Electronic Supplementary Material (ESI) for ChemComm.

N-Heterocyclic Carbene (NHC)-Catalyzed Tandem Imine Umpolung–aza-Michael Addition–Oxidationof β-Carboline Cyclic Imines

Killari Satyam,[a,b] Battu Harish,[a,b] Jagadeesh Babu Nanubolu,[c] Surisetti Suresh*[,a,b]

[a]Department of Organic Synthesis and Process Chemistry, CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad 500 007, India.
[b]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad 201002, India.
[c]Laboratory of X-Ray Crystallography, Department of Analytical Chemistry, CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad 500 007, India.

Contents:

1. General information

All the reactions were carried out with an oven dried Schlenk tube under argon atmosphere. Reactions were magnetically stirred and monitored by analytical thin layer chromatography (TLC). TLC was performed on Merck silica gel 60 F_{254}; UV lamp was used as visualizing agent. Purification of products was carried out by column chromatography by using 60-120 mesh silica and EtOAc, n-hexane were used as eluents and concentration under reduced pressure was performed by rotary evaporator at 40-45 ^{o}C, at appropriate pressure. The yields were given to the isolated products.

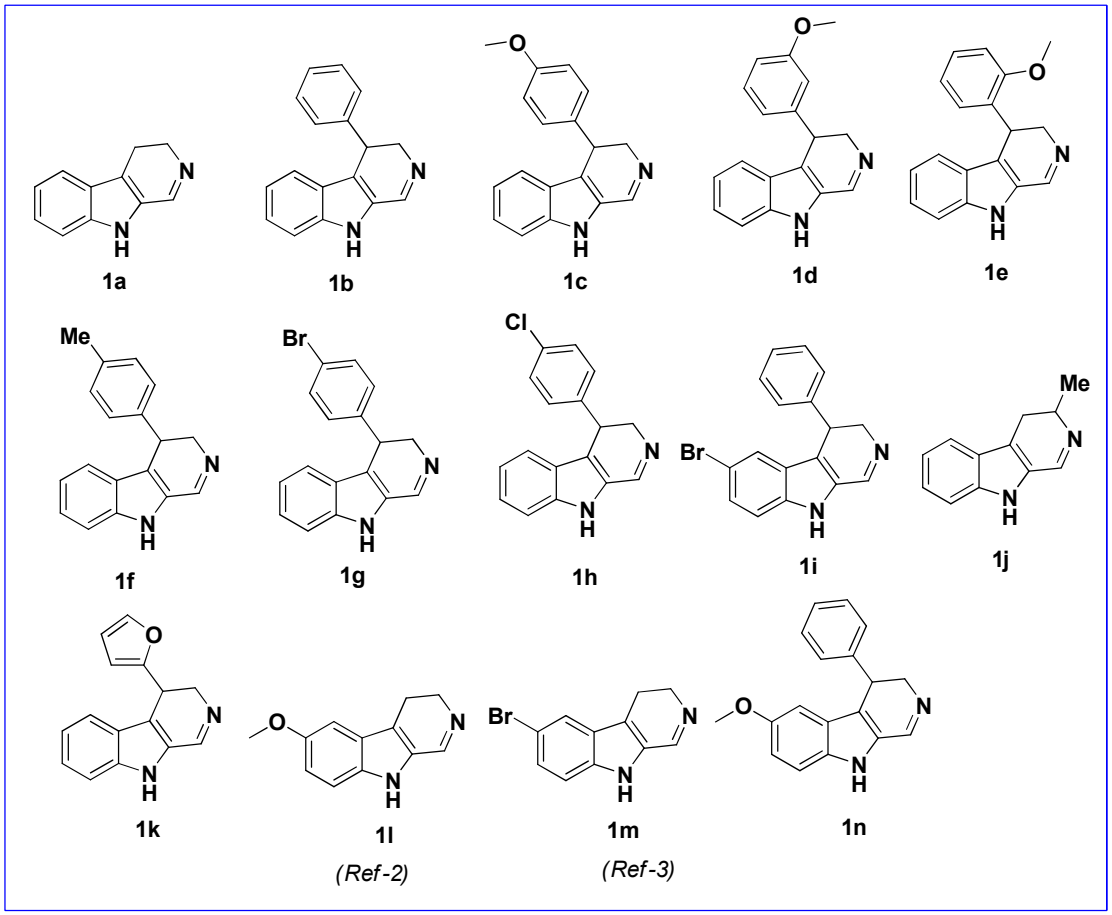
All the solvents, which were used in the reactions were dried and freshly distilled solvents according to their standard procedures, wherever required, and transferred under argon. Dry solvents like DMF, DMSO, CH_3CN, *t*-BuOH, DME and 1,4-dioxane were purchased from Finar Scientifics. Which were stored over activated 4 Å molecular sieves.

All the reagents, substrates, catalysts, deuterated solvents were purchased from commercial suppliers like as Alfa Aesar, Sigma Aldrich, TCI, S. D Fine chemicals, India, those were used without further purification.

^{1}H-NMR spectra were recorded on 300, 400 and 500 MHz instruments. Chemical shifts are reported in ppm with the reference solvent as the internal standards (TMS = 0; $CDCl_3$ = 7.26; DMSO-d_6 = 2.50). The following abbreviations were used to explain the multiplicity of the spectra (s = singlet, d = doublet, dd = doublet of doublet, t = triplet, m = multiplet, brs = broad singlet). ^{13}C-NMR spectra were recorded on 75, 100, and 125 MHz spectrometers. peaks which appears at 1.26, 0.86 in ^{1}H-NMR and 29.7 in ^{13}C-NMR corresponds to the residual grease present in the solvent (H. E. Gottlieb, V. Kotlyar, A. Nudelman, NMR Chemical Shifts of Common Laboratory Solvents as Trace Impurities. *J. Org. Chem.* 1997, **62**, 7512). Mass spectra were analysed by Electrospray Ionization (ESI) method and was obtained on a Shimadzu LCMS-2020 mass spectrometer. High resolution mass spectra were recorded on a Thermo scientific Exactive^{TM} Orbitrap mass spectrometer or Q STAR XL Hybrid MS/M. Melting points (MP) were determined using a Super Fit capillary point apparatus. MPs reported in this work are uncorrected. Infrared spectroscopy (IR-neat) was performed on a BRUKER FT-IR spectrophotometer in chloroform, and IR [KBr] spectra were recorded on a THERMO NICOLET NEXUS 670 FT-IR instrument.

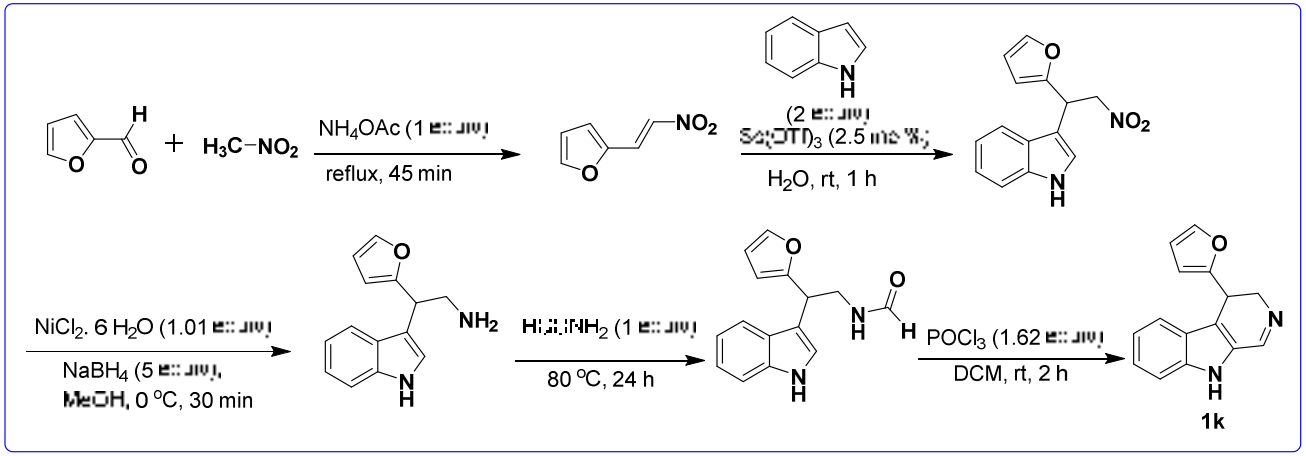
2. Synthesis of 4,9-dihydro-3*H*-pyrido[3,4-*b*]indole derivatives (1a-n)

a. **4,9-Dihydro-3*H*-pyrido[3,4-*b*]indole derivatives (1a-n) were synthesized by using literature reports and references cited therein**: [1]

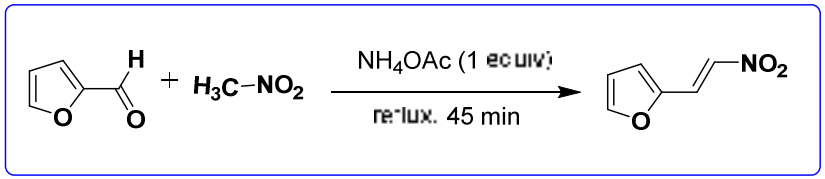


CAUTION: The dihydro *β*-carboline imines **1a-n** are found to be stable for one week at 0-4 °C.

b. Experimental procedures for the synthesis of 4-(furan-2-yl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (1k):

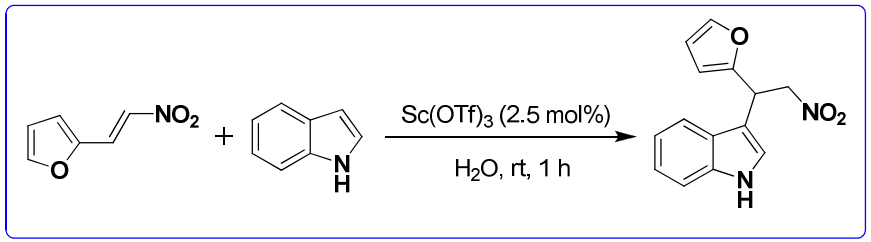


Step-1:- (*E*)-2-(2-nitrovinyl)furan preparation:



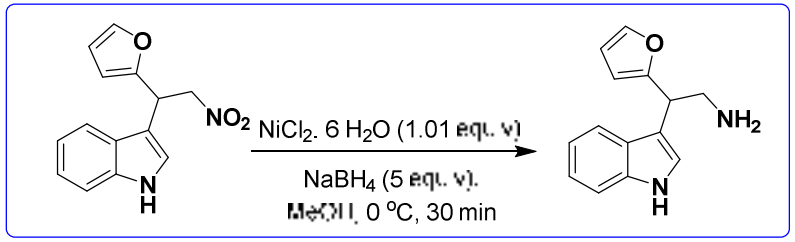
2-Furaldehyde (1.12 equiv, 30 mmol, 2.88 g) and ammonium acetate (1 equiv, 26.78 mmol, 2.06 g) were added to nitro methane (27 mL) and the reaction mixture was heated to reflux for 45 minutes. After cooling to room temperature, the solvent was evaporated and the residue was extracted with EtOAc (2 x 100 mL) and washed with saturated aqueous solution of $NaHCO_3$ (50 mL) . The combined organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography (EtOAc/Hexane, 3:97) on silica gel to afford the (*E*)-2-(2-nitrovinyl)furan as a brown solid in 80% yield. [4]

Step-2:- 3-(1-(furan-2-yl)-2-nitroethyl)-1*H*-indole preparation:



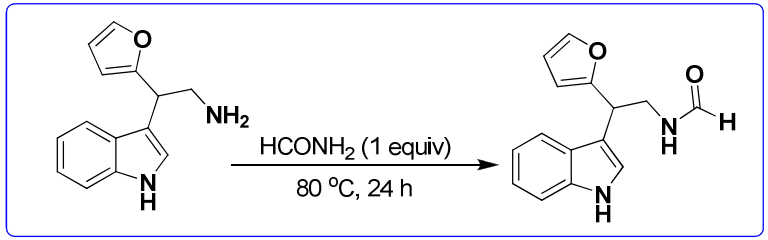
Indole (2 equiv, 48 mmol, 5.616 g) and (*E*)-2-(2-nitrovinyl)furan (1 equiv, 24 mmol, 3.336 g) were added to a solution of $Sc(OTf)_3$ (0.60 mmol, 2.5 mol%, 0.295 g) in water (48 mL). The mixture was stirred at room temperature for 1 h. The reaction mixture was then diluted with water (2 x 50 mL) and extracted with EtOAc (2 x 100 mL). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Thus obtained residue was purified by column chromatography on silica gel (EtOAc/Hexane, 20:80) to give the substituted 3-(1-(furan-2-yl)-2-nitroethyl)-1*H*-indole as a brown liquid in 84% yield. [5]

Step-3:- 2-(furan-2-yl)-2-(1*H*-indol-3-yl)ethanamine preparation:



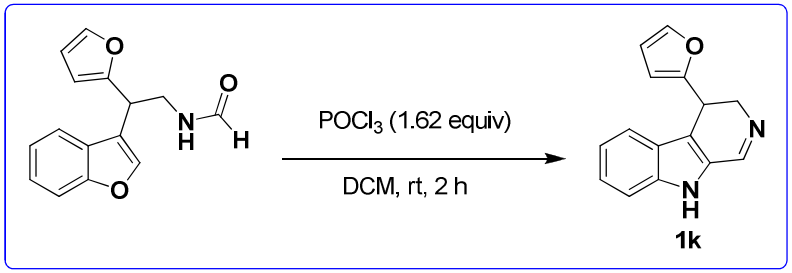
To a suspension of 3-(1-(furan-2-yl)-2-nitroethyl)-1*H*-indole (1 equiv, 19 mmol, 4.864 g) and $NiCl_2$**.** 6 H_2O (1.01 equiv, 19.19 mmol, 4.528 g) in methanol (50 mL) was added $NaBH_4$ (5 equiv, 95 mmol, 3.515 g) at 0 ^oC and the mixture was stirred at 0 ^oC for 30 min. The reaction mixture was quenched by addition of sat. NH_4Cl (50 mL) at 0 ^oC and extracted with CH_2Cl_2 (2 x 100 mL). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4. After filtration of the drying agent, the filtrate was concentrated under reduced pressure to give the required 2-(furan-2-yl)-2-(1*H*-indol-3-yl)ethanamine as a white solid in 95% yield. [6]

Step-4:- *N*-(2-(furan-2-yl)-2-(1*H*-indol-3-yl)ethyl)formamide preparation:



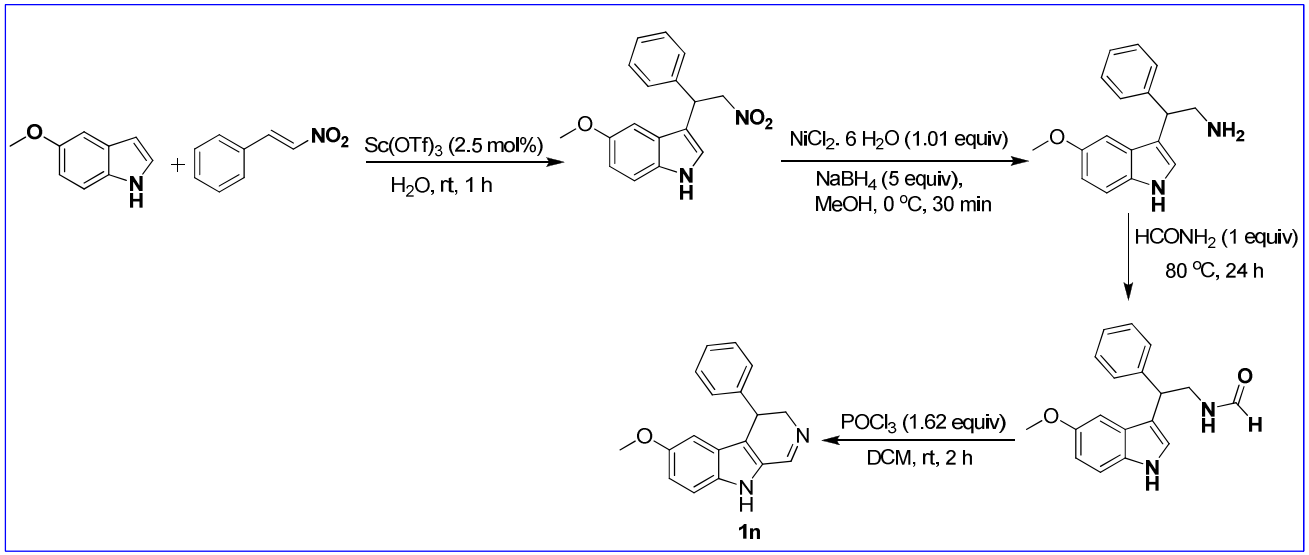
A mixture of 2-(furan-2-yl)-2-(1*H*-indol-3-yl)ethanamine (1 equiv, 18 mmol, 4.068 g) and formamide (1 equiv, 18 mmol, 0.810 g) under neat conditions was stirred for 24 h at 80 °C. After stirring for 24 h the reaction mixture was cooled to room temperature and the crude product was directly used in the next step without further purification. [7]

Step-5:- 4-(furan-2-yl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole **1k** preparation:

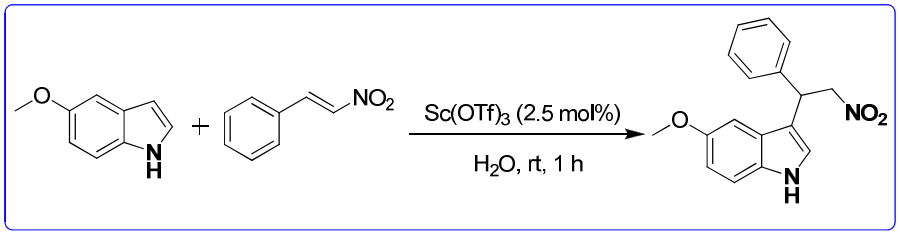


N-(2-(furan-2-yl)-2-(1*H*-indol-3-yl)ethyl)formamide (1 equiv, 16.20 mmol, 4.114 g) was dissolved in DCM solvent (12 mL) and $POCl_3$ (1.62 equiv, 26.24 mmol, 2.44 mL) was added to this solution at 0-5 °C. After the addition, reaction mixture was stirred at room temperature for another 2 h. Then it was concentrated under reduced pressure to remove volatiles. Thus obtained dark solid residue was suspended in EtOAc (100 mL) and extracted with 10% AcOH/water (20 mL). The combined aqueous extract was basified with conc. NaOH until pH = 9. The precipitated solid was extracted with DCM (3 x 100 mL) to afford the 4-(furan-2-yl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole **1k** in 86% yield. [8]

c. Experimental procedures for the synthesis of 6-methoxy-4-phenyl-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (1n):



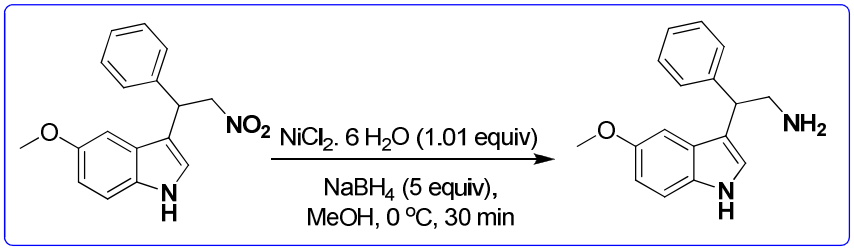
Step-1:- 5-methoxy-3-(2-nitro-1-phenylethyl)-1*H*-indole preparation:



5-methoxyIndole (2 equiv, 48 mmol, 7.056 g) and trans-*β*-nitrostyrene (1 equiv, 24 mmol, 3.576 g) were added to a solution of $Sc(OTf)_3$ (0.60 mmol, 2.5 mol%, 0.295 g) in water (48 mL). The mixture was stirred at room temperature for 1 h. The reaction mixture was then diluted with water (2 x 50 mL) and extracted with EtOAc (2 x 100 mL). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Thus obtained residue was purified by

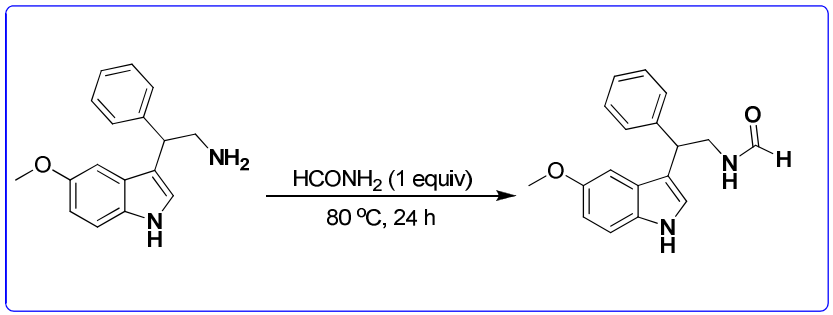
column chromatography on silica gel (EtOAc/Hexane, 25:75) to give the 5-methoxy-3-(2-nitro-1-phenylethyl)-1*H*-indole as a brown liquid in 94% yield. [5]

Step-2:- 2-(5-methoxy-1*H*-indol-3-yl)-2-phenylethanamine preparation:



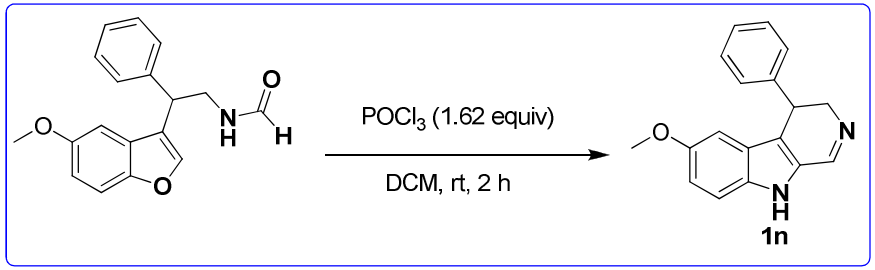
To a suspension of 5-methoxy-3-(2-nitro-1-phenylethyl)-1*H*-indole (1 equiv, 22 mmol, 6.512 g) and $NiCl_2$**.** 6 H_2O (1.01 equiv, 22.22 mmol, 5.243 g) in methanol (60 mL) was added $NaBH_4$ (5 equiv, 110 mmol, 4.070 g) at 0 ^oC and the mixture was stirred at 0 ^oC for 30 min. The reaction mixture was quenched by addition of sat. NH_4Cl (50 mL) at 0 ^oC and extracted with CH_2Cl_2 (2 x 100 mL). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4. After filtration of the drying agent, the filtrate was concentrated under reduced pressure to give the required 2-(5-methoxy-1*H*-indol-3-yl)-2-phenylethanamine as a white solid in 93% yield. [6]

Step-3:- *N*-(2-(5-methoxy-1*H*-indol-3-yl)-2-phenylethyl)formamide preparation:



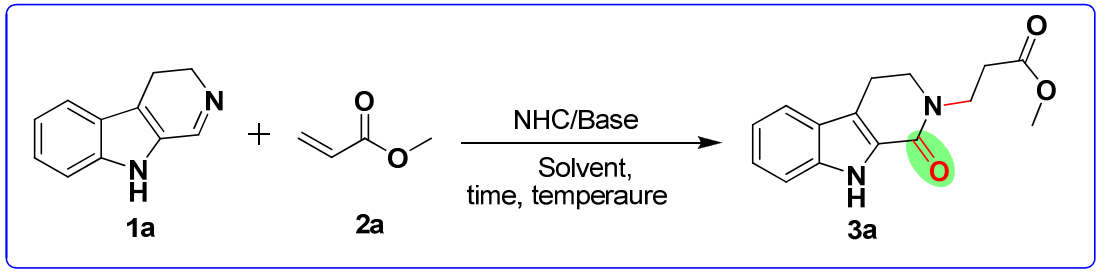
A mixture of 2-(5-methoxy-1*H*-indol-3-yl)-2-phenylethanamine (1 equiv, 18 mmol, 4.788 g) and formamide (1 equiv, 18 mmol, 0.810 g) under neat conditions was stirred for 24 h at 80 ^{o}C. After stirring for 24 h the reaction mixture was cooled to room temperature and the crude product was directly used in the next step without further purification. [7]

Step-5:- 6-methoxy-4-phenyl-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole **1n** preparation:



N-(2-(5-methoxy-1*H*-indol-3-yl)-2-phenylethyl)formamide (1 equiv, 18 mmol, 5.292 g) was dissolved in DCM solvent (12 mL) and $POCl_3$ (1.62 equiv, 26.24 mmol, 2.44 mL) was added to this solution at 0-5 ^{o}C. After the addition, reaction mixture was stirred at room temperature for another 2 h. Then it was concentrated under reduced pressure to remove volatiles. Thus obtained dark solid residue was suspended in EtOAc (100 mL) and extracted with 10% AcOH/water (20 mL). The combined aqueous extract was basified with conc. NaOH until pH = 9. The precipitated solid was extracted with DCM (3 x 100 mL) to afford the 6-methoxy-4-phenyl-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole **1n** in 89% yield. [8]

3. General procedure for the optimization study

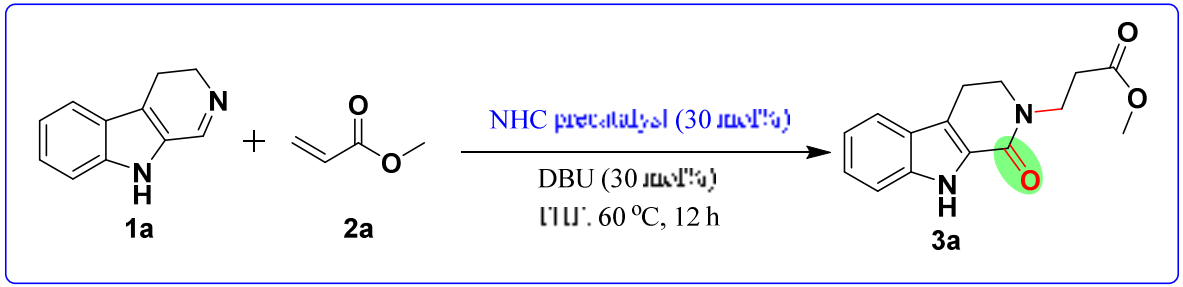


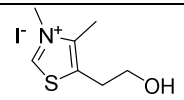
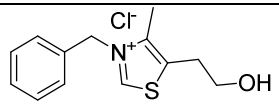
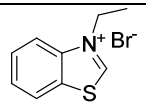
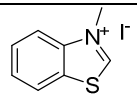
The 4,9-dihydro-3*H*-pyrido[3,4-*b*]indole **1a** (1 equiv, 0.50 mmol, 85 mg) and NHC precatalyst (0.15 mmol, 30 mol%) were taken in a clean and oven dried Schlenk tube, it was evacuated and back filled with argon gas (2-3 cycles). Then added dry solvent (5 mL, un-degassed) followed by the addition of methyl acrylate **2a** (1 equiv, 0.50 mmol, 0.04 mL) and base (0.15 mmol, 30 mol%). Then reaction mixture was stirred at the temperature and time as mentioned in optimization Tables S1-S4. After completion of the reaction, the reaction mixture was diluted with water (2 x 20 mL), extracted with dichloromethane (2 x 10 mL), dried over on anhydrous Na_2SO_4 and the filtrate was concentrated under reduced pressure. The crude was purified by column chromatography (Hexane/EtOAc) on 60-120 mesh silica gel to afford the methyl 3-(1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate **3a** as a pure product.

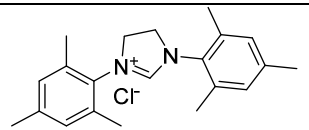
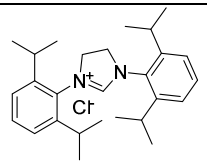
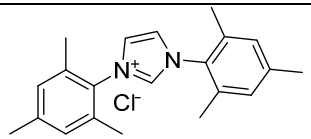
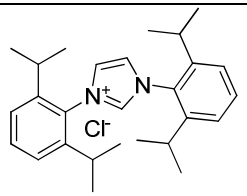
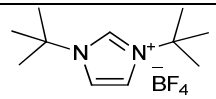
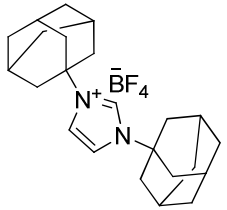
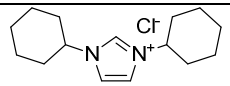
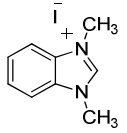
Note: **please see tables S1-S4, for screening of various NHCs, bases, solvents and their ratios/quantities**

4. Optimization survey

Table S1: Screening of various NHC precatalysts



Entry	NHC precatalyst (30 mol %)	Structure of the NHC precatalyst	% Yield of 3a
1.	5-(2-Hydroxyethyl)-3,4-dimethylthiazolium iodide **A1**		25
2.	3-Benzyl-5-(2-hydroxyethyl)-4-methylthiazolium chloride **A2**		traces
3.	3-Ethylbenzothiazolium bromide **A3**		traces
4.	3-Methylbenzothiazolium iodide **A4**		40

5.	1,3-Bis(2,4,6-trimethylphenyl)imidazolinium chloride **B1**		traces
6.	1,3-Bis-(2,6-diisopropylphenyl)imidazolinium chloride **B2**		28
7.	**1,3-Bis(2,4,6-trimethylphenyl)imidazolium chloride C1**		**81**
8.	1,3-Bis(2,6-diisopropylphenyl)imidazolium chloride **C2**		47
9.	1,3-Di-*ter*t-butylimidazolium tetrafluoroborate **C3**		traces
10.	1,3-Bis(1-adamantyl)imidazolium tetrafluoroborate **C4**		49
11.	1,3-Dicyclohexylimidazolium chloride **C5**		44
12.	1,3-Dimethyl-1*H*-benzimidazolium iodide **C6**		50

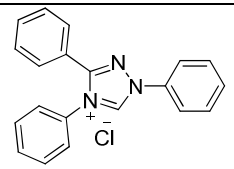
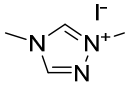
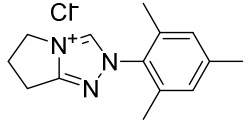
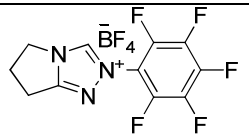
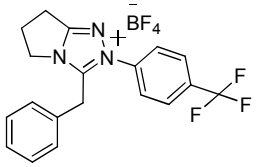
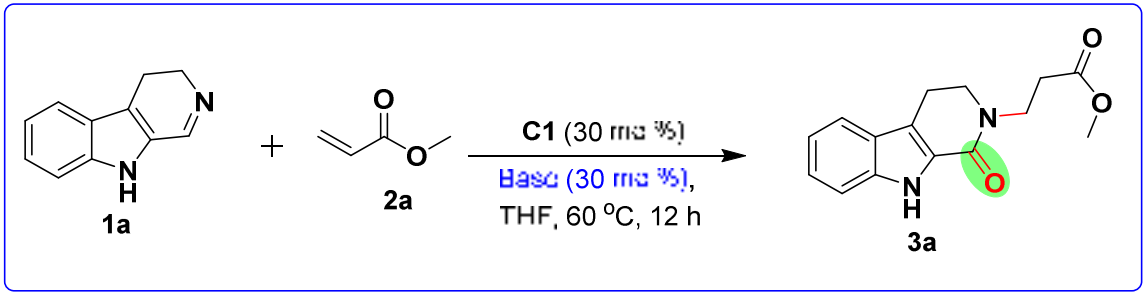
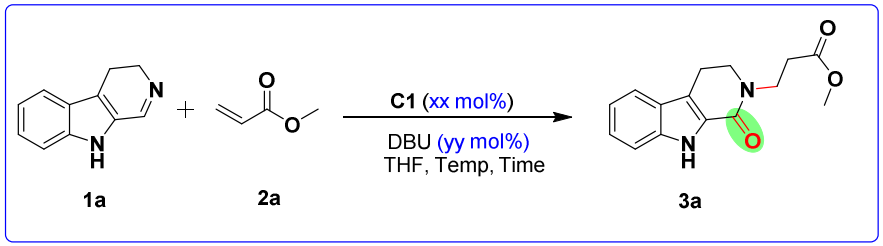
13.	1,3,4-triphenyl-1*H*-1,2,4-triazol-4-ium chloride **D1**		27
14.	1,4-Dimethyl-1,2,4-triazolium iodide **D2**		traces
15.	2-Mesityl-2,5,6,7-tetrahydropyrrolo[2,1-*c*][1,2,4] triazol-4-ium chloride **D3**		traces
16.	6,7-Dihydro-2-pentafluorophenyl-5*H*-pyrrolo[2,1-*c*]-1,2,4-triazolium tetrafluoroborate **D4**		traces
17.	(*S*)-Benzyl-2-[4-(trifluoroMethyl)phenyl]-6,7-dihydro-5*H*-pyrrolo[2,1-*c*][1,2,4]triazolium tetrafluoroborate **D5**		traces

Table S2: Screening of various bases



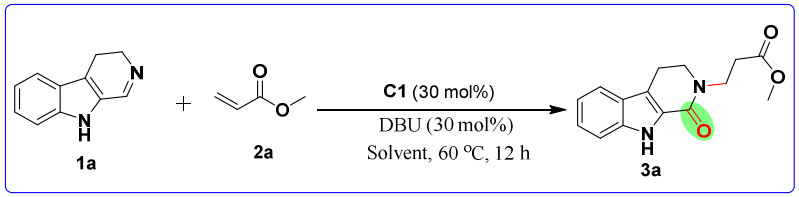
Entry	Base (30 mol%)	% Yield of 3a
1.	K_2CO_3	55
2.	K_3PO_4	50
3.	Et_3N	20
4.	1,4-Diazabicyclo[2.2.2]octane (DABCO)	62
5.	NaH	-
6.	Cs_2CO_3	31
7.	**1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU)**	**81**

Table S3: Screening of molar equivalents of NHC, DBU and reaction conditions



Entry	NHC precatalyst C1	DBU (yy mol%)	Temp. (^{o}C)	Time (h)	% Yield of 3a
1.	10	30	60	12	45
2.	20	30	60	12	78
3.	**30**	**30**	**60**	**12**	**81**
4.	30	20	60	12	76
5.	30	60	60	12	65
6.	30	100	60	12	25
7.	30	30	40	12	52
8.	30	30	rt	12	40
9.	30	30	80	12	-
10.	30	30	60	24	81

Table S4: Screening of various solvents



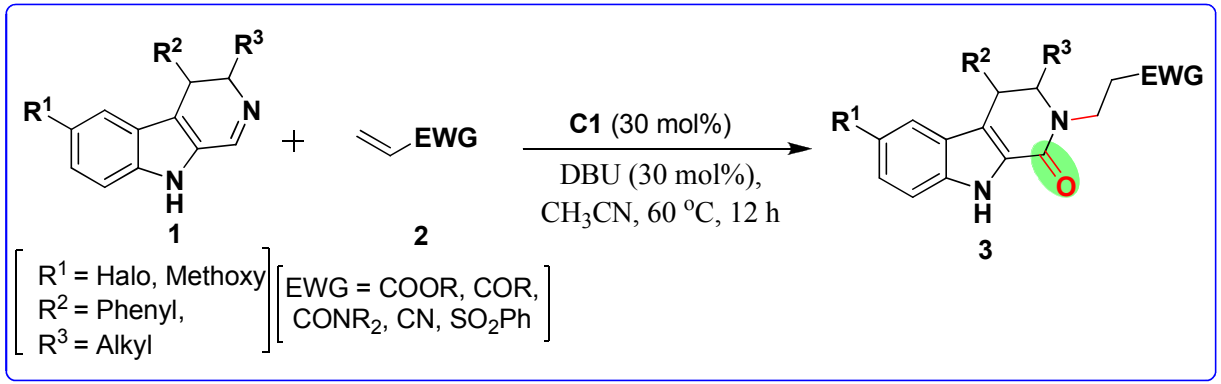
Entry	NHC.C1 (mol%)	DBU (mol%)	Solvent	Temp. (°C)	Time (h)	% Yield of 3a
1.	30	30	THF	60	12	81
2.	**30**	**30**	**CH_3CN**	**60**	**12**	**86**
3.	30	30	1,4-Dioxane	60	12	25
4.	30	30	Dimethyl sulfoxide (DMSO)	60	12	-
5.	30	30	*N,N*-Dimethylformamide (DMF)	60	12	-
6.	30	30	1,2-Dimethoxyethane (DME)	60	12	-
7.	30	30	*t*-BuOH	60	12	-
8.	30	30	1,2-Dichloroethane (DCE)	60	12	-
9.	30	30	EtOAc	60	12	-
10.	30	30	THF:H_2O (1:10)	60	12	-

Table S5: **Reaction without using NHC precatalyst (or) base**

(Optimized conditions mentioned entry 2, Table S4 were used)

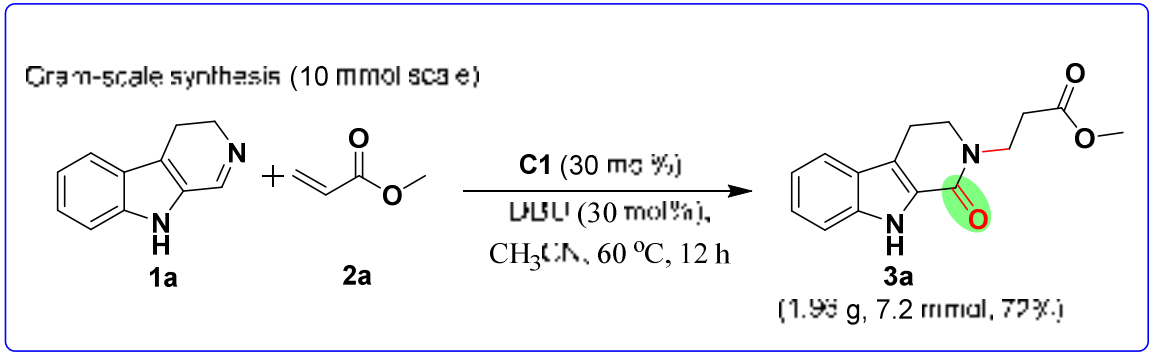
Entry	NHC precatalyst	Base	Solvent	% Yield of 3a
1.	1,3-Bis(2,4,6-trimethylphenyl)imidazolium chloride **C1**	**No base**	CH_3CN	27
2.	**No catalyst**	DBU	CH_3CN	traces

5. General procedure for the synthesis of 3a-3aa



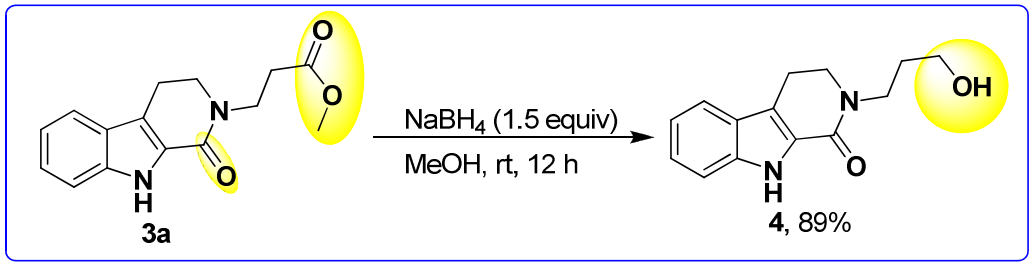
The substituted 4,9-dihydro-3*H*-pyrido[3,4-*b*]indole **1** (0.50 mmol) and NHC precatalyst **C1** (0.15 mmol, 30 mol%, 51 mg) were taken in a clean and dried Schlenk tube, it was evacuated and back filled with argon gas (2-3 cycles). Then were added dry CH_3CN (5 mL, un-degassed) by syringe and Michael acceptor **2** (0.50 mmol) followed by the addition of DBU (0.15 mmol, 30 mol%, 0.02 mL) under positive pressure of argon. Then reaction mixture was stirred at the 60 ^oC for 12 h. After completion of the reaction, reaction mixture was diluted with water (2 x 20 mL), extracted with dichloromethane (2 x 10 mL), dried over on anhydrous Na_2SO_4 and the filtrate was concentrated under reduced pressure. The crude was purified by column chromatography (EtOAc/Hexane) on silica gel to afford the derivatives of **3a-3aa** as pure products.

6. Experimental procedure for the gram-scale synthesis of 3a

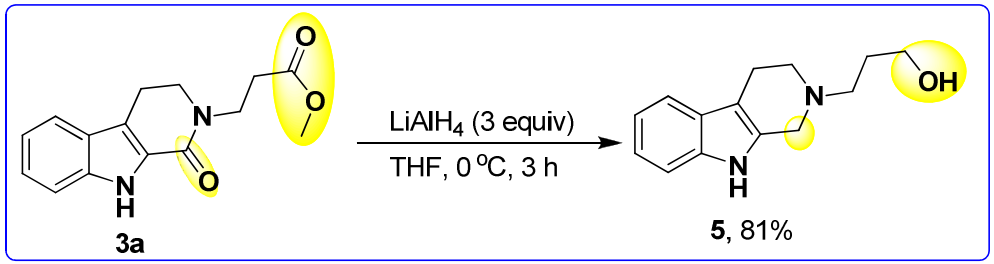


The 4,9-dihydro-3*H*-pyrido[3,4-*b*]indole **1a** (1 equiv, 10 mmol, 1.70 g) and NHC precatalyst **C1** (3 mmol, 30 mol%, 1.02 g) were taken in a clean and dried Schlenk tube, it was evacuated and back filled with argon gas (2-3 cycles). Then were added dry CH_3CN (80 mL, un-degassed) by syringe and methyl acrylate **2a** (1 equiv, 10 mmol, 0.80 mL) followed by the addition of DBU (3 mmol, 30 mol%, 0.42 mL) under positive pressure of argon. Then reaction mixture was stirred at the 60 °C for 12 h. After completion of the reaction, reaction mixture was diluted with water (2 x 200 mL), extracted with dichloromethane (2 x 100 mL), dried over on anhydrous Na_2SO_4 and the filtrate was concentrated under reduced pressure. The crude was purified by column chromatography (EtOAc/Hexane, 40:60) on silica gel to afford the methyl 3-(1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate **3a** as a pure product in 72% yield (1.96 g).

7. Experimental procedure for the chemoselective reduction of 3a by using $NaBH_4$ and $LiAlH_4$



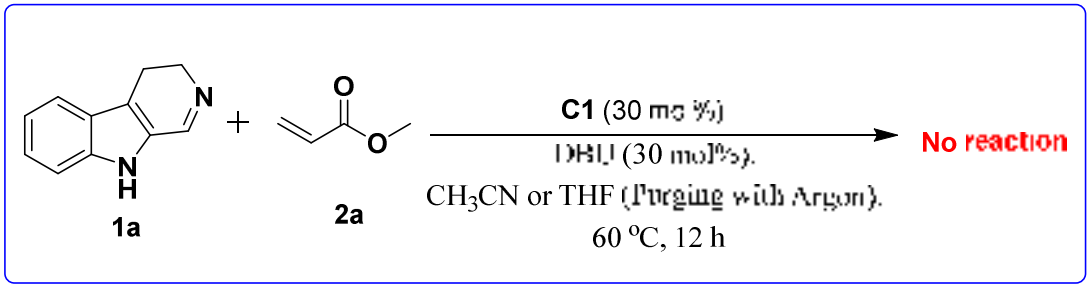
Methyl 3-(1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate **3a** (1 equiv, 0.50 mmol, 136 mg) was dissolved in MeOH (5 mL) and kept at 0 ^{o}C, then $NaBH_4$ (1.5 equiv, 0.75 mmol, 28 mg) was added slowly at the same temperature and the resulting reaction mixture was stirred at room temperature for 12 h. After this time, the reaction mixture was quenched with saturated aqueous NH_4Cl solution (10 mL) and diluted with water (2 x 20 mL), extracted with dichloromethane (2 x 10 mL), dried over on anhydrous Na_2SO_4 and the filtrate was concentrated under reduced pressure. The crude was purified by column chromatography (MeOH/DCM, 3:97) on silica gel to afford the 2-(3-hydroxypropyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-1-one **4** as a yellow solid in 89% yield.



Methyl 3-(1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate **3a** (1 equiv, 0.50 mmol, 136 mg) was dissolved in THF (5 mL) and the reaction mixture kept at 0 ^{o}C, $LiAlH_4$ (3 equiv, 1.50 mmol, 56 mg) was slowly added at the same temperature and the resulting reaction mixture was stirred at the same temperature for 3 h. After this time, the reaction mixture was quenched with saturated aq. NH_4Cl solution (10 mL) and diluted with water (2 x 20 mL), extracted with dichloromethane (2 x 10 mL), dried over on anhydrous Na_2SO_4 and the filtrate was concentrated under reduced pressure. The crude was purified by column chromatography (MeOH/DCM, 5:95) on silica gel to afford the 3-(3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propan-1-ol **5** as a yellow solid in 81% yield.

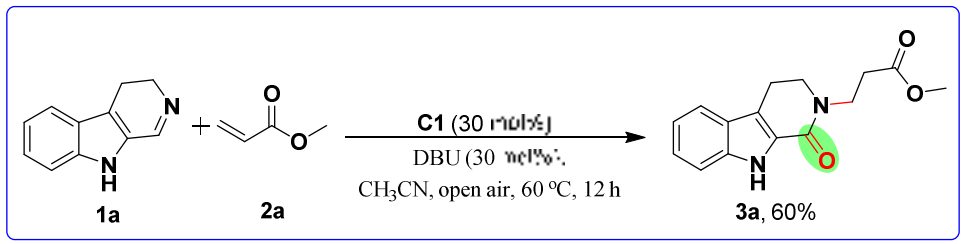
8. Control experiments

a. By using degassed solvents (with argon purging):



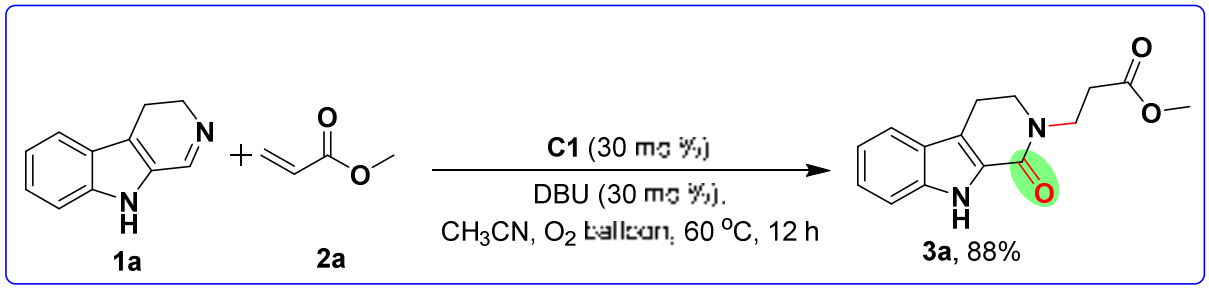
4,9-Dihydro-3*H*-pyrido[3,4-*b*]indole **1a** (1 equiv, 0.50 mmol, 85 mg) and NHC precatalyst **C1** (0.15 mmol, 30 mol%, 51 mg) were taken in a clean and oven dried Schlenk tube, it was evacuated and back filled with argon gas (2-3 cycles). Then added dry CH_3CN or THF (5 mL), which was priorly purged with argon. Methyl acrylate **2a** (1 equiv, 0.50 mmol, 0.04 mL) were added to the reaction mixture, and DBU (0.15 mmol, 30 mol%, 0.02 mL). Then the reaction mixture was stirred at the 60 °C temperature for 12 h. The desired product was not observed. Unreacted 4,9-dihydro-3*H*-pyrido[3,4-*b*]indole **1a** (81%) starting material was recovered by using column chromatography.

b. In open air:



4,9-Dihydro-3*H*-pyrido[3,4-*b*]indole **1a** (1 equiv, 0.50 mmol, 85 mg) and NHC precatalyst **C1** (0.15 mmol, 30 mol%, 51 mg) were taken in a clean and oven dried Schlenk tube. To this were added CH_3CN (5 mL, un-degassed) and methyl acrylate **2a** (1 equiv, 0.50 mmol, 0.04 mL) followed by the addition of DBU (0.15 mmol, 30 mol%, 0.02 mL). Then reaction mixture was stirred at the 60 ^oC temperature for 12 h, in presence of open air. After this time, the reaction mixture was diluted with water (2 x 10 mL), extracted with dichloromethane (2 x 20 mL), dried over on anhydrous Na_2SO_4 and the filtrate was concentrated under reduced pressure. The crude was purified by column chromatography (EtOAc/Hexane, 40:60) on silica gel to afford methyl 3-(1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate **3a** of as a pure product in 60% yield.

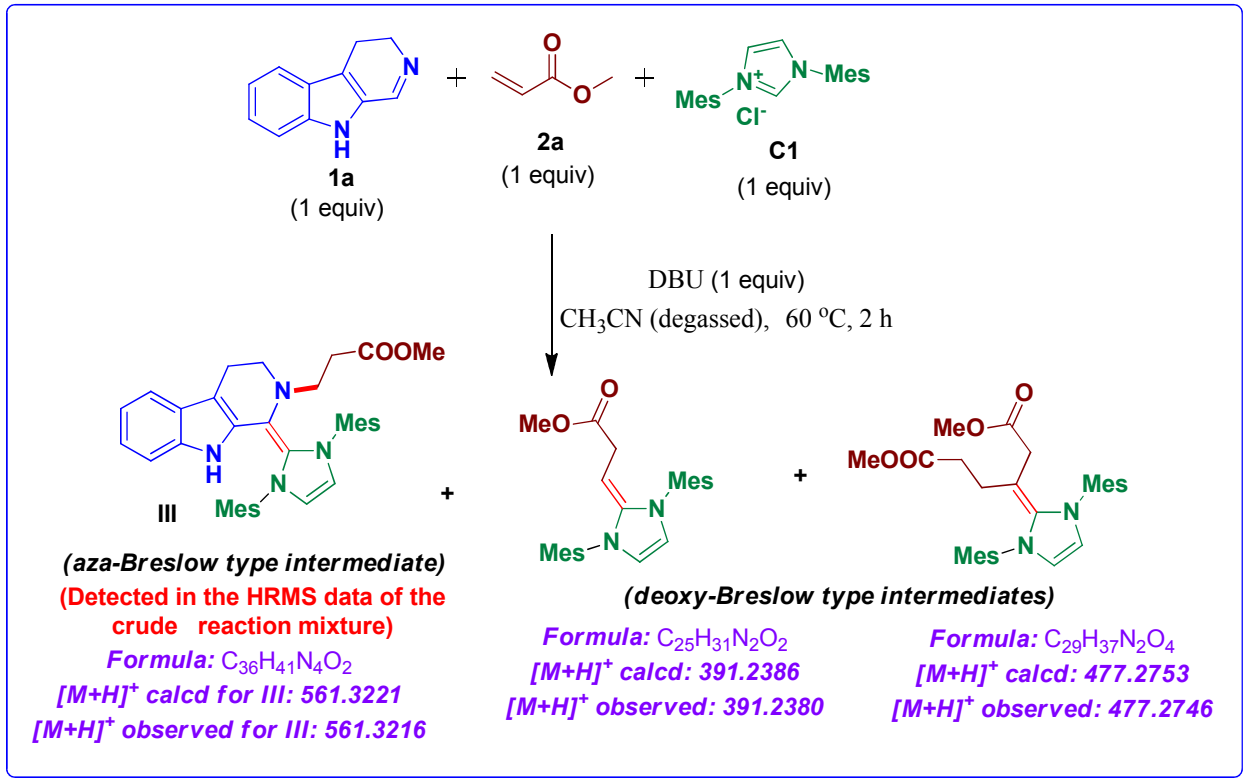
c. Under oxygen atmosphere:



4,9-Dihydro-3*H*-pyrido[3,4-*b*]indole **1a** (1 equiv, 0.50 mmol, 85 mg) and NHC precatalyst **C1** (0.15 mmol, 30 mol%, 51 mg) were taken in a clean and dry Schlenk tube, it was evacuated and back filled with argon gas (2-3 cycles). Then were added dry CH_3CN (5 mL) via syringe and methyl acrylate **2a** (1 equiv, 0.50 mmol, 0.04 mL) followed by the addition of DBU (0.15 mmol, 30 mol%, 0.02 mL) under positive pressure of argon. Then removed the argon balloon and the reaction mixture was stirred at the 60 ^oC for 12 h, in the presence of oxygen atmosphere. After completion of the reaction, reaction mixture was diluted with water (2 x 10 mL), extracted with dichloromethane (2 x 20 mL), dried over on anhydrous Na_2SO_4 and the filtrate was concentrated under reduced pressure. The crude was purified by column chromatography (EtOAc/Hexane, 40:60) on silica gel to afford methyl 3-(1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate **3a** of as a pure product in 88% yield.

9. Mechanistic studies to detect the intermediate III

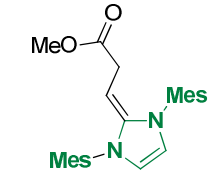
i). Experimental procedure for the stiochiometric reaction of 1a, 2a, C1 and DBU:



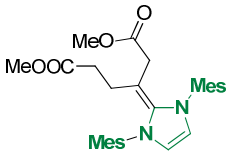
The 4,9-dihydro-3*H*-pyrido[3,4-*b*]indole **1a** (1 equiv, 0.50 mmol, 85 mg) and NHC precatalyst **C1** (1 equiv, 0.50 mmol, 170 mg) were taken in a clean and dried Schlenk tube, it was evacuated and back filled with argon gas (2-3 cycles). Then were added dry CH_3CN (5 mL, degassed) by syringe and Michael acceptor **2a** (1 equiv, 0.50 mmol, 0.04 mL) followed by the addition of DBU (1 equiv, 0.50 mmol, 0.07 mL) under positive pressure of argon. Then reaction mixture was stirred at the 60 °C for 12 h. The solvent was evaporated and crude was analyzed by HRMS. We have detected the aza-Breslow intermediate III in the HRMS. In the crude HRMS, we have

also detected the corresponding deoxy-Breslow type intermediates composed in a 1:1 (**2a**:**C1**) and 2:1 (**2a**:**C1**) mixtures (Ref: Guy Bertrand and co-Workers, *J. Am. Chem. Soc.* 2014, **136**, 5023).[9]

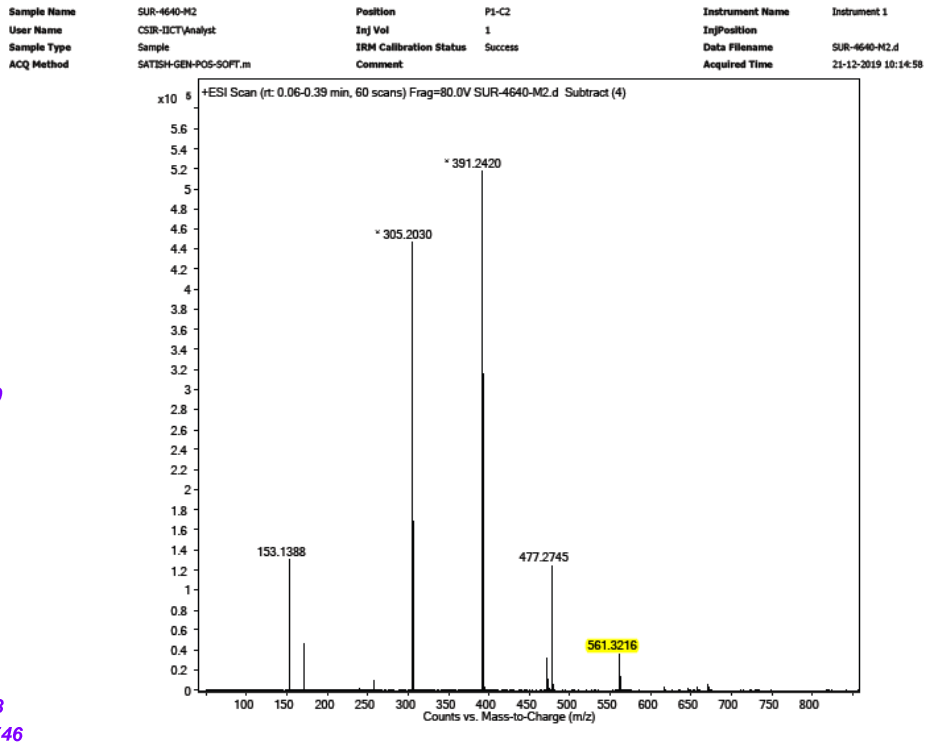
HRMS spectra of crude reaction mixture after 2 h

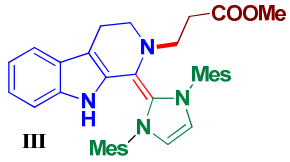


Formula: $C_{25}H_{31}N_2O_2$
$[M+H]^+$ calcd: 391.2386
$[M+H]^+$ observed: 391.2380



Formula: $C_{29}H_{37}N_2O_4$
$[M+H]^+$ calcd: 477.2753
$[M+H]^+$ observed: 477.2746





III

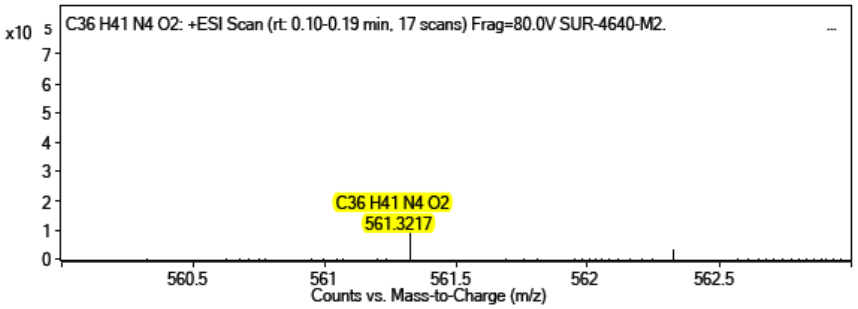
Formula: $C_{36}H_{41}N_4O_2$
$[M+H]^+$ calcd for III: 561.3221
$[M+H]^+$ observed for III: 561.3216

Qualitative Analysis Report

Data File	SUR-4640-M2.d	**Sample Name**	SUR-4640-M2
Sample Type	Sample	**Position**	P1-C2
Instrument Name	Instrument 1	**User Name**	CSIR-IICT\Analyst
Acq Method	SATISH-GEN-POS-SOFT.m	**Acquired Time**	21-12-2019 10:14:58
IRM Calibration Status	Success	**DA Method**	HRMS TEMPLATE.m
Comment			
Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6172 SP1)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
80	0	ESI



Peak List

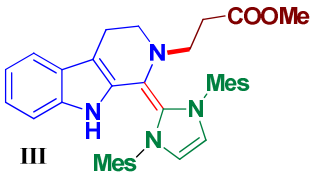
m/z	Abund
305.2049	637854.19
391.2463	641676.44

Formula Calculator Element Limits

Element	Min	Max
C	0	36
H	0	42
O	2	2
N	1	4
S	0	0
F	0	0

Formula Calculator Results

Formula	Best	Mass	Tgt Mass	Diff (ppm)	Ion Species	Score
C36 H41 N4 O2	True	561.3221	561.323	1.59	C36 H41 N4 O2	95.83



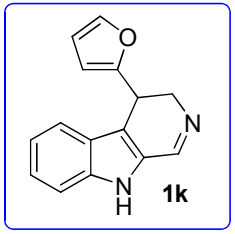
III

Formula: $C_{36}H_{41}N_4O_2$

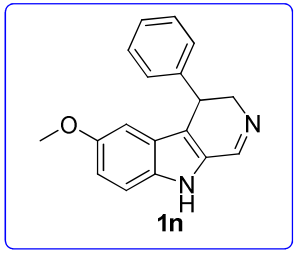
$[M+H]^+$ calcd for III: 561.3221

$[M+H]^+$ observed for III: 561.3216

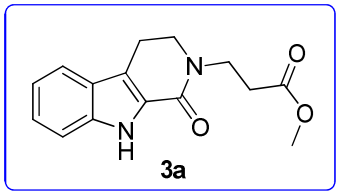
10. Spectroscopic data



4-(Furan-2-yl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (1k):- Light yellow solid, 1.880 g (8 mmol), 80%, R_f = 0.3 (MeOH/DCM, 2:98); **MP** 172-124 °C; (**IR-KBr**) 741, 1298, 1549, 1625, 2925, 3057, 3418 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 4.10 (dd, *J* = 16.3, 6.7 Hz, 1H), 4.26 (dd, *J* = 15.6, 8.4 Hz, 1H), 4.49 (t, *J* = 8.0 Hz, 1H), 6.01 (d, *J* = 2.7 Hz, 1H), 6.29 (s, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 7.26-7.34 (m, 2H), 7.35-7.41 (m, 2H), 8.40 (s, 1H), 8.43 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 31.5, 53.6, 106.4, 110.3, 112.1, 116.2, 120.6, 120.9, 124.8, 125.0. 136.8, 141.8, 151.2, 154.8; **MS** (ESI, *m/z*): $[M+H]^+$ 237; **HRMS** (ESI, *m/z*): calcd for $C_{15}H_{13}N_2O$ $[M+H]^+$ 237.1022, found 237.1033.

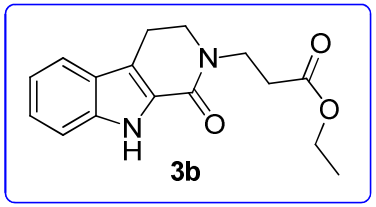


6-methoxy-4-phenyl-4,9-dihydro-3H-pyrido[3,4-b]indole (1n):- Yellow solid, 1.269 g (4.6 mmol), 92%, R_f = 0.3 (MeOH/DCM, 2:98); **MP** 152-154 °C; (**IR-neat**) 760, 1219, 1610, 2945, 3062, 3210 cm^{-1}; **^{1}H-NMR** (500 MHz, DMSO-d_6) δ = 3.55 (s, 3H), 3.96-3.86 (m, 1H), 4.01-4.08 (d, J = 7.9 Hz, 1H), 4.39-4.42 (m, 1H), 6.41 (d, *J* = 2.1 Hz, 1H), 6.86 (dd, *J* = 8.9, 2.3 Hz, 1H), 7.24 (t, *J* = 6.9 Hz, 2H), 7.34-7.28 (m, 2H), 7.37 (d, *J* = 8.9 Hz, 1H), 8.31 (s, 1H), 8.51 (s, 1H), 11.48 (brs, 1H); **^{13}C-NMR** (101 MHz, DMSO-d_6) δ = 55.5, 56.3, 79.6, 101.3, 114.1, 115.6, 117.1, 125.1, 127.1, 128.3, 128.9, 133.1, 142.6, 143.2, 152.5, 154.0; **MS** (ESI, *m/z*): $[M+H]^+$ 277; **HRMS** (ESI, *m/z*): calcd for $C_{18}H_{17}N_2O$ $[M+H]^+$, 277.13354, found 277.13513.



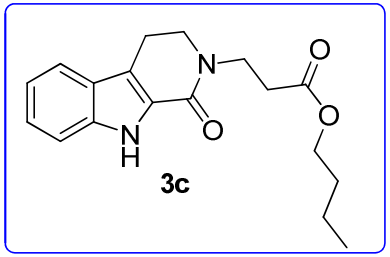
3a

Methyl 3-(1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3a):- Light brown solid, 117 mg (0.430 mmol), 86%, R_f = 0.4 (EtOAc/Hexane, 40:60); **MP** 168-170 ^oC; (**IR-neat**)772, 1290, 1648, 1693, 1732, 2922, 3222 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.75 (t, *J* = 6.3 Hz, 2H), 3.05 (t, *J* = 6.6 Hz, 2H), 3.70 (s, 3H), 3.79 (t, *J* = 6.6 Hz, 2H), 3.87 (t, *J* = 6.2 Hz, 2H), 7.14 (t, *J* = 7.2 Hz, 1H), 7.27-7.34 (m, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 7.8 Hz, 1H), 9.72 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 21.0, 33.2, 43.3, 49.3, 51.8, 112.5, 118.5, 120.2, 124.9, 125.2, 127.0, 137.5, 161.6, 172.5; **MS** (ESI, *m/z*): $[M+H]^+$ 273; **HRMS** (ESI, *m/z*): calcd for $C_{15}H_{17}N_2O_3$ $[M+H]^+$ 273.1234, found 273.1232.



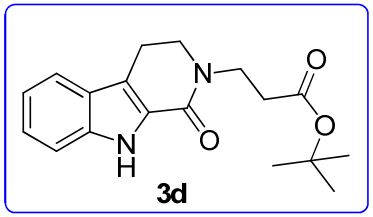
3b

Ethyl 3-(1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3b):- Brown solid, 117 mg (0.410 mmol), 82%, R_f = 0.5 (EtOAc/Hexane, 40:60); **MP** 162-164 ^oC; (**IR-neat**) 772, 1294, 1637, 1692, 1733, 2925, 3217 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 1.26 (t, *J* = 7.1 Hz, 3H), 2.74 (t, *J* = 6.8 Hz, 2H), 3.05 (dd, *J* = 9.1, 5.0 Hz, 2H), 3.80 (t, *J* = 7.0 Hz, 2H), 3.87 (t, *J* = 6.8 Hz, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 7.11-7.16 (m, 1H), 7.27-7.32 (m, 1H), 7.46 (d, *J* = 8.3 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 9.71 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 14.2, 21.0, 33.5, 43.3, 49.3, 60.7, 112.6, 118.5, 120.1, 124.8, 125.2, 127.0, 137.6, 161.7, 172.1; **MS** (ESI, *m/z*): $[M+H]^+$ 287; **HRMS** (ESI, *m/z*): calcd for $C_{16}H_{18}N_2O_3Na$ $[M+Na]^+$ 309.1210, found 309.1218. The spectroscopic data were in good agreement with the reported data.[10]



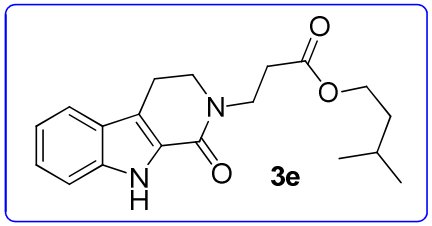
3c

Butyl 3-(1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate. (3c):- Light brown solid, 116 mg (0.370 mmol), 74%, R_f = 0.4 (EtOAc/Hexane, 40:60); **MP** 124-126 ^oC; (**IR-neat**) 743, 1250, 1636, 1730, 2957, 3224 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 0.89 (t, *J* = 7.4 Hz, 3H), 1.32-1.41 (m, 2H), 1.57-1.62 (m, 2H), 2.75 (t, *J* = 6.8 Hz, 2H), 3.05 (t, *J* = 7.0 Hz, 2H), 3.80 (t, *J* = 7.0 Hz, 2H), 3.88 (t, *J* = 6.8 Hz, 2H), 4.11 (t, *J* = 6.7 Hz, 2H), 7.09-7.17- (m, 1H), 7.27-7.32 (m, 1H), 7.46 (d, *J* = 8.3 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 9.80 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 13.7, 19.1, 21.0, 30.6, 33.5, 43.4, 49.3, 64.7, 112.7, 118.5, 120.1, 124.8, 125.2, 127.0, 137.7, 161.8, 172.2; **MS** (ESI, *m/z*): $[M+H]^+$ 315; **HRMS** (ESI, *m/z*): calcd for $C_{18}H_{23}N_2O_3$ $[M+H]^+$ 315.1703, found 315.1714.

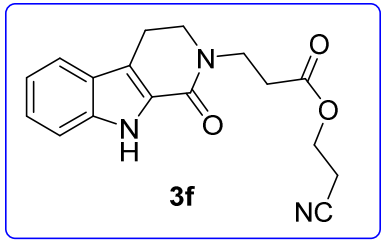


3d

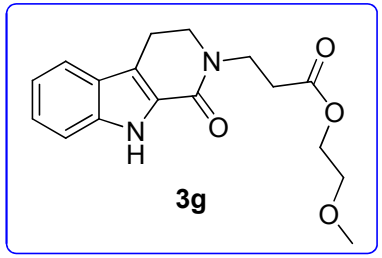
Tert-butyl 3-(1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3d):- Brown solid, 118 mg (0.375 mmol), 75%, R_f = 0.4 (EtOAc/Hexane, 40:60); **MP** 122-124 ^oC; (**IR-neat**) 743, 1250, 1636, 1730, 2956, 3216 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 1.45 (s, 9H), 2.65 (t, *J* = 6.8 Hz, 2H), 3.05 (t, *J* = 7.0 Hz, 2H), 3.79 (t, *J* = 7.0 Hz, 2H), 3.83 (t, *J* = 6.8 Hz, 2H), 7.11-7.17 (m, 1H), 7.27-7.31 (m, 1H), 7.46 (d, *J* = 8.3 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 9.60 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 20.9, 28.1, 34.7, 43.2, 49.1, 80.9, 112.6, 118.4, 120.1, 124.8, 125.2, 127.1, 137.6, 161.6, 171.3; **MS** (ESI, *m/z*): $[M+H]^+$ 315; **HRMS** (ESI, *m/z*): calcd for $C_{18}H_{23}N_2O_3$ $[M+H]^+$ 315.1703, found 315.1714.



Isopentyl 3-(1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3e):- Brown yellowish solid, 128 mg (0.390 mmol), 78%, R_f = 0.4 (EtOAc/Hexane, 40:60); **MP** 151-153 °C; (**IR-neat**) 743, 1250, 1636, 1730, 2956, 3216 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 0.89 (d, = 6.6 Hz, 6H), 1.51 (q, *J* = 6.9 Hz, 2H), 1.62-1.70 (m, 1H), 2.74 (t, *J* = 6.8 Hz, 2H), 3.05 (t, *J* = 7.0 Hz, 2H), 3.79 (t, *J* = 7.0 Hz, 2H), 3.87 (t, *J* = 6.8 Hz, 2H), 4.13 (t, *J* = 6.9 Hz, 2H), 7.14 (t, *J* = 7.9 Hz, 1H), 7.29 (t, *J* = 8.2 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 9.84 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 20.9, 22.4, 25.0, 33.4, 37.3, 43.3, 49.2, 63.5, 112.5, 118.5, 120.2, 124.9, 125.2, 127.0, 137.5, 161.6, 172.1; **MS** (ESI, *m/z*): $[M+H]^+$ 329; **HRMS** (ESI, *m/z*): calcd for $C_{19}H_{25}N_2O_3$ $[M+H]^+$ 329.1860, found 329.1865.

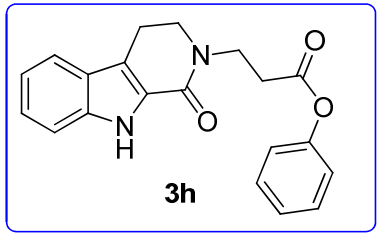


2-Cyanoethyl 3-(1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3f):- Brown solid, 126 mg (0.405 mmol), 81%, R_f = 0.4 (EtOAc/Hexane, 40:60); **MP** 156-158 °C; (**IR-neat**) 745, 1183, 1289, 1552, 1636, 1733, 2250, 2923, 3218 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.70 (t, *J* = 6.4 Hz, 2H), 2.79 (t, *J* = 6.7 Hz, 2H), 3.07 (t, *J* = 7.0 Hz, 2H), 3.80 (t, *J* = 7.0 Hz, 2H), 3.87 (t, *J* = 6.7 Hz, 2H), 4.31 (t, *J* = 6.4 Hz, 2H), 7.15 (t, *J* = 7.2 Hz, 1H), 7.31 (t, *J* = 7.7 Hz, 1H), 7.44 (d, *J* = 8.3 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 9.22 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 17.9, 20.9, 33.1, 43.1, 49.1, 58.9, 112.5, 116.7, 118.7, 120.2, 120.3, 125.0, 125.2, 126.8, 137.5, 161.7, 171.4; **MS** (ESI, *m/z*): $[M+H]^+$ 312; **HRMS** (ESI, *m/z*): calcd for $C_{17}H_{18}N_3O_3$ $[M+H]^+$ 312.1348, found 312.1358.



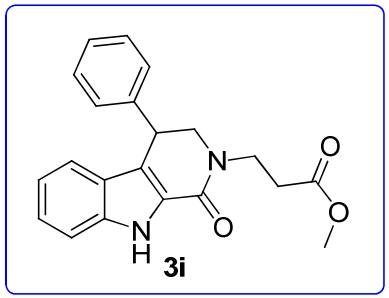
3g

2-Methoxyethyl 3-(1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3g):- Light yellow solid, 118 mg (0.375 mmol), 75%, R_f = 0.4 (EtOAc/Hexane, 40:60); **MP** 161-163 °C; (**IR-neat**) 745, 1153, 1290, 1546, 1649, 1735, 2923, 3221 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.79 (t, *J* = 6.7 Hz, 2H). 3.05 (t, *J* = 7.0 Hz, 2H), 3.34 (s, 3H), 3.55-3.61 (m, 2H), 3.79 (t, *J* = 7.0 Hz, 2H), 3.88 (t, *J* = 6.7 Hz, 2H), 4.23-4.29 (m, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 7.29 (t, *J* = 7.9 Hz, 1H), 7.46 (d, *J* = 8.3 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 9.87 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 20.9, 33.3, 43.2, 49.2, 59.0, 63.7, 70.4, 112.6, 118.5, 120.1, 124.8, 125.2, 127.0, 137.6, 161.7, 172.0; **MS** (ESI, *m/z*): $[M+H]^+$ 317; **HRMS** (ESI, *m/z*): calcd for $C_{17}H_{21}N_2O_4$ $[M+H]^+$ 317.1501, found 317.1511.



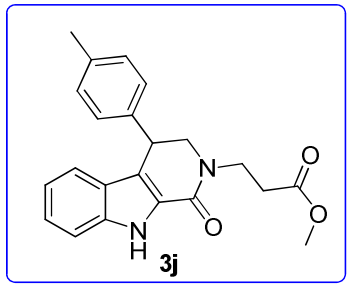
3h

Phenyl 3-(1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3h):- Yellow solid, 134 mg (0.400 mmol), 80%, R_f = 0.5 (EtOAc/Hexane, 40:60); **MP** 145-147 °C; (**IR-neat**) 748, 1187, 1645, 1757, 2851, 2923, 3175 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 3.02 (t, *J* = 6.6 Hz, 2H), 3.08 (t, *J* = 7.0 Hz, 2H), 3.86 (t, *J* = 7.0 Hz, 2H), 3.98 (t, *J* = 6.6 Hz, 2H), 7.09 (d, *J* = 7.7 Hz, 2H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.22 (t, *J* = 7.4 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.46 (d, *J* = 8.3 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 9.62 (brs, 1H); **^{13}C-NMR** (126 MHz, $CDCl_3$) δ = 21.0, 33.6, 43.3, 49.5, 112.5, 118.7, 120.2, 120.3, 121.5, 125.0, 125.3, 126.0, 126.9, 129.5, 137.5, 150.5, 161.7, 170.7; **MS** (ESI, *m/z*): $[M+H]^+$ 335; **HRMS** (ESI, *m/z*): calcd for $C_{20}H_{19}N_2O_3$ $[M+H]^+$ 335.1396, found 335.1411.



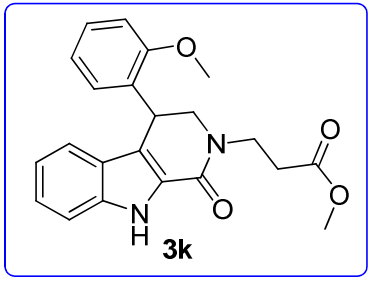
3i

Methyl 3-(1-oxo-4-phenyl-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3i):- Yellow solid, 127 mg (0.365 mmol), 73%, R_f = 0.5 (EtOAc/Hexane, 35:65); **MP** 122-124 ^oC; (**IR-neat**) 772, 1218, 1550, 1640, 1735, 2922, 3221 cm^{-1}; **^{1}H-NMR** (300 MHz, $CDCl_3$) δ = 2.52-2.71 (m, 2H), 3.62 (s, 3H), 3.73-3.88 (m, 3H), 3.99 (dd, *J* = 12.3, 5.9 Hz, 1H), 4.46-4.55 (m, 1H), 6.94-7.02 (m, 2H), 7.21-7.36 (m, 6H), 7.45 (d, *J* = 8.2 Hz, 1H), 9.33 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 33.0, 39.6, 43.0, 51.8, 57.2, 112.3, 120.3, 120.6, 121.3, 121.5, 125.0, 127.4, 128.2, 128.7, 137.5, 140.6, 161.1, 172.2; **MS** (ESI, *m/z*): $[M+H]^+$ 349; **HRMS** (ESI, *m/z*): calcd for $C_{21}H_{21}N_2O_3$ $[M+H]^+$ 349.1557, found 349.1546.



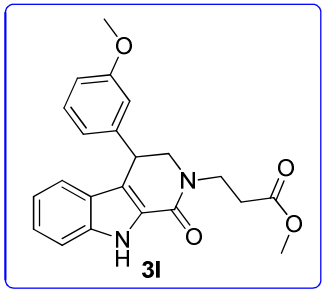
3j

Methyl 3-(1-oxo-4-p-tolyl-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3j):- Light brown solid, 146 mg (0.405 mmol), 81%, R_f = 0.4 (EtOAc/Hexane, 40:60); **MP** 132-134 ^oC; (**IR-neat**) 772, 1219, 1693, 1711, 2922, 3227 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.34 (s, 3H), 2.50-2.74 (m, 2H), 3.63 (s, 3H), 3.69-3.81 (m, 4H), 4.47-4.49 (m, 1H), 6.96-6.98 (m, 2H), 7.01-7.02 (m, 4H), 7.21-7.23 (m, 1H), 7.44 (d, *J* = 8.2 Hz, 1H), 9.27 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 14.1, 21.1, 29.3, 29.7, 39.3, 50.4, 112.5, 118.4, 119.6, 120.3, 121.3, 122.2, 124.1, 125.1, 125.2, 126.6, 128.2, 129.4, 137.1, 137.5, 162.8, 188.8; **MS** (ESI, *m/z*): $[M+H]^+$ 363; **HRMS** (ESI, *m/z*): calcd for $C_{22}H_{23}N_2O_3$ $[M+H]^+$ 363.1709, found 363.1714.



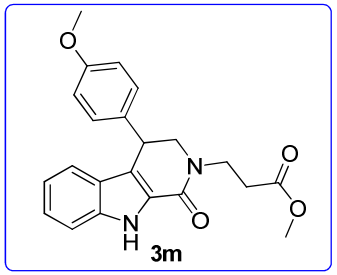
3k

Methyl 3-(4-(2-methoxyphenyl)-1-oxo-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indol-2-yl)propanoate (3k):- Yellow solid, 134 mg (0.355 mmol), 71%, R_f = 0.3 (EtOAc/Hexane, 40:60); **MP** 147-149 ^oC; (**IR-neat**) 772, 1219, 1656, 1727, 2853, 2923, 3227 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.43-2.61 (m, 2H), 3.59 (s, 3H), 3.63-3.75 (m, 2H), 3.83-3.91 (m, 1H), 3.94 (s, 3H), 4.02-4.04 (m, 1H), 4.95 (t, *J* = 5.7 Hz, 1H), 6.73-6.81 (m, 2H), 6.92-7.03 (m, 2H), 7.14-7.25 (m, 3H), 7.47 (d, *J* = 8.3 Hz, 1H), 9.55 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 31.7, 32.8, 42.9, 51.7, 55.1, 55.5, 110.3, 112.4, 120.2, 120.5, 120.6, 121.1, 124.9, 125.0, 128.0, 128.2, 128.4, 129.2, 137.7, 156.8, 161.3, 172.1; **MS** (ESI, *m/z*) $[M+H]^+$ 379; **HRMS** (ESI, *m/z*): calcd for $C_{22}H_{23}N_2O_4$ $[M+H]^+$ 379.1658, found 379.1666.

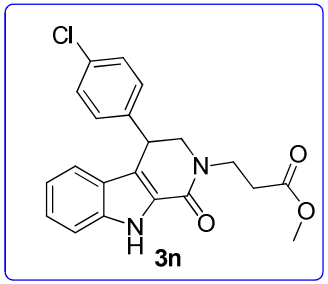


3l

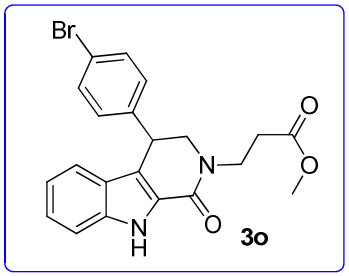
Methyl 3-(4-(3-methoxyphenyl)-1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3l):- Brown solid, 128 mg (0.340 mmol), 68%, R_f = 0.3 (EtOAc/Hexane, 40:60); **MP** 144-146 ^oC; (**IR-neat**) 772, 1219, 1656, 1727, 2923, 3227 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.59-2.65 (m, 2H), 3.63 (s, 3H), 3.75-3.78 (m, 6H), 3.94-3.96 (m, 1H), 4.46-4.48 (m, 1H), 6.82 (d, *J* = 15.2 Hz, 3H), 7.02 (dd, *J* = 26.0, 7.3 Hz, 3H), 7.43 (d, *J* = 8.2 Hz, 2H), 9.07 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 31.7, 32.8, 42.9, 51.7, 55.1, 55.5, 110.3, 112.4, 120.2, 120.5, 121.0, 121.1, 124.9, 125.0, 128.0, 128.2, 128.3, 129.2, 137.7, 156.8, 161.3, 172.1; **MS** (ESI, *m/z*): $[M+H]^+$ 379; **HRMS** (ESI, *m/z*): calcd for $C_{22}H_{23}N_2O_4$ $[M+H]^+$ 379.1658, found 379.1664.



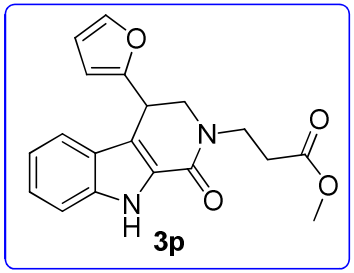
Methyl 3-(4-(4-methoxyphenyl)-1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3m):- Brown solid, 136 mg (0.360 mmol), 72%, R_f = 0.4 (EtOAc/Hexane, 40:60); **MP** 112-114 ^oC; (**IR-neat**) 772, 1289, 1635, 1732, 2924, 3222 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.54-2.74 (m, 2H), 3.63 (s, 3H), 3.71-3.78 (m, 1H), 3.80 (s, 4H), 3.83-3.89 (m, 1H), 3.94 (dd, *J* = 12.0, 5.7 Hz, 1H), 4.43-4.54 (m, 1H), 6.85 (d, *J* = 8.2 Hz, 2H), 6.92-7.05 (m, 3H), 7.17 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 8.1 Hz, 1H), 9.81 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 33.0, 38.8, 43.1, 51.8, 55.3, 57.4, 112.5, 114.0, 120.2, 121.0, 121.1, 124.9, 127.3, 129.2, 132.6, 137.8, 158.8, 161.4, 172.2; **MS** (ESI, *m/z*): $[M+H]^+$ 379; **HRMS** (ESI, *m/z*): calcd for $C_{22}H_{23}N_2O_4$ $[M+H]^+$ 379.1658, found 379.1659.



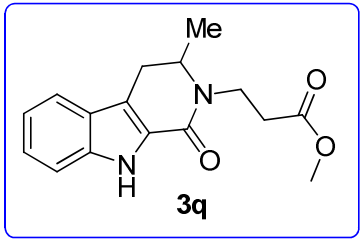
Methyl 3-(4-(4-chlorophenyl)-1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3n):- Yellow solid, 132 mg (0.345 mmol), 69%, R_f = 0.5 (EtOAc/Hexane, 35:65); **MP** 117-119 ^oC; (**IR-neat**) 772, 826, 1091, 1546, 1660, 1733, 2923, 3222 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.53-2.60 (m, 1H), 2.63-2.69 (m, 1H), 3.62 (s, 3H), 3.90-3.70 (m, 3H), 3.98 (dd, *J* = 12.2, 5.8 Hz, 1H), 4.48-4.53 (m, 1H), 6.94-7.02 (m, 2H), 7.29-7.33 (m, 5H), 7.44-7.45 (m, 1H), 9.29 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 33.0, 39.0, 43.2, 51.9, 57.1, 112.7, 120.0, 120.5, 120.9, 121.4, 124.8, 125.2, 127.5, 130.0, 131.9, 137.8, 139.8, 161.4, 172.3; **MS** (ESI, *m/z*): $[M+H]^+$ 383; **HRMS** (ESI, *m/z*): calcd for $C_{21}H_{20}ClN_2O_3$ $[M+H]^+$ 383.1162, found 383.1162.



Methyl 3-(4-(4-bromophenyl)-1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3o):- Brown solid, 175 mg (0.410 mmol), 82%, R_f = 0.5 (EtOAc/Hexane, 35:65); **MP** 132-134 ^oC; (**IR-neat**) 772, 1219, 1550, 1656, 1727, 2923, 3227 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.51-2.72 (m, 2H), 3.62 (s, 3H), 3.72-3.77 (m, 2H), 3.82-3.92 (m, 1H), 3.99-4.03 (m, 1H), 4.45-4.47 (m, 1H), 6.99-7.02 (m, 2H), 7.10-7.12 (m, 2H), 7.26-7.28 (m, 1H), 7.42-7.48 (m, 3H), 9.90 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 33.0, 39.0, 43.1, 51.8, 57.0, 112.5, 119.9, 120.5, 120.8, 121.3, 124.7, 125.1, 127.4, 129.9, 131.8, 137.7, 139.7, 161.3, 172.2; **MS** (ESI, *m/z*): $[M+H]^+$ 427; **HRMS** (ESI, *m/z*): calcd for $C_{21}H_{20}BrN_2O_3$ $[M+H]^+$ 427.0657, found 427.0664.

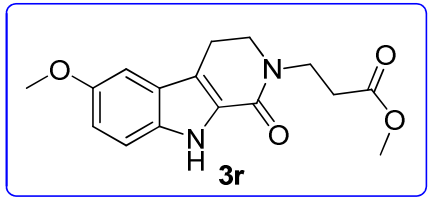


Methyl 3-(4-(furan-2-yl)-1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3p):- Yellow solid, 122 mg (0.360 mmol), 72%, R_f = 0.4 (EtOAc/Hexane, 40:60); **MP** 155-157 ^oC; (**IR-KBr**) 779, 1202, 1648, 1740, 2922, 3208 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.50-2.61 (m, 2H), 3.66 (s, 3H), 3.93-4.00 (m, 4H), 4.55-4.57 (m, 1H), 5.88-5.91 (m, 1H), 6.25-6.27 (m, 1H), 7.06-7.08 (m, 1H), 7.29-7.35 (t, *J* = 7.3 Hz, 3H), 7.46-7.48 (m, 1H), 9.51 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 32.6, 32.9, 43.0, 51.8, 53.5, 107.6, 110.4, 112.5, 118.3, 120.5, 120.6, 124.9, 125.1, 127.2, 137.3, 142.0, 153.5, 160.8, 172.2; **MS** (ESI, *m/z*): $[M+H]^+$ 339; **HRMS** (ESI, *m/z*): calcd for $C_{19}H_{19}N_2O_4$ $[M+H]^+$ 339.1339, found 339.1341.



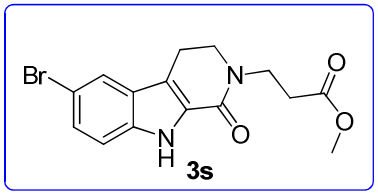
3q

Methyl 3-(3-methyl-1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3q):- Light brown solid, 119 mg (0.415 mmol), 83%, R_f = 0.4 (EtOAc/Hexane, 35:65); **MP** 137-139 ^oC; (**IR-neat**) 772, 1219, 1656, 1727, 2923, 3227 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 1.29 (d, *J* = 6.6 Hz, 3H), 2.80-2.89 (m, 1H), 3.25-3.33 (m, 2H), 3.62-3.67 (m, 1H), 3.70 (s, 3H), 4.06-4.09 (m, 1H), 4.18-4.23 (m, 1H), 4.26-4.34 (m, 1H), 7.11-7.17 (m, 1H), 7.30 (dd, *J* = 13.4, 5.5 Hz, 1H), 7.45 (t, *J* = 7.9 Hz, 1H), 7.58 (dd, *J* = 12.4, 8.1 Hz, 1H), 9.59 (brs,1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 27.2, 29.7, 33.8, 41.7, 51.8, 55.4, 112.5, 116.3, 120.1, 124.8, 126.0, 128.8, 130.9, 137.5, 160.6, 172.6; **MS** (ESI, *m/z*): $[M+H]^+$ 287; **HRMS** (ESI, *m/z*): $C_{16}H_{19}N_2O_3Na$ $[M+Na]^+$ 309.1210, found 309.1218.



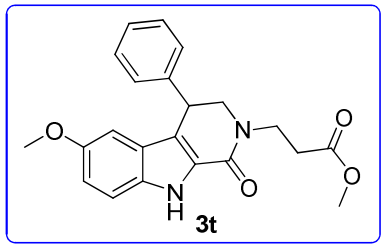
3r

Methyl 3-(6-methoxy-1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3r):- Brown solid, 104 mg (0.344 mmol), 69%, R_f = 0.3 (EtOAc/Hexane, 40:60); **MP** 184-186 ^oC; (**IR-neat**) 754, 1251, 1637, 1735, 2844, 3219 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.47 (t, *J* = 6.7 Hz, 2H), 2.90 (t, *J* = 5.0 Hz, 2H), 3.45 (t, *J* = 6.7 Hz, 2H), 3.62 (s, 3H), 3.63 (s, 3H), 3.71 (t, *J* = 5.0 Hz, 2H), 6.82 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.07 (d, *J* = 1.6 Hz, 1H), 7.28 (s, 1H), 8.01 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 21.9, 33.2, 36.4, 38.3, 45.1, 50.7, 113.5, 119.5, 121.1, 125.7, 126.2, 128.1, 138.5, 159.9, 162.8, 172.4; **MS** (ESI, *m/z*): $[M+H]^+$ 303; **HRMS** (ESI, *m/z*): calcd for $C_{16}H_{19}N_2O_4$ $[M+H]^+$, 303.10157, found 303.10308.



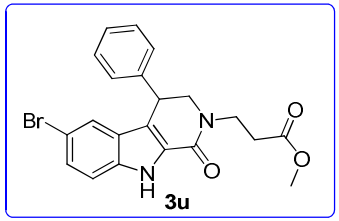
3s

Methyl 3-(6-bromo-1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3s):- Brown solid, 135 mg (0.385 mmol), 77%, R_f = 0.3 (EtOAc/Hexane, 40:60); **MP** 165-167 ^oC; (**IR-neat**) 764, 1197, 1638, 1736, 2944, 3213 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.75 (t, *J* = 6.8 Hz, 2H), 3.01 (t, *J* = 7.0 Hz, 2H), 3.70 (s, 3H), 3.80 (t, *J* = 7.0 Hz, 2H), 3.86 (t, *J* = 6.8 Hz, 2H), 7.39-7.32 (m, 2H), 7.72-7.69 (m, 1H), 9.75 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 20.8, 33.1, 44.0, 49.2, 51.9, 113.4, 114.0, 117.8, 122.8, 126.9, 127.8, 128.0, 136.0, 161.2, 172.4; **MS** (ESI, *m/z*): $[M]^+$ 350, $[M+2]^+$ 352; **HRMS** (ESI, *m/z*): calcd for $C_{15}H_{16}BrN_2O_3$ $[M+H]^+$, 351.0339, found 351.0361 & calcd for $C_{15}H_{16}{}^{81}BrN_2O_3$ $[M+H]^+$, 351.0318, found 351.0339.



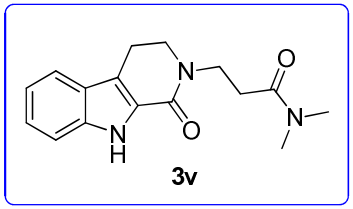
3t

Methyl 3-(6-methoxy-1-oxo-4-phenyl-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3t):- Brown solid, 117 mg (0.309 mmol), 62%, R_f = 0.3 (EtOAc/Hexane, 40:60); **MP** 195-197 ^oC; (**IR-neat**) 752, 1249, 1633, 1734, 2843, 3214 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.84 (t, *J* = 6.9 Hz, 2H), 3.57 (s, 3H), 3.67 (s, 3H), 3.87 (m, 1H), 4.22 (m, 1H), 4.33 (m, 1H), 4.58 (t, *J* = 7.0 Hz, 2H), 6.29 (d, *J* = 2.4 Hz, 1H), 6.92 (dd, *J* = 9.0, 2.5 Hz, 1H), 7.25 (s, 1H), 7.35-7.27 (m, 5H), 8.58 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 35.1, 38.9, 39.1, 52.1, 55.4, 57.2, 102.1, 110.8, 115.6, 117.8, 125.1, 126.9, 128.3, 128.6, 129.3, 132.5, 142.2, 150.0, 154.3, 171.3; **MS** (ESI, *m/z*): $[M+H]^+$ 379; **HRMS** (ESI, *m/z*): calcd for $C_{22}H_{23}N_2O_4$ $[M+H]^+$,379.1658, found 379.1664.



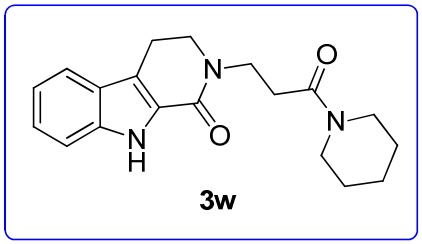
3u

Methyl 3-(6-bromo-1-oxo-4-phenyl-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanoate (3u):- White solid, 158 mg (0.370 mmol), 74%, R_f = 0.4 (EtOAc/Hexane, 35:65); **MP** 132-134 ^oC; (**IR-neat**) 745, 767, 1285, 1639, 1735, 2922, 3221 cm^{-1}; **^{1}H-NMR** (300 MHz, $CDCl_3$) δ = 2.49-2.74 (m, 2H), 3.62 (s, 3H), 3.68-3.92 (m, 3H), 4.01 (dd, *J* = 12.3, 5.8 Hz, 1H), 4.43-4.52 (m, 1H), 7.01 (q, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 1H), 7.45 (t, *J* = 8.6 Hz, 3H), 9.50 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 33.0, 39.0, 43.0, 51.8, 57.0, 112.5, 119.9, 120.5, 120.9, 124.8, 125.1, 127.5, 129.9, 131.8, 137.6, 139.7, 161.1, 172.1; **MS** (ESI, *m/z*): $[M+H]^+$ 427; **HRMS** (ESI, *m/z*): calcd for $C_{21}H_{20}BrN_2O_3$ $[M+H]^+$ 427.0657, found 427.0671.



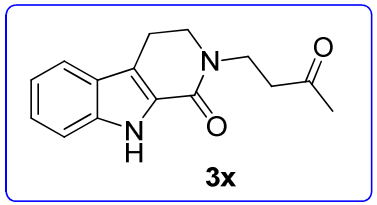
3v

***N,N*-Dimethyl-3-(1-oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propenamide (3v):-** White solid, 121 mg (0.425 mmol), 85%, R_f = 0.3 (Pure EtOAc); **MP** 168-170 ^oC; (**IR-neat**) 745, 1286, 1632, 2923, 3217 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.78 (t, *J* = 6.7 Hz, 2H), 2.96 (s, 3H), 3.01 (s, 3H), 3.04 (t, *J* = 7.1 Hz, 2H), 3.92-3.83 (m, 4H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.29 (d, *J* = 7.3 Hz, 1H), 7.45 (d, *J* = 8.2 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 9.78 (brs, 1H), **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 20.1, 32.3, 35.5, 37.4, 44.2, 49.7, 112.5, 118.6, 120.1, 120.2, 124.8, 125.3, 127.1, 137.6, 161.9, 171.2; **MS** (ESI, *m/z*): $[M+H]^+$ 286; **HRMS** (ESI, *m/z*): calcd for $C_{16}H_{20}N_3O_2$ $[M+H]^+$ 286.1556, found 286.1563. The spectroscopic data were in good agreement with the reported data. [10]



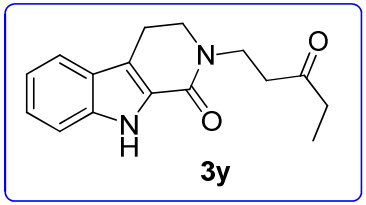
3w

2-(3-Oxo-3-(piperidin-1-yl)propyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-1-one (3w):- Light red liquid, 128 mg (0.395 mmol), 79%, R_f = 0.3 (Pure EtOAc); (**IR-neat**) 744, 1291, 1631, 2929, 3220 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 1.52-1.60 (m, 4H), 2.78-2.84 (m, 3H), 3.05 (t, *J* = 6.5 Hz, 2H), 3.40 (d, *J* = 25.3 Hz, 3H), 3.54-3.56 (m, 2H), 3.84-3.90 (m, 4H), 7.10-7.12 (m, 1H), 7.25-7.27 (m, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.57 (d, *J* = 7.4 Hz, 1H), 10.41 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 20.9, 24.5, 25.6, 26.5, 32.1, 42.8, 44.4, 46.8, 49.6, 112.6, 118.5, 120.0, 120.2, 124.7, 125.2, 127.1, 137.7, 161.9, 169.3; **MS** (ESI, *m/z*): $[M+H]^+$ 326; **HRMS** (ESI, *m/z*): calcd for $C_{19}H_{24}N_3O_2$ $[M+H]^+$ 326.1863, found 326.1868.



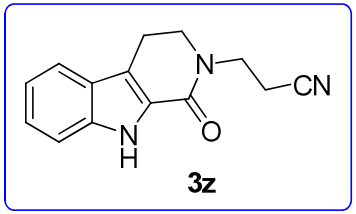
3x

2-(3-Oxobutyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-1-one (3x):- Light brown solid, 58 mg (0.225 mmol), 45%, R_f = 0.5 (EtOAc/Hexane, 40:60); **MP** 118-120 ^oC; (**IR-neat**) 744, 1287, 1633, 1712, 2922, 3221 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.20 (s, 3H), 2.88-2.89 (m, 2H), 3.02-3.05 (m, 2H), 3.77-3.81 (m, 4H), 7.11-7.18 (m, 1H), 7.29-7.31 (m, 1H), 7.44-7.51 (m, 1H), 7.51-7.58 (m, 1H), 9.82 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 14.1, 30.3, 42.3, 42.5, 49.6, 112.5, 118.6, 120.2, 124.9, 125.2, 127.0, 137.5, 161.8, 207.4; **MS** (ESI, *m/z*): $[M+H]^+$ 257; **HRMS** (ESI, *m/z*): calcd for $C_{15}H_{17}N_2O_2$ $[M+H]^+$ 257.1290, found 257.1300.



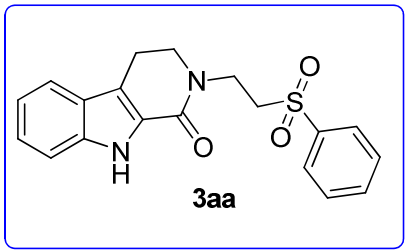
3y

2-(3-Oxopentyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-1-one (3y):- Light brown solid, 68 mg (0.250 mmol), 50%, R_f = 0.5 (EtOAc/Hexane, 40:60); **MP** 135-137 °C; (**IR-neat**) 740, 1165, 1290, 1550, 1636, 1711, 2936, 3217 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 1.07 (t, *J* = 7.3 Hz, 3H), 2.48 (q, *J* = 7.2 Hz, 2H), 2.86 (t, *J* = 6.5 Hz, 2H), 3.03 (t, *J* = 7.0 Hz, 2H), 3.80 (dd, *J* = 15.2, 7.0 Hz, 4H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.27-7.32 (m, 1H), 7.43 (d, *J* = 8.2 Hz, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 9.37 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 7.7, 20.9, 36.4, 41.0, 42.6, 49.5, 112.4, 118.6, 120.2, 124.9, 125.3, 127.0, 137.4, 161.7, 210.3; **MS** (ESI, *m/z*): $[M+H]^+$ 271; **HRMS** (ESI, *m/z*): calcd for $C_{16}H_{19}N_2O_2$ $[M+H]^+$ 271.1447, found 271.1464.



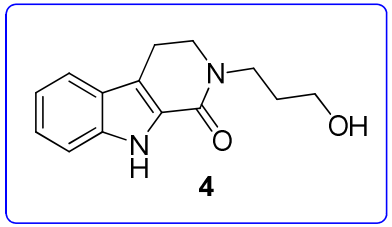
3z

3-(1-Oxo-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propanenitrile (3z):- Brown solid, 97 mg (0.405 mmol), 81%, R_f = 0.4 (EtOAc/Hexane, 40:60); **MP** 128-130 °C; (**IR-neat**) 746, 1278, 1636, 2250, 2924, 3224 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.76 (t, *J* = 6.4 Hz, 2H), 3.14 (t, *J* = 7.0 Hz, 2H), 3.83 (t, *J* = 6.4 Hz, 2H), 3.89 (t, *J* = 7.0 Hz, 2H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.33 (t, *J* = 7.3 Hz, 1H), 7.43 (d, *J* = 8.3 Hz, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 8.91 (brs, 1H); **^{13}C-NMR** (126 MHz, $CDCl_3$) δ = 17.3, 21.0, 43.7, 49.8, 112.4, 118.3, 119.4, 120.4, 120.5, 125.2, 125.4, 126.3, 137.5, 161.6; **MS** (ESI, *m/z*): $[M+H]^+$ 240; **HRMS** (ESI, *m/z*): calcd for $C_{14}H_{14}N_3O$ $[M+H]^+$ 240.1131, found 240.1137.



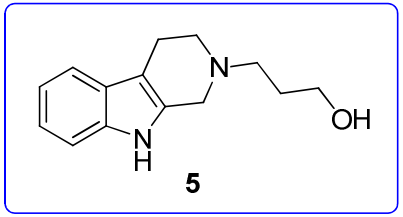
3aa

2-(2-(Phenylsulfonyl)ethyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-1-one (3aa):- White solid, 126 mg (0.355 mmol), 71%, R_f = 0.4 (EtOAc/Hexane, 40:60); **MP** 142-144 ^oC; (**IR-neat**) 772, 1081 1290, 1713, 2321, 2921, 3330 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 3.05 (t, *J* = 7.0 Hz, 2H), 3.52 (t, *J* = 6.7 Hz, 2H), 3.81 (t, *J* = 7.0 Hz, 2H), 3.95 (t, *J* = 6.7 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.28-7.33 (m, 1H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 3H), 7.95 (d, *J* = 7.3 Hz, 2H), 9.12 (brs, 1H); **^{13}C-NMR** (126 MHz, $CDCl_3$) δ = 20.8, 41.5, 49.5, 54.2, 112.4, 120.3, 120.4, 125.3, 126.4, 127.6, 127.9, 129.0, 129.4, 134.0, 137.4, 139.4, 161.6; **MS** (ESI, *m/z*): $[M+H]^+$ 355; **HRMS** (ESI, *m/z*): calcd for $C_{19}H_{19}N_2O_3S$ $[M+H]^+$ 355.1111, found 355.1126.



4

2-(3-Hydroxypropyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-1-one (4):- Yellow solid, 108 mg (0.445 mmol), 89%, R_f = 0.3 (MeOH/DCM, 2:98); **MP** 140-142 ^oC; (**IR-neat**) 745, 1289, 1633, 2923, 3079, 3242 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 1.80-1.85 (m, 2H), 3.09 (t, *J* = 7.1 Hz, 2H), 3.60-3.61 (m, 2H), 3.70-3.79 (m, 4H), 3.88 (brs, 1H), 7.13 - 7.18 (m, 1H), 7.30 - 7.34 (m, 1H), 7.45 (d, *J* = 8.3 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 9.20 (brs, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ = 20.7, 30.1, 42.8, 48.3, 58.1, 112.5, 118.6, 120.2, 120.4, 125.2, 126.5, 137.5, 162.3; **MS** (ESI, *m/z*): $[M+H]^+$ 245; **HRMS** (ESI, *m/z*): calcd for $C_{14}H_{17}N_2O_2$ $[M+H]^+$ 245.1290, found 245.1291.



5

3-(3,4-Dihydro-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)propan-1-ol (5):- Brown solid, 93 mg (0.405 mmol), 81%, R_f = 0.3 (MeOH/DCM, 4:96); **MP** 136-138 ^oC; (**IR-neat**) 751, 1281, 1462, 2923, 3330 cm^{-1}; **^{1}H-NMR** (400 MHz, DMSO-d_6) δ = 1.68-1.70 (m, 2H), 2.60-2.81 (m, 6H), 3.33-3.62 (m, 4H), 4.60 (brs, 1H), 6.93-7.00 (m, 2H), 7.26-7.35 (m, 2H), 10.69 (brs, 1H); **^{13}C-NMR** (101 MHz, DMSO-d_6) δ = 21.6, 30.5, 50.6, 51.3, 55.0, 59.8, 106.9, 111.3, 117.8, 118.7, 120.8, 127.1, 133.1, 136.3; **MS** (ESI, *m/z*): $[M+H]^+$ 231; **HRMS** (ESI, *m/z*): calcd for $C_{14}H_{19}N_2O$ $[M+H]^+$ 231.1492, found 231.1494.

11. References

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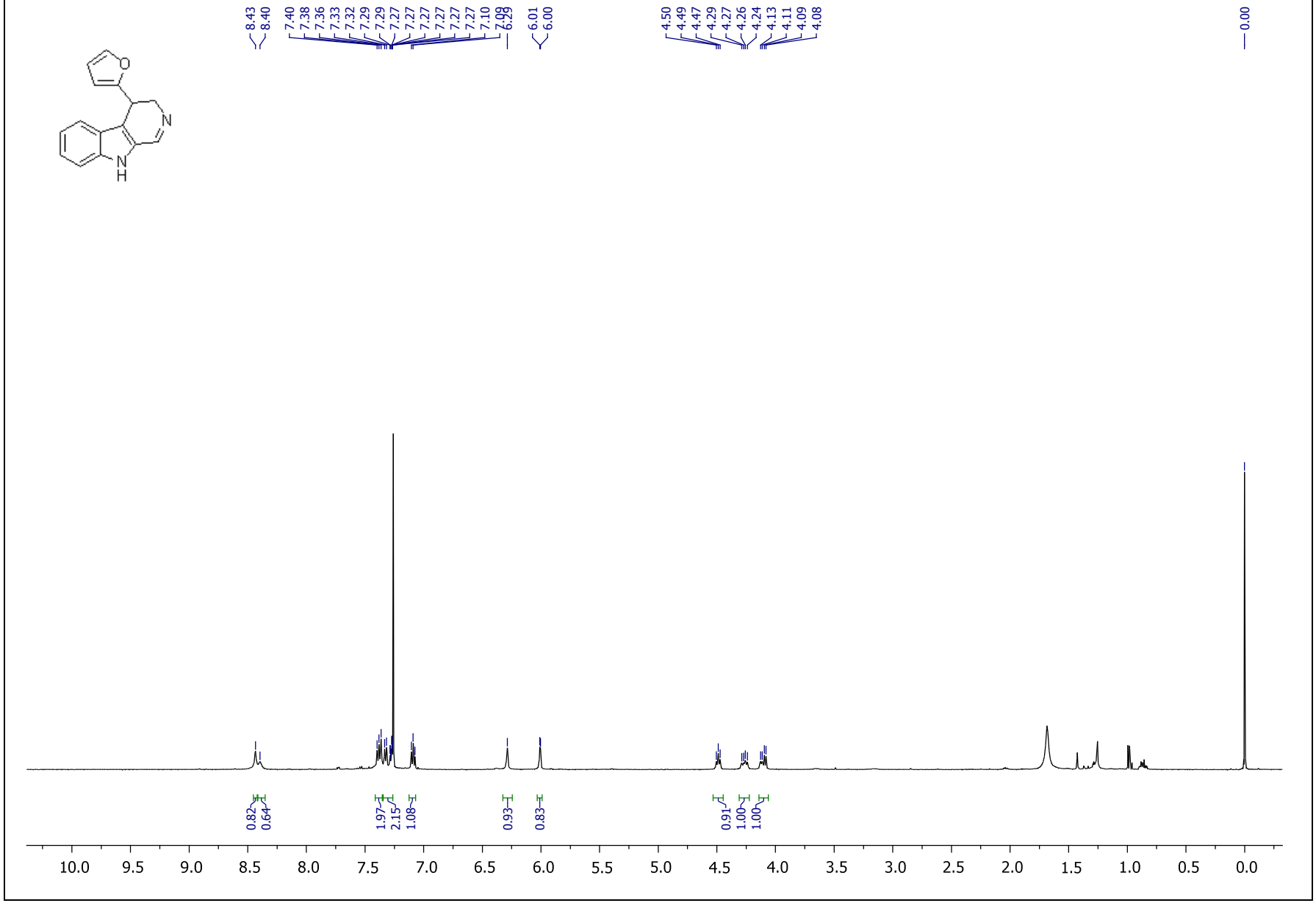
12. Copies of ^{1}H and ^{13}C NMR spectra of the products

^{1}H NMR of **1k**



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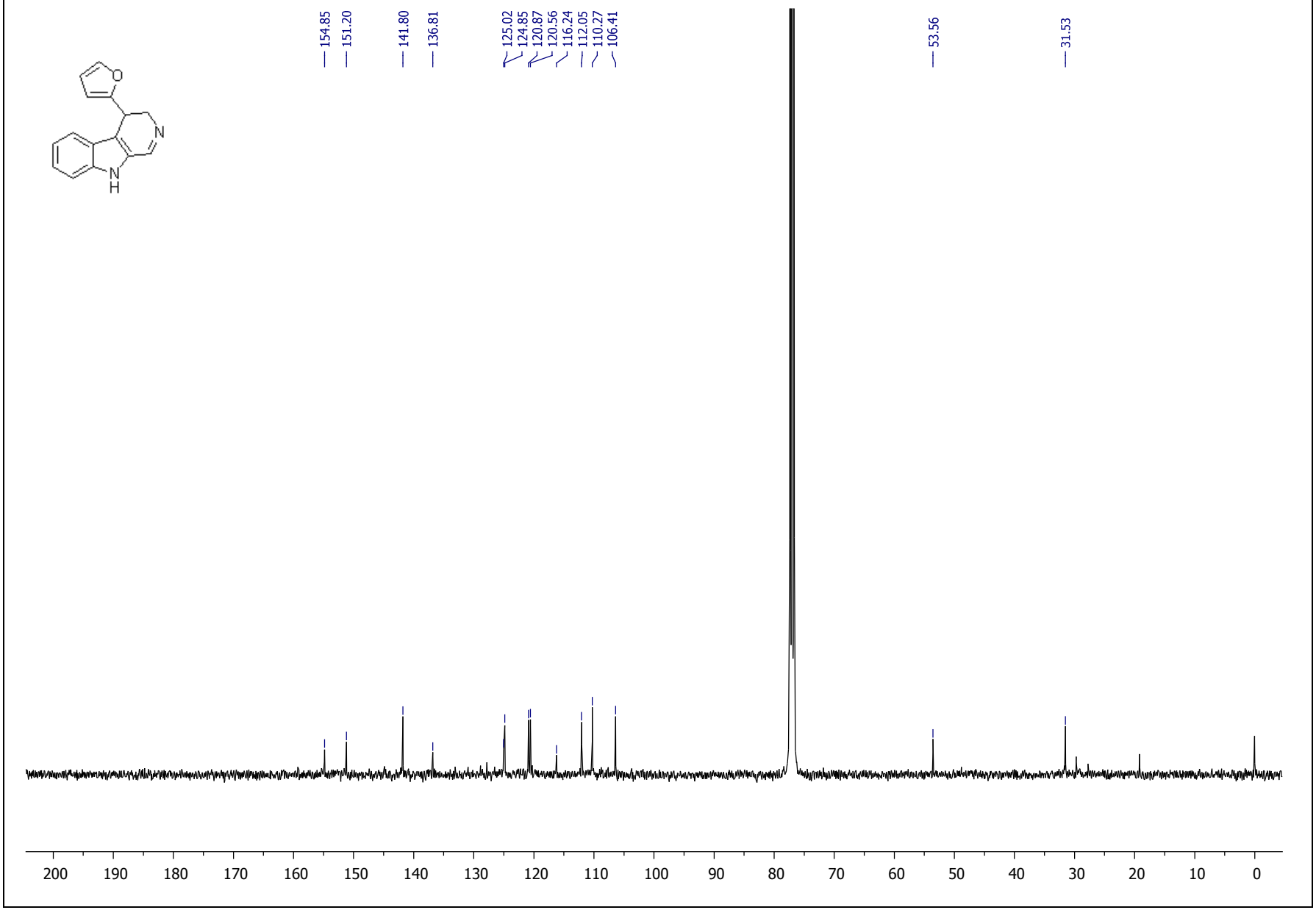
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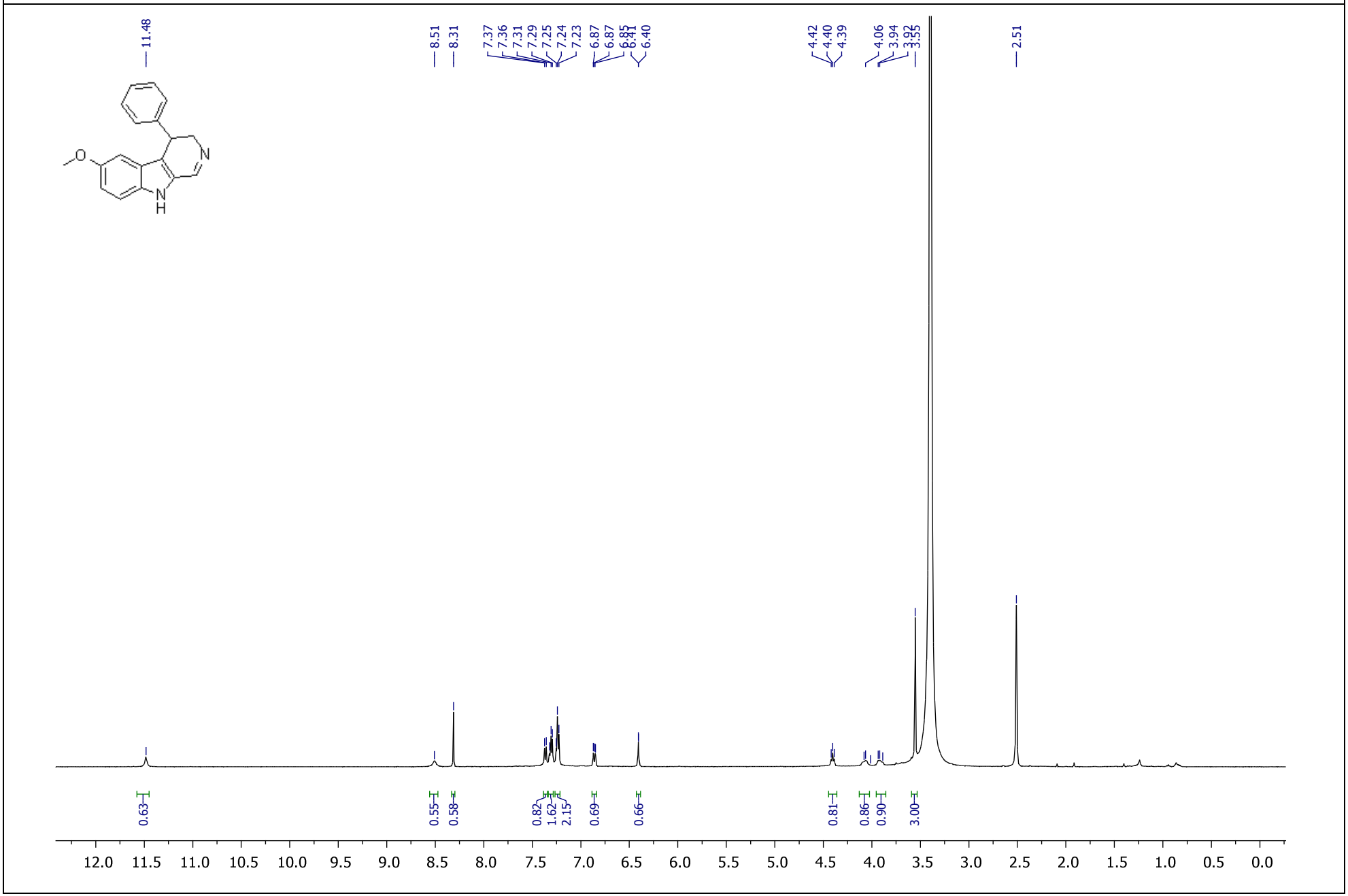
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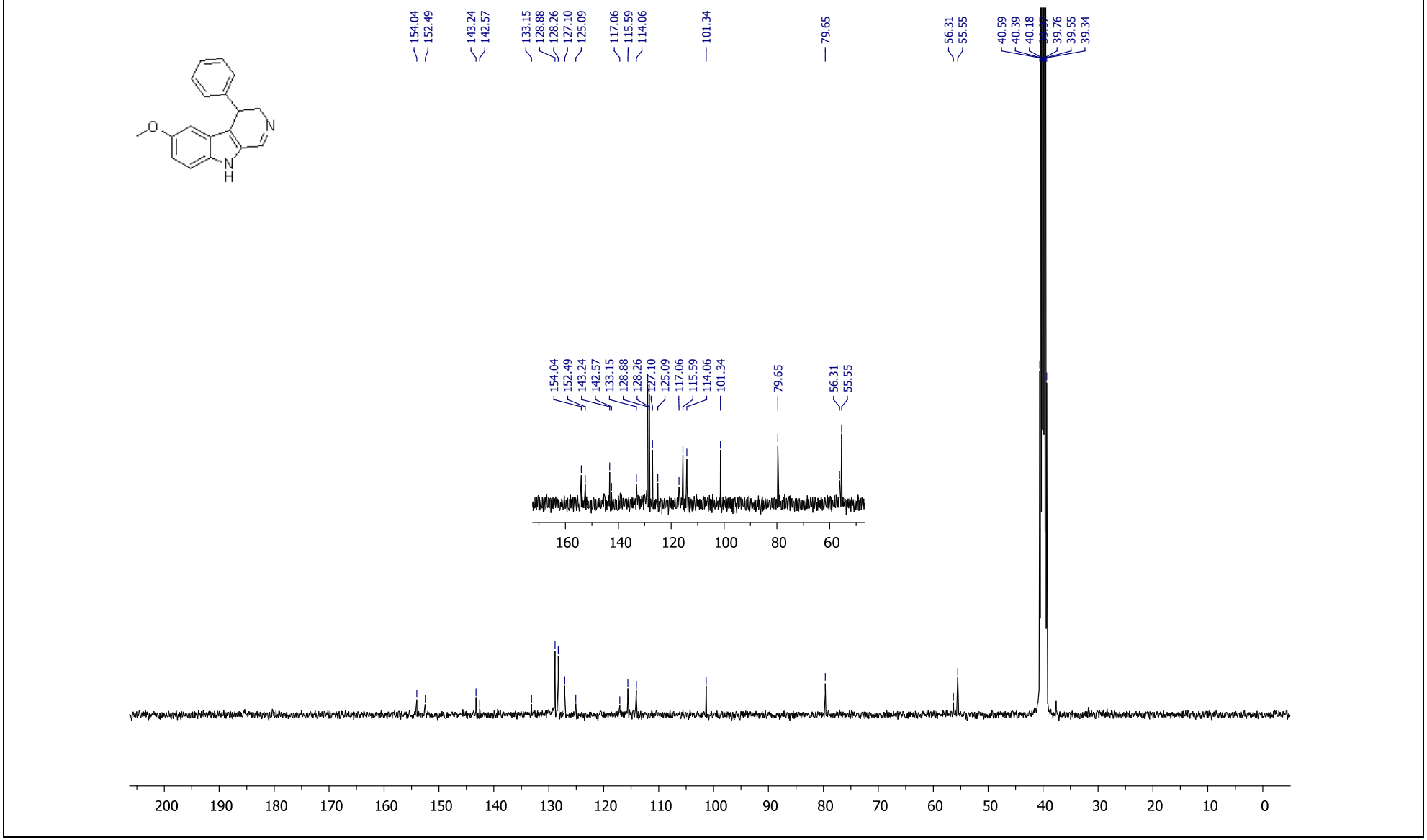
^{13}C NMR of **1n**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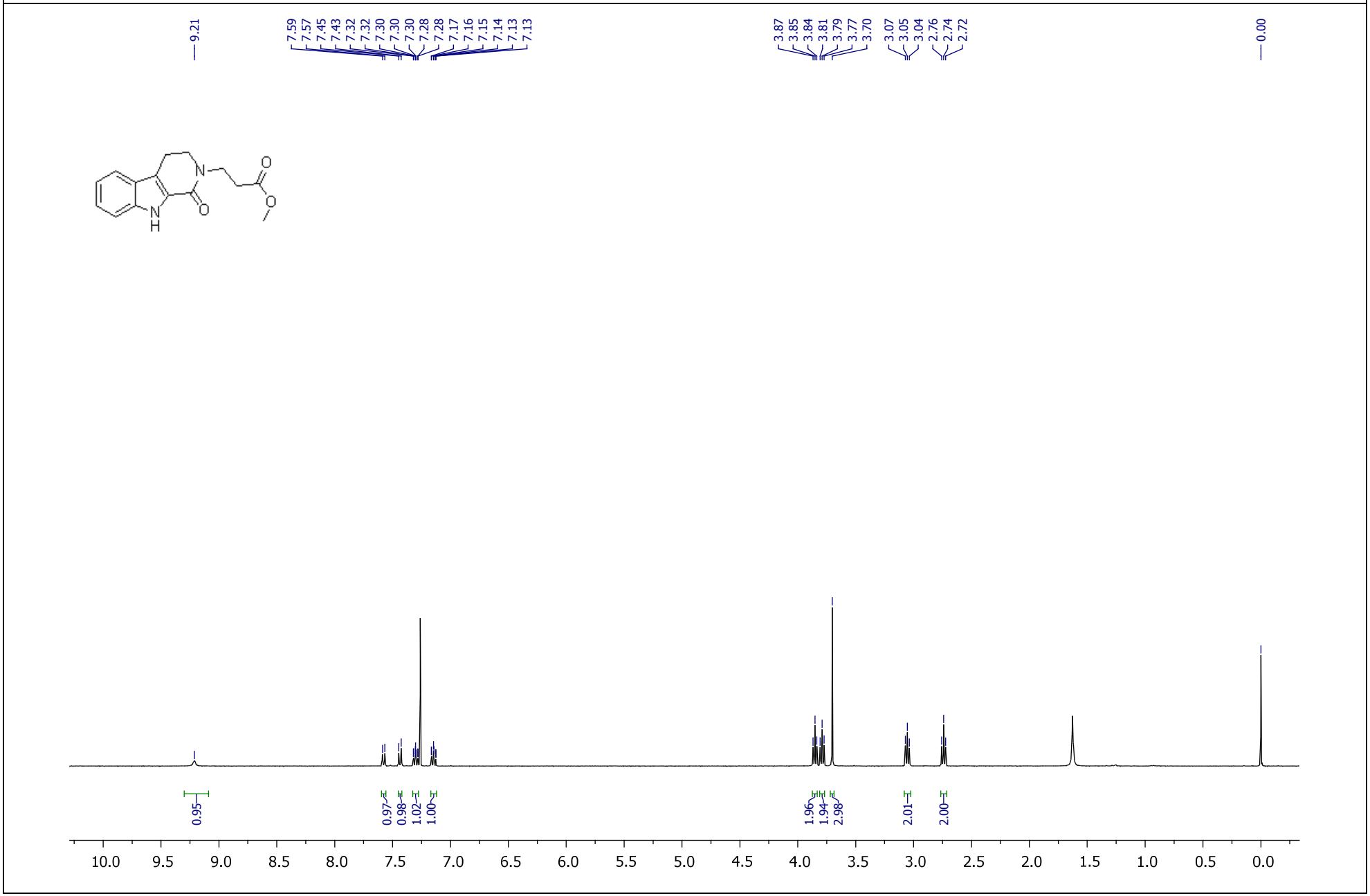
^{1}H NMR of **3a**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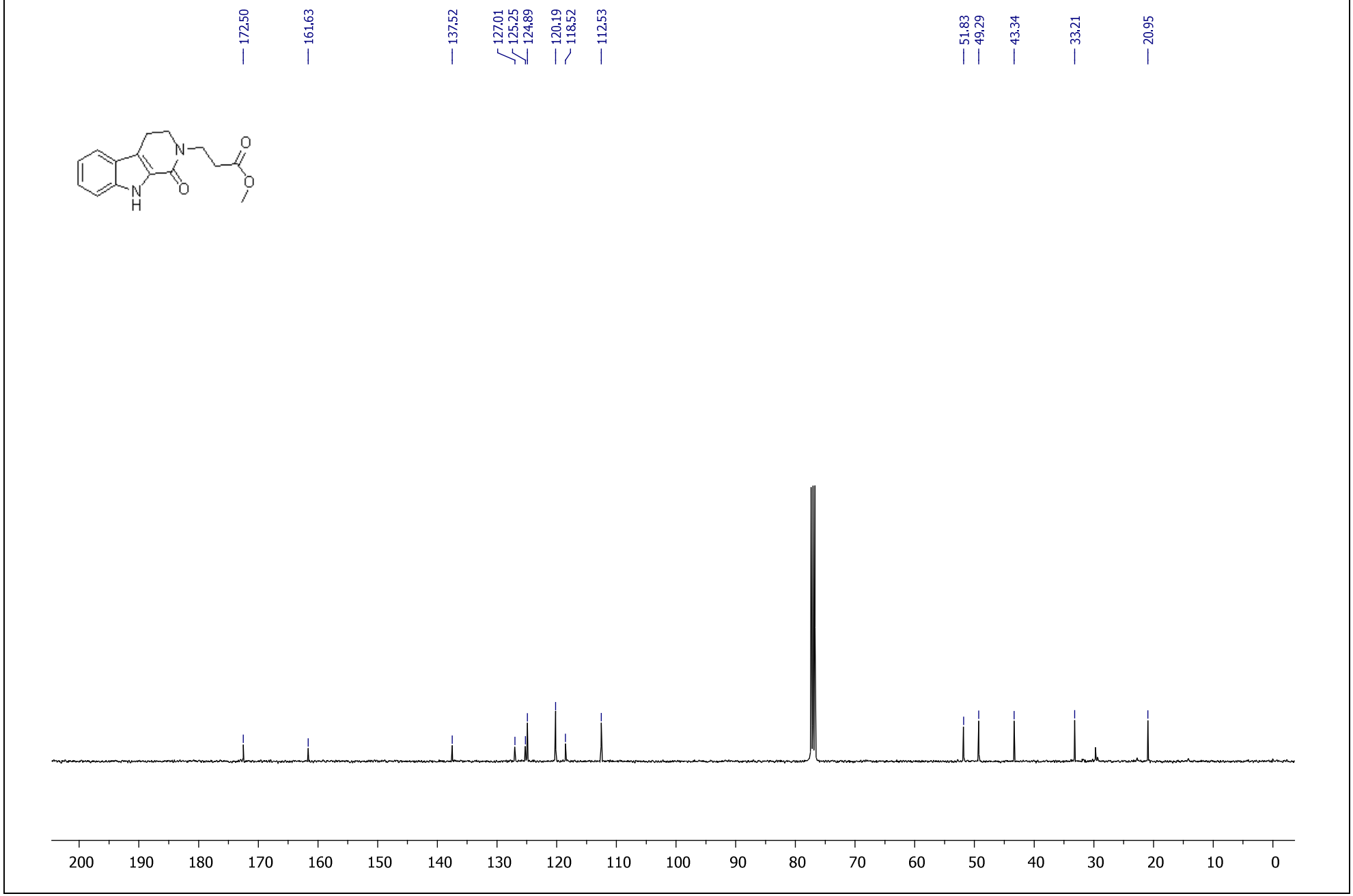
^{13}C NMR of **3a**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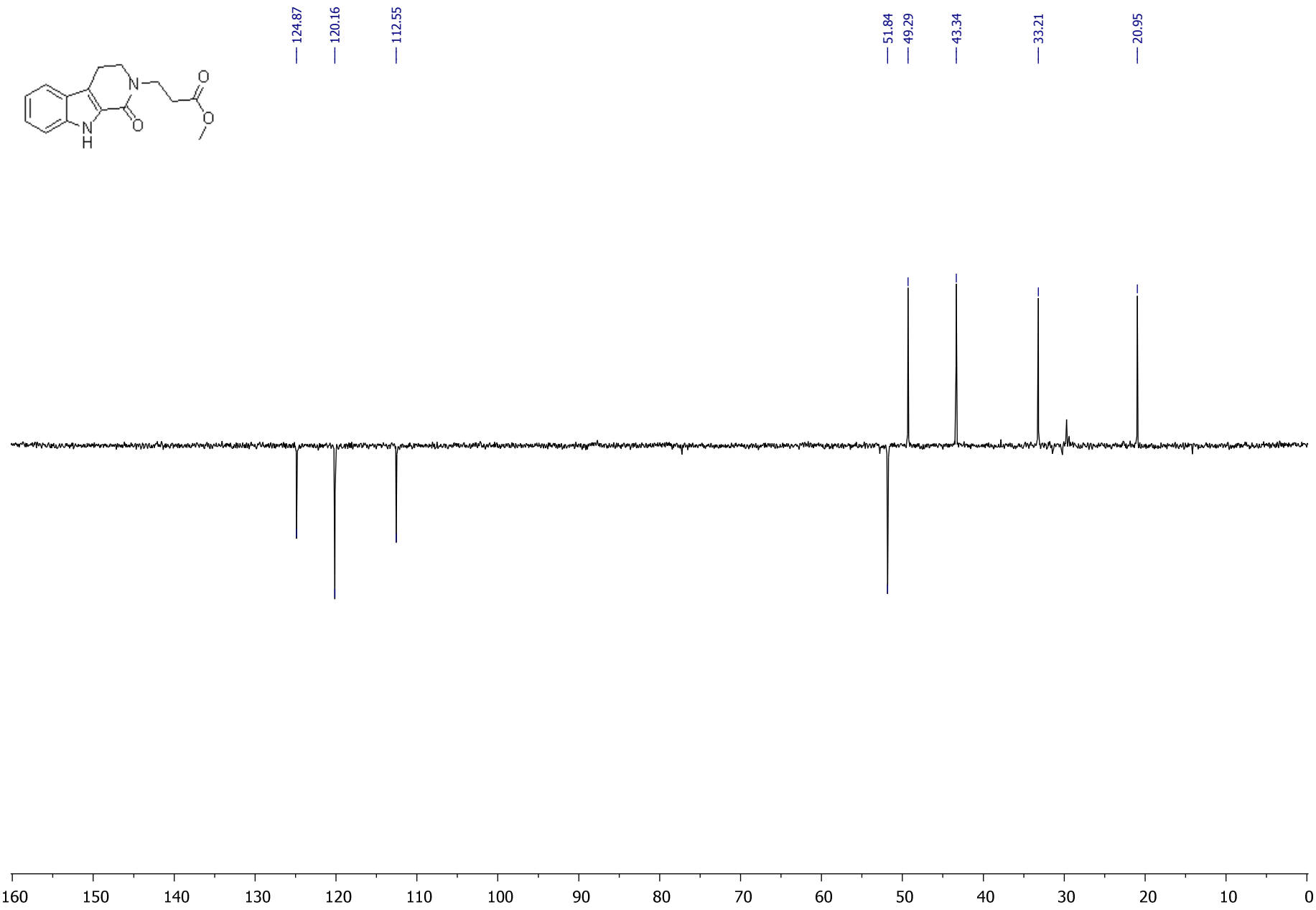
DEPT-135 of **3a**



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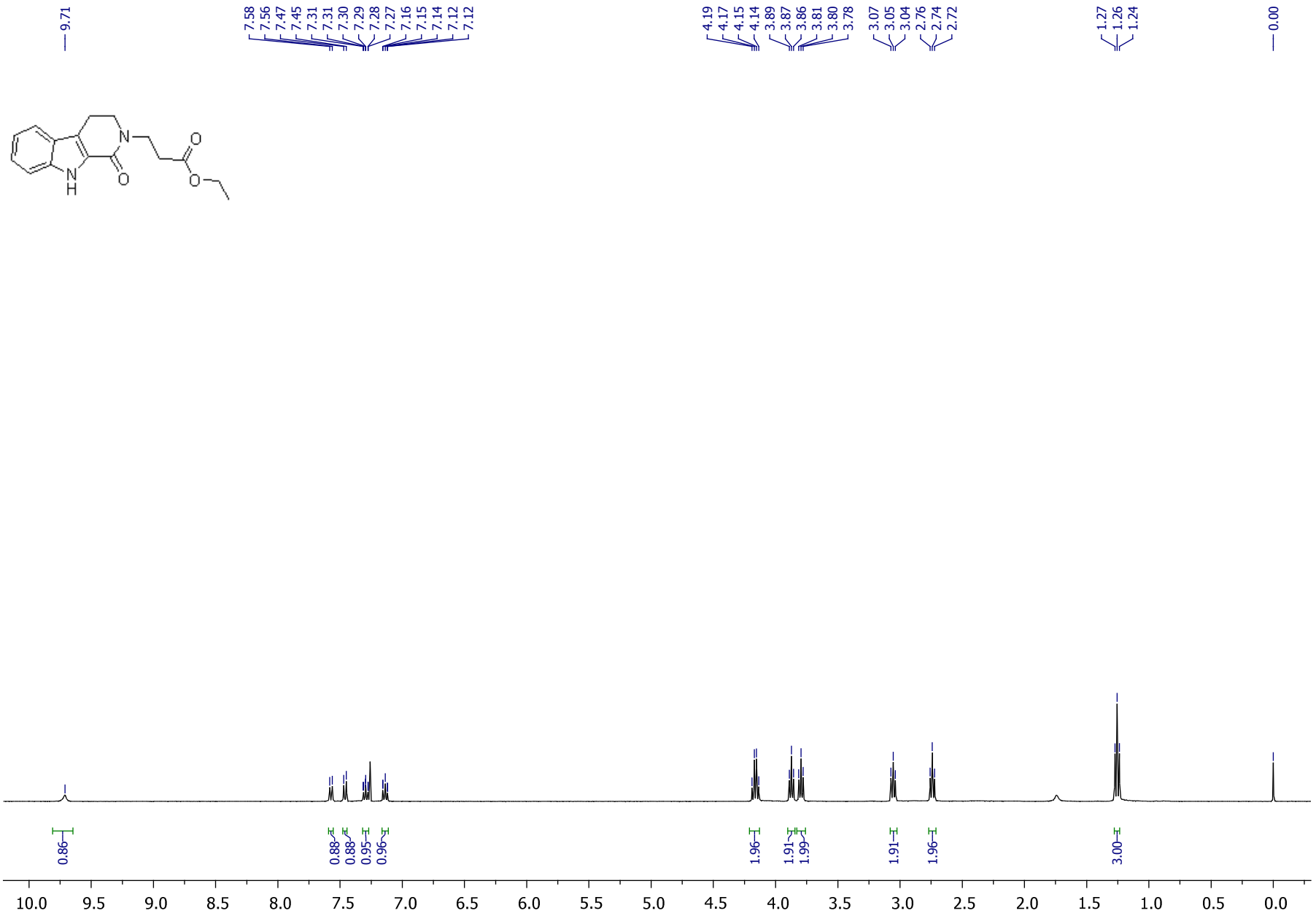
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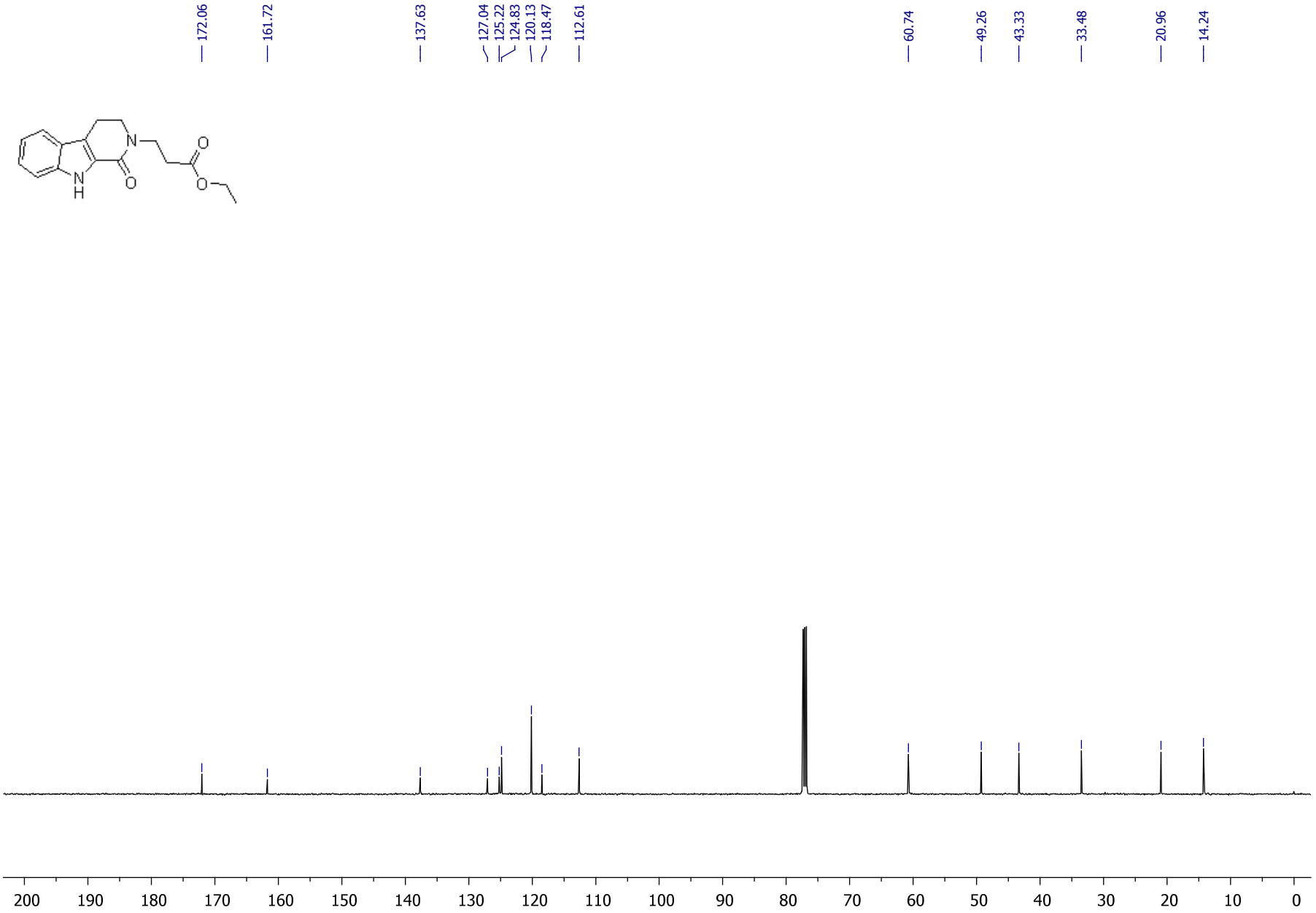
^{13}C NMR of **3b**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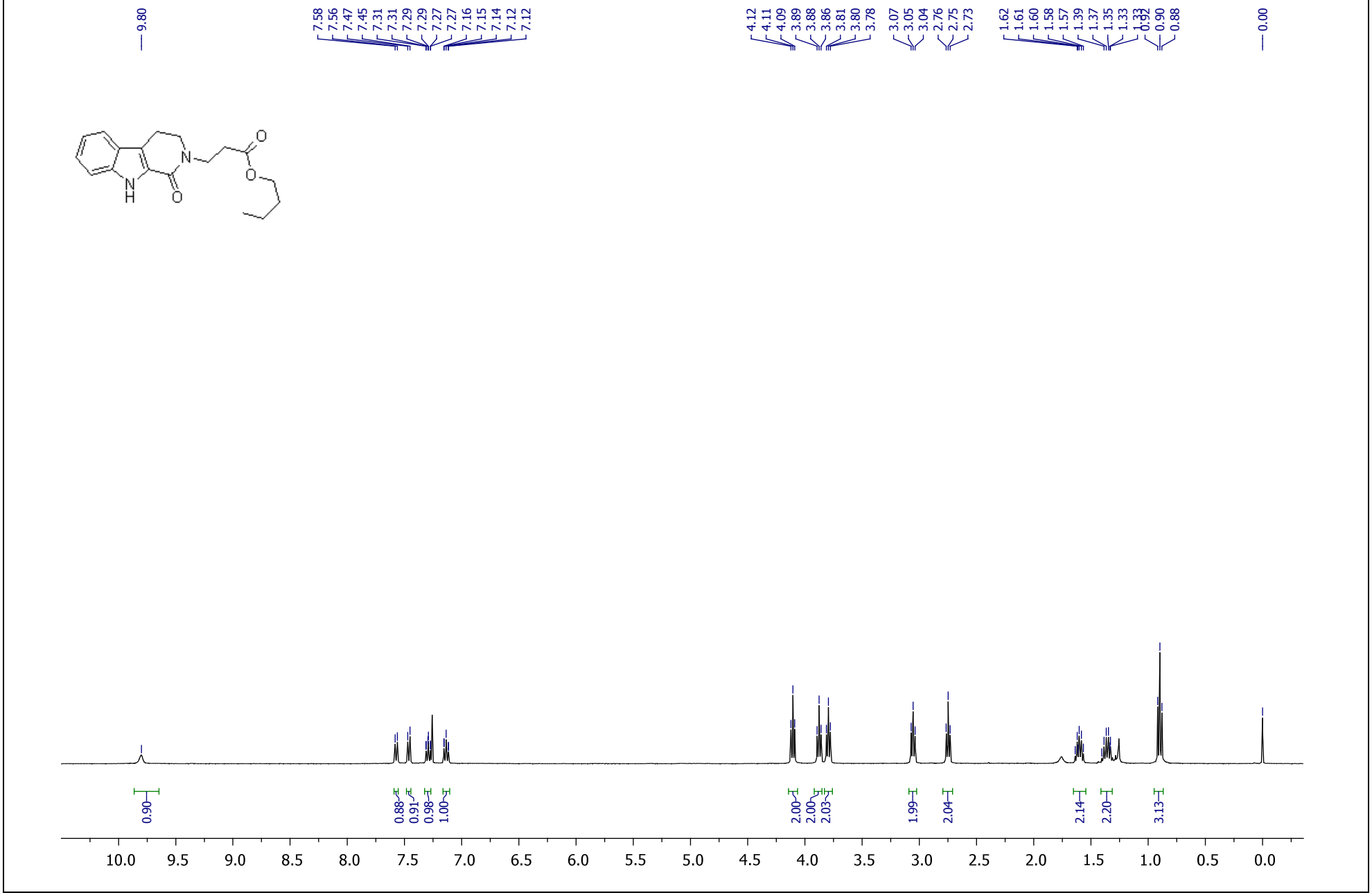
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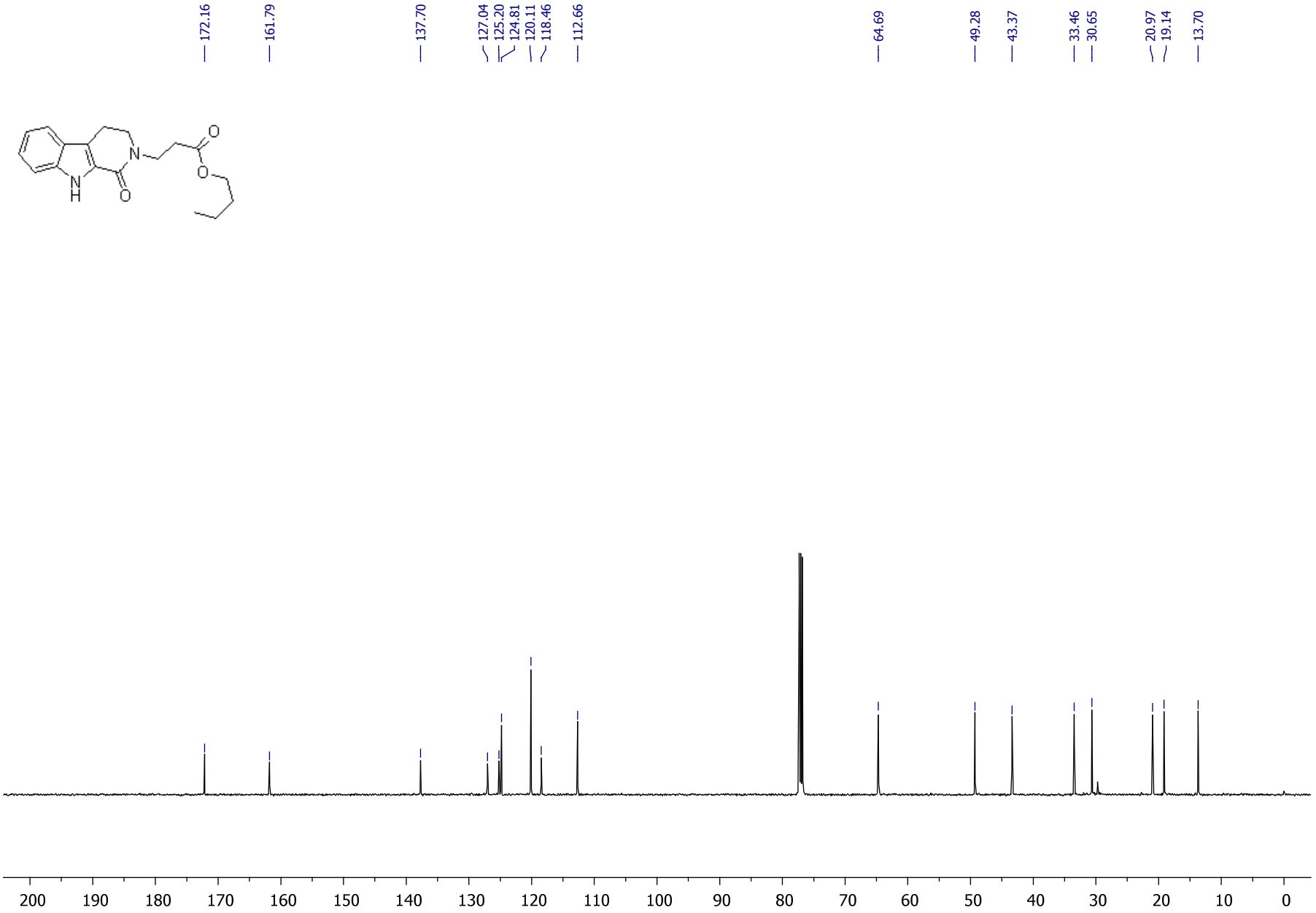
^{13}C NMR of **3c**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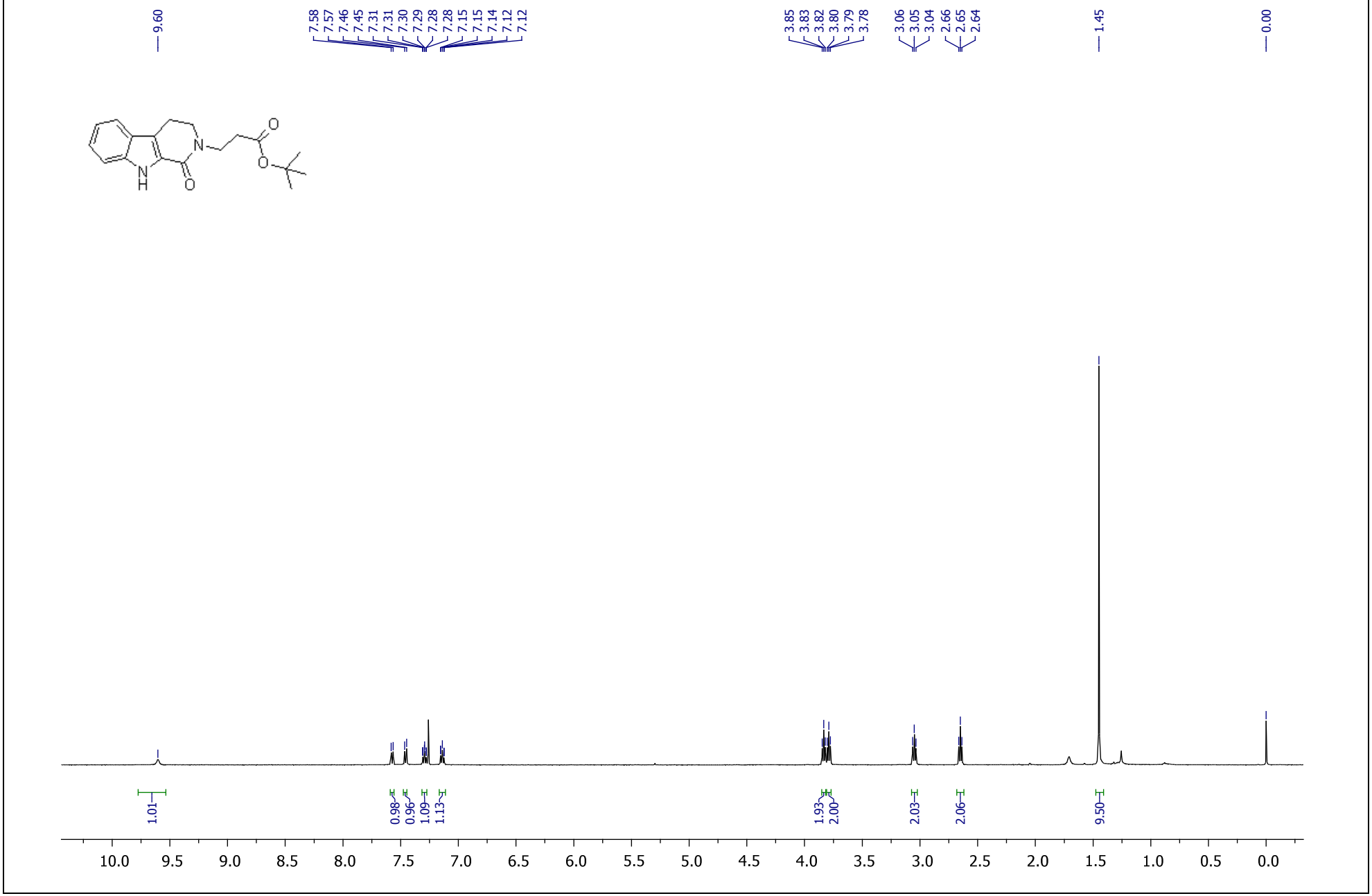
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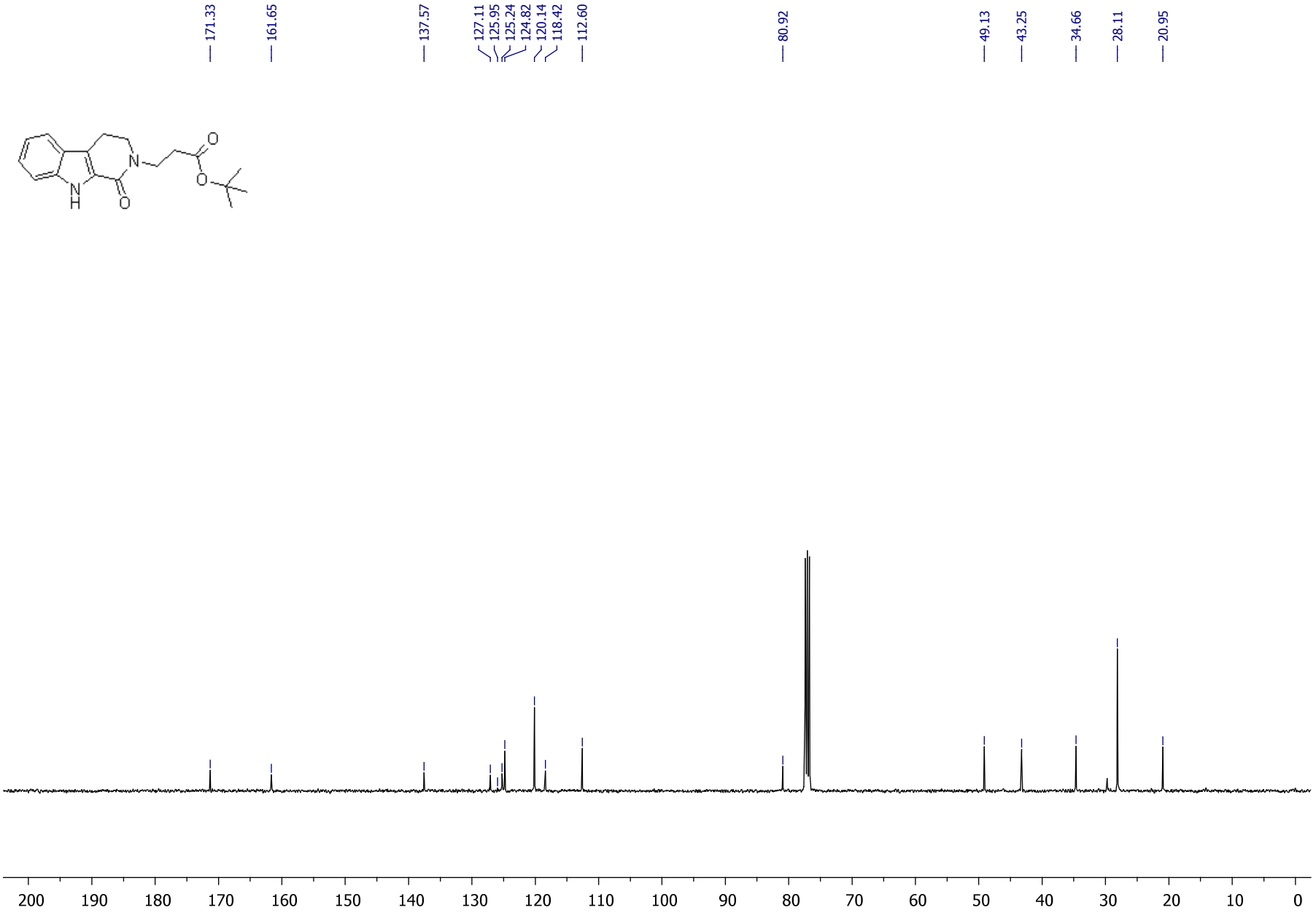
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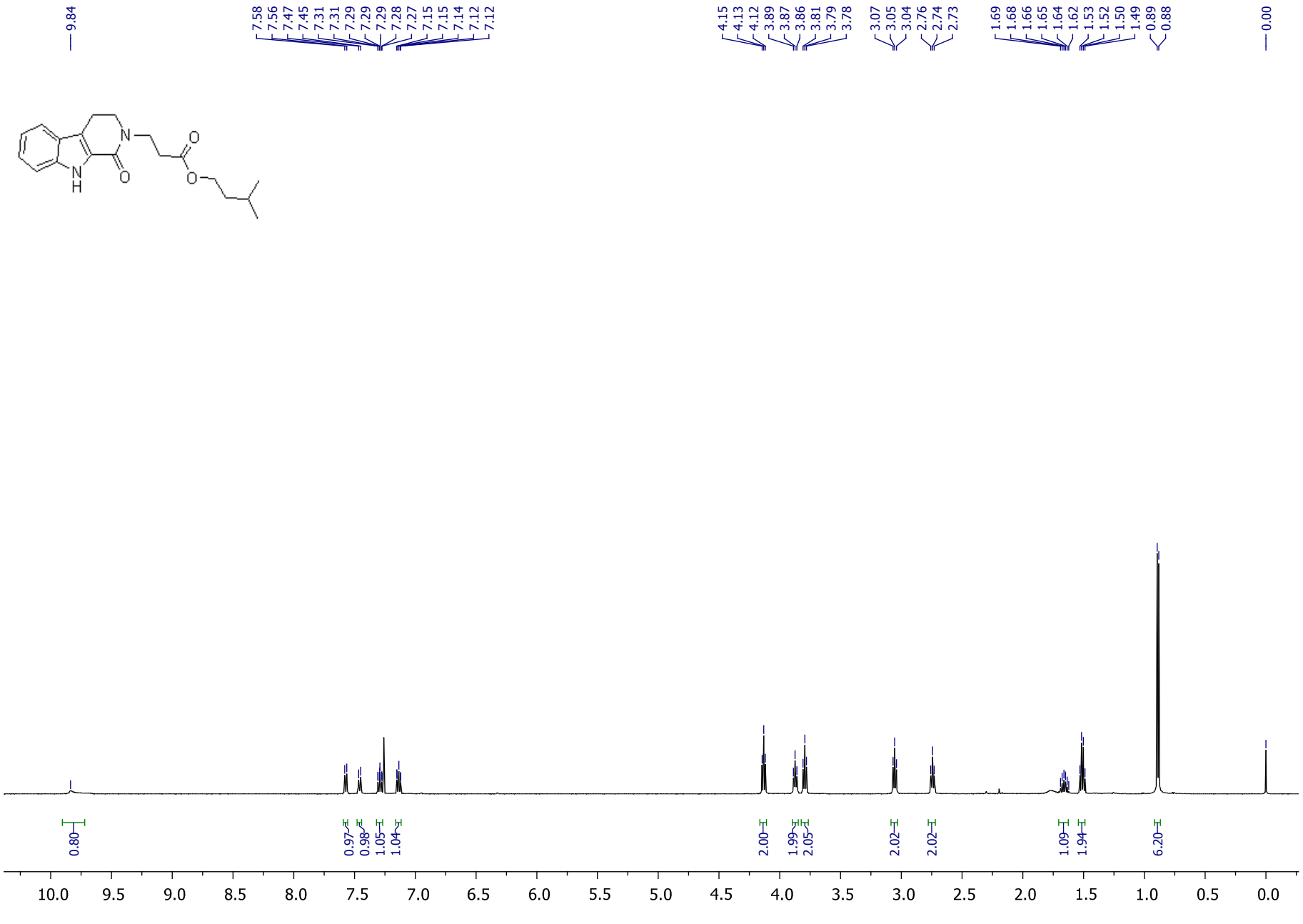
^{1}H NMR of **3e**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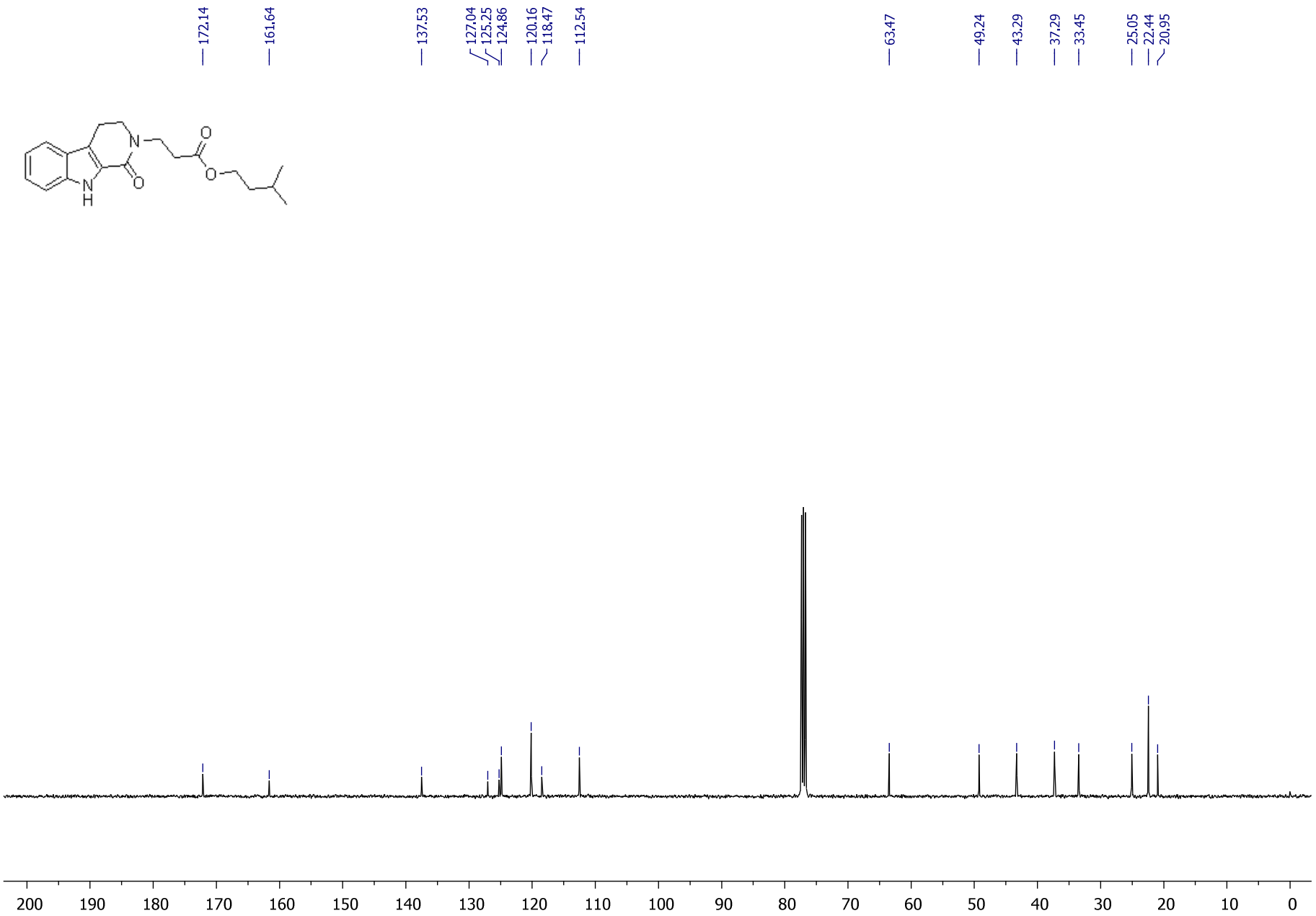
^{13}C NMR of **3e**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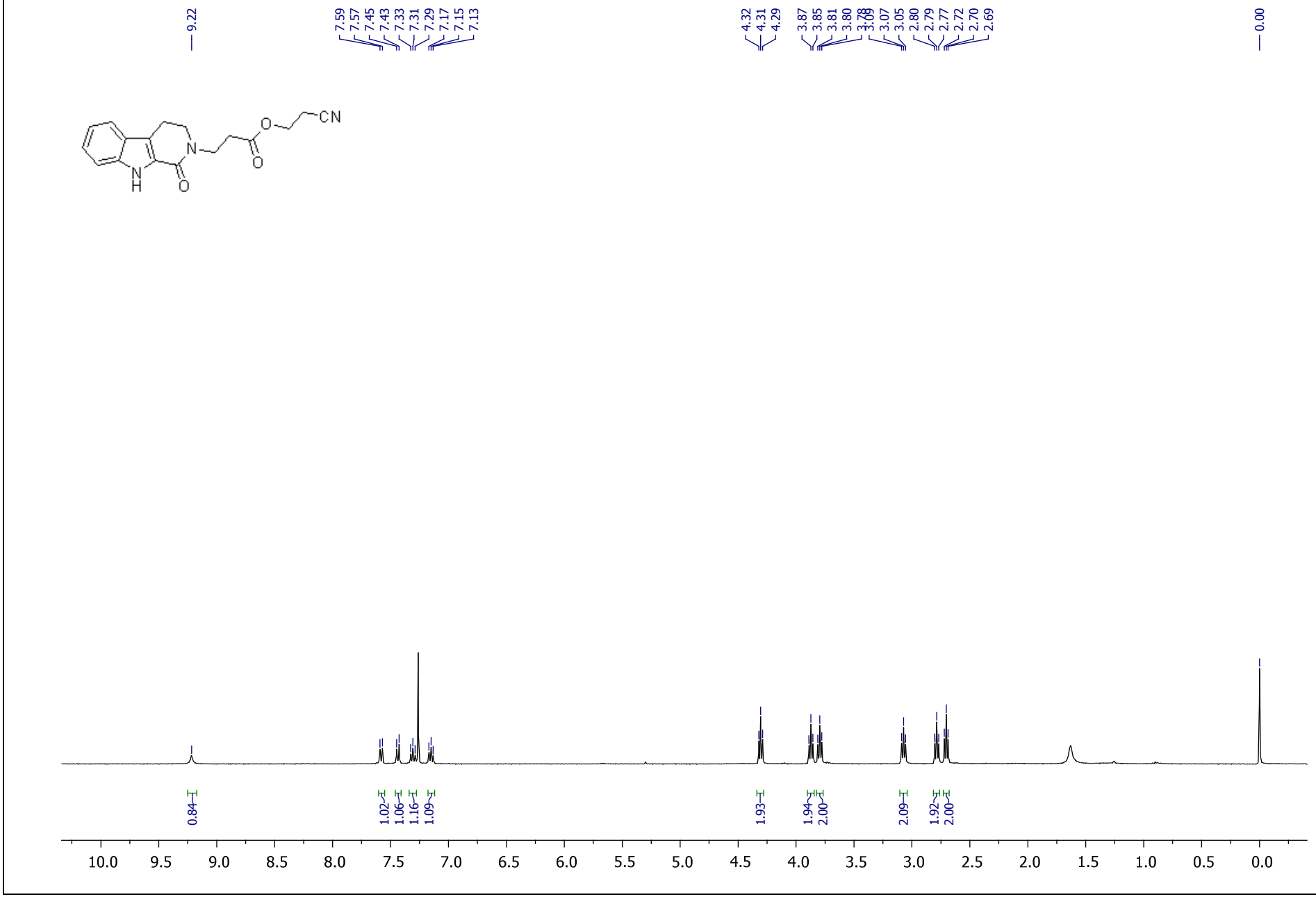
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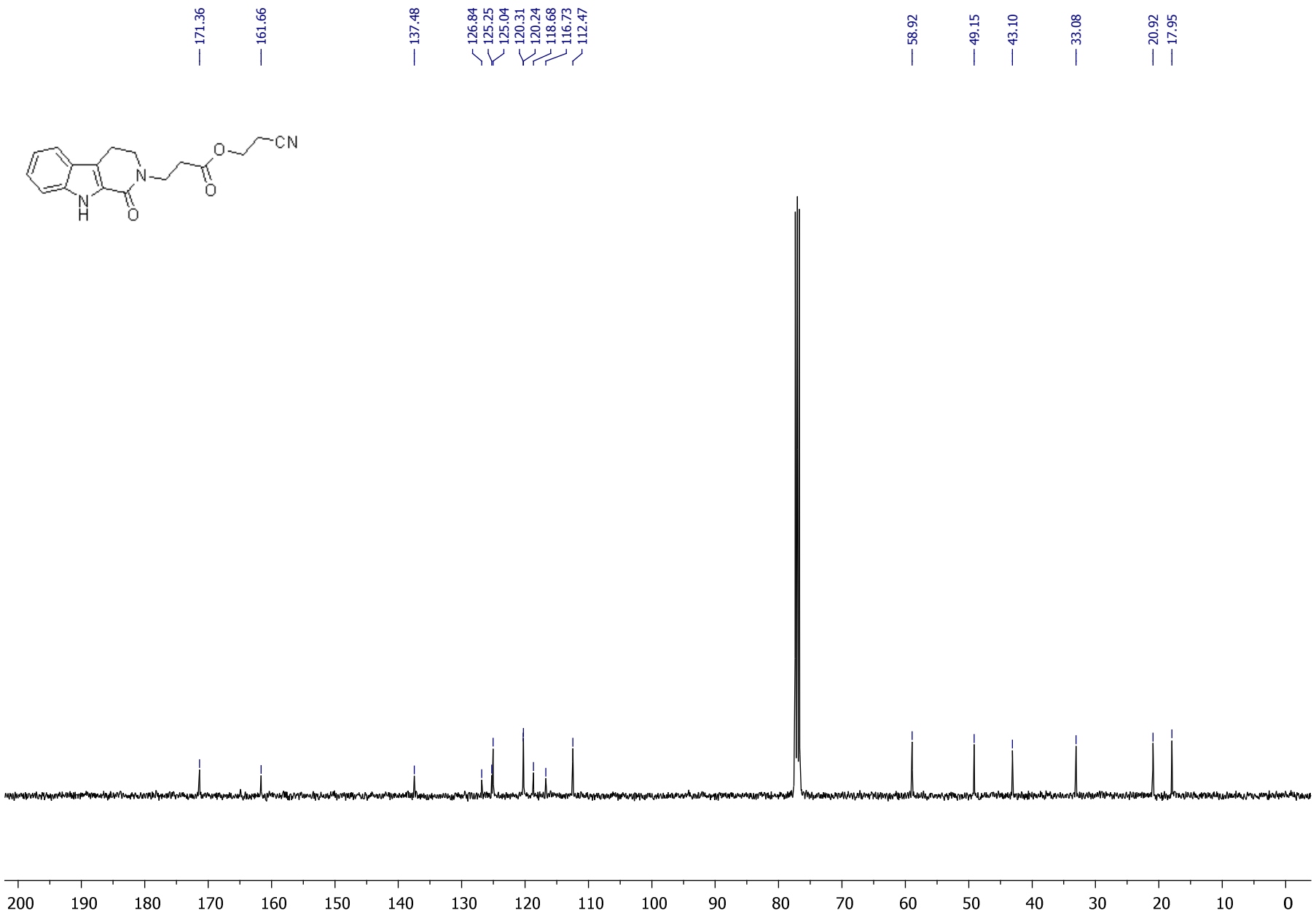
^{13}C NMR of **3f**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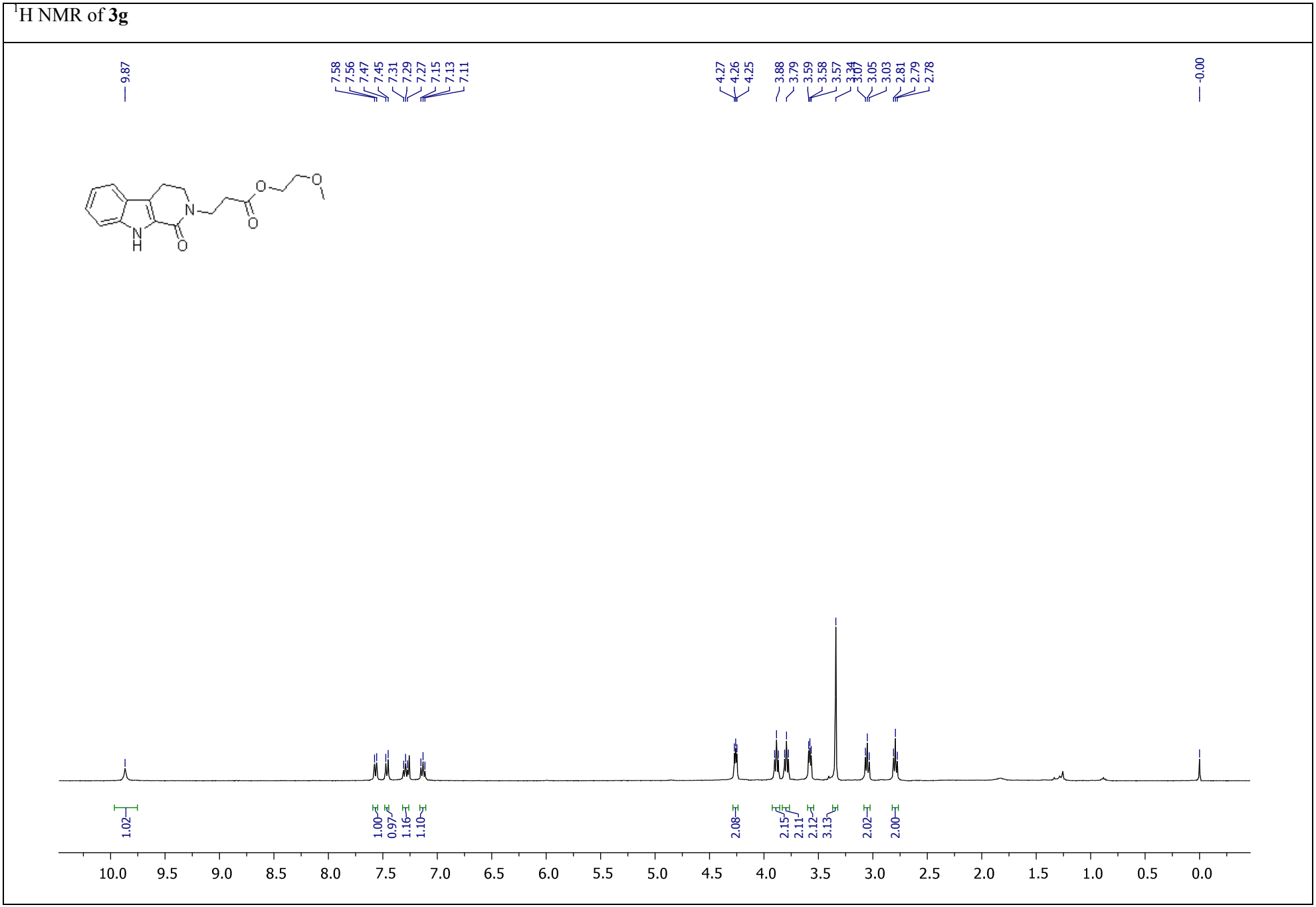
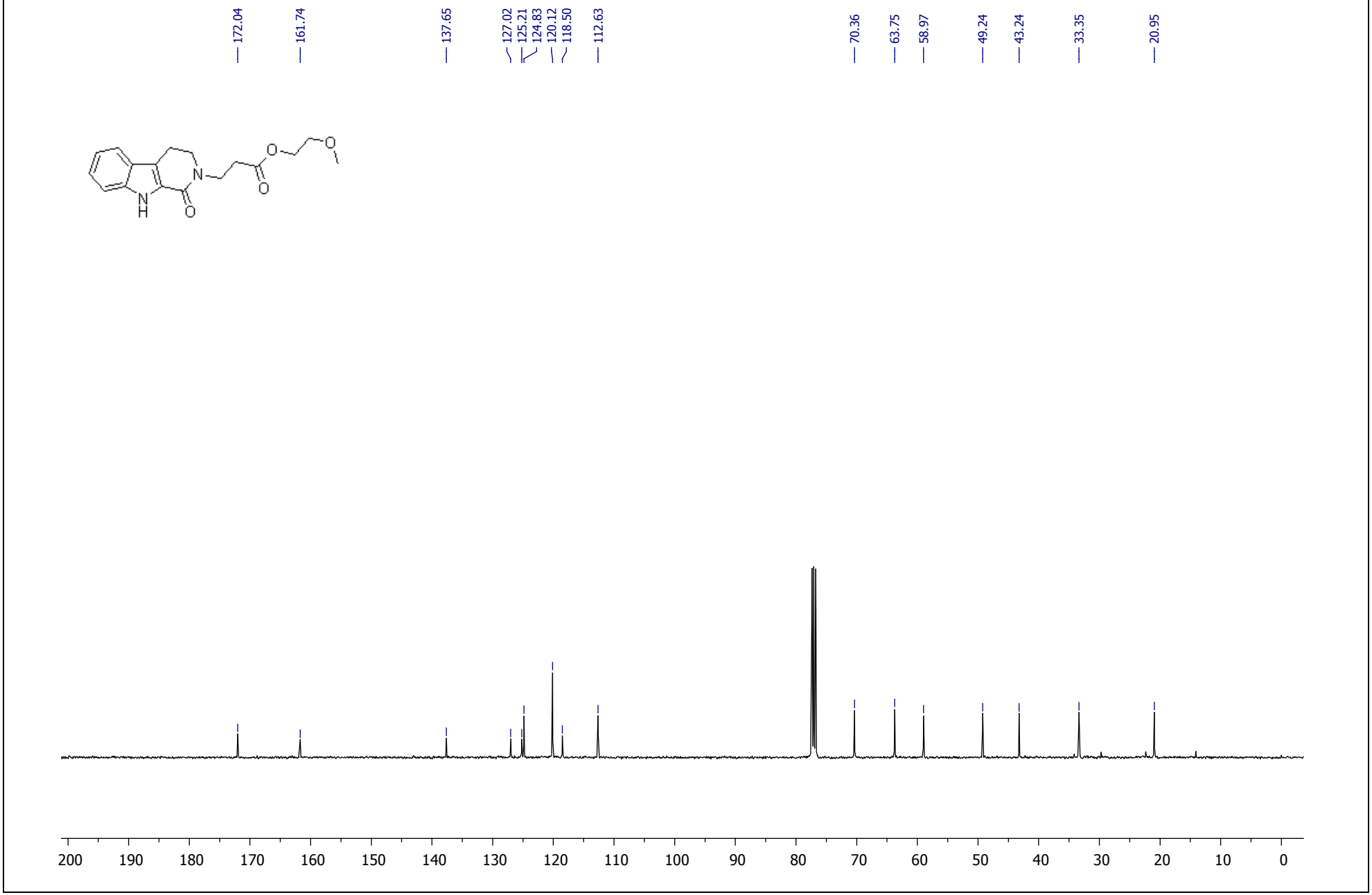
90
80
70
60
50
40
30
20
10
0

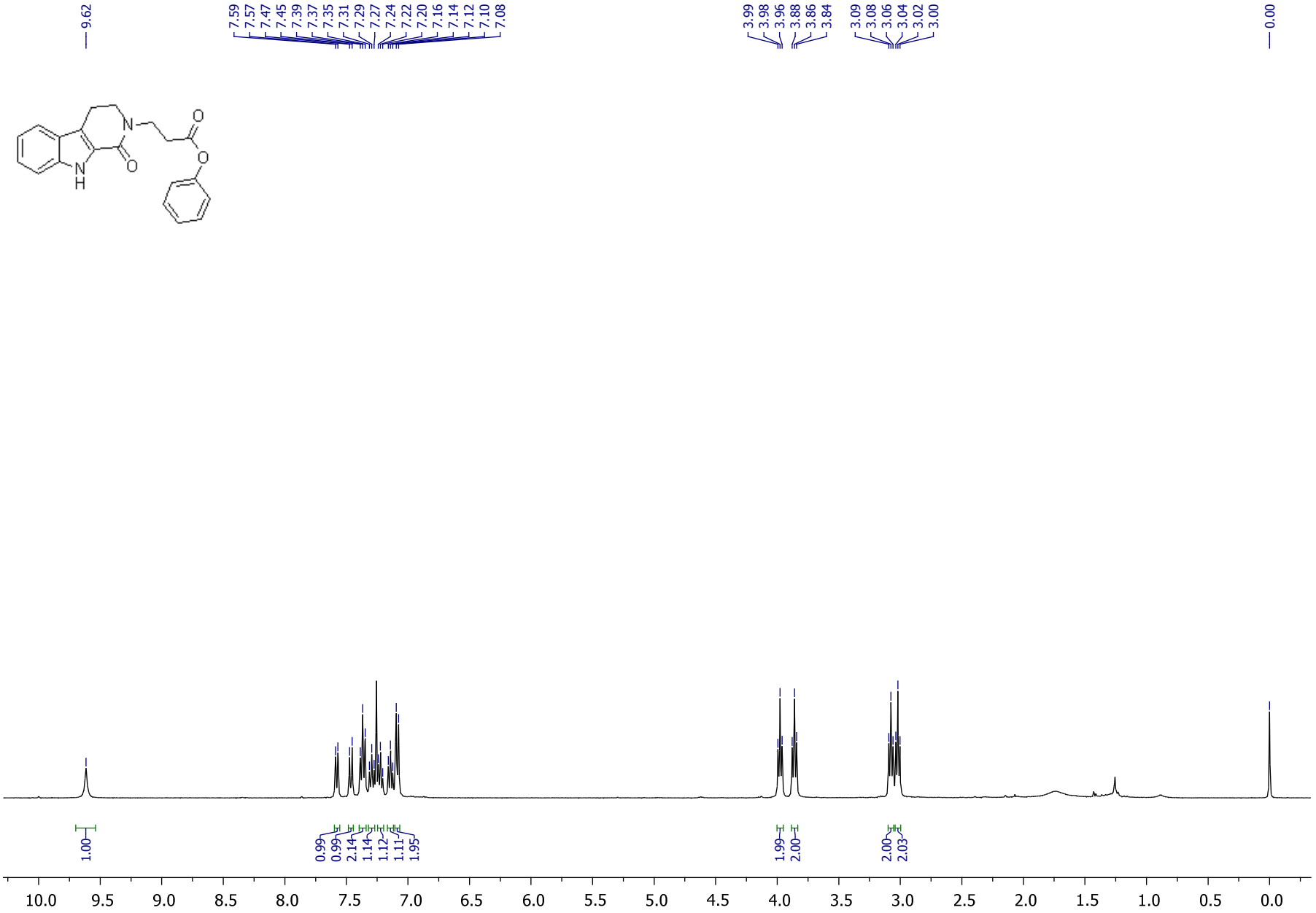
^{1}H NMR of **3g**


9.87
7.58
7.56
7.47
7.45
7.31
7.29
7.27
7.15
7.13
7.11
4.27
4.26
4.25
3.88
3.79
3.59
3.58
3.57
3.05
3.03
2.81
2.79
2.78
-0.00
1.02
1.00
0.97
1.16
1.10
2.08
2.15
2.11
2.12
3.13
2.02
2.00
10.0
9.5
9.0
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
0.0

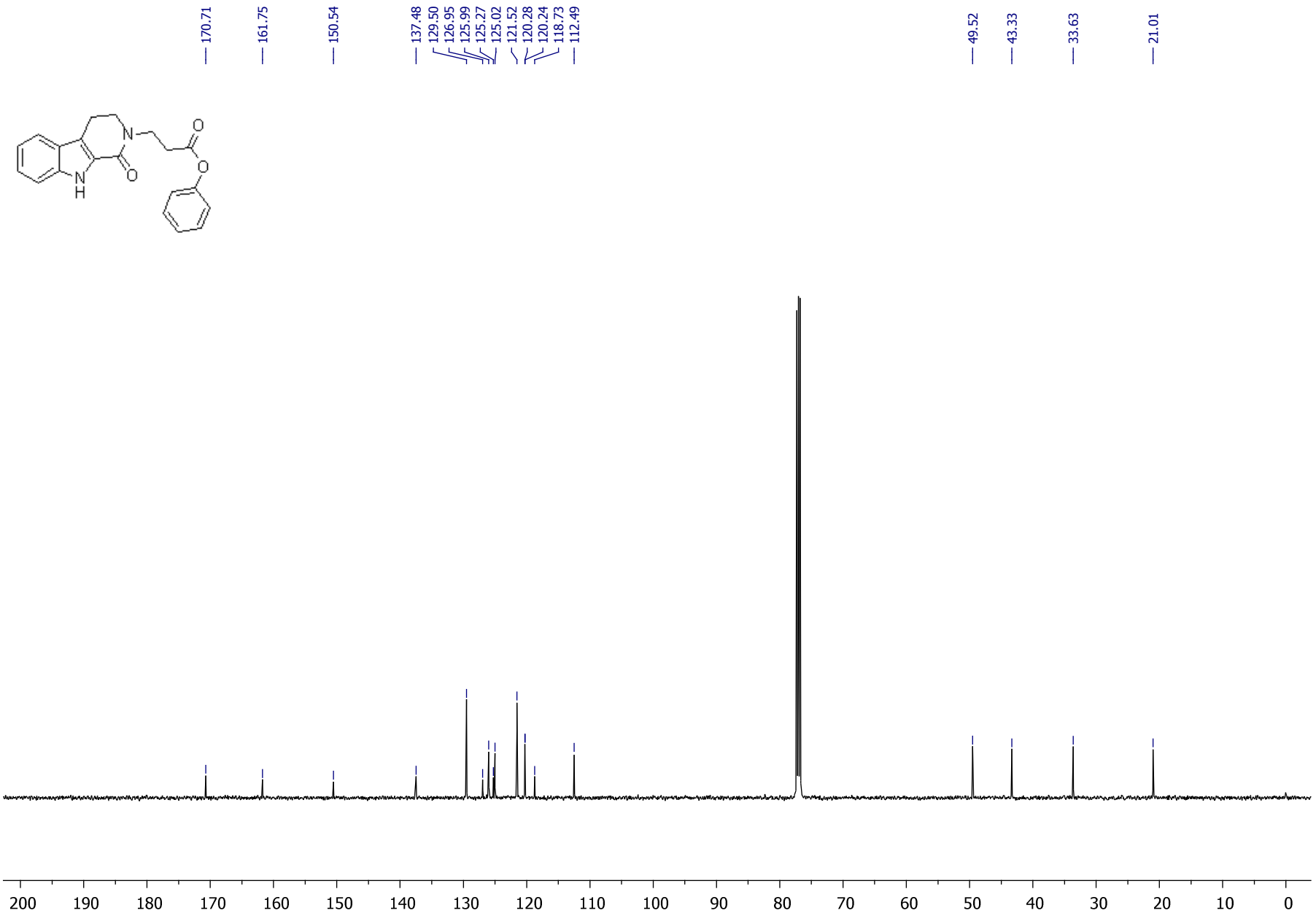
^{13}C NMR of **3g**


172.04
161.74
137.65
127.02
125.21
124.83
120.12
118.50
112.63
70.36
63.75
58.97
49.24
43.24
33.35
20.95
O
O
O
N
H
N
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{1}H NMR of **3h**


9.62
7.59
7.57
7.47
7.45
7.39
7.37
7.35
7.31
7.29
7.27
7.24
7.22
7.20
7.16
7.14
7.12
7.10
7.08
3.99
3.98
3.96
3.88
3.86
3.84
3.09
3.08
3.06
3.04
3.02
3.00
0.00
O
N
H
O
O
1.00
0.99
0.99
2.14
1.14
1.12
1.11
1.95
1.99
2.00
2.00
2.03
10.0
9.5
9.0
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
0.0

^{13}C NMR of **3h**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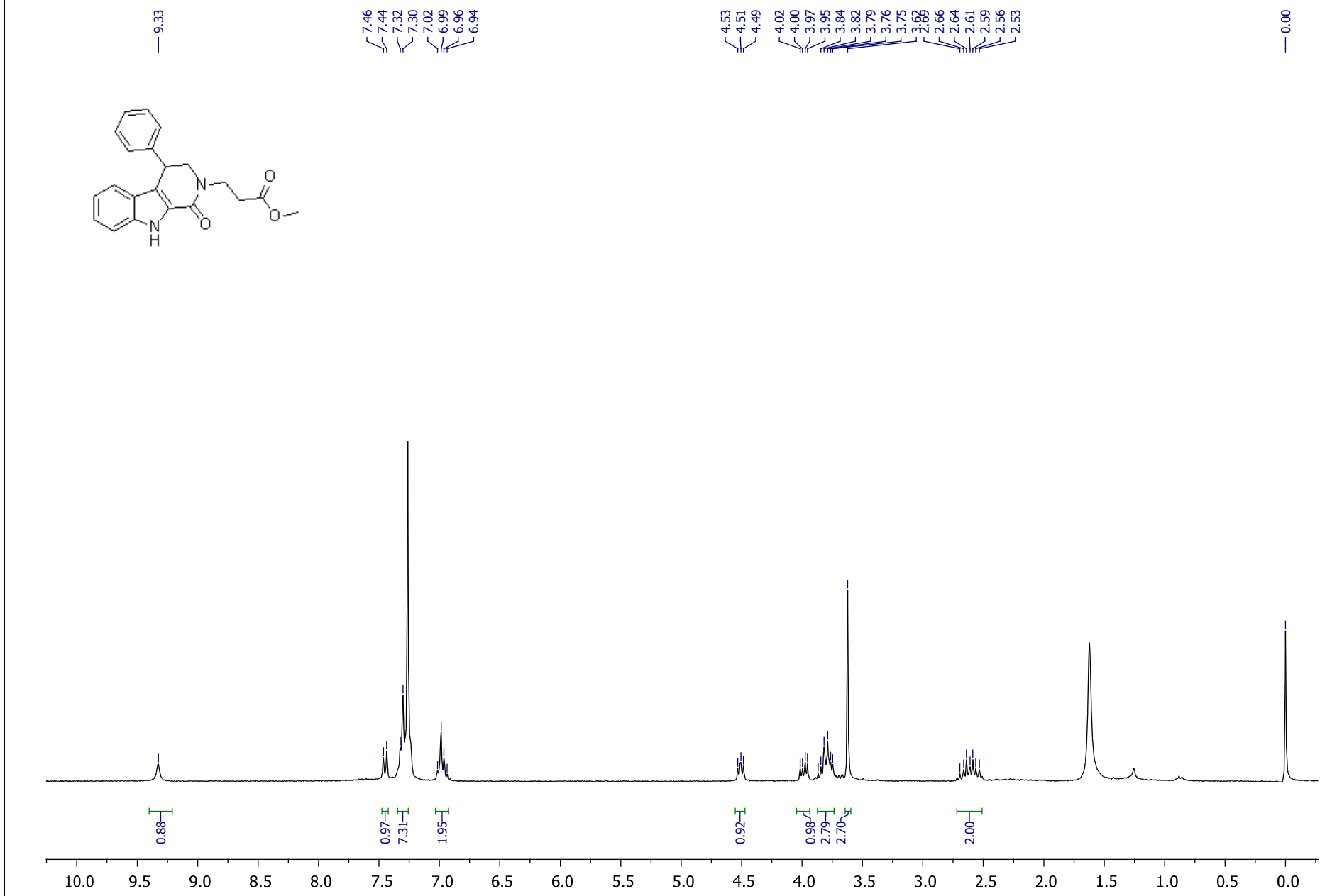
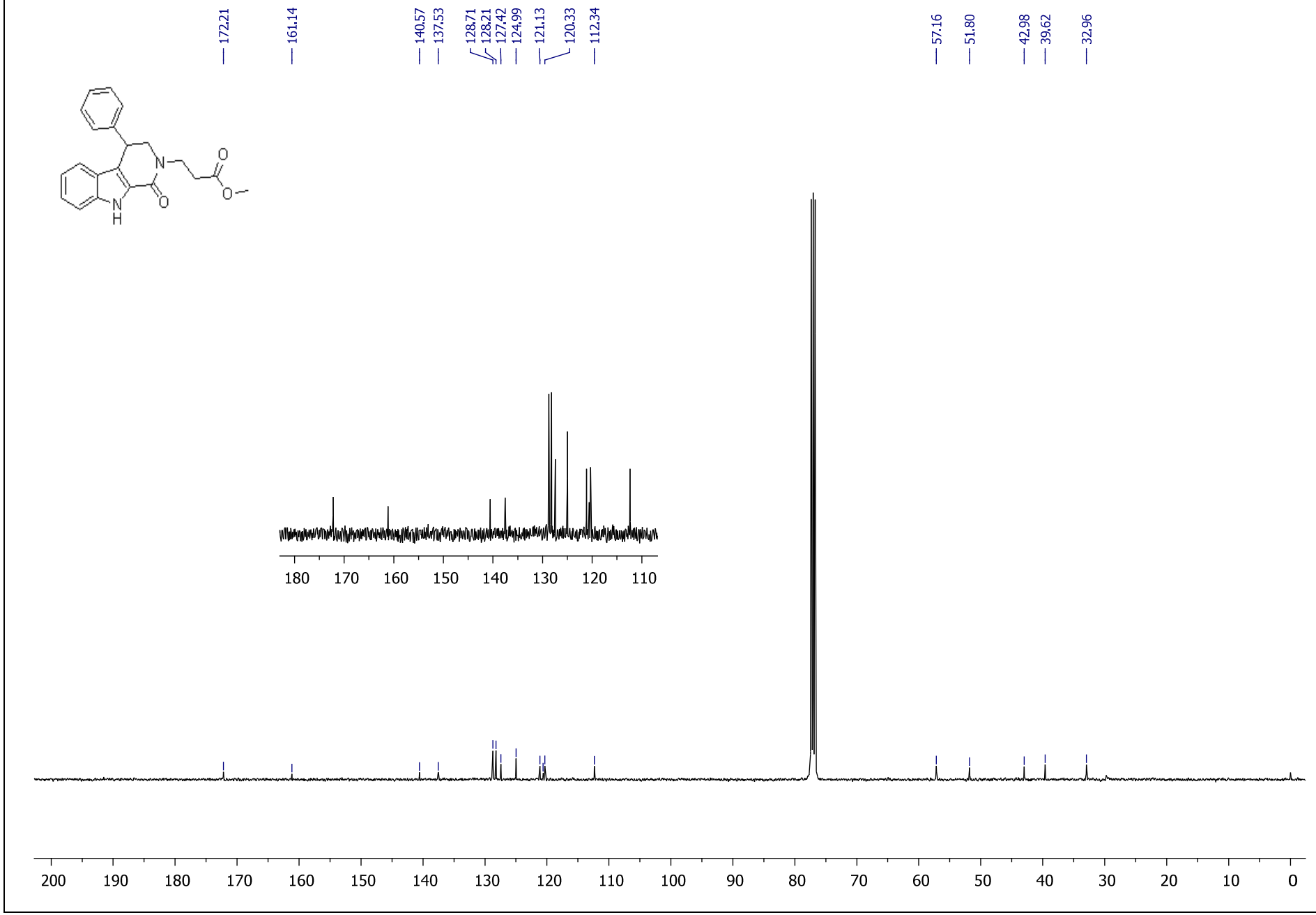
161.75
150.54
137.48
129.50
126.95
125.99
125.27
125.02
121.52
120.28
120.24
118.73
112.49
49.52
43.33
33.63
21.01
N
H
O
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

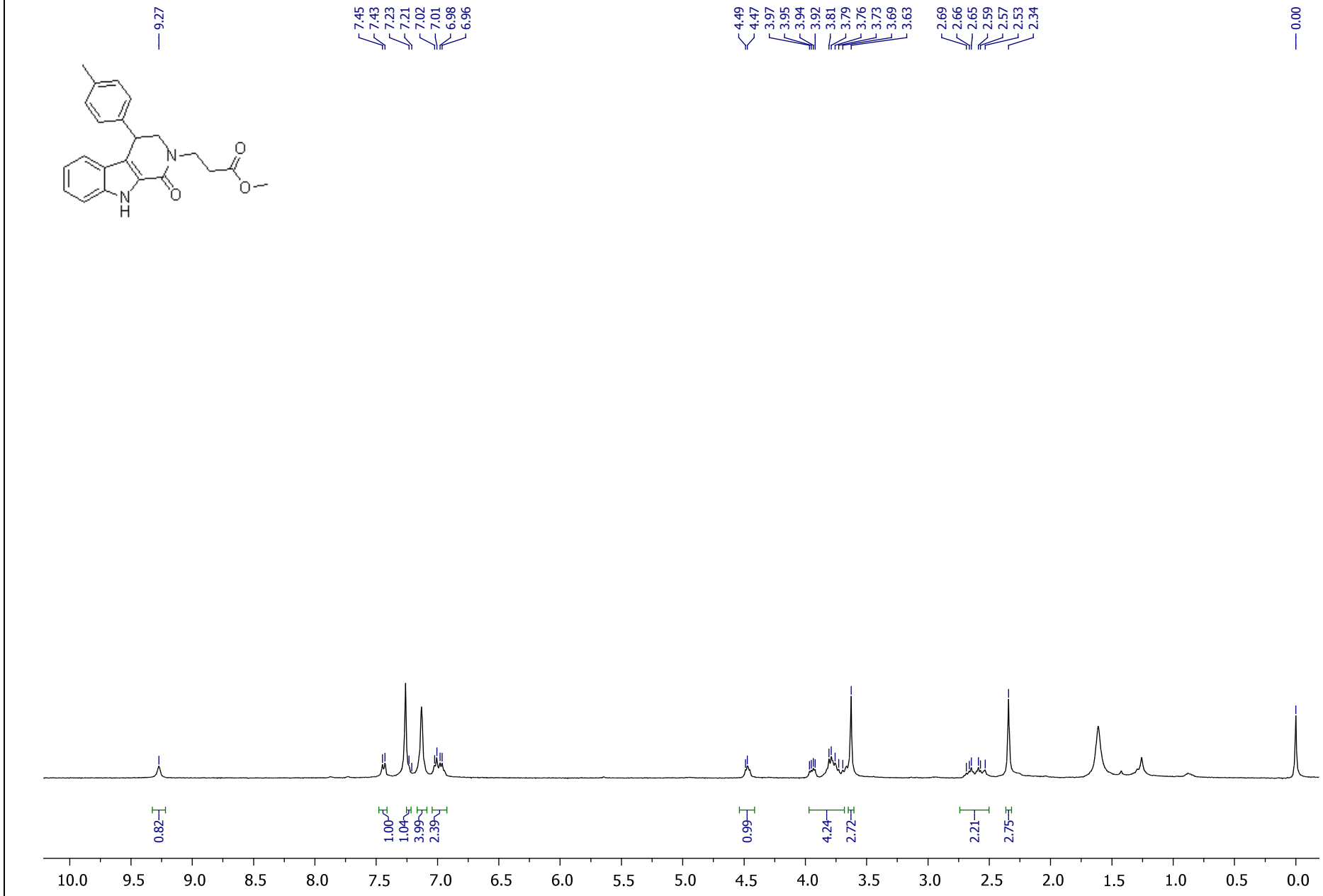
^{1}H NMR of **3i**


9.33
7.46
7.44
7.32
7.30
7.02
6.99
6.96
6.94
4.53
4.51
4.49
4.02
4.00
3.97
3.95
3.84
3.82
3.79
3.76
3.75
2.66
2.64
2.61
2.59
2.56
2.53
0.00
0.88
0.97
7.31
1.95
0.92
0.98
2.79
2.70
2.00
10.0
9.5
9.0
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
0.0

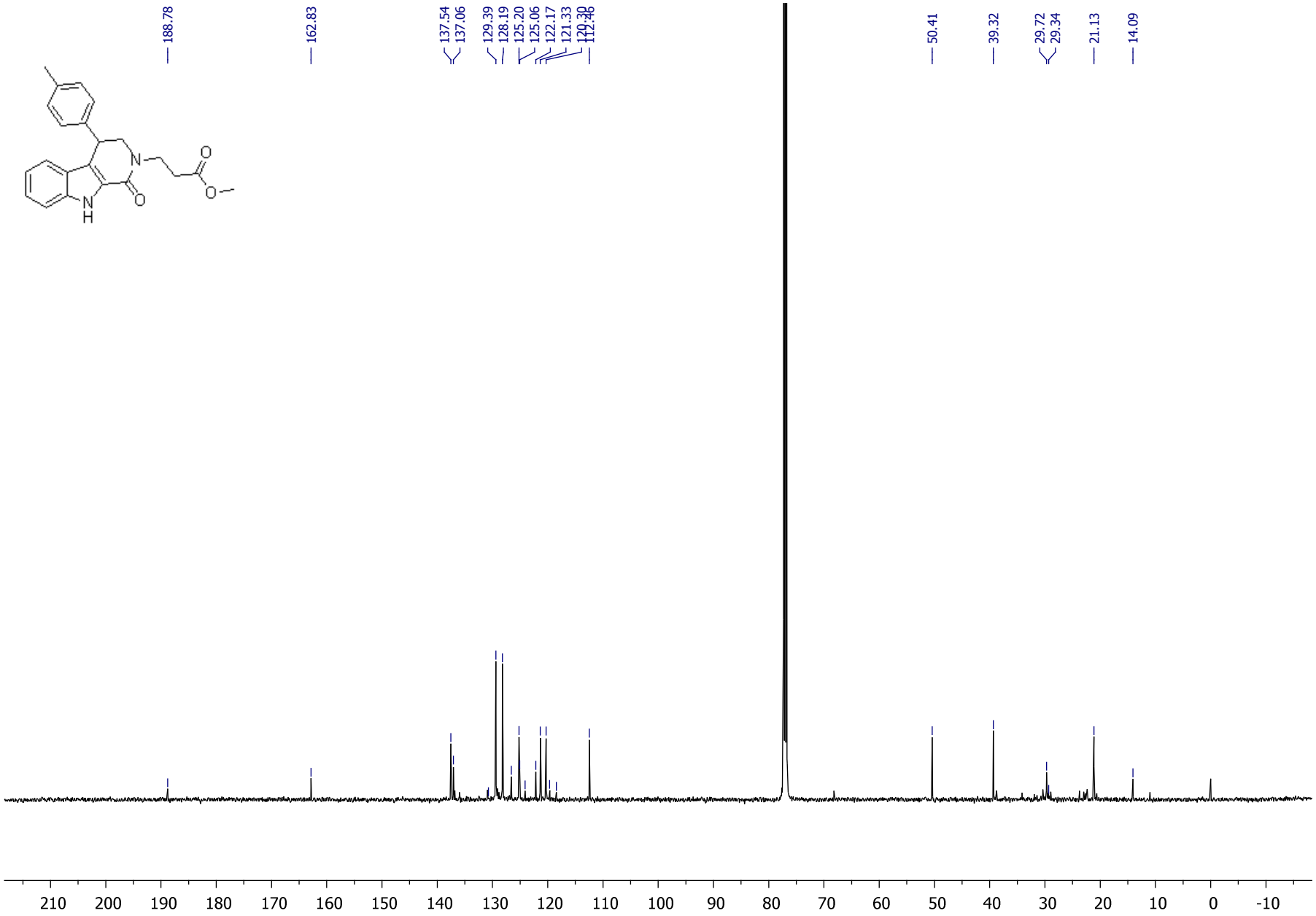
^{13}C NMR of **3i**


172.21
161.14
140.57
137.53
128.71
128.21
127.42
124.99
121.13
120.33
112.34
57.16
51.80
42.98
39.62
32.96
O
N
O
O
N
H
180
170
160
150
140
130
120
110
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

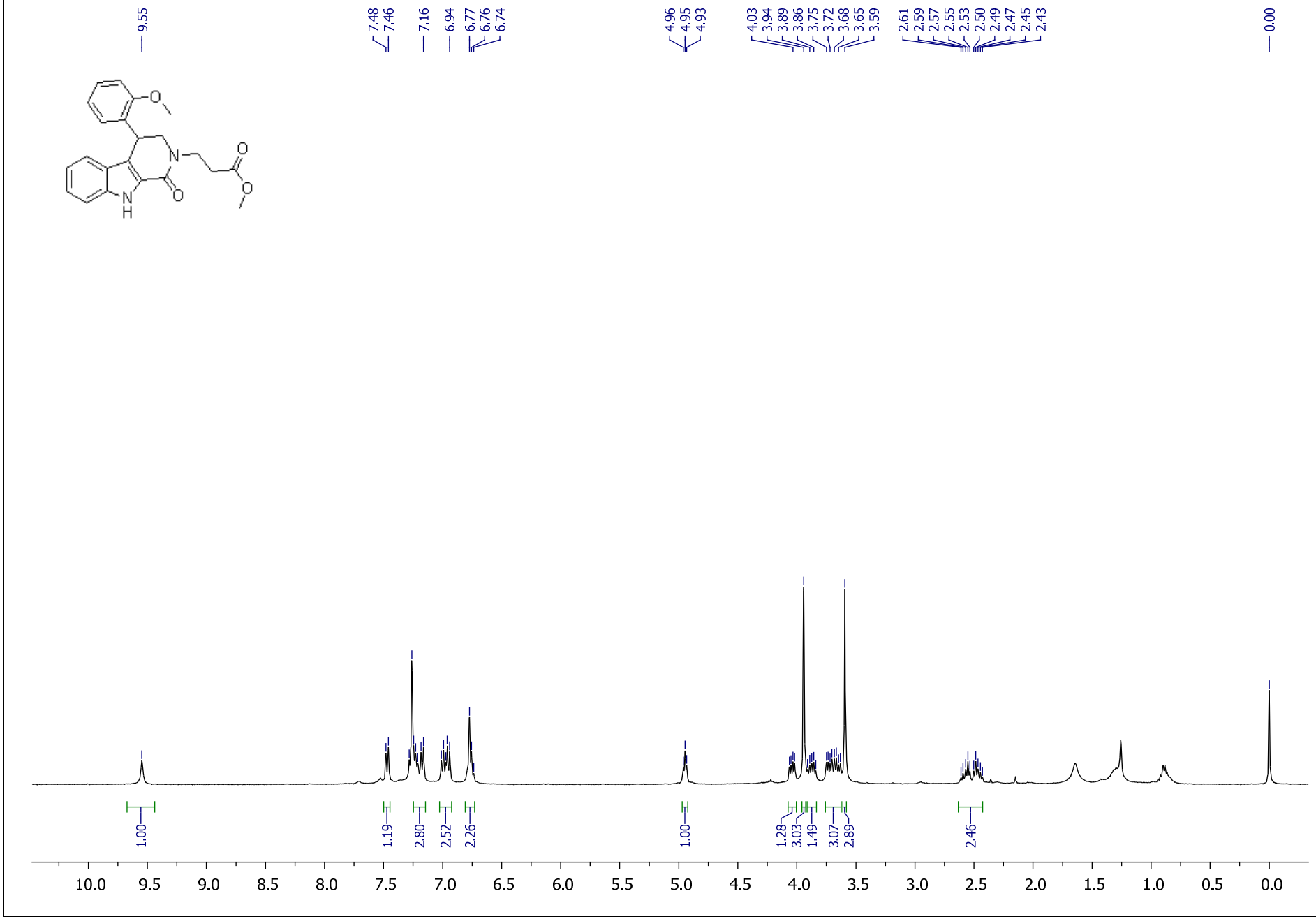
^{1}H NMR of **3j**


9.27
7.45
7.43
7.23
7.21
7.02
7.01
6.98
6.96
4.49
4.47
3.97
3.95
3.94
3.92
3.81
3.79
3.76
3.73
3.69
3.63
2.69
2.66
2.65
2.59
2.57
2.53
2.34
0.00
O
N
O
O
N
H
0.82
1.00
1.04
3.99
2.39
0.99
4.24
2.72
2.21
2.75
10.0
9.5
9.0
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
0.0

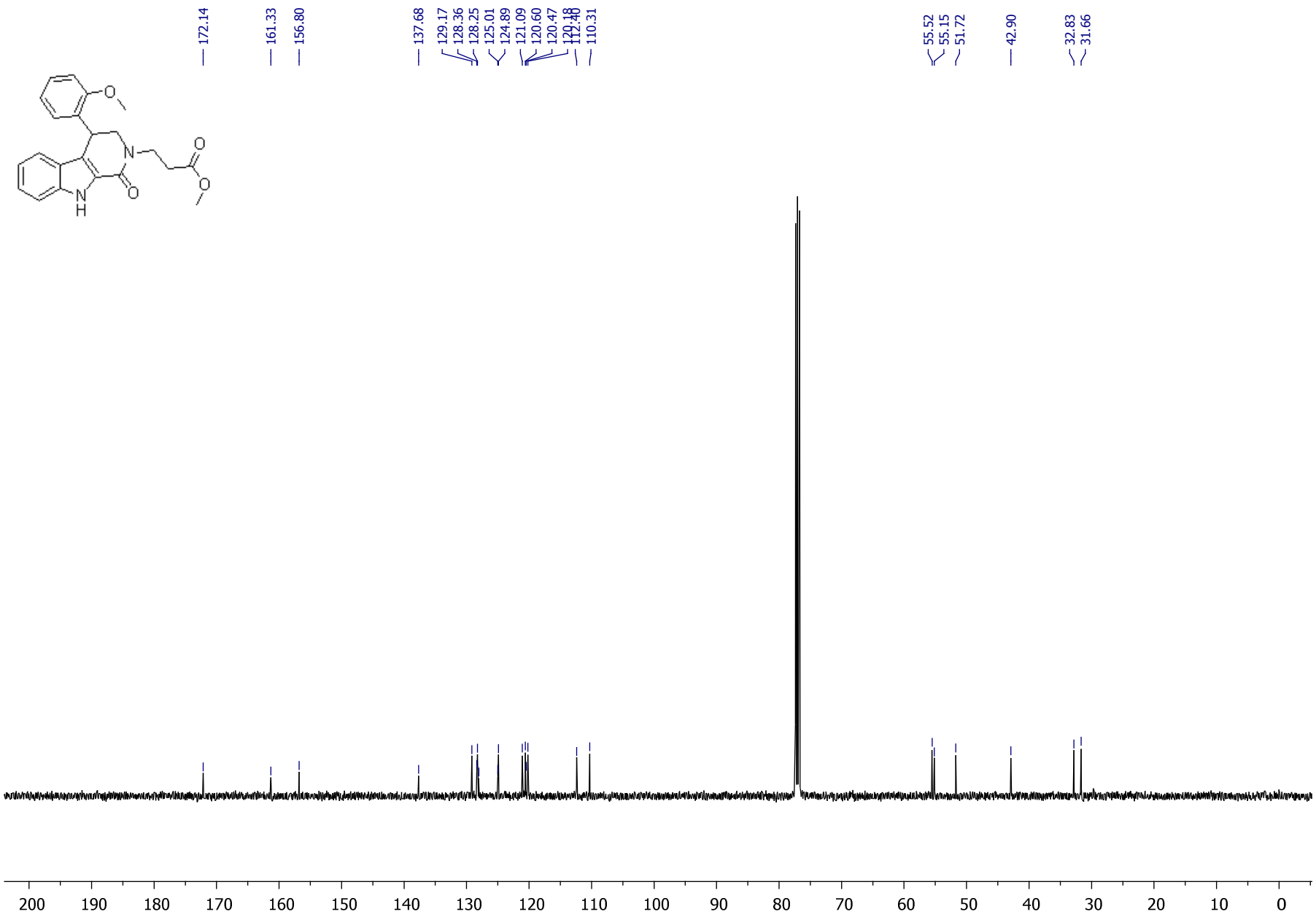
^{13}C NMR of **3j**


188.78
162.83
137.54
137.06
129.39
128.19
125.20
125.06
122.17
121.33
112.46
50.41
39.32
29.72
29.34
21.13
14.09
O
N
O
O
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

^{1}H NMR of **3k**


9.55
7.48
7.46
7.16
6.94
6.77
6.76
6.74
4.96
4.95
4.93
4.03
3.94
3.89
3.86
3.75
3.72
3.68
3.65
3.59
2.61
2.59
2.57
2.55
2.53
2.50
2.49
2.47
2.45
2.43
0.00
O
O
N
O
O
N
H
1.00
1.19
2.80
2.52
2.26
1.00
1.28
3.03
1.49
3.07
2.89
2.46
10.0
9.5
9.0
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
0.0

^{13}C NMR of **3k**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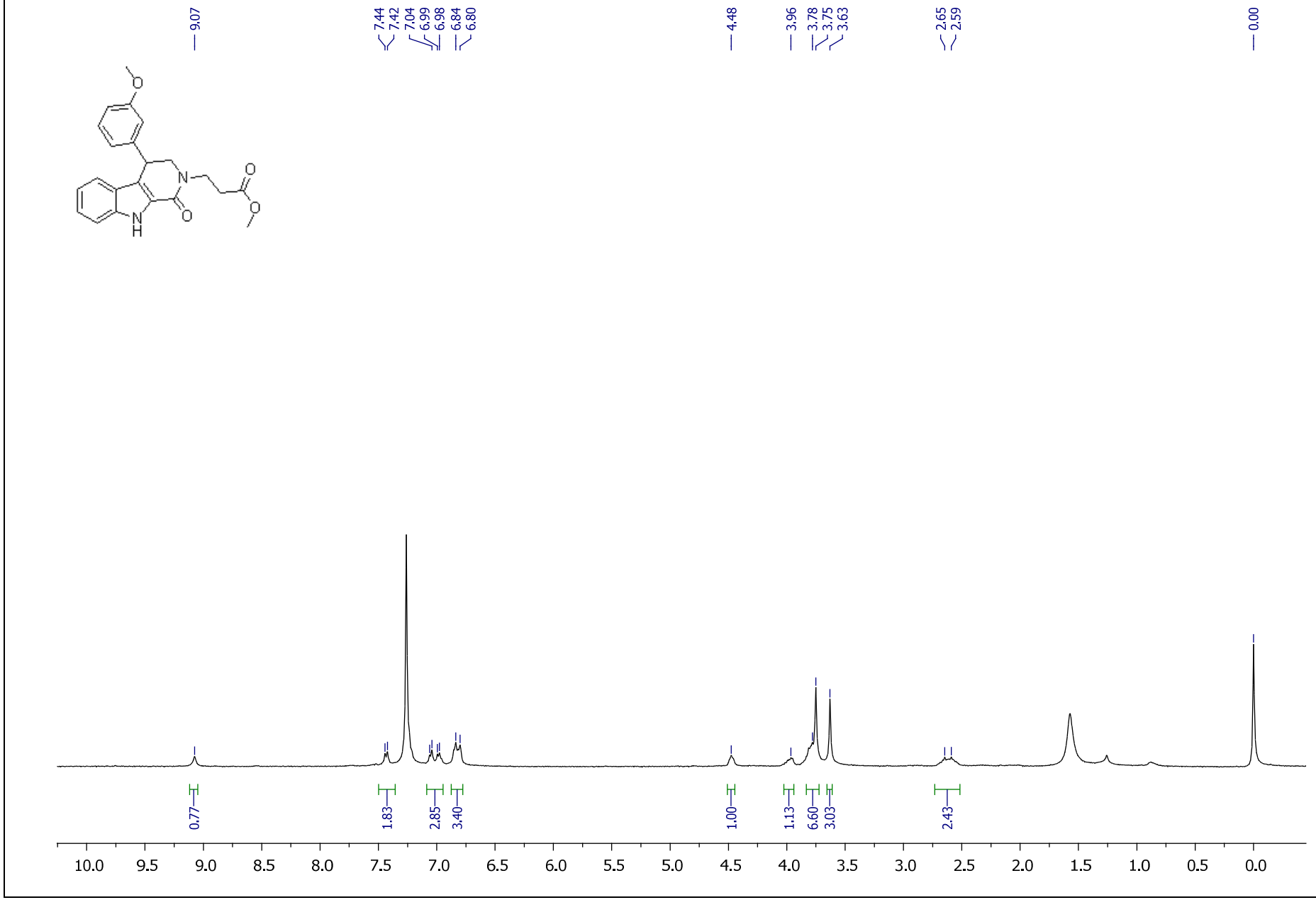
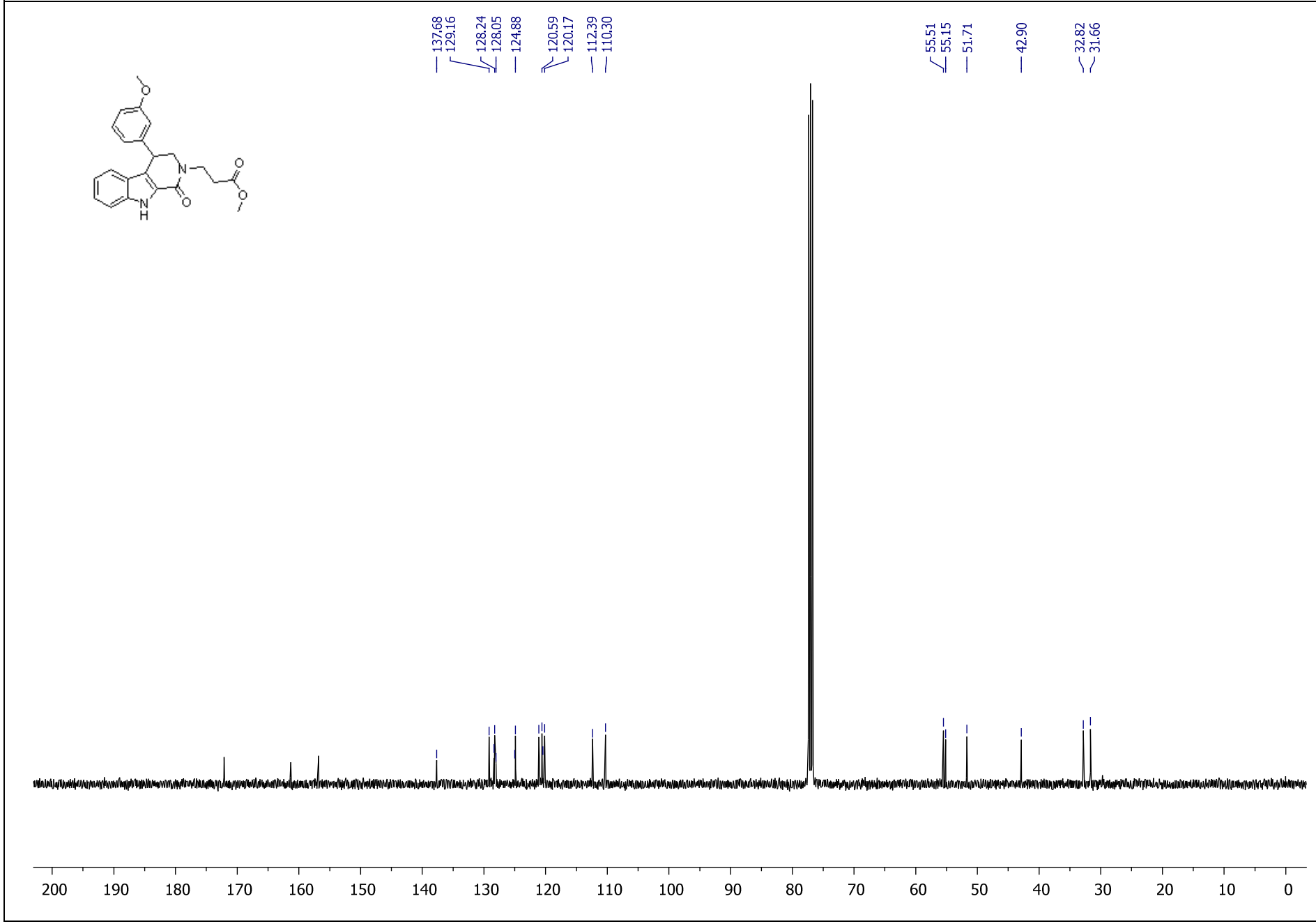
161.33
156.80
137.68
129.17
128.36
128.25
125.01
124.89
121.09
120.60
120.47
120.18
112.40
110.31
55.52
55.15
51.72
42.90
32.83
31.66
O
N
O
O
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

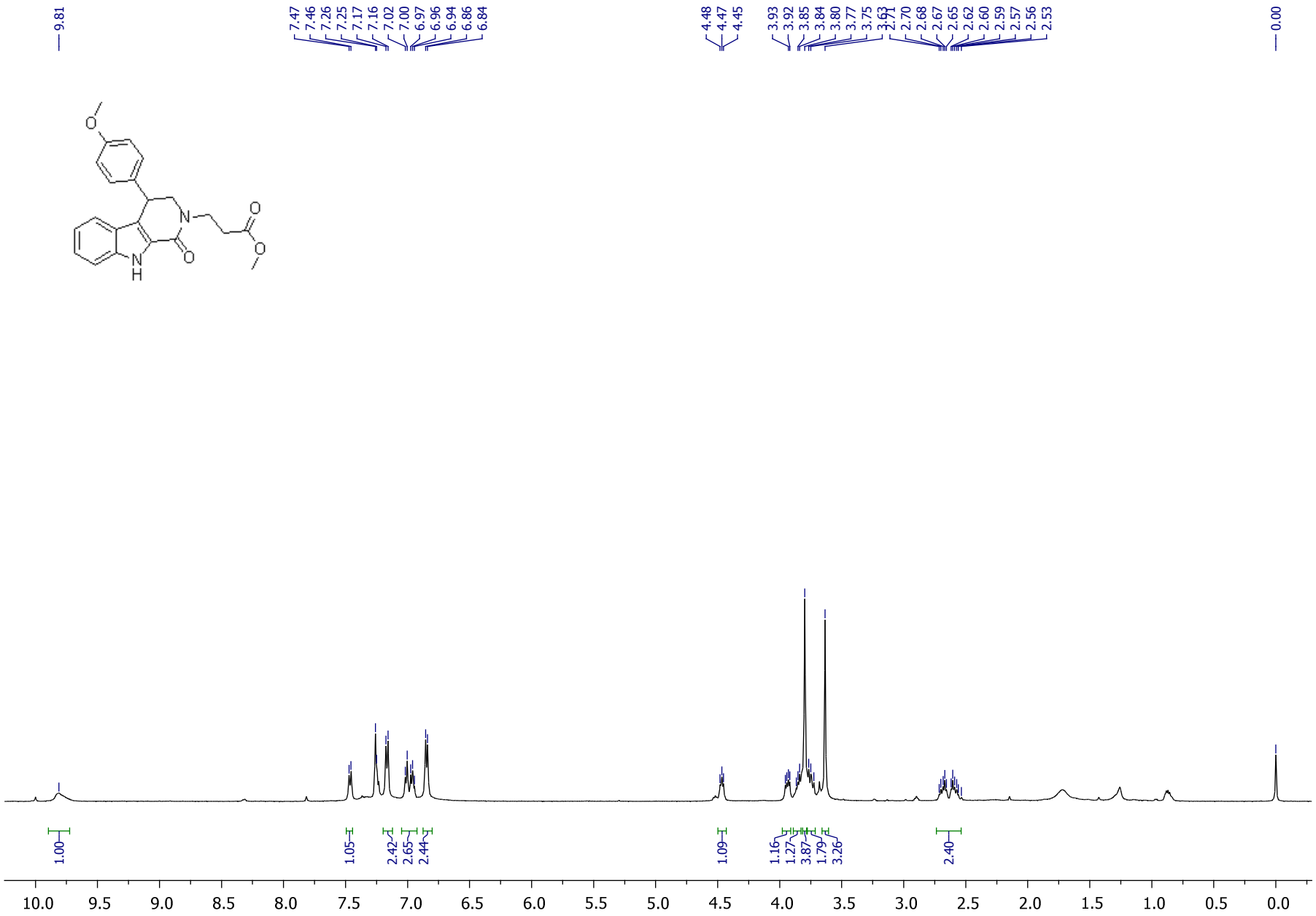
^{1}H NMR of **3l**


9.07
7.44
7.42
7.04
6.99
6.98
6.84
6.80
4.48
3.96
3.78
3.75
3.63
2.65
2.59
0.00
O
N
O
O
N
H
O
0.77
1.83
2.85
3.40
1.00
1.13
6.60
3.03
2.43
10.0
9.5
9.0
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
0.0

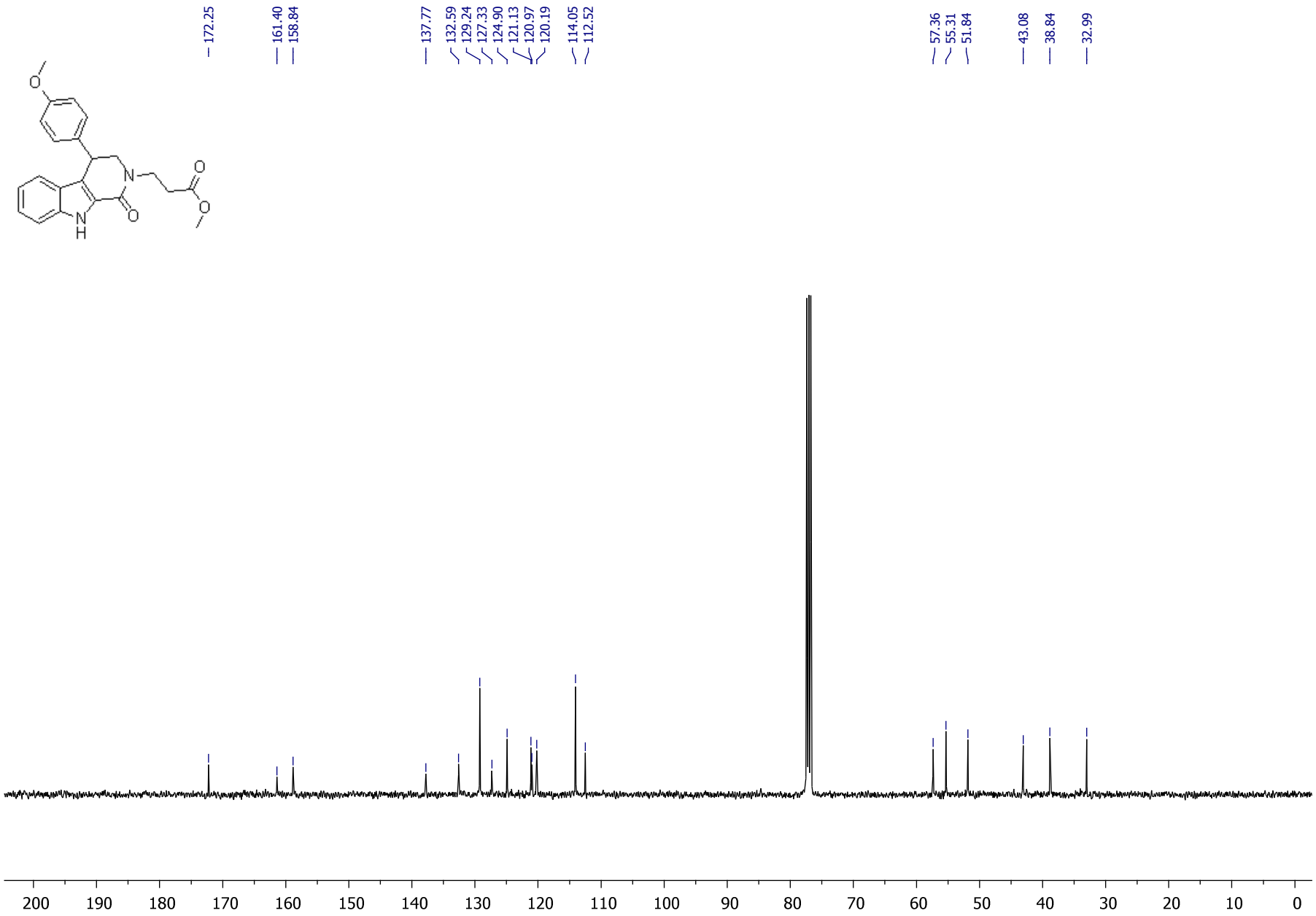
^{13}C NMR of **3l**


137.68
129.16
128.24
128.05
124.88
120.59
120.17
112.39
110.30
55.51
55.15
51.71
42.90
32.82
31.66
O
N
H
O
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

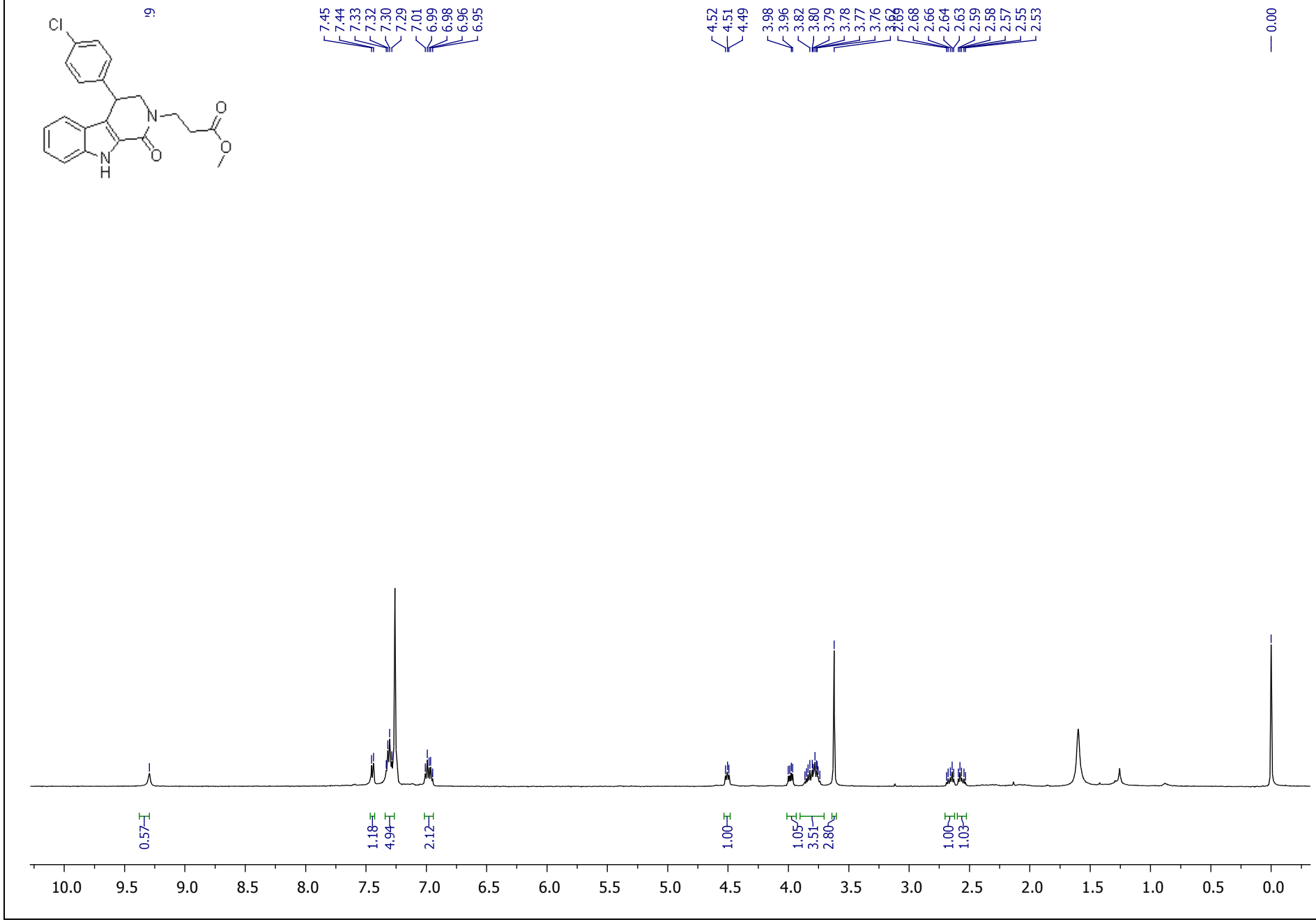
^{1}H NMR of **3m**


9.81
7.47
7.46
7.26
7.25
7.17
7.16
7.02
7.00
6.97
6.96
6.94
6.86
6.84
4.48
4.47
4.45
3.93
3.92
3.85
3.84
3.80
3.77
3.75
3.63
2.71
2.70
2.68
2.67
2.65
2.62
2.60
2.59
2.57
2.56
2.53
0.00
O
N
O
O
N
H
1.00
1.05
2.42
2.65
2.44
1.09
1.16
1.27
3.87
1.79
3.26
2.40
10.0
9.5
9.0
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
0.0

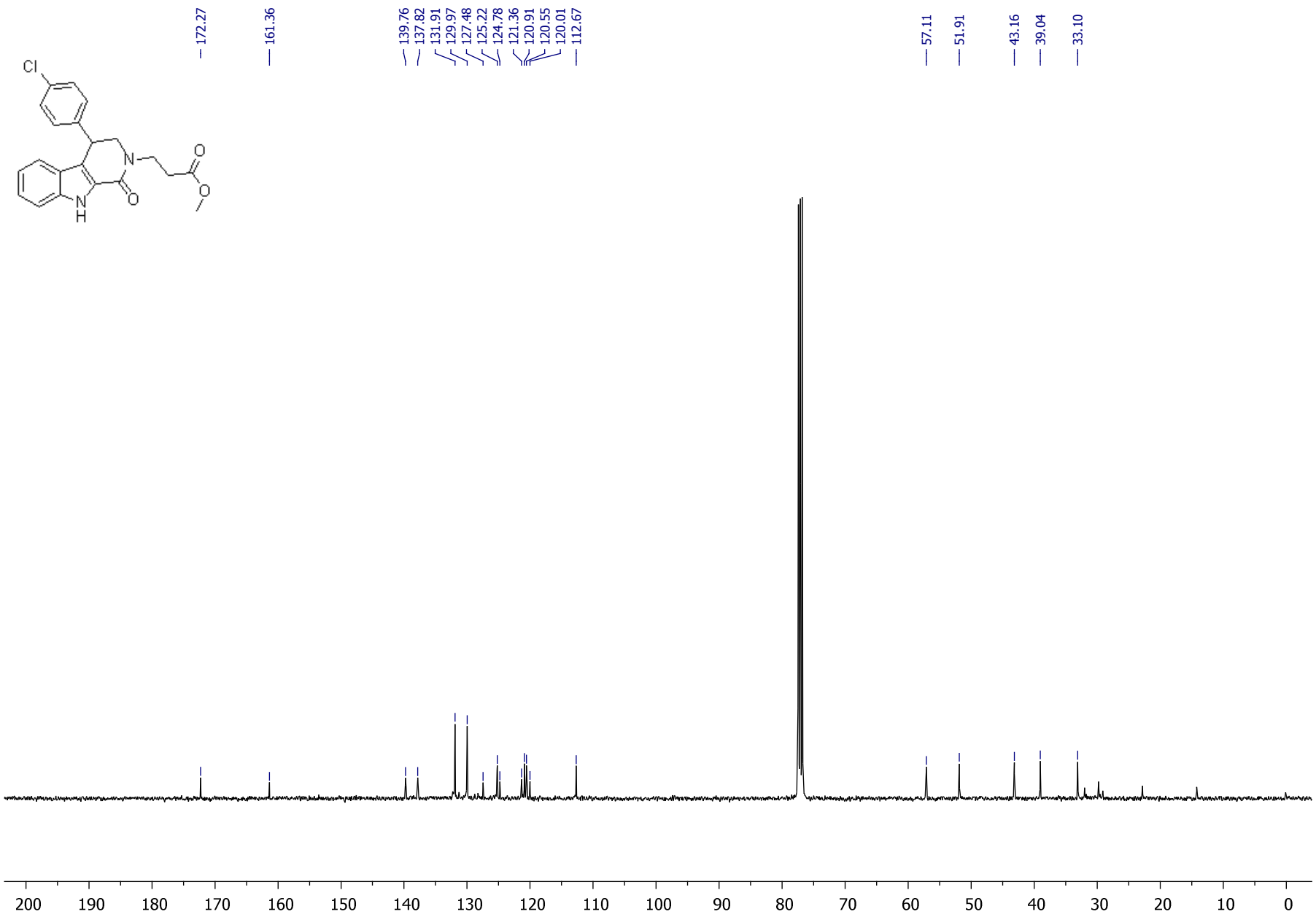
^{13}C NMR of **3m**


172.25
161.40
158.84
137.77
132.59
129.24
127.33
124.90
121.13
120.97
120.19
114.05
112.52
57.36
55.31
51.84
43.08
38.84
32.99
O
N
O
O
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{1}H NMR of **3n**


Cl
O
N
O
O
N
H
7.45
7.44
7.33
7.32
7.30
7.29
7.01
6.99
6.98
6.96
6.95
4.52
4.51
4.49
3.98
3.96
3.82
3.80
3.79
3.78
3.77
3.76
2.68
2.66
2.64
2.63
2.59
2.58
2.57
2.55
2.53
0.00
0.57
1.18
4.94
2.12
1.00
1.05
3.51
2.80
1.00
1.03
10.0
9.5
9.0
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
0.0

^{13}C NMR of **3n**


172.27
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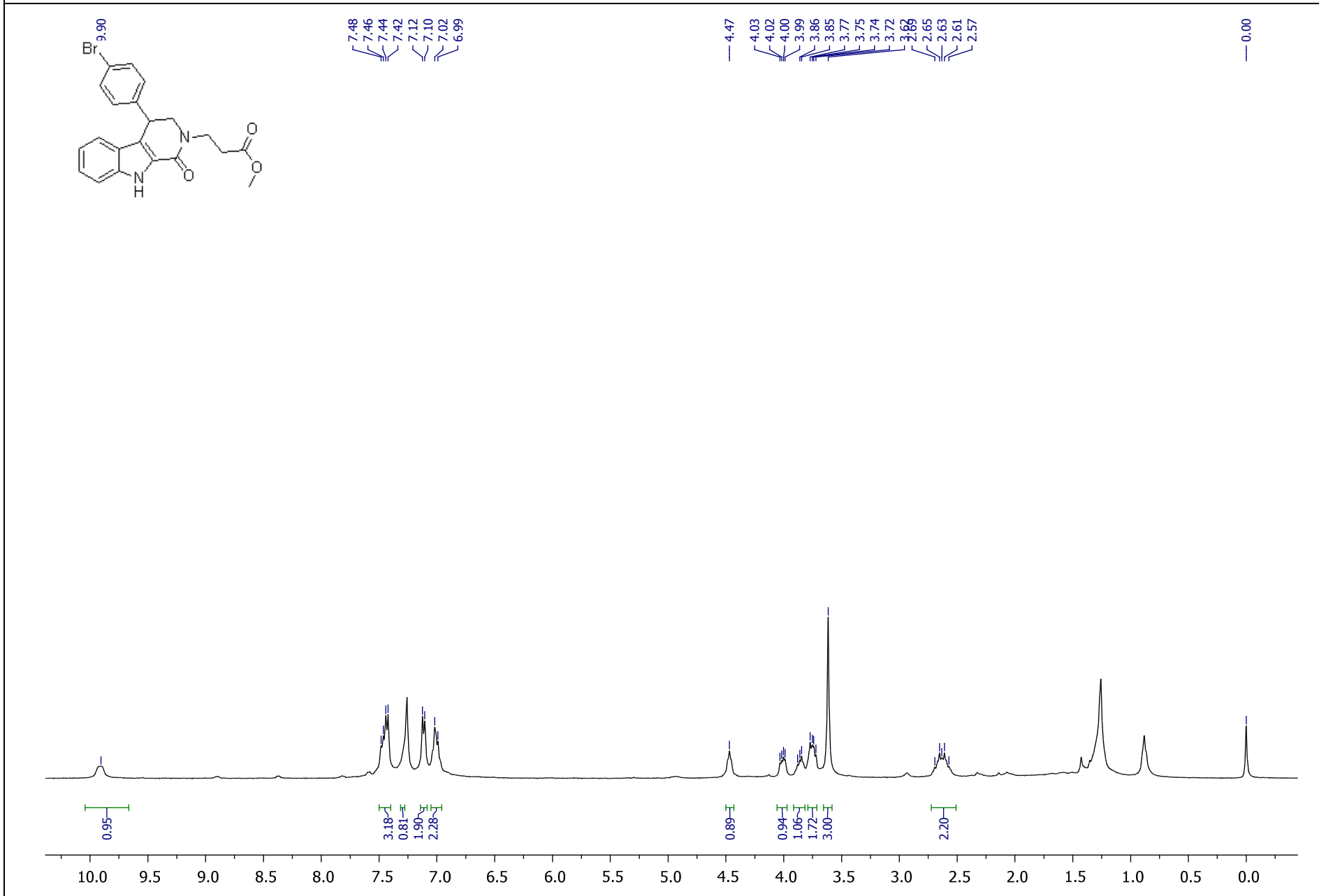
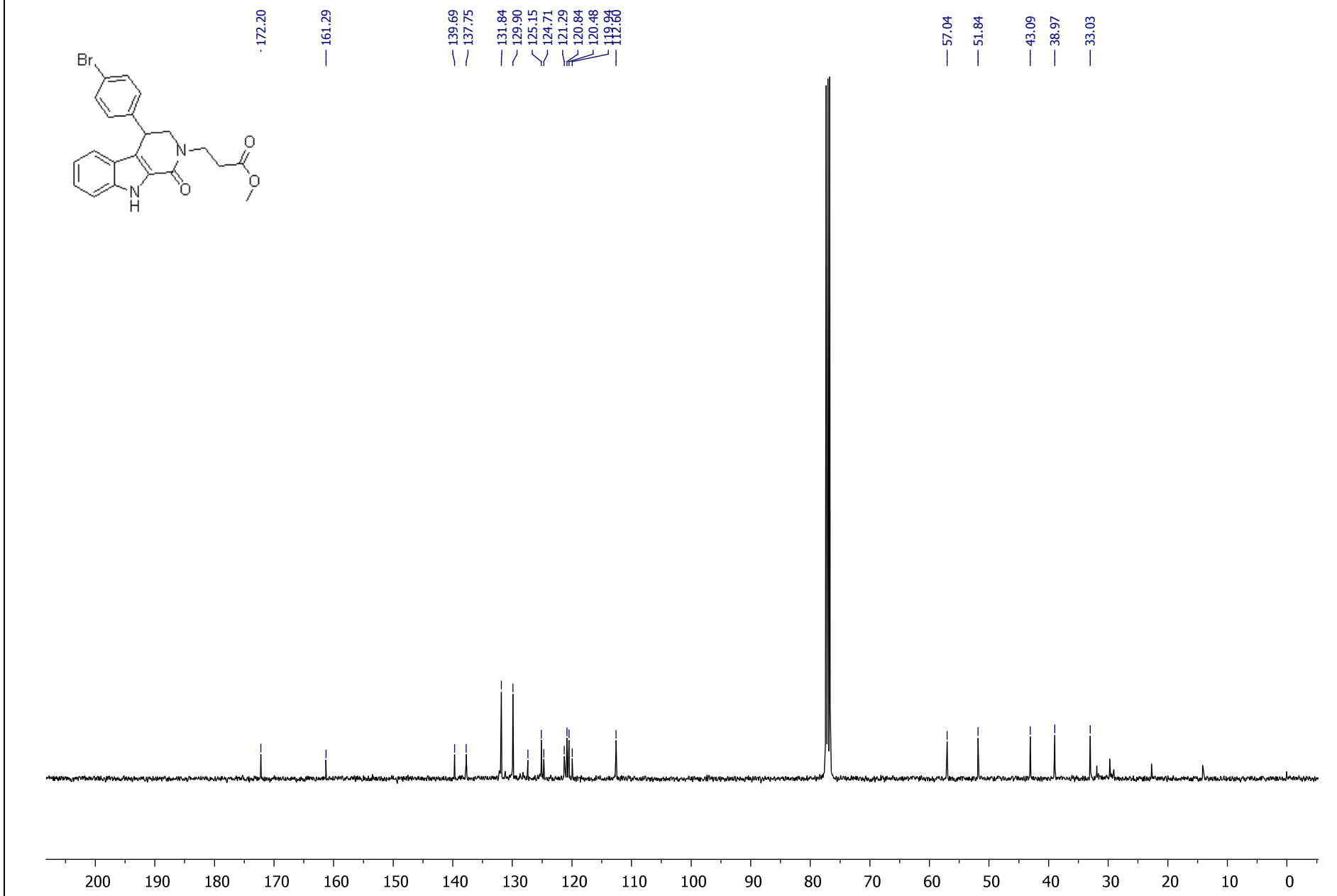
139.76
137.82
131.91
129.97
127.48
125.22
124.78
121.36
120.91
120.55
120.01
112.67
57.11
51.91
43.16
39.04
33.10
Cl
N
O
O
N
H
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

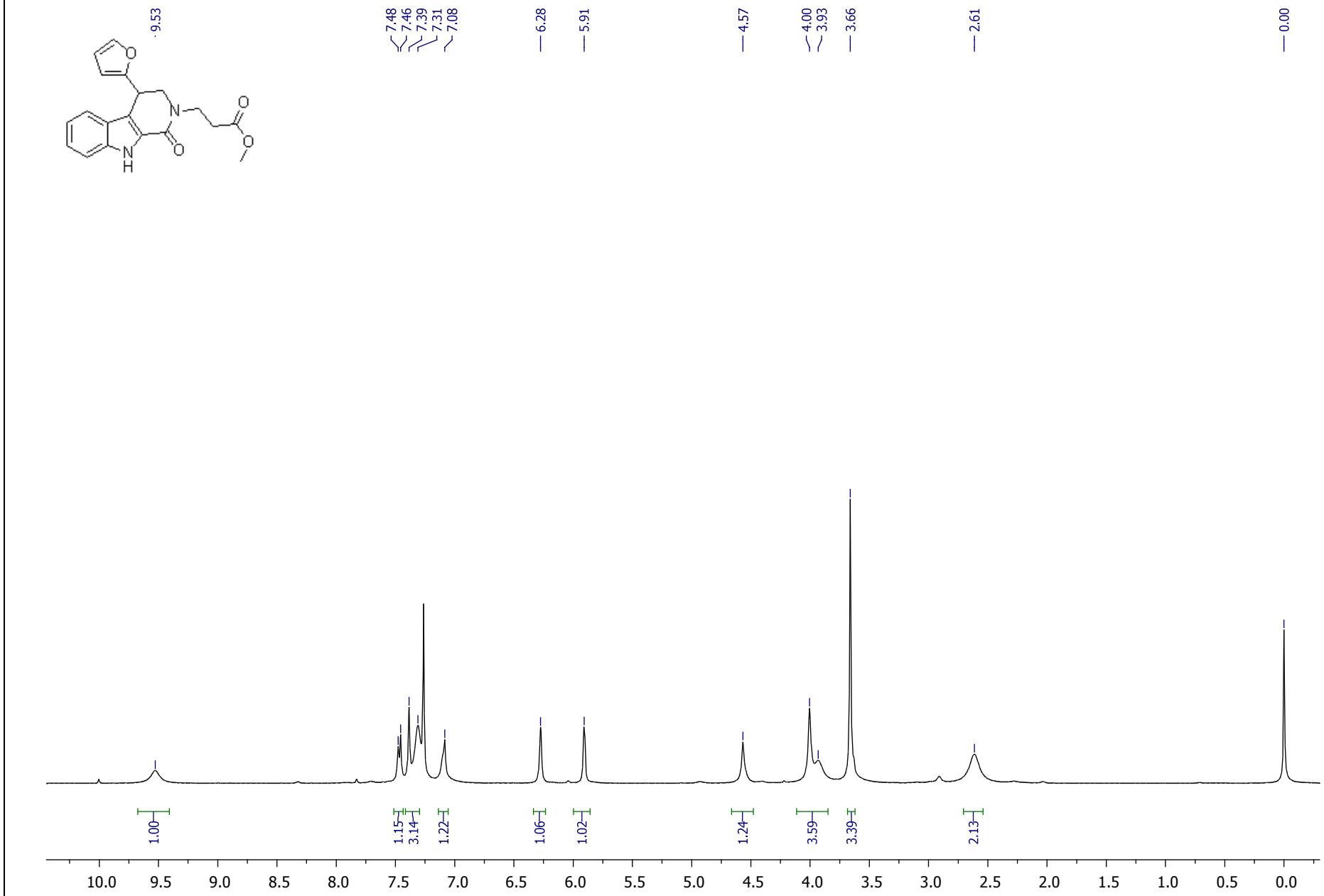
^{1}H NMR of **3o**


Br
N
O
O
N
H
O
9.90
7.48
7.46
7.44
7.42
7.12
7.10
7.02
6.99
4.47
4.03
4.02
4.00
3.99
3.86
3.85
3.77
3.75
3.74
3.72
2.65
2.63
2.61
2.57
0.00
0.95
3.18
0.81
1.90
2.28
0.89
0.94
1.06
1.72
3.00
2.20
10.0
9.5
9.0
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
0.0

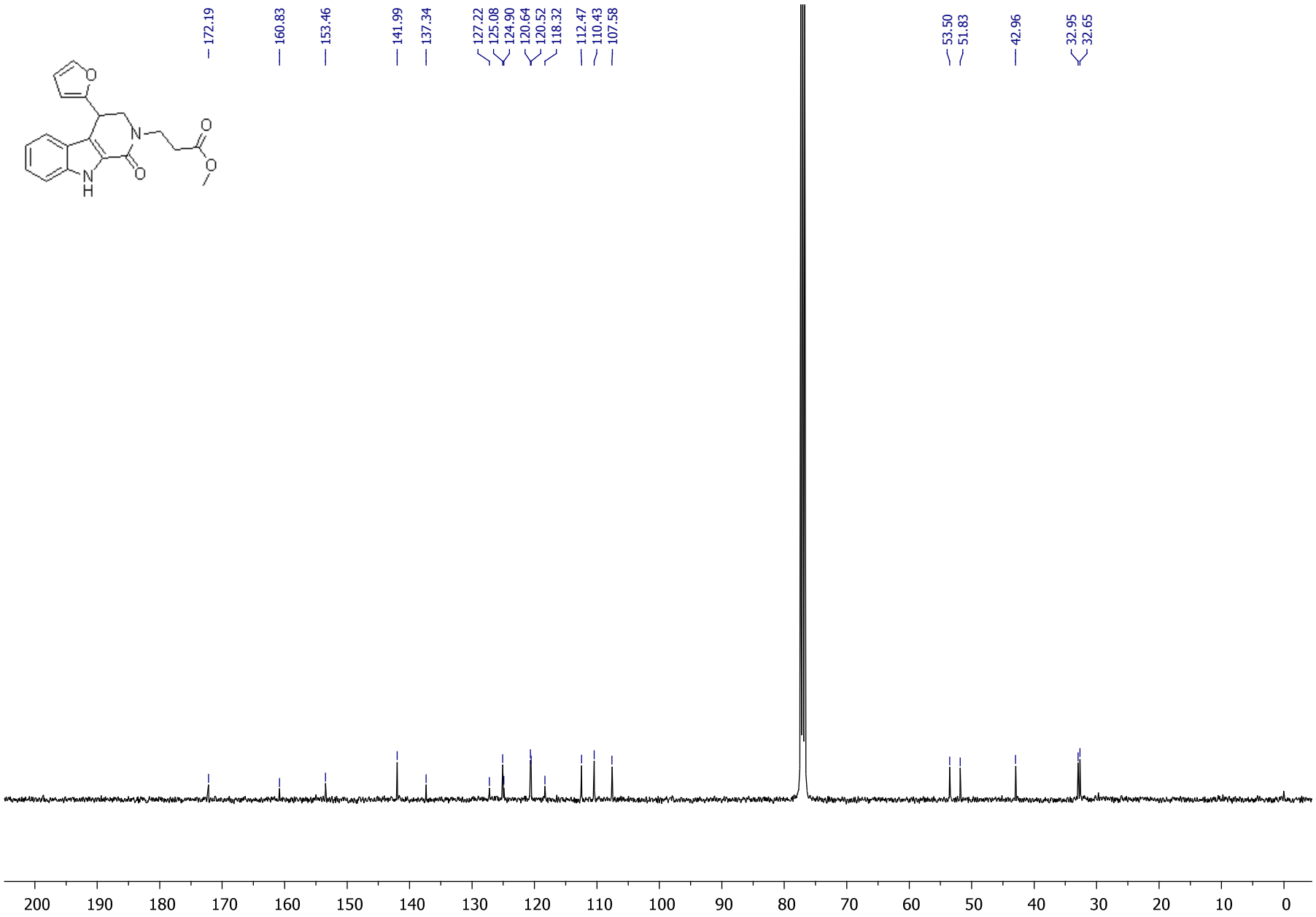
^{13}C NMR of **3o**


172.20
161.29
139.69
137.75
131.84
129.90
125.15
124.71
121.29
120.84
120.48
119.94
112.60
57.04
51.84
43.09
38.97
33.03
Br
N
O
O
N
H
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

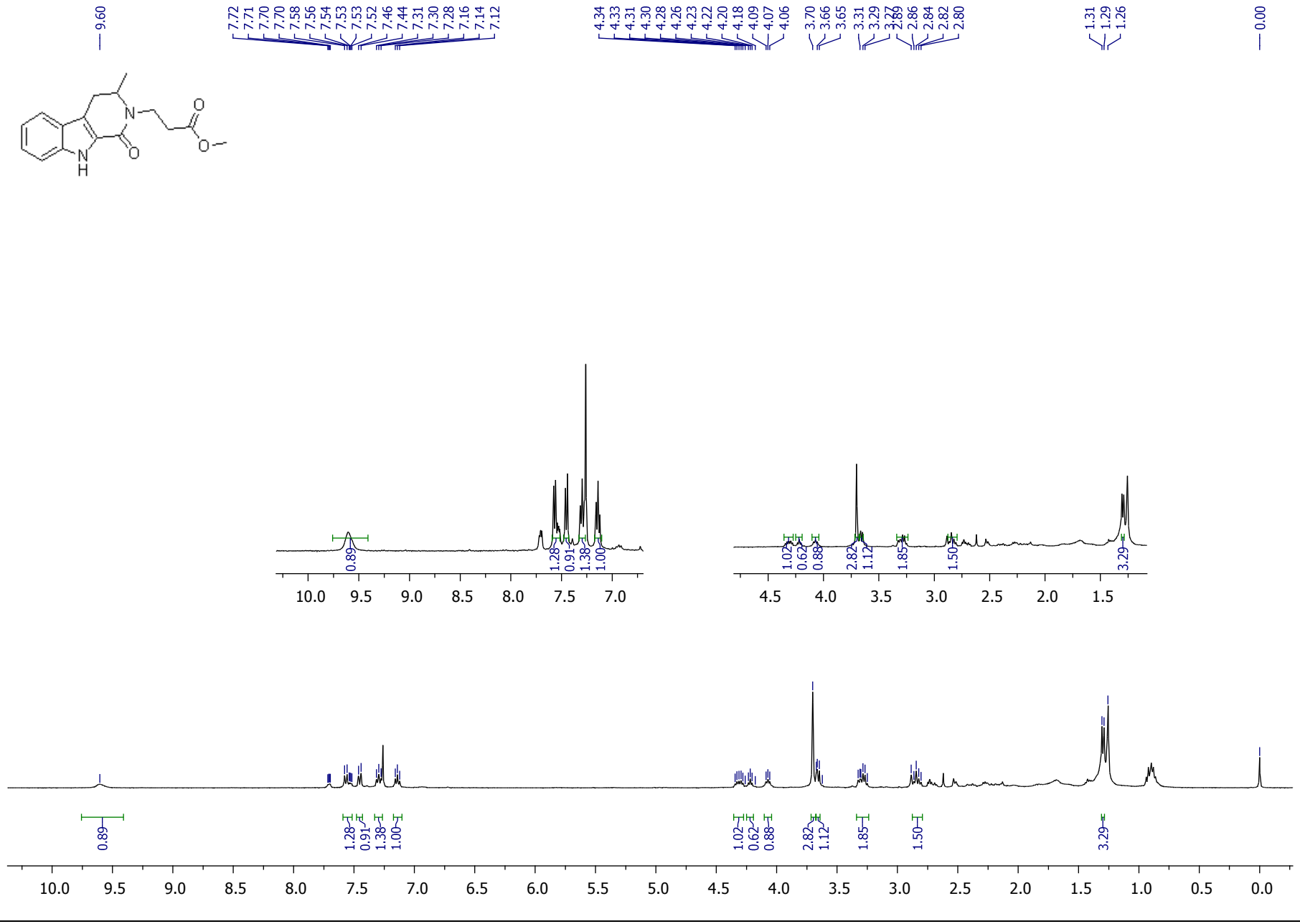
^{1}H NMR of **3p**


9.53
7.48
7.46
7.39
7.31
7.08
6.28
5.91
4.57
4.00
3.93
3.66
2.61
0.00
1.00
1.15
3.14
1.22
1.06
1.02
1.24
3.59
3.39
2.13
10.0
9.5
9.0
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
0.0

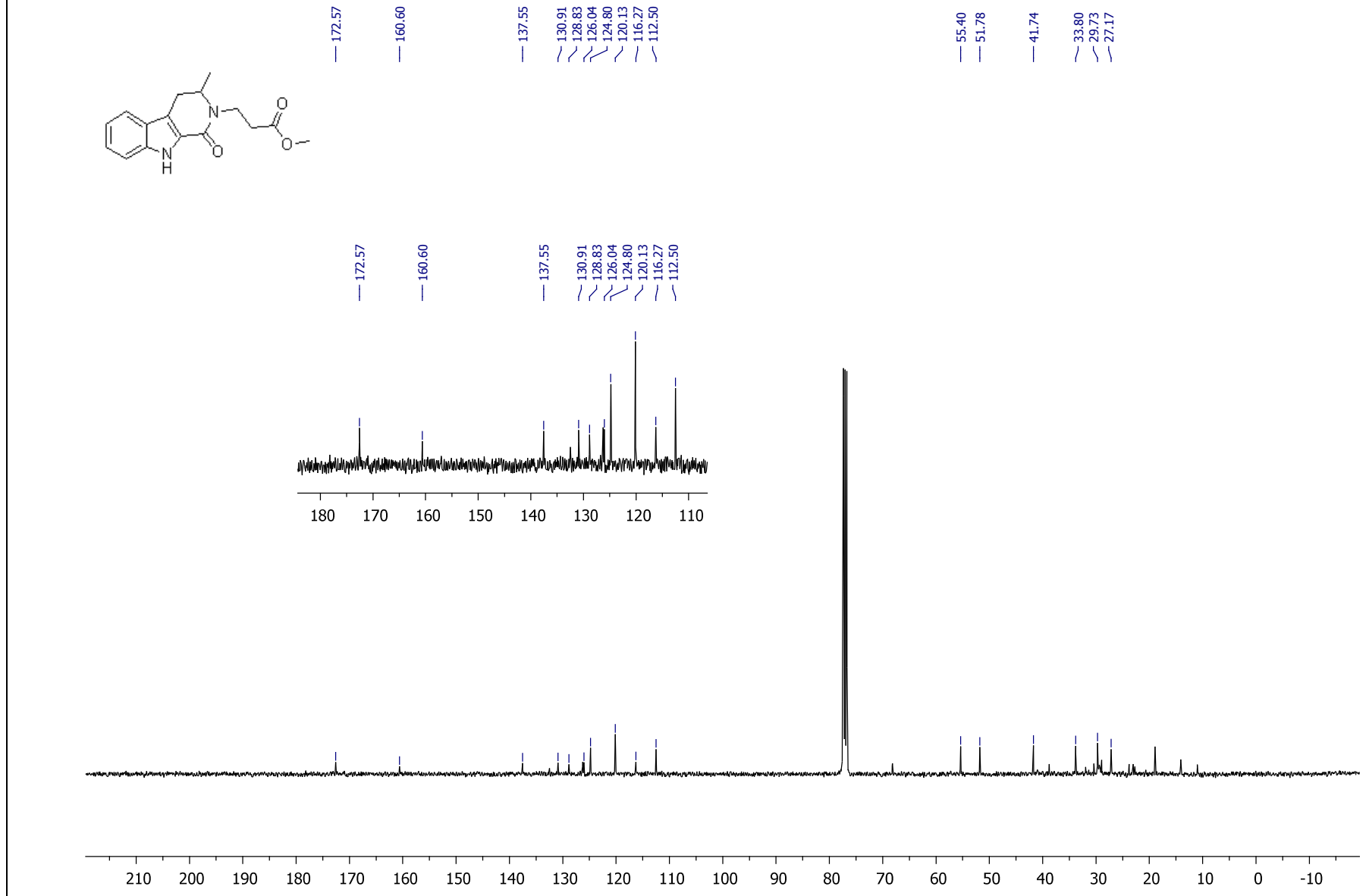
^{13}C NMR of **3p**


172.19
160.83
153.46
141.99
137.34
127.22
125.08
124.90
120.64
120.52
118.32
112.47
110.43
107.58
53.50
51.83
42.96
32.95
32.65
O
N
H
O
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

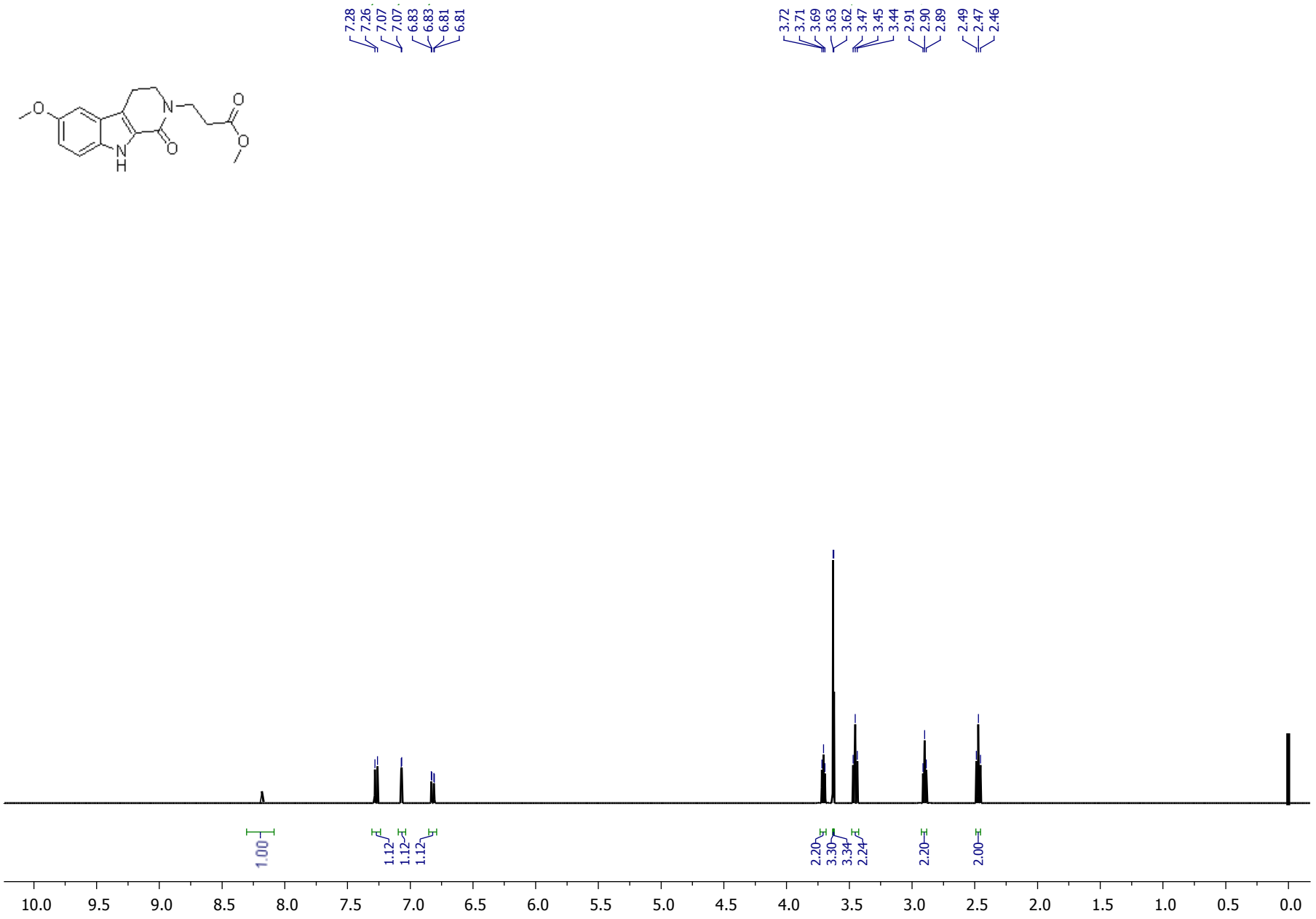
^{1}H NMR of **3q**


9.60
7.72
7.71
7.70
7.70
7.58
7.56
7.54
7.53
7.53
7.52
7.46
7.44
7.31
7.30
7.28
7.16
7.14
7.12
4.34
4.33
4.31
4.30
4.28
4.26
4.23
4.22
4.20
4.18
4.09
4.07
4.06
3.70
3.66
3.65
3.31
3.29
2.89
2.86
2.84
2.82
2.80
1.31
1.29
1.26
0.00
N
O
O
N
H
O
0.89
1.28
0.91
1.38
1.00
1.02
0.62
0.88
2.82
1.12
1.85
1.50
3.29

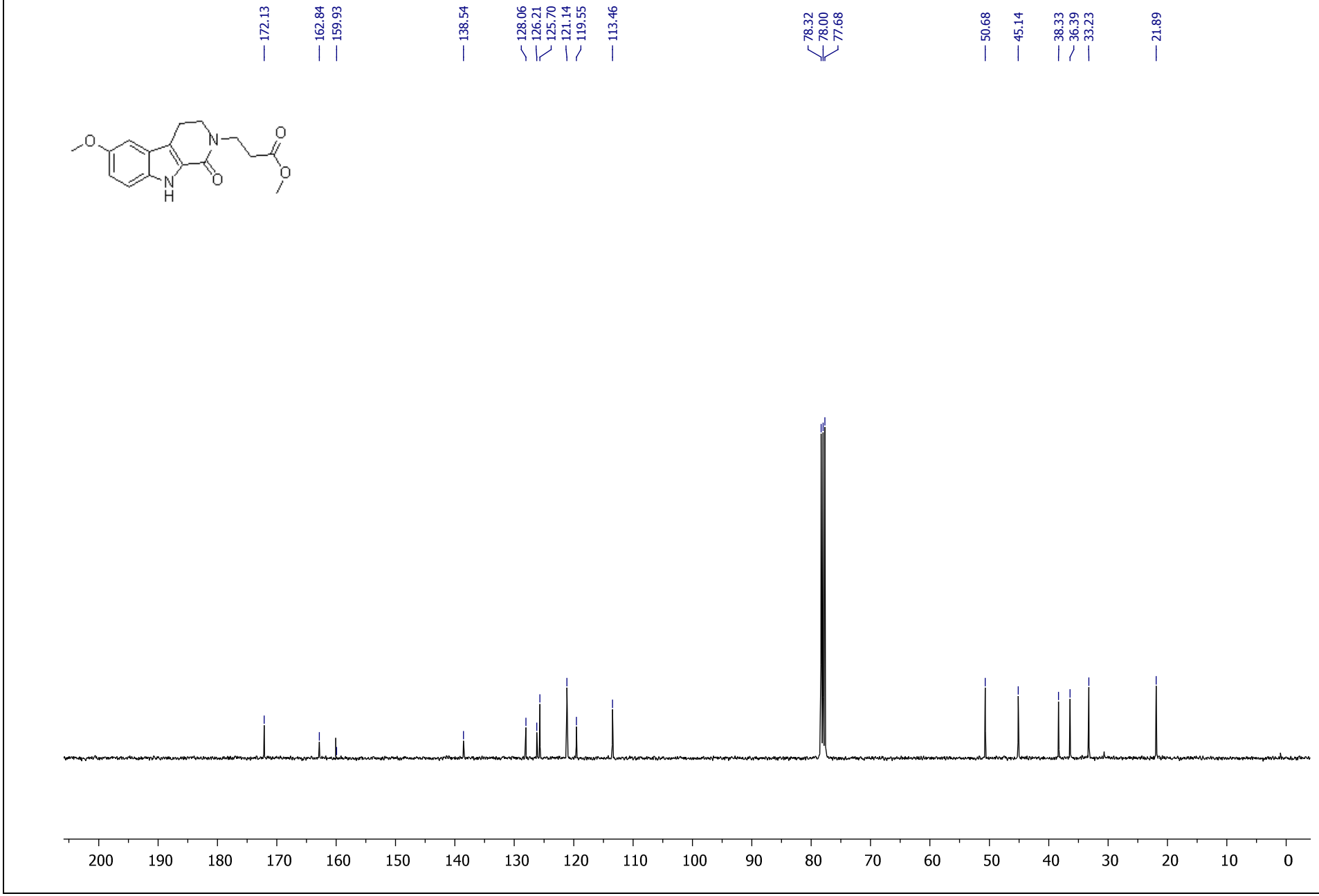
^{13}C NMR of **3q**


172.57
160.60
137.55
130.91
128.83
126.04
124.80
120.13
116.27
112.50
55.40
51.78
41.74
33.80
29.73
27.17
O
N
O
O
N
H
180
170
160
150
140
130
120
110
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

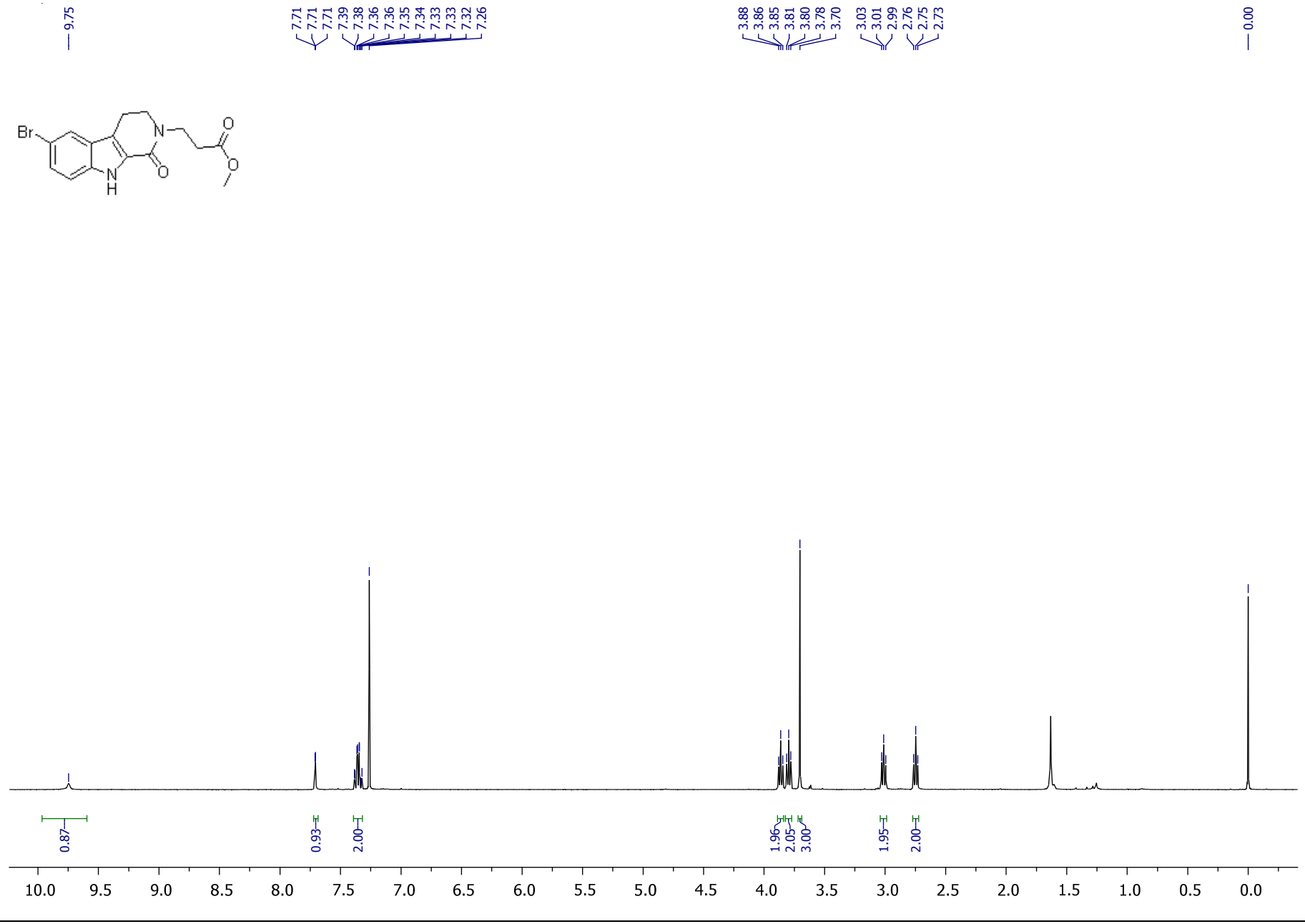
^{1}H NMR of **3r**


7.28
7.26
7.07
7.07
6.83
6.83
6.81
6.81
3.72
3.71
3.69
3.63
3.62
3.47
3.45
3.44
2.91
2.90
2.89
2.49
2.47
2.46
O
N
O
O
O
N
H
1.00
1.12
1.12
1.12
2.20
3.30
3.34
2.24
2.20
2.00
10.0
9.5
9.0
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
0.0

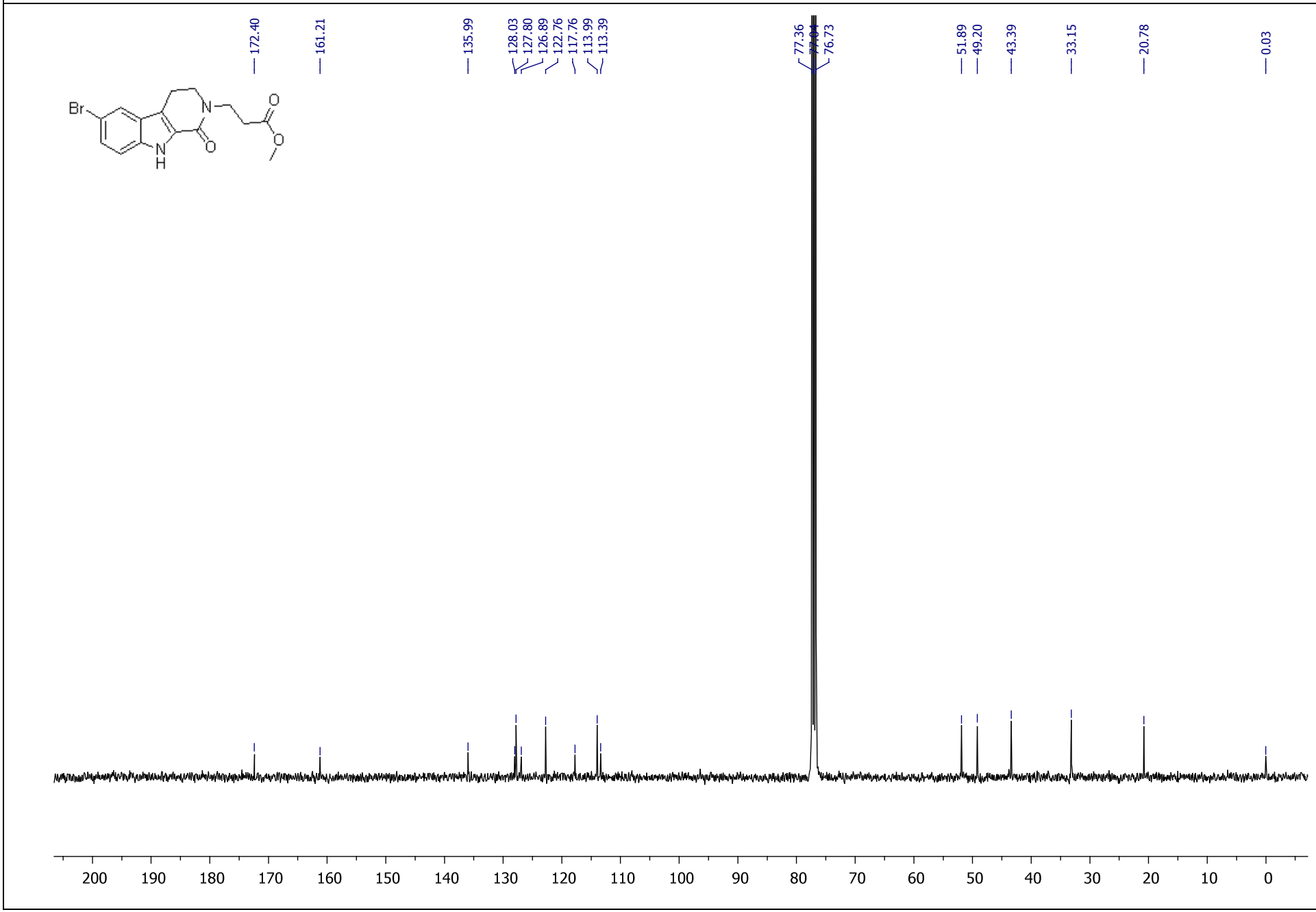
^{13}C NMR of **3r**


172.13
162.84
159.93
138.54
128.06
126.21
125.70
121.14
119.55
113.46
78.32
78.00
77.68
50.68
45.14
38.33
36.39
33.23
21.89
O
N
O
O
N
H
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

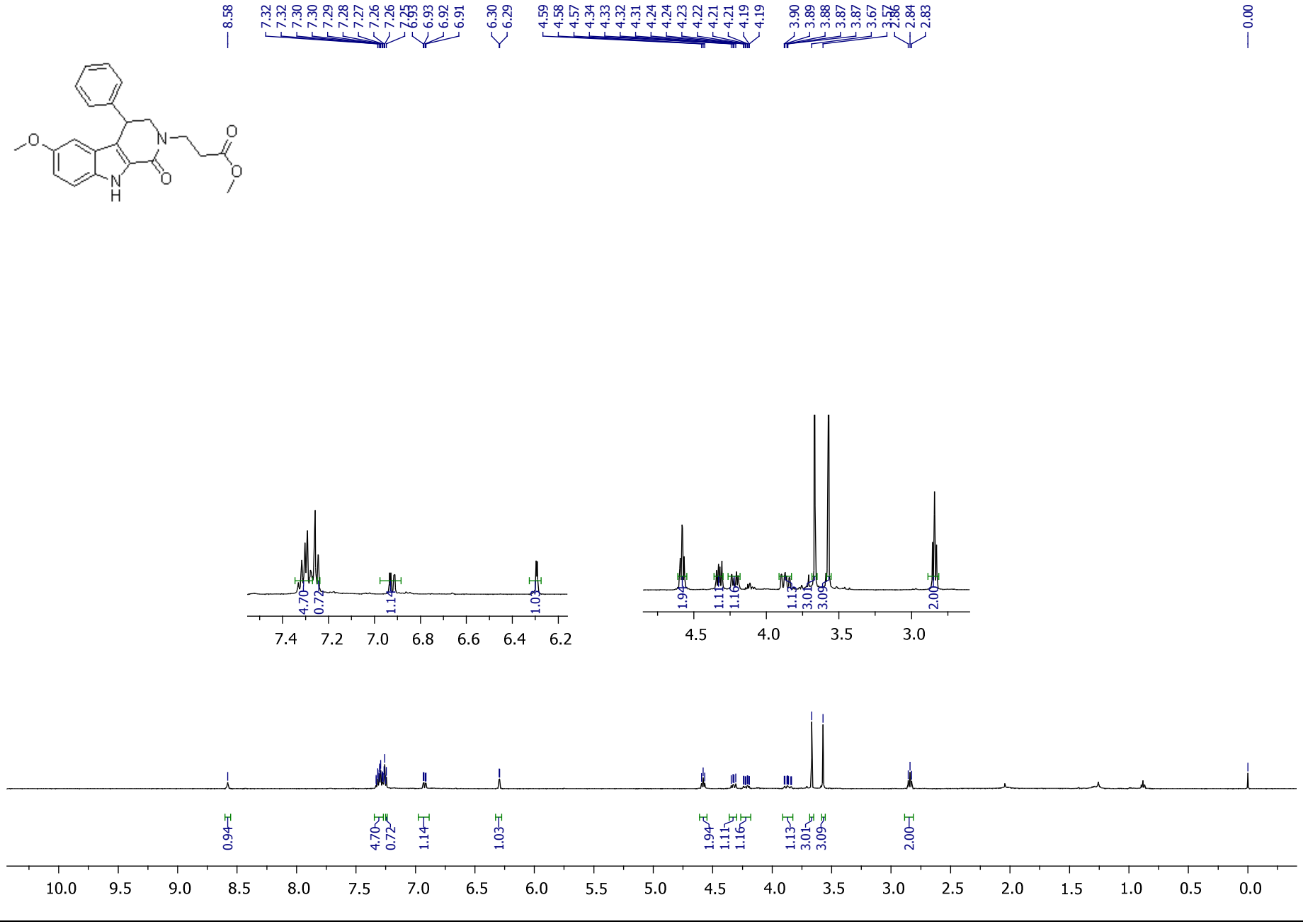
^{1}H NMR of **3s**


9.75
7.71
7.71
7.71
7.39
7.38
7.36
7.36
7.35
7.34
7.33
7.33
7.32
7.26
3.88
3.86
3.85
3.81
3.80
3.78
3.70
3.03
3.01
2.99
2.76
2.75
2.73
0.00
Br
N
O
O
O
N
H
0.87
0.93
2.00
1.96
2.05
3.00
1.95
2.00
10.0
9.5
9.0
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
0.0

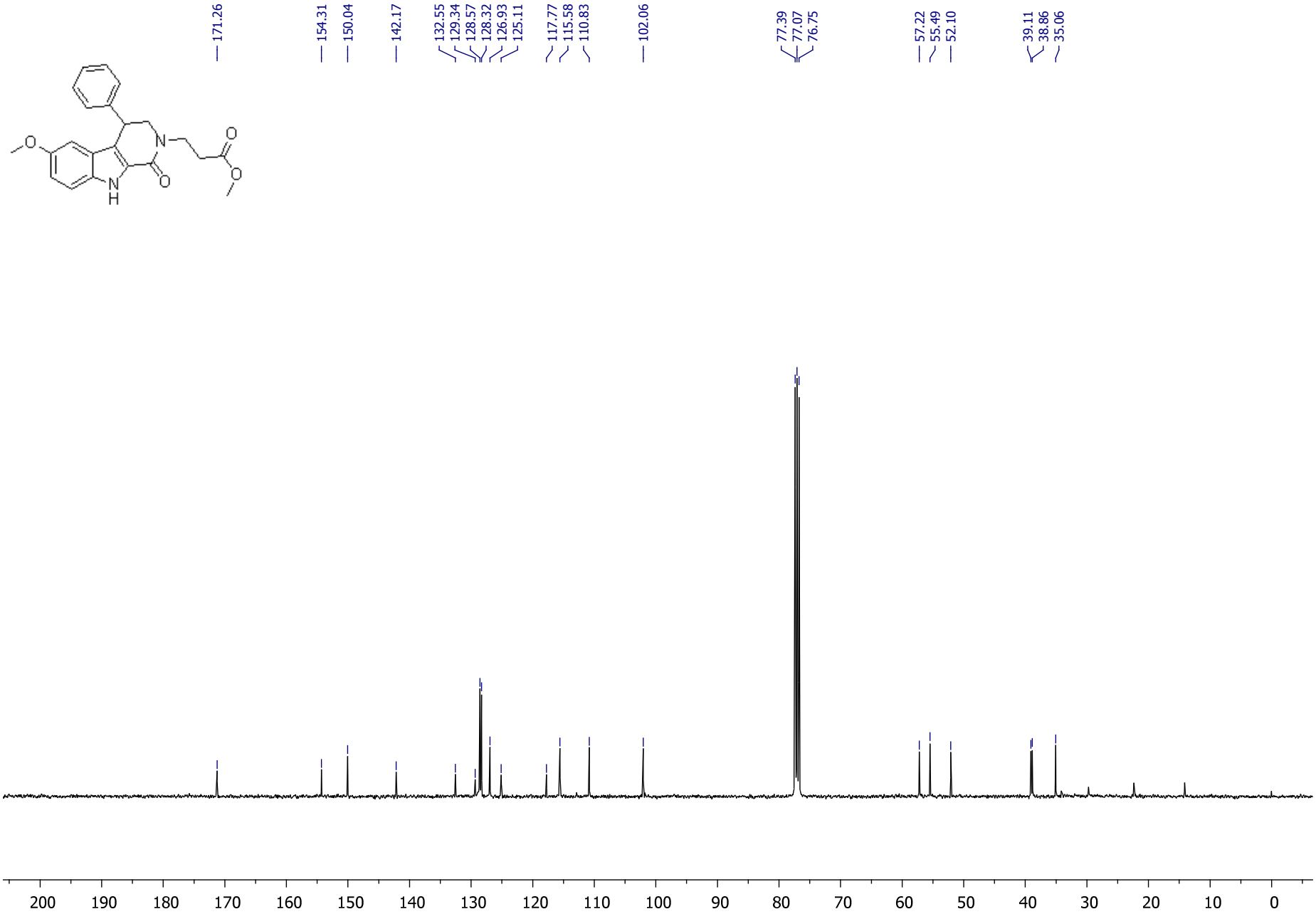
^{13}C NMR of **3s**


172.40
161.21
135.99
128.03
127.80
126.89
122.76
117.76
113.99
113.39
77.36
77.04
76.73
51.89
49.20
43.39
33.15
20.78
0.03
Br
N
O
O
N
H
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

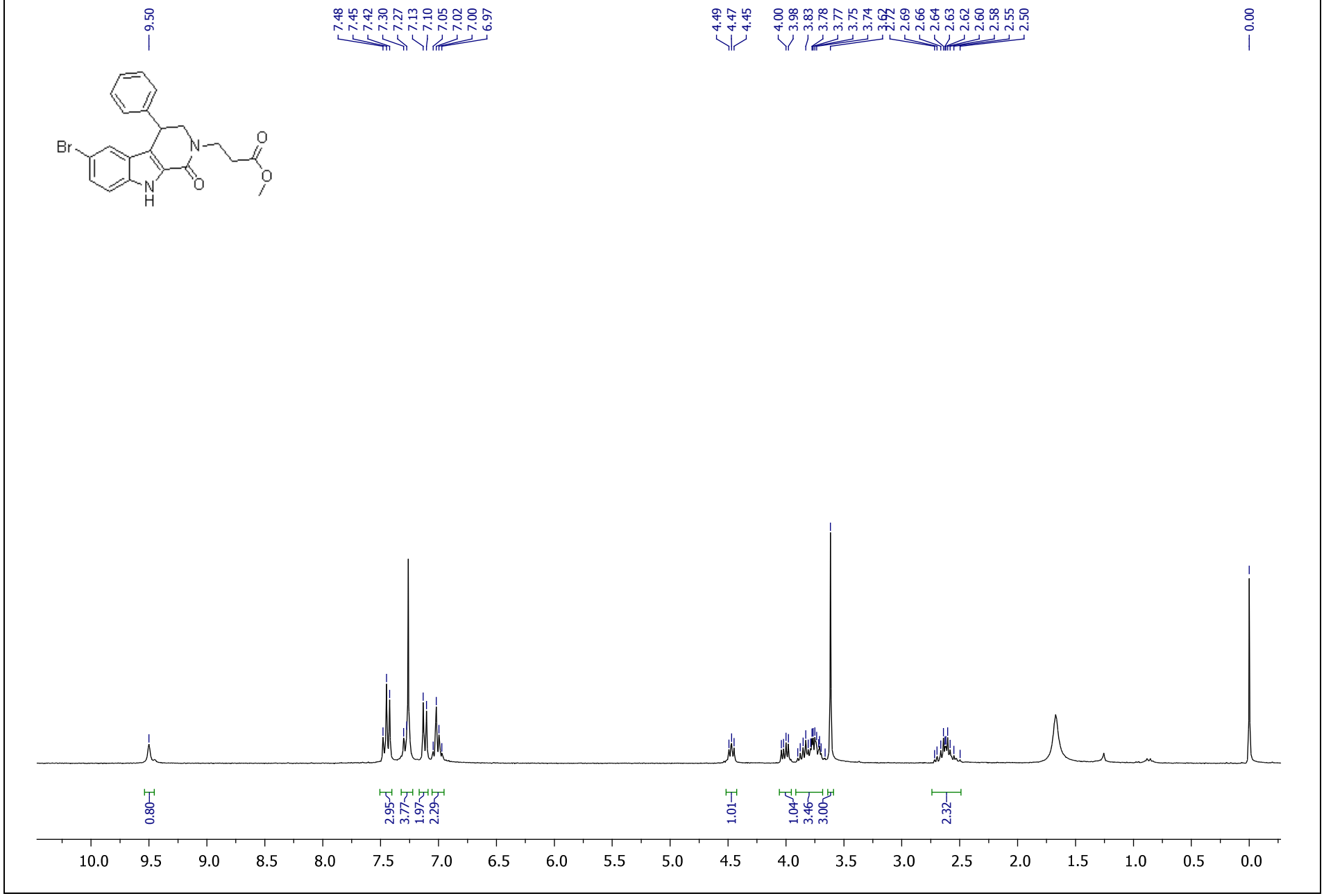
^{1}H NMR of **3t**


8.58
7.32
7.32
7.30
7.30
7.29
7.28
7.27
7.26
7.26
6.93
6.93
6.92
6.91
6.30
6.29
4.59
4.58
4.57
4.34
4.33
4.32
4.31
4.24
4.24
4.23
4.22
4.21
4.21
4.19
4.19
3.90
3.89
3.88
3.87
3.87
3.67
2.84
2.83
0.00
O
O
N
O
O
N
H
4.70
0.72
1.14
1.03
1.94
1.11
1.16
1.13
3.01
3.09
2.00
0.94
4.70
0.72
1.14
1.03
1.94
1.11
1.16
1.13
3.01
3.09
2.00
10.0
9.5
9.0
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
0.0

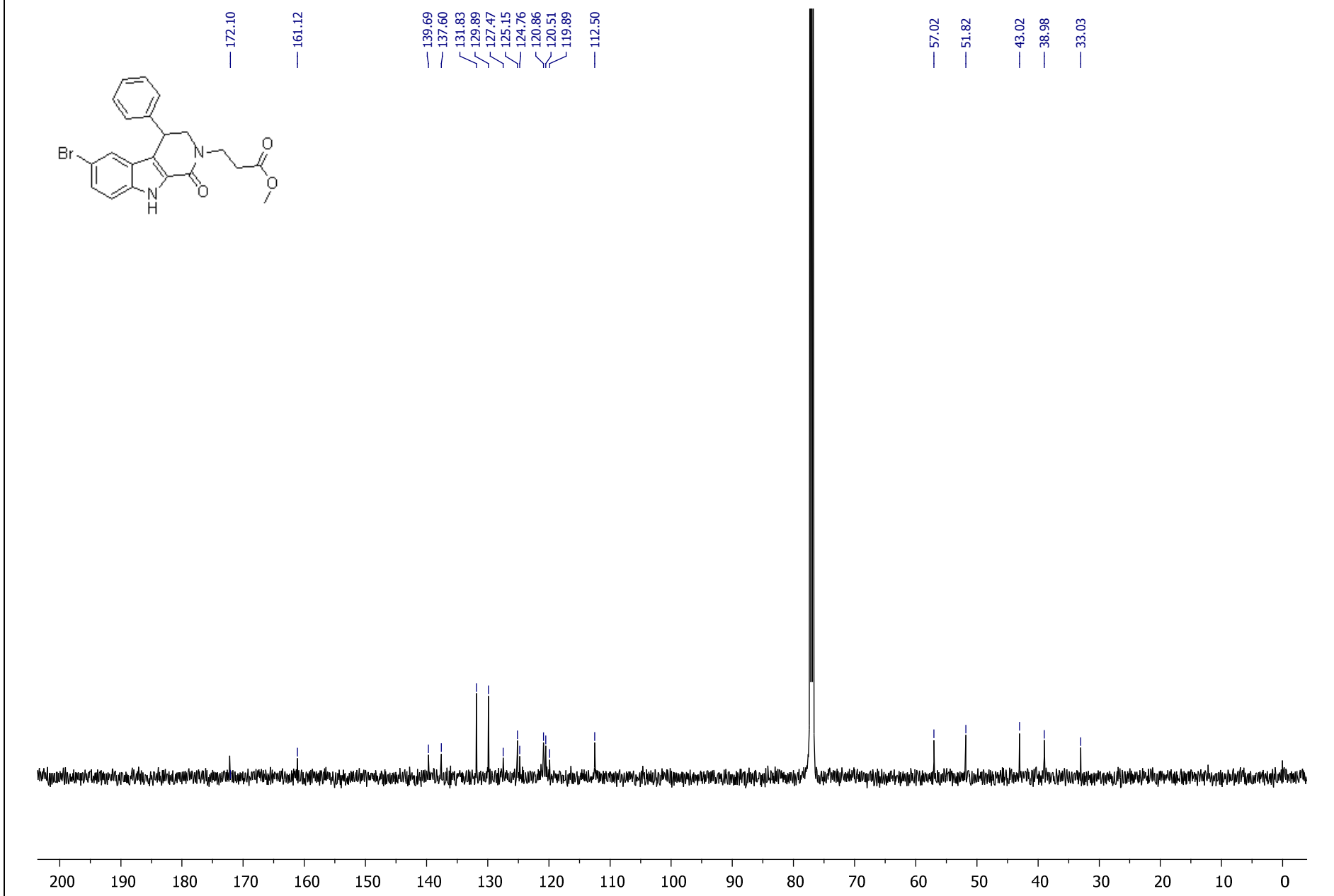
^{13}C NMR of **3t**


171.26
154.31
150.04
142.17
132.55
129.34
128.57
128.32
126.93
125.11
117.77
115.58
110.83
102.06
77.39
77.07
76.75
57.22
55.49
52.10
39.11
38.86
35.06
O
N
O
O
O
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

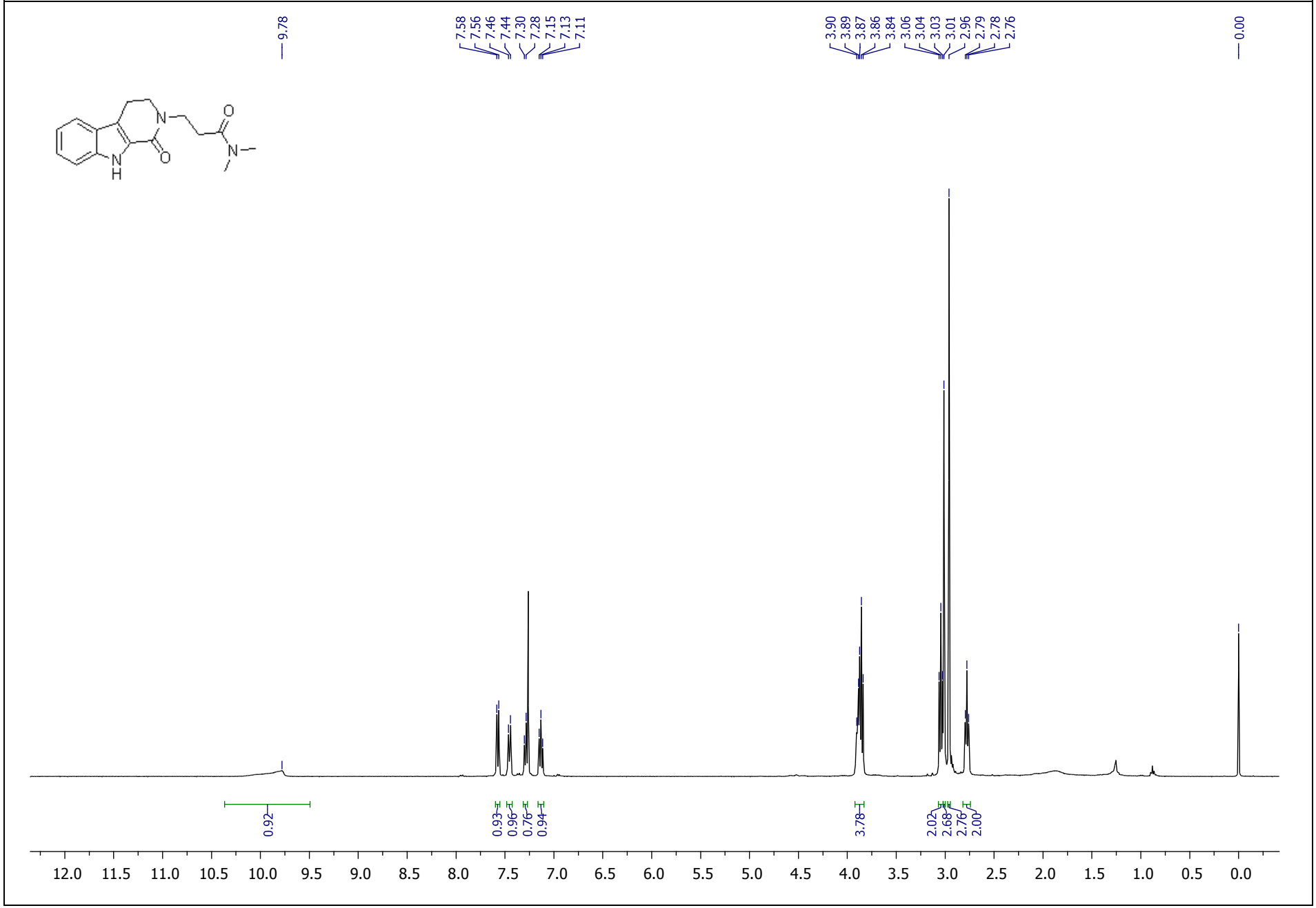
^{1}H NMR of **3u**


9.50
7.48
7.45
7.42
7.30
7.27
7.13
7.10
7.05
7.02
7.00
6.97
4.49
4.47
4.45
4.00
3.98
3.83
3.78
3.77
3.75
3.74
3.62
2.72
2.69
2.66
2.64
2.63
2.62
2.60
2.58
2.55
2.50
0.00
Br
N
O
O
N
H
O
0.80
2.95
3.77
1.97
2.29
1.01
1.04
3.46
3.00
2.32
10.0
9.5
9.0
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
0.0

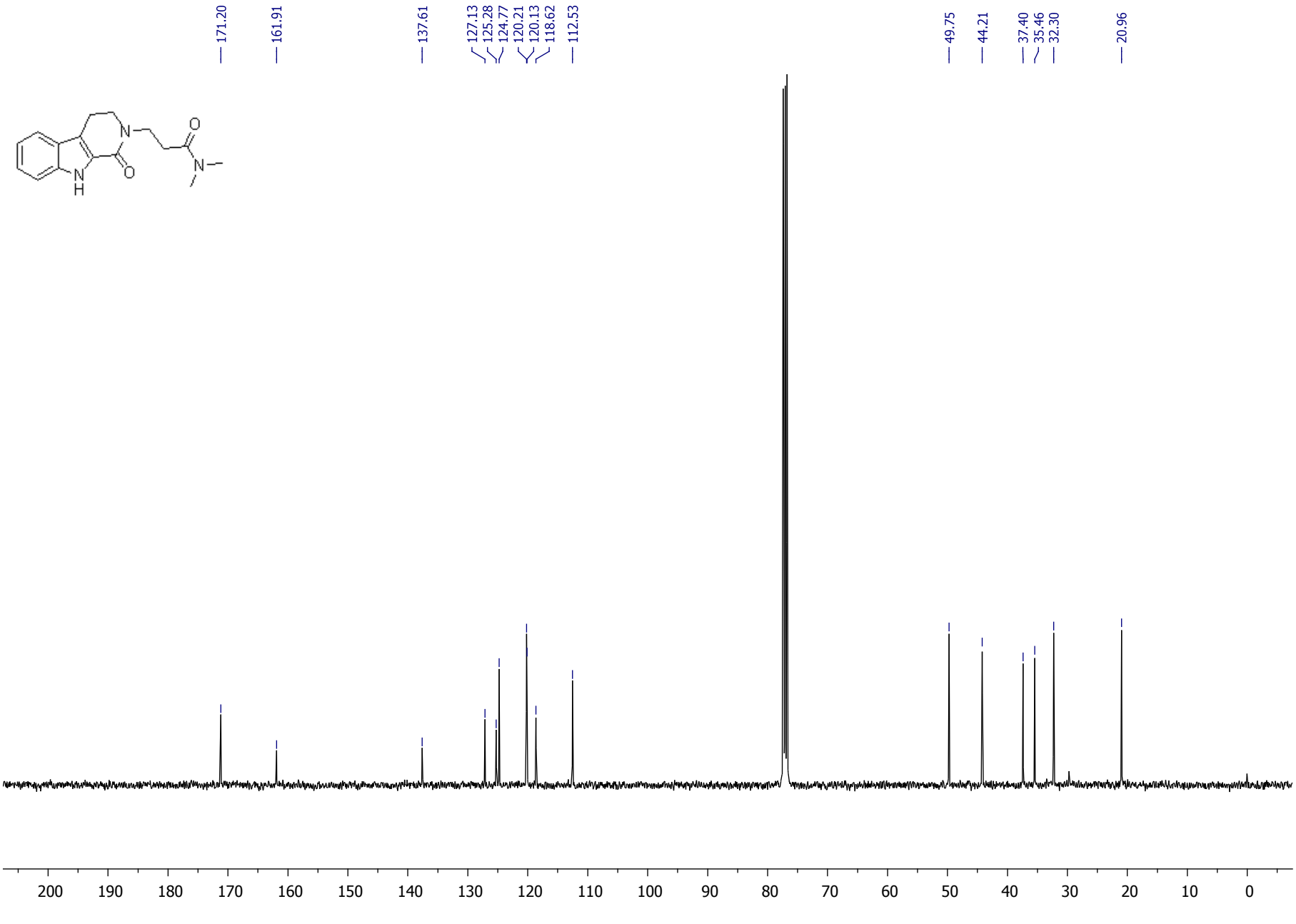
^{13}C NMR of **3u**


172.10
161.12
139.69
137.60
131.83
129.89
127.47
125.15
124.76
120.86
120.51
119.89
112.50
57.02
51.82
43.02
38.98
33.03
Br
N
O
O
N
H
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

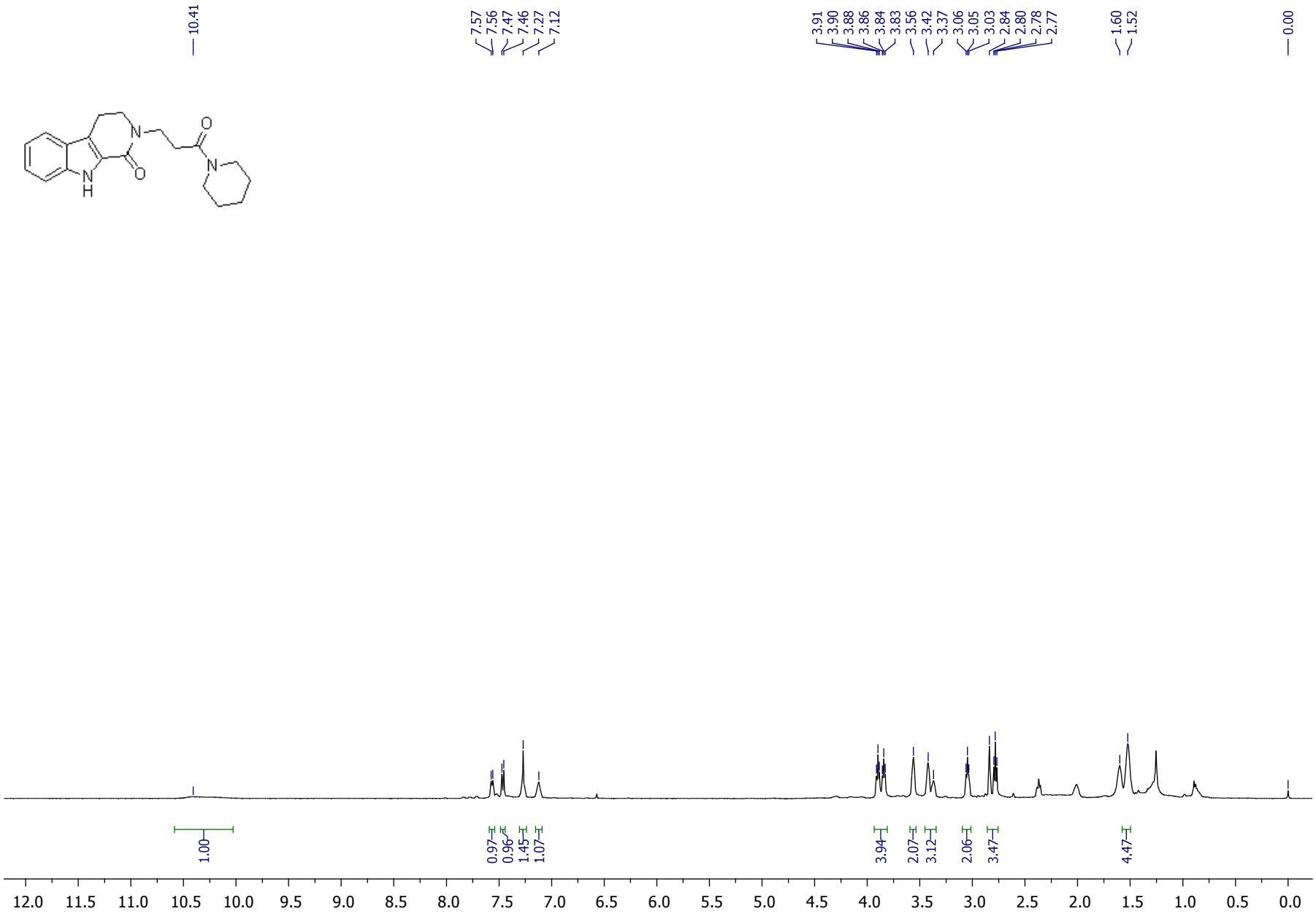
^{1}H NMR of **3v**


9.78
7.58
7.56
7.46
7.44
7.30
7.28
7.15
7.13
7.11
3.90
3.89
3.87
3.86
3.84
3.06
3.04
3.03
3.01
2.96
2.79
2.78
2.76
0.00
0.92
0.93
0.96
0.76
0.94
3.78
2.02
2.68
2.76
2.00
12.0
11.5
11.0
10.5
10.0
9.5
9.0
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
0.0

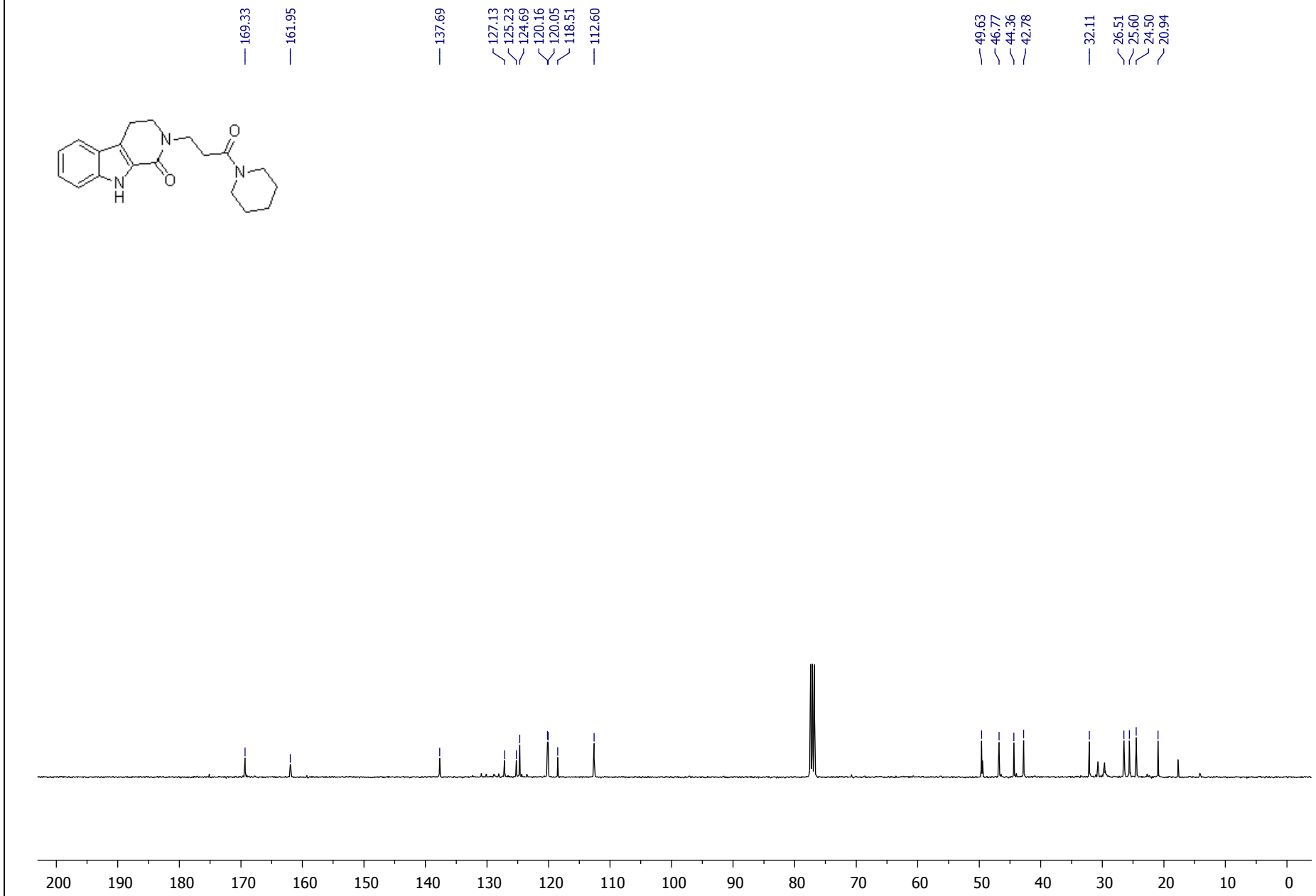
^{13}C NMR of **3v**


171.20
161.91
137.61
127.13
125.28
124.77
120.21
120.13
118.62
112.53
49.75
44.21
37.40
35.46
32.30
20.96
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

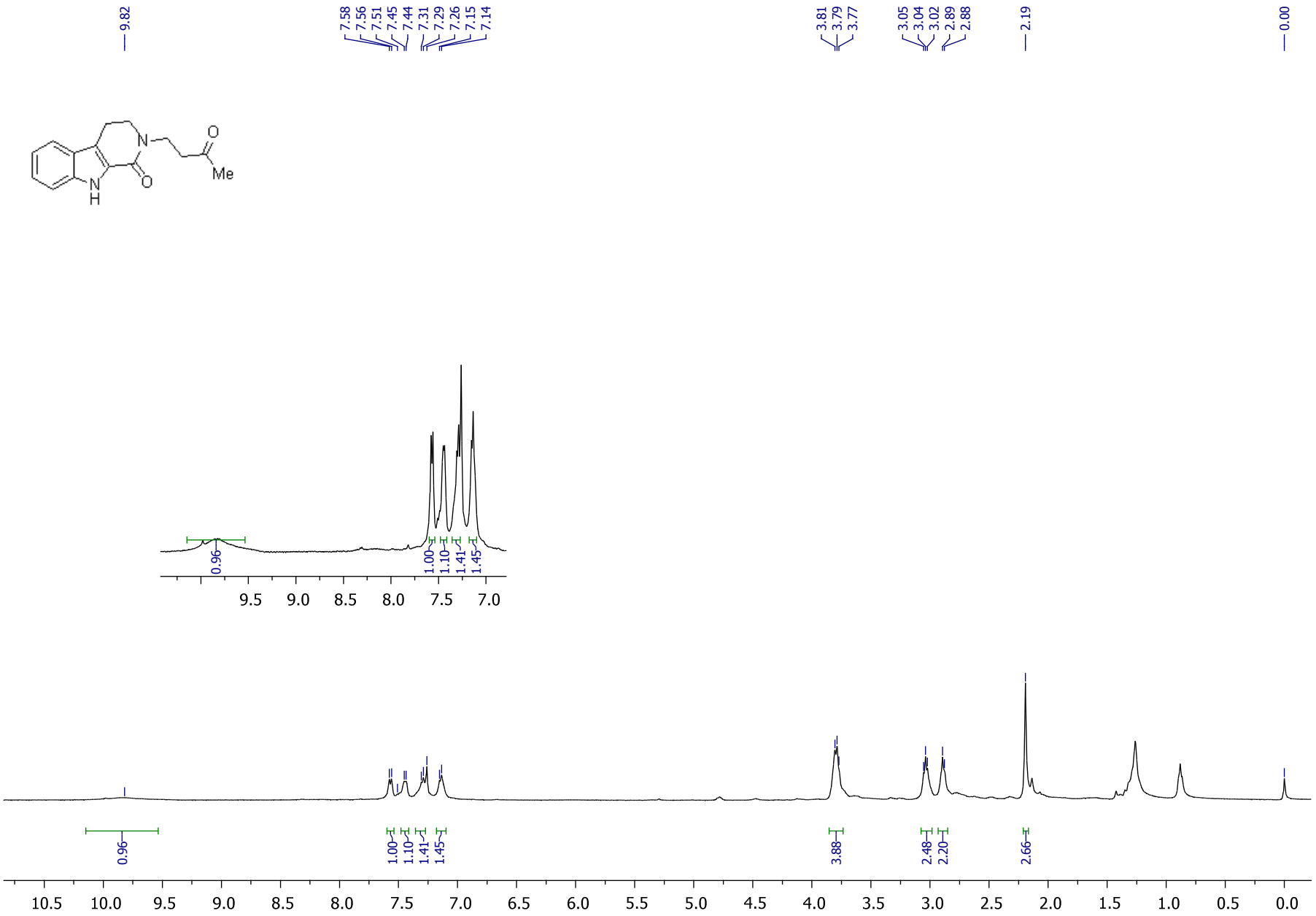
^{1}H NMR of **3w**


10.41
7.57
7.56
7.47
7.46
7.27
7.12
3.91
3.90
3.88
3.86
3.84
3.83
3.56
3.42
3.37
3.06
3.05
3.03
2.84
2.80
2.78
2.77
1.60
1.52
0.00
1.00
0.97
0.96
1.45
1.07
3.94
2.07
3.12
2.06
3.47
4.47
12.0
11.5
11.0
10.5
10.0
9.5
9.0
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
0.0

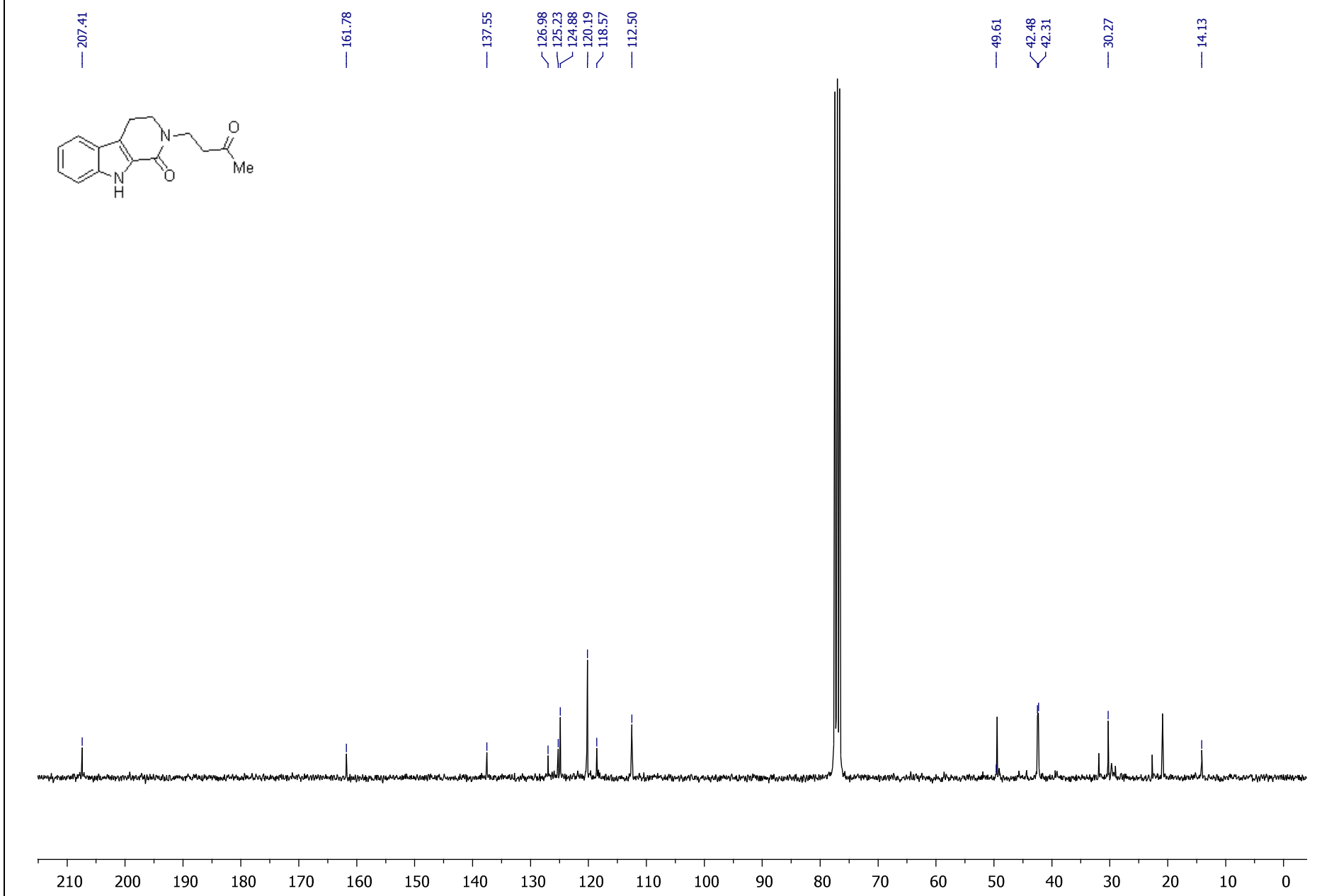
^{13}C NMR of **3w**


169.33
161.95
137.69
127.13
125.23
124.69
120.16
120.05
118.51
112.60
49.63
46.77
44.36
42.78
32.11
26.51
25.60
24.50
20.94
O
N
O
N
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

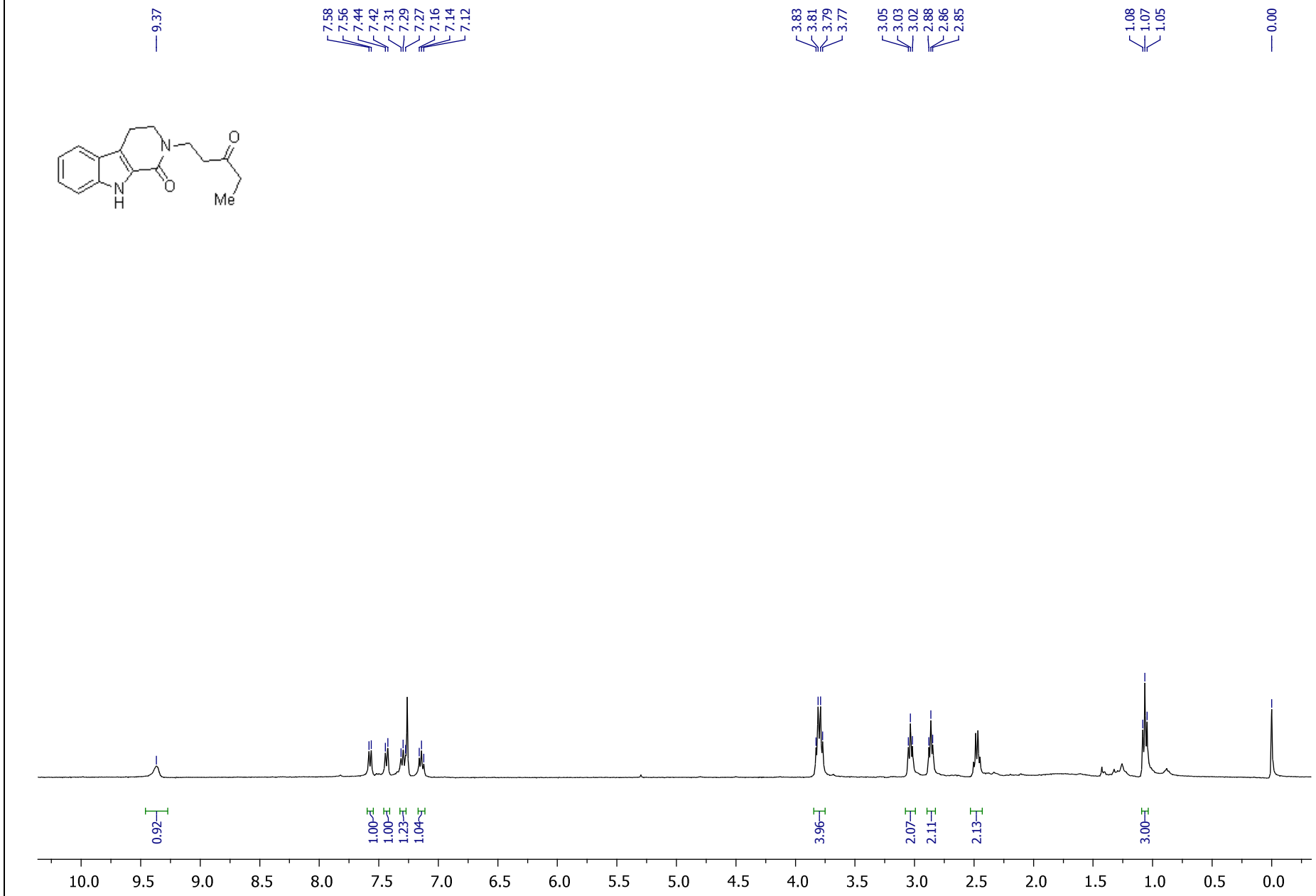
^{1}H NMR of **3x**


9.82
7.58
7.56
7.51
7.45
7.44
7.31
7.29
7.26
7.15
7.14
3.81
3.79
3.77
3.05
3.04
3.02
2.89
2.88
2.19
0.00
O
N
Me
N
H
O
0.96
1.00
1.10
1.41
1.45
9.5
9.0
8.5
8.0
7.5
7.0
0.96
1.00
1.10
1.41
1.45
3.88
2.48
2.20
2.66
10.5
10.0
9.5
9.0
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
0.0

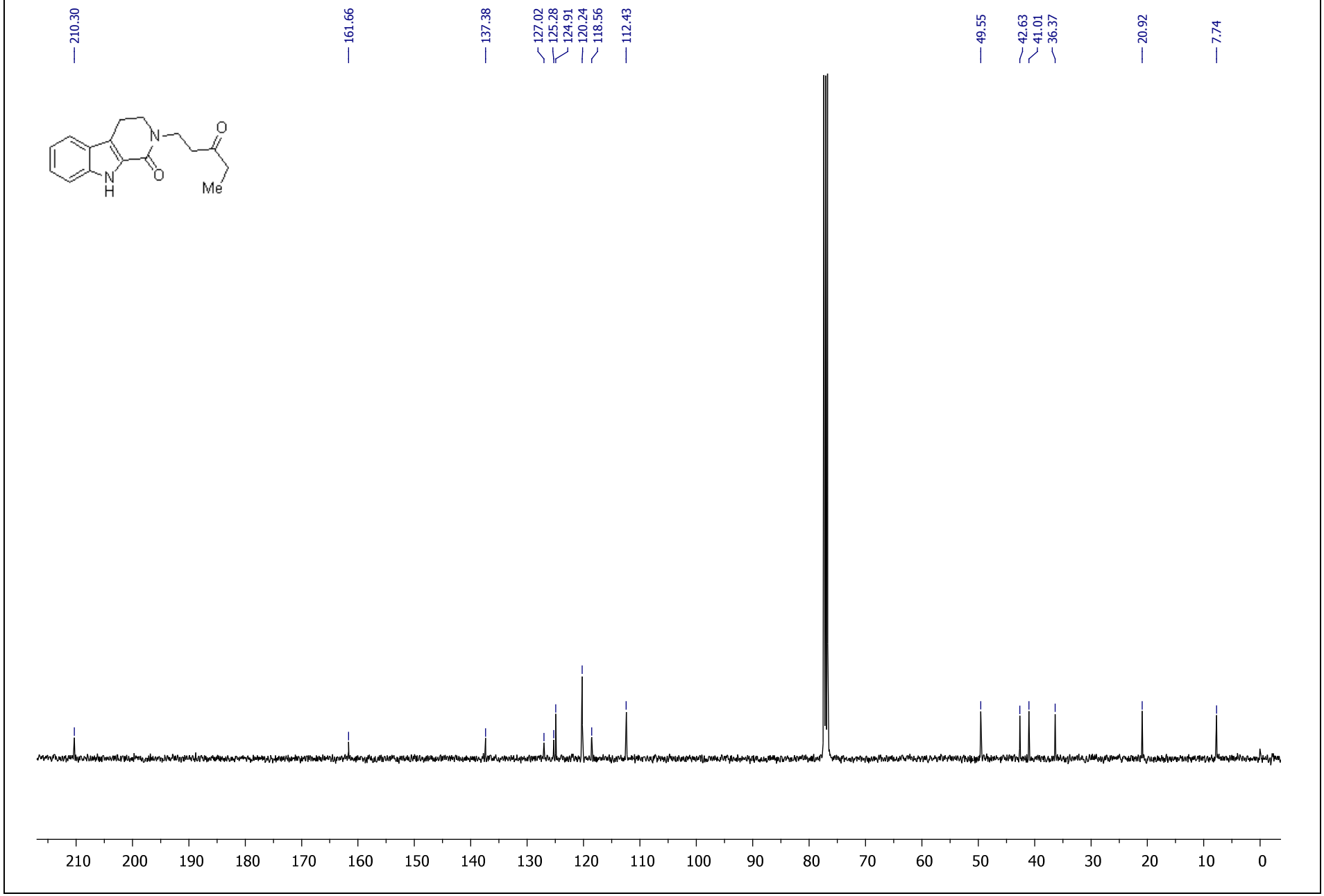
^{13}C NMR of **3x**


207.41
161.78
137.55
126.98
125.23
124.88
120.19
118.57
112.50
49.61
42.48
42.31
30.27
14.13
N
O
Me
O
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

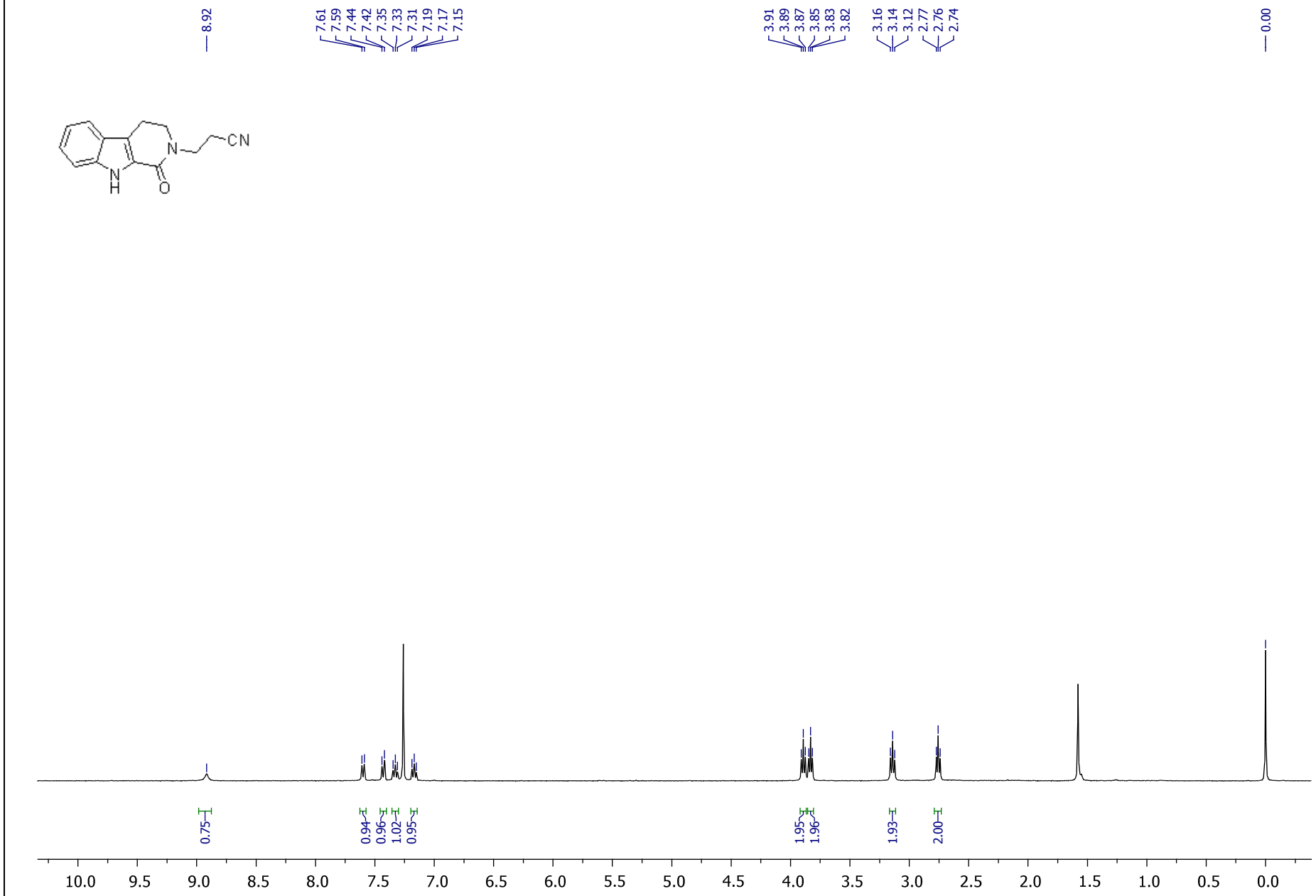
^{1}H NMR of **3y**


9.37
7.58
7.56
7.44
7.42
7.31
7.29
7.27
7.16
7.14
7.12
3.83
3.81
3.79
3.77
3.05
3.03
3.02
2.88
2.86
2.85
1.08
1.07
1.05
0.00
N
O
N
H
O
Me
0.92
1.00
1.00
1.23
1.04
3.96
2.07
2.11
2.13
3.00
10.0
9.5
9.0
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
0.0

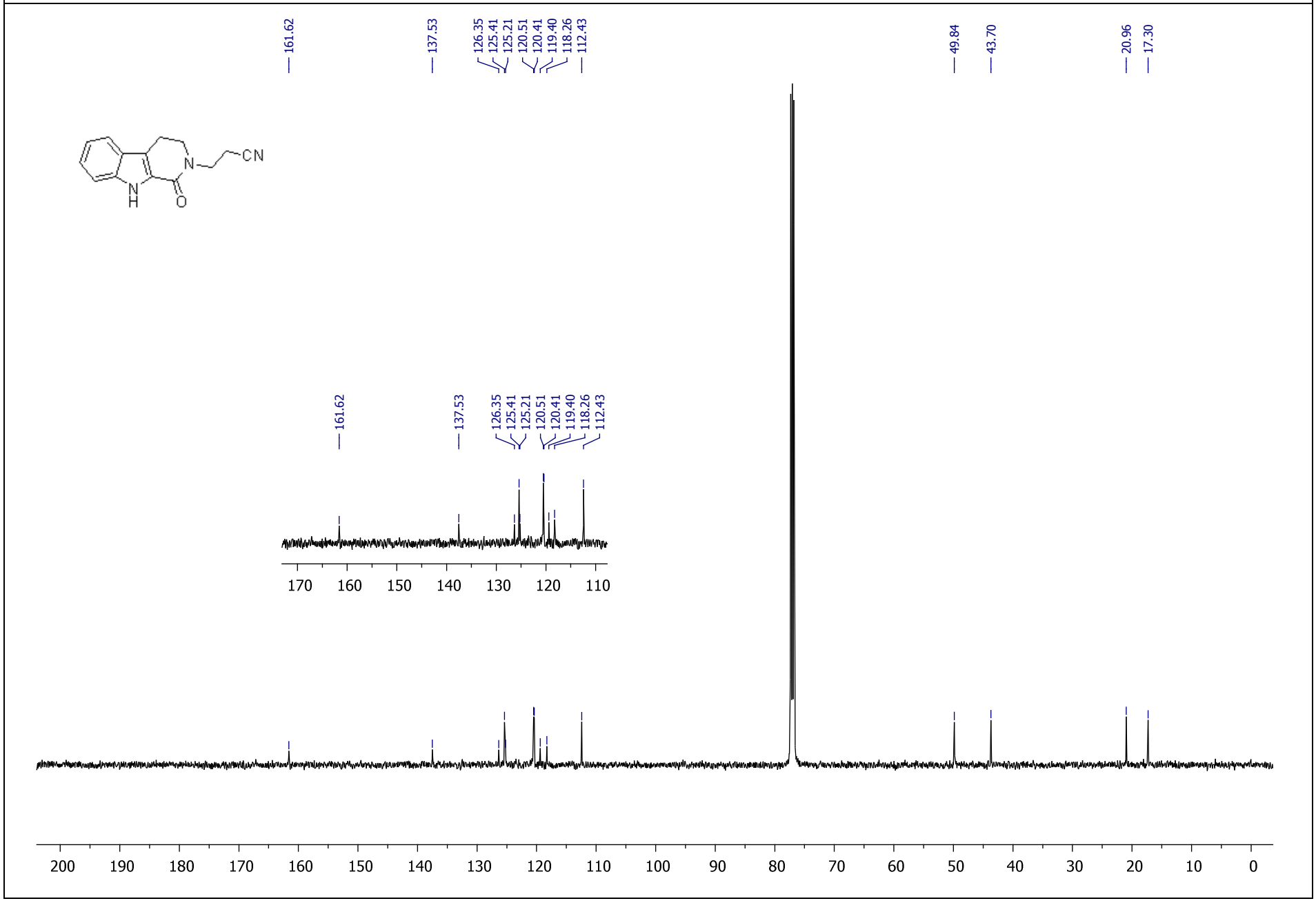
^{13}C NMR of **3y**


210.30
161.66
137.38
127.02
125.28
124.91
120.24
118.56
112.43
49.55
42.63
41.01
36.37
20.92
7.74
N
O
N
H
O
Me
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

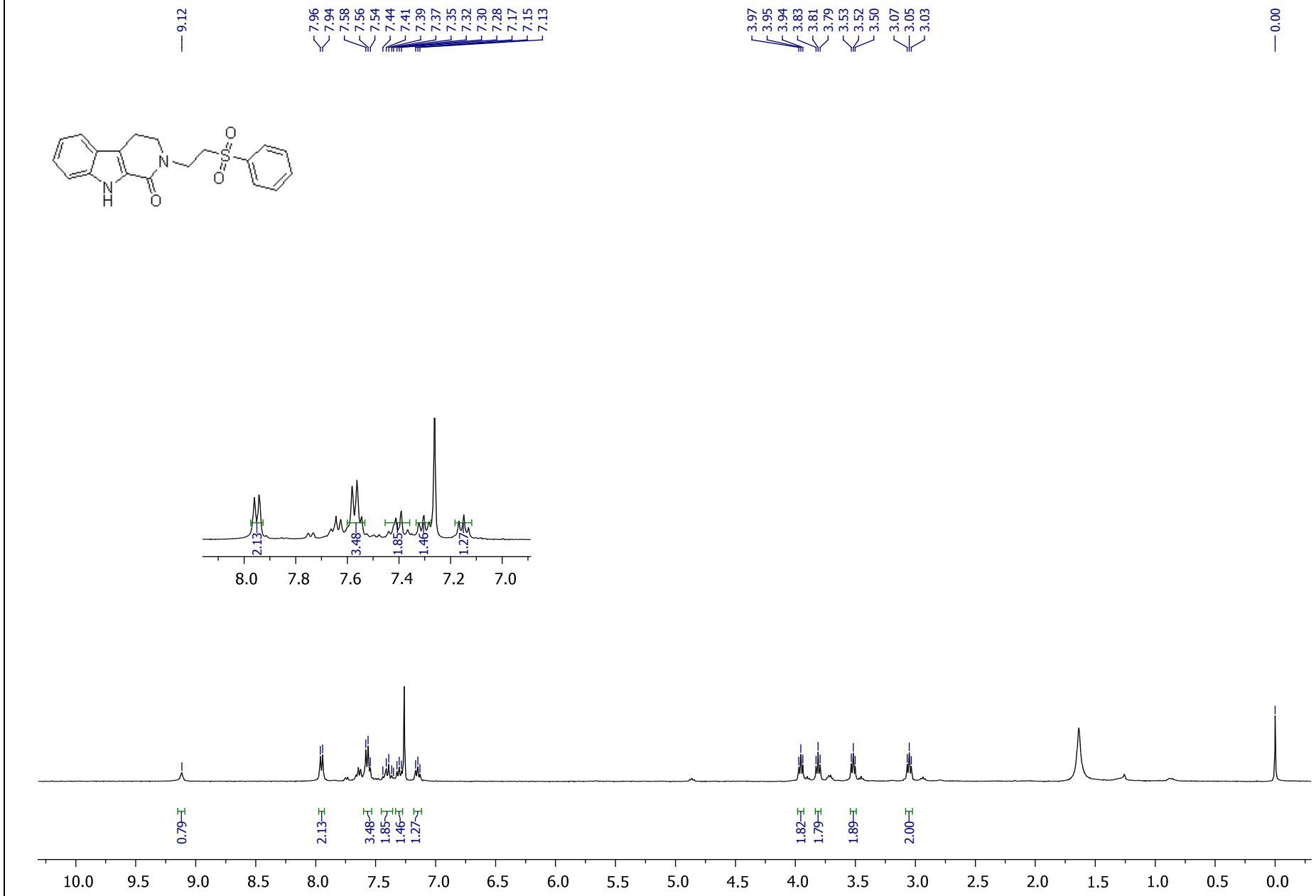
^{1}H NMR of **3z**


8.92
7.61
7.59
7.44
7.42
7.35
7.33
7.31
7.19
7.17
7.15
3.91
3.89
3.87
3.85
3.83
3.82
3.16
3.14
3.12
2.77
2.76
2.74
0.00
CN
N
H
O
0.75
0.94
0.96
1.02
0.95
1.95
1.96
1.93
2.00
10.0
9.5
9.0
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
0.0

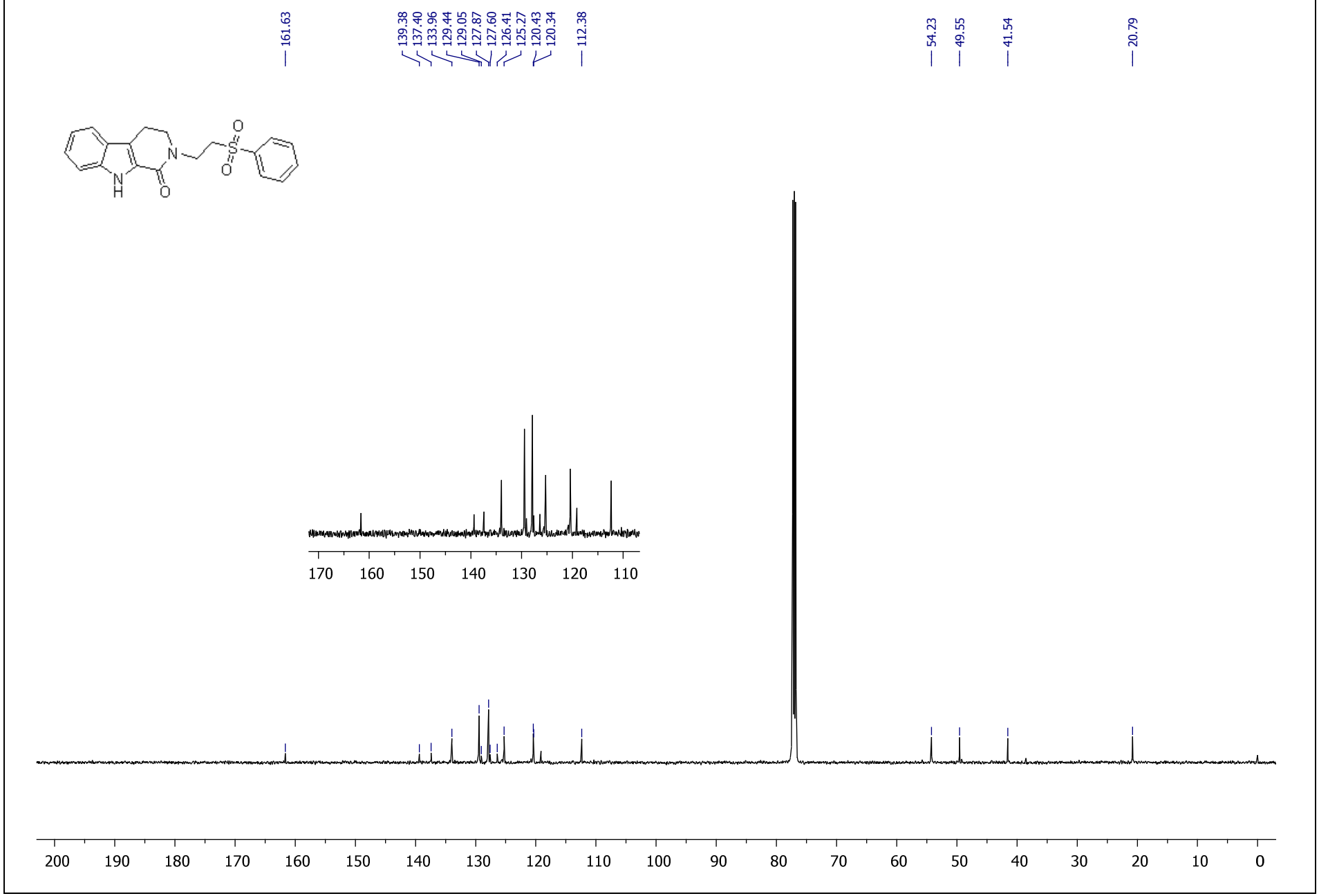
^{13}C NMR of **3z**


161.62
137.53
126.35
125.41
125.21
120.51
120.41
119.40
118.26
112.43
49.84
43.70
20.96
17.30
CN
N
H
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

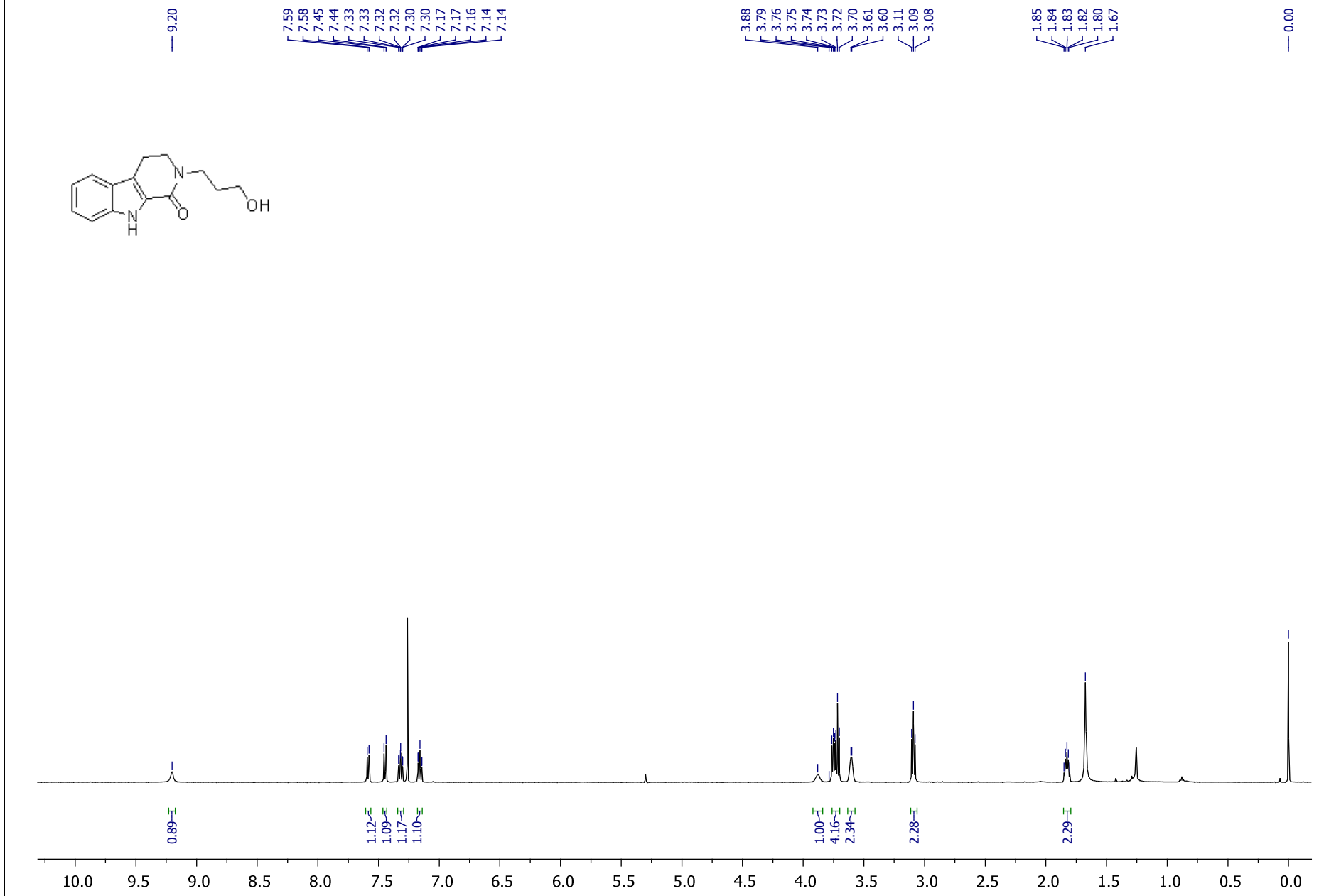
^{1}H NMR of **3aa**


9.12
7.96
7.94
7.58
7.56
7.54
7.44
7.41
7.39
7.37
7.35
7.32
7.30
7.28
7.17
7.15
7.13
3.97
3.95
3.94
3.83
3.81
3.79
3.53
3.52
3.50
3.07
3.05
3.03
0.00
2.13
3.48
1.85
1.46
1.27
0.79
1.82
1.79
1.89
2.00

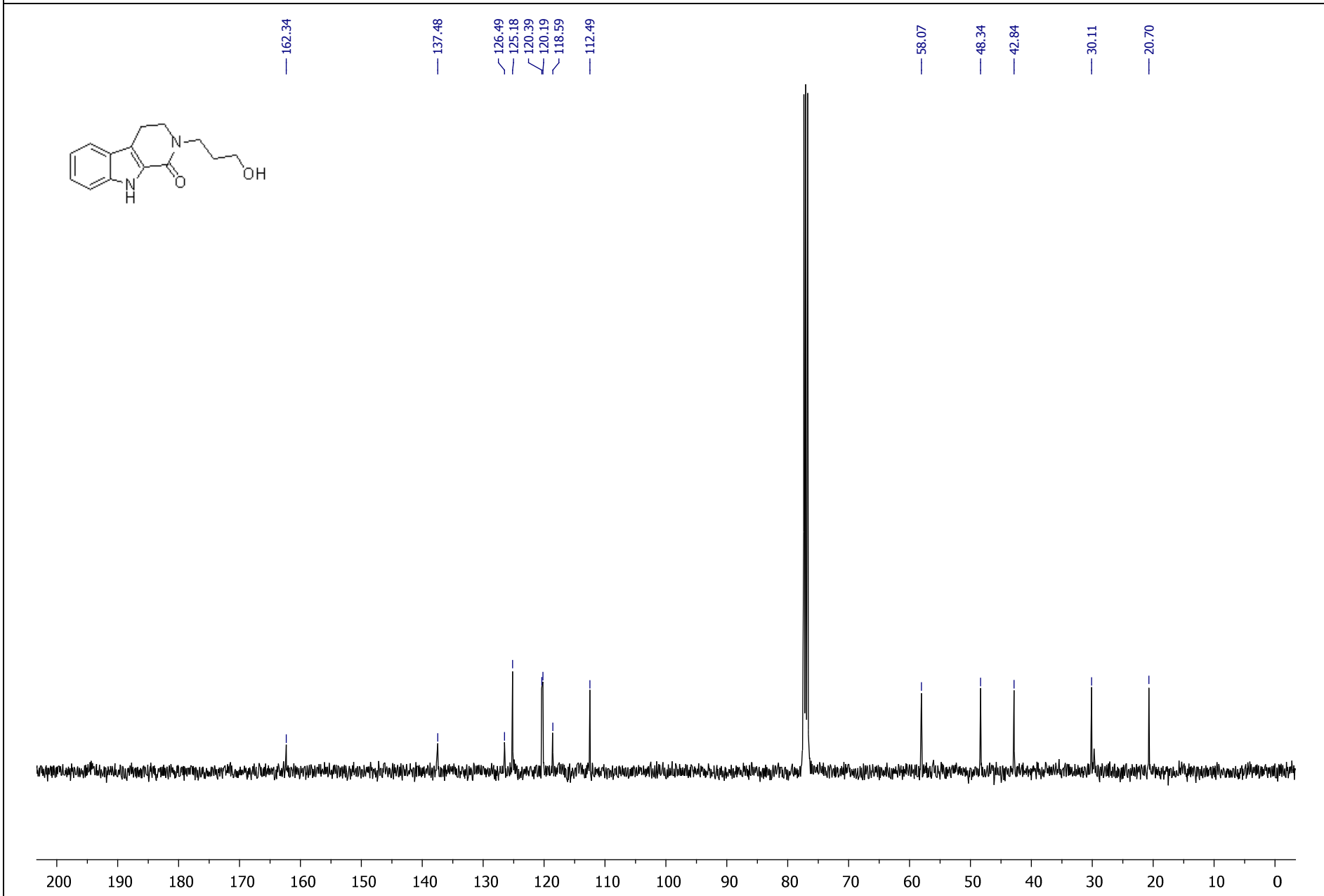
^{13}C NMR of **3aa**



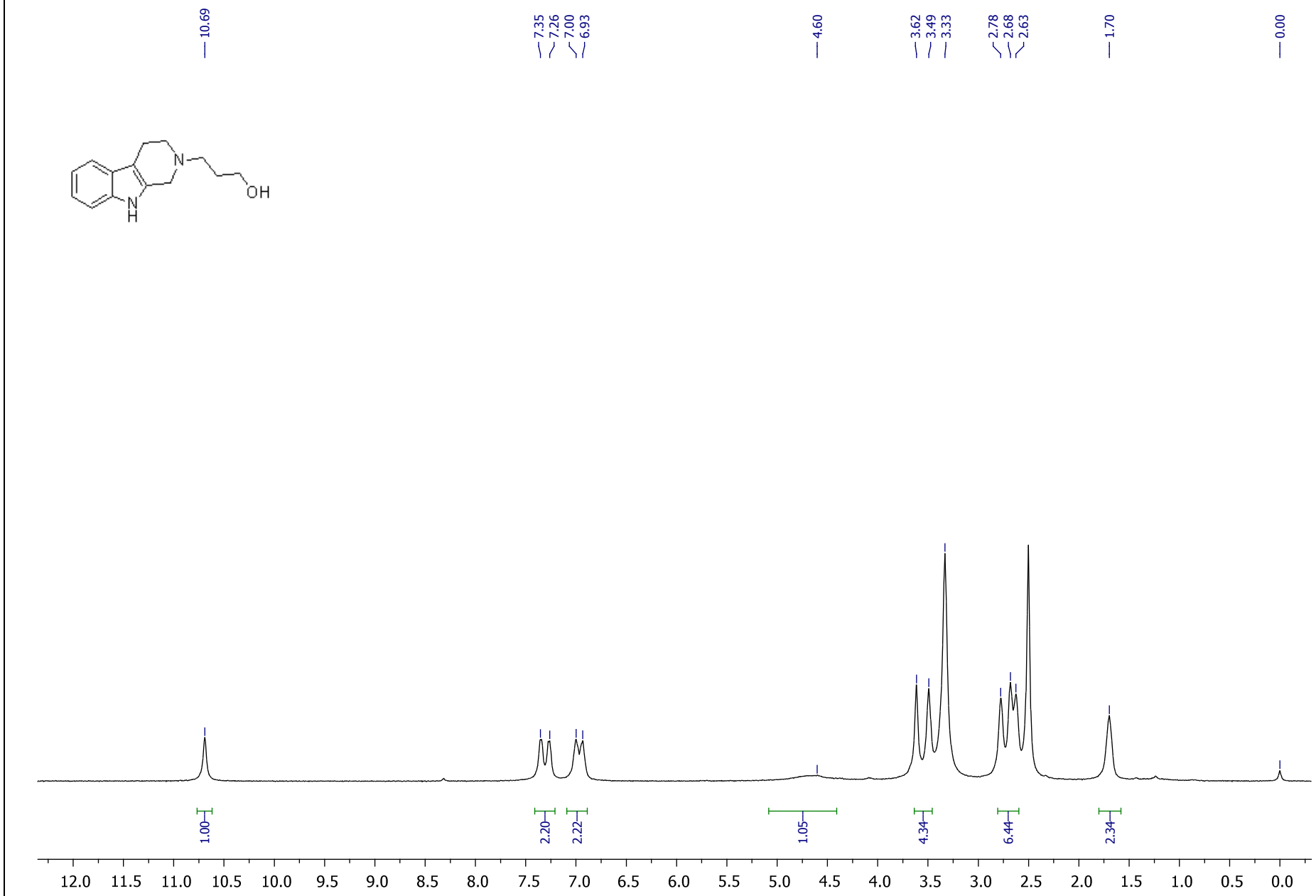
^{1}H NMR of **4**


9.20
7.59
7.58
7.45
7.44
7.33
7.33
7.32
7.32
7.30
7.30
7.17
7.17
7.16
7.14
7.14
3.88
3.79
3.76
3.75
3.74
3.73
3.72
3.70
3.61
3.60
3.11
3.09
3.08
1.85
1.84
1.83
1.82
1.80
1.67
0.00
N
O
N
H
OH
0.89
1.12
1.09
1.17
1.10
1.00
4.16
2.34
2.28
2.29
10.0
9.5
9.0
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
0.0

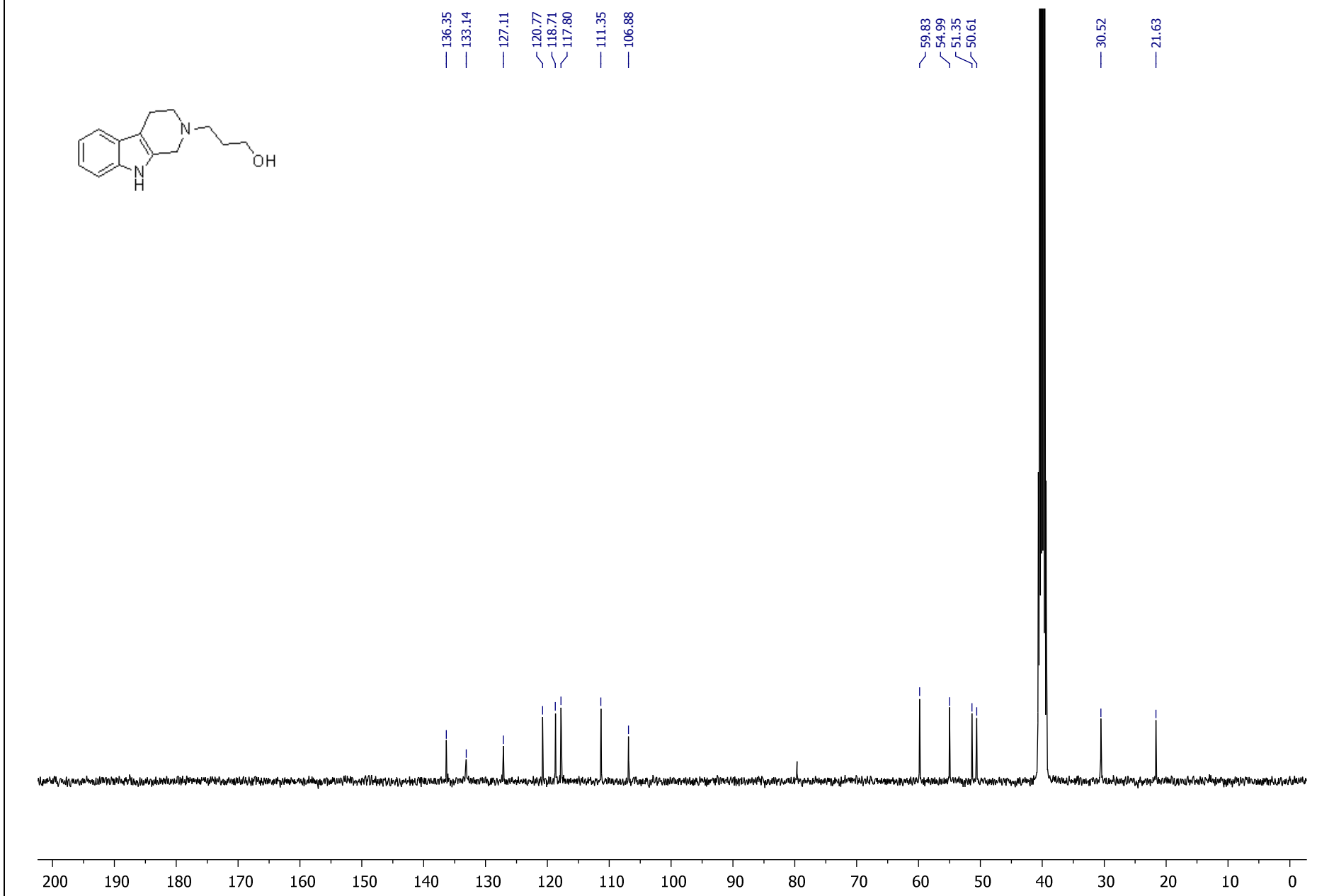
^{13}C NMR of **4**


162.34
137.48
126.49
125.18
120.39
120.19
118.59
112.49
58.07
48.34
42.84
30.11
20.70
N
O
N
H
OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

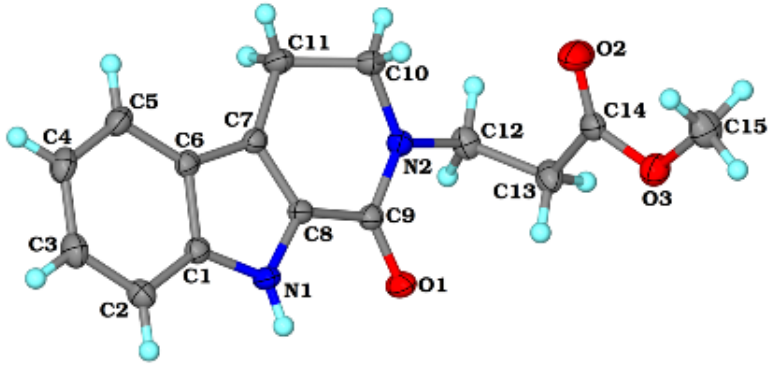
^{1}H NMR of **5**


10.69
7.35
7.26
7.00
6.93
4.60
3.62
3.49
3.33
2.78
2.68
2.63
1.70
0.00
N
OH
N
H
1.00
2.20
2.22
1.05
4.34
6.44
2.34
12.0
11.5
11.0
10.5
10.0
9.5
9.0
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
0.0

^{13}C NMR of **5**


136.35
133.14
127.11
120.77
118.71
117.80
111.35
106.88
59.83
54.99
51.35
50.61
30.52
21.63
N
N
H
OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

13. Crystallographic data for 3a



ORTEP diagram of KA270 with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radius. CCDC 1953542 contains the supplementary crystallographic data for this paper.

Data Collection and Structure Refinement details: Single crystal X-ray data for **3a** compound were collected at room temperature on a Bruker D8 QUEST equipped with a four-circle kappa diffractometer and Photon 100 detector. An Iμs microfocus Mo source (λ = 0.71073Å) supplied the multi-mirror monochromated incident beam. A combination of Phi and Omega scans were used to collect the necessary data and unit cell dimensions were determined using 7286 reflections. Integration and scaling of intensity data were accomplished using SAINT program.[11] The structures were solved by Direct Methods using SHELXS97[12] and refinement was carried out by full-matrix least-squares technique using SHELXL-2018/3.[10] Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms with C-H distances of 0.93--0.97 Å, and with $U_{iso}(H) = 1.2U_{eq}$ (C) or $1.5U_{eq}$ for methyl atoms. The two carbon atoms of tetrahydropyrido ring were disordered over two sites with site occupancy factor of 0.877(10) for C10/C11 atoms (major component) and 0.123(10) for C10D/C11D atoms (minor component). PART and FVAR commands were employed for the disorder model treatment. The anisotropic displacement parameters of the disordered carbon atoms were restrained to be similar (SIMU instruction) and the direction of motion along the axis between

these atoms was also restrained (DELU instruction).[13] CCDC 1953542 contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://summary.ccdc.cam.ac.uk/structure-summary-form or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk.

11. SMART & SAINT. Software Reference manuals. Versions 6.28a & 5.625, Bruker Analytical X-ray Systems Inc., Madison, Wisconsin, U.S.A., 2001.

12. Sheldrick, G. M. SHELXS97 and SHELXL Version 2018/3, http://shelx.uni-ac.gwdg.de/SHELX/index.php

13. Muller, P, Herbst-Imer, R, Spek, A. L, Schneider, T. R, and Sawaya, M. R. Crystal Structure Refinement: A Crystallographer's Guide to SHELXL. Muller, P. Ed. 2006 Oxford University Press: Oxford, New York, pp. 57–91.