Pd-Catalyzed O-Arylation of Ethyl Acetohydroximate: Synthesis of *O*-Arylhydroxylamines and Substituted Benzofurans

Thomas J. Maimone and Stephen L. Buchwald*

Contribution from the Department of Chemistry, Massachusetts Institute of Technology

77 Massachusetts Ave, Cambridge, MA 92037

SUPPORTING INFORMATION

General Procedures. All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry toluene was obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. The preparation of *t*-BuBrettPhos has been previously described (see: *Tetrahedron* **2009**, *65*, 6576). $(AllylPdCl)_2$ was purchased from Strem and used as received. Ethyl acetohydroximate was purchased from Aldrich and used as received (the bottle was very gently warmed to induce melting prior to use and the compound manipulated as a liquid). Free-flowing, anhydrous Cs_2CO_3 was generously donated by Chemetall and stored in a glovebox. Small portions were removed and stored in a desiccator for up to 2 weeks (All reactions were set-up outside of the glovebox). Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. Satisfactory elemental analyses were obtained for all compounds. All yields stated are the average of at least two experiments. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Aryl iodides were passed through a short plug of alumina prior to use. Reactions were monitored by GC and thin-layer chromatography (TLC) carried out on 0.25 mm E.

Merck silica gel plates (60F-254) using UV light as a visualizing agent and *p*-anisaldehyde in ethanol/aqueous H_2SO_4/CH_3CO_2H (for *N*-hydroxyacetimidate coupled products and benzofurans) or $KMnO_4$ solution (for free *O*-arylhydroxylamines) and heat as developing agents. Flash silica gel chromatography was performed using Silicycle SiliaFlashP60 (230-400 mesh) silica gel. NMR spectra were recorded on a Bruker AMX 400 spectrometer and were calibrated using residual solvent as an internal reference ($CDCl_3$: 7.26 ppm for ^1H NMR and 77.16 ppm for ^{13}C NMR). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad, at = apparent triplet, ad = apparent doublet. IR spectra were recorded on a Perkin-Elmer 2000 FTIR spectrometer using KBr plates (thin film). Melting points (m.p.) were obtained on a Mel-Temp capillary melting point apparatus. Gas chromatographic analyses were performed on an Agilent 6890 gas chromatograph. Elemental analyses were performed by Atlantic Microlabs Inc., Norcross, GA

General Procedure A: Ligand Evaluation (Table 1)

To an oven-dried re-sealable screw cap vial was added $(allylPdCl)_2$ (2.7 mg, 0.5 mol %), ligand **1**-**6** (2.0 mol %) and Cs_2CO_3 (730 mg, 2.24 mmol, 1.5 equiv.). The vial was evacuated and back-filled with argon (this process was repeated a total of 3 times). Under argon, PhBr (157.5 μl, 1.5 mmol, 1 equiv.) was added followed by toluene (3 ml), and finally ethyl acetohydroximate (190 μl, 1.9 mmol, 1.25 equiv.). The argon source was removed and the sealed vial placed into a pre-heated 65°C oil bath with vigorous stirring. After stirring for 1 hour at 65°C, the vessel was cooled to room temperature, diluted with EtOAc (10 ml), and dodecane added. The mixture was filtered through a small plug of

silica gel and then analyzed by GC. [Note: In general, GC can only be used to accurately monitor the consumption of the aryl halide, since the O-arylated products decompose during vaporization]

General Procedure B: O-Arylation of Ethyl Acetohydroximate (Table 2)

To an oven-dried re-sealable screw cap vial was added $(allylPdCl)_2$ (0.5 – 2.5 mol %), ligand **1** or **4** (2.0 – 10 mol %, Pd:L = 1:2), Cs_2CO_3 (490 mg, 1.5 mmol, 1.5 equiv.), and the aryl halide (if it is a solid) (1.0 mmol, 1.0 equiv.). The vial was evacuated and back-filled with argon (this process was repeated a total of 3 times). Under argon, the aryl halide (if it is a liquid) (1.0 mmol, 1.0 equiv.) was added followed by toluene (2 ml), and finally ethyl acetohydroximate (125 μl, 1.25 mmol, 1.25 equiv.). The argon source was removed and the sealed vial placed into a pre-heated 65°C oil bath with vigorous stirring. After stirring for 1-12 hours at 65°C (see Table 2 for reaction times), the vessel was cooled to room temperature, opened, and diluted with EtOAc. The mixture was then filtered through a short 1 cm pad of silica gel (2.5 cm diameter) eluting with EtOAc. The solvent was removed *in vacuo* and the crude product purified by silica gel flash chromatography. [Note: many of the products are somewhat volatile and should not be placed under high vacuum for extended periods of time]

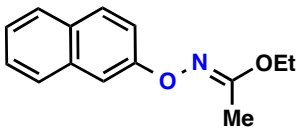
Representative Procedure C: Synthesis of Free *O*-arylhydroxylamines (Table 3)

To a re-sealable screw cap vial was added the O-aryl ethyl acetohydroximate product (0.75 mmol, 1 equiv.) and anhydrous dioxanes (1.5 ml). The mixture was cooled to 0 °C under argon at which point the solution froze. HCl (6 M aqueous solution, 750 μl, 4.5 mmol, 6 equiv.) was added dropwise to the solution at 0 °C and the solution stirred for 5 minutes at this temperature, then warmed to room temperature. After 1 hour of vigorous

stirring at room temperature, the mixture was diluted with Et_2O (10 ml), and poured into 1 M NaOH (25 ml). The aqueous layer was extracted with Et_2O (2 x 10 ml), and the combined organic layers were washed with 1 M NaOH (25 ml), brine (25 ml), and dried (Na_2SO_4). The solvent was removed *in vacuo* and the crude material purified by silica gel flash chromatography. [Note: many of the products are volatile and should not be placed under high vacuum]

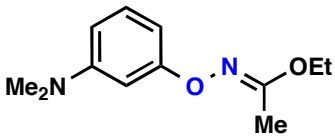
Representative Procedure D: One-Pot Synthesis of Benzofurans (Table 4)

To a re-sealable screw cap vial was added the O-aryl ethyl acetohydroximate product (0.65 mmol, 1 equiv.), ketone (1.3 mmol, 2 equiv.), H_2O (58 µl, 3.2 mmol, 5 equiv.), and dioxane (2.4 ml). The vessel was purged with argon and HCl (4.0 M solution in dioxanes, 810 µl, 3.2 mmol, 5 equiv.) was added dropwise to the stirring solution. The argon source was removed and the sealed vial placed into a pre-heated 70 °C oil bath. After heating for 1-2 hours (see Table 4), the mixture was cooled to room temperature, diluted with Et_2O (10 ml), and poured into 1 M NaOH (25 ml). The aqueous layer was extracted with Et_2O (2 x 10 ml), and the combined organic layers were washed with 1 M NaOH (25 ml), brine (25 ml), and dried ($MgSO_4$). The solvent was removed *in vacuo* and the crude material purified by silica gel flash chromatography.

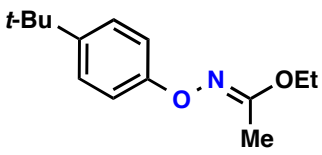


Ethyl *N*-naphthalen-2-yloxyacetimidate (Table 2, 1% Pd). Following procedure B, 2-bromonapthalene (207 mg, 1 mmol), ethyl acetohydroximate (125 µl, 1.25 mmol), $(allylPdCl)_2$ (1.9 mg, 0.5 mol %), **1** (9.7 mg, 2.0 mol %), Cs_2CO_3 (490 mg, 1.5 mmol), and toluene (2 ml) were heated at 65 °C for 1 hour. The crude product was purified by flash column chromatography (silica gel,

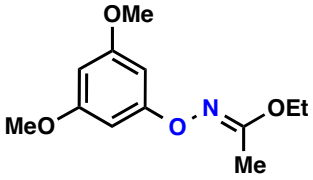
gradient from 20:1→10:1→5:1 hexanes:DCM) to afford the title compound as a colorless oil (214 mg, 93% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.78 (m, 3 H), 7.60 (d, *J* = 2.3 Hz, 1 H), 7.47 (at, *J* = 7.5 Hz, 1 H), 7.36 (at, *J* = 7.5 Hz, 1 H), 7.33 (dd, *J* = 9.0, 2.3 Hz, 1 H), 4.32 (q, *J* = 7.0 Hz, 2 H), 2.21 (s, 3 H), 1.44 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 157.5, 134.7, 129.4, 129.1, 127.7, 127.1, 126.3, 123.6, 116.5, 108.0, 63.1, 14.5, 14.4; IR (film) ν_{max} 3058, 2981, 2939, 2901, 1646, 1626, 1600, 1510, 1464, 1378, 1251, 1212, 1162, 1116, 1054, 981, 847, 809, 746, 625, 473 cm^{-1} ; Anal. Calcd. For $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59. Found: C, 73.62; H, 6.40.



Ethyl *N*-3-(dimethylamino)phenoxyacetimidate (Table 2, 1% Pd). Following procedure B, 3-bromo-*N*,*N*-dimethylaniline (145 μl, 1 mmol), ethyl acetohydroximate (125 μl, 1.25 mmol), $(allylPdCl)_2$ (1.9 mg, 0.5 mol %), **1** (9.7 mg, 2.0 mol %), Cs_2CO_3 (490 mg, 1.5 mmol), and toluene (2 ml) were heated at 65 °C for 1 hour. The crude product was purified by flash column chromatography (silica gel, gradient from 20:1→10:1→5:1→2:1 hexanes:Et_2O) to afford the title compound as a colorless oil (212 mg, 94% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (at, *J* = 8.0 Hz, 1 H), 6.60 – 6.56 (m, 2 H), 6.40 (dd, *J* = 8.0, 2.0 Hz, 1 H), 4.23 (q, *J* = 7.0 Hz, 2 H), 2.97 (s, 6 H), 2.15 (s, 3 H), 1.39 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 160.9, 151.9, 129.6, 106.2, 102.5, 98.5, 62.9, 40.7, 14.5, 14.3; IR (film) ν_{max} 2980, 2939, 2803, 1646, 1606, 1572, 1500, 1445, 1377, 1233, 1145, 1056, 1008, 985, 824, 756, 686 cm^{-1} ; Anal. Calcd. For $C_{12}H_{18}N_2O_2$: C, 64.84; H, 8.16. Found: C, 65.11; H, 8.06.

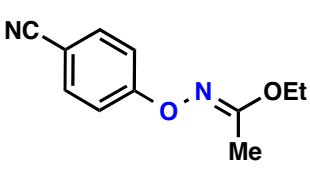


Ethyl *N*-4-(*tert*-butyl)phenoxyacetimidate (Table 2, 1% Pd). Following procedure B, 1-(*tert*-butyl)-4-iodobenzene (177.5 μl, 1 mmol), ethyl acetohydroximate (125 μl, 1.25 mmol), $(allylPdCl)_2$ (1.9 mg, 0.5 mol %), **1** (9.7 mg, 2.0 mol %), Cs_2CO_3 (490 mg, 1.5 mmol), and toluene (2 ml) were heated at 65 °C for 8 hours. The crude product was purified by flash column chromatography (silica gel, gradient from 20:1→10:1→5:1→hexanes:DCM) to afford the title compound as a colorless oil (207 mg, 87% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.34 (m, 2 H), 7.15 – 7.11 (m, 2 H), 4.25 (q, *J* = 7.0 Hz, 2 H), 2.16 (s, 3 H), 1.40 (t, *J* = 7.0 Hz, 3 H), 1.36 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 157.6, 144.0, 126.0, 113.5, 62.9, 34.2, 31.6, 14.5, 14.2; IR (film) ν_{max} 2963, 2902, 2868, 1648, 1607, 184, 1508, 1377, 1314, 1303, 1236, 1170, 1111, 1055, 981, 907, 828, 545 cm^{-1}; Anal. Calcd. For $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99. Found: C, 71.20; H, 9.18.

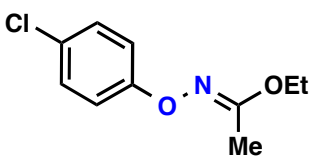


Ethyl *N*-3,5-dimethoxyphenoxyacetimidate (Table 2, 2.5% Pd). Following procedure B, 1-bromo-3,5-dimethoxybenzene (217 mg, 1 mmol), ethyl acetohydroximate (125 μl, 1.25 mmol), $(allylPdCl)_2$ (4.6 mg, 1.25 mol %), **1** (24 mg, 5 mol %), Cs_2CO_3 (490 mg, 1.5 mmol), and toluene (2 ml) were heated at 65 °C for 1 hour. The crude product was purified by flash column chromatography (silica gel, gradient from 2:1→1:1→1:2 hexanes:DCM → pure DCM) to afford the title compound as a white crystalline solid (223 mg, 93% yield): mp = 46 – 48 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.35 (d, *J* = 2.2 Hz, 2 H), 6.1 (t, *J* = 2.2 Hz, 1 H), 4.18 (q, *J* = 7.0 Hz, 2 H), 3.78 (s, 6 H), 2.10 (s, 3 H), 1.35 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 161.6, 161.4, 93.7, 92.8, 63.1, 55.5, 14.5, 14.4; IR

(film) ν_{max} 3015, 2972, 1650, 1605, 1481, 1447, 1397, 1371, 1310, 1207, 1148, 1068, 1048, 1013, 962, 815, 800, 677, 541 cm^{-1}; Anal. Calcd. For $C_{12}H_{17}NO_4$: C, 60.24; H, 7.16. Found: C, 60.53; H, 7.19.

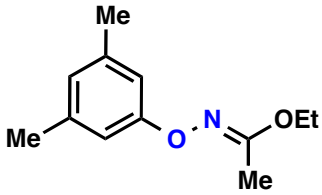


Ethyl *N*-4-cyanophenoxyacetimidate (Table 2, 1% Pd). Following procedure B, 4-chlorobenzonitrile (138 mg, 1 mmol), ethyl acetohydroximate (125 μl, 1.25 mmol), $(allylPdCl)_2$ (1.9 mg, 0.5 mol %), **1** (9.7 mg, 2 mol %), Cs_2CO_3 (490 mg, 1.5 mmol), and toluene (2 ml) were heated at 65 °C for 1 hour. The crude product was purified by flash column chromatography (silica gel, gradient from 5:1→3:1→1:1 hexanes:DCM → pure DCM) to afford the title compound as a colorless oil (142 mg, 70% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.54 (m, 2 H), 7.22 – 7.18 (m, 2 H), 4.18 (q, *J* = 7.0 Hz, 2 H), 2.12 (s, 3 H), 1.35 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 162.8, 133.8, 119.4, 114.5, 104.2, 63.3, 14.5, 14.3; IR (film) ν_{max} 2984, 2942, 2224, 1645, 1603, 1502, 1379, 1318, 1248, 1162, 1052, 980, 835, 545 cm^{-1}; Anal. Calcd. For $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92. Found: C, 64.91; H, 6.10.

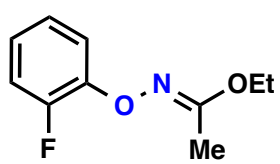


Ethyl *N*-4-chlorophenoxyacetimidate (Table 2, 1% Pd). Following procedure B, 1-bromo-4-chlorobenzene (191 mg, 1 mmol), ethyl acetohydroximate (125 μl, 1.25 mmol), $(allylPdCl)_2$ (1.9 mg, 0.5 mol %), **1** (9.7 mg, 2 mol %), Cs_2CO_3 (490 mg, 1.5 mmol), and toluene (2 ml) were heated at 65 °C for 1 hour. The crude product was purified by flash column chromatography (silica gel, gradient from 20:1→10:1→5:1 hexanes:DCM) to afford the title compound as a colorless oil (186 mg, 87% yield) [Note: This reaction has been performed on a 10 mmol scale in 88% yield]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 –

7.21 (m, 2 H), 7.09 – 7.05 (m, 2 H), 4.18 (q, J = 7.0 Hz, 2 H), 2.11 (s, 3 H), 1.35 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 158.4, 129.2, 126.0, 115.3, 63.1, 14.5, 14.5; IR (film) ν_{max} 2983, 2941, 2902, 2917, 1876, 1647, 1583, 1485, 1406, 1378, 1315, 1233, 1157, 108, 1054, 1007, 981, 907, 823, 694, 637, 601, 501 cm^{-1}; Anal. Calcd. For $C_{10}H_{12}NO_2Cl$: C, 56.21; H, 5.66. Found: C, 56.47; H, 5.83.

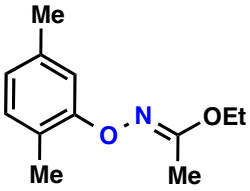


Ethyl *N*-3,5-dimethylphenoxyacetimidate (Table 2, 1% Pd). Following procedure B, 1-iodo-3,5-dimethylbenzene (145 μl, 1 mmol), ethyl acetohydroximate (125 μl, 1.25 mmol), $(allylPdCl)_2$ (1.9 mg, 0.5 mol %), **1** (9.7 mg, 2 mol %), Cs_2CO_3 (490 mg, 1.5 mmol), and toluene (2 ml) were heated at 65 °C for 4 hours. The crude product was purified by flash column chromatography (silica gel, gradient from 20:1→10:1→5:1 hexanes:DCM) to afford the title compound as a volatile colorless liquid (186 mg, 90% yield) [Note: this compound should not be subjected to high vacuum]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 (s, 2 H), 6.64 (s, 1 H), 4.23 (q, J = 7.0 Hz, 2 H), 2.33 (s, 6 H), 2.13 (s, 3 H), 1.39 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 159.8, 139.0, 123.1, 111.6, 63.0, 21.6, 14.5, 14.3; IR (film) ν_{max} 2980, 2939, 2897, 1647, 1588, 1439, 1318, 1136, 1033, 983, 866, 830, 685 cm^{-1}; Anal. Calcd. For $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27. Found: C, 69.33; H, 8.08.

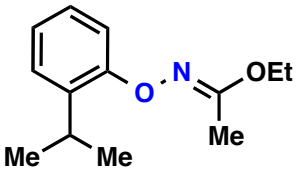


Ethyl *N*-2-fluorophenoxyacetimidate (Table 2, 2.5% Pd). Following procedure B, 1-bromo-2-fluorobenzene (110 μl, 1 mmol), ethyl acetohydroximate (125 μl, 1.25 mmol), $(allylPdCl)_2$ (4.6 mg, 1.25 mol %), **1** (24 mg, 2 mol %), Cs_2CO_3 (490 mg, 1.5 mmol), and toluene (2 ml) were heated at 65 °C for 2 hours. The crude product was purified by flash column

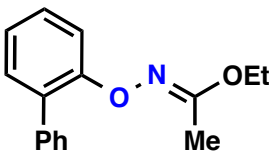
chromatography (silica gel, gradient from 20:1→10:1→5:1 hexanes:DCM) to afford the title compound as a volatile colorless liquid (170 mg, 86% yield) [Note: This reaction has been performed on a 5 mmol scale in 88% yield. This compound should not be subjected to high vacuum]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.43 (m, 1 H), 7.11 – 7.05 (m, 2 H), 6.93 – 6.88 (m, 1 H), 4.21 (q, *J* = 7.0 Hz, 2 H), 2.18 (s, 3 H), 1.37 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) [complexity observed due to C-F splitting] δ 166.70, 152.1, 149.6, 147.7, 147.6, 124.3, 124.3, 121.4, 121.3, 116.1, 116.0, 115.8, 63.2, 14.4, 14.4; IR (film) ν_{max} 2983, 1645, 1497, 1379, 1317, 1257, 1199, 1102, 980, 747 cm^{-1}; Anal. Calcd. For $C_{10}H_{12}NO_2F$: C, 60.90; H, 6.13. Found: C, 61.17; H, 6.25.



Ethyl *N*-2,5-dimethylphenoxyacetimidate (Table 2, 1% Pd). Following procedure B, 2-bromo-1,4-dimethylbenzene (140 μl, 1 mmol), ethyl acetohydroximate (125 μl, 1.25 mmol), $(allylPdCl)_2$ (1.9 mg, 0.5 mol %), **4** (8.5 mg, 2 mol %), Cs_2CO_3 (490 mg, 1.5 mmol), and toluene (2 ml) were heated at 65 °C for 2 hours. The crude product was purified by flash column chromatography (silica gel, gradient from 20:1→10:1→5:1 hexanes:DCM) to afford the title compound as a volatile colorless liquid (155 mg, 75% yield) [Note: this compound should not be subjected to high vacuum]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (s, 1 H), 6.99 (d, *J* = 7.5 Hz, 1 H), 6.69 (d, *J* = 7.5 Hz, 1 H), 4.22 (q, *J* = 7.0 Hz, 2 H), 2.32 (s, 3 H), 2.21 (s, 3 H), 2.14 (s, 3 H), 1.37 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 157.4, 136.6, 130.2, 121.5, 121.0, 113.4, 63.0, 21.5, 15.6, 14.5, 14.3; IR (film) ν_{max} 2981, 2924, 1648, 1613, 1583, 1503, 1413, 1376, 1310, 1260, 1120, 1055, 997, 982, 801 cm^{-1}; Anal. Calcd. For $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27. Found: C, 69.69; H, 8.35.

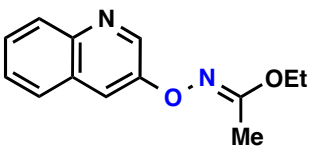


Ethyl *N*-2-isopropylphenoxyacetimidate (Table 2, 1% Pd). Following procedure B, 1-bromo-2-isopropylbenzene (155 μl, 1 mmol), ethyl acetohydroximate (125 μl, 1.25 mmol), $(allylPdCl)_2$ (1.9 mg, 0.5 mol %), **4** (8.5 mg, 2 mol %), Cs_2CO_3 (490 mg, 1.5 mmol), and toluene (2 ml) were heated at 65 °C for 2 hours. The crude product was purified by flash column chromatography (silica gel, gradient from 20:1→10:1→5:1→2:1 hexanes:DCM) to afford the title compound as a volatile colorless liquid (175 mg, 79% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 8.2, 1.2 Hz, 1 H), 7.21 (dd, *J* = 7.5, 1.7 Hz, 1 H), 7.15 (td, *J* = 7.5, 1.7 Hz, 1 H), 6.94 (td, *J* = 7.4, 1.2 Hz, 1 H), 4.21 (q, *J* = 7.0 Hz, 2 H), 3.31 (septet, *J* = 6.9 Hz, 1 H), 1.37 (t, *J* = 7.0 Hz, 3 H), 1.26 (d, *J* = 6.9 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 156.6, 134.5, 126.7, 125.8, 121.2, 113.2, 63.0, 27.2, 22.7, 14.5, 14.5; IR (film) ν_{max} 2034, 2962, 2870, 1647, 1599, 1482, 1451, 1377, 1313, 1228, 1085, 1054, 1007, 911, 751, 642 cm^{-1}; Anal. Calcd. For $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65. Found: C, 70.37; H, 8.69.

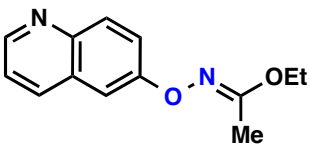


Ethyl *N*-[1,1'-biphenyl]-2-yloxyacetimidate (Table 2, 1% Pd). Following procedure B, 2-bromo-1,1'-biphenyl (172.5 μl, 1 mmol), ethyl acetohydroximate (125 μl, 1.25 mmol), $(allylPdCl)_2$ (1.9 mg, 0.5 mol %), **4** (8.5 mg, 2 mol %), Cs_2CO_3 (490 mg, 1.5 mmol), and toluene (2 ml) were heated at 65 °C for 2 hours. The crude product was purified by flash column chromatography (silica gel, gradient from 20:1→10:1→5:1→2:1 hexanes:DCM) to afford the title compound as a colorless oil (229 mg, 90% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.61 (m, 3 H), 7.51 – 7.47 (m, 2 H), 7.42 – 7.38 (m, 3 H), 7.13 (td, *J* = 7.4, 1.2 Hz, 1 H), 4.27 (q, *J* = 7.0 Hz, 2 H), 2.06 (s, 3 H), 1.42 (t, *J* = 7.0 Hz, 3 H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 165.7, 156.4, 138.5, 130.5, 129.6, 128.7 (2 C), 128.0, 126.9, 121.5, 114.2, 63.1, 14.7, 14.5; IR (film) ν_{max} 3060, 2981, 1644, 1597, 1474, 1433, 1377, 1312, 1224, 1053, 979, 752, 699 cm^{-1}; Anal. Calcd. For $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71. Found: C, 75.57; H, 6.98.

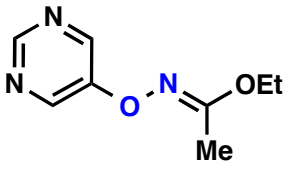


Ethyl *N*-quinolin-3-yloxyacetimidate (Table 2, 2.5% Pd). Following procedure B, 3-bromoquinoline (135 μl, 1 mmol), ethyl acetohydroximate (125 μl, 1.25 mmol), $(allylPdCl)_2$ (4.6 mg, 1.25 mol %), **1** (24 mg, 5 mol %), Cs_2CO_3 (490 mg, 1.5 mmol), and toluene (2 ml) were heated at 65 °C for 4 hours. The crude product was purified by flash column chromatography (silica gel, gradient from 10:1→5:1→3:1→1:1 hexanes:Et_2O) to afford the title compound as a colorless oil (211 mg, 92% yield): ^1H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 2.6 Hz, 1 H), 8.04 (d, *J* = 8.0 Hz, 1 H), 7.82 (d, *J* = 2.6 Hz, 1 H), 7.75 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.55 (td, *J* = 7.0, 1.5 Hz, 1 H), 7.50 (td, *J* = 7.0, 1.5 Hz, 1 H), 4.27 (q, *J* = 7.0 Hz, 2 H), 2.19 (s, 3 H), 1.40 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 153.1, 144.0, 142.0, 129.1, 129.0, 127.0, 126.7, 115.0, 63.3, 14.5, 14.4; IR (film) ν_{max} 3064, 2982, 1645, 1602, 1496, 1465, 1400, 1342, 1312, 1209, 1158, 1054, 987, 882, 781, 752, 615 cm^{-1}; Anal. Calcd. For $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13. Found: C, 67.57; H, 6.15.

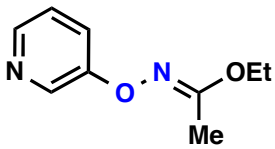


Ethyl *N*-quinolin-6-yloxyacetimidate (Table 2, 2.5% Pd). Following procedure B, 6-chloroquinoline (164 mg, 1 mmol), ethyl acetohydroximate (125 μl, 1.25 mmol), $(allylPdCl)_2$ (4.6 mg, 1.25 mol %), **1** (24 mg, 5 mol %), Cs_2CO_3 (490 mg, 1.5 mmol), and toluene (2 ml) were heated at 65 °C for 2 hours. The crude product was purified by flash column chromatography (silica gel, gradient from 3:1→2:1→1:1 hexanes:Et_2O) to afford the title compound as a colorless oil

(212 mg, 92% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (dd, *J* = 4.0, 2.0 Hz, 1 H), 8.05 (d, *J* = 8.0 Hz, 1 H), 8.01 (d, *J* = 8.0 Hz, 1 H), 7.50 (d, *J* = 2.6 Hz, 1 H), 7.48 (d, *J* = 2.6 Hz, 1 H), 7.34 (dd, *J* = 8.0, 4.0 Hz, 1 H), 4.27 (q, *J* = 7.0 Hz, 2 H), 2.18 (s, 3 H), 1.40 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 157.4, 148.0, 144.7, 135.0, 130.5, 129.3, 121.3, 120.0, 107.3, 63.1, 14.4, 14.4; IR (film) ν_{max} 2982, 1646, 1619, 1597, 1499, 1466, 1378, 1310, 1253, 1219, 1150, 1112, 1054, 981, 859, 831, 765, 628 cm^{-1}; Anal. Calcd. For $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13. Found: C, 67.52; H, 5.96.

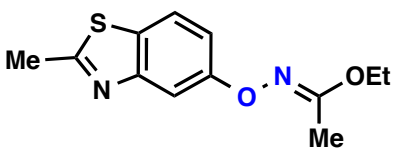


Ethyl *N*-pyrimidin-5-yloxyacetimidate (Table 2, 2.5% Pd). Following procedure B, 5-bromopyrimidine (159 mg, 1 mmol), ethyl acetohydroximate (125 μl, 1.25 mmol), $(allylPdCl)_2$ (4.6 mg, 1.25 mol %), **1** (24 mg, 5 mol %), Cs_2CO_3 (490 mg, 1.5 mmol), and toluene (2 ml) were heated at 65 °C for 6 hours. The crude product was purified by flash column chromatography (silica gel, gradient from 2:1→1:1 hexanes:Et_2O) to afford the title compound as a colorless oil which slowy solidified into a waxy solid (163 mg, 90% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (s, 1 H), 8.61 (s, 2 H), 4.18 (q, *J* = 7.0 Hz, 2 H), 2.14 (s, 3 H), 1.36 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 153.8, 151.9, 143.0, 63.3, 14.3, 14.2; IR (film) ν_{max} 2983, 1646, 1561, 1438, 1415, 1379, 1319, 1261, 1181, 1048, 978, 887, 718 cm^{-1}

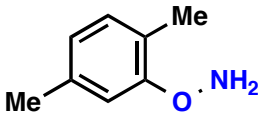


Ethyl *N*-pyrimidin-5-yloxyacetimidate (Table 2, 2.5% Pd). Following procedure B, 3-chloropyrimidine (95 μl, 1 mmol), ethyl acetohydroximate (125 μl, 1.25 mmol), $(allylPdCl)_2$ (4.6 mg, 1.25 mol %), **1** (24 mg, 5 mol %), Cs_2CO_3 (490 mg, 1.5 mmol), and toluene (2 ml) were heated at 65 °C for 4 hours. The crude product was purified by flash column

chromatography (silica gel, gradient from 2:1→1:1 hexanes:Et_2O) to afford the title compound as a volatile colorless liquid (153 mg, 85% yield) [Note: this compound should not be subjected to high vacuum]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 2.8 Hz, 1 H), 8.22 (dd, *J* = 4.5, 1.5 Hz, 1 H), 7.47 (ddd, *J* = 8.5, 2.8, 1.5 Hz, 1 H), 7.21 (dd, *J* = 8.5, 4.5 Hz, 1 H), 4.19 (q, *J* = 7.0 Hz, 2 H), 2.13 (s, 3 H), 1.36 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 155.9, 142.5, 137.1, 123.6, 120.8, 63.1, 14.3, 14.3; IR (film) ν_{max} 3059, 2982, 1644, 1574, 1474, 1425, 1379, 1312, 1224, 978, 799, 706 cm^{-1}; Anal. Calcd. For $C_9H_{12}N_2O_2$: C, 59.99; H, 6.71. Found: C, 60.33; H, 7.07.

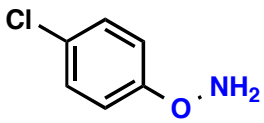


Ethyl *N*-(2-methylbenzo[*d*]thiazol-5-yl)oxyacetimidate (Table 2, 5% Pd). Following procedure B, 5-chloro-2-methylbenzo[*d*]thiazole (184 mg, 1 mmol), ethyl acetohydroximate (125 μl, 1.25 mmol), $(allylPdCl)_2$ (9.2 mg, 2.5 mol %), **1** (48 mg, 10 mol %), Cs_2CO_3 (490 mg, 1.5 mmol), and toluene (2 ml) were heated at 65 °C for 12 hours. The crude product was purified by flash column chromatography (silica gel, gradient from 10:1→5:1 hexanes:Et_2O) to afford the title compound as a white solid (188 mg, 75% yield): mp = 75 – 78 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 2.4 Hz, 1 H), 7.65 (d, *J* = 8.8 Hz, 1 H), 7.13 (dd, *J* = 8.8, 2.4 Hz, 1 H), 4.22 (q, *J* = 7.0 Hz, 2 H), 2.81 (s, 3 H), 2.14 (s, 3 H), 1.36 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 165.6, 158.9, 154.5, 127.8, 121.2, 113.0 106.7, 63.0, 210.2, 14.4, 14.3; IR (film) ν_{max} 3048, 2974, 1644, 1552, 1445, 1375, 1315, 1157, 1057, 983, 892, 802, 645 cm^{-1}; Anal. Calcd. For $C_{12}H_{14}N_2O_2S$: C, 57.58; H, 5.64. Found: C, 57.51; H, 5.67.

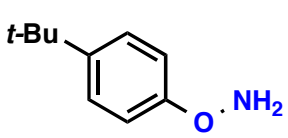


***O*-(2,5-dimethylphenyl)hydroxylamine (Table 3)**. Following procedure C, ethyl *N*-2,5-dimethylphenoxyacetimidate (135 mg,

0.65 mmol), HCl (6 M aq. solution, 0.65 ml, 3.9 mmol), and dioxane (1.3 ml) were stirred at room temperature for 1 hour. The crude product was purified by flash column chromatography (silica gel, gradient from 5:1→4:1→3:1 hexanes:Et_2O) to afford the title compound as a volatile yellow liquid (80 mg, 90% yield) [Note: this compound should not be subjected to high vacuum]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (s, 1 H), 7.00 (d, *J* = 7.4 Hz, 1 H), 6.71 (d, *J* = 7.4, 1 H), 5.83 (bs, 2 H), 2.36 (s, 3 H), 2.17 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 136.7, 130.3, 121.3, 120.9, 112.3, 21.5, 15.5; IR (film) ν_{max} 3318, 3242, 2922, 1619, 1583, 1502, 1460, 1414, 1262, 1187, 1101, 993, 937, 866, 804 cm^{-1}; Anal. Calcd. For $C_8H_{11}NO$: C, 70.04; H, 8.08. Found: C, 70.10; H, 8.10.

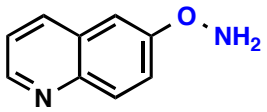


***O*-(4-chlorophenyl)hydroxylamine (Table 3)**. Following procedure C, ethyl *N*-4-chlorophenoxyacetimidate (133 mg, 0.62 mmol), HCl (6 M aq. solution, 0.62 ml, 3.7 mmol), and dioxane (1.25 ml) were stirred at room temperature for 1 hour. The crude product was purified by flash column chromatography (silica gel, gradient from 5:1→4:1→3:1 hexanes:Et_2O) to afford the title compound as a volatile yellow liquid (81 mg, 91% yield) [Note: this compound should not be subjected to high vacuum]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.21 (m, 2 H), 7.10 – 7.06 (m, 2 H), 5.87 (bs, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 129.1, 125.8, 114.6; IR (film) ν_{max} 3324, 1597, 1484, 1248, 1133, 1089, 826, 649, 501 cm^{-1}; Anal. Calcd. For C_6H_6NOCl: C, 50.19; H, 4.21. Found: C, 49.95; H, 4.35.

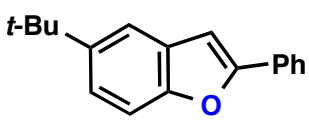


***O*-(4-(*tert*-butyl)phenyl)hydroxylamine (Table 3)**. Following procedure C, ethyl *N*-4-(*tert*-butyl)phenoxyacetimidate (154 mg, 0.65 mmol), HCl (6 M aq. solution, 0.65 ml, 3.9 mmol), and dioxane (1.3 ml) were stirred at room temperature for 1 hour. The crude product was purified by flash column

chromatography (silica gel, gradient from 5:1→4:1→3:1 hexanes:Et_2O) to afford the title compound as a volatile yellow liquid (92 mg, 85% yield) [Note: this compound should not be subjected to high vacuum]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.31 (m, 2 H), 7.12 – 7.08 (m, 2 H), 5.84 (bs, 2 H), 1.34 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 143.9, 126.0, 112.7, 34.1, 31.6; IR (film) ν_{max} 3320, 2962, 1610, 1506, 1363, 1250, 1136, 831 cm^{-1}; Anal. Calcd. For $C_{10}H_{15}NO$: C, 72.69; H, 9.15. Found: C, 72.91; H, 9.33.

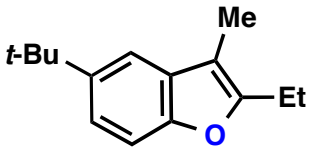


***O*-(quinolin-6-yl)hydroxylamine (Table 3)**. Following procedure C, ethyl *N*-quinolin-6-yloxyacetimidate (125 mg, 0.54 mmol), HCl (6 M aq. solution, 0.54 ml, 3.9 mmol), and dioxane (1.1 ml) were stirred at room temperature for 1 hour. The crude product was purified by flash column chromatography (silica gel, gradient from 3:1→2:1→1:1 hexanes:Et_2O→pure Et_2O→pure EtOAc) to afford the title compound as slightly yellow crystalline solid (61 mg, 70% yield):): mp = 114 – 116 °C (decomp.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (dd, *J* = 4.2, 1.4 Hz, 1 H), 8.02 (d, *J* = 8.2 Hz, 1 H), 7.97 (d, *J* = 9.2 Hz, 1 H), 7.55 (d, *J* = 2.7 Hz, 1 H), 7.38 (dd, *J* = 9.2, 2.7 Hz, 1 H), 7.31 (dd, *J* = 8.2, 4.2 Hz, 1 H), 6.02 (bs, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 148.1, 144.6, 135.1, 130.5, 129.3, 121.4, 119.6 106.4; IR (film) ν_{max} 3293, 3219, 3135, 2920, 1626, 1501, 1382, 1259, 1197, 1098, 919, 869, 827, 801, 717, 623 cm^{-1}; Anal. Calcd. For $C_9H_8N_2O$: C, 67.49; H, 5.03. Found: C, 67.27; H, 5.20.

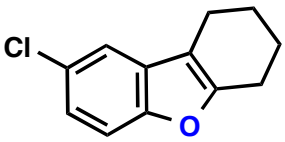


5-(*tert*-butyl)-2-phenylbenzofuran (Table 4). Following procedure D, ethyl *N*-4-(*tert*-butyl)phenoxyacetimidate (130 mg, 0.55 mmol), acetophenone (130 µl, 1.1 mmol), H_2O (50 µl, 2.8 mmol), HCl (4.0 M solution in dioxane, 0.7 ml, 2.8 mmol), and dioxane (2.1 ml) were heated at 70 °C for 1 hour. The crude product was purified by flash column chromatography (silica gel,

hexanes) to afford the title compound as white solid (118 mg, 86% yield): mp = 103 – 105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (ad, *J* = 8.0 Hz, 2 H), 7.62 (d, *J* = 1.8 Hz, 1 H), 7.46 (at, *J* = 8.0 Hz, 3 H), 7.40 – 7.35 (m, 2 H), 7.02 (s, 1 H), 1.43 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.1, 153.2, 146.0, 130.7, 130.0, 128.9, 128.4, 124.9, 122.3, 117.1, 110.5, 101.5, 34.8, 31.9; IR (film) ν_{max} 2960, 1605, 1563, 1474, 1443, 1364, 1330, 1277, 1164, 1021, 912, 882, 806, 760, 748, 687, 657 cm^{-1}; Anal. Calcd. For $C_{18}H_{18}O$: C, 86.36; H, 7.25. Found: C, 86.09; H, 7.40.

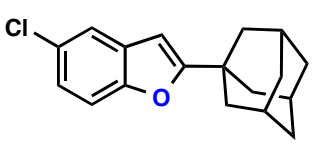


5-(*tert*-butyl)-2-ethyl-3-methylbenzofuran (Table 4). Following procedure D, ethyl *N*-4-(*tert*-butyl) phenoxyacetimidate (155 mg, 0.66 mmol), pentan-3-one (139 µl, 1.32 mmol), H_2O (60 µl, 3.3 mmol), HCl (4.0 M solution in dioxane, 0.83 ml, 3.3 mmol), and dioxane (2.5 ml) were heated at 70 °C for 1 hour. The crude product was purified by flash column chromatography (silica gel, hexanes) to afford the title compound as colorless oil (96 mg, 68% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 1.7 Hz, 1 H), 7.36 (d, *J* = 8.6 Hz, 1 H), 7.32 (dd, *J* = 8.6, 1.7 Hz, 1 H), 2.79 (q, *J* = 7.5 Hz, 2 H), 2.22 (s, 3 H), 1.44 (s, 9 H), 1.33 (t, *J* = 7.5 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 152.0, 145.1, 130.1, 120.9, 114.9, 109.9, 108.9, 34.8, 32.0, 19.8, 12.9, 7.9; IR (film) ν_{max} 2965, 1632 1605, 1477, 1460, 1362, 1280 1256, 1184, 1017, 807, 640 cm^{-1}; Anal. Calcd. For $C_{15}H_{20}O$: C, 83.28; H, 9.32. Found: C, 83.52; H, 9.42.

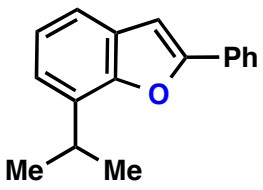


8-chloro-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan (Table 4). Following procedure D, ethyl *N*-4-chlorophenoxyacetimidate (156 mg, 0.73 mmol), cyclohexanone (150 µl, 1.45 mmol), H_2O (65 µl, 3.6 mmol), HCl (4.0 M solution in dioxane, 0.91 ml, 3.6 mmol), and dioxane (2.7 ml) were heated at 70 °C for

1 hour. The crude product was purified by flash column chromatography (silica gel, hexanes) to afford the title compound as a white crystalline solid (131 mg, 88% yield): mp = 74 – 76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 2.0 Hz, 1 H), 7.30 (d, *J* = 8.6 Hz, 1 H), 7.14 (dd, *J* = 8.6, 2.0 Hz, 1 H), 2.75 – 2.71 (m, 2 H), 2.60 – 2.56 (m, 2 H), 1.90 – 1.96 (m, 2 H), 1.89 – 1.81 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 152.80, 130.4, 127.8, 123.0, 118.3, 112.8, 111.8, 23.6, 22.9, 22.6, 20.4; IR (film) ν_{max} 2938, 2855, 1458, 1435, 1384, 1121, 856, 799, 751, 583 cm^{-1}; Anal. Calcd. For $C_{12}H_{11}OCl$: C, 69.74; H, 5.36. Found: C, 69.71; H, 5.49.

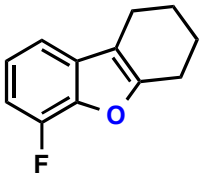


2-(adamantan-1-yl)-5-chlorobenzofuran (Table 4). Following procedure D, ethyl *N*-4-chlorophenoxyacetimidate (138 mg, 0.65 mmol), 1-adamantyl methyl ketone (230 mg, 1.3 mmol), H_2O (58 μl, 3.2 mmol), HCl (4.0 M solution in dioxane, 0.81 ml, 3.2 mmol), and dioxane (2.4 ml) were heated at 70 °C for 2 hour. The crude product was purified by flash column chromatography (silica gel, hexanes) to afford the title compound as a white solid (153 mg, 83% yield): mp = 147 – 150 °C (decomp.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 2 Hz, 1 H), 7.33 (d, *J* = 8.6 Hz, 1 H), 7.17 (dd, *J* = 8.6, 2.0 Hz, 1 H), 6.26 (s, 1 H), 2.12 (bs, 3 H), 2.02 (m, 6 H), 1.85 – 1.78 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 152.8, 130.3, 127.8, 123.1, 120.0, 111.7, 98.4, 40.8, 36.7, 35.0, 28.2; IR (film) ν_{max} 2908, 2852, 2360, 1580, 1446, 1262, 1031, 931, 870, 801, 790, 694, 668, 586 cm^{-1}; Anal. Calcd. For $C_{18}H_{19}OCl$: C, 75.38; H, 6.68. Found: C, 75.16; H, 6.57.

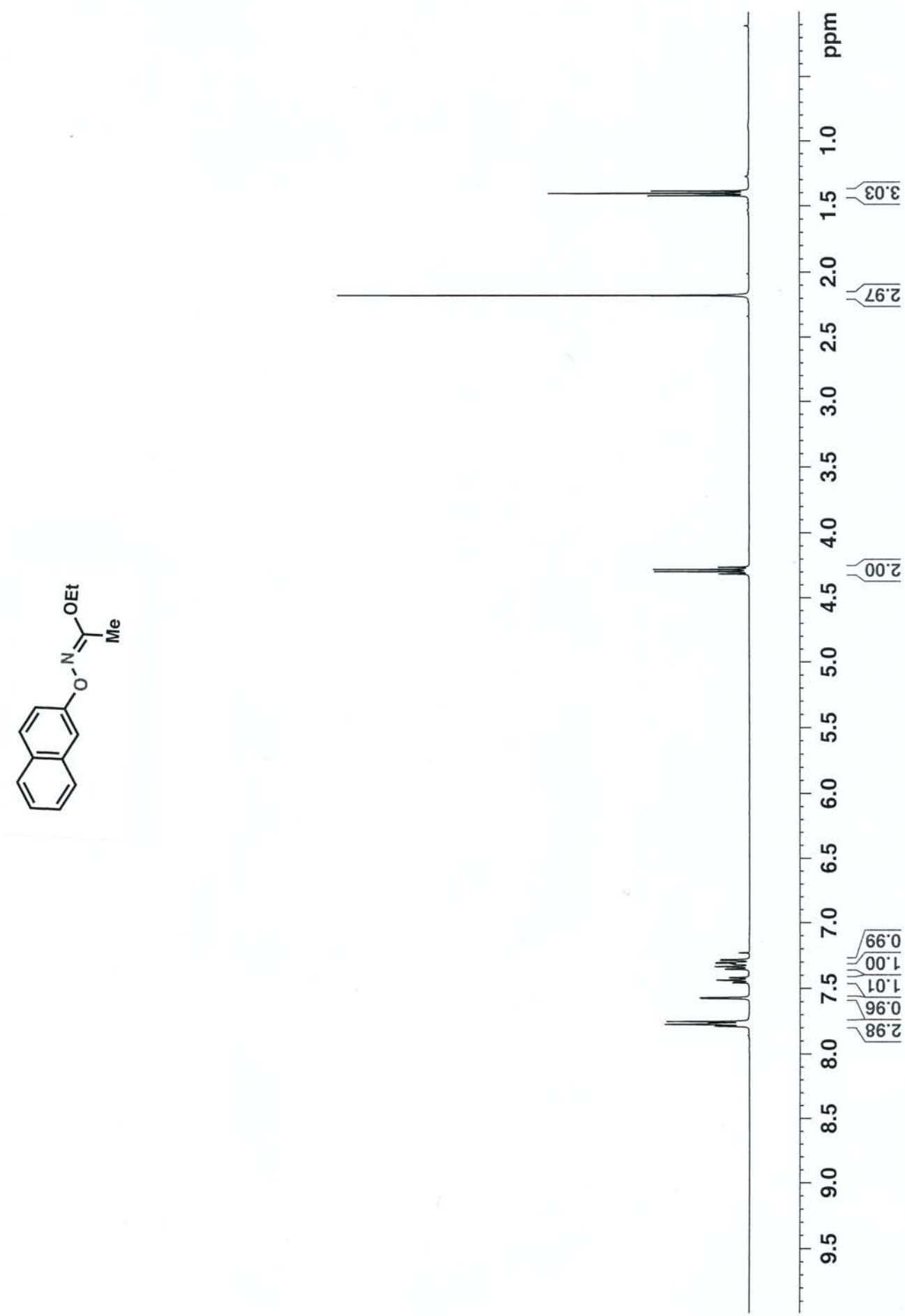


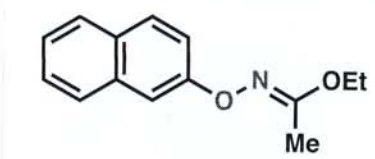
7-isopropyl-2-phenylbenzofuran (Table 4). Following procedure D, ethyl *N*-2-isopropylphenoxyacetimidate (156 mg, 0.70 mmol), acetophenone (165 μl, 1.41 mmol), H_2O (63 μl, 3.5

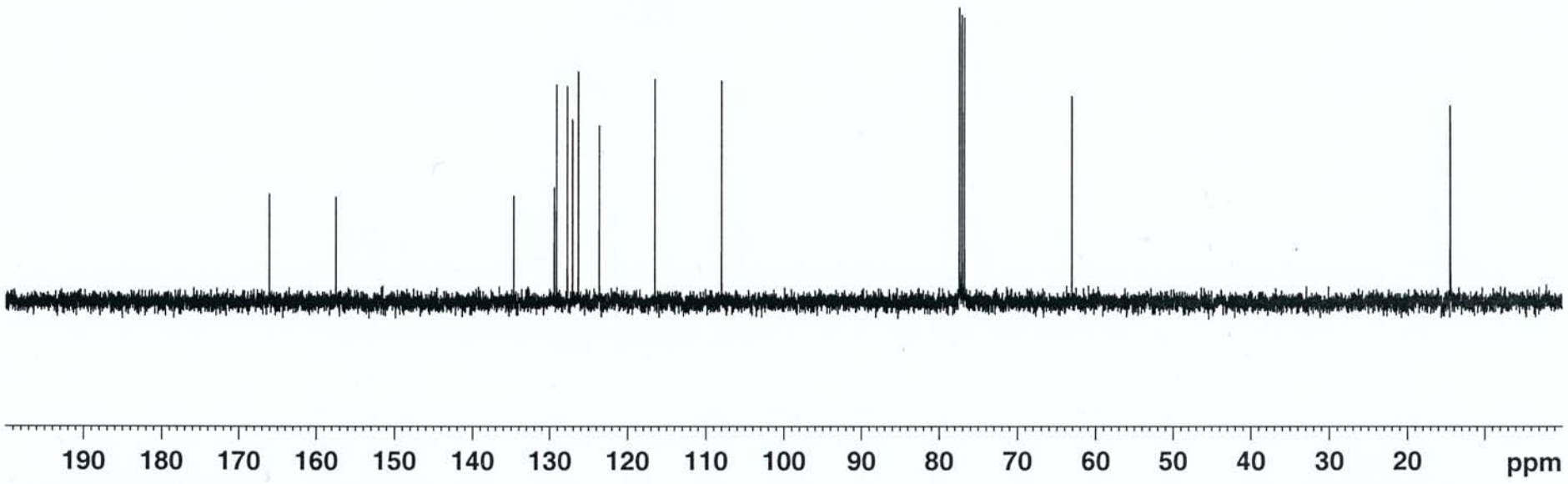
mmol), HCl (4.0 M solution in dioxane, 0.88 ml, 3.5 mmol), and dioxane (2.6 ml) were heated at 70 °C for 2 hour. The crude product was purified by flash column chromatography (silica gel, hexanes) to afford the title compound as an oil which slowly solidified (113 mg, 68% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.89 (m, 2 H), 7.49 – 7.42 (m, 3 H), 7.39 – 7.34 (m, 1 H), 7.21 – 7.14 (m, 2 H), 7.03 (s, 1 H), 3.54 (septet, *J* = 7 Hz, 1 H), 1.46 (d, *J* = 7 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.5, 153.0, 132.4, 130.9, 129.2, 128.9, 128.5, 125.0, 123.25, 121.5, 118.6, 101.6, 29.2, 22.8; IR (film) ν_{max} 3039, 2969, 2871, 1608, 1482, 1448, 1383, 1273, 1167, 1037, 1019, 816, 745, 487 cm^{-1}; Anal. Calcd. For $C_{17}H_{16}O$: C, 86.40; H, 6.82. Found: C, 86.22; H, 6.84.

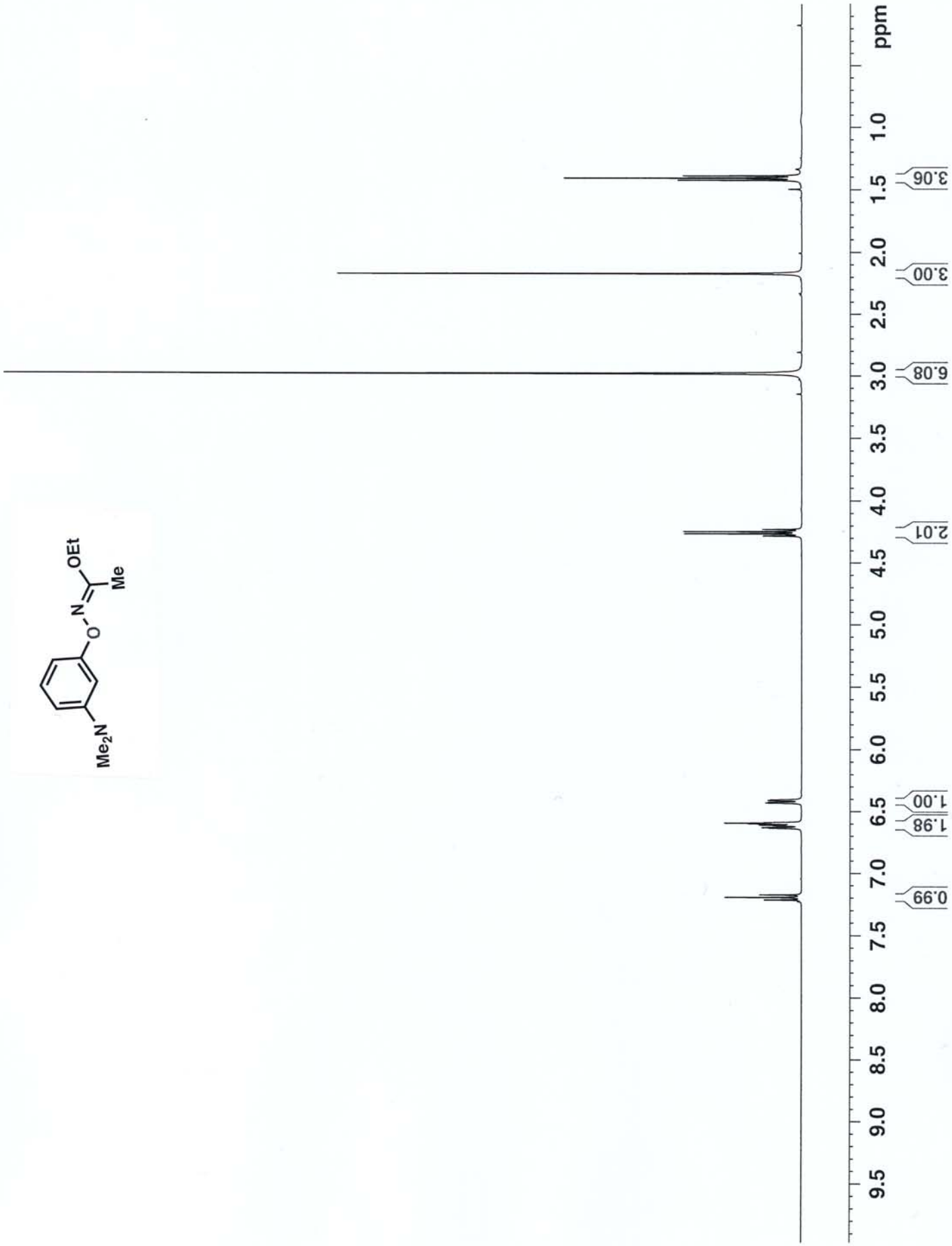


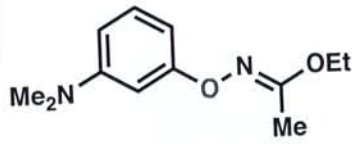
6-fluoro-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan (Table 4). Following procedure D, ethyl *N*-2-fluorophenoxyacetimidate (159 mg, 0.81 mmol), cyclohexanone (167 μl, 1.61 mmol), H_2O (73 μl, 4.1 mmol), HCl (4.0 M solution in dioxane, 1.0 ml, 4.0 mmol), and dioxane (3.0 ml) were heated at 70 °C for 2 hour. The crude product was purified by flash column chromatography (silica gel, hexanes) to afford the title compound as a volatile colorless oil (85 mg, 55% yield) [Note: this compound should not be exposed to high vacuum]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 7.6, 1.0 Hz, 1 H); 7.13 – 7.08 (m, 1 H), 6.99 – 6.92 (m, 1 H), 2.79 – 2.75 (m, 2 H), 2.64 – 2.60 (m, 2 H), 1.98 – 1.92 (m, 2 H), 1.88 – 1.82 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) [complexity observed due to C-F splitting] δ 155.3, 149.2, 146.8, 141.1, 141.0, 132.7, 132.7, 122.9, 122.8, 114.2, 114.2, 113.5, 113.5, 109.7, 109.6, 23.5, 23.0, 22.7, 20.7; IR (film) ν_{max} 2938, 2849, 1633, 1590, 1490, 1443, 1300, 1252, 1201, 1123, 1077, 933, 854, 778, 729, 618 cm^{-1}; Anal. Calcd. For $C_{12}H_{11}OF$: C, 75.77; H, 5.83. Found: C, 75.52; H, 5.87.

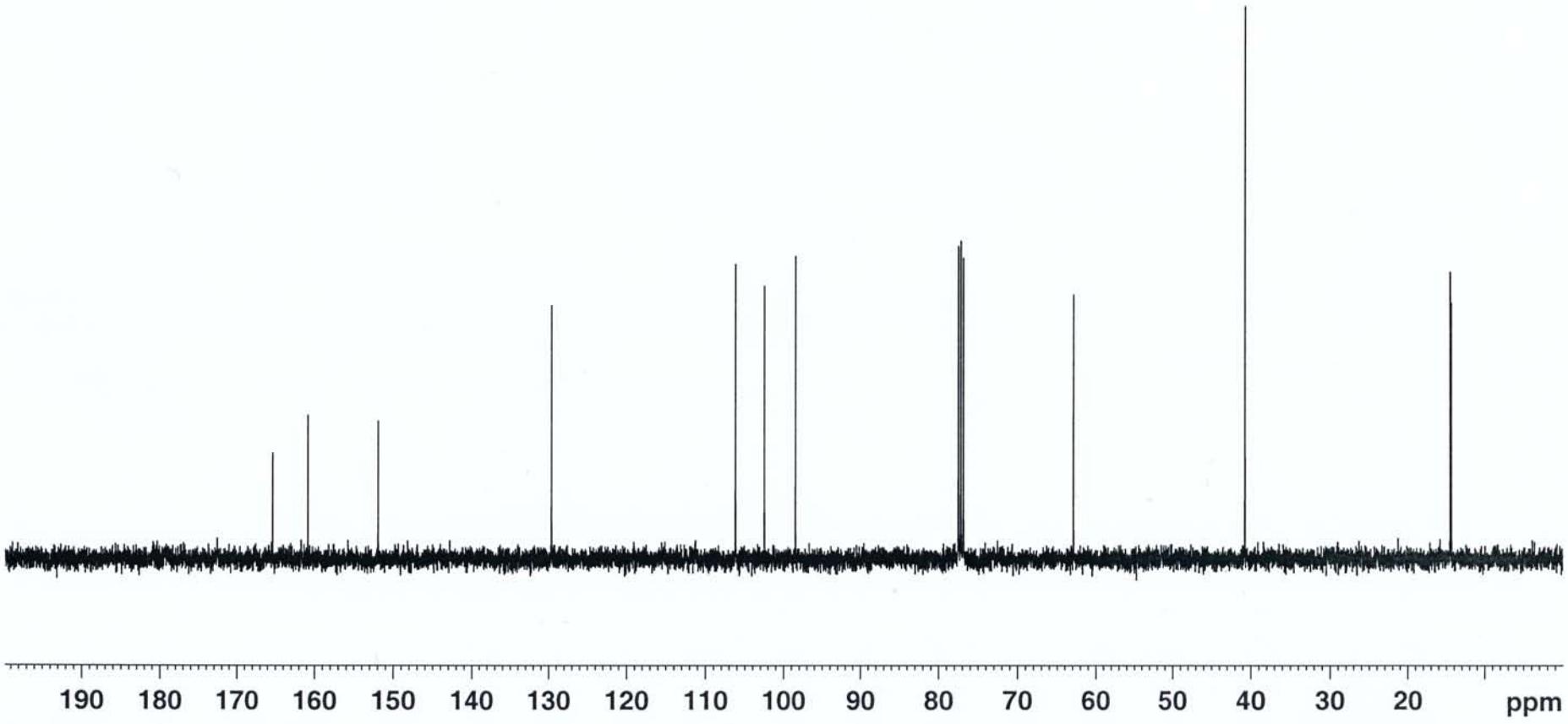

OEt
N
O
Me
ppm
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
2.98
0.96
1.01
1.00
0.99
2.00
2.97
3.03

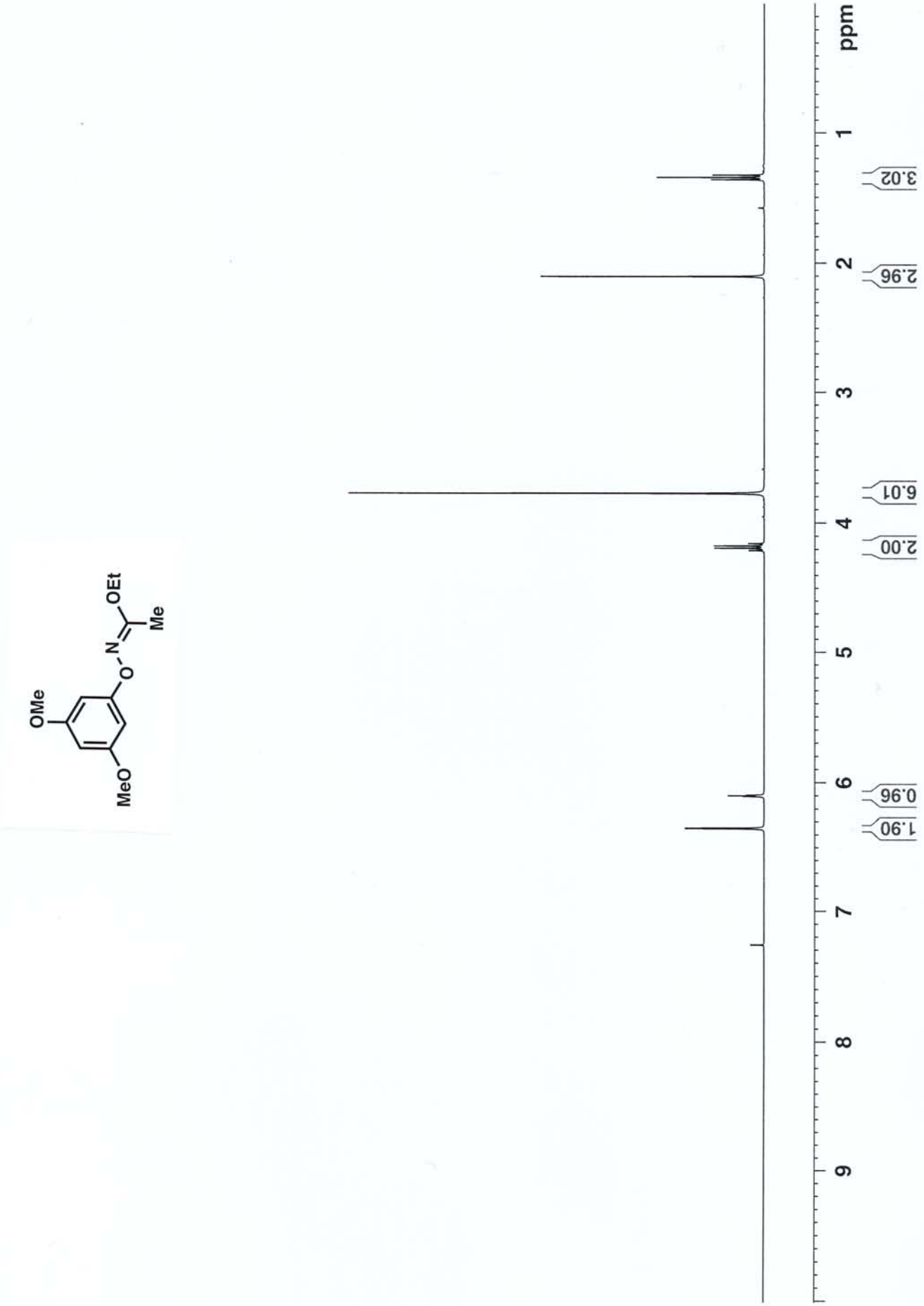

O
N
OEt
Me

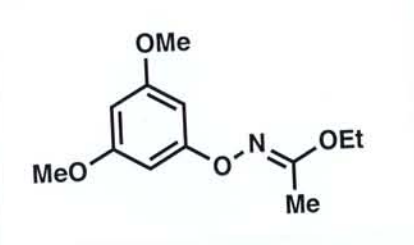

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

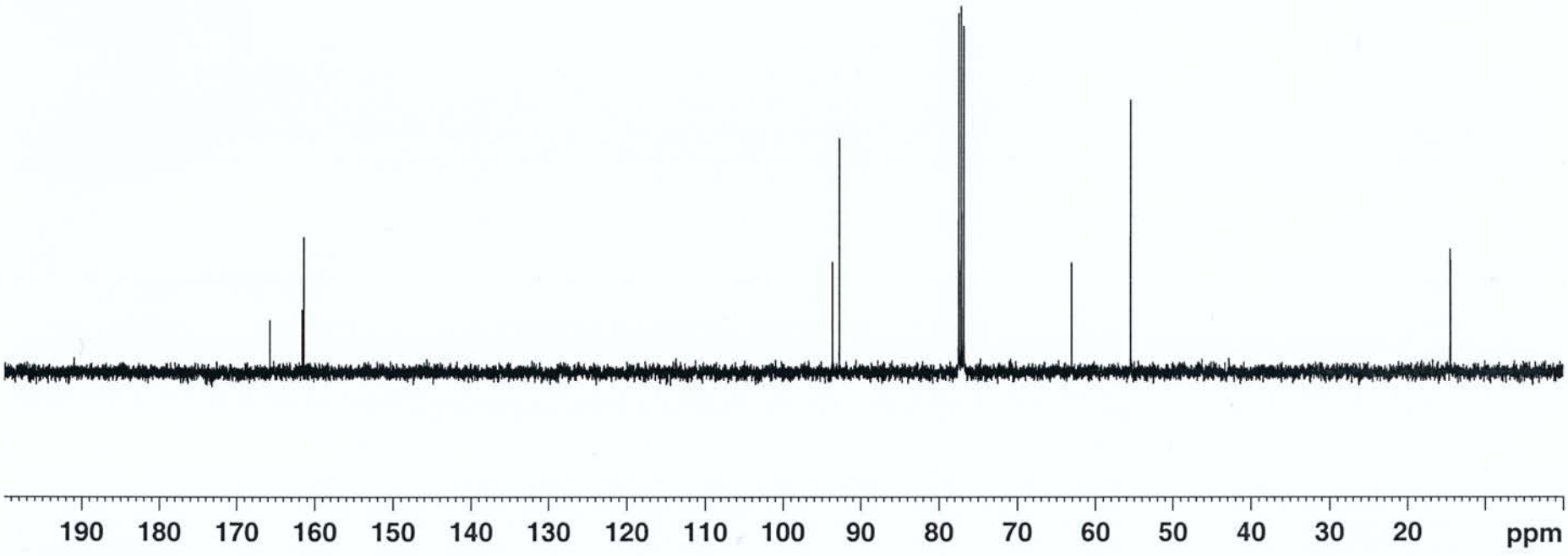

OEt
N
Me
O
Me2N
ppm
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.99
1.98
1.00
2.01
6.08
3.00
3.06

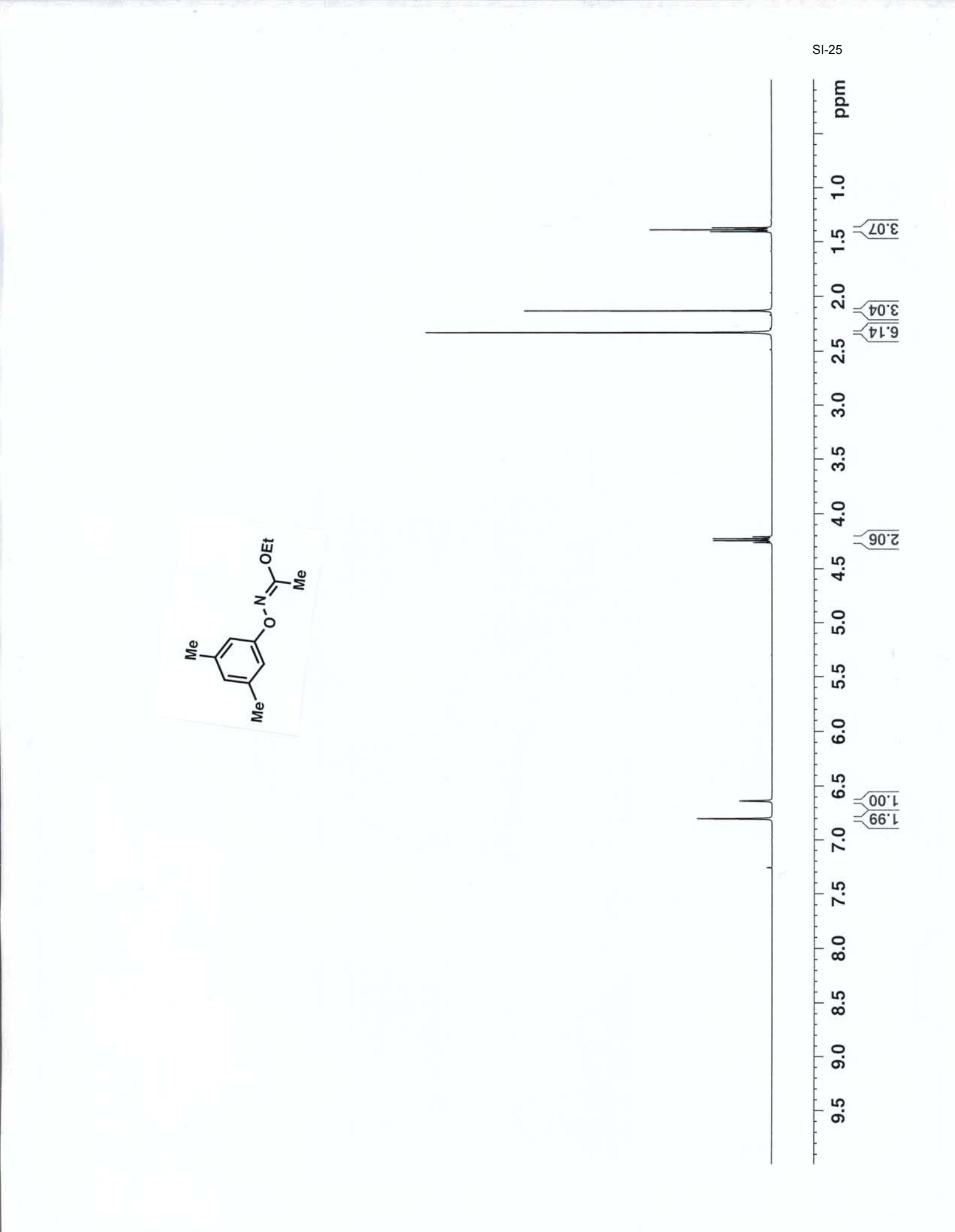

Me2N
O
N
OEt
Me

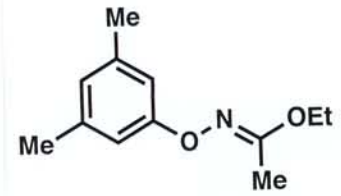

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

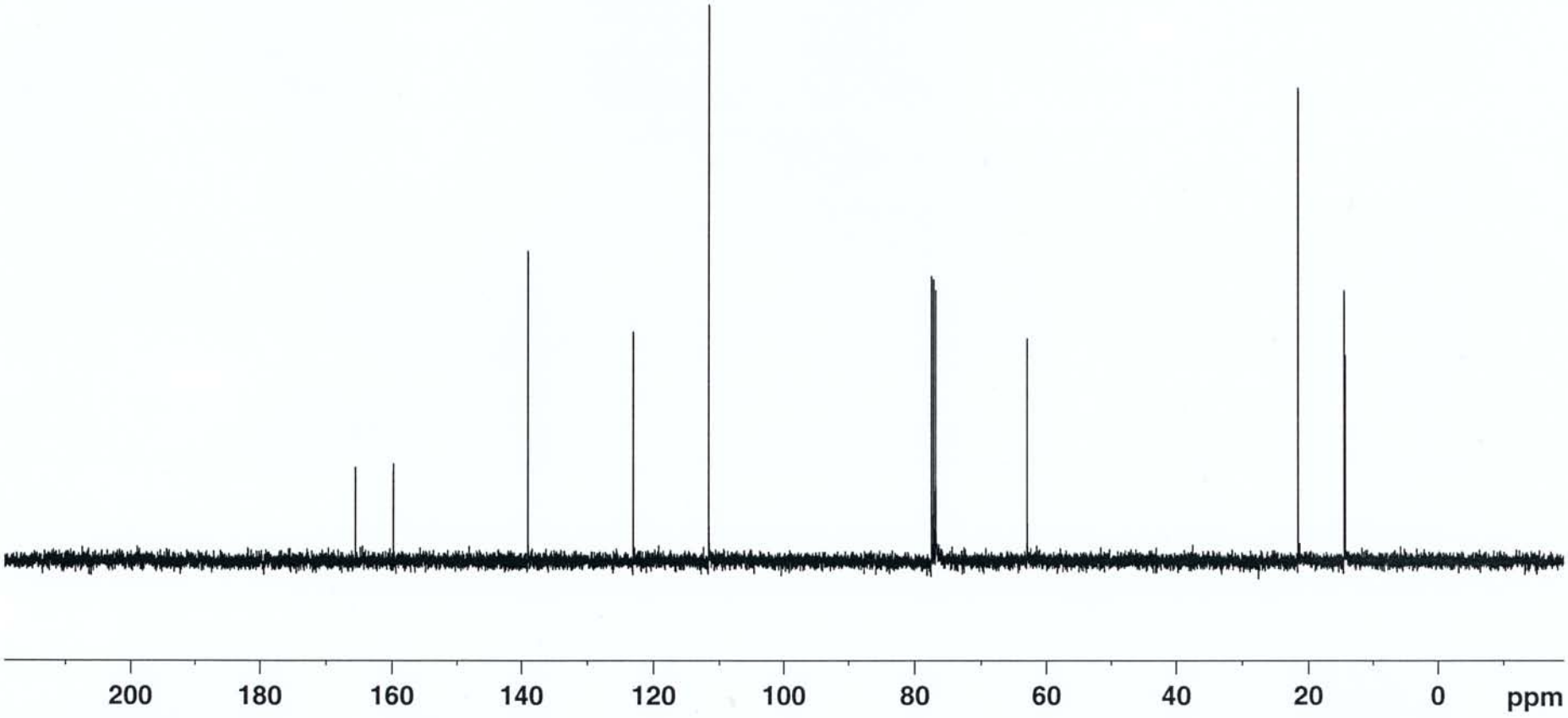

OMe
MeO
O
N
OEt
Me
ppm
1
2
3
4
5
6
7
8
9
3.02
2.96
6.01
2.00
0.96
1.90

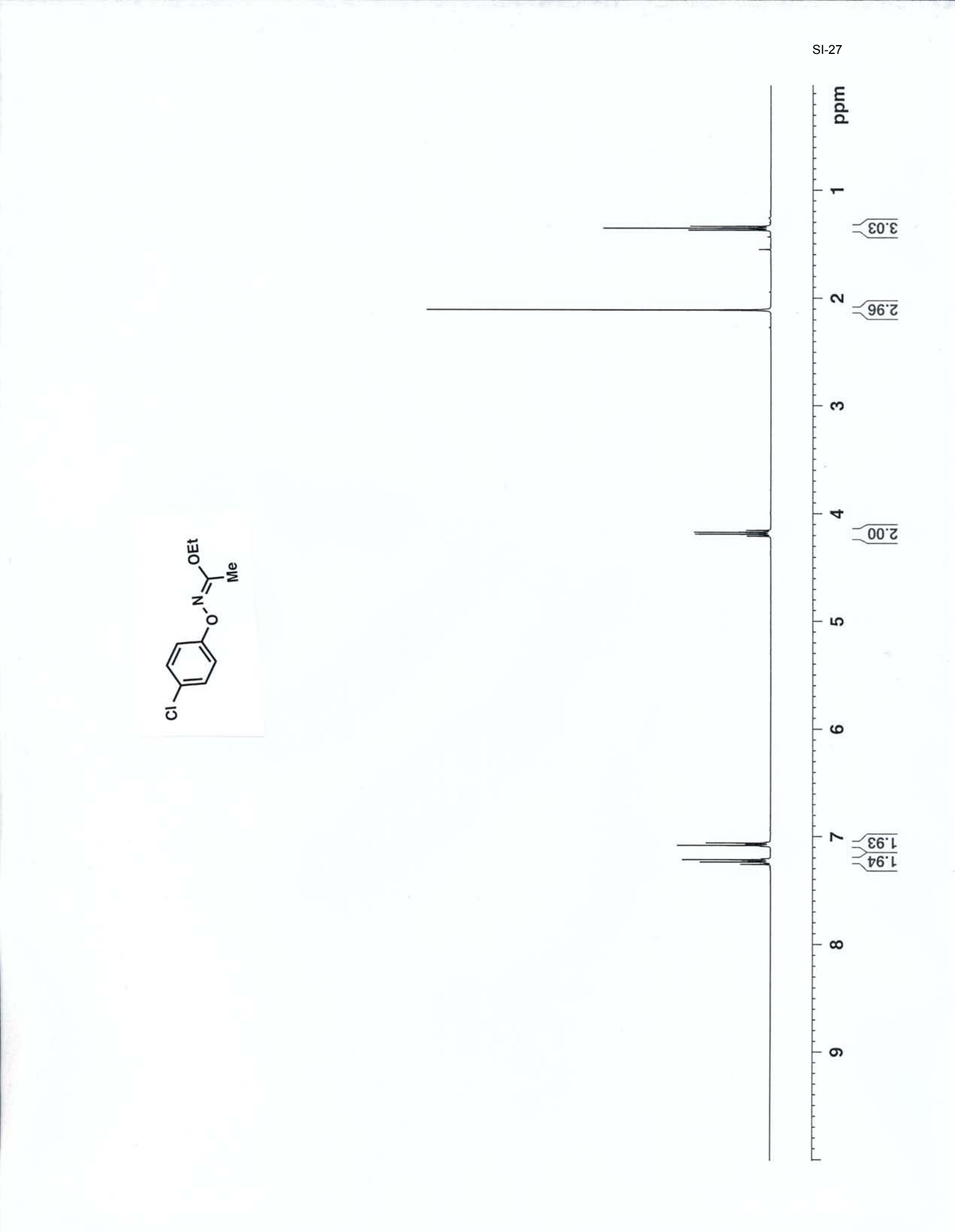

OMe
MeO
O
N
OEt
Me

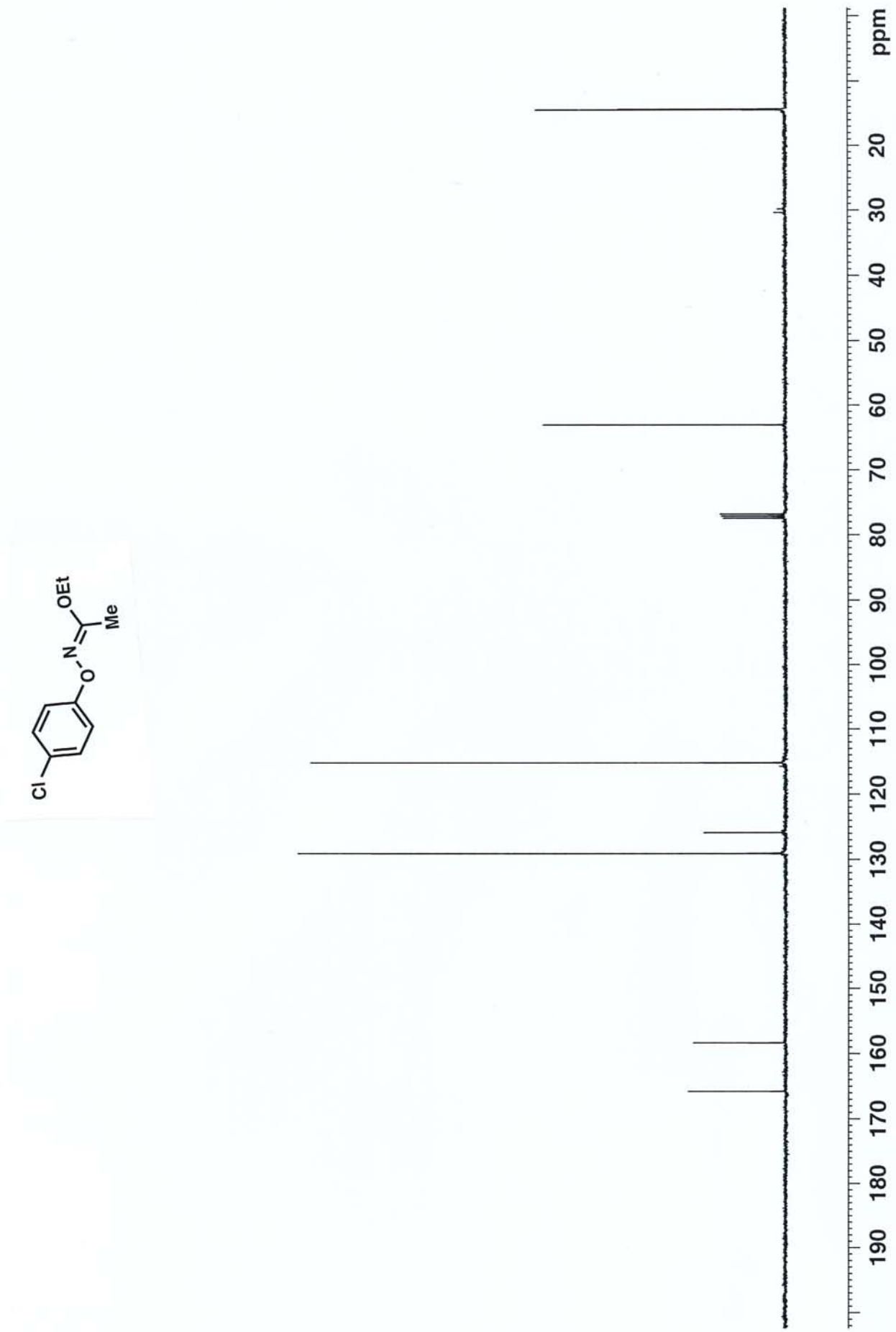

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

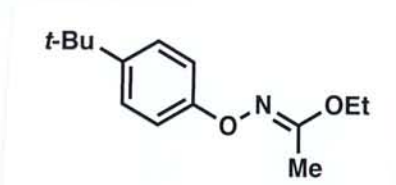

Me
Me
O
N
OEt
Me
ppm
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
1.99
1.00
2.06
6.14
3.04
3.07

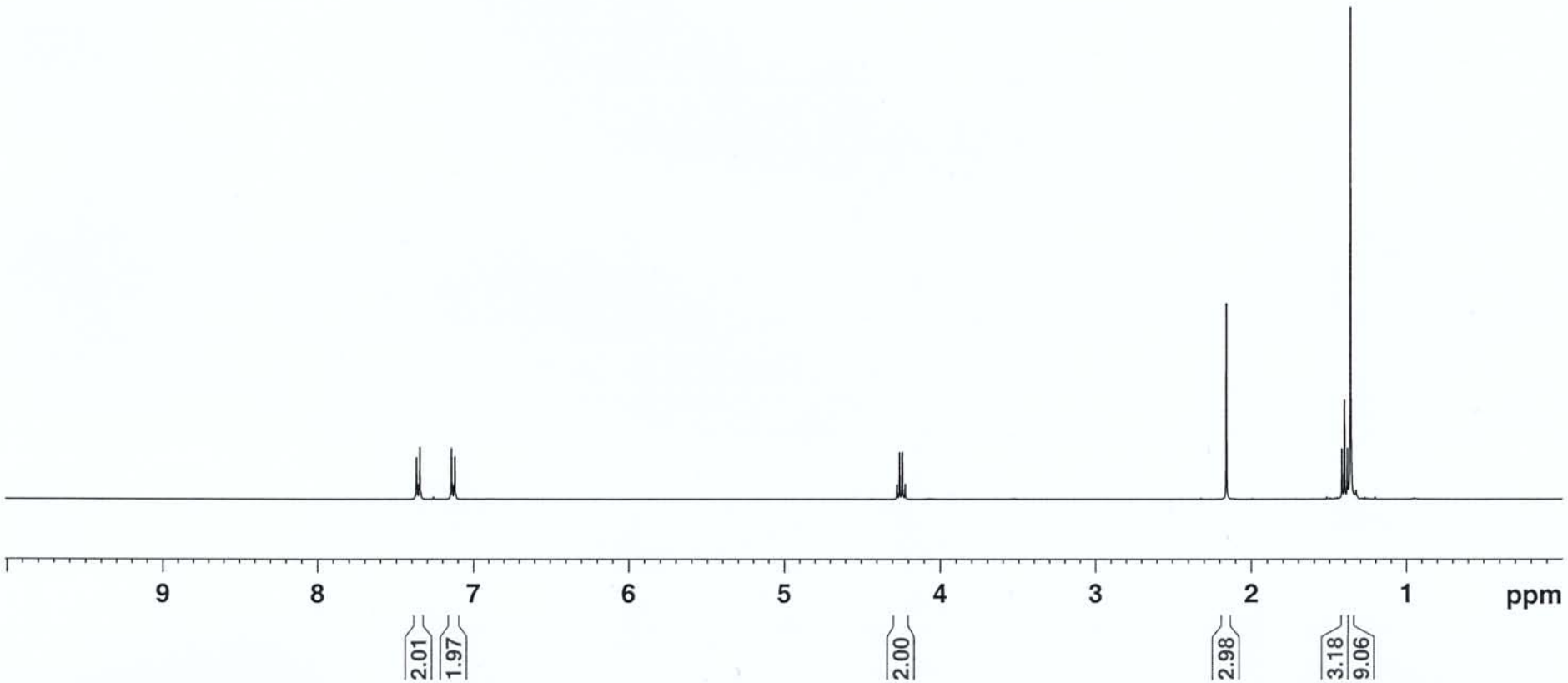

Me
Me
O
N
OEt
Me

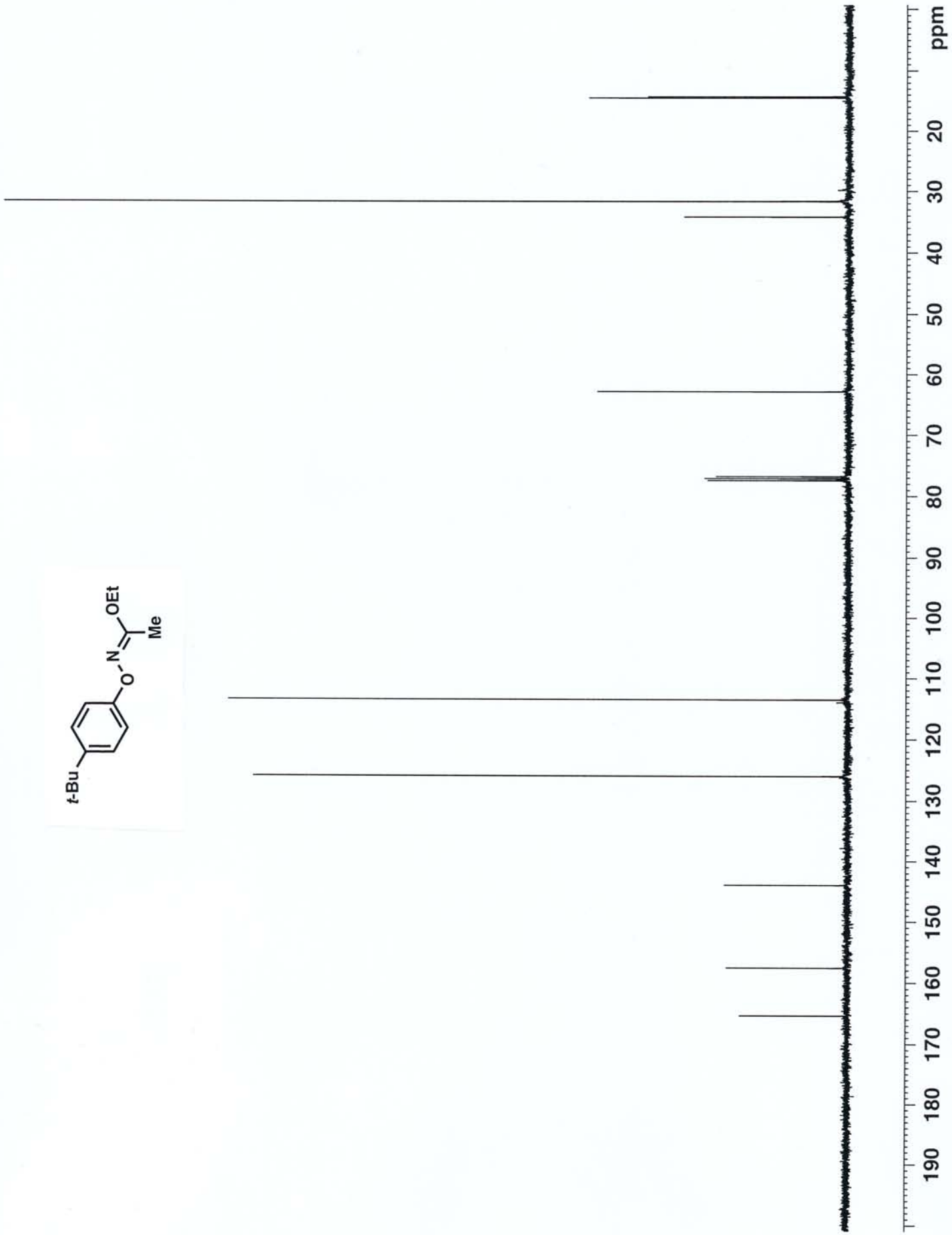

200
180
160
140
120
100
80
60
40
20
0
ppm

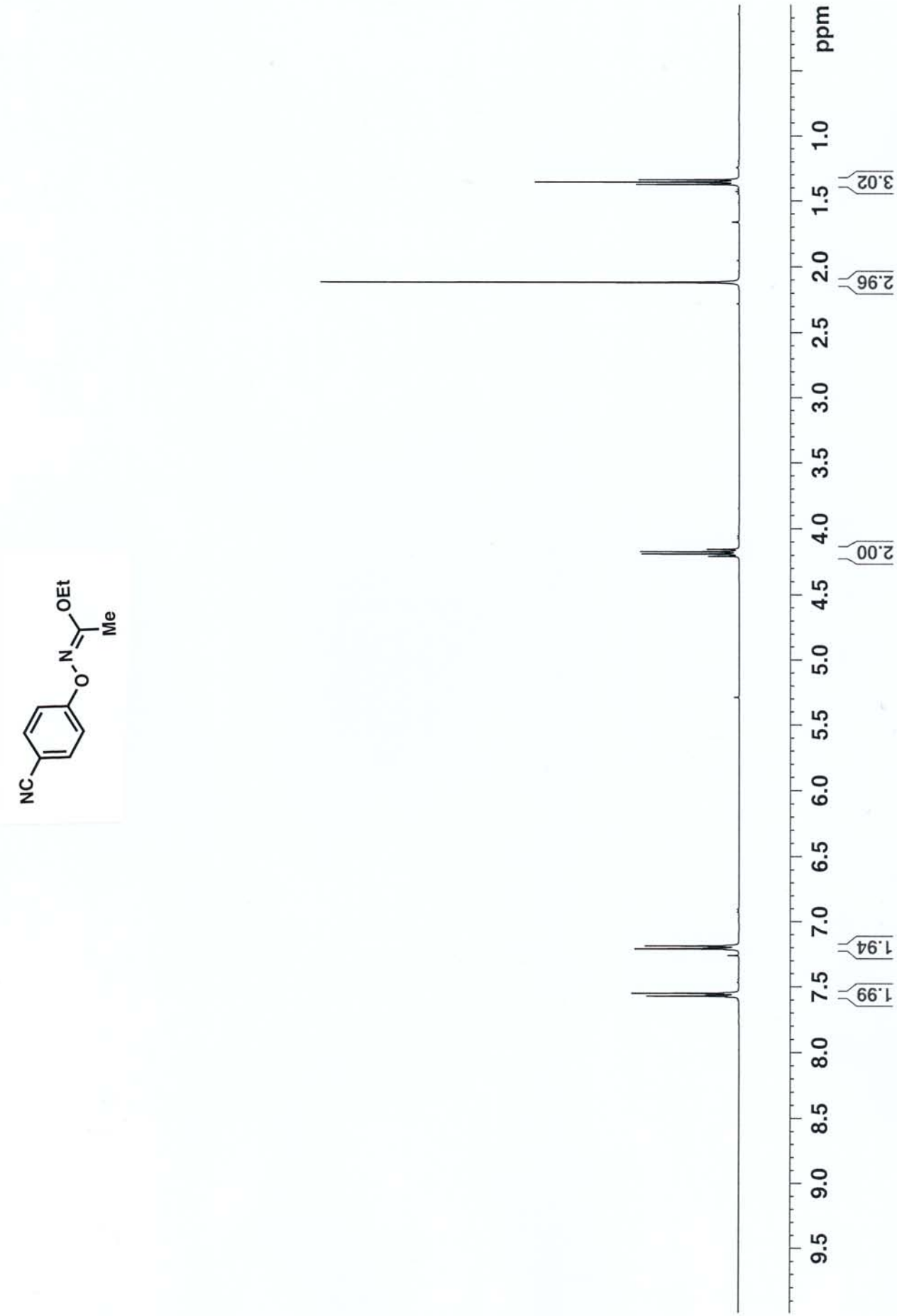

Cl
O
N
OEt
Me
ppm
1
2
3
4
5
6
7
8
9
3.03
2.96
2.00
1.94
1.93

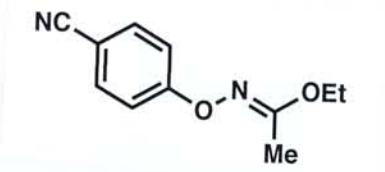

Cl
O
N
OEt
Me
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

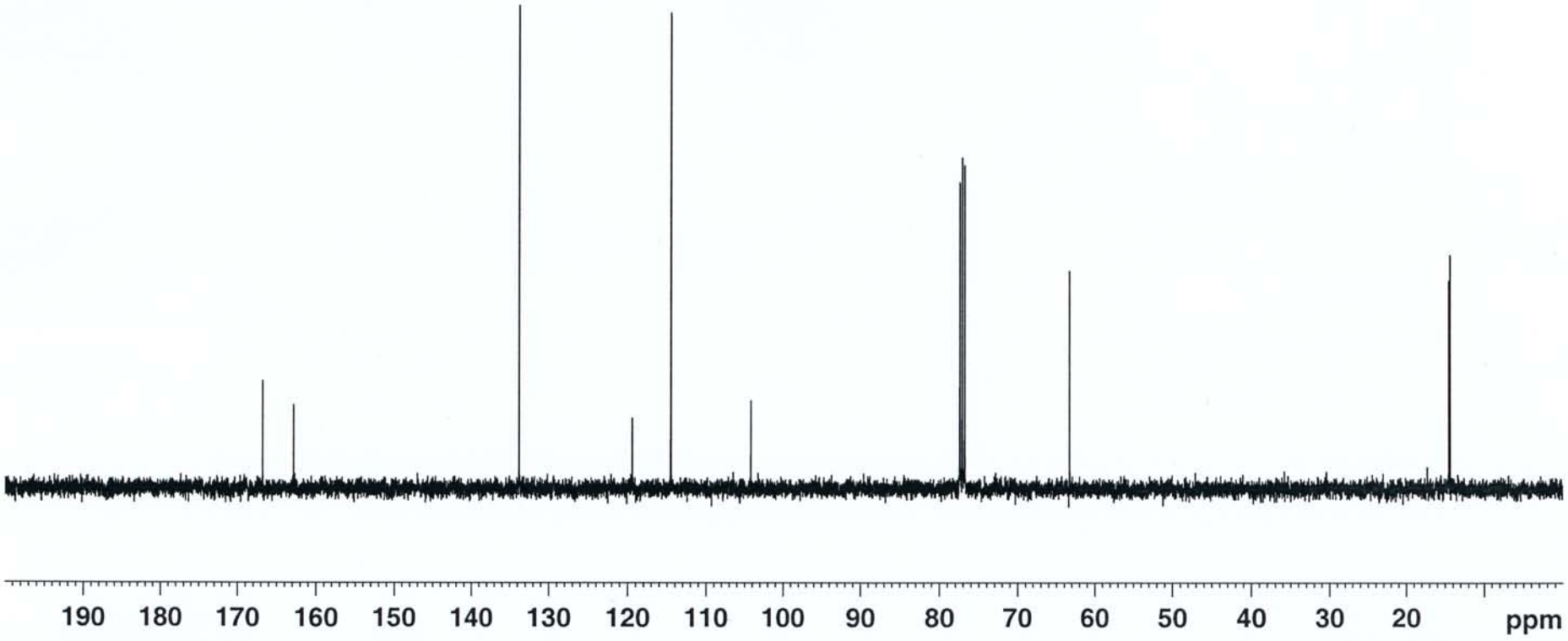

t-Bu
O
N
OEt
Me

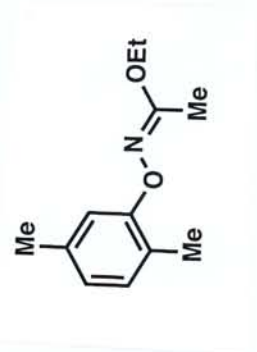

9
8
7
6
5
4
3
2
1
ppm
2.01
1.97
2.00
2.98
3.18
9.06

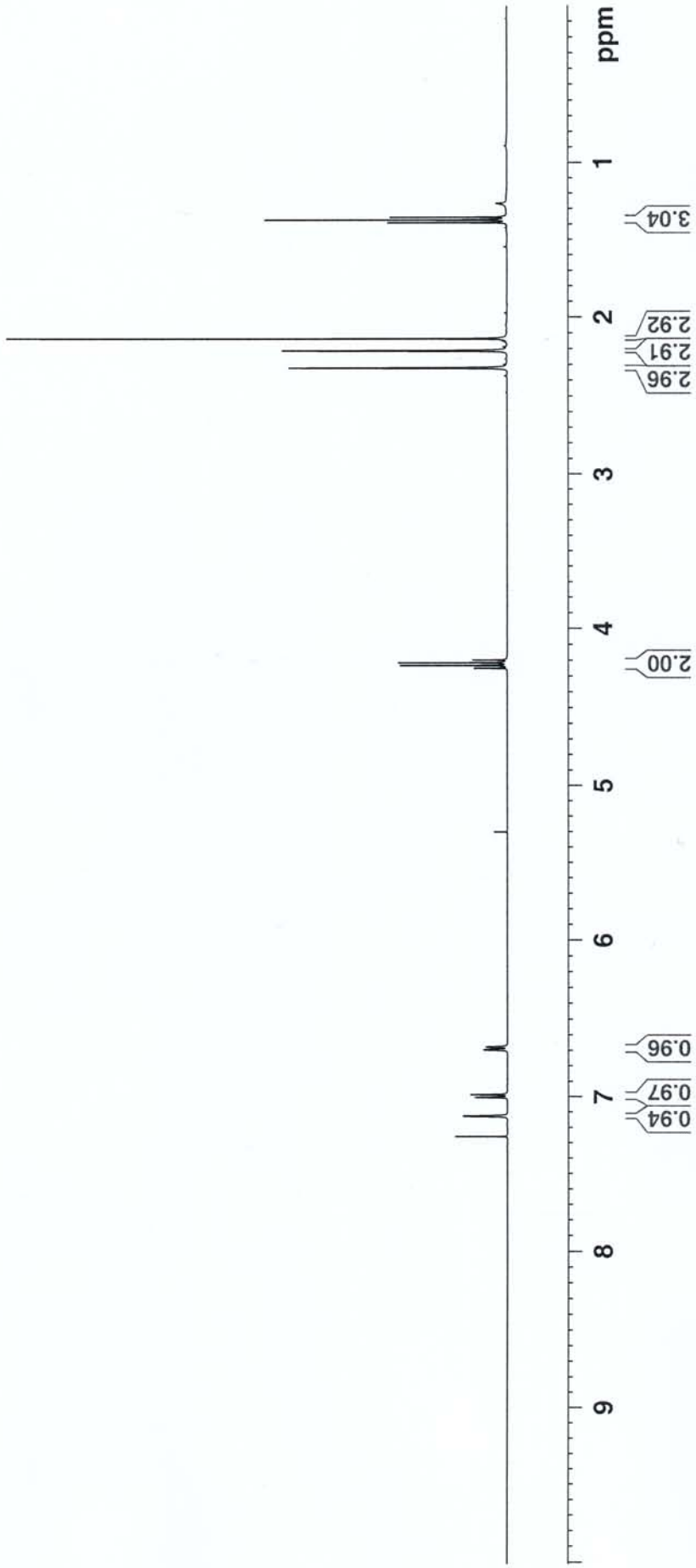

t-Bu
O
N
OEt
Me
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

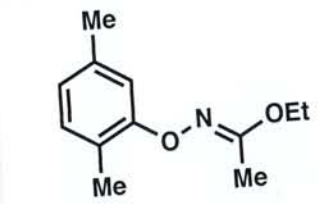

NC
O
N
OEt
Me
ppm
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
1.99
1.94
2.00
2.96
3.02

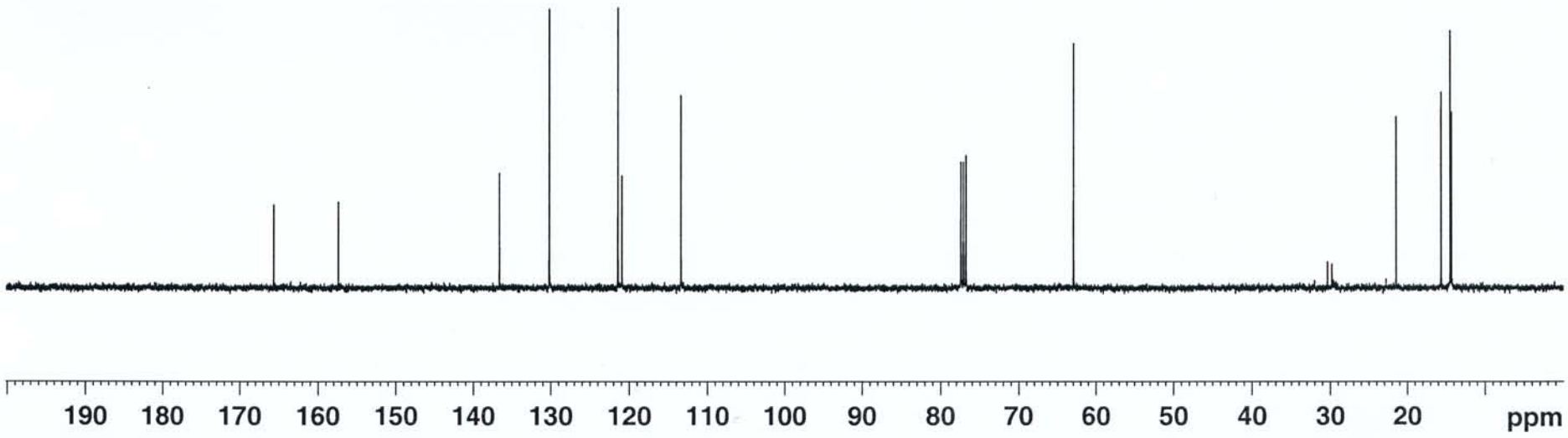

NC
O
N
OEt
Me

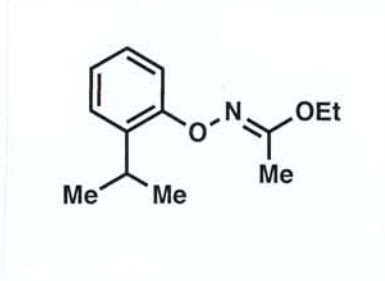

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

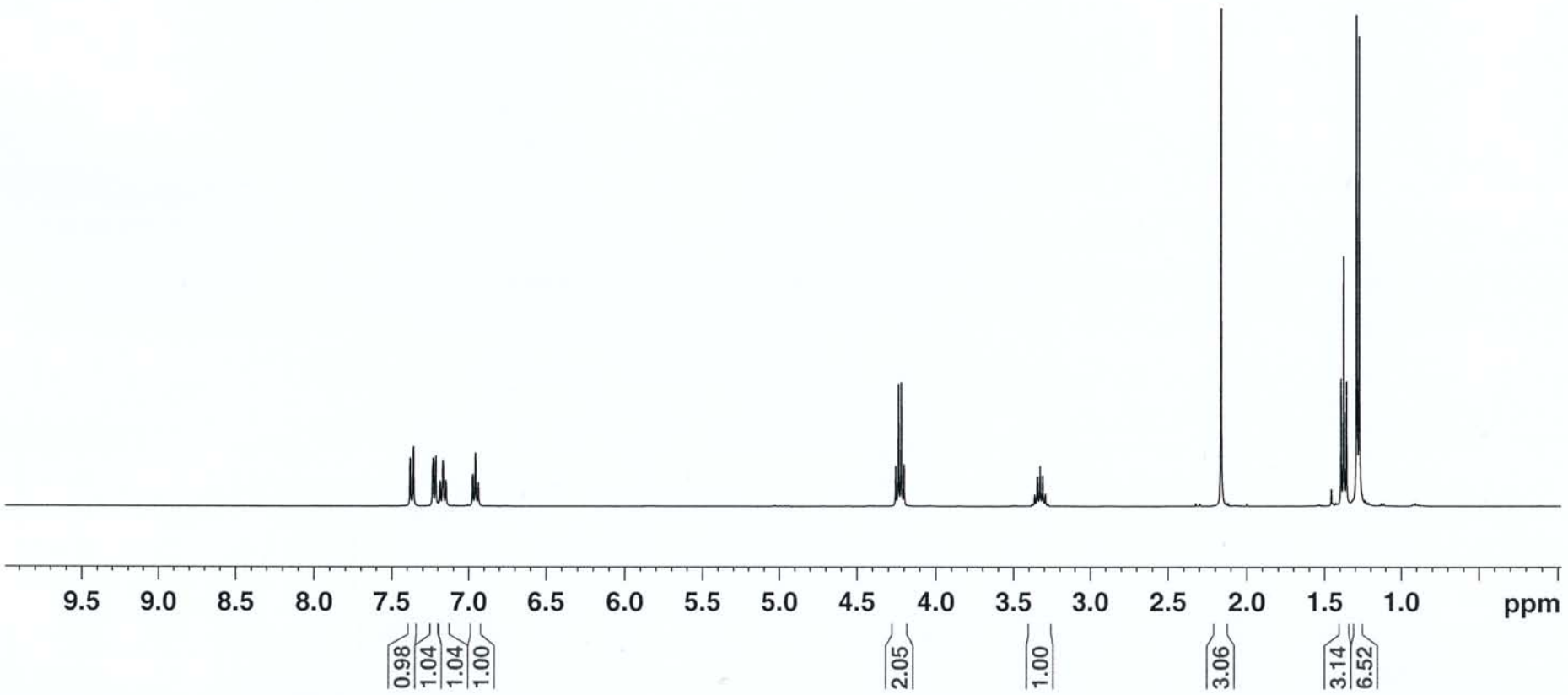

Me
O
N
OEt
Me
Me

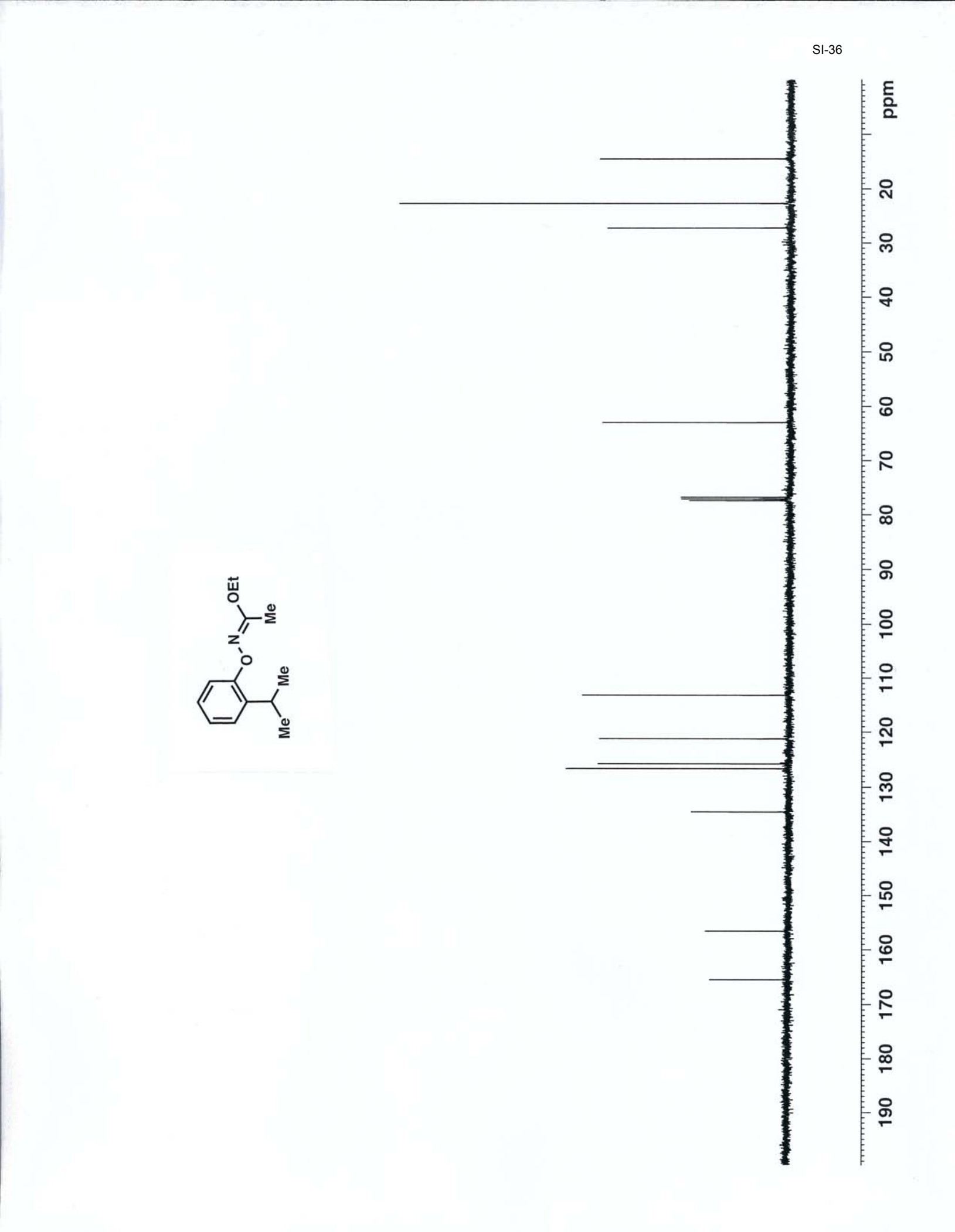

ppm
1
2
3
4
5
6
7
8
9
3.04
2.92
2.91
2.96
2.00
0.96
0.97
0.94

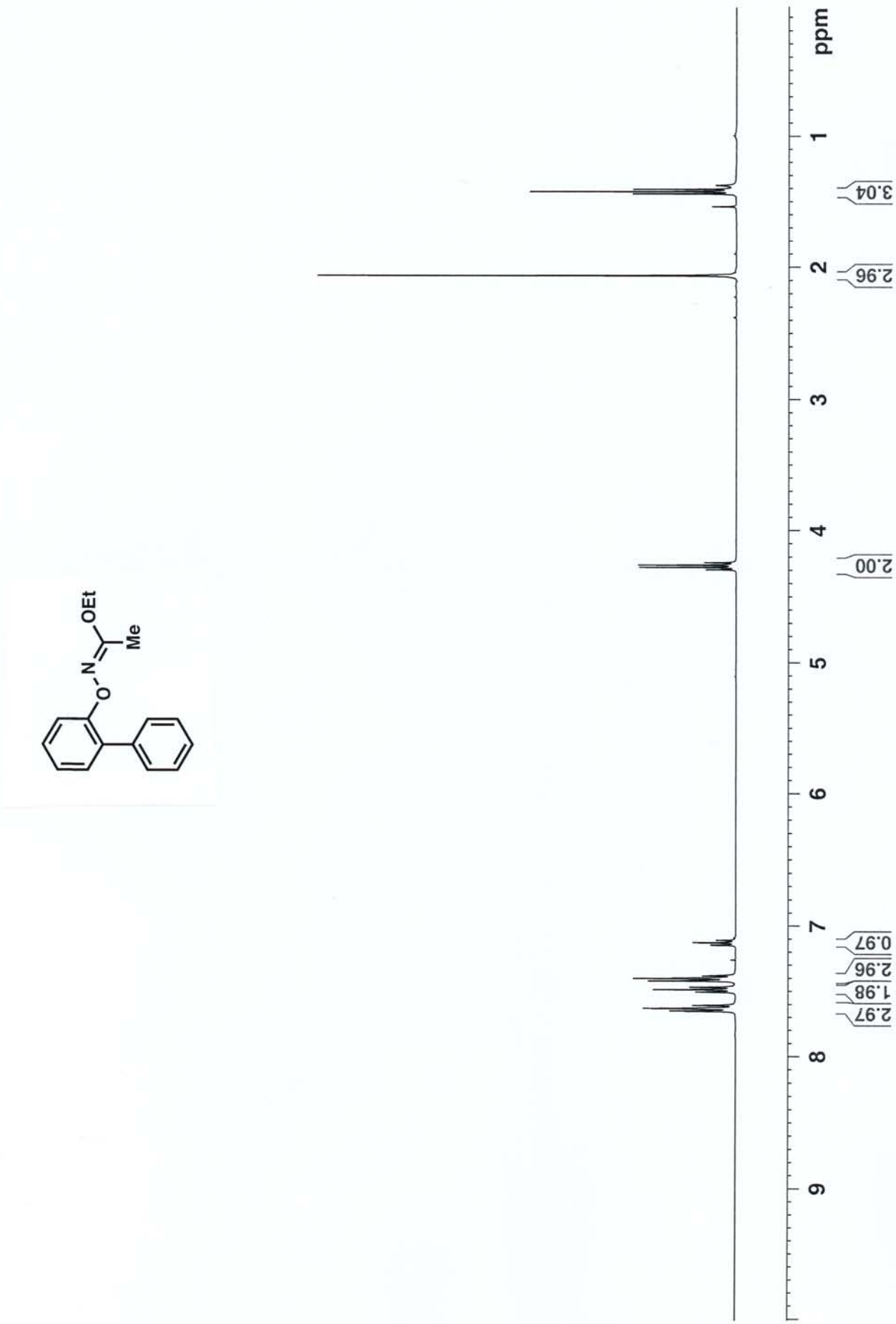

Me
O
N
OEt
Me
Me

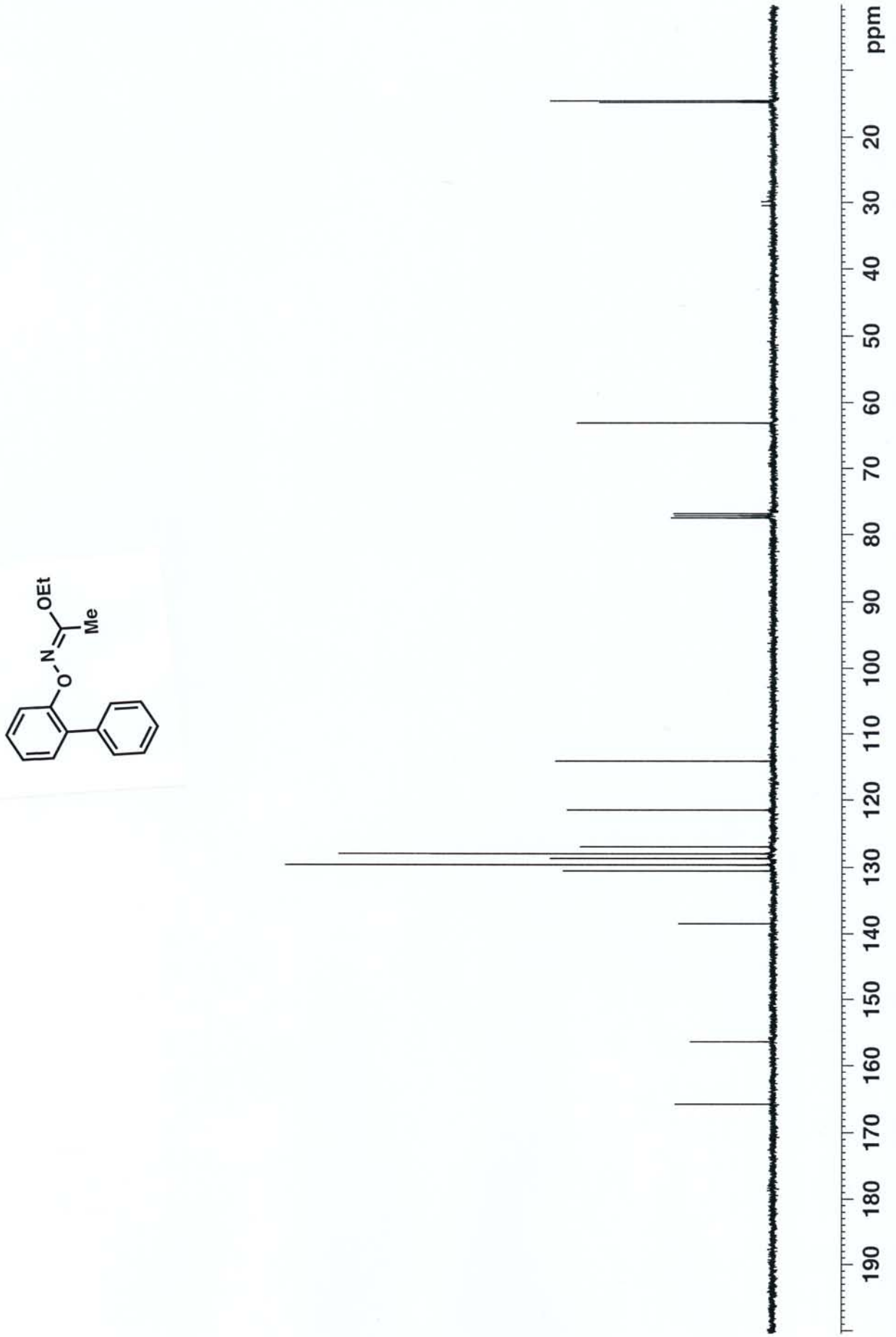

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

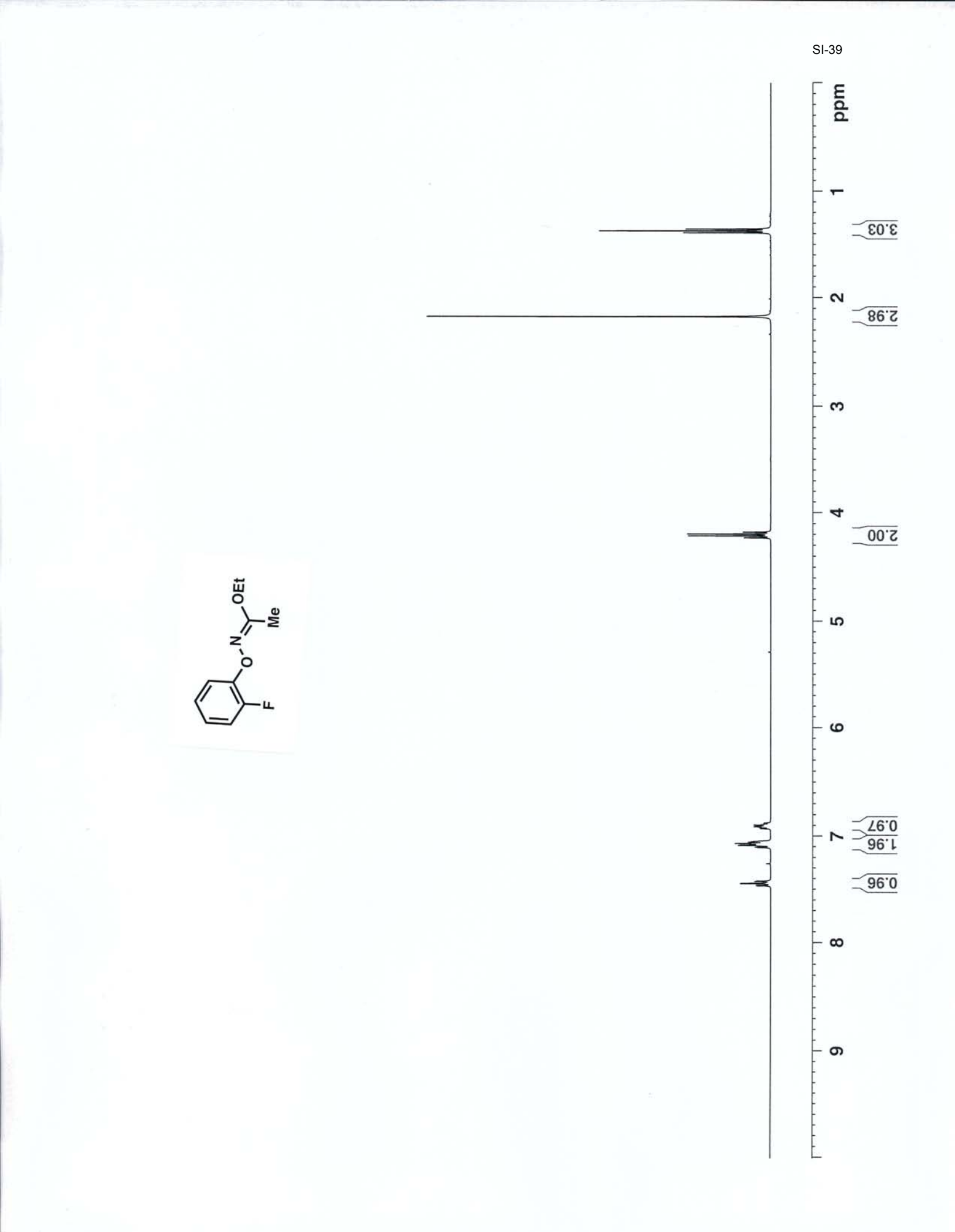

O
N
OEt
Me
Me
Me

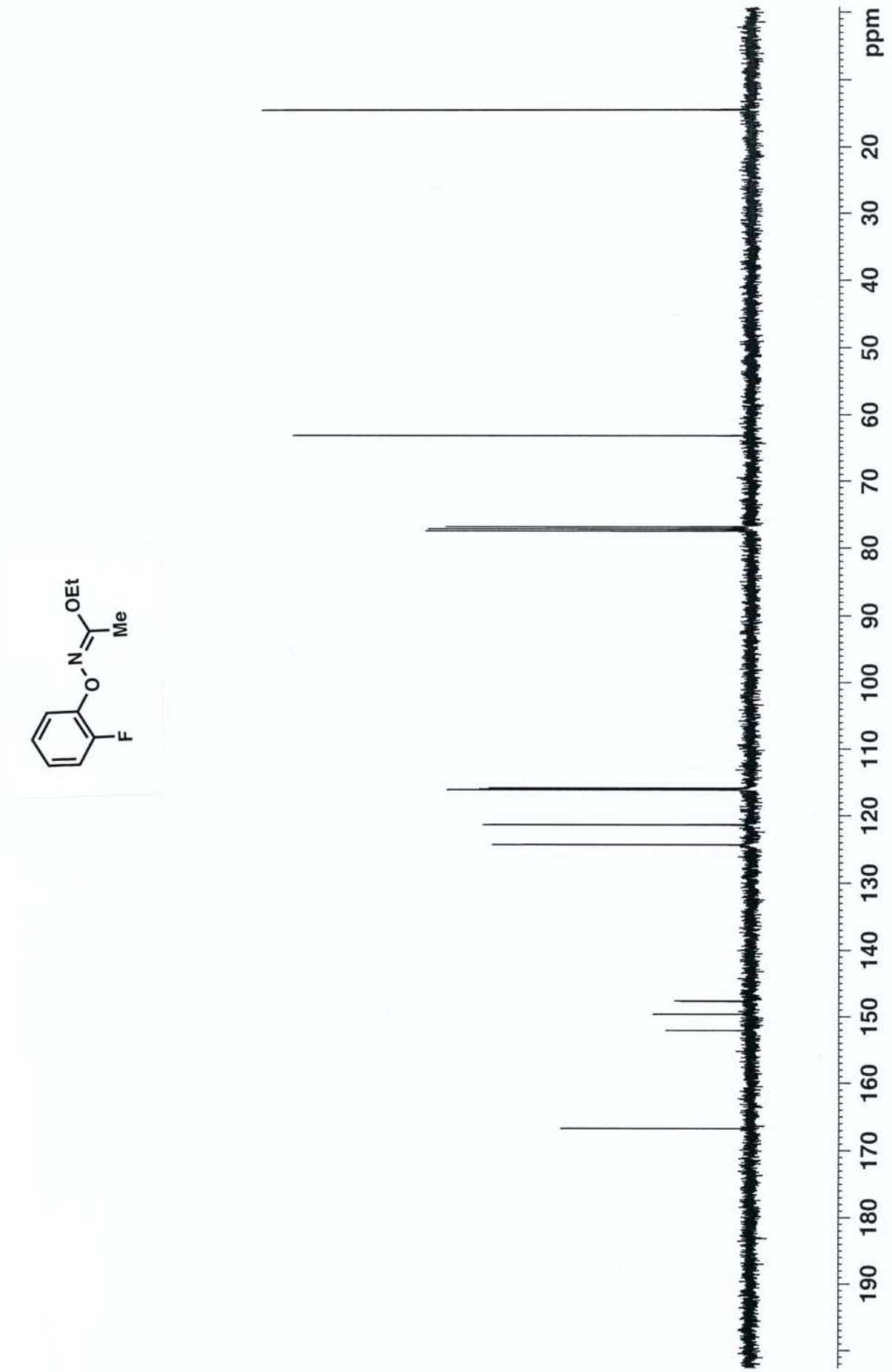

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.98
1.04
1.04
1.00
2.05
1.00
3.06
3.14
6.52

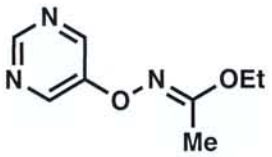

OEt
N
O
Me
Me
Me
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

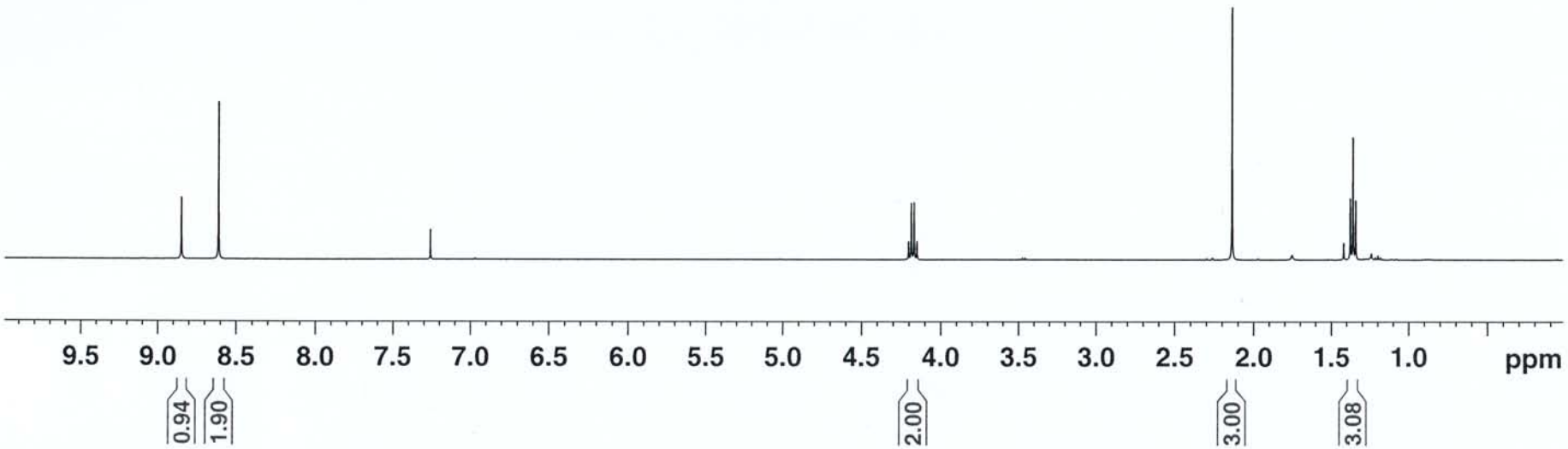

OEt
N
Me
O
ppm
1
2
3
4
5
6
7
8
9
3.04
2.96
2.00
0.97
2.96
1.98
2.97

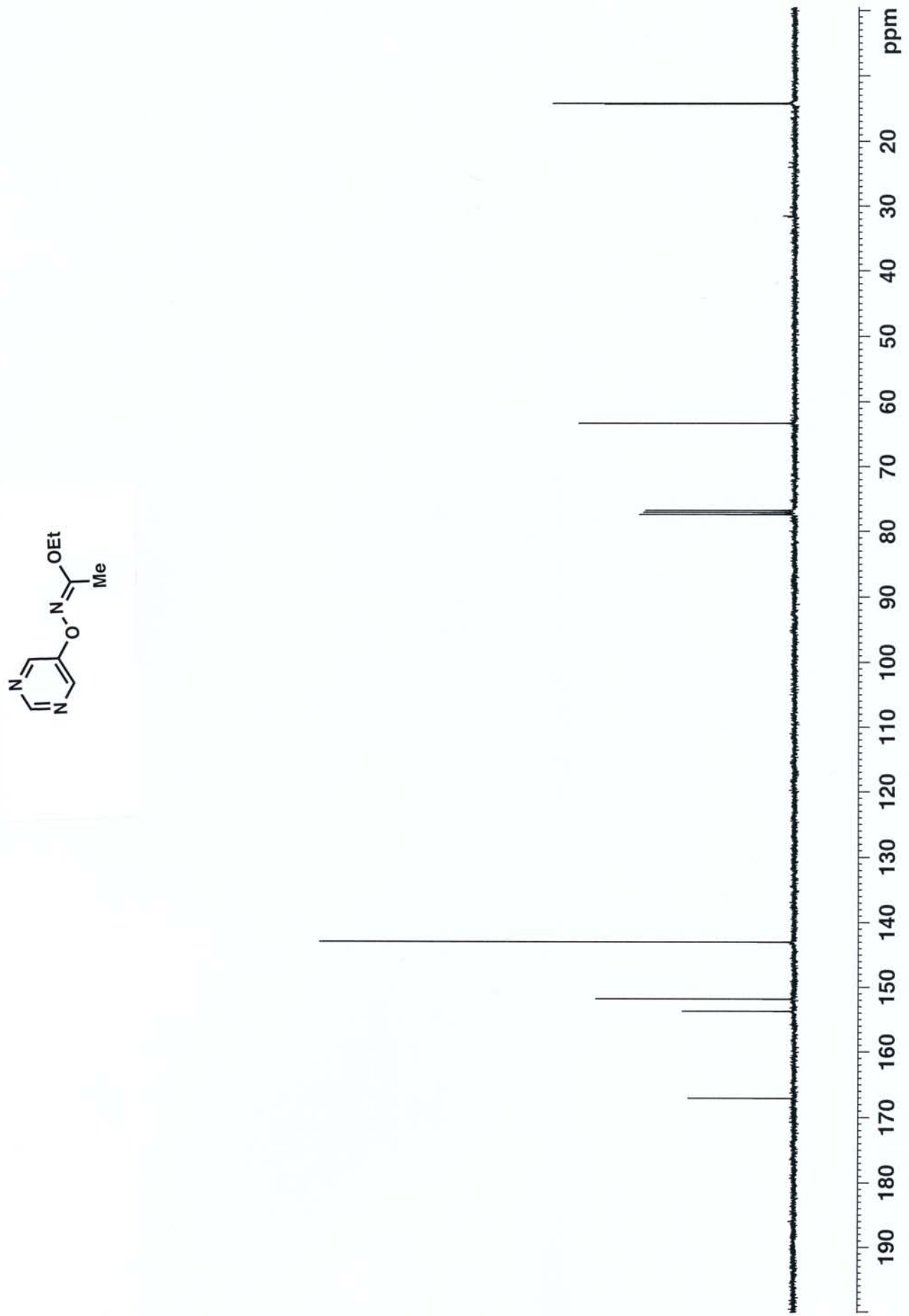

OEt
Me
N
O
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

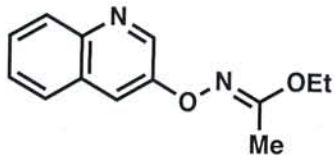

OEt
N
Me
O
F
ppm
1
2
3
4
5
6
7
8
9
3.03
2.98
2.00
0.96
1.96
0.97

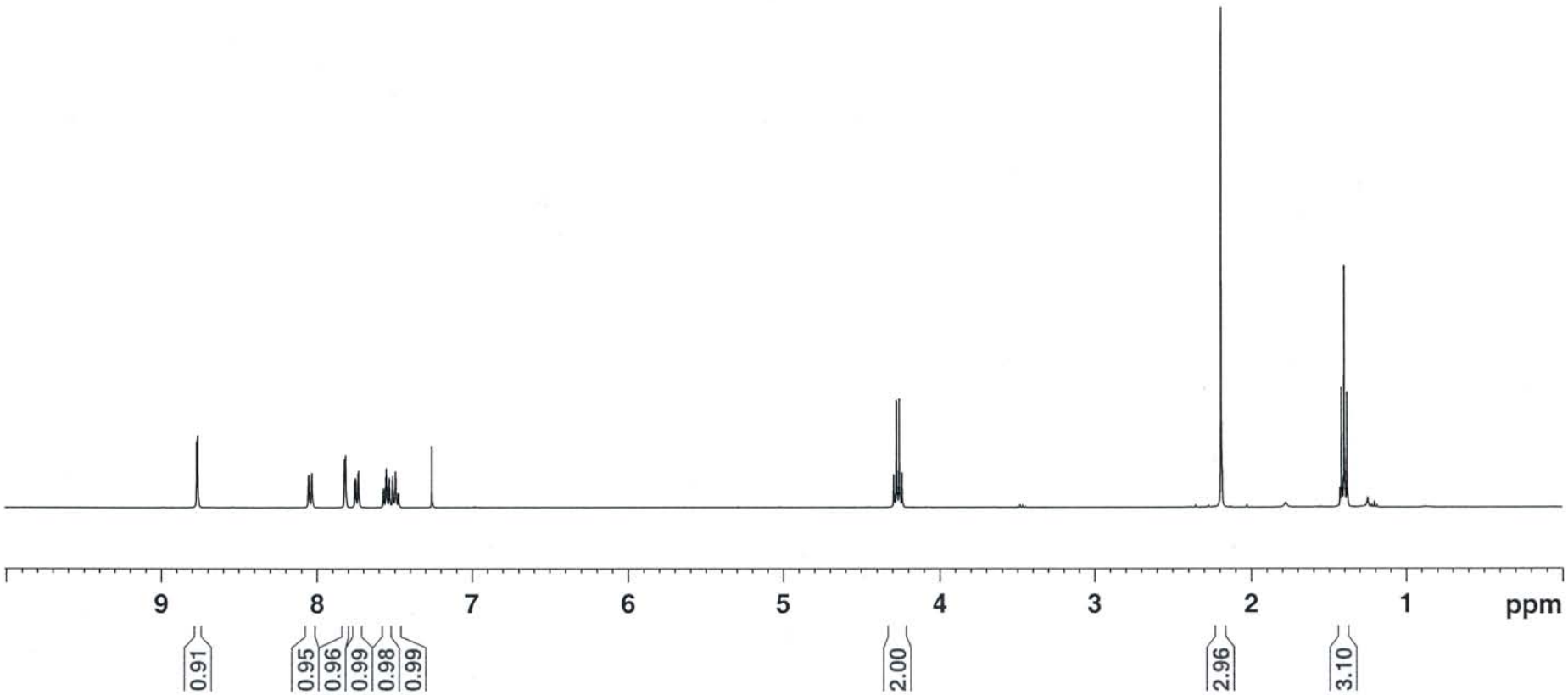

OEt
N
Me
O
F
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

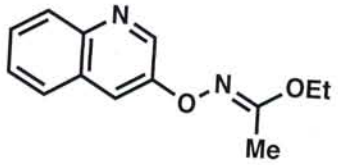

N
N
O
N
OEt
Me

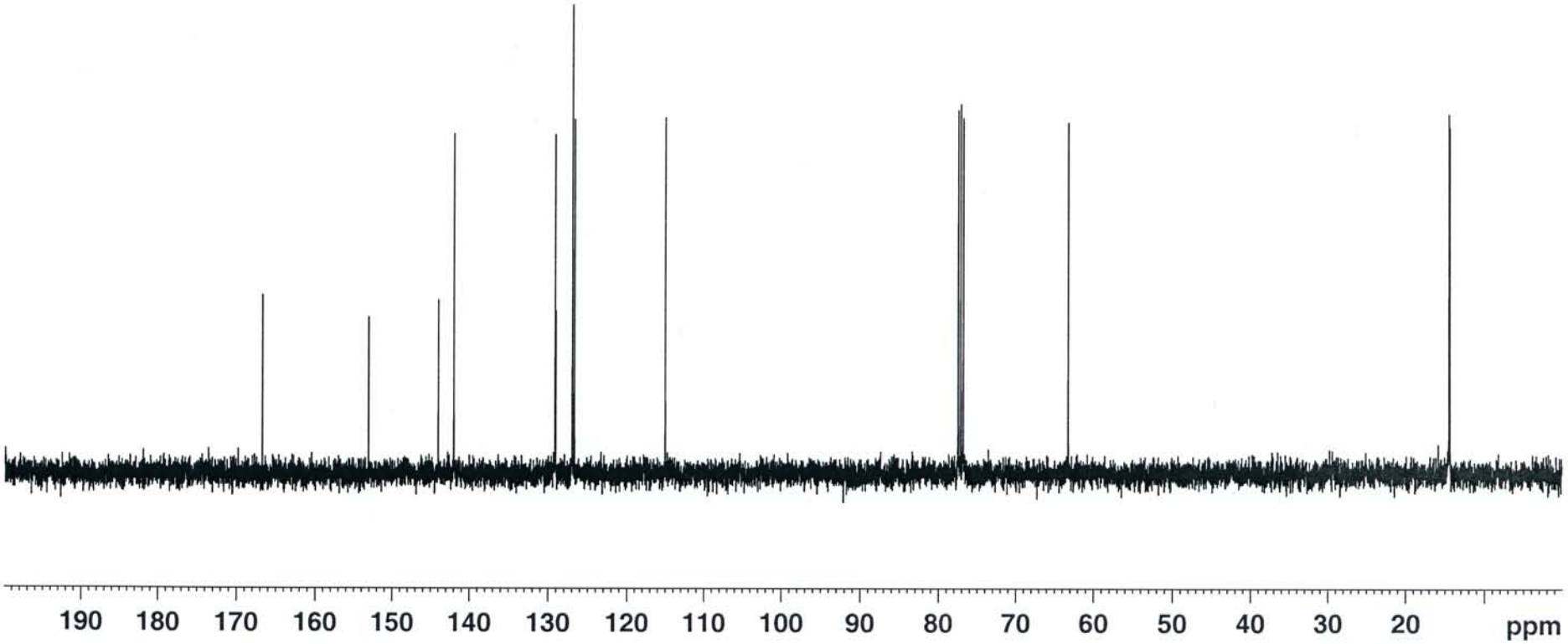

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.94
1.90
2.00
3.00
3.08

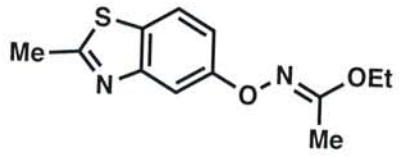

OEt
Me
N
O
N
N
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

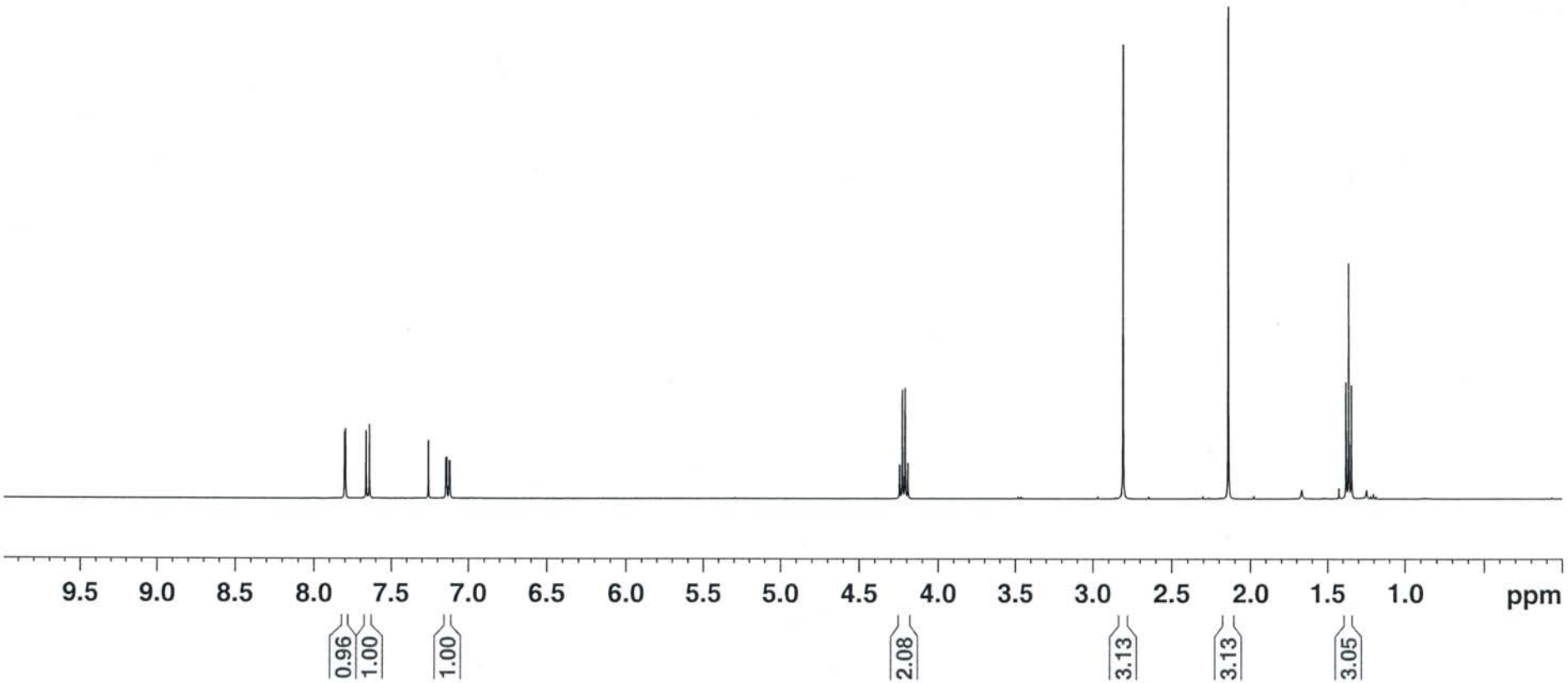

N
O
N
OEt
Me

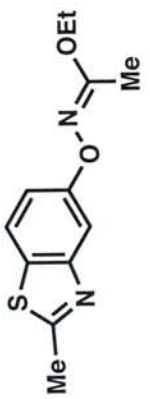

9
8
7
6
5
4
3
2
1
ppm
0.91
0.95
0.96
0.99
0.98
0.99
2.00
2.96
3.10

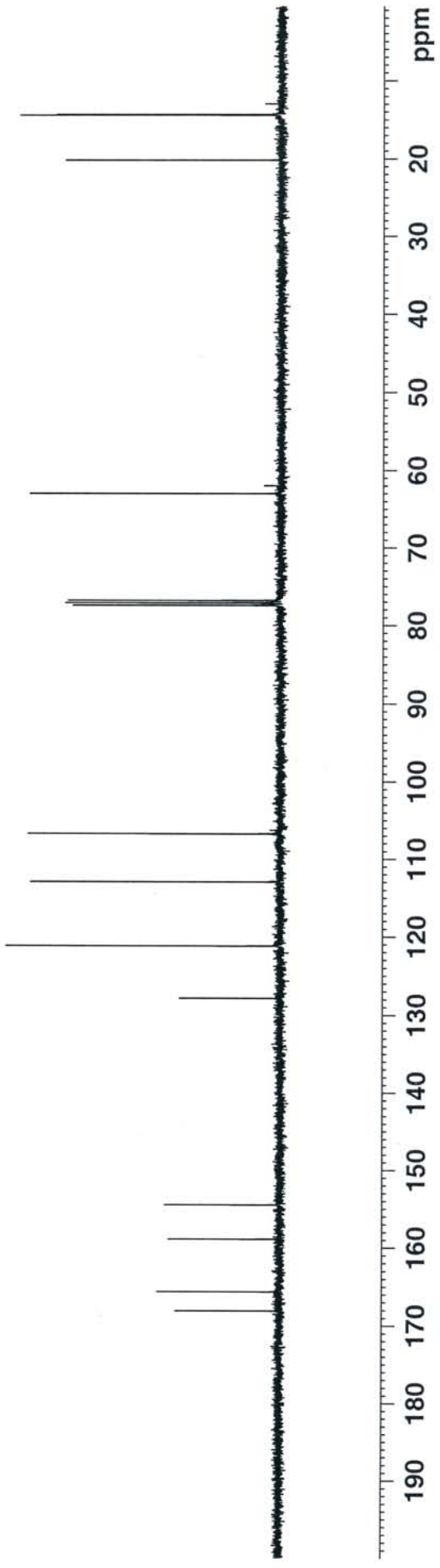

N
O
N
OEt
Me

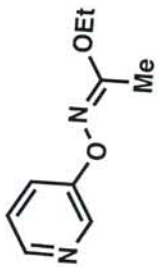

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

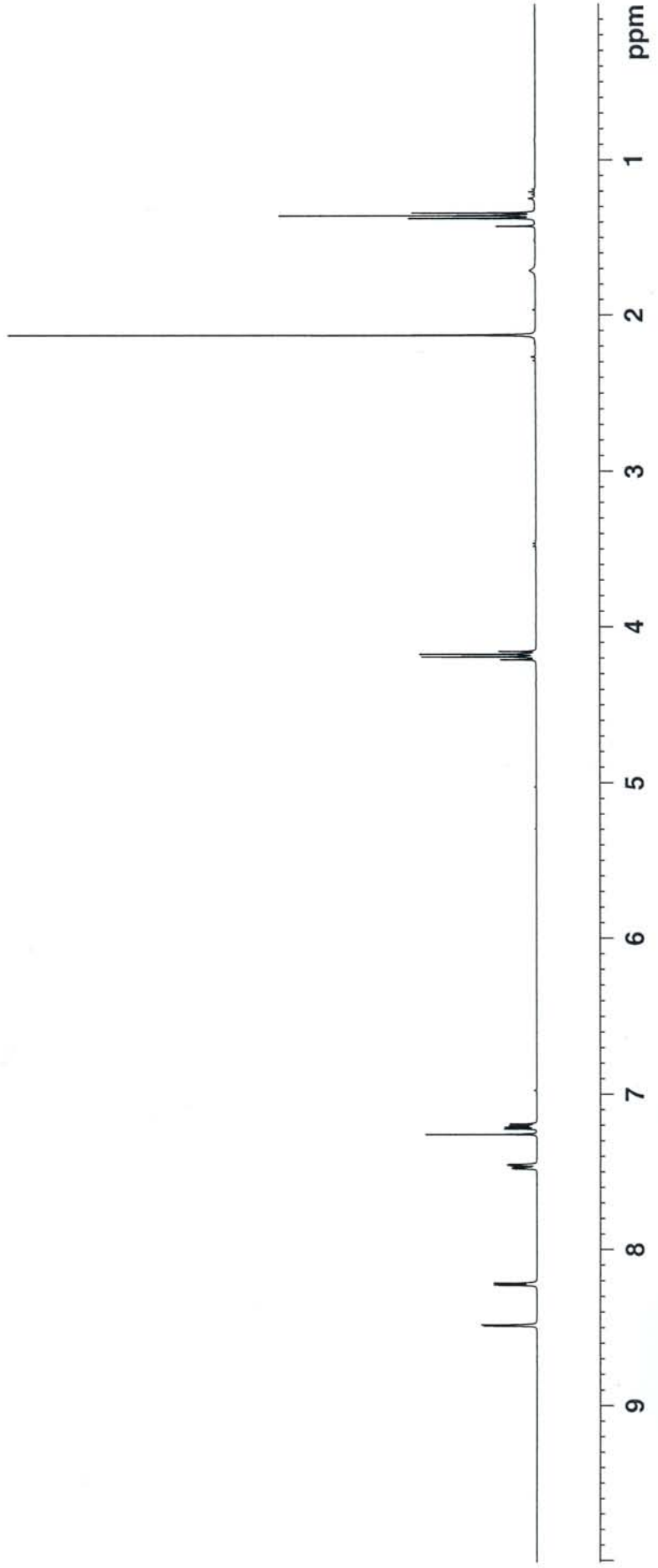

S
Me
N
O
N
OEt
Me

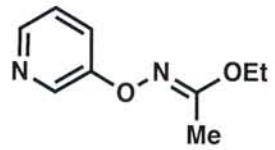

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.96
1.00
1.00
2.08
3.13
3.13
3.05

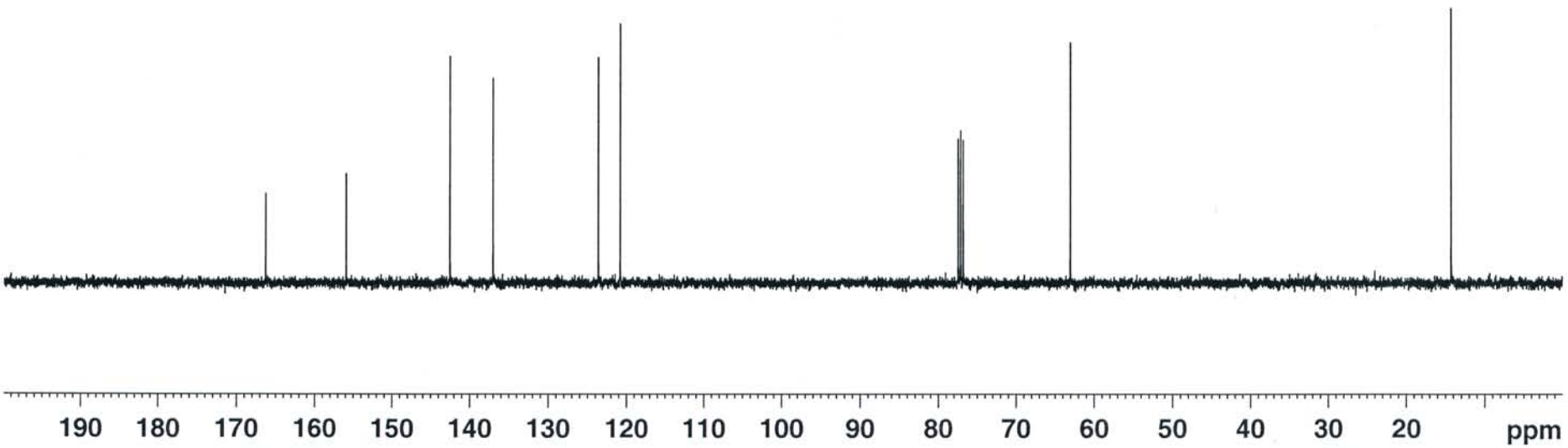

OEt
N
Me
O
S
N
Me

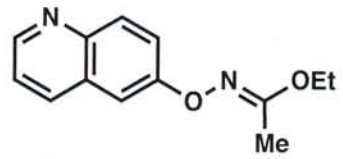

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

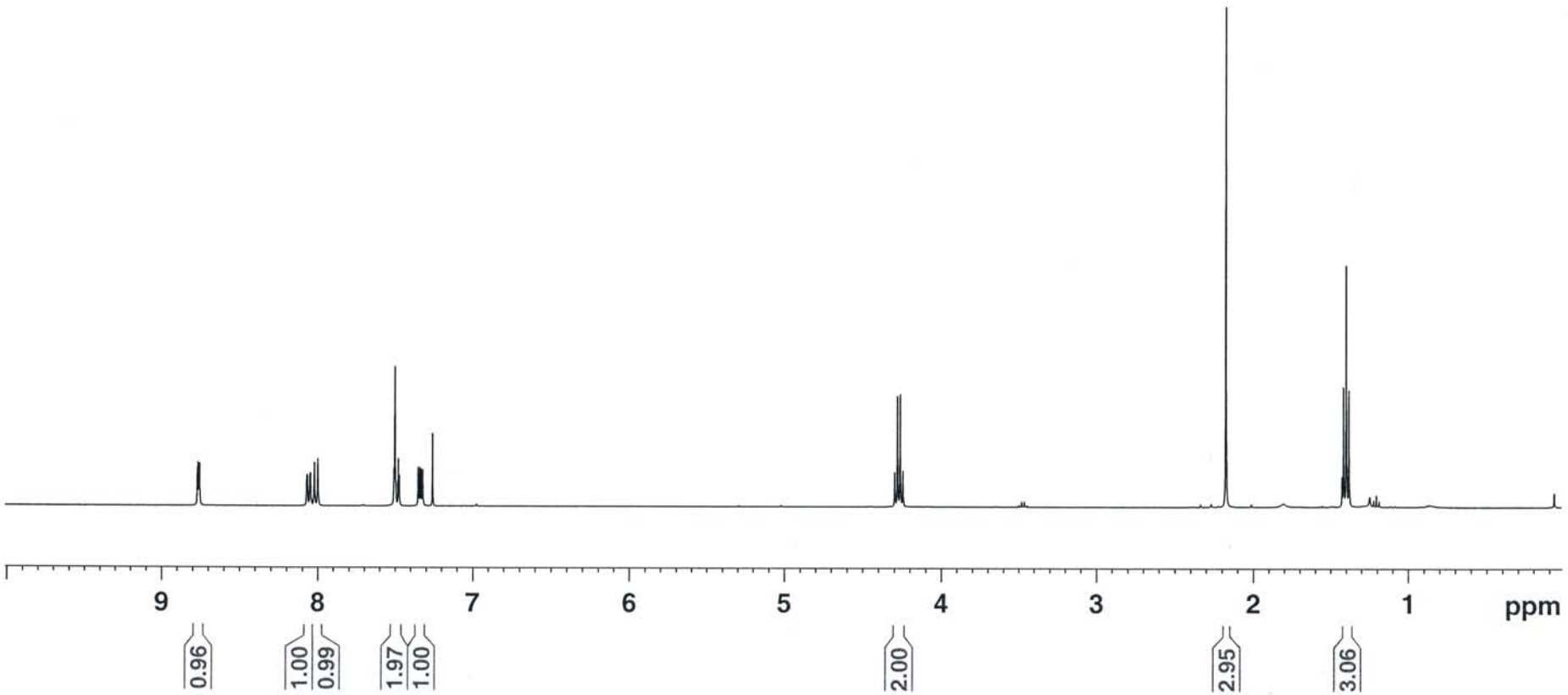

OEt
N
Me
O
N

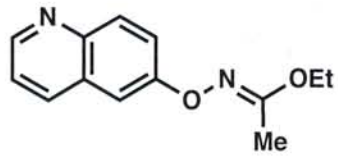

ppm
1
2
3
4
5
6
7
8
9

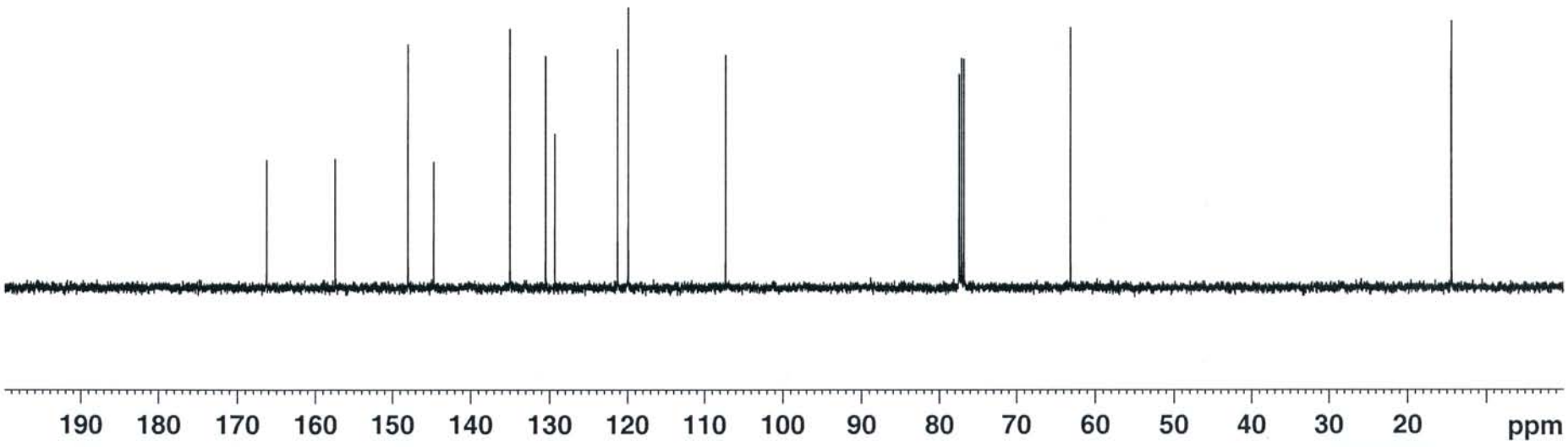

N
O
N
OEt
Me

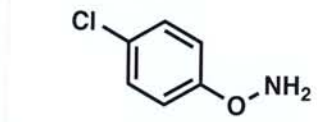

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

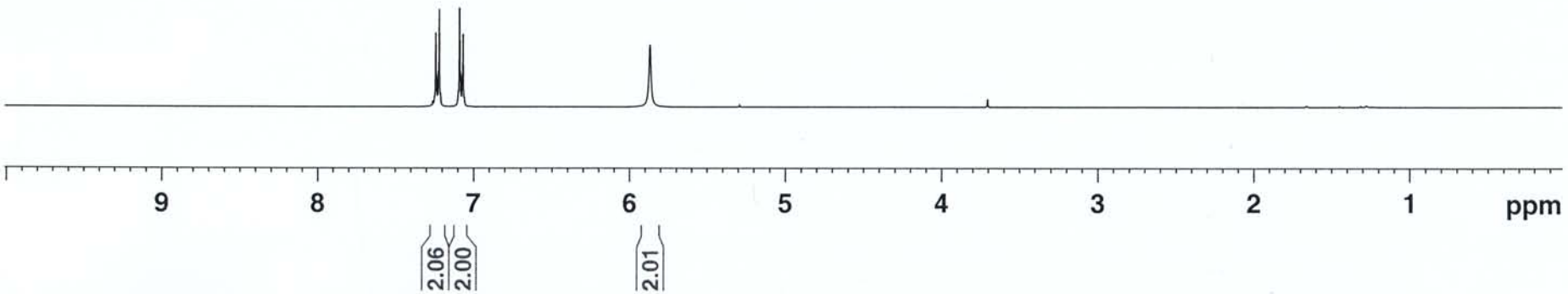

N
O
N
OEt
Me

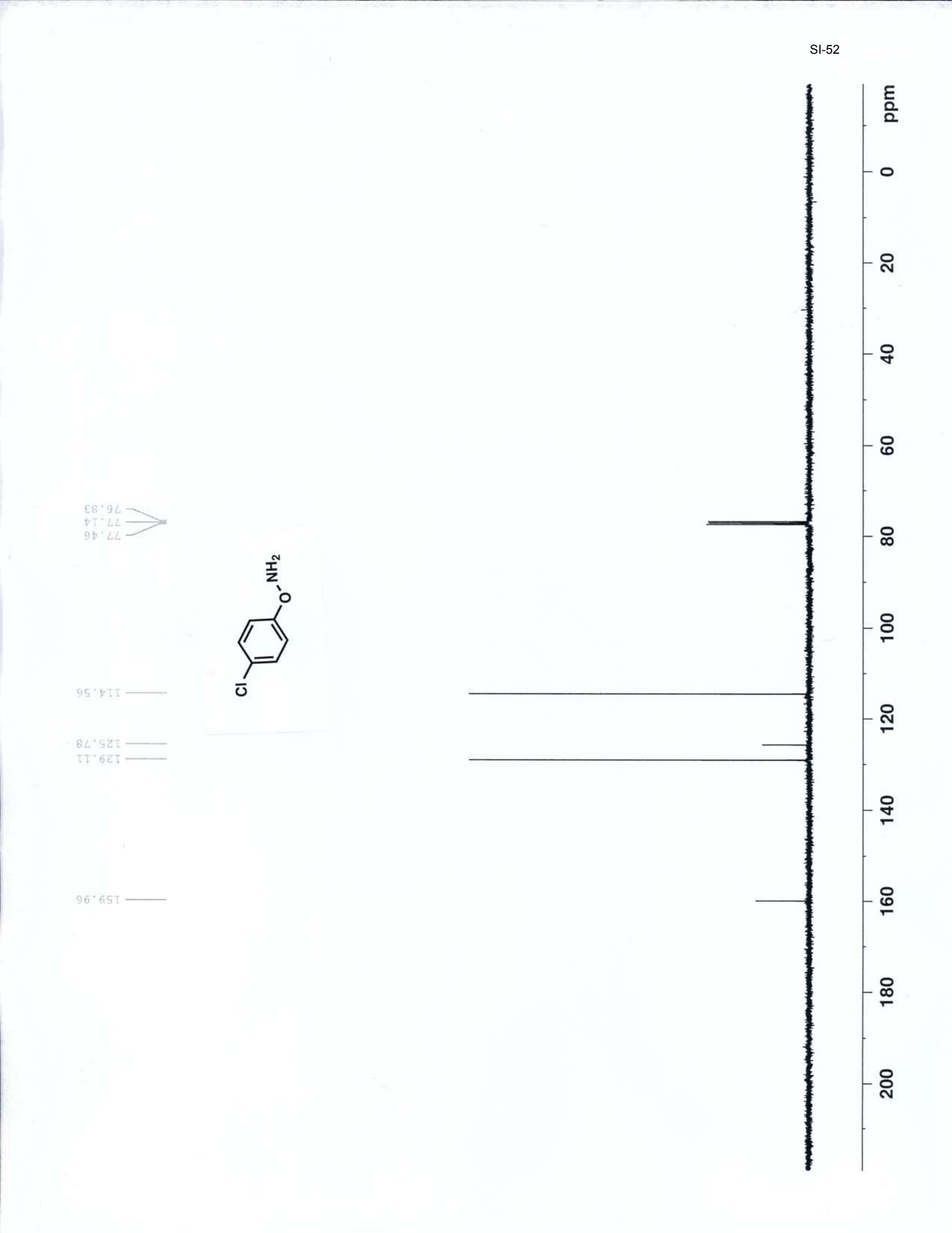

9
8
7
6
5
4
3
2
1
ppm
0.96
1.00
0.99
1.97
1.00
2.00
2.95
3.06

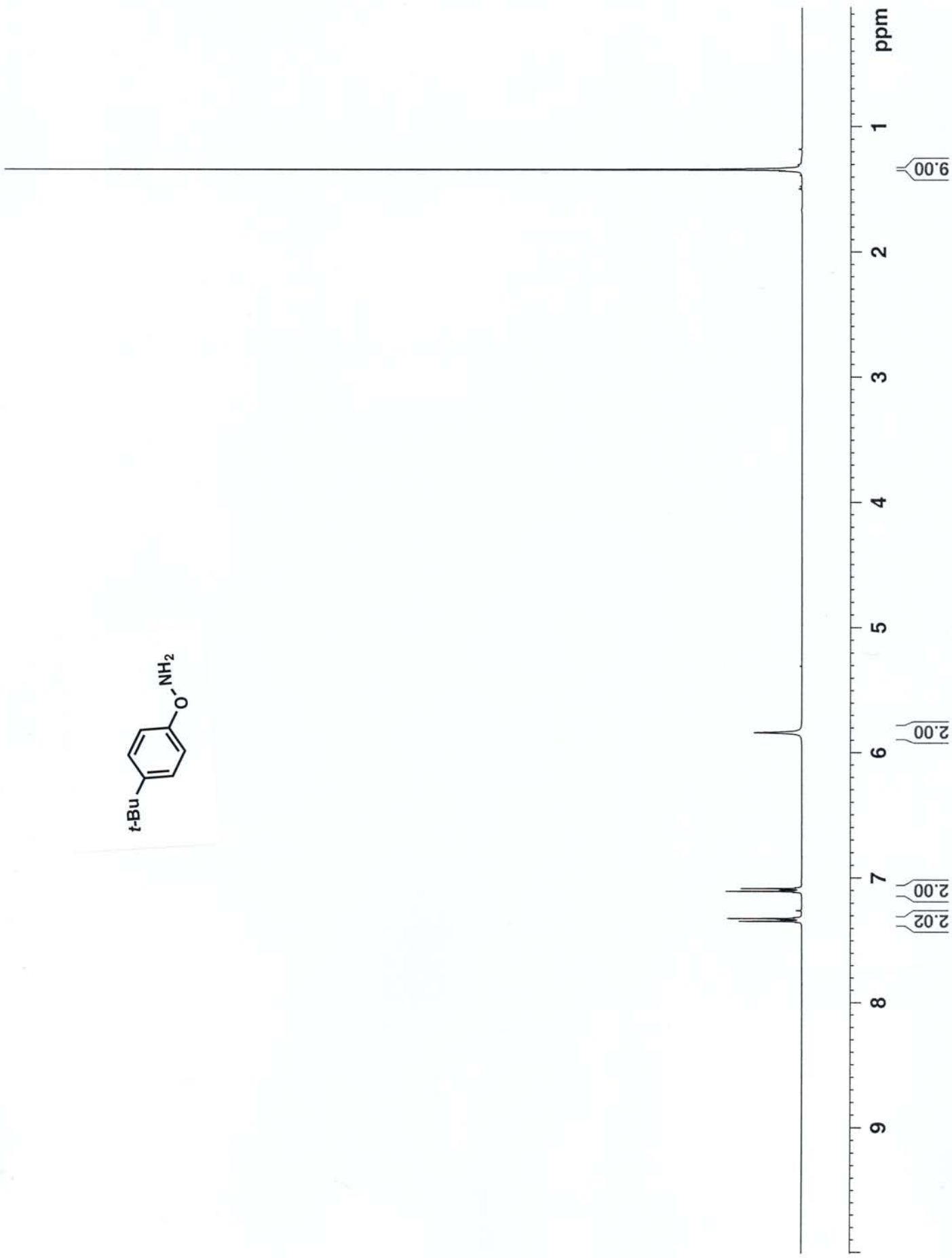

N
O
N
OEt
Me

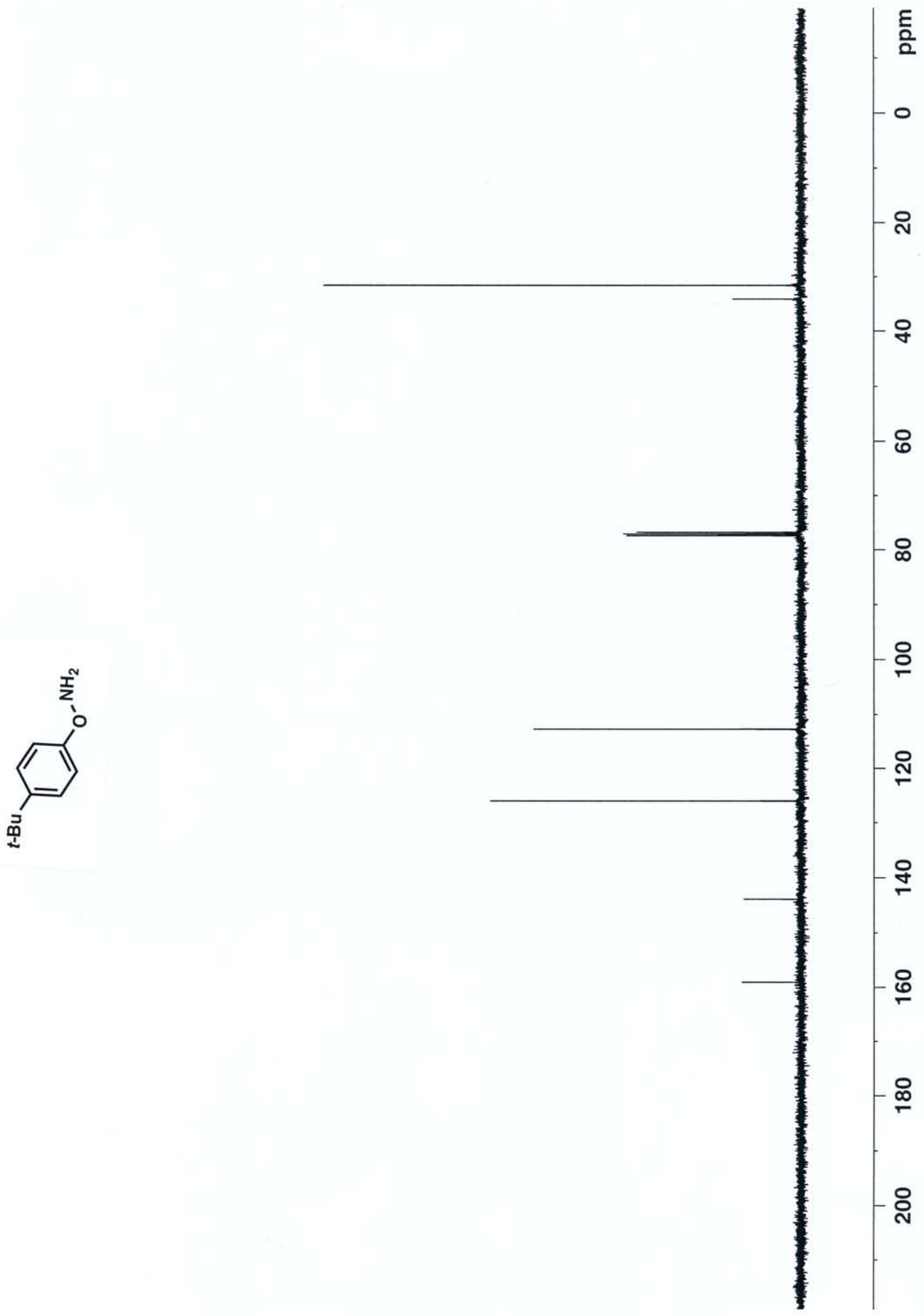

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

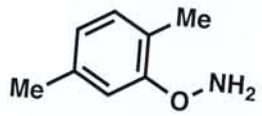

Cl
O
NH2

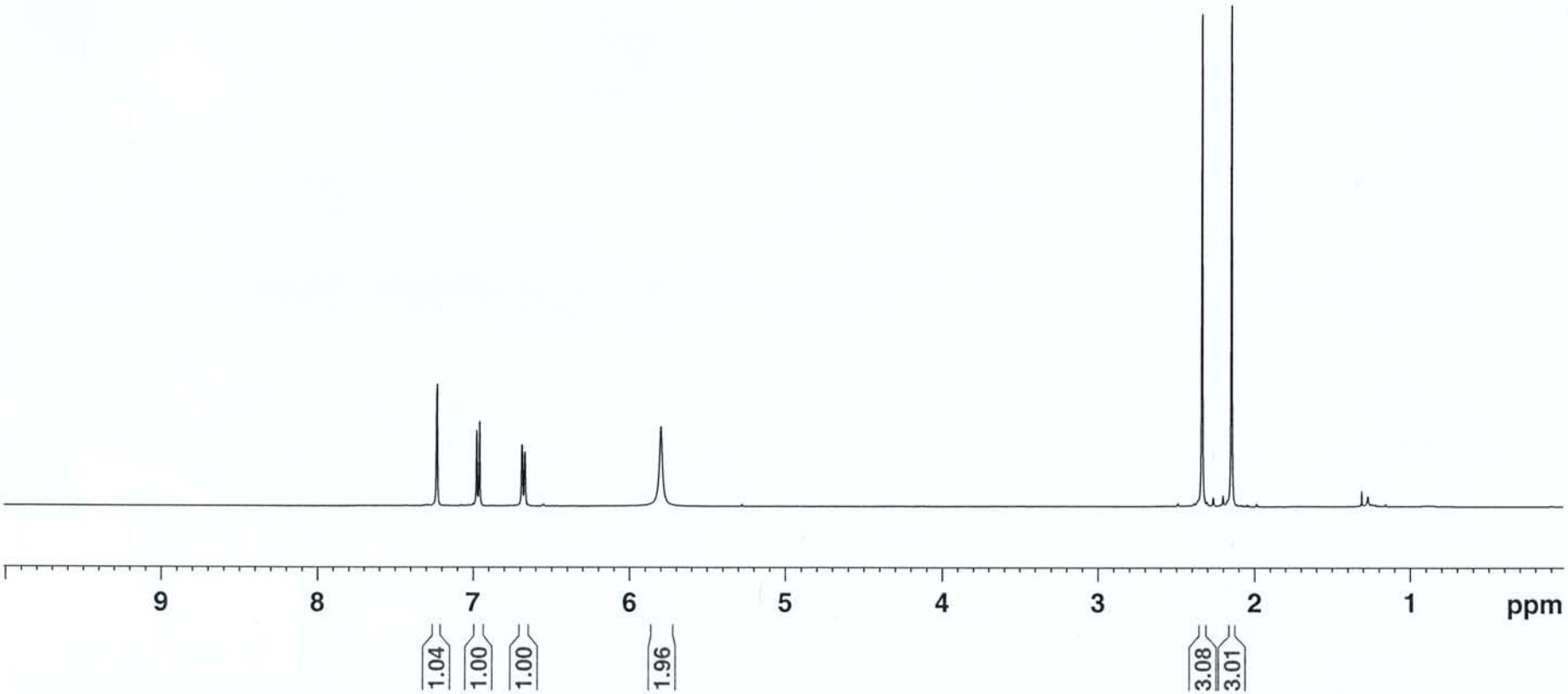

9
8
7
6
5
4
3
2
1
ppm
2.06
2.00
2.01

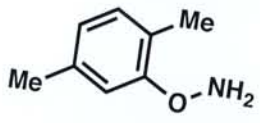

ppm
200
180
160
140
120
100
80
60
40
20
0
159.96
129.11
125.78
114.56
77.46
77.14
76.83
Cl
O
NH2

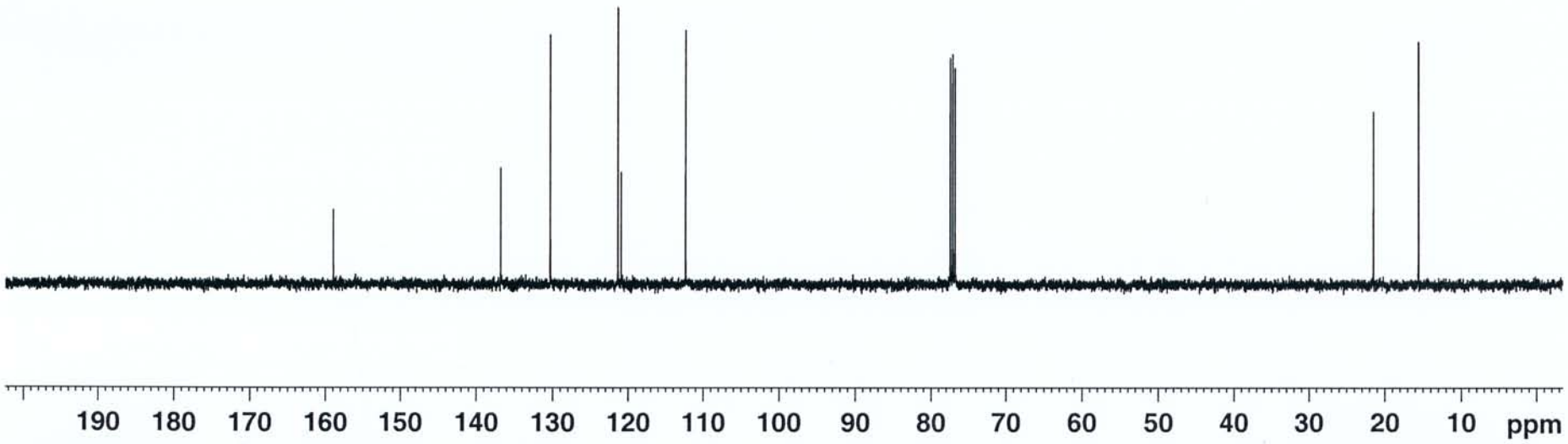

t-Bu
O
NH2
ppm
1
2
3
4
5
6
7
8
9
9.00
2.00
2.00
2.02

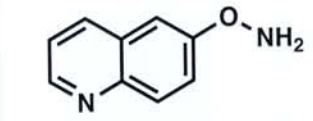

t-Bu
O
NH2
200
180
160
140
120
100
80
60
40
20
0
ppm

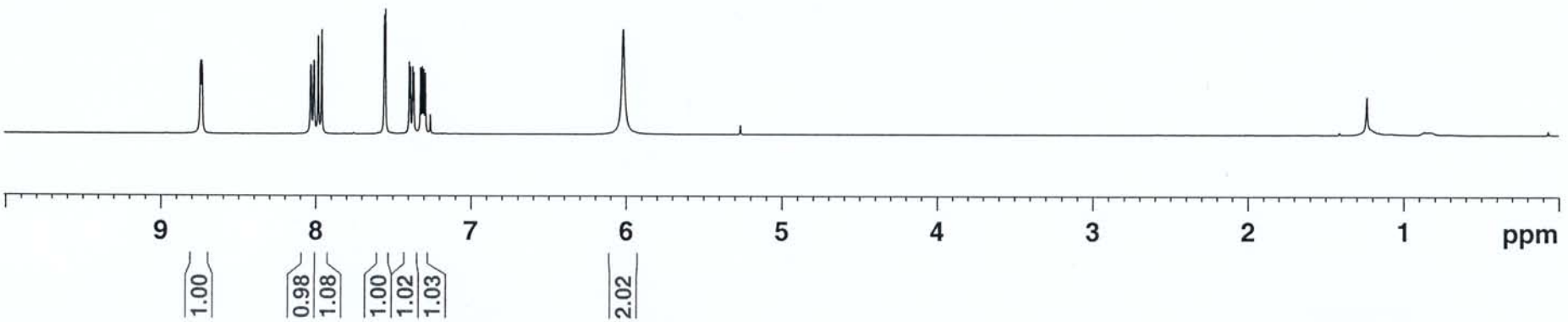

Me
Me
O
NH2

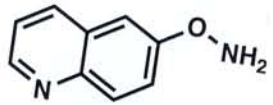

9
8
7
6
5
4
3
2
1
ppm
1.04
1.00
1.00
1.96
3.08
3.01

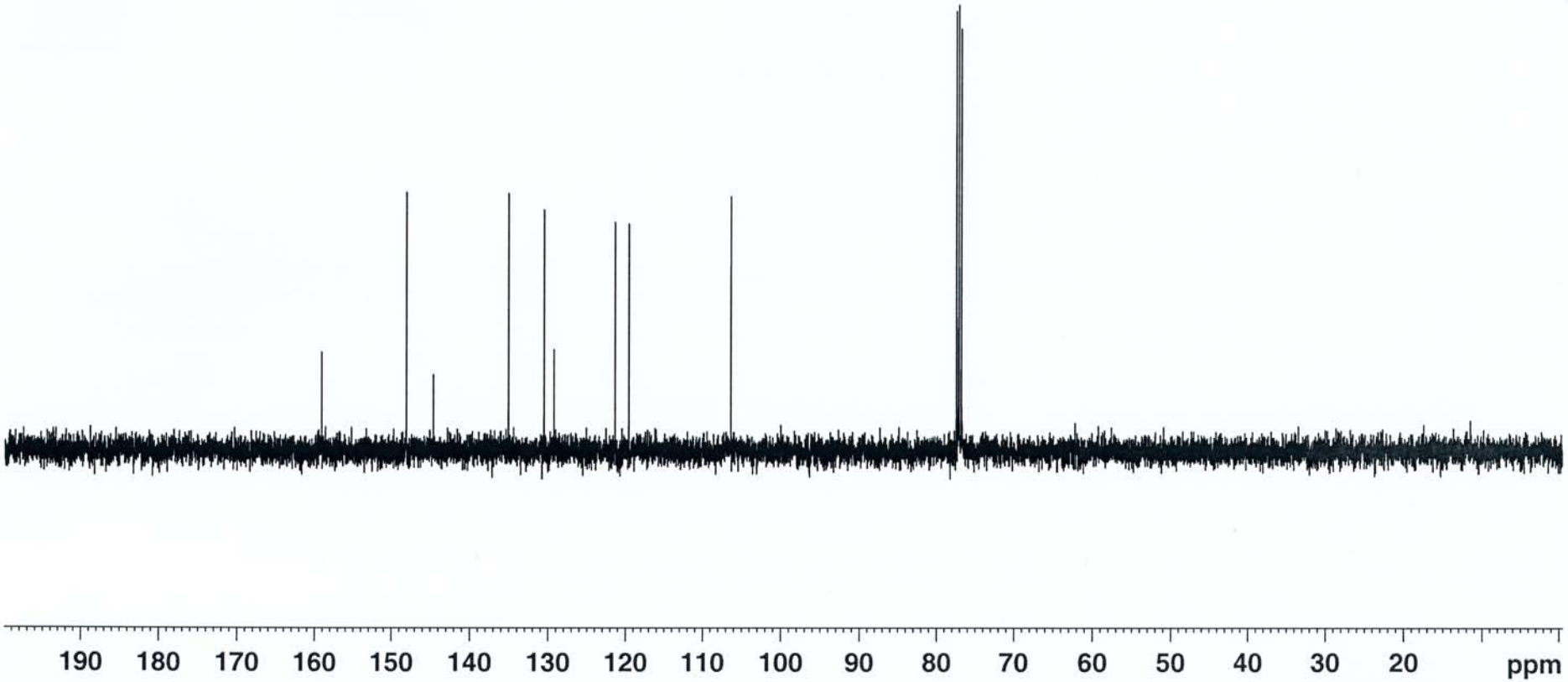

Me
Me
O
NH2

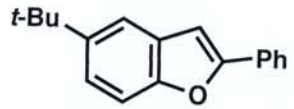

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


O
NH2
N

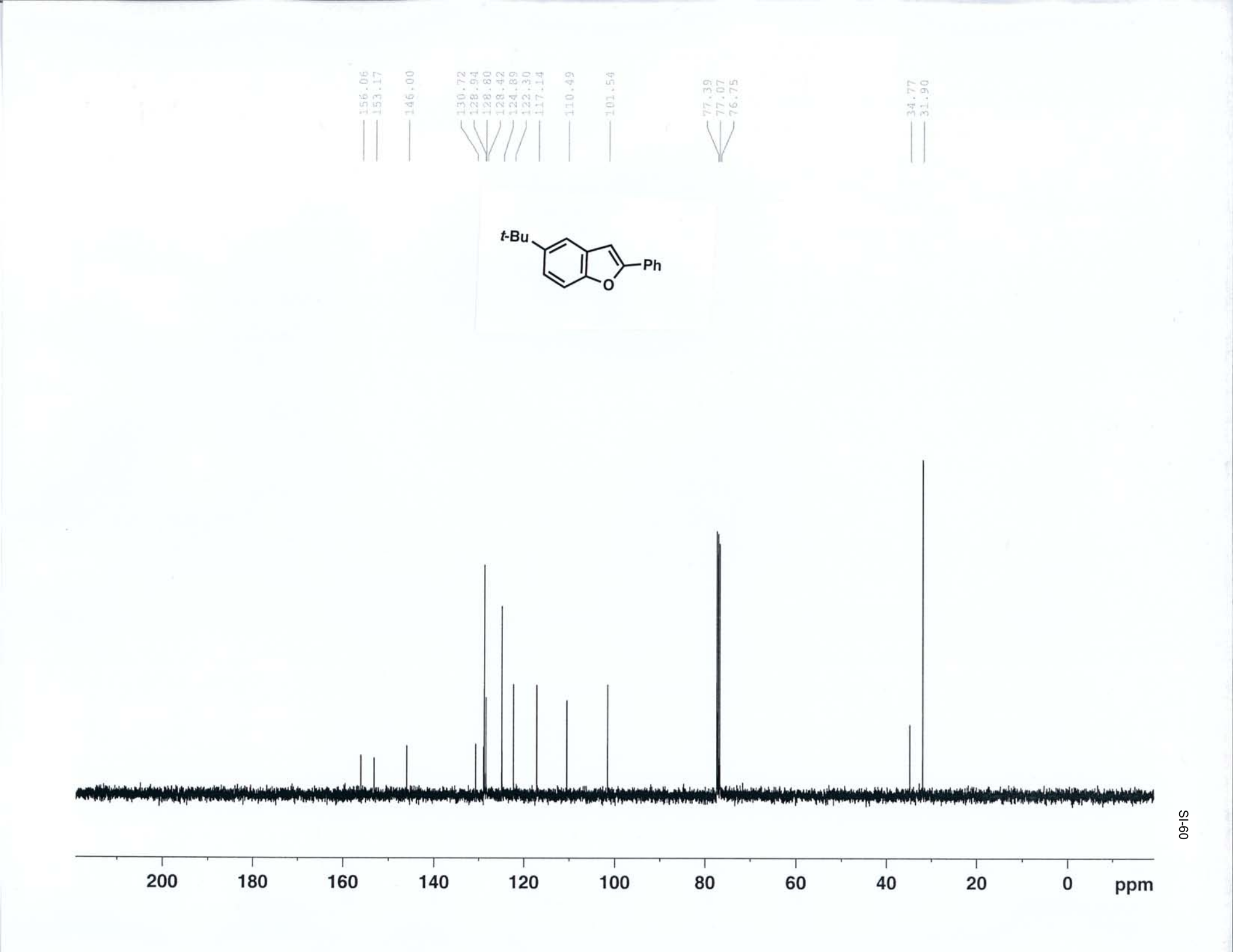

9
8
7
6
5
4
3
2
1
ppm
1.00
0.98
1.08
1.00
1.02
1.03
2.02

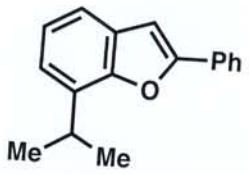

O
NH2
N

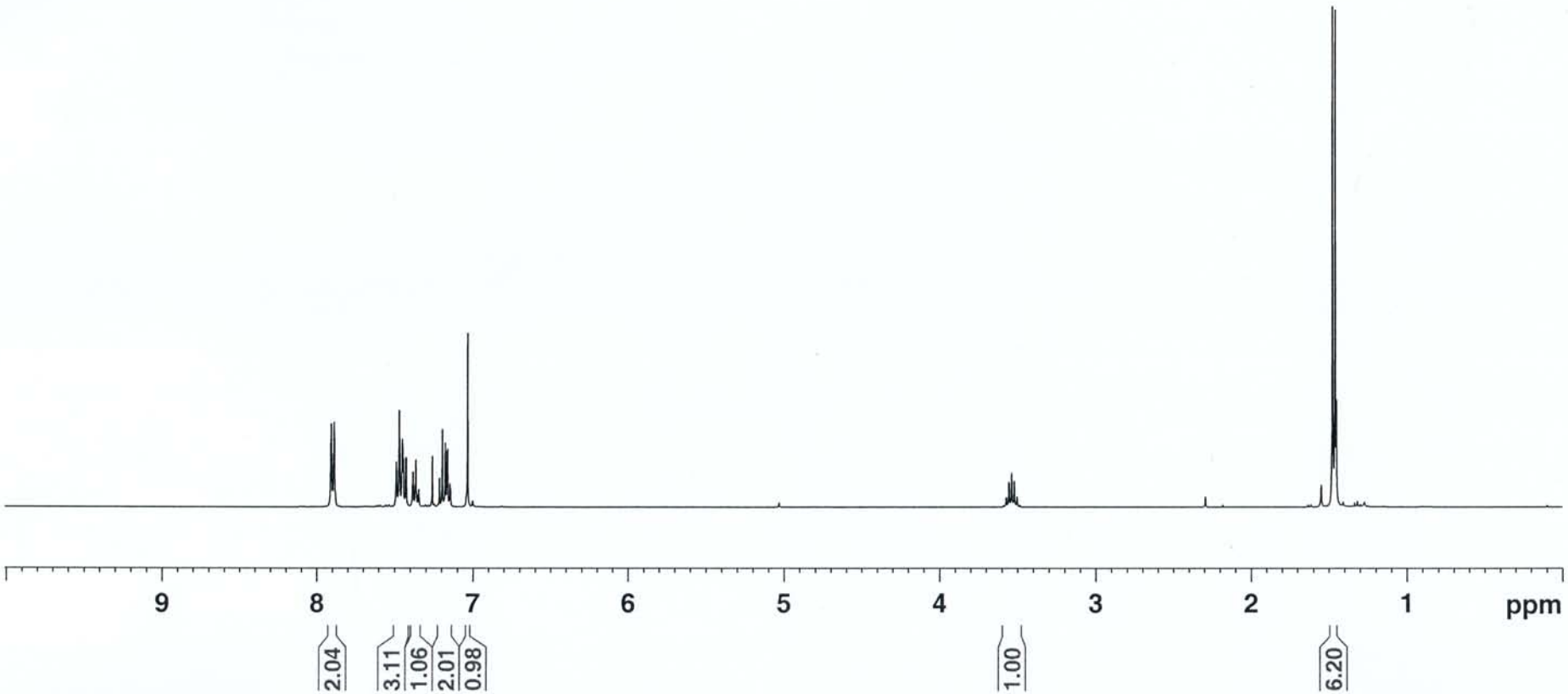

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

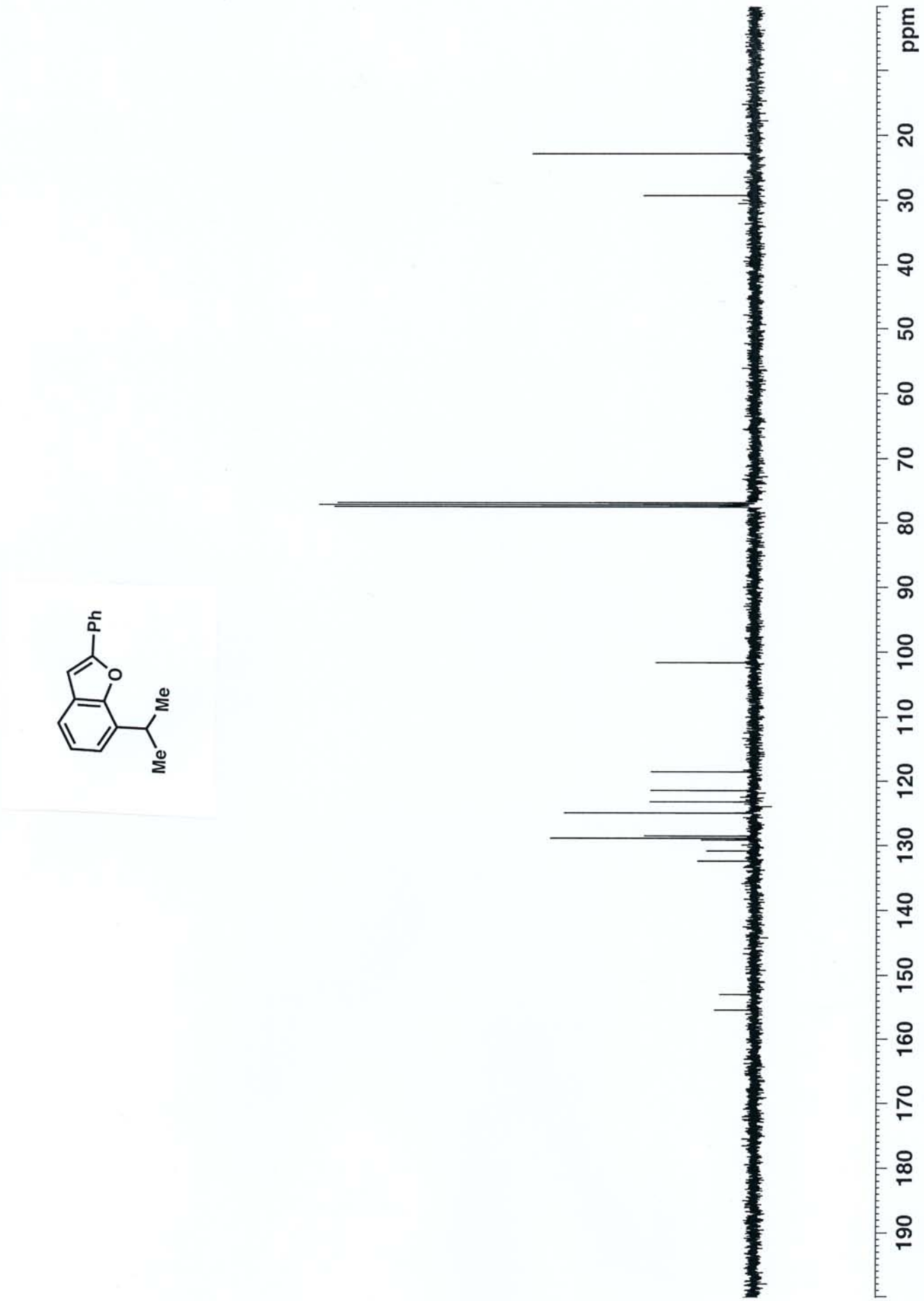

t-Bu
Ph
O

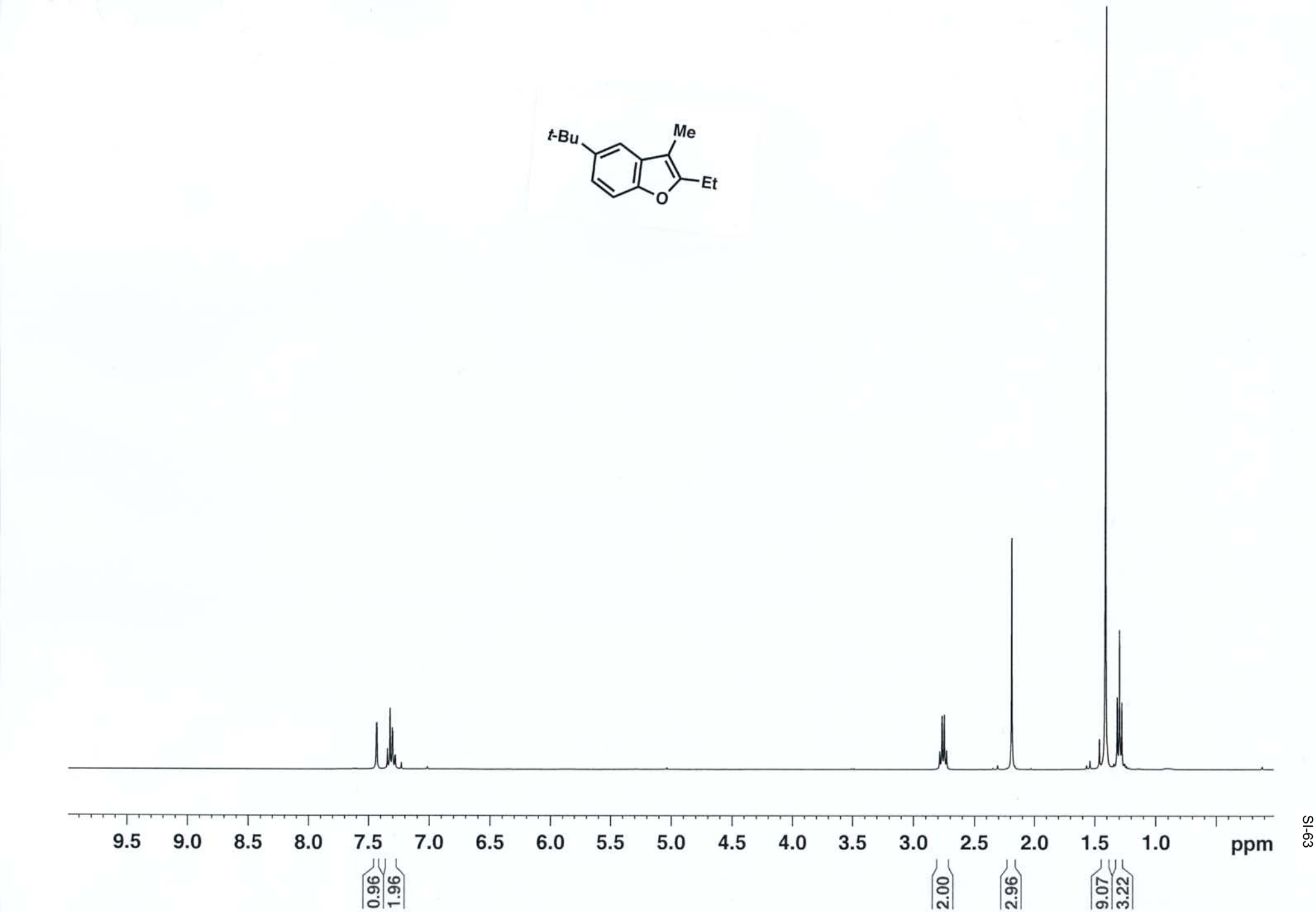
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.98
0.98
2.97
1.98
1.00
9.02

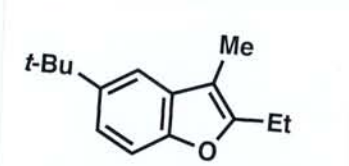

156.06
153.17
146.00
130.72
128.94
128.80
128.42
124.89
122.30
117.14
110.49
101.54
77.39
77.07
76.75
34.77
31.90
t-Bu
Ph
O
200
180
160
140
120
100
80
60
40
20
0
ppm

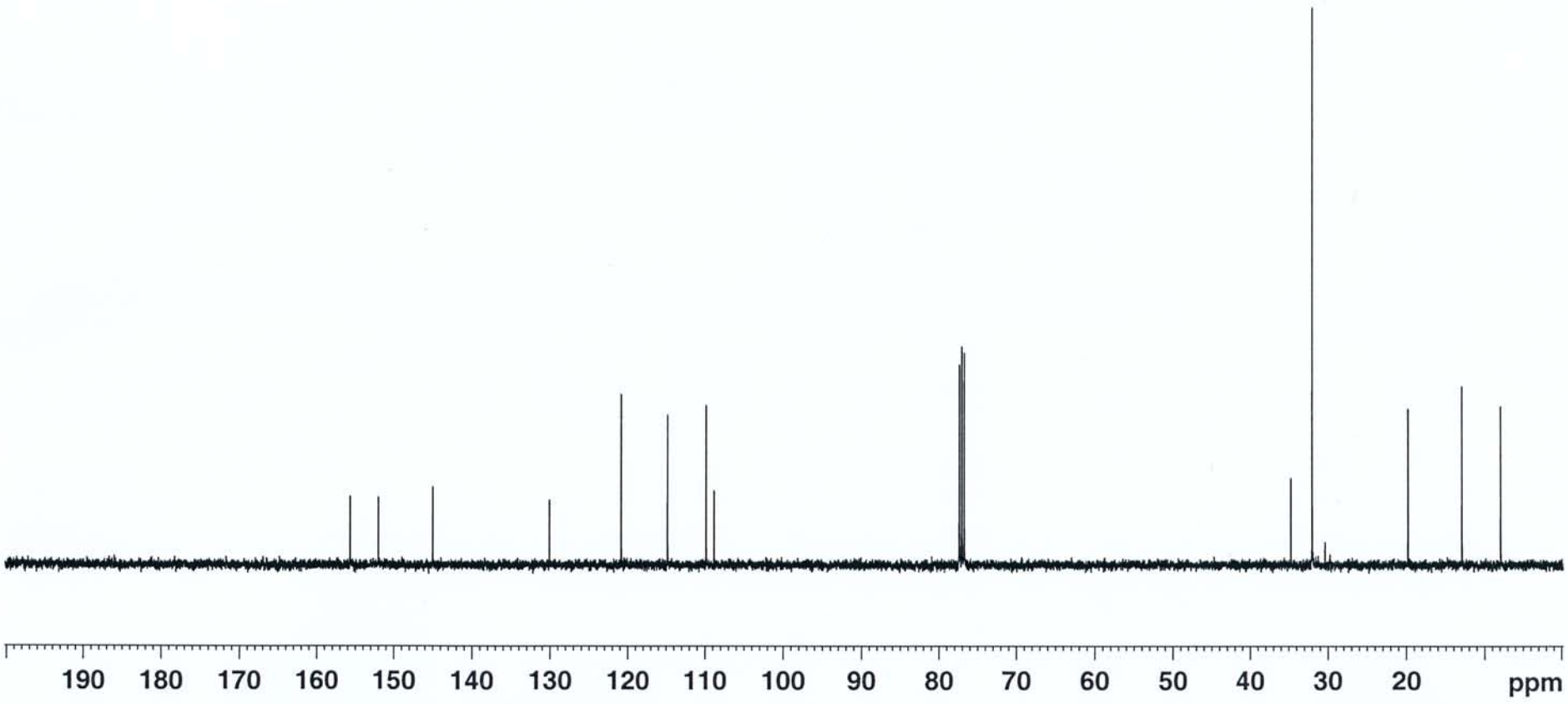

Ph
O
Me
Me

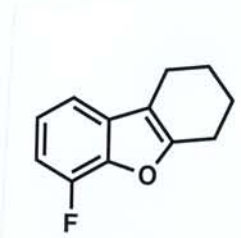

9
8
7
6
5
4
3
2
1
ppm
2.04
3.11
1.06
2.01
0.98
1.00
6.20

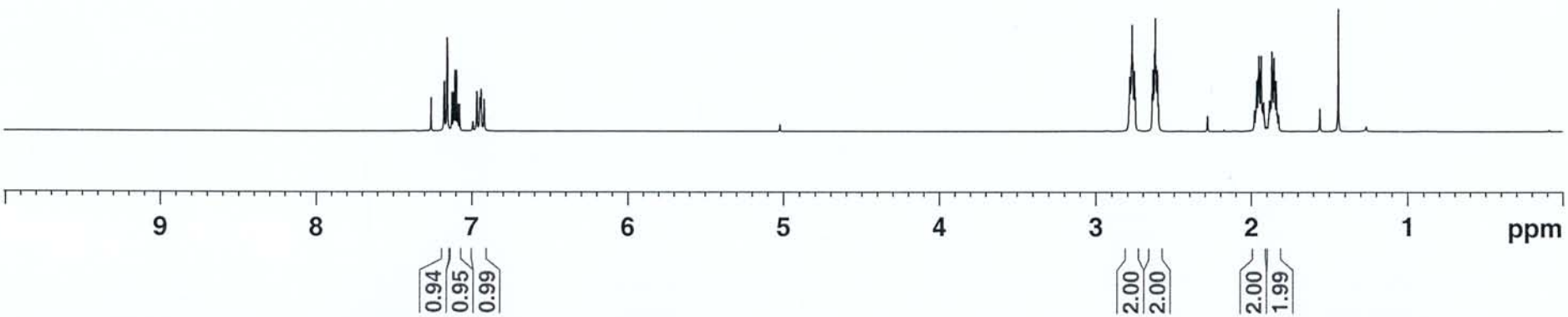

Ph
O
Me
Me
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

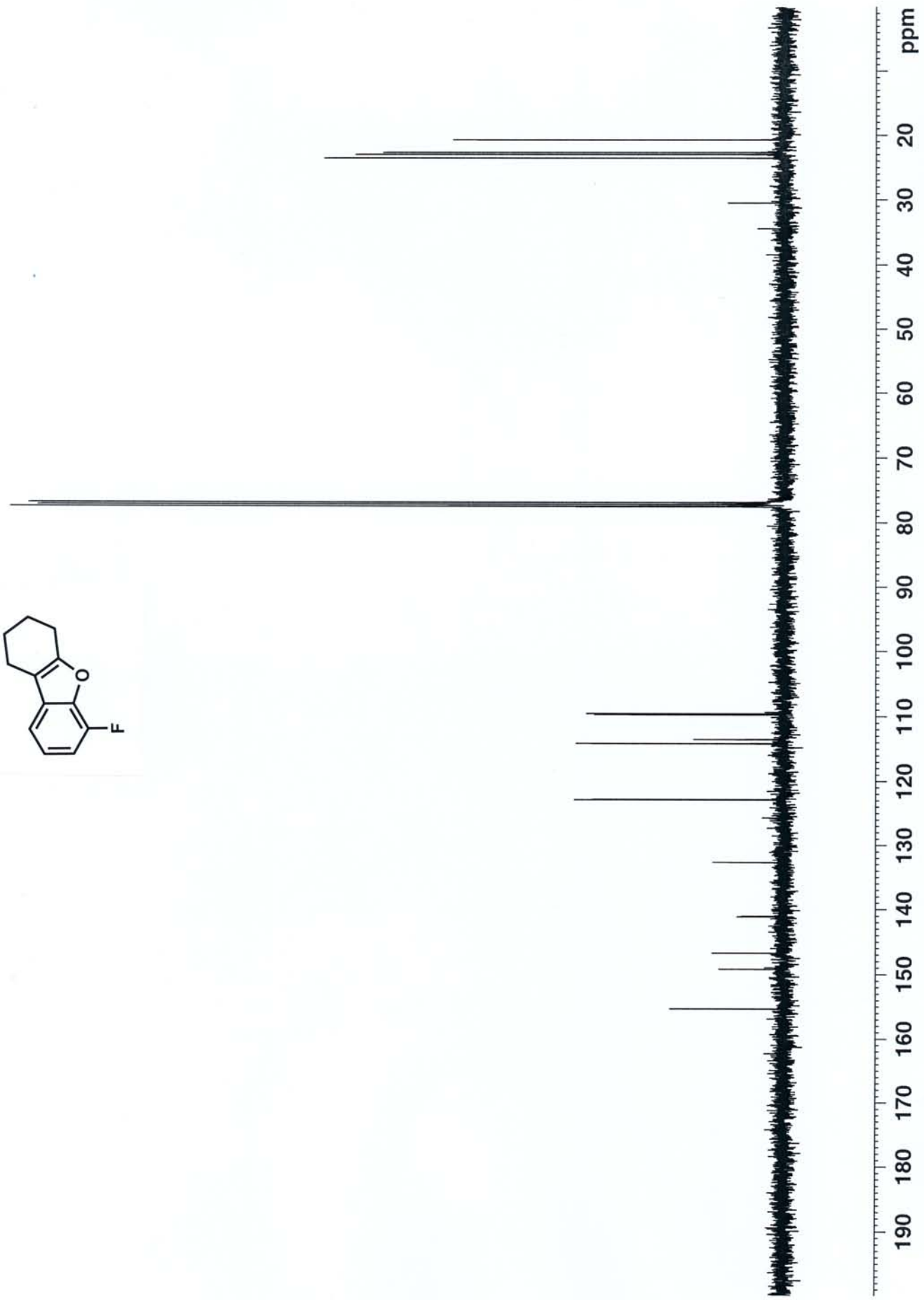

t-Bu
Me
Et
O
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.96
1.96
2.00
2.96
9.07
3.22

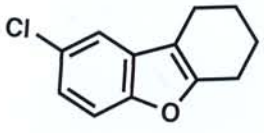

t-Bu
Me
Et
O

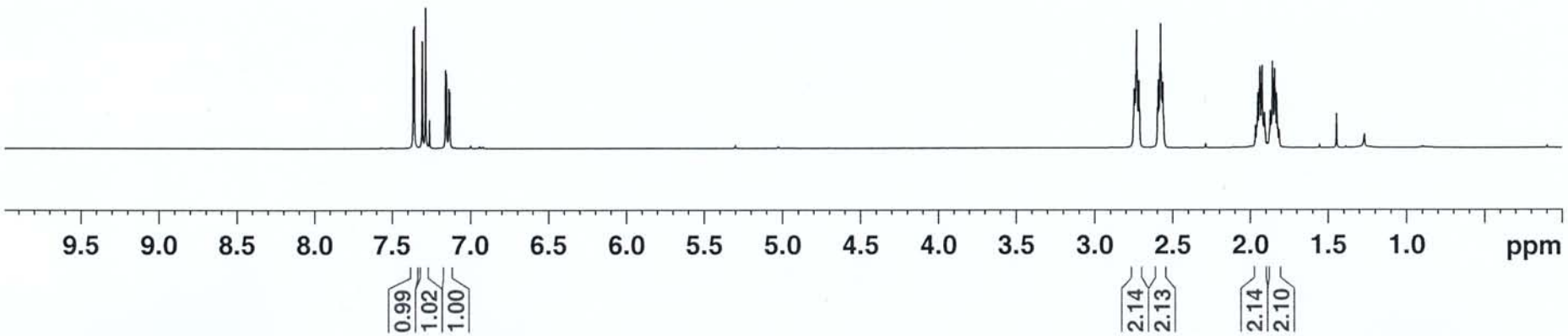

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

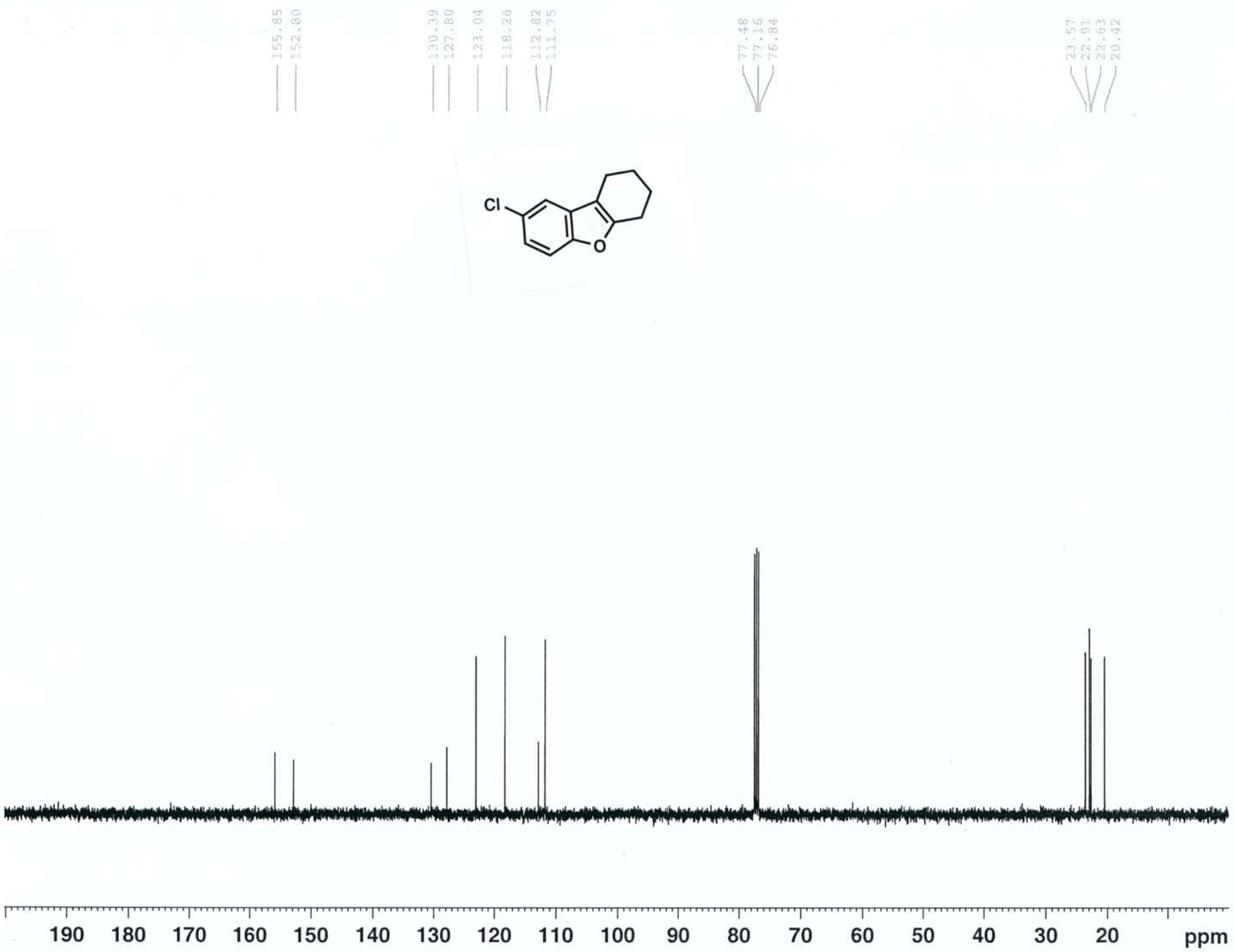

O
F

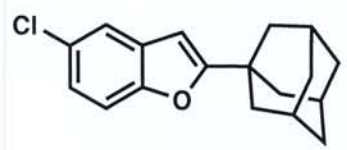

9
8
7
6
5
4
3
2
1
ppm
0.94
0.95
0.99
2.00
2.00
2.00
1.99

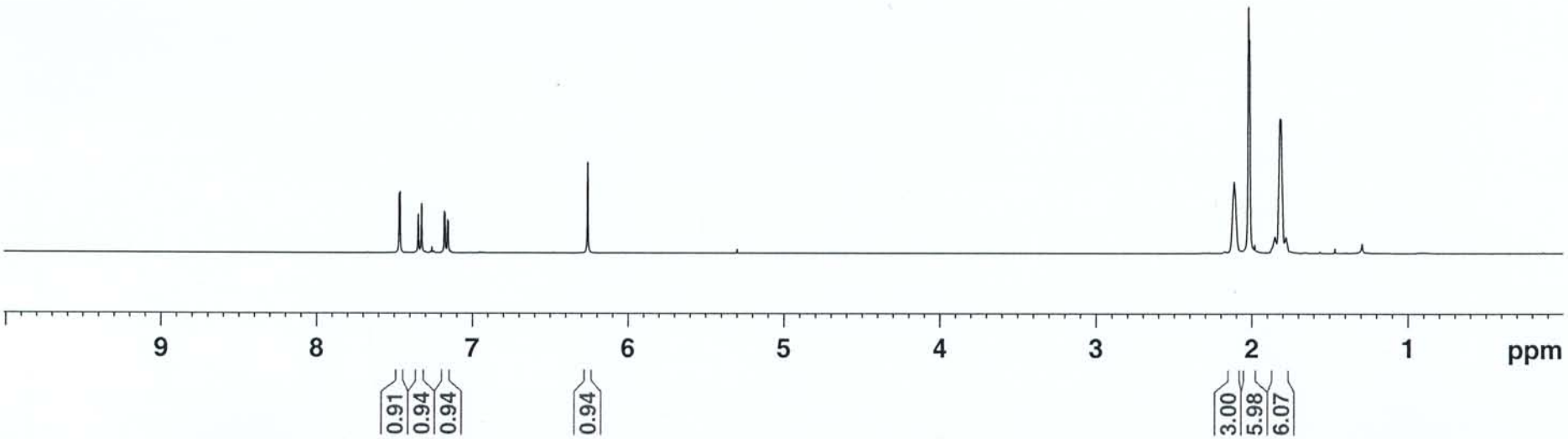

O
F
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

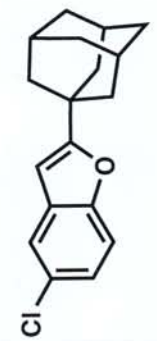

Cl
O

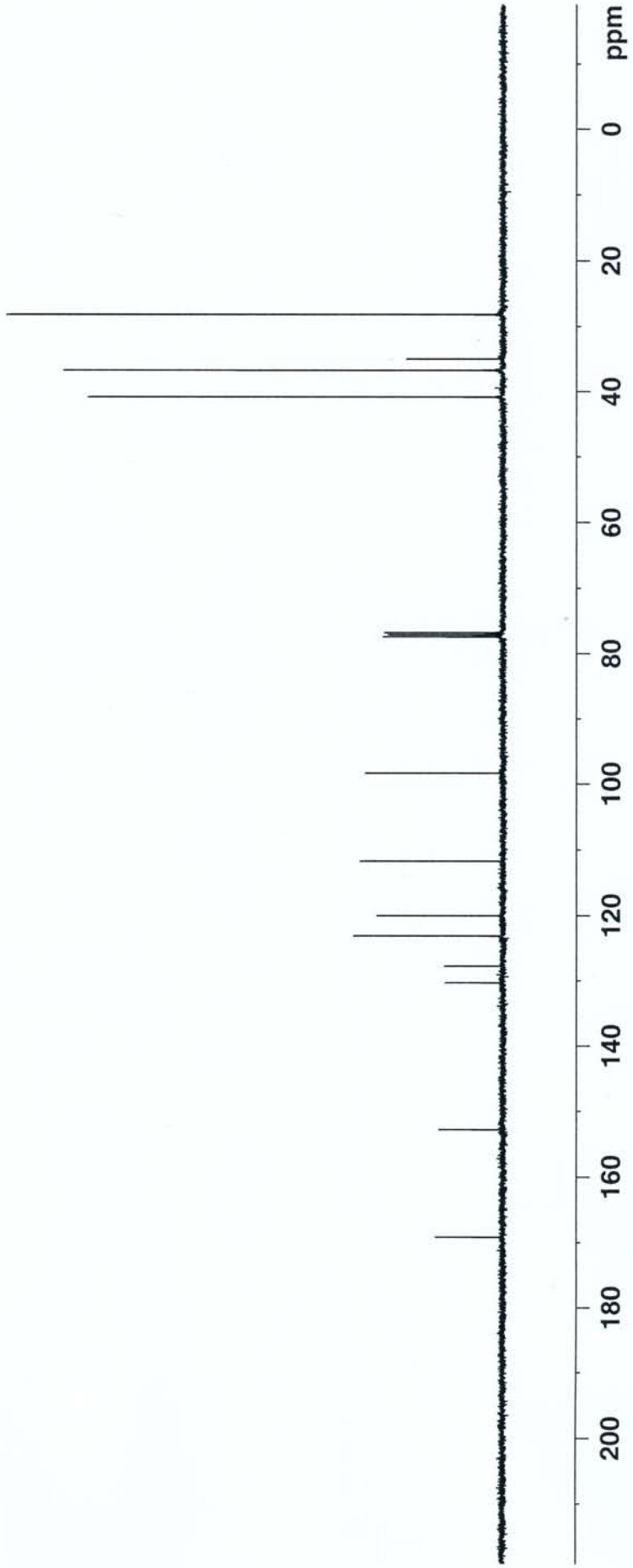

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.99
1.02
1.00
2.14
2.13
2.14
2.10


155.85
152.80
130.39
127.80
123.04
118.26
112.82
111.75
77.48
77.16
76.84
23.57
22.91
22.63
20.42
Cl
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


Cl
O


9
8
7
6
5
4
3
2
1
ppm
0.91
0.94
0.94
0.94
3.00
5.98
6.07


O
Cl


ppm
0
20
40
60
80
100
120
140
160
180
200