Supporting Information for

1,6 Conjugate Addition of Zinc Alkyls to *para*-Quinone Methides in a continuous-Flow Microreactor

Abhijeet S. Jadhav and Ramasamy Vijaya Anand*

Department of Chemical Sciences, Indian Institute of Science Education and Research (IISER) Mohali, Sector 81, Knowledge City, S. A. S. Nagar, Manauli (PO), Punjab – 140306, India.

E-mail: rvijayan@iisermohali.ac.in

Contents:

Experimental Section

General Information:

Continuous-flow experiments were carried out using FlowStart Evo B-401 instrument purchased from Future Chemistry Holding B.V. The microreactor unit was made up of borosilicate glass (channel width 600 μm, channel depth 500 μm) with effective reaction volume of 100 μL. Melting points were recorded on SMP20 melting point apparatus and are uncorrected. Most of the reagents and starting materials were purchased from commercial sources and used as such. All *p*-quinone methides were prepared by following a literature procedure.[1] ^{1}H, ^{13}C and ^{19}F spectra were recorded in $CDCl_3$ (400, 100 and 376 MHz respectively) on Bruker FT-NMR spectrometer. Chemical shift (δ) values are reported in parts per million relative to TMS and the coupling constants (J) are reported in Hz. High resolution mass spectra were recorded on Waters Q-TOF Premier-HAB213 spectrometer. FT-IR spectra were recorded on a Perkin–Elmer FT-IR spectrometer. Thin layer chromatography was performed on Merck silica gel 60 F_{254} TLC plates. Column chromatography was carried out through silica gel (100-200 mesh) using EtOAc/hexane as an eluent.

General procedure for the synthesis of unsymmetrical alkyl diarylmethane derivatives under continuous flow method:

p-Quinone methide (1 equiv, dissolved in 1 mL of toluene) and dialkylzinc solution (in hexane or diethyl ether) (2 equiv, diluted with toluene to make the total volume 1 mL) were pumped simultaneously through the microractor at the flow rates of 5 μL/min each. The temperature of microreactor was maintained at 25 °C throughout the reaction. The reaction mixture collected at the outlet was carefully quenched by the addition of aqueous ammonium chloride solution. The organic phase was separated and aqueous layer was extracted diethyl ether (10 mL x 2). The combined organic solutions were then washed with brine, dried over

anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the crude was purified through silica-gel chromatography using hexane/EtOAc to obtain the pure alkyl diarylmethane derivatives.

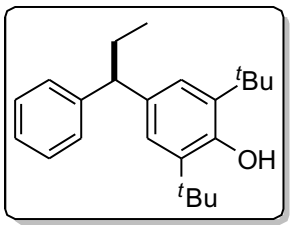
General procedure for the synthesis of 3 in the conventional method:

A solution of diethylzinc (15 w/w solution in hexane) (0.15 mL, 0.122 mmol) was added in a drop-wise manner to a solution of 2,6-di-tert-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone **1** (20 mg, 0.061 mmol) in toluene (2 mL) kept in a rb flask at 0 ºC. After the addition of diethylzinc, the ice bath was removed and the reaction mixture was stirred at room temperature. After the reaction was complete (30 min), reaction mixture was carefully quenched by addition of aqueous ammonium chloride solution. The organic phase was separated and aqueous layer was extracted with Et_2O (10 mL x 2). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the crude was purified through silica-gel chromatography using hexane/EtOAc to obtain pure 2,6-di-*tert*-butyl-4-(1-[4-methoxyphenyl]propyl)phenol **3** (19 mg, 90% yield).

2,6-di-*tert*-butyl-4-(1-[4-methoxyphenyl]propyl)phenol (3)

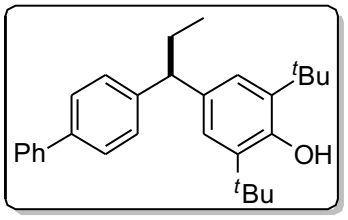
The reaction was performed in 0.061 mmol scale of **1**; R_f = 0.3 (5% EtOAc in hexane); white solid (20 mg, 92 % yield [in microreactor], 19.5 mg, 90% yield [in conventional method]); m. p. = 74-76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19-7.16 (m, 2H), 7.03 (s, 2H), 6.87-6.83 (m, 2H), 5.02 (s, 1H), 3.79 (s, 3H), 3.66 (t, J = 7.8 Hz, 1H), 2.01 (quin, J = 7.4 Hz, 2H), 1.42 (s, 18H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 151.9, 137.9, 136.4, 135.5, 129.0, 124.3, 113.8, 55.3, 52.6, 34.5, 30.5, 29.6, 13.1; FT-IR (neat): 3649, 2958, 2871, 1610, 1511, 1435, 1248, 1121 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{24}H_{33}O_2$ $[M-H]^+$: 353.2481; found : 353.2468.

2,6-di-*tert*-butyl-4-(1-phenylpropyl)phenol (3a)



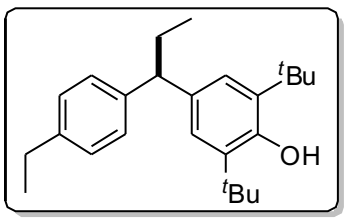
The reaction was performed in 0.068 mmol scale of **1a**; R_f = 0.5 (5% EtOAc in hexane); pale yellow gummy solid (14.9 mg, 85% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.24 (m, 4H), 7.18-7.15 (m, 1H), 7.03 (s, 2H), 5.02 (s, 1H), 3.69 (t, J = 7.8 Hz, 1H), 2.09-1.98 (m, 2H), 1.41 (s, 18H), 0.88 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 145.7, 136.0, 135.5, 128.4, 128.1, 125.9, 124.4, 53.5, 34.5, 30.5, 29.4, 13.1; FT-IR (neat): 3645, 2959, 2876, 1605, 1232, 1156, 764, 699 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{23}H_{31}O$ [M-H]$^+$: 323.2375; found : 323.2363.

4-(1-{[1,1'-biphenyl]-4-yl}propyl)-2,6-di-*tert*-butylphenol (3b)



The reaction was performed in 0.04 mmol scale of **1b**; R_f = 0.4 (5% EtOAc in hexane); white solid (16 mg, 99% yield); m. p. = 87-89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.57 (m, 2H), 7.53-7.51 (m, 2H), 7.44-7.40 (m, 2H), 7.33-7.29 (m, 3H), 7.06 (s, 2H), 5.03 (s, 1H), 3.73 (t, J = 7.6 Hz, 1H), 2.12-2.01 (m, 2H), 1.42 (s, 18H), 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 145.0, 141.2, 138.7, 135.9, 135.6, 128.8, 128.5, 127.14, 127.1, 127.07, 124.4, 53.2, 34.5, 30.5, 29.4, 13.2; FT-IR (neat): 3640, 2958, 2877, 1486, 1235, 1156, 1124, 697 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{35}O$ [M-H]$^+$: 399.2688; found : 399.2677.

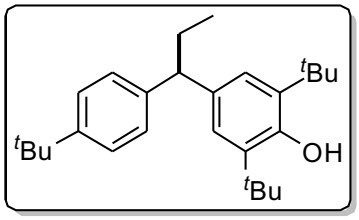
2,6-di-*tert*-butyl-4-(1-[4-ethylphenyl]propyl)phenol (3c)



The reaction was performed in 0.062 mmol scale of **1c**; R_f = 0.5 (5% EtOAc in hexane); pale yellow solid (17.5 mg, 80% yield); m. p. = 71-73 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19-7.17 (m,

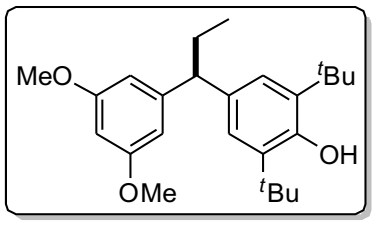
2H), 7.13-7.11 (m, 2H), 7.05 (s, 2H), 5.02 (s, 1H), 3.67 (t, *J* = 7.7 Hz, 1H), 2.62 (q, *J* = 7.6 Hz, 2H), 2.03-2.01 (m, 2H), 1.42 (s, 18H), 1.23 (t, *J* = 7.6 Hz, 3H), 0.89 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 143.0, 141.7, 136.2, 135.5, 127.9, 127.8, 124.3, 53.2, 34.5, 30.5, 29.5, 28.5, 15.7, 13.2; FT-IR (neat): 3645, 2961, 2873, 1512, 1361, 1232, 1157, 1120, 1073, 767 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{25}H_{35}O$ $[M-H]^+$: 351.2688; found : 351.2674.

2,6-di-*tert*-butyl-4-(1-[4-(*tert*-butyl)phenyl]propyl)phenol (3d)



The reaction was performed in 0.025 mmol scale of **1d**; R_f = 0.5 (5% EtOAc in hexane); pale yellow solid (8.3 mg, 88% yield); m. p. = 89-91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.29 (m, 2H), 7.20-7.18 (m, 2H), 7.05 (s, 2H), 5.02 (s, 1H), 3.66 (t, *J* = 7.8 1H), 2.07-1.97 (m, 2H), 1.42 (s, 18H), 1.31 (s, 9H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 148.5, 142.8, 136.1, 135.5, 127.5, 125.3, 124.4, 53.1, 34.5, 34.4, 31.6, 30.5, 29.6, 13.2; FT-IR (neat): 3645, 2960, 2872, 1462, 1362, 1271, 1232, 1157, 768, 743 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{27}H_{39}O$ $[M-H]^+$: 379.3001; found : 379.2987.

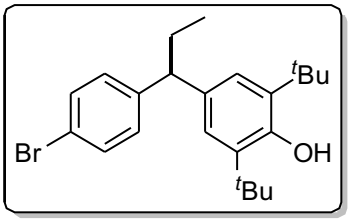
2,6-di-*tert*-butyl-4-(1-[3,5-dimethoxyphenyl]propyl)phenol (3e)



The reaction was performed in 0.056 mmol scale of **1e**; R_f = 0.2 (5% EtOAc in hexane); colourless gummy solid (16 mg, 74% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (s, 2H), 6.44 (d, *J* = 2.3 Hz, 2H), 6.29 (t, *J* = 2.3 Hz, 1H), 5.03 (s, 1H), 3.78 (s, 6H), 3.62 (t, *J* = 7.6 Hz, 1H), 2.05-1.96 (m, 2H), 1.42 (s, 18H), 0.89 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 152.1, 148.3, 135.6, 135.5, 124.3, 106.3, 97.6, 55.3, 53.8, 34.5, 30.5, 29.4, 13.1; FT-IR (neat): 3641, 2958, 1596, 1462, 1289, 1233, 1204, 1156,

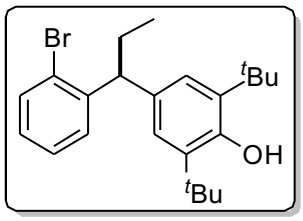
1064, 830, 710 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{25}H_{35}O_3$ $[M-H]^+$: 383.2586; found : 383.2574.

4-(1-[4-bromophenyl]propyl)-2,6-di-*tert*-butylphenol (3f)



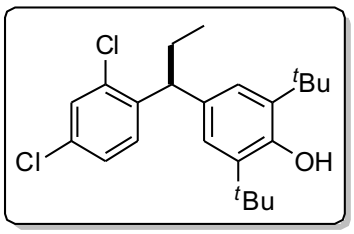
The reaction was performed in 0.053 mmol scale of **1f**; R_f = 0.5 (5% EtOAc in hexane); colourless gummy solid (16.79 mg, 78% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.37 (m, 2H), 7.12-7.10 (m, 2H), 6.98 (s, 2H), 5.04 (s, 1H), 3.65 (t, J = 7.8 Hz 1H), 2.05-1.94 (m, 2H), 1.40 (s, 18H), 0.86 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 144.8, 135.7, 135.4, 131.4, 129.9, 124.2, 119.6, 52.9, 34.5, 30.5, 29.2, 13.0; FT-IR (neat): 3650, 2927, 2870, 1461, 1438, 1289, 1275, 1120, 1073, 690 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{23}H_{30}BrO$ $[M-H]^+$: 401.1480; found : 401.1493.

4-(1-[2-bromophenyl]propyl)-2,6-di-*tert*-butylphenol (3g)



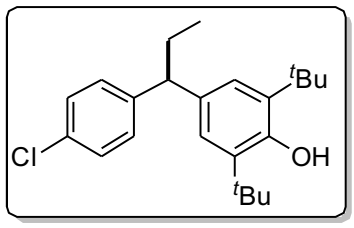
The reaction was performed in 0.053 mmol scale of **1g**; R_f = 0.5 (5% EtOAc in hexane); colourless gummy solid (17 mg, 79 % yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, J = 7.9, 1 Hz, 1H), 7.29-7.23 (m, 2H), 7.09 (s, 2H), 7.01 (ddd, J = 8.0, 6.6, 2.3 Hz, 2H), 5.04 (s, 1H), 4.31 (t, J = 7.8 Hz, 1H), 2.03 (quin, J = 7.4 Hz, 2H), 1.41 (s, 18H), 0.90 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 145.0, 135.5, 134.4, 133.0, 128.6, 127.6, 127.3, 125.6, 124.7, 50.9, 34.5, 30.5, 29.0, 12.8; FT-IR (neat): 3644, 2959, 2873, 1600, 1361, 1316, 1232, 1157, 836, 763, 699, 635 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{23}H_{30}BrO$ $[M-H]^+$: 401.1480; found : 401.1467.

2,6-di-*tert*-butyl-4-(1-[2,4-dichlorophenyl]propyl)phenol (3h)



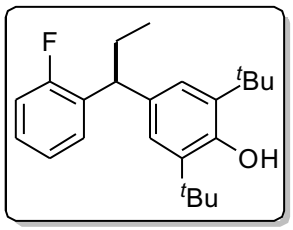
The reaction was performed in 0.049 mmol scale of **1h**; R_f = 0.6 (5% EtOAc in hexane); white solid (16.7 mg, 86% yield); m. p. = 95-97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 1.8 Hz, 1H), 7.23-7.18 (m, 2H), 7.04 (s, 2H), 5.06 (s, 1H), 4.27 (t, J = 7.8 Hz, 1H), 2.09-1.93 (m, 2H), 1.42 (s, 18H), 0.90 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 142.0, 135.7, 135.0, 133.9, 131.9, 129.4, 129.3, 127.3, 124.5, 47.9, 34.5, 30.5, 28.7, 12.7; FT-IR (neat): 3644, 2960, 2869, 1469, 1233, 1157, 1046, 844 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{23}H_{29}Cl_2O$ $[M-H]^+$: 391.1595; found : 391.1581.

2,6-di-*tert*-butyl-4-(1-[4-chlorophenyl]propyl)phenol (3i)



The reaction was performed in 0.06 mmol scale of **1i**; R_f = 0.6 (5% EtOAc in hexane); colourless gummy solid (19.8 mg, 91% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, J = 8.2 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H), 6.99 (s, 2H), 5.05 (s, 1H), 3.67 (t, J = 7.8 Hz, 1H), 2.06-1.95 (m, 2H), 1.41 (s, 18H), 0.87 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 144.3, 135.7, 135.5, 131.5, 129.5, 128.5, 124.3, 52.8, 34.5, 30.5, 29.3, 13.0; FT-IR (neat): 3644, 2958, 2878, 1602, 1232, 1156, 1121, 1027, 734, 700 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{23}H_{30}ClO$ $[M-H]^+$: 357.1985; found: 357.1969.

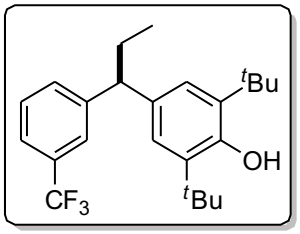
2,6-di-*tert*-butyl-4-(1-[2-fluorophenyl]propyl)phenol (3j)



The reaction was performed in 0.058 mmol scale of **1j**; R_f = 0.6 (5% EtOAc in hexane); colourless gummy solid (17.1 mg, 86% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (td, J = 7.6, 1.8 Hz ,1H), 7.18-7.06 (m, 4H), 7.03-6.98 (m, 1H), 5.05 (s, 1H), 4.10 (t, J = 7.8 Hz, 1H), 2.11-2.00 (m, 2H), 1.42 (s, 18H), 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0 (d, $J_{C\text{-}F}$ = 242.9 Hz), 152.1, 135.6, 134.8, 132.6 (d, $J_{C\text{-}F}$ = 14.6 Hz), 128.8 (d, $J_{C\text{-}F}$ =

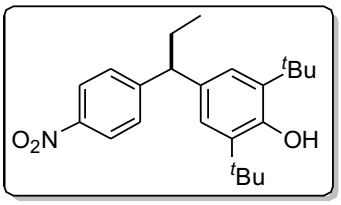
4.8 Hz), 127.3 (d, $J_{C\text{-}F}$ = 8.3 Hz), 124.5, 124.1 (d, $J_{C\text{-}F}$ = 3.5 Hz), 115.5 (d, $J_{C\text{-}F}$ = 23.0 Hz), 45.3 (d, $J_{C\text{-}F}$ = 1.9 Hz), 34.5, 30.5, 28.4, 12.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.09; FT-IR (neat): 3643, 2961, 2873, 1585, 1488, 1365, 1316, 1229, 1157, 1119, 755 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{23}H_{30}FO$ $[M\text{-}H]^+$: 341.2281; found: 341.2268

2,6-di-*tert*-butyl-4-(1-[3-{trifluoromethyl}phenyl]propyl)phenol (3k)



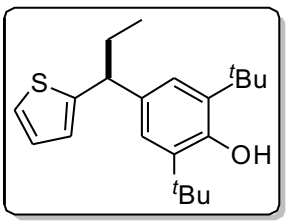
The reaction was performed in 0.049 mmol scale of **1k**; R_f = 0.6 (5% EtOAc in hexane); colourless gummy solid (19.5 mg, 64 % yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (brs, 1H), 7.46-7.36 (m, 3H), 7.01(s, 2H), 5.08 (s, 1H), 3.77 (t, *J* = 7.8 Hz, 1H), 2.06 (quin, *J* = 7.4 Hz, 2H), 1.42 (s, 18H), 0.89 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 146.6, 135.8, 135.0, 131.6, 130.6 (q, $J_{C\text{-}F}$ = 31.6 Hz), 128.9, 124.8 (q, $J_{C\text{-}F}$ = 3.8 Hz), 124.5 (q, $J_{C\text{-}F}$ = 270.7 Hz), 124.3, 122.9 (q, $J_{C\text{-}F}$ = 3.6 Hz), 53.3, 34.5, 30.4, 29.4, 13.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.46; FT-IR (neat): 3644, 2961, 2873, 1589, 1328, 1163, 1126, 1232, 1074, 805, 704, 658 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{24}H_{30}F_3O$ $[M\text{-}H]^+$: 391.2249; found : 391.2235.

2,6-di-*tert*-butyl-4-(1-[4-nitrophenyl]propyl)phenol (3l)



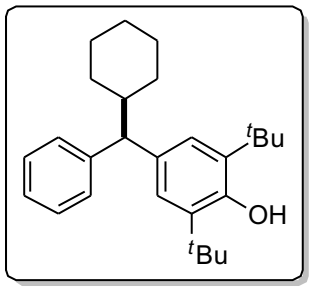
The reaction was performed in 0.054 mmol scale of **1l**; R_f = 0.5 (5% EtOAc in hexane); white solid (17.89 mg, 91% yield); m.p. = 112-114 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17-8.13 (m, 2H), 7.41-7.38 (m, 2H), 6.98 (s, 2H), 5.10 (s, 1H), 3.81 (t, *J* = 7.8 Hz, 1H), 2.11-2.01 (m, 2H), 1.41 (s, 18H), 0.90 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.7, 152.5, 146.3, 136.0, 134.1, 128.8, 124.3, 123.8, 53.3, 34.5, 30.4, 28.9, 12.9; FT-IR (neat): 3639, 2960, 1595, 1521, 1345, 1234, 1157, 1120, 857, 703 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{23}H_{30}NO_3$ $[M\text{-}H]^+$: 368.2226; found : 368.2214.

2,6-di-*tert*-butyl-4-(1-[thiophen-2-yl]propyl)phenol (3m)



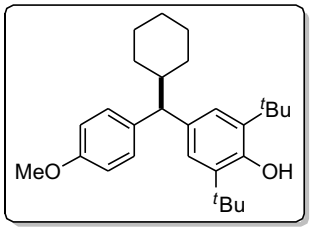
The reaction was performed in 0.06 mmol scale of **1m**; R_f = 0.4 (5% EtOAc in hexane); pale yellow gummy solid (14.9 mg, 76 % yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (dd, J = 5.1, 1.2 Hz, 1H), 7.10 (s, 2H), 6.93 (dd, J = 5.1, 3.4 Hz, 1H), 6.84 (dt, J = 3.4, 0.9 Hz, 1H), 5.09 (s, 1H), 3.97 (t, J = 7.7 Hz, 1H), 2.13-2.00 (m, 2H), 1.45 (s, 18H), 0.94 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 150.4, 135.6, 135.4, 126.5, 124.3, 123.8, 123.2, 49.0, 34.5, 31.5, 30.5, 13.0; FT-IR (neat): 3642, 2929, 2873, 1600, 1463, 1380, 1278, 1125, 1072, 742 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{21}H_{29}OS$ $[M-H]^+$: 329.1939; found : 329.1927.

2,6-di-*tert*-butyl-4-(cyclohexyl[phenyl]methyl)phenol (3n)



The reaction was performed in 0.049 mmol scale of **1n**; R_f = 0.5 (5% EtOAc in hexane); white solid (22.6 mg, 98% yield); m. p. = 100-102 °C; ^{1}H NMR (400 MHz, $CDCl_3$); δ 7.31-7.24 (m, 4H), 7.16-7.12 (m, 1H), 7.07 (s, 2H), 4.98 (s, 1H), 3.46 (d, J = 11.2 Hz, 1H), 2.65-2.60 (m, 1H), 1.64-1.53 (m, 7H), 1.42 (s, 18H), 1.14-1.13 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 146.4, 136.1, 135.4, 128.3, 128.1, 125.7, 124.4, 58.7, 45.2, 34.4, 32.5, 32.4, 30.5, 25.6, 25.5; FT-IR (neat): 3644, 2955, 2869, 1602, 1435, 1232, 1124, 750, 700 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{27}H_{37}O$ $[M-H]^+$: 377.2844; found : 377.2829.

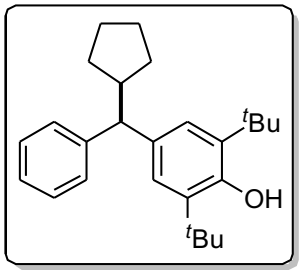
2,6-di-*tert*-butyl-4-(cyclohexyl[4-methoxyphenyl]methyl)phenol (3o)



The reaction was performed in 0.043 mmol scale of **1o**; R_f = 0.5 (5% EtOAc in hexane); white solid (13.19 mg, 75% yield); m. p. = 144-146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20-7.16 (m,

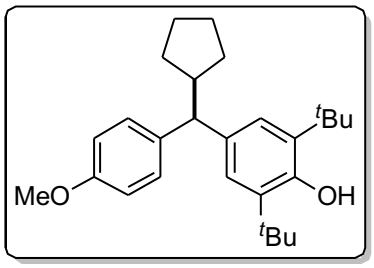
2H), 7.01 (s, 2H), 6.82-6.79 (m, 2H), 4.96 (s, 1H), 3.76 (s, 3H), 3.31 (d, J = 10.8 Hz, 1H), 1.97-1.93 (m, 1H), 1.65-1.60 (m, 4H), 1.41 (s, 18H), 1.26-1.16 (m, 4H), 0.86-0.79 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 151.8, 137.8, 135.4, 135.3, 129.0, 124.5, 113.8, 58.7, 55.3, 42.1, 34.4, 32.34, 32.29, 30.5, 26.8, 26.6, 26.56; FT-IR (neat): 3640, 2921, 2851, 1611, 1510, 1247, 1180, 1042, 839, 637 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{39}O_2$ $[M-H]^+$: 407.2950; found : 407.2936

2,6-di-*tert*-butyl-4-(cyclopentyl[phenyl]methyl)phenol (3p)



The reaction was performed in 0.049 mmol scale of **1p**; R_f = 0.5 (5% EtOAc in hexane); white solid (21 mg, 93%); m. p. = 101-103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.24 (m, 4H), 7.16-7.12 (m, 1H), 7.07 (s, 2H), 4.98 (s, 1H), 3.46 (d, J = 11.2 Hz, 1H), 2.65-2.60 (m, 1H), 1.64-1.50 (m, 6H), 1.42 (s, 18H), 1.20-1.09 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 146.4, 136.1, 135.4, 128.3, 128.1, 125.7, 124.4, 58.7, 45.2, 34.4, 32.5, 32.4, 30.5, 25.6, 25.5; FT-IR (neat): 3644, 2955, 2870, 1599, 1391, 1361, 1232, 1159, 1120, 804, 700 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{26}H_{35}O$ $[M-H]^+$: 363.2688; found : 363.2673.

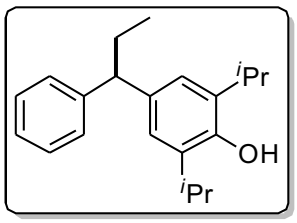
2,6-di-*tert*-butyl-4-(cyclopentyl[4-methoxyphenyl]methyl)phenol (3q)



The reaction was performed in 0.049 mmol scale of **1q**; R_f = 0.5 (5% EtOAc in hexane); colourless gummy solid (17.4 mg, 89% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21-7.18 (m, 2H), 7.03 (s, 2H), 6.82-6.78 (m, 2H), 4.96 (s, 1H), 3.77 (s, 3H), 3.41 (d, J = 11.2 Hz, 1H), 2.63-2.52 (m, 1H), 1.61-1.51 (m, 4H), 1.40 (s, 18H), 1.26-1.11 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 151.8, 138.8, 136.4, 135.4, 128.9, 124.3, 113.7, 57.8, 55.3, 45.4, 34.4, 32.5, 32.4, 30.5, 25.57, 25.55; FT-IR (neat): 3644, 2954, 2969, 1615,

1510, 1434, 1247, 1176, 1042, 770, 839 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{27}H_{37}O_2$ $[M-H]^+$: 393.2794; found : 393.2780.

2,6-diisopropyl-4-(1-phenylpropyl)phenol (3r)

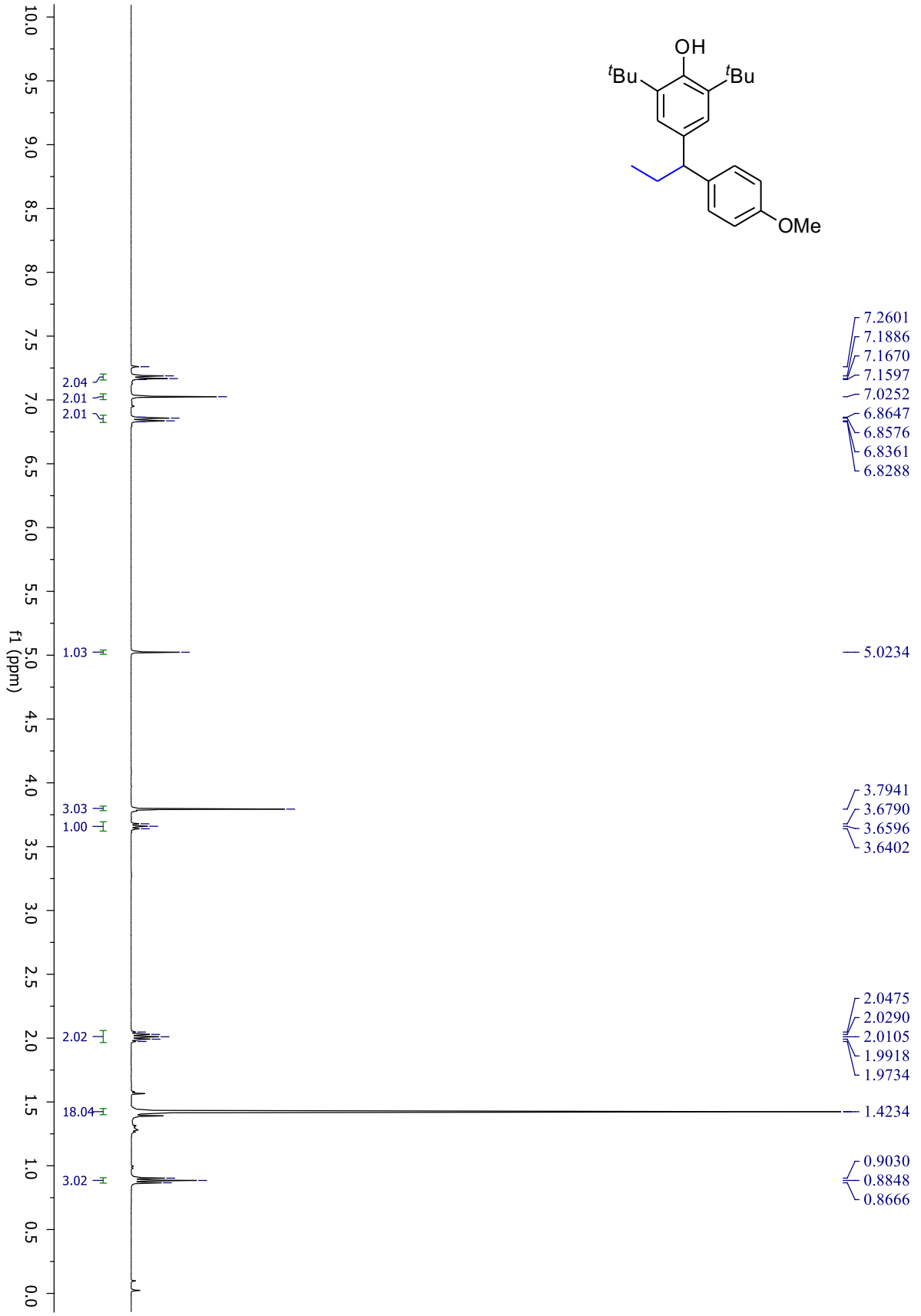


The reaction was performed in 0.075 mmol scale of **1r**; R_f = 0.4 (10% EtOAc in hexane); colourless gummy solid (19 mg, 85% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 7.31-7.24 (m, 4H), 7.19-7.15 (m, 1H), 6.93 (s, 2H), 4.65 (s, 1H), 3.73 (t, *J* = 7.8 Hz, 1H), 3.13 (sept, *J* = 6.9 Hz, 2H), 2.09-2.02 (m, 2H), 1.26 (d, *J* = 1.4 Hz, 6H), 1.24 (d, *J* = 1.4 Hz, 6H), 0.90 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 145.9, 137.1, 133.4, 128.4, 128.0, 125.9, 122.9, 53.2, 29.3, 27.4, 22.9, 13.1; FT-IR (neat): 3521, 2962, 2929, 2874, 1470, 1291, 1203, 1128, 1074, 702 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{21}H_{27}O$ $[M-H]^+$: 295.2062; found : 295.2048.

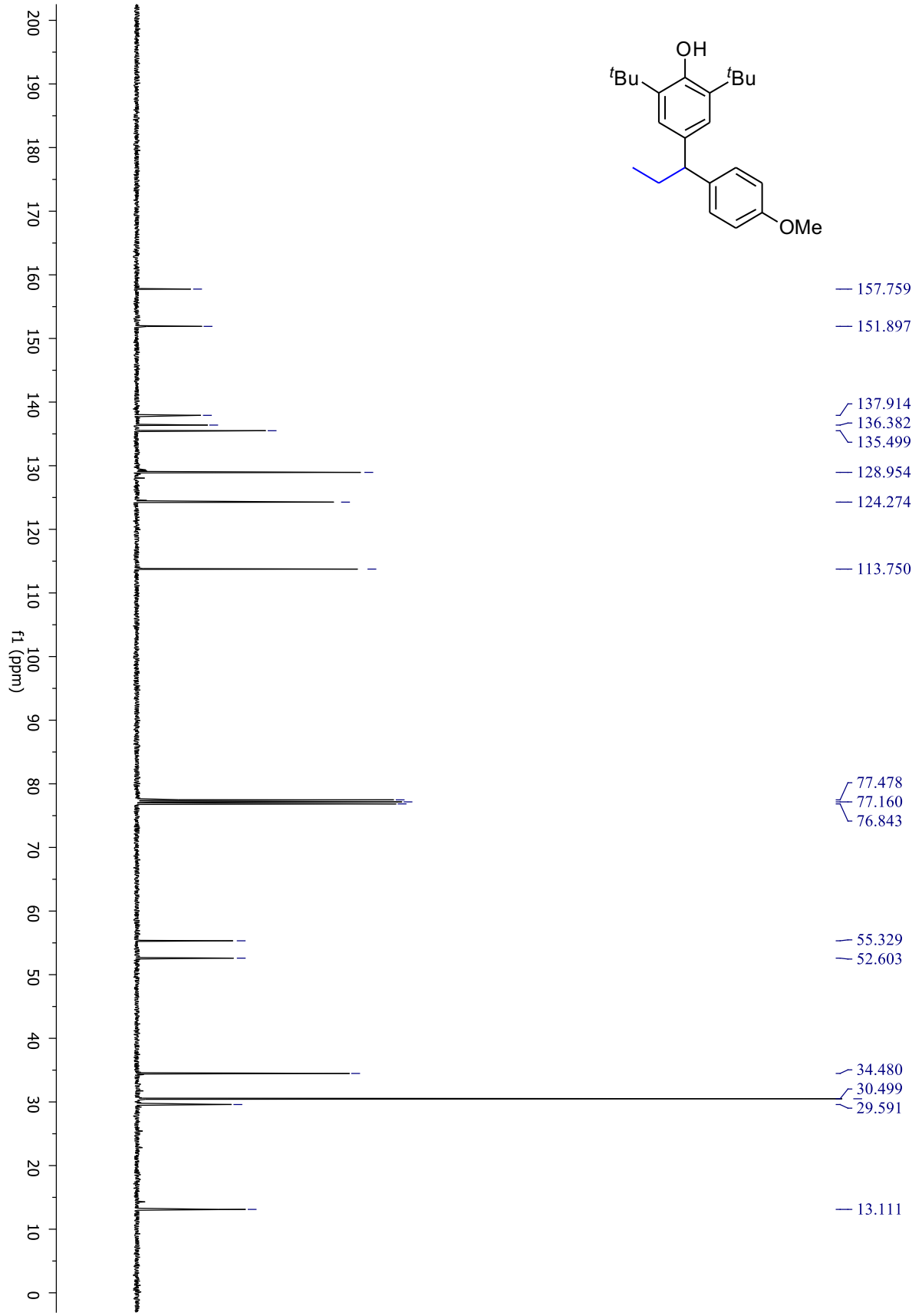
References:

1. W. D. Chu, L. F. Zhang, X. Bao, X. H. Zhao, C. Zeng, J. Y. Du, G. B. Zhang, F. X. Wang, X. Y. Ma, C. A. Fan, *Angew. Chem.*, *Int.*, *Ed.* 2013, **52**, 9229–9233; (b) V. Reddy, R. V. Anand, *Org. Lett.*, 2015, **17**, 3390–3393.

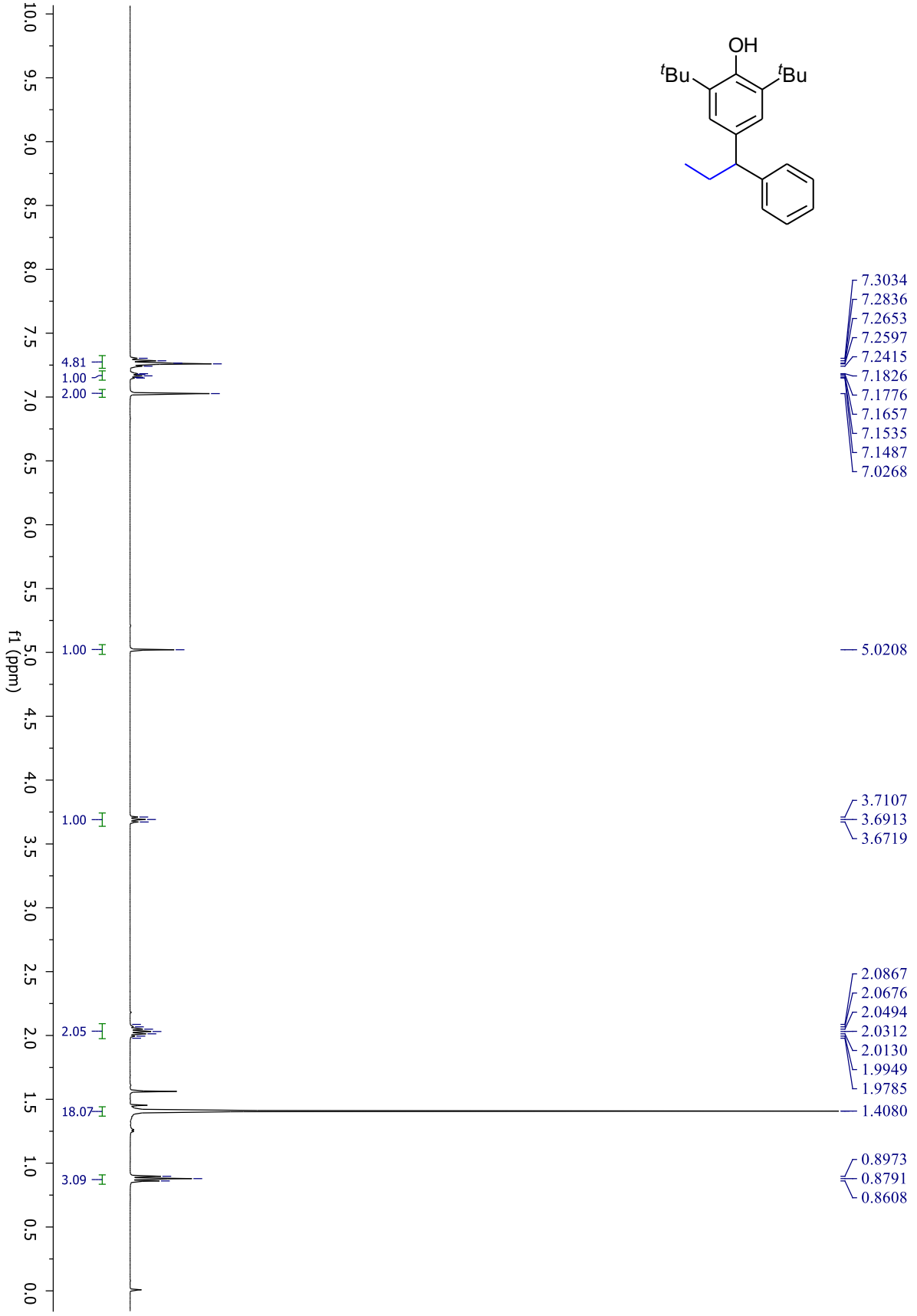
^{1}H NMR spectrum of compound **3**



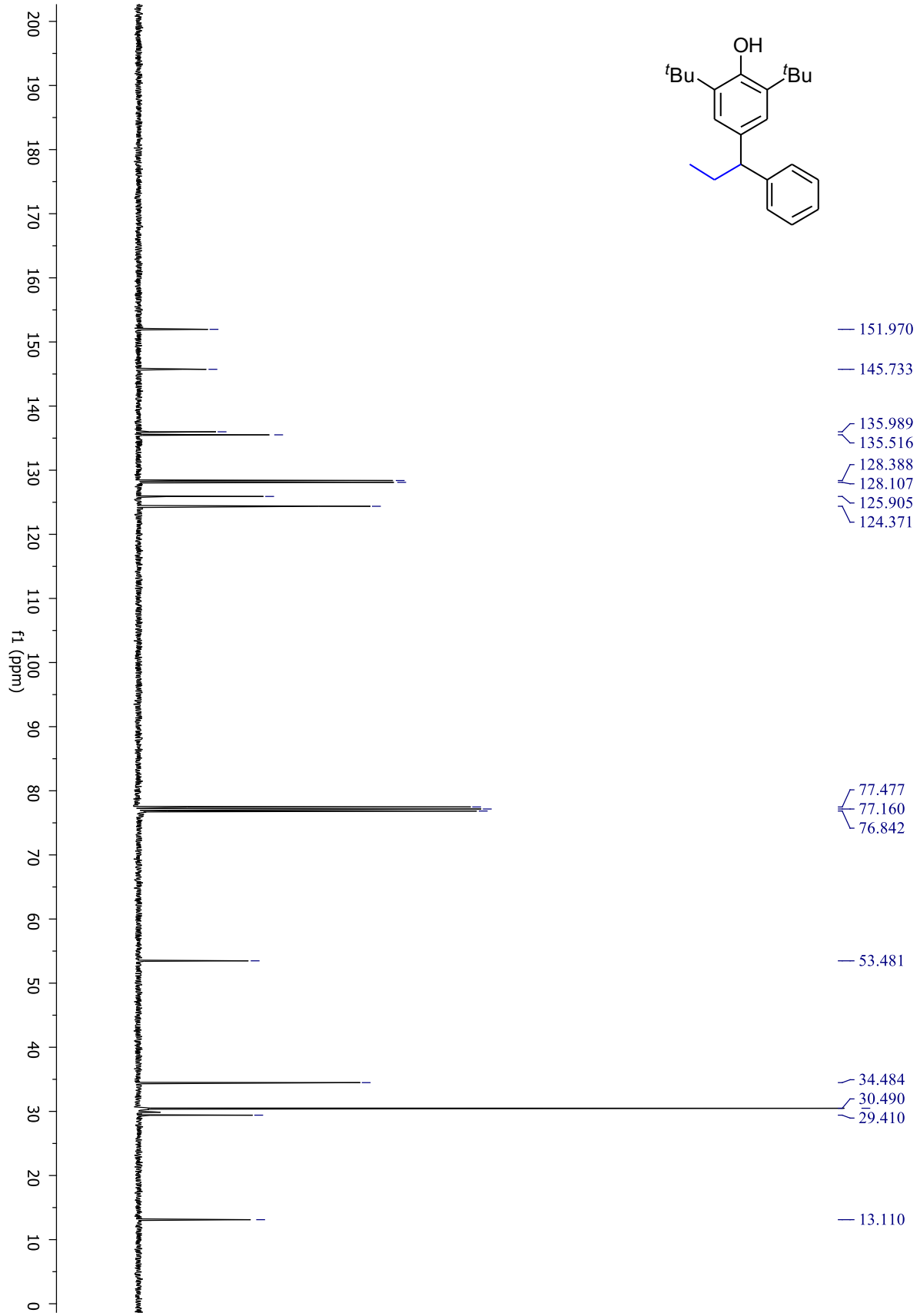
^{13}C NMR spectrum of compound **3**



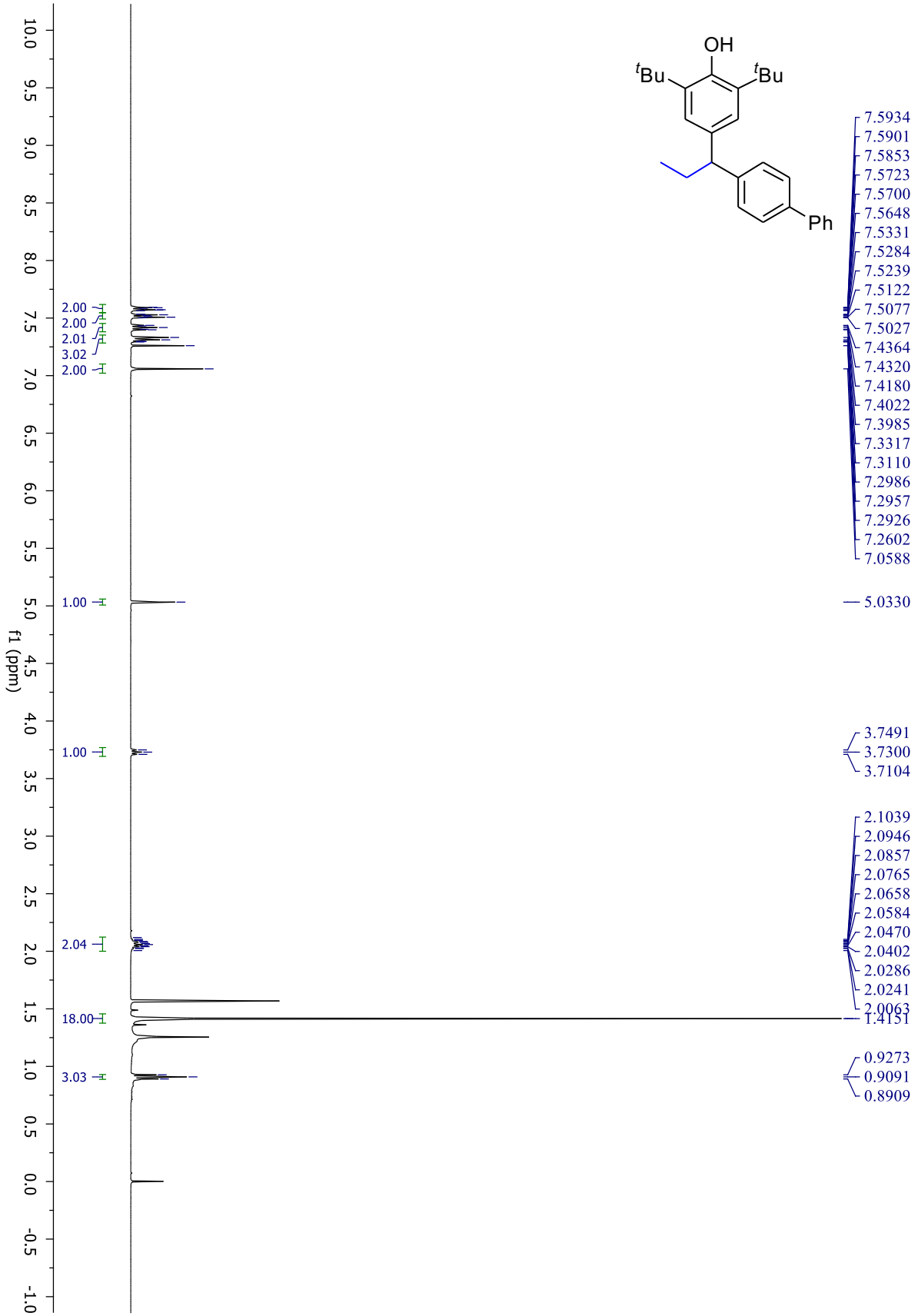
^{1}H NMR spectrum of compound **3a**



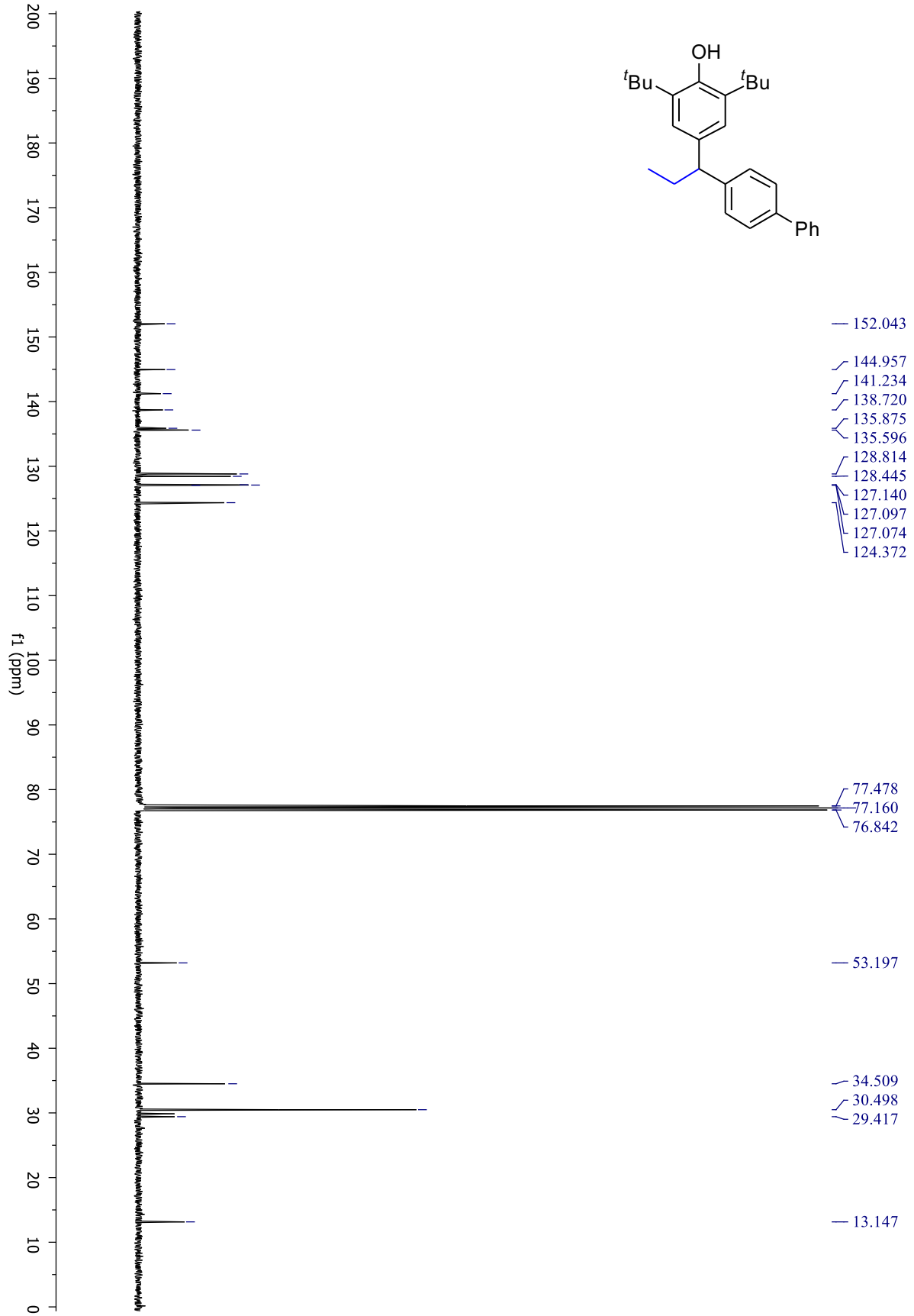
^{13}C NMR spectrum of compound **3a**



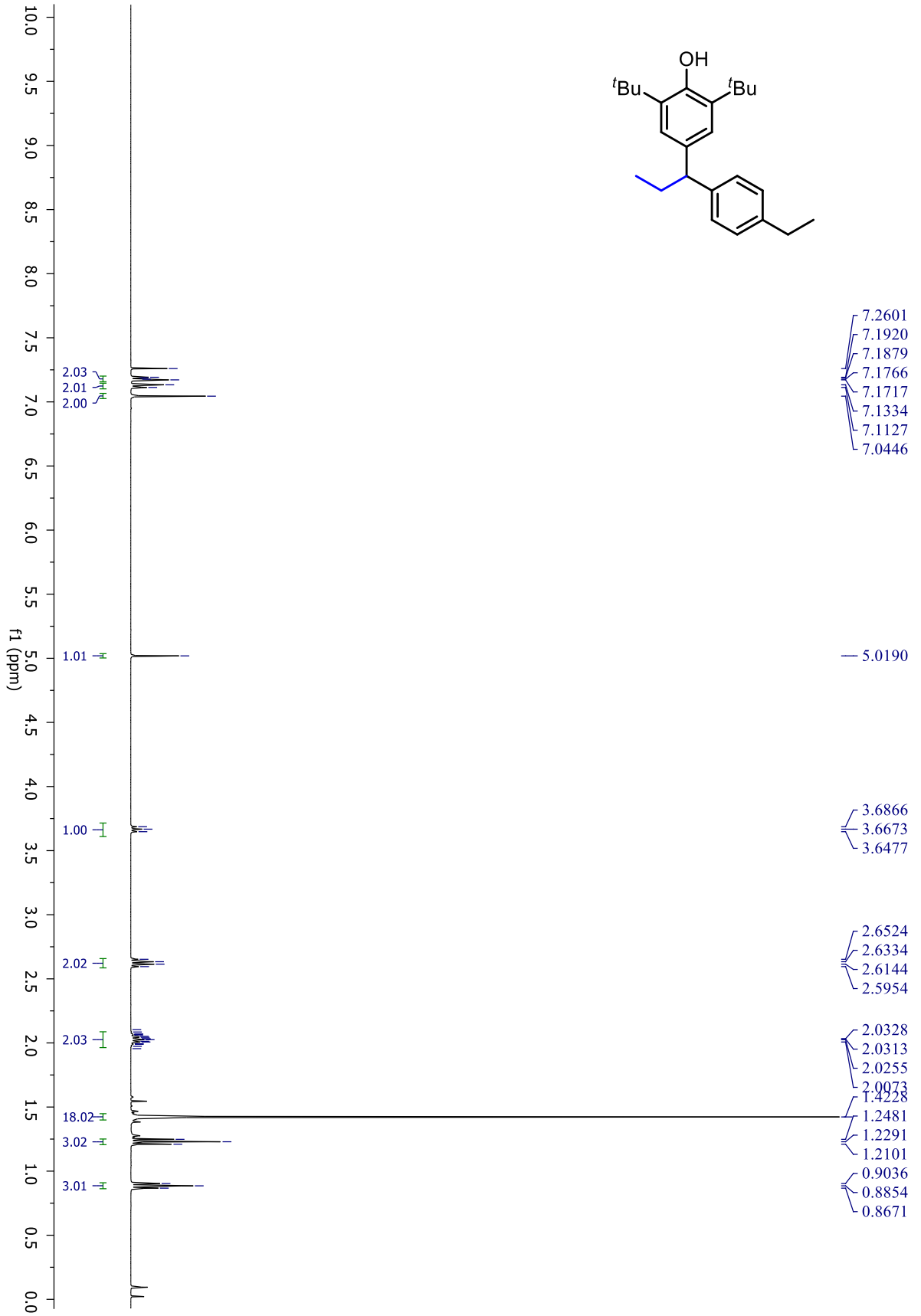
^{1}H NMR spectrum of compound **3b**



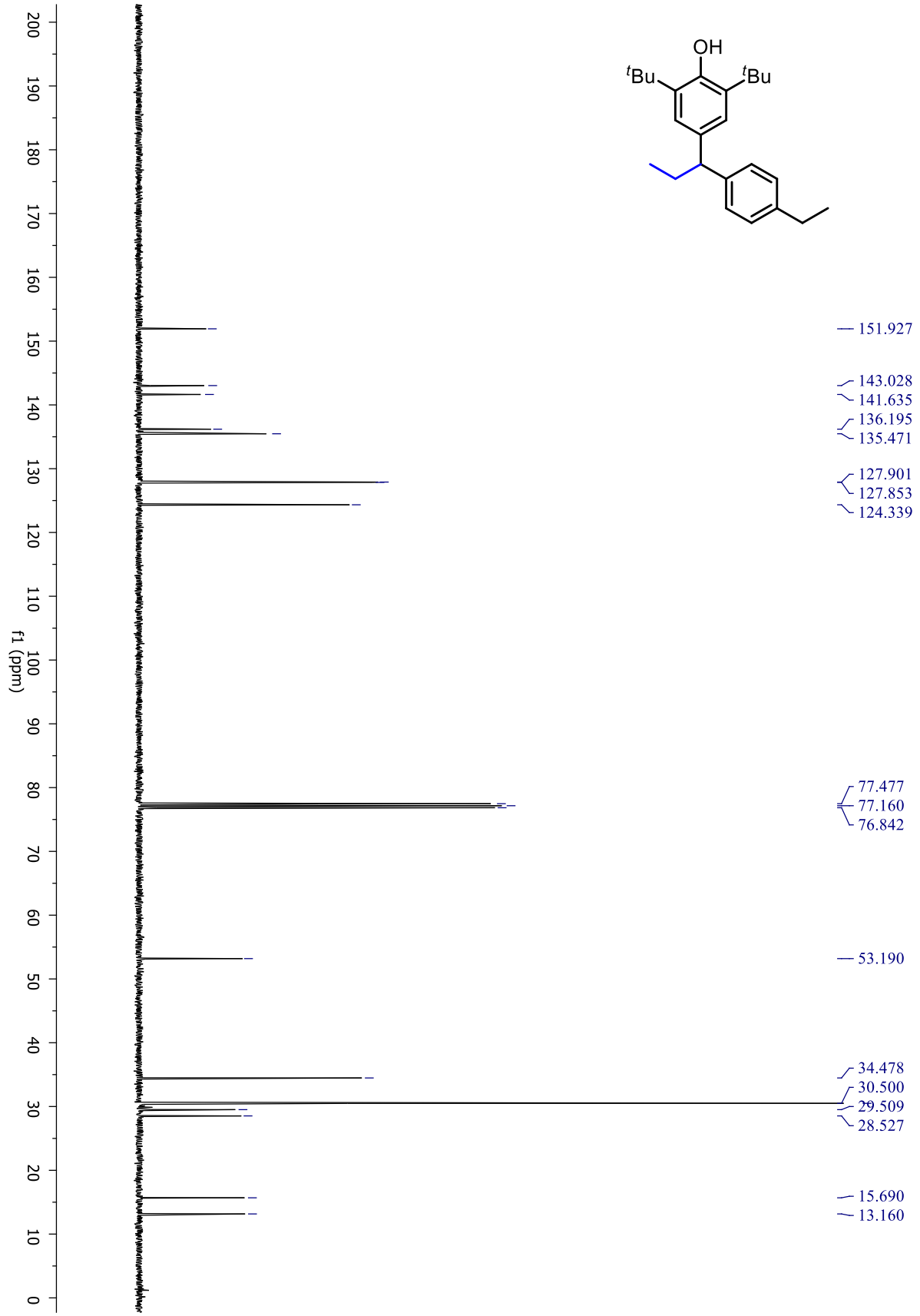
^{13}C NMR spectrum of compound **3b**



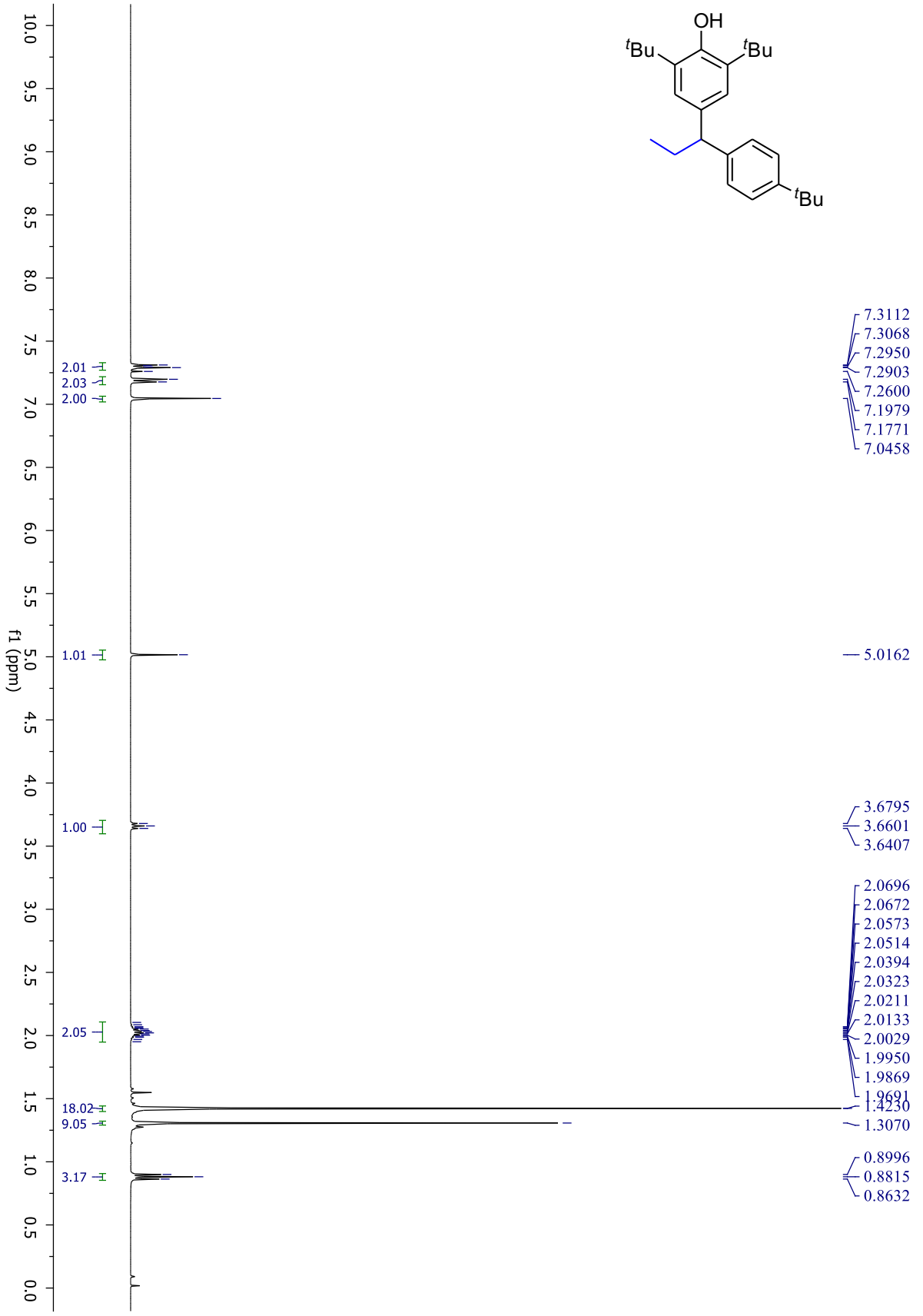
^{1}H NMR spectrum of compound **3c**



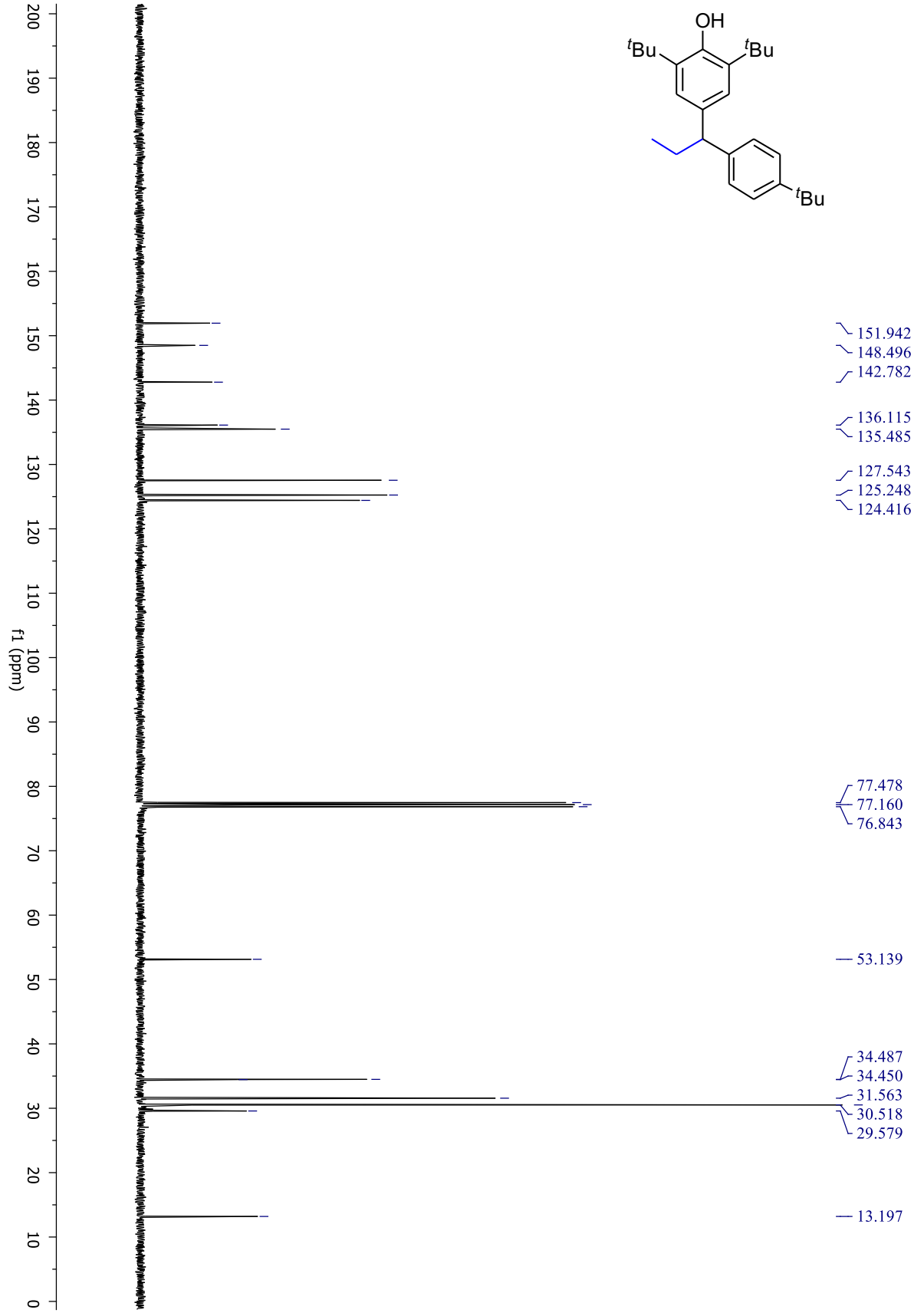
^{13}C NMR spectrum of compound **3c**



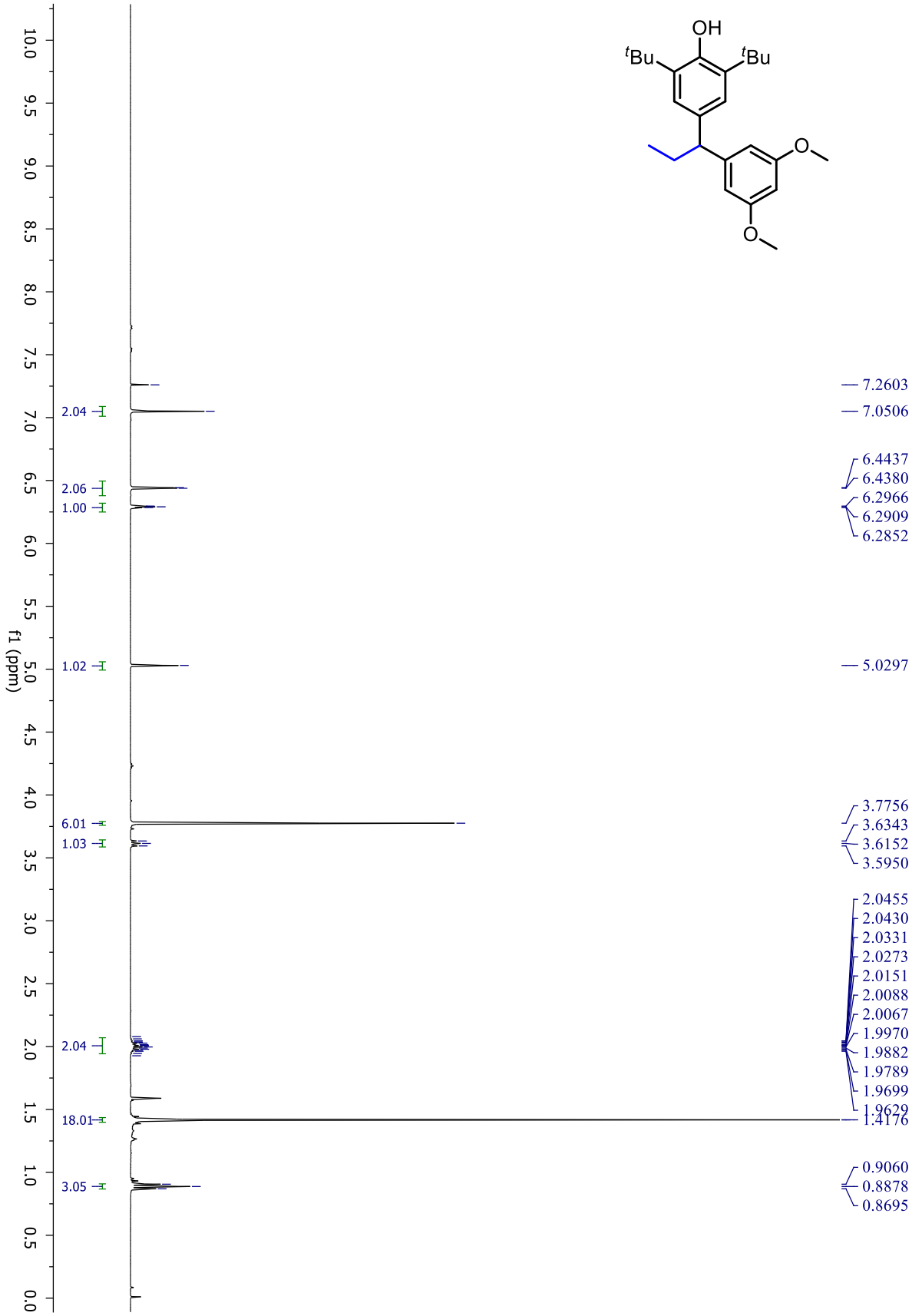
^{1}H NMR spectrum of compound **3d**



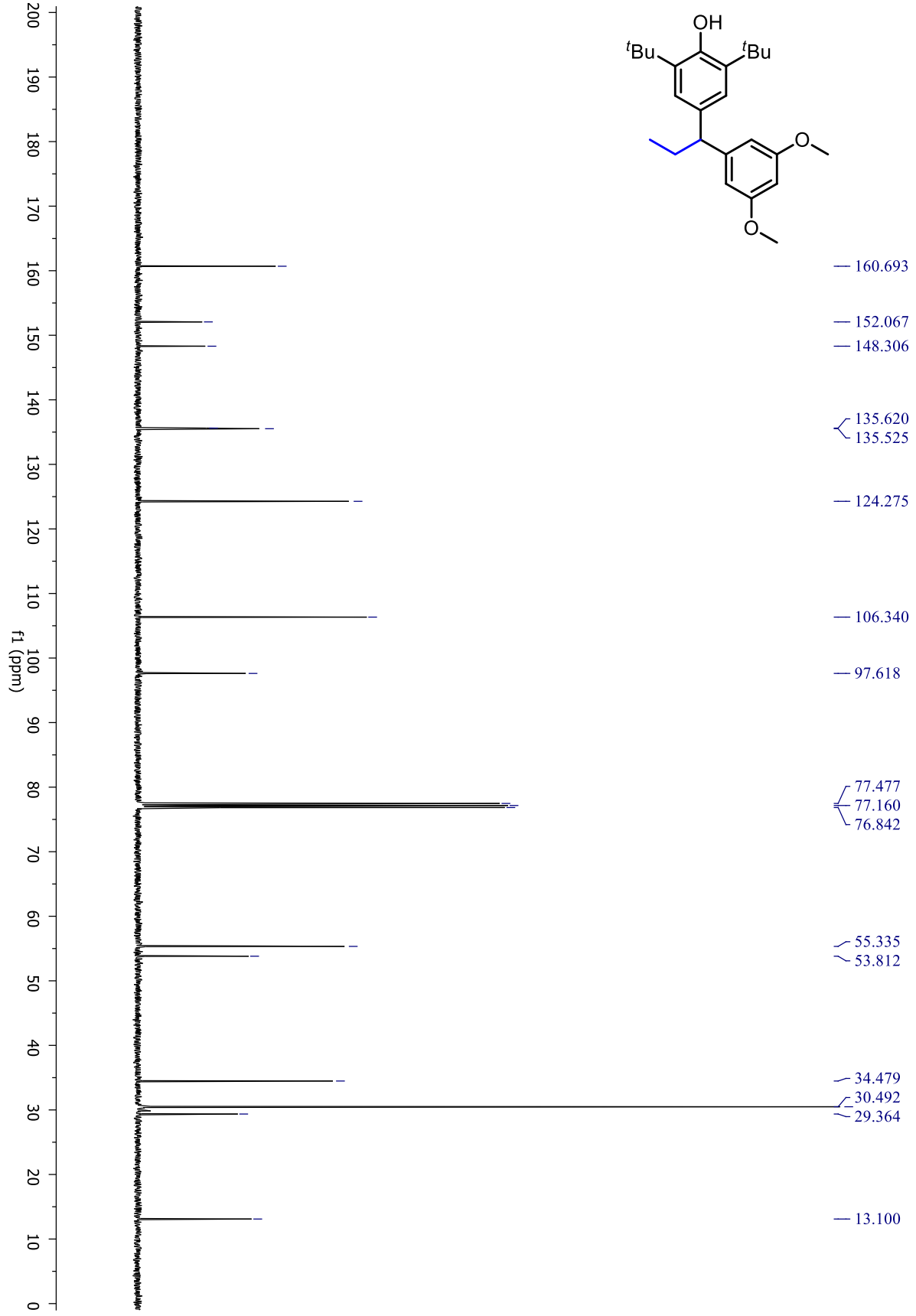
^{13}C NMR spectrum of compound **3d**



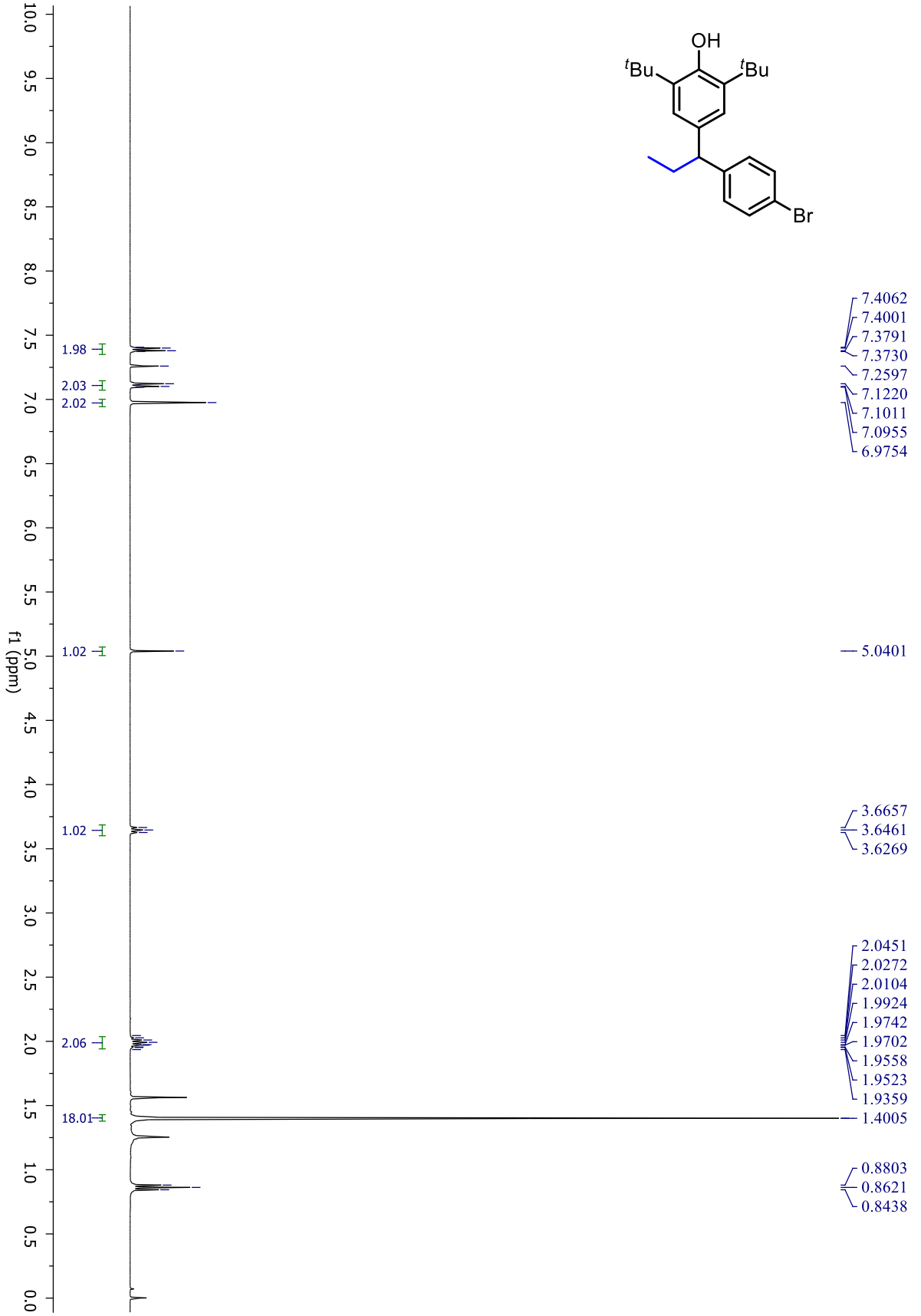
^{1}H NMR spectrum of compound **3e**



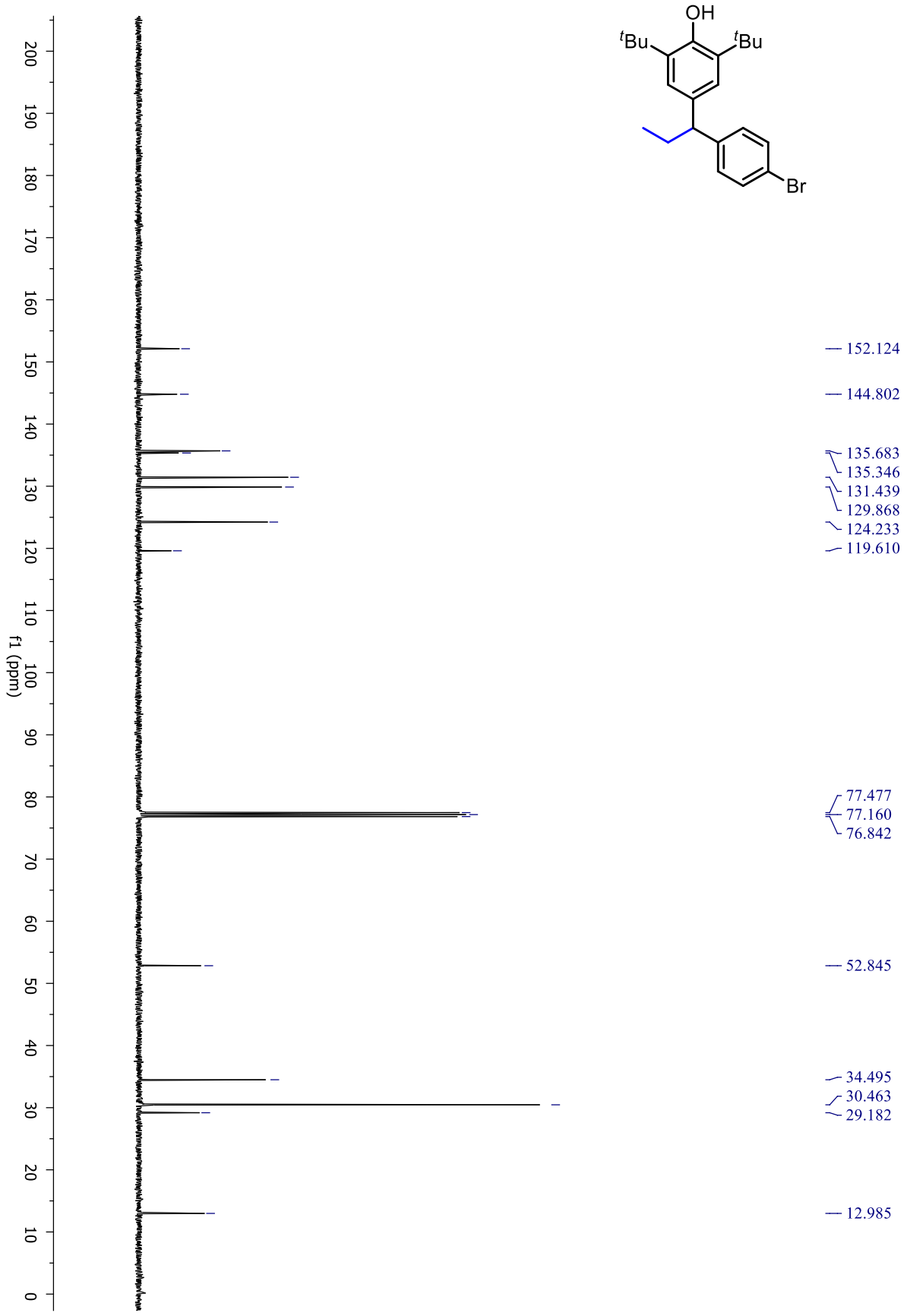
^{13}C NMR spectrum of compound **3e**



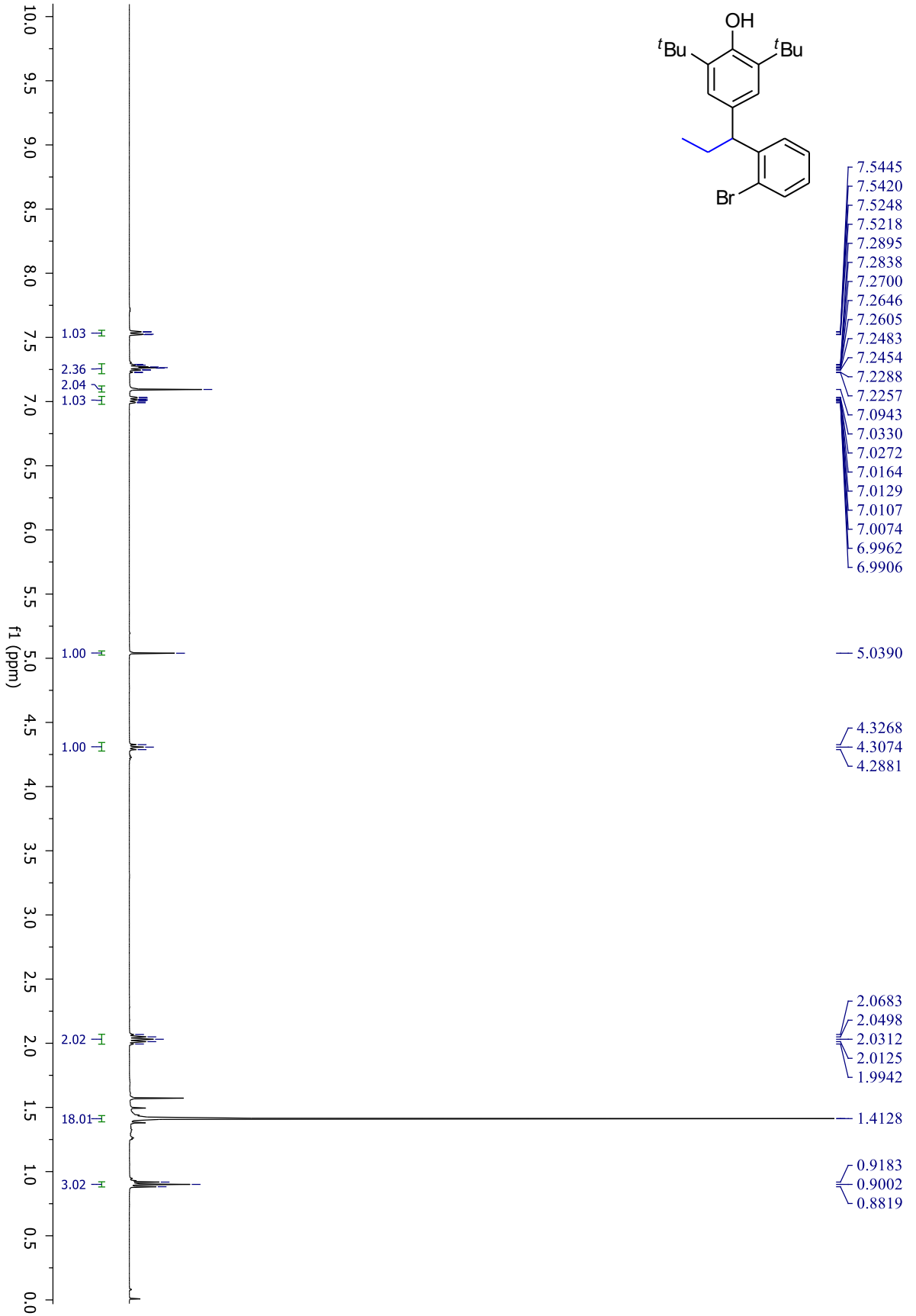
^{1}H NMR spectrum of compound **3f**



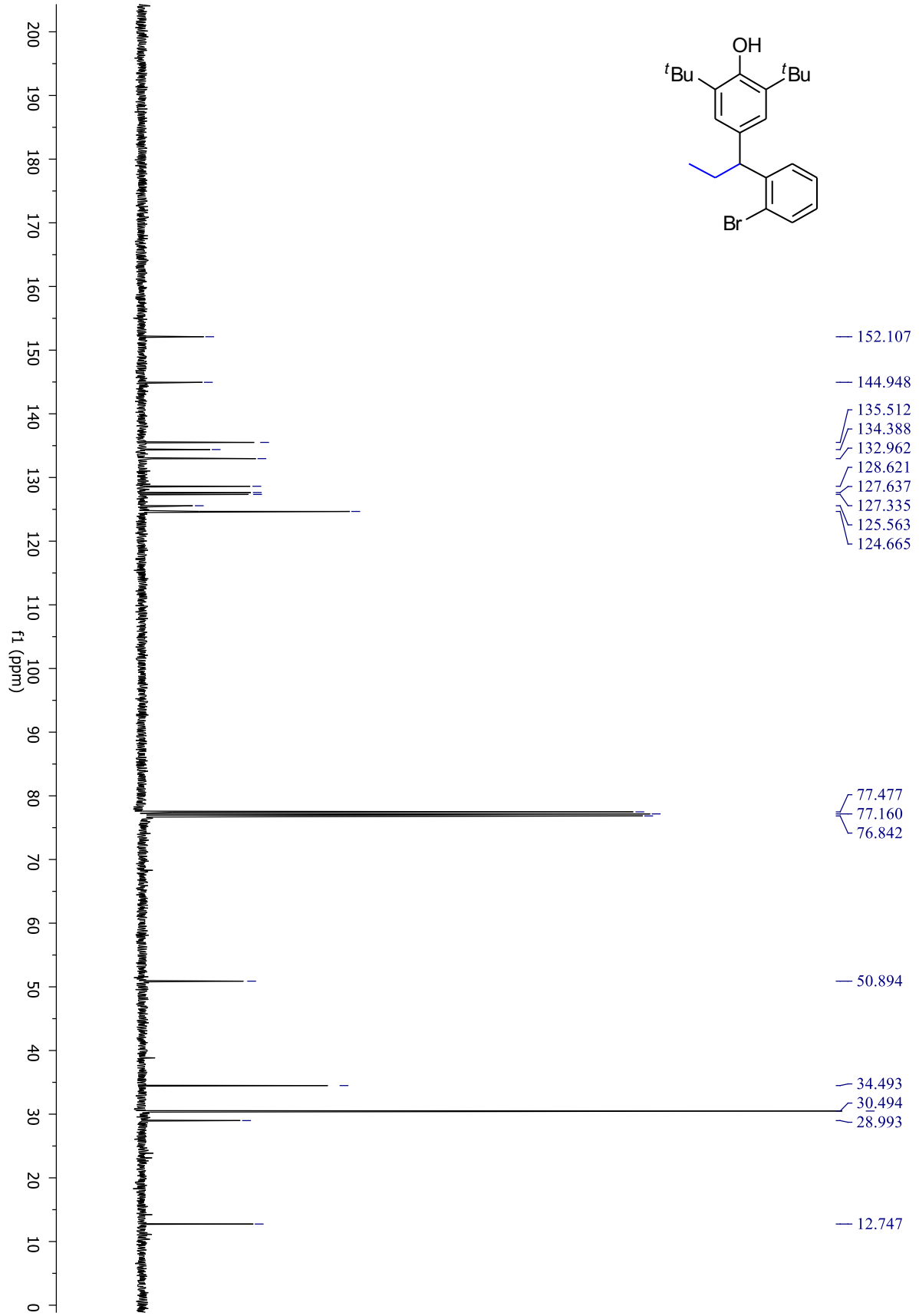
^{13}C NMR spectrum of compound **3f**



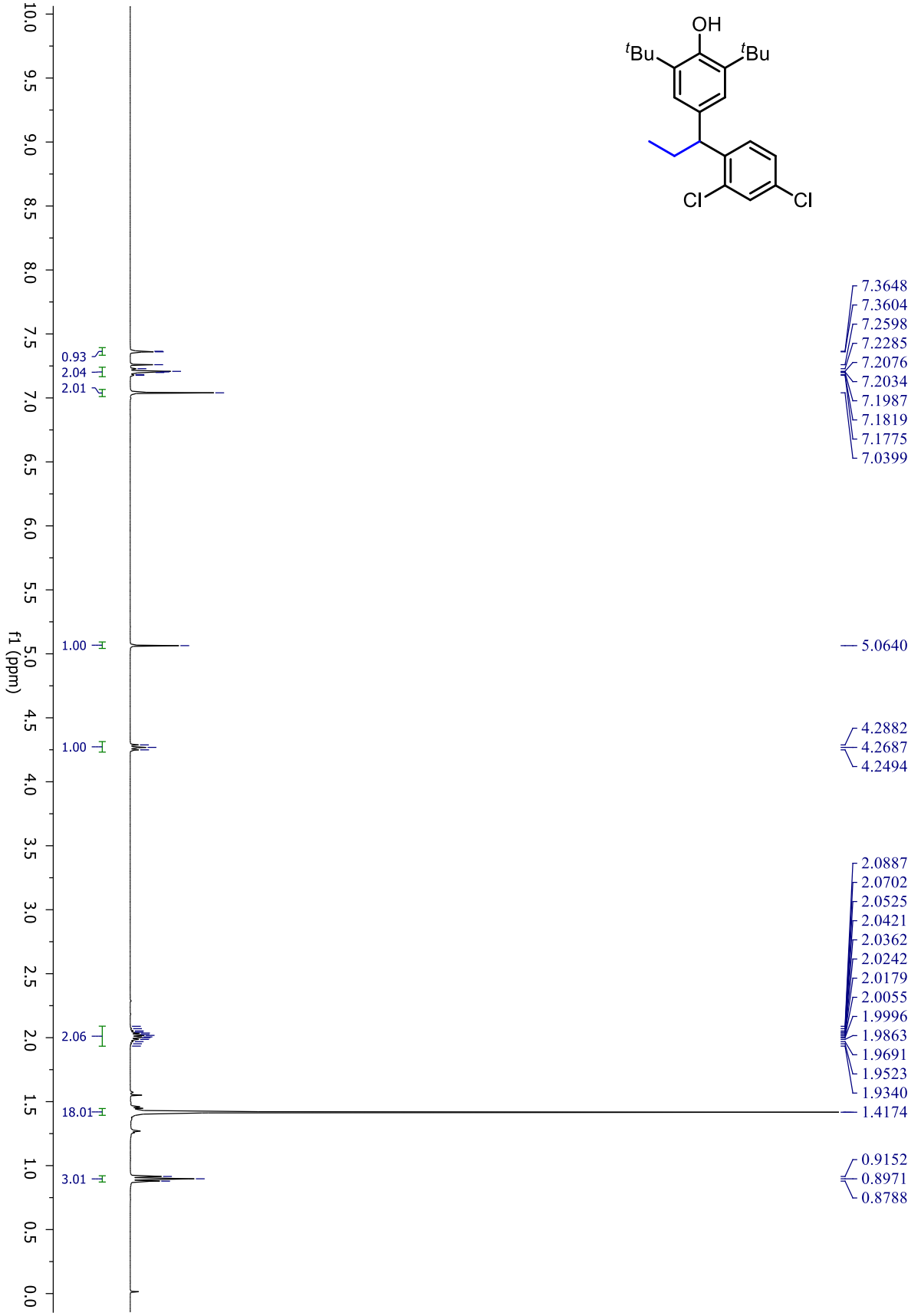
^{1}H NMR spectrum of compound **3g**



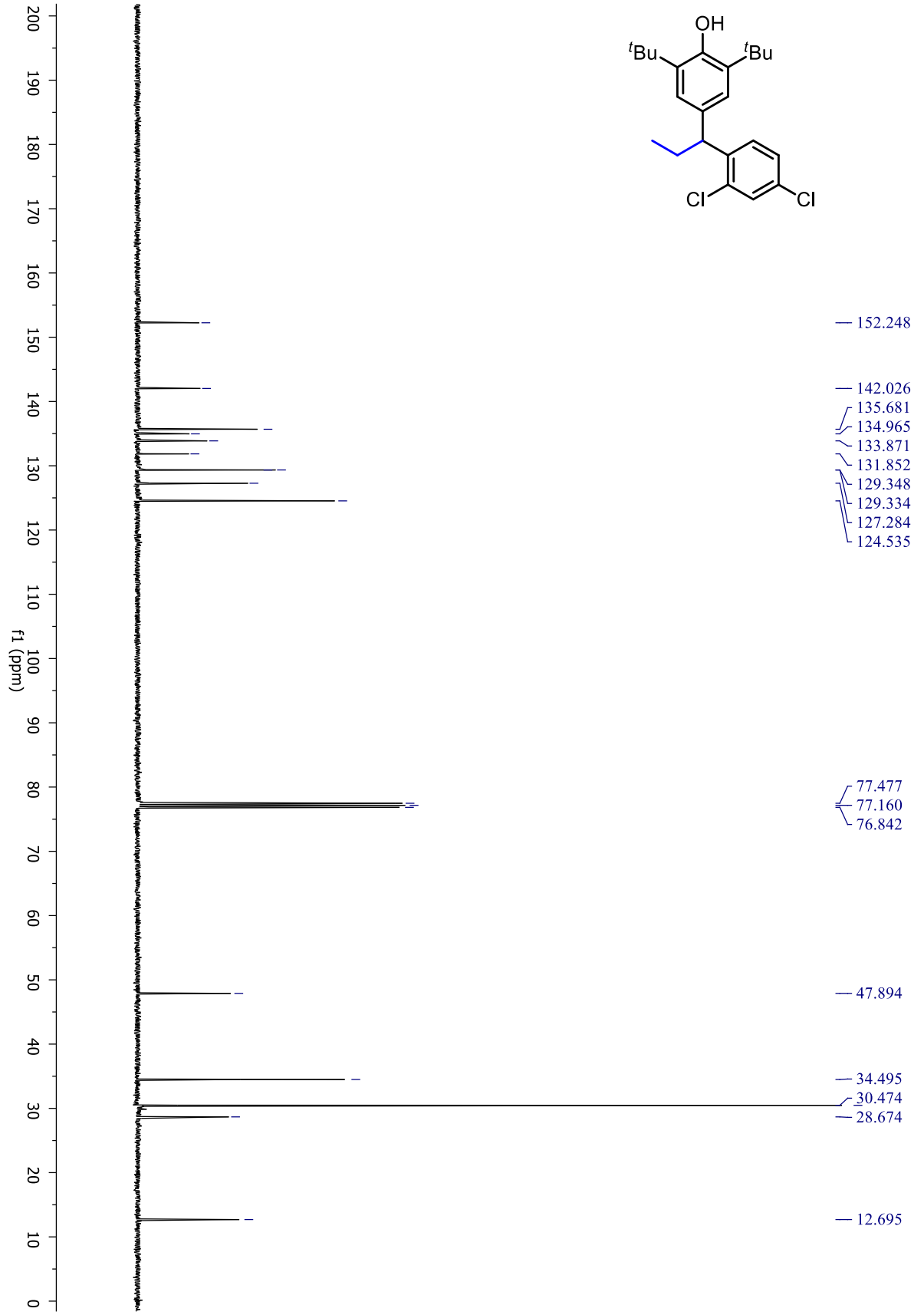
^{13}C NMR spectrum of compound **3g**



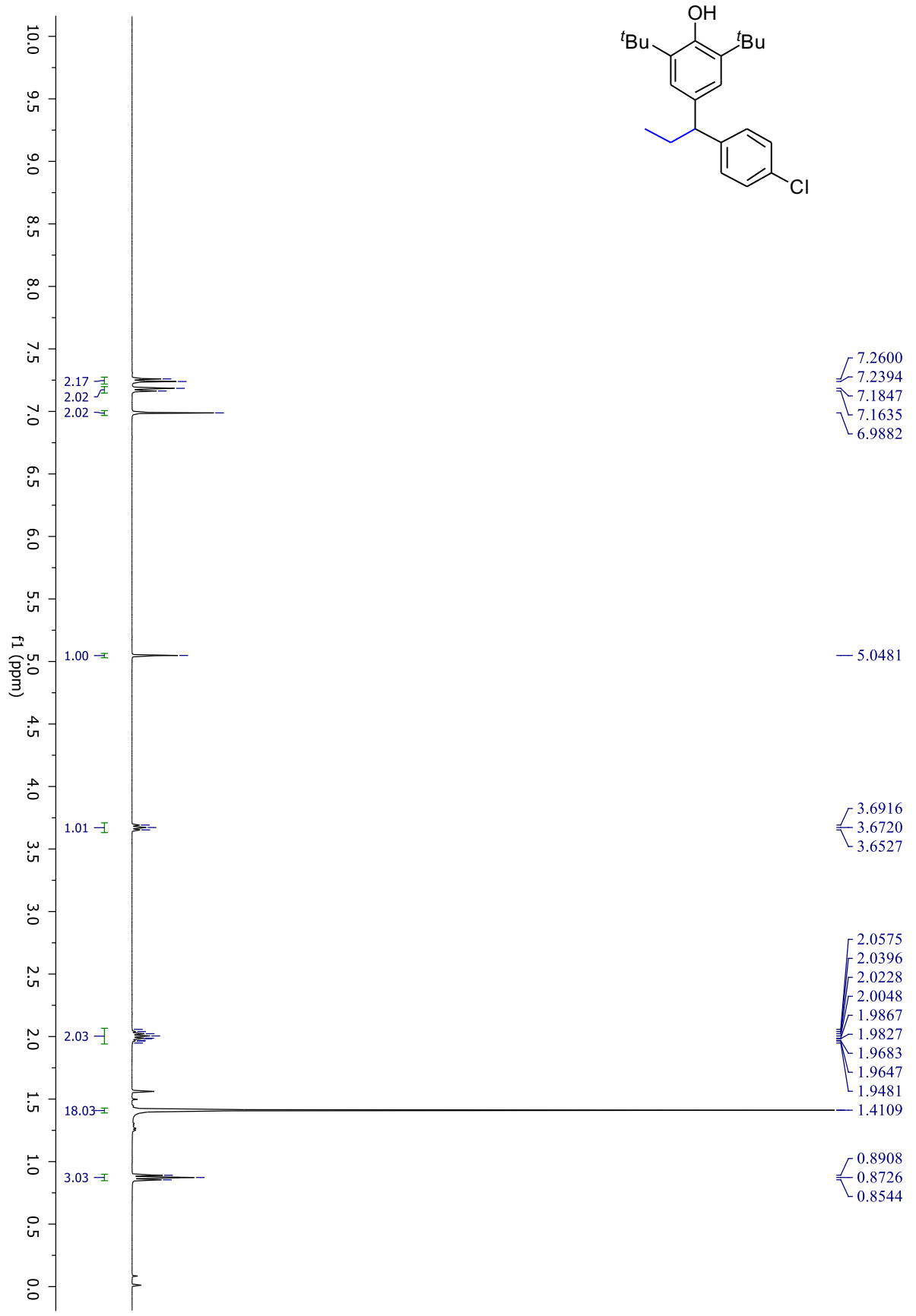
^{1}H NMR spectrum of compound **3h**



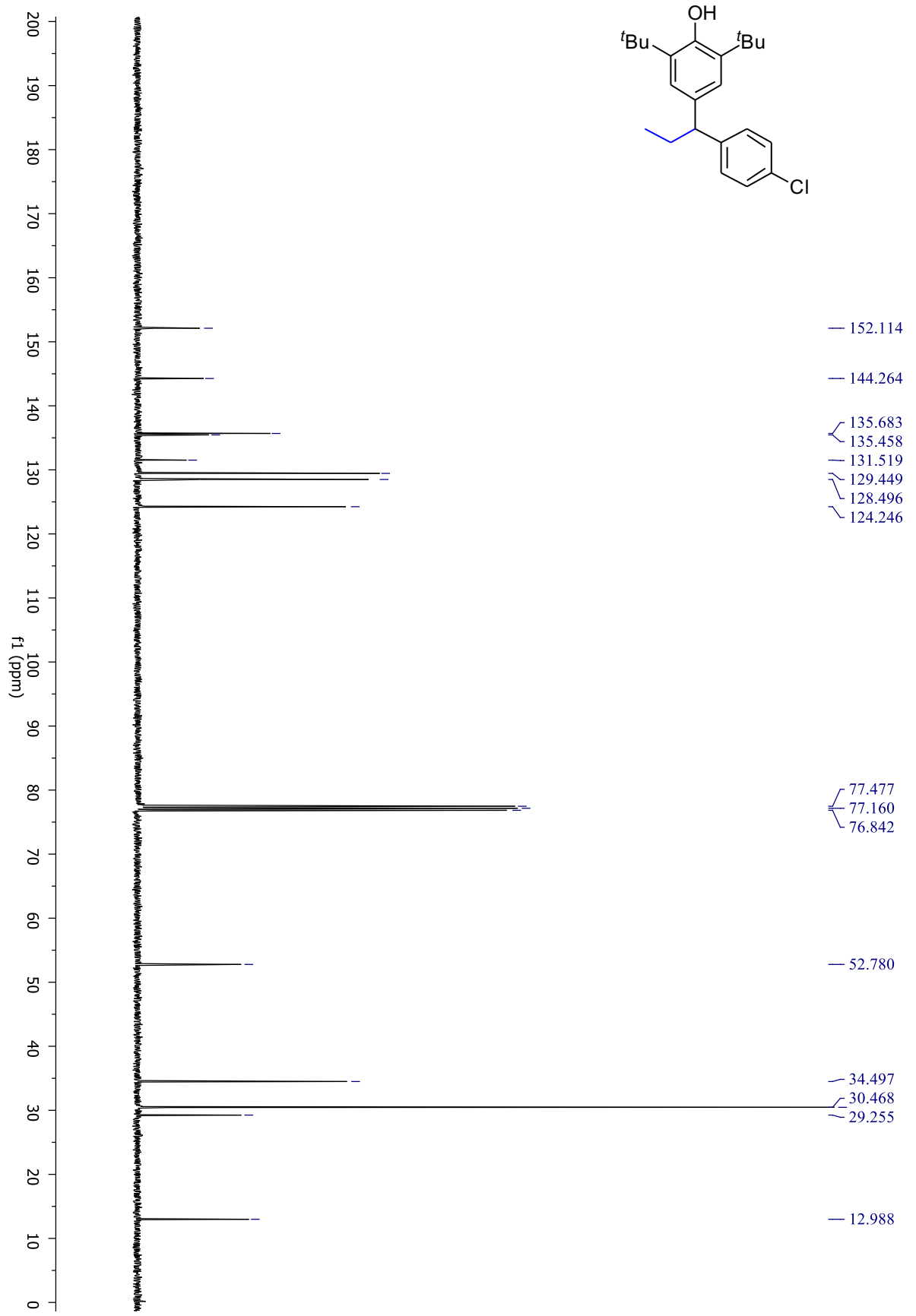
^{13}C NMR spectrum of compound **3h**



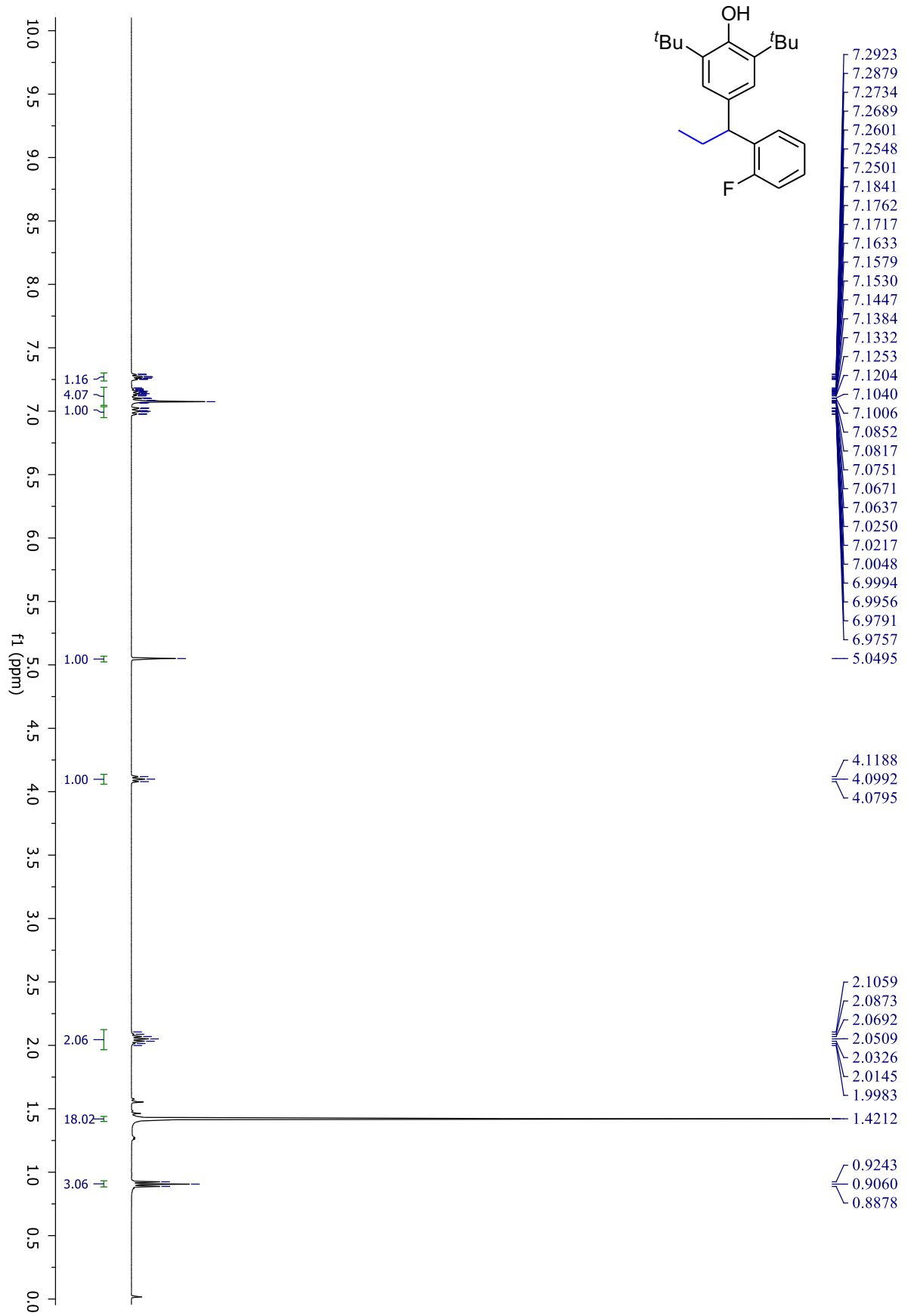
^{1}H NMR spectrum of compound **3i**



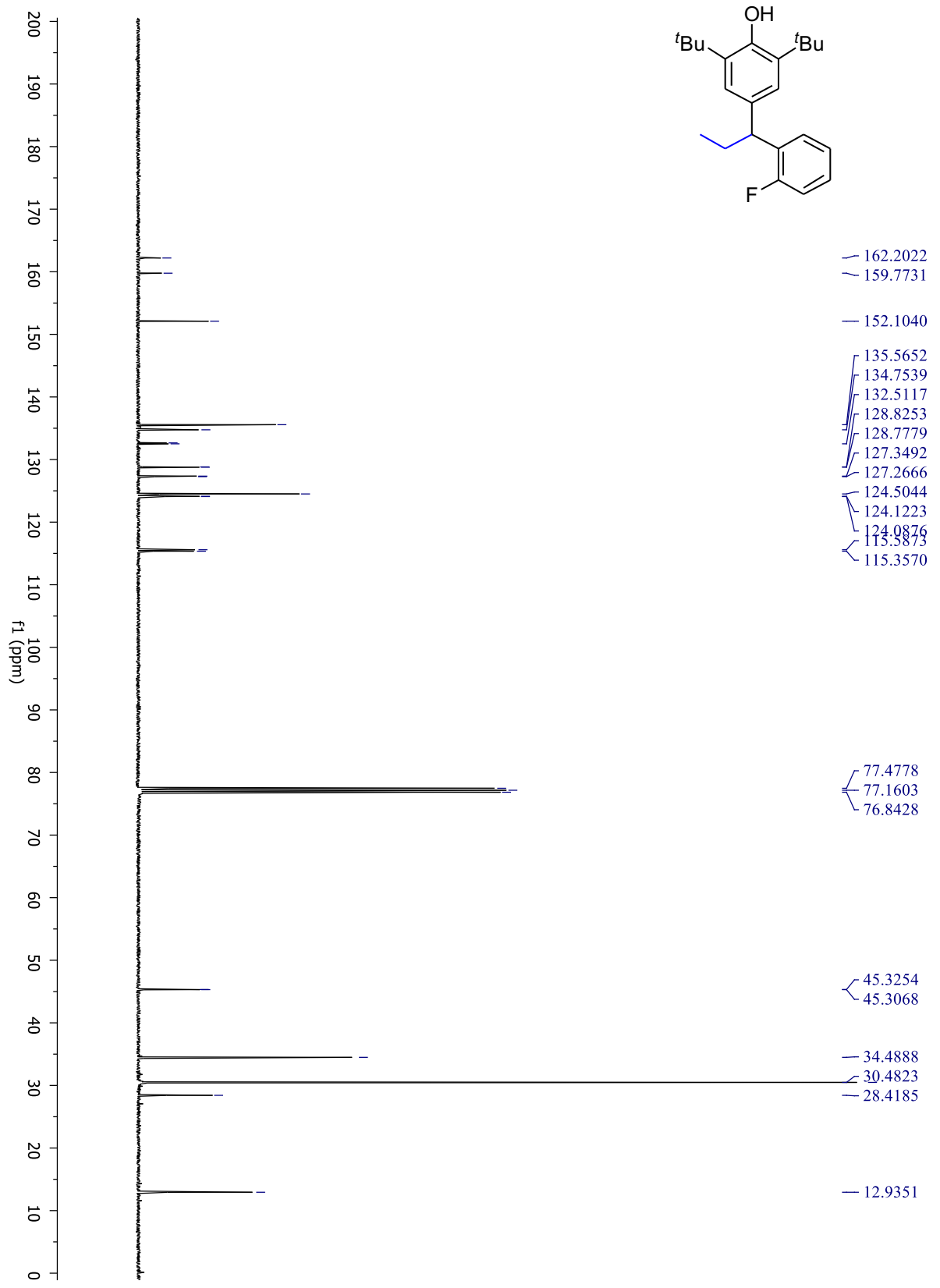
^{13}C NMR spectrum of compound **3i**



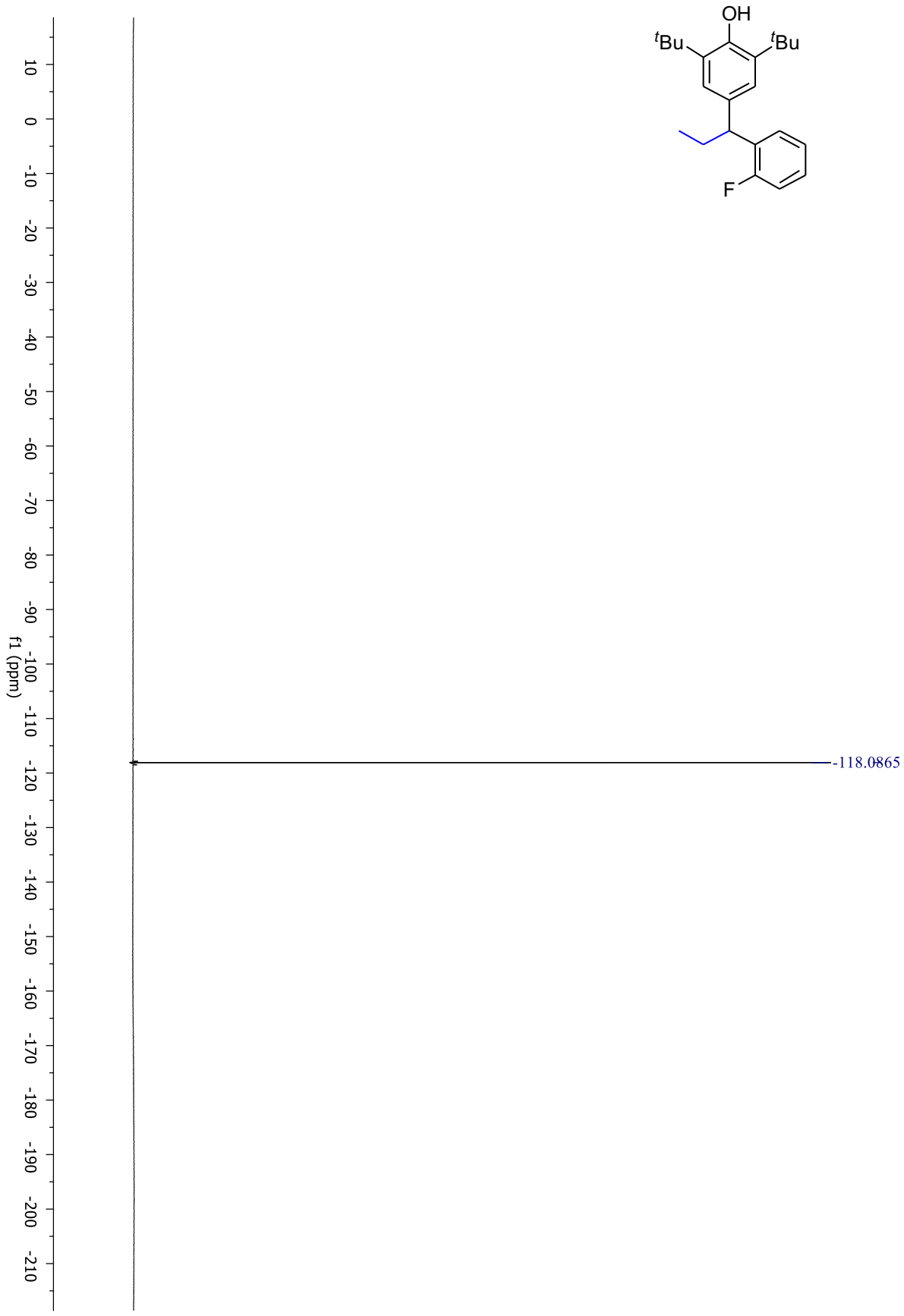
^{1}H NMR spectrum of compound **3j**



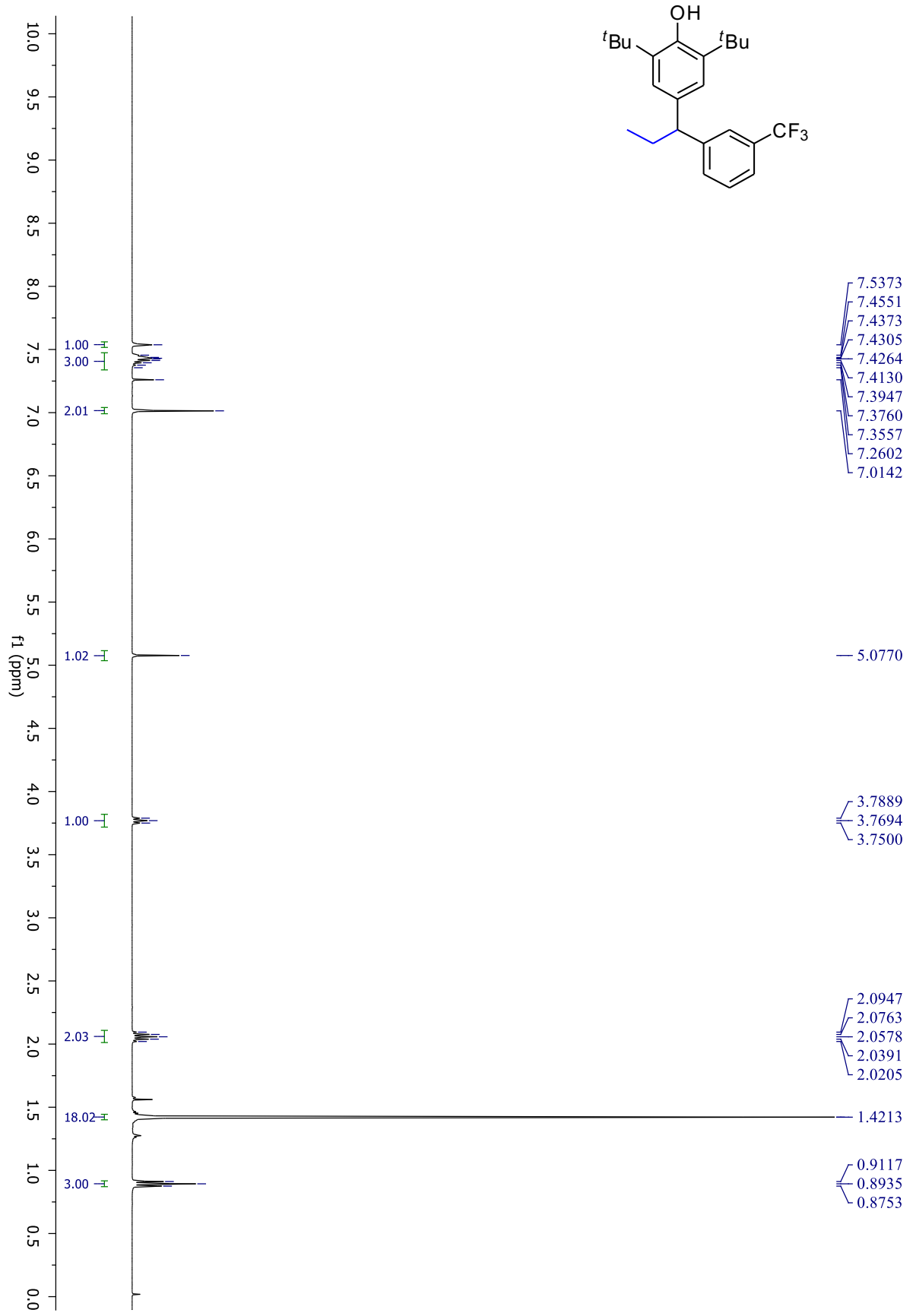
^{13}C NMR spectrum of compound **3j**



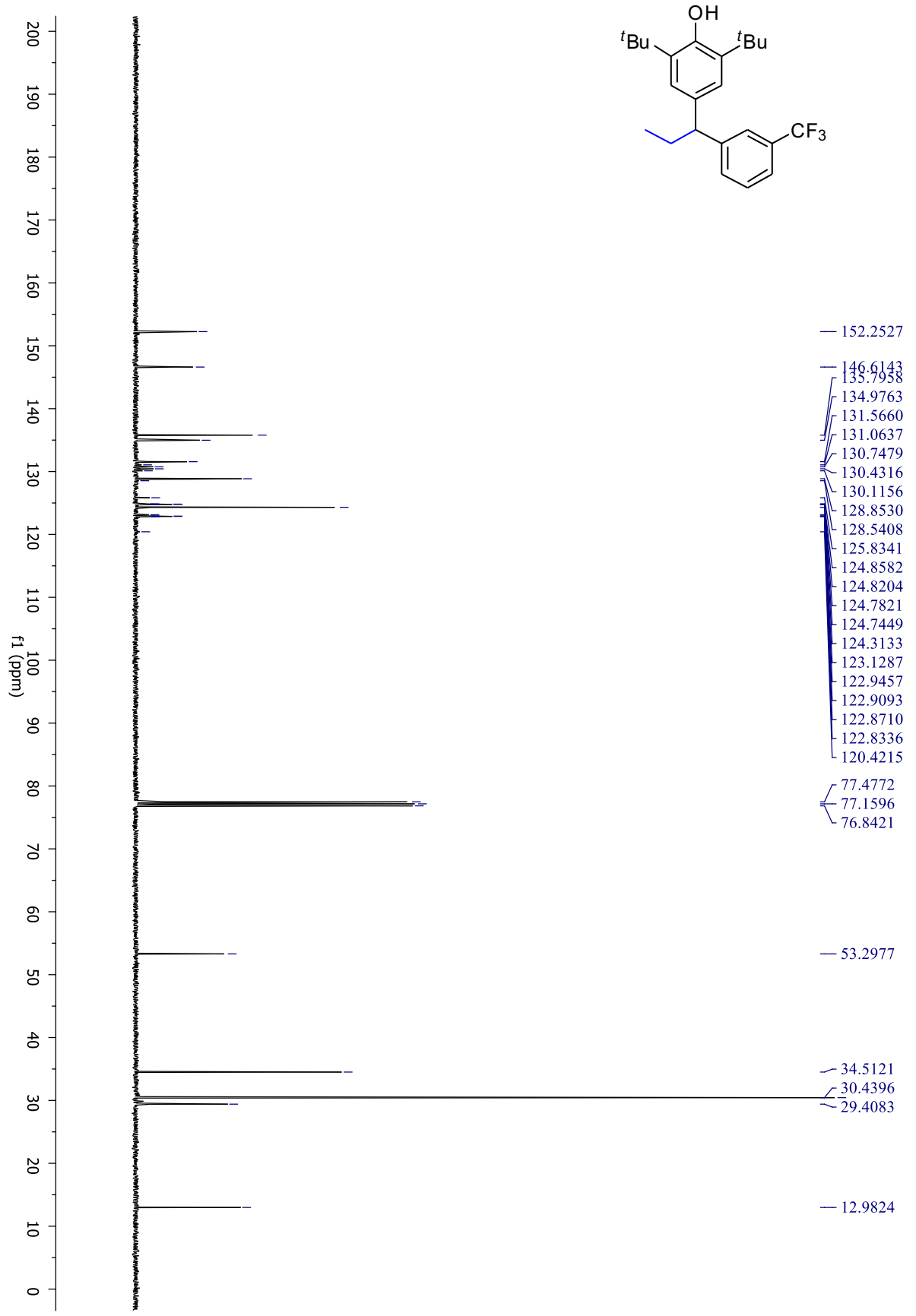
^{19}F NMR spectrum of compound **3j**



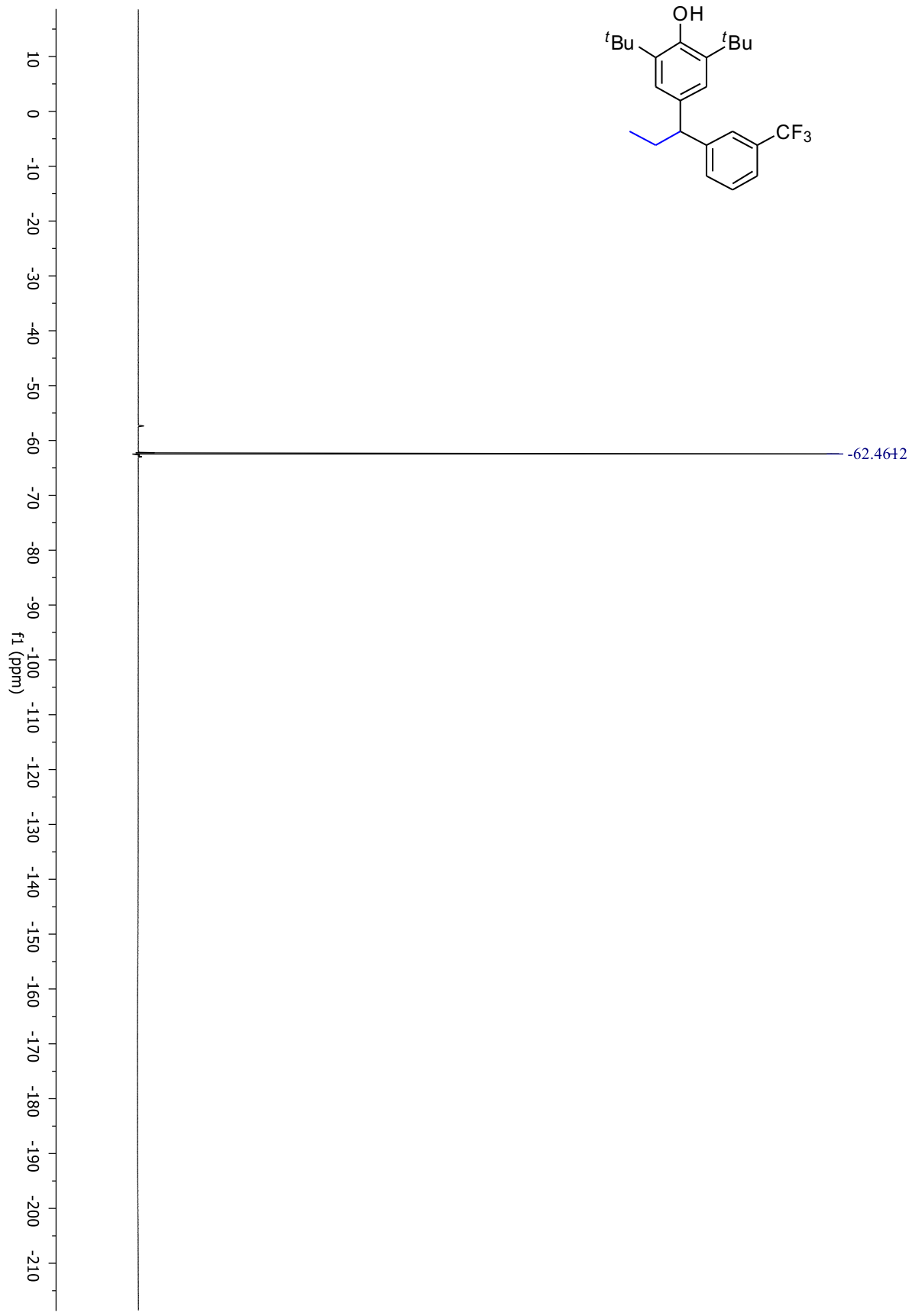
^{1}H NMR spectrum of compound **3k**



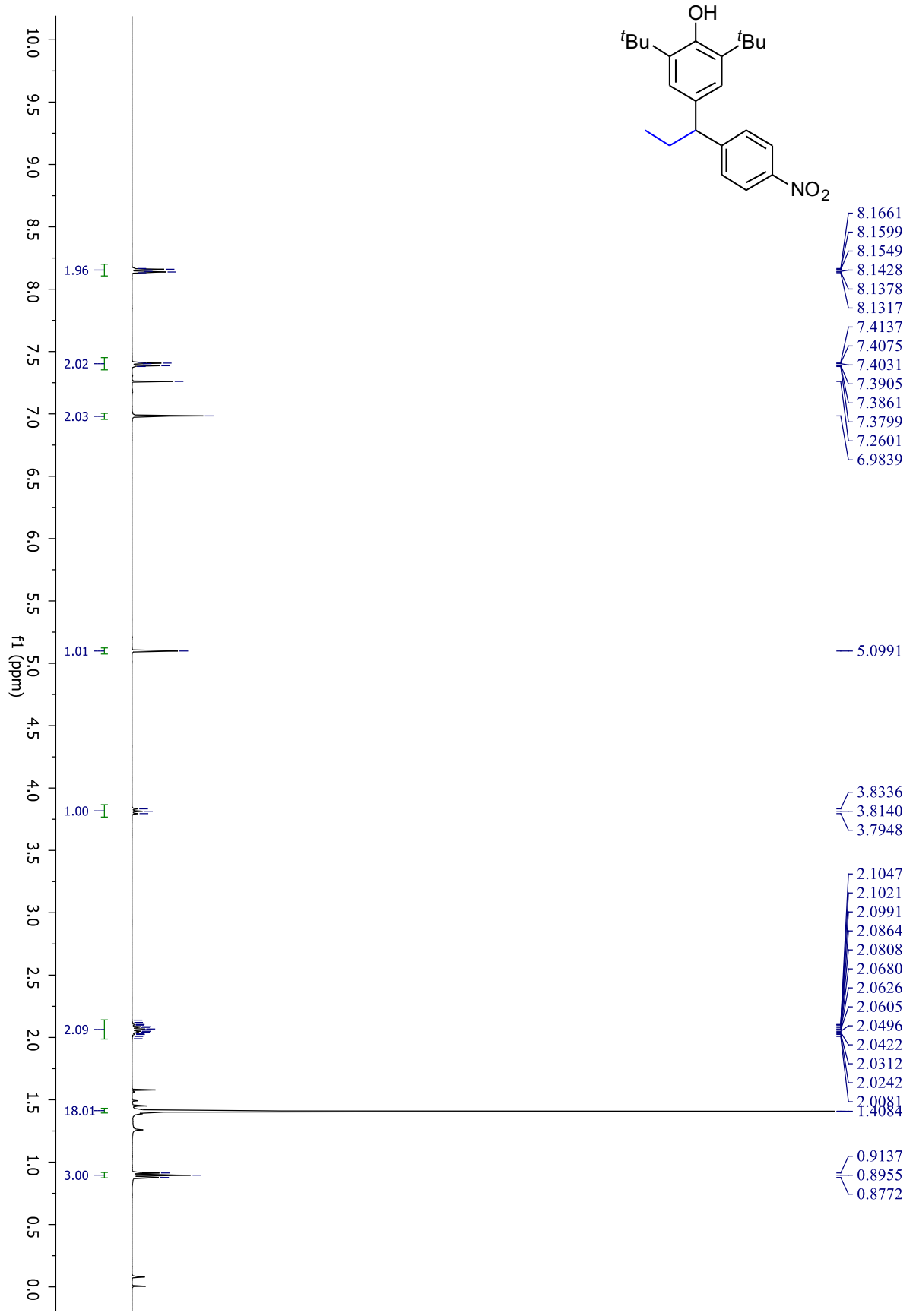
^{13}C NMR spectrum of compound **3k**



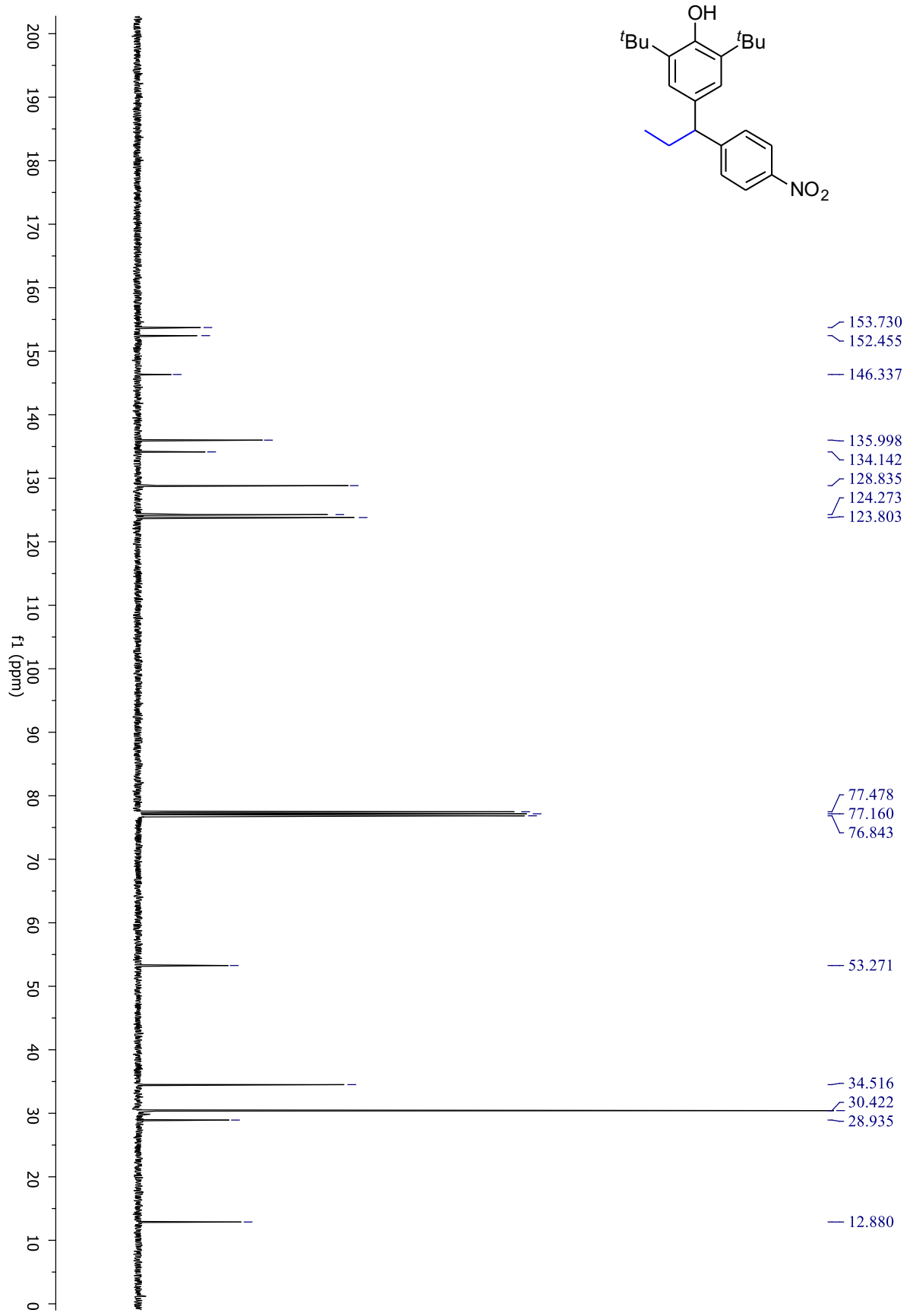
^{19}F NMR spectrum of compound **3k**



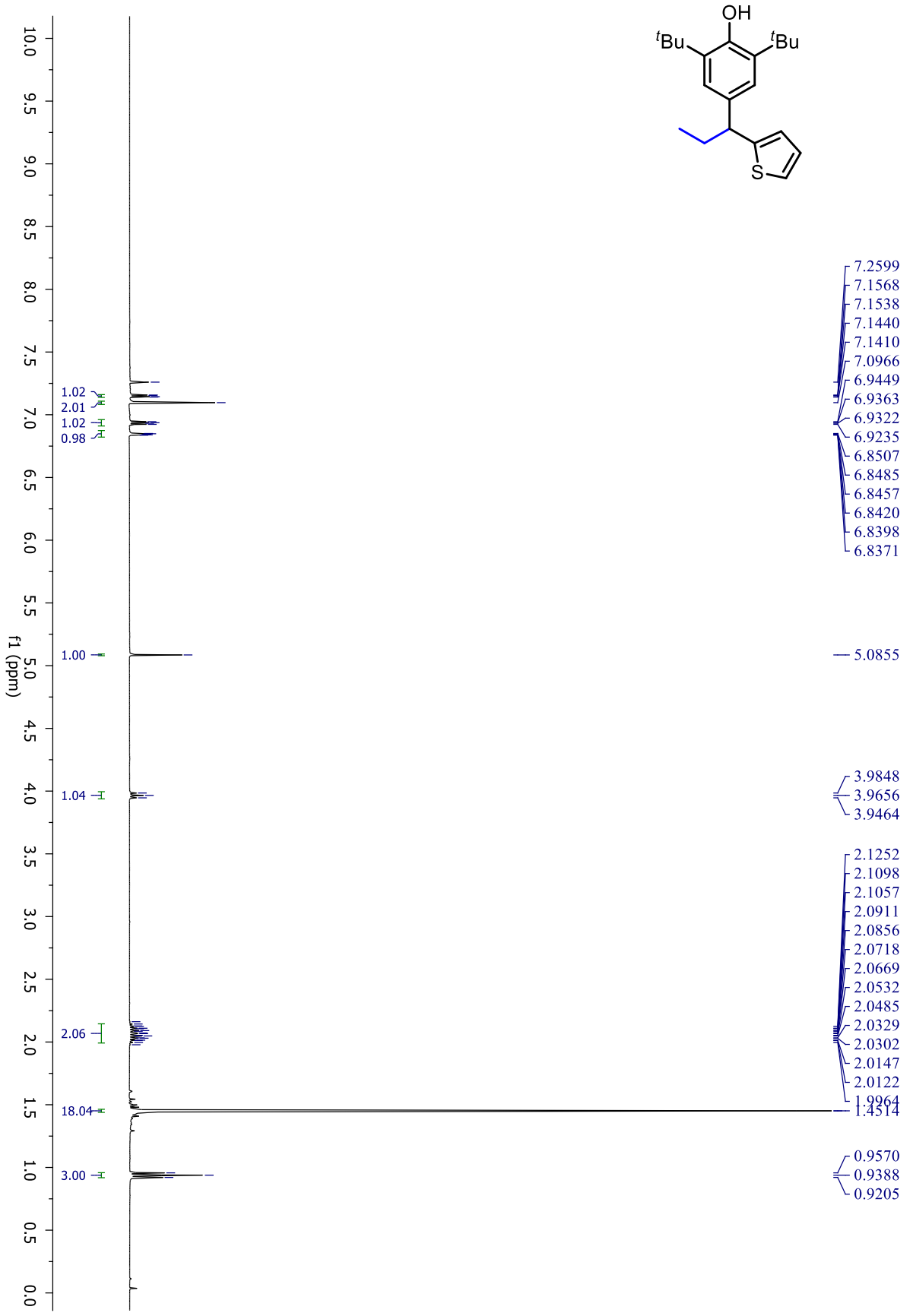
^{1}H NMR spectrum of compound **3l**



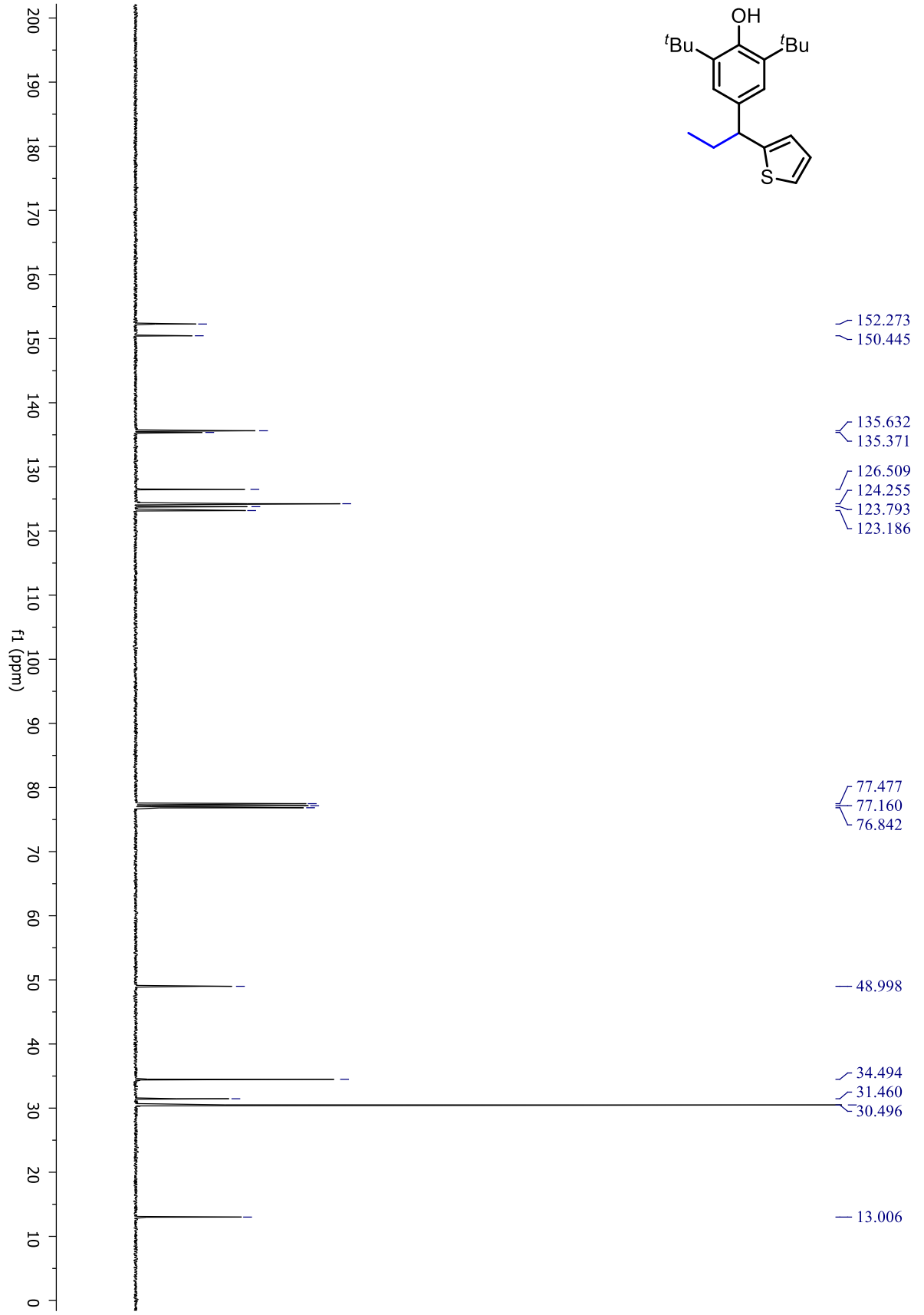
^{13}C NMR spectrum of compound **3l**



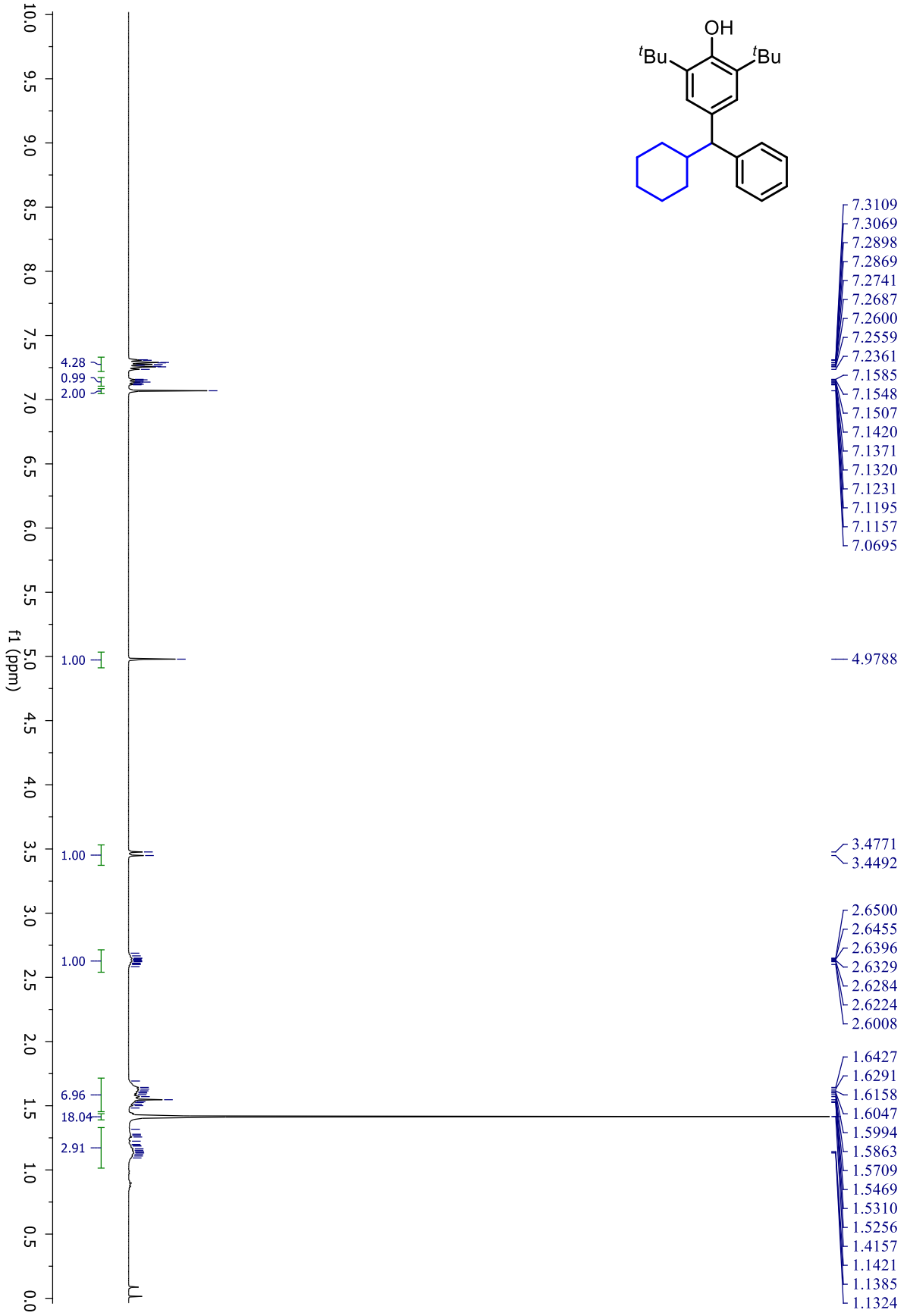
^{1}H NMR spectrum of compound **3m**



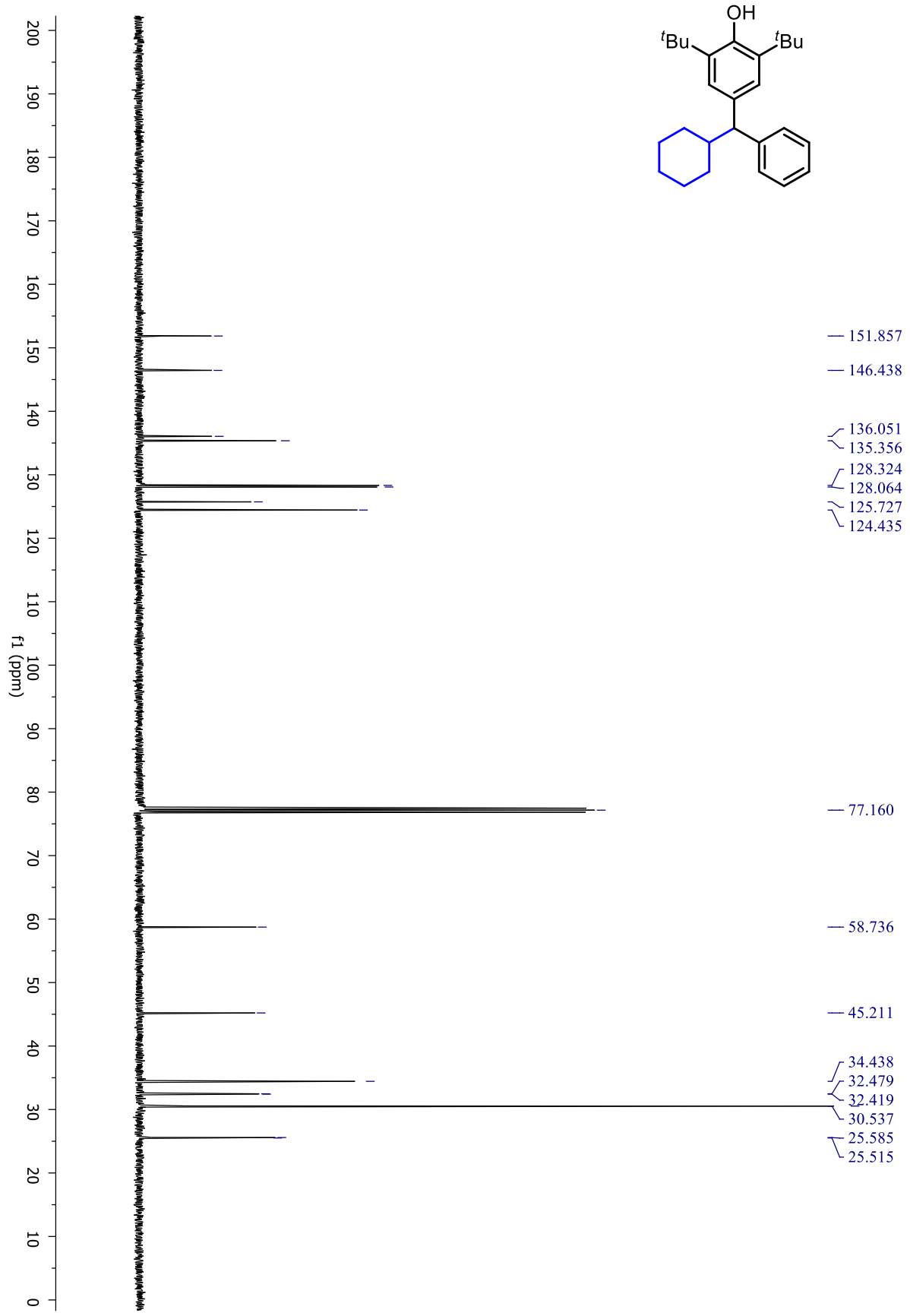
^{13}C NMR spectrum of compound **3m**



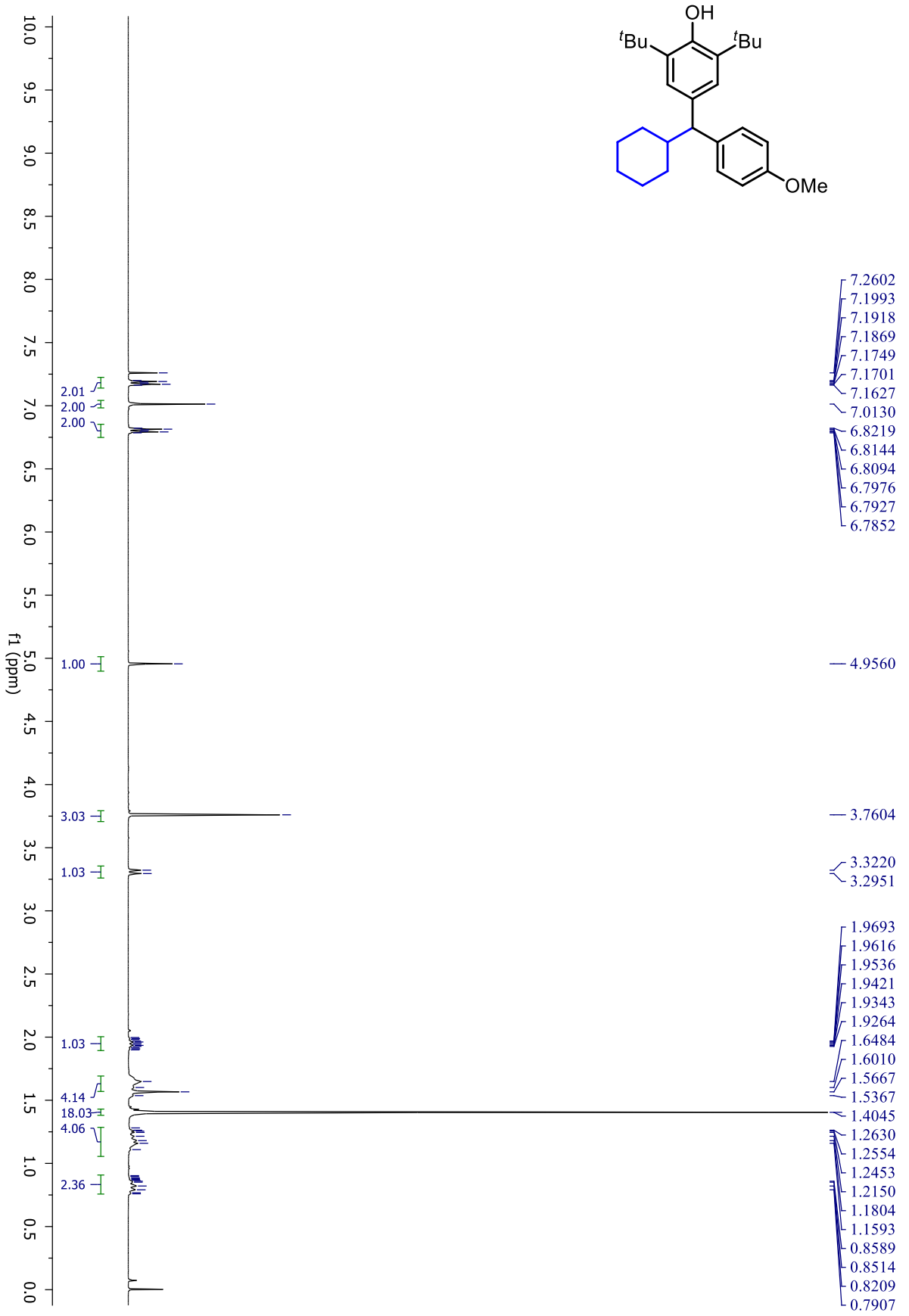
^{1}H NMR spectrum of compound **3n**



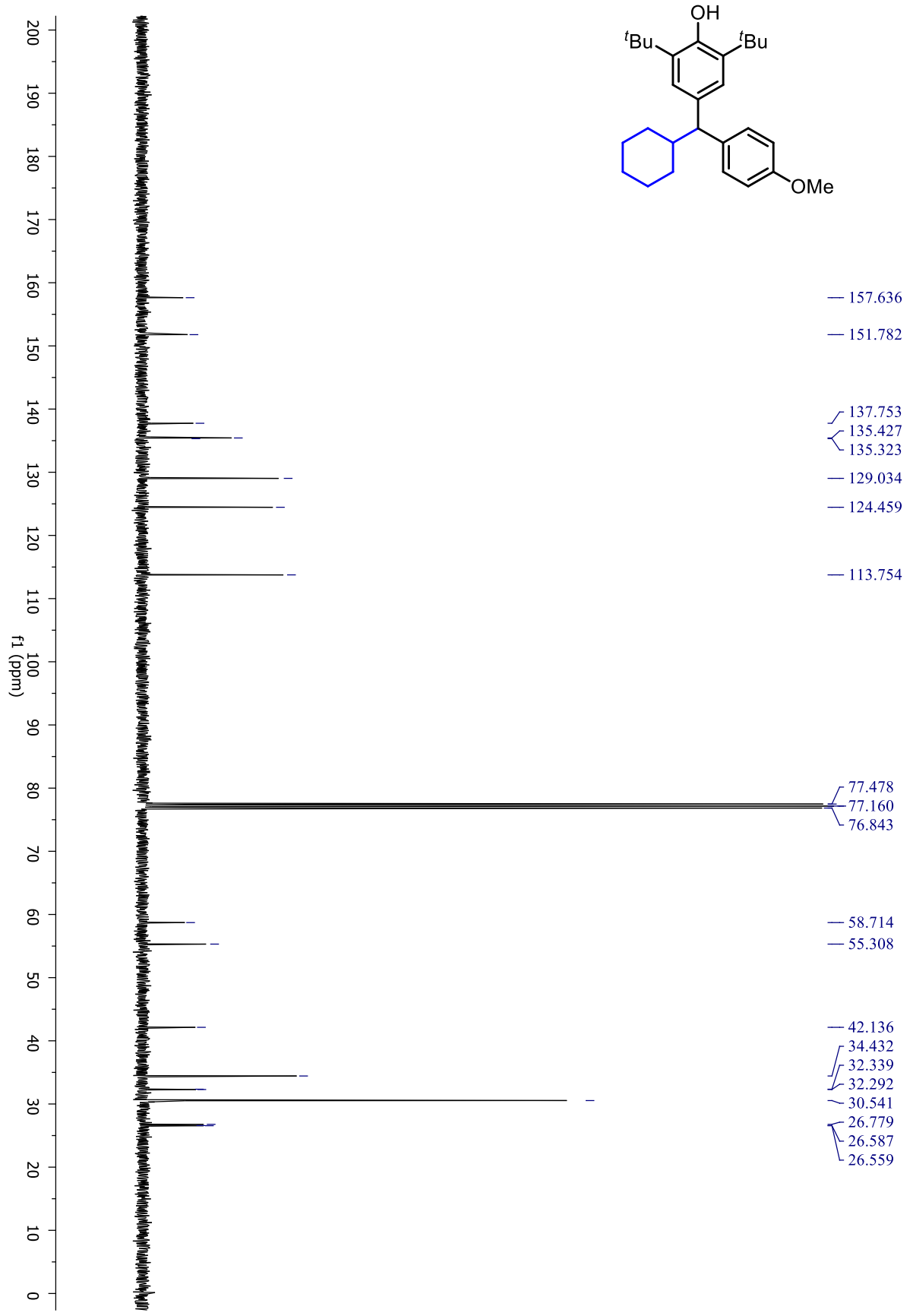
^{13}C NMR spectrum of compound **3n**



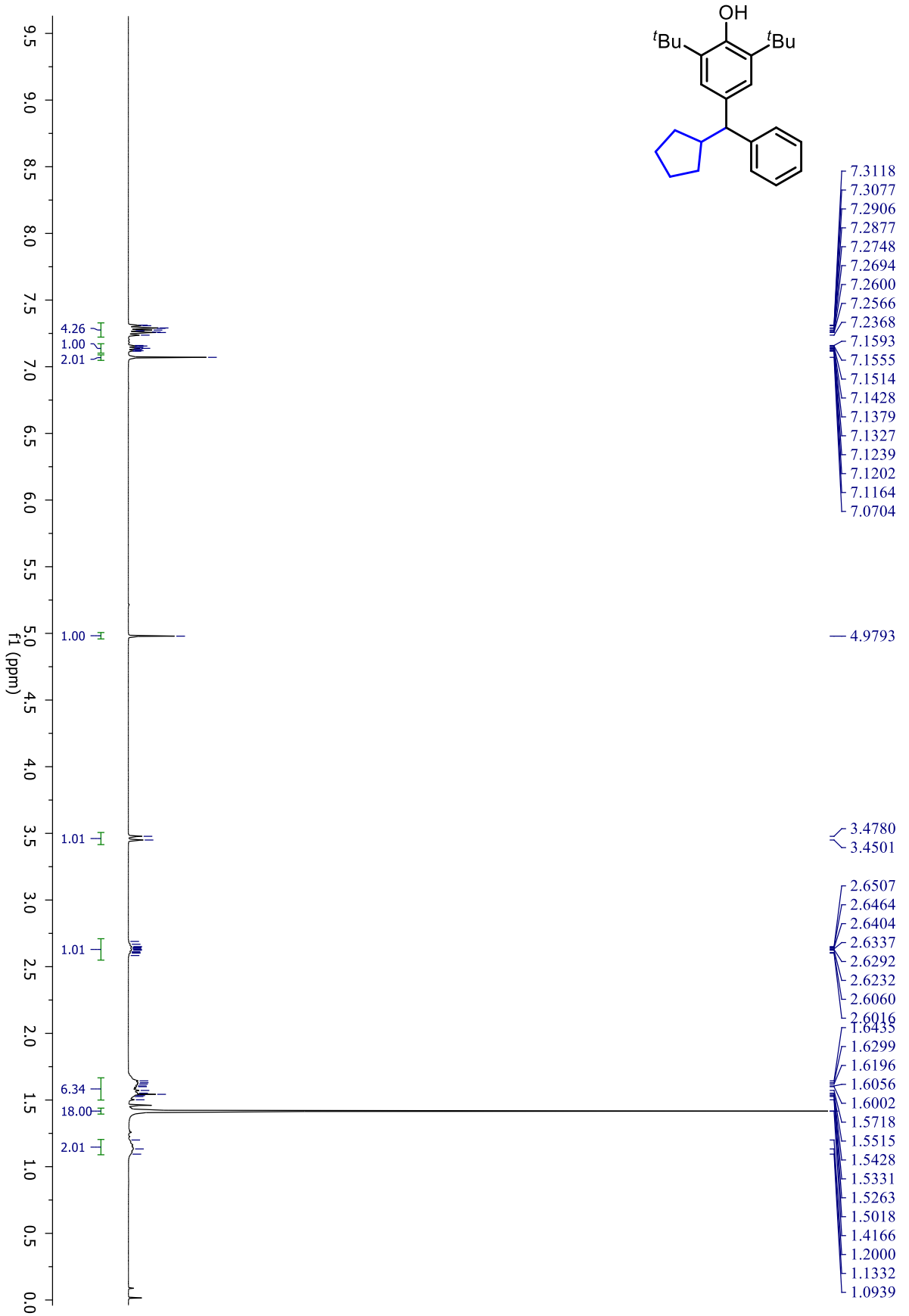
^{1}H NMR spectrum of compound **3o**



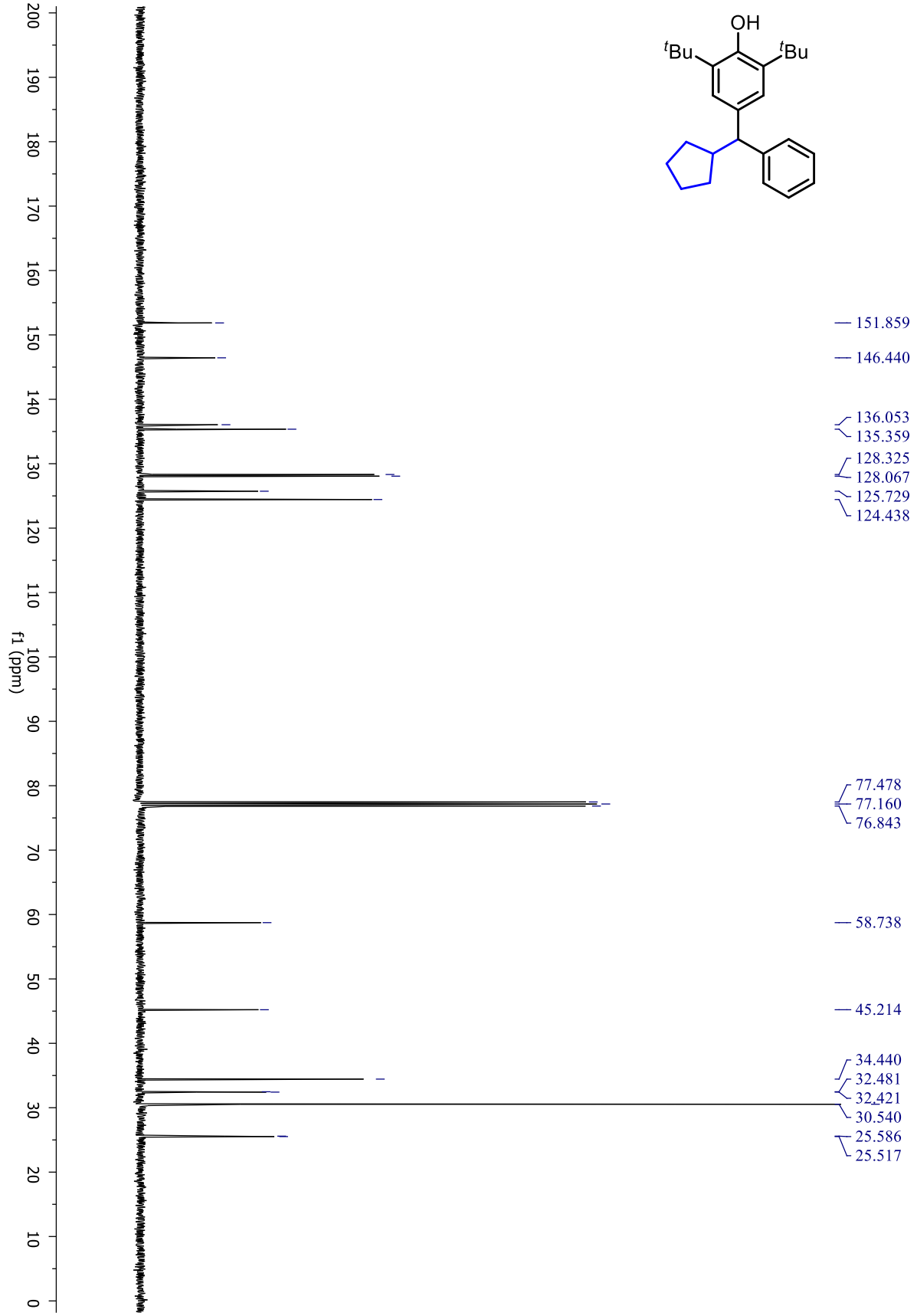
^{13}C NMR spectrum of compound **3o**



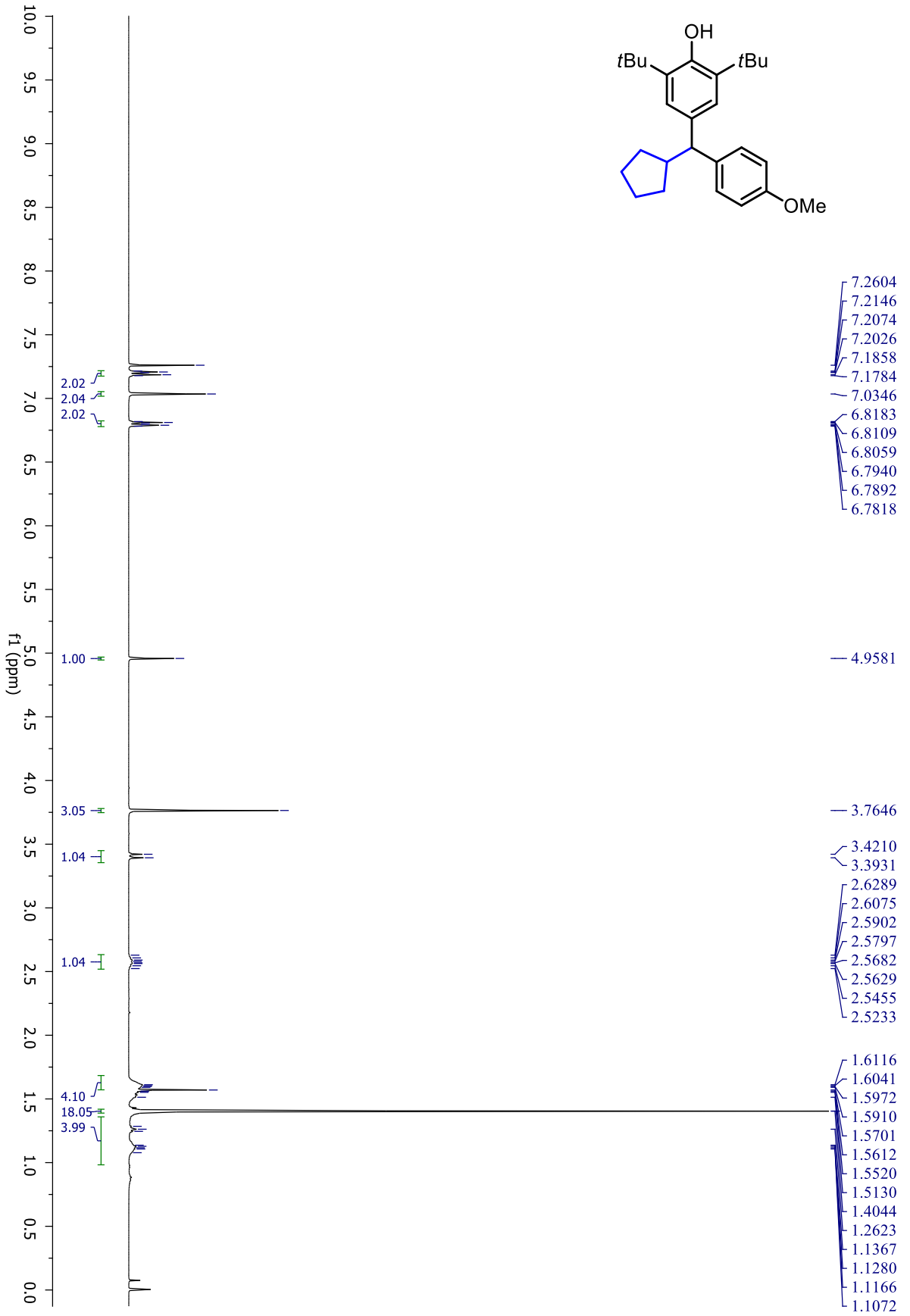
^{1}H NMR spectrum of compound **3p**



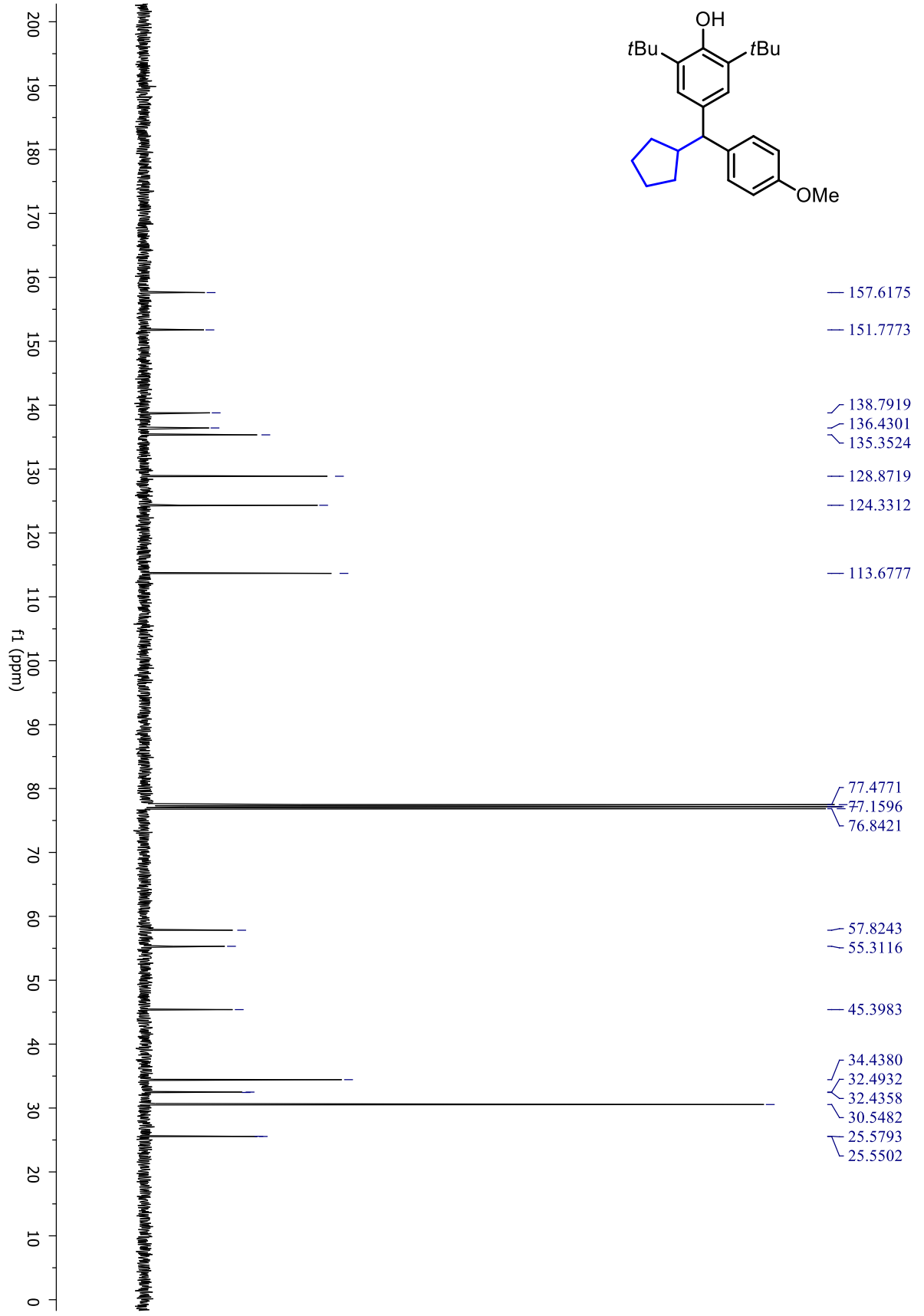
^{13}C NMR spectrum of compound **3p**



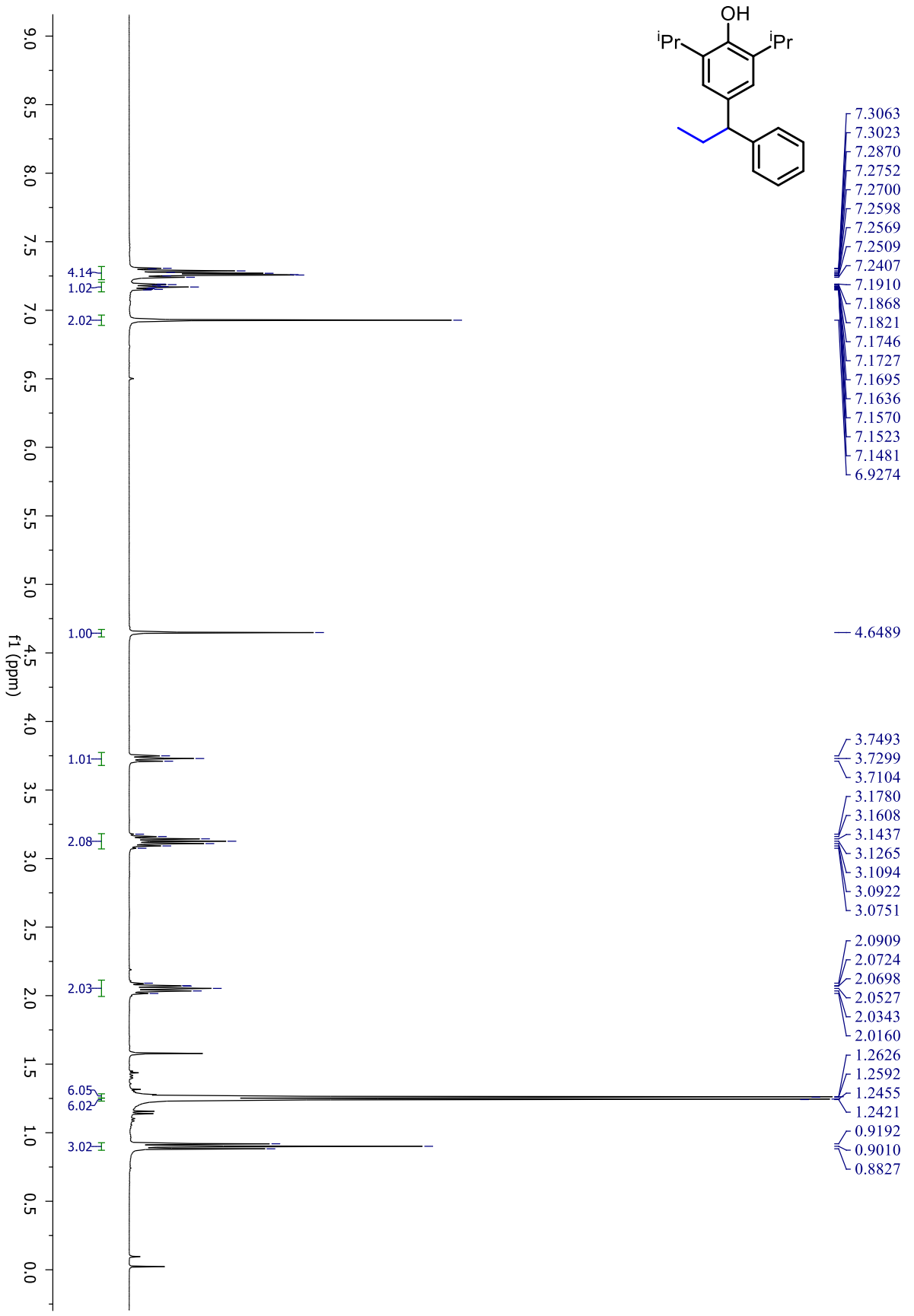
^{1}H NMR spectrum of compound **3q**



^{13}C NMR spectrum of compound **3q**



^{1}H NMR spectrum of compound **3r**



^{13}C NMR spectrum of compound **3r**