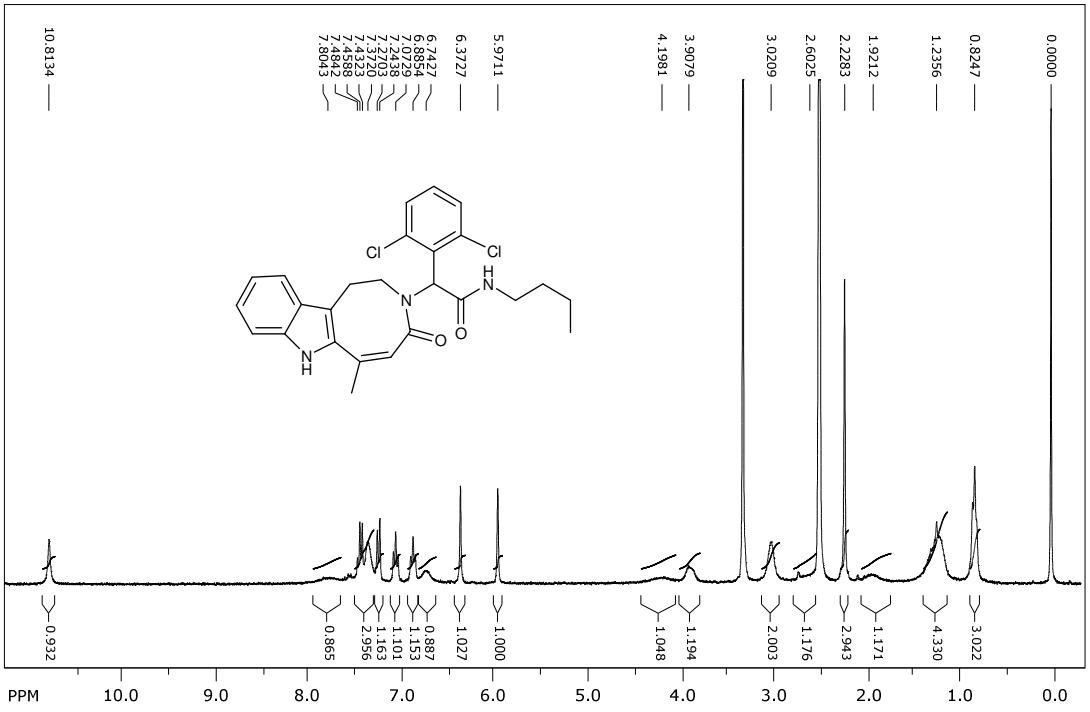


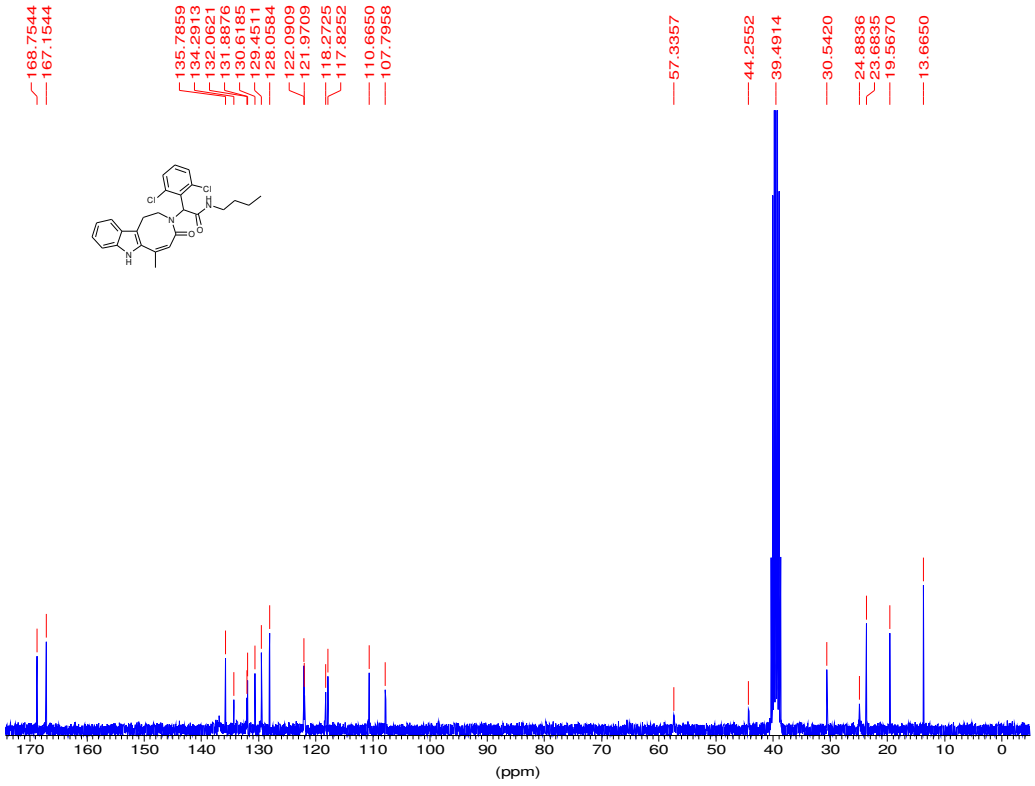
^{1}H and ^{13}C NMR of compound **6i** (300 MHz, DMSO-d_6)



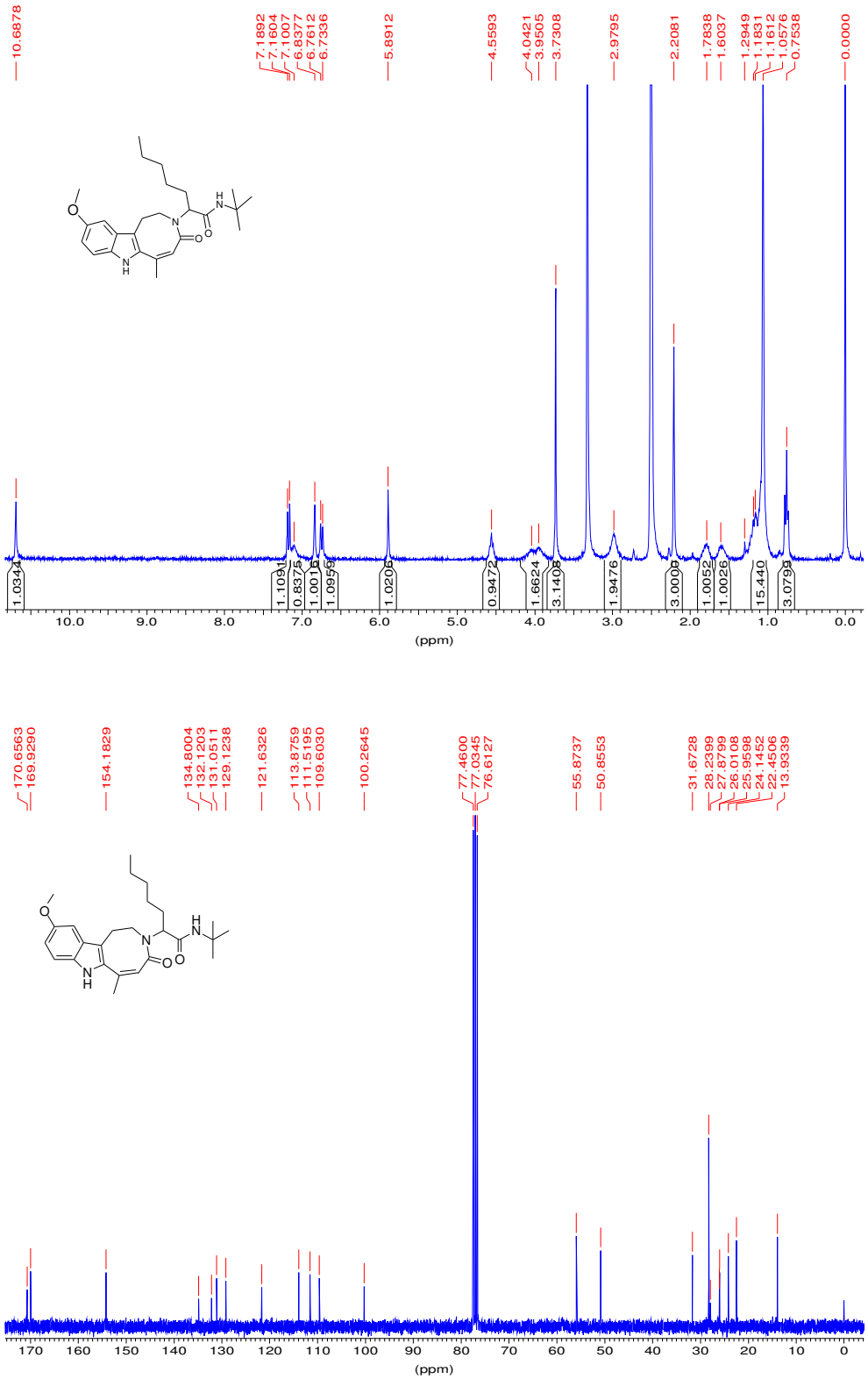


^{1}H NMR (300 MHz, DMSO-d$_6$) and ^{13}C NMR (75 MHz, DMSO-d$_6$) of compound **6j**

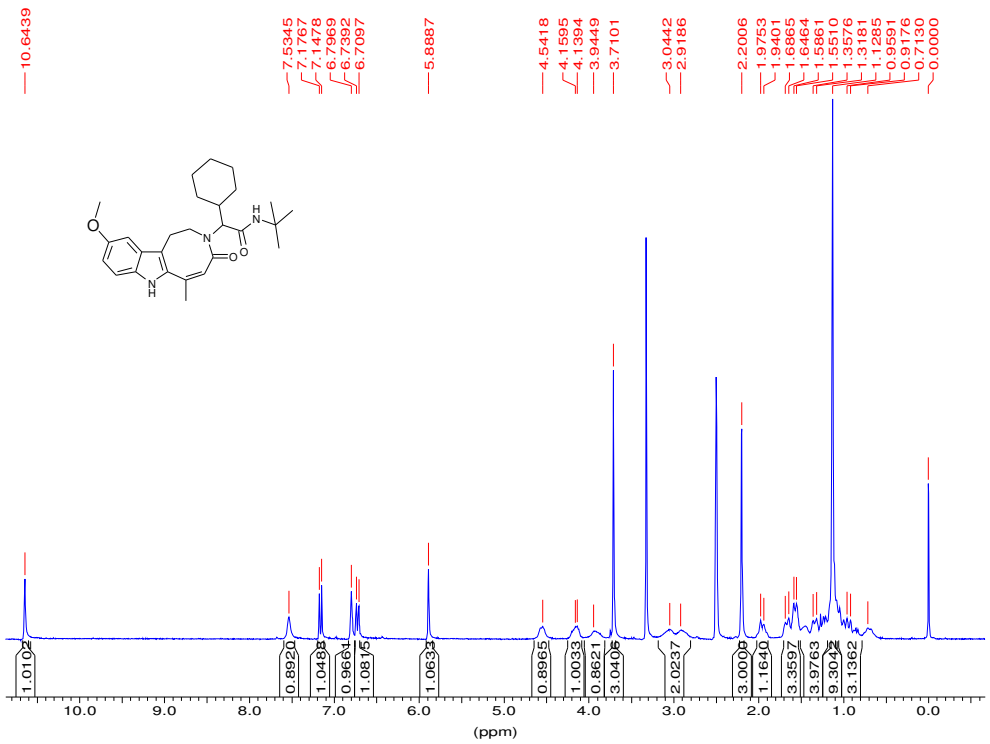


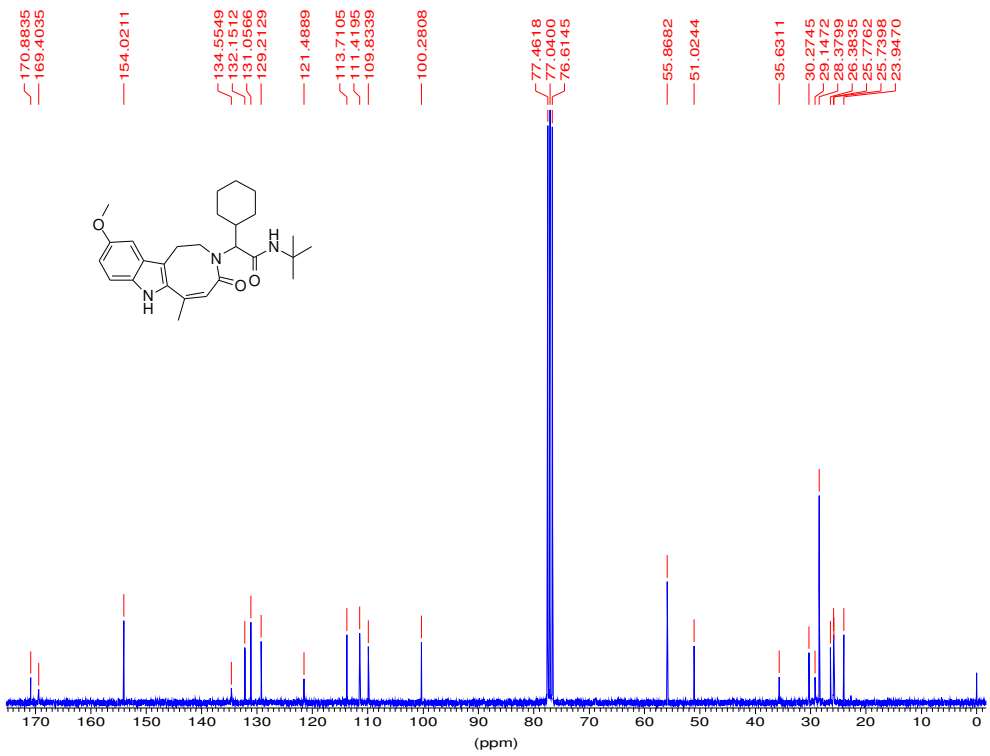


^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR (75 MHz, $CDCl_3$) of compound **6k**

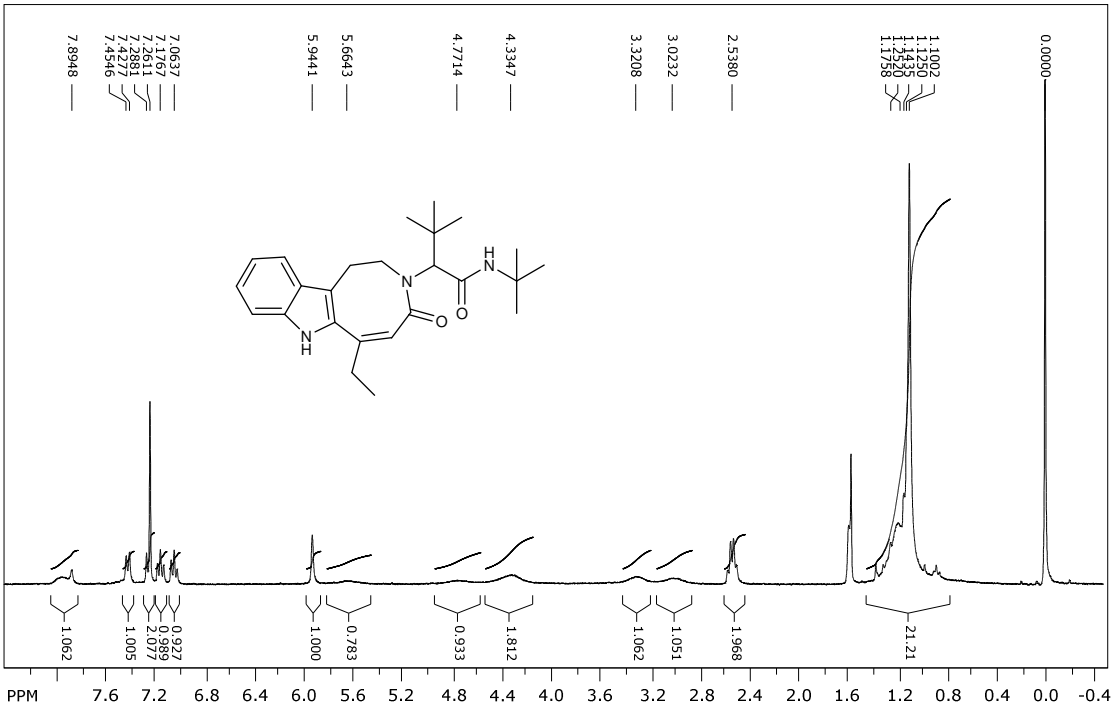


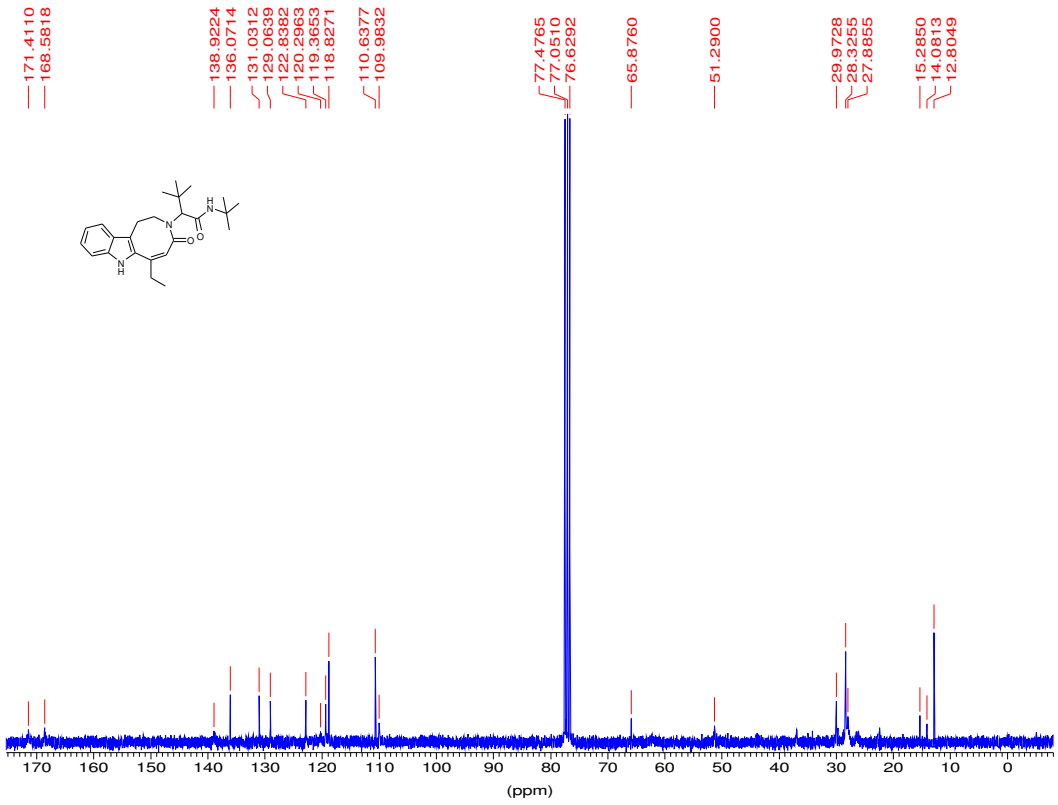
^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR (75 MHz, $CDCl_3$) of compound **6l**



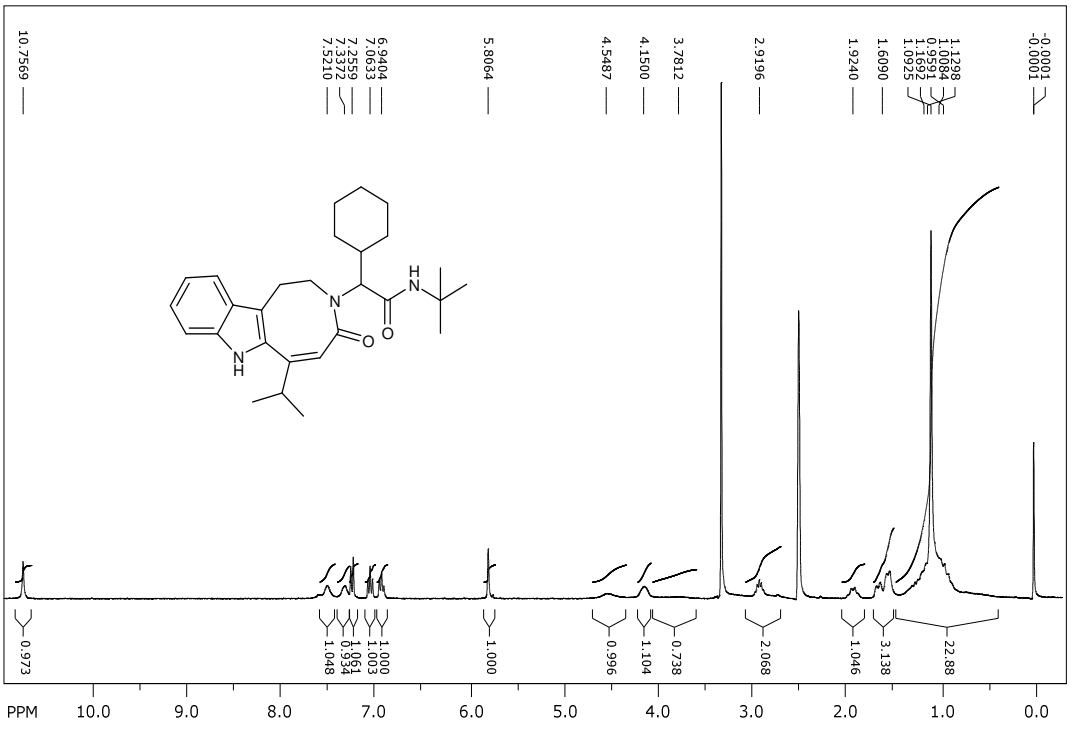


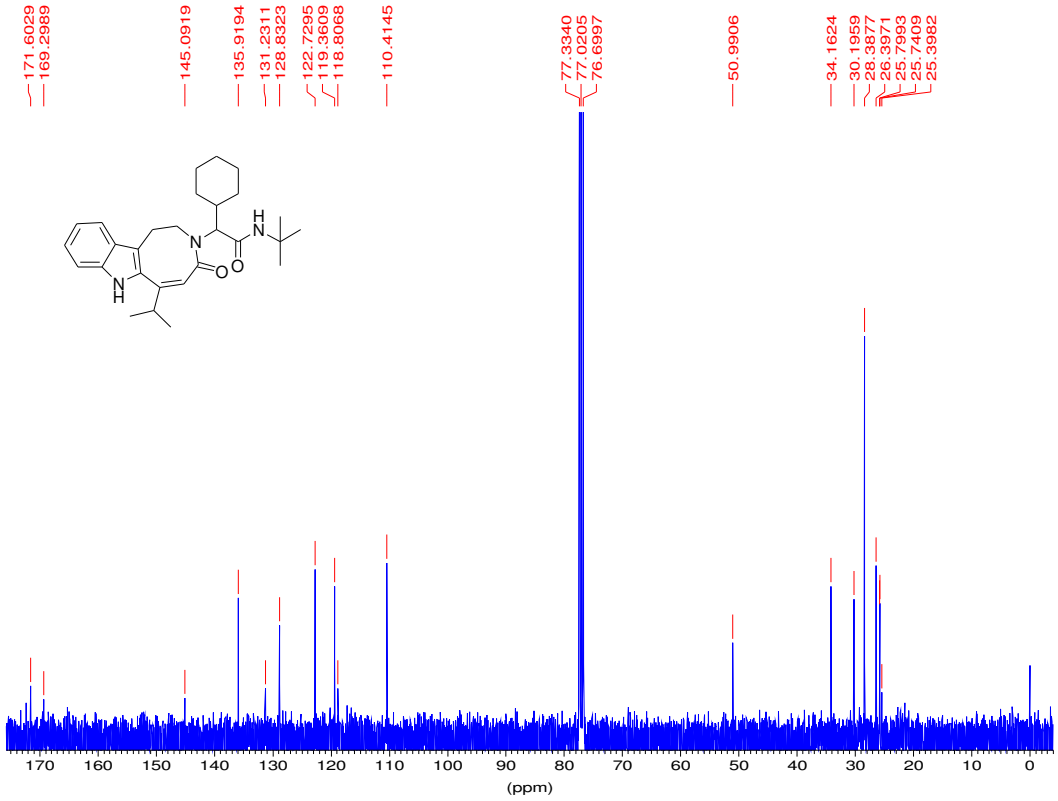
^{1}H NMR and ^{13}C NMR of compound **6m** (300 MHz, $CDCl_3$)



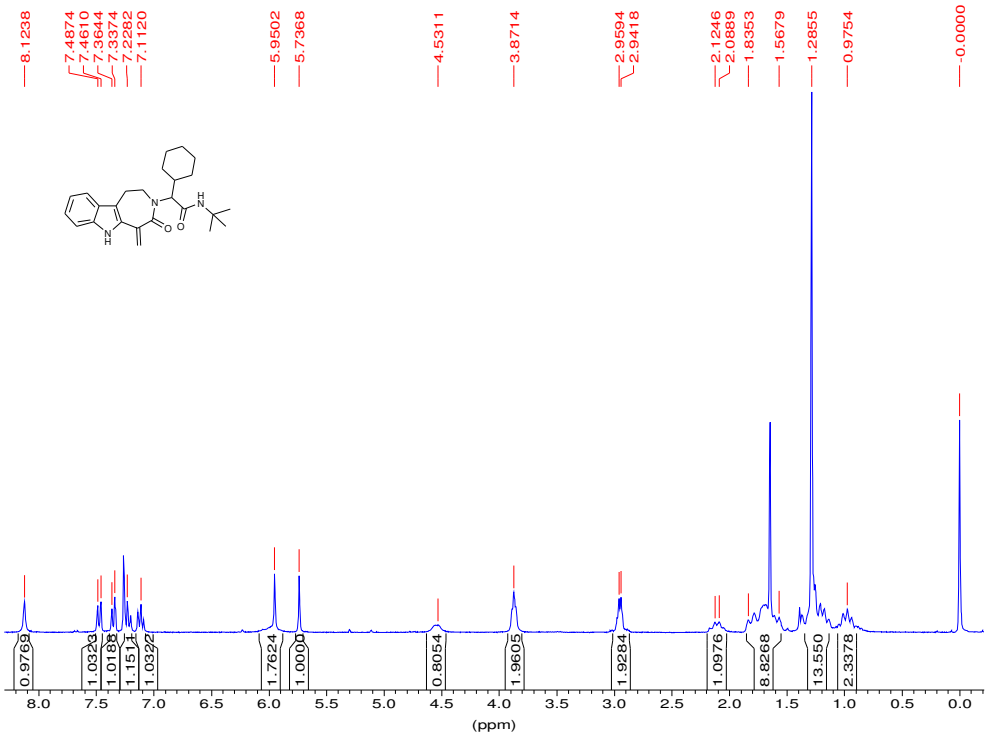


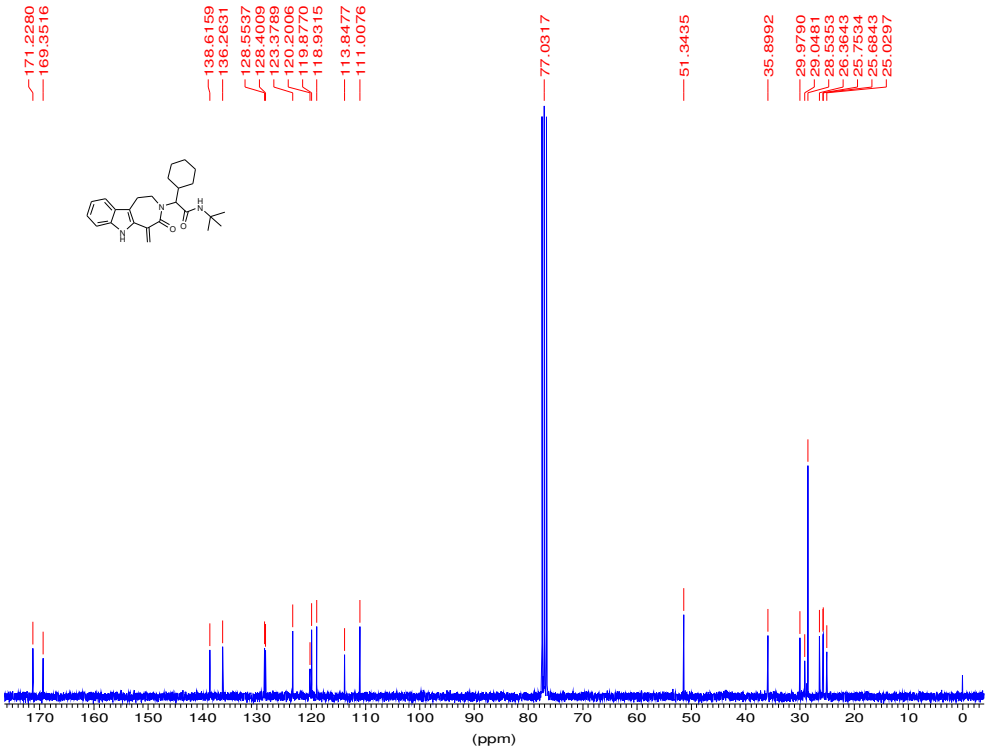
^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR (100 MHz, $CDCl_3$) of compound **6o**



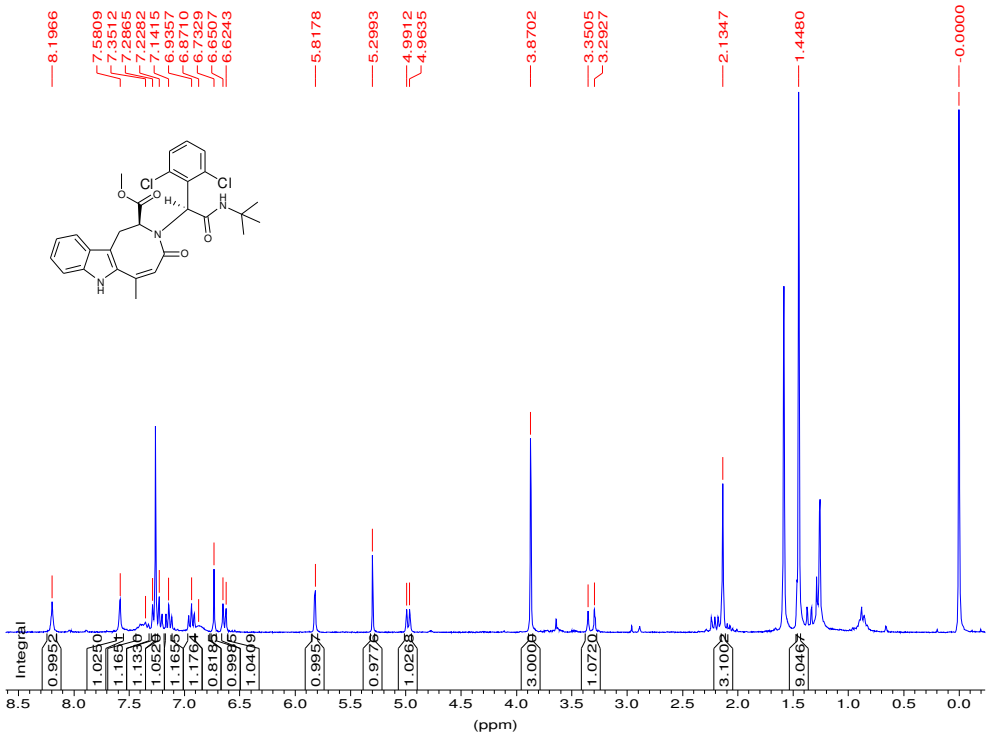


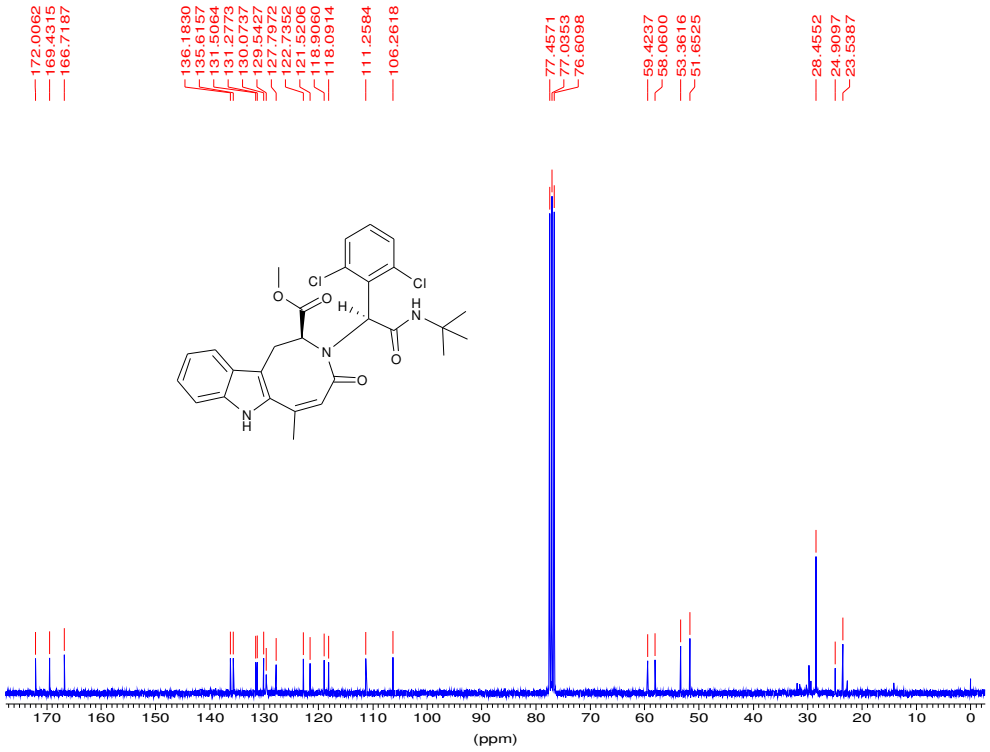
^{1}H and ^{13}C NMR spectra of compound **6q** (300 MHz, $CDCl_3$)





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





^{1}H and ^{13}C NMR spectra of compound **6s** (400 MHz, $CDCl_3$)