Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

An efficient one-pot decarboxylative aromatization of tetrahydro-β-carbolines by using *N*-chlorosuccinimide: Total synthesis of norharmane, harmane and eudistomins

Ahmed Kamal,* Manda Sathish, A. V. G. Prasanthi, Jadala Chetna, Yellaiah Tangella, Vunnam Srinivasulu, Nagula Shankaraiah and Abdullah Alarifi

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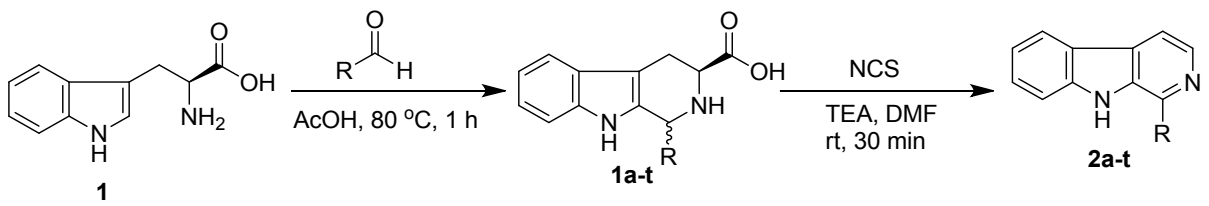
Experimental Section

General information

Unless otherwise stated, all the starting materials and other reagents of the best grade were commercially available and were used without further purification. TLC was performed on 0.25 mm silica gel 60-F254 plates. Spots were visualized by UV light. All the melting points were taken by Electrothermal apparatus and the values are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on 300 MHz, 400 MHz and 500 MHz NMR instruments using tetramethylsilane as the internal standard. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane. Spin multiplicities are described as s (singlet), bs (broad singlet), d (doublet), dd (double doublet), t (triplet), q (quartet), or m (multiplet). Coupling constants are reported in hertz (Hz). HRMS analyses were acquired on single quadruple and carried out using the ESI techniques at 70 eV. Wherever required column chromatography was performed using silica gel of 60–120 mm with hexane, ethyl acetate and methanol as eluents.

Pictet-Spengler reaction and decarboxylative aromatization of L-tryptophan.

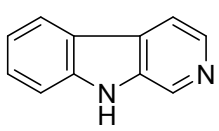


Scheme S1: Synthesis of β-carboline (**2a-t**) unsing NCS.

General Procedure

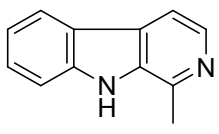
To a stirred solution of L-tryptophan (**1**, 1 mmol) in acetic acid was added aldehyde (1.1 mmol), stirred at 80 °C for 1 h and the acetic acid was removed under reduced pressure and dried well. This residue was taken in DMF, added TEA (3 mmol) and solution of NCS (2.1 mmol) in DMF. Then the reaction mixture was stirred for 30 min at room temperature. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with water, extracted with ethyl acetate and washed with saturated Na_2CO_3 solution. The combined organic layers were washed with water, brine solution, dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue obtained was purified by column chromatography by using ethyl acetate and hexane to afford the desired β-carbolines (**2a-t**).

9*H*-Pyrido[3,4-*b*]indole (norharmane, 2a).[1]



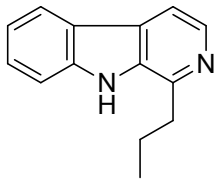
Yellow solid: 80% yield; mp:195–198 °C (ref. 1: (195–197 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.16 (bs, 1H), 8.94 (s, 1H), 8.47 (d, *J* = 4.9 Hz, 1H), 8.14 (d, *J* = 7.9 Hz, 1H), 7.98 (d, *J* = 4.9 Hz, 1H), 7.58–7.51 (m, 2H), 7.30 (t, *J* = 7.7 Hz, 1H); ^{13}C NMR (125 MHz, DMSO−d_6) δ; 140.4, 137.9, 135.8, 133.9, 128.0, 127.3, 121.6, 120.5, 119.1, 114.5, 111.8; MS (ESI): *m/z* 169 $[M + H]^+$; HRMS (ESI): calcd for $C_{11}H_9N_2$ *m/z* 169.0760 $[M + H]^+$; found: 169.0757.

1-Methyl-9*H*-pyrido[3,4-*b*]indole (harmane, 2b).[2]



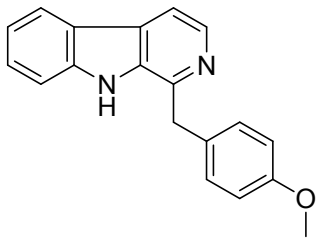
Off white solid: 82% yield; mp: 230–233 °C (ref. 2: 235–236 °C); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6) δ: 10.77 (bs, 1H), 8.30 (d, *J* = 4.7 Hz, 1H), 8.10 (d, *J* = 7.5 Hz, 1H), 7.81 (d, *J* = 4.7 Hz, 1H), 7.63–7.48 (m, 2H), 7.23 (t, *J* = 6.9 Hz, 1H), 2.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO–d_6) δ: 141.6, 140.2, 136.8, 134.3, 127.3, 126.9, 121.0, 120.7, 118.8, 112.1, 111.5, 20.0; MS (ESI): *m/z* 183 $[M + H]^+$; HRMS (ESI): calcd for $C_{12}H_{11}N_2$ *m/z* 183.0916 $[M + H]^+$; found: 183.0916.

1-Propyl-9*H*-pyrido[3,4-*b*]indole (2c).[3]



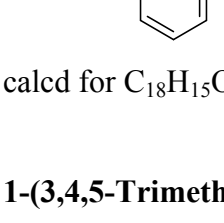
Brown colour solid: 78% yield; mp: 170−175 °C (ref. 3: 218–220 °C); ^{1}H NMR (300 MHz, DMSO−d_6) δ: 11.05 (bs, 1H), 8.30 (d, *J* = 5.3 Hz, 1H), 8.09 (d, *J* = 7.7 Hz, 1H), 7.80 (d, *J* = 5.3 Hz, 1H), 7.58 (d, *J* = 8.1 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 3.14 (t, *J* = 7.5 Hz, 2H), 1.92 (q, *J* = 7.5, 15.1 Hz, 2H), 1.05 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO–d_6) δ: 145.6, 140.2, 137.3, 134.0, 127.6, 126.9, 121.5, 120.9, 119.0, 112.4, 111.7, 35.3, 21.3, 13.8; MS (ESI): *m/z* 211 $[M + H]^+$; HRMS (ESI): calcd for $C_{14}H_{15}N_2$ *m/z* 211.1229 $[M + H]^+$; found: 211.1216.

1-(4-Methoxybenzyl)-9*H*-pyrido[3,4-*b*]indole (2d)



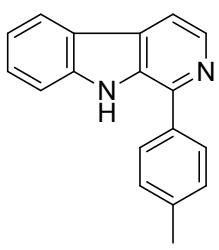
Yellow solid: 90% yield; mp: 142–144 °C; ^{1}H NMR (300 MHz, DMSO−d_6) δ: 11.67 (s, 1H), 8.26 (d, J = 5.3 Hz, 1H), 8.21 (d, J = 7.7 Hz, 1H), 7.96 (d, J = 5.1 Hz, 1H), 7.62 (d, J = 8.1 Hz, 1H), 7.54 (t, J = 7.2 Hz, 1H), 7.31 (d, J = 8.7 Hz, 2H), 7.23 (t, J = 7.7 Hz, 1H), 6.82 (d, J = 8.5 Hz, 2H), 4.38 (s, 2H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, DMSO−d_6) δ: 157.5, 144.7, 140.3, 137.6, 133.8, 131.1, 129.6, 127.9, 127.6, 121.6, 120.9, 119.2, 113.6, 112.8, 111.8, 54.8, 38.4; MS (ESI): *m/z* 289 $[M + H]^+$; HRMS (ESI): calcd for $C_{19}H_{17}ON_2$ *m/z* 289.1335 $[M + H]^+$; found: 289.1328.

1-Phenyl-9*H*-pyrido[3,4-*b*]indole (2e).[2]



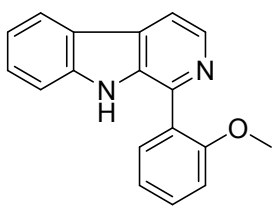
Yellow solid: 85% yield; mp: 241–244 °C (ref. 2: 241–242 °C); ^{1}H NMR (300 MHz, DMSO−d_6) δ: 11.52 (bs, 1H), 8.47 (d, J = 5.2 Hz, 1H), 8.26 (d, J = 7.7 Hz, 1H), 8.13 (d, J = 5.3 Hz, 1H), 8.03 (d, J = 7.0 Hz, 2H), 7.67−7.49 (m, 5H), 7.26 (t, J = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, DMSO−d_6) δ: 142.1, 141.0, 138.3, 138.3, 132.9, 129.0, 128.6, 128.4, 128.3, 128.0, 121.5, 120.7, 119.4, 113.8, 112.3; MS (ESI): *m/z* 245 $[M + H]^+$; HRMS (ESI): calcd for $C_{19}H_{15}O_2N_2$ *m/z* 245.1073 $[M + H]^+$; found: 245.1074.

1-(*p*-Tolyl)-9*H*-pyrido[3,4-*b*]indole (2f).[4]



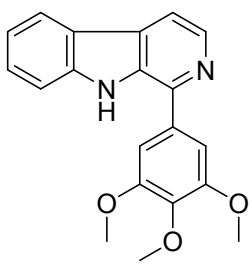
White solid: 88% yield; mp: 192–195 °C (ref. 4: 190.3–191.6 °C); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6) δ: 11.23 (bs, 1H), 8.38 (d, J = 5.1 Hz, 1H), 8.11 (d, J = 7.9 Hz, 2H), 7.89 (t, J = 5.4 Hz, 3H), 7.59 (d, J = 8.2 Hz, 1H), 7.45 (t, J = 7.3 Hz, 1H), 7.34 (d, J = 7.9 Hz, 2H), 7.19 (t, J = 7.3 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO−d_6) δ: 142.2, 140.8, 137.8, 137.5, 135.4, 132.8, 128.8, 127.9, 127.5, 120.8, 120.6, 118.9, 112.9, 112.0, 20.6; MS (ESI): *m/z* 259 $[M + H]^+$; HRMS (ESI): calcd for $C_{18}H_{15}N_2$ *m/z* 259.1229 $[M + H]^+$; found: 259.1219.

1-(2-Methoxyphenyl)-9*H*-pyrido[3,4-*b*]indole (2g).[5]



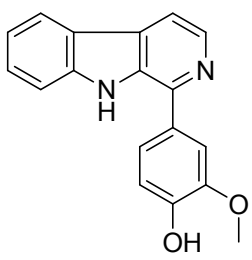
White solid: 93% yield; mp: 157–160 °C (ref. 5: 172–174 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.58 (bs, 1H), 8.55 (d, J = 5.2 Hz, 1H), 8.17 (d, J = 7.9 Hz, 1H), 7.93–7.90 (m, 3H), 7.55 (t, J = 7.1 Hz, 1H), 7.51 (t, J = 8.1 Hz, 1H), 7.32 (t, J = 7.6 Hz, 1H), 7.11 (d, J = 8.6 Hz, 2H), 3.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO−d_6) δ: 158.7, 141.5, 140.2, 137.2, 132.2, 130.1, 128.7, 128.2, 126.8, 120.1, 118.3, 113.0, 111.9, 111.3, 54.2; MS (ESI): *m/z* 275 $[M + H]^+$; HRMS (ESI): calcd for $C_{18}H_{15}ON_2$ *m/z* 275.1178 $[M + H]^+$; found: 275.1166.

1-(3,4,5-Trimethoxyphenyl)-9*H*-pyrido[3,4-*b*]indole (2h).[6]



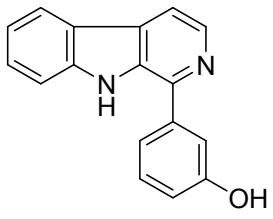
White solid: 92% yield; mp: 169–172 °C (ref. 6: 167–169 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.77 (bs, 1H), 8.55 (d, J = 5.1 Hz, 1H), 8.16 (d, J = 7.9 Hz, 1H), 7.94 (d, J = 5.1 Hz, 1H), 7.60–7.52 (m, 2H), 7.33 (t, J = 7.5 Hz, 1H), 7.13 (s, 1H), 3.92 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 153.5, 143.0, 140.5, 139.0, 138.2, 134.0, 133.4, 129.8, 128.4, 121.8, 121.7, 120.1, 113.7, 111.6, 105.2, 60.8, 56.1; MS (ESI): *m/z* 335 $[M + H]^+$; HRMS (ESI): calcd for $C_{19}H_{15}O_2N_2$ *m/z* 335.1390 $[M + H]^+$; found: 335.1391.

2-Methoxy-4-(9*H*-pyrido[3,4-*b*]indol-1-yl)phenol (2i).[7]



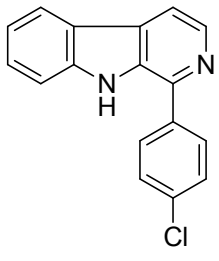
White solid: 83% yield; mp: 262–264 °C (ref. 7: 260–262 °C); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6) δ: 11.17 (s, 0.8H), 8.98 (s, 0.8H), 8.35 (d, J = 5.1 Hz, 1H), 8.07 (d, J = 7.9 Hz, 2H), 7.87–7.83 (m, 1H), 7.58 (d, J = 8.1 Hz, 1H), 7.51 (d, J = 1.7 Hz, 0.8H), 7.46−7.40 (m, 2H), 7.17 (d, J = 7.7 Hz, 1H), 6.98 (d, J = 8.1 Hz, 1H), 3.92 (s, 2.5H), peaks at 11.29, 9.22, 7.54 and 3.96 are due to 20% minor rotamers; ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO−d_6) δ: 147.4, 146.9, 142.5, 140.8, 137.6, 132.6, 129.5, 128.6, 127.4, 120.9, 120.7, 118.9, 115.2, 112.5, 112.1, 111.8, 55.2; MS (ESI): *m/z* 291 $[M + H]^+$; HRMS (ESI): calcd for $C_{18}H_{15}O_2N_2$ *m/z* 291.1128 $[M + H]^+$; found: 291.1115.

3-(9*H*-Pyrido[3,4-*b*]indol-1-yl)phenol (2j).[5]



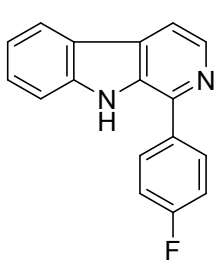
Cream colour solid: 78% yield; mp: 213–216 °C (ref. 5: 215–216 °C); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6) δ: 10.79 (s, 1H), 9.14 (bs, 1H), 8.38 (d, *J* = 5.1 Hz, 1H), 7.85 (d, *J* = 7.7 Hz, 1H), 7.54 (d, *J* = 5.1 Hz, 1H), 7.61 (d, *J* = 3.0 Hz, 1H), 7.47−7.37 (m, 3H), 7.30 (t, *J* = 7.7 Hz, 1H), 7.17 (t, *J* = 7.4 Hz, 1H), 6.87 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO−*d6*) δ: 156.9, 142.1, 140.4, 139.0, 137.4, 132.6, 128.9, 128.6, 127.1, 120.4, 120.4, 118.6, 115.0, 114.8, 112.6, 111.5; MS (ESI): *m/z* 261 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{13}ON_2$ *m/z* 261.1022 $[M + H]^+$; found: 261.1019.

1-(4-Chlorophenyl)-9*H*-pyrido[3,4-*b*]indole (2k).



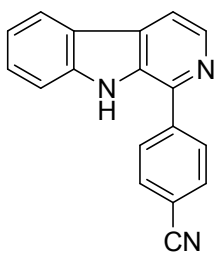
Light yellow solid: 80% yield; mp: 200−265 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6) δ: 11.42 (s, 1H), 8.39 (d, *J* = 5.3 Hz, 1H), 8.13 (d, *J* = 7.7 Hz, 1H), 8.00 (s, 1H), 7.99 (d, *J* = 8.3 Hz, 2H), 7.61 (d, *J* = 8.3 Hz, 1H), 7.55 (d, *J* = 8.5 Hz, 2H), 7.48 (t, *J* = 7.2 Hz, 1H), 7.21 (t, *J* = 7.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO−*d6*) δ: 141.1, 140.7, 137.8, 136.7, 133.4, 132.9, 129.8, 129.4, 128.4, 127.9, 121.1, 120.6, 119.3, 113.7, 112.1; MS (ESI): *m/z* 279 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{12}ClN_2$ *m/z* 279.0689 $[M + H]^+$; found: 279.0942.

1-(4-Fluorophenyl)-9*H*-pyrido[3,4-*b*]indole (2l).[4]



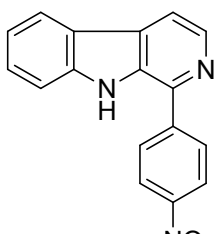
White solid: 83% yield; mp: 206–209 °C (ref. 4: 203–205 °C); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6) δ: 11.03 (bs, 1H), 8.39 (d, *J* = 5.3 Hz, 1H), 8.06 (d, *J* = 7.7 Hz, 1H), 7.98 (q, *J* = 5.5, 8.5 Hz, 2H), 7.87 (d, *J* = 5.1 Hz, 1H), 7.56 (d, *J* = 8.1 Hz, 1H),7.45 (t, *J* = 7.5 Hz, 1H), 7.25−7.14 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO−d_6) δ: 163.7 and 160.4 (d, *J* = 247.5 Hz), 141.1, 140.8, 137.8, 134.4, 132.8, 129.9 (d, *J* = 7.7 Hz), 1289.1, 127.5, 120.7, 120.6, 119.0, 115.0 (d, *J* = 20.9 Hz), 113.6, 111.8; MS (ESI): *m/z* 263 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{12}N_2F$ *m/z* 263.0979 $[M + H]^+$; found: 263.0979.

4-(9*H*-Pyrido[3,4-*b*]indol-1-yl)benzonitrile (2m).[5]



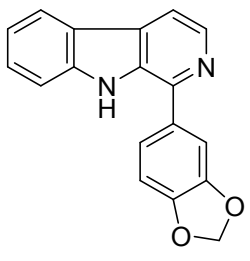
White solid: 81% yield; mp: 230–233 °C (ref. 5: 230−232 °C); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6) δ: 11.03 (bs, 1H), 8.45 (d, *J* = 5.3 Hz, 1H), 8.15 (d, *J* = 8.1 Hz, 2H), 8.07 (d, *J* = 7.7 Hz, 1H), 7.93 (d, *J* = 5.3 Hz, 1H), 7.80 (d, *J* = 8.1 Hz, 2H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.47 (t, *J* = 5.5 Hz, 1H), 7.20 (t, *J* = 7.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO−d_6) δ: 142.6, 140.9, 139.6, 138.2, 133.2, 131.8, 129.8, 128.7, 127.9, 120.9, 120.6, 119.4, 118.3, 114.1, 111.8, 110.9; MS (ESI): *m/z* 270 $[M + H]^+$; HRMS (ESI): calcd for $C_{18}H_{12}N_3$ *m/z* 270.1025 $[M + H]^+$; found: 270.1026.

1-(4-Nitrophenyl)-9*H*-pyrido[3,4-*b*]indole (2n).[5]



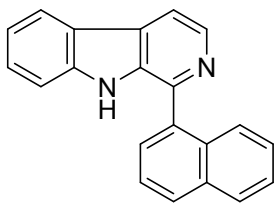
Yellow solid: 79% yield; mp: 243–246 °C (ref. 5: 244–246 °C); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6) δ: 10.82 (bs, 1H), 8.31 (d, *J* = 5.3 Hz, 1H), 8.17 (d, *J* = 8.9 Hz, 2H), 8.06 (d, *J* = 8.9 Hz, 2H), 7.92 (d, *J* = 7.9 Hz, 1H), 7.79 (d, *J* = 5.1 Hz, 1H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.32 (t, *J* = 7.7 Hz, 1H), 7.06 (t, *J* = 7.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO–d_6) δ: 146.8, 144.5, 141.0, 139.2, 138.2, 133.3, 129.9, 129.0, 128.0, 123.2, 120.9, 120.5, 119.4, 114.4, 111.9; MS (ESI): *m/z* 290 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{12}O_2N_3$ *m/z* 290.0924 $[M + H]^+$; found: 290.0927.

1-(Benzo[*d*][1,3]dioxol-5-yl)-9*H*-pyrido[3,4-*b*]indole (2o).[2]



White solid: 91% yield; mp: 169–173 °C (Ref. 2: 171–172 °C); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO–d_6) δ: 11.06 (bs, 1H), 8.35 (d, *J* = 5.1 Hz, 1H), 8.06 (d, *J* = 7.9 Hz, 1H), 7.84 (d, *J* = 5.1 Hz, 1H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.52−7.40 (m, 3H), 7.17 (t, *J* = 7.2 Hz, 1H), 6.95 (d, *J* = 7.9 Hz, 1H), 6.02 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO−d_6) δ: 146.6, 146.5, 140.9, 140.0, 136.9, 131.8, 131.4, 128.1, 126.7, 121.1, 119.9, 119.8, 118.2, 112.0, 111.1, 107.6, 107.1, 99.9; MS (ESI): *m/z* 289 $[M + H]^+$; HRMS (ESI): calcd for $C_{18}H_{13}O_2N_2$ *m/z* 289.0971 $[M + H]^+$; found: 289.0973.

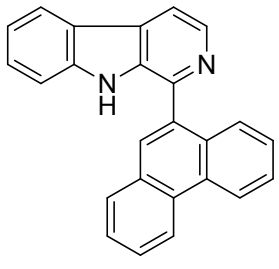
1-(Naphthalen-1-yl)-9*H*-pyrido[3,4-*b*]indole (2p).[5]



Off white solid: 94% yield; mp: 177–180 °C (ref. 5: 178–180 °C); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6) δ: 10.80 (bs, 1H), 8.46 (d, *J* = 5.3 Hz, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 8.00 (d, *J* = 5.5 Hz, 1H), 7.95 (d, *J* = 5.5 Hz, 1H), 7.84–7.79 (m,

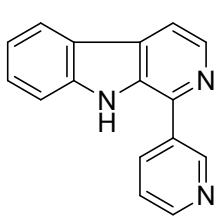
1H), 7.72–7.67 (m, 2H), 7.62 (d, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 1H), 7.45−7.40 (m, 2H),7.34 (t, *J* = 8.1 Hz, 1H), 7.21−7.15 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO−d_6) δ: 141.3, 139.7, 136.4, 134.3, 133.4, 132.3, 130.0, 127.4, 127.2, 126.7, 126.6, 126.0, 124.8, 124.5, 124.3, 124.0, 119.9, 119.5, 117.9, 112.3, 110.8; MS (ESI): *m/z* 295 $[M + H]^+$; HRMS (ESI): calcd for $C_{21}H_{14}N_2$ *m/z* 295.1229 $[M+H]^+$; found: 295.1232.

1-(Phenanthren-9-yl)-9*H*-pyrido[3,4-*b*]indole (2q).



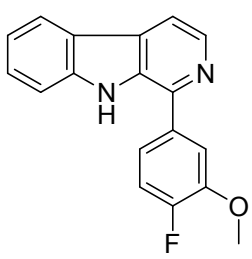
Off white solid: 95% yield; mp: 230−235 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6) δ: 11.51 (bs, 1H), 8.88 (t, *J* = 8.6 Hz, 2H), 8.52 (d, *J* = 5.3 Hz, 1H), 8.22 (d, *J* = 7.9 Hz, 1H), 7.95 (d, *J* = 5.5 Hz, 1H), 8.13 (d, *J* = 5.3 Hz, 1H), 8.04 (s, 1H), 8.03 (d, *J* = 5.5 Hz, 1H), 7.78−7.64 (m, 4H), 7.53−7.42 (m, 3H), 7.26−7.19 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO−d_6) δ: 142.4, 140.9, 137.6, 137.5, 134.8, 133.8, 130.9, 130.3, 130.0, 128.9, 128.7, 128.2, 127.9, 127.2, 126.8, 126.6, 126.6, 126.3, 122.8, 122.4, 121.3, 120.7, 119.2, 113.8, 112.0; MS (ESI): *m/z* 345 $[M + H]^+$; HRMS (ESI): calcd for $C_{25}H_{17}N_2$ *m/z* 345.1386 $[M + H]^+$; found: 345.1369.

1-(Pyridin-3-yl)-9*H*-pyrido[3,4-*b*]indole (2r).[5]



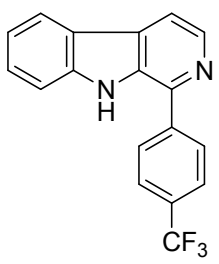
White solid: 91% yield; mp: 203–208 °C (ref. 5: 205–208 °C); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6) δ: 11.08 (bs, 1H), 9.32 (s, 1H), 8.69 (dd, *J* = 1.1, 4.5 Hz, 1H), 8.55 (d, *J* = 5.2 Hz, 1H), 8.38 (d, *J* = 7.9 Hz, 1H), 8.16 (d, *J* = 7.9 Hz, 1H), 7.99 (d, *J* = 5.1 Hz, 1H), 7.63 (d, *J* = 8.1 Hz, 1H), 7.57−7.49 (m, 2H), 7.28 (t, *J* = 7.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO−d_6) δ: 149.3, 148.9, 141.1, 139.3, 138.5, 135.8, 134.0, 133.2, 129.3, 128.3, 123.8, 121.6, 120.6, 119.5, 114.4, 112.3; MS (ESI): *m/z* 246 $[M + H]^+$; HRMS (ESI): calcd for $C_{16}H_{12}N_3$ *m/z* 246.1025 $[M + H]^+$; found: 246.1012.

1-(4-Fluoro-3-methoxyphenyl)-9*H*-pyrido[3,4-*b*]indole (2s).



Creamish solid: 88% yield; mp: 130−135 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6) δ: 11.45 (bs, 1H), 8.41 (d, *J* = 5.1 Hz, 1H), 8.17 (d, *J* = 6.7 Hz, 1H), 8.01 (d, *J* = 5.1 Hz, 1H), 7.71 (dd, *J* = 1.7, 8.5 Hz, 1H), 7.62 (d, *J* = 8.3 Hz, 1H), 7.59–7.53 (m, 1H), 7.50 (t, *J* = 7.9 Hz, 1H), 7.33 (dd, *J* = 8.3, 11.1 Hz, 1H), 7.22 (t, *J* = 7.2 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO−d_6) δ: 152.7 and 150.7 (d, *J* = 247.0 Hz), 147.1 (d, *J* = 10.9 Hz), 141.2, 141.0, 137.7 (d, *J* = 17.2 Hz), 134.8 (d, *J* = 2.7 Hz), 132.8, 129.1, 127.9, 127.8, 121.1, 120.6, 119.2, 115.6 (dd, *J* = 3.6, 17.2 Hz), 113.6, 113.5, 112.2, 55.7; MS (ESI): *m/z* 293 $[M + H]^+$; HRMS (ESI): calcd for $C_{18}H_{14}ON_2F$ *m/z* 293.1084 $[M + H]^+$; found: 293.1066.

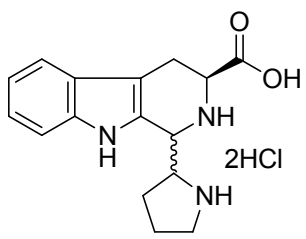
1-(4-(trifluoromethyl)phenyl)-9H-pyrido[3,4-b]indole (2t).



Light yellow solid: 85% yield; mp: 150−153 °C; ^{1}H NMR (400 MHz, DMSO−d_6) δ: 8.51 (d, *J* = 5.1 Hz, 1H), 8.30 (d, *J* = 7.9 Hz, 1H), 8.25 (d, *J* = 8.1 Hz, 2H), 8.20 (d, *J* = 5.2 Hz, 1H), 7.97 (d, *J* = 8.2 Hz, 2H), 7.65 (d, *J* = 1H), 7.58 (t, *J* = 5.8 Hz, 1H), 7.29 (t, *J* = 6.7 Hz, 1H); ^{13}C NMR (125 MHz, DMSO−d_6) δ: 142.2, 141.1, 140.3, 138.4, 133.1, 129.5, 129.1, 128.7, 128.4, 128.3, 125.4, 121.6, 120.6, 119.6, 114.6, 112.3; MS (ESI): *m/z* 313 $[M + H]^+$.

Synthesis of Eudistomin I (6)

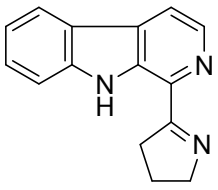
1-(Pyrrolidin-2-yl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole-3-carboxylic acid dihydrochloride (5)



A stirred solution of L-tryptophan (1.0 g, 4.90 mmol) and *N*-boc-L-prolinal (0.975 g, 4.90 mmol) in glacial acetic acid was heated at 80 ^{o}C for 2 h. After cooling to rt, the acetic acid was removed, the residue was taken in 1,4-dioxane (10 mL) and was added 2N HCl in 1,4-dioxane (5 ml) at 0 ^{o}C. The resulting reaction mixture was stirred at room temperature for 4 h. After total consumption of the starting material (monitored by TLC), the reaction mixture was concentrated under reduced pressure and dried well. The crude product was triturated in acetone, the resulted solid filtered and dried to afford the dihydrochloride salt **5** as white solid (1.57 g, 90% yield). mp: 238–240 °C; ^{1}H NMR (300 MHz, DMSO−d_6) δ: 11.61 (s, 0.2H), 11.47 (s, 0.8H), 10.36 (bs, 0.3H), 9.98 (bs, 0.8H), 9.61 (bs, 1H), 7.53 (d, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.16 (t, *J* = 7.3 Hz, 1H), 7.04 (t, *J* = 7.1 Hz, 1H), 5.44−5.24 (m, 1H), 4.74−4.63 (m, 1H), 4.61−4.51 (m, 1H), 4.30−4.15 (m, 1H), 3.46−3.27 (m, 3H),

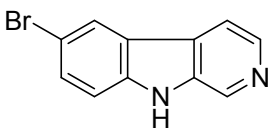
3.04−2.92 (m, 1H), 2.22−1.76 (m, 4H); ^{13}C NMR (75 MHz, DMSO−d_6) δ: 169.9, 136.5, 125.2, 125.1, 122.5, 119.2, 118.3, 111.6, 106.4, 59.2, 51.5, 51.2, 44.5, 27.5, 22.7, 22.1; MS (ESI): *m/z* 286 $[M + H]^+$; HRMS (ESI): calcd for $C_{16}H_{20}O_2N_3$ *m/z* 286.1550 $[M + H]^+$; found: 286.1545.

1-(3,4-Dihydro-2*H*-pyrrol-5-yl)-9*H*-pyrido[3,4-*b*]indole (or) eudistomin I (6).[8]



To a stirred solution of dihydrochloride salt **5** (500 mg, 1.39 mmol) in DMF (4 mL) was added TEA (0.97 mL, 6.98 mmol), cooled to 0 °C and added a solution of NCS (0.575 mg, 4.32 mmol) in DMF (5 mL) and the reaction mixture was allowed to stir at room temperature 30 min. After the completion of starting material (monitored by TLC) reaction mixture was diluted with water and extracted with ethyl acetate (2x50 mL), washed with water (50 mL), brine (50 mL), dried over sodium sulfate and concentrated under reduced pressure. The crude product was purified by column chromatography using 20% ethyl acetate in `n-hexane to afford the eudistomin I (**6**, 288 mg, 70% yield) as a light yellow solid, mp: 151–154 °C (ref. 8: 153–155 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 10.85 (s, 1H), 8.50 (d, *J* = 5.0 Hz, 1H), 8.15 (d, *J* = 7.9 Hz, 1H), 8.00 (d, *J* = 5.1 Hz, 1H), 7.61−7.53 (m, 2H), 7.32−7.28 (m, 1H), 4.30−4.26 (m, 2H), 3.37−3.31 (m, 2H), 2.14−2.05 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 176.8, 140.8, 138.2, 135.8, 135.4, 129.5, 128.5, 121.8, 121.2, 120.1, 116.1, 111.9, 62.2, 34.9, 21.9; MS (ESI): *m/z* 236 $[M + H]^+$. HRMS (ESI): calcd for $C_{15}H_{14}N_3$ *m/z* 236.1182 $[M + H]^+$; found: 236.1185.

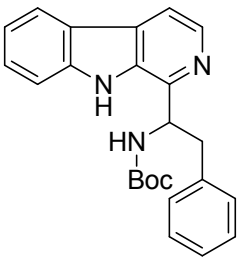
6-Bromo-9*H*-pyrido[3,4-*b*]indole (or) Eudistomin N (7)[8]



To a mixture of 0.1 N H_2SO_4 (1.5 mL) and 37% formaldehyde (0.8 mL) was added L-tryptophane (0.5 g, 2.4 mmol) with stirring. After being stirred for 4 h at room temperature, the resulted white solid was collected by filtration and dried well. The solid material was taken in DMF (7 mL), added TEA (0.61 mL, 7.34 mmol), cooled to 0 °C and added solution of NCS (0.69 g, 5.14 mmol) in DMF. The reaction mixture was stirred for 30 min at room temperature, diluted with water (50 mL), extracted with ethylacetate (2x50 mL) and washed with water (50 mL). The combined extracts were dried over sodium sulfate, filtered, concentrated *in vacuo* and the crude product was purified by silica gel column chromatography using ethyl acetate:n-hexane (1:1) to afford norharmane (**2a**, 0.33 g, 80% yield). To the stirred solution of **2a** in acetic acid (10 mL) was added NBS (0.38 g, 2.16 mmol) and stirred for 5 h at room temperature. The solvent most removed *in vacuo* and neutralized with saturated Na_2HCO_3 solution and extracted with ethylacetate (2x30 mL) and washed with water (30 mL). The combined extracts were dried over sodium sulfate, filtered, concentrated *in vacuo* and the crude product was purified by silica gel column chromatography using ethyl acetate:n-hexane (1:1) to afford eudistomin N (**7**, 0.43 g, 89% yield) as creamish solid. Mp: 265−270 °C (ref. 8: 265–268 °C); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6) δ: 11.09 (bs, 1H), 8.84 (s, 1H), 8.31 (d, *J* = 5.3 Hz, 1H), 8.16 (S, 1H), 7.83 (d, *J* = 5.1 Hz, 1H), 7.51 (dd, *J* = 1.7, 8.6 Hz, 1H), 7.38 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO−d_6) δ: 139.1, 137.6, 136.0, 133.7, 130.2, 126.8, 123.6, 122.2, 114.0, 113.1, 111.3; MS (ESI): *m/z* 247 $[M]^+$ and 249 $[M + 2H]^+$; HRMS (ESI): calcd for $C_{11}H_8N_2Br$ *m/z* 246.9865 $[M + H]^+$; found: 246.9855.

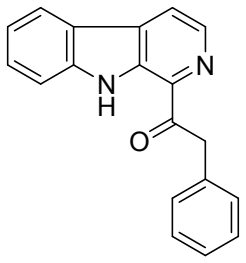
Synthesis of eudistomin T (9)

tert-Butyl 2-phenyl-1-(9*H*-pyrido[3,4-*b*]indol-1-yl)ethylcarbamate (8)[9]



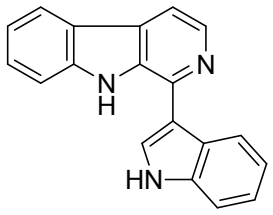
A stirred solution of L-tryptophan (1.0 g, 4.90 mmol) and *N*-boc-L-alaninal (1.22 g, 4.90 mmol) in glacial acetic acid was heated at 80 °C for 2 h. After cooling to rt, the acetic acid was removed, the residue was taken DMF (7 mL), added TEA (2.0 mL, 14.70 mmol), cooled to 0 °C and added solution of NCS (1.37 g, 10.29 mmol) in DMF. The reaction mixture was stirred for 30 min at room temperature, diluted with water (70 mL), extracted with ethyl acetate (2x70 mL) and washed with water (100 mL). The combined extracts were dried over sodium sulfate, filtered, concentrated *in vacuo* and the crude product was purified by silica gel column chromatography using ethyl acetate:n-hexane (1:1) to afford compound **8** (1.51 g, 80% yield) as white solid. Mp: 236−240 °C (ref. 9: 230−232 °C); ^{1}H NMR (400 MHz, DMSO−d_6) δ: 8.29 (d, *J* = 5.1 Hz, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 8.01 (d, *J* = 5.1 Hz, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.32–7.1 (m, 7H), 5.50 (q, *J* = 6.9, 13.8 Hz, 0.8H), 3.21–3.09 (m, 2H), 1.28 (s, 8H), peaks at 5.32 and 0.99 are due to the 20% minor rotamer; ^{13}C NMR (100 MHz, DMSO−d_6) δ: 155.1, 145.1, 140.3, 138.1, 137.1, 137.0, 132.6, 129.3, 127.9, 127.8, 127.7, 125.9, 121.6, 121.5, 120.7, 119.2, 113.5, 111.8, 77.8, 53.1, 28.0; MS (ESI): *m/z* 388 $[M + H]^+$; HRMS (ESI): calcd for $C_{24}H_{26}O_2N_3$ *m/z* 388.2019 $[M + H]^+$; found: 388.2020.

2-Phenyl-1-(9*H*-pyrido[3,4-*b*]indol-1-yl)ethanone (or) Eudistomin T (9)[9]



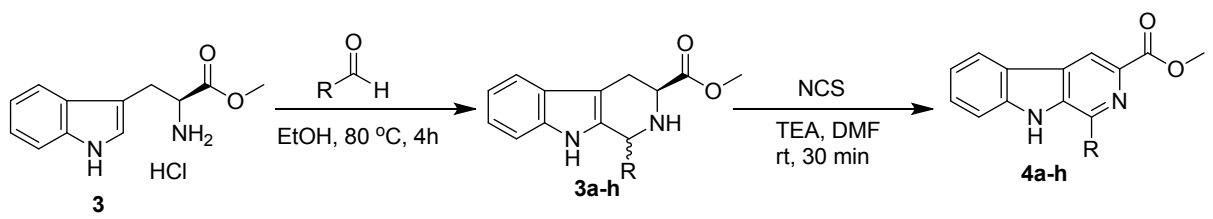
To a stirred solution of boc product **8** (0.3 g, 1.04 mmol) in 1,4-dioxane (20 mL) was added 2 N HCl in 1,4-dioxane solution (1 mL) at 0°C and stirred for 3 h. After consumption of the starting material (monitored by TLC), the solvent removed *in vacuo* and dried. The crude product was dissolved in methanol (10 mL) and added sodium carbonate (4 g), followed by aq. NaOCl (1 mL, 5.9 % w/w) over a period of 15 mins. After being stirred for 1 h at room temperature, reaction mixture was diluted with 1 N HCl solution (30 mL), extracted with DCM (2x30 mL), washed with saturated sodium bicarbonate solution (30 mL) and water (50 mL). The combined organic phases were dried over sodium sulfate, filtered and evaporated *in vacuo*. The crude product was purified by column chromatography using ethyl acetate and n-hexane (3:7) to afford eudistomin T (**9**) as yellow solid (0.19 g, 88% yield). Mp: 163–165°C (ref. 9: 155−157 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.26 (bs, 1H), 8.59 (d, J = 4.9 Hz, 1H), 8.15 (d, J = 5.5 Hz, 1H), 8.14 (d, J = 8.9 Hz, 1H), 7.61–7.56 (m, 1H), 7.51 (d, J = 8.2 Hz, 1H), 7.43–7.40 (m, 2H), 7.37–7.30 (m, 3H), 7.29–7.24 (m, 1H), 4.74 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.3, 141.0, 138.2, 135.9, 135.3, 134.9, 131.6, 130.0, 129.2, 128.4, 126.7, 121.8, 120.7, 120.5, 119.2, 111.9, 43.9; MS (ESI): *m/z* 287 $[M + H]^+$; HRMS (ESI): calcd for $C_{19}H_{15}ON_2$ *m/z* 287.1178 $[M + H]^+$; found: 287.1175.

Synthesis of 1-(1*H*-indol-3-yl)-9*H*-pyrido[3,4-*b*]indole (or) Eudistomin U (10)[10]



A stirred solution of L-tryptophan (0.50 g, 2.45 mmol) and indole-3-carbaldehyde (0.35 g, 2.45 mmol) in glacial acetic acid (5 mL) was heated at 80 °C for 2 h. After cooling to rt, the solvent most was removed *in vacuo*, the residue was taken DMF (5 mL), added TEA (1.02 mL, 7.35 mmol), cooled to 0 °C and added solution of NCS (0.69 g, 5.14 mmol) in DMF (5 mL). The reaction mixture was stirred for 30 min at room temperature, diluted with water (30 mL), extracted with ethyl acetate (2x50 mL) and washed with water (30 mL). The combined extracts were dried over sodium sulfate, filtered, evaporated *in vacuo* and the crude product was purified by silica gel column chromatography using ethyl acetate/methanol (9:1) to afford eudistomin U (**10**, 0.59 g, 85% yield) as light yellow solid. Mp: 230−235 °C (ref. 10: 235−236 °C); ^{1}H NMR (500 MHz, DMSO−d_6) δ: 11.72 (s, 1H), 11.31 (s, 1H), 8.55 (d, J = 7.9 Hz, 1H), 8.4 (d, J = 5.1 Hz, 1H), 8.30 (d, J = 2.7 Hz, 1H), 8.23 (d, J = 7.9 Hz, 1H), 7.95 (d, J = 5.1 Hz, 1H), 7.69 (d, J = 8.1 Hz, 1H), 7.56–7.50 (m, 2H), 7.25 (t, J = 7.3 Hz, 1H), 7.21 (t, J = 7.0 Hz, 1H), 7.14 (t, J = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, DMSO−d_6) δ: 140.6, 140.3, 137.8, 136.4, 131.9, 128.0, 127.6, 126.1, 125.9, 122.2, 121.9, 121.3, 121.1, 119.7, 119.3, 113.1, 112.3, 111.5, 111.4; MS (ESI): *m/z* 284 $[M + H]^+$; HRMS (ESI): calcd for $C_{19}H_{14}N_3$ *m/z* 284.1182 $[M + H]^+$; found: 284.1185.

Pictet-Spengler reaction and aromatization of tetrahydro-β-carboline esters.

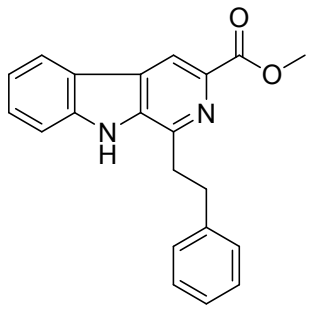


Scheme S2: Synthesis of methyl-β-carbolinecarboxylates (**4a-h**)

General Procedure

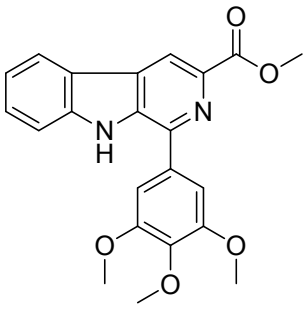
To a stirred solution of L-tryptophan methyl ester hydrochloride (**3**, 1 mmol) in ethanol was added aldehyde (1 mmol), stirred at 80 °C for 4 h and the ethanol was evaporated *in vacuo* and dried well. This residue was directly taken in DMF, added TEA (2.5 mmol) and NCS (2.1 mmol) in DMF. Then the reaction mixture was stirred for 30 min at room temperature and after completion of the reaction (monitored by TLC), added ice cold water, the resulted solid was filtered, washed with water and dried well. The solid product was then triturated in 20-50% ethyl acetate and hexane solvent system, filtered and dried to afford the pure desired β-carboline esters (**4a-h**).

Methyl 1-phenethyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4a).



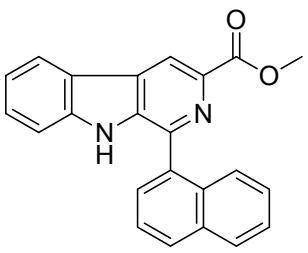
Brown solid: 81% yield; mp: 165−170 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.77 (s, 1H), 8.30 (bs, 1H), 8.13 (d, J = 7.9 Hz, 1H), 7.52 (t, J = 8.2 Hz, 1H), 7.37 (d, J = 8.2 Hz, 1H), 7.30 (t, J = 7.1 Hz, 1H), 7.21–7.15 (m, 3H), 7.12 (d, J = 7.9 Hz, 2H), 4.05 (s, 3H), 3.47 (t, J = 7.3 Hz, 2H), 3.18 (t, J = 7.7 Hz, 2H); ^{13}C NMR (100 MHz, DMSO−d_6) δ: 166.1, 144.8, 141.5, 140.6, 135.9, 135.6, 128.4, 128.3, 128.1, 127.1, 125.8, 121.9, 121.2, 120.6, 116.0, 112.2, 51.8, 35.1, 33.5; MS (ESI): *m/z* 331 $[M + H]^+$; HRMS (ESI): calcd for $C_{21}H_{19}O_2N_2$ *m/z* 331.1441 $[M + H]^+$; found: 331.1428.

Methyl 1-(3,4,5-trimethoxyphenyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4b).[11]



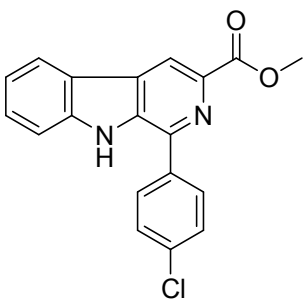
Off white solid: 94% yield; mp: 226–229 °C (ref. 11: 229−230 °C); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6) δ: 8.79 (s, 1H), 8.22 (d, *J* = 7.9 Hz, 1H), 7.64 (d, *J* = 8.3 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.26 (t, *J* = 7.2 Hz, 1H), 7.17 (s, 2H), 3.93 (s, 3H), 3.92 (s, 6H), 3.79 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 165.8, 152.7, 142.2, 141.2, 137.8, 136.2, 134.5, 132.9, 128.7, 128.0, 121.1, 120.9, 119.9, 116.1, 112.4, 105.5, 59.9, 55.5, 51.6; MS (ESI): *m/z* 393 $[M + H]^+$; HRMS (ESI): calcd for $C_{22}H_{21}O_5N_2$ *m/z* 393.1445 $[M + H]^+$; found: 393.1432.

Methyl 1-(naphthalen-1-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4c).



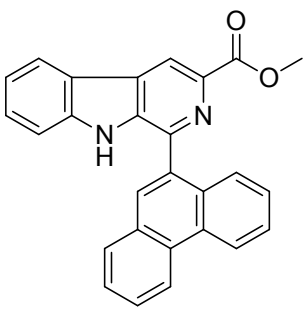
White solid: 95% yield; mp: 294–297 °C; ^{1}H NMR (300 MHz, DMSO−d_6) δ: 11.61 (s, 1H), 9.05 (s, 1H), 8.48 (d, *J* = 7.7 Hz, 1H), 8.16 (dd, *J* = 2.5, 6.8 Hz, 1H), 8.11 (d, *J* = 8.1 Hz, 1H), 7.78–7.73 (m, 2H), 7.62–7.53 (m, 4H), 7.44 (t, *J* = 6.9 Hz, 1H), 7.33 (t, *J* = 7.7 Hz, 1H), 3.90 (s, 3H): ^{13}C NMR (125 MHz, DMSO−d_6) δ: 166.0, 142.4, 141.2, 136.3, 136.2, 134.6, 133.4, 131.1, 128.9, 128.6, 128.4, 128.2, 127.5, 126.5, 126.1, 125.5, 125.2, 122.1, 121.1, 120.2, 116.9, 112.5, 51.9; MS (ESI): *m/z* 353 $[M + H]^+$; HRMS (ESI): calcd for $C_{23}H_{17}O_2N_2$ *m/z* 353.1284 [M + H]+; found: 353.1288.

Methyl 1-(4-chlorophenyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4d).[12]



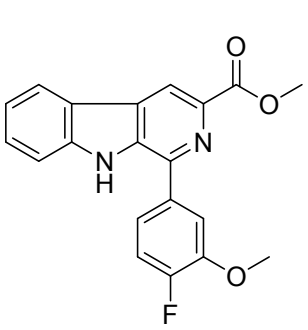
Yellow solid: 92% yield; mp: 268−272 °C (ref. 12: 270 °C); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6) δ (ppm): 8.81 (s, 1H), 8.23 (d, *J* = 7.7 Hz, 1H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.64 (d, *J* = 8.3 Hz, 1H), 7.59–7.51 (m, 3H), 7.27 (t, *J* = 7.2 Hz, 1H), 6.92 (d, *J* = 7.4 Hz, 1H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, DMSO−d_6) δ (ppm); 165.8, 141.4, 140.6, 136.5, 136.2, 134.4, 133.6, 130.3, 129.3, 128.7, 125.4, 121.9, 120.9, 120.4, 116.8, 112.6, 51.9; MS (ESI): *m/z* 337 $[M + H]^+$; HRMS (ESI): calcd for $C_{19}H_{14}O_2N_2Cl$ *m/z* 337.0738 $[M + H]^+$; found: 337.0729.

Methyl 1-(phenanthren-9-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4e).[9]



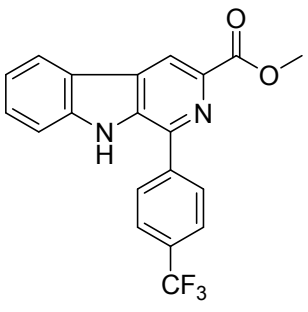
White solid: 96% yield; mp: 290–295 °C; ^{1}H NMR (300 MHz, DMSO−d_6 + $CDCl_3$) δ: 11.56 (s, 1H), 8.98 (s, 1H), 8.89 (t, *J* = 8.7 Hz, 2H), 8.34 (d, *J* = 7.9 Hz, 1H), 8.03 (d, *J* = 6.6 Hz, 2H), 7.80–7.60 (m, 4H), 7.52–7.45 (m, 3H), 7.29 (t, *J* = 7.9 Hz, 1H), 3.92 (s, 3H): ^{13}C NMR (125 MHz, DMSO−d_6 + $CDCl_3$) δ: 165.9, 142.3, 141.2, 136.4, 136.2, 133.2, 130.8, 130.2, 130.1, 130.0, 128.9, 128.4, 128.3, 127.2, 126.8, 126.7, 126.6, 126.1, 122.8, 122.5, 121.5, 121.0, 120.0, 116.8, 112.3, 51.8; MS (ESI): *m/z* 403 $[M + H]^+$; HRMS (ESI): calcd for $C_{27}H_{19}O_2N_2$ *m/z* 403.1441 [M + H]+; found: 403.1427.

Methyl 1-(4-fluoro-3-methoxyphenyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4f).



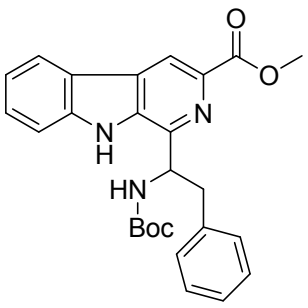
Off white solid: 94% yield; mp: 215−220 °C; ^{1}H NMR (300 MHz, DMSO−d_6) δ: 8.94 (s, 1H), 8.44 (d, *J* = 7.9 Hz, 1H), 7.73–7.66 (m, 2H), 7.61 (t, *J* = 7.2 Hz, 1H), 7.55−7.43 (m, 2H), 7.34 (t, *J* = 7.4 Hz, 1H), 3.99 (s, 3H), 3.93 (s, 3H); ^{13}C NMR (725 MHz, DMSO−d_6) δ: 165.8, 152.8 and 150.9 (d, *J* = 246.1 Hz), 147.1 (d, *J* = 10.9 Hz), 141.3 (d, *J* = 3.6 Hz), , 136.4, 134.5, 134.2 (d, *J* = 3.6 Hz), 129.0, 128.6, 121.9, 121.1 (d, *J* = 7.2 Hz), 121.0, 120.3, 116.7, 116.1, 116.0, 114.0 (1.8 Hz), 112.6, 55.9, 51.9; MS (ESI): *m/z* 351 $[M + H]^+$; HRMS (ESI): calcd for $C_{20}H_{16}O_3N_2$ F *m/z* 351.1139 $[M + H]^+$; found: 351.1128.

Methyl 1-(4-(trifluoromethyl)phenyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4g).[5]



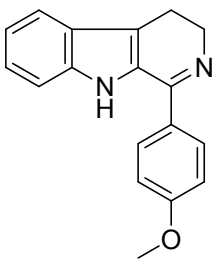
White solid: 91% yield; mp: 303–306°C (ref. 5: 306−310 °C); ^{1}H NMR (300 MHz, DMSO−d_6) δ: 8.80 (s, 1H), 8.13 (t, *J* = 7.4 Hz, 3H), 7.75 (d, *J* = 8.3 Hz, 2H), 7.60 (d, *J* = 8.1 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 1H), 7.26 (t, *J* = 7.5 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (75 MHz, DMSO−d_6) δ: 165.6, 141.4, 141.2, 140.2, 136.6, 134.6, 129.4, , 129.3, 129.2, 129.2, 128.5, 125.3 (q, *J* = 3.8, 7.7 Hz), 121.7, 120.9, 120.3, 116.9, 112.5, 51.8; MS (ESI): *m/z* 371 $[M + H]^+$; HRMS (ESI): calcd for $C_{20}H_{14}O_2N_2F_3$ *m/z* 371.1001 $[M + H]^+$; found: 371.0993.

Methyl 1-(1-((*tert*-butoxycarbonyl)amino)-2-phenylethyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4h)



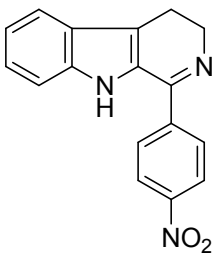
White solid: 88% yield; mp: 147–150 °C; ^{1}H NMR (400 MHz, DMSO−d_6) δ: 12.01 (bs, 1H), 8.85 (s, 1H), 8.38 (d, J = 7.8 Hz, 1H), 7.69 (d, J = 8.2 Hz, 1H), 7.62 (t, J = 7.2 Hz, 1H), 7.37–7.26 (m, 4H), 7.22 (t, J = 7.2 Hz, 2H), 7.14 (d, J = 7.2 Hz, 1H), 5.52 (q, J = 7.2, 14.7 Hz, 1H), 3.94 (s, 3H), 3.22 (d, J = 7.1 Hz, 2H), 1.30 and 0.96 (s, 8H and s, 1H); ^{13}C NMR (100 MHz, DMSO−d_6) δ: 165.8, 155.1, 145.2, 140.7, 137.9, 135.7, 134.5, 129.4, 128.5, 127.9, 127.7, 126.0, 121.9, 120.9, 120.2, 116.7, 112.2, 78.0, 53.6, 51.9, 40.0, 28.0; MS (ESI): *m/z* 446 [M + H]$^+$; HRMS (ESI): calcd for $C_{26}H_{28}O_4N_3$ *m/z* 446.2074 [M + H]$^+$; found: 446.2063.

1-(4-Methoxyphenyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (14).[13]



Creamish solid: 85% yield; mp: 185–188 °C (ref. 13: 196−197 °C); ^{1}H NMR (300 MHz, DMSO−d_6) δ: 7.78 (d, J = 7.6 Hz, 1H), 7.46–7.39 (m, 1H), 7.34–7.28 (m, 2H), 6.76 (d, J = 8.8 Hz, 2H), 6.29 (d, J = 8.8 Hz, 2H), 4.67–4.55 (m, 1H), 4.51–4.39 (m, 1H), 3.52 (s, 3H), 2.94 (m, 1H), 2.31–2.21 (m, 1H); ^{13}C NMR (75 MHz, DMSO−d_6) δ: 174.1, 167.5, 160.1, 153.5, 143.8, 128.6, 128.5, 127.7, 125.3, 122.6, 121.9, 113.1, 72.5, 59.8, 54.6, 36.9; MS (ESI): *m/z* 277 [M + H]$^+$.

1-(4-Nitrophenyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (15)[14]



Yellow solid: 82% yield; mp: 218–220 °C (ref. 14: 220−222 °C); ^{1}H NMR (300 MHz, DMSO−d_6 + $CDCl_3$) δ: 11.04 (s, 1H), 8.30 (d, J = 8.7 Hz, 2H), 7.99 (d, J = 8.7 Hz, 2H), 7.55 (d, J = 7.9 Hz, 1H), 7.38 (d, J = 8.1 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H), 7.04 (t, J = 7.5 Hz, 1H), 3.96 (t, J = 7.9 Hz, 2H), 2.89 (t, J = 8.3 Hz, 2H); ^{13}C NMR (75 MHz, DMSO−d_6 + $CDCl_3$) δ: 155.8, 146.4, 141.6, 135.5, 127.6, 125.3, 123.0, 122.3, 121.6, 118.0, 117.8, 115.3, 110.9, 47.1, 17.3; MS (ESI): *m/z* 292 [M + H]$^+$.

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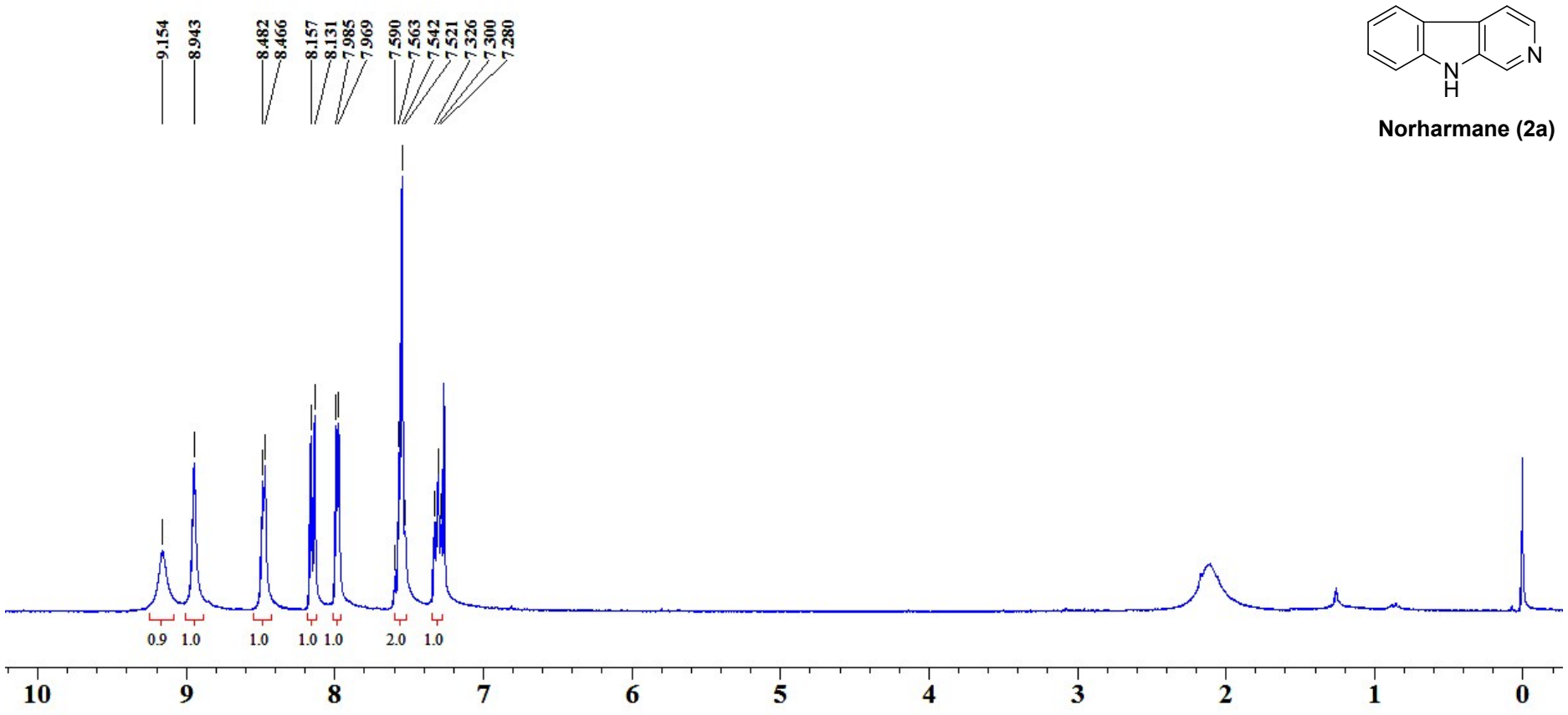
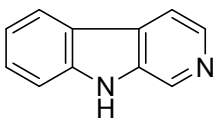
9*H*-Pyrido[3,4-*b*]indole (norharmane, 2a)

^{1}H NMR (300 MHz, $CDCl_3$)



Norharmane (2a)

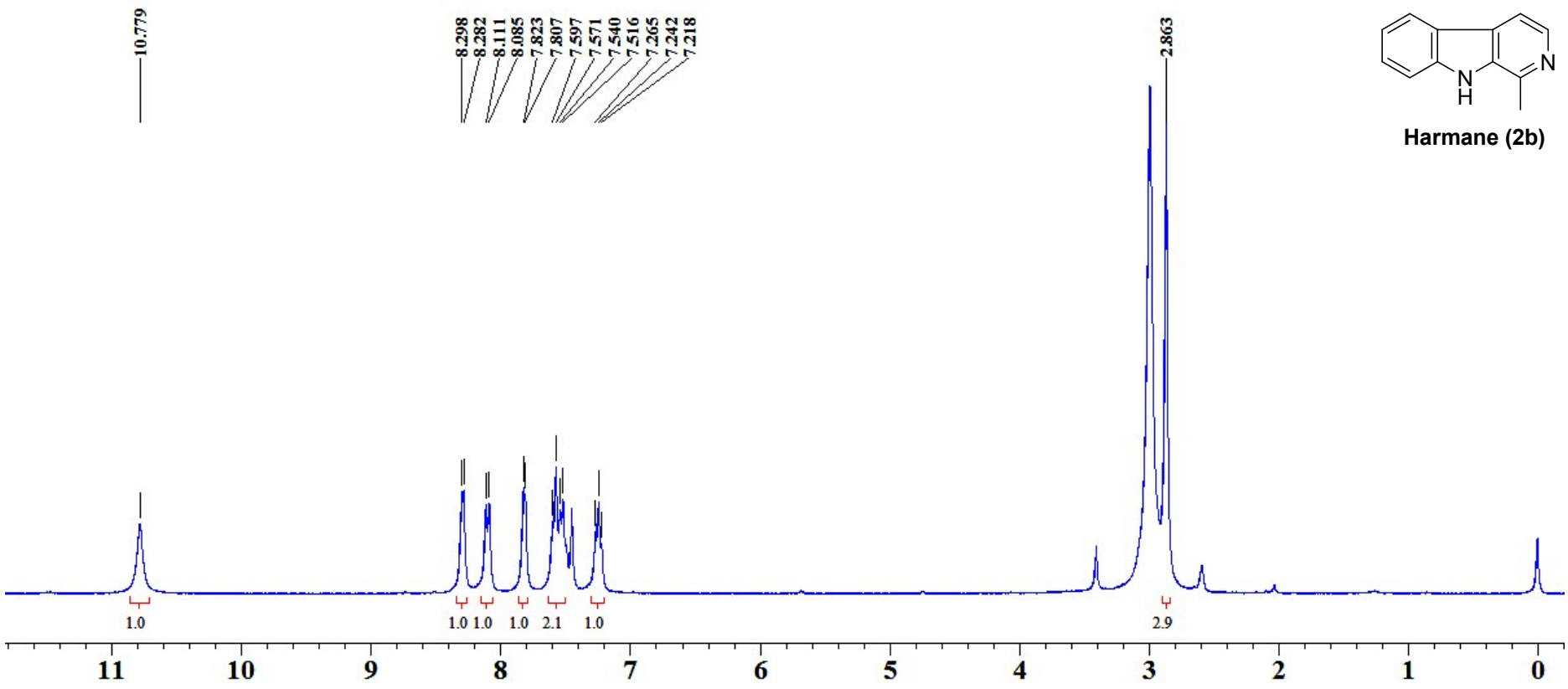
^{13}C NMR (125 MHz, DMSO−d_6)



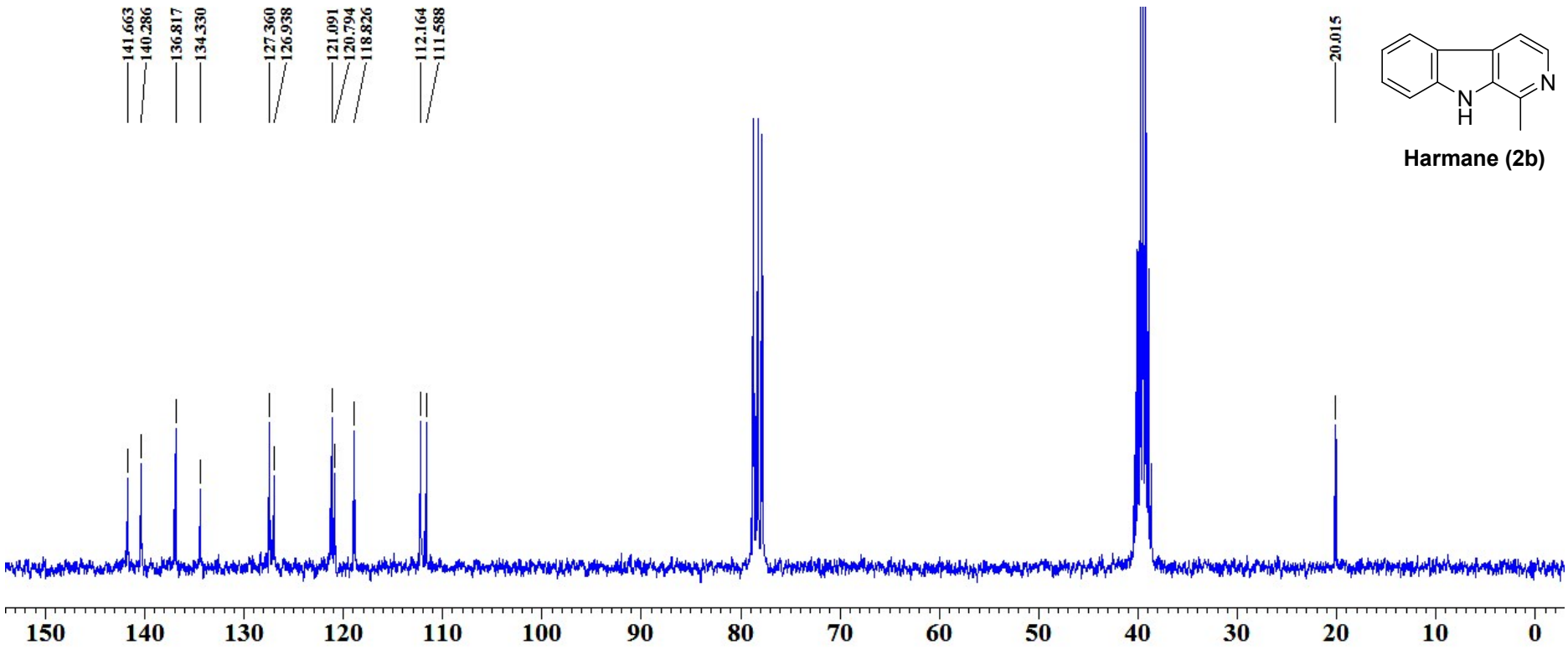
Norharmane (2a)

1-Methyl-9*H*-pyrido[3,4-*b*]indole (harmane, 2b)

^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6)

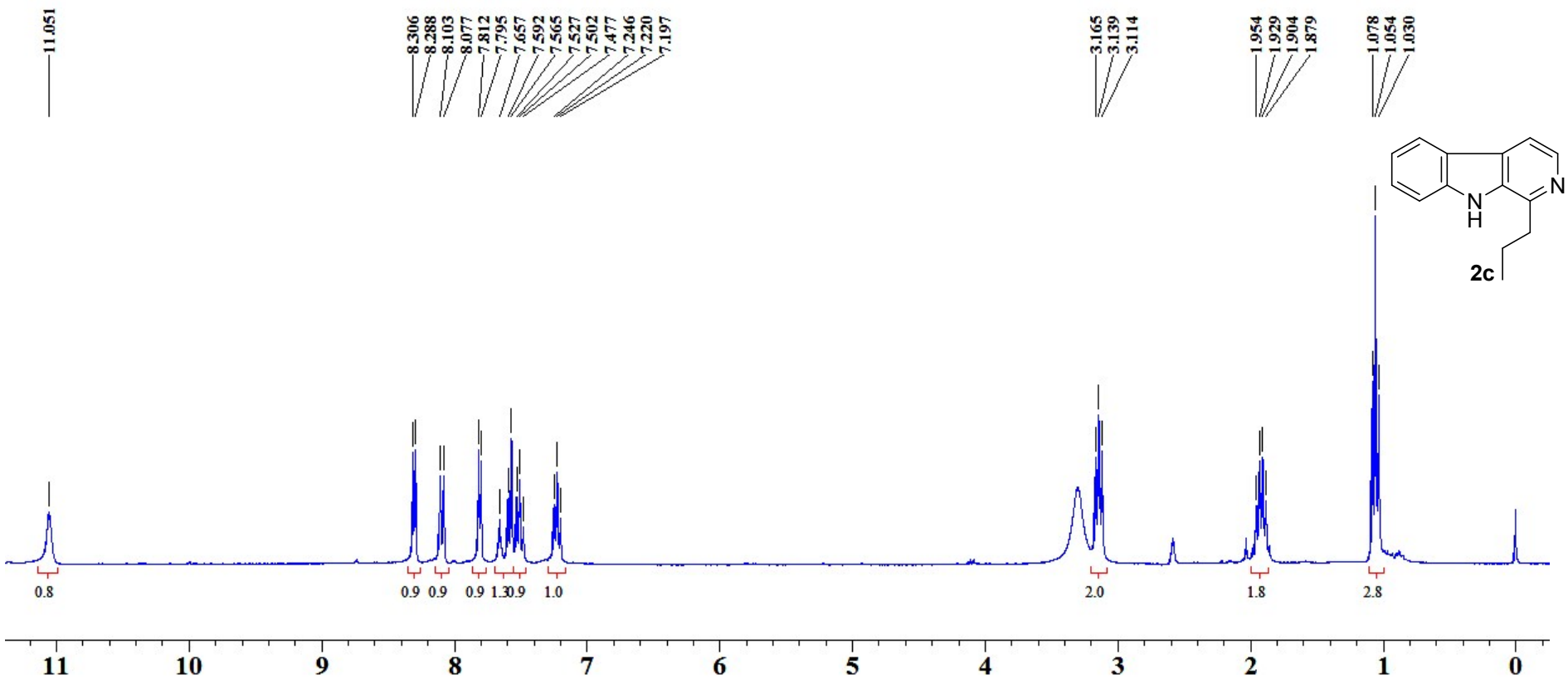


^{13}C NMR (75 MHz, $CDCl_3$ + DMSO–d_6)

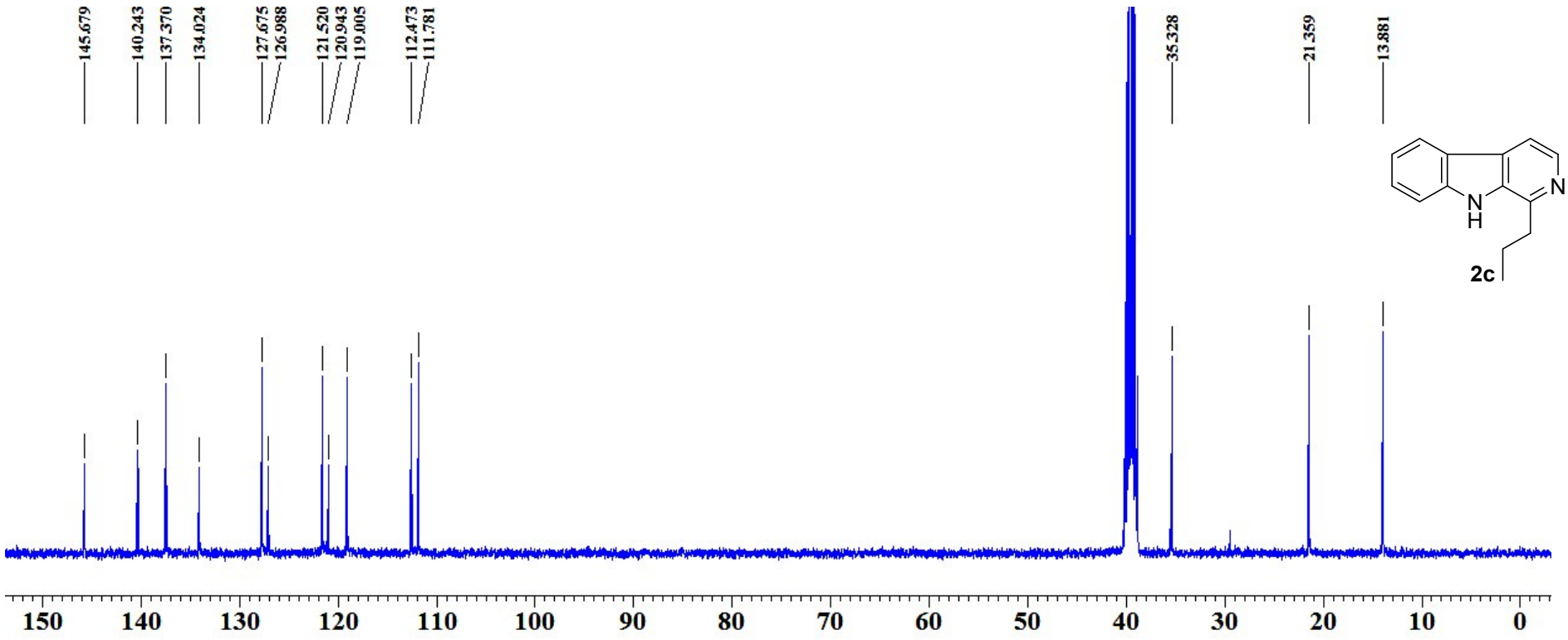


1-Propyl-9*H*-pyrido[3,4-*b*]indole (2c)

^{1}H NMR (300 MHz, DMSO−d_6)

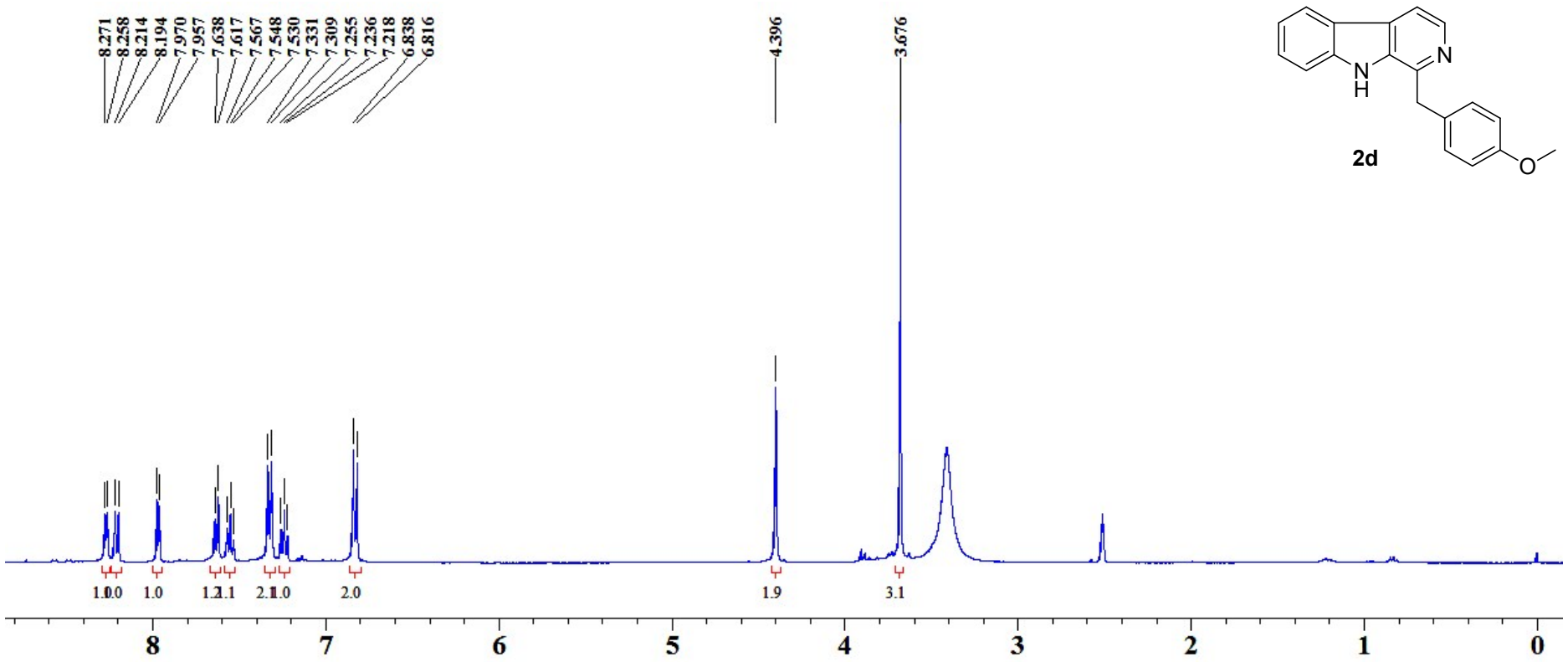


^{13}C NMR (100 MHz, DMSO–d_6)

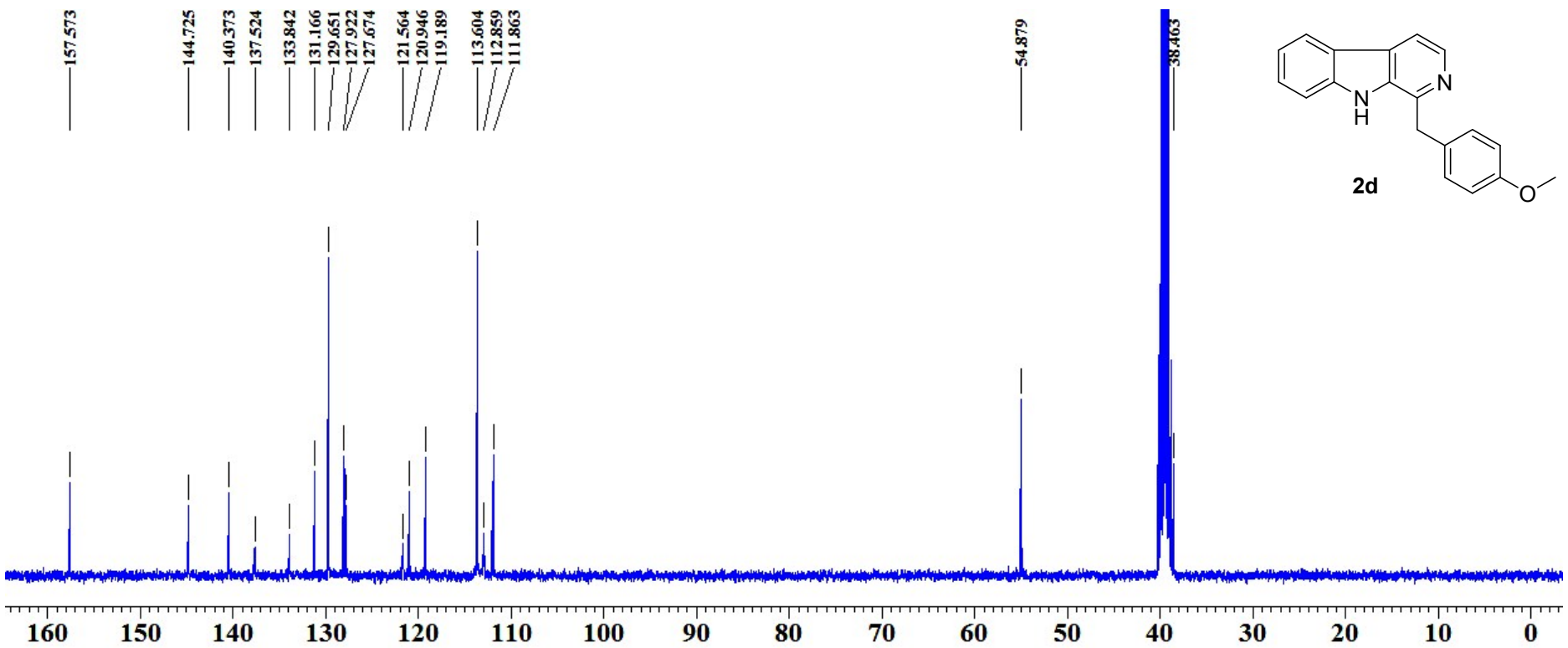


1-(4-Methoxybenzyl)-9*H*-pyrido[3,4-*b*]indole (2d)

^{1}H NMR (300 MHz, DMSO−d_6)

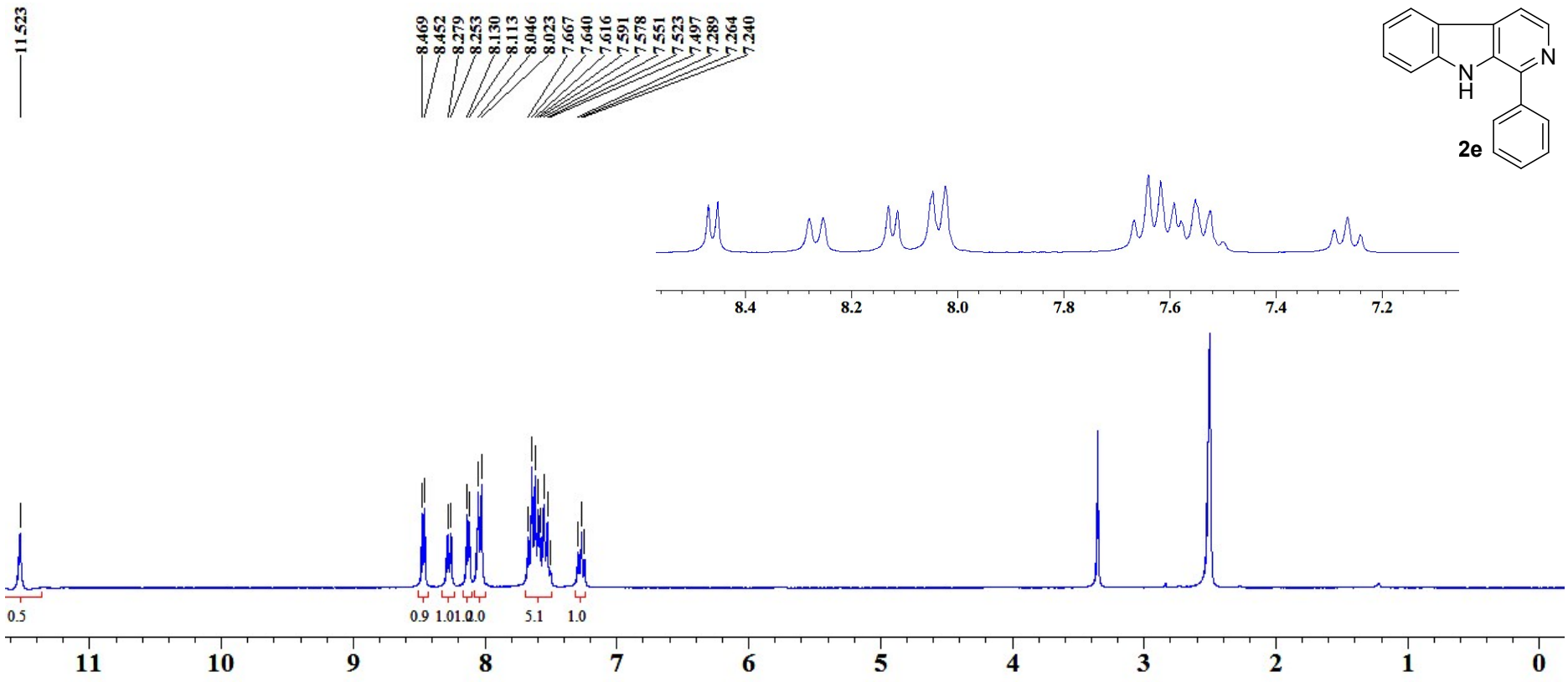


^{13}C NMR (100 MHz, DMSO−d_6)

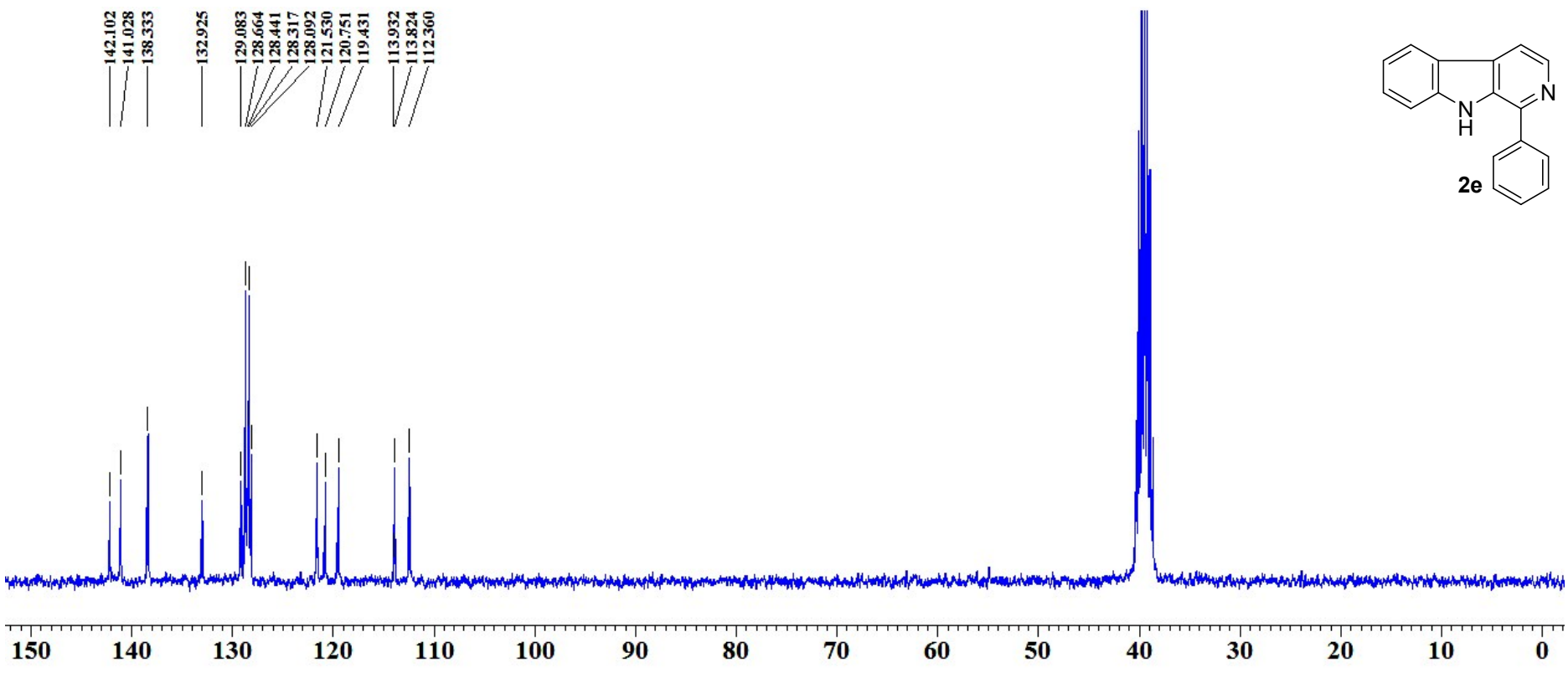


1-Phenyl-9*H*-pyrido[3,4-*b*]indole (2e)

^{1}H NMR (300 MHz, DMSO−d_6)

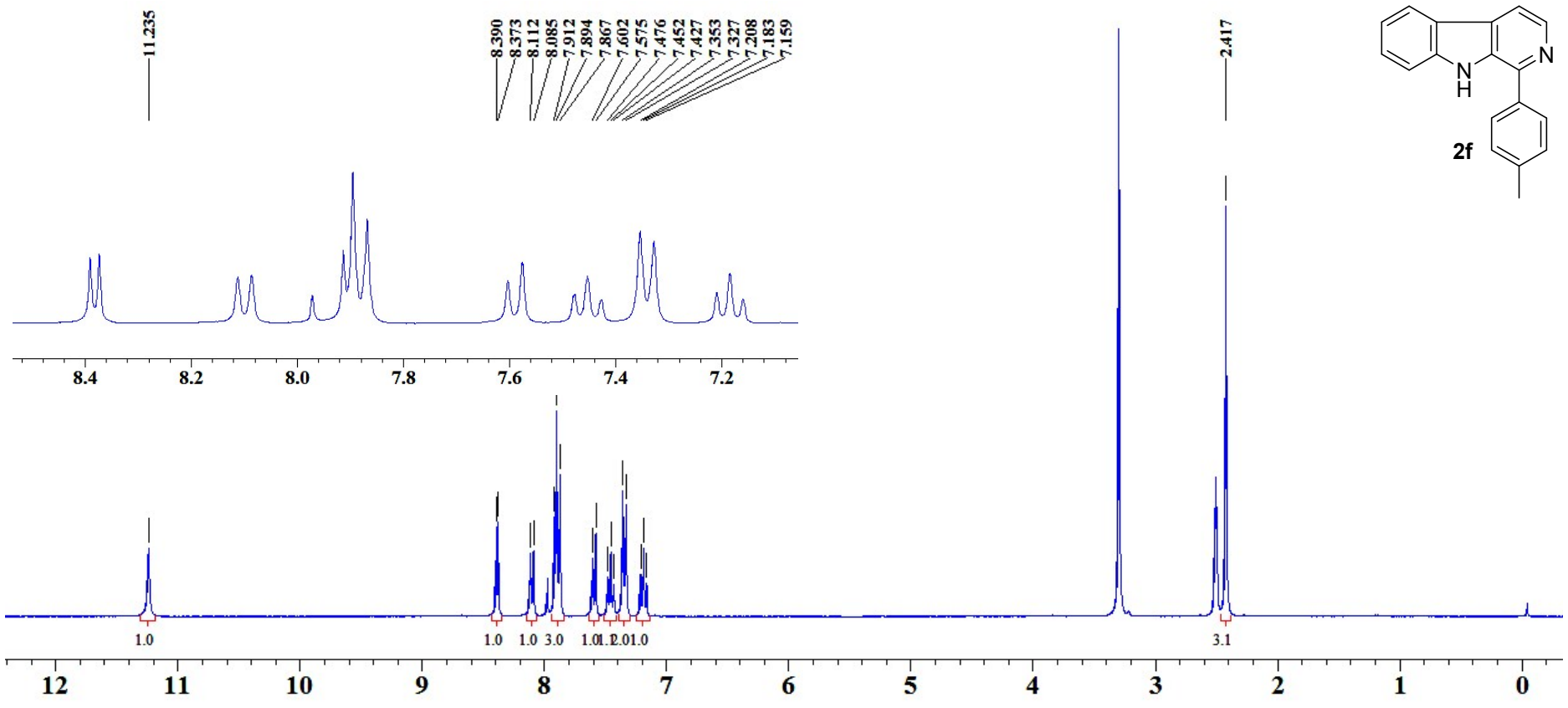


^{13}C NMR (75 MHz, DMSO−d_6)

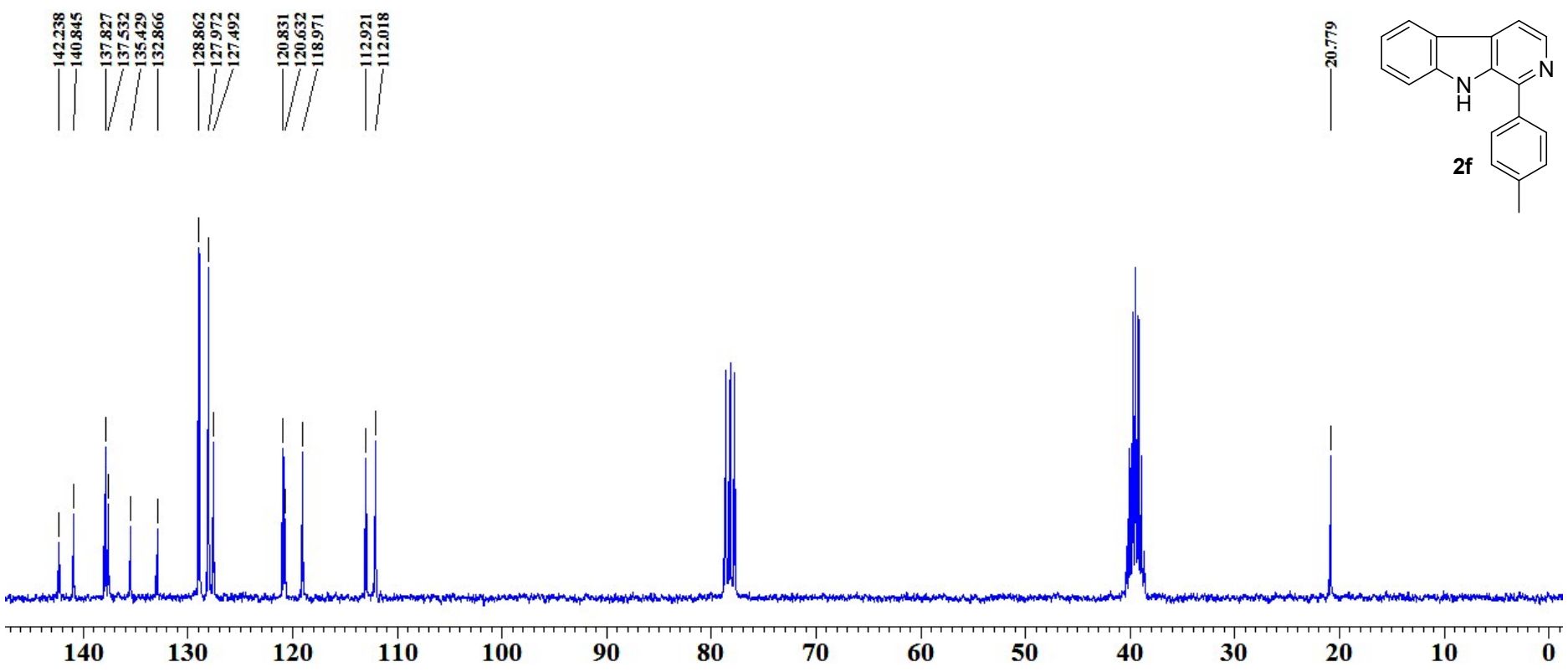


1-(*p*-Tolyl)-9*H*-pyrido[3,4-*b*]indole (2f)

^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6)

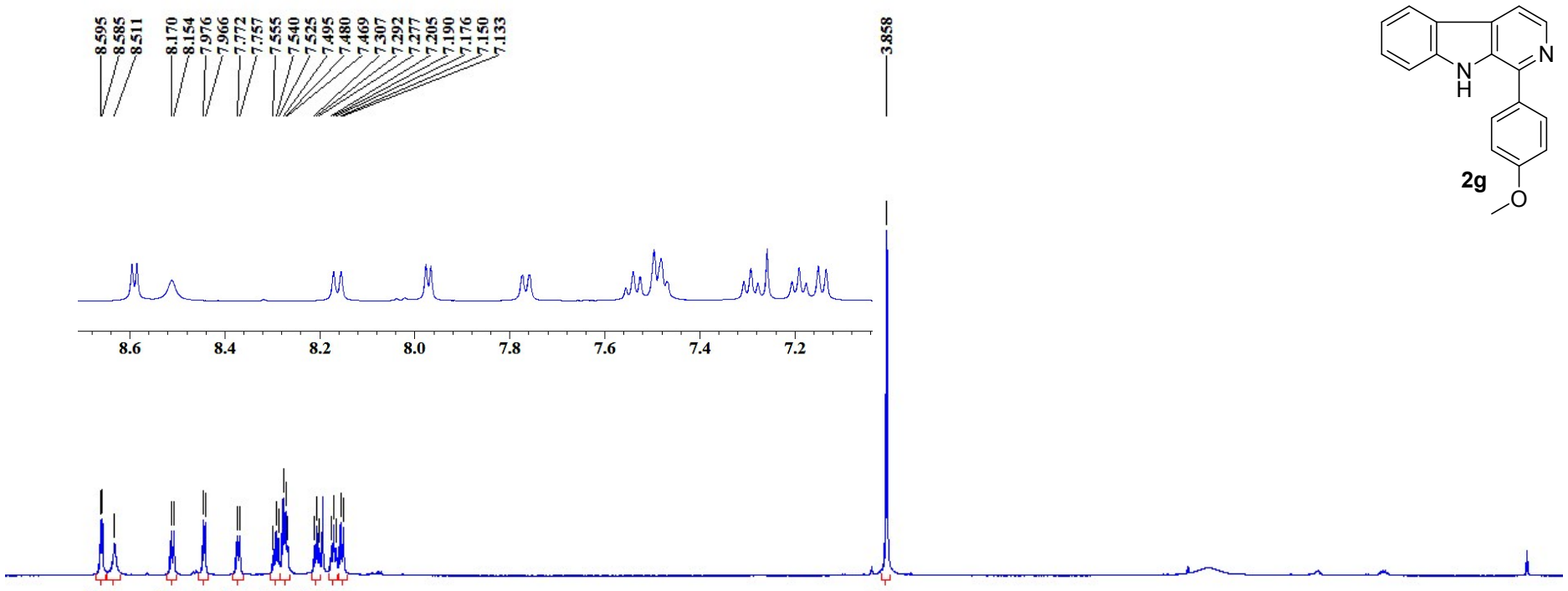


^{13}C NMR (75 MHz, $CDCl_3$ + DMSO−d_6)

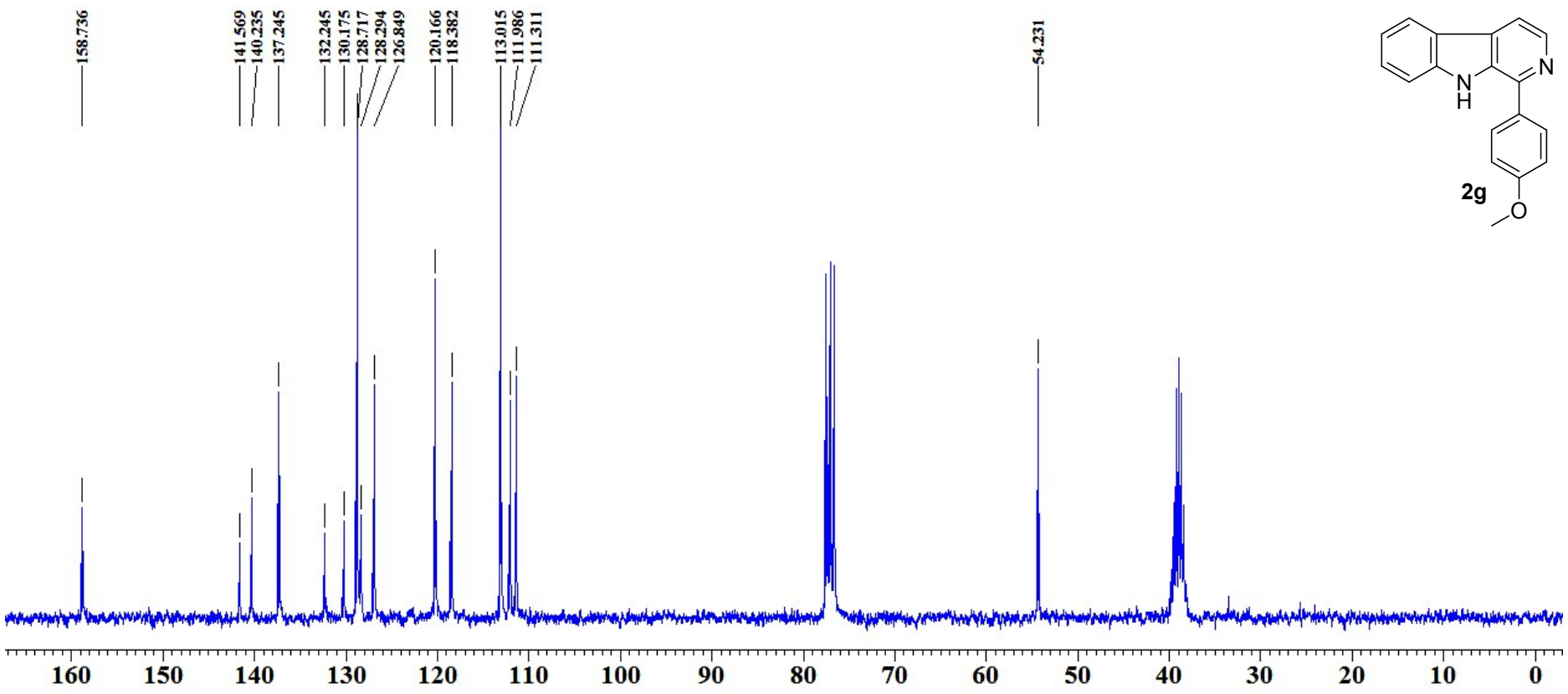


1-(2-Methoxyphenyl)-9*H*-pyrido[3,4-*b*]indole (2g)

^{1}H NMR (500 MHz, $CDCl_3$)

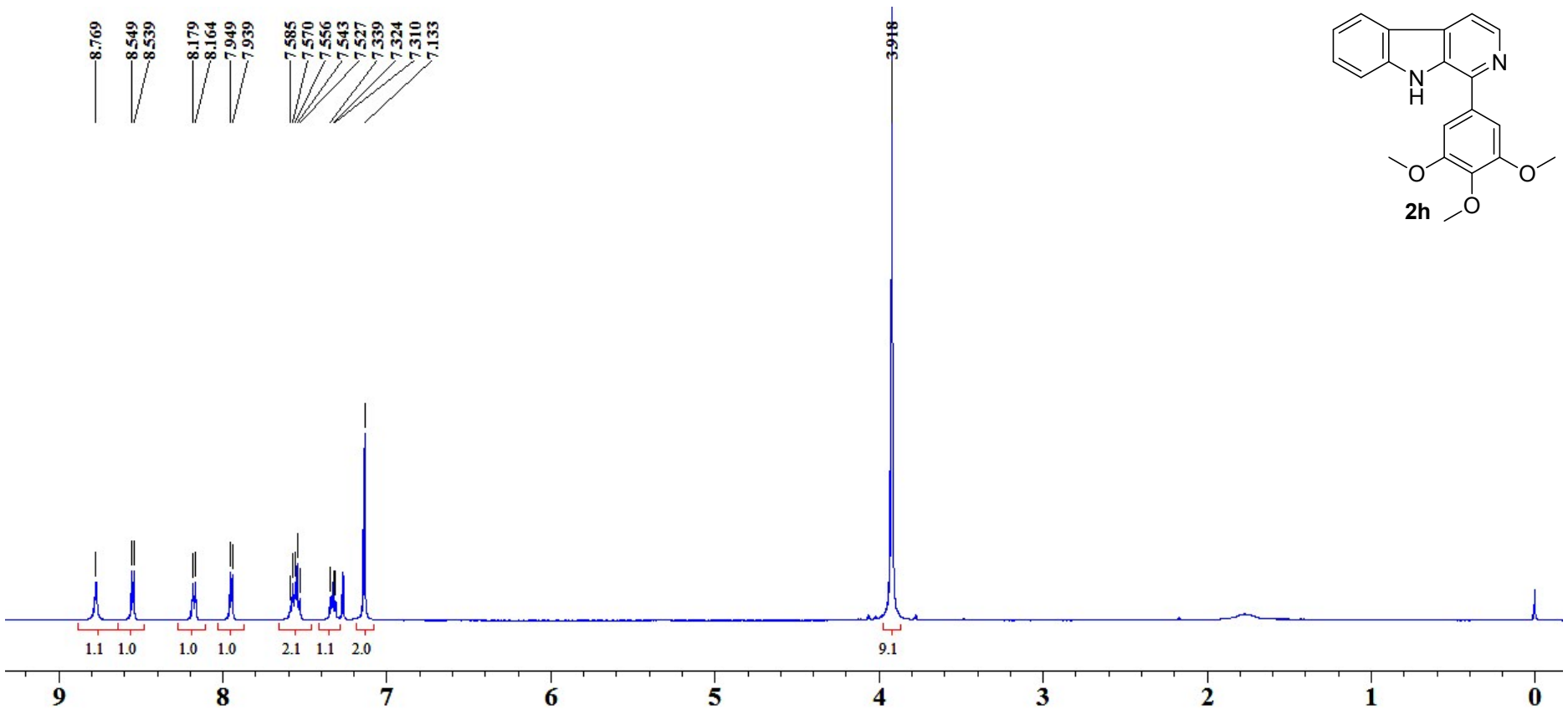


^{13}C NMR (75 MHz, $CDCl_3$ + DMSO−d_6)

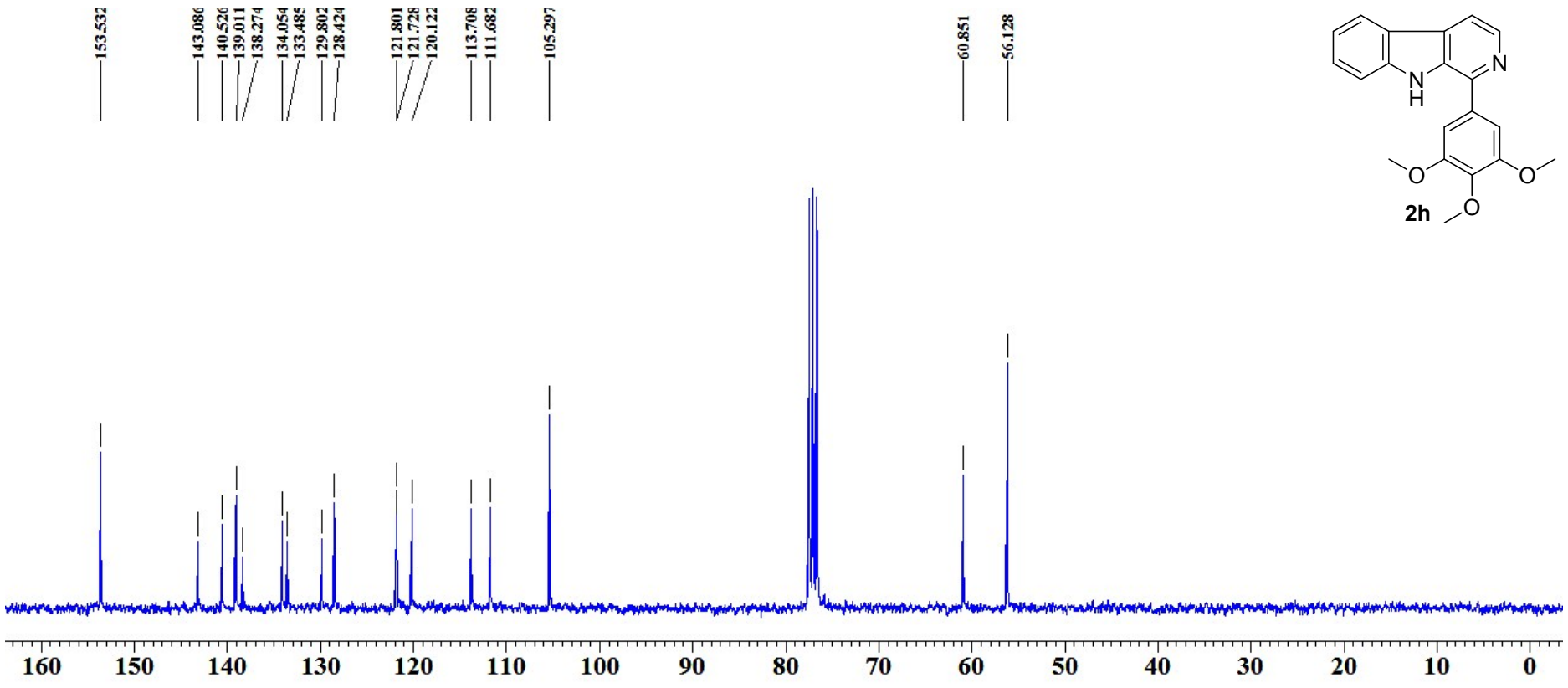


1-(3,4,5-Trimethoxyphenyl)-9*H*-pyrido[3,4-*b*]indole (2h)

^{1}H NMR (500 MHz, $CDCl_3$)

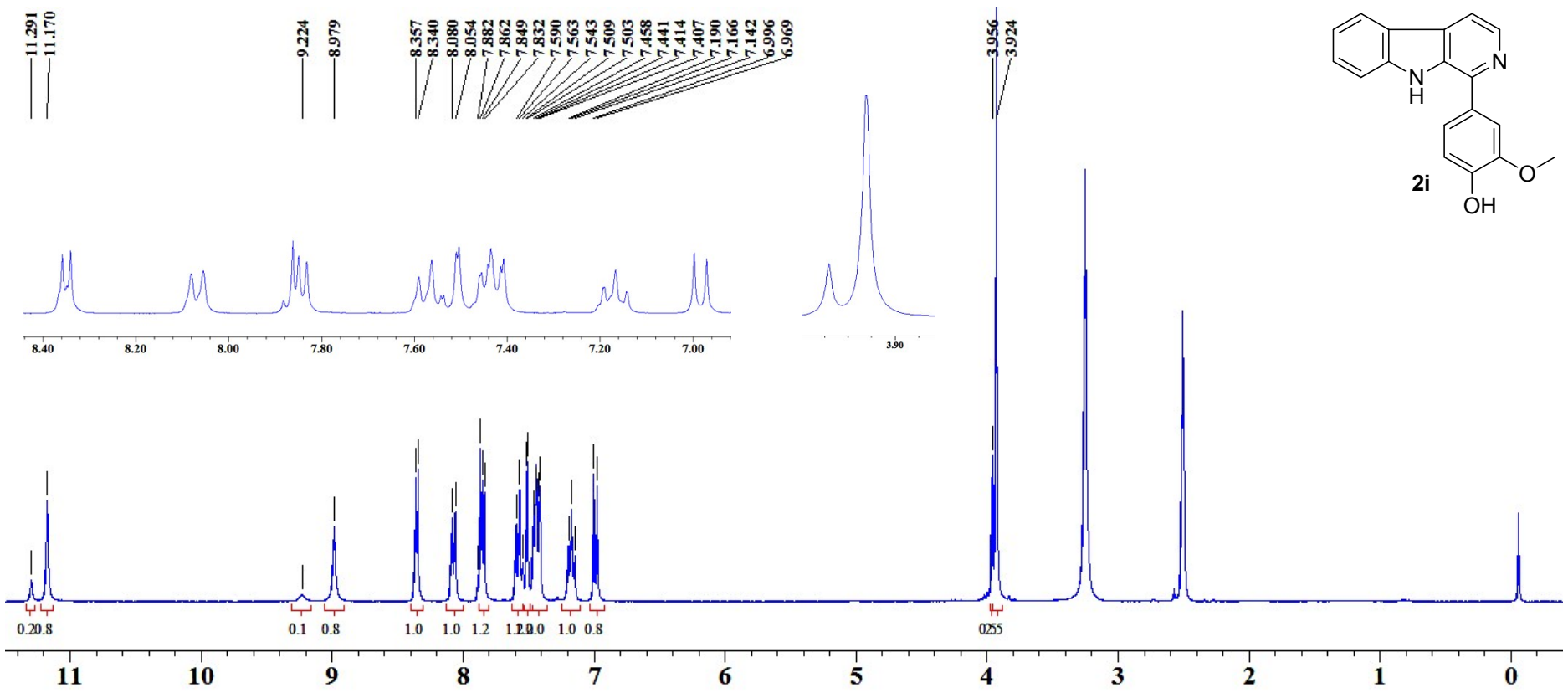


^{13}C NMR ($CDCl_3$, 75 MHz)

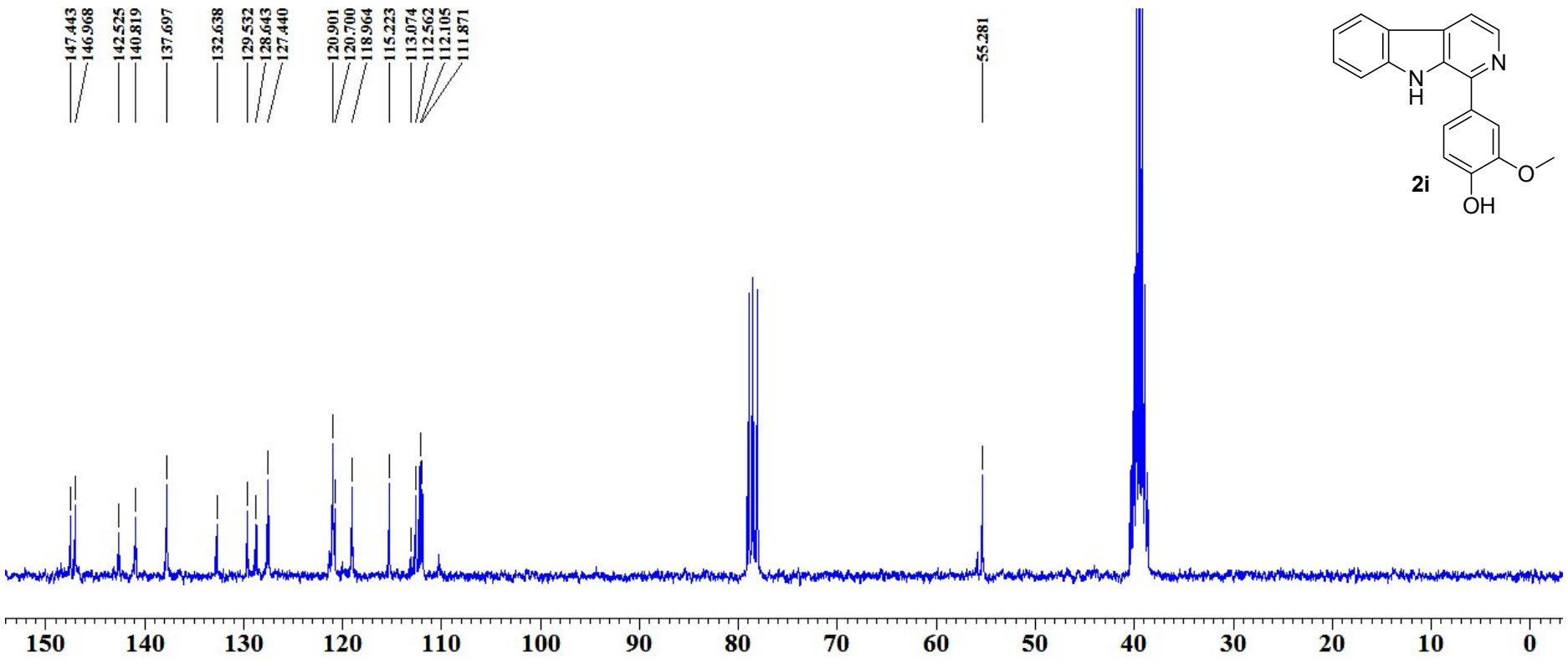


2-Methoxy-4-(9*H*-pyrido[3,4-*b*]indol-1-yl)phenol (2i)

^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6)

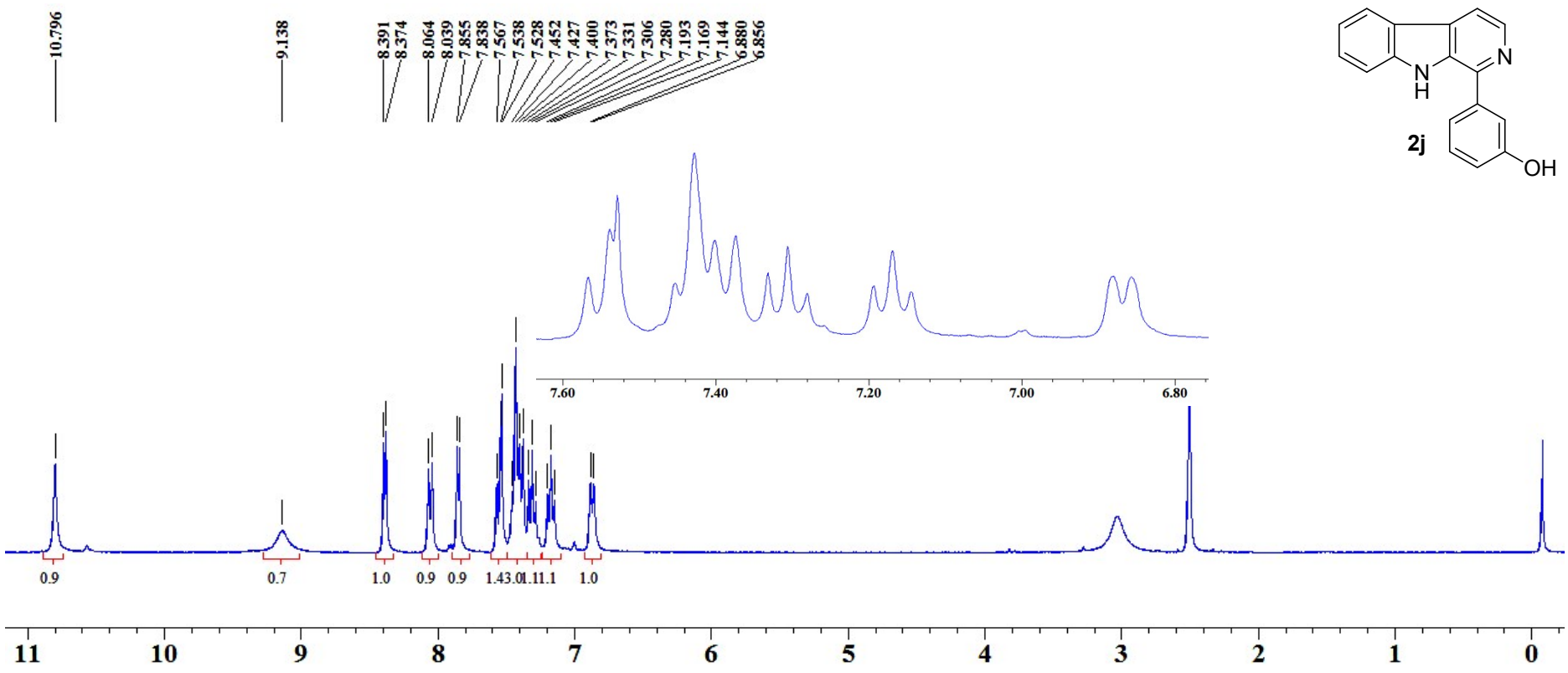


^{13}C NMR (75 MHz, $CDCl_3$ + DMSO−d_6)

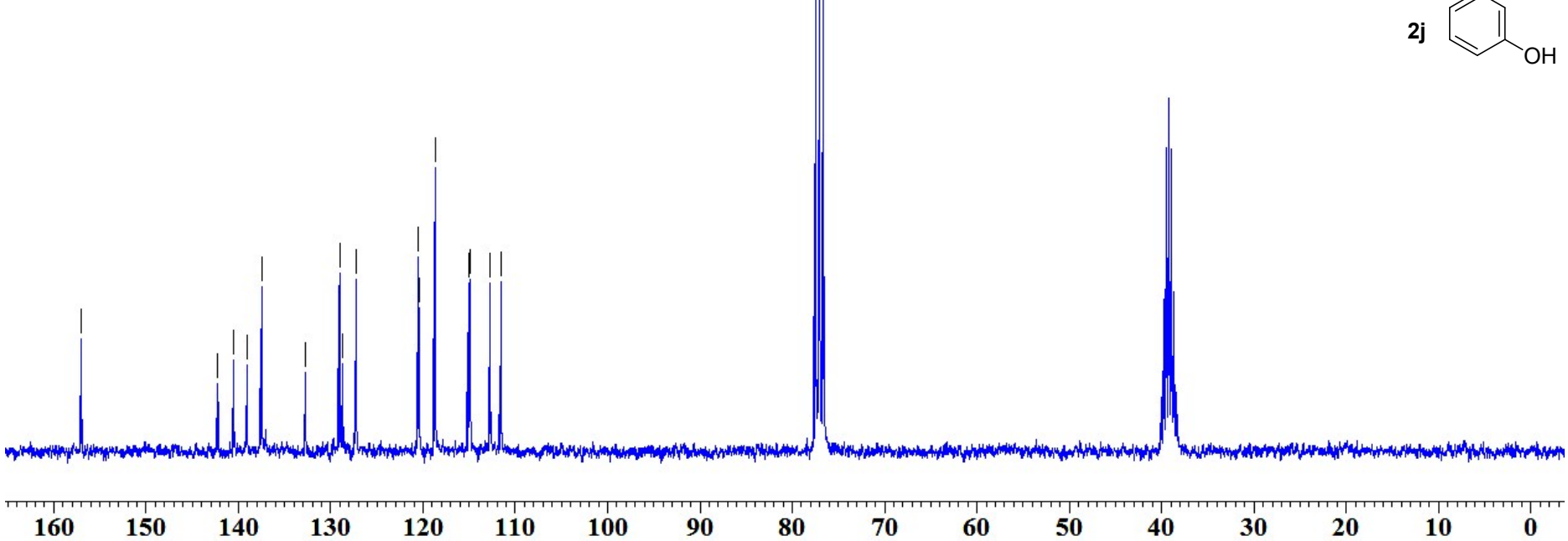


3-(9*H*-Pyrido[3,4-*b*]indol-1-yl)phenol (2j)

NMR (300 MHz, $CDCl_3$ + DMSO−d_6)

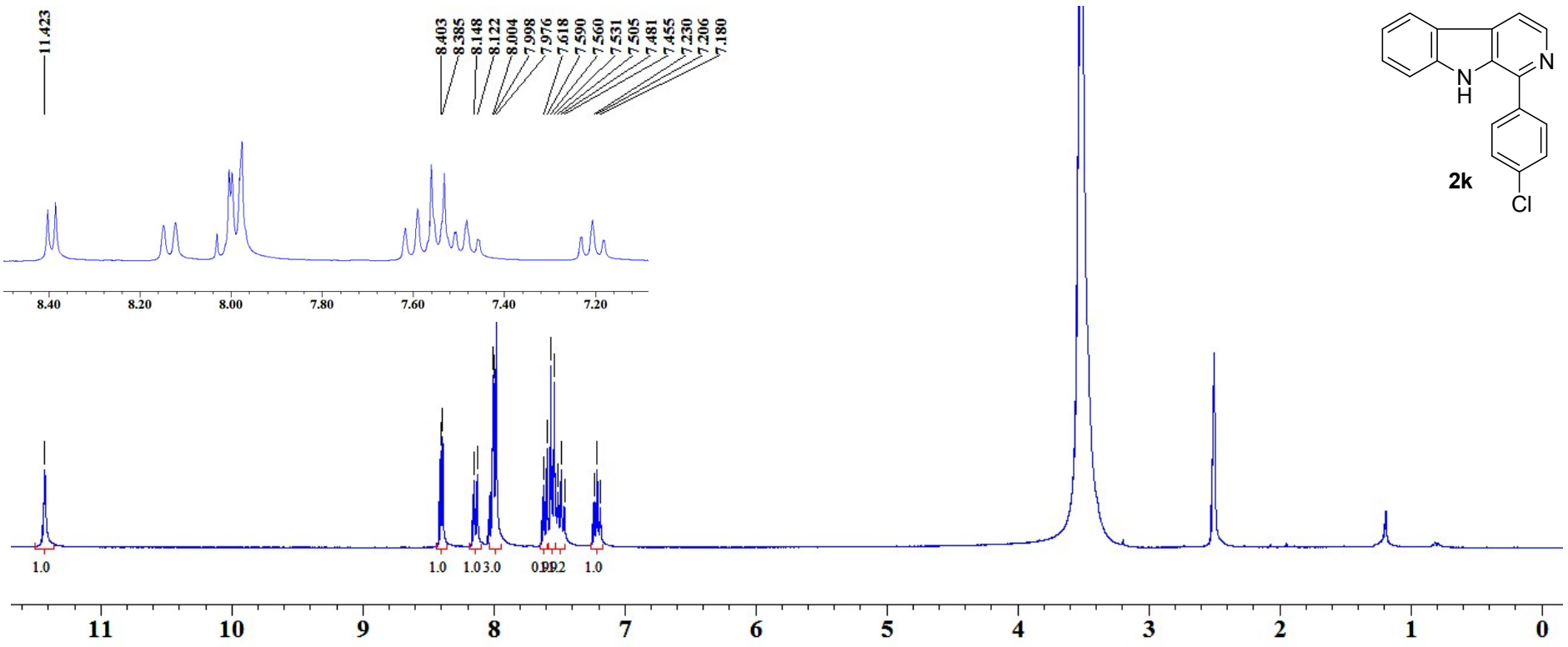


^{13}C NMR (75 MHz, $CDCl_3$ + DMSO−*d6*)

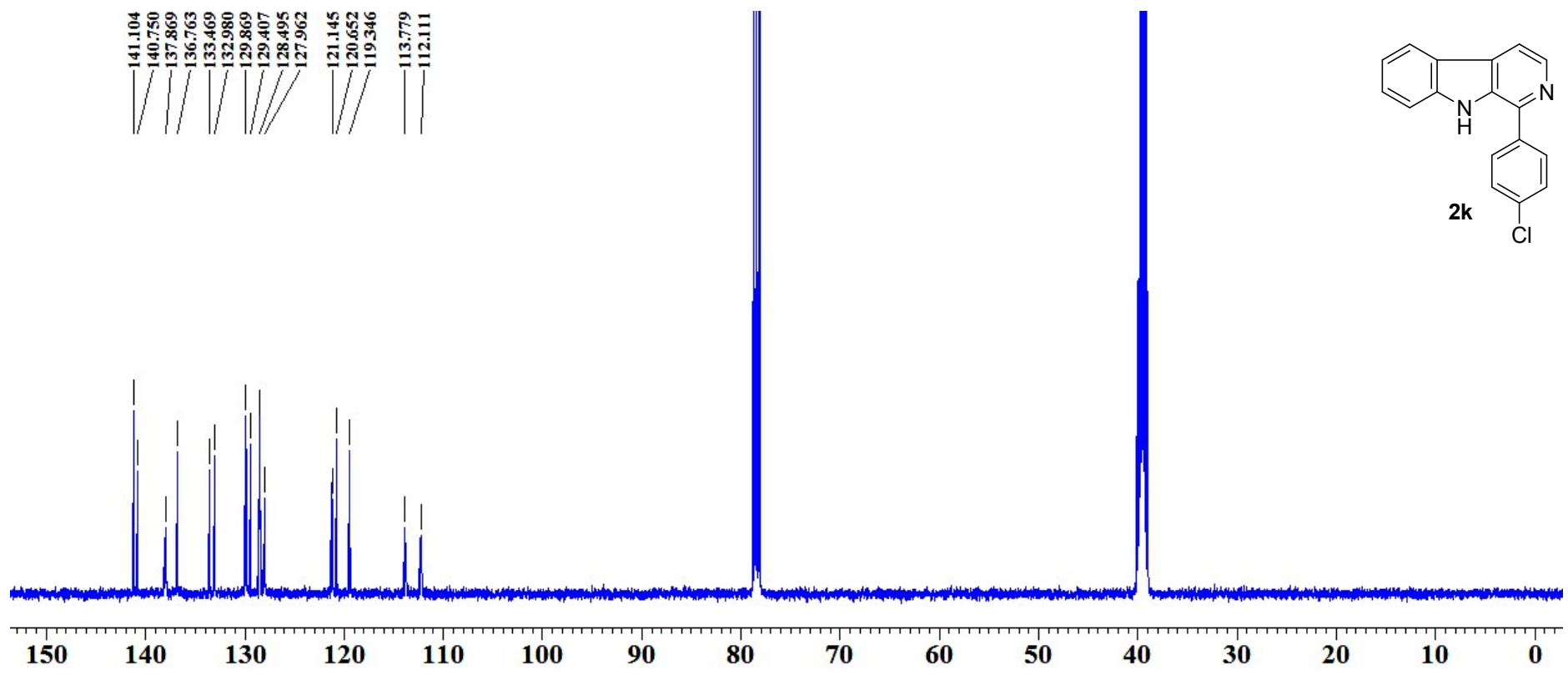


1-(4-Chlorophenyl)-9*H*-pyrido[3,4-*b*]indole (2k)

^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6)

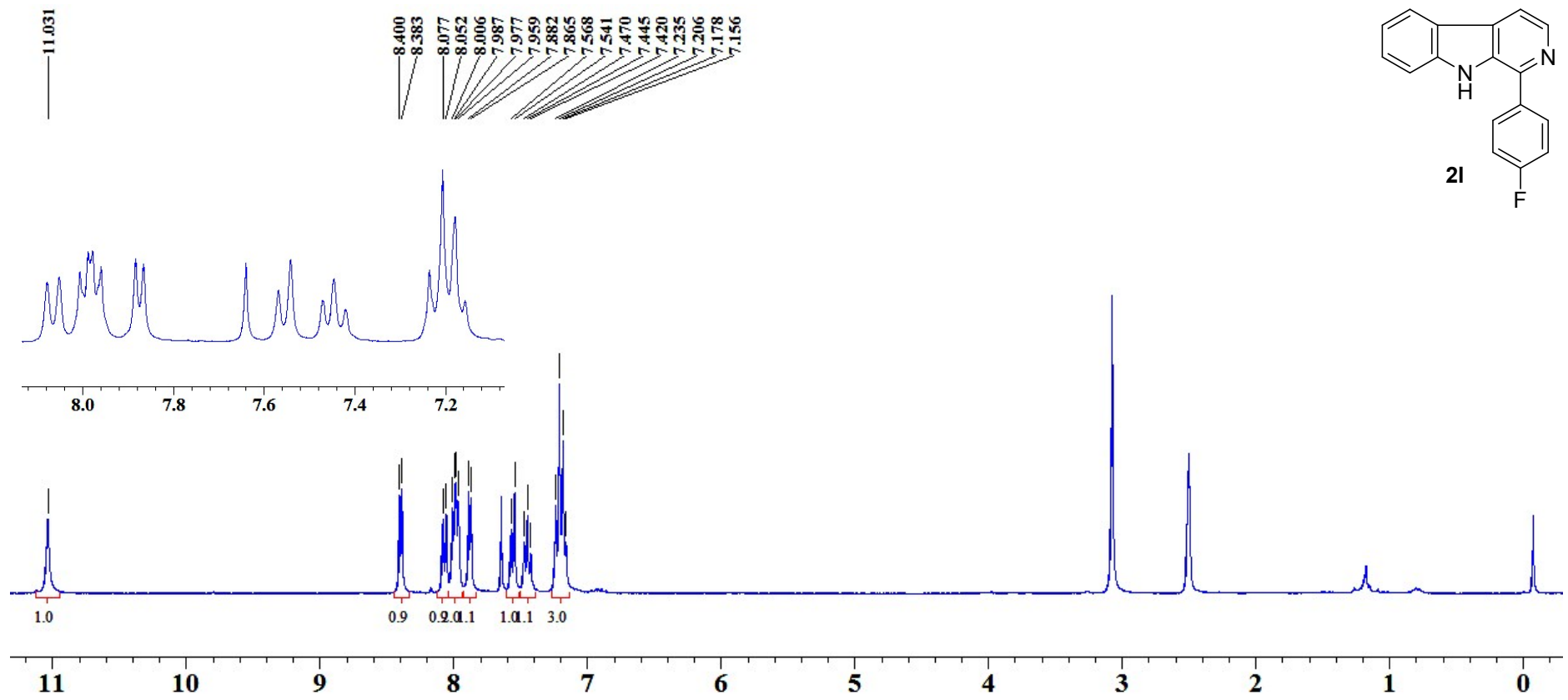


^{13}C NMR (125 MHz, $CDCl_3$ + DMSO−*d6*)

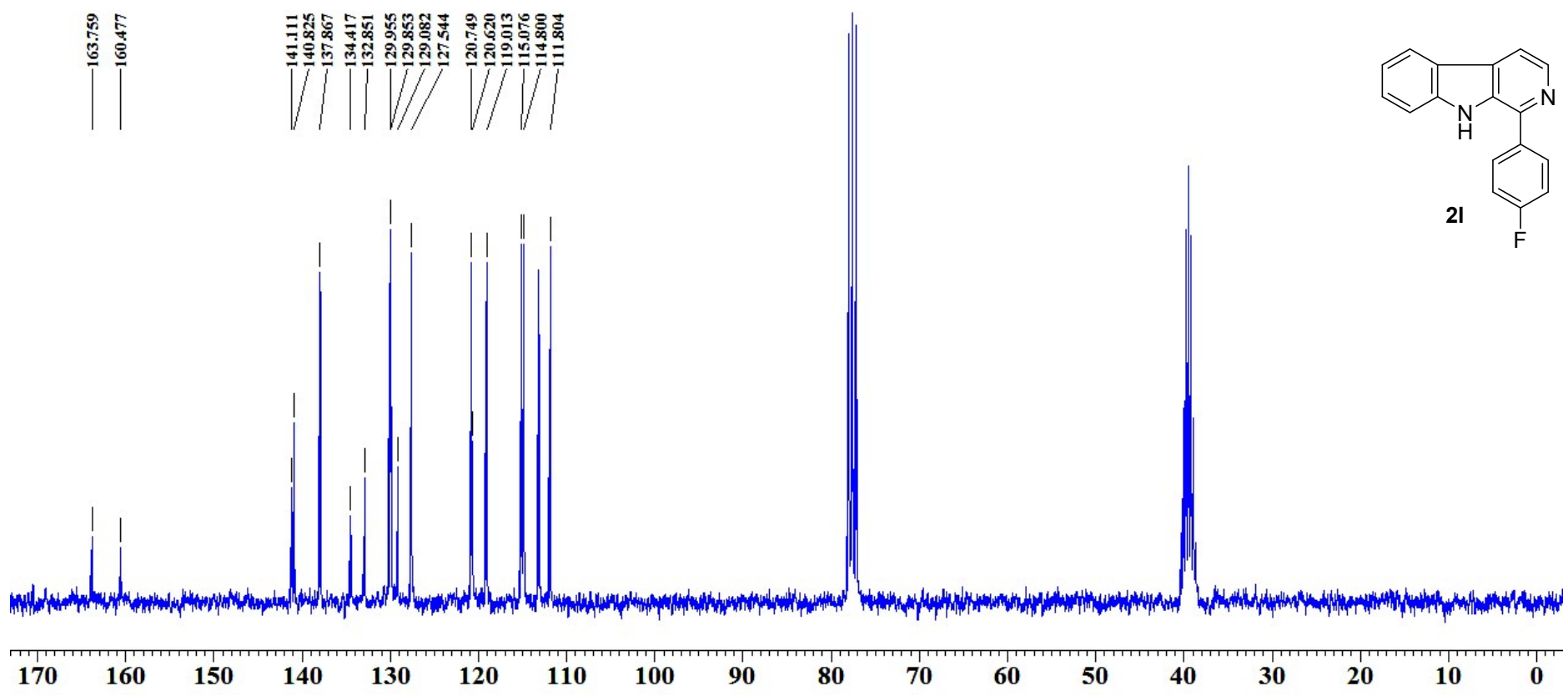


1-(4-Fluorophenyl)-9*H*-pyrido[3,4-*b*]indole (2l)

^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6)

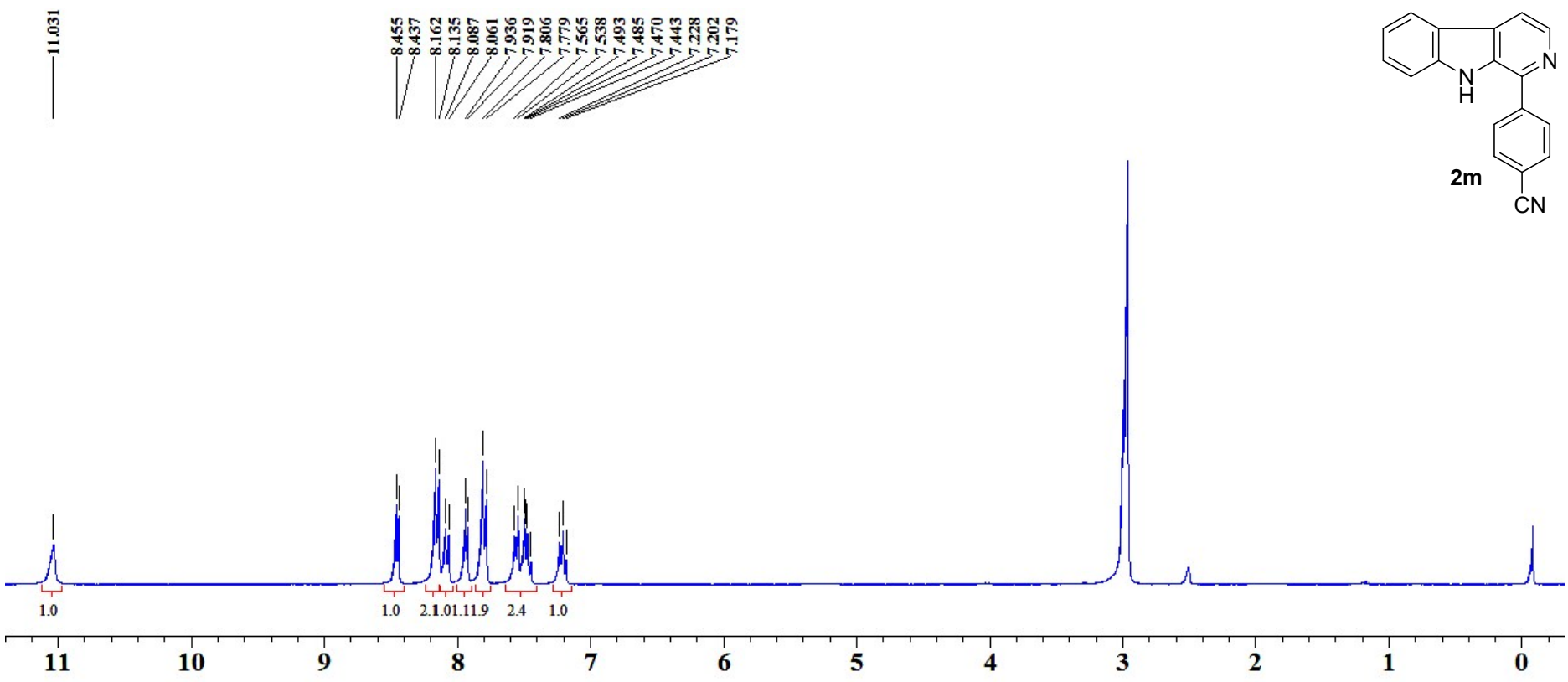


^{13}C NMR (75 MHz, $CDCl_3$ + DMSO−d_6)

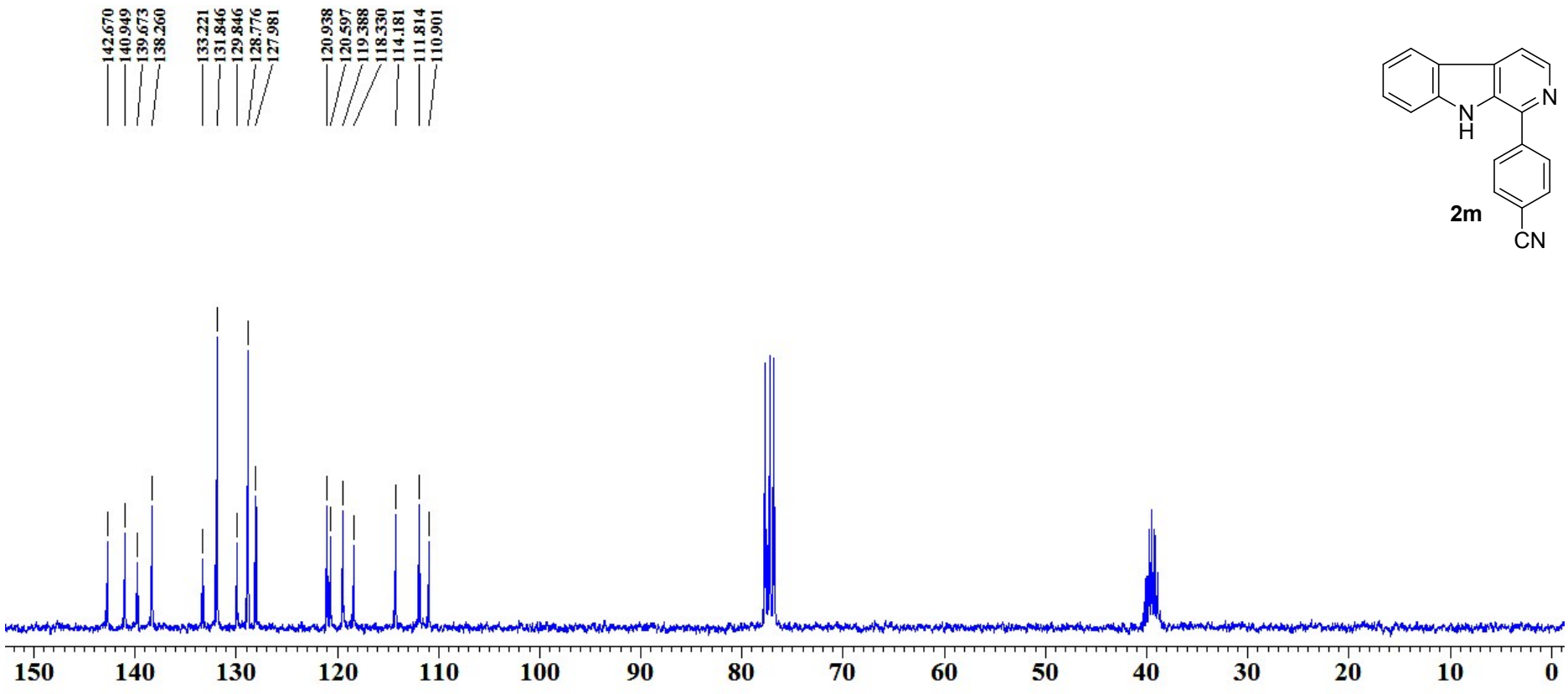


4-(9*H*-Pyrido[3,4-*b*]indol-1-yl)benzonitrile (2m)

^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6)

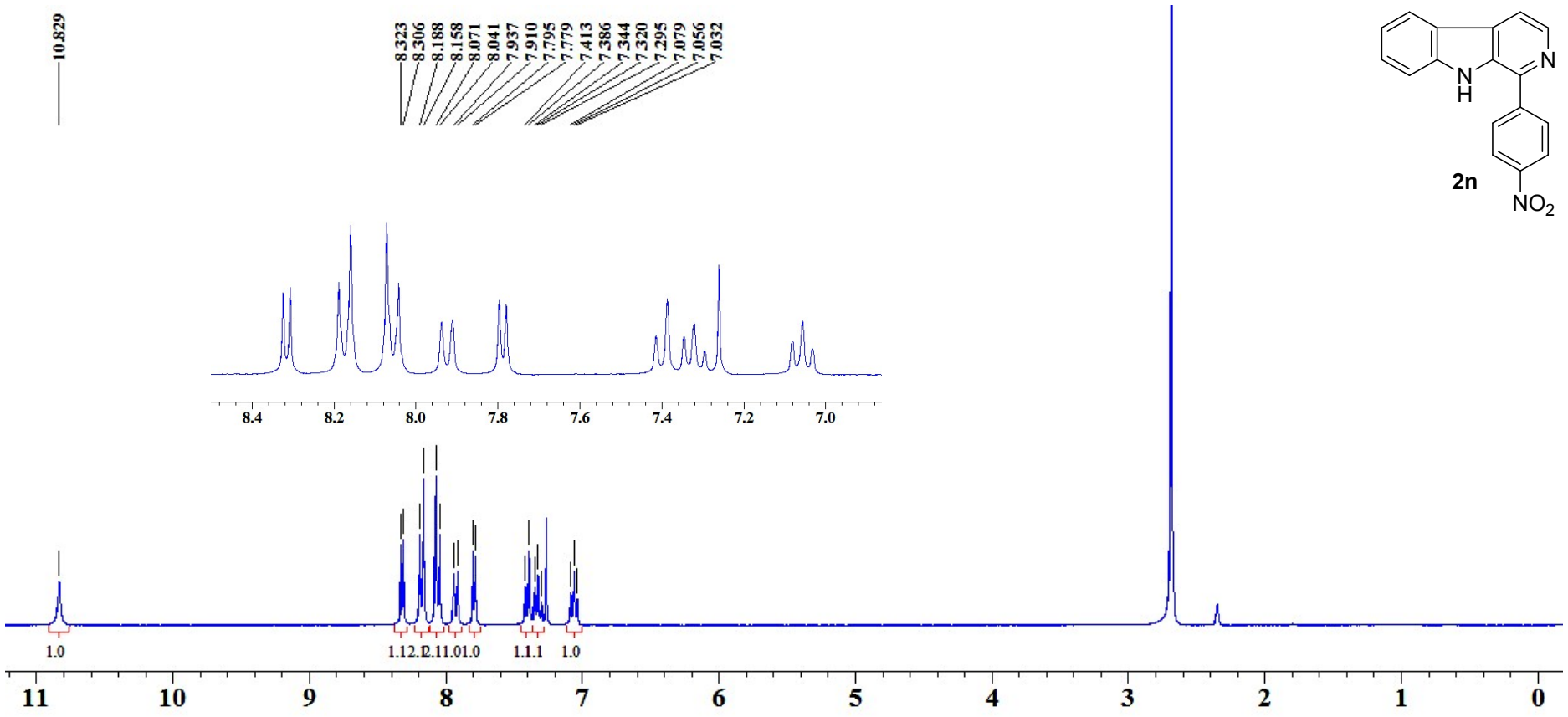


13 C NMR (75 MHz, $CDCl_3$ + DMSO−d_6)

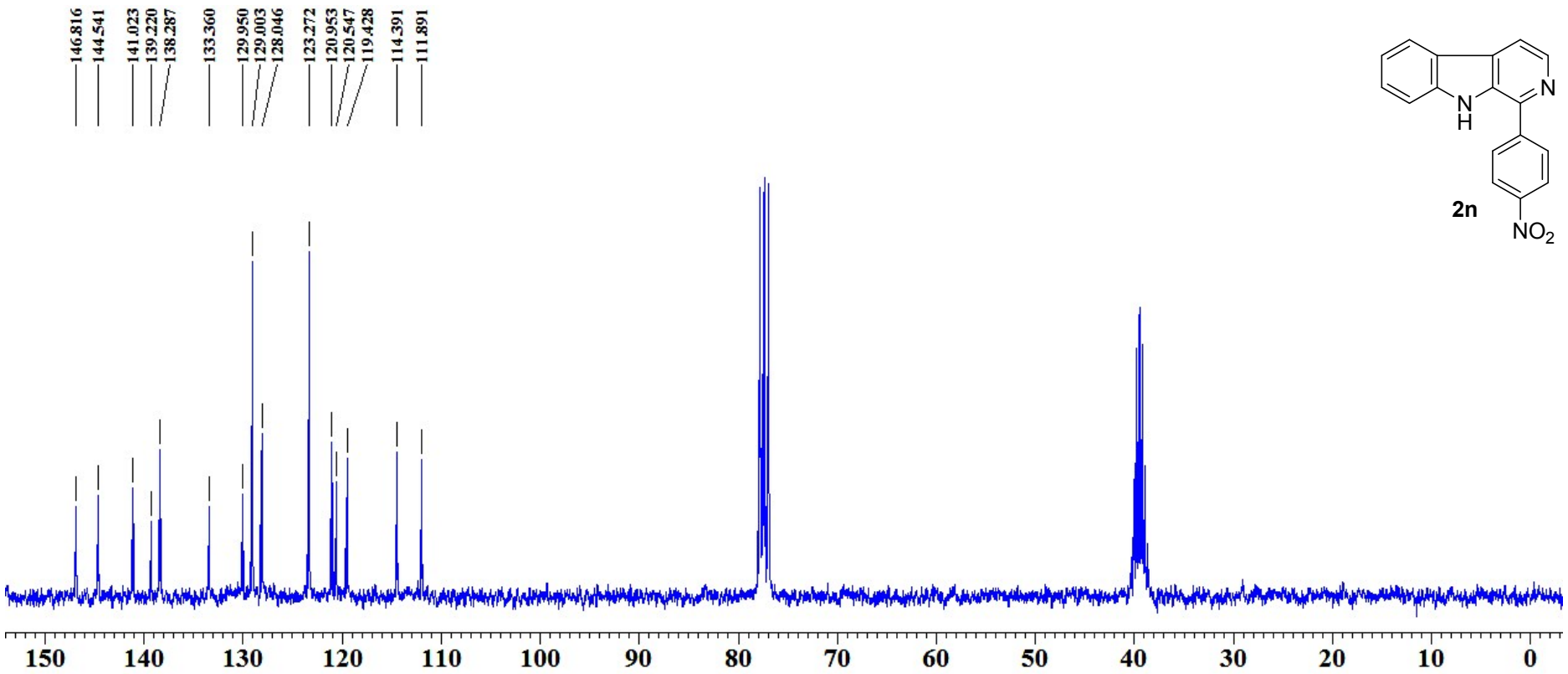


1-(4-Nitrophenyl)-9*H*-pyrido[3,4-*b*]indole (2n)

^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6)

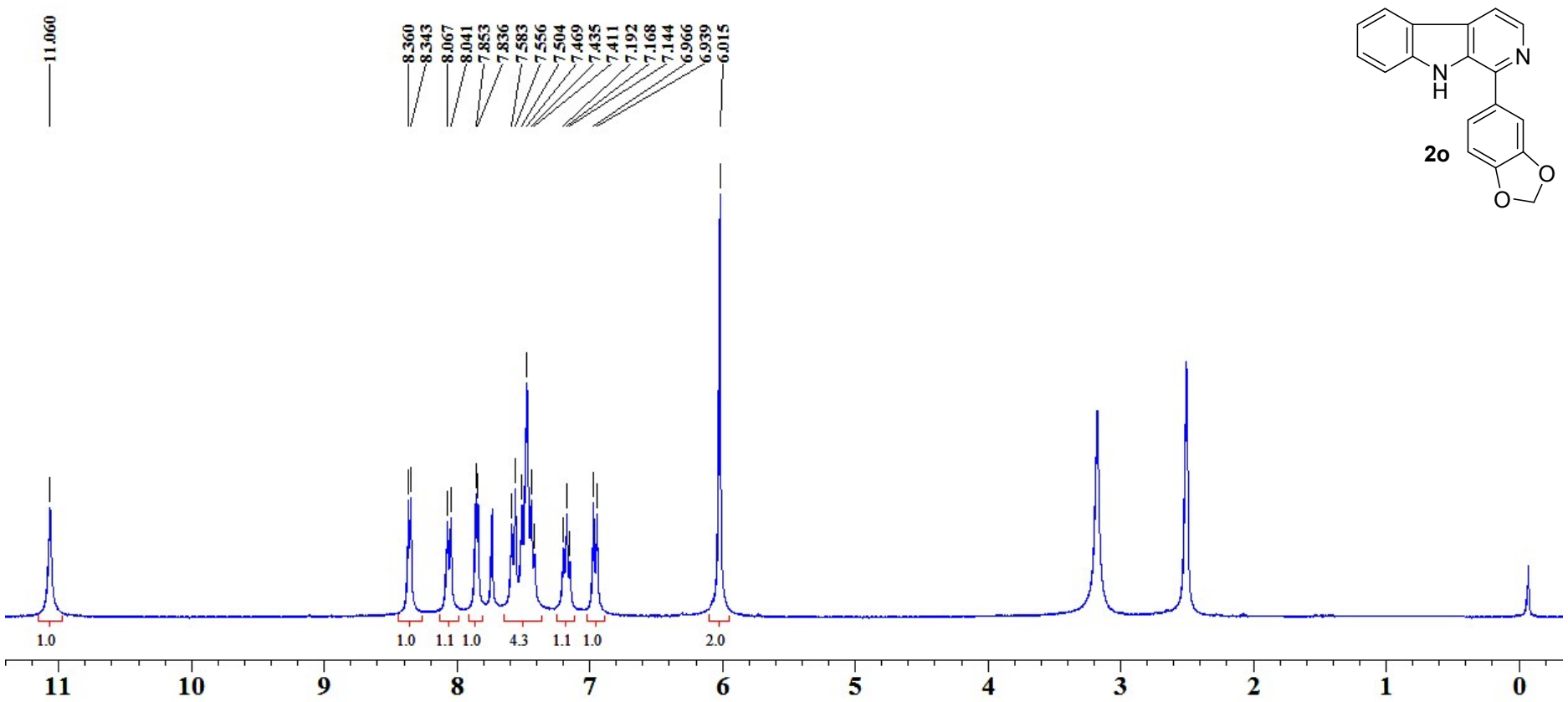


^{13}C NMR (75 MHz, $CDCl_3$ + DMSO–d_6)

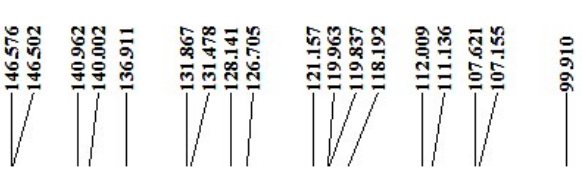


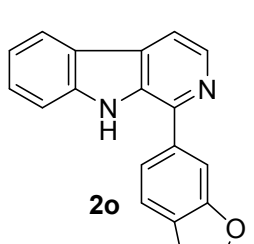
1-(Benzo[*d*][1,3]dioxol-5-yl)-9*H*-pyrido[3,4-*b*]indole (2o)

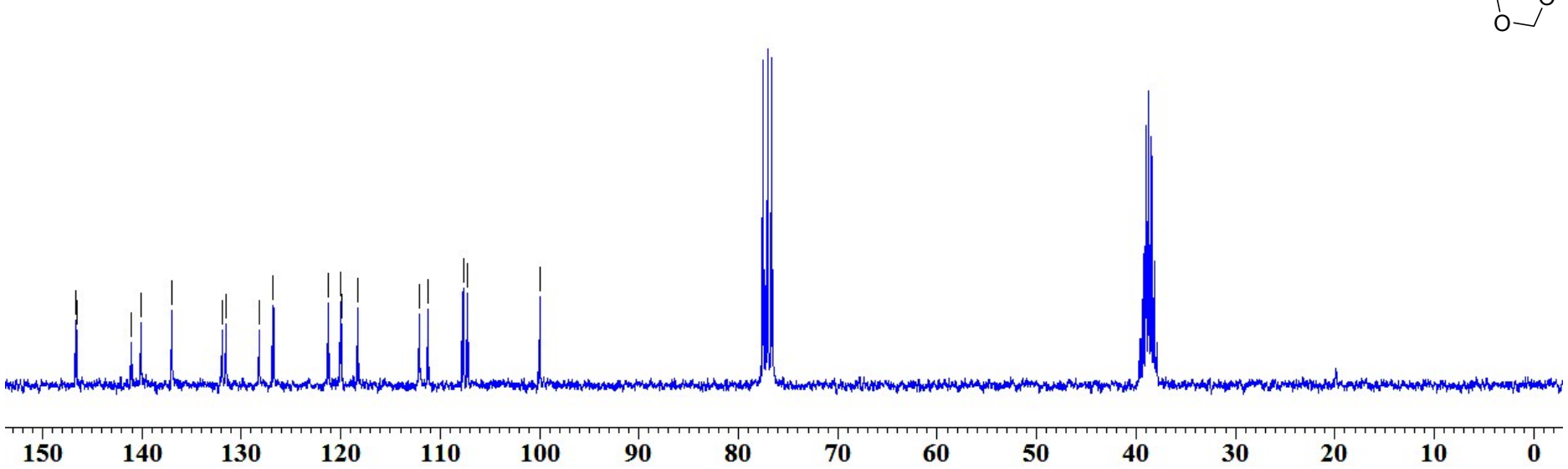
^{1}H NMR (300 MHz, $CDCl_3$ + DMSO–d_6)



^{13}C NMR (75 MHz, $CDCl_3$ + DMSO−d_6)

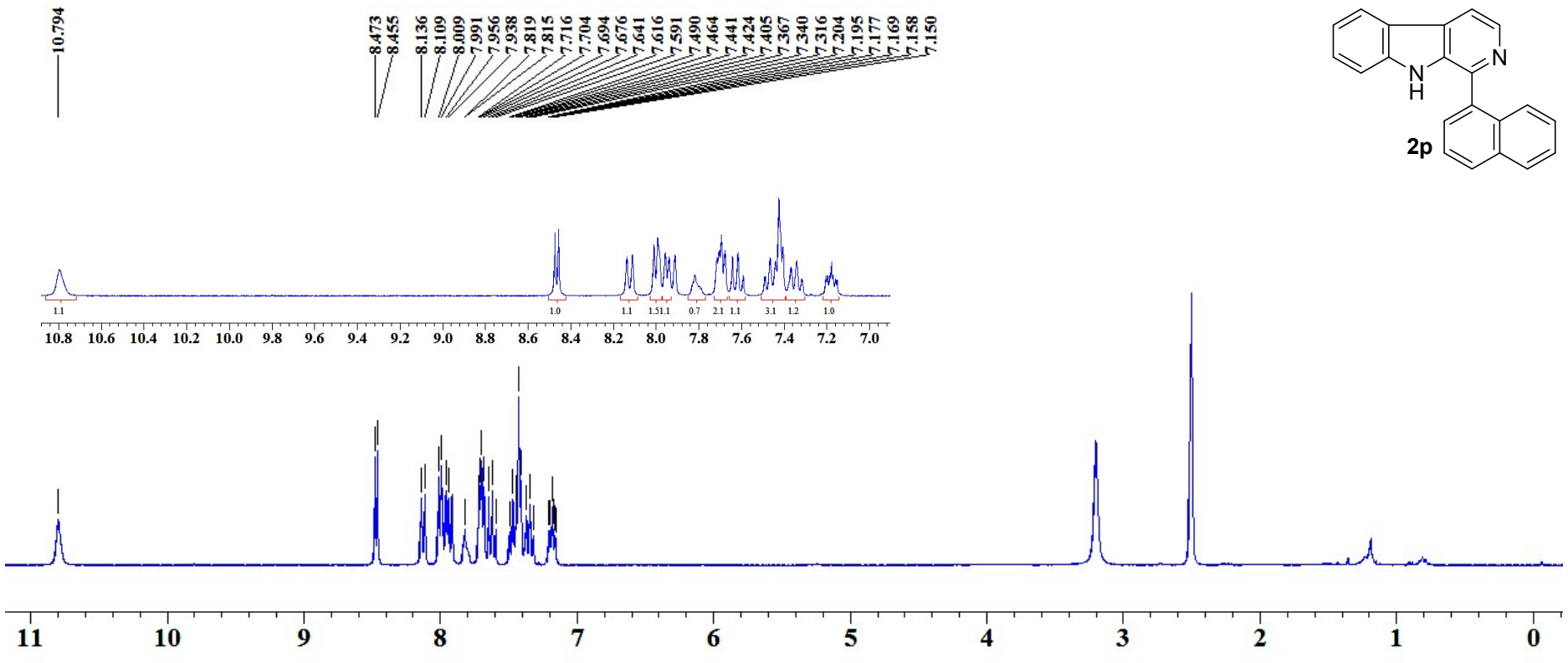




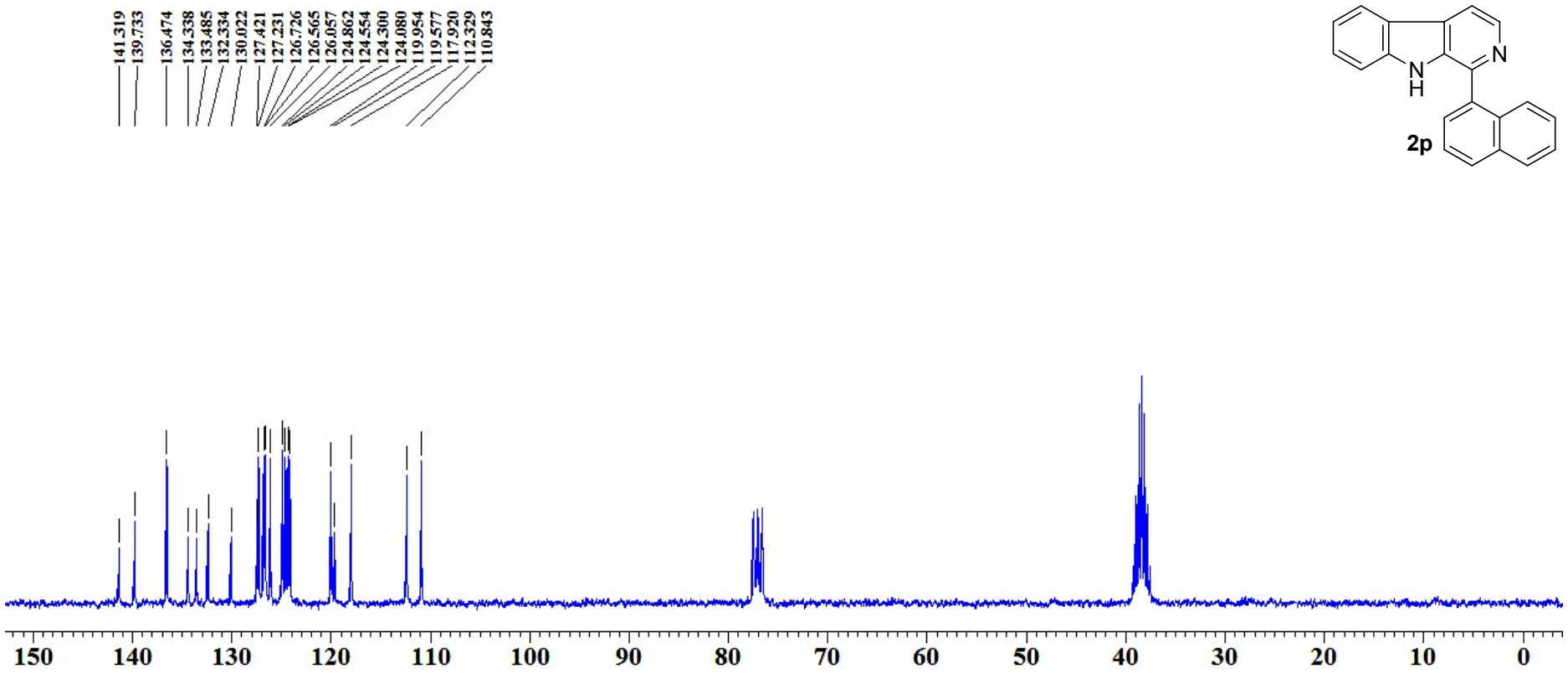


1-(Naphthalen-1-yl)-9*H*-pyrido[3,4-*b*]indole (2p)

^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6)

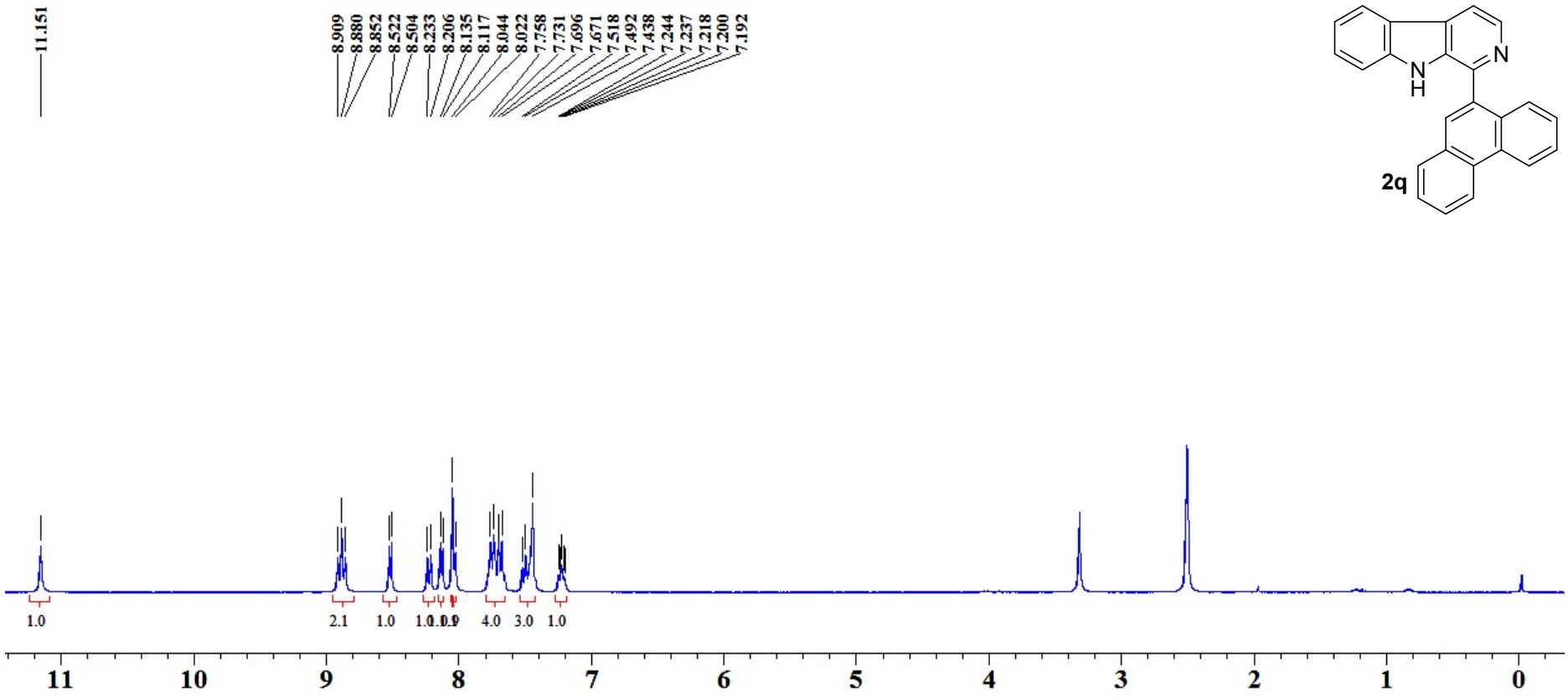


^{13}C NMR (75 MHz, $CDCl_3$ + DMSO−d_6)

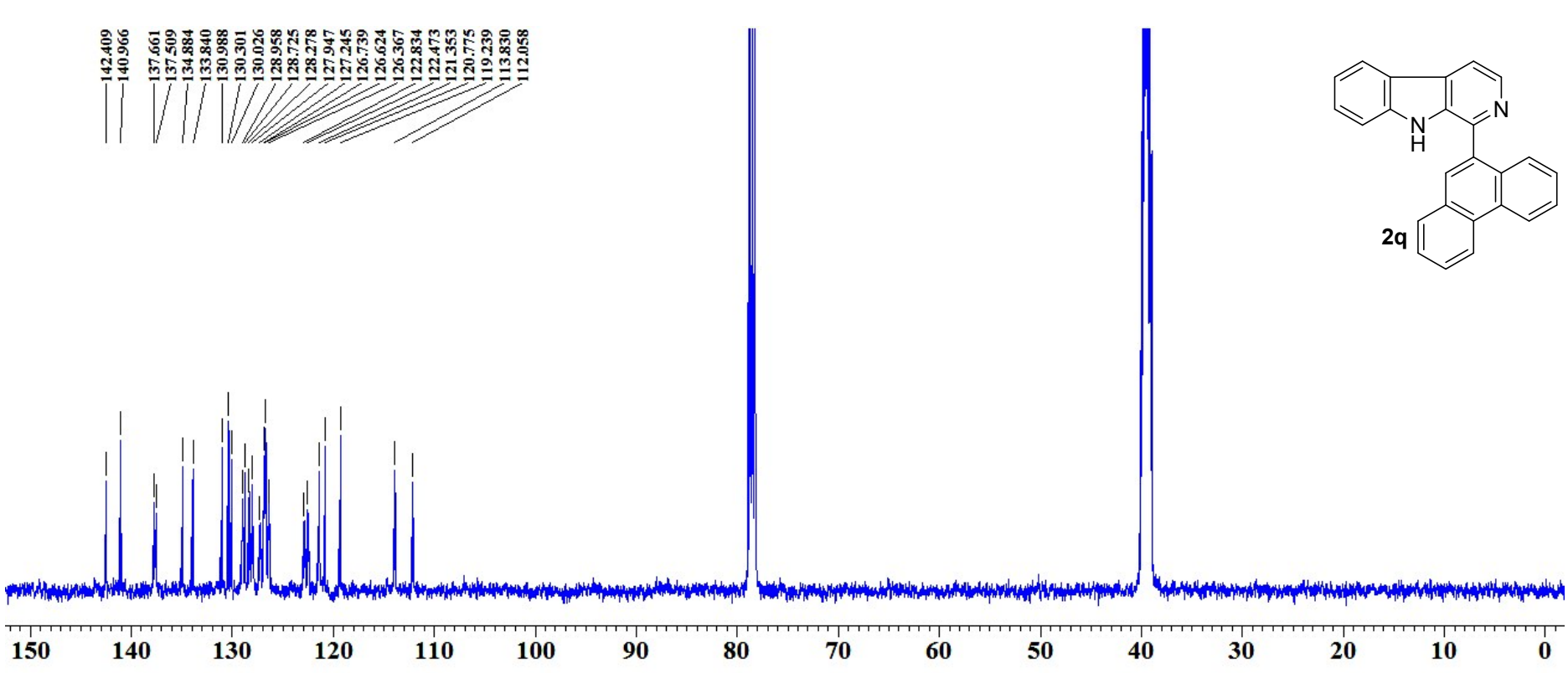


1-(Phenanthren-9-yl)-9*H*-pyrido[3,4-*b*]indole (2q)

^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6)

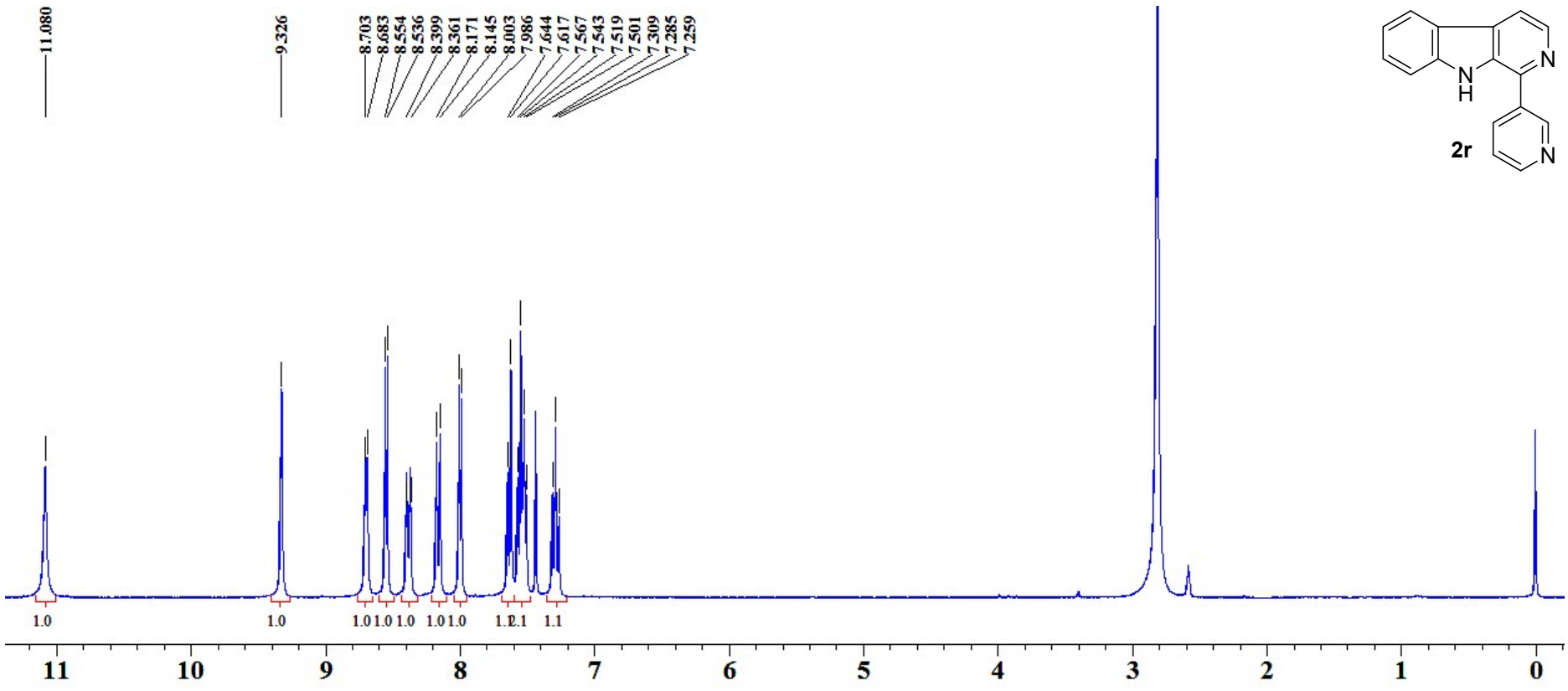


^{13}C NMR (125 MHz, $CDCl_3$ + DMSO−d_6)

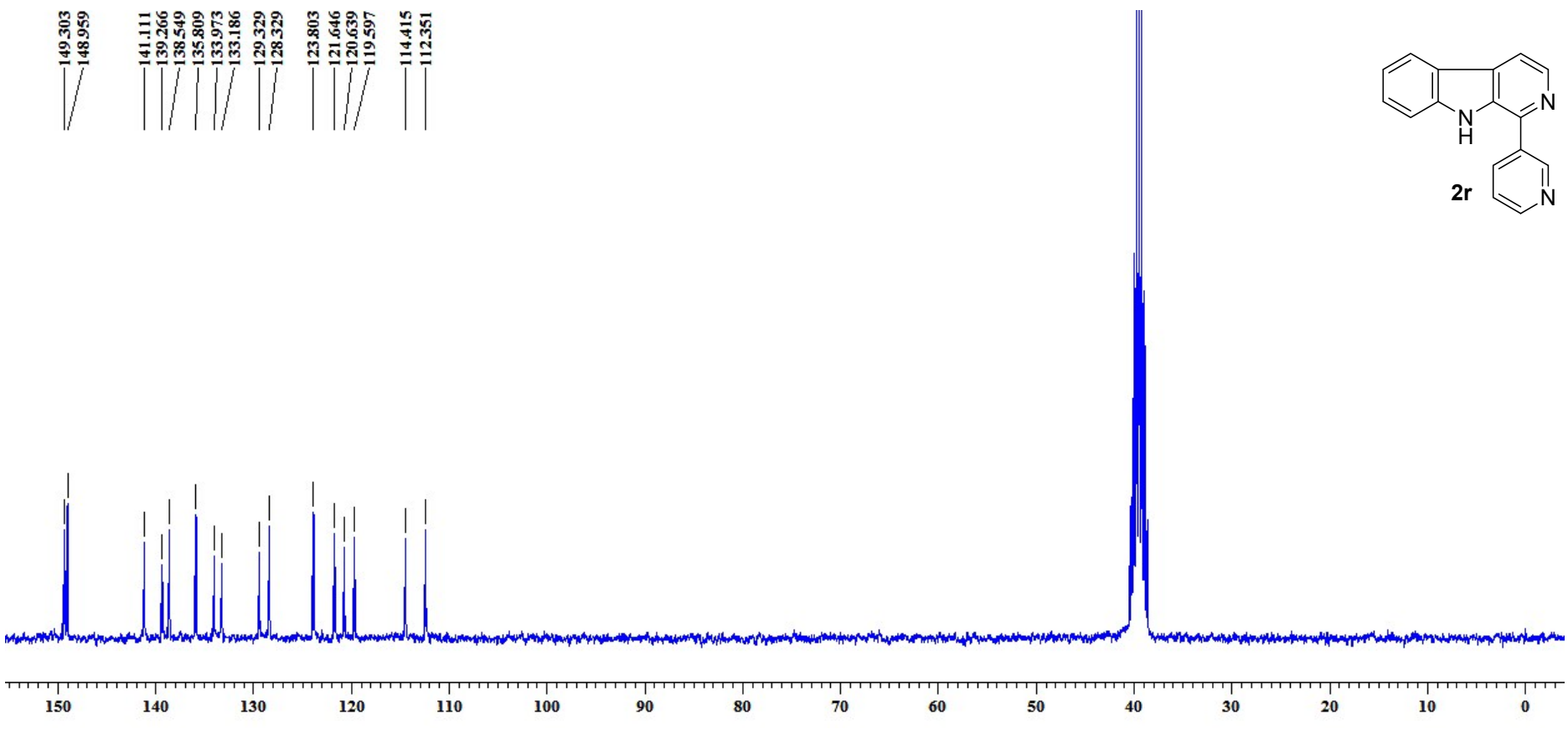


1-(Pyridin-3-yl)-9*H*-pyrido[3,4-*b*]indole (2r)

^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6)

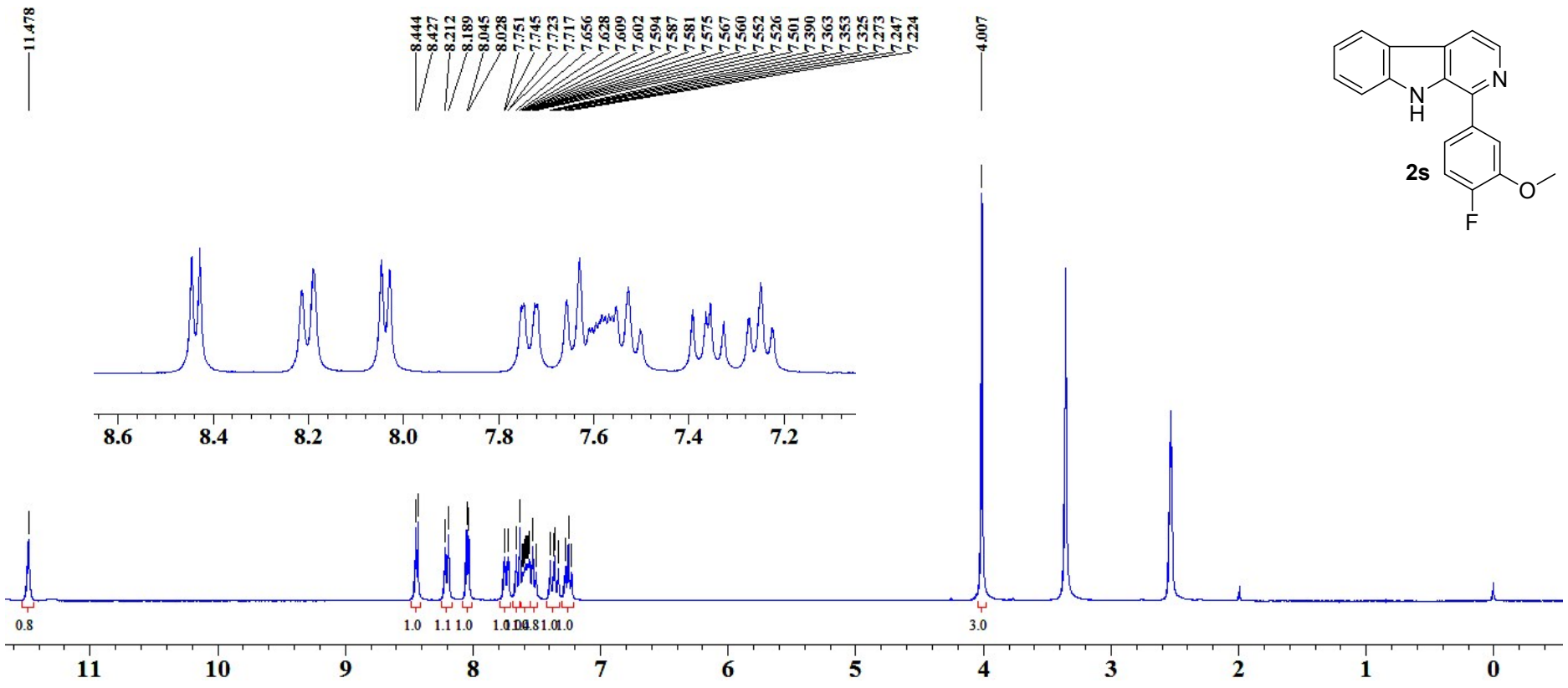


^{13}C NMR (75 MHz, DMSO−d_6)

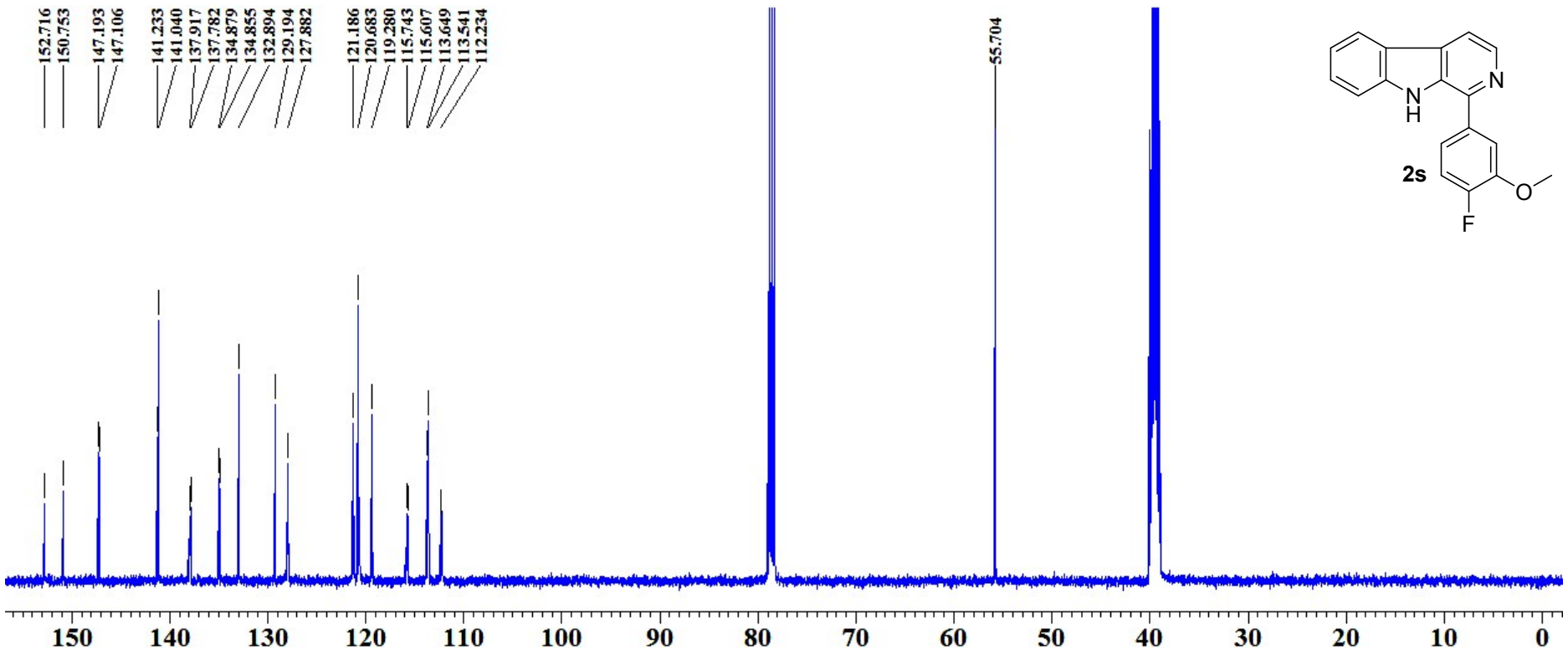


1-(4-Fluoro-3-methoxyphenyl)-9*H*-pyrido[3,4-*b*]indole (2s)

^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6)

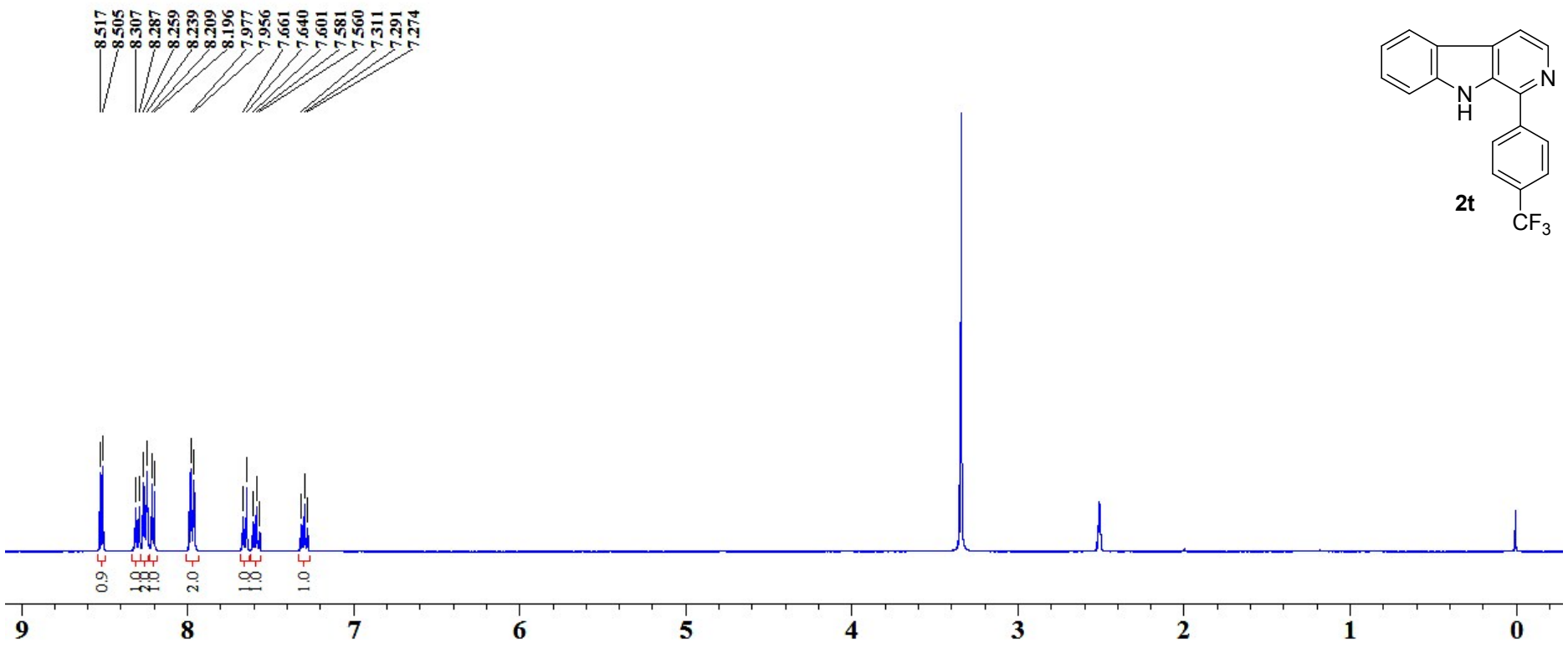


^{13}C NMR (125 MHz, $CDCl_3$ + DMSO−d_6)

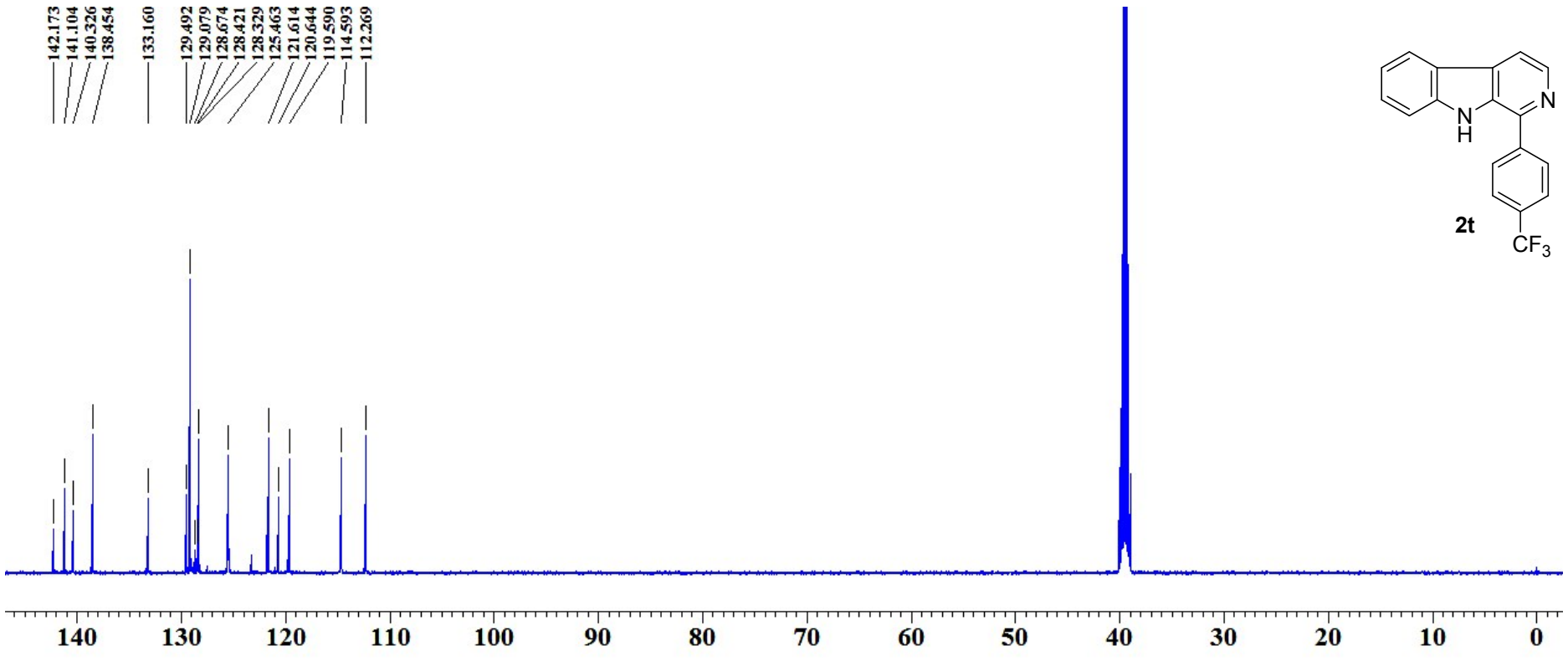


1-(4-(trifluoromethyl)phenyl)-9H-pyrido[3,4-b]indole (2t)

^{1}H NMR (400 MHz, DMSO−d_6)

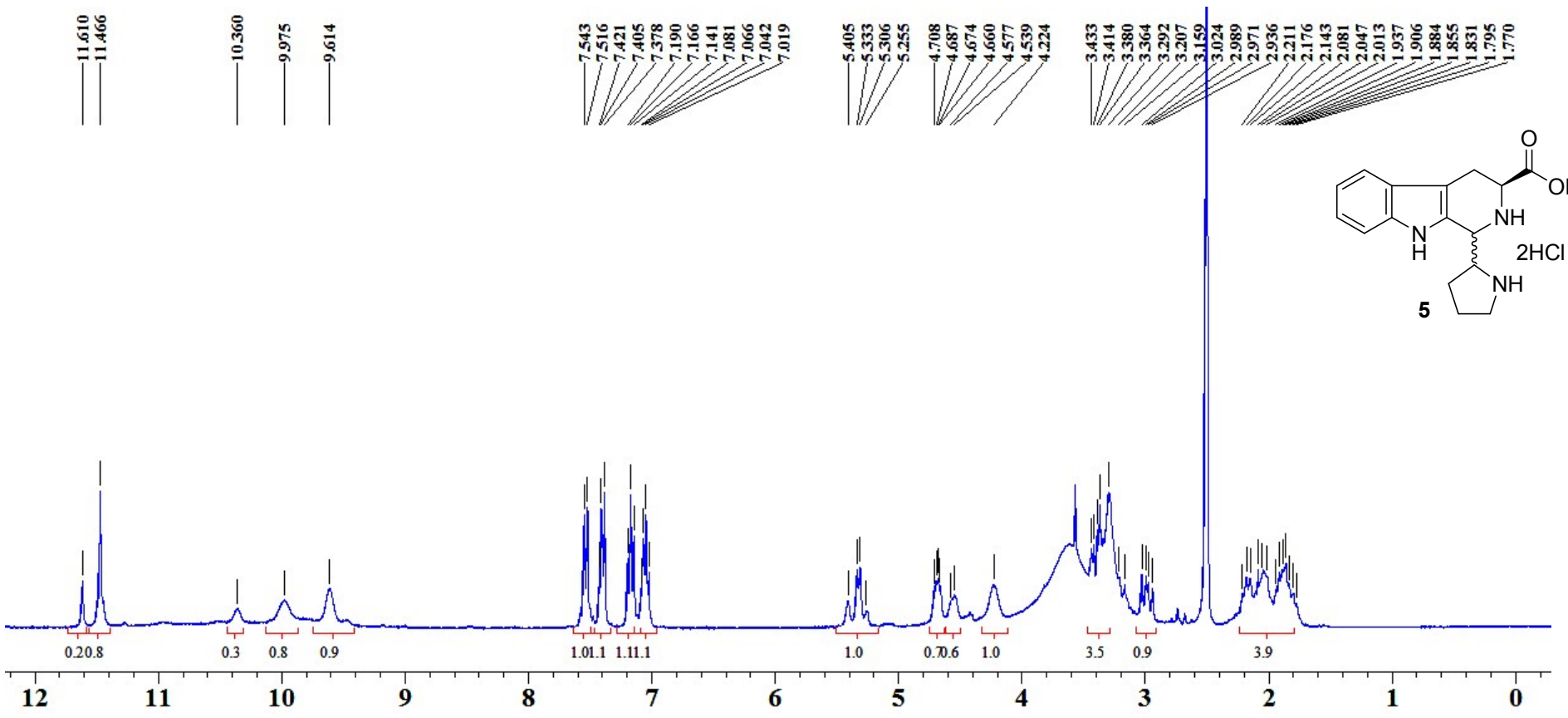


^{13}C NMR (125 MHz, DMSO−d_6)

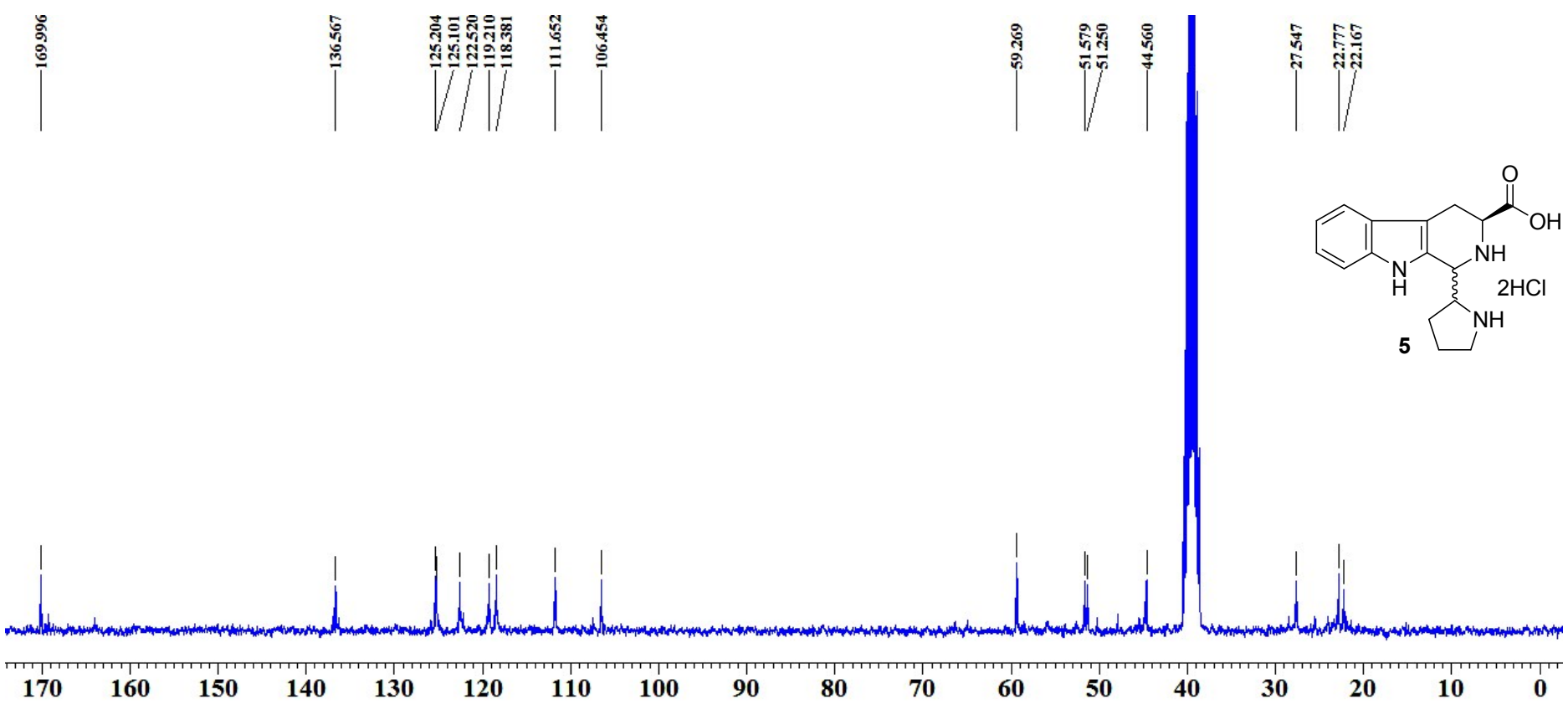


1-(Pyrrolidin-2-yl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole-3-carboxylic acid dihydrochloride (5)

^{1}H NMR (300 MHz, DMSO−d_6)

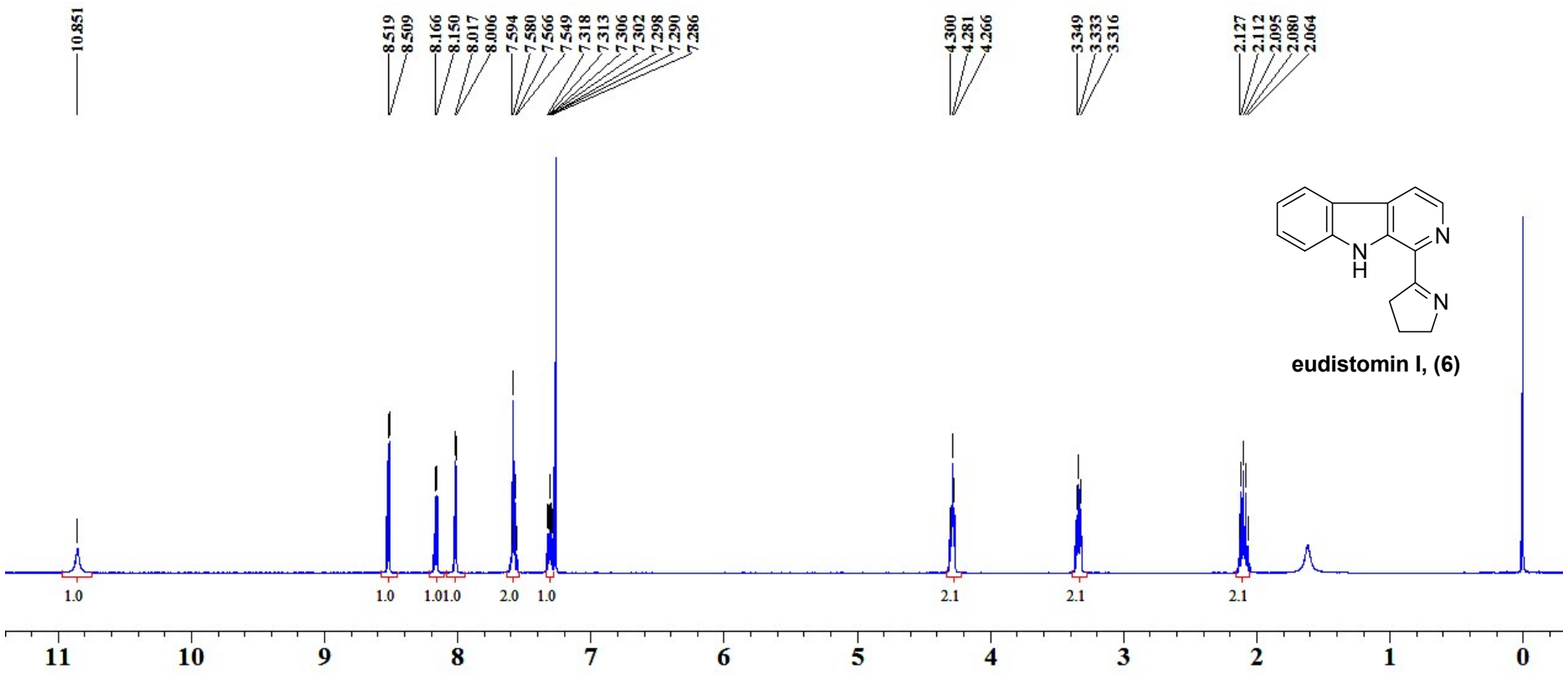


^{13}C NMR (75 MHz, DMSO−d_6)

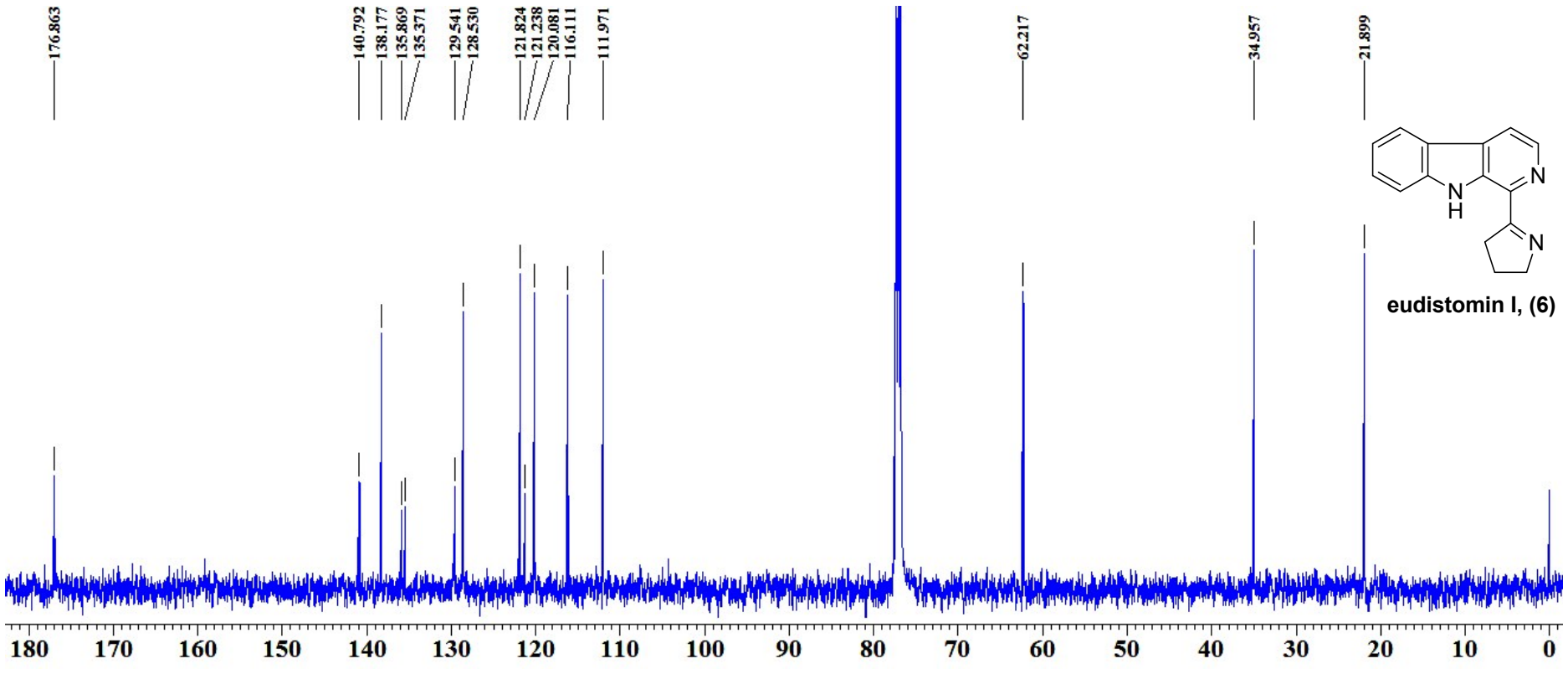


1-(3,4-Dihydro-2*H*-pyrrol-5-yl)-9*H*-pyrido[3,4-*b*]indole (or) eudistomin I (6)

^{1}H NMR (500 MHz, $CDCl_3$)

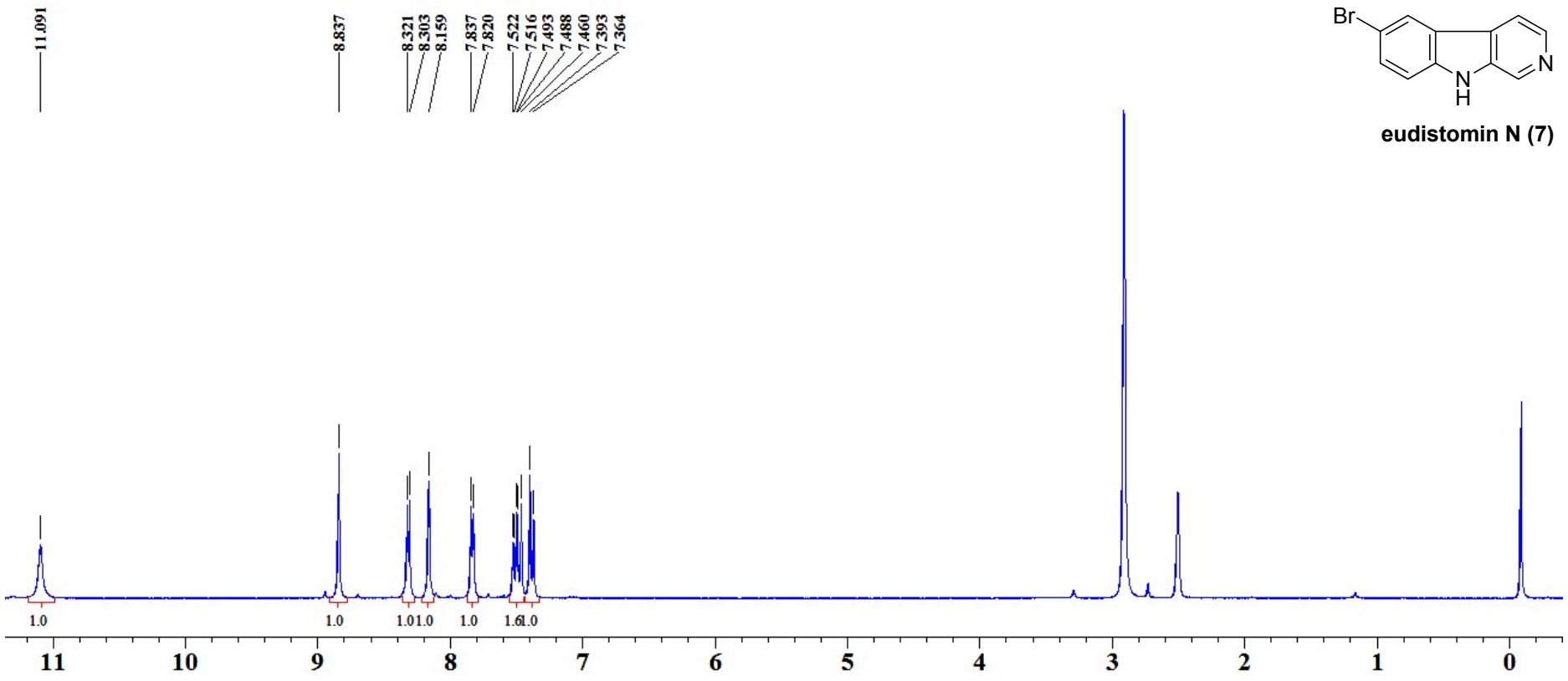


^{3}C NMR (125 MHz, $CDCl_3$)

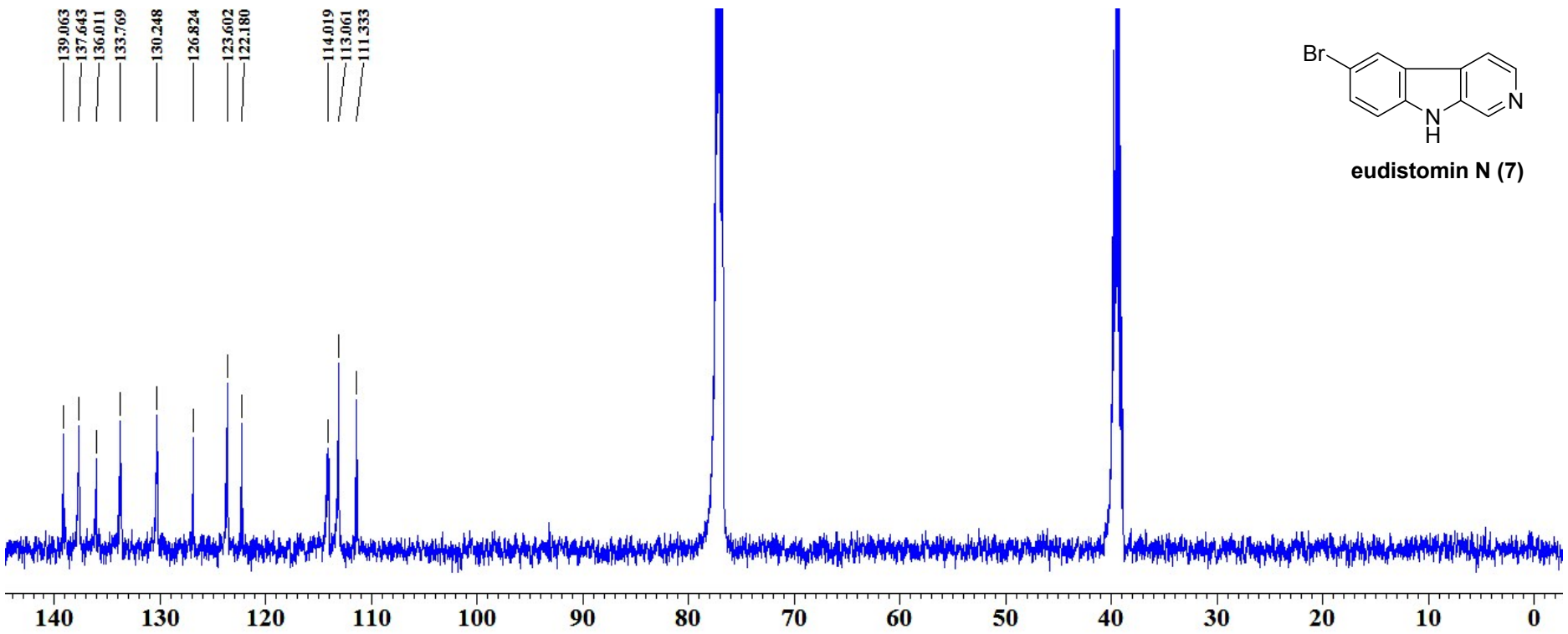


6-Bromo-9*H*-pyrido[3,4-*b*]indole (or) Eudistomin N (7)

^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6)

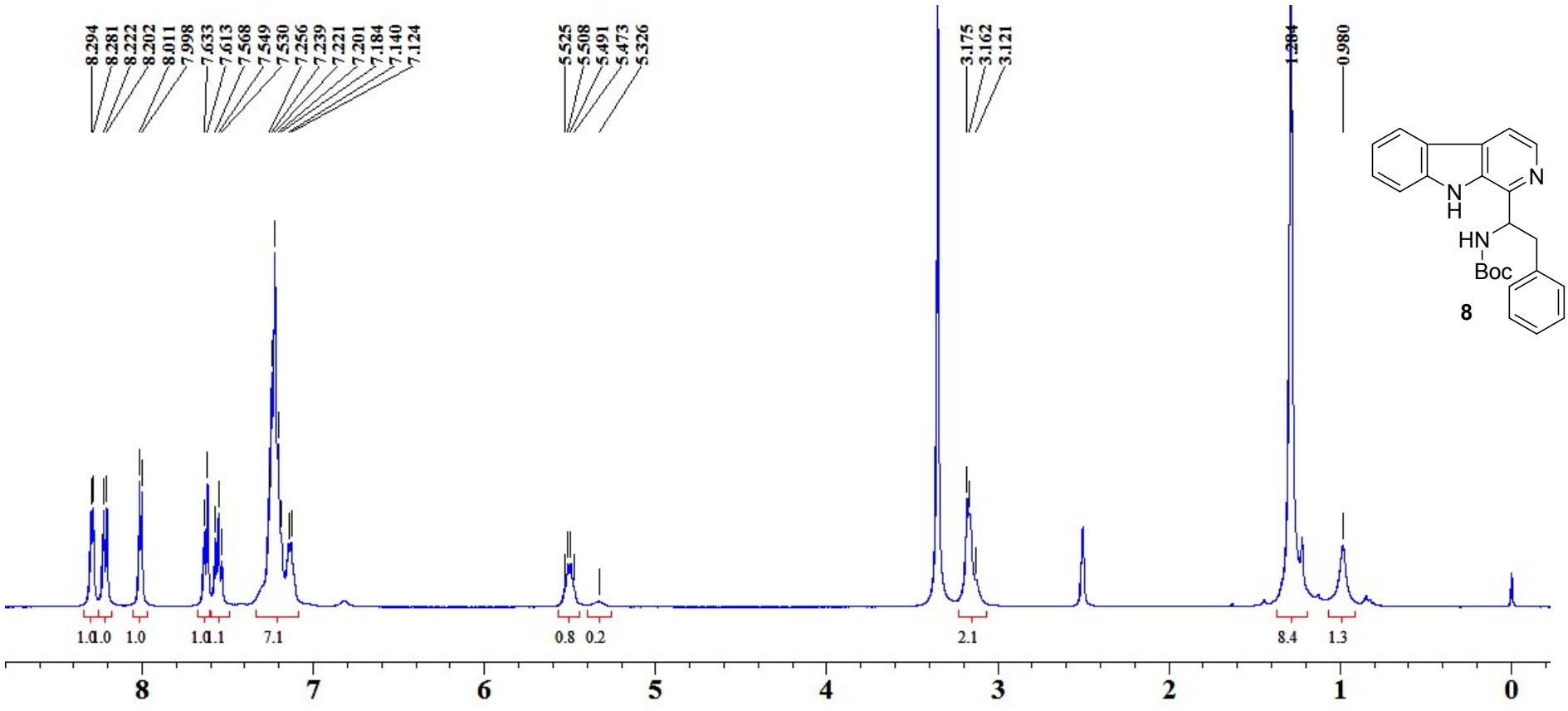


^{13}C NMR (125 MHz, $CDCl_3$ + DMSO−d_6)

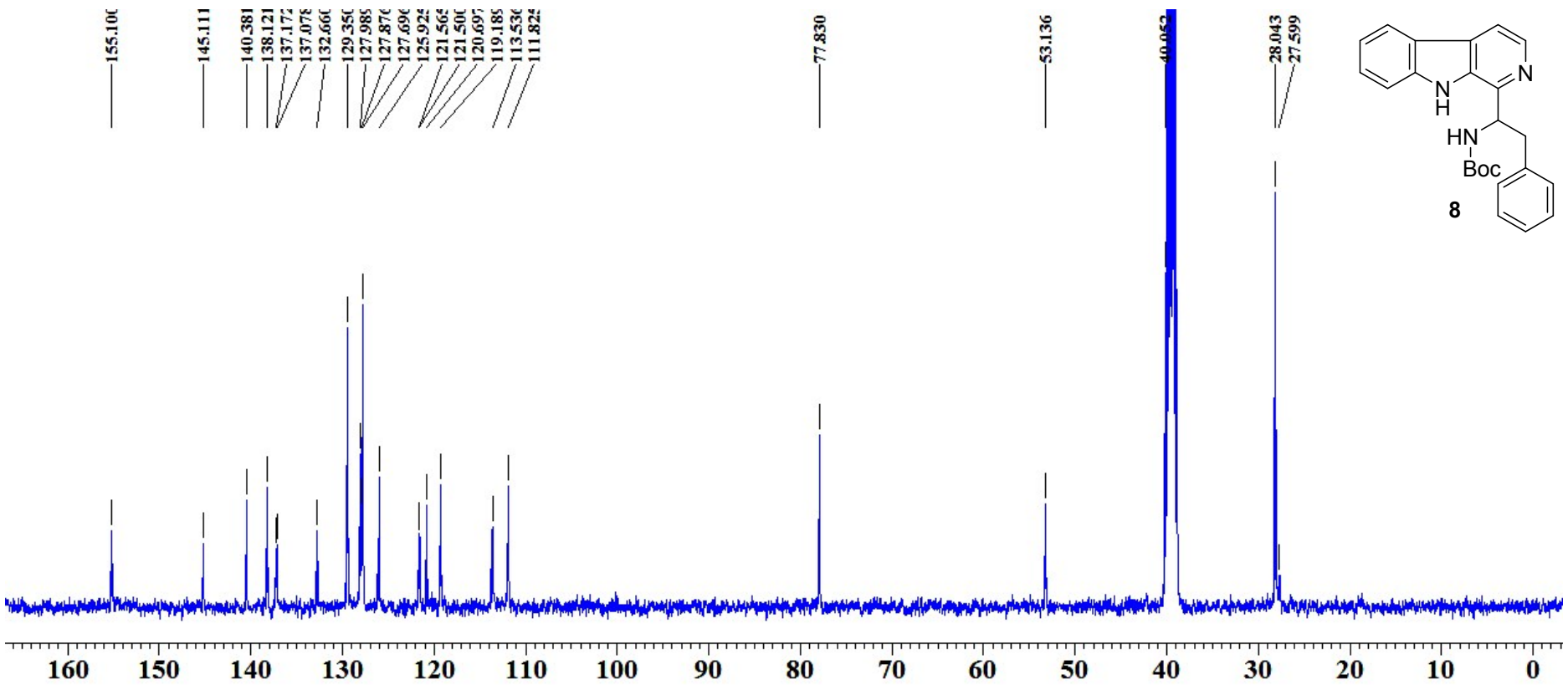


tert-Butyl 2-phenyl-1-(9*H*-pyrido[3,4-*b*]indol-1-yl)ethylcarbamate (8)

^{1}H NMR (400 MHz, DMSO−d_6)

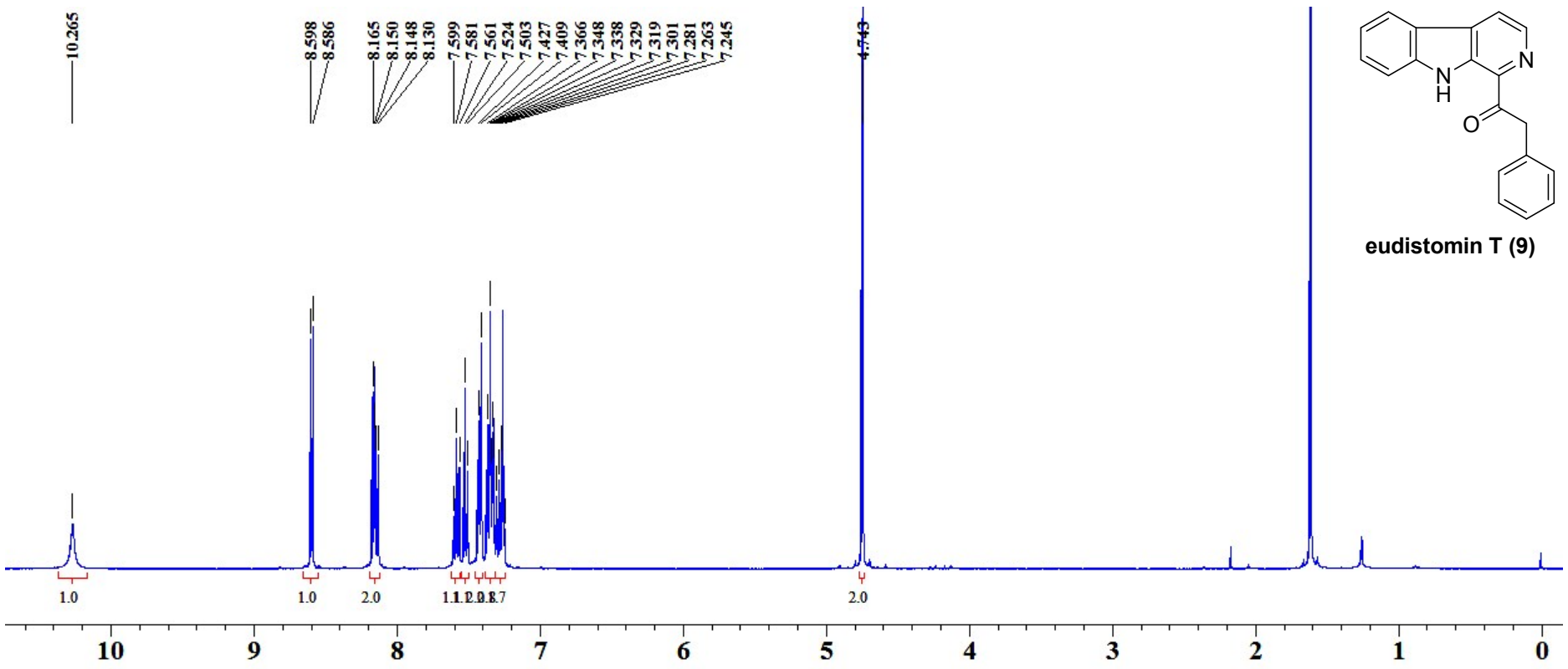


^{13}C NMR (100 MHz, DMSO−d_6)

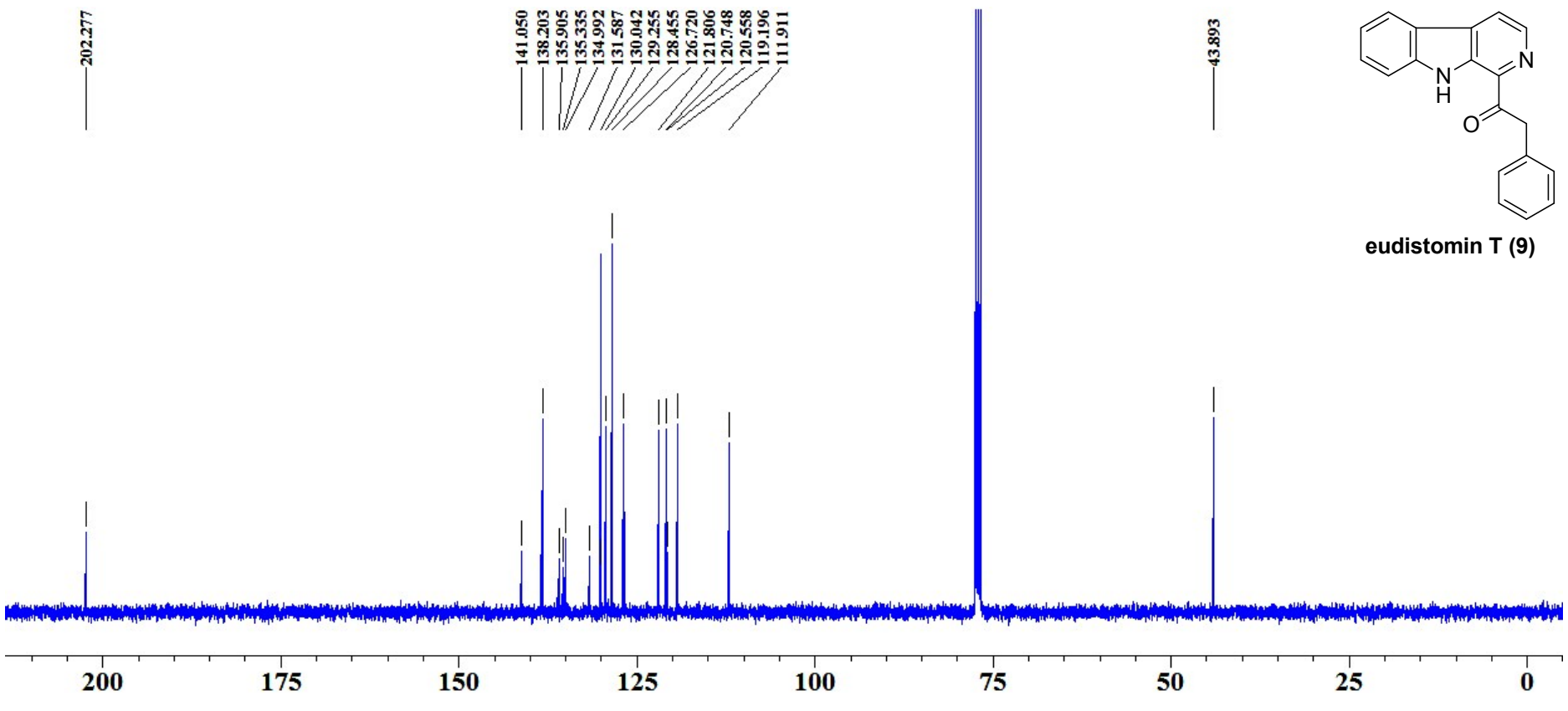


2-Phenyl-1-(9*H*-pyrido[3,4-*b*]indol-1-yl)ethanone (or) Eudistomin T (9)

^{1}H NMR (400 MHz, $CDCl_3$)

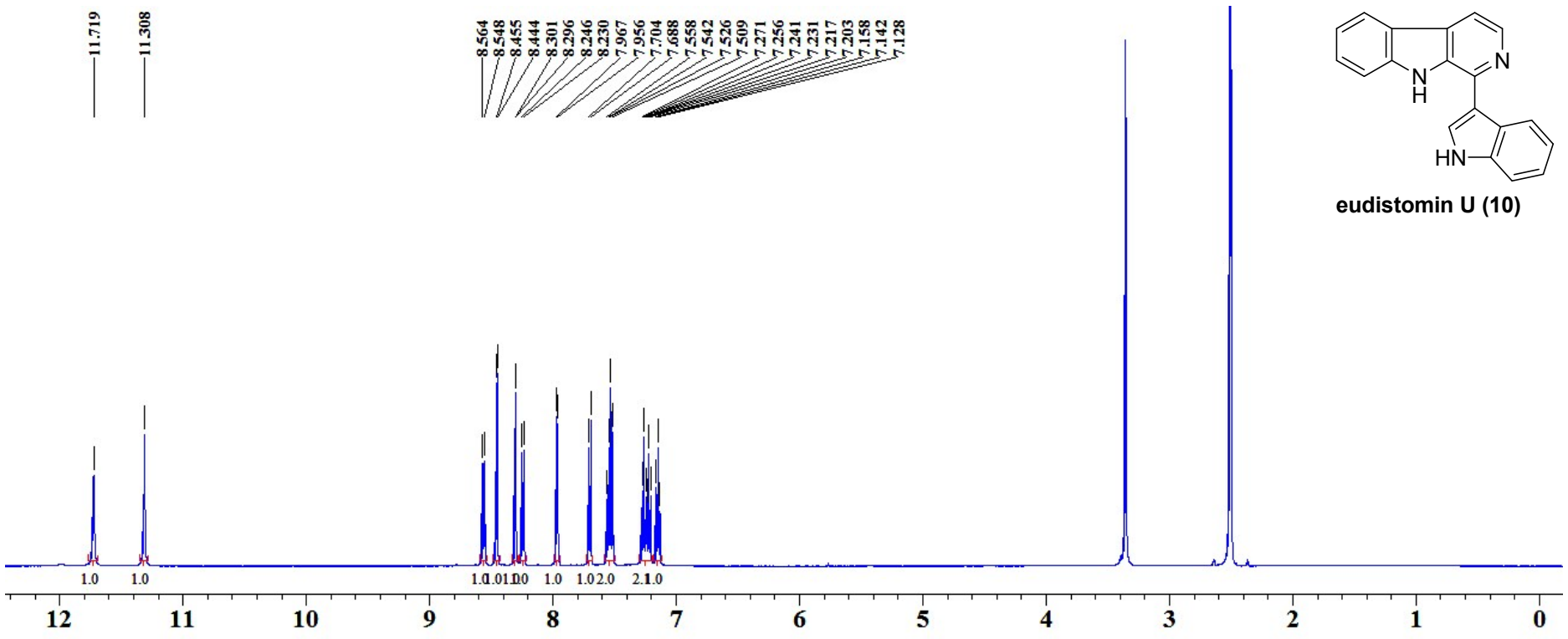


^{13}C NMR (100 MHz, $CDCl_3$)



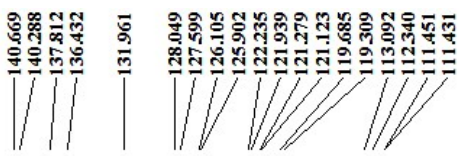
Synthesis of 1-(1*H*-indol-3-yl)-9*H*-pyrido[3,4-*b*]indole (or) Eudistomin U (10)

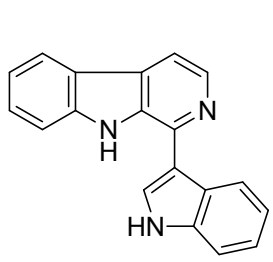
^{1}H NMR (500 MHz, DMSO−d_6)



eudistomin U (10)

^{13}C NMR (100 MHz, DMSO−d_6)

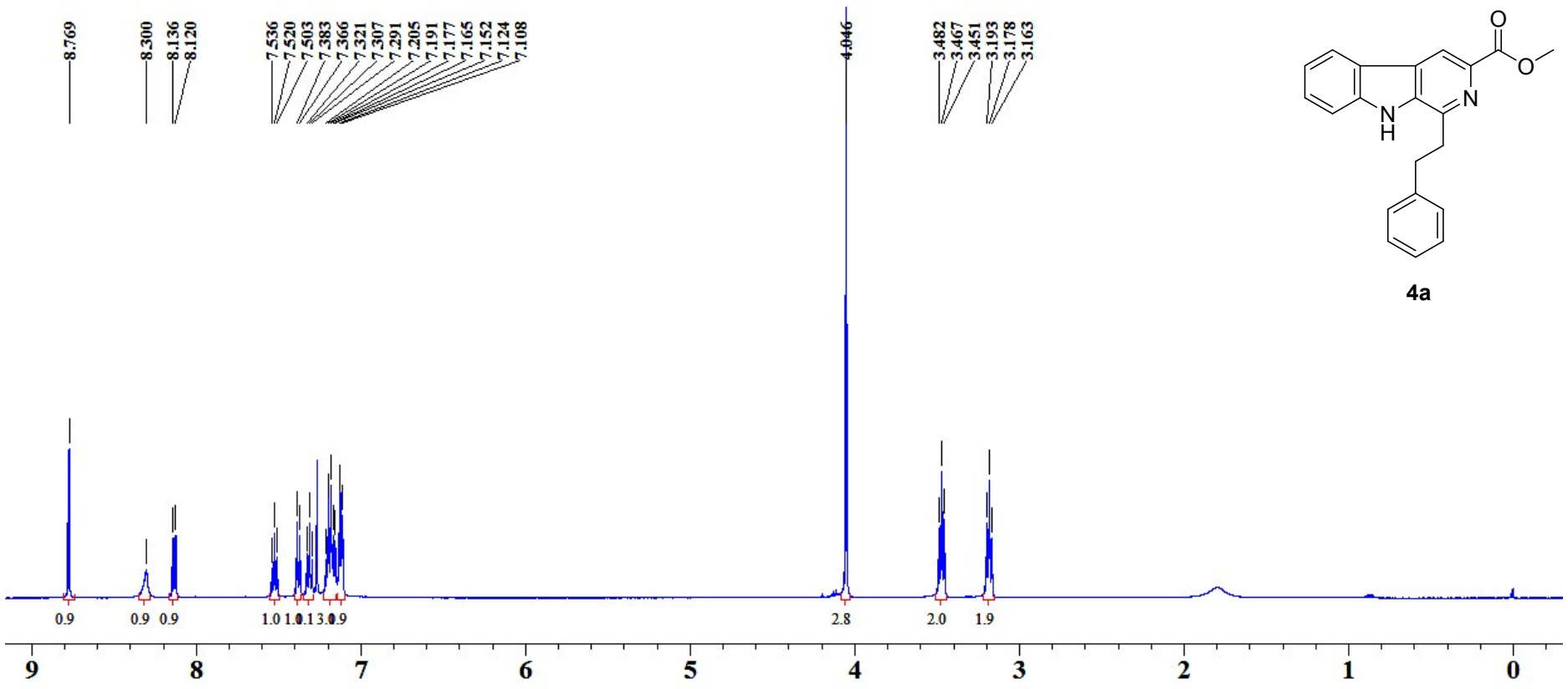




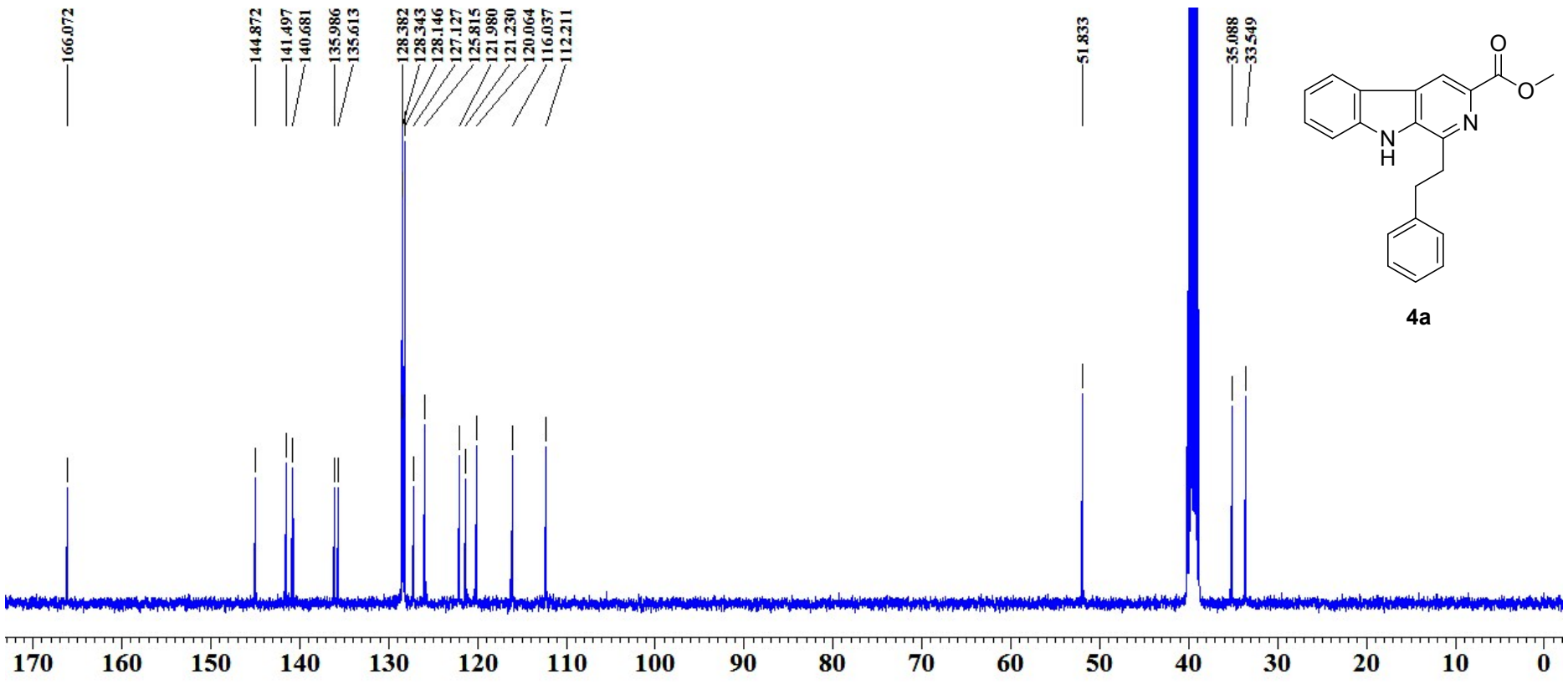
eudistomin U (10)

Methyl 1-phenethyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4a)

^{1}H NMR (300 MHz, $CDCl_3$)

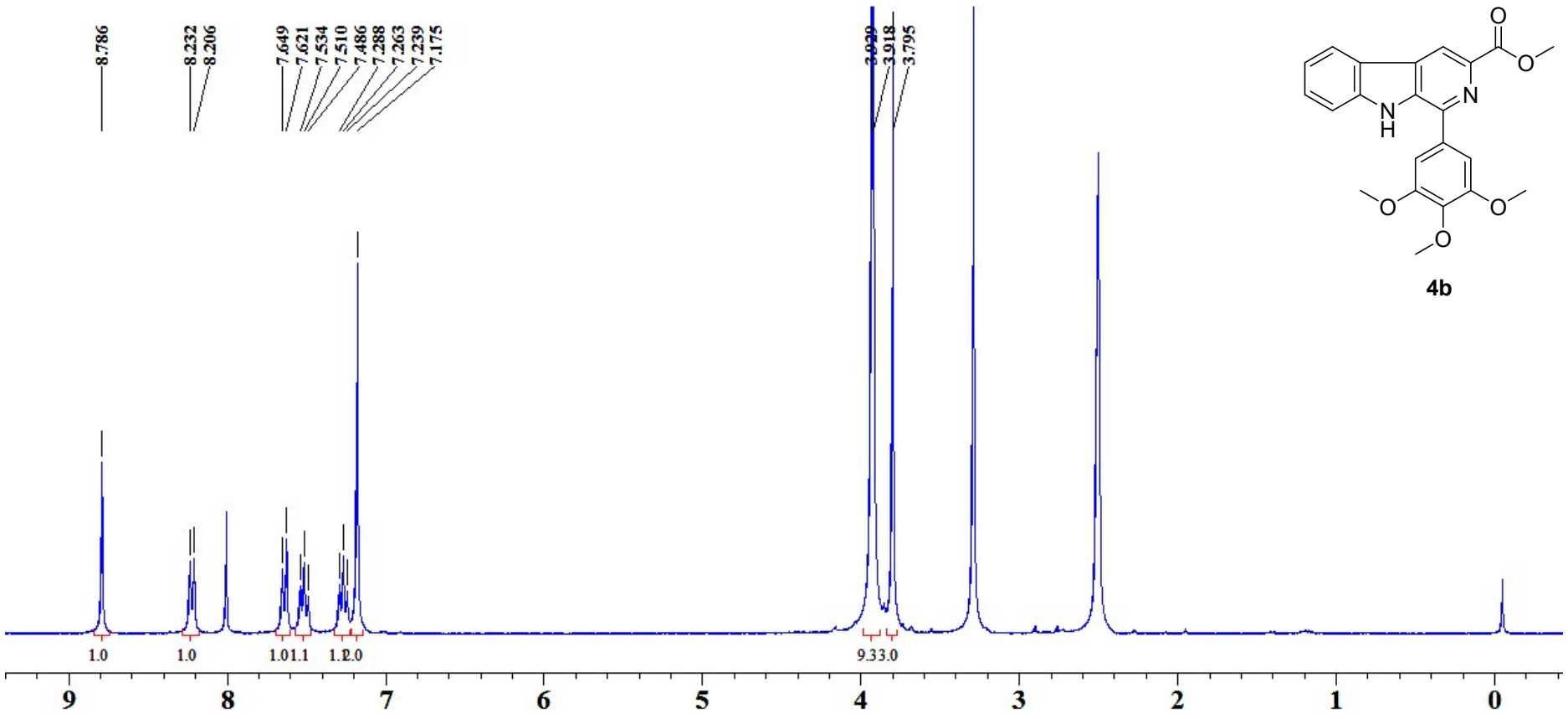


^{13}C NMR (100 MHz, DMSO−d_6)

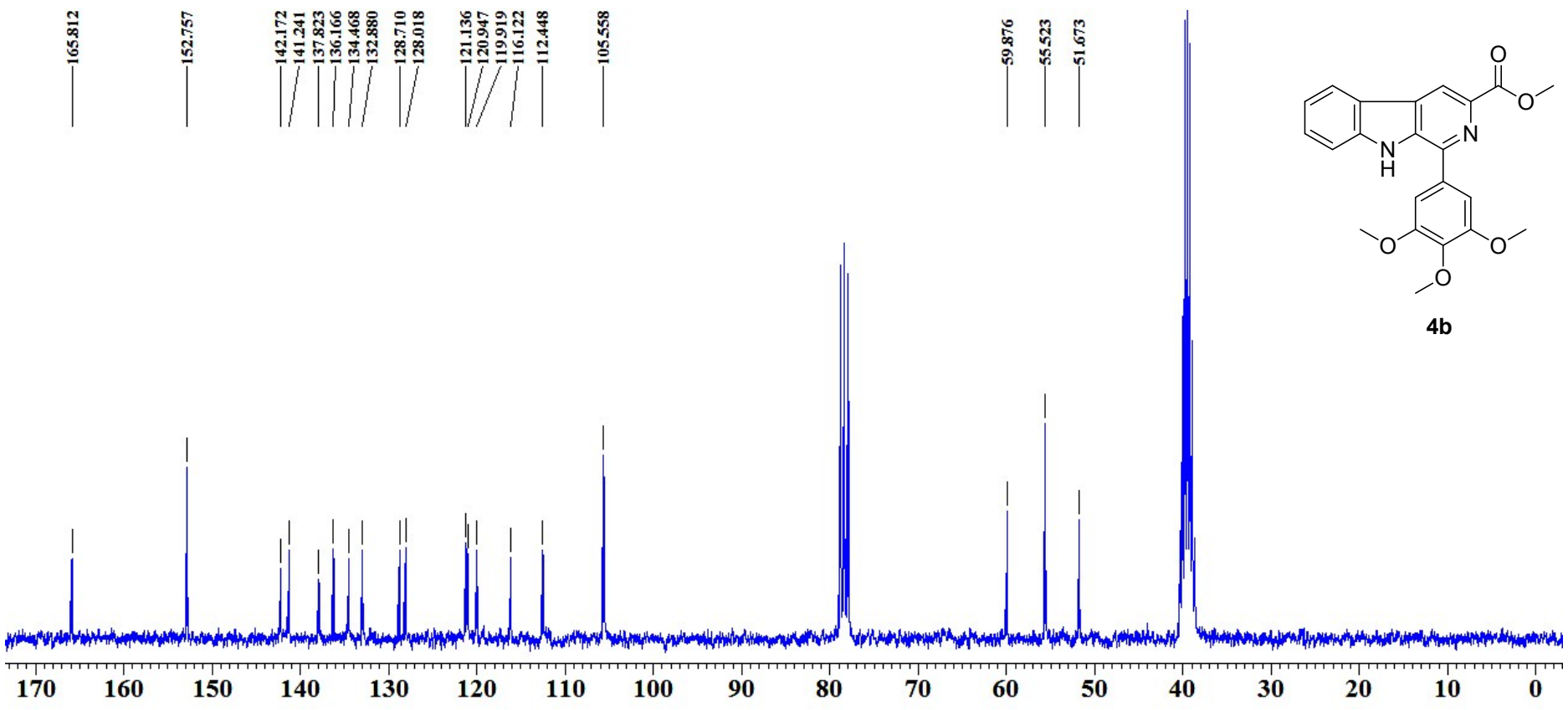


Methyl 1-(3,4,5-trimethoxyphenyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4b)

^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6)

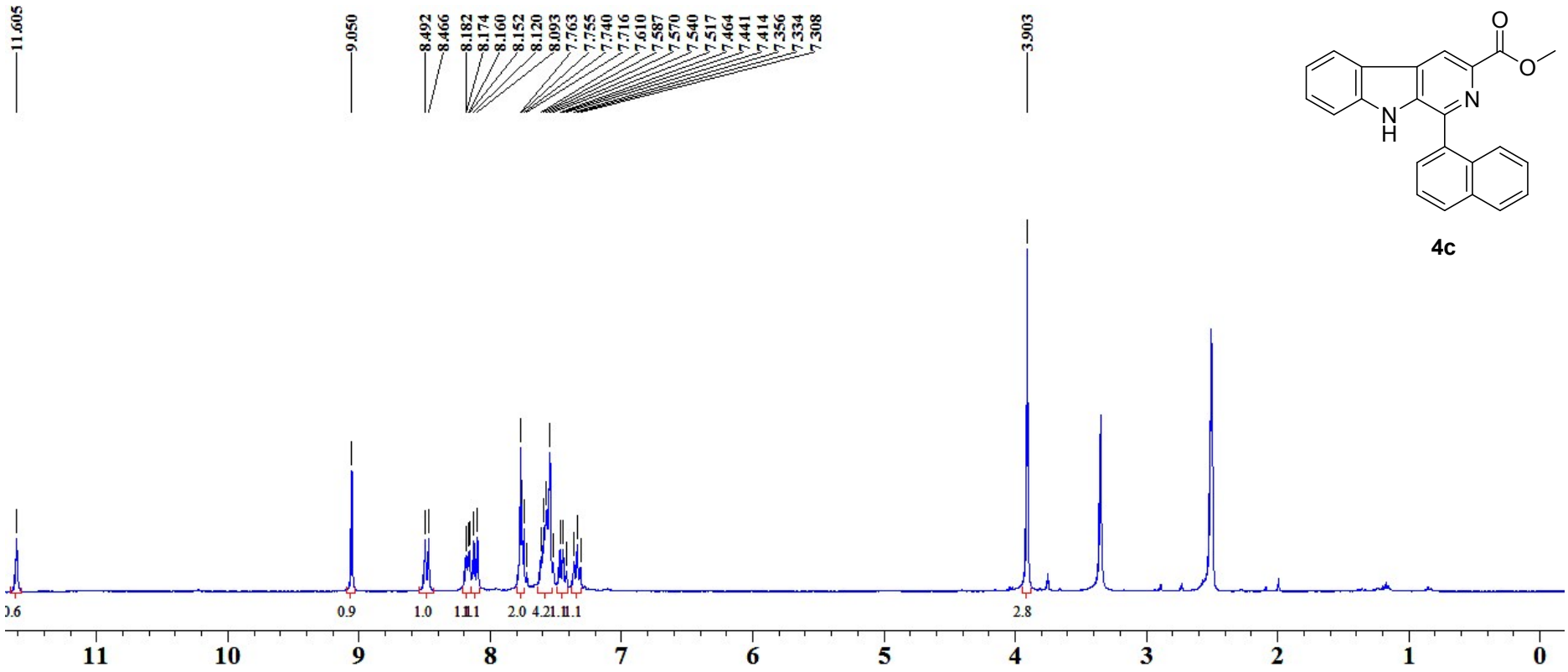


^{13}C NMR ($CDCl_3$, 75 MHz)

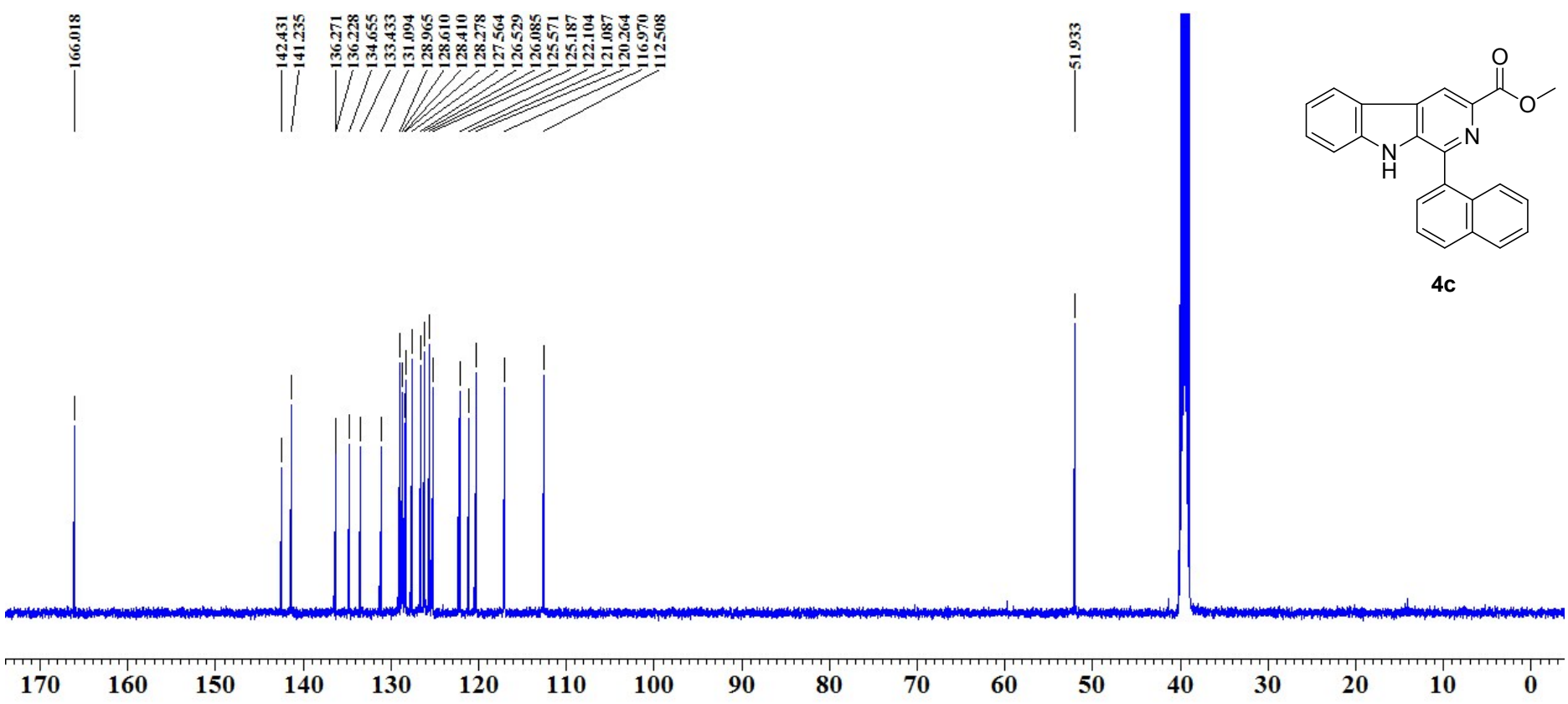


Methyl 1-(naphthalen-1-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4c)

^{1}H NMR (300 MHz, DMSO−d_6)

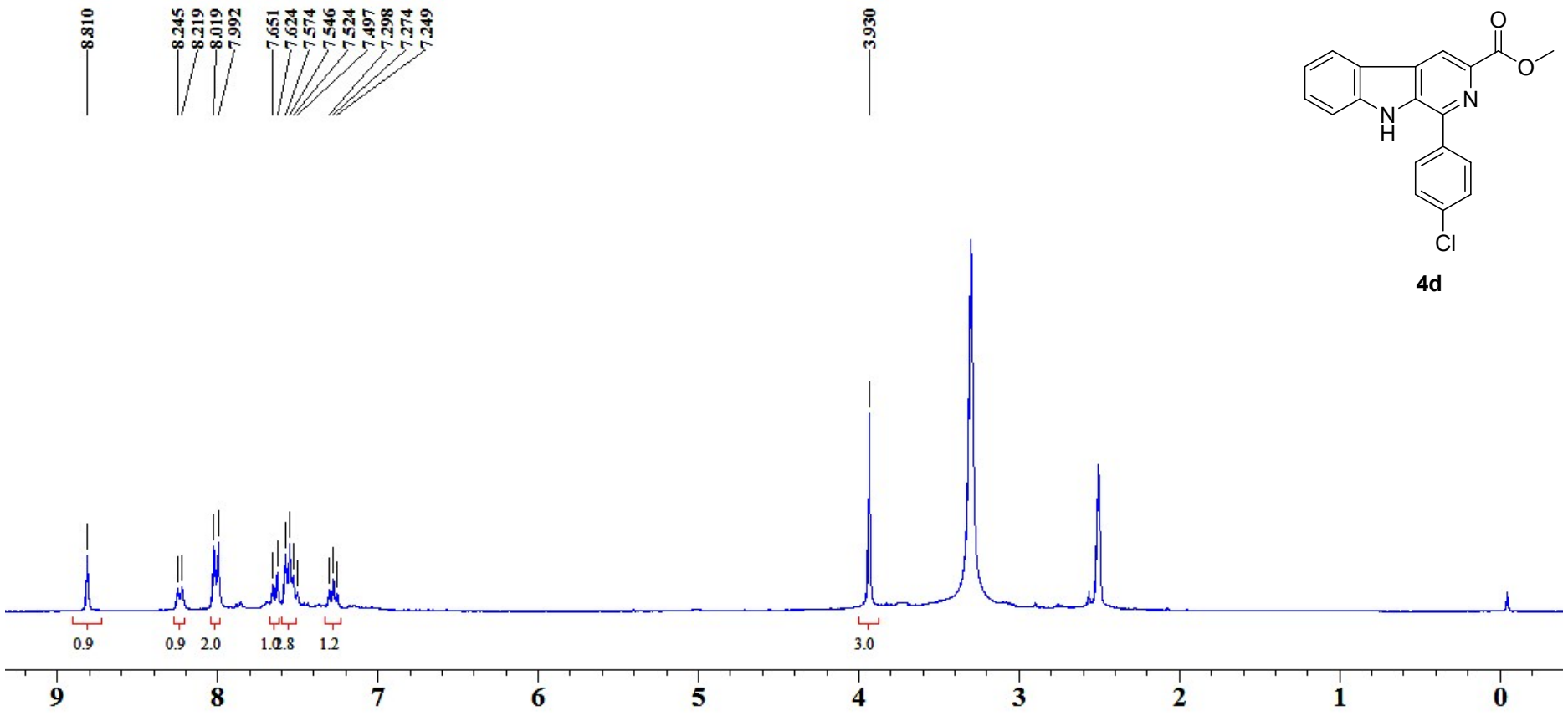


^{13}C NMR (125 MHz, DMSO−d_6)

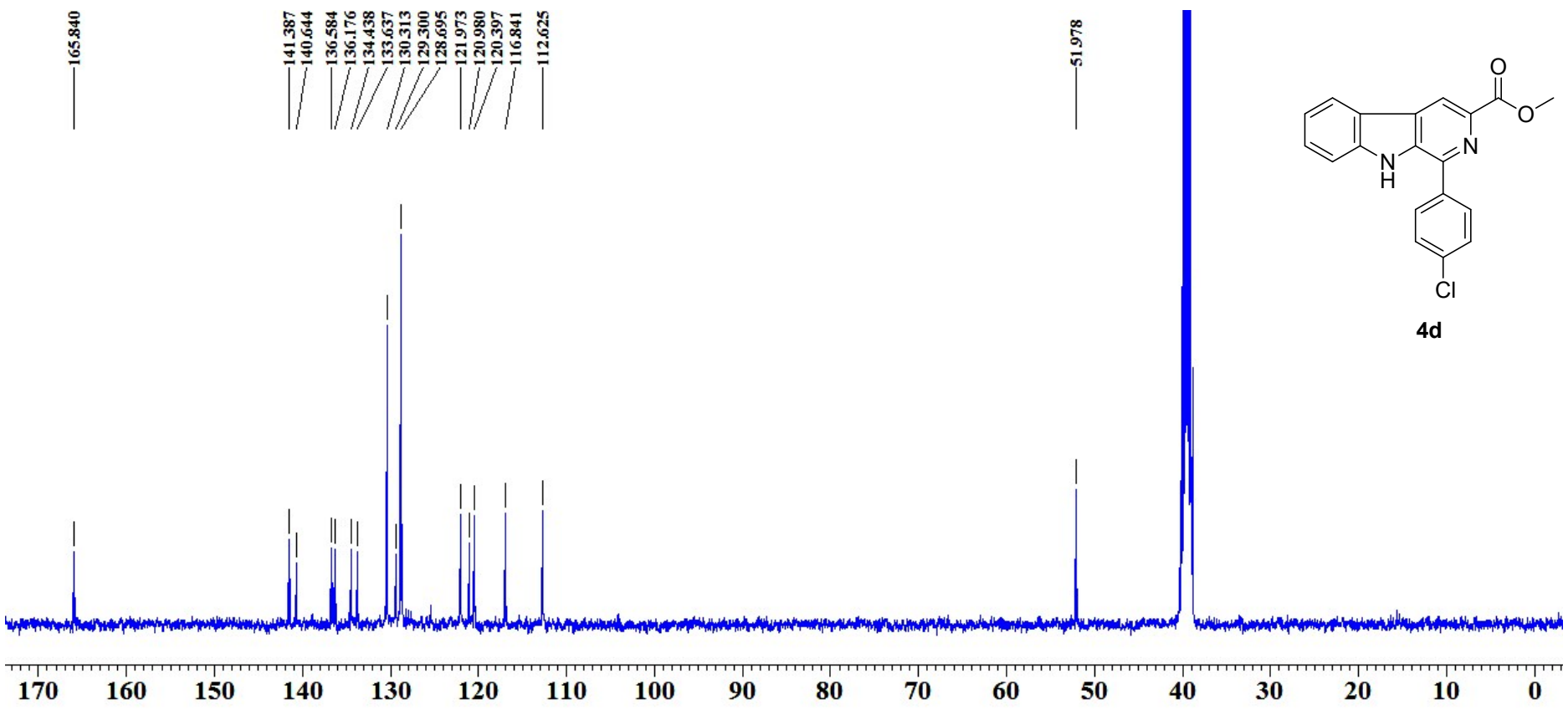


Methyl 1-(4-chlorophenyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4d)

^{1}H NMR (300 MHz, $CDCl_3$ + DMSO−d_6)

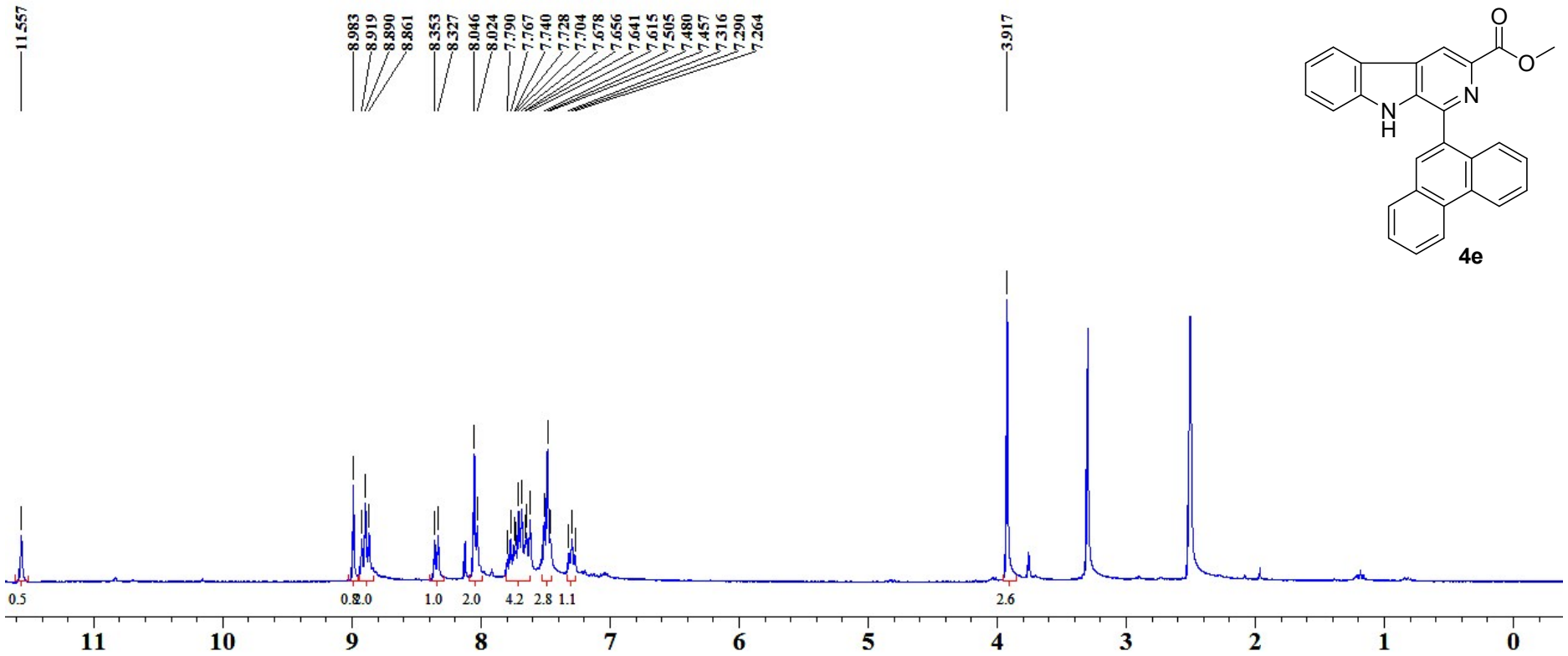


^{13}C NMR (100 MHz, DMSO−d_6)

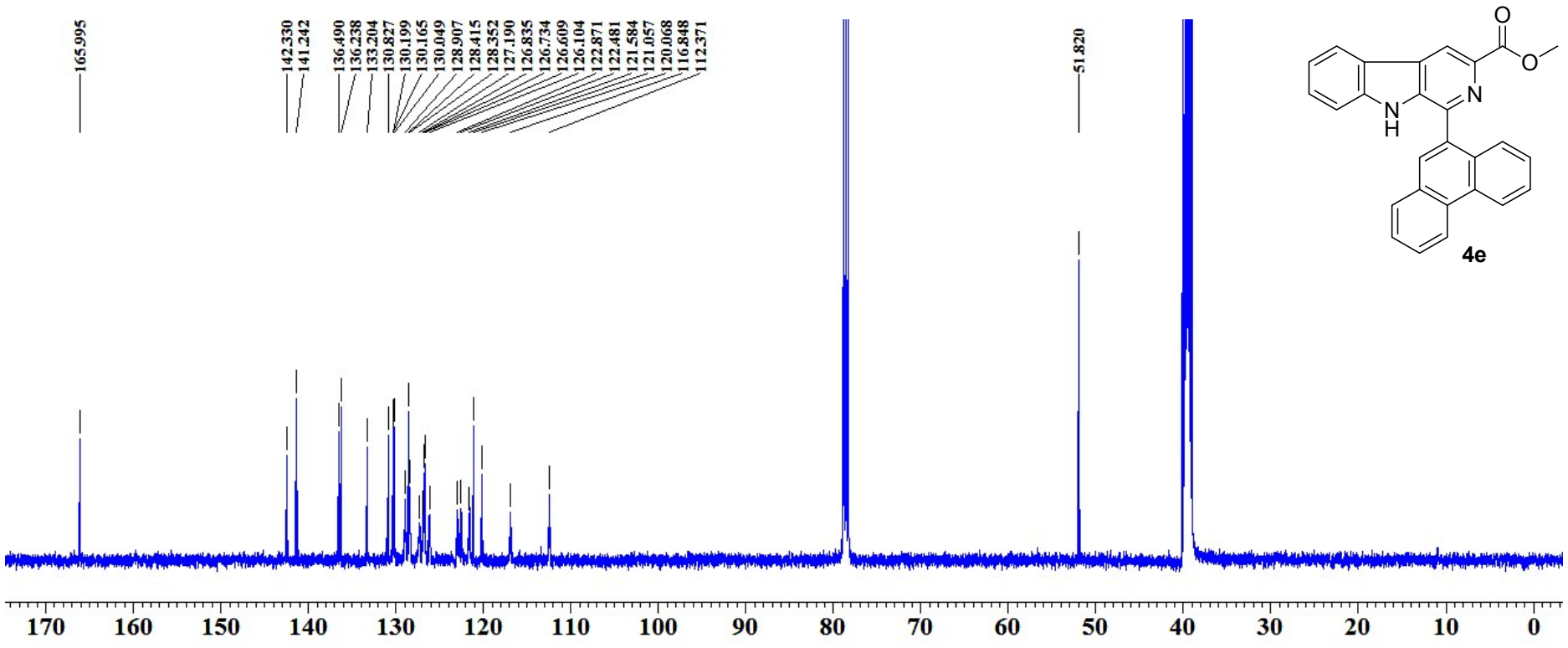


Methyl 1-(phenanthren-9-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4e)

^{1}H NMR (300 MHz, DMSO−d_6 + $CDCl_3$)

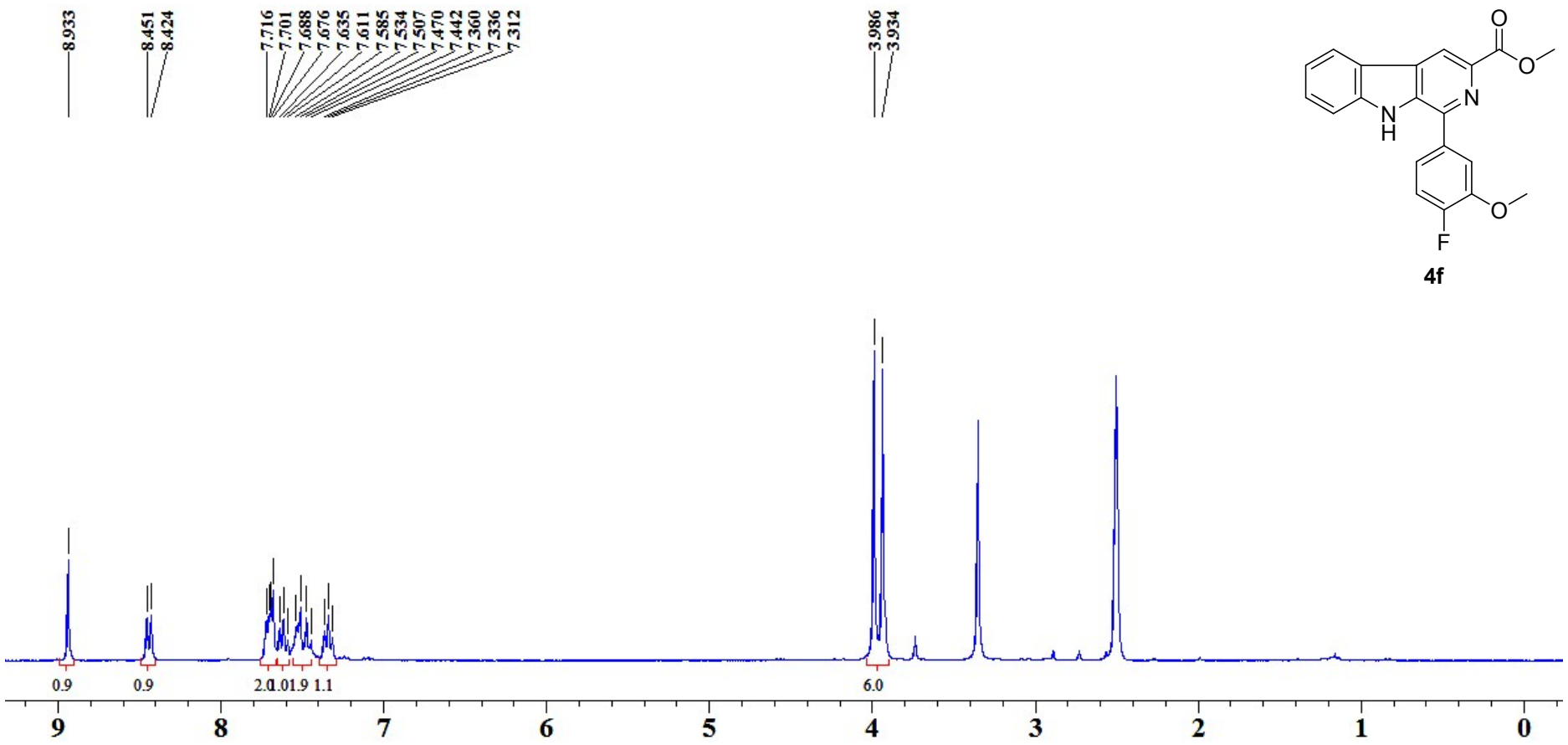


^{13}C NMR (125 MHz, DMSO−d_6 + $CDCl_3$)



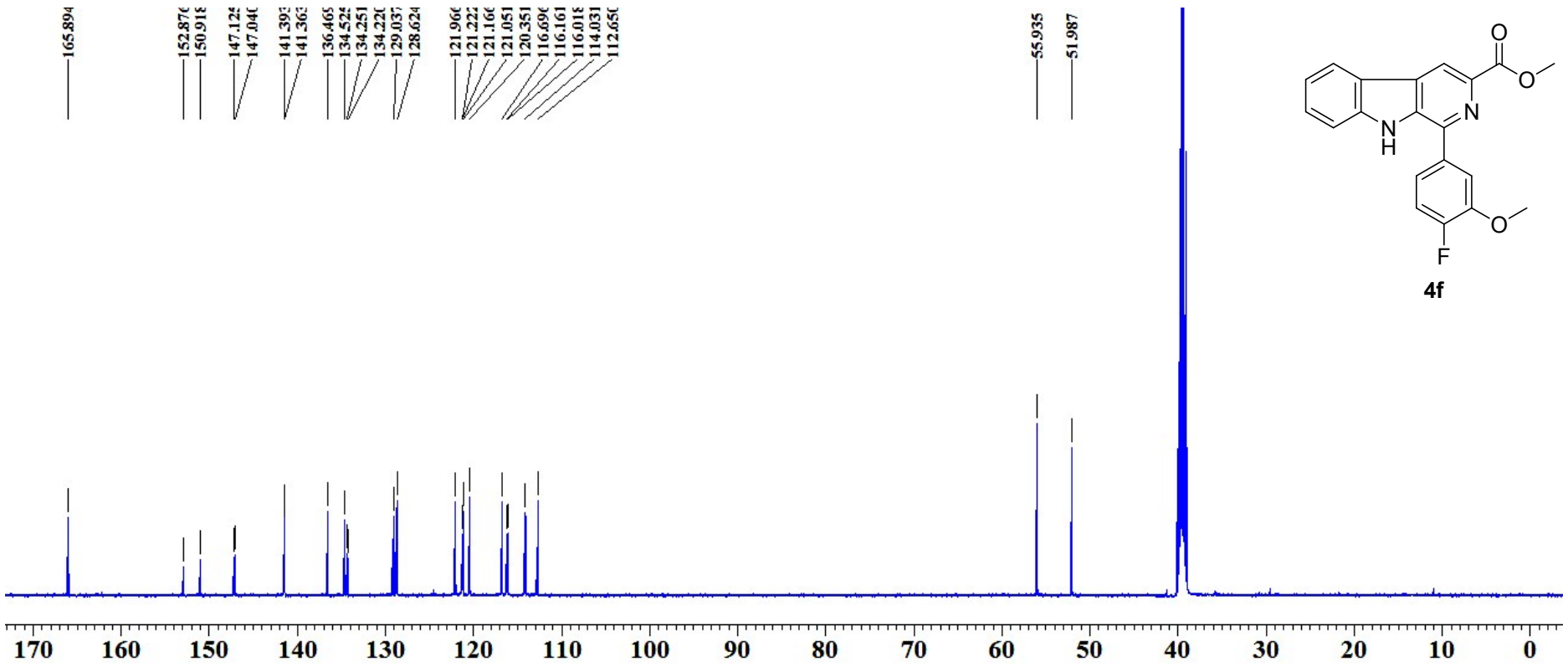
Methyl 1-(4-fluoro-3-methoxyphenyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4f)

^{1}H NMR (300 MHz, DMSO−d_6)



4f

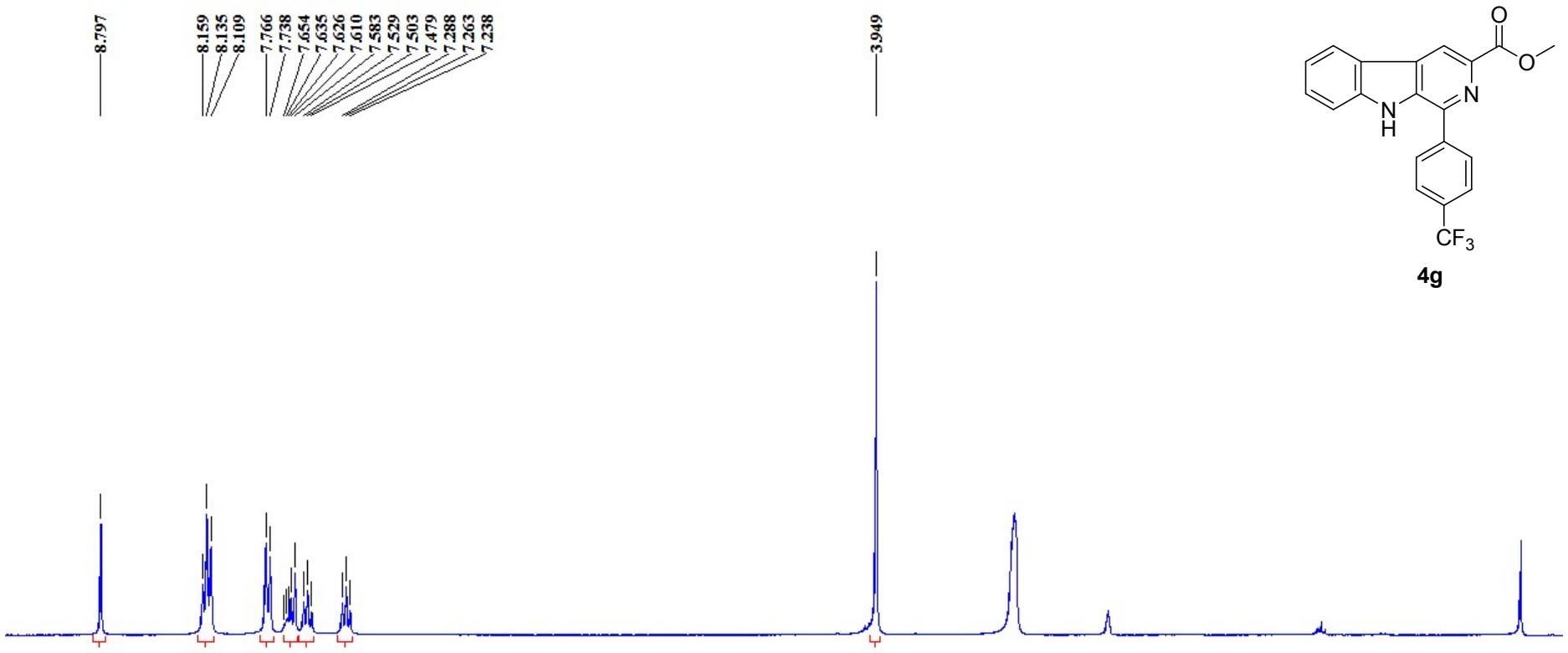
^{13}C NMR (725 MHz, DMSO−d_6)



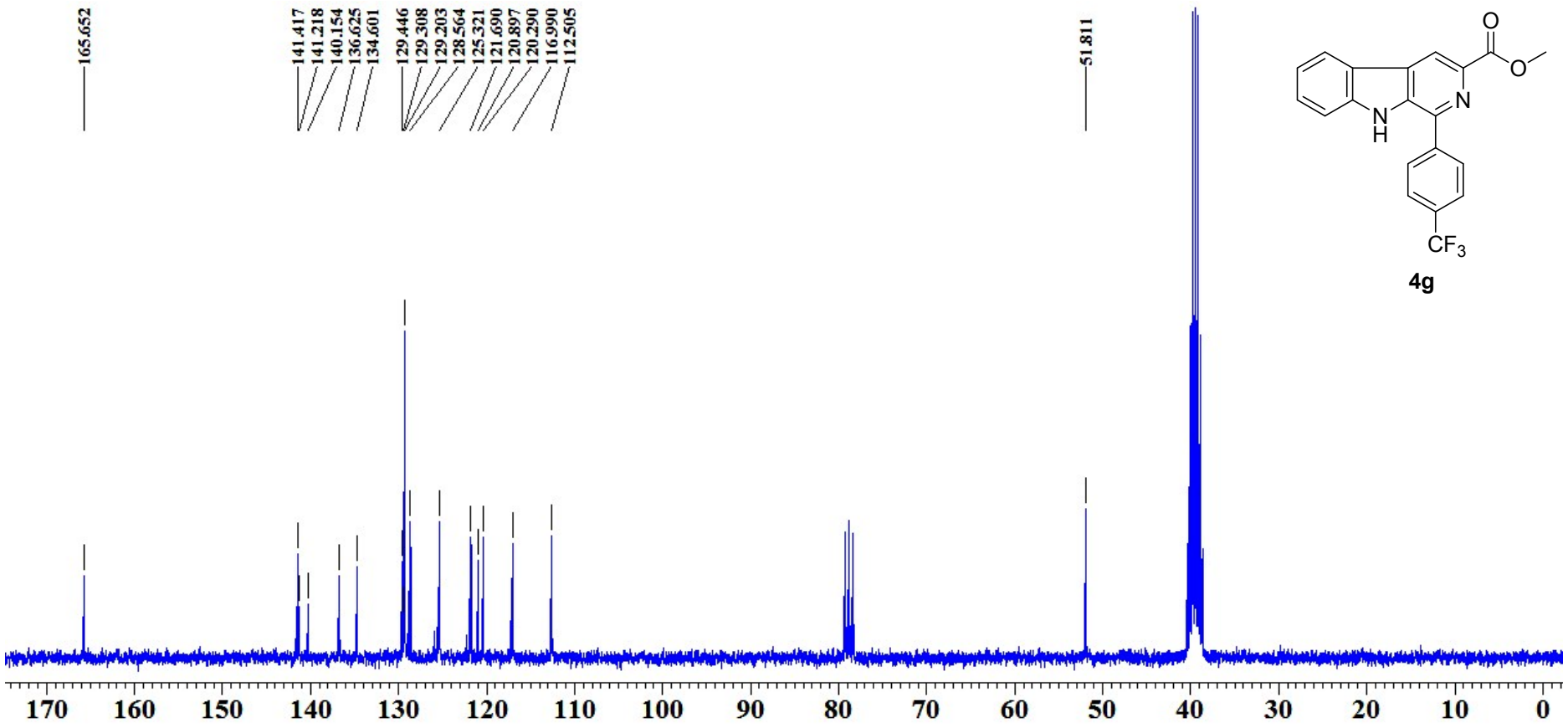
4f

Methyl 1-(4-(trifluoromethyl)phenyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4g)

^{1}H NMR (300 MHz, DMSO−d_6)

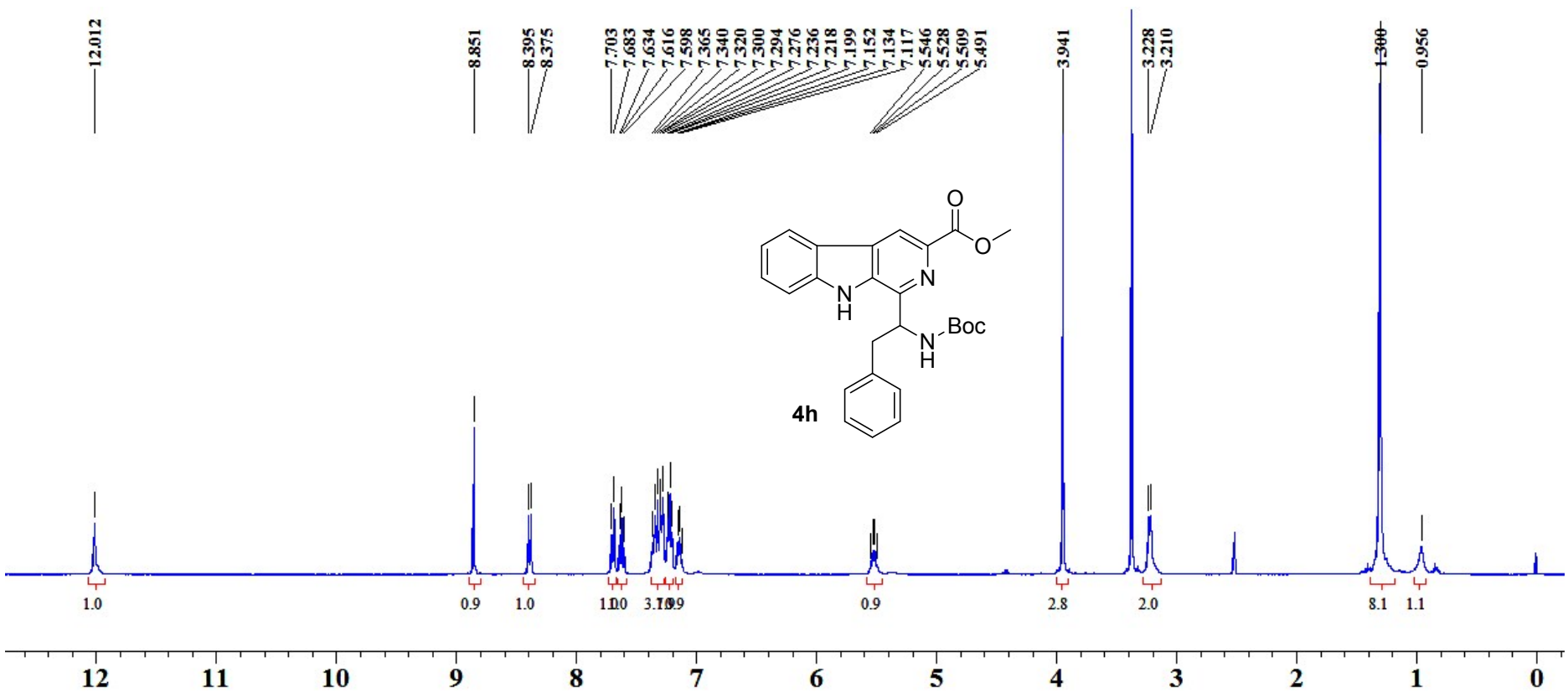


^{13}C NMR (75 MHz, DMSO−d_6)

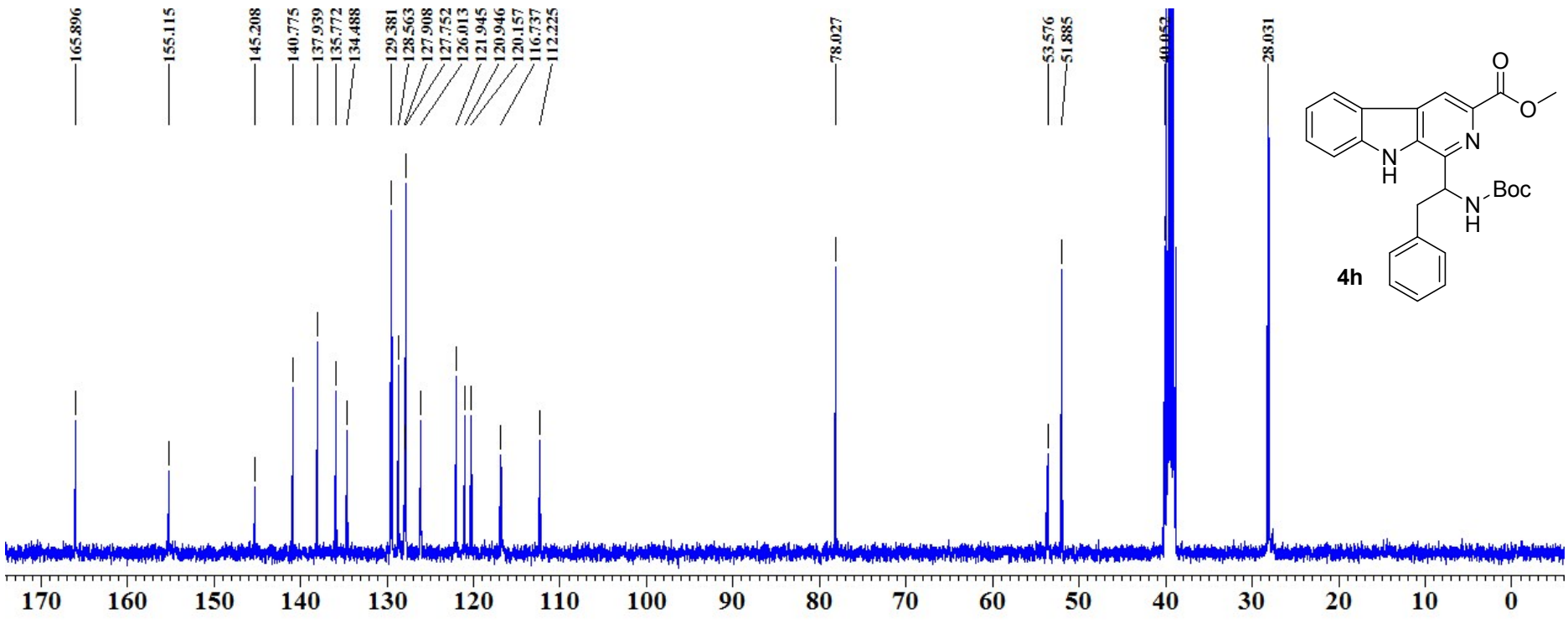


Methyl 1-(1-((*tert*-butoxycarbonyl)amino)-2-phenylethyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4h)

^{1}H NMR (400 MHz, DMSO−d_6)

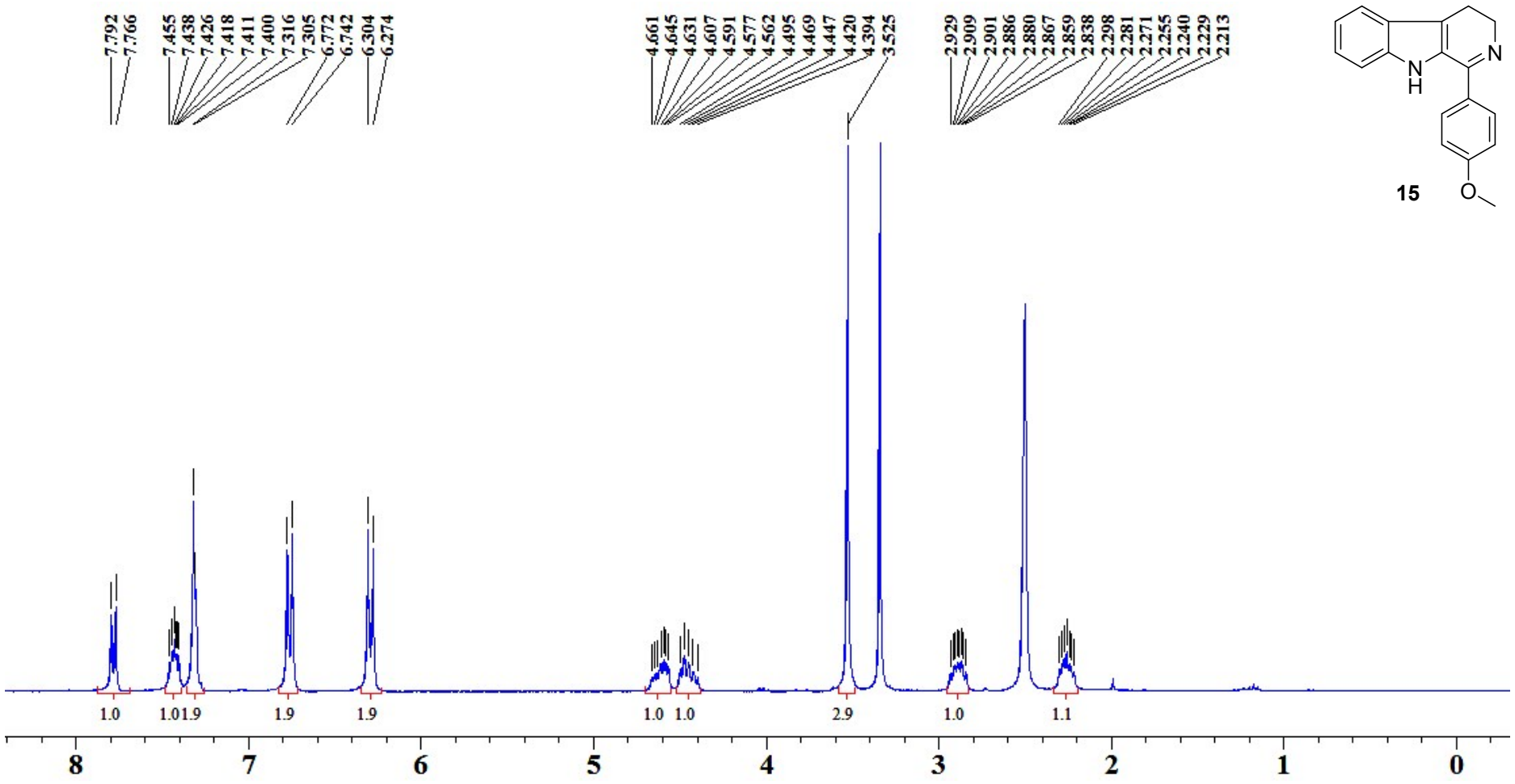


^{13}C NMR (100 MHz, DMSO−d_6)

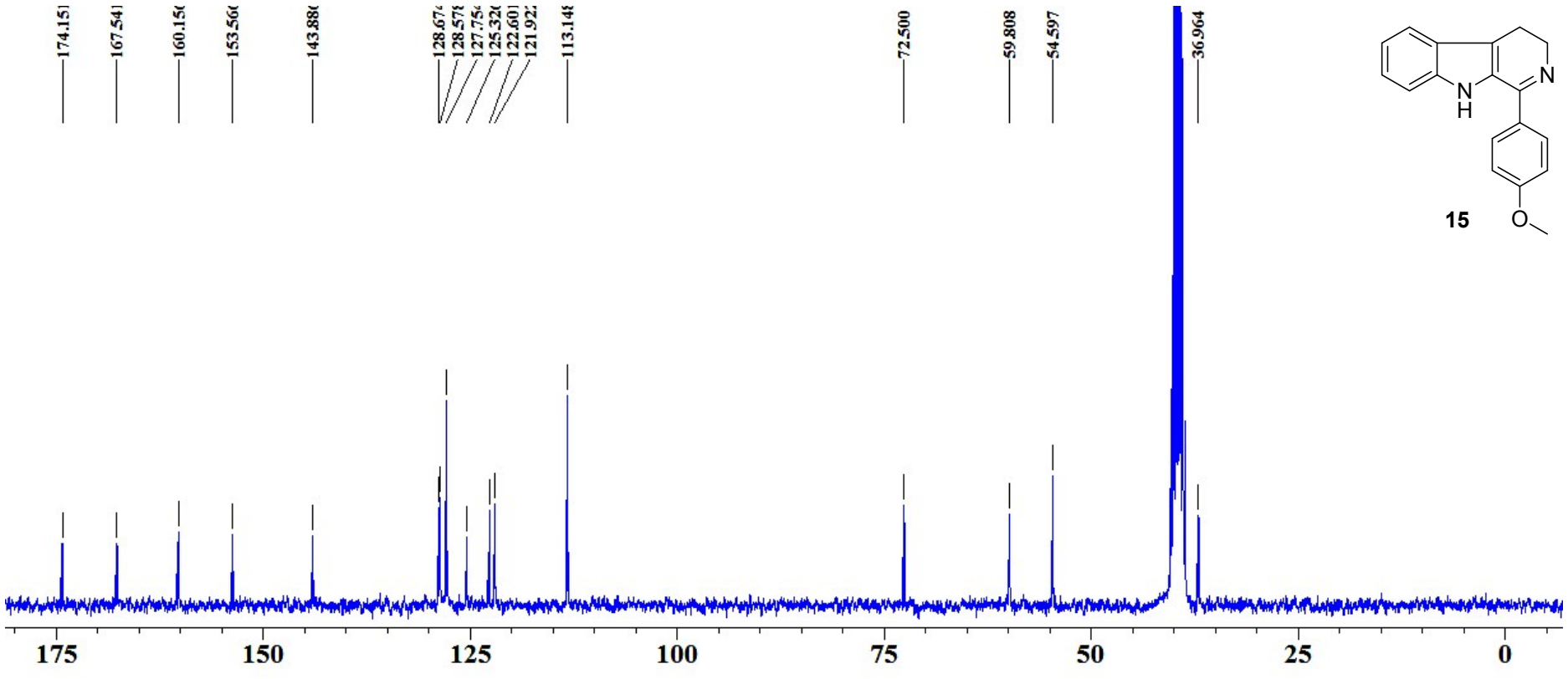


1-(4-Methoxyphenyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (15)

^{1}H NMR (300 MHz, DMSO−d_6)

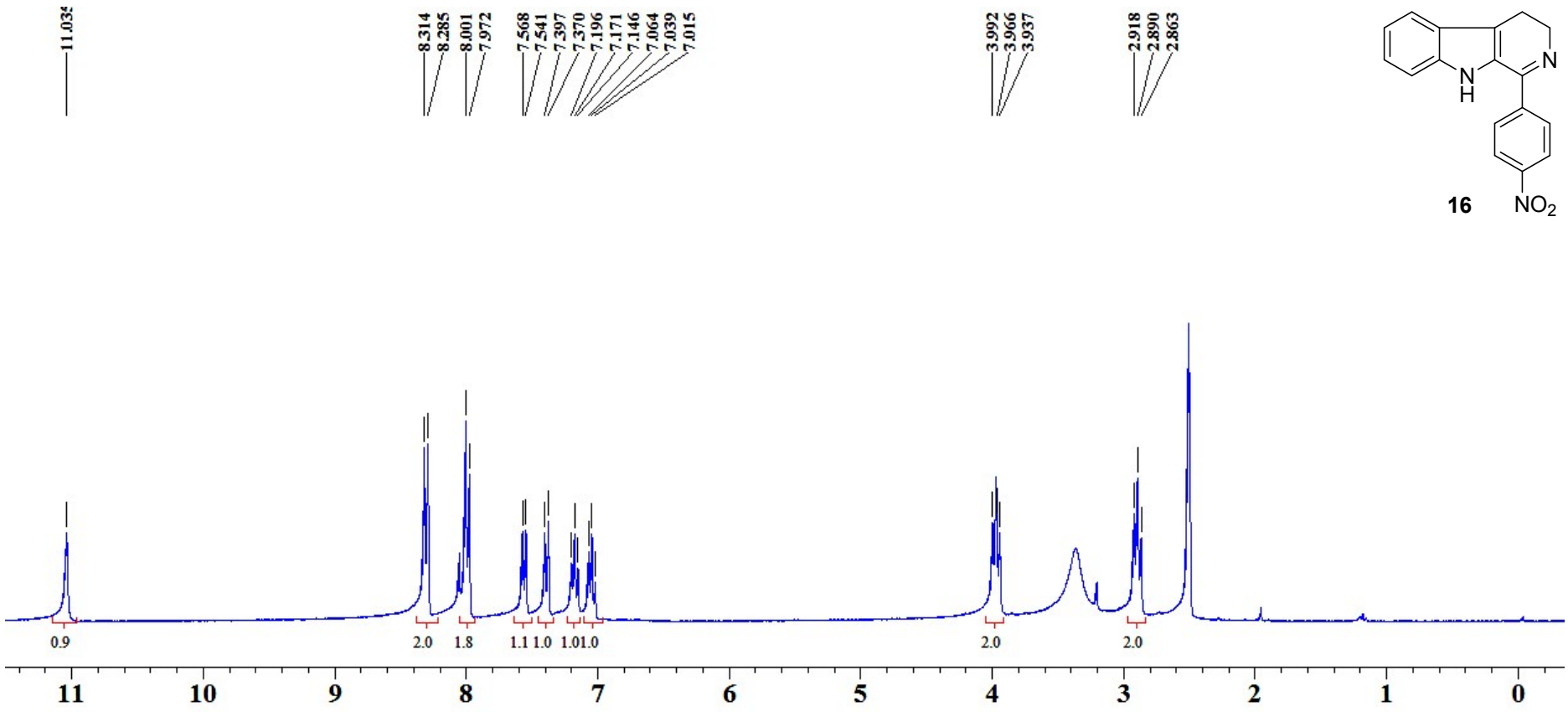


^{13}C NMR (75 MHz, DMSO−d_6)



1-(4-Nitrophenyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (16)

^{1}H NMR (300 MHz, DMSO−d_6 + $CDCl_3$)



^{13}C NMR (75 MHz, DMSO−d_6 + $CDCl_3$)