Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Electronic Supplementary Information

Baylis-Hillman Acetates in Organic Synthesis: Convenient One-Pot Synthesis of α-Carboline Framework-A Concise Synthesis of Neocryptolepine

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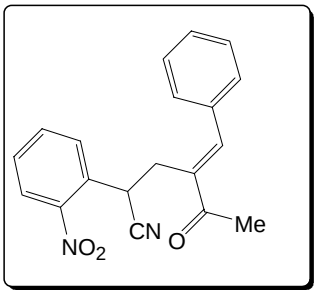
EXPERIMENTAL SECTION

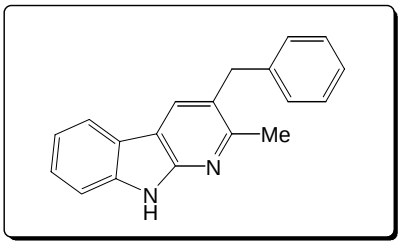
General Remarks: Melting Points were recorded on a Superfit (India) capillary melting point apparatus and were uncorrected. Infrared spectra were recorded on a JASCO FT / IR 5300 spectrophotometer. All the spectra were calibrated against polystyrene absorption at 1601 cm^{-1}. Solid samples were recorded as KBr wafers and liquid samples as thin film between NaCl plates. Proton magnetic resonance spectra and carbon-13 magnetic resonance spectra were recorded on a Bruker-AVANCE-400 spectrometer. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in chloroform-d or dimethyl sulfoxide-d_6. Elemental analyses were recorded on a Thermo-Finnigan Flash EA 1112 analyzer. Mass spectra were recorded on Shimadzu-LCMS-2010A mass spectrometer. HRMS spectra were recorded on Bruker maXis ESI-TOF spectrometer. The X-ray diffraction measurements were carried out at 298 K on a Bruker SMART APEX CCD area detector system equipped with a graphite monochromator and a Mo-Kα fine-focus sealed tube (λ = 0.71073 Å).

Representative procedure: Synthesis of (*E*)-3-benzylidine-5-cyano-5-(2-nitrophenyl)pentan-2-one (5a): To a stirred solution of 4-acetoxy-3-methylene-4-phenylbutan-2-one (**4a**) (2 mmol, 0.436 g) and 2-nitrophenylacetonitrile (**3a**) (2 mmol, 0.324 g) in THF (6 mL) was added K_2CO_3 (2 mmol, 0.276 g). After stirring the reaction mixture at room temperature for 12 h (monitored by TLC), solvent was removed under reduced pressure. The residue, thus obtained, was diluted with water and extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the residue thus obtained was purified by column chromatography (silica gel, 10 % EtOAc in hexanes) to provide the title compound **5a** as pale yellow viscous liquid.



Reaction time = 12 h; yield = 0.570 g (89 %); ^{1}H NMR (400 MHz, $CDCl_3$) = δ 2.47 (s, 3H), 3.18 & 3.30 [dABq, 2H, J = 13.2 Hz, J = 8.4 (7.6 Hz)], 4.99 (dd, 1H, J = 7.6, 7.6 Hz), 7.17-7.22 (m, 2H), 7.32-7.57 (m, 6H), 7.70 (s, 1H), 7.89 (dd, 1H, J = 8.0, 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) = δ 25.62, 31.09, 31.83, 119.51, 125.14, 128.49, 128.73, 129.03, 129.37, 130.13, 130.50, 133.78, 134.41, 136.69, 144.59, 148.10, 199.21; IR (Neat) = ν 2235, 1665, 1627, 1528, 1347 cm^{-1}; LCMS (m/z): 321 $(M+H)^+$; elemental analysis calcd (%) for $C_{19}H_{16}N_2O_3$: C 71.24, H 5.03, N 8.74; found: C 71.12, H 5.09, N 8.63.

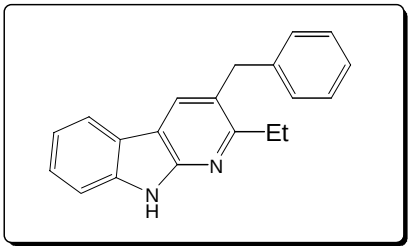
3-Benzyl-2-methyl-9*H*-pyrido[2,3-*b*]indole (6a): To a stirred solution of (*E*)-3-benzylidine-5-cyano-5-(2-nitrophenyl)pentan-2-one (**5a**) (1 mmol, 0.320 g) in acetic acid (5 mL) was added Fe powder (electrolytic, 6 mmol, 0.335g). The resulting reaction mixture was heated under reflux for 1 h. Then the reaction mixture was cooled to room temperature, acetic acid was removed under reduced pressure and was diluted with ethyl acetate (15 mL). The reaction mixture was filtered to remove any iron impurities. Iron residue was washed with ethyl acetate (2 x 15 mL). Filtrate and washings were combined and dried over anhydrous Na_2SO_4. Solvent was evaporated and the residue thus obtained was purified by column chromatography (silica gel, 7% EtOAc in hexanes) to provide the title compound (**6a)** as a colorless solid.



Reaction time = 1 h; yield = 0.166 g (61%); m.p. 208-210 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 2.47 (s, 3H), 4.11 (s, 2H), 7.12-7.20 (m, 4H), 7.24-7.31 (m, 2H), 7.34-7.41 (m, 1H), 7.44 (d, 1H, J = 8.0 Hz), 8.03 (d, 1H, J = 8.0 Hz), 8.26 (s, 1H), 11.54 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 23.05, 38.44, 111.39, 113.42, 119.40, 120.67, 120.95, 125.53, 126.16, 126.21, 128.68, 129.98, 138.98, 140.87, 150.72, 153.97; IR (KBr) = ν 3140, 1604, 1454, 1413, 733 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{19}H_{16}N_2H$ $(M+H)^+$, 273.1391; Found, 273.1393.

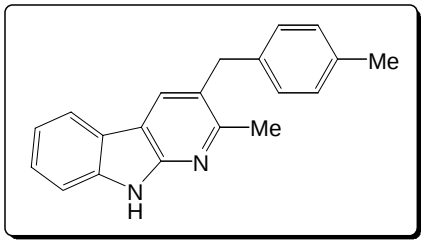
3-Benzyl-2-methyl-9*H*-pyrido[2,3-*b*]indole (6a): To a stirred solution of 4-acetoxy-3-methylene-4-phenylbutan-2-one (**4a**) (1 mmol, 0.218 g) and 2-nitrophenylacetonitrile (**3a**) (1 mmol, 0.162 g) in THF (3 mL) was added K_2CO_3 (1 mmol, 0.138 g). After stirring at room temperature for 12 h (monitored by TLC), solvent was removed under reduced pressure. The residue, thus obtained, was diluted with acetic acid (5 mL) and Fe powder (electrolytic, 6 mmol, 0.335 g) was added. The resulting reaction mixture was heated under reflux for 1h. Then the reaction mixture was cooled to room temperature, acetic acid was removed under reduced pressure and was diluted with ethyl acetate (15 mL). The reaction mixture was filtered to remove any iron impurities. Iron residue was washed with ethyl acetate (2 x 15 mL). Filtrate and washings were combined and dried over anhydrous Na_2SO_4. Solvent was evaporated and the residue thus obtained was purified by column chromatography (silica gel, 7% EtOAc in hexanes) to provide the title compound (**6a)** as a colorless solid. Yield = 0.141 g (52%); reaction time = 13 h (12 h + 1 h); m.p. 208-210 °C. Spectral data (IR, ^{1}H, ^{13}C NMR, HRMS) and m.p. of the compound (**6a**) are in complete agreement with that prepared in a two step process.

3-Benzyl-2-ethyl-9*H*-pyrido[2,3-*b*]indole (6b):



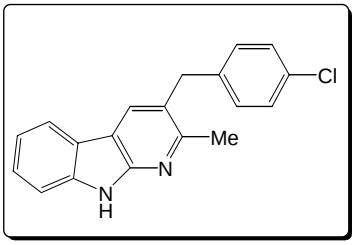
Reaction time = 11 h (10 h + 1 h); yield = 67%; colorless solid; m.p. 191-193 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 1.15 (t, 3H, J = 7.6 Hz), 2.79 (q, 2H, J = 7.6 Hz), 4.13 (s, 2H), 7.12-7.20 (m, 4H), 7.23-7.29 (m, 2H), 7.35-7.41 (m, 1H), 7.43 (d, 1H, J = 8.0 Hz), 8.03 (d, 1H, J = 8.0 Hz), 8.26 (s, 1H), 11.62 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 13.42, 28.06, 38.02, 111.28, 113.21, 119.31, 120.61, 120.93, 124.78, 126.14, 128.60, 130.29, 139.04, 141.29, 150.94, 158.32; IR (KBr) = ν 3130, 1608, 1450, 1412, 738 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{20}H_{18}N_2H$ $(M+H)^+$, 287.1548; Found, 287. 1552.

2-Methyl-3-(4-methylbenzyl)-9*H*-pyrido[2,3-*b*]indole (6c):



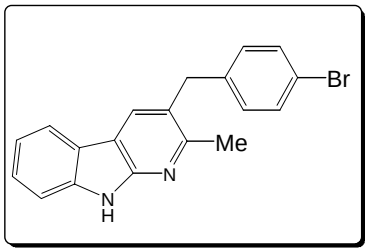
Reaction time = 9 h (8 h + 1 h); yield = 53%; colorless solid; m.p. 234-236 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 2.23 (s, 3H), 2.46 (s, 3H), 4.05 (s, 2H), 7.01-7.10 (m, 4H), 7.11-7.20 (m, 1H), 7.33-7.41 (m, 1H), 7.44 (d, 1H, J = 8.0 Hz), 8.02 (d, 1H, J = 7.6 Hz), 8.23 (s, 1H), 11.54 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 20.76, 22.96, 38.00, 111.28, 113.30, 119.27, 120.62, 120.86, 125.62, 126.02, 128.48, 129.16, 129.77, 135.01, 137.67, 138.90, 150.64, 153.86; IR (KBr) = v 3142, 1606, 1458, 1415, 734 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{20}H_{18}N_2H$ $(M+H)^+$, 287.1548; Found, 287. 1551.

3-(4-Chlorobenzyl)-2-methyl-9*H*-pyrido[2,3-*b*]indole (6d):



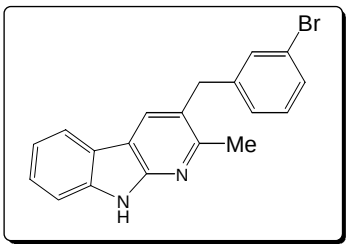
Reaction time = 13 h (12 h + 1 h); yield = 55%; colorless solid; m.p. 250-252 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 2.45 (s, 3H), 4.10 (s, 2H), 7.12-7.23 (m, 3H), 7.32 (d, 2H, J = 8.4 Hz), 7.34-7.41 (m, 1H), 7.44 (d, 1H, J = 8.0 Hz), 8.03 (d, 1H, J = 7.6 Hz), 8.25 (s, 1H), 11.57 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 22.97, 37.65, 111.32, 113.39, 119.34, 120.60, 120.92, 124.99, 126.12, 128.54, 129.93, 130.45, 130.74, 138.94, 139.88, 150.75, 153.87; IR (KBr) = v 3138, 1606, 1458, 1415, 734 cm^{-1}; LCMS (*m/z*): 307 $(M+H)^+$, 309 $(M+H+2)^+$; elemental analysis cacld (%) for $C_{19}H_{15}ClN_2$: C 74.38, H 4.93, N 9.13; found: C 74.51, H 4.84, N 9.07.

3-(4-Bromobenzyl)-2-methyl-9*H*-pyrido[2,3-*b*]indole (6e):



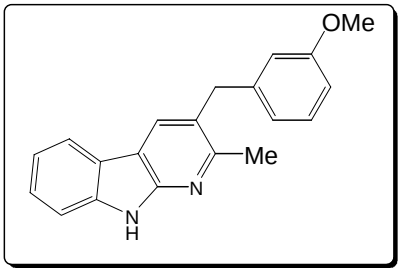
Reaction time = 9 h (8 h + 1 h); yield = 59%; colorless solid; m.p. 263-265 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 2.47 (s, 3H), 4.10 (s, 2H), 7.11-7.22 (m, 3H), 7.36-7.42 (m, 1H), 7.44-7.53 (m, 3H), 8.05 (d, 1H, J = 8.0 Hz), 8.28 (s, 1H), 11.60 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 22.97, 37.71, 111.31, 113.38, 119.19, 119.33, 120.59, 120.92, 124.91, 126.11, 129.94, 130.85, 131.45, 138.93, 140.31, 150.75, 153.86; IR (KBr) = v 3136, 1606, 1458, 1415, 734 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{19}H_{15}BrN_2H$ $(M+H)^+$, 351.0497; Found, 351.0501.

3-(3-Bromobenzyl)-2-methyl-9*H*-pyrido[2,3-*b*]indole (6f):



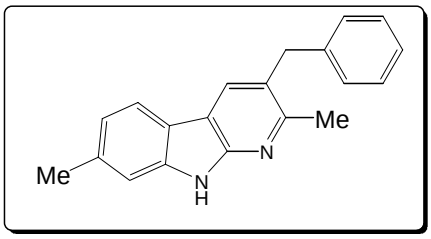
Reaction time = 9 h (8 h + 1 h); yield = 57%; colorless solid; m.p. 210-212 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 2.45 (s, 3H), 4.11 (s, 2H), 7.11-7.20 (m, 2H), 7.20-7.28 (m, 1H), 7.32-7.42 (m, 3H), 7.46 (d, 1H, J = 8.0 Hz), 8.04 (d, 1H, J = 7.6 Hz), 8.28 (s, 1H), 11.58 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 23.09, 38.01, 111.54, 113.58, 119.58, 120.71, 121.12, 122.14, 124.89, 126.36, 127.89, 129.25, 130.26, 130.94, 131.31, 139.10, 143.96, 150.87, 154.05; IR (KBr) = v 3136, 1602, 1458, 1415, 736 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{19}H_{15}BrN_2H$ $(M+H)^+$, 351.0497; Found, 351.0496.

3-(3-Methoxybenzyl)-2-methyl-9*H*-pyrido[2,3-*b*]indole (6g):



Reaction time = 31 h (30 h + 1 h); yield = 50%; pale brown solid; m.p. 200-202 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 2.50 (s, 3H)*, 3.70 (s, 3H), 4.10 (s, 2H), 6.71-6.82 (m, 3H), 7.14-7.24 (m, 2H), 7.36-7.44 (m, 1H), 7.46 (d, 1H, J = 8.0 Hz), 8.05 (d, 1H, J = 7.6 Hz), 8.26 (s, 1H), 11.59 (s, 1H); * DMSO peak merges with this singlet. ^{13}C NMR (100 MHz, DMSO- d_6) = δ 23.01, 38.37, 55.09, 111.27, 111.29, 113.32, 114.58, 119.30, 120.63, 120.87, 125.28, 126.06, 129.63, 129.86, 138.93, 142.44, 150.69, 153.92, 159.55; IR (KBr): v 3140, 1595, 1458, 1410, 731 cm^{-1}; LCMS (m/z): 303 $(M+H)^{+}$; elemental analysis cacld (%) for $C_{20}H_{18}N_2O$: C 79.44, H 6.00, N 9.26; found:C 79.32, H 6.08, N 9.13.

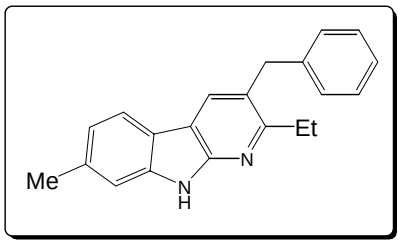
3-Benzyl-2,7-dimethyl-9*H*-pyrido[2,3-*b*]indole (6h):



Reaction time = 13 h (12 h + 1 h); yield = 56%; colorless solid; m.p. 252-254 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 2.44 (s, 3H), 2.45 (s, 3H), 4.09 (s, 2H), 6.97 (d, 1H, J = 7.2 Hz), 7.14-7.20 (m, 3H), 7.22-7.30 (m, 3H), 7.88 (d, 1H, J = 8.0 Hz), 8.17 (s, 1H), 11.43 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 21.91, 22.92, 38.37, 111.30, 113.47, 118.30, 120.58, 120.75, 125.22, 126.09, 128.58, 129.40, 135.62, 139.36, 140.84, 150.76, 153.09; IR (KBr) = v 3142, 1610, 1415,

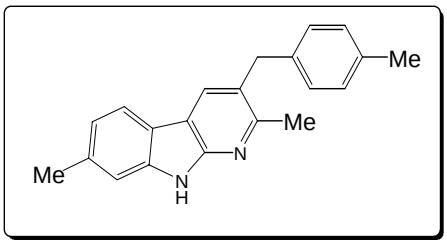
721 cm^{-1}; LCMS (*m/z*): 287 $(M+H)^+$; elemental analysis cacld (%) for $C_{20}H_{18}N_2$: C 83.88, H 6.34, N 9.78; found: C 83.76, H 6.41, N 9.65.

3-Benzyl-2-ethyl-7-methyl-9*H*-pyrido[2,3-*b*]indole (6i):



Reaction time = 25 h (24 h + 1 h); yield = 62%; colorless solid; m.p. 229-231 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 1.17 (t, 3H, J = 7.2 Hz), 2.46 (s, 3H), 2.79 (q, 2H, J = 7.2 Hz), 4.13 (s, 2H), 6.99 (d, 1H, J = 8.0 Hz), 7.14-7.33 (m, 6H), 7.90 (d, 1H, J = 8.0 Hz), 8.19 (s, 1H), 11.51 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 13.41, 21.92, 27.96, 37.99, 111.28, 113.32, 118.27, 120.63, 120.76, 124.57, 126.09, 128.56, 129.79, 135.65, 139.47, 141.31, 150.99, 157.52; IR (KBr) = v 3146, 1610, 1454, 1410, 721 cm^{-1}; LCMS (*m/z*): 301 $(M+H)^+$; elemental analysis cacld (%) for $C_{21}H_{20}N_2$: C 83.96, H 6.71, N 9.33; found: C 84.06, H 6.65, N 9.45.

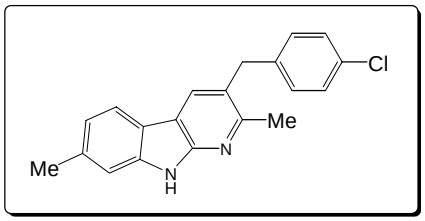
2,7-Dimethyl-3-(4-methylbenzyl)-9*H*-pyrido[2,3-*b*]indole (6j):



Reaction time = 13 h (12 h + 1 h); yield = 50%; colorless solid; m.p. 222-224 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 2.23 (s, 3H), 2.44 (s, 6H), 4.03 (s, 2H), 6.97 (d, 1H, J = 7.6 Hz), 7.02-7.12 (m, 4H), 7.22 (s, 1H), 7.88 (d, 1H, J = 7.6 Hz), 8.15 (s, 1H), 11.41 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 20.77, 21.92, 22.90, 38.00, 111.31, 113.45, 118.32, 120.59, 120.75, 125.45, 128.49, 129.15, 129.32, 134.99, 135.61, 137.73, 139.36, 150.72, 153.08; IR (KBr) = v 3074,

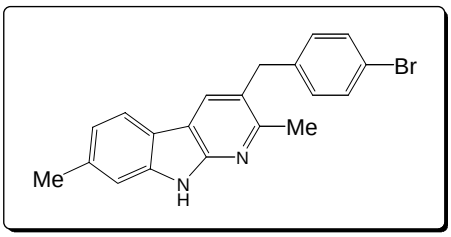
1608, 1413, 796 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{21}H_{20}N_2H$ $(M+H)^+$, 301.1704; Found, 301.1706.

3-(4-Chlorobenzyl)-2,7-dimethyl-9*H*-pyrido[2,3-*b*]indole (6k):



Reaction time = 25 h (24 h + 1 h); yield = 53%; colorless solid; m.p. 235-237 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 2.44 (s, 6H), 4.09 (s, 2H), 6.98 (d, 1H, J = 8.0 Hz), 7.18 (d, 2H, J = 8.4 Hz), 7.23 (s, 1H), 7.32 (d, 2H, J = 8.4 Hz), 7.89 (d, 1H, J = 8.0 Hz), 8.17 (s, 1H), 11.43 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 21.92, 22.88, 37.65, 111.34, 113.53, 118.29, 120.64, 120.81, 124.81, 128.52, 129.45, 130.44, 130.72, 135.70, 139.39, 139.92, 150.82, 153.08; IR (KBr) = ν 3148, 1610, 1489, 1415, 731 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{20}H_{17}ClN_2H$ $(M+H)^+$, 321.1158; Found, 321.1155.

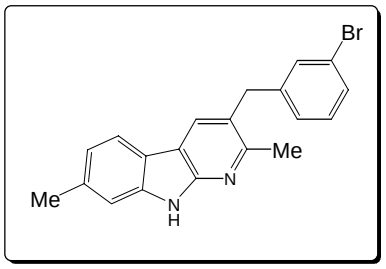
3-(4-Bromobenzyl)-2,7-dimethyl-9*H*-pyrido[2,3-*b*]indole (6l):



Reaction time = 13 h (12 h + 1 h); yield = 58%; colorless solid; m.p. 254-256 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 2.43 (s, 6H), 4.06 (s, 2H), 6.98 (d, 1H, J = 7.6 Hz), 7.12 (d, 2H, J = 8.4 Hz), 7.23 (s, 1H), 7.45 (d, 2H, J = 8.0 Hz), 7.89 (d, 1H, J = 8.0 Hz), 8.18 (s, 1H), 11.45 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 21.95, 22.91, 37.72, 111.35, 113.54, 118.29, 119.18, 120.67, 120.84, 124.76, 129.50, 130.87, 131.45, 135.73, 139.40, 140.38, 150.83, 153.10; IR

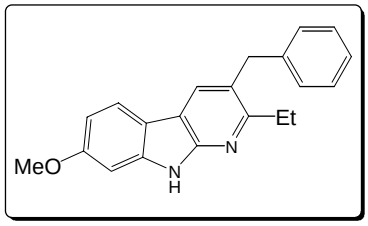
(KBr) = ν 3151, 1610, 1487, 1415, 731 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{20}H_{17}BrN_2H$ $(M+H)^+$, 365.0653; Found, 365.0656.

3-(3-Bromobenzyl)-2,7-dimethyl-9*H*-pyrido[2,3-*b*]indole (6m):



Reaction time = 10 h (9 h + 1 h); yield = 55%; colorless solid; m.p. 223-225 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 2.44 (s, 6H), 4.11 (s, 2H), 6.98 (d, 1H, J = 8.0 Hz), 7.17 (d, 1H, J = 7.6 Hz), 7.20-7.28 (m, 2H), 7.32-7.41 (m, 2H), 7.90 (d, 1H, J = 7.6 Hz), 8.20 (s, 1H), 11.45 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 21.92, 22.91, 37.86, 111.34, 113.53, 118.27, 120.68, 120.83, 121.96, 124.49, 127.73, 129.05, 129.57, 130.75, 131.18, 135.74, 139.40, 143.86, 150.85, 153.09; IR (KBr) = ν 3070, 1608, 1471, 1415, 796 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{20}H_{17}BrN_2H$ $(M+H)^+$, 365.0653; Found, 365.0656.

3-Benzyl-2-ethyl-7-methoxy-9*H*-pyrido[2,3-*b*]indole (6n):

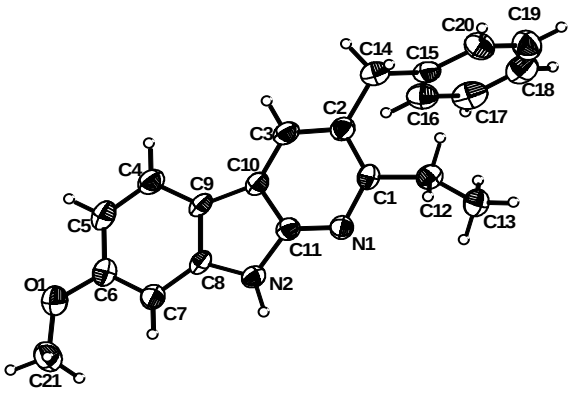


Reaction time = 29 h (28 h + 1 h); yield = 60%; colorless solid; m.p. 212-214 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 1.16 (t, 3H, J = 7.6 Hz), 2.78 (q, 2H, J = 7.6 Hz), 3.83 (s, 3H), 4.12 (s, 2H), 6.77 (dd, 1H, J = 8.4 Hz, 1.6 Hz), 6.93 (d, 1H, J = 1.6 Hz), 7.14-7.21 (m, 3H), 7.25-7.32 (m, 2H), 7.91 (d, 1H, J = 8.4 Hz), 8.14 (s, 1H), 11.52 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6)

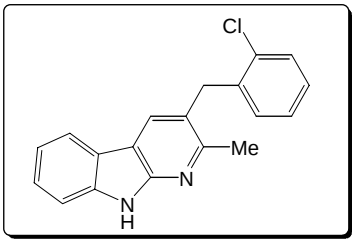
= δ 13.49, 27.89, 38.00, 55.41, 94.85, 108.37, 113.57, 114.16, 121.80, 124.63, 126.07, 128.55, 129.18, 140.51, 141.35, 151.08, 156.42, 158.81; IR (KBr) = ν 3138, 1612, 1464, 1410, 719 cm^{-1}; LCMS (*m/z*): 317 $(M+H)^+$; elemental analysis cacld (%) for $C_{21}H_{20}N_2O$: C 79.72, H 6.37, N 8.85; found: C 79.82, H 6.31, N 8.79.

Crystal data for **6n:** Empirical formula, $C_{21}H_{20}N_2O$; Formula weight, 316.39; crystal color, colorless; habit, rectangular; crystal dimensions, 0.30 x 0.12 x 0.10 mm^3 ; crystal system, triclinic; lattice type, primitive; lattice parameters, a = 5.7251(10) Å, b = 12.062(2) Å, c = 12.371(2) Å, α = 82.492(3), β = 80.563(3), γ = 81.462(3); V = 828.4(3) $Å^3$; space group, p-1; Z = 2; D_{cald} = 1.268 g / cm^3; F_{000} = 336; λ (Mo-Kα) = 0.71073 Å; $R(I \geq 2\sigma_1)$ = 0.0601, wR^2 = 0.1314. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (for compound **6n** CCDC # 873380).

Figure 1. ORTEP diagram of compound **6n**

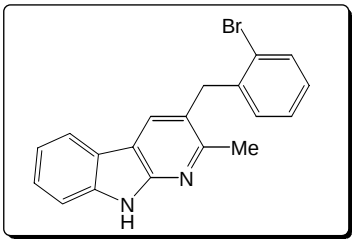


3-(2-Chlorobenzyl)-2-methyl-9*H*-pyrido[2,3-*b*]indole (6o):



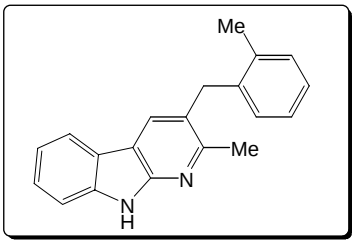
Reaction time = 5 h (4 h + 1 h); yield = 51%; colorless solid; m.p. 228-230 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 2.47 (s, 3H), 4.17 (s, 2H), 6.98 (d, 1H, J = 7.6 Hz), 7.10-7.17 (m, 1H), 7.20-7.30 (m, 2H), 7.35-7.41 (m, 1H), 7.42-7.52 (m, 2H), 7.97 (d, 1H, J = 8.0 Hz), 8.06 (s, 1H), 11.59 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 22.90, 35.83, 111.44, 113.47, 119.47, 120.58, 120.95, 123.72, 126.26, 127.67, 128.42, 129.62, 130.68, 133.48, 138.02, 139.01, 150.82, 154.02; IR (KBr) = v 3142, 1606, 1458, 1412, 733 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{19}H_{15}ClN_2H$ $(M+H)^+$, 307.1002; Found, 307.1005.

3-(2-Bromobenzyl)-2-methyl-9*H*-pyrido[2,3-*b*]indole (6p):



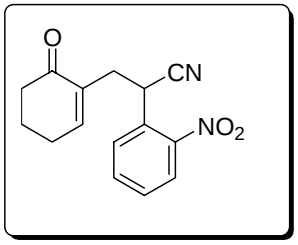
Reaction time = 5 h (4 h + 1 h); yield = 48%; colorless solid; m.p. 224-226 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 2.46 (s, 3H), 4.16 (s, 2H), 6.96 (d, 1H, J = 8.0 Hz), 7.10-7.16 (m, 1H), 7.17-7.22 (m, 1H), 7.26-7.31 (m, 1H), 7.35-7.40 (m, 1H), 7.45 (d, 1H, J = 8.0 Hz), 7.67 (d, 1H, J = 8.0 Hz), 7.96 (d, 1H, J = 7.6 Hz), 8.03 (s, 1H), 11.59 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 22.93, 38.56, 111.47, 113.50, 119.51, 120.60, 120.95, 123.87, 124.52, 126.29, 128.27, 128.73, 129.56, 130.78, 132.94, 139.03, 139.68, 150.82, 154.05; IR (KBr) = v 3142, 1606, 1460, 1412, 733 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{19}H_{15}BrN_2H$ $(M+H)^+$, 351.0497; Found, 351.0496.

2-Methyl-3-(2-methylbenzyl)-9*H*-pyrido[2,3-*b*]indole (6q):



Reaction time = 5 h (4 h + 1 h); yield = 52%; colorless solid; m.p. 218-200 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 2.28 (s, 3H), 2.47 (s, 3H), 4.04 (s, 2H), 6.77 (d, 1H, J = 7.2 Hz), 7.02-7.16 (m, 3H), 7.20 (d, 1H, J = 7.2 Hz), 7.33-7.40 (m, 1H), 7.45(d, 1H, J = 8.0 Hz), 7.93 (d, 1H, J = 8.0 Hz), 7.96 (s, 1H), 11.56 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 19.53, 22.90, 35.72, 111.42, 113.43, 119.41, 120.61, 120.85, 124.70, 126.16, 126.25, 126.43, 128.60, 129.30, 130.31, 136.38, 138.75, 138.97, 150.69, 154.15; IR (KBr) = ν 3140, 1608, 1458, 1412, 731 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{20}H_{18}N_2H$ $(M+H)^+$, 287.1548; Found, 287.1550.

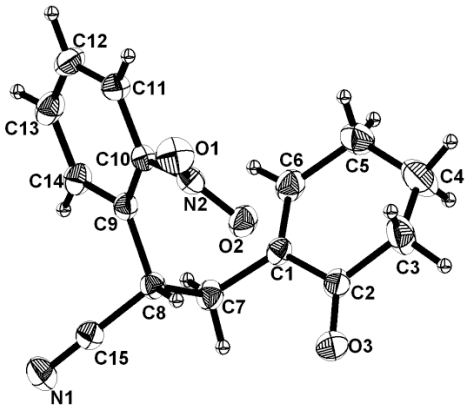
2-[2-Cyano-2-(2-nitrophenyl)]ethylcyclohex-2-enone (8): To a stirred solution of 2-acetoxymethylcyclohex-2-eone (**7**) (1 mmol, 0.168 g) and 2-nitrophenylacetonitrile (**3a**) (1 mmol, 0.162 g) in THF (3 mL) was added K_2CO_3 (1 mmol, 0.138 g). After stirring at room temperature for 48 h (monitored by TLC) solvent was removed under reduced pressure. The reaction mixture was diluted with water and extracted with EtOAc (3 x 5 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was removed and the resulting crude product was purified by column chromatography (silica gel, 15% EtOAc in hexanes) to furnish the compound **8** as a colorless solid.



Reaction time = 48 h; yield = 0.216 g (80 %); colorless solid; m.p.78-80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) = δ 1.94-2.08 (m, 2H), 2.35-2.48 (m, 4H), 2.70-2.82 (m. 1H), 2.89-3.00 (m,1H), 4.91-5.01 (m, 1H), 6.88 (s, 1H)*, 7.48-7.58 (m, 1H), 7.65-7.77 (m, 2H), 8.01 (d, 1H, J = 8.0 Hz); *This looks like an unresolved triplet. ^{13}C NMR (100 MHz, $CDCl_3$) = δ 22.75, 26.24, 33.27, 35.11, 37.99, 119.53, 125.50, 129.54, 130.41, 133.99, 134.40, 148.10, 149.85, 198.33; IR (KBr) = ν 2243, 1670, 1608, 1541, 1359 cm^{-1}; LCMS (m/z): 271 $(M+H)^+$; elemental analysis cacld (%) for $C_{15}H_{14}N_2O_3$: C 66.66, H 5.22, N 10.36; found: C 66.51, H 5.28, N 10.25.

Crystal data for **8:** Empirical formula, $C_{15}H_{14}N_2O_3$; Formula weight, 270.28; crystal color, colorless; habit, rectangular; crystal dimensions, 0.36 x 0.28 x 0.14 mm^3; crystal system, monoclinic; lattice type, primitive; lattice parameters, a = 7.9981(14) Å, b = 10.3530(18) Å, c = 16.174(3) Å, α = 90.00, β = 92.804(3), γ = 90.00; V = 1337.7(4) $Å^3$; space group, p 2(1)/c; Z = 4; D_{cald} = 1.342 g / cm^3; F_{000} = 568; λ (Mo-Kα) = 0.71073 Å; R($I \geq 2\sigma_1$) = 0.0585, wR^2 = 0.1589. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (for compound **8** CCDC # 873381).

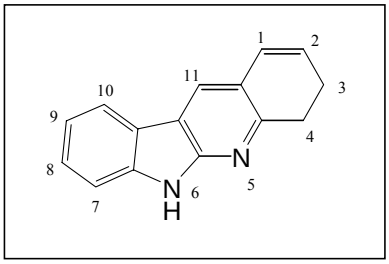
Figure 2. ORTEP diagram of compound **8**



Synthesis of compounds 9 and 10: To a stirred solution of 2-acetoxymethylcyclohex-2-enone (**7**) (5 mmol, 0.841 g) and 2-nitrophenylacetonitrile (**3a**) (5 mmol, 0.810 g) in THF (15 mL) was added K_2CO_3 (5 mmol, 0.690 g) and stirring continued at room temperature for 48 h (monitored by TLC). Solvent was removed under reduced pressure. The residue, thus obtained, was diluted with acetic acid (25 mL) and the resulting solution was heated at 120 °C for 1 h in the presence of Fe powder (electrolytic, 30 mmol, 1.66 g). Then the reaction mixture was cooled to room temperature, acetic acid was removed under reduced pressure and diluted with ethyl acetate (75 mL). The reaction mixture was filtered to remove any iron impurities. Iron residue was washed with ethyl acetate (2 x 75 mL). Filtrate and washings were combined and dried over anhydrous Na_2SO_4. Solvent was evaporated and the residue thus obtained was purified by column chromatography (silica gel, 5 % EtOAc in hexanes) to furnish the compounds **9** and **10** as

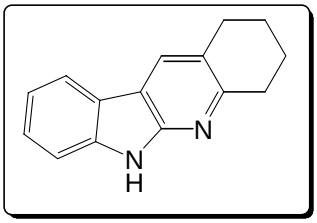
colorless solids in 12% (0.132 g) and 22% (0.244 g) respectively. In addition, we have also isolated the mixture of **9** and **10** in about 6% (0.066 g) yield.

3,4-Dihydro-6*H*-indolo[2,3-*b*]quinoline (9):



m.p. 304-306 °C; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 2.40-2.49 (m, 2H), 3.00 (t, 2H, J = 8.4 Hz), 5.96-6.05 (m, 1H), 6.63 (d, 1H, J = 9.6 Hz), 7.15-7.23 (m, 1H), 7.36-7.44 (m, 1H), 7.46 (d, 1H, J = 8.0 Hz), 8.05 (d, 1H, J = 8.0 Hz), 8.12 (s, 1H), 11.67 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 23.13, 30.94, 111.44, 113.51, 119.49, 120.85, 120.93, 121.54, 125.30, 126.03, 127.30, 138.70, 150.61, 154.18; IR (KBr) = v 3130, 1604, 1558, 1458, 740 cm^{-1}; LCMS (*m/z*): 221 $(M+H)^{+}$; elemental analysis cacld (%) for $C_{15}H_{12}N_2$: C 81.79, H 5.49, N 12.72; found: C 81.68, H 5.56, N 12.62.

1,2,3,4-Tetrahydro-6*H*-indolo[2,3-*b*]quinoline (10):



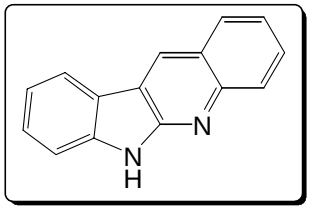
m.p. 224-226 °C [lit.[1] m.p. 220-221 °C], ^{1}H NMR (400 MHz, DMSO- d_6) = δ 1.76-1.93 (m, 4H), 2.86-2.98 (m, 4H), 7.11-7.19 (m, 1H), 7.34-7.46 (m, 2H), 8.03 (d, 1H, J = 7.6 Hz), 8.12 (s, 1H), 11.40 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 23.08, 23.12, 28.66, 32.83, 111.14, 113.59, 119.12, 120.58, 120.85, 122.93, 126.05, 128.74, 139.15, 150.65, 153.78; IR (KBr) = v

3138, 1606, 1458, 1408, 734 cm^{-1}; LCMS (*m/z*): 223 $(M+H)^+$; elemental analysis cacld (%) for $C_{15}H_{14}N_2$: C 81.05, H 6.35, N 12.60; found: C 80.91, H 6.41, N 12.71

6*H*-Indolo[2,3-*b*]quinoline (11):

Aromatization of mixture of compounds **9**, **10** and (**9** + **10**) was carried out using DDQ.[1]

To a stirred mixture of compound **9**, **10** and (**9** + **10**) (1 mmol, 0.221 g) in dry 1, 4- dioxane (6 mL) was added a solution of DDQ (2.2 mmol, 0.499 g) in 1, 4- dioxane (6 mL) under nitrogen atmosphere. After heating the reaction mixture under reflux for 8 h, it was cooled to room temperature and filtered through sintered funnel. The filtrate was diluted with water (10 mL) and extracted with chloroform (3 x 20 mL), washed with water (3 x 20 mL) and dried over anhydrous Na_2SO_4. Solvent was evaporated and the resulting crude product was purified by column chromatography (silica gel, 10 % EtOAc in hexanes) to afford **11** as pale yellow solid.

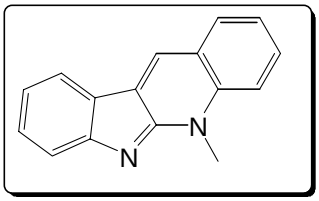


Reaction time = 8 h; yield = 0.148 g (68%), pale yellow solid; m.p. 332-334 °C [lit.[2] m.p. 346 °C]; ^{1}H NMR (400 MHz, DMSO- d_6) = δ 7.23-7.31 (m, 1H), 7.46-7.58 (m, 3H), 7.68-7.77 (m, 1H), 7.99 (d, 1H, J = 8.4 Hz), 8.11 (d, 1H, J = 8.0 Hz), 8.27 (d, 1H, J = 7.6 Hz), 9.05 (s, 1H), 11.71 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) = δ 111.12, 118.10, 119.86, 120.49, 122.03, 122.92, 123.88, 127.20, 127.73, 128.40, 128.86, 141.66, 146.53, 153.10; IR (KBr) = ν 3146, 1612, 1460, 1404, 736 cm^{-1}; LCMS (*m/z*): 219 $(M+H)^+$; elemental analysis cacld (%) for $C_{15}H_{10}N_2$: C 82.55, H 4.62, N 12.84; found: C 82.65, H 4.58, N 12.76. This compound is known in the literature. Melting point and spectral data of our compound are in agreement with the known data.[1]

5-*N*-Methyl-5*H*-indolo[2,3-*b*]quinoline (2):

This molecule was prepared according to literature procedure.[3]

To a stirred solution of compound **11** (0.25 mmol, 0.055 g) in dry THF (4 mL) was added MeI (excess, 0.5 mL). The reaction mixture was then refluxed for 12 h. Solvent was removed under reduced pressure and the resulting residue was purified by column chromatography (neutral alumina, 15 % EtOAc in hexanes) to provide the compound **2** as orange amorphous solid.



Reaction time = 12 h; yield = 0.047 g (82%); orange (amorphous) solid; m.p. 105-107 °C [lit.[4] m.p.104-108 °C]; ^{1}H NMR (400 MHz, $CDCl_3$) = δ 4.34 (s, 3H), 7.19-7.27 (m, 1H), 7.41-7.48 (m, 1H), 7.50-7.59 (m, 1H), 7.69-7.79 (m, 3H), 7.96 (d, 1H, J = 8.0 Hz), 8.03 (d, 1H, J = 7.6 Hz), 8.49 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) = δ 33.09, 114.19, 117.73, 119.91, 120.86, 121.07, 121.96, 124.04, 128.15, 128.20, 129.38, 130.02, 130.43, 137.01, 155.45, 156.29; IR (KBr) = ν 1647, 1566, 1518, 1496, 1296, 1201, 746 cm^{-1}; LCMS (*m/z*): 233 $(M+H)^+$; elemental analysis cacld (%) for $C_{16}H_{12}N_2$: C 82.73, H 5.21, N 12.06; found: C 82.65, H 5.28, N 11.91. This compound is known in the literature. Melting point and spectral data of our compound are in agreement with the known data.[5]

References:

1. G. S. M. Sundaram, C. Venkatesh, U. K. Syam Kumar, H. Ila and H. Junjappa, *J. Org. Chem*., 2004, **69**, 5760.
2. S. J. Holt and V. Petrow, *J. Chem. Soc.* 1948, 922.
3. T.-L. Ho and D.-G. Jou, *Helv. Chim. Acta*., 2002, **85**, 3823.
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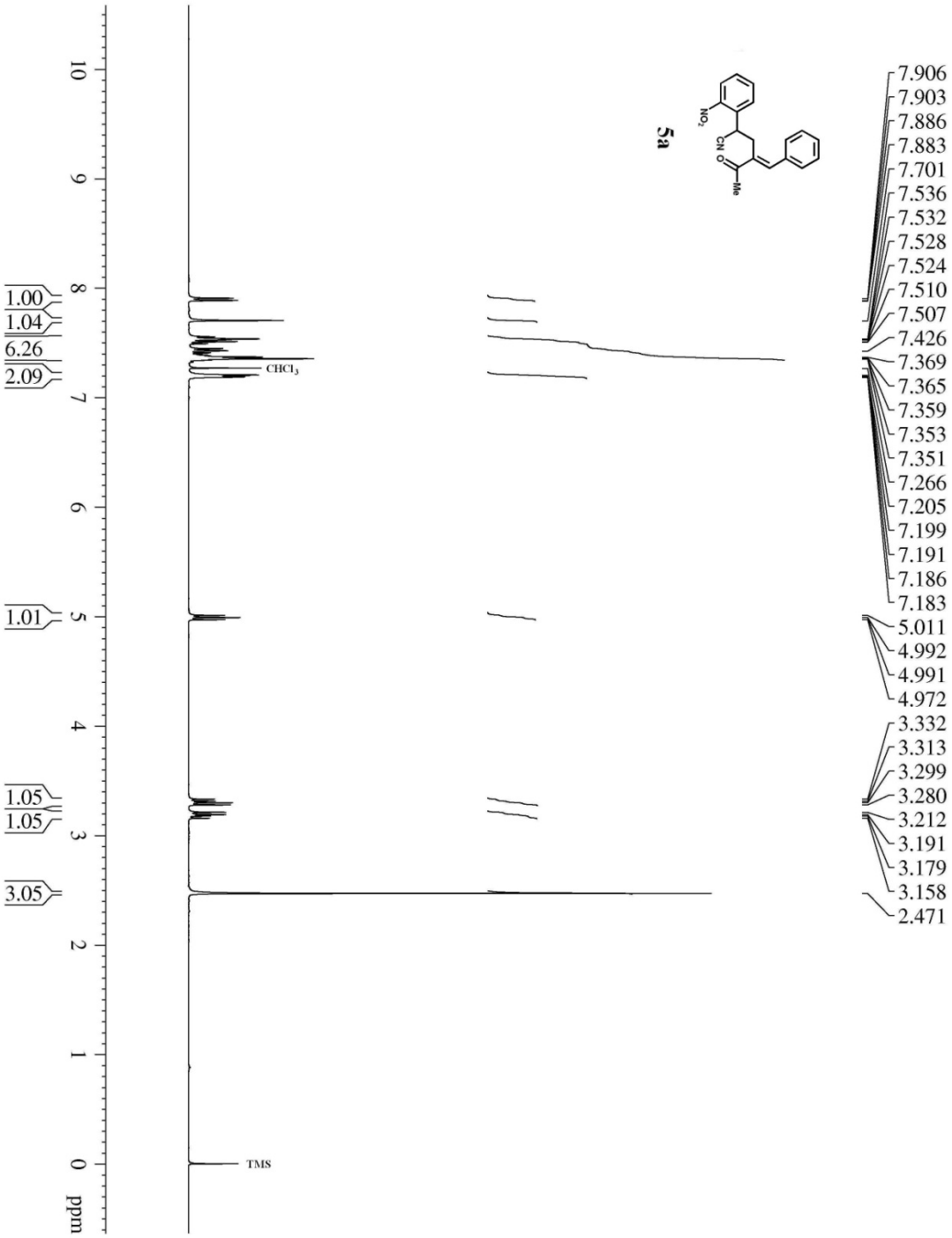
5. A. L. Pumphrey, H. Dong and T. G. Driver, *Angew. Chem. Int. Ed.,* 2012, **51**, 5920.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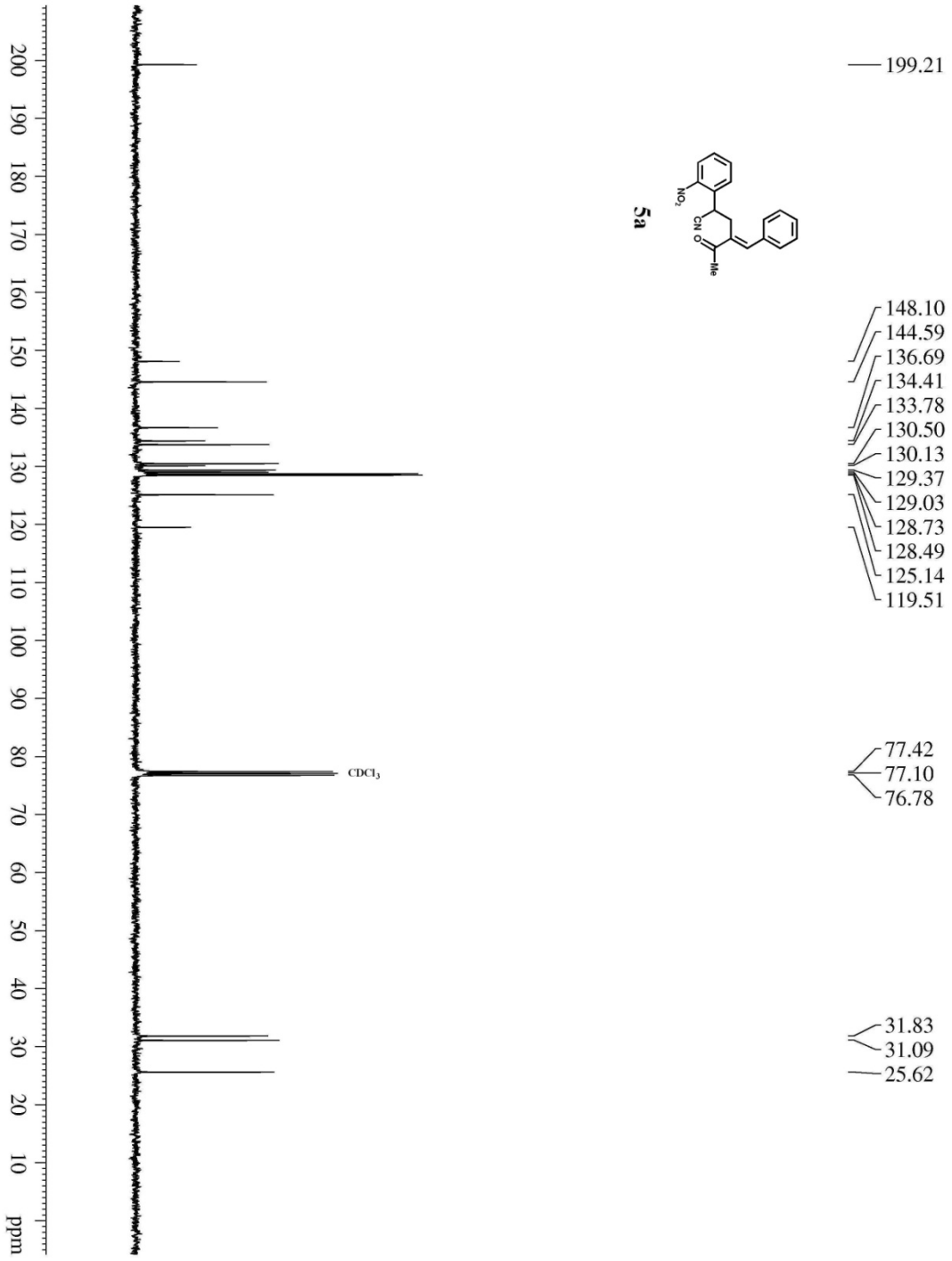

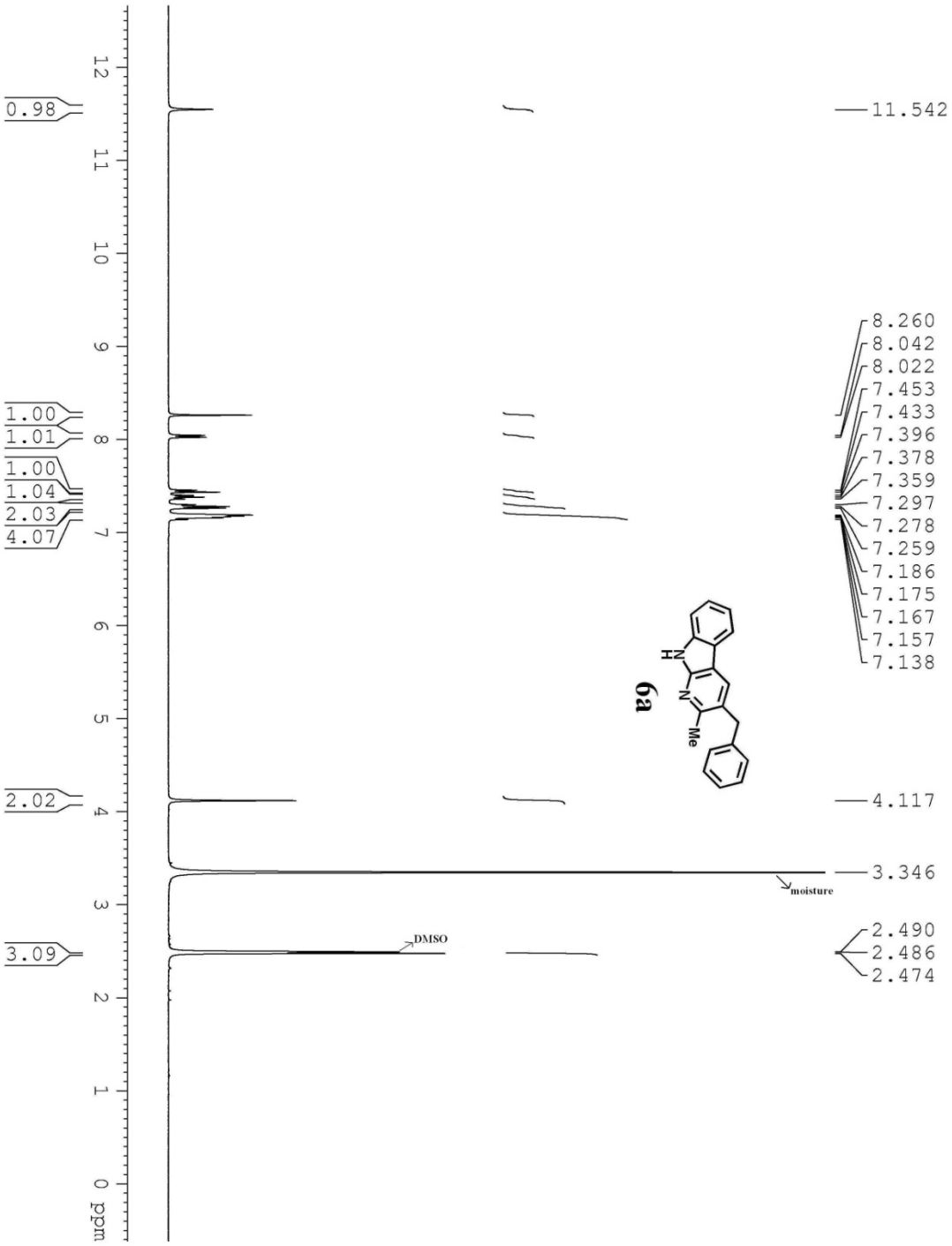

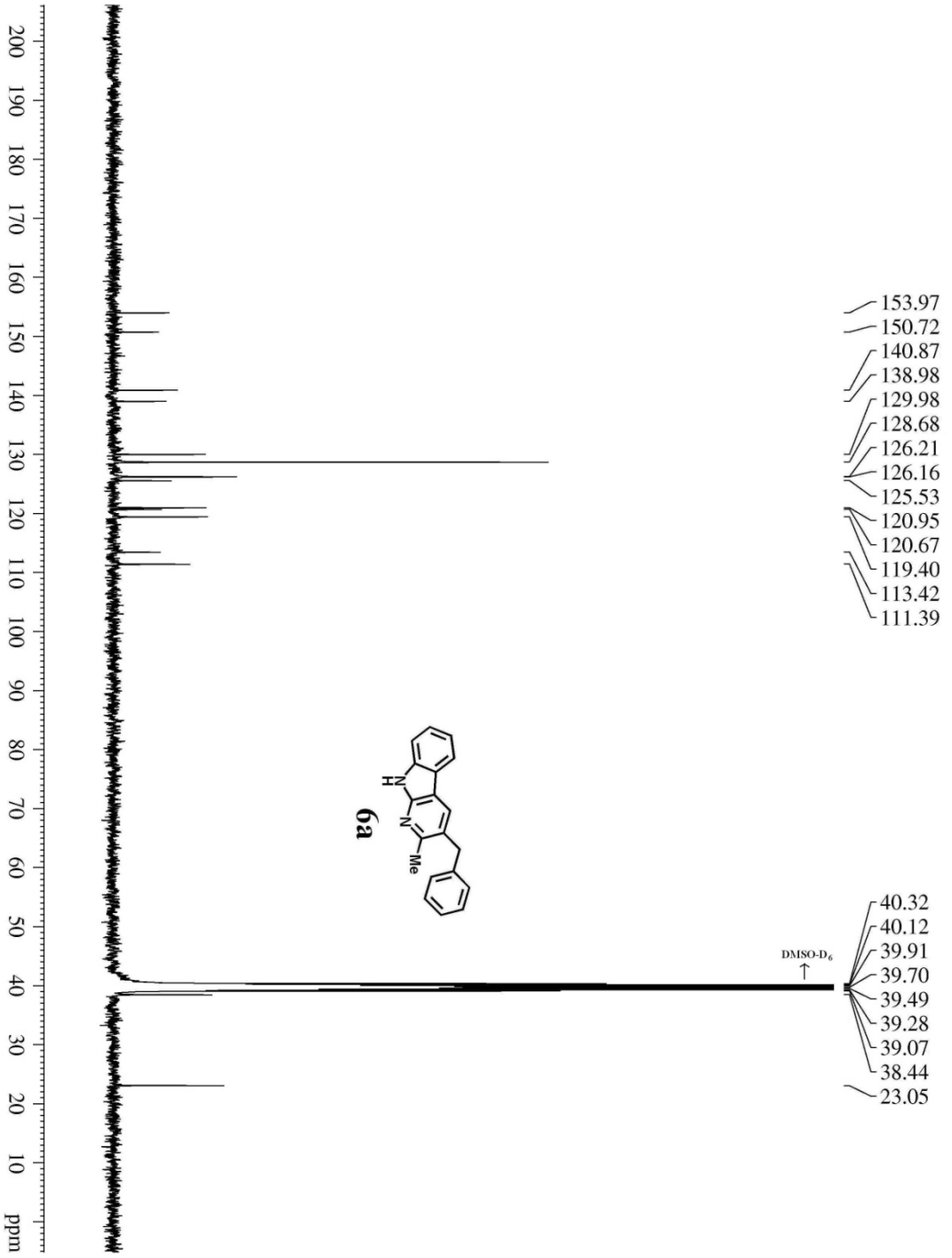

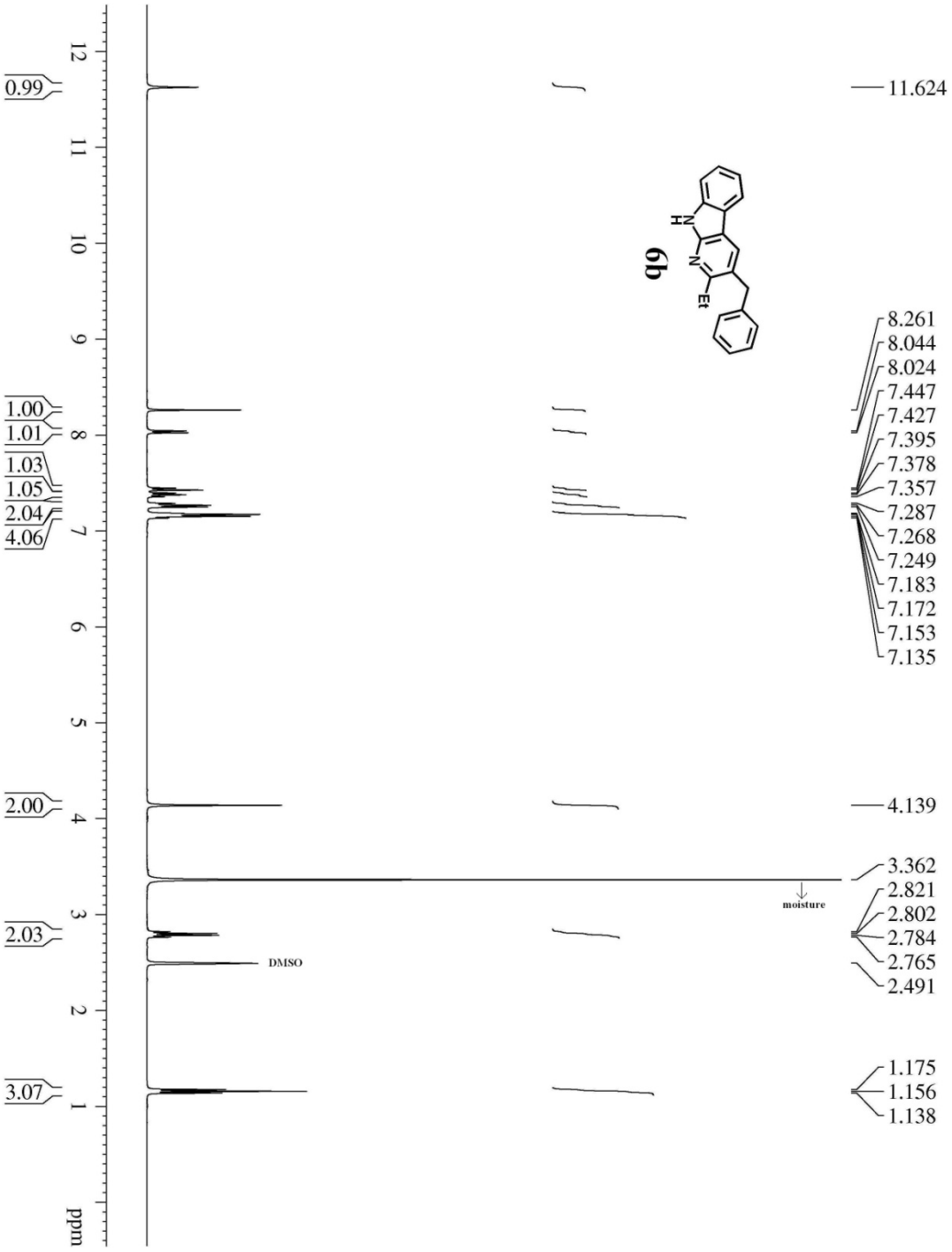
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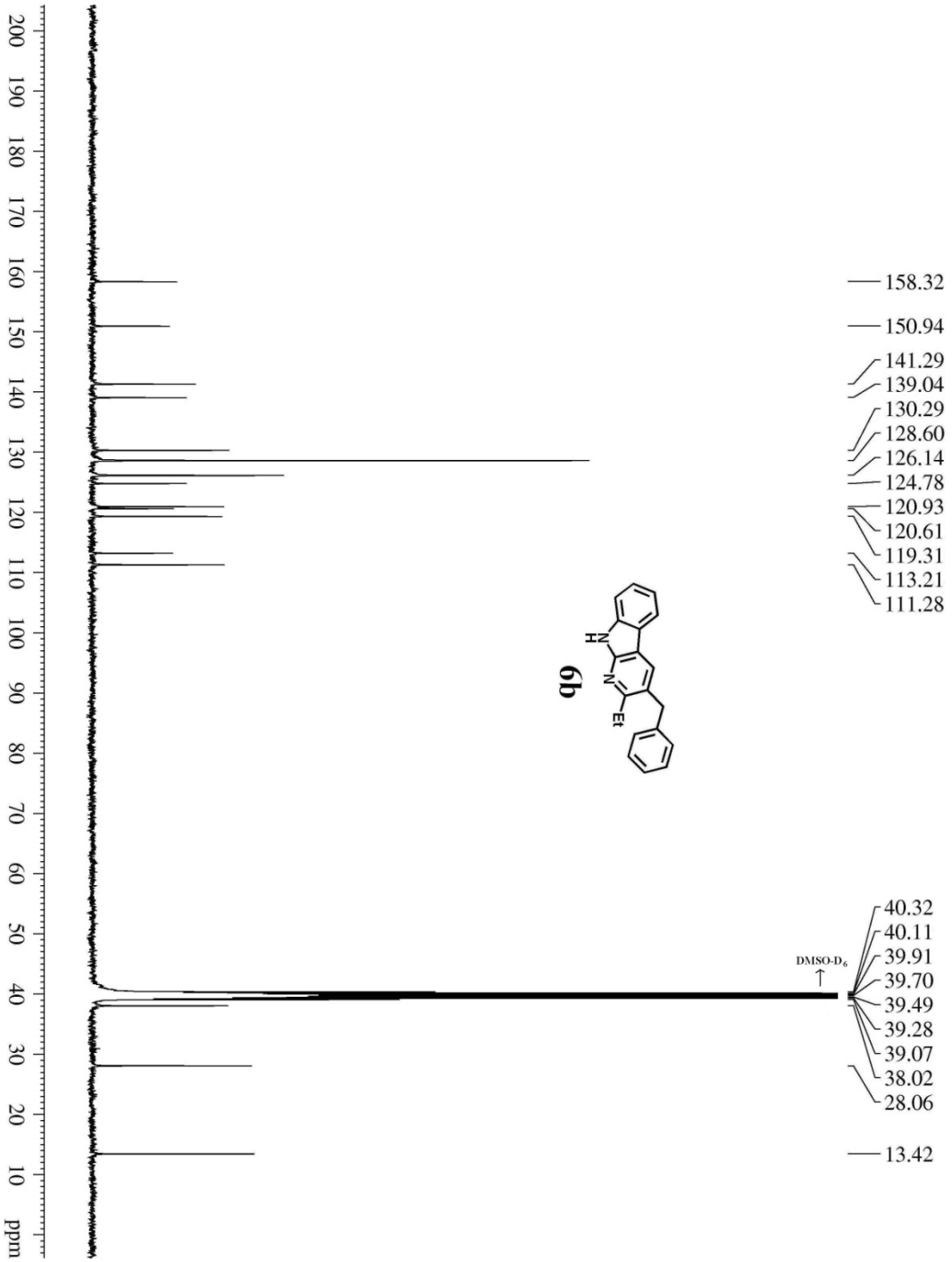

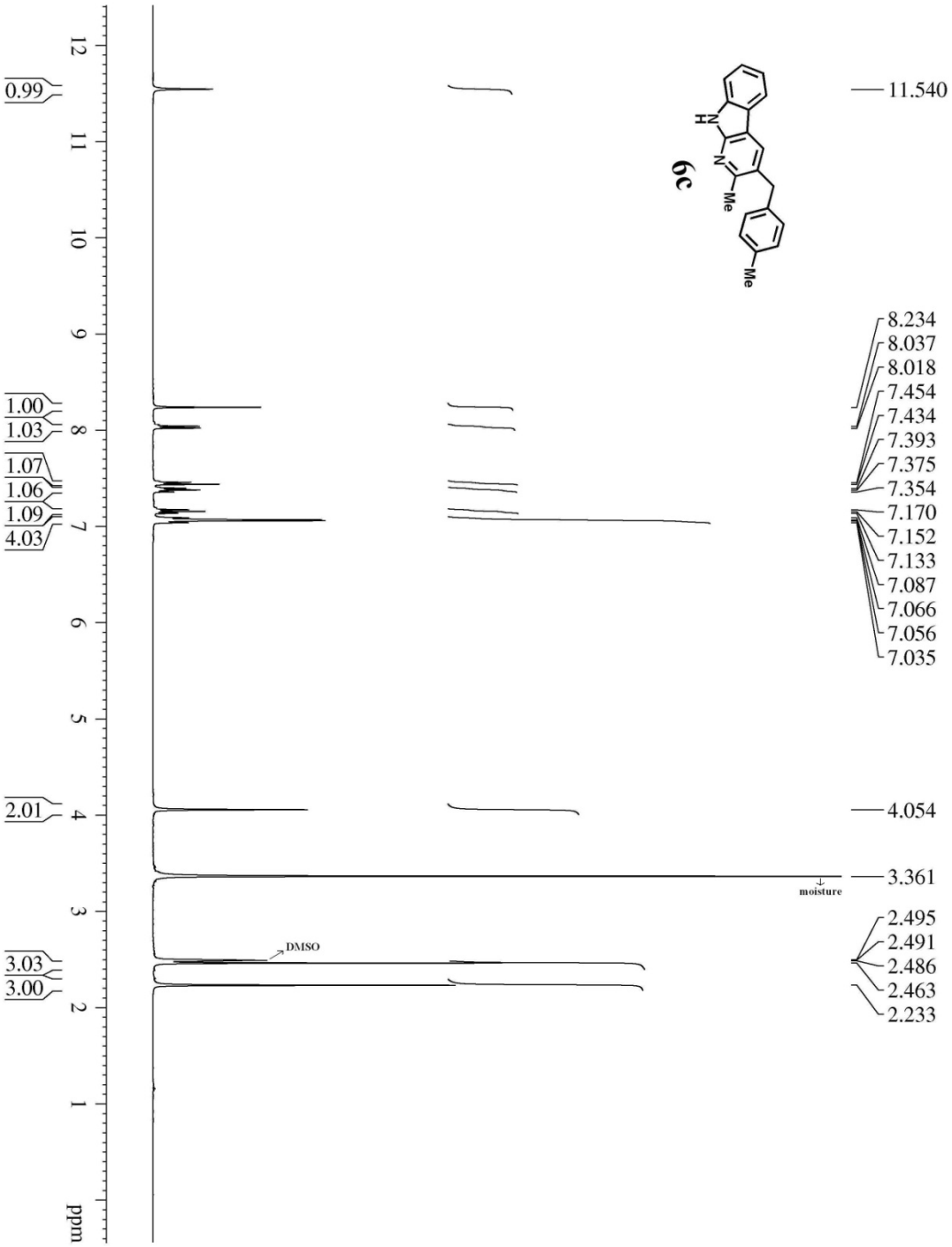
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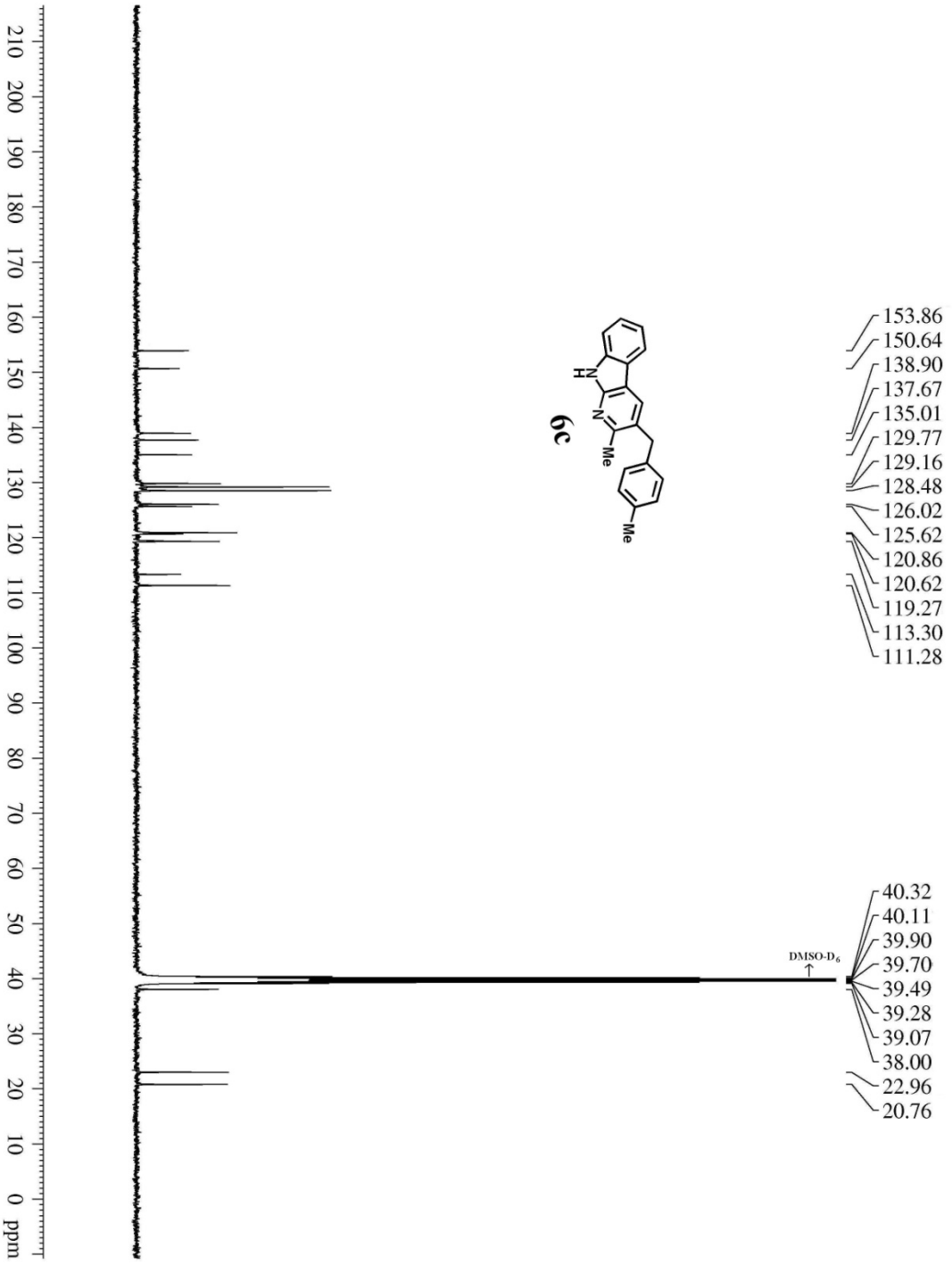
3.00
12
11
10
9
8
7
6
5
4
3
2
1
ppm
DMSO
moisture
6c
Me
Me
11.540
8.234
8.037
8.018
7.454
7.434
7.393
7.375
7.354
7.170
7.152
7.133
7.087
7.066
7.056
7.035
4.054
3.361
2.495
2.491
2.486
2.463
2.233


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
3c
Me
Me
153.86
150.64
138.90
137.67
135.01
129.77
129.16
128.48
126.02
125.62
120.86
120.62
119.27
113.30
111.28
DMSO-D6
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40.11
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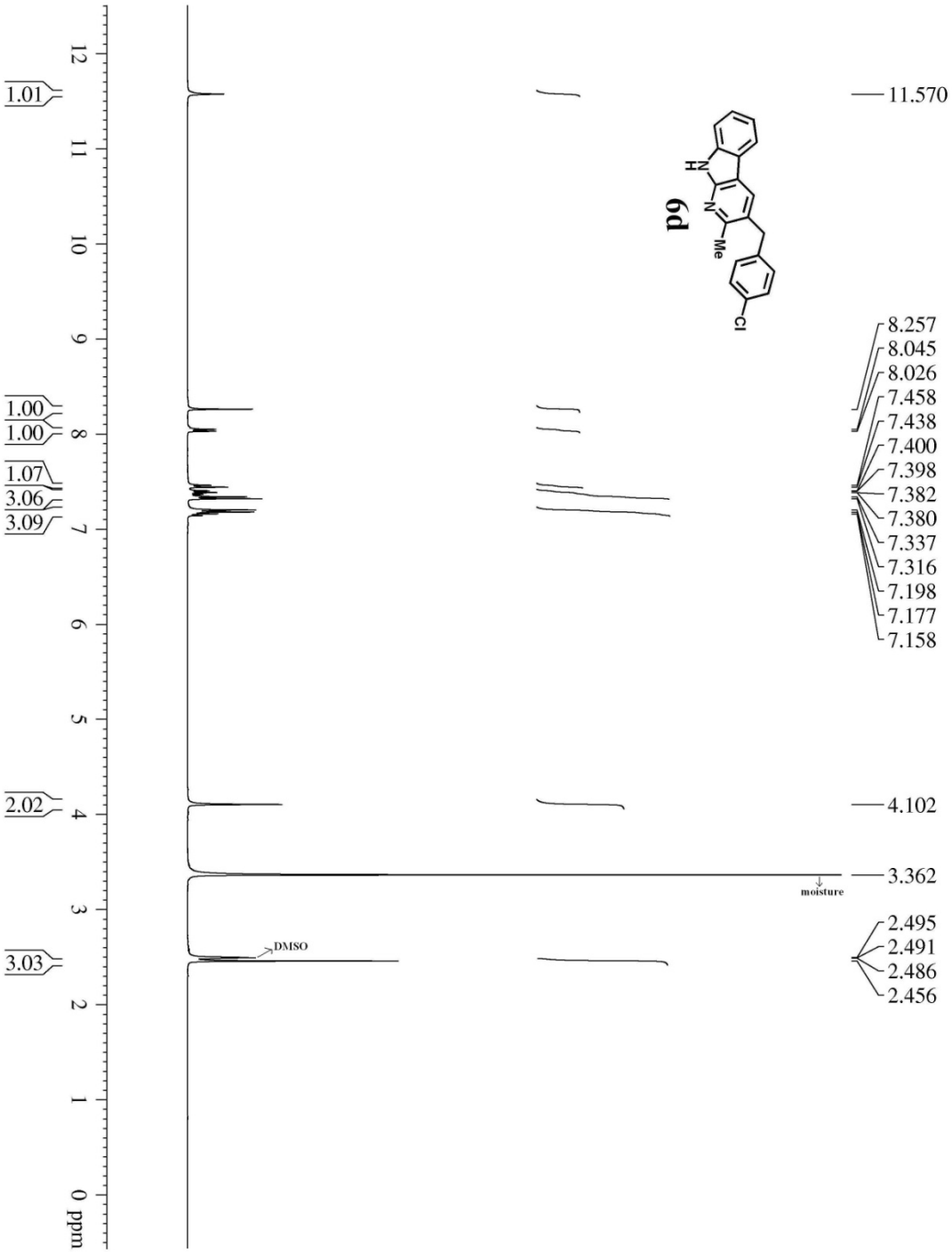
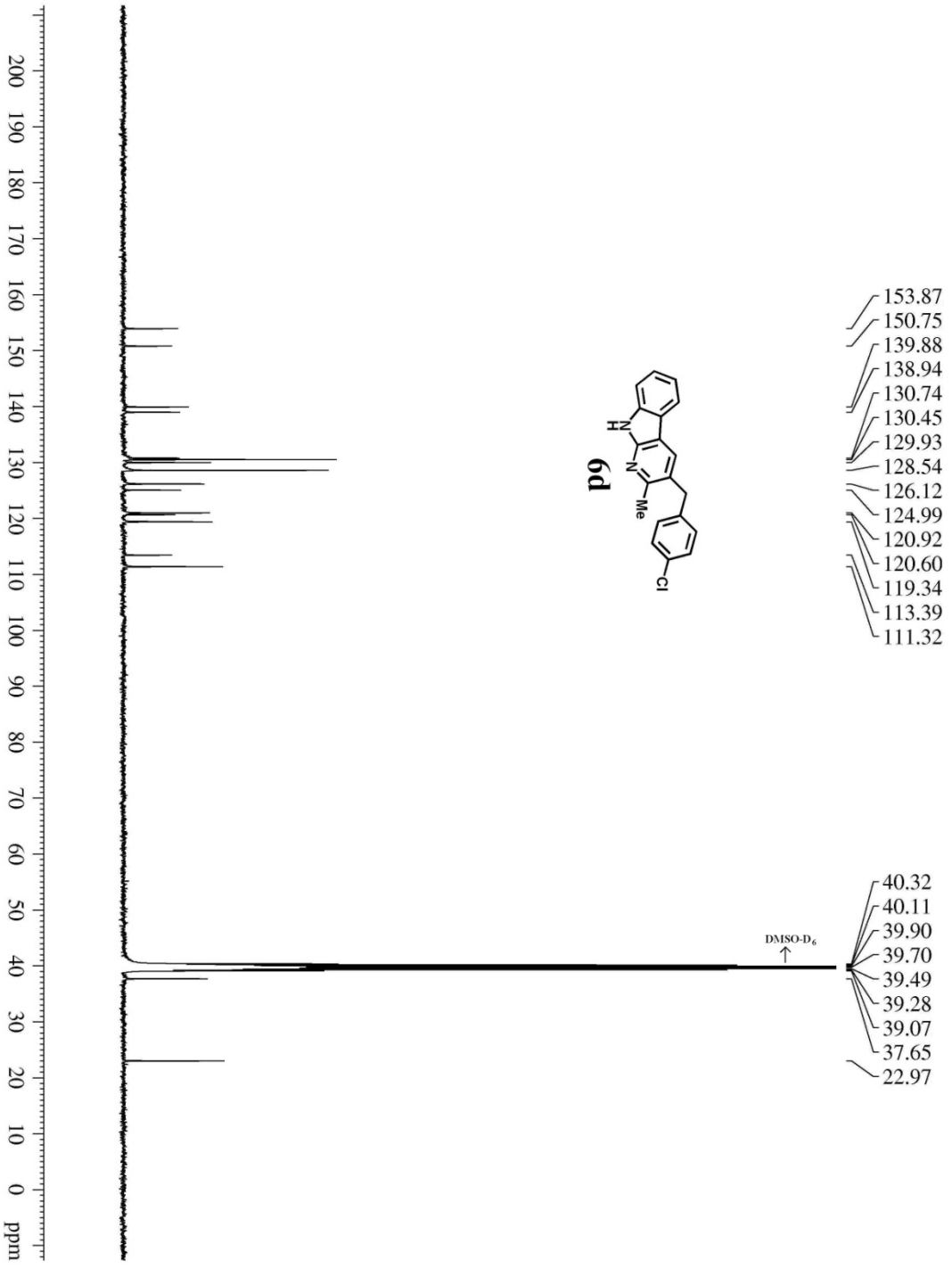
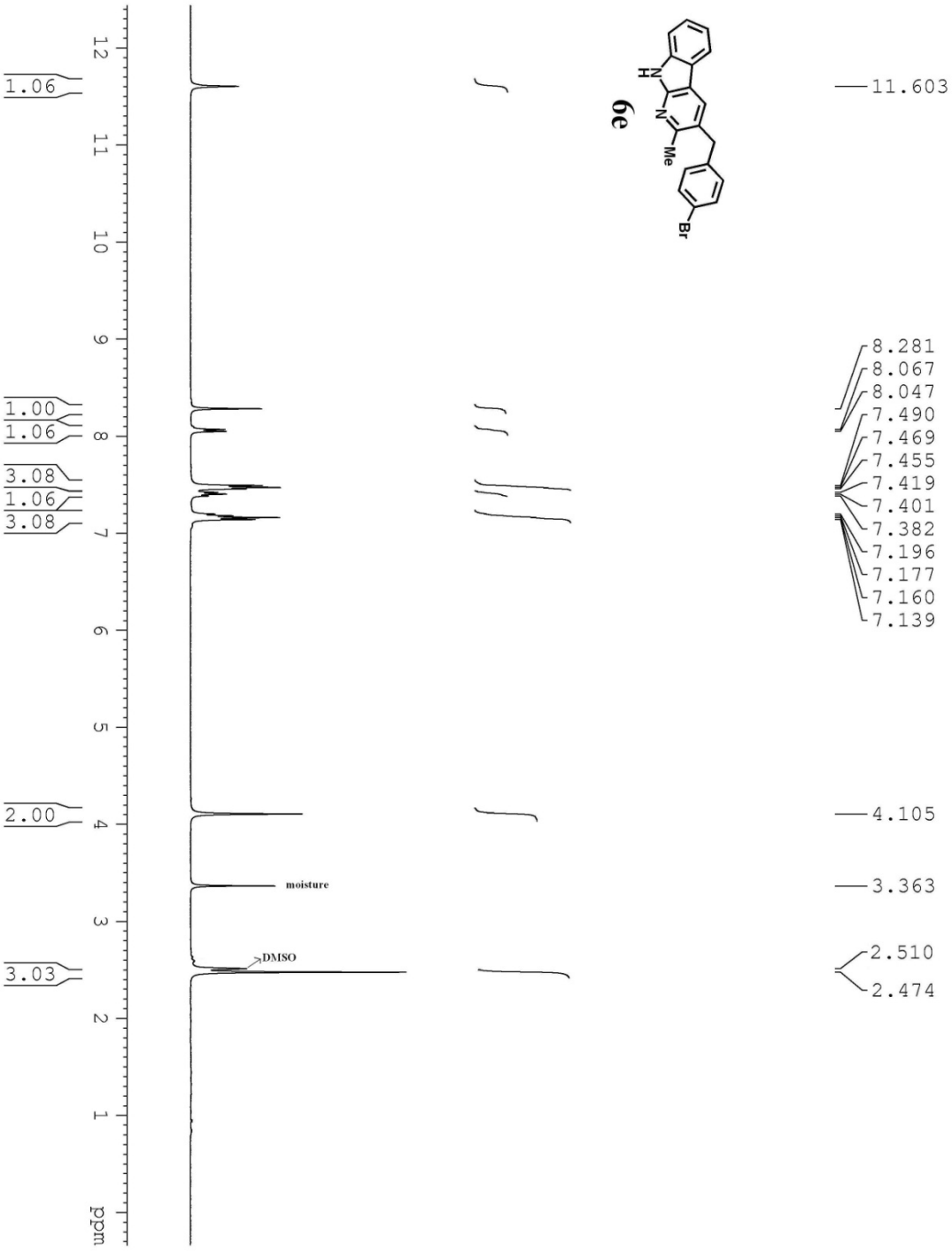
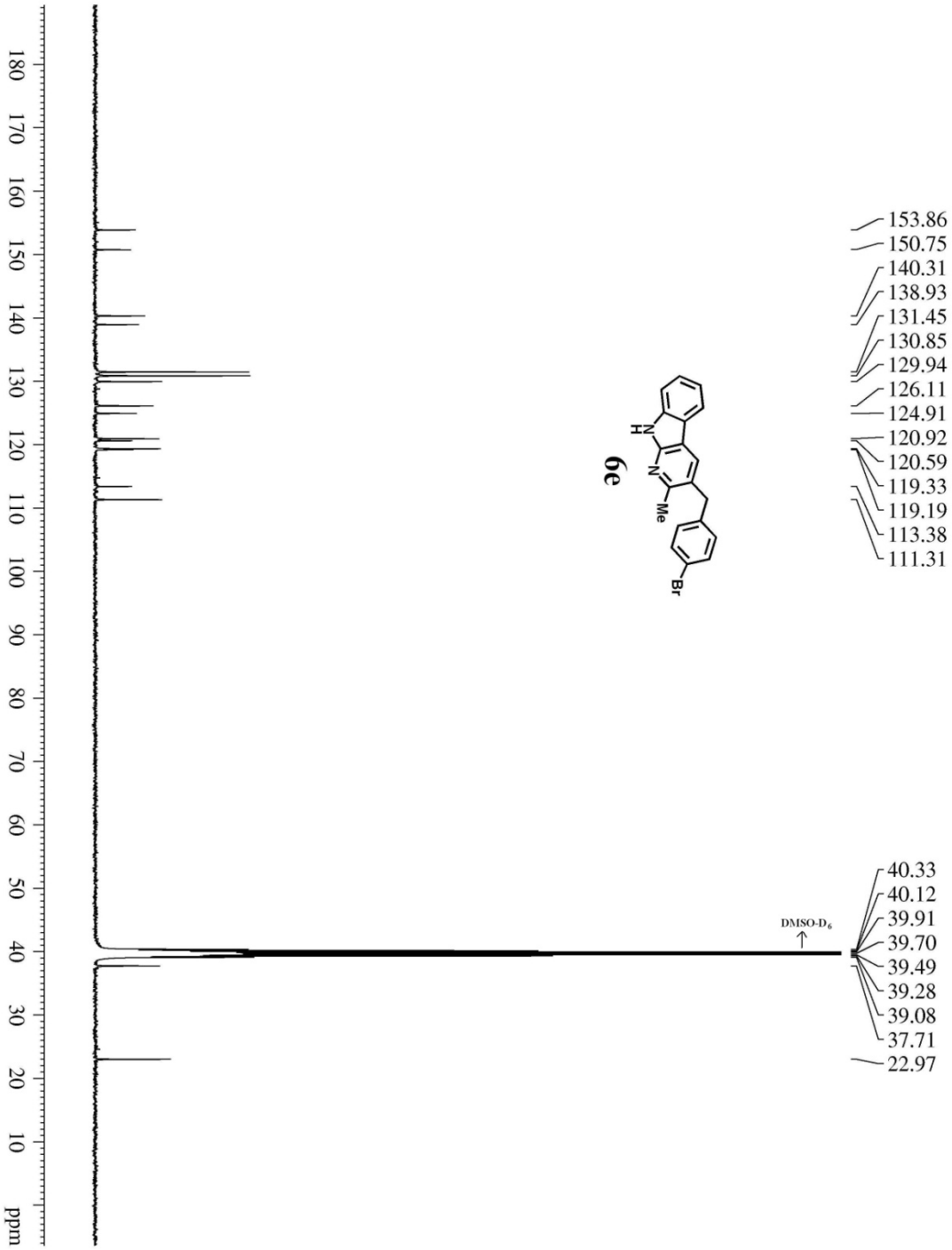
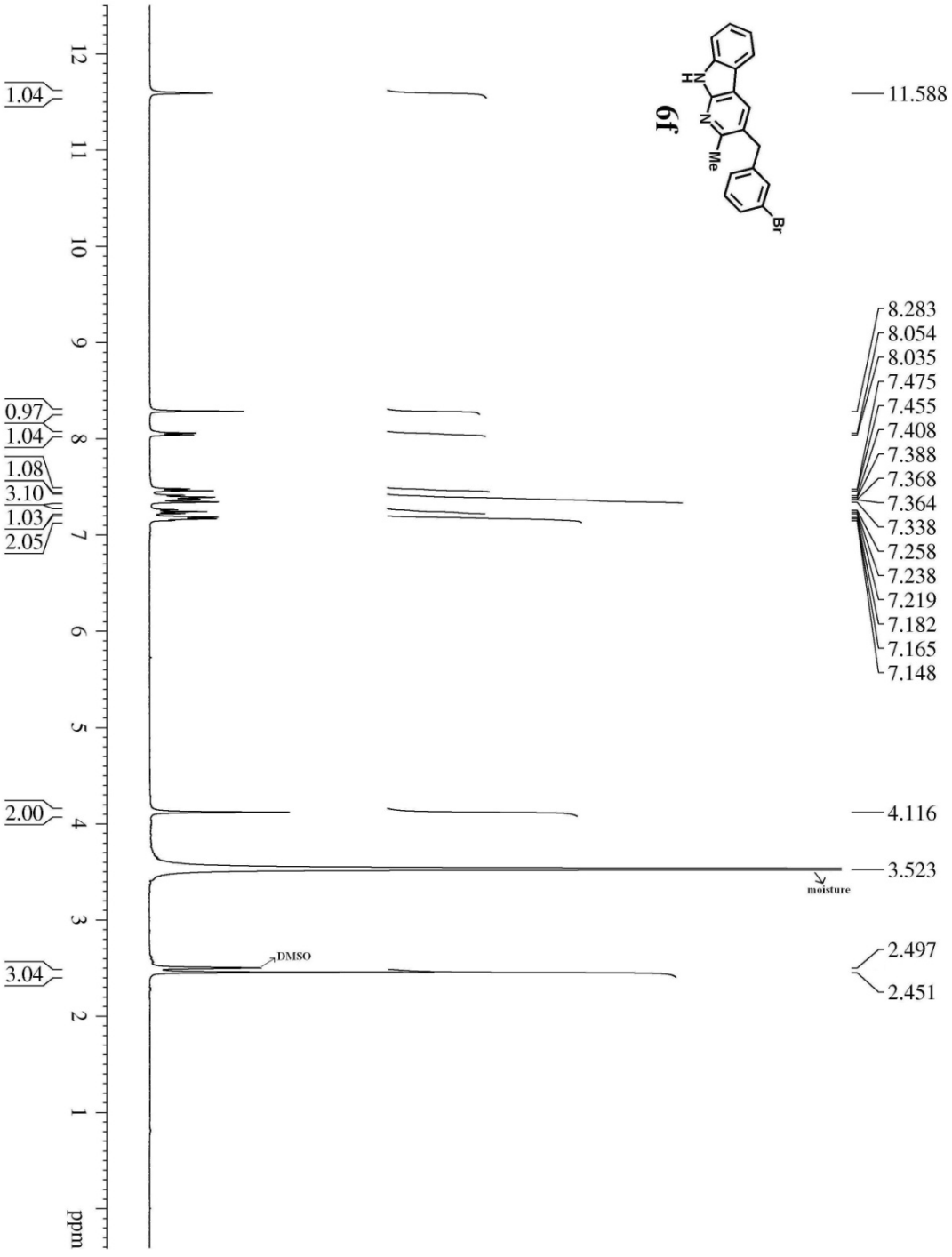
39.70
39.49
39.28
39.07
38.00
22.96
20.76

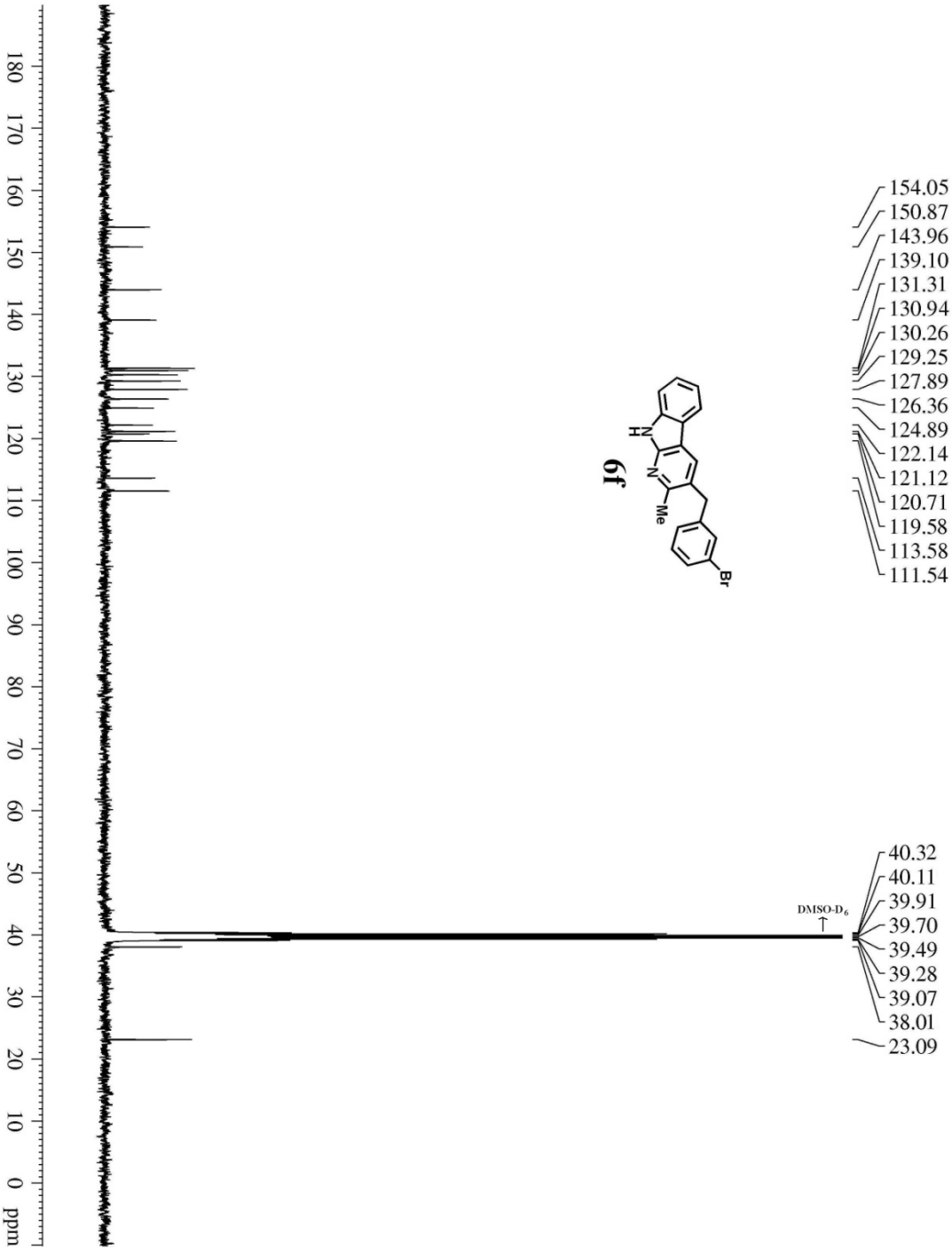

9d
11.570
8.257
8.045
8.026
7.458
7.438
7.400
7.398
7.382
7.380
7.337
7.316
7.198
7.177
7.158
4.102
3.362
moisture
2.495
2.491
2.486
2.456
DMSO
1.01
1.00
1.00
1.07
3.06
3.09
2.02
3.03
ppm

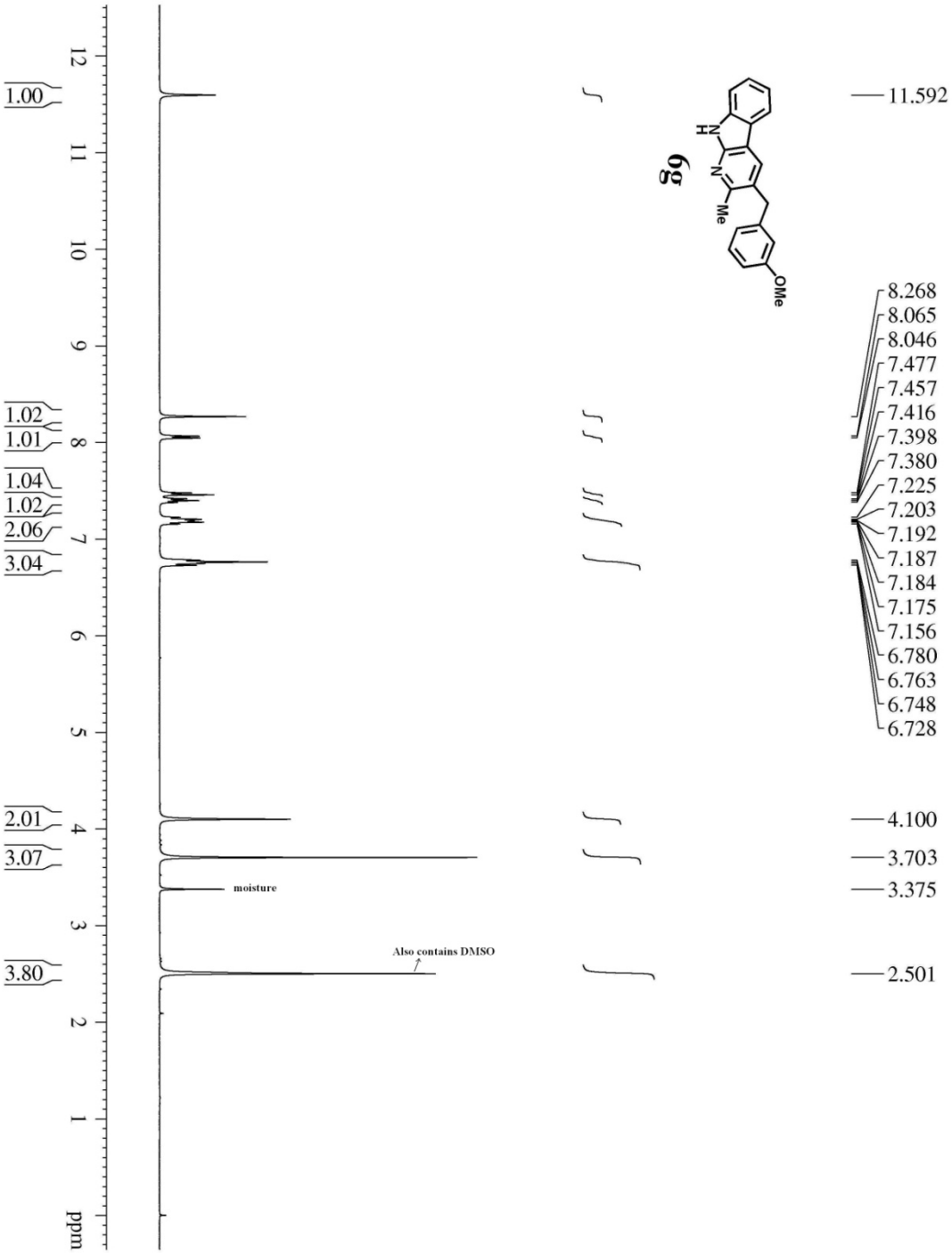


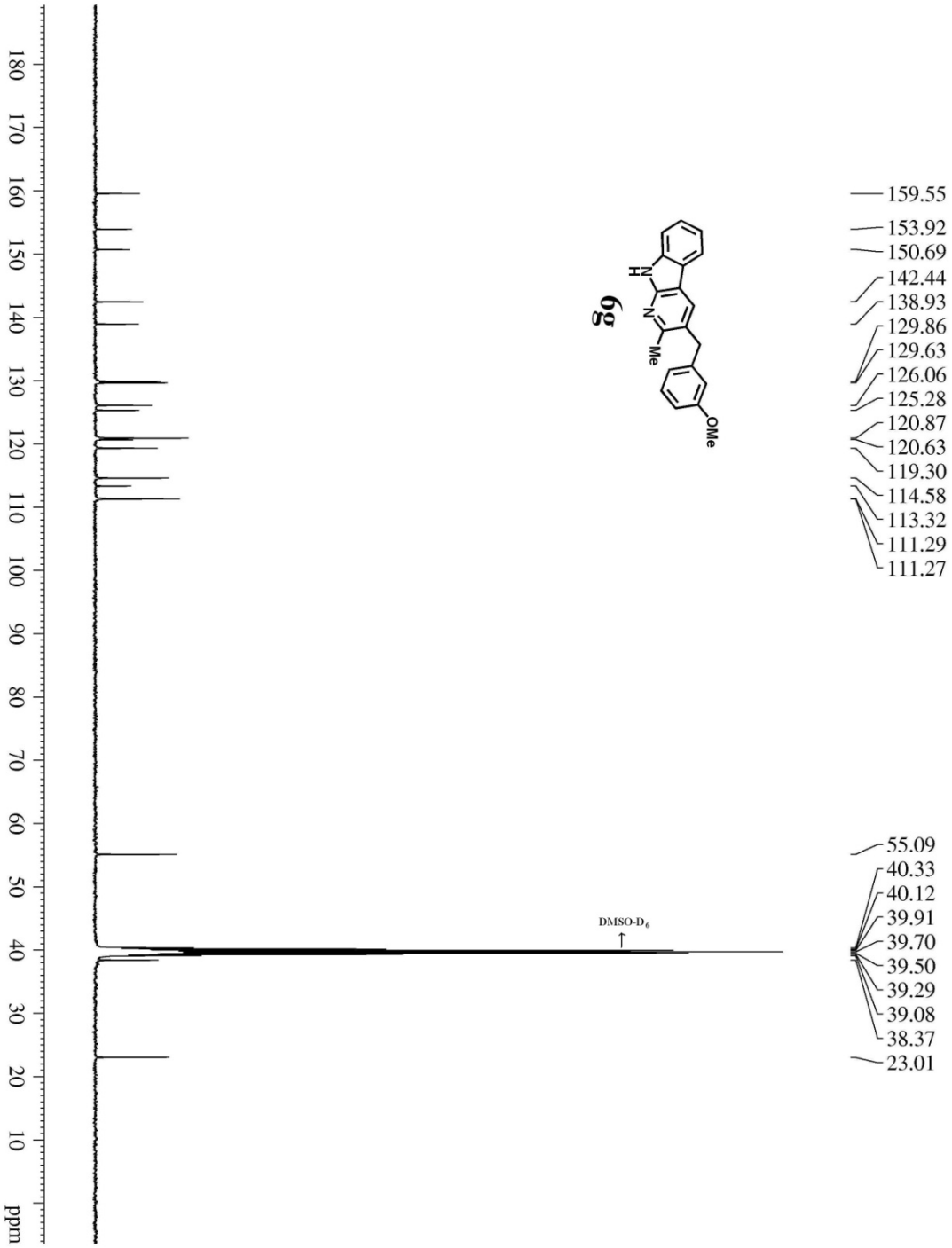

6e
11.603
8.281
8.067
8.047
7.490
7.469
7.455
7.419
7.401
7.382
7.196
7.177
7.160
7.139
4.105
3.363
2.510
2.474
moisture
DMSO
1.06
1.00
1.06
3.08
1.06
3.08
2.00
3.03
ppm

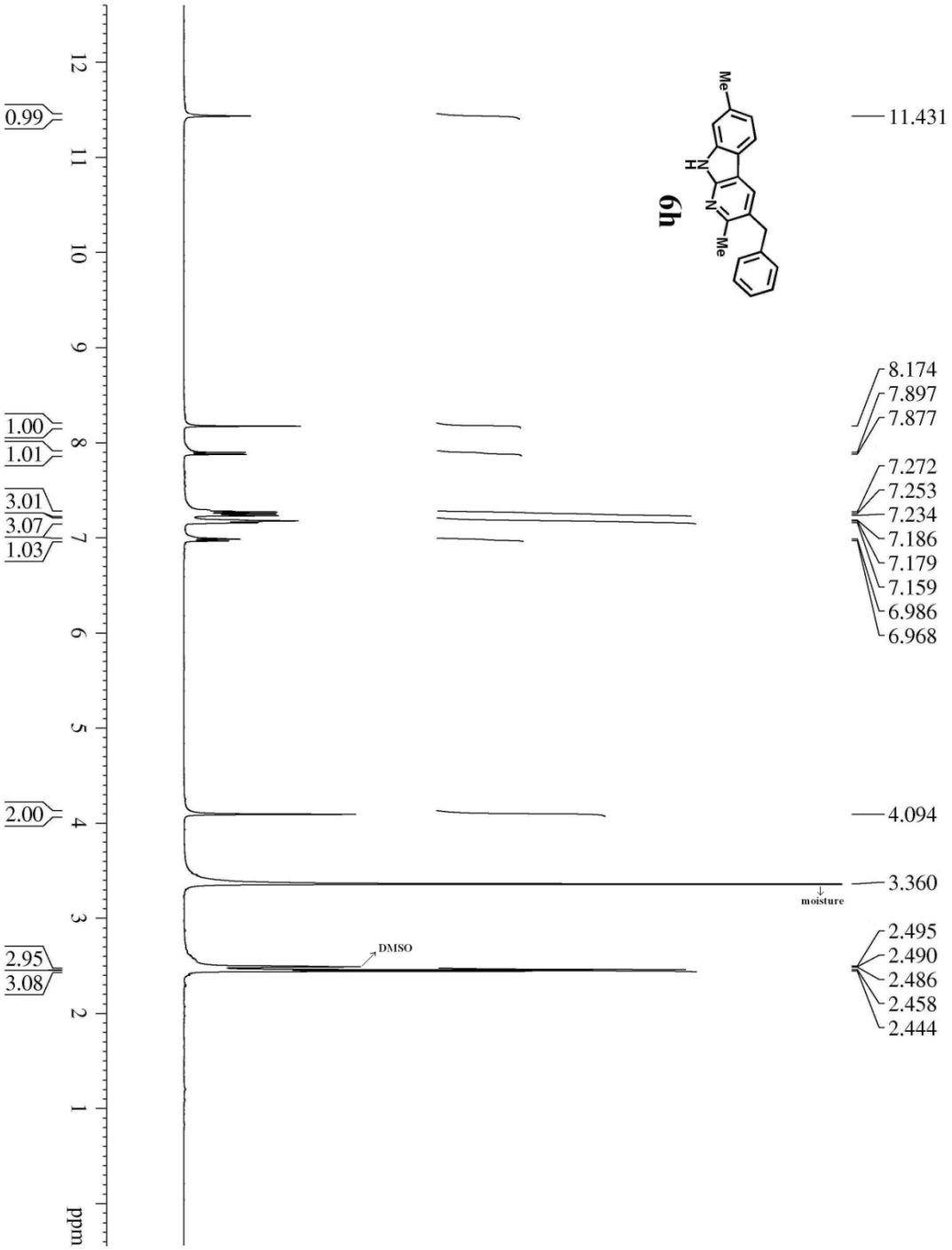


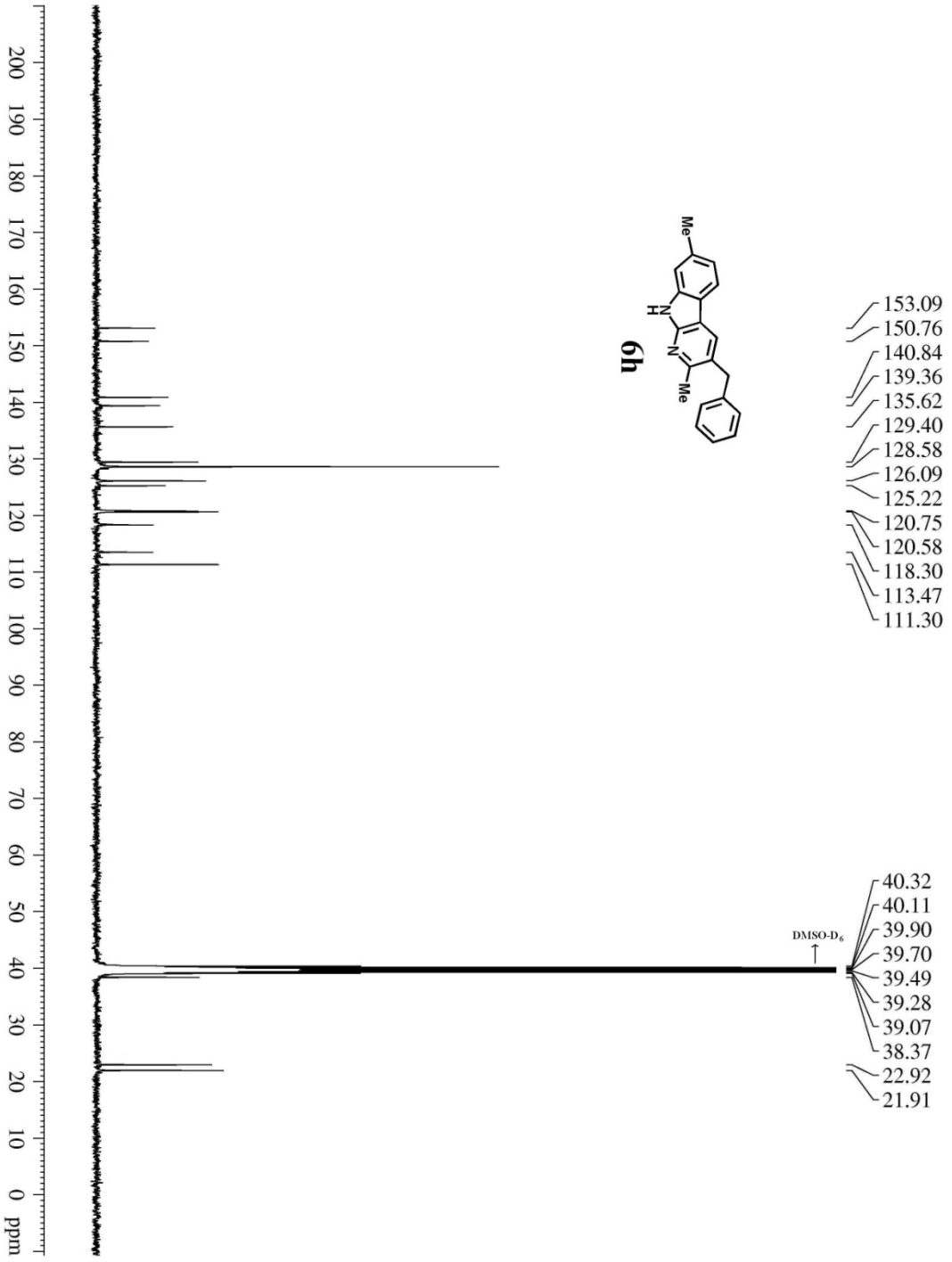

6f
H
N
N
Me
Br
11.588
8.283
8.054
8.035
7.475
7.455
7.408
7.388
7.368
7.364
7.338
7.258
7.238
7.219
7.182
7.165
7.148
4.116
3.523
moisture
2.497
2.451
DMSO
1.04
0.97
1.04
1.08
3.10
1.03
2.05
2.00
3.04
12
11
10
9
8
7
6
5
4
3
2
1
ppm

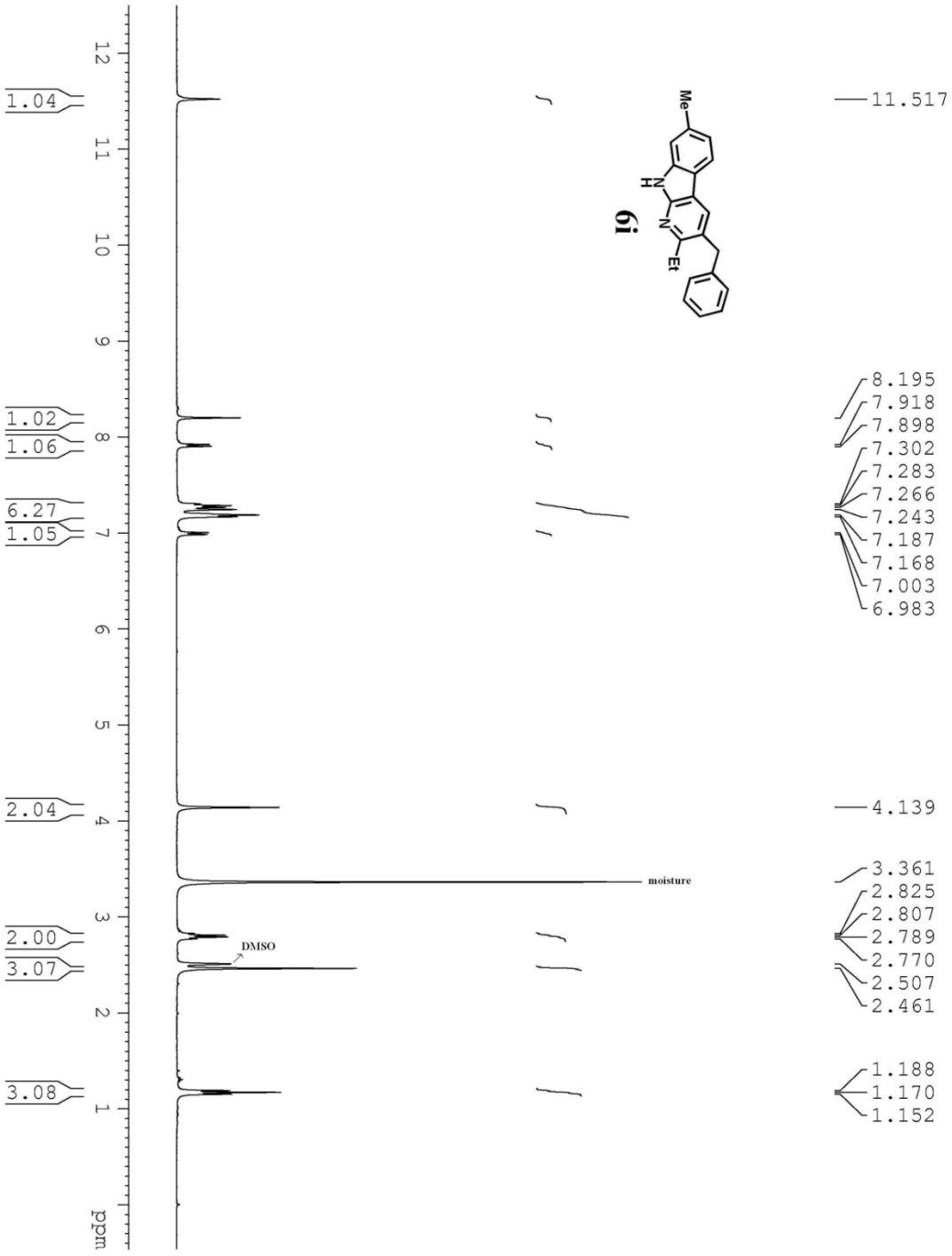


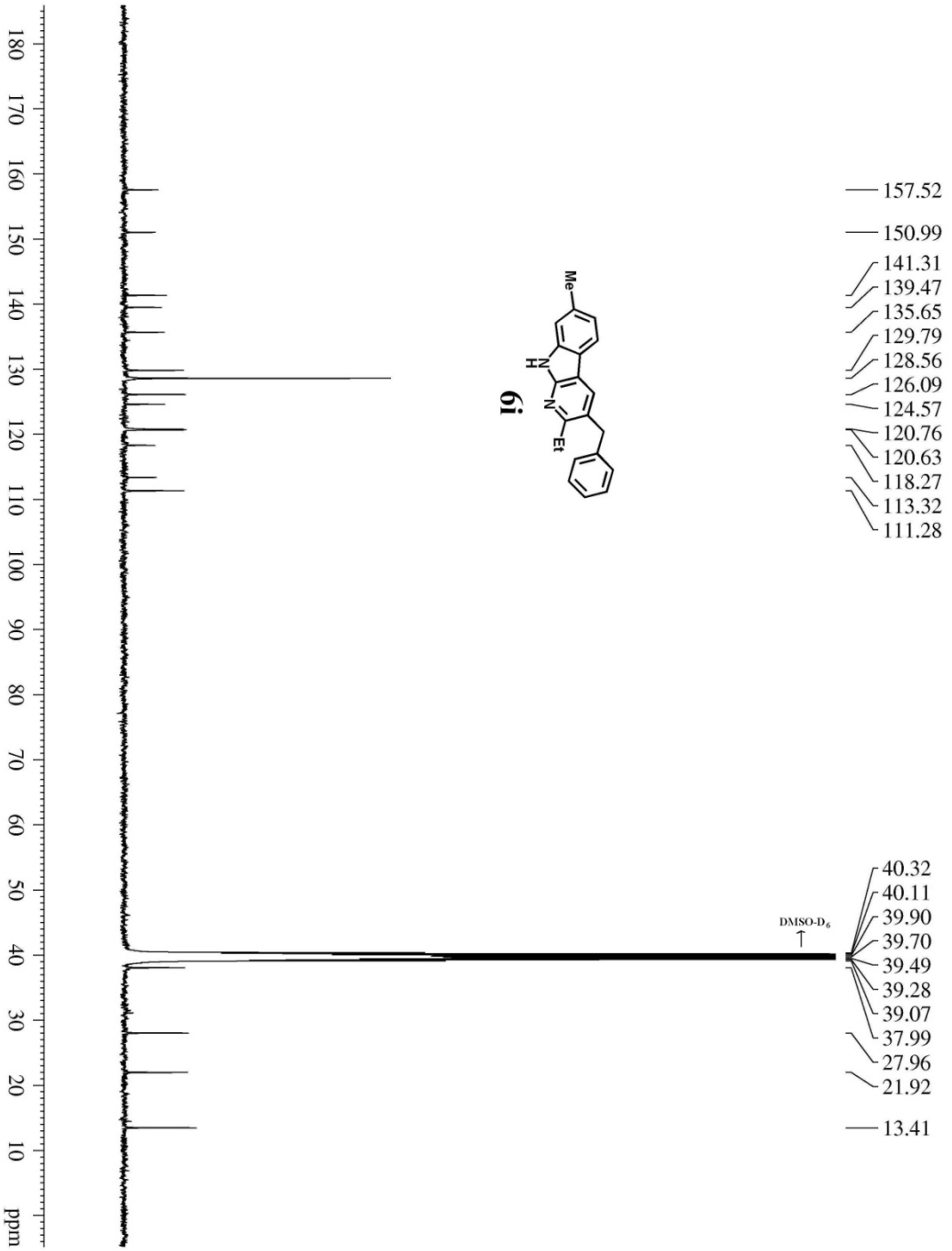


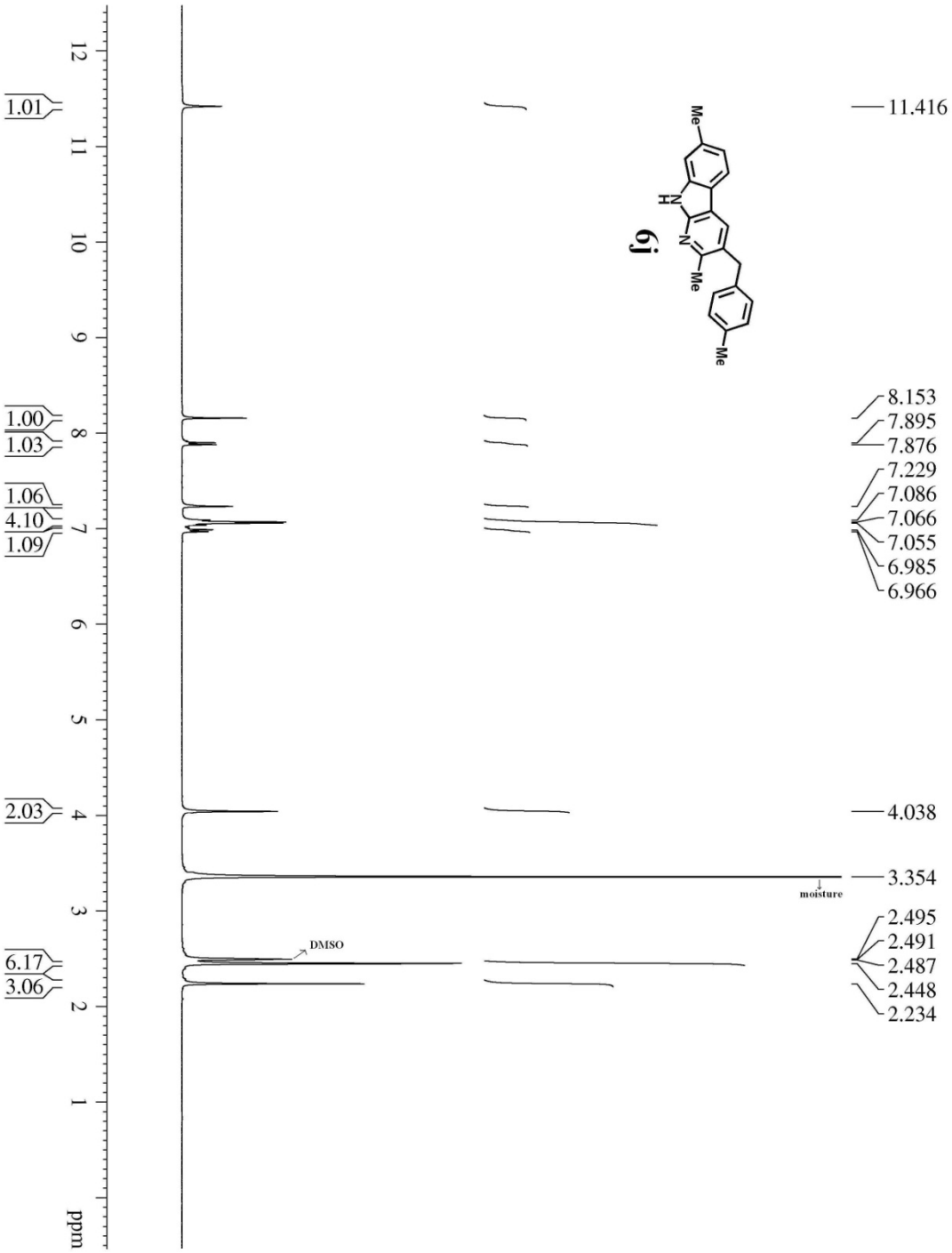


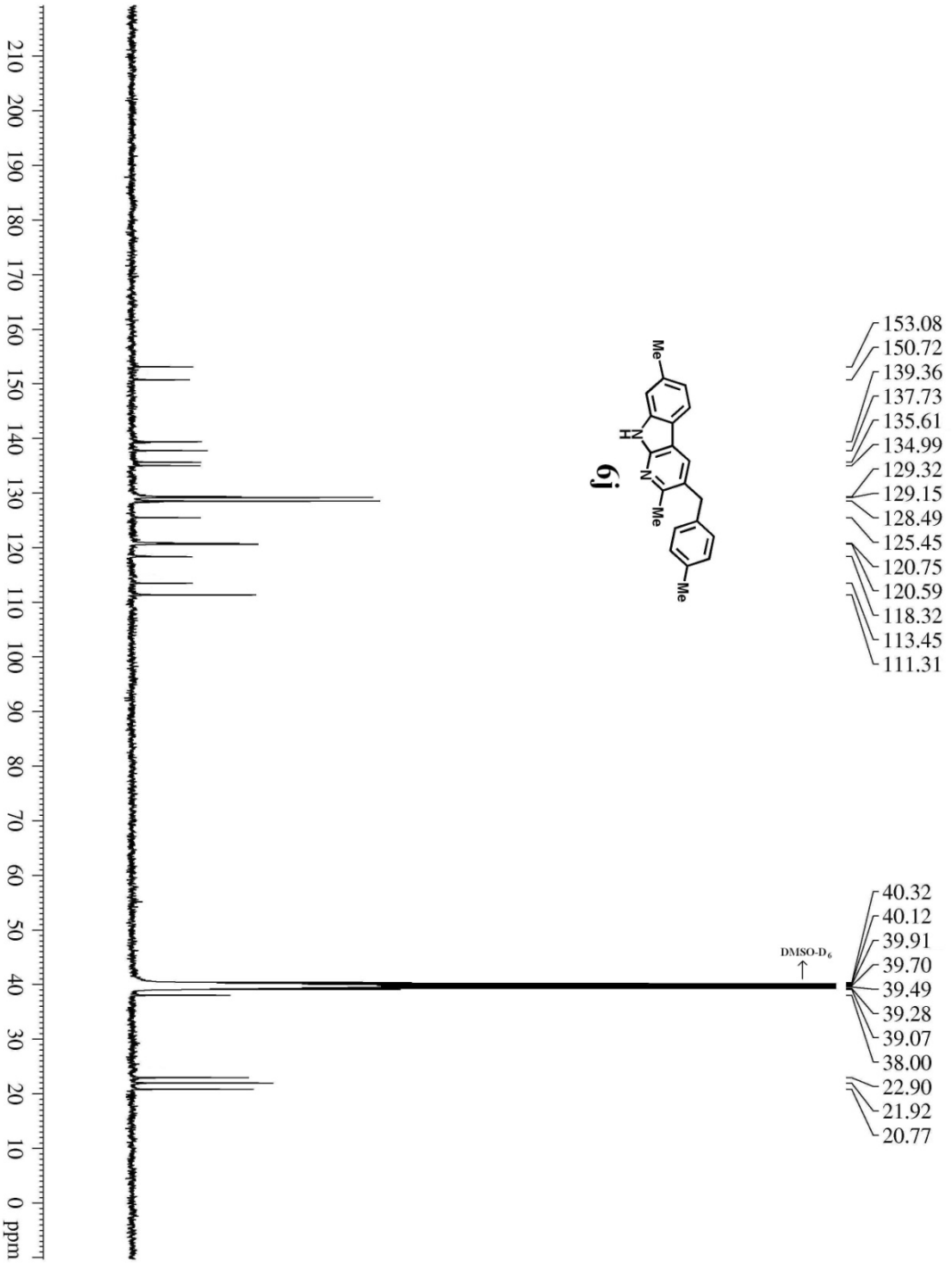

6h
Me
N
H
N
N
Me
11.431
8.174
7.897
7.877
7.272
7.253
7.234
7.186
7.179
7.159
6.986
6.968
4.094
3.360
moisture
DMSO
2.495
2.490
2.486
2.458
2.444
0.99
1.00
1.01
3.01
3.07
1.03
2.00
2.95
3.08
12
11
10
9
8
7
6
5
4
3
2
1
ppm

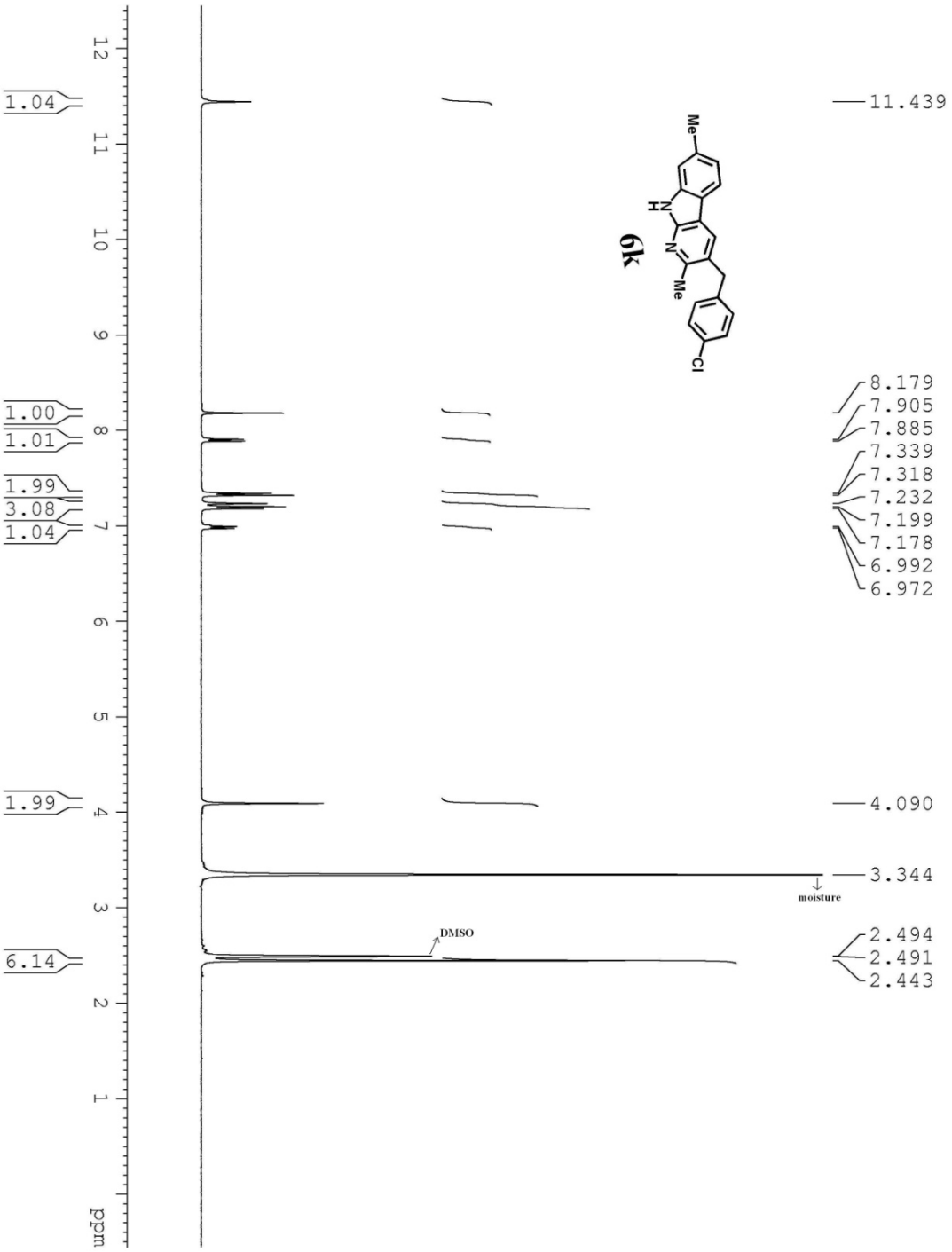


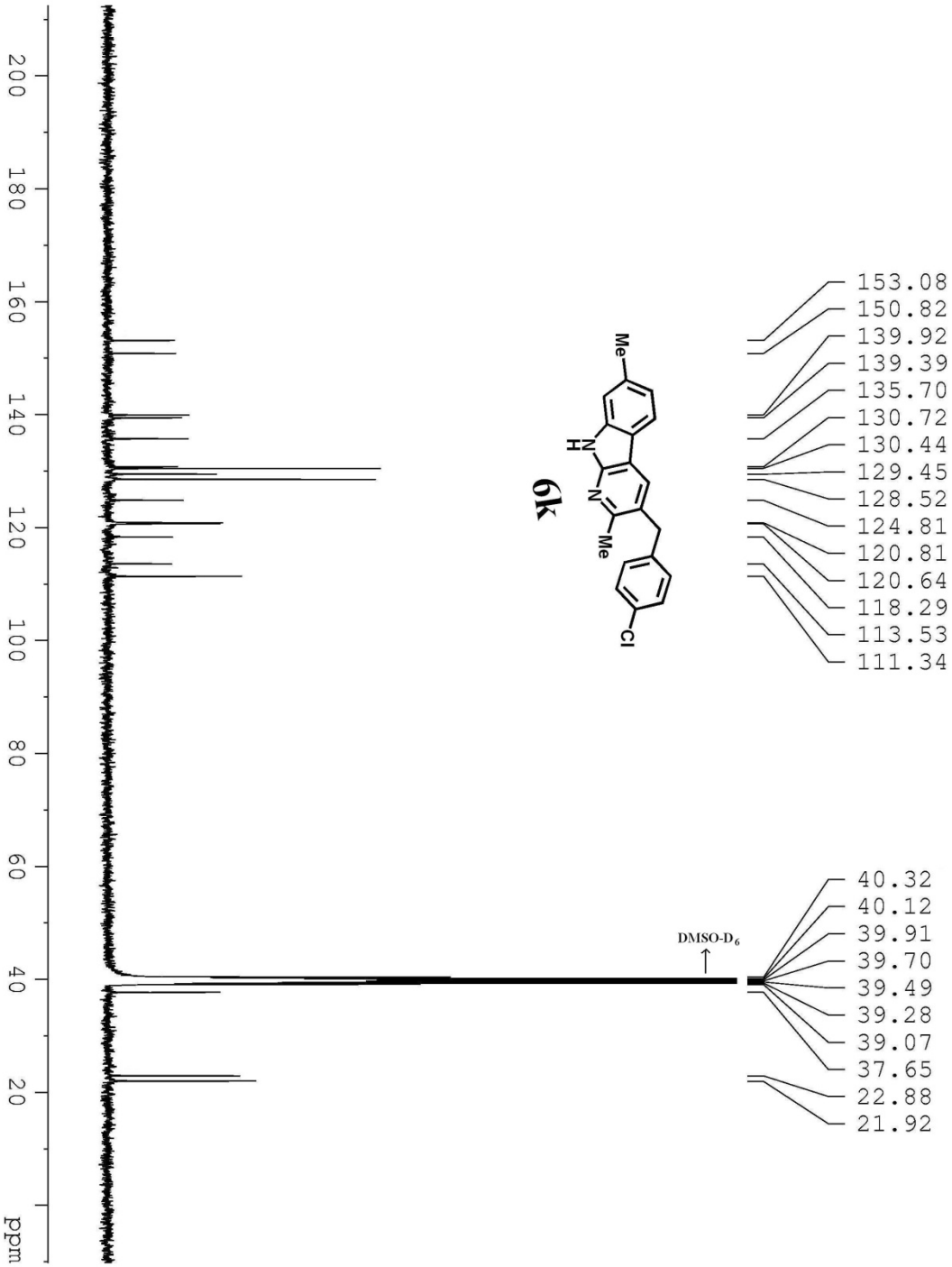


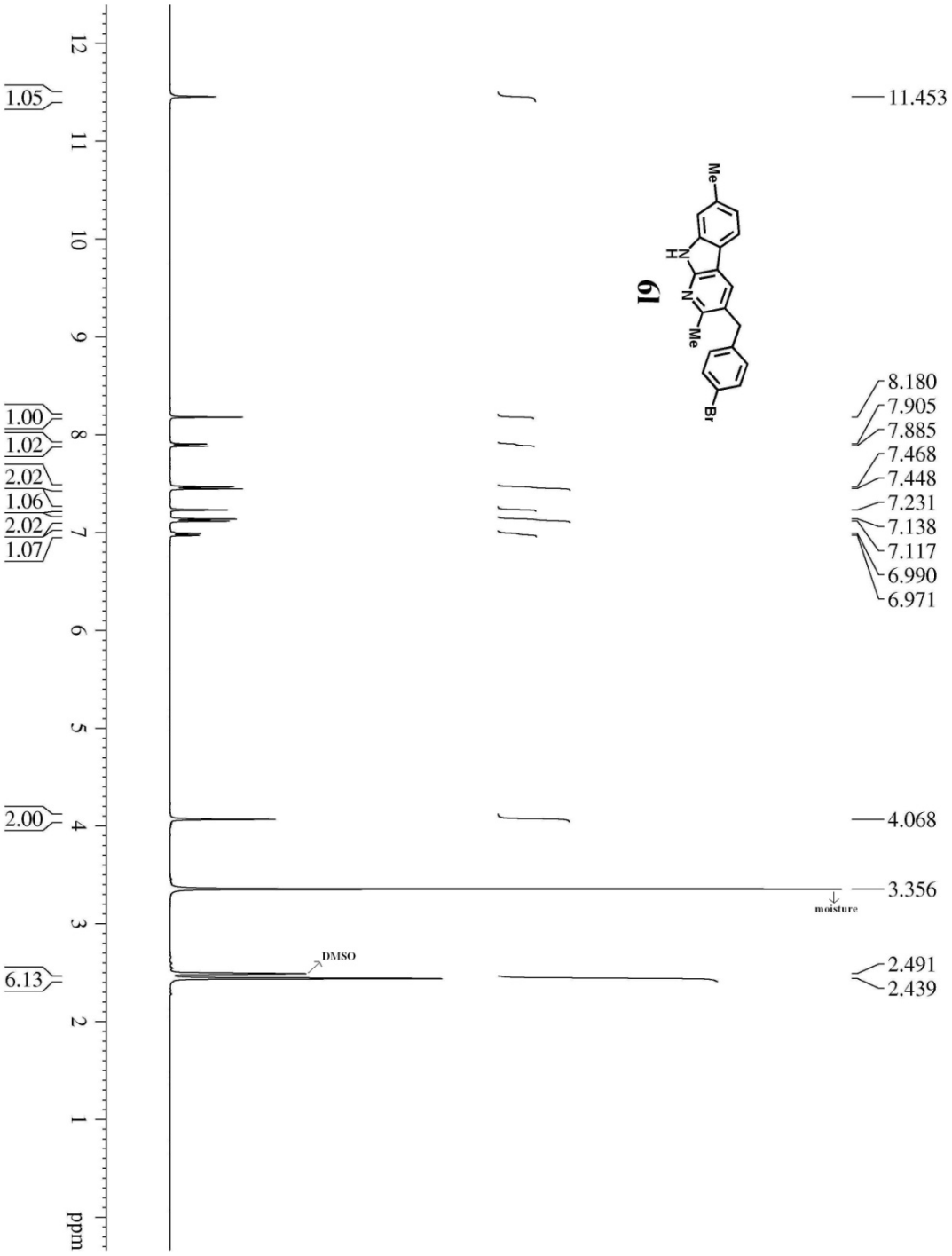

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
Me
H
N
N
Et
6j
157.52
150.99
141.31
139.47
135.65
129.79
128.56
126.09
124.57
120.76
120.63
118.27
113.32
111.28
DMSO-D6
40.32
40.11
39.90
39.70
39.49
39.28
39.07
37.99
27.96
21.92
13.41

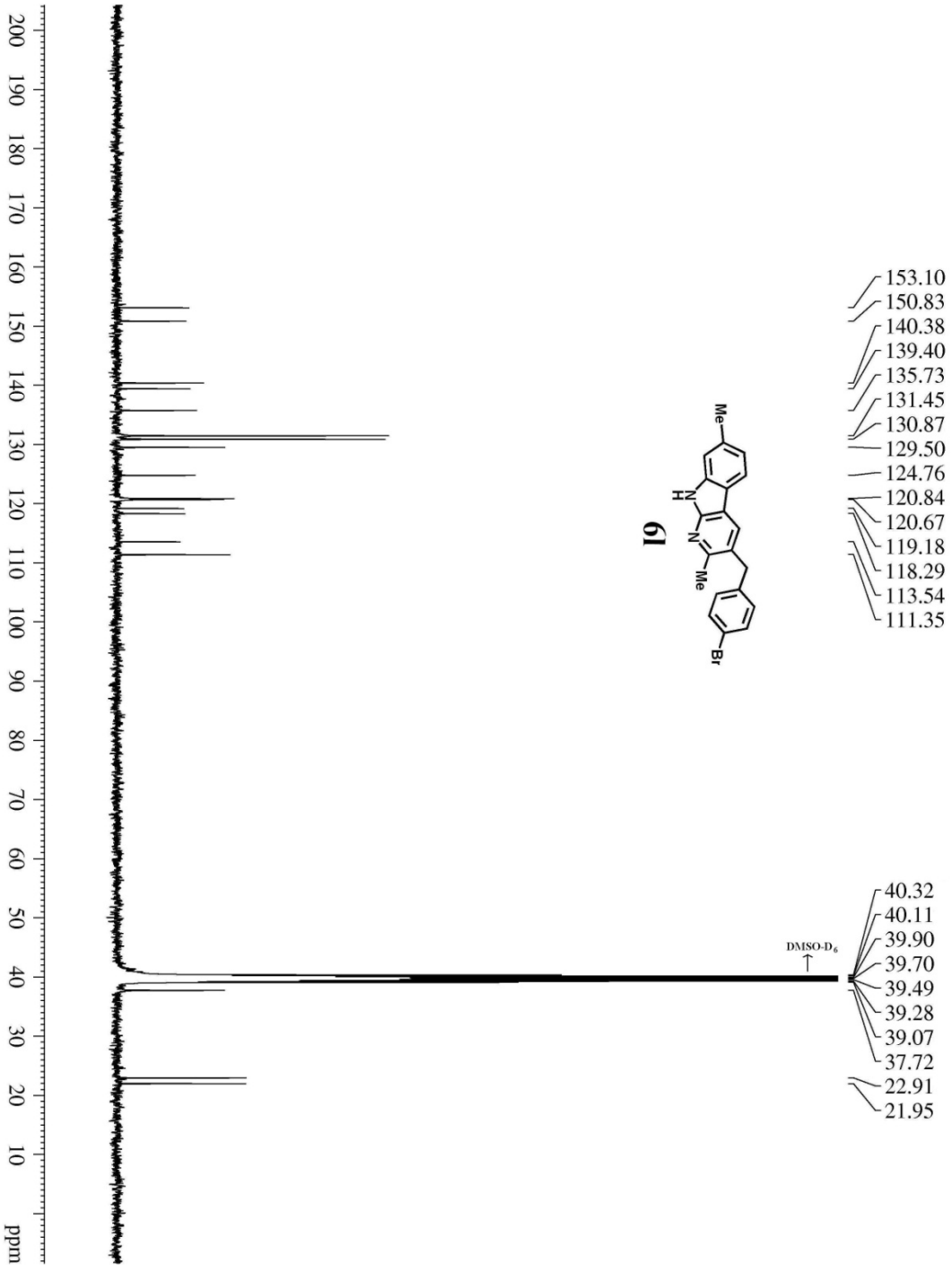

6j
Me
H
N
N
Me
Me
11.416
8.153
7.895
7.876
7.229
7.086
7.066
7.055
6.985
6.966
4.038
3.354
moisture
2.495
2.491
2.487
2.448
2.234
DMSO
1.01
1.00
1.03
1.06
4.10
1.09
2.03
6.17
3.06
ppm

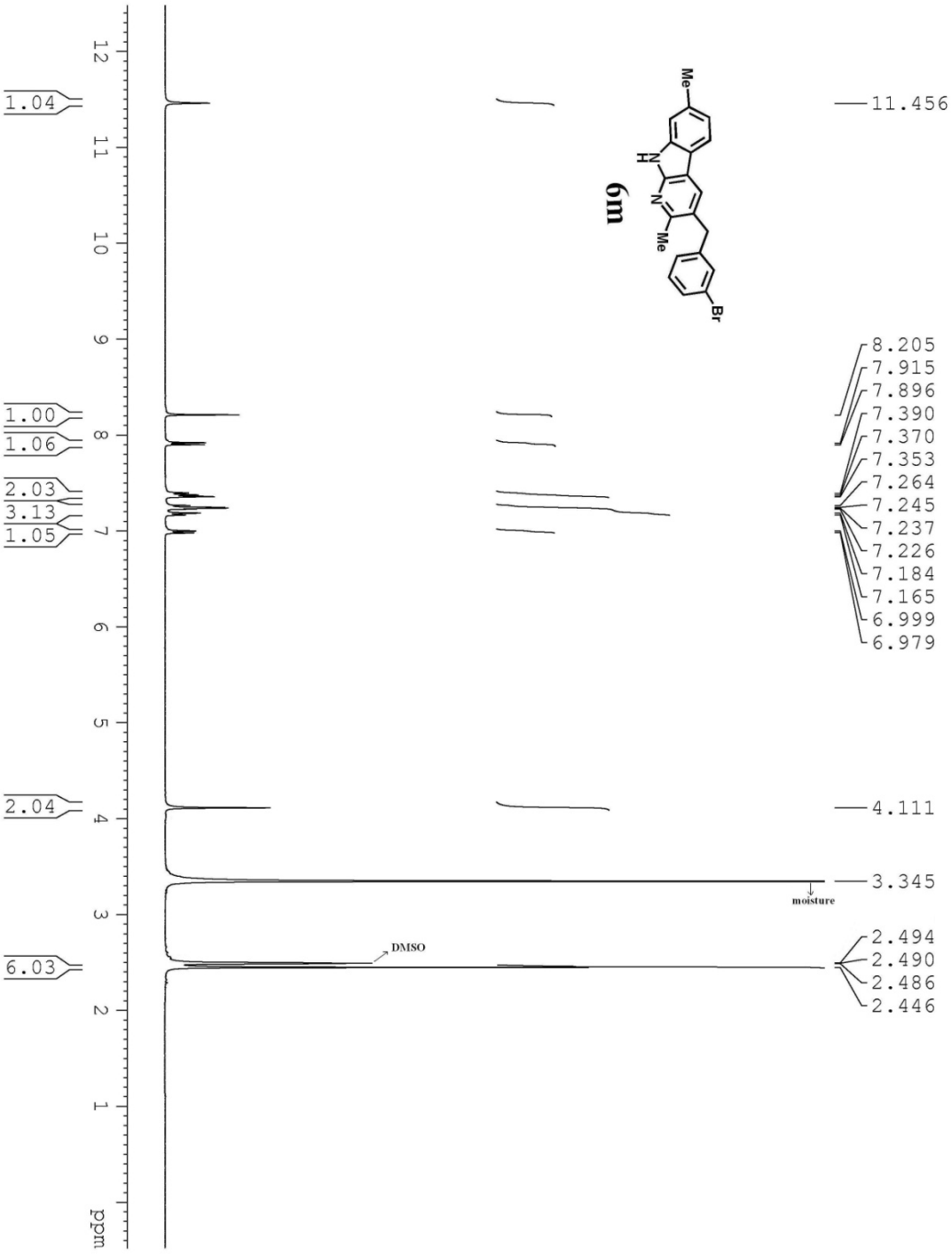


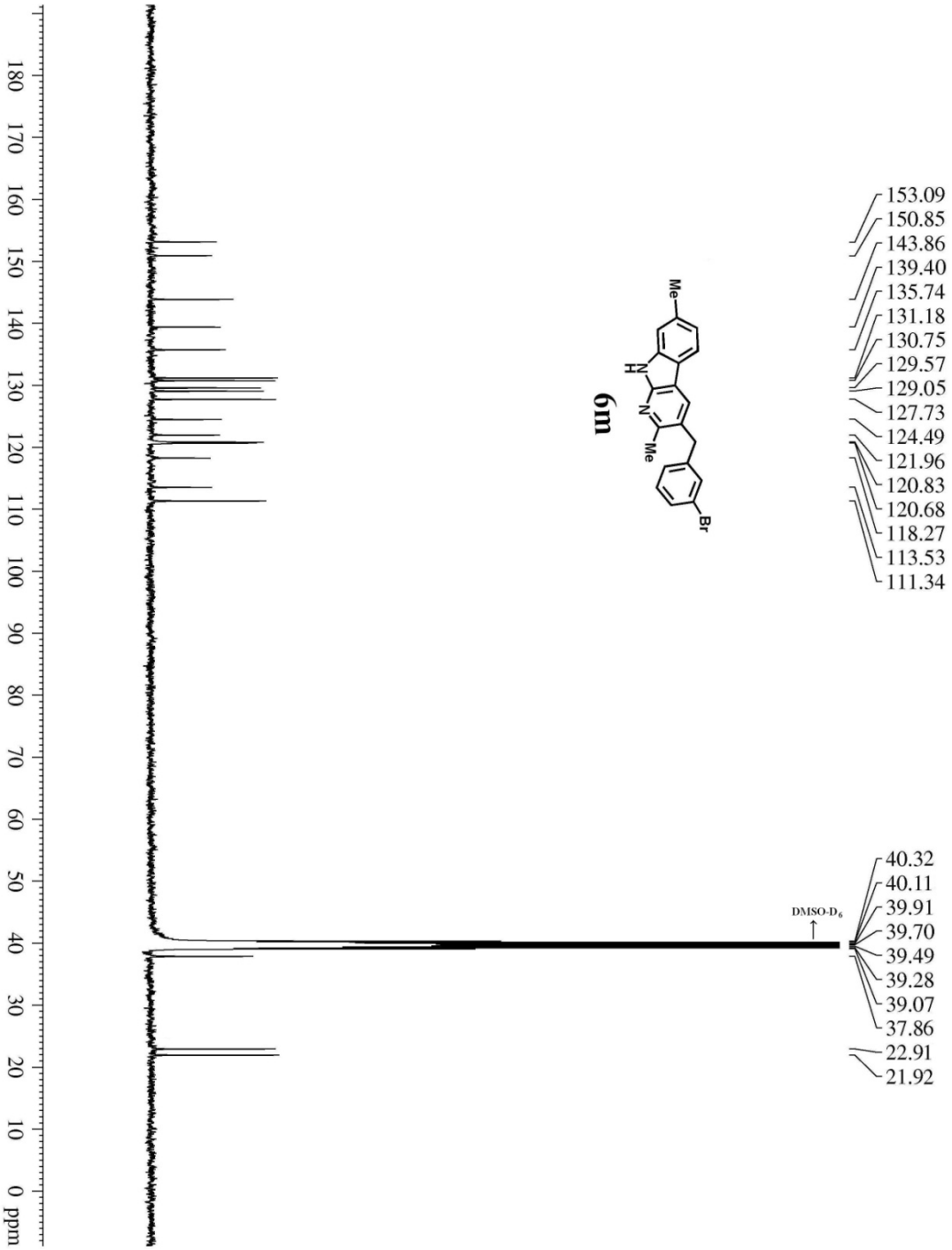


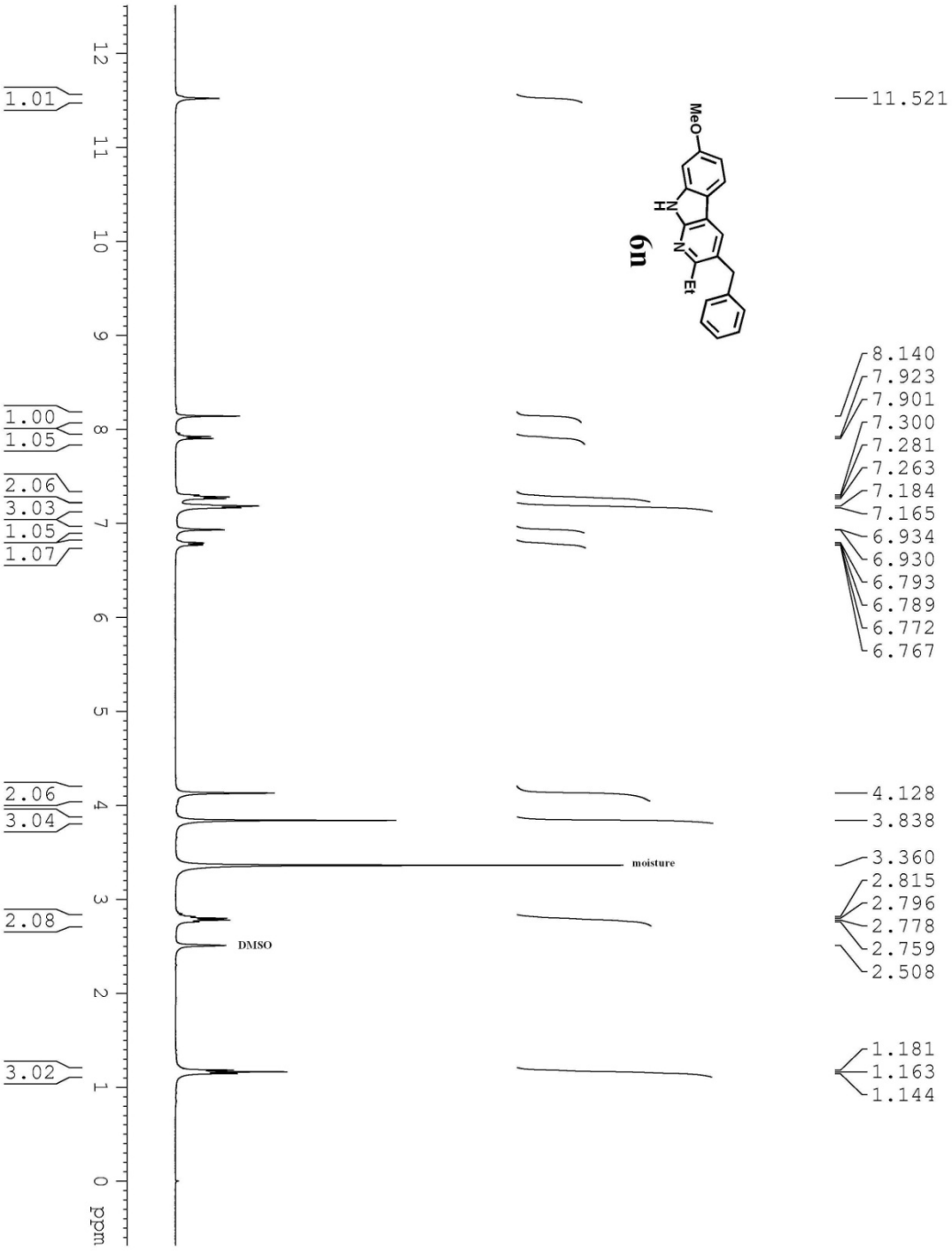


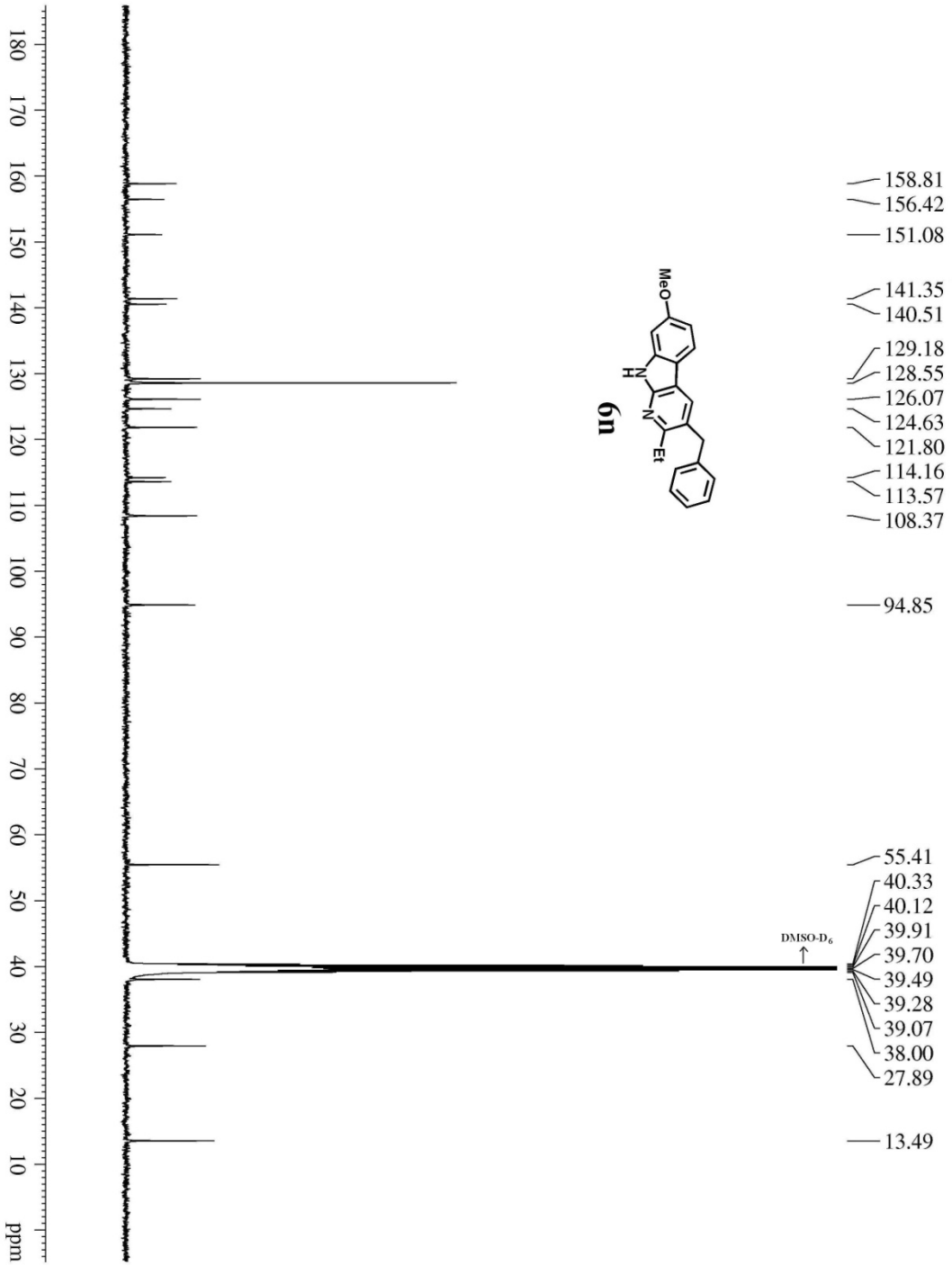

1.05
1.00
1.02
2.02
1.06
2.02
1.07
2.00
6.13
11.453
8.180
7.905
7.885
7.468
7.448
7.231
7.138
7.117
6.990
6.971
4.068
3.356
moisture
2.491
2.439
DMSO
ppm
6l
Me
H
N
N
Me
Br

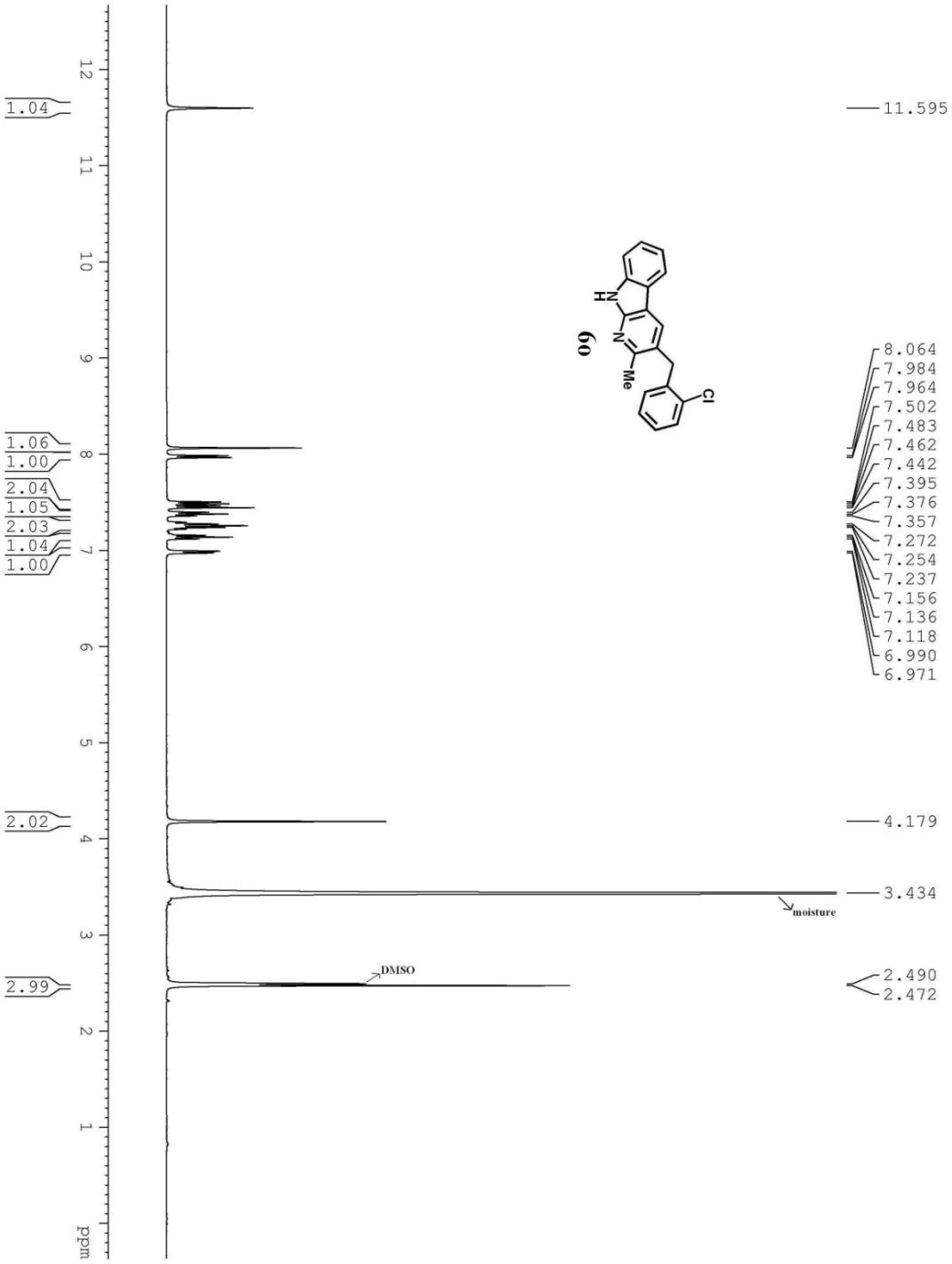









158.81
156.42
151.08
141.35
140.51
129.18
128.55
126.07
124.63
121.80
114.16
113.57
108.37
94.85
55.41
40.33
40.12
39.91
39.70
39.49
39.28
39.07
38.00
27.89
13.49
DMSO-D6
MeO
H
N
Et
ug
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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1.06
1.00
2.04
1.05
2.03
1.04
1.00
2.02
2.99
ppm
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7.984
7.964
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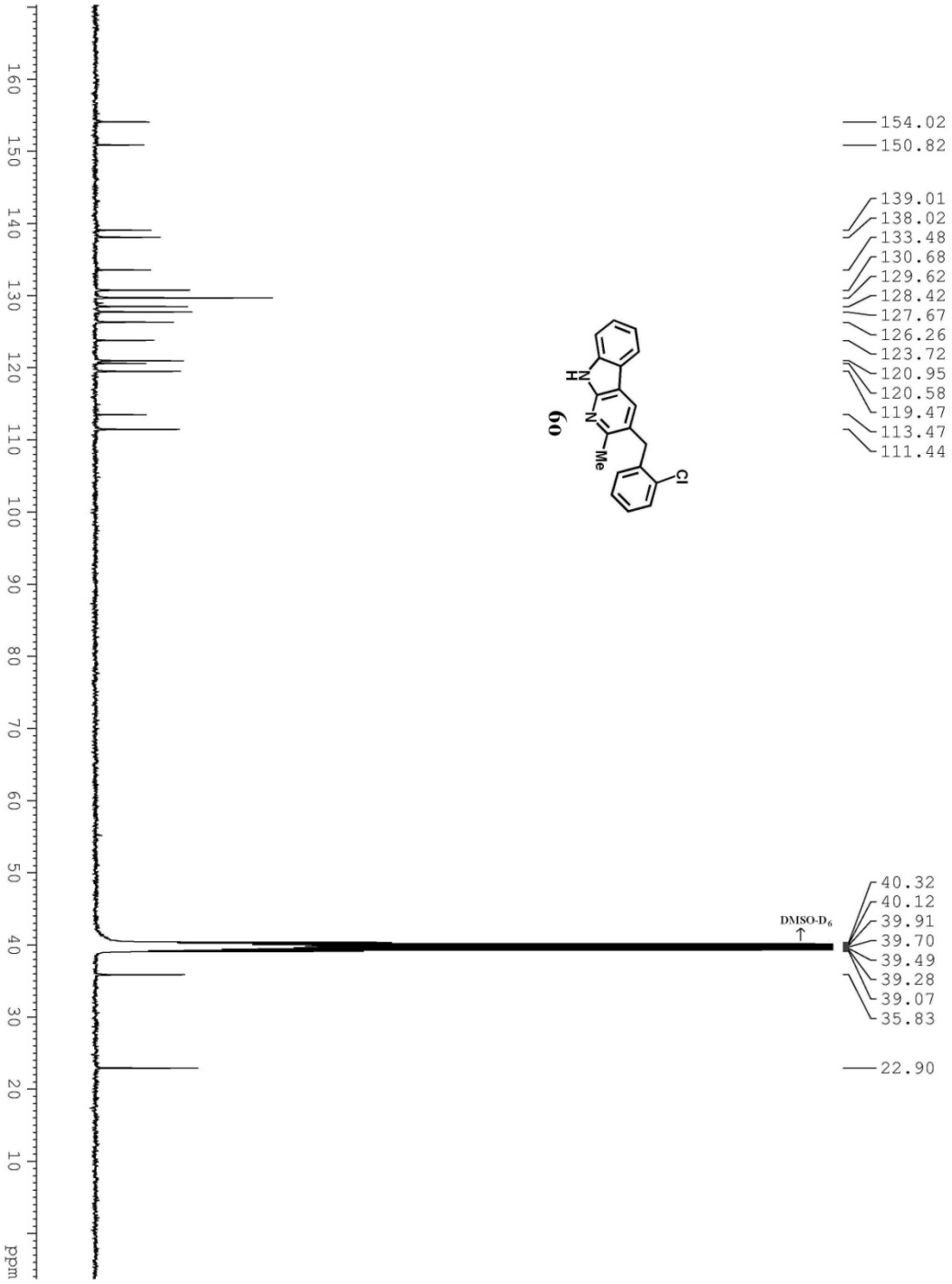
7.483
7.462
7.442
7.395
7.376
7.357
7.272
7.254
7.237
7.156
7.136
7.118
6.990
6.971
4.179
3.434
moisture
DMSO
2.490
2.472
6g
Me
Cl



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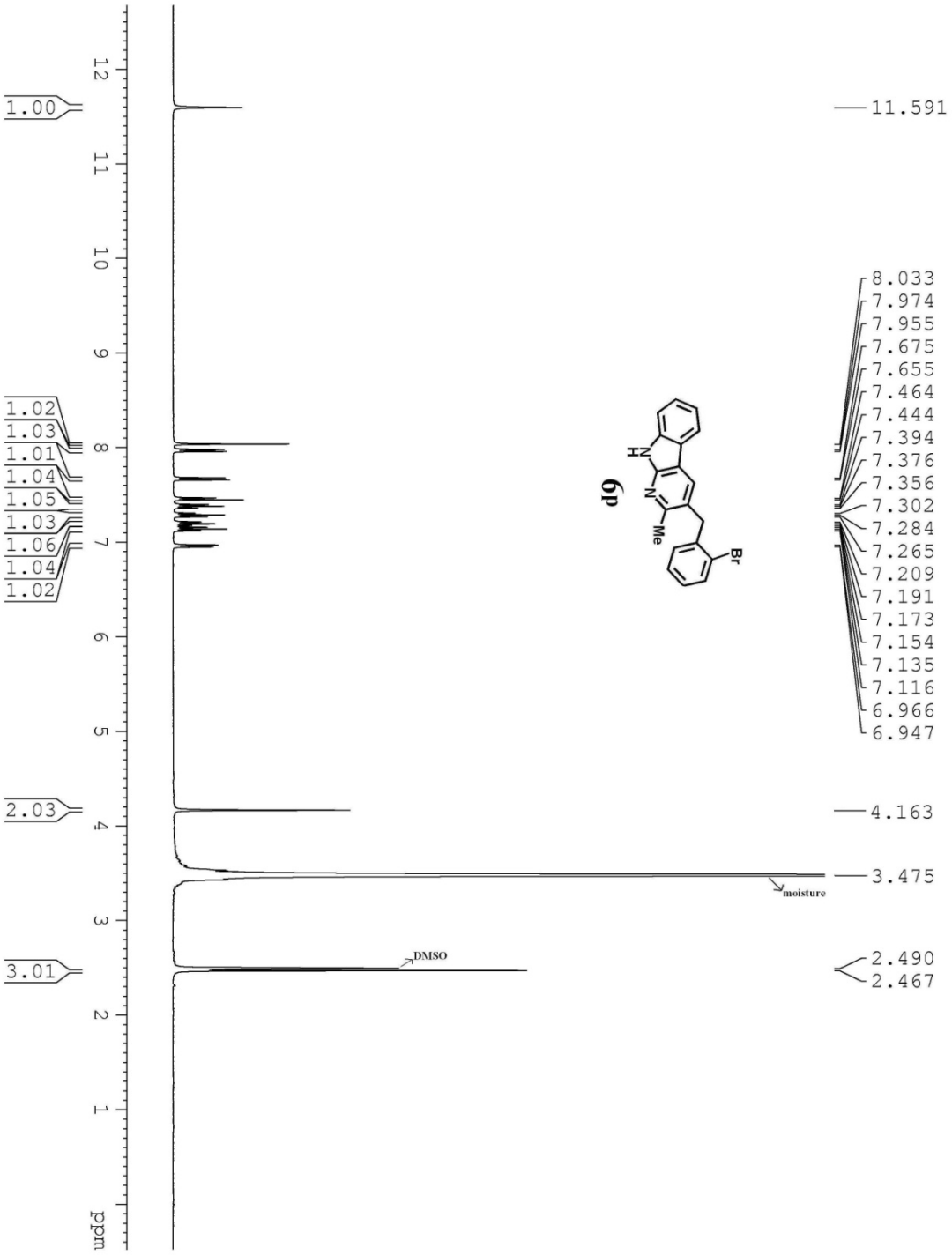
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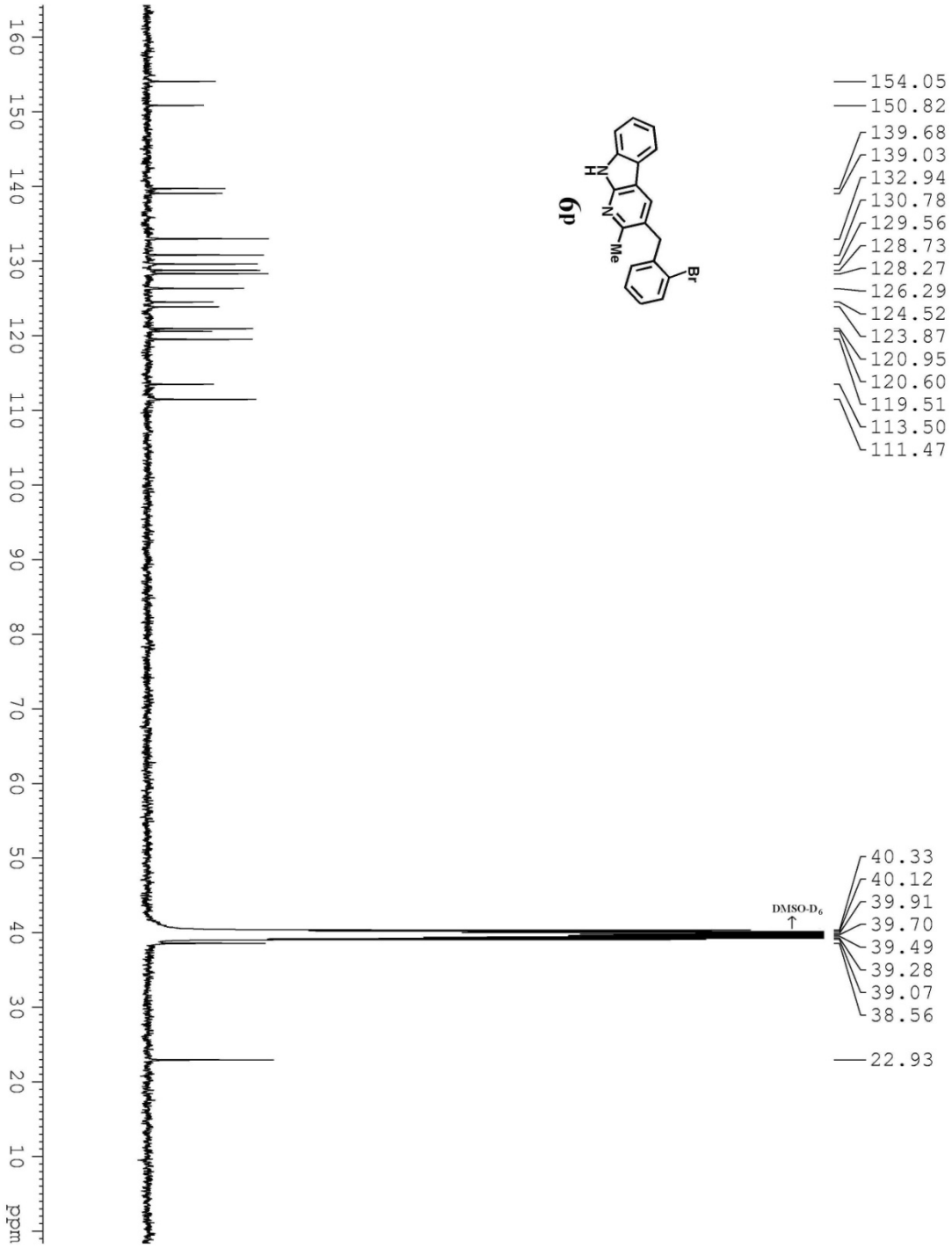
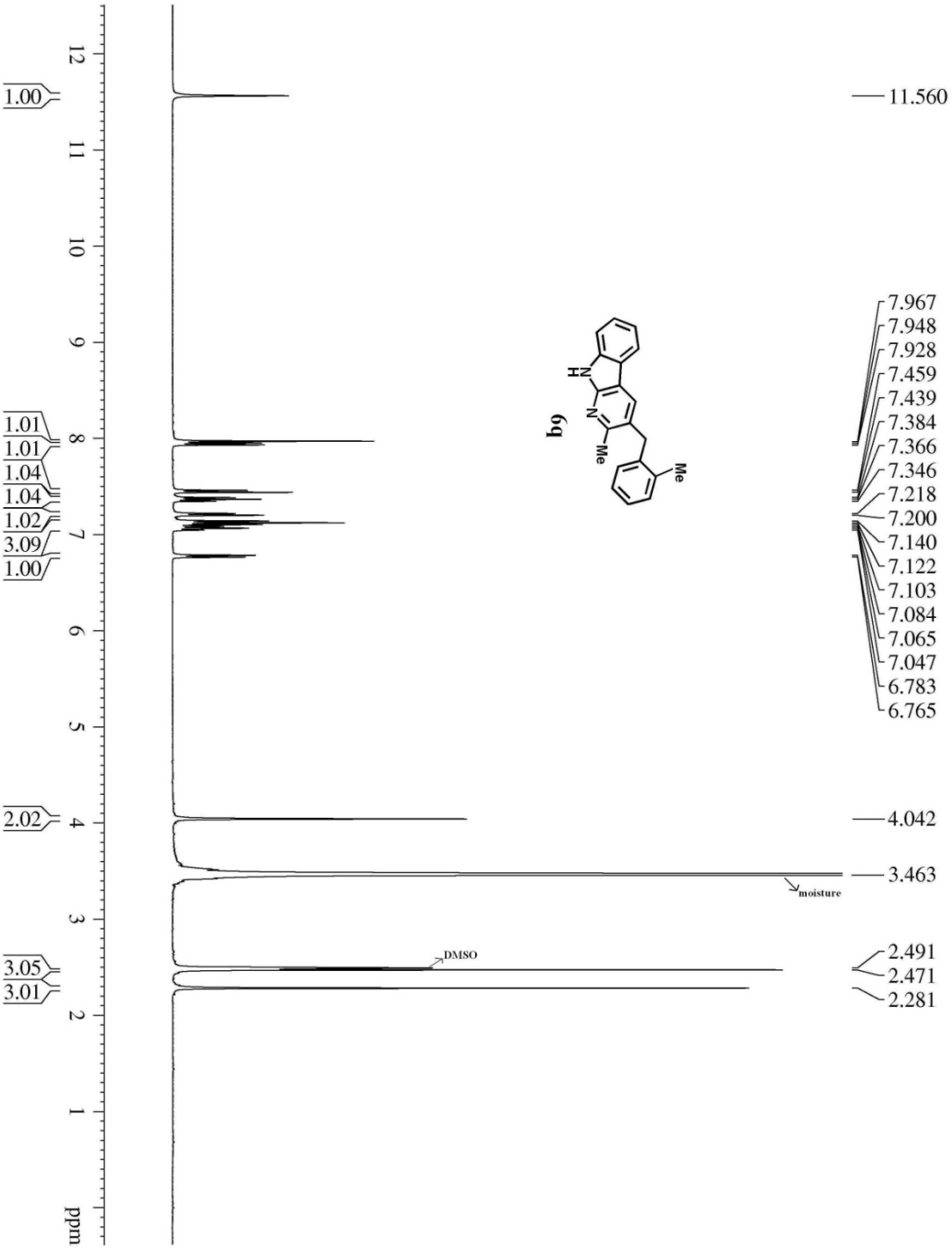
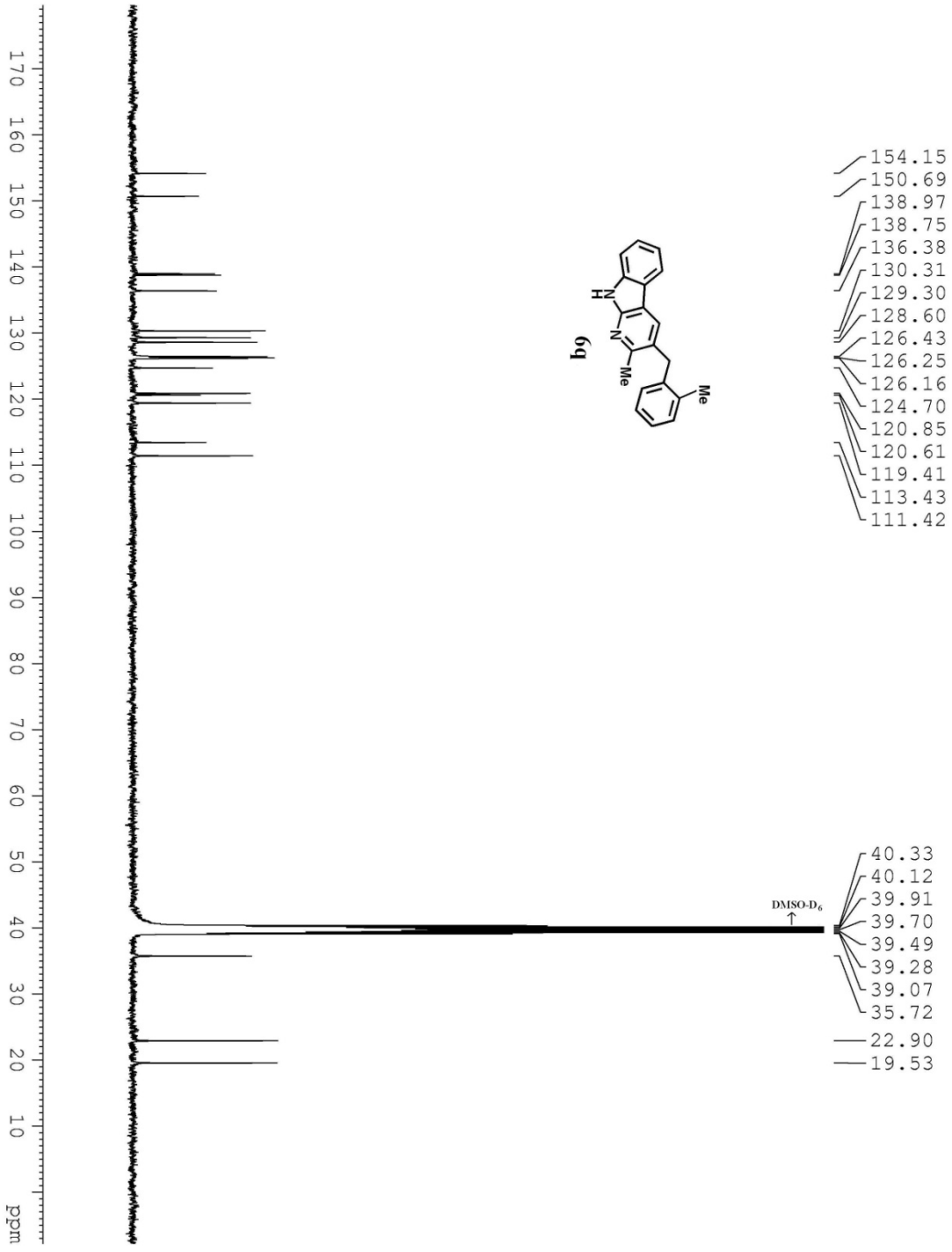
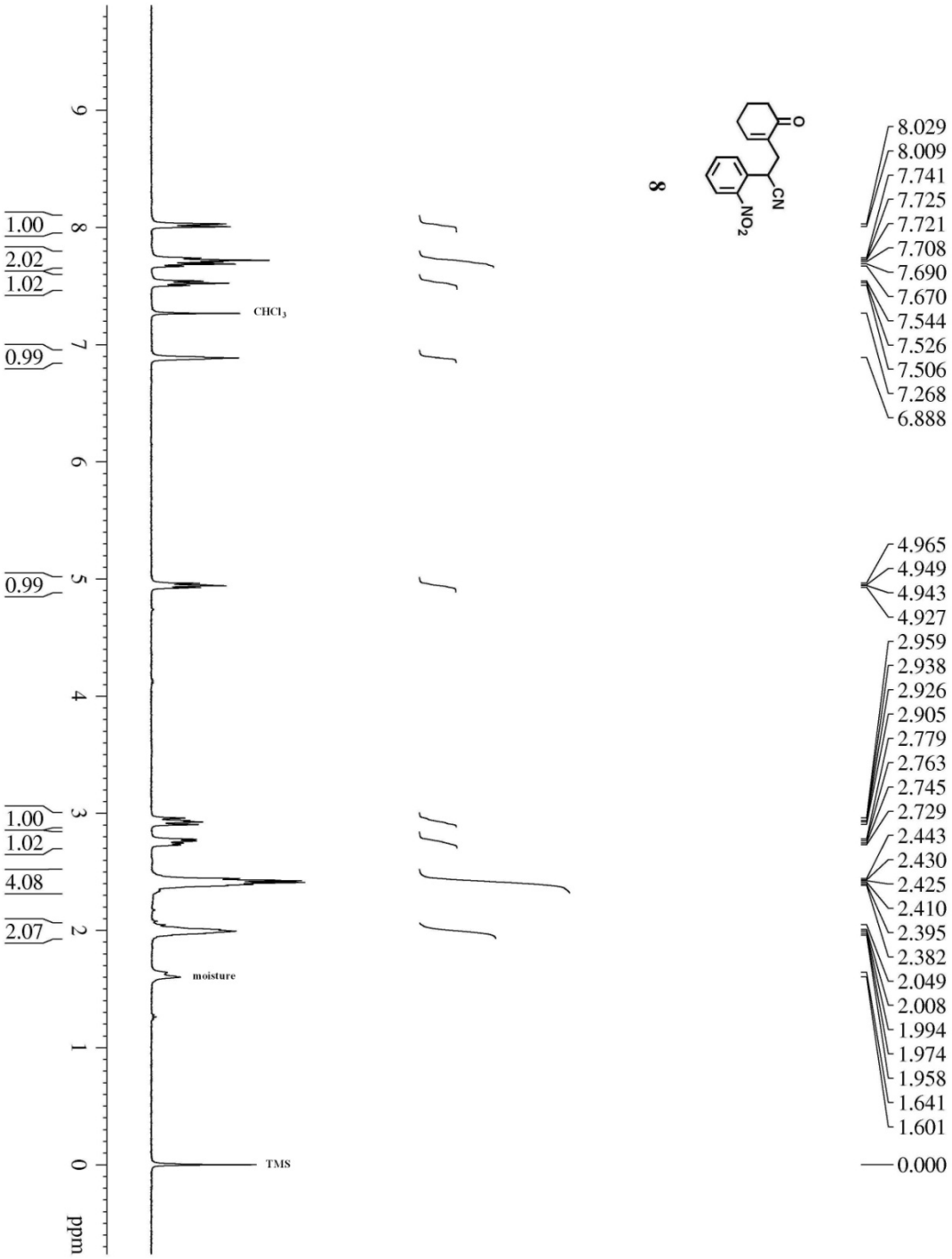
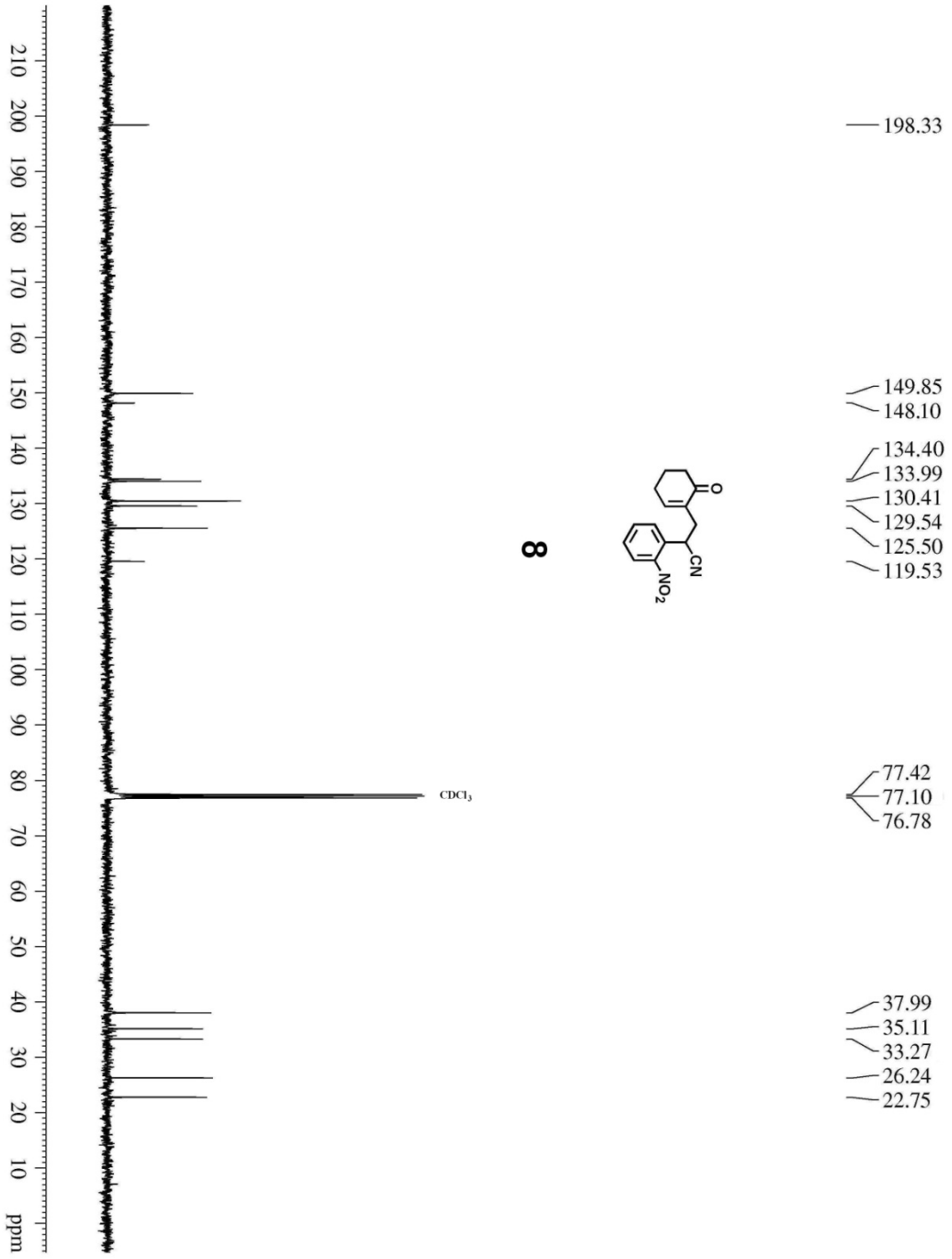
1.02
1.03
1.01
1.04
1.05
1.03
1.06
1.04
1.02
2.03
3.01
11.591
8.033
7.974
7.955
7.675
7.655
7.464
7.444
7.394
7.376
7.356
7.302
7.284
7.265
7.209
7.191
7.173
7.154
7.135
7.116
6.966
6.947
4.163
3.475
2.490
2.467
moisture
DMSO
6p
H
N
N
Me
Br
ppm

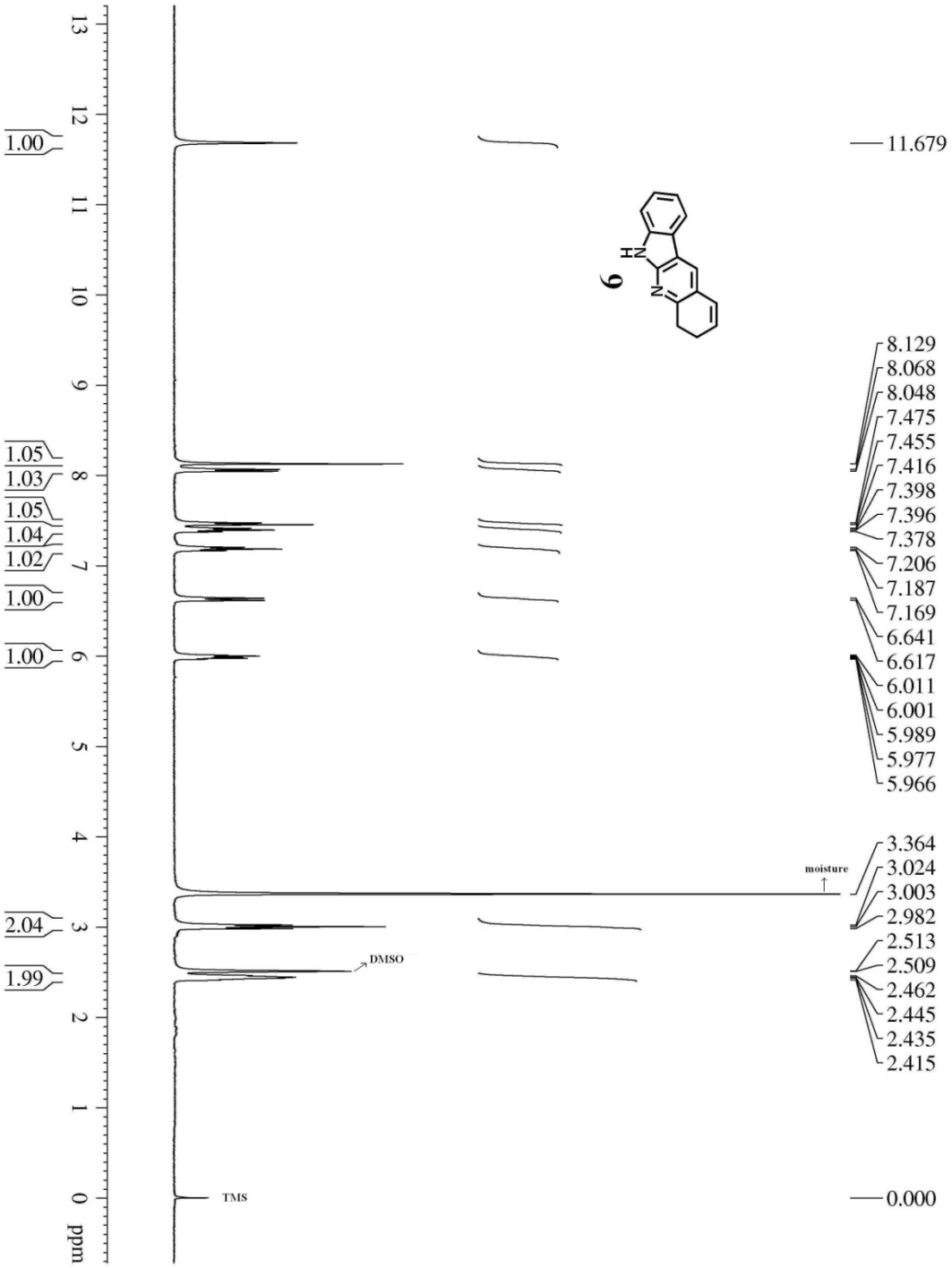


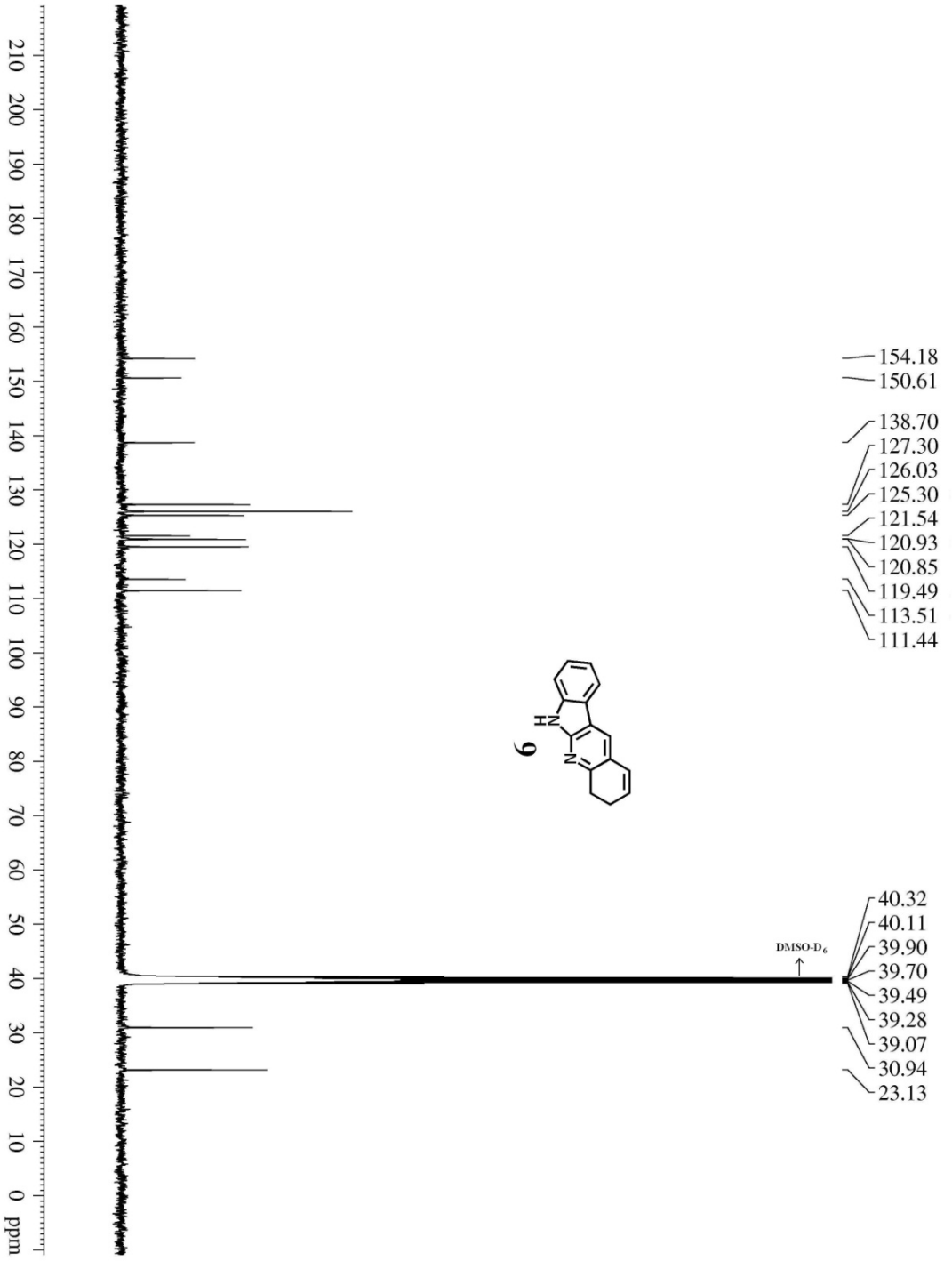

1.00
1.01
1.01
1.04
1.04
1.02
3.09
1.00
2.02
3.05
3.01
ppm
11.560
7.967
7.948
7.928
7.459
7.439
7.384
7.366
7.346
7.218
7.200
7.140
7.122
7.103
7.084
7.065
7.047
6.783
6.765
4.042
3.463
moisture
DMSO
2.491
2.471
2.281
6g
Me
Me

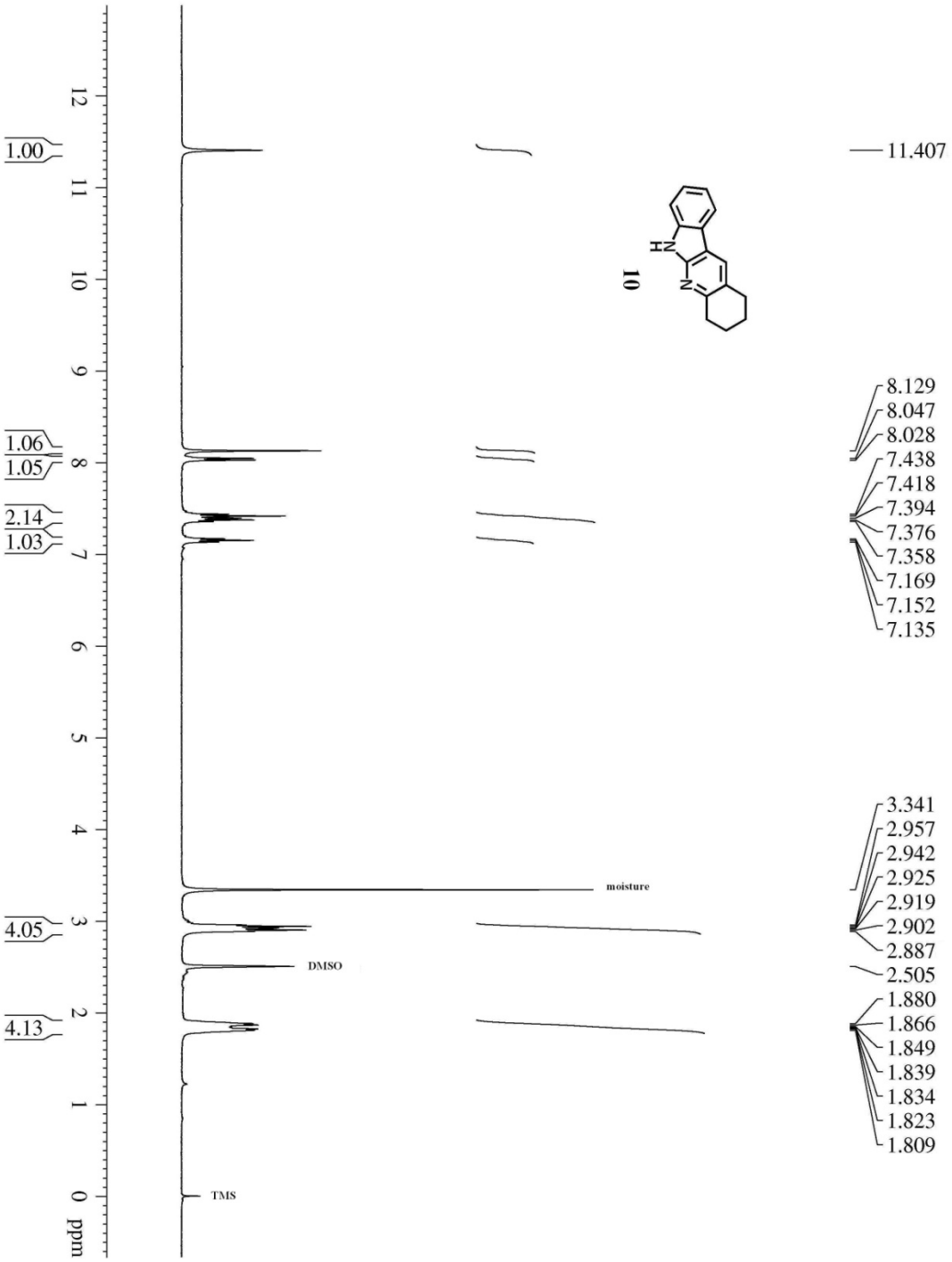


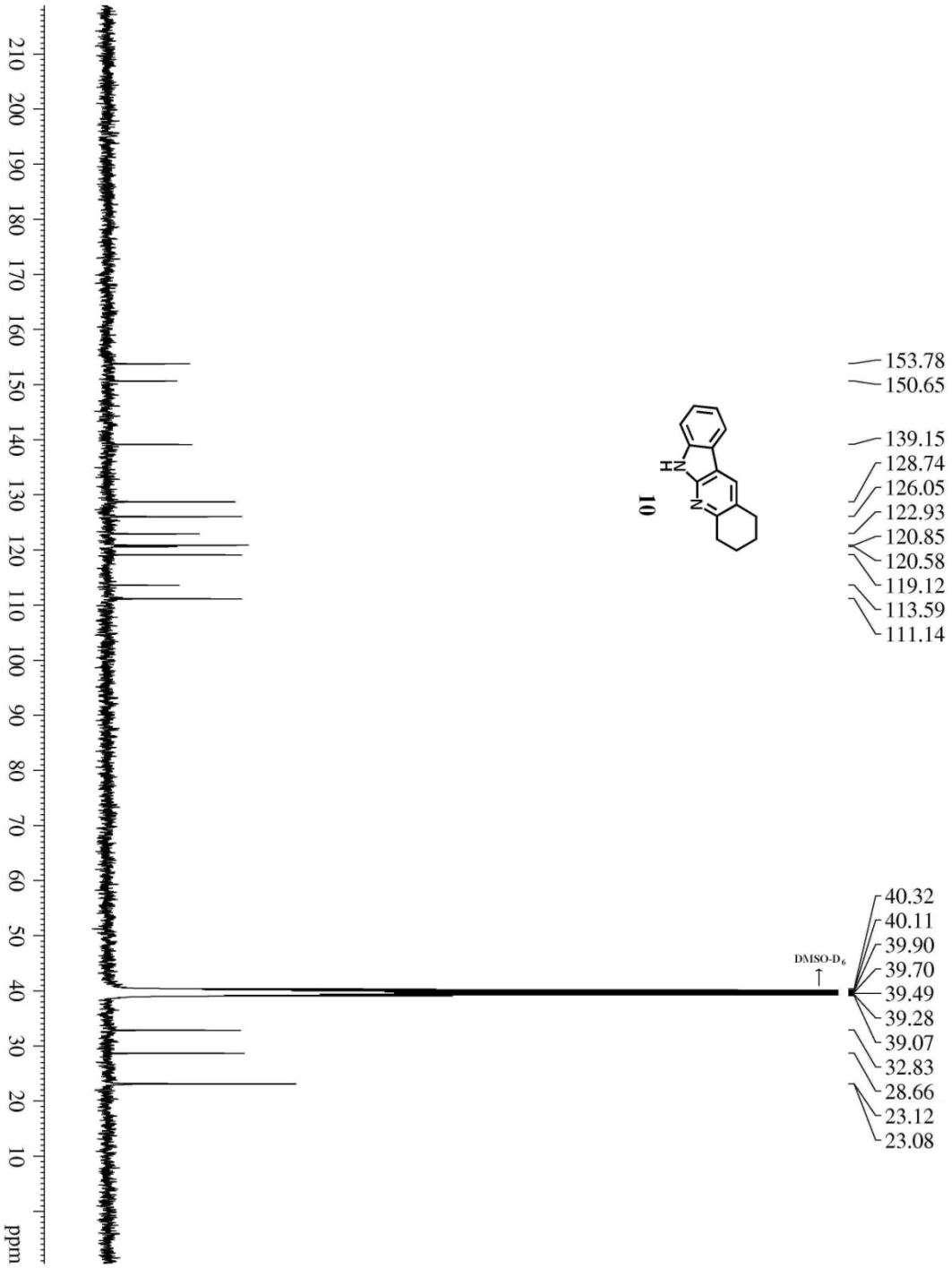


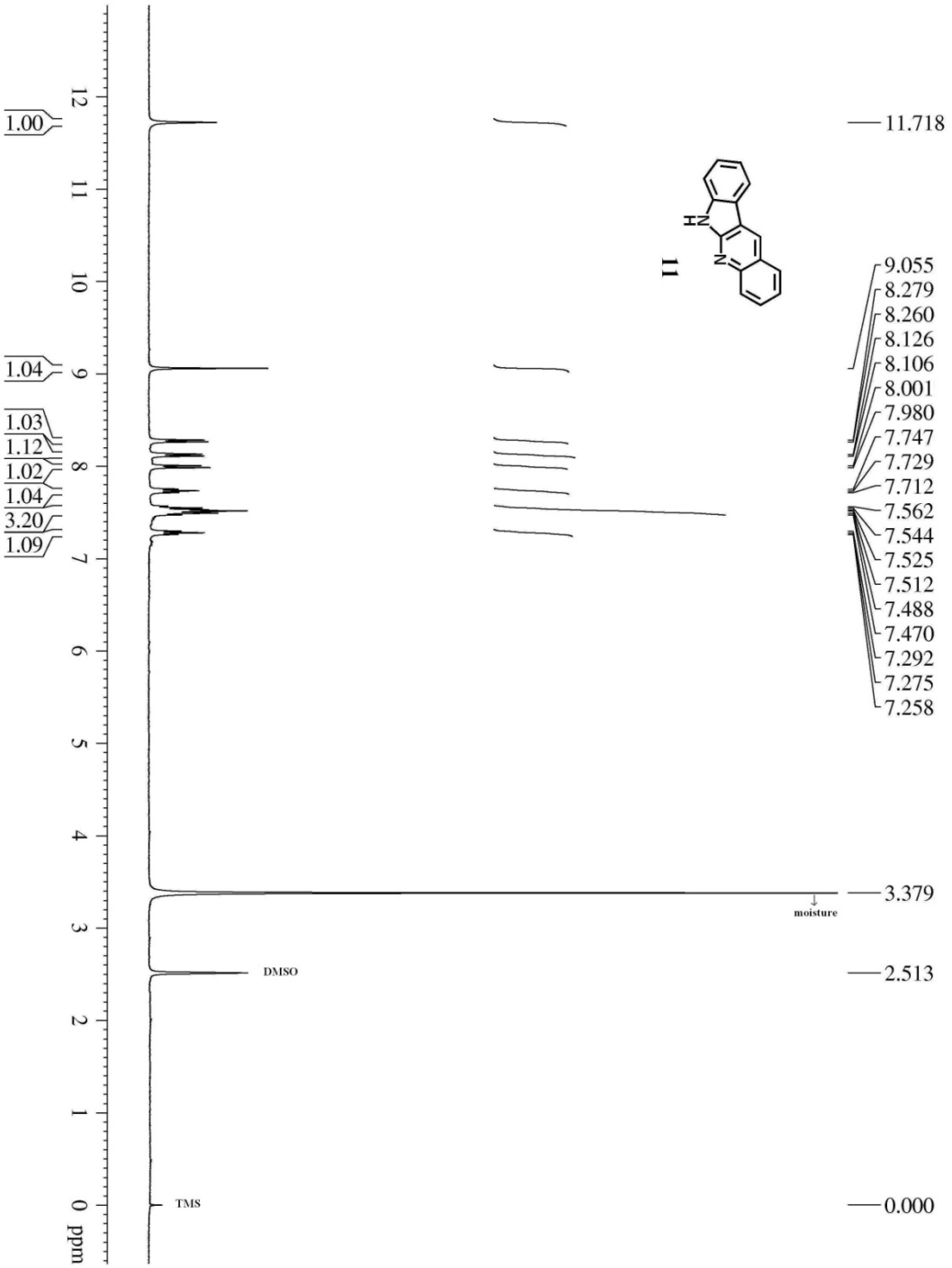

198.33
149.85
148.10
134.40
133.99
130.41
129.54
125.50
119.53
77.42
77.10
76.78
37.99
35.11
33.27
26.24
22.75
CDCl3
8
O
CN
NO2
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm






1.00
1.06
1.05
2.14
1.03
4.05
4.13
11.407
8.129
8.047
8.028
7.438
7.418
7.394
7.376
7.358
7.169
7.152
7.135
3.341
2.957
2.942
2.925
2.919
2.902
2.887
2.505
1.880
1.866
1.849
1.839
1.834
1.823
1.809
moisture
DMSO
TMS
10
ppm




1.00
1.04
1.03
1.12
1.02
1.04
3.20
1.09
11.718
9.055
8.279
8.260
8.126
8.106
8.001
7.980
7.747
7.729
7.712
7.562
7.544
7.525
7.512
7.488
7.470
7.292
7.275
7.258
3.379
moisture
2.513
0.000
DMSO
TMS
11
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm