Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

for

A Simple, Tandem Approach to the Construction of Pyridine Derivatives under Metal-free Conditions: A One-step Synthesis of the Monoterpene Natural Product, (-)-Actinidine

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EXPERIMENTAL SECTION

General experimental: Glassware was dried in an oven (120 °C), heated under reduced pressure, and cooled under argon before use. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Reactions were monitored by thin-layer chromatography on Analtech silica gel plates using UV-light and ceric sulfate or *β*-naphthol for visualization. Column chromatography was performed on silica gel (230–400 mesh) using *n*-hexane/ethyl acetate, diethyl ether/hexanes as eluents. Evaporation of solvents was conducted under reduced pressure at 50 °C. FTIR spectra were recorded neat on a Perkin-Elmer Spectrum 65. NMR spectra were recorded on a Bruker Avance III 400 NMR spectrometer at 400 MHz (^{1}H) and 100 MHz (^{13}C), respectively. Deuterated chloroform was used as the solvent unless otherwise noted, and spectra were calibrated against the residual solvent peak (7.24 ppm for ^{1}H and 77.0 ppm for ^{13}C). Chemical shifts (δ) and coupling constants (J) are given in ppm (parts per million) and Hz (Hertz), respectively. The following abbreviations were used to explain multiplicities: s=singlet, d=doublet, t=triplet, m=multiplet, bs=broad singlet. High Resolution mass spectra were obtained on a VG 70–70H or LC/MSD trapSL spectrometer operating at 70 eV using a direct inlet system.

Figure 1: Structures of aldehyde starting materials (1a-s):

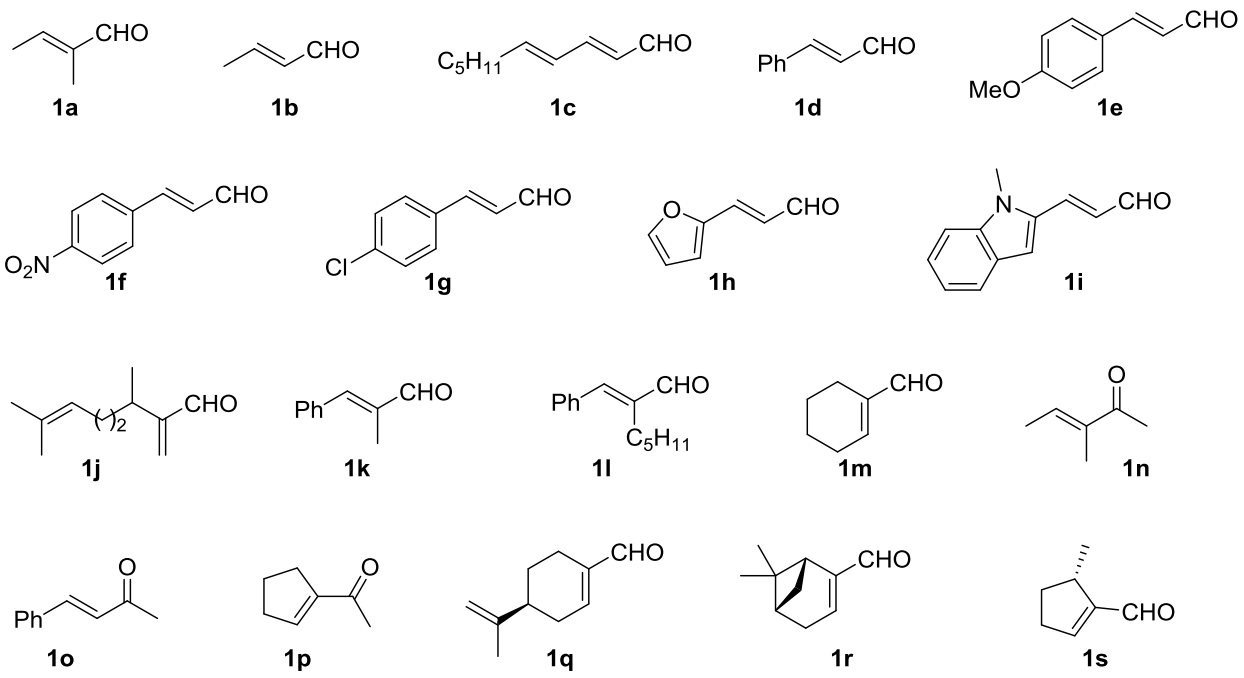
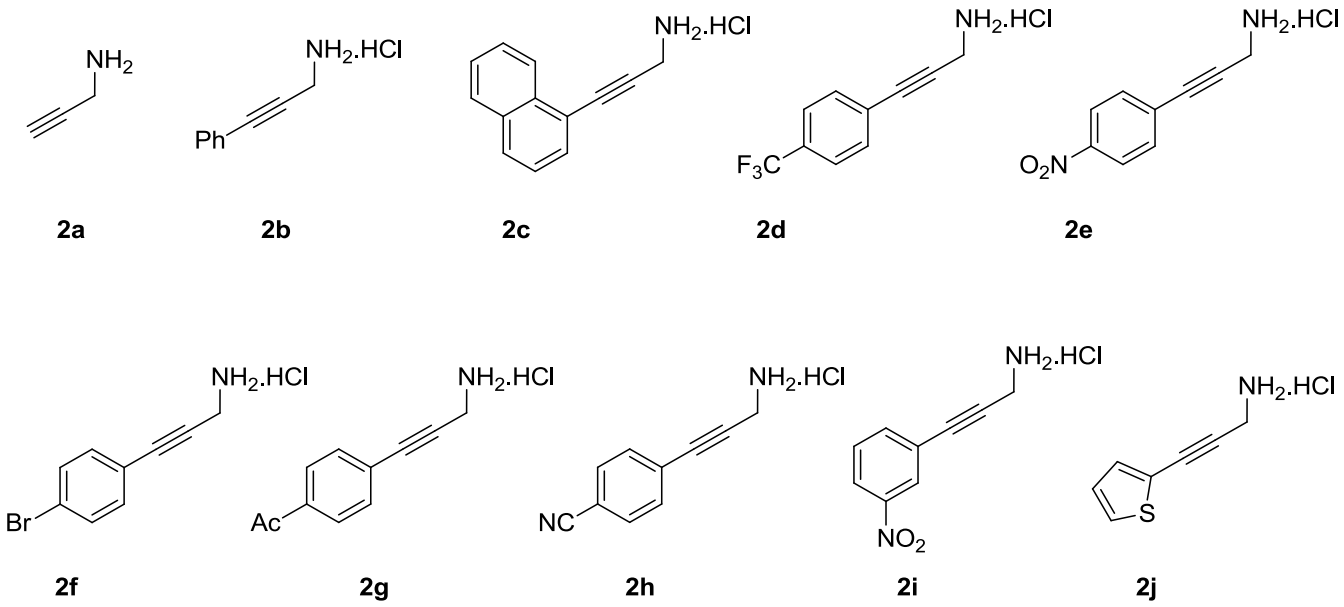
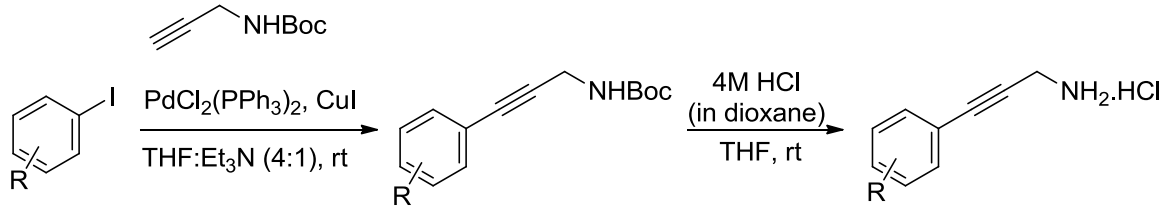


Figure 2: Structures of propargylic amines (2a-j):



Commercially available aldehydes (**1a-h** and **1k-r**) and propargylic amines (**2a** and **2b**) were used without further purification. All remaining starting aldehydes (**1i**[1] and **1j**, **1s**[2]) and propargylic amines (**2e**, **2h**,[3] **2f**,[4] and **2j**[5]) were synthesized according to literature procedures.

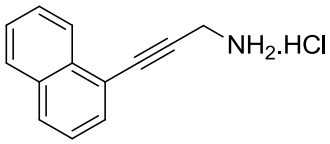
General procedure for the synthesis of propargylic amine hydrochloride salts 2c-j:



To a degassed solution of aryl iodide (5.5 mmol) and *tert*-butyl prop-2-yn-1-yl carbamate (0.77 g, 5.0 mmol) in THF/Et_3N (0.45 M, 4:1) under argon, were added CuI (38.1 mg, 0.20 mmol) and $PdCl_2(PPh_3)_2$ (70.2 mg, 0.10 mmol) at room temperature. The mixture was stirred overnight, and an aqueous solution of saturated NH_4Cl was added, and the mixture was extracted with Et_2O (3 x 30 mL). The combined organic layer was washed with brine (50 mL) and dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (gradient, 0→20% EtOAc/hexanes) to give the corresponding propargylic amine derivatives in high yield (81-91%).

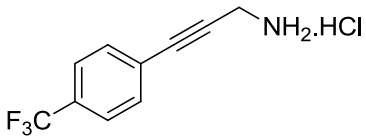
To a solution of the coupling product (4.0 mmol) in THF (4 mL) was added 4.0 M HCl in 1,4-dioxane solution (4.0 mL, 16 mmol) at room temperature, and the reaction mixture was stirred overnight. The solution was diluted with Et_2O upon completion. The organic layer was removed by decantation, and the precipitate was washed with Et_2O (3 x 15 mL). The solid compound was dried under vacuum to give the corresponding propargylic amine hydrochloride salts **2c-j**.

3-(Naphthalen-1-yl)prop-2-yn-1-amine hydrochloride (2c):



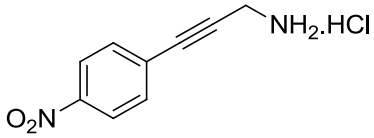
^{1}H NMR (400 MHz, DMSO-d_6): δ 8.79 (s, 3H), 8.40 (dd, J = 8.1, 0.9 Hz, 1H), 8.02 (t, J = 7.4 Hz, 2H), 7.74 (dd, J = 7.1, 1.0 Hz, 1H), 7.70-7.59 (m, 2H), 7.58-7.51 (m, 1H), 4.14 (s, 2H); ^{13}C{^{1}H}NMR (100 MHz, DMSO-d_6): δ 133.2, 133.1, 131.1, 130.0, 129.0, 127.7, 127.3, 126.2, 126.0, 119.3, 88.1, 83.9, 29.6.

3-(4-(Trifluoromethyl)phenyl)prop-2-yn-1-amine hydrochloride (2d):



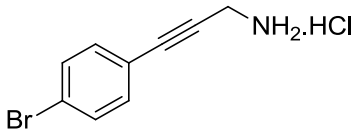
^{1}H NMR (400 MHz, DMSO-d_6): δ 8.72 (s, 3H), 7.81 (d, J = 8.2 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H), 4.02 (s, 2H); ^{13}C{^{1}H}NMR (100 MHz, DMSO-d_6): δ 132.3, 127.7 (q, J = 373.4 Hz), 125.8 (q, J = 3.7 Hz), 125.4, 122.5, 85.7, 84.1, 28.8.

3-(4-Nitrophenyl)prop-2-yn-1-amine hydrochloride (2e):



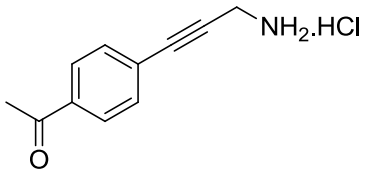
^{1}H NMR (400 MHz, DMSO-d_6): δ 8.67 (s, 3H), 7.68-7.57 (m, 2H), 7.45-7.35 (m, 2H), 3.95 (s, 2H); ^{13}C{^{1}H}NMR (100 MHz, DMSO-d_6): δ 147.3, 132.8, 128.0, 124.1, 88.0, 83.8, 28.9.

3-(4-Bromophenyl)prop-2-yn-1-amine hydrochloride (2f):



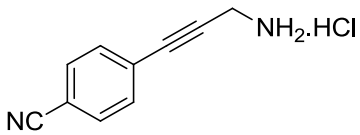
^{1}H NMR (400 MHz, DMSO-d_6): δ 8.73 (bs, 3H), 8.35-8.18 (m, 2H), 7.80-7.66 (m, 2H), 4.05 (s, 2H); ^{13}C{^{1}H}NMR (100 MHz, DMSO-d_6): δ 133.4, 132.0, 122.7, 120.5, 84.5, 84.2, 28.8.

1-(4-(3-Aminoprop-1-yn-1-yl)phenyl)ethanone hydrochloride (2g):



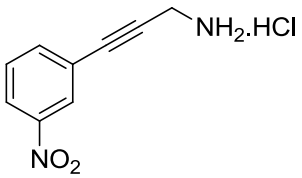
^{1}H NMR (400 MHz, DMSO-d_6): δ 8.68 (bs, 3H), 8.03-7.94 (m, 2H), 7.64-7.58 (m, 2H), 4.03 (s, 2H), 2.60 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, DMSO-d_6): δ 197.3, 136.7, 131.7, 128.6, 125.8, 85.9, 84.8, 28.9, 26.8.

4-(3-Aminoprop-1-yn-1-yl)benzonitrile hydrochloride (2h):



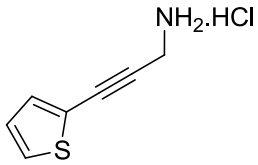
^{1}H NMR (400 MHz, DMSO-d_6): δ 8.67 (bs, 3H), 7.92 (d, J = 8.6 Hz, 2H), 7.65 (d, J = 8.6 Hz, 2H), 4.03 (s, 2H); ^{13}C{^{1}H}NMR (100 MHz, DMSO-d_6): δ 132.8, 132.3, 126.1, 118.3, 111.6, 87.1, 84.1, 28.9.

3-(3-Nitrophenyl)prop-2-yn-1-amine hydrochloride (2i):



^{1}H NMR (400 MHz, DMSO-d_6): δ 8.77 (s, 3H), 8.27 (m, 1H), 8.23-8.18 (m, 1H), 7.93-7.87 (m, 1H), 7.76-7.67 (m, 1H), 4.01 (s, 2H); ^{13}C{^{1}H}NMR (100 MHz, DMSO-d_6): δ 147.8, 137.5, 130.7 125.9, 124.0, 122.8, 85.4, 83.3, 28.7.

3-(Thiophen-2-yl)prop-2-yn-1-amine hydrochloride (2j):



^{1}H NMR (400 MHz, DMSO-d_6): δ 8.62 (s, 3H), 7.68 (dd, J = 5.1, 1.1 Hz, 1H), 7.37 (dd, J = 3.6, 0.9 Hz, 1H), 7.11 (dd, J = 5.1, 3.7 Hz, 1H), 4.00 (s, 2H); ^{13}C{^{1}H}NMR (100 MHz, DMSO-d_6): δ 133.2, 129.2, 127.5, 120.5, 86.5, 78.7, 28.8.

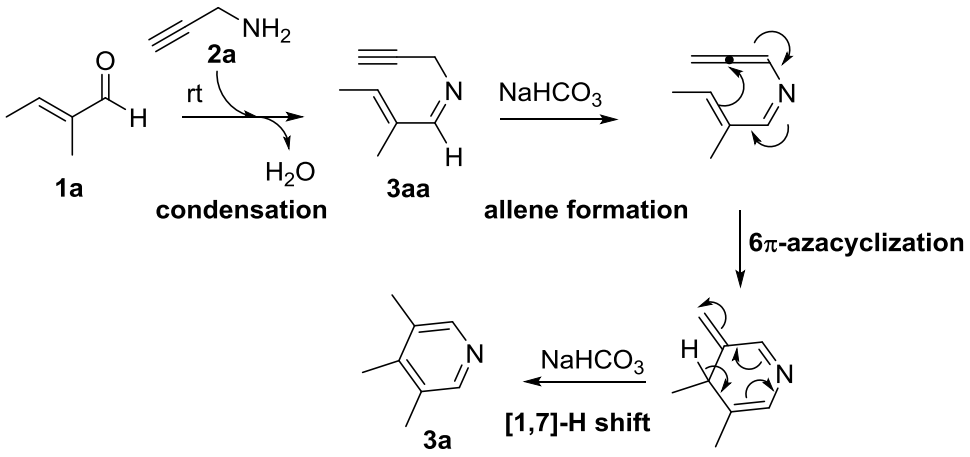
General procedure for the synthesis of substituted pyridines:

To a stirred solution of α, β-unsaturated carbonyl compounds **1a-s** (0.6 mmol) and propargylic amine/propargylic amine hydrochloride (0.9 mmol) in DMF (3 mL) were added 4 Å molecular sieves (200 mg) and $NaHCO_3$ (1.2 mmol for free propargylic amines and 1.8 mmol for propargylic amine hydrochlorides) at room temperature under an argon atmosphere. The reaction mixture was stirred for 3 h at room temperature, followed by 12 h at 80 °C. The mixture was filtered through Celite, washed with Et_2O (10 mL) and water (10 mL) was added to the filtrate. The two layers were separated, and the aqueous layer was extracted with Et_2O (2 x 10 mL). The combined organic layer was washed with ice cold water (2 x 15 mL), dried over magnesium sulfate and evaporated

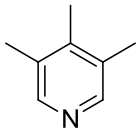
under reduced pressure. The crude product was purified by flash column chromatography on silica gel to afford the corresponding pyridines.

Plausible reaction mechanism:

Based on our preliminary studies and previous reports, a plausible mechanism for construction of pyridine ring was proposed. First, taglic aldehyde **1a** condenses with propargylamine **2a** to give the stable imine intermediate **3aa**, which converts into the allene in the presence of base. The allene intermediate further undergoes 6π-azacyclization followed by aromatization through a [1,7]-H shift leading to the formation of substituted pyridine **3a**.

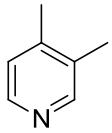


3,4,5-Collidine (3a):[6] (CAS NO: 20579-43-5)



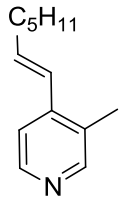
Tiglic aldehyde (**1a**, 50 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (Et_2O/hexanes 5:95 to 20:80), 60 mg (83%) of a pale, yellow liquid was obtained. R_f = 0.3 (Et_2O/hexanes 30:70); ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (s, 2H), 2.24 (s, 6H), 2.18 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 147.9, 144.2, 131.4, 16.8, 14.9.

3,4-Lutidine (3b):[7] (CAS NO: 583-58-4)



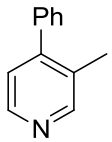
Crotonaldehyde (**1b**, 42 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (Et_2O/hexanes 5:95 to 30:70), 46 mg (72%) of a pale yellow liquid was obtained. R_f = 0.4 (Et_2O/hexanes 30:70); ^1H NMR (400 MHz, $CDCl_3$): δ 8.32 (s, 1H), 8.30 (d, J = 4.9 Hz, 1H), 7.04 (d, J = 4.9 Hz, 1H), 2.26 (s, 3H), 2.24 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 150.0, 147.3, 145.5, 132.1, 124.5, 19.0, 16.3.

(*E*)-4-(Hept-1-en-1-yl)-3-methylpyridine (3c):



(2*E*,4*E*)-Deca-2,4-dienal (**1c**, 91 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 20:80), 88 mg (78%) of a pale, yellow liquid was obtained. R_f = 0.4 (EtOAc/hexanes 30:70); ^1H NMR (400 MHz, $CDCl_3$): δ 8.35-8.33 (m, 2H), 7.26 (d, J = 5.2 Hz, 1H), 6.49 (d, J = 15.7 Hz, 1H), 6.34 (dt, J = 15.7, 6.8 Hz, 1H), 2.29 (s, 3H), 2.25 (ddd, J = 10.4, 5.5, 1.9 Hz, 2H), 1.54-1.44 (m, 2H), 1.37-1.29 (m, 4H), 0.91 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 151.0, 147.4, 144.1, 136.8, 129.6, 125.2, 119.1, 33.3, 31.3, 28.7, 22.4, 16.4, 14.0; FTIR (neat): 2929, 2856, 1710, 1602, 1384, 1278, 1037, 856, 699 cm^{-1}; MS (ESI): *m/z* 190 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{13}H_{20}N$ $(M+H)^+$: 190.1590, found: 190.1595.

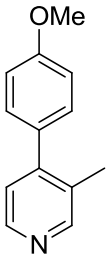
3-Methyl-4-phenylpyridine (3d):[8]



trans-Cinnamaldehyde (**1d**, 80 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (Et_2O/hexanes 5:95 to 20:80), 90 mg (89%) of a pale, yellow liquid was obtained. R_f = 0.4 (Et_2O/hexanes 30:70);

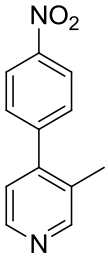
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (s, 1H), 8.47 (d, J = 5.0 Hz, 1H), 7.50-7.37 (m, 3H), 7.36-7.30 (m, 2H), 7.15 (d, J = 5.0 Hz, 1H), 2.28 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 151.3, 149.1, 147.3, 139.0, 130.6, 128.5, 128.4, 127.9, 124.0, 17.2.

4-(4-Methoxyphenyl)-3-methylpyridine (3e):[9]



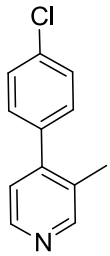
trans-p-Methoxycinnamaldehyde (**1e**, 97 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 20:80), 107 mg (90%) of a pale, yellow solid was obtained. R_f = 0.5 (EtOAc/hexanes 30:70), mp = 112-114 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (s, 1H), 8.44 (d, J = 4.8 Hz, 1H), 7.29-7.24 (m, 2H), 7.13 (d, J = 5.0 Hz, 1H), 7.01-6.95 (m, 2H), 3.85 (s, 3H), 2.29 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 159.3, 151.2, 148.6, 147.3, 131.2, 130.5, 129.7, 123.9, 113.7, 55.2, 17.3.

3-Methyl-4-(4-nitrophenyl)pyridine (3f):



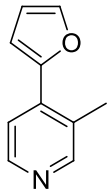
4-Nitrocinnamaldehyde (**1f**, 106 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 25:75), 106 mg (83%) of a pale, yellow solid was obtained. R_f = 0.4 (EtOAc/hexanes 30:70), mp = 139-141 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (s, 1H), 8.54 (d, J = 5.0 Hz, 1H), 8.36-8.31 (m, 2H), 7.55-7.50 (m, 2H), 7.16 (d, J = 5.0 Hz, 1H), 2.29 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 151.5, 147.6, 146.9, 145.5, 130.2, 129.6, 123.8, 123.8, 123.1, 17.1; FTIR (neat): 2928, 1590, 1512, 1344, 1106, 994, 855, 735, 697 cm^{-1}; MS (ESI): *m/z* 215 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{12}H_1N_2O_2$ $(M+H)^+$: 215.0815, found: 215.0818.

4-(4-Chlorophenyl)-3-methylpyridine (3g):[10]



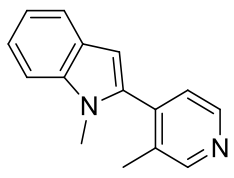
4-Chlorocinnamaldehyde (**1g**, 100 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 20:80), 111 mg (93%) of a pale, yellow liquid was obtained. R_f = 0.4 (EtOAc/hexanes 30:70); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (s, 1H), 8.47 (d, J = 5.0 Hz, 1H), 7.47-7.40 (m, 2H), 7.30-7.23 (m, 2H), 7.12 (d, J = 5.0 Hz, 1H), 2.27 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 151.3, 147.8, 147.4, 137.3, 134.0, 130.4, 129.8, 128.6, 123.7, 17.1.

4-(Furan-2-yl)-3-methylpyridine (3h):



(*E*)-3-(Furan-2-yl)acrylaldehyde (**1h**, 73 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 25:75), 83 mg (87%) of a pale, yellow semi solid was obtained. R_f = 0.4 (EtOAc/hexanes 30:70); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47 (d, J = 3.9 Hz, 2H), 7.62 (d, J = 5.2 Hz, 1H), 7.59 (dd, J = 1.8, 0.6 Hz, 1H), 6.80 (dd, J = 3.5, 0.5 Hz, 1H), 6.57 (dd, J = 3.5, 1.8 Hz, 1H), 2.50 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 151.9, 150.9, 147.5, 143.3, 136.6, 128.1, 119.4, 112.0, 111.9, 19.0; FTIR (neat): 2921, 1619, 1445, 1330, 1268, 1159, 1024, 980, 882, 791, 741 cm^{-1}; MS (ESI): *m/z* 160 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{10}H_{10}NO$ $(M+H)^+$: 160.0757, found: 160.0756.

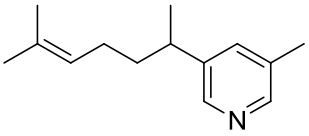
1-Methyl-2-(3-methylpyridin-4-yl)-1*H*-indole (3i):



(*E*)-3-(1-Methyl-1*H*-indol-2-yl)acrylaldehyde (**1i**, 111 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 30:70), 114 mg (86%) of a yellow

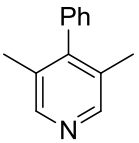
semisolid was obtained. R_f = 0.4 (EtOAc/hexanes 30:70); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (s, *J* = 0.6 Hz, 1H), 8.52 (d, *J* = 4.9 Hz, 1H), 7.69-7.62 (m, 1H), 7.38 (dd, *J* = 8.2, 0.8 Hz, 1H), 7.29 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.21 (d, *J* = 4.9 Hz, 1H), 7.17 (ddd, *J* = 7.0, 5.5, 1.0 Hz, 1H), 6.51 (d, *J* = 0.8 Hz, 1H), 3.55 (s, 3H), 2.25 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 151.3, 147.1, 140.2, 137.7, 137.2, 132.8, 127.7, 125.0, 122.1, 120.7, 120.0, 109.6, 102.6, 30.6, 17.0; FTIR (neat): 2976, 1576, 1495, 1400, 1254, 1145, 892, 757, 698 cm^{-1}; MS (ESI): *m/z* 223 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{15}H_{15}N_2$ $(M+H)^+$: 223.1230, found: 223.1233.

3-Methyl-5-(6-methylhept-5-en-2-yl)pyridine (3j):



3,7-Dimethyl-2-methyleneoct-6-enal (**1j**, 100 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 12 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 20:80), 98 mg (81%) of a pale, yellow liquid was obtained. R_f = 0.3 (EtOAc/hexanes 30:70); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (s, 1H), 8.23 (s, 1H), 7.29 (s, 1H), 5.07 (m, 1H), 2.69 (h, *J* = 7.1 Hz, 1H), 2.32 (s, 3H), 1.95-1.83 (m, 2H), 1.67 (s, 3H), 1.61 (q, *J* = 7.6 Hz, 2H), 1.51 (s, 3H), 1.24 (d, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 147.8, 146.3, 142.0, 134.8, 132.7, 131.8, 124.0, 38.0, 36.7, 26.0, 25.7, 22.1, 18.4, 17.6; FTIR (neat): 2961, 1682, 1577, 1438, 1376, 1147, 1028, 983, 873, 719 cm^{-1}; MS (ESI): *m/z* 204 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{14}H_{22}N$ $(M+H)^+$: 204.1747, found: 204.1741.

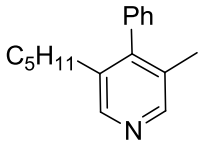
2,6-Dimethyl-1,1'-biphenyl (3k):[11]



α-Methyl-*trans*-cinnamaldehyde (**1k**, 87 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 20:80), 90 mg (83%) of a white solid was obtained. R_f = 0.4

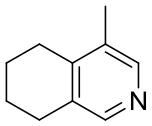
(EtOAc/hexanes 30:70), mp = 106-108 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35 (s, 2H), 7.50-7.43 (m, 2H), 7.42-7.35 (m, 1H), 7.15-7.08 (m, 2H), 2.03 (s, 6H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 149.3, 148.3, 138.0, 130.8, 128.7, 127.9, 127.5, 17.3.

3-Methyl-5-pentyl-4-phenylpyridine (3l):



(*E*)-*alpha*-Amyl cinnamaldehyde (Jasmonal A, **1l**, 121 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 25:75), 129 mg (91%) of a colorless liquid was obtained. R_f = 0.3 (EtOAc/hexanes 30:70); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (s, 1H), 8.33 (s, 1H), 7.48-7.35 (m, 3H), 7.16-7.08 (m, 2H), 2.40-2.30 (m, 2H), 2.00 (s, 3H), 1.42-1.32 (m, 2H), 1.20-1.08 (m, 4H), 0.78 (t, J = 6.9 Hz, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 148.9, 148.1, 148.0, 137.7, 135.4, 130.9, 128.4, 128.2, 127.4, 31.4, 30.5, 30.5, 22.1, 17.4, 13.8; FTIR (neat): 2955, 1582, 1464, 1380, 1158, 1041, 885, 758, 702 cm^{-1}; MS (ESI): *m/z* 240 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{17}H_{22}N$ $(M+H)^+$: 240.1747, found: 240.1749.

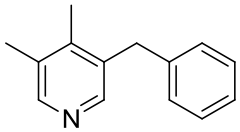
4-Methyl-5,6,7,8-tetrahydroisoquinoline (3m):



1-Cyclohexene-1-carboxaldehyde (**1m**, 66 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (Et_2O/hexanes 5:95 to 20:80), 76 mg (87%) of a pale, yellow liquid was obtained. R_f = 0.5 (Et_2O/hexanes 30:70); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (s, 1H), 8.14 (s, 1H), 2.73 (t, J = 6.1 Hz, 2H), 2.60 (t, J = 6.3 Hz, 2H), 2.17 (s, 3H), 1.89-1.74 (m, 4H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 148.1, 147.0, 144.5, 132.2, 131.4, 26.6, 26.0, 22.5, 22.3, 15.9; FTIR (neat): 2929, 1680,

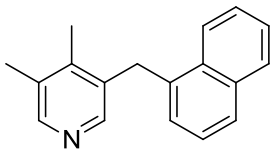
1588, 1449, 1421, 1192, 1141, 909, 800, 718 cm^{-1}; MS (ESI): *m/z* 148 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{10}H_{14}N$ $(M+H)^+$: 148.1121, found: 148.1125.

3-Benzyl-4,5-dimethylpyridine (**3n**):



Tiglic aldehyde (**1a**, 50 mg, 0.60 mmol), 3-phenylprop-2-yn-1-amine hydrochloride (**2b**, 150 mg, 0.90 mmol) and $NaHCO_3$ (151 mg, 1.80 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 20:80), 93 mg (79%) of a pale, yellow semi solid was obtained. R_f = 0.4 (EtOAc/hexanes 30:70); ^1H NMR (400 MHz, $CDCl_3$): δ 8.25 (s, 1H), 8.24 (s, 1H), 7.30-7.23 (m, 2H), 7.22-7.15 (m, 1H), 7.09 (ddd, *J* = 8.1, 2.4, 1.8 Hz, 2H), 3.99 (s, 2H), 2.24 (s, 3H), 2.11 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 148.7, 148.7, 144.6, 139.5, 133.8, 132.2, 128.5, 128.4, 126.2, 36.9, 16.9, 15.1; FTIR (neat): 2925, 1669, 1598, 1491, 1385, 1197, 1125, 797, 757, 695 cm^{-1}; MS (ESI): *m/z* 198 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{14}H_{16}N$ $(M+H)^+$: 198.1277, found: 198.1280.

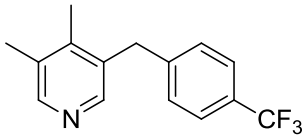
3,4-Dimethyl-5-(naphthalen-1-ylmethyl)pyridine (3o):



Tiglic aldehyde (**1a**, 50 mg, 0.60 mmol), 3-(naphthalen-1-yl)prop-2-yn-1-amine hydrochloride (**2c**, 195 mg, 0.90 mmol) and $NaHCO_3$ (151 mg, 1.80 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 20:80), 127 mg (86%) of a pale, yellow solid was obtained. R_f = 0.5 (EtOAc/hexanes 30:70), mp = 121-123 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.29 (s, 1H), 8.11 (s, 1H), 8.04 (d, *J* = 7.9 Hz, 1H), 7.91-7.85 (m, 1H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.57-7.47 (m, 2H), 7.33 (t, *J* = 7.7 Hz, 1H), 6.89 (d, *J* = 7.0 Hz, 1H), 4.41 (s, 2H), 2.29 (s, 3H), 2.14 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 148.9, 148.8, 144.7, 135.1, 133.7, 133.2, 132.0, 131.9, 128.8, 127.1, 126.2, 125.8, 125.7, 125.5, 123.3, 33.6, 17.0, 15.0; FTIR

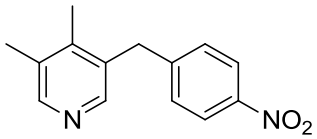
(neat): 2917, 1597, 1440, 1399, 1186, 1074, 887, 793, 774, 757 cm^{-1}; MS (ESI): *m/z* 248 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{18}H_{18}N$ $(M+H)^+$: 248.1434, found: 248.1437.

3,4-Dimethyl-5-(4-(trifluoromethyl)benzyl)pyridine (3p):



Tiglic aldehyde (**1a**, 50 mg, 0.60 mmol), 3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-amine hydrochloride (**2d**, 211 mg, 0.90 mmol) and $NaHCO_3$ (151 mg, 1.80 mmol) in DMF (3 mL) were stirred for 3 h at room temperature 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 20:80), 145 mg (93%) of a pale, yellow solid was obtained. R_f = 0.5 (EtOAc/hexanes 30:70), mp = 127-129 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (s, 1H), 8.25 (s, 1H), 7.52 (d, *J* = 8.1 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 4.05 (s, 2H), 2.25 (s, 3H), 2.09 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 149.1, 148.7, 144.5, 143.7, 132.9, 132.4, 128.7, 128.6 (q, *J* = 32.4 Hz), 125.4 (q, *J* = 3.9 Hz), 124.1 (q, *J* = 271.9 Hz), 36.7, 16.9, 15.1; FTIR (neat): 2925, 1618, 1416, 1321, 1160, 1107, 1065, 1017, 815, 726 cm^{-1}; MS (ESI): *m/z* 266 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{15}H_{15}F_3N$ $(M+H)^+$: 266.1151, found: 266.1154.

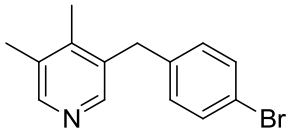
3,4-Dimethyl-5-(4-nitrobenzyl)pyridine (3q):



Tiglic aldehyde (**1a**, 50 mg, 0.60 mmol), 3-(4-nitrophenyl)prop-2-yn-1-amine hydrochloride (**2e**, 190.8 mg, 0.90 mmol) and $NaHCO_3$ (151 mg, 1.80 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 20:80), 126 mg (87%) of a pale, yellow solid was obtained. R_f = 0.6 (EtOAc/hexanes 30:70), mp = 163-165 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (s, 1H), 8.26 (s, 1H), 8.14 (d, *J* = 8.8 Hz, 2H), 7.26 (d, *J* = 8.9 Hz, 2H), 4.11 (s, 2H), 2.26 (s, 3H), 2.09 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 149.5, 148.7, 147.3, 146.6, 144.5, 132.6, 132.3, 129.1, 123.8, 36.8, 16.9, 15.2; FTIR (neat): 2923, 1594, 1440, 1340, 1105,

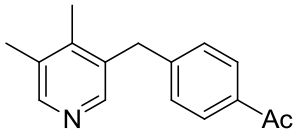
930, 834, 733, 698 cm^{-1}; MS (ESI): *m/z* 243 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{14}H_{15}N_2O_2$ $(M+H)^+$: 243.1128, found: 243.1132.

3-(4-Bromobenzyl)-4,5-dimethylpyridine (3r):



Tiglic aldehyde (**1a**, 50 mg, 0.60 mmol), 3-(4-bromophenyl)prop-2-yn-1-amine hydrochloride (**2f**, 219 mg, 0.90 mmol) and $NaHCO_3$ (151 mg, 1.80 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 20:80), 146 mg (88%) of a pale, yellow solid was obtained. R_f = 0.5 (EtOAc/hexanes 30:70), mp = 127-129 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.27 (s, 1H), 8.23 (s, 1H), 7.38 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 8.5 Hz, 2H), 3.94 (s, 2H), 2.24 (s, 3H), 2.08 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 149.0, 148.7, 144.4, 138.5, 133.2, 132.3, 131.5, 130.1, 120.0, 36.3, 16.9, 15.1; FTIR (neat): 2920, 1585, 1485, 1414, 1072, 1012, 897, 793, 746 cm^{-1}; MS (ESI): *m/z* 276 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{14}H_{15}BrN$ $(M+H)^+$: 276.0382, found: 276.0385.

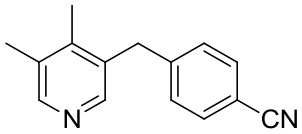
1-(4-((4,5-Dimethylpyridin-3-yl)methyl)phenyl)ethanone (3s):



Tiglic aldehyde (**1a**, 50 mg, 0.60 mmol), 1-(4-(3-aminoprop-1-yn-1-yl)phenyl)ethanone hydrochloride (**2g**, 188 mg, 0.90 mmol) and $NaHCO_3$ (151 mg, 1.80 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 20:80) 120 mg (84%) of a pale yellow solid was obtained. R_f = 0.5 (EtOAc/hexanes 30:70), mp = 122-124 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.28 (s, 1H), 8.26 (s, 1H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.5 Hz, 2H), 4.05 (s, 2H), 2.57 (s, 3H), 2.25 (s, 3H), 2.09 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 197.6, 149.1, 148.7, 145.2, 144.5, 135.3, 133.0, 132.4, 128.6, 128.5, 36.9, 26.5, 16.9, 15.1; FTIR (neat):

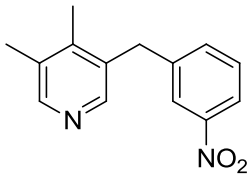
2919, 1677, 1606, 1412, 1356, 1269, 1018, 958, 895, 749 cm^{-1}; MS (ESI): *m/z* 240 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{16}H_{18}NO$ $(M+H)^+$: 240.1383, found: 240.1386.

4-((4,5-Dimethylpyridin-3-yl)methyl)benzonitrile (3t):



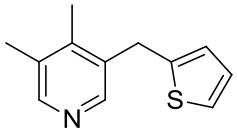
Tiglic aldehyde (**1a**, 50 mg, 0.60 mmol), 4-(3-aminoprop-1-yn-1-yl)benzonitrile hydrochloride (**2h**, 172.8 mg, 0.90 mmol) and $NaHCO_3$ (151 mg, 1.80 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (gradient: EtOAc/hexanes 5:95 to 20:80) 120 mg (90 %) of a pale, yellow solid was obtained. R_f = 0.5 (EtOAc/hexanes 30:70), mp = 145-147 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (s, 1H), 8.24 (s, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.21 (dd, *J* = 8.0, 0.5 Hz, 2H), 4.06 (s, 2H), 2.26 (s, 3H), 2.08 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 149.3, 148.7, 145.2, 144.4, 132.5, 132.3, 132.3, 129.1, 118.7, 110.2, 36.9, 16.9, 15.1; FTIR (neat): 2945, 2224, 1584, 1500, 1412, 1172, 995, 892, 812, 755 cm^{-1}; MS (ESI): *m/z* 223 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{15}H_{15}N_2$ $(M+H)^+$ 223.1230, found: 223.1234.

3,4-Dimethyl-5-(3-nitrobenzyl)pyridine (3u):



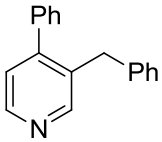
Tiglic aldehyde (**1a**, 50 mg, 0.60 mmol), 3-(3-nitrophenyl)prop-2-yn-1-amine hydrochloride (**2i**, 190.8 mg, 0.90 mmol) and $NaHCO_3$ (151 mg, 1.80 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 20:80), 132 mg (91%) of a pale, yellow solid was obtained. R_f = 0.6 (EtOAc/hexanes 30:70), mp = 170-172 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, *J* = 10.9 Hz, 1H), 8.26 (s, 1H), 8.07 (d, *J* = 6.8 Hz, 1H), 7.99 (s, 1H), 7.45 (m, 2H), 4.11 (s, 2H), 2.27 (s, 3H), 2.11 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 149.5, 148.7, 148.4, 144.3, 141.7, 134.5, 132.5, 132.3, 129.4, 123.2, 121.5, 36.5, 16.9, 15.2; FTIR (neat): 2921, 1530, 1438, 1384, 1093, 996, 928, 804, 726, 691 cm^{-1}; MS (ESI): *m/z* 243 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{14}H_{15}N_2O_2$ $(M+H)^+$: 243.1128, found: 243.1129.

3,4-Dimethyl-5-(thiophen-2-ylmethyl)pyridine (3v):



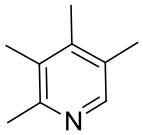
Tiglic aldehyde (**1a**, 50 mg, 0.60 mmol), 3-(thiophen-2-yl)prop-2-yn-1-amine hydrochloride (**2j**, 155.7 mg, 0.90 mmol) and $NaHCO_3$ (151 mg, 1.80 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 ^oC. After column chromatography (EtOAc/hexanes 5:95 to 20:80) 102 mg (84 %) of a pale, yellow liquid was obtained. R_f = 0.5 (EtOAc/hexanes 30:70); ^1H NMR (400 MHz, $CDCl_3$): δ 8.28 (s, 1H), 8.27 (s, 1H), 7.13 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.90 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.72-6.64 (m, 1H), 4.15 (s, 2H), 2.25 (s, 3H), 2.18 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 149.0, 148.3, 144.3, 142.8, 133.6, 132.3, 126.8, 124.9, 123.8, 31.3, 16.9, 14.9; FTIR (neat): 2919, 1586, 1437, 1286, 1230, 1108, 1017, 886, 821, 694 cm^{-1}; MS (ESI): *m/z* 204 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{12}H_{14}NOS$ $(M+H)^+$: 204.0841, found: 204.0843.

3-Benzyl-4-phenylpyridine (3w):



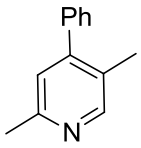
trans-Cinnamaldehyde (**1d**, 80 mg, 0.60 mmol), 3-phenylprop-2-yn-1-amine hydrochloride (**2b**, 150 mg, 0.90 mmol) and $NaHCO_3$ (151 mg, 1.80 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 $^{\circ}C$. After column chromatography (EtOAc/hexanes 5:95 to 30:70), 117 mg (80%) of a pale, yellow semi-solid was obtained. R_f = 0.5 (EtOAc/hexanes 30:70); ^1H NMR (400 MHz, $CDCl_3$): δ 8.63-8.25 (m, 2H), 7.41-7.35 (m, 3H), 7.23-7.13 (m, 6H), 6.96-6.89 (m, 2H), 3.98 (s, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 151.6, 149.7, 147.6, 140.1, 138.7, 133.6, 128.6, 128.5, 128.4, 128.3, 128.0, 126.1, 124.5, 36.3; FTIR (neat): 3057, 1668, 1588, 1493, 1407, 1179, 838, 752, 695 cm^{-1}; MS (ESI): *m/z* 246 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{18}H_{16}N$ $(M+H)^+$: 246.1277, found: 246.1279.

2,3,4,5-Tetramethylpyridine (3x):[12]



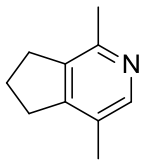
(*E*)-3-Methylpent-3-en-2-one (**1n**, 59 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (Et_2O/hexanes 5:95 to 20:80), 59 mg (73%) of a pale, yellow liquid was obtained. R_f = 0.4 (Et_2O/hexanes 30:70); ^1H NMR (400 MHz, $CDCl_3$): δ 8.07 (s, 1H), 2.49 (s, 3H), 2.22 (s, 3H), 2.20 (s, 3H), 2.19 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 154.0, 146.3, 143.9, 129.4, 129.3, 23.2, 17.1, 15.4, 15.1.

2,5-Dimethyl-4-phenylpyridine (3y):[13]



4-Phenyl-3-buten-2-one (**1o**, 88 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 20:80), 82 mg (75%) of a pale, yellow liquid was obtained. R_f = 0.4 (EtOAc/hexanes 30:70); ^1H NMR (400 MHz, $CDCl_3$): δ 8.37 (s, 1H), 7.47-7.35 (m, 3H), 7.33-7.28 (m, 2H), 7.02 (s, 1H), 2.54 (s, 3H), 2.22 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 155.6, 150.4, 149.5, 139.2, 128.4, 128.3, 127.7, 127.4, 123.5, 23.7, 16.7.

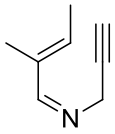
1,4-Dimethyl-6,7-dihydro-5*H*-cyclopenta[c]pyridine (3z):



1-Acetylcyclopentene (**1p**, 66 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (Et_2O/hexanes 5:95 to 20:80) 130 mg (70%) of a pale, yellow liquid was obtained. R_f = 0.3 (Et_2O/hexanes 30:70); ^1H NMR (400 MHz, $CDCl_3$): δ 8.07 (s, 1H), 2.91-2.81 (m, 4H), 2.43 (s, 3H), 2.20 (s, 3H), 2.14-2.05 (m, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 152.2, 151.1, 146.8, 137.2, 126.8, 31.4, 30.9, 23.8, 21.7, 15.9; FTIR (neat): 2920, 1669, 1596, 1434, 1312, 1045, 926,

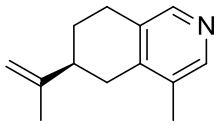
906, 722 cm^{-1}; MS (ESI): *m/z* 148 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{10}H_{14}N$ $(M+H)^+$: 148.1121, found: 148.1125.

(*Z*)-*N*-((*E*)-2-methylbut-2-en-1-ylidene)prop-2-yn-1-amine (3aa):



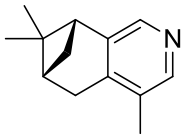
Tiglic aldehyde (**1a**, 50 mg, 0.60 mmol) and propargylamine (**2a**, 49.5 mg, 0.90 mmol) in DMF (3 mL) were stirred for 36 h at room temperature. After column chromatography (Et_2O/hexanes 5:95 to 10:80), 62 mg (85%) of a pale, yellow liquid was obtained. R_f = 0.6 (Et_2O/hexanes 20:70); ^1H NMR (400 MHz, $CDCl_3$): δ 8.08 (t, *J* = 1.5 Hz, 1H), 6.26 – 5.86 (m, 1H), 4.36 (dd, *J* = 2.5, 1.5 Hz, 2H), 2.44 (t, *J* = 2.5 Hz, 1H), 1.86 (d, *J* = 5.5 Hz, 3H), 1.85 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 167.0, 137.5, 136.5, 79.6, 74.6, 46.7, 14.2, 11.1; FTIR (neat): 3010, 2919, 1630, 1423, 1298, 1125, 1013, 978, 847, 726 cm^{-1}; MS (ESI): *m/z* 122 $(M+H)^+$.

(*S*)-4-Methyl-6-(prop-1-en-2-yl)-5,6,7,8-tetrahydroisoquinoline (4a):



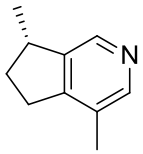
(*S*)-(-)-Perillaldehyde (**1q**, 90 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 30:70), 95 mg (85%) of a brown liquid was obtained. R_f = 0.2 (EtOAc/hexanes 30:70); $[\alpha]^{25}_D$ = -37.8 (c = 0.53, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 8.15 (s, 1H), 4.83-4.80 (m, 1H), 4.79-4.76 (m, 1H), 2.92-2.70 (m, 3H), 2.51-2.32 (m, 2H), 2.19 (s, 3H), 2.06-1.97 (m, 1H), 1.82 (s, 3H), 1.68-1.54 (m, 1H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 148.8, 147.9, 147.2, 144.1, 131.5, 131.3, 109.6, 41.1, 31.5, 27.1, 26.6, 20.6, 16.0; FTIR (neat): 2923, 1644, 1586, 1435, 1376, 1149, 1034, 886, 720 cm^{-1}; MS (ESI): *m/z* 188 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{13}H_{18}N$ $(M+H)^+$: 188.1434, found: 188.1436.

(6*R*,8*R*)-4,7,7-Trimethyl-5,6,7,8-tetrahydro-6,8-methanoisoquinoline (4b):



(1*R*)-(-)-Myrtenal (**1r**, 90 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (EtOAc/hexanes 5:95 to 30:70), 91 mg (81%) of a brown liquid was obtained. R_f = 0.2 (EtOAc/hexanes 30:70); $[\alpha]_D^{25}$-34.7 (c 1.12, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (s, 1H), 7.99 (s, 1H), 2.88-2.72 (m, 3H), 2.66 (dt, *J* = 9.7, 5.8 Hz, 1H), 2.34 (dq, *J* = 8.7, 2.8 Hz, 1H), 2.20 (s, 3H), 1.40 (s, 3H), 1.18 (d, *J* = 9.5 Hz, 1H), 0.60 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 148.5, 143.8, 142.4, 141.5, 131.0, 44.4, 39.9, 38.7, 31.6, 31.3, 25.8, 21.2, 15.2; FTIR (neat): 2921, 1588, 1472, 1424, 1289, 1221, 1132, 955, 844, 792, 735 cm^{-1}; MS (ESI): *m/z* 188 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{13}H_{18}N$ $(M+H)^+$: 188.1434, found: 188.1437.

(*R*)-4,7-Dimethyl-6,7-dihydro-5*H*-cyclopenta[c]pyridine ((-)-actinidine) (5):[14]



(*R*)-5-Methylcyclopent-1-enecarbaldehyde (**1s**, 66 mg, 0.60 mmol), propargylamine (**2a**, 49.5 mg, 0.90 mmol) and $NaHCO_3$ (101 mg, 1.20 mmol) in DMF (3 mL) were stirred for 3 h at room temperature followed by 12 h at 80 °C. After column chromatography (Et_2O/hexanes 05:95 to 20:80), 73 mg (85%) of a pale, yellow liquid was obtained. R_f = 0.3 (Et_2O/hexanes 30:70); $[\alpha]_D^{25}$ -14.6 (c 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (s, 1H), 8.19 (s, 1H), 3.34-3.16 (m, 1H), 2.86 (ddd, *J* = 16.7, 8.8, 4.1 Hz, 1H), 2.73 (dt, *J* = 16.7, 8.3 Hz, 1H), 2.42-2.29 (m, 1H), 2.24 (s, 3H), 1.62 (ddd, *J* = 16.7, 12.7, 8.3 Hz, 1H), 1.31 (d, *J* = 6.9 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 151.9, 147.7, 143.6, 142.5, 129.1, 37.9, 33.8, 29.7, 20.0, 16.0;

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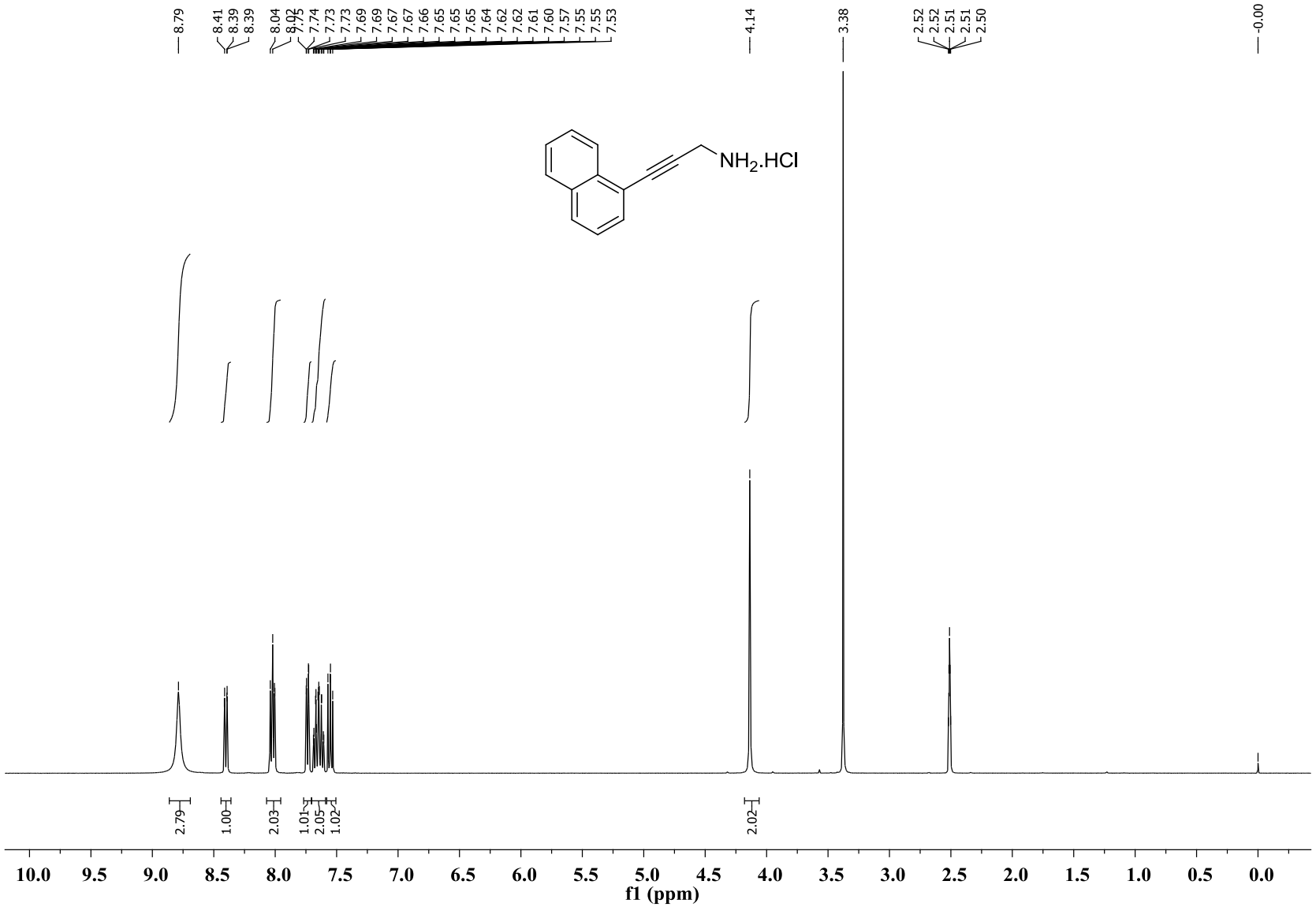
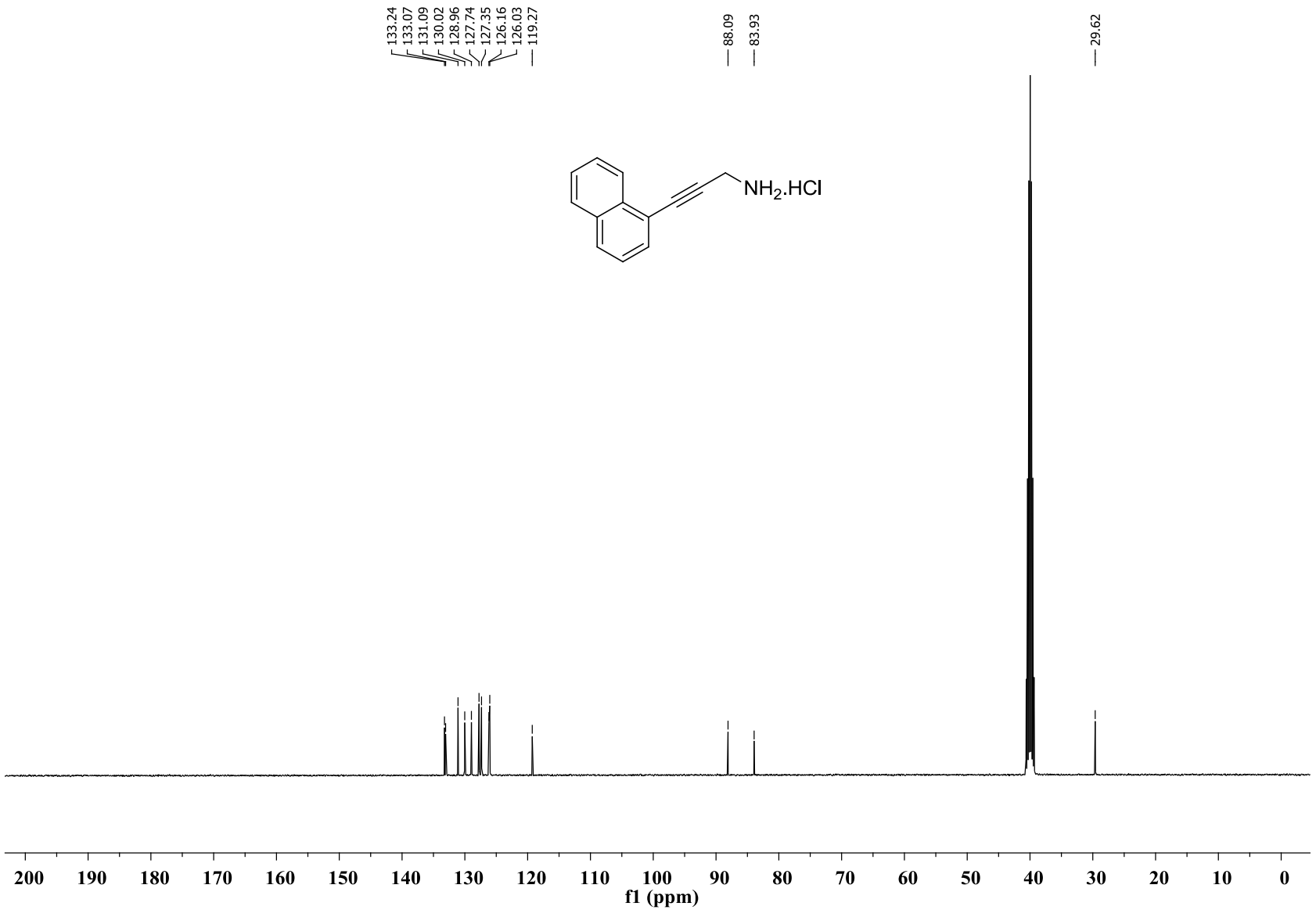
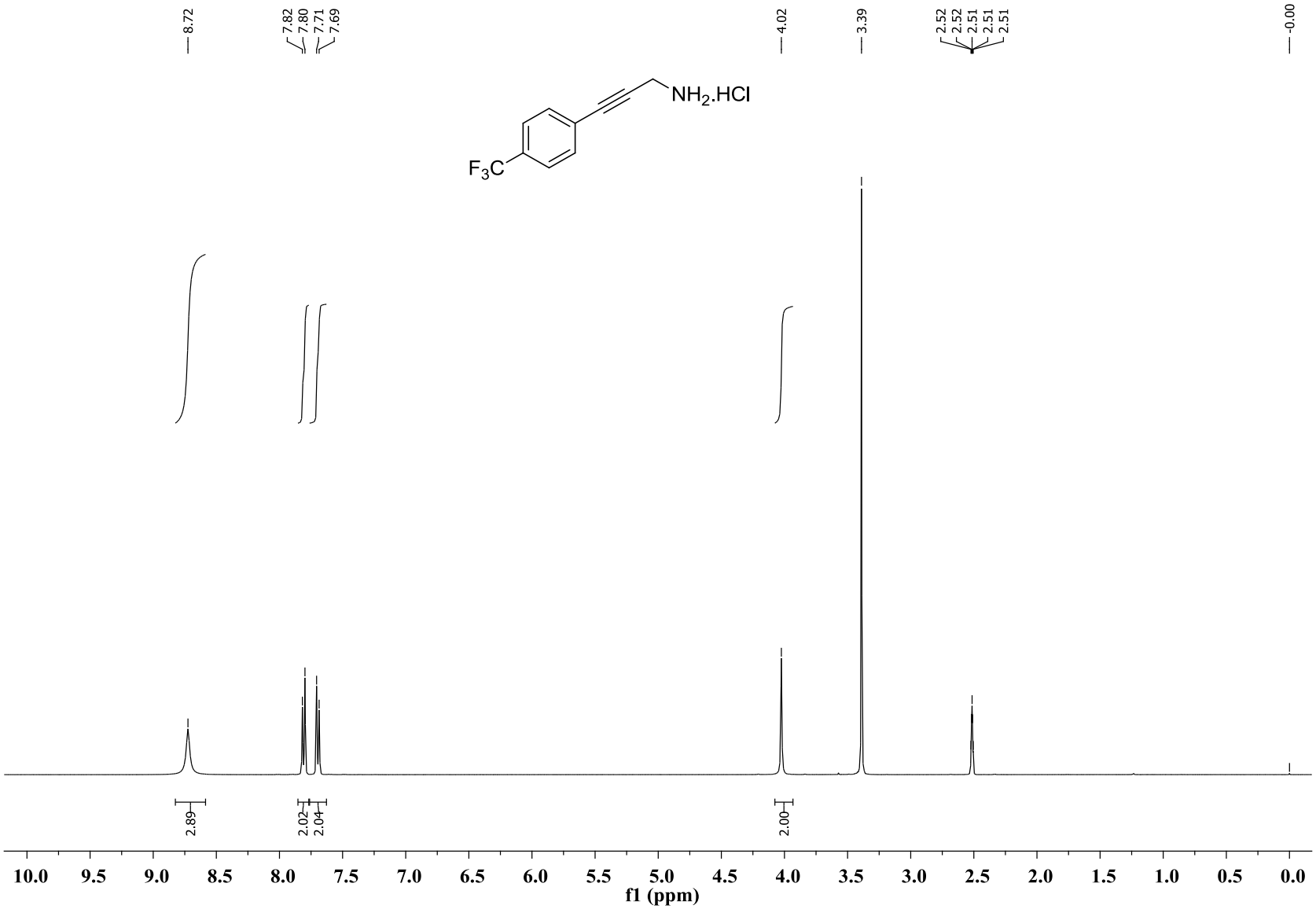
^{1}H NMR spectrum of **2c** (DMSO-d_6, 400 MHz)**:**



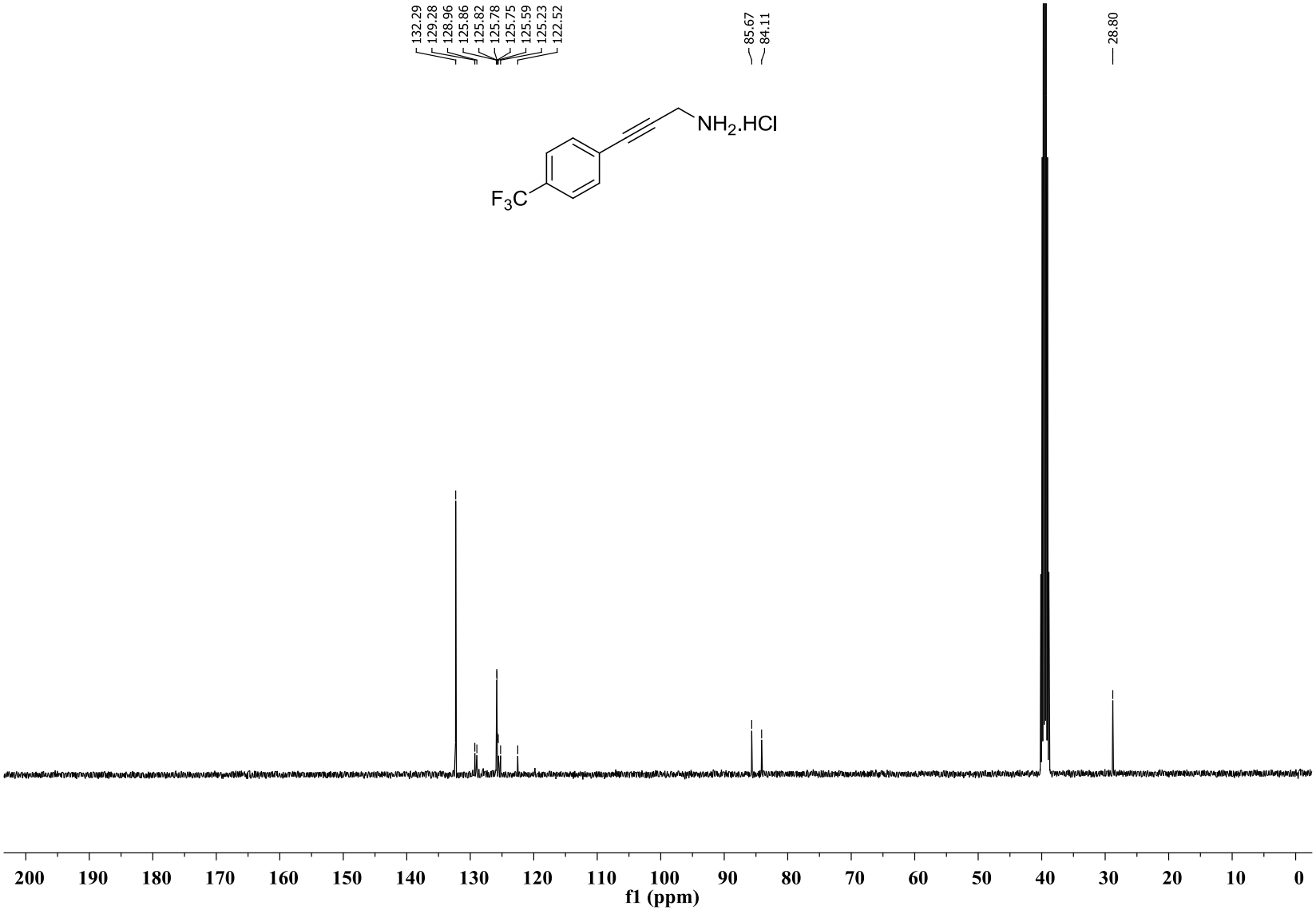
$^{13}C\{1H\}$NMR spectrum of **2c** (DMSO-d_6, 100 MHz)**:**



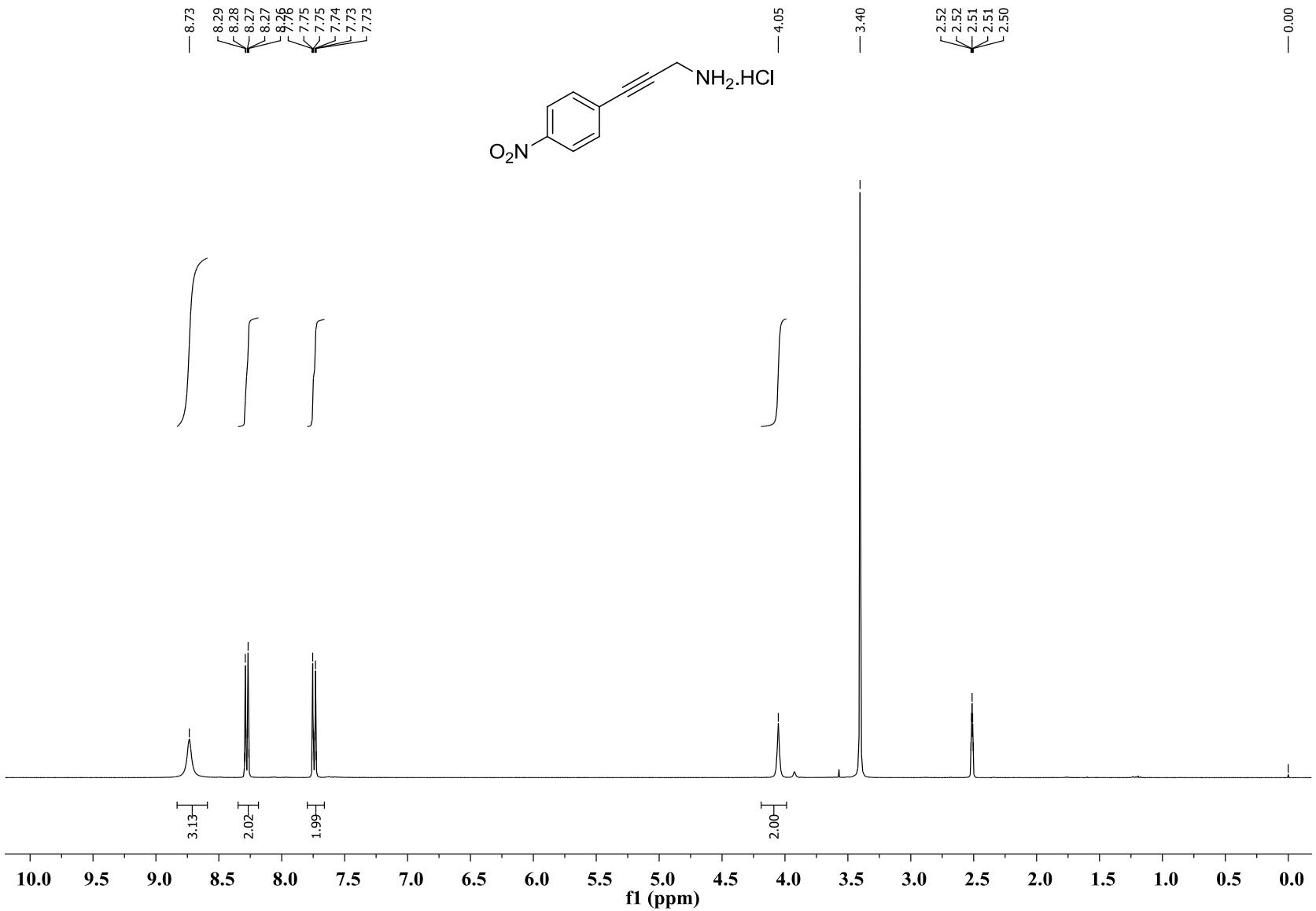
^{1}H NMR spectrum of **2d** (DMSO-d_6, 400 MHz)**:**



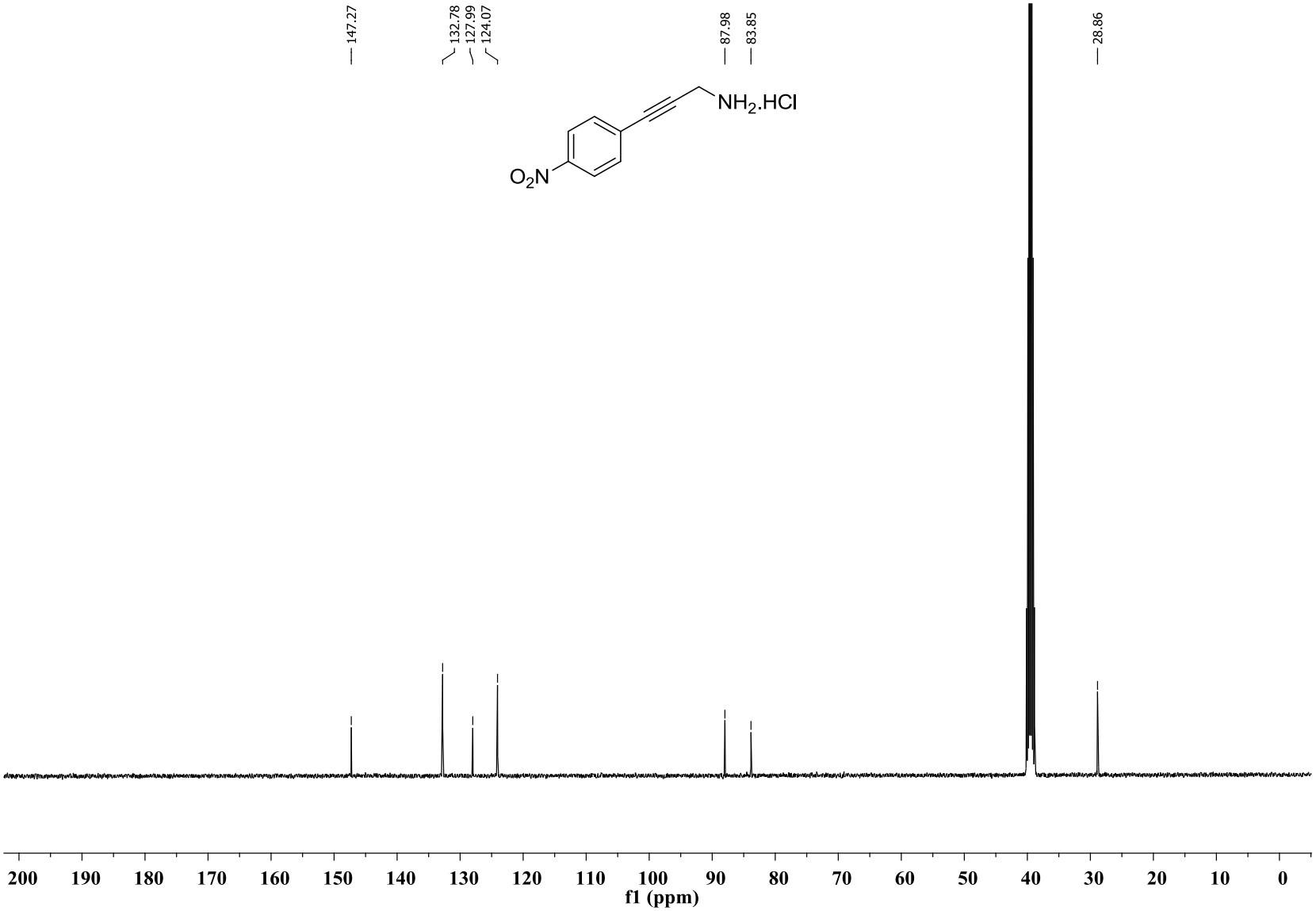
^{13}C{1H}NMR spectrum of **2d** (DMSO-d_6, 100 MHz)**:**



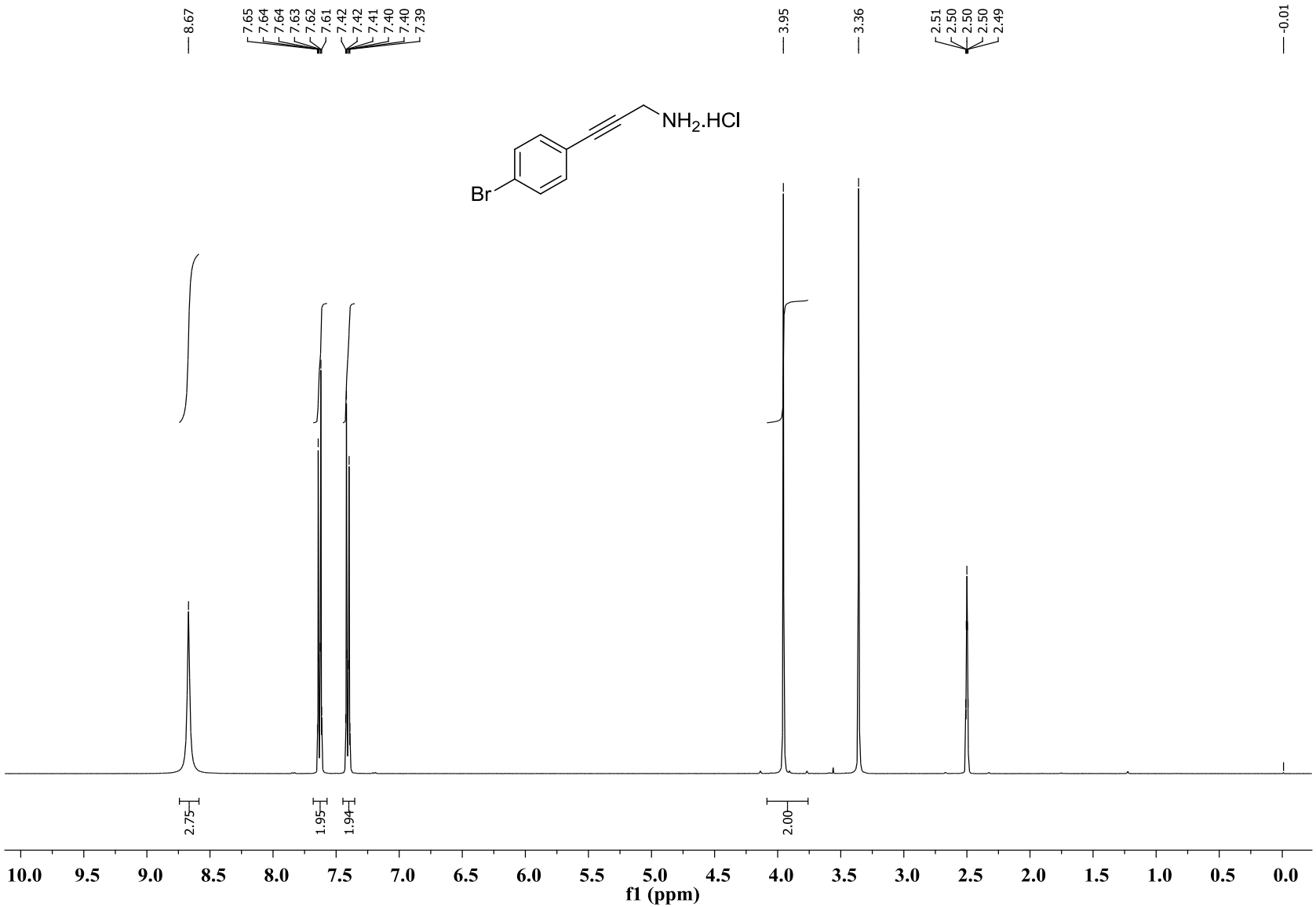
^{1}H NMR spectrum of **2e** (DMSO-d_6, 400 MHz)**:**



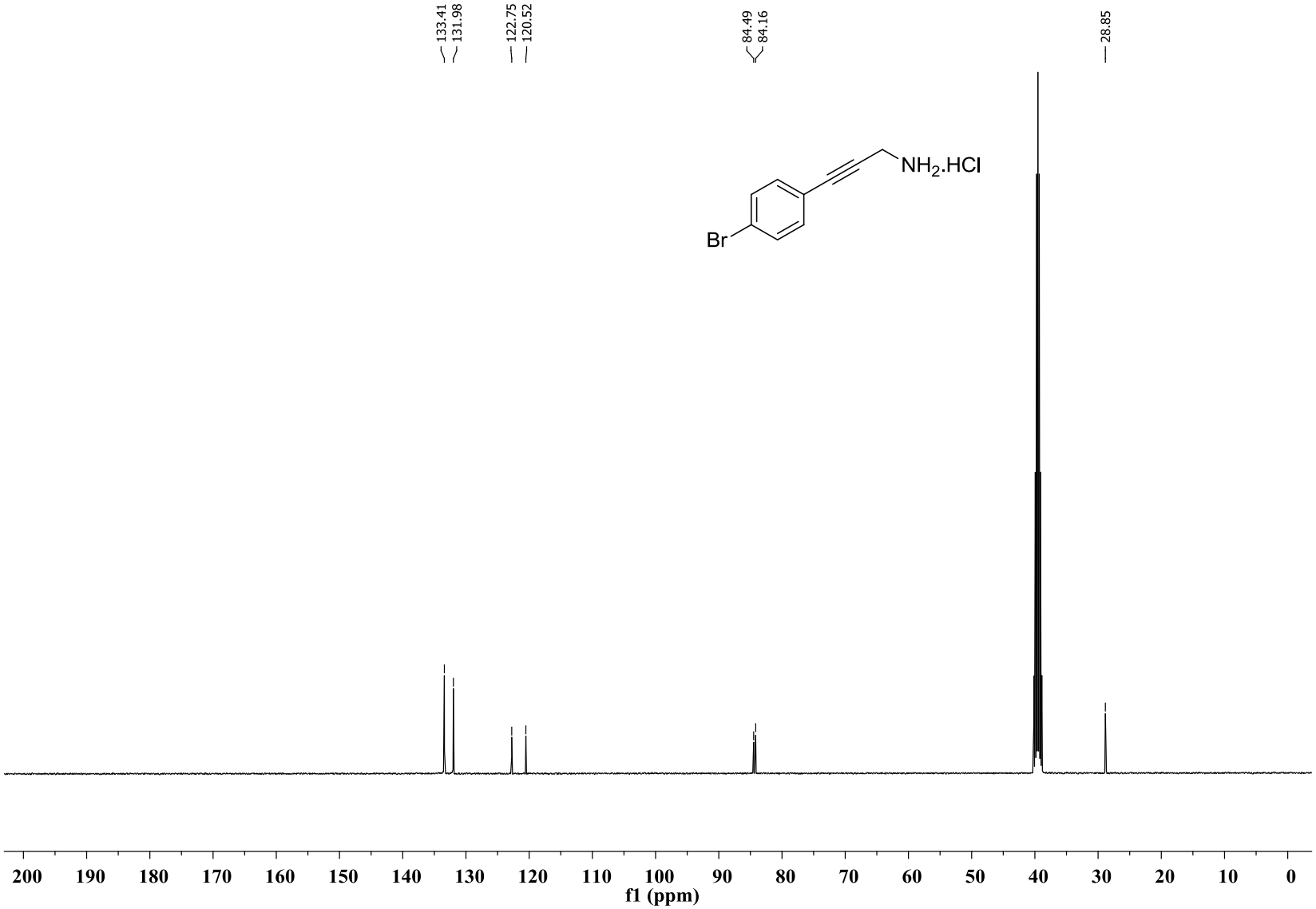
^{13}C{1H}NMR spectrum of **2e** (DMSO-d_6, 100 MHz)**:**



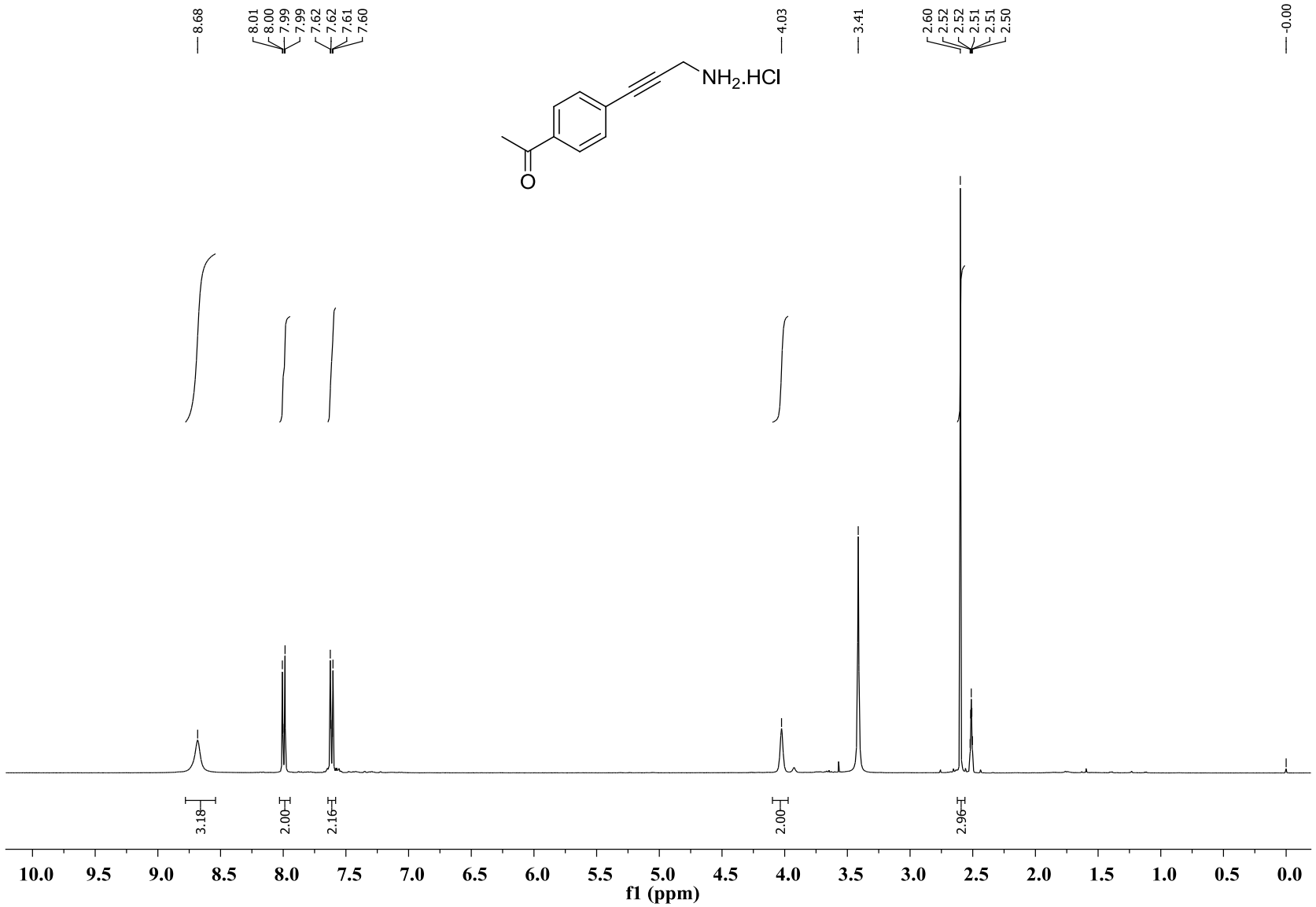
^{1}H NMR spectrum of **2f** (DMSO-*d*$_6$, 400 MHz)**:**



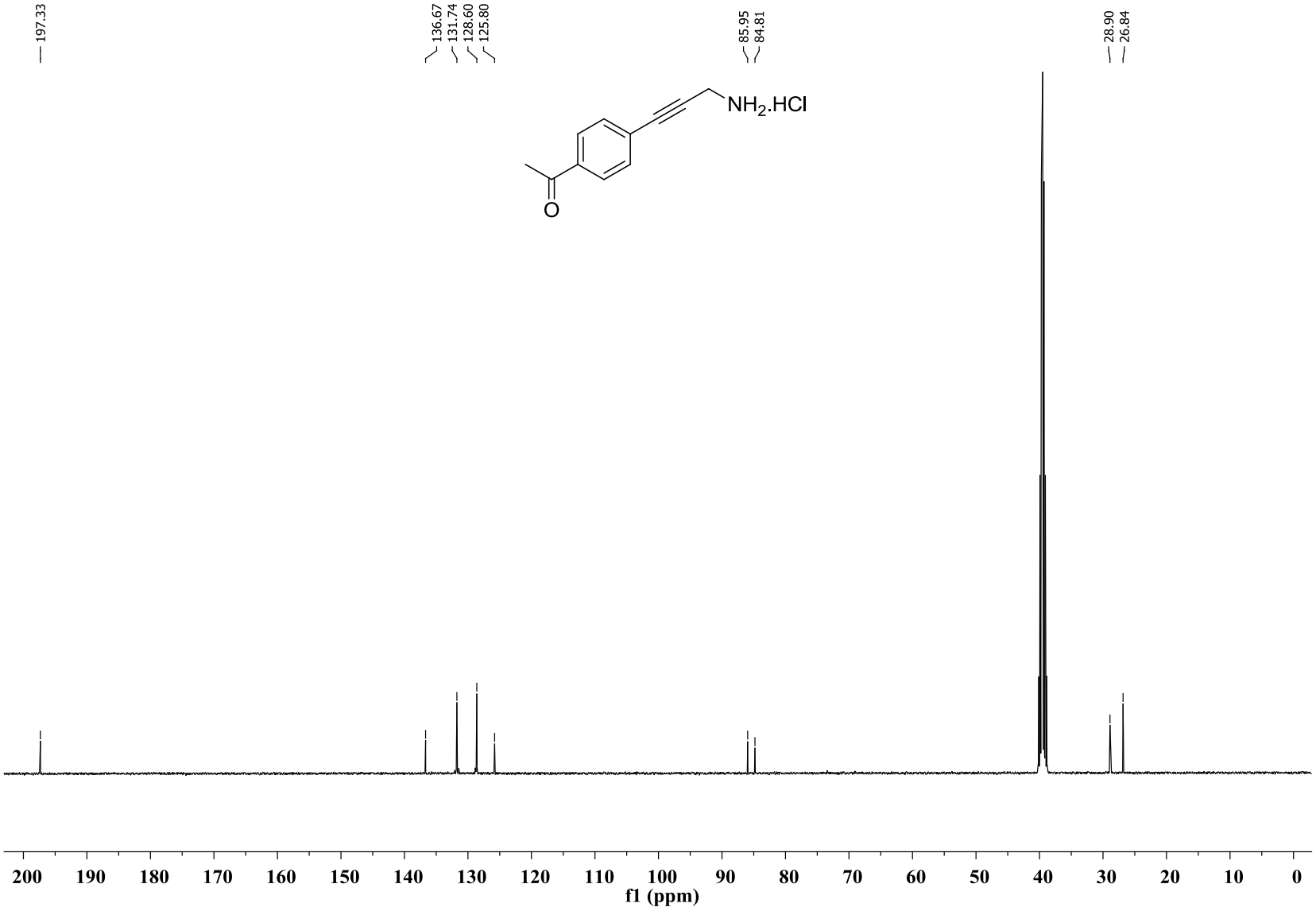
^{13}C{1H}NMR spectrum of **2f** (DMSO-d_6, 100 MHz)**:**



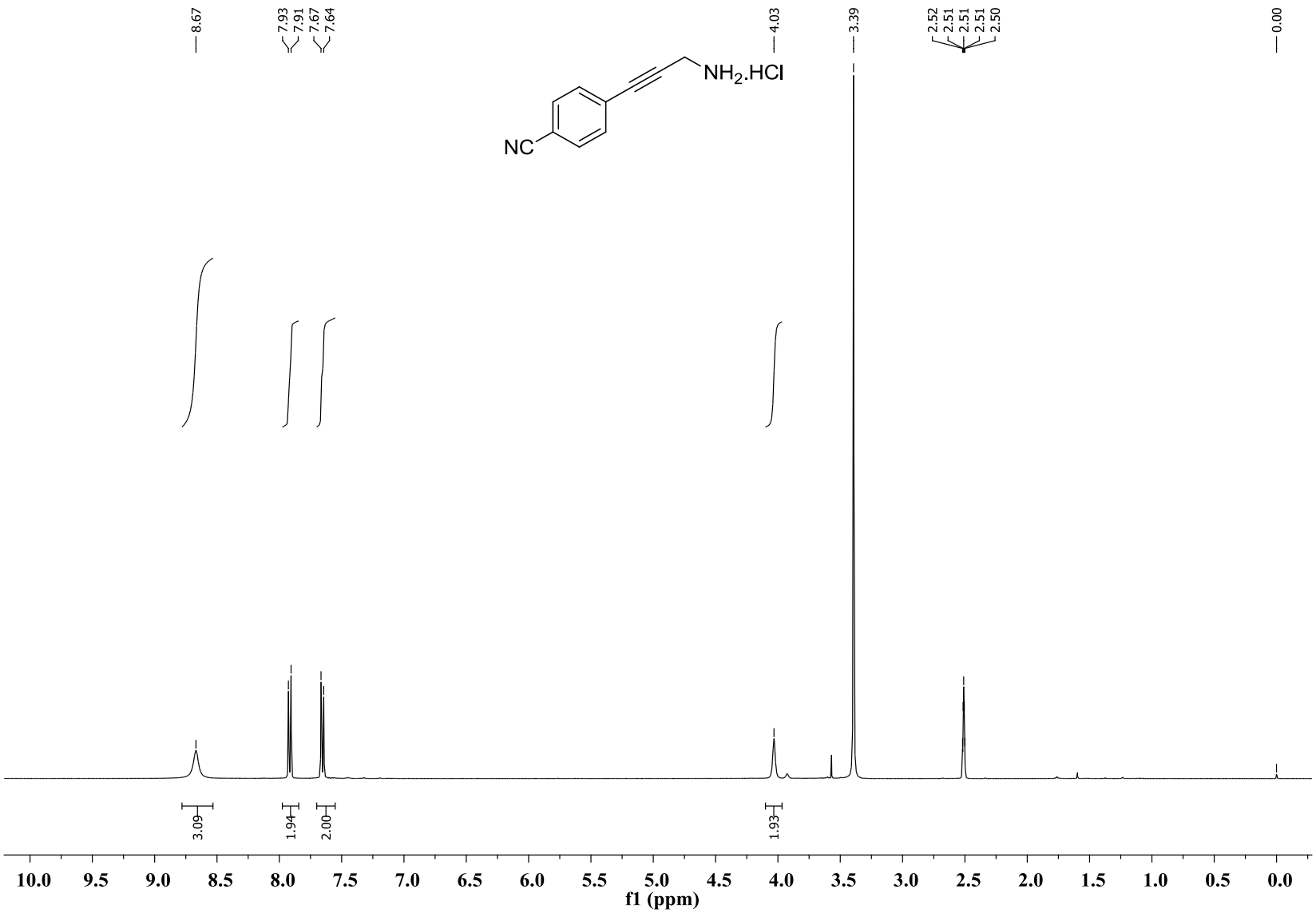
^{1}H NMR spectrum of **2g** (DMSO-d_6, 400 MHz)**:**



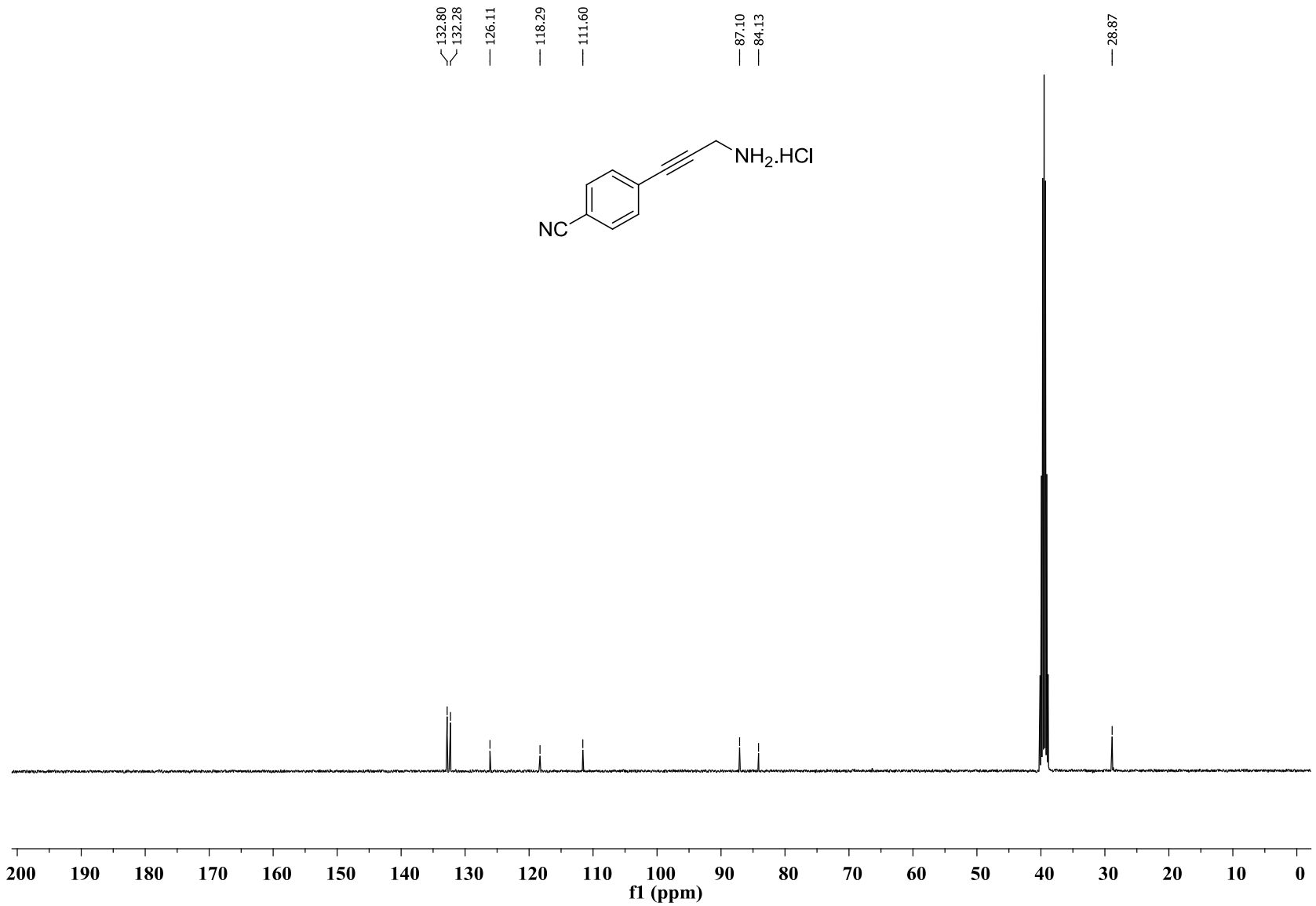
^{13}C{1H}NMR spectrum of **2g** (DMSO-d_6, 100 MHz)**:**



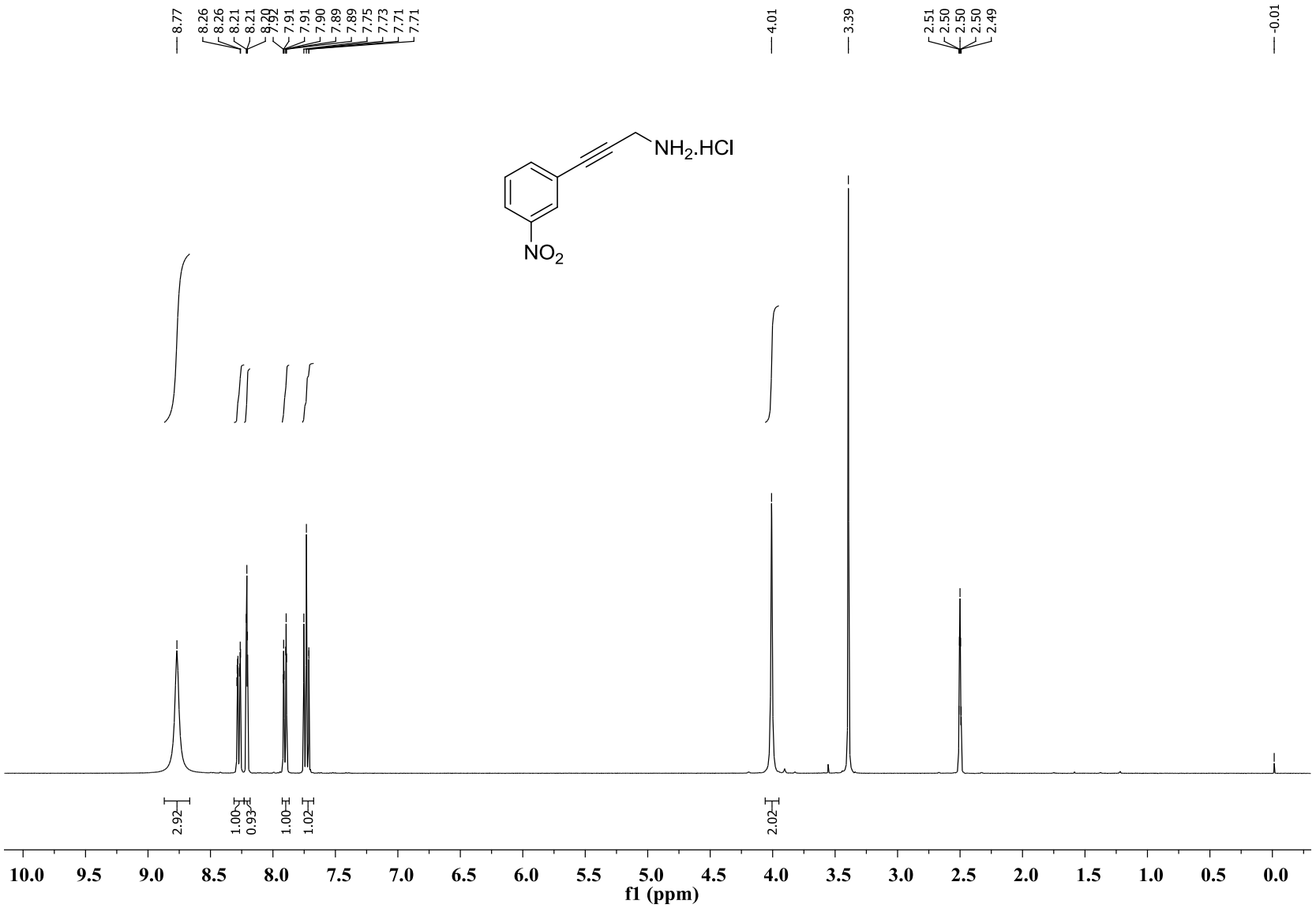
^{1}H NMR spectrum of **2h** (DMSO-d_6, 400 MHz)**:**



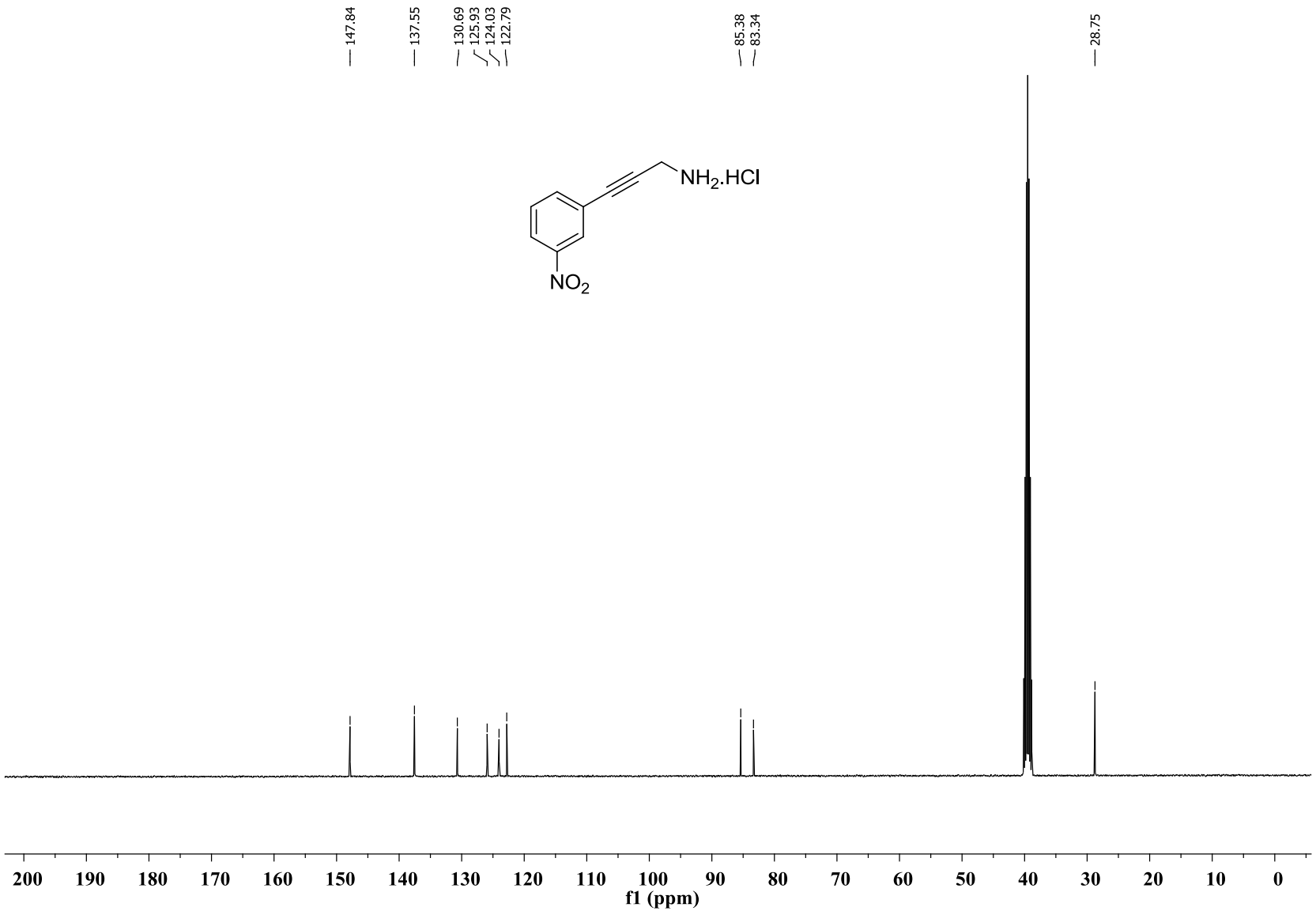
^{13}C{1H}NMR spectrum of **2h** (DMSO-d_6, 100 MHz)**:**



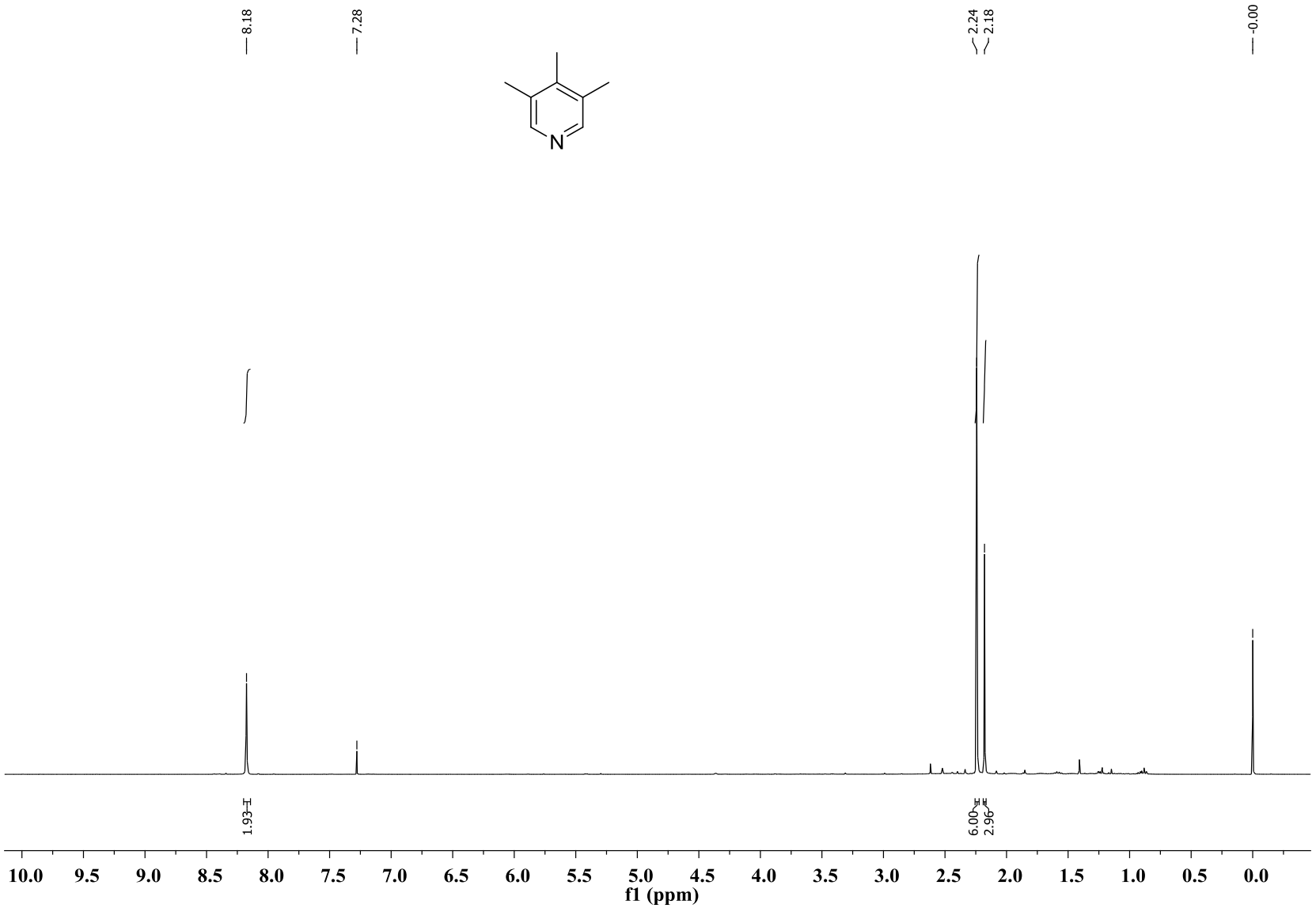
^{1}H NMR spectrum of **2i** (DMSO-d_6, 400 MHz)**:**



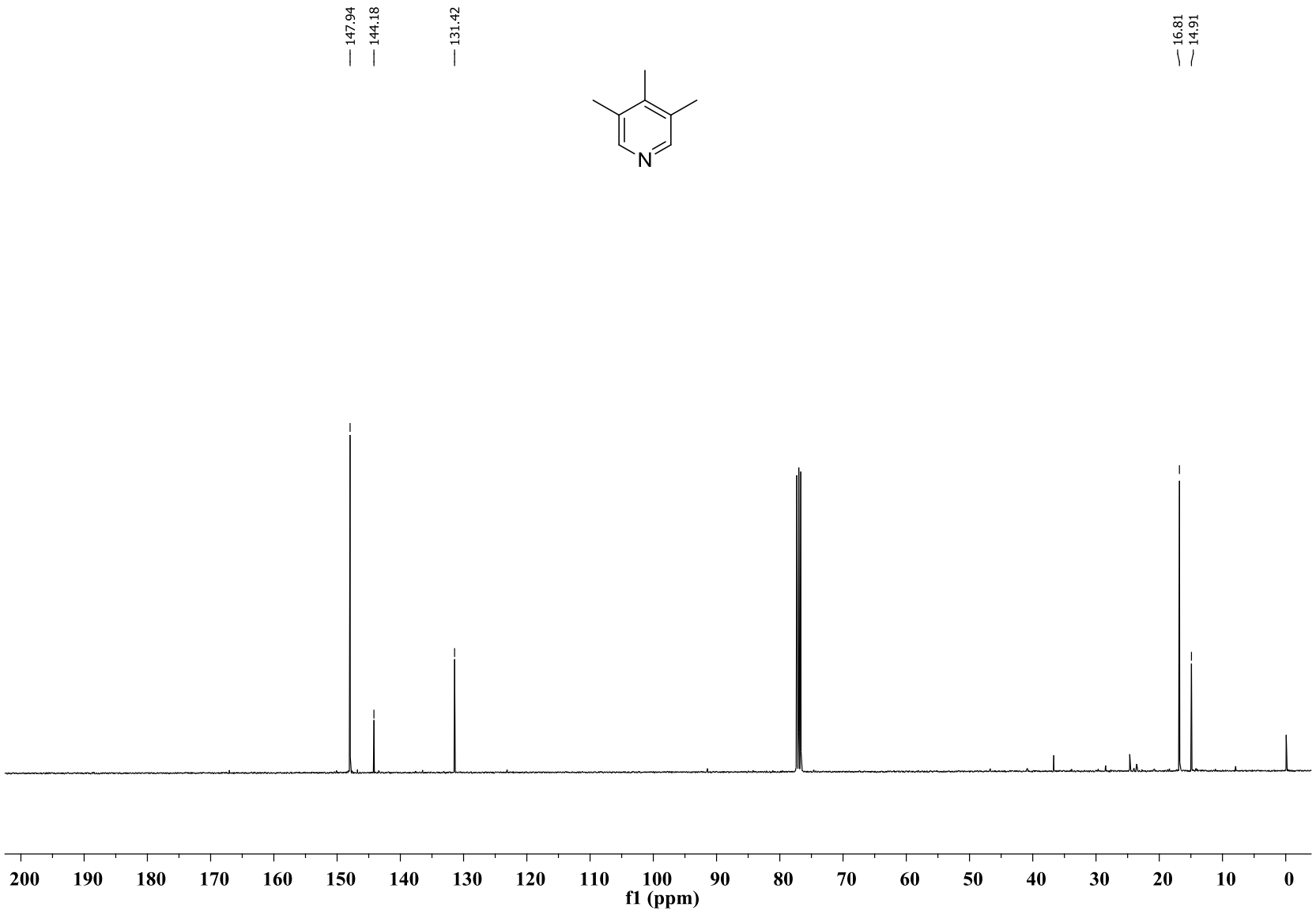
^{13}C{1H}NMR spectrum of **2i** (DMSO-d_6, 100 MHz)**:**



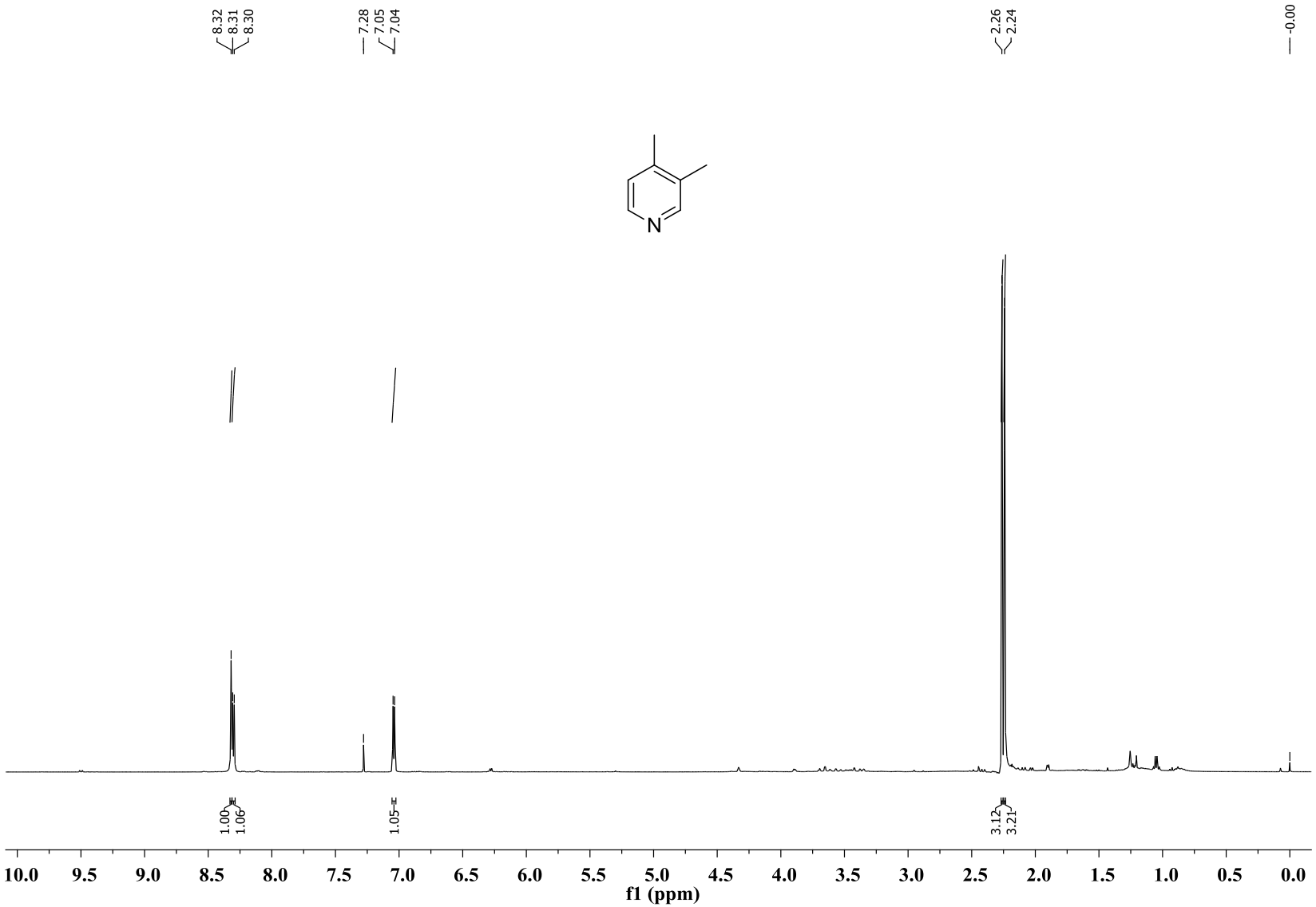
^{1}H NMR spectrum of **3a** ($CDCl_3$, 400 MHz)**:**



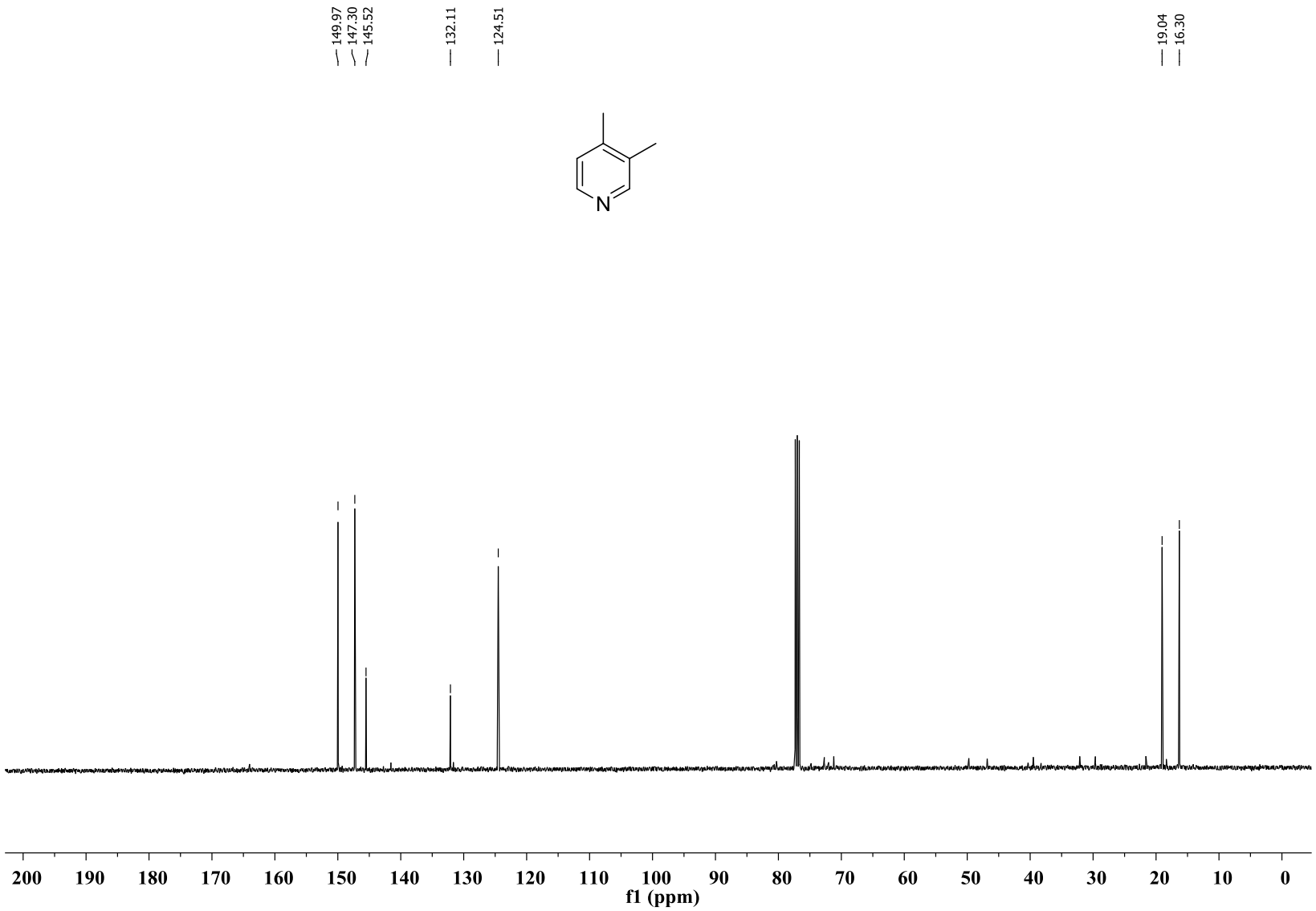
$^{13}C\{^{1}H\}$NMR spectrum of **3a** ($CDCl_3$, 100 MHz)**:**



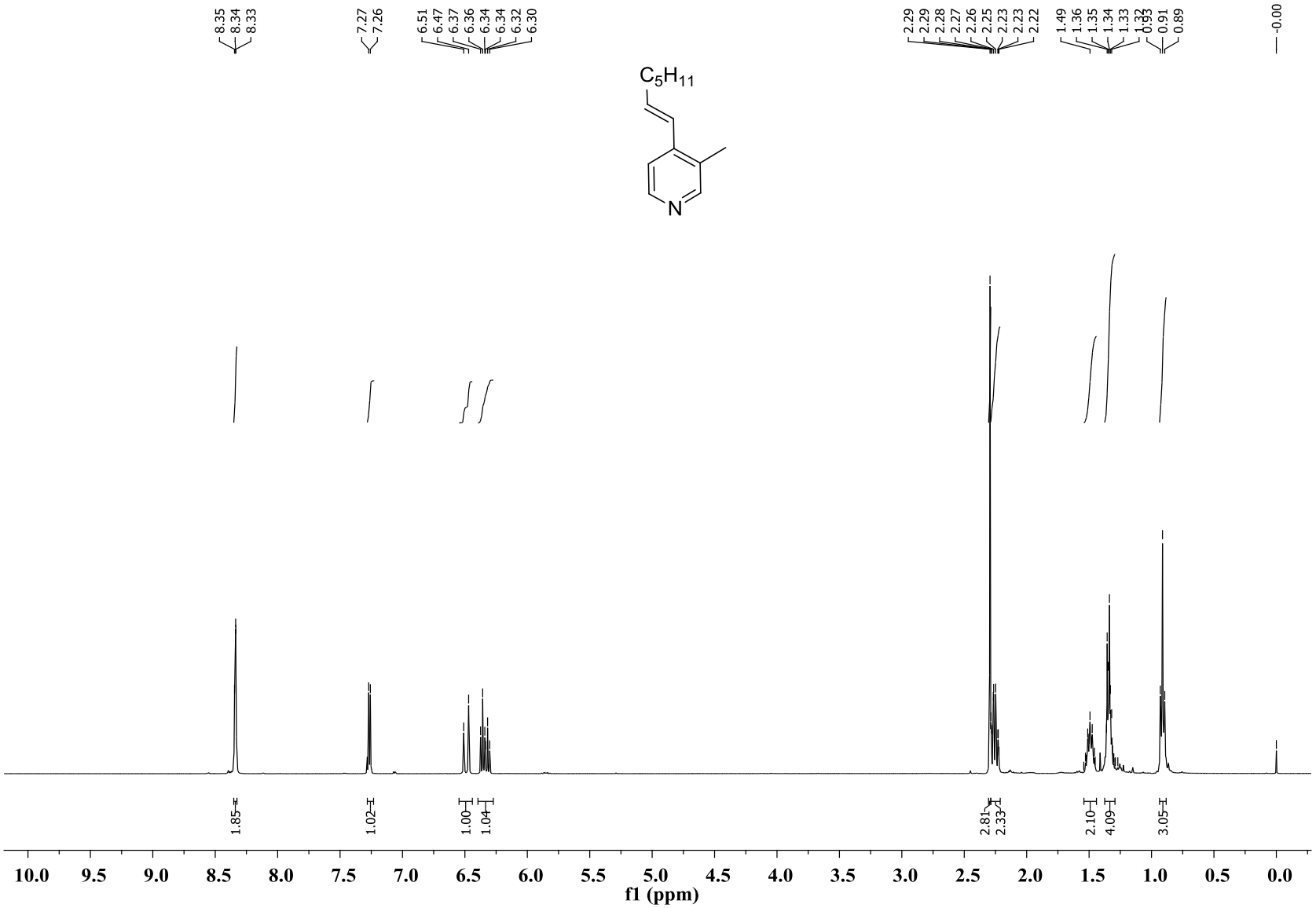
^{1}H NMR spectrum of **3b** ($CDCl_3$, 400 MHz)**:**



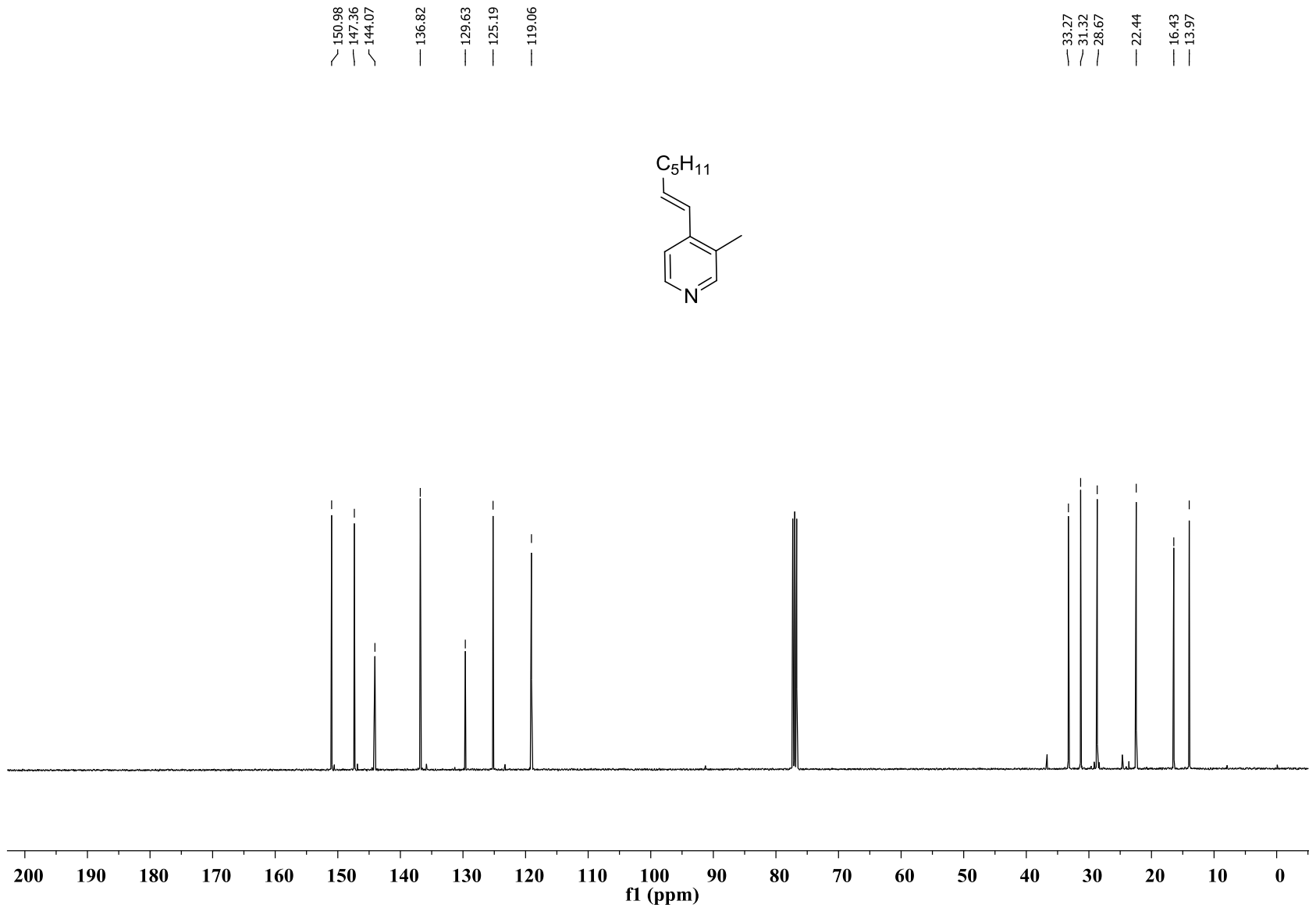
$^{13}C\{1H\}$NMR spectrum of **3b** ($CDCl_3$, 100 MHz)**:**



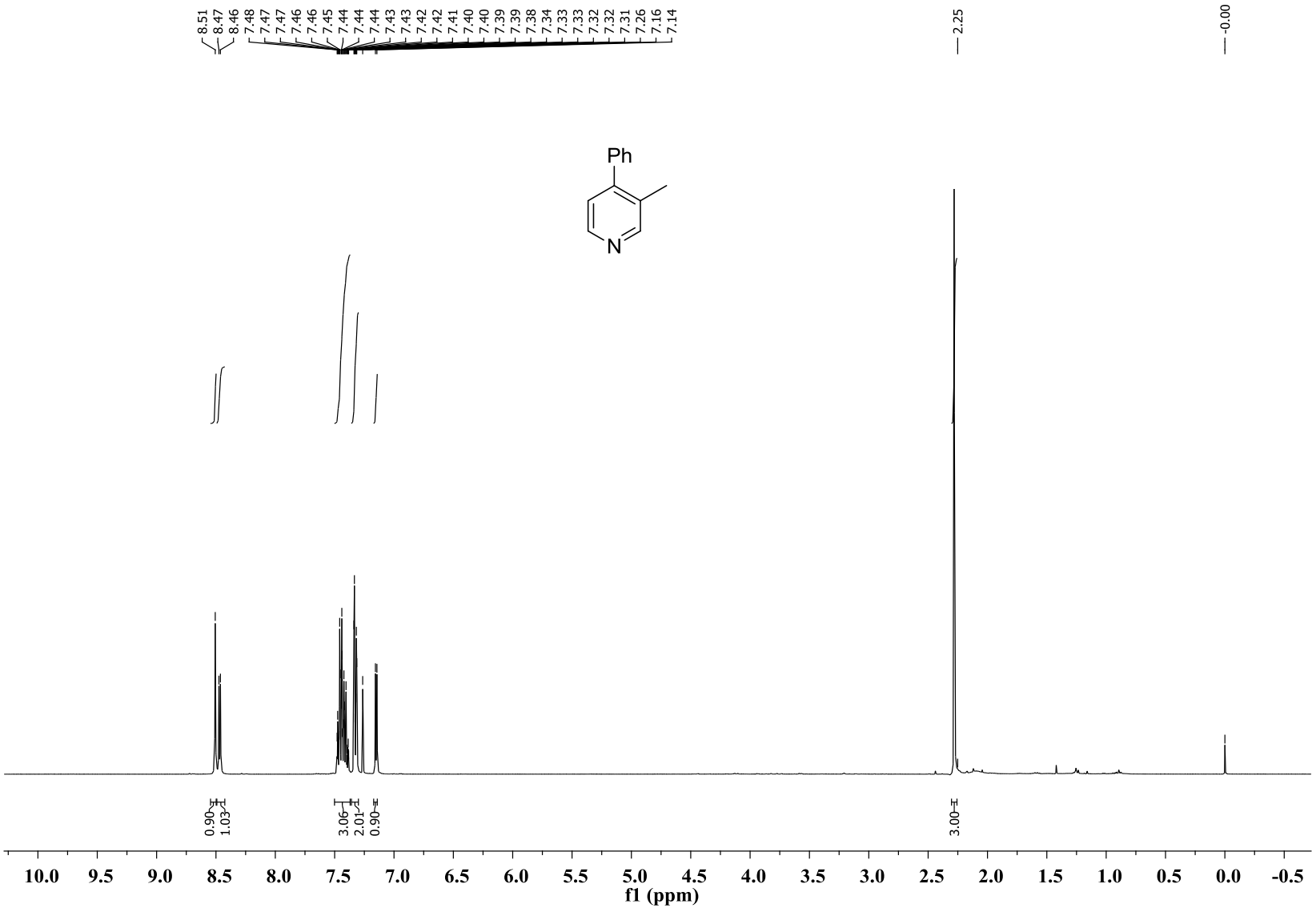
^{1}H NMR spectrum of **3c** ($CDCl_3$, 400 MHz)**:**



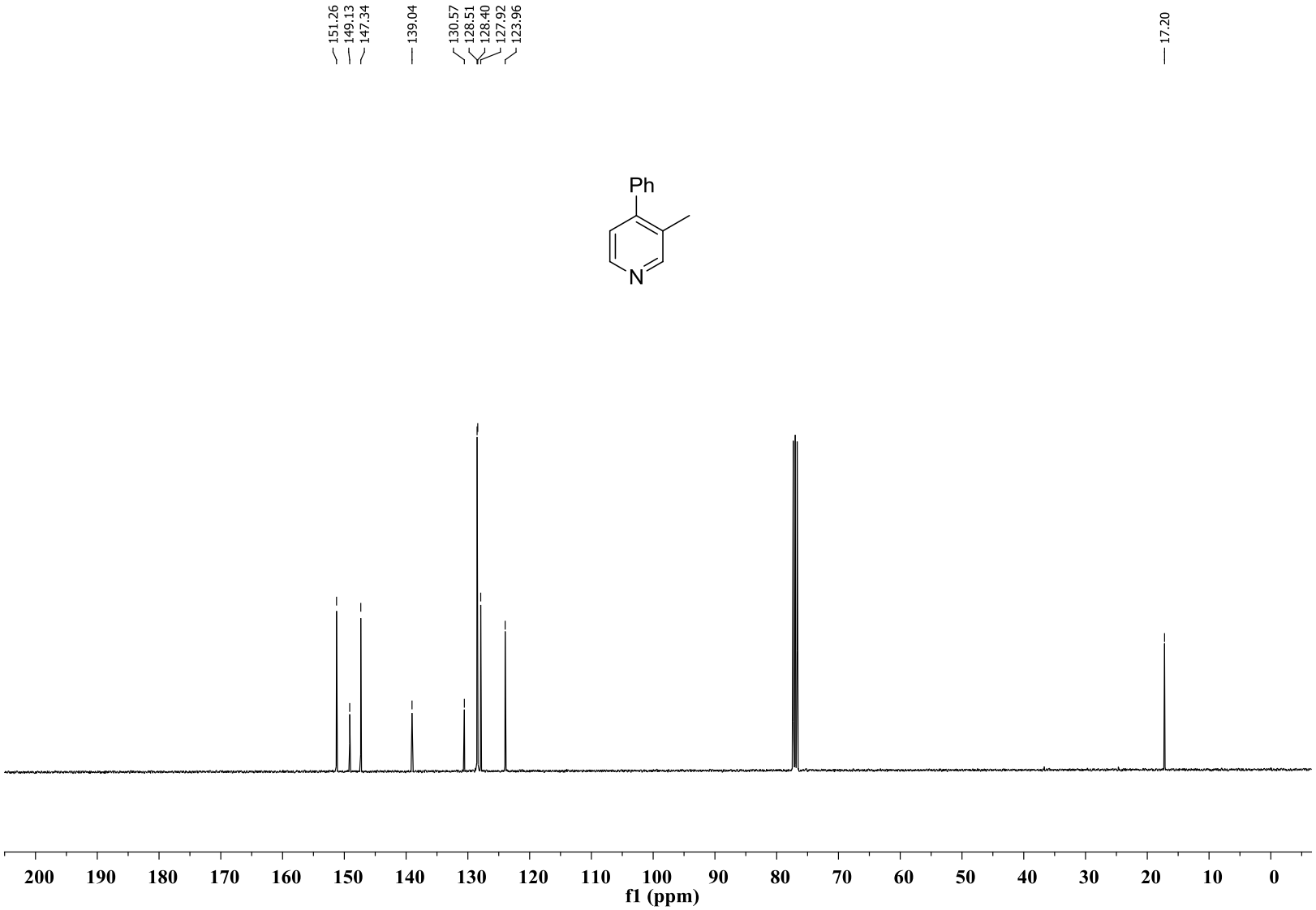
$^{13}C\{1H\}$NMR spectrum of **3c** ($CDCl_3$, 100 MHz)**:**



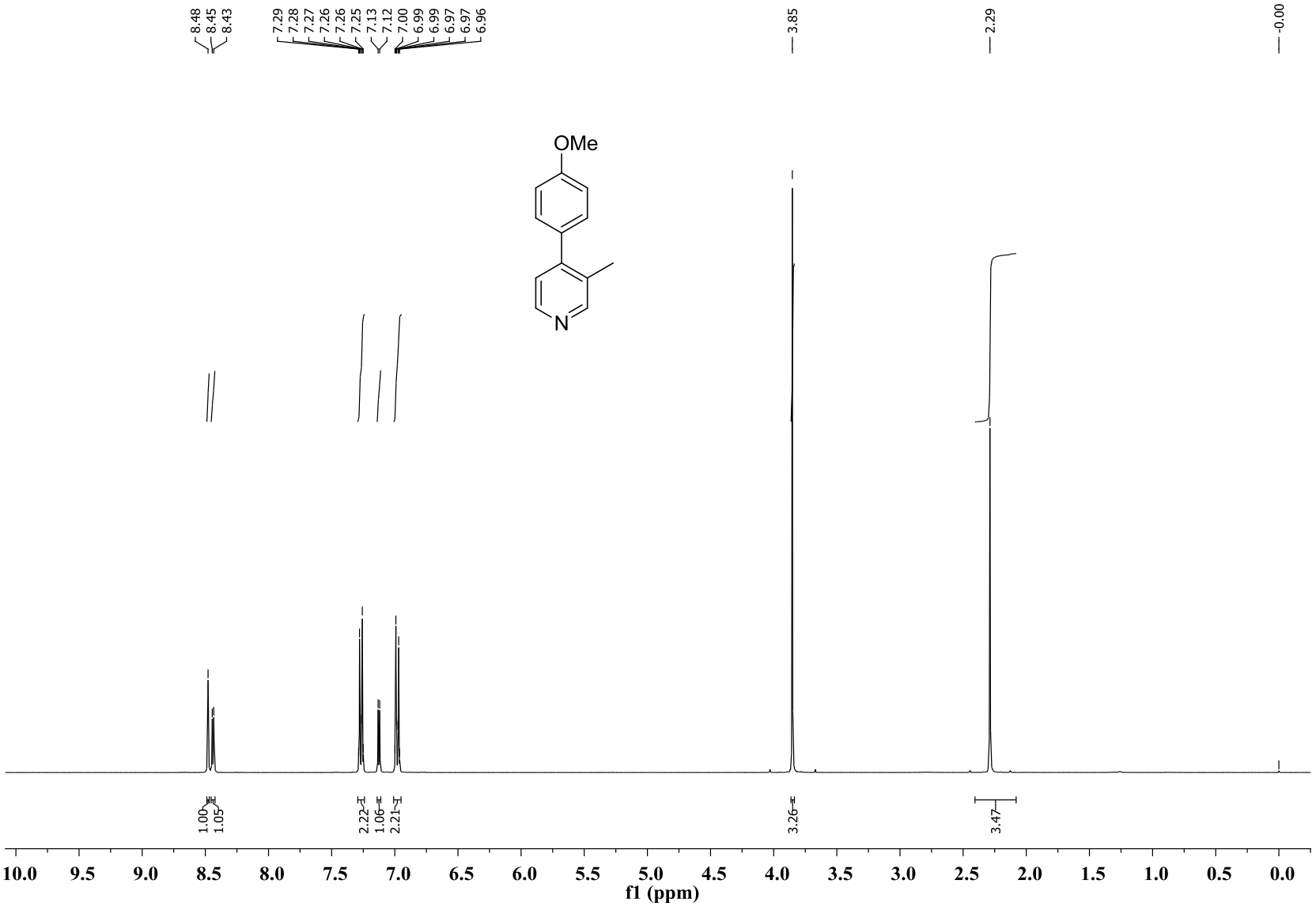
^{1}H NMR spectrum of **3d** ($CDCl_3$, 400 MHz)**:**



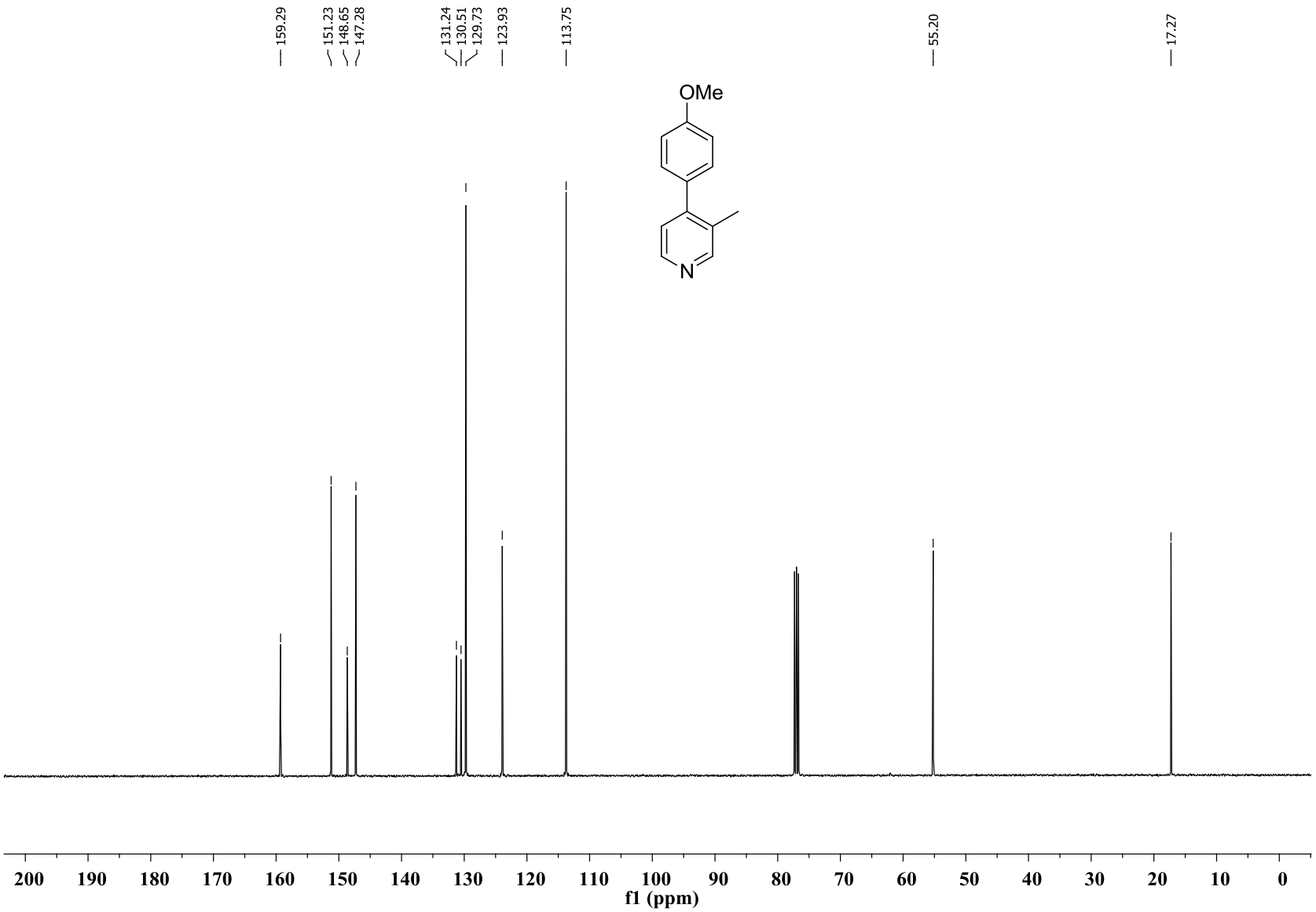
$^{13}C\{^{1}H\}$NMR spectrum of **3d** ($CDCl_3$, 100 MHz)**:**



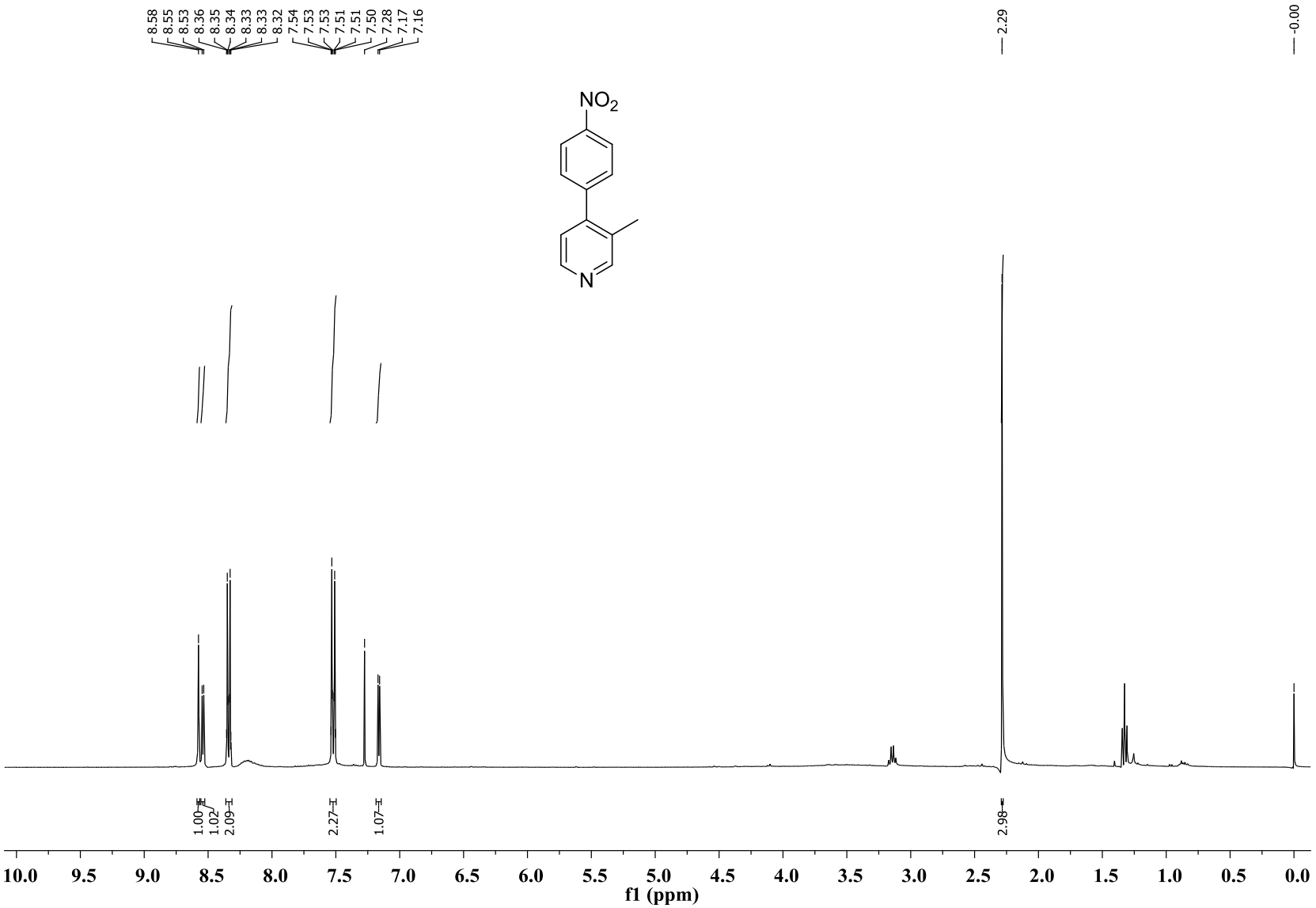
^{1}H NMR spectrum of **3e** ($CDCl_3$, 400 MHz)**:**



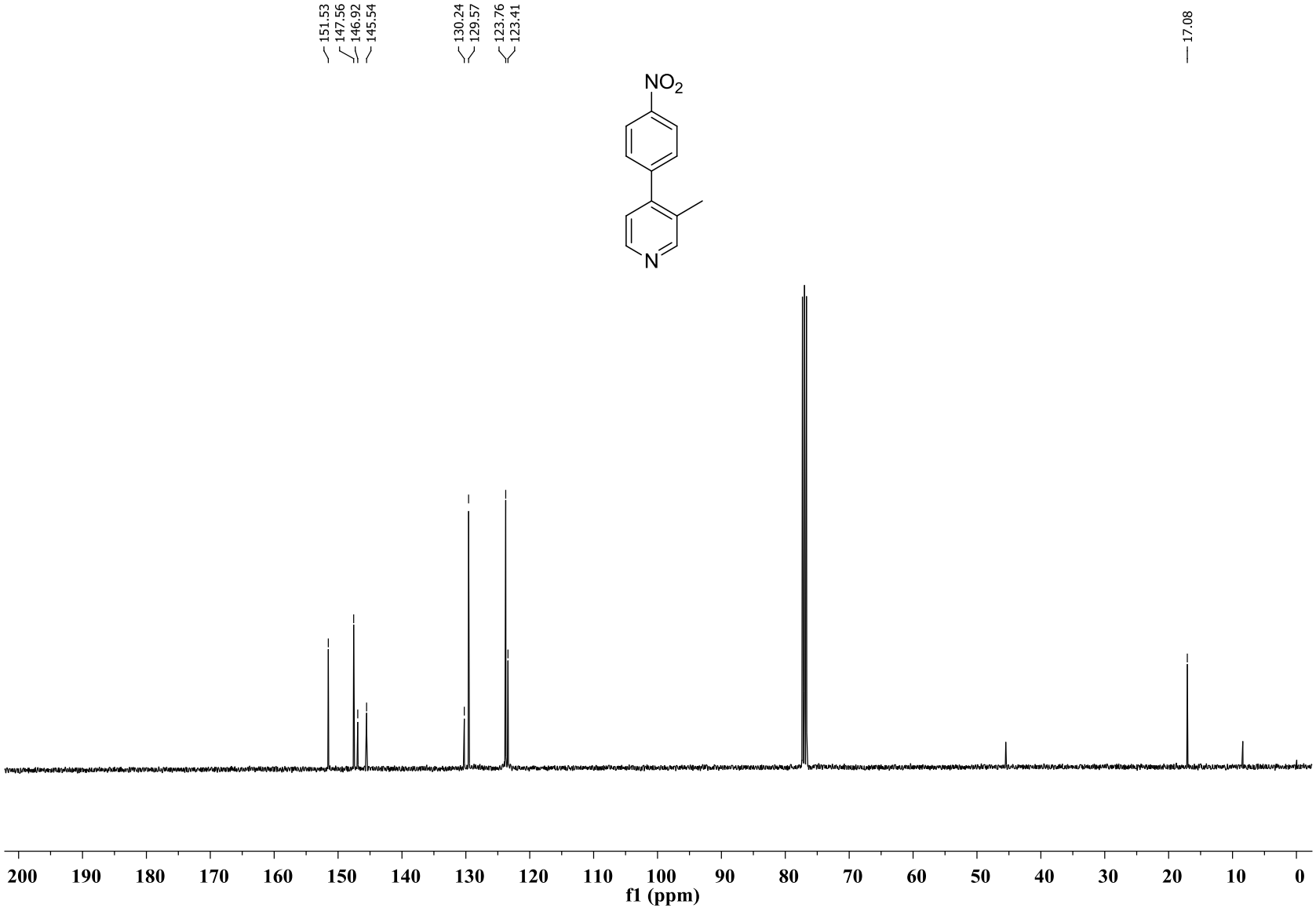
$^{13}C\{1H\}$NMR spectrum of **3e** ($CDCl_3$, 100 MHz)**:**



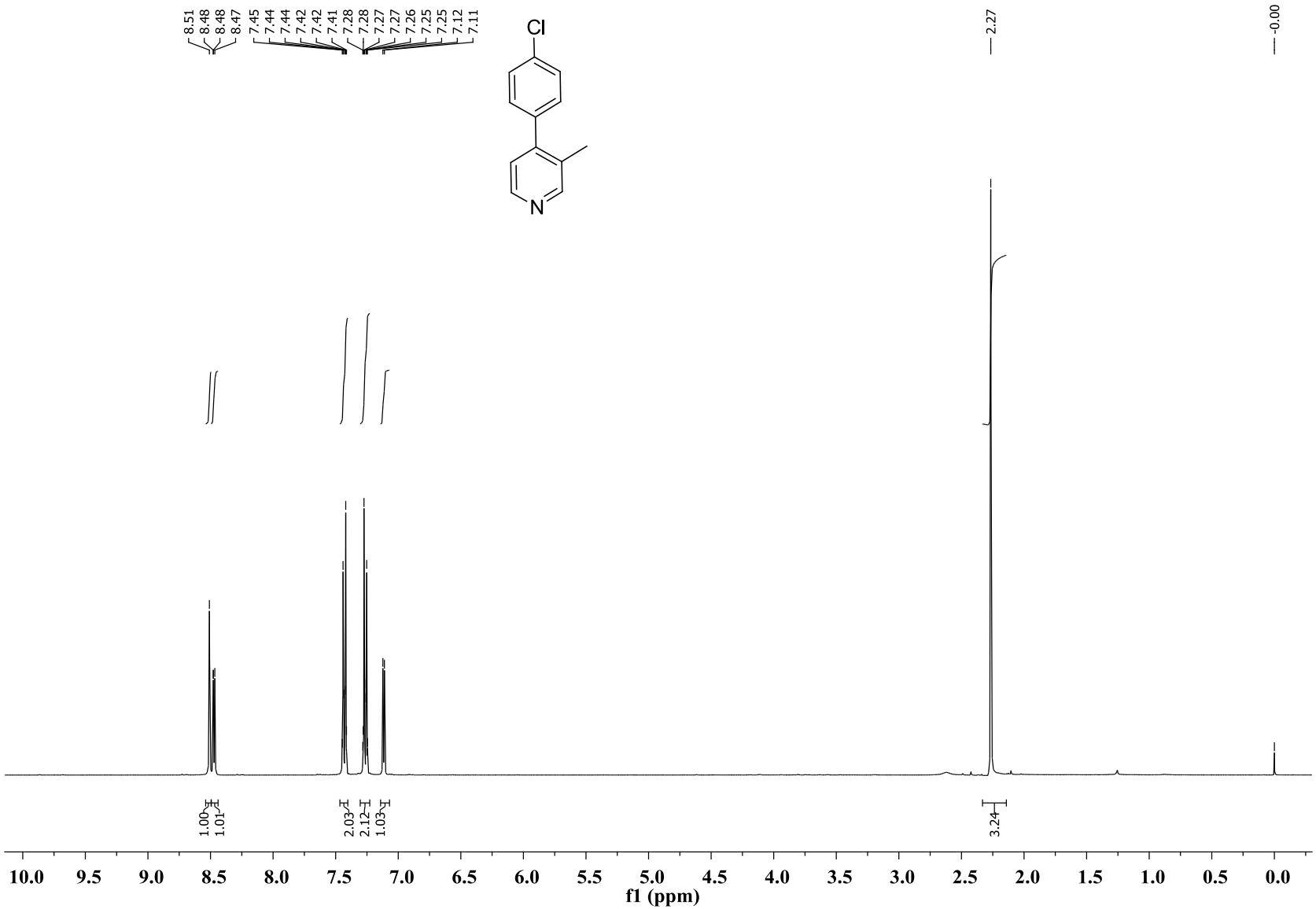
^{1}H NMR spectrum of **3f** ($CDCl_3$, 400 MHz)**:**



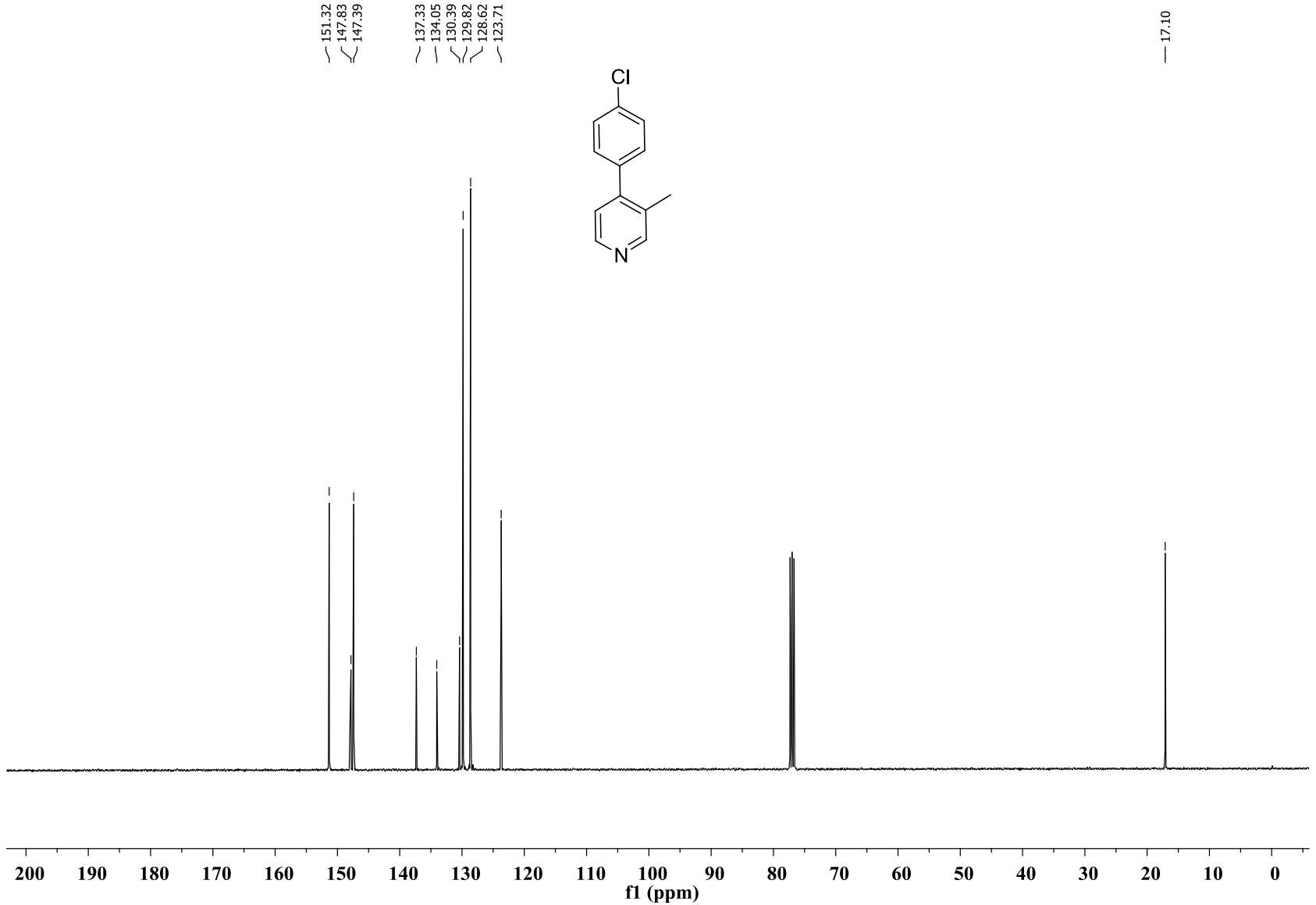
$^{13}C\{1H\}$NMR spectrum of **3f** ($CDCl_3$, 100 MHz)**:**



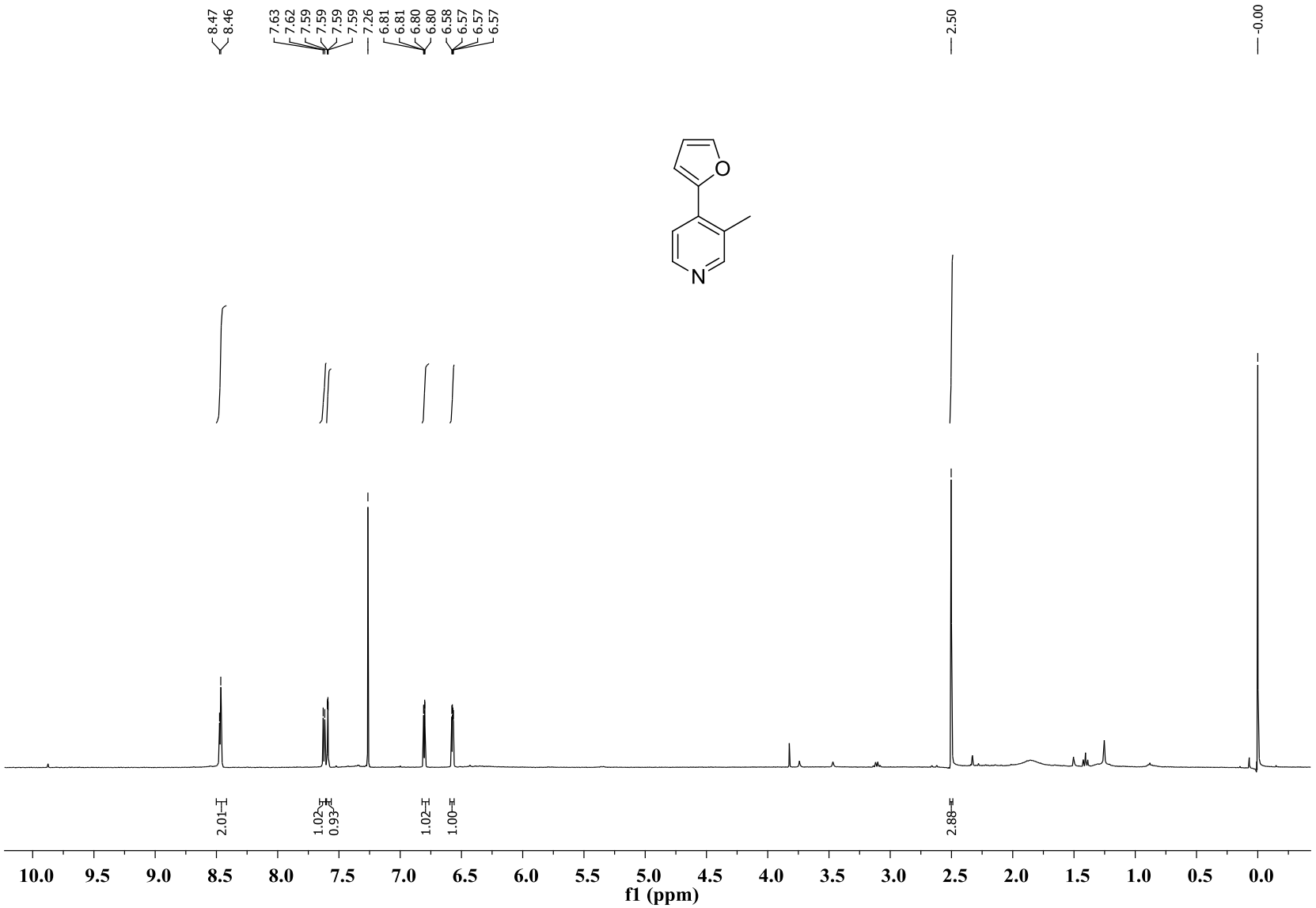
^{1}H NMR spectrum of **3g** ($CDCl_3$, 400 MHz)**:**



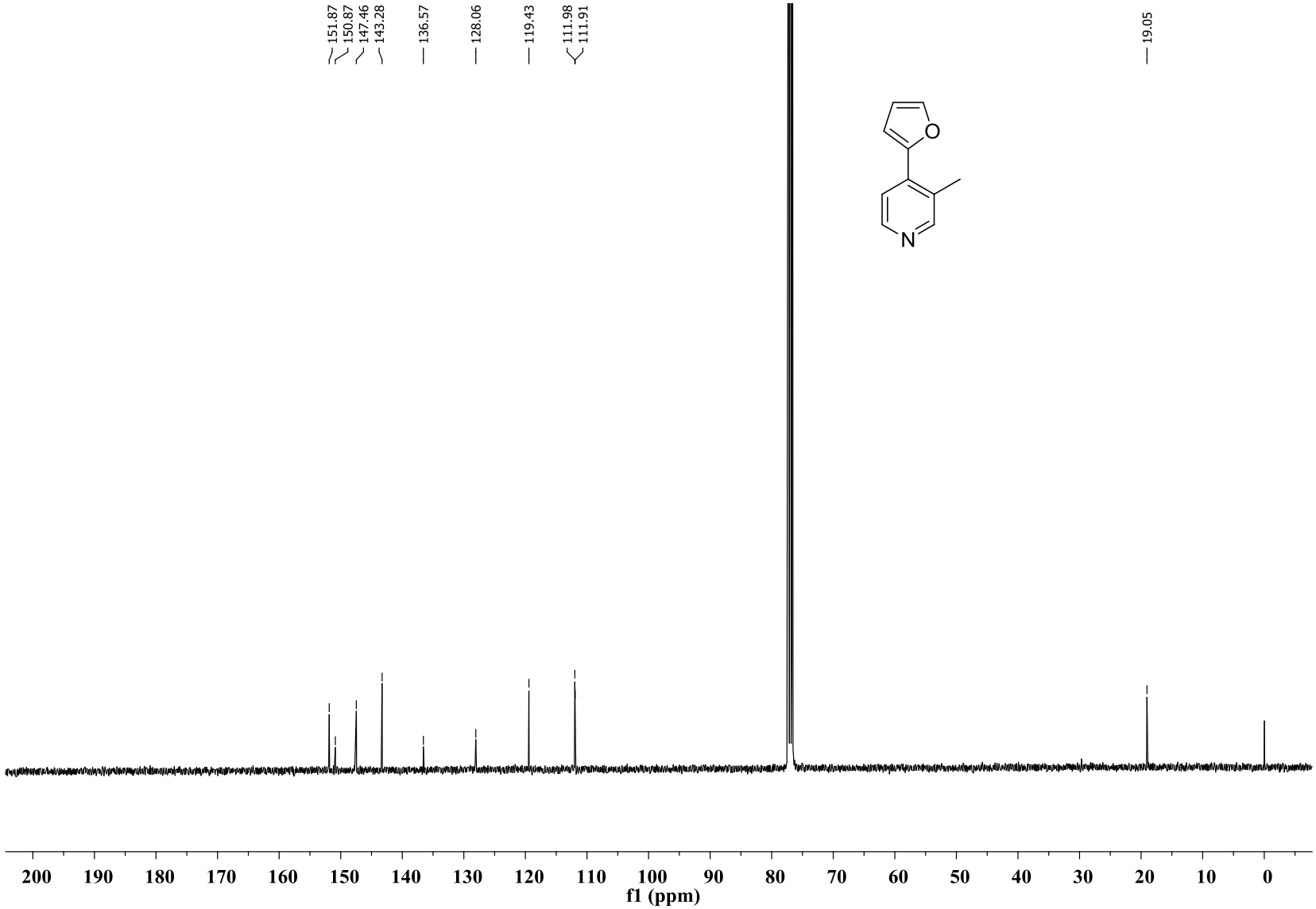
$^{13}C\{1H\}$NMR spectrum of **3g** ($CDCl_3$, 100 MHz)**:**



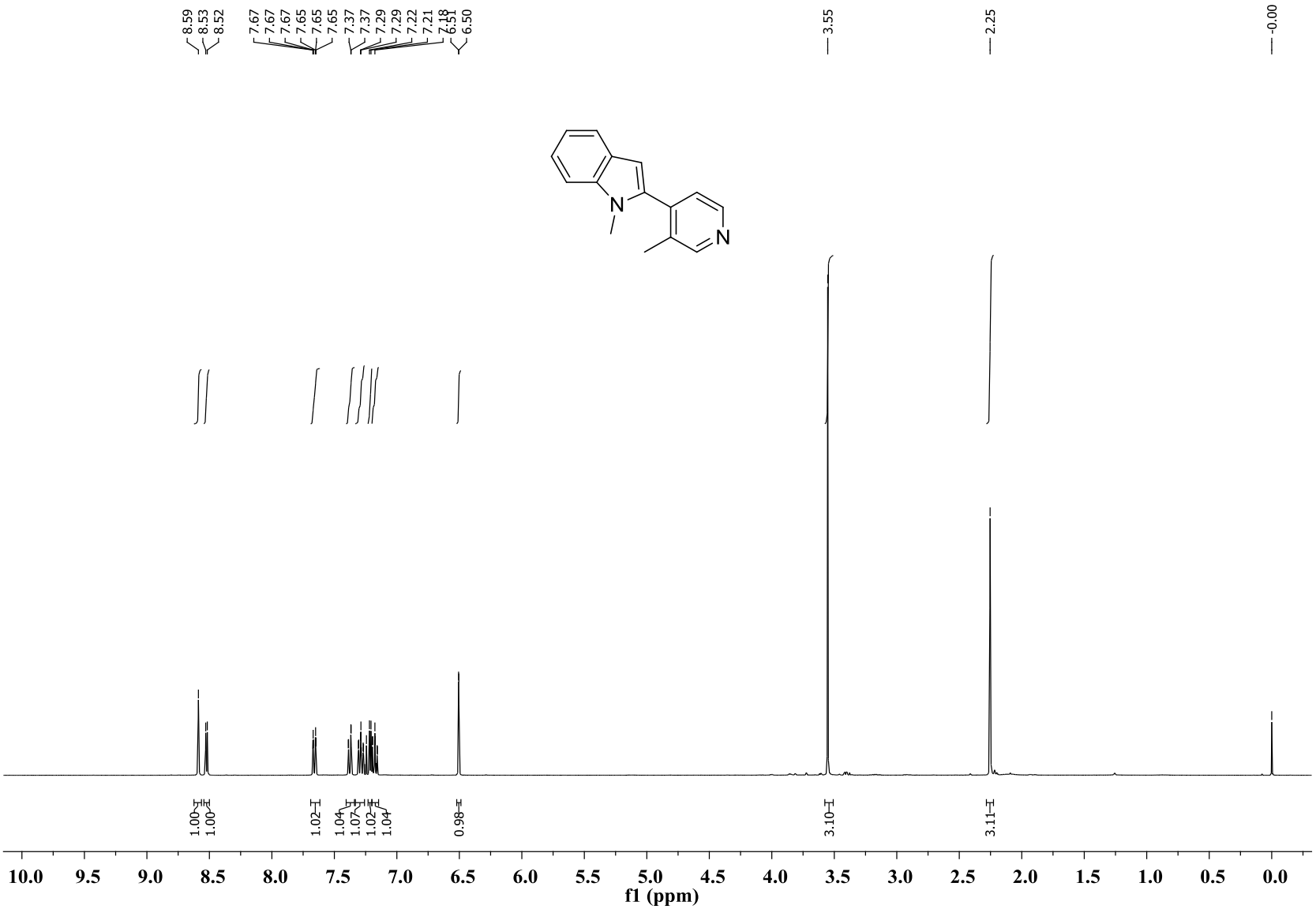
^{1}H NMR spectrum of **3h** ($CDCl_3$, 400 MHz)**:**



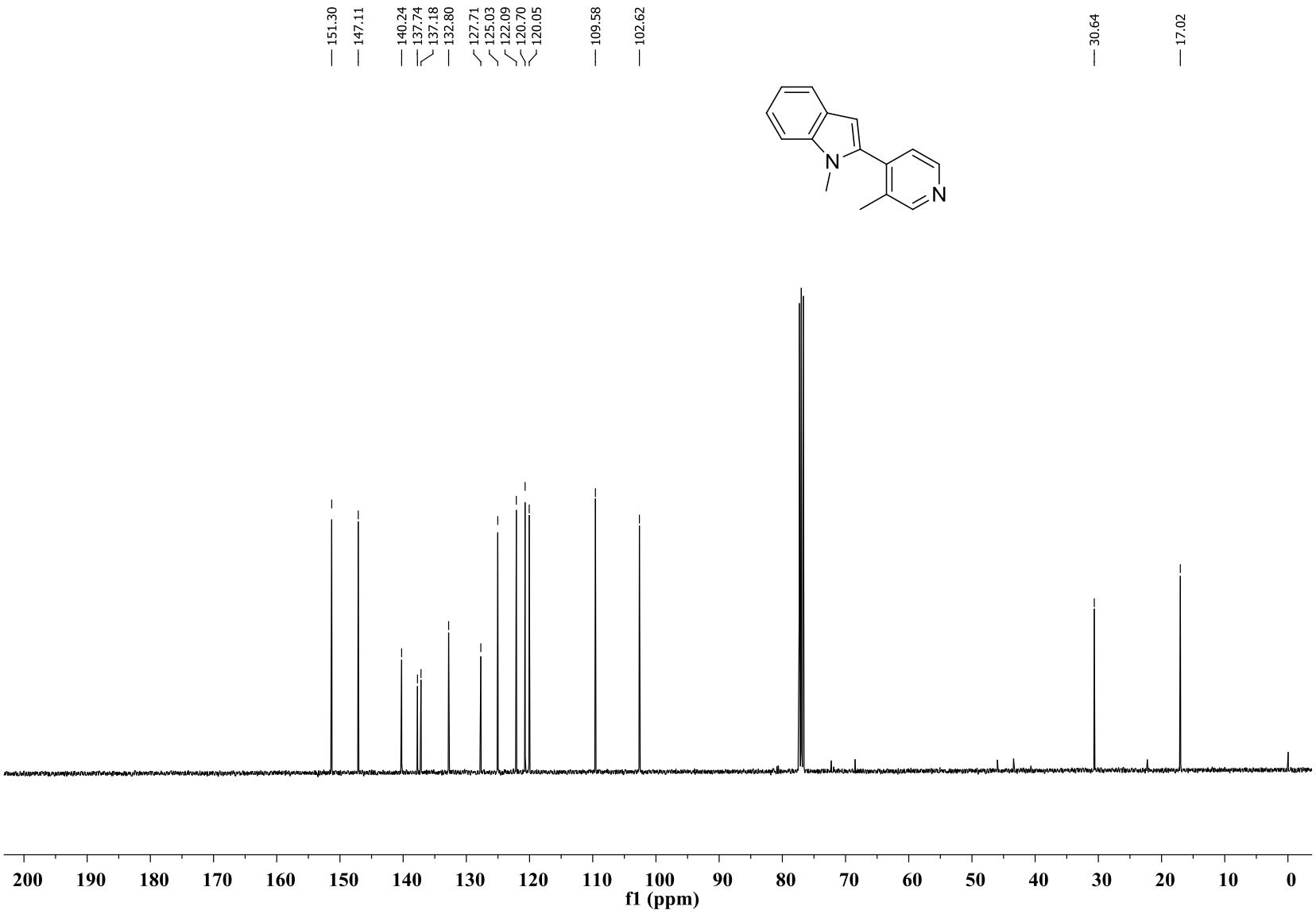
$^{13}C\{1H\}$NMR spectrum of **3h** ($CDCl_3$, 100 MHz)**:**



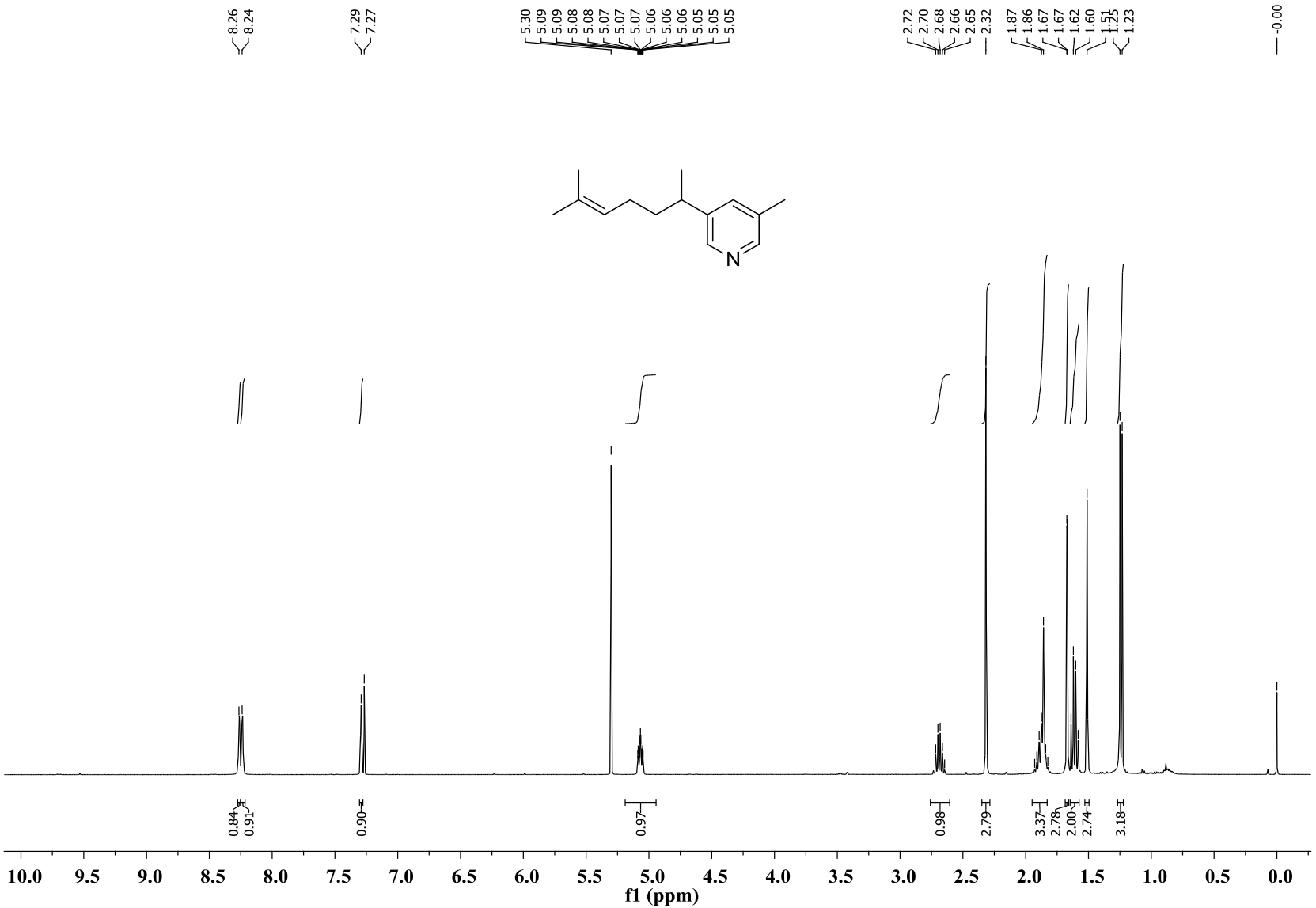
^{1}H NMR spectrum of **3i** ($CDCl_3$, 400 MHz)**:**



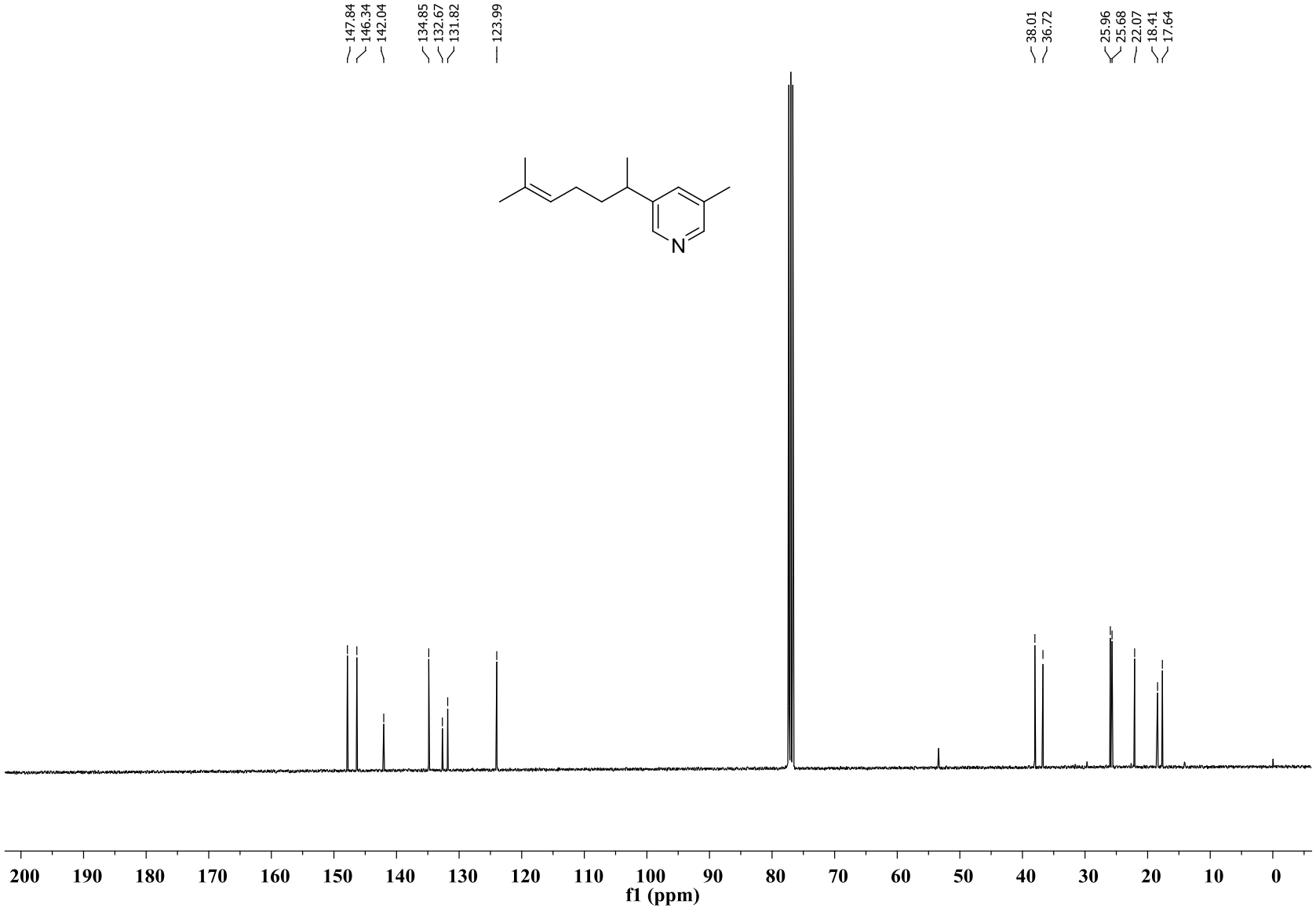
$^{13}C\{1H\}$NMR spectrum of **3i** ($CDCl_3$, 100 MHz)**:**



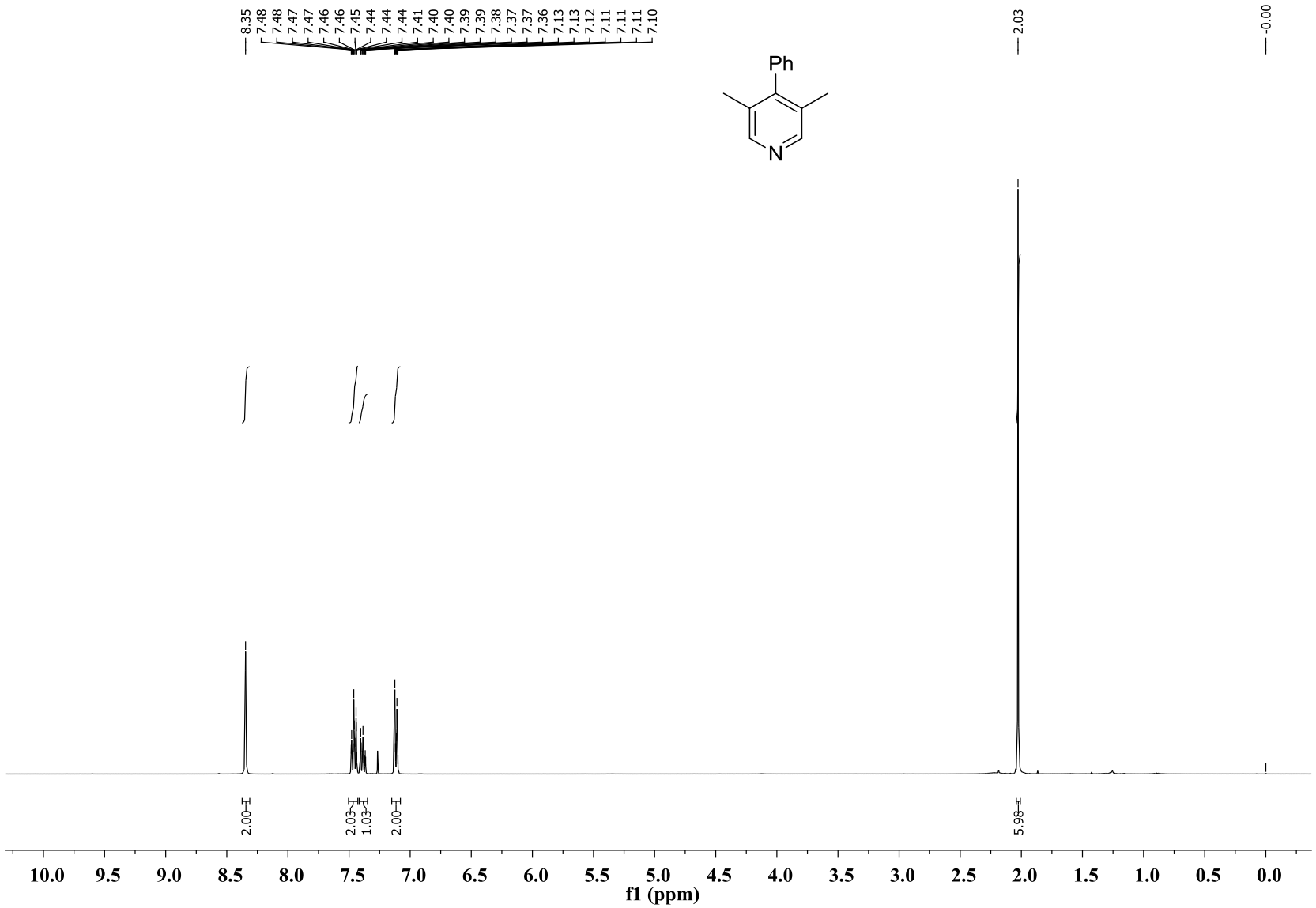
^{1}H NMR spectrum of **3j** ($CDCl_3$, 400 MHz)**:**



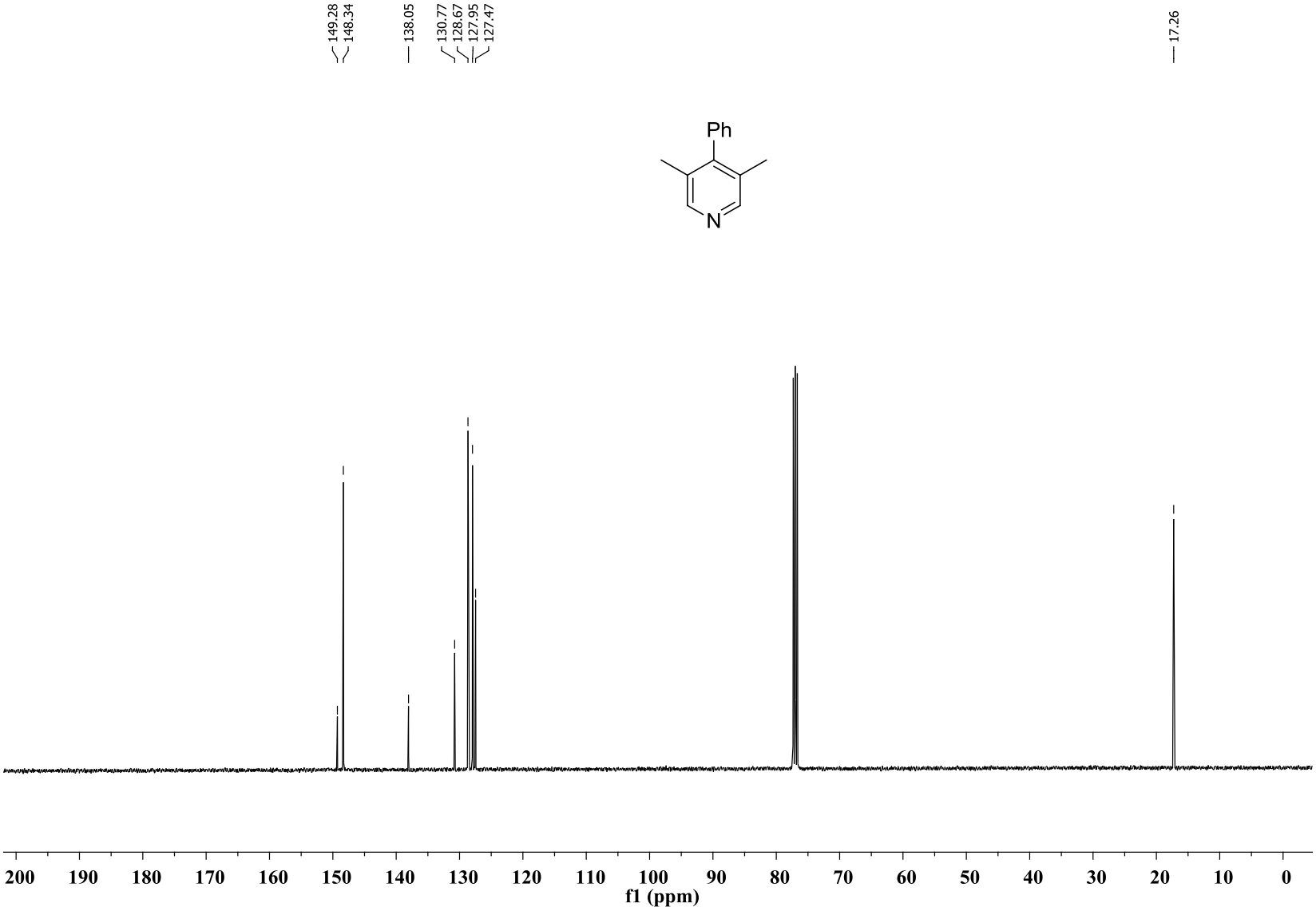
$^{13}C\{1H\}$NMR spectrum of **3j** ($CDCl_3$, 100 MHz)**:**



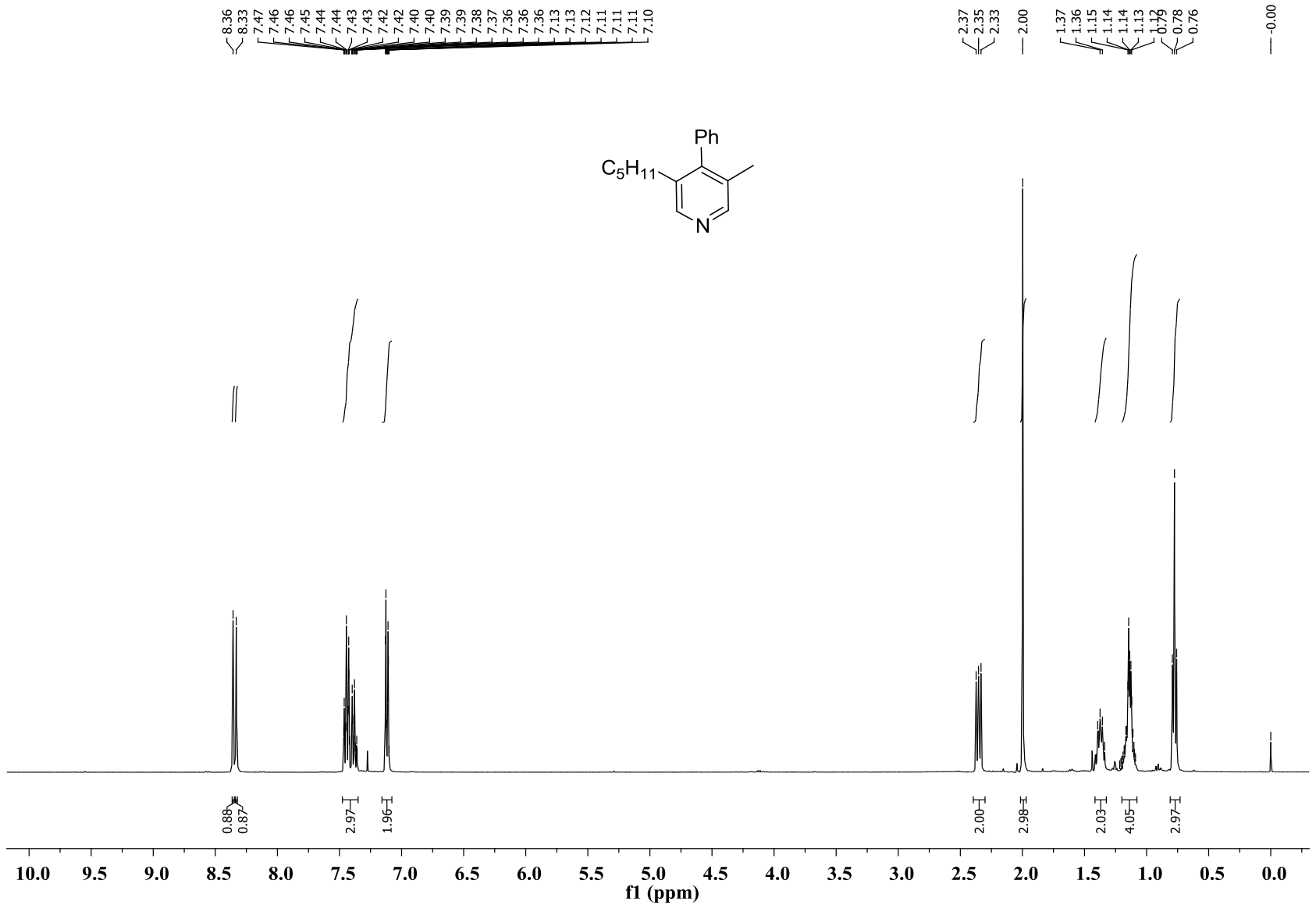
^{1}H NMR spectrum of **3k** ($CDCl_3$, 400 MHz)**:**



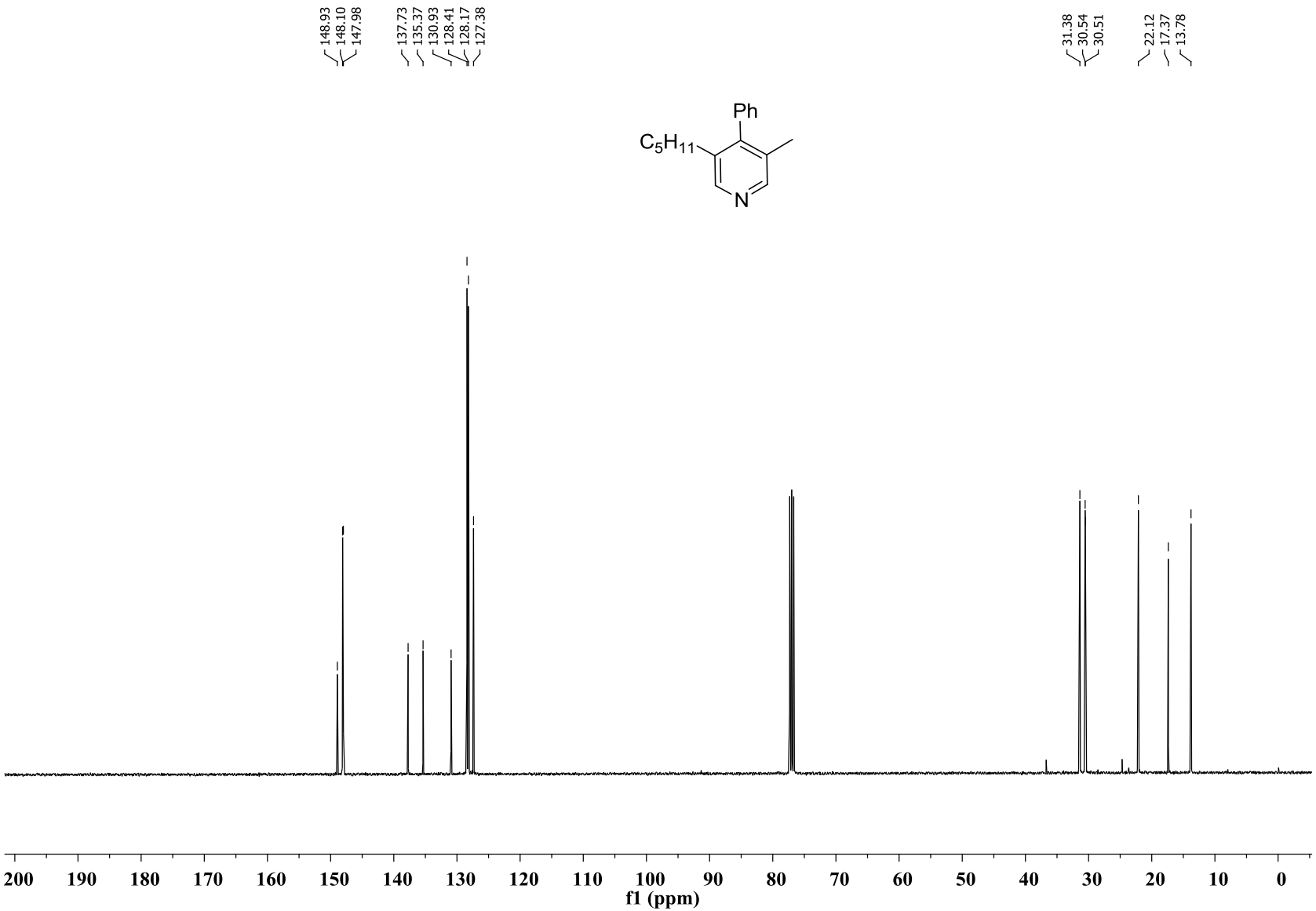
$^{13}C\{1H\}$NMR spectrum of **3k** ($CDCl_3$, 100 MHz)**:**



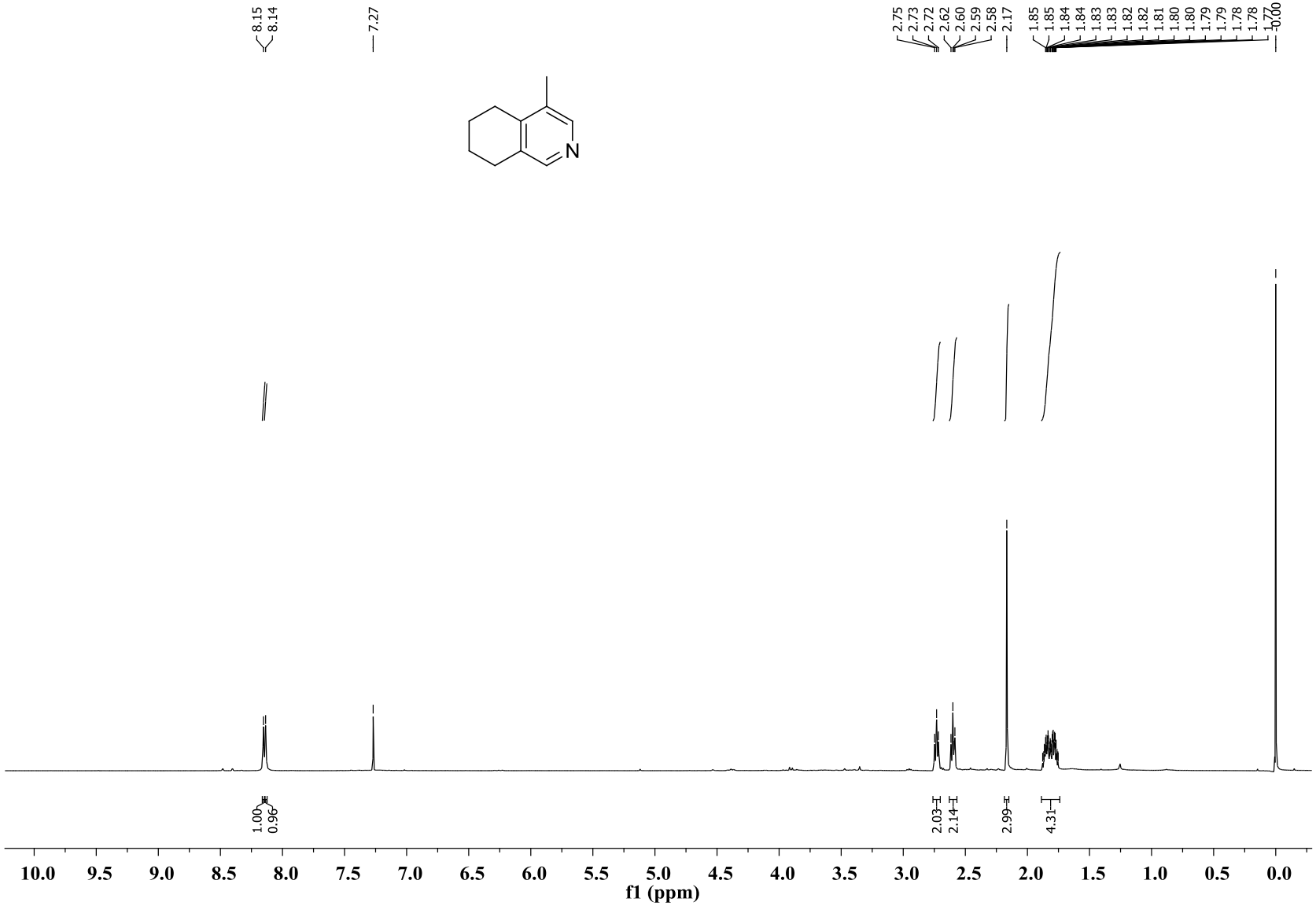
^{1}H NMR spectrum of **3l** ($CDCl_3$, 400 MHz)**:**



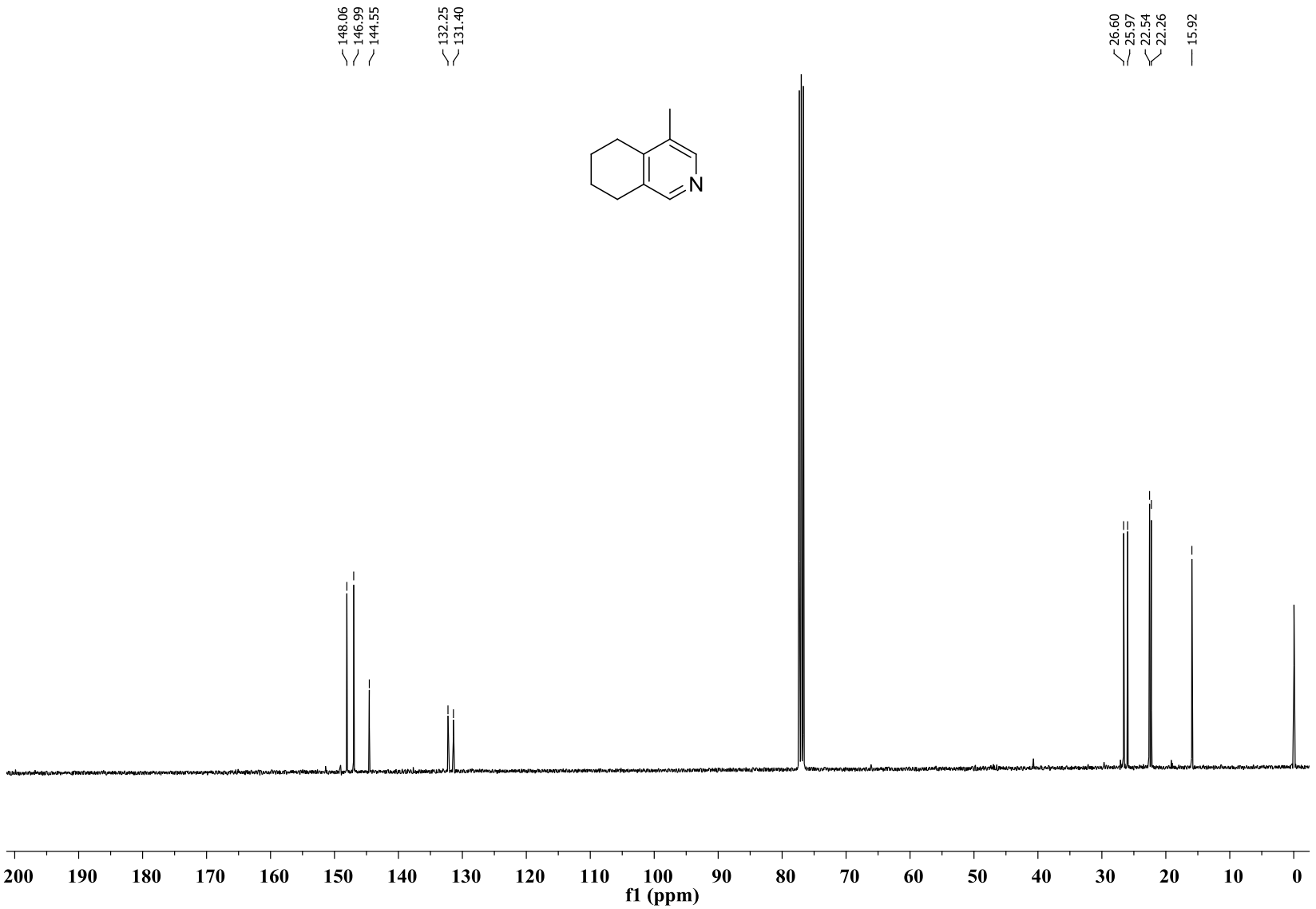
$^{13}C\{1H\}$NMR spectrum of **3l** ($CDCl_3$, 100 MHz)**:**



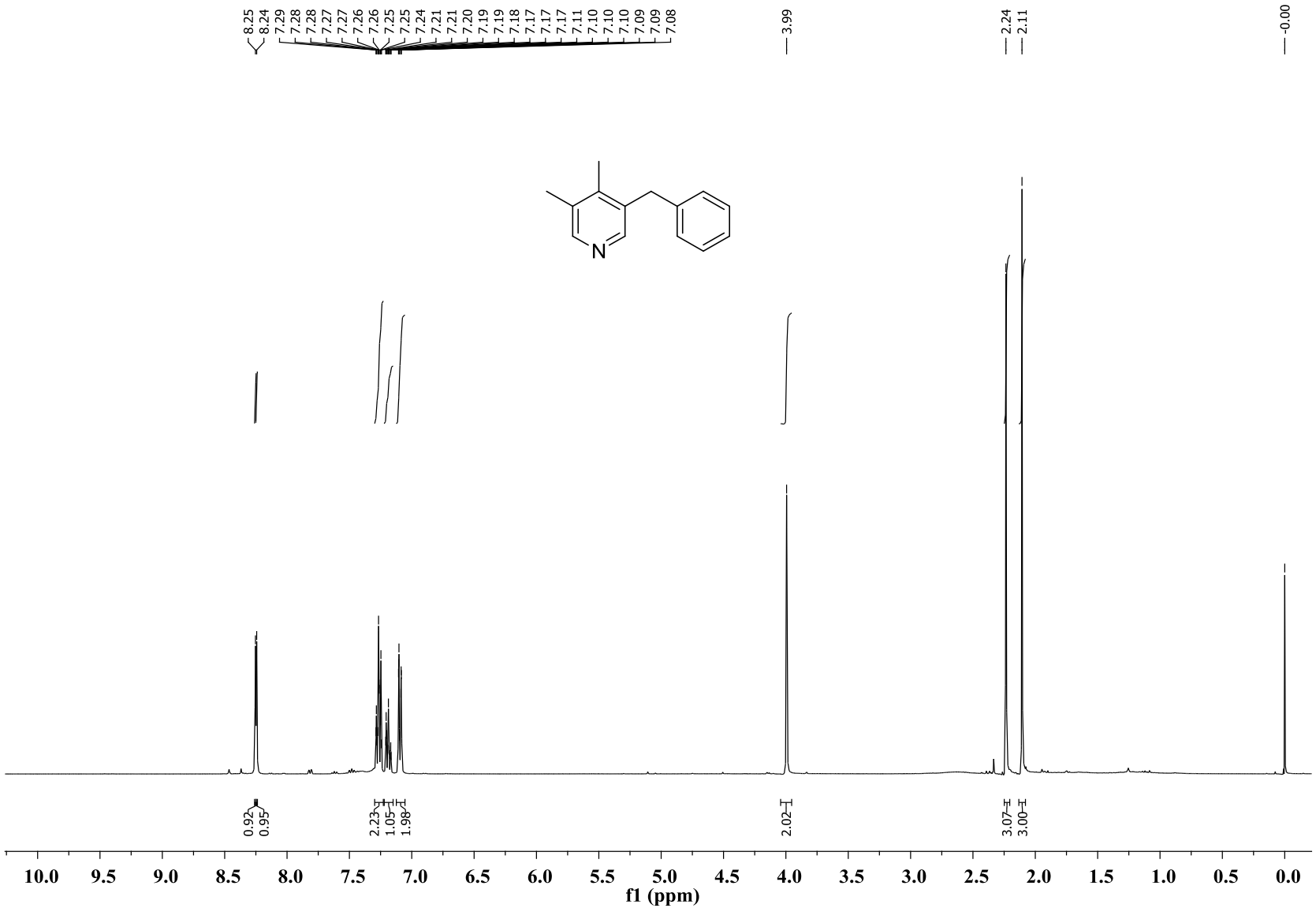
^{1}H NMR spectrum of **3m** ($CDCl_3$, 400 MHz)**:**



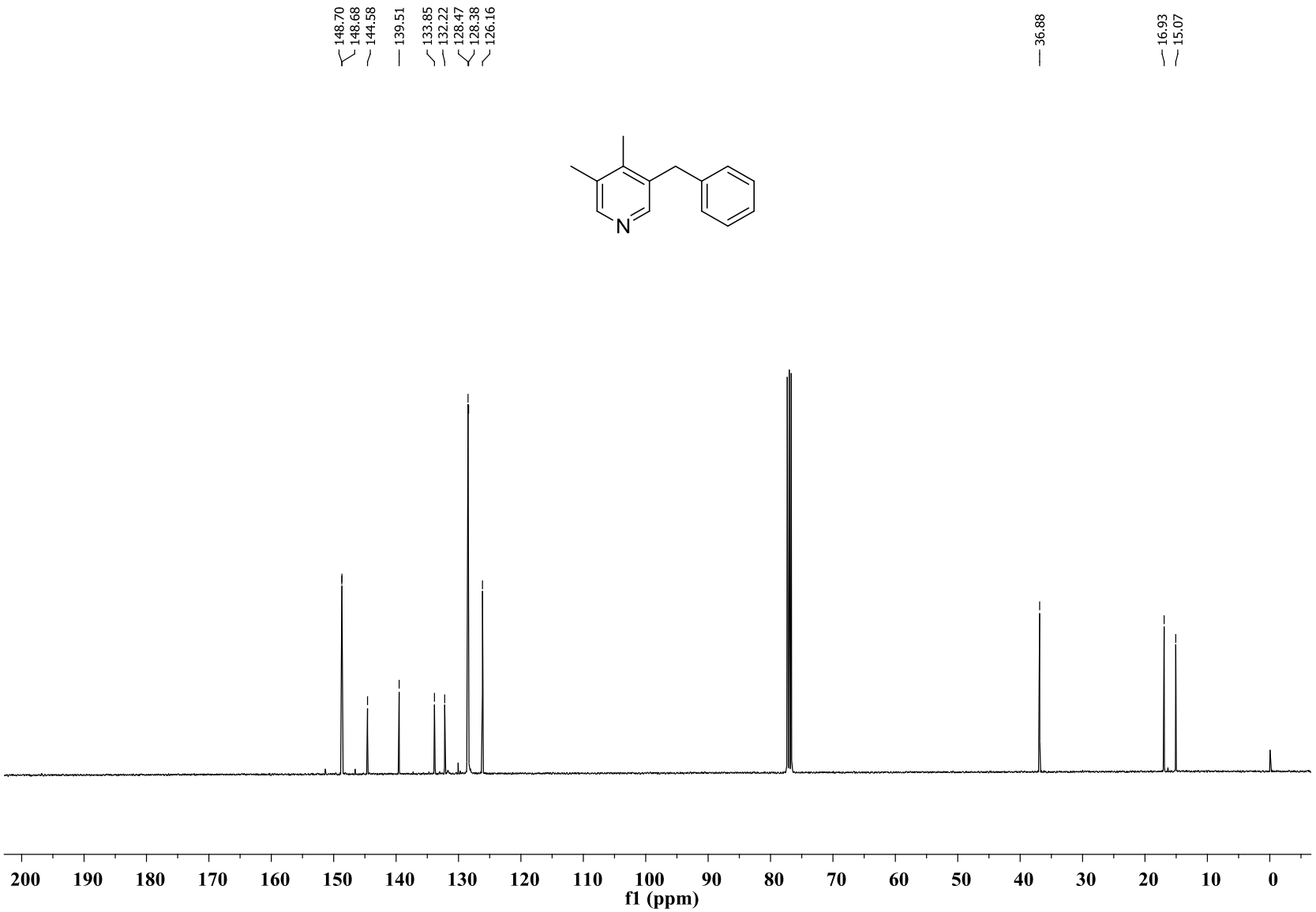
$^{13}C\{^{1}H\}$NMR spectrum of **3m** ($CDCl_3$, 100 MHz)**:**



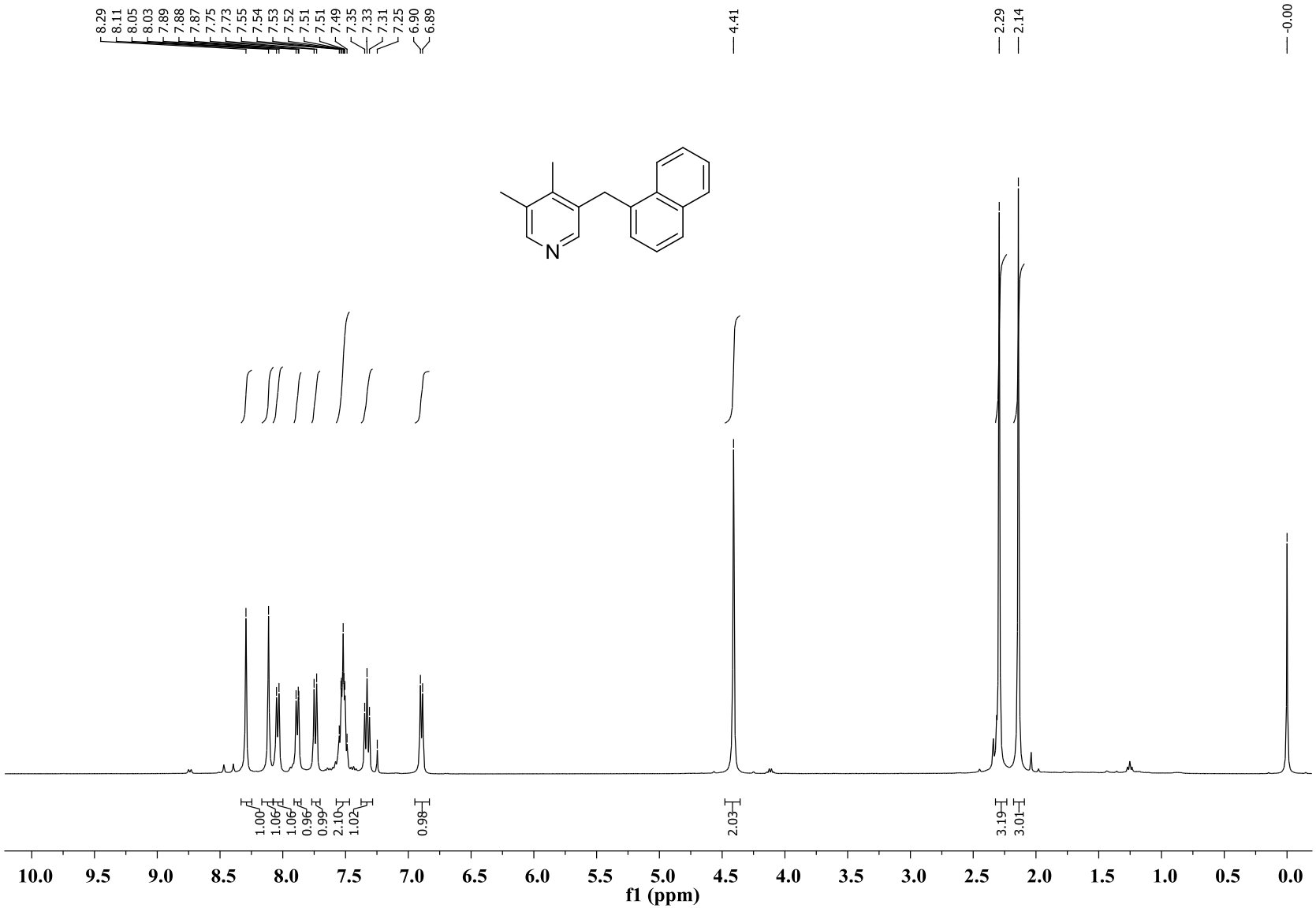
^{1}H NMR spectrum of **3n** ($CDCl_3$, 400 MHz)**:**



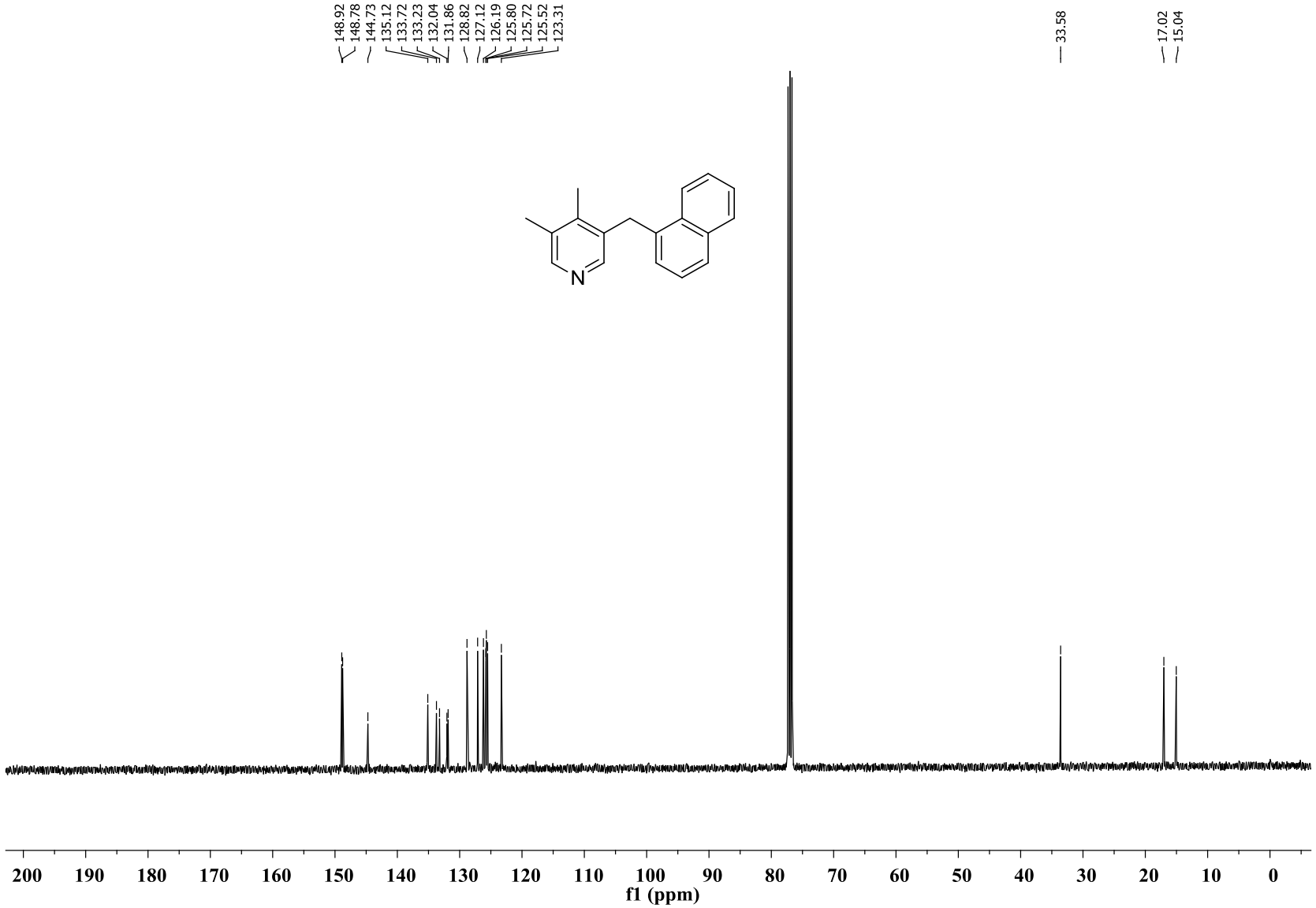
$^{13}C\{^{1}H\}$NMR spectrum of **3n** ($CDCl_3$, 100 MHz)**:**



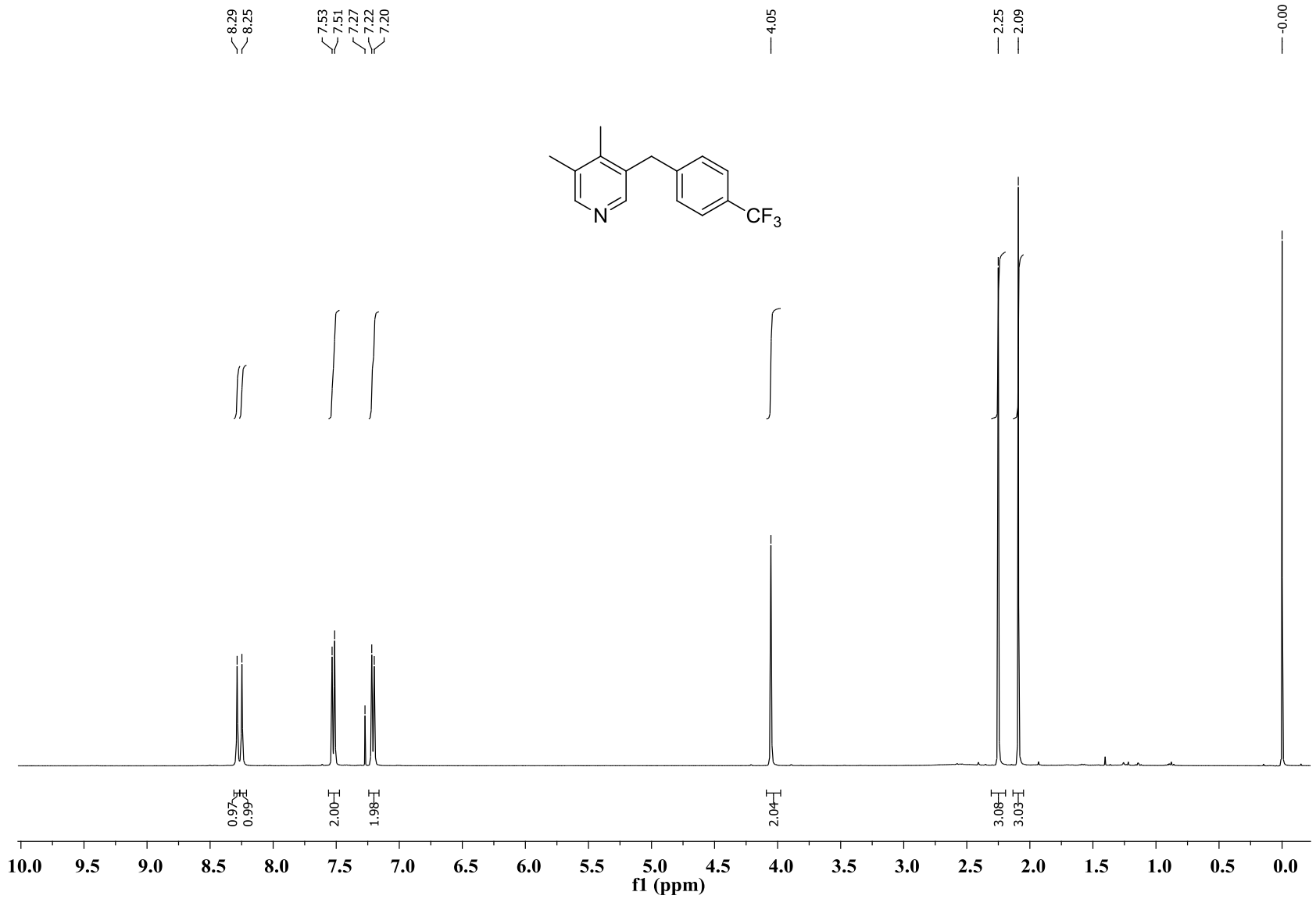
^{1}H NMR spectrum of **3o** ($CDCl_3$, 400 MHz)**:**



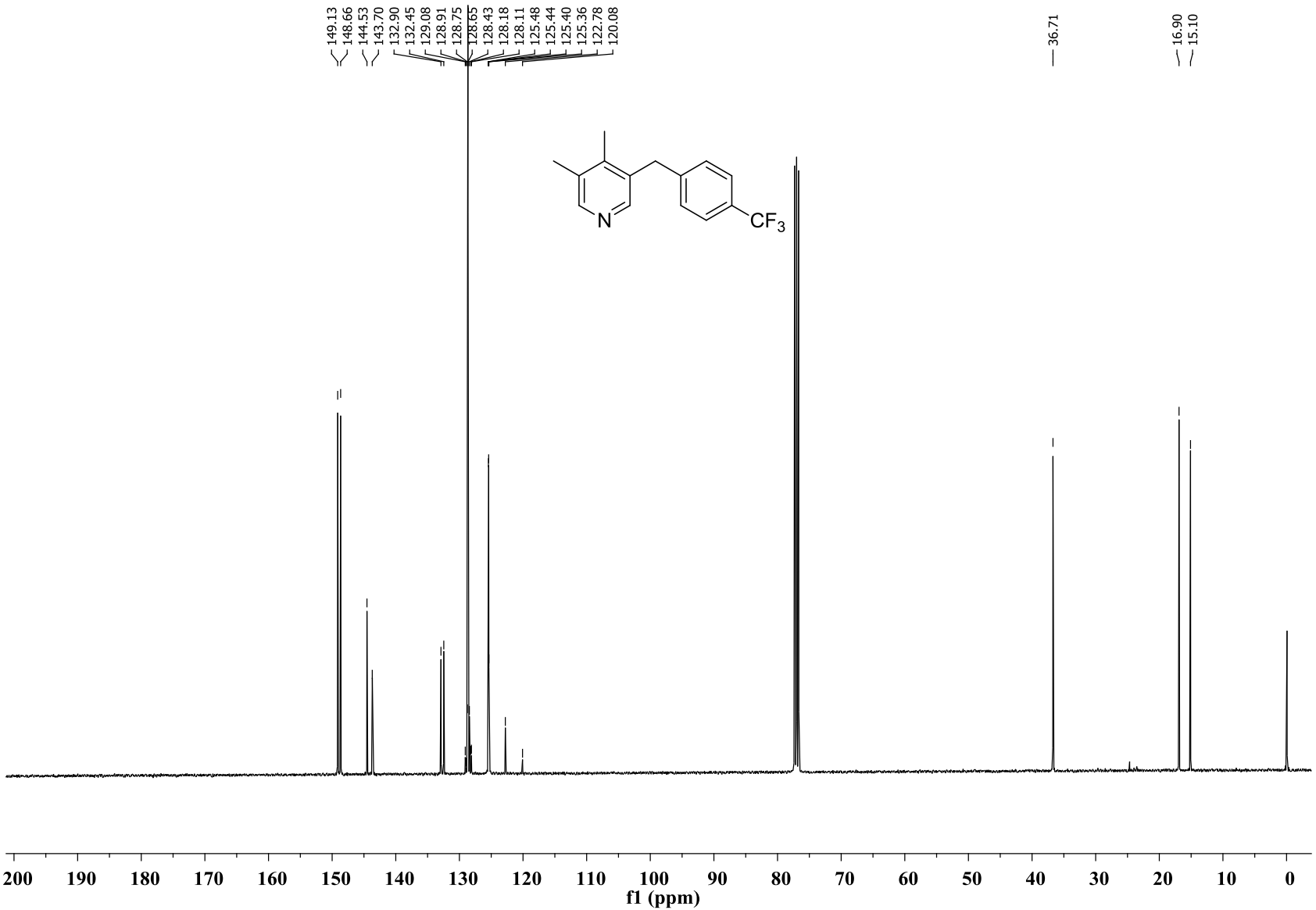
$^{13}C\{1H\}$NMR spectrum of **3o** ($CDCl_3$, 100 MHz)**:**



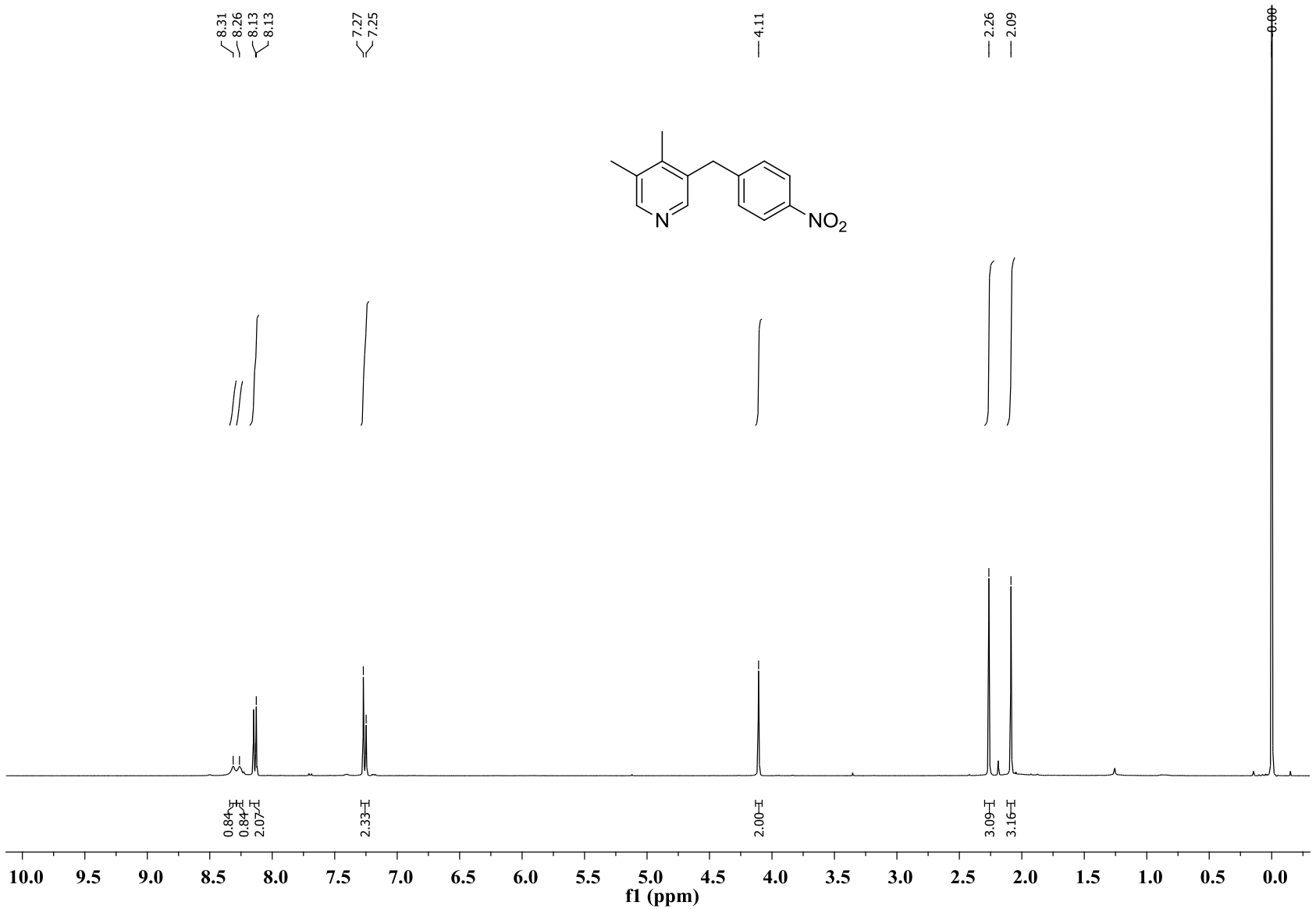
^{1}H NMR spectrum of **3p** ($CDCl_3$, 400 MHz)**:**



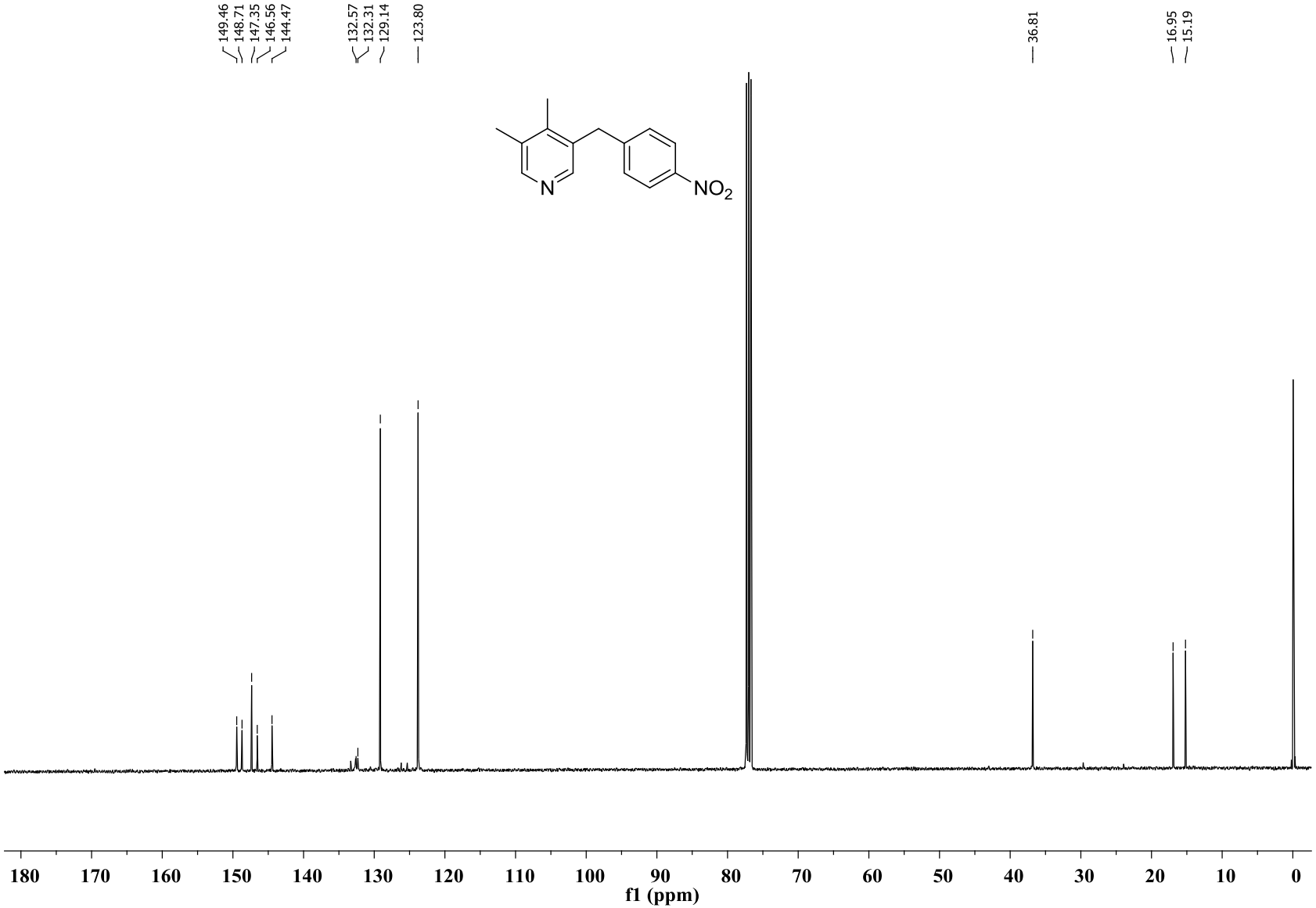
$^{13}C\{1H\}$NMR spectrum of **3p** ($CDCl_3$, 100 MHz)**:**



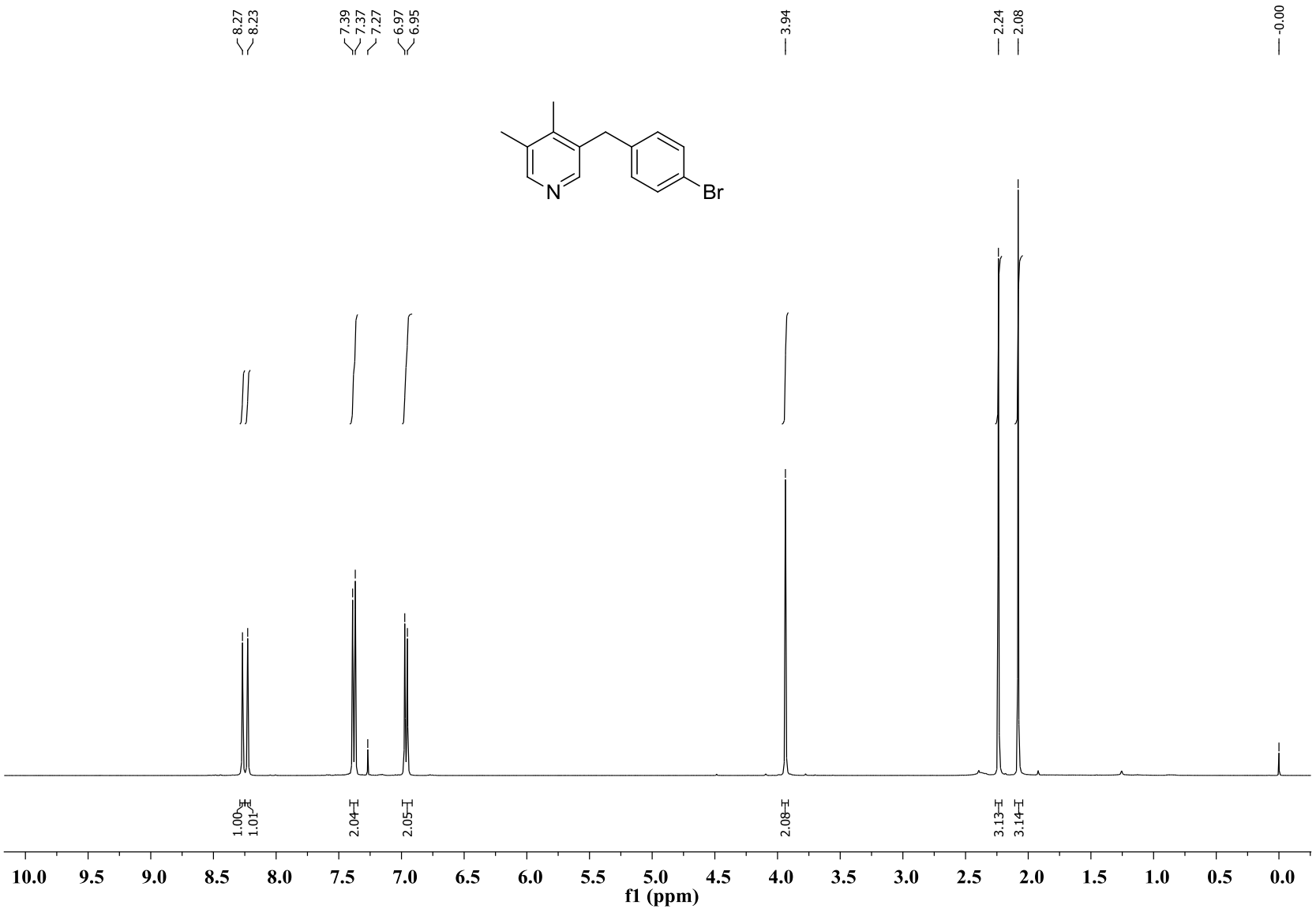
^{1}H NMR spectrum of **3q** ($CDCl_3$, 400 MHz)**:**



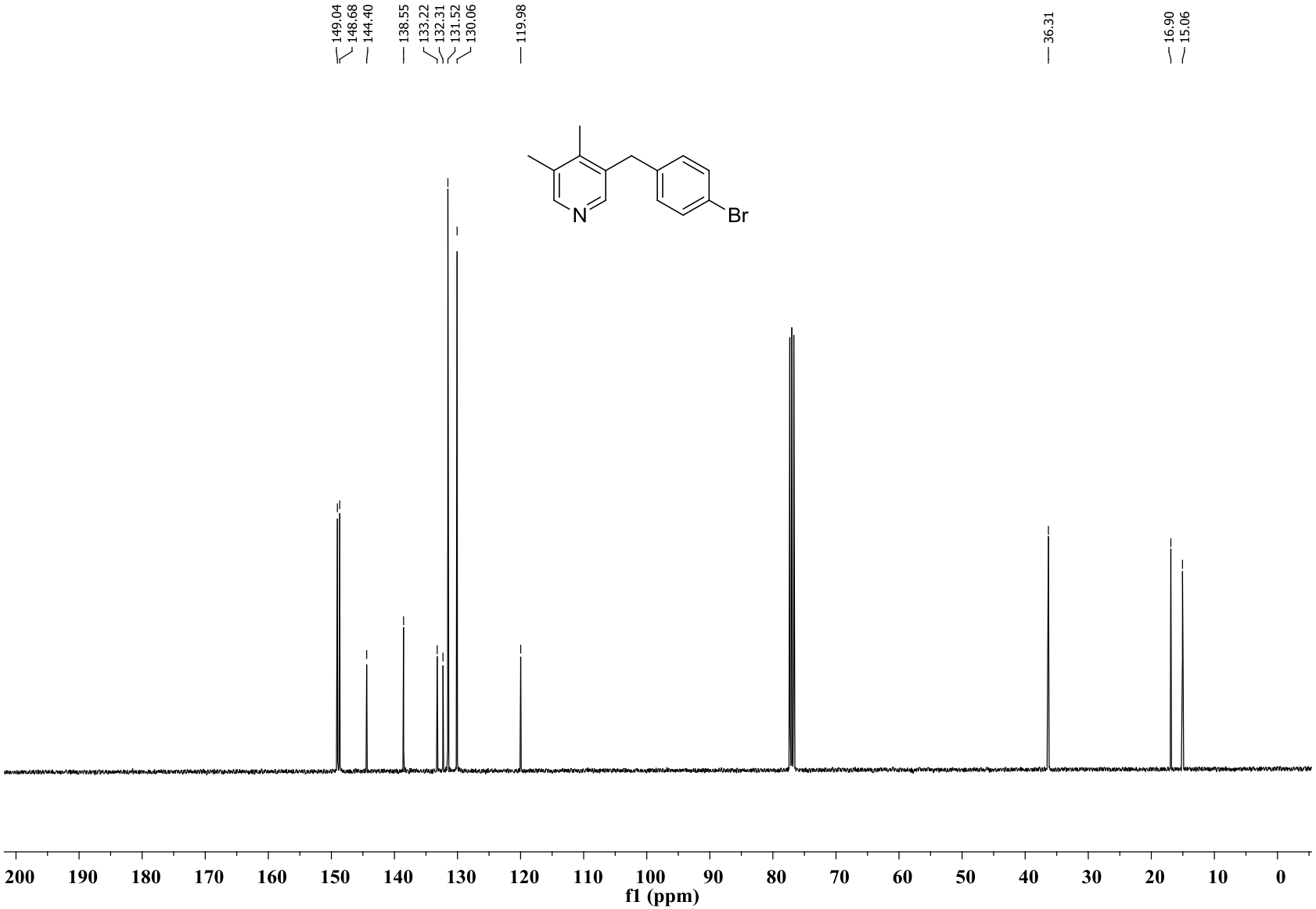
$^{13}C\{1H\}$NMR spectrum of **3q** ($CDCl_3$, 100 MHz)**:**



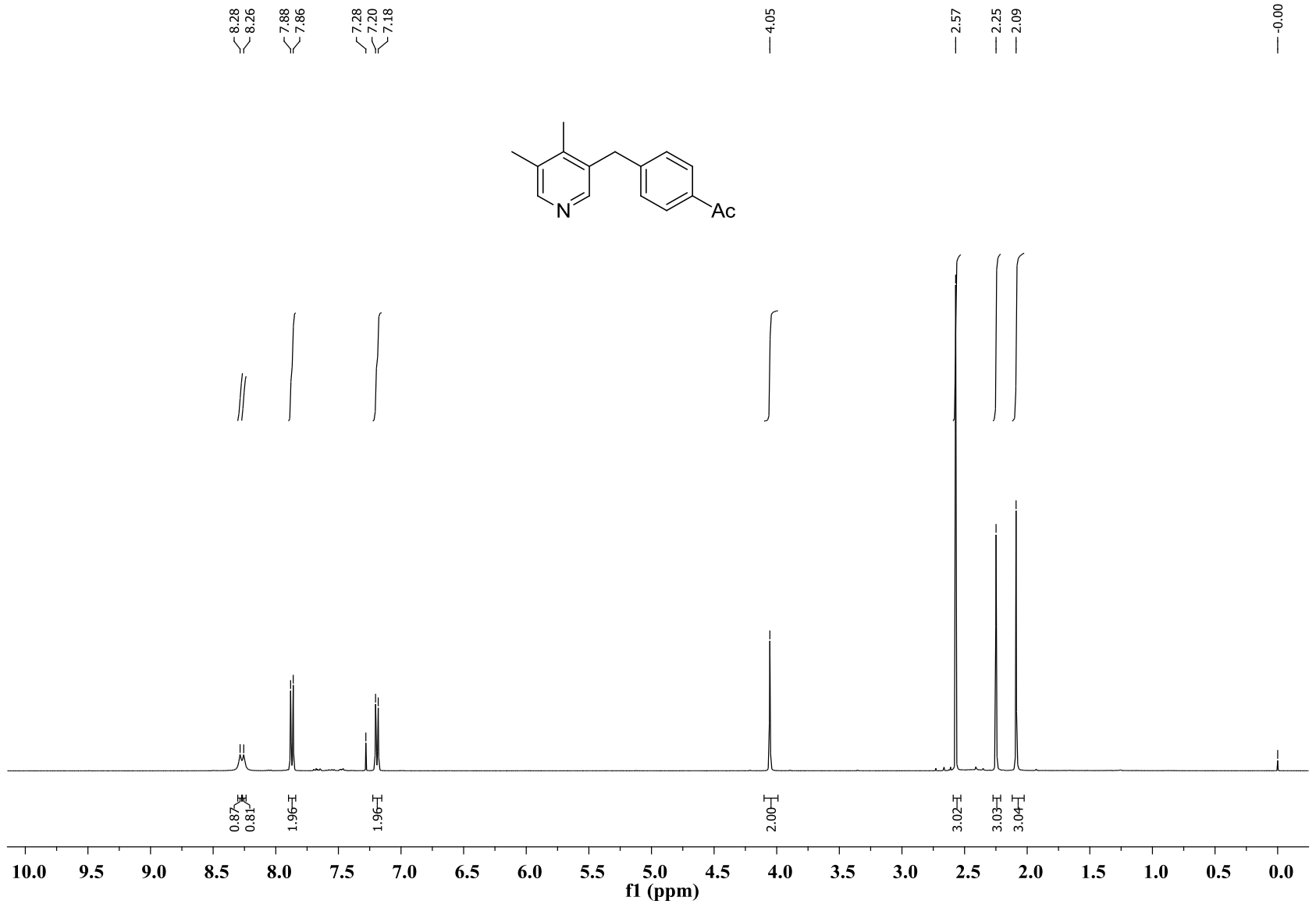
^{1}H NMR spectrum of compound **3r** ($CDCl_3$, 400 MHz)**:**



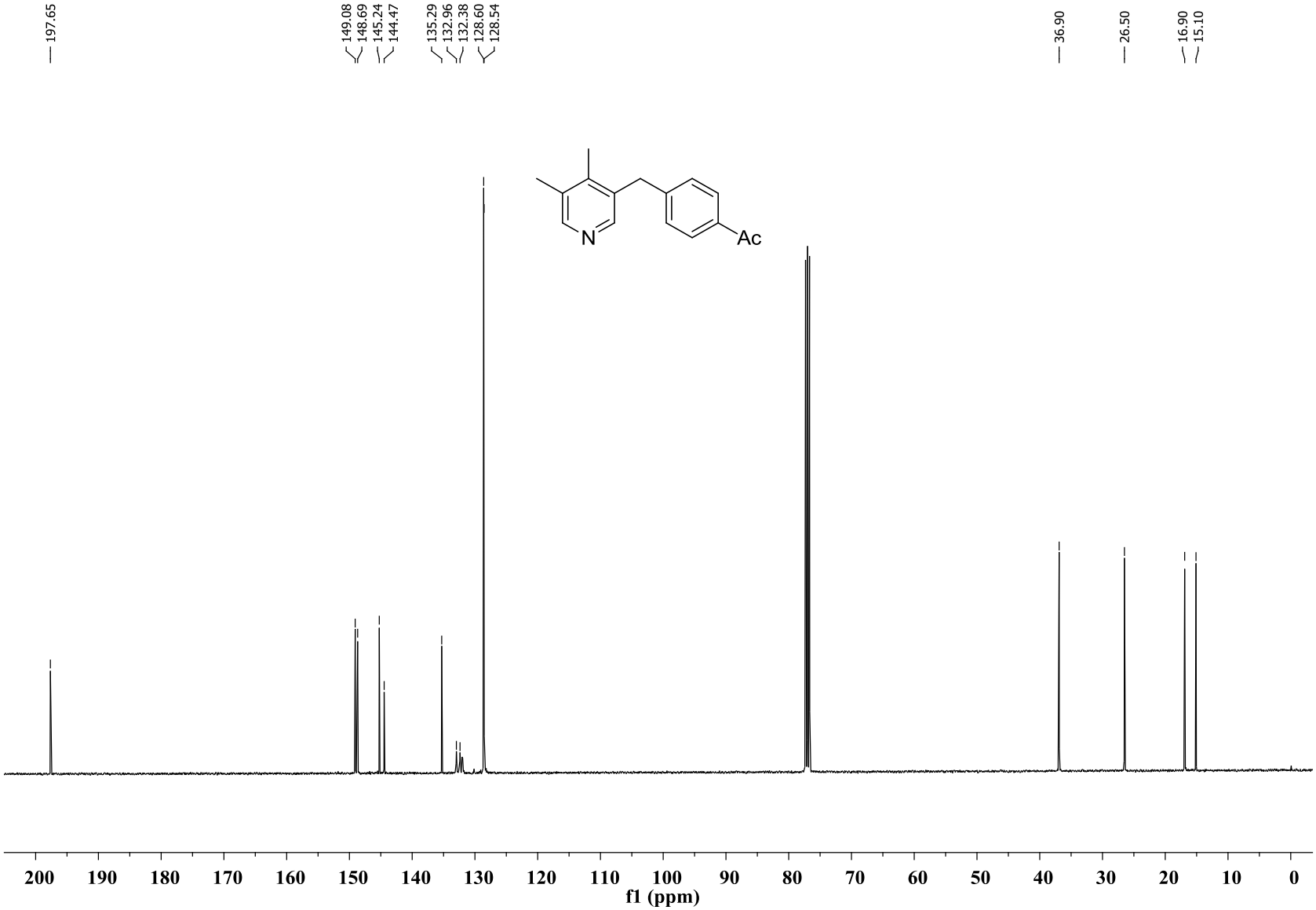
$^{13}C\{1H\}NMR$ spectrum of compound **3r** ($CDCl_3$, 100 MHz)**:**



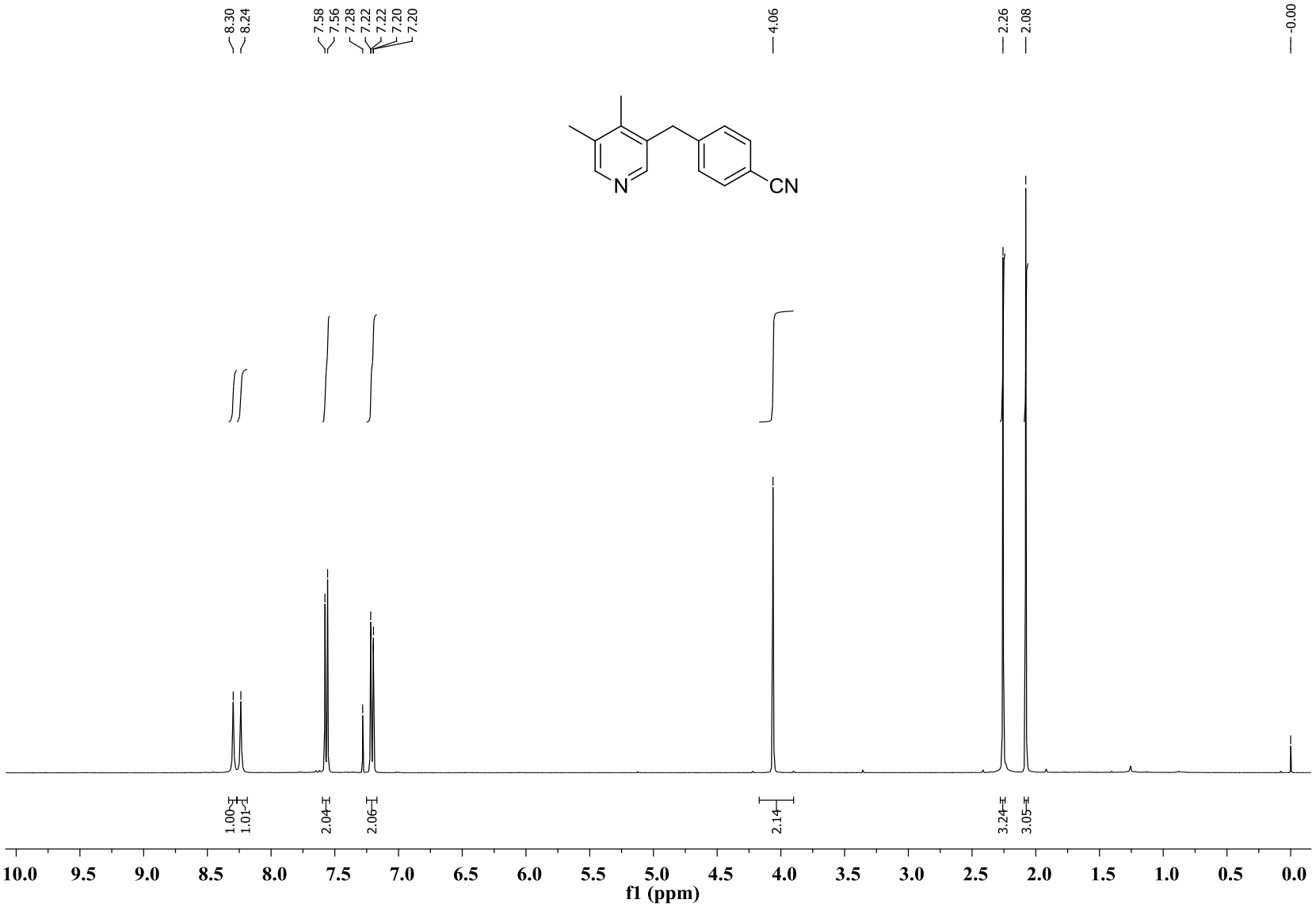
^{1}H NMR spectrum of **3s** ($CDCl_3$, 400 MHz)**:**



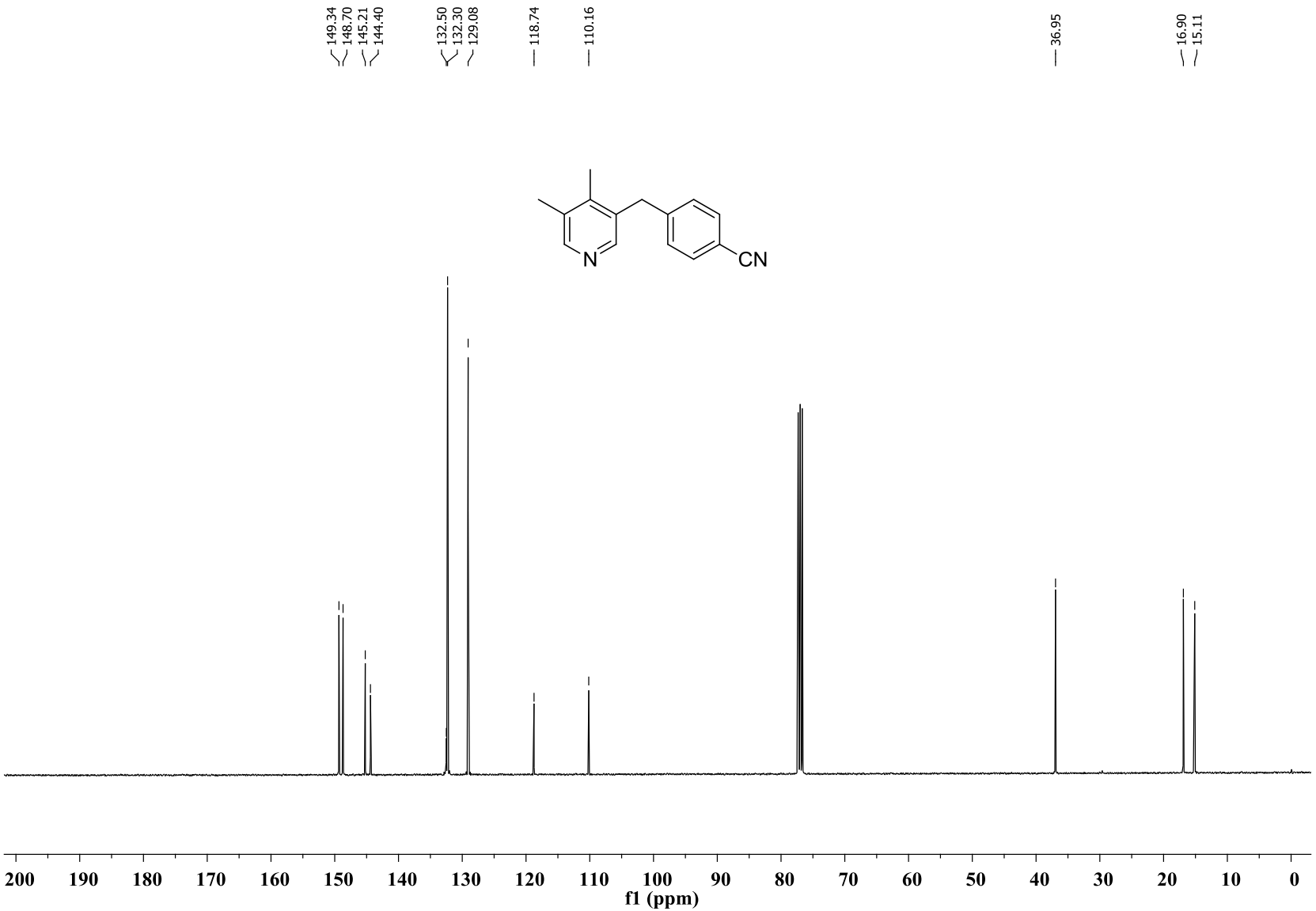
$^{13}C\{1H\}$NMR spectrum of **3s** ($CDCl_3$, 100 MHz)**:**



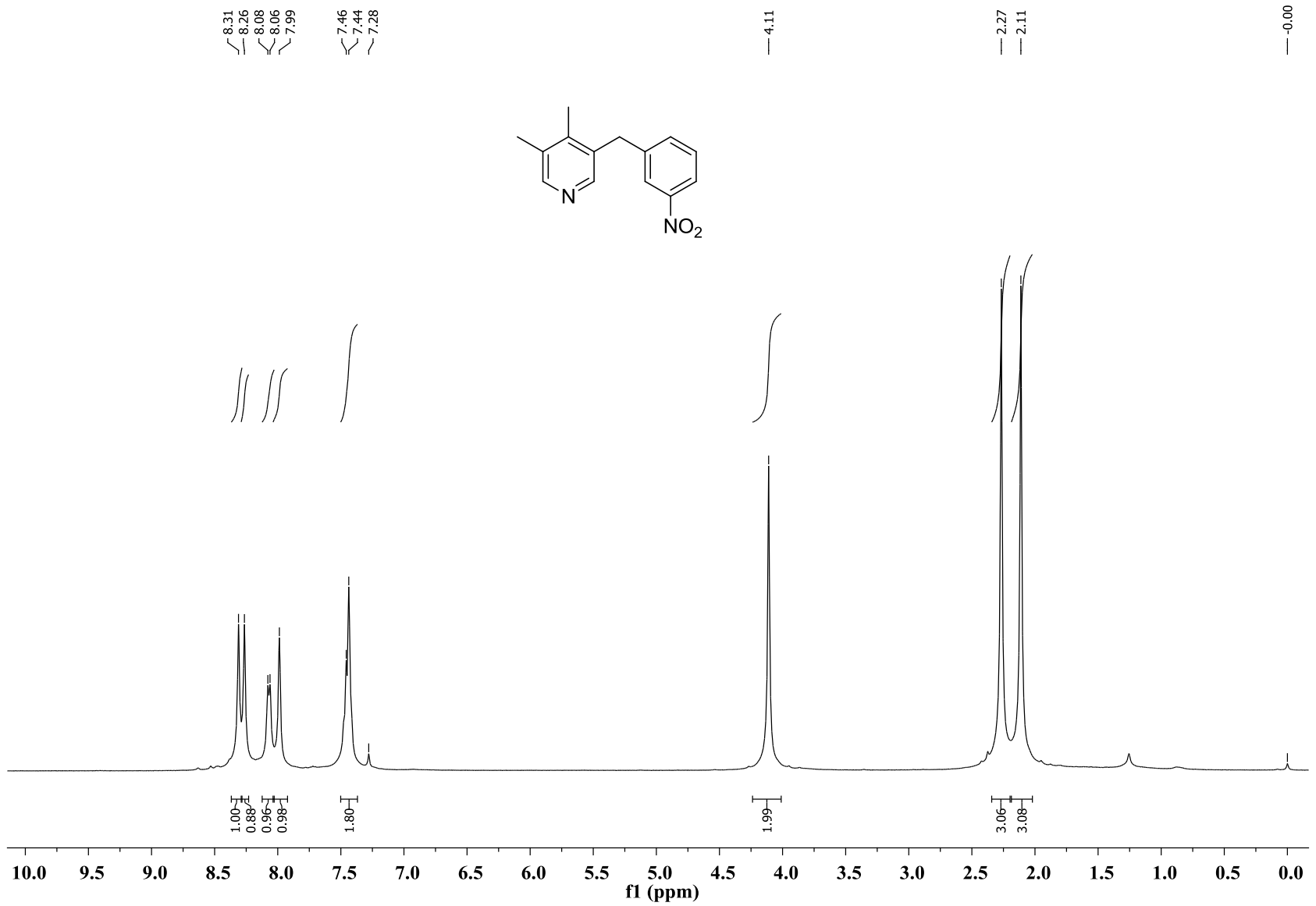
^{1}H NMR spectrum of **3t** ($CDCl_3$, 400 MHz)**:**



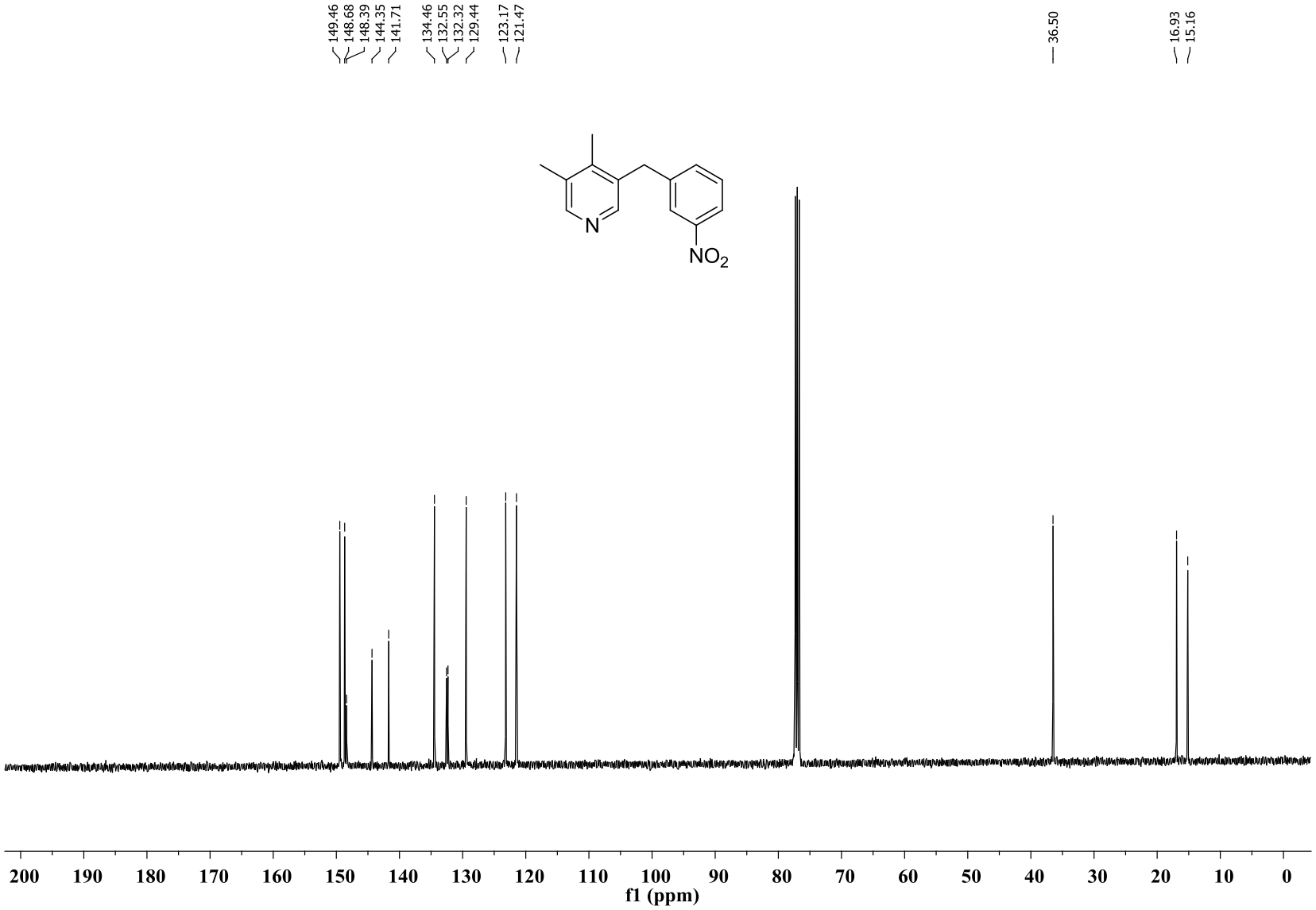
$^{13}C\{1H\}$NMR spectrum of **3t** ($CDCl_3$, 100 MHz)**:**



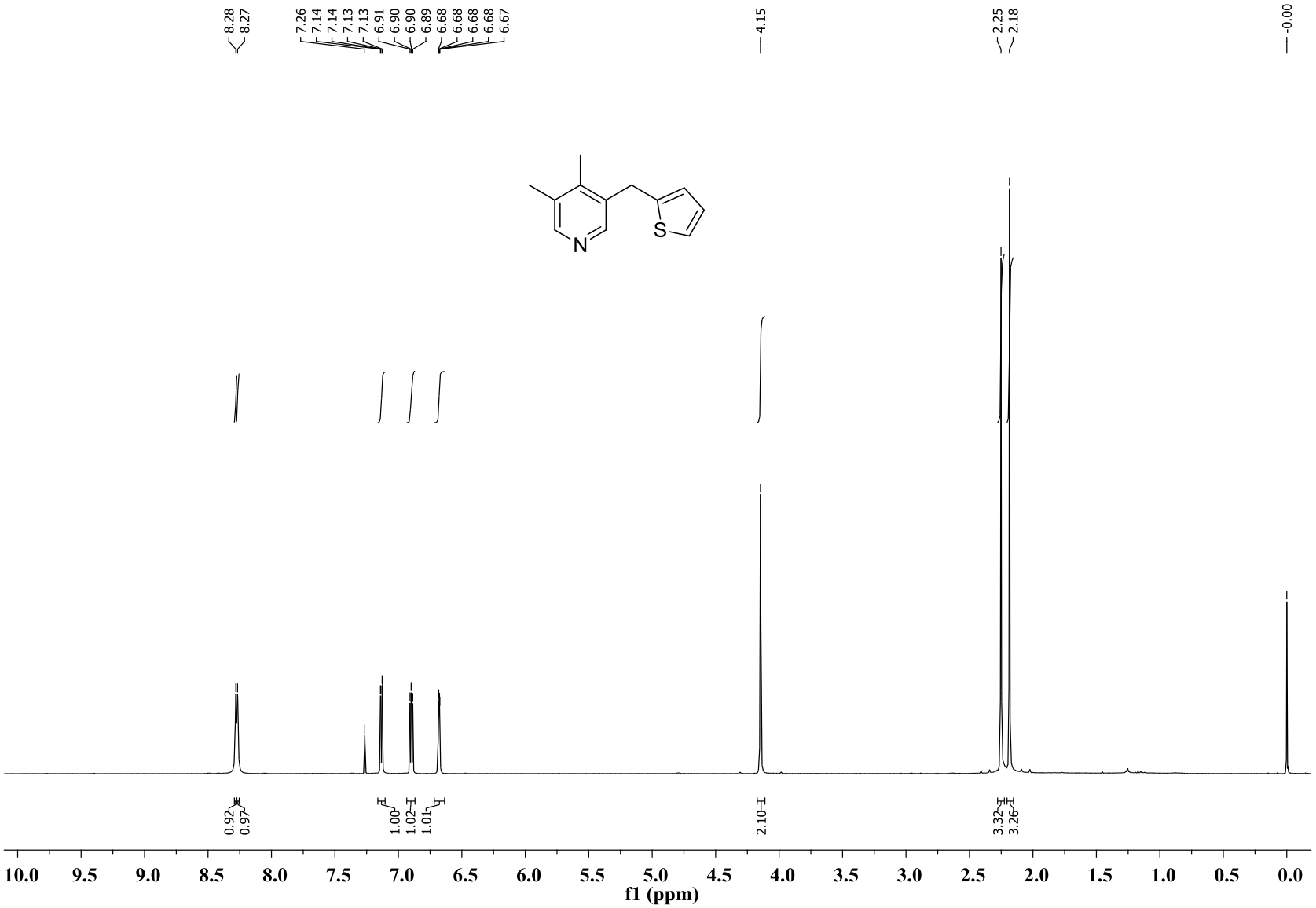
[1]H NMR spectrum of compound **3u** ($CDCl_3$, 400 MHz)**:**



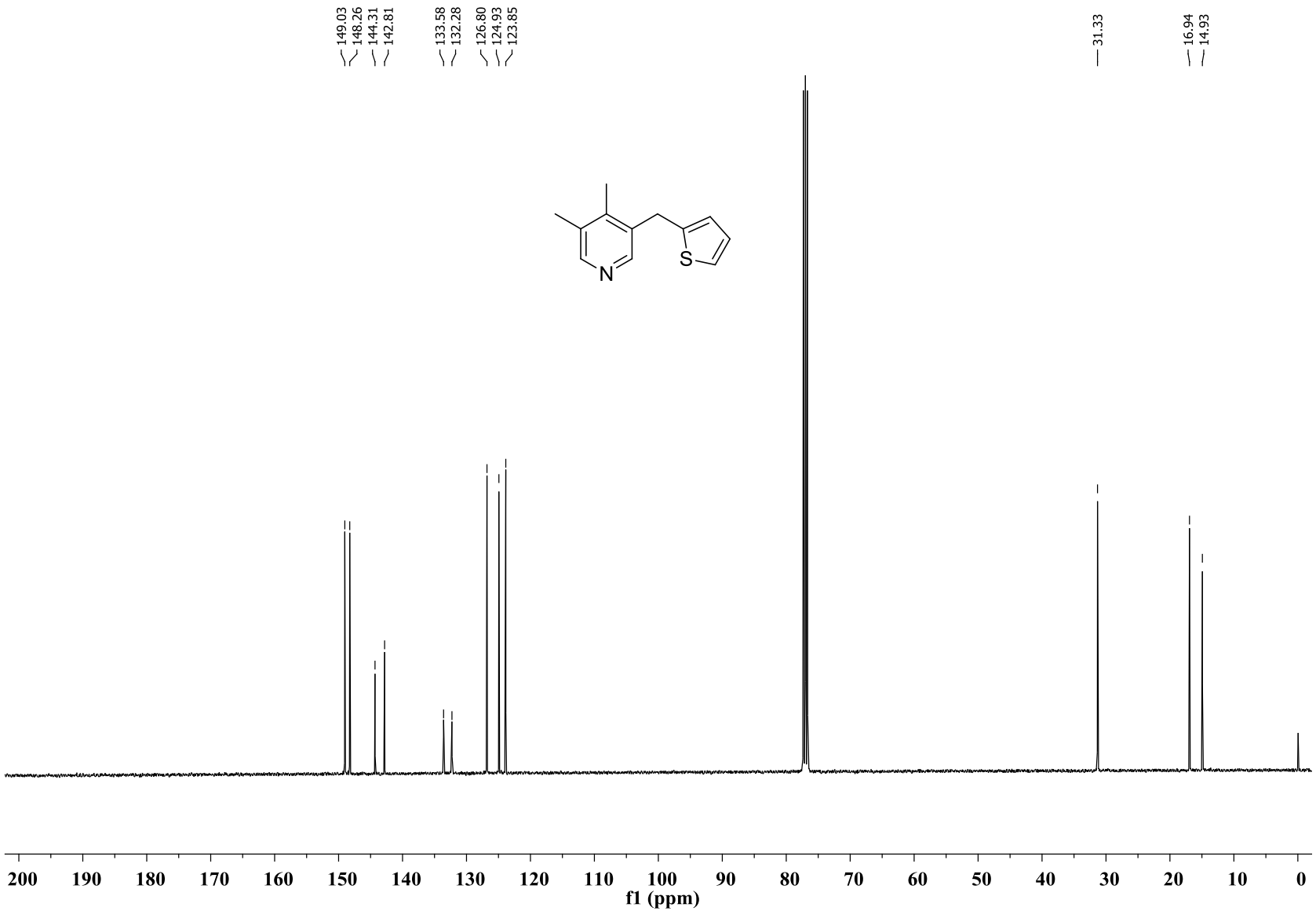
$^{13}C\{1H\}NMR$ spectrum of compound **3u** ($CDCl_3$, 100 MHz)**:**



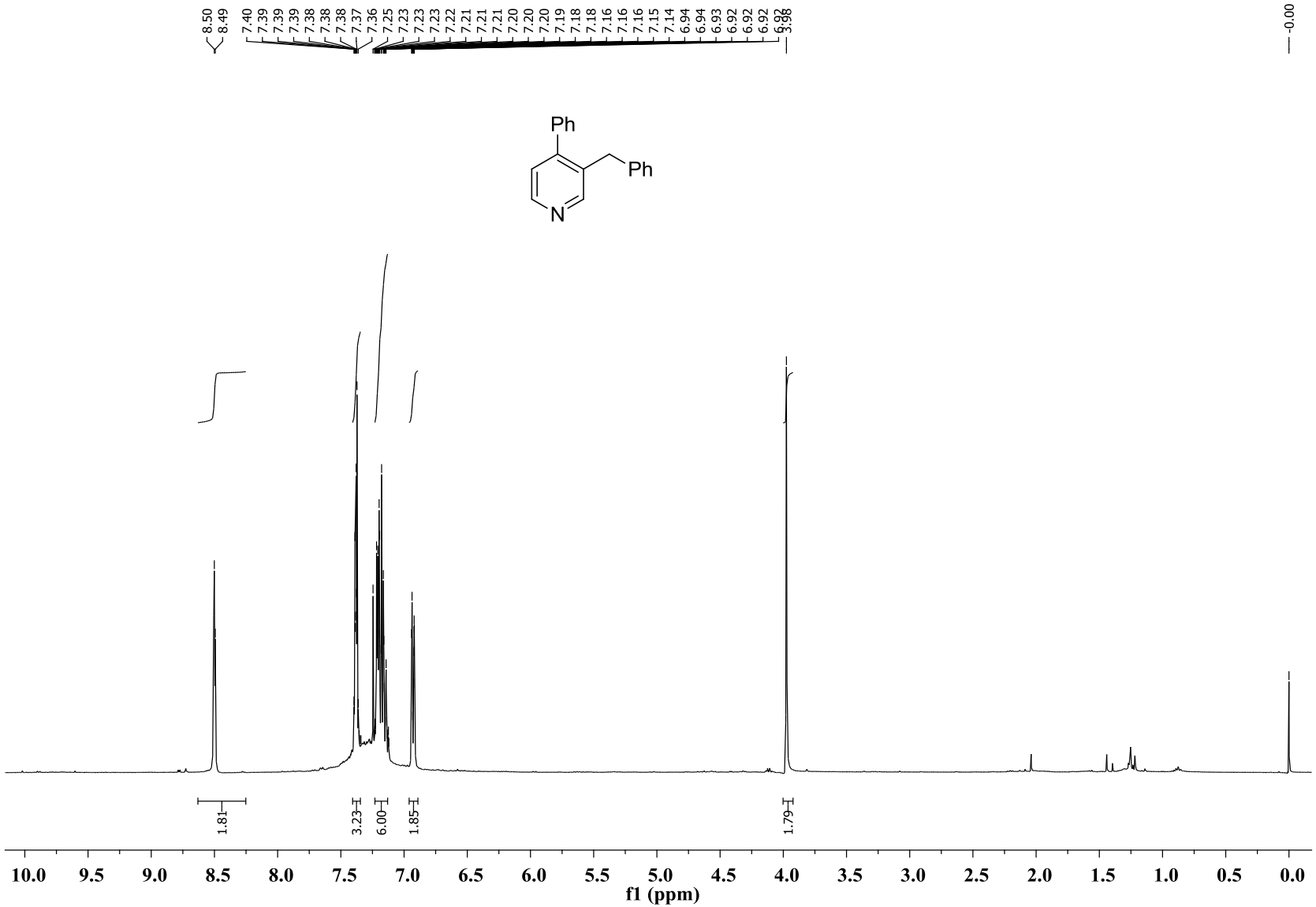
^{1}H NMR spectrum of **3v** ($CDCl_3$, 400 MHz)**:**



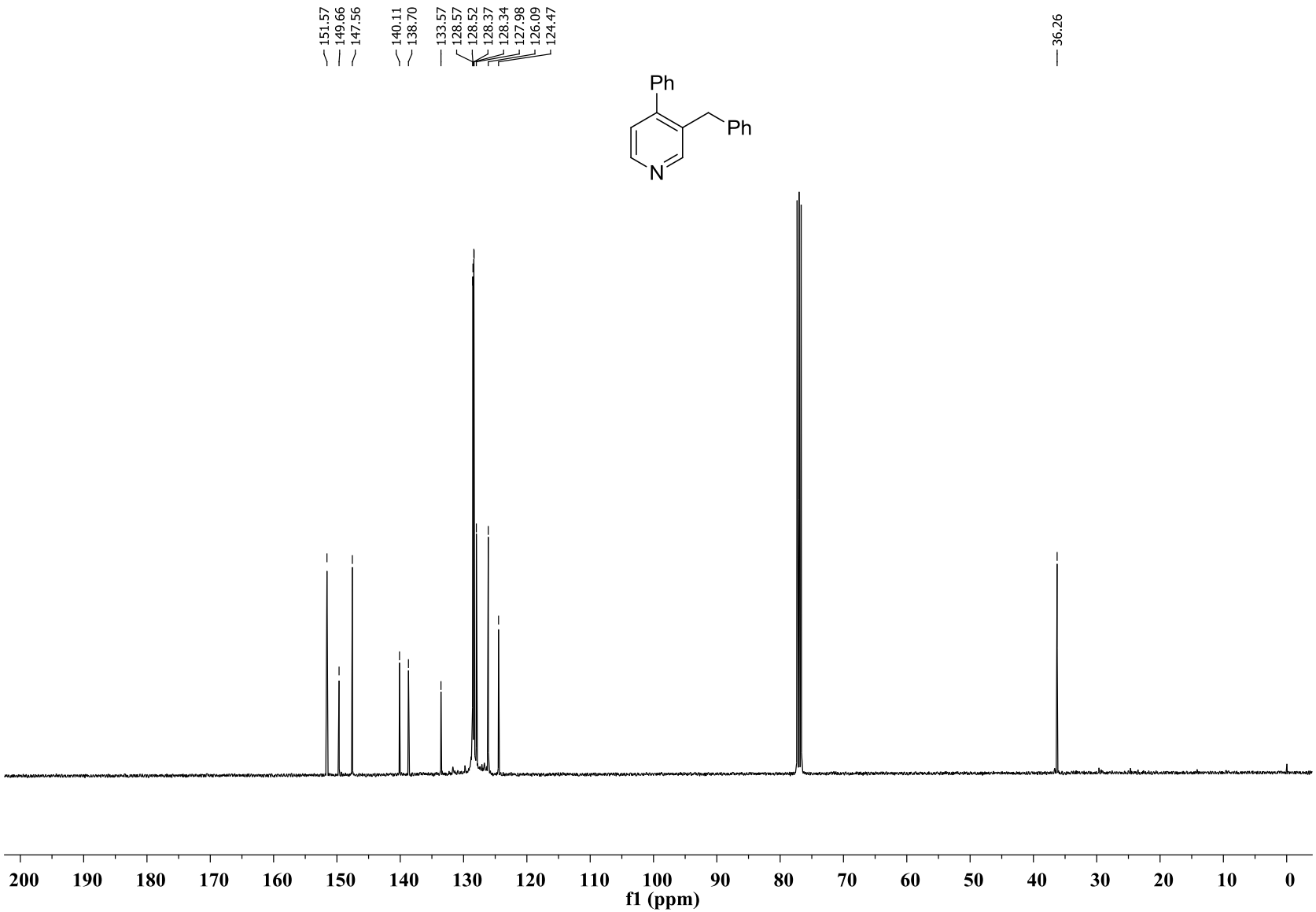
$^{13}C\{1H\}$NMR spectrum of **3v** ($CDCl_3$, 100 MHz)**:**



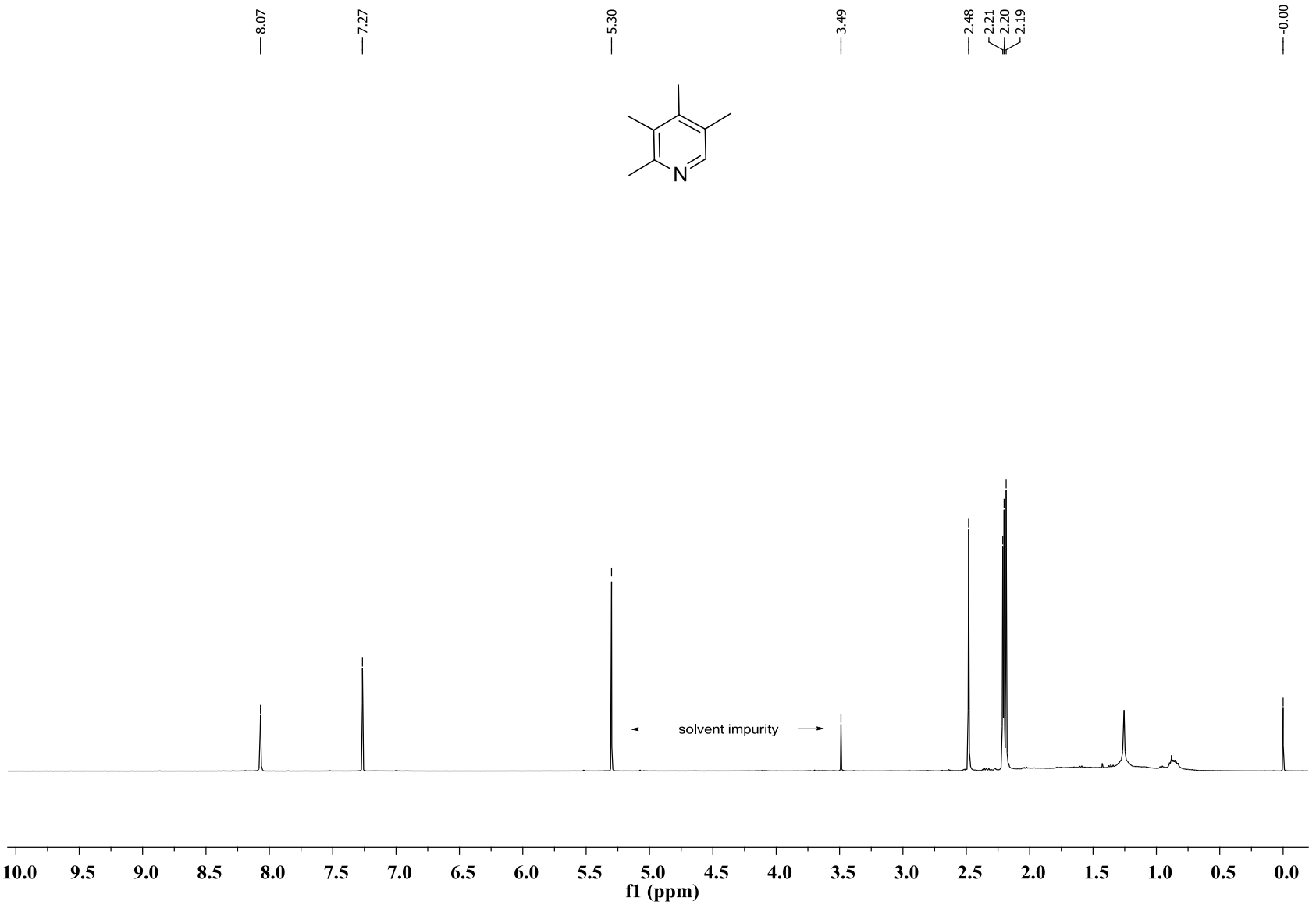
^{1}H NMR spectrum of **3w** ($CDCl_3$, 400 MHz)**:**



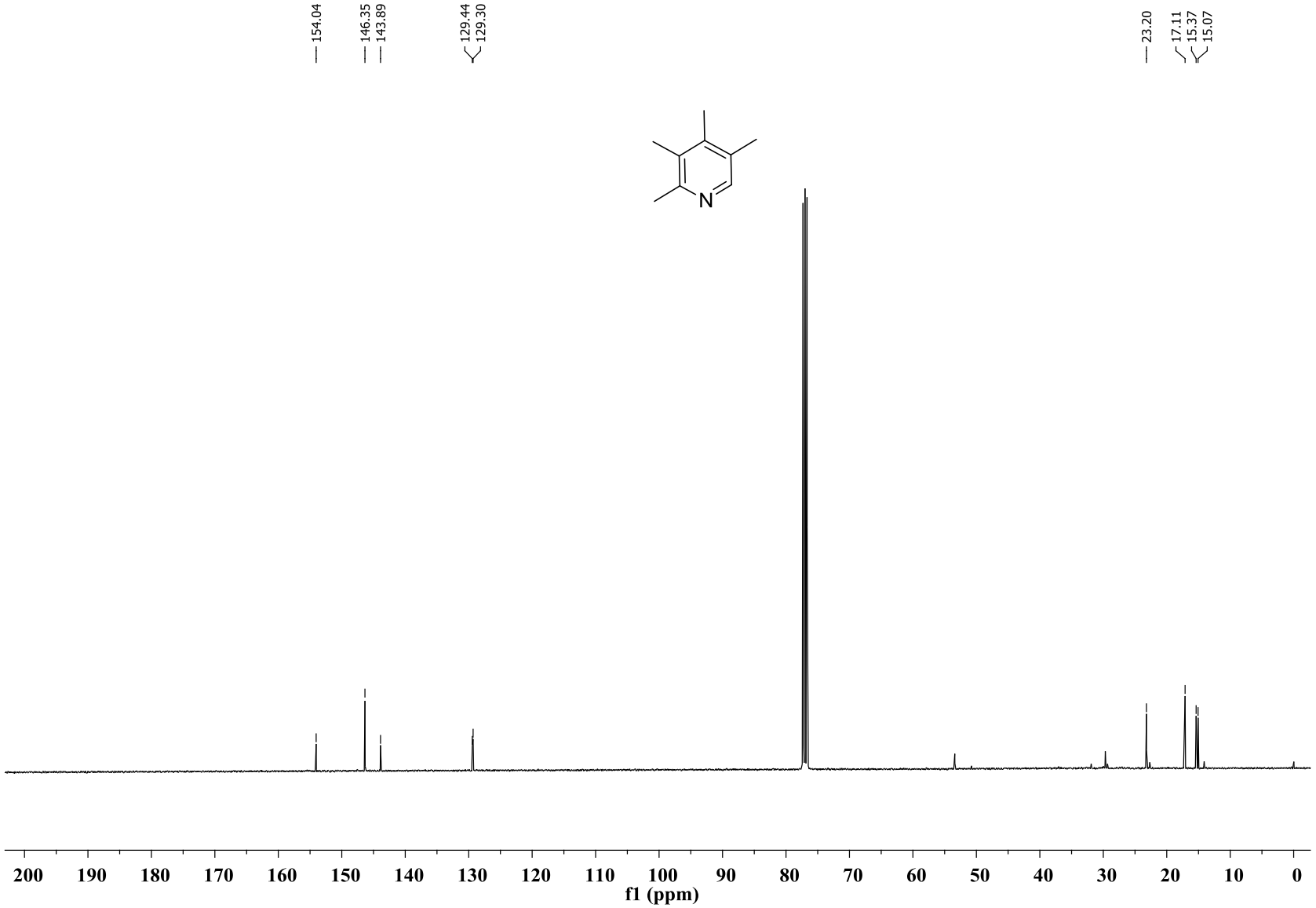
$^{13}C\{^{1}H\}$NMR spectrum of **3w** ($CDCl_3$, 100 MHz)**:**



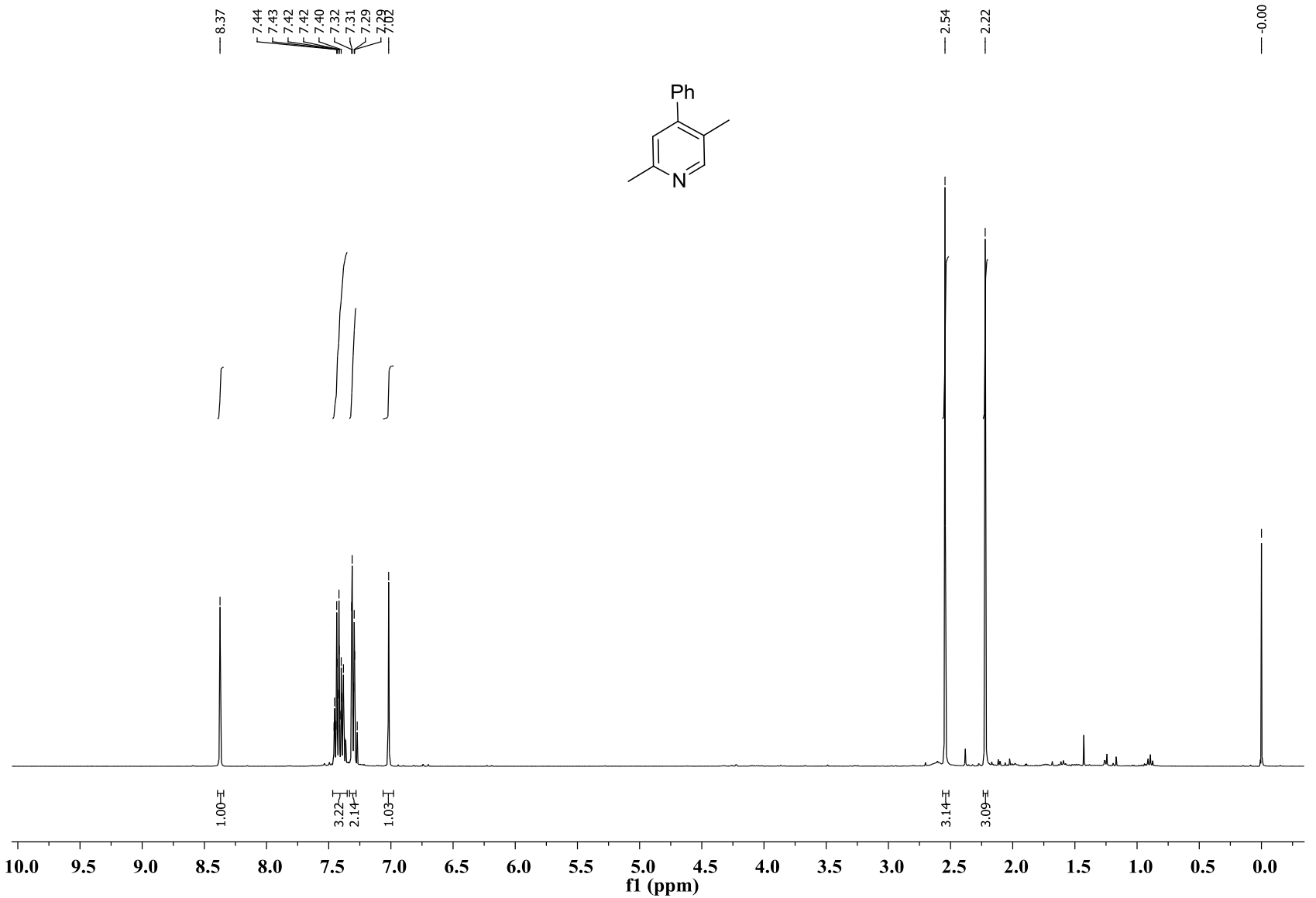
^{1}H NMR spectrum of **3x** ($CDCl_3$, 400 MHz)**:**



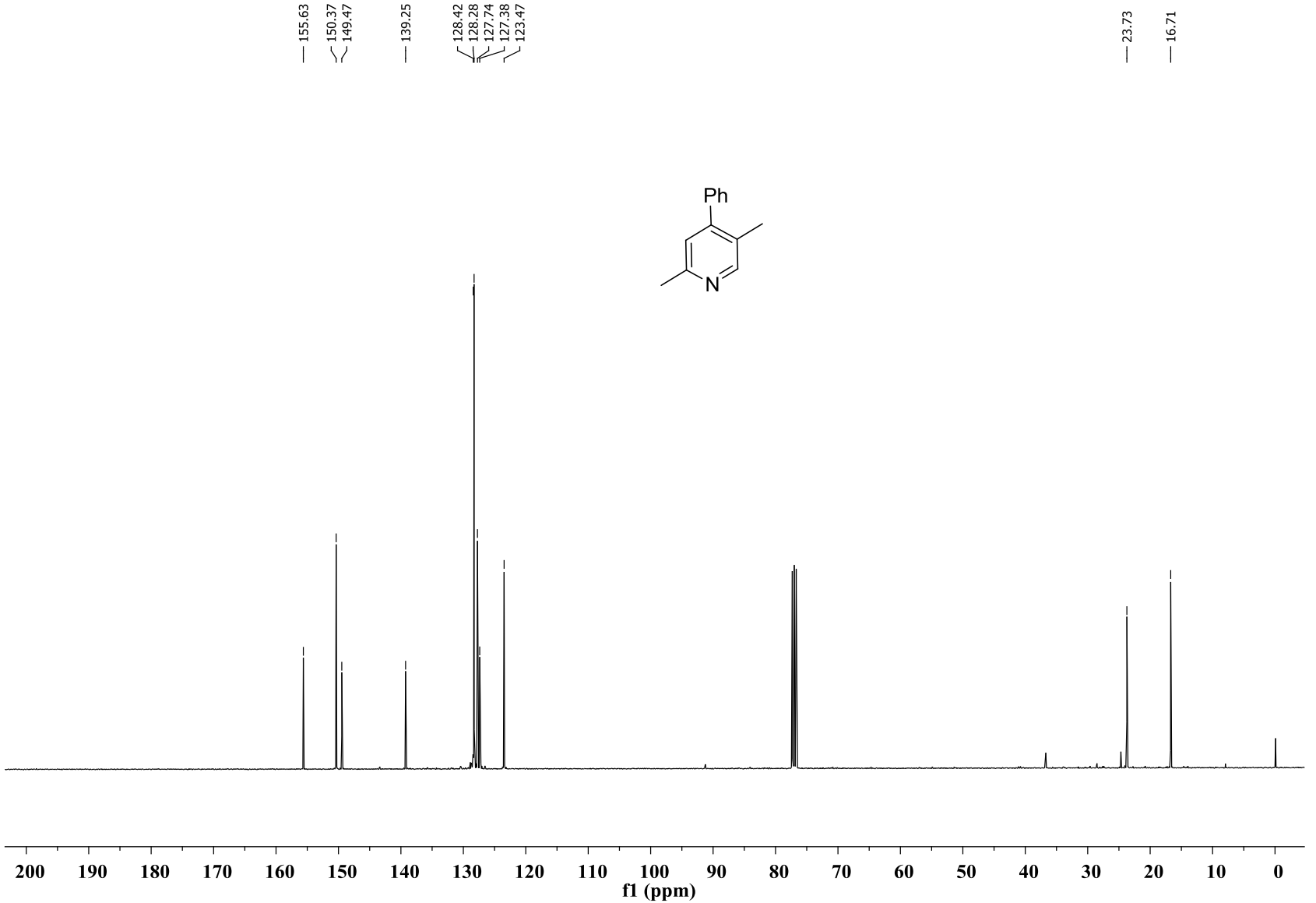
$^{13}C\{1H\}$NMR spectrum of **3x** ($CDCl_3$, 100 MHz)**:**



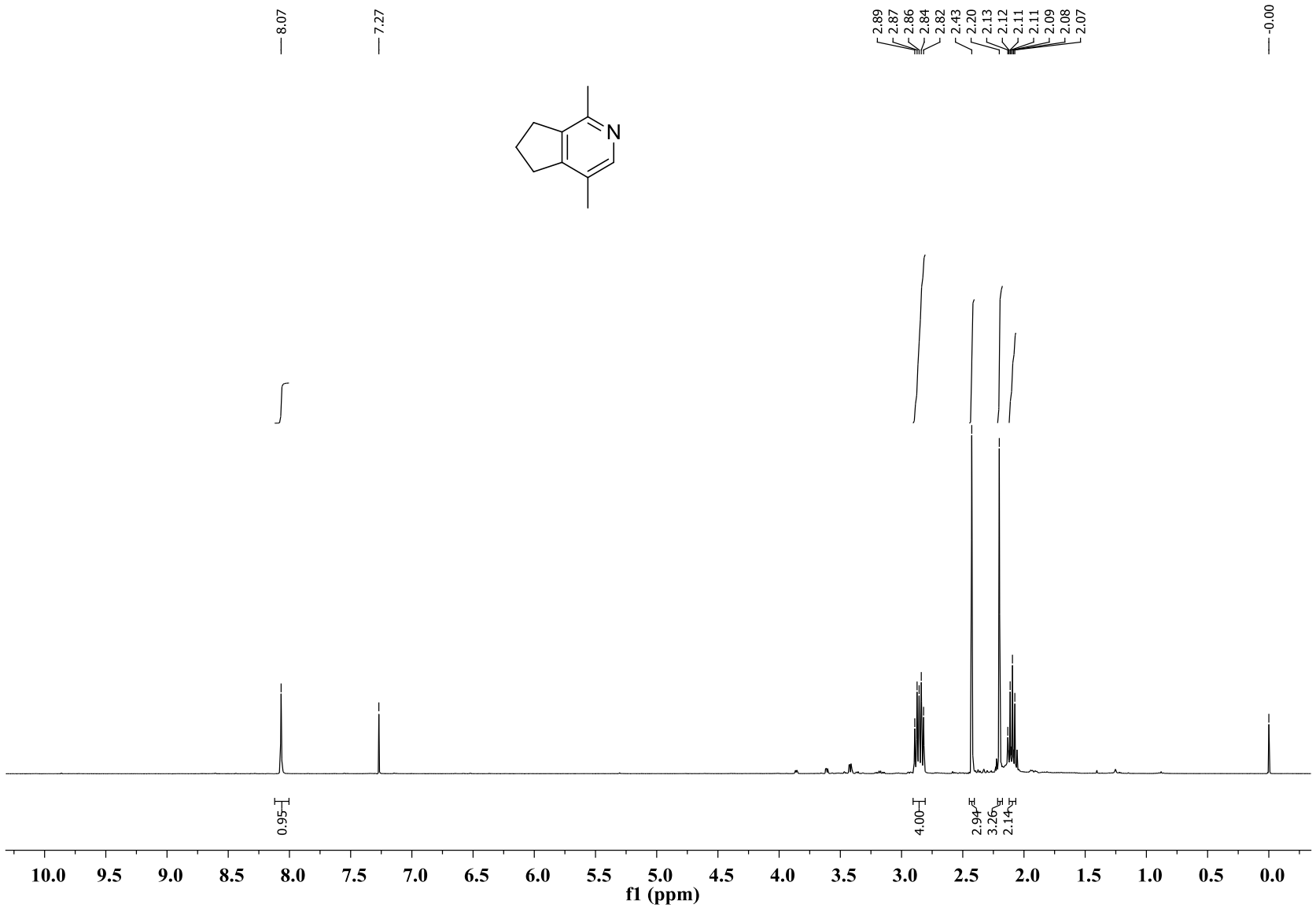
^{1}H NMR spectrum of **3y** ($CDCl_3$, 400 MHz)**:**



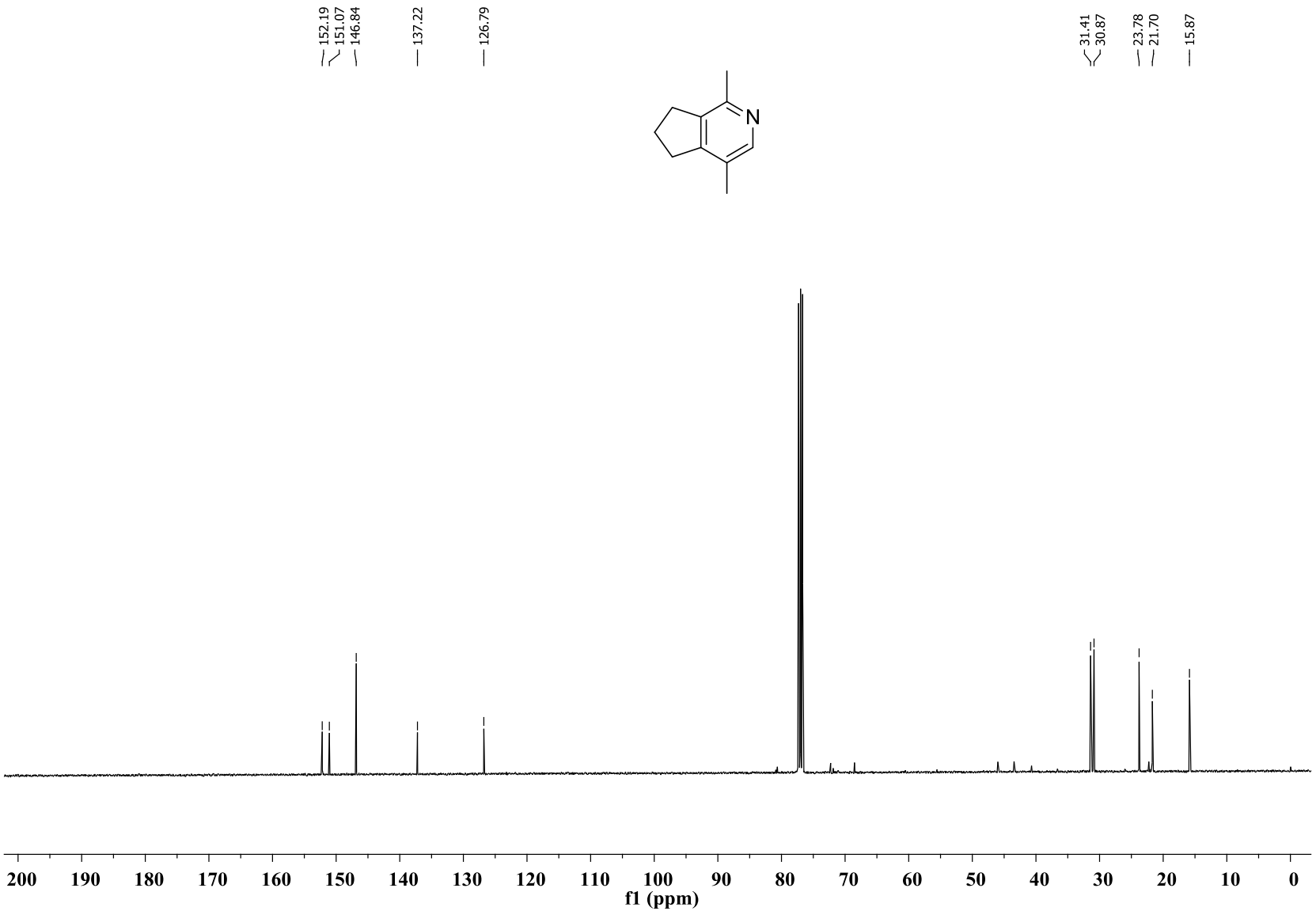
$^{13}C\{1H\}$NMR spectrum of **3y** ($CDCl_3$, 100 MHz)**:**



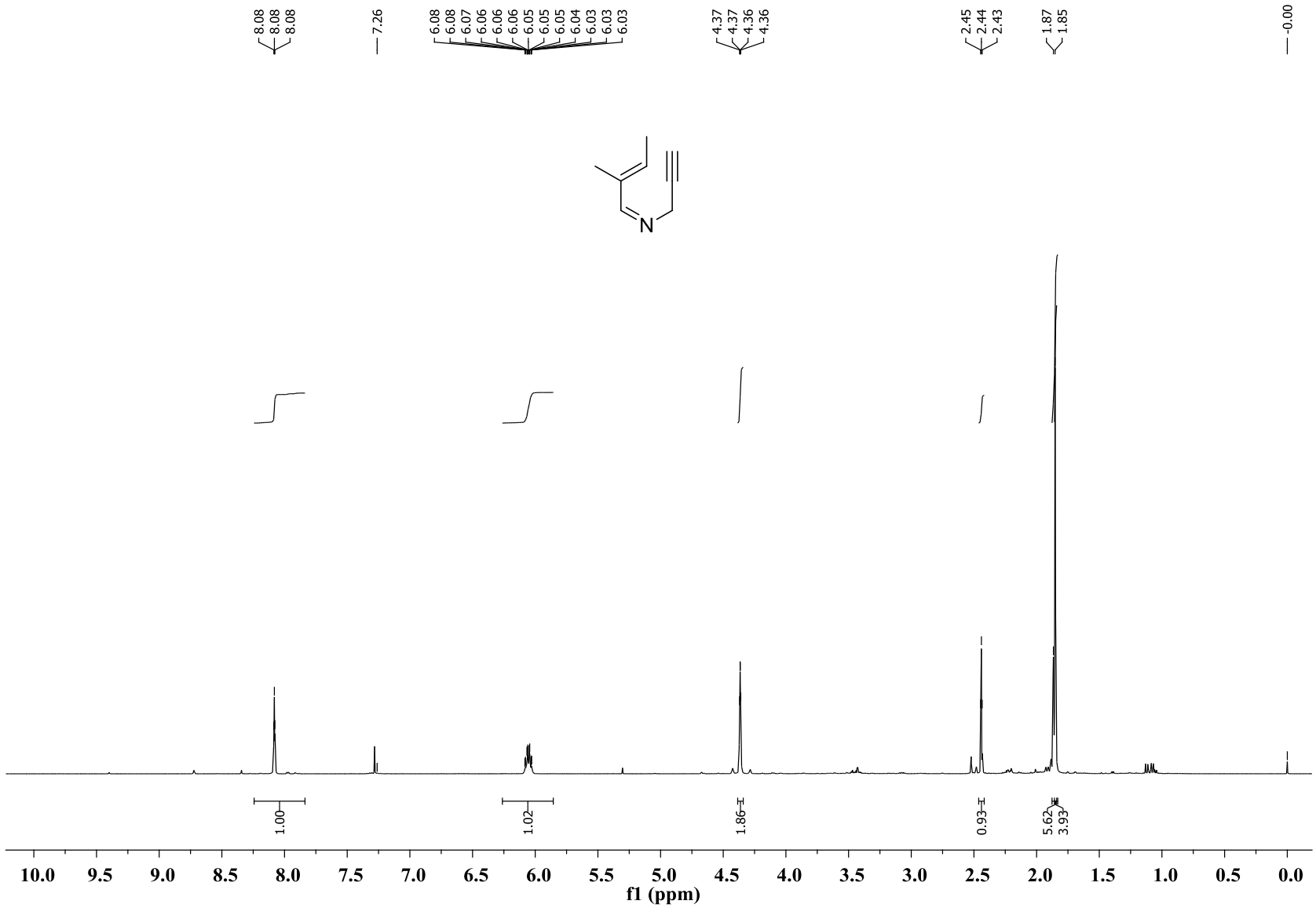
^{1}H NMR spectrum of **3z** ($CDCl_3$, 400 MHz)**:**



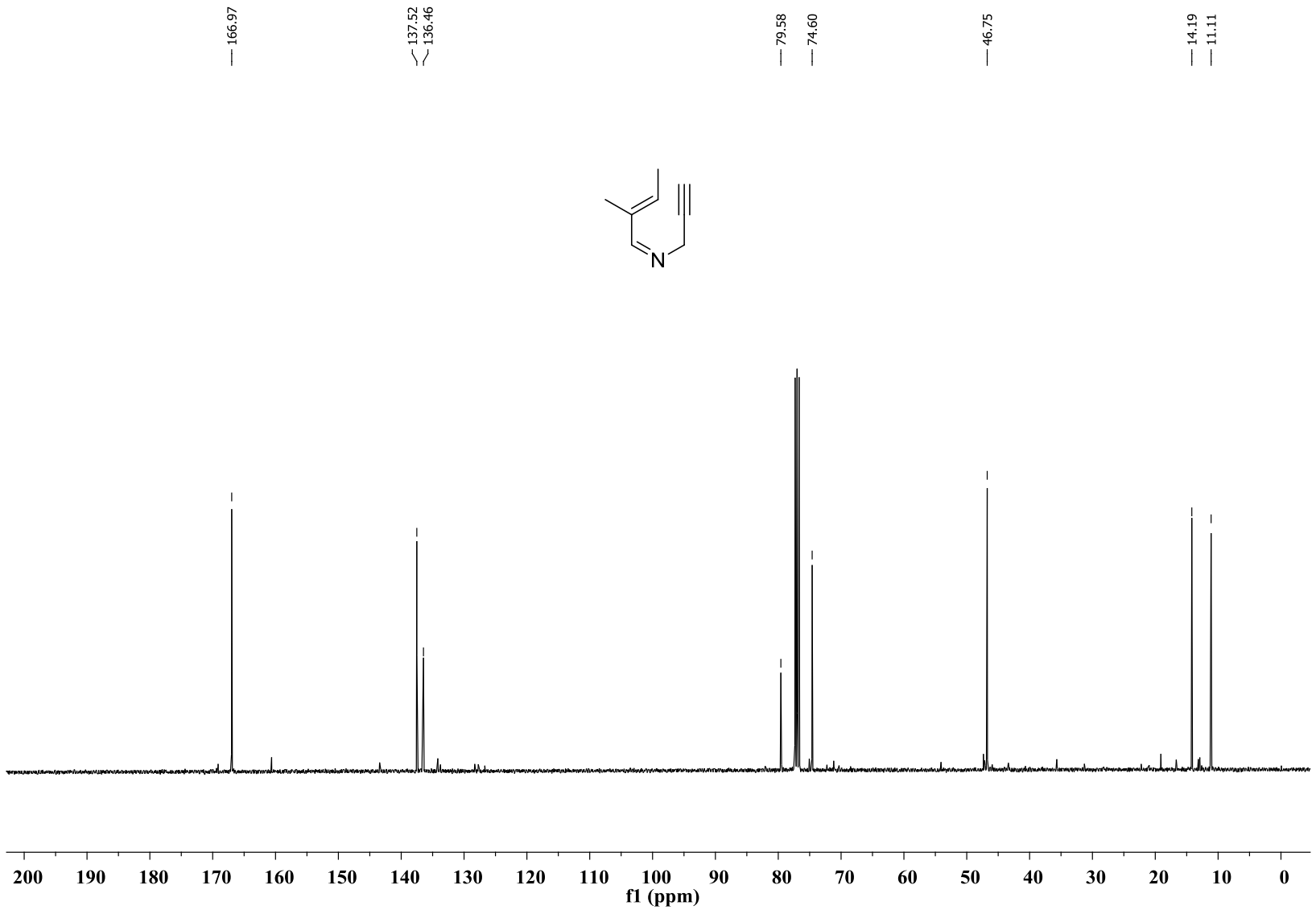
$^{13}C\{1H\}$NMR spectrum of **3z** ($CDCl_3$, 100 MHz)**:**



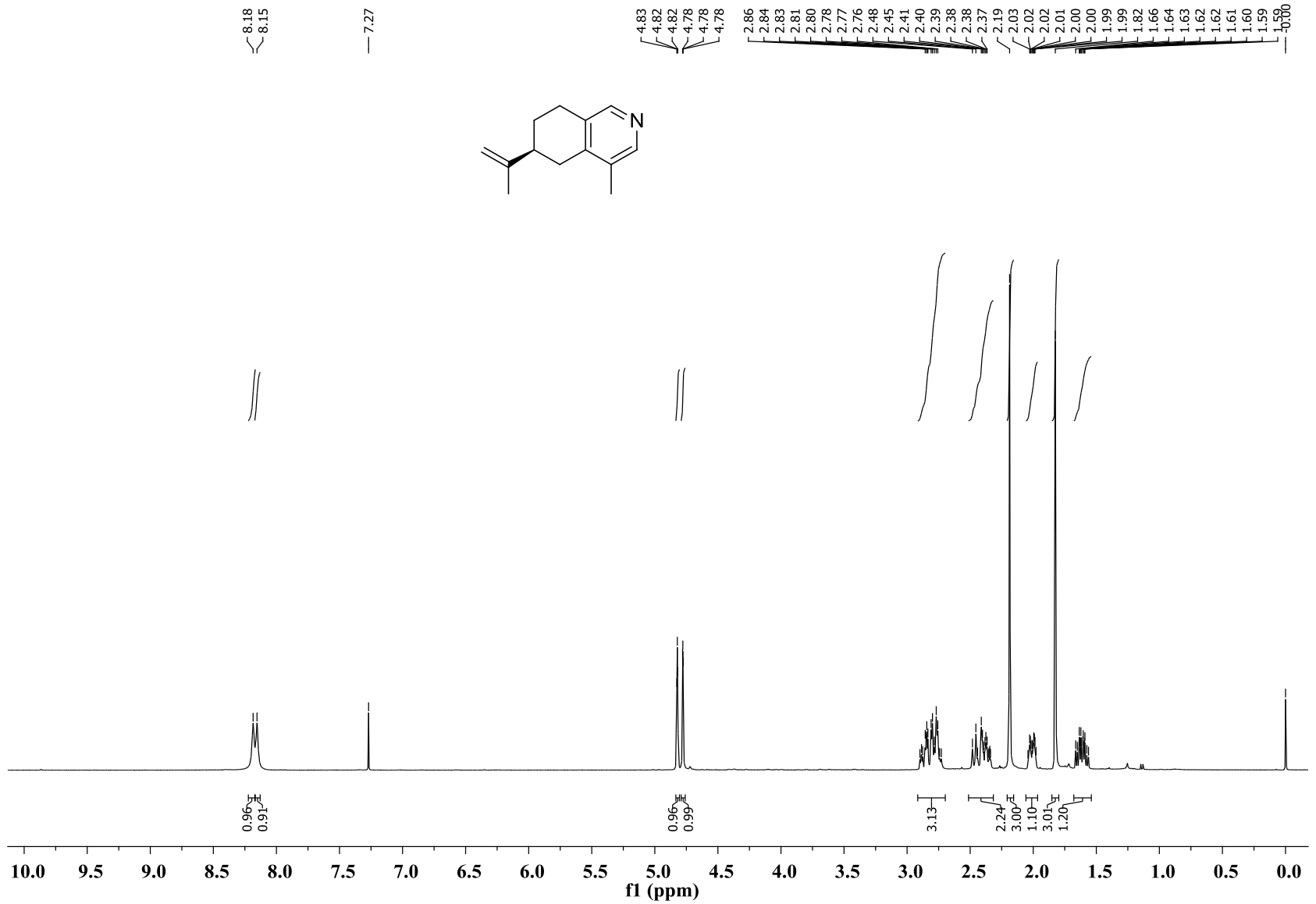
^{1}H NMR spectrum of **3aa** ($CDCl_3$, 400 MHz)**:**



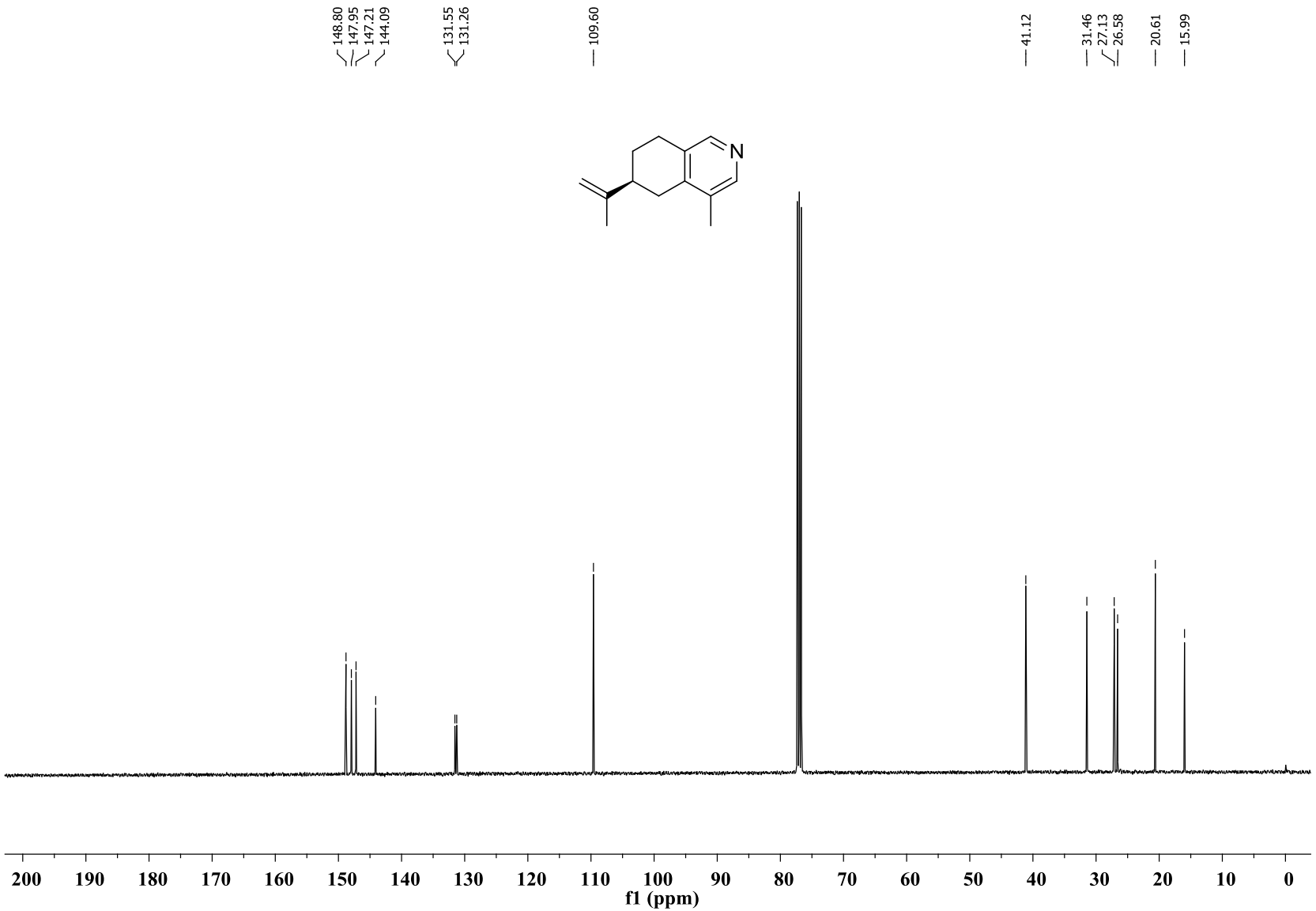
$^{13}C\{1H\}$NMR spectrum of **3aa** ($CDCl_3$, 100 MHz)**:**



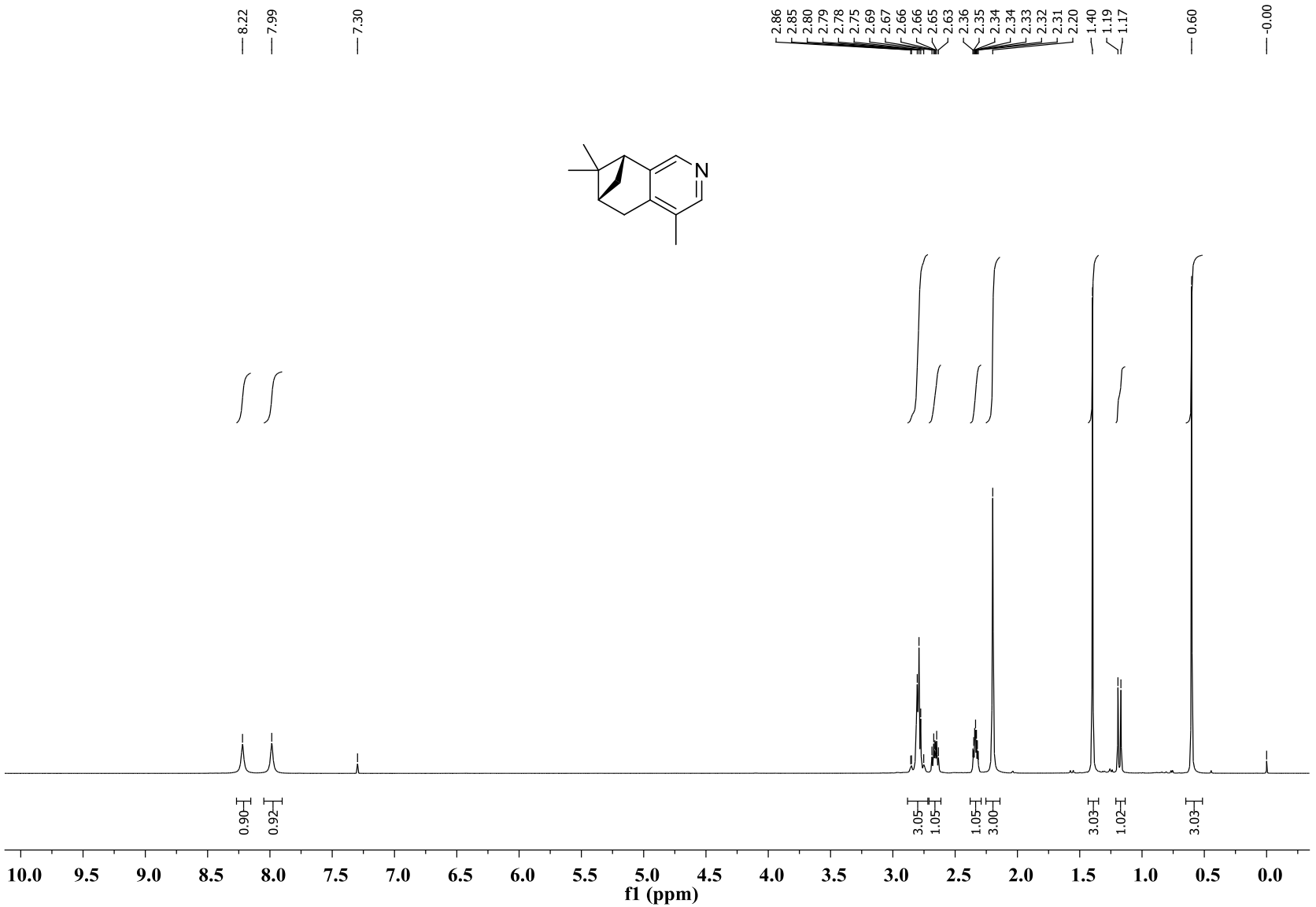
^{1}H NMR spectrum of **4a** ($CDCl_3$, 400 MHz)**:**



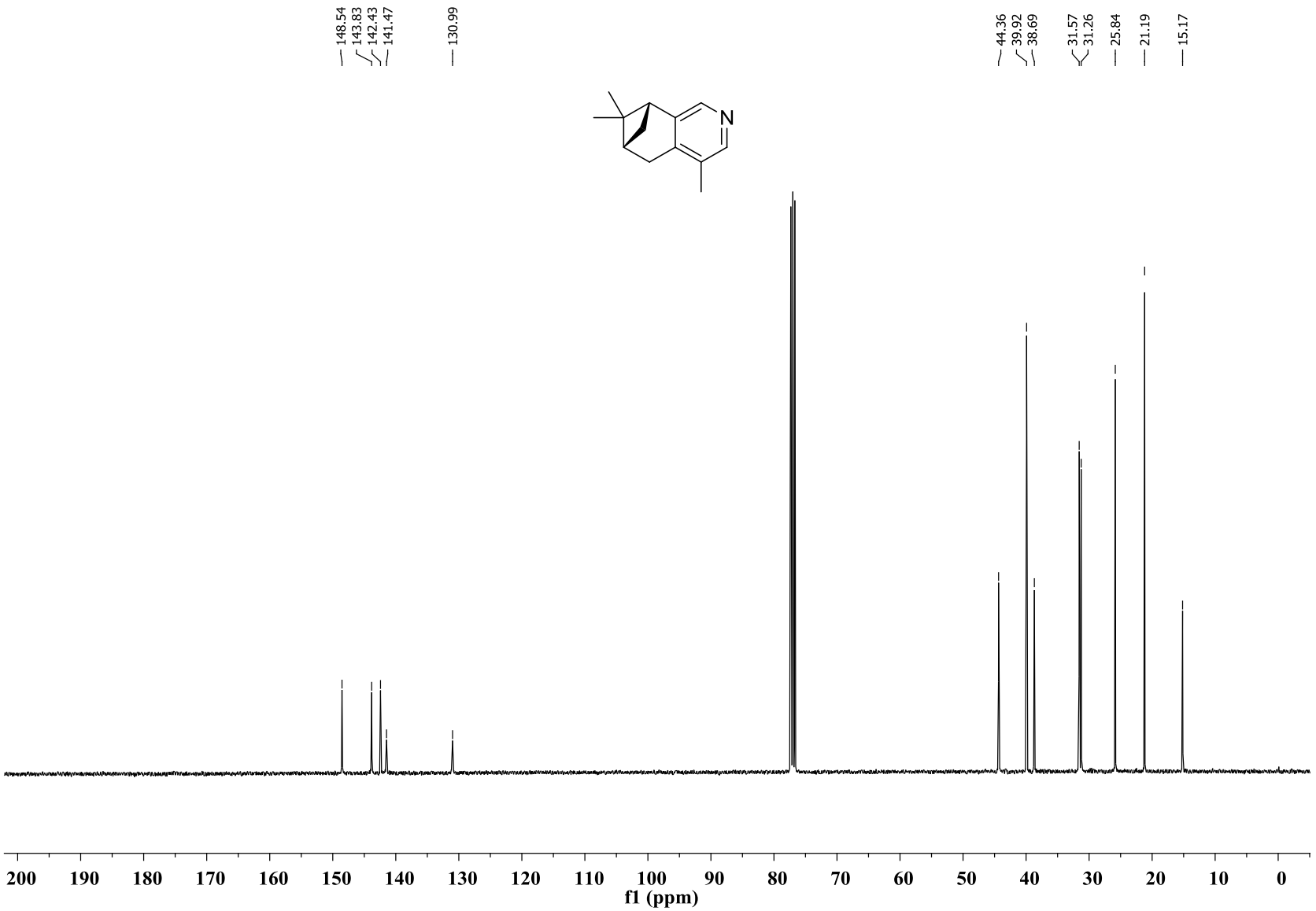
$^{13}C\{1H\}$NMR spectrum of **4a** ($CDCl_3$, 100 MHz)**:**



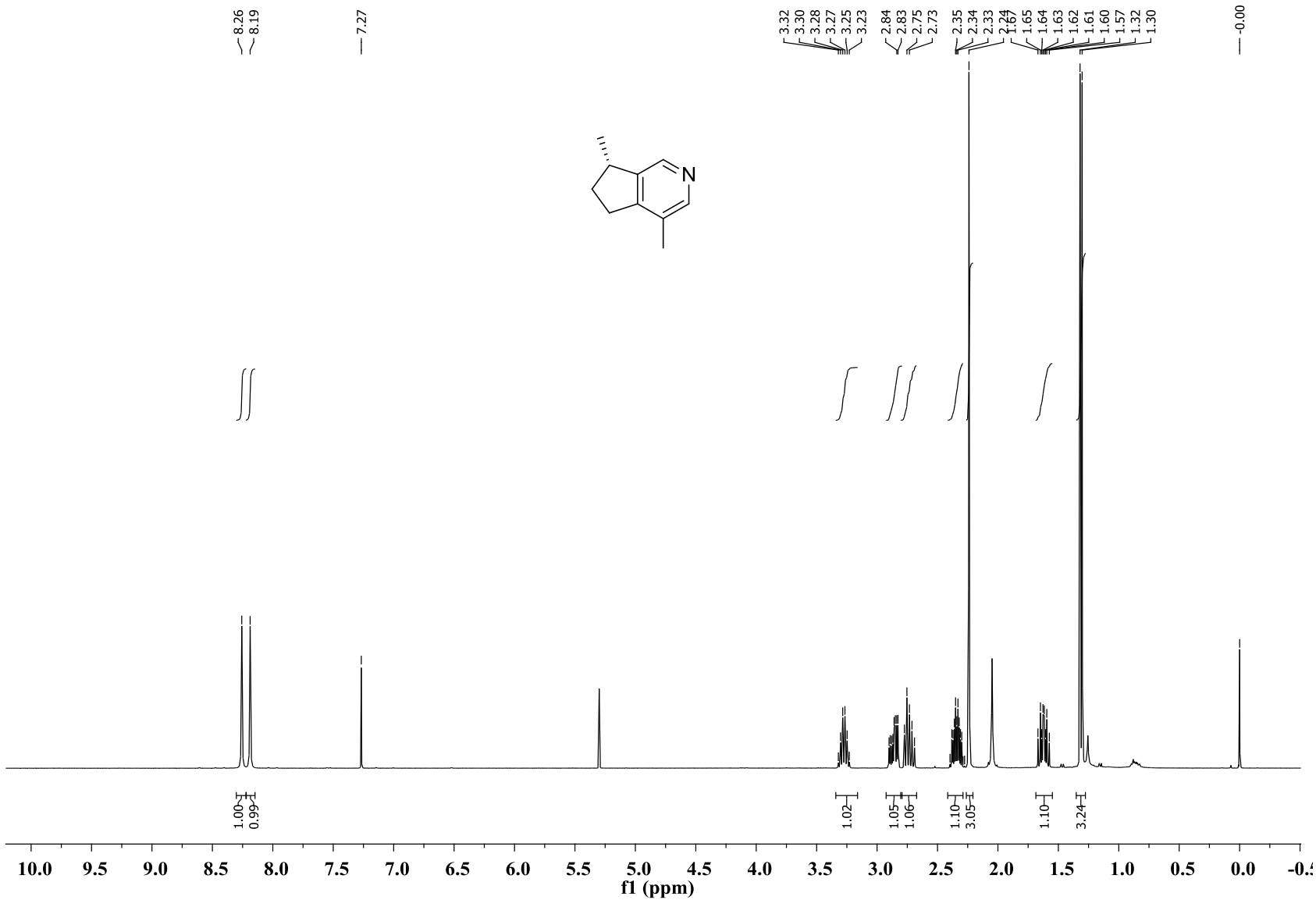
^{1}H NMR spectrum of **4b** ($CDCl_3$, 400 MHz)**:**



$^{13}C\{1H\}$NMR spectrum of **4b** ($CDCl_3$, 100 MHz)**:**



^{1}H NMR spectrum of compound **5** ($CDCl_3$, 400 MHz)**:**



$^{13}C\{1H\}NMR$ spectrum of compound **5** ($CDCl_3$, 100 MHz)**:**