Electronic Supporting Information

IBX-mediated oxidative addition of isocyanides to cyclic secondary amines: total syntheses of alangiobussine and alangiobussinine

Mayur D. Ambule,[a,b] Shashank Tripathi,[a,b] Anirban Ghoshal,[a,b] and Ajay K. Srivastava*[a,b]

[a]*Division of Medicinal and Process Chemistry, CSIR-Central Drug Research Institute, Sector-10, Jankipuram Extension, Lucknow-226031, India.*

[b]*Chemical Sciences Division, AcSIR, New Delhi-110025, India*

Table of Contents

1. **General Information**. All the reagents and solvents were used as received from commercial sources without further purification. All air and moisture sensitive reactions were conducted under inert atmosphere of nitrogen. Reactions were monitored by thin-layer chromatography carried out on silica plates (silica gel 60 F254, Merck) using uv-light, iodine, ninhydrin and *p*-anisaldehyde for visualization. Column chromatography was carried out using silica gel (100-200 mesh) packed in glass columns. Technical grade ethyl acetate and petroleum ether used for column chromatography were distilled prior to use. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ as solvent on 300 MHz or 400 MHz spectrometer at ambient temperature. The coupling constant *J* is given in Hz. The chemical shifts (δ) are reported in ppm on scale downfield from TMS and using the residual solvent peak in $CDCl_3$ (H: δ = 7.26 ppm and C: δ = 77.00 ppm) or TMS (δ = 0.00) as internal standard and signal patterns are indicated as follows: s = singlet, d= doublet, dd = doublet of doublet, ddd = doublet of doublet of doublet, dt = doublet of triplet, t = triplet, q = quartet, m = multiplet. High-resolution mass spectra (HRMS) were recorded on a Thermo Scientific Exactive "ORBITRAP" spectrometer using H_2O/MeOH mixed with 0.1% formic acid as mobile phase. 2-Iodoxybenzoic acid (IBX),[1] tryptoline **1a**,[2] 6-bromotryptoline **1b**,[3] 6-methoxy-1,2,3,4-tetrahydroisoquinoline **6b**,[4] 3,4-dihydro-*β*-carboline **5**,[5] 3,4-dihydrohydroisoquinoline (DHIQ) **17**,[6] *N*(2)-benzyl-tryptoline **21**,[7] C(1)-phenyl-tryptoline **23**,[8] benzylisocyanide **2d**,[9] 2-bromobenzylisocyanide **2e**,[10] phenethylisocyanide **2f**,[11] 1-(2-isocyanoethyl)-4-methoxybenzene **2g**,[12] 4-(2-isocyanoethyl)-1,2-dimethoxybenzene **2h**,[13] 1-bromo-2-isocyanobenzene **2k**,[14] 3-(2-isocyanoethyl)-1*H*-indole **2m**,[15] (3aR,4R,7S,7aS)-2,3,3a,4,7,7a-hexahydro-1*H*-4,7-epoxyisoindole **10**,[16] were prepared and characterized as previously reported.

Isocyanides used in the study:

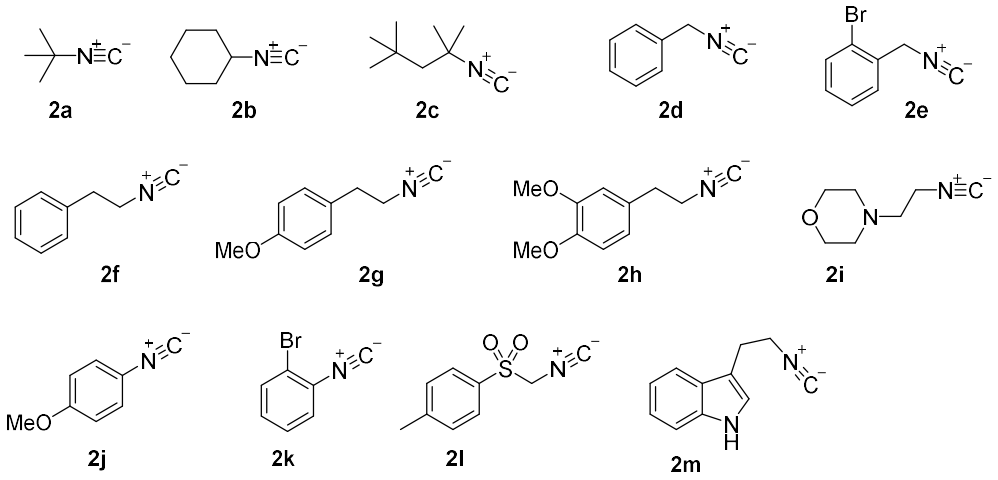
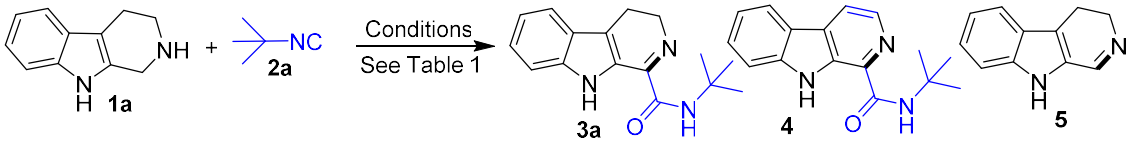


Table S1. Optimization of the Reaction Conditions[a]



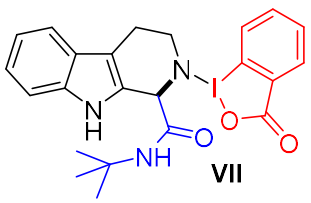
Entry	Oxidant (equiv.)	Solvent	Temp (°C)	Time/(h)	**3a** (% yield)[b]
1.	IBX (2.5)	THF	rt	12	15
2.	IBX (2.5)	THF	60	12	20[c]
3.	IBX (2.5)	DMSO	rt	2	68
4.	IBX (1.0)	DMSO	rt	12	--[d]
5.	IBX (2.0)	DMSO	rt	12	40[e]
6.	IBX (2.5)	DCM	rt	5	--[f]
7.	IBX (2.5)	HFIP	rt	12	14[g]
8.	PIDA (2.5)	DMSO	rt	5	--[f]
9.	PIFA (2.5)	DMSO	rt	12	--[f]
10.	DMP (2.5)	DMSO	rt	2	60

[a]Reaction conditions: **1a** (0.11 mmol), **2a** (0.11 mmol), oxidant, solvent (1.0 mL). [b]Isolated yields. [c]along with **VII** (25%) and **4** (16%). [d]only oxidized product **5** (75%), [e]along with **5** (15%). [f]Complex mixture. [g]uncharacterized side products. IBX = 2-Iodoxybenzoic acid; DMP = Dess–Martin periodinane; PIDA = Phenyliodiodiacetate; PIFA = (Bis(trifluoroacetoxy)iodo)benzene; THF = Tetrahydrofuran; DCM = Dichloromethane; HFIP = Hexafluoroisopropanol; DMSO = Dimethyl sulfoxide; IBA = 2-iodosobenzoic acid

We began our investigation by reacting tryptoline **1a** with *tert*-butyl isocyanide **2a** in the presence of hypervalent iodine containing oxidizing agents (Table S1). Initially, the use of IBX in THF led to the formation of desired carboxamide **3a** after 12 h albeit in a low yield of 15% with incomplete consumption of tryptoline **1a** (Table S1, entry 1). After heating the reaction mixture at 60 °C for 12 h, product **3a** was obtained in 20% yield along with two more byproducts; (i) a complex of **3a** with 2-iodosobenzoic acid (IBA) (**VII**, 25%) and the over oxidized product (**4**, 16%) (Table S1, entry 2). Change of solvent from THF to DMSO gave encouraging results and tryptoline **1a** got consumed at room temperature in 2 h affording **3a** in 68% yield (Table S1, entry 3). Reducing the amount of IBX to 1.0 equivalent provided oxidized tryptoline **5** (75%), whereas with 2.0 equivalents of IBX, product **3a** was formed in 40% yield with unreacted **5** (15%) (Table 1, entries 4 and 5). However, the reaction did not proceed in DCM and HFIP, and a mixture of uncharactizable products was obtained along with a low yield of **3a** of 14% (Table S1, entries 6 and 7).

Screening of different hypervalent iodine reagents as oxidizing agents reflects that with PIDA and PIFA, a complex mixture was obtained whereas DMP favors the reaction to provide **3a** in 60% (Table S1, entries 8–10). It was inferred that IBX (2.5 equiv.) in DMSO provided the best results with complete conversion (Table S1, entry 3). Products **3a**, **4** and **VII** were fully characterized by spectroscopic analysis such as ^{1}H-, ^{13}C-NMR, and HRMS analyses.

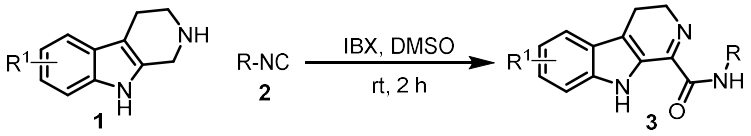
A probable complex of product **3a** with IBA was obtained as following structure based on NMR and Mass analysis:



VII

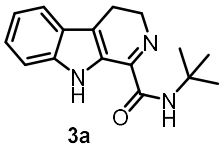
2. Experimental Procedures and characterization data:

2.1. General procedure A for the synthesis of 3a-3m



IBX (2.5 equiv) was taken in a round bottom flask, then DMSO (2.0 mL) was added and stirred at room temperature for 15 minutes. After complete solubilisation of IBX, tryptoline **1** (1.0 equiv) and isocyanide **2** (1.0 equiv) were added and stirred at room temperature for 2 h. After completion of reaction (based on TLC), the reaction mixture was diluted with ethyl acetate (10 mL) and then saturated solution of sodium thiosulfate (10 mL) was added and stirred for 10 minutes. The organic layer was separated; aqueous layer was again washed with ethyl acetate. The combined organic layers were washed with saturated solution of sodium bicarbonate (15 mL), dried over anhydrous Na_2SO_4, concentrated in *vacuo* and crude was purified by silica gel column chromatography to afford different tryptoline derived imino-carboxamides **3**.

***N*-(*tert*-butyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole-1-carboxamide (3a)**

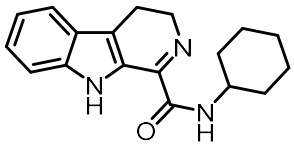


3a

According to general procedure A by using tryptoline **1a** (50.0 mg, 0.29 mmol), *tert*-butyl isocyanide **2a** (0.04 mL, 0.29 mmol) and IBX (203.2 mg, 0.72 mmol), the titled compound was prepared to yield **3a** as a pale yellow solid (53.5 mg, 68%); **m.p**: 136-137 °C; R_f = 0.5 (20% EtOAc in hexane); **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.57 (d, J = 8.1 Hz, 1H), 7.53 (s, 1H), 7.37 (d, J = 8.3 Hz, 1H), 7.30 – 7.25 (m, 2H), 7.14 – 7.09 (m, 1H), 4.00 (dd, J = 9.5, 8.2 Hz, 2H), 2.94 (dd, J = 9.5, 8.2 Hz, 2H), 1.47 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 163.6, 152.0, 136.9, 126.7, 124.9, 124.5, 120.0, 119.8, 117.6, 112.2, 51.0, 48.4, 28.6, 19.1; **IR**

($CHCl_3$) ν_{max} (cm^{-1}) = 3438, 3020, 2401, 1669, 1525, 1215, 1068, 760, 669; **HRMS (ESI)**: calcd. for $C_{16}H_{20}N_3O$ $[M+H]^+$: 270.1606, found: 270.1602.

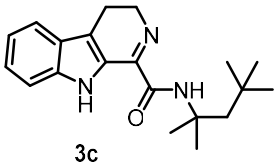
***N*-cyclohexyl-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole-1-carboxamide (3b)**



3b

According to general procedure A by using tryptoline **1a** (50.0 mg, 0.29 mmol), cyclohexyl isocyanide **2b** (0.04 mL, 0.29 mmol) and IBX (203.2 mg, 0.72 mmol), the titled compound was prepared to yield **3b** as a yellow oil (51.5 mg, 60%); R_f = 0.5 (20% EtOAc in hexane); **^{1}H NMR (300 MHz, $CDCl_3$)**: δ 10.00 (s, 1H), 7.54 (t, J = 9.9 Hz, 2H), 7.38 (d, J = 8.3 Hz, 1H), 7.31 – 7.22 (m, 1H), 7.11 (dd, J = 11.0, 3.9 Hz, 1H), 4.07 – 3.95 (m, 2H), 3.94 – 3.79 (m, 1H), 3.03 – 2.87 (m, 2H), 2.04 – 1.93 (m, 2H), 1.82 – 1.72 (m, 2H), 1.69 – 1.60 (m, 1H), 1.46 – 1.39 (m, 1H), 1.33 (d, J = 12.3 Hz, 2H), 1.26 (dd, J = 7.2, 4.3 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 163.3, 151.6, 136.9, 126.7, 124.8, 124.6, 119.9, 119.8, 117.4, 112.3, 48.4, 48.0, 32.8, 25.4, 24.7, 19.1; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3360, 2931, 2854, 1663, 1589, 1523, 1447, 1371, 1319, 1249, 1188, 1066, 872, 756, 637; **HRMS (ESI)**: calcd. for $C_{18}H_{22}N_3O$ $[M+H]^+$: 296.1763, found: 296.1754.

***N*-(2,4,4-trimethylpentan-2-yl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole-1-carboxamide (3c)**

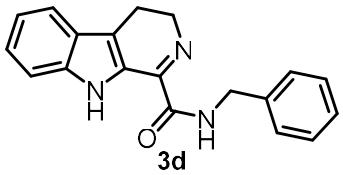


3c

According to general procedure A by using tryptoline **1a** (50.0 mg, 0.29 mmol), 2-isocyano-2,4,4-trimethylpentane **2c** (0.05 mL, 0.29 mmol) and IBX (203.2 mg, 0.72 mmol), the titled compound was prepared to yield **3c** as a yellow oil (61.4 mg, 65%); R_f = 0.5 (20% EtOAc in hexane); ^{1}H NMR **(400 MHz, $CDCl_3$)**: δ 10.03 (s, 1H), 7.62 (s, 1H), 7.55 (dd, J = 8.0, 0.7 Hz,

1H), 7.36 (d, *J* = 8.3 Hz, 1H), 7.28 – 7.23 (m, 1H), 7.14 – 7.08 (m, 1H), 3.99 (dd, *J* = 9.5, 8.2 Hz, 2H), 2.92 (dd, *J* = 9.5, 8.2 Hz, 2H), 1.83 (s, 2H), 1.51 (s, 6H), 1.03 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 163.3, 151.9, 136.8, 126.7, 124.8, 124.5, 119.8, 117.4, 112.2, 54.7, 51.9, 48.4, 31.5, 28.9, 19.1; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3743, 3430, 3357, 2952, 1673, 1590, 1523, 1447, 1367, 1320, 1231, 1188, 875, 743, 628, 510; **HRMS (ESI)**: calcd. for $C_{20}H_{28}N_3O$ $[M+H]^+$: 326.2232, found: 326.2231.

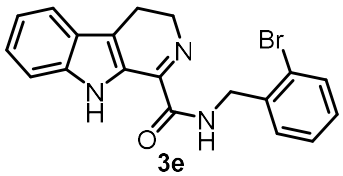
***N*-benzyl-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole-1-carboxamide (3d)**



3d

According to general procedure A by using tryptoline **1a** (50.0 mg, 0.29 mmol), benzylisocyanide **2d** (0.035 mL, 0.29 mmol) and IBX (203.2 mg, 0.72 mmol), the titled compound was prepared to yield **3d** as a yellow solid (54.0 mg, 61%); **m.p**: 129-130 °C; R_f = 0.4 (30% EtOAc in hexane); **^{1}H NMR (300 MHz, $CDCl_3$)** δ 9.94 (s, 1H), 7.95 (s, 1H), 7.58 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.40 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.37 – 7.32 (m, 4H), 7.32 – 7.26 (m, 2H), 7.12 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 4.58 (d, *J* = 6.2 Hz, 2H), 4.07 – 3.97 (m, 2H), 2.99 – 2.90 (m, 2H); **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 164.2, 151.3, 137.7, 136.9, 128.8, 127.8, 127.6, 126.6, 125.0, 124.7, 120.1, 119.9, 117.6, 112.3, 48.5, 43.2, 19.1; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3438, 3020, 1644, 1526, 1216, 761, 669; **HRMS (ESI)**: calcd. for $C_{19}H_{18}N_3O$ $[M+H]^+$: 304.1450, found: 304.1445.

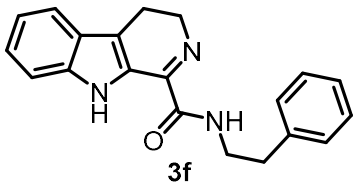
***N*-(2-bromobenzyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole-1-carboxamide (3e)**



3e

According to general procedure A by using tryptoline **1a** (50.0 mg, 0.29 mmol), 2-bromobenzylisocyanide **2e** (0.035 mL, 0.29 mmol) and IBX (203.2 mg, 0.72 mmol), the titled compound was prepared to yield **3e** as a yellow oil (67.0 mg, 60%); R_f = 0.4 (30% EtOAc in hexane); **^{1}H NMR (300 MHz, $CDCl_3$)**: δ 9.90 (s, 1H), 8.13 – 7.98 (m, 1H), 7.58 (ddd, J = 8.1, 2.2, 1.1 Hz, 2H), 7.47 – 7.36 (m, 2H), 7.34 – 7.26 (m, 2H), 7.21 – 7.09 (m, 2H), 4.67 (d, J = 6.4 Hz, 2H), 4.04 (dd, J = 9.6, 8.2 Hz, 2H), 2.95 (dd, J = 9.6, 8.3 Hz, 2H); **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 164.2, 151.2, 136.9, 136.8, 132.9, 129.9, 129.3, 127.7, 126.6, 125.0, 124.6, 123.7, 120.1, 119.9, 117.6, 112.3, 48.6, 43.4, 19.1; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3368, 2924, 1668, 1522, 1067, 747; **HRMS (ESI)**: calcd. for $C_{19}H_{17}BrN_3O$ $[M+H]^+$: 382.0555, found: 382.0555.

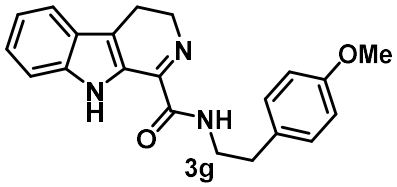
***N*-phenethyl-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole-1-carboxamide (3f)**[17]



3f

According to general procedure A by using tryptoline **1a** (50.0 mg, 0.29 mmol), (2-isocyanoethyl)benzene **2f** (0.035 mL, 0.29 mmol) and IBX (203.2 mg, 0.72 mmol), the titled compound was prepared to yield **3f** as a yellow oil (53.5 mg, 58%); R_f = 0.5 (30% EtOAc in hexane); **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 9.97 (s, 1H), 7.71 (s, 1H), 7.58 – 7.54 (m, 1H), 7.38 (d, J = 8.3 Hz, 1H), 7.34 – 7.27 (m, 3H), 7.26 – 7.21 (m, 3H), 7.11 (ddd, J = 8.0, 7.0, 0.9 Hz, 1H), 3.98 (dd, J = 9.5, 8.3 Hz, 2H), 3.68 – 3.60 (m, 2H), 2.96 – 2.87 (m, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 164.3, 151.3, 138.6, 136.9, 128.7, 128.6, 126.6, 126.5, 124.9, 124.6, 120.04, 119.8, 117.5, 112.3, 48.5, 40.4, 35.7, 19.1; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3438, 3020, 1669, 1528, 1215, 1067, 760, 669; **HRMS (ESI)**: calcd. for $C_{20}H_20N_3O$ $[M+H]^+$: 318.1606, found: 318.1602.

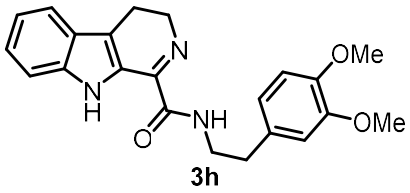
***N*-(4-methoxyphenethyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole-1-carboxamide (3g)**



3g

According to general procedure A by using tryptoline **1a** (50.0 mg, 0.29 mmol), 1-(2-isocyanoethyl)-4-methoxybenzene **2g** (46.2 mg, 0.29 mmol) and IBX (203.2 mg, 0.72 mmol), the titled compound was prepared to yield **3g** as a yellow oil (64.6 mg, 64%); R_f = 0.4 (30% EtOAc in hexane); **^{1}H NMR (400 MHz, CDCl$_3$)**: δ 9.97 (s, 1H), 7.69 (s, 1H), 7.56 (dd, J = 8.0, 0.6 Hz, 1H), 7.38 (d, J = 8.3 Hz, 1H), 7.31 – 7.24 (m, 1H), 7.18 – 7.09 (m, 3H), 6.89 – 6.83 (m, 2H), 3.99 (dd, J = 9.5, 8.3 Hz, 2H), 3.78 (s, 3H), 3.64 – 3.57 (m, 2H), 2.92 (dd, J = 9.5, 8.3 Hz, 2H), 2.84 (t, J = 7.3 Hz, 2H); **^{13}C NMR (100 MHz, CDCl$_3$)**: δ 164.2, 158.3, 151.3, 136.9, 130.6, 129.6, 126.6, 124.9, 124.6, 120.0, 119.8, 117.5, 114.1, 112.3, 55.2, 48.5, 40.6, 34.9, 19.1; **IR (CHCl$_3$) ν_{max} (cm^{-1})** = 3441, 3019, 2401, 1671, 1591, 1519, 1440, 1215, 1037, 760, 669; **HRMS (ESI)**: calcd. for $C_{21}H_{22}N_3O_2$ $[M+H]^+$: 348.1712, found: 348.1708.

***N*-(3,4-dimethoxyphenethyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole-1-carboxamide (3h)**

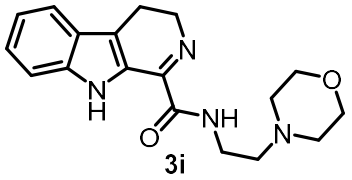


3h

According to general procedure A by using tryptoline **1a** (50.0 mg, 0.29 mmol), 4-(2-isocyanoethyl)-1,2-dimethoxybenzene **2h** (55.5 mg, 0.29 mmol) and IBX (203.2 mg, 0.72 mmol), the titled compound was prepared to yield **3h** as a yellow oil (75.0 mg, 68%); R_f = 0.4 (30% EtOAc in hexane); **^{1}H NMR (400 MHz, CDCl$_3$)**: δ 9.96 (s, 1H), 7.72 (s, 1H), 7.56 (dd, J = 8.0, 0.7 Hz, 1H), 7.39 (d, J = 8.3 Hz, 1H), 7.27 (ddd, J = 8.2, 7.0, 1.1 Hz, 1H), 7.12 (ddd, J = 8.0, 7.0, 0.9 Hz, 1H), 6.83 – 6.75 (m, 3H), 3.99 (dd, J = 9.6, 8.3 Hz, 2H), 3.86 (d, J = 3.8 Hz, 6H), 3.62 (dd, J = 13.6, 7.0 Hz, 2H), 2.92 (dd, J = 9.6, 8.3 Hz, 2H), 2.85 (t, J = 7.2 Hz, 2H); **^{13}C NMR (100 MHz, CDCl$_3$)**: δ 164.2, 151.3, 148.9, 147.7, 136.9, 131.1, 126.6,

124.9, 124.6, 120.6, 120.1, 119.8, 117.5, 112.3, 111.9, 111.4, 55.9, 55.8, 48.4, 40.5, 35.3, 19.1; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3438, 3020, 2401, 1666, 1519, 1215, 1067, 758, 669; **HRMS (ESI)**: calcd. for $C_{22}H_{24}N_3O_3$ $[M+H]^+$: 378.1818, found: 378.1814.

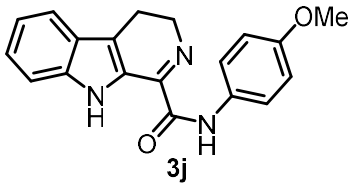
***N*-(2-morpholinoethyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole-1-carboxamide (3i)**



3i

According to general procedure A by using tryptoline **1a** (50.0 mg, 0.29 mmol), 4-(2-isocyanoethyl)morpholine **2i** (0.035 mL, 0.29 mmol) and IBX (203.2 mg, 0.72 mmol), the titled compound was prepared to yield **3i** as a yellow oil (52.5 mg, 55%); R_f = 0.4 (5% MeOH in DCM); **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 9.93 (s, 1H), 7.90 (s, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.40 (d, J = 8.3 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.15 – 7.10 (m, 1H), 4.04 (dd, J = 9.5, 8.3 Hz, 2H), 3.77 – 3.72 (m, 4H), 3.51 (q, J = 6.1 Hz, 2H), 2.95 (dd, J = 9.5, 8.3 Hz, 2H), 2.59 (t, J = 6.3 Hz, 2H), 2.55 – 2.48 (m, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 164.4, 151.4, 136.9, 126.7, 124.9, 124.7, 120.1, 119.9, 117.6, 112.3, 66.9, 57.2, 53.4, 48.6, 35.6, 19.1; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3368, 2925, 1667, 1524, 1450, 1068, 748; **HRMS (ESI)**: calcd. for $C_{18}H_{23}N_4O_2$ $[M+H]^+$: 327.1821, found: 327.1821.

***N*-(4-methoxyphenyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole-1-carboxamide (3j)**

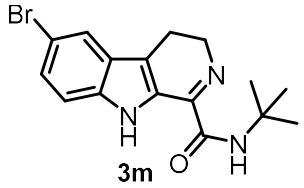


3j

According to general procedure A by using tryptoline **1a** (50.0 mg, 0.29 mmol), 1-isocyano-4-methoxybenzene **2j** (38.6 mg, 0.29 mmol) and IBX (203.2 mg, 0.72 mmol), the titled compound was prepared to yield **3j** as a yellow oil (37.2 mg, 40%); R_f = 0.4 (30% EtOAc in hexane); **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 9.97 (s, 1H), 9.42 (s, 1H), 7.63 – 7.57 (m, 3H), 7.41

(d, *J* = 8.3 Hz, 1H), 7.29 (s, 1H), 7.13 (s, 1H), 6.95 – 6.88 (m, 2H), 4.09 (dd, *J* = 9.6, 8.3 Hz, 2H), 3.81 (s, 3H), 2.99 (dd, *J* = 9.6, 8.3 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 161.7, 156.6, 151.6, 137.1, 130.3, 126.5, 125.2, 124.6, 121.3, 120.2, 119.9, 117.9, 114.3, 112.4, 55.5, 48.5, 19.2; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3433, 2927, 1673, 1591, 1526, 1447, 1373, 1246, 1161, 1034, 828, 747, 666, 520; **HRMS (ESI)**: calcd. for $C_{19}H_{18}N_3O_2$ $[M+H]^+$: 320.1399, found: 320.1392.

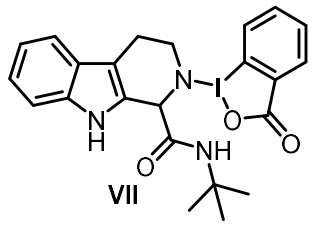
6-bromo-N-(*tert*-butyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole-1-carboxamide (3m)



3m

According to general procedure A by using 6-Bromo-1,2,3,4-tetrahydro-*β*-carboline **1b** (50.0 mg, 0.2 mmol), *tert*-butyl isocyanide **2a** (38.6 mg, 0.2 mmol) and IBX (139.38 mg, 0.49 mmol), the titled compound was prepared to yield **3m** as a yellow oil (43.0 mg, 62%); R_f = 0.6 (30% EtOAc in hexane); **^{1}H NMR (300 MHz, $CDCl_3$)**: δ 10.06 (s, 1H), 7.69 (d, *J* = 1.6 Hz, 1H), 7.51 (s, 1H), 7.33 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.26 – 7.21 (m, 1H), 4.04 – 3.96 (m, 2H), 2.93 – 2.84 (m, 2H), 1.46 (s, 9H); **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 163.7, 151.9, 135.6, 127.9, 127.8, 126.5, 122.6, 116.9, 113.9, 113.4, 51.3, 48.5, 28.8, 19.2; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3434, 3359, 3018, 2959, 2926, 2401, 1591, 1526, 1458, 1365, 1314, 1281, 1216, 932, 866, 760, 669, 586, 513; **HRMS (ESI)**: calcd. for $C_{16}H_{19}BrN_3O$ $[M+H]^+$: 348.0711, found: 348.0703 .

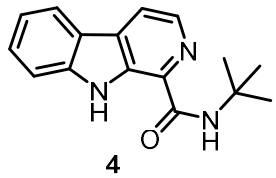
***N*-(*tert*-butyl)-2-(3-oxo-1λ^3-benzo[*d*][1,2]iodaoxol-1(3*H*)-yl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole-1-carboxamide (VII)**



VII

Yellow solid (15.1 mg, 25%); **m.p**: 95-97 °C; R_f = 0.2 (20% EtOAc in hexane); **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 11.40 (s, 1H), 7.81 (d, J = 8.1 Hz, 2H), 7.39 (d, J = 3.7 Hz, 3H), 7.31 – 7.26 (m, 1H), 7.20 – 7.14 (m, 2H), 7.06 – 7.01 (m, 1H), 6.14 (s, 1H), 3.84 – 3.78 (m, 2H), 3.54 (t, J = 6.7 Hz, 2H), 1.46 (s, 9H); **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 176.5, 169.38, 162.2, 142.3, 139.8, 137.4, 130.8, 129.4, 128.1, 128.1, 127.9, 127.3, 121.4, 121.0, 112.8, 92.4, 51.7, 40.6, 29.6, 28.3, 25.0; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3431, 3020, 2401, 1641, 1514, 1216, 1047, 762, 669; **HRMS (ESI)**: calcd. for $C_{23}H_{25}IN_3O_3$ $[M+H]^+$: 518.0941, found: 518.0935.

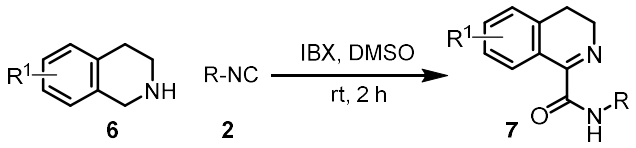
***N*-(*tert*-butyl)-9*H*-pyrido[3,4-*b*]indole-1-carboxamide (4)**



4

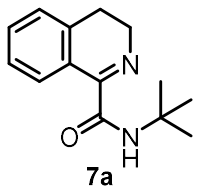
Pale yellow oil (5.0 mg, 16%); R_f = 0.5 (20% EtOAc in hexane); **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 10.37 (s, 1H), 8.34 (d, J = 5.1 Hz, 1H), 8.12 (dd, J = 5.4, 2.4 Hz, 2H), 8.06 (dd, J = 5.1, 0.5 Hz, 1H), 7.57 (ddd, J = 8.1, 7.0, 1.1 Hz, 1H), 7.54 – 7.48 (m, 1H), 7.29 (ddd, J = 8.0, 7.0, 1.1 Hz, 1H), 1.57 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 166.0, 141.0, 136.9, 135.4, 132.9, 131.3, 129.1, 121.8, 120.6, 120.1, 117.5, 111.8, 51.1, 28.9; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3434, 3020,2401, 1657, 1527, 1215, 1048, 761,669; **HRMS (ESI)**: calcd. for $C_{16}H_{18}N_3O$ $[M+H]^+$: 268.1450, found: 268.1450.

2.2 General procedure B for the synthesis of 7a-7m



IBX (2.5 equiv) was taken in a round bottom flask, then DMSO (2.0 mL) was added and stirred at room temperature for 15 minutes. After complete solubilisation of IBX, 1,2,3,4-tetrahydrosioquinoline (THIQ) **6** (1.0 equiv) and isocyanide **2** (1.0 equiv) were added and stirred at room temperature for 2 h. After completion of reaction (based on TLC), the reaction mixture was diluted with ethyl acetate (10 mL) and then saturated solution of sodium thiosulfate (10 mL) was added and stirred for 10 minutes. The organic layer was separated and aqueous layer was again washed with ethyl acetate. The combined organic layers were washed with saturated solution of sodium bicarbonate (15 mL), dried over anhydrous Na_2SO_4, concentrated *in vacuo* and the crude was purified by silica gel column chromatography to afford different THIQ derived imino-carboxamides **7**.

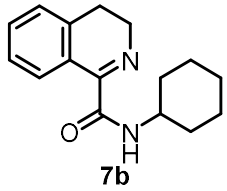
***N*-(*tert*-butyl)-3,4-dihydroisoquinoline-1-carboxamide (7a)**[18]



According to general procedure B by using THIQ **6a** (50.0 mg, 0.37 mmol), *tert*-butyl isocyanide **2a** (0.035 mL, 0.37 mmol) and IBX (262.7 mg, 0.93 mmol), the titled compound was prepared to yield **7a** as a pale yellow oil (60.6 mg, 71%); R_f = 0.5 (20% EtOAc in hexane); **^{1}H NMR (300 MHz, $CDCl_3$)**: δ 8.18 (dd, J = 7.6, 1.3 Hz, 1H), 7.41 – 7.26 (m, 3H), 7.20 – 7.14 (m, 1H), 3.79 – 3.70 (m, 2H), 2.74 – 2.66 (m, 2H), 1.46 (s, 9H); **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 163.7, 160.5, 138.1, 131.1, 128.6, 127.0, 126.8, 126.3, 51.0, 47.1, 28.6,

25.9; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3393, 2925, 1674, 1515, 1247, 1069, 750; HRMS (ESI): calcd. for $C_{14}H_{19}N_2O$ $[M+H]^+$: 231.1497, found: 231.1494.

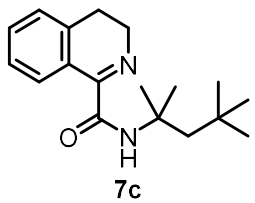
***N*-cyclohexyl-3,4-dihydroisoquinoline-1-carboxamide (7b)**



7b

According to general procedure B by using THIQ **6a** (50.0 mg, 0.37 mmol), cyclohexyl isocyanide **2b** (0.035 mL, 0.37 mmol) and IBX (203.2 mg, 0.93 mmol), the titled compound was prepared to **7b** as a pale yellow solid (65.5 mg, 68%); m.p: 75-78 °C; R_f = 0.5 (20% EtOAc in hexane); **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.19 (dd, J = 7.7, 1.0 Hz, 1H), 7.37 (td, J = 7.4, 1.4 Hz, 1H), 7.31 (td, J = 7.6, 1.4 Hz, 2H), 7.17 (dd, J = 7.3, 0.7 Hz, 1H), 3.92 – 3.83 (m, 1H), 3.79 – 3.73 (m, 2H), 2.75 – 2.68 (m, 2H), 2.04 – 1.97 (m, 2H), 1.79 – 1.72 (m, 2H), 1.69 – 1.60 (m, 2H), 1.42 (ddd, J = 13.2, 10.1, 4.1 Hz, 2H), 1.30 – 1.23 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 163.5, 160.1, 137.9, 131.2, 128.5, 127.1, 126.9, 126.3, 48.1, 47.2, 32.9, 25.8, 25.6, 24.9; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3392, 3016, 2933,2855, 1665, 1517, 1215, 757, 669; **HRMS (ESI)**: calcd. for $C_{16}H_{21}N_2O$ $[M+H]^+$: 257.1654, found: 257.1649.

***N*-(2,4,4-trimethylpentan-2-yl)-3,4-dihydroisoquinoline-1-carboxamide (7c)**

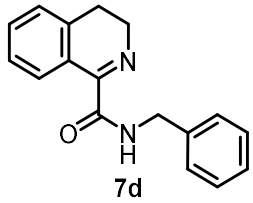


7c

According to general procedure B by using THIQ **6a** (50.0 mg, 0.37 mmol), 2-isocyano-2,4,4-trimethylpentane **2c** (52.2 mg, 0.37 mmol) and IBX (262.7 mg, 0.93 mmol), the titled compound was prepared to yield **7c** as a pale yellow oil (66.7 mg, 62%); R_f = 0.5 (20% EtOAc in hexane); **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.20 (dd, J = 7.7, 1.1 Hz, 1H), 7.42 (s, 1H), 7.32 (dtd, J = 22.2, 7.5, 1.4 Hz, 2H), 7.16 (dd, J = 7.2, 0.7 Hz, 1H), 3.77 – 3.70 (m, 2H),

2.72 – 2.65 (m, 2H), 1.85 (s, 2H), 1.51 (s, 6H), 1.04 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 163.2, 160.2, 138.1, 130.9, 128.6, 126.9, 126.7, 126.3, 54.7, 51.6, 47.1, 31.6, 31.5, 28.9, 25.9; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3377, 2952, 1676, 1611, 1517, 1240, 1066, 755, 605; HRMS (ESI): calcd. for $C_{18}H_{27}N_2O$ $[M+H]^+$: 287.2123, found: 287.2116.

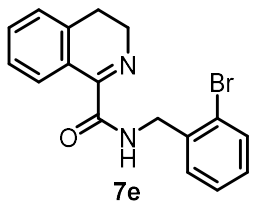
***N*-benzyl-3,4-dihydroisoquinoline-1-carboxamide (7d)**



7d

According to general procedure B by using THIQ **6a** (50.0 mg, 0.37 mmol), benzyl isocyanide **2d** (0.027 mL, 0.37 mmol) and IBX (262.7 mg, 0.93 mmol), the titled compound was prepared to yield **7d** as a colourless oil 64.6 mg, 65%); R_f = 0.4 (30% EtOAc in hexane); **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.24 (dd, J = 7.7, 0.9 Hz, 1H), 7.77 (s, 1H), 7.41 – 7.27 (m, 7H), 7.18 (d, J = 6.7 Hz, 1H), 4.58 (d, J = 6.1 Hz, 2H), 3.75 (dd, J = 8.4, 6.6 Hz, 2H), 2.74 – 2.69 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 164.2, 159.7, 138.1, 137.9, 131.3, 128.7, 128.5, 127.9, 127.5, 127.1, 126.9, 126.3, 47.2, 43.4, 25.8; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3391, 3018, 1672, 1611, 1520, 1454, 1216, 1064, 765, 669; **HRMS (ESI)**: calcd. for $C_{17}H_{17}N_2O$ $[M+H]^+$: 265.1341, found: 265.1337.

***N*-(2-bromobenzyl)-3,4-dihydroisoquinoline-1-carboxamide (7e)**

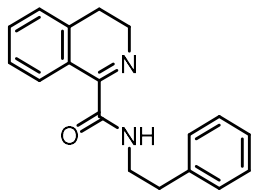


7e

According to general procedure B by using THIQ **6a** (50.0 mg, 0.37 mmol), 2-bromo benzyl isocyanide **2e** (73.6 mg, 0.37 mmol) and IBX (262.7 mg, 0.93 mmol) the titled compound

was prepared to yield **7e** as a pale yellow oil (77.60 mg, 60%); R_f = 0.4 (30% EtOAc in hexane); **^{1}H NMR (300 MHz, $CDCl_3$)**: δ 8.22 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.91 (s, 1H), 7.56 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.45 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.37 (td, *J* = 7.4, 1.5 Hz, 1H), 7.34 – 7.26 (m, 2H), 7.20 – 7.11 (m, 2H), 4.66 (d, *J* = 6.3 Hz, 2H), 3.81 – 3.73 (m, 2H), 2.75 – 2.67 (m, 2H); **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 164.2, 159.5, 137.9, 137.2, 132.8, 131.3, 130.1, 129.1, 128.5, 127.7, 127.1, 126.9, 126.2, 123.8, 47.2, 43.6, 25.8; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3394, 3019, 2401, 1674, 1611, 1518, 1215, 1030, 931, 557, 669; **HRMS (ESI)**: calcd. for $C_{17}H_{16}BrN_2O$ $[M+H]^+$: 343.0446, found: 343.0433.

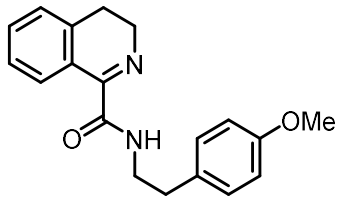
***N*-phenethyl-3,4-dihydroisoquinoline-1-carboxamide (7f)**[19]



7f

According to general procedure B by using THIQ **6a** (50.0 mg, 0.37 mmol), (2-isocyanoethyl)benzene **2f** (49.2 mg, 0.37 mmol) and IBX (262.7 mg, 0.93 mmol), the titled compound was prepared to yield **7f** as a pale yellow oil mixture (64.0 mg, 61%); R_f = 0.5 (40% EtOAc in hexane); **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.16 (d, *J* = 7.5 Hz, 1H), 7.52 – 7.46 (m, 1H), 7.36 (dt, *J* = 7.4, 3.7 Hz, 1H), 7.33 – 7.29 (m, 2H), 7.24 (dd, *J* = 7.4, 4.3 Hz, 3H), 7.20 – 7.14 (m, 2H), 3.77 – 3.69 (m, 2H), 3.68 – 3.61 (m, 2H), 2.91 (t, *J* = 7.3 Hz, 2H), 2.73 – 2.66 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 164.3, 159.8, 138.9, 137.9, 131.2, 128.7, 128.5, 128.4, 127.1, 126.9, 126.4, 47.1, 40.6, 35.8, 25.7; **IR** ($CHCl_3$) ν_{max} (cm^{-1}) = 3400, 3020, 1671, 1522, 1215, 1068, 760, 669; **HRMS (ESI)**: calcd. for $C_{18}H_{19}N_2O$ $[M+H]^+$: 279.1497, found: 279.1495.

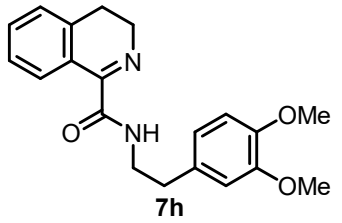
***N*-(4-methoxyphenethyl)-3,4-dihydroisoquinoline-1-carboxamide (7g)**



7g

According to general procedure B by using THIQ **6a** (50.0 mg, 0.37 mmol), 1-(2-isocyanoethyl)-4-methoxybenzene **2g** (60.5 mg, 0.37 mmol) and IBX (262.7 mg, 0.93 mmol), the titled compound was prepared to yield **7g** as a yellow oil (76.5, 66%); R_f = 0.5 (40% EtOAc in hexane); **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.15 (dd, *J* = 7.7, 0.9 Hz, 1H), 7.47 (d, *J* = 4.4 Hz, 1H), 7.37 (td, *J* = 7.4, 1.4 Hz, 1H), 7.33 – 7.28 (m, 1H), 7.16 (dd, *J* = 6.9, 4.6 Hz, 3H), 6.89 – 6.83 (m, 2H), 3.79 (s, 3H), 3.74 (dd, *J* = 8.9, 6.1 Hz, 2H), 3.65 – 3.57 (m, 2H), 2.85 (t, *J* = 7.3 Hz, 2H), 2.73 – 2.67 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 164.3, 159.8, 158.2, 137.9, 131.2, 130.9, 129.7, 128.4, 127.1, 126.9, 126.2, 113.9, 55.2, 47.2, 40.8, 34.9, 25.8; **IR ($CHCl_3$) ν_{max} (cm^{-1})** =3408, 3020, 1616, 1514, 1216, 1068, 764, 669; **HRMS (ESI)**: calcd. for $C_{19}H_{21}N_2O_2$ $[M+H]^+$: 309.1603, found: 309.1592.

***N*-(3,4-dimethoxyphenethyl)-3,4-dihydroisoquinoline-1-carboxamide (7h)**

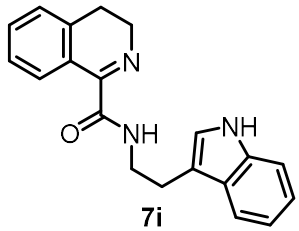


7h

According to general procedure B by using THIQ **6a** (50.0 mg, 0.37 mmol), 4-(2-isocyanoethyl)-1,2-dimethoxybenzene **2h** (71.8 mg, 0.37 mmol) and IBX (262.7 mg, 0.93 mmol) the titled compound was prepared to yield **7h** as a yellow oil (85.1 mg, 67%); R_f = 0.5 (40% EtOAc in hexane); **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.16 (dd, *J* = 7.7, 0.9 Hz, 1H), 7.51 (s, 1H), 7.37 (td, *J* = 7.4, 1.4 Hz, 1H), 7.31 (td, *J* = 7.6, 1.3 Hz, 1H), 7.20 – 7.15 (m, 1H), 6.84 – 6.77 (m, 3H), 3.87 (d, *J* = 5.3 Hz, 6H), 3.76 – 3.70 (m, 2H), 3.62 (dd, *J* = 13.5, 6.9 Hz,

2H), 2.86 (t, *J* = 7.1 Hz, 2H), 2.73 – 2.67 (m, 2H); **^{13}C NMR (100 MHz, CDCl$_3$)**: δ 164.3, 159.8, 148.9, 147.6, 137.8, 131.4, 131.2, 128.3, 127.0, 126.9, 126.2, 120.6, 112.0, 111.4, 55.8, 55.8, 47.1, 40.7, 35.3, 25.7; **IR (CHCl$_3$) ν_{max} (cm^{-1})** = 3421, 3020, 1638, 1516,1069, 760, 669; **HRMS (ESI)**: calcd. for $C_{20}H_{23}N_2O_3$ $[M+H]^+$: 339.1709, found: 339.1706.

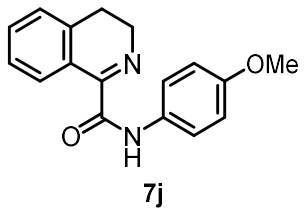
***N*-(2-(1*H*-indol-3-yl)ethyl)-3,4-dihydroisoquinoline-1-carboxamide (7i)**



7i

According to general procedure B by using THIQ **6a** (50.0 mg, 0.37 mmol), 3-(2-isocyanoethyl)-1*H*-indole **2m** (63.9 mg , 0.37 mmol) and IBX (262.7 mg, 0.93 mmol), the titled compound was prepared to yield **7i** as a pale brown solid (74.0 mg, 62%); m.p: 60-62 °C; R_f = 0.4 (40% EtOAc in hexane); **^{1}H NMR (400 MHz, CDCl$_3$)**: δ 8.26 (s, 1H), 8.17 (d, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.53 (s, 1H), 7.39 – 7.28 (m, 3H), 7.21 – 7.15 (m, 2H), 7.13 – 7.09 (m, 1H), 7.04 (s, 1H), 3.79 – 3.67 (m, 4H), 3.07 (t, *J* = 7.0 Hz, 2H), 2.73 – 2.64 (m, 2H); **^{13}C NMR (100 MHz, CDCl$_3$)**: δ 164.5, 159.9, 137.9, 136.4, 131.2, 128.4, 127.3, 127.1, 126.9, 126.2, 122.0, 119.3, 118.7, 112.9, 111.2, 47.1, 39.6, 25.7, 25.4; **IR (CHCl$_3$) ν_{max} (cm^{-1})** = 3401, 3019, 1669, 1523, 1426, 1216, 1068, 762, 669; **HRMS (ESI)**: calcd. for $C_{20}H_{20}N_3O$ $[M+H]^+$: 318.1606, found: 318.1602.

***N*-(4-methoxyphenyl)-3,4-dihydroisoquinoline-1-carboxamide (7j)**

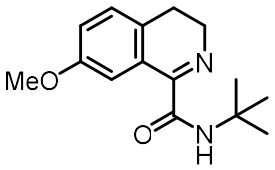


7j

According to general procedure by using THIQ **6a** (50.0 mg, 0.37 mmol), 1-isocyano-4-methoxybenzene **2j** (50.0 mg, 0.37 mmol) and IBX (262.7 mg, 0.93 mmol), the titled

compound was prepared to yield **7j** as a pale yellow oil (44.2 mg, 42%); R_f = 0.4 (30% EtOAc in hexane); **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 9.97 (s, 1H), 9.42 (s, 1H), 7.63 – 7.57 (m, 3H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.29 (s, 1H), 7.13 (s, 1H), 6.95 – 6.88 (m, 2H), 4.09 (dd, *J* = 9.6, 8.3 Hz, 2H), 3.81 (s, 3H), 2.99 (dd, *J* = 9.6, 8.3 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 161.7, 156.6, 151.6, 137.1, 130.3, 126.5, 125.2, 124.6, 121.4, 120.2, 119.9, 117.9, 114.3, 112.4, 55.5, 48.5, 19.2; ; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3396, 3020, 1613, 1522, 1215, 1045, 758, 669; **HRMS (ESI)**: calcd. for $C_{17}H_{17}N_2O_2$ $[M+H]^+$: 281.1290, found: 281.1282.

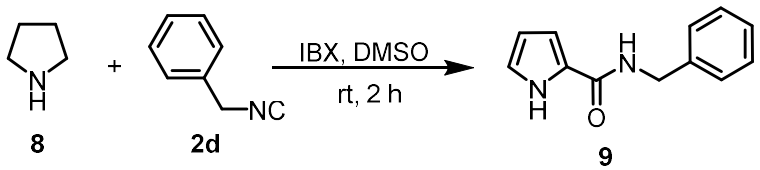
***N*-(*tert*-butyl)-7-methoxy-3,4-dihydroisoquinoline-1-carboxamide (7m)**



7m

According to general procedure B by using 6-methoxy-1,2,3,4-tetrahydroisoquinoline **6b** (50.0 mg, 0.306 mmol), *tert*-butyl isocyanide **2a** (0.03 mL, 0.306 mmol) and IBX (214.4 mg, 0.76 mmol), the titled compound was prepared to yield **7m** as a pale yellow oil (28.0 mg, 35%); R_f = 0.5 (30% EtOAc in hexane); **^{1}H NMR (300 MHz, $CDCl_3$)**: δ 7.87 (d, *J* = 2.7 Hz, 1H), 7.33 (s, 1H), 7.08 (d, *J* = 8.3 Hz, 1H), 6.93 (dd, *J* = 8.3, 2.7 Hz, 1H), 3.83 (s, 3H), 3.75 – 3.67 (m, 2H), 2.69 – 2.58 (m, 2H), 1.46 (s, 9H); **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 163.7, 160.1, 158.3, 130.2, 127.8, 126.9, 117.7, 113.5, 55.5, 50.9, 47.5, 28.6, 25.1; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3401, 3020, 1672, 1518, 1216, 1045, 762, 669; **HRMS (ESI)**: calcd. for $C_{15}H_{21}N_2O_2$ $[M+H]^+$: 261.1603, found: 261.1592.

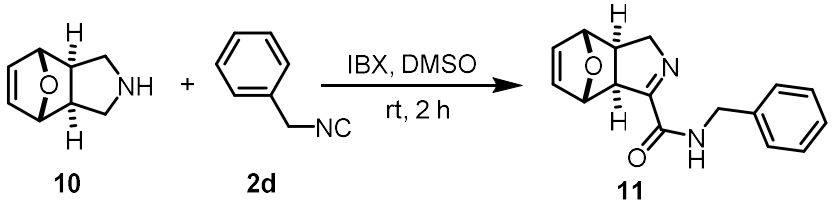
***N*-benzyl-1*H*-pyrrole-2-carboxamide (9)**



8 **2d** **9**

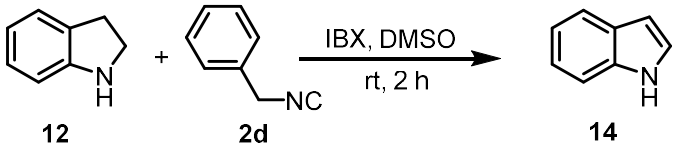
According to general procedure A by using pyrrolidine **8** (100.0 mg, 1.41 mmol), benzylisocyanide **2d** (164.7 mg, 1.41 mmol) and IBX (984.2 mg, 3.52 mmol), the titled compound was prepared to yield **9** as a pale brown sticky oil (40.0 mg, 14%); R_f = 0.7 (30% EtOAc in hexane); **^{1}H NMR (300 MHz, $CDCl_3$)**: δ 9.90 (s, 1H), 7.37 – 7.27 (m, 5H), 6.94 – 6.86 (m, 1H), 6.58 – 6.53 (m, 1H), 6.25 (d, J = 14.4 Hz, 1H), 6.23 – 6.18 (m, 1H), 4.61 (d, J = 5.9 Hz, 2H); **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 161.2, 138.4, 128.7, 127.7, 127.5, 125.7, 121.8, 109.7, 108.9, 43.4; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3355, 2924, 1638, 1448, 1323, 1217, 1088, 770; **HRMS (ESI)**: calcd. for $C_{12}H_{13}N_2O$ $[M+H]^+$: 201.1028, found: 201.1021.

(3aS,4S,7R,7aR)-*N*-benzyl-3a,4,7,7a-tetrahydro-1*H*-4,7-epoxyisoindole-3-carboxamide (11)



According to general procedure A by using pyrrolidine **10** (100.0 mg, 1.41 mmol), benzyl isocyanide **2d** (85.4 mg, 1.41 mmol) and IBX (510.3 mg, 3.52 mmol), the titled compound was prepared to yield **11** as a white solid (60.0 mg, 31%); **m.p**: 124-125 °C; R_f = 0.3 (40% EtOAc in hexane); **^{1}H NMR (300 MHz, $CDCl_3$)**: δ 7.43 (s, 1H), 7.37 – 7.26 (m, 5H), 6.44 (dd, J = 5.9, 1.7 Hz, 1H), 6.36 (dd, J = 5.9, 1.6 Hz, 1H), 5.22 (d, J = 1.2 Hz, 1H), 4.77 (d, J = 1.1 Hz, 1H), 4.51 (qd, J = 14.8, 6.0 Hz, 2H), 4.09 (ddd, J = 18.0, 8.7, 1.1 Hz, 1H), 3.79 (dt, J = 18.0, 3.2 Hz, 1H), 3.45 (dd, J = 7.4, 1.7 Hz, 1H), 2.62 (ddd, J = 8.6, 7.5, 3.6 Hz, 1H); **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 167.6, 161.8, 137.6, 136.7, 136.6, 128.7, 127.8, 127.6, 84.3, 80.9, 63.5, 57.1, 43.9, 43.3; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3396, 1624, 1531, 1071; **HRMS (ESI)**: calcd. for $C_{16}H_{17}N_2O_2$ $[M+H]^+$: 269.1290, found: 269.1292.

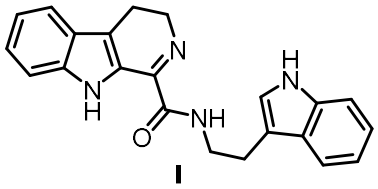
1*H*-indole (14)



According to general procedure A by using indoline **12** (100.0 mg, 1.41 mmol), benzylisocyanide **2d** (98.3 mg, 1.41 mmol) and IBX (587.4 mg, 3.52 mmol), the titled compound was prepared to yield **14** as a white solid (40.0 mg, 14%); **m.p**: 50-54 °C; R_f = 0.6 (20% EtOAc in hexane); **^{1}H NMR (300 MHz, $CDCl_3$)**: δ 8.03 (s, 1H), 7.64 (dd, J = 7.8, 0.7 Hz, 1H), 7.39 – 7.33 (m, 1H), 7.23 – 7.08 (m, 3H), 6.54 (ddd, J = 3.0, 2.0, 0.9 Hz, 1H); **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 135.8, 127.8, 124.1, 121.9, 120.7, 119.8, 110.9, 102.6; **IR ($CHCl_3$) ν_{max} (cm^{-1})** =3414, 1632, 1409, 1217, 1087, 767; **HRMS (ESI)**: calcd. for C_8H_8N $[M+H]^+$: 118.0657, found: 118.065.

2.3 Total synthesis of Alangiobussine (I) and Alangiobussinine (II)

2.3.1. Total synthesis of Alangiobussine (I)[17]

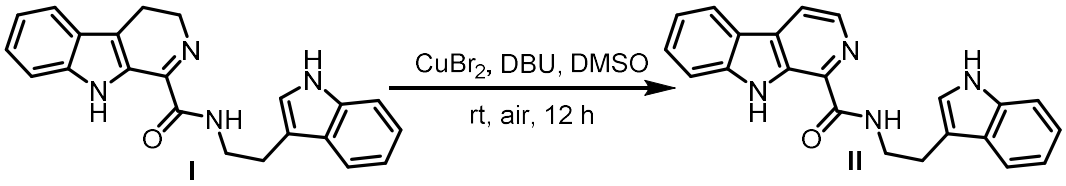


I

According to general procedure A by using tryptoline **1a** (50.0 mg, 0.3 mmol), 3-(2-isocyanoethyl)-1*H*-indole **2m** (49.4 mg, 0.3 mmol) and IBX (203.2 mg, 0.7 mmol), alangiobussine **I** was obtained as a yellow solid (66.0 mg, 63%); **m.p**: 152-153 °C; R_f = 0.4 (40% EtOAc in hexane); **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 9.99 (s, 1H), 8.10 (s, 1H), 7.76 (t, J = 5.5 Hz, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.35 (dd, J = 17.1, 8.2 Hz, 2H), 7.26 (dd, J = 11.3, 3.9 Hz, 1H), 7.23 – 7.16 (m, 1H), 7.11 (t, J = 7.5 Hz, 2H), 7.01 (d, J = 2.0 Hz, 1H), 4.01 – 3.91 (m, 2H), 3.71 (q, J = 6.9 Hz, 2H), 3.05 (t, J = 7.1 Hz, 2H), 2.94 – 2.85 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 164.3, 151.4, 136.9, 136.3, 127.2, 126.7,

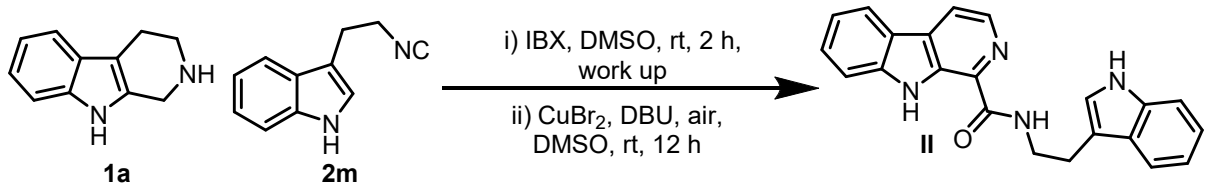
124.9, 124.6, 122.1, 121.9, 120.0, 119.8, 119.4, 118.7, 117.5, 112.8, 112.3, 111.2, 48.4, 39.4, 25.3, 19.1; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3419, 2924, 1663, 1526, 1451, 1074, 769; HRMS (ESI): calcd. for $C_{22}H_{21}N_4O$ $[M+H]^+$: 357.1715, found: 357.1706.

2.3.2 Total synthesis of Alangiobussinine (II)[20]



To a stirred solution of alangiobussine **I** (50.0 mg, 0.37 mmol) in DMSO (1.5 mL), $CuBr_2$ (3.1 mg, 0.014 mmol) and DBU (0.02 mL, 0.37 mmol) were added and stirred at rt for 12 h under air. After completion of reaction (based on TLC), the reaction mixture was diluted with ammonia aqueous solution (5% w/w) and dichloromethane. Two phases were separated, and the aqueous phase was twice extracted with dichloromethane. The combined organic layers were separated and dried over Na_2SO_4, concentrated *in vacuo* and the crude was purified by silica gel column chromatography to afford alangiobussinine **II** as a pale yellow solid (35.0 mg, 70%); **m.p**: 190-192 °C; R_f = 0.4 (40% EtOAc in hexane); **^{1}H NMR (300 MHz, DMSO-*d*$_6$)**: δ 11.76 (s, 1H), 10.82 (s, 1H), 9.03 (t, *J* = 6.0 Hz, 1H), 8.39 (d, *J* = 5.0 Hz, 1H), 8.33 (d, *J* = 5.1 Hz, 1H), 8.27 (d, *J* = 7.9 Hz, 1H), 7.82 (d, *J* = 8.2 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.61 – 7.54 (m, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.30 – 7.22 (m, 2H), 7.12 – 7.05 (m, 1H), 7.03 – 6.96 (m, 1H), 3.73 (dd, *J* = 14.4, 6.7 Hz, 2H), 3.06 (t, *J* = 7.5 Hz, 2H); **^{13}C NMR (75 MHz, DMSO-*d*$_6$)**: δ 165.4 141.6, 136.6, 136.3, 134.4, 132.6, 130.6, 128.7, 127.3, 122.6, 121.7, 120.9, 119.9, 119.7, 118.4, 118.2, 117.8, 112.9, 111.8, 111.4, 39.4, 25.4; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3431, 3019, 1654, 1528, 1453, 1215, 758, 669; HRMS (ESI): calcd. for $C_{22}H_{19}N_4O$ $[M+H]^+$: 355.1559, found: 355.1559.

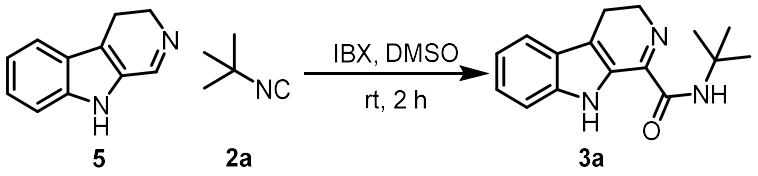
2.3.3. Gram-scale alangibussinine (II) sequential manner synthesis



IBX (8.31 g, 1.16 mmol) was taken in a round bottom flask, then DMSO (60.0 mL) was added and stirred at room temperature for 15 minutes. After complete solubilisation of IBX, tryptoline **1** (2.0 g, 11.61 mmol) and 3-(2-isocyanoethyl)-1*H*-indole **2m** (1.98 g, 11.61 mmol) were added and stirred at room temperature for 2 h. After completion of reaction (based on TLC), the reaction mixture was diluted with ethyl acetate (15 mL) and saturated solution of sodium thiosulfate (15 mL) was added and stirred for 10 minutes. The organic layer was separated and the aqueous layer was again washed with ethyl acetate. The combined organic layers were washed with saturated solution of sodium bicarbonate (15 mL), dried over anhydrous Na_2SO_4, concentrated in *vacuo* and the crude obtained was used for next step without further purification. The crude was dissolved in DMSO, then $CuBr_2$ (259.37 mg, 1.16 mmol) and DBU (1.73 mL, 11.61 mmol) were added and stirred for 12 h under air. After completion of reaction (based on TLC), the reaction mixture was diluted with ammonia aqueous solution (5% w/w) and dichloromethane. Two phases were separated, and the aqueous phase was twice extracted with dichloromethane. The combined organic layers were separated and dried over Na_2SO_4, concentrated *in vacuo* and the crude was purified by silica gel column chromatography to afford alangiobussinine **II** as a pale yellow solid (1.85 g, 45%)

3. Control Experiments

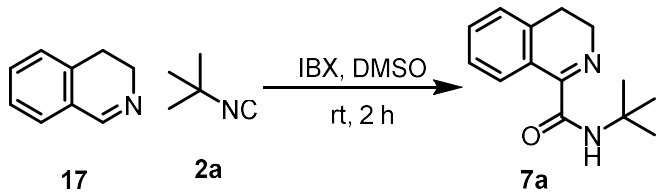
3.1. Reaction of 3,4-dihydro-*β*-carboline 5 with *tert*-butyl isocyanide 2a:



5 2a 3a

IBX (205.6 mg, 0.73 mmol) was taken in a round bottom flask, then DMSO (2.0 mL) was added and stirred at room temperature for 15 minutes. After complete solubilisation of IBX, 3,4-dihydro-*β*-carboline **5** (50.0 mg, 0.29 mmol) and *tert*-butyl isocyanide **2a** (0.03 mL, 0.29 mmol) were added and stirred at room temperature for 2 h. After completion of reaction (based on TLC), the reaction mixture was diluted with ethyl acetate (10 mL) and then saturated solution of sodium thiosulfate (10 mL) was added and stirred for 10 minutes. The organic layer was separated and aqueous layer was again washed with ethyl acetate. The combined organic layers were washed with saturated solution of sodium bicarbonate (15 mL), dried over anhydrous Na_2SO_4, concentrated *in vacuo* and crude was purified by silica gel column chromatography to afford **3a** (54.5 mg, 69%).

3.2. Reaction of 3,4-dihydroisoquinoline 17 with *tert*-butyl isocyanide 2a:



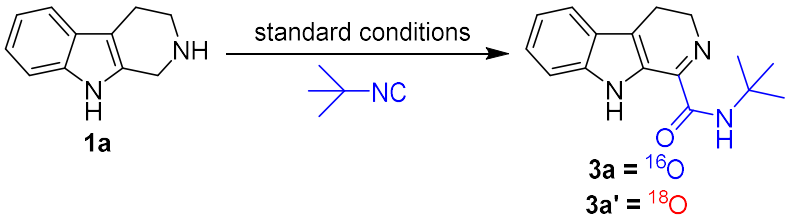
17 2a 7a

IBX (266.8 mg, 0.95 mmol) was taken in a round bottom flask, then DMSO (2.0 mL) was added and stirred at room temperature for 15 minutes. After complete solubilisation of IBX, 3,4-Dihydroisoquinoline (DHIQ) **17** (50.0 mg, 0.38 mmol) and *tert*-butyl isocyanide **2a** (0.043 mL, 0.38 mmol) were added and stirred at room temperature for 2 h. After completion of reaction (based on TLC), the reaction mixture was diluted with ethyl acetate (10 mL) and then saturated solution of sodium thiosulfate (10 mL) was added and stirred for 10 minutes.

The organic layer was separated and aqueous layer was again washed with ethyl acetate. The combined organic layers were washed with saturated solution of sodium bicarbonate (15 mL), dried over anhydrous Na_2SO_4, concentrated *in vacuo* and crude was purified by silica gel column chromatography to afford **7a** (60.0 mg, 68%).

3.3. Effect of additives

Table S2.



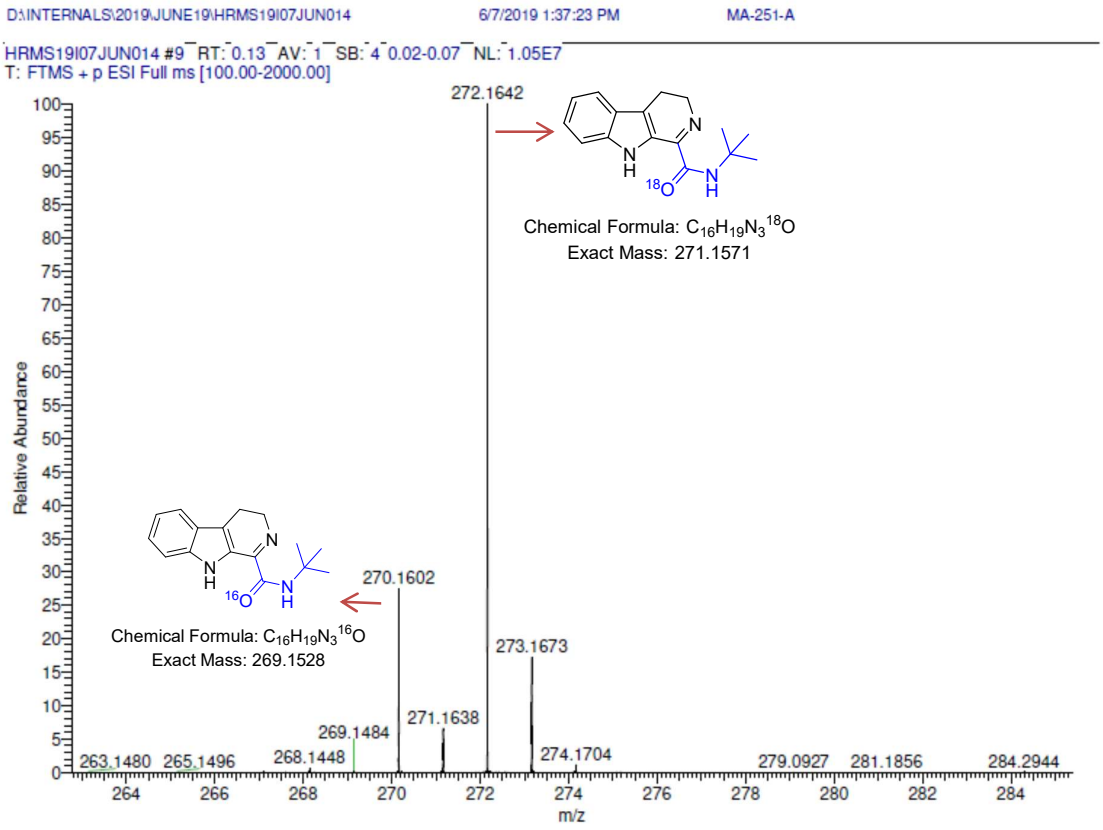
Entry	variation from standard condition	yield of 3a/3a'
1	Anhydrous DMSO, $H_2{}^{18}O$ under Ar	62% (**3a'**)
2	Anhydrous DMSO, 4 Å MS under Ar	50%
3	AcOH (1.0 equiv.)	60%
4	PhCOOH (1.0 equiv.)	59%

Reaction Conditions:

1) IBX (81.3 mg, 0.29 mmol) was taken in a round bottom flask, then anhydrous DMSO (1.5 mL) was added and stirred at room temperature for 15 minutes under argon atmosphere. After complete solubilisation of IBX, $H_2{}^{18}O$ (0.2 mL, 35.0 equiv.) was added, simultaneously **1a** (20.0 mg, 0.116 mmol) and *tert*-butyl isocyanide **2a** (0.014 mL, 0.116mmol) were added and stirred at room temperature for 2 h. After completion of reaction (based on TLC), the reaction mixture was diluted with ethyl acetate (8 mL) and then saturated solution of sodium thiosulfate (8.0 mL) was added and stirred for 10 minutes. The organic layer was separated and aqueous layer was again washed with ethyl acetate. The combined organic layers were washed with saturated solution of sodium bicarbonate (10.0 mL), dried over anhydrous Na_2SO_4, concentrated *in vacuo* and crude was purified by silica gel column chromatography to afford **3a'** (19.5 mg, 62%). The percentage of ^{18}O

enrichment was examined by mass spectrometry as shown in following Figure S1. The calculated data showed 80% ^{18}O enrichment of **3a'**. HRMS (ESI): calcd. for $C_{16}H_{20}N_3{}^{18}O$ $[M+H]^+$: 272.1649, found: 272.1642.

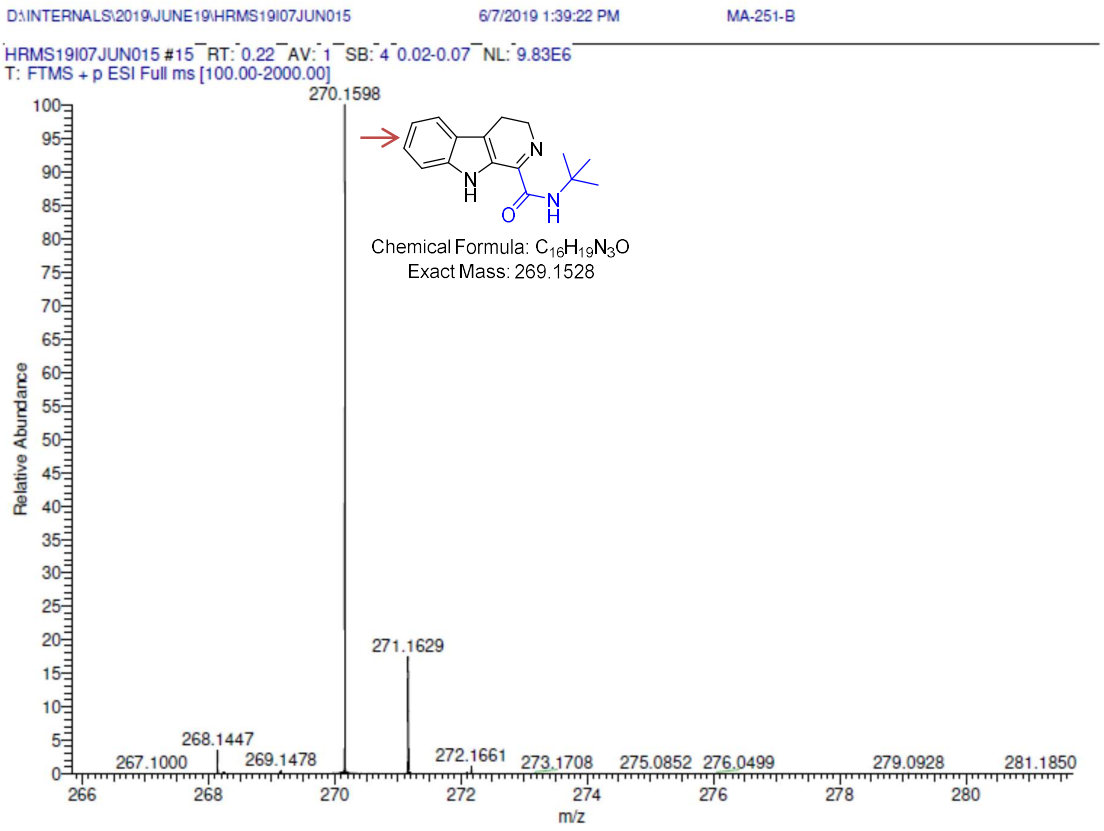
1) **Figure S1: Observation of ^{18}O incorporation by HRMS analysis**



2) IBX (81.3 mg, 0.29 mmol) was taken in a round bottom flask, then anhydrous DMSO (1.8 mL) was added and stirred at room temperature for 15 minutes under argon atmosphere. After complete solubilisation of IBX, 4 Å MS (50 mg) was added, simultaneously **1a** (20.0 mg, 0.116 mmol) and *tert*-butyl isocyanide **2a** (0.014 mL, 0.116 mmol) were added stirred at room temperature for 2 h. After completion of reaction (based on TLC), the reaction mixture was diluted with ethyl acetate (8 mL) and then saturated solution of sodium thiosulfate (8 mL) was added and stirred for 10 minutes. The organic layer was separated and aqueous layer was again washed with ethyl acetate. The combined organic layers were washed with saturated solution of sodium bicarbonate (10 mL), dried

over anhydrous Na_2SO_4, concentrated *in vacuo* and crude was purified by silica gel column chromatography to afford **3a** (15.8 mg, 50%).

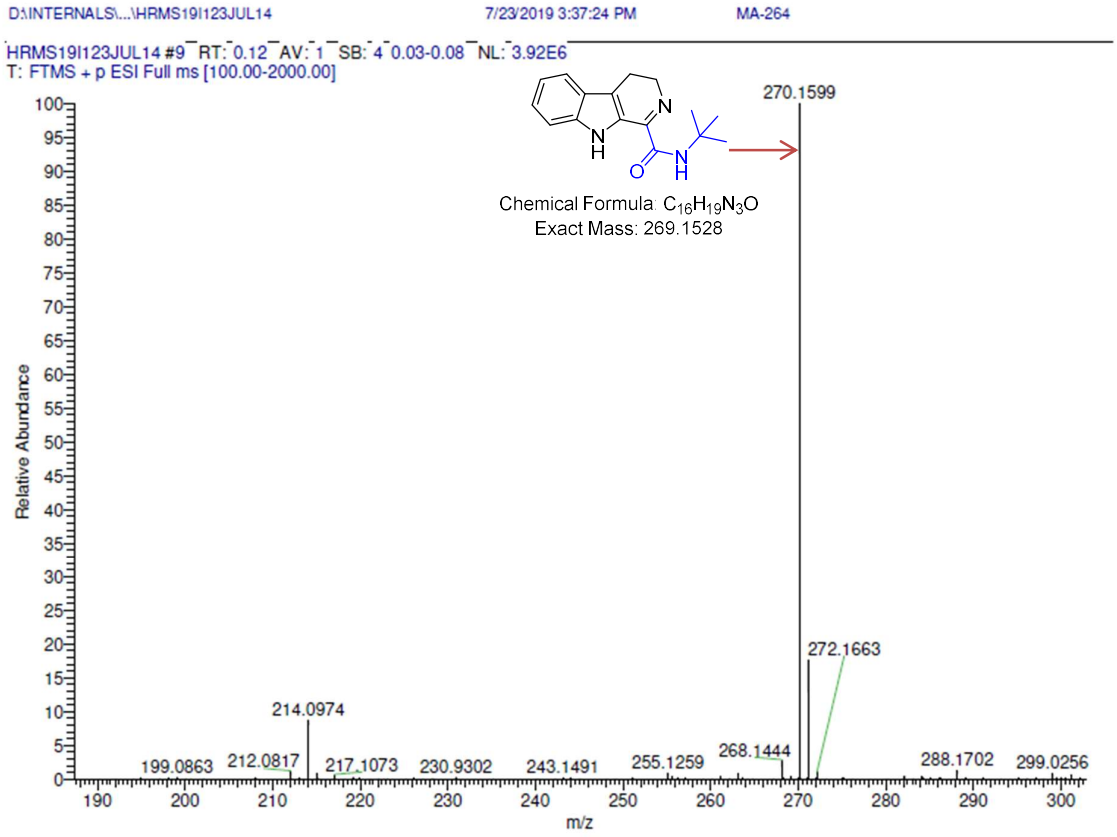
Figure S2: HRMS analysis of compound 3a (entry 3, Table 1)



3) IBX (81.3 mg, 0.29 mmol) was taken in a round bottom flask, then anhydrous DMSO (2.2 mL) was added and stirred at room temperature for 15 minutes under argon atmosphere. After complete solubilisation of IBX, **1a** (20.0 mg, 0.116 mmol), acetic acid (0.02 ml, 0.116 mmol 1.0 equiv.) and *tert*-butyl isocyanide **2a** (0.013 mL, 0.16 mmol) were added and stirred at room temperature for 2 h. After completion of reaction (based on TLC), the reaction mixture was diluted with ethyl acetate (8 mL) and then saturated solution of sodium thiosulfate (8 mL) was added and stirred for 10 minutes. The organic layer was separated and aqueous layer was again washed with ethyl acetate. The combined organic layers were washed with saturated solution of sodium bicarbonate (10 mL), dried over anhydrous

Na_2SO_4, concentrated *in vacuo* and crude was purified by silica gel column chromatography to afford **3a** (19.0 mg, 60%).

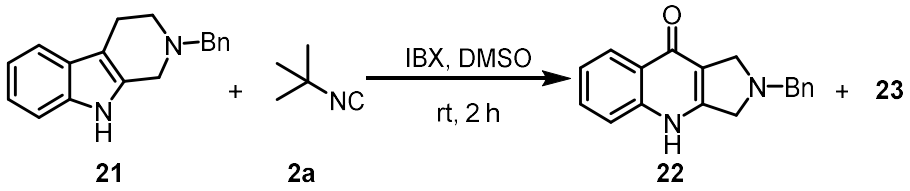
Figure S3: HRMS analysis of compound 3a (entry 4, Table 1)s



4) IBX (81.3 mg, 0.29 mmol) was taken in a round bottom flask, then anhydrous DMSO (2.2 mL) was added and stirred at room temperature for 15 minutes under argon atmosphere. After complete solubilisation of IBX, **1a** (20.0 mg, 0.116 mmol), benzoic acid (14.18 mg, 0.116 mmol 1.0 equiv.) and *tert*-butyl isocyanide **2a** (0.013 mL, 0.16 mmol) were added and stirred at room temperature for 2 h. After completion of reaction (based on TLC), the reaction mixture was diluted with ethyl acetate (8 mL) and then saturated solution of sodium thiosulfate (8 mL) was added and stirred for 10 minutes. The organic layer was separated and aqueous layer was again washed with ethyl acetate. The combined organic layers were washed with saturated solution of sodium bicarbonate (10 mL), dried over anhydrous

Na_2SO_4, concentrated *in vacuo* and crude was purified by silica gel column chromatography to afford **3a** (18.5 mg, 59%).

3.4. Reaction of *N*(2)-benzyl-tryptoline 23 with *tert*-butyl isocyanide 2a:

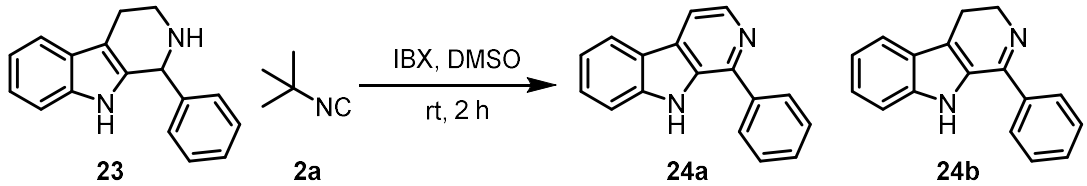


21 **2a** **22**

IBX (133.4 mg, 0.47 mmol) was taken in a round bottom flask, then DMSO (2.0 mL) was added and stirred at room temperature for 15 minutes. After complete solubilisation of IBX, *N*(2)-benzyl-tryptoline **21** (50.0 mg, 0.19 mmol) and *tert*-butyl isocyanide **2a** (0.021 mL, 0.19 mmol) were added and stirred at room temperature for 2 h. After completion of reaction (based on TLC), the reaction mixture was diluted with ethyl acetate (10 mL) and then saturated solution of sodium thiosulfate (10 mL) was added and stirred for 10 minutes. The organic layer was separated and aqueous layer was again washed with ethyl acetate. The combined organic layers were washed with saturated solution of sodium bicarbonate (15 mL), dried over anhydrous Na_2SO_4, concentrated *in vacuo* and crude was purified by silica gel column chromatography to afford compound **22**.

2-benzyl-1,2,3,4-tetrahydro-9*H*-pyrrolo[3,4-*b*]quinolin-9-one (22)[21]: Yellow solid (24.0 mg, 45%); **m.p**: 178-180 °C; R_f = 0.3 (60% EtOAc in hexane); **^{1}H NMR (300 MHz, DMSO-d_6)**: δ 11.94 (s, 1H), 7.95 – 7.87 (m, 1H), 7.44 (dd, J = 6.1, 2.4 Hz, 1H), 7.36 (d, J = 4.0 Hz, 4H), 7.34 – 7.28 (m, 1H), 7.19 (pd, J = 7.2, 3.7 Hz, 2H), 3.87 (s, 2H), 3.78 (s, 2H), 3.24 (s, 2H); **^{13}C NMR (75 MHz, DMSO- d_6)**: δ 189.7, 150.5, 137.6, 136.1, 128.9, 128.4, 127.3, 123.7, 122.9, 121.9, 120.1, 112.0, 110.3, 61.3, 60.3, 48.5; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3229, 3020, 2401, 1638, 1477, 1215, 1070, 758, 669; **HRMS (ESI)**: calcd. for $C_{18}H_{17}N_2O$ $[M+H]^+$: 277.1341, found: 277.1347.

3.5. Reaction of C(1)-phenyl-tryptoline 25 with *tert*-butyl isocyanide 2a:



23 **2a** **24a** **24b**

IBX (140.9 mg 0.5 mmol) was taken in a round bottom flask, then DMSO (2.0 mL) was added and stirred at room temperature for 15 minutes. After complete solubilisation of IBX, C(1)-phenyl-tryptoline **23** (50.0 mg, 0.2 mmol) and *tert*-butyl isocyanide **2a** (0.02 mL, 0.2 mmol) were added and stirred at room temperature for 2 h. After completion of reaction (based on TLC), the reaction mixture was diluted with ethyl acetate (10 mL) and then saturated solution of sodium thiosulfate (10 mL) was added and stirred for 10 minutes. The organic layer was separated and aqueous layer was again washed with ethyl acetate. The combined organic layers were washed with saturated solution of sodium bicarbonate (15 mL), dried over anhydrous Na_2SO_4, concentrated *in vacuo* and crude was purified by silica gel column chromatography to afford **24a** and **24b** respectively.

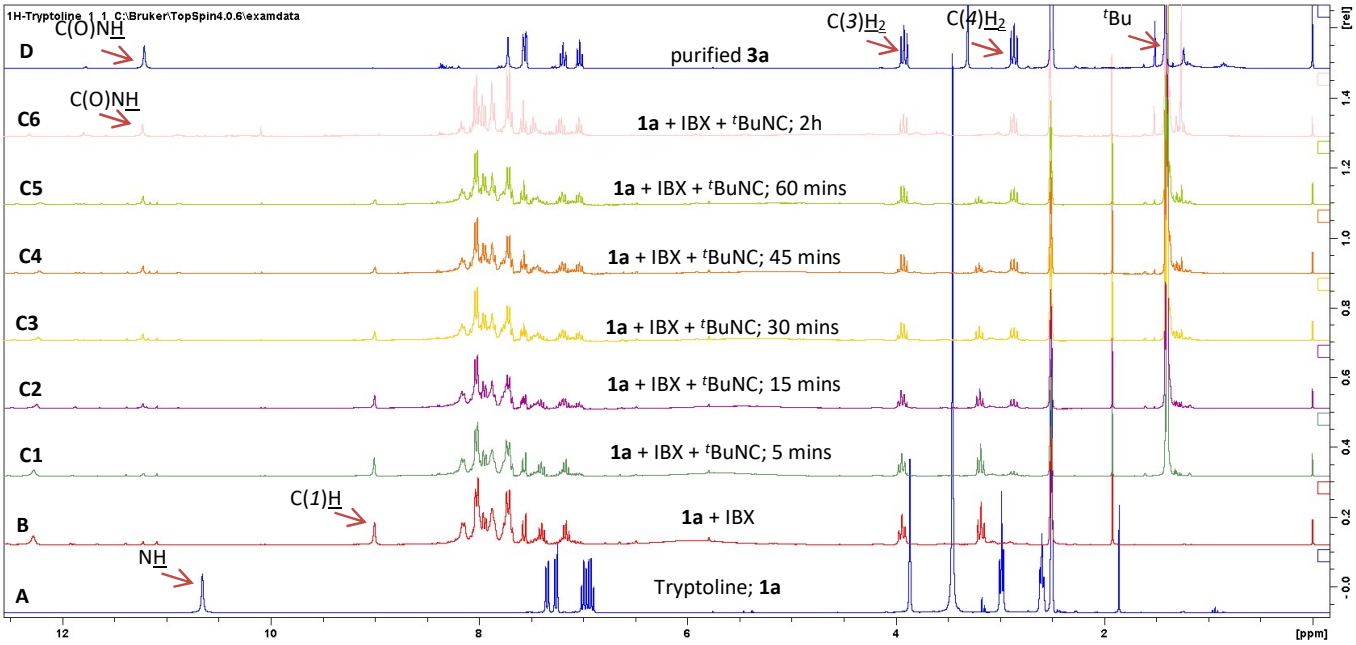
1-phenyl-9*H*-pyrido[3,4-*b*]indole (24a)[22]: White solid (5.0 mg, 10.0%); **m.p**: 240-241 °C; R_f = 0.6 (60% EtOAc in hexane); **^{1}H NMR (300 MHz, $CDCl_3$)**: δ 8.58 (d, J = 5.2 Hz, 1H), 8.52 (s, 1H), 8.17 (d, J = 7.9 Hz, 1H), 7.98 (t, J = 1.7 Hz, 1H), 7.95 (t, J = 3.6 Hz, 2H), 7.63 – 7.46 (m, 5H), 7.31 (ddd, J = 8.0, 6.8, 1.3 Hz, 1H); **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 143.0, 140.3, 139.7, 138.6, 133.5, 129.8, 129.2, 128.8, 128.5, 128.1, 121.9, 121.8, 120.3, 113.8, 111.5; **IR ($CHCl_3$) ν_{max} (cm^{-1})** = 3402, 3020, 1625, 1416, 1215, 1066, 759, 669; HRMS (ESI): calcd. for $C_{17}H_{13}N_2$ $[M+H]^+$: 245.1079, found: 245.1070.

1-phenyl-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (24b)[23]: Pale yellow solid (20.0 mg, 40%); **m.p**: 213-214 °C; R_f = 0.2 (60% EtOAc in hexane); **^{1}H NMR (300 MHz, $CDCl_3$)**: δ 8.15 (s, 1H), 7.78 – 7.69 (m, 2H), 7.65 (d, J = 7.9 Hz, 1H), 7.50 (dd, J = 6.7, 3.6 Hz, 3H), 7.36 (d, J = 8.2 Hz, 1H), 7.30 (dd, J = 6.9, 1.1 Hz, 1H), 7.22 – 7.13 (m, 1H), 4.05 (dd, J = 9.0, 7.7 Hz, 2H), 2.98 (dd, J = 9.1, 7.6 Hz, 2H); **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 159.3, 137.6, 136.5,

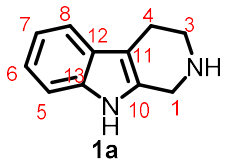
129.9, 128.8, 127.8, 127.7, 125.6, 124.6, 120.4, 120.0, 117.9, 111.9, 48.9, 19.2; **IR ($CHCl_3$)** ν_{max} **(cm^{-1})** = 3459, 3020, 1638, 1542, 1215, 1069, 760, 669; **HRMS (ESI)**: calcd. for $C_{17}H_{15}N_2$ $[M+H]^+$: 247.1235, found: 247.1226.

4. Real-time NMR Studies:

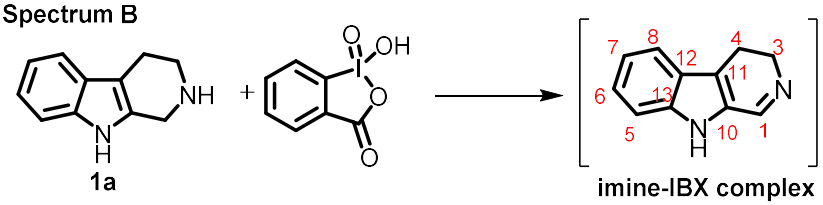
Figure S4: ^{1}H NMR studies on the reaction mechanism.



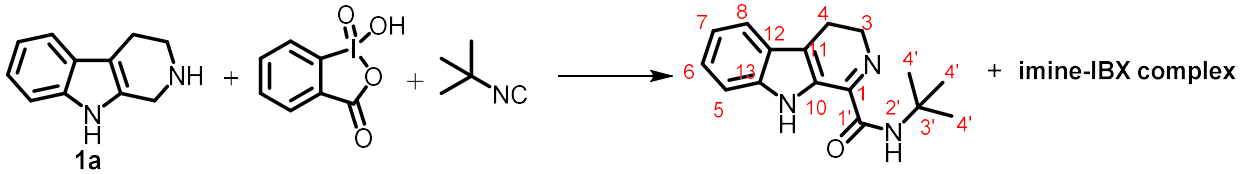
Spectrum A



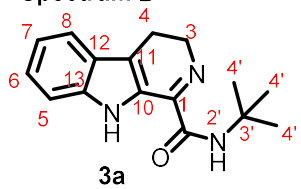
Spectrum B



Spectrum C1-C6: Progress of reaction



Spectrum D



Procedure: To a dry NMR tube were added tryptoline **1a** (10.0 mg, 0.1 mmol) and DMSO-d_6 (0.5 mL) at room temperature. The NMR tube was shaken. At this point, ^{1}H NMR was recorded giving **spectrum A**.

To a dry NMR tube were added IBX (40.0 mg, mmol) and DMSO-d_6 at room temperature and shaken for 3 minutes. After complete solubilization, compound **1a** (10.0 mg, mmol) was added. The NMR tube was again shaken for 5 minutes, at this point ^{1}H NMR was recorded giving **spectrum B**.

After the ^{1}H NMR measurement, *tert*-butyl isocyanide (5.0 mg, mmol) was added to the mixture at room temperature. After addition, NMR tube was slightly shaken and ^{1}H NMR was recorded at this point giving **spectrum C1**.

Then reaction progress was monitored at 15 minutes interval for 1 h. After that, ^{1}H NMR was recorded after 2 h for respective time interval, giving **spectrum C2-C6**.

The **spectrum D** was taken for pure isolated compound **3a**.

Summary: **Spectrum A** represents the ^{1}H NMR of tryptoline **1a**. S**pectrum B** gave the information about intermediate imine-IBX complex formation; as C(*1*)-C$\underline{H}_2$- disappearance of the compound **1a** and C(*1*)-C$\underline{H}$- appeared more downfield (δ 8.99) region as compared to the 3,4-dihydro-β-carboline C(*1*)-C$\underline{H}$- (δ 8.34) proton as shown in **spectrum B**. As *tert*-butyl isocyanide was added there is appearance of *tert*-butyl peak, -C$\underline{H}_2$ at *C*4 carbon shifted more shielded region and the -NH of amide peak appeared as shown in **spectrum C1**. Further progress of reaction was checked at 15 minutes interval of time. These results indicate that as the reaction proceeds, the -C$\underline{H}_2$ at *C*4 carbon (δ 2.83-2.89); -N$\underline{H}$ of amide, Ar-C$\underline{H}$ peak intensity goes on increasing while -C$\underline{H}_2$ at *C*4 carbon (δ 3.16-3.22), C(*1*)-C$\underline{H}$-(δ 8.99) peak intensity goes on decreasing as shown in **spectrum C2-C6**.

5. References

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6. Copies of ^{1}H and ^{13}C NMR Spectra

Figure S5: ^{1}H NMR of compound **3a**

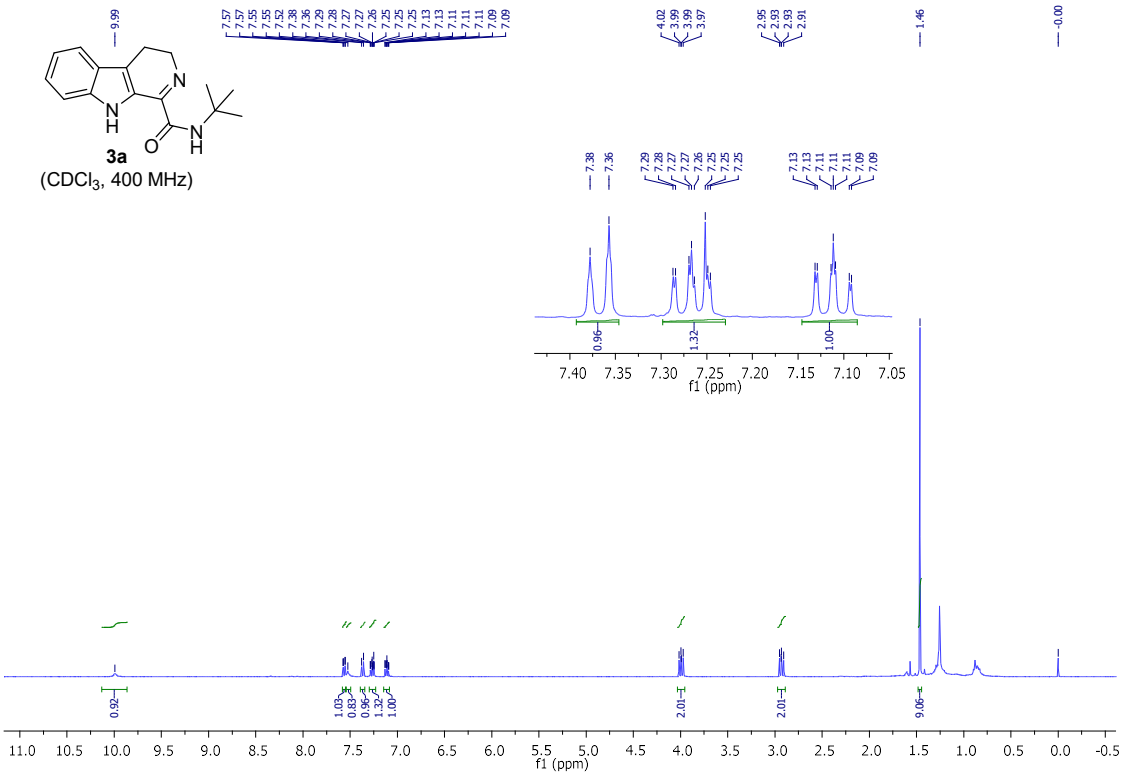

Figure S6: ^{13}C NMR of compound **3a**

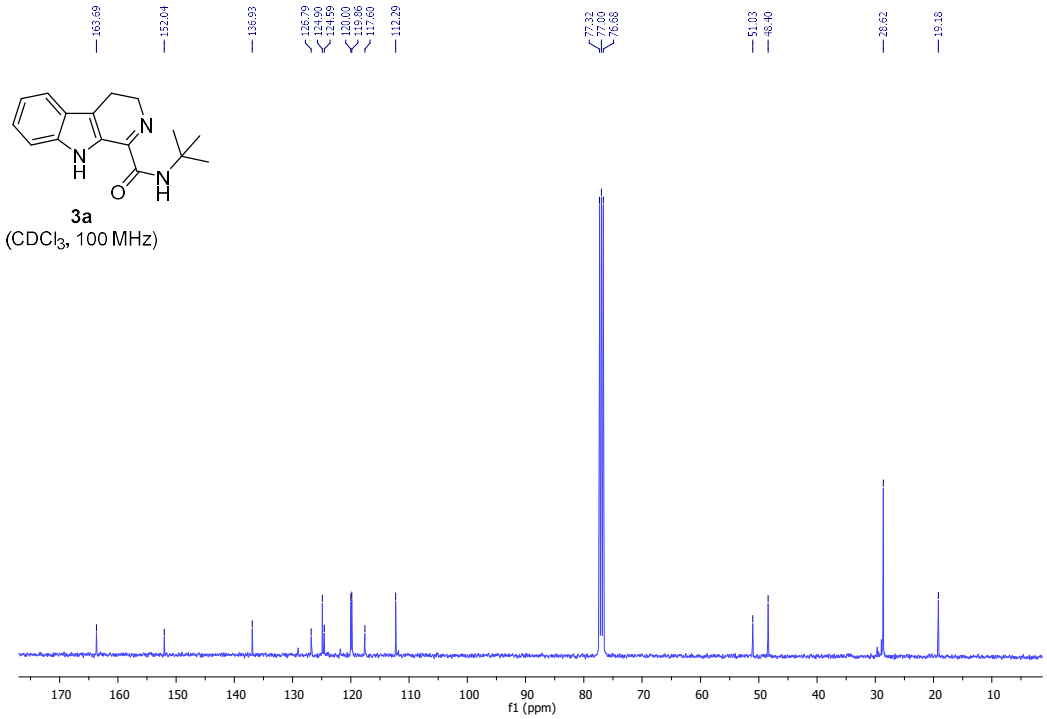

Figure S7: ^{1}H NMR of compound **3b**

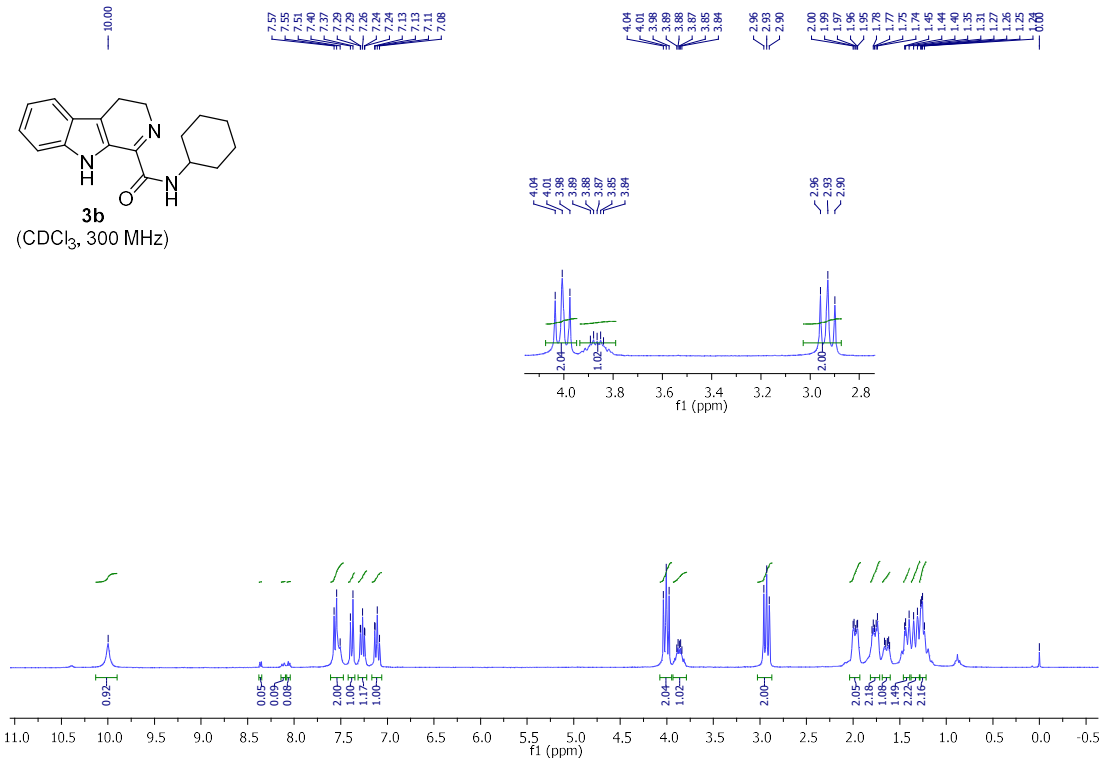

Figure S8: ^{13}C NMR of compound **3b**

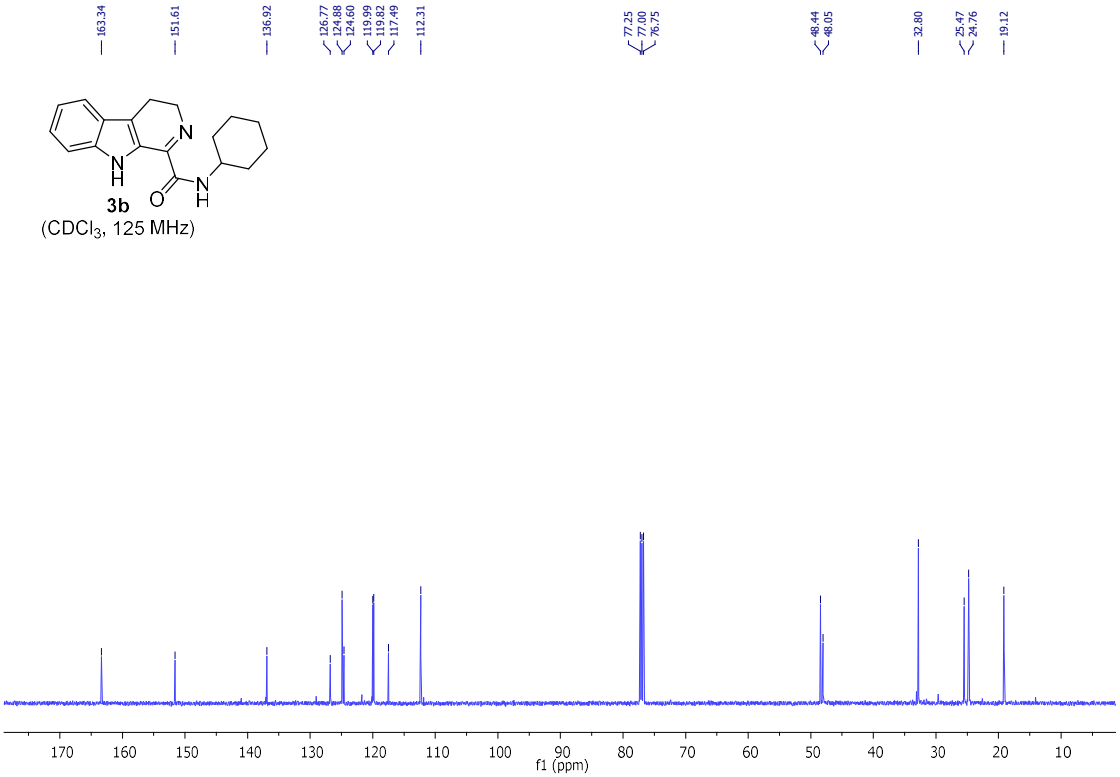

Figure S9: ^{1}H NMR of compound **3c**

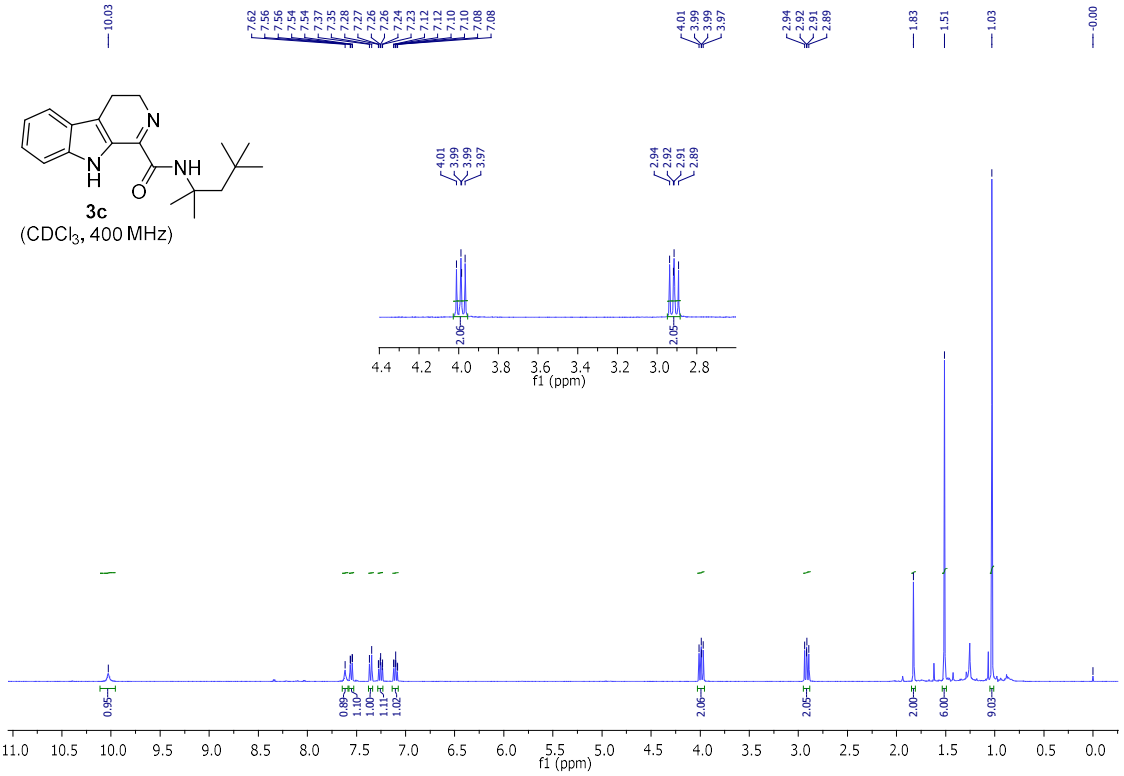

Figure S10: ^{13}C NMR of compound **3c**

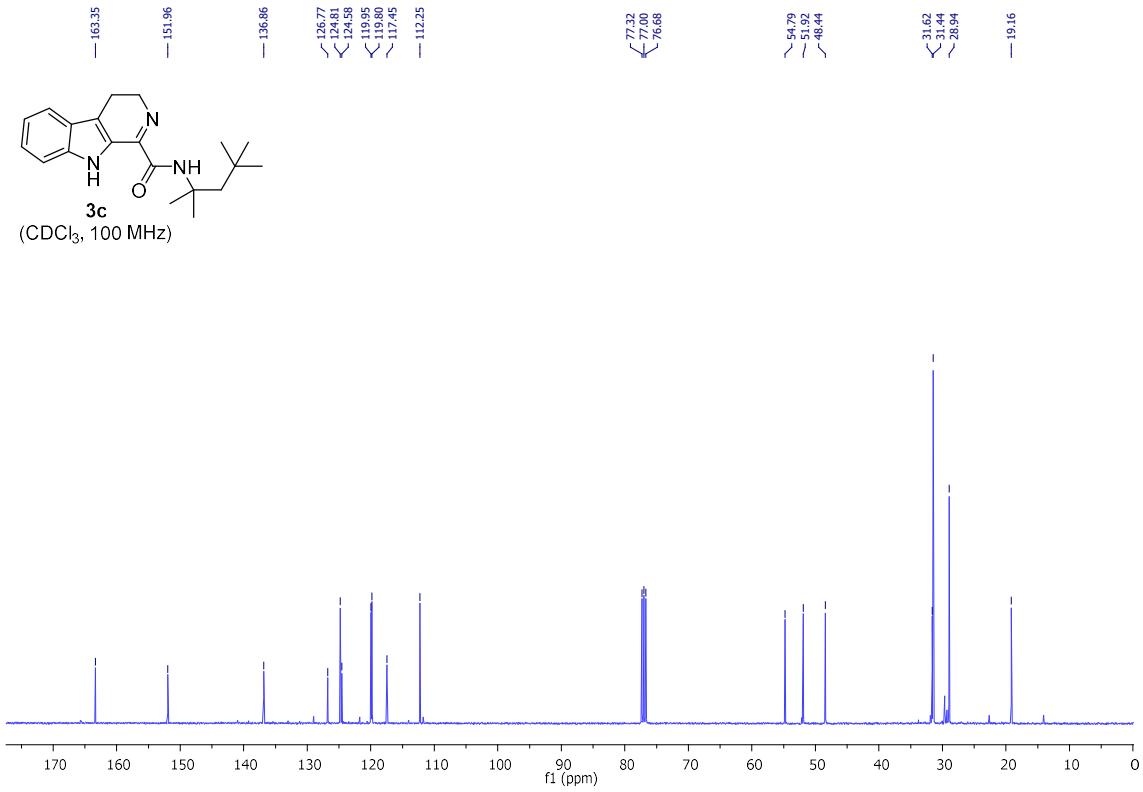

Figure S11: ^{1}H NMR of compound **3d**

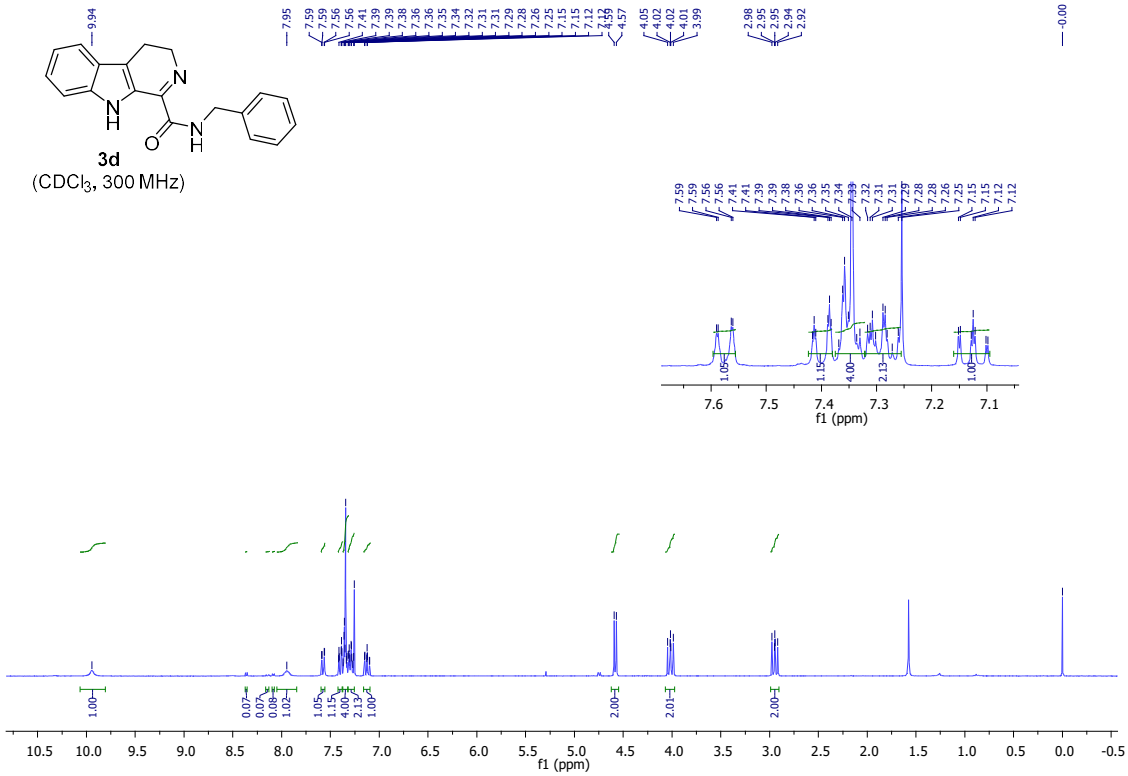

Figure S12: ^{13}C NMR of compound **3d**

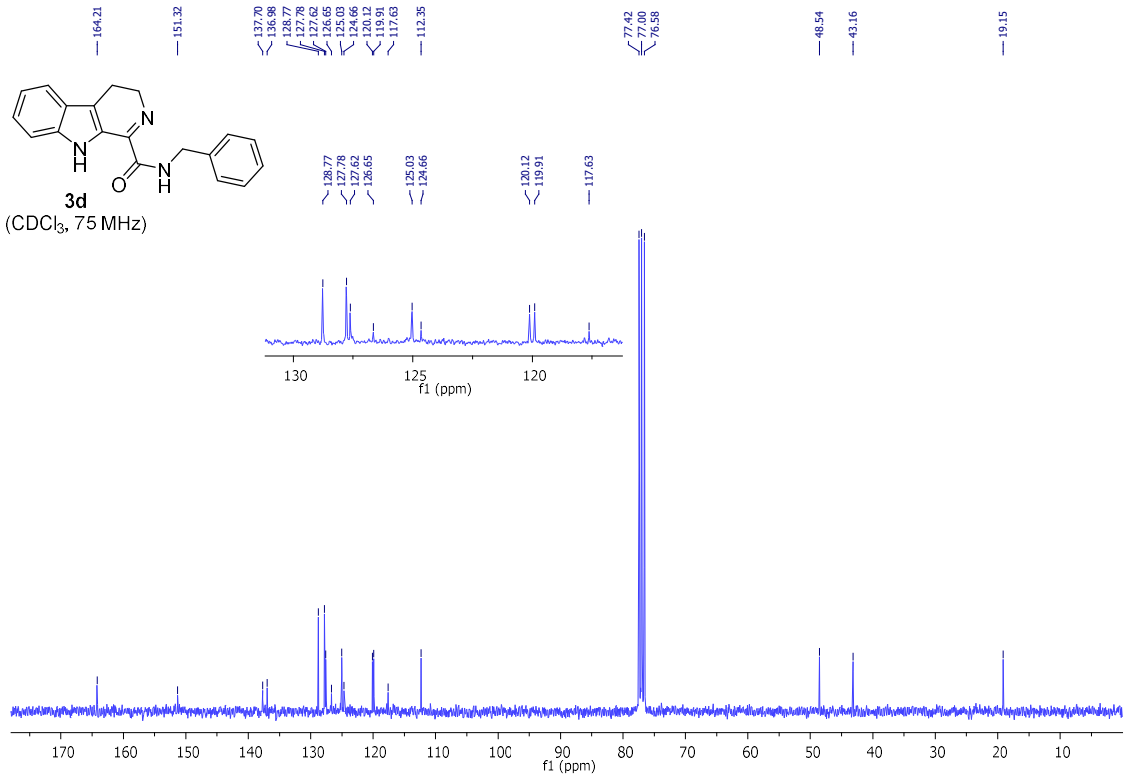

Figure S13: ^{1}H NMR of compound **3e**

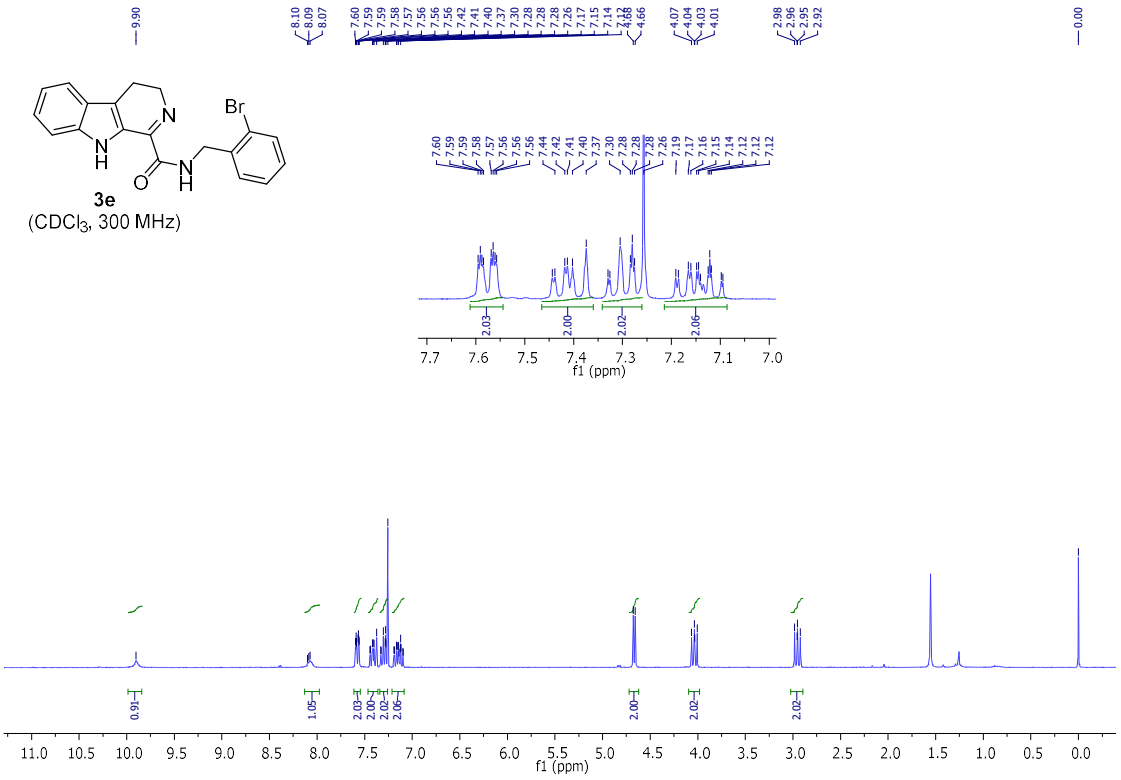

Figure S14: ^{13}C NMR of compound **3e**

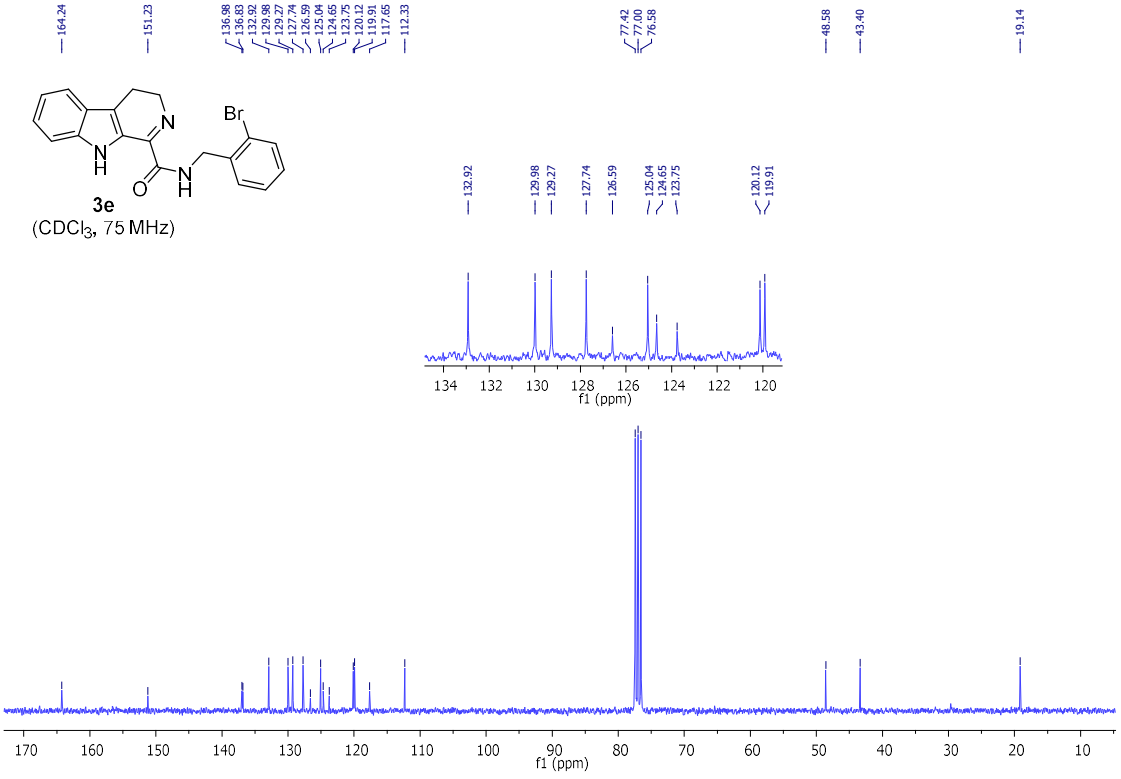

Figure S15: ^{1}H NMR of compound **3f**

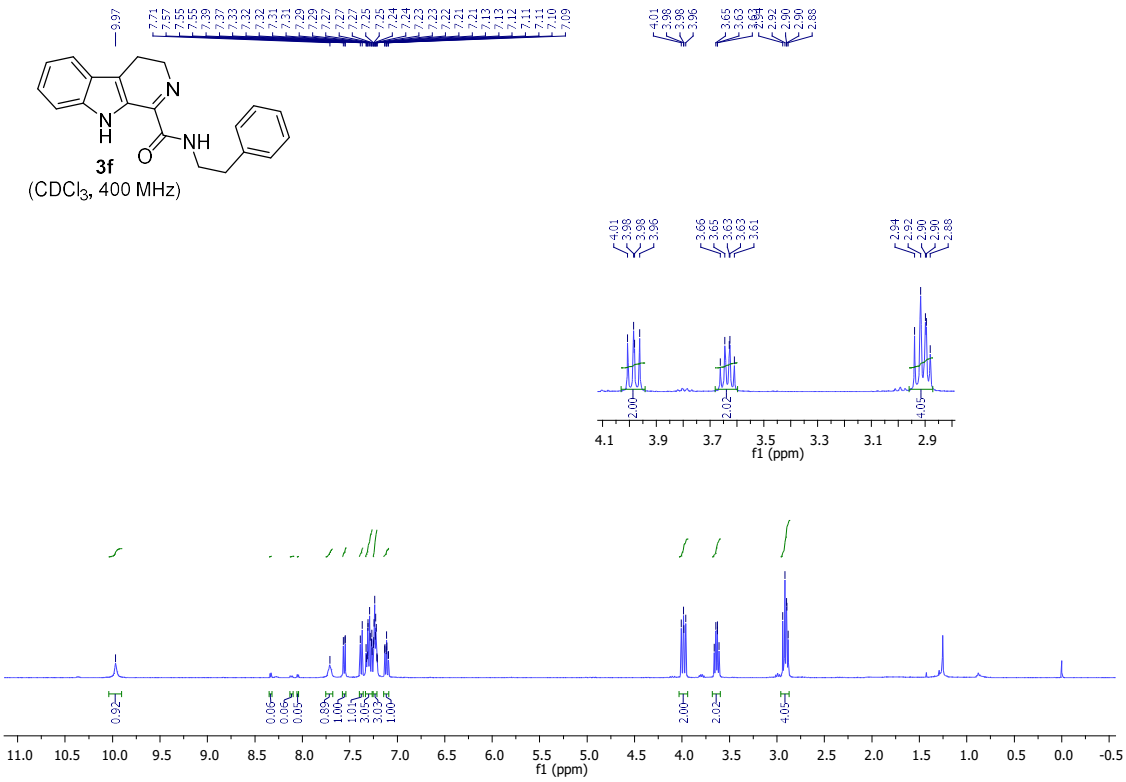

Figure S16: ^{13}C NMR of compound **3f**

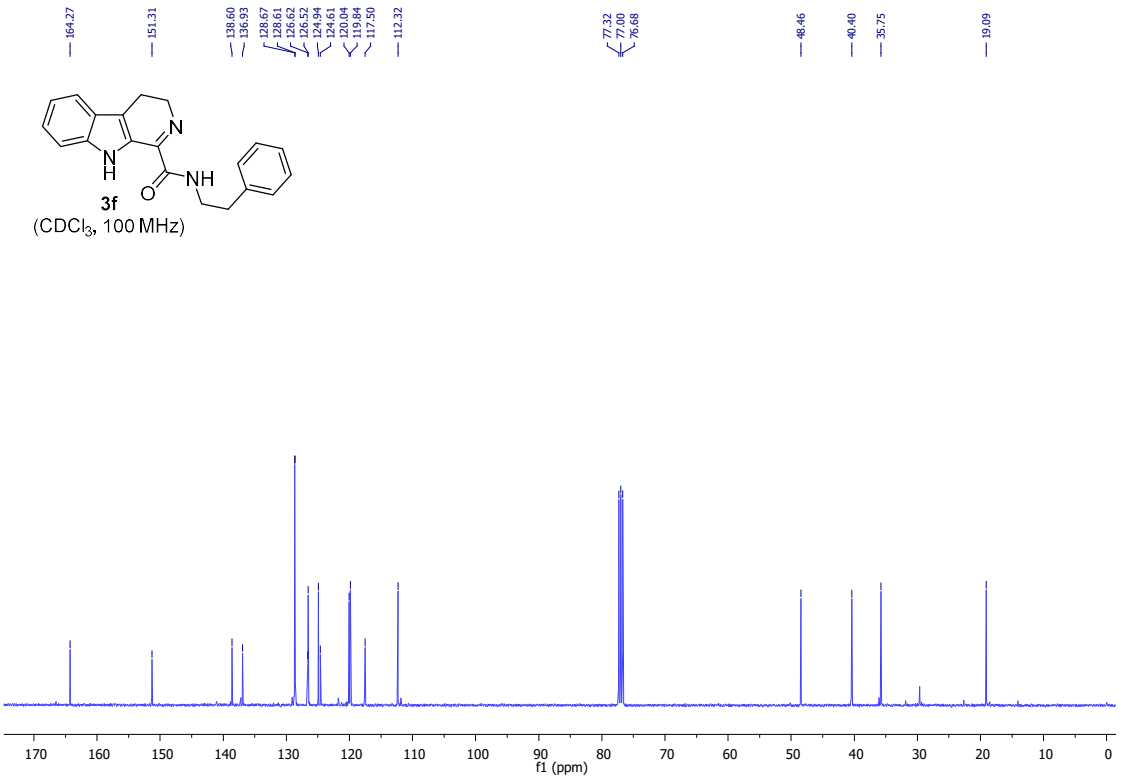

Figure S17: ^{1}H NMR of compound **3g**

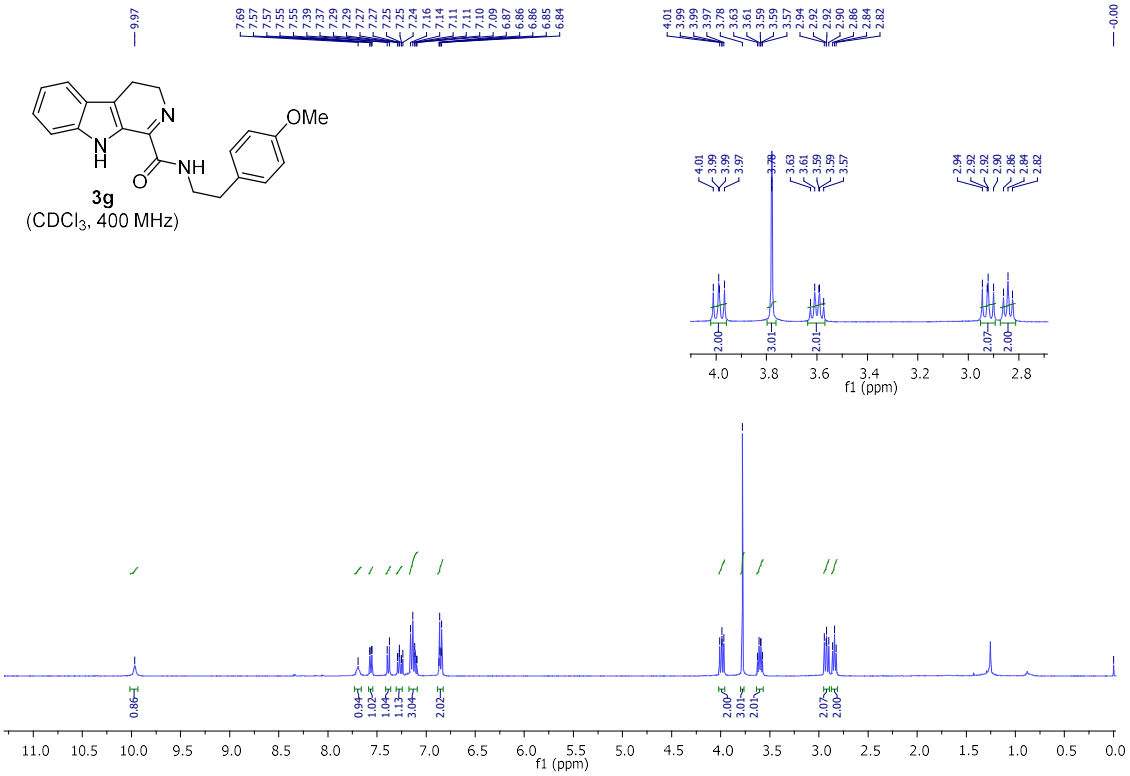

Figure S18: ^{1}H NMR of compound **3g**

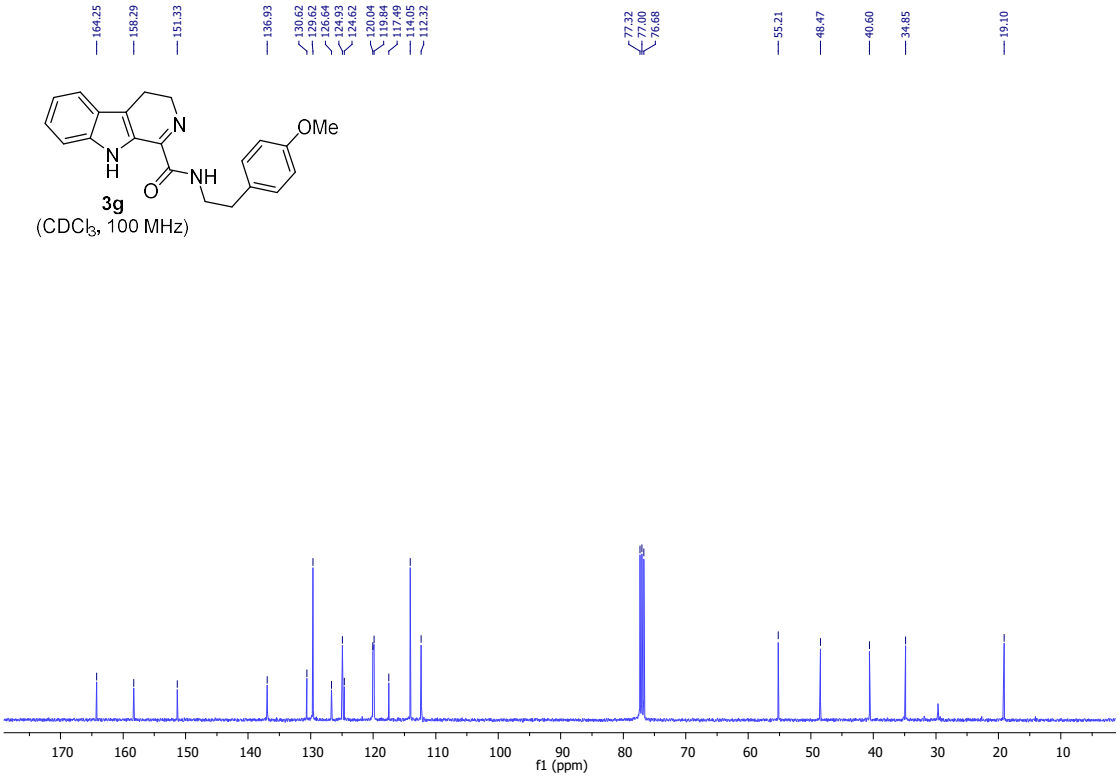

Figure S19: ^{1}H NMR of compound **3h**

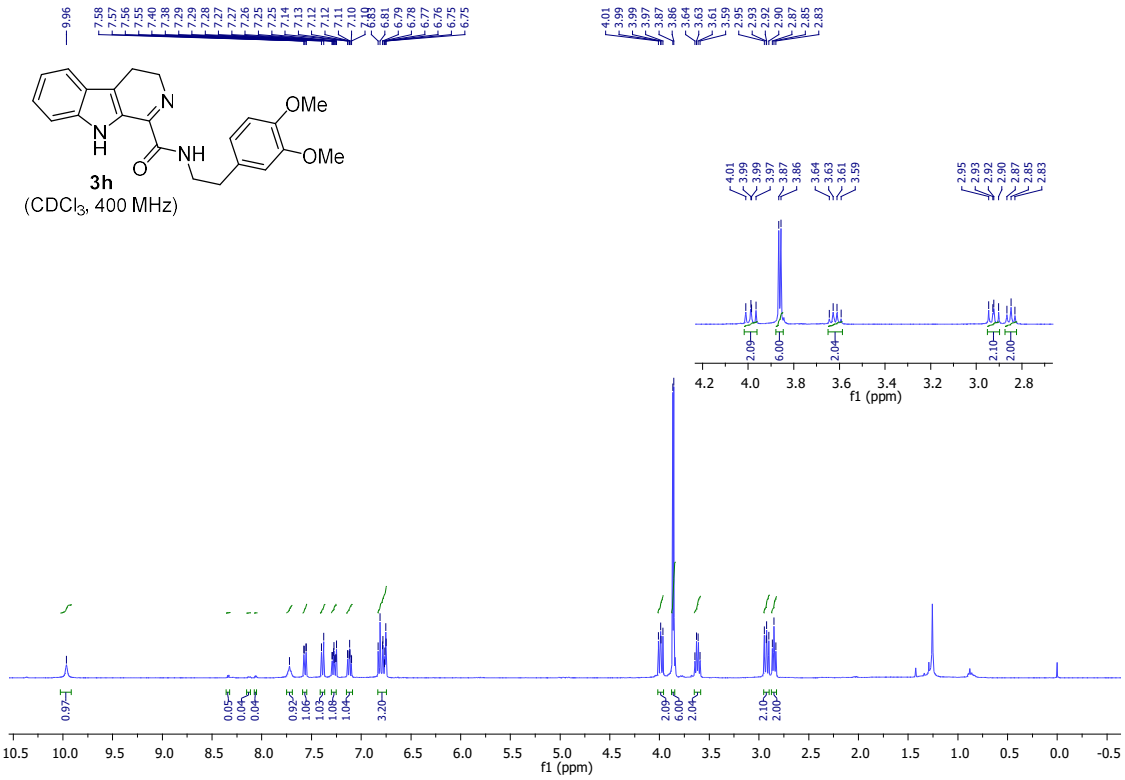

Figure S20: ^{13}C NMR of compound **3h**

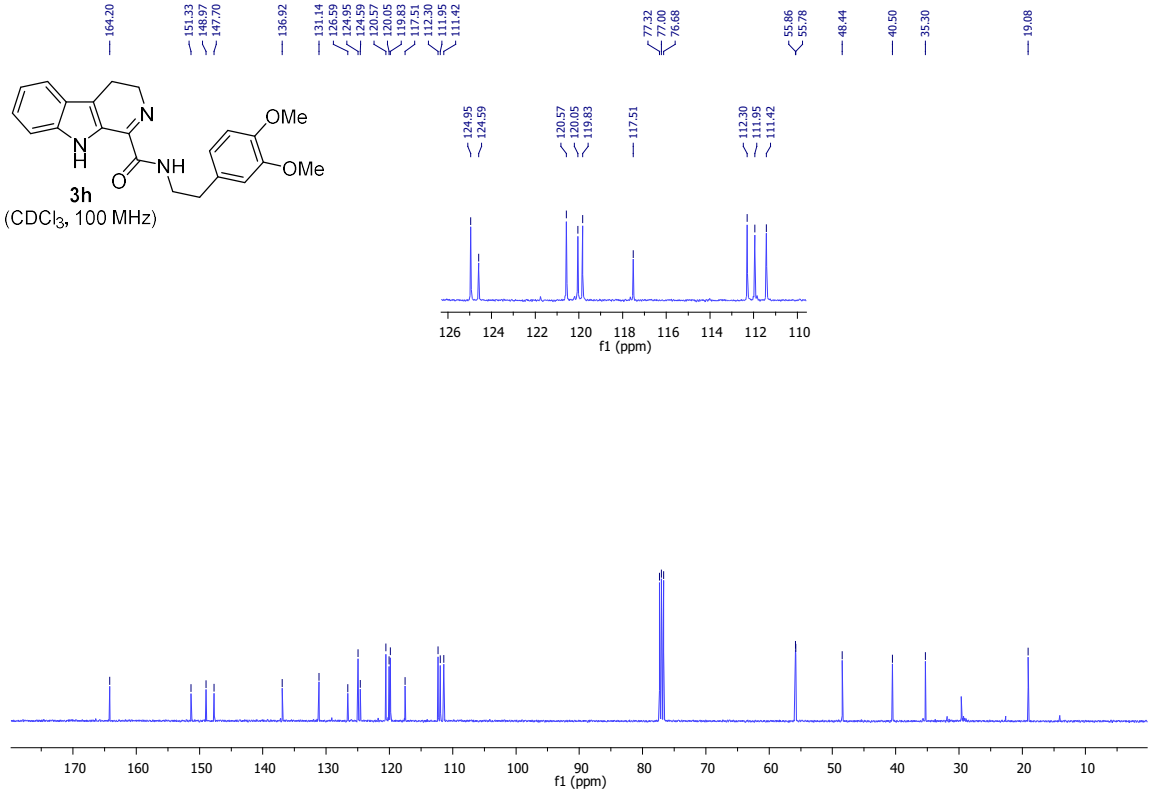

Figure S21: ^{1}H NMR of compound **3i**

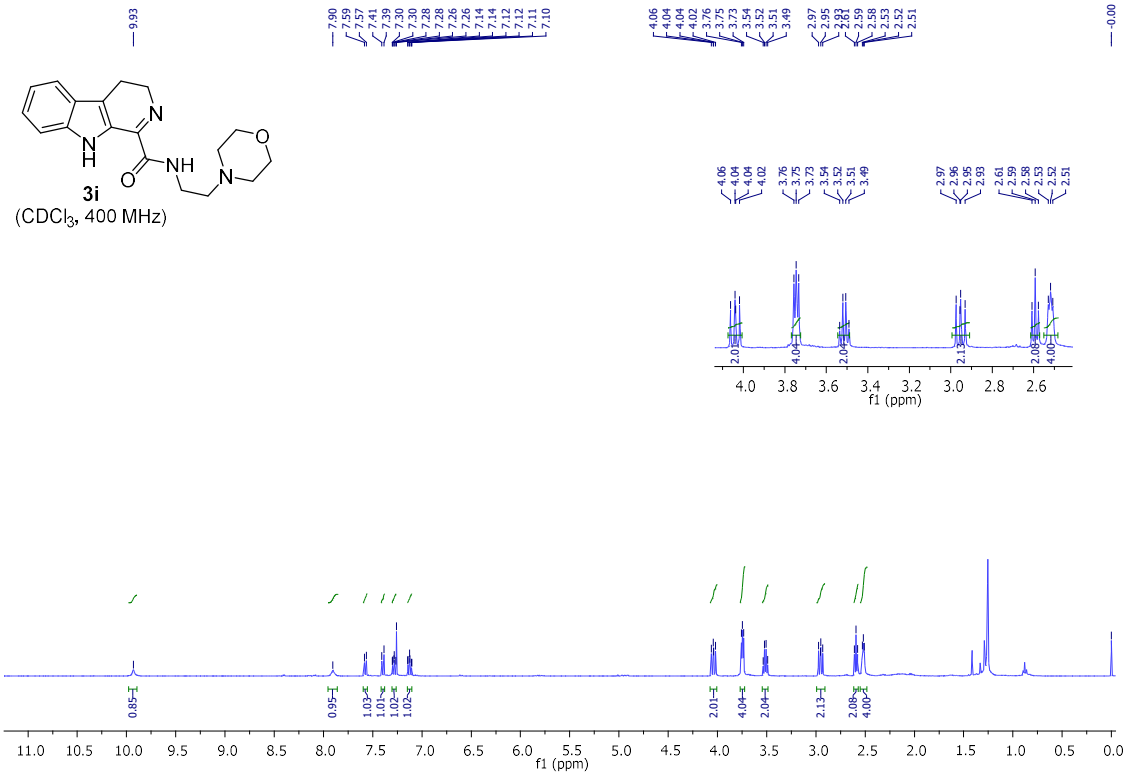

Figure S22: ^{13}C NMR of compound **3i**

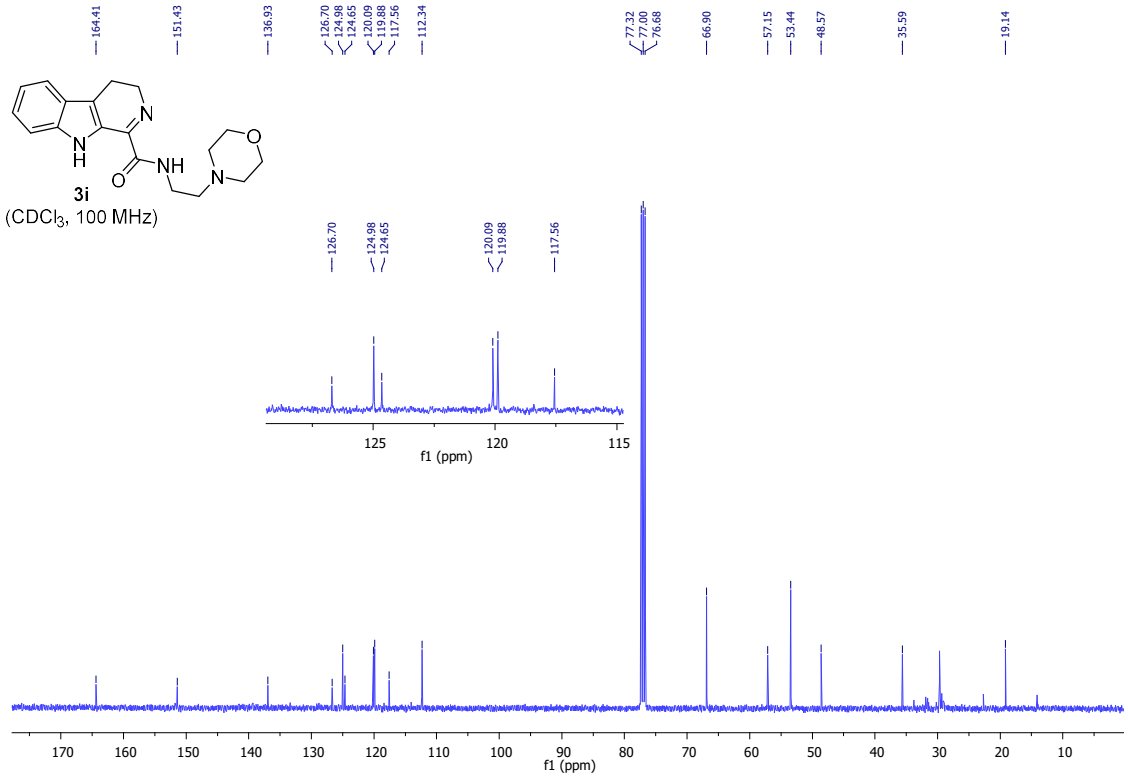

Figure S23: ^{1}H NMR of compound **3j**

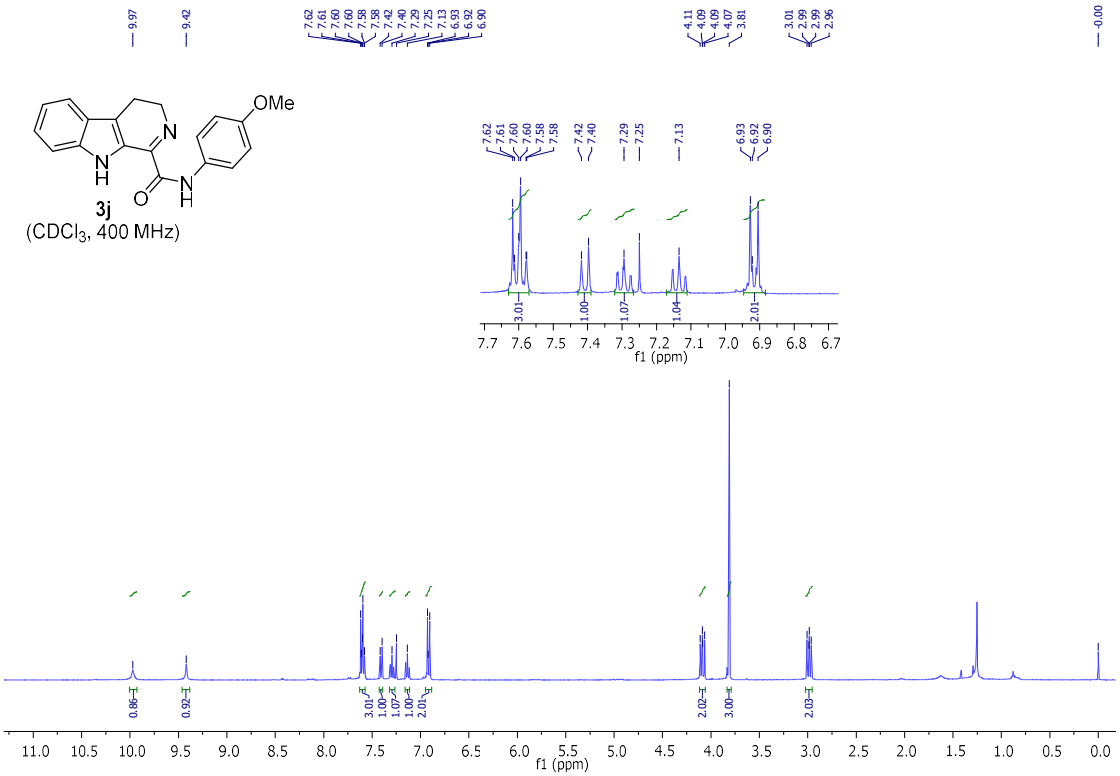

Figure S24: ^{13}C NMR of compound **3j**

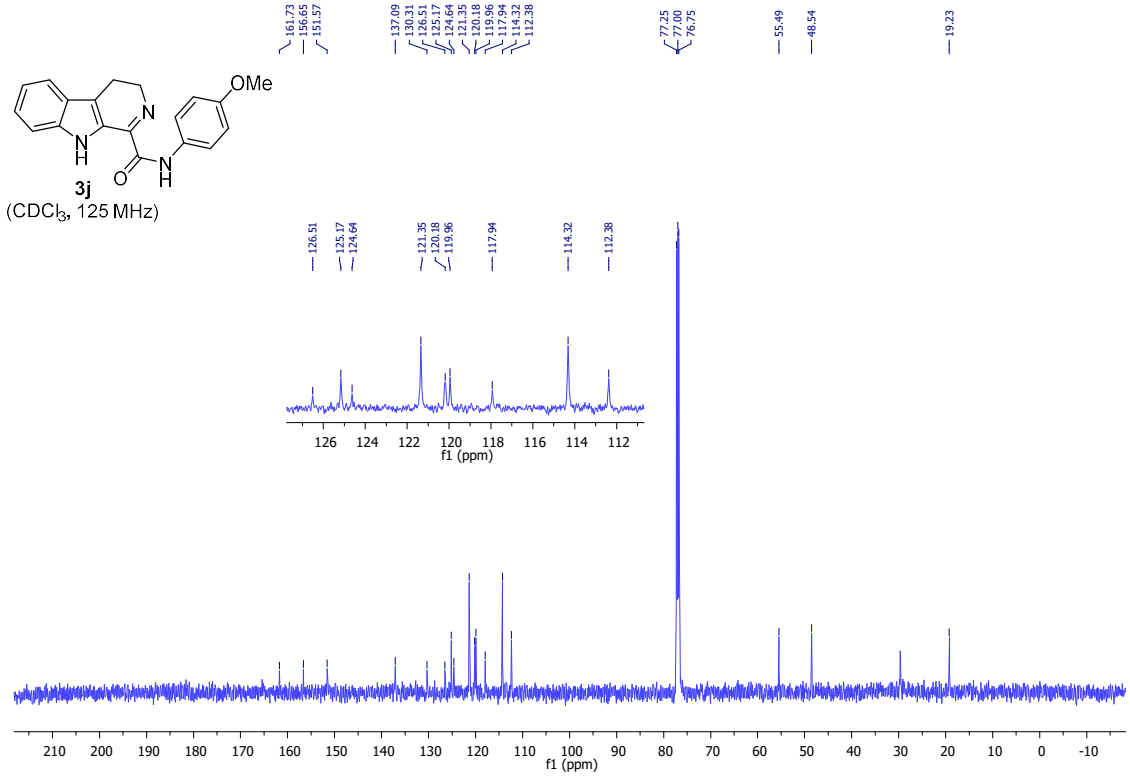

Figure S25: ^{1}H NMR of compound **3m**

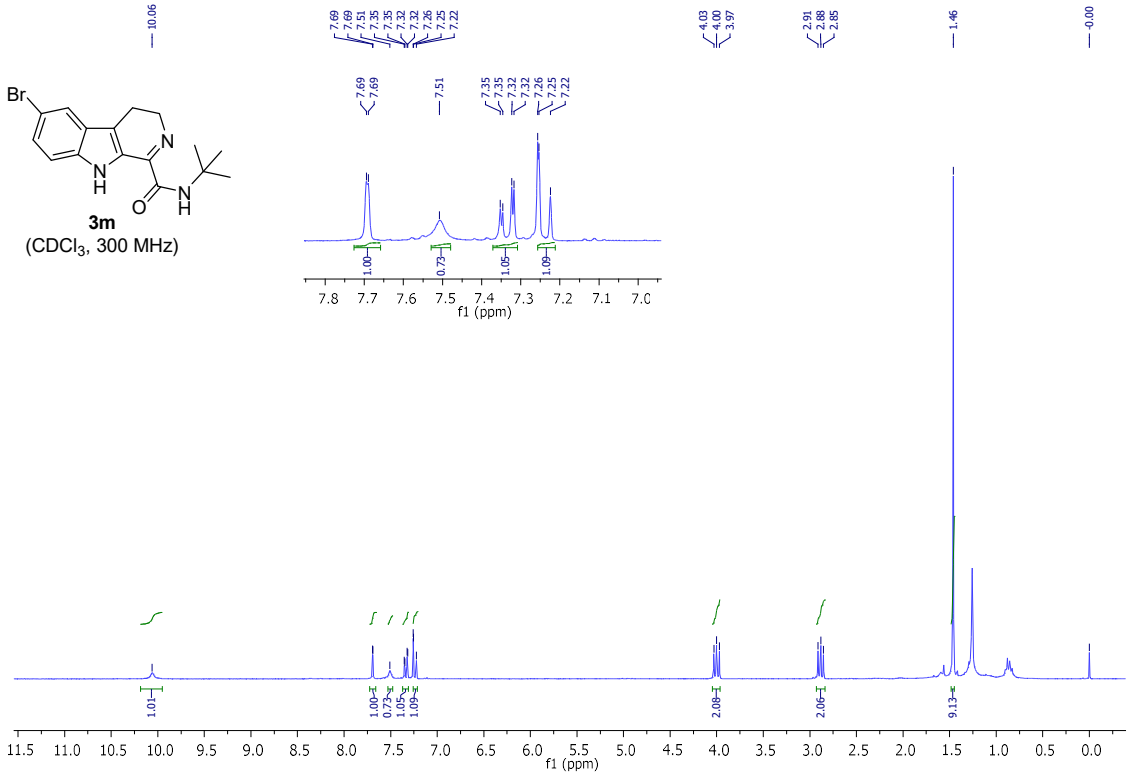

Figure S26: ^{13}C NMR of compound **3m**

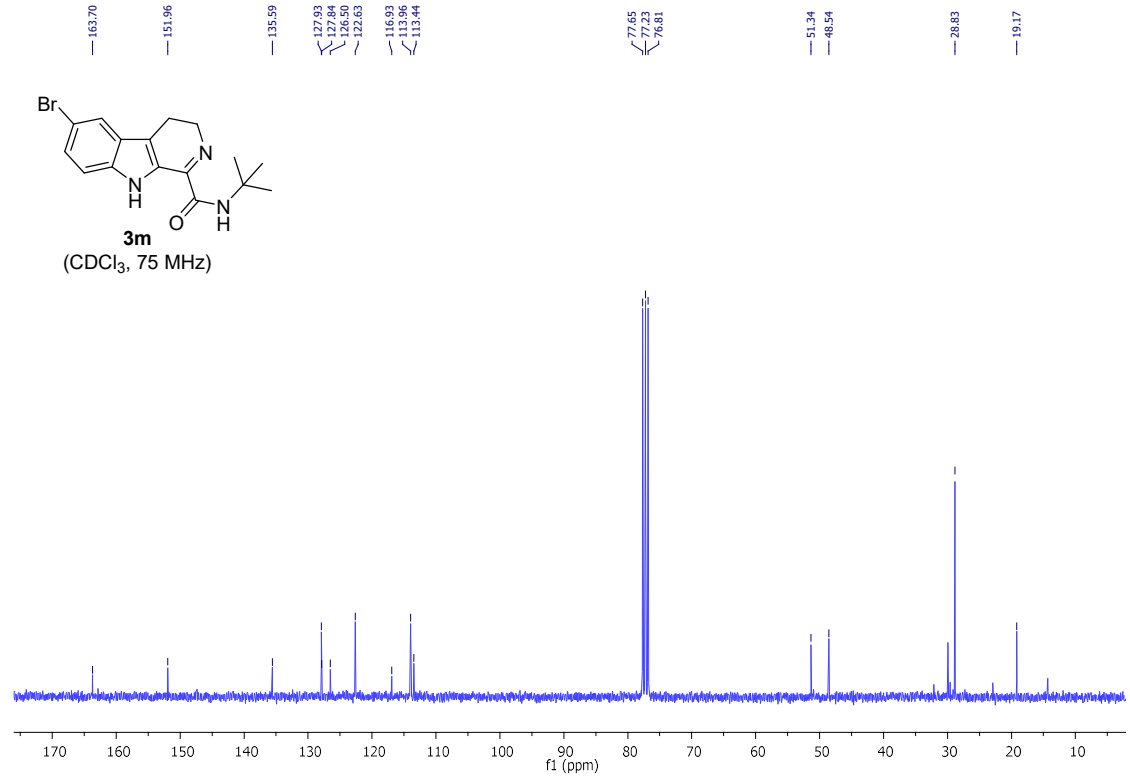

Figure S27: ^{1}H NMR of compound **VII**

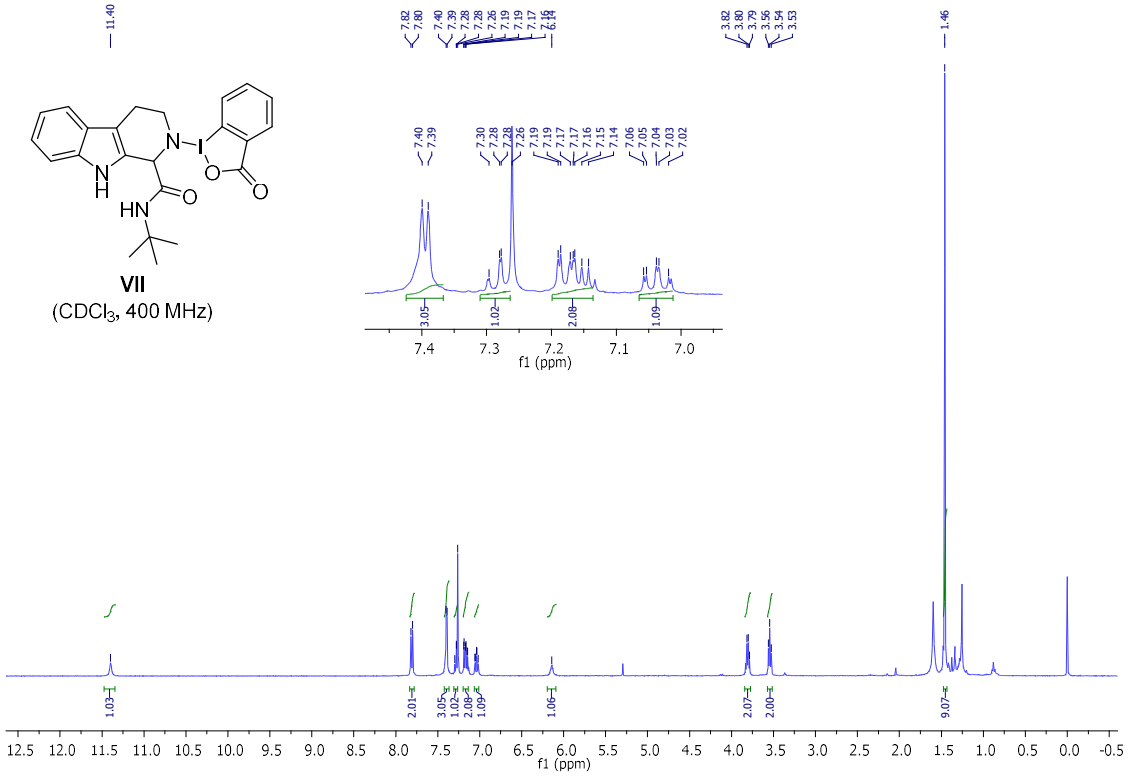

Figure S28: ^{13}C NMR of compound **VII**

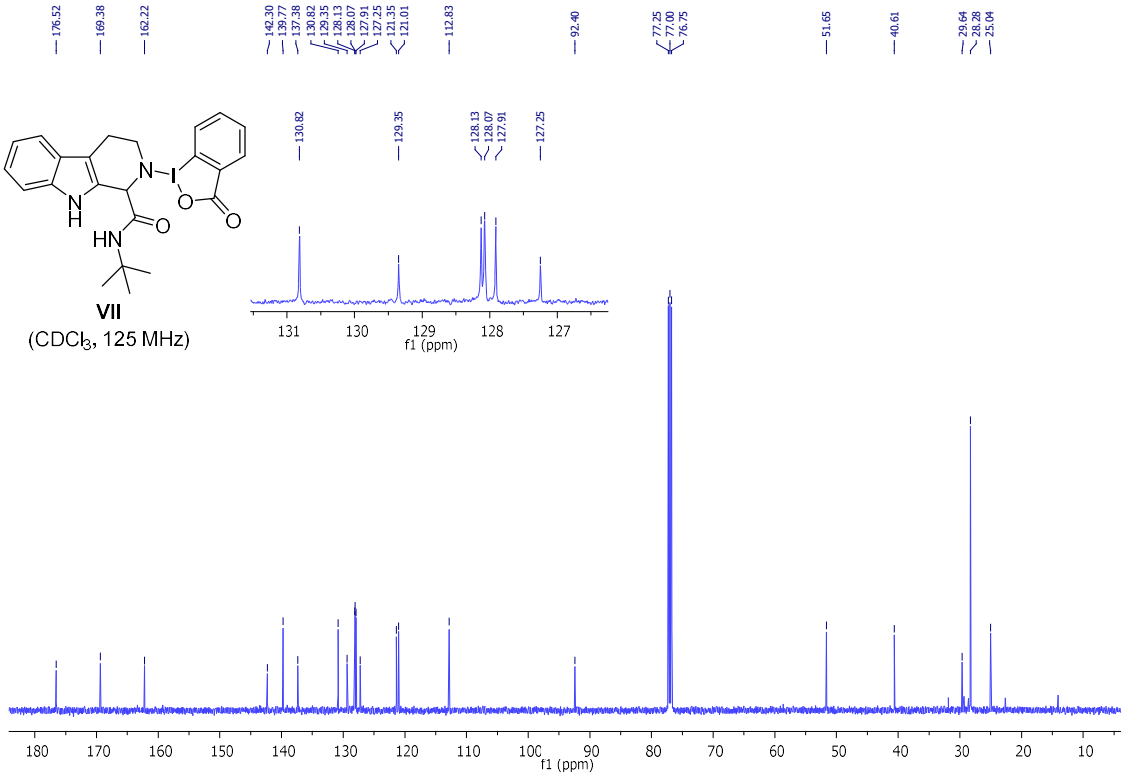

Figure S29: ^{1}H NMR of compound **4**

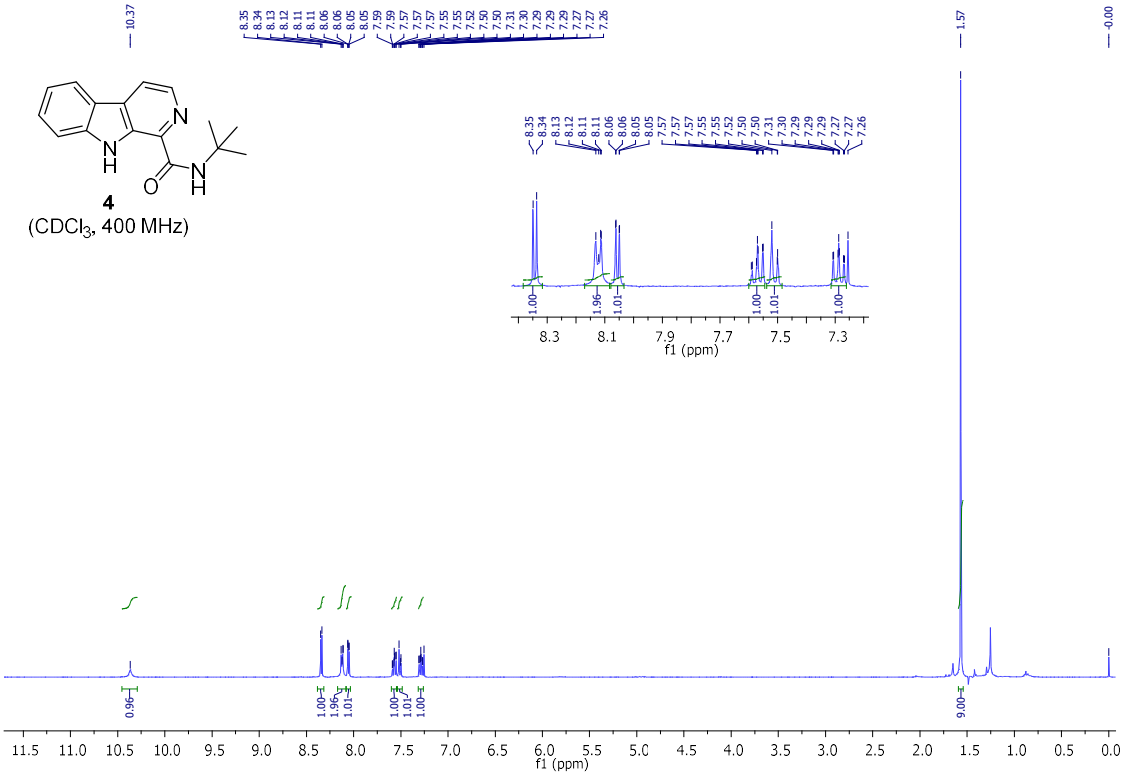

Figure S30: ^{13}C NMR of compound **4**

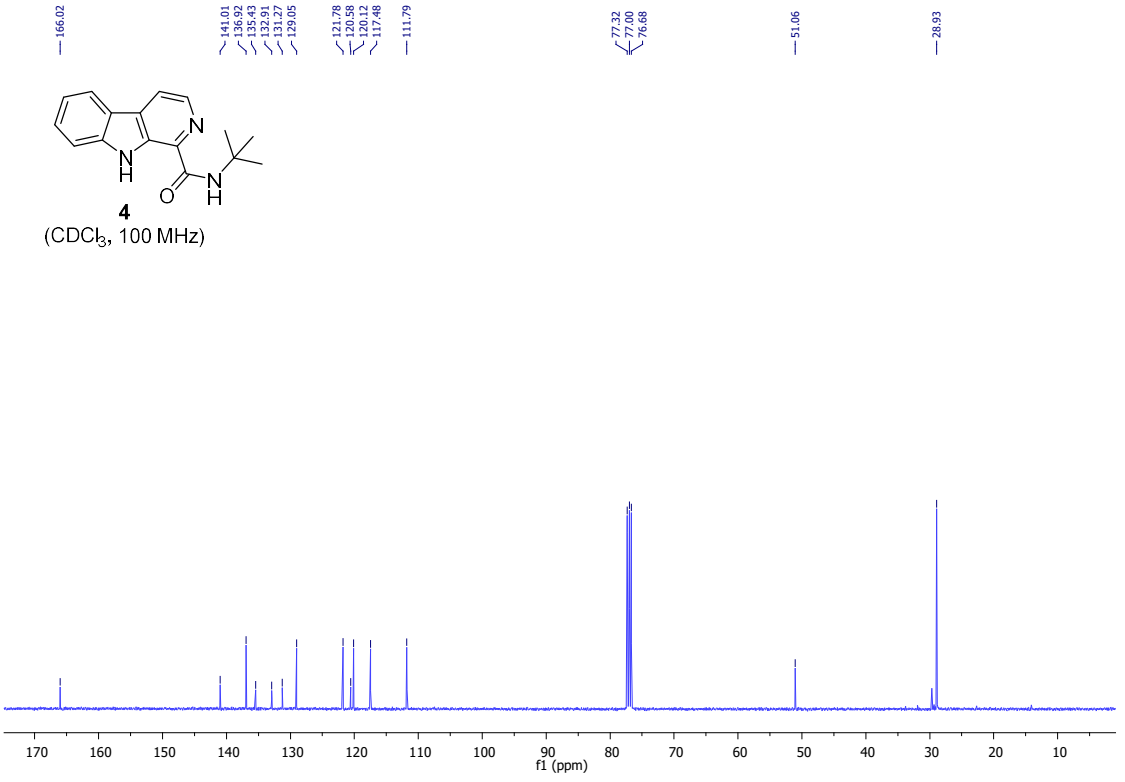

Figure S31: ^{1}H NMR of compound **7a**

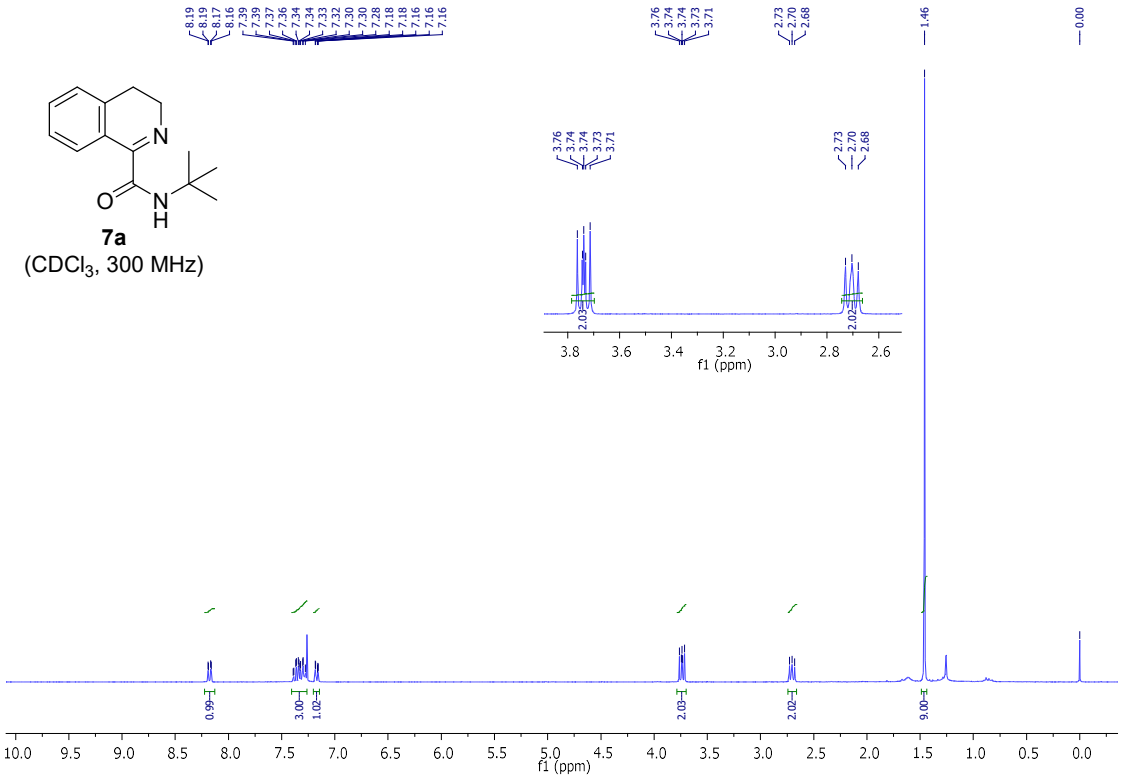

Figure S32: ^{13}C NMR of compound **7a**

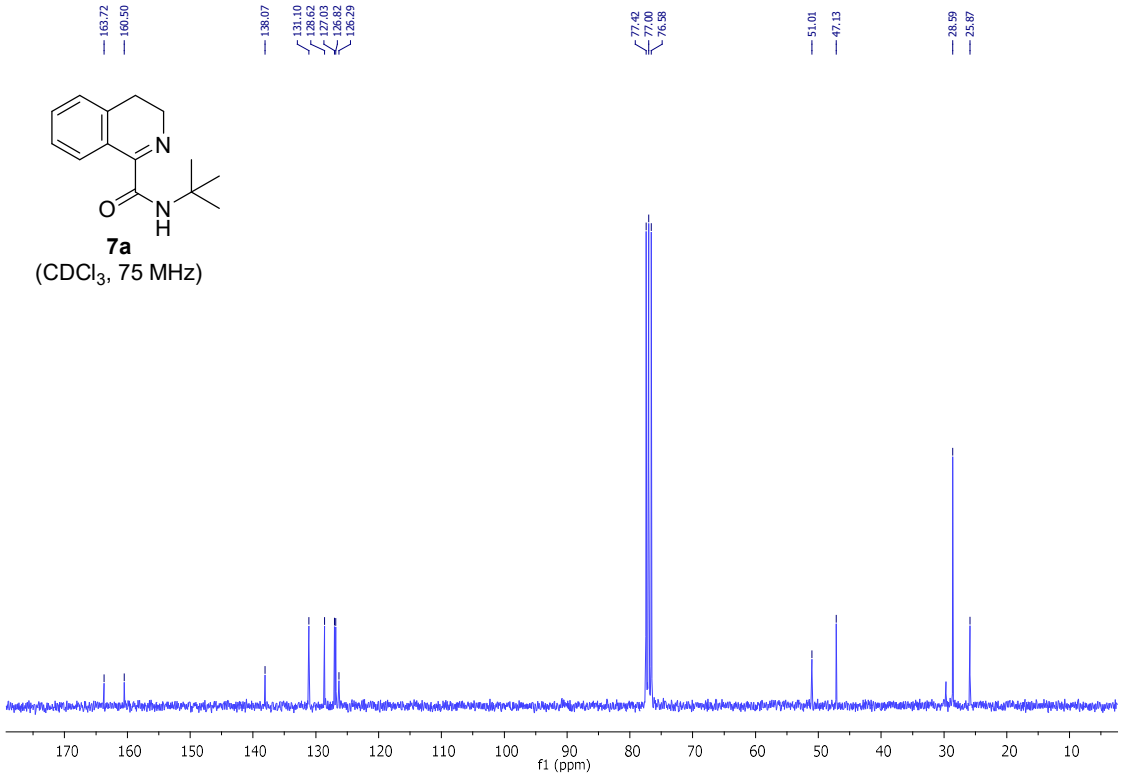

Figure S33: ^{1}H NMR of compound **7b**

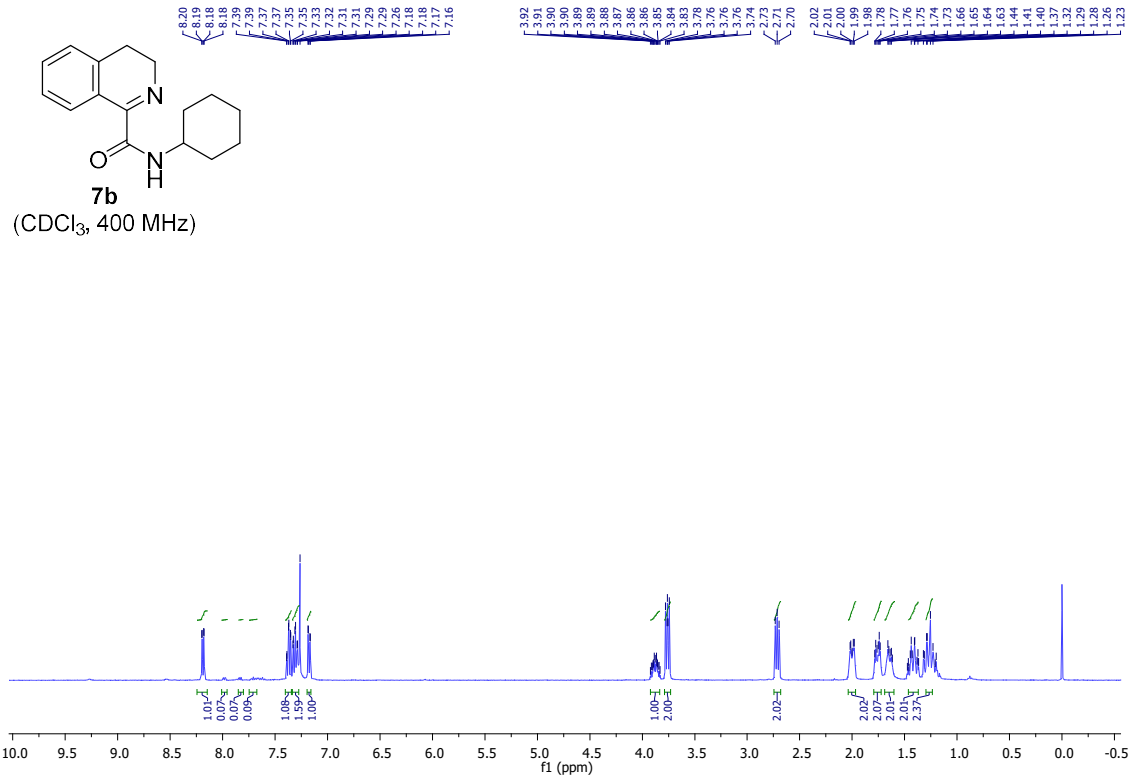

Figure S34: ^{13}C NMR of compound **7b**

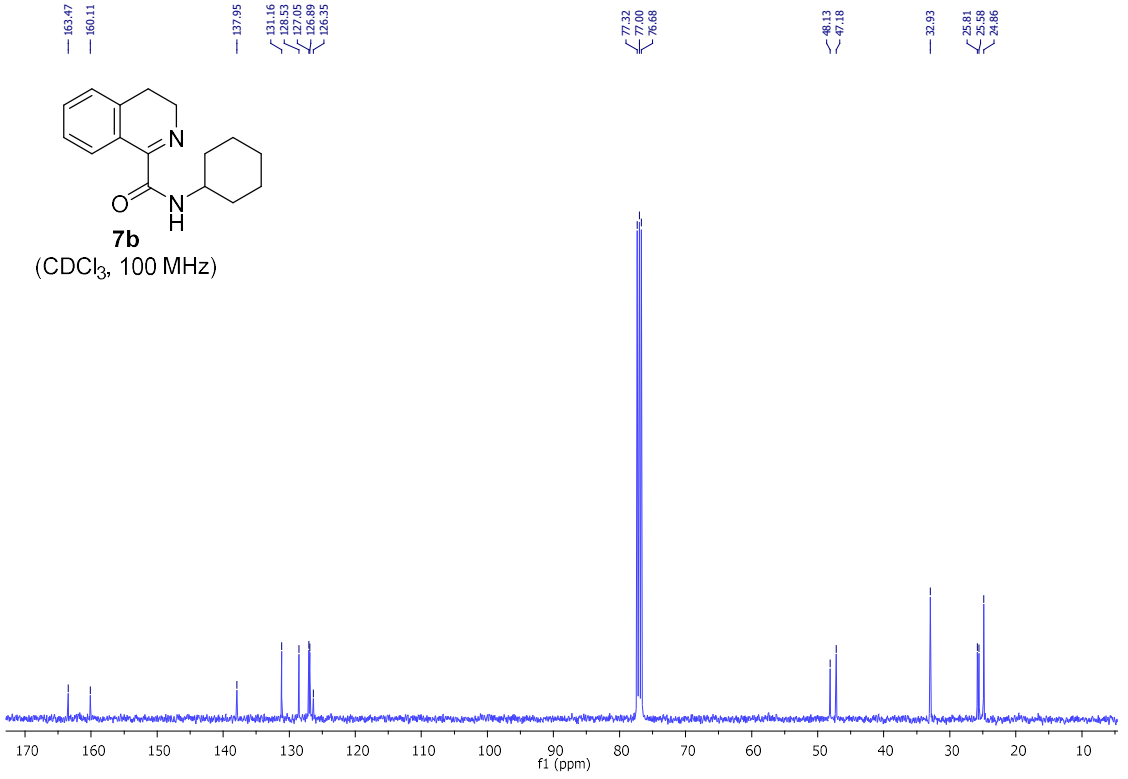

Figure S35: ^{1}H NMR of compound **7c**

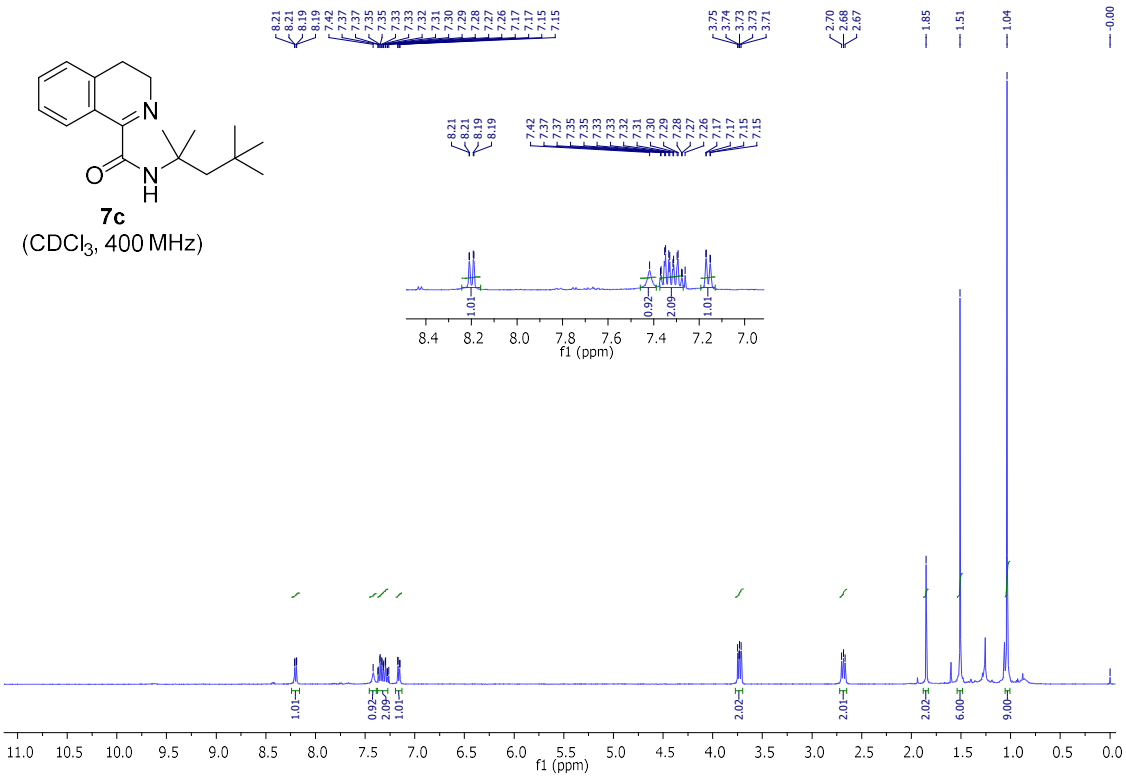

Figure S36: ^{13}C NMR of compound **7c**

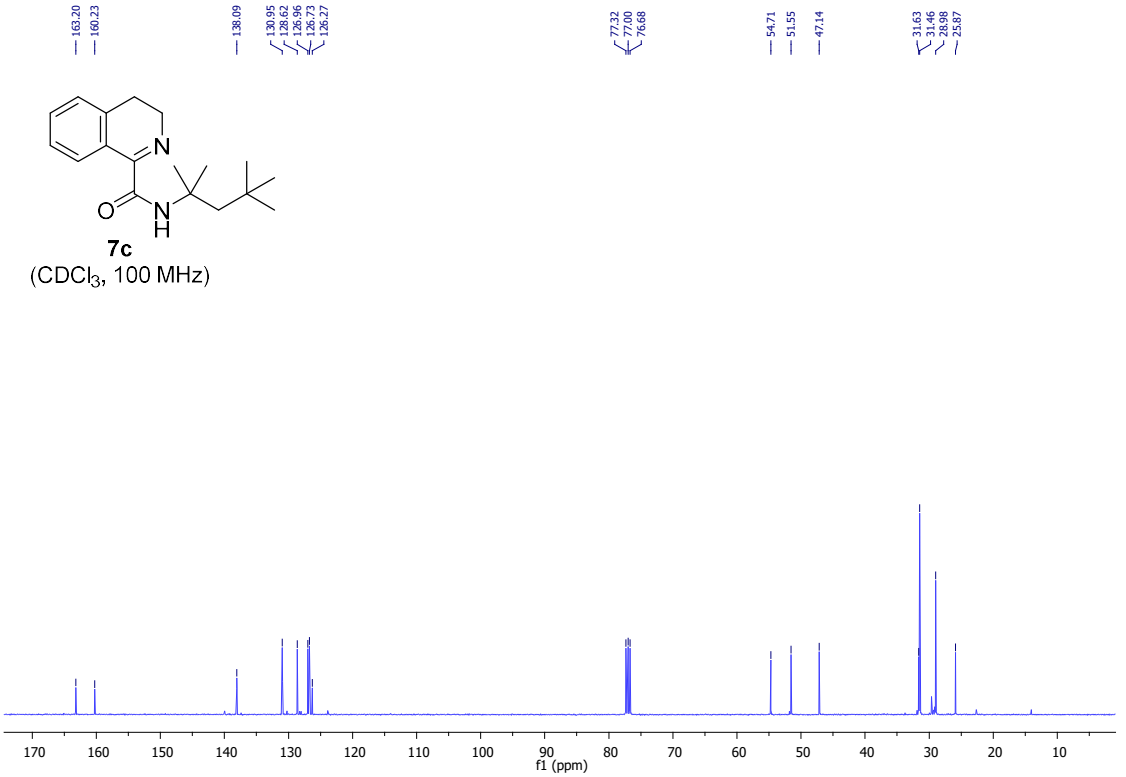

Figure S37: ^{1}H NMR of compound **7d**

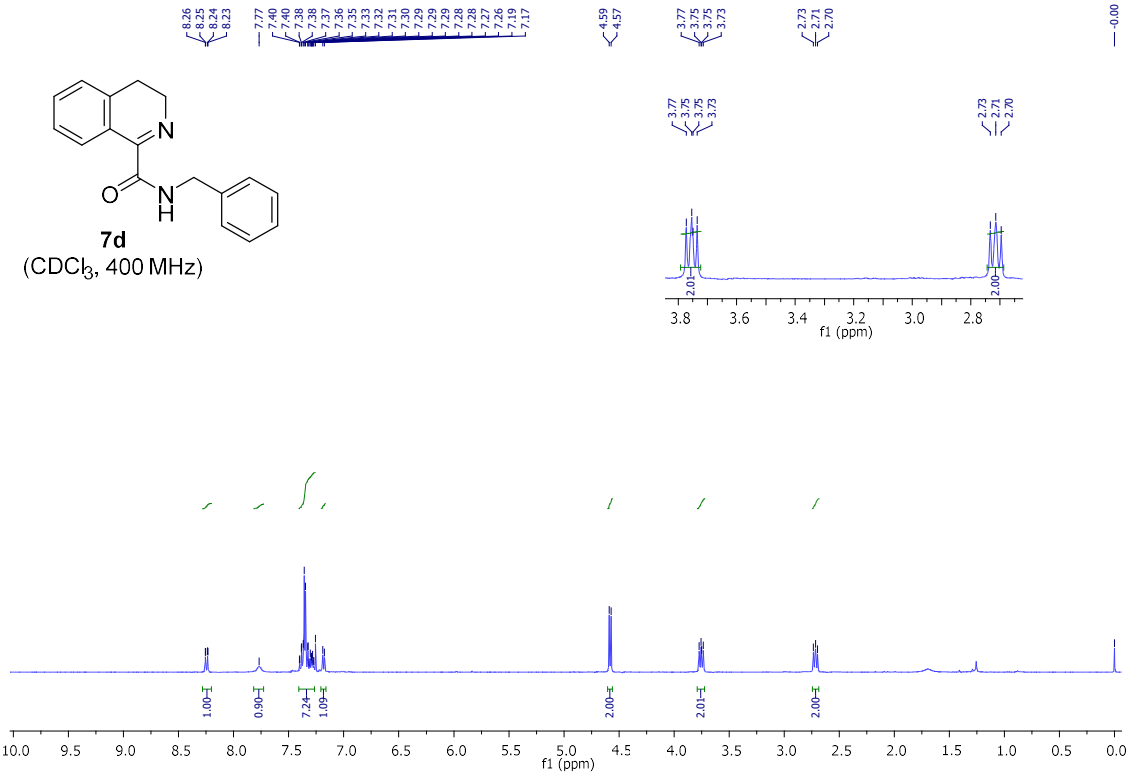

Figure S38: ^{13}C NMR of compound **7d**

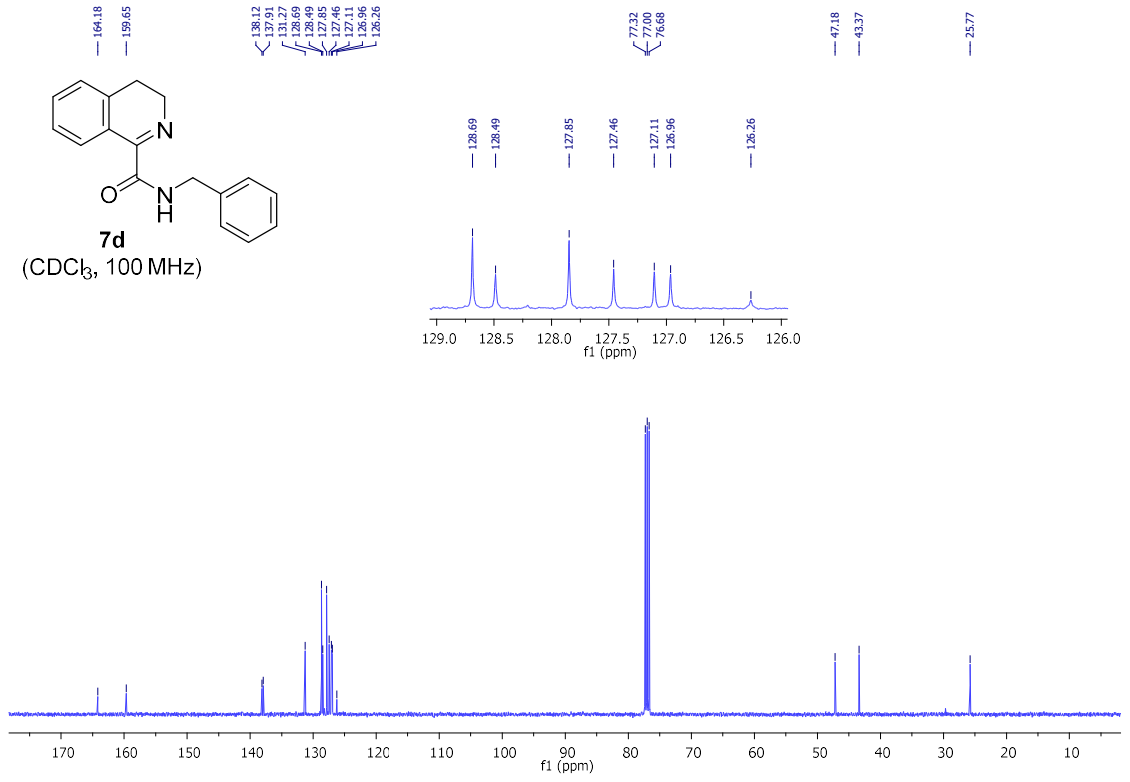

Figure S39: ^{1}H NMR of compound **7e**

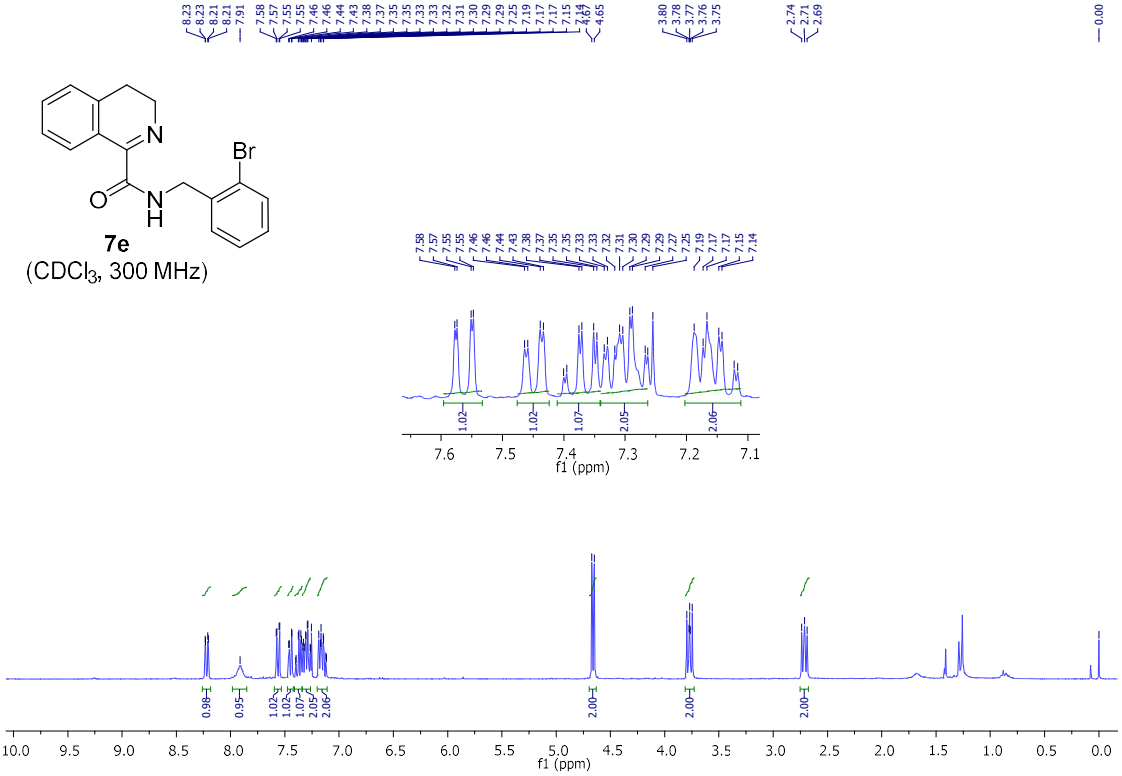

Figure S40: ^{13}C NMR of compound **7e**

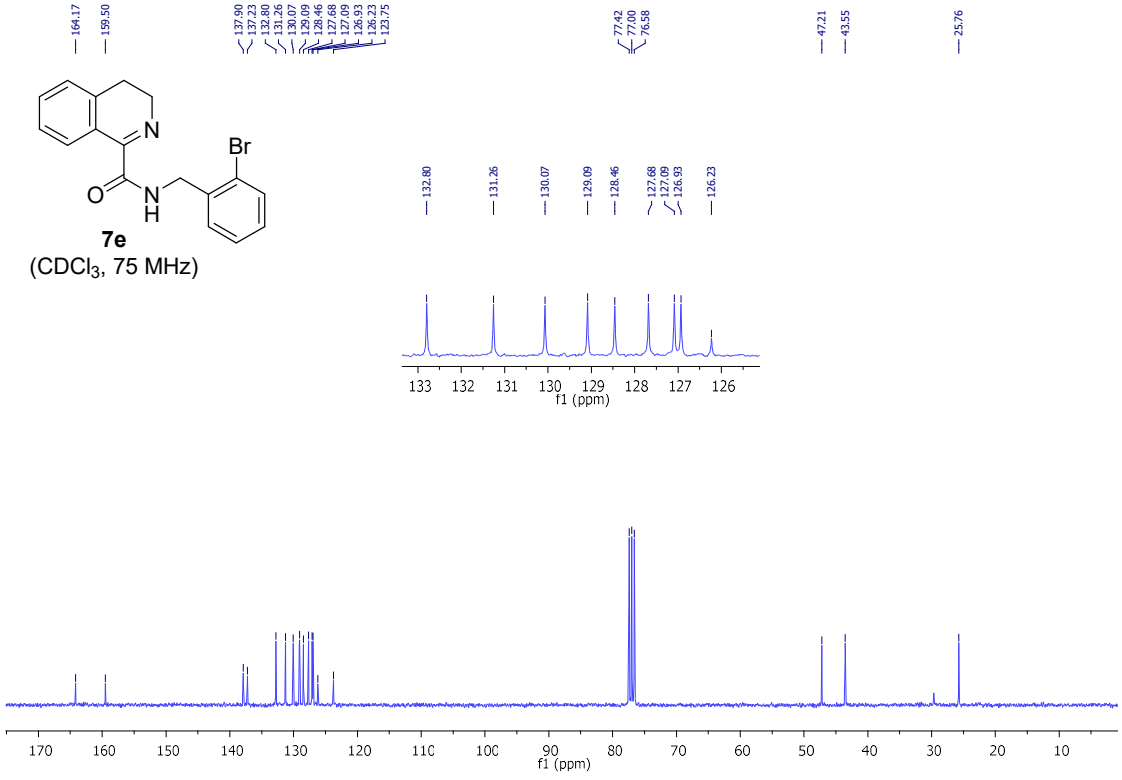

Figure S41: ^{1}H NMR of compound **7f**

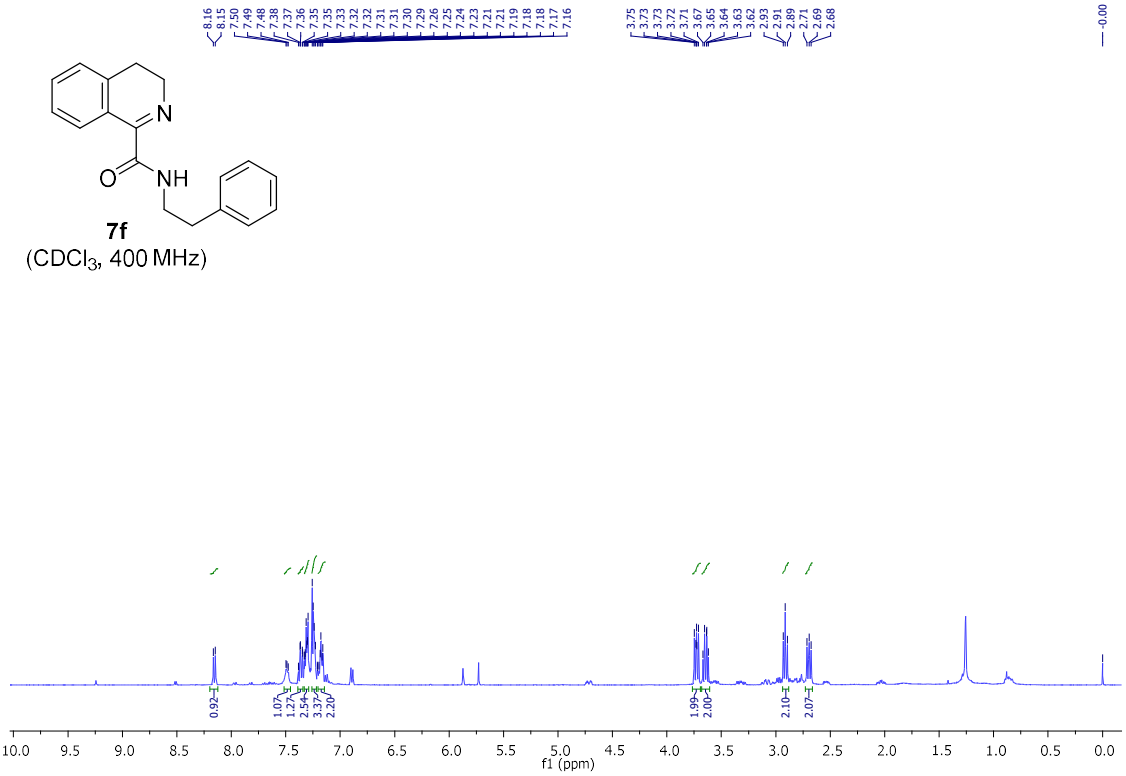

Figure S42: ^{13}C NMR of compound **7f**

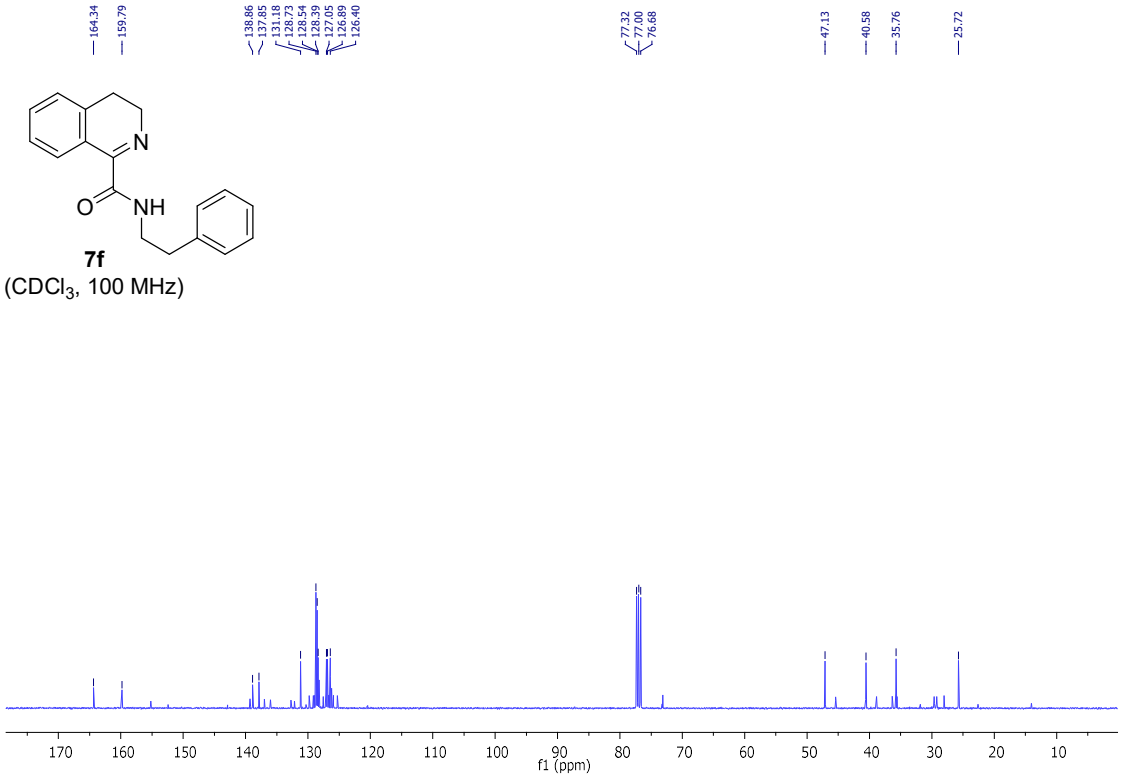

Figure S43: ^{1}H NMR of compound **7g**

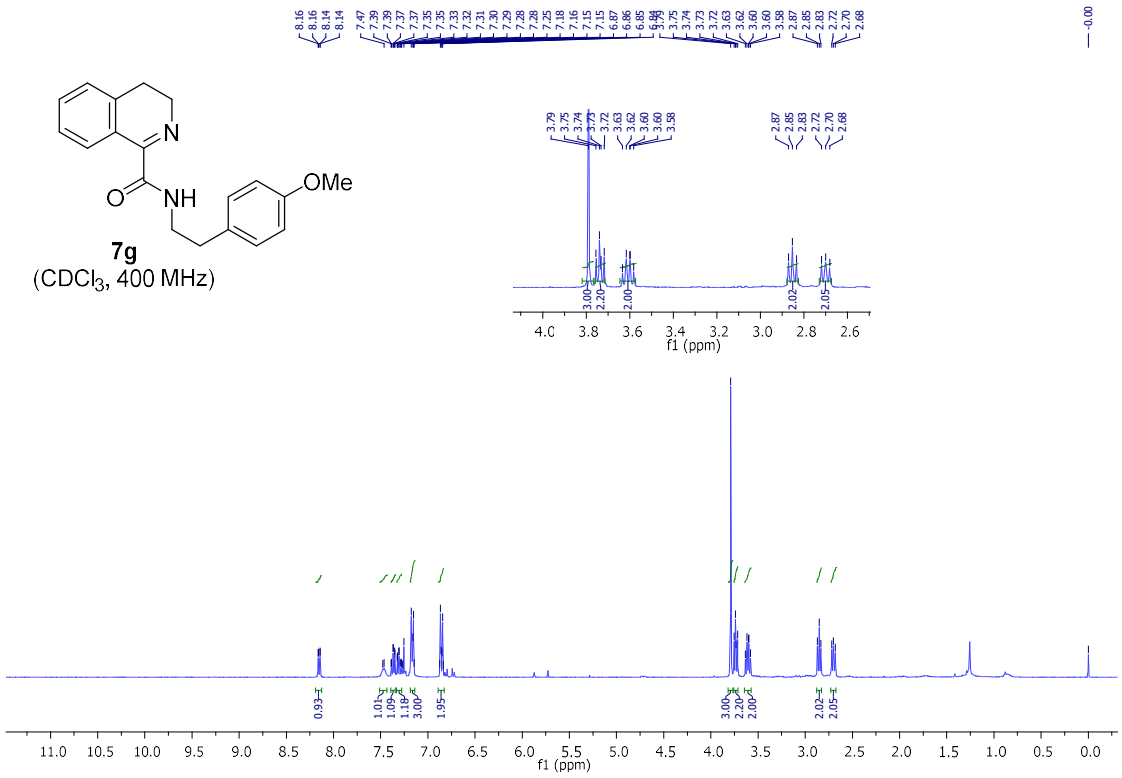

Figure S44: ^{1}H NMR of compound **7g**

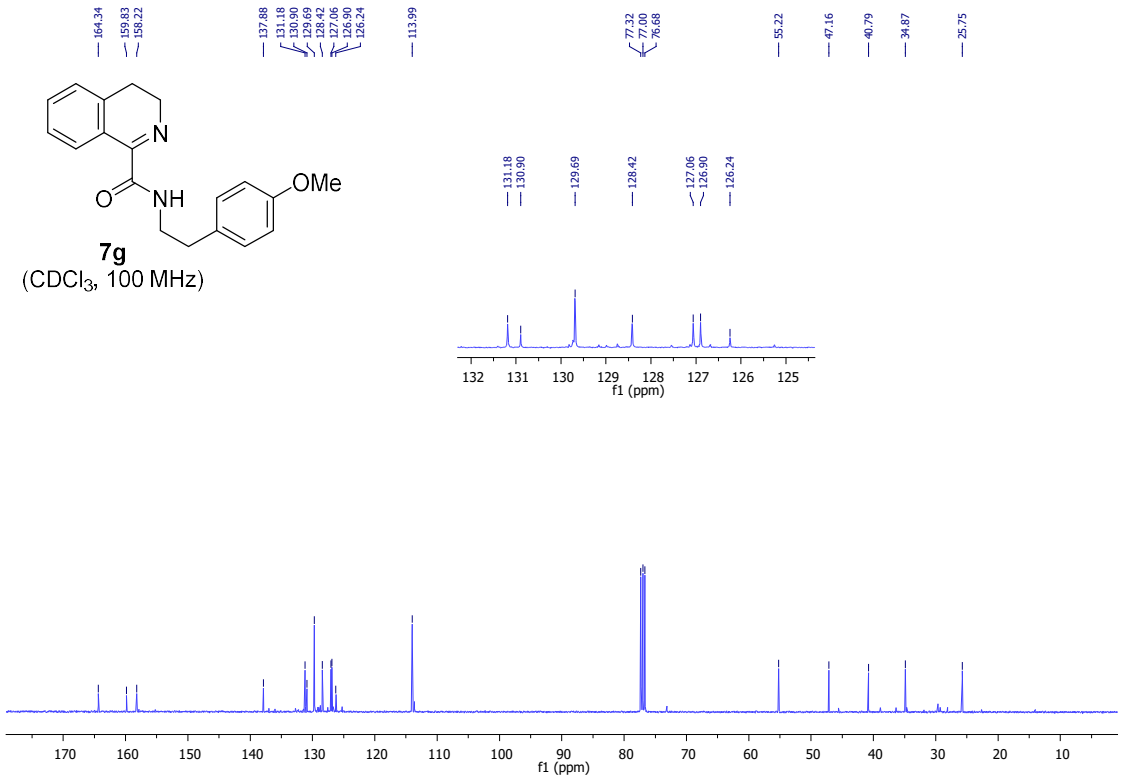

Figure S45: ^{1}H NMR of compound **7h**

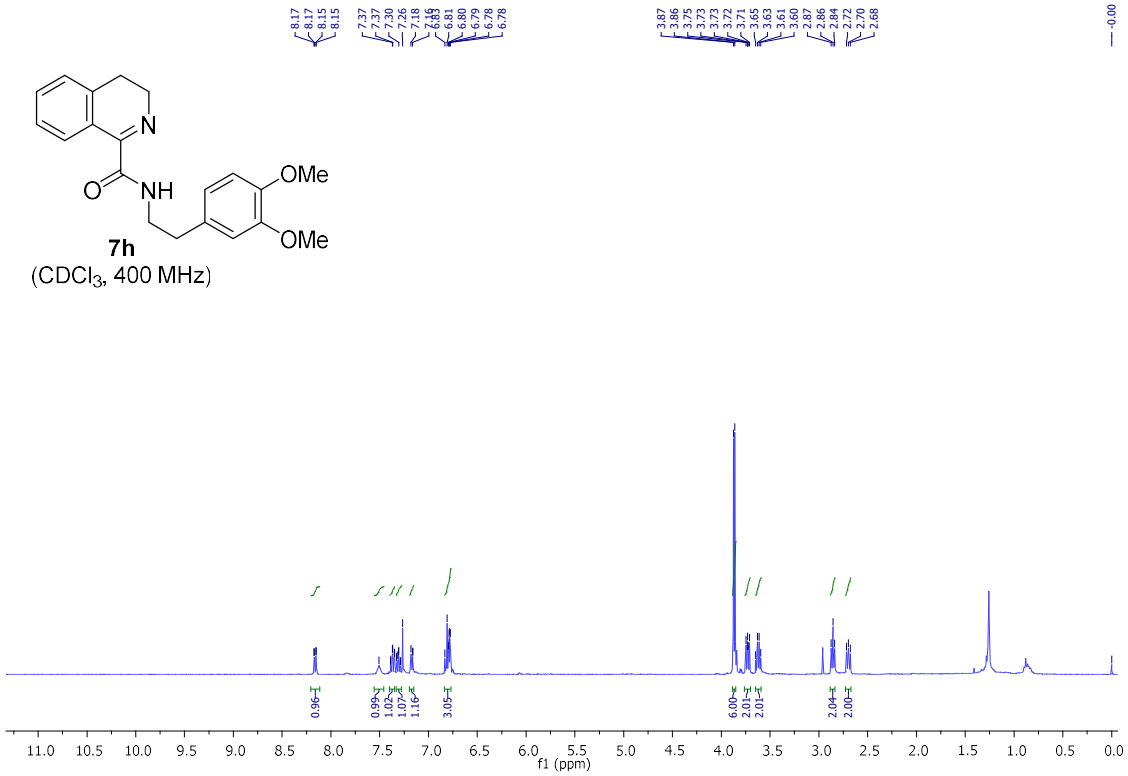

Figure S46: ^{1}H NMR of compound **7h**

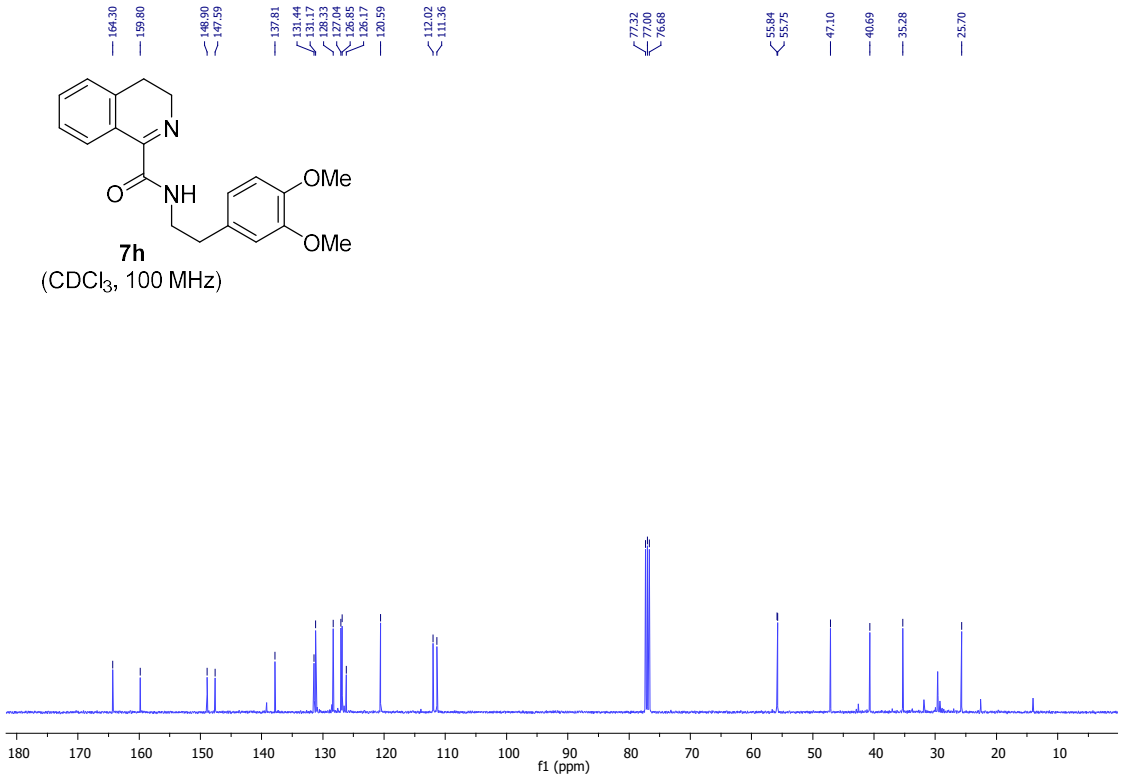

Figure S47: ^{1}H NMR of compound **7i**

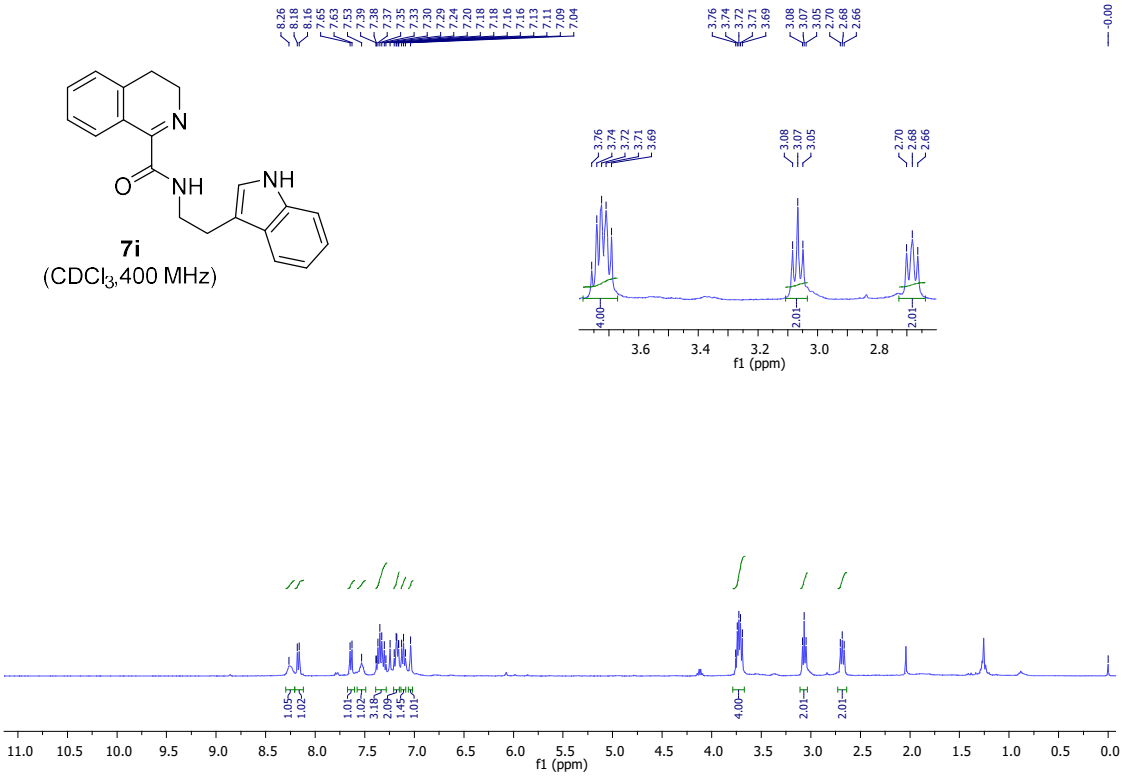

Figure S48: ^{13}C NMR of compound **7i**

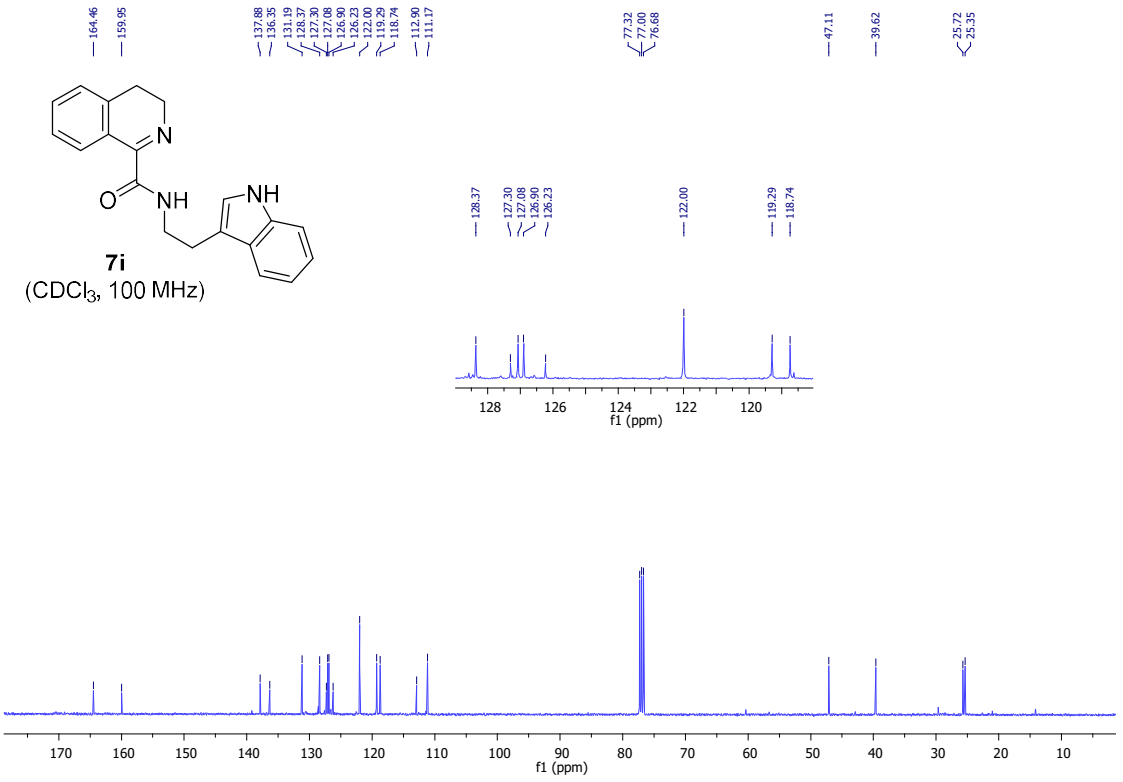

Figure S49: ^{1}H NMR of compound **7j**

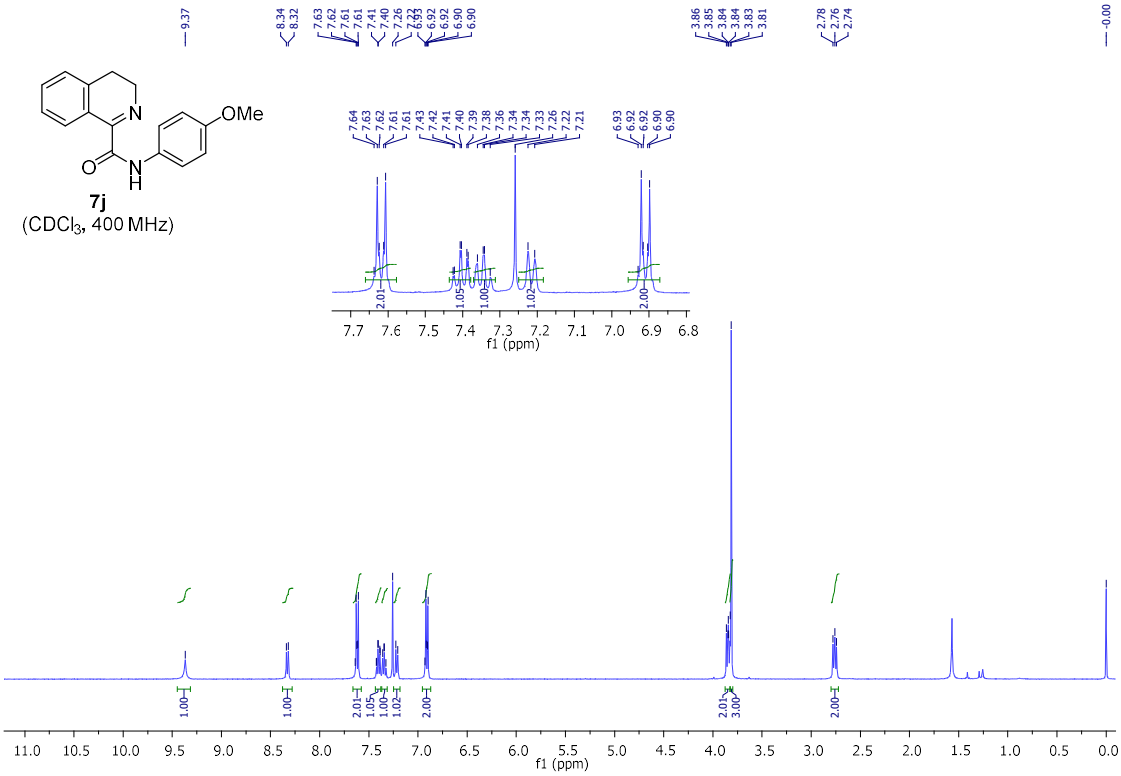

Figure S50: ^{13}C NMR of compound **7j**

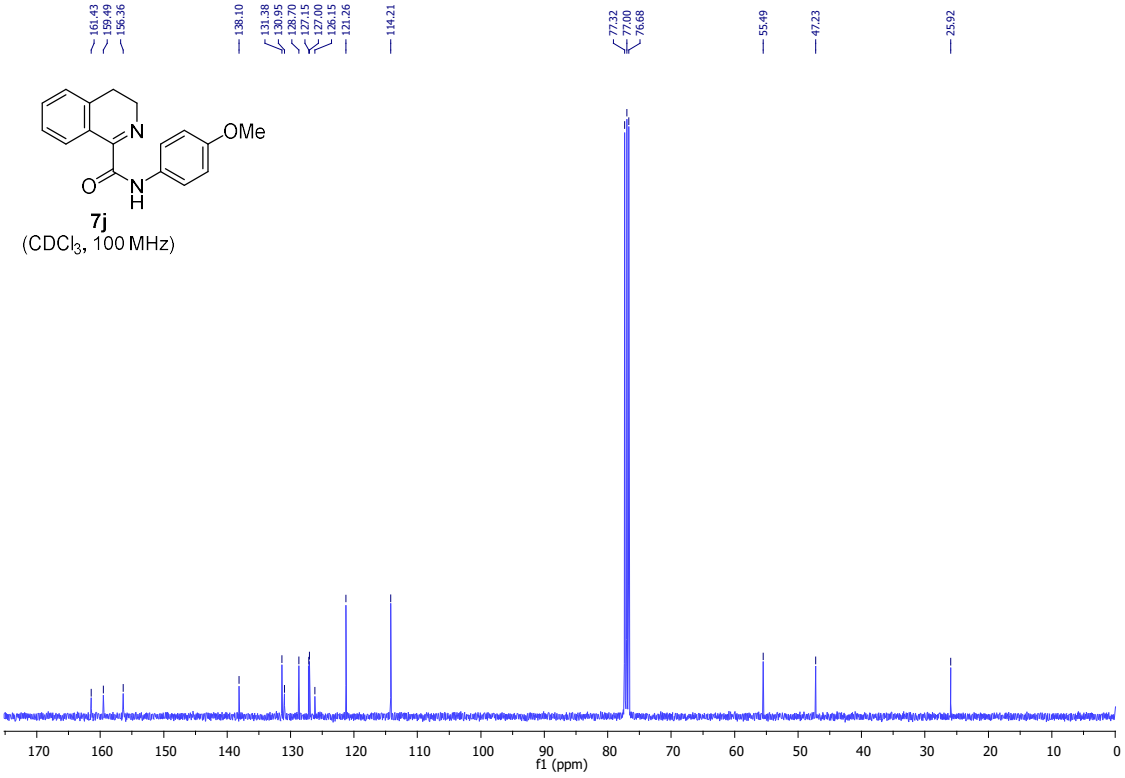

Figure S51: ^{1}H NMR of compound **7m**

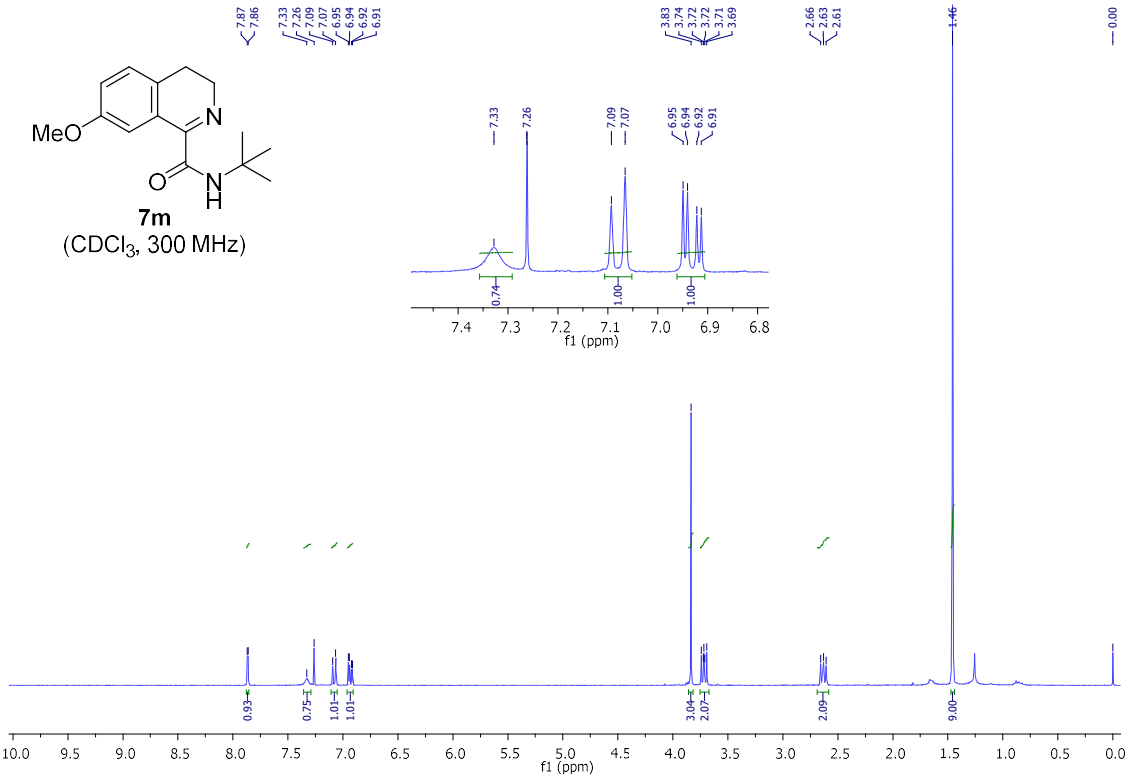

Figure S52: ^{13}C NMR of compound **7m**

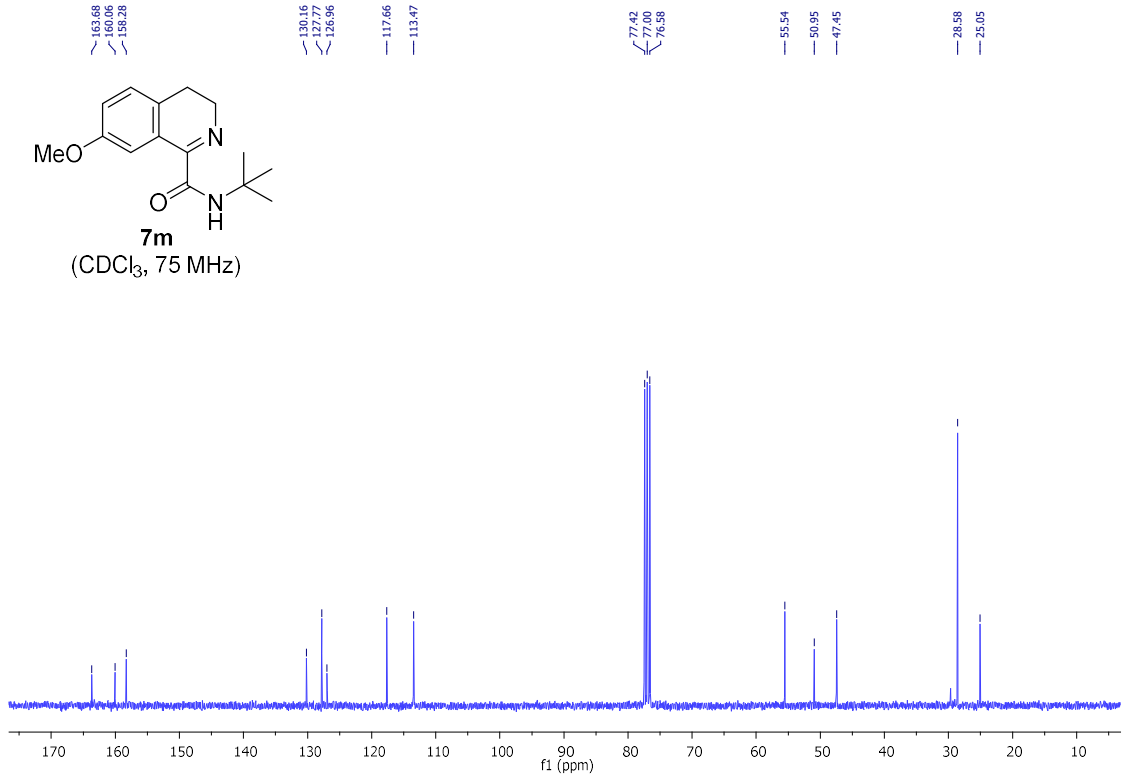

Figure S53: ^{1}H NMR of compound **9**

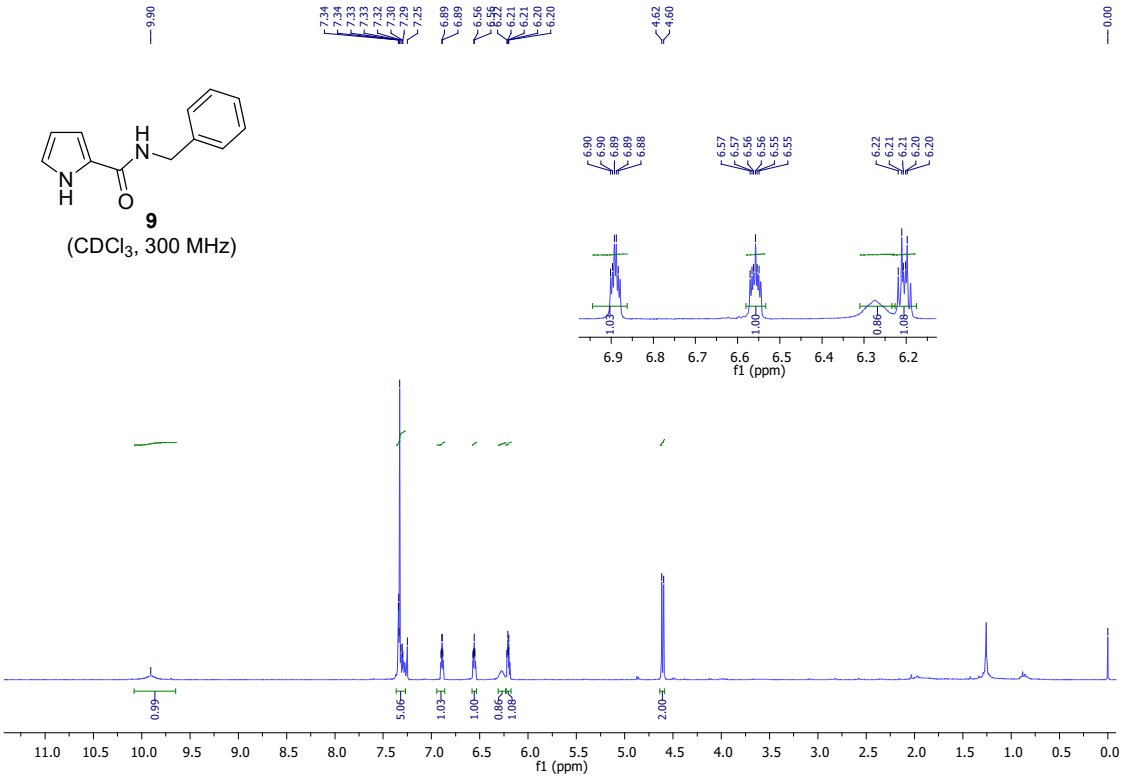

Figure S54: ^{13}C NMR of compound **9**

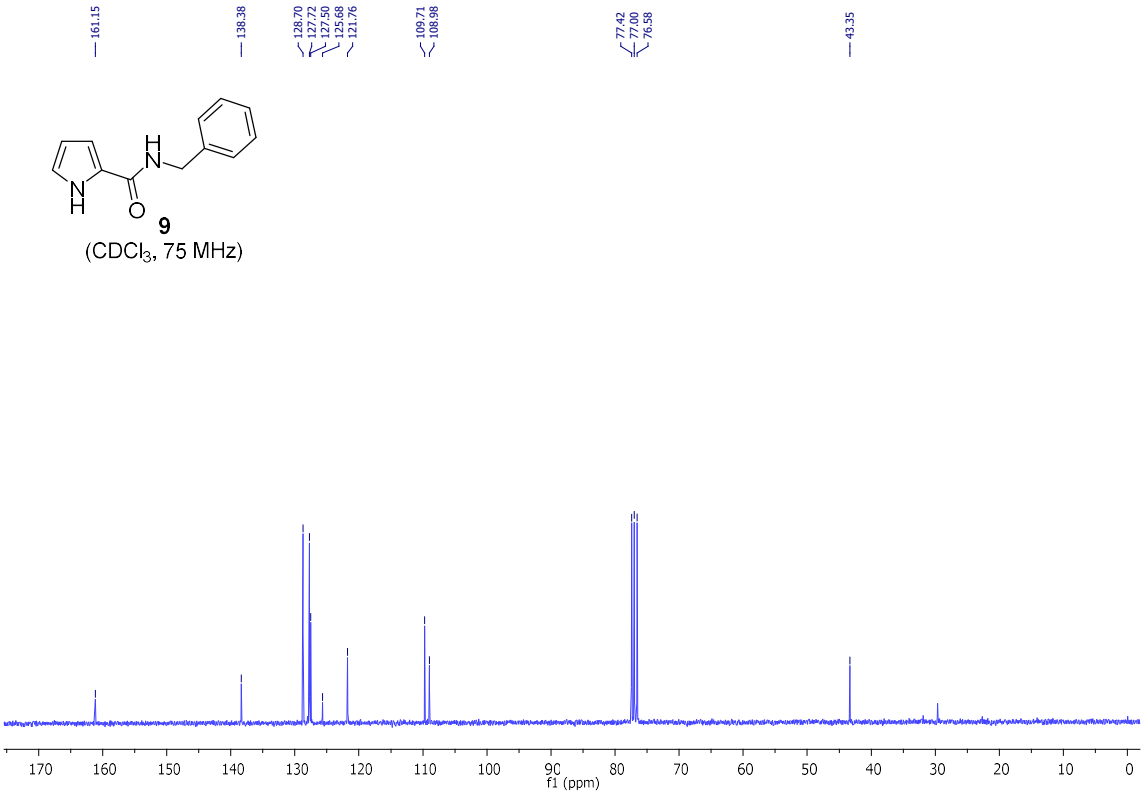

Figure S55: ^{1}H NMR of compound **11**

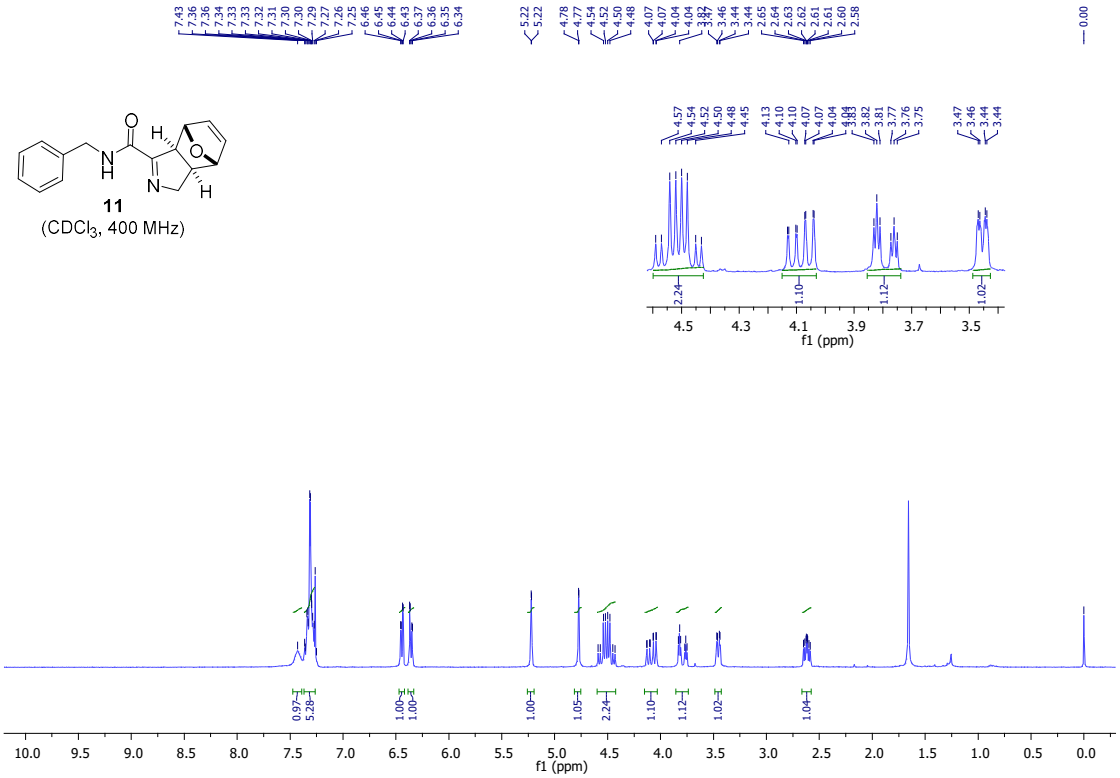

Figure S56: ^{13}C NMR of compound **11**

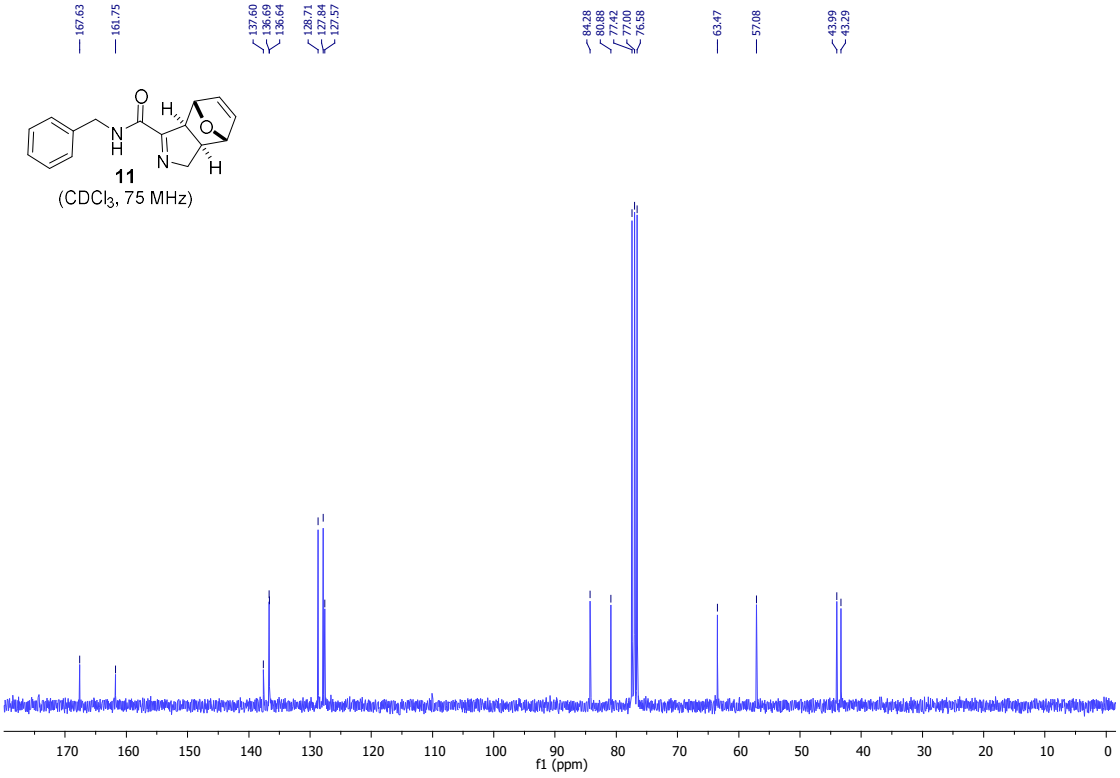

Figure S57: ^{1}H NMR of compound **14**

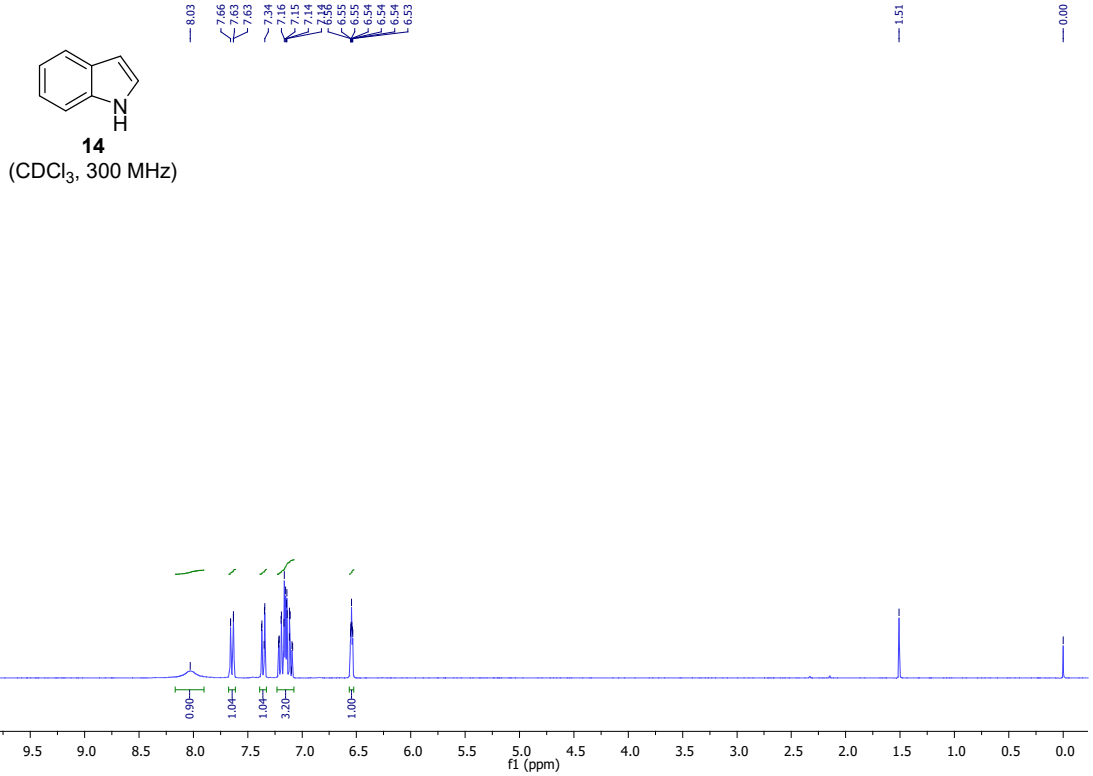

Figure S58: ^{13}C NMR of compound **14**

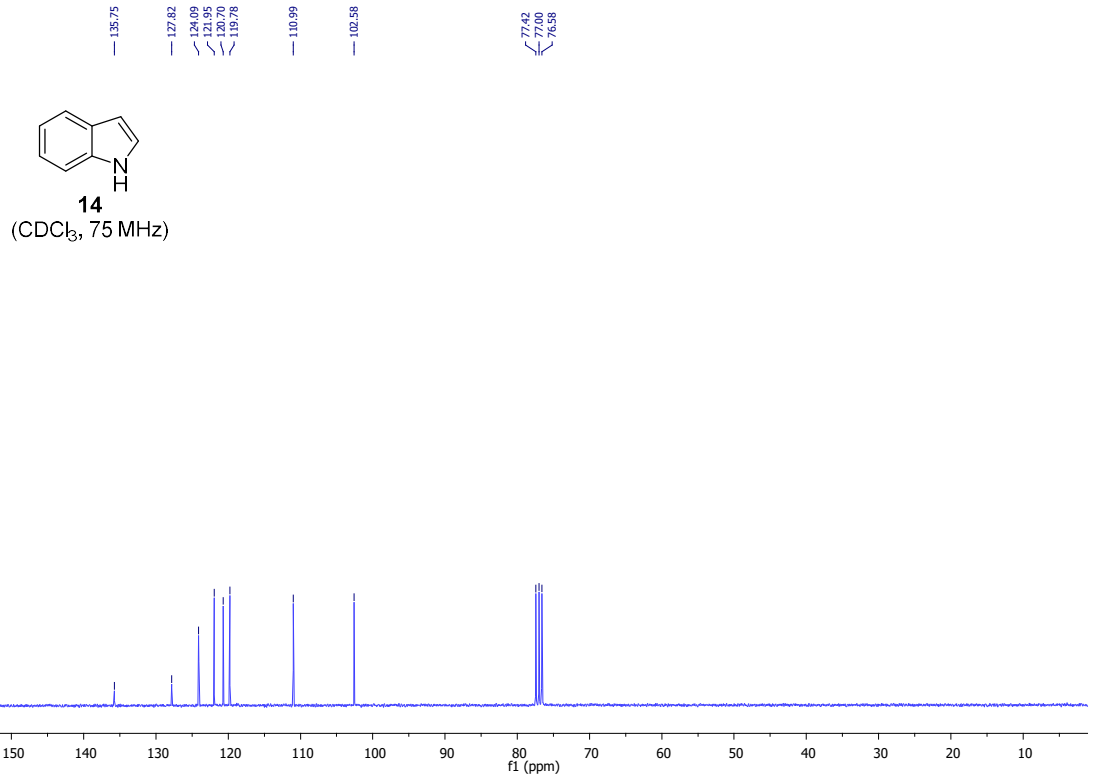

Figure S59: ^{1}H NMR of compound **I**

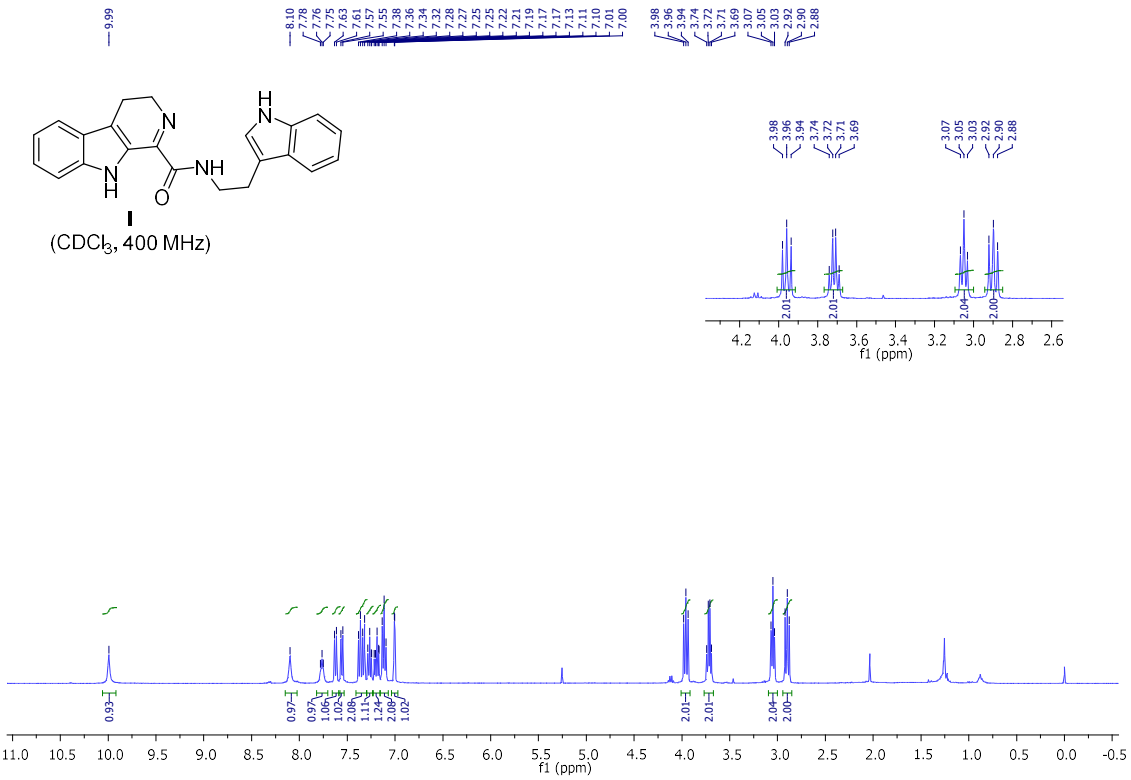

Figure S60: ^{13}C NMR of compound **I**

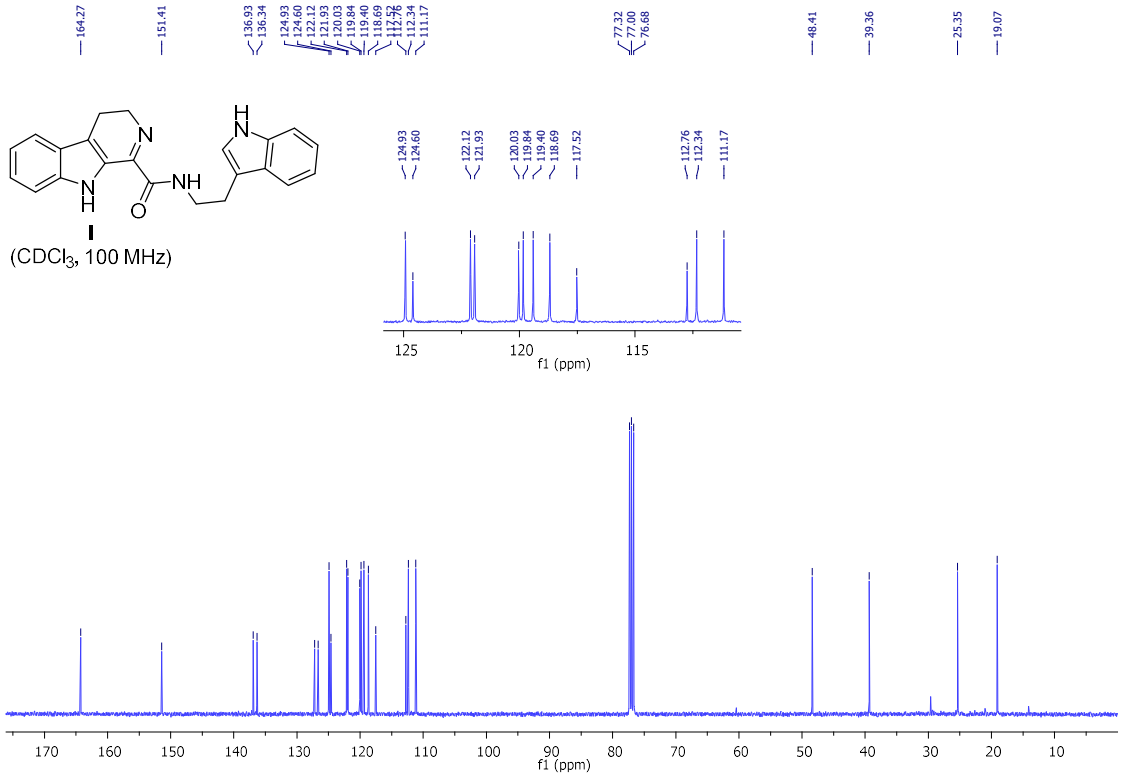

Figure S61: ^{1}H NMR of compound **II**

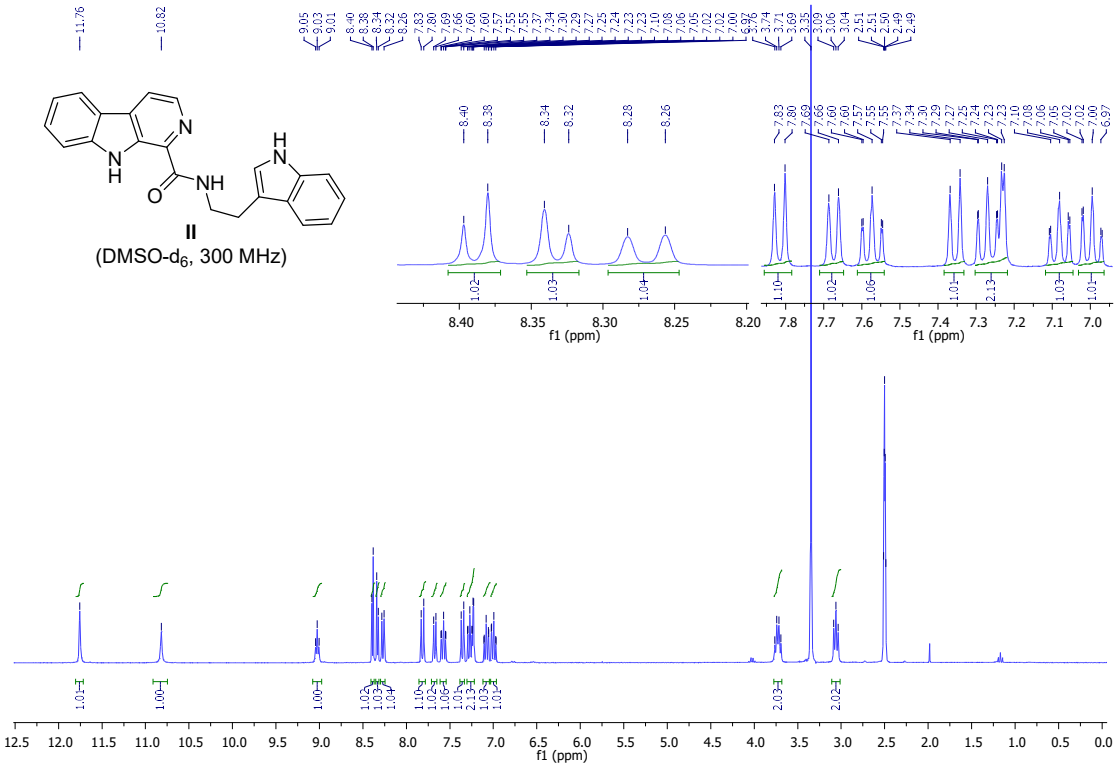

Figure S62: ^{13}C NMR of compound **II**

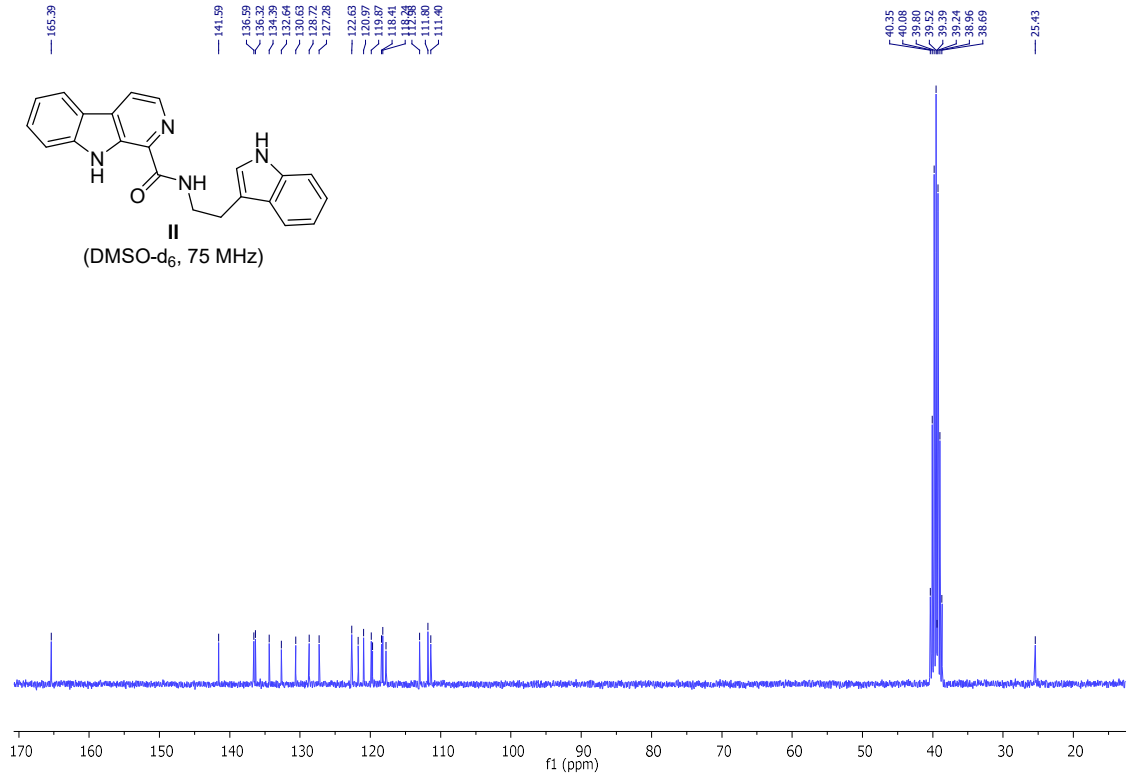

Figure S63: ^{1}H NMR of compound **22**

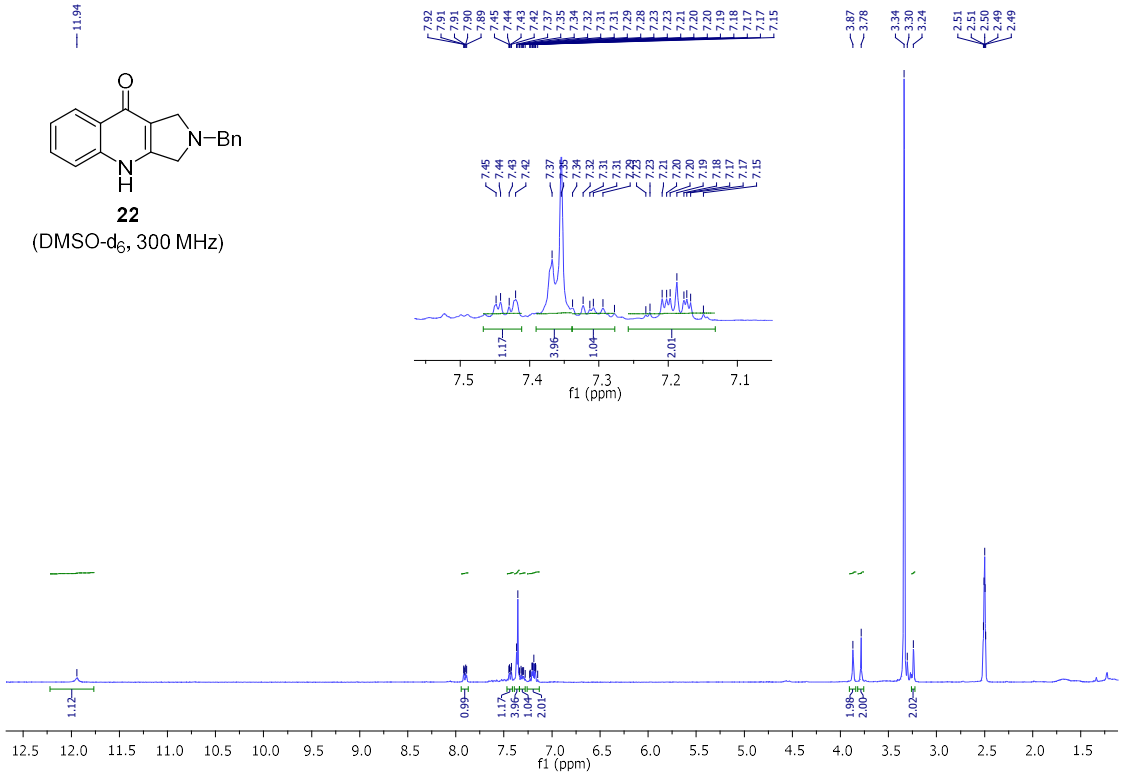

Figure S64: ^{13}C NMR of compound **22**

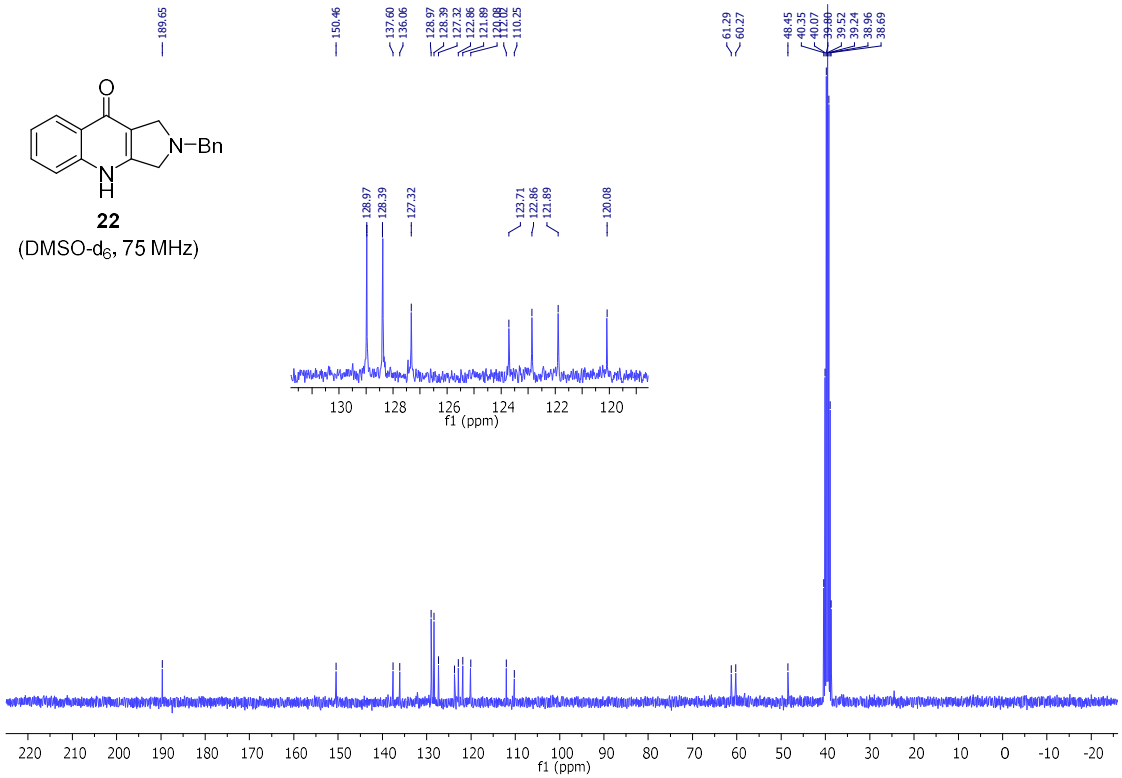

Figure S65: ^{1}H NMR of compound **24a**

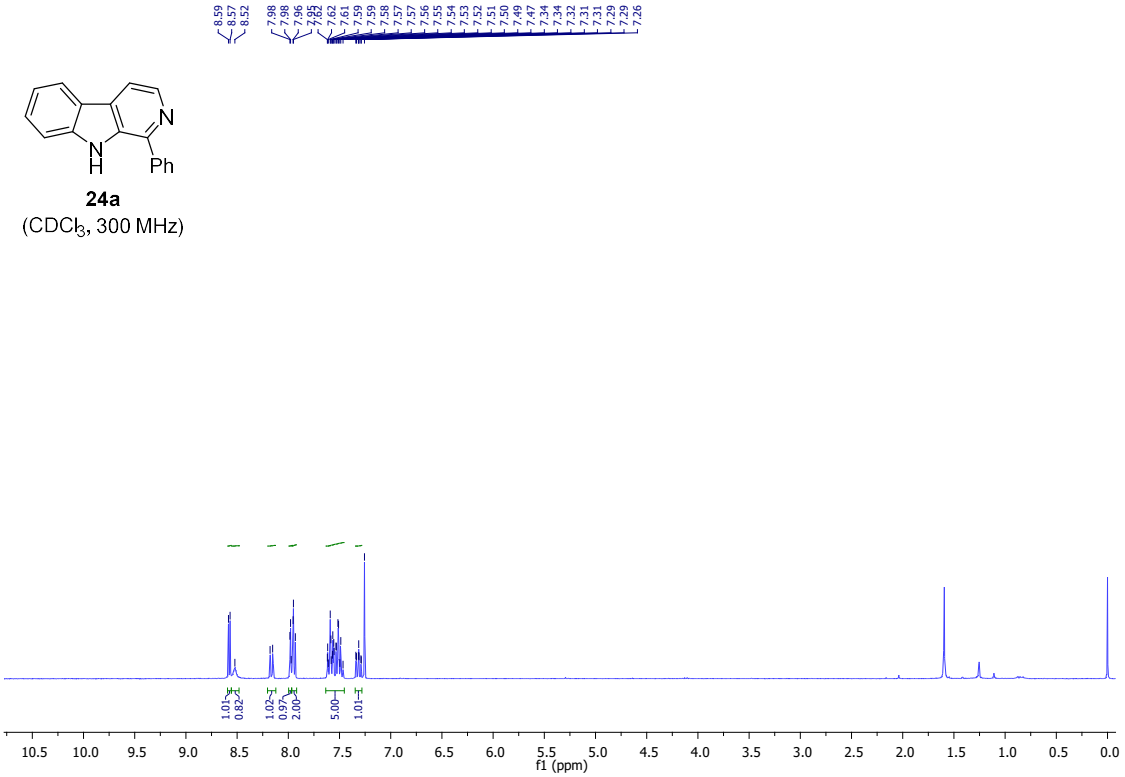

Figure S66: ^{13}C NMR of compound **24a**

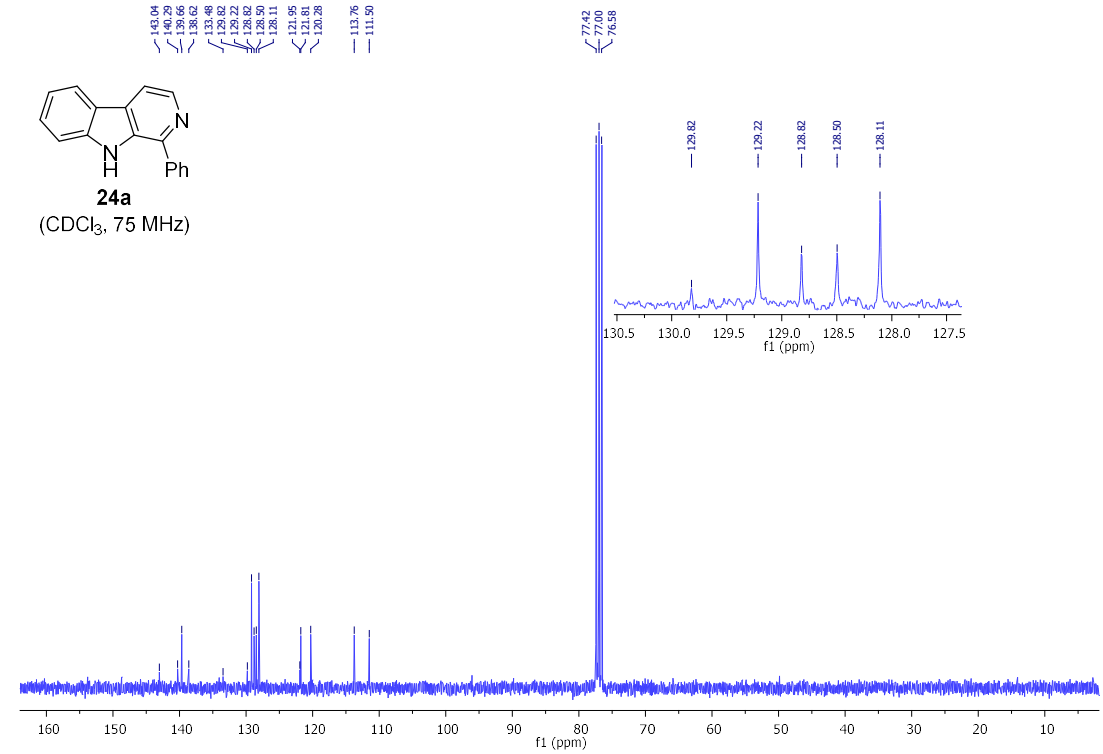

Figure S67: ^{1}H NMR of compound **24b**

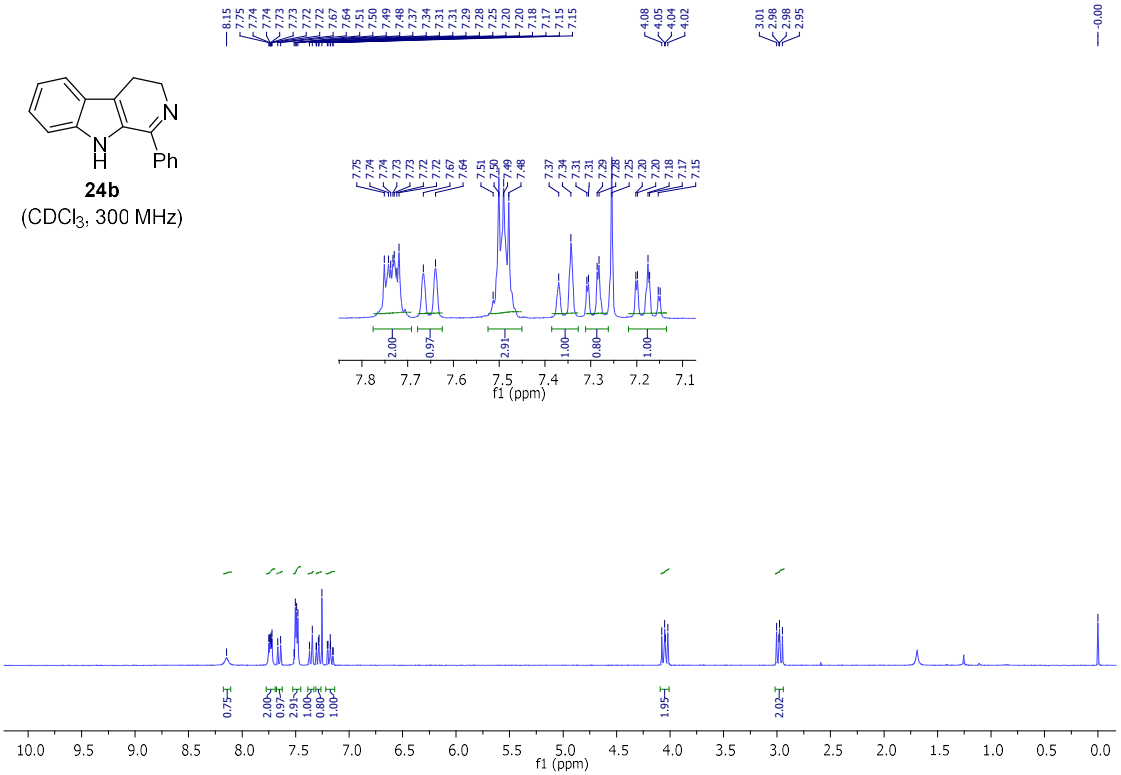

Figure S68: ^{13}C NMR of compound **24b**