Supporting Information for

Rapid and selective access to three distinct sets of indole-based heterocycles from a single set of Ugi-adducts under microwave heating

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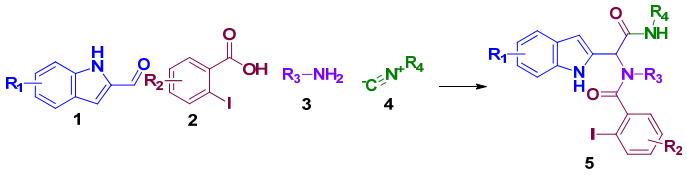
Contents:

General Experimental

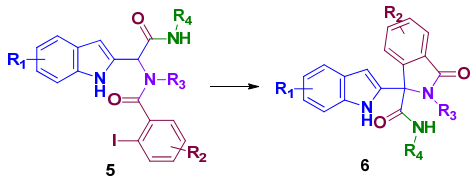
All of the microwave-assisted reactions were performed in sealed tubes (capacity 10 mL) under nitrogen atmosphere under microwave heating system (CEM Corp.) at the specified temperature using the standard mode of operation. All target products were characterized by ^{1}H NMR, ^{13}C NMR, MS and HRMS. Nuclear magnetic resonance spectra were recorded on a Brucker AMX-300 or 400 MHz instrument (TMS as IS). Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). Low- and high-resolution mass spectra were given with an electric ionization (EI) and electrospray and a LCQ-DECA spectrometer produced by Finnigan MAT-95.

General procedure for preparation of Ugi products 5.



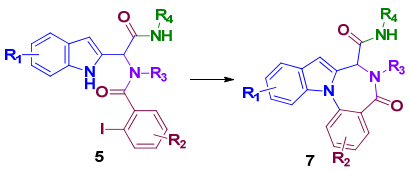
To a solution of amine **3** (1.0 mmol) in dry MeOH (5.0 mL) was added aldehyde **1** (1.0 mmol), and the reaction mixture was stirred at room temperature for 10 min. After addition of acid **2** (1.0 mmol), the reaction mixture was stirred for 5 min followed by addition of isocyanide **4** (1.0 mmol), and the reaction mixture was stirred at room temperature for 3 days. The solvent was removed under reduced pressure. The residue was purified by flash chromatography to give the corresponding Ugi products **5**.

General procedure for the preparation of compounds 6.



A high-pressure microwave vessel was loaded with the Ugi adduct **5** (0.04 mmol, 1.0 equiv) and Cs_2CO_3 (0.08 mmol, 2.0 equiv) in DMSO (0.02 M). The vessel was degassed, refilled with argon, and sealed. The mixture was subjected to microwave heating at 80 ^{o}C for 40 min. After cooling, the reaction mixture was extracted with ethyl acetate. The organic extracts were washed with water and brine, dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography to give the corresponding products **6**.

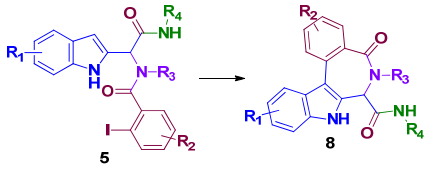
General procedure for the preparation of compounds 7.



A high-pressure microwave vessel was loaded with the Ugi adduct **5** (0.04 mmol, 1.0 equiv), CuI (0.002 mmol, 0.05 equiv), *L*-proline (0.004 mmol, 0.1 equiv), and K_2CO_3 (0.08 mmol, 2.0 equiv) in

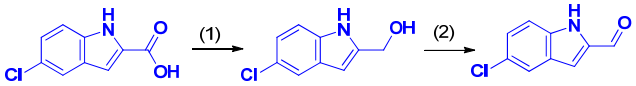
DMSO (0.02 M). The vessel was degassed, refilled with argon, and sealed. The mixture was subjected to microwave heating at 90 °C for 40 min. After cooling, the reaction mixture was extracted with ethyl acetate. The organic extracts were washed with water and brine, dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography to give the corresponding products **7**.

General procedure for the preparation of compounds 8.



A high-pressure microwave vessel was loaded with the Ugi adduct **5** (0.04 mmol, 1.0 equiv), $Pd(OAc)_2$ (0.002 mmol, 0.05 equiv), PPh_3 (0.004 mmol, 0.1 equiv), and K_2CO_3 (0.08 mmol, 2.0 equiv) in dry dioxane/acetonitrile (v/v =3/1, 0.02 M). The vessel was degassed, refilled with argon, and sealed. The mixture was subjected to microwave heating at 110 °C for 2 h. After cooling, the crude was filtered through celite, and the resulting solution was concentrated and purified by flash chromatography to give the corresponding products **8**.

Preparation of 5-chloro-1*H*-indole-2-carbaldehyde.

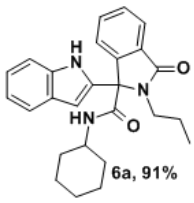


(1) A solution of 5-chloro-1*H*-indole-2-carboxylic acid (1 g, 5.11 mmol) in dry THF (20 mL) was treated carefully with $LiAlH_4$ (388 mg, 10.22 mmol) at room temperature for 6 h. Additional small portions of lithium aluminum hydride were added until the conversion of starting material was complete via TLC. The reaction was quenched by 80% aqueous MeOH solution (2.0 mL), and the resulting suspension filtered and concentrated in vacuo. Purification by flash column chromatography on silica gave 5-chloro-1*H*-2-hydroxymethylindole as a white solid (863 mg, 93%).

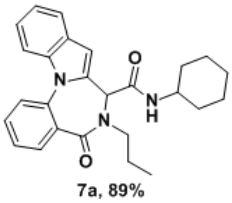
(2) A mixture of 5-chloro-1*H*-2-hydroxymethylindole (800 mg, 4.40 mmol) and activated manganese dioxide (3.83 g) in dichloromethane (30 mL) was stirred at room temperature for 18 h. The reaction solution was filtered followed by concentrating the filtrate under a reduced pressure. The residue was purified by silica gel column chromatography to give 5-chloro-1*H*-indole-2-carbaldehyde as a pale brown solid (672 mg, 85%).

Compound 5-methoxy-1*H*-indole-2-carbaldehyde was prepared by a similar procedure to 5-chloro-1*H*-indole-2-carbaldehyde from 5-methoxy-1*H*-indole-2-carboxylic acid.

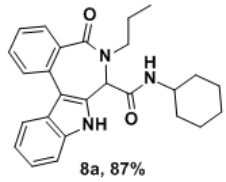
Spectroscopy Data.



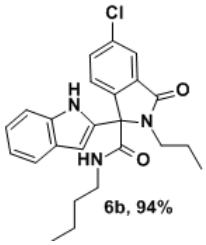
***N*-Cyclohexyl-1-(1*H*-indol-2-yl)-3-oxo-2-propylisoindoline-1-carboxamide (6a).** ^{1}H NMR (400 MHz,$CDCl_3$) δ 9.93 (s, 1H), 7.76 (d, J = 7.2 Hz, 1H), 7.51-7.43 (m, 4H), 7.40 (d, J = 8.4 Hz, 1H), 7.19 (t, J = 7.2 Hz, 1H), 7.08 (t, J = 7.2 Hz, 1H), 6.19 (s, 2H), 3.81-3.73 (m, 1H), 3.58-3.50 (m, 1H), 3.38-3.30 (m, 1H), 1.94-1.92 (m, 1H), 1.71-1.69 (m, 2H), 1.60-1.58 (m, 4H), 1.37-1.26 (m, 2H), 1.19-1.06 (m, 2H), 0.99-0.91 (m, 1H), 0.83 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.79, 168.19, 146.41, 136.14, 133.74, 132.87, 129.81, 129.48, 127.71, 124.08, 122.70, 122.53, 120.76, 120.18, 111.58, 102.59, 71.17, 49.34, 44.90, 32.72, 32.44, 25.36, 24.94, 24.80, 21.60, 11.95; MS (EI, m/z) 415 $[M]^+$; HRMS (EI) calcd for $C_{26}H_{29}N_3O_2$ $[M]^+$ 415.2260, found 415.2261.



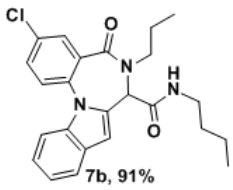
***N*-Cyclohexyl-5-oxo-6-propyl-6,7-dihydro-5*H*-benzo[6,7][1,4]diazepino[1,2-a]indole-7-carboxamide (7a).** ^{1}H NMR (400 MHz,$CDCl_3$) δ 7.96 (d, J = 8.4 Hz, 1H), 7.69-7.67 (m, 2H), 7.62 (d, J = 8.0 Hz, 1H), 7.53 (t, J = 8.0 Hz, 1H), 7.35 (t, J = 8.0 Hz, 1H), 7.29 (t, J = 8.4 Hz, 1H), 7.23 (t, J = 8.0 Hz, 1H), 6.72 (s, 1H), 5.33 (d, J = 8.4 Hz, 1H), 5.08 (s, 1H), 3.74-3.60 (m, 2H), 3.41-3.32 (m, 1H), 1.79-1.64 (m, 2H), 1.55-1.43 (m, 4H), 1.16-1.04 (m, 3H), 0.98-0.88 (m, 1H), 0.93 (t, J = 7.2 Hz, 3H), 0.81-0.73 (m, 1H), 0.56-0.47 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.39, 165.16, 137.08, 136.06, 134.68, 132.77, 131.59, 130.36, 128.76, 126.45, 123.68, 122.59, 121.65, 121.42, 111.55, 104.40, 60.00, 51.57, 48.68, 32.63, 32.42, 25.20, 24.78, 24.64, 21.27, 11.33; MS (EI, m/z) 415 $[M]^+$; HRMS (EI) calcd for $C_{26}H_{29}N_3O_2$ $[M]^+$ 415.2260, found 415.2267.



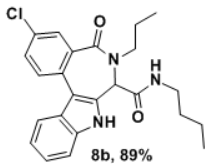
***N*-Cyclohexyl-5-oxo-6-propyl-5,6,7,8-tetrahydrobenzo[5,6]azepino[3,4-b]indole-7-carboxamide (8a).** ^{1}H NMR (400 MHz,$CDCl_3$) δ 10.48 (s, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 7.6 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.28 (t, J = 8.0 Hz, 1H), 7.20-7.18 (m, 3H), 5.55 (br s, 1H), 5.17 (s, 1H), 3.84 (m, 1H), 3.47-3.39 (m, 2H), 1.63-1.52 (m, 2H), 1.47-1.37 (m, 4H), 1.12-1.09 (m, 2H), 0.97-0.90 (m, 2H), 0.73 (t, J = 7.2 Hz, 3H), 0.71-0.67 (m, 1H), 0.54-0.52 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.83, 165.56, 135.28, 133.91, 132.92, 131.49, 131.37, 130.99, 130.24, 125.81, 124.97, 124.26, 121.97, 120.06, 118.46, 111.35, 76.48, 76.16, 75.84, 58.49, 52.14, 47.84, 31.46, 31.35, 24.29, 23.81, 23.72, 20.54, 10.35; MS (EI, m/z) 415 $[M]^+$; HRMS (EI) calcd for $C_{26}H_{29}N_3O_2$ $[M]^+$ 415.2260, found 415.2262.



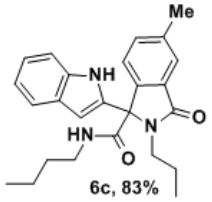
***N*-Butyl-5-chloro-1-(1*H*-indol-2-yl)-3-oxo-2-propylisoindoline-1-carboxamide (6b).** ^{1}H NMR (400 MHz,$CDCl_3$) δ 10.05 (s, 1H), 7.51-7.46 (m, 3H), 7.43-7.40 (m, 2H), 7.19 (t, J = 7.2 Hz, 1H), 7.08 (t, J = 8.0 Hz, 1H), 7.01 (t, J = 5.2 Hz, 1H), 6.21 (s, 1H), 3.46-3.41 (m, 2H), 3.38-3.31 (m, 1H), 3.29-3.22 (m, 1H), 1.66-1.46 (m, 4H), 1.32-1.23 (m, 2H), 0.90 (t, J = 7.2 Hz, 3H), 0.79 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ168.56, 168.53, 144.70, 136.28, 135.76, 133.16, 131.44, 127.66, 124.14, 123.71, 122.68, 120.79, 120.27, 111.66, 102.75, 71.19, 45.22, 40.09, 31.35, 21.24, 20.15, 13.79, 11.86; MS (EI, m/z) 423 $[M]^+$; HRMS (EI) calcd for $C_{24}H_{26}ClN_3O_2$ $[M]^+$ 423.1714, found 423.1719.



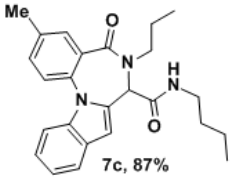
***N*-Butyl-3-chloro-5-oxo-6-propyl-6,7-dihydro-5*H*-benzo[6,7][1,4]diazepino[1,2-a]indole-7-carboxamide (7b).** ^{1}H NMR (400 MHz,$CDCl_3$) δ 7.95 (s, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.63-7.56 (m, 2H), 7.48-7.46 (m, 1H), 7.31 (t, J = 7.2 Hz, 1H), 7.25-7.22 (m, 1H), 6.71 (s, 1H), 5.58 (t, J = 6.0 Hz, 1H), 5.07 (s, 1H), 3.68-3.63 (m, 2H), 3.02-2.97 (m, 1H), 2.85-2.79 (m, 1H), 1.76-1.63 (m, 2H), 0.97-0.96 (m, 4H), 0.92 (t, J = 7.6 Hz, 3H), 0.76 (t, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.10, 165.97, 136.73, 136.00, 133.28, 132.57, 132.03, 131.78, 131.64, 128.78, 124.06, 123.87, 122.02, 121.62, 111.39, 104.86, 59.97, 51.82, 39.84, 31.66, 21.29, 19.91, 13.73, 11.40; MS (EI, m/z) 423 $[M]^+$; HRMS (EI) calcd for $C_{24}H_{26}ClN_3O_2$ $[M]^+$ 423.1714, found 423.1712.



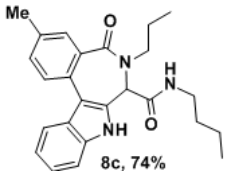
***N*-Butyl-3-chloro-5-oxo-6-propyl-5,6,7,8-tetrahydrobenzo[5,6]azepino[3,4-b]indole-7-carboxamide (8b).** ^{1}H NMR (400 MHz,$CDCl_3$) δ 11.25 (s, 1H), 7.99 (s, 1H), 7.89-7.87 (m, 1H), 7.79 (d, J = 8.4 Hz, 1H), 7.22-7.19 (m, 4H), 5.72 (s, 1H), 5.25 (s, 1H), 3.85 (m, 1H), 3.39 (m, 1H), 3.03 (m, 1H), 2.71 (m, 1H), 1.64-1.51 (m, 2H), 0.88-0.84 (m, 4H), 0.70-0.66 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.37, 167.15, 136.28, 135.42, 135.08, 132.54, 131.37, 131.10, 127.93, 125.06, 123.04, 121.16, 119.22, 112.45, 111.26, 59.06, 53.20, 39.72, 31.48, 21.37, 19.73, 13.74, 11.24; MS (EI, m/z) 423 $[M]^+$; HRMS (EI) calcd for $C_{24}H_{26}ClN_3O_2$ $[M]^+$ 423.1714, found 423.1705.



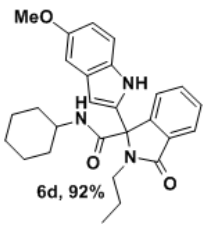
***N*-Butyl-1-(1*H*-indol-2-yl)-5-methyl-3-oxo-2-propylisoindoline-1-carboxamide (6c).** ^{1}H NMR (400 MHz,$CDCl_3$) δ 10.01 (s, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.41-7.37 (m, 2H), 7.32-7.29 (m, 2H), 7.17 (t, J = 8.0 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 6.84 (t, J = 5.6 Hz, 1H), 6.22 (s, 1H), 3.47-3.41 (m, 2H), 3.35-3.28 (m, 1H), 3.26-3.18 (m, 1H), 2.32 (s, 3H), 1.75-1.41 (m, 6H), 0.88 (t, J = 7.2 Hz, 3H), 0.78 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.80, 169.23, 143.82, 139.55, 136.18, 134.05, 133.75, 130.08, 127.74, 123.99, 122.52, 122.39, 120.72, 120.05, 111.58, 102.57, 71.02, 44.91, 39.94, 31.35, 21.44, 21.34, 20.11, 13.79, 11.88; MS (EI, m/z) 403 $[M]^+$; HRMS (EI) calcd for $C_{25}H_{29}N_3O_2$ $[M]^+$ 403.2260, found 403.2262.



***N*-Butyl-3-methyl-5-oxo-6-propyl-6,7-dihydro-5*H*-benzo[6,7][1,4]diazepino[1,2-a]indole-7-carboxamide (7c)**. ^{1}H NMR (400 MHz,$CDCl_3$) δ 7.77 (s, 1H), 7.66 (t, J = 7.6 Hz, 2H), 7.51 (d, J = 8.4 Hz, 1H), 7.33-7.27 (m, 2H), 7.22 (t, J = 8.0 Hz, 1H), 6.69 (s, 1H), 5.54 (t, J = 6.0 Hz, 1H), 5.06 (s, 1H), 3.74-3.58 (m, 2H), 3.02-2.93 (m, 1H), 2.81-2.73 (m, 1H), 2.40 (s, 3H), 1.78-1.64 (m, 2H), 0.97-0.86 (m, 4H), 0.93 (t, J = 7.6 Hz, 3H), 0.73 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.49, 161.34, 131.93, 131.41, 131.09, 127.86, 127.53, 127.29, 124.95, 123.66, 118.65, 117.40, 116.58, 116.40, 106.64, 99.12, 55.08, 46.68, 34.74, 26.63, 16.34, 15.98, 14.88, 8.76, 6.43; MS (EI, m/z) 403 $[M]^+$; HRMS (EI) calcd for $C_{25}H_{29}N_3O_2$ $[M]^+$ 403.2260, found 403.2256.

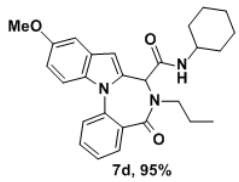


***N*-Butyl-3-methyl-5-oxo-6-propyl-5,6,7,8-tetrahydrobenzo[5,6]azepino[3,4-b]indole-7-carboxamide (8c).** ^{1}H NMR (400 MHz,$CDCl_3$) δ 10.91 (s, 1H), 7.93-7.91 (m, 1H), 7.81 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.19-1.17 (m, 3H), 5.65 (br s, 1H), 5.20 (s, 1H), 3.87-3.84 (m, 1H), 3.42-3.39 (m, 1H), 3.04-3.01 (m, 1H), 2.67-2.65 (m, 1H), 2.32 (s, 3H), 1.62-1.50 (m, 2H), 0.83-0.78 (m, 4H), 0.68-0.65 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.93, 167.56, 136.29, 135.62, 134.46, 133.72, 132.21, 129.57, 126.67, 125.23, 122.85, 120.90, 119.48, 112.35, 112.21, 59.26, 53.19, 39.69, 31.45, 21.44, 21.20, 19.71, 13.79, 11.29; MS (EI, m/z) 403 $[M]^+$ HRMS (EI) calcd for $C_{25}H_{29}N_3O_2$ $[M]^+$ 403.2260, found 403.2254.



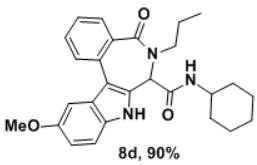
6d, 92%

***N*-Cyclohexyl-1-(5-methoxy-1*H*-indol-2-yl)-3-oxo-2-propylisoindoline-1-carboxamide (6d).** ^{1}H NMR (400 MHz,$CDCl_3$) δ 9.88 (s, 1H), 7.71 (d, J = 7.2 Hz, 1H), 7.50-7.49 (m, 2H), 7.45-7.41 (m, 1H), 7.29 (d, J = 8.8 Hz, 1H), 6.94 (s, 1H), 6.85 (d, J = 8.8 Hz, 1H), 6.28 (d, J = 8.0 Hz, 1H), 6.11 (s, 1H), 3.79 (s, 3H), 3.78-3.73 (m, 1H), 3.56-3.48 (m, 1H), 3.38-3.31 (m, 1H), 1.94-1.91 (m, 1H), 1.71-1.68 (m, 2H), 1.61-1.57 (m, 4H), 1.37-1.28 (m, 2H), 1.18-1.08 (m, 2H), 1.00-0.94 (m, 1H), 0.82 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.76, 168.16, 154.41, 146.42, 134.30, 132.83, 131.36, 129.83, 129.41, 128.11, 124.01, 122.69, 113.05, 112.36, 102.32, 102.04, 71.22, 55.87, 49.34, 44.87, 32.70, 32.42, 25.36, 24.95, 24.81, 21.56, 11.94; MS (EI, m/z) 445 $[M]^+$; HRMS (EI) calcd for $C_{27}H_{31}N_3O_3$ $[M]^+$ 445.2365, found 445.2363.



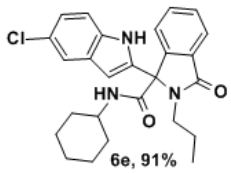
7d, 95%

***N*-Cyclohexyl-10-methoxy-5-oxo-6-propyl-6,7-dihydro-5*H*-benzo[6,7][1,4]diazepino[1,2-a]indole-7-carboxamide (7d).** ^{1}H NMR (400 MHz,$CDCl_3$) δ 7.96 (d, J = 7.6 Hz, 1H), 7.59-7.55 (m, 2H), 7.51 (t, J = 7.6 Hz, 1H), 7.34 (t, J = 8.0 Hz, 1H), 7.13 (s, 1H), 6.95 (d, J = 8.2 Hz, 1H), 6.64 (s, 1H), 5.25 (d, J = 8.4 Hz, 1H), 5.04 (s, 1H), 3.88 (s, 3H), 3.76-3.63 (m, 2H), 3.42-3.34 (m, 1H), 1.79-1.66 (m, 2H), 1.55-1.42 (m, 4H), 1.17-1.08 (m, 3H), 0.93 (t, J = 7.6 Hz, 3H), 0.87-0.76 (m, 2H), 0.54-0.49 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ167.47, 165.25, 155.39, 137.55, 134.90, 132.89, 131.74, 131.12, 130.26, 129.48, 126.40, 122.40, 113.72, 112.58, 104.15, 103.02, 77.48, 77.16, 76.84, 60.11, 55.95, 51.70, 48.71, 32.79, 32.59, 25.31, 24.88, 24.73, 21.40, 11.47; MS (EI, m/z) 445 $[M]^+$; HRMS (EI) calcd for $C_{27}H_{31}N_3O_3$ $[M]^+$ 445.2365, found 445.2371.



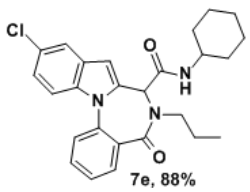
8d, 90%

***N*-Cyclohexyl-11-methoxy-5-oxo-6-propyl-5,6,7,8-tetrahydrobenzo[5,6]azepino[3,4-b]indole-7-carboxamide (8d).** ^{1}H NMR (400 MHz,$CDCl_3$) δ 11.01 (s, 1H), 7.97 (d, J = 7.2 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.51 (t, J = 7.2 Hz, 1H), 7.35 (s, 1H), 7.25 (t, J = 7.2 Hz, 1H), 7.07 (d, J = 8.8 Hz, 1H), 6.83 (d, J = 8.8 Hz, 1H), 5.51 (d, J = 8.0 Hz, 1H), 5.18 (s, 1H), 3.87 (s, 3H), 3.83-3.76 (m, 1H), 3.48-3.38 (m, 2H), 1.63-1.53 (m, 2H), 1.44-1.37 (m, 4H), 1.30-1.25 (m, 2H), 1.15-1.07 (m, 4H), 0.72 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.60, 166.63, 155.09, 135.73, 134.13, 132.72, 131.68, 131.43, 131.03, 126.23, 125.78, 125.73, 113.06, 112.92, 112.03, 101.25, 59.41, 52.96, 48.67, 32.41, 32.38, 25.30, 24.83, 24.70, 21.49, 11.34; MS (EI, m/z) 445 $[M]^+$; HRMS (EI) calcd for $C_{27}H_{31}N_3O_3$ $[M]^+$ 445.2365, found 445.2365.



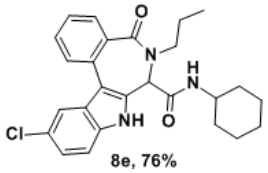
6e, 91%

1-(5-Chloro-1*H*-indol-2-yl)-*N*-cyclohexyl-3-oxo-2-propylisoindoline-1-carboxamide (6e). ^{1}H NMR (400 MHz,CD_3OD) δ 10.48 (s, 1H), 7.68 (d, J = 6.0 Hz, 1H), 7.46-7.33 (m, 3H), 7.18 (d, J = 8.0 Hz, 1H), 6.95 (t, J = 7.2 Hz, 1H), 6.87 (t, J = 7.2 Hz, 1H), 6.36 (s, 1H), 3.48-3.42 (m, 1H), 3.21-3.19 (m, 1H), 3.18-3.13 (m, 1H), 1.63-1.29 (m, 6H), 1.22-1.08 (m, 6H), 0.71 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.71, 167.03, 145.23, 134.38, 133.48, 131.95, 128.71, 128.54, 127.71, 124.77, 123.07, 121.82, 121.60, 119.05, 111.59, 101.11, 76.48, 76.16, 75.84, 69.97, 48.40, 43.88, 31.67, 31.37, 24.33, 23.95, 23.80, 20.53, 10.90; MS (EI, m/z) 449 $[M]^+$; HRMS (EI) calcd for $C_{26}H_{28}ClN_3O_2$ $[M]^+$ 449.1870, found 449.1878.



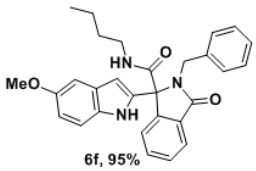
7e, 88%

10-Chloro-*N*-cyclohexyl-5-oxo-6-propyl-6,7-dihydro-5*H*-benzo[6,7][1,4]diazepino[1,2-a]indole-7-carboxamide (7e). ^{1}H NMR (400 MHz,$CDCl_3$) δ 7.96 (d, J = 7.6 Hz, 1H), 7.63 (d, J = 1.6 Hz, 1H), 7.58-7.54 (m, 3H), 7.39-7.35 (m, 1H), 7.23 (dd, J = 8.8 Hz, 1.6 Hz, 1H), 6.66 (s, 1H), 5.34 (d, J = 8.4 Hz, 1H), 5.08 (s, 1H), 3.74-3.61 (m, 2H), 3.41-3.34 (m, 1H), 1.78-1.64 (m, 2H), 1.55-1.42 (m, 4H), 1.22-1.07 (m, 3H), 1.00-0.97 (m, 1H), 0.92 (t, J = 7.2 Hz, 3H), 0.82-0.74 (m, 1H), 0.62-0.53 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.32, 164.88, 138.44, 134.40, 134.38, 132.83, 131.86, 130.32, 129.84, 127.20, 126.79, 123.94, 122.57, 120.85, 112.59, 103.77, 77.48, 77.16, 76.84, 59.94, 51.64, 48.72, 32.67, 32.47, 25.22, 24.75, 24.65, 21.33, 11.36; MS (EI, m/z) 449 $[M]^+$; HRMS (EI) calcd for $C_{26}H_{28}ClN_3O_2$ $[M]^+$ 449.1870, found 449.1862.



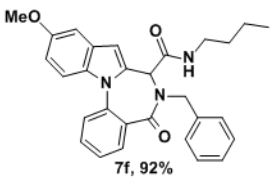
8e, 76%

11-Chloro-*N*-cyclohexyl-5-oxo-6-propyl-5,6,7,8-tetrahydrobenzo[5,6]azepino[3,4-b]indole-7-carboxamide (8e). ^{1}H NMR (400 MHz,$CDCl_3$) δ 10.78 (s, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.82-7.80 (m, 2H), 7.58 (t, J = 7.6 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.01 (d, J = 8.0 Hz, 1H), 6.81 (d, J = 8.4 Hz, 1H), 5.79 (d, J = 7.6 Hz, 1H), 5.16 (s, 1H), 3.90-3.87 (m, 1H), 3.45-3.43 (m, 2H), 1.62-1.48 (m, 6H), 1.30-1.24 (m, 2H), 1.19-1.12 (m, 2H), 1.01-0.95 (m, 1H), 0.89-0.85 (m, 1H), 0.75 (t, J = 7.2Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.81, 166.91, 136.09, 134.47, 133.74, 131.89, 131.52, 126.77, 126.69, 126.18, 125.99, 123.10, 118.58, 113.13, 111.72, 59.36, 53.00, 48.97, 32.52, 32.21, 25.24, 24.73, 21.53, 11.31; MS (EI, m/z) 449 $[M]^+$; HRMS (EI) calcd for $C_{26}H_{28}ClN_3O_2$ $[M]^+$ 449.1870, found 449.1872.



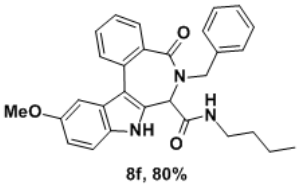
6f, 95%

2-Benzyl-*N*-butyl-1-(5-methoxy-1*H*-indol-2-yl)-3-oxoisoindoline-1-carboxamide (6f). ^{1}H NMR (400 MHz,$CDCl_3$) δ 10.05 (s, 1H), 7.79 (d, J = 7.2 Hz, 1H), 7.58 (d, J = 7.6 Hz, 1H), 7.48 (t, J = 8.4 Hz, 1H), 7.43 (d, J = 7.6 Hz, 1H), 7.39-7.37 (m, 2H), 7.30-7.25 (m, 5H), 6.97 (s, 1H), 6.85 (d, J = 8.8 Hz, 1H), 6.18 (s, 1H), 5.87-5.84 (m, 1H), 5.25 (d, J = 14.4 Hz, 1H), 4.19 (d, J =15.2 Hz, 1H), 3.80 (s, 3H), 2.86-2.81 (m, 1H), 2.68-2.64 (m, 1H), 0.89-0.82 (m, 4H), 0.70 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ170.78, 168.36, 154.40, 147.05, 137.62, 133.91, 133.14, 131.42, 131.00, 129.33, 129.10, 128.97, 128.49, 128.07, 124.11, 122.93, 113.03, 112.38, 102.04, 101.96, 71.74, 55.86, 46.10, 39.51, 30.41, 19.82, 13.58; MS (EI, m/z) 467 $[M]^+$; HRMS (EI) calcd for $C_{29}H_{29}N_3O_3$ $[M]^+$ 467.2209, found 467.2201.



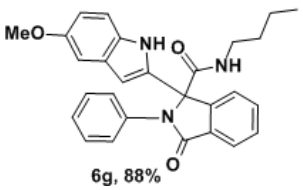
7f, 92%

6-Benzyl-*N*-butyl-10-methoxy-5-oxo-6,7-dihydro-5*H*-benzo[6,7][1,4]diazepino[1,2-a]indole-7-carboxamide (7f). ^{1}H NMR (400 MHz,$CDCl_3$) δ 8.01 (d, J = 7.2 Hz, 1H), 7.62-7.51 (m, 3H), 7.36-7.38 (m, 5H), 7.05 (s, 1H), 6.93 (d, J = 8.4 Hz, 1H), 6.29 (s, 1H), 5.30 (br s, 1H), 5.02 (d, J = 14.8 Hz, 1H), 5.00 (s, 1H), 4.84 (d, J = 14.8 Hz, 1H), 3.86 (s, 3H), 2.86-2.82 (m, 1H), 2.67-2.62 (m, 1H), 0.87 (m, 4H), 0.70-0.69 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.96, 166.14, 155.32, 136.99, 136.13, 135.23, 132.86, 132.03, 131.13, 129.74, 129.47, 129.03, 128.99, 128.20, 126.20, 122.55, 113.57, 112.39, 104.24, 103.10, 58.59, 55.91, 52.67, 39.54, 31.33, 19.80, 13.68; MS (EI, m/z) 468 $[M]^+$; HRMS (EI) calcd for $C_{29}H_{29}N_3O_3$ $[M]^+$ 467.2209, found 467.2210.



8f, 80%

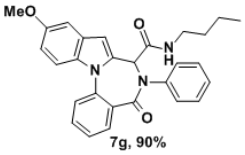
6-Benzyl-*N*-butyl-11-methoxy-5-oxo-5,6,7,8-tetrahydrobenzo[5,6]azepino[3,4-b]indole-7-carboxamide (8f). ^{1}H NMR (400 MHz,$CDCl_3$) δ 9.91 (s, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.63-7.46 (m, 2H), 7.34 (s, 1H), 7.11 (m, 5H), 6.90 (d, J = 8.0 Hz, 1H), 6.78 (d, J = 8.4 Hz, 1H), 5.59 (br s, 1H), 5.09 (s, 1H), 5.04 (d, J = 14.8 Hz, 1H), 4.68 (d, J = 15.2 Hz, 1H), 3.85 (s, 3H), 2.84 (m, 1H), 2.62 (m, 1H), 0.78 (m, 4H), 0.65 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.95, 166.13, 155.27, 136.94, 136.09, 135.19, 132.83, 132.03, 131.09, 129.69, 129.42, 129.00, 128.19, 126.20, 122.54, 113.56, 112.37, 104.22, 103.03, 77.48, 77.16, 76.84, 58.56, 55.89, 52.64, 39.53, 31.32, 19.80, 13.69; MS (EI, m/z) 467 $[M]^+$; HRMS (EI) calcd for $C_{29}H_{29}N_3O_3$ $[M]^+$ 467.2209, found 467.2218.



6g, 88%

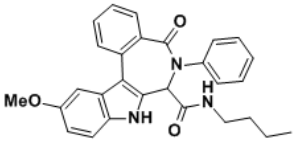
***N*-Butyl-1-(5-methoxy-1*H*-indol-2-yl)-3-oxo-2-phenylisoindoline-1-carboxamide (6g).** ^{1}H NMR (400 MHz,$CDCl_3$) δ 10.41 (s, 1H), 7.70 (d, J = 7.6 Hz, 1H), 7.63-7.61 (m, 3H), 7.52 (t, J = 7.6 Hz, 1H), 7.41 (t, J = 7.2 Hz, 1H), 7.30 (d, J = 9.2 Hz, 1H), 7.22 (d, J = 8.4 Hz, 1H), 7.11 (t, J = 7.6 Hz, 1H), 6.82-6.80 (m, 2H), 6.61 (t, J = 5.6 Hz, 1H), 5.97 (s, 1H), 3.73 (s, 3H), 3.36-3.31 (m, 1H), 3.12-3.07 (m, 1H), 1.32-1.27 (m, 2H), 1.05-0.99 (m, 2H), 0.76 (t, J = 7.2Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.15, 168.70, 154.26, 146.26, 137.12, 134.77, 133.53, 131.25, 129.43, 129.04, 128.56, 128.09, 125.36, 124.72, 122.14, 121.67, 112.73, 112.29, 102.01, 101.22, 71.20, 55.82, 39.87,

31.05, 19.79, 13.69; MS (EI, m/z) 453 $[M]^+$; HRMS (EI) calcd for $C_{28}H_{27}N_3O_3$ $[M]^+$ 453.2052, found 453.2053.



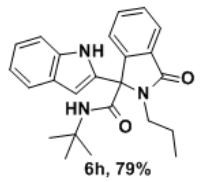
7g, 90%

***N*-Butyl-10-methoxy-5-oxo-6-phenyl-6,7-dihydro-5*H*-benzo[6,7][1,4]diazepino[1,2-a]indole-7-carboxamide (7g).** ^{1}H NMR (400 MHz,$CDCl_3$) δ 8.05 (d, J = 7.6 Hz, 1H), 7.64-7.62 (m, 2H), 7.56 (t, J = 7.2 Hz, 1H), 7.42-7.31 (m, 6H), 7.12 (s, 1H), 6.99 (d, J = 8.8 Hz, 1H), 6.62 (s, 1H), 5.55-5.52 (m, 1H), 5.39 (s, 1H), 3.89 (s, 3H), 3.07-3.02 (m, 1H), 2.78-2.74 (m, 1H), 0.96-0.94 (m, 4H), 0.73 (t, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.24, 165.19, 154.51, 143.05, 135.91, 133.93, 132.32, 131.07, 130.27, 128.99, 128.59, 128.48, 126.78, 125.99, 125.55, 121.33, 113.05, 111.74, 103.53, 102.06, 76.48, 76.16, 75.84, 62.28, 54.94, 38.87, 30.60, 18.90, 12.75; MS (EI, m/z) 453 $[M]^+$; HRMS (EI) calcd for $C_{28}H_{27}N_3O_3$ $[M]^+$ 453.2052, found 453.2048.



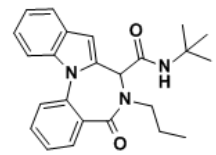
8g, 81%

***N*-Butyl-11-methoxy-5-oxo-6-phenyl-5,6,7,8-tetrahydrobenzo[5,6]azepino[3,4-b]indole-7-carboxamide (8g).** ^{1}H NMR (400 MHz,$CDCl_3$) δ 10.14 (s, 1H), 7.93 (d, J = 7.6 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 8.0 Hz, 1H), 7.41 (s, 1H), 7.29-7.09 (m, 7H), 6.90 (d, J = 7.6 Hz, 1H), 5.64 (br s, 1H), 5.24 (s, 1H), 3.89 (s, 3H), 3.03 (s, 1H), 2.58 (s, 1H), 0.80 (s, 4H), 0.65 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.52, 166.99, 155.36, 144.90, 134.61, 133.51, 132.61, 132.25, 132.14, 131.46, 131.35, 129.40, 127.49, 126.93, 126.35, 126.12, 125.85, 113.38, 113.30, 101.34, 77.48, 77.16, 76.84, 62.30, 56.12, 39.76, 31.40, 19.75, 13.82; MS (EI, m/z) 453 $[M]^+$; HRMS (EI) calcd for $C_{28}H_{27}N_3O_3$ $[M]^+$ 453.2052, found 453.2050.



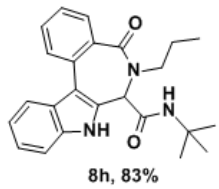
6h, 79%

***N*-(*tert*-Butyl)-1-(1*H*-indol-2-yl)-3-oxo-2-propylisoindoline-1-carboxamide (6h).** ^{1}H NMR (400 MHz,$CDCl_3$) δ 9.93 (s, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.51-7.48 (m, 4H), 7.40 (d, J = 8.0 Hz, 1H), 7.18 (t, J = 7.2 Hz, 1H), 7.07 (t, J = 7.6 Hz, 1H), 6.14 (s, 1H), 5.89 (br s, 1H), 3.63-3.55 (m, 1H), 3.35-3.27 (m, 1H), 1.66-1.61 (m, 2H), 1.29 (s, 9H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.87, 168.39, 146.56, 136.15, 133.82, 132.93, 129.75, 129.51, 127.69, 124.24, 122.58, 122.53, 120.77, 120.20, 111.56, 102.47, 71.35, 52.30, 44.91, 28.45, 21.83, 12.00; MS (EI, m/z) 389 $[M]^+$; HRMS (EI) calcd for $C_{24}H_{27}N_3O_3$ $[M]^+$ 389.2103 found 389.2103.



7h, 88%

***N*-(*tert*-Butyl)-5-oxo-6-propyl-6,7-dihydro-5*H*-benzo[6,7][1,4]diazepino[1,2-a]indole-7-carboxamide (7h).** ^{1}H NMR (400 MHz,$CDCl_3$) δ 7.98 (d, J = 8.0 Hz, 1H), 7.69-7.64 (m, 3H), 7.54 (t, J = 6.8 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.23 (t, J = 7.6 Hz, 1H), 6.71 (s, 1H), 5.06 (s, 1H), 3.67 (t, J = 6.8 Hz, 2H), 1.81-1.65 (m, 2H), 0.91 (s, 9H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.49, 165.19, 137.35, 136.09, 134.98, 132.92, 131.76, 130.52, 128.87, 126.50, 123.71, 122.64, 121.71, 121.51, 111.62, 104.47, 60.61, 51.86, 51.67, 28.16, 21.37, 11.46; MS (EI, m/z) 389 $[M]^+$; HRMS (EI) calcd for $C_{24}H_{27}N_3O_3$ $[M]^+$ 389.2103 found 389.2107.

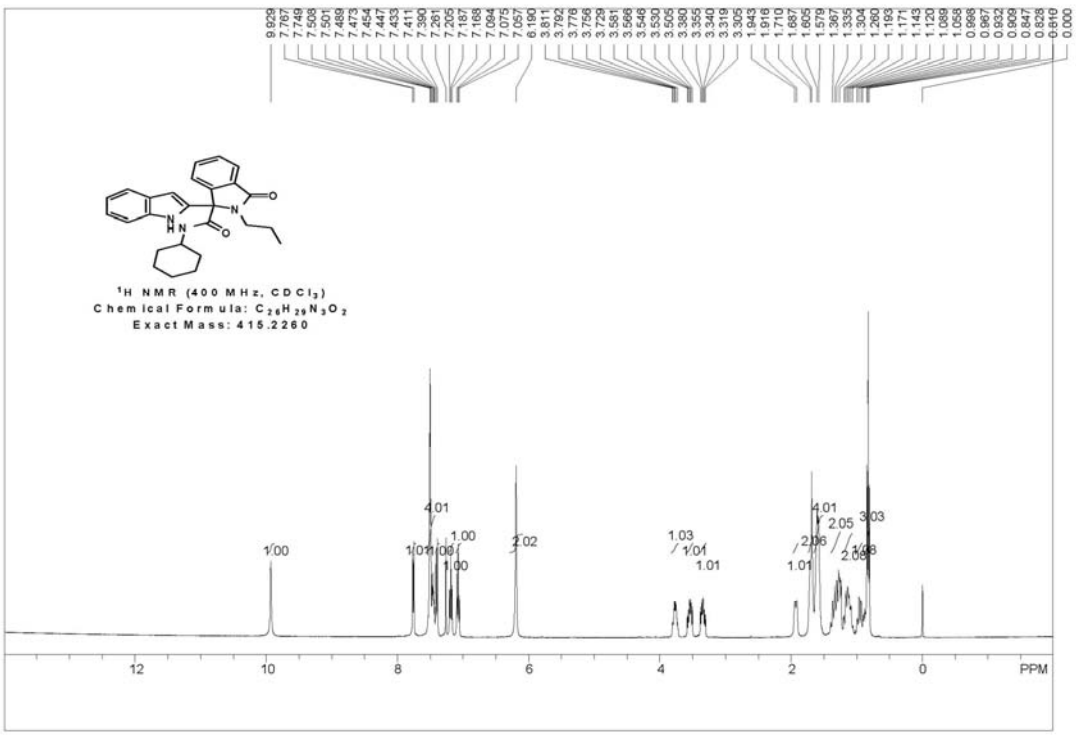


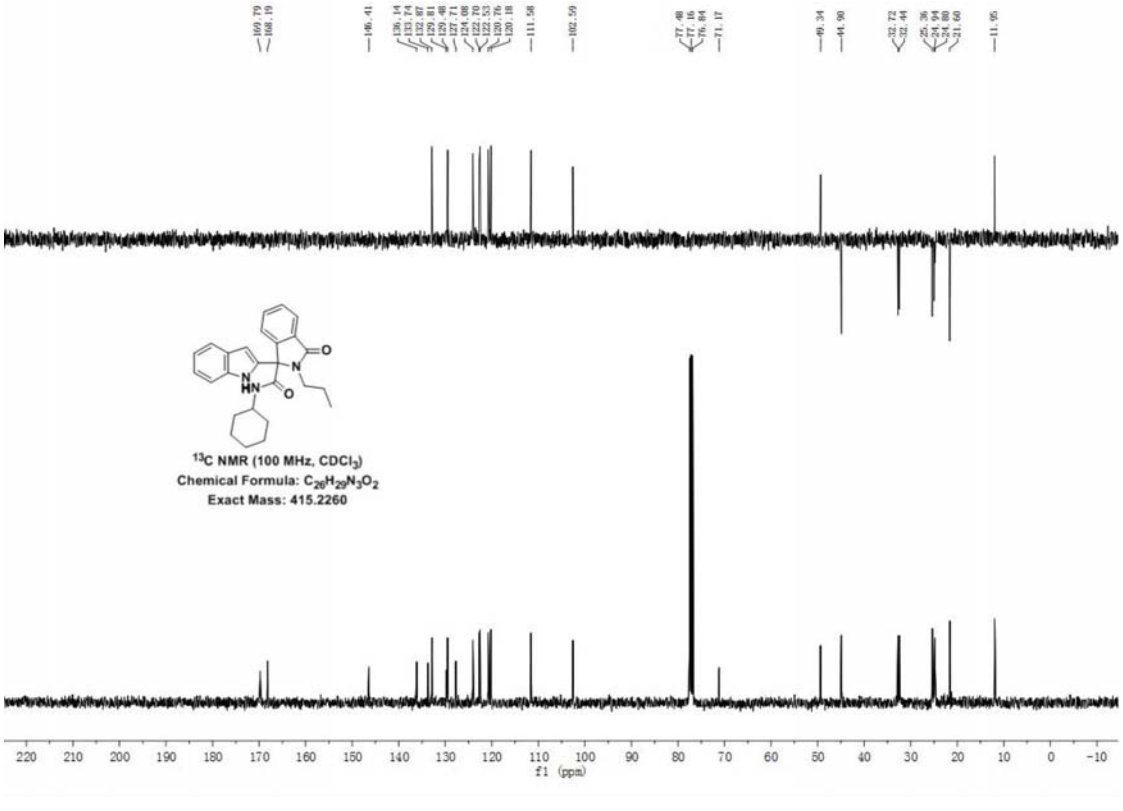
8h, 83%

***N*-(*tert*-Butyl)-5-oxo-6-propyl-5,6,7,8-tetrahydrobenzo[5,6]azepino[3,4-b]indole-7-carboxamide (8h).** ^{1}H NMR (400 MHz, DMSO) δ 11.65 (s, 1H), 7.83 (d, J = 7.6 Hz, 1H), 7.76-7.72 (m, 2H), 7.54-7.51 (m, 2H), 7.27 (t, J = 7.2 Hz, 1H), 7.21 (t, J = 7.2 Hz, 1H), 7.15 (t, J = 7.2 Hz, 1H), 6.31 (s, 1H), 5.24 (s, 1H), 3.97-3.90 (m, 1H), 3.36-3.30 (m, 1H), 1.61-1.48 (m, 2H), 0.83 (s, 9H), 0.72 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, DMSO) δ 168.40, 165.90, 137.33, 135.72, 134.62, 131.62, 130.50, 125.96, 125.04, 121.97, 120.42, 118.66, 112.40, 110.18, 58.52, 51.80, 50.69, 40.15, 39.94, 39.73, 39.52, 39.31, 39.10, 38.89, 27.77, 20.99, 11.15; MS (EI, m/z) 389 $[M]^+$; HRMS (EI) calcd for $C_{24}H_{27}N_3O_3$ $[M]^+$ 389.2103 found 389.2106.

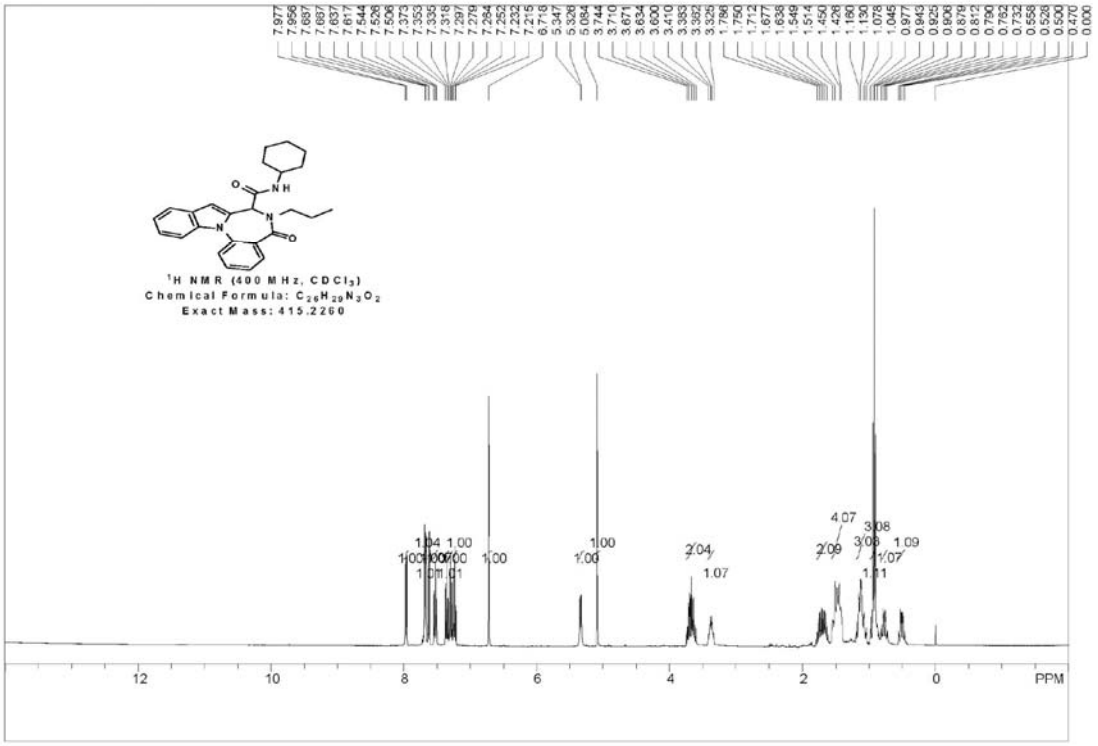
^{1}H and ^{13}C NMR Spectra.

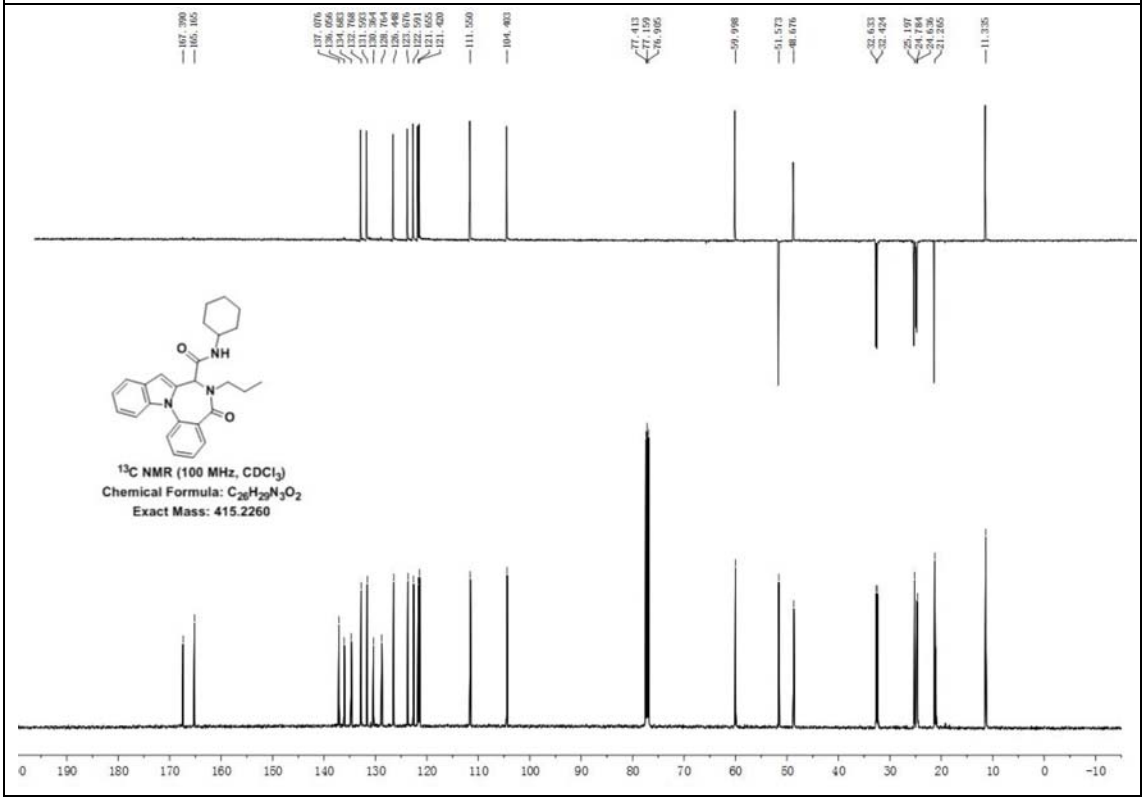
***N*-Cyclohexyl-1-(1*H*-indol-2-yl)-3-oxo-2-propylisoindoline-1-carboxamide (6a).**



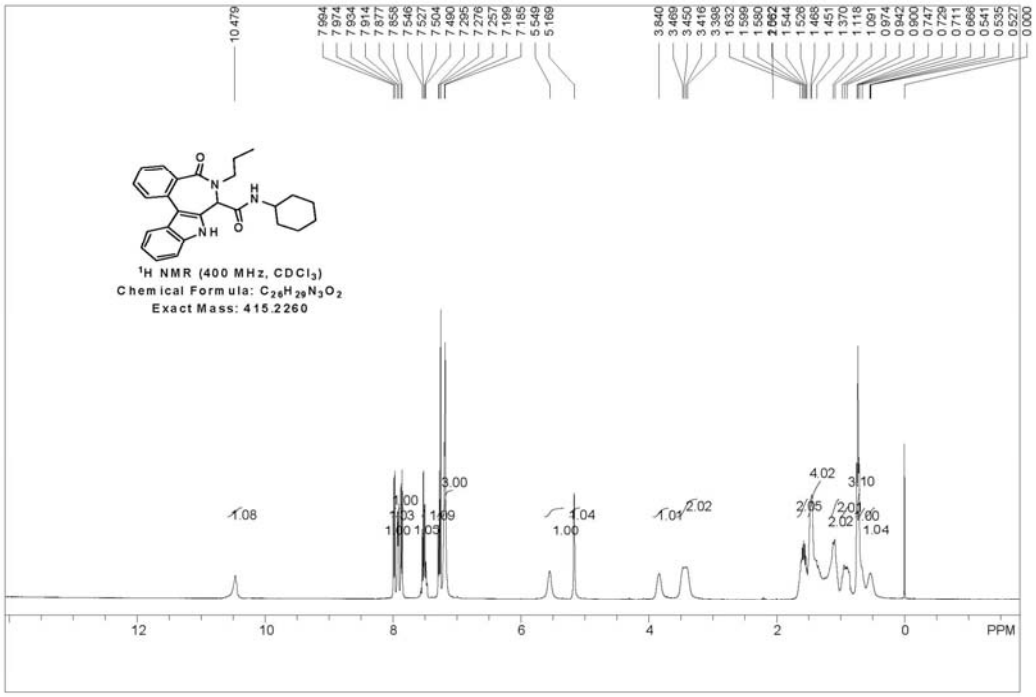


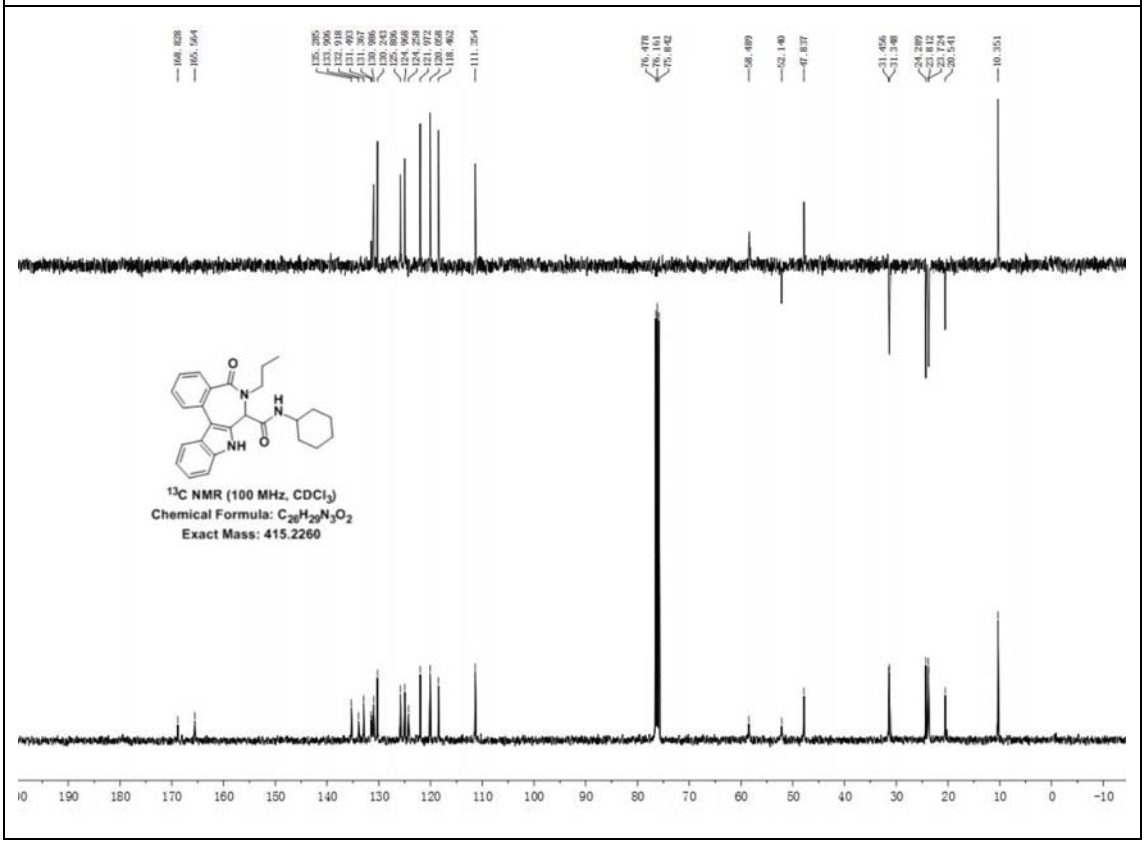
***N*-Cyclohexyl-5-oxo-6-propyl-6,7-dihydro-5*H*-benzo[6,7][1,4]diazepino[1,2-a]indole-7-carboxamide (7a).**



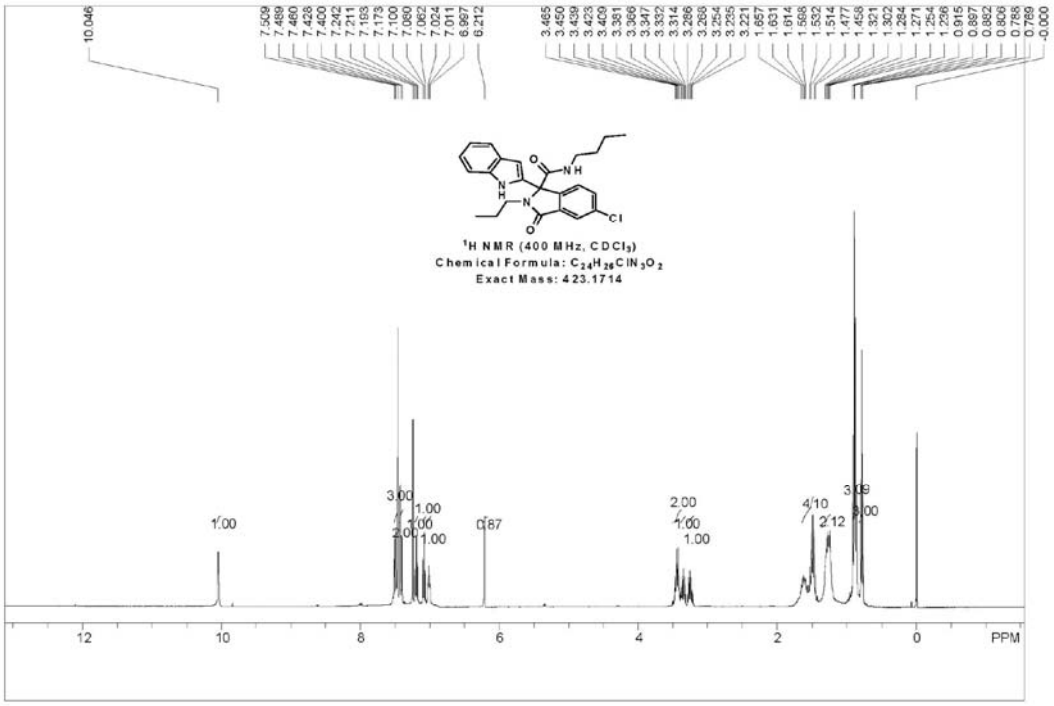


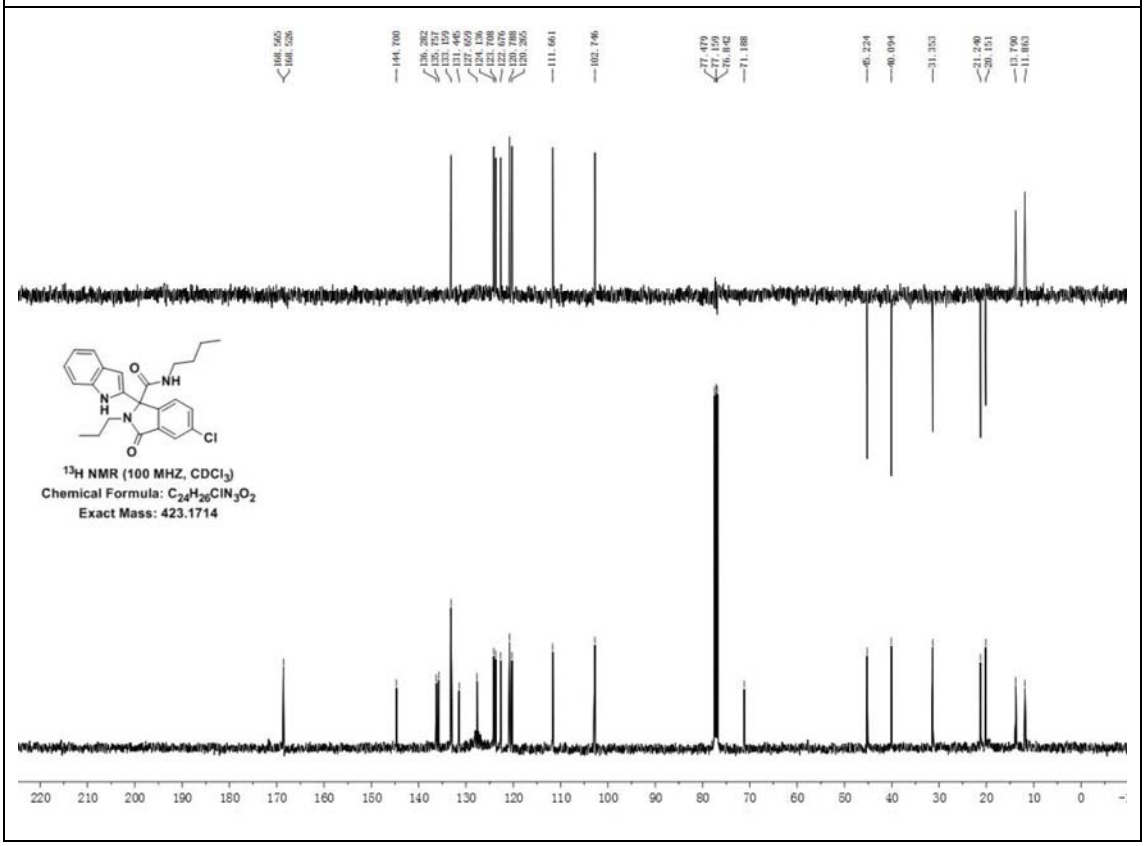
***N*-Cyclohexyl-5-oxo-6-propyl-5,6,7,8-tetrahydrobenzo[5,6]azepino[3,4-b]indole-7-carboxamide (8a).**



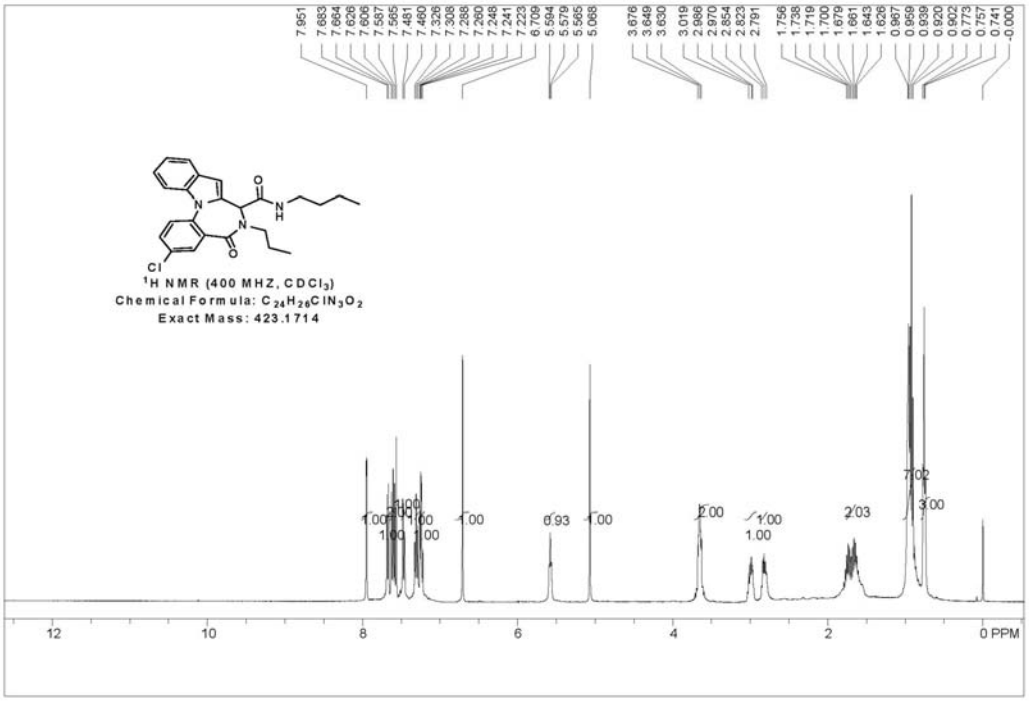


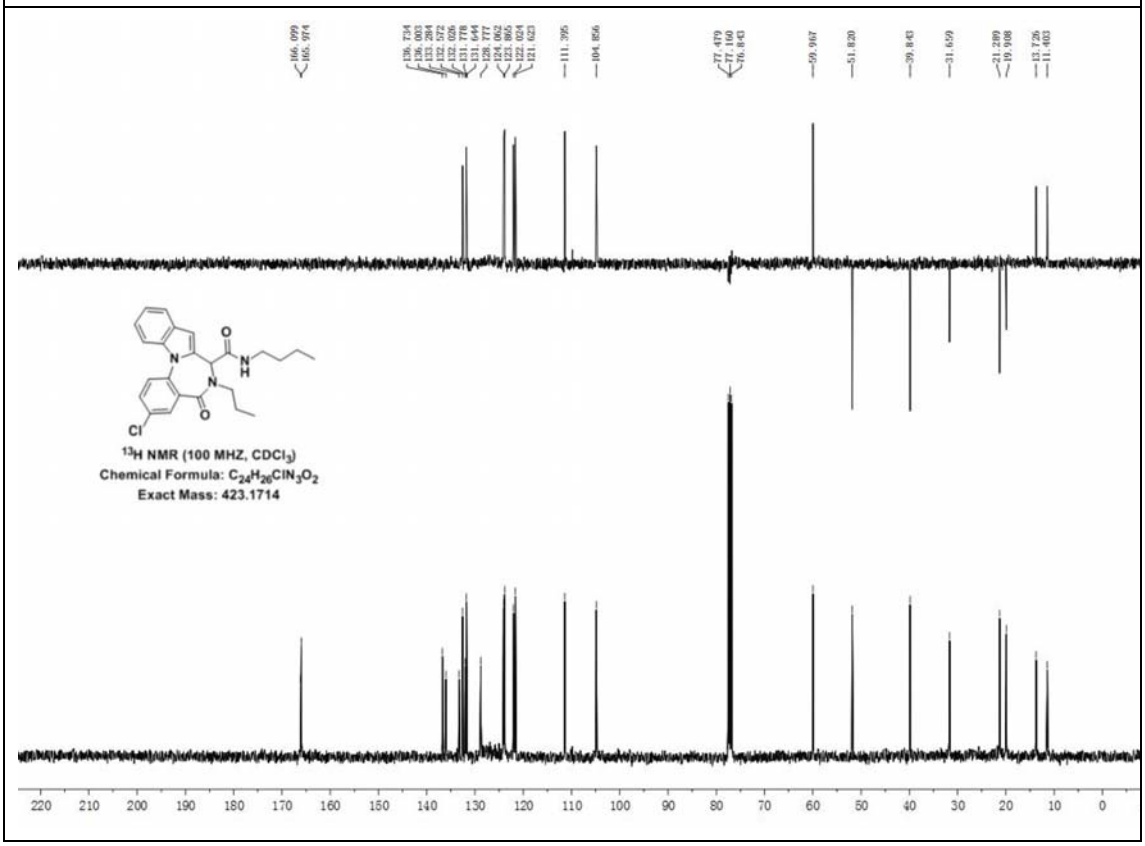
***N*-Butyl-5-chloro-1-(1*H*-indol-2-yl)-3-oxo-2-propylisoindoline-1-carboxamide (6b).**



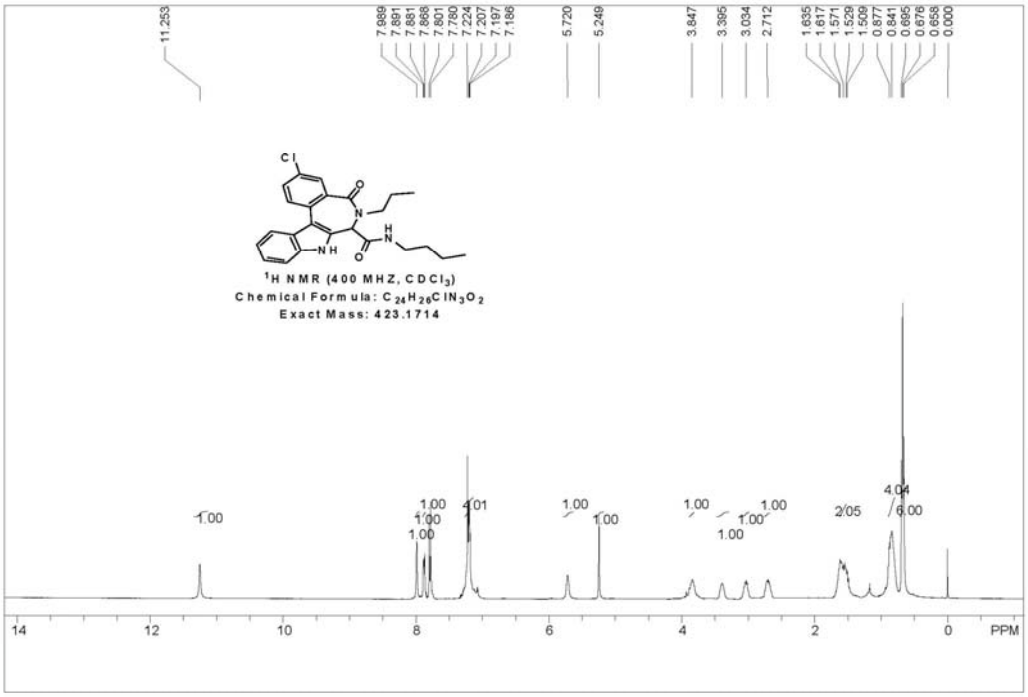


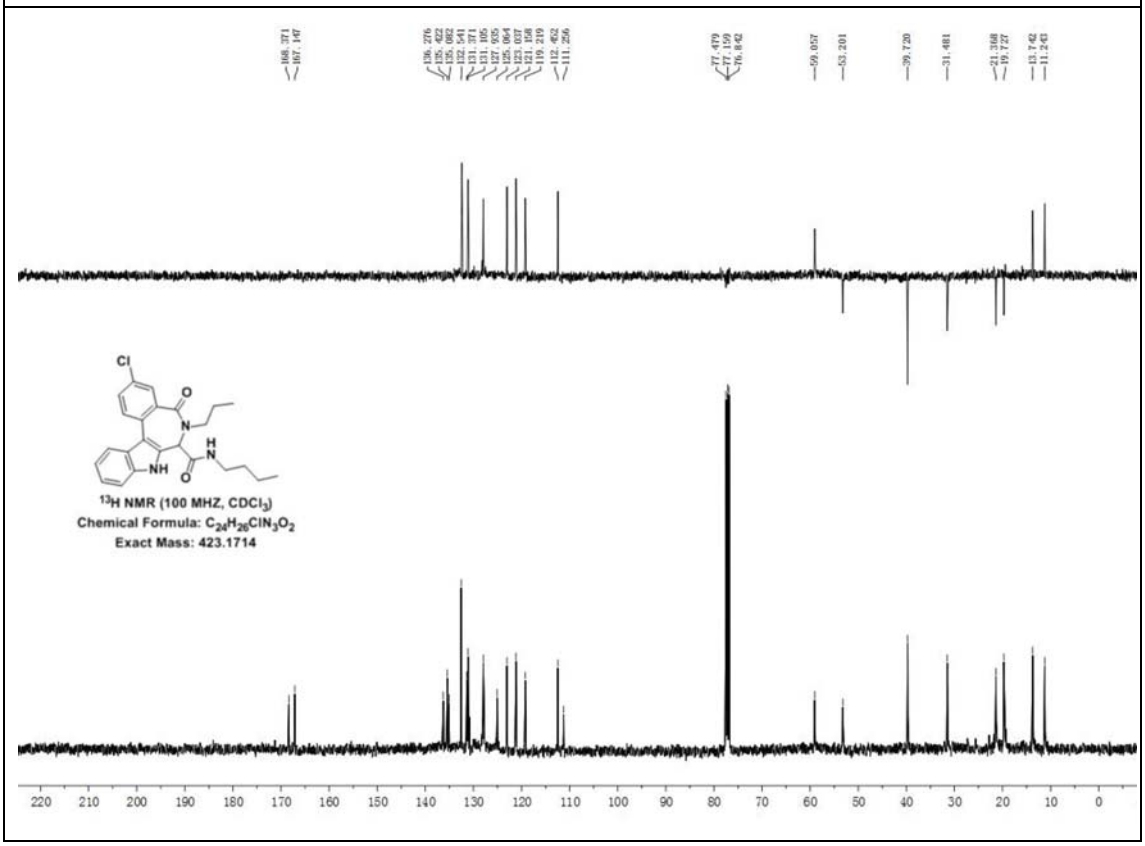
_N_-Butyl-3-chloro-5-oxo-6-propyl-6,7-dihydro-5_H_-benzo[6,7][1,4]diazepino[1,2-a]indole-7-carboxamide (7b).



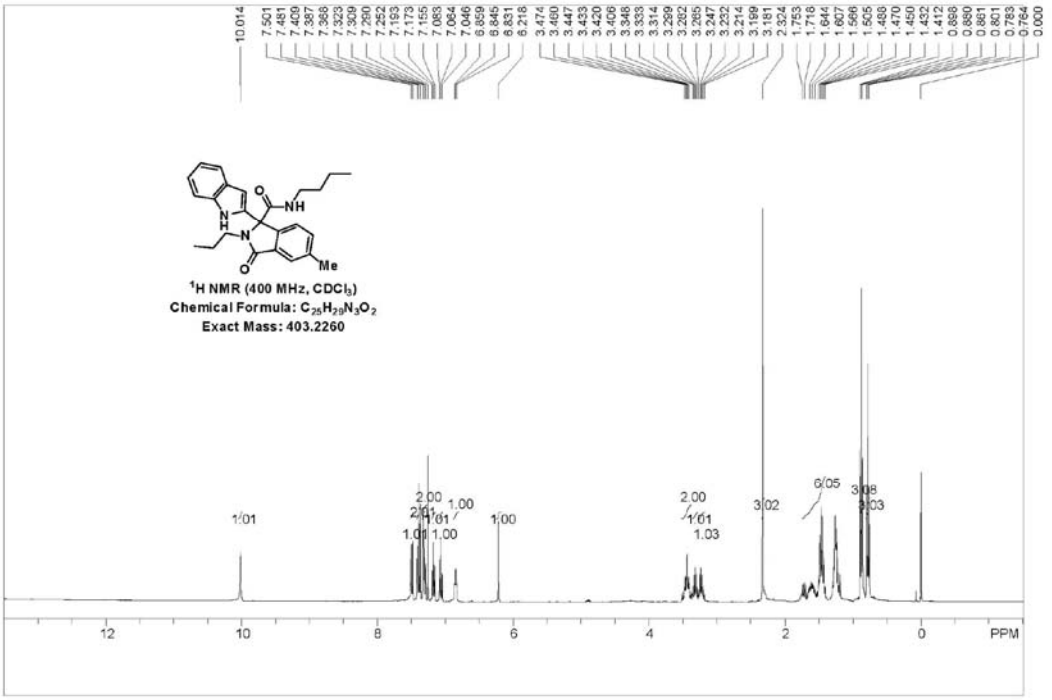


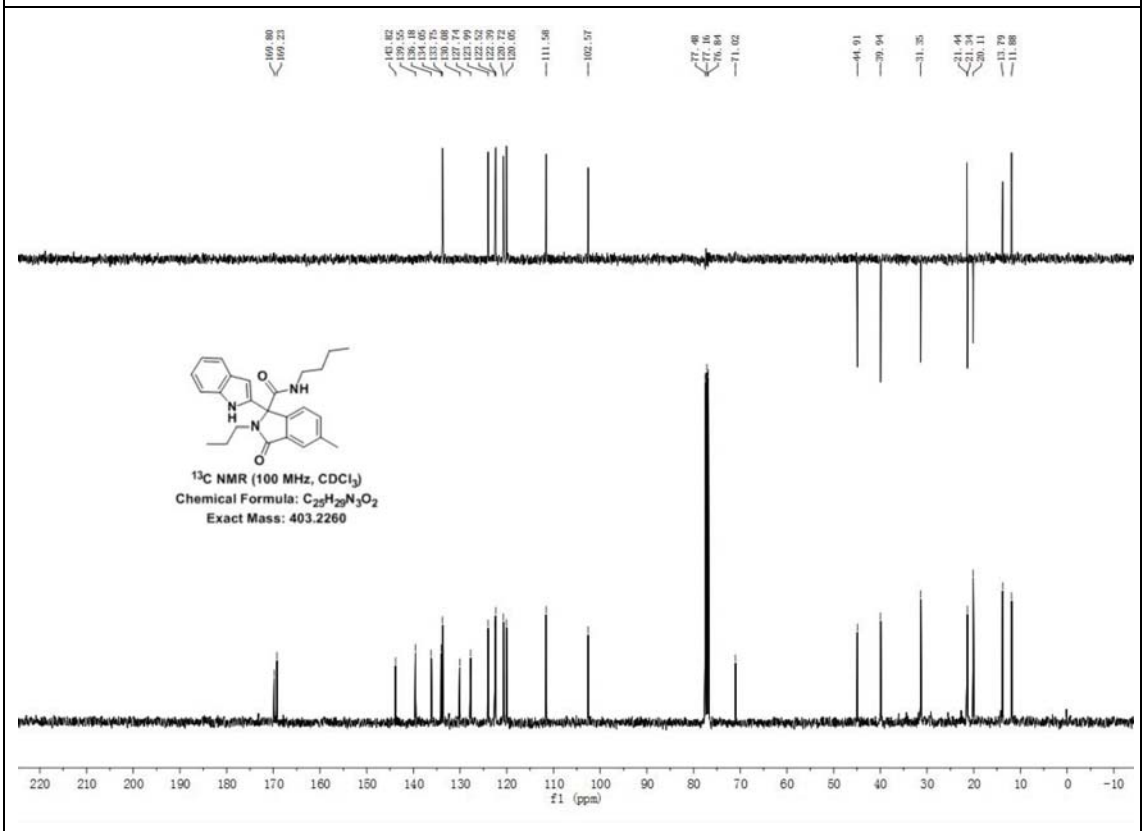
***N*-Butyl-3-chloro-5-oxo-6-propyl-5,6,7,8-tetrahydrobenzo[5,6]azepino[3,4-b]indole-7-carboxamide (8b).**



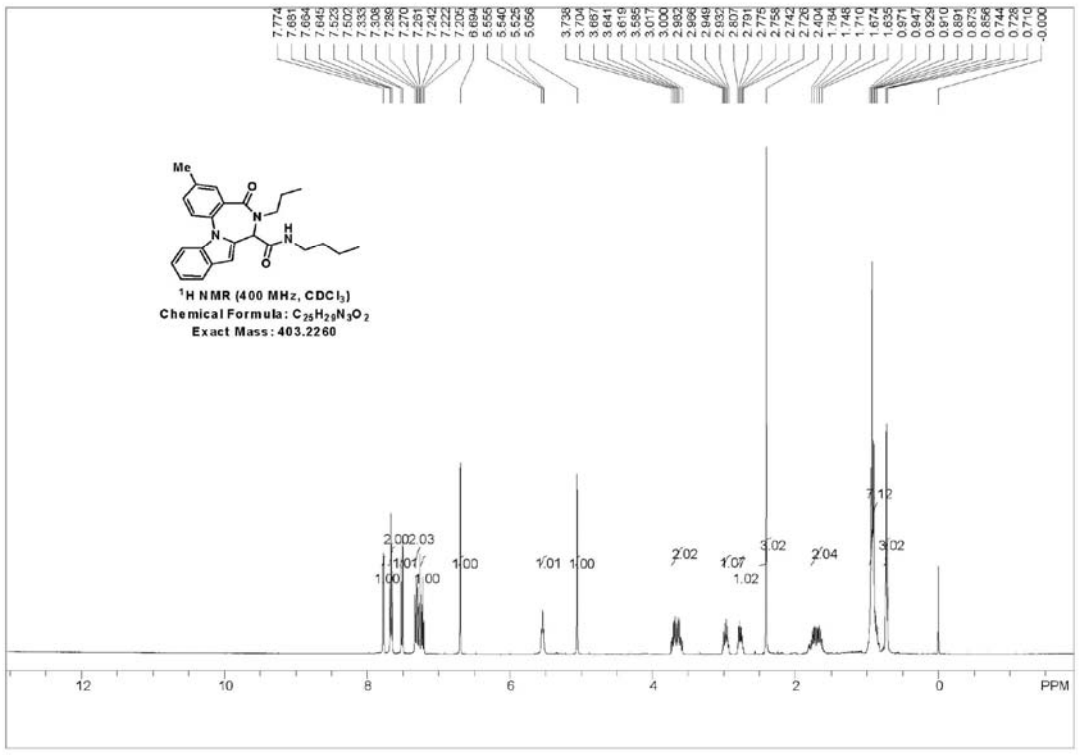


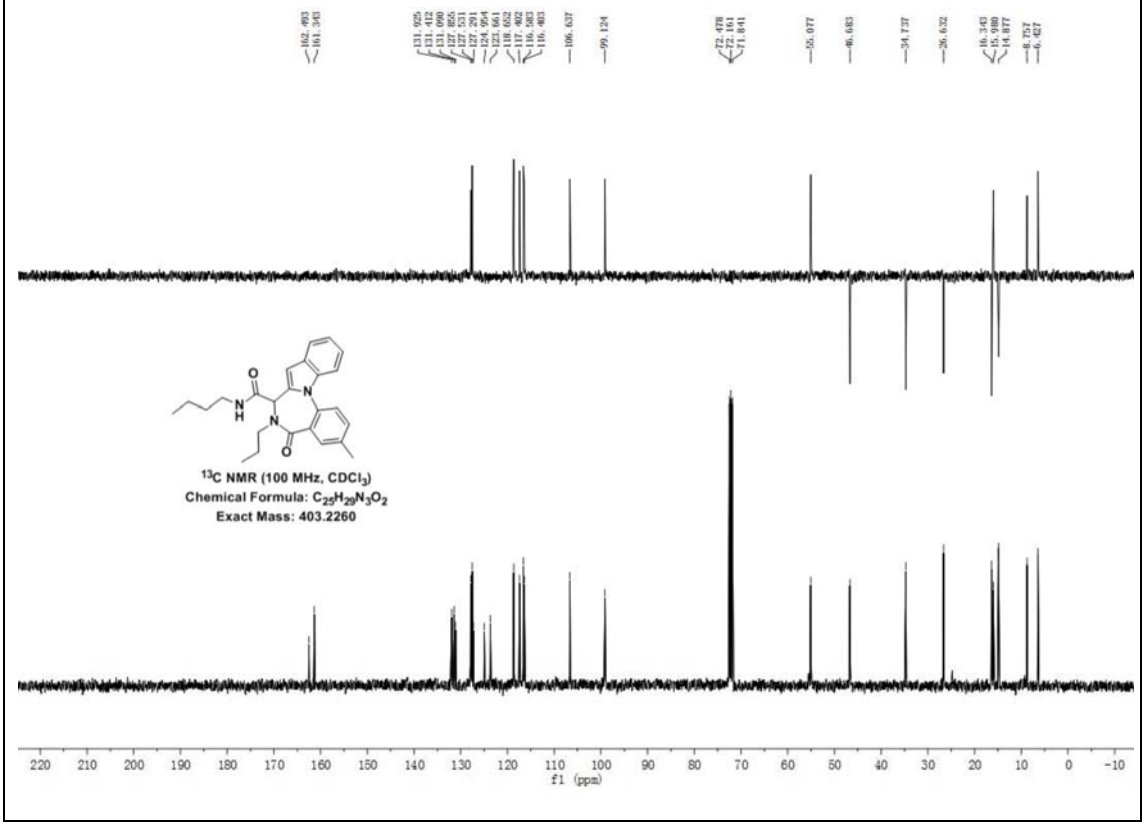
***N*-Butyl-1-(1*H*-indol-2-yl)-5-methyl-3-oxo-2-propylisoindoline-1-carboxamide (6c).**



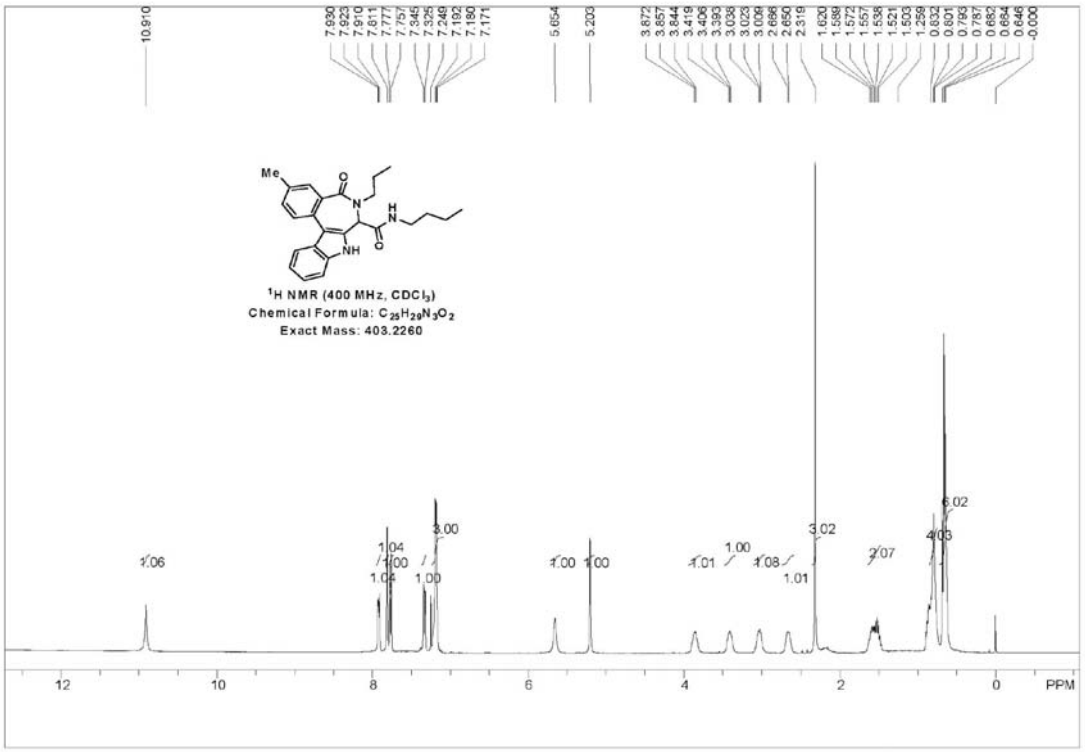


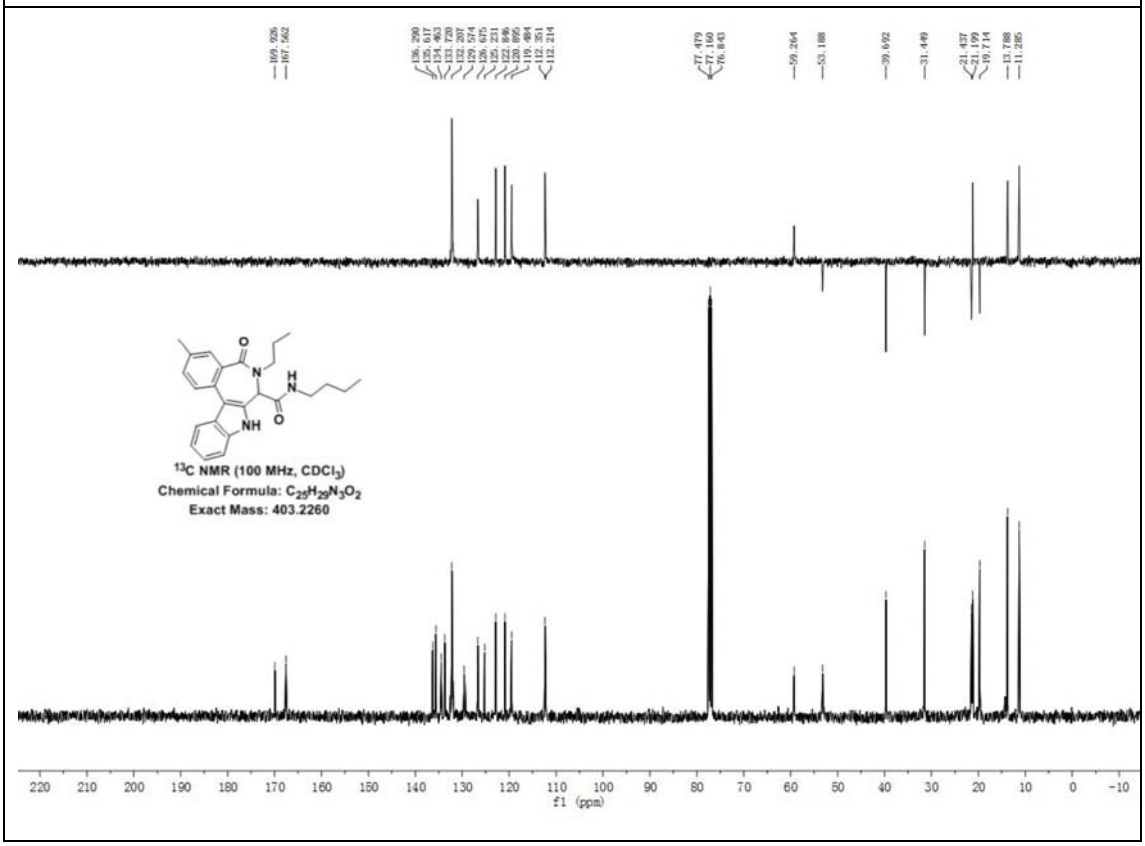
***N*-Butyl-3-methyl-5-oxo-6-propyl-6,7-dihydro-5*H*-benzo[6,7][1,4]diazepino[1,2-a]indole-7-carboxamide (7c).**



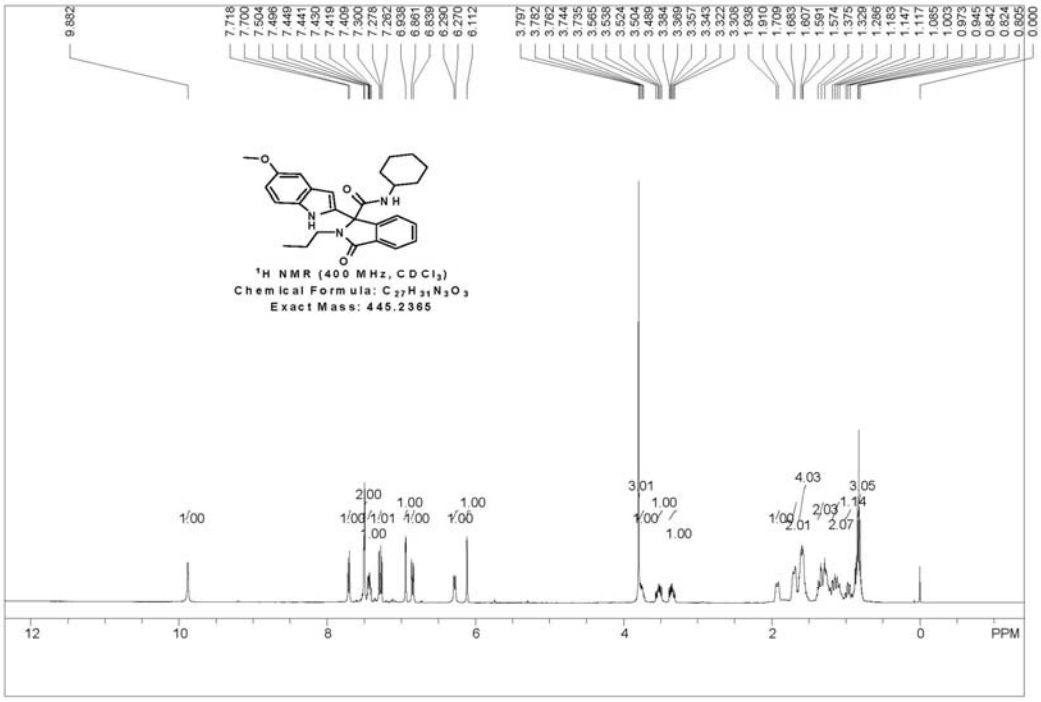


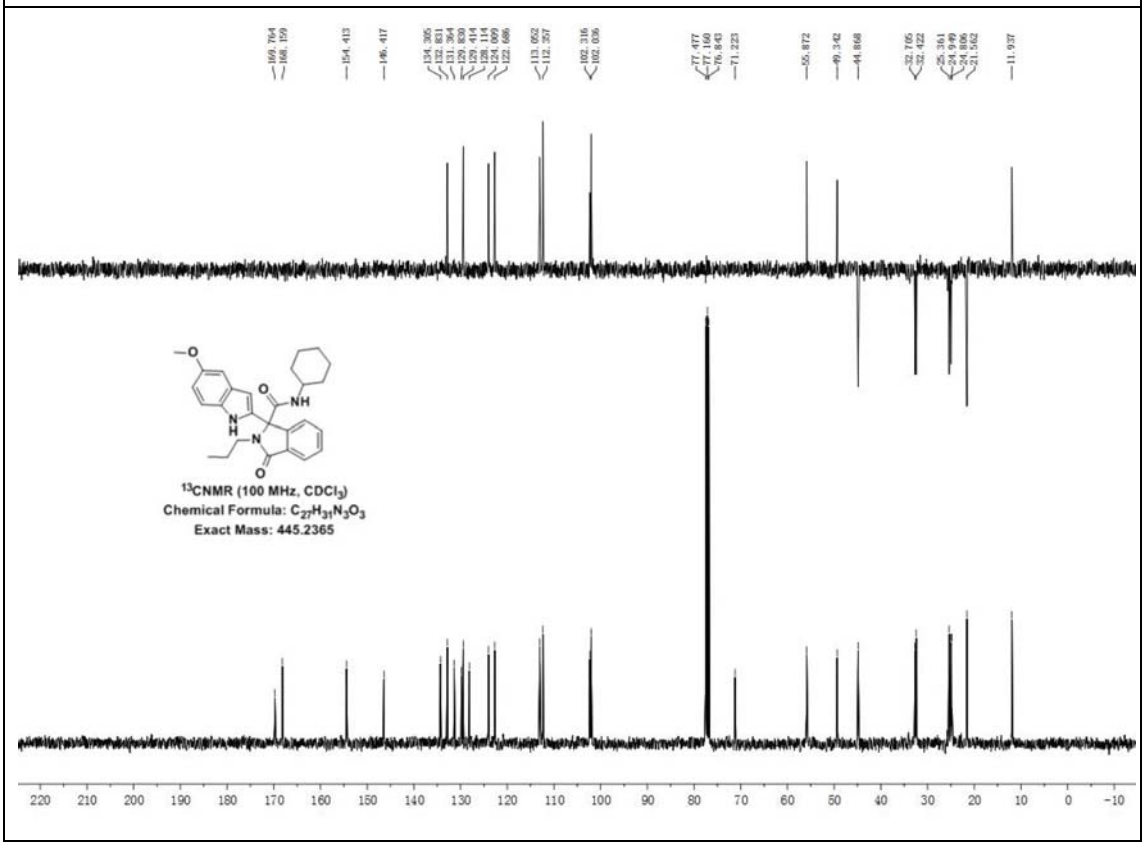
***N*-Butyl-3-methyl-5-oxo-6-propyl-5,6,7,8-tetrahydrobenzo[5,6]azepino[3,4-b]indole-7-carboxamide (8c).**



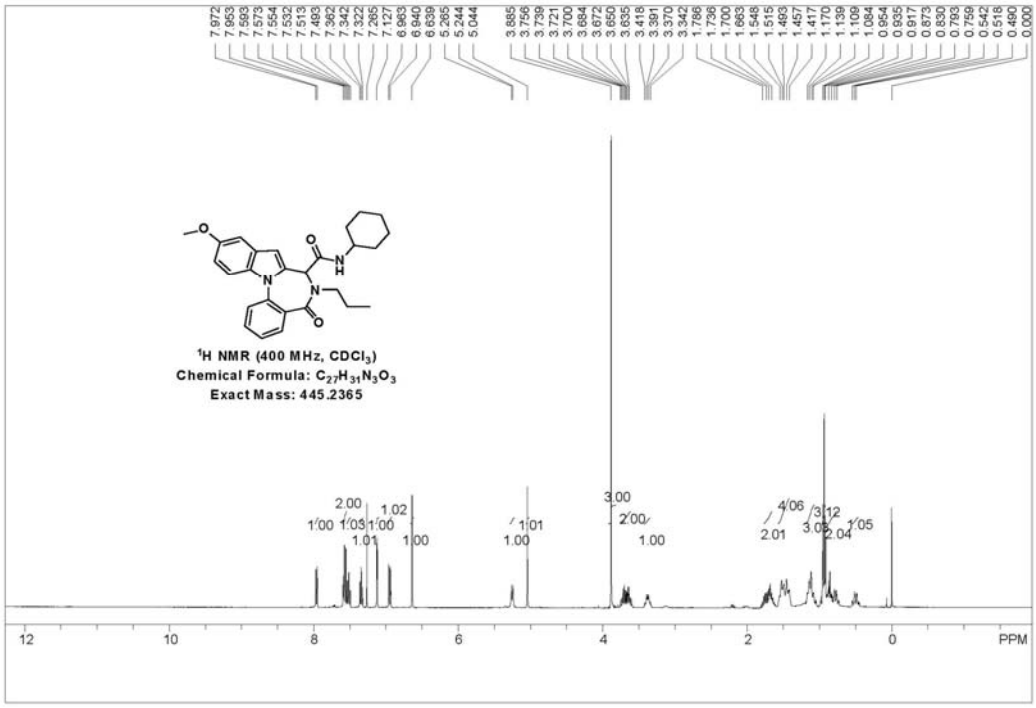


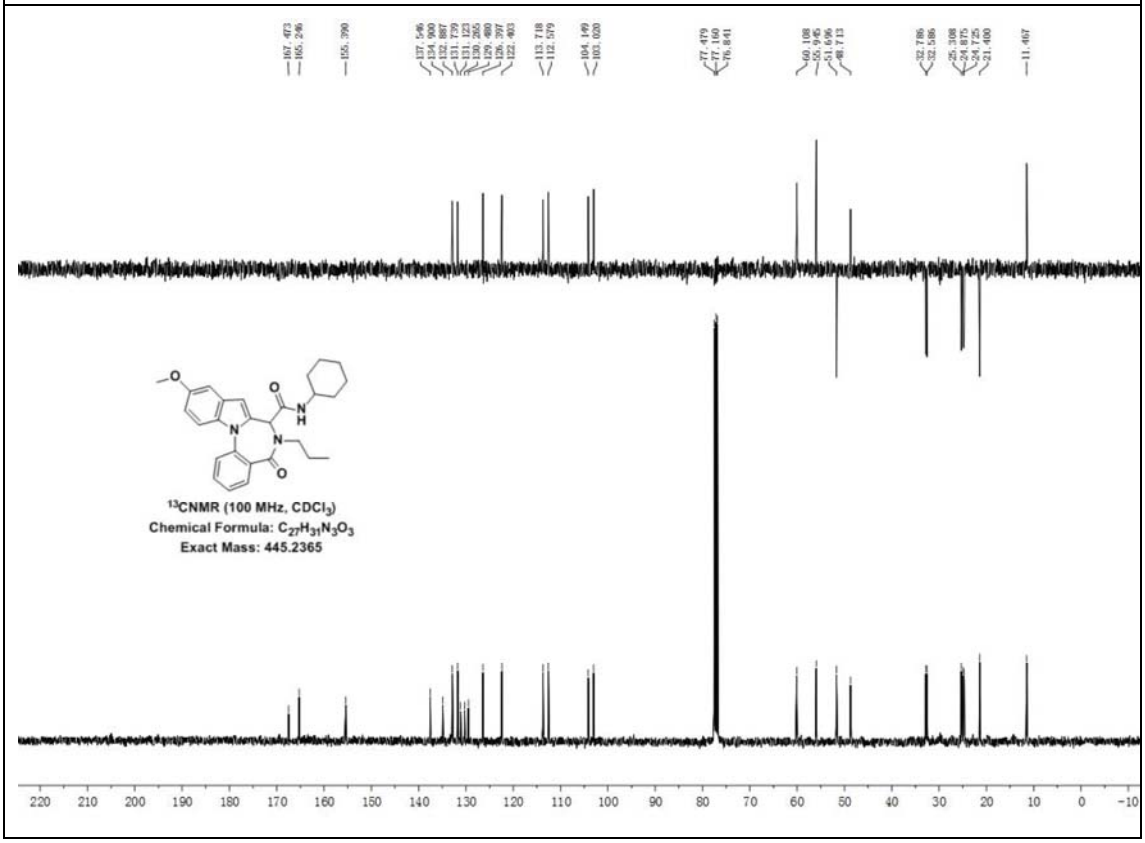
***N*-Cyclohexyl-1-(5-methoxy-1*H*-indol-2-yl)-3-oxo-2-propylisoindoline-1-carboxamide (6d).**



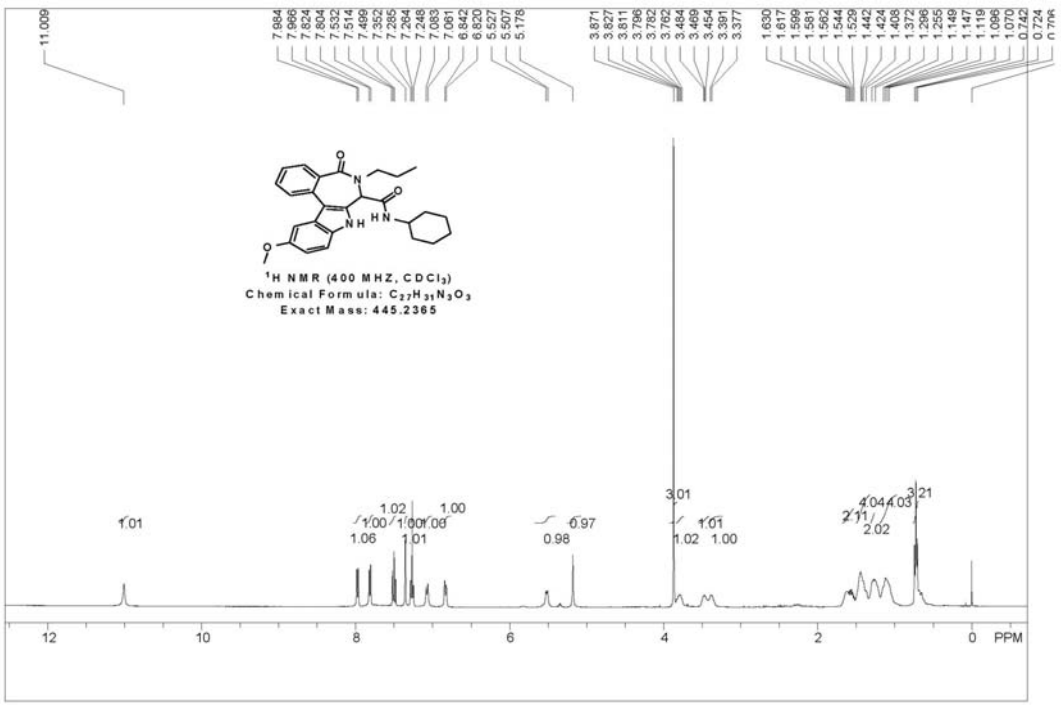


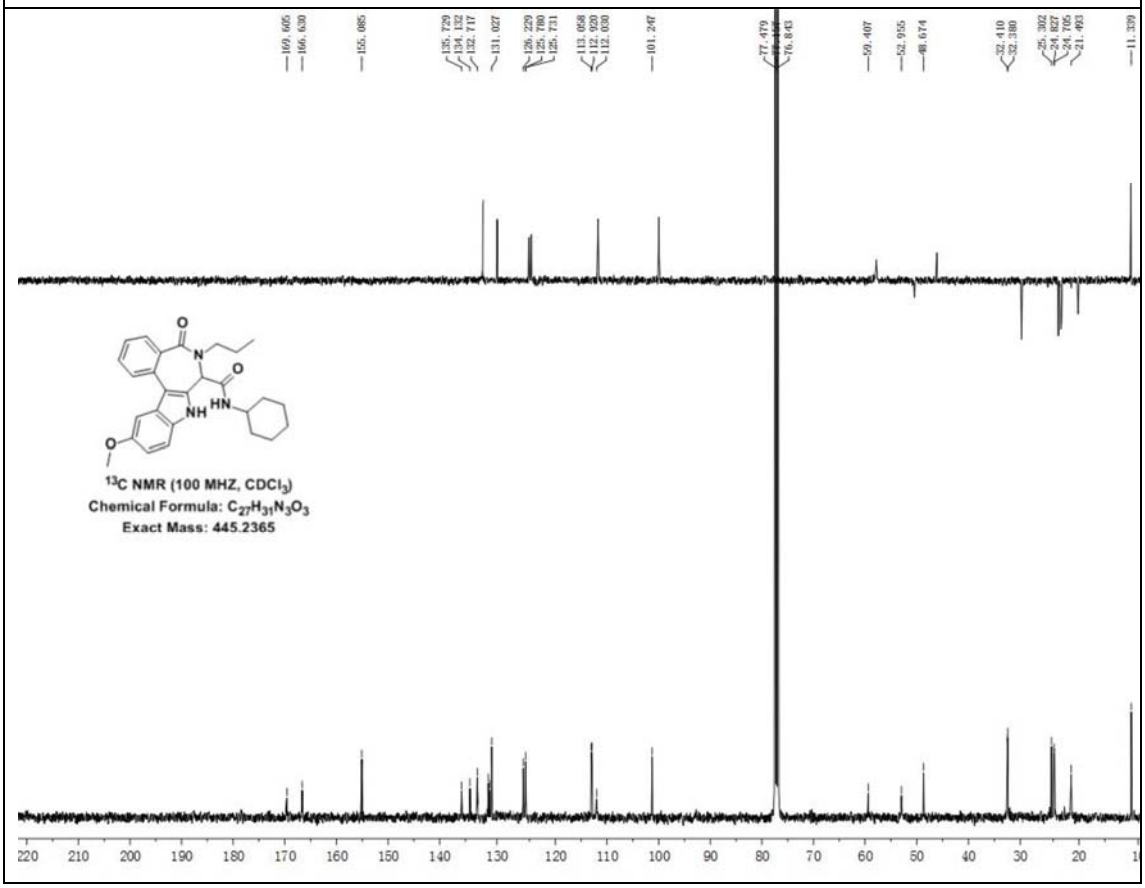
***N*-Cyclohexyl-10-methoxy-5-oxo-6-propyl-6,7-dihydro-5*H*-benzo[6,7][1,4]diazepino[1,2-a]indole-7-carboxa mide (7d).**



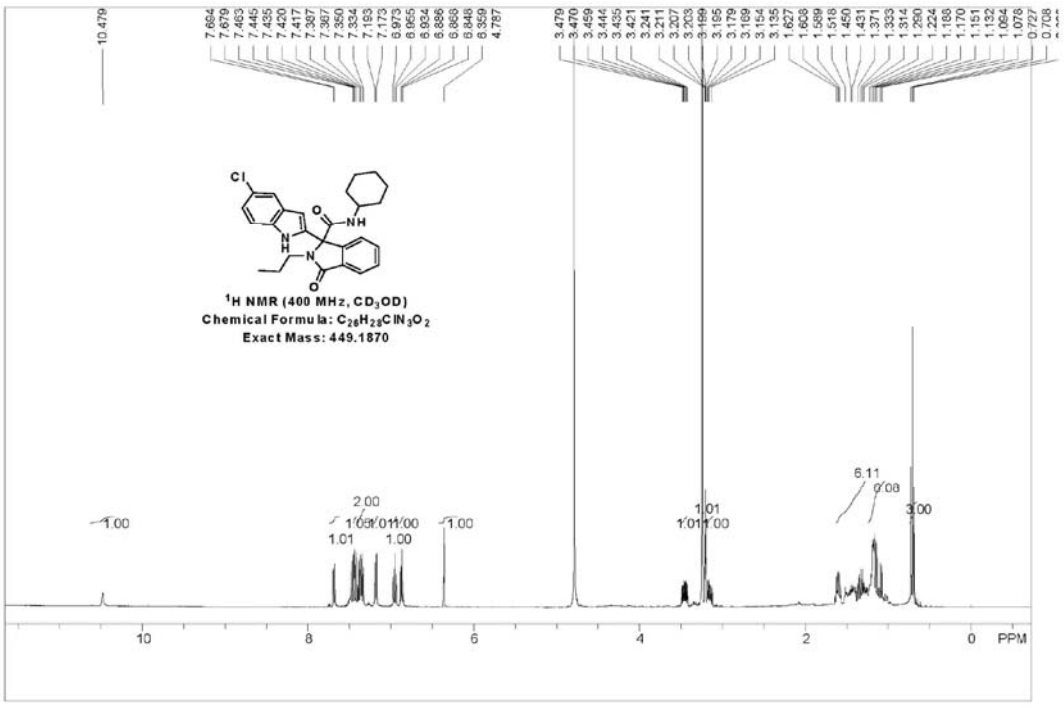


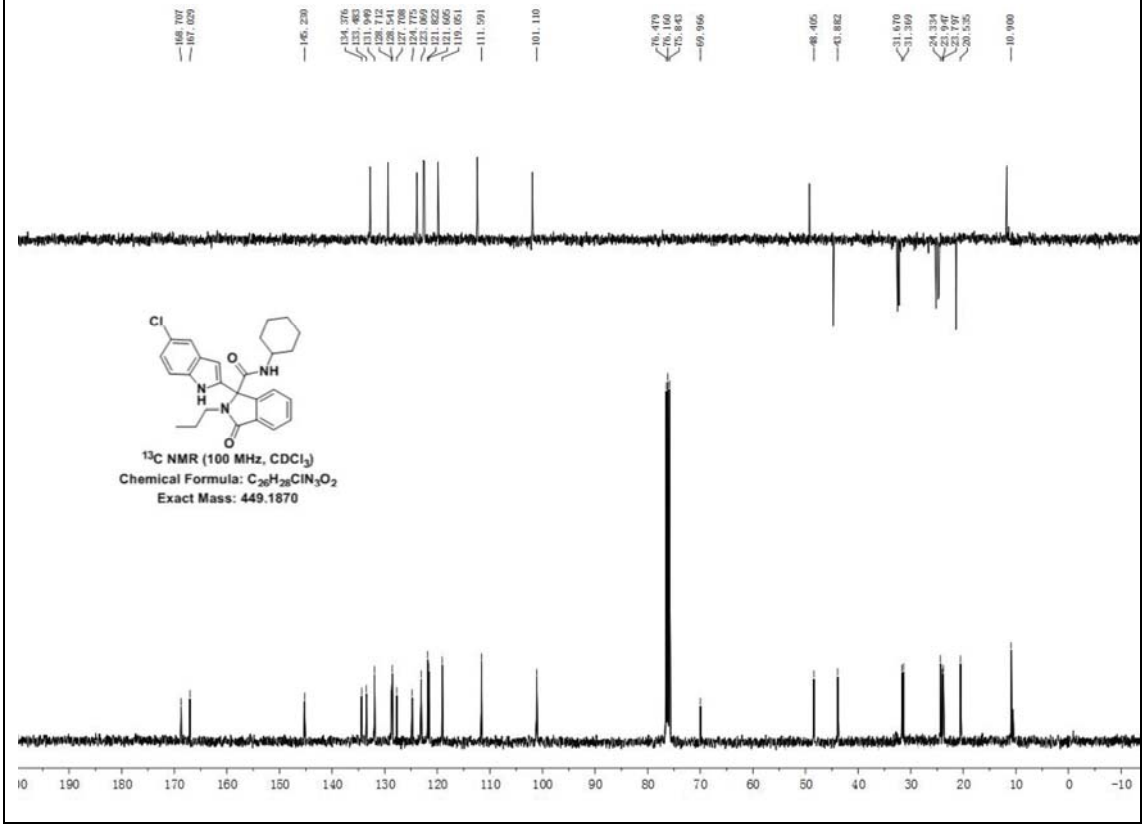
_N_-Cyclohexyl-11-methoxy-5-oxo-6-propyl-5,6,7,8-tetrahydrobenzo[5,6]azepino[3,4-b]indole-7-carboxamide (8d).



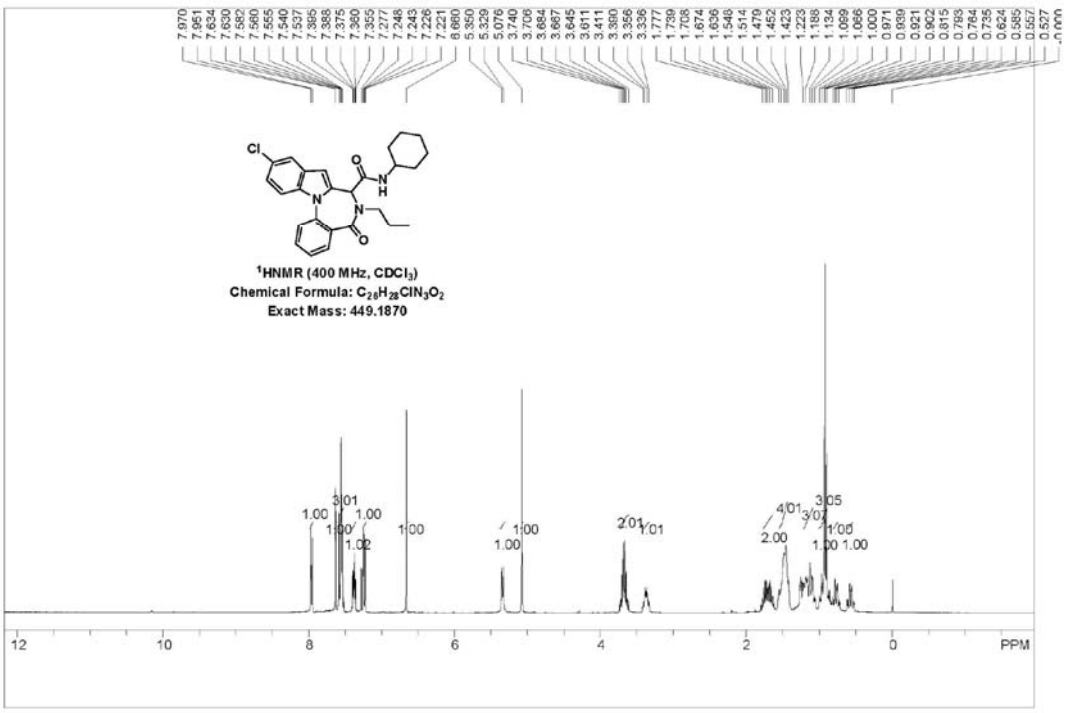


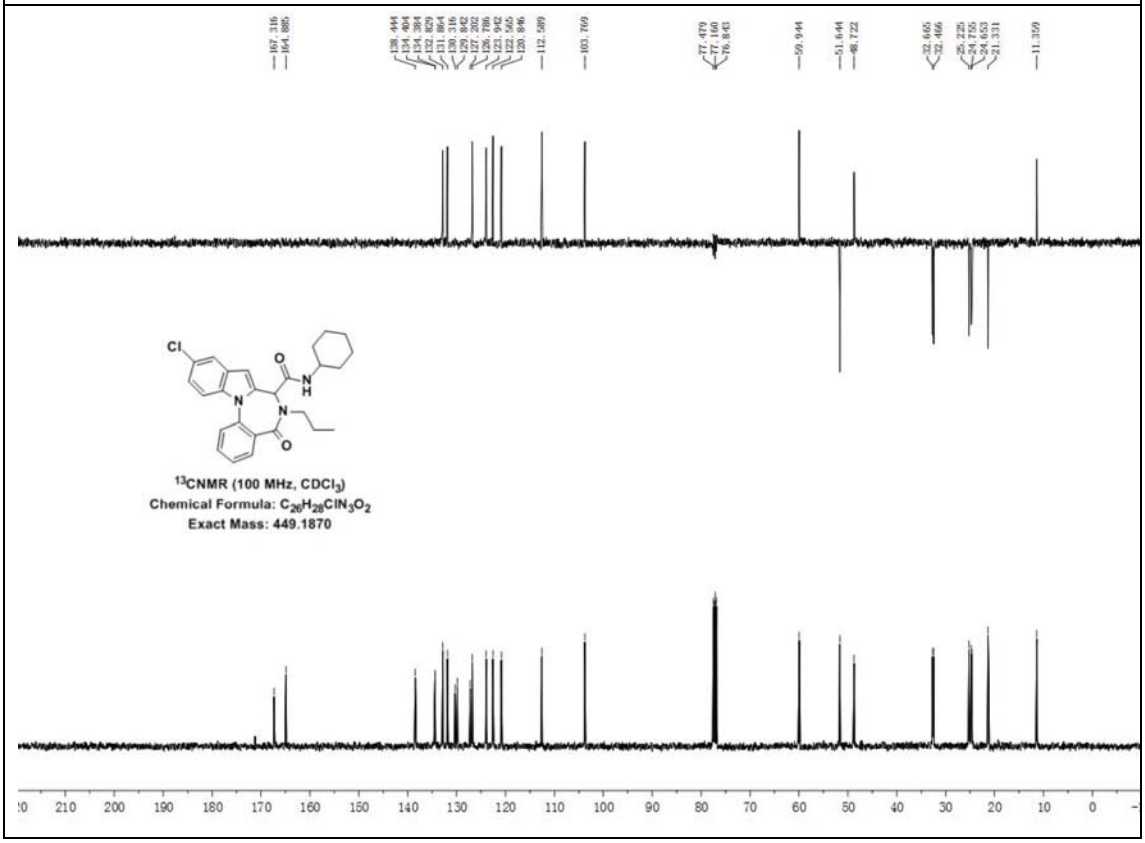
1-(5-Chloro-1*H*-indol-2-yl)-*N*-cyclohexyl-3-oxo-2-propylisoindoline-1-carboxamide (6e).



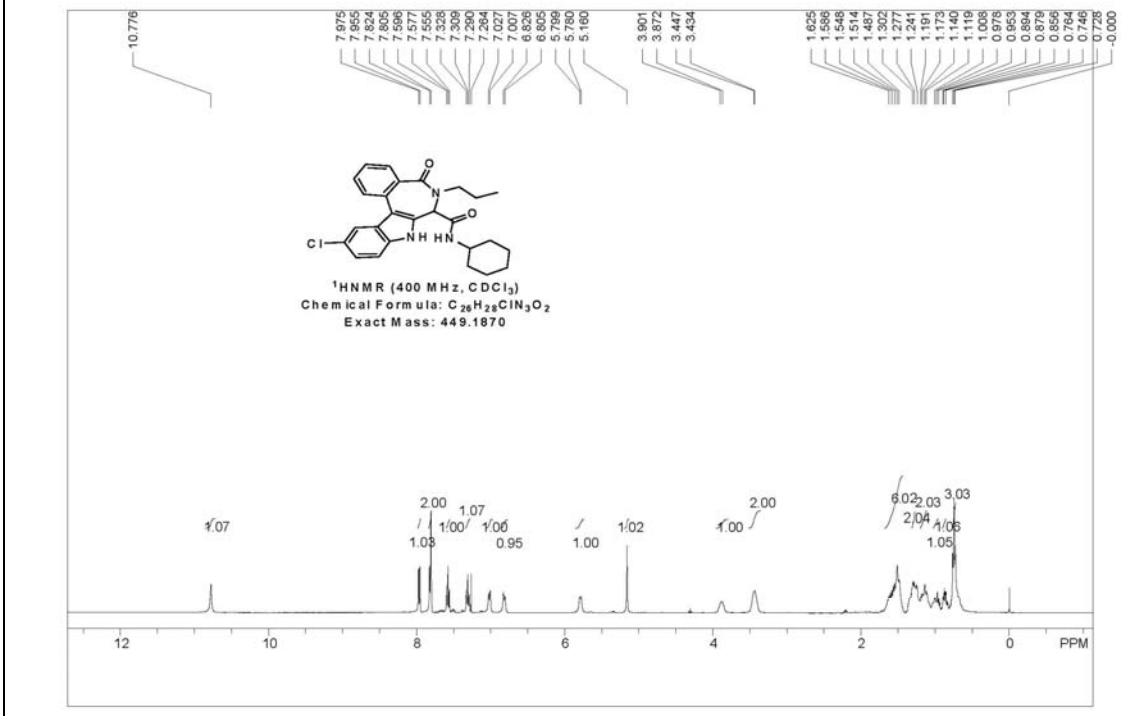


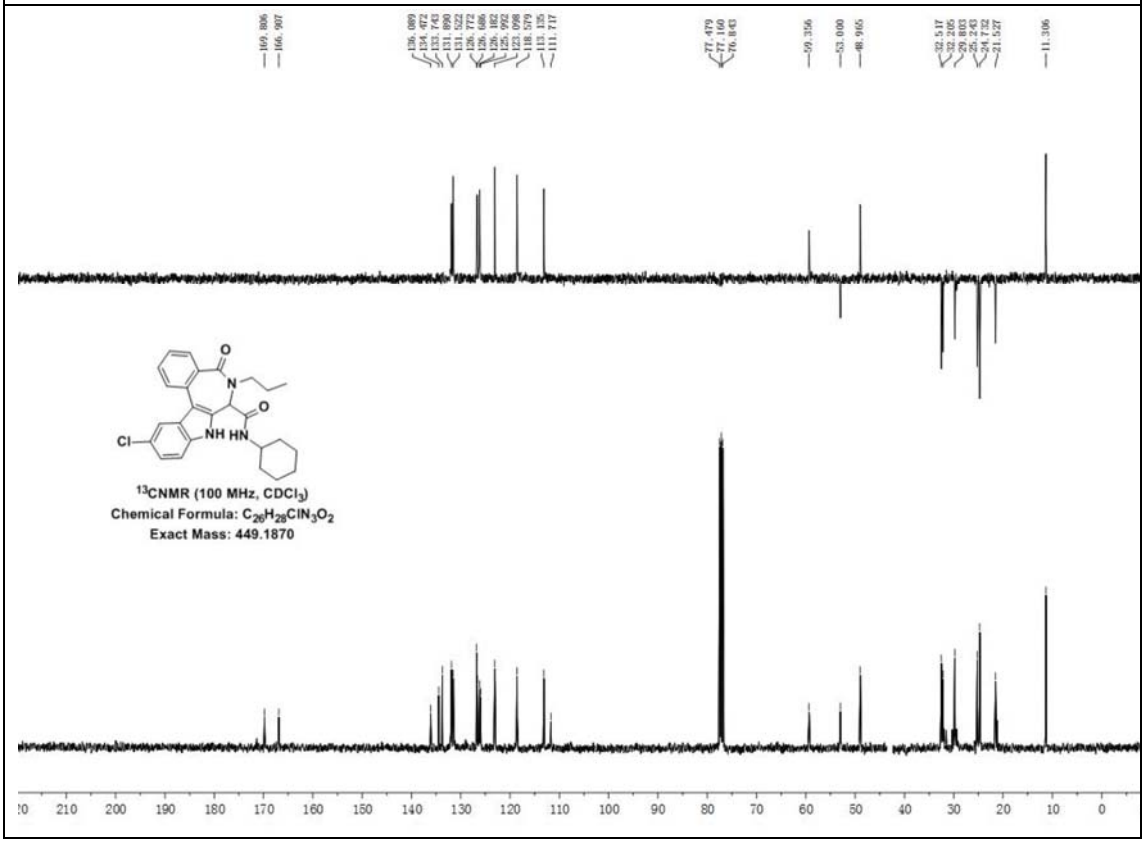
10-Chloro-*N*-cyclohexyl-5-oxo-6-propyl-6,7-dihydro-5*H*-benzo[6,7][1,4]diazepino[1,2-a]indole-7-carboxamide (7e).



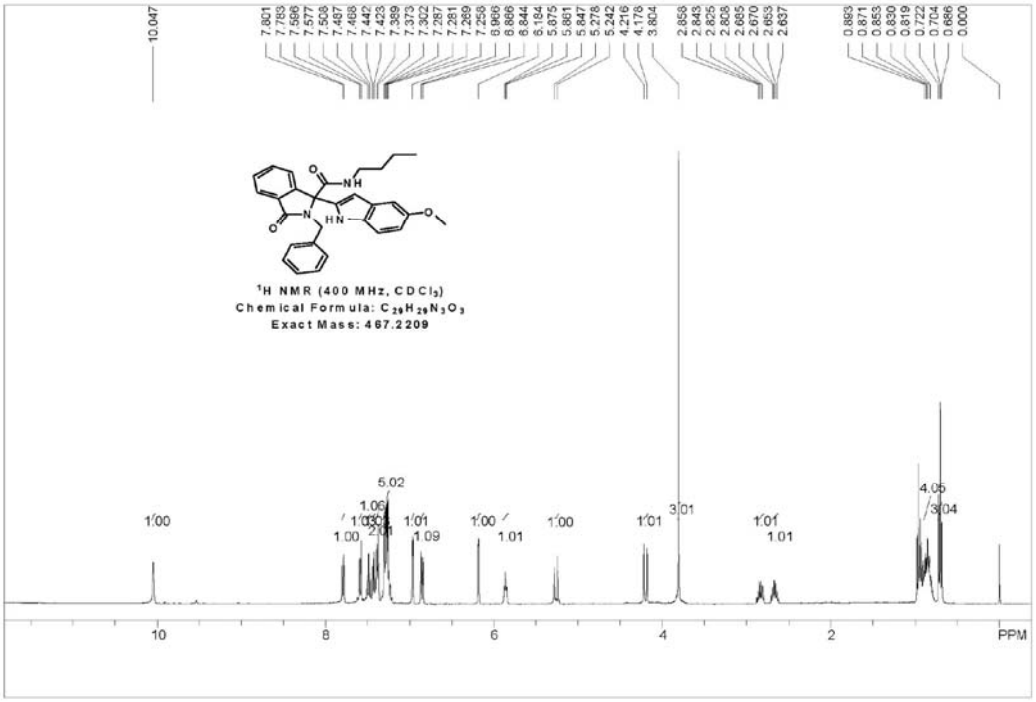


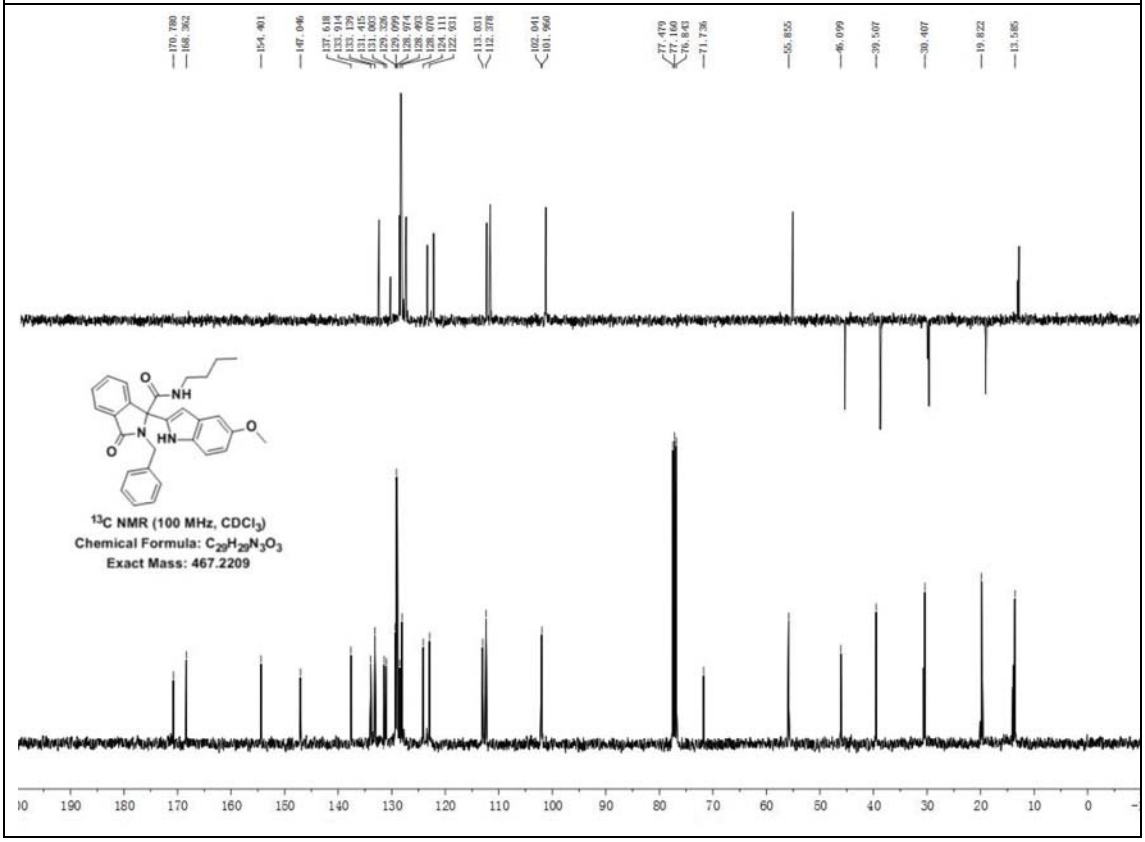
11-Chloro-*N*-cyclohexyl-5-oxo-6-propyl-5,6,7,8-tetrahydrobenzo[5,6]azepino[3,4-b]indole-7-carboxamide (8e).



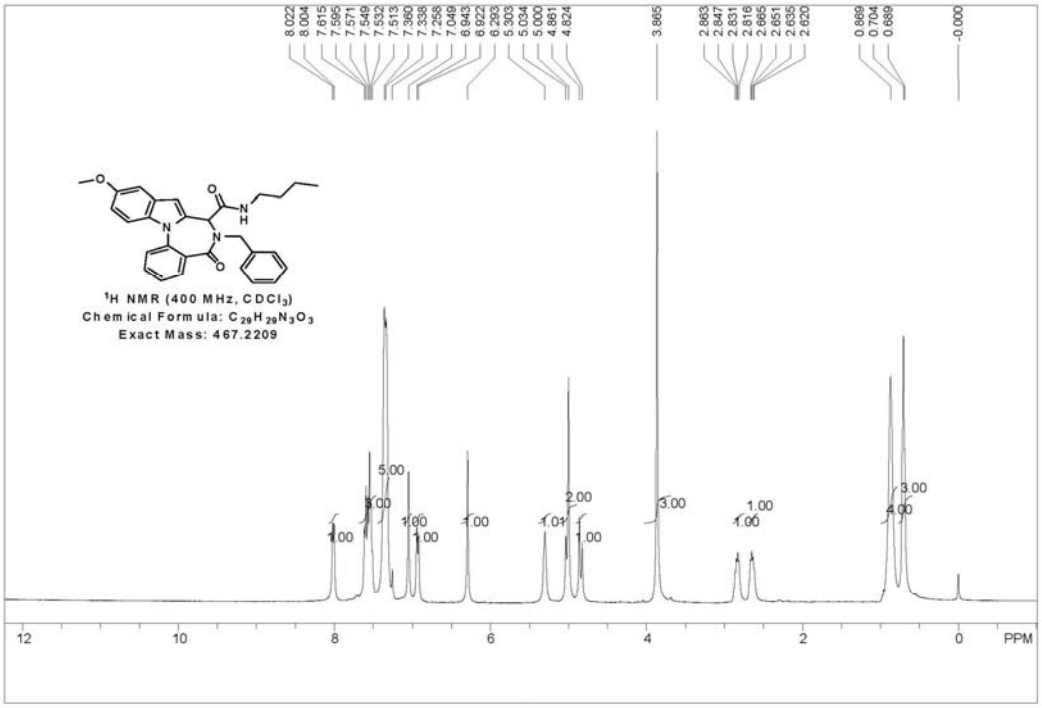


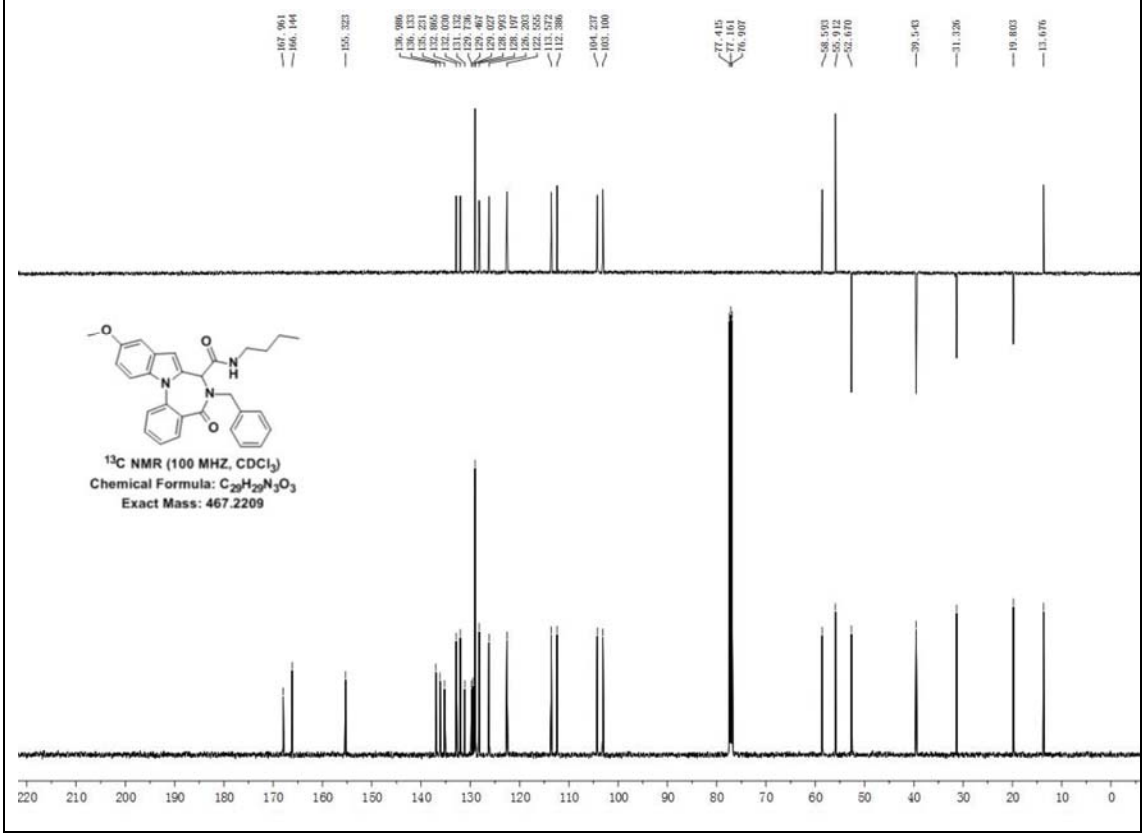
2-Benzyl-*N*-butyl-1-(5-methoxy-1*H*-indol-2-yl)-3-oxoisoindoline-1-carboxamide (6f).



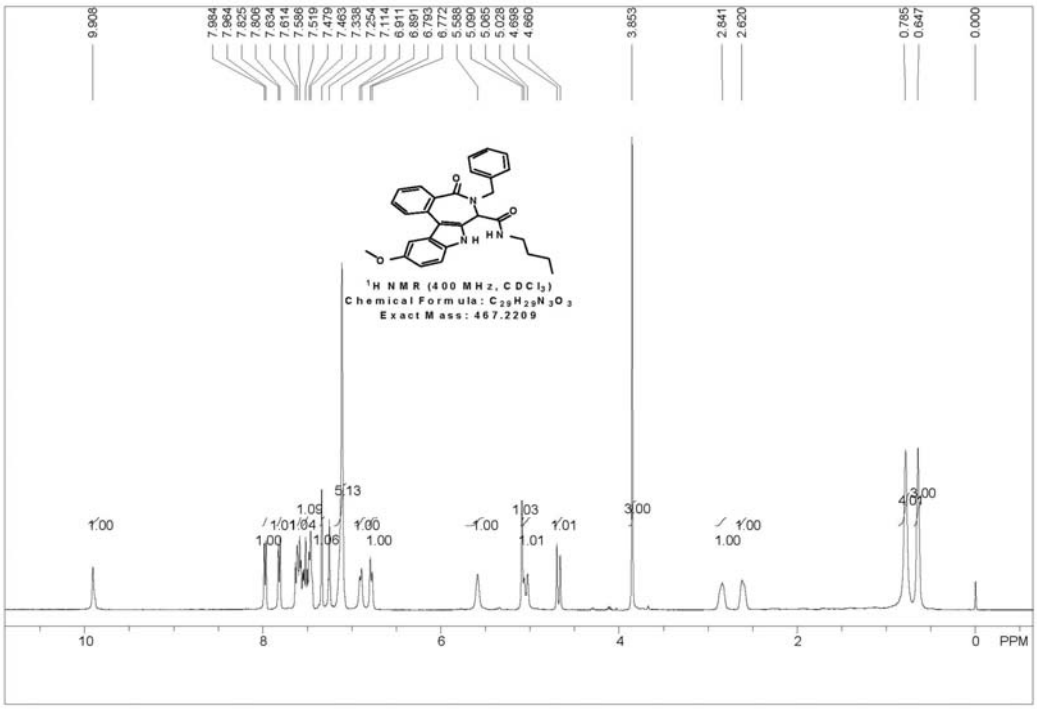


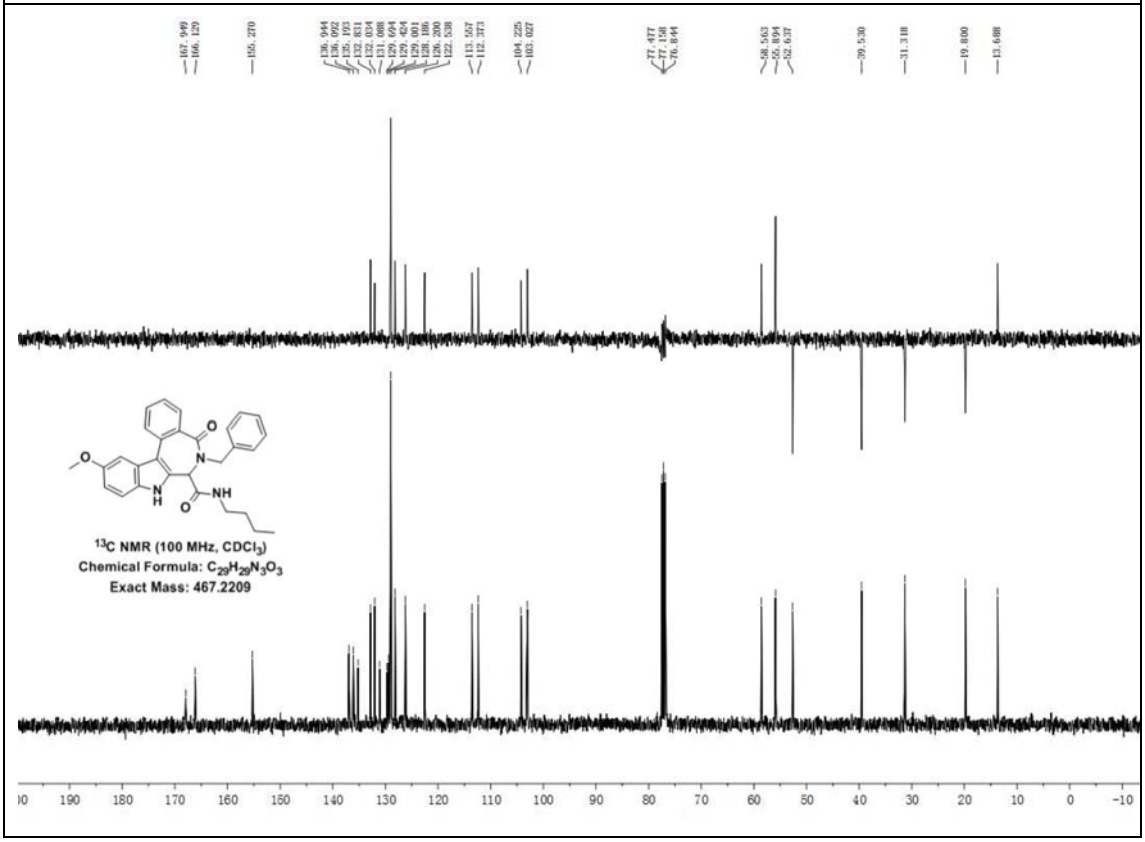
6-Benzyl-*N*-butyl-10-methoxy-5-oxo-6,7-dihydro-5*H*-benzo[6,7][1,4]diazepino[1,2-a]indole-7-carboxamide (7f).



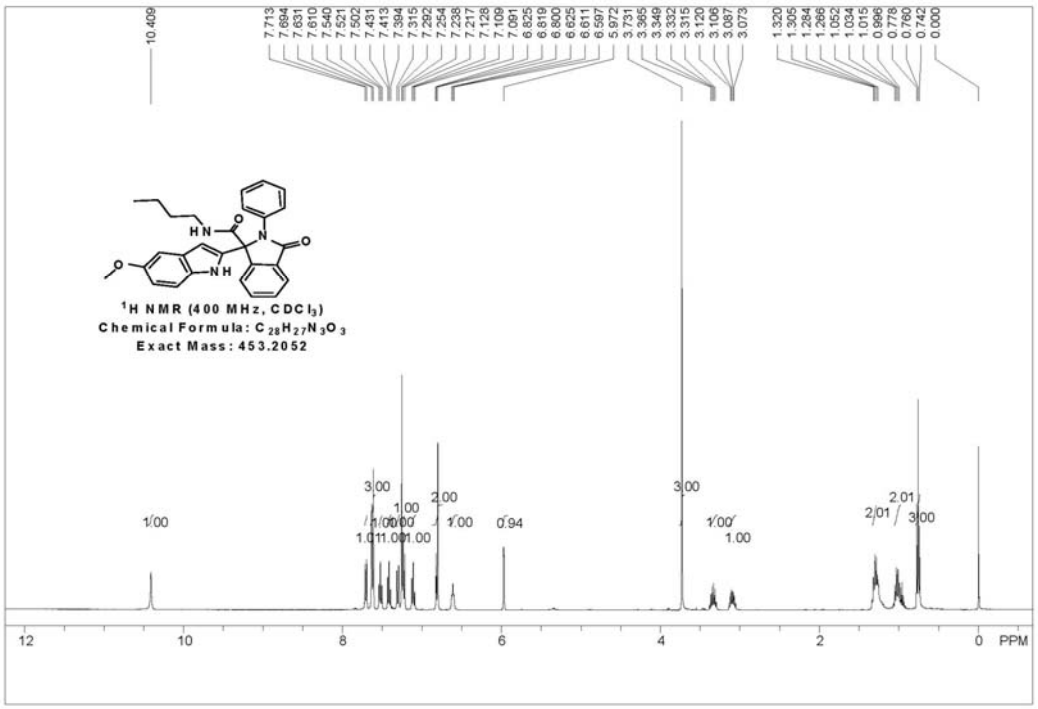


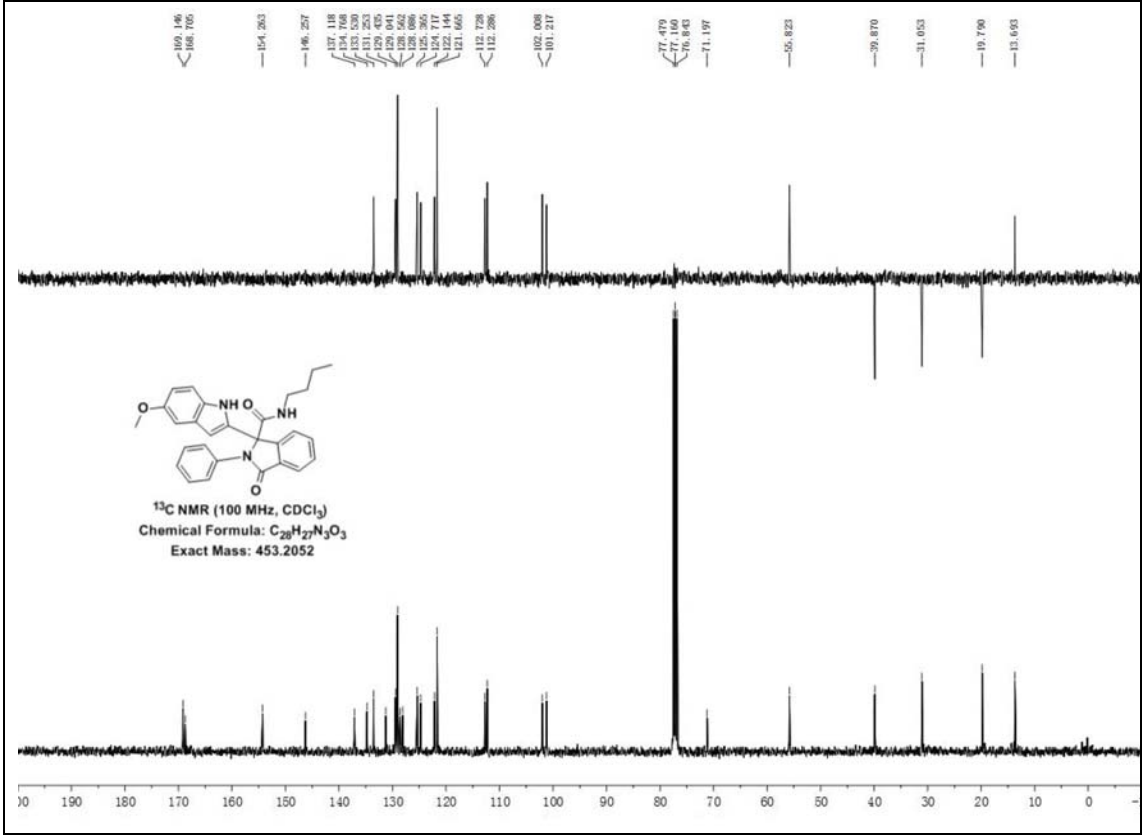
6-Benzyl-*N*-butyl-11-methoxy-5-oxo-5,6,7,8-tetrahydrobenzo[5,6]azepino[3,4-b]indole-7-carboxamide (8f).



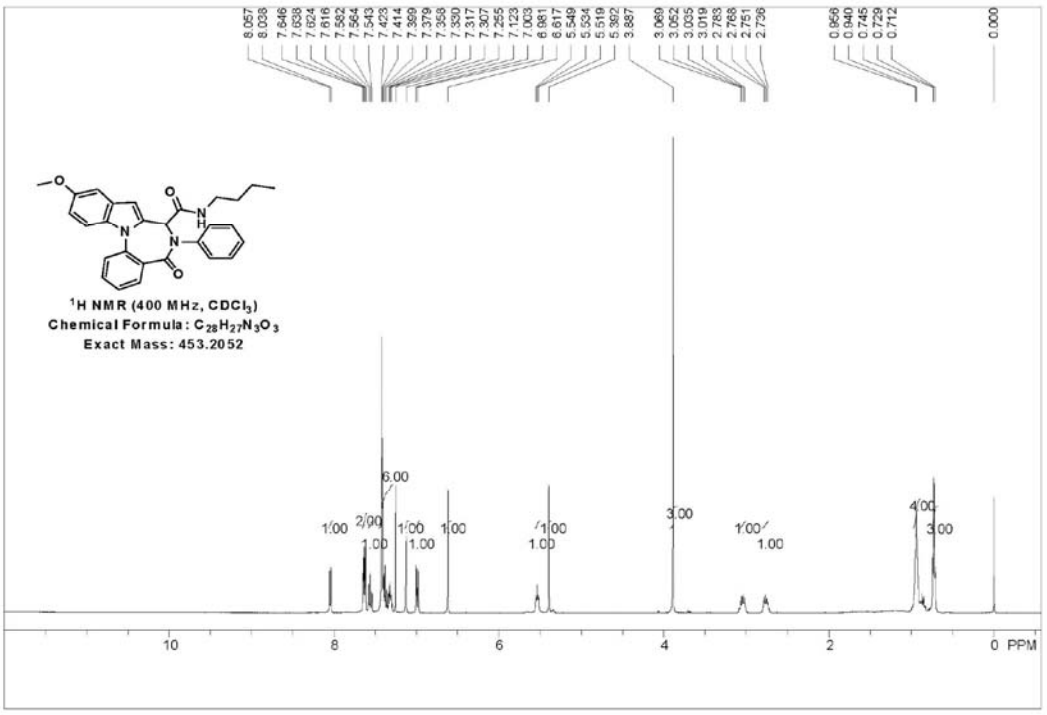


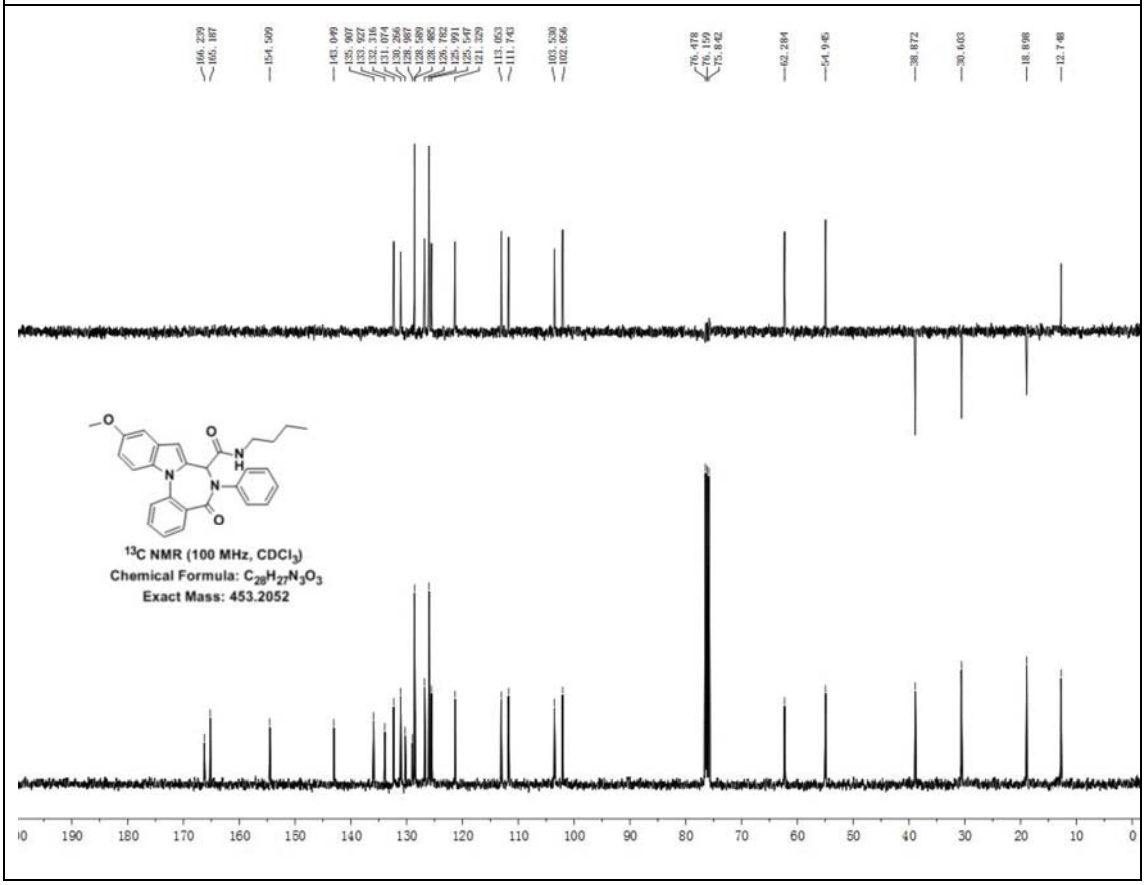
***N*-Butyl-1-(5-methoxy-1*H*-indol-2-yl)-3-oxo-2-phenylisoindoline-1-carboxamide (6g).**



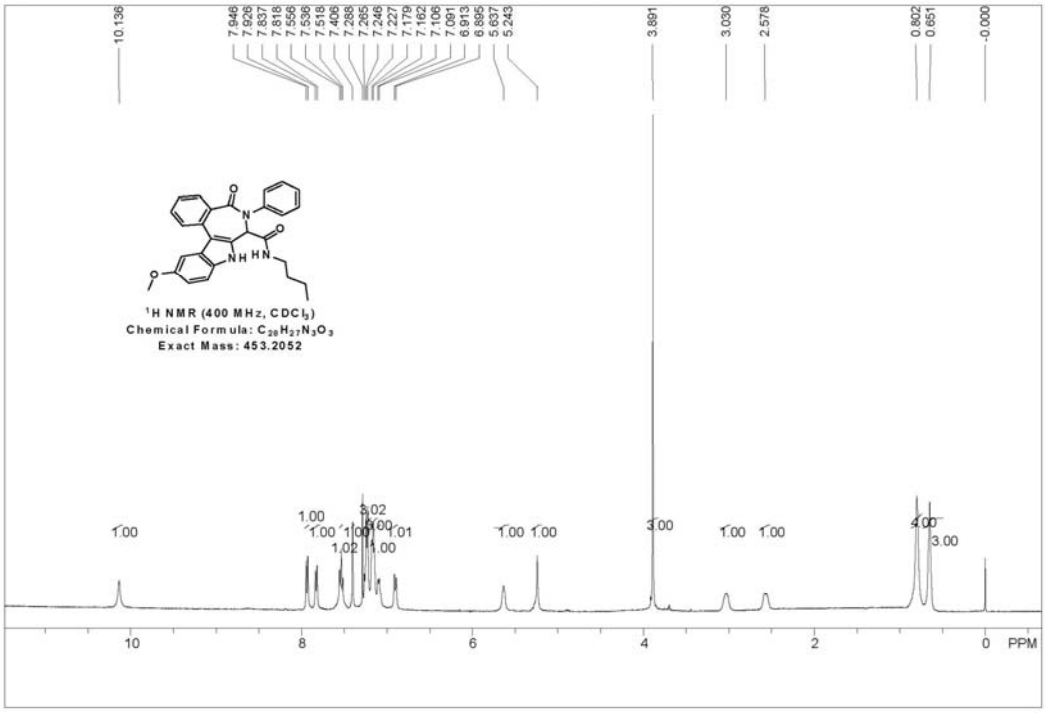


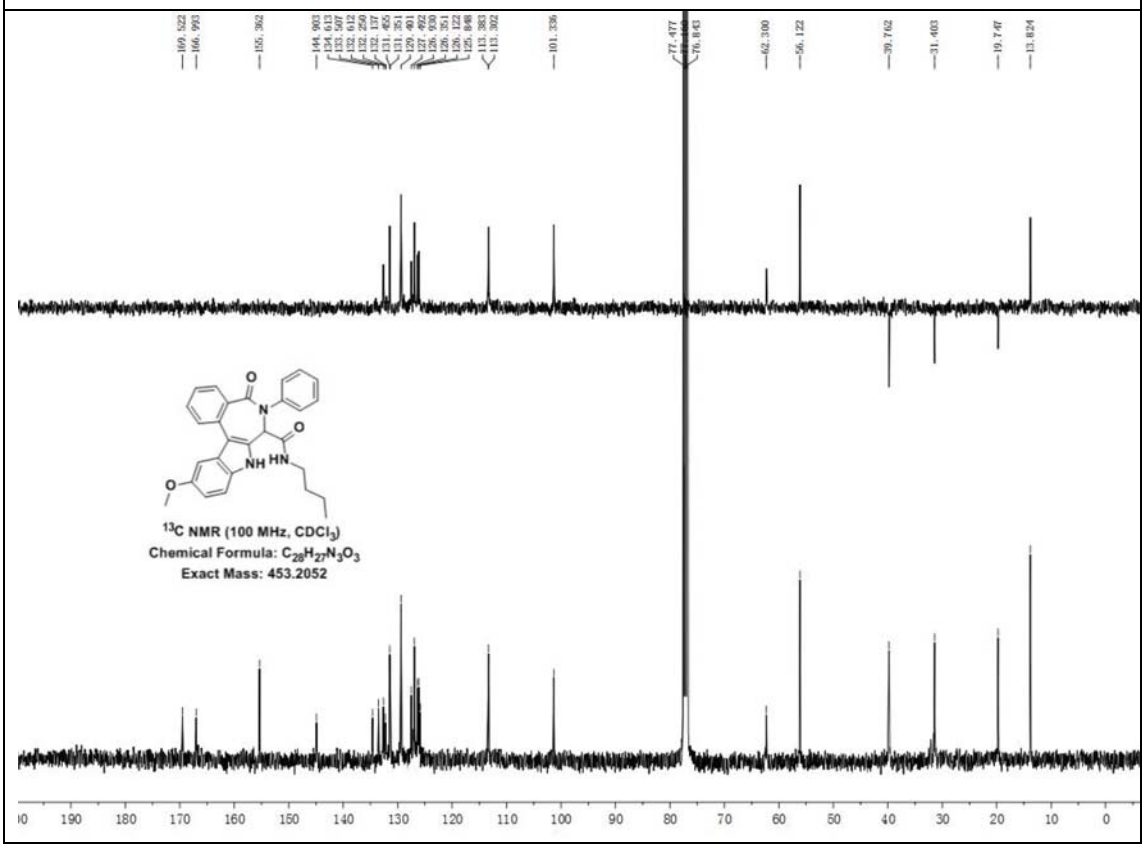
***N*-Butyl-10-methoxy-5-oxo-6-phenyl-6,7-dihydro-5*H*-benzo[6,7][1,4]diazepino[1,2-a]indole-7-carboxamide (7g).**



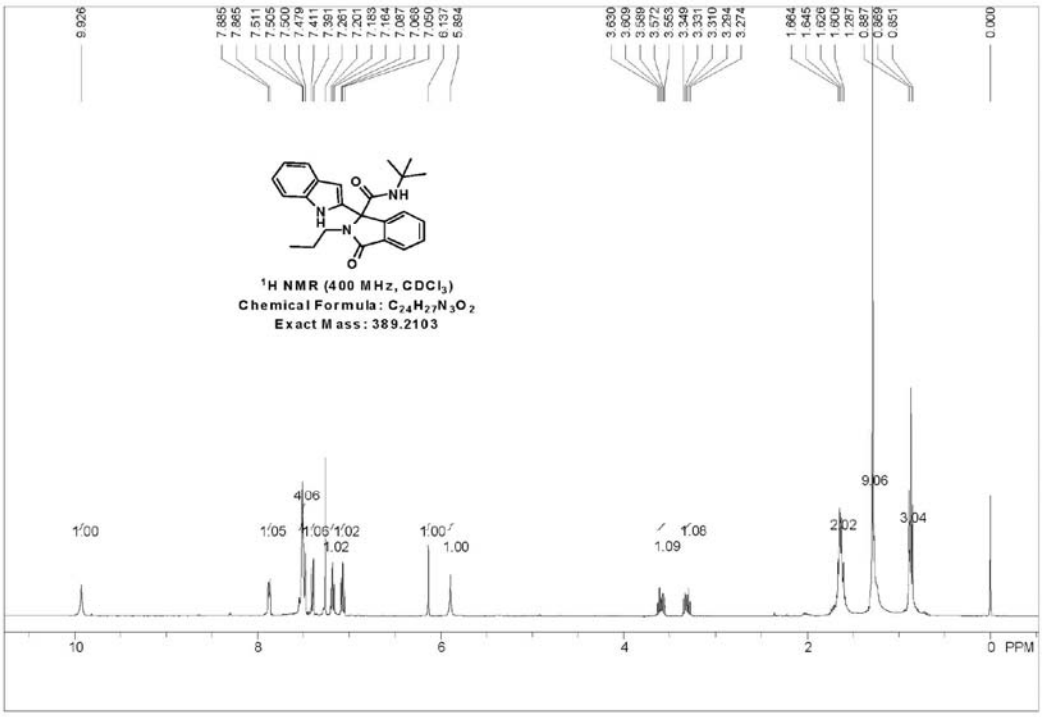


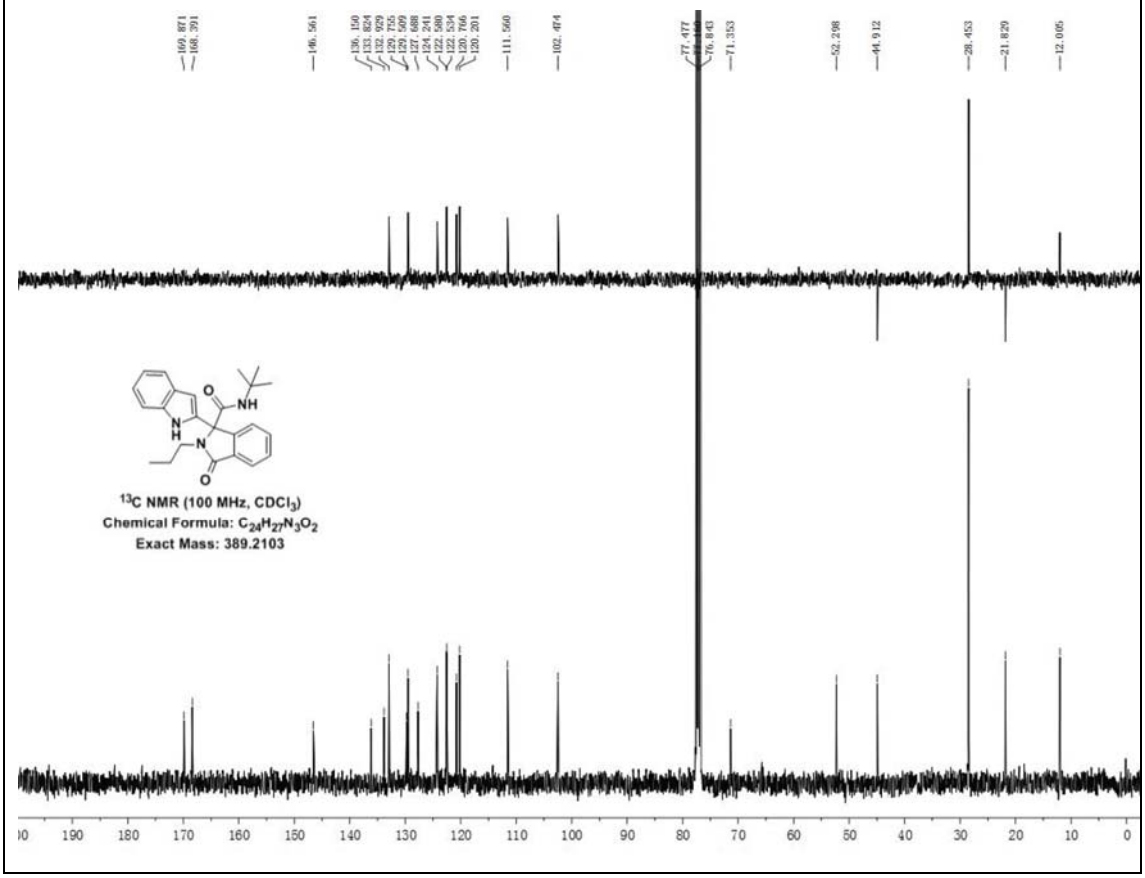
***N*-Butyl-11-methoxy-5-oxo-6-phenyl-5,6,7,8-tetrahydrobenzo[5,6]azepino[3,4-b]indole-7-carboxamide (8g).**



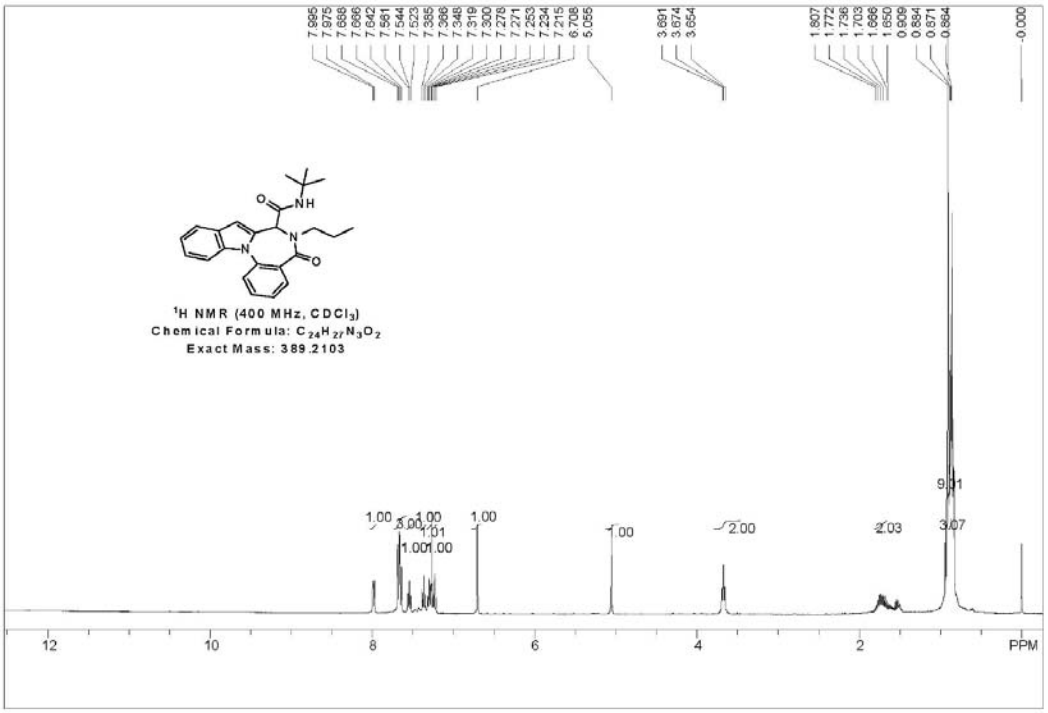


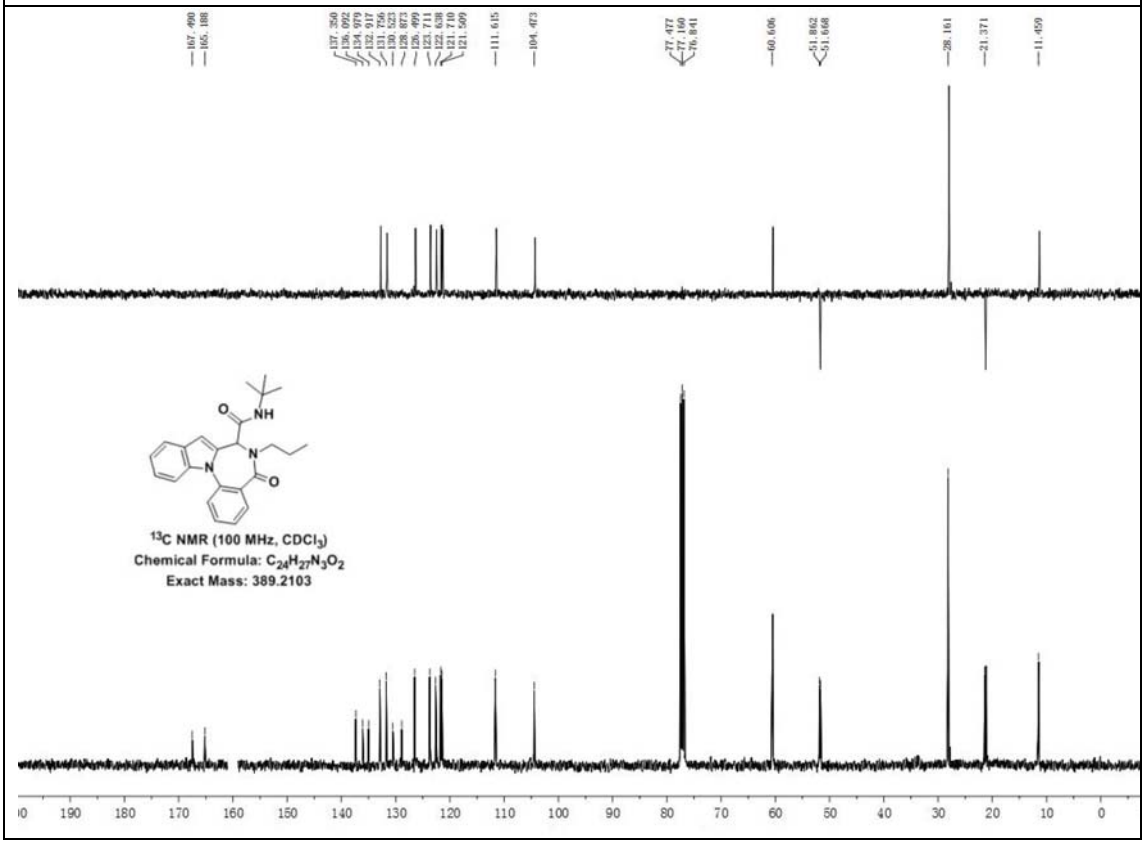
***N*-(*tert*-Butyl)-1-(1*H*-indol-2-yl)-3-oxo-2-propylisoindoline-1-carboxamide (6h).**





***N*-(*tert*-Butyl)-5-oxo-6-propyl-6,7-dihydro-5*H*-benzo[6,7][1,4]diazepino[1,2-a]indole-7-carboxamide (7h).**





***N*-(*tert*-Butyl)-5-oxo-6-propyl-5,6,7,8-tetrahydrobenzo[5,6]azepino[3,4-b]indole-7-carboxamide (8h).**