Electronic Supplementary Material (ESI) for Chemical Communications.

Access to 1-Indolyltetrahydro-β-carbolines via Metal-Free Cross-Dehydrogenative Coupling: Total Synthesis of Eudistomin U, Isoeudistomin U and 19-Bromoisoeudistomin U

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Electronic Supplementary Information

Contents

General Experimental

The reactions were monitored by thin layer chromatography using ethyl acetate/hexane system. All reaction solvents used were of GR grade and were distilled before using. All the other commercial reagents were used as received. Evaporation of solvents were performed using a rotary evaporator connected to a membrane pump at various temperatures. All new compounds were characterized by TLC, melting point (m.p.), ^{1}H NMR and ^{13}C NMR, IR, and HRMS (ESI). Analytical TLC was conducted using Merck aluminium sheets covered with silica gel. The plates were either visualized under UV-light and/or stained by dipping in Seebach's magic TLC stain. All the obtained products were purified by column chromatography using silica gel (100–200 mesh). Melting points were measured using a capillary melting point apparatus. ^{1}H and ^{13}C NMR spectra were recorded at Bruker 400 and 100 MHz, respectively, or at 500 and 125 MHz, respectively. Chemical shifts are calculated in ppm and the coupling constants (*J*) in Hz. DMSO-d_6, and $CDCl_3$ were used as the solvents and signal positions were measured relative to the signal for DMSO (δ 2.50 ppm for ^{1}H NMR and δ 39.52 ppm for ^{13}C NMR), and $CDCl_3$ (δ 7.26 ppm for ^{1}H NMR and δ 77.16 ppm for ^{13}C NMR). Data are presented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, dd = doublet doublet, t = triplet, q = quartet, m = multiplet). IR spectra were recorded on FT/IR-5300 instrument and are reported in frequency of absorption (cm^{-1}). TOF and quadrupole mass analyser types are used for the HRMS measurements. Single crystal X-ray diffraction data were collected on a Rigaku Oxford XtaLAB Pro-Pilatus3 R 200K-A detector system equipped with a CuK_α (λ = 1.54184 Å) MicroMax-003 micro focus sealed tube operated at 50 kV and 0.6 mA or a Bruker D8 Quest-Photon II detector system equipped with a MoKα (λ = 0.71073 Å) micro focus sealed tube operated at 50 kV and 1 mA. Data was collected at 293 K, and the reduction performed using CrysAlisPro or Bruker SAINT Software; the structure was solved and refined using the Bruker SHELXL-2017/1 software.

Synthesis of starting materials:

Starting materials **1a**, **1b**, **1c**, **2p**, **2q** were synthesized by using literature procedures.[1-4]

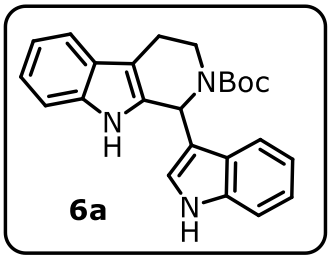
Synthesis of 1-(1*H*-indol-3-yl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylates (6a-s)

General procedure:

Boc protected tetrahydro-β-carboline **1a-c** (0.74 mmol, 1.0 equiv) was dissolved in 12 mL of dry dichloromethane in a RB flask, purged with nitrogen, closed with a glass stopper and then cooled using ice and salt mixture. Trityl tetrafluoroborate (0.88 mmol, 1.2 equiv) was added in one stretch, after 2.5 minutes of stirring at -20 ^{o}C, indoles **2a-q** (0.81 mmol, 1.1 equiv) was added in one stretch. After 30 seconds, the reaction mixture was quenched with water, extracted with EtOAc, the organic layer was washed with water, dried with anhydrous sodium sulfate and the product formation was checked by TLC. Then the organic layer was concentrated under vacuum to afford the crude compound (**6a-s**). The crude compound thus obtained was further purified using column chromatography on silica gel using EtOAc in hexanes.

Note: It is difficult to remove residual solvents (EtOAc, hexanes, DCM and $CHCl_3$) from these compounds. After drying under vacuum oven for several hours also we could observe little solvent peaks in the NMR spectra of the compounds. Rotamers are formed in most of the cases. These rotamers can be observed only at the aliphatic regions and Boc group using NMR spectroscopy and these carbons observed as broad peaks and as doublets, Peak intensities were not improved even after taking 30-45 mg (maximum solubility) of compound and also after running approximately 10000 scans in the ^{13}C NMR.

Tert-butyl 1-(1*H*-indol-3-yl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate (6a)

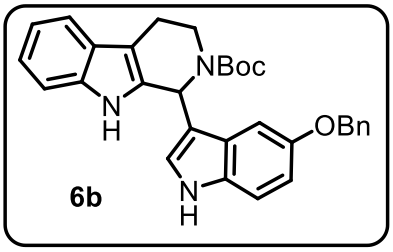


6a

Colorless solid; Yield: (178 mg, 88 %), mp 142-144 ^{o}C; R_f = 0.43, EtOAc/hexanes (2:8), Column chromatography: 0.8:9.2 (EtOAc/Hexanes), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (1H, br s), 7.77 (2H, s), 7.56 (1H, d, *J* = 7.5 Hz), 7.35 (1H, d, *J* = 8.1 Hz),

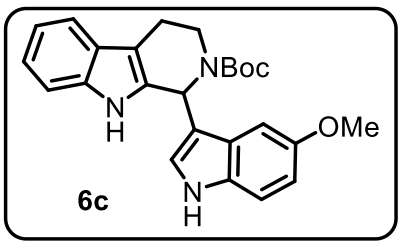
7.27 (1H, d, *J* = 7.7 Hz), 7.22-7.08 (4H, m), 6.84 (1H, s), 6.78 (1H, br s), 4.18 (1H, s), 3.22-3.15 (1H, m), 2.93 (1H, t, *J* = 10.3 Hz), 2.79-2.74 (1H, dd, *J* = 15.2, 3.0 Hz), 1.53 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 154.0, 136.4, 136.0, 133.5, 126.4, 126.2, 125.1, 121.4, 121.0, 118.9, 118.4, 117.4, 114.7, 111.7, 111.2, 107.8, 79.0, 47.0 (2C), 37.9, 28.2, 21. IR (neat, cm^{-1}) 3413, 3286, 2978, 2926, 2844, 1653, 1453, 1419, 1363, 1343, 1322, 1291, 1251, 1250. HRMS (ESI-TOF) Calcd for $C_{24}H_{25}N_3O_2$ [M+H]$^+$ 388.2020, Found: 388.2018.

Tert-butyl 1-(5-(benzyloxy)-1*H*-indol-3-yl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate (6b)



Colorless solid; Yield: (318 mg, 88 %), mp 128-130 ^{o}C; R_f = 0.43, EtOAc/hexanes (2:8), Column chromatography: 0.8:9.2 (EtOAc/Hexanes), ^{1}H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 7.94 (1H, br s,), 7.88 (1H, br s), 7.56 (1H, d, *J* = 7.4 Hz), 7.37-7.28 (7H, m), 7.21 (1H, d, *J* = 8.7 Hz), 7.19-7.13 (2H, m), 6.92 (1H, dd, *J* = 8.9, 2.2 Hz), 6.77 (1H, s), 6.60 (1H, br s), 4.89 (2H, s), 4.1 (1H, s), 3.10 (1H, t, *J* = 10.4), 2.93 (1H, s), 2.72 (1H, dd, *J* = 15.4, 3.3 Hz,), 1.53 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$ + DMSO-d_6) δ 154.3, 152.6, 137.3, 135.9, 133.0, 131.4, 128.0 (2C), 127.2, 126.5, 126.3, 125.4, 120.9, 118.4, 117.5, 115.1, 112.7, 111.8, 110.9, 108.5, 102.1, 79.0, 69.8, 47.1, 37.9, 28.2, 21.4. IR (neat, cm^{-1}) 3398, 3311, 2922, 2923, 2851, 2361, 2331, 1659, 1622, 1581, 1478, 1451, 1414, 1364, 1317, 1285, 1250, 1228. HRMS (ESI-TOF) Calcd for $C_{31}H_{31}N_3O_3$ [M+Na]$^+$ 516.2258, Found: 516.2257.

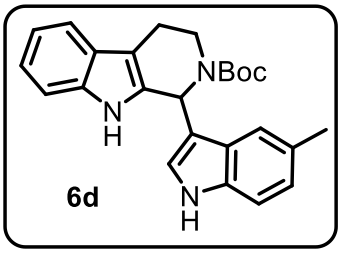
Tert-butyl 1-(5-methoxy-1*H*-indol-3-yl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate (6c)



Colorless solid; Yield: (206.8 mg, 90 %), mp 168-170 ^{o}C (melts with decomposition); R_f = 0.37, EtOAc/hexanes (2:8), Column chromatography: 0.8:9.2 (EtOAc /Hexanes), ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.98 (1H, br s), 10.84 (1H, br s), 7.47 (1H, d, *J* = 7.6 Hz), 7.27 (2H, d, *J* = 8.4 Hz), 7.20-6.53 (6H, m), 4.15-4.01 (1H, m), 3.66 (3H, s), 3.20-3.04 (1H, m), 2.82-2.76 (2H, m), 1.47 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 154.1, 153.3, 136.0, 133.4, 131.5, 126.6, 126.4, 125.5,121.0, 118.5, 117.8, 114.6, 112.3, 111.8, 111.2, 107.9, 100.7, 79.0, 54.9, 47.1, 37.8, 28.1, 21.4. DEPT-135 NMR (125 MHz, DMSO-d_6) δ 125.2, 120.7, 118.2, 117.5, 112.0, 111.5, 110.9, 100.5, 55.8, 47.9, 36.7, 27.9, 21.3. IR (neat, cm^{-1}) 3416, 3304, 2928,

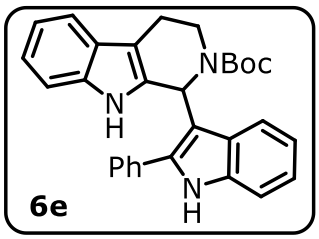
2323, 2161, 1656, 1623, 1588, 1484, 1455, 1421, 1364, 1315. HRMS (ESI-TOF) Calcd for $C_{27}H_{27}N_3O_3$ $[M+Na]^+$ 440.1945, Found: 440.1941.

***Tert*-butyl 1-(5-methyl-1*H*-indol-3-yl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate (6d)**



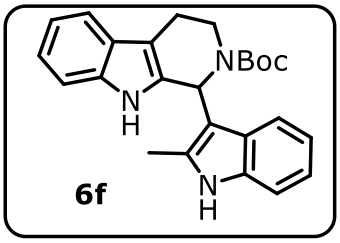
Pale pink solid; Yield: (184.0 mg, 84 %), mp 176-178 ^oC (melt with decomposition), R_f = 0.46, EtOAc/hexanes (2:8), Column chromatography: 0.8:9.2 (EtOAc/Hexanes), ^1H NMR (500 MHz, DMSO-d_6) δ 10.98 (1H, br s), 10.86 (1H, br s), 7.50 (1H, s), 7.46 (1H, d, *J* = 7.8 Hz), 7.27 (2H, d, *J* = 7.7 Hz), 7.09 (1H, t, *J* = 7.3 Hz), 7.00 (1H, t, *J* = 7.1 Hz), 6.99 (1H, d, *J* = 8.1 Hz), 6.70 (1H, s), 6.68 (1H, s), 4.13 (1H, br) 3.09-3.04 (1H, m), 2.78-2.71 (2H, m), 2.35 (3H, s), 1.49 (9H, s). ^{13}C {^1H} NMR (125 MHz, DMSO-d_6) δ 154.0, 136.0, 134.8, 133.5, 127.1, 126.4, 126.4, 125.5, 122.9, 120.7, 118.7, 118.4, 117.7, 114.2, 111.3, 111.1, 107.7, 79.0, 47.1, 37.7, 28.1, 21.3, 20.6. IR (neat, cm^{-1}) 3414, 3313, 2978, 2922, 2851, 2334, 1658, 1622, 1454, 1421, 1361, 1330, 1231. HRMS (ESI-TOF) Calcd for $C_{25}H_{27}N_3O_2$ $[M+Na]^+$ 424.1995, Found: 424.1993.

***Tert*-butyl 1-(2-phenyl-1*H*-indol-3-yl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate (6e)**



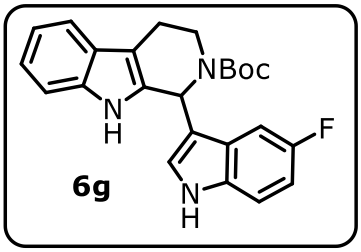
Pale pink solid; Yield: (232.0 mg, 91 %), mp 144-146 ^oC; R_f = 0.56, EtOAc/hexanes (2:8), Column chromatography: 0.8:9.2 (EtOAc/Hexanes). ^1H NMR (500 MHz, DMSO-d_6) δ 11.48 (1H, br s), 10.89 (1H, br s), 7.63 (2H, d, *J* = 7.4 Hz), 7.48-7.38 (4H, m), 7.33 (1H, d, *J* = 8.1 Hz), 7.21 (1H, d, *J* = 7.7 Hz), 7.05-6.98 (3H, m), 6.77 (1H, d, *J* = 7.9 Hz), 6.70 (1H, t, *J* = 7.5 Hz), 6.66 (1H, s), 4.18-4.14 (1H, m), 3.44-3.35 (1H, m), 2.89-2.84 (1H, m), 2.79-2.66 (1H, m), 1.24 (9H, s). ^{13}C {^1H} NMR (125 MHz, DMSO-d_6) δ 154.3, 137.7, 136.1, 135.8, 134.0, 132.8, 129.5, 128.3, 128.0, 127.9, 126.4, 121.2, 120.9, 119.3, 119.1, 118.5, 118.48, 117.9, 117.5, 111.3, 111.0, 110.1, 107.6, 79.1, 47.7, 28.1, 27.8, 20.8. IR (neat, cm^{-1}) 3393, 3288, 2972, 2925, 2844, 1622, 1450, 1411, 1364, 1300, 1229, 1158, 1098. HRMS (ESI-TOF) Calcd for $C_{30}H_{29}N_3O_2$ $[M+Na]^+$ 486.2152, Found: 486.2155.

***Tert*-butyl 1-(2-methyl-1*H*-indol-3-yl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate (6f)**



Pale pink solid; Yield: (176.5 mg, 80 %), mp 138-140 ºC, R_f = 0.4, EtOAc/hexanes (2:8), Column chromatography: 0.8:9.2 (EtOAc/Hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.0 (1H, br s), 10.87 (1H, br s), 7.49 (1H, d, *J* = 7.6 Hz), 7.24-7.23 (2H, m), 7.05 (1H, dt, *J* = 7.03, 1.2 Hz), 7.00 (1H, dt, *J* = 7.7, 1.2 Hz), 6.95-6.92 (2H, m), 6.74 (1H, dt, *J* = 7.6, 0.8 Hz), 6.61 (1H, s), 4.12 (1H, d, *J* = 5.2 Hz), 3.23-3.16 (1H, m), 2.87-2.78 (2H, m), 2.18 (3H, s), 1.46 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 153.9, 136.0, 134.9, 134.6, 133.7, 128.0, 126.3, 120.9, 120.1, 118.7, 118.4, 117.9, 117.8, 111.1, 110.4, 109.4, 107.7, 79.1, 47.3, 34.1, 28.1, 21.1, 11.6. IR (neat, cm^{-1}) 3393, 3302, 2976, 2921, 2848, 2160, 1961, 1660, 1620, 1458, 1412, 1364, 1299, 1249, 1229. HRMS (ESI-TOF) Calcd for $C_{25}H_{27}N_3O_2$ $[M+Na]^+$ 424.1996, Found: 424.1995.

***Tert*-butyl 1-(5-fluoro-1*H*-indol-3-yl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate (6g)**

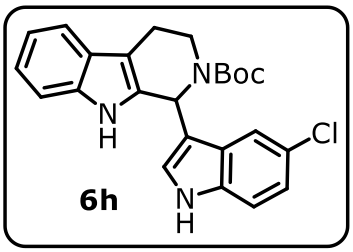


Pale pink solid; Yield: (164.6 mg, 74 %), mp 208-210 ºC, R_f = 0.67, EtOAc/hexanes (3:7), Column chromatography: 0.7:9.3 (EtOAc/Hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.13 (9H, br s), 10.94 (1H, br s), 7.47 (1H, d, *J* = 7.3 Hz), 7.39-7.26 (3H, m), 7.08 (1H, t, *J* = 7.5 Hz), 7.00 (1H, t, *J* = 7.0 Hz), 6.95 (1H, t, *J* = 8.6 Hz), 6.87 (1H, br s), 6.62 (1H, br s), 4.04 (1H, br s), 3.08-3.02 (1H, m), 2.76 (2H, s), 1.48 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 158.3, 156.4, 154.5, 136.4, 133.53, 133.47, 127.5, 126.8 (d, *J* = 8.4 Hz), 121.5, 118.9, 118.3, 115.4, 113.2, 111.6, 110 (d, *J* = 21.3 Hz), 108.4, 104.0, 79.6, 47.4, 38.3, 28.6, 21.8. IR (neat, cm^{-1}) 3409, 3289, 2977, 2928, 2850, 1653, 1583, 1481, 1454, 1422, 1392, 1366, 1313, 1286, 800. HRMS (ESI-TOF) Calcd for $C_{24}H_{24}FN_3O_2$ $[M+H]^+$ 406.1925, Found: 406.1922.

***Tert*-butyl 1-(5-chloro-1*H*-indol-3-yl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate (6h)**

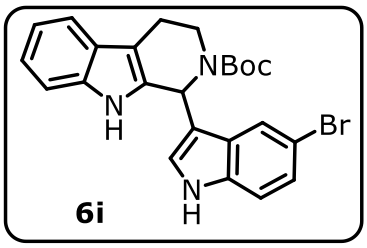
Pale pink solid; Yield: (308.0 mg, 68 %), mp 222-224 ºC; R_f = 0.72, EtOAc/hexanes (3:7), Column chromatography: 0.7:9.3 (EtOAc/Hexanes), ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.23 (1H, br s), 10.98 (1H, br s), 7.72 (1H, d, *J* = 1.6 Hz), 7.47 (1H, d, *J* = 8.0 Hz), 7.42 (1H, d, *J*

= 8.5 Hz), 7.29 (1H, d, *J* = 8.04 Hz), 7.12 (1H, dd, *J* = 8.5, 1.5 Hz), 7.08 (1H, dt, *J* = 7.4, 0.9 Hz), 7.02 (1H, dt, *J* = 7.6, 0.7 Hz), 6.86 (1H, br s), 6.65 (1H, br s), 4.15-4.04 (1H, m), 3.07-3.02 (1H, m), 2.81-2.72 (2H, m), 1.48 (9H, s), 1.33 (1H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-*d*$_6$) δ 154.0, 136.0, 134.9, 132.9, 127.1, 126.8, 126.3, 123.7, 121.3, 121.1, 118.5, 118.3, 117.8, 114.7, 113.3, 111.1, 108.0, 79.14, 46.9, 37.8, 28.1, 21.2. IR (neat, cm^{-1}) 3416, 3327, 3015, 2974, 2926, 2850, 1653, 1619, 1572, 1451, 1419, 1391, 1364, 1343, 1298, 1249, 1230, 842. HRMS (ESI-TOF) Calcd for $C_{24}H_{24}ClN_3O_2$ [M+H]$^+$ 422.1630, Found: 422.1618.



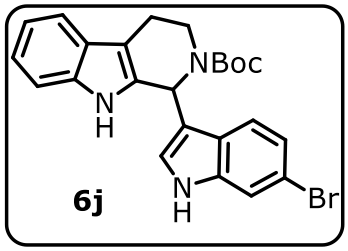
Tert-butyl 1-(5-bromo-1*H*-indol-3-yl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate (6i)

Pale pink solid; Yield: (55 mg, 64 %), mp 214-216^{o}C; R$_f$ = 0.40, EtOAc/hexanes (2:8), Column chromatography: 0.7:9.3 (EtOAc/Hexanes). ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 11.24 (1H, br s), 10.99 (1H, br s), 7.91 (1H, s), 7.41 (1H, d, *J* = 7.7 Hz), 7.37 (1H, d, *J* = 8.6 Hz), 7.28 (1H, d, *J* = 8.1 Hz), 7.23 (1H, d, *J* = 8.6 Hz), 7.08 (1H, t, *J* = 7.2 Hz), 7.01 (1H, t, *J* = 7.1 Hz), 6.83 (1H, br s), 6.63 (1H, br s), 4.06-4.03 (1H, m), 3.06-2.99 (1H, m), 2.81-2.71 (2H, m), 1.50 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-*d*$_6$+$CDCl_3$) δ 153.6, 135.3, 134.4, 132.1, 127.1, 125.6, 123.3, 121.4, 120.8, 120.2, 117.8, 116.9, 114.4, 112.3, 111.3, 110.4, 107.6, 78.6, 46.2, 37.1, 27.6, 20.8. IR (neat, cm^{-1}) 3418, 3332, 2972, 2926, 1654, 1449, 1418, 1364, 1342, 1298, 1249, 1230, 1162, 1103. HRMS (ESI-TOF) Calcd for $C_{24}H_{24}BrN_3O_2$ 465.1052 [M+Na]$^+$ 488.0944 Found: 488.0941.



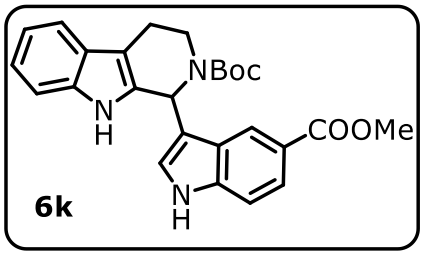
Tert-butyl 1-(6-bromo-1*H*-indol-3-yl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate (6j)

Colorless solid; Yield: (212.0 mg, 62.4 %), mp 128-130 ^{o}C, R$_f$ = 0.47, EtOAc/hexanes (2:8), Column chromatography: 0.7:9.3 (EtOAc/Hexanes). ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 11.17 (1H, br s), 10.95 (1H, br s), 7.58 (2H, d, *J* = 1.16 Hz), 7.47 (1H, d, *J* = 7.8 Hz), 7.27 (1H, d, *J* =7.96 Hz), 7.13 (1H, dd, *J* = 8.5, 1.8 Hz), 7.07 (1H, t, *J* = 7.1 Hz), 7.00 (1H, m), 6.84 (1H, s), 6.65 (1H, s), 4.04 (1H, s), 3.09-3.03 (1H, m), 2.78-2.75 (2H, m), 1.46 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-*d*$_6$) δ 154.0,



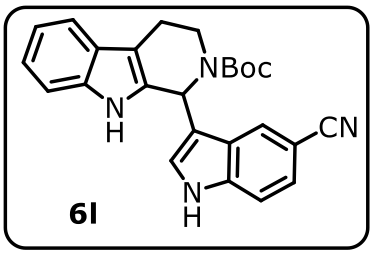
137.3, 136.0, 133.0, 126.2, 126.1, 125.1, 121.8, 121.1, 120.7, 118.4, 117.8, 115.0, 114.3, 114.2, 111.2, 107.9, 79.2, 46.8, 37.8, 28.1, 21.3. IR (neat, cm^{-1}) 3395, 3300, 2923, 2849, 2332, 2161, 1978, 1661, 1618, 1538, 1451, 1416, 1365. HRMS (ESI-TOF) Calcd for $C_{24}H_{24}BrN_3O_2$ $[M+Na]^+$ 488.0944, Found: 488.0940.

Tert-butyl 1-(5-(methoxycarbonyl)-1_H_-indol-3-yl)-1,3,4,9-tetrahydro-2_H_-pyrido[3,4-_b_]indole-2-carboxylate (6k)



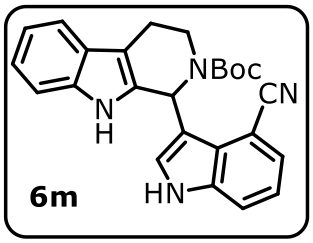
Colourless solid; Yield: (97 mg, 61 %), mp 210-212°C, R_f = 0.50, EtOAc/hexanes (3:7), Column chromatography: 1.5:8.5 (EtOAc/Hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.42 (1H, br s), 10.90 (1H, br s), 8.55 (1H, d, J = 5.7 Hz), 7.77 (1H, d, J = 7.7 Hz), 7.47 (2H, d, J = 7.6 Hz), 7.28 (1H, d, J = 6.8 Hz), 7.08 (1H, dt, J = 7.6, 1.0 Hz), 7.00 (1H, dt, J = 7.4, 0.9 Hz), 6.87 (1H, d, J = 2.11 Hz), 6.72-6.65 (1H, br), 4.11-4.00 (1H, m), 3.83 (3H, s), 3.06-3.00 (1H, m), 2.81-2.70 (2H, m), 1.59 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 167.3, 153.2, 139.1, 136.0, 133.0, 127.0, 126.4, 125.6, 122.5, 121.6, 120.5, 118.5, 117.9, 116.2, 111.8, 111.2, 108.0, 80.0, 51.6, 47.6, 36.5, 28.0, 21.3. IR (neat, cm^{-1}) 3396, 3311, 2919, 2917, 2849, 2162, 2037, 2014, 1975, 1681, 1618, 1436, 1413, 1363, 1318, 1273, 1246. HRMS (ESI-TOF) Calcd for $C_{26}H_{27}N_3O_4$ $[M+H]^+$ 446.2074, Found: 446.2079.

Tert-butyl 1-(5-cyano-1_H_-indol-3-yl)-1,3,4,9-tetrahydro-2_H_-pyrido[3,4-_b_]indole-2-carboxylate (6l)



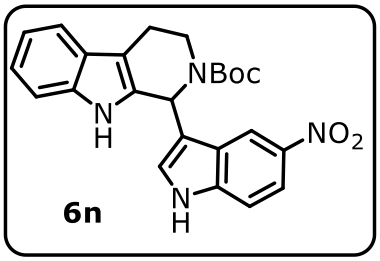
Colorless solid; Yield: (187.0 mg, 62 %), mp 220-222 °C, R_f = 0.37, EtOAc/hexanes (3:7), Column chromatography: 1.8:8.2 (EtOAc/Hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.62 (1H, br s), 10.95 (1H, br s), 8.13 (1H, s), 7.57 (1H, d, J = 8.4 Hz), 7.48 (2H, d, J =8.3 Hz), 7.29 (1H, d, J = 8.1 Hz), 7.08 (1H, m), 7.01 (2H, dt, J = 7.5, 0.96 Hz), 6.69 (1H, s), 4.07-4.00 (1H, m), 3.06-3.00 (1H, m), 2.81-2.75 (2H, m), 1.50 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 154.1, 138.2, 136.1, 132.5, 127.8, 126.3, 125.9, 124.8, 124.1, 121.2, 120.7, 118.6, 117.9, 116.0, 113.2, 111.2, 108.1, 101.1, 79.5, 46.7, 37.9, 28.1, 21.3. IR (neat, cm^{-1}) 3399, 3329, 2972, 2924, 2845, 2221, 1650, 1619, 1473, 1456, 1422, 1392, 1364, 1250, 1230, 1158, 1138, 1111, 982, 912. HRMS (ESI-TOF) Calcd for $C_{25}H_{24}N_4O_2$ $[M+H]^+$ 413.1972, Found: 413.1972.

***Tert*-butyl 1-(4-cyano-1*H*-indol-3-yl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate (6m)**



Colourless solid; Yield: (180 mg, 61 %), mp 218-220ºC, R_f = 0.33, EtOAc/hexanes (3:7), Column chromatography: 1.8:8.2 (EtOAc/Hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.72 (1H, br s), 10.67 (1H, br s), 7.75 (1H, d, *J* = 8.04 Hz), 7.60 (1H, d, *J* = 7.53 Hz), 7.45 (1H, d, *J* = 7.53 Hz), 7.28 (2H, t, *J* = 7.8 Hz), 7.24 (1H, d, *J* = 8.0 Hz), 7.03 (1H, t, *J* = 7.5 Hz), 6.97 (1H, t, *J* = 7.3 Hz), 6.90 (1H, s), 4.42-4.28 (1H, m), 2.80 (2H, s), 1.47-1.40 (1H, m), 1.26 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 154.6, 136.3, 135.9, 134.4, 127.6, 126.2, 124.9, 120.9, 120.7, 120.5, 119.3, 118.4, 117.7, 117.1, 117.0, 111.2, 106.7, 101.3, 79.1, 46.5, 30.6, 27.9, 20.8. IR (neat, cm^{-1}) 3332, 3008, 2966, 2920, 2850, 2222, 2048, 1669, 1453, 1387, 1364, 1346, 1301, 1224, 1160, 1138. HRMS (ESI-TOF) Calcd for $C_{25}H_{24}N_4O_2$ $[M+H]^+$ 413.1972 Found: 413.1975.

***Tert*-butyl 1-(5-nitro-1*H*-indol-3-yl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate (6n)**

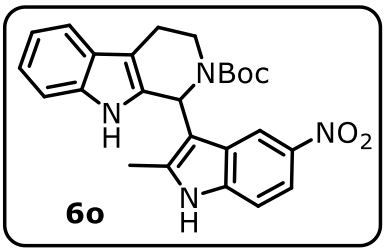


Yellow solid; Yield: (184 mg, 58 %), mp 218-220 ºC; R_f = 0.40, EtOAc/hexanes (3:7), Column chromatography: 2:8 (EtOAc/Hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.77 (1H, br s), 11.02 (1H, br s), 8.80 (1H, s), 8.05 (1H, d, *J* = 8.7 Hz), 7.58 (1H, d, *J* = 8.9 Hz), 7.48 (1H, d, *J* = 7.7 Hz), 7.30 (1H, d, *J* = 7.6 Hz), 7.10-7.00 (3H, m), 6.74 (1H, s), 4.08 (1H, s), 3.07-3.01 (1H, m), 2.83-2.72 (2H, m), 1.54 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 154.1, 140.7, 139.7, 136.0, 132.4, 129.0, 126.3, 125.3, 121.2, 118.6, 117.9, 117.7, 116.9, 116.5, 112.3, 111.2, 108.2, 79.6, 46.6, 37.8, 28.1, 21.3. IR (neat, cm^{-1}) 3392, 3312, 2965, 2917, 2848, 2618, 2432, 2366, 2324, 2186, 2162, 2013, 1651, 1516, 1471, 1460, 1365, 1250. HRMS (ESI-TOF) Calcd for $C_{24}H_{24}N_4O_4$ $[M+H]^+$ 433.1870, Found: 433.1868.

***Tert*-butyl 1-(2-methyl-5-nitro-1*H*-indol-3-yl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate (6o)**

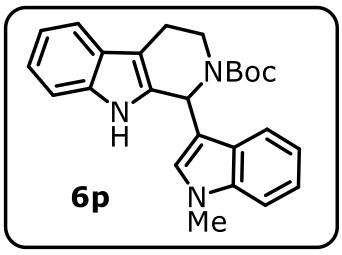
Yellow solid; Yield: (224 mg, 69 %), mp 216-218 ºC; R_f = 0.32, EtOAc/hexanes (3:7), Column chromatography: 2:8 (EtOAc/Hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.75 (1H, br s), 10.95 (1H, br s), 8.32 (1H, s), 7.92 (1H, dd, *J* = 9.0, 2.1 Hz), 7.50 (1H, d, *J* = 7.9

Hz), 7.43 (1H, d, *J* = 9.13 Hz), 7.27 (1H, d, *J* = 8.14 Hz), 7.09-7.06 (1H, m), 7.03-7.00 (1H, m), 6.70 (1H, s), 4.13 (1H, d, *J* = 9.98 Hz), 3.13-3.07 (1H, m), 2.89-2.78 (2H, m), 1.97 (3H, s), 1.49 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 153.9, 140.6, 138.8, 138.2, 136.0, 132.4, 127.4, 126.3, 121.2, 118.7, 117.9, 116.1, 115.1, 112.0, 111.3, 110.9, 108.2, 79.7, 46.9, 36.6, 28.0, 21.0, 11.4. IR (neat, cm^{-1}) 3363, 3277, 2977, 2933, 2844, 1647, 1566, 1517, 1474, 1455, 1418, 1366, 1335, 1287, 1250, 1229, 1157. HRMS (ESI-TOF) Calcd for $C_{25}H_{26}N_4O_4$ $[M+H]^+$ 447.2027 Found: 447.2025.



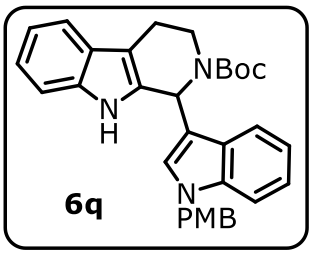
Tert-butyl 1-(1-methyl-1*H*-indol-3-yl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate (6p)

Colorless solid; Yield: (32.6 mg, 89 %), mp 206-208 ºC melts with decomposition, R_f = 0.70, EtOAc/hexanes (3:7), Column chromatography: 0.5:9.5 (EtOAc/Hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.95 (1H, br s), 7.67 (1H, s), 7.47 (1H, d, *J* = 7.78 Hz), 7.41 (1H, d, *J* = 8.1 Hz), 7.24 (1H, d, *J* = 7.5 Hz), 7.17 (1H, dt, *J* = 7.7, 1.0 Hz), 7.08-7.05 (1H, m), 7.03-6.99 (2H, m), 6.84 (1H, br s), 6.69 (1H, br s), 4.17 (1H, s), 3.70 (3H, s), 3.14-3.09 (1H, m), 2.82-2.73 (2H , m), 1.46 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 153.9, 136.8, 136.0, 133.3, 129.3, 126.5, 126.4, 121.5, 120.9, 119.2, 119.0, 118.9, 118.4, 117.8, 113.8, 111.1, 109.8, 107.8, 79.1, 46.8, 37.9, 32.3, 28.2, 21.3. IR (neat, cm^{-1}) 3308, 3065, 2970, 2927, 2847, 1655, 1588, 1473, 1451, 1418, 1364, 1300. HRMS (ESI-TOF) Calcd for $C_{25}H_{27}N_3O_3$ $[M+H]^+$ 424.1995, Found: 424.1999.



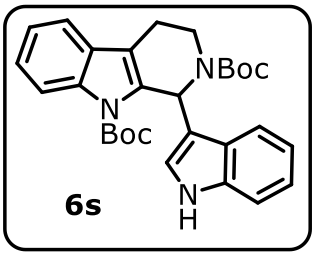
Tert-butyl 1-(1-(4-methoxybenzyl)-1*H*-indol-3-yl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate (6q)

Colorless solid; Yield: (80 mg, 85 %), mp 178 ºC melts with decomposition, R_f = 0.70, EtOAc/hexanes (3:7), Column chromatography: 0.6:9.4 (EtOAc/Hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.19 (1H, br s), 7.66 (1H, s), 7.48 (1H, d, *J* = 7.7 Hz), 7.44 (1H, s), 7.28 (1H, d, *J* = 6.3 Hz), 7.14-6.99 (7H, m), 6.84 (2H, d, *J* = 6.90 Hz), 6.72 (1H, br s), 5.27 (2H, s), 4.20 (1H, s), 3.69 (3H, s), 3.15-3.09 (1H, m), 2.78 (2H, s), 1.46 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 158.5, 154.0 136.1, 133.2, 130.0, 128.8, 128.5, 126.8, 126.4, 121.5, 121.0, 119.2, 118.5, 117.8, 114.3, 113.9,



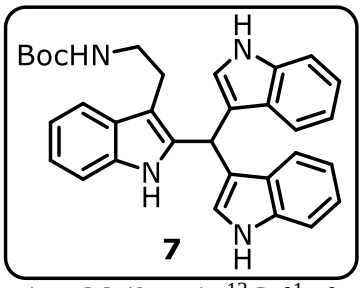
111.2, 110.5, 107.8, 79.1, 55.0, 48.5, 40.0, 38.0, 28.1, 21.4. IR (neat, cm^{-1}) 3312, 3056, 2976, 2925, 2839, 2163, 1670, 1612, 1542, 1511, 1462, 1416, 1391, 1364, 1295. HRMS (ESI-TOF) Calcd for $C_{32}H_{33}N_3O_3$ $[M+H]^+$ 508.2595, Found: 508.2597.

Di-*tert*-butyl 1-(1*H*-indol-3-yl)-3,4-dihydro-1*H*-pyrido[3,4-*b*]indole-2,9-dicarboxylate (6s)



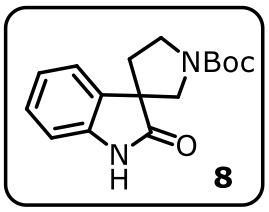
The title compound was obtained only in trace amounts and was confirmed by TLC using Seebach's magic TLC stain (characteristic pink color).

Tert-butyl (2-(2-(di(1*H*-indol-3-yl)methyl)-1*H*-indol-3-yl)ethyl)carbamate (7)



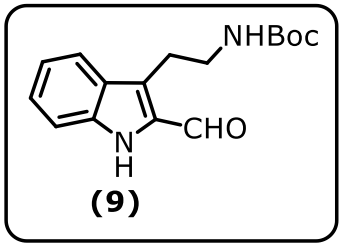
Pink Colored powder; Yield: (37 mg, 40 %); R_f = 0.33, EtOAc/hexanes (3:7), Column chromatography: 1.8:8.2 (EtOAc/Hexanes), ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.87 (2H, br s), 10.43 (1H, br, s), 7.45 (1H, d, *J* = 7.2 Hz), 7.36 (4H, d, *J* = 8.2 Hz), 7.21 (1H, d, *J* = 8.0 Hz), 7.05-7.02 (2H, m), 6.98-6.85 (m, 7H), 6.09 (1H, s), 3.10 (2H, t, *J* = 5.9 Hz), 2.94 (2H, t, *J* = 7.0 Hz), 1.36 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 155.8, 138.6, 136.5, 135.5, 128.2, 126.6, 123.9, 121.0, 120.1, 119.0, 118.4, 118.2, 117.7, 116.4, 111.5, 106.7, 107.8, 77.6, 41.3, 31.4, 31.0, 28.4. IR (neat, cm^{-1}) 3396, 3337, 3302, 3267, 2920, 2851, 1970, 1987, 1682, 1617, 1505, 1455, 1412, 1364, 1337, 1241. HRMS (ESI-TOF) Calcd for $C_{32}H_{32}N_4O_2$ $[M+Na]^+$ 527.2423, Found: 527.2422.

Tert-butyl 2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate (8)



Colorless solid; Yield: (26 mg, 50 %), R_f = 0.28, EtOAc/hexanes (3:7), Column chromatography: 1.8:8.2 (EtOAc/Hexanes), ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.51 (1H, br s), 7.23-7.19 (2H, m), 6.98 (1H, d, *J* = 8.1 Hz), 6.87 (1H, d, *J* = 7.6 Hz), 3.69-3.56 (4H, m), 2.19-2.08 (2H, m), 1.42 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 179.3, 153.6, 141.6, 131.9, 128.4, 122.8, 122.0, 109.7, 78.9, 53.7, 51.8, 45.1, 35.2, 28.3. IR (neat, cm^{-1}) 3139, 3085, 2972, 2921, 2851, 1990, 1970, 1888, 1698, 1620, 1469, 1391, 1366, 1341, 1311, 1266, 1255, 1160, 1118. HRMS (ESI-TOF) Calcd for $C_{16}H_{20}N_2O_3$ $[M+Na]^+$ 311.1372, Found: 311.1372.

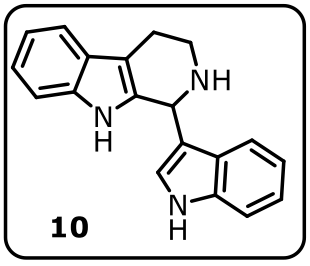
Synthesis of *tert*-butyl [2-(2-formyl-1*H*-indol-3-yl)ethyl]carbamate (9):



Colorless solid; Yield: (74.3 mg, 70 %), mp 136-138 ^{o}C; R_f = 0.40, EtOAc/hexanes (3:7), Column chromatography: 2.5:7.5 (EtOAc/Hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.64 (1H, br s,), 9.92 (1H, br s), 7.75 (1H, d, *J* = 7.9 Hz), 7.39 (1H, d, *J* = 8.1 Hz), 7.33-7.30 (1H, m), 7.10-7.07 (1H, m), 6.92 (1H, s), 3.19 (4H, s), 1.33 (9H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 181.4, 155.6, 137.8, 132.3, 127.1, 126.4, 125.2, 121.1, 119.9, 112.7, 77.5, 41.5, 28.1, 23.6. IR (neat, cm^{-1}) 3430, 3296, 3052, 2974, 2925, 2858, 1721, 1676, 1639, 1573, 1530, 1455. HRMS (ESI-TOF) Calcd for $C_{16}H_{20}N_2O_3$ $[M+H]^+$ 289.1552, Found: 289.1556.

Total synthesis of Eudistomin U (3):[5]

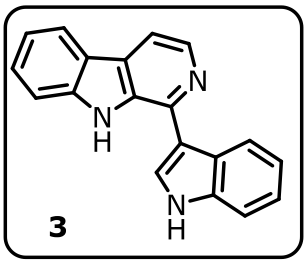
i) Synthesis of 1-(1*H*-indol-3-yl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (10)[5]



Compound **6a** (100 mg, 0.258 mmol) was dissolved in 1 mL of 1,4-dioxane, then 1.0 mL of 4.0 M HCl in 1,4-dioxane was added slowly. The resulting mixture was stirred for 2 hours, after checking the completion of reaction by TLC, the reaction mixture was neutralized with saturated sodium bicarbonate solution. EtOAc extraction (3 × 25 mL) followed by water wash (50 mL), drying over anhydrous Na_2SO_4 and concentration under vacuum afforded the deprotected compound **8** quantitatively and was further used as such without any further purification.

Yellow powder; R_f = 0.30, MeOH/$CHCl_3$ (2:8), Column chromatography: 0.7:9.3 (EtOAc /Hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.01 (1H, br s), 10.40 (1H, br s), 7.44 (1H, d, *J* = 7.4 Hz), 7.37 (2H, t, *J* = 8.5 Hz), 7.20 (1H, d, *J* = 7.5 Hz), 7.16 (1H, d, *J* = 1.6 Hz), 7.05 (1H, t, *J* = 7.3 Hz), 7.00-6.95 (2H, m), 6.88 (1H, t, *J* = 7.3 Hz), 5.48 (1H, br s), 3.23-3.20 (1H, m), 3.04-3.00 (1H, m), 2.85-2.80 (1H, m), 2.75-2.72 (1H, m), 1.89 (1H, s). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 136.6, 135.8, 128.7, 126.9, 126.4, 124.6, 121.0, 120.3, 119.4, 118.4, 118.0, 117.5, 115.4, 111.4, 111.1, 107.4, 49.6, 41.8, 22.1. IR (neat, cm^{-1}) 3394, 3102, 3061, 2958, 2921, 2851, 1722, 1617, 1545, 1451, 1340, 1300, 1228. HRMS (ESI-TOF) Calcd for $C_{19}H_{17}N_3$ $[M+H]^+$ 288.1501, Found: 288.1503.

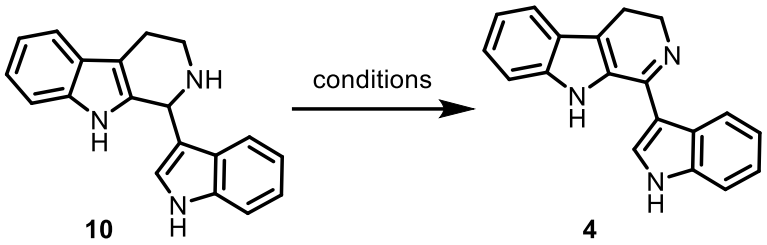
ii) 1-(1*H*-Indol-3-yl)-9*H*-pyrido[3,4-*b*]indole (Eudistomin U) (3)[5]



Compound **8** (20 mg, 0.0696 mmol) was dissolved in dry *o*-xylene (1.0 mL) and the 10 mol% of Pd/C was added and the reaction was refluxed for 6 hours. After ensuring the reaction completion by TLC, the reaction mixture was filtered using celite, washed with EtOAc (25 mL) and concentrated under vacuum. The crude product was further purified using column chromatography using EtOAc in hexanes (4:6).

Yellow solid; Yield: (13.0 mg, 66 %), mp 242-244 ^{o}C (Lit[5b] 242.7-243.2 ^{o}C), R_f = 0.35, MeOH/$CHCl_3$ (0.5:9.5). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.72 (1H, br s), 11.30 (1H, br s), 8.57 (1H, d, *J* = 7.9 Hz), 8.46 (1H, d, *J* = 5.2 Hz), 8.30 (1H, d, *J* = 2.5 Hz), 8.25 (1H, d, *J* = 7.8 Hz), 7.98 (1H, d, *J* = 5.2 Hz), 7.71 (1H, d, *J* = 8.1 Hz), 7.57-7.52 (2H, m), 7.27 (1H, t, *J* = 7.2 Hz), 7.23 (1H, t, *J* = 7.2 Hz), 7.16 (1H, t, *J* = 7.06 Hz). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 140.8, 140.5, 138.0, 136.6, 132.1, 128.1, 127.7, 126.2, 125.9, 122.3, 122.0, 121.4, 121.3, 119.8, 119.4, 113.3, 112.4, 111.6, 111.5. IR (neat, cm^{-1}) 3183, 3059, 2921, 2852, 2360, 1598, 1553, 1216, 746; HRMS (ESI-TOF) Calcd for $C_{19}H_{13}N_3$ $[M+H]^+$ 284.1185, Found: 284.1182.

Table S1: Reaction Optimization for the synthesis of Isoeudistomin U (4):



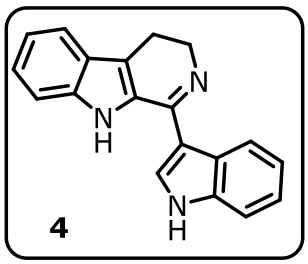
10 **4**

S. No.	Oxidation Reagent	Additive	Solvent	Temp (^{o}C)	Time (min.)	Yield (%) (**4**)
1	DDQ (1.1 equiv.)	-	DCM	rt	60	-
2	DIB (1.0 equiv.)[a]	-	DMF	rt	60	-
3	NBS (1.0 equiv.)[b]	NaOH	DCM-H_2O	rt	10	trace
4	NCS 1.0 equiv.)	-	DMF	rt	30	5
5	NCS (1.0 equiv.)[c]	Et_3N	DMF	rt	30	10
6	IBX (1.3 equiv.)		CH_3CN	rt	120	30
7	IBX (1.2 equiv.)[d]	TBAB	CH_3CN	rt	18 hours	56

Reaction conditions: Compound **10** (1.0 equiv.), Yields mentioned are isolated yields.

[a-d] References 6a-d.

1-(1*H*-Indol-3-yl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (Isoeudistomin U) (4)[7]



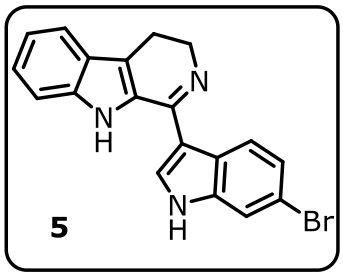
4

Compound **10** (30 mg, 0.0770 mmol) was dissolved in dry CH_3CN (2.0 mL) then IBX (26 mg, 0.0920 mmol, 1.2 equiv.) and 12.4 mg of TBAB (0.5 equiv.) was added. The resulting solution was stirred at rt for 18 hours, after completion of the reaction as shown in TLC, solvent was evaporated, the residue was dissolved in EtOAc (10 mL), washed with sat. $NaHCO_3$ solution, then with water, dried over Na_2SO_4 and concentrated under vacuum. The crude product was further purified using preparative TLC using MeOH in EtOAc (2:8).

Yellow powder; Yield: (16.0 mg, 56 %), R_f = 0.3, MeOH/$CHCl_3$ (2.0:8.0). ^{1}H NMR (500 MHz, CD_3OD + TFA) δ 8.34 (1H, s), 7.98-7.96 (1H, m), 7.79 (1H, d, *J* = 8.2 Hz), 7.65-7.64 (1H, m), 7.56 (1H, d, *J* = 8.5 Hz), 7.45 (1H, d, *J* = 8.3 Hz), 7.43-7.36 (2H, m), 7.24 (1H, t, *J* = 8.0 Hz), 4.06 (2H, t, *J* = 7.8 Hz), 3.35 (2H, t, *J* = 7.7 Hz). ^{13}C {^{1}H} NMR (125 MHz,

CD_3OD + TFA) δ 158.5, 142.8, 139.1, 137.8, 129.4, 126.6, 126.3, 125.8, 125.7, 124.2, 122.8, 122.4, 120.9, 114.3, 114.2 (2C), 107.4, 42.6, 20.4. IR (neat, cm^{-1}) 3226, 2960, 2916, 2849, 1731, 1670, 1578, 1556, 1448, 1423, 1334, 1229, 1197, 1080. HRMS (ESI-TOF) Calcd for $C_{19}H_{15}N_3$ $[M+H]^+$ 286.1342, Found: 286.1342.

1-(6-Bromo-1*H*-indol-3-yl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (19-Bromoisoeudistomin U) (5)[8]



5

Compound **6j** (100 mg, 0.2144 mmol) was dissolved in 1 mL of 1,4-dioxane, then 2.0 mL of 4.0 M HCl in 1,4-dioxane was added slowly. The resulting mixture was stirred for 2 hours at rt, after checking the completion of reaction by TLC, the reaction mixture was neutralized with saturated sodium bicarbonate solution. EtOAc extraction (3 × 25 mL) followed by water wash (50 mL), drying over anhydrous Na_2SO_4 and concentration under vacuum afforded the deprotected compound **11** quantitatively as yellow powder and was further used as such without any further Purification. Compound **11** (30 mg, 0.0819 mmol) was dissolved in dry CH_3CN (2.0 mL) then IBX (27.5 mg, 0.0983 mmol, 1.2 equiv.) and 13.2 mg of TBAB (0.04095 mmol, 0.5 equiv.) was added. The resulting solution was stirred at rt for 12 hours, after completion of the reaction as shown in TLC, solvent was evaporated, the residue was dissolved in EtOAc (10 mL), washed with sat. $NaHCO_3$ solution, then with water, dried over Na_2SO_4 and concentrated under vacuum. The crude product was further purified using preparative TLC using MeOH in EtOAc (2:8).

Yellow powder; Yield: (18.0 mg, 60 %), R_f = 0.35, MeOH/$CHCl_3$ (2.0:8.0). ^{1}H NMR (400 MHz, CD_3OD) δ 8.20 (1H, s), 7.81 (1H, d, *J* = 8.6 Hz), 7.75 (s, 1H), 7.73 (1H, d, *J* = 8.2 Hz), 7.49 (1H, d, *J* = 8.4 Hz), 7.39 (1H, d, *J* = 8.2 Hz), 7.38 (1H, t, *J* = 8.9 Hz), 7.18 (1H, t, *J* = 7.5 Hz), 3.99 (2H, t, *J* = 7.8 Hz), 3.24 (2H, t, *J* = 7.8 Hz). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.9 (1H, br, s), 11.2 (1H, br, s), 8.27 (1H, d, *J* = 8.6 Hz), 8.00 (1H, s), 7.67 (1H, d, *J* = 1.5 Hz), 7.62 (1H, d, *J* = 8.0 Hz), 7.49 (1H, d, *J* = 8.2 Hz), 7.24 (1H, dd, *J* = 8.5, 1.8 Hz), 7.23-7.20 (1H, m), 7.08 (1H, t, *J* = 7.3 Hz), 3.89 (2H, t, *J* = 8.3 Hz), 2.83 (2H, t, *J* = 8.0 Hz). ^{13}C {^{1}H} NMR (100 MHz, CD_3OD) δ 158.2, 142.2, 139.9, 136.5, 128.7, 127.2, 126.6, 126.4, 125.1, 123.2, 122.7, 122.5, 122.1, 118.4, 116.8, 114.2, 108.9, 44.0, 20.6. IR (neat, cm^{-1}) 3207, 3135, 2956, 2919, 2850, 2356, 2185, 1990, 1535, 1404, 1333, 1229, 1198, 1149, 1082, 1043. HRMS (ESI-TOF) Calcd for $C_{19}H_{14}BrN_3$ $[M+H]^+$ 364.0449, Found: 364.0449.

Comparison of spectral data of natural product 19-Bromoisoeudistomin U) (5) with that of the isolated compound:[8]

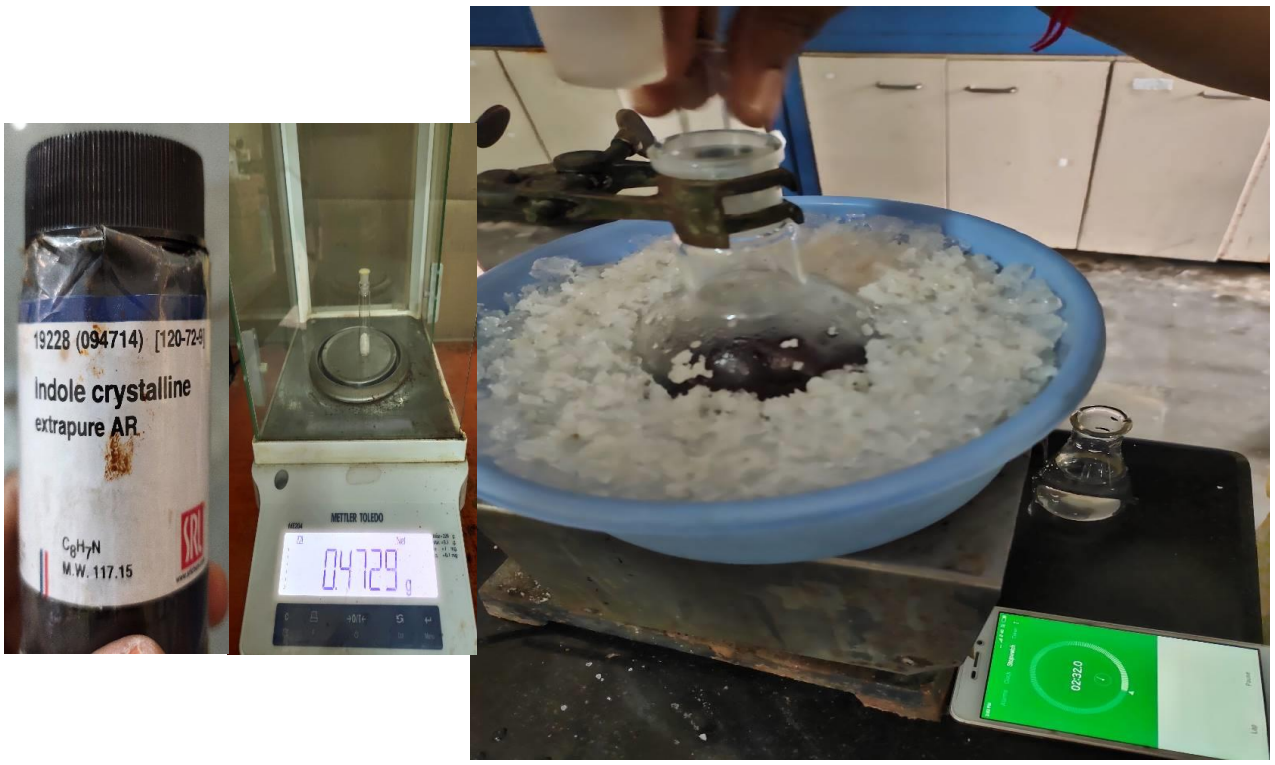
S. No.	^{1}H (Reported) 500 MHz, CD_3OD	^{1}H (Observed), 400 MHz, CD_3OD	^{13}C (Reported), 125 MHz, CD_3OD	^{13}C (Observed), 100 MHz, CD_3OD
1	8.09 (1H, s)	8.20 (1H, s)	158.5	158.2
2	7.84 (1H, d, *J* = 7.7 Hz)	7.81 (1H, d, *J* = 8.6 Hz)	142.0	142.2
3	7.74 (1H, d, *J* = 1.5 Hz)	7.75 (1H, s)	140.4	139.9
4	7.72 (1H, d, *J* = 8.3 Hz)	7.73 (1H, d, *J* = 8.2 Hz)	135.8	136.5
5	7.50 (1H, d, *J* = 8.3 Hz)	7.49 (1H, d, *J* = 8.4 Hz)	128.5	128.7
6	7.38 (1H, d, *J* = 8.3 Hz)	7.39 (1H, d, *J* = 8.3 Hz)	128.3	127.2
7	7.36 (1H, t, *J* = 8.3 Hz)	7.38 (1H, t, *J* = 8.2 Hz)	127.0	126.6
8	7.18 (1H t, *J* = 8.3 Hz)	7.18 (1H t, *J* = 8.9 Hz)	126.7	126.4
9	4.00 (2H, t, *J* = 8.3 Hz)	3.99 (2H, t, *J* = 8.3 Hz)	125.9	125.1
10	3.18 (2H, t, *J* = 8.3 Hz)	3.24 (2H, t, *J* = 7.5 Hz)	124.2	123.3
11	12.1 (1H, br, s) [DMSO-d_6]	11.9 (1H, br, s) [DMSO-d_6]	123.4	122.7
12	11.5 (1H, br, 1H) [DMSO-d_6]	11.2 (1H, br, 1H) [DMSO-d_6]	122.7	122.5
13			122.3	122.1
14			118.6	118.4
15			117.1	116.8
16			114.6	114.2
17			110.6	108.9
18			45.5	44.0
19			21.0	20.6

Gram scale synthesis of 6a: Tetrahydro-β-carboline (**1a**) (1.003 g, 1.0 equiv, 3.69 mol) was dissolved in 60 mL of dry dichloromethane in a RB flask, purged with nitrogen, closed with a glass stopper and then cooled using ice and salt mixture. Trityl tetrafluoroborate (1.46 g, 1.2 equiv, 4.43 mol) was in one stretch, after 2.5 minutes of stirring indole (0.473 g, 1.1 equiv, 4.1 mol) was added in one stretch. After 30 seconds, the reaction mixture was quenched with water, extracted with EtOAc, the organic layer was washed with water, dried with anhydrous sodium sulfate and the product formation was checked by TLC. Then the organic layer was concentrated under vacuum to afford the crude compound (**6a**). The crude compound thus obtained was further purified using column chromatography on silica gel using 8% EtOAc in hexane. Colorless solid (turns to pale pink on air), Yield: 1.16 g, (82%).

a) Addition of tetrahydro-β-carboline derivative (**1a**)

b) Addition of solvent followed by cooling with ice-salt freezing mixture

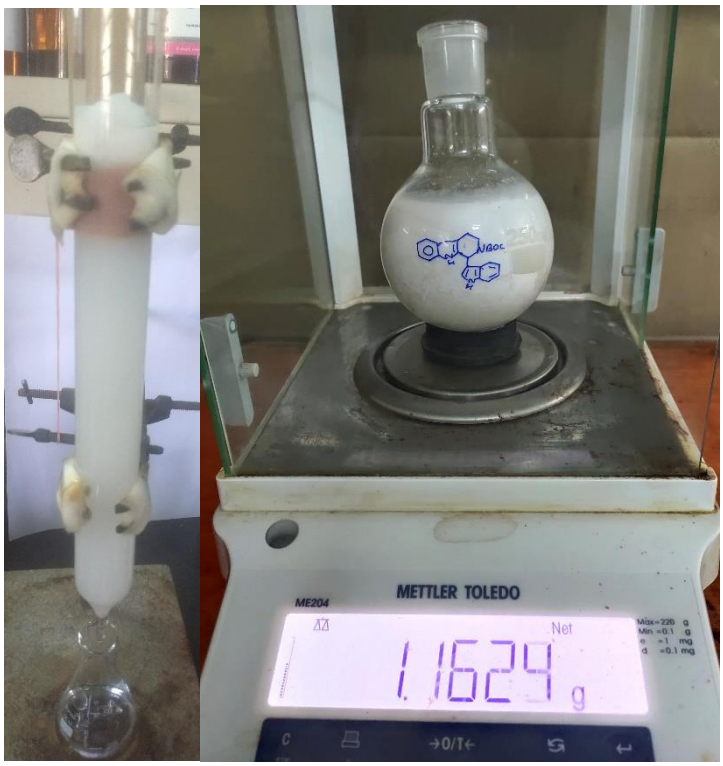
c) Addition of Trityl salt at -20 ºC



d) Addition of indole (**2a**) at -20 ºC after 150 seconds

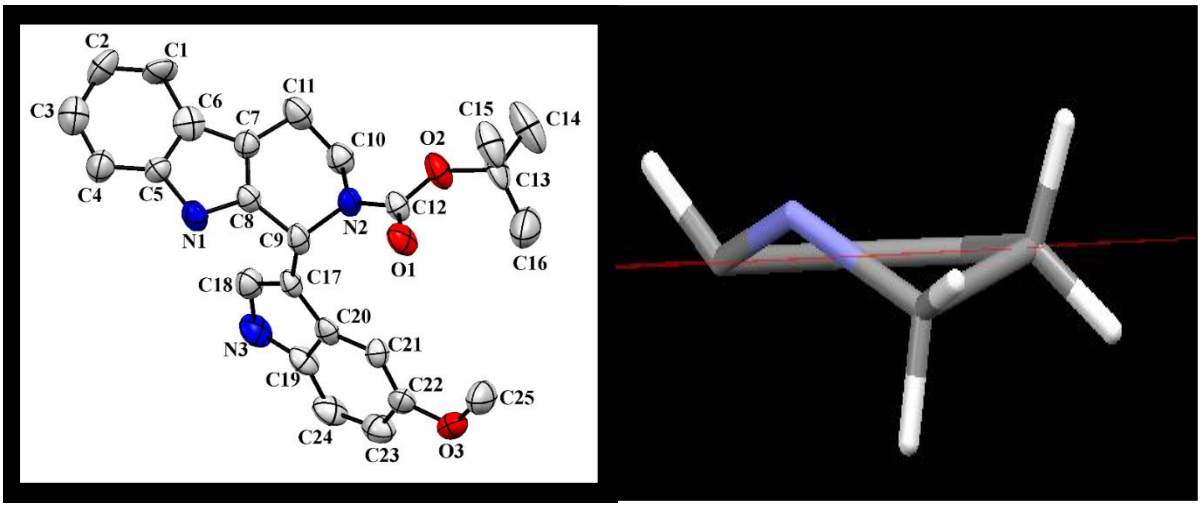
e) Quenching the reaction at 180 seconds

f) Extraction with EtOAc, drying using Na_2SO_4, TLC confirmation and crude compound **6a** after evaporation of the solvent



g) Purification by column chromatography and isolated coupled product **6a**.

Table S1. Crystal data and structure refinement for 6c:



Identification code	rn142_0m_a_a_a
Empirical formula	$C_{25}H_{27}Cl_0N_3O_3$
Formula weight	417.50
Temperature/K	300(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
a/Å	8.2512(12)
b/Å	10.4301(14)
c/Å	15.810(2)
α/°	80.059(6)
β/°	79.541(6)
γ/°	87.359(6)
Volume/Å^3	1317.7(3)

Z	2
ρcalcg/m^3	1.052 mg/m3
μ/mm^{-1}	0.070
F(000)	444
Crystal size/mm^3	0.32 x 0.28 x 0.25
2Θ range for data collection/°	2.19 to 25.00
Index ranges	9<=h<=9, -12<=k<=12, -18<=l<=18
Reflections collected	25836
Independent reflections	4659 [R(int) = 0.1707]
Data/restraints/parameters	4659 / 0 / 280
Goodness-of-fit on F2	0.884
Final R indexes [I>=2σ (I)]	R1 = 0.0916, wR2 = 0.2604
Final R indexes [all data]	R1 = 0.2127, wR2 = 0.3220
Largest diff. peak/hole/e $Å^{-3}$	0.220 and -0.230
CCDC number	1973061

The disordered solvent molecules were removed using SQUEEZE option in PLATON.32 The total electron count removed by SQUEEZE corresponds to 2 dichloromethane molecules.

References:

1. (a) E. J. Cochrane, L. A. Hassall and L. Coldham, *J. Org. Chem.*, 2015, **80**, 5964–5969. (b) J. H. Kalin, K. V. Butler, T. Akimova, W. W. Hancock, and A. P. Kozikowski, *J. Med. Chem.*, 2012, **55**, 639–651.
2. M. E. Kuehne, *US 4283,536*, 1981.
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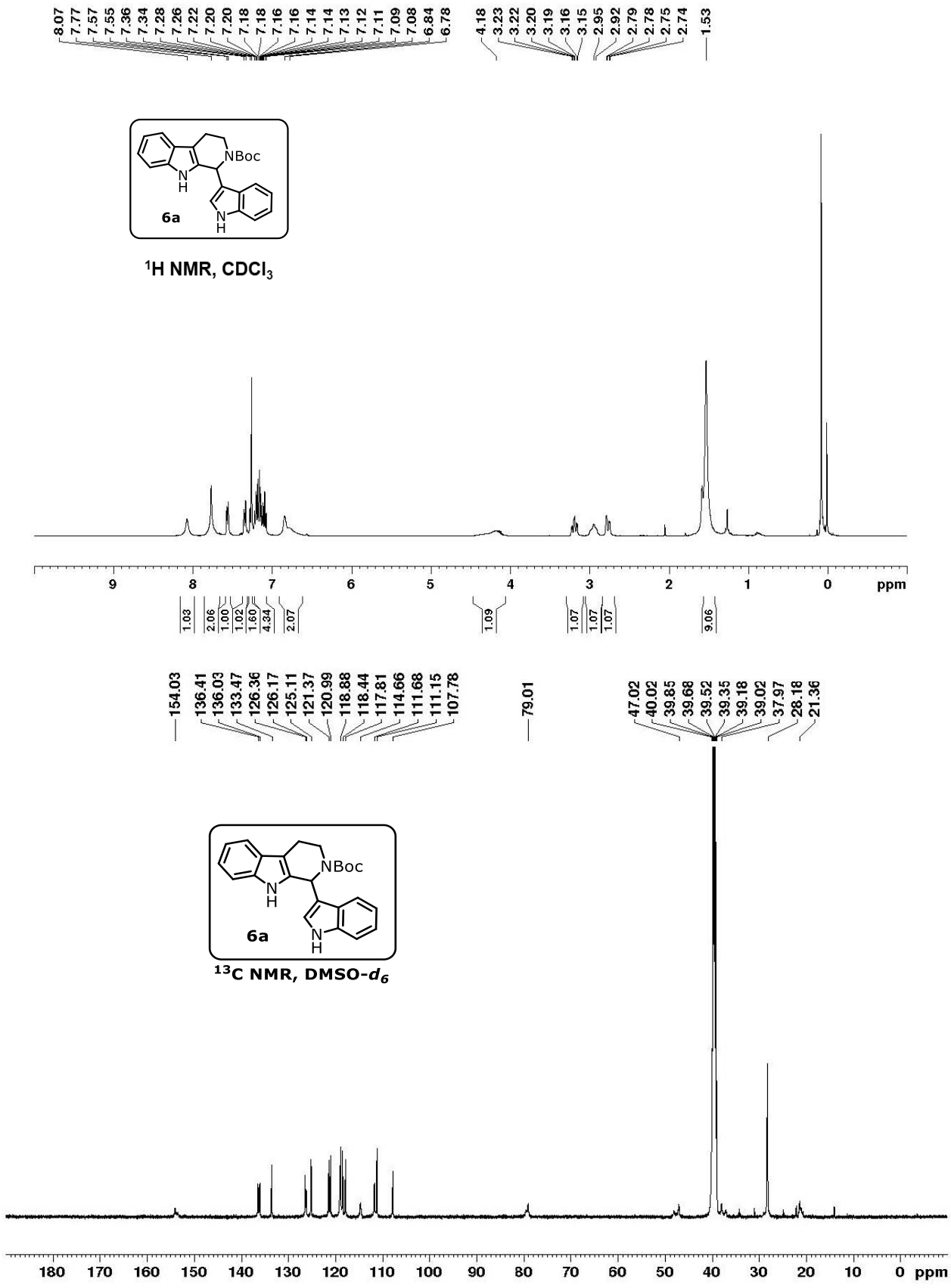
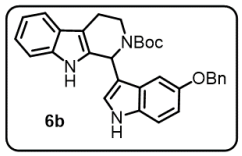
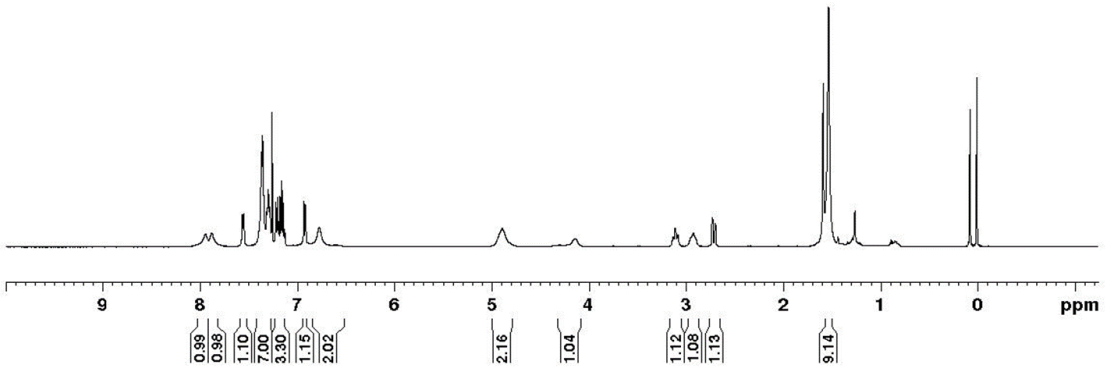
4. L. Zhang, C. Peng, D. Zhao, Y. Wang, H.-J. Fu, Q. Shena and J.-X. Li, *Chem. Commun.*, 2012, *48*, 5928–5930.
5. (a) D. S. Pakhare and R. S. Kusurkar, *Tetrahedron Lett.*, 2015, **56**, 6012–6015. (b) D. Xu, F. Ye, J. Ye, Y. Gao and H. Chen, *Org. Lett.*, 2019, **21**, 6160−6163.
6. (a) A. Kamal, M. Sathish, J. Chetna, Y. Tahgella, S. Vunnam, N. Srinivasulu and A. Alarifi, *Org. Biomol. Chem.*, 2015, **13**, 8652–8662. (b) J. C. Pelletier and M. P. Cava, *J. Org. Chem.*, 1987, **52**, 616-622. (c) A. Kamal, M. Sathish, A. V. G. Prasanthi, J. Chetna, Y. Tahgella, S. Vunnam, N. Srinivasulu and A. Alarifi, *RSC Adv.*, 2015, **5**, 90121–90126. (d) J. D. Panarese and S. P. Waters, *Org. Lett.*, 2010, **12**, 4086-4089.
7. G. Massiot, S. Nazabadioko and Bliard, C. *J. Nat. Prod.*, 1995, **58**, 1636–1639.
8. H. Kang and W. Fenical, *Nat. Prod. Lett*., 1996, **9**, 7–12.

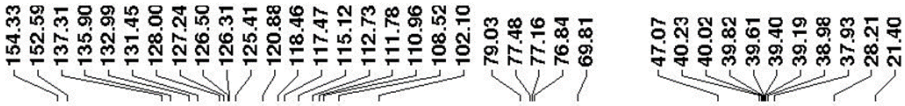
^{1}H and ^{13}C NMR Spectra

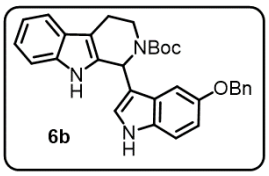




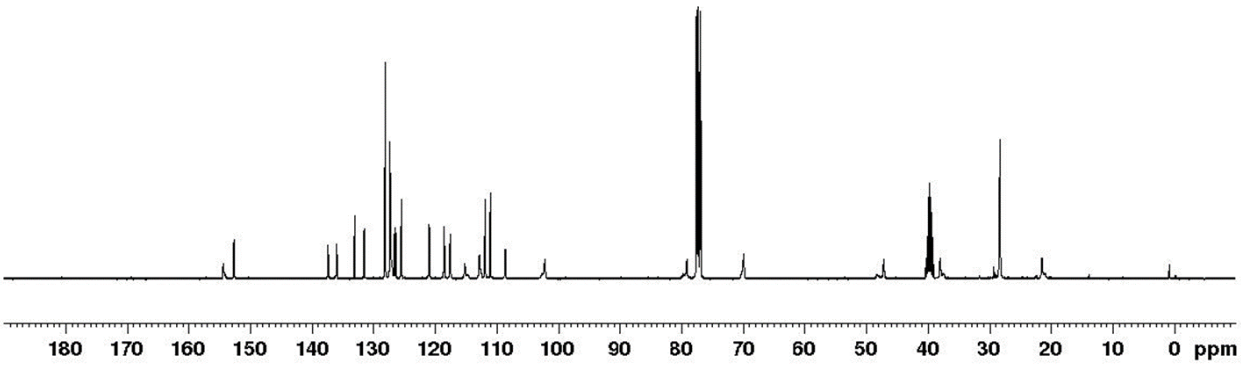
^{1}H NMR, $CDCl_3$ + DMSO-d_6

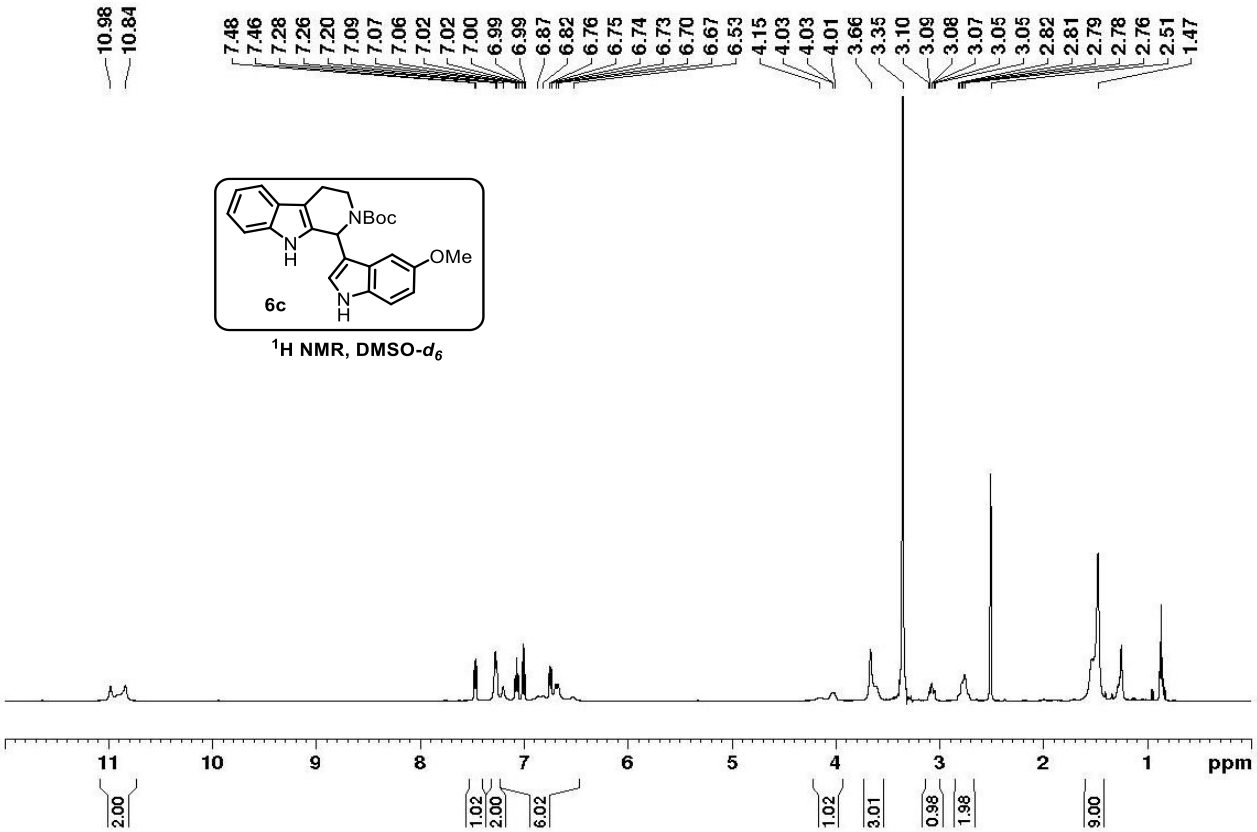




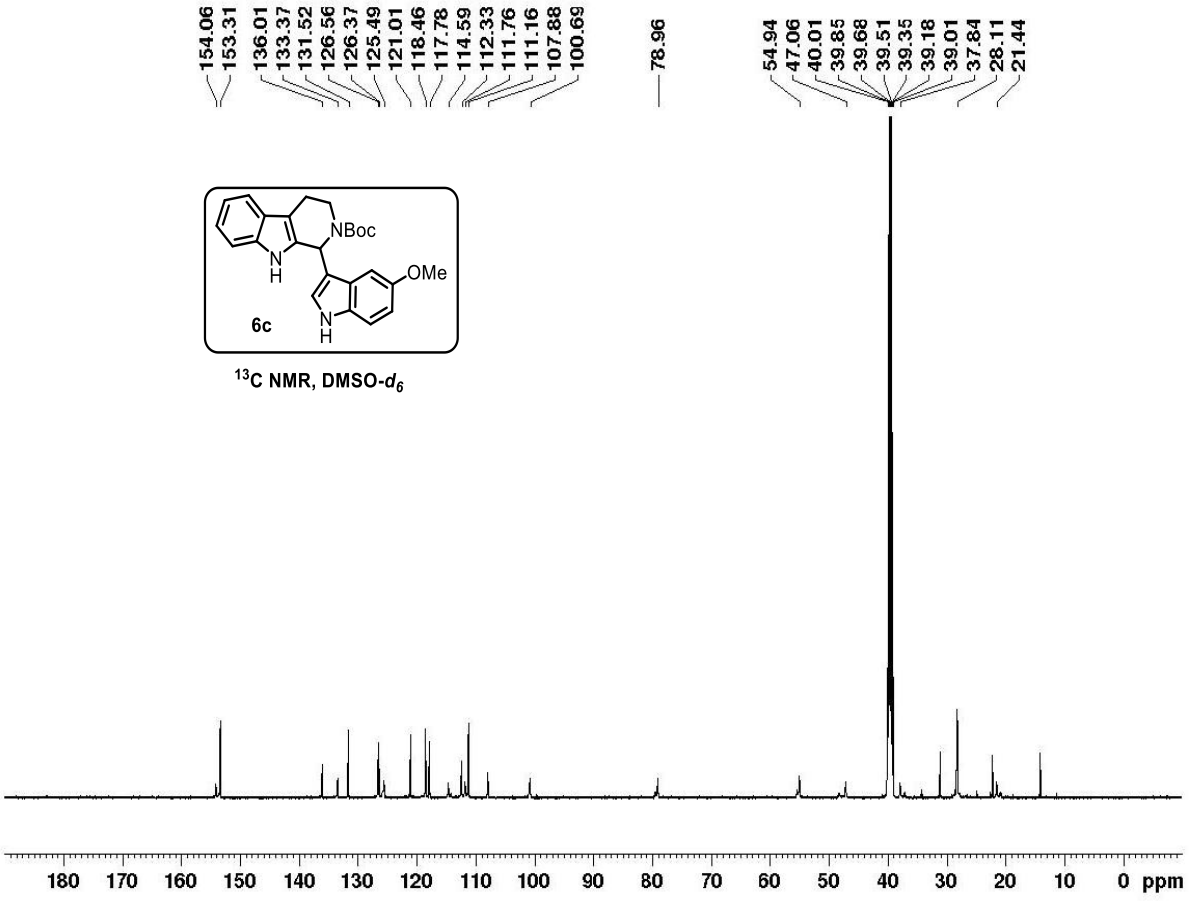


^{13}C NMR, $CDCl_3$ + DMSO-d_6

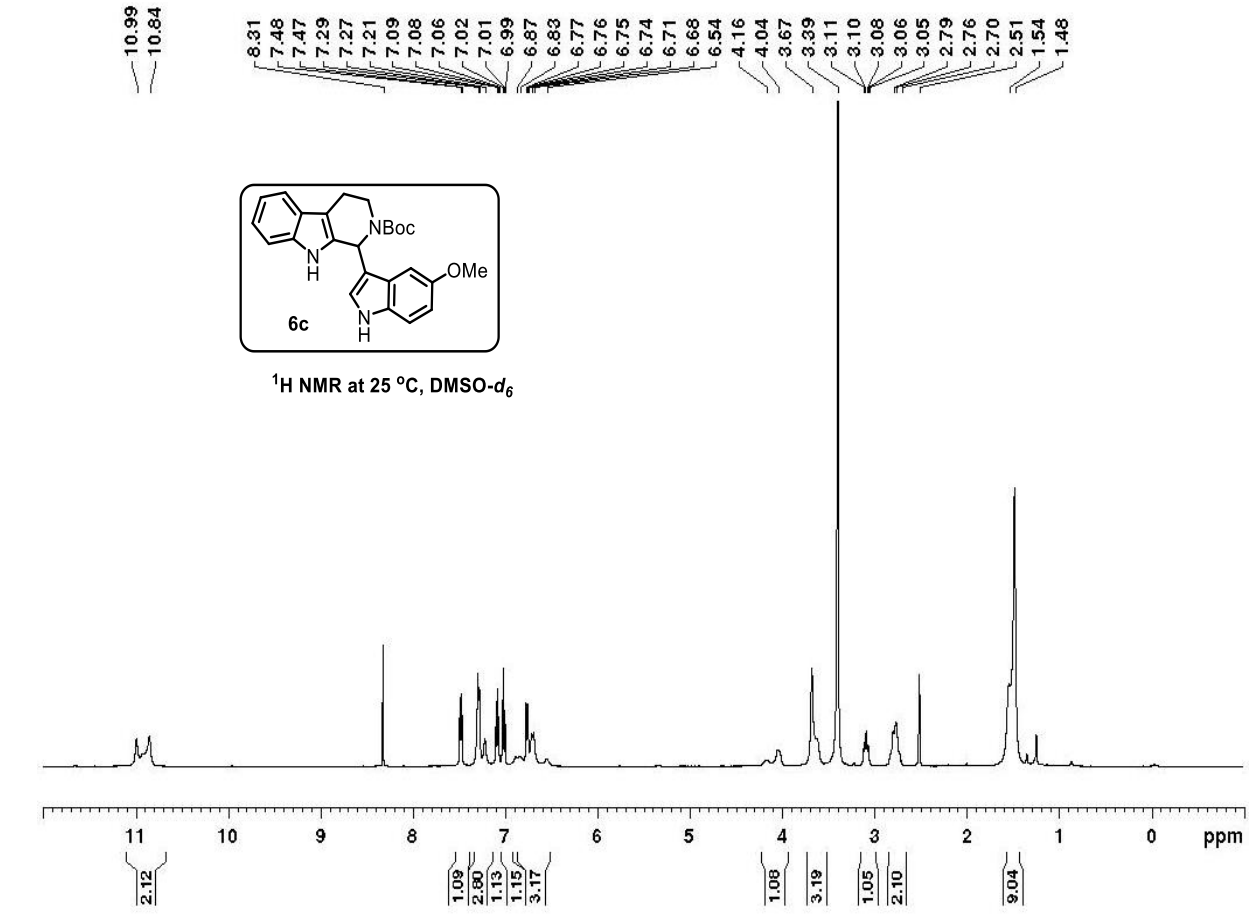




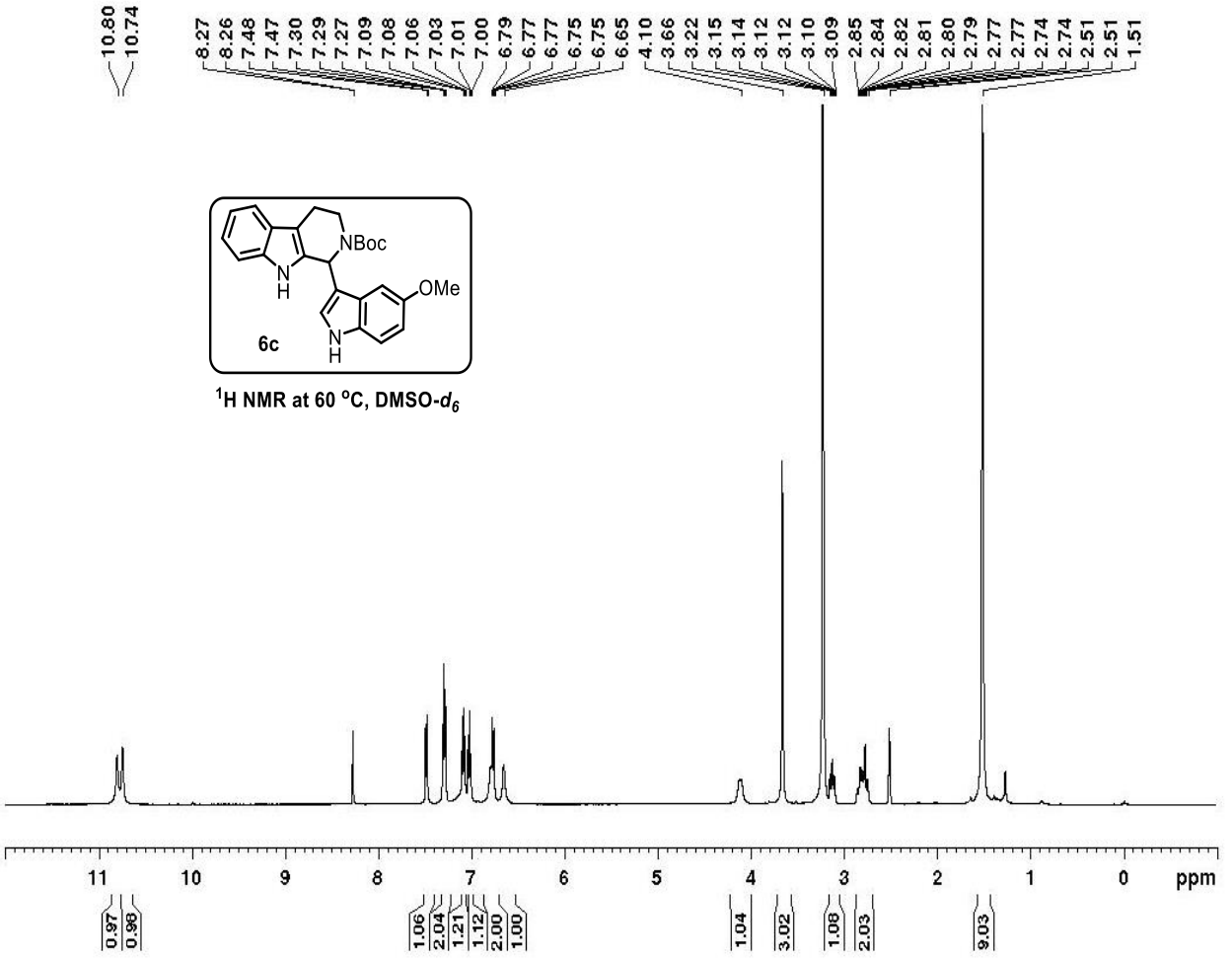
^{1}H NMR, DMSO-d_6



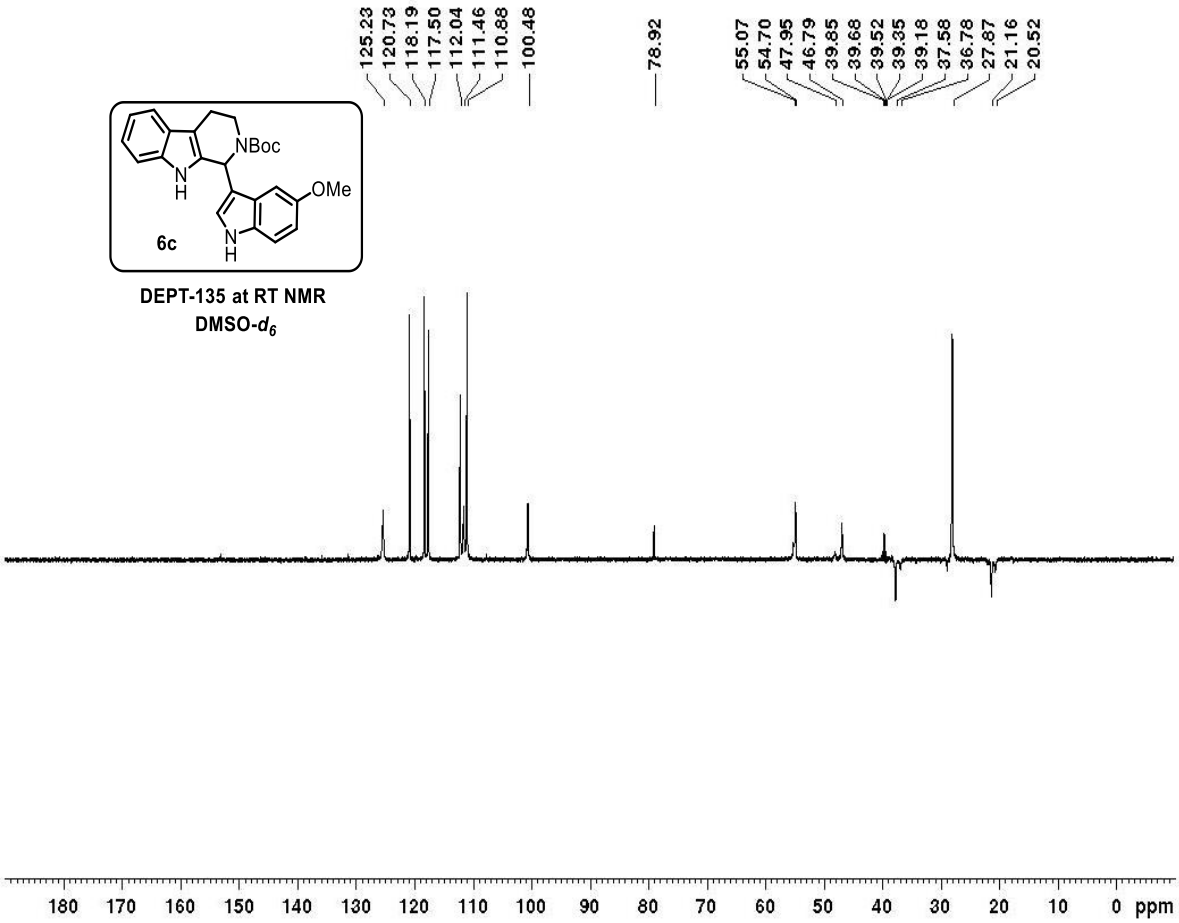
^{13}C NMR, DMSO-d_6

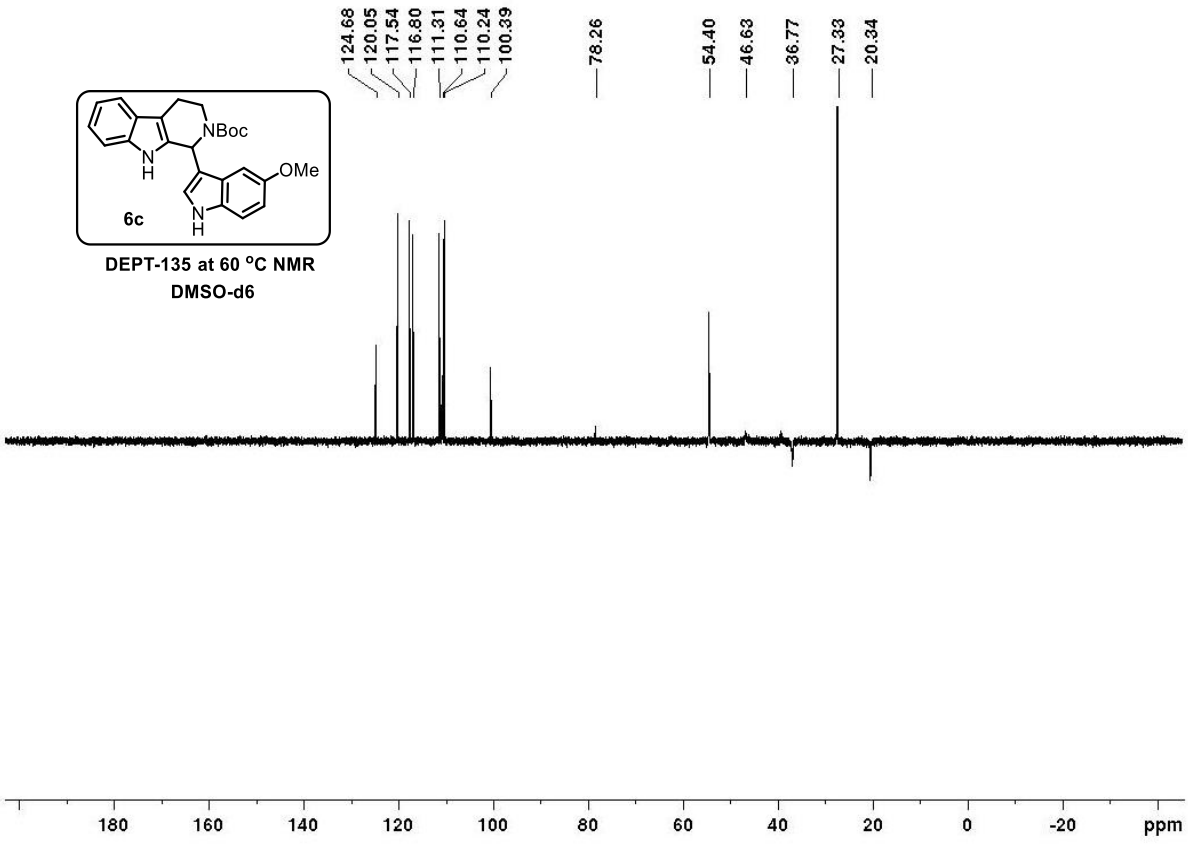


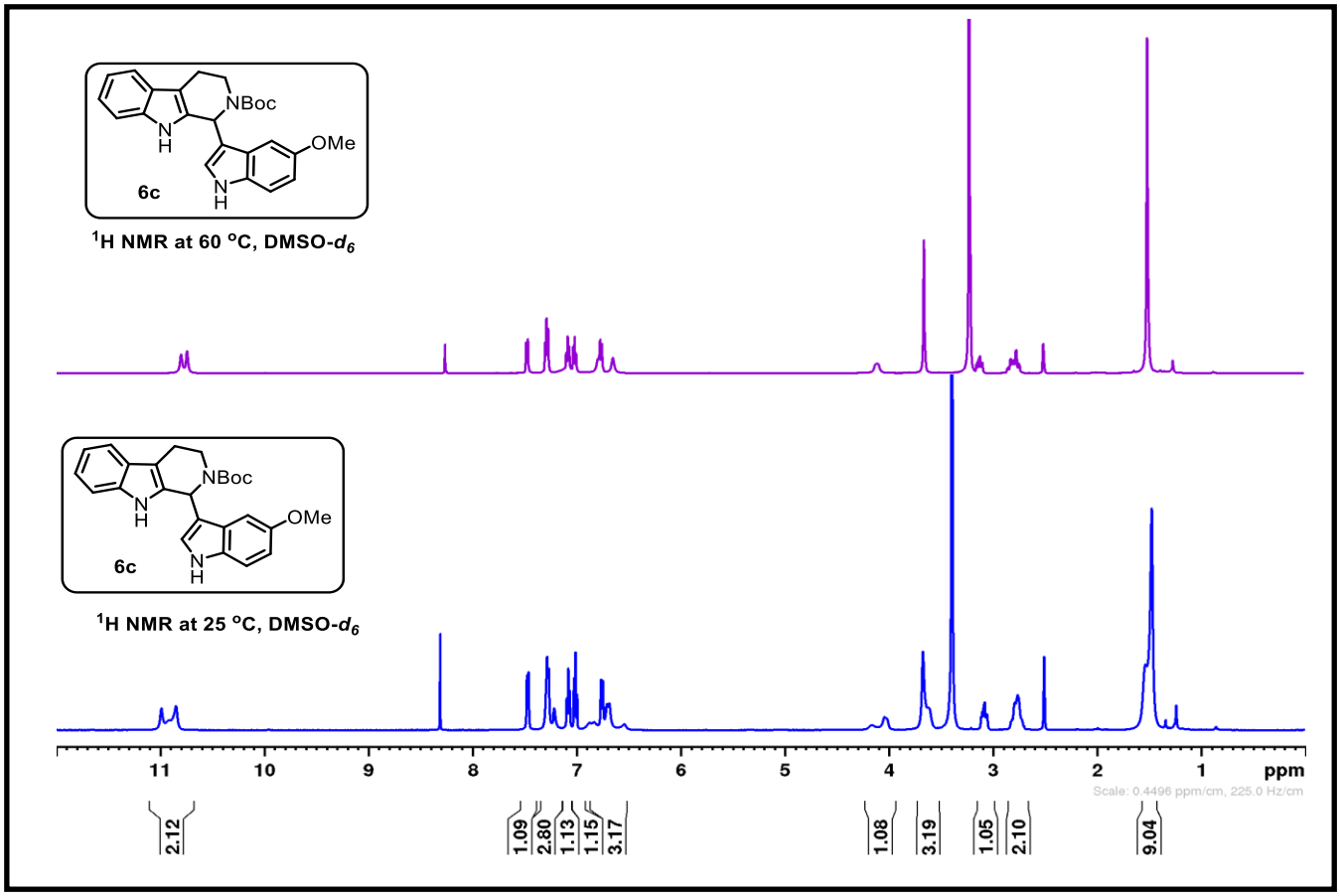
^{1}H NMR at 25 °C, DMSO-d_6

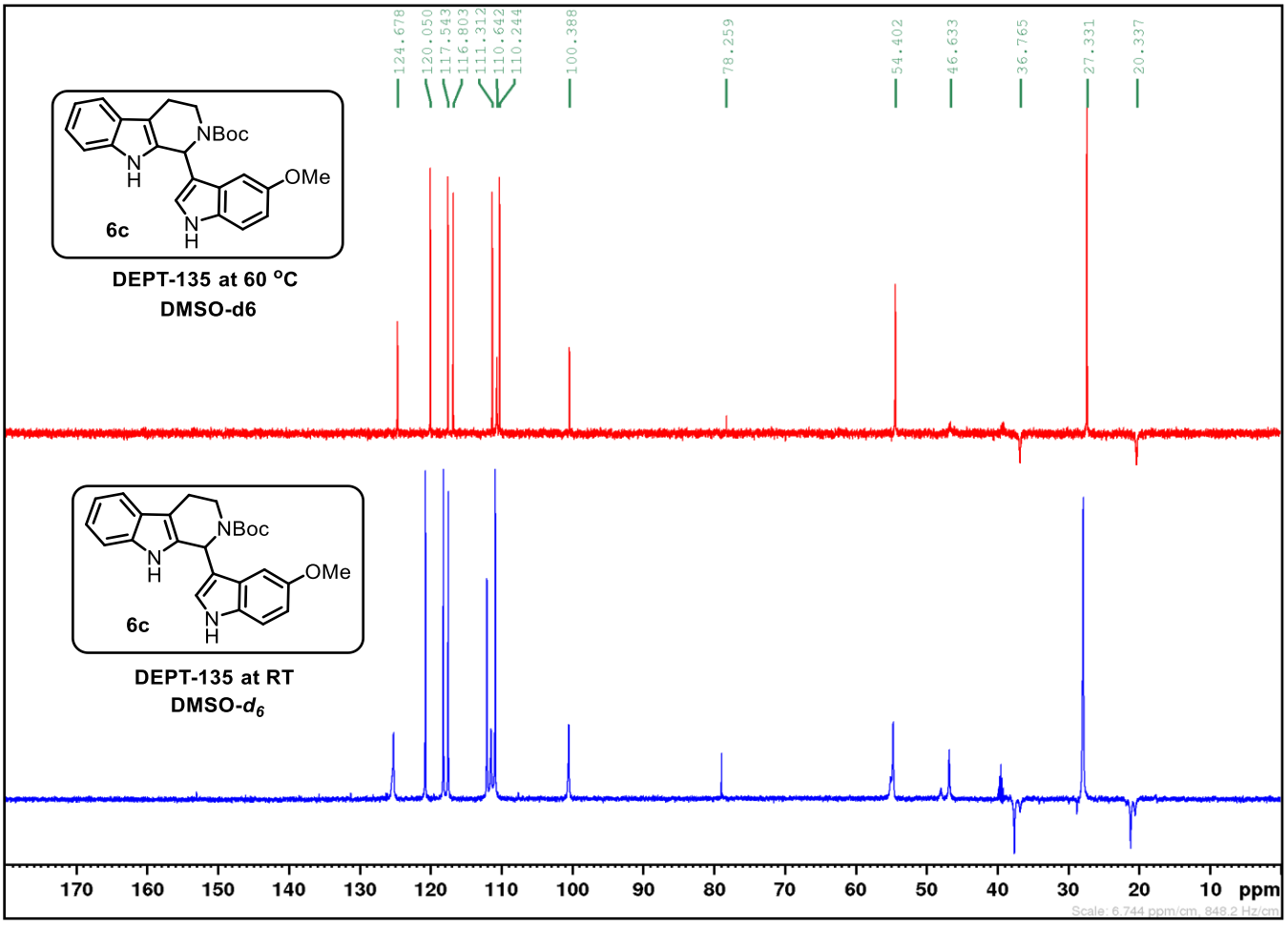


^{1}H NMR at 60 °C, DMSO-d_6


125.23
120.73
118.19
117.50
112.04
111.46
110.88
100.48
78.92
55.07
54.70
47.95
46.79
39.85
39.68
39.52
39.35
39.18
37.58
36.78
27.87
21.16
20.52
NBoc
OMe
6c
DEPT-135 at RT NMR
DMSO-d_6
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


124.68
120.05
117.54
116.80
111.31
110.64
110.24
100.39
78.26
54.40
46.63
36.77
27.33
20.34
NBoc
OMe
6c
DEPT-135 at 60 °C NMR
DMSO-d6
180 160 140 120 100 80 60 40 20 0 -20 ppm


NBoc
OMe
6c
^{1}H NMR at 60 °C, DMSO-d_6
^{1}H NMR at 25 °C, DMSO-d_6
11 10 9 8 7 6 5 4 3 2 1 ppm
Scale: 0.4496 ppm/cm, 225.0 Hz/cm
2.12
1.09
2.80
1.13
1.15
3.17
1.08
3.19
1.05
2.10
9.04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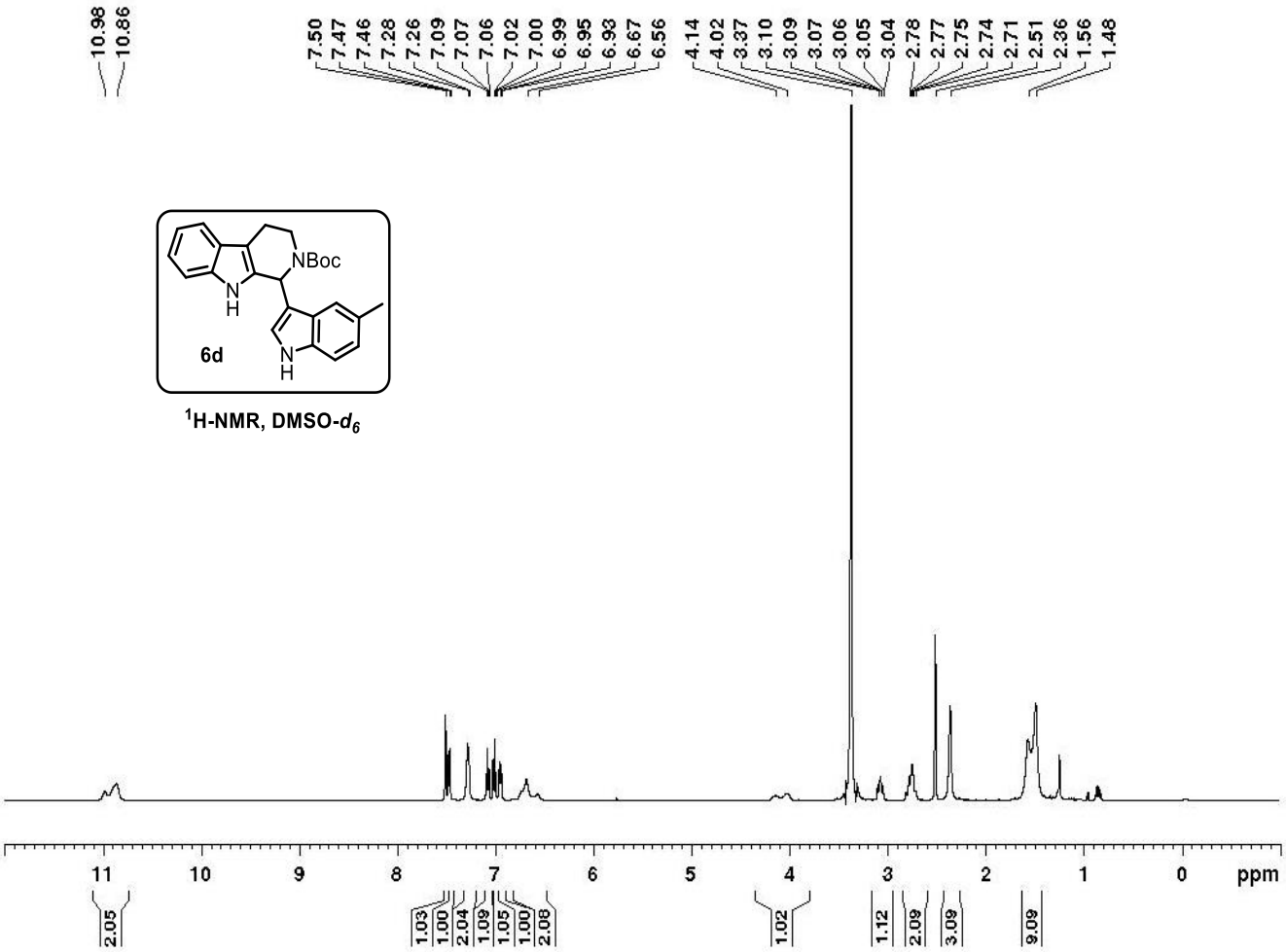
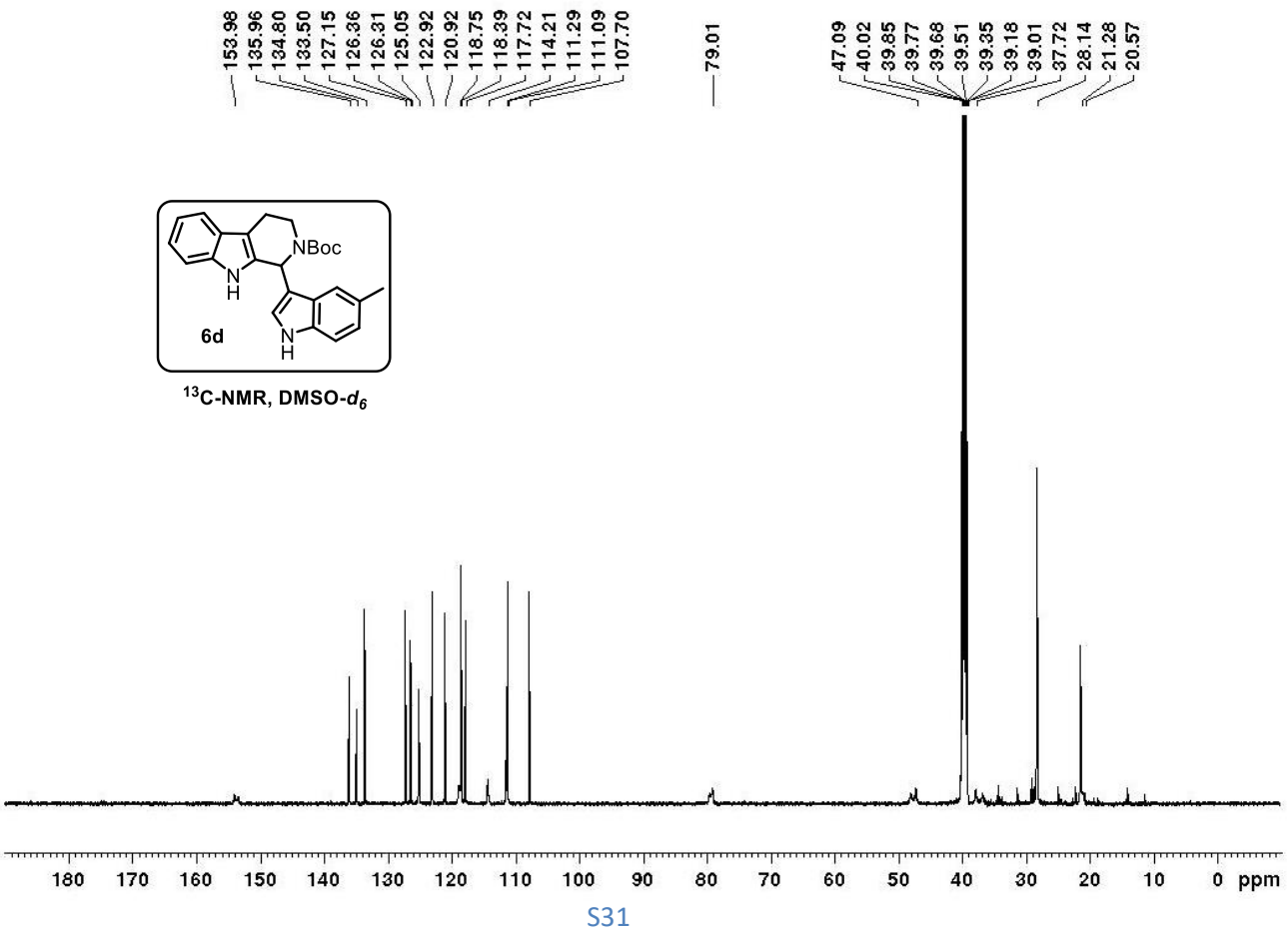
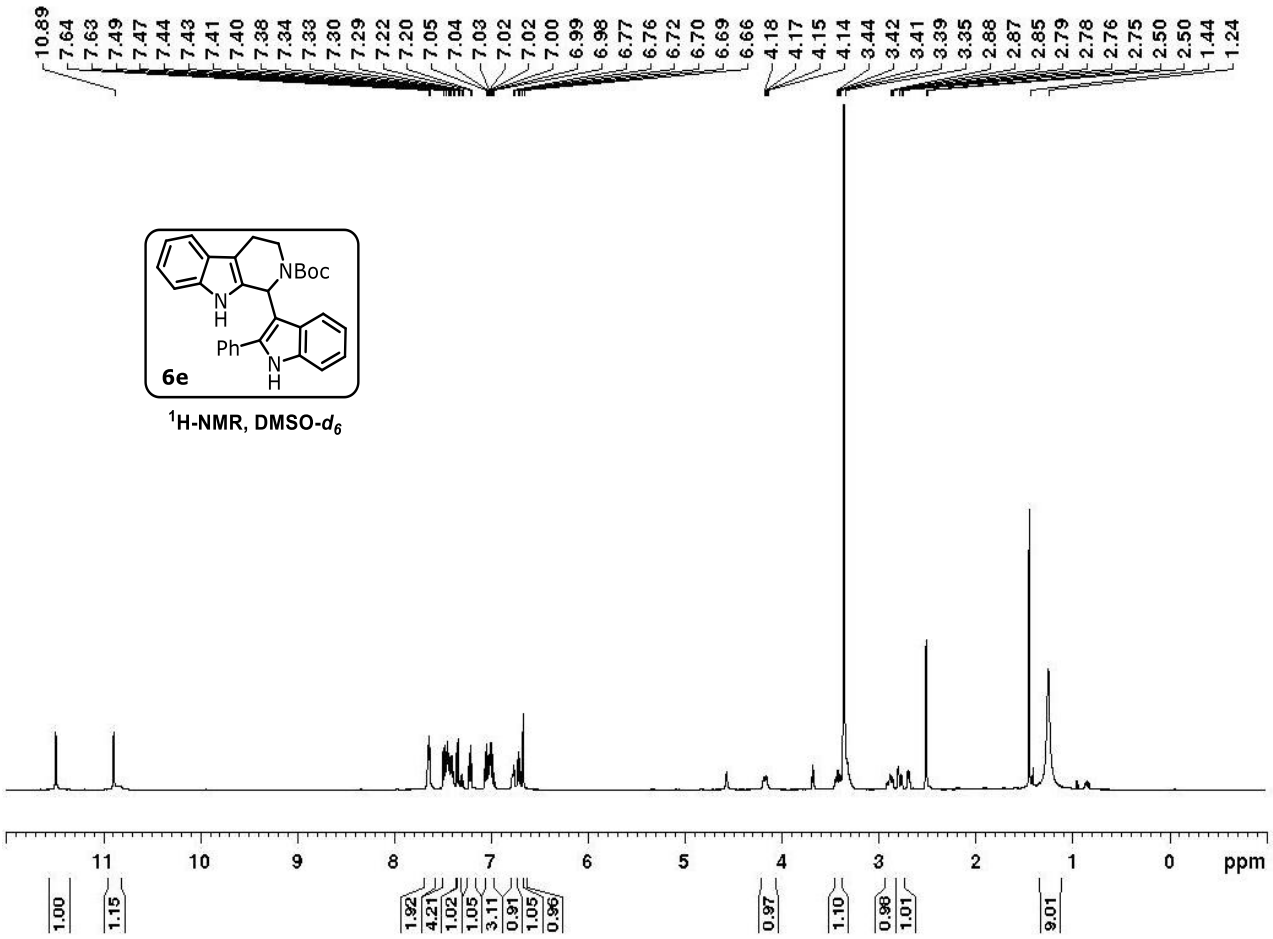
36.765
27.331
20.337
NBoc
OMe
6c
DEPT-135 at 60 °C
DMSO-d6
DEPT-135 at RT
DMSO-d_6
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
Scale: 6.744 ppm/cm, 848.2 Hz/cm



^{1}H-NMR, DMSO-d_6



^{13}C-NMR, DMSO-d_6



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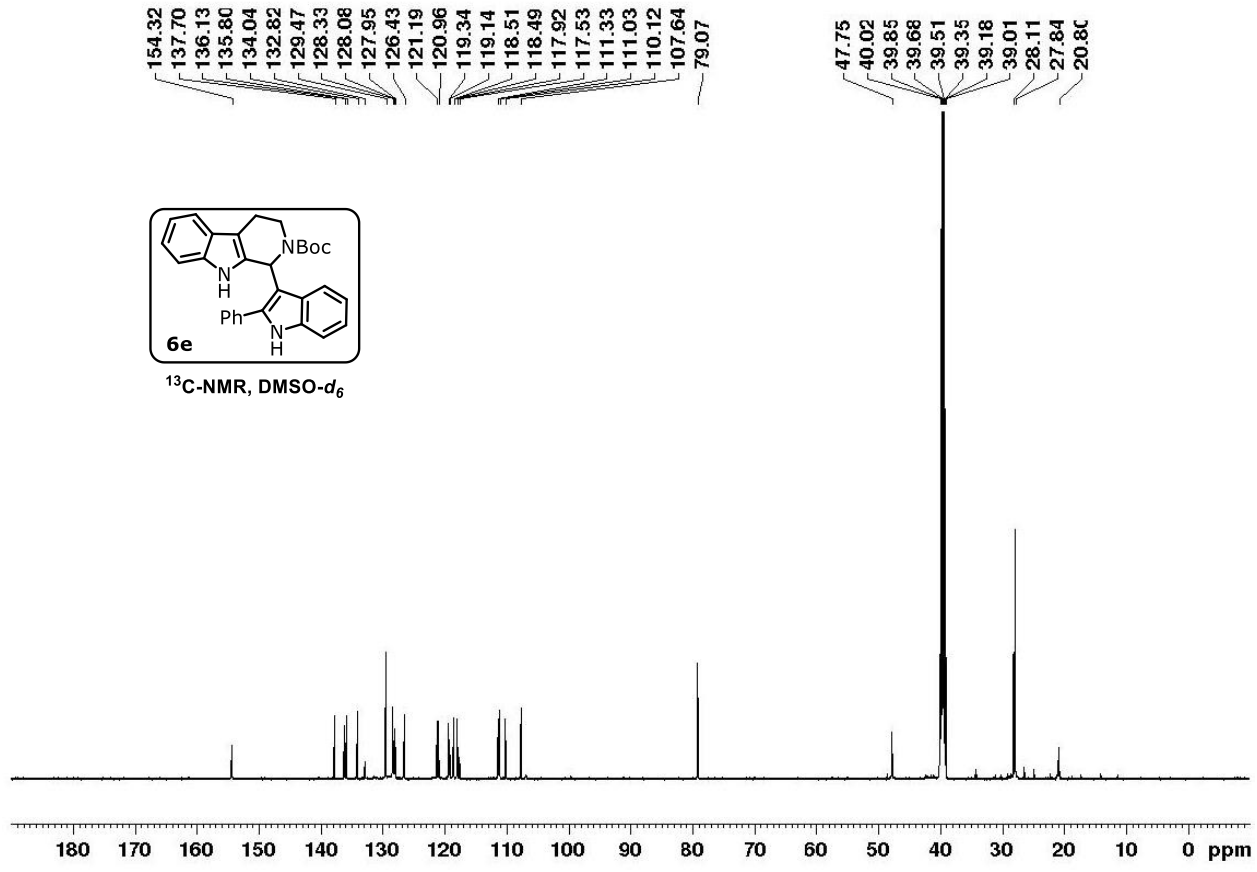

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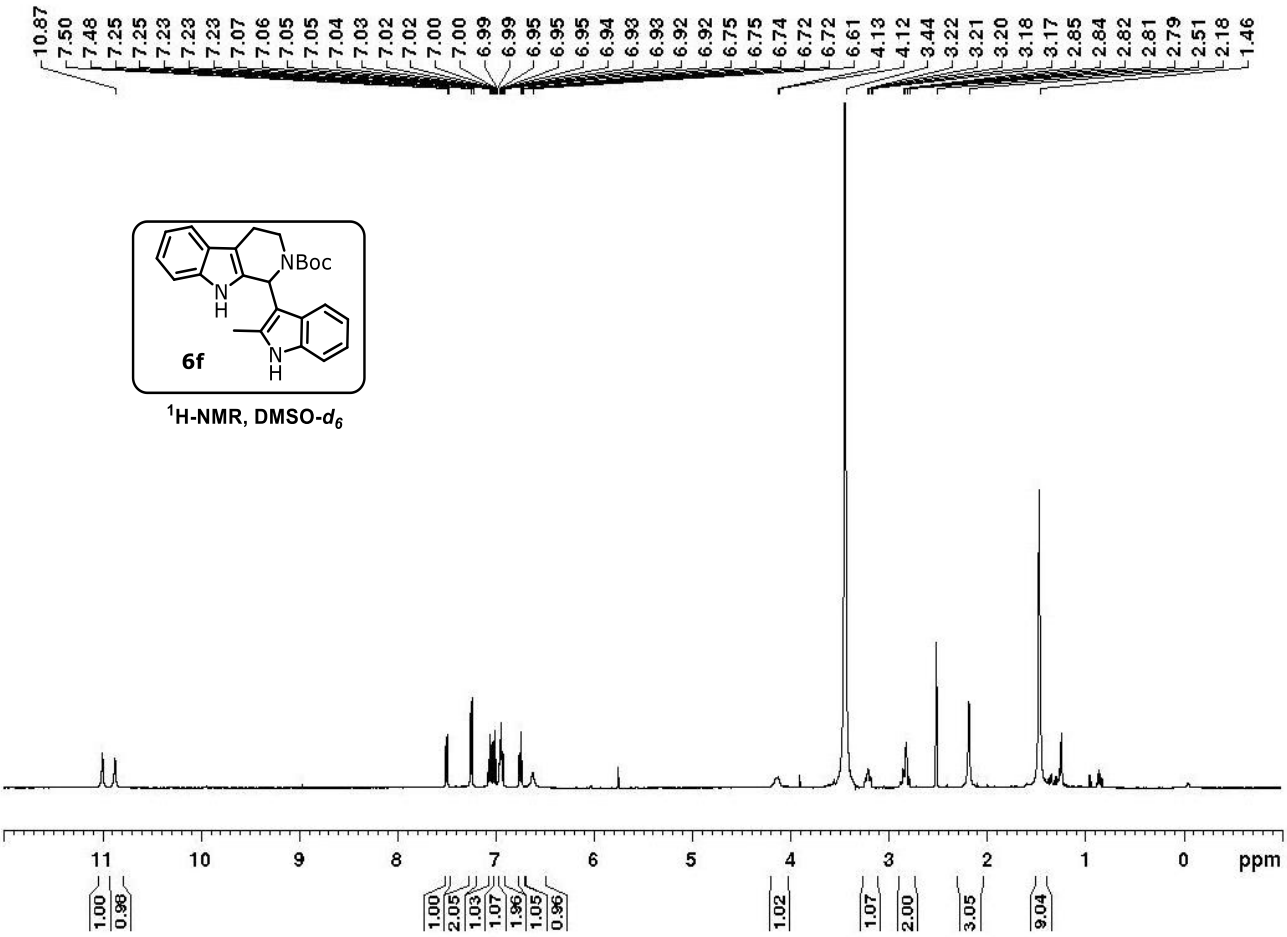

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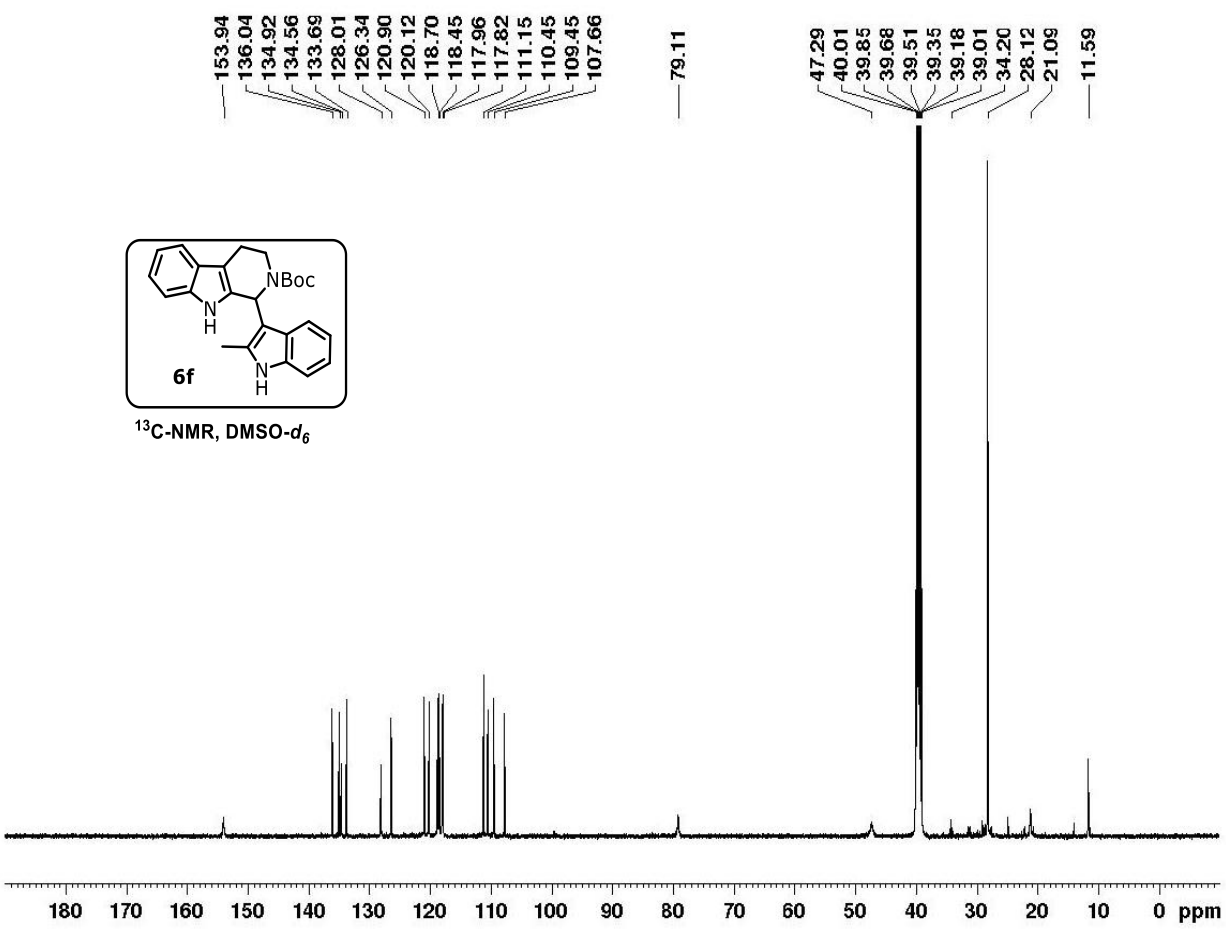

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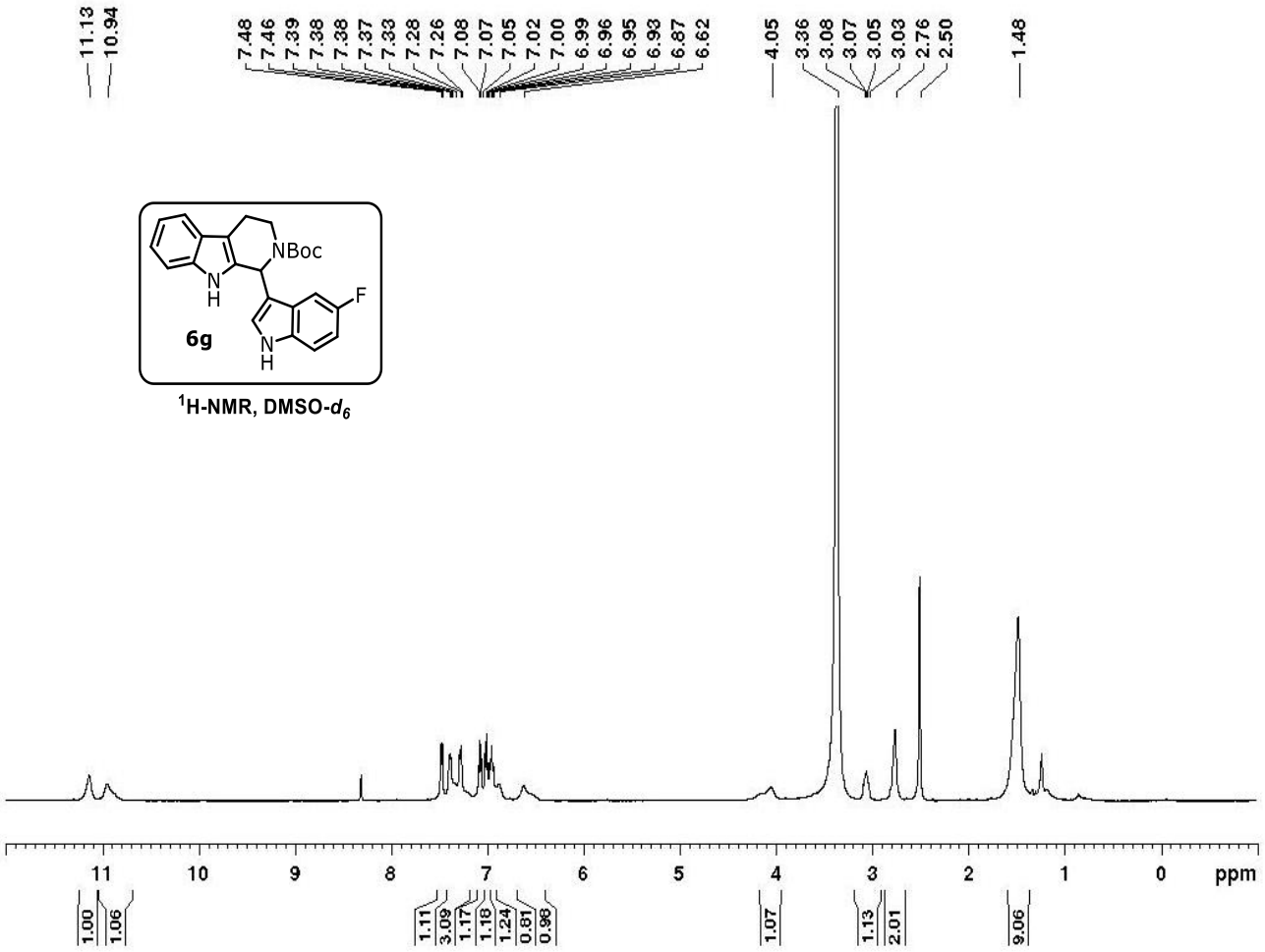

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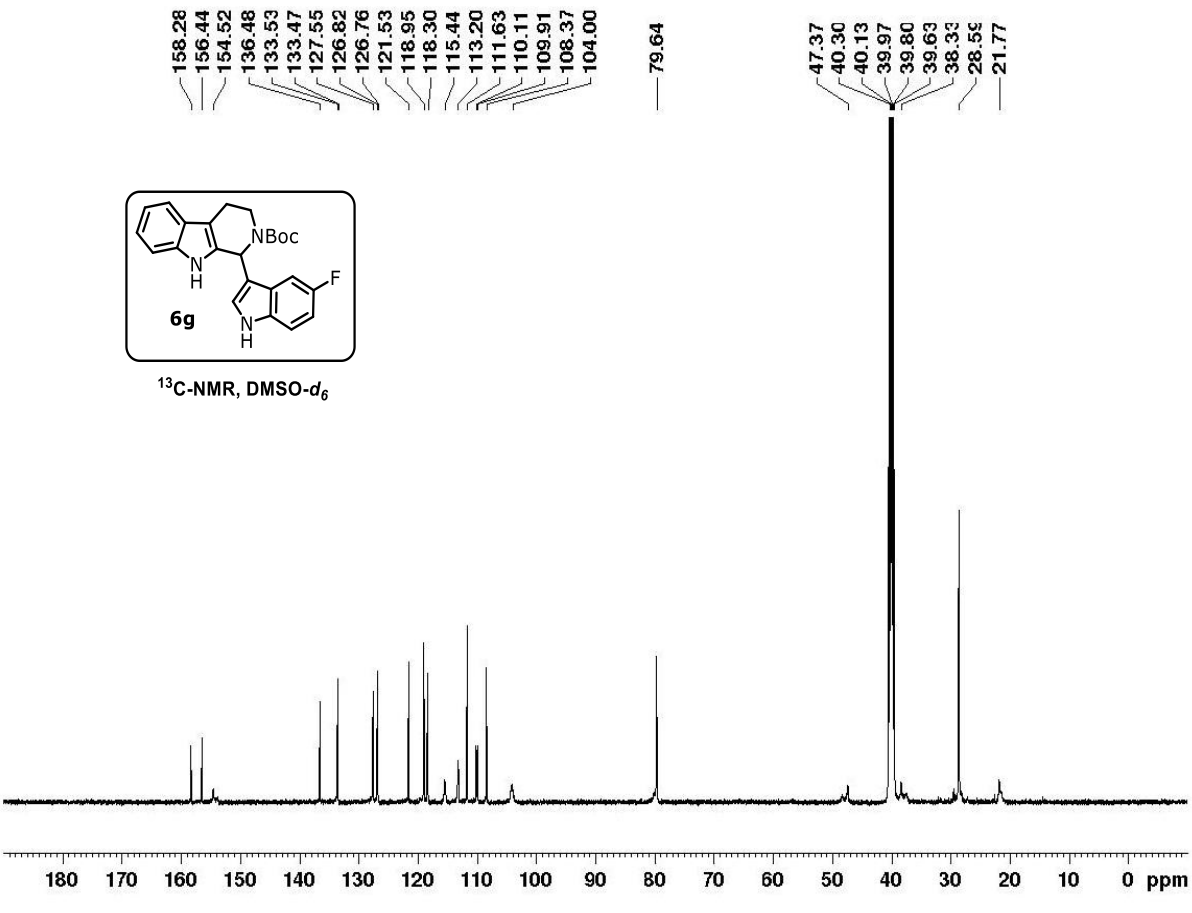

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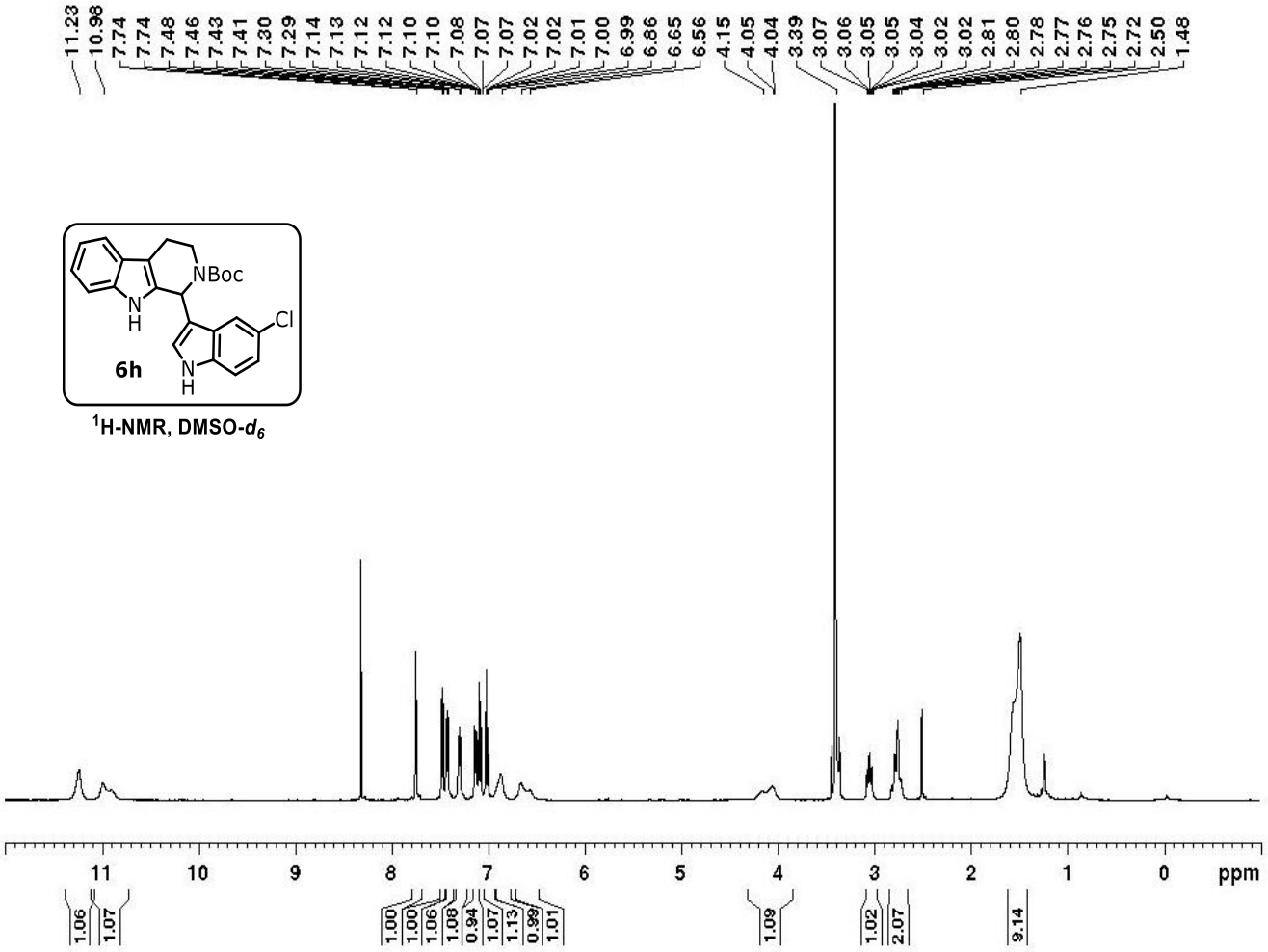

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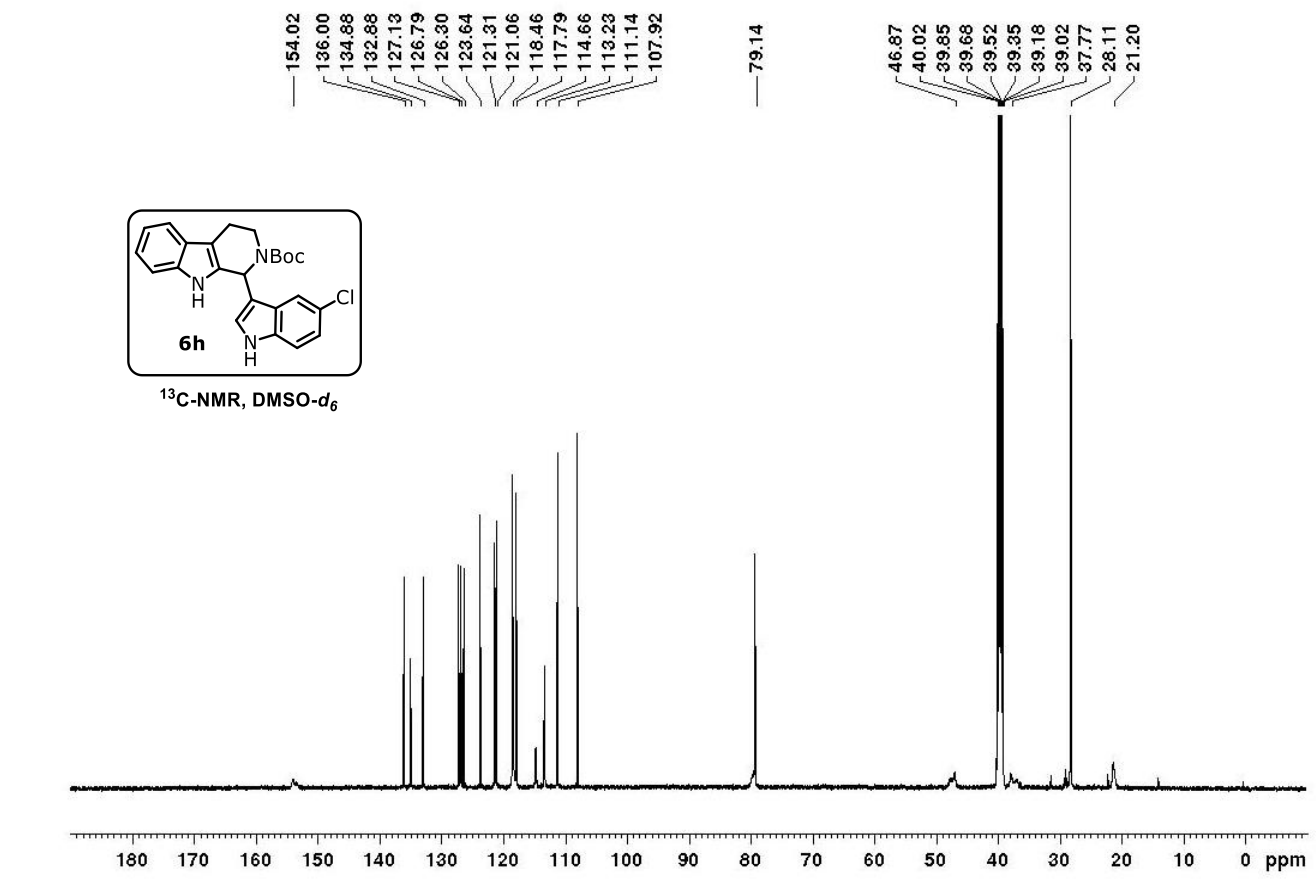

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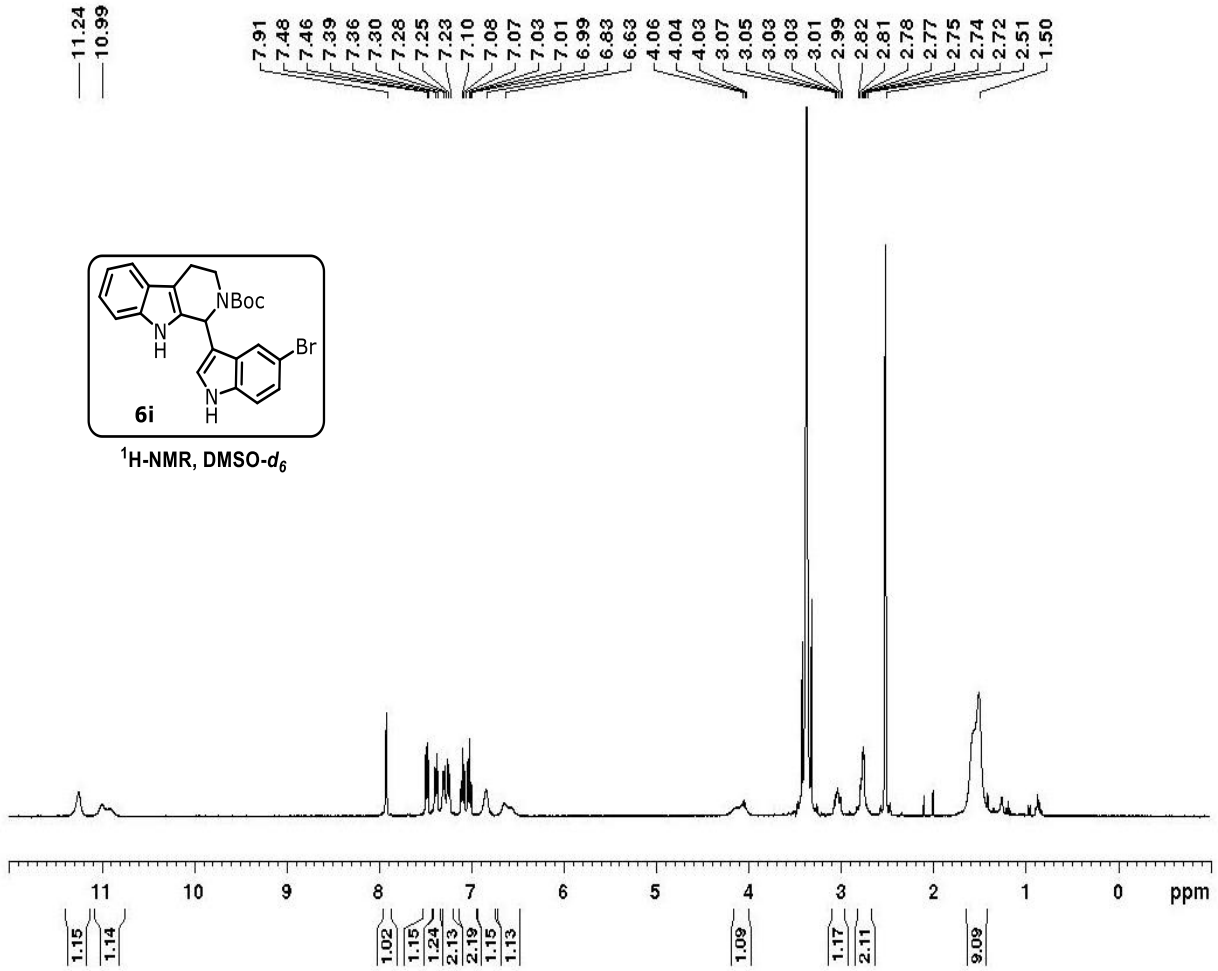

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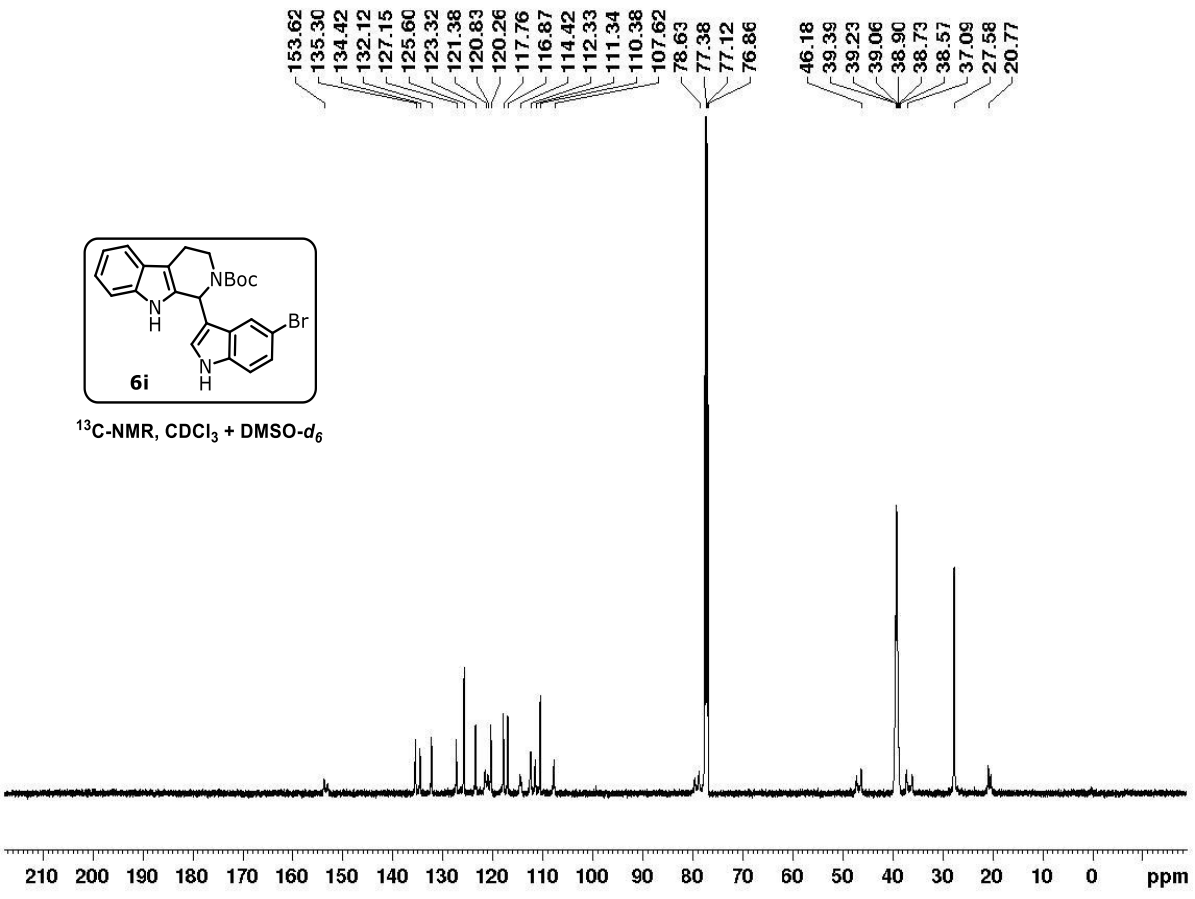
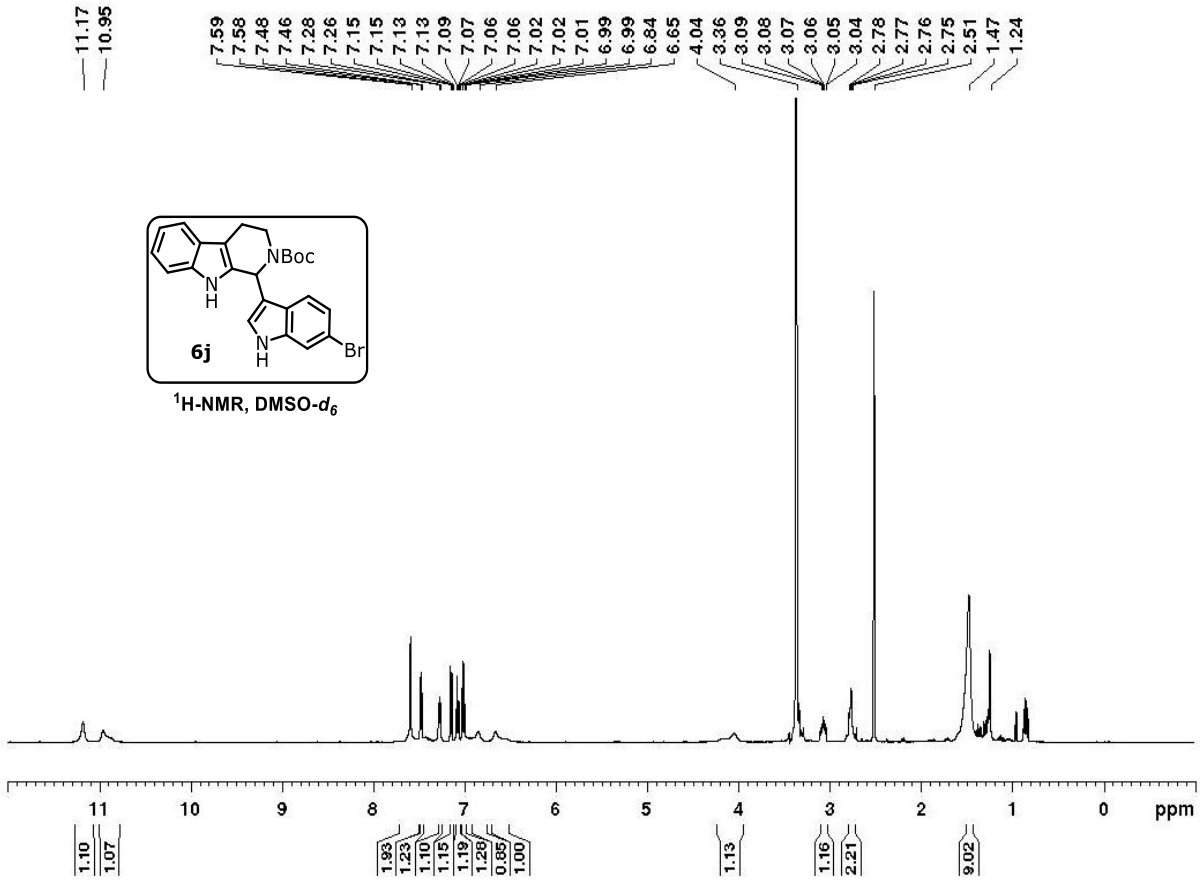


^{13}C-NMR, $CDCl_3$ + DMSO-d_6



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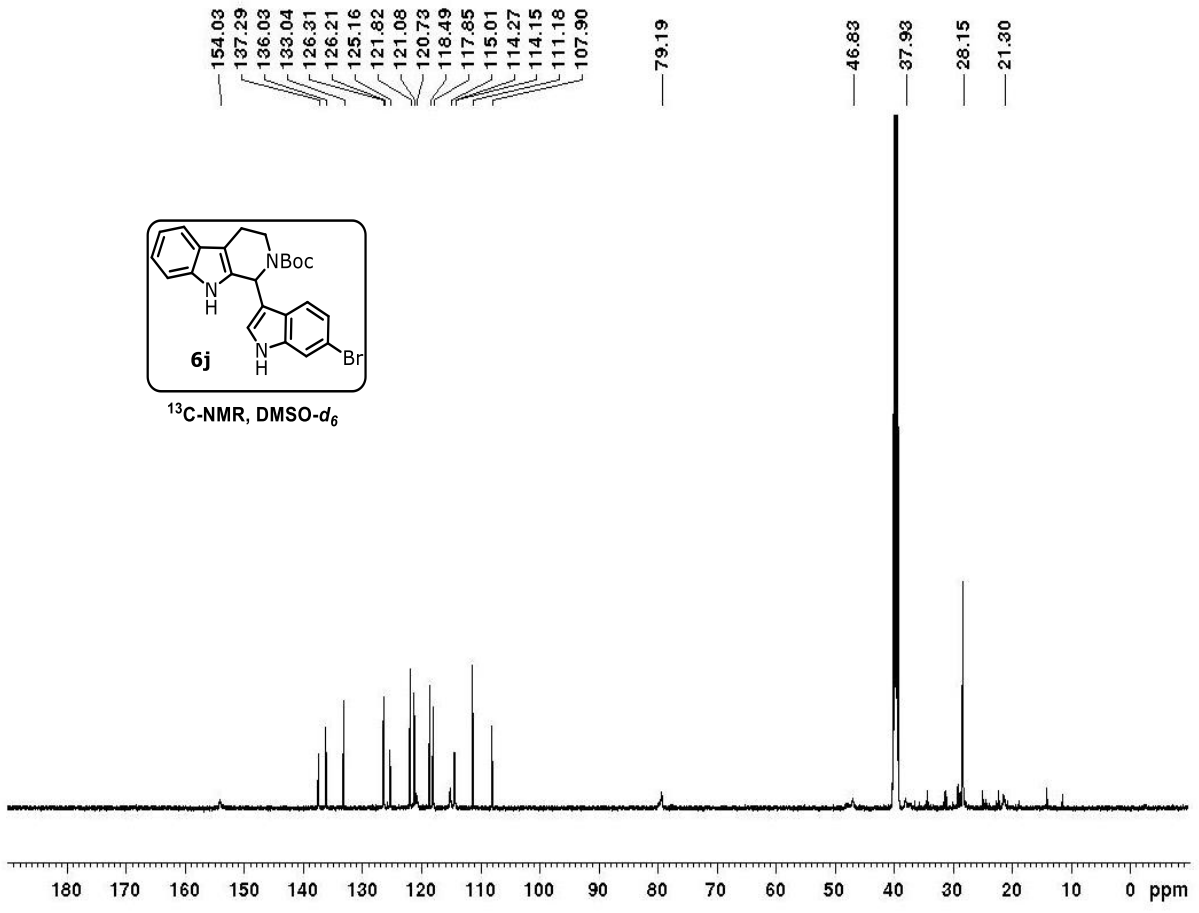
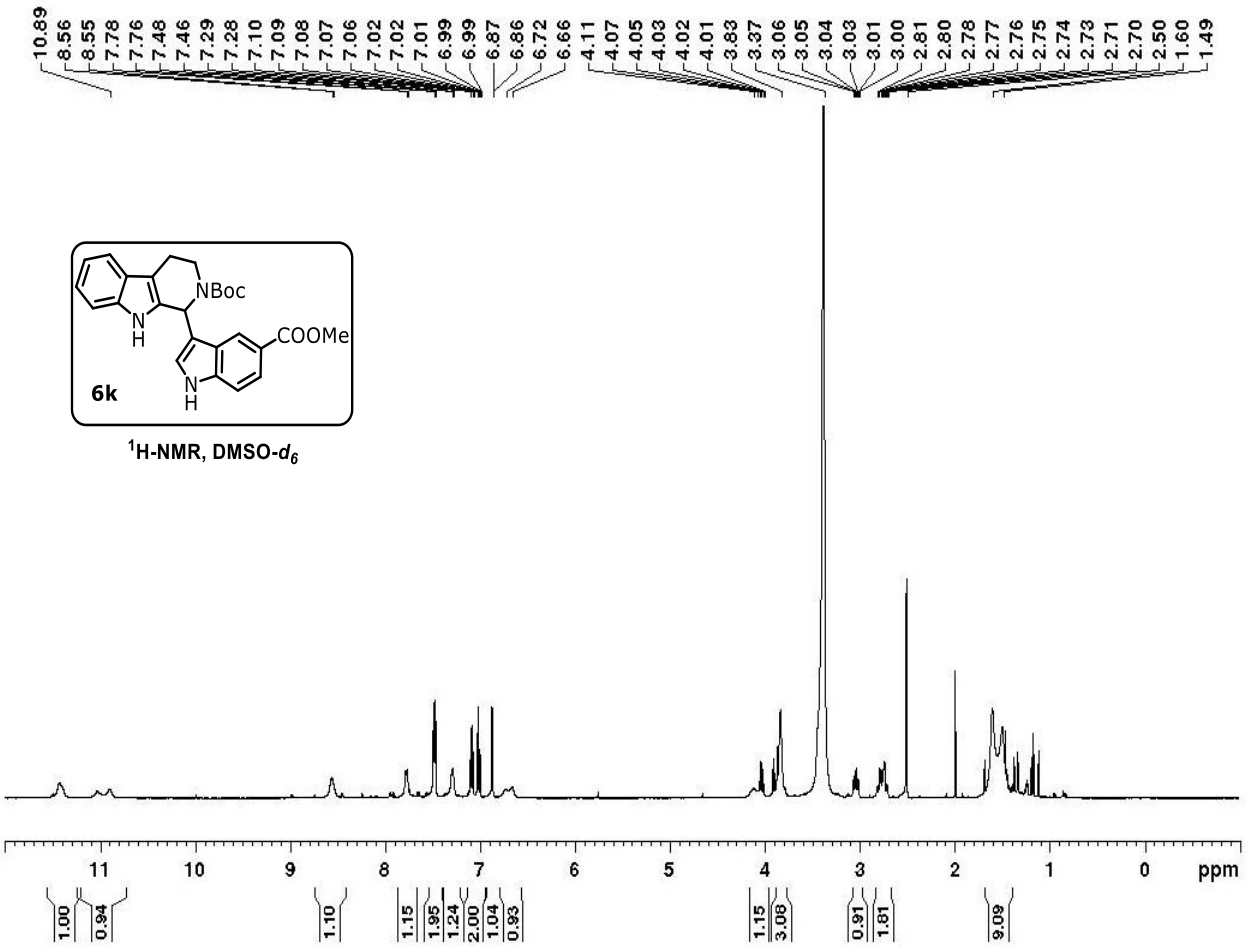


^{13}C-NMR, DMSO-d_6



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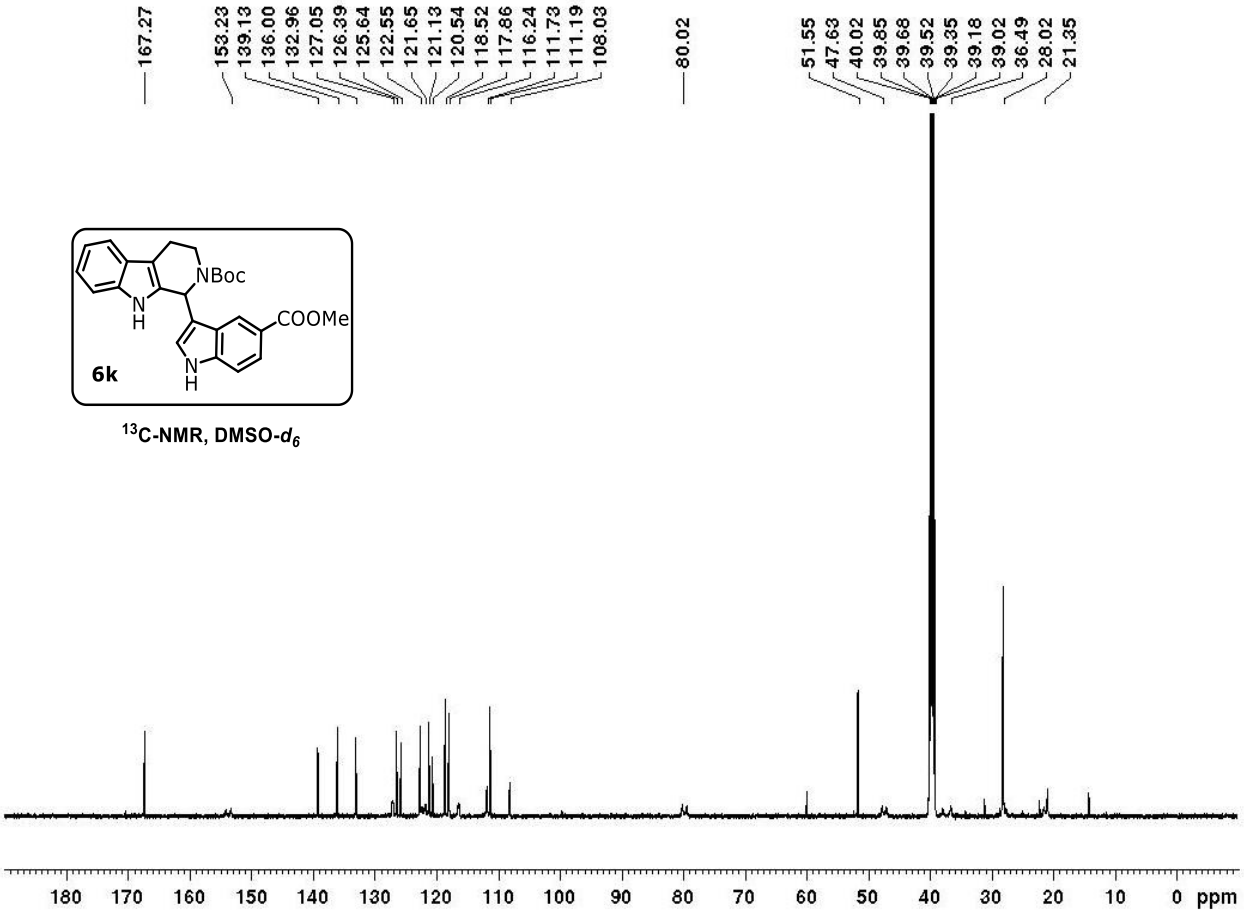

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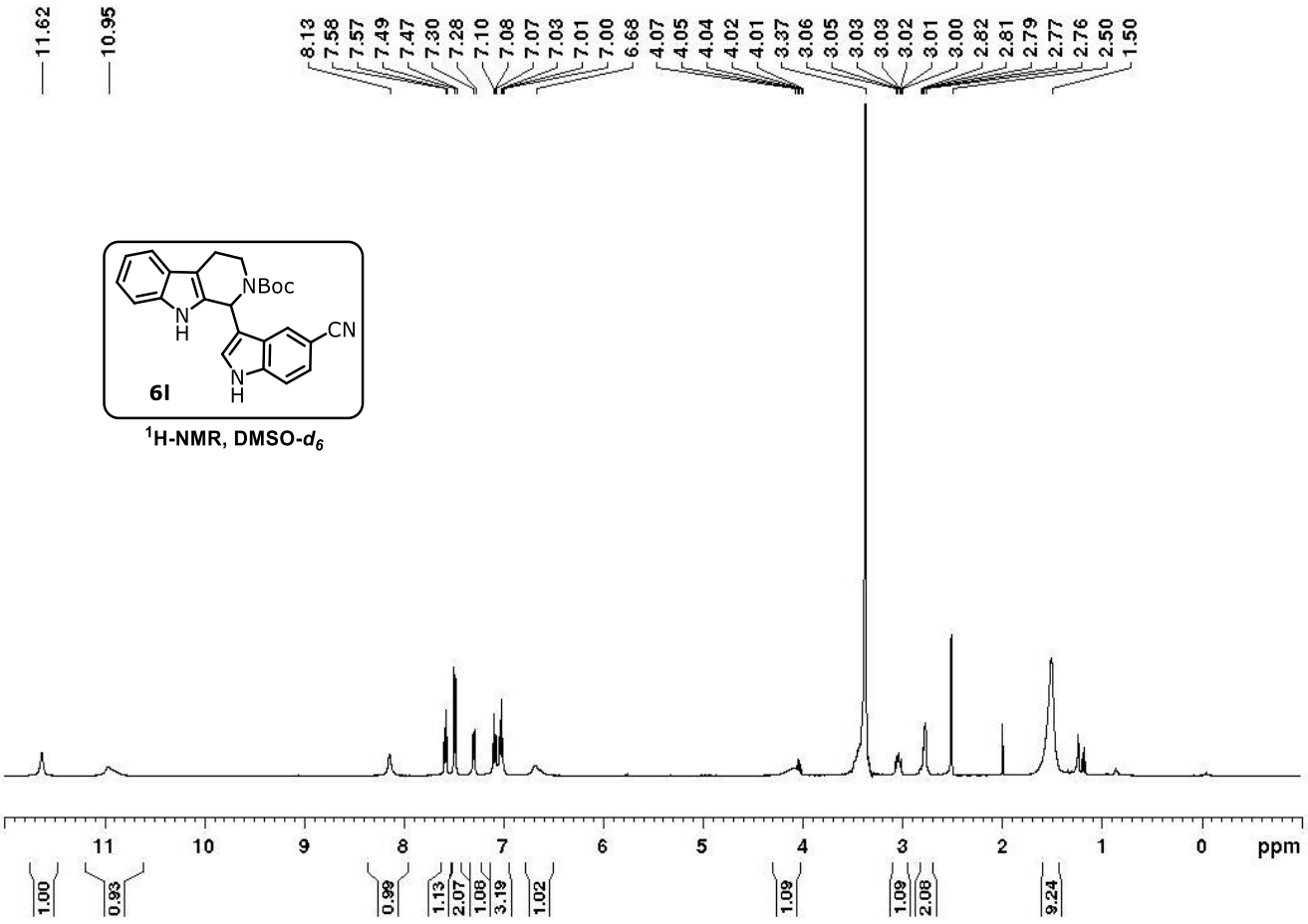

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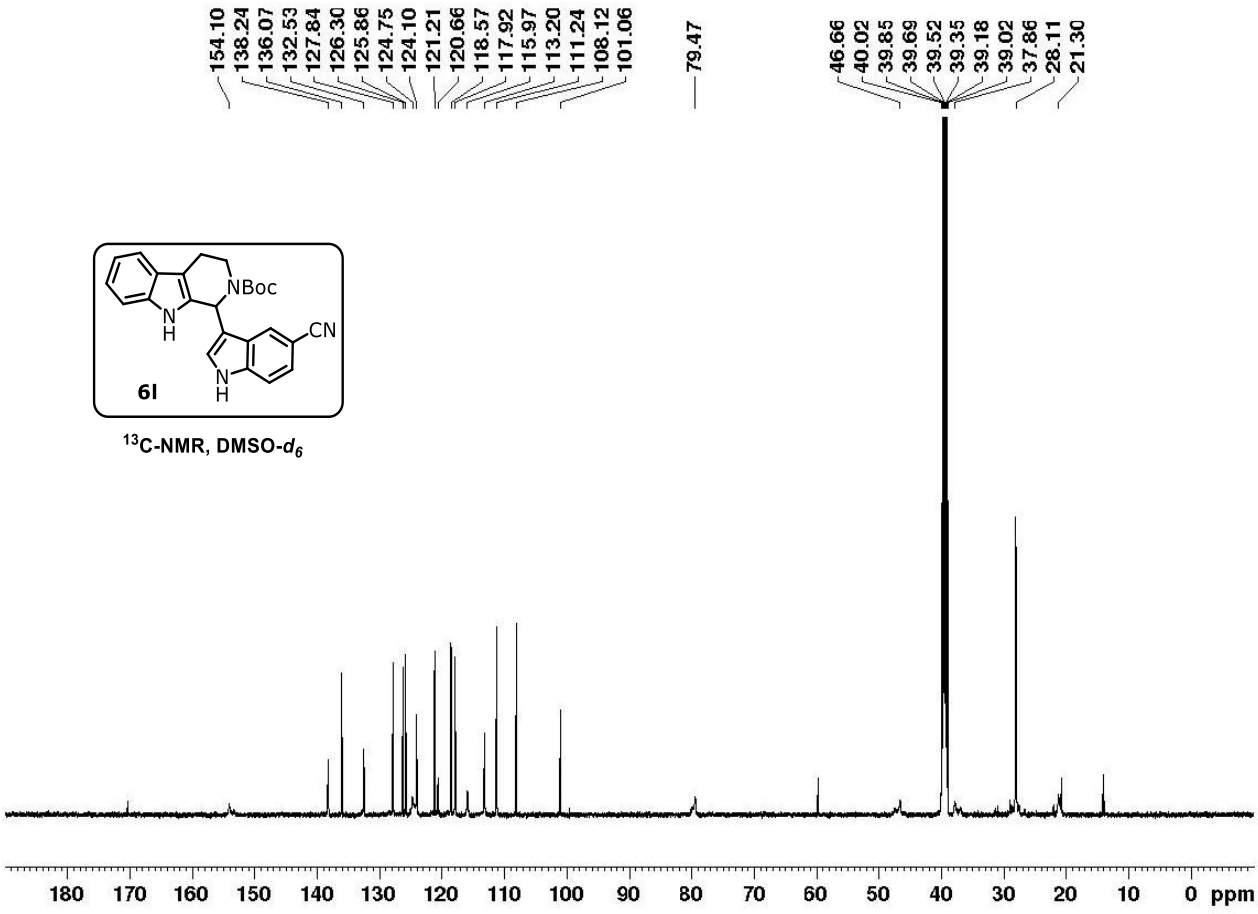

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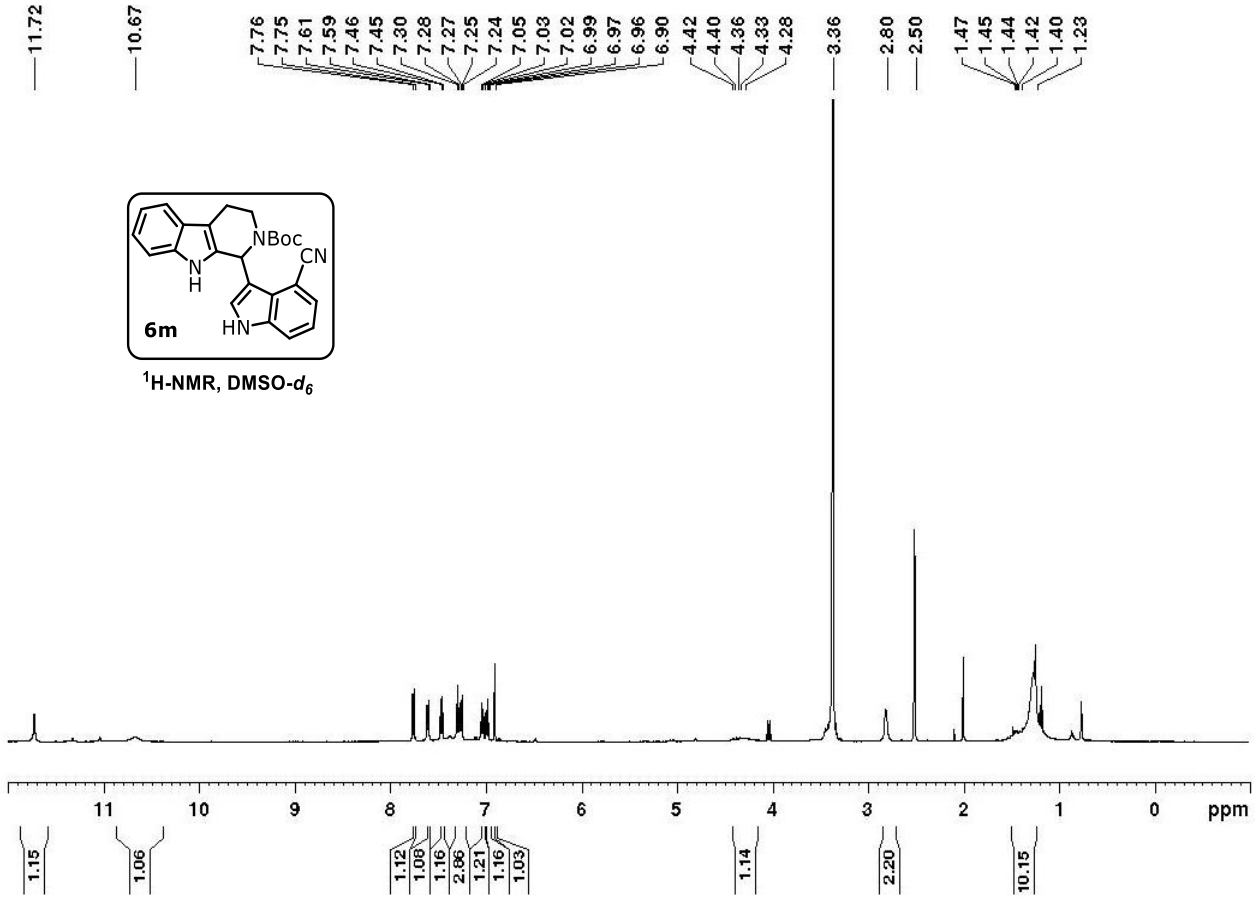

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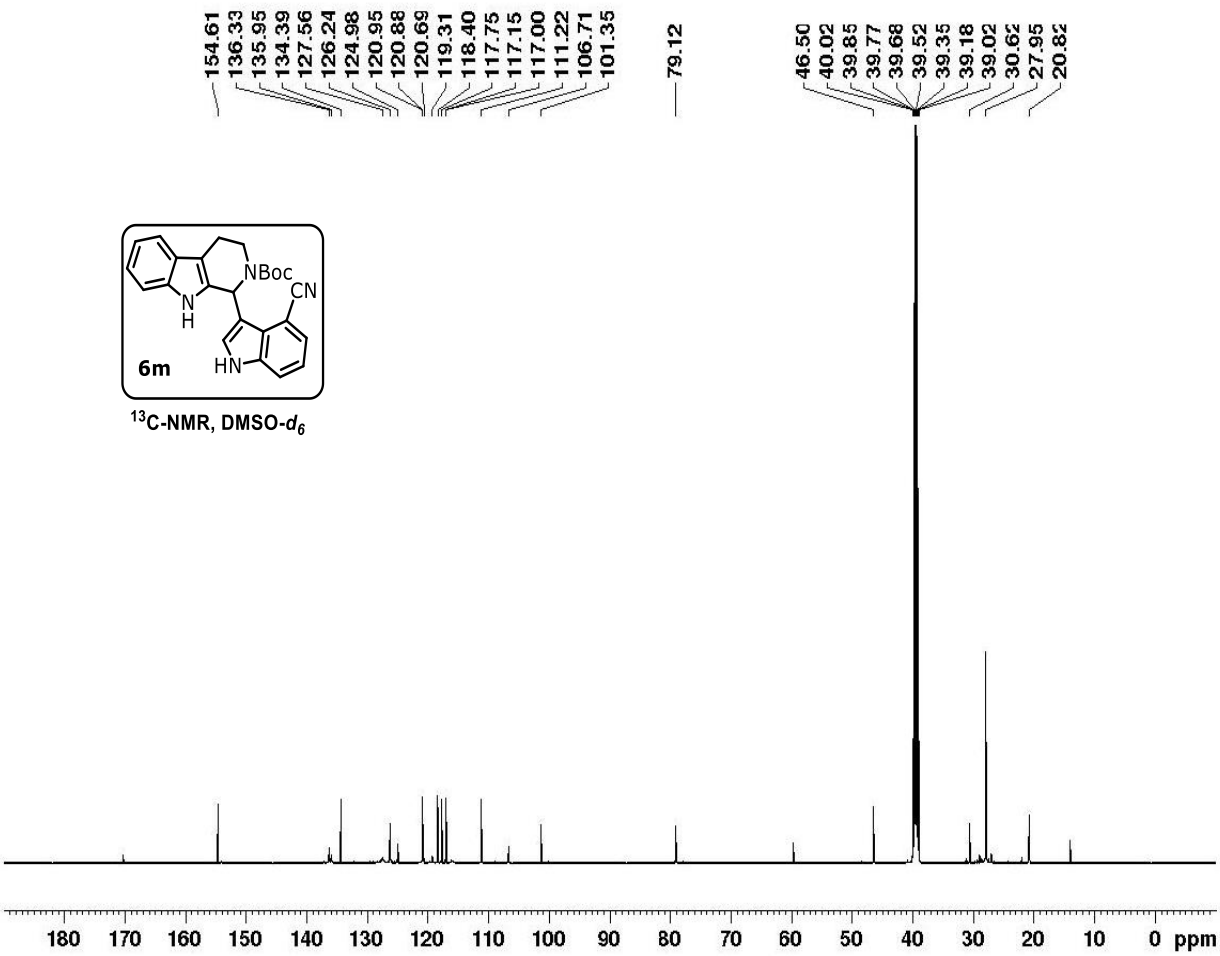

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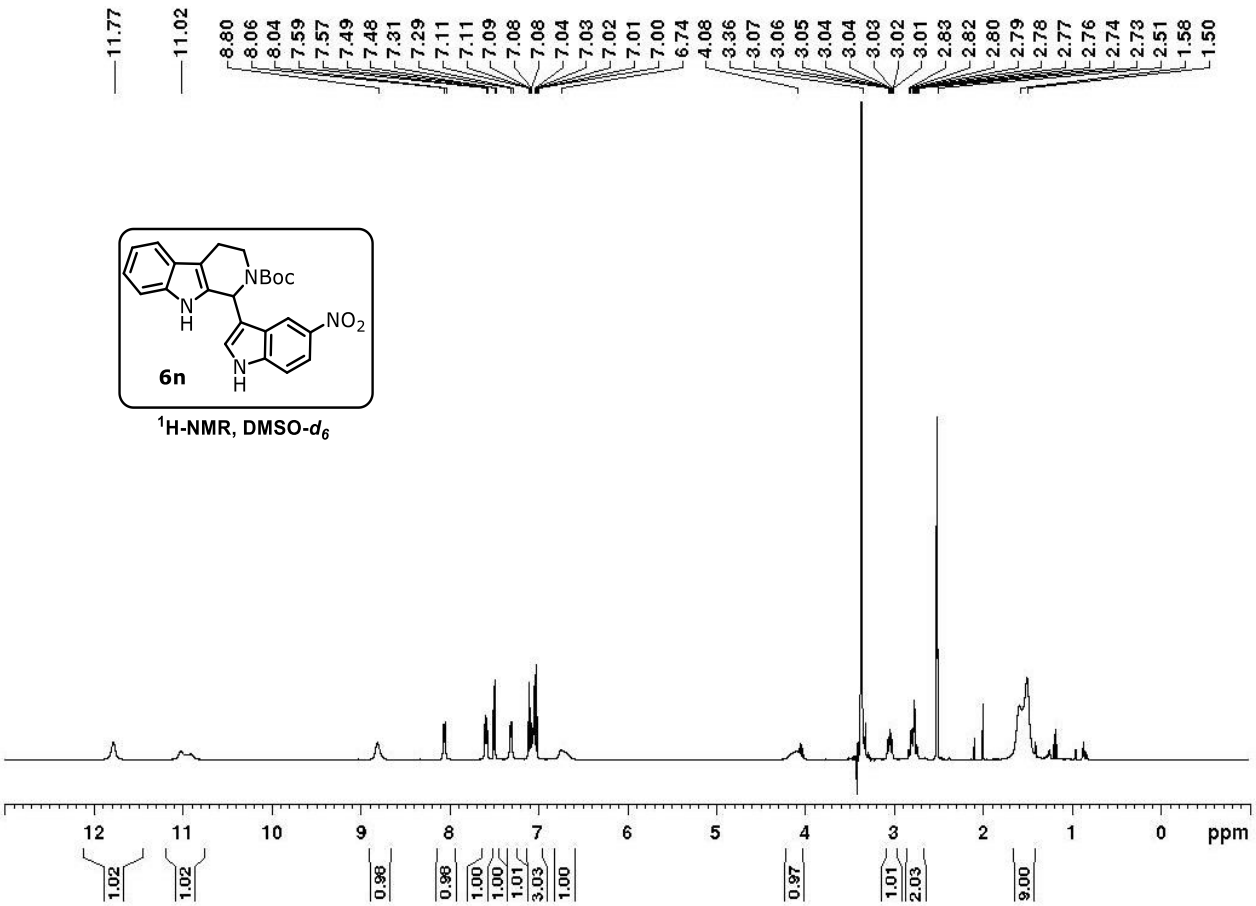

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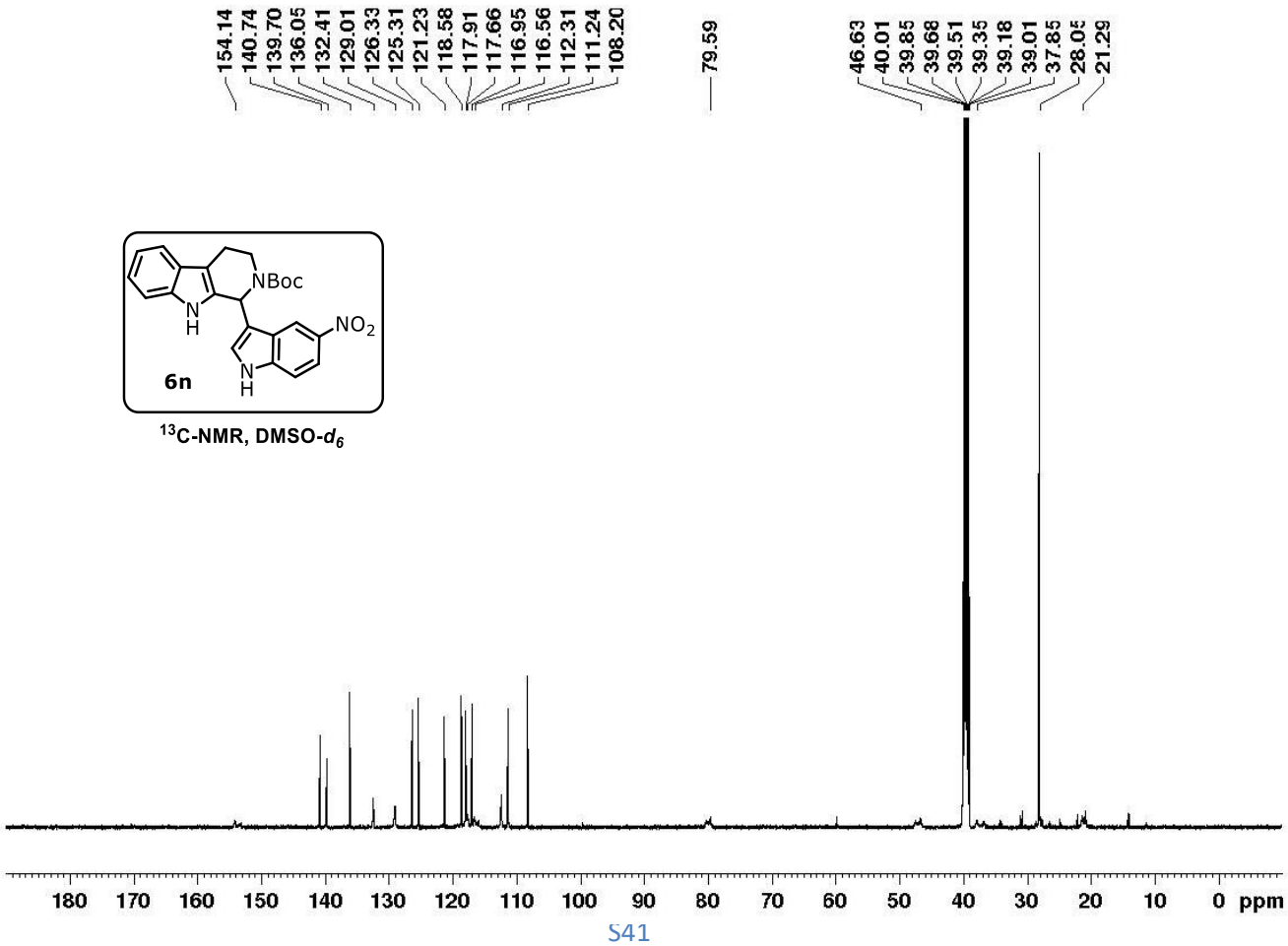

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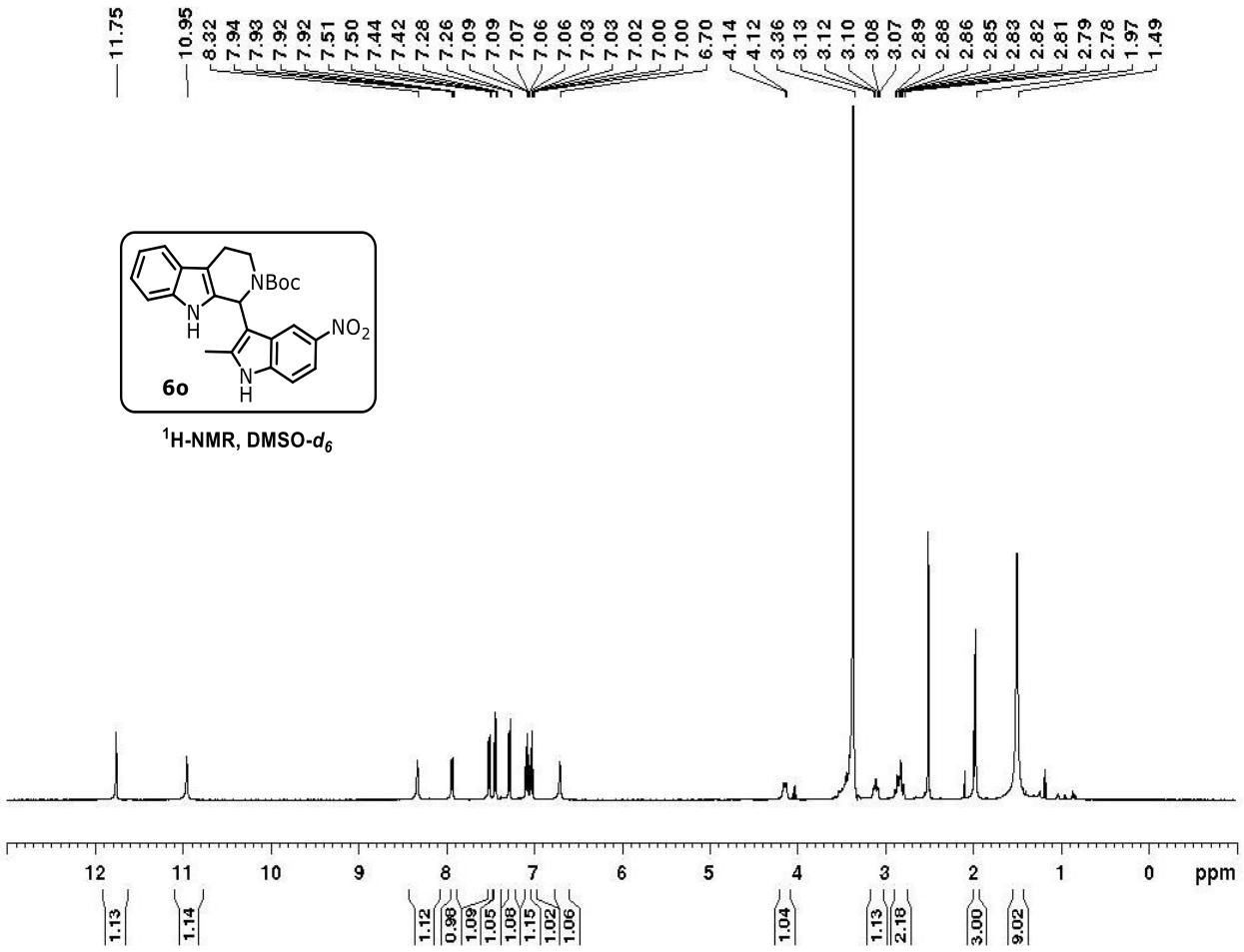
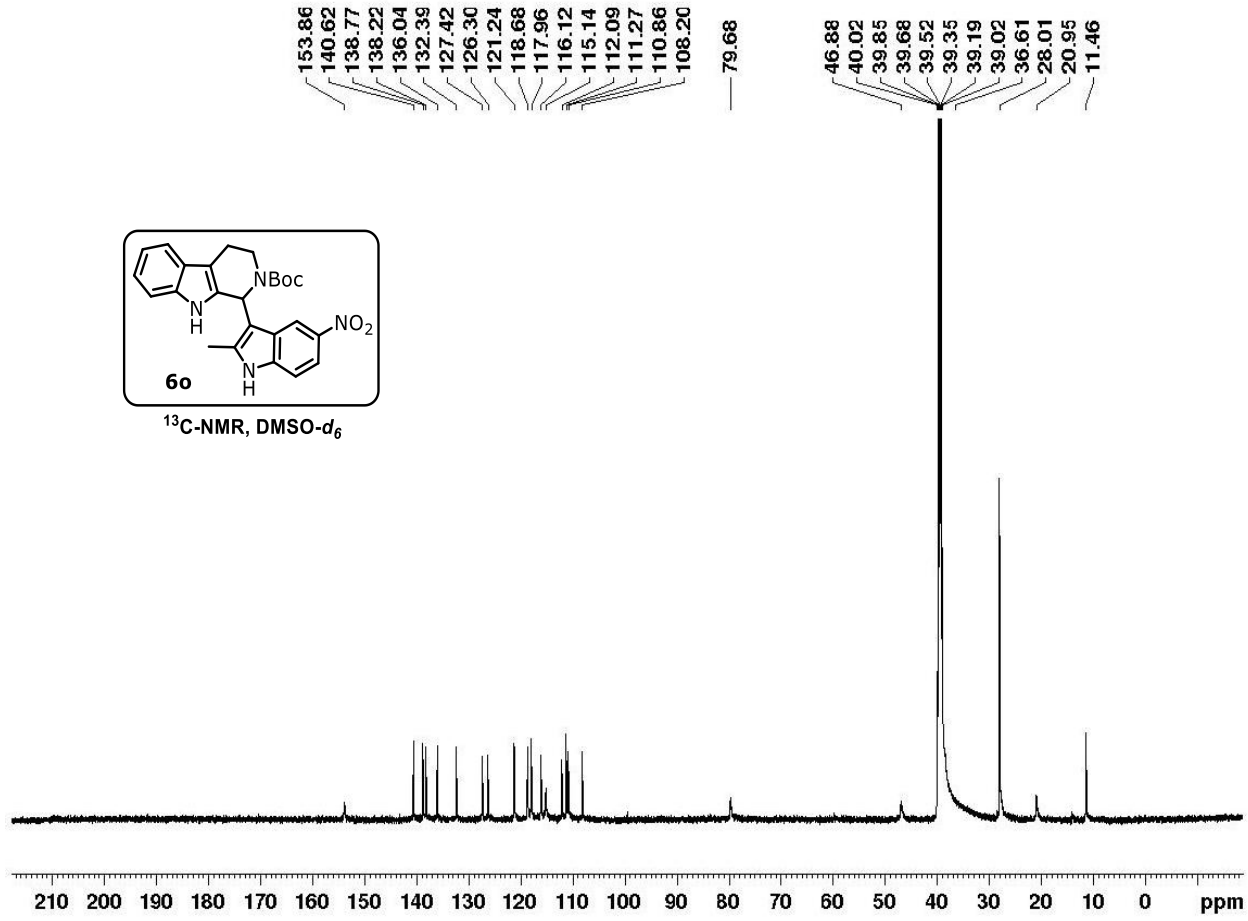


^{1}H-NMR, DMSO-d_6



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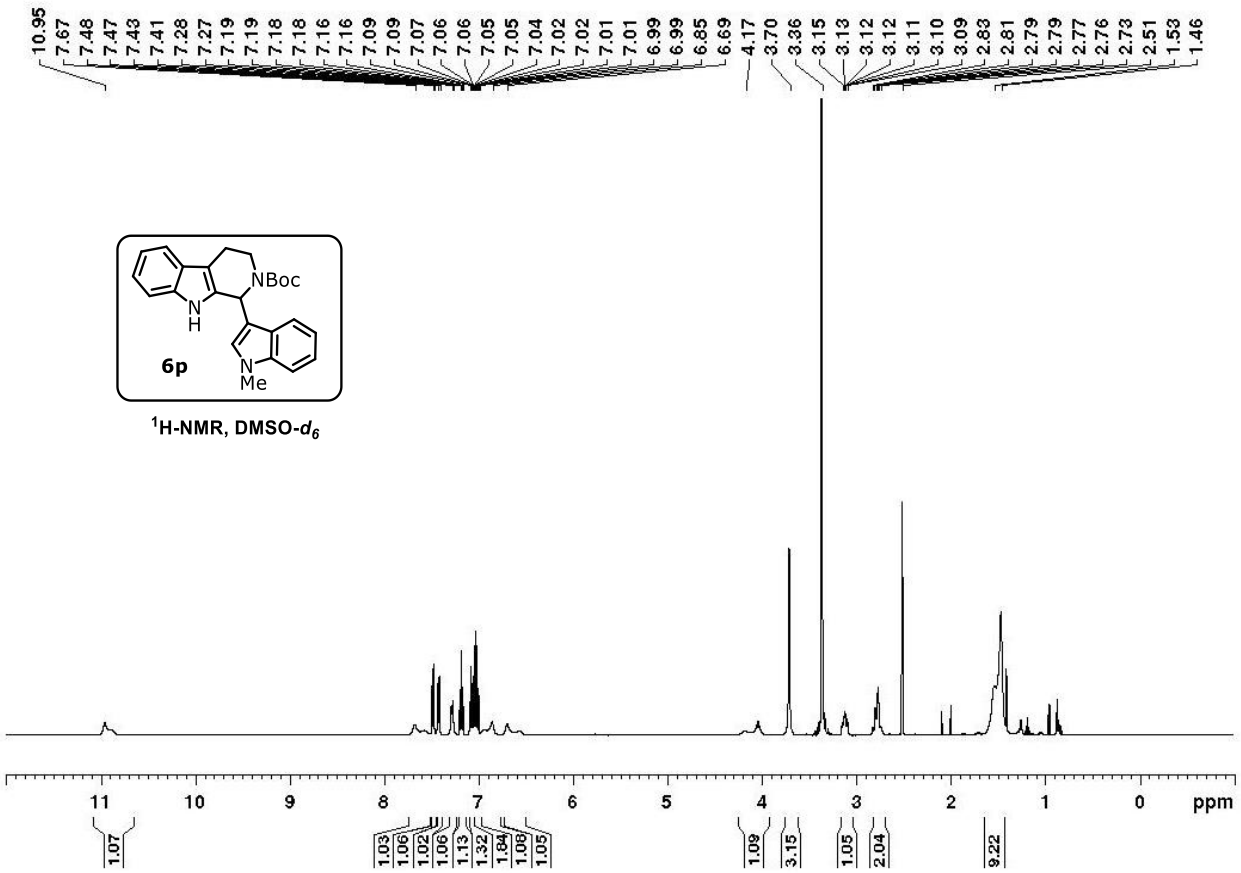

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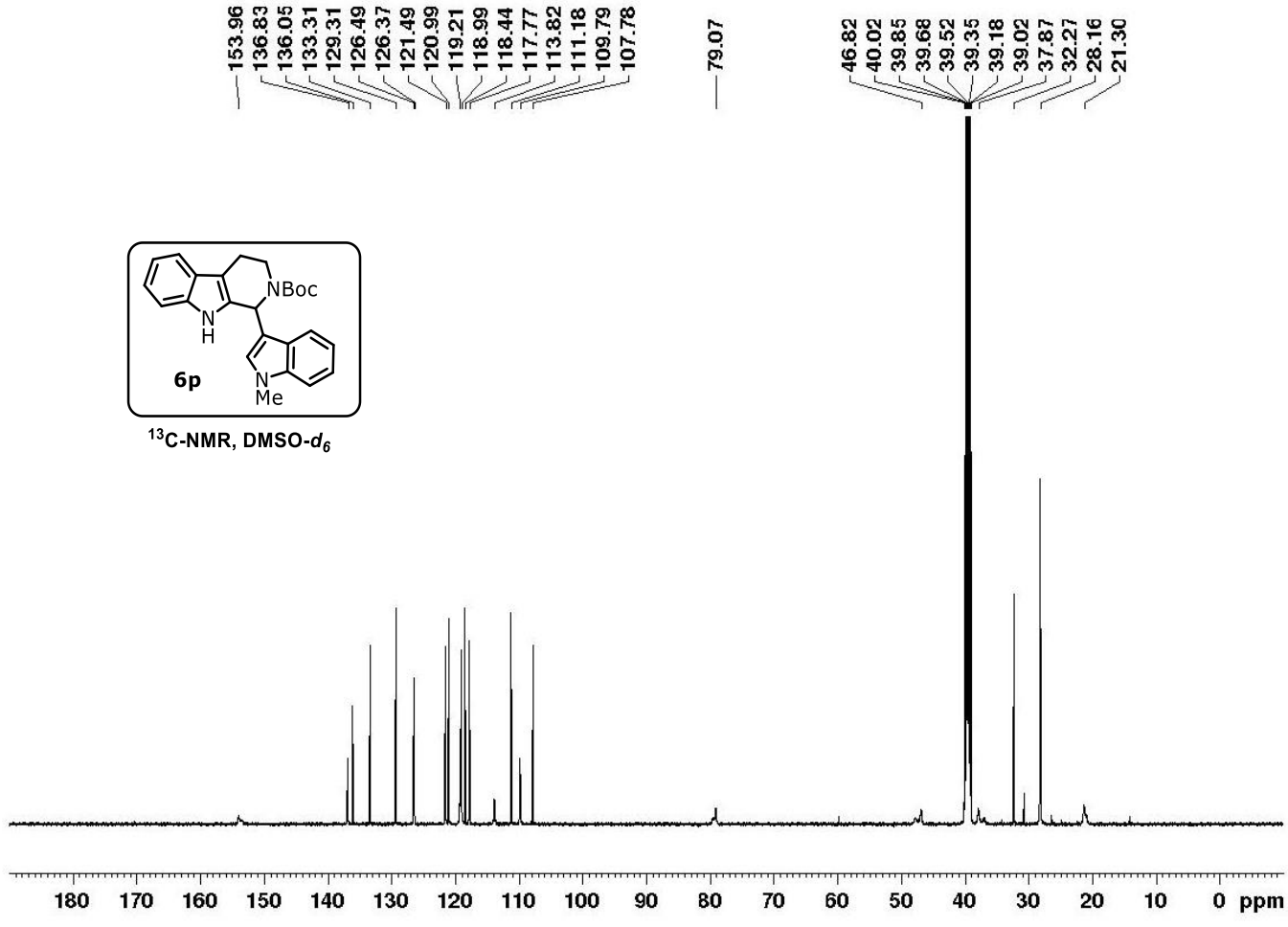

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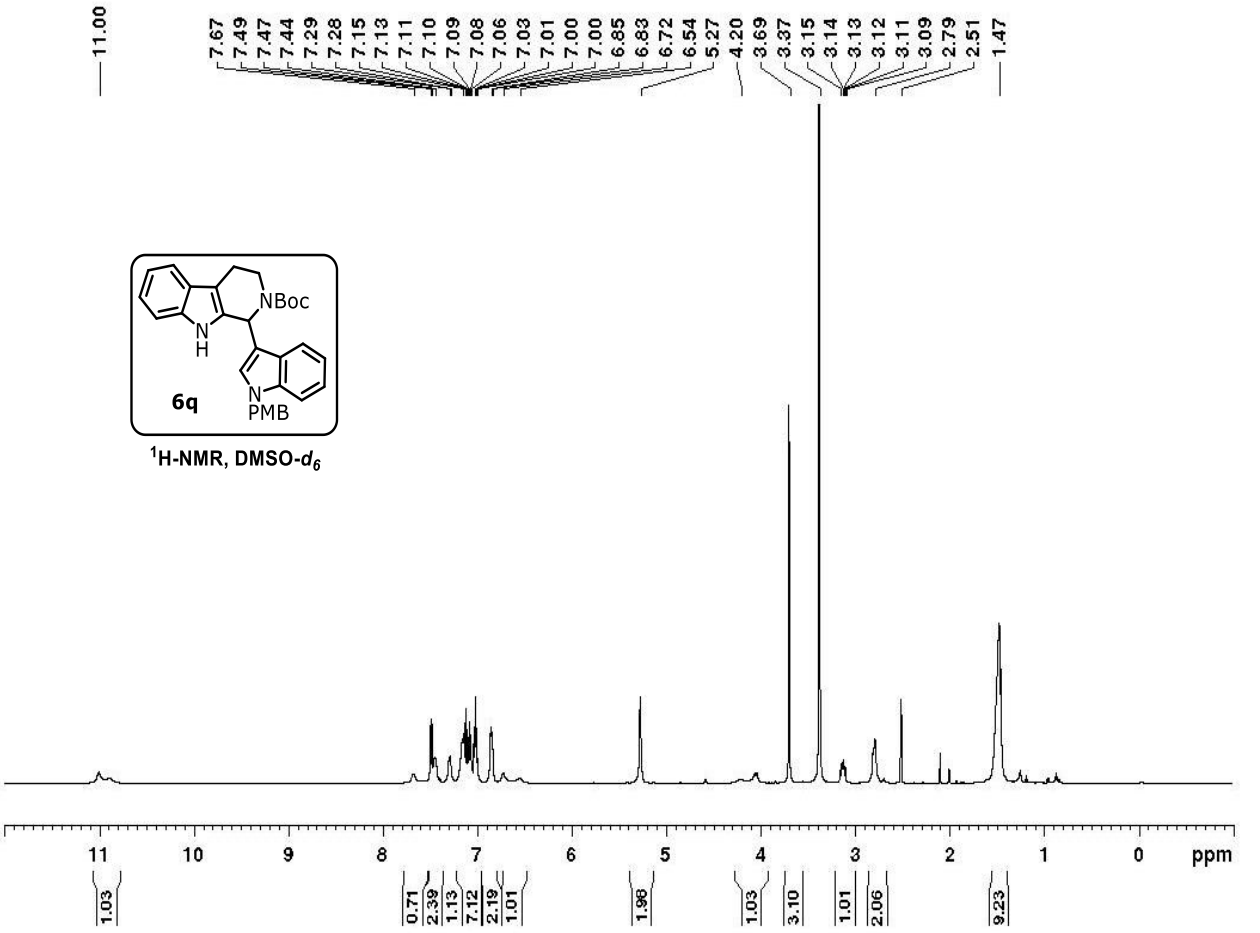

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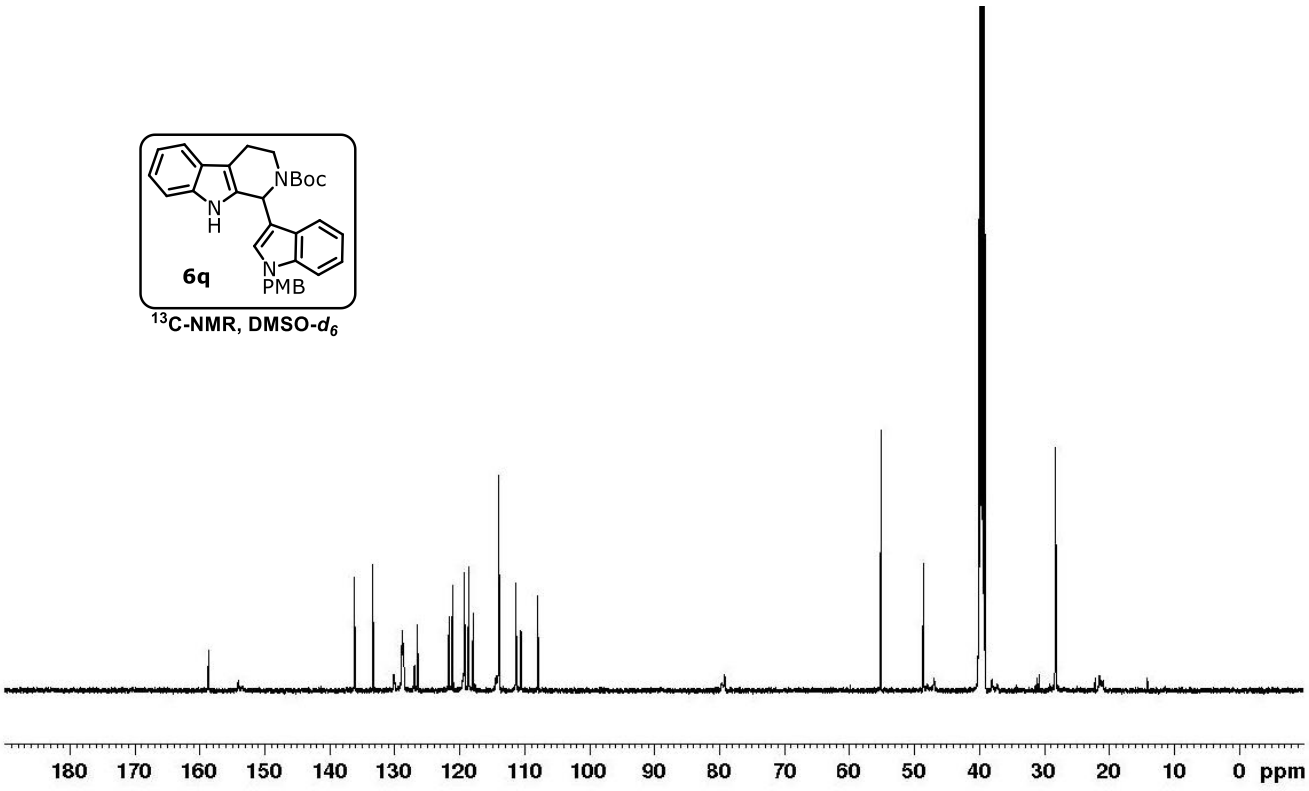

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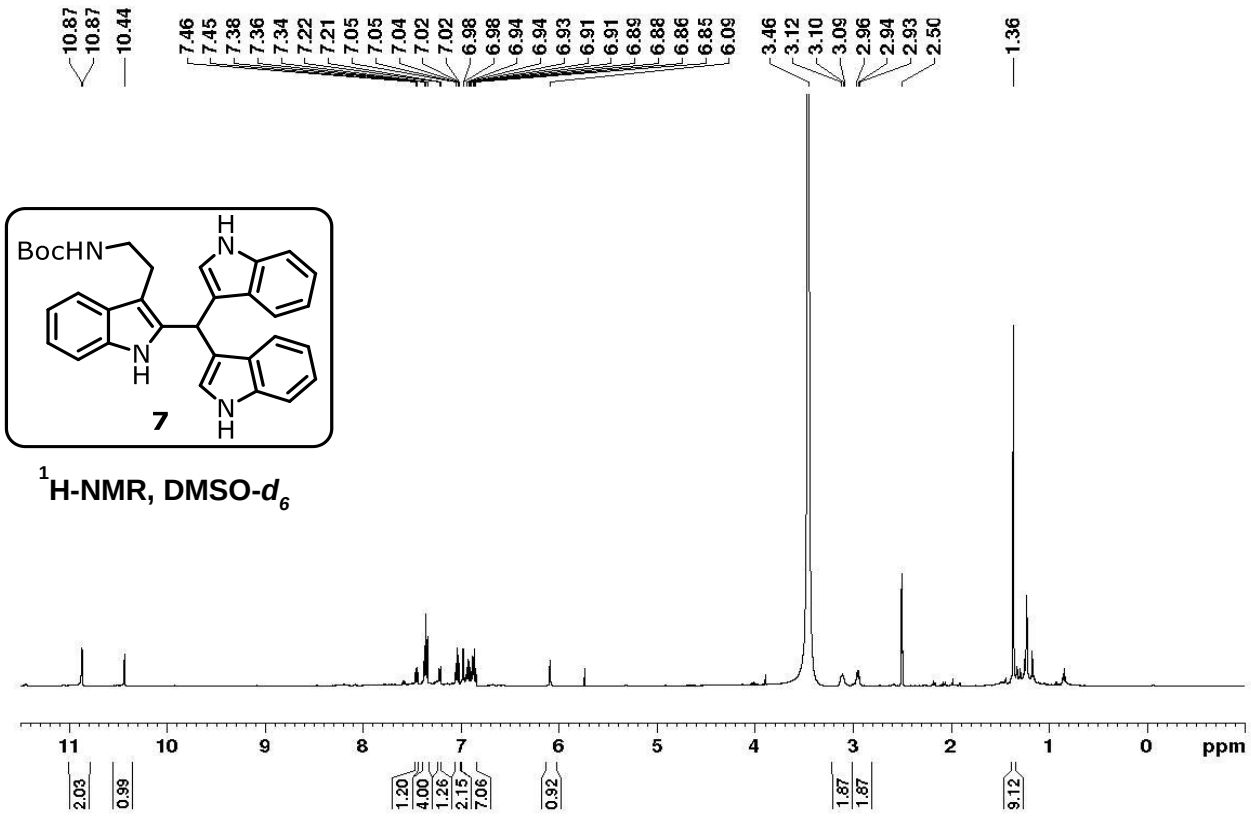

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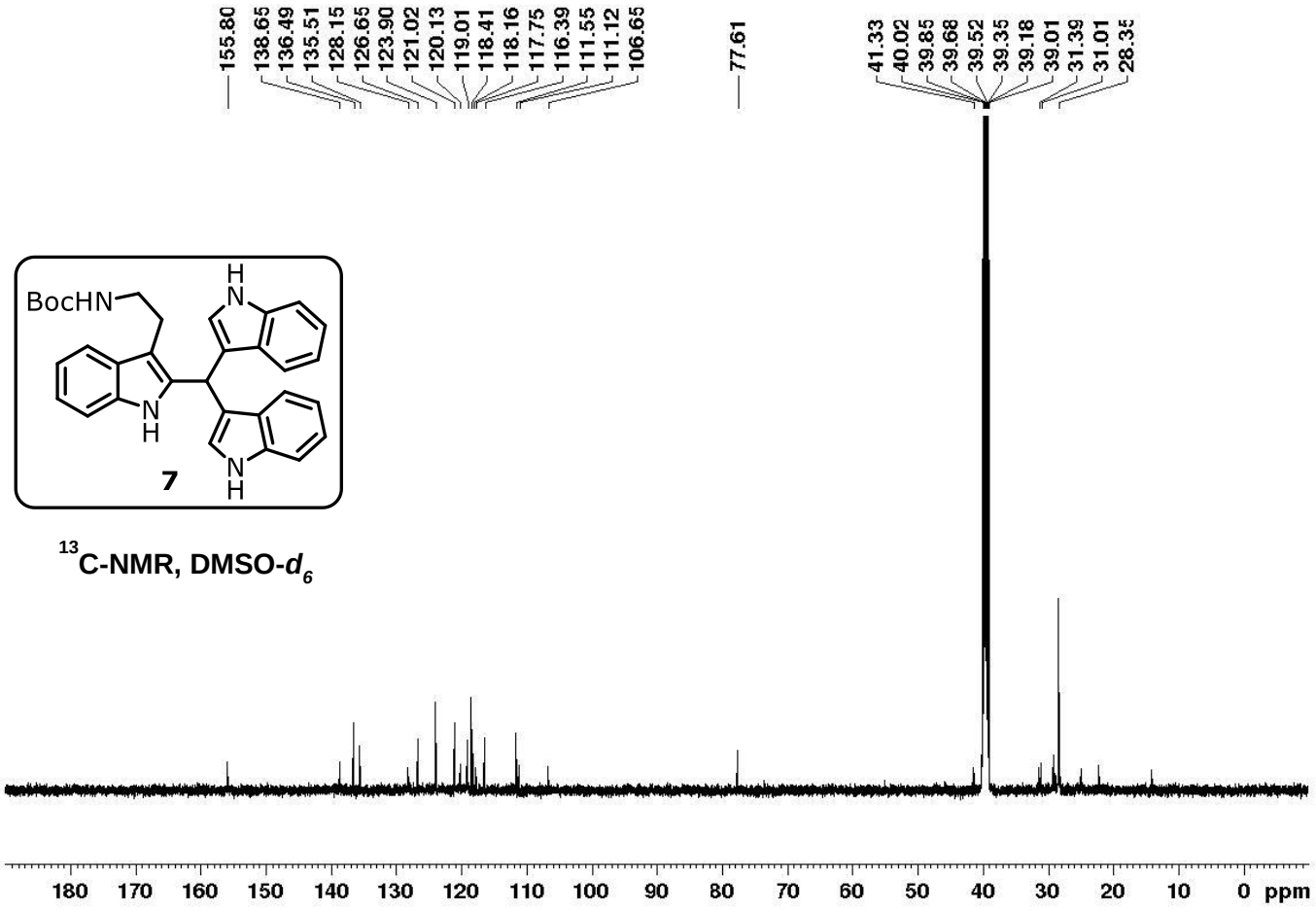

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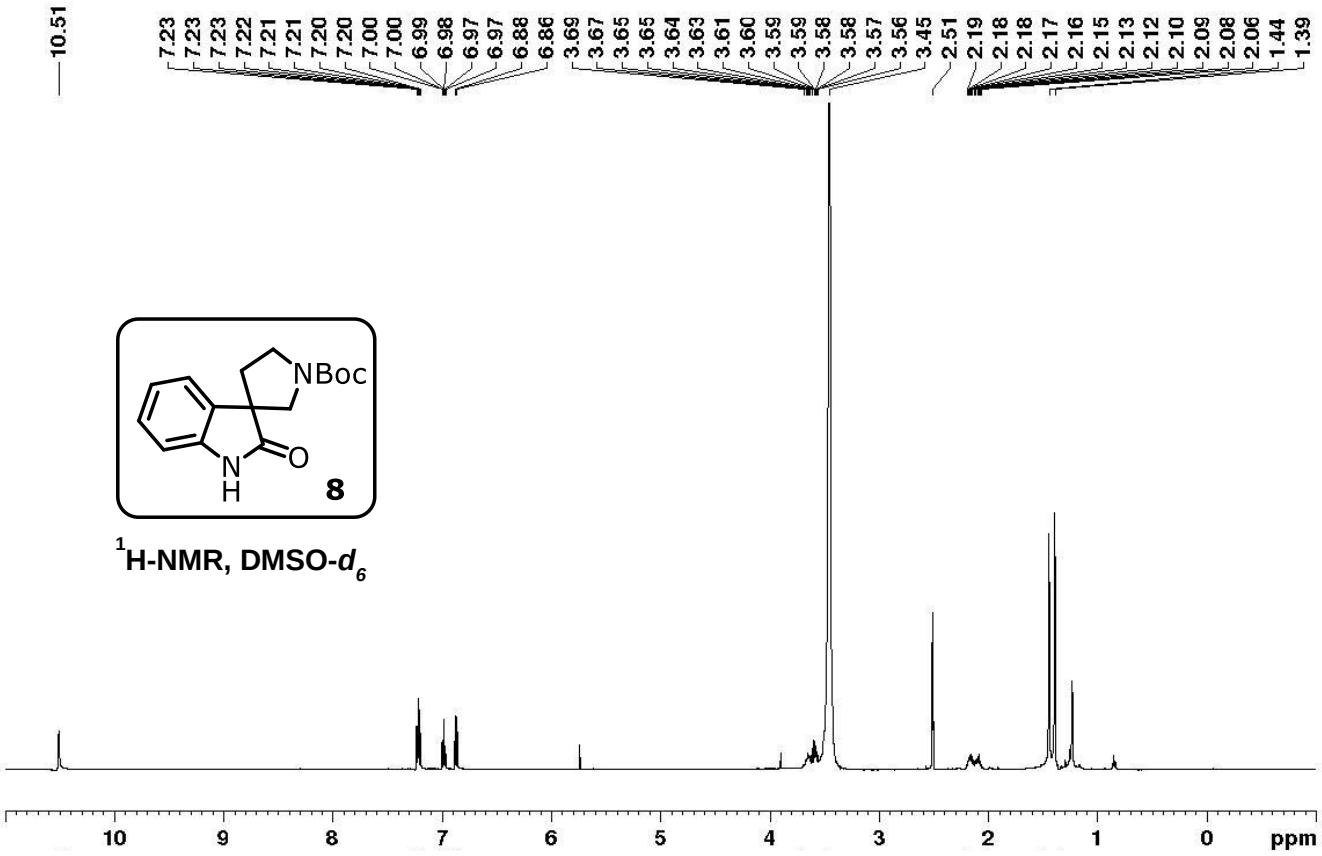

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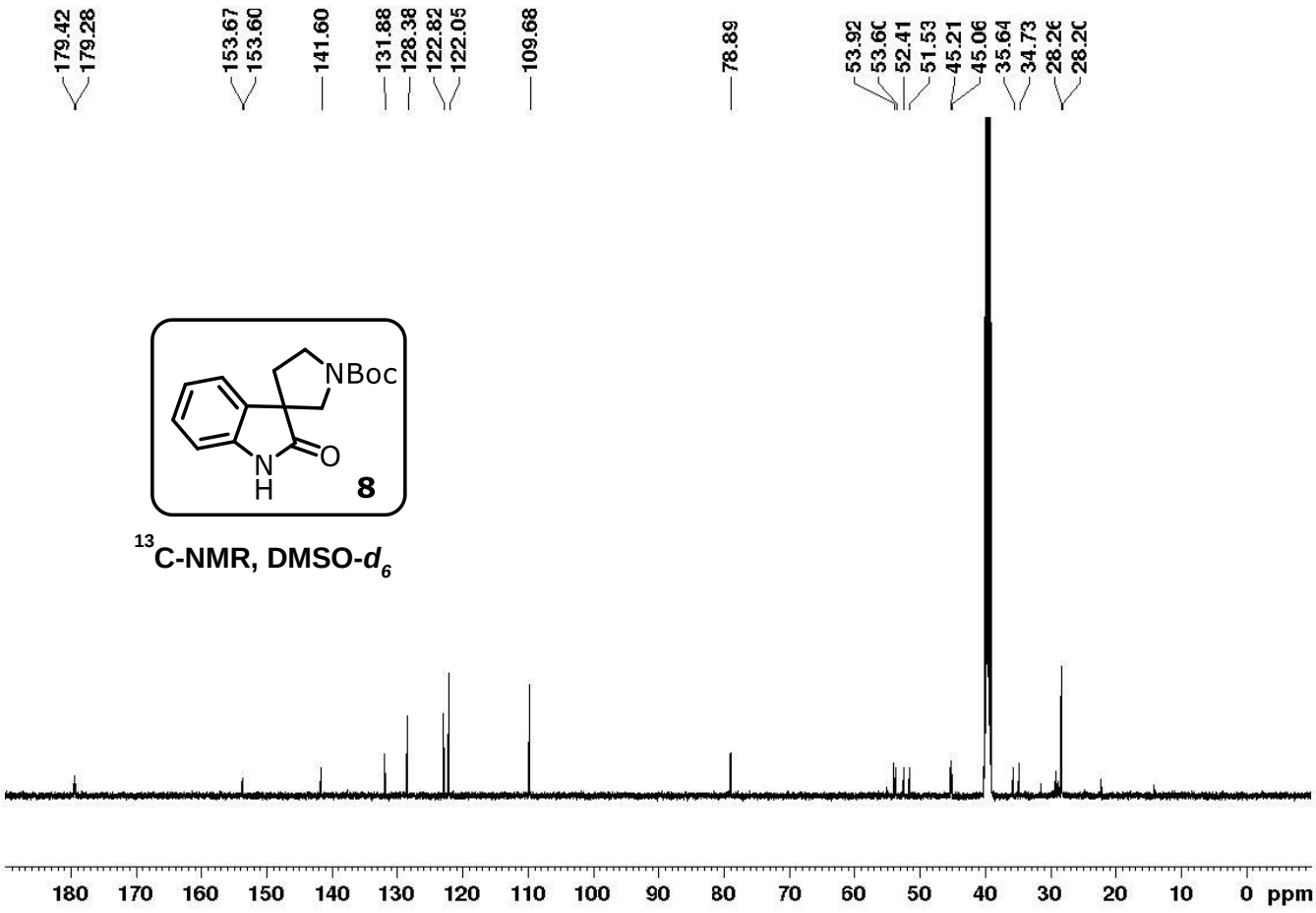

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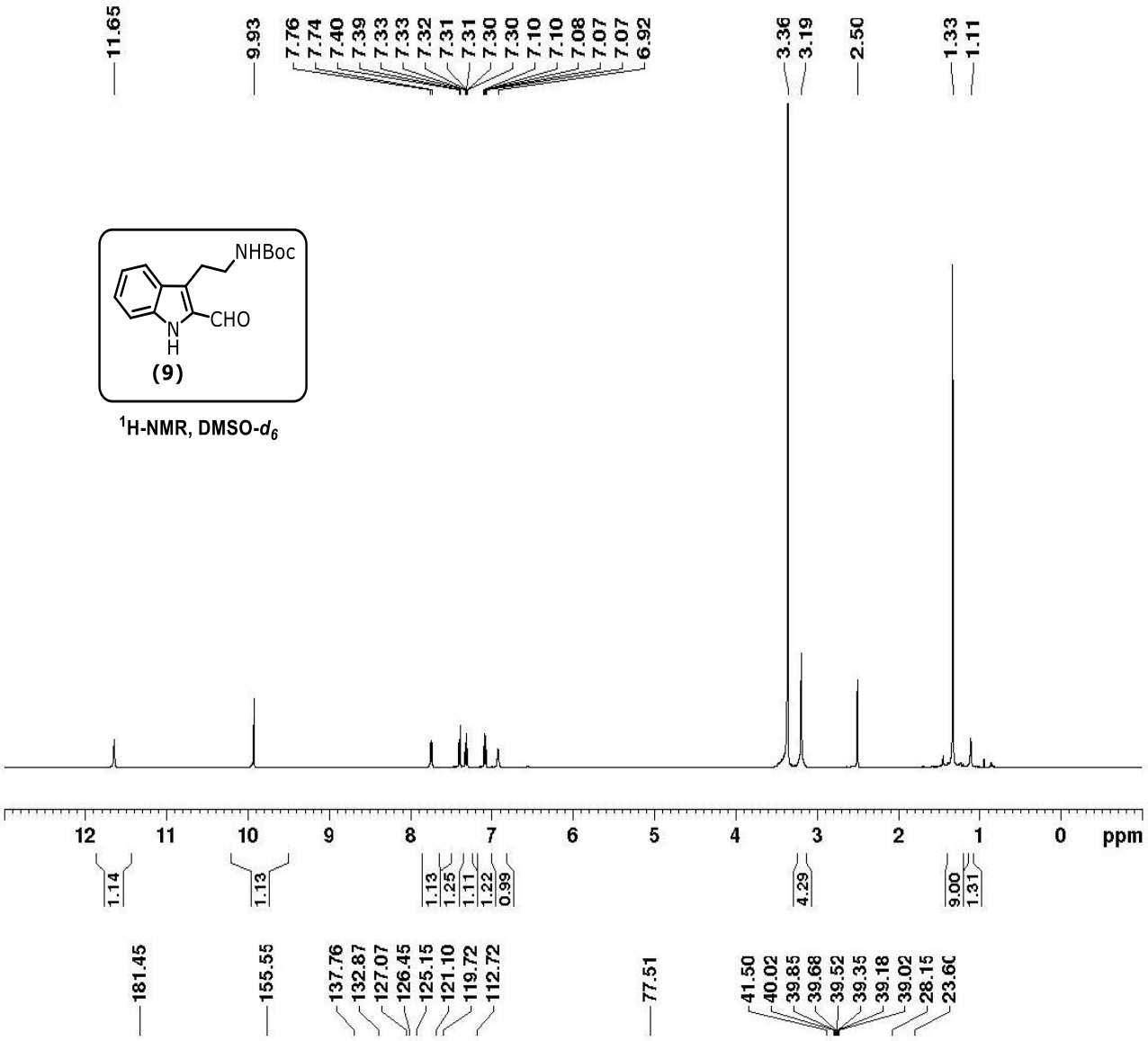

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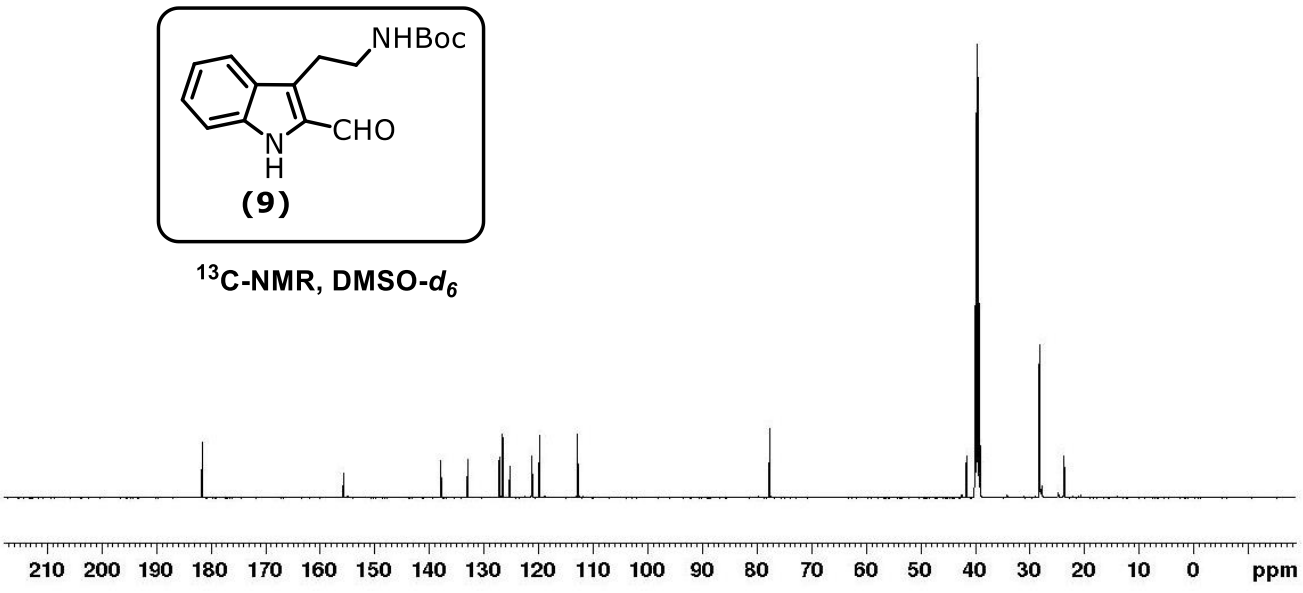

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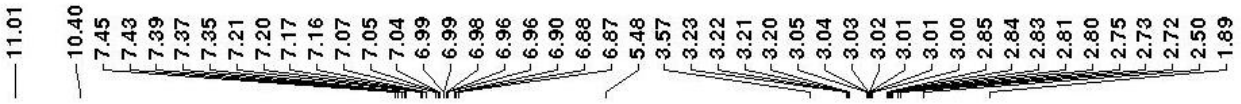
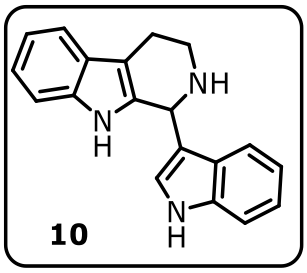
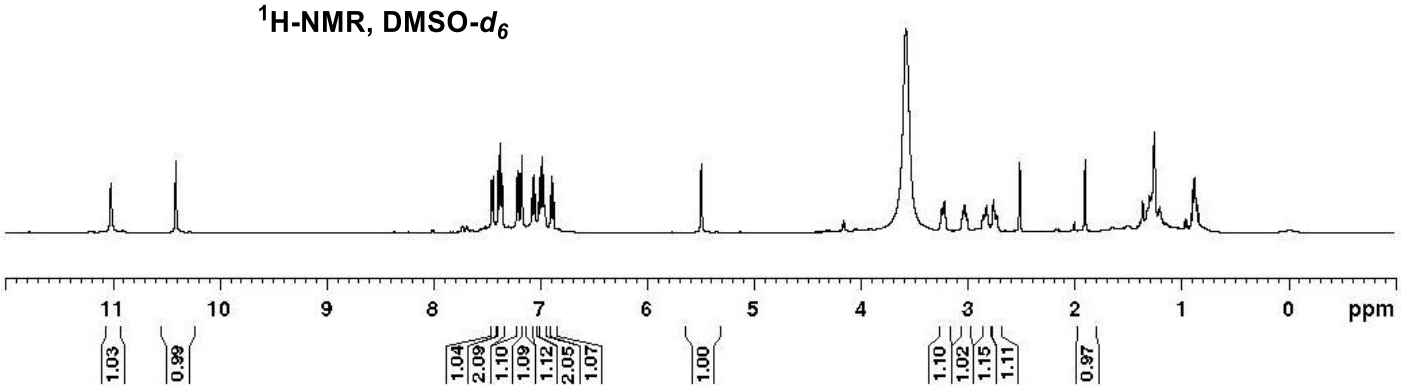
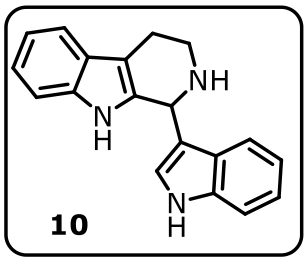


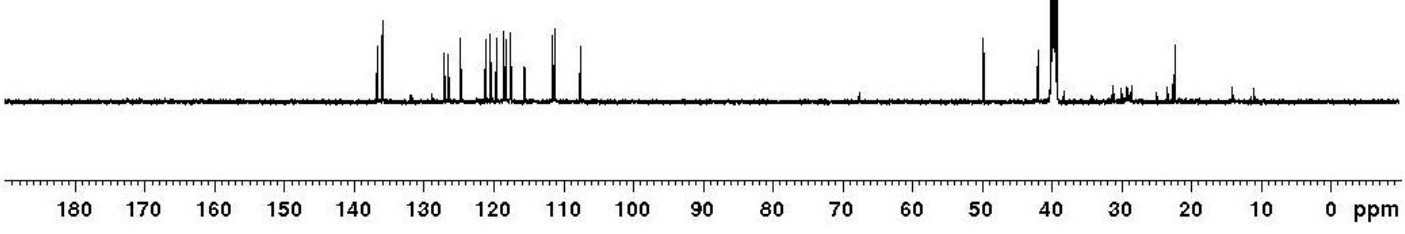


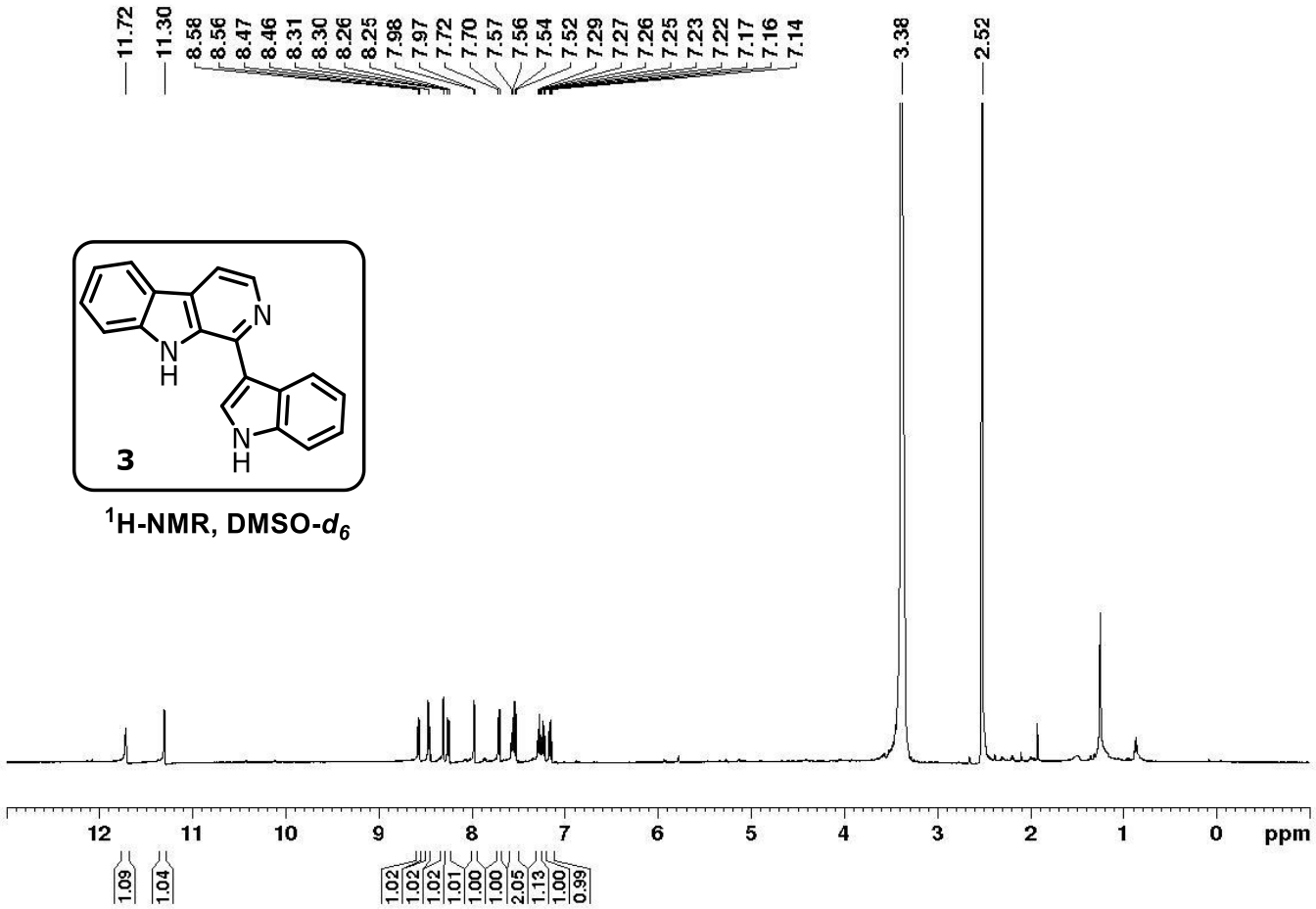
^{1}H-NMR, DMSO-*d*$_{6}$



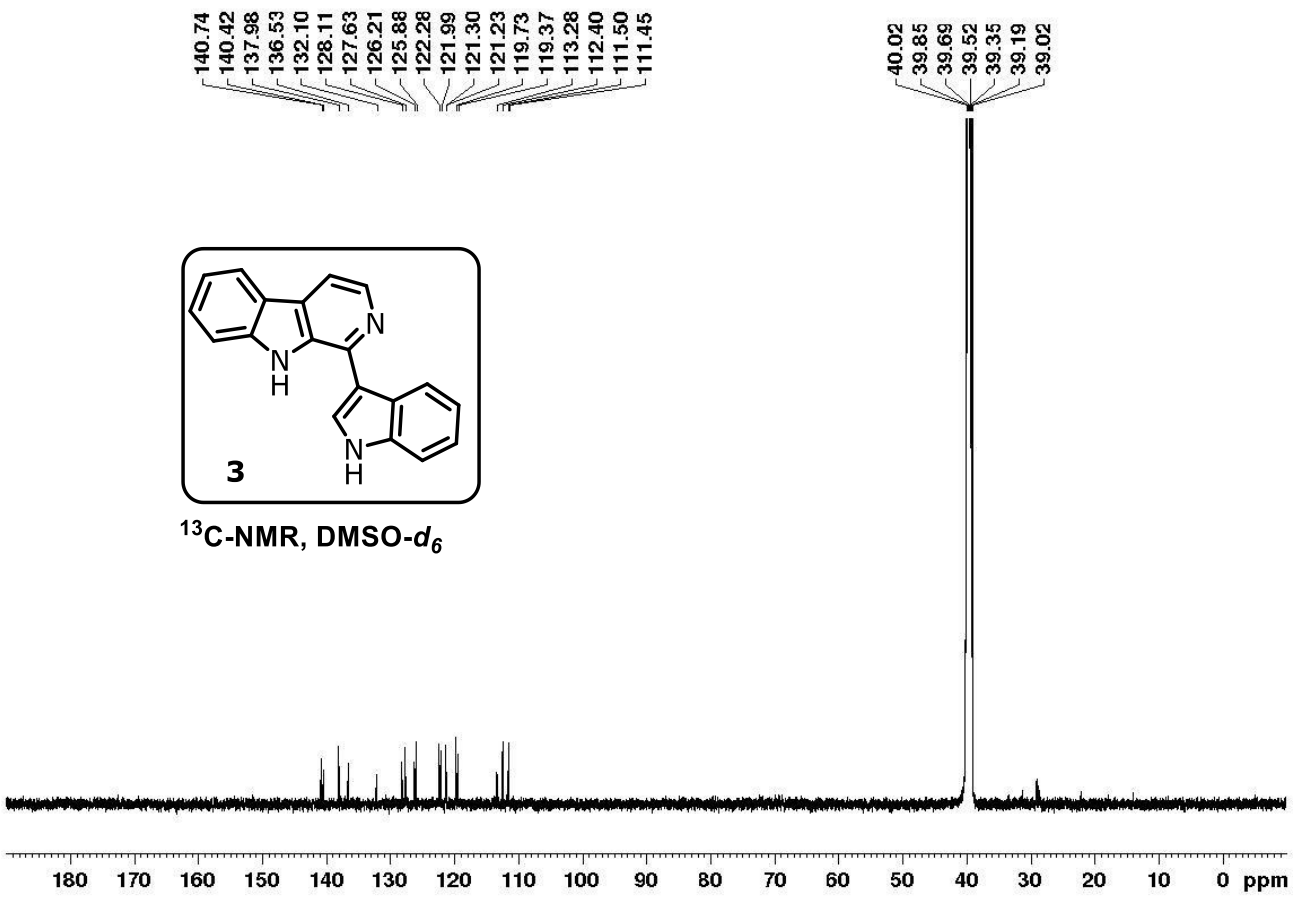


^{13}C-NMR, DMSO-*d*$_{6}$





^{1}H-NMR, DMSO-d_6



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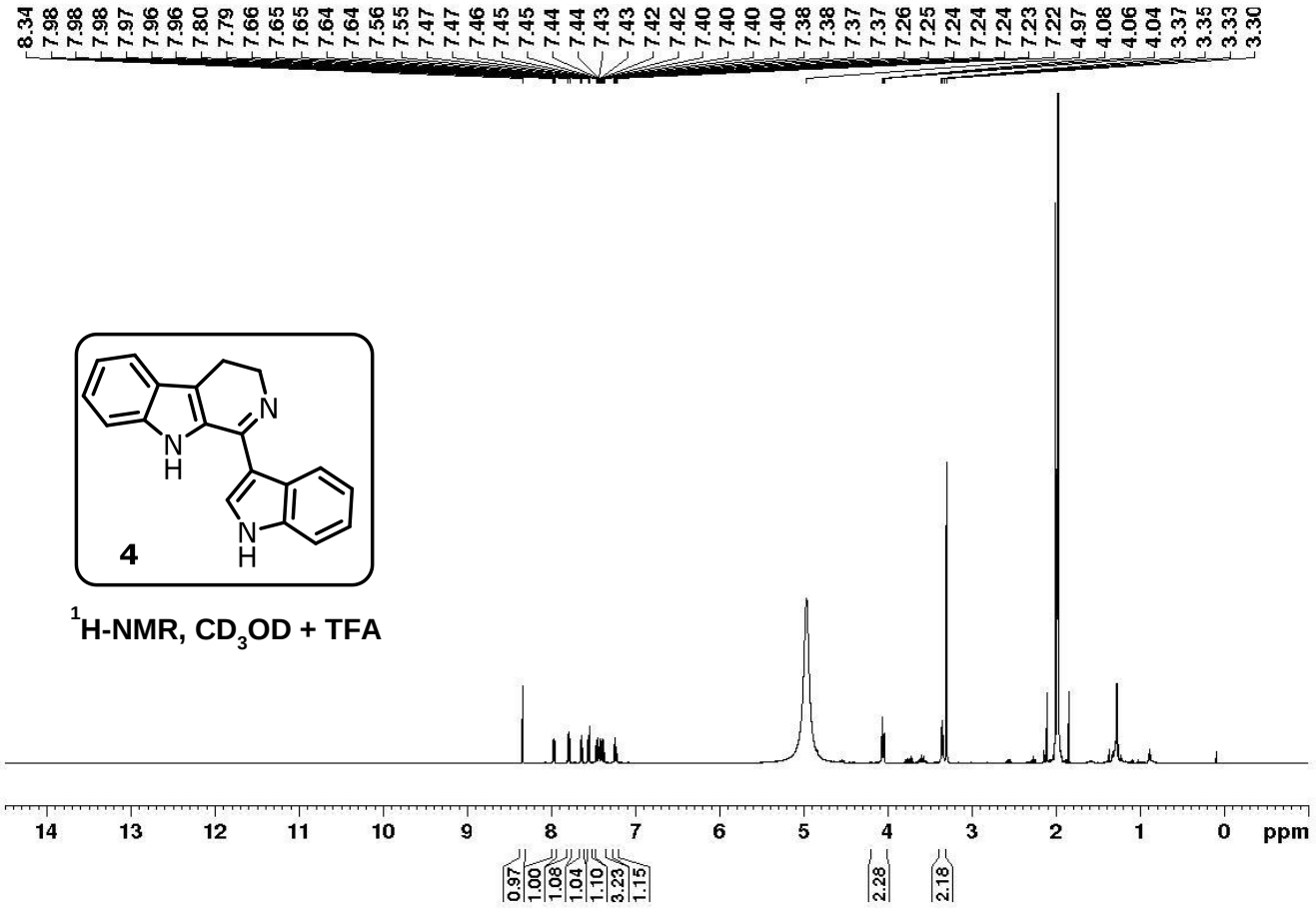
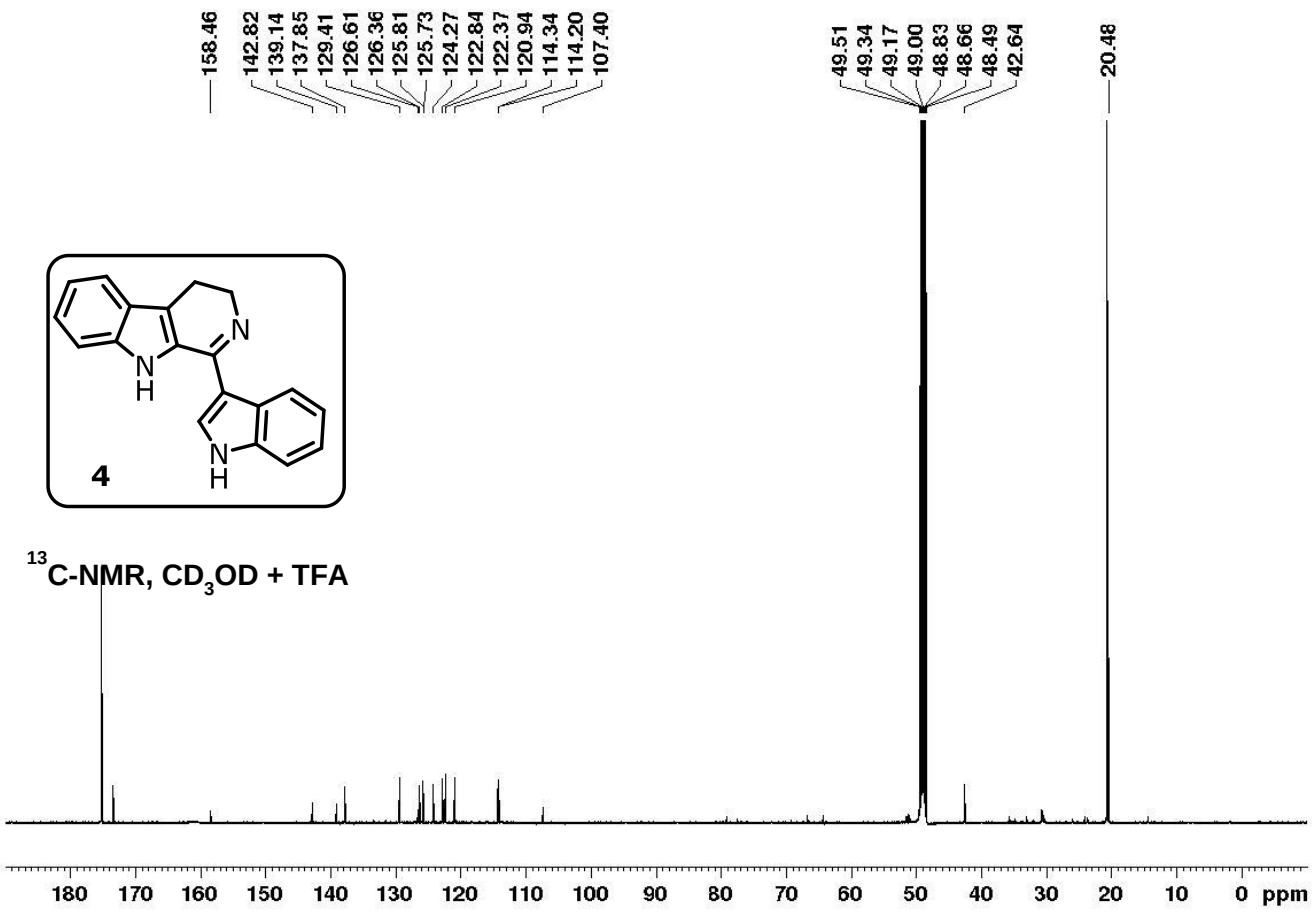
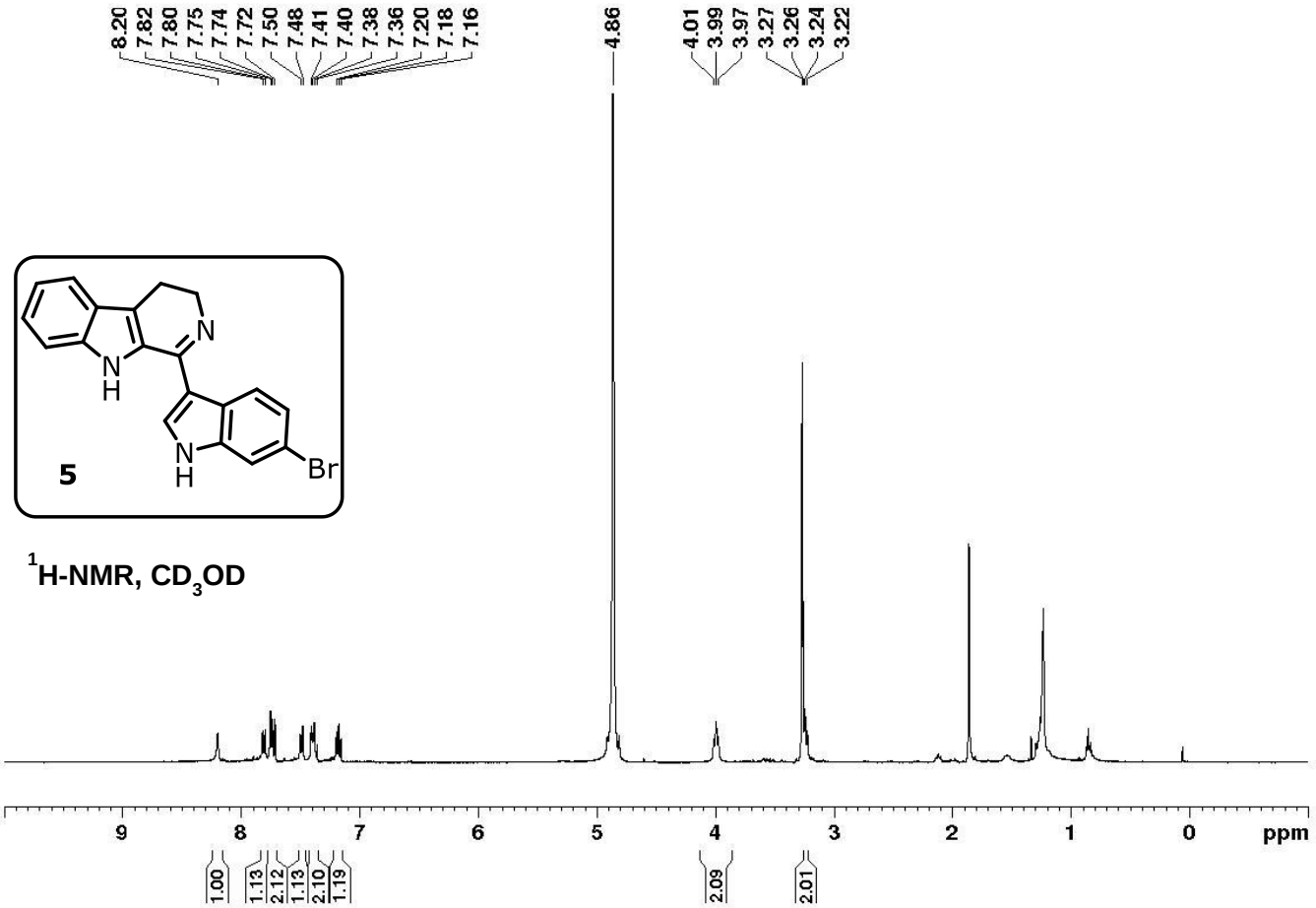


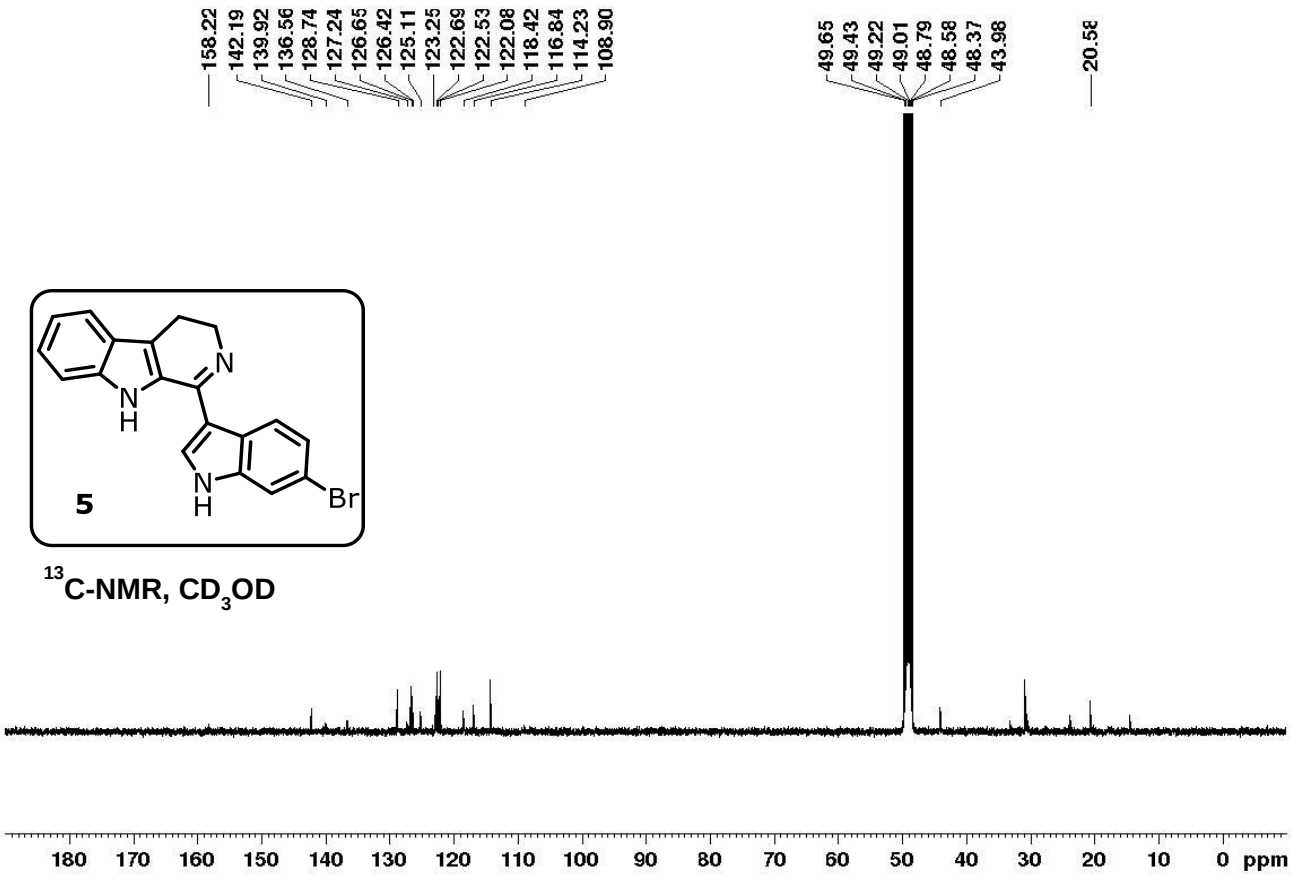
^{1}H-NMR, CD_3OD + TFA



^{13}C-NMR, CD_3OD + TFA



^{1}H-NMR, CD_3OD



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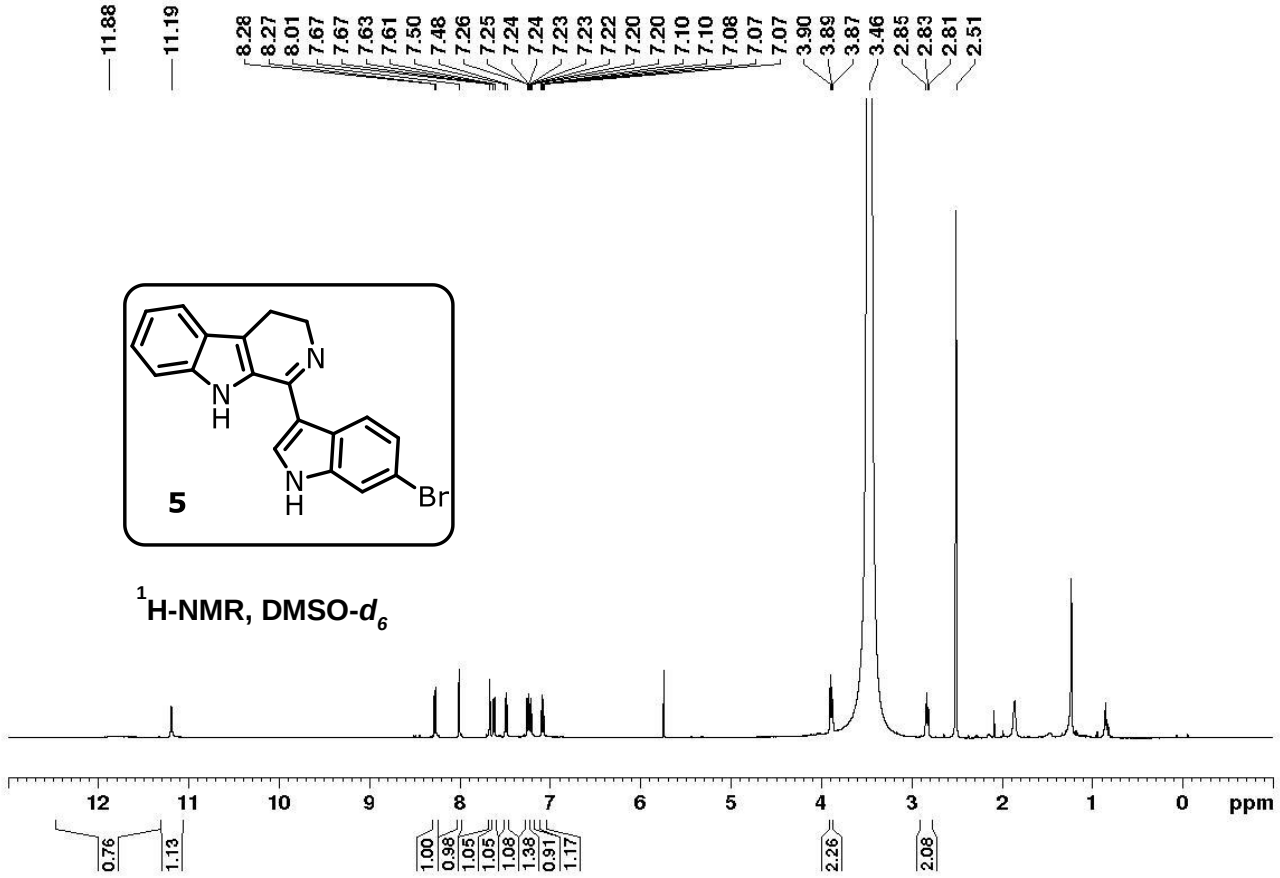
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Br
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