Tunable Copper-Catalyzed Multicomponent Reaction Towards Alkaloid-Inspired Indole/Lactam polycycles

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General Experimental

^{1}H nuclear magnetic resonance (NMR) spectra were recorded using an internal deuterium lock at ambient temperatures on the following instruments: Bruker AC400 (400 MHz). The internal references of δ_H 7.26 and 2.05 ppm were used for the residual protons in $CDCl_3$ and $(CD_3)_2CO$. Data are presented as follows: chemical shift (in ppm), integration, interpretation, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, dd = doublet of doublet, dt = doublet of triplet, br = broad) and coupling constant (*J* in Hz). ^{13}C NMR spectra were recorded on a Bruker AC400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the internal solvent signal (peak at 77.16 ppm in the case of $CDCl_3$ and 206.26 ppm in the case of $(CD_3)_2CO$). NMR spectra were assigned using information ascertained from DEPT, HMQC, COSY and NOESY experiments.

Melting point was determined by means of Büchi Melting Point B-540 apparatus.

Infra-red spectra were recorded on a Bruker VERTEX70 Fourier transform infrared spectrometer fitted with a single reflection diamond ATR Bruker A222 accessory. The measurements were done for pure samples. For each individual spectrum, about 30 scans were averaged at 4 cm^{-1} resolution. The diamond crystal without sample served as reference. All the system was purged with dry air. The identification of peaks was done with the standard method proposed in OPUS 6.0 software. Wavelengths of maximum absorbance (ν_{max}) are quoted in cm^{-1}.

High resolution MS experiments were performed with a QSTAR Elite mass spectrometer (Applied Biosystems SCIEX) or a SYNAPT G2 HDMS mass spectrometer (Waters) equipped with an electrospray ionization source operated in the positive ion mode. In this hybrid instrument, ions were measured using an orthogonal acceleration time-of-flight (oa-TOF) mass analyzer.

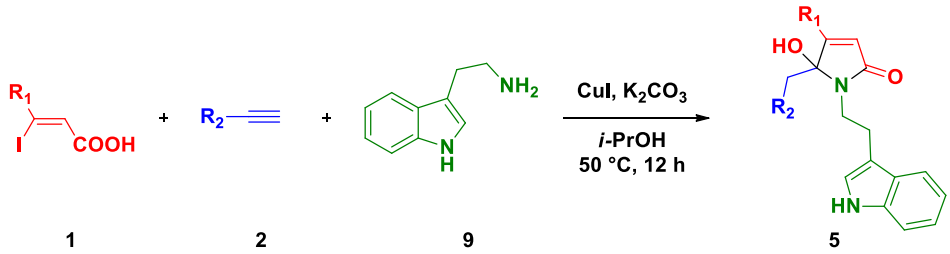
Analytical thin layer chromatography (TLC) was carried out on Merck® Kieselgel 60 F254 plates and achieved under a 254 nM UV light, visualized with a $KMNO_4$ solution.

Flash column chromatography was carried out on Acros Organic Kieselgel 60 (0.035-0.07 mm) silica gel. Reagents and solvents were purified by standard means.[1]

All experiments were performed under anhydrous conditions and an inert atmosphere of argon. Petroleum ether refers to the petroleum ether fraction boiling between 40°C and 60°C. All reagents were weighed and handled in air at room temperature. The reactions were magnetically stirred.

[1] Perrin, D. D.; Amarego, W. L.; *Purification of Laboratory Chemicals;* Pergamon Press, **1988**.

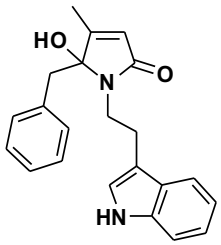
General Procedure to synthesize Indolo-γ-hydroxybutyrolactams 5



1 2 9 5

(*Z*)-3-Substituted-3-iodoprop-2-enoic acid derivative **1** (2.0 mmol, 1 equiv.) was dissolved in *i*-PrOH (7 mL) in oven-dried-Schlenk tube. K_2CO_3 (553 mg, 4.0 mmol, 2 equiv.) was then added to the solution and the suspension was stirred for 10 min under Argon. The mixture was then degassed at -78 °C for 2x10 min and the vessel was backfilled with argon. After warming to room temperature, terminal alkyne **2** (4.0 mmol, 2 equiv.), tryptamine **9** (641 mg, 4.0 mmol, 2 equiv.) and CuI (76 mg, 0.4 mmol, 0.2 equiv) were respectively added into the mixture. The mixture was then rapidly degassed and the vessel was backfilled with argon. The sealed Schlenck tube was placed in the preheated oil bath (50 °C) and was stirred overnight. The reaction mixture was cooled to 0 °C, then quenched by the addition of an aqueous saturated NH_4Cl solution and stirred for further 15 min. The mixture was filtered through a pad of Celite®. The aqueous phase was extracted with ethyl acetate and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was then purified by flash chromatography on silica gel using petroleum ether: ethyl acetate as eluent.

1-(2-(1*H*-indol-3-yl)ethyl)-5-benzyl-5-hydroxy-4-methyl-1,5-dihydro-2*H*-pyrrol-2-one (5a)



Purification: flash chromatography on silica gel (PE/EtOAc : from 80/20 to 30/70)

Yield: 83% (576 mg)

Physical appearance: brown solid

m.p. (amorphous): 167°C; **^{1}H-NMR** ($(CD_3)_2CO$, 400 MHz): δ (ppm) 2.07 (3H, CH_3, br d, *J* = 1.5 Hz), 3.10-3.27 (2H, CH_2, m), 3.19 (1H, C*H*$_2$, d, *J* = 14.2 Hz), 3.37 (1H, C*H*$_2$, d, *J* = 14.2 Hz), 3.54-3.64 (1H, C*H*$_2$, m), 3.84-3.94 (1H, C*H*$_2$, m), 5.38 (1H, OH, br s), 5.58 (1H, CH, br q, *J* = 1.5 Hz), 7.04-7.25 (8H, 8 x CH_{Ar}, m), 7.42 (1H, CH_{Ar}, br d, *J* = 7.9 Hz), 7.42 (1H, CH_{Ar}, br d, *J* = 7.8 Hz), 10.05 (1H, NH, br s); **^{13}C-NMR** ($(CD_3)_2CO$, 100 MHz): δ (ppm) 12.7 (CH_3), 26.1 (CH_2), 41.0 (CH_2), 41.2 (CH_2), 94.1 (C), 112.1 (CH_{Ar}), 113.7 (C_{Ar}), 119.3 (CH_{Ar}), 119.5 (CH_{Ar}), 122.0 (CH_{Ar}), 123.1 (CH_{Ar}), 123.5 (CH), 127.4 (CH_{Ar}), 128.5 (C_{Ar}), 128.7 (2 x CH_{Ar}), 130.3 (2 x CH_{Ar}), 136.2 (C_{Ar}), 137.6 (C_{Ar}), 160.1 (C), 169.8 (C); **IR** (nujol): 3282, 3234, 2921, 1664, 1629, 1436, 1093, 1072, 740, 696 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{22}H_{23}N_2O_2$ $[M+H]^+$ 347.1754, found 347.1757.

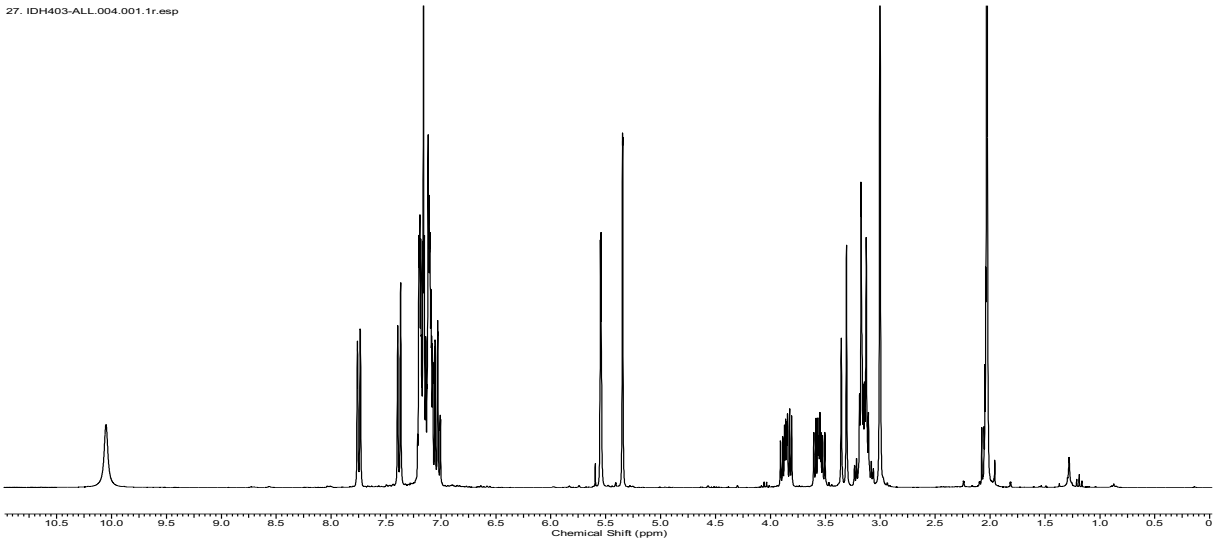


Figure S1 ^{1}H-NMR spectrum of **5a** in $(CD_3)_2CO$

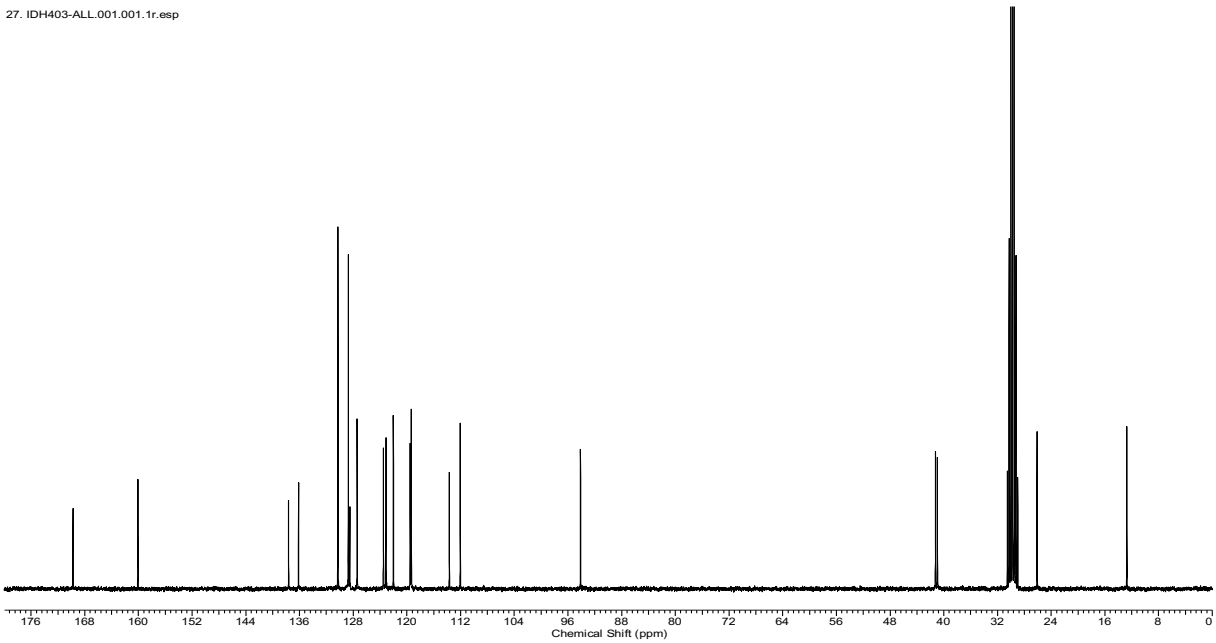


Figure S2 ^{13}C-NMR spectrum of **5a** in $(CD_3)_2CO$

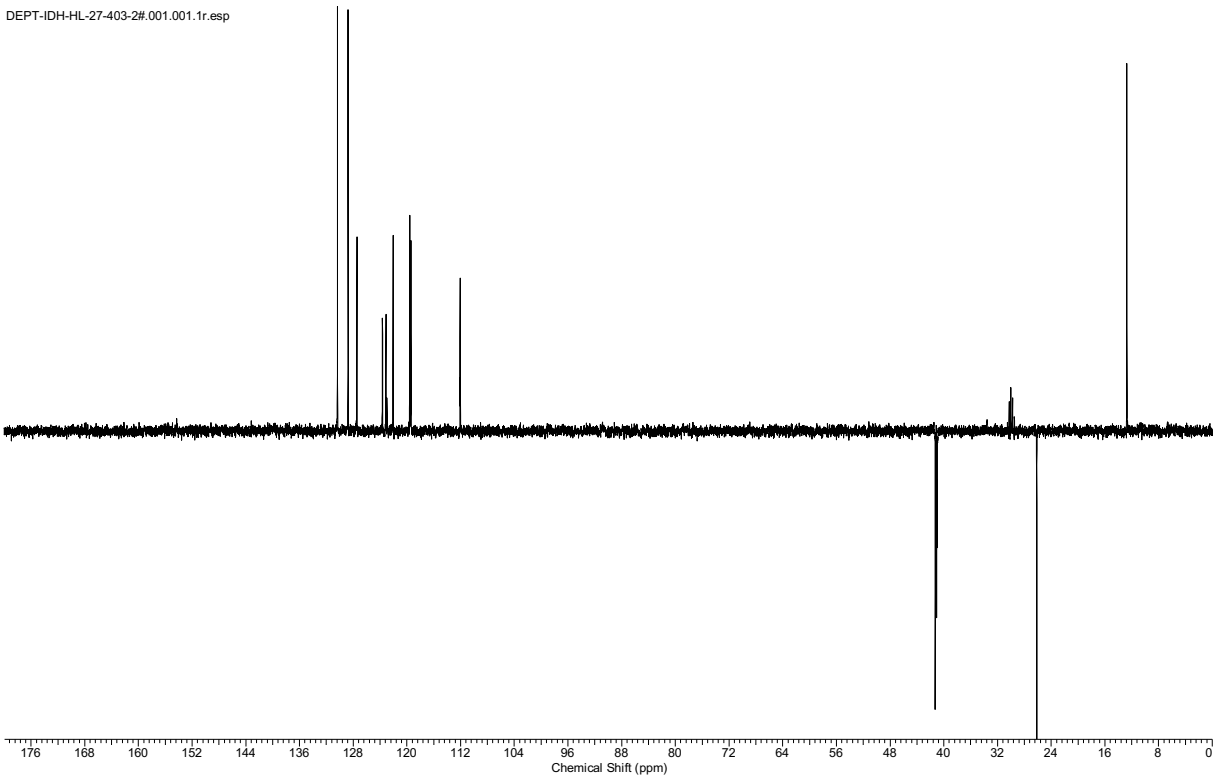
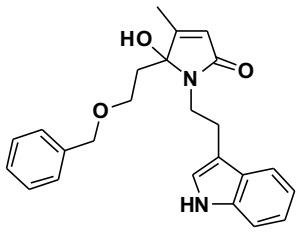


Figure S3 DEPT 135 spectrum of **5a** in $(CD_3)_2CO$

1-(2-(1H-indol-3-yl)ethyl)-5-(2-(benzyloxy)ethyl)-5-hydroxy-4-methyl-1H-pyrrol-2(5H)-one (5b)



Purification: flash chromatography on silica gel (PE/EtOAc : from 85/15 to 40/60)

Yield: 77% (601 mg)

Physical appearance: brown solid

m.p. (amorphous): 120 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 1.91 (3H, CH_3, d, *J* = 1.5 Hz), 2.11-2.27 (2H, CH_2, m), 2.51 (1H, OH, br s), 3.04-3.18 (3H, $CH_2$and CH_2, m), 3.21-3.26 (1H, CH_2, m), 3.36-3.43 (1H, CH_2, m), 3.77-3.85 (1H, CH_2, m), 4.31(1H, CH_2, d, *J* = 12.0 Hz), 4.34 (1H, CH_2, d, *J* = 12.0 Hz), 5.71 (1H, CH, brq, *J* = 1.5 Hz), 7.02 (1H, CH_{Ar}, br s), 7.11 (1H, CH_{Ar}, br t, *J* = 7.6 Hz), 7.18 (1H, CH_{Ar}, br t, *J* = 7.8 Hz), 7.22-7.35 (6H, 6 x CH_{Ar}, m), 7.66 (1H, CH_{Ar}, br d, *J* = 7.8 Hz), 8.06 (1H, NH, br s);**^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 12.6 (CH_3), 24.8 (CH_2), 33.8 (CH_2), 39.9 (CH_2), 65.3 (CH_2), 73.5 (CH_2), 92.3 (C), 111.3 (CH_{Ar}), 113.6 (C_{Ar}), 119.1 (CH_{Ar}), 119.6 (CH_{Ar}), 121.9 (CH), 122.2$_1$ (CH_{Ar}), 122.2$_4$ (CH_{Ar}), 127.5 (C_{Ar}), 127.8 (2 x CH_{Ar}), 127.9 (CH_{Ar}), 128.5 (2 x CH_{Ar}), 135.4 (C_{Ar}), 137.9 (C_{Ar}), 160.5 (C), 170.4 (C); **IR** (nujol): 3299, 2958, 1677, 1633, 1404, 1060, 844, 734 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{24}H_{26}N_2O_3Na[M+Na]^+$ 413.1836, found 413.1836.

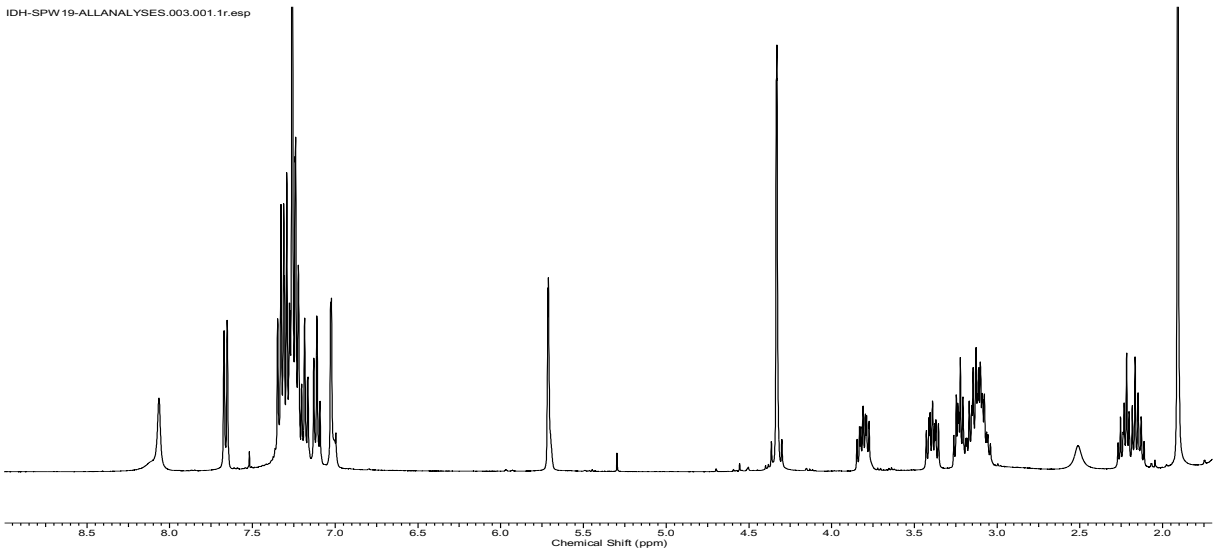


Figure S4 ^{1}H-NMR spectrum of **5b** in $CDCl_3$

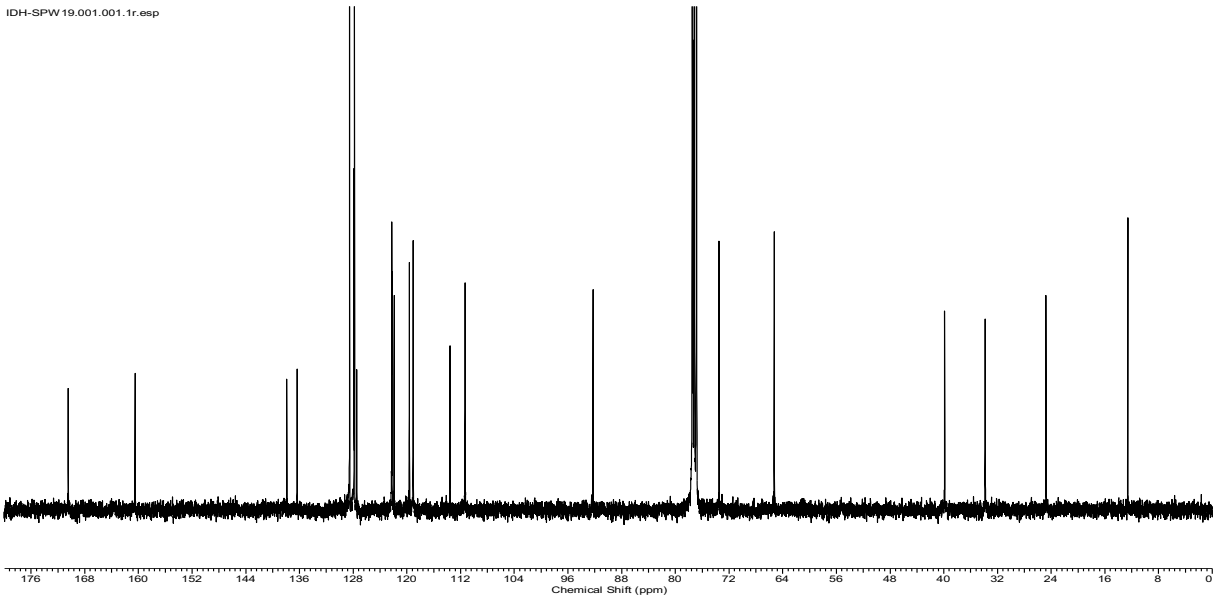


Figure S5 ^{13}C-NMR spectrum of **5b** in $CDCl_3$

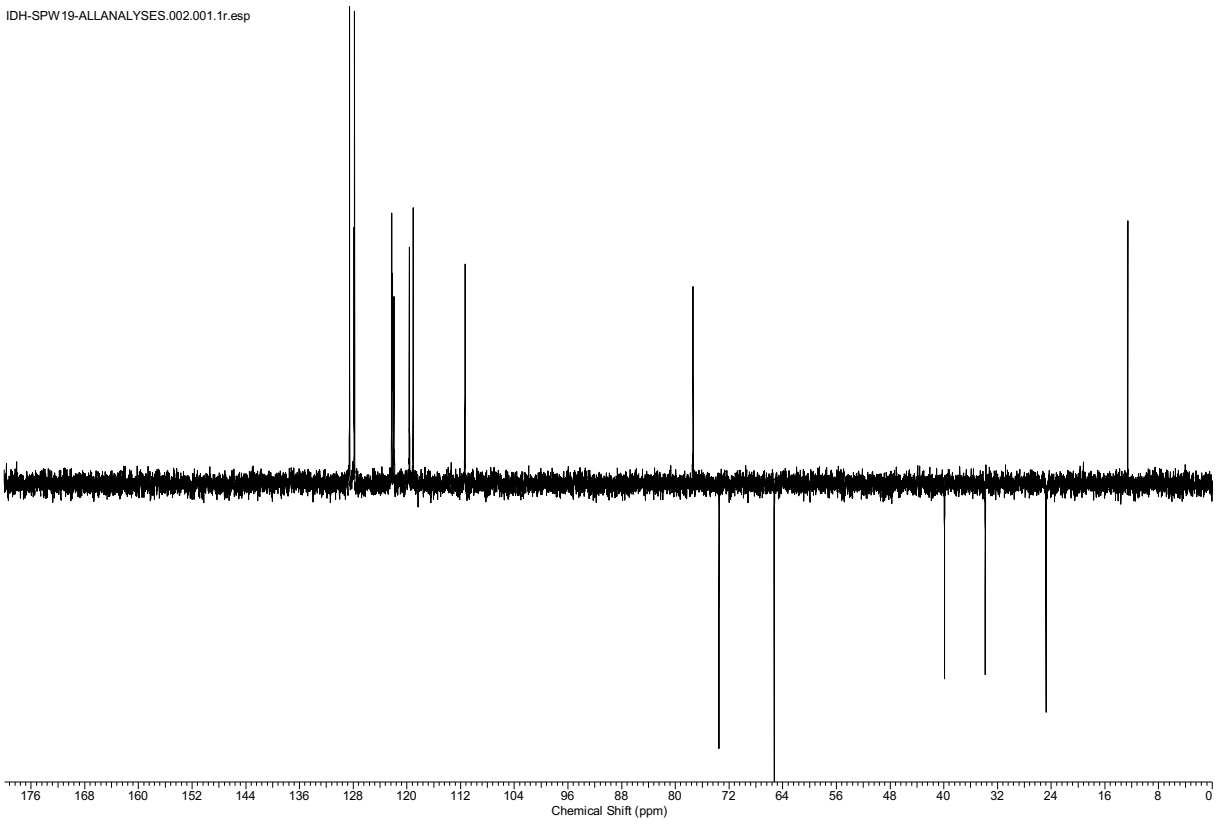
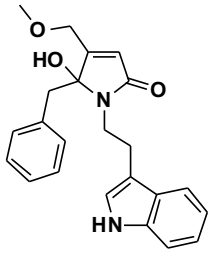


Figure S6 DEPT 135 spectrum of **5b** in $CDCl_3$

1-(2-(1H-indol-3-yl)ethyl)-5-benzyl-5-hydroxy-4-(methoxymethyl)-1H-pyrrol-2(5H)-one (5c)



Note: the reaction was performed with 1 mmol of acid

Purification: flash chromatography on silica gel (PE/EtOAc : from 85/15 to 40/60)

Yield: 85% (320 mg)

Physical appearance: yellow solid

m.p. (amorphous): 77 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 2.89 (1H, OH, br s), 3.08 (1H, C*H*$_2$, d, *J* = 14.4 Hz), 3.13-3.20 (2H, CH_2, m), 3.17 (1H, C*H*$_2$, d, *J* = 14.4 Hz), 3.29 (3H, CH_3, s), 3.51 (1H, C*H*$_2$, ddd, *J* = 15.9, 9.1 and 6.9 Hz), 3.92-3.99 (1H, C*H*$_2$, m), 4.07 (1H, C*H*$_2$, dd, *J* = 15.4 and 1.7 Hz), 4.13 (1H, C*H*$_2$, dd, *J* = 15.4 and 1.7 Hz), 5.84 (1H, CH, t, *J* = 1.7Hz), 7.03-7.06 (3H, 3 x CH_{Ar}, m), 7.13 (1H, CH_{Ar}, m), 7.17-7.24 (4H, 4 x CH_{Ar}, m), 7.35 (1H, CH_{Ar}, d, *J* = 8.0 Hz), 7.69 (1H, CH_{Ar}, d, *J* = 7.8 Hz), 8.15 (1H, NH, br s);**^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 24.7 (CH_2), 40.6 (CH_2), 41.5 (CH_2), 59.2 (CH_3), 68.0 (CH_2), 92.7 (C), 111.4 (CH_{Ar}), 113.7 (C_{Ar}), 119.1 (CH_{Ar}), 119.7 (CH_{Ar}), 122.3 (CH_{Ar}), 122.4 (CH_{Ar}), 123.0 (CH), 127.4 (CH_{Ar} and C_{Ar}), 128.54 (2 x CH_{Ar}), 129.6 (2 x CH_{Ar}), 134.4 (C_{Ar}), 136.4 (C_{Ar}), 158.9 (C), 169.3 (C); **IR** (nujol): 3299, 3062, 2931, 1652, 1409, 1340, 746, 702 cm^{-1} **HRMS** (ESI-MS) calcd for $C_{23}H_{24}N_2O_3$ $[M+H]^+$ 399.1679, found 399.1680.

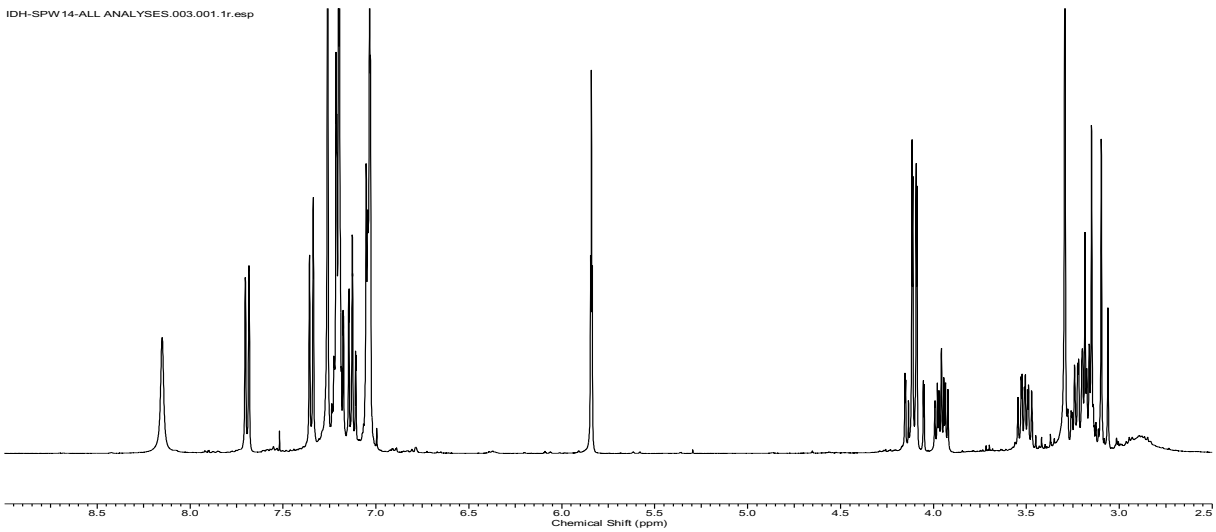


Figure S7 ^{1}H-NMR spectrum of **5c** in $CDCl_3$

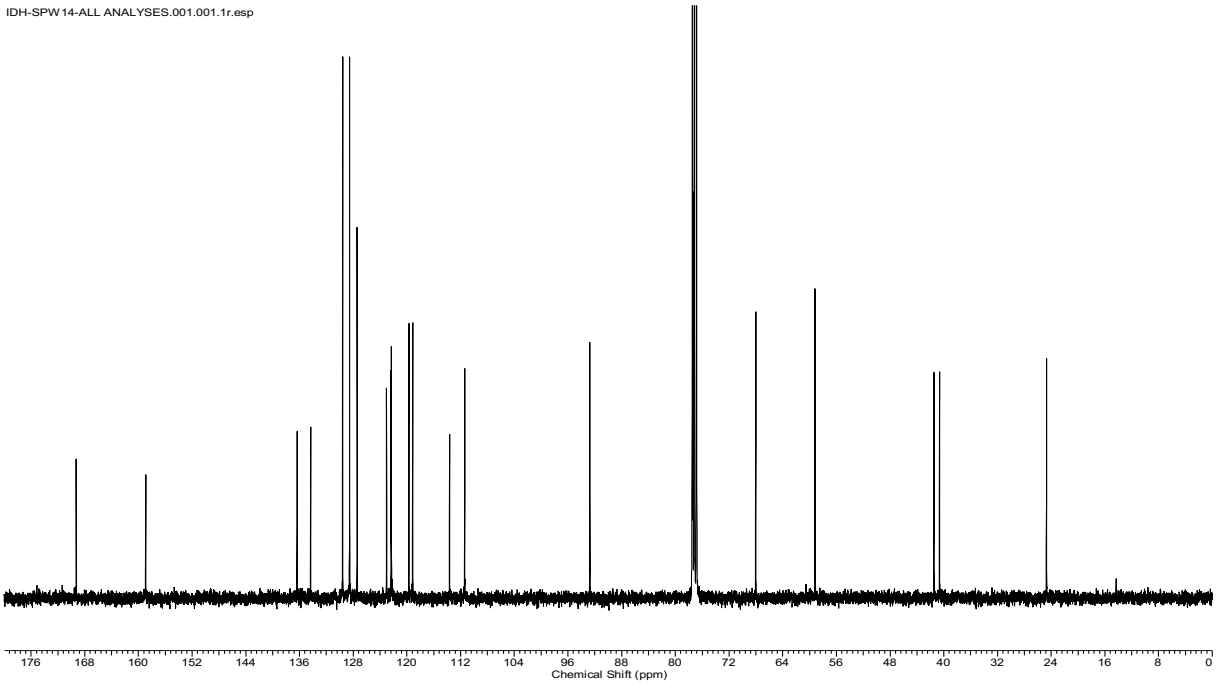


Figure S8 ^{13}C-NMR spectrum of **5c** in $CDCl_3$

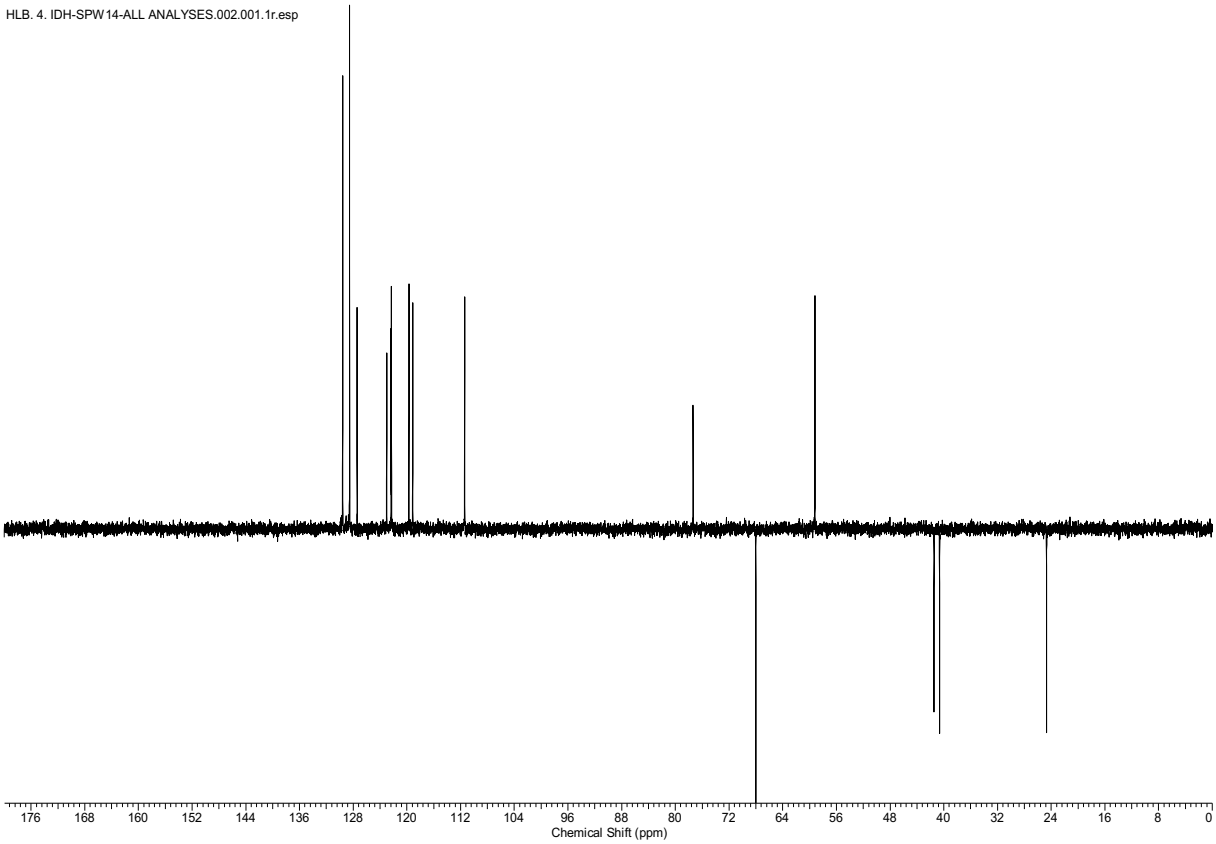
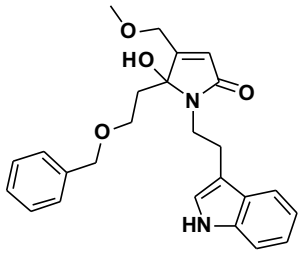


Figure S9 DEPT 135 spectrum of **5c** in $CDCl_3$

1-(2-(1H-indol-3-yl)ethyl)-5-(2-(benzyloxy)ethyl)-5-hydroxy-4-(methoxymethyl)-1H-pyrrol-2(5H)-one (5d)



Note:the reaction was performed with 1 mmol of acid

Purification: flash chromatography on silica gel (PE/EtOAc : from 85/15 to 40/60)

Yield: 63% (266 mg)

Physical appearance: brown gel

^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 2.09-2.16 (1H, C*H*$_2$, m), 2.22-2.28 (1H, C*H*$_2$, m), 2.95 (1H, OH, br s), 3.05-3.21 (3H, C*H*$_2$, CH_2, m), 3.25-3.30 (1H, C*H*$_2$, m), 3.31 (3H, CH_3, s), 3.35-3.43 (1H, C*H*$_2$, m), 3.76-3.83 (1H, C*H*$_2$, m), 4.18 (2H, CH_2, d, *J* = 1.7 Hz), 4.31 (2H, CH_2, s), 5.97 (1H, CH, br t, *J* = 1.7 Hz), 7.04 (1H, CH_{Ar}, br s), 7.11 (1H, CH_{Ar},br t, *J* = 7.8 Hz), 7.18 (1H, CH_{Ar}, br t, *J* = 7.8 Hz), 7.22-7.35 (6H, 6 x CH_{Ar}, m), 7.67 (1H, CH_{Ar}, d, *J* = 7.8 Hz), 8.06 (1H, NH, br s);**^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 24.7 (CH_2), 34.9 (CH_2), 39.7 (CH_2), 59.2 (CH_3), 65.3 (CH_2), 67.9 (CH_2) 73.6 (CH_2), 91.6 (C), 111.3 (CH_{Ar}), 113.6 (C_{Ar}), 119.1 (CH_{Ar}), 120.0 (CH_{Ar}), 121.6 (CH), 122.2 (CH_{Ar}), 122.3 (CH_{Ar}), 127.5 (C_{Ar}), 127.9 (3 x CH_{Ar}), 128.5 (2 x CH_{Ar}), 136.4 (C_{Ar}), 137.8 (C_{Ar}), 160.1 (C), 169.9 (C); **IR** (Nujol) : 3317, 3058, 1679, 1265, 730, 700 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{25}H_{29}N_2O_4$ $[M+H]^+$ 421.2122, found 421.2122.

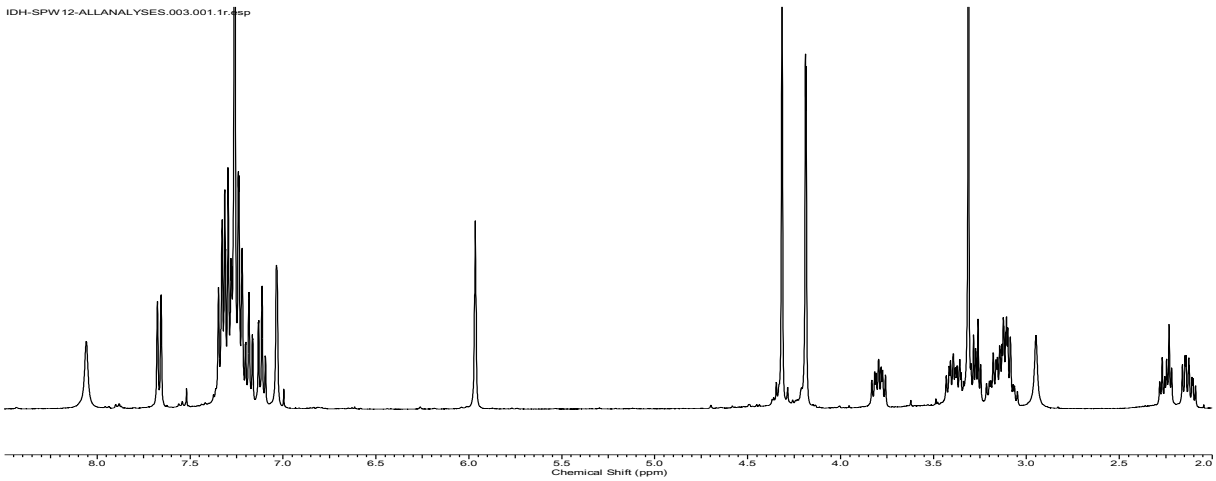


Figure S10 ^{1}H-NMR spectrum of **5d** in $CDCl_3$

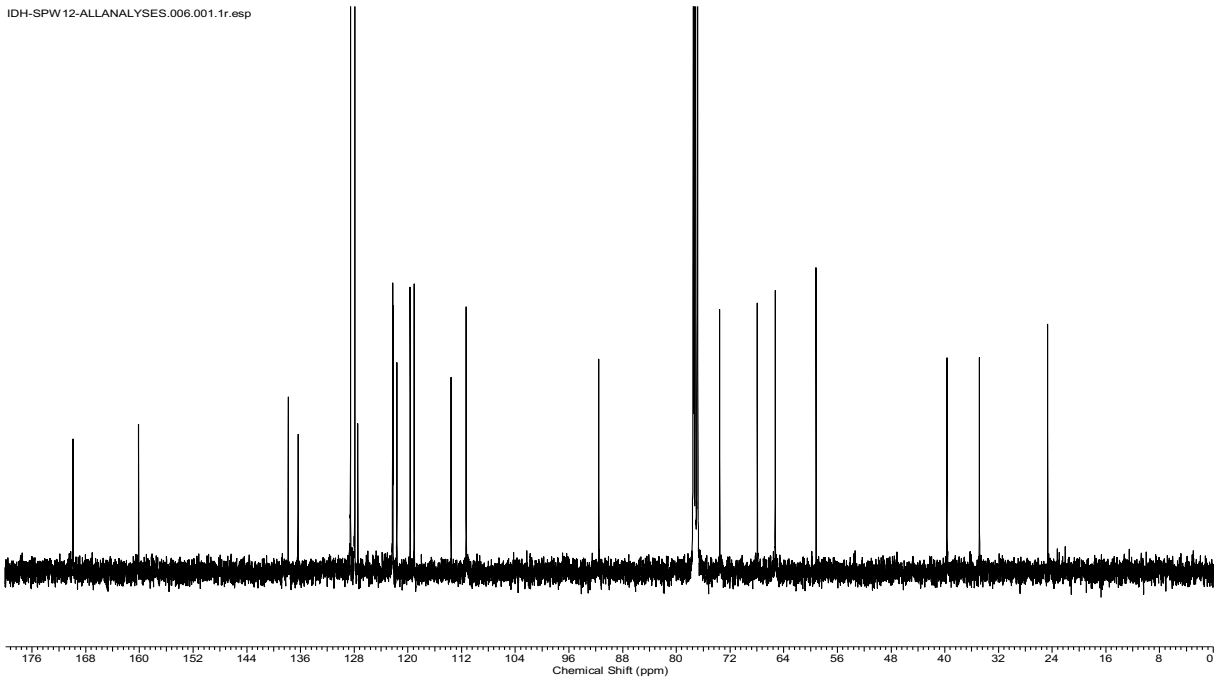


Figure S11 ^{13}C-NMR spectrum of **5d** in $CDCl_3$

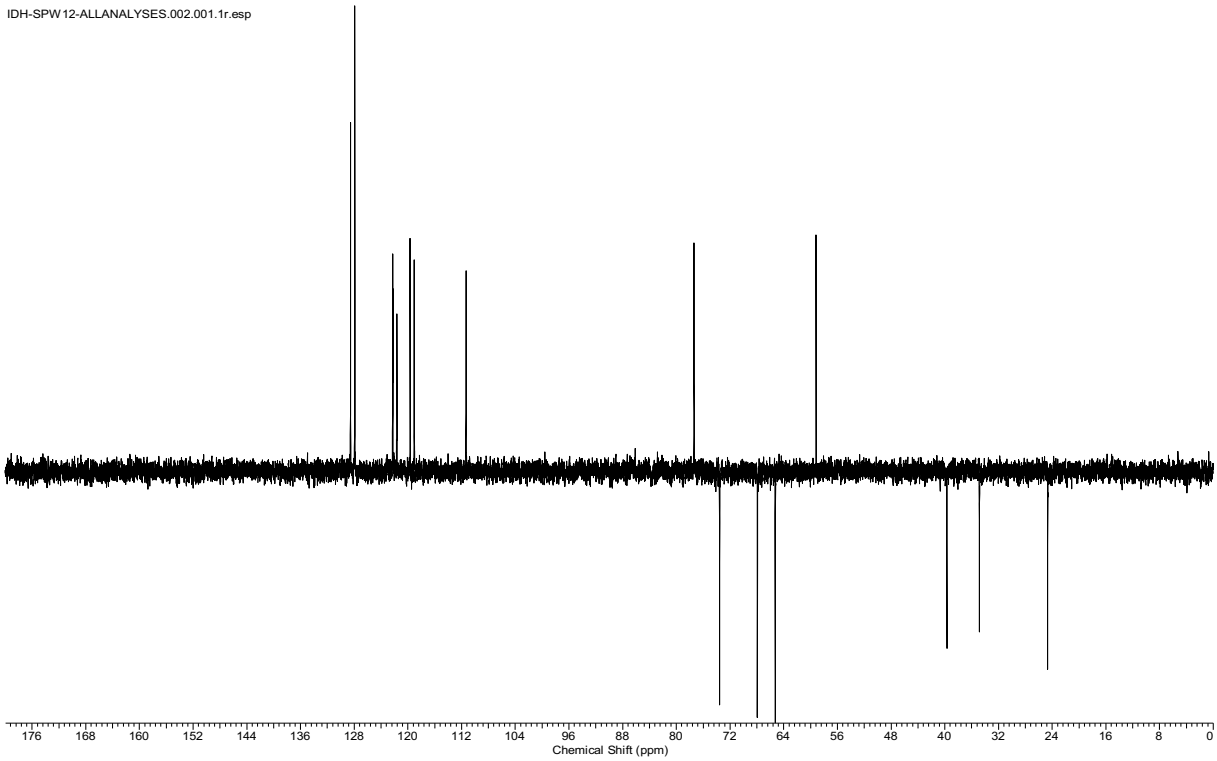
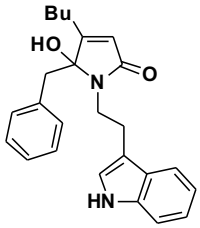


Figure S12 DEPT 135 spectrum of **5d** in $CDCl_3$

1-(2-(1*H*-indol-3-yl)ethyl)-5-benzyl-4-butyl-5-hydroxy-1,5-dihydro-2*H*-pyrrol-2-one (5e)



Purification: flash chromatography on silica gel (PE/EtOAc : from 9/1 to 3/7)

Yield: 81% (629 mg)

Physical appearance: brown solid

m.p. (amorphous): 163°C; **^{1}H-NMR** ($(CD_3)_2CO$, 400 MHz): δ (ppm) 0.94 (3H, CH_3, t, *J* = 7.3 Hz), 1.35-1.47 (2H, CH_2, m), 1.49-1.61 (2H, CH_2, m), 2.31-2.53 (2H, CH_2, m), 3.05-3.22 (2H, CH_2, m), 3.17 (1H, C*H*$_2$, d, *J* = 14.2 Hz), 3.35 (1H, C*H*$_2$, d, *J* = 14.2 Hz), 3.49-3.59 (1H, C*H*$_2$, m), 3.77-3.89 (1H, C*H*$_2$, m), 5.14 (1H, OH, br s), 5.53 (1H, CH, br t, *J* = 1.9 Hz), 7.01-7.22 (8H, 8 x CH_{Ar}, m), 7.39 (2H, 2 x CH_{Ar}, br d, *J* = 7.9 Hz), 7.74 (2H, 2 x CH_{Ar}, br d, *J* = 7.8 Hz), 10.01 (1H, NH, br s); **^{13}C-NMR** ($(CD_3)_2CO$, 100 MHz): δ (ppm) 14.3 (CH_3), 23.3 (CH_2), 26.3 (CH_2), 26.9 (CH_2), 29.3 (CH_2), 41.3 (CH_2), 41.4 (CH_2), 94.4 (C), 112.2 (CH_{Ar}), 113.9 (C_{Ar}), 119.5 (CH_{Ar}), 119.7 (CH_{Ar}), 121.9 (CH_{Ar}), 122.2 (CH), 123.4 (CH_{Ar}), 127.5 (CH_{Ar}), 128.7 (C_{Ar}), 128.9 (2 x CH_{Ar}), 130.5 (2 x CH_{Ar}), 136.4 (C_{Ar}), 137.8 (C_{Ar}), 164.7 (C), 169.8 (C); **IR** (nujol): 3355, 2931, 1664, 1633, 1454, 1419, 1041, 746, 700, 646 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{25}H_{29}N_2O_2$ $[M+H]^+$389.2224, found 389.2220.

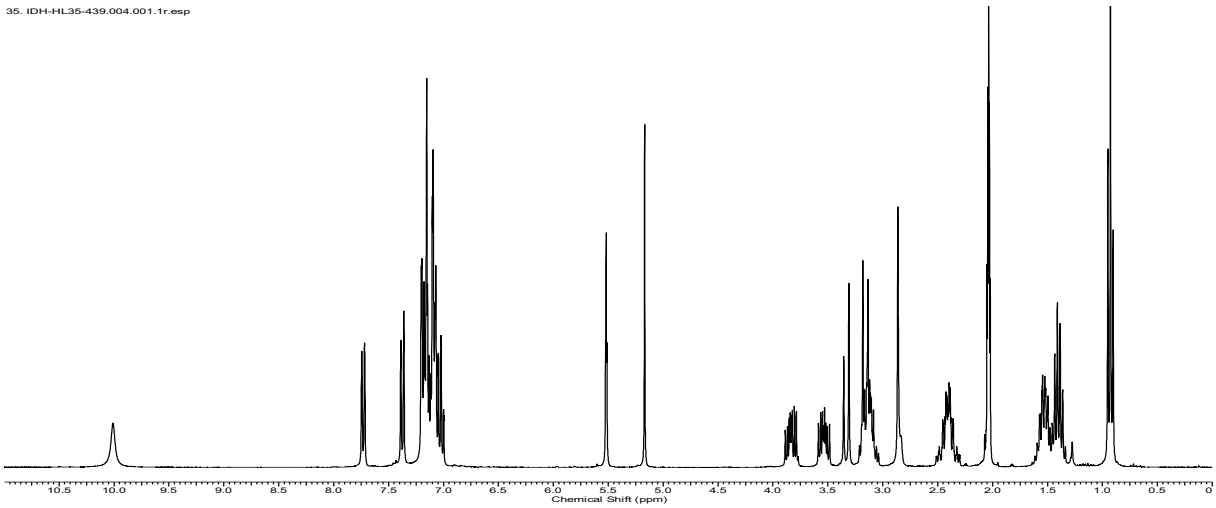


Figure S13 ^{1}H-NMR spectrum of **5e** in $(CD_3)_2CO$

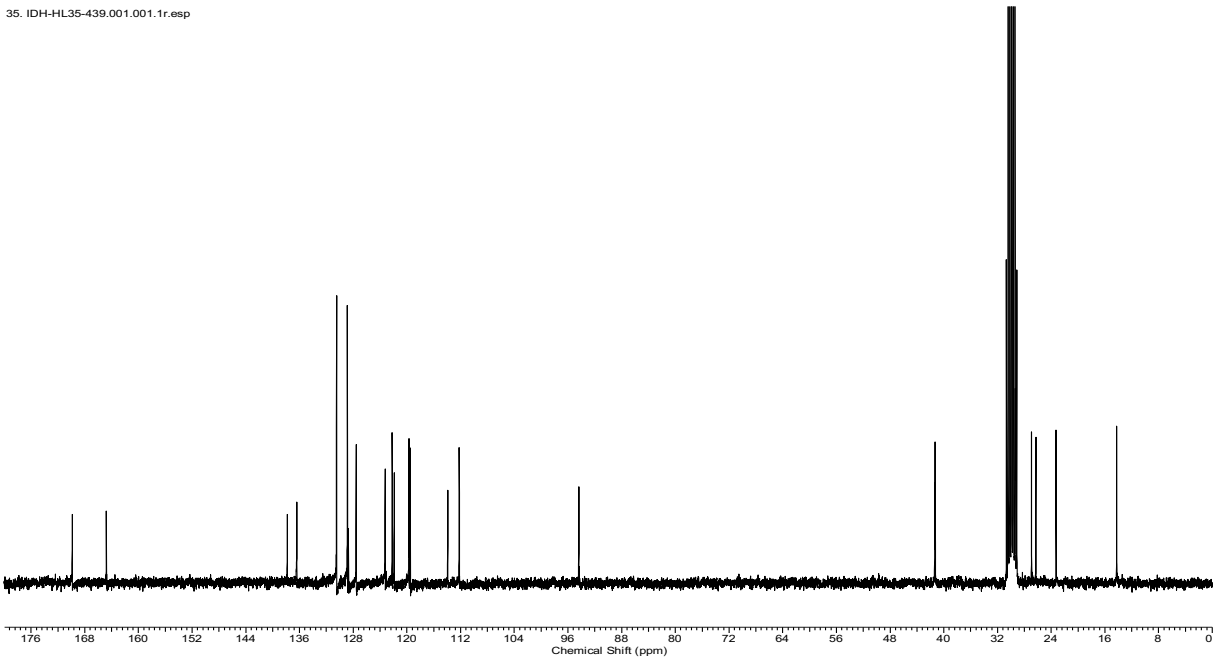


Figure S14 ^{13}C-NMR spectrum of **5e** in $(CD_3)_2CO$

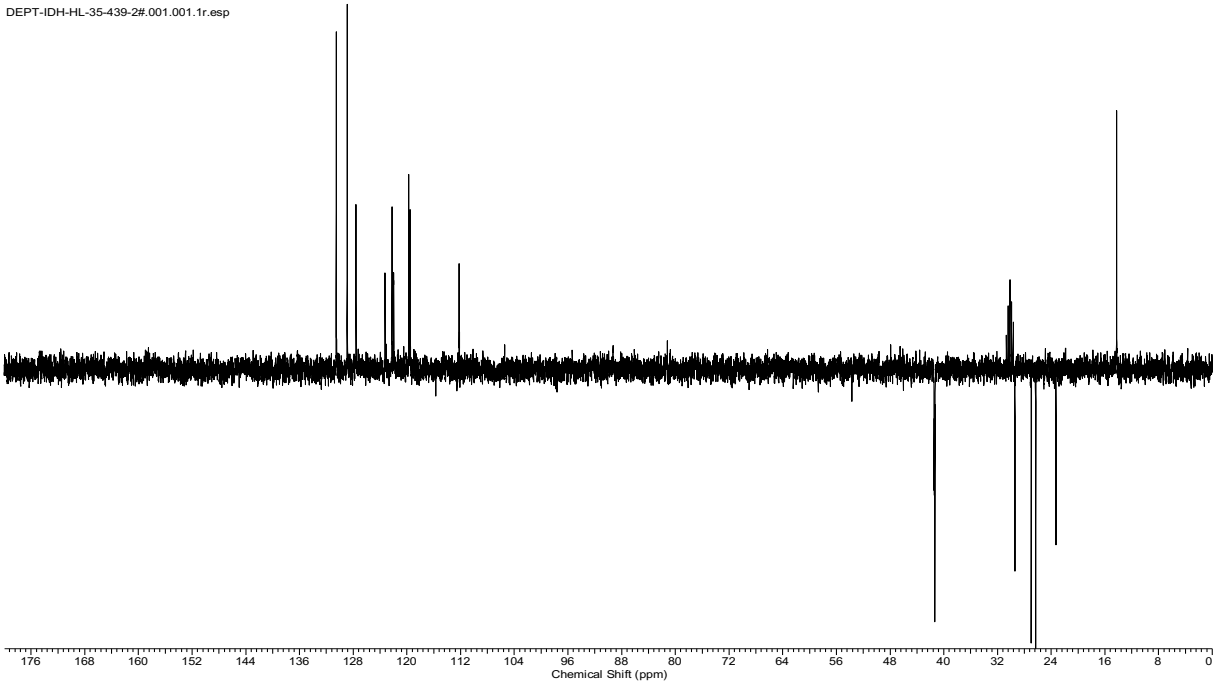
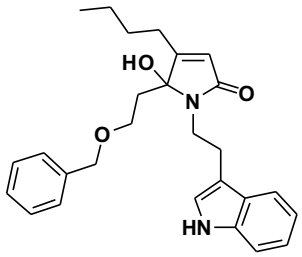


Figure S15 DEPT 135 spectrum of **5e** in $(CD_3)_2CO$

1-(2-(1H-indol-3-yl)ethyl)-5-(2-(benzyloxy)ethyl)-4-butyl-5-hydroxy-1H-pyrrol-2(5H)-one (5f)



Purification: flash chromatography on silica gel (PE/EtOAc : from 8/2 to 6/4)

Yield: 64% (275 mg)

Physical appearance: light yellow gel

^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 0.86 (3H, CH_3, t, *J* = 7.2 Hz), 1.24-1.33 (2H, CH_2, m), 1.39-1.46 (2H, CH_2, m), 2.11-2.28 (4H, 2 xCH_2, m), 2.69 (1H, OH, br s), 3.03-3.16 (3H, CH_2 and C*H*$_2$, m), 3.19-3.24 (1H, C*H*$_2$, m), 3.35-3.42 (1H, C*H*$_2$, m), 3.75-3.83 (1H, C*H*$_2$, m), 4.30 (2H, CH_2, d, *J* = 11.7 Hz), 4.35 (2H, CH_2, d, *J* = 11.7 Hz), 5.69 (1H, CH, br t, *J* = 1.8 Hz), 7.04 (1H, CH_{Ar}, br d, *J* = 2.2 Hz), 7.11 (1H, CH_{Ar}, br dd, *J* = 8.1 and 7.8Hz), 7.18 (1H, CH_{Ar}, br dd, *J* = 8.1 and 7.1 Hz), 7.22-7.34 (6H, 6 x CH_{Ar}, m), 7.65 (1H, CH_{Ar}, br d, *J* = 7.8 Hz), 8.11 (1H, NH, br s); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 14.0 (CH_3), 22.6 (CH_2), 24.8 (CH_2), 26.1 (CH_2), 28.5 (CH_2), 34.1 (CH_2), 39.8 (CH_2), 65.3 (CH_2), 73.5 (CH_2), 92.4 (C), 111.3 (CH_{Ar}), 113.6 (C_{Ar}), 119.1 (CH_{Ar}), 119.6 (CH_{Ar}), 120.1 (CH), 122.2$_0$ (CH_{Ar}), 122.2$_1$ (CH_{Ar}), 127.5 (C_{Ar}), 127.8$_2$ (2 x CH_{Ar}), 127.8$_4$ (CH_{Ar}), 128.5 (2 x CH_{Ar}), 136.4 (C_{Ar}), 137.9 (C_{Ar}), 165.3 (C), 170.6 (C); **IR** (Nujol) : 3313, 2929, 1672, 1417, 1265, 1095, 732, 698cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{27}H_{33}N_2O_3$ $[M+H]^+$ 433.2486, found 433.2486.

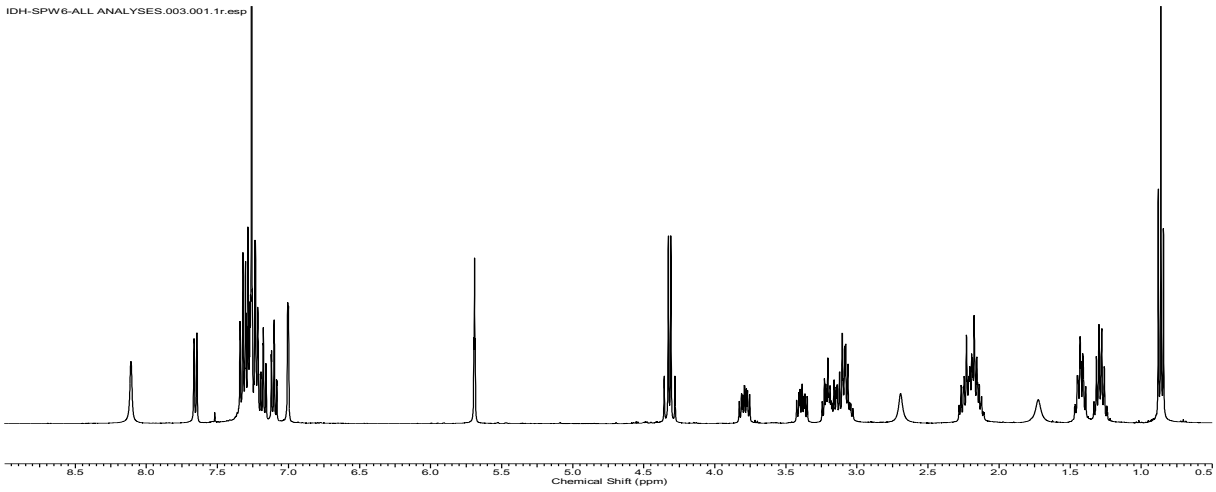


Figure S16 ^{1}H-NMR spectrum of **5f** in $CDCl_3$

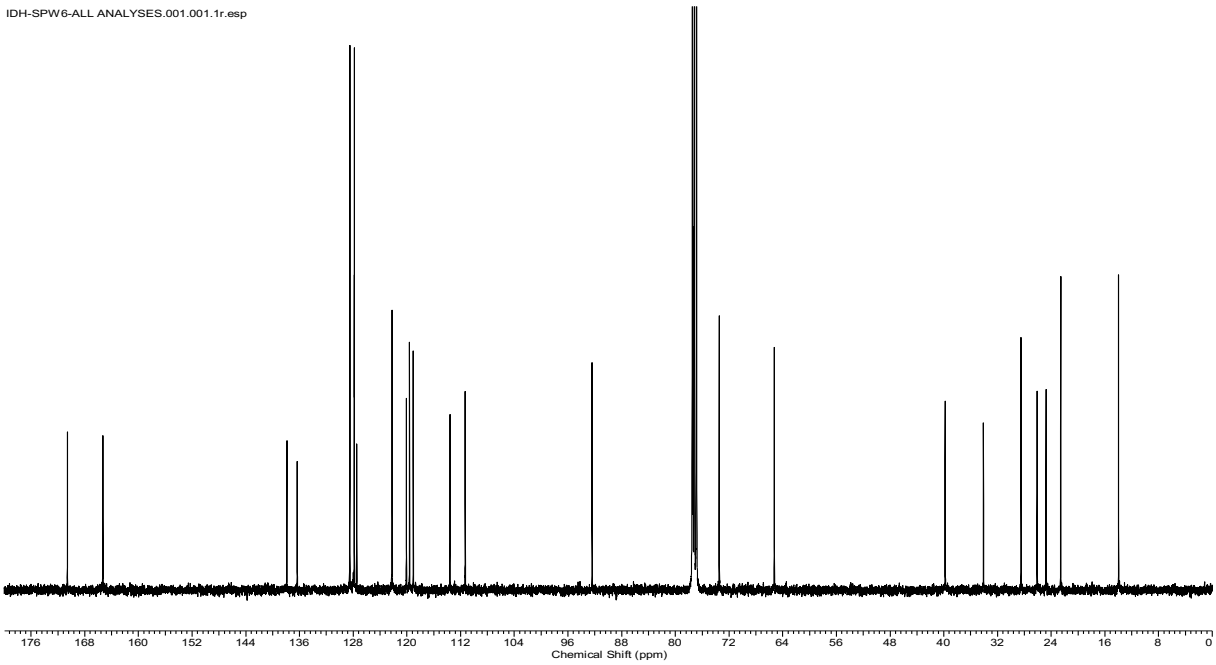


Figure S17 ^{13}C-NMR spectrum of **5f** in $CDCl_3$

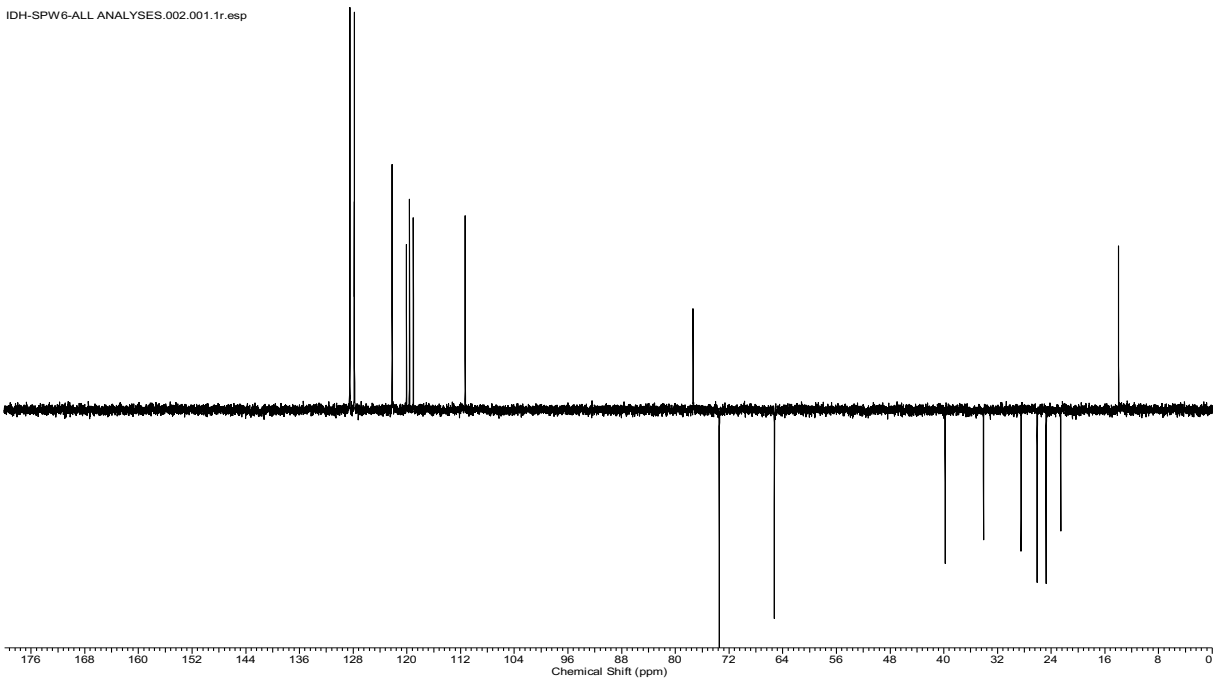
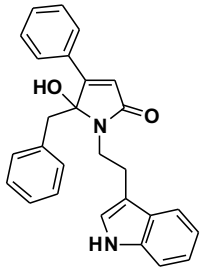


Figure S18 DEPT 135 spectrum of **5f** in $CDCl_3$

1-(2-(1H-Indol-3-yl)ethyl)-5-benzyl-5-hydroxy-4-phenyl-1H-pyrrol-2(5H)-one (5g)



Purification: flash chromatography on silica gel (PE/EtOAc : from 8/2 to 3/7)

Yield: 51% (414 mg)

Physical appearance: light brown

m.p. (amorphous): 180 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 2.15 (1H, br s, OH), 3.19 (1H, CH_2, d, *J* = 14.2 Hz), 3.21-3.27 (1H, CH_2, m), 3.26(1H, CH_2, d, *J* = 14.2 Hz), 3.32-3.39 (1H, CH_2, m), 3.64 (1H, CH_2, dt, , *J* = 13.7 and 7.8 Hz), 4.08 (1H, CH_2, br ddd, *J* = 13.7, 7.8 and 4.6 Hz), 6.07 (1H, CH, s), 6.64 (2H, 2 x CH_{Ar}, m), 7.03-7.11 (4H, 4 x CH_{Ar}, m), 7.15 (1H, CH_{Ar}, br dd, *J* = 7.8and 7.1 Hz), 7.21 (1H, CH_{Ar}, br dd, *J* = 7.8 and 7.1 Hz), 7.37 (1H, CH_{Ar}, br d, *J* = 7.8 Hz), 7.38-7.42 (3H, 3 x CH_{Ar}, m), 7.65-7.70 (2H, 2 x CH_{Ar}, m), 7.73 (1H, CH_{Ar}, br d, *J* = 7.8 Hz), 8.07 (1H, NH, br s); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 24.5 (CH_2), 41.0 (CH_2), 41.5 (CH_2), 94.0 (C), 111.5 (CH_{Ar}), 113.8 (C_{Ar}), 119.1 (CH_{Ar}), 120.0 (CH_{Ar}), 121.7 (CH), 122.5 (CH_{Ar}), 122.6 (CH_{Ar}), 127.2 (CH_{Ar}),127.3 (C_{Ar}),127.8 (2 x CH_{Ar}), 128.2 (2 x CH_{Ar}), 129.0 (2 x CH_{Ar}), 129.6 (2 x CH_{Ar}), 130.2 (CH_{Ar}),131.6 (C_{Ar}), 134.0 (C_{Ar}), 136.4 (C_{Ar}), 157.6 (C), 169.1 (C); **IR** (nujol): 3317, 3054, 1654, 1417, 1062, 744, 690 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{27}H_{25}N_2O_2[M+H]^+$409.1911, found 409.1904.

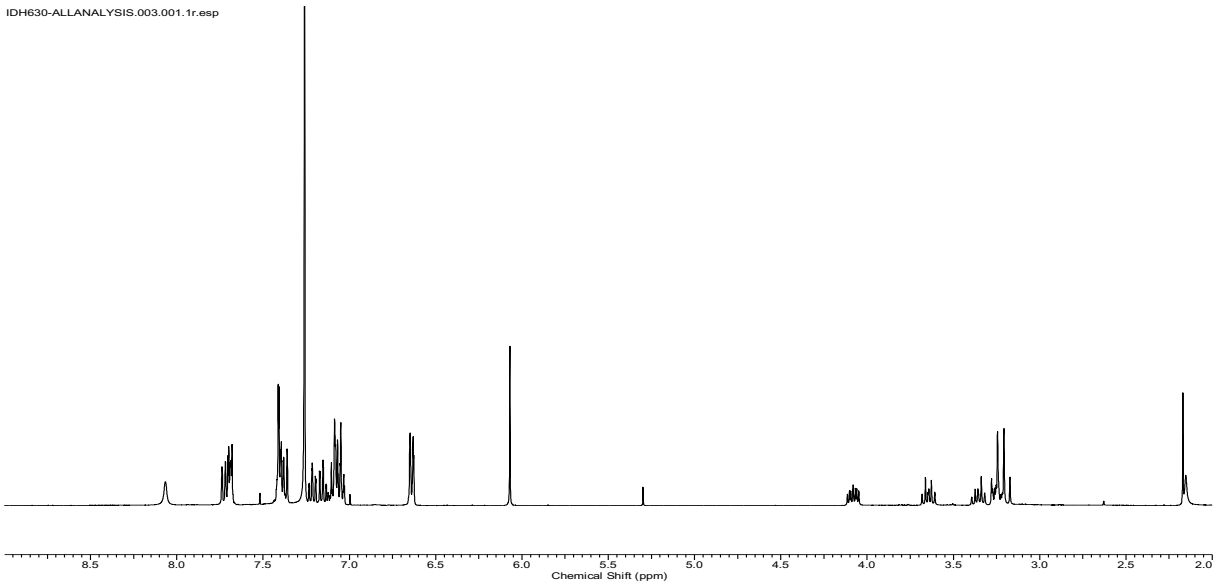


Figure S19 ^{1}H-NMR spectrum of **5g** in $CDCl_3$

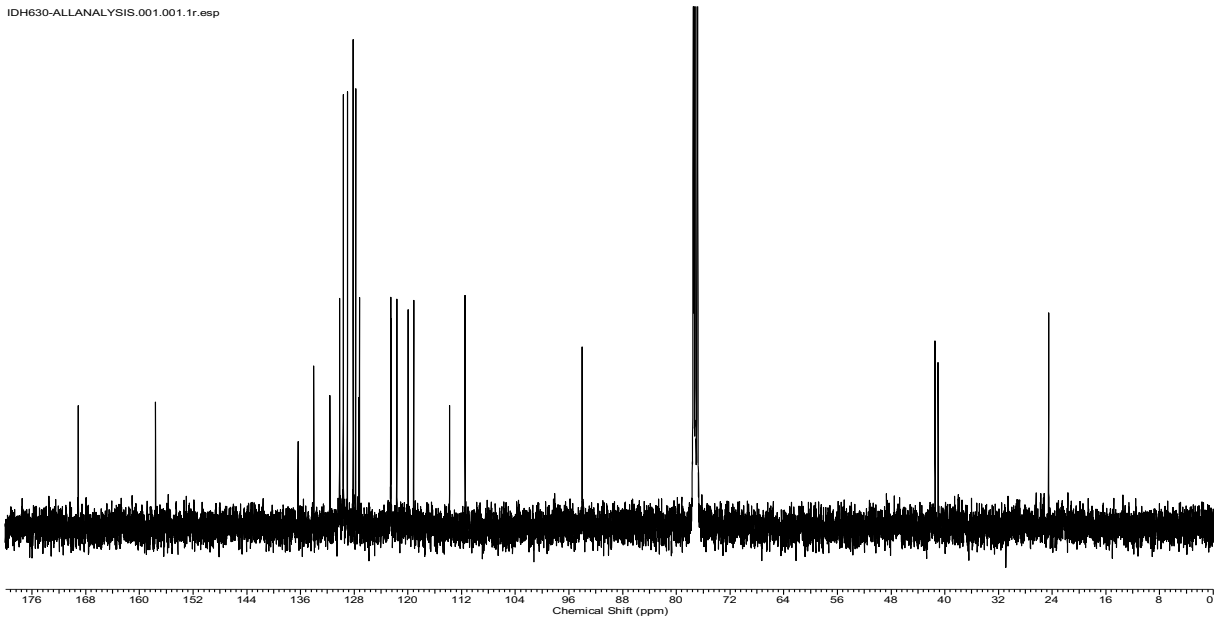


Figure S20 ^{13}C-NMR spectrum of **5g** in $CDCl_3$

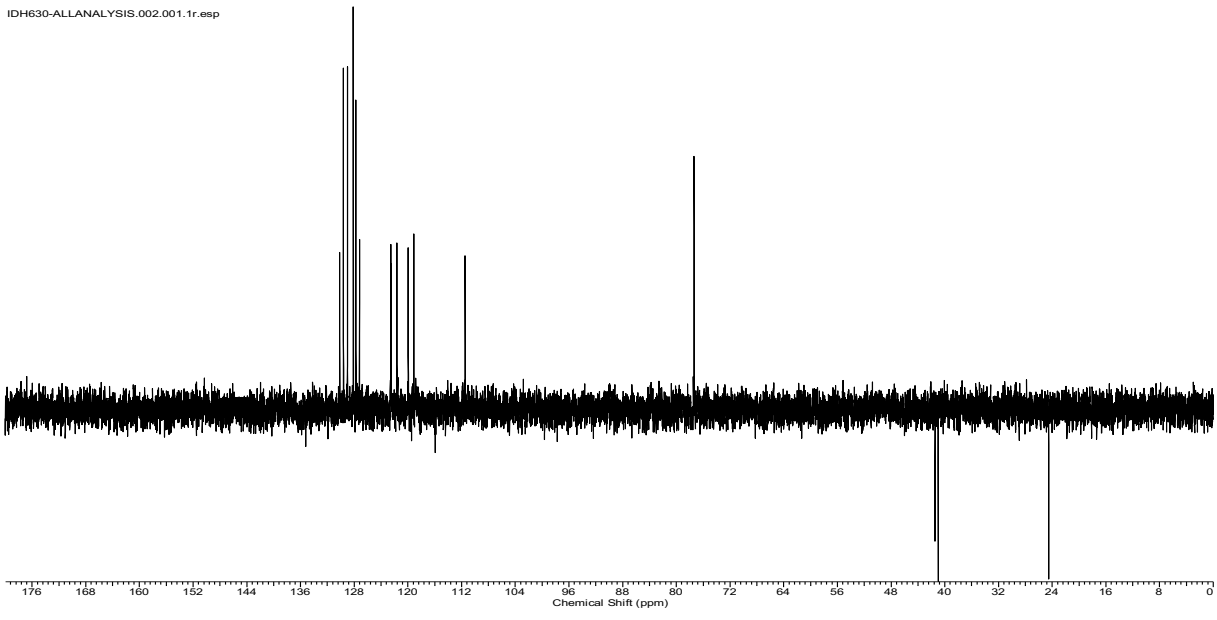
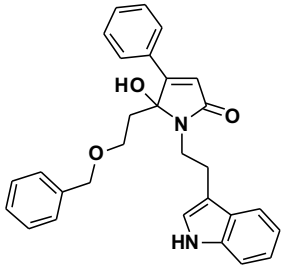


Figure S21 DEPT 135 spectrum of **5g** in $CDCl_3$

1-(2-(1H-indol-3-yl)ethyl)-5-(2-(benzyloxy)ethyl)-5-hydroxy-4-phenyl-1H-pyrrol-2(5H)-one (5h)



Purification: flash chromatography on silica gel (PE/EtOAc : from 85/15 to 40/60)

Yield: 38% (343 mg)

Physical appearance: yellow solid

m.p. (amorphous): 81 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 1.75, (1H, OH, br s), 2.34-2.41 (2H, CH_2, m), 3.05-3.17 (3H, $CH_2$and C*H*$_2$, m), 3.20-3.28 (1H, C*H*$_2$, m), 3.47-3.54 (1H, C*H*$_2$, m), 3.82-3.90 (1H, C*H*$_2$, m), 4.21 (2H, CH_2, br s), 6.19 (1H, CH, s), 7.01 (1H, CH_{Ar}, br d, *J* = 2.2 Hz), 7.07-7.11 (3H, 3 x CH_{Ar}, m), 7.18 (1H, CH_{Ar}, br dd, *J* = 8.1 and 7.1 Hz), 7.21-7.25 (3H, 3 x CH_{Ar}, m), 7.31-7.38 (4H, 4 x CH_{Ar}, m), 7.65-7.69 (3H, 3 x CH_{Ar}, m), 8.07 (1H, NH, br s);**^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 24.6 (CH_2), 35.2 (CH_2), 40.0 (CH_2), 65.3 (CH_2), 73.2 (CH_2), 92.7 (C), 111.3 (CH_{Ar}), 113.6 (C_{Ar}), 119.1 (CH_{Ar}), 119.7 (CH_{Ar}), 120.0 (CH), 122.2 (CH_{Ar}), 122.3 (CH_{Ar}), 127.5 (C_{Ar}), 127.6 (2 x CH_{Ar}), 127.7 (CH_{Ar}), 127.8 (2 x CH_{Ar}), 128.4 (2 x CH_{Ar}), 128.9 (2 x CH_{Ar}), 130.1 (CH_{Ar}), 131.4 (C_{Ar}), 136.3 (C_{Ar}), 137.8 (C_{Ar}), 158.7 (C), 169.5 (C); **IR** (Nujol) : 3311, 2862, 1670, 1452, 1415, 1095, 1074, 732, 696 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{29}H_{29}N_2O_3$ $[M+H]^+$ 453.2173, found 453.2166.

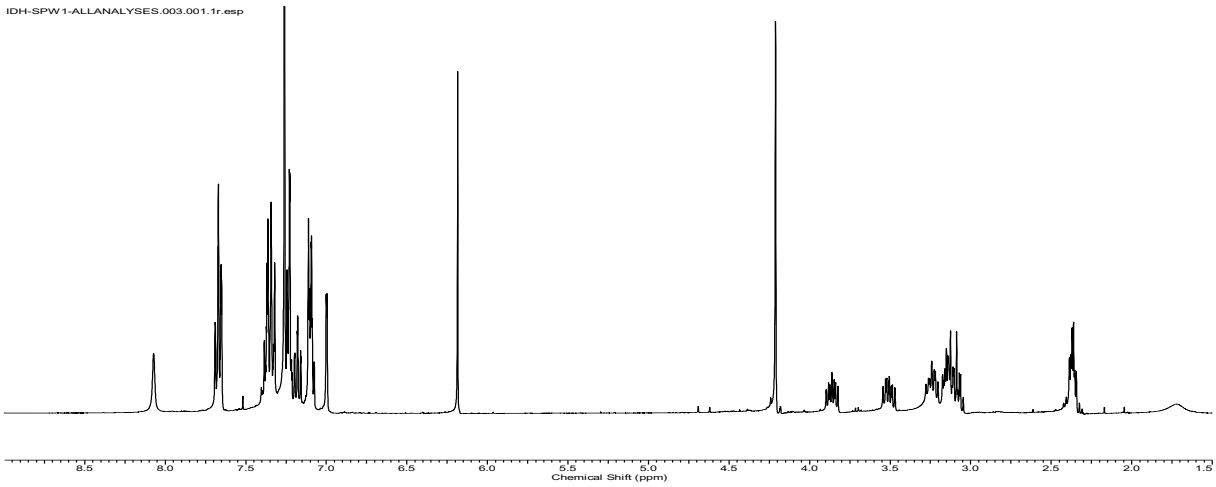


Figure S22 ^{1}H-NMR spectrum of **5h** in $CDCl_3$

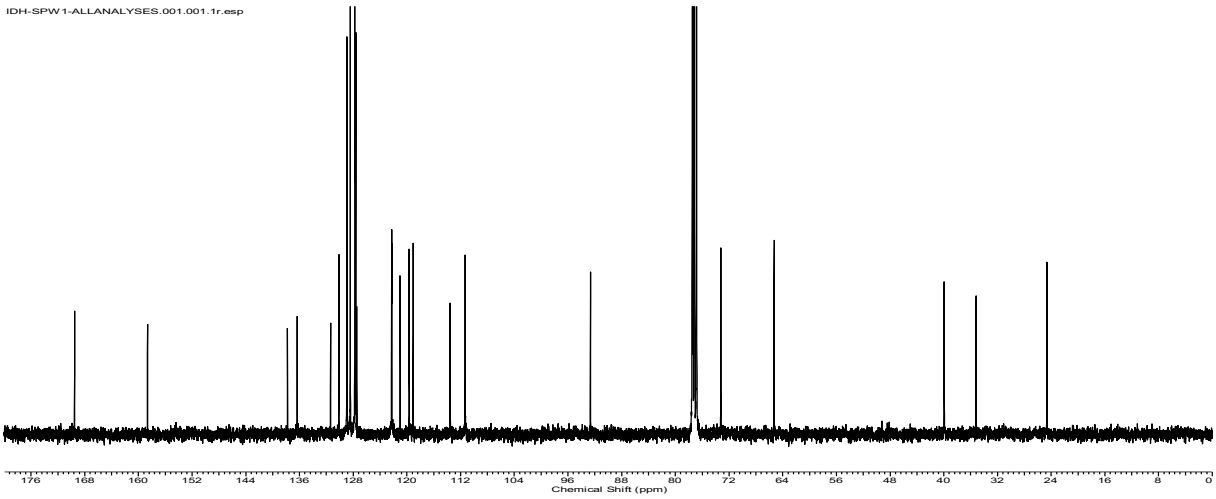


Figure S23 ^{13}C-NMR spectrum of **5h** in $CDCl_3$

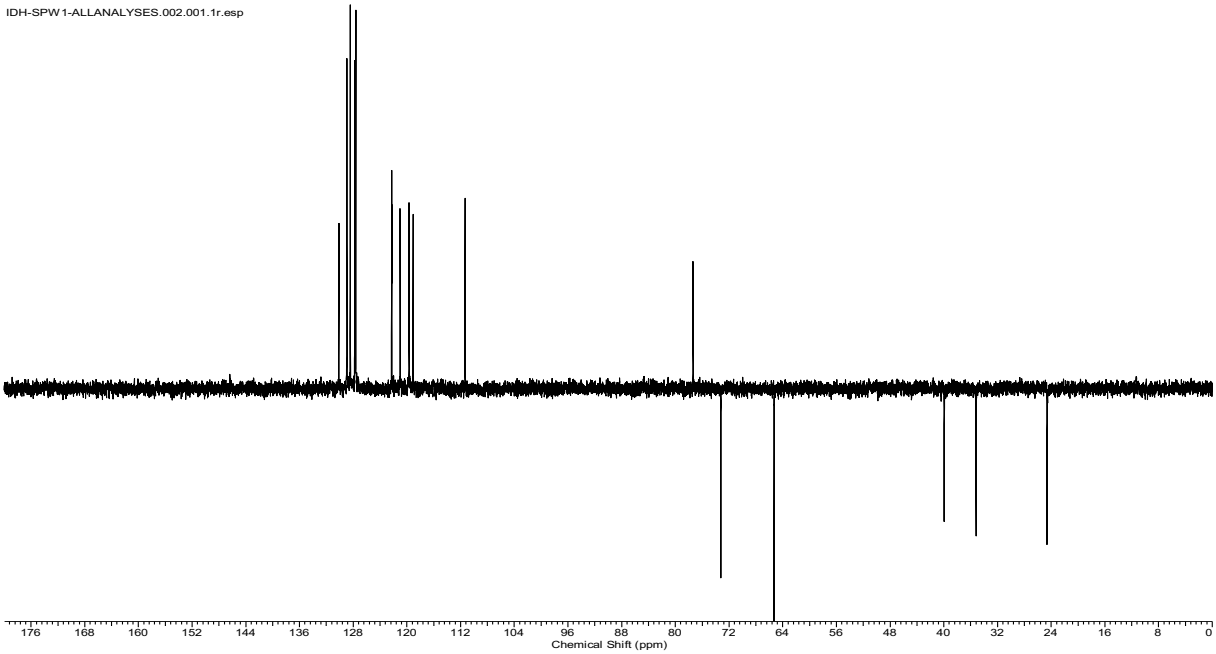
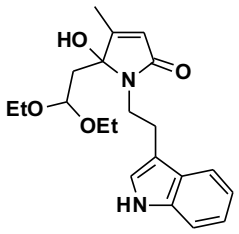


Figure S24 DEPT 135 spectrum of **5h** in $CDCl_3$

1-(2-(1H-indol-3-yl)ethyl)-5-(2,2-diethoxyethyl)-5-hydroxy-4-methyl-1H-pyrrol-2(5H)-one (5i)



Purification: flash chromatography on silica gel (PE/EtOAc : from 85/15 to 30/70)

Yield: 73% (270 mg)

Physical appearance: light brown solid

m.p. (amorphous): 139 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 1.11 (3H, CH_3, t, *J* = 7.1 Hz), 1.15 (3H, CH_3, t, *J* = 7.1 Hz), 1.95 (3H, CH_3, br d, *J* = 1.7 Hz), 2.17 (1H, C*H*$_2$, dd, *J* = 14.4, 6.4 Hz), 2.26 (1H, C*H*$_2$, dd, *J* = 14.4, 3.9 Hz), 2.51 (1H, OH, br s), 3.10-3.23 (2H, CH_2, m), 3.26-3.34 (1H, C*H*$_2$, m), 3.37-3.46 (2H, C*H*$_2$ and C*H*$_2$, m), 3.49-3.61 (2H, CH_2, m), 3.82-3.90 (1H, C*H*$_2$, m), 4.14-4.16 (1H, CH, dd, *J* = 6.4 and 3.9 Hz), 5.72 (1H, CH, br q,*J* = 1.7 Hz), 7.04 (1H, CH_{Ar}, br s), 7.11 (1H, CH_{Ar}, br dd,*J* =8.1 and 7.8 Hz), 7.18 (1H, CH_{Ar}, br dd, *J* = 8.1 and 7.1 Hz), 7.35 (1H, CH_{Ar}, br d, *J* = 8.1 Hz), 7.67 (1H, CH_{Ar}, br d, *J* = 8.1 Hz), 8.11 (1H, NH, br s);**^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 12.8 (CH_3), 15.1 (CH_3), 15.4 (CH_3), 24.8 (CH_3), 38.6 (CH_2), 40.2 (CH_2), 61.7 (CH_2), 62.9 (CH_2), 91.5 (C), 99.7 (CH), 111.3 (CH_{Ar}), 113.7 (C_{Ar}), 119.1 (CH_{Ar}), 119.7 (CH_{Ar}), 121.5 (CH), 122.2 (CH_{Ar}), 122.3 (CH_{Ar}), 127.5 (C_{Ar}), 136.4 (C_{Ar}), 161.1 (C), 170.4 (C); **IR** (nujol): 3323, 2973, 1674, 1415, 1150, 1091, 1053, 742 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{21}H_{29}N_2O_4$ $[M+H]^+$ 373.2122, found 373.2122.

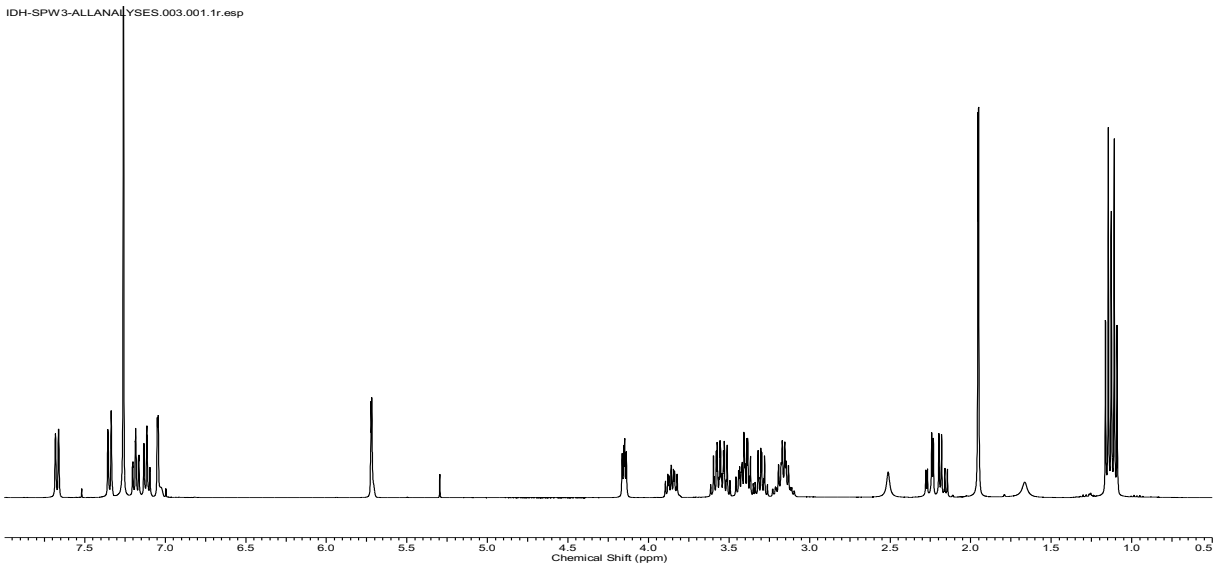


Figure S25 ^{1}H-NMR spectrum of **5i** in $CDCl_3$

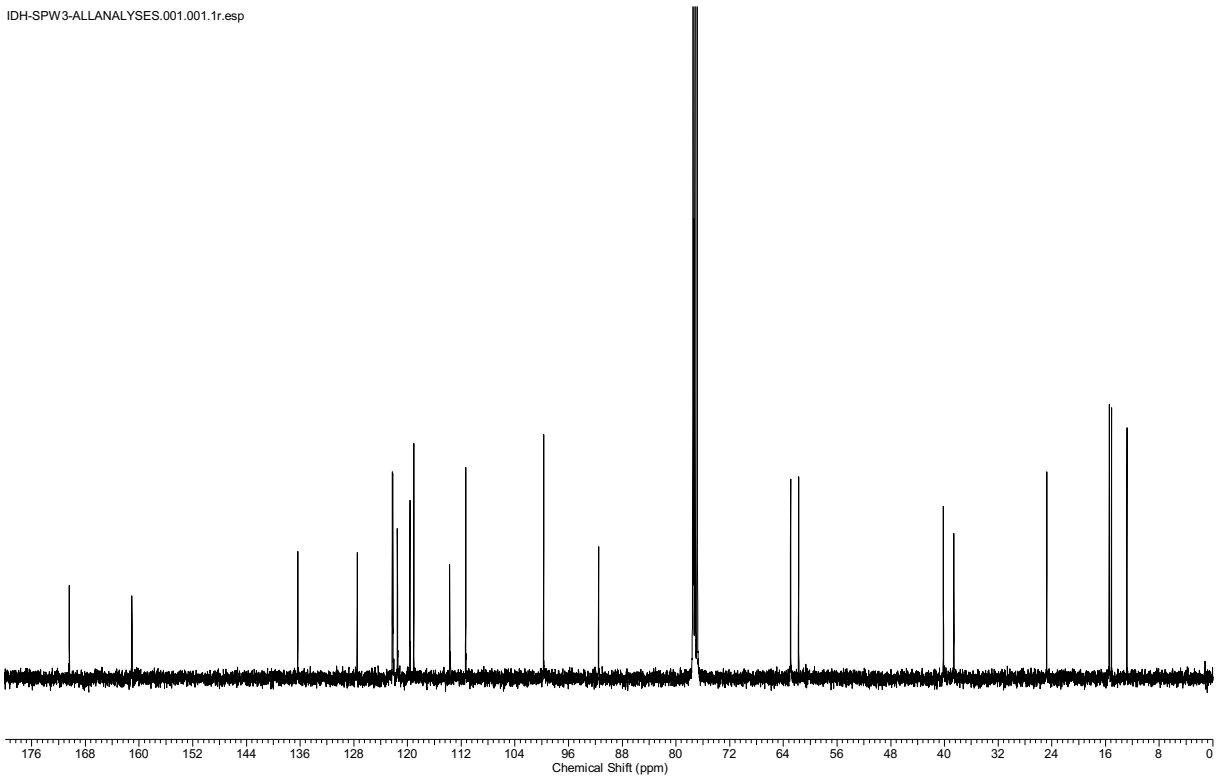


Figure S26 ^{13}C-NMR spectrum of **5i** in $CDCl_3$

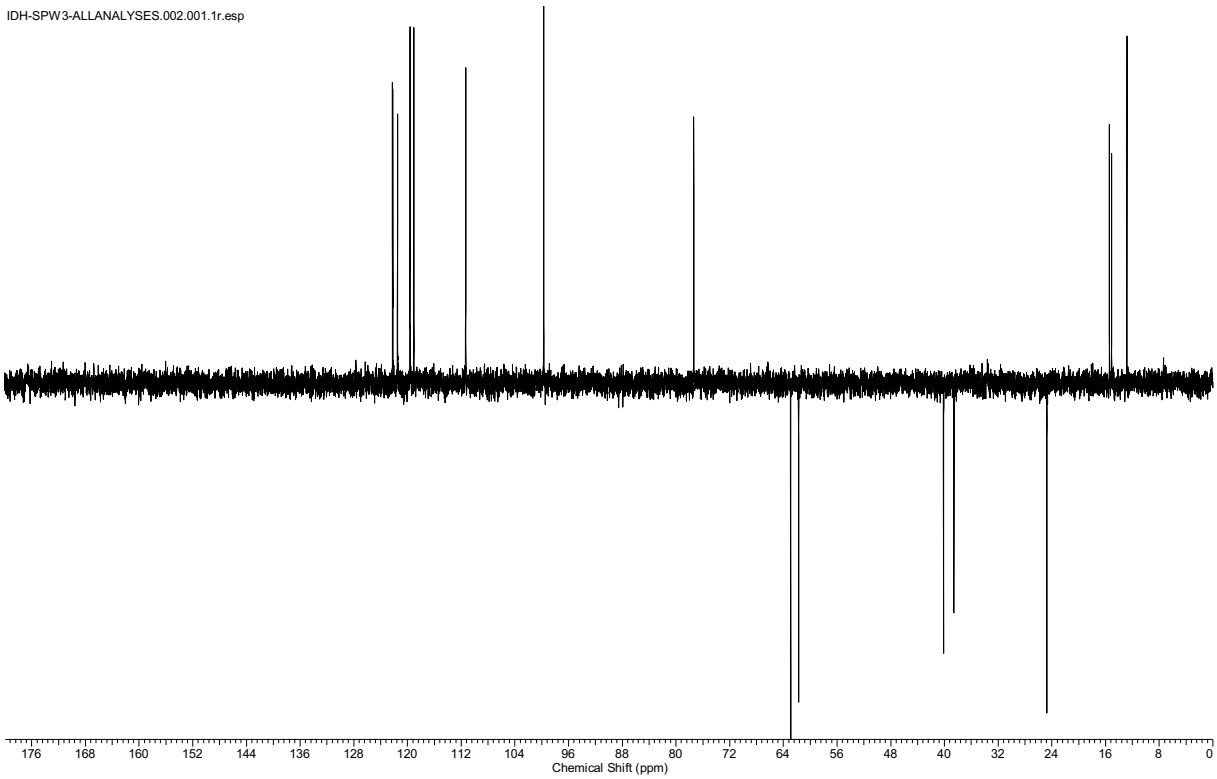


Figure S27 DEPT 135 spectrum of **5i** in $CDCl_3$

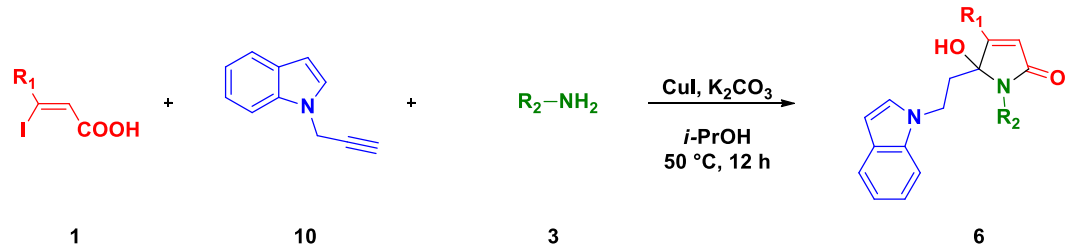
Synthesis of 1-prop-2-yn-1-yl-1*H*-indole 10 [2]

To a solution of indole (2.0 g, 17.1 mmol, 1 equiv.) and propargyl bromide (3.8 g, 2.76 mL of a 80% solution in toluene, 25.6 mmol, 1.5 equiv.) in toluene (51 mL) were respectively added tetrabutylammonium bromide (0.275 g, 0.85 mmol, 0.05 equv.) and 50% aqueous NaOH solution (6 mL, 7.5 equiv.). The two-phase system was vigorously stirred for 3 h at room temperature. The mixture was diluted with toluene (51 mL). The organic layer was washed several times with water and then with brine, dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was purified using flash chromatography (petroleum ether : ethyl acetate = 9:1) to give 1-prop-2-yn-1-yl-1*H*-indole as light brown solid in 53% yield (1.4 g).

m.p. (amorphous): 48 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 2.41 (1H, CH, t, *J* = 2.5 Hz), 4.89 (2H, CH_2, d, *J* = 2.5 Hz), 6.55 (1H, CH_{Ar}, d, *J* = 3.3 Hz), 7.15 (1H, CH_{Ar}, t, *J* = 7.8 Hz), 7.23 (1H, CH_{Ar}, d, *J* = 3.3 Hz), 7.25-7.28 (1H, CH_{Ar}, m), 7.42 (1H, CH_{Ar}, d, *J* = 8.2 Hz), 7.66 (1H, CH_{Ar}, d, *J* = 7.8 Hz).

[2] N. Haider, T. Kabicher, J. Käferböck and A. Plenk**,** *Molecules*, **2007**, *12*, 1900-1909.

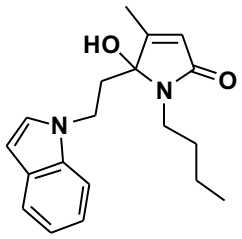
General Procedure to synthesize Indolo-γ-hydroxybutyrolactams 6



1 10 3 6

(*Z*)-3-Substituted-3-iodoprop-2-enoic acid derivative **1** (1.0 mmol, 1 equiv.) was dissolved in *i*-PrOH (3.5 mL) in oven-dried-Schlenk tube. K_2CO_3 (277 mg, 2.0 mmol, 2 equiv.) was then added to the solution and the suspension was stirred for 10 min under Argon. The mixture was then degassed at -78 °C for 2x10 min and the vessel was backfilled with argon. After warming to room temperature, 1-prop-2-yn-1-yl-1*H*-indole **10** (310 mg, 2.0 mmol, 2 equiv.), primary amine **3** (3.0 mmol, 3 equiv.) and CuI (190 mg, 1.0 mmol, 1 equiv) were respectively added into the mixture. The mixture was then rapidly degassed and the vessel was backfilled with argon. The sealed Schlenk tube was placed in the preheated oil bath (50 °C) and was stirred overnight. The reaction mixture was cooled to 0 °C, then quenched by the addition of an aqueous saturated NH_4Cl solution and stirred for further 15 min. The mixture was filtered through a pad of Celite®. The aqueous phase was extracted with ethyl acetate and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was then purified by flash chromatography on silica gel using petroleum ether: ethyl acetate as eluent.

5-(2-(1H-Indol-1-yl)ethyl)-1-butyl-5-hydroxy-4-methyl-1H-pyrrol-2(5H)-one (6a)



Purification: flash chromatography on silica gel (PE/EtOAc : from 80/20 to 30/70)

Yield: 60% (188 mg)

Physical appearance: brown gel

^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 0.95 (3H, CH_3, t, *J* = 7.3 Hz), 1.32-1.44 (2H, CH_2, m), 1.56-1.75 (2H, CH_2, m), 1.81 (3H, CH_3, br d, *J* = 1.7 Hz), 2.37 (1H, OH, br s), 2.44 (2H, CH_2, t, *J* = 7.4 Hz), 3.13 (1H, C*H*$_2$, ddd, *J* = 15.5, 9.6, 5.9 Hz), 3.49 (1H, C*H*$_2$, ddd, *J* = 15.9, 10.0, 5.9 Hz), 3.70-3.81 (1H, C*H*$_2$, m), 3.81-3.94 (1H, C*H*$_2$, m), 5.81 (1H, CH, br q, *J* = 1.7 Hz), 6.47 (1H, CH_{Ar}, d, *J* = 3.2 Hz), 6.93 (1H, CH_{Ar}, d, *J* = 3.2 Hz), 7.08-7.13 (1H, CH_{Ar}, m), 7.19-7.23 (2H, 2 x CH_{Ar}, m), 7.62 (1H, CH_{Ar}, d, *J* = 7.7 Hz); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 12.1 (CH_3), 13.9 (CH_3), 20.8 (CH_2), 31.8 (CH_2), 33.8 (CH_2), 38.9 (CH_2), 41.1 (CH_2), 92.3 (C), 101.9 (CH_{Ar}), 109.1 (CH_{Ar}), 119.8 (CH_{Ar}), 121.4 (CH_{Ar}), 121.9 (CH_{Ar}), 123.5 (CH), 127.8 (CH_{Ar}), 128.8 (C_{Ar}), 135.9 (C_{Ar}), 158.8 (C), 169.9 (C). **IR** (nujol): 3284, 2958, 2931, 1677, 1643, 1463, 1313, 740 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{19}H_{25}N_2O_4$ $[M+H]^+$ 313.1911, found 313.1911.

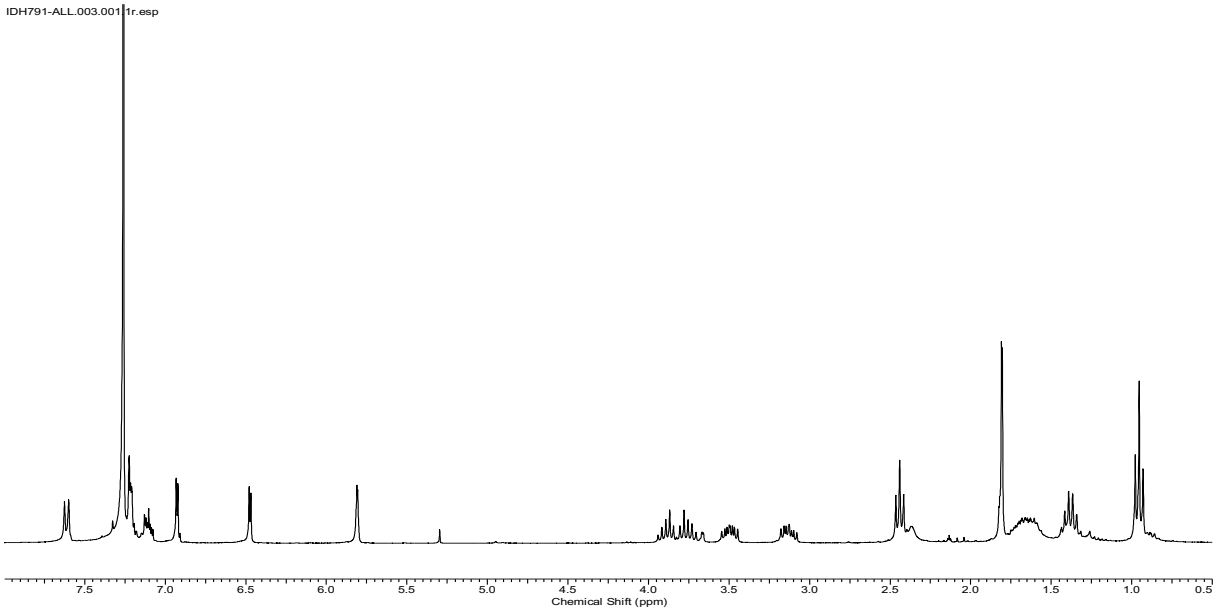


Figure S28 ^{1}H-NMR spectrum of **6a** in $CDCl_3$

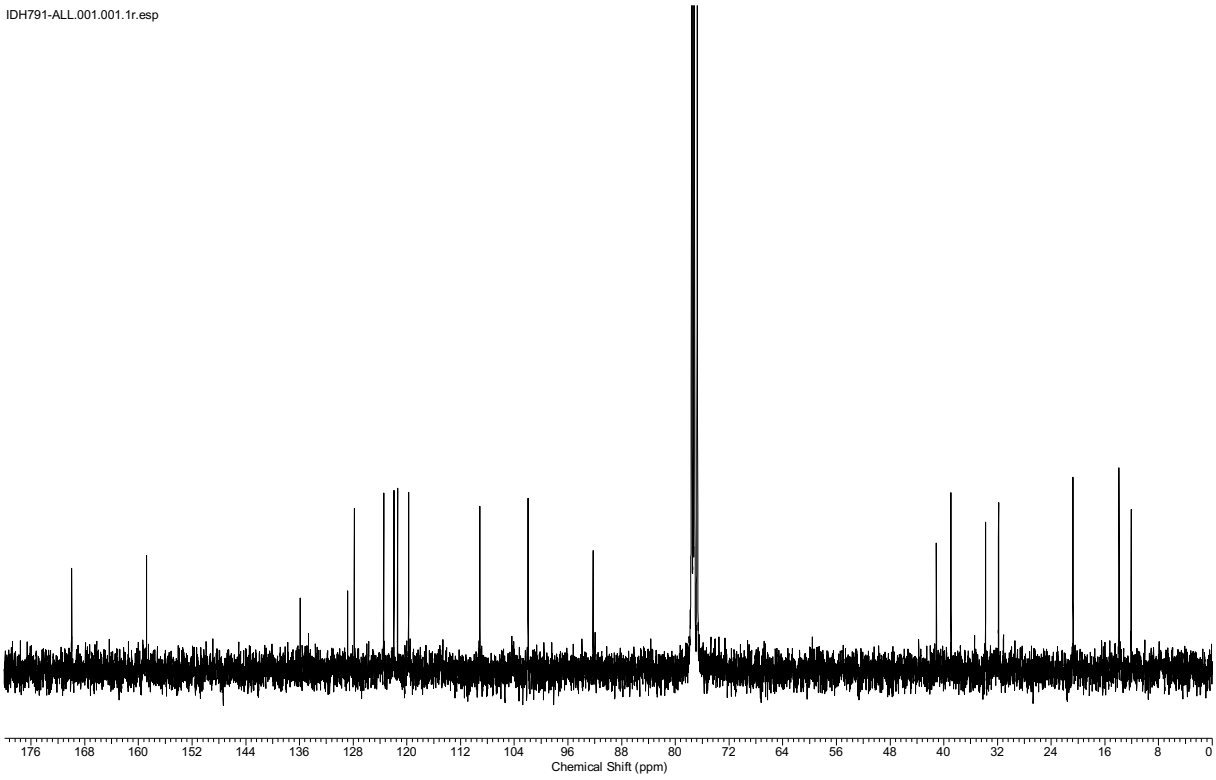


Figure S29 ^{13}C-NMR spectrum of **6a** in $CDCl_3$

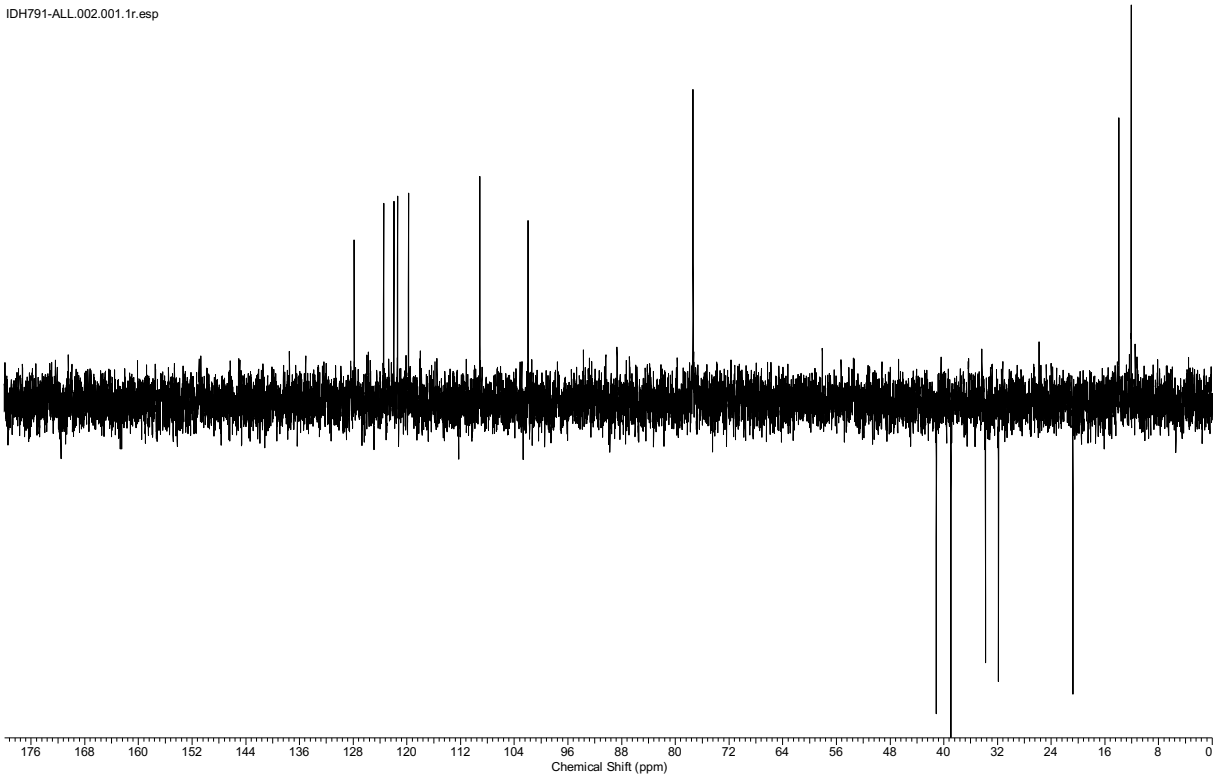
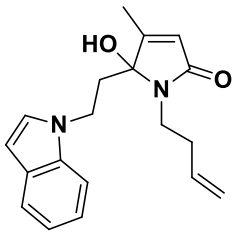


Figure S30 DEPT 135 spectrum of **6a** in $CDCl_3$

5-(2-(1H-Indol-1-yl)ethyl)-1-(but-3-en-1-yl)-5-hydroxy-4-methyl-1H-pyrrol-2(5H)-one (6b)



Purification: flash chromatography on silica gel (PE/EtOAc : from 80/20 to 40/60)

Yield: 64% (199 mg)

Physical appearance: brown gel

^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 1.81 (3H, CH_3, br d, *J* = 1.5 Hz), 2.43 (2H, CH_2, t, *J* = 7.4 Hz), 2.46-2.58 (2H, CH_2, m), 3.08-3.18 (1H, C*H*$_2$, m), 3.58-3.65 (1H, C*H*$_2$, m), 3.74-3.92 (2H, CH_2, m), 5.06-5.12 (2H, CH_2, m), 5.76-5.90 (2H, 2 x CH, m), 6.47 (1H, CH_{Ar}, d, *J* = 3.2 Hz), 6.91 (1H, CH_{Ar}, d, *J* = 3.2 Hz), 7.08-7.13 (1H, CH_{Ar}, m), 7.20-7.23 (2H, 2 x CH_{Ar}, m), 7.62 (1H, CH_{Ar}, d, *J* = 7.7 Hz)*;* **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 12.1 (CH_3), 33.5 (CH_2), 33.7 (CH_2), 38.5 (CH_2), 41.1 (CH_2), 92.0 (C), 101.9 (CH_{Ar}), 109.1 (CH_{Ar}), 117.4 (CH_2), 119.7 (CH_{Ar}), 121.4 (CH_{Ar}), 121.9 (CH_{Ar}), 123.2 (CH), 127.9 (CH_{Ar}), 128.8 (C_{Ar}), 135.8 (C_{Ar}), 136.1 (CH), 159.3 (C), 170.0 (C). **IR** (nujol): 3286, 2935, 1672, 1641, 1459, 1440, 1413, 1315, 1085, 738 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{19}H_{22}N_2O_2Na^+$ $[M+Na]^+$ 333.1573, found 333.1573.

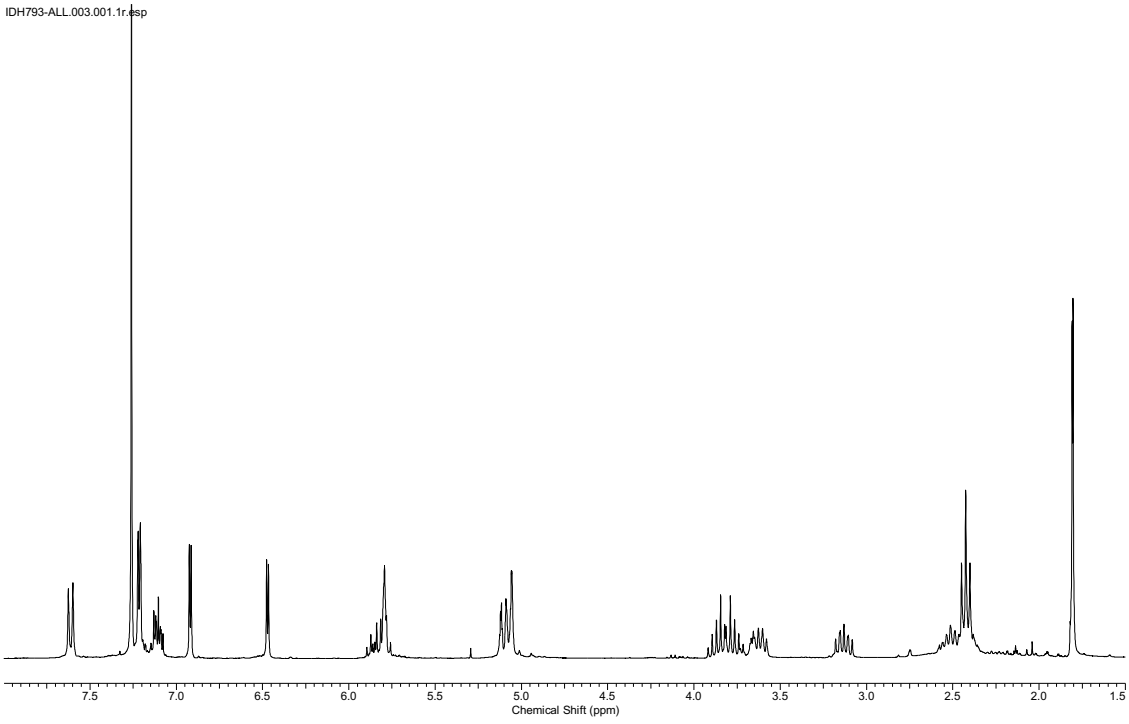


Figure S31 ^{1}H-NMR spectrum of **6b** in $CDCl_3$

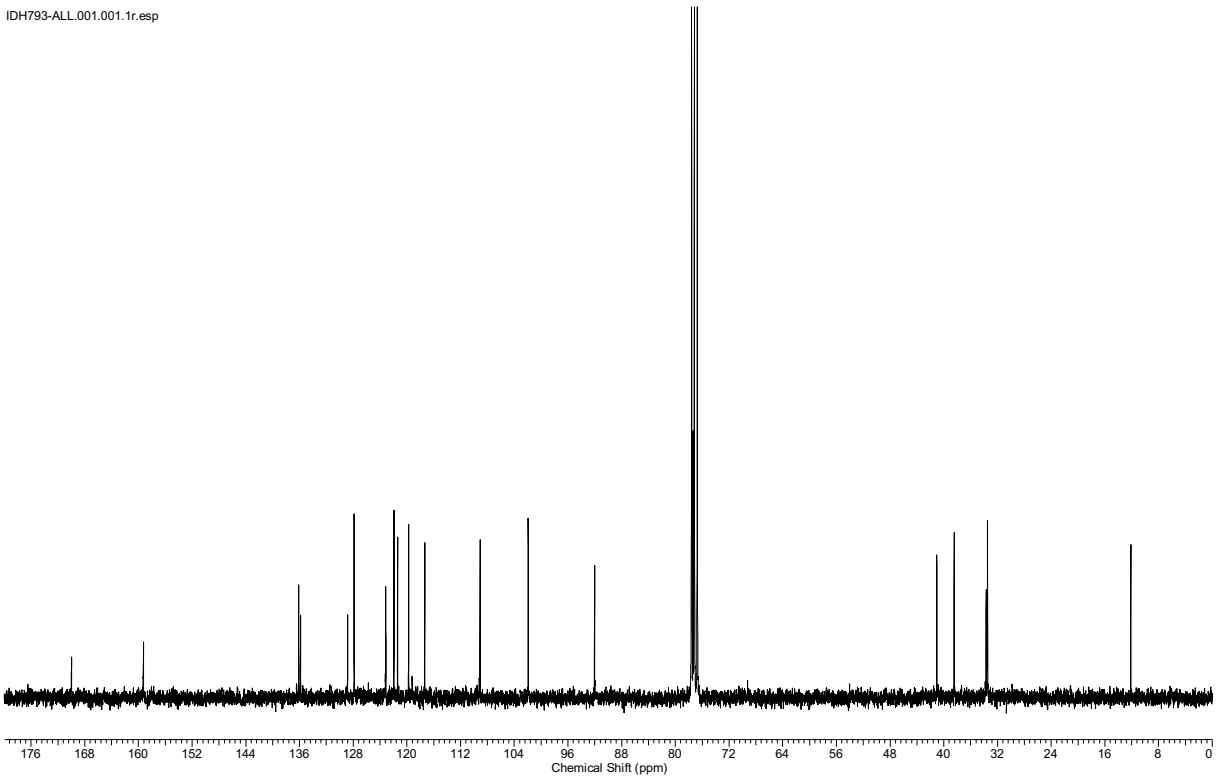


Figure S32 ^{13}C-NMR spectrum of **6b** in $CDCl_3$

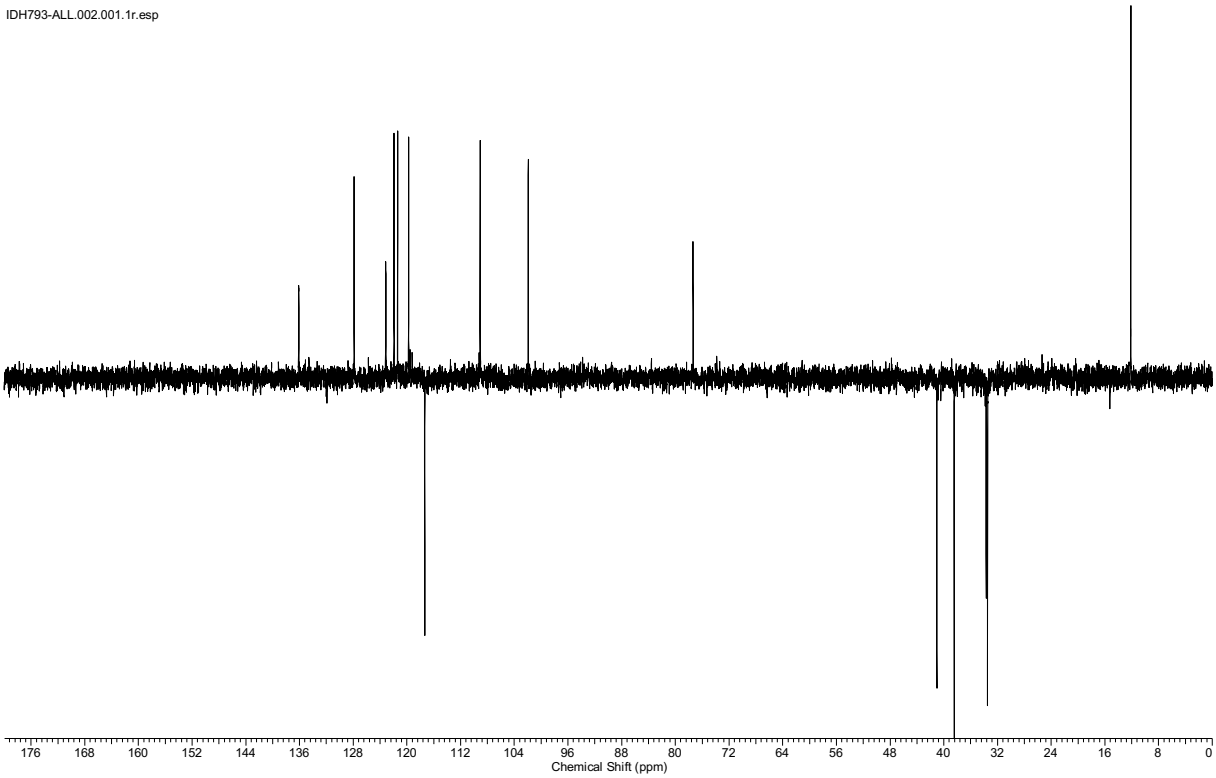
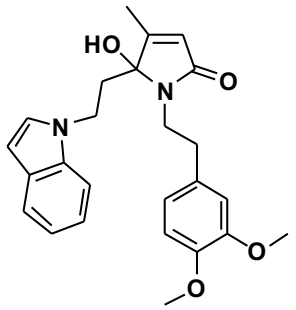


Figure S33 DEPT 135 spectrum of **6b** in $CDCl_3$

5-(2-(1H-indol-1-yl)ethyl)-1-(3,4-dimethoxyphenethyl)-5-hydroxy-4-methyl-1H-pyrrol-2(5H)-one (6c)



Purification: flash chromatography on silica gel (PE/EtOAc : from 80/20 to 10/90)

Yield: 55% (232 mg)

Physical appearance: brown solid

m.p. (amorphous): 126 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 1.77 (3H, CH_3, br d, *J* = 1.7 Hz), 2.36 (2H, CH_2, t, *J* = 7.2 Hz), 2.83-2.91 (1H, C*H*$_2$, m), 3.08-3.18 (1H, C*H*$_2$, m), 3.19-3.30 (1H, C*H*$_2$, m), 3.72-3.84 (3H, CH_2 and C*H*$_2$, m), 3.84 (3H, CH_3, s), 3.85 (3H, CH_3, s), 5.83 (1H, CH, br q, *J* = 1.7 Hz), 6.47 (1H, CH_{Ar}, d, *J* = 3.2 Hz), 6.73-6.81 (3H, 3 x CH_{Ar}, m), 6.92 (1H, CH_{Ar}, d, *J* = 3.2 Hz), 7.07-7.13 (1H, CH_{Ar}, m), 7.20-7.21 (2H, 2 x CH_{Ar}, m), 7.61 (1H, CH_{Ar}, d, *J* = 7.7 Hz)*;* **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 12.4 (CH_3), 33.7 (CH_2), 34.2 (CH_2), 40.9 (CH_2), 41.0 (CH_2), 56.0 (CH_3), 56.1 (CH_3), 91.9 (C), 101.9 (CH_{Ar}), 109.1 (CH_{Ar}), 111.6 (CH_{Ar}), 112.4 (CH_{Ar}), 119.8 (CH_{Ar}), 121.0 (CH_{Ar}), 121.4 (CH_{Ar}), 121.9 (CH_{Ar}), 123.8 (CH), 127.9 (CH_{Ar}), 128.9 (C_{Ar}), 131.8 (C_{Ar}), 135.8 (C_{Ar}), 148.0 (C_{Ar}), 149.3(C_{Ar}), 159.2 (C), 169.9 (C). **IR** (nujol): 3270, 2964, 2935, 1675, 1513, 1463, 1263, 1234, 1155, 1027, 740 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{25}H_{28}N_2O_4Na^+$ $[M+Na]^+$ 443.1941, found 443.1941.

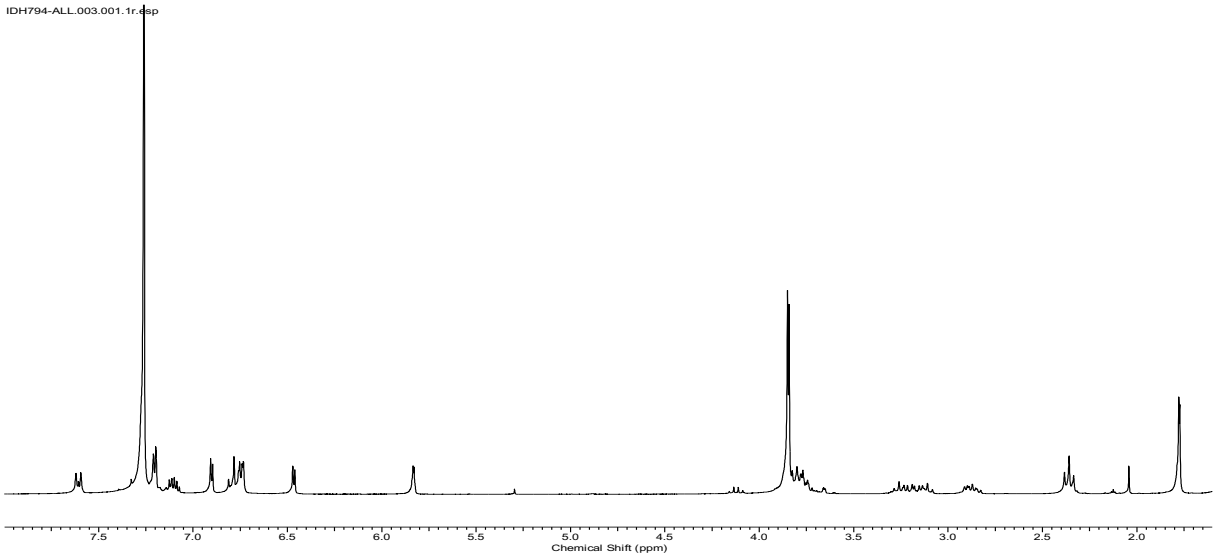


Figure S34 ^{1}H-NMR spectrum of **6c** in $CDCl_3$

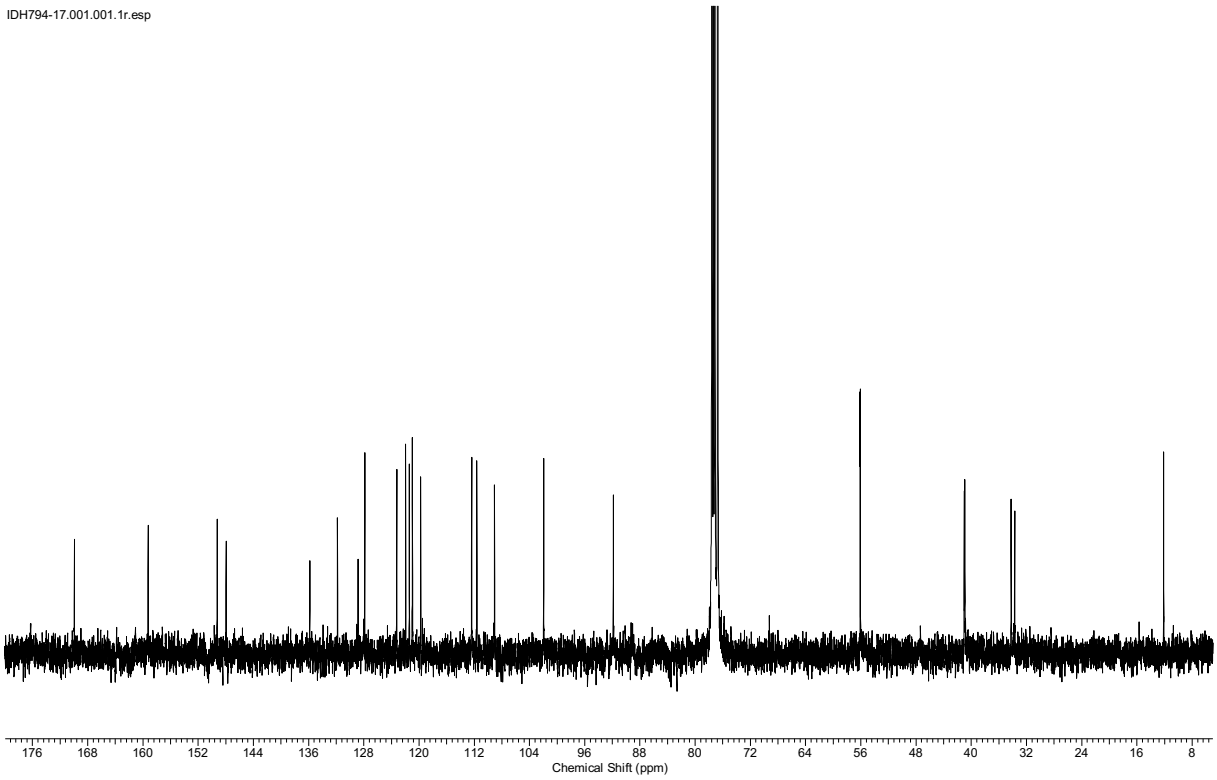


Figure S35 ^{13}C-NMR spectrum of **6c** in $CDCl_3$

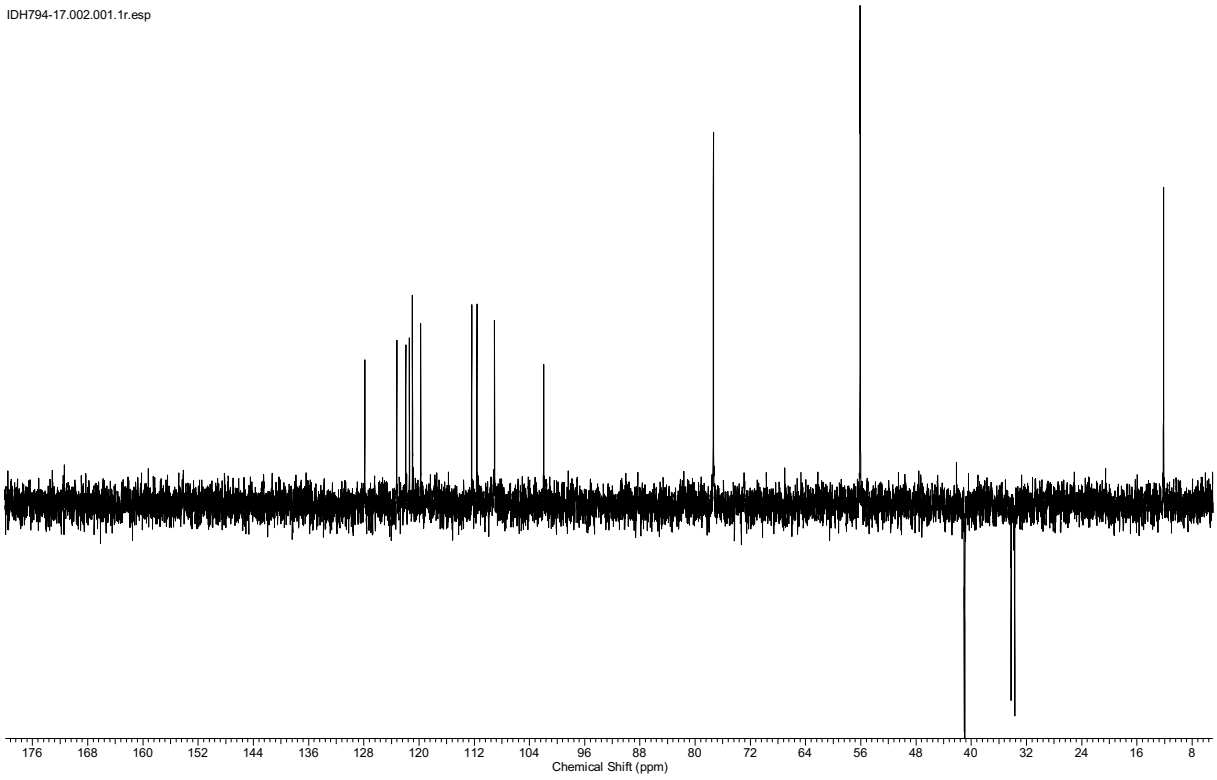
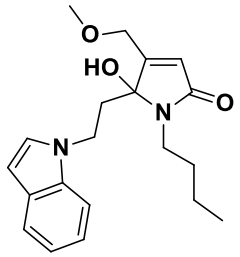


Figure S36 DEPT 135 spectrum of **6c** in $CDCl_3$

5-(2-(1H-indol-1-yl)ethyl)-1-butyl-5-hydroxy-4-(methoxymethyl)-1H-pyrrol-2(5H)-one (6d)



Purification: flash chromatography on silica gel (PE/EtOAc : from 80/20 to 40/60)

Yield: 53% (182 mg)

Physical appearance: brown gel

^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 0.96 (3H, CH_3, t, *J* = 7.3 Hz), 1.33-1.43 (2H, CH_2, m), 1.60-1.77 (2H, CH_2, m), 2.48 (2H, CH_2, br t, *J* = 7.7 Hz), 3.09-3.19 (1H, C*H*$_2$, m), 3.30 (3H, CH_3, s), 3.44-3.55 (1H, C*H*$_2$, m), 3.80-3.93 (3H, CH_2 and C*H*$_2$, m), 4.00 (1H, C*H*2, dd, *J* = 14.5 and 1.7 Hz), 5.98 (1H, CH, br t, *J* = 1.7 Hz), 6.47 (1H, CH_{Ar}, br d, *J* = 3.2 Hz), 6.92 (1H, CH_{Ar}, d, *J* = 3.2 Hz), 7.07-7.13 (1H, CH_{Ar}, m), 7.18-7.24 (2H, 2 x CH_{Ar}, m), 7.62 (1H, CH_{Ar}, d, *J* = 7.9 Hz)*;* **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 13.9 (CH_3), 20.7 (CH_2), 31.6 (CH_2), 35.0 (CH_2), 38.8 (CH_2), 41.2 (CH_2), 59.3 (CH_3), 67.4 (CH_2), 91.6 (C), 101.9 (CH_{Ar}), 109.3 (CH_{Ar}), 119.8 (CH_{Ar}), 121.4 (CH_{Ar}), 121.9 (CH_{Ar}), 123.8 (CH), 127.9 (CH_{Ar}), 128.8 (C_{Ar}), 135.8 (C_{Ar}), 157.9 (C), 169.5 (C). **IR** (nujol): 3276, 2954, 2931, 1679, 1648, 1461, 1313, 1193, 1112, 740 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{20}H_{26}N_2O_3Na^+$ $[M+Na]^+$ 365.1836, found 365.1836.

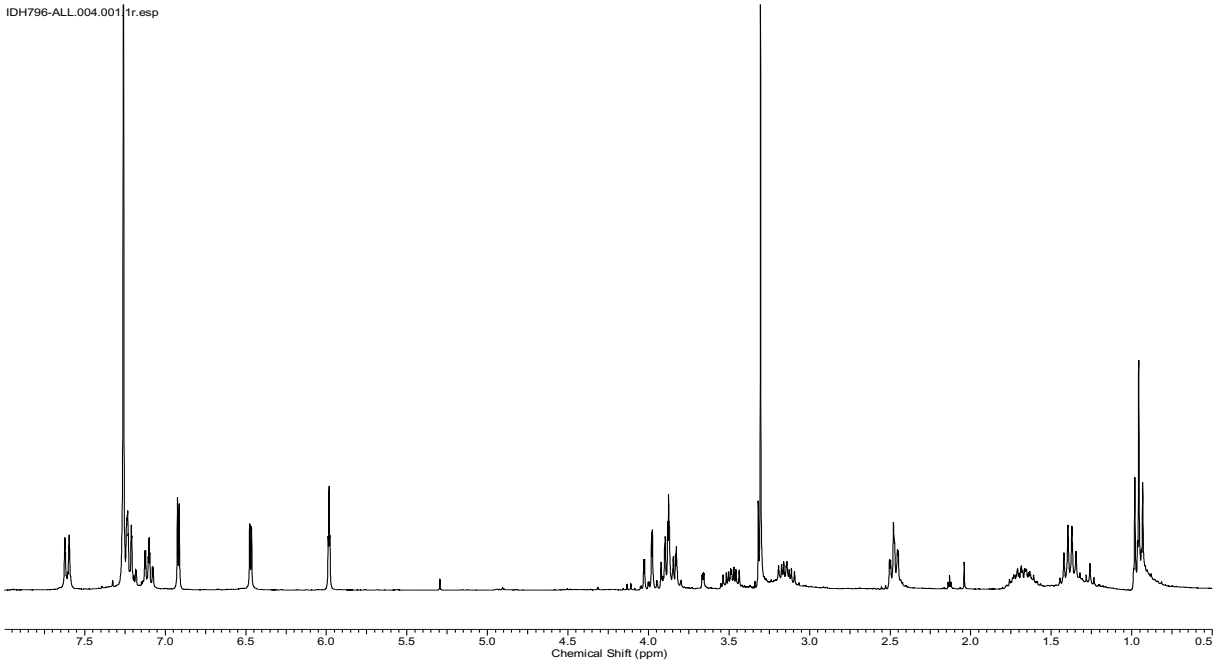


Figure S37 ^{1}H-NMR spectrum of **6d** in $CDCl_3$

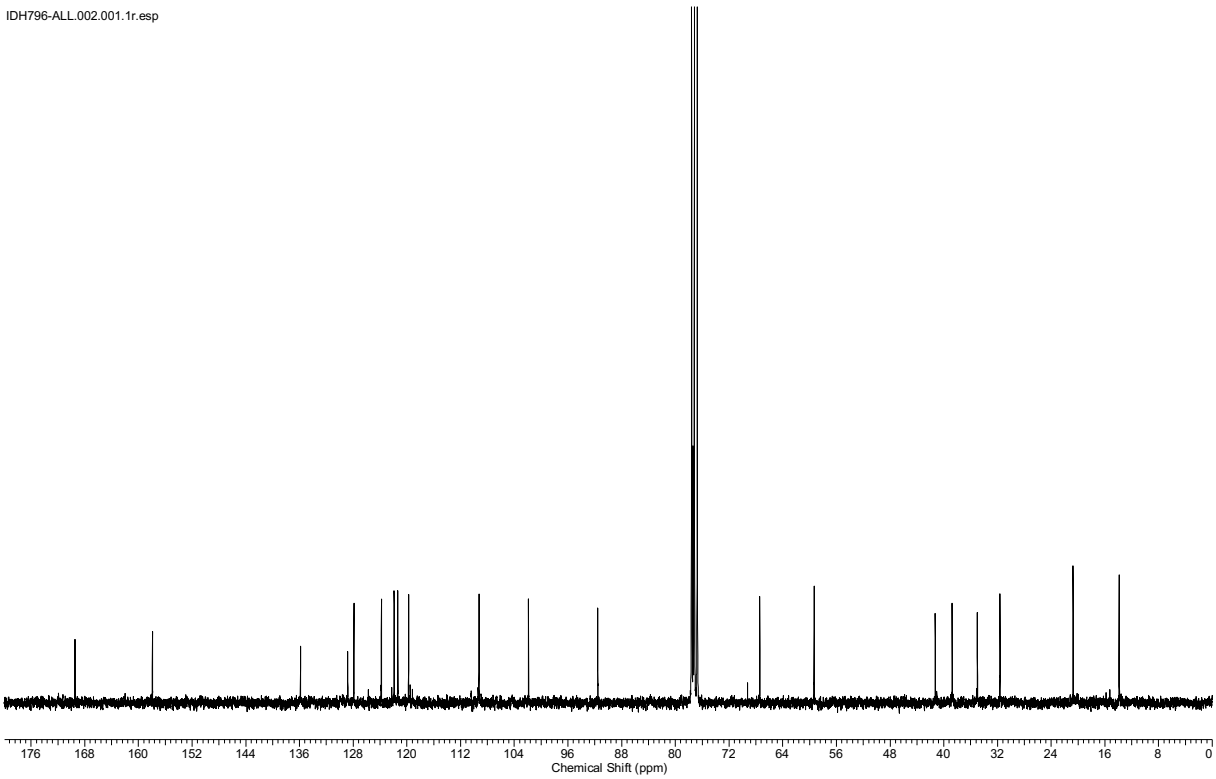


Figure S38 ^{13}C-NMR spectrum of **6d** in $CDCl_3$

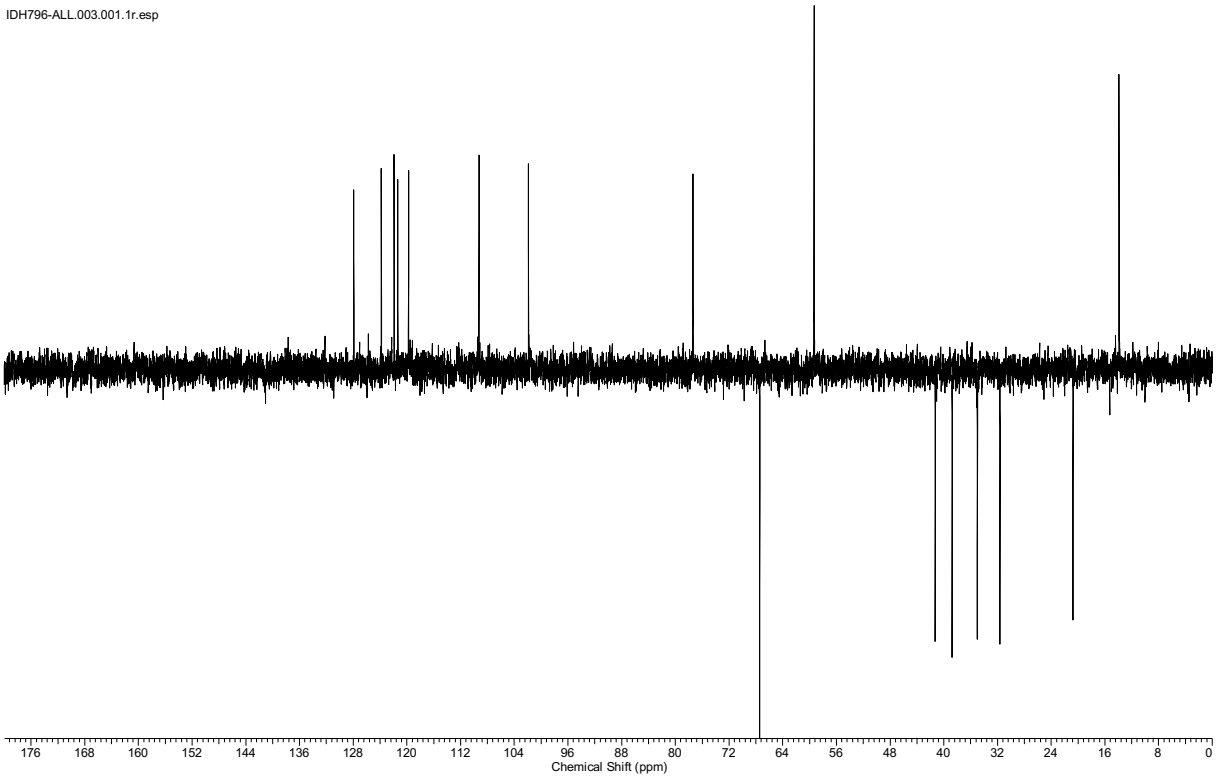
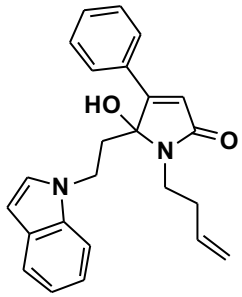


Figure S39 DEPT 135 spectrum of **6d** in $CDCl_3$

5-(2-(1H-Indol-1-yl)ethyl)-1-(but-3-en-1-yl)-5-hydroxy-4-phenyl-1H-pyrrol-2(5H)-one (6e)



Purification: flash chromatography on silica gel (PE/EtOAc : from 80/20 to 50/50)

Yield: 47% (175 mg)

Physical appearance: brown solid

m.p. (amorphous): 163 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 2.44-2.69 (4H, 2x CH_2, m), 3.22-3.31 (1H, C*H*$_2$, m), 3.66-3.80 (3H, C*H*$_2$ and CH_2, m), 5.09-5.16 (2H, CH_2, m), 5.81-5.95 (1H, CH, m), 6.35-6.37 (2H, CH and CH_{Ar}, m), 6.62-6.65 (1H, CH_{Ar}, m), 6.76 (1H, CH_{Ar}, d, *J* = 3.2 Hz), 6.96-7.04 (2H, 2 x CH_{Ar}, m), 7.39-7.54 (4H, 4 x CH_{Ar}, m), 7.74-7.77 (2H, 2 x CH_{Ar}, m); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 33.4 (CH_2), 35.2 (CH_2), 38.4 (CH_2), 41.1 (CH_2), 92.3 (C), 101.8 (CH_{Ar}), 108.9 (CH_{Ar}), 117.5 (CH_2), 119.5 (CH_{Ar}), 121.1 (CH_{Ar}), 121.4 (CH_{Ar}), 121.7 (CH), 127.4 (CH_{Ar}), 127.6 (2x CH_{Ar}), 128.7 (C_{Ar}), 129.3 (2x CH_{Ar}), 130.69 (CH_{Ar}), 130.72 (C_{Ar}), 135.7 (C_{Ar}), 136.1 (CH), 158.0 (C), 169.4 (C); **IR** (nujol): 3257, 2925, 1670, 1444, 1411, 1083, 736, 690 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{24}H_{24}N_2O_2Na^+$ $[M+H]^+$ 395.1730, found 395.1730.

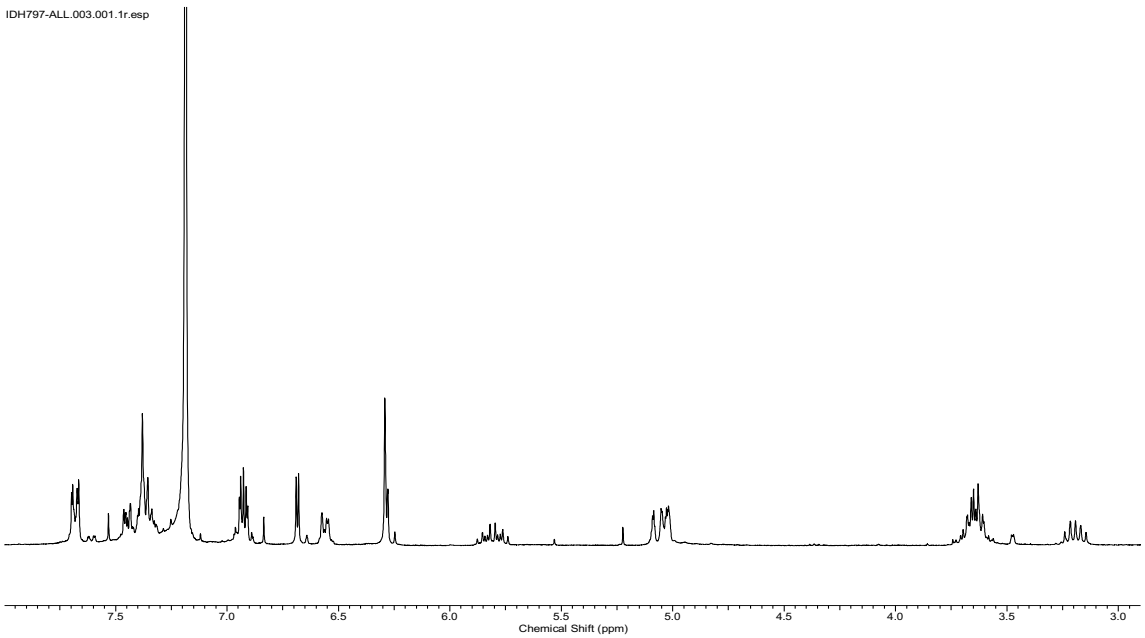


Figure S40 ^{1}H-NMR spectrum of **6e** in $CDCl_3$

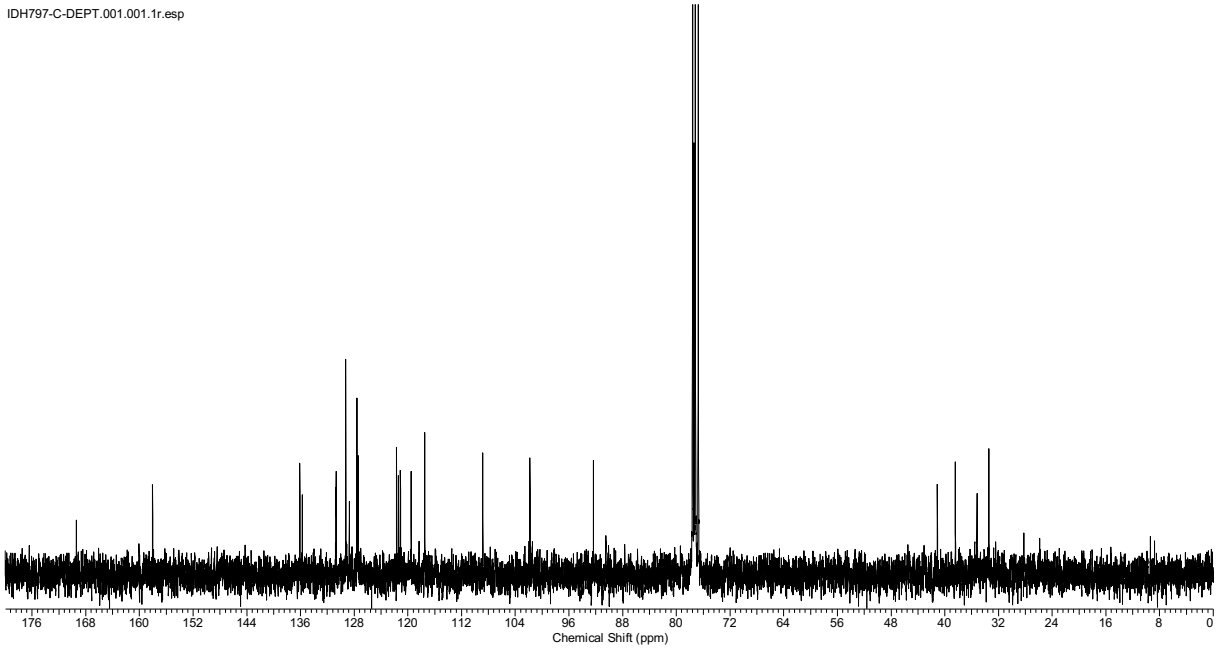


Figure S41 ^{13}C-NMR spectrum of **6e** in $CDCl_3$

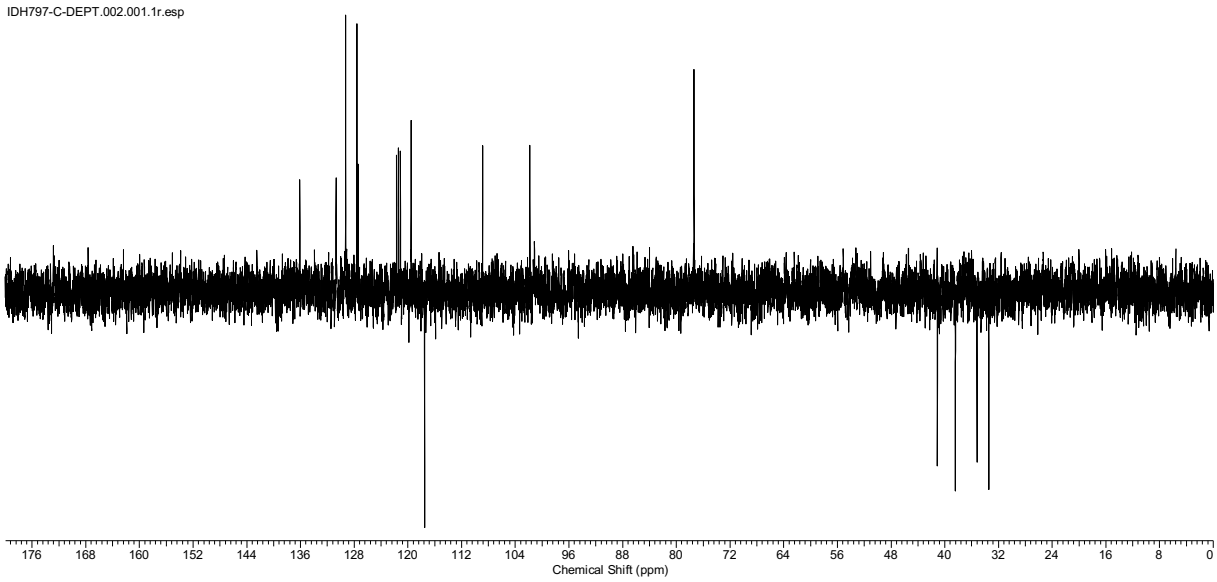
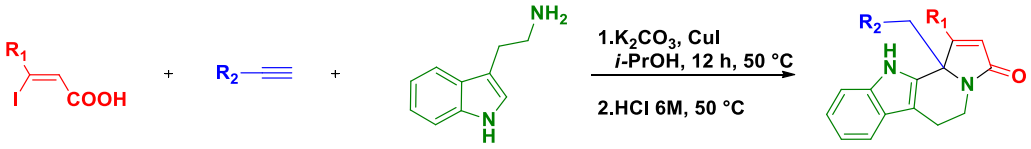


Figure S42 DEPT 135 spectrum of **6e** in $CDCl_3$

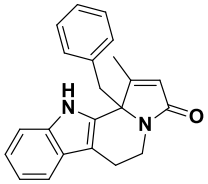
General Procedure to synthesize fused tetrahydro-β-carboline-lactam derivatives 7



(*Z*)-3-Substituted-3-iodoprop-2-enoic acid derivative **1** (1.0 mmol, 1 equiv.) was dissolved in *i*-PrOH (3.5 mL) in oven-dried-Schlenk tube. K_2CO_3 (277 mg, 2.0 mmol, 2 equiv.) was then added to the solution and the suspension was stirred for 10 min under Argon. The mixture was then degassed at -78 °C for 2x10 min and the vessel was backfilled with argon. After warming to room temperature, terminal alkyne **2** (2.0 mmol, 2 equiv.), tryptamine **9** (320 mg, 2.0 mmol, 2 equiv.) and CuI (38 mg, 0.2 mmol, 0.2 equiv.) were respectively added into the mixture. The mixture was then rapidly degassed and the vessel was backfilled with argon. The sealed Schlenk tube was placed in the preheated oil bath (50 °C) and was stirred overnight. The reaction mixture was cooled to 0 °C, then a solution of hydrochloric acid (3.4 mL, 6 M, 20 equiv.) was added dropwise. The reaction was then heated at 50 °C until the disappearance of the γ-hydroxybutyrolactam checked by TLC. The reaction mixture was cooled to 0 °C then filtered through a pad of Celite®. The aqueous phase was extracted with ethyl acetate and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was then purified by flash chromatography on silica gel using petroleum ether: ethyl acetate as eluent.

Or (*Z*)-3-Substituted-3-iodoprop-2-enoic acid derivative **1** (0.5. mmol, 1 equiv.) was dissolved in *i*-PrOH (1.75 mL) in oven-dried-Schlenk tube. K_2CO_3 (138 mg, 1.0 mmol, 2 equiv.) was then added to the solution and the suspension was stirred for 10 min under Argon. The mixture was then degassed at -78 °C for 2x10 min and the vessel was backfilled with argon. After warming to room temperature, terminal alkyne **2** (1.0 mmol, 2 equiv.), tryptamine **9** (160 mg, 1.0 mmol, 2 equiv.) and CuI (19 mg, 0.1 mmol, 0.2 equiv.) were respectively added into the mixture. The mixture was then rapidly degassed and the vessel was backfilled with argon. The sealed Schlenk tube was placed in the preheated oil bath (50 °C) and was stirred overnight. The reaction mixture was cooled to 0 °C, then a solution of hydrochloric acid (3.5 mL, 1 M, 7 equiv.) was added dropwise. The reaction was then heated at 50 °C until the disappearance of the γ-hydroxybutyrolactam checked by TLC. The reaction mixture was cooled to 0 °C then filtered through a pad of Celite®. The aqueous phase was extracted with ethyl acetate and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was then purified by flash chromatography on silica gel using petroleum ether: ethyl acetate (stated below) as eluent.

11b-Benzyl-1-methyl-5,6,6a,11,11a,11b-hexahydro-3*H*-indolizino[8,7-*b*]indol-3-one (7a)



Purification: flash chromatography on silica gel (PE/EtOAc : from 8/2 to 3/7)

Yield: 82% (269 mg, quenched with HCl 6 M, 20 equiv.), 86% (142 mg, quenched with HCl 1M, 7 equiv.)

Physical appearance: light brown solid

m.p. (amorphous): 257 °C; **^{1}H-NMR** ($(CD_3)_2CO$, 400 MHz): δ (ppm) 2.41 (3H, CH_3, br d, *J* = 1.6 Hz), 2.60-2.73 (2H, CH_2, m), 2.96 (1H, C*H*$_2$, ddd, *J* = 13.1, 11.0 and 4.8 Hz), 3.36 (1H, C*H*$_2$, d, *J* = 13.8 Hz), 3.49 (1H, C*H*$_2$, d, *J* = 13.8 Hz), 4.41 (1H, C*H*$_2$, br dd, *J* = 13.1 and 5.5 Hz), 5.62 (1H, CH, br q,*J* = 1.6 Hz), 7.02-7.08 (3H, 3 x CH_{Ar}, m), 7.13 (1H, CH_{Ar}, br dd, *J* = 8.2 and 7.1 Hz), 7.17-7.21 (3H, 3 x CH_{Ar}, m), 7.42 (1H, CH_{Ar}, br d, *J* = 8.2 Hz), 7.46 (1H, CH_{Ar}, br d, *J* = 7.8 Hz), 10.46 (1H, NH, br s); **^{13}C-NMR** ($(CD_3)_2CO$, 100 MHz): δ (ppm) 14.9 (CH_3), 22.5 (CH_2), 37.2 (CH_2), 42.9 (CH_2), 69.9 (C), 109.8 (C_{Ar}), 112.2 (CH_{Ar}), 119.4 (CH_{Ar}), 120.2 (CH_{Ar}), 122.8 (CH_{Ar}), 123.9 (CH), 127.6$_9$ (C_{Ar}), 127.7$_2$ (CH_{Ar}), 128.8 (2 x CH_{Ar}), 130.6 (2 x CH_{Ar}), 134.1 (C_{Ar}), 136.5 (C_{Ar}), 137.9 (C_{Ar}), 162.4 (C), 172.4 (C); **IR** (nujol): 3255, 2923, 1664; 1448, 1405, 742, 702 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{22}H_{21}N_2O[M+H]^+$ 329.1648, found 329.1649.

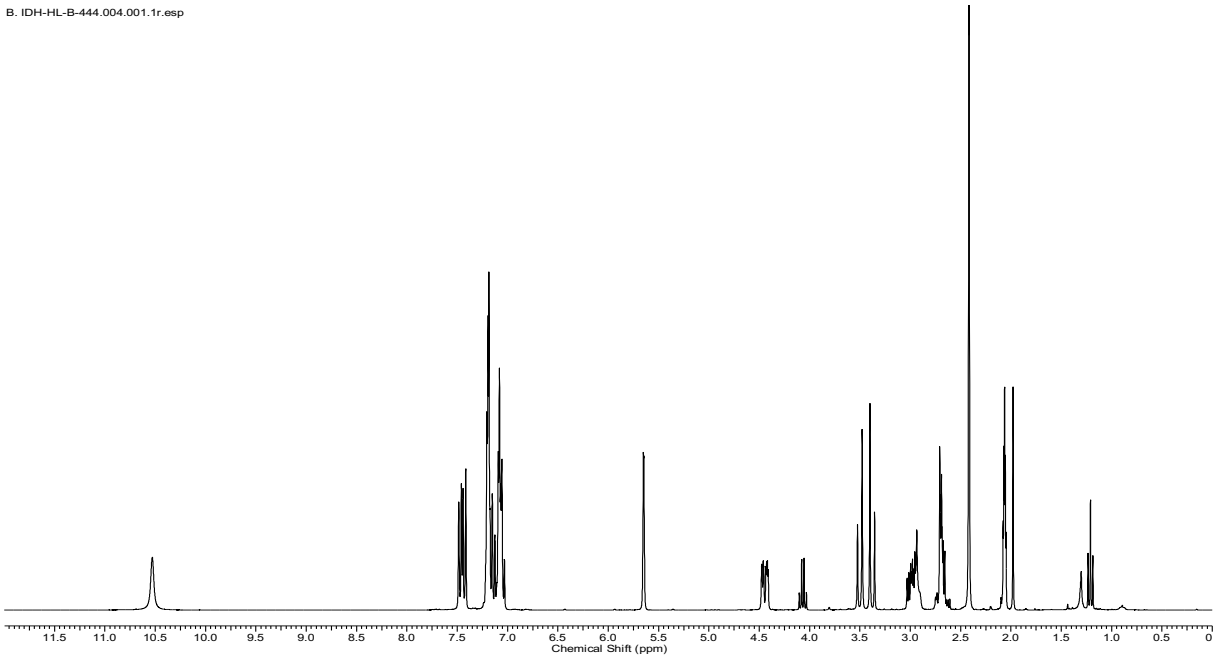


Figure S43 ^{1}H-NMR spectrum of **7a** in $CDCl_3$

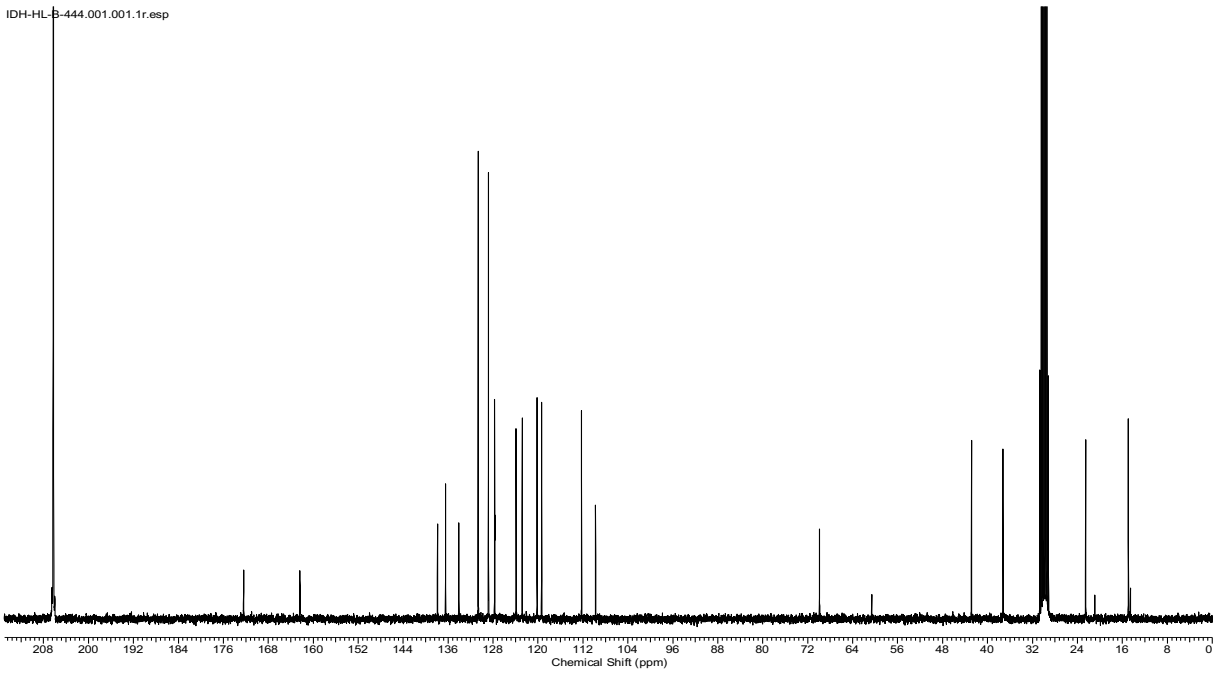


Figure S44 ^{13}C-NMR spectrum of **7a** in $CDCl_3$

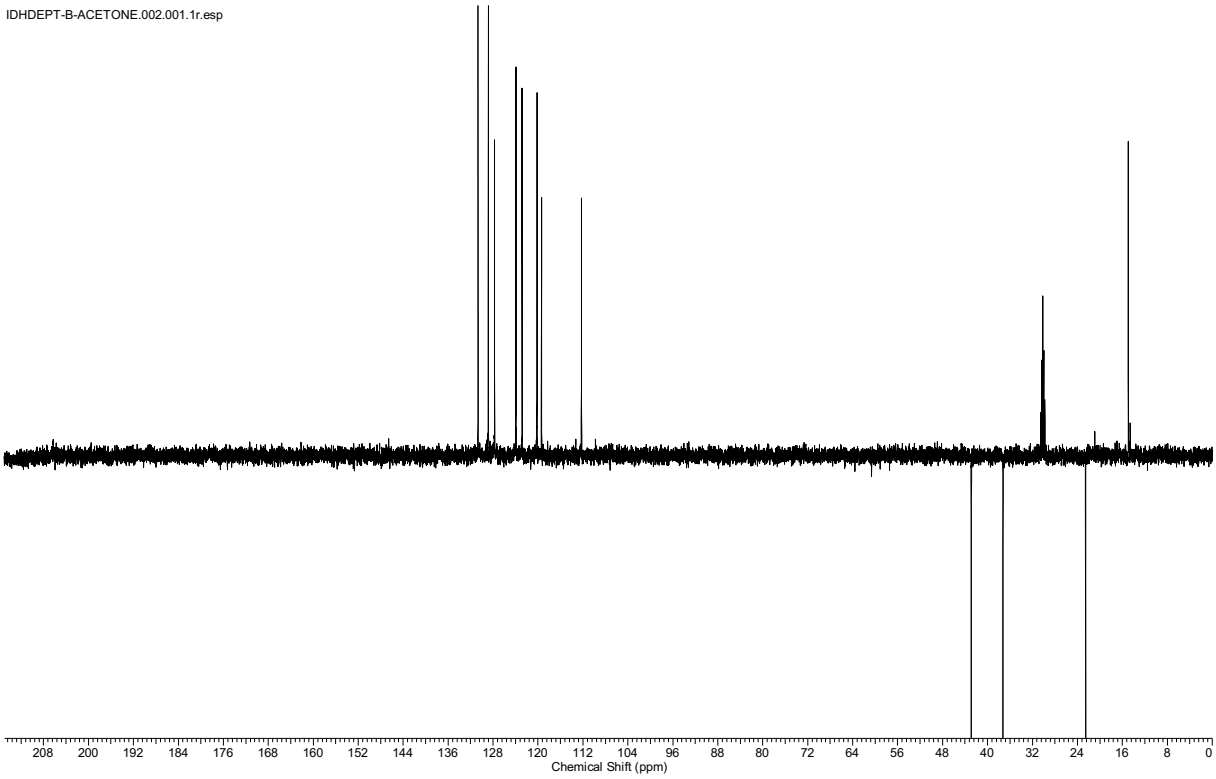
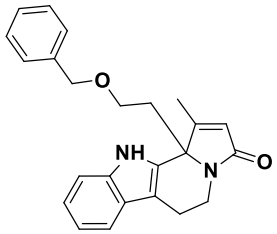


Figure S45 DEPT 135 spectrum of **7a** in $CDCl_3$

11b-(2-(Benzyloxy)ethyl)-1-methyl-5,6,11,11b-tetrahydro-3H-indolizino[8,7-b]indol-3-one (7b)



Purification: flash chromatography on silica gel (PE/EtOAc : from 8/2 to 5/5)

Yield: 58% (108 mg, quenched with HCl 1M, 7 equiv.)

Physical appearance: light brown solid

m.p. (amorphous): 206 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 2.27 (3H, CH_3, br s), 2.27-2.34 (1H, C*H*$_2$, m), 2.39-2.49 (1H, C*H*$_2$, m), 2.71-2.91 (2H, CH_2, m), 3.08 (1H, C*H*$_2$, m), 3.33-3.47 (2H, CH_2, m), 4.39 (2H, CH_2, br s), 4.57 (1H, C*H*$_2$, br dd, *J* = 13.2 and 5.3 Hz), 5.86 (1H, CH, br s), 7.12 (1H, CH_{Ar}, br t, *J* = 7.2 Hz), 7.20 (1H, CH_{Ar}, br t, *J* = 7.8 Hz), 7.25-7.35 (6H, 6 x CH_{Ar}, m), 7.49 (1H, CH_{Ar}, d, *J* = 7.8 Hz), 8.32 (1H, NH, br s); **^{13}C-NMR (**$CDCl_3$,100 MHz): δ (ppm) 15.0 (CH_3), 22.0 (CH_2), 36.5 (CH_2), 36.6 (CH_2), 65.4 (CH_2), 67.4 (C), 73.5 (CH_2),109.4 (C_{Ar}), 111.2 (CH_{Ar}), 119.0 (CH_{Ar}), 120.1 (CH_{Ar}), 122.7 (CH_{Ar}), 123.1 (CH), 126.7 (C_{Ar}), 127.8 (2 x CH_{Ar}), 127.9 (CH_{Ar}), 128.6 (2 x CH_{Ar}), 133.2 (C_{Ar}), 136.5 (C_{Ar}), 138.0 (C_{Ar}), 161.4 (C), 172.4 (C); **IR**(nujol): 3295, 2852, 1662, 1452, 1398, 1299, 1105, 740, 698 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{24}H_{25}N_2O_2[M+H]^+$ 373.1911, found 373.1911.

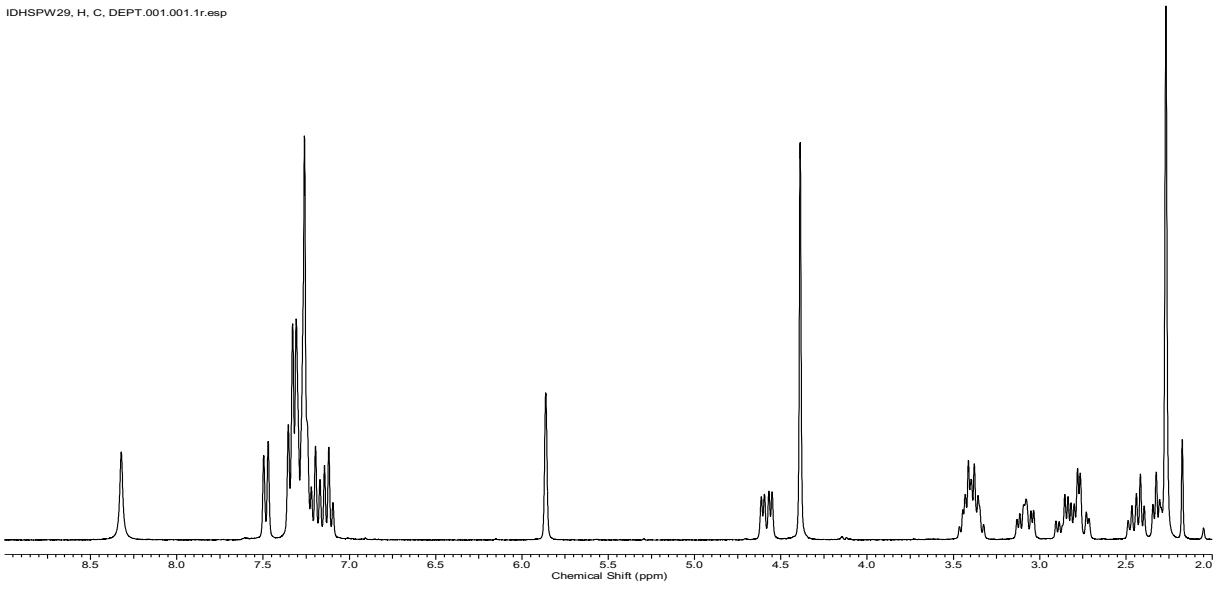


Figure S46 DEPT 135 spectrum of **7b** in $CDCl_3$

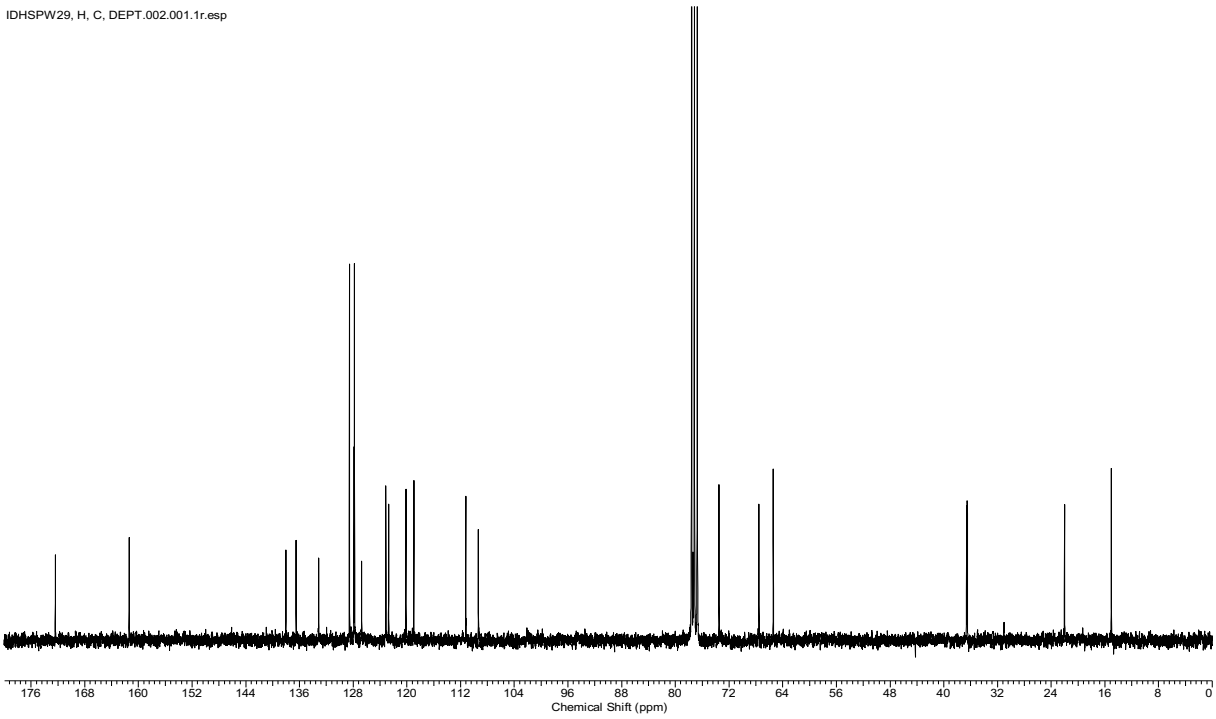


Figure S47 ^{13}C-NMR spectrum of **7b** in $CDCl_3$

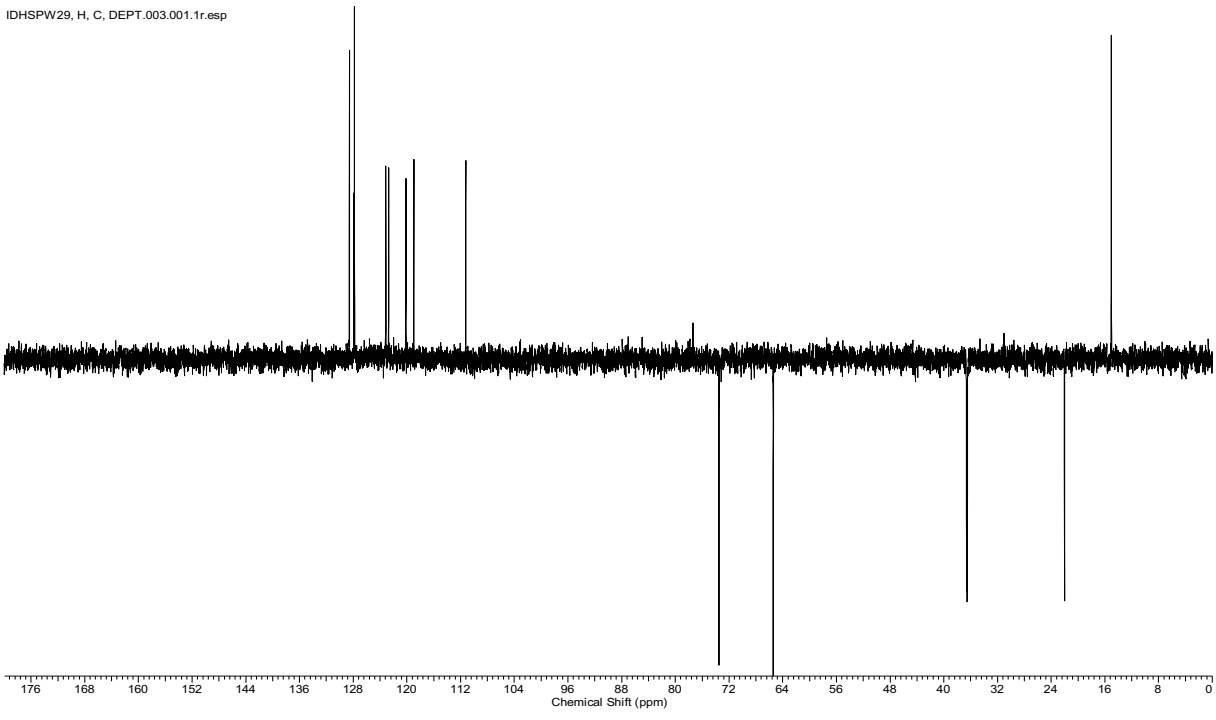
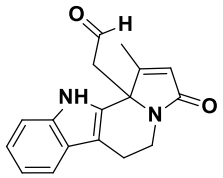


Figure S48 DEPT 135 spectrum of **7b** in $CDCl_3$

2-(1-Methyl-3-oxo-6,11-dihydro-3H-indolizino[8,7-b]indol-11b(5H)-yl)acetaldehyde (7c)



Purification: flash chromatography on silica gel (PE/EtOAc : from 85/15 to 50/50)

Yield: 36% (102 mg, quenched with HCl 6 M, 20 equiv.), 53% (75 mg, quenched with HCl 1M, 7 equiv.)

Physical appearance: yellow solid

m.p. (amorphous): 230 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 2.34 (3H, CH_3, br d, *J* = 1.7 Hz), 2.79-2.94 (2H, CH_2, m), 3.05 (2H, CH_2, br d, *J* = 2.5 Hz),3.18 (1H, C*H*$_2$, ddd, *J* = 13.4, 10.7 and 4.9 Hz), 4.66 (1H, C*H*$_2$, ddd, *J* = 13.4, 5.6 and 1.2 Hz), 5.98 (1H, CH, br q,*J* = 1.7 Hz), 7.14 (1H, CH_{Ar}, br t, *J* = 7.8 Hz), 7.23 (1H, CH_{Ar}, br dd,*J* = 8.1 and 7.1 Hz), 7.38 (1H, CH_{Ar}, br d, *J* = 8.1 Hz), 7.51 (1H, CH_{Ar}, br d, *J* = 7.8 Hz), 8.37 (1H, NH, br s), 9.48 (1H, CH, t,*J* = 2.5Hz): **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 15.1 (CH_3), 21.8 (CH_2), 36.7 (CH_2), 48.4 (CH_2), 66.2 (C), 110.2 (C_{Ar}), 111.3 (CH_{Ar}), 119.2 (CH_{Ar}), 120.4 (CH_{Ar}), 123.3 (CH_{Ar}), 124.5 (CH), 126.5 (C_{Ar}), 131.2 (C_{Ar}), 136.6 (C_{Ar}), 160.0 (C), 171.63 (C), 198.8 (C); **IR** (nujol): 3261, 2925, 1720, 1664, 1440, 1396, 1299, 740cm^{-1}; **HRMS** (ESI-MS) unstable to be measured by HRMS.

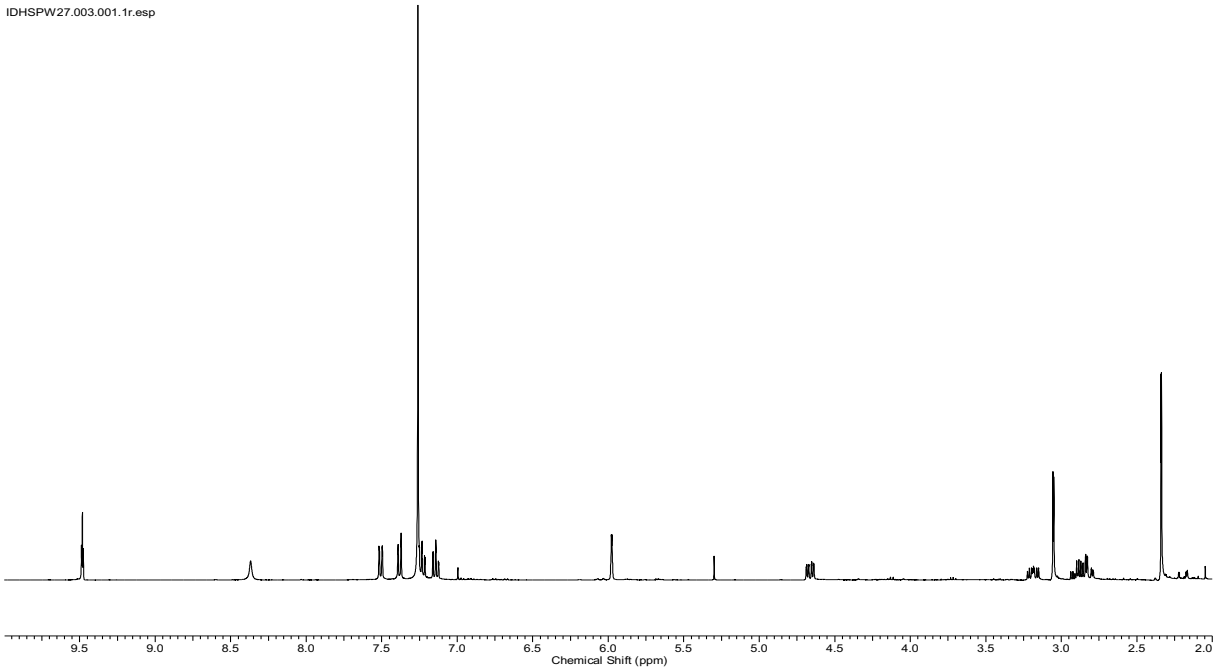


Figure S49 ^{1}H-NMR spectrum of **7c** in $CDCl_3$

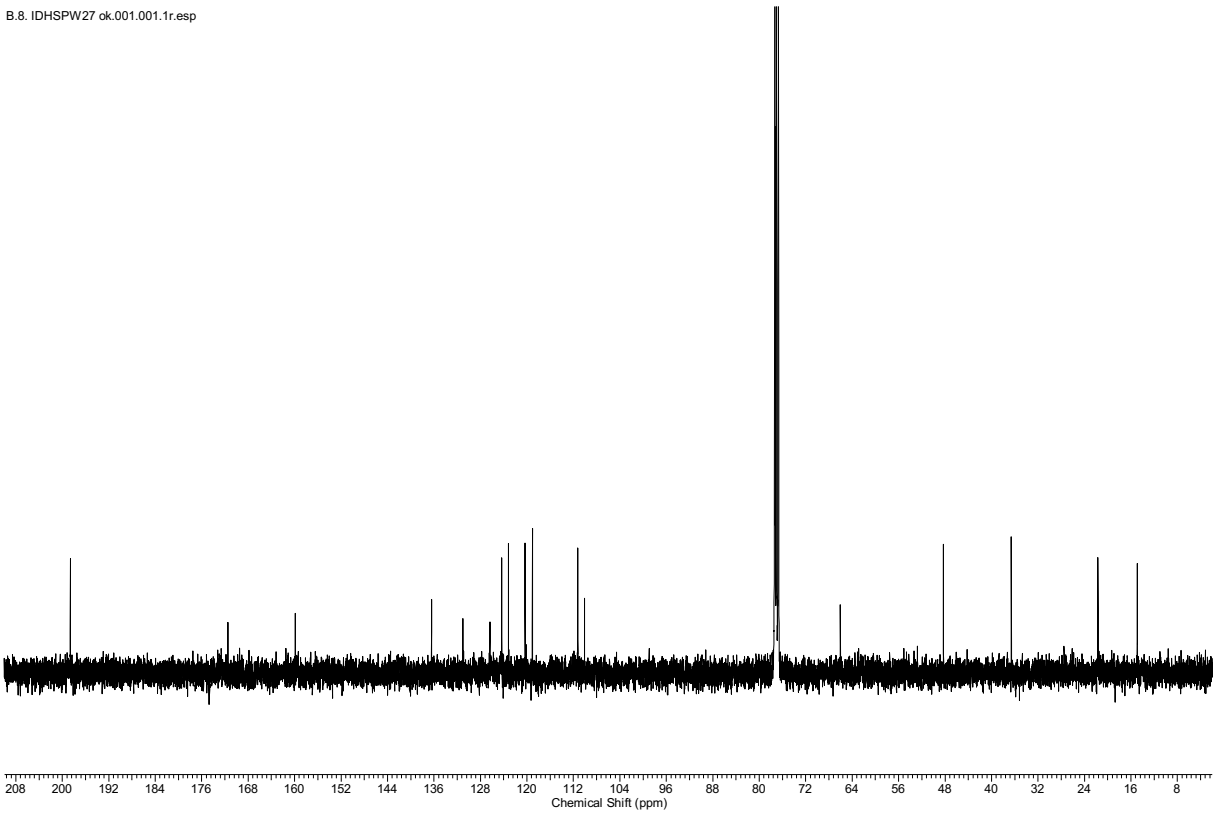


Figure S50 ^{13}C-NMR spectrum of **7c** in $CDCl_3$

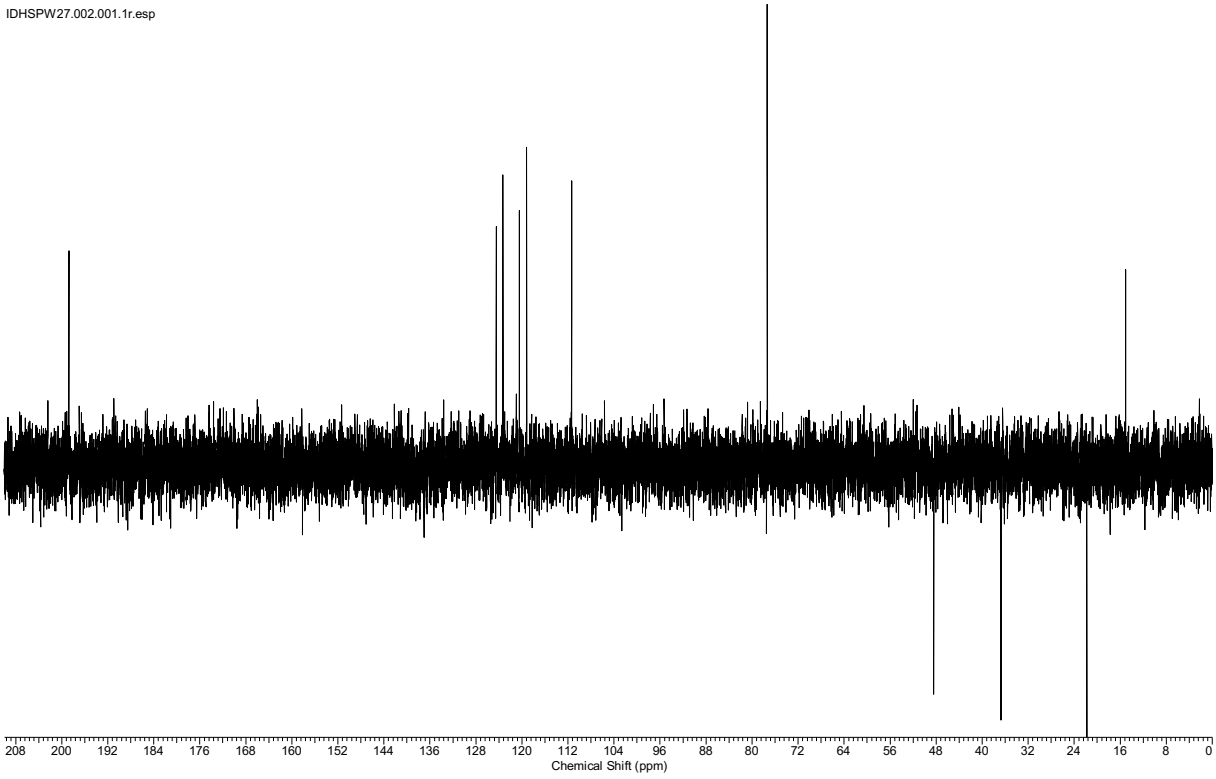
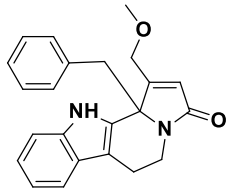


Figure S51 DEPT 135 spectrum of **7c** in $CDCl_3$

11b-Benzyl-1-(methoxymethyl)-5,6,11,11b-tetrahydro-3H-indolizino[8,7-b]indol-3-one (7d)



Purification: flash chromatography on silica gel (PE/EtOAc : from 85/15 to 50/50)

Yield: 52% (185 mg, quenched with HCl 6 M, 20 equiv.), 65% (118 mg, quenched with HCl 1M, 7 equiv.)

Physical appearance: grey solid

m.p. (amorphous): 229 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 2.77 (1H, C*H*$_2$, dd, *J* = 15.4 and 4.7 Hz), 2.90 (1H, C*H*$_2$, ddd,*J* = 15.4 and 11.3 and 6.1 Hz), 3.10 (1H, C*H*$_2$, br ddd, *J* = 13.2 and 11.5 and 4.9 Hz), 3.38 (1H, C*H*$_2$, d, *J* = 14.2 Hz), 3.46 (1H, C*H*$_2$, d, *J* = 14.2 Hz), 3.58 (3H, CH_3, s), 4.45 (1H, C*H*$_2$, br d, *J* = 14.4 and 1.0 Hz), 4.57-4.62 (2H, 2 x C*H*$_2$, m), 5.80 (1H, CH, br t,*J* = 1.0 Hz),7.00-7.02 (2H, 2x CH_{Ar}, m), 7.12 (1H, CH_{Ar}, br t, *J* = 7.8 Hz), 7.20-7.24 (4H, 4x CH_{Ar}, m), 7.39 (1H, CH_{Ar}, br d, *J* = 8.1 Hz), 7.49 (1H, CH_{Ar}, br d, *J* = 7.8Hz), 9.33 (1H, NH, br s); **^{13}C-NMR** ($CDCl_3$,100 MHz): δ (ppm) 21.8 (CH_3), 36.0 (CH_2), 43.1 (CH_2), 59.2 (CH_3), 69.6 (C), 70.0 (CH_2), 109.4 (C_{Ar}), 111.4 (CH_{Ar}), 119.0 (CH_{Ar}), 119.8 (CH_{Ar}), 122.6 (CH_{Ar}), 124.3 (CH), 126.9 (C_{Ar}), 127.4 (CH_{Ar}), 128.5 (2 x CH_{Ar}), 129.6 (2 x CH_{Ar}), 132.9 (C_{Ar}), 135.1 (C_{Ar}), 136.2 (C_{Ar}), 158.8 (C), 170.4 (C); **IR** (nujol): 3242, 2927, 1662, 1452, 1402, 742, 702 cm^{-1}; **HRMS**(ESI-MS) calcd for $C_{23}H_{23}N_2O_2[M+H]^+$ 359.1754, found 359.1756.

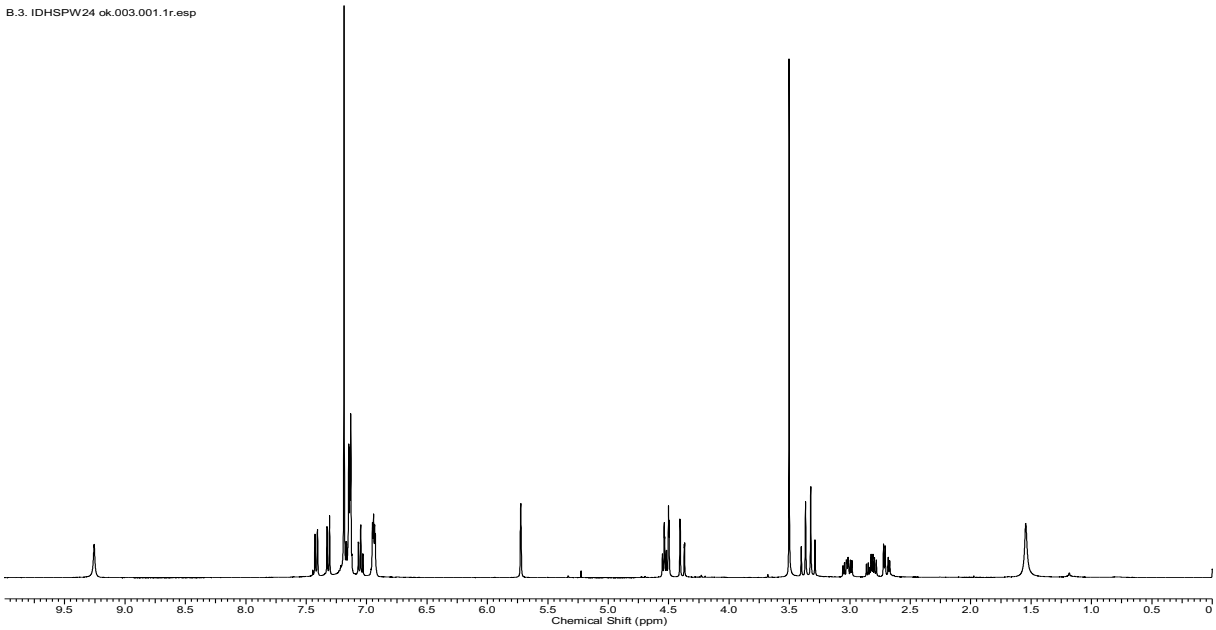


Figure S52 ^{1}H-NMR spectrum of **7d** in $CDCl_3$

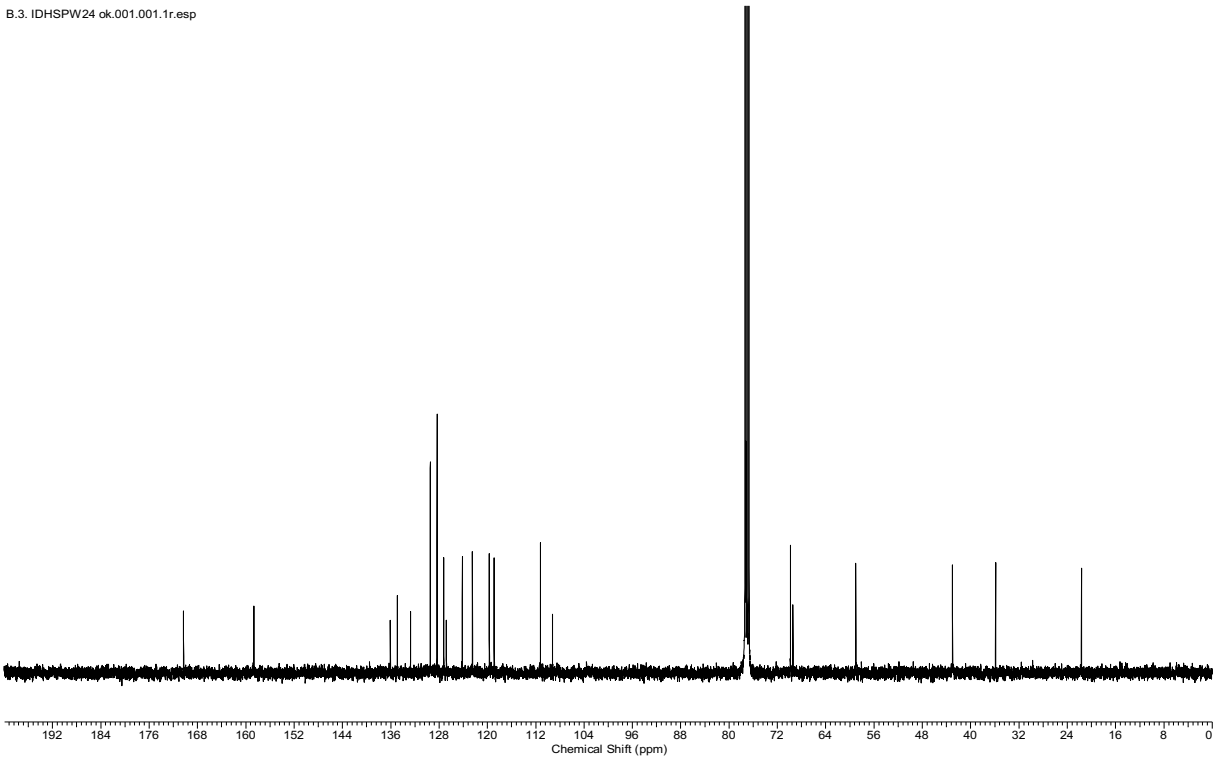


Figure S53 ^{13}C-NMR spectrum of **7d** in $CDCl_3$

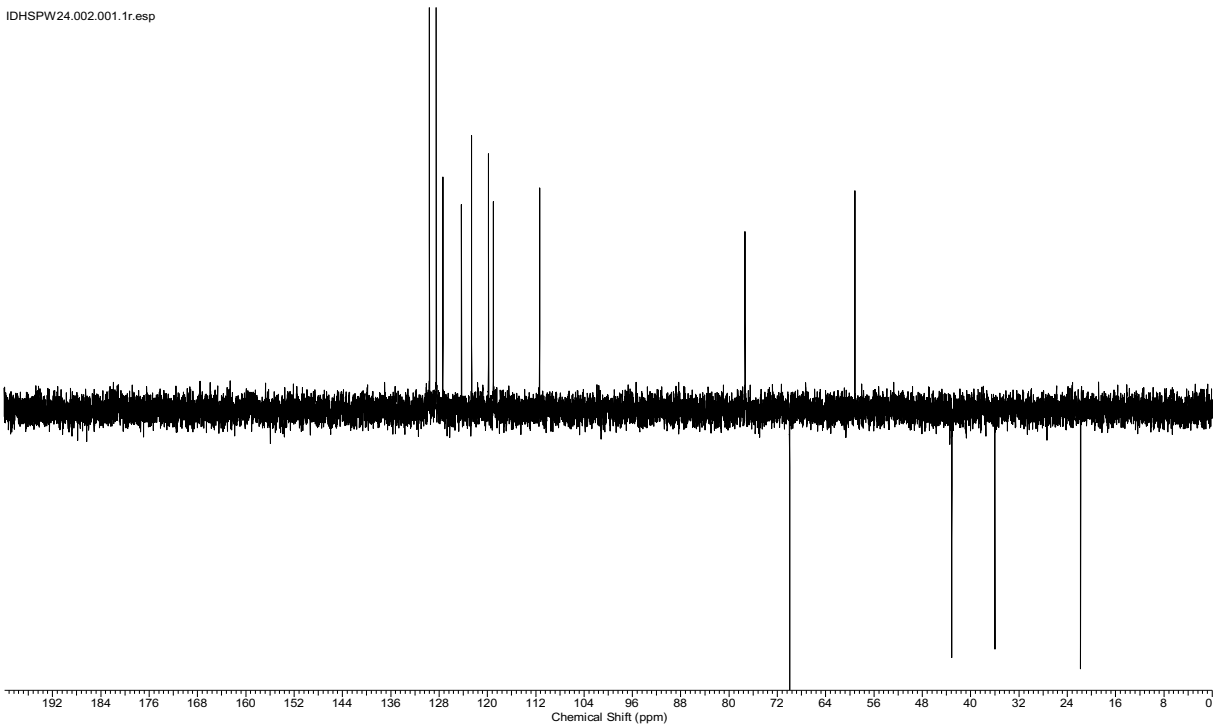
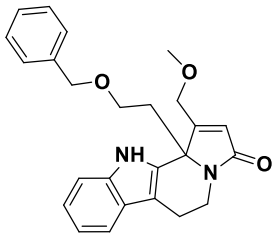


Figure S54 DEPT 135 spectrum of **7d** in $CDCl_3$

11b-(2-(Benzyloxy)ethyl)-1-(methoxymethyl)-5,6,11,11b-tetrahydro-3H-indolizino[8,7-b]indol-3-one (7e)



Purification: flash chromatography on silica gel (PE/EtOAc : from 85/15 to 50/50)

Yield: 32% (130 mg, quenched with HCl 6 M, 20 equiv.), 65% (131 mg, quenched with HCl 1M, 7 equiv.)

Physical appearance: brown solid

m.p. (amorphous): 135 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 2.32 (1H, CH_2, dt, *J* = 14.9 and 5.3 Hz), 2.63 (1H, CH_2, ddd, *J* = 14.9, 8.1 and 5.8 Hz), 2.79 (1H, CH_2, dd,*J* = 15.4 and 4.9 Hz), 2.92 (1H, CH_2, ddd, *J* = 15.4, 11.2 and 6.4 Hz), 3.15 (1H, CH_2, ddd, *J* = 13.5, 11.5 and 5.2 Hz), 3.31-3.37 (1H, CH_2, m), 3.40-3.45 (1H, CH_2, m), 3.41 (3H, CH_3, s), 4.34-4.41 (3H, CH_2 and CH_2, m), 4.59 (1H, CH_2, br dd, *J* = 13.5 and 5.6 Hz), 4.69 (1H, CH_2, dd, *J* = 14.2 and 2.0 Hz), 5.99 (1H, br s), 7.10 (1H, CH_{Ar}, br dd, *J* = 8.1 and 7.1 Hz), 7.18 (1H, CH_{Ar}, br dd, *J* = 8.1 and 7.1 Hz), 7.25-7.37 (6H, 6 x CH_{Ar}, m, H11, H12), 7.47 (1H, CH_{Ar}, d, *J* = 8.1 Hz), 9.24 (1H, NH, br s); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 21.7 (CH_2), 35.8 (CH_2), 36.8 (CH_2), 58.9 (CH_3),65.4 (CH_2), 67.9 (C), 69.8 (CH_2), 73.5 (CH_2), 108.2(C_{Ar}), 111.4 (CH_{Ar}), 118.9 (CH_{Ar}), 119.8 (CH_{Ar}), 122.5 (CH_{Ar}), 124.6 (CH), 126.9 (C_{Ar}), 127.8 (2 x CH_{Ar}), 127.9 (CH_{Ar}), 128.6 (2 x CH_{Ar}), 133.8 (C_{Ar},), 136.2 (C_{Ar}), 138.0 (C_{Ar}), 159.6 (C), 170.5 (C). **IR** (nujol): 3253, 2929, 1656, 1452, 1405, 1297, 740, 700 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{25}H_{27}N_2O_3[M+H]^+$ 403.2016, found 403.2016.

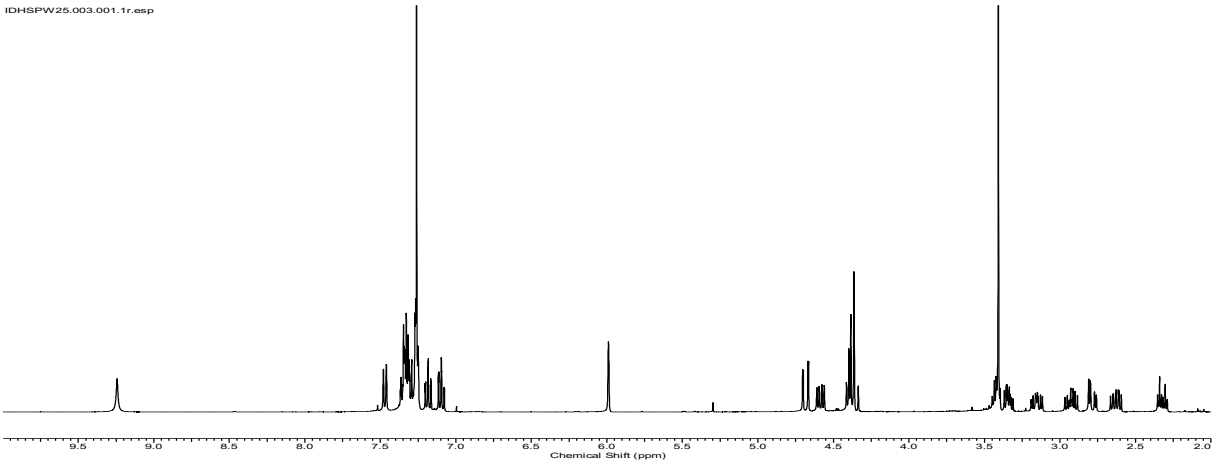


Figure S55 ^{1}H-NMR spectrum of **7e** in $CDCl_3$

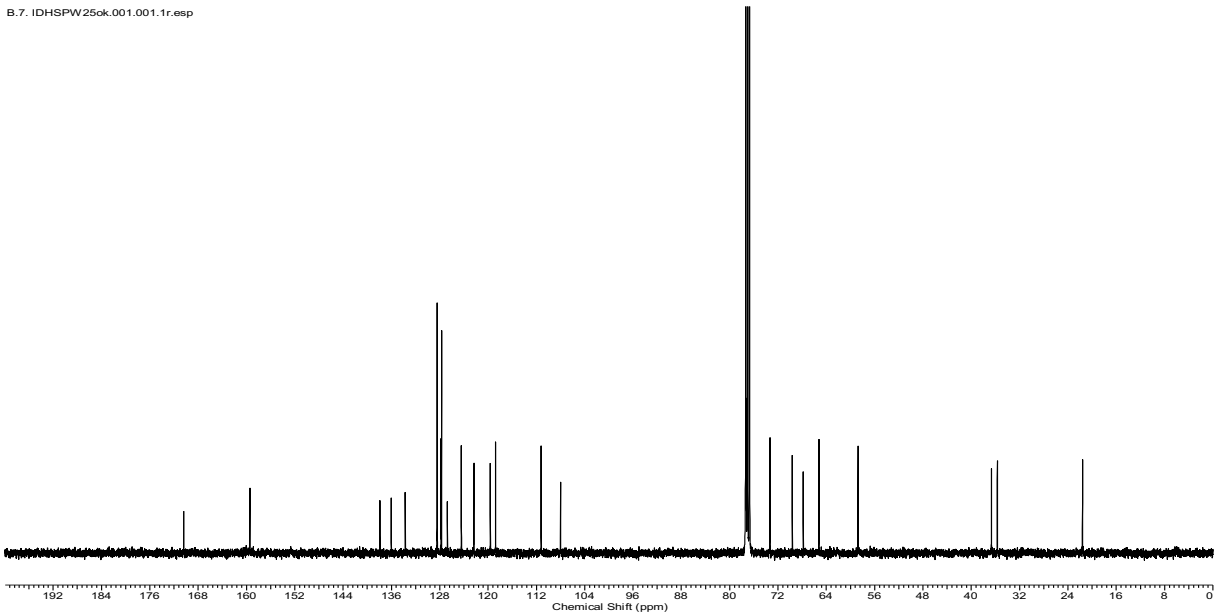


Figure S56 ^{13}C-NMR spectrum of **7e** in $CDCl_3$

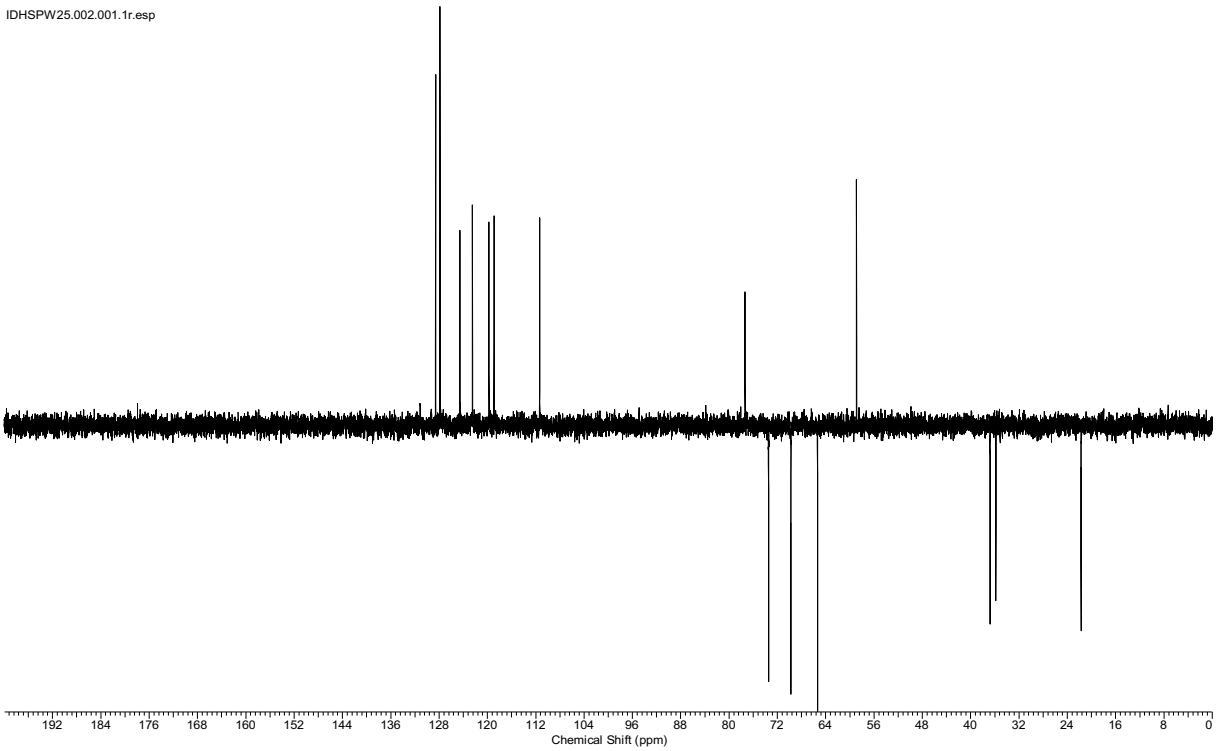
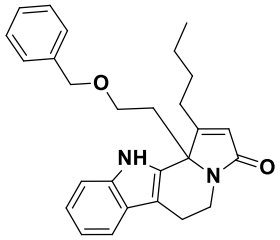


Figure S57 DEPT 135 spectrum of **7e** in $CDCl_3$

11b-(2-(Benzyloxy)ethyl)-1-butyl-5,6,11,11b-tetrahydro-3H-indolizino[8,7-b]indol-3-one (7f)



Purification: flash chromatography on silica gel (PE/EtOAc : from 8/2 to 3/7)

Yield: 39% (160 mg, quenched with HCl 6 M, 20 equiv.), 56% (116 mg, quenched with HCl 1M, 7 equiv.)

Physical appearance: light brown solid

m.p. (amorphous): 143 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 0.89 (3H, CH_3, t, *J* = 7.3 Hz, H7), 1.30-1.39 (2H, CH_2, m, H6), 1.43-1.60 (2H, CH_2, m, H5), 2.26-2.32 (1H, C*H*$_2$, m, H9), 2.38-2.43 (1H, C*H*$_2$, m, H4), 2.38-2.48 (1H, C*H*$_2$, m, H9), 2.55-2.64 (1H, C*H*$_2$, m, H4), 2.73-2.88 (2H, CH_2, m, H17), 3.07 (1H, C*H*$_2$, ddd, *J* =15.9, 11.0 and 4.9 Hz, H16), 3.29-3.35 (1H, C*H*$_2$, m, H10), 3.36-3.43 (1H, C*H*$_2$, m, H10), 4.34-4.41 (2H, CH_2, m, H11), 4.55 (1H, C*H*$_2$, dd, *J* =13.2, 5.6 Hz, H16), 5.86 (1H, br q, H2), 7.12 (1H, CH_{Ar}, dt, *J* = 7.8 and 1.0 Hz), 7.20 (1H, CH_{Ar}, dt, *J* = 7.2 and 1.2 Hz), 7.24-7.40 (6H, 6 x $CH_{Ar,}$ m), 7.47 (1H, CH_{Ar}, d, *J* = 7.8 Hz), 8.04 (1H, NH, br s, H26); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 14.1 (CH_3, C7), 22.0 (CH_2, C17), 22.7 (CH_2, C6), 28.4 (CH_2, C14), 28.9 (CH_2, C5), 36.5 (CH_2, C16), 36.8 (CH_2, C9), 65.3 (CH_2, C10), 67.5 (C, C8), 73.5 (CH_2, C11), 109.5 (C_{Ar}), 111.2 (CH_{Ar}), 119.0 (CH_{Ar}), 120.2 (CH, C2), 121.0 (CH_{Ar}), 122.8 (CH_{Ar}), 126.7 (C_{Ar}), 127.9 (2 x CH_{Ar}), 127.9 (CH_{Ar}), 128.6 (2 x CH_{Ar}), 133.2 (C_{Ar}), 136.3 (C_{Ar}), 138.0 (C_{Ar}), 166.1 (C, C8), 172.4 (C, C1); **IR** (nujol): 3253, 2929, 2862, 1660, 1452, 1402, 1105, 742 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{27}H_{31}N_2O_2$ $[M+H]^+$ 415.2380, found 415.2380.

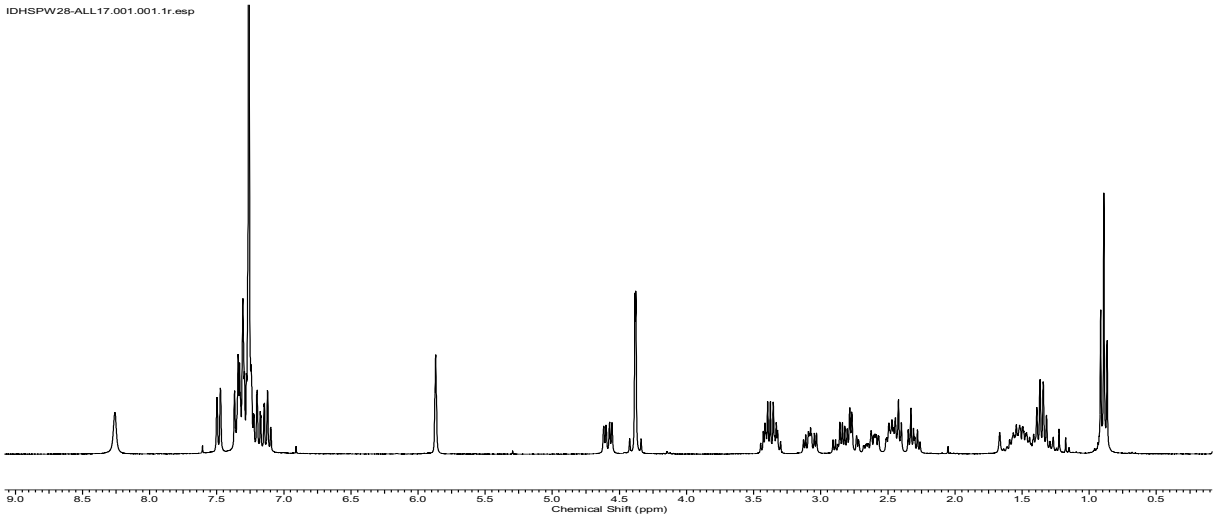


Figure S58 ^{1}H-NMR spectrum of **7f** in $CDCl_3$

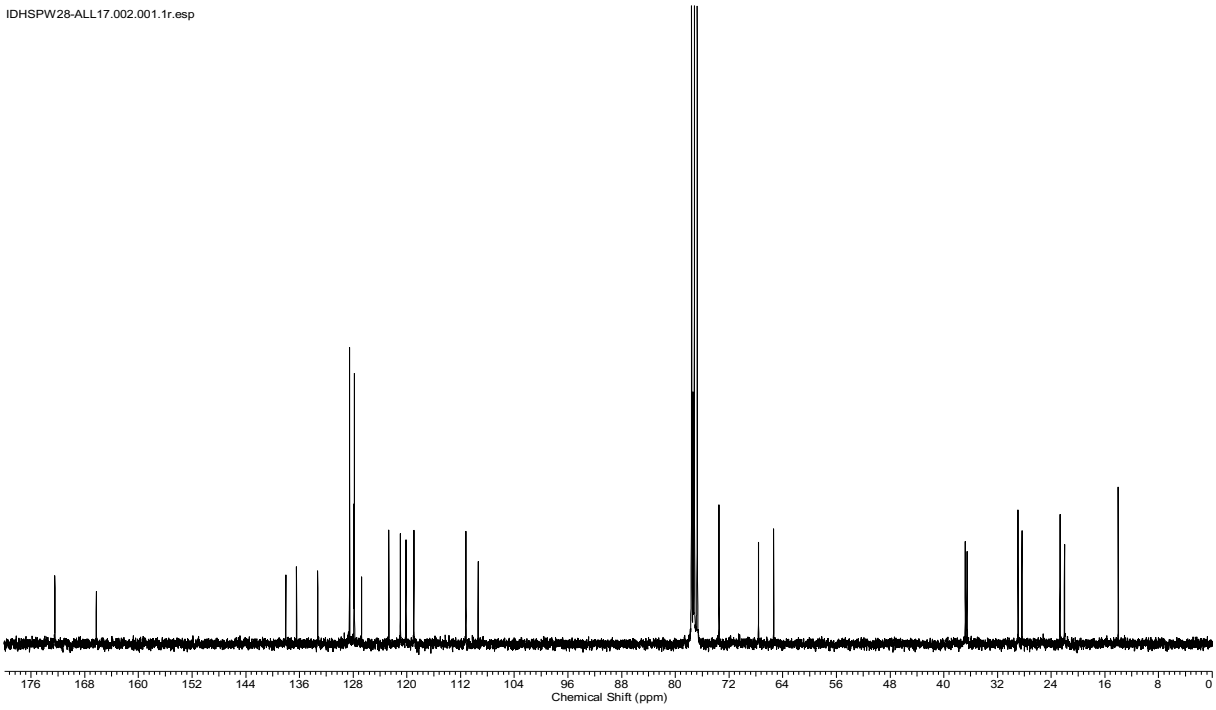


Figure S59 ^{13}C-NMR spectrum of **7f** in $CDCl_3$

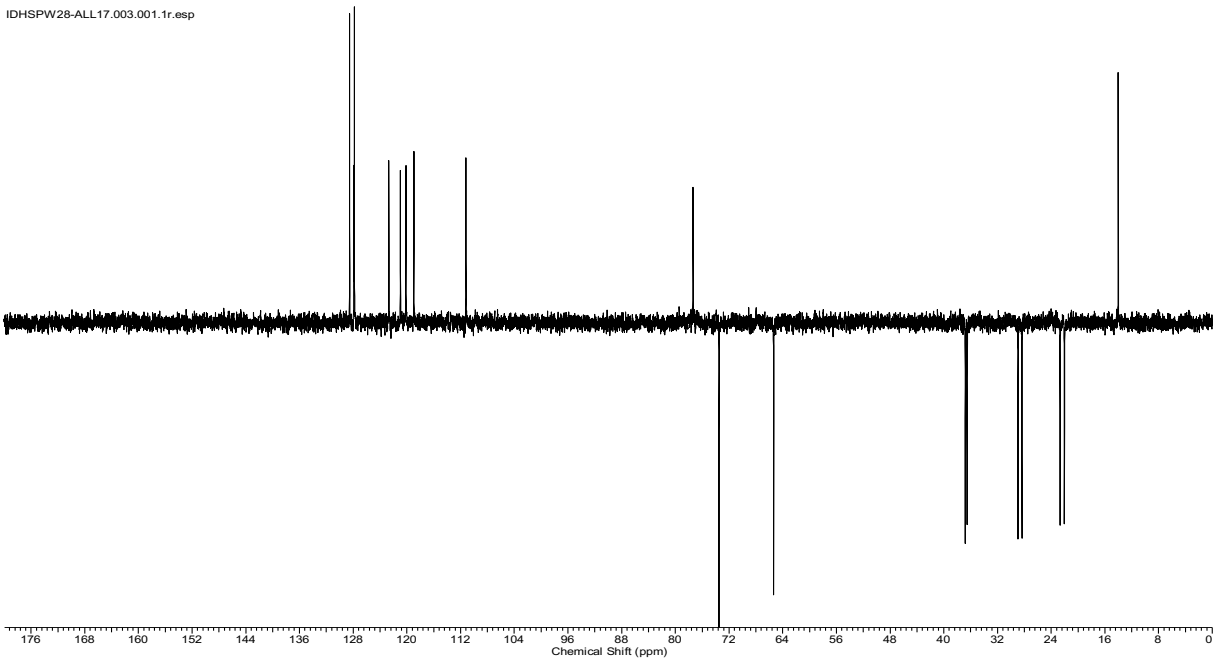
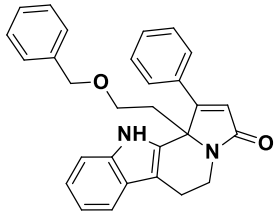


Figure S60 DEPT 135 spectrum of **7f** in $CDCl_3$

11b-(2-(Benzyloxy)ethyl)-1-phenyl-5,6,11,11b-tetrahydro-3H-indolizino[8,7-b]indol-3-one (7g)



Purification: flash chromatography on silica gel (PE/EtOAc : from 8/2 to 5/5)

Yield: 62% (1360mg, quenched with HCl 1M, 7 equiv.)

Physical appearance: light brown solid

m.p. (amorphous): 201 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 2.47-2.54 (1H, C*H*$_2$, m), 2.79-2.86 (2H, 2 x C*H*$_2$, m), 2.89-2.97(1H, C*H*$_2$, m), 3.23 (1H, C*H*$_2$, ddd, *J* = 13.5 and 11.0 and 4.9 Hz), 3.53-3.63 (2H, CH_2, m), 4.41 (1H, C*H*$_2$, d, *J* = 11.7 Hz), 4.46 (1H, C*H*$_2$, d, *J* = 11.7 Hz), 4.66 (1H, C*H*$_2$, dd, *J* = 13.5 and 5.6 Hz), 6.21 (1H, CH, s), 7.06-7.15 (3H, 3 x CH_{Ar}, m), 7.22-7.33 (5H, 5 x CH_{Ar}, m), 7.47 (1H, br d, *J* = 7.3 Hz), 7.49-7.52 (5H, 5 x CH_{Ar}, m); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 21.8 (CH_2), 35.9 (CH_2), 36.8 (CH_2), 65.5 (CH_2), 67.5 (C), 73.5 (CH_2), 108.9 (C_{Ar}), 111.2 (CH_{Ar}), 119.0 (CH_{Ar}), 120.1 (CH_{Ar}), 122.7 (CH_{Ar}), 124.7 (CH), 126.6 (C_{Ar}), 127.8 (2 x CH_{Ar}), 127.9 (CH_{Ar}), 128.2 (2 x CH_{Ar}), 128.5 (2 x CH_{Ar}), 129.5 (2 x CH_{Ar}), 130.0 (CH_{Ar}), 133.2 (C_{Ar}), 133.9 (C_{Ar}), 136.1 (C_{Ar}), 138.0 (C_{Ar}), 161.8 (C), 170.8 (C); **IR** (nujol): 3253, 2929, 1656, 1452, 1405, 740, 700 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{29}H_{27}N_2O_2[M+H]^+$ 435.2067, found 435.2068.

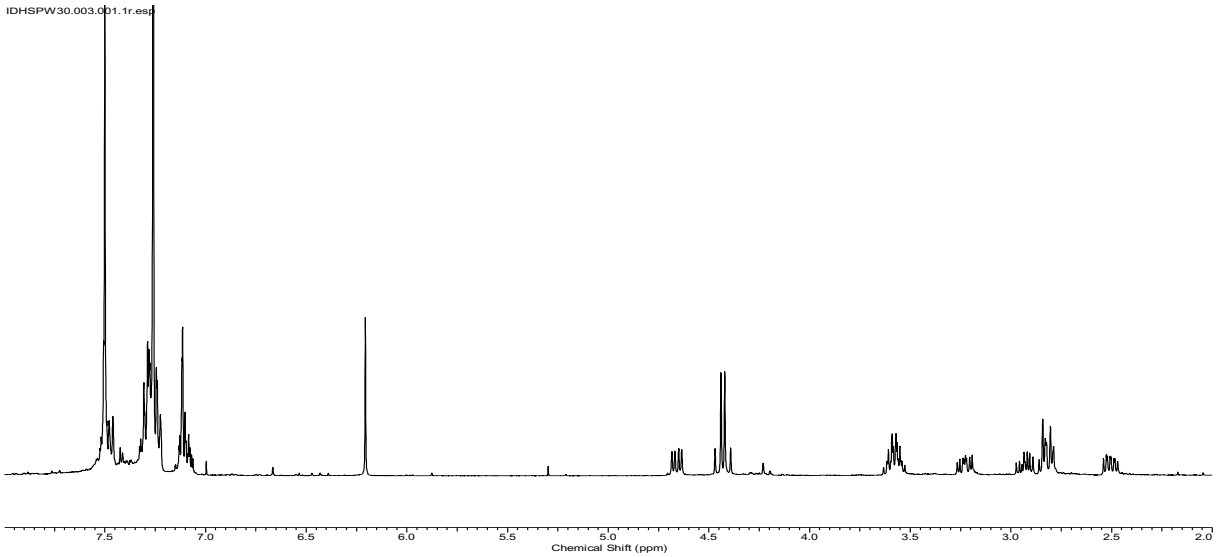


Figure S61 ^{1}H-NMR spectrum of **7g** in $CDCl_3$

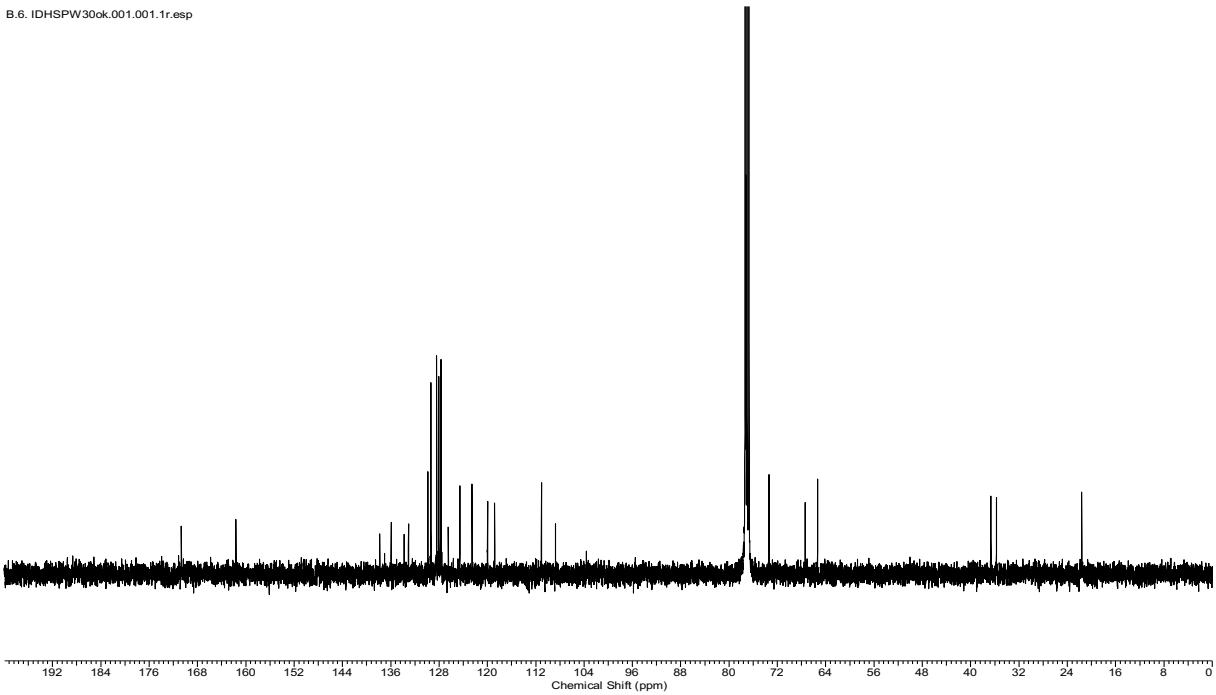


Figure S62 ^{13}C-NMR spectrum of **7g** in $CDCl_3$

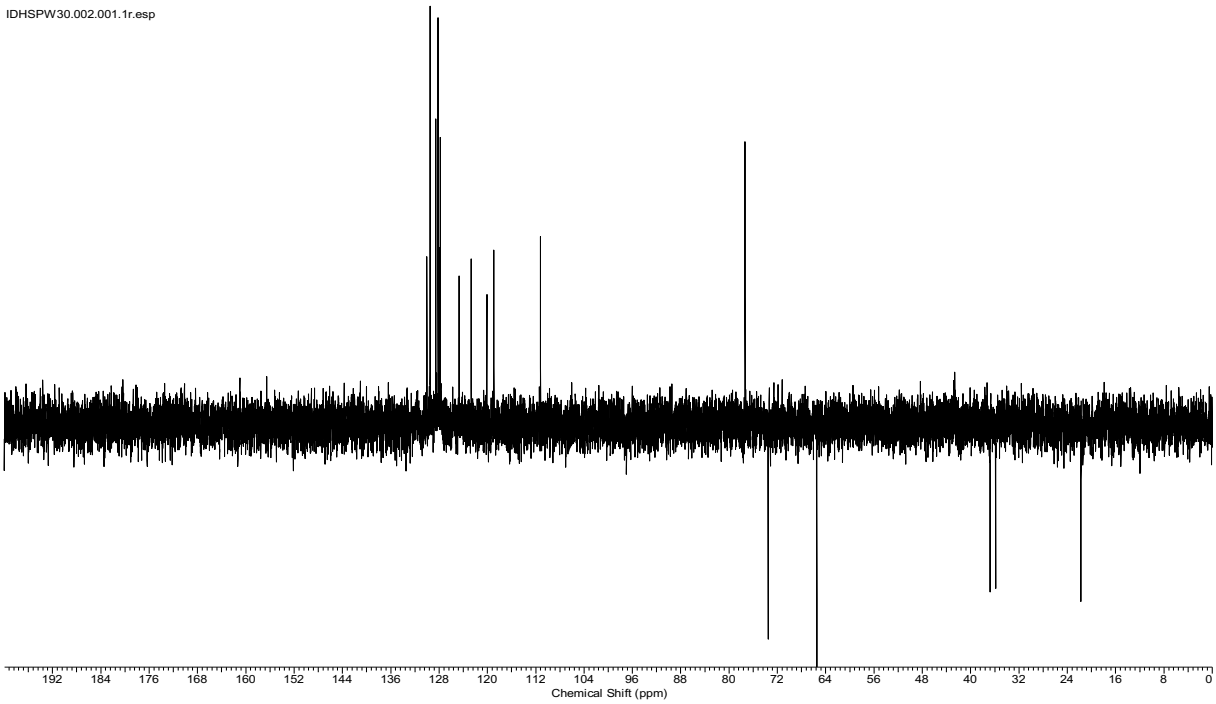
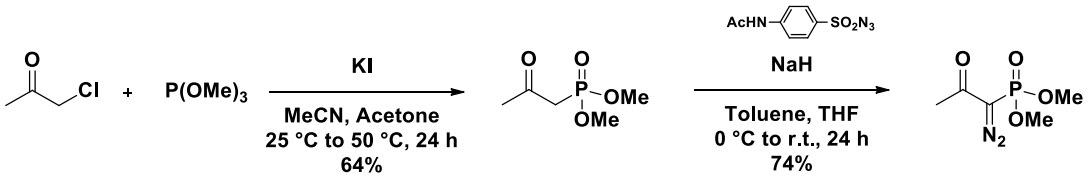


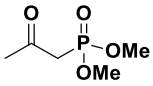
Figure S63 DEPT 135 spectrum of **7g** in $CDCl_3$

General Procedure to synthesize terminal alkyne derivatives 11

Synthesis of Bestmann-Ohira reagent



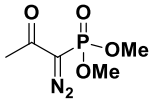
Synthesis of dimethyl 2-oxopropylphosphonate



To a suspension of KI (4.98 g, 30 mmol, 1 equiv.) in acetone (5.4 mL) and acetonitrile (10 mL) was added chloroacetone (2.4 mL, 30 mmol, 1 equiv.). The mixture was stirred at r.t. for 1h. Trimethylphosphite (3.5 mL, 30 mmol, 1 equiv.) was slowly added to the mixture. After heating the mixture for 24h at 50 °C, it was then filtered through a pad of celite. The solvent was removed under reduced pressure. The crude product was distilled under reduced pressure (0.67 mbar) at 85 °C to give dimethyl 2-oxopropylphosphonate as colorless liquid in 64% yield (3.19 g).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 2.31 (3H, CH_3, s), 3.09 (2H, CH_2, d, *J* = 22.8 Hz), 3.76 (3H, CH_3, s), 3.80 (3H, CH_3, s).

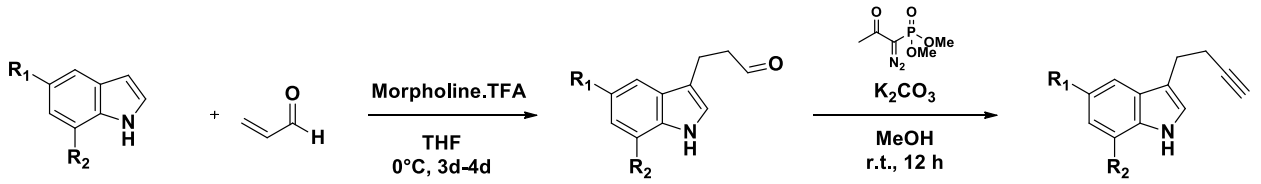
Synthesis of dimethyl 1-diazo-2-oxopropylphosphonate (Bestmann-Ohira reagent)



To a stirred solution of dimethyl 2-oxopropylphosphonate (1 g, 6.02 mmol, 1.11 equiv.) in toluene (12 mL) was added NaH (0.29 g, 5.42 mmol, 1.33 equiv.) in portions at 0 °C. Stirring was continued for 1h at 0 °C. A solution of azide (1.30 g, 5.42 mmol, 1 equiv.) in THF (4 mL) was added dropwise at 0 °C. The mixture was stirred at r.t. for 24h. Petroleum ether was added and the precipitate was filtered off through a pad of celite®. The filtrate was concentrated under reduced pressure. The crude product was purified by flash chromatography (petroleum ether : ethyl acetate = 7:3 to 3:7) to give Bestmann-Ohira reagent as light yellow oil in 74% yield (0.77 g).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 2.27 (3H, CH_3, s), 3.82 (3H, CH_3, s), 3.86 (3H, CH_3, s).

Synthesis 3-(But-3-yn-1-yl)-1H-indole derivatives

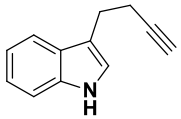


11a: R_1 = H, R_2 = H
11c: R_1 =H, R_2 = F
11d: R_1 = Br, R_2 = H

Indole derivative (4.27 mmol, 1 equiv.) and morpholine trifluoroacetic salt (0.17 g, 0.85 mmol, 0.2 equiv.) were dissolved in THF (5.3 mL). Acrolein (0.34 mL, 5.12 mmol, 1.2 equiv.) was dropwise added to the mixture at 0 °C. The reaction mixture was stirred at 0 °C for 24h. The solvent was then evaporated and water was added to the crude mixture. The aqueous layer was extracted with dichloromethane. The combined organic layers were dried and concentrated under reduced pressure. The crude product was purified using flash chromatography (petroleum ether : ethyl acetate = 8 : 2 to 7:3) to yield the aldehyde which was used immediately for the next step.

Aldehyde derivative (1.73 mmol, 1 equiv.) were dissolved in methanol (29 mL). Potassium carbonate (431 g, 3.12 mmol, 1.8 equiv.) and Bestmann-Ohira reagent [dimethyl (1-diazo-2-oxopropyl)phosphonate, 433 mg, 2.25 mmol, 1.3 equiv.] were respectively added to the solution. The reaction mixture was stirred at room temperature overnight then filtered through a pad of celite®. The filter cake was washed with diethyl ether. The filtrate was evaporated and water was added to the residue. The aqueous layer was extracted with diethyl ether. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash chromatography (petroleum ether : ethyl acetate = 8 : 2).

*3-(But-3-yn-1-yl)-1H-indole (**11a**)*



Yield: 40% over two steps

Physical appearance: white solid

m.p. (amorphous): 67 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 2.00 (1H, CH, t, *J* = 2.6 Hz), 2.59 (2H, CH_2, td, *J* = 7.7 and 2.6 Hz), 3.03 (2H, CH, t, *J* = 7.7 Hz), 7.08 (1H, CH_{Ar}, br s), 7.13 (1H, CH_{Ar}, br dd, J =8.1 and 7.2 Hz), 7.20 (1H, CH_{Ar}, br dd, *J* = 8.1 and 7.2 Hz), 7.37 (1H,CH_{Ar}, d, *J* = 8.1 Hz), 7.61 (1H,CH_{Ar}, d, *J* = 8.1 Hz), 7.94 (1H, NH, br s); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 19.9 (CH_2), 24.8 (CH_2), 68.8 (CH), 84.7 (C), 111.3 (CH_{Ar}), 115.3 (C_{Ar}), 118.9 (CH_{Ar}), 119.2 (CH_{Ar}), 121.6 (CH_{Ar}), 122.2 (CH_{Ar}), 127.4 (C_{Ar}), 136.4 (C_{Ar}); **IR** (Nujol): 3392, 3299, 2941, 1456, 1091, 759, 646, 624, 507 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{12}H_{10}N[M+H]^-$ 168.0819, found 168.0819.

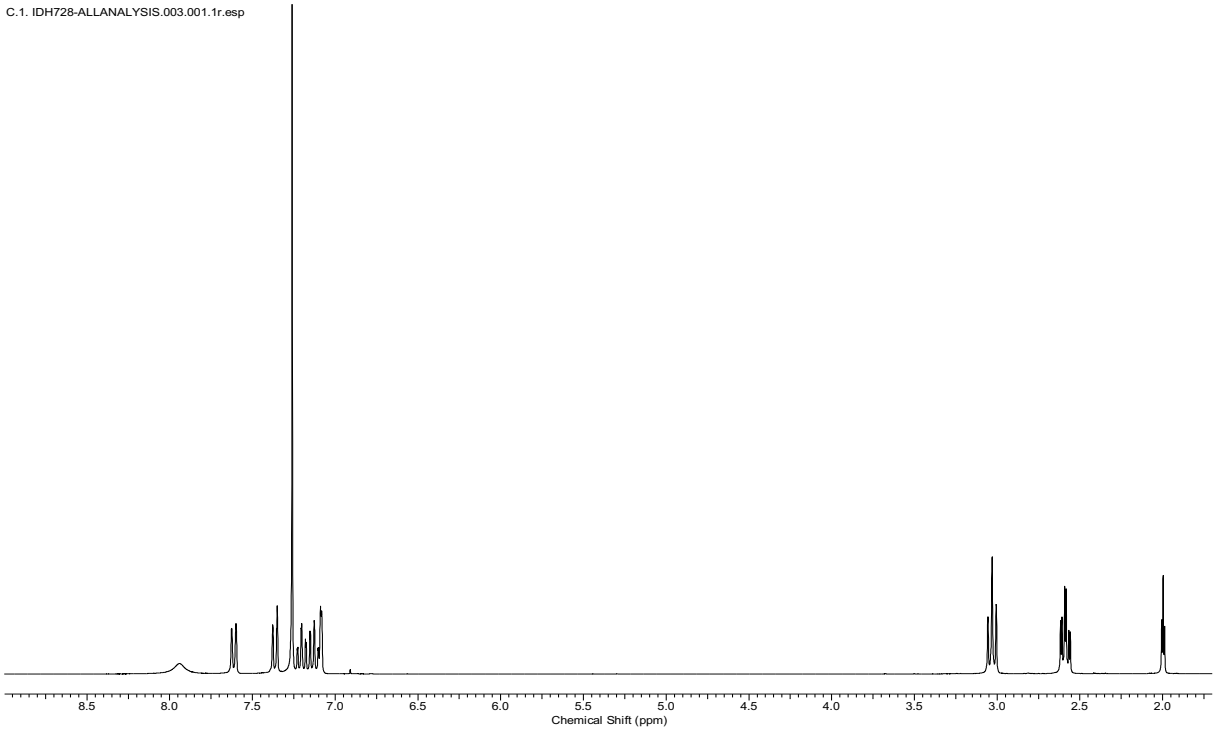


Figure S64 ^{1}H-NMR spectrum of **11a** in $CDCl_3$

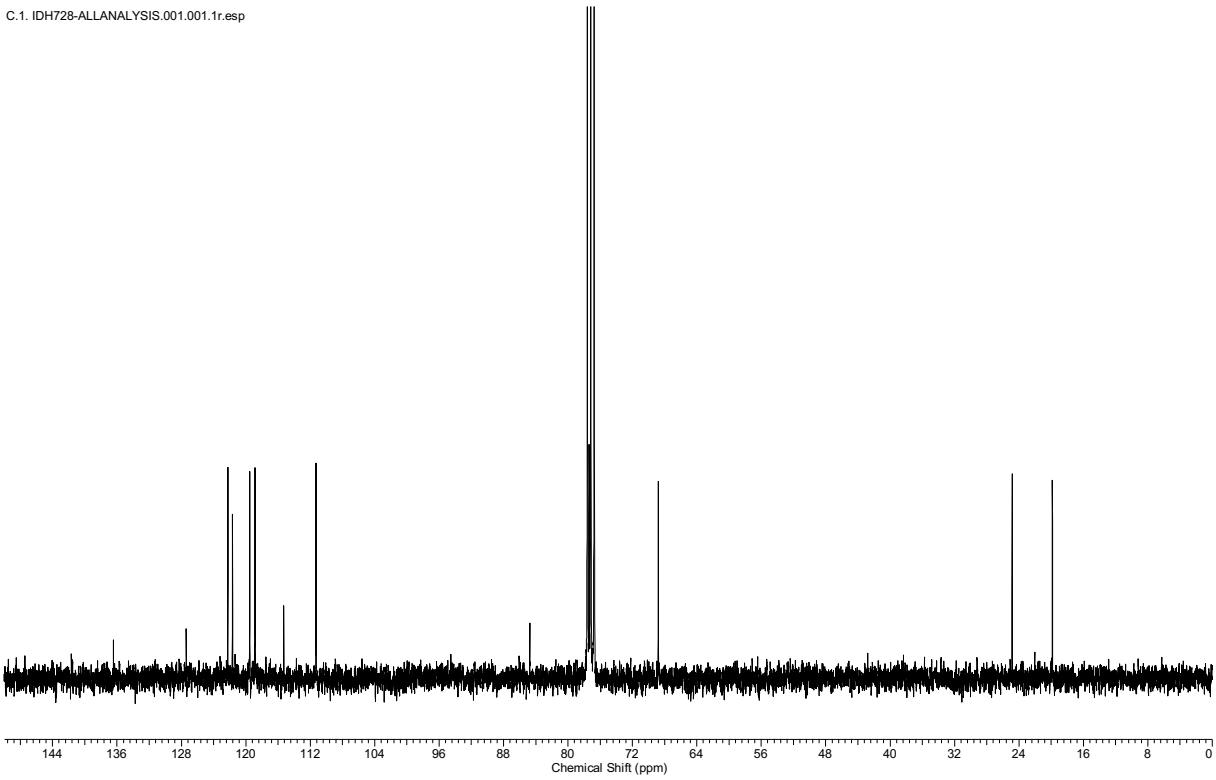


Figure S65 ^{13}C-NMR spectrum of **11a** in $CDCl_3$

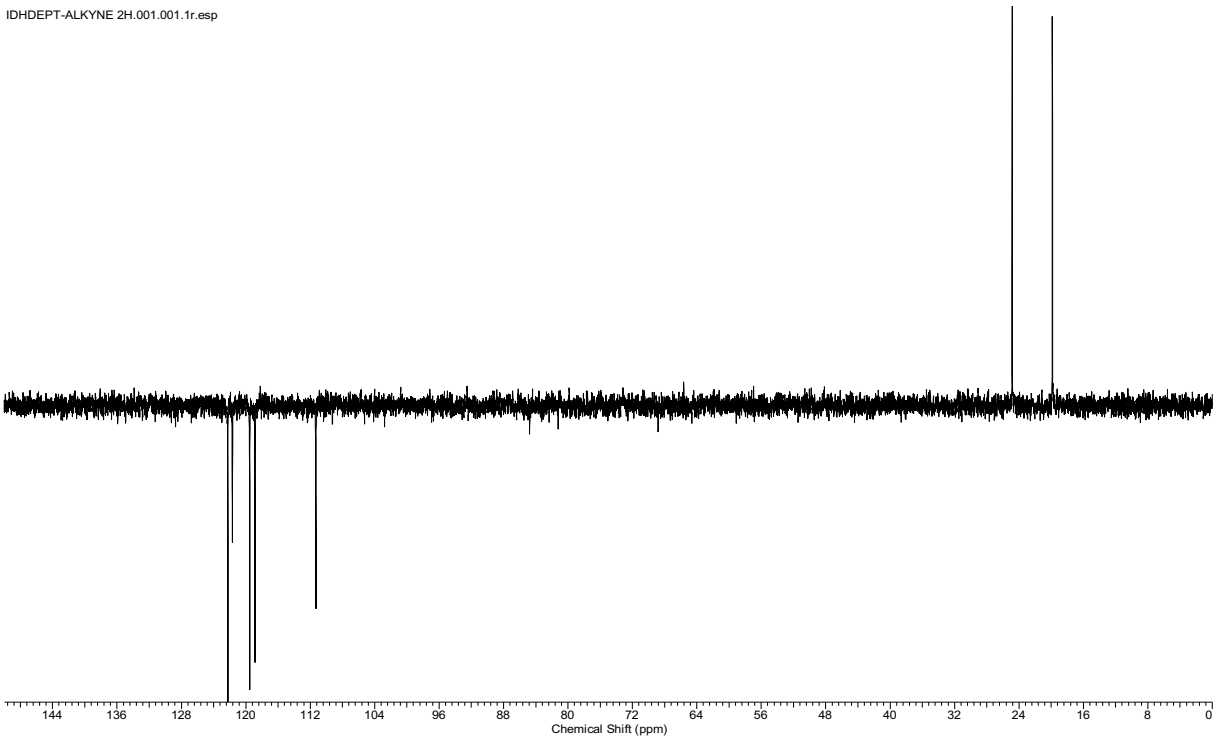
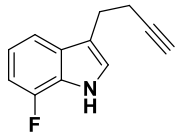


Figure S66 DEPT 135 spectrum of **11a** in $CDCl_3$

*3-(But-3-yn-1-yl)-7-fluoro-1H-indole (**11c**)*



Yield: 22% over two steps

Physical appearance: brown oil

^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 2.01 (1H, CH, t, *J* = 2.6 Hz), 2.58 (2H, CH_2, td, *J* = 7.3 and 2.5 Hz), 3.01 (1H, CH, t, *J* = 7.3 Hz), 6.89-6.94 (1H, CH_{Ar}, m), 7.01-7.06 (1H, CH_{Ar}, m), 7.12 (1H, CH_{Ar}, br s), 7.37 (1H, CH_{Ar}, d, *J* = 8.1 Hz), 8.14 (1H, NH, br s); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 19.8 (CH_2), 24.8 (CH_2), 69.0 (CH), 84.5 (C), 107.0 (CH_{Ar}, d, *J* = 16 Hz), 114.6 ($CH_{Ar,}$ d, *J* = 4 Hz), 116.0 (C_{Ar}, d, *J* = 2 Hz), 119.7 (CH_{Ar}, d, *J* = 6 Hz), 122.4 (CH_{Ar}), 124.7 (C_{Ar}, d, *J* = 13 Hz), 131.1 (C_{Ar}, d, *J* = 5 Hz), 149.8 (C_{Ar}, d, *J* = 243 Hz); **IR** (Nujol): 3425, 3290, 2113, 1458, 1093,792, 634 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{12}H_{10}NFNa[M+Na]^+$ 210.0689, found 210.0689.

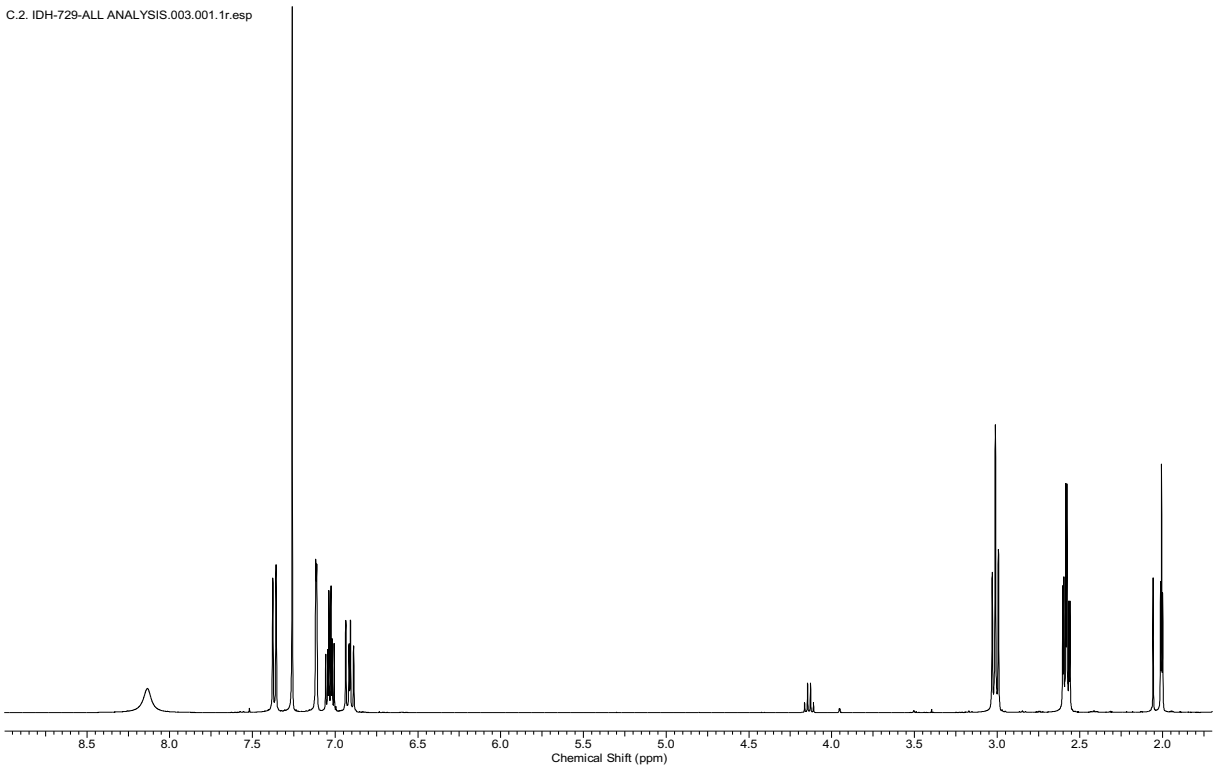


Figure S67 ^{1}H-NMR spectrum of **11c** in $CDCl_3$

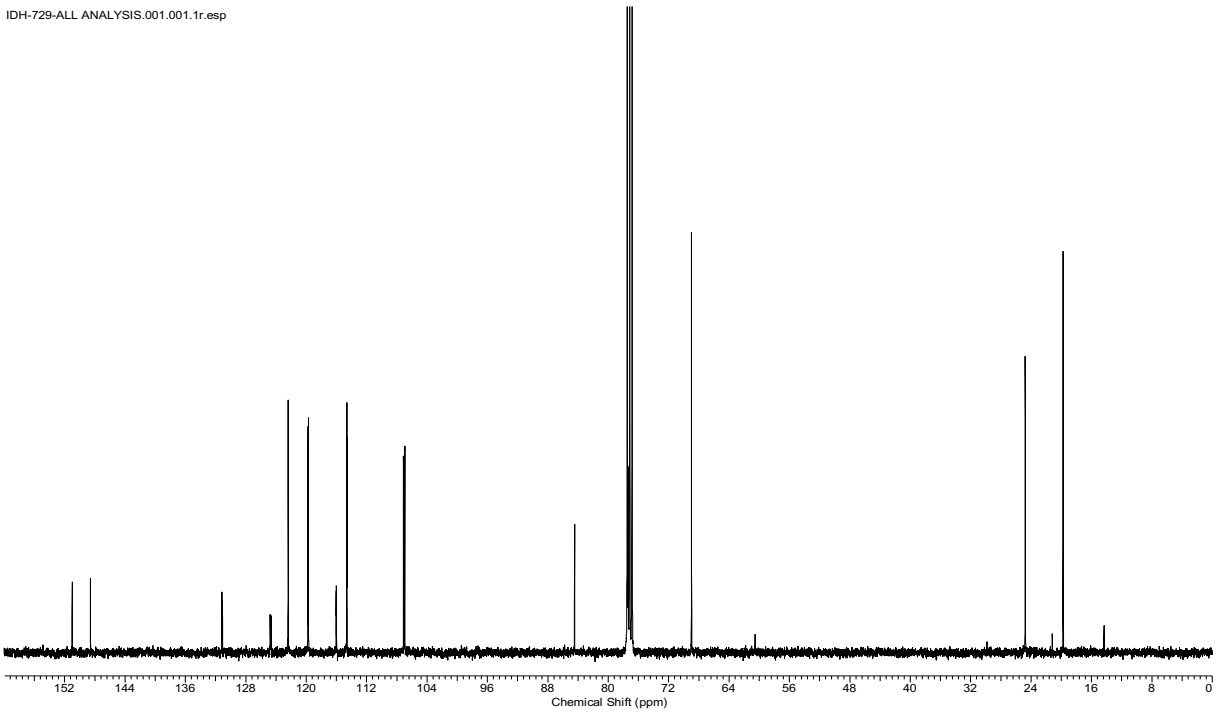


Figure S68 ^{13}C-NMR spectrum of **11c** in $CDCl_3$

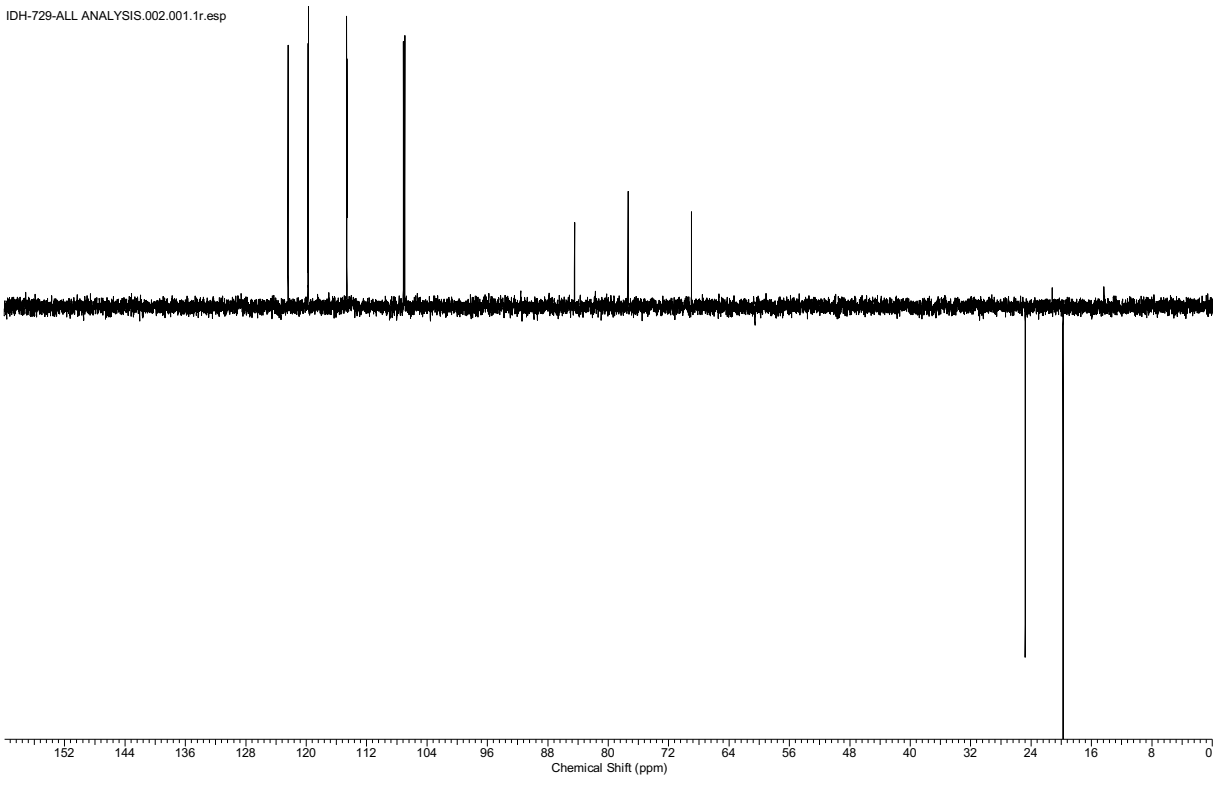
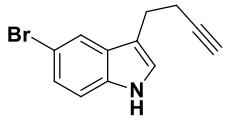


Figure S69 DEPT 135 spectrum of **11c** in $CDCl_3$

*5-Bromo-3-(but-3-yn-1-yl)-1H-indole (**11d**)*



Yield: 47% over two steps

Physical appearance: light brown solid

m.p. (amorphous): 72°C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 1.99 (1H, CH, t, *J* = 2.6 Hz), 2.55 (2H, CH_2, dt, *J* = 7.4 and 2.6 Hz), 2.96 (1H, CH, t, *J* = 7.4 Hz), 7.09 (1H, CH_{Ar}, br s), 7.21-7.29 (2H, 2 x CH_{Ar}, m), 7.73 (1H, CH_{Ar}, br s), 7.99 (1H, NH, br s); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 19.8 (CH_2), 24.6 (CH_2), 69.0 (CH), 84.4 (C), 112.7 (CH_{Ar}), 112.9 (C_{Ar}), 115.0 (C_{Ar}), 121.6 (CH_{Ar}), 123.0 (CH_{Ar}), 125.1 (CH_{Ar}), 129.2 (C_{Ar}), 135.0 (C_{Ar}); **IR** (Nujol): 3427, 3290, 1459, 1226, 1093, 879, 792, 582, 474, 420 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{12}H_9NBr[M+H]^-$ 245.9924, found 245.9922.

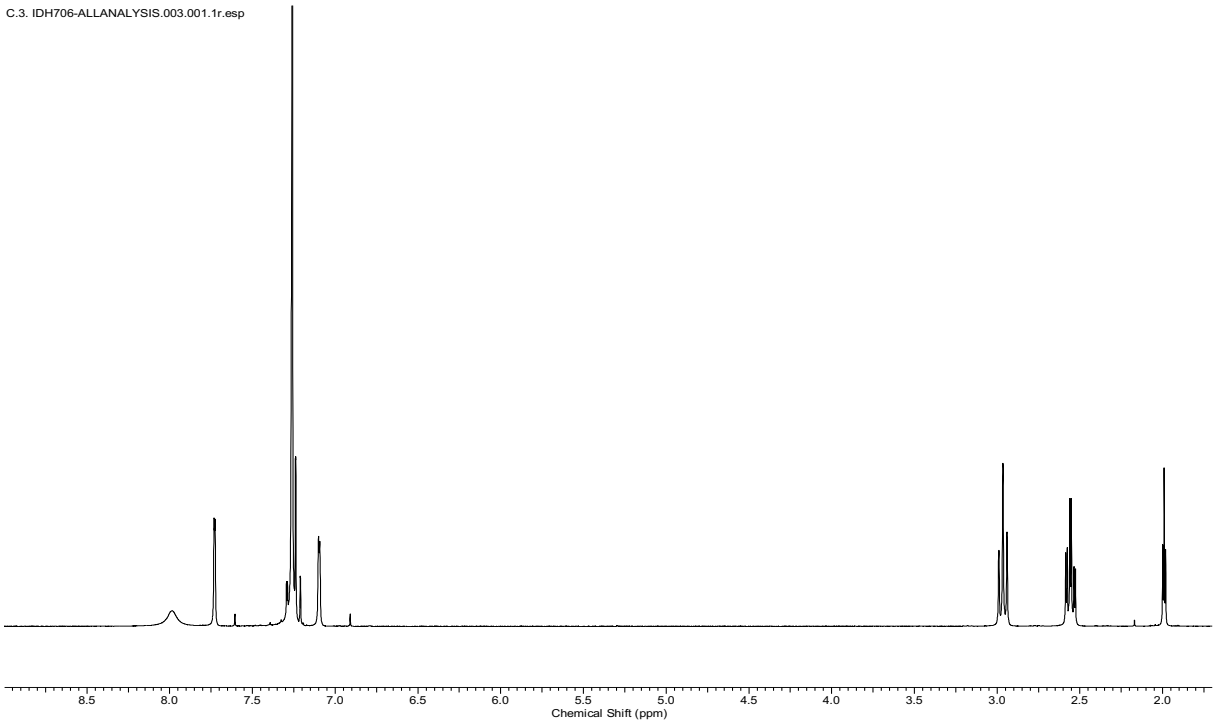


Figure S70 ^{1}H-NMR spectrum of **11d** in $CDCl_3$

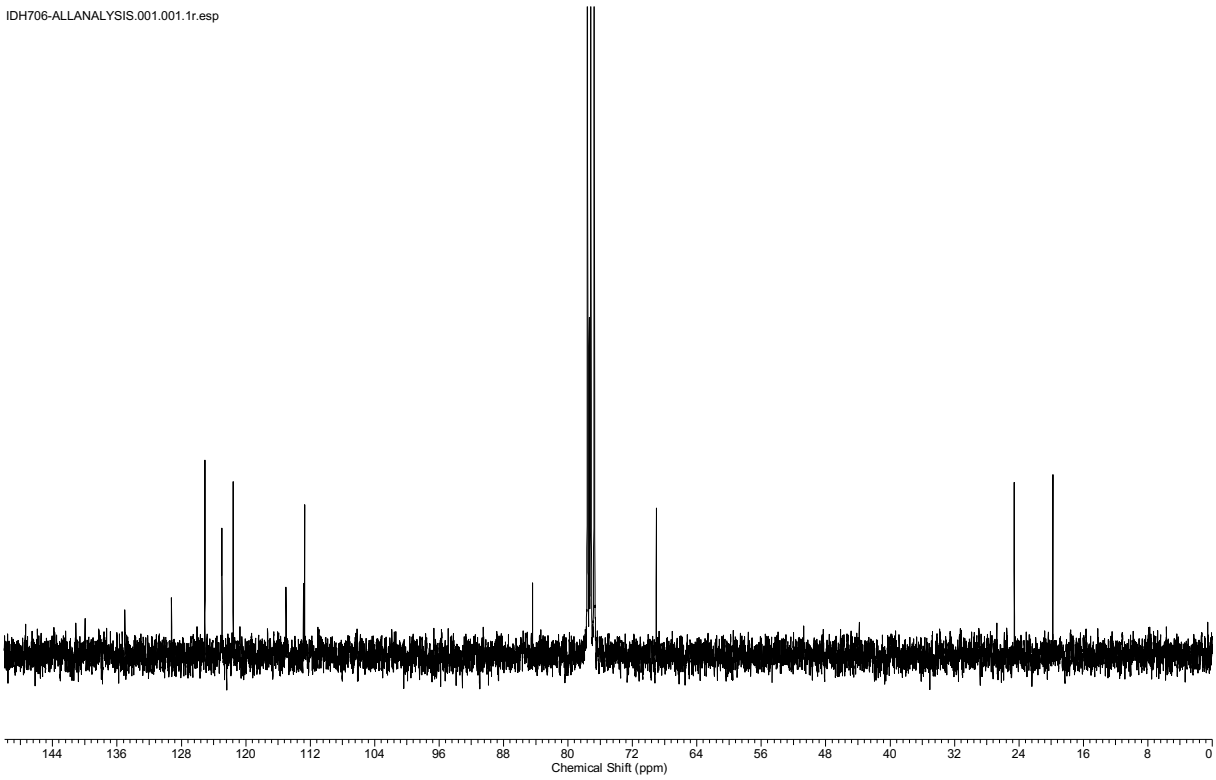


Figure S71 ^{13}C-NMR spectrum of **11d** in $CDCl_3$

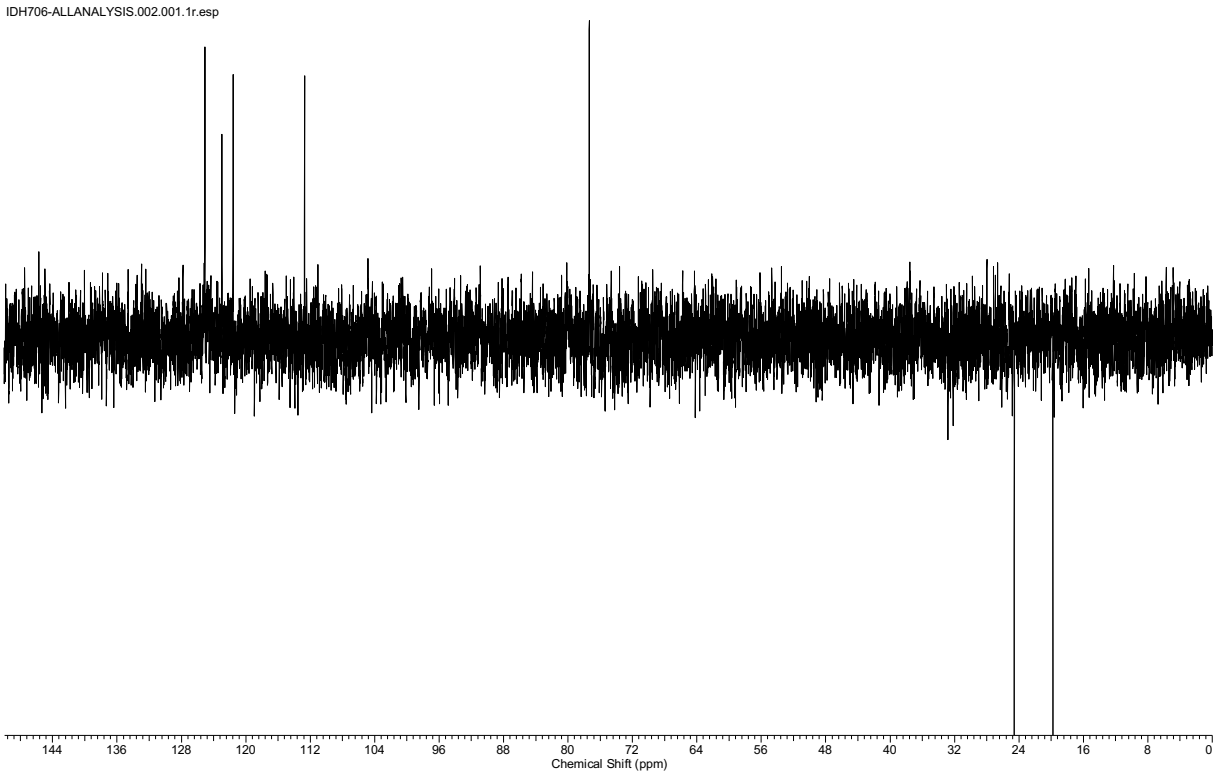
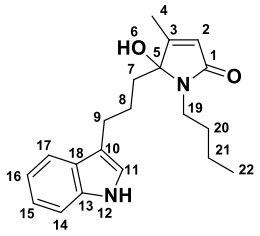


Figure S72 DEPT 135 spectrum of **11d** in $CDCl_3$

Synthesize of 5-(3-(1H-indol-3-yl)propyl)-1-butyl-5-hydroxy-4-methyl-1H-pyrrol-2(5H)-one (14a)



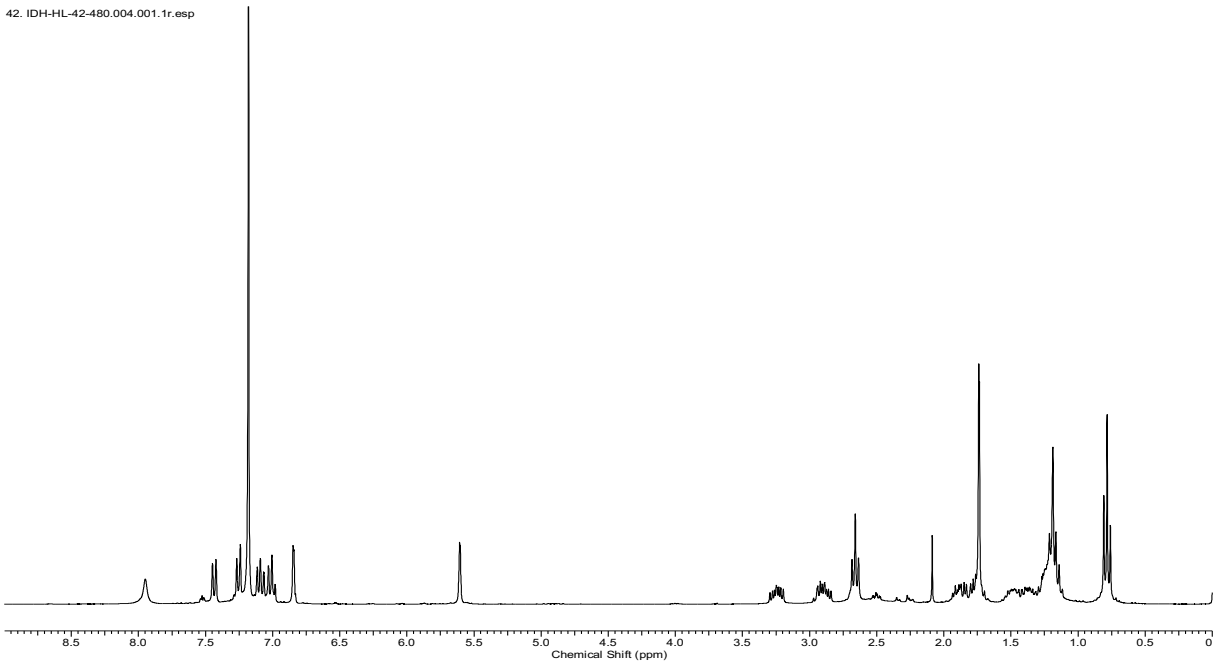
1a (424 mg, 2 mmol, 1 equiv.) was dissolved in *i*-PrOH (7 mL) in oven-dried-Schlenk tube. K_2CO_3 (553 mg, 4.0 mmol, 2 equiv.) was then added to the solution and the suspension was stirred for 10 min under Argon. The mixture was then degassed at -78 °C for 2x10 min and the vessel was backfilled with argon. After warming to room temperature, terminal alkyne **11a** (677 mg, 4.0 mmol, 2 equiv.), butyl amine **3a** (0.790 mL, 8.0 mmol, 4 equiv.) and CuI (76 mg, 0.4 mmol, 0.2 equiv.) were respectively added into the mixture. The mixture was then rapidly degassed and the vessel was backfilled with argon. The sealed Schlenk tube was placed in the preheated oil bath (45 °C) and was stirred overnight. The reaction mixture was cooled to 0 °C, then quenched by the addition of an aqueous saturated NH_4Cl solution and stirred for further 15 min. The mixture was filtered through a pad of Celite®. The aqueous phase was extracted with ethyl acetate and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was then purified by flash chromatography on silica gel using petroleum ether: ethyl acetate (stated below) as eluent.

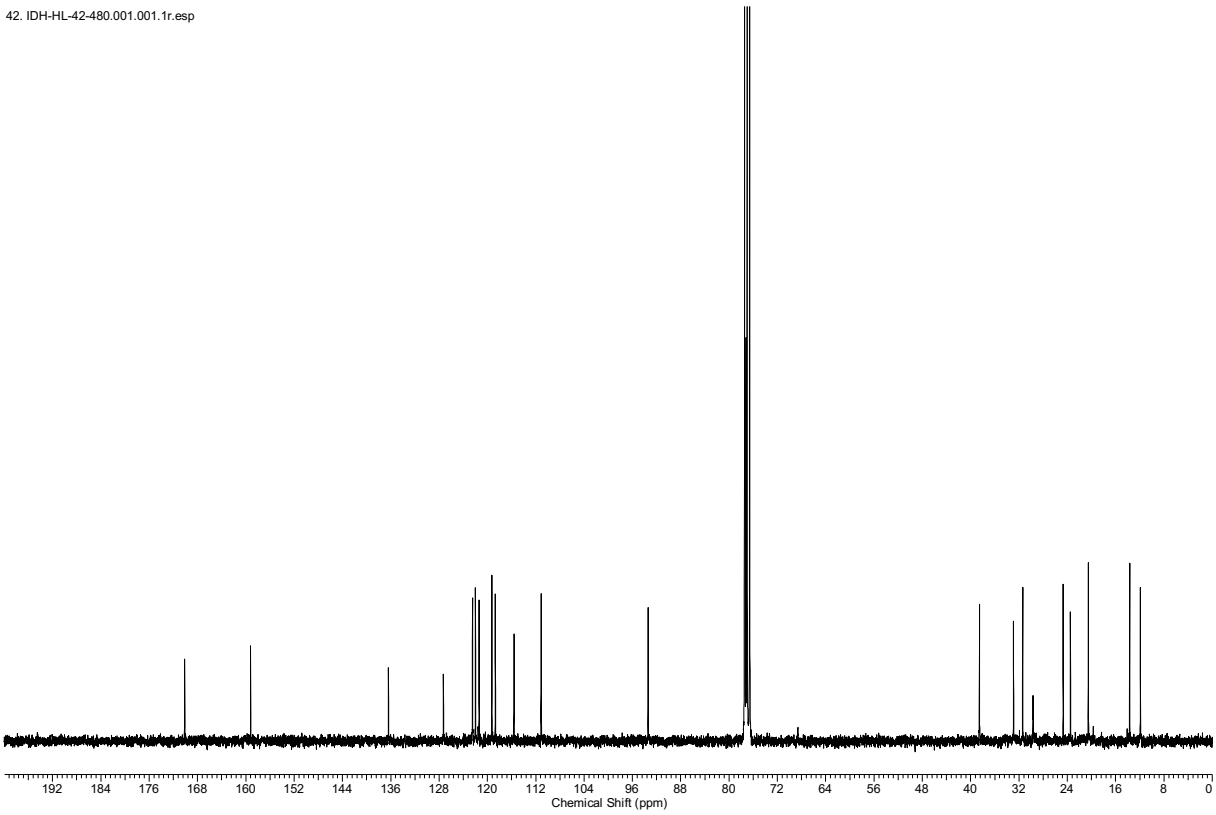
Purification: flash chromatography on silica gel (PE/EtOAc : from 8/2 to 3/7)

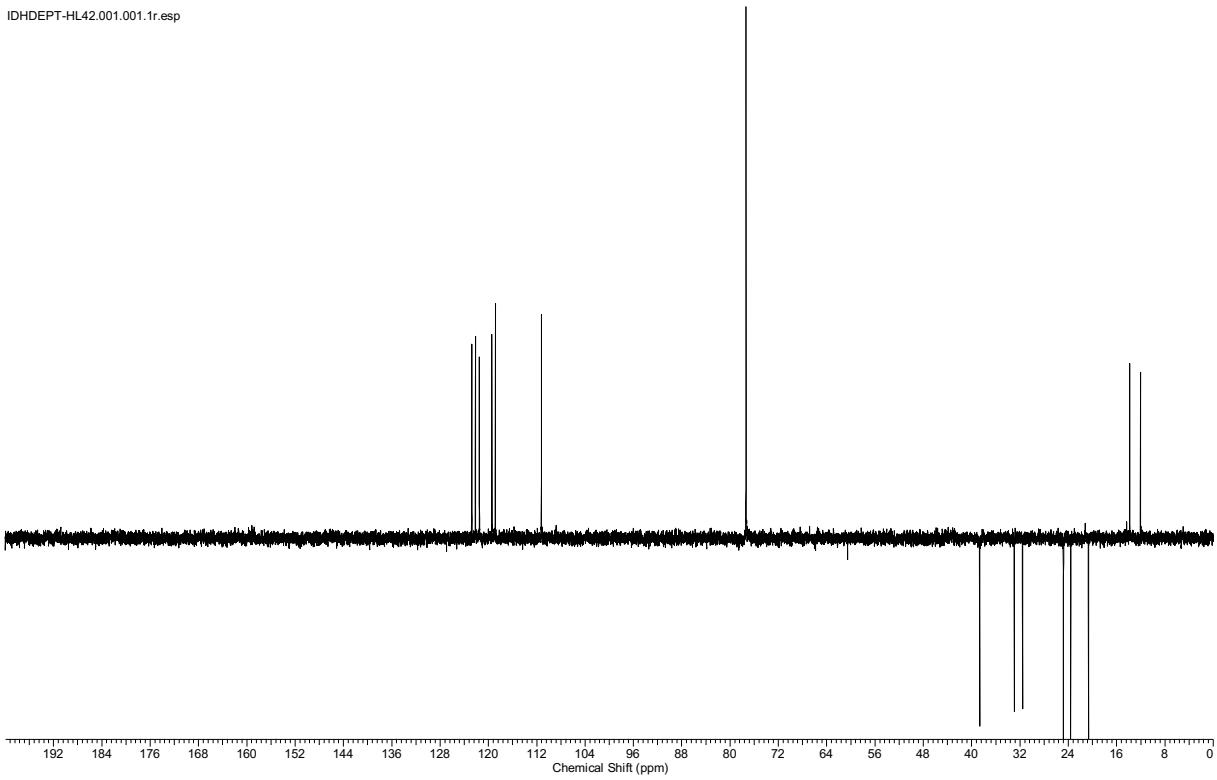
Yield: 43% (277 mg)

Physical appearance: light brown solid

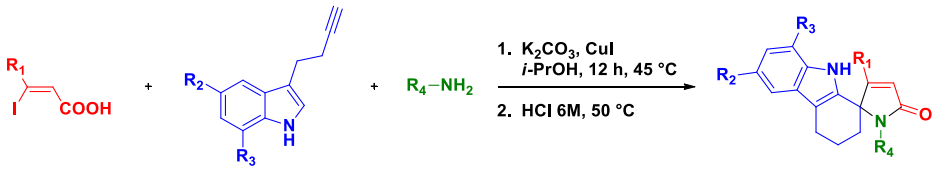
m.p. (amorphous): 128°C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 0.86 (3H, CH_3, t, *J* = 7.3 Hz, H22), 1.20-1.35 (4H, 2 x CH_2, m, H8 and H21), 1.39-1.62 (2H, CH_2, m, H20), 1.78-1.88 (1H, C*H*$_2$, m, H7), 1.81 (3H, CH_3, br d, *J* = 1.3 Hz, H4), 1.91-2.01 (1H, C*H*$_2$, m, H7), 2.74 (2H, CH_2, t, *J* = 7.3 Hz, H9), 2.92-3.05 (1H, C*H*$_2$, m, H19), 3.28-3.37 (1H, C*H*$_2$, m, H19), 5.69 (1H, CH, br q, *J* = 1.3 Hz, H2), 6.93 (1H, H_{Ar}, br s, H11), 7.09 (1H, H_{Ar}, m, H16), 7.17 (1H, H_{Ar}, m H15), 7.34 (1H, H_{Ar}, br d, *J* = 7.9 Hz, H14), 7.52 (1H, H_{Ar}, br d, *J* = 7.7 Hz, H17), 8.03 (1H, br s, NH); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 12.1 (CH_3, C4), 13.8 (CH_3, C22), 20.7 (CH_2, C21), 23.6 (CH_2, C8), 24.8 (CH_2, C9), 31.5 (CH_2, C20), 33.1 (CH_2, C7), 38.7 (CH_2, C19), 93.6 (C, C5), 111.3 (CH_{Ar}, C14), 115.8 (C_{Ar}, C10), 118.9 (CH_{Ar}, C17), 119.4 (CH_{Ar}, C16), 121.5 (CH_{Ar}, C11), 122.1 ($CH_{Ar,}$ C15), 122.6 (CH, C2),127.4 (C_{Ar}, C18), 136.6 ($C_{Ar,}$ C13), 159.4 (C, C3), 170.3 (C, C1); **IR** (Nujol): 3286, 2958, 1677, 1463, 1444, 1313, 740 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{20}H_{26}N_2O_2Na[M+Na]^+$349.1886, found 349.1885.


42. IDH-HL-42-480.004.001.1r.esp
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


42. IDH-HL-42-480.001.001.1r.esp
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

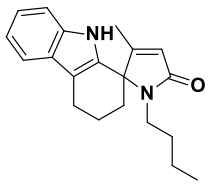

IDHDEPT-HL42.001.001.1r.esp
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

General Procedure to synthesize indolo-(6,5)-spirolactams 14



(*Z*)-3-Substituted-3-iodoprop-2-enoic acid derivative **1** (0.5 mmol, 1 equiv.) was dissolved in *i*-PrOH (1.75 mL) in oven-dried-Schlenk tube. K_2CO_3 (139 mg, 1.0 mmol, 2 equiv.) was then added to the solution and the suspension was stirred for 10 min under Argon. The mixture was then degassed at -78 °C for 2x10 min and the vessel was backfilled with argon. After warming to room temperature, terminal alkyne **2** (1.0 mmol, 2 equiv.), primary amine **3** (2.0 mmol, 4 equiv.) and CuI (19 mg, 0.1 mmol, 0.2 equiv.) were respectively added into the mixture. The mixture was then rapidly degassed and the vessel was backfilled with argon. The sealed Schlenk tube was placed in the preheated oil bath (45 °C) and was stirred overnight. The reaction mixture was cooled to 0 °C, then 1.7 mL of a solution of hydrochloric acid (6 M, 20 equiv.) was added dropwise. The reaction was then heated at 50 °C until the disappearance of the γ-hydroxybutyrolactam checked by TLC. The reaction mixture was cooled to 0 °C then filtered through a pad of Celite®. The aqueous phase was extracted with ethyl acetate and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was then purified by flash chromatography on silica gel using petroleum ether: ethyl acetate as eluent.

1'-Butyl-3'-methyl-2,3,4,9-tetrahydrospiro[carbazole-1,2'-pyrrol]-5'(1'H)-one (14a)



Purification: flash chromatography on silica gel (PE/EtOAc : from 8/2 to 6/4)

Yield: 43% (66 mg)

Physical appearance: white solid

m.p. (crystal): 105°C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 0.81 (3H, CH_3, t, *J* = 7.3 Hz), 1.15-1.25 (2H, CH_2, m), 1.30-1.41 (1H, C*H*$_2$, m), 1.53-1.63 (1H, C*H*$_2$, m), 1.81 (3H, CH_3, br d, *J* = 1.5 Hz), 2.01-2.17 (4H, 2 x CH_2, m), 2.74-2.81 (1H, C*H*$_2$, m), 2.88-2.98 (2H, 2 xC*H*$_2$, m), 3.29 (1H, C*H*$_2$, ddd, *J* = 15.9, 10.5 and 5.4 Hz), 5.91 (1H, CH, br q, *J* = 1.5 Hz), 7.12 (1H, H_{Ar}, br dd, *J* = 8.0 and 7.1 Hz), 7.20 (1H, H_{Ar}, br dd, *J* = 8.0 and 7.1 Hz), 7.26-7.30 (1H, H_{Ar}, m), 7.55 (1H, H_{Ar}, d, *J* = 8.0 Hz), 7.96 (1H, NH, br s); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 13.8 (CH_3), 14.2 (CH_3), 20.6 (CH_2), 20.8 (CH_2), 21.5 (CH_2), 31.5 (CH_2), 32.6 (CH_2), 41.0 (CH_2), 67.9 (C), 111.6 (CH_{Ar}),115.8 (C_{Ar}), 118.6 (CH_{Ar}),119.2 (CH_{Ar}), 122.0 (CH), 122.7 (CH_{Ar}), 127.0 (C_{Ar}), 129.1 (C_{Ar}),136.9 (C_{Ar}), 163.1 (C), 171.3 (C); **IR** (nujol): 3178, 2931, 1672, 1641, 1407, 1228, 779, 729 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{20}H_{25}N_2O[M+H]^+$309.1961, found 309.1962.

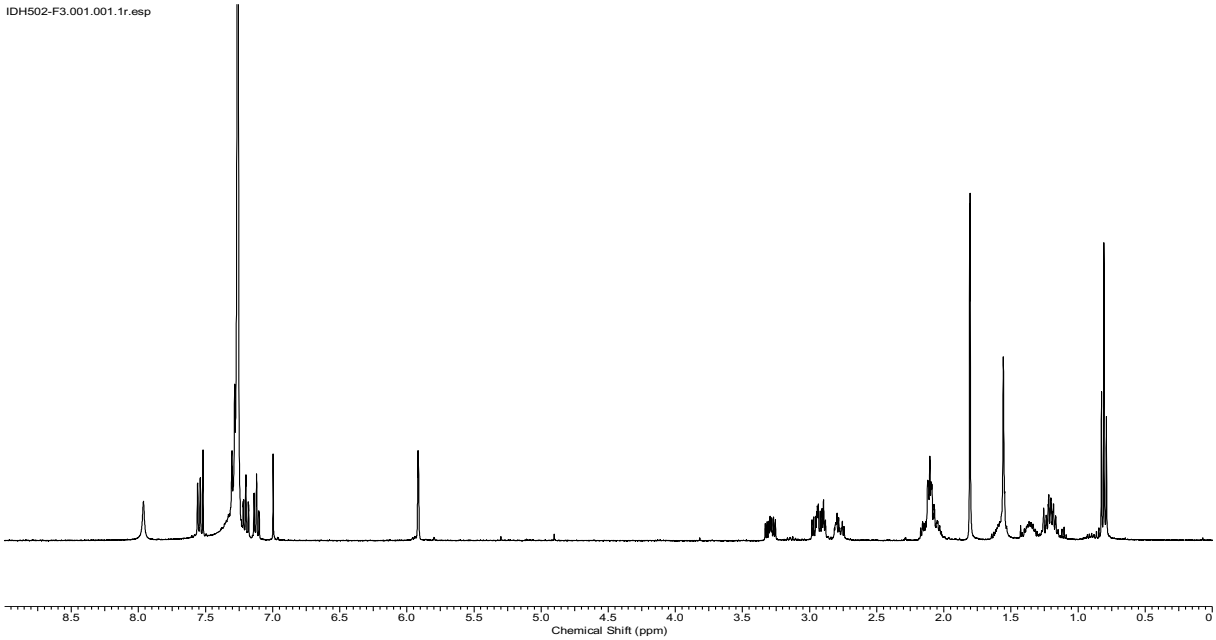


Figure S73 ^{1}H-NMR spectrum of **14a** in $CDCl_3$

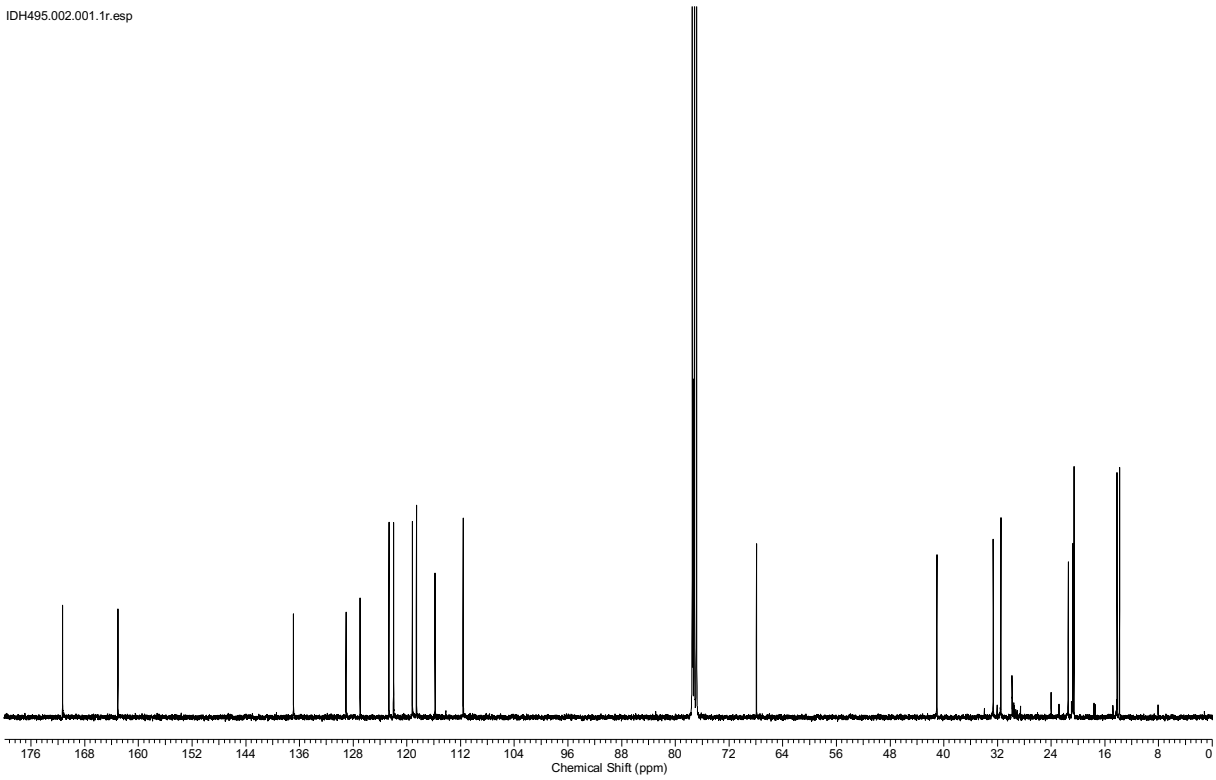


Figure S74 ^{13}C-NMR spectrum of **14a** in $CDCl_3$

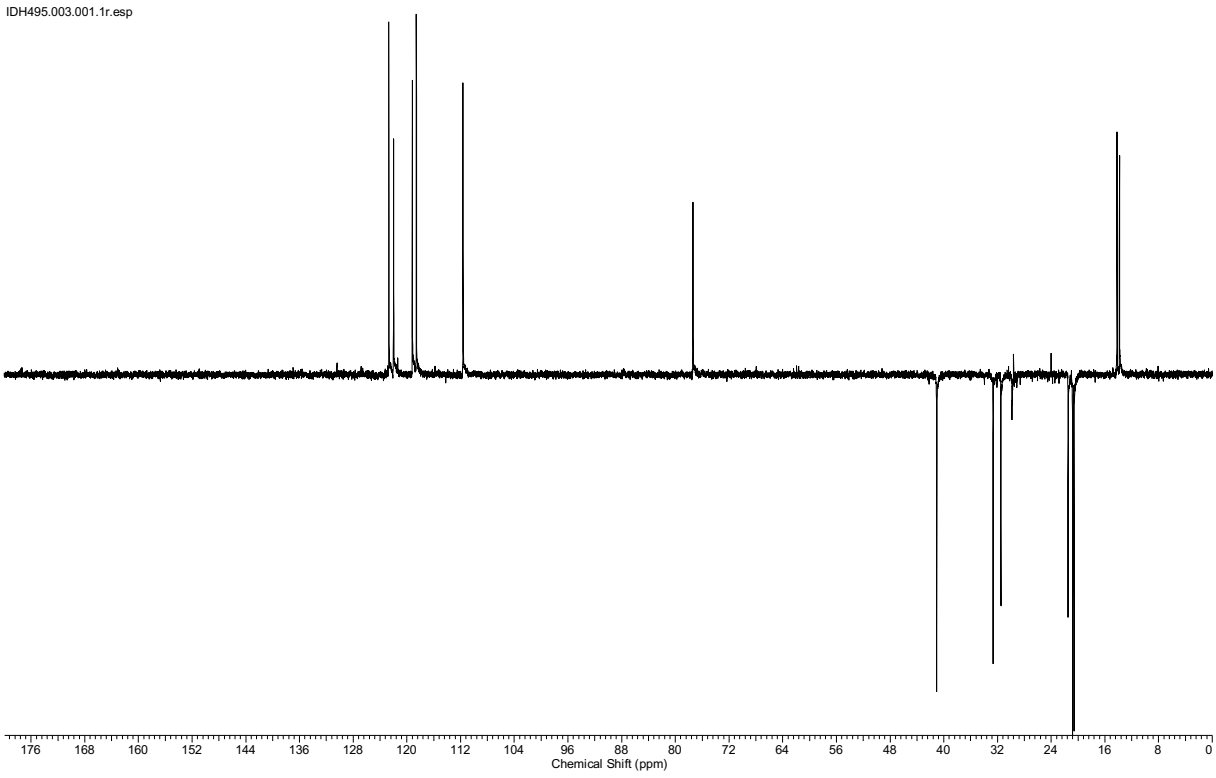
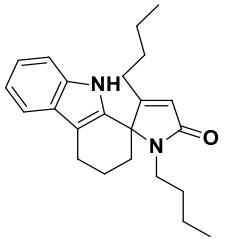


Figure S75 DEPT 135 spectrum of **14a** in $CDCl_3$

1',3'-Dibutyl-2,3,4,9-tetrahydrospiro[carbazole-1,2'-pyrrol]-5'(1'H)-one (14b)



Purification: flash chromatography on silica gel (PE/EtOAc : from 8/2 to 6/4)

Yield: 33% (57 mg)

Physical appearance: white solid

m.p. (amorphous): 164°C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 0.80 (3H, CH_3, t, *J* = 7.3 Hz), 0.82 (3H, CH_3, t, *J* = 7.6 Hz), 1.14-1.31 (4H, 2 x CH_2, m), 1.34-1.55 (3H, C*H*$_2$ and CH_2, m), 1.58-1.68 (1H, C*H*$_2$, m), 1.82-1.91 (1H, C*H*$_2$, m), 1.99-2.22 (5H, 2 x CH_2 and C*H*$_2$), 2.75-2.82 (1H, C*H*$_2$, m), 2.86-2.95 (2H, 2 x C*H*$_2$, m), 3.29 (1H, C*H*$_2$, ddd, *J* = 16.2, 10.8 and 5.4 Hz), 5.87 (1H, CH, br t, *J* = 1.7 Hz), 7.11 (1H, H_{Ar}, br t, *J* = 7.8 Hz), 7.19 (1H, H_{Ar}, br dd, *J* = 7.8 and 7.1 Hz), 7.35 (1H, H_{Ar}, br d, *J* = 7.8 Hz), 7.55 (1H, H_{Ar}, br d, *J* = 7.8 Hz), 8.91 (1H, NH, br s); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 13.8 (CH_3), 14.0 (CH_3), 20.6 (CH_2), 20.8 (CH_2, d, *J* = 1 Hz), 21.6 (CH_2, d, *J* = 1 Hz), 22.5 (CH_2), 27.5 (CH_2, d, *J* = 3 Hz), 29.2 (CH_2, d, *J* = 1 Hz), 31.5 (CH_2), 32.9 (CH_2, d, *J* = 4 Hz), 40.9 (CH_2, d, *J* = 4.4 Hz), 67.8 (CH_2, d, *J* = 10 Hz), 111.6 (CH_{Ar}, d, *J* = 10 Hz),115.8 (C_{Ar}, d, *J* = 11 Hz), 118.6 ($CH_{Ar,}$ d, *J* = 6 Hz), 119.2 ($CH_{Ar,}$d, *J* = 10 Hz), 120.3 (CH, d, *J* = 7 Hz), 122.7 ($CH_{Ar,}$d, *J* = 8 Hz), 127.0 ($C_{Ar,}$d, *J* = 2 Hz), 129.4 ($C_{Ar,}$d, *J* = 4 Hz), 136.8 ($C_{Ar,}$ d, *J* = 13 Hz), 167.8 (C, d, *J* = 8 Hz), 171.3 (C, d, *J* = 7 Hz); **IR** (nujol): 3228, 2929, 1670, 1452, 1407, 1317, 846, 736 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{23}H_{31}N_2O[M+H]^+$351.2431, found 351.2432.

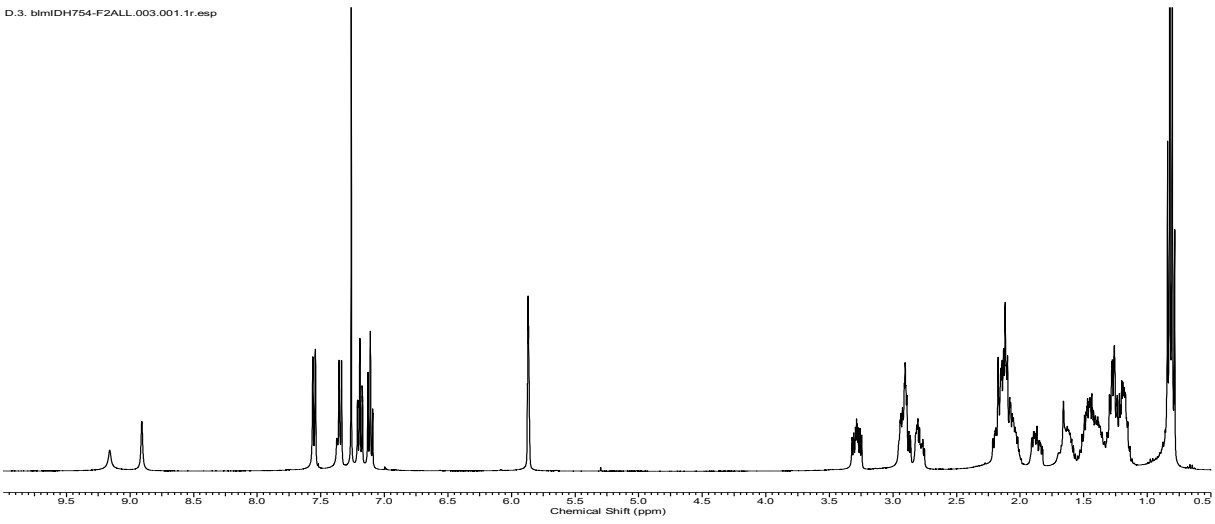


Figure S76^{1}H-NMR spectrum of **14b** in $CDCl_3$

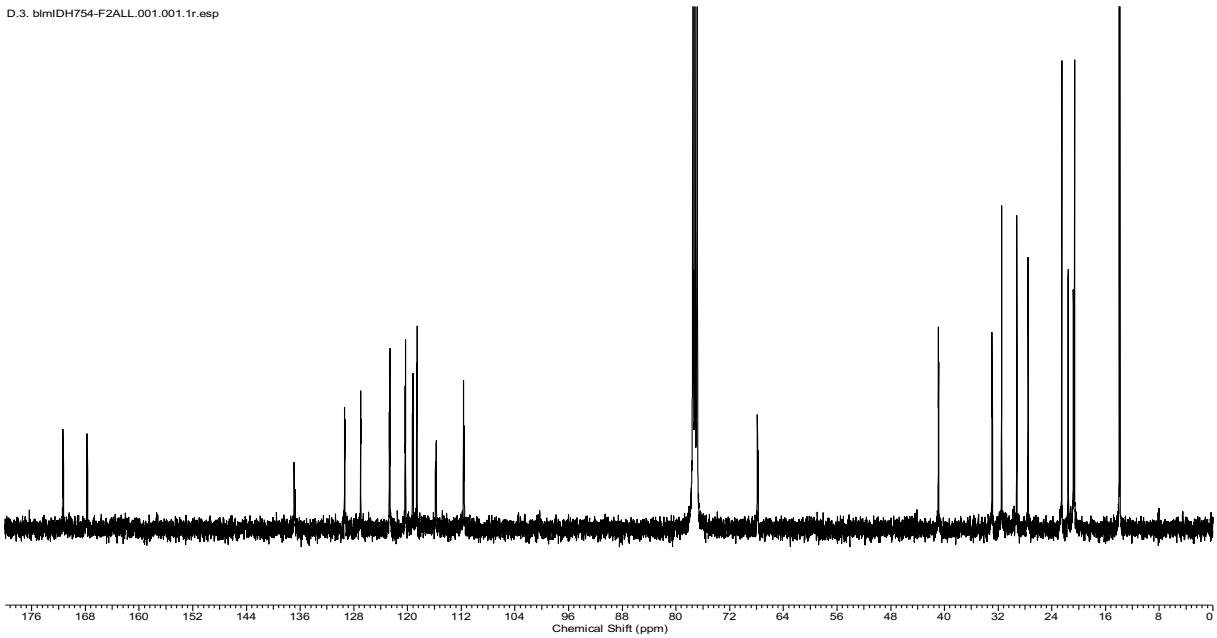


Figure S77 ^{13}C-NMR spectrum of **14b** in $CDCl_3$

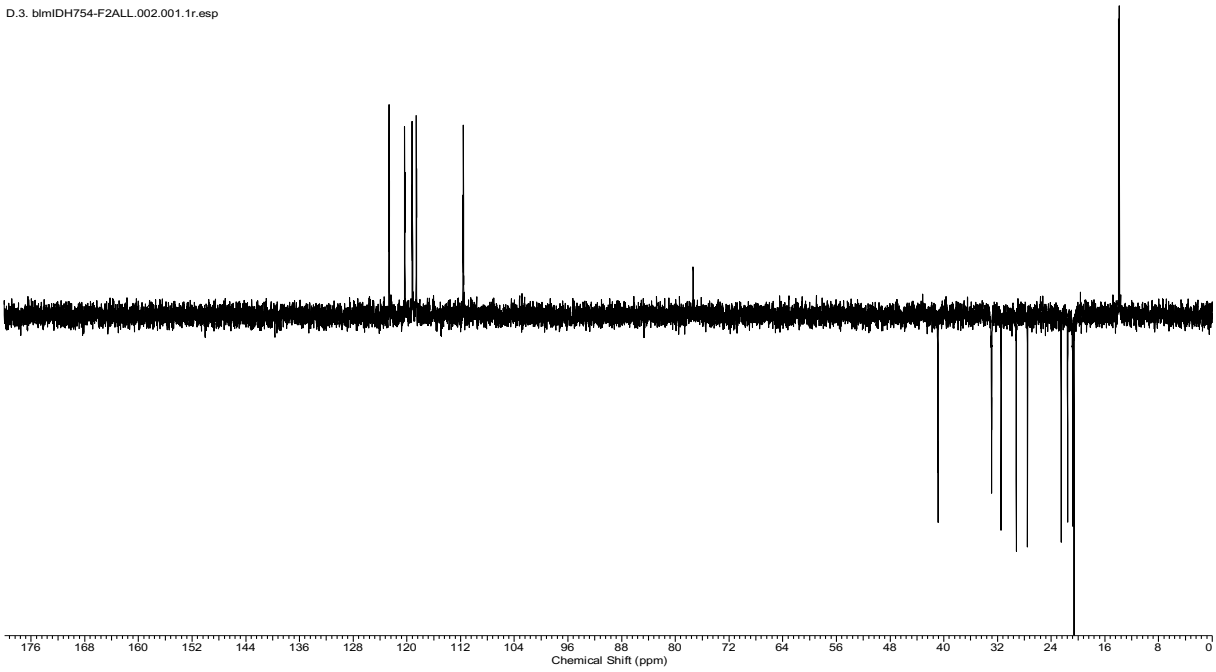
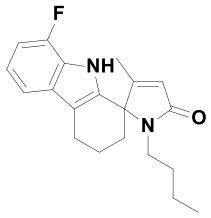


Figure S78DEPT 135 spectrum of **14b** in $CDCl_3$

1'-Butyl-8-fluoro-3'-methyl-2,3,4,9-tetrahydrospiro[carbazole-1,2'-pyrrol]-5'(1'H)-one (14c)



Purification: flash chromatography on silica gel (PE/EtOAc : from 8/2 to 5/5)

Yield: 32% (52 mg)

Physical appearance: light yellow solid

m.p. (amorphous): 174°C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 0.80 (3H, CH_3, t, *J* = 7.3 Hz), 1.14-1.25 (2H, CH_2, m), 1.31-1.43 (1H, C*H*$_2$, m), 1.57-1.68 (1H, C*H*$_2$, m), 1.82 (3H, CH_3, br d, *J* = 1.2 Hz), 2.02-2.18 (4H, 2 x CH_2, m), 2.74-2.82 (1H, C*H*$_2$, m), 2.87-2.96 (2H, 2 x C*H*$_2$, m), 3.31 (1H, C*H*$_2$, ddd, *J* = 16.2, 10.8 and 5.4 Hz), 5.92 (1H, CH, br q, *J* = 1.2 Hz), 6.91 (1H, H_{Ar}, m), 7.02 (1H, H_{Ar}, td, 8.1 and 4.5 Hz), 7.30 (1H, H_{Ar}, d, *J* = 8.1 Hz), 8.81 (1H, NH, br s); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 13.8 (CH_3), 14.2 (CH_3), 20.6 (CH_2), 20.9 (CH_2), 21.4 (CH_2), 31.4 (CH_2), 32.6 (CH_2), 41.0 (CH_2), 67.5 (C), 107.9 (CH_{Ar}, d, *J* = 16 Hz), 114.5 ($CH_{Ar,}$ d, *J* = 4 Hz), 116.8 ($C_{Ar,}$ d, *J* = 2 Hz), 119.7 ($CH_{Ar,}$ d, *J* = 6 Hz), 122.5 (CH), 124.9 ($C_{Ar,}$ d, *J* = 13 Hz), 130.2 (C_{Ar}), 130.7 ($C_{Ar,}$ d, *J* = 6 Hz), 149.7 ($C_{Ar,}$ d, *J* = 245 Hz), 162.4 (C), 171.1 (C); **IR** (Nujol): 3419, 3294, 1574, 1222 1083, 966, 781, 729, 632 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{20}H_{24}N_2OF[M+H]^+$327.1867, found 327.1866.

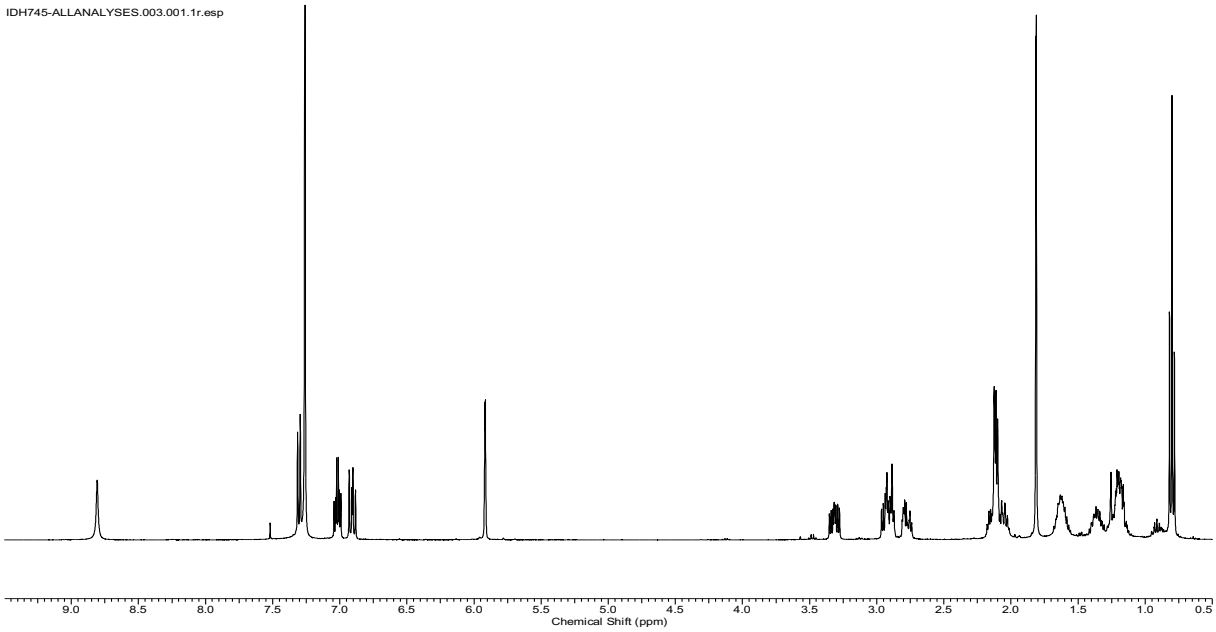


Figure S79^{1}H-NMR spectrum of **14c** in $CDCl_3$

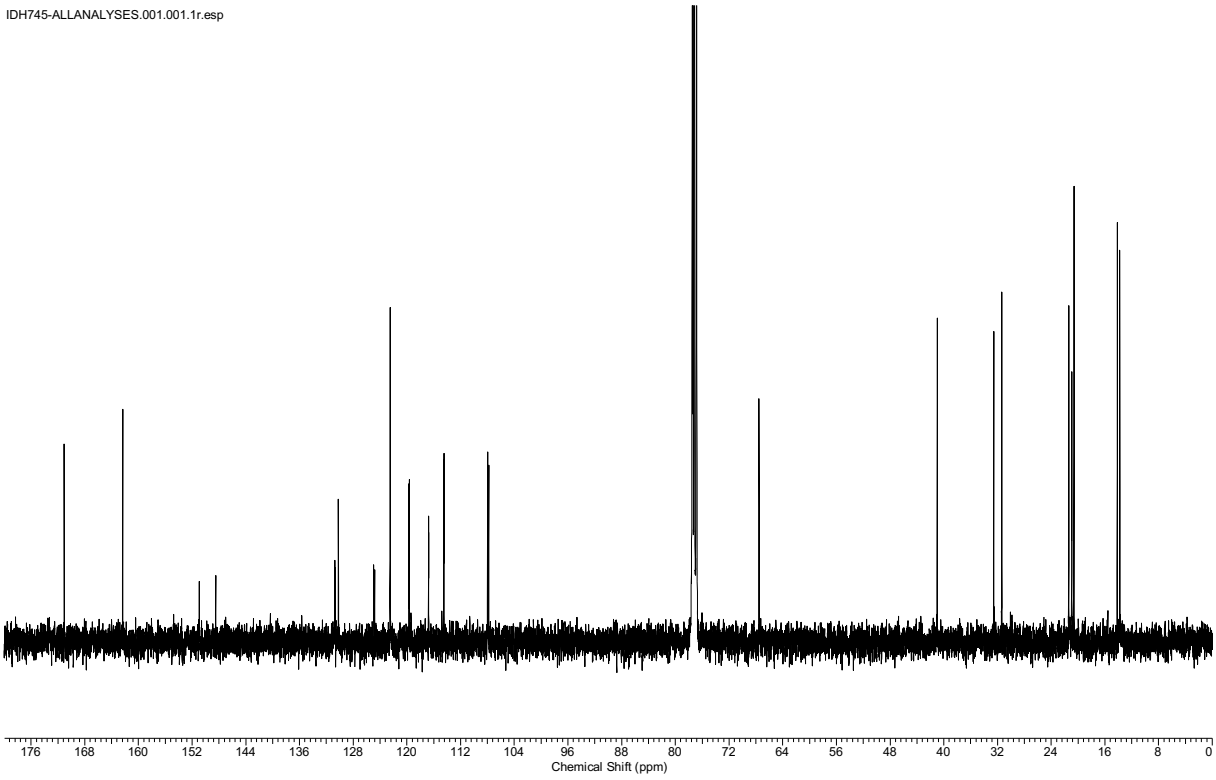


Figure S80 ^{13}C-NMR spectrum of **14c** in $CDCl_3$

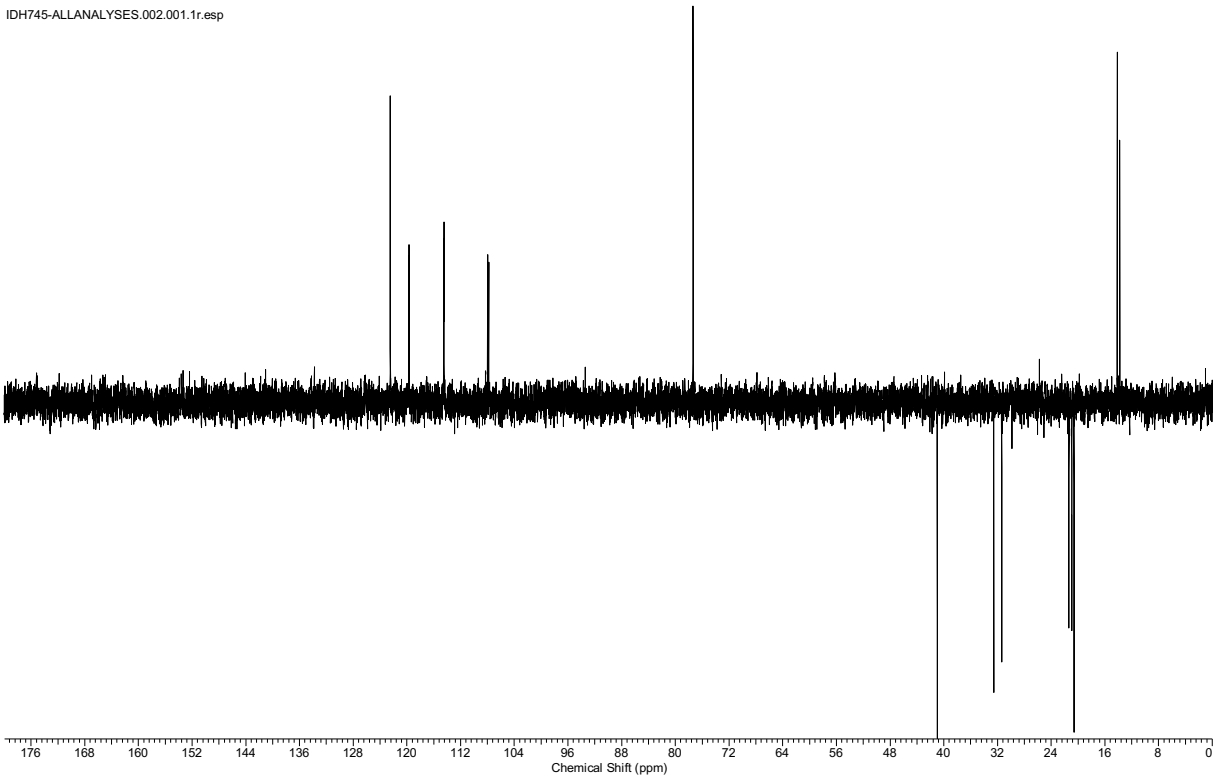
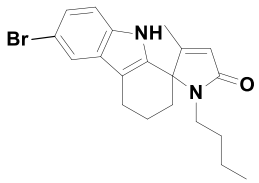


Figure S81 DEPT 135 spectrum of **14c** in $CDCl_3$

6-Bromo-1'-butyl-3'-methyl-2,3,4,9-tetrahydrospiro[carbazole-1,2'-pyrrol]-5'(1'H)-one (14d)



Purification: flash chromatography on silica gel (PE/EtOAc : from 8/2 to 5/5)

Yield: 32% (62 mg)

Physical appearance: brown solid

^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 0.78 (3H, CH_3, t, *J* = 7.3 Hz), 1.11-1.20 (2H, CH_2, m), 1.29-1.41 (1H, C*H*$_2$, m), 1.50-1.66 (1H, C*H*$_2$, m), 1.80 (3H, CH_3, br d, *J* = 1.5 Hz), 2.01-2.17 (4H, 2 x CH_2, m), 2.71-2.78 (1H, C*H*$_2$, m), 2.82-2.90 (2H, 2 x C*H*$_2$, m), 3.27 (1H, C*H*$_2$, ddd, *J* = 16.1, 10.8 and 5.4 Hz), 5.91 (1H, CH, br q, *J* = 1.5 Hz), 7.24-7.25 (2H, 2 x H_{Ar}, m), 7.66 (1H, H_{Ar}, br s), 9.67 (1H, NH, br s); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 13.8 (CH_3), 14.2 (CH_3), 20.6 (CH_2), 20.7 (CH_2), 21.5 (CH_2), 31.5 (CH_2), 32.6 (CH_2), 41.0 (CH_2), 67.8 (C), 112.5 (C_{Ar}), 113.1 (CH_{Ar}), 115.3 (C_{Ar}), 121.3 (CH_{Ar}), 122.0 (CH_{Ar}), 125.4 (CH_{Ar}), 128.7 (C_{Ar}), 130.6 (C_{Ar}), 135.0 (C_{Ar}), 163.0 (C), 171.3 (C); **IR** (nujol): 3211, 2933, 1668, 1442, 1407, 1305, 1259, 902, 842, 798, 736 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{20}H_{24}N_2OBr[M+H]^+$387.1067, found 387.1069.

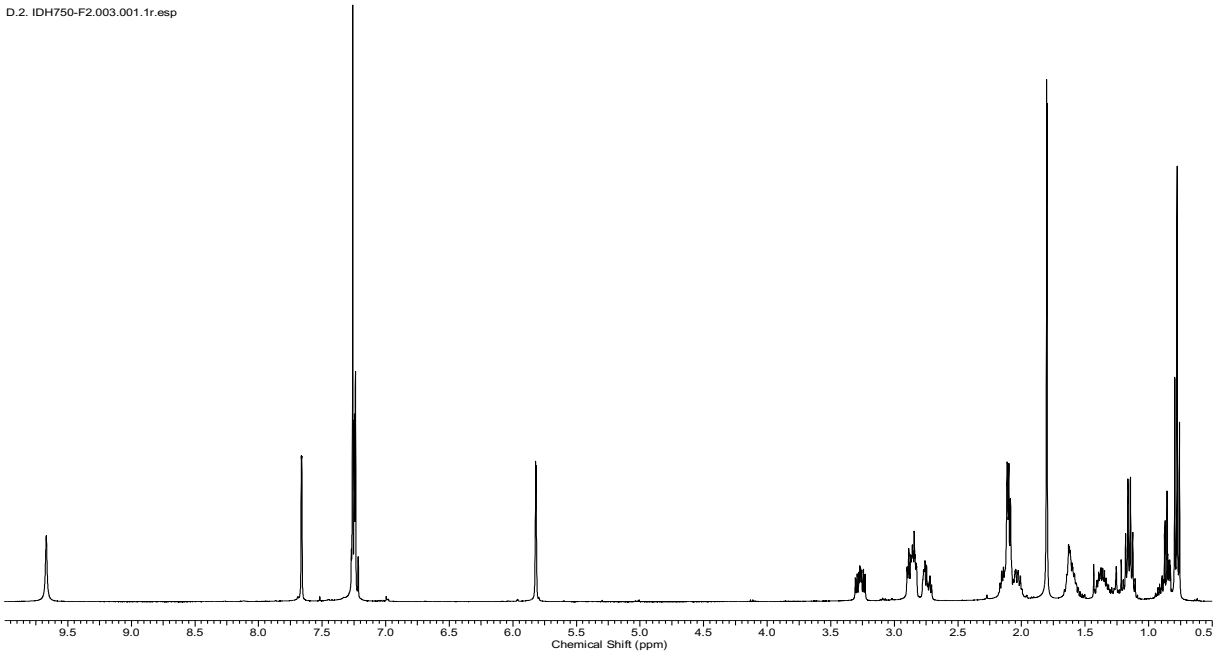


Figure S82 ^{1}H-NMR spectrum of **14d** in $CDCl_3$

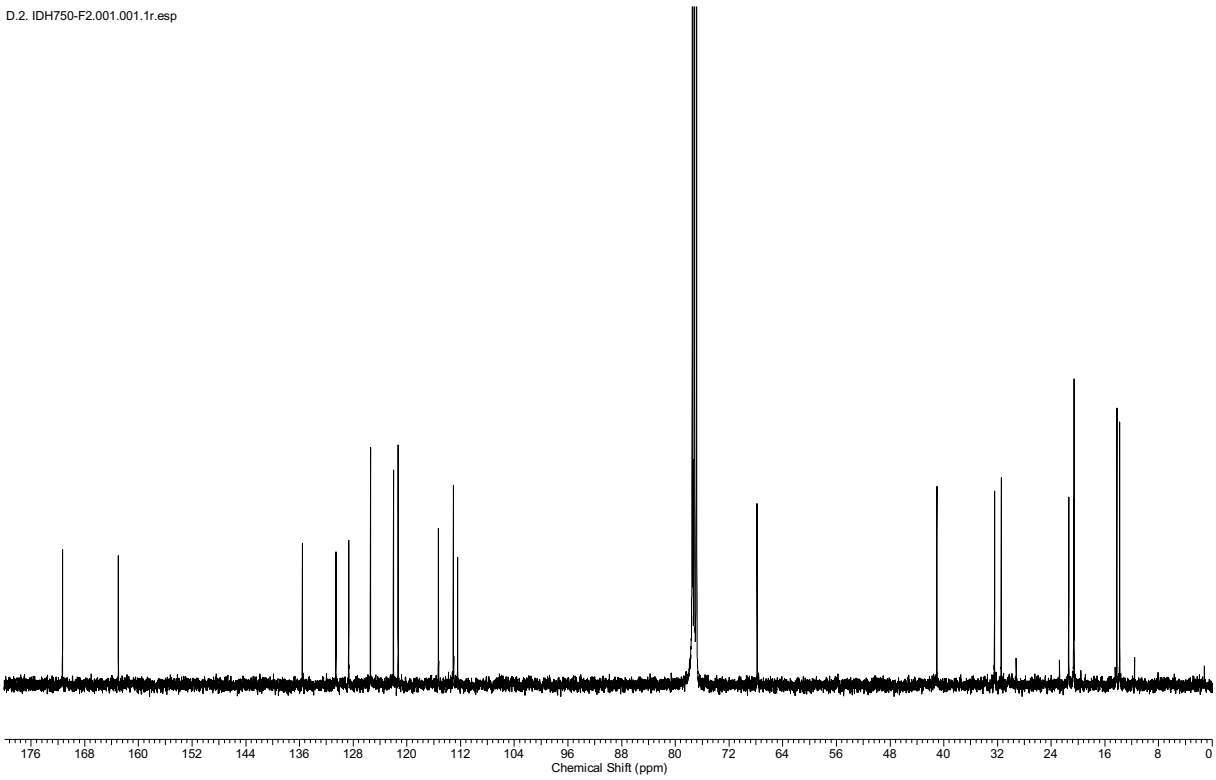


Figure S83 ^{13}C-NMR spectrum of **14d** in $CDCl_3$

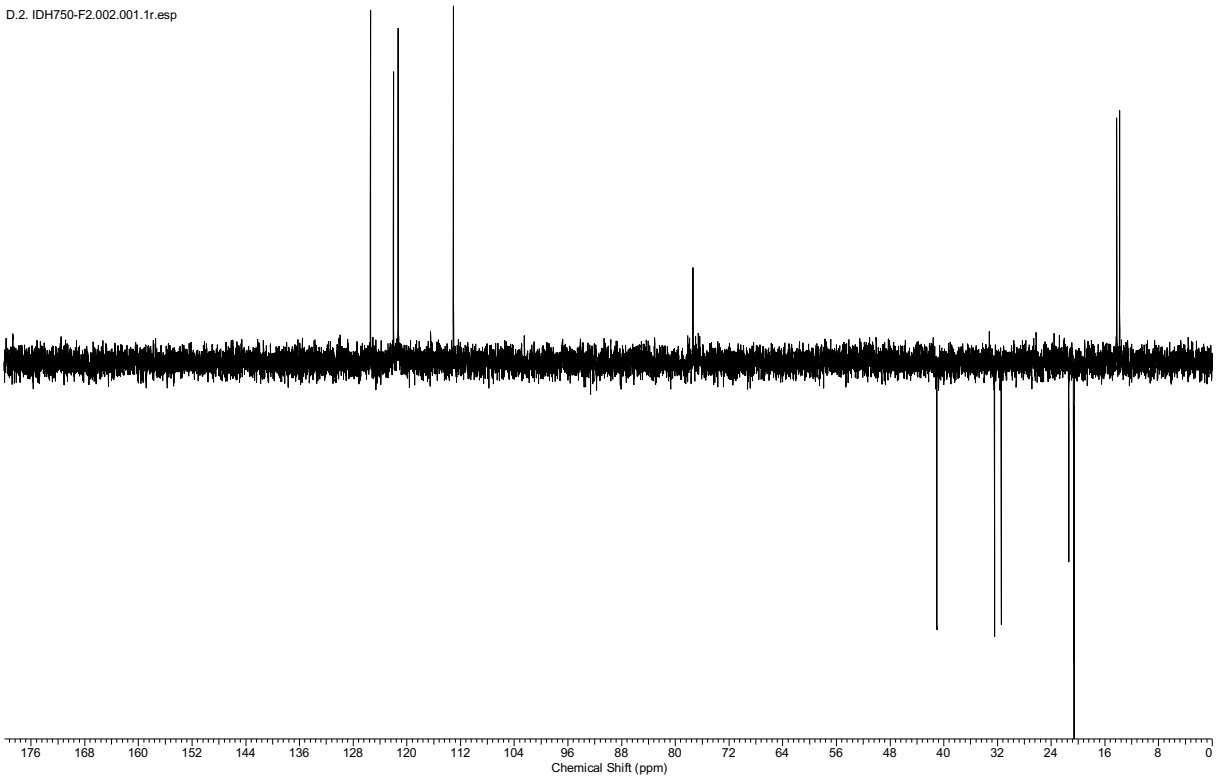
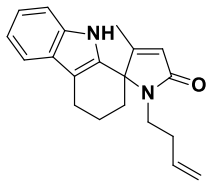


Figure S84 DEPT 135 spectrum of **14d** in $CDCl_3$

1'-(But-3-en-1-yl)-3'-methyl-2,3,4,9-tetrahydrospiro[carbazole-1,2'-pyrrol]-5'(1'H)-one (14e)



Purification: flash chromatography on silica gel (PE/EtOAc : from 8/2 to 6/4)

Yield: 33% (51 mg)

Physical appearance: light yellow solid

m.p. (amorphous): 269 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 1.81 (3H, CH_3, br d, *J* = 1.5 Hz), 2.05-2.18 (5H, 2 x CH_2 and C*H*$_2$, m), 2.27-2.39 (1H, C*H*$_2$, m), 2.73-2.83 (1H, C*H*$_2$, m), 2.88-2.97 (1H, C*H*$_2$, m), 3.13 (1H, C*H*$_2$, ddd, *J* = 15.4, 10.0 and 6.0 Hz), 3.36 (1H, C*H*$_2$, ddd, *J* = 15.4, 9.8 and 5.6 Hz), 4.90-4.98 (2H, CH_2, m), 5.60-5.73 (1H, CH, m), 5.92 (1H, CH, br q, *J* = 1.5 Hz), 7.12 (1H, H_{Ar}, br dd, *J* = 8.1 and 7.1 Hz), 7.20 (1H, H_{Ar}, br dd, *J* = 8.1 and 7.1 Hz), 7.26-7.31 (1H, H_{Ar}, m), 7.55 (1H, H_{Ar}, d, *J* = 8.1 Hz), 8.81 (1H, NH, br s); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 14.1 (CH_3), 20.8 (CH_2), 21.5 (CH_2), 32.6 (CH_2), 33.5 (CH_2), 40.3 (CH_2), 67.5 (C), 111.4 (CH_{Ar}), 116.3 (C_{Ar}), 116.6 (CH_2), 118.9 (CH_{Ar}), 119.6 (CH_{Ar}), 122.2 (CH), 123.1 (CH_{Ar}), 127.1 (C_{Ar}), 128.9 (C_{Ar}), 135.6 (CH), 136.6 (C_{Ar}), 163.1 (C), 171.1 (C); **IR** (Nujol): 3245, 2935, 1668, 1637, 1450, 1405, 1317, 1297, 738 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{20}H_{23}N_2O[M+H]^+$307.1805, found 307.1808.

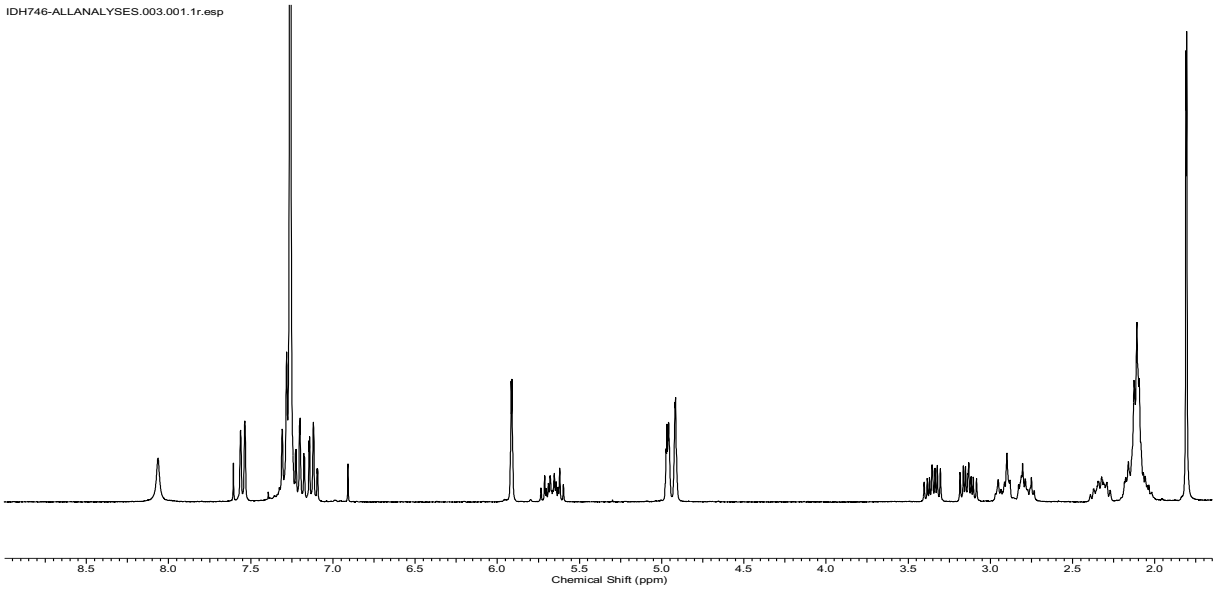


Figure S85 ^{1}H-NMR spectrum of **14e** in $CDCl_3$

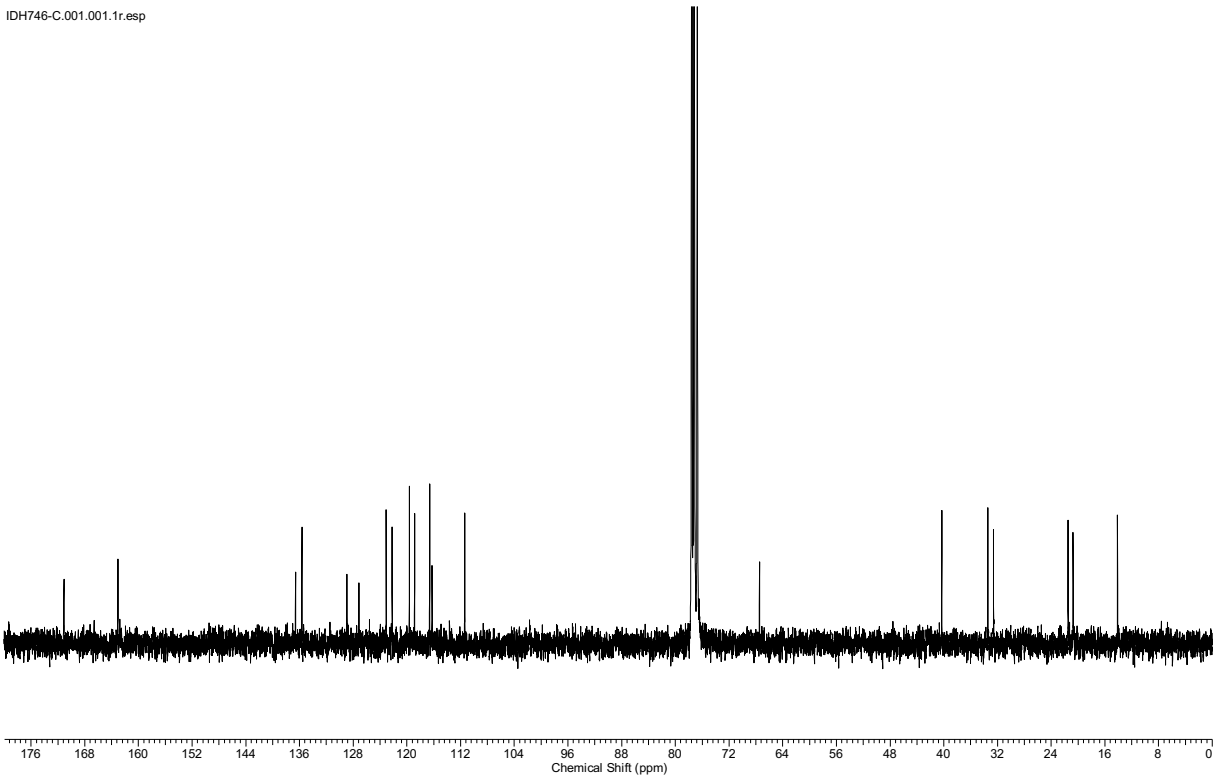


Figure S86 ^{13}C-NMR spectrum of **14e** in $CDCl_3$

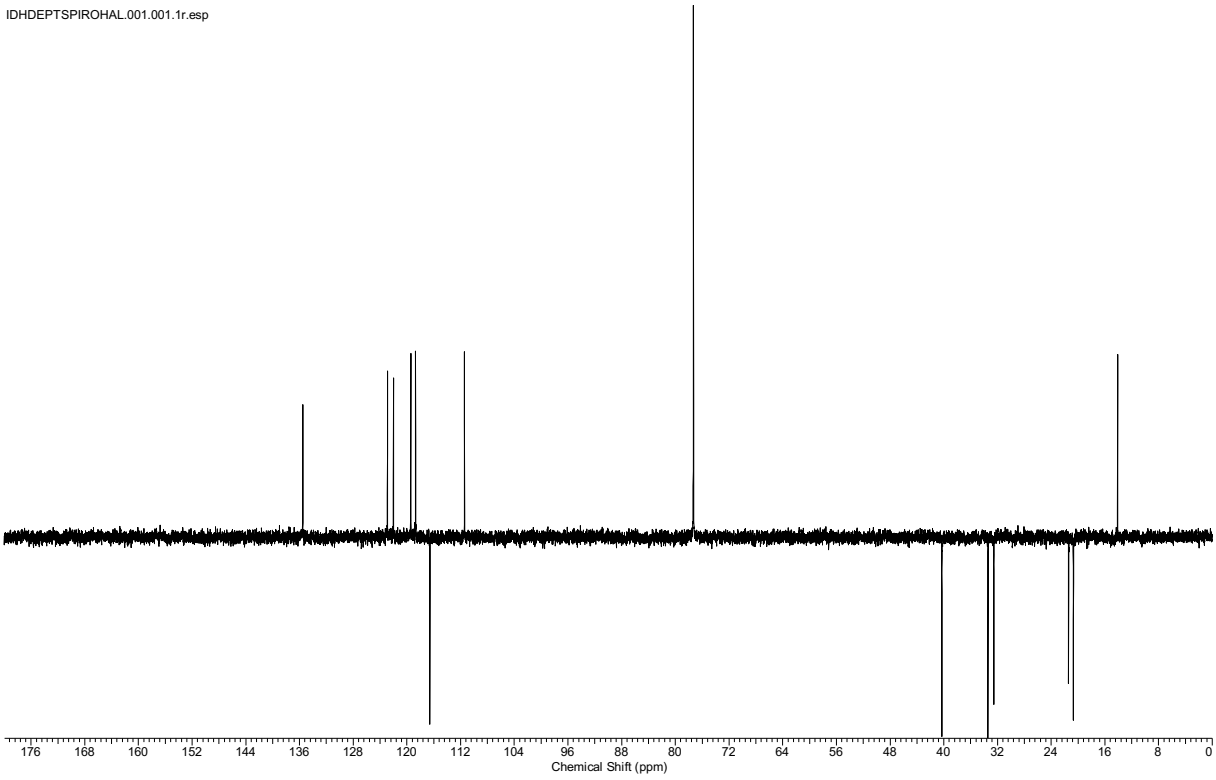
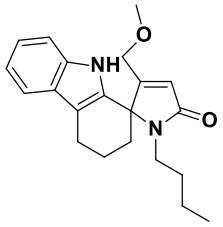


Figure S87 DEPT 135 spectrum of **14e** in $CDCl_3$

1'-Butyl-3'-(methoxymethyl)-2,3,4,9-tetrahydrospiro[carbazole-1,2'-pyrrol]-5'(1'H)-one (14f)



Purification: flash chromatography on silica gel (PE/EtOAc : from 8/2 to 6/4)

Yield: 20% (34 mg)

Physical appearance: white solid

m.p. (amorphous): 170°C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ (ppm) 0.80 (3H, CH_3, t, *J* = 7.4 Hz), 1.14-1.26 (2H, CH_2, m), 1.30-1.46 (1H, C*H*$_2$, m), 1.55-1.71 (1H, C*H*$_2$, m), 1.97-2.09 (2H, CH_2, m), 2.10-2.22 (2H, CH_2, m), 2.77-2.97 (3H, $CH_2$and C*H*$_2$, m), 3.24-3.34 (1H, C*H*$_2$, m), 3.29 (3H, CH_3, s), 3.76 (1H, C*H*$_2$, dd, *J* = 15.3 and 1.5 Hz), 4.13 (1H, C*H*$_2$, dd, *J* = 15.3 and 1.5 Hz), 6.13 (1H, CH, br s), 7.11 (1H, H_{Ar}, br t, *J* = 7.9 Hz), 7.20 (1H, H_{Ar}, br t, *J* = 7.9 Hz), 7.33 (1H, H_{Ar}, d, *J* = 7.9 Hz), 7.54 (1H, H_{Ar}, d, *J* = 7.9 Hz), 8.76 (1H, NH, br s); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 13.8 (CH_3), 20.6 (CH_2), 20.7 (CH_2), 21.7 (CH_2), 31.3 (CH_2), 32.9 (CH_2), 40.8 (CH_2), 59.00 (CH_3), 66.5 (C), 68.4 (CH_2), 111.6 (CH_{Ar}),115.8 (C_{Ar}), 118.7 (CH_{Ar}),119.5 (CH_{Ar}), 121.8 (CH), 123.0 (CH_{Ar}),127.0 ($C_{Ar,}$), 128.9 ($C_{Ar,}$),136.9 (C_{Ar}), 163.0 (C), 170.6 (C); **IR** (nujol): 3228, 2931, 1668, 1452, 1405, 1317, 736 cm^{-1}; **HRMS**(ESI-MS) calcd for $C_{21}H_{27}N_2O_2[M+H]^+$339.2067, found 339.2067.

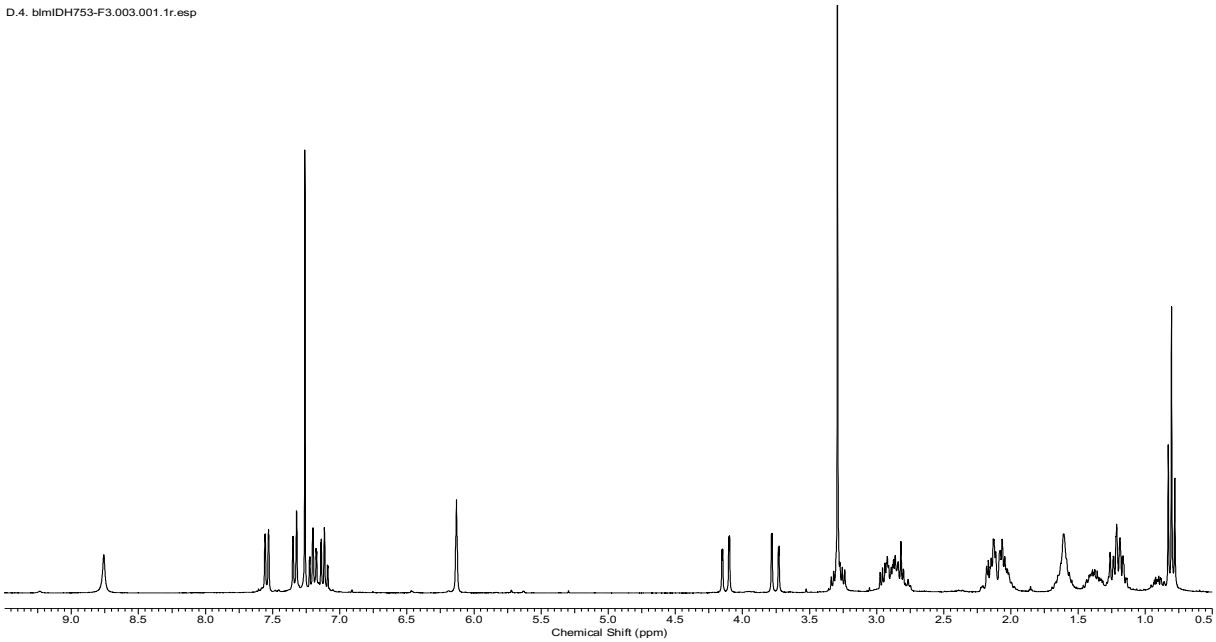


Figure S88 ^{1}H-NMR spectrum of **14f** in $CDCl_3$

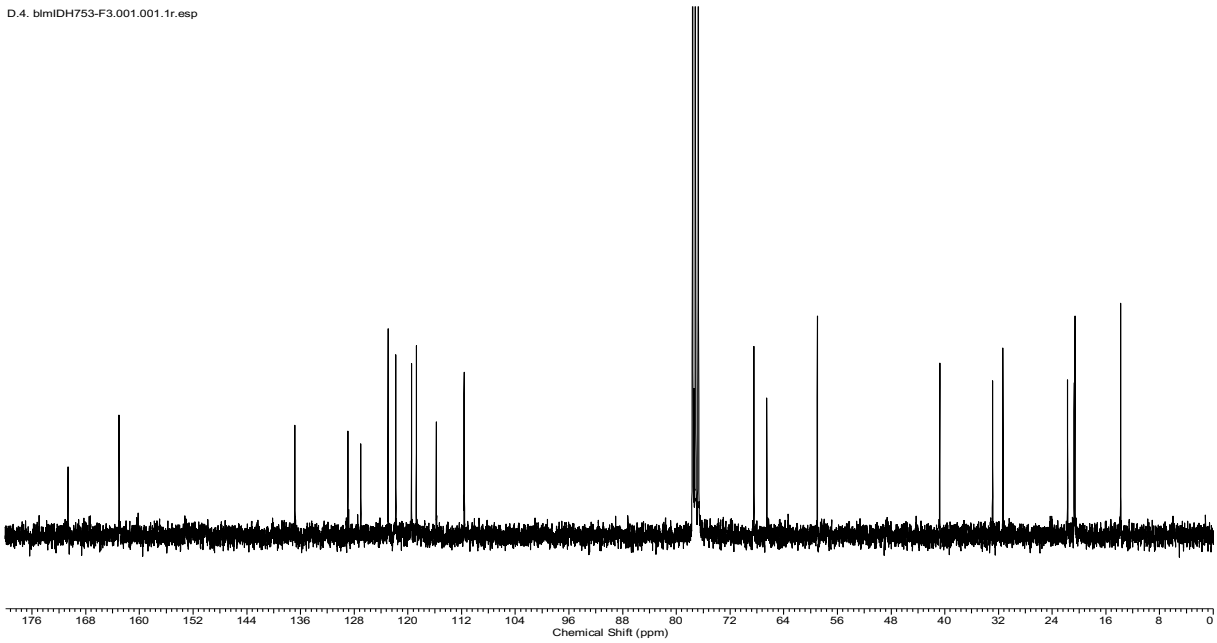


Figure S89 ^{13}C-NMR spectrum of **14f** in $CDCl_3$

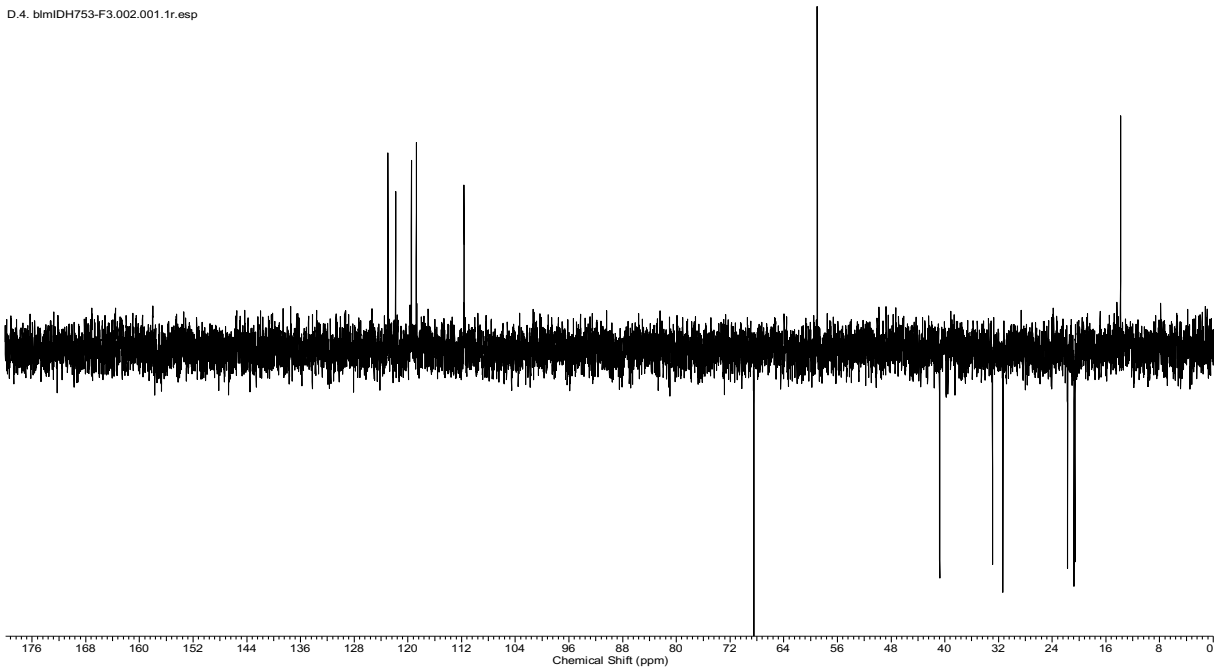
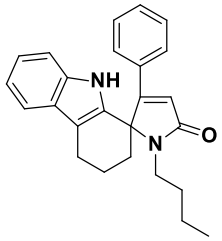


Figure S90 DEPT 135 spectrum of **14f** in $CDCl_3$

1'-Butyl-3'-phenyl-2,3,4,9-tetrahydrospiro[carbazole-1,2'-pyrrol]-5'(1'H)-one (14g)



Purification: flash chromatography on silica gel (PE/EtOAc : from 8/2 to 7/3)

Yield: 11% (21 mg)

Physical appearance: brown solid

^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 0.81 (3H, CH_3, t, *J* = 7.3 Hz), 1.14-1.29 (2H, CH_2, m), 1.35-1.50 (1H, C*H*$_2$, m), 1.63-1.70 (1H, C*H*$_2$, m), 1.89-2.01 (1H, C*H*$_2$, m), 2.02-2.11 (1H, C*H*$_2$, m), 2.17-2.27 (1H, C*H*$_2$, m),2.66-2.76 (1H, C*H*$_2$, m), 2.88-3.06 (2H, CH_2, m), 3.38 (1H, C*H*$_2$, m, ddd, *J* = 16.1, 10.8 and 5.5 Hz), 6.37 (1H, CH, br s), 6.93 (2H, 2 x H_{Ar}, br d, *J* = 7.2 Hz), 7.14-7.30 (5H, 5 x H_{Ar}, m), 7.35 (1H, H_{Ar}, br d, *J* = 7.9 Hz), 7.62 (1H, H_{Ar}, br d, *J* = 7.6 Hz), 8.70 (1H, NH, br s);**^{13}C-NMR** ($CDCl_3$, 100 MHz): δ (ppm) 13.8 (CH_3), 20.6 (2 x CH_2), 20.9 (CH_2), 31.6 (CH_2), 34.2 (CH_2), 41.0 (CH_2), 66.9 (C), 111.8 (CH_{Ar}),116.3 (C_{Ar}), 119.0 (CH_{Ar}),119.6 (CH_{Ar}),122.5 (CH), 123.1 (CH_{Ar}),127.0 (C_{Ar}), 127.5 (2 x CH_{Ar}), 128.5 (C_{Ar}), 128.9 (2 x CH_{Ar}), 129.7 (CH_{Ar}), 132.7 (C_{Ar}), 136.9 (C_{Ar}), 163.1 (C), 170.4 (C);); **IR** (nujol): 3228, 2931, 1668, 1451, 1405, 1317, 844, 735 cm^{-1}; **HRMS** (ESI-MS) calcd for $C_{25}H_{27}N_2O[M+H]^+$371.2118, found 371.2119.

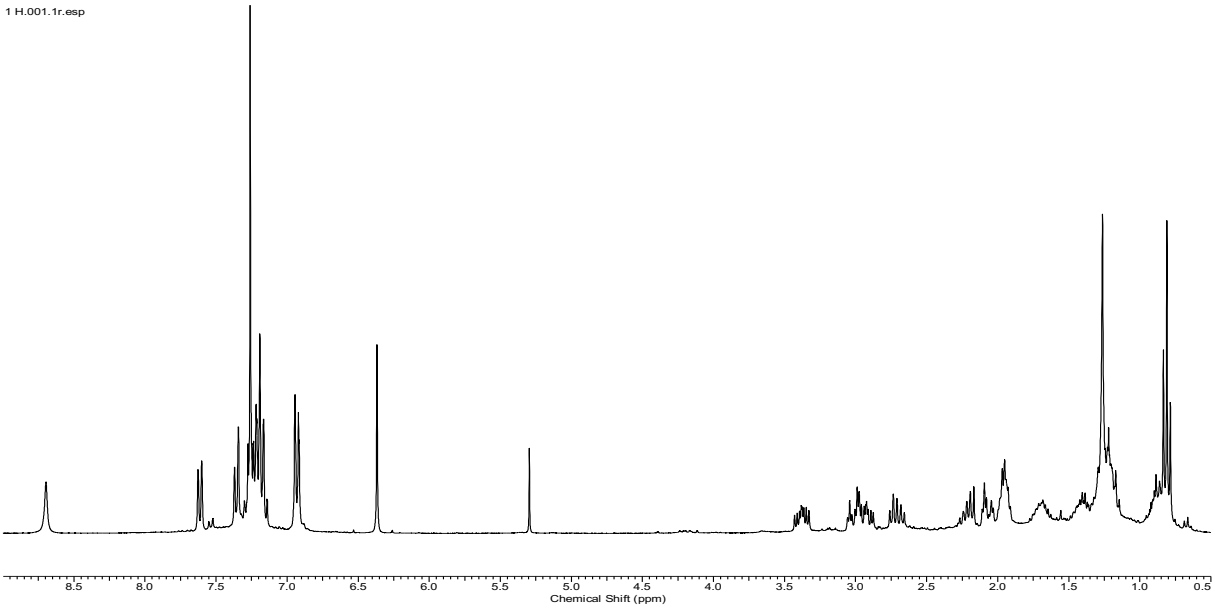


Figure S91 ^{1}H-NMR spectrum of **14g** in $CDCl_3$

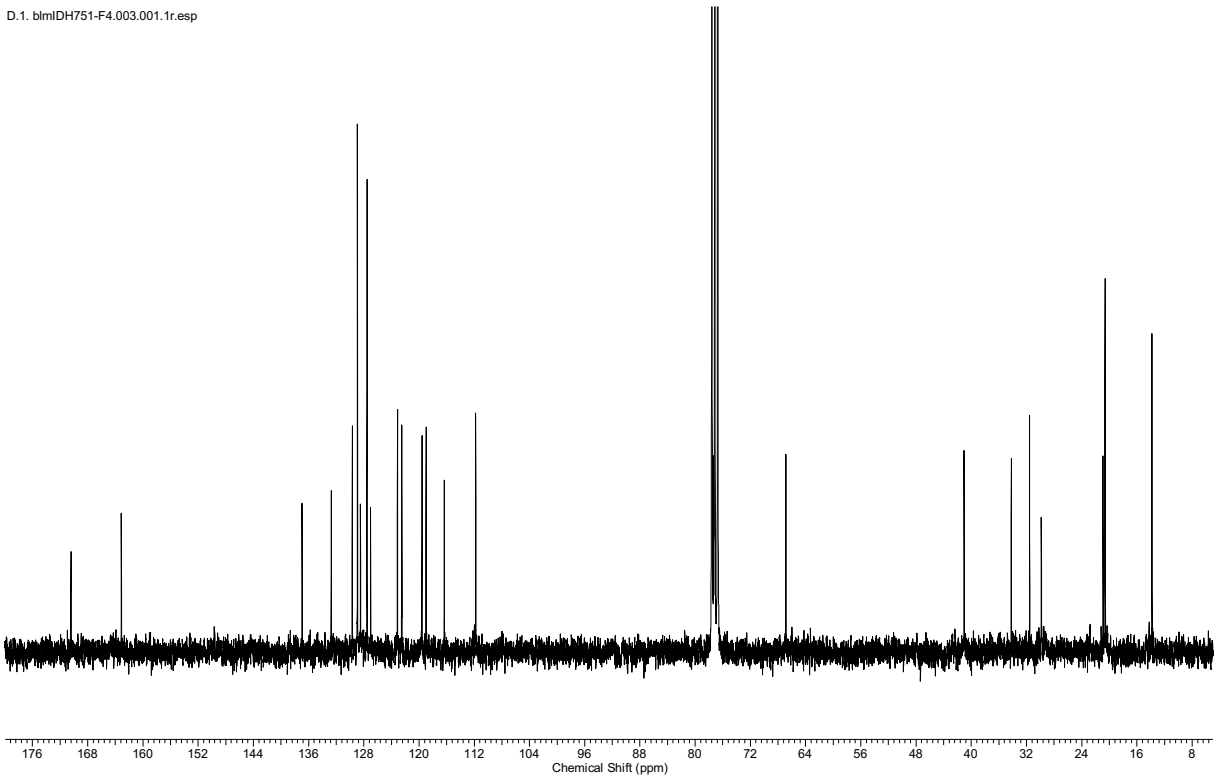


Figure S92 ^{13}C-NMR spectrum of **14g** in $CDCl_3$

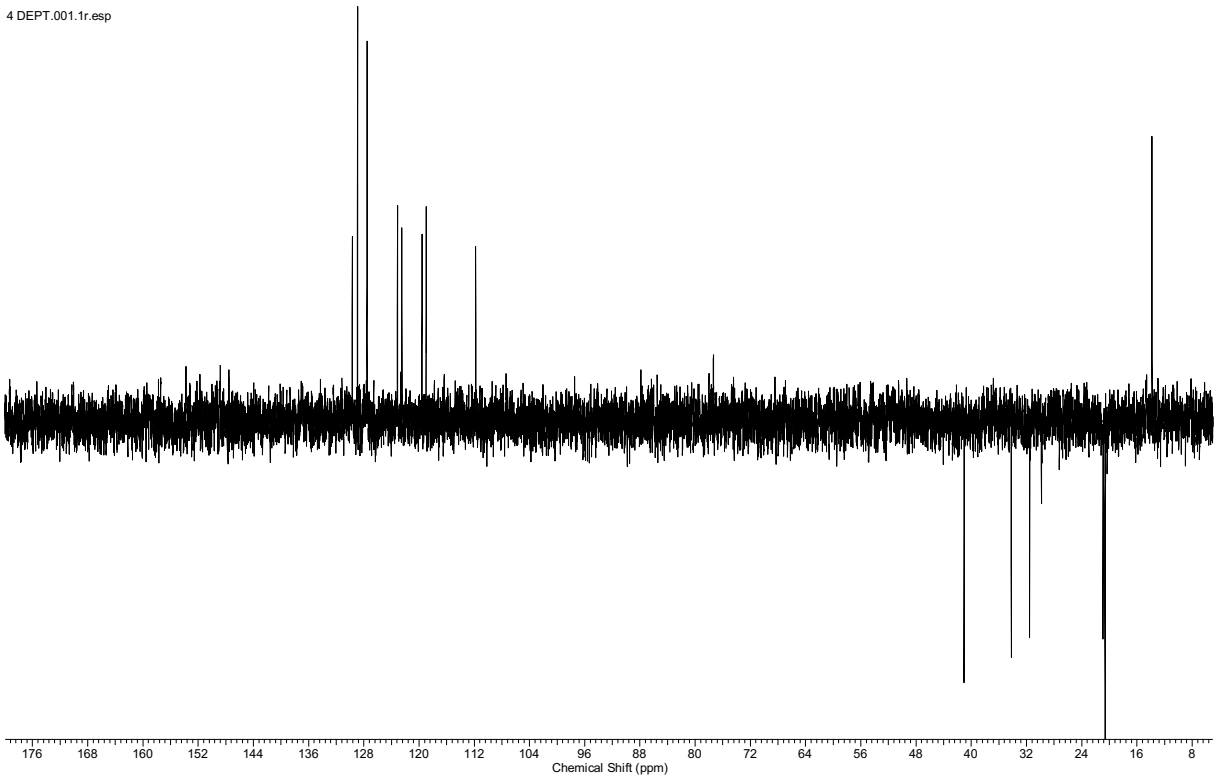


Figure S93 DEPT 135 spectrum of **14g** in $CDCl_3$