Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Base-Free van Leusen Reaction of Cyclic Imines on Water: Synthesis of *N*-Fused Imidazo 6,11-Dihydro β-Carboline Derivatives

Killari Satyam,[†,‡] V. Murugesh,[†,‡] and Surisetti Suresh*[,†,‡]

[†]Organic Synthesis and Process Chemistry, CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad 500 007, India

[‡]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad 201002, India

Contents:

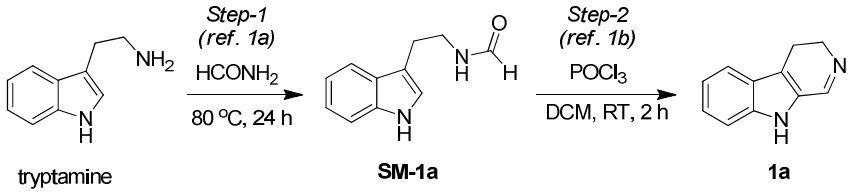
1. General experimental

All the reactions were carried out in an oven dried glassware or screw caped vials. pH values were measured on a Thermo Scientific Orion Star A111 pH benchtop meter. Reactions are 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. Iodine, 5% aqueous potassium permanganate solution were used as a developing agents followed by heating. Purification of products was carried out by column chromatography by using 60-120 mesh silica and DCM, methanol were used as eluents. Concentration under reduced pressure was performed by rotary evaporator at 40-45 ^{o}C, at appropriate pressure. The yields were given to the purified products.

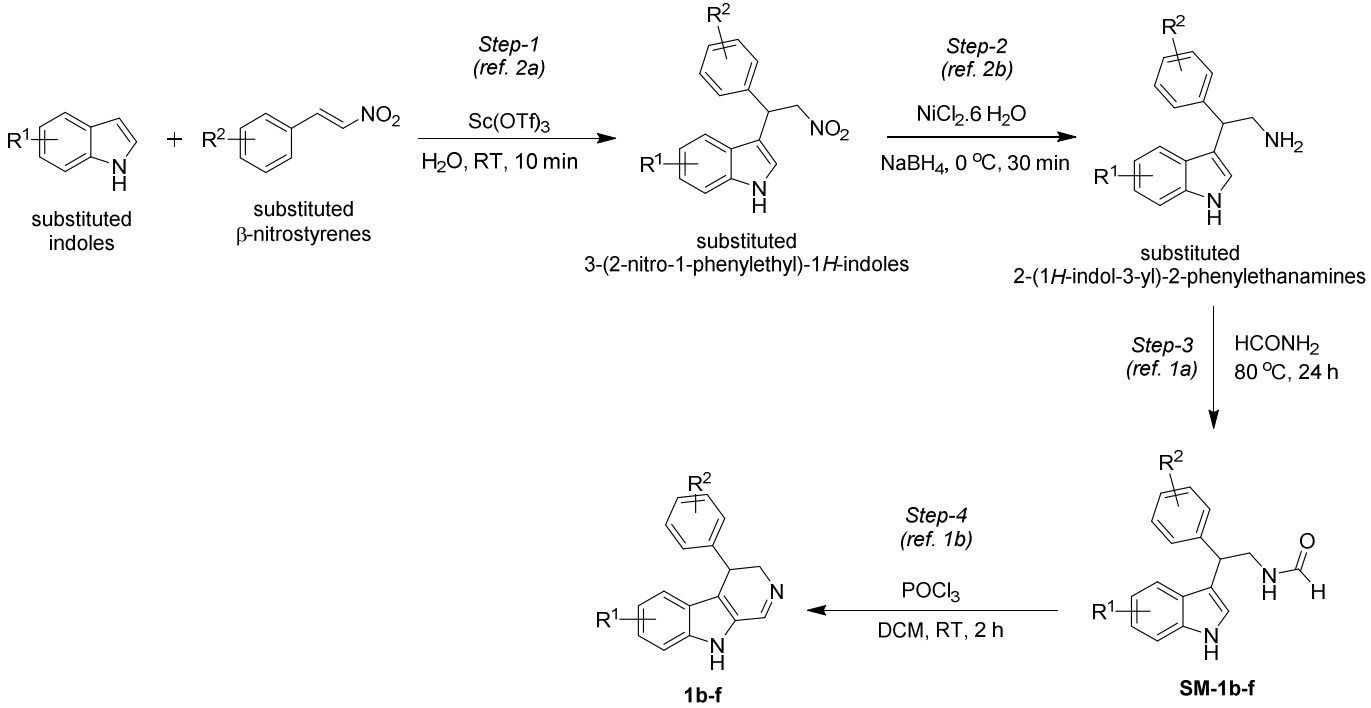
All the required starting materials, reagents and (deuterated) solvents were purchased from commercial suppliers and those were used without further purification. ^{1}H NMR spectra were recorded on 300, 400 and 500 MHz instruments. Chemical shifts are reported in ppm with the reference solvent as the 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). ^{13}C{H}NMR spectra were recorded on 75, 100, and 125 MHz spectrometers. Mass spectra were analyzed by Electrospray Ionization (ESI) method which were obtained on a mass spectrometer. High resolution mass spectra (HRMS) were recorded on a QSTAR XL Hybrid MS/MS mass spectrometer or Orbitrap Mass Spectrometer. Melting points (MP) were determined using a capillary point apparatus. MPs are uncorrected. Infrared (IR) spectroscopy was performed in neat (in chloroform) and as KBr pellets on a FT-IR spectrophotometer.

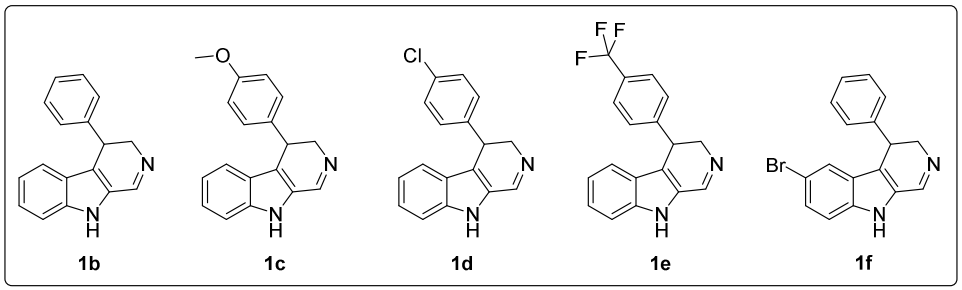
2. Schemes for the synthesis of starting materials

Synthesis of 4,9-dihydro-3*H*-pyrido[3,4-*b*]indole 1a:

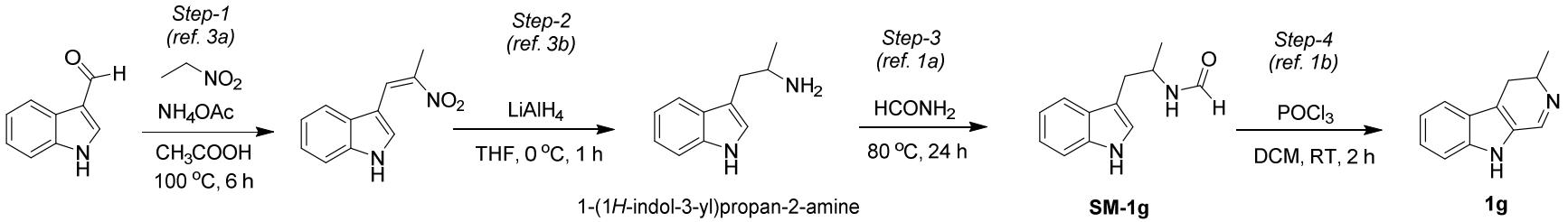


Synthesis of substituted 4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (1b-1f):



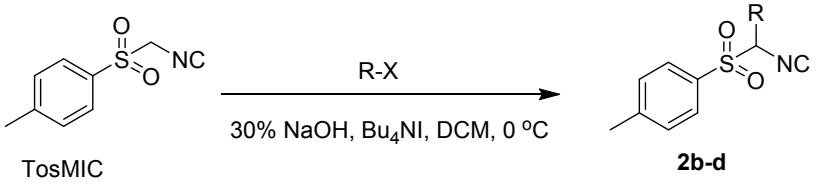


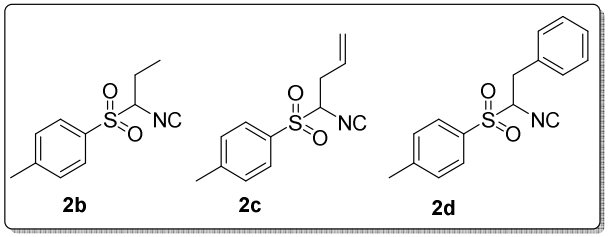
Synthesis of 3-methyl-4,9-dihydro-3*H*-pyrido[3,4-b]indole (1g)



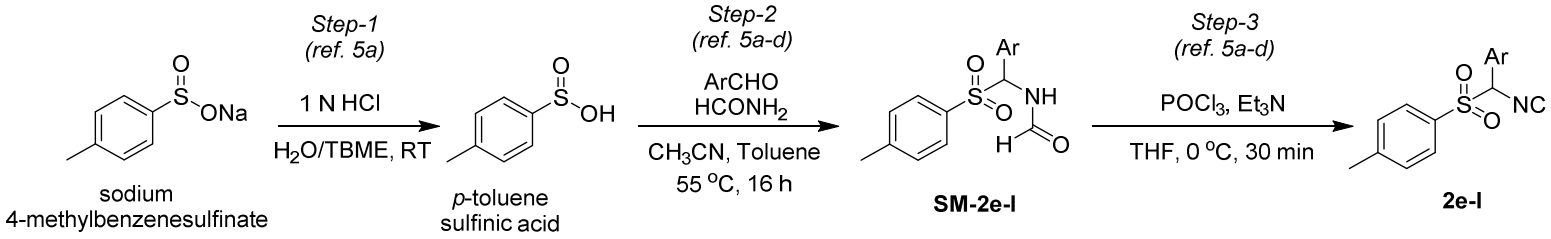
*CAUTION: the dihydro β-carboline imines **1a-g** are found to be stable for one week at 0-4 °C.*

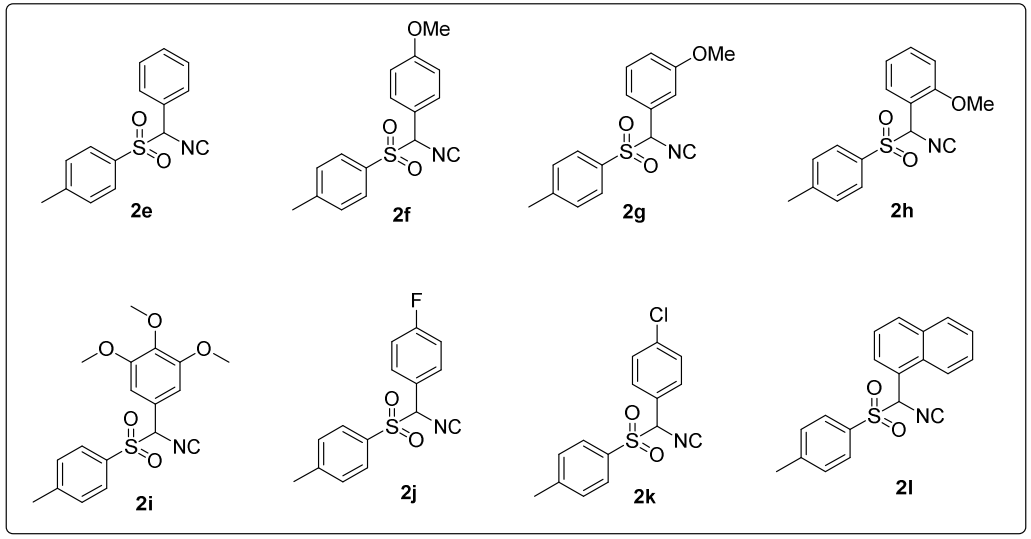
Synthesis of alkyl substituted *p*-toluenesulfonylmethyl isocyanides 2b-2d[4]:





Synthesis of aryl substituted *p*-toluenesulfonylmethyl isocyanides 2e-2l[5a-d]:

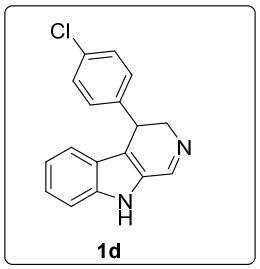




CAUTION: the TosMIC derivatives ***2b-l*** *are found to be stable for one-two days at 0-4 °C.*

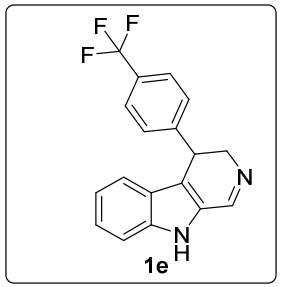
Synthesis of starting materials 1a-g, 2b-l and spectral data of 1d-f: The starting imine **1a** was prepared in two steps by formylation of tryptamine[1a] followed by Bischler-Napieralski cyclization[1b] using known methods. The imines **1b-c** have been prepared in four steps: (i) Friedel-Crafts type reaction of indole with β-nitrostyrenes,[2a] (ii) reduction of the corresponding nitro group to amine,[2b] (iii) formylation of the amine[1a] and (iv) Bischler-Napieralski cyclization[1b] using the reported procedures. The imines **1d-f** have been prepared by adopting the above mentioned four steps[1,2] used for the preparation of **1b-c** starting with the appropriate indole and β-nitrostyrene derivatives. The imine **1g** was prepared in four steps: (i) condensation of indole-3-carbaldehyde and nitroethane,[3a] (ii) reduction of the corresponding nitro group,[3b] (iii) formylation of the amine[1a] and (iv) Bischler-Napieralski cyclization[1b]using the reported procedures.Alkyl substituted TosMIC derivatives**2b-d** have been synthesized by alkylation of TosMIC using the reported procedure.[4] Aryl substituted TosMIC derivatives**2e-l** have been synthesized from sodium salt of sodium 4-methylbenzenesulfinate in three steps: (i) hydrolysis of the 4-methylbenzenesulfinate,[5a] (ii) reaction of sulfinic acid with aryl aldehyde and formamide to give N-(aryl(tosyl)methyl)formamide,[5a-d] (iii) dehydration.[5a-d]

Spectral data of 1d-f:



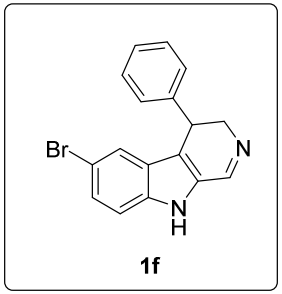
1d

4-(4-Chlorophenyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (1d): on 1 mmol scale for Bischler-Napieralski cyclizationreaction; Yellow solid, 252 mg, (0.900 mmol), 90%, R_f = 0.3 (DCM/MeOH, 98:2); **MP**: 120-122 ^{o}C; **IR** ($CHCl_3$): 1014, 1157, 1453, 1672, 2924, 3376 cm^{-1};**^{1}H NMR** (400 MHz, DMSO-d_6): δ = 3.82-3.91 (m, 1H), 4.02-4.09 (m, 1H), 4.40 (t, *J* = 8.1 Hz, 1H), 6.93 (t, *J* = 7.4 Hz, 1H), 7.01 (d, *J* = 8.0 Hz, 1H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.45 (d, *J* = 8.3 Hz, 1H), 8.48 (s, 1H), 11.55 (br, s, 1H); **MS** (ESI):*m/z* 281 $[M+H]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{17}H_{14}N_2Cl[M+H]^+$, 281.0840; found, 281.0851.



1e

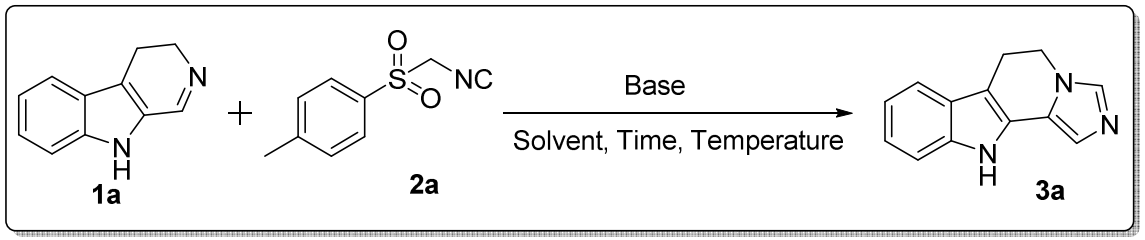
4-(4-(Trifluoromethyl)phenyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (1e): on 1 mmol scale for Bischler-Napieralski cyclizationreaction; Yellow solid, 0.194 mg, (0.620 mmol), 62%, R_f = 0.4 (DCM/MeOH, 98:2); **MP**: 132-134 ^{o}C; **IR** ($CHCl_3$): 1065, 1112, 1326, 1621, 2926, 3417 cm^{-1}; **^{1}H NMR** (500MHz, $CDCl_3$) δ = 3.77-3.97 (m, 1H), 4.16-4.28 (m, 1H), 4.40-4.49 (m, 1H), 6.95-7.05 (m, 2H), 7.27-7.44 (m, 4H), 7.53-7.64 (s, 2H), 8.50 (s, 1H), 8.64 (br, s, 1H); **MS** (ESI) m/z 315 $[M+H]^+$**HRMS** (ESI, m/z): calcd for $C_{18}H_{14}N_2F_3[M+H]^+$ 315.1104, found 315.1117.



1f

6-Bromo-4-phenyl-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (1f): on 1 mmol scale for Bischler-Napieralski cyclizationreaction; Yellow solid, 0.305 mg, (0.940 mmol), 94%, R_f = 0.4 (DCM/MeOH, 98:2); **MP**: 145-147 ^{o}C; **IR** ($CHCl_3$): 1019, 1311, 1452, 1628, 2924, 3416 cm^{-1}; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 3.83-3.94 (m,1H), 4.02-4.12 (m, 1H), 4.33-4.41 (m, 1H), 6.90 (dd, *J* = 11.0, 3.9 Hz, 1H), 6.97 (d, *J* = 8.1 Hz, 2H), 7.13-7.32 (m, 5H), 7.43 (dd, *J* = 8.5, 4.0 Hz, 1H), 8.49 (br, s, 1H); **MS** (ESI):*m/z* 325 $[M+H]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{17}H_{14}N_2Br[M+H]^+$, 325.0335; found 325.0349.

3. General procedure for the optimization study



In a 15 mL screw caped vial 4,9-dihydro-3*H*-pyrido[3,4-*b*]indole **1a** (0.5 mmol), *p*-toluenesulfonylmethyl isocyanide **2a** (0.75 mmol) and solvent, were taken, then the reaction vial was closed in the presence of air and the reaction mixture was allowed to stirred at specified temperature and time. After completion of the reaction, reaction mixture (heterogeneous in case of water as a solvent) was diluted with water (50 mL), extracted with dichloromethane (2 x 40 mL), dried over on anhydrous Na_2SO_4 and the filtrate was concentrated under reduced pressure. The crude was purified by column chromatography (DCM/MeOH, 98:2) on silica gel to afford the *N*-fused imidazole **3a**.

4. Optimization survey

Table 1

Entry[a]	Solvent	Temp. (^oC)	Time (h)	Concentration (M)	% Yield of 3a[b]
1.	Tap water	RT	2	0.1 M	76
2.	Tap water	40	2	0.1 M	74
3.	Tap water	50	2	0.1 M	73
4.	Tap water	60	2	0.1 M	71

5.	Tap water	80	2	0.1 M	65
6.	Tap water	100	2	0.1 M	40
7.	Tap water	RT	12	0.1 M	76
8.	t-BuOH	RT	2	0.1 M	74
9.	EtOH	RT	2	0.1 M	76
10.	t-AmOH	RT	2	0.1 M	72
11.	DMSO	RT	2	0.1 M	48
12.	DMF	RT	2	0.1 M	40
13.	THF	RT	2	0.1 M	30
14.	Toluene	RT	2	0.1 M	64
15.	Neat	RT	2	_	51
16.	Distilled water	RT	2	0.1 M	76
17.	HPLC grade water	RT	2	0.1 M	76
18.	**Tap water**	**RT**	**2**	**0.2 M**	**81**
19.	Tap water	RT	2	0.2 M	85[c]
20.	Tap water	RT	2	0.2 M	74[d]

21.	Tap water	RT	2	0.5 M	81
22.	Tap water	RT	2	0.05 M	70
23.	Tap water	60 ^{o}C	2	0.2 M	78
24.	Tap water	80 ^{o}C	2	0.2 M	72
25.	Tap water	100 ^{o}C	2	0.2 M	61
26.	Tap water	RT	4	0.2 M	81
27.	Tap water	RT	6	0.2 M	81
28.	Tap water	RT	12	0.2 M	81
29.	Tap water	RT	24	0.2 M	81

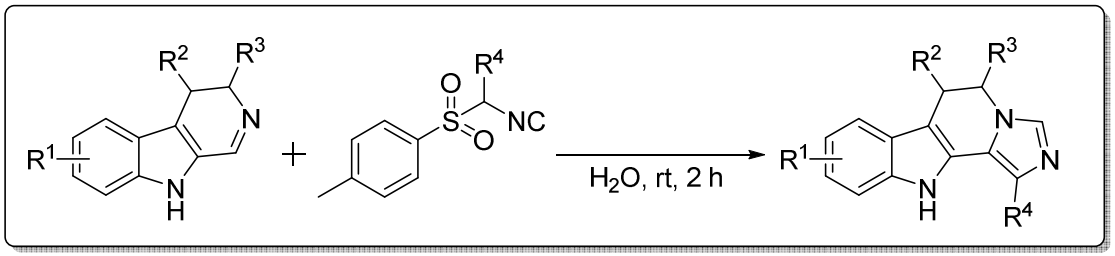
a) Reaction conditions: **1a** (0.5 mmol), **2a** (0.75 mmol). b) Isolated yields

c) entry 19: base (0.75 mmol) was used

d) entry 20: 1.2 equiv (0.6 mmol) of TosMIC **2a** was used

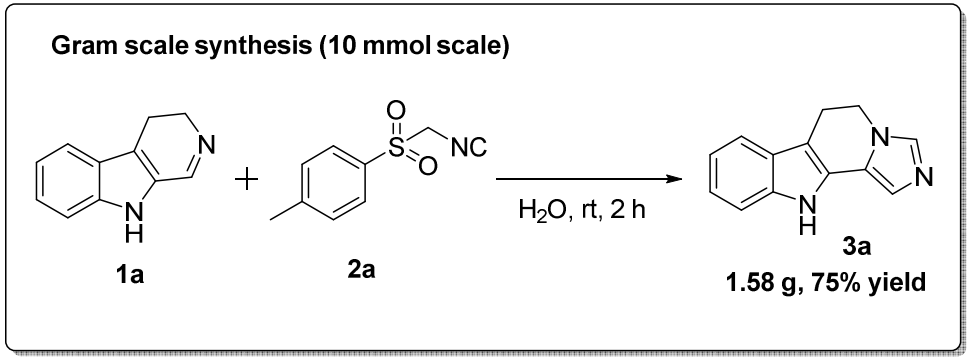
Tap water (pH = 7.85); Distilled water (pH = 7.34); HPLC grade water (pH = 7.65)

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



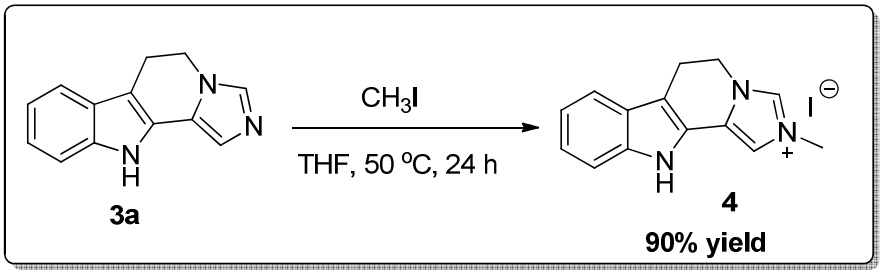
General procedure for the synthesis of 3a-r: In a 15 mL screw caped vial 4,9-dihydro-3*H*-pyrido[3,4-*b*]indoles **1a-g** (0.5 mmol), *p*-toluenesulfonylmethyl isocyanides **2a-l** (0.75 mmol) and H_2O (2.5 mL) were taken. The reaction mixture was allowed to stir at room temperature for 2 h. After this time, the heterogeneous reaction mixture was diluted with water (50 mL), extracted with dichloromethane (25 mL), dried over anhydrous Na_2SO_4 and the filtrate was concentrated under reduced pressure. Thus obtained crude was purified by column chromatography (DCM/MeOH, 98:2) on silica gel to afford 6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole derivatives **3a-r**.

6. Gram scale synthesis of 6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole 3a



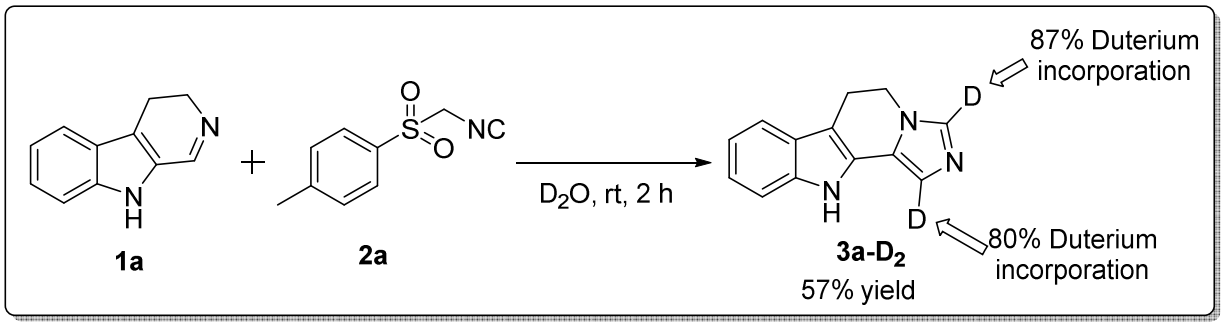
Gram scale synthesis of 6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole 3a: In a 100 mL round bottom flask 4,9-dihydro-3*H*-pyrido[3,4-*b*]indole **1a** (10 mmol, 1.70 g), *p*-toluenesulfonylmethyl isocyanide **2a** (15 mmol, 2.93 g) and H_2O (40 mL) were taken, then the round bottom flask was closed in the presence of air and the reaction mixture was allowed to be stirred at room temperature for 2 h. After completion of the reaction, reaction mixture was diluted with water (150 mL), extracted with dichloromethane (2 x 200 mL), dried over on anhydrous Na_2SO_4 and filtrate was concentrated under reduced pressure. The crude was purified by column chromatography (DCM/MeOH, 98:2) on silica gel to afford the 6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole **3a** (1.57 g) as a light yellow color solid in 75% yield.

7. Experimental procedure for NHC precatalyst 4



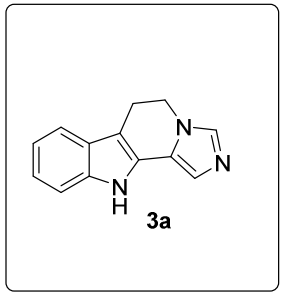
Experimental procedure for the synthesis of NHC pre-catalysts 4: To a solution of 6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole **3a** (0.5 mmol, 105 mg) in anhydrous THF (7.5 mL) was added CH_3I (2.5 mmol, 0.15 mL). The reaction mixture was stirred at 50 ^oC for 24 h; a light yellow colored precipitate was formed, which was collected by filtration and washed with anhydrous THF to afford the NHC pre-catalyst **4.**

8. Control experiments and mechanistic studies



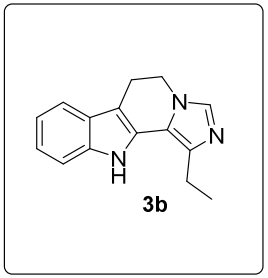
Experimental procedure for the synthesis of 3a-D_2: In a 15 mL screw caped vial 4,9-dihydro-3*H*-pyrido[3,4-*b*]indole **1a** (0.5 mmol, 85 mg), *p*-toluenesulfonylmethyl isocyanide **2a** (0.75 mmol, 146 mg) and D_2O (5 mL) were taken, then the reaction vial was closed in the presence of air and the reaction mixture was allowed to stir at room temperature for 2 h. After completion of the reaction, the heterogeneous reaction mixture was extracted with dichloromethane (2 x 20 mL), dried over on anhydrous Na_2SO_4 and concentrated. The crude was purified by column chromatography (DCM/MeOH, 98:2) on silica gel to afford the 6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole-1,3-d2 **3a-D_2**.

9. Spectral data of products 3a-r, 3a-D_2, 4



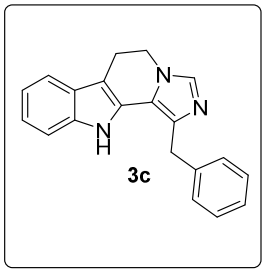
3a

6,11-Dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (**3a**)**:** Light yellow solid, 85 mg (0.407 mmol), 81%, R_f = 0.3 (DCM/MeOH, 98:2); **MP**: 162-164 °C; **IR** ($CHCl_3$): 1020, 1415, 1449, 2830, 2942, 3315 cm^{-1}; **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 3.08 (t, *J* = 6.9 Hz, 2H), 4.26 (t, *J* = 6.9 Hz, 2H), 7.01 (t, *J* = 7.4 Hz, 1H), 7.08 (t, *J* = 7.4 Hz, 1H), 7.13 (s, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 7.7 Hz, 1H), 7.76 (s, 1H), 11.49 (br, s, 1H); **^{13}C{H}NMR** (101 MHz, DMSO-d_6): δ = 20.4, 42.5, 105.4, 111.3, 118.1, 119.1, 121.3, 121.7, 123.9, 126.0, 126.3, 136.6, 137.3; **MS** (ESI): *m/z* 210 $[M + H]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{13}H_{12}N_3$ $[M + H]^+$, 210.1026; found, 210.1017.

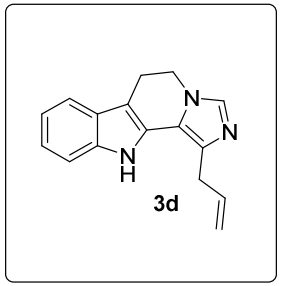


3b

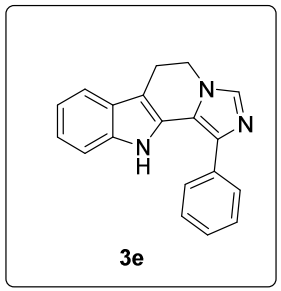
1-Ethyl-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3b): Yellow solid, 91 mg (0.384 mmol), 77%, R_f = 0.5 (DCM/MeOH, 98:2); **MP**: 164-166 °C; **IR** ($CHCl_3$): 1020, 1113, 1414, 1449, 1660, 2943, 3322 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 1.38 (t, *J* = 7.6 Hz, 3H), 2.86 (q, *J* = 7.6 Hz, 2H), 3.16 (t, *J* = 6.8 Hz, 2H), 4.22 (t, *J* = 6.8 Hz, 2H), 7.12-7.23 (m, 2H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.50-7.51 (m, 2H), 8.25 (br, s, 1H); **^{13}C{H}NMR** (101 MHz, $CDCl_3$): δ = 14.4, 21.1, 21.9, 43.3, 106.3, 111.2, 118.1, 119.2, 120.3, 122.1, 126.5, 126.8, 135.7, 136.7, 137.2; **MS** (ESI): *m/z* 238 $[M + H]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{15}H_{16}N_3$ $[M + H]^+$, 238.1339; found, 238.1329.



1-Benzyl-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3c): Light yellow solid, 113 mg (0.378 mmol), 76%, R_f = 0.4 (DCM/MeOH, 98:2); **MP**: 100-102 °C; **IR** ($CHCl_3$): 1020, 1113, 1414, 1449, 1660, 2831, 2943, 3322 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 3.12 (t, *J* = 6.7 Hz, 2H), 4.21 (t, *J* = 6.6 Hz, 2H), 4.25 (s, 2H), 7.05-7.15 (m, 4H), 7.34 (d, *J* = 6.4 Hz, 1H), 7.36-7.42 (m, 4H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.57 (s, 1H); **^{13}C{H}NMR** (126 MHz, $CDCl_3$): δ = 20.8, 31.9, 43.6, 111.2, 118.1, 120.1, 120.9, 122.2, 122.8, 125.8, 126.0, 126.9, 128.3, 129.1, 130.4, 136.5, 137.6; **MS** (ESI): *m/z* 300 $[M + H]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{20}H_{18}N_3$ $[M + H]^+$, 300.1495; found, 300.1495.

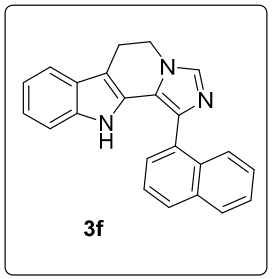


1-Allyl-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3d): Light yellow solid, 97 mg (0.389 mmol), 78%, R_f = 0.6 (DCM/MeOH, 98:2); **MP**: 166-168 °C; **IR** ($CHCl_3$): 1017, 1113, 1410, 1449, 1658, 2833, 2944, 3330 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 3.15 (t, *J* = 6.9 Hz, 2H), 3.65 (d, *J* = 6.2 Hz, 2H), 4.22 (t, *J* = 6.8 Hz, 2H), 5.29-5.37 (m, 2H), 6.18-6.24 (m, 1H), 7.10-7.20 (m, 2H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.49-7.50 (m, 1H), 7.52 (s, 1H), 8.57 (br, s, 1H); **^{13}C{H}NMR** (126 MHz, $CDCl_3$): δ = 21.0, 33.5, 43.5, 106.4, 111.3, 116.3, 118.1, 120.3, 120.7, 122.1, 126.4, 129.8, 133.3, 135.6, 136.7, 137.6; **MS** (ESI): *m/z* 250 $[M + H]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{16}H_{16}N_3$ $[M + H]^+$, 250.1339; found, 250.1328.



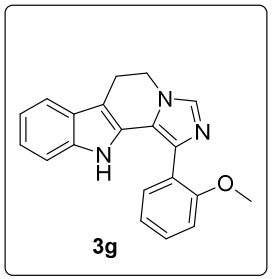
3e

1-Phenyl-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3e): Yellow solid, 101 mg (0.354 mmol), 71%, R_f = 0.4 (DCM/MeOH, 98:2); **MP**: 144-146 °C; **IR** ($CHCl_3$): 1024, 1219, 1643, 2132, 2260, 3360 cm^{-1}; **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 3.11 (t, *J* = 6.6 Hz, 2H), 4.23 (t, *J* = 6.6 Hz, 2H), 7.01-7.09 (m, 2H), 7.34 (t, *J* = 7.3 Hz, 1H), 7.41-7.53 (m, 4H), 7.80 (d, *J* = 7.5 Hz, 2H), 7.87 (s, 1H), 10.76 (br, s, 1H); **^{13}C{H}NMR** (101 MHz, DMSO-d_6): δ = 20.9, 43.4, 108.5, 112.8, 118.3, 119.9, 120.1, 122.1, 126.5, 126.6, 127.1, 127.2, 129.2, 135.0, 135.5, 137.5, 138.1; **MS** (ESI): *m/z* 286 $[M + H]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{19}H_{16}N_3$ $[M + H]^+$, 286.1339; found, 286.1336.

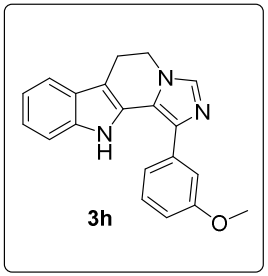


3f

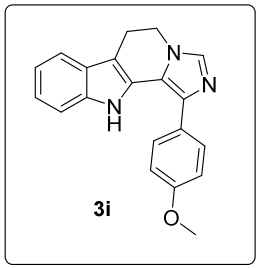
1-(Naphthalen-1-yl)-6,11-dihydro-5H-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3f): Light yellow solid, 128 mg (0.382 mmol), 77%, R_f = 0.4 (DCM/MeOH, 98:2); **MP**: 188-190 °C; **IR** ($CHCl_3$): 926, 1354, 1490, 1562, 1720, 2923, 3054 cm^{-1}; **^{1}H NMR** (500MHz, DMSO-d_6): δ = 3.10-3.20 (m, 2H), 4.20-4.30 (m, 2H), 7.01-7.06 (m, 2H), 7.41 (d, *J* = 7.3 Hz, 1H), 7.45-7.76 (m, 3H), 7.85-8.20 (m, 5H), 8.29 (s, 1H), 10.91 (br, s, 1H); **^{13}C{H}NMR** (101 MHz, DMSO-d_6): δ = 21.0, 43.5, 108.6, 112.8, 118.4, 119.9, 120.6, 122.1, 125.2, 126.0, 126.1, 126.5, 126.6, 126.7, 128.0, 128.6, 128.7, 132.7, 133.0, 134.0, 134.9, 138.0, 138.2; **MS** (ESI): *m/z* 336 $[M + H]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{23}H_{18}N_3$ $[M + H]^+$, 336.1495; found, 336.1493.



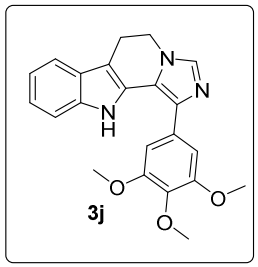
1-(2-Methoxyphenyl)-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3g): Light yellow solid, 116 mg (0.368 mmol), 74%, R_f = 0.6 (DCM/MeOH, 98:2); **MP**: 128-130 ^{o}C; **IR** ($CHCl_3$): 1087, 1278, 1443, 1463, 1578, 1598, 2923 cm^{-1}; **^{1}H NMR** (400MHz, DMSO-d_6): δ = 3.10 (t, *J* = 6.8 Hz, 2H), 3.69 (s, 3H), 4.27 (t, *J* = 6.8 Hz, 2H), 6.96-7.07 (m, 3H), 7.14 (d, *J* = 8.3 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.42-7.55 (m, 3H), 7.82 (s, 1H), 10.12 (br, s, 1H); **^{13}C{H}NMR** (75 MHz, DMSO-d_6): δ = 20.4, 42.9, 54.9, 106.1, 111.8, 111.9, 117.7, 119.0, 120.2, 121.0, 121.2, 124.1, 125.6, 126.7, 128.4, 130.9, 136.9, 137.0, 156.3; **MS** (ESI): *m/z* 316 $[M + H]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{20}H_{18}ON_3$ $[M + H]^+$, 316.1444; found, 316.1442.



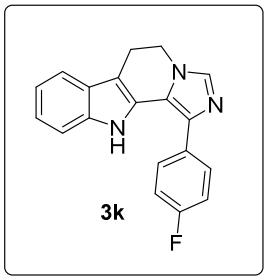
1-(3-Methoxyphenyl)-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3h): Light yellow solid, 118 mg (0.375 mmol), 75%, R_f = 0.6 (DCM/MeOH, 98:2); **MP**: 188-190 ^{o}C; **IR** ($CHCl_3$): 1024, 1381, 1463, 1492, 1548, 1679, 3395 cm^{-1}; **^{1}H NMR**(300MHz, DMSO-d_6): δ = 3.11 (t, *J* = 6.5 Hz, 2H), 3.80 (s, 3H), 4.23 (t, *J* = 6.5 Hz, 2H), 6.87-6.93 (m, 1H), 7.00-7.12 (m, 2H), 7.34-7.46 (m, 4H), 7.52 (d, *J* = 7.4 Hz, 1H), 7.87 (s, 1H), 10.86 (br, 1H); **^{13}C{H}NMR** (75 MHz,DMSO-d_6): δ = 20.4, 43.0, 54.8, 108.1, 111.1, 112.2, 113.2, 117.9, 118.8, 119.4, 119.6, 121.6, 125.9, 126.0, 129.8, 134.3, 136.1, 137.0, 137.4, 159.4; **MS** (ESI): *m/z* 316 $[M + H]^+$**HRMS** (ESI, *m/z*): calcd for $C_{20}H_{18}ON_3$ $[M + H]^+$, 316.1444; found, 316.1443.



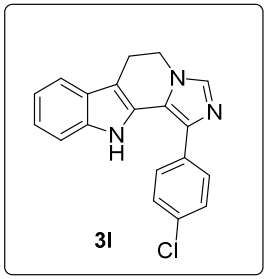
1-(4-Methoxyphenyl)-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3i): Light yellow solid, 126 mg (0.400 mmol), 80%, R_f = 0.4 (DCM/MeOH, 98:2); **MP**: 184-186 °C; **IR** ($CHCl_3$): 1319, 1412, 1455, 1529, 1646, 3337 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 3.21 (t, *J* = 6.8 Hz, 2H), 3.89 (s, 3H), 4.26 (t, *J* = 6.8 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 2H), 7.09-7.20 (m, 2H), 7.31 (d, *J* = 7.3 Hz, 1H), 7.52 (d, *J* = 7.0 Hz, 1H), 7.60 (s, 1H), 7.70 (d, *J* = 8.4 Hz, 2H), 8.25 (br, s, 1H); **^{13}C{H}NMR** (126 MHz, $CDCl_3$): δ = 20.9, 43.6, 55.4, 107.3, 111.3, 114.6, 118.1, 119.5, 120.3,122.4, 126.3, 127.7, 128.6, 129.2, 135.5,136.1, 136.7, 159.3; **MS** (ESI): *m/z* 316 $[M + H]^+$ **HRMS** (ESI, *m/z*): calcd for $C_{20}H_{18}ON_3$ $[M + H]^+$ 316.1444; found, 316.1442. The spectroscopic data were in good agreement with the reported data.[6]



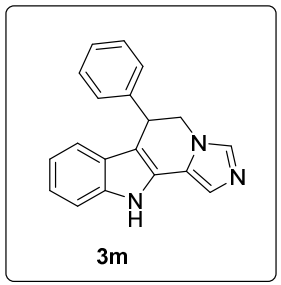
1-(3,4,5-Trimethoxyphenyl)-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3j): Yellow solid, 136 mg (0.363 mmol), 73%, R_f = 0.3 (DCM/MeOH, 98:2); **MP**: 130-132 °C; **IR** ($CHCl_3$): 1020, 1419, 1448, 2830, 2945, 3319 cm^{-1}; **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 3.11 (t, *J* = 6.7 Hz, 2H), 3.73 (s, 3H), 3.82 (s, 6H), 4.23 (t, *J* = 6.7 Hz, 2H), 7.04-7.08 (m, 2H), 7.10 (s, 2H), 7.42 (d, *J* = 7.1 Hz, 1H), 7.51 (d, *J* = 7.1 Hz, 1H), 7.88 (s, 1H), 10.95 (br, s, 1H); **^{13}C{H}NMR** (126 MHz, DMSO-d_6): δ = 34.2, 49.1, 60.9, 65.3, 109.4, 110.3, 117.5, 123.6, 125.0, 127.8, 130.8, 133.3, 134.7, 134.9, 142.6, 143.0, 150.7, 157.8, 158.5; **MS** (ESI): m/z 376 $[M + H]^+$ **HRMS** (ESI, m/z): calcd for $C_{22}H_{22}N_3O_3$ $[M + H]^+$, 376.1656; found, 376.1662.



1-(4-Fluorophenyl)-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3k): Light yellow solid, 113 mg (0.373 mmol), 75%, R_f = 0.4 (DCM/MeOH, 98:2); **MP**: 108-110°C; **IR** ($CHCl_3$): 1013, 1222, 1503, 1702, 2852, 2967, 3305 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.21 (t, *J* = 6.9 Hz, 2H), 4.25 (t, *J* = 6.9 Hz, 2H), 7.11-7.21 (m, 4H),7.31 (d, *J* = 7.5 Hz, 1H), 7.52 (d, *J* = 7.4 Hz, 1H), 7.61 (s, 1H), 7.70-7.75 (m, 2H), 8.23 (br, s, 1H); **^{13}C{H}NMR** (101 MHz, $CDCl_3$): δ = 20.9, 43.6, 107.9, 111.4, 116.0 (*J* = 22.0 Hz), 118.2, 120.0, 120.4, 122.7, 125.9, 126.3, 128.9 (*J* = 8.0 Hz), 129.0, 131.2, 134.4, 136.3, 136.8, 161.1, 163.5; **MS** (ESI): *m/z* 304 $[M + H]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{19}H_{15}FN_3$ $[M + H]^+$, 304. 1244; found, 304.1243.

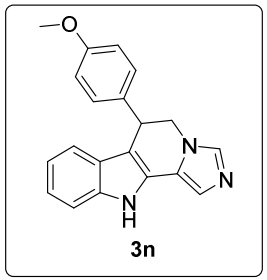


1-(4-Chlorophenyl)-6,11-dihydro-5H-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3l): Light yellow solid, 124 mg (0.389 mmol), 78%, R_f = 0.6 (DCM/MeOH, 98:2); **MP**: 100-102°C; **IR** ($CHCl_3$): 1090, 1444, 1575, 1670, 2851, 2922 cm^{-1}; **^{1}H NMR** (300MHz, DMSO-d_6) δ = 3.11 (t, *J* = 6.7 Hz, 2H), 4.23 (t, *J* = 6.7 Hz, 2H), 7.01-7.11 (m, 2H), 7.38-7.47 (m, 1H), 7.51 (d, *J* = 8.4 Hz, 3H), 7.78 (d, *J* = 8.5 Hz, 2H), 7.89 (s, 1H), 10.81 (br, s, 1H); **^{13}C{H}NMR** (75 MHz, DMSO-d_6): δ = 20.4, 42.9, 108.2, 112.2, 117.9, 119.4, 119.9, 121.7, 125.8, 125.9, 128.3, 128.7, 131.1, 133.2, 133.8, 137.0, 137.7; **MS** (ESI): *m/z* 320 $[M + H]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{19}H_{15}ClN_3$ $[M + H]^+$, 320.0949; found, 320.0948.



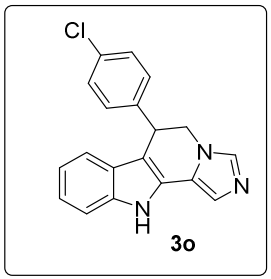
3m

6-Phenyl-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3m): Yellow solid, 100 mg (0.351 mmol), 70%, R_f = 0.4 (DCM/MeOH, 98:2); **MP**: 138-140 ^{o}C; **IR** ($CHCl_3$): 1024, 1219, 1643, 2132, 2260, 3360 cm^{-1}; **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 4.36-4.41 (m, 1H), 4.47-4.59 (m, 1H), 4.66-4.72 (m, 1H), 6.87 (d, *J* = 7.0 Hz, 1H), 6.97 (d, *J* = 7.4 Hz, 1H), 7.01-7.09 (m, 1H), 7.14-7.28 (m, 6H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.74 (s, 1H), 11.68 (br, s, 1H); **^{13}C{H}NMR** (75 MHz, DMSO-d_6): δ = 43.4, 54.9, 113.7, 116.7, 123.5, 124.4, 126.6, 127.4, 128.9, 131.1, 131.6, 132.1, 132.9, 133.7, 142.0, 142.7, 147.6; **MS** (ESI): *m/z* 286 $[M + H]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{19}H_{16}N_3$ $[M + H]^+$, 286.1339; found, 286.1325.



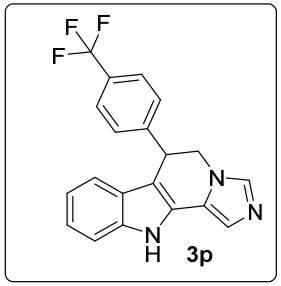
3n

6-(4-Methoxyphenyl)-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3n): Light yellow solid, 108 mg (0.342 mmol), 69%, R_f = 0.4 (DCM/MeOH, 98:2); **MP**: 126-130 ^{o}C; **IR** ($CHCl_3$): 1085, 1445, 1511, 1692, 2853, 2924, 3327 cm^{-1}; **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 3.69 (s, 3H), 4.32 (dd, *J* = 12.8, 5.6 Hz, 1H), 4.45 (dd, *J* = 12.5, 5.7 Hz, 1H), 4.62 (t, *J* = 5.4 Hz, 1H), 6.85 (dd, *J* = 19.3, 8.0 Hz, 3H), 6.96 (d, *J* = 7.8 Hz, 1H), 7.06 (dd, *J* = 16.7, 8.1 Hz, 3H), 7.24 (s, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.80 (s, 1H), 11.67 (br, s, 1H); **^{13}C{H}NMR** (75 MHz, DMSO-d_6): δ = 37.3, 49.8, 54.9, 108.7, 111.3, 118.3, 119.1, 121.3, 122.0, 123.6, 125.8, 126.2, 128.6, 134.1, 136.7,137.3, 158.0; **MS** (ESI): *m/z* 316 $[M + H]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{20}H_{18}N_3O$ $[M + H]^+$, 316.1442; found, 316.1444.



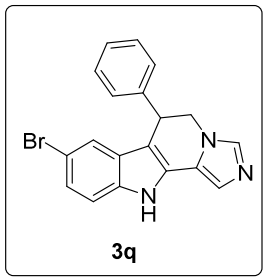
3o

6-(4-Chlorophenyl)-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3o): Yellow solid, 108 mg (0.338 mmol), 68%, R_f = 0.3 (DCM/MeOH, 98:2); **MP**: 128-130 ^{o}C; **IR** ($CHCl_3$): 770, 1142, 1682, 2853, 2923, 3254 cm^{-1}; **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 4.41 (dd, *J* = 13.0, 5.2 Hz, 1H), 4.50 (dd, *J* = 13.0, 5.8 Hz, 1H), 4.74 (t, *J* = 5.4 Hz, 1H), 6.90 (t, *J* = 7.4 Hz, 1H), 7.02 (d, *J* = 7.9 Hz, 1H), 7.08 (t, *J* = 7.1 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 5.9 Hz, 2H), 7.34 (s, 1H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.95 (s, 1H), 11.77 (br, s, 1H); **^{13}C{H}NMR** (75 MHz, DMSO-d_6): δ = 37.2, 49.7, 108.4, 111.6, 118.3, 119.4, 120.6, 121.7, 125.6, 125.8, 127.6, 128.4, 129.5, 131.5, 136.9, 137.1, 141.2; **MS** (ESI): *m/z* 320 $[M + H]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{19}H_{15}ClN_3$ $[M + H]^+$, 320.0949; found, 320.0949.



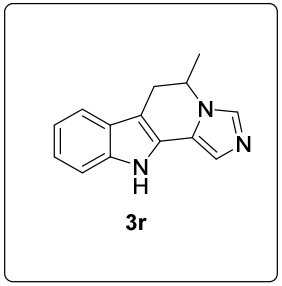
3p

6-(4-(Trifluoromethyl)phenyl)-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3p): Yellow solid, 114 mg (0.323 mmol), 65%, R_f = 0.4 (DCM/MeOH, 98:2); **MP**: 116-118 ^{o}C; **IR** ($CHCl_3$): 768, 1420, 1680, 2853, 2924, 3305 cm^{-1}; **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 4.44 (m, 2H), 4.50 (dd, *J* = 13.0, 5.8 Hz, 1H), 6.90 (t, *J* = 7.4 Hz, 1H), 7.02-7.12 (m, 2H), 7.25 (s, 1H), 7.38 (dd, *J* = 17.8, 8.1 Hz, 3H), 7.63 (d, *J* = 8.1 Hz, 2H), 7.73 (s, 1H), 11.75 (br, s, 1H); **^{13}C{H}NMR** (75 MHz, DMSO-d_6): δ = 37.6, 48.8, 107.5, 111.5, 118.0, 119.4, 121.5, 122.3, 123.5, 125.3, 125.4, 125.7, 126.5, 127.7, 128.4, 136.8, 137.6, 147.4; **MS** (ESI): *m/z* 354 $[M + H]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{20}H_{15}F_3N_3$ $[M + H]^+$, 354. 1213; found, 354.1214.



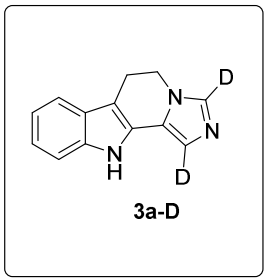
3q

8-Bromo-6-phenyl-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3q): Yellow solid, 127 mg (0.350 mmol), 70%, R_f = 0.4 (DCM/MeOH, 98:2); **MP**: 184-186 °C; **IR** ($CHCl_3$): 667, 1024, 1219, 1643, 2132, 2260, 3360 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 4.21-4.30 (m, 1H), 4.40-4.50 (m, 1H), 4.52-4.65 (m, 1H), 6.94 (dd, *J* = 17.9, 8.0 Hz, 1H), 7.06 (s, 1H), 7.19 (dd, *J* = 13.7, 8.3 Hz, 2H), 7.24 (s, 1H), 7.29 (s, 2H), 7.30 (s, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.54 (s, 1H), 9.42 (br, s, 1H); **^{13}C{H}NMR** (101 MHz, $CDCl_3$): δ = 39.6, 50.8, 112.7, 113.4, 119.2, 120.2, 121.6, 122.5, 125.2, 127.4, 127.7, 127.9, 128.1, 128.9, 129.0, 135.7, 140.6; **MS** (ESI): *m/z* 364 $[M + H]^+$; **HRMS** (ESI, *m/z*) calcd for $C_{19}H_{15}BrN_3$ $[M + H]^+$, 364.0444, found 364.0448.



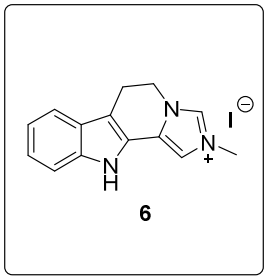
3r

5-Methyl-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole (3r): Light yellow solid, 73 mg (0.327 mmol), 66%, R_f = 0.3 (DCM/MeOH, 98:2); **MP**: 106-108 °C; **IR** ($CHCl_3$): 1077, 1185, 1448, 1720, 2925, 3061 cm^{-1}; **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 1.53 (d, *J* = 6.5 Hz, 3H), 2.81 (dd, *J* = 15.8, 8.3 Hz, 1H), 3.21 (dd, *J* = 15.8, 5.7 Hz, 1H), 4.49 (dd, *J* = 14.2, 6.2 Hz, 1H), 6.97-7.04 (m, 1H), 7.05-7.12 (m, 1H), 7.19 (s, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.87 (s, 1H), 11.50 (br, s, 1H); **^{13}C{H}NMR** (126 MHz, DMSO-d_6): δ = 20.3, 28.0, 49.8, 104.6, 111.8, 111.3, 117.9, 118.0, 119.1, 121.3, 121.9, 125.6, 126.4, 136.7; **MS** (ESI): *m/z* 224 $[M + H]^+$; **HRMS**(ESI, *m/z*) calcd for $C_{14}H_{14}N_3$ $[M + H]^+$, 224.1182; found, 224.1184.



3a-D

6,11-Dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole-1,3-d2 (3a-D_2): Light yellow solid, 60 mg (0.284 mmol), 57%, R_f = 0.3 (DCM/MeOH, 98:2); **MP**: 163-165 ^oC; **IR** (KBr): 1098, 1329, 1430, 1663, 2925, 3255 cm^{-1}; **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 3.08 (t, *J* = 6.9 Hz, 2H), 4.26 (t, *J* = 6.9 Hz, 2H), 6.98-7.04 (m, 1H), 7.05-7.11 (m, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 8.0Hz, 1H), 11.49 (br, s, 1H); **^{13}C{H}NMR** (126 MHz, DMSO-d_6): δ = 20.8, 43.0, 105.8, 111.7, 111.8, 118.5, 119.6, 121.8, 124.2, 126.5, 126.7, 137.0, 137.1; **MS** (ESI): *m/z* 212 $[M]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{13}H_9{}^2H_2N_3$ $[M]^+$, 212.1136; found, 212.1140.



6

2-Methyl-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indol-2-ium iodide (4):- Light yellow solid, 158 mg (0.450 mmol), 90%, **MP**: 268-270 ^oC; **IR** (KBr): 1014, 1219, 1644, 2844, 2953, 3289 cm^{-1}; **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 3.23 (t, *J* = 7.0 Hz, 2H), 3.94 (s, 3H), 4.50 (t, *J* = 7.0 Hz, 2H), 7.11 (t, *J* = 7.2 Hz, 1H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.48 (d, *J* = 8.2 Hz, 1H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.68 (s, 1H), 9.21 (s, 1H), 11.87 (br, s, 1H); **^{13}C{H}NMR** (75 MHz, DMSO-d_6): δ = 19.2, 36.1, 44.4, 109.3, 111.9, 114.9, 119.1, 119.9, 121.4, 123.3, 125.4, 136.5, 137.1; **MS** (ESI): *m/z* 224 $[M]^+$; **HRMS** (ESI, *m/z*): calcd for $C_{14}H_{14}N_3{}^+$ $[M]^+$, 224.1180; found, 224.1182.

10. References

1. 4,9-dihydro-3*H*-pyrido[3,4-*b*]indole **1a** preparation.

a) T. Lebleu, H. Kotsuki, J. Maddaluno and J. Legros, *Tetrahedron Lett.,* 2014, **55**, 362.

b) G. Huang, B. Kling, F. H. Darras, J. Heilmann and M. Decker, *Eur. J. Med. Chem*., 2014, **81***,* 15.

2. Substituted 4,9-dihydro-3*H*-pyrido[3,4-*b*]indole **1b-1f** preparation.

a) J. Xie, X. Zhu, M. Huang, F. Meng, M. Wang and Y. Wan, *Synth.Commun*., 2010, **40**, 3259.

b) J. Itoh, K. Fuchibe and T. Akiyama, *Angew. Chem., Int. Ed*., 2008, **47**, 4016.

3. Substituted 4,9-dihydro-3*H*-pyrido[3,4-*b*]indole **1g** preparation.

a) M. Rodrıguez-Mata, V. Gotor-Fernandez, J. Gonzalez-Sabin, F. Rebolledoa and V. Gotor, *Org. Biomol. Chem*., 2011, **9**, 2274.

b) D. Robaa, C. Enzensperger, S. E. AbulAzm, M. M. Hefnawy, H. I. El-Subbagh, T. A. Wani and J. Lehmann, *J. Med. Chem*., 2011, **54**, 7422.

4. Alkyl substituted *p*-toluenesulfonylmethyl isocyanides **2b**-**2d** preparation.

B. Wu, J. Wen, J. Zhang, J. Li, Y. -Z. Xiang and X. -Q. Yu, *Synlett,* 2009, **3**, 500.

5. Aryl substituted *p*-toluenesulfonylmethyl isocyanides **2e**-**2l** preparation.

a) F. Morana, A. Basso, M. Bella, R. Riva and L. Banfi, *Adv. Synth. Catal*., 2012, **354**, 2199.

b) W. Antuch, S. Menon, Q. -Z. Chen, Y. Lu, S. Sakamuri, B. Beck, V. Schauer-Vukašinović, S. Agarwal, S. Hess and A. Dömling, *Bioorg. Med. Chem. Lett*., 2006, **16**, 1740.

c) J. Sisko, M. Mellinger, P. W. Sheldrake and N. H.Baine, *Org. Syn.,* 2000*,* **77,** 198.

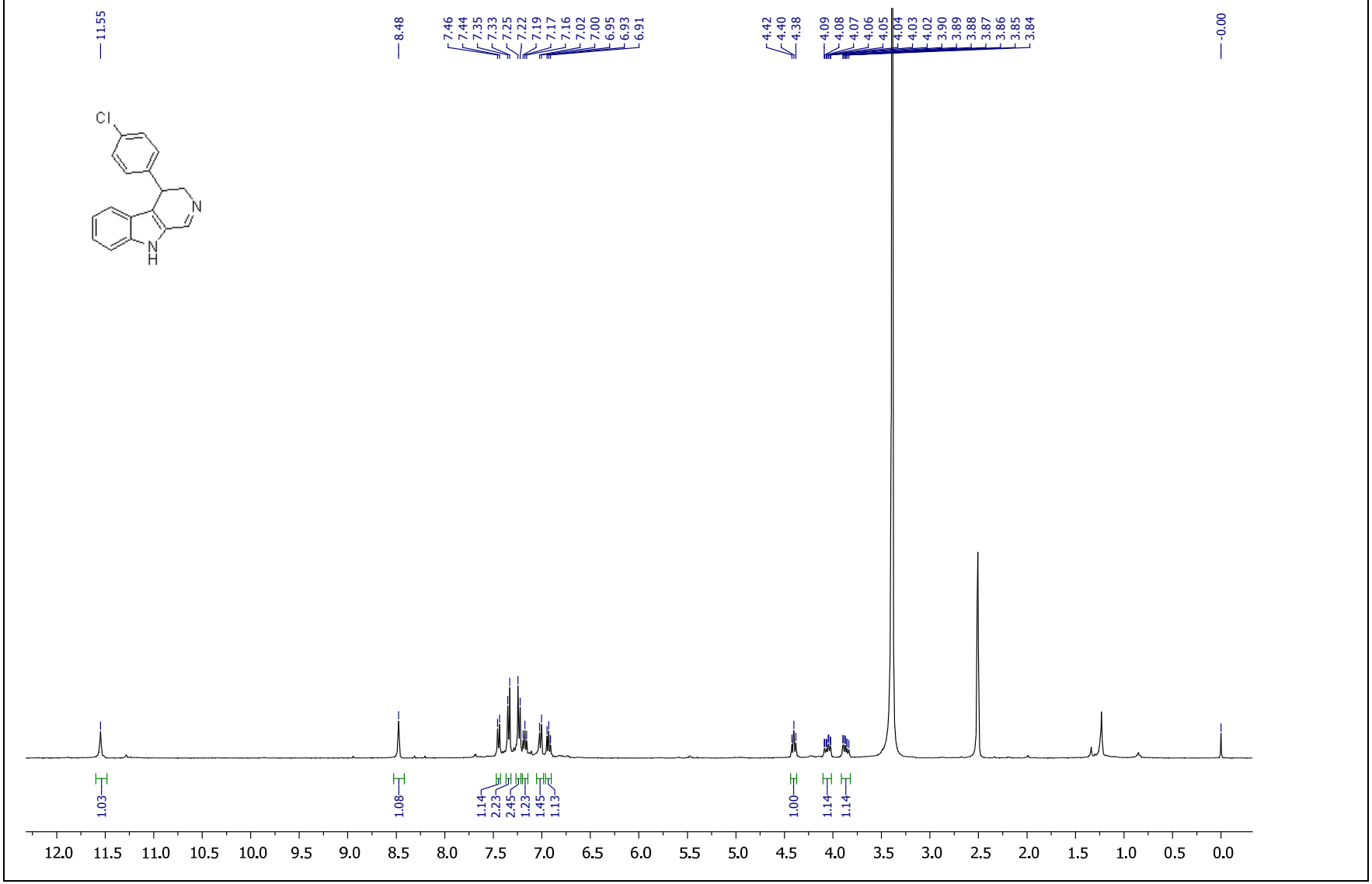
d) T. Stefański, R. Mikstacka, R. Kurczab, Z. Dutkiewicz, M. Kucińska, M. Murias, M. Zielińska-Przyjemska, M. Cichocki, A. Teubert, M. Kaczmarek, A. Hogendorf and S. Sobiak, *Eur. J. Med. Chem.,* 2018, **144,** 797.

6. 1-(4-methoxyphenyl)-6,11-dihydro-5*H*-imidazo[1',5':1,2]pyrido[3,4-*b*]indole **3i** spectral data.

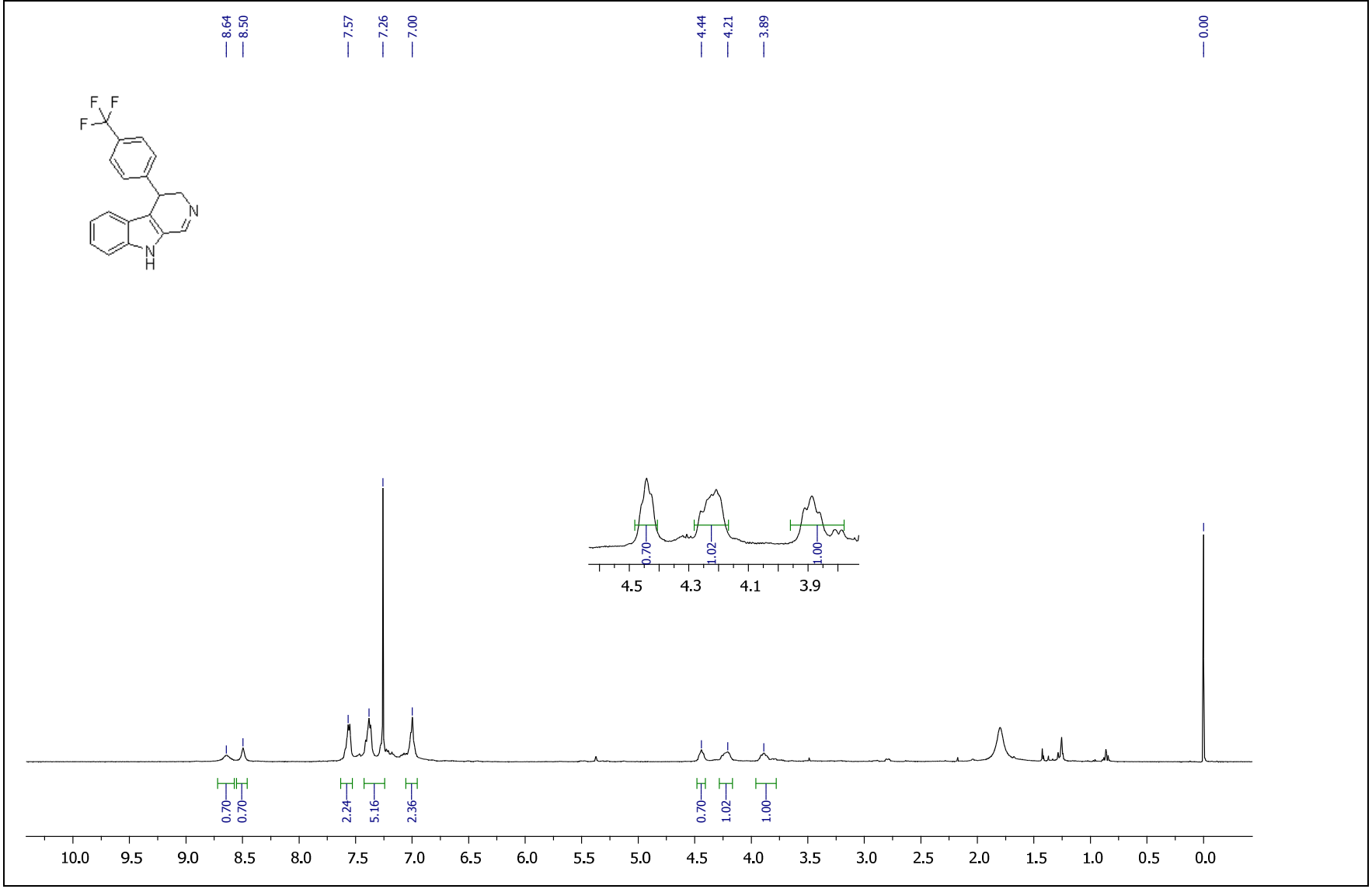
a. A. Silvani, G. Lesma, S. Crippa and V. Vece, *Tetrahedron,* 2014, **70**, 3994.

11. Copies of ^{1}H NMR spectra of the β-carboline imines 1d, 1f, 1e

^{1}H NMR of 1d



1H NMR of 1e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7.26
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3.89
0.00
F
F
F
N
H
0.70
1.02
1.00
4.5
4.3
4.1
3.9
0.70
0.70
2.24
5.16
2.36
0.70
1.02
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.5
3.0
2.5
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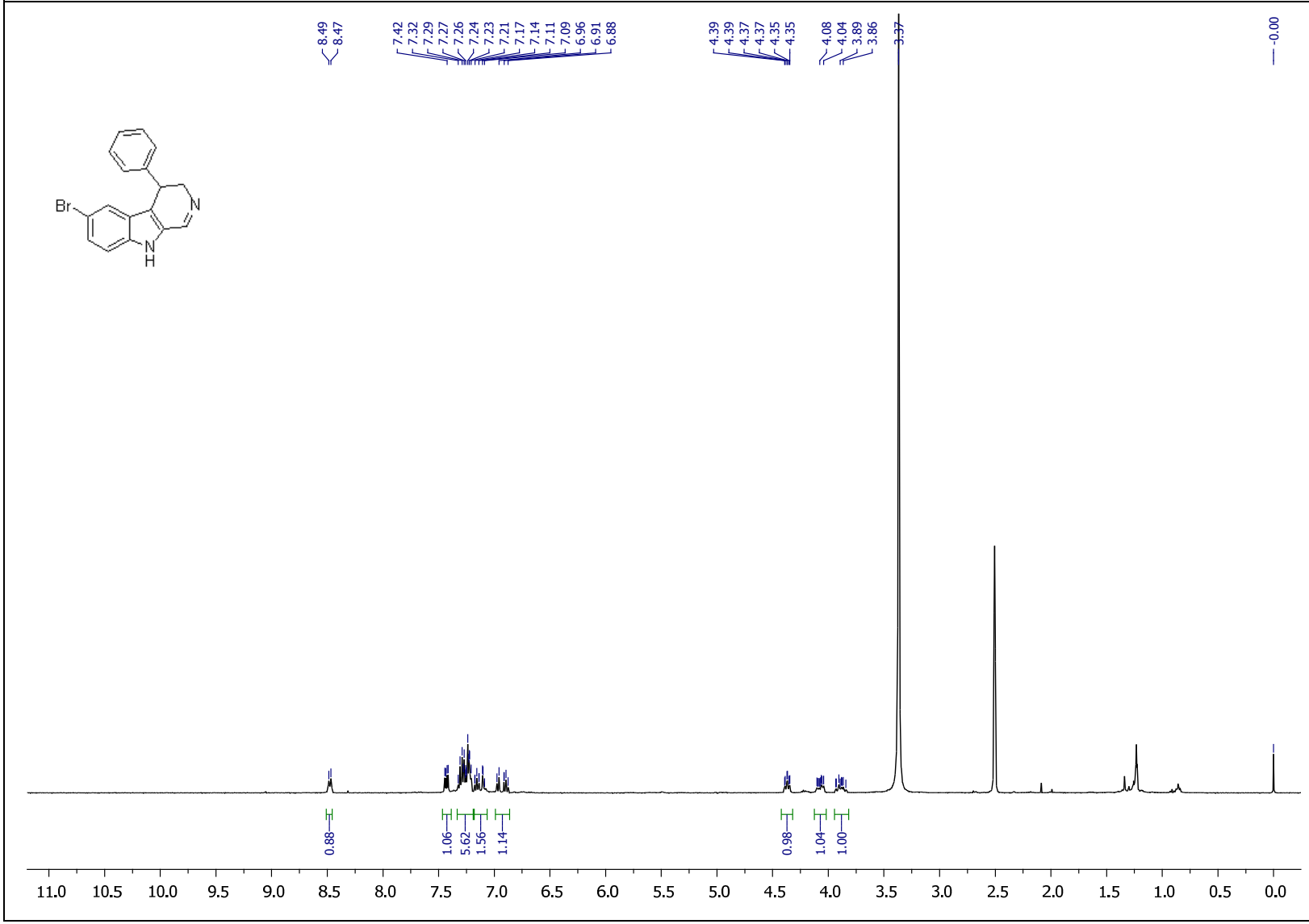
1.0
0.5
0.0

^{1}H NMR of 1f


8.49
8.47
7.42
7.32
7.29
7.27
7.26
7.24
7.23
7.21
7.17
7.14
7.11
7.09
6.96
6.91
6.88
4.39
4.39
4.37
4.37
4.35
4.35
4.08
4.04
3.89
3.86
3.37
-0.00
Br
N
N
H
0.88
1.06
5.62
1.56
1.14
0.98
1.04
1.00
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
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4.0
3.5
3.0
2.5
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0.0

12. Copies of ^{1}H and ^{13}C NMR spectra of the products 3a-r, 3a-D_2, 4

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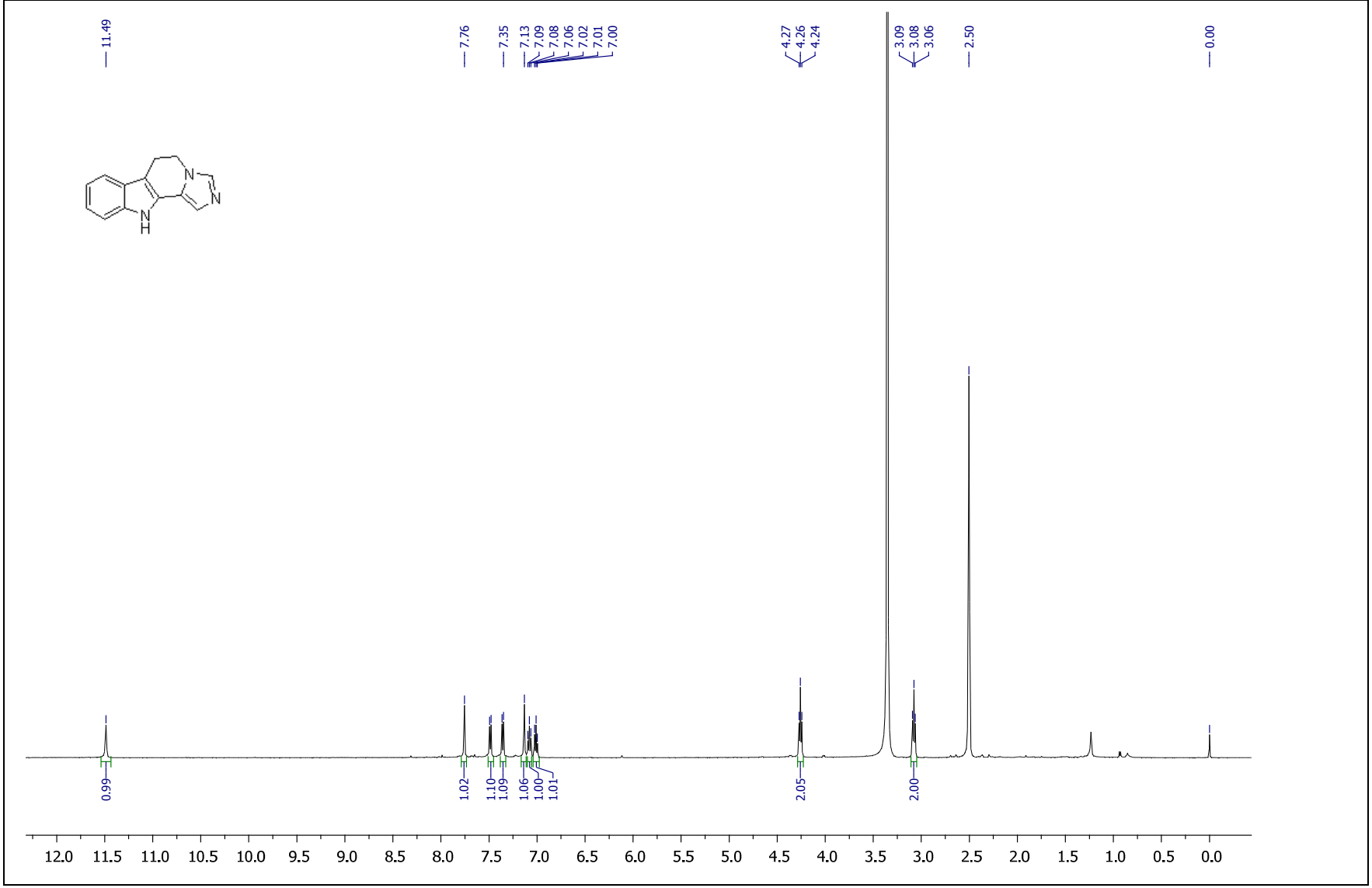
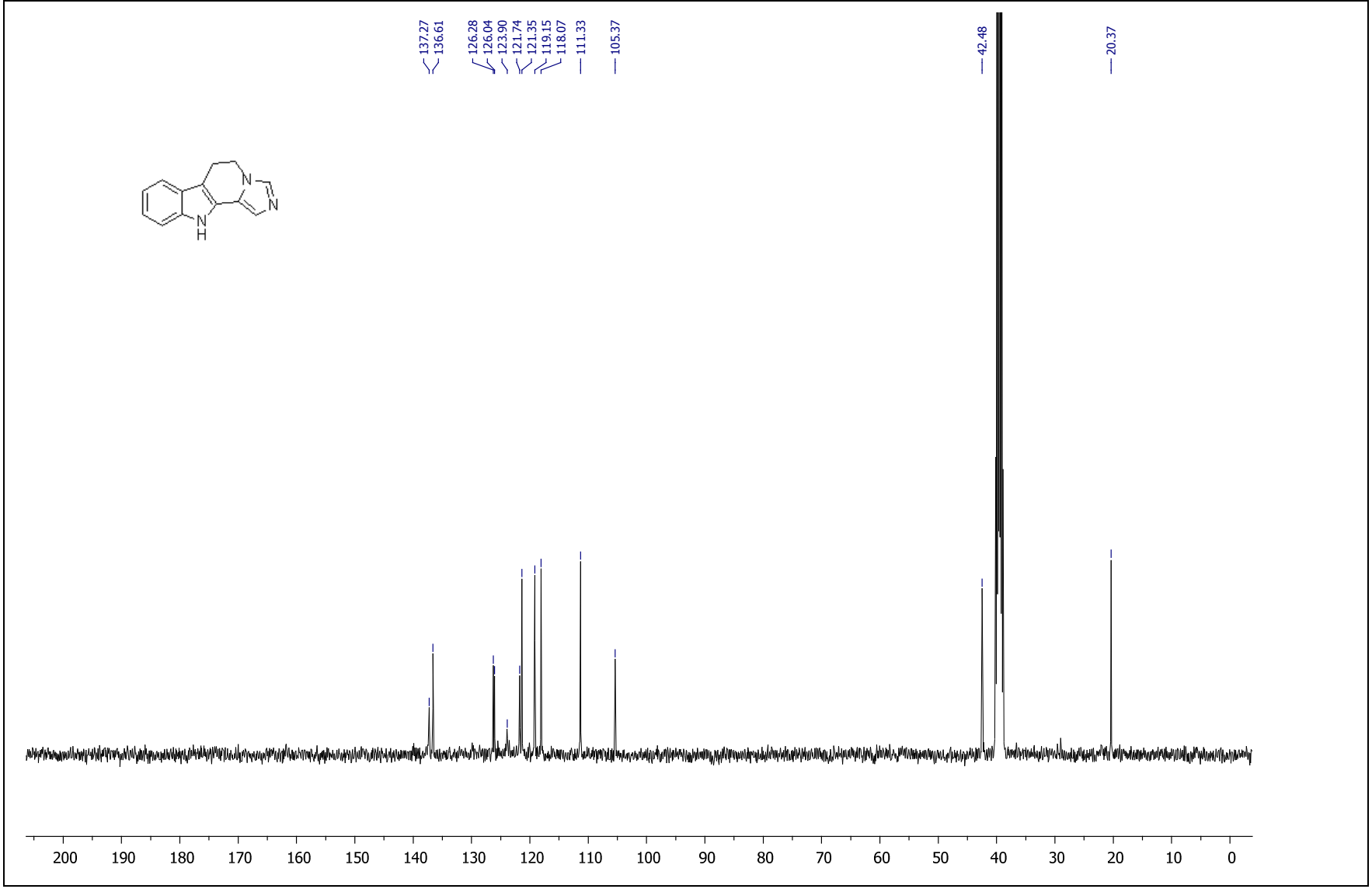


^{13}C NMR of 3a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N
H
200
190
180
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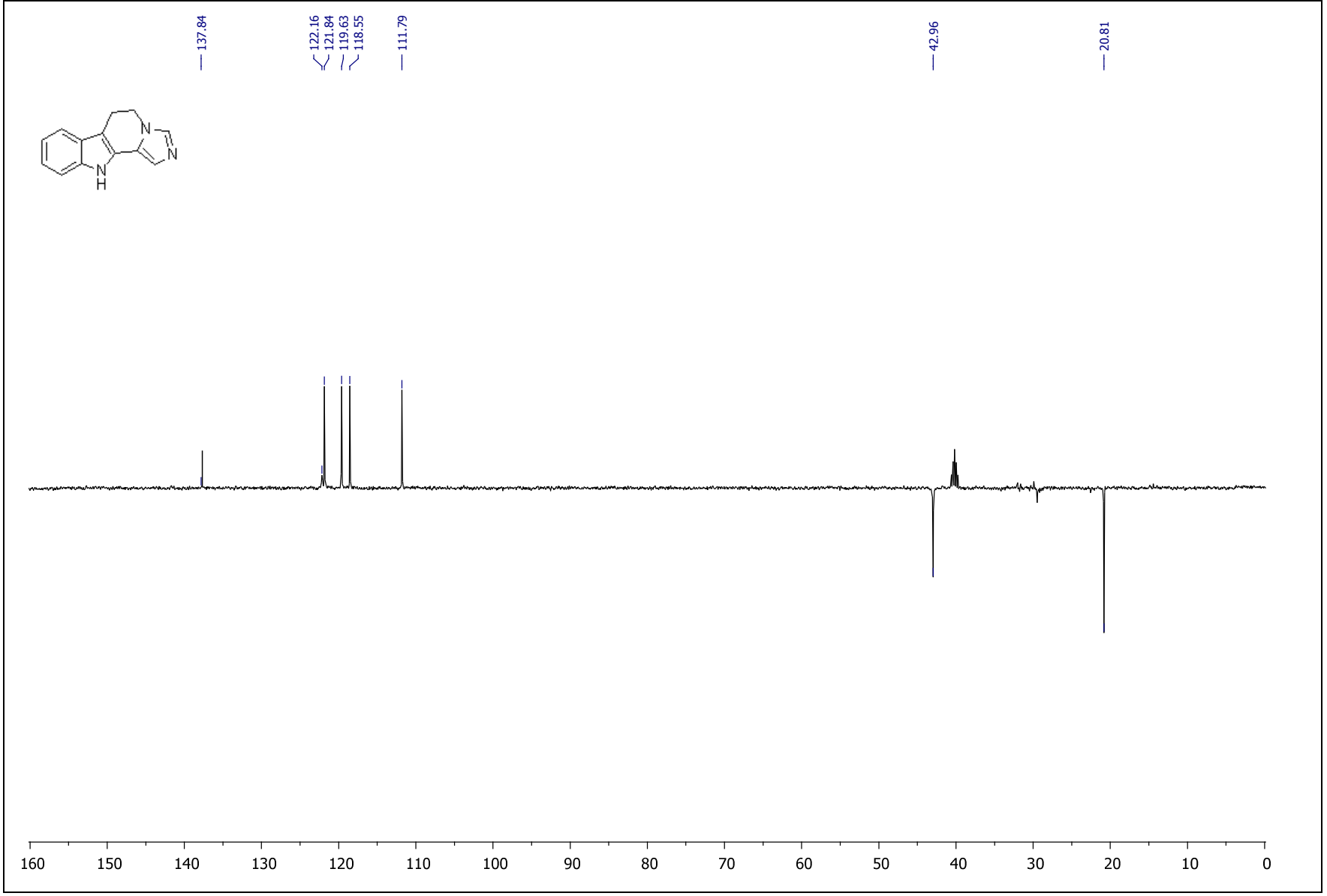
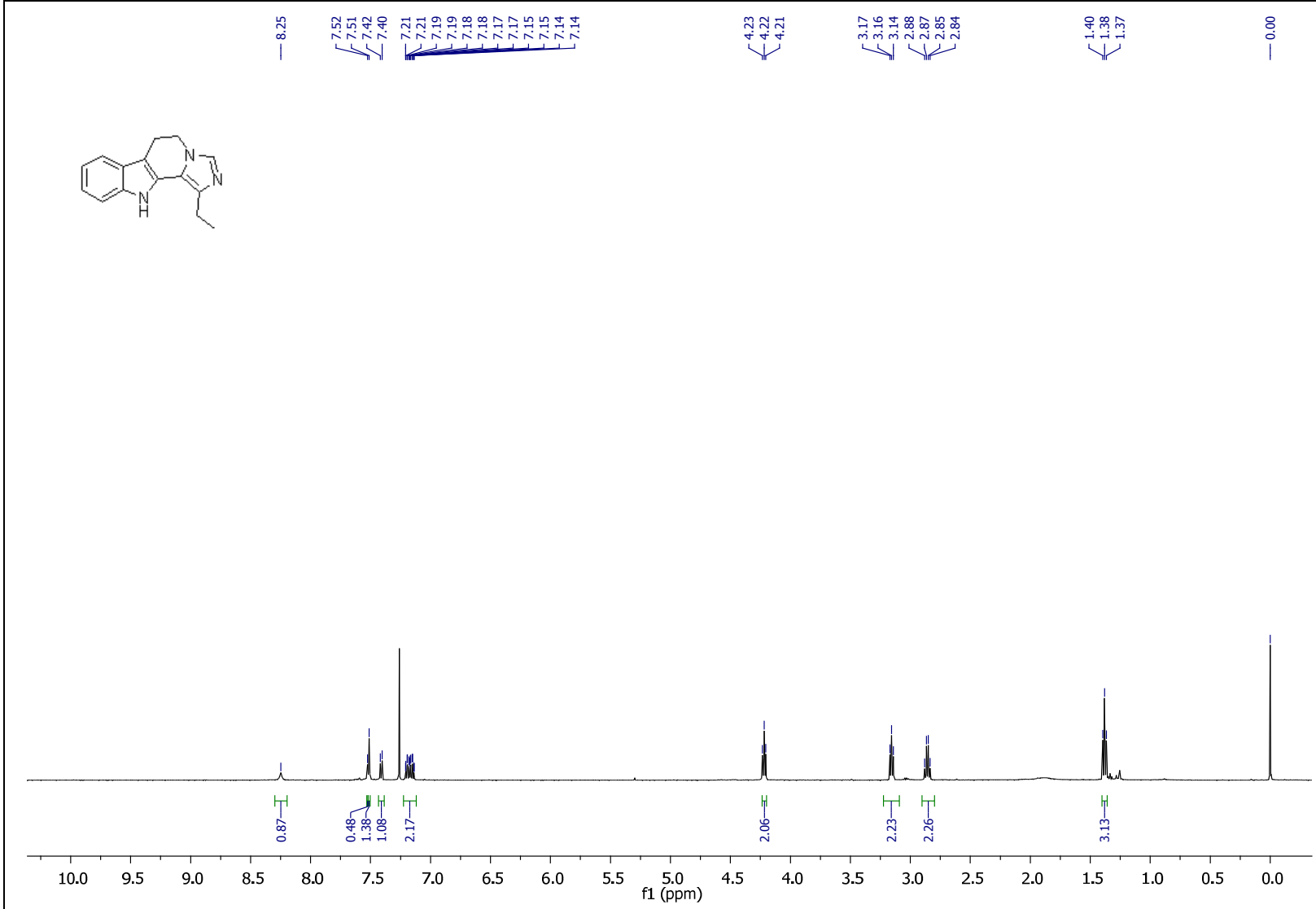
DEPT-135 of 3a



^{1}H NMR of 3b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7.17
7.15
7.15
7.14
7.14
4.23
4.22
4.21
3.17
3.16
3.14
2.88
2.87
2.85
2.84
1.40
1.38
1.37
0.00
0.87
0.48
1.38
1.08
2.17
2.06
2.23
2.26
3.13
10.0
9.5
9.0
8.5
8.0
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6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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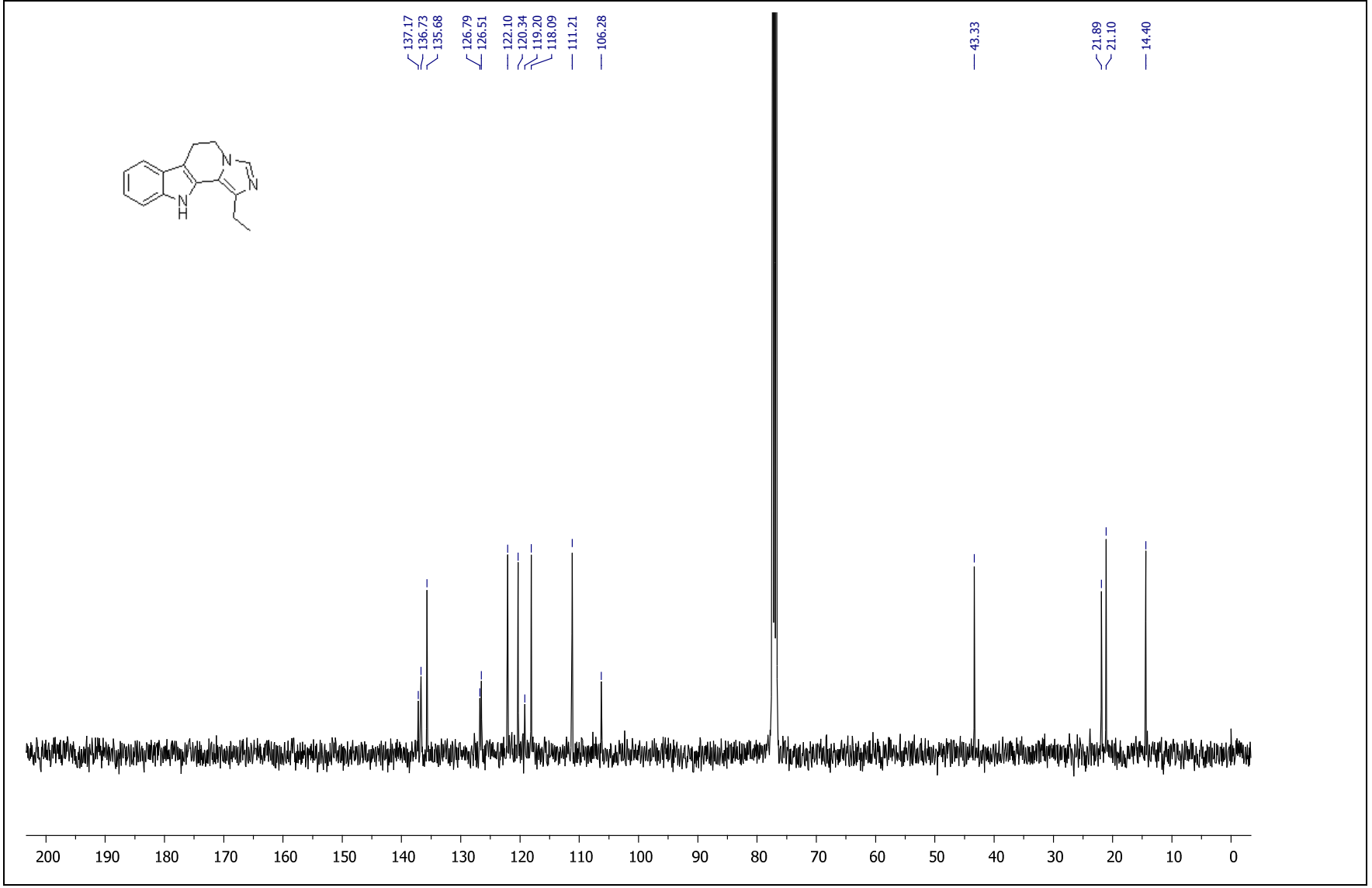
1.5
1.0
0.5
0.0
f1 (ppm)

^{13}C NMR of 3b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N
H
200
190
180
170
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40
30
20
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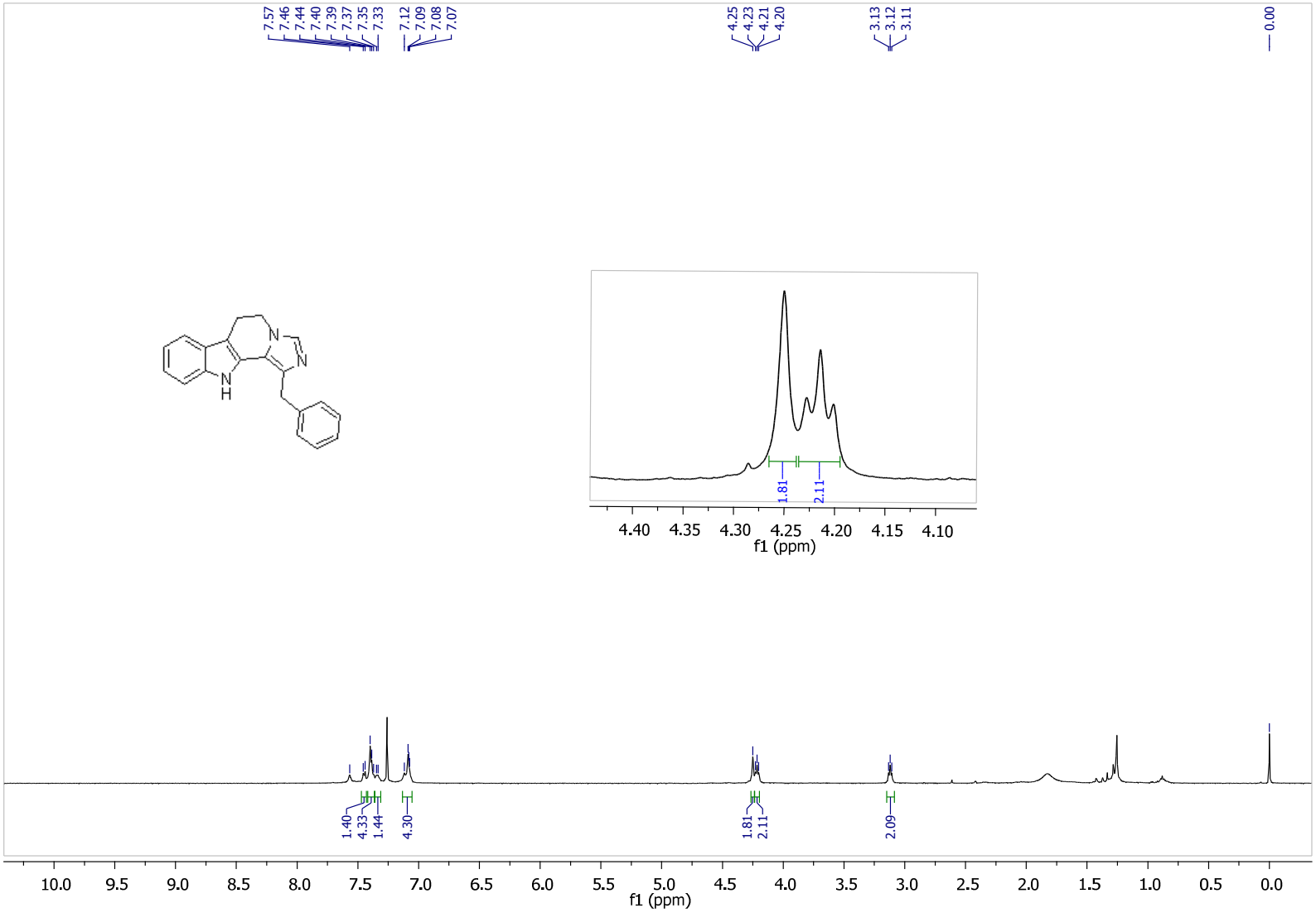
0

^{1}H NMR of 3c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4.23
4.21
4.20
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3.12
3.11
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N
H
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2.11
4.40 4.35 4.30 4.25 4.20 4.15 4.10
f1 (ppm)
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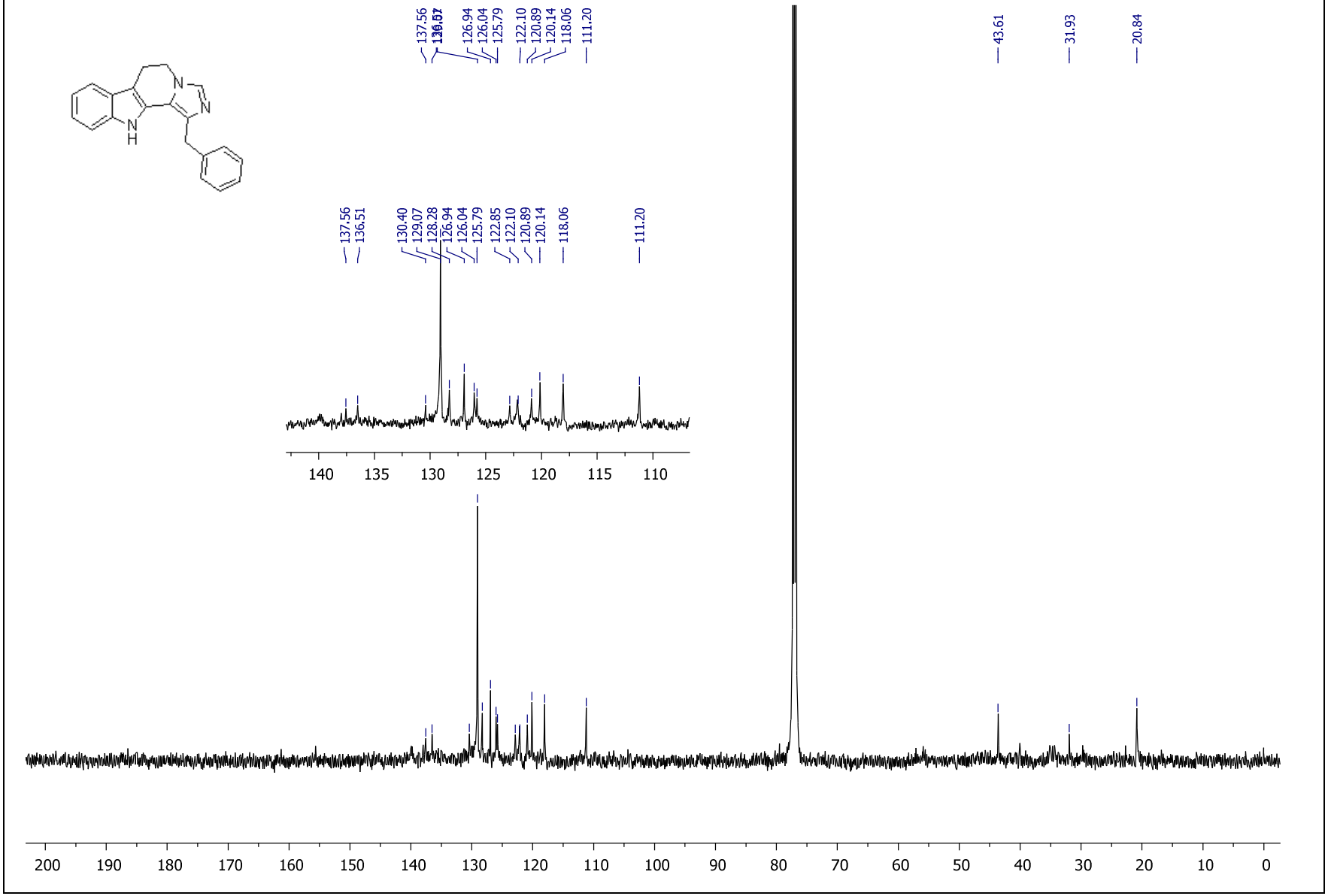
4.33
1.44
4.30
1.81
2.11
2.09
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

^{13}C NMR of 3c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200
190
180
170
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40
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20
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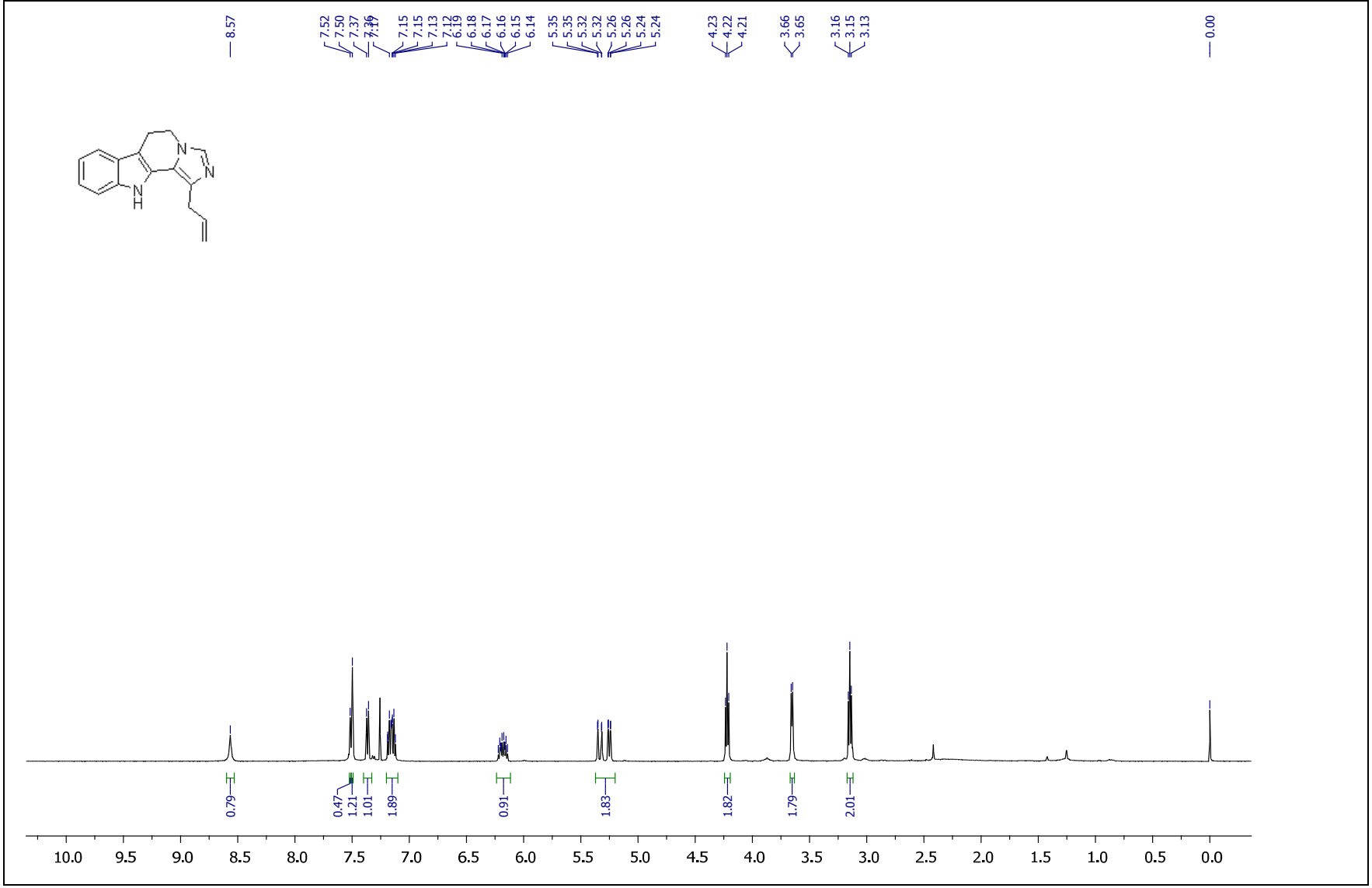
0

^{1}H NMR of 3d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5.35
5.35
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5.32
5.26
5.26
5.24
5.24
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4.22
4.21
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3.65
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3.15
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1.83
1.82
1.79
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10.0
9.5
9.0
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5.0
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2.5
2.0
1.5
1.0
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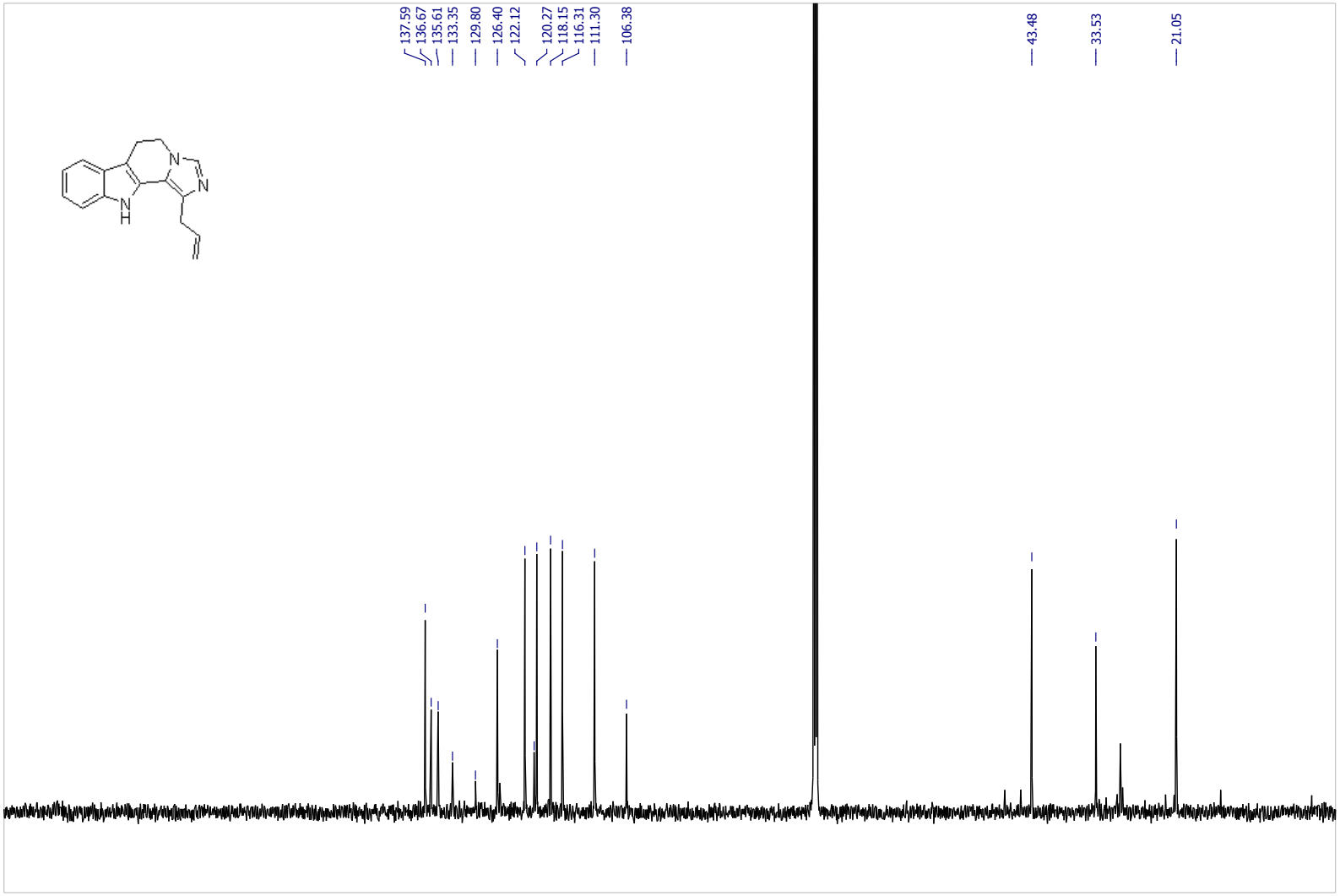
0.0

^{13}C NMR of 3d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90
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70
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50
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30
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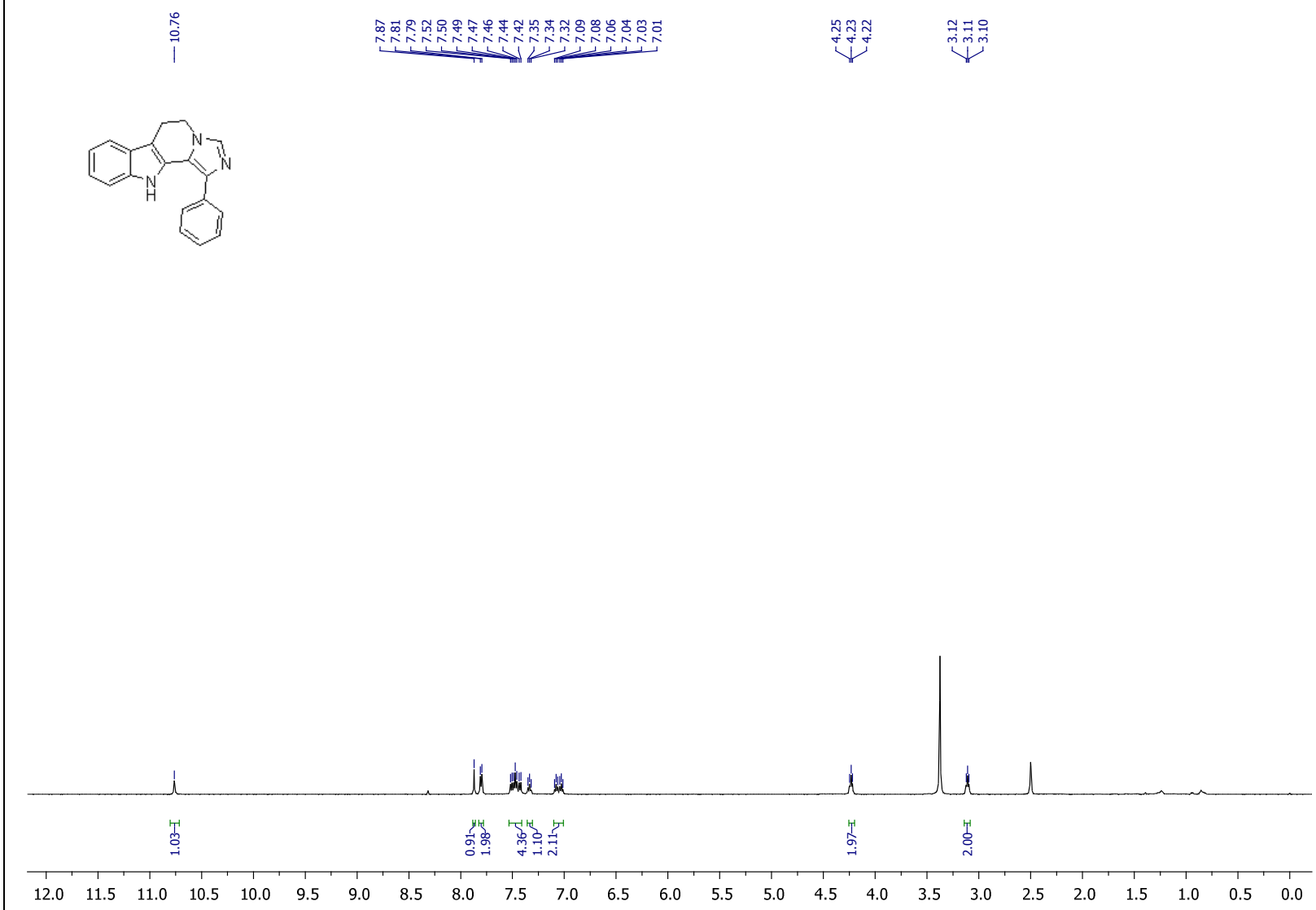
0

^{1}H NMR of 3e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7.42
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7.08
7.06
7.04
7.03
7.01
4.25
4.23
4.22
3.12
3.11
3.10
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H
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1.98
4.36
1.10
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1.97
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10.0
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9.0
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6.0
5.5
5.0
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2.0
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1.0
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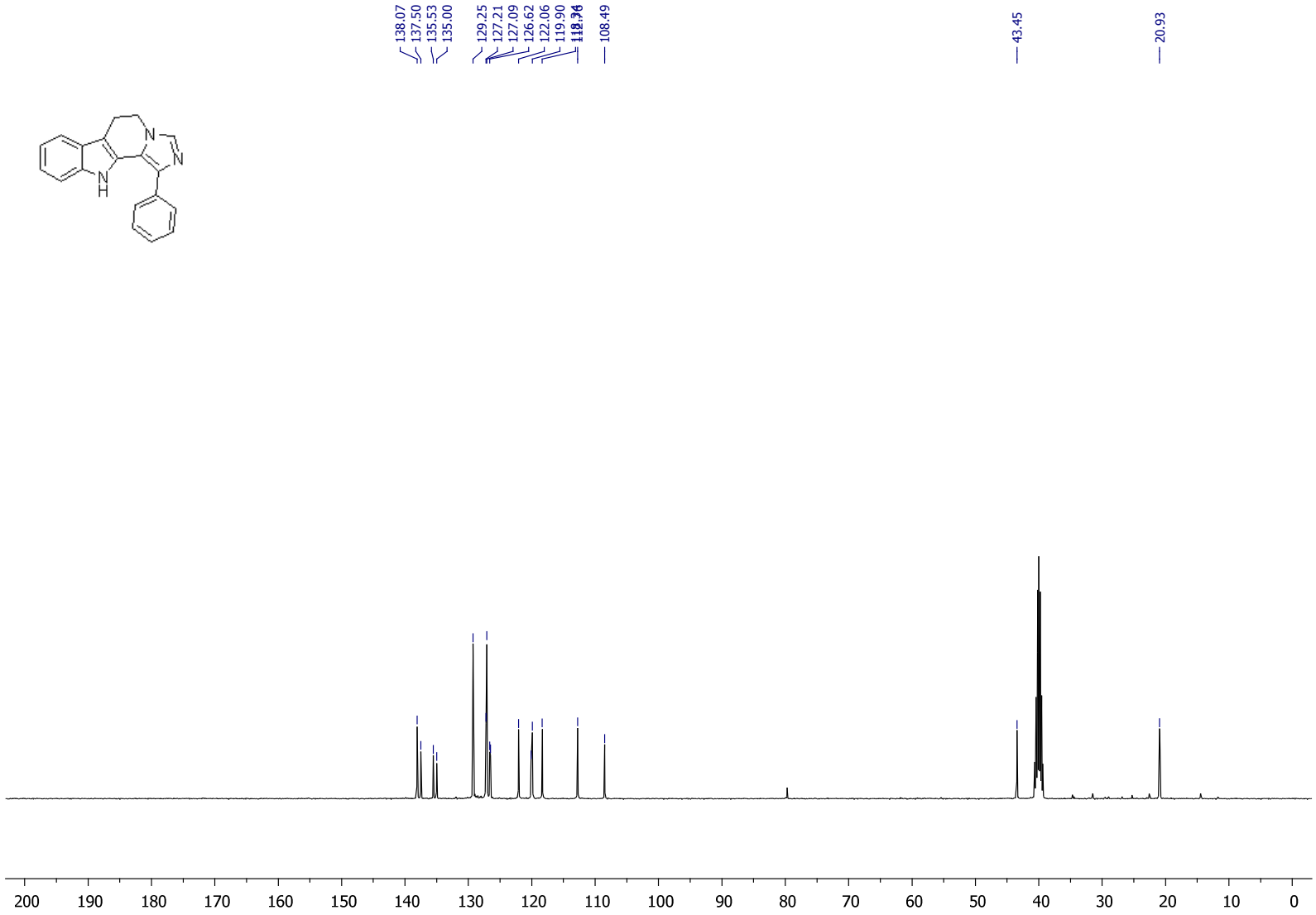
^{13}C NMR of 3e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122.06
119.90
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20.93
200
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180
170
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120
110
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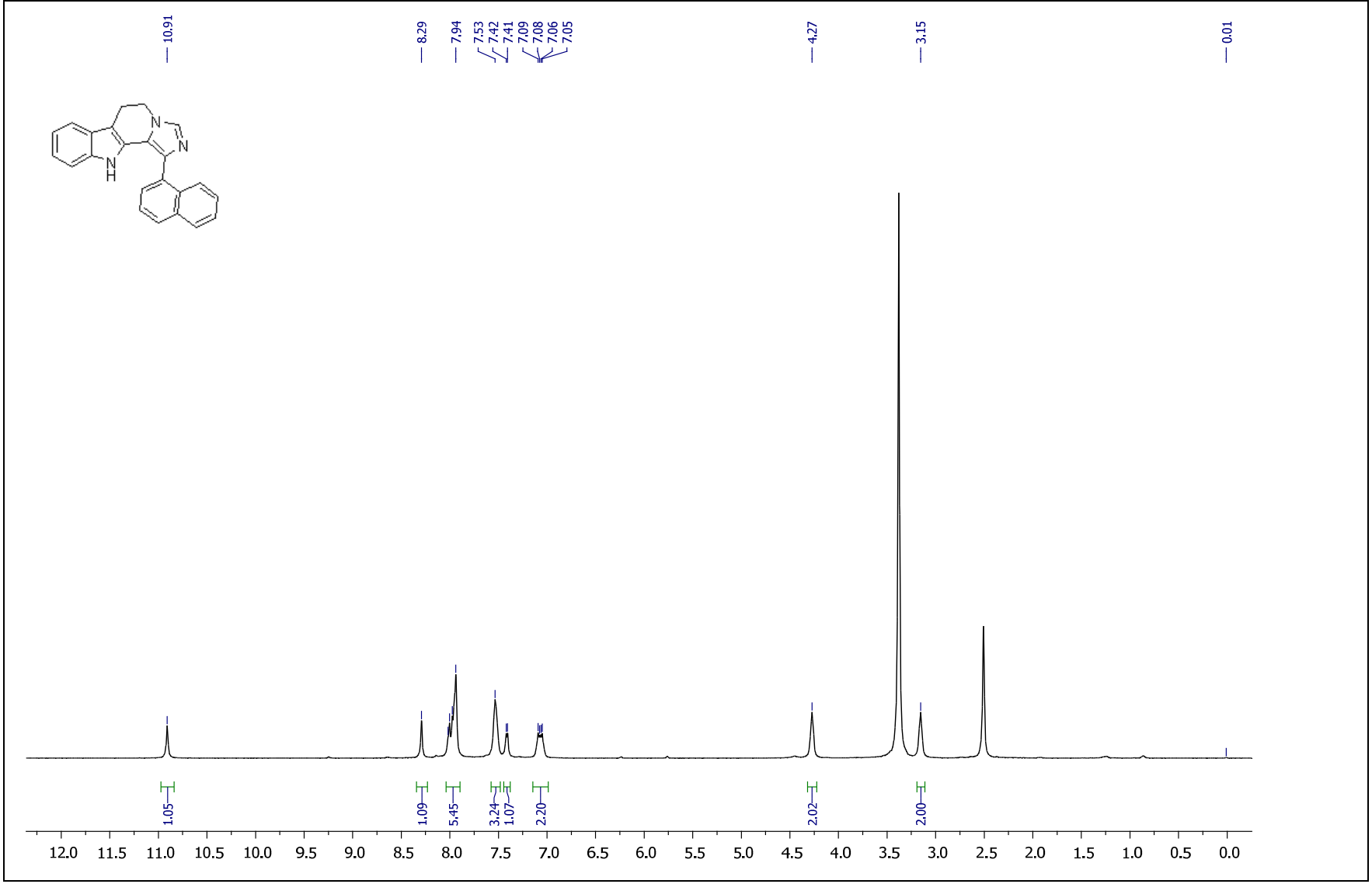
90
80
70
60
50
40
30
20
10
0

^{1}H NMR of 3f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1.05
1.09
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12.0
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11.0
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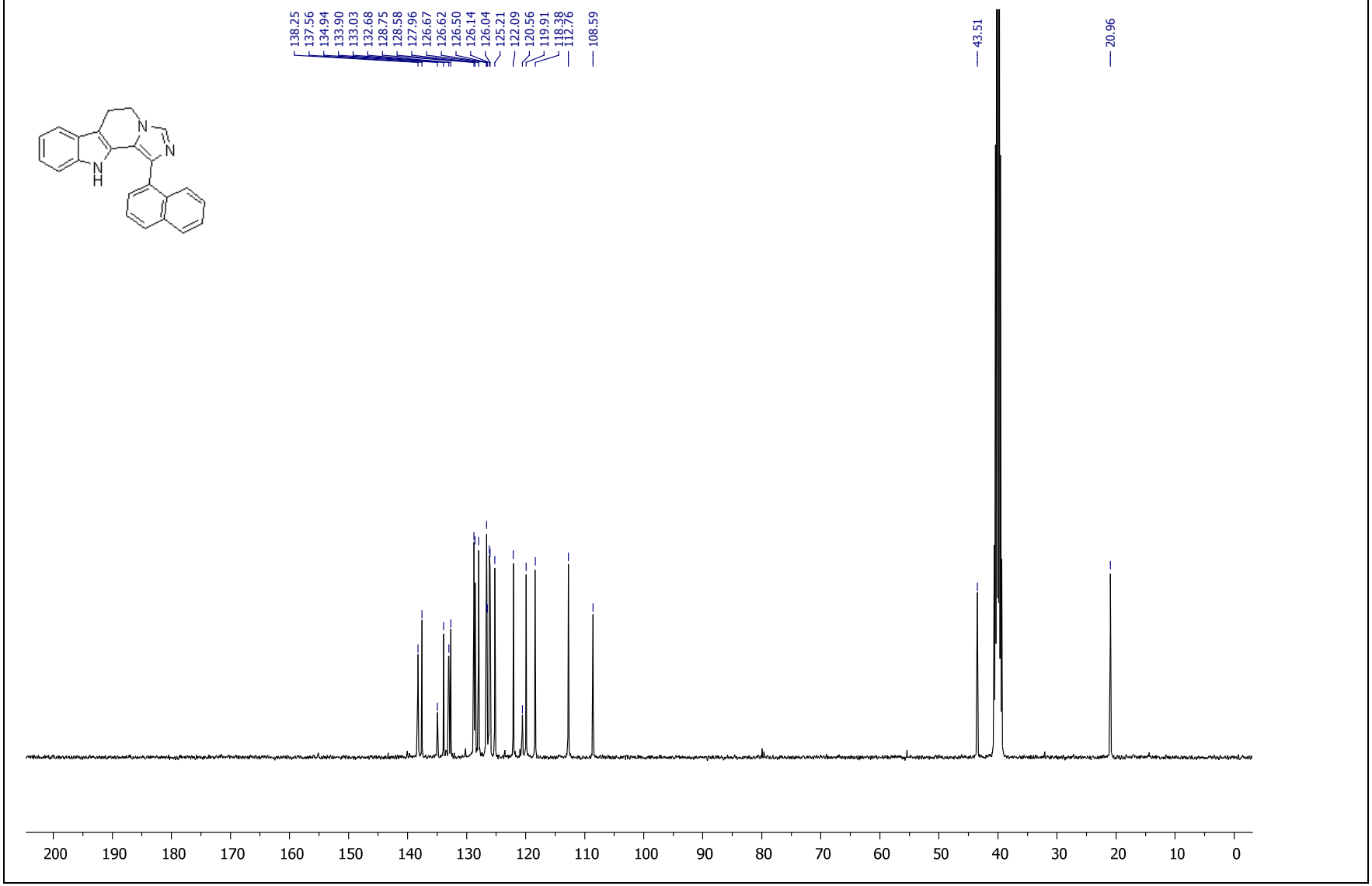
^{13}C NMR of 3f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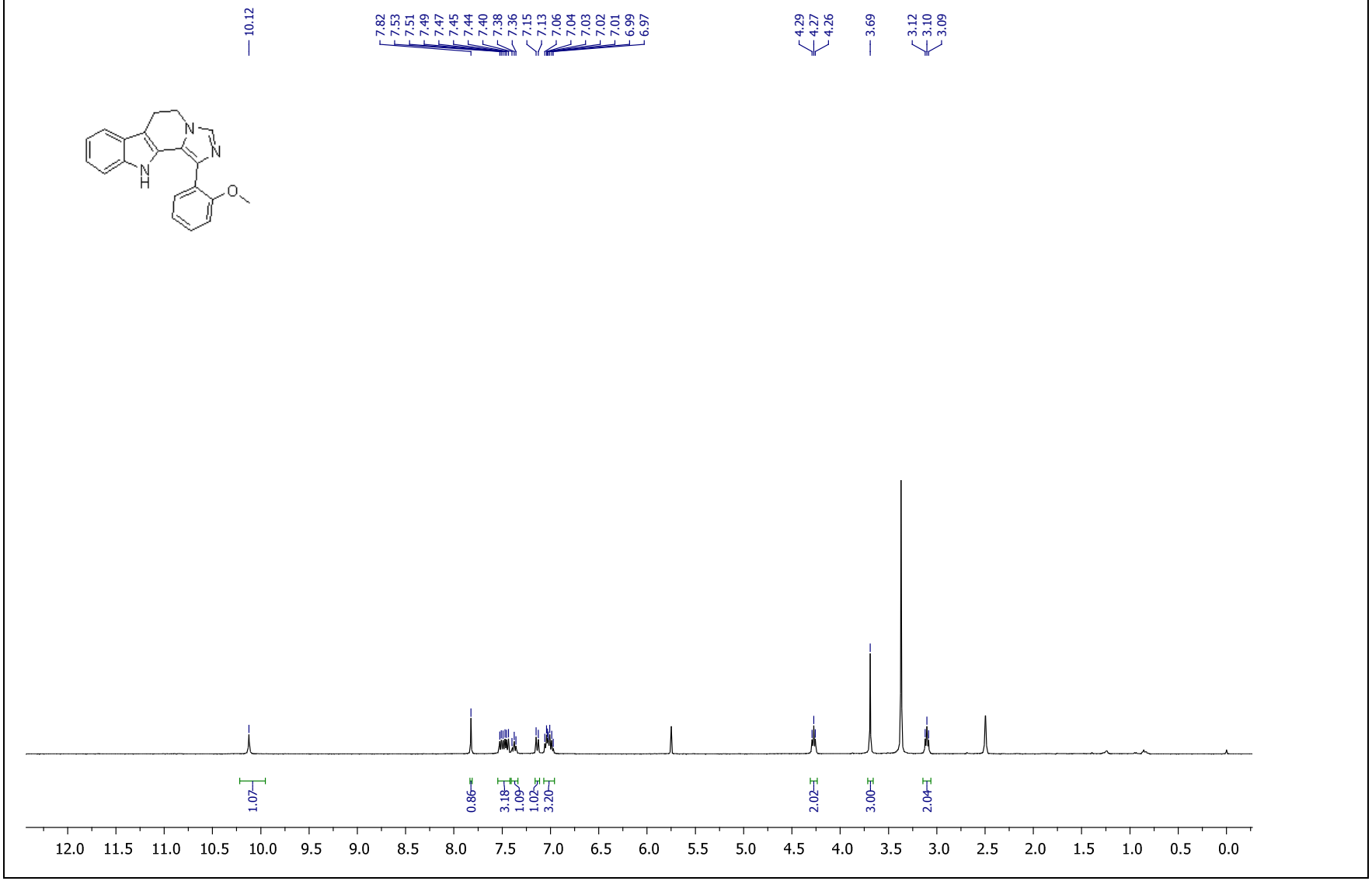
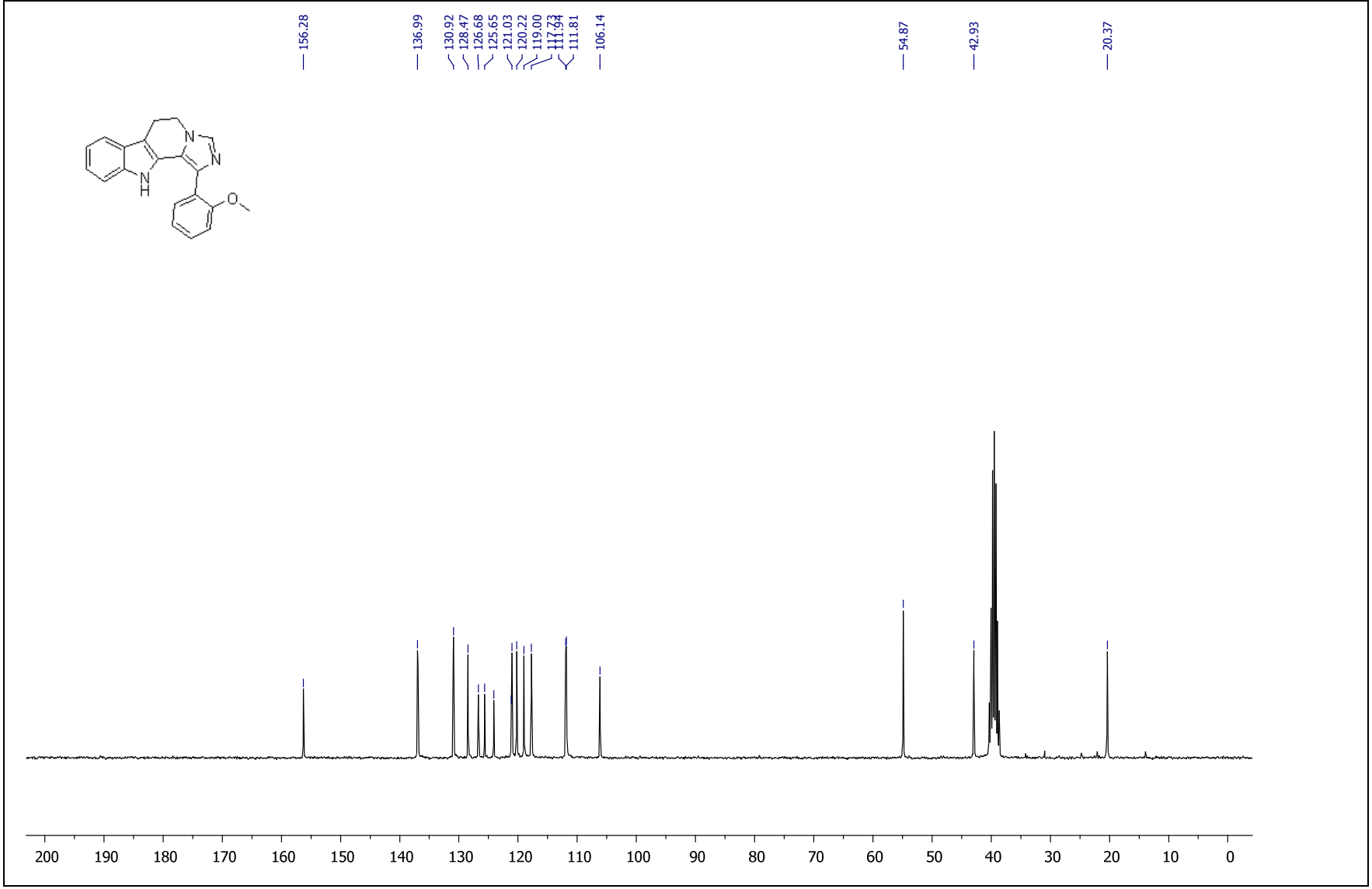
126.62
126.50
126.14
126.04
125.21
122.09
120.56
119.91
118.38
112.76
108.59
43.51
20.96
N
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

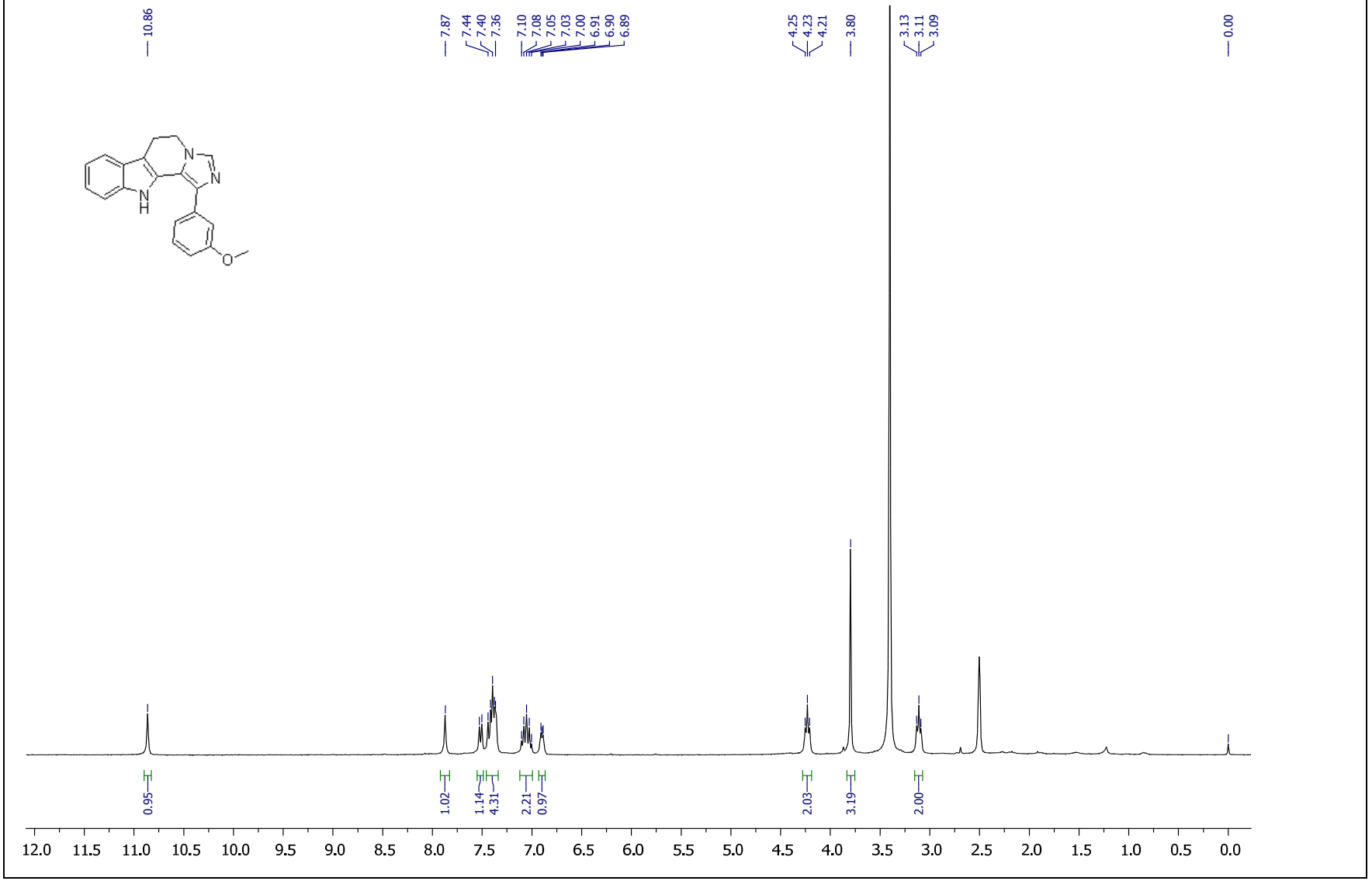
^{1}H NMR of 3g


10.12
7.82
7.53
7.51
7.49
7.47
7.45
7.44
7.40
7.38
7.36
7.15
7.13
7.06
7.04
7.03
7.02
7.01
6.99
6.97
4.29
4.27
4.26
3.69
3.12
3.10
3.09
1.07
0.86
3.18
1.09
1.02
3.20
2.02
3.00
2.04
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

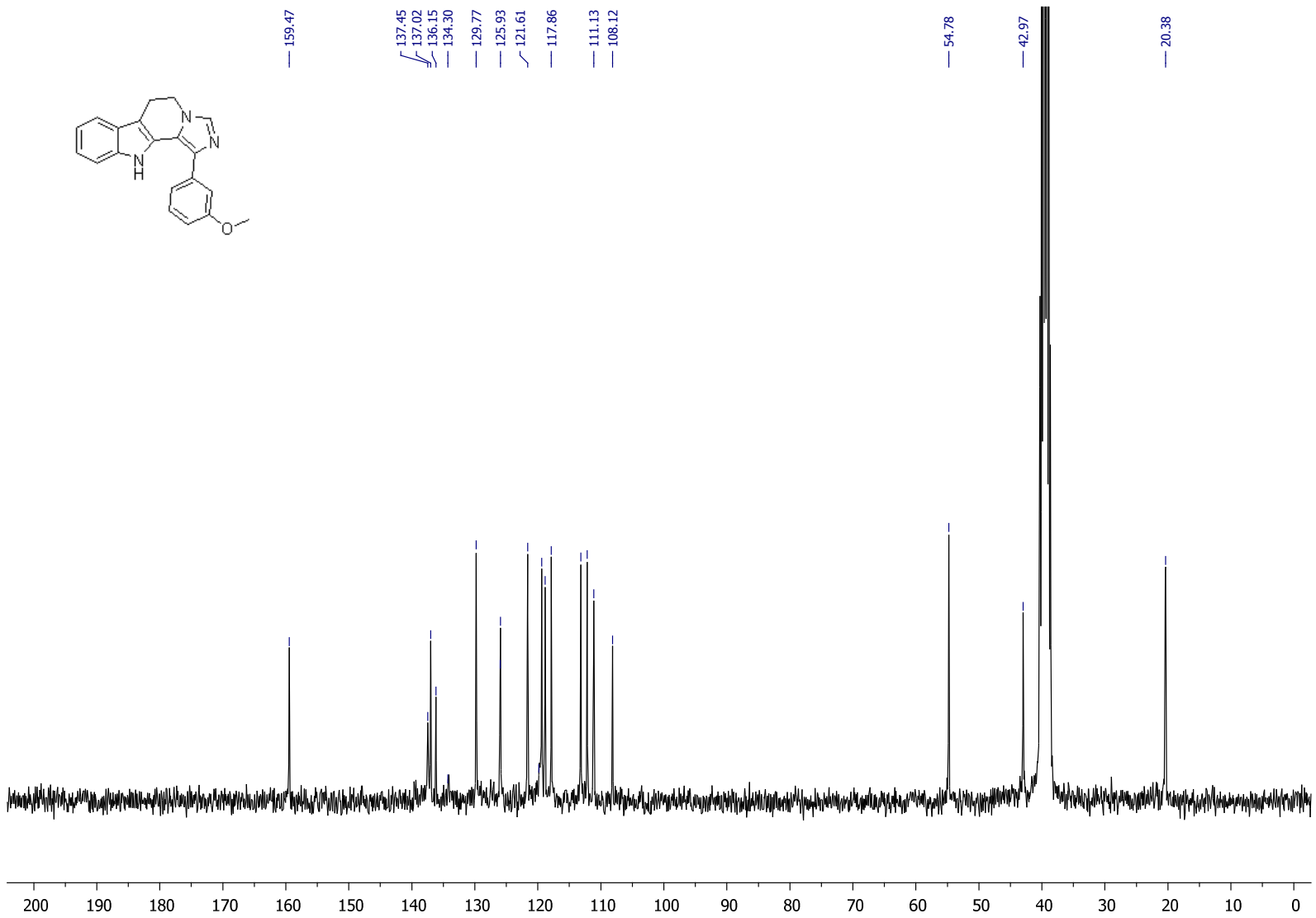
^{13}C NMR of 3g


156.28
136.99
130.92
128.47
126.68
125.65
121.03
120.22
119.00
111.81
106.14
54.87
42.93
20.37
N
N
H
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

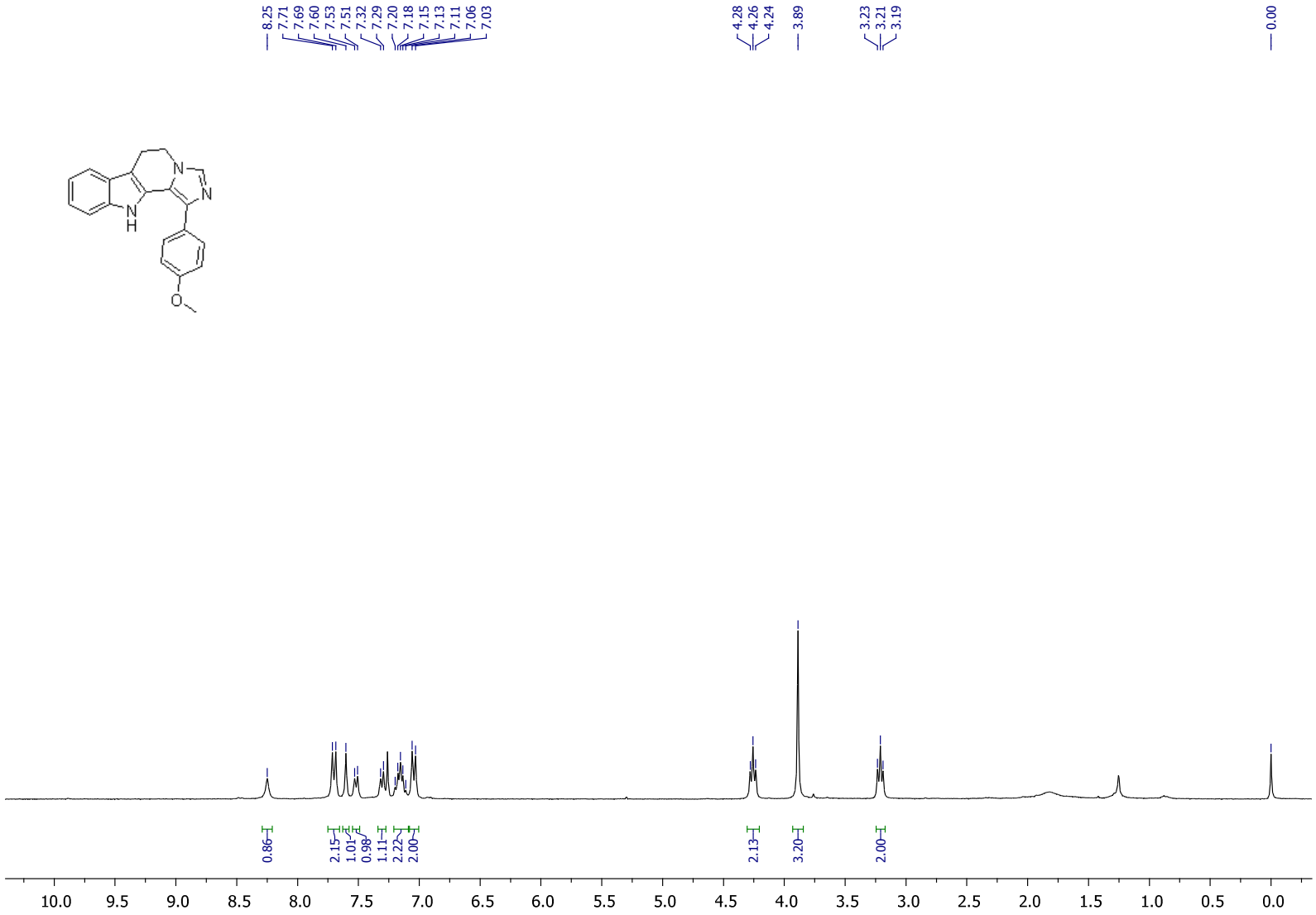
^{1}H NMR of 3h


10.86
7.87
7.44
7.40
7.36
7.10
7.08
7.05
7.03
7.00
6.91
6.90
6.89
4.25
4.23
4.21
3.80
3.13
3.11
3.09
0.00
N
N
H
O
0.95
1.02
1.14
4.31
2.21
0.97
2.03
3.19
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

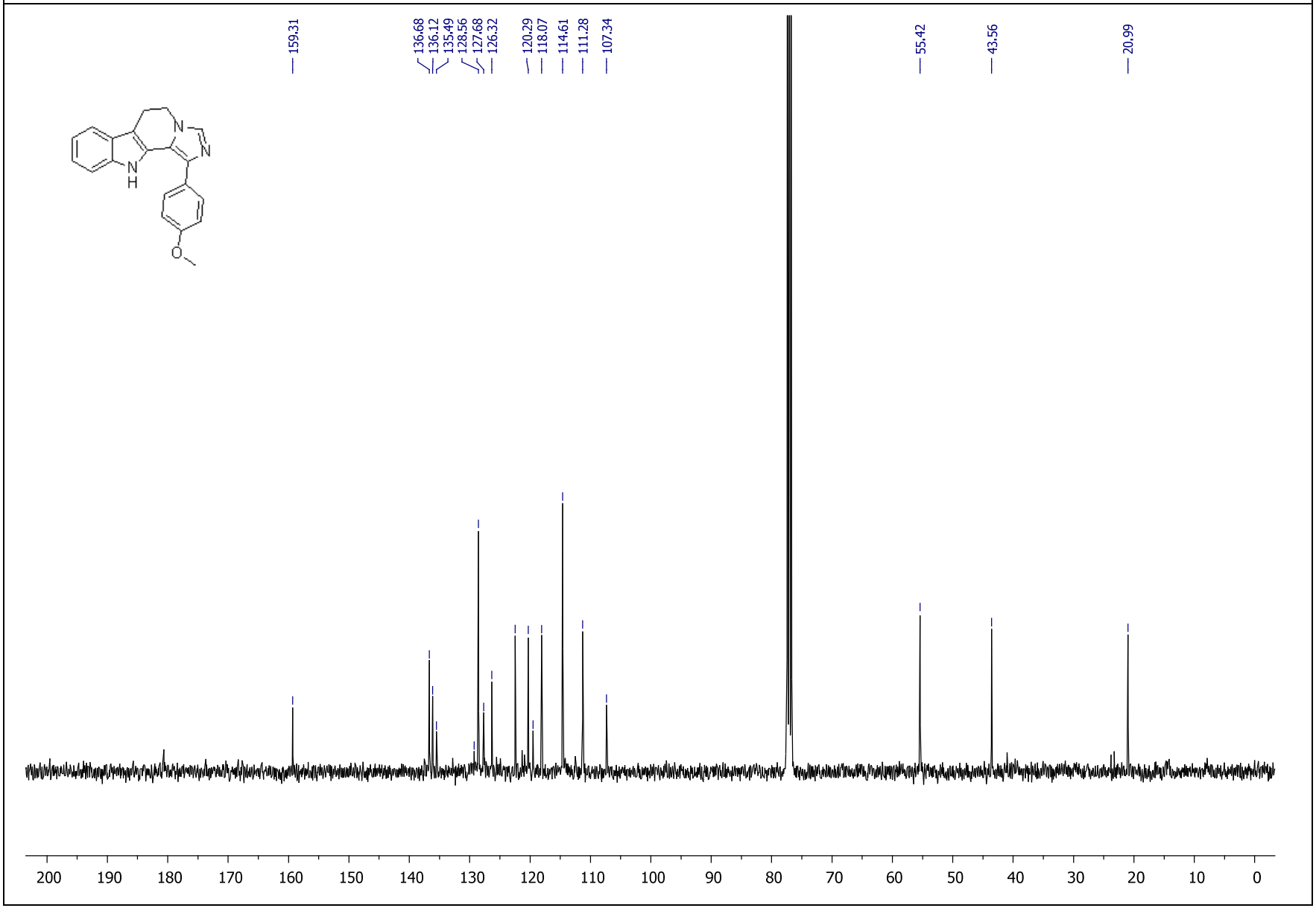
^{13}C NMR of 3h


159.47
137.45
137.02
136.15
134.30
129.77
125.93
121.61
117.86
111.13
108.12
54.78
42.97
20.38
N
N
H
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

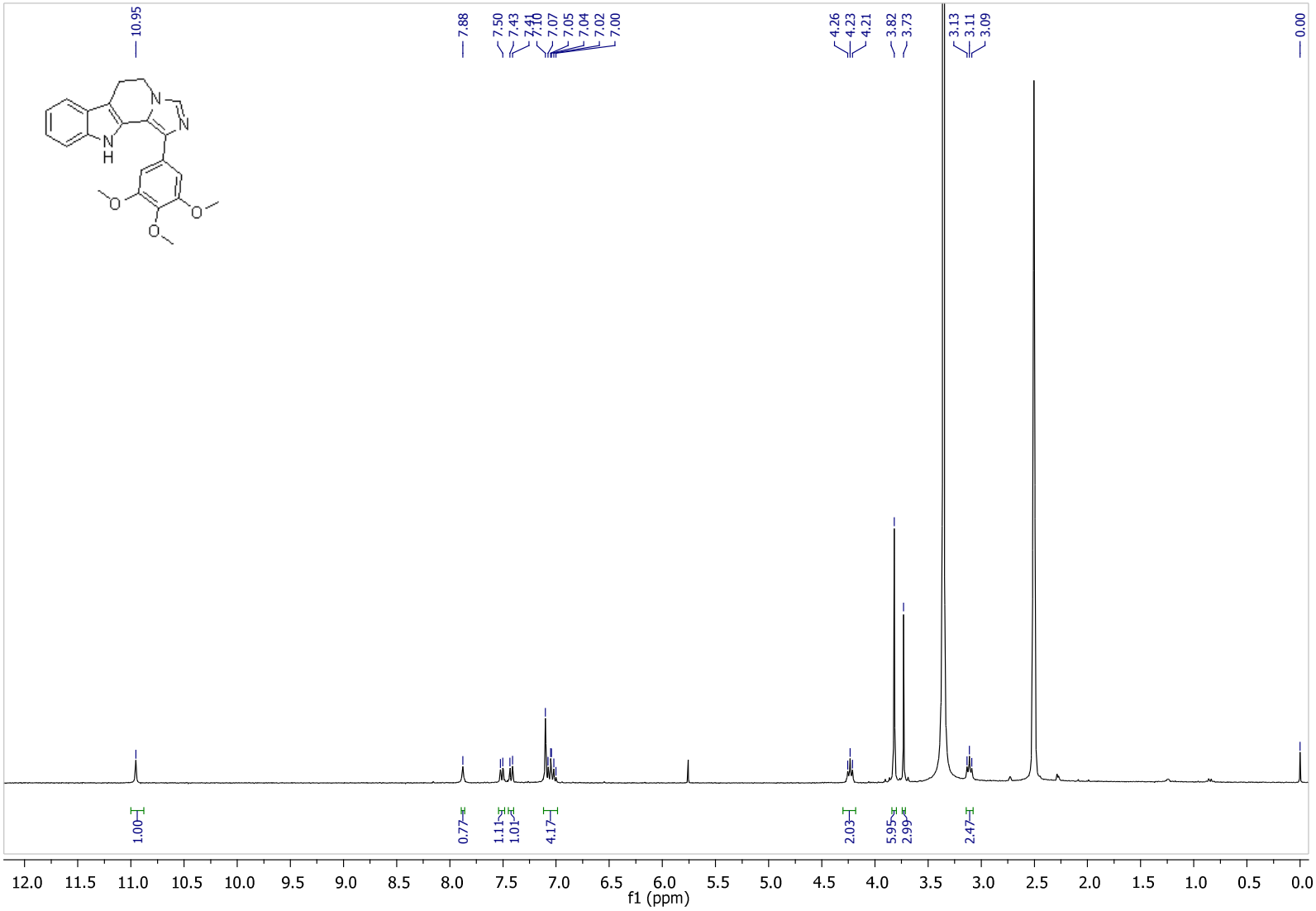
^{1}H NMR of 3i


8.25
7.71
7.69
7.60
7.53
7.51
7.32
7.29
7.20
7.18
7.15
7.13
7.11
7.06
7.03
4.28
4.26
4.24
3.89
3.23
3.21
3.19
0.00
N
N
H
O
0.86
2.15
1.01
0.98
1.11
2.22
2.00
2.13
3.20
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

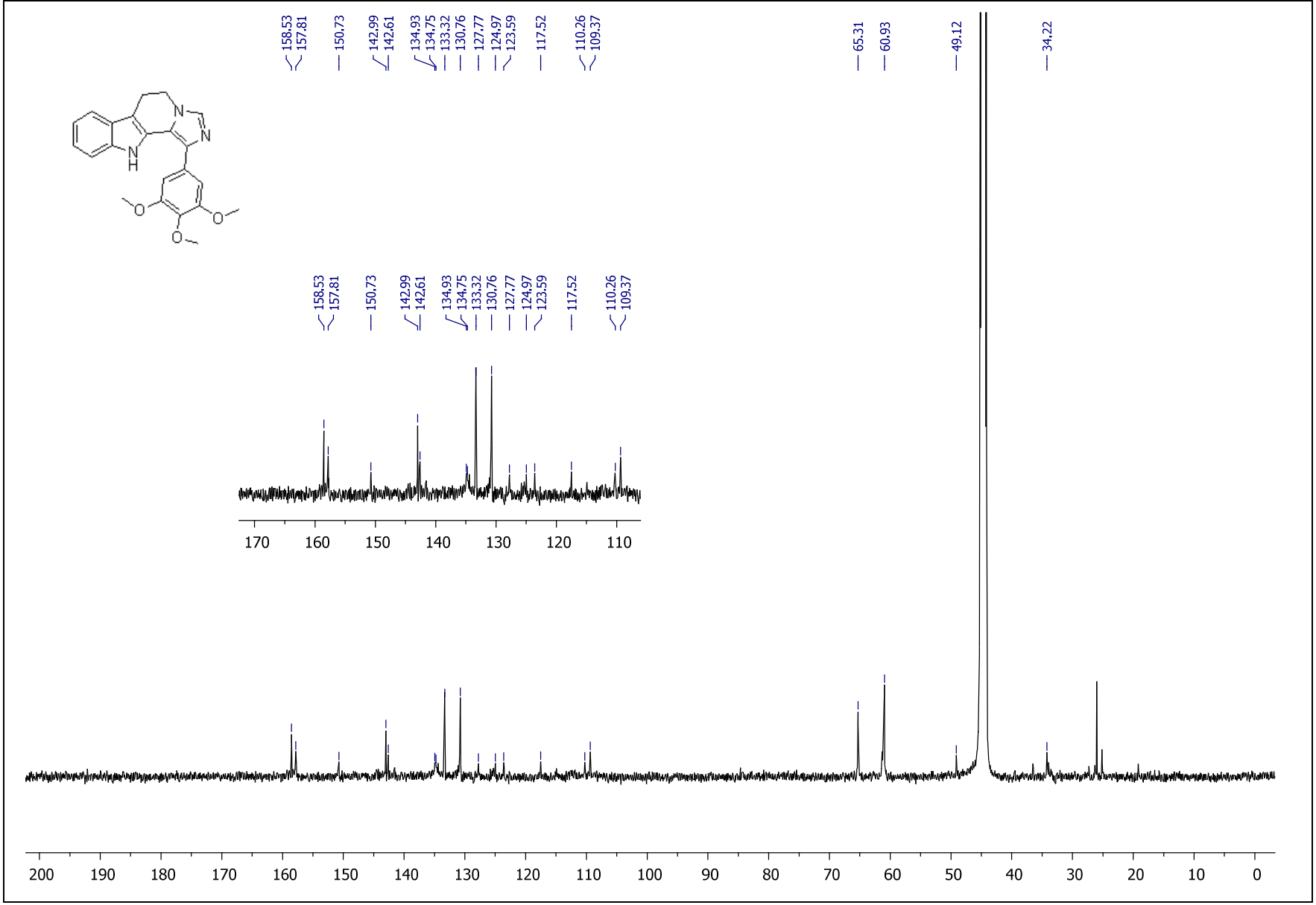
^{13}C NMR of 3i


159.31
136.68
136.12
135.49
128.56
127.68
126.32
120.29
118.07
114.61
111.28
107.34
55.42
43.56
20.99
N
N
H
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

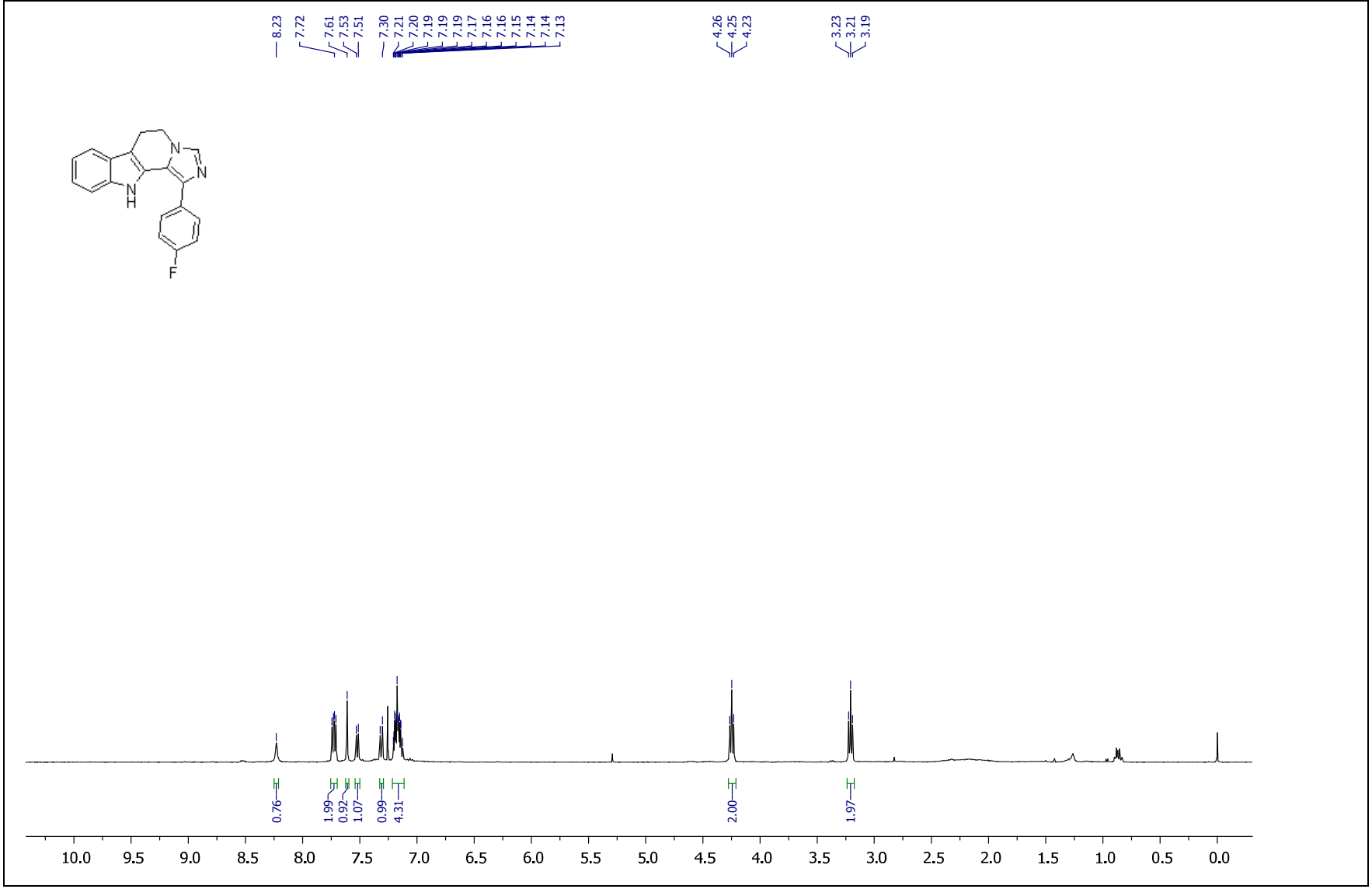
^{1}H NMR of 3j


10.95
7.88
7.50
7.43
7.41
7.10
7.07
7.05
7.04
7.02
7.00
4.26
4.23
4.21
3.82
3.73
3.13
3.11
3.09
0.00
1.00
0.77
1.11
1.01
4.17
2.03
5.95
2.99
2.47
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
f1 (ppm)

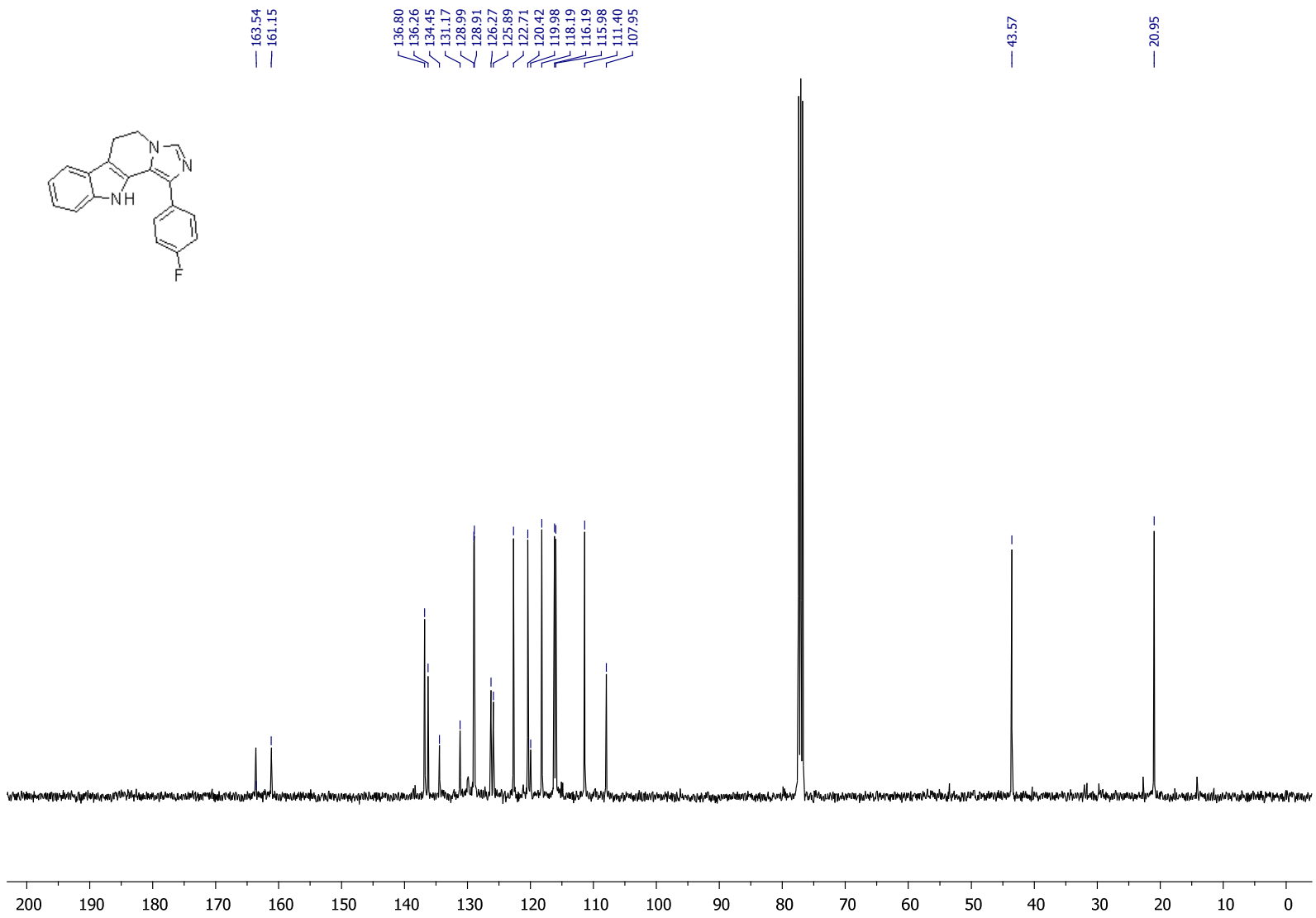
^{13}C NMR of 3j


158.53
157.81
150.73
142.99
142.61
134.93
134.75
133.32
130.76
127.77
124.97
123.59
117.52
110.26
109.37
65.31
60.93
49.12
34.22
N
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

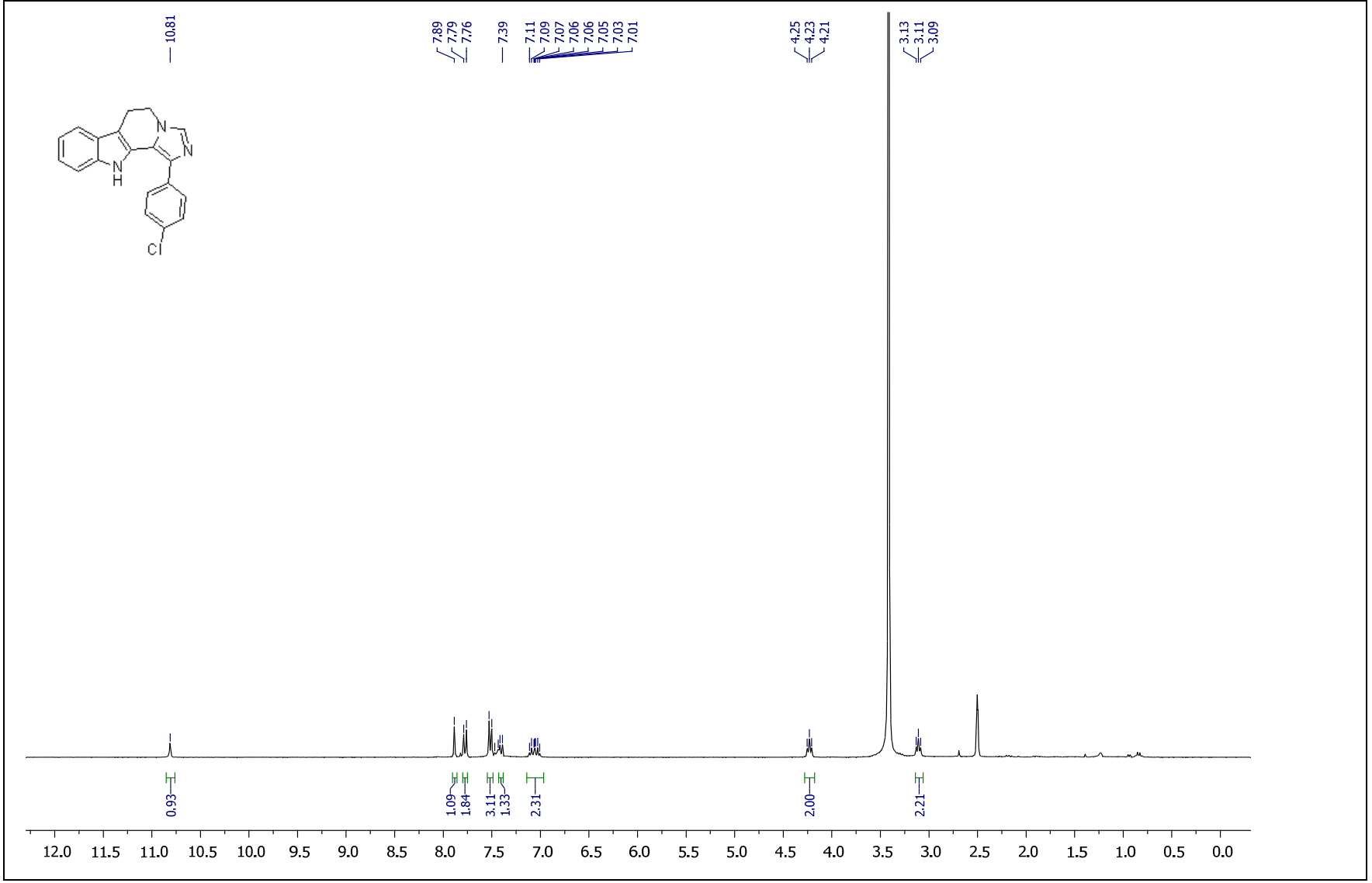
^{1}H NMR of 3k


8.23
7.72
7.61
7.53
7.51
7.30
7.21
7.20
7.19
7.19
7.19
7.17
7.16
7.16
7.15
7.14
7.14
7.13
4.26
4.25
4.23
3.23
3.21
3.19
N
N
H
F
0.76
1.99
0.92
1.07
0.99
4.31
2.00
1.97
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

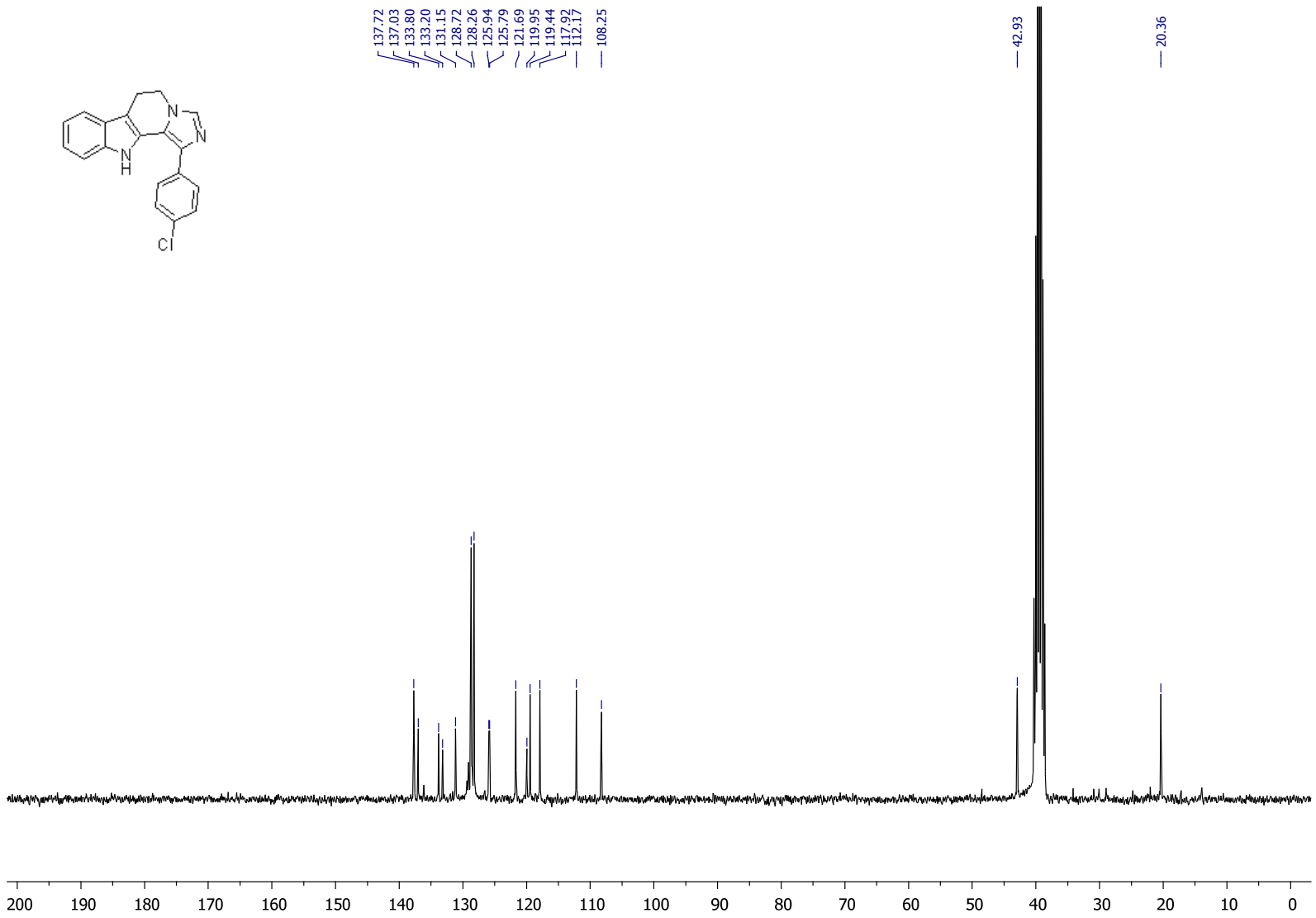
^{13}C NMR of 3k


163.54
161.15
136.80
136.26
134.45
131.17
128.99
128.91
126.27
125.89
122.71
120.42
119.98
118.19
116.19
115.98
111.40
107.95
43.57
20.95
N
N
NH
F
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

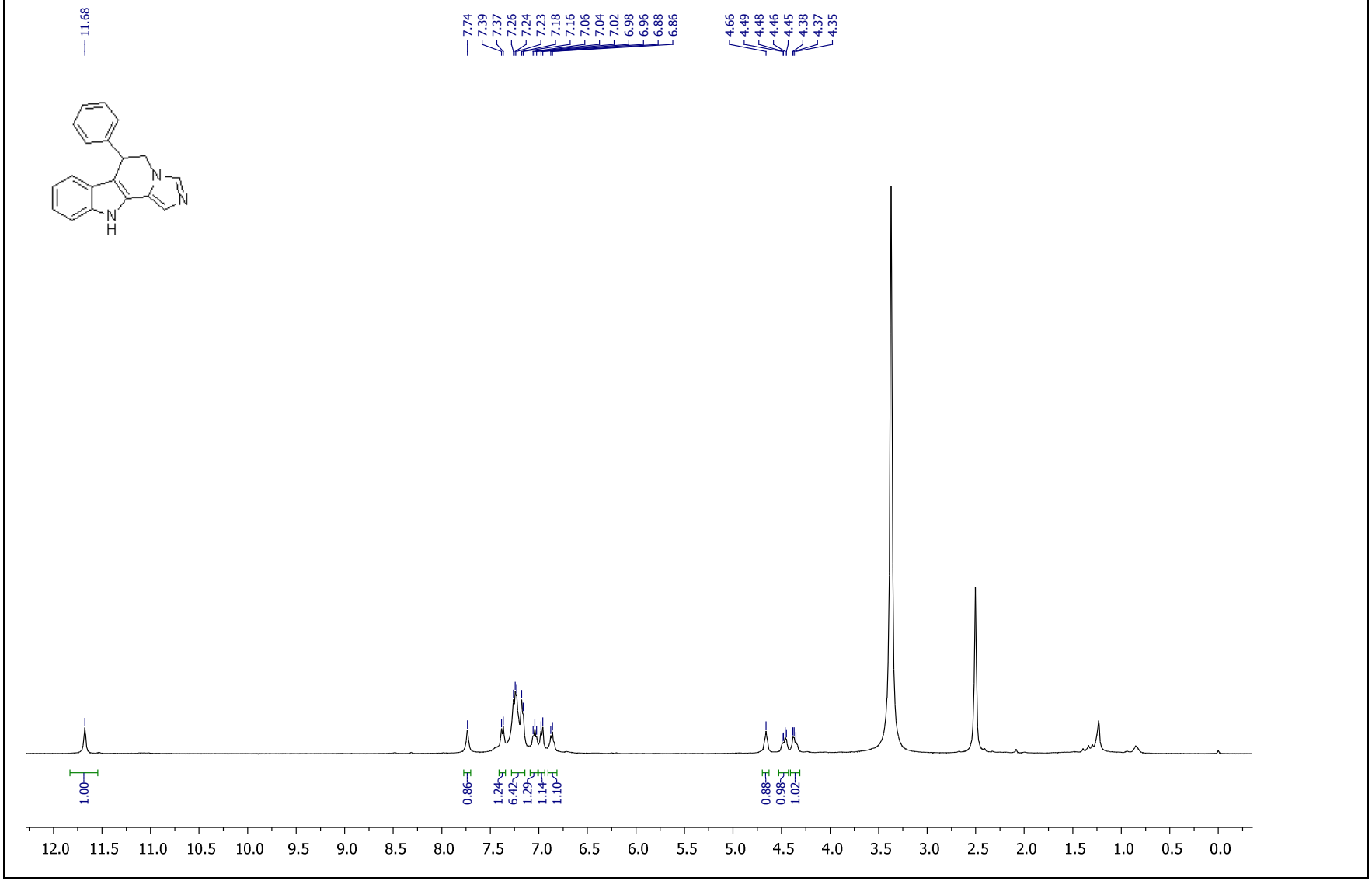
^{1}H NMR of 3l


10.81
7.89
7.79
7.76
7.39
7.11
7.09
7.07
7.06
7.06
7.05
7.03
7.01
4.25
4.23
4.21
3.13
3.11
3.09
N
N
H
Cl
0.93
1.09
1.84
3.11
1.33
2.31
2.00
2.21
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

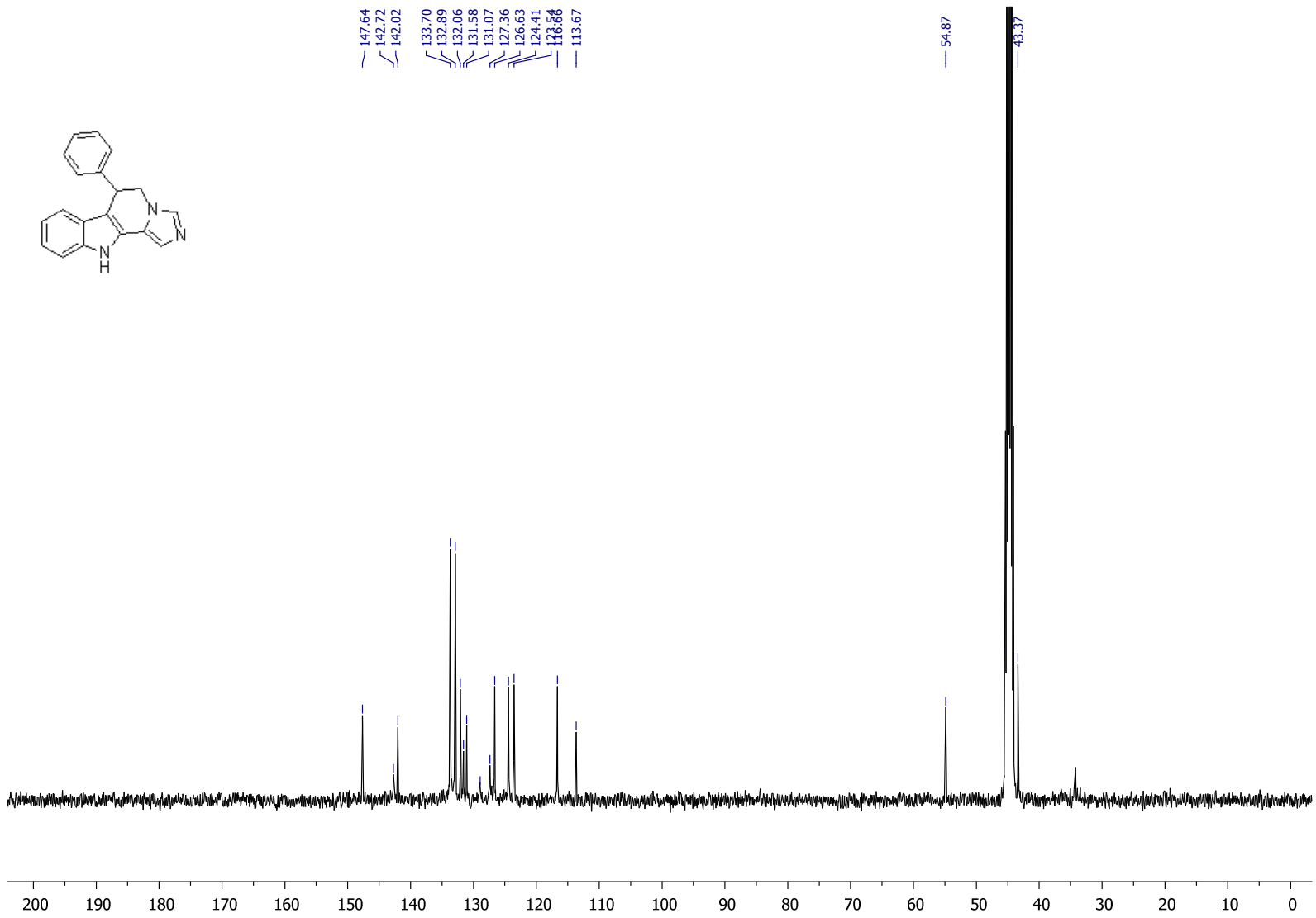
^{13}C NMR of 3l


137.72
137.03
133.80
133.20
131.15
128.72
128.26
125.94
125.79
121.69
119.95
119.44
117.92
112.17
108.25
42.93
20.36
N
N
H
Cl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

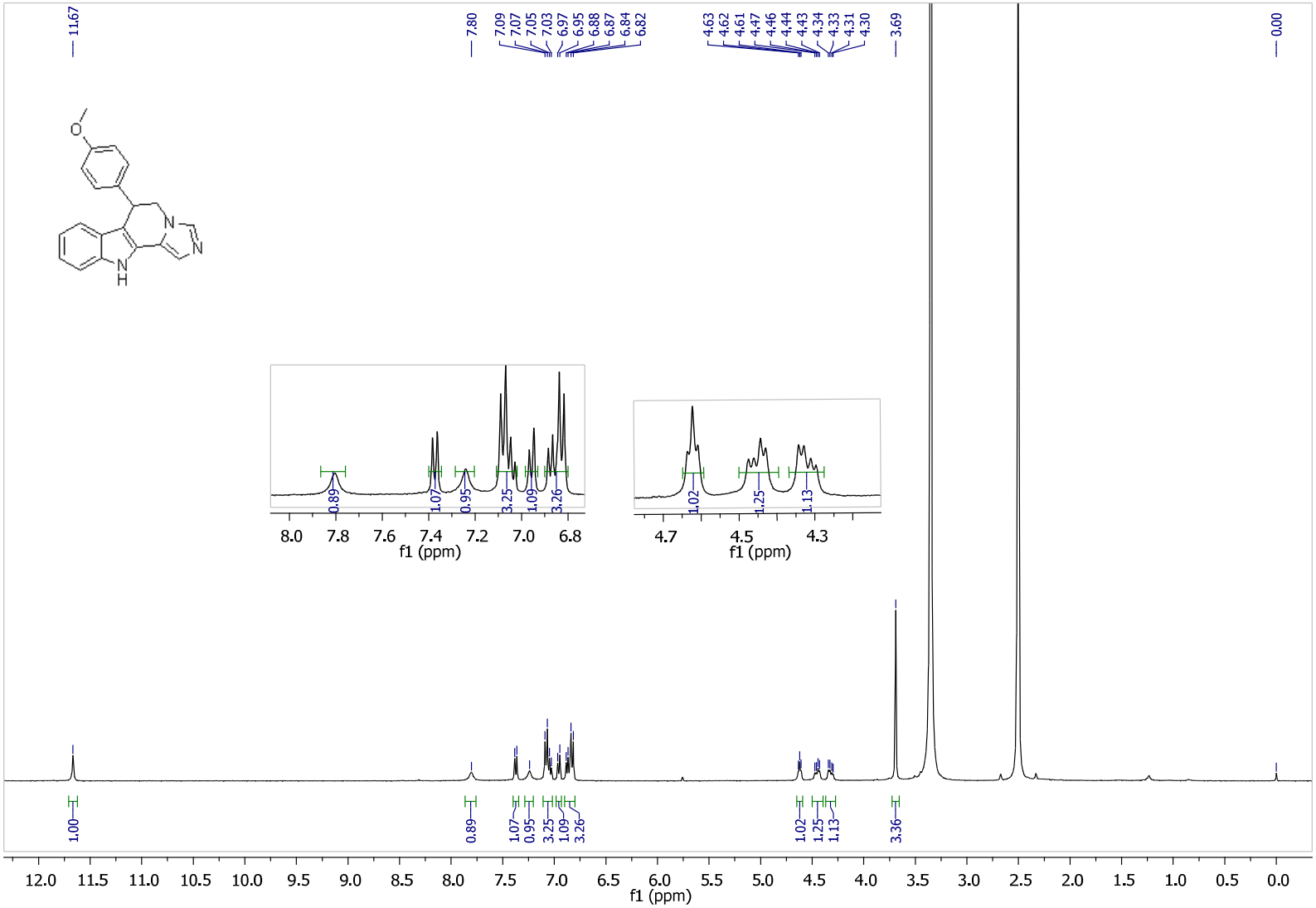
^{1}H NMR of 3m


11.68
7.74
7.39
7.37
7.26
7.24
7.23
7.18
7.16
7.06
7.04
7.02
6.98
6.96
6.88
6.86
4.66
4.49
4.48
4.46
4.45
4.38
4.37
4.35
N
N
N
H
1.00
0.86
1.24
6.42
1.29
1.14
1.10
0.88
0.98
1.02
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

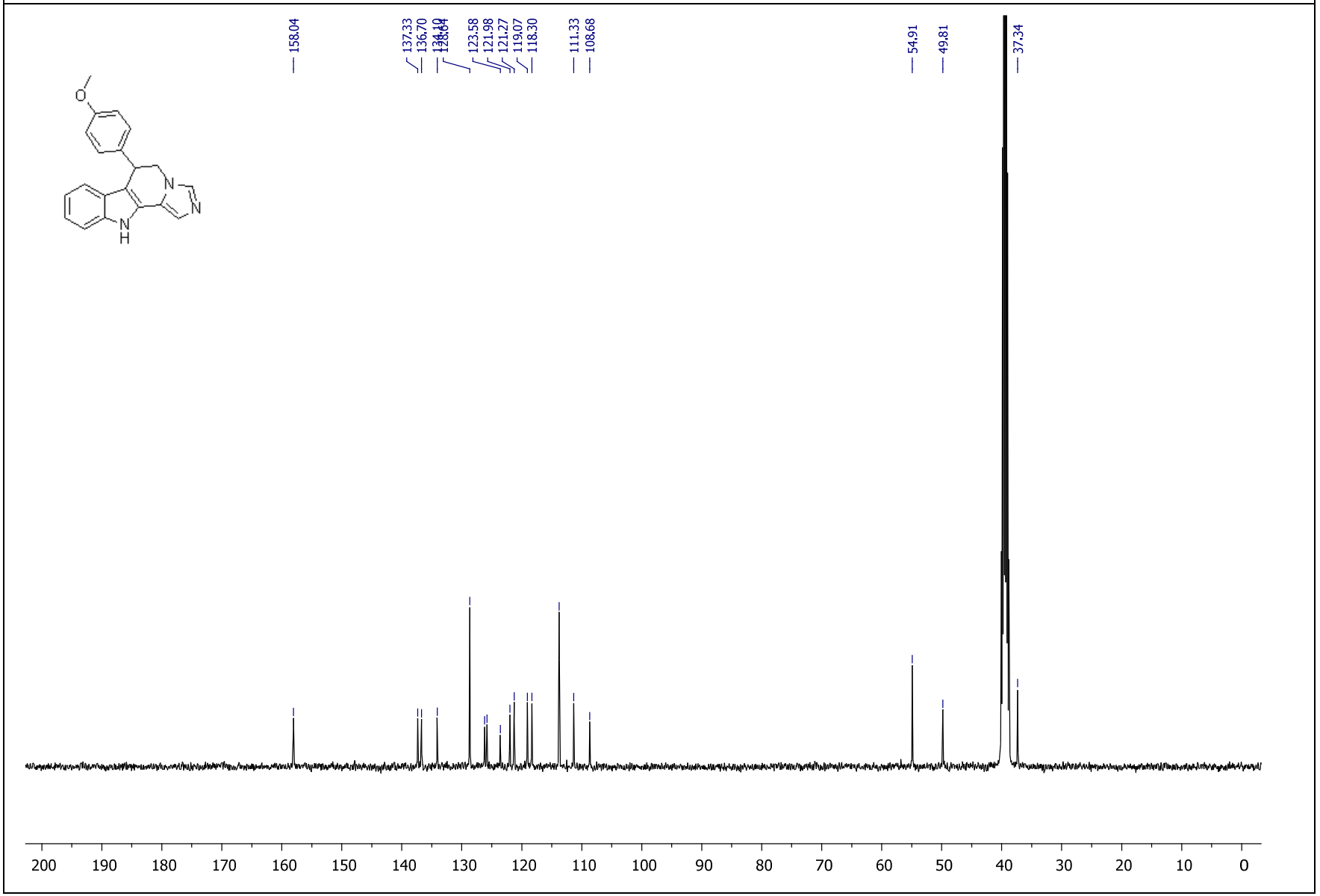
^{13}C NMR of 3m


147.64
142.72
142.02
133.70
132.89
132.06
131.58
131.07
127.36
126.63
124.41
113.67
54.87
43.37
N
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

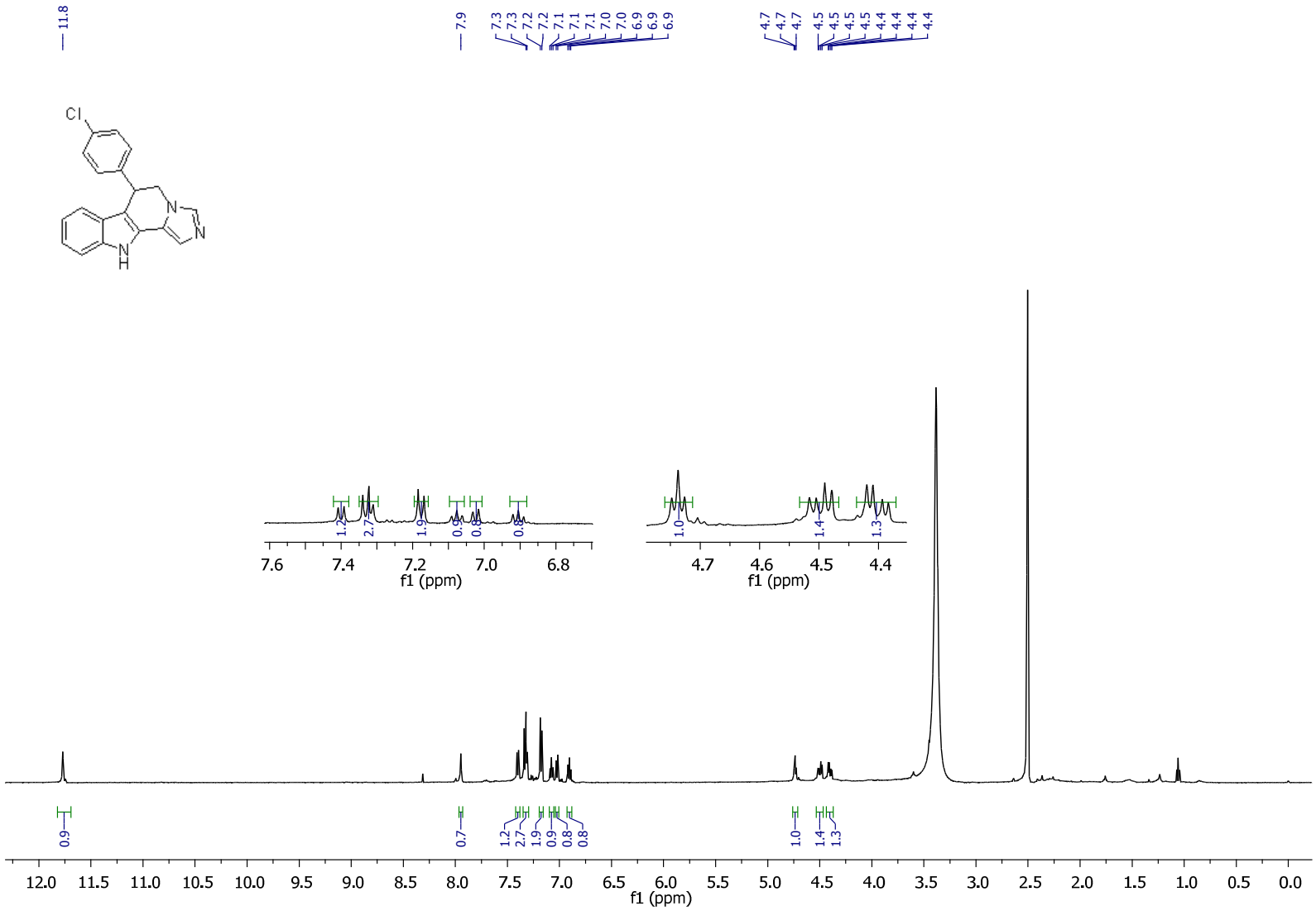
^{1}H NMR of 3n


11.67
7.80
7.09
7.07
7.05
7.03
6.97
6.95
6.88
6.87
6.84
6.82
4.63
4.62
4.61
4.47
4.46
4.44
4.43
4.34
4.33
4.31
4.30
3.69
0.00
O
N
N
H
0.89
1.07
0.95
3.25
1.09
3.26
1.02
1.25
1.13
f1 (ppm)
1.00
0.89
1.07
0.95
3.25
1.09
3.26
1.02
1.25
1.13
3.36
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
f1 (ppm)

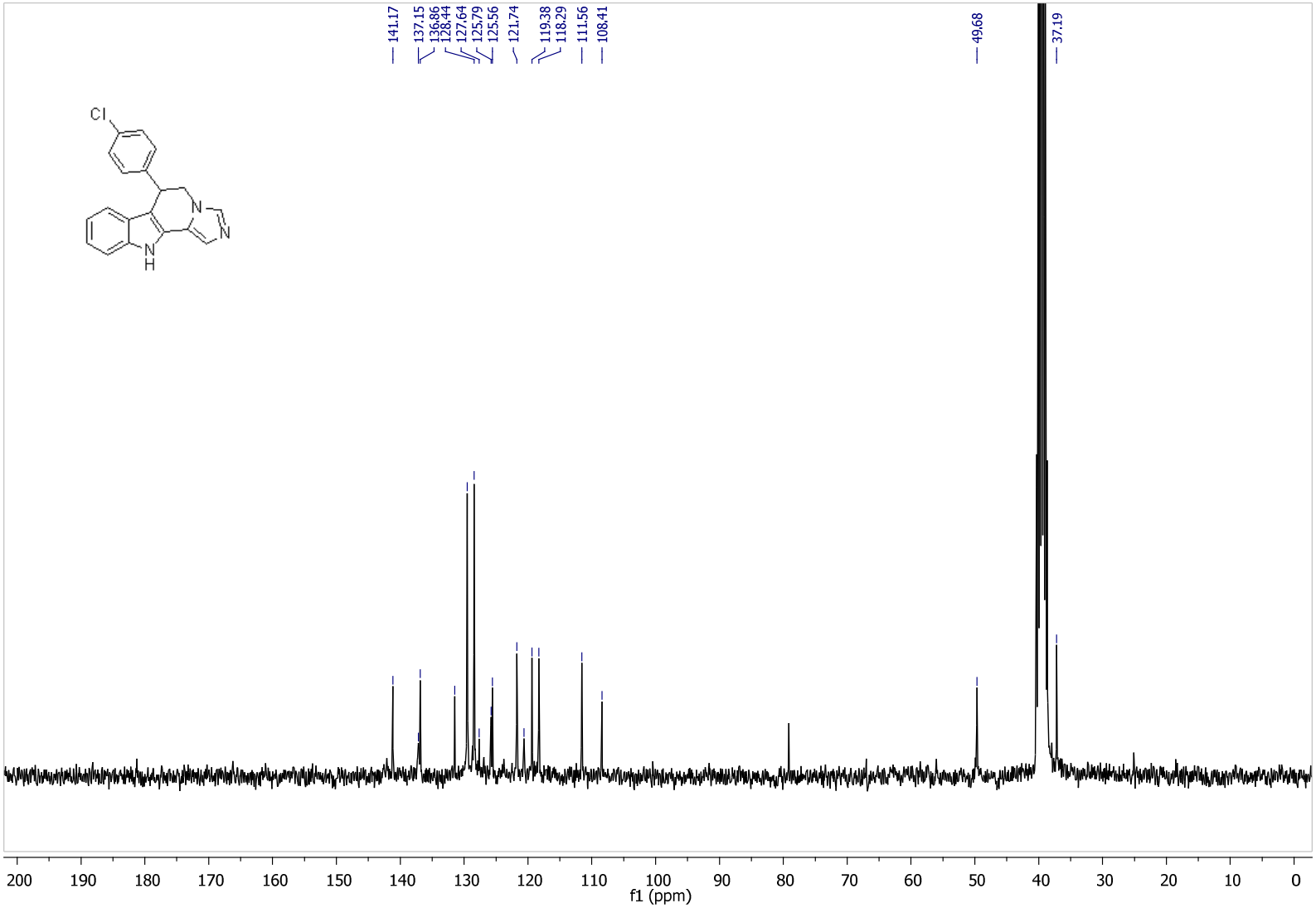
^{13}C NMR of 3n


158.04
137.33
136.70
123.58
121.98
121.27
119.07
118.30
111.33
108.68
54.91
49.81
37.34
O
N
N
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

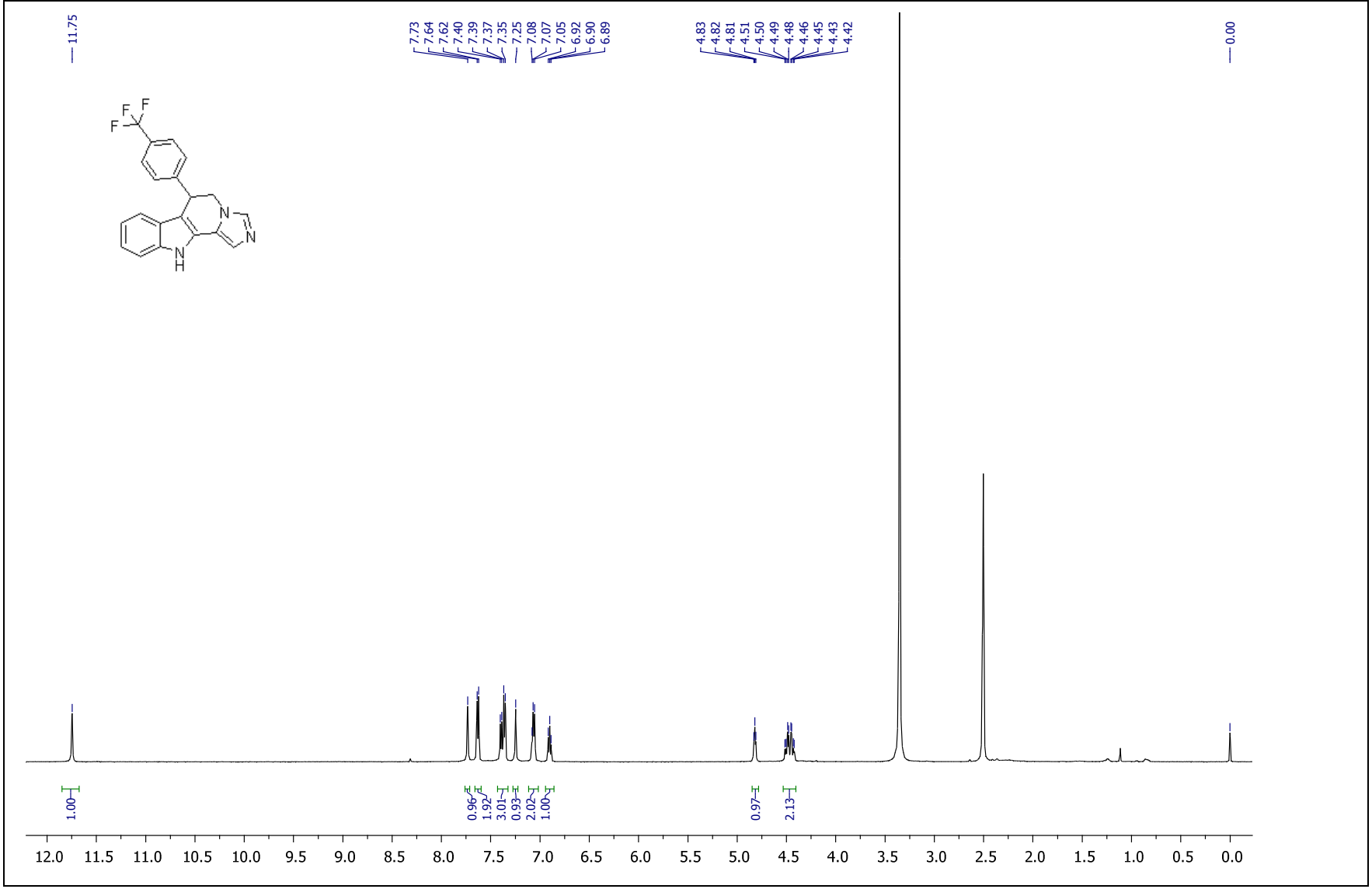
^{1}H NMR of 3o


11.8
7.9
7.3
7.3
7.2
7.2
7.1
7.1
7.1
7.0
7.0
6.9
6.9
6.9
4.7
4.7
4.7
4.5
4.5
4.5
4.5
4.4
4.4
4.4
4.4
Cl
N
N
H
1.2
2.7
1.9
0.9
0.8
0.8
7.6
7.4
7.2
7.0
6.8
f1 (ppm)
1.0
1.4
1.3
4.7
4.6
4.5
4.4
f1 (ppm)
0.9
0.7
1.2
2.7
1.9
0.9
0.8
0.8
1.0
1.4
1.3
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
f1 (ppm)

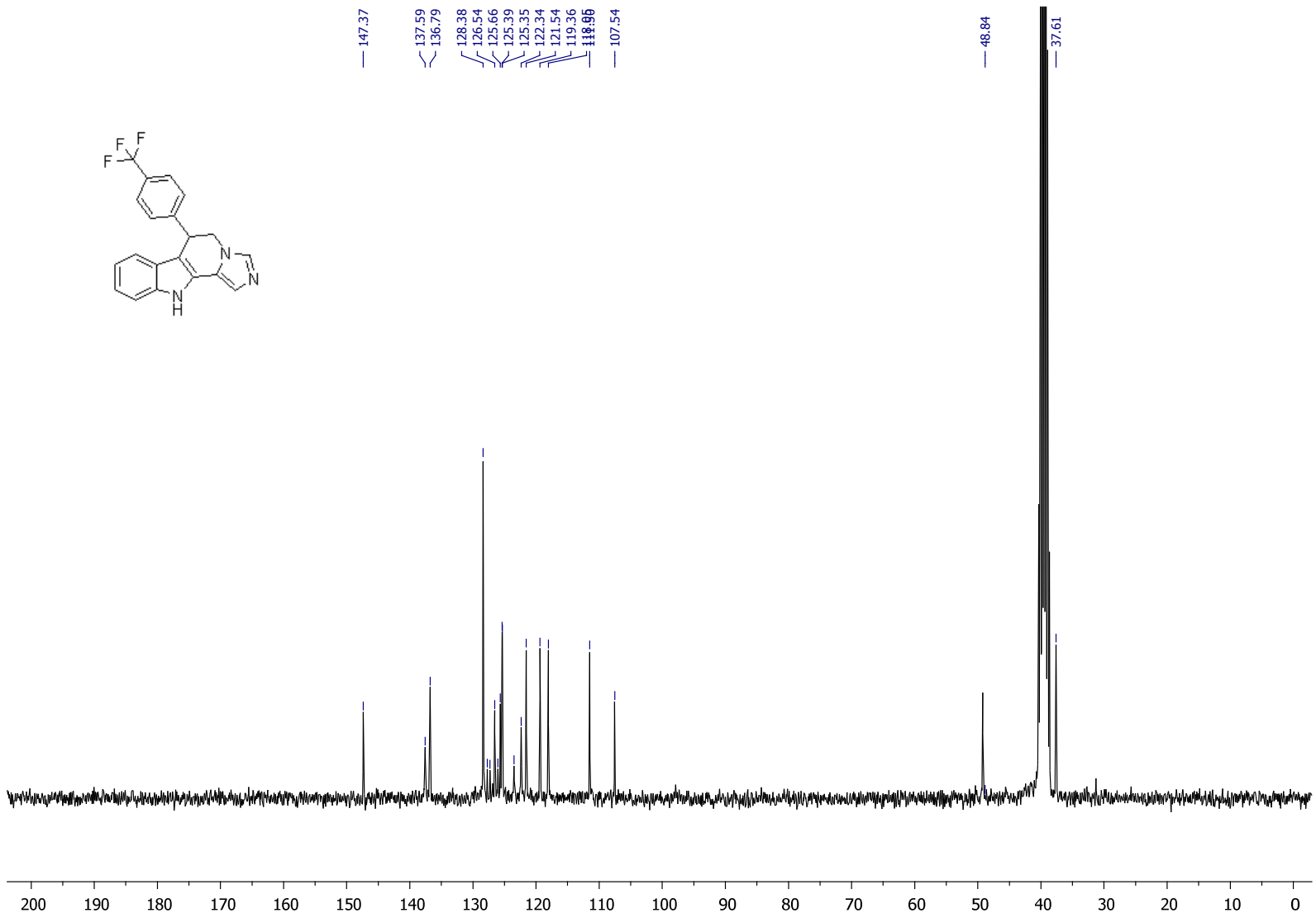
^{13}C NMR of 3o


141.17
137.15
136.86
128.44
127.64
125.79
125.56
121.74
119.38
118.29
111.56
108.41
49.68
37.19
Cl
N
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

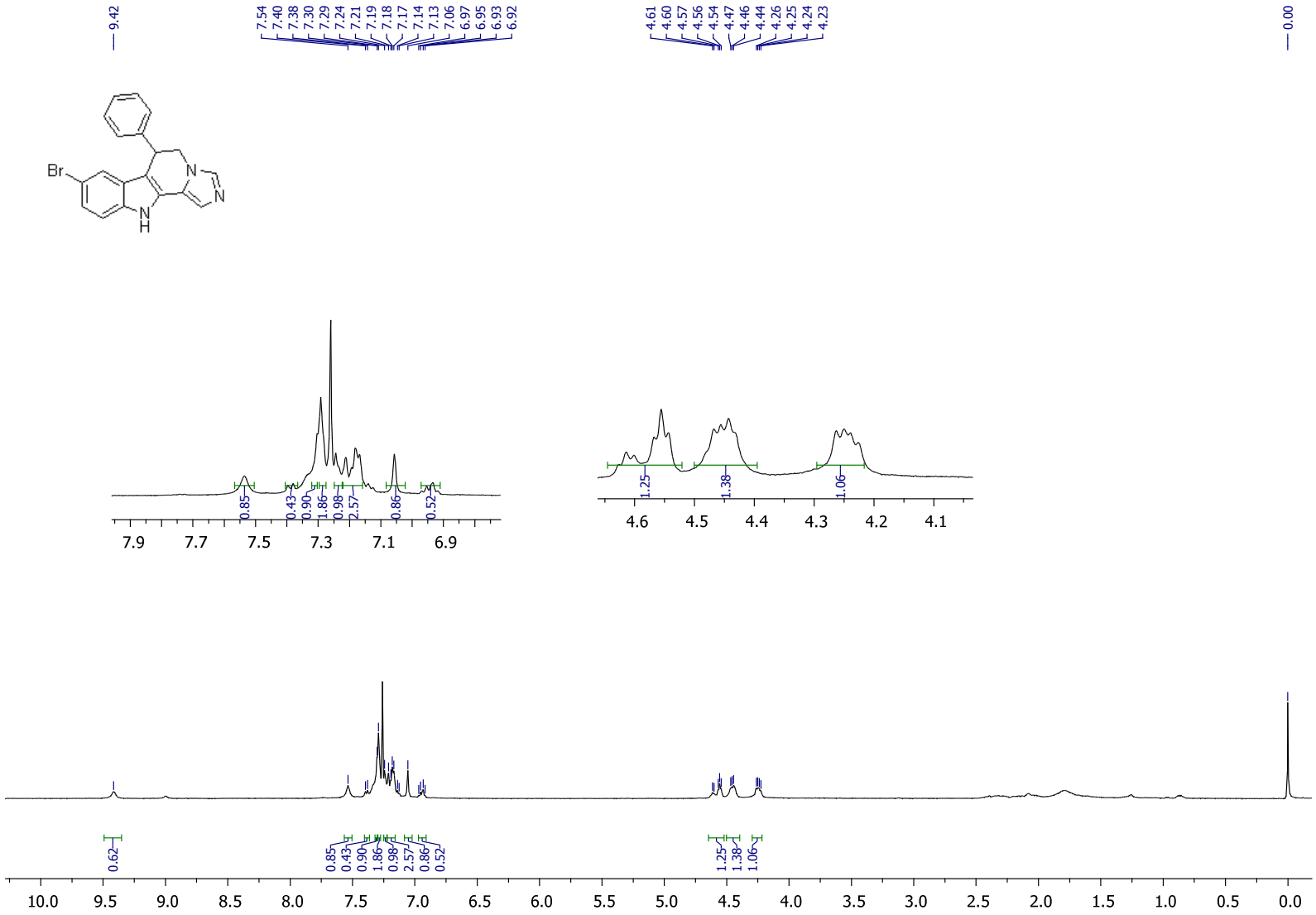
^{1}H NMR of 3p


11.75
7.73
7.64
7.62
7.40
7.39
7.37
7.35
7.25
7.08
7.07
7.05
6.92
6.90
6.89
4.83
4.82
4.81
4.51
4.50
4.49
4.48
4.46
4.45
4.43
4.42
0.00
F
F
F
N
N
H
1.00
0.96
1.92
3.01
0.93
2.02
1.00
0.97
2.13
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

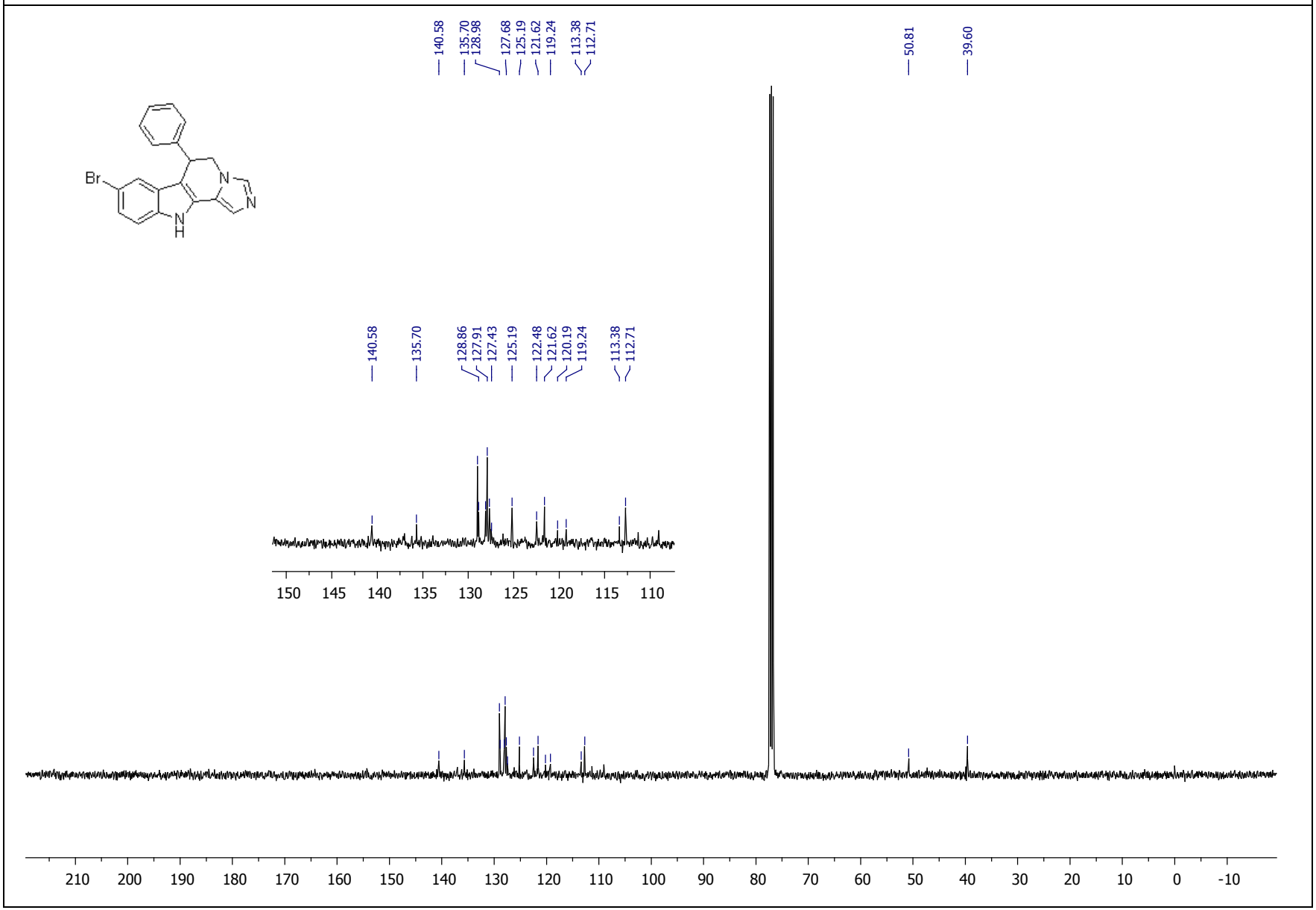
^{13}C NMR of 3p


147.37
137.59
136.79
128.38
126.54
125.66
125.39
125.35
122.34
121.54
119.36
107.54
48.84
37.61
F
F
F
N
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

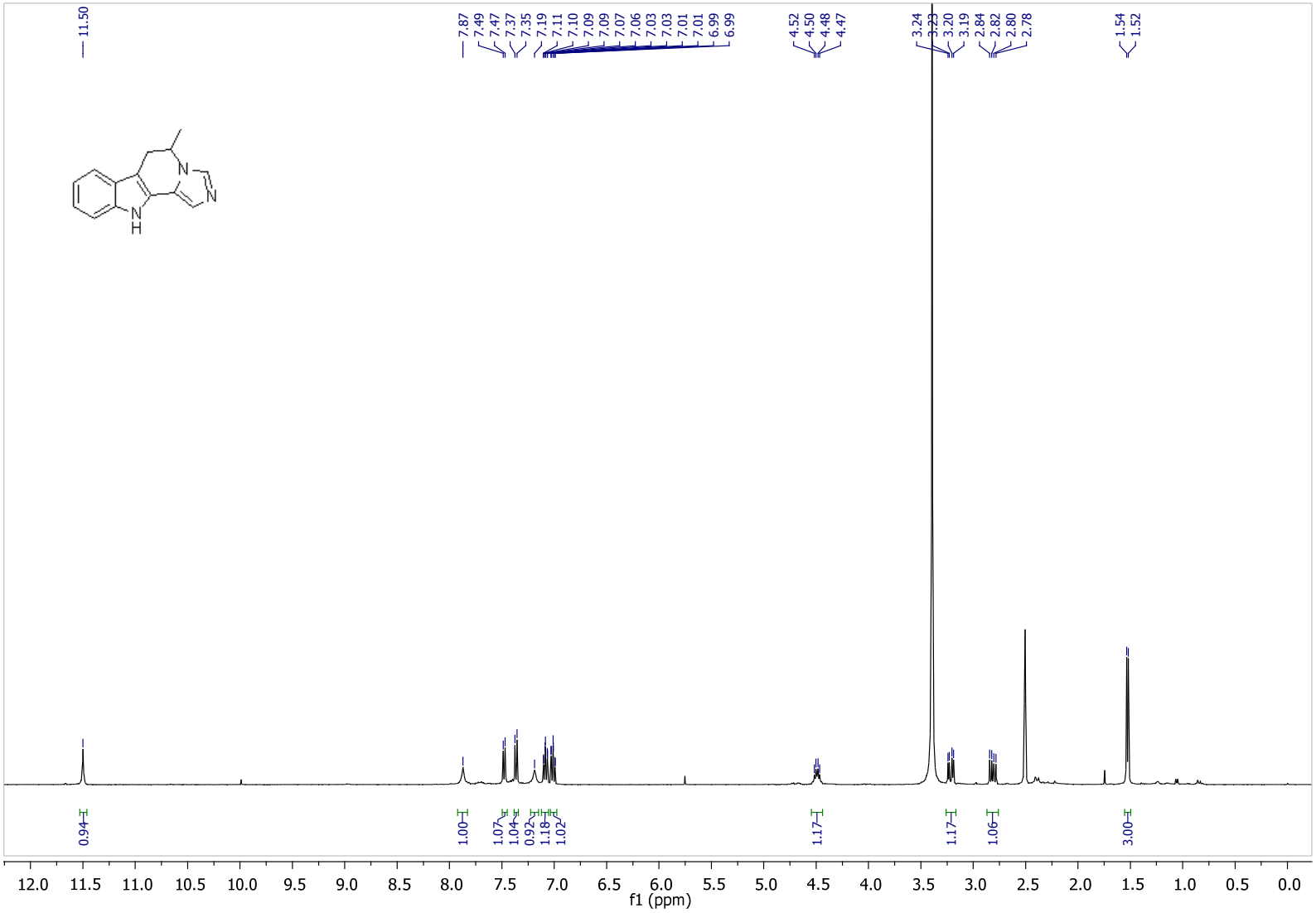
^{1}H NMR of 3q


9.42
7.54
7.40
7.38
7.30
7.29
7.24
7.21
7.19
7.18
7.17
7.14
7.13
7.06
6.97
6.95
6.93
6.92
4.61
4.60
4.57
4.56
4.54
4.47
4.46
4.44
4.26
4.25
4.24
4.23
0.00
Br
N
N
N
H
0.85
0.43
0.90
1.86
0.98
2.57
0.86
0.52
1.25
1.38
1.06
0.62
7.9
7.7
7.5
7.3
7.1
6.9
4.6
4.5
4.4
4.3
4.2
4.1
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

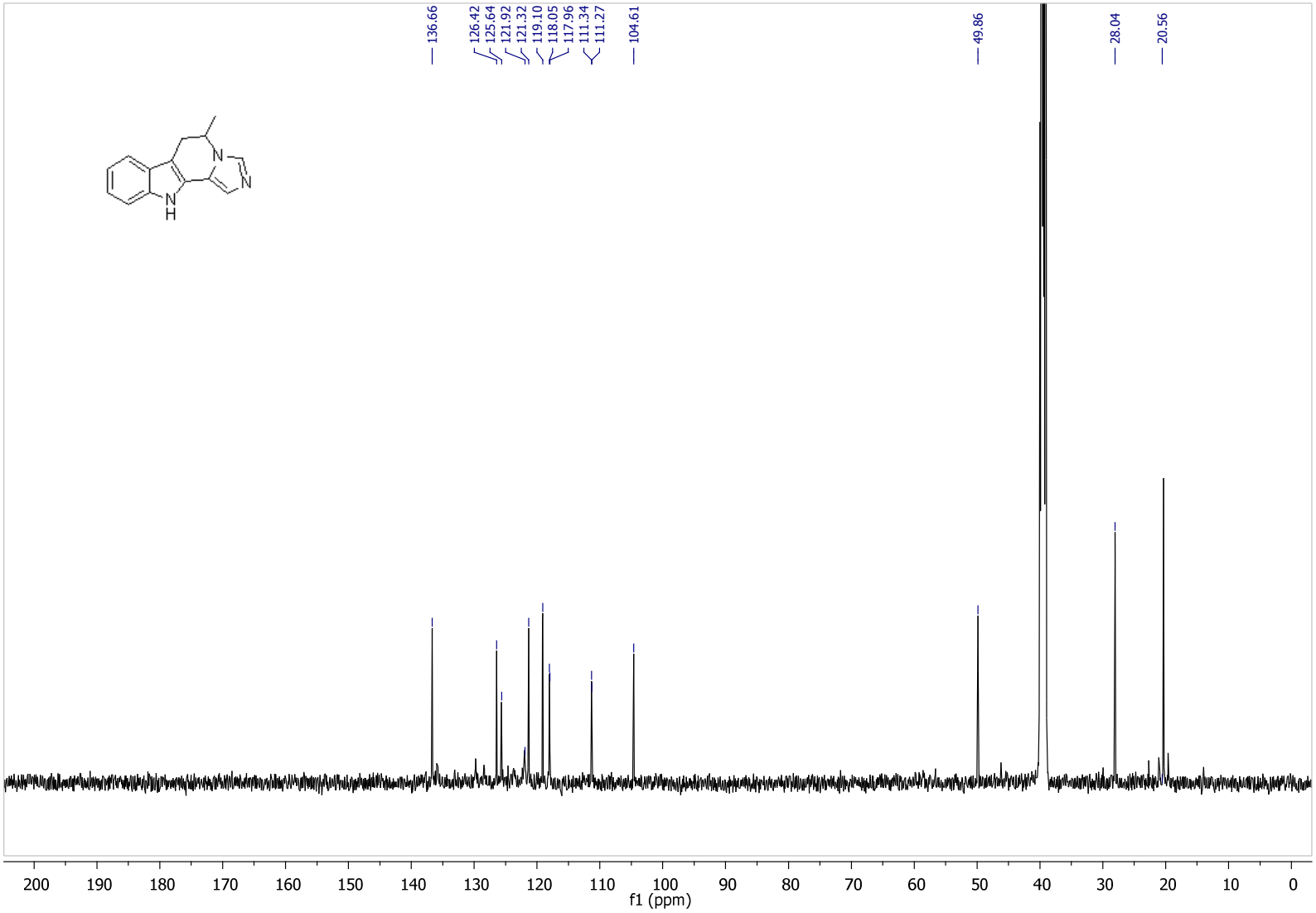
^{13}C NMR of 3q


140.58
135.70
128.98
127.68
125.19
121.62
119.24
113.38
112.71
50.81
39.60
Br
N
N
N
H
140.58
135.70
128.86
127.91
127.43
125.19
122.48
121.62
120.19
119.24
113.38
112.71
150 145 140 135 130 125 120 115 110
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

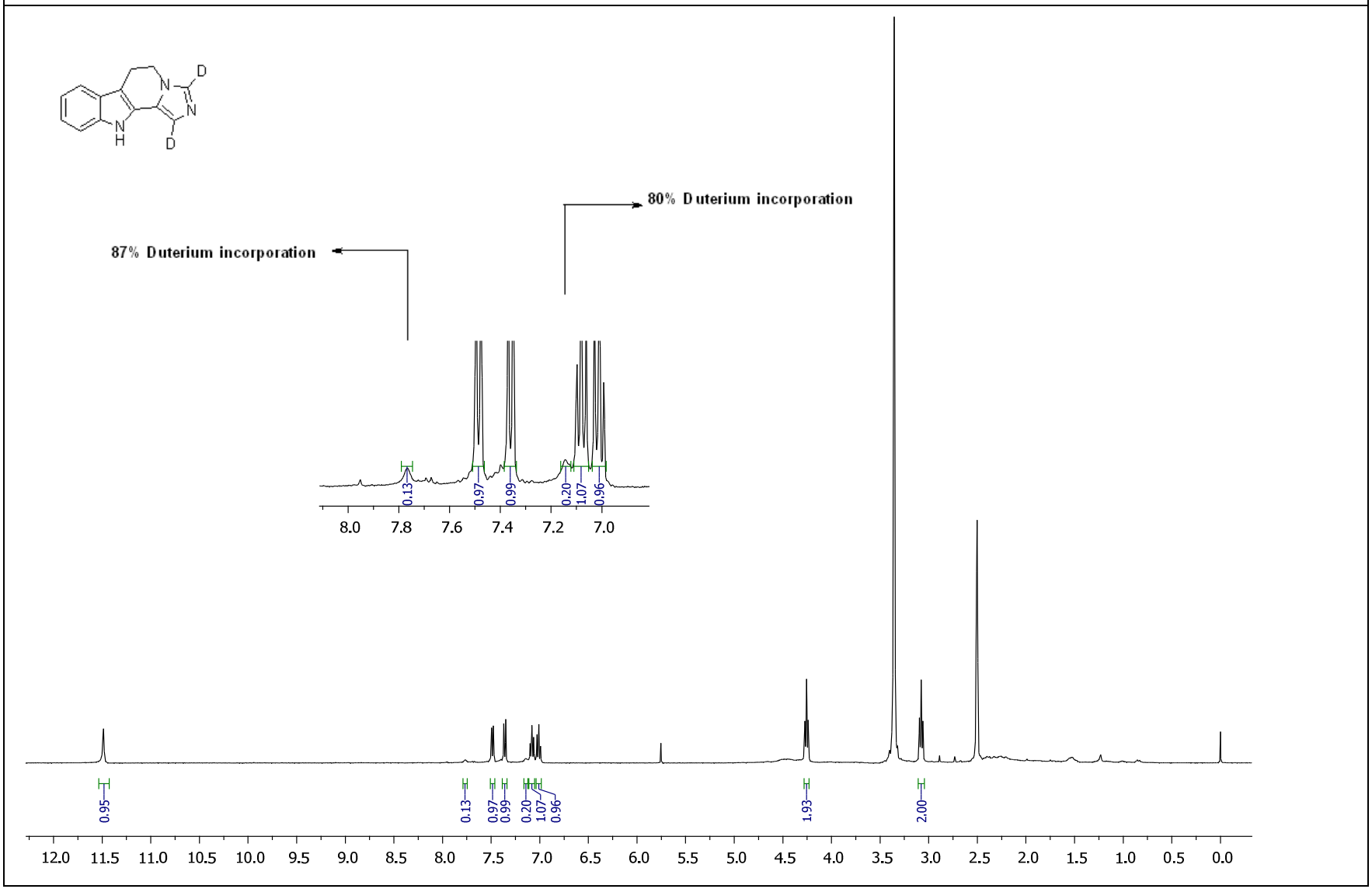
^{1}H NMR of 3r


11.50
7.87
7.49
7.47
7.37
7.35
7.19
7.11
7.10
7.09
7.09
7.07
7.06
7.03
7.03
7.01
7.01
6.99
6.99
4.52
4.50
4.48
4.47
3.24
3.23
3.20
3.19
2.84
2.82
2.80
2.78
1.54
1.52
0.94
1.00
1.07
1.04
0.92
1.18
1.02
1.17
1.17
1.06
3.00
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
f1 (ppm)

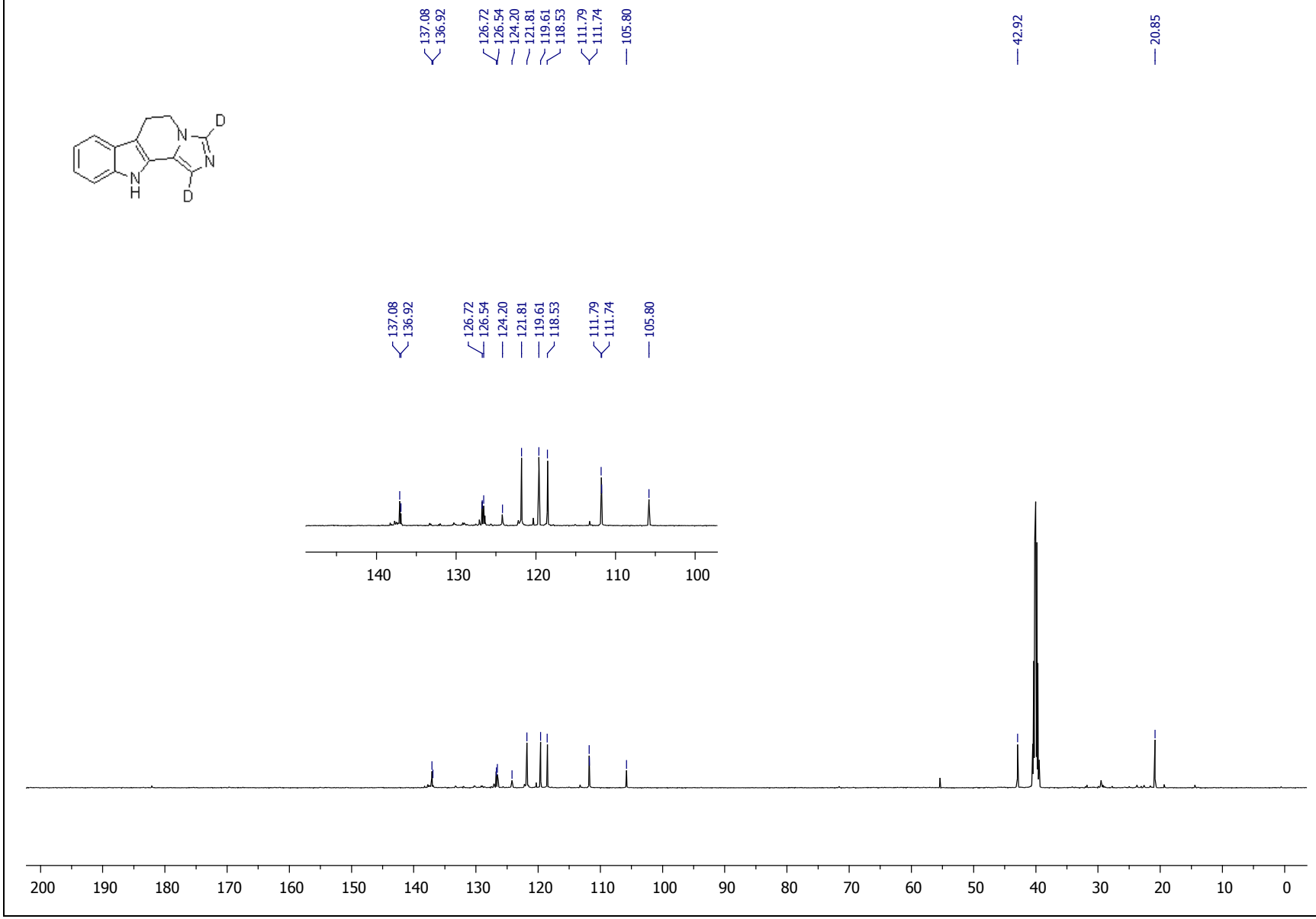
^{13}C NMR of 3r


136.66
126.42
125.64
121.92
121.32
119.10
118.05
117.96
111.34
111.27
104.61
49.86
28.04
20.56
N
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

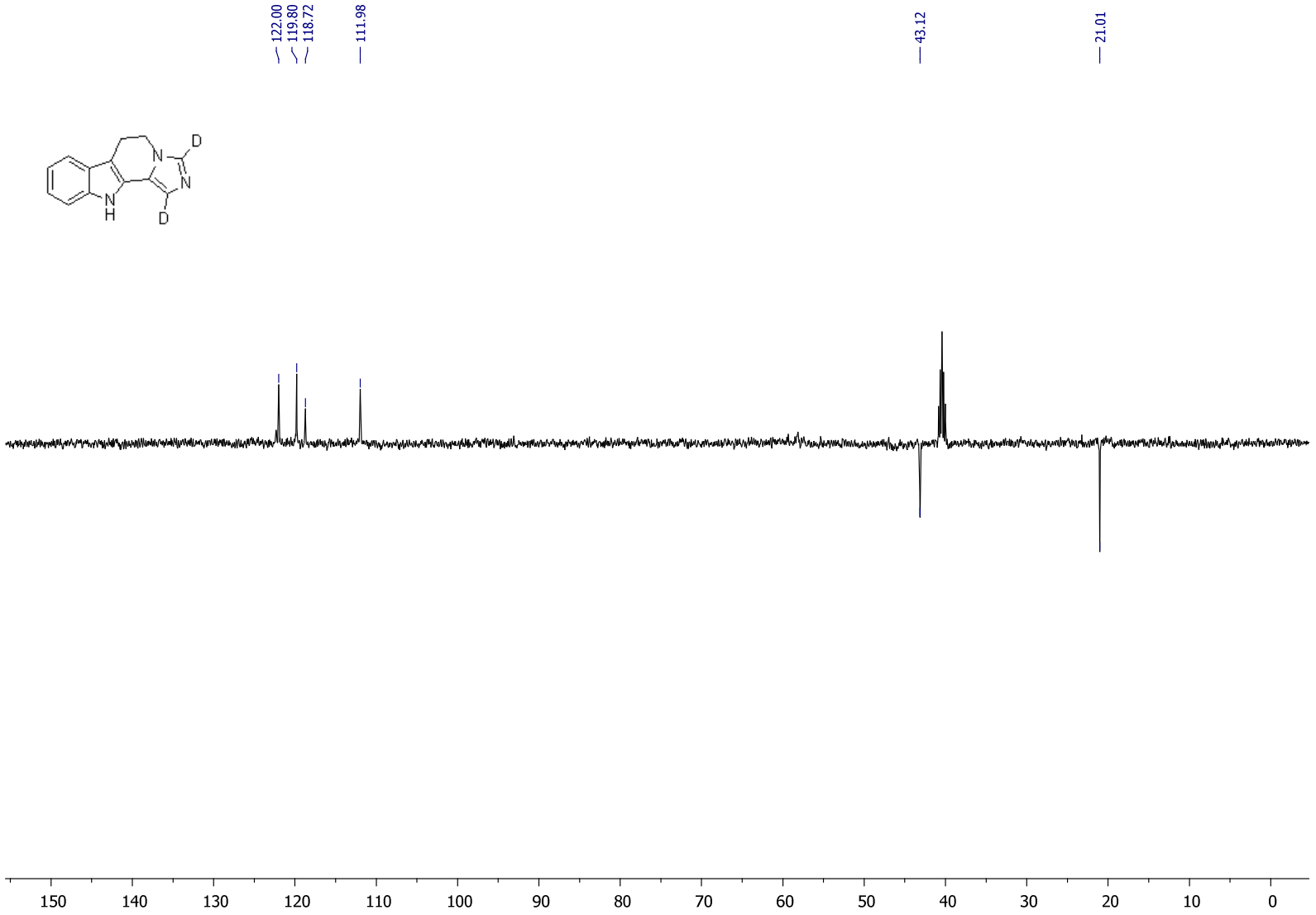
^{1}H NMR of 3a-D_2



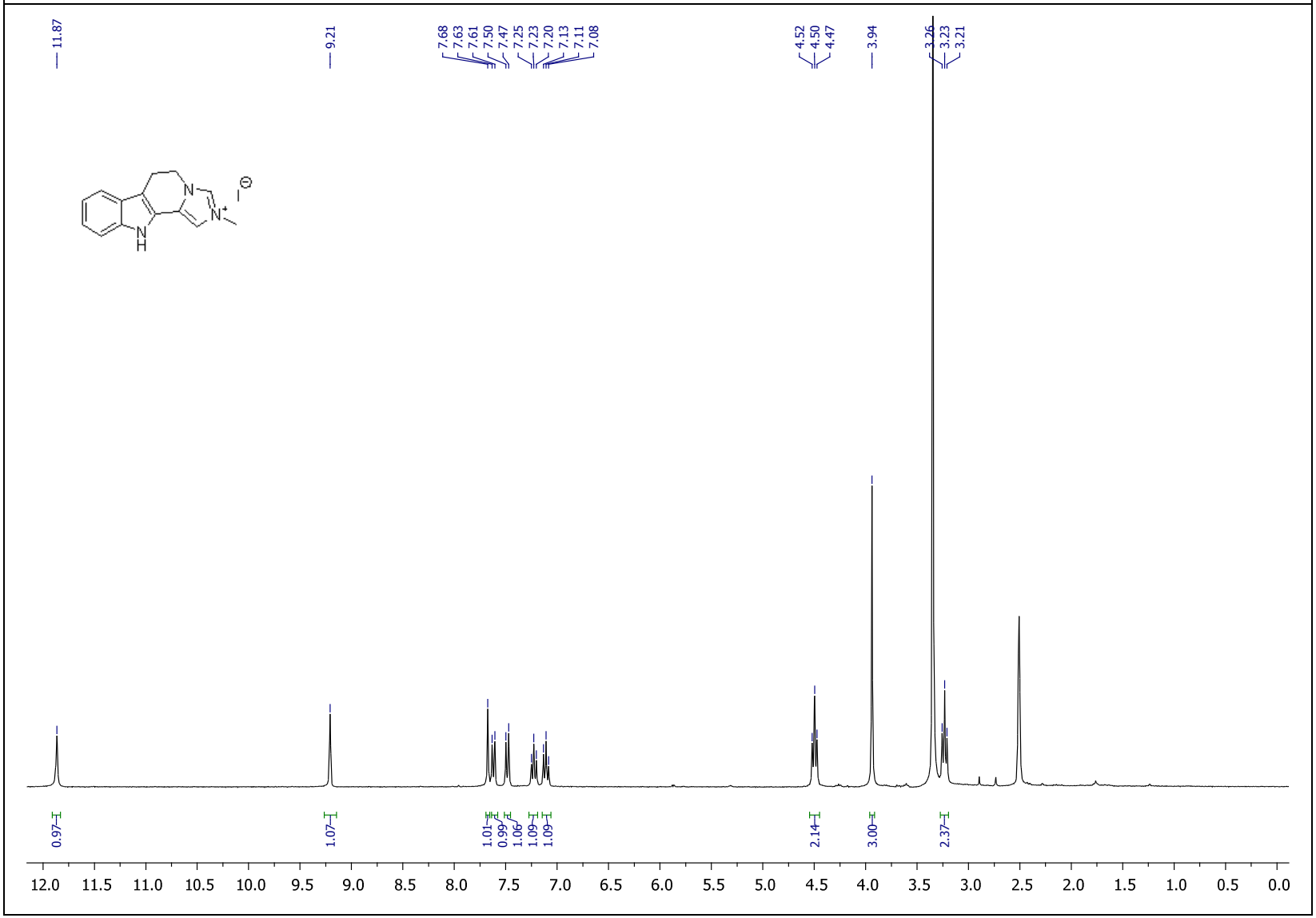
^{13}C NMR of 3a-D_2



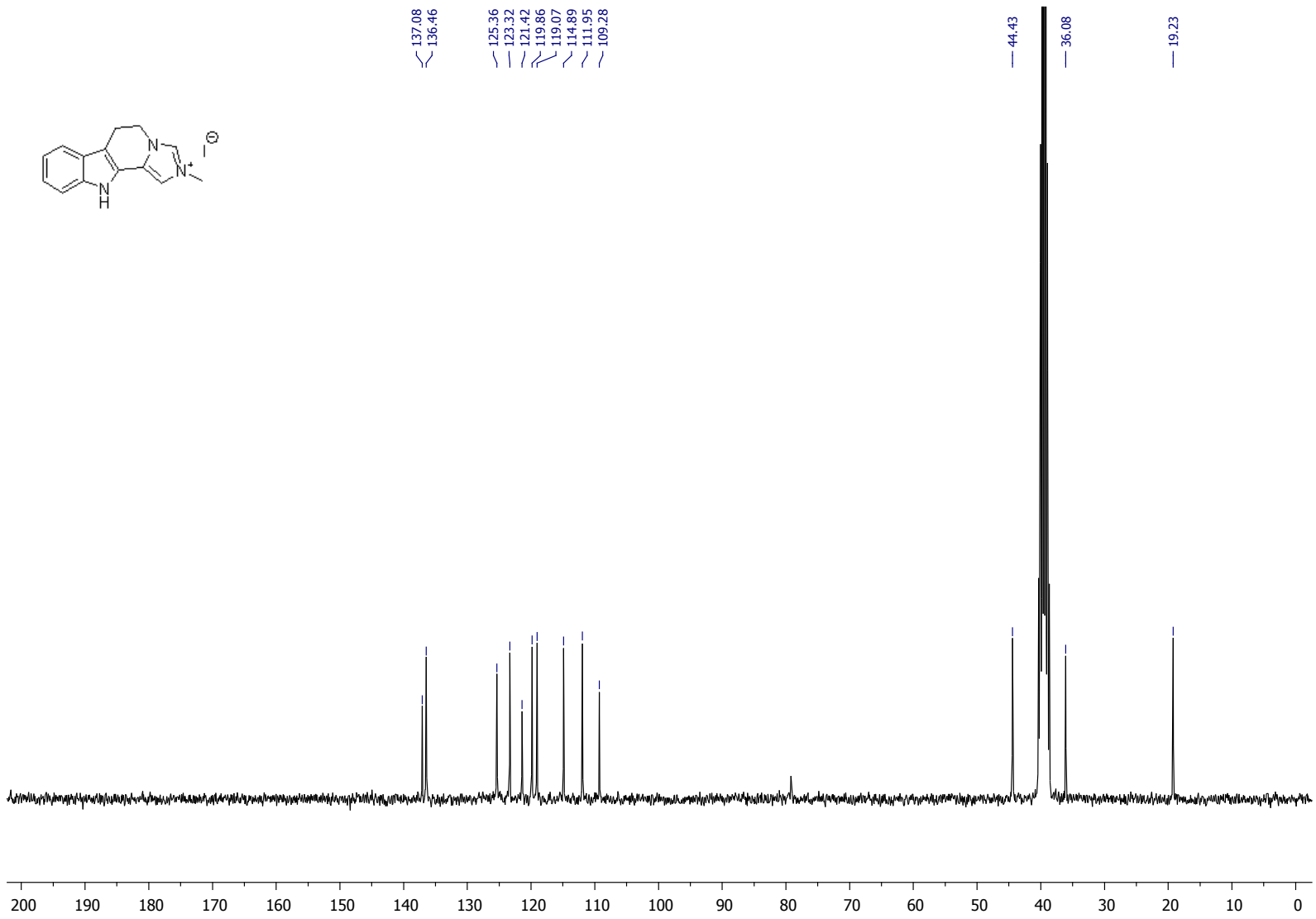
DEPT-135 of 3a-D_2



^{1}H NMR of 4


11.87
9.21
7.68
7.63
7.61
7.50
7.47
7.25
7.23
7.20
7.13
7.11
7.08
4.52
4.50
4.47
3.94
3.26
3.23
3.21
0.97
1.07
1.01
0.99
1.06
1.09
1.09
2.14
3.00
2.37
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 4


137.08
136.46
125.36
123.32
121.42
119.86
119.07
114.89
111.95
109.28
44.43
36.08
19.23
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0