Twofold C–H Functionalization: Palladium-catalyzed *ortho* Arylation of Anilides

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Supporting Information

Content

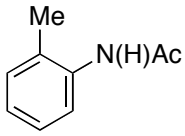
General Considerations

Reagents. All anilines were commercially available and were used as received. Pivaloyl chloride (99%) was purchased from Acros. Acetic anhydride (99.5%) was obtained from Aldrich. $Pd(OAc)_2$ was a gift from BASF. Benzene (anhydrous, 99.8%) and DMSO (anhydrous, 99.9+%) were purchased from Aldrich in SureSeal™ bottles. TFA (99%) was purchased either from Alfa Aesar or Strem Chemicals. Oxygen (extra dry, size 200, minimum purity 99.8%) was obtained from Airgas. All other commercially available materials as solvents and reagents were used as received. Flash chromatography was either performed on SilicaFlash® F60 silica gel available from SILICYCLE by standard technique or using a Biotage SP4™ EXP Flash Purification System. For the latter, 25+S KP-Sil silica cartridges were used to purify the biphenyls. EtOAc was used to transfer the crude reaction material onto the silica gel samplet. The samplet was dried under vacuum prior to usage.

Analytical Methods. All new compounds were characterized by ^{1}H NMR, ^{13}C NMR ^{19}F NMR (where applicable), IR spectroscopy and in most cases, elemental analysis. ^{1}H NMR, ^{13}C NMR, ^{19}F NMR (where applicable) and melting points (where applicable) are included for all known compounds. Nuclear magnetic resonance (NMR) spectra were recorded on a Varian Mercury-300 and Varian Inova-500 instrument. Chemical shifts (δ) are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (^{1}H NMR $CDCl_3$: δ 7.27; ^{13}C NMR $CDCl_3$: δ 77.23) or fluorobenzene (^{19}F NMR C_6H_5F: δ -113.15) as external standard. ^{13}C NMR spectra were recorded with complete proton decoupling. Infrared (IR) spectra were recorded on a Perkin Elmer System 2000 FT-IR spectrophotometer. Melting points (mp) were taken on a MEL-TEMP® apparatus and are uncorrected. Gas chromatographic (GC) analyses were performed with a Hewlett-Packard 6890 Series GC System with a capillary column with cross-linked methyl siloxane as the stationary phase (25 m × 0.20 mm) using a FID detector. Elemental analyses were carried out by Atlantic Microlab, Inc. (Norcross, GA). The yield reported in Tables 2, 3 and 4 refer to isolated yields and represent an average of at least two independent runs. The pure compounds are estimated to be ≥ 95% pure as determined by ^{1}H NMR and GC analysis and/or combustion analysis. In the cases where regioisomers were obtain and was not possible to separate them by means of column chromatography, the purity is based on the mixture of all of them. GC conversions and GC yields were calculated using dodecane as internal standard.

Preparation and Analytical Data of Chemical Compounds

Synthesis and Analytical Data of the Anilides

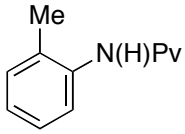


1b

2-Methylacetanilide.[1] To a solution of 2-methylaniline (1.60 mL, 15 mmol) in CH_2Cl_2 (15 mL) at 0 °C in a one-neck round bottom flask were slowly added H_2SO_4 (1 mL) and acetic anhydride (2.84 mL, 30 mmol, 2.00 equiv) by syringe. After complete addition, the cooling bath was removed, and the mixture was stirred for 24 h at room temperature under a nitrogen atmosphere before CH_2Cl_2 (10 mL) and H_2O (25 mL) were added. The organic layer was separated, washed with saturated $NaHCO_3$ (1 × 25 mL), dried over $MgSO_4$, filtered, and concentrated.

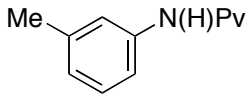
The title compound was obtained after recrystallization (Hexanes/EtOAc) as light orange needles, yield: 0.94 g (42%, mp 108 °C; lit.[2] mp 110 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 1H), 7.34-7.03 (m, 4H), 2.25 (s, 3H), 2.19 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 135.8, 130.7, 129.8, 126.9, 125.6, 123.8, 24.4, 18.0. IR (KBr plate, $CDCl_3$) ν 3290, 1644, 1588, 1531, 1486, 1460, 1369, 1287, 1272, 1118, 1039, 1018, 756, 713, 700, 653, 608, 562, 534, 447 cm^{-1}. Anal. Calcd. for $C_9H_{11}NO$: C, 72.46; H, 7.43; Found: C, 72.54; H, 7.42.

General procedure for the synthesis of pivalanilides from anilines and pivaloyl chloride: The reactions were carried out in a one-neck round bottom flask. The corresponding aniline (25.0 mmol) and Na_2CO_3 (5.30 g, 50.0 mmol, 2.00 equiv) were added to a vigorously stirred mixture of CH_2Cl_2 (25 mL) and H_2O (25 mL). A reflux condenser was attached to the flask, and pivaloyl chloride (6.16 mL, 50.0 mmol, 2.00 equiv) was slowly added by syringe through the condenser while maintaining vigorous stirring. The flask was lowered into an oil bath heated to 80 °C and the reaction mixture was stirred for 2 h. After cooling to room temperature, CH_2Cl_2 (50 mL) and 1 N NaOH (50 mL) were added. The layers were separated, and the organic layer was washed with H_2O (2 × 50 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was subsequently purified by silica gel chromatography or recrystallization.



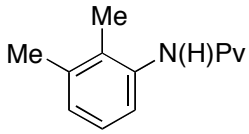
1a

2-Methylpivalanilide.[3] Following the general procedure. Recrystallization (Hexanes/ EtOAc). White needles; yield: 4.48 g (94%, mp 110-112 °C; lit.[3] mp 111-112 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94-7.82 (m, 1H), 7.40-7.15 (m, 3H), 7.07 (td, *J* = 7.4, 1.2 Hz, 1H), 2.26 (s, 3H), 1.35 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.6, 136.0, 130.5, 128.9, 127.0, 125.1, 123.0, 39.9, 27.9, 17.8. IR (KBr plate, $CDCl_3$) ν 3347, 2966, 1659, 1585, 1515, 1457, 1365, 1297, 1253, 1170, 1042, 949, 921, 756, 634, 447 cm^{-1}. Anal. Calcd. for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; Found: C, 75.42; H, 9.15.



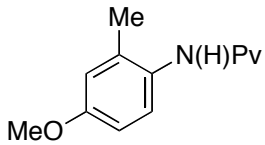
1c

3-Methylpivalanilide. Following the general procedure. Recrystallization (Hexanes/ EtOAc). White needles; yield: 4.35 g (91%, mp 125 °C; lit.[4] mp 126.5 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (s, 1H), 7.38-7.25 (m, 2H), 7.20 (t, *J* = 7.8 Hz, 1H), 6.97-6.89 (m, 1H), 2.34 (s, 3H), 1.32 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.8, 139.1, 138.1, 128.9, 125.1, 120.8, 117.1, 39.8, 27.8, 21.7. IR (KBr plate, $CDCl_3$) ν 3305, 2967, 1652, 1593, 1543, 1475, 1428, 1302, 1195, 783, 697 cm^{-1}. Anal. Calcd. for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; Found: C, 75.61; H, 9.11.



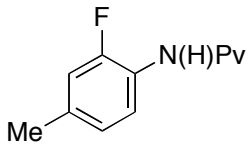
1d

2,3-Dimethylpivalanilide. Following the general procedure. Recrystallization (Hexanes/ EtOAc). Fine white needles; yield: 4.51 g (88%, mp 123 °C; lit.[5] mp 121.5-122 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, *J* = 4.8 Hz, 1H), 7.23 (s, 1H), 7.11 (t, *J* = 4.8 Hz, 1H), 7.01 (d, *J* = 4.8 Hz, 1H), 2.31 (s, 3H), 2.15 (s, 3H), 1.35 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.8, 137.4, 135.6, 129.2, 127.3, 126.1, 122.1, 39.7, 27.9, 20.8, 13.8. IR (KBr plate, $CDCl_3$) ν 3270, 2956, 1645, 1603, 1519, 1475, 1456, 1383, 1365, 1232, 1184, 776, 714 cm^{-1}. Anal. Calcd. for $C_{13}H_{19}NO$: C, 76.06; H, 9.33; Found: C, 76.06; H, 9.41.



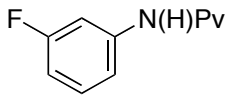
1e

4-Methoxy-2-methylpivalanilide. Following the general procedure. Recrystallization (Hexanes/EtOAc). Fine white needles; yield: 5.17 g (93%, mp 102 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58-7.53 (m, 1H), 7.09 (s, 1H), 6.78-6.71 (m, 2H), 3.79 (s, 3H), 2.22 (s, 3H), 1.34 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.9, 157.2, 132.5, 128.9, 125.7, 116.0, 111.6, 55.5, 39.5, 27.8, 18.1. IR (KBr plate, $CDCl_3$) ν 3271, 2955, 1647, 1616, 1587, 1502, 1465, 1364, 1293, 1229, 1159, 1117, 1055, 883, 799 cm^{-1}. Anal. Calcd. for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; Found: C, 70.70; H, 8.69.



1f

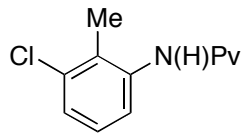
2-Fluoro-4-methylpivalanilide. Following the general procedure. Silica gel chromatography (Hexanes/EtOAc, gradient 4% to 10% EtOAc). White solid; yield: 4.81 g (92%, mp 74 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (t, *J* = 8.7 Hz, 1H), 7.54 (s, 1H), 6.97-6.87 (m, 2H), 2.32 (s, 3H), 1.33 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.7, 154.3, 151.1, 134.7, 134.6, 125.1, 125.1, 124.0, 123.9, 121.7. 121.7, 115.5, 115.2, 40.0, 27.7, 21.0, 21.0. ^{19}F NMR (282 MHz, $CDCl_3$) δ -132.5 (m). IR (KBr plate, $CDCl_3$) ν 3319, 2975, 1654, 1587, 1522, 1489, 1366, 1287, 1116, 941, 848, 815, 727, 595 cm^{-1}. Anal. Calcd. for $C_{12}H_{16}FNO$: C, 68.88; H, 7.71; Found: C, 68.93; H, 7.77.



1g

3-Fluoropivalanilide. Following the general procedure. Recrystallization (Hexanes/EtOAc). Fine white needles; yield: 4.58 g (94%, mp 114-115 °C; lit.[6] mp 112-114 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (dt, *J* = 11.1, 2.4 Hz, 1H), 7.44 (s, 1H), 7.29-7.20 (td, *J* = 8.1, 6.3 Hz, 1H), 7.14 (dq, *J* = 8.1, 0.9 Hz, 1H), 6.79 (tdd, *J* = 8.1, 2.4, 0.9 Hz, 1H), 1.31 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.9, 164.8, 161.5, 139.8, 139.7, 130.2, 130.0, 115.3, 115.3, 111.2, 110.9, 107.9, 107.5, 39.9, 27.7. ^{19}F NMR (282 MHz, $CDCl_3$)

δ -111.57 (m). IR (KBr plate, $CDCl_3$) ν 3315, 2967, 1654, 1606, 1527, 1476, 1434, 1384, 1277, 1188, 1130, 966, 920, 863, 815, 779, 749, 684, 520 cm^{-1}. Anal. Calcd. for $C_{11}H_{14}FNO$: C, 67.67; H, 7.23; Found: C, 67.83; H, 7.28.

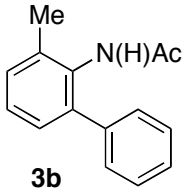


1h

3-Chloro-2-methylpivalanilide. Following the general procedure. Recrystallization (Hexanes). Light yellow needles; yield: 5.33 g (95%, mp 104 °C). ^1H NMR (300 MHz, $CDCl_3$) δ 7.72-7.67 (m, 1H), 7.26 (s, 1H), 7.21 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.14 (t, *J* = 8.1 Hz, 1H), 2.31 (s, 3H), 1.35 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.0, 137.2, 134.9, 128.8, 127.1, 126.4, 122.7, 39.9, 27.9, 14.7. IR (KBr plate, $CDCl_3$) ν 3281, 2973, 1652, 1573, 1504, 1440, 1167, 1011, 772, 702, 662 cm^{-1}. Anal. Calcd. for $C_{12}H_{16}ClNO$: C, 63.85; H, 7.14; Found: C, 63.97; H, 7.23.

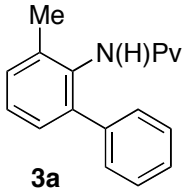
Synthesis and Analytical Data of the Biphenyls

General procedure A for the arylation of anilides with benzene: An oven-dried Schlenk tube equipped with a stir bar and a teflon stopper was cooled to room temperature under vacuum and backfilled with O_2. With the tube open to the air, the anilide (1.00 mmol) and $Pd(OAc)_2$ (11.3-22.6 mg, 5-10 mol%) were added. The tube was evacuated and backfilled with O_2, followed by addition of benzene (1 mL, ~11 equiv), TFA (370 μL, 5.00 equiv), and DMSO (7-14 μL, 10-20 mol%) by syringe under a positive O_2 pressure with the tube open to the air. The tube was sealed and lowered into a preheated oil bath at 55-100 °C and stirred for the indicated time. *(Note: Agitation is very important for the reaction outcome! The reaction mixture has to be vigorously stirred to obtain high yields and reproducible results.)* After allowing the reaction mixture to cool to room temperature, the teflon stopper was removed and ethyl acetate (8 mL), distilled water (4 mL), and aqueous 30% NH_4OH (4 mL) were added sequentially. The aqueous layer was extracted with ethyl acetate (2 × 8 mL). The combined organic layers were dried over $MgSO_4$, filtered through Celite™, and concentrated under reduced pressure. The residue was purified by silica gel chromatography or recrystallization.



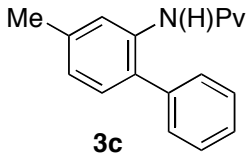
3b

2-Acetamino-3-methylbiphenyl (Table 2, entry 1).[7] Following the general procedure A using 5 mol% $Pd(OAc)_2$ and 10 mol% DMSO for 18h at 80°C. Column chromatography: Silica gel, 1:1 Hexanes/EtOAc. White solid; yield: 158 mg (70%, mp 127-129 °C; lit. mp 132-133 °C).[7] ^{1}H NMR (500 MHz, $CDCl_3$) δ ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44-7.37 (m, 2H), 7.37-7.28 (m, 3H), 7.28-7.22 (m, 2H), 7.18 (t, *J* = 4.6 Hz, 1H), 6.79 (s, 1H), 2.30 (s, 3H), 1.98 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.6, 139.8, 139.7, 137.0, 132.8, 130.3, 129.0, 128.5, 128.0, 127.6, 127.5, 23.2, 18.8. IR (KBr plate, $CDCl_3$) ν 3246, 3027, 1711, 1654, 1524, 1465, 1438, 1369, 1290, 791, 758, 701 cm^{-1}.



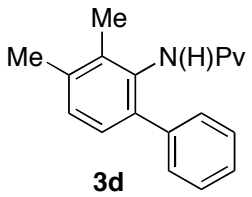
3a

3-Methyl-2-pivalaminobiphenyl (Table 1, entry 7). Following the general procedure A using 5 mol% $Pd(OAc)_2$ and 10 mol% DMSO for 18h at 90°C. Column chromatography: Silica gel, Hexanes/EtOAc, gradient 4% to 30% EtOAc. White solid; yield: 240 mg (90%, mp 173 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.32 (m, 3H), 7.32-7.28 (m, 2H), 7.27-7.22 (m, 2H), 7.19-7.14 (m, 1H), 6.85 (s, 1H), 2.26 (s, 3H), 1.12 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 139.8, 139.7, 136.8, 133.0, 130.2, 129.2, 128.4, 127.8, 127.5, 127.2, 39.2, 27.7, 18.7. IR (KBr plate, $CDCl_3$) ν 3282, 2954, 1646, 1513, 1466, 1365, 1293, 1225, 1178, 1072, 939, 788, 754, 734, 702, 653 cm^{-1}.



3c

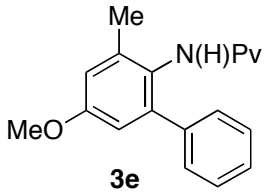
4-Methyl-2-pivalaminobiphenyl (Table 2, entry 2). Following the general procedure A using 5 mol% $Pd(OAc)_2$ and 10 mol% DMSO for 18h at 90°C. Column chromatography: Silica gel, Hexanes/EtOAc, gradient 4% to 25% EtOAc. Off-white solid; yield: 244 mg (91%, mp 77-78 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.53-7.33 (m, 6H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.02-6.96 (m, 1H), 2.41 (s, 3H), 1.10 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.6, 138.7, 138.3, 135.1, 129.7, 129.6, 129.6, 129.2, 128.1, 124.9, 121.6, 40.0, 27.6, 21.7. IR (KBr plate, $CDCl_3$) ν 3435, 3258, 2959, 1687, 1618, 1579, 1530, 1495, 1479, 1458, 1416, 1366, 1292, 1184, 1151, 818, 765, 703, 597, 541 cm^{-1}. Anal. Calcd. for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; Found: C, 80.64; H, 7.94.



3d

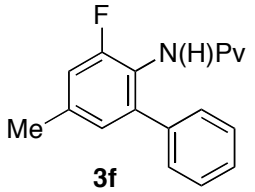
3,4-Dimethyl-2-pivalaminobiphenyl (Table 2, entry 3). Following the general procedure A using 10 mol% $Pd(OAc)_2$ and 20 mol% DMSO for 18h at 90°C. Column chromatography: Silica gel, Hexanes/EtOAc, gradient 4% to 50% EtOAc. Off-white

solid; yield: 237 mg (84%, mp 182 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.23 (m, 5H), 7.15 (d, *J* = 7.5 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 6.83 (s, 1H), 2.34 (s, 3H), 2.14 (s, 3H), 1.11 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.0, 140.1, 137.3, 137.3, 135.2, 132.8, 129.2, 128.7, 128.4, 127.4, 127.1, 39.2, 27.7, 20.8, 15.0. IR (KBr plate, $CDCl_3$) ν 3275, 2963, 1650, 1515, 1473, 1366, 1225, 1188, 1072, 1020, 943, 921, 819, 762, 736, 702, 571 cm^{-1}. Anal. Calcd. for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; Found: C, 81.01; H, 8.32.



3e

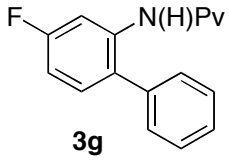
5-Methoxy-3-methyl-2-pivalaminobiphenyl (Table 2, entry 4). Following the general procedure A using 7.5 mol% $Pd(OAc)_2$ and 15 mol% DMSO for 18h at 80°C. Column chromatography: Silica gel, Hexanes/EtOAc, gradient 4% to 40% EtOAc. White solid; yield: 259 mg (87%, mp 169-170 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.24 (m, 5H), 6.79 (d, *J* = 3.0 Hz, 1H), 6.71 (s, 1H), 6.70 (d, *J* = 3.0 Hz, 1H), 3.80 (s, 3H), 2.22 (s, 3H), 1.10 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.3, 158.2, 141.1, 139.9, 138.3, 129.0, 128.3, 127.6, 126.0, 115.5, 113.0, 55.6, 39.1, 27.7, 18.9. IR (KBr plate, $CDCl_3$) ν 3297, 2956, 1647, 1601, 1507, 1475, 1341, 1233, 1204, 1164, 1110, 1059, 858, 845, 758, 701, 653 cm^{-1}. Anal. Calcd. for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.80; Found: C, 76.43; H, 7.85.



3f

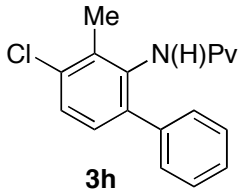
2-Fluoro-5-methyl-2-pivalaminobiphenyl (Table 2, entry 5). Following the general procedure A using 10 mol% $Pd(OAc)_2$ and 20 mol% DMSO for 18h at 90°C. Column chromatography: Silica gel, Hexanes/EtOAc, gradient 4% to 40% EtOAc. Off-white solid; yield: 244 mg (86%, mp 176 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.28 (m, 5H), 6.99-6.92 (m, 2H), 6.72 (s, 1H), 2.38 (s, 3H), 1.15 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.3, 159.7, 156.4, 140.9, 140.9, 138.6, 138.5, 138.4, 138.4, 129.0, 128.5, 127.9, 126.3, 126.2, 119.8, 119.6, 116.0, 115.7, 39.3, 27.6, 21.4, 21.4. ^{19}F NMR (282 MHz, $CDCl_3$) δ -120.2 (d, *J* = 10.7 Hz). IR (KBr plate, $CDCl_3$) ν 3275, 2964, 1653, 1618,

1584, 1508, 1335, 1233, 1180, 1113, 981, 948, 846, 761, 700, 649 cm^{-1}. Anal. Calcd. for $C_{18}H_{20}FNO$: C, 75.76; H, 7.06; Found: C, 75.77; H, 7.12.



3g

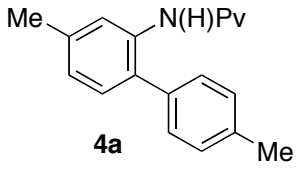
4-Fluoro-2-pivalaminobiphenyl (Table 2, entry 6).[6] Following the general procedure A using 10 mol% $Pd(OAc)_2$ and 20 mol% DMSO for 18h at 90°C. Column chromatography: Silica gel, 9:1 Hexanes/EtOAc. Off-white solid; yield: 185 mg (68%, mp 58-59 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (dd, *J* = 11.5, 2.6 Hz, 1H), 7.55 (s, 1H), 7.50 (m, 2H), 7.44 (m, 1H), 7.33 (m, 2H), 7.18 (dd, *J* = 8.3, 6.3 Hz, 1H), 6.84 (td, *J* = 8.3, 2.6 Hz, 1H), 1.09 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.5, 163.6, 161.6, 137.3, 136.7, 136.6, 130.8, 130.7, 129.6, 129.4, 128.5, 127.7, 127.7, 110.6, 110.4, 108.0, 107.8, 40.0, 27.4. ^{19}F NMR (470 MHz, $CDCl_3$) δ -112.3 (m). IR (KBr plate, $CDCl_3$) ν 3432, 3061, 2962, 2870, 1693, 1599, 1526, 1495, 1458, 1445, 1424, 1278, 1176, 974, 871, 814, 767, 704, 613, 556, 542 cm^{-1}. Anal. Calcd. for $C_{17}H_{18}FNO$: C, 75.25; H, 6.69; Found: C, 75.39; H, 6.70.



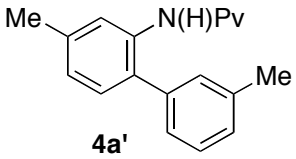
3h

4-Chloro-3-methyl-2-pivalaminobiphenyl (Table 2, entry 7). Following the general procedure A using 10 mol% $Pd(OAc)_2$ and 20 mol% DMSO for 96h at 55°C. Column chromatography: Silica gel, Hexanes/EtOAc, gradient 4% to 25% EtOAc. Off-white solid; yield: 178 mg (59%, mp 211-212 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.31 (m, 4H), 7.27-7.20 (m, 2H), 7.09 (d, *J* = 8.1 Hz, 1H), 6.90 (s, 1H), 2.26 (s, 3H), 1.09 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.1, 139.1, 138.5, 135.1, 134.6, 134.3, 129.0, 128.6, 128.0, 128.0, 127.9, 39.3, 27.6, 16.0. IR (KBr plate, $CDCl_3$) ν 3278, 2969, 1649, 1505, 1460, 1366, 1293, 1225, 1178, 1144, 1073, 1014, 940, 821, 763, 704, 663 cm^{-1}. Anal. Calcd. for $C_{18}H_{20}ClNO$: C, 71.63; H, 6.68; Found: C, 71.39; H, 6.64.

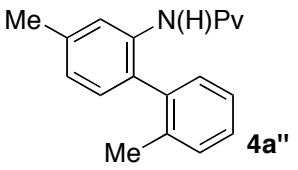
General procedure B for the arylation of anilides with other arenes (Tables 3 and 4): An oven-dried Schlenk tube equipped with a stir bar and a teflon stopper was cooled to room temperature under vacuum and backfilled with O_2. With the tube open to the air, the anilide (0.5 mmol, 1 eq), $Pd(OAc)_2$ (8.5-11.3 mg, 7.5-10 mol%) and 25 mg of 4 Å molecular sieves in powder (previously activated by heating under vacuum) were added. The tube was evacuated and backfilled with O_2, followed by addition of arene (2.0 mmol, 4 eq), TFA (370 μL, 10.00 equiv), and DMSO (5-7 μL, 15-20 mol%) by syringe under a positive O_2 pressure with the tube open to the air. The tube was sealed and lowered into a preheated oil bath at 100 °C and stirred for 10 h. *(Note: Agitation is very important for the reaction outcome! The reaction mixture has to be vigorously stirred to obtain high yields and reproducible results.)* After allowing the reaction mixture to cool to room temperature, the teflon stopper was removed and ethyl acetate (5 mL), distilled water (2 mL), and aqueous 30% NH_4OH (2 mL) were added sequentially. The aqueous layer was extracted with ethyl acetate (2 × 8 mL). The combined organic layers were dried over $MgSO_4$, filtered through Celite, and concentrated under reduced pressure. The residue was purified by silica gel chromatography. **Note:** The identity of each regioisomer was verified by synthesizing the product by an alternative route.[7]



4a



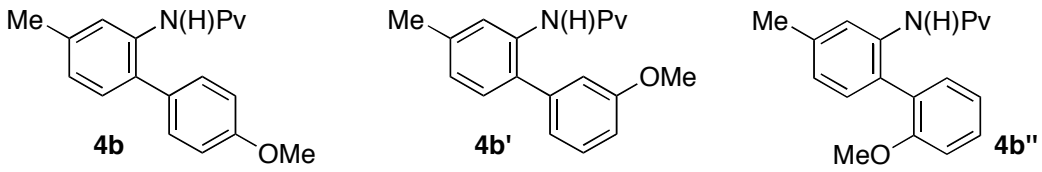
4a'



4a''

4,4'-dimethyl-2-pivalaminobiphenyl (4a), **3',4-dimethyl-2-pivalaminobiphenyl (4a') and 2',4-dimethyl-2-pivalaminobiphenyl (4a'') (Table 2, entry 1).** Following the general procedure B using 215 μL of toluene, 7.5 mol% $Pd(OAc)_2$ and 15 mol% DMSO. Column chromatography: Silica gel, 9:1 Hexanes/EtOAc. Yellow oil; yield: 115 mg (82%). Inseparable mixture of regioisomers **4a**:**4a'**:**4a''** (16:16:1). Due to the low yield of the **4a''** isomer, it is not possible to report its spectroscopic data. The following ^{1}H NMR belongs to a mixture of regioisomers **4a**:**4a'** (1:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (s, 2H), 7.54 (s, 2H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.34-7.21 (m, 5H), 7.21-7.10 (m, 4H), 6.98 (d, *J* = 6.9 Hz, 2H), 2.44 (s, 3H), 2.43 (s, 3H), 2.42 (s, 6H), 1.14 (s, 9H), 1.14 (s, 9H). *The individual assignment of the ^{13}C-NMR for regioisomers **4a** and **4a'** was based on pure samples of these compounds prepared by other means:*[7] ^{13}C NMR (125 MHz, $CDCl_3$) **4a** δ 176.4, 138.3, 135.1, 135.0, 129.8, 129.7, 129.4, 124.7, 121.4, 39.9, 27.5, 21.6, 21.3. **4a'** δ 176.4, 138.8, 138.4, 138.1, 135.0, 130.2, 129.6, 129.5, 129.0, 126.5, 121.4, 39.9, 27.5,

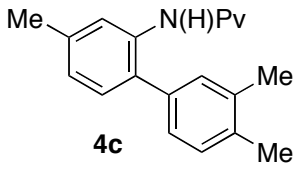
21.6, 21.5. IR spectra belongs to a mixture of regioisomers **4a**:**4a'** (1:1). IR (KBr plate, $CDCl_3$) ν 3433, 2959, 2923, 1687, 1576, 1531, 1512, 1478, 1458, 1419, 1293, 1181, 1151, 810, 789, 732, 710 cm^{-1}.



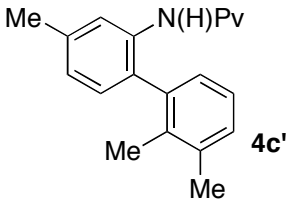
4'-methoxy-4-methyl-2-pivalaminobiphenyl (4b), 3'-methoxy-4-methyl-2-pivalaminobiphenyl (4b') and 2'-methoxy-4-methyl-2-pivalaminobiphenyl (4b'') (Table 2, entry 2). Following the general procedure B using 220 μL of anisole, 7.5 mol% $Pd(OAc)_2$ and 15 mol% DMSO. Column chromatography: Silica gel, 9:1 Hexanes/ EtOAc. Yield: 115 mg (82%). Mixture of regioisomers **4b**:**4b'**:**4b''** (12:2:1) separable by column chromatography. Due to the low yield of the **4b''** isomer, it is not possible to report its spectroscopic data.

4'-methoxy-4-methyl-2-pivalaminobiphenyl (4b). Off-white solid (mp 70-72 °C). ^1H NMR (500 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.51 (s, 1H), 7.27 (d, *J* = 8.3 Hz, 2H), 7.11 (d, *J* = 7.6 Hz, 1H), 7.01 (d, *J* = 8.3 Hz, 2H), 6.96 (d, *J* = 7.6 Hz, 1H), 3.87 (s, 3H), 2.40 (s, 3H), 1.13 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.4, 159.3, 138.2, 135.1, 130.7, 130.3, 129.8, 129.1, 124.7, 121.4, 114.5, 55.4, 39.9, 27.5, 21.6. IR (KBr plate, $CDCl_3$) ν 3431, 2959, 2870, 2837, 1685, 1609, 1569, 1531, 1512, 1478, 1458, 1421, 1294, 1247, 1181, 1038, 921, 839, 814, 733 cm^{-1}.

3'-methoxy-4-methyl-2-pivalaminobiphenyl (4b'). Light yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.55 (s, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.02-6.91 (m, 3H), 6.88 (app m, 1H), 3.84 (s, 3H), 2.41 (s, 3H), 1.12 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.6, 160.3, 139.7, 138.8, 135.1, 130.2, 129.6, 129.3, 124.8, 121.7, 121.4, 115.1, 113.7, 55.5, 40.0, 27.6, 21.7. IR (KBr plate, $CDCl_3$) ν 3431, 2959, 2360, 1685, 1580, 1532, 1477, 1458, 1413, 12945, 1245, 1182, 1050, 1023, 816, 788, 706 cm^{-1}.



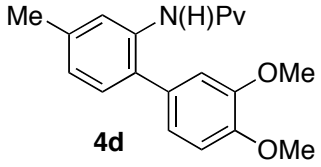
4c



4c'

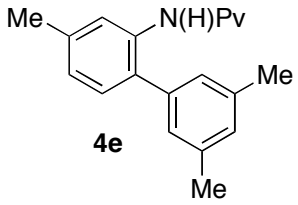
3',4,4'-trimethylbiphenyl-2-pivalaminobiphenyl (4c) and 2',3',4-trimethylbiphenyl-2-pivalaminobiphenyl (4c') (Table 3, entry 3). Following the general procedure B using 240 μL of *o*-xylene, 7.5 mol% $Pd(OAc)_2$ and 15 mol% DMSO. Column chromatography: Silica gel, 9:1 Hexanes/EtOAc. Yield: 136 mg (92%). Mixture of regioisomers **4c**:**4c'** (40:1) separable by column chromatography. Due to the low yield of the **4c'** isomer, it is not possible to report its spectroscopic data. The following data belongs to **4c**.

3',4,4'-trimethylbiphenyl-2-pivalaminobiphenyl (4c). Orange oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.62 (s, 1H), 7.26 (d, *J* = 7.7 Hz, 1H), 7.16 (s, 1H), 7.15 (d, *J* = 7.7 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 7.6 Hz, 1H), 2.43 (s, 3H), 2.36 (s, 3H), 2.34 (s, 3H), 1.16 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.4, 138.2, 137.3, 136.3, 135.6, 135.0, 130.7, 130.4, 129.7, 129.4, 126.8, 124.7, 121.3, 39.9, 27.5, 21.6, 19.9, 19.7. IR (KBr plate, $CDCl_3$) ν 3431, 2960, 2920, 2869, 1687, 1577, 1532, 1477, 1457, 1420, 1292, 1188, 1150, 1023, 922, 811, 732 cm^{-1}.

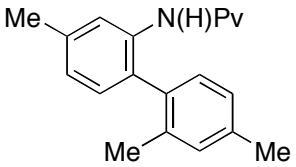


4d

3',4'-dimethoxy-4-methylbiphenyl-2-pivalaminobiphenyl (Table 3, entry 4). Following the general procedure B using 255 μL of veratrole, 7.5 mol% $Pd(OAc)_2$ and 15 mol% DMSO. Column chromatography: Silica gel, 4:1 Hexanes/EtOAc. Lightly yellow solid; yield: 154 mg (94%, mp 117-119 °C). Single regioisomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.55 (s, 1H), 7.09 (d, *J* = 7.7 Hz, 1H), 6.95 (d, *J* = 8.2 Hz, 1H), 6.93 (d, *J* = 7.7 Hz, 1H), 6.91-6.80 (m, 2H), 3.92 (s, 3H), 3.86 (s, 3H), 2.37 (s, 3H), 1.10 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.4, 149.3, 148.7, 138.4, 135.2, 130.6, 129.7, 129.1, 124.6, 121.6, 121.1, 112.5, 111.4, 56.0, 56.0, 39.9, 27.5, 21.6. IR (KBr plate, $CDCl_3$) ν 3427, 2958, 2869, 2836, 1685, 1603, 1574, 1531, 1463, 1419, 1404, 1294, 1251, 1172, 1140, 1028, 811, 766, 737, 609 cm^{-1}.



4e

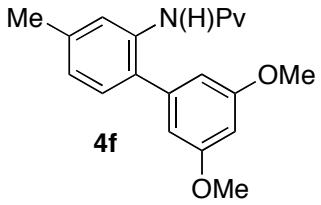


4e'

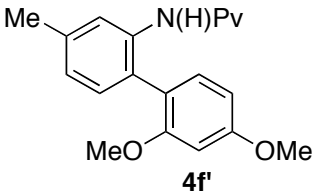
3',4,5'-trimethylbiphenyl-2-pivalaminobiphenyl (4e) and 2',4,4'-trimethylbiphenyl-2-pivalaminobiphenyl (4e') (Table 3, entry 5). Following the general procedure B using 245 μL of *m*-xylene, 10 mol% $Pd(OAc)_2$ and 20 mol% DMSO. Column chromatography: Silica gel, 9:1 Hexanes/EtOAc. Yield: 92 mg (62%). Mixture of regioisomers **4e**:**4e'** (4.1:1) separable by column chromatography.

3',4,5'-trimethylbiphenyl-2-pivalamino-biphenyl (4e). Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.61 (s, 1H), 7.14 (d, *J* = 7.7 Hz, 1H), 7.05 (s, 1H), 6.99 (s, 2H), 6.97 (d, *J* = 7.7 Hz, 1H), 2.41 (s, 3H), 2.39 (s, 6H), 1.15 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.4, 138.7, 138.4, 138.0, 135.0, 129.6, 129.5, 129.5, 127.3, 124.7, 121.3, 40.0, 27.5, 21.7, 21.5. IR (KBr plate, $CDCl_3$) ν 3430, 2959, 2868, 2248, 1686, 1601, 1575, 1532, 1478, 1457, 1366, 1292, 1181, 1150, 1031, 922, 855, 813, 733, 711 cm^{-1}.

2',4,4'-trimethylbiphenyl-2-pivalaminobiphenyl (4e'). Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.17 (s, 1H), 7.16 (s, 1H), 7.11 (d, *J* = 7.6 Hz, 1H), 7.06 (d, *J* = 7.6 Hz, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 2.41 (s, 3H), 2.39 (s, 3H), 2.05 (s, 3H), 1.02 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.5, 138.5, 138.3, 136.9, 135.7, 134.2, 131.4, 130.2, 129.4, 128.5, 127.4, 124.5, 120.5, 39.9, 27.4, 21.8, 21.4, 19.8. IR (KBr plate, $CDCl_3$) ν 3425, 2959, 2868, 1689, 1532, 1458, 1419, 1292, 1181, 1026, 814 cm^{-1}.



4f

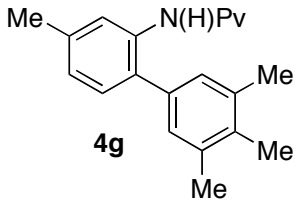


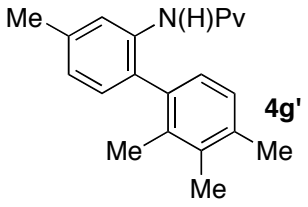
4f'

3',5'-dimethoxy-4-methylbiphenyl-2-pivalaminobiphenyl (4f) and 2',4'-dimethoxy-4-methylbiphenyl-2-pivalaminobiphenyl (4f') (Table 3, entry 6). Following the general procedure B using 260 μL of 1,3-dimethoxybenzene, 10 mol% $Pd(OAc)_2$ and 20 mol% DMSO. Column chromatography: Silica gel, 85:15 Hexanes/EtOAc. Yield: 129 mg (79%). Mixture of regioisomers **4f**:**4f'** (11:1) separable by column chromatography.

Due to the low yield of the **4f'** isomer, it is not possible to report its spectroscopic data. The following data belongs to the major regioisomer.

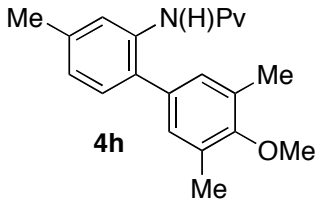
3',5'-dimethoxy-4-methylbiphenyl-2-pivalaminobiphenyl (4f). Lightly yellow solid (mp 70-72 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.79 (s, 1H), 7.13 (d, *J* = 8.1 Hz, 1H), 7.09 (d, *J* = 7.8 Hz, 1H), 6.98 (d, *J* = 7.7 Hz, 1H), 6.64-6.58 (m, 2H), 3.87 (s, 3H), 3.80 (s, 3H), 2.40 (s, 3H), 1.12 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.5, 161.0, 156.9, 138.0, 135.7, 132.8, 130.7, 127.1, 125.1, 122.6, 119.8, 105.3, 98.7, 55.8, 55.5, 39.6, 27.4, 21.5. IR (KBr plate, $CDCl_3$) ν 3429, 2960, 1684, 1609, 1576, 1532, 1507, 1458, 1415, 1304, 1208, 1159, 1049, 1031, 1003, 923, 822, 732 cm^{-1}.



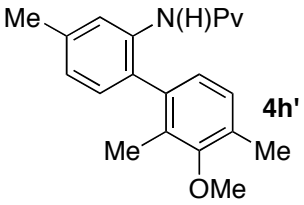


3',4,4',5'-tretramethylbiphenyl-2-pivalaminobiphenyl (4g) and 2',3',4,4'-tretramethylbiphenyl-2-pivalaminobiphenyl (4g') (Table 3, entry 7). Following the general procedure B using 270 μL of 1,2,3-trimethylbenzene, 185 μL of TFA (*5 equivalents*), 10 mol% $Pd(OAc)_2$ and 20 mol% DMSO. Column chromatography: Silica gel, 4:1 Hexanes/ EtOAc. Orange oil. Yield: 136 mg (88%). Mixture of regioisomers **4g**:**4g'** (10:1) inseparable by column chromatography. The following data belongs to the major regioisomer.

3',4,4',5'-tretramethylbiphenyl-2-pivalaminobiphenyl (**4g**). Orange oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.7 (s, 1H), 7.15 (d, *J* = 7.7 Hz, 1H), 7.04 (s, 2H), 6.97 (d, *J* = 7.7 Hz, 1H), 2.42 (s, 3H), 2.36 (s, 6H), 2.26 (s, 3H), 1.17 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.4, 138.1, 137.3, 135.0, 134.9, 134.8, 129.7, 129.4, 128.6, 124.7, 121.3, 40.0, 27.5, 21.6, 20.7, 15.4. IR (KBr plate, $CDCl_3$) ν 3428, 2959, 2920, 2868, 1687, 1577, 1532, 1457, 1420, 1293, 1188, 1169, 1150, 923, 878, 813, 732 cm^{-1}.



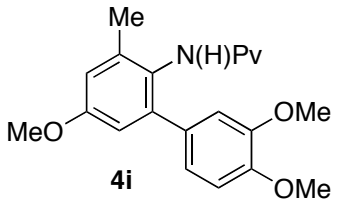
4h



4h'

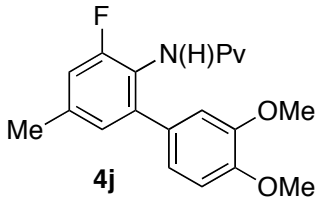
4'-methoxy-3',4,5'-trimethylbiphenyl-2-pivalaminobiphenyl (4h) and 3'-methoxy-2',4,4'-trimethylbiphenyl-2-pivalaminobiphenyl (4h') (Table 3, entry 8). Following the general procedure B using 260 μL of 1,6-dimethoxyanisole, 10 mol% $Pd(OAc)_2$ and 20 mol% DMSO. Column chromatography: Silica gel, 9:1 Hexanes/EtOAc. Yellow solid; yield: 108 mg (66%, mp 74-76 °C). Mixture of regioisomers **4h**:**4h'** (20:1) inseparable by column chromatography. The following data belongs to the major regioisomer.

4'-methoxy-3',4,5'-trimethylbiphenyl-2-pivalaminobiphenyl (**4h)**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.57 (s, 1H), 7.11 (d, *J* = 7.8 Hz, 1H), 7.01 (s, 2H), 6.94 (d, *J* = 7.8 Hz, 1H), 3.78 (s, 3H), 2.39 (s, 3H), 2.34 (s, 6H), 1.14 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.4, 156.7, 138.3, 135.0, 133.5, 131.7, 130.0, 129.5, 129.1, 124.7, 121.4, 59.9, 39.9, 27.5, 21.6, 16.2. IR (KBr plate, $CDCl_3$) ν 3430, 2956, 1685, 1574, 1531, 1458, 1420, 1293, 1231, 1199, 1165, 1121, 1010, 883, 815 cm^{-1}.



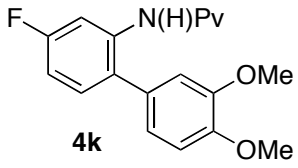
4i

3',4',5-trimethoxy-3-methylbiphenyl-2-pivalaminobiphenyl (Table 4, entry 1). Following the general procedure B using 255 μL of veratrole, 7.5 mol% $Pd(OAc)_2$, 15 mol% DMSO and *without molecular sieves*. Column chromatography: Silica gel, 3:1 Hexanes/EtOAc. Orange solid; yield: 126 mg (70%, mp 167-169 °C). Single regioisomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.86-6.77 (m, 5H), 6.73 (d, *J* = 2.8 Hz, 1H), 6.65 (d, *J* = 2.8 Hz, 1H), 3.87 (s, 3H), 3.81 (s, 3H), 3.76 (s, 3H), 2.17 (s, 3H), 1.09 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.3, 158.0, 148.5, 148.4, 141.0, 138.1, 132.5, 126.0, 121.0, 115.0, 113.0, 112.2, 110.8, 56.0, 55.9, 55.4, 39.0, 27.6, 18.7 IR (KBr plate, $CDCl_3$) ν 3320, 2959, 2837, 2254, 1649, 1601, 1515, 1466, 1256, 1226, 1157, 1055, 1029, 913, 762, 732, 646, 614 cm^{-1}. Calcd. for $C_{21}H_{27}NO_4$: C, 70.56; H, 7.61; Found: C, 70.58; H, 6.67.



4j

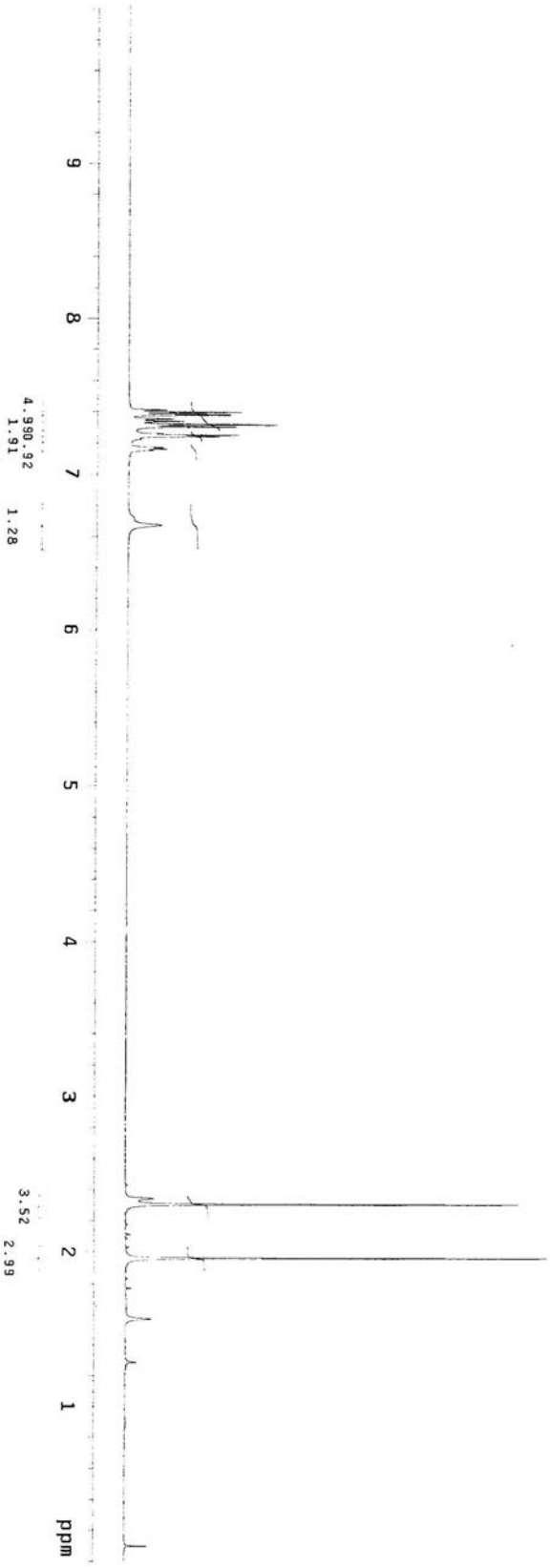
3-Fluoro-3',4'-dimethoxy-5-methylbiphenyl-2-pivalaminobiphenyl (Table 4, entry 2). Following the general procedure B using 255 μL of veratrole, 10 mol% $Pd(OAc)_2$, 20 mol% DMSO and *without molecular sieves*. Column chromatography: Silica gel, 7:3 Hexanes/EtOAc. Yellow solid; yield: 121 mg (70%, mp 134-136 °C). Single regioisomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.92-6.81 (m, 5H), 6.78 (s, 1H), 3.88 (s, 3H), 3.83 (s, 3H), 2.33 (s, 3H), 1.14 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.4, 159.0, 157.0, 148.7, 140.8, 138.4, 138.3, 131.0, 131.0, 126.2, 126.1, 121.2, 119.8, 119.7, 115.6, 115.4, 112.1, 110.9, 56.0, 56.0, 39.1, 27.6, 21.2. ^{19}F NMR (470 MHz, $CDCl_3$) δ -120.4 (d, J = 10.8 Hz). IR (KBr plate, $CDCl_3$) ν 3310, 2961, 2254, 1657, 1516, 1464, 1256, 1120, 1142, 1028, 913, 763, 731, 611 cm^{-1}. Anal. Calcd. for $C_{19}H_{22}FNO_3$: C, 68.86; H, 6.69; Found: C, 68.58; H, 6.77.

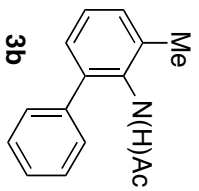


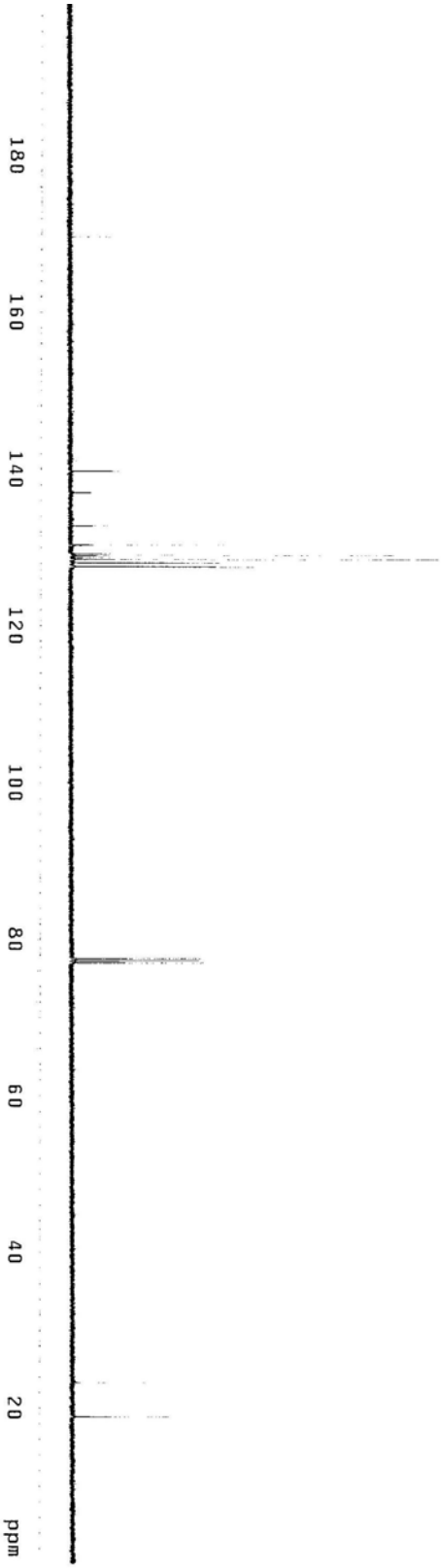
4k

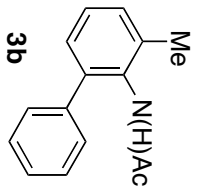
4-Fluoro-3',4'-dimethoxybiphenyl-2-pivalaminobiphenyl (Table 4, entry 3). Following the general procedure B using 255 μL of veratrole, 10 mol% $Pd(OAc)_2$, 20 mol% DMSO and *without molecular sieves*. Column chromatography: Silica gel, 7:3 Hexanes/ EtOAc. Yellow solid; yield: 121 mg (73%, mp 131-133 °C). Single regioisomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, J = 10.8 Hz 1H), 7.63 (s, 1H), 7.13 (dd, J = 8.0, 6.7 Hz, 1 H), 6.95 (d, J = 8.0 Hz), 6.85 (d, J = 8.0 Hz, 1H), 6.82-6.74 (m, 1H), 6.80 (s, 1H), 3.92 (s, 3H), 3.86 (s, 3H), 1.08 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.5, 163.3, 161.4, 149.5, 149.0, 136.8, 136.7, 130.8, 130.8, 129.6, 127.3, 127.3, 121.7, 112.5, 111.6, 110.3, 110.1, 107.6, 107.4, 56.1, 56.0, 40.0, 27.4. ^{19}F NMR (470 MHz, $CDCl_3$) δ -112.5 (quint., J = 6.5 Hz). IR (KBr plate, $CDCl_3$) ν 3424, 2961, 2361, 1990, 1599, 1525, 1460, 1429, 1250, 1173, 1140, 976, 872, 809, 765, 557 cm^{-1}. Anal. Calcd. for $C_{18}H_{22}FNO_3$: C, 68.86; H, 6.69; Found: C, 68.58; H, 6.77.

Selected Spectra

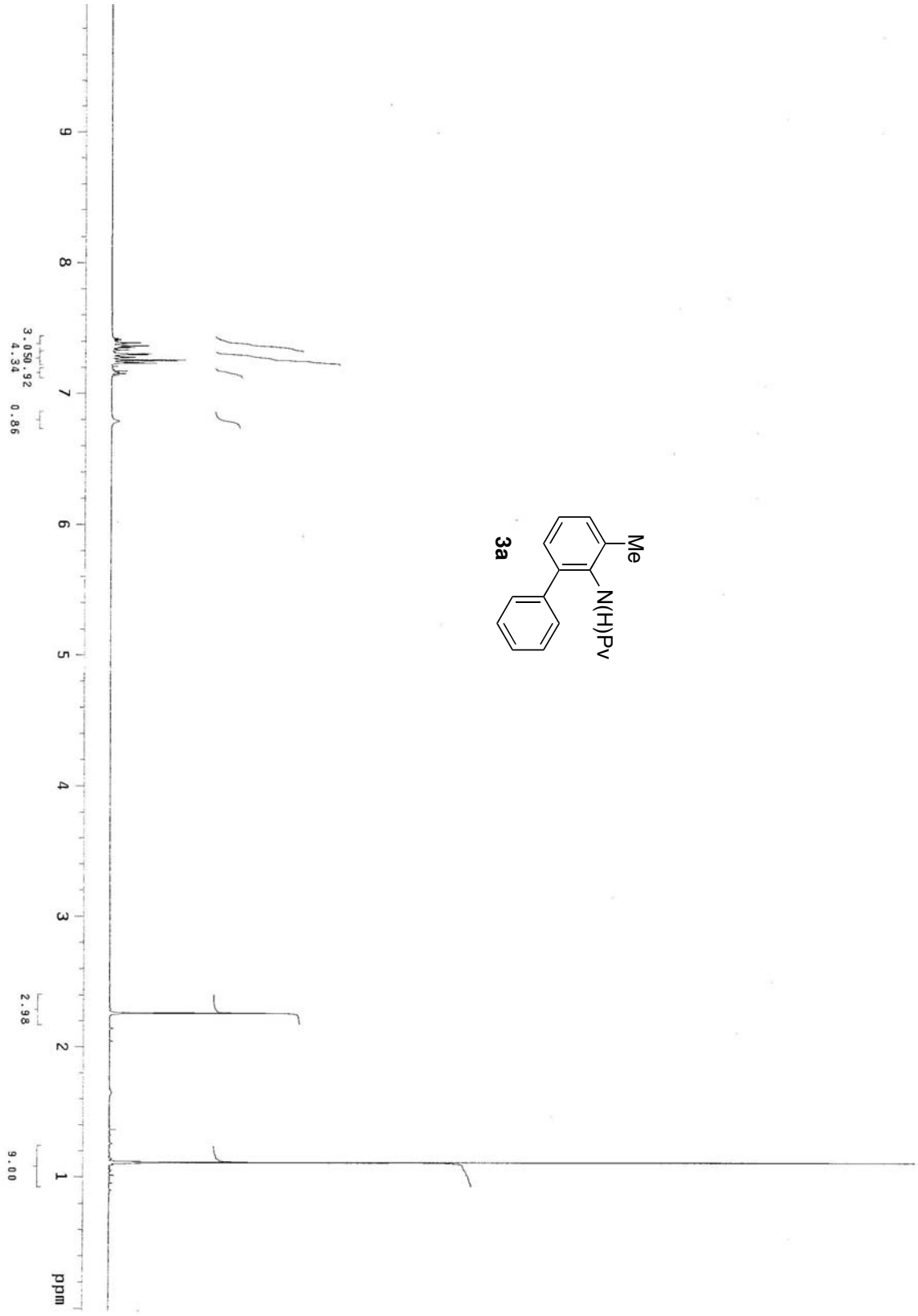








3b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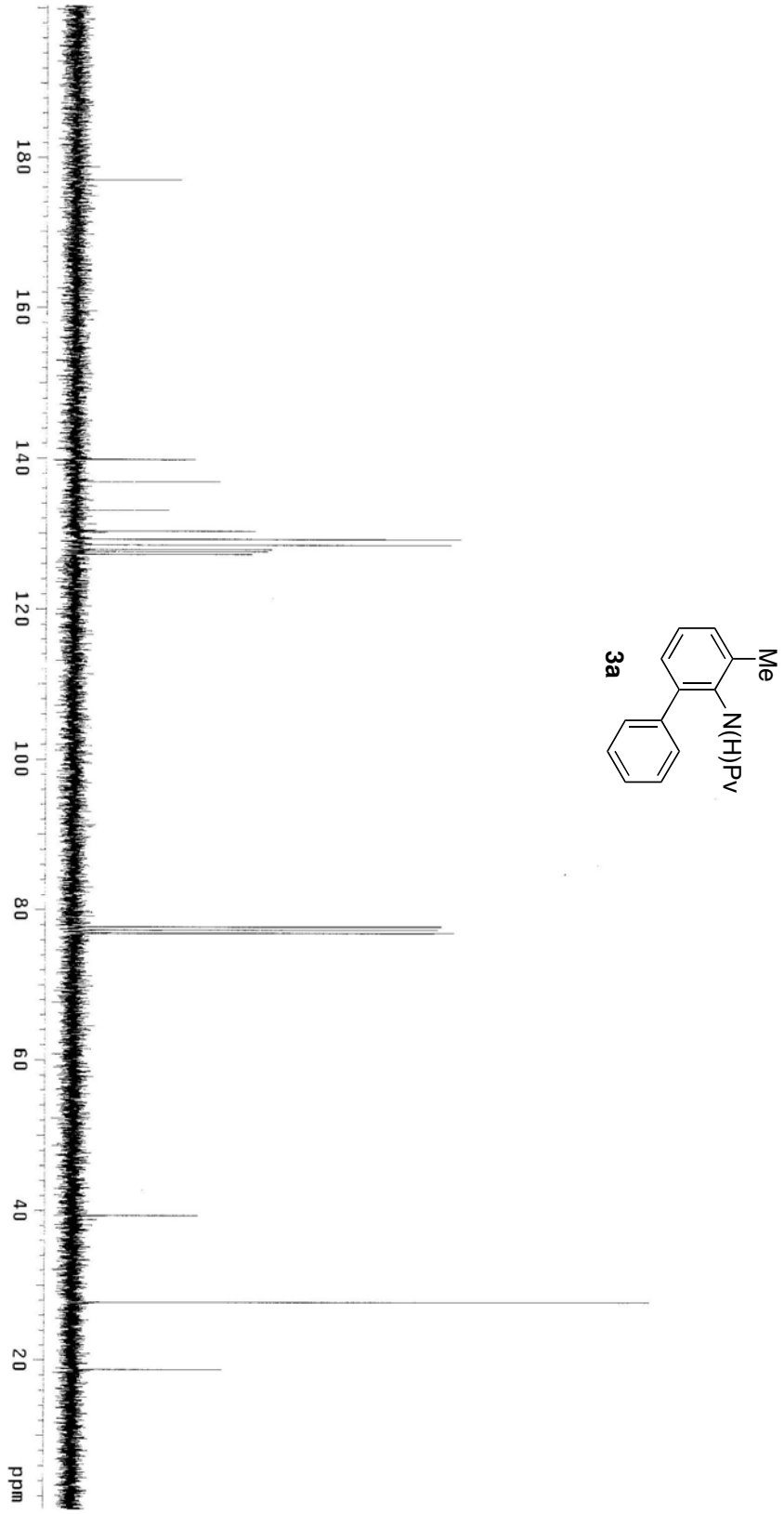
9.00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120
100
80
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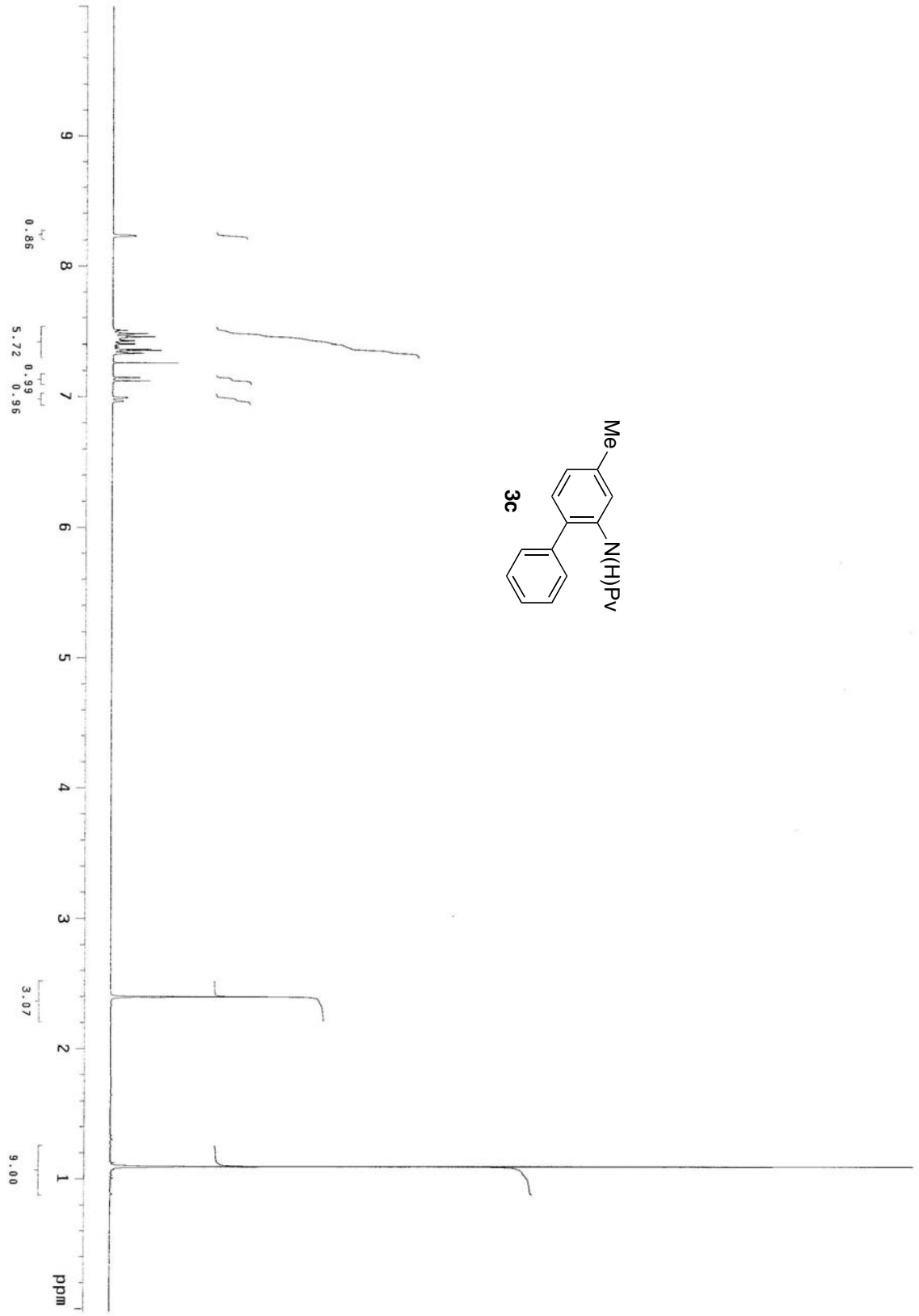
40
20
ppm
Me
N(H)Pv
3a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4
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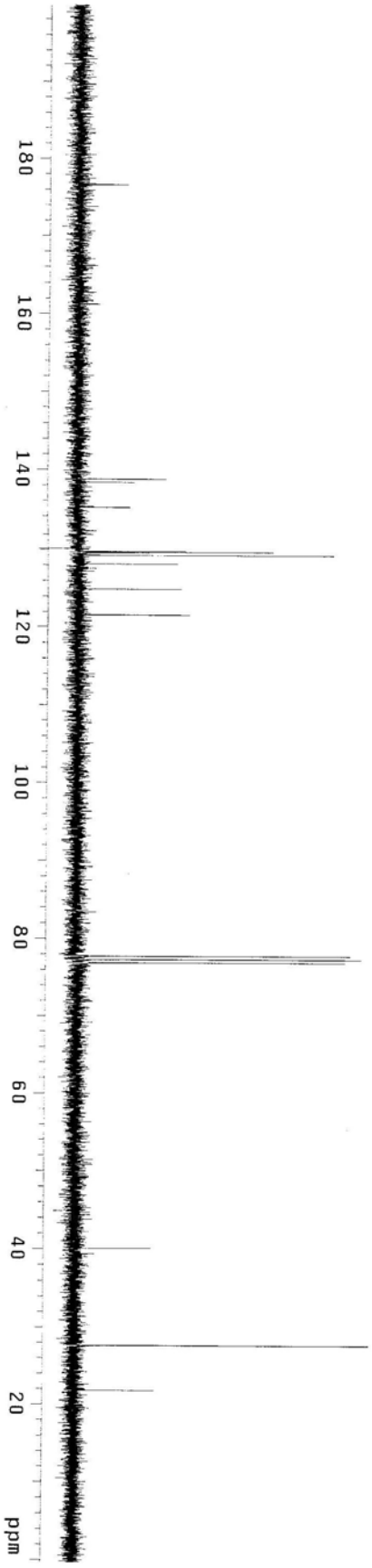
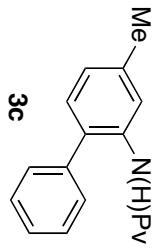
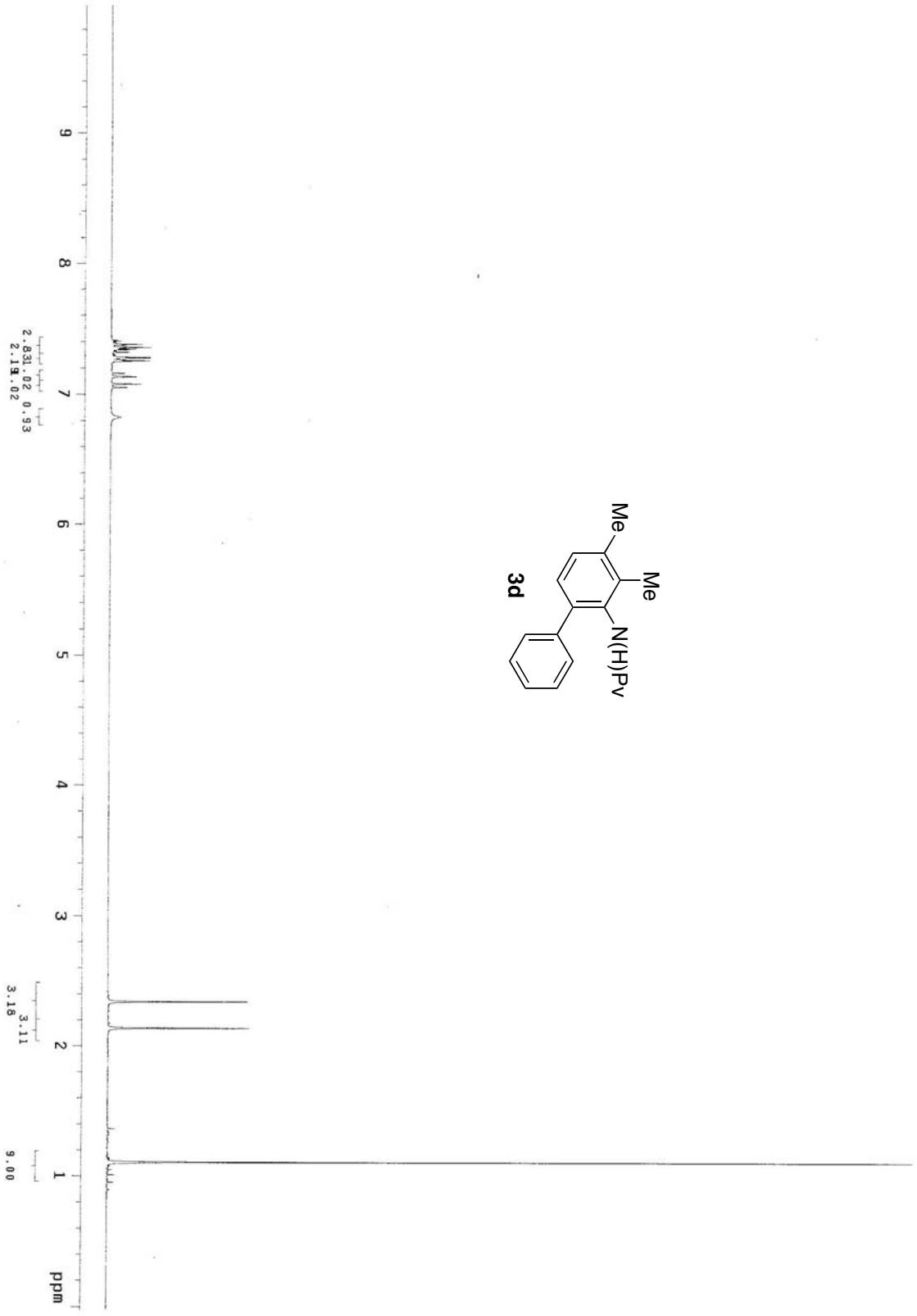
9.00





3c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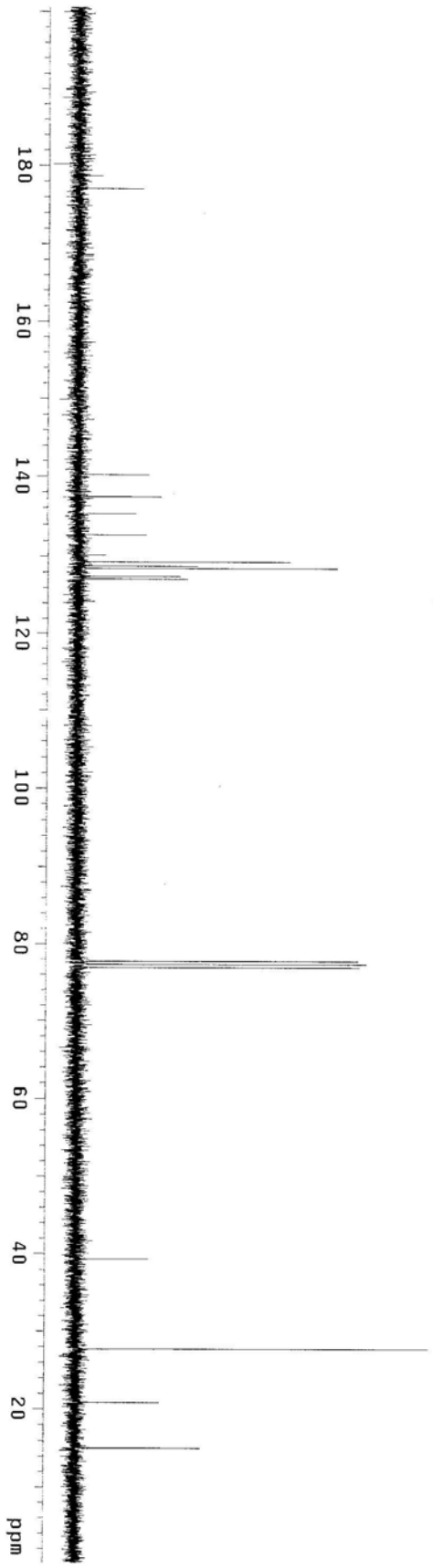
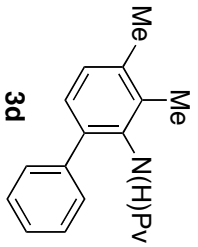
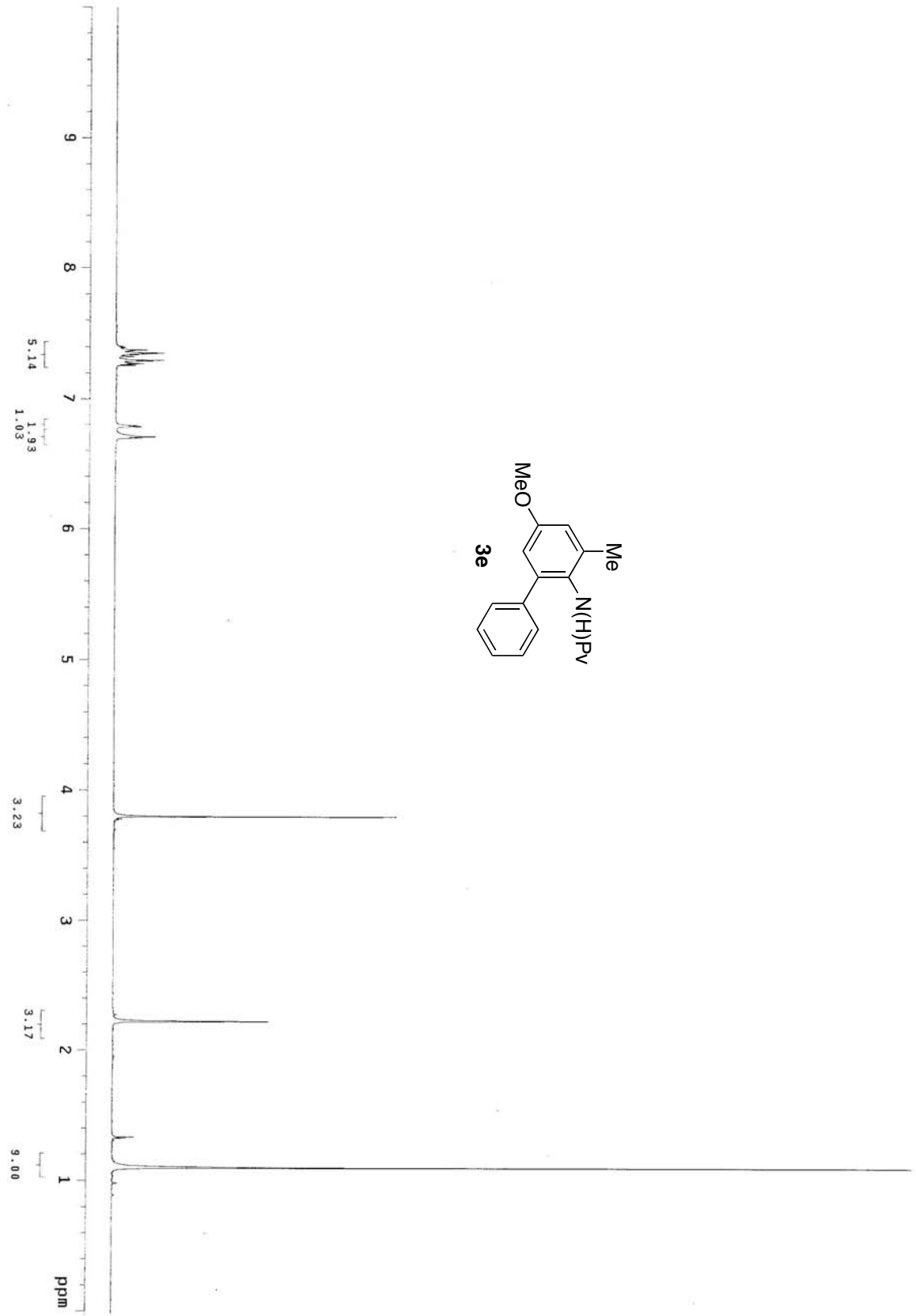
1.02
ppm





3d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ppm
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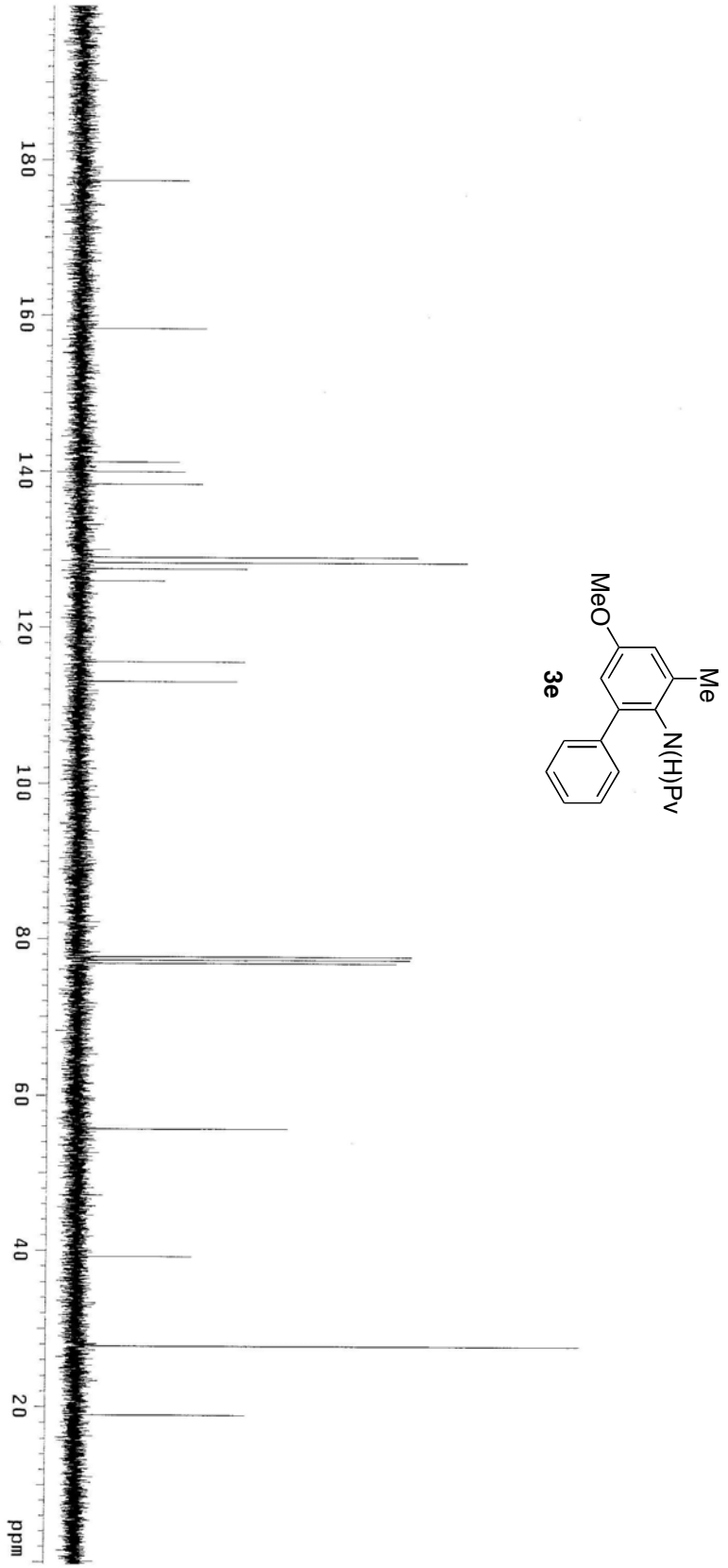
9.00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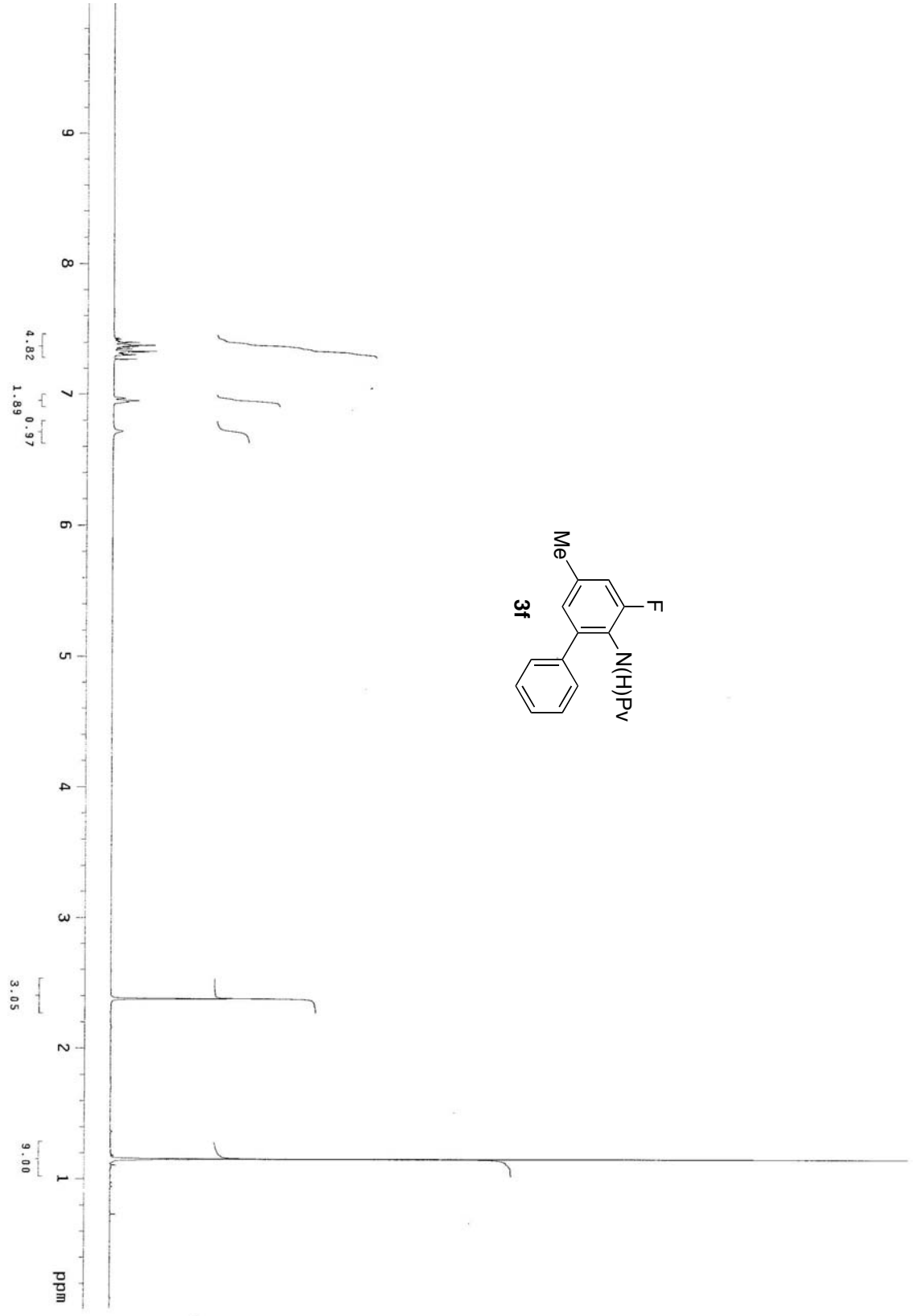
140
120
100
80
60
40
20
ppm
MeO
Me
N(H)Pv
3e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N(H)Pv
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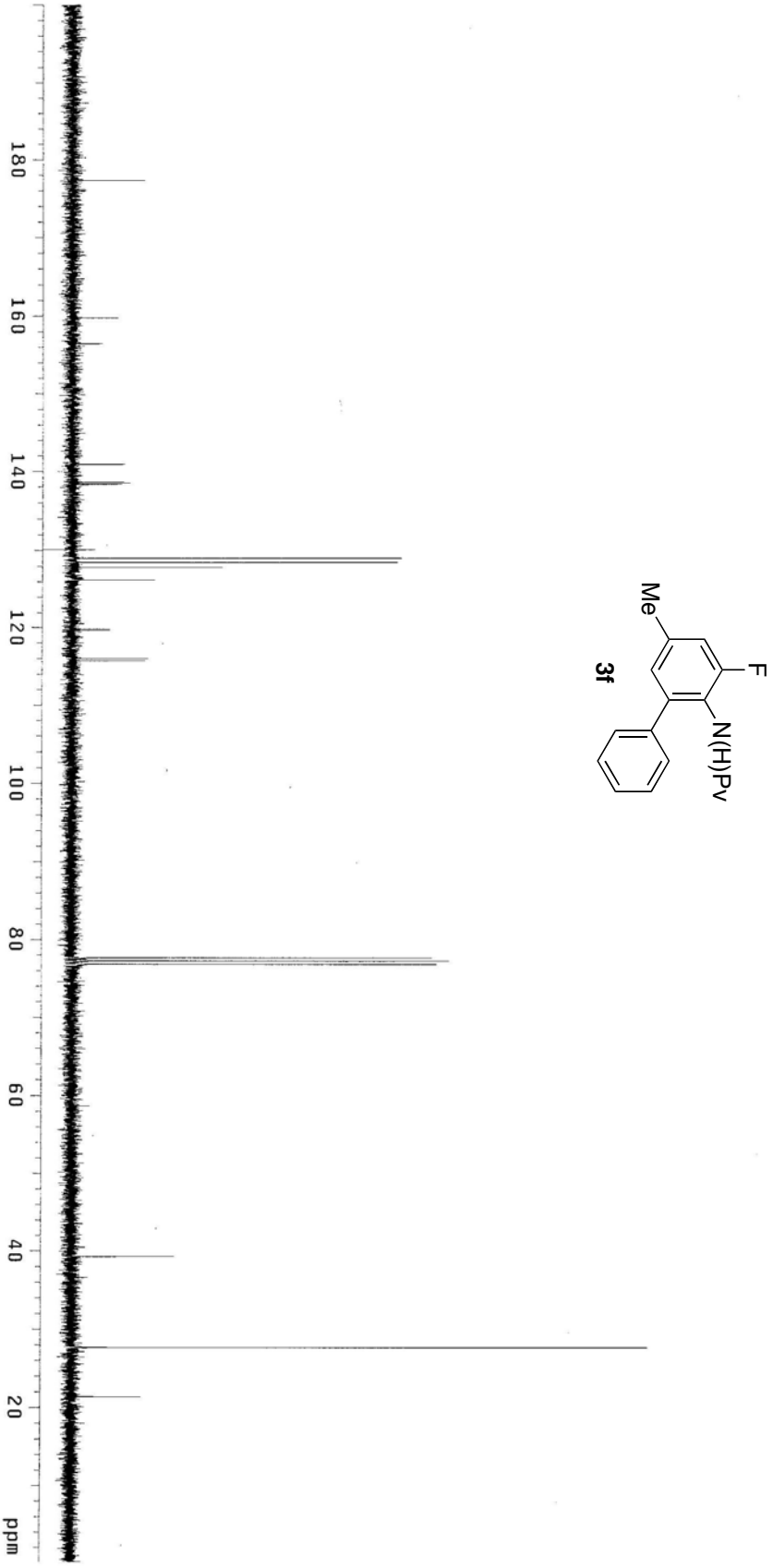
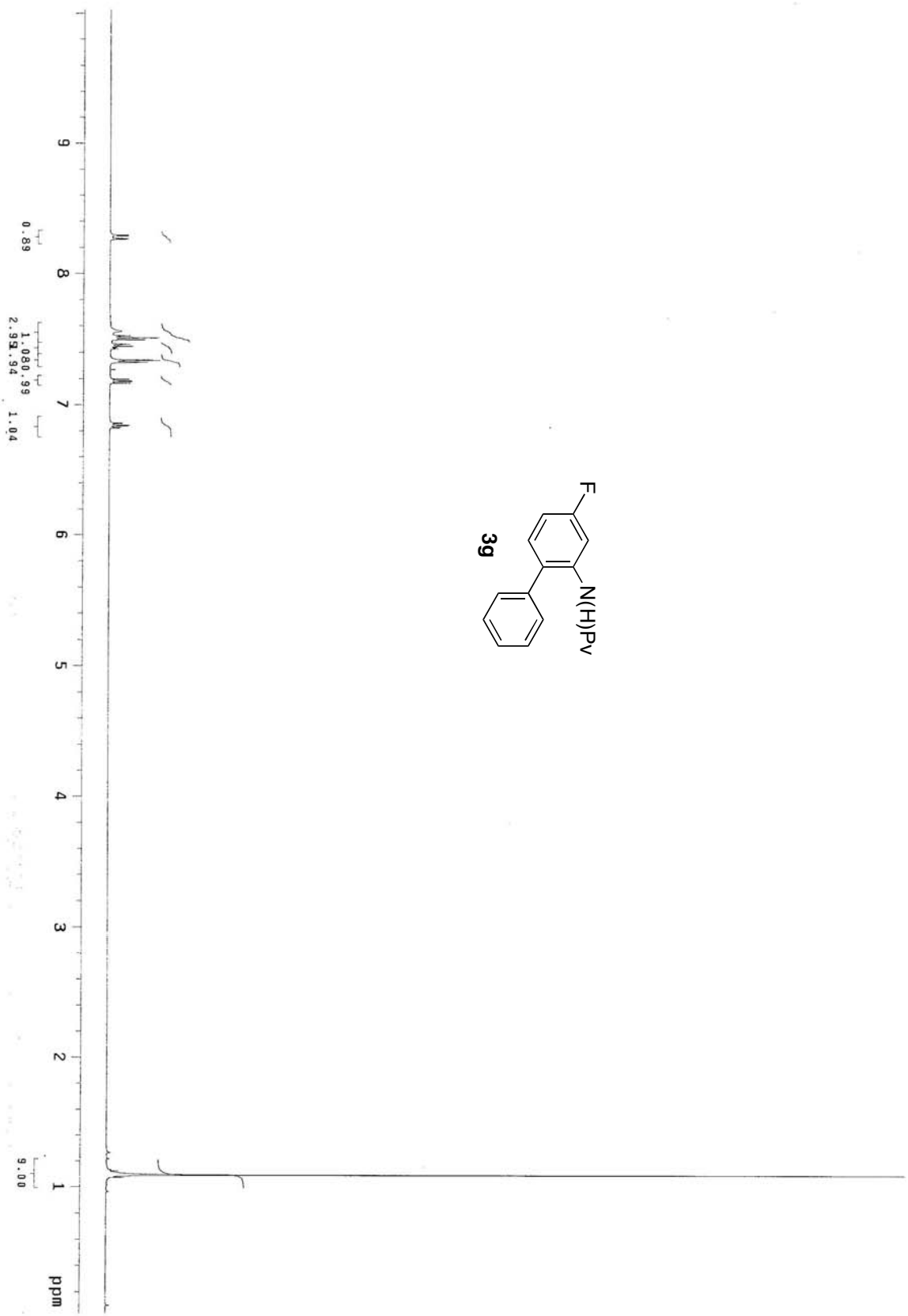


3f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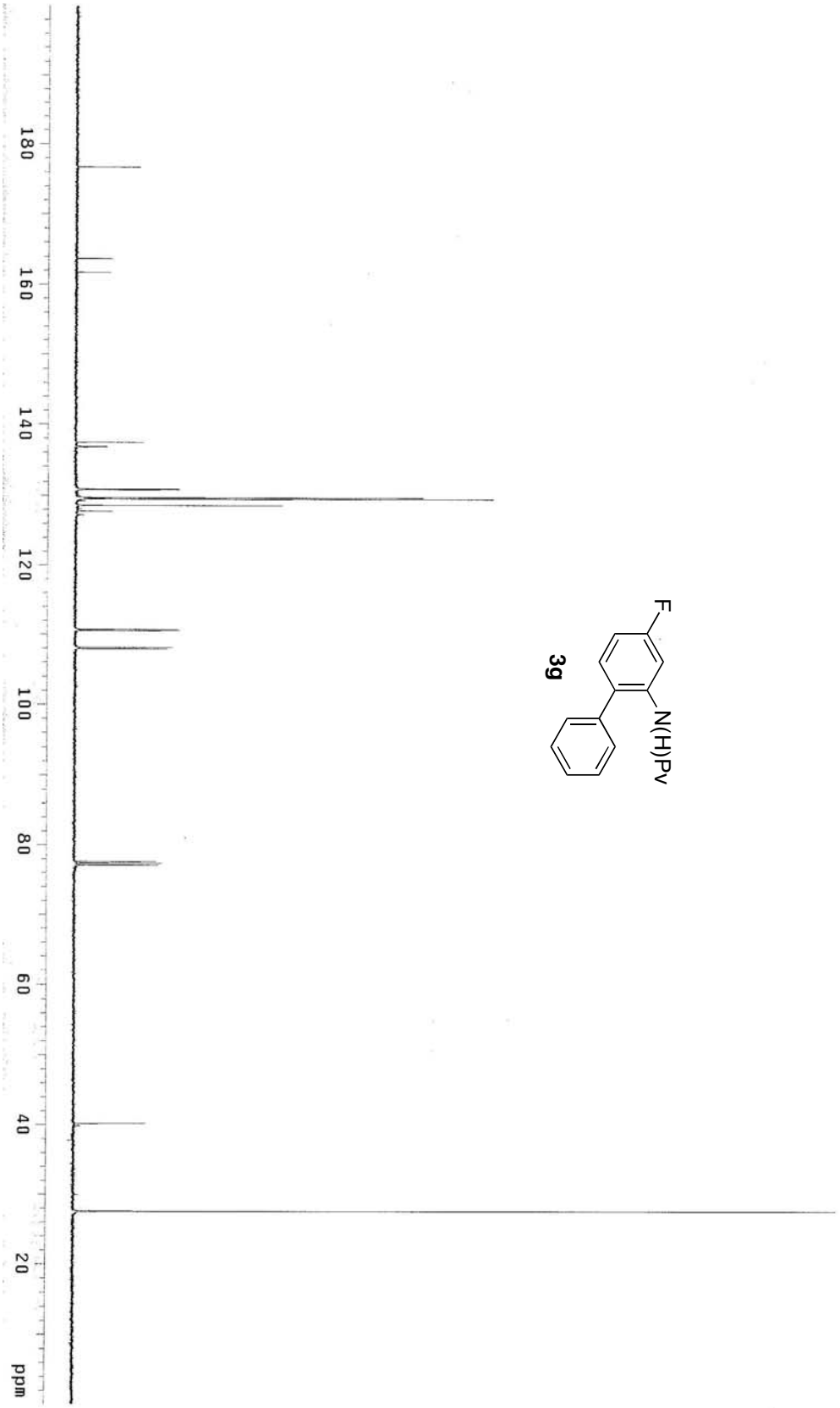
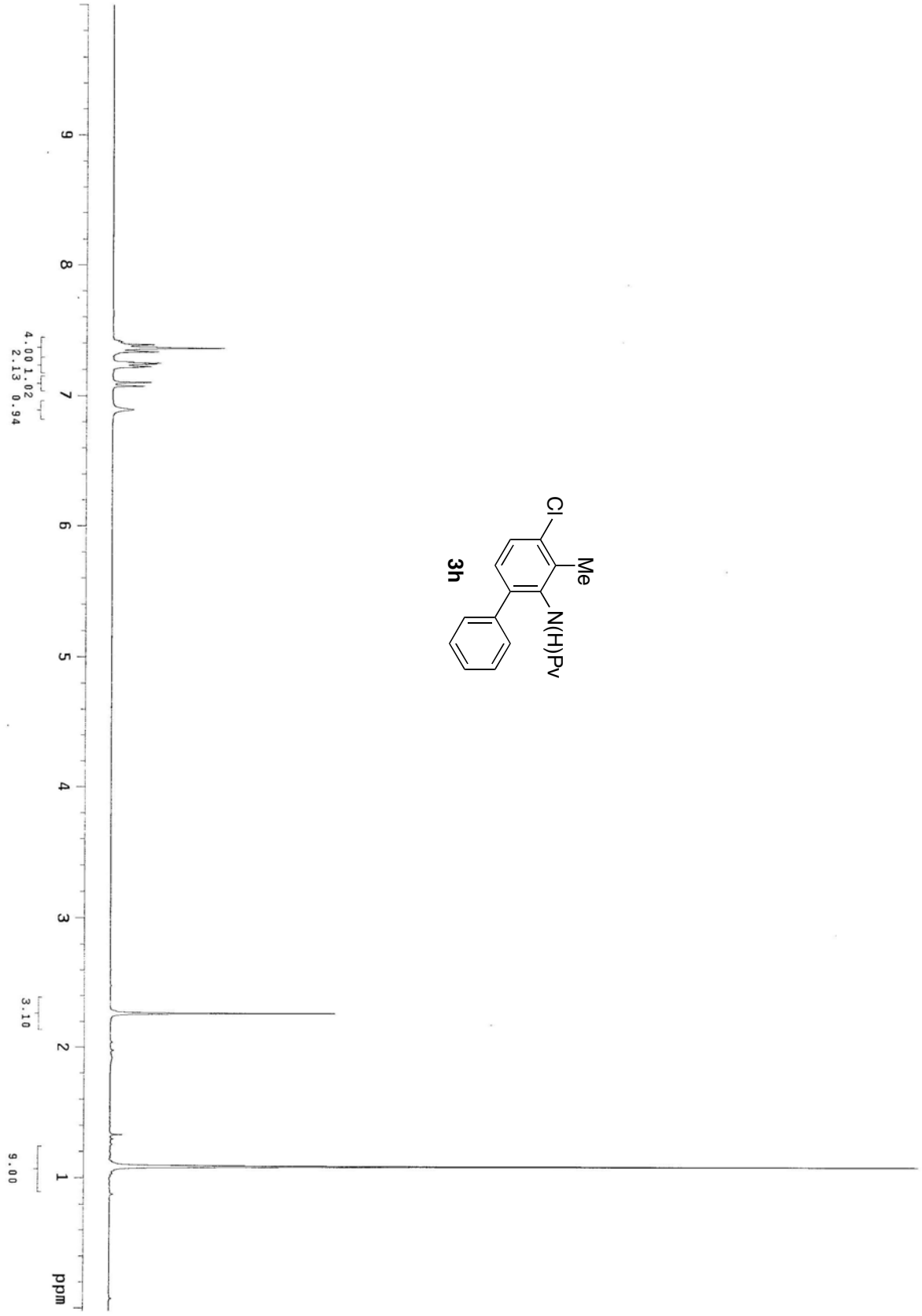
9.00



3g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3
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ppm
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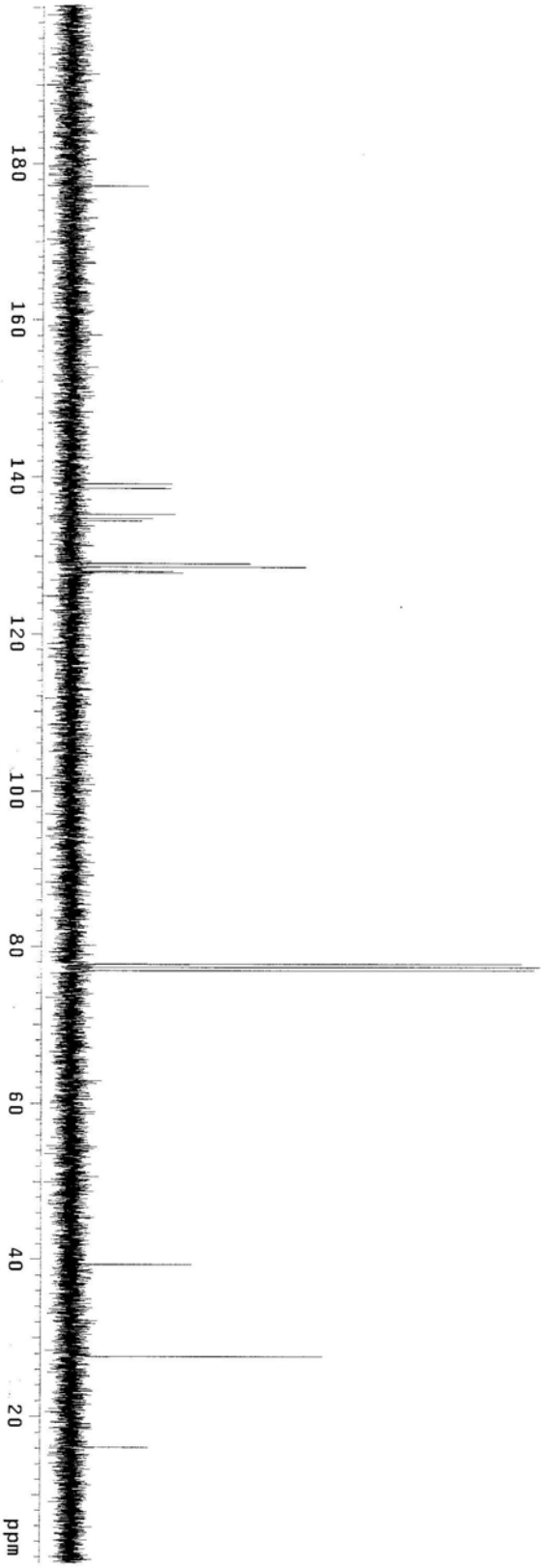
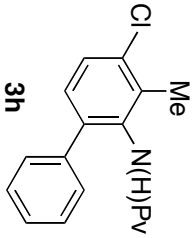
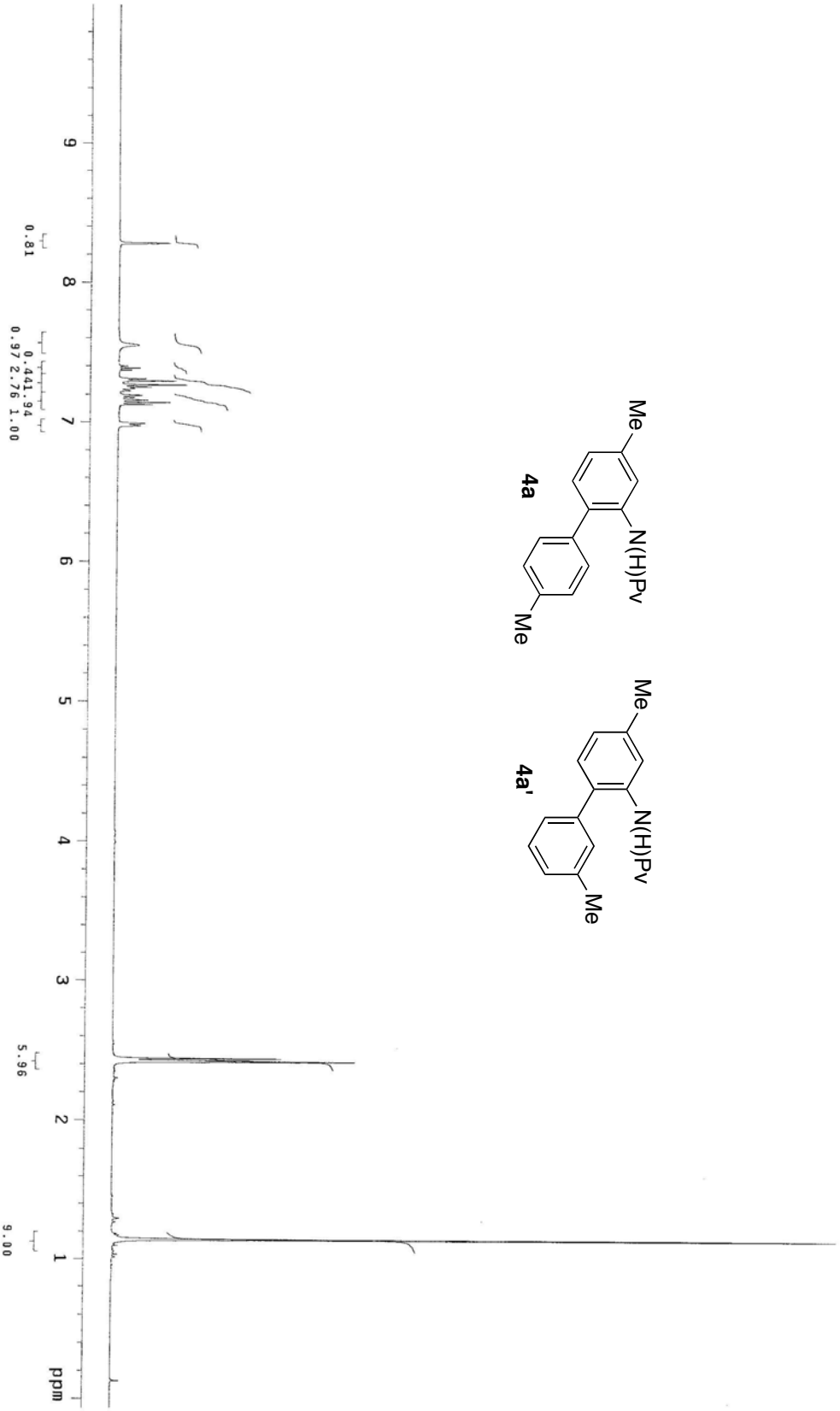
9.00





3h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Me
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Me
N(H)Pv
Me
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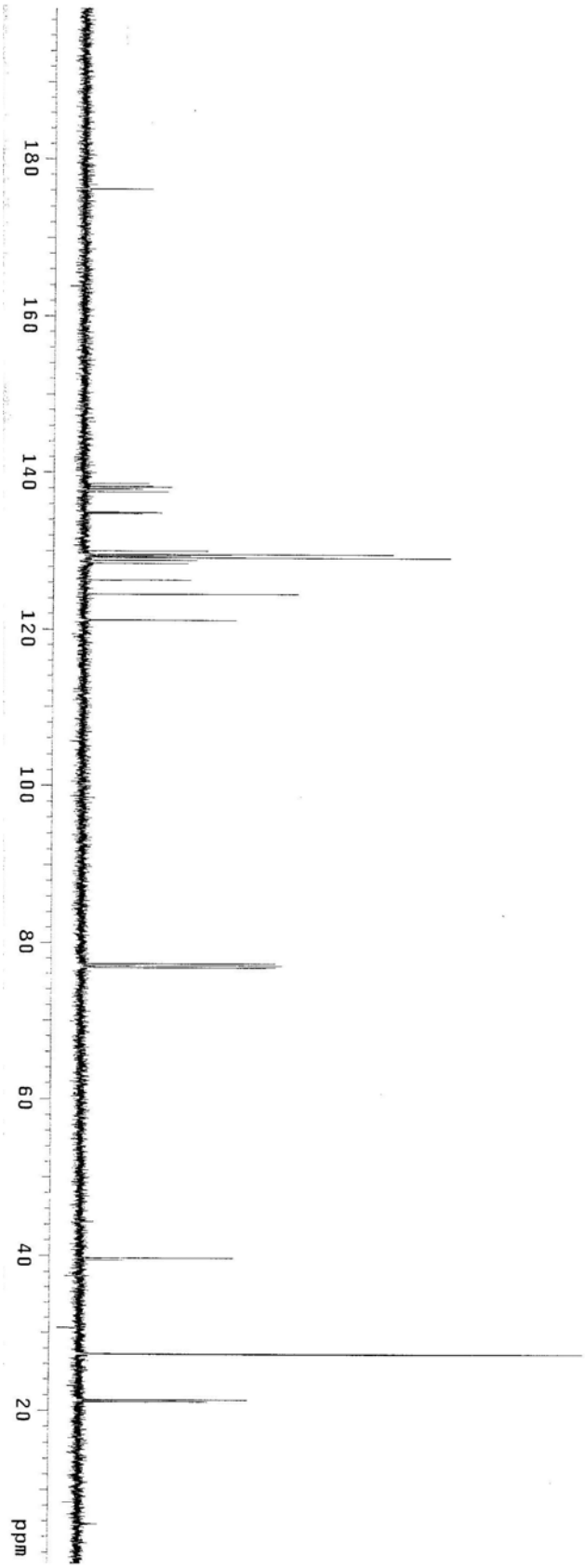
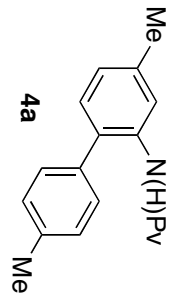
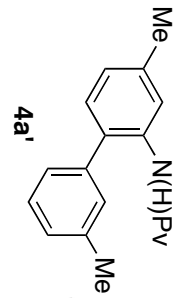
ppm

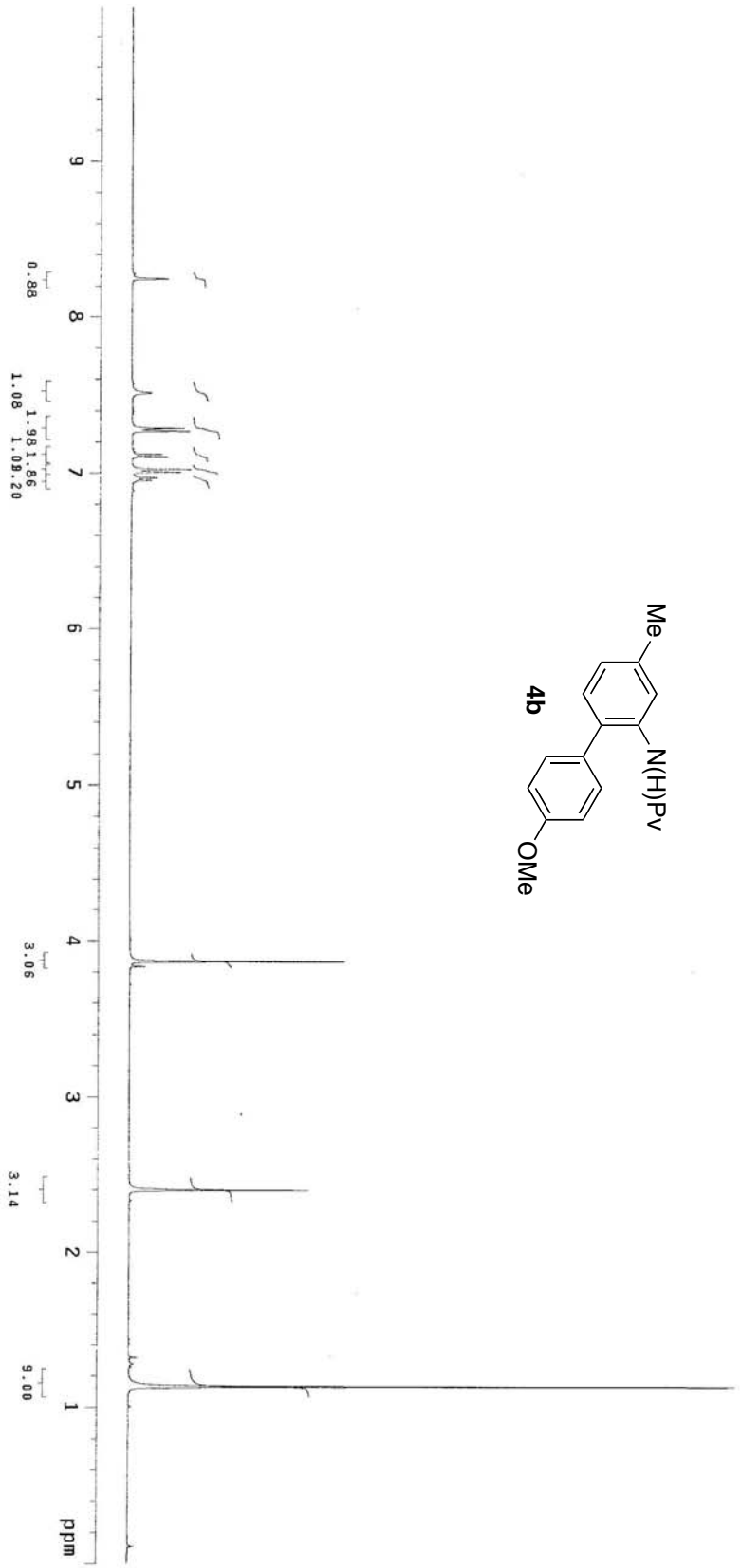




4a



4a'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4b
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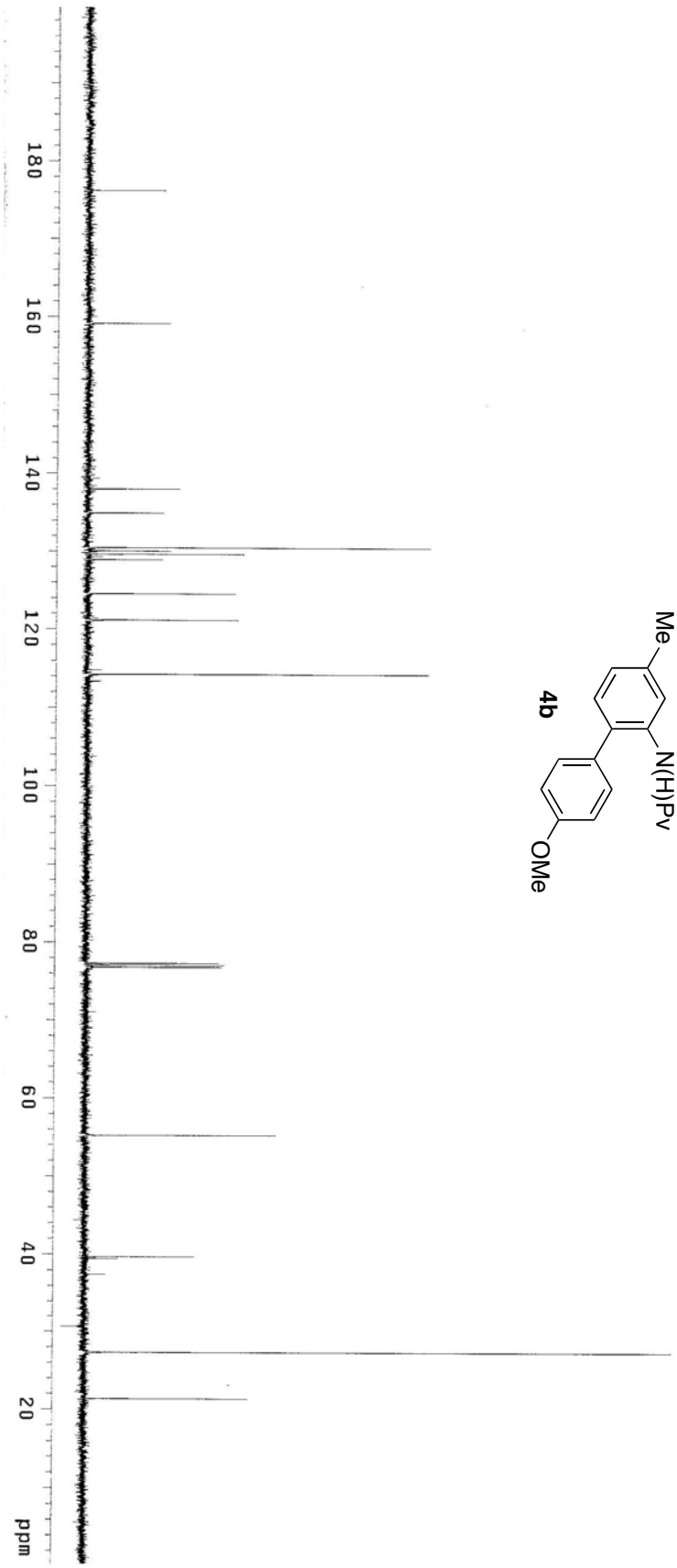
9.00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OMe
4b
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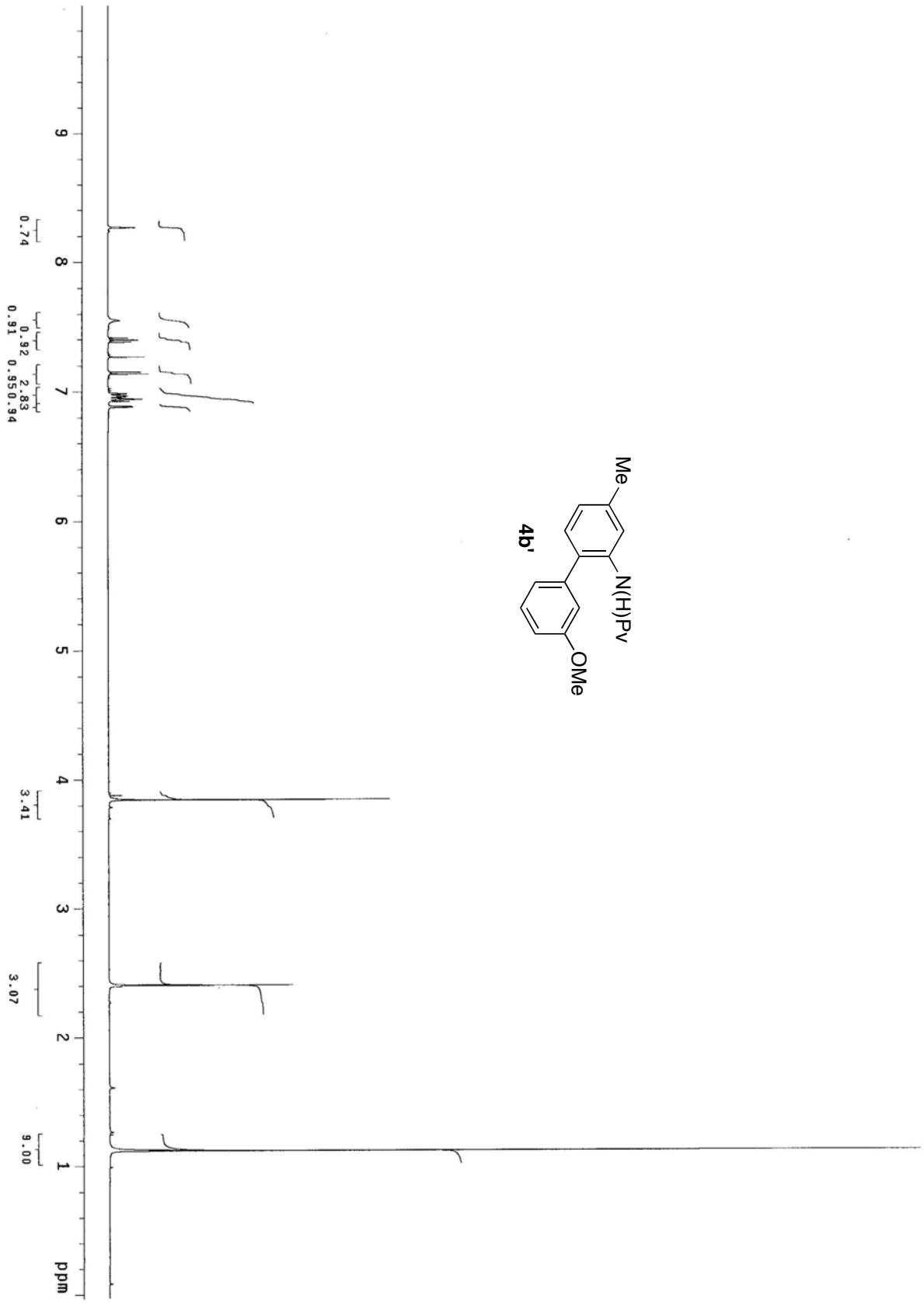
ppm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N(H)Pv
OMe
4b'
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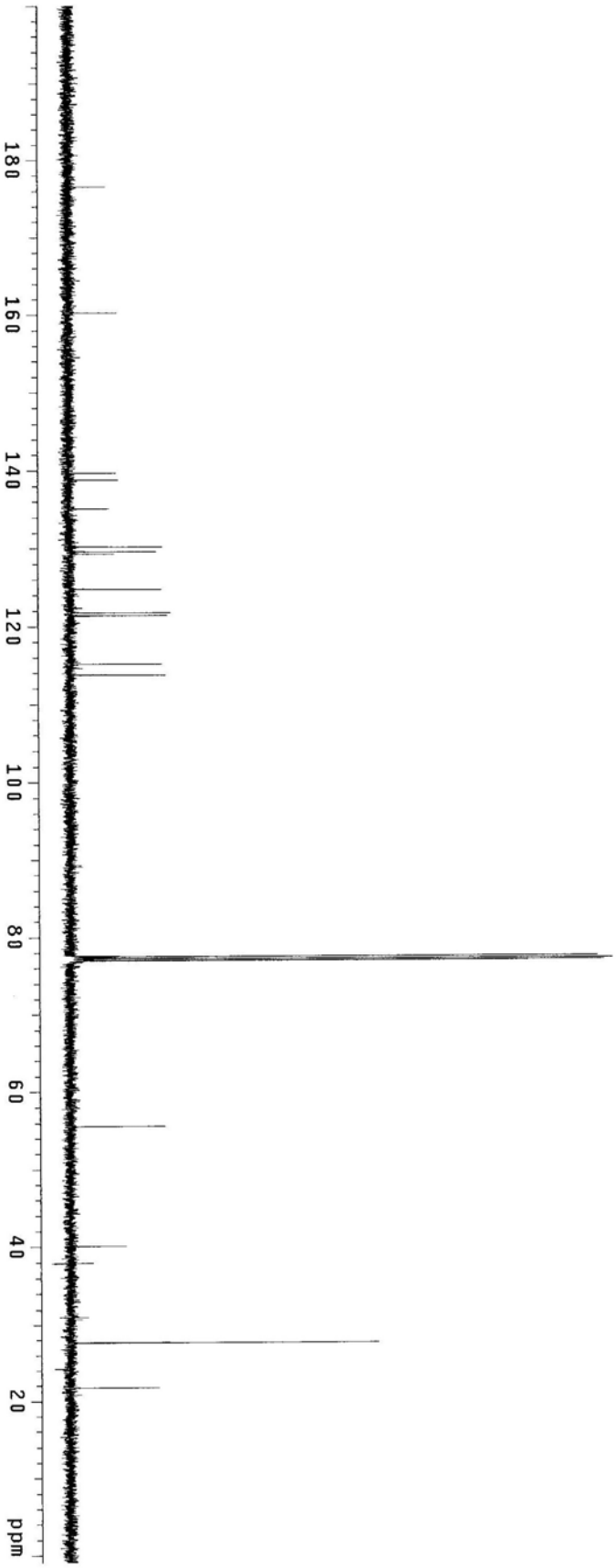
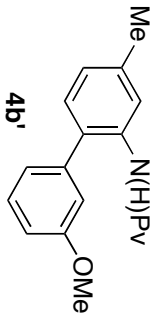
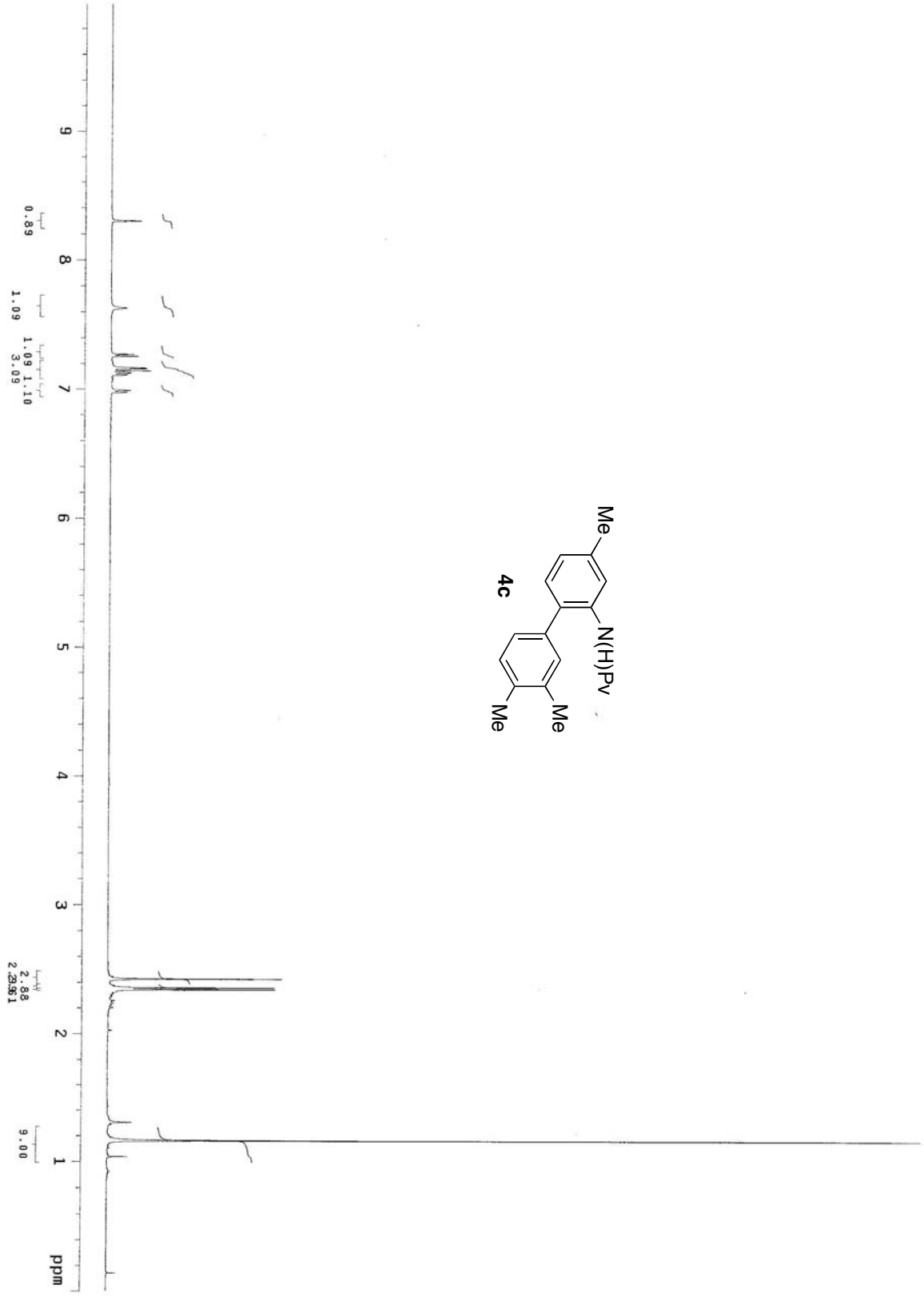
0.94





4b'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N(H)Pv
Me
Me
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1.09
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3.09
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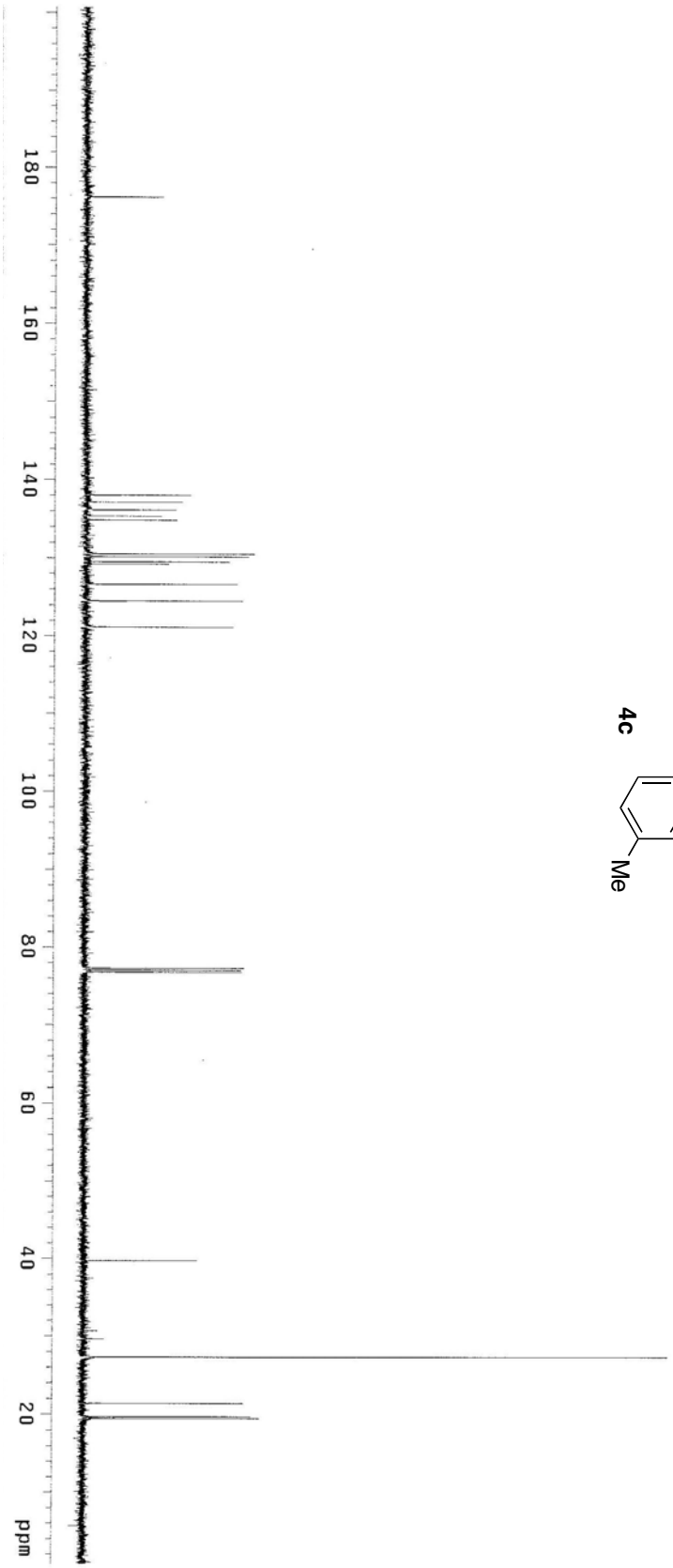
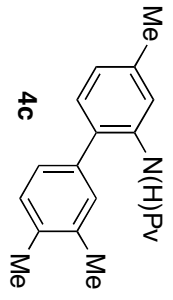
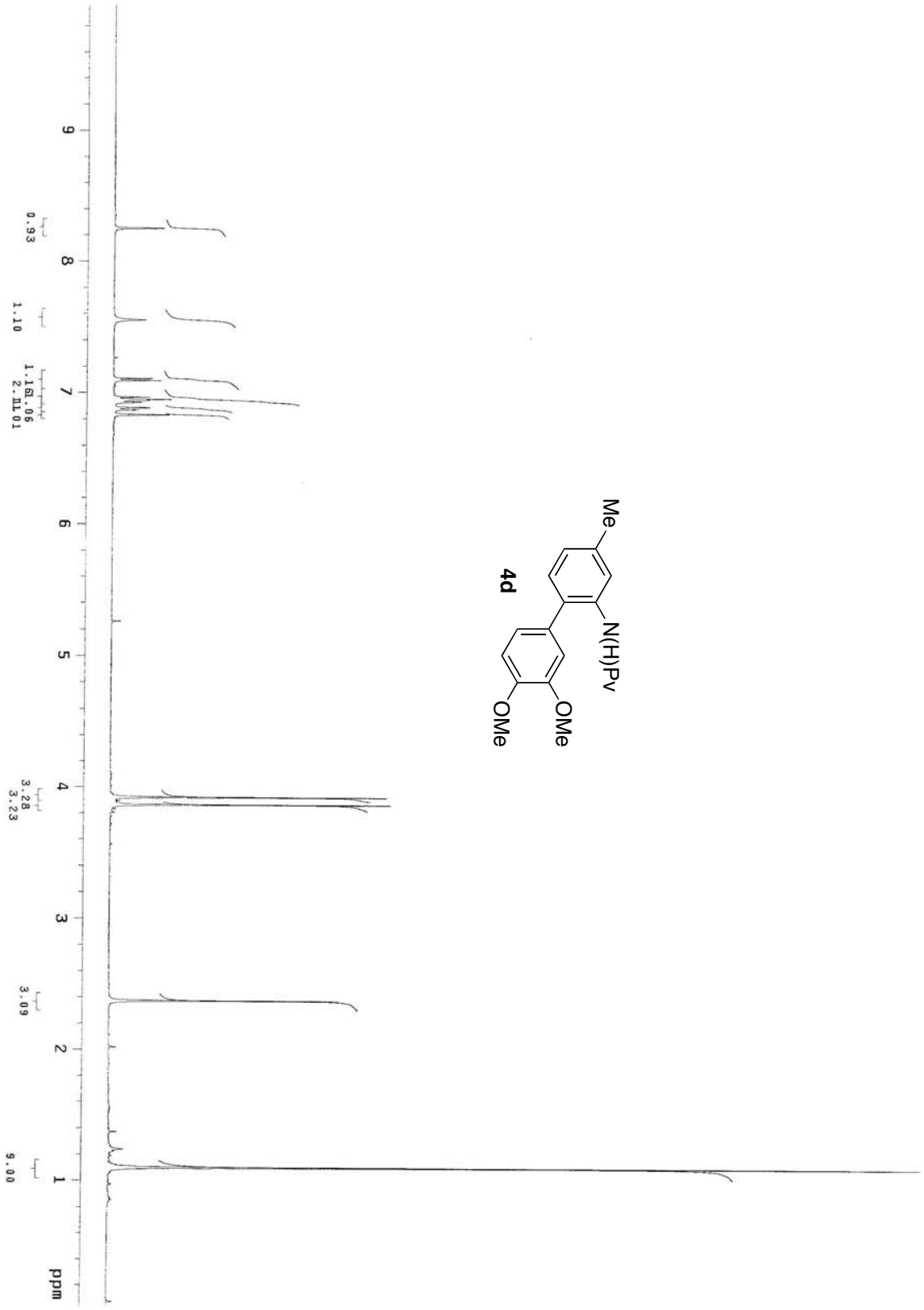
2.29
2.31
9.00





4c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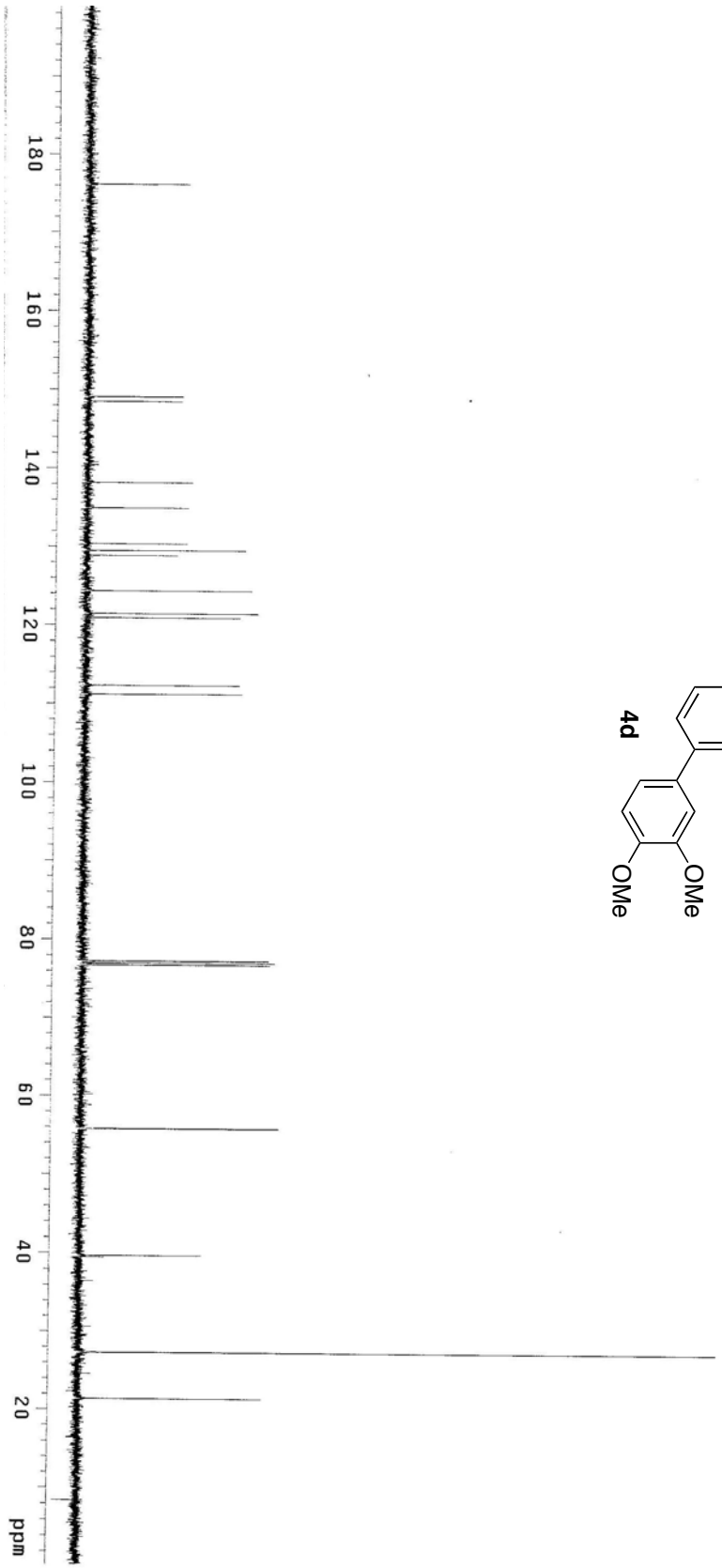
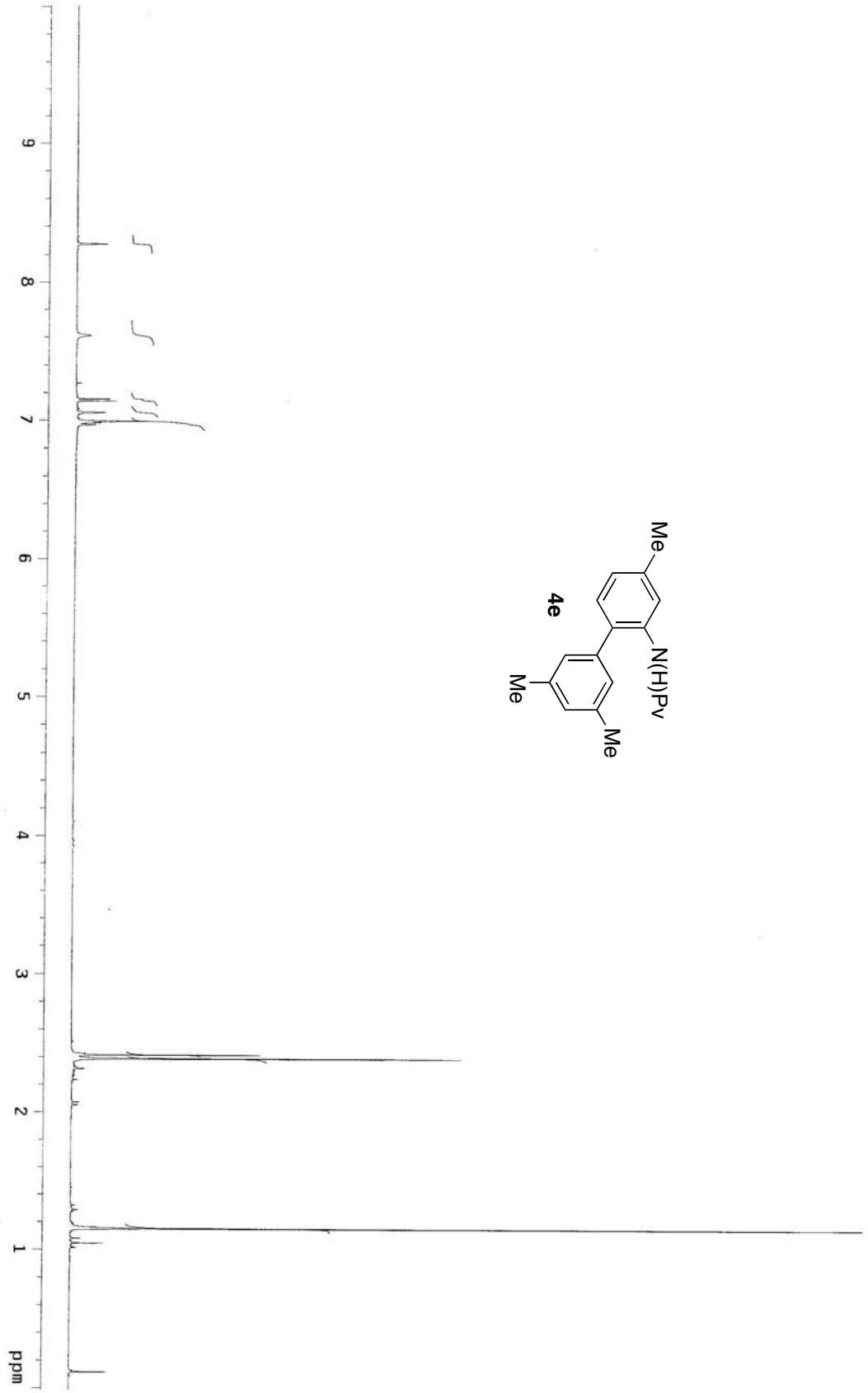
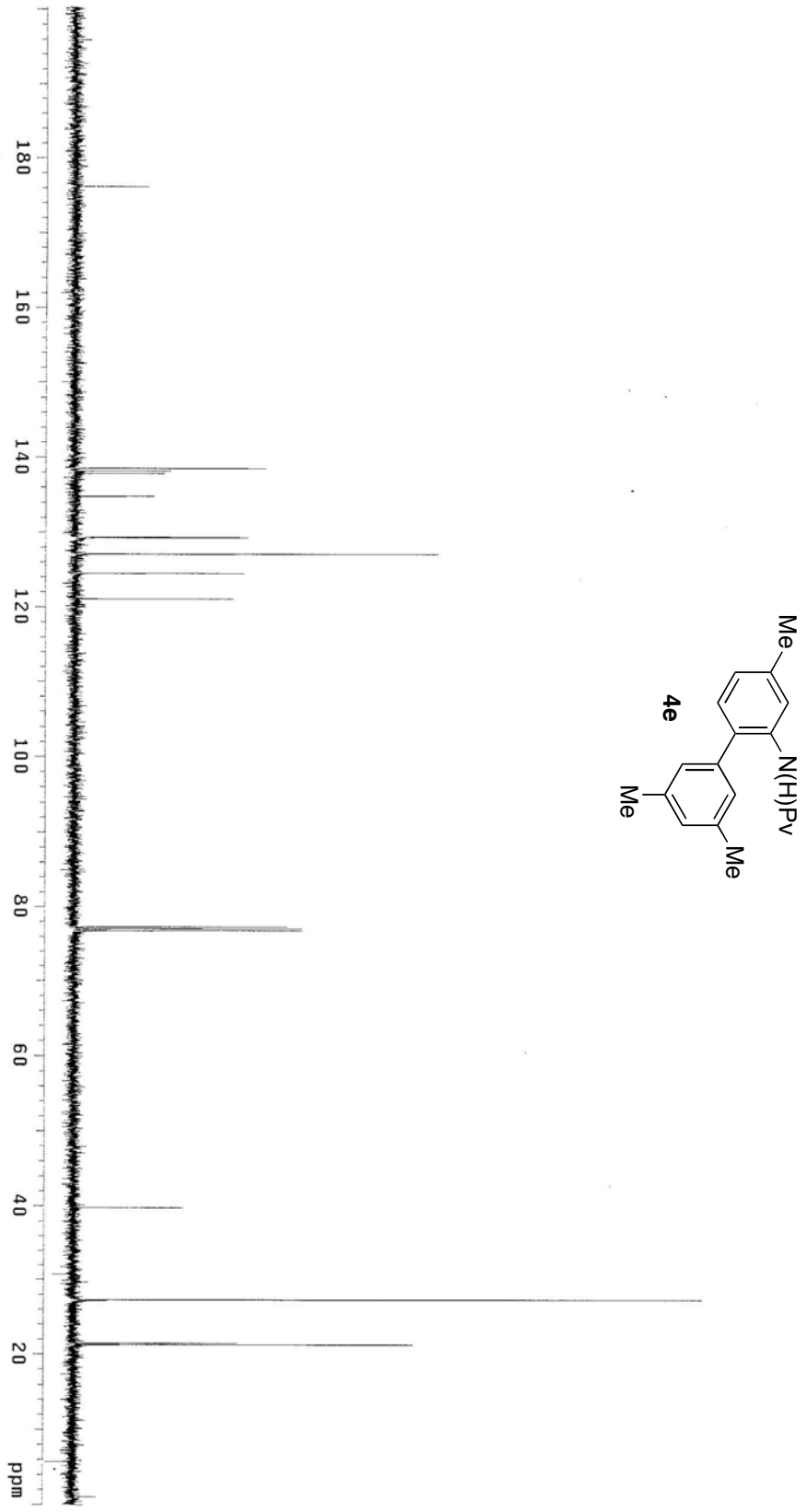
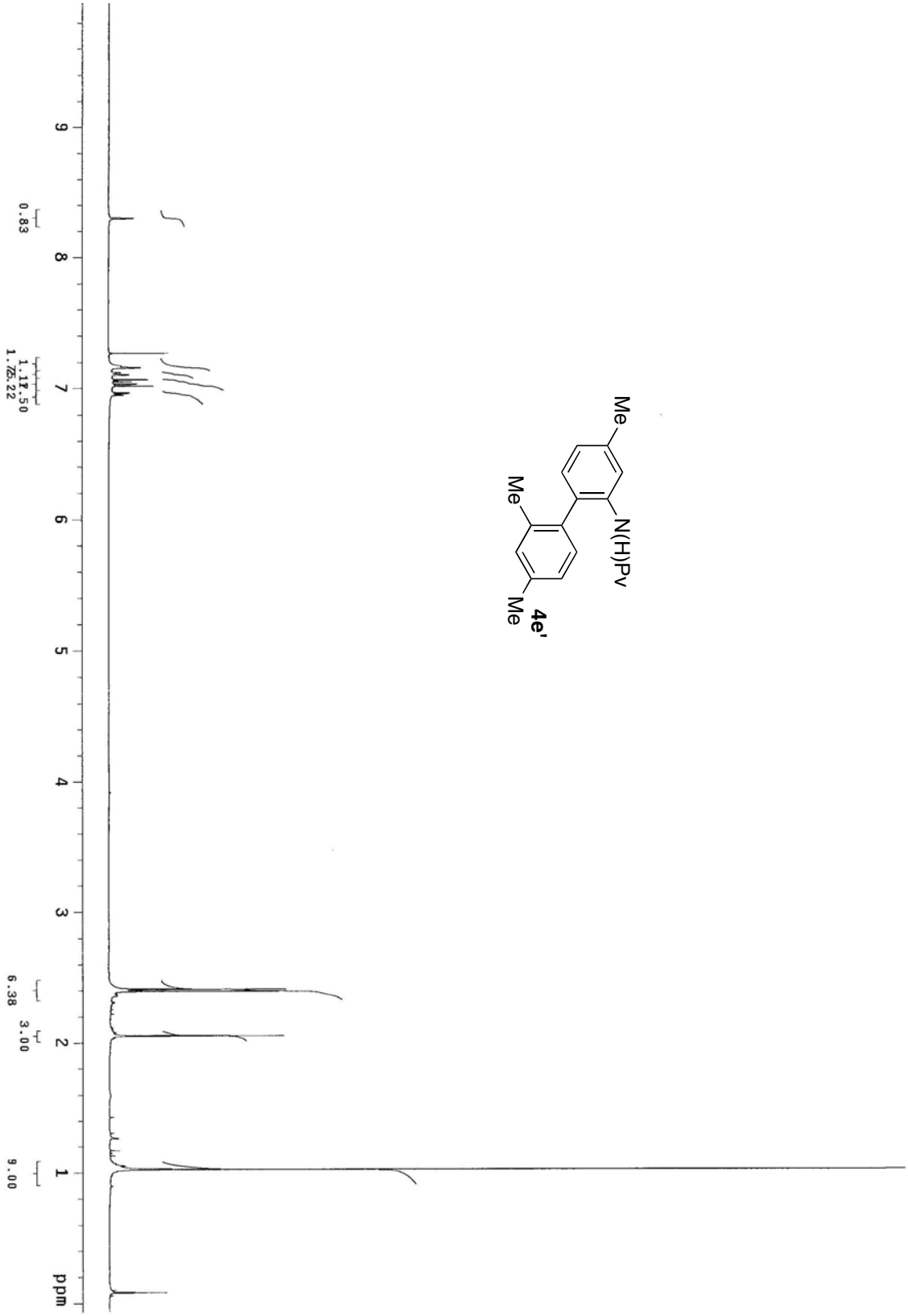
9.00
ppm

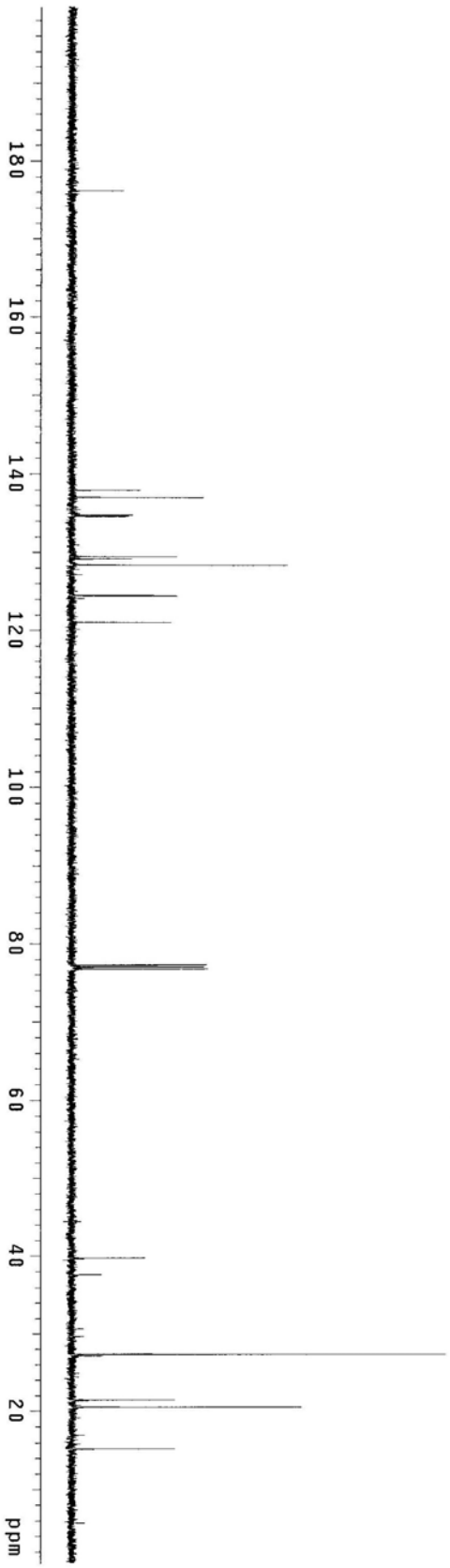

Me
N(H)Piv
OMe
OMe
4d
180
160
140
120
100
80
60
40
20
ppm

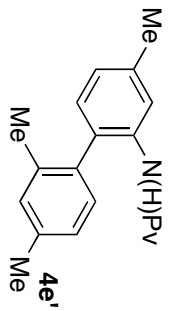

Me
N(H)Pv
Me
Me
4e
9
8
7
6
5
4
3
2
1
ppm



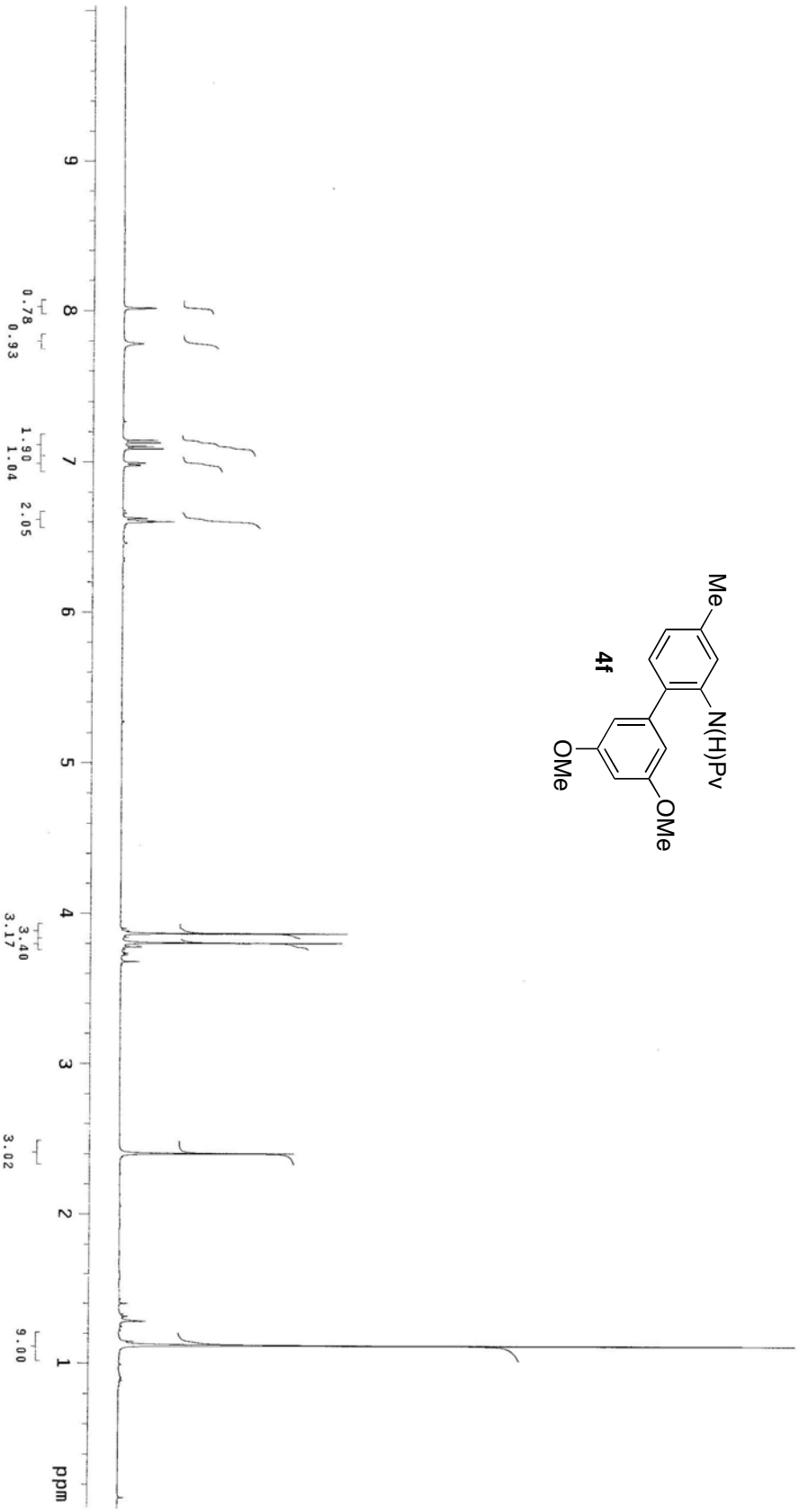
4e

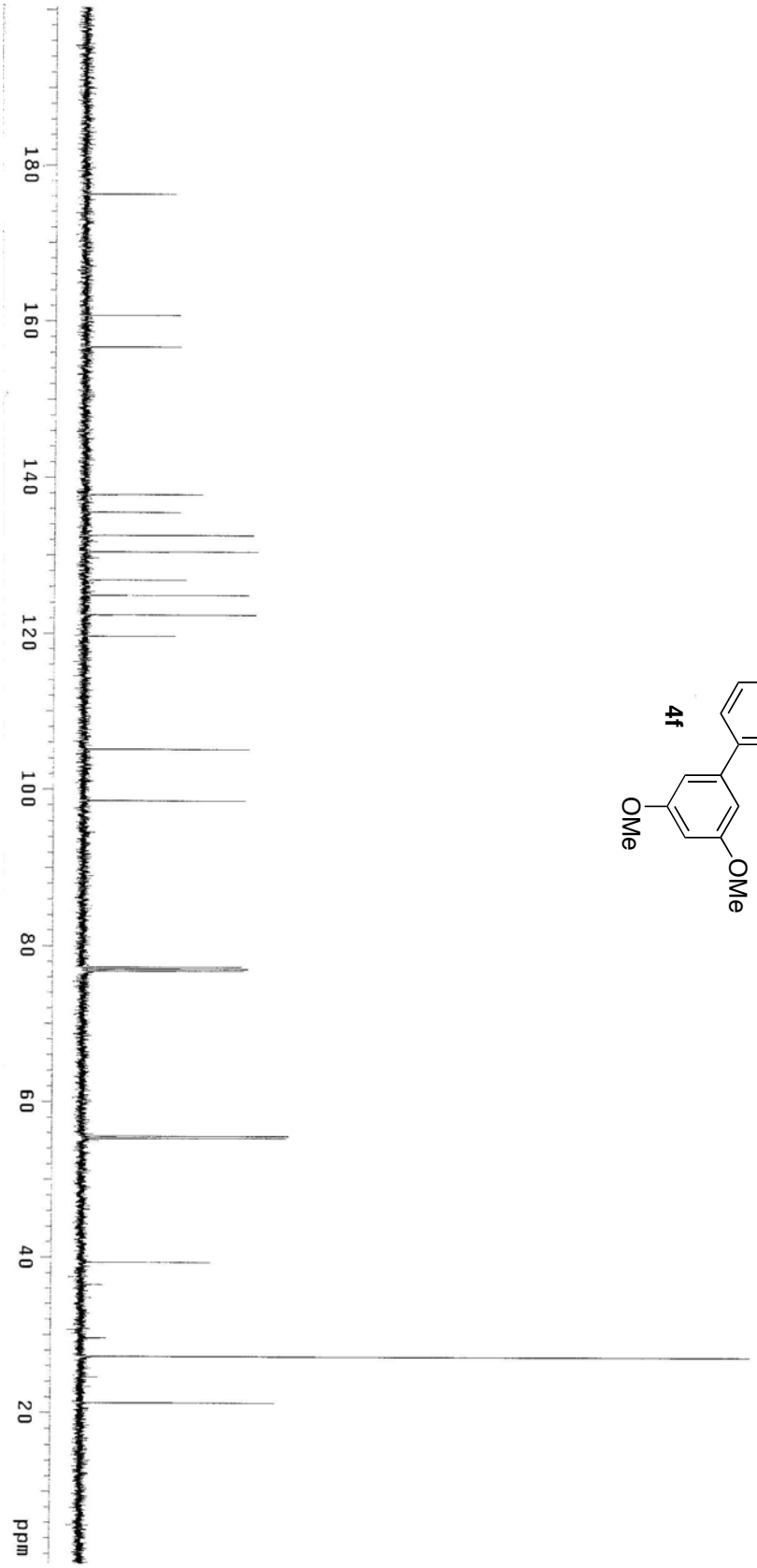

Me
N(H)Pv
Me
Me
4e'
9.00
3.00
6.38
1.17.50
1.75.22
0.83
ppm

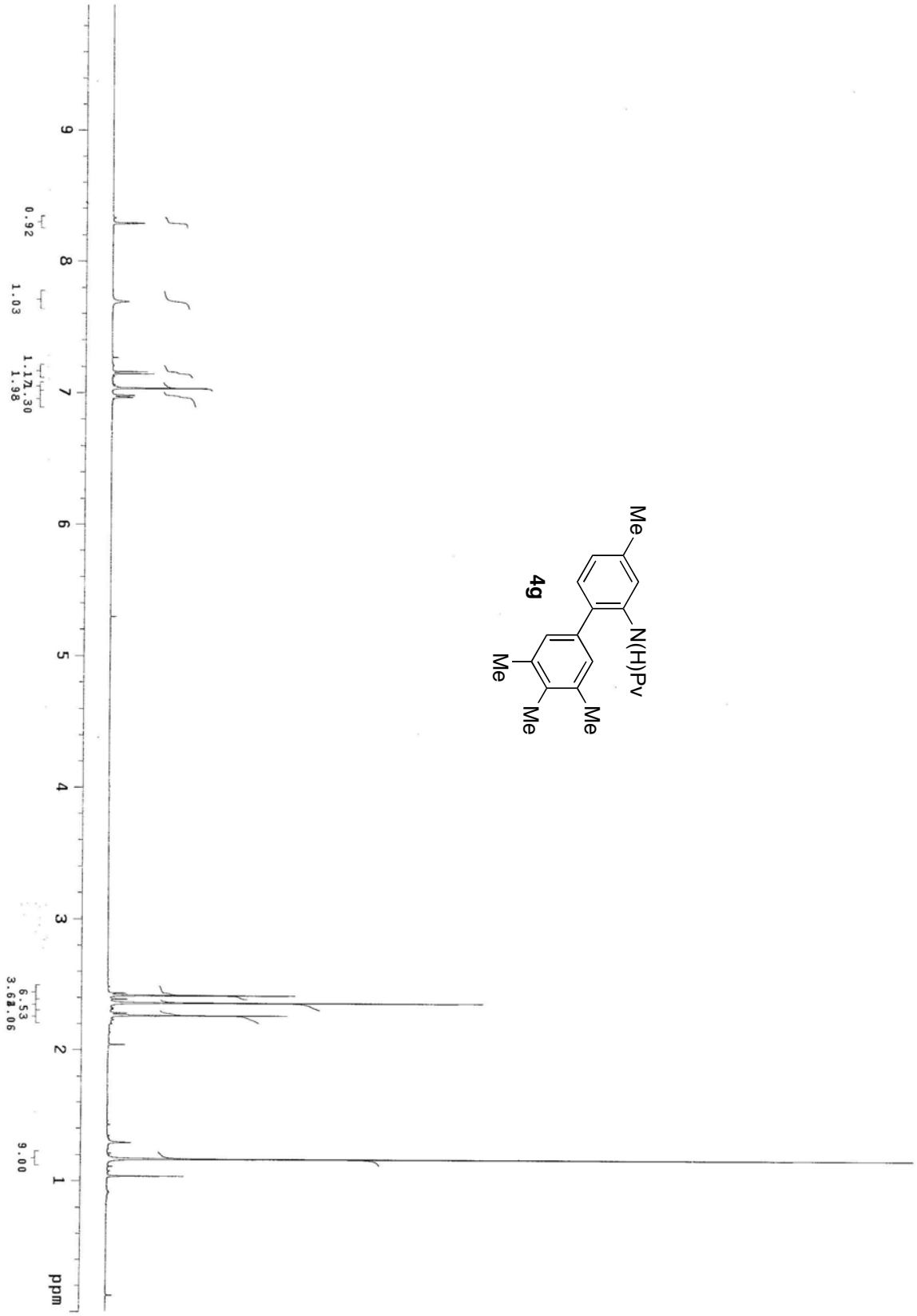


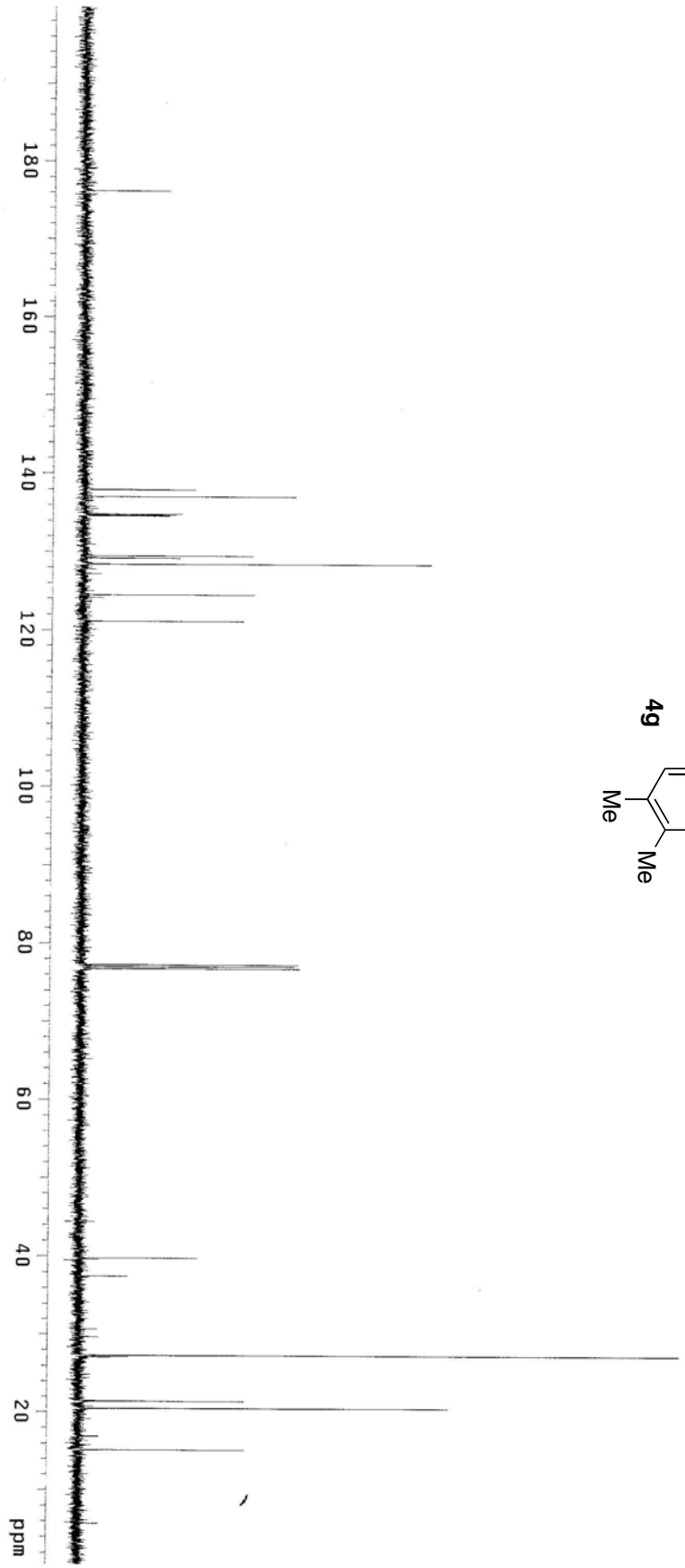


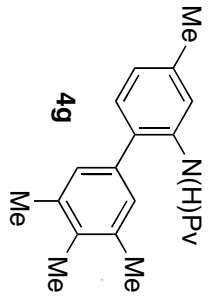
4e'


Me
N(H)Pv
OMe
OMe
4f
9
8
7
6
5
4
3
2
1
ppm
0.78
0.93
1.90
1.04
2.05
3.40
3.17
3.02
9.00

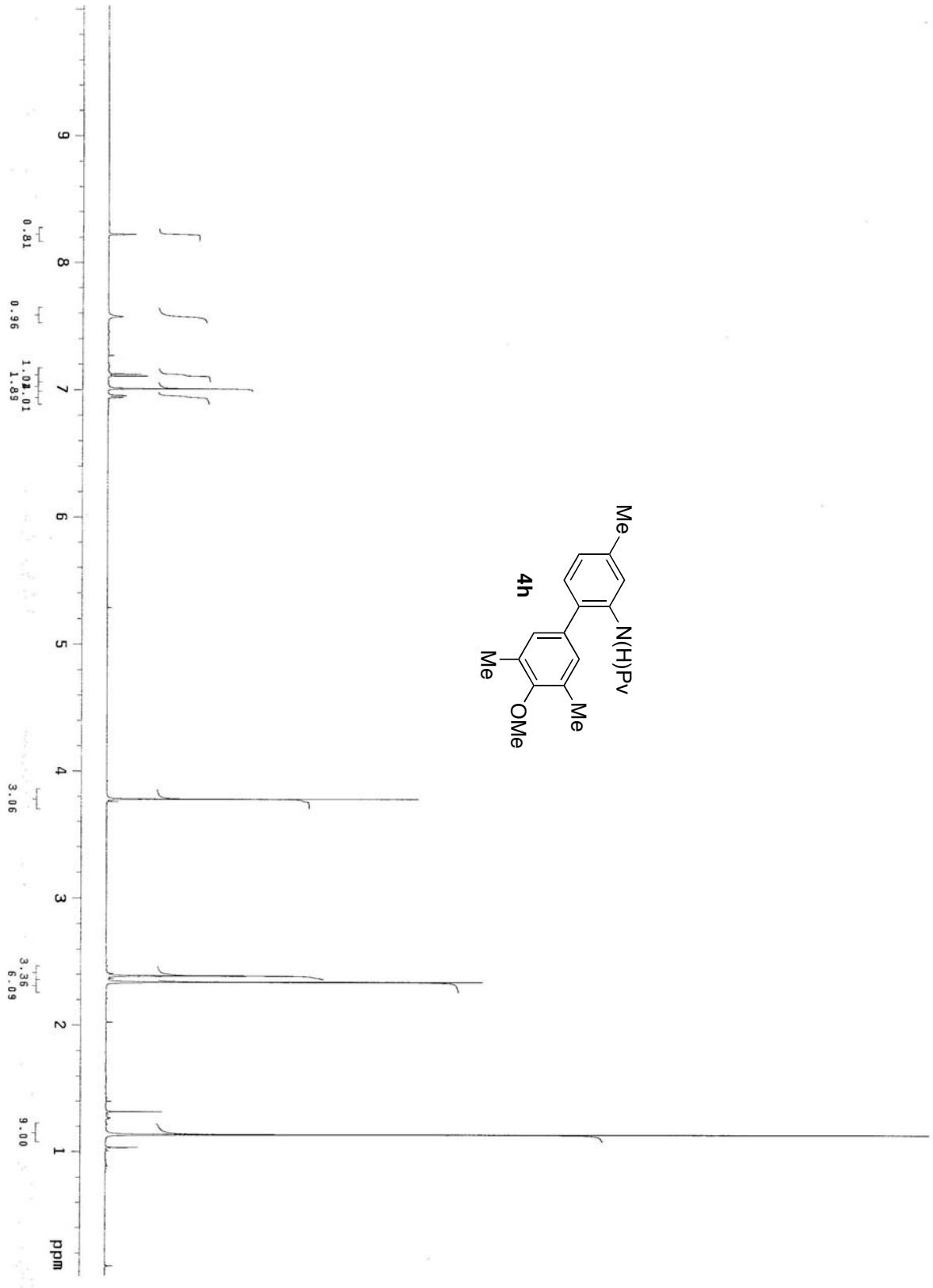

Me
N(H)Pv
OMe
OMe
4f
180
160
140
120
100
80
60
40
20
ppm

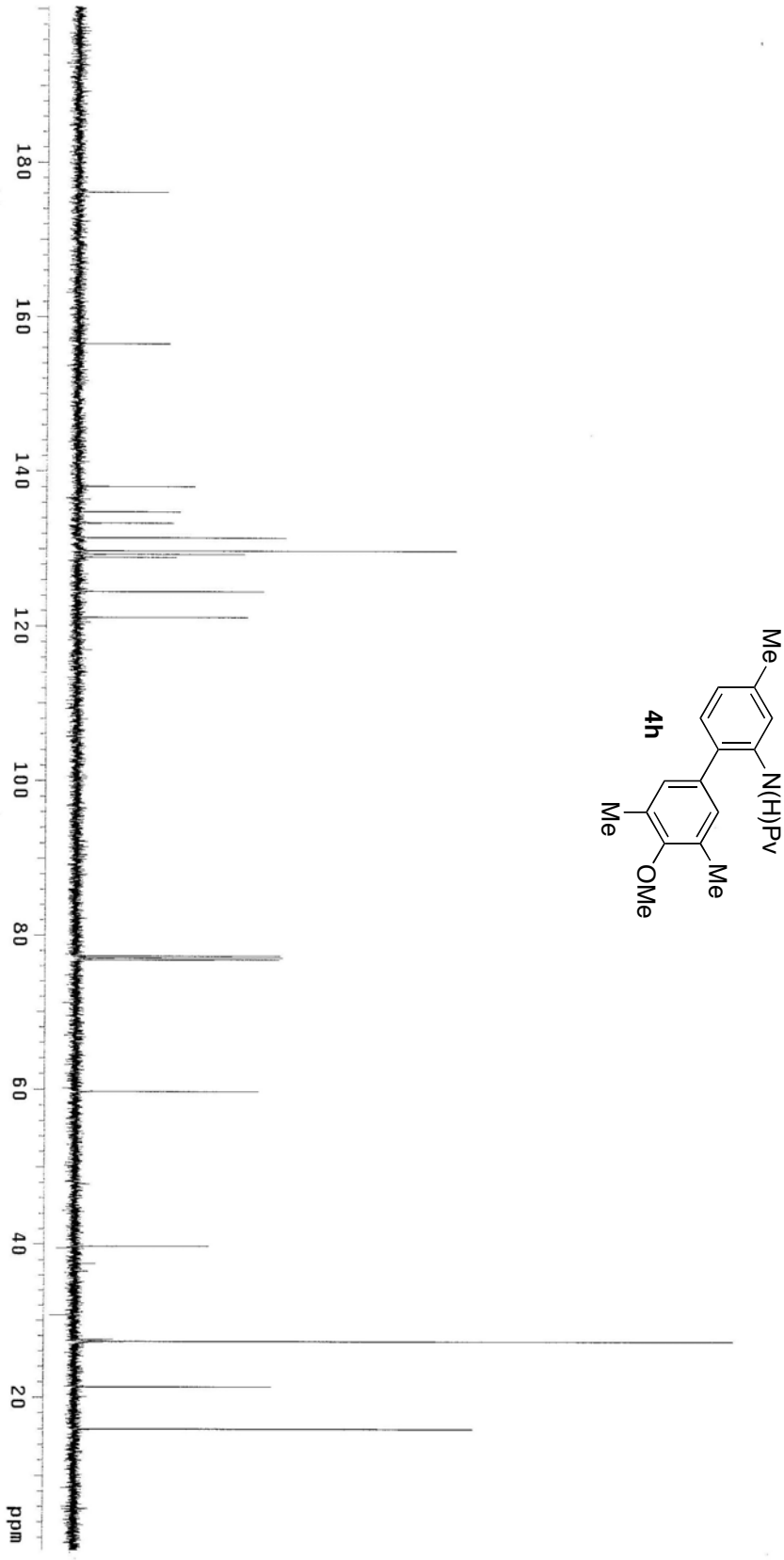

Me
N(H)Pv
4g
Me
Me
Me
9.00
6.53
3.68
2.06
1.98
1.17
1.30
1.03
0.92
ppm

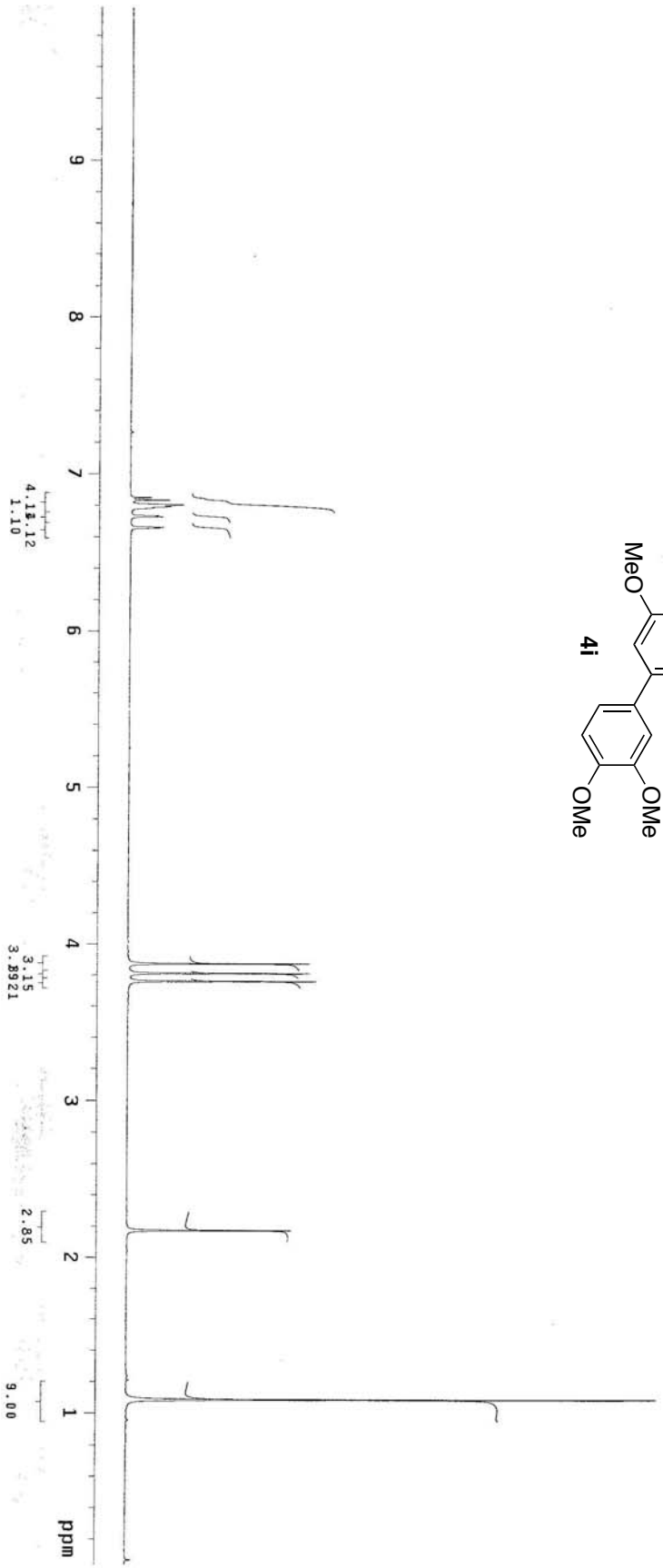


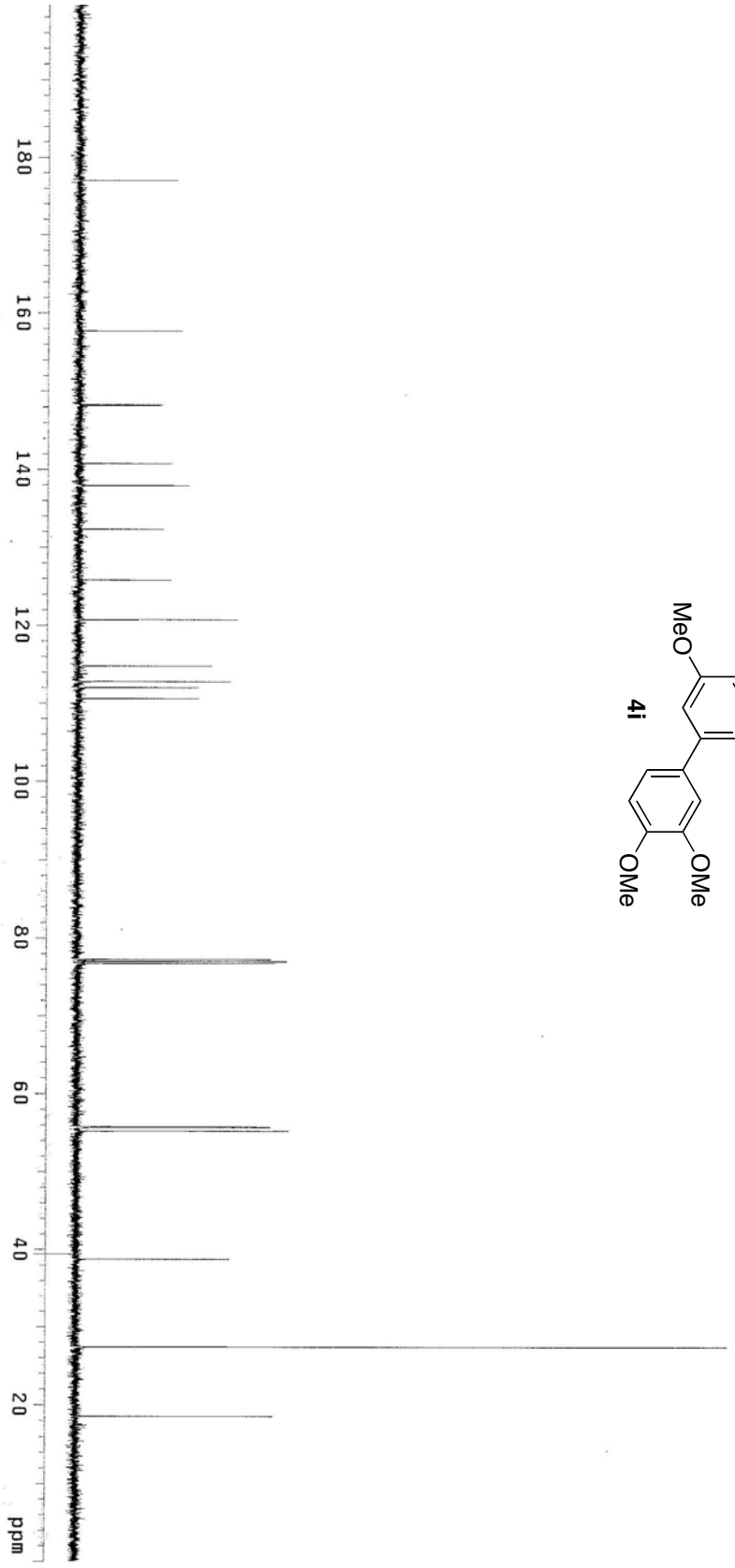


4g

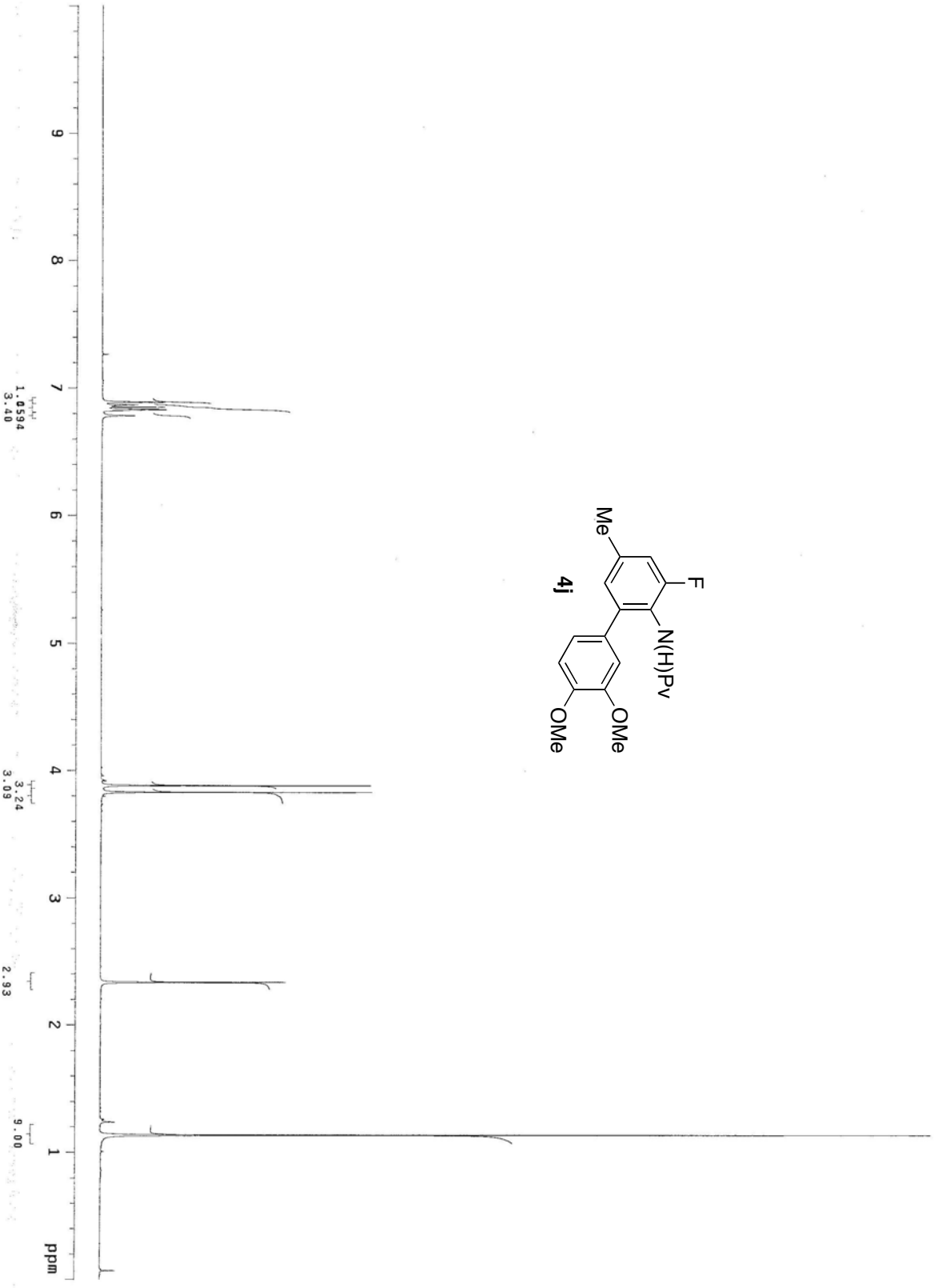

Me
N(H)Pv
4h
Me
Me
OMe
0.81
0.96
1.02
1.01
1.89
3.06
3.35
6.09
9.00
ppm


Me
N(H)Piv
4h
Me
Me
OMe
180
160
140
120
100
80
60
40
20
ppm


MeO
Me
N(H)Pv
OMe
OMe
4i
9
8
7
6
5
4
3
2
1
ppm
4.12
1.10
3.15
3.00
2.85
9.00



4i


Me
F
N(H)Pv
OMe
OMe
4j
9
8
7
6
5
4
3
2
1
ppm
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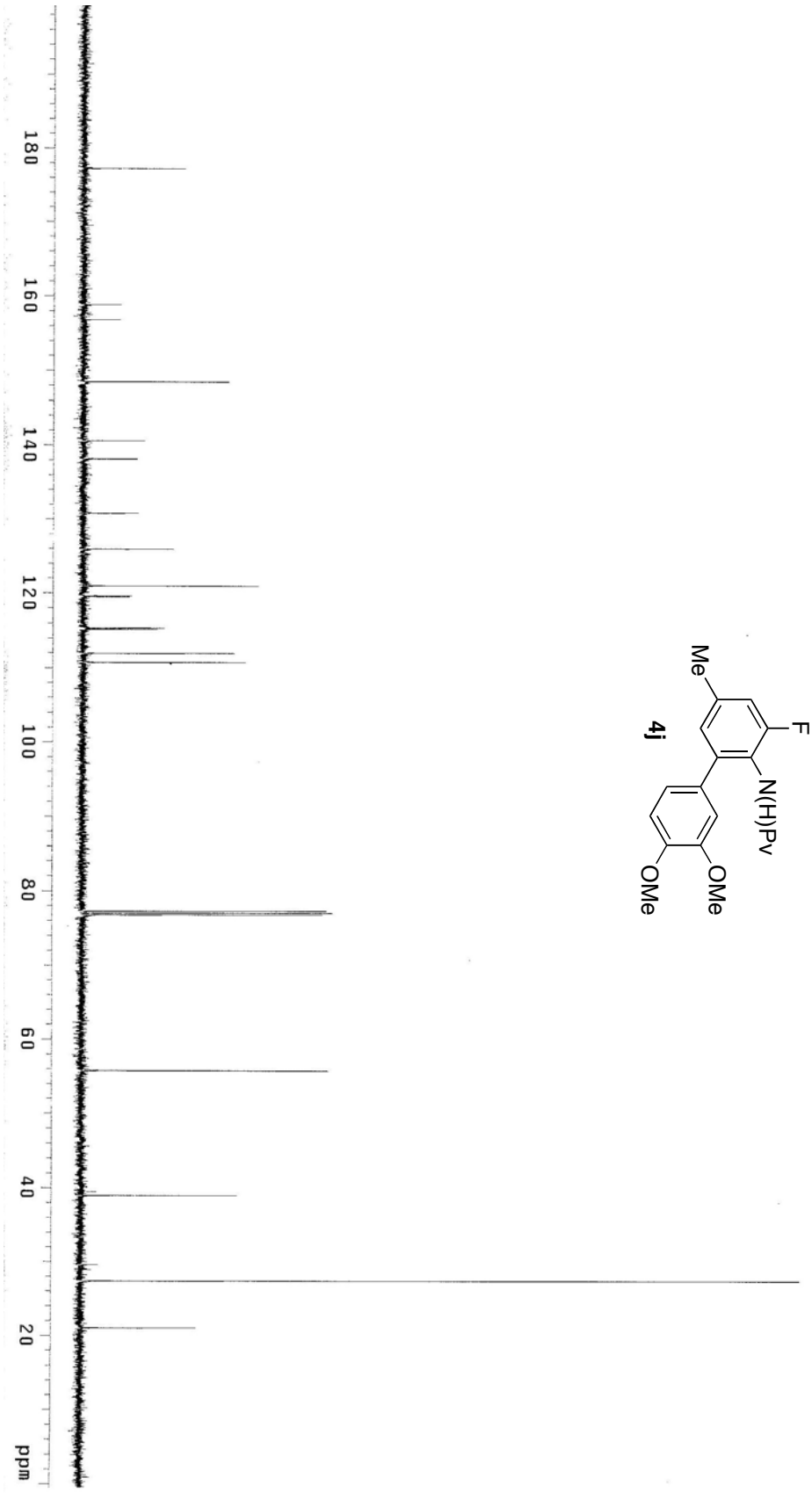
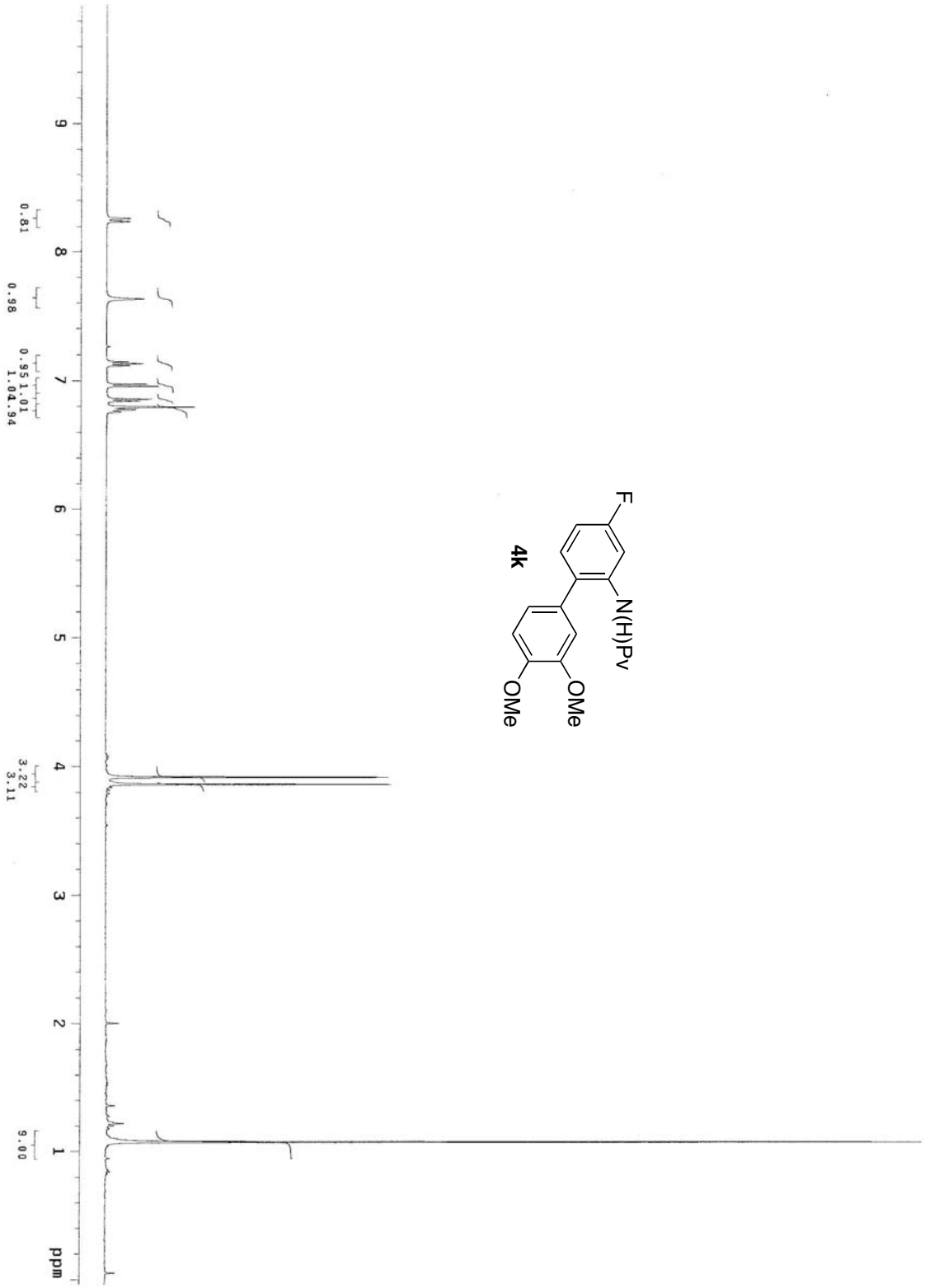
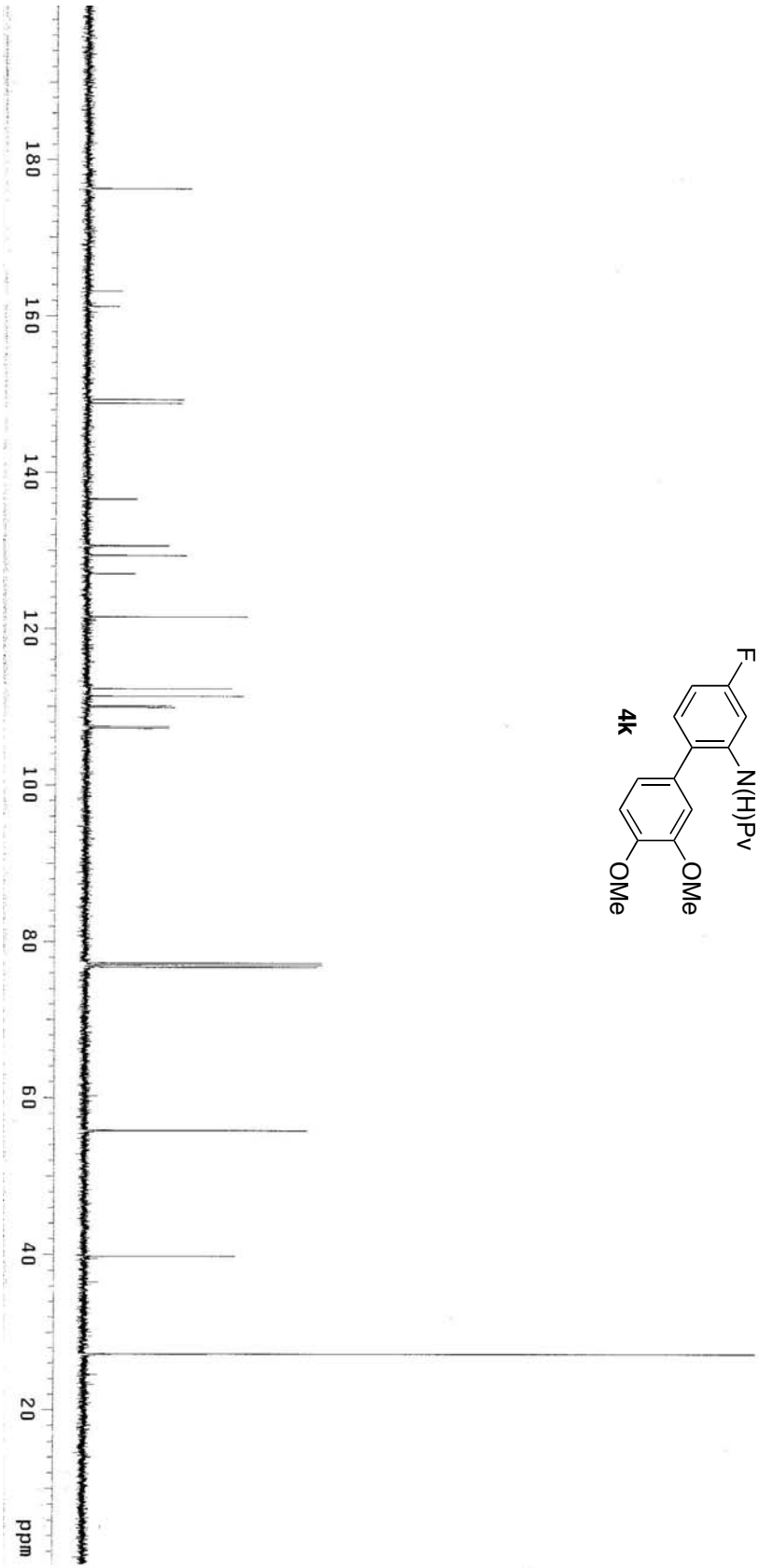
3.40
3.24
3.03
2.93
9.00


Me
F
N(H)Pv
OMe
OMe
4j
180
160
140
120
100
80
60
40
20
ppm


F
N(H)Pv
OMe
OMe
4k
ppm


F
N(H)Pv
OMe
OMe
4k
180
160
140
120
100
80
60
40
20
ppm

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