Supplementary Material (ESI) for Chemical Communications

A Diastereo- and Enantioselective Synthesis of α-Substituted *anti*-α,β-Diaminophosphonic Acid Derivatives

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Experimental Section

Flame-dried (under vacuum) glassware was used for all reactions. All reagents and solvents were commercial grade and purified prior to use when necessary. Diethyl ether (Et_2O), tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), and toluene were dried by passage through a column of activated alumina as described by Grubbs.[1] Imines[2], $Pd(dba)_2$[3], 4-phenylthiobenzaldehyde,[4] diethyl-1-nitroethyl phosphonate,[5] and diisopropyl-1-nitroethyl phosphonate[6] were prepared according to their respective literature procedures. α-Hydroxyiminophosphonates were prepared by modifications of known literature protocols.[6] Buchwald's protocol was used for palladium-mediated aryl amination.[7]

Thin layer chromatography (TLC) was performed using glass-backed silica gel (250 μm) plates and flash chromatography utilized 230–400 mesh silica gel from Scientific Adsorbents. UV light, and/or the use of potassium permanganate, phosphomolybdic acid, and ninhydrin solutions were used to visualize products.

IR spectra were recorded on a Thermo Nicolet IR100 spectrophotometer and are reported in wavenumbers (cm^{-1}). Liquids and oils were analyzed as neat films on a NaCl plate (transmission), whereas solids were applied to a diamond plate (ATR). Nuclear magnetic resonance spectra (NMR) were acquired on either a Bruker DRX-400 (400 MHz) or DRX-500 (500 MHz) instrument. Chemical shifts are measured relative to residual solvent peaks as an internal standard set to δ 7.27 and δ 77.0 ($CDCl_3$). Mass spectra were recorded on a Kratos MS-80 spectrometer by use of chemical ionization (CI) or electrospray ionization (EI). The absolute and relative configuration of *anti*-*ent*-**5h** and *anti*-**5i** were determined by X-ray diffraction. The absolute and relative configurations of the remaining products were assigned by analogy.

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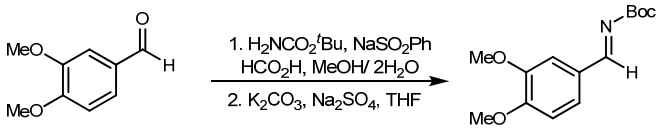
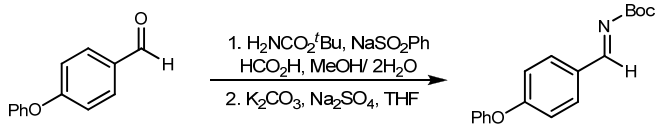
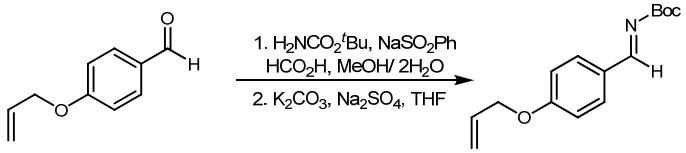


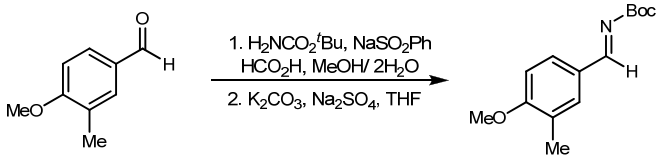
***tert*-Butyl 3,4-dimethoxybenzylidenecarbamate (2b)**. Following the Greene protocol, **2b** was obtained as a colorless oil. IR (film) 2976, 2935, 1708, 1621, 1597, 1580, 1511, 1245, 1136 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.85 (s, 1H), 7.58 (s, 1H), 7.38 (d, *J* = 8.2 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 1H), 3.95 (s, 3H), 3.94 (s, 3H), 1.59 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 170.1, 162.8, 154.0, 149.5, 127.6, 127.2, 110.4, 109.5, 82.0, 56.1, 27.9; HRMS (CI): Exact mass calcd for $C_{14}H_{19}NO_4$ $[M]^+$ = 265.1314. Found 265.1315.



***tert*-Butyl 4-phenoxybenzylidenecarbamate (2d)**. Following the Greene protocol, **2d** was obtained as a colorless oil. IR (film) 2976, 1684, 1601, 1582, 1572, 1505, 1488, 1238, 1146 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.88 (s, 1H), 7.90 (d, *J* = 8.5 Hz, 2H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 2H), 7.02 (d, *J* = 8.5 Hz, 2H), 1.59 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 169.2, 162.6, 162.5, 155.2, 132.3, 130.0, 128.5, 124.7, 120.2, 117.6, 82.0, 27.9; HRMS (CI): Exact mass calcd for $C_{18}H_{20}NO_3$ $[M+H]^+$ 298.1438. Found 298.1443.

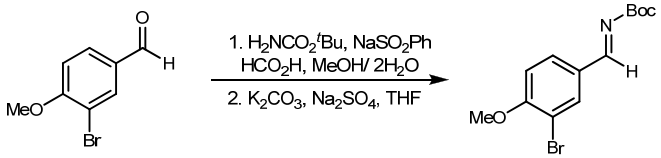


***tert*-Butyl 4-(allyloxy)benzylidenecarbamate (2e)**. Following the Greene protocol, **2e** was obtained as a white solid. IR (film) 2977, 1694, 1591, 1573, 1514, 1367, 1260, 1222, 1144 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.88 (s, 1H), 7.88 (d, *J* = 8.5 Hz, 2H), 6.97 (d, *J* = 8.5 Hz, 2H), 6.05 (ddt, *J* = 17.5, 10.0, 5.0 Hz, 1H), 5.43 (d, *J* = 17.5 Hz, 1H), 5.32 (d, *J* = 10.0 Hz, 1H), 4.61 (d, *J* = 5.0 Hz, 2H), 1.58 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 169.7, 163.1, 162.8, 132.4, 132.3, 126.9, 118.2, 115.0, 81.8, 68.9, 27.9; HRMS (CI): Exact mass calcd for $C_{15}H_{20}NO_3$ $[M+H]^+$ 262.1438. Found 262.1436.

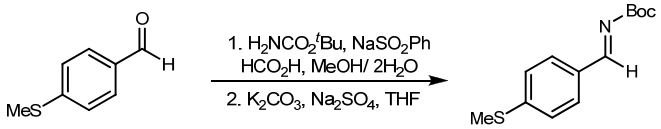


***tert*-Butyl 4-methoxy-3-methylbenzylidenecarbamate (2f)**. Following the Greene protocol, **2f** was obtained as a white solid. IR (film) 2978, 1693, 1601, 1572, 1506, 1247, 1223, 1152 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ

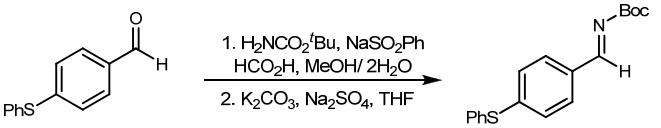
8.88 (s, 1H), 7.81 (s, 1H), 7.72 (dd, *J* = 8.5, 1.5 Hz, 1H), 6.88 (d, *J* = 8.5 Hz, 1H), 3.90 (s, 3H), 2.23 (s, 3H), 1.59 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 170.3, 162.9, 162.5, 131.8, 131.4, 127.6, 126.3, 109.6, 81.7, 55.5, 27.9, 16.0; HRMS (CI): Exact mass calcd for $C_{14}H_{20}NO_3$ $[M+H]^+$ 250.1438. Found 250.1433.



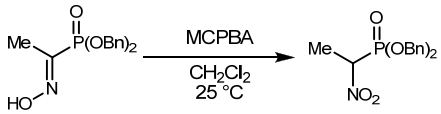
***tert*-Butyl 3-bromo-4-methoxybenzylidenecarbamate (2g)**. Following the Greene protocol, **2g** was obtained as a pale yellow solid. IR (film) 2976, 1692, 1591, 1503, 1250, 1207, 1157, 1140 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.21 (s, 1H), 7.82 (dd, *J* = 8.5, 1.5 Hz, 1H), 6.96 (d, *J* = 8.5 Hz, 1H), 3.97 (s, 3H), 1.58 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 168.2, 162.3, 160.0, 134.6, 131.8, 128.0, 112.5, 111.4, 82.2, 56.5, 27.8; HRMS (CI): Exact mass calcd for $C_{13}H_{17}BrNO_3$ $[M+H]^+$ 314.0386. Found 314.0375.



***tert*-Butyl 4-(methylthio)benzylidenecarbamate (2h)**. Following the Greene protocol, **2h** was obtained as a pale yellow solid. IR (film) 2978, 2924, 1708, 1620, 1591 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 2.52 (s, 3H), 1.59 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 169.5, 162.7. 146.7, 130.5, 130.3, 125.2, 82.1, 27.9, 14.7; HRMS (CI): Exact mass calcd for $C_{13}H_{18}NO_2S$ $[M+H]^+$ 252.1053. Found 252.1047.

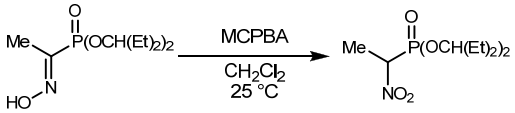


***tert*-Butyl 4-(phenylthio)benzylidenecarbamate (2i)**. Following the Greene protocol, **2i** was obtained as a pale yellow solid. IR (film) 2985, 1702, 1639, 1592, 1268, 1252, 1220, 1151, 1078 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 (s, 1H), 7.78 (d, *J* = 8.5 Hz, 2H), 7.53-7.51 (m, 2H), 7.43-7.41 (m, 3H), 7.21 (d, *J* = 8.5 Hz, 2H), 1.59 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 169.1, 162.6, 145.7, 133.9, 131.8, 131.4, 130.6, 129.7, 128.9, 127.5, 82.1, 27.8; HRMS (CI): Exact mass calcd for $C_{18}H_{19}NO_2S$ $[M]^+$ 313.1136. Found 313.1132.

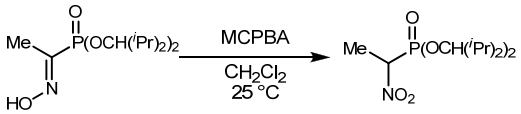


Dibenzyl-1-nitroethyl phosphonate (3b). To a stirred solution of dibenzyl-1-hydroxyiminoethylphosphonate (1.71 g, 4.0 mmol) in a minimal amount of CH_2Cl_2 was added 77% MCPBA (1.44 g, 6.4 mmol) in one portion

at 25 °C, and the total volume of CH_2Cl_2 was increased until a clear, homogeneous solution was obtained. The reaction mixture was stirred at 25 °C for 48 h. The solvent was removed under reduced pressure and the residue was purified by column chromatography (SiO_2, 20% ethyl acetate in hexanes) to give the title compound as a clear, colorless oil (1.4 g, 78%). R_f = 0.3 (20% EtOAc/hexanes); IR (film) 3065, 3034, 2959, 2895, 1555, 1270, 997 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38-7.29 (m, 10H), 5.13-5.03 (m, 4H), 4.95 (dq, J_{PH} = 15.2 Hz, J_{HH} = 7.2 Hz, 1H), 1.79 (dd, J_{PH} = 16.5 Hz, J_{HH} = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 135.2 (d, J_{PC} = 4.8 Hz), 135.1 (d, J_{PC} = 4.8 Hz), 128.9, 128.7, 128.2, 128.1, 79.6 (d, J_{PC} = 146.0 Hz), 69.5 (d, J_{PC} = 5.8 Hz), 69.4 (d, J_{PC} = 5.8 Hz), 14.5 (d, J_{PC} = 3.9 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) ppm 15.7; HRMS (CI): Exact mass calcd for $C_{16}H_{19}NO_5P$ $[M+H]^+$ 336.0995. Found 336.1000. *Anal.* Calcd for $C_{16}H_{18}NO_5P$: C, 57.31; H, 5.41; N, 4.18. Found: C, 57.32; H, 5.44; N, 4.01.



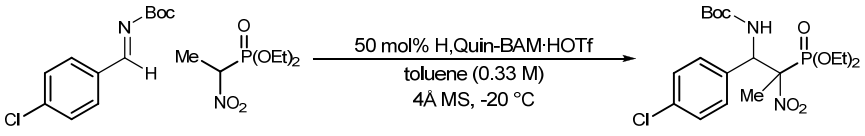
Di(3-pentyl)-1-nitroethylphosphonate (3d). Di(3-pentyl)-1-hydroxyiminoethyl phosphonate (600 mg, 2.2 mmol) was dissolved in a minimal amount of CH_2Cl_2, and 77% MCPBA (578 mg, 2.6 mmol) was added. The reaction mixture was diluted with CH_2Cl_2 (~ 3 mL) until the solution was homogeneous, and was stirred at 25 °C for 48 h. Crude ^1H and ^{31}P NMR spectroscopy of an aliquot indicated that the reaction was complete. The reaction mixture was washed with satd aq $NaHCO_3$, water, and brine; the organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to leave an oily residue. Column chromatography (SiO_2, 15% ethyl acetate in hexanes) provided the title compound (521 mg, 82%) as a clear, colorless oil. R_f = 0.34 (20% EtOAc/hexanes); IR (neat) 2971, 2942, 2882, 1556, 1460, 1384, 1352, 1266, 1040 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.98 (dq, J_{PH}= 15.5 Hz, J_{HH} = 7.2 Hz, 1H), 4.47 (m, 2H), 1.83 (dd, J_{PH} = 16.1 Hz, J_{HH} = 7.2 Hz); 1.73-1.68 (m, 8H), 1.0-0.91 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 82.4 (d, J_{PC} = 7.7 Hz), 82.3 (d, J_{PC} = 7.7 Hz), 80.11 (d, J_{PC} = 147.0 Hz), 27.2 (d, J_{PC} = 3.8 Hz), 27.1 (d, J_{PC} = 3.8 Hz), 27.0 (d, J_{PC} = 3.8 Hz), 26.7 (d, J_{PC} = 3.8 Hz), 14.7 (d, J_{PC} = 3.8 Hz), 8.9 (2C), 8.9, 8.8; ^{31}P NMR (162 MHz, $CDCl_3$) ppm 12.6; HRMS (CI): Exact mass calcd for $C_{12}H_{26}NO_5P$ $[M+H]^+$ 296.1627. Found 296.1617. *Anal.* Calcd for $C_{12}H_{27}NO_5P$: C, 48.81; H, 8.87; N, 4.74. Found C, 48.61; H, 8.85; N, 4.33.



Di(diisopropylmethyl)-1-nitroethylphosphonate (3e). Di(diisopropylmethyl)-1-hydroxyiminoethyl phosphonate (2.27 g, 6.76 mmol) was dissolved in a minimal amount of CH_2Cl_2, and 77% MCPBA (1.82 g, 8.11 mmol) was added. The reaction mixture was diluted with CH_2Cl_2 (~ 15 mL) until the solution was homogeneous, and was stirred at 25 °C for 48 h. Crude ^{1}H and ^{31}P NMR spectroscopy of an aliquot indicated that the reaction was complete. The reaction mixture was washed with satd aq $NaHCO_3$, water, and brine; the organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to leave an oily residue. Column chromatography (SiO_2, 15% ethyl acetate in hexanes) provided the title compound (2.08 g, 88%) as a clear, colorless oil. R_f = 0.35 (20% EtOAc/hexanes); IR (neat) 2965, 1555, 1264, 978 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.99 (dq, J_{PH} = 14.7, J_{HH} = 7.2 Hz, 1H), 4.16 (dt, J_{PH} = 8.4, J_{HH} = 4.6 Hz, 1H), 4.10 (dt, J_{PH} = 8.4, J_{HH} = 4.6 Hz, 1H), 2.06-1.92 (m, 4H), 1.82 (dd, J_{PH} = 16.0, J_{HH} = 7.2 Hz, 3H), 1.04 (d, J = 7.2 Hz, 3H), 1.02-0.95 (m, 15H), 0.93 (d, J = 7.2 Hz, 3H), 0.92 (d, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 90.5 (d, J_{PC} = 7.6 Hz), 90.0 (d, J_{PC} = 9.5 Hz), 80.0 (d, J_{PC} = 147.9 Hz), 31.4, 31.3, 30.9, 30.8, 20.3, 20.2, 20.0, 19.8, 19.0, 18.2, 18.0, 17.8, 15.3; ^{31}P NMR (202 MHz, $CDCl_3$) ppm 11.0; HRMS (CI): Exact mass calcd for $C_{16}H_{35}NO_5P$ $[M+H]^+$ 352.2247. Found 352.2247. *Anal*. Calcd for $C_{16}H_{34}NO_5P$: C, 54.68; H, 9.75; N, 3.99. Found: C, 54.75; H, 9.71; N, 4.07.

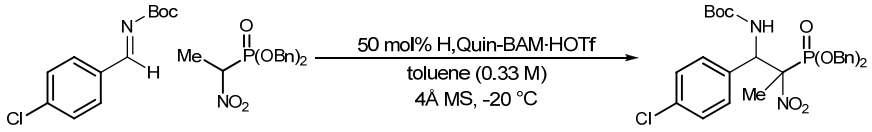
General Procedure for Preparation of 4a – 4d.

An oven-dried vial was charged with a stir bar, 4Å MS, imine (1.0 equiv), and H,Quin-BAM·HOTf (**1**, 0.5 equiv) successively; the vial was capped with a septum and placed under an Ar atmosphere. Toluene was added (0.3 M), followed by the nitrophosphonate (1.0 equiv). The resulting solution was stirred at -20 °C for the indicated time. The solution was then concentrated; the % conversion and diastereomeric ratio were determined by ^{1}H and ^{31}P NMR spectroscopic analysis of the crude reaction mixture.

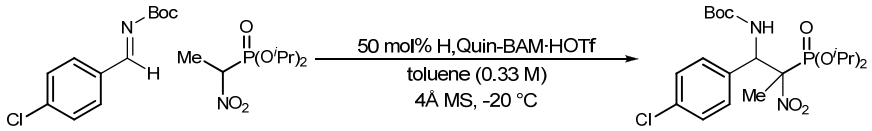


***tert*-Butyl 1-(4-chlorophenyl)-2-(diethoxyphosphoryl)-2-nitropropylcarbamate (4a)**. According to the general procedure and after flash column chromatography (25-50% ethyl acetate in hexanes), **4a** was isolated as

a white foam which was determined to be 65% ee by chiral HPLC analysis (Chiralcel AD, 2% ^{i}PrOH/hexanes, 1.0 mL/min, t_r = 12.2 (major), 14.0 (minor) min). Major Diastereomer: R_f = 0.46 (50% EtOAc/hexanes); IR (film) 3292, 2980, 2930, 1718, 1554, 1492, 1249, 1163 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 6.24 (br s, 1H), 5.56 (dd, J_{PH} = 17.2 Hz, J_{HH} = 8.8 Hz, 1H), 4.44-4.32 (m, 1H), 4.30-3.95 (m, 3H), 1.66 (d, J_{PH} = 12.8 Hz, 3H), 1.39-1.35 (m, 12H), 1.17 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 154.4, 134.6, 134.5, 129.4, 128.5, 92.2 (d, J_{PC} = 150.8 Hz), 80.5, 65.2 (d, J_{PC} = 7.4 Hz), 63.6 (d, J_{PC} = 7.9 Hz), 59.0, 28.2, 18.2, 16.4 (d, J_{PC} = 5.6 Hz), 15.9 (d, J_{PC} = 5.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) ppm 15.9; HRMS (CI): Exact mass calcd for $C_{18}H_{29}ClN_2O_7P$ $[M+H]^+$ 451.1395. Found 451.1397.

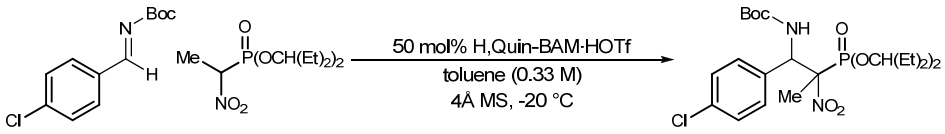


***tert*-Butyl 2-(bis(benzyloxy)phosphoryl)-1-(4-chlorophenyl)-2-nitropropylcarbamate (4b)**. According to the general procedure and after flash column chromatography (25% ethyl acetate in hexanes), **4b** was isolated as a white foam which was determined to be 70% ee by chiral HPLC analysis (Chiralcel AD, 10% EtOH/hexanes, 1.0 mL/min, t_r = 14.4 (minor), 74.9 (major) min). R_f = 0.35 (25% EtOAc/hexanes); IR (film) 3304, 2977, 1717, 1553, 1493, 1366, 1249, 1163 cm^{-1}; ^{1}H NMR (both diastereomers, 500 MHz, $CDCl_3$) δ 7.41-7.16 (m, 26H), 7.0 (m, 2H), 6.44 (br s, 2H), 5.58 (dd, J_{PH} = 21.0 Hz, J_{HH} = 9.0 Hz, 1H), 5.46 (dd, J_{PH} = 8.5 Hz, J_{HH} = 8.5 Hz, 1H), 5.27 (dd, J_{HH} = 11.5 Hz, J_{PH} = 8.0 Hz, 1H), 5.10-4.97 (m, 5H), 4.75 (m, 2H), 1.76 (d, J_{PH} = 14.0 Hz, 3H), 1.74 (d, J_{PH} = 14.0 Hz, 3H), 1.41 (s, 18H); ^{13}C NMR (both diastereomers, 100 MHz, $CDCl_3$) ppm 154.4, 154.3, 135.5-134.2 (m, 6C), 129.6-127.8 (m, 30C), 92.7 (d, J_{PC} = 151.2 Hz), 92.5 (d, J_{PC} = 146.3 Hz, 1C), 80.5 (2C), 70.6, 69.9, 69.6, 68.4, 59.4, 57.9, 28.2 (6C), 19.7, 19.0; ^{31}P NMR (202 MHz, $CDCl_3$, both diastereomers) ppm 16.9, 16.6; HRMS (CI): Exact mass calcd for $C_{28}H_{33}ClN_2O_7P$ $[M+H]^+$ 575.1708. Found 575.1700.



***tert*-Butyl 1-(4-chlorophenyl)-2-(diisopropoxyphosphoryl)-2-nitropropylcarbamate (4c)**. According to the general procedure and after flash column chromatography (35% ethyl acetate in hexanes), **4c** was isolated as a white foam which was determined to be 80% ee by chiral HPLC analysis (Chiralcel AD, 5% EtOH/hexanes, 1.0 mL/min, t_r = 16.3 min (major), 11.6 min (minor) min). Major Diastereomer: R_f = 0.75 (50% EtOAc/hexanes);

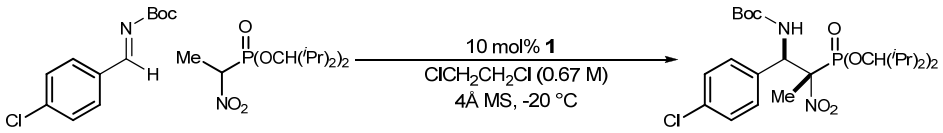
IR (film) 3292, 2981, 1719, 1697, 1553, 1247, 1167 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 6.17 (br s, 1H), 5.57 (dd, J_{PH} = 14.0 Hz, J_{HH} = 8.0 Hz, 1H), 4.94-4.84 (m, 1H), 4.78-4.68 (m, 1H), 1.63 (d, J_{PH} = 13.5 Hz, 3H), 1.43-1.18 (m, 12H), 1.38 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 154.4, 134.6, 134.3, 129.4, 128.5, 92.3 (d, J_{PC} = 147.4 Hz), 80.3, 74.3 (d, J_{PC} = 7.3 Hz), 73.6 (d, J_{PC} = 8.1 Hz), 58.8, 28.2, 24.3 (d, J_{PC} = 2.8 Hz), 24.0 (d, J_{PC} = 2.8 Hz), 23.4 (d, J_{PC} = 7.0 Hz), 23.3 (d, J_{PC} = 6.4 Hz), 17.6; ^{31}P NMR (202 MHz, $CDCl_3$) ppm 14.1; HRMS (EI): Exact mass calcd for $C_{20}H_{32}ClNaN_2O_7P$ $[M+Na]^+$ 501.1528. Found 501.1528.



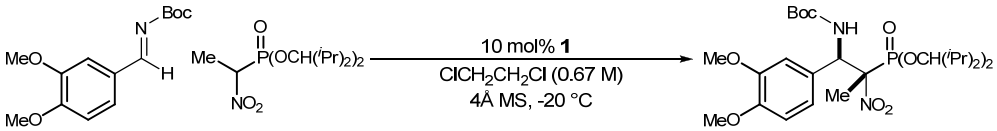
***tert*-Butyl-2-(bis(pentan-3-yloxy)phosphoryl)-1-(4-chlorophenyl)-2-nitropropylcarbamate (4d)**. According to the general procedure and after flash column chromatography (20% ethyl acetate in hexanes), **4d** was isolated as a white foam which was determined to be 84% ee by chiral HPLC analysis (Chiralcel AD, 5% ^{i}PrOH/hexanes, 1.0 mL/min, t_r = 20.1 (major), 21.5 (minor) min). Major Diastereomer: R_f = 0.46 (25% EtOAc/hexanes); IR (film) 3298, 2970, 1719, 1699, 1551, 1491, 1242, 1164 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 7.6 Hz, 2H), 7.20 (d, J = 7.6 Hz, 2H), 6.17 (br s, 1H), 5.59 (dd, J_{PH} = 12.8 Hz, J_{HH} = 6.8 Hz, 1H), 4.54 (dquint, J_{PH} = 6.0 Hz, J_{HH} = 6.0 Hz, 1H), 4.40 (dquint, J_{PH} = 6.0 Hz, J_{HH} = 6.0 Hz, 1H), 1.80-1.60 (m, 8H), 1.64 (d, J_{PH} = 13.5 Hz, 3H), 1.37 (s, 9H), 1.0-0.8 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 154.4, 134.7, 134.4, 129.3, 128.6, 92.0 (d, J_{PC} = 146.8 Hz), 83.2 (d, J_{PC} = 7.9 Hz), 82.8 (d, J_{PC} = 7.8 Hz), 80.3, 58.8, 28.2, 27.3, 26.9, 26.4, 26.3, 17.2, 9.0, 8.70, 8.68, 8.60; ^{31}P NMR (162 MHz, $CDCl_3$) ppm 14.2; HRMS (CI): Exact mass calcd for $C_{24}H_{41}ClN_2O_7P$ $[M+H]^+$ 535.2334. Found 535.2343.

General Procedure for Preparation of 5a – 5m.

An oven-dried vial was charged with a stir bar, 4Å MS, imine (203 μmol), and **1** (10.6 mg, 20.3 μmol) successively; the vial was capped with a septum and placed under an Ar atmosphere. 1,2-Dichloroethane (300 μL) was added, followed by di(diisopropylmethyl)1-nitroethyl phosphonate (70.2 mg, 203 μmol). The resulting solution was stirred at -20 °C for 7 d. The solution was then concentrated; the % conversion and diastereomeric ratio were determined by crude ^1H and ^{31}P NMR spectroscopy. Flash column chromatography (SiO_2) provided the desired addition product.

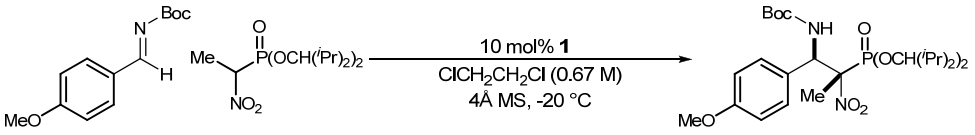


***tert*-Butyl-(1*R*,2*S*)-2-(bis(2,4-dimethylpentan-3-yloxy)phosphoryl)-1-(4-chlorophenyl)-2-nitropropylcarbamate (5a).** According to the general procedure and after flash column chromatography (20% ethyl acetate in hexanes), **5a** was isolated as a white foam (58 mg, 49%) which was determined to be 88% ee by chiral HPLC analysis (Pirkle Whelk-O covalent, 2% ^{i}PrOH/hexanes, 1.0 mL/min, t_r = 7.82 (major), 7.24 (minor) min). Major Diastereomer: R_f = 0.29 (10% EtOAc/hexanes); IR (neat) 3283, 2965, 2927, 1719, 1552, 1239 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 6.35 (br s, 1H), 5.65 (dd, J_{PH} = 10.0 Hz, J_{HH} = 5.5 Hz, 1H), 4.27 (dt, J_{PH} = 6.8 Hz, J_{HH} = 4.8 Hz, 1H), 4.14 (dt, J_{PH} = 6.8 Hz, J_{HH} = 4.8 Hz, 1H), 2.24 (m, 1H), 2.11 (m, 1H), 2.00 (m, 1H), 1.92 (m, 1H), 1.68 (d, J_{PH} = 14.0 Hz, 3H), 1.36 (s, 9H), 1.11-1.02 (m, 12H), 0.98-0.95 (m, 9H), 0.86 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 154.3, 134.7, 134.2, 129.2, 128.6, 91.8 (d, J_{PC} = 143.4 Hz), 91.2 (d, J_{PC} = 9.6 Hz), 90.8 (d, J_{PC} = 9.6 Hz), 80.2, 58.6, 31.8, 31.4, 30.7 (d, J_{PC} = 4.1 Hz), 30.4 (d, J_{PC} = 3.5 Hz), 28.2, 20.1, 19.8, 19.4, 19.1, 18.8, 18.7, 18.5, 17.9, 16.9; ^{31}P NMR (162 MHz, $CDCl_3$) ppm 12.4; HRMS (CI): Exact mass calcd for $C_{28}H_{49}ClN_2O_7P$ $[M+H]^+$ 591.2960. Found 591.2960.

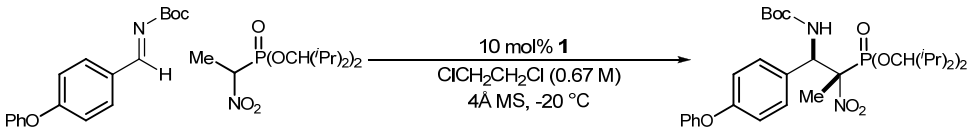


***tert*-Butyl-(1*R*,2*S*)-2-(bis(2,4-dimethylpentan-3-yloxy)phosphoryl)-1-(3,4-dimethoxyphenyl)-2-nitropropylcarbamate (5b).** According to the general procedure and after flash column chromatography (25% ethyl acetate in hexanes), **5b** was isolated as a white foam (84 mg, 68%) which was determined to be 67% ee by chiral HPLC analysis (Chiralcel IA, 5% ^{i}PrOH/hexanes, 1.0 mL/min, t_r = 14.6 (major), 13.6 (minor) min). Major Diastereomer: R_f = 0.15 (20% EtOAc/hexanes); IR (film) 3294, 2965, 2935, 1718, 1552, 1516, 1241, 1167 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.79 (br s, 2H), 6.70 (s, 1H), 6.28 (br s, 1H), 5.65 (dd, J_{PH} = 12.0 Hz, J_{HH} = 6.0 Hz, 1H), 4.26 (dt, J_{PH} = 6.5 Hz, J_{HH} = 4.5 Hz, 1H), 4.13 (dt, J_{PH} = 6.5 Hz, J_{HH} = 4.5 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 2.25 (m, 1H), 2.12 (m, 1H), 2.10 (m, 1H), 1.93 (m, 1H), 1.66 (d, J_{PH} = 14.0 Hz, 3H), 1.38 (s, 9H), 1.11-1.04 (m, 12H), 0.99-0.93 (m, 9H), 0.88 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 154.3, 148.9, 148.8, 128.3, 120.0, 110.9, 110.6, 92.1 (d, J_{PC} = 143.5 Hz), 91.0 (d, J_{PC} = 8.3 Hz), 90.6 (d, J_{PC} = 9.5 Hz), 80.0, 58.8, 55.8, 55.7, 31.7 (d, J_{PC} = 2.8 Hz), 31.5 (d, J_{PC} = 2.8 Hz), 30.7 (d, J_{PC} = 4.3 Hz), 30.4 (d, J_{PC} = 4.3

Hz), 28.2, 20.0, 19.9, 19.4, 19.1, 18.9, 18.7, 18.5, 18.0, 16.9; ^{31}P NMR (202 MHz, $CDCl_3$) ppm 12.9; HRMS (CI): Exact mass calcd for $C_{30}H_{54}N_2O_9P$ $[M+H]^+$ 617.3561. Found 617.3539.

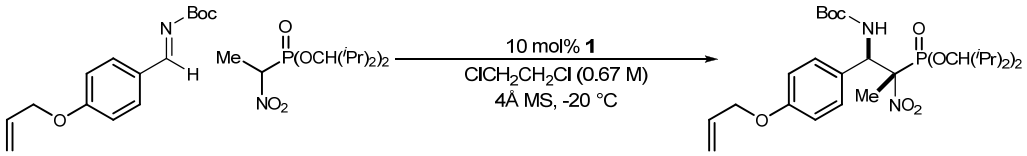


***tert*-Butyl-(1*R*,2*S*)-2-(bis(2,4-dimethylpentan-3-yloxy)phosphoryl)-1-(4-methoxyphenyl)-2-nitropropylcarbamate (5c).** According to the general procedure and after flash column chromatography (20% ethyl acetate in hexanes), **5c** was isolated as a white foam (98 mg, 84%) which was determined to be 99% ee by chiral HPLC analysis (Chiralcel AD, 5% ^{i}PrOH/hexanes, 1.0 mL/min, t_r = 10.4 (major), 11.1 (minor) min). Major Diastereomer: R_f = 0.20 (15% EtOAc/hexanes); IR (film) 3293, 2965, 2934, 1718, 1551, 1512, 1245, 1171 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, J = 8.5 Hz, 2H), 6.82 (d, J = 8.5 Hz, 2H), 6.24 (br s, 1H), 5.63 (dd, J_{PH} = 9.6 Hz, J_{HH} = 5.6 Hz, 1H), 4.27 (dt, J_{PH} = 6.4 Hz, J_{HH} = 4.0 Hz, 1H), 4.13 (dt, J_{PH} = 6.4 Hz, J_{HH} = 4.0 Hz, 1H), 3.78 (s, 3H), 2.26 (m, 1H), 2.12 (m, 1H), 2.00 (m, 1H), 1.93 (m, 1H), 1.68 (d, J_{PH} = 13.6 Hz, 3H), 1.36 (s, 9H), 1.12-1.04 (m, 12H), 0.99-0.93 (m, 9H), 0.86 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 159.5, 154.3, 128.9, 127.9, 113.8, 92.2 (d, J_{PC} = 143.6 Hz), 90.9 (d, J_{PC} = 9.3 Hz), 90.5 (d, J_{PC} = 9.9 Hz), 79.9, 58.7, 55.2, 31.8 (d, J_{PC} = 2.8 Hz), 31.5 (d, J_{PC} = 2.8 Hz), 30.7 (d, J_{PC} = 5.5 Hz), 30.4 (d, J_{PC} = 4.5 Hz), 28.3, 20.1, 19.9, 19.4, 19.1, 18.9, 18.8, 18.6, 18.0, 17.0; ^{31}P NMR (162 MHz, $CDCl_3$) ppm 12.8; HRMS (CI): Exact mass calcd for $C_{29}H_{52}N_2O_8P$ $[M+H]^+$ 587.3456. Found 587.3463.

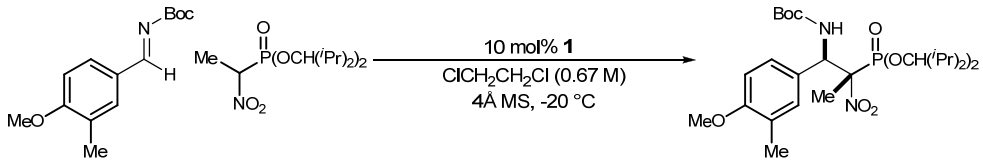


***tert*-Butyl-(1*R*,2*S*)-2-(bis(2,4-dimethylpentan-3-yloxy)phosphoryl)-1-(4-phenyloxyphenyl)-2-nitropropylcarbamate (5d).** According to the general procedure and after flash column chromatography (20% ethyl acetate in hexanes), **5d** was isolated as a white foam (96 mg, 74%) which was determined to be 99% ee by chiral HPLC analysis (Chiralcel IA, 2% ^{i}PrOH/hexanes, 1.0 mL/min, t_r = 22.0 (major), 24.5 (minor) min). Major Diastereomer: R_f = 0.54 (25% EtOAc/hexanes); IR (film) 3300, 2966, 1719, 1699, 1552, 1489, 1241 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (t, J = 7.6 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 7.11 (t, J = 7.6 Hz, 1H), 7.00 (d, J = 8.0 Hz, 2H), 69.3 (d, J = 8.0 Hz, 2H), 6.33 (br s, 1H), 5.66 (dd, J_{PH} = 10.8 Hz, J_{HH} = 6.0 Hz, 1H), 4.28 (dt, J_{PH} = 6.8 Hz, J_{HH} = 4.0 Hz, 1H), 4.14 (dt, J_{PH} = 6.8 Hz, J_{HH} = 4.0 Hz, 1H), 2.26 (m, 1H), 2.11 (m, 1H), 2.01

(m, 1H), 1.93 (m, 1H), 1.71 (d, J_{PH} = 14.0 Hz, 3H), 1.37 (s, 9H), 1.12-1.03 (m, 12H), 1.00-0.93 (m, 9H), 0.86 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 157.4, 156.6, 154.3, 130.1, 129.7, 129.2, 123.5, 119.2, 118.2, 92.1 (d, J_{PC} = 144.3 Hz), 91.0 (d, J_{PC} = 9.8 Hz), 90.6 (d, J_{PC} = 9.7 Hz), 80.0, 58.8, 31.8, 31.4 (d, J_{PC} = 2.9 Hz), 30.6 (d, J_{PC} = 4.0 Hz), 30.4 (d, J_{PC} = 4.2 Hz), 28.2, 20.0, 19.8, 19.4, 19.0, 18.9, 18.7, 18.6, 17.8, 17.1; ^{31}P NMR (162 MHz, $CDCl_3$) ppm 12.6; HRMS (CI): Exact mass calcd for $C_{34}H_{54}N_2O_8P$ $[M+H]^+$ 649.3612. Found 649.3603.

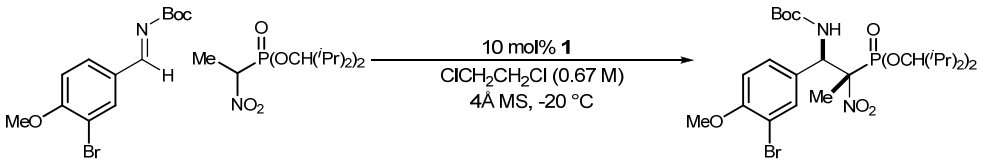


***tert*-Butyl-(1*R*,2*S*)-2-(bis(2,4-dimethylpentan-3-yloxy)phosphoryl)-1-(4-allyloxyphenyl)-2-nitropropylcarbamate (5e).** According to the general procedure and after flash column chromatography (20% ethyl acetate in hexanes), **5e** was isolated as a white foam (97 mg, 78%) which was determined to be 99% ee by chiral HPLC analysis (Chiralcel AD, 5% ^{i}PrOH/hexanes, 1.0 mL/min, t_r = 9.0 (minor), 9.4 (major) min). Major Diastereomer: R_f = 0.48 (25% EtOAc/hexanes); IR (film) 3297, 2966, 2934, 1719, 1699, 1551, 1510, 1244, 1169 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (d, J = 8.5 Hz, 2H), 6.83 (d, J = 8.5 Hz, 2H), 6.27 (br s, 1H), 6.04 (ddt, J = 17.5, 11.0, 5.0 Hz, 1H), 5.63 (dd, J_{PH} = 10.0 Hz, J_{HH} = 5.5 Hz, 1H), 5.40 (d, J = 17.5 Hz, 1H), 5.28 (d, J = 11.0 Hz, 1H), 4.50 (d, J = 5.0 Hz, 2H), 4.27 (dt, J_{PH} = 7.0 Hz, J_{HH} = 4.5 Hz, 1H), 4.12 (dt, J_{PH} = 7.0 Hz, J_{HH} = 4.5 Hz, 1H), 2.25 (m, 1H), 2.11 (m, 1H), 2.00 (m, 1H), 1.93 (m, 1H), 1.68 (d, J_{PH} = 14.5 Hz, 3H), 1.37 (s, 9H), 1.10-1.04 (m, 12H), 0.99-0.94 (m, 9H), 0.85 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 158.5, 154.2, 133.1, 128.9, 127.9, 117.6, 114.5, 92.2 (d, J_{PC} = 143.8 Hz), 90.9 (d, J_{PC} = 9.3 Hz), 90.4 (d, J_{PC} = 9.9 Hz), 79.9, 68.7, 58.7, 31.7, 31.4, 30.6, 30.4, 28.2, 20.0, 19.8, 19.4, 19.0, 18.8, 18.7, 18.5, 17.9, 17.5, 16.9; ^{31}P NMR (202 MHz, $CDCl_3$) ppm 12.8; HRMS (CI): Exact mass calcd for $C_{31}H_{54}N_2O_8P$ $[M+H]^+$ 613.3612. Found 613.3633.

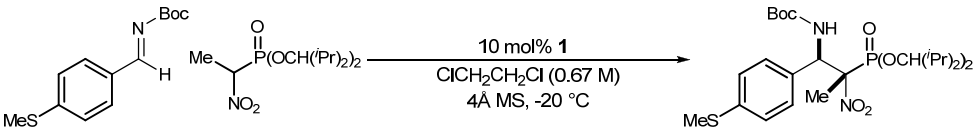


***tert*-Butyl-(1*R*,2*S*)-2-(bis(2,4-dimethylpentan-3-yloxy)phosphoryl)-1-(4-methoxy-3-methylphenyl)-2-nitropropylcarbamate (5f).** According to the general procedure and after flash column chromatography (20%

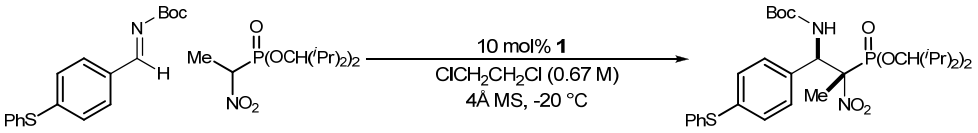
ethyl acetate in hexanes), **5f** was isolated as a white foam (90 mg, 75%) which was determined to be 85% ee by chiral HPLC analysis (Chiralcel AD, 5% ^{i}PrOH/hexanes, 1.0 mL/min, t_r = 8.3 (minor), 10.3 (major) min). Major Diastereomer: R_f = 0.5 (25% EtOAc/hexanes); IR (film) 3284, 2965, 2932, 1716, 1530, 1239 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (d, J = 8.4 Hz, 1H), 6.97 (s, 1H), 6.72 (d, J = 8.4 Hz, 1H), 6.25 (br s, 1H), 5.59 (dd, J_{PH} = 10.8 Hz, J_{HH} = 6.4 Hz, 1H), 4.27 (dt, J_{PH} = 6.8 Hz, J_{HH} = 4.4 Hz, 1H), 4.11 (dt, J_{PH} = 6.8 Hz, J_{HH} = 4.4 Hz, 1H), 3.79 (s, 3H), 2.25 (m, 1H), 2.16 (s, 3H), 2.11 (m, 1H), 2.00 (m, 1H), 1.90 (m, 1H), 1.69 (d, J_{PH} = 14.0 Hz, 3H), 1.36 (s, 9H), 1.11-1.03 (m, 12H), 0.98-0.92 (m, 9H), 0.84 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 157.6, 154.3, 129.9, 127.3, 126.4, 126.3, 109.6, 92.2 (d, J_{PC} = 145.3 Hz), 90.8 (d, J_{PC} = 8.1 Hz), 90.4 (d, J_{PC} = 9.8 Hz), 79.8, 58.8, 55.2, 31.7, 31.4 (d, J_{PC} = 2.4 Hz), 30.7 (d, J_{PC} = 5.5 Hz), 30.4 (d, J_{PC} = 3.3 Hz), 28.2, 20.0, 19.8, 19.4, 19.1, 18.9, 18.8, 18.6, 17.8, 17.1, 16.3; ^{31}P NMR (162 MHz, $CDCl_3$) ppm 12.8; HRMS (CI): Exact mass calcd for $C_{30}H_{53}N_2O_8P$ $[M]^+$ 600.3534. Found 600.3508.



***tert*-Butyl-(1*R*,2*S*)-2-(bis(2,4-dimethylpentan-3-yloxy)phosphoryl)-1-(3-bromo-4-methoxyphenyl)-2-nitropropylcarbamate (5g).** According to the general procedure and after flash column chromatography (20% ethyl acetate in hexanes), **5g** was isolated as a white foam (95 mg, 71%) which was determined to be 83% ee by chiral HPLC analysis (Chiralcel AD, 5% ^{i}PrOH/hexanes, 1.0 mL/min, t_r = 11.2 (minor), 21.3 (major) min). Major Diastereomer: R_f = 0.51 (25% EtOAc/hexanes); IR (film) 3280, 2965, 2933, 1717, 1551, 1239, 1164 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.14 (d, J = 8.4 Hz, 1H), 6.81 (d, J = 8.4 Hz, 1H), 6.35 (br s, 1H), 5.60 (dd, J_{PH} = 10.4 Hz, J_{HH} = 6.0 Hz, 1H), 4.27 (dt, J_{PH} = 6.4 Hz, J_{HH} = 4.4 Hz, 1H), 4.14 (dt, J_{PH} = 6.4 Hz, J_{HH} = 4.4 Hz, 1H), 3.87 (s, 3H), 2.25 (m, 1H), 2.10 (m, 1H), 2.00 (m, 1H), 1.92 (m, 1H), 1.71 (d, J_{PH} = 14.0 Hz, 3H), 1.37 (s, 9H), 1.13-1.02 (m, 12H), 1.00-0.91 (m, 9H), 0.84 (d, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 155.7, 154.3, 132.4, 129.5, 128.2, 111.7, 111.5, 91.9 (d, J_{PC} = 144.3 Hz), 91.1 (d, J_{PC} = 9.4 Hz), 90.7 (d, J_{PC} = 9.9 Hz), 80.2, 58.3, 56.2, 31.7, 31.4 (d, J_{PC} = 2.8 Hz), 30.6 (d, J_{PC} = 4.9 Hz), 30.3 (d, J_{PC} = 4.6 Hz), 28.2, 20.0, 19.8, 19.3, 19.0, 18.8, 18.7, 18.6, 17.8, 17.1; ^{31}P NMR (162 MHz, $CDCl_3$) ppm 12.4; HRMS (CI): Exact mass calcd for $C_{29}H_{51}BrN_2O_8P$ $[M+H]^+$ 665.2561. Found 665.2551.

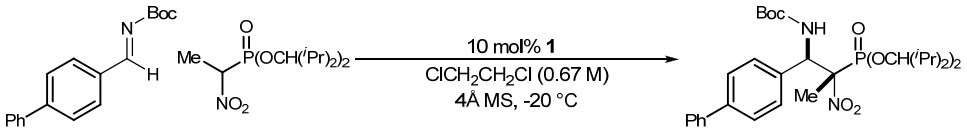


***tert*-Butyl-(1*R*,2*S*)-2-(bis(2,4-dimethylpentan-3-yloxy)phosphoryl)-1-(4-(methylthio)phenyl)-2-nitropropylcarbamate (5h).** According to the general procedure and after flash column chromatography (20% ethyl acetate in hexanes), **5h** was isolated as a white foam (104 mg, 86%) which was determined to be 99% ee by chiral HPLC analysis (Chiralcel AD, 2% ^{i}PrOH/hexanes, 1.0 mL/min, t_r = 31.9 (major), 38.0 (minor) min). Major Diastereomer: R_f = 0.46 (25% EtOAc/hexanes); IR (film) 3288, 2966, 2934, 1718, 1551, 1240, 1168 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, J = 8.6 Hz, 2H), 7.14 (d, J = 8.6 Hz, 2H), 6.30 (br s, 1H), 5.63 (dd, J_{PH} = 10.0 Hz, J_{HH} = 6.0 Hz, 1H), 4.26 (dt, J_{PH} = 7.0 Hz, J_{HH} = 4.5 Hz, 1H), 4.12 (dt, J_{PH} = 7.0 Hz, J_{HH} = 4.5 Hz, 1H), 2.44 (s, 3H), 2.23 (m, 1H), 2.10 (m, 1H), 1.99 (m, 1H), 1.92 (m, 1H), 1.67 (d, J_{PH} = 13.5 Hz, 3H), 1.36 (s, 9H), 1.10-1.03 (m, 12H), 0.98-0.92 (m, 9H), 0.84 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 154.2, 138.7, 132.6, 128.2, 126.2, 91.9 (d, J_{PC} = 144.7 Hz), 91.0 (d, J_{PC} = 8.9 Hz), 90.6 (d, J_{PC} = 9.7 Hz), 80.0, 58.7, 31.7 (d, J_{PC} = 3.3 Hz), 31.4 (d, J_{PC} = 3.2 Hz), 30.6 (d, J_{PC} = 3.2 Hz), 30.3 (d, J_{PC} = 4.3 Hz), 28.2, 20.0, 19.8, 19.4, 19.0, 18.8, 18.7, 18.5, 17.9, 16.9, 15.5; ^{31}P NMR (202 MHz, $CDCl_3$) ppm 12.6; HRMS (CI): Exact mass calcd for $C_{29}H_{52}N_2O_7PS$ $[M+H]^+$ 603.3227. Found 603.3201.

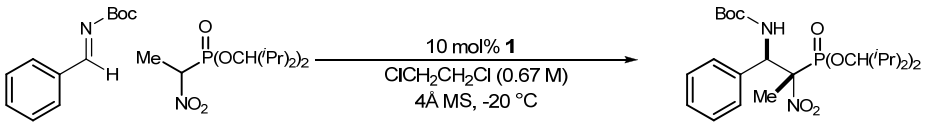


***tert*-Butyl-(1*R*,2*S*)-2-(bis(2,4-dimethylpentan-3-yloxy)phosphoryl)-1-(4-(phenylthio)phenyl)-2-nitropropylcarbamate (5i).** According to the general procedure and after flash column chromatography (15% ethyl acetate in hexanes), **5i** was isolated as a white foam (92 mg, 69%) which was determined to be 99% ee by chiral HPLC analysis (Chiralcel AD, 5% ^{i}PrOH/hexanes, 1.0 mL/min, t_r = 12.0 (major), 12.9 (minor) min). Major Diastereomer: R_f = 0.51 (25% EtOAc/hexanes); IR (film) 3295, 2965, 2934, 1719, 1699, 1551, 1244, 1167 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.25 (m, 5H), 7.20 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 6.36 (br s, 1H), 5.63 (dd, J_{PH} = 10.8 Hz, J_{HH} = 6.4 Hz, 1H), 4.27 (dt, J_{PH} = 7.2 Hz, J_{HH} = 4.4 Hz, 1H), 4.11 (dt, J_{PH} = 7.2 Hz, J_{HH} = 4.4 Hz, 1H), 2.24 (m, 1H), 2.01 (m, 1H), 1.99 (m, 1H), 1.89 (m, 1H), 1.68 (d, J_{PH} = 13.6 Hz, 3H), 1.36 (s, 9H), 1.12-1.02 (m, 12H), 0.99-0.92 (m, 9H), 0.83 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 154.4, 136.6, 134.3, 131.8, 131.3, 129.8, 129.2, 128.5, 127.4, 91.9 (d, J_{PC} = 145.9 Hz), 91.1 (d, J_{PC} = 10.4 Hz), 90.6 (d, J_{PC} = 9.8 Hz), 80.1, 53.8, 31.8 (d, J_{PC} = 3.6 Hz), 31.3 (d, J_{PC} = 3.2 Hz), 30.6 (d, J_{PC} = 4.5

Hz), 30.3 (d, J_{PC} = 3.4 Hz), 28.2, 20.0, 19.8, 19.4, 19.0, 18.8, 18.7, 18.6, 17.8, 17.2; ^{31}P NMR (162 MHz, $CDCl_3$) ppm 12.4; HRMS (CI): Exact mass calcd for $C_{34}H_{53}N_2O_7PS$ $[M]^+$ 664.3306. Found 664.3303.

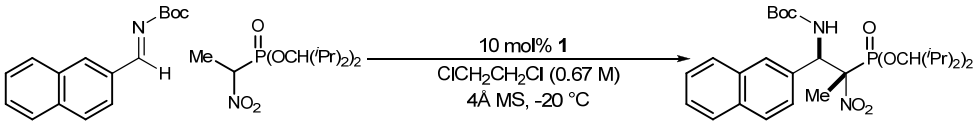


***tert*-Butyl-(1*R*,2*S*)-2-(bis(2,4-dimethylpentan-3-yloxy)phosphoryl)-2-nitro-1-*p*-tolylpropylcarbamate (5j).** According to the general procedure and after flash column chromatography (20% ethyl acetate in hexanes), **5j** was isolated as a white foam (59 mg, 46%) which was determined to be 88% ee by chiral HPLC analysis (Chiralcel IA, 2% ^{i}PrOH/hexanes, 1.0 mL/min, t_r = 17.1 (major), 21.2 (minor) min). Major Diastereomer: R_f = 0.47 (25% EtOAc/hexanes); IR (film) 3300, 2966, 2935, 1720, 1699, 1552, 1366, 1245, 1169 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, J = 7.2 Hz, 2H), 7.49 (d, J = 7.9 Hz, 2H), 7.40 (t, J = 7.5 Hz, 2H), 7.34-7.26 (m, 3H), 6.39 (br s, 1H), 5.70 (dd, J_{HH} = 10.4 Hz, J_{PH} = 5.5 Hz, 1H), 4.28 (m, 1H), 4.11 (m, 1H), 2.24 (m, 1H), 2.10 (m, 1H), 1.97 (m, 1H), 1.89 (m, 1H), 1.72 (d, J_{PH} = 13.8 Hz, 3H), 1.36 (s, 9H), 1.11-1.02 (m, 12H), 0.97-0.90 (m, 9H), 0.81 (br s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 154.3, 141.1, 140.5, 134.8, 128.7, 128.2, 127.3, 127.1, 127.0, 92.1 (d, J_{PC} = 145.6 Hz), 91.0 (d, J_{PC} = 9.7 Hz), 90.6 (d, J_{PC} = 10.4 Hz), 80.0, 58.9, 31.8, 31.3, 30.6 (d, J_{PC} = 5.8 Hz), 30.3 (d, J_{PC} = 3.8 Hz), 28.2 (3C), 20.0, 19.8, 19.4, 19.0, 18.9, 18.7, 18.6, 17.7, 17.3; ^{31}P NMR (202 MHz, $CDCl_3$) ppm 12.6; HRMS (CI): Exact mass calcd for $C_{34}H_{54}N_2O_7P$ $[M+H]^+$ 633.3669. Found 633.3663.

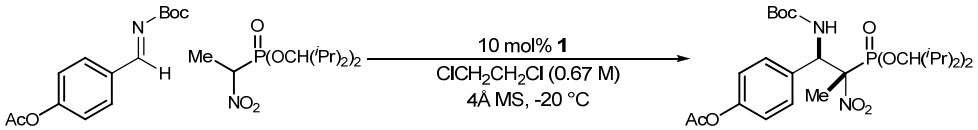


***tert*-Butyl-(1*R*,2*S*)-2-(bis(2,4-dimethylpentan-3-yloxy)phosphoryl)-2-nitro-1-phenylpropylcarbamate (5k).** According to the general procedure and after flash column chromatography (20% ethyl acetate in hexanes), **5k** was isolated as a white foam (60 mg, 54%) which was determined to be 82% ee by chiral HPLC analysis (Chiralcel AD, 5% ^{i}PrOH/hexanes, 1.0 mL/min, t_r = 7.3 (major), 8.2 (minor) min). Major Diastereomer: R_f = 0.48 (25% EtOAc/hexanes); IR (film) 3298, 2965, 1720, 1701, 1550, 1390, 1242, 1168 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.26 (m, 3H), 7.23 (d, J = 7.2 Hz, 2H), 6.34 (br s, 1H), 5.68 (dd, J_{PH} = 10.0 Hz, J_{HH} = 5.5 Hz, 1H), 4.28 (dt, J_{PH} = 6.5 Hz, J_{HH} = 4.5 Hz, 1H), 4.11 (dt, J_{PH} = 6.5 Hz, J_{HH} = 4.5 Hz, 1H), 2.26 (m, 1H), 2.11 (m, 1H), 2.00 (m, 1H), 1.91 (m, 1H), 1.68 (d, J_{PH} = 14.0 Hz, 3H), 1.37 (s, 9H), 1.11-1.04 (m, 12H), 0.98-0.93

(m, 9H), 0.83 (d, J = 5.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 154.2, 128.4, 128.3, 128.2, 127.7, 92.0 (d, J_{PC} = 144.1 Hz), 90.9 (d, J_{PC} = 9.9 Hz), 90.5 (d, J_{PC} = 10.0 Hz), 79.9, 58.8, 31.7, 31.3 (d, J_{PC} = 2.1 Hz), 30.6 (d, J_{PC} = 4.8 Hz), 30.3 (d, J_{PC} = 4.2 Hz), 28.2, 20.0, 19.8, 19.4, 19.0, 18.9, 18.7, 18.6, 17.8, 17.1; ^{31}P NMR (202 MHz, $CDCl_3$) ppm 12.7; HRMS (CI): Exact mass calcd for $C_{28}H_{50}N_2O_7P$ $[M+H]^+$ 557.3350. Found 557.3371.

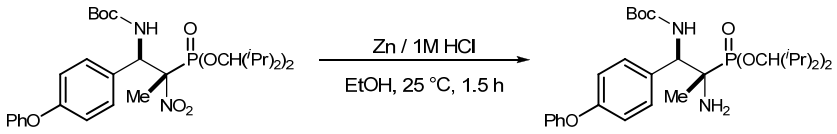


***tert*-Butyl-(1*R*,2*S*)-2-(bis(2,4-dimethylpentan-3-yloxy)phosphoryl)-1-(naphthalen-2-yl)-2-nitropropylcarbamate (5l).** According to the general procedure and after flash column chromatography (20% ethyl acetate in hexanes), **5l** was isolated as a white foam (61 mg, 50%) which was determined to be 88% ee by chiral HPLC analysis (Chiralcel AD, 5% ^{i}PrOH/hexanes, 1.0 mL/min, t_r = 7.9 (minor), 13.2 (major) min). Major Diastereomer: R_f = 0.14 (10% EtOAc/hexanes); IR (film) 3298, 2966, 2935, 1719, 1699, 1552, 1245, 1167 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83-7.76 (m, 3H), 7.71 (s, 1H), 7.46 (d, J = 6.0 Hz, 1H), 7.45 (d, J = 6.0 Hz, 1H), 7.38 (d, J = 8.5 Hz, 1H), 6.49 (br s, 1H), 5.86 (dd, J_{PH} = 11.0 Hz, J_{HH} = 6.0 Hz, 1H), 4.32 (dt, J_{PH} = 7.0 Hz, J_{HH} = 4.0 Hz, 1H), 4.12 (dt, J_{PH} = 7.0 Hz, J_{HH} = 4.0 Hz, 1H), 2.28 (m, 1H), 2.14 (m, 1H), 1.97 (m, 1H), 1.82 (m, 1H), 1.75 (d, J_{PH} = 13.5 Hz, 3H), 1.38 (s, 9H), 1.15-1.05 (m, 12H), 0.97-0.89 (m, 9H), 0.78 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 154.3, 133.4, 133.1, 133.0, 128.2, 128.0, 127.4, 127.3, 126.1, 126.0, 125.2, 92.1 (d, J_{PC} = 145.5 Hz), 91.0 (d, J_{PC} = 10.4 Hz), 90.6 (d, J_{PC} = 9.8 Hz), 80.0, 59.3, 31.7, 31.3 (d, J_{PC} = 3.2 Hz), 30.6 (d, J_{PC} = 4.4 Hz), 30.3 (d, J_{PC} = 3.4 Hz), 28.2, 20.0, 19.7, 19.4, 19.0, 18.9, 18.7, 18.5, 17.7, 17.4; ^{31}P NMR (202 MHz, $CDCl_3$) ppm 12.6; HRMS (EI): Exact mass calcd for $C_{32}H_{51}NaN_2O_7P$ $[M+Na]^+$ 629.3326. Found 629.3332.

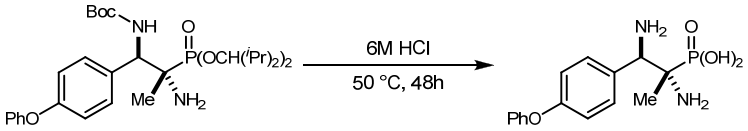


***tert*-Butyl-(1*R*,2*S*)-2-(bis(2,4-dimethylpentan-3-yloxy)phosphoryl)-1-(4-acetoxyphenyl)-2-nitropropylcarbamate (5m).** According to the general procedure and after flash column chromatography (25% ethyl acetate in hexanes), **5m** was isolated as a white foam (59 mg, 48%) which was determined to be 97% ee by chiral HPLC analysis (Chiralcel OD, 2% ^{i}PrOH/hexanes, 1.0 mL/min, t_r = 6.3 (major), 9.3 (minor) min). Major Diastereomer: R_f = 0.40 (25% EtOAc/hexanes); IR (film) 3298, 2967, 2935, 1765, 1719, 1699, 1552,

1367, 1248, 1201, 1168 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, J = 8.8 Hz, 2H), 7.04 (d, J = 8.8 Hz, 2H), 6.38 (br s, 1H), 5.67 (dd, J_{PH} = 11.2 Hz, J_{HH} = 6.4 Hz, 1H), 4.28 (dt, J_{PH} = 6.8 Hz, J_{HH} = 4.0 Hz, 1H), 4.12 (dt, J_{PH} = 6.8 Hz, J_{HH} = 4.0 Hz, 1H), 2.27 (s, 3H), 2.25 (m, 1H), 2.09 (m, 1H), 1.99 (m, 1H), 1.90 (m, 1H), 1.70 (d, J_{PH} = 13.6 Hz, 3H), 1.36 (s, 9H), 1.11-0.99 (m, 12H), 0.98-0.91 (m, 9H), 0.82 (d, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 169.0, 154.3, 150.7, 133.5, 128.9, 121.4, 92.1 (d, J_{PC} = 148.2 Hz), 91.1 (d, J_{PC} = 10.3 Hz), 90.8 (d, J_{PC} C = 9.8 Hz), 80.2, 58.8, 31.9, 31.4 (d, J_{PC} = 2.8 Hz), 30.7 (d, J_{PC} = 5.6 Hz), 30.4 (d, J_{PC} = 4.8 Hz), 28.2, 21.2, 20.1, 19.8, 19.5, 19.0, 18.9, 18.8, 18.7, 17.8, 17.4; ^{31}P NMR (162 MHz, $CDCl_3$) ppm 12.4; HRMS (CI): Exact mass calcd for $C_{30}H_{52}N_2O_9P$ $[M+H]^+$ 615.3405. Found 615.3420.



***tert*-Butyl-2-amino-2-(bis(2,4-dimethylpentan-3-yloxy)phosphoryl)-1-(4-phenoxyphenyl)propylcarbamate (6)**. To a solution of *tert*-butyl-2-(bis(2,4-dimethylpentan-3-yloxy)phosphoryl)-2-nitro-1-(4-phenoxyphenyl)propylcarbamate (457 mg, 0.70 mmol) in EtOH (17 mL) was added 1 M HCl (14 mL, 14 mmol) and Zn dust (1.66 g, 25.4 mmol) in rapid succession. The reaction mixture was allowed to stir at 25 °C for 2 h, and was quenched by pouring into satd aq $NaHCO_3$ (50 mL) and EtOAc (75 mL). The quenched reaction was stirred for 20 min, filtered through a pad of Celite, and washed through with EtOAc. The filtrate was transferred to a separatory funnel, and the aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated to leave the crude product as an oil. Column chromatography (SiO_2, 25% Ethyl acetate in hexanes) provided the title compound as a clear, colorless oil (320 mg, 74%). R_f = 0.35 (25% EtOAc/hexanes); IR (film) 3313, 2965, 2933, 2875, 1713, 1590, 1505, 1489, 1239, 1167 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37-7.30 (m, 4H), 7.10 (t, J = 7.5 Hz, 1H), 7.01 (d, J = 8.0 Hz, 2H), 7.01 (d, J = 8.5 Hz, 2H), 6.67 (br s, 1H), 4.65 (dd, J_{PH} = 18.5 Hz, J_{HH} = 7.5 Hz, 1H), 4.23 (m, 1H), 4.01 (m, 1H), 2.22-2.10 (m, 2H), 1.99-1.81 (m, 2H), 1.39 (s, 9H), 1.33 (d, J_{PH} = 15.0 Hz, 3H), 1.08-0.88 (m, 21H), 0.72 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 157.0, 156.5, 155.4, 133.6, 129.8, 129.6, 123.2, 119.0, 117.7, 88.4 (d, J_{PC} = 9.8 Hz), 88.3 (d, J_{PC} = 9.8 Hz), 79.3, 62.5, 56.2 (d, J_{PC} = 157.4 Hz), 31.7, 30.9, 30.5, 30.4 (d, J_{PC} = 4.3 Hz), 28.3, 22.1, 20.1, 19.9, 19.7 (2C), 19.4, 19.2, 18.9, 17.1; ^{31}P NMR (202 MHz, $CDCl_3$) ppm 25.7; HRMS (CI): Exact mass calcd for $C_{34}H_{56}N_2O_6P$ $[M+H]^+$ 619.3871. Found 619.3864.



1,2-Diamino-1-(4-phenoxyphenyl)propan-2-ylphosphonic acid (7). To *tert*-butyl-2-amino-2-(bis(2,4-dimethylpentan-3-yloxy)phosphoryl)-1-(4-phenoxyphenyl)propylcarbamate **6** (23 mg, 37.2 μmol) was added 6M HCl (0.5 mL) and 2 drops of EtOH, and the resulting suspension was heated at 50 °C for 48 h. The reaction mixture was then concentrated and dried under vacuum to leave the desired product as the *n*-hydrochloride salt (17.7 mg). ^{1}H NMR (500 MHz, MeOH-d^4) δ 7.68 (d, J = 8.0 Hz, 2H), 7.44 (t, J = 8.0 Hz, 2H), 7.22 (t, J = 8.0 Hz, 1H), 7.16 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 4.91 (d, J_{PH} = 9.0 Hz, 1H), 1.68 (d, J_{PH} = 12.5 Hz, 3H); ^{13}C NMR (150 MHz, MeOH-d^4) ppm 161.8, 158.3, 133.1, 132.0, 126.3 (2C), 121.6, 120.8, 58.7, 56.8 (d, J_{PC} = 137.8 Hz), 16.2; ^{31}P NMR (202 MHz, $CDCl_3$) ppm 13.9; HRMS (CI): Exact mass calcd for $C_{15}H_{17}NO_4P$ $[M\text{-}NH_2]^+$ 306.0895. Found 306.0880.

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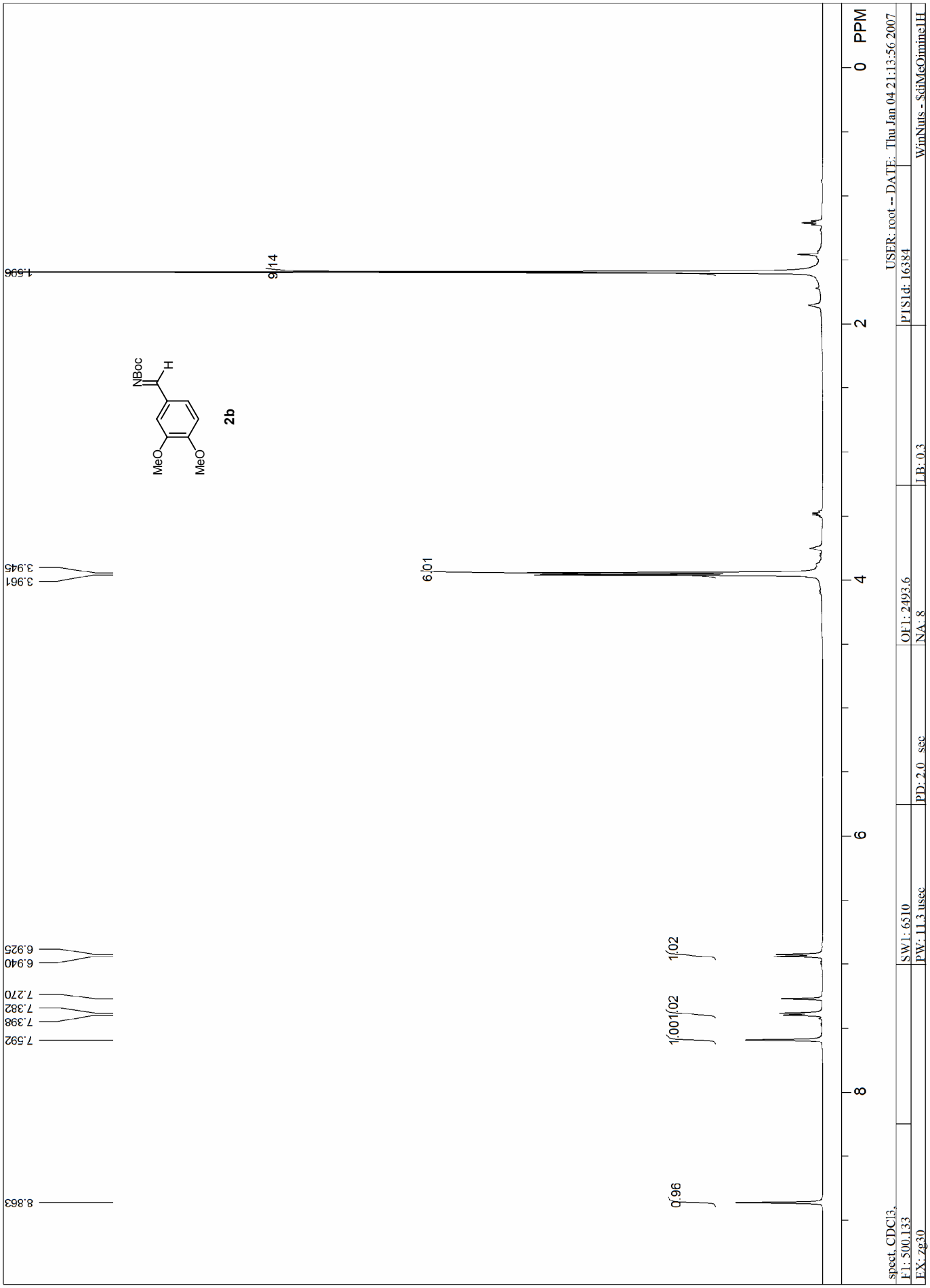

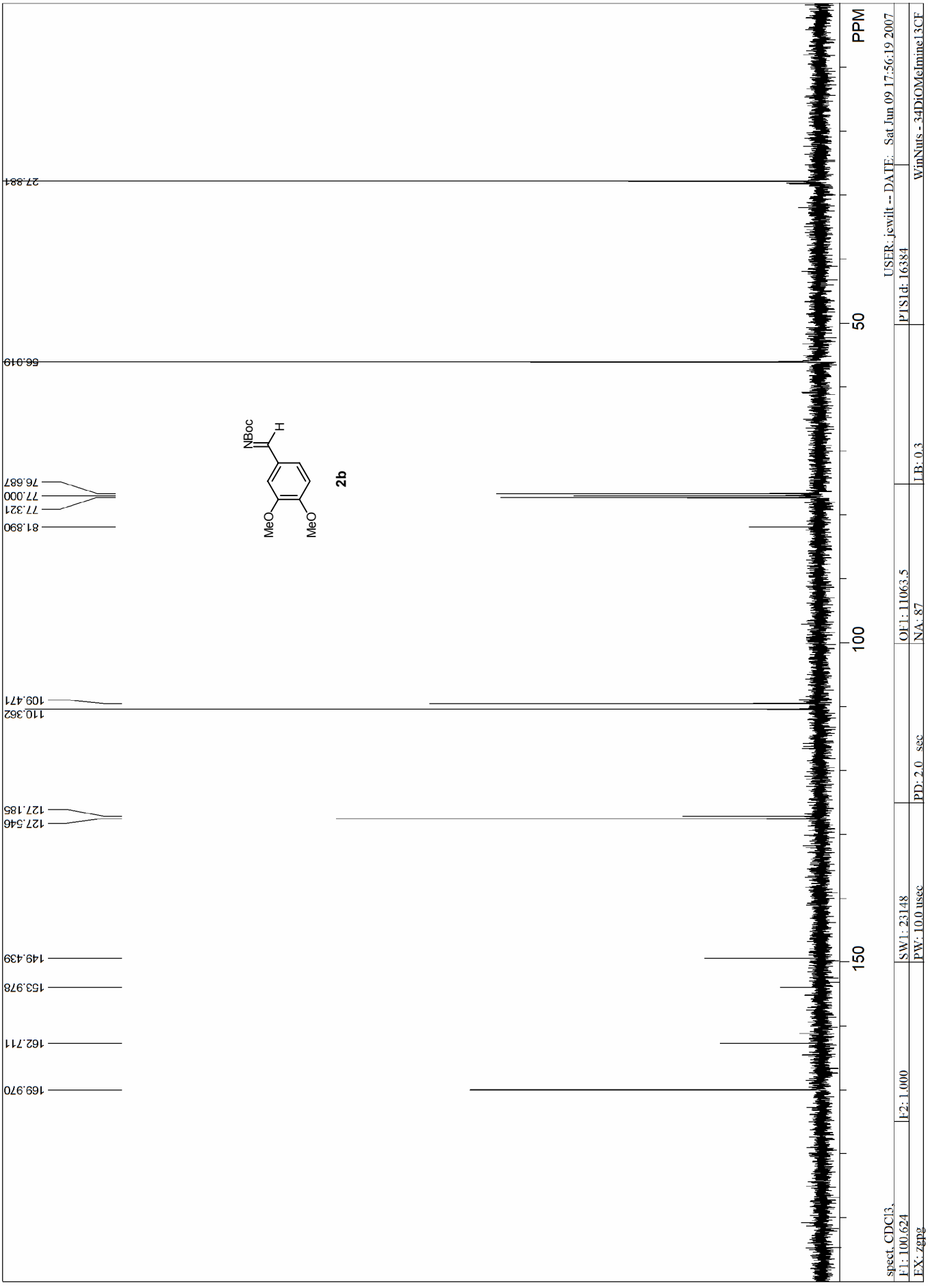

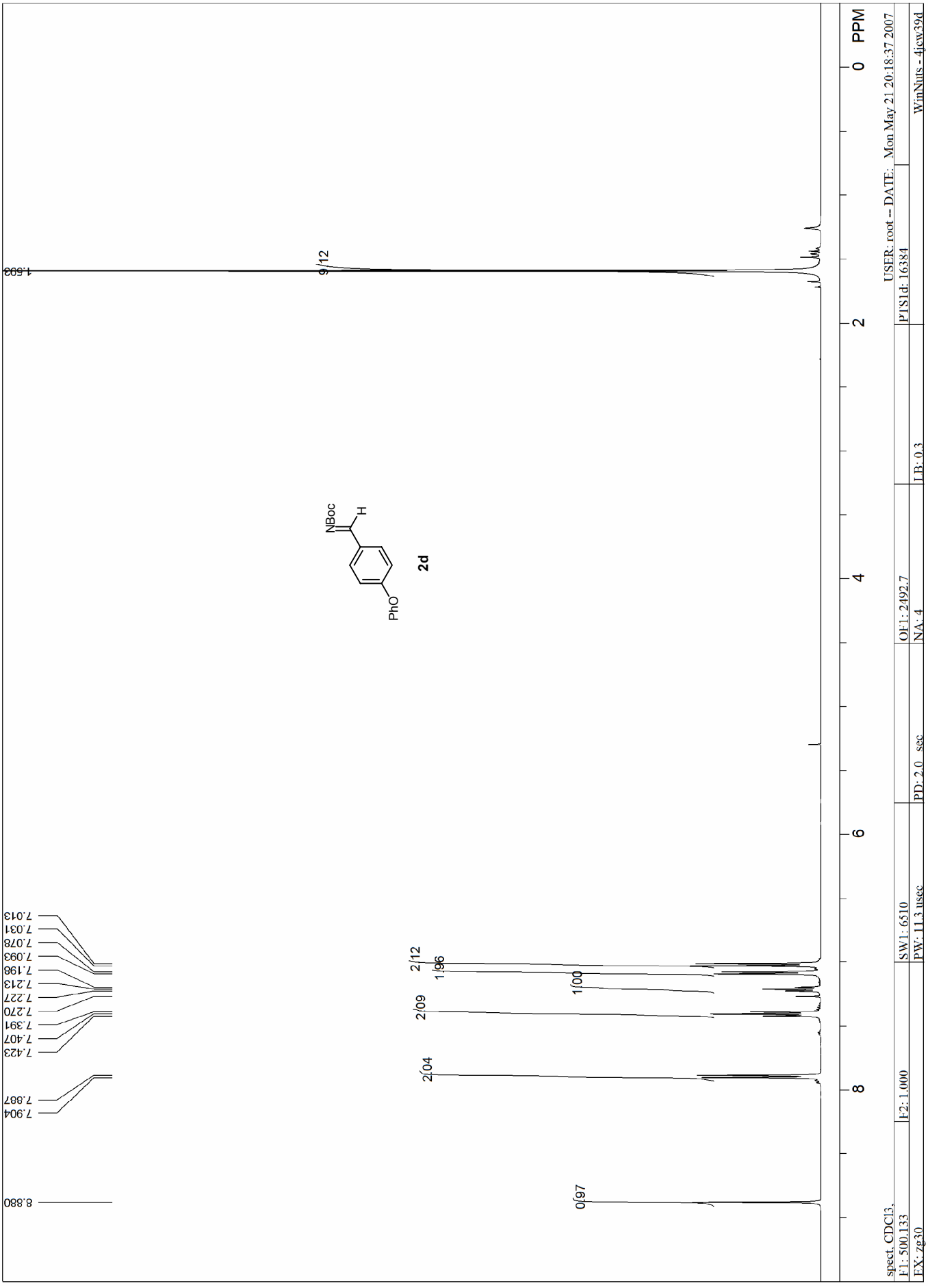

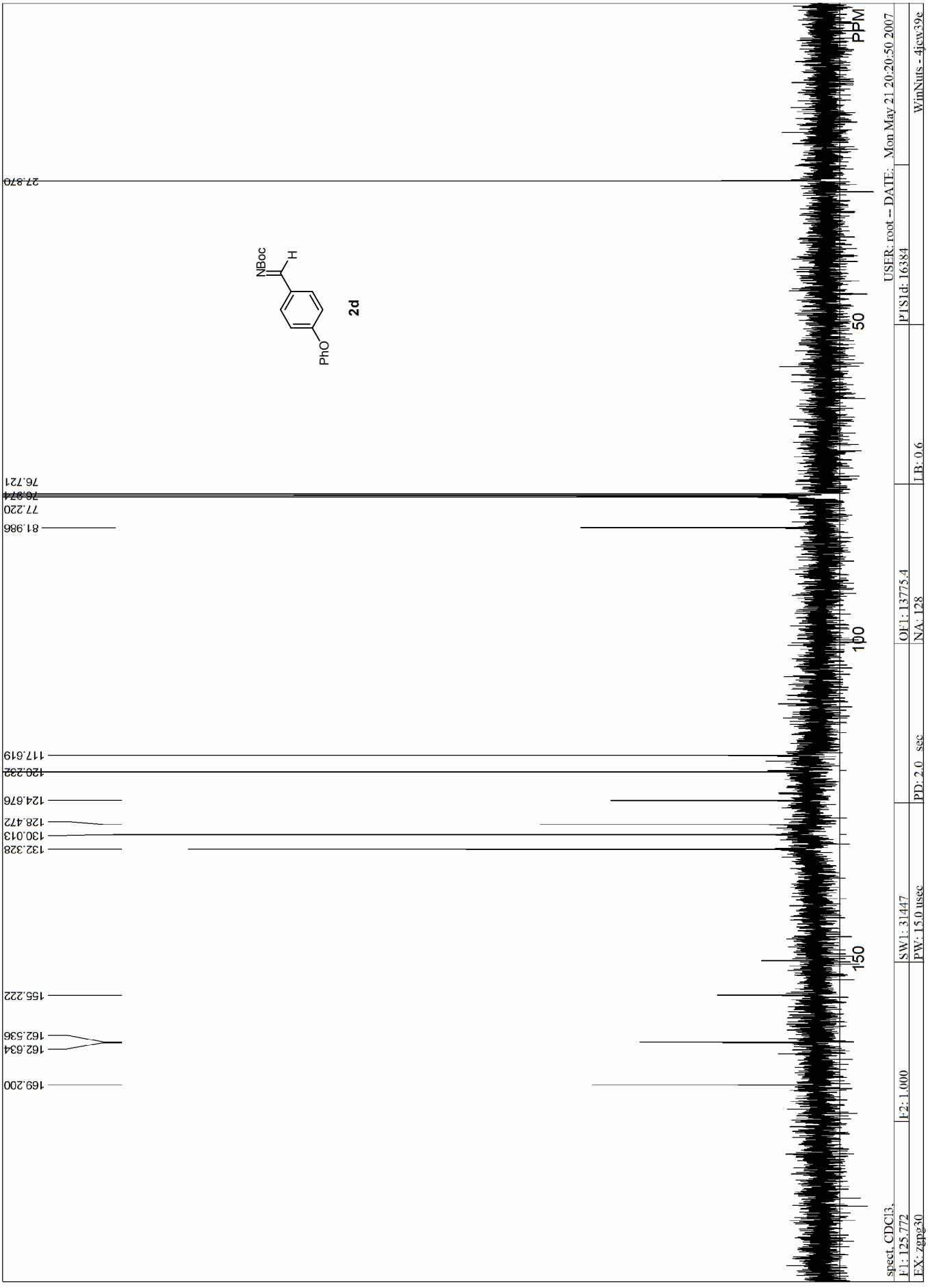

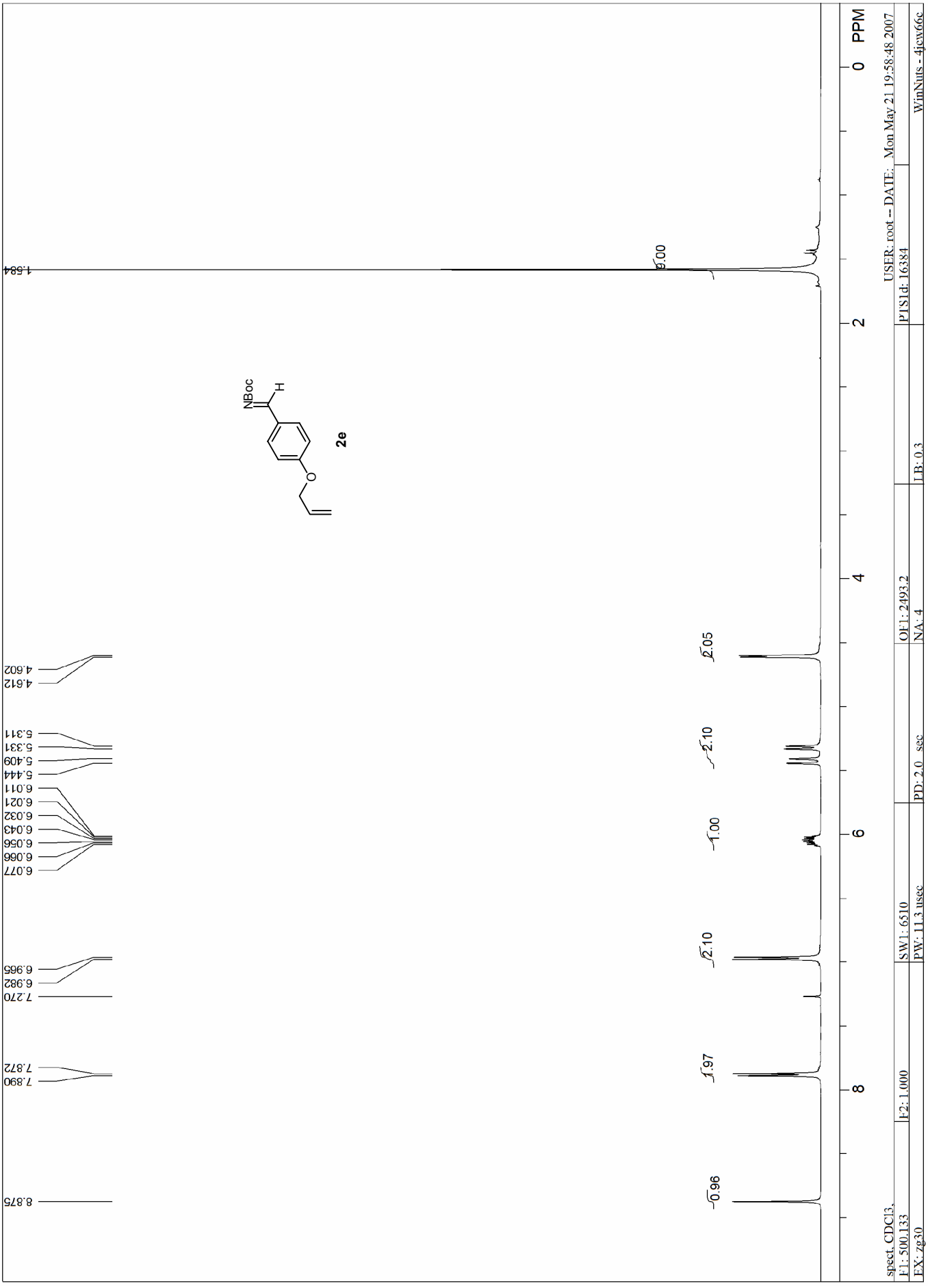

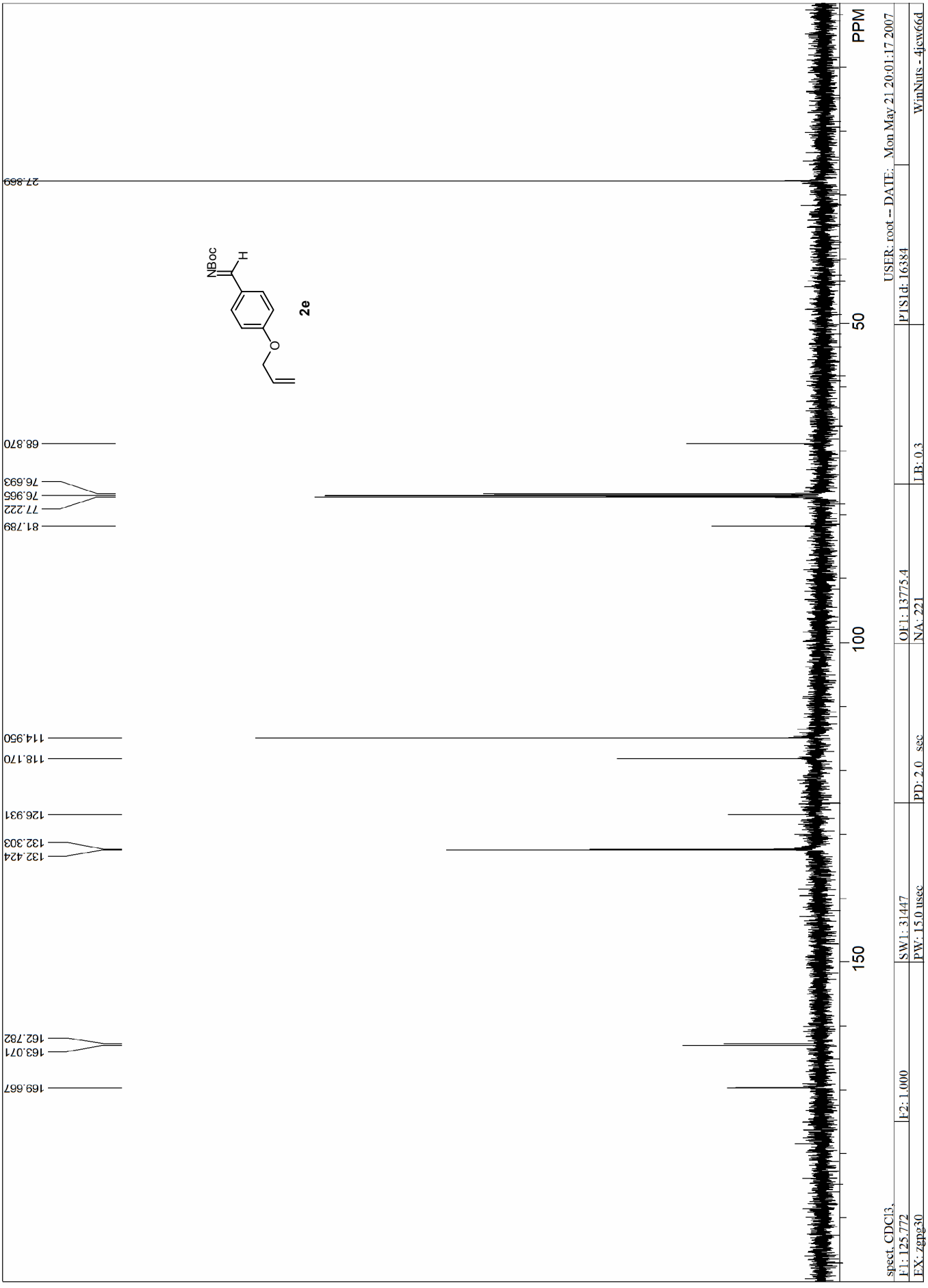

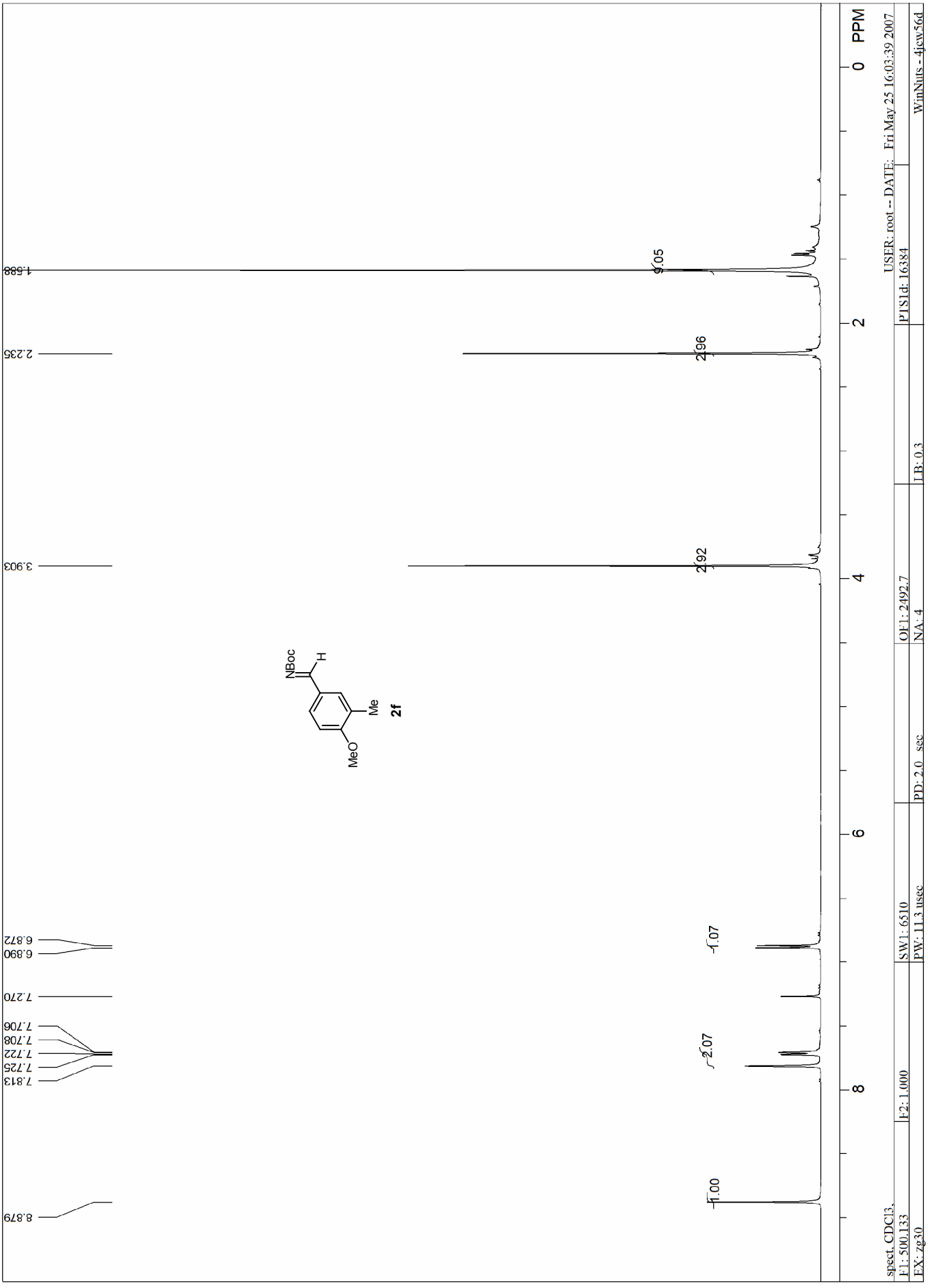

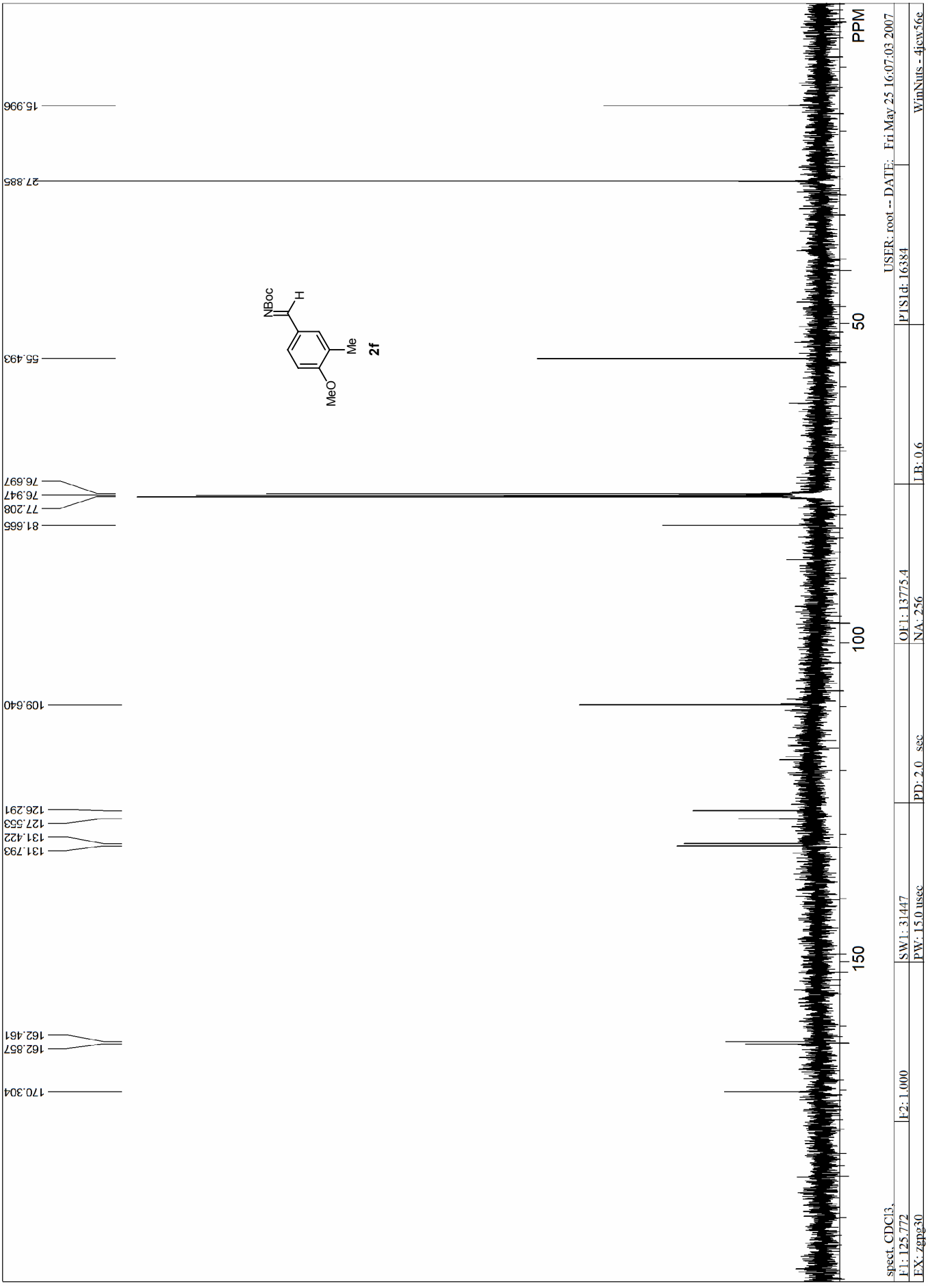

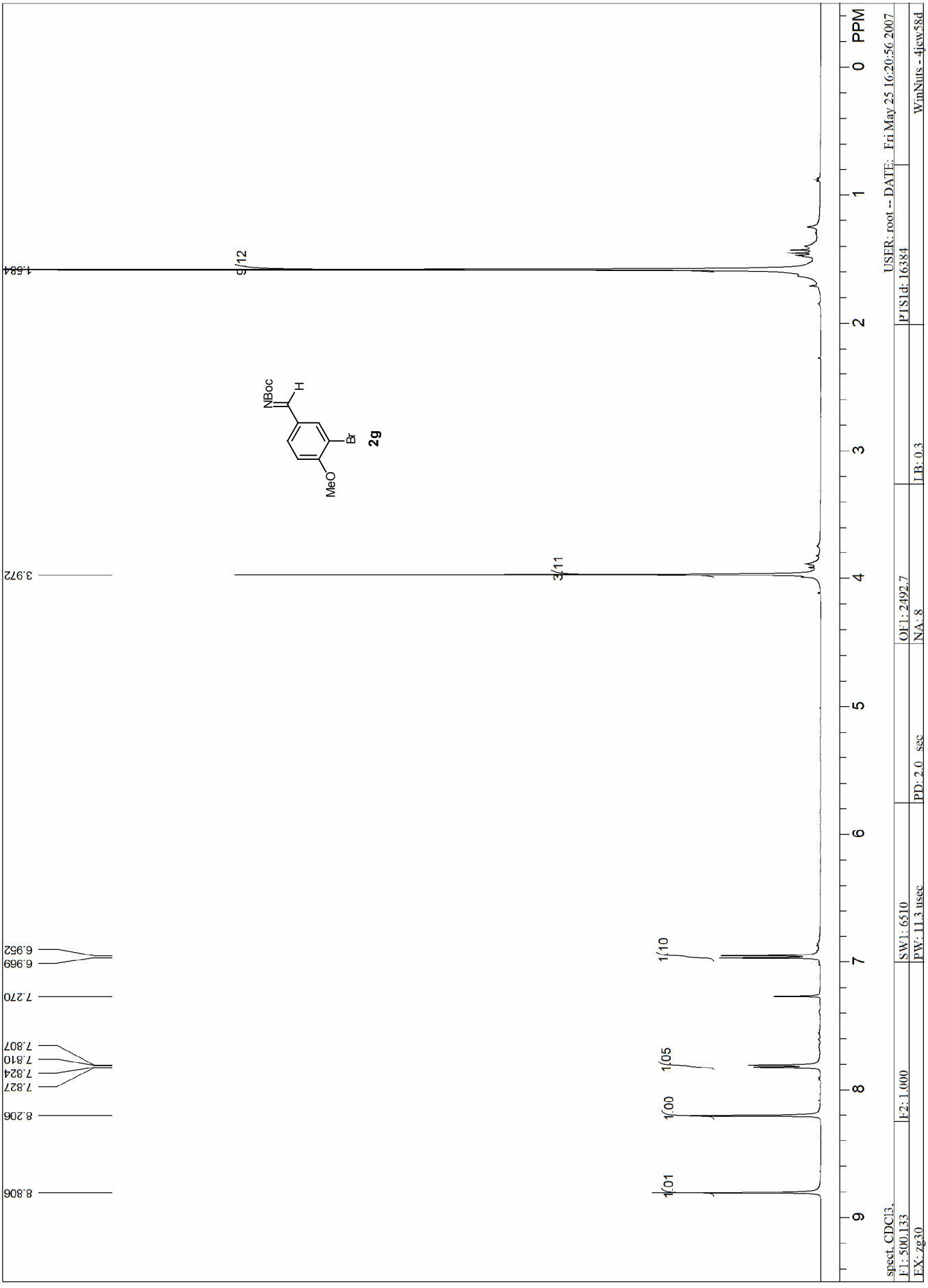

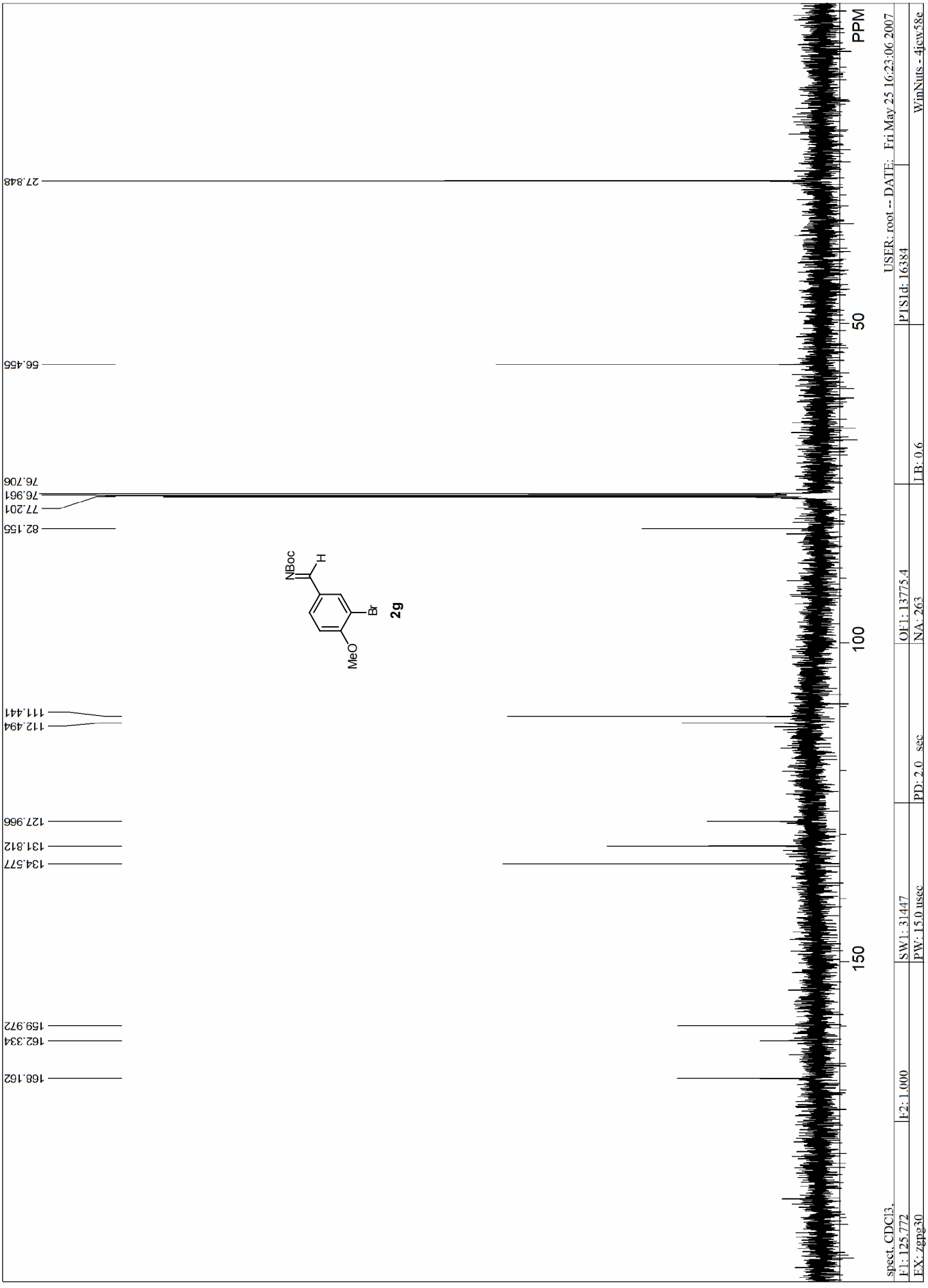

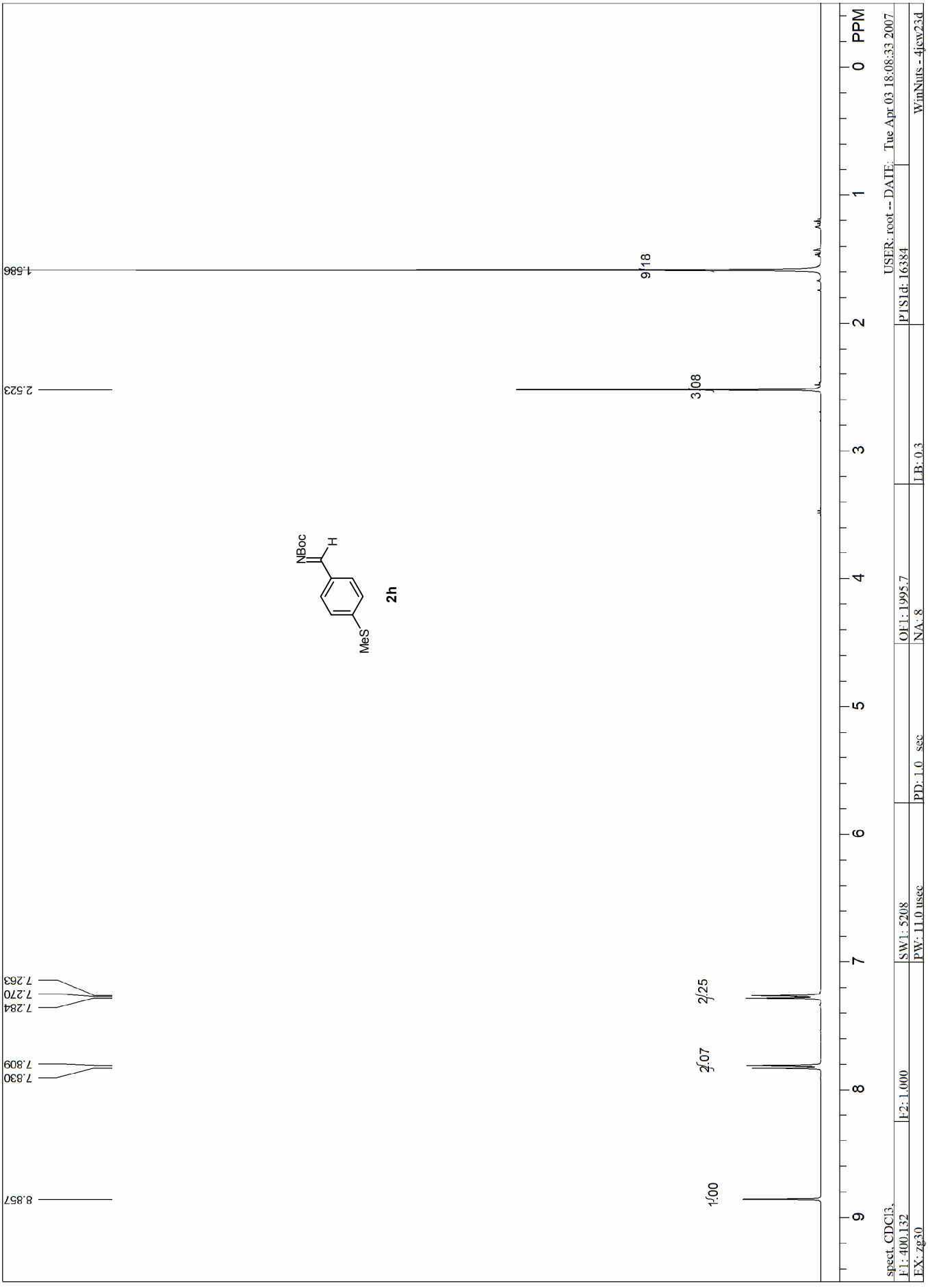

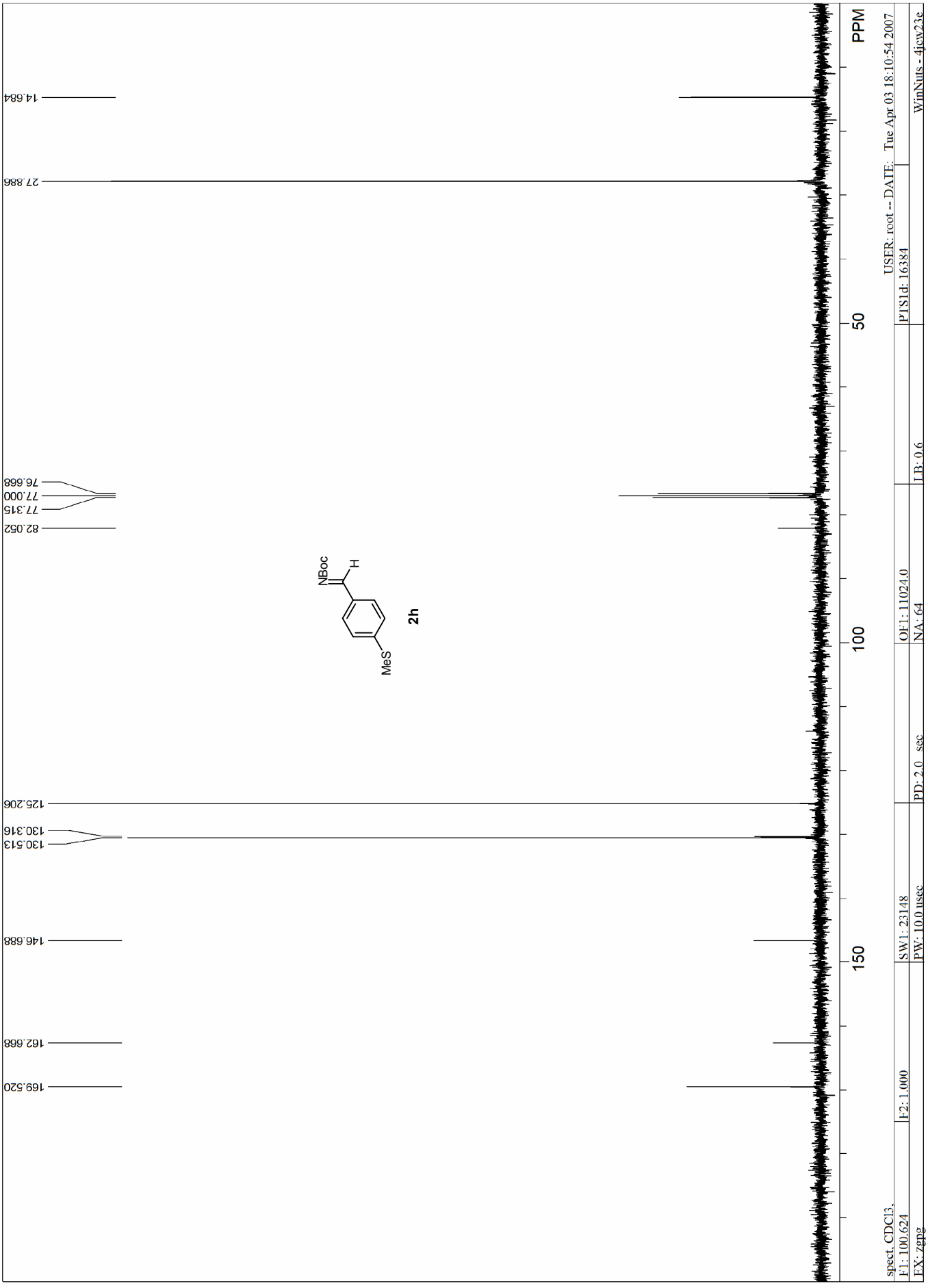

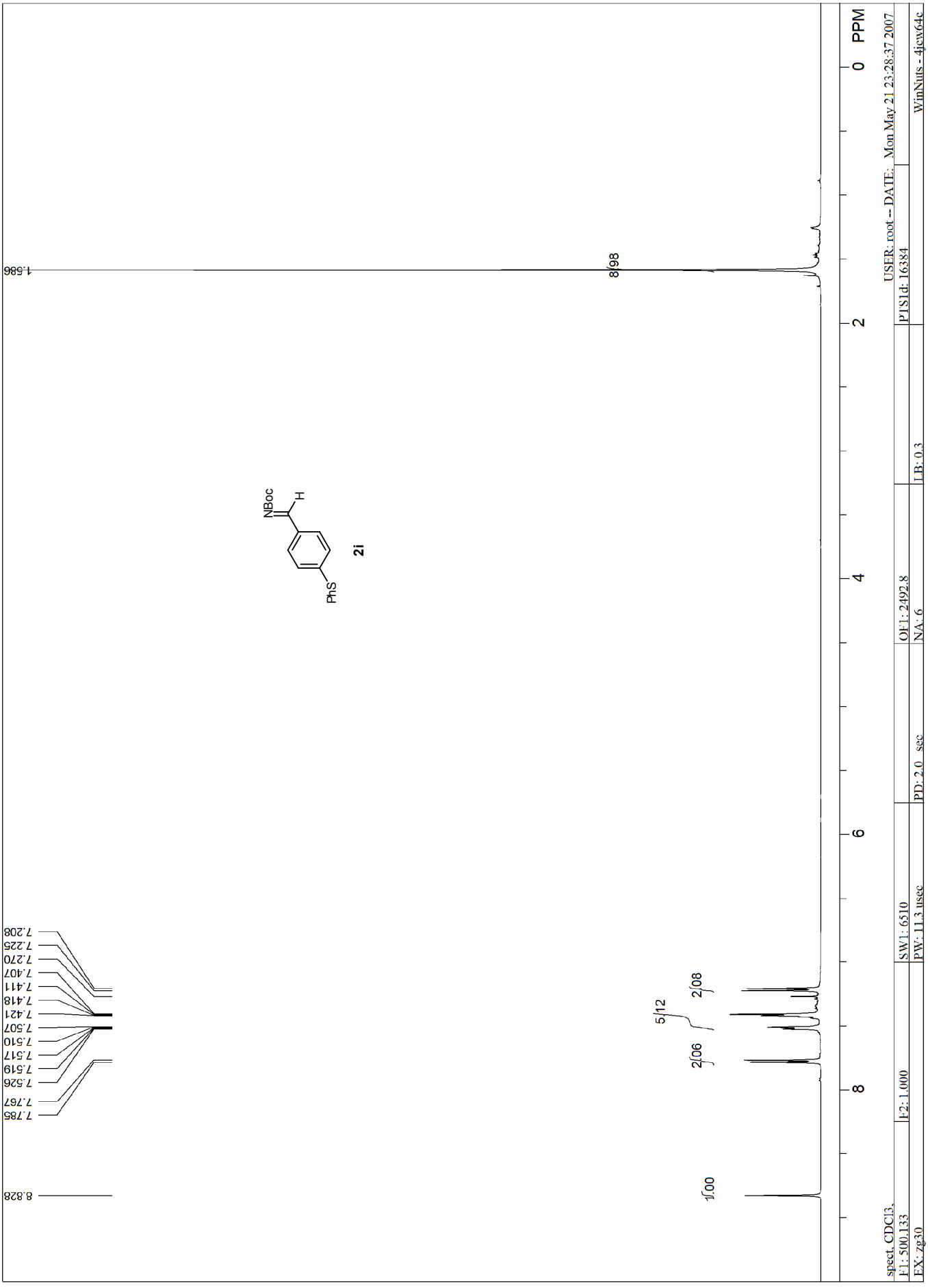

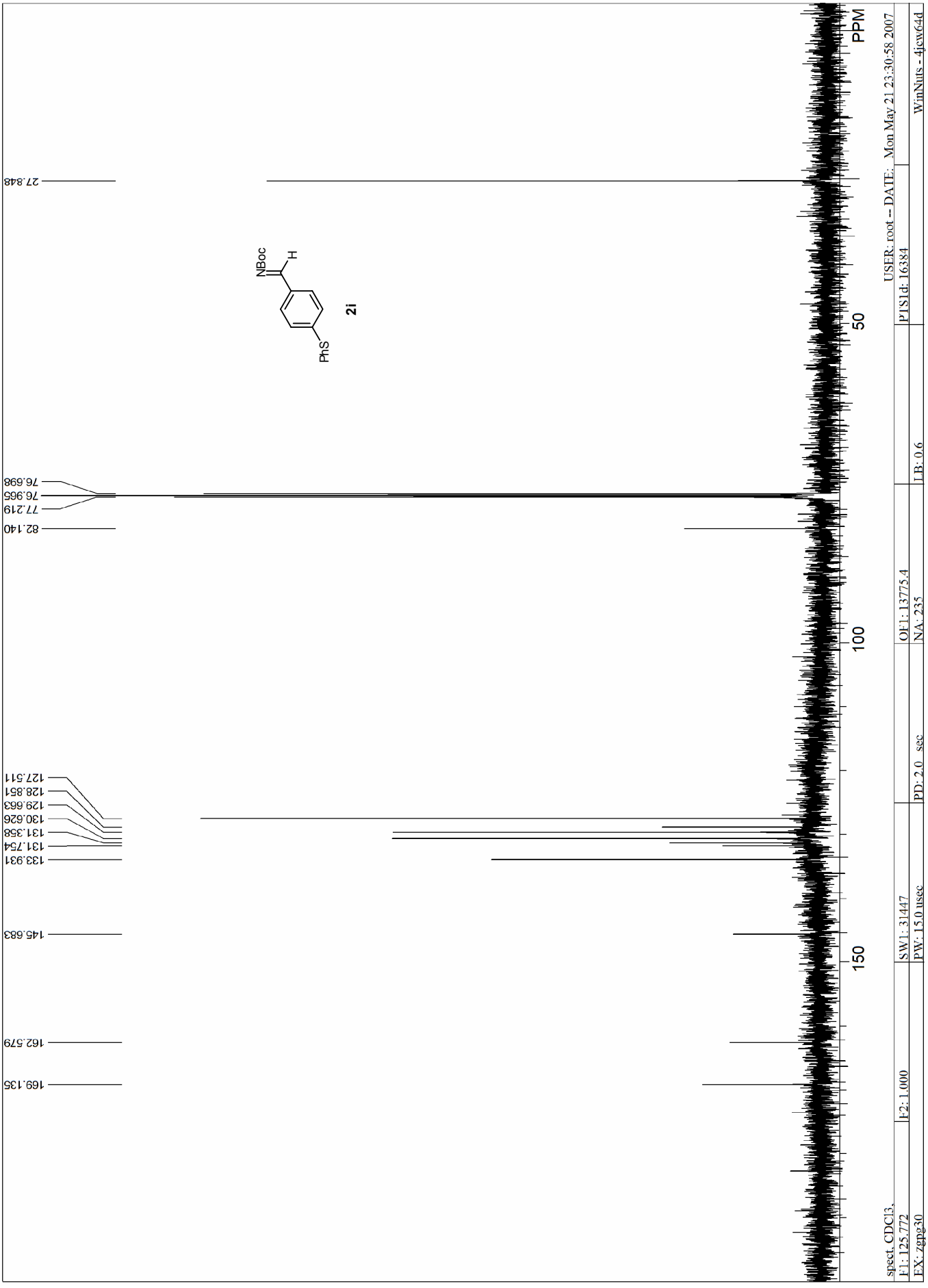

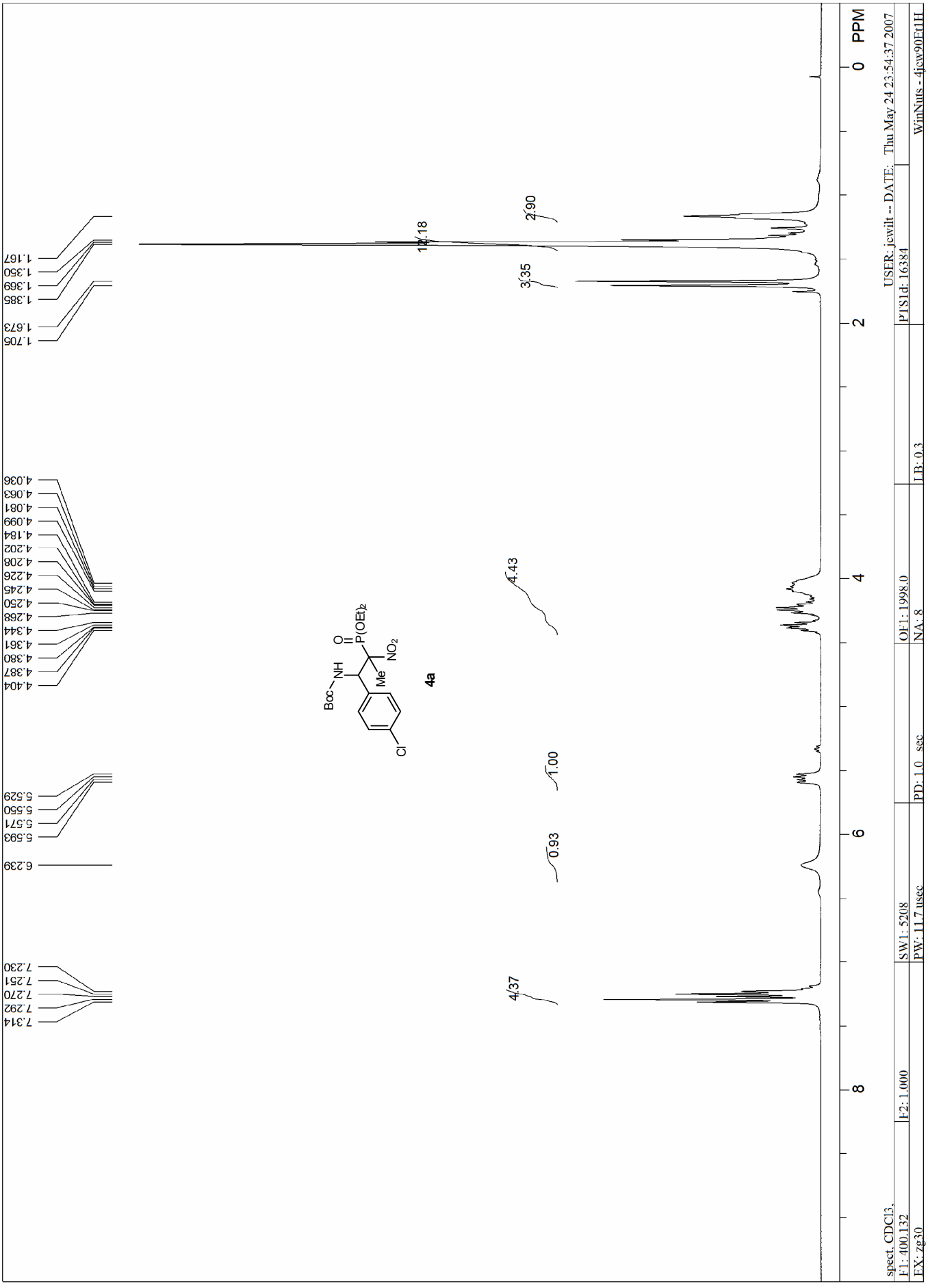

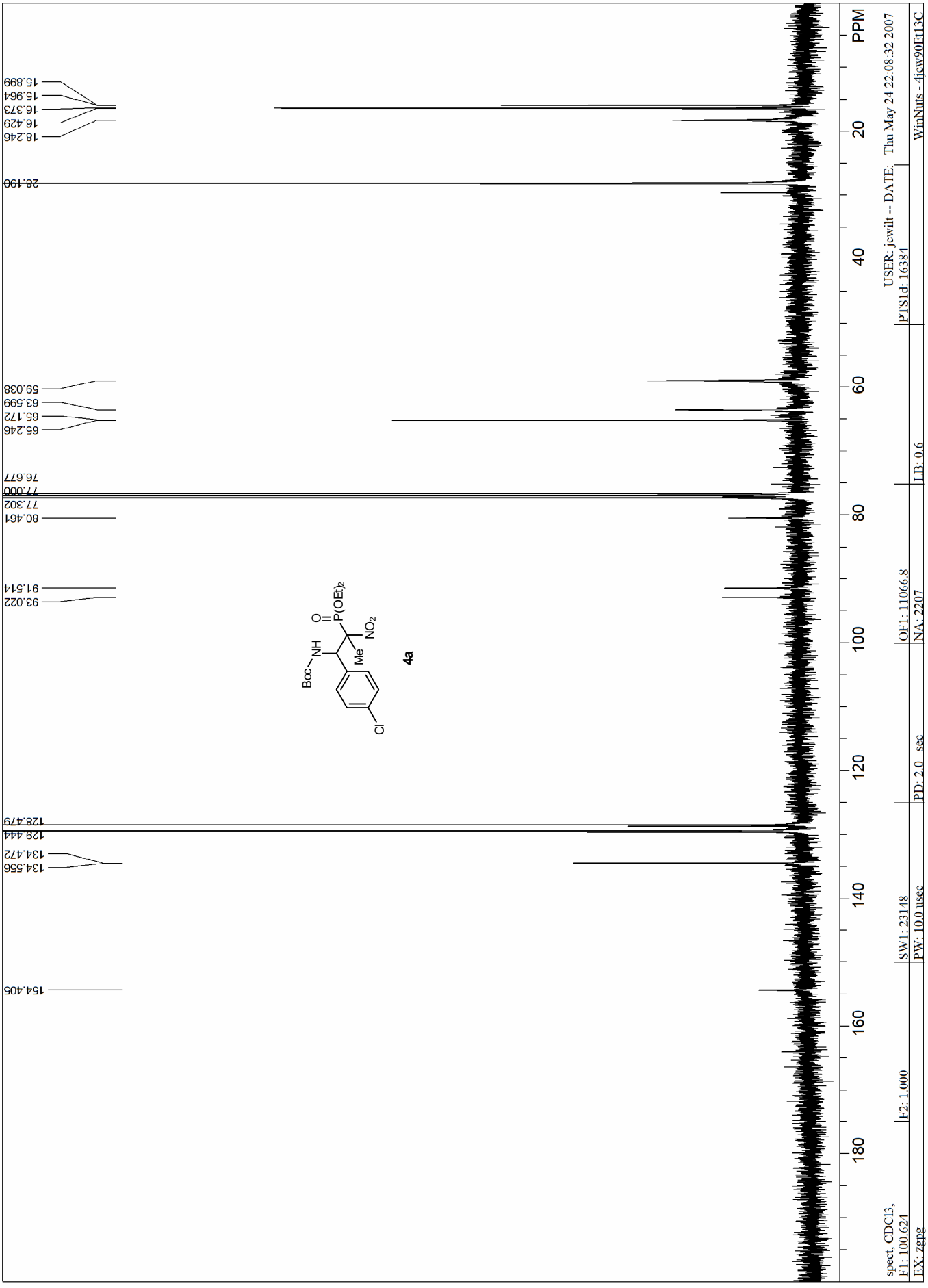

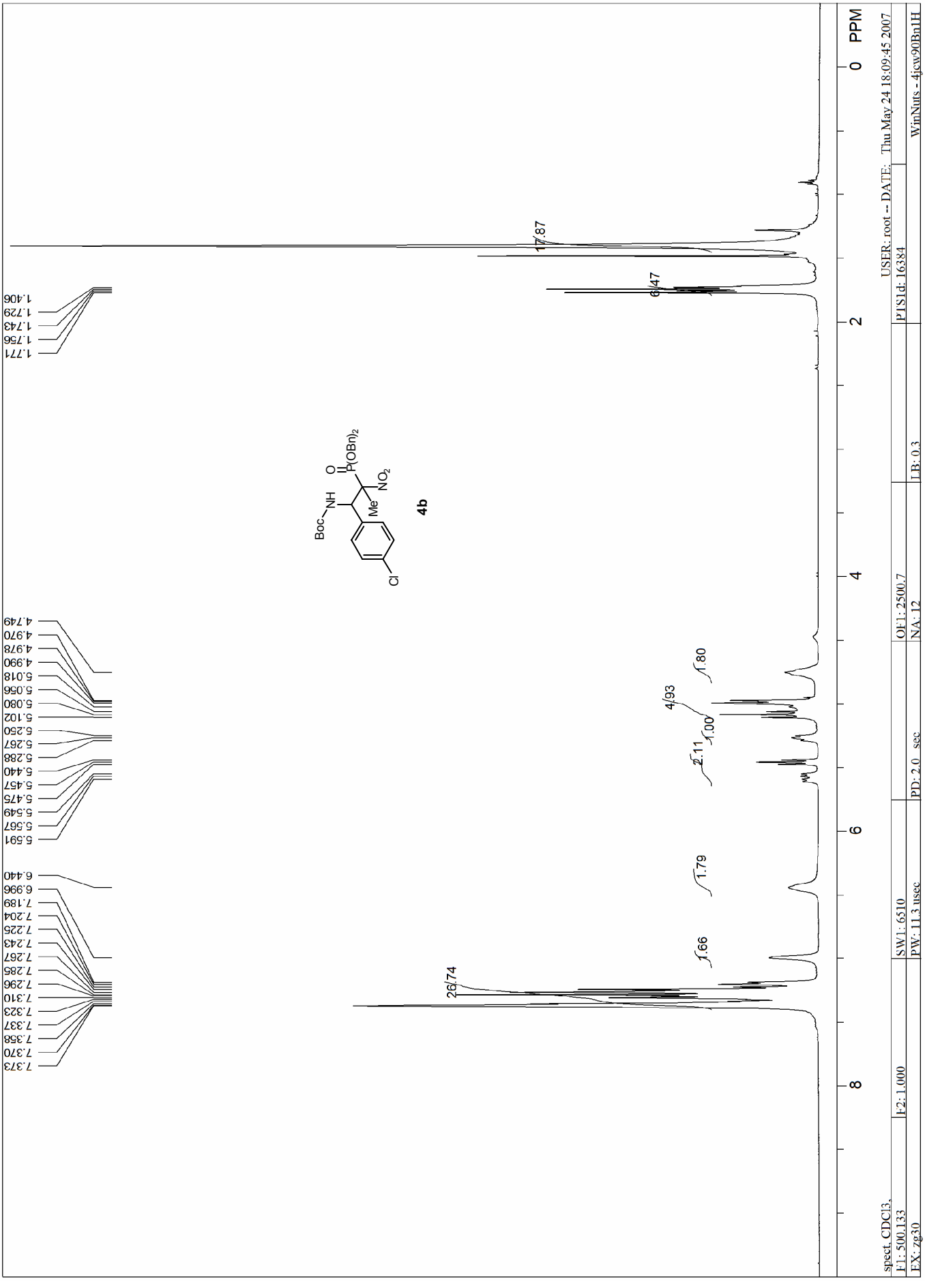

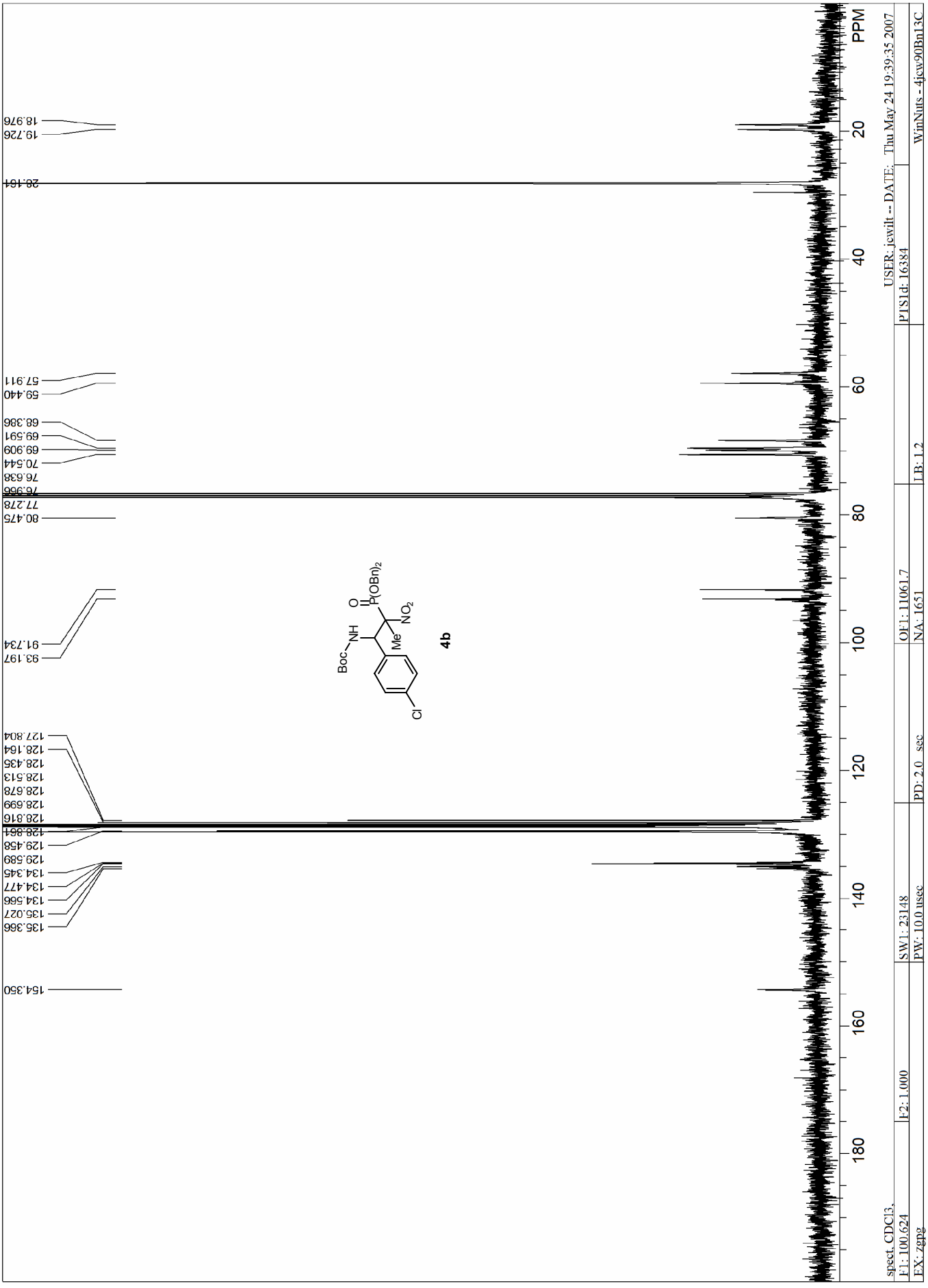

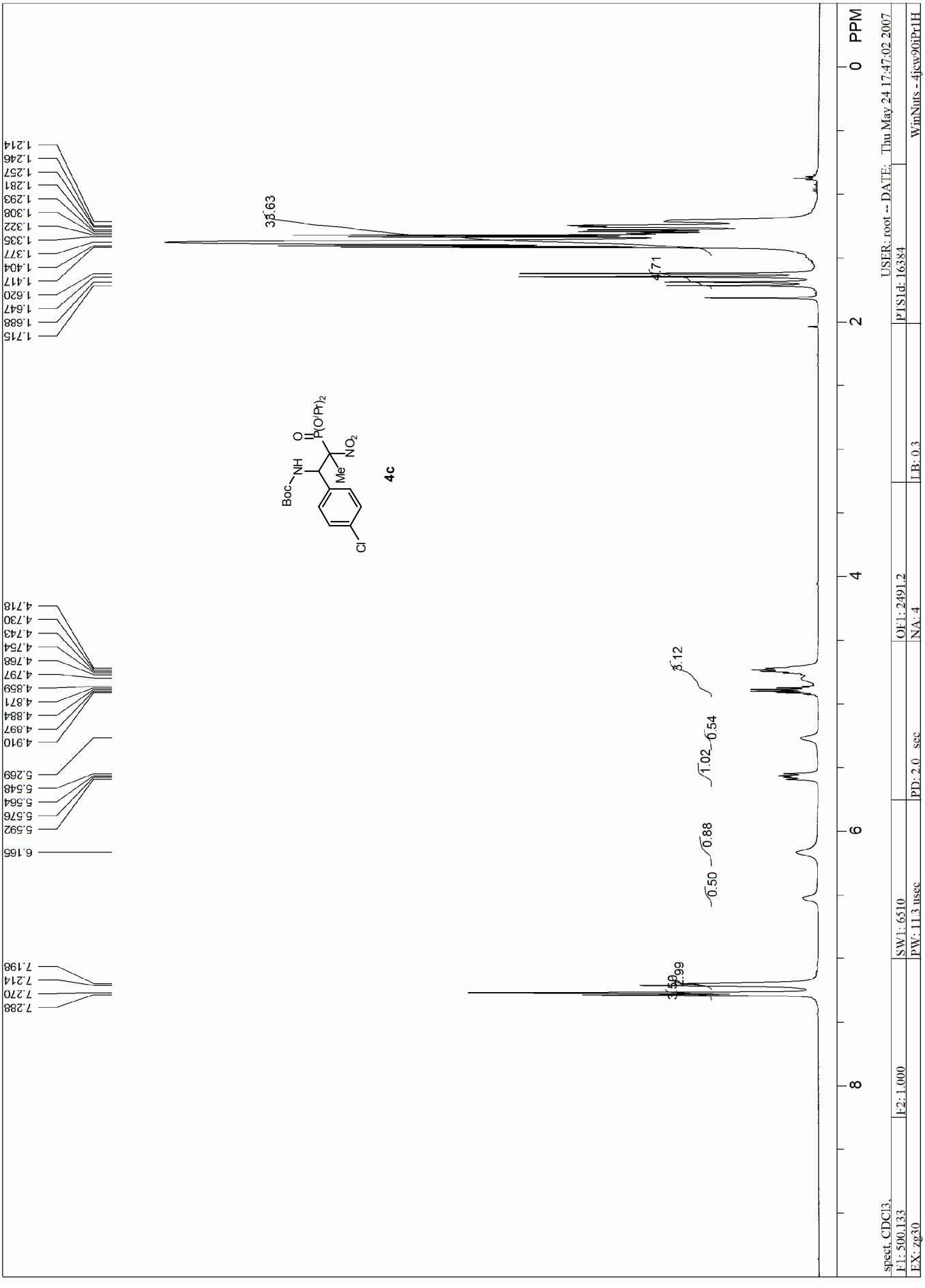

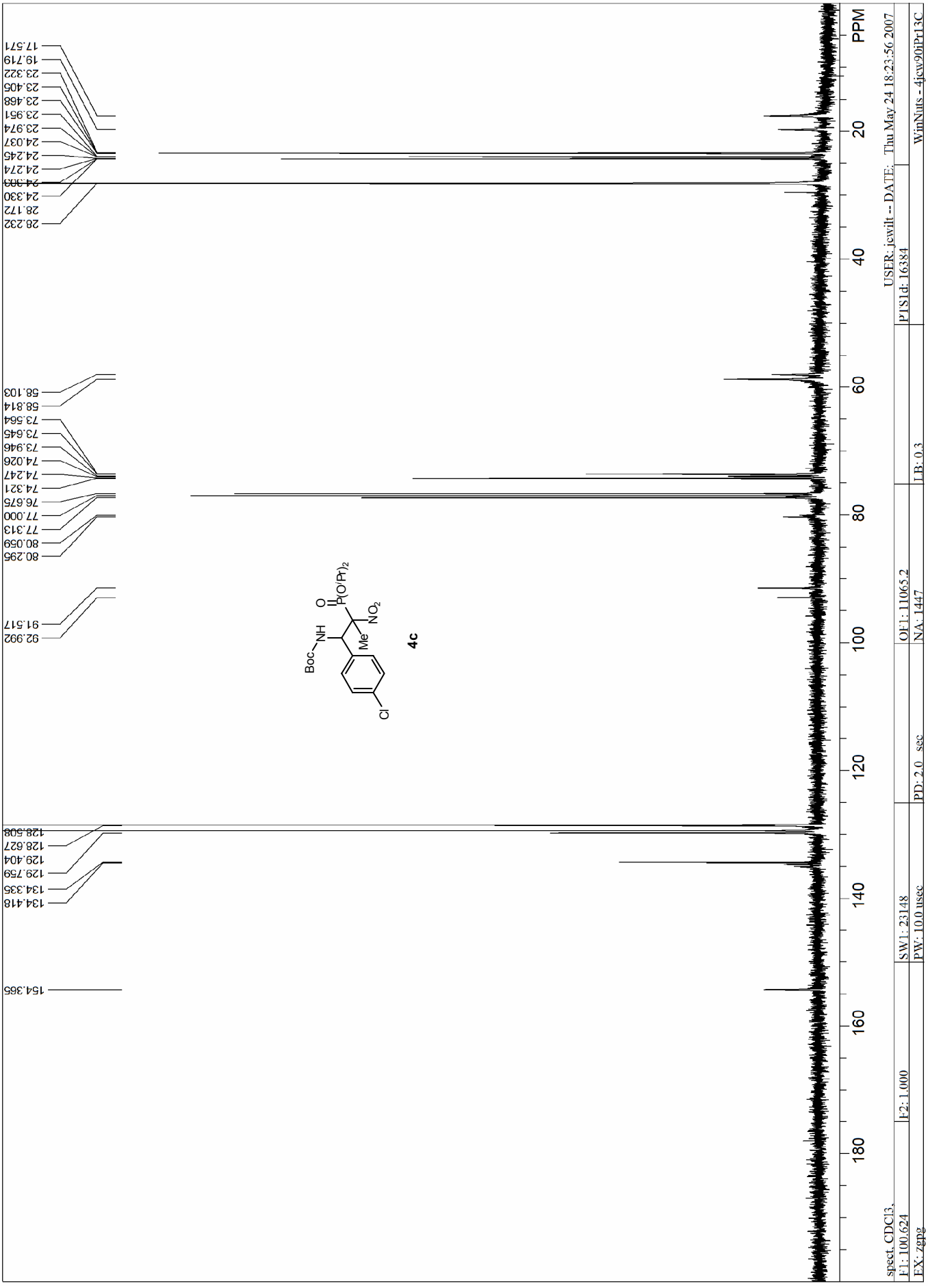

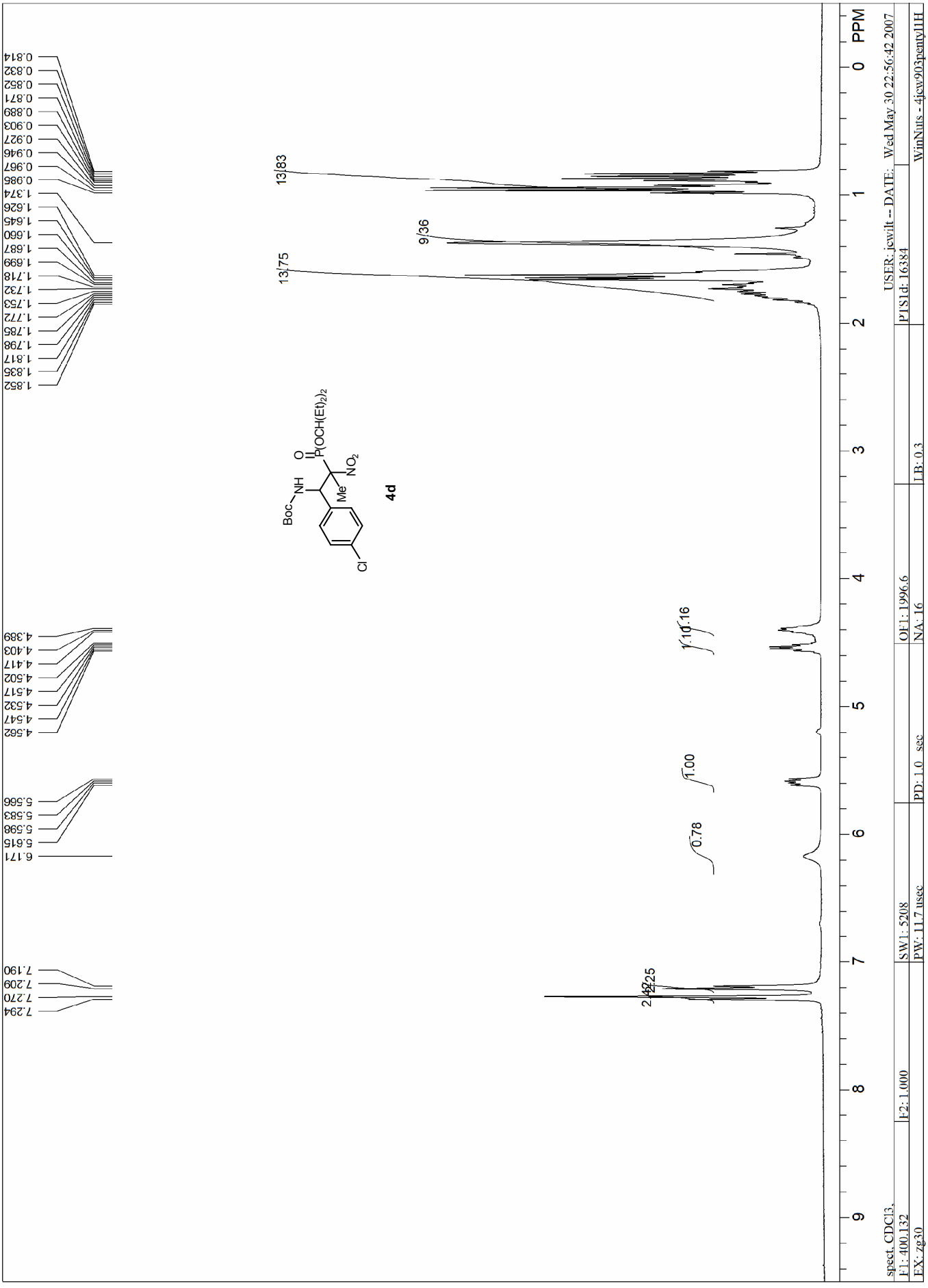

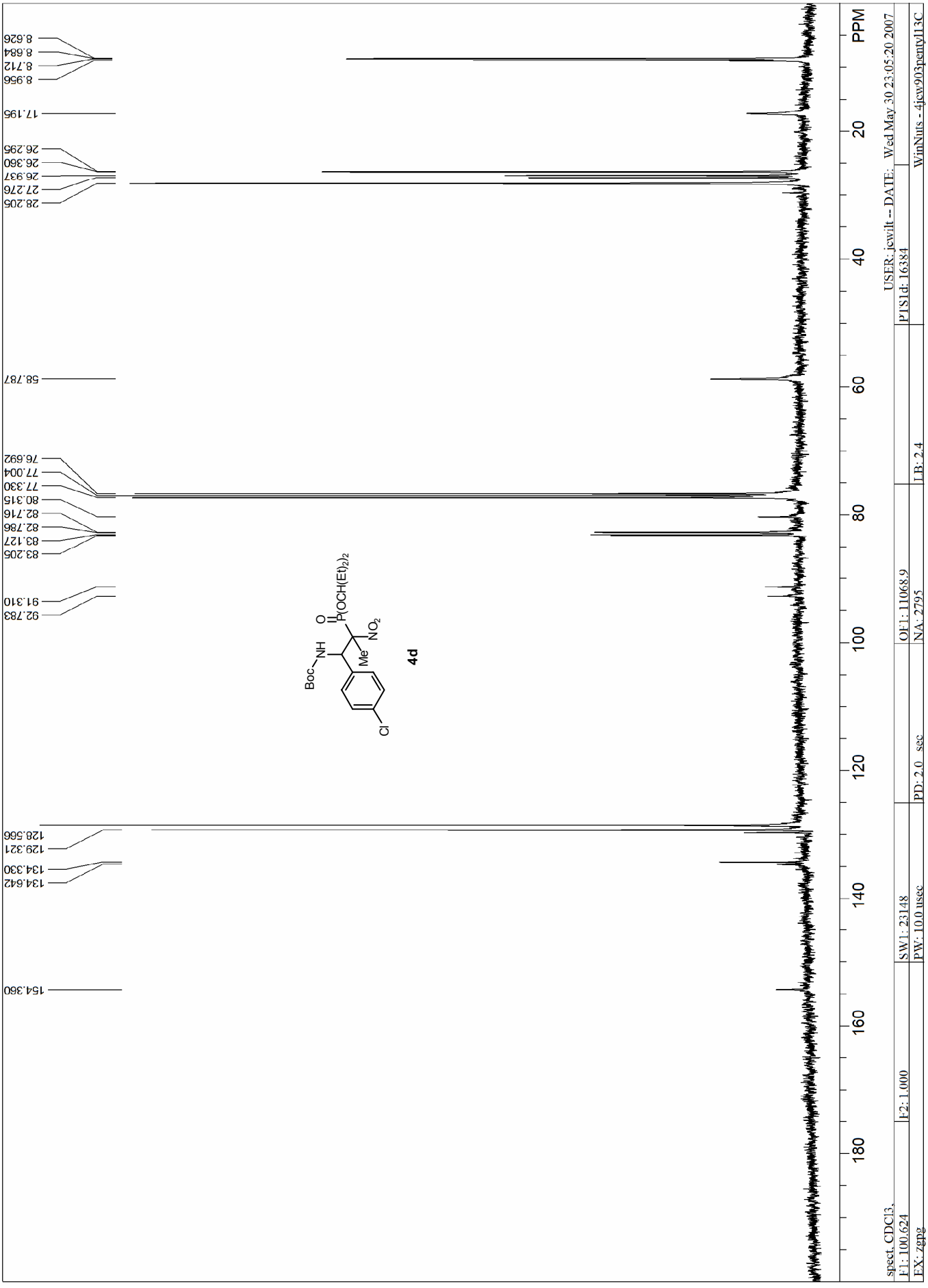

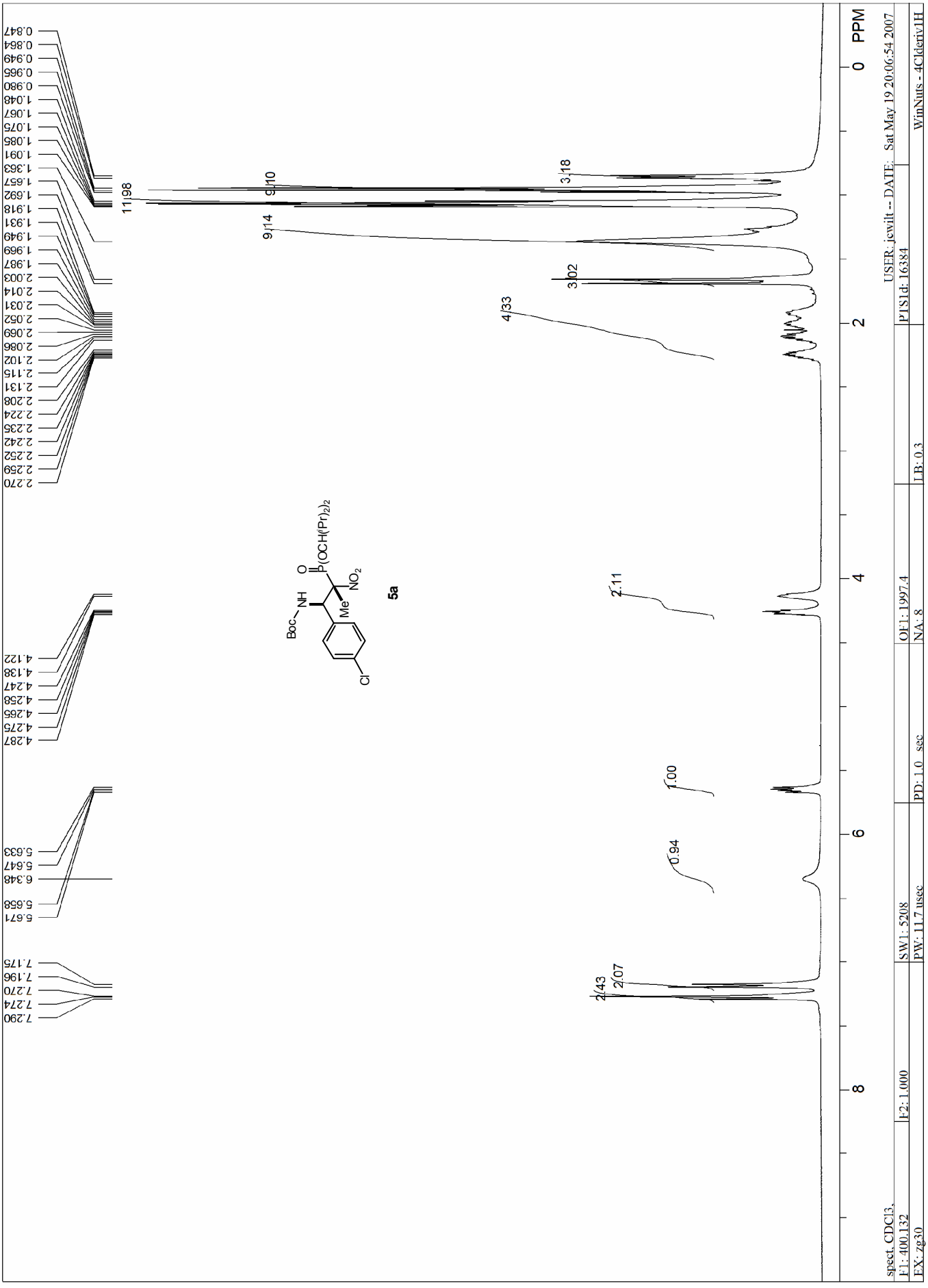
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P(OCH(iPr)2)2
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NO2
Cl
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PPM
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6
8
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EX: zg30
F2: 1.000
SW1: 5208
PW: 11.7 usec
PD: 1.0 sec
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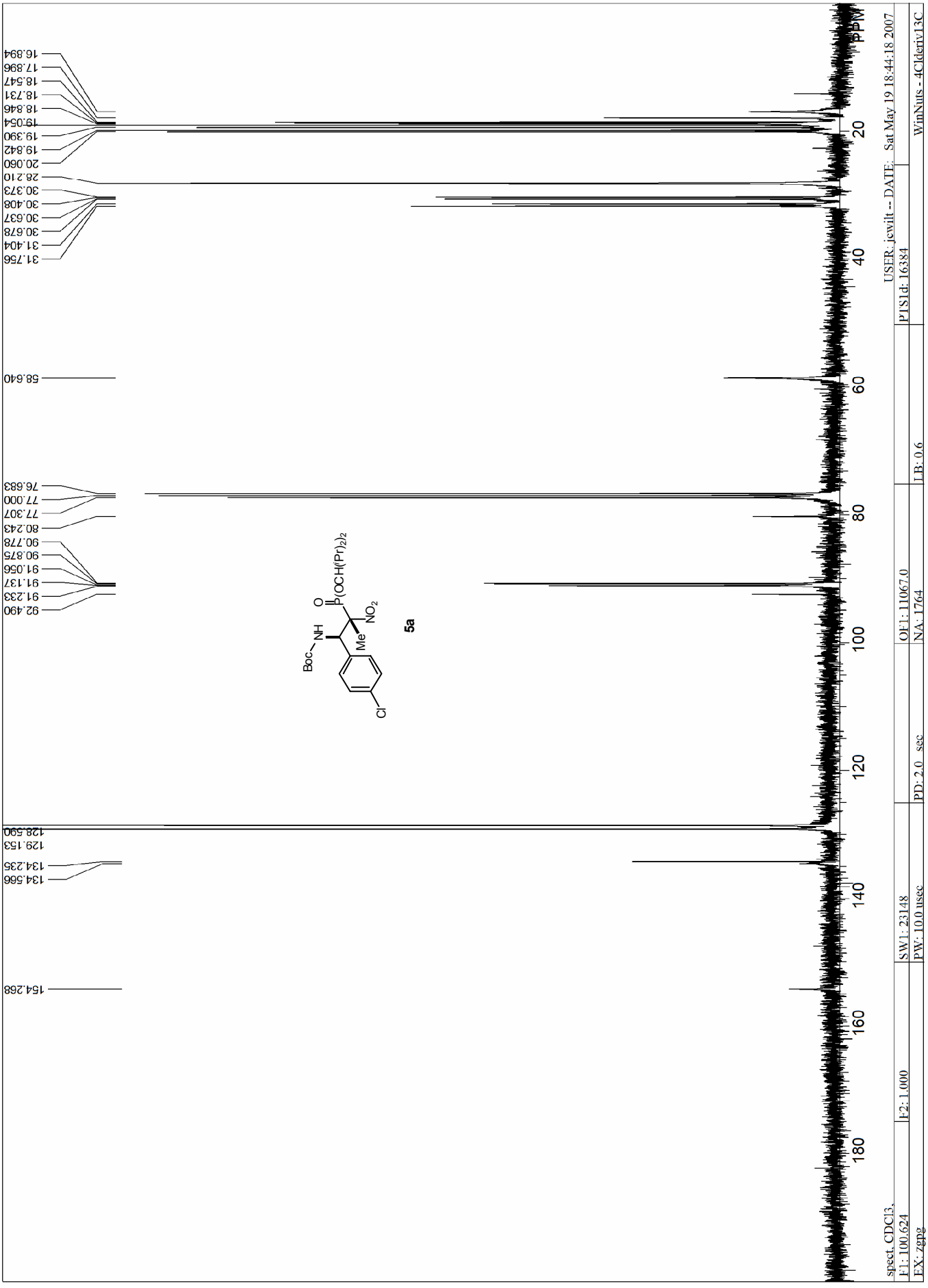
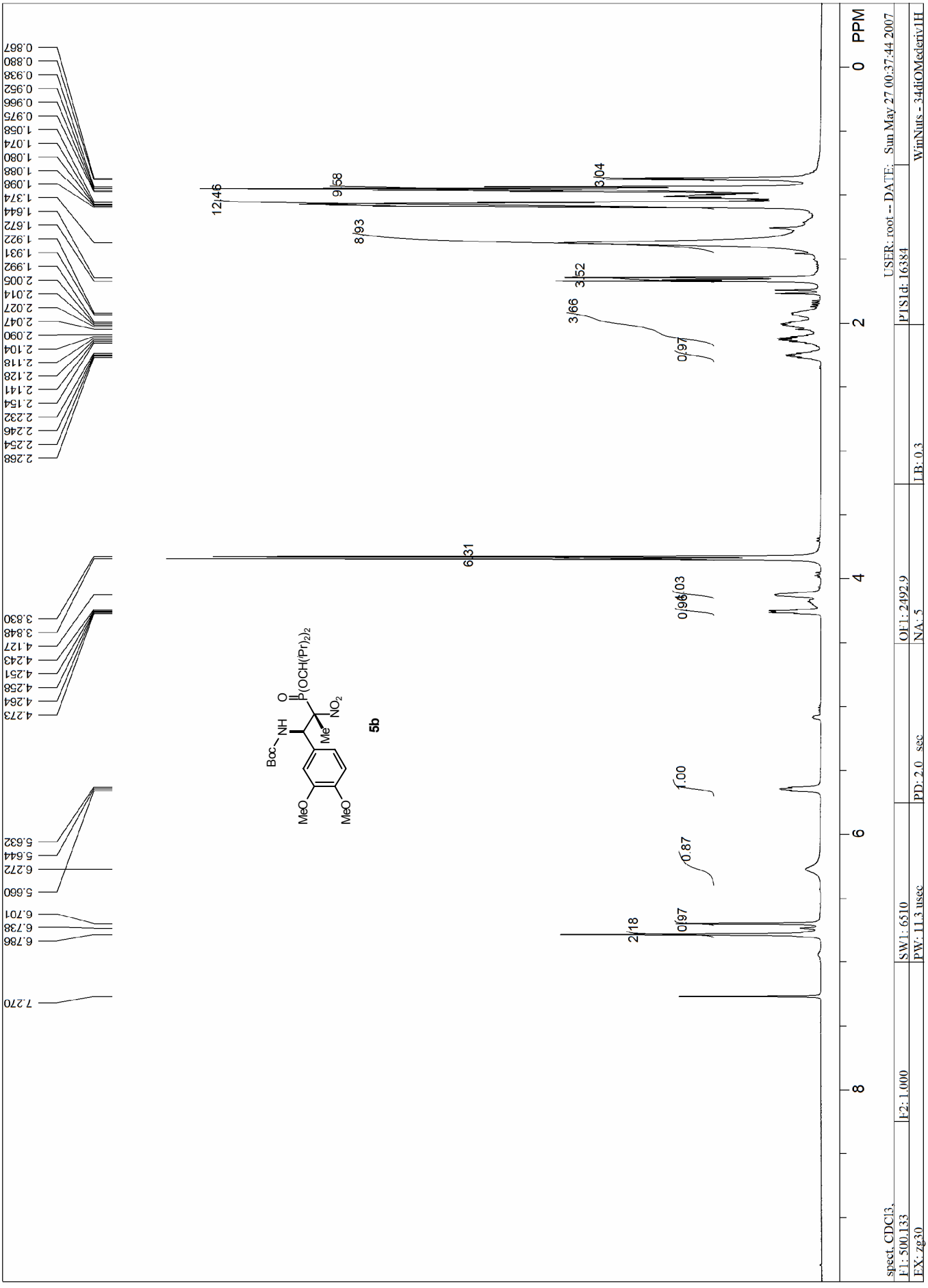
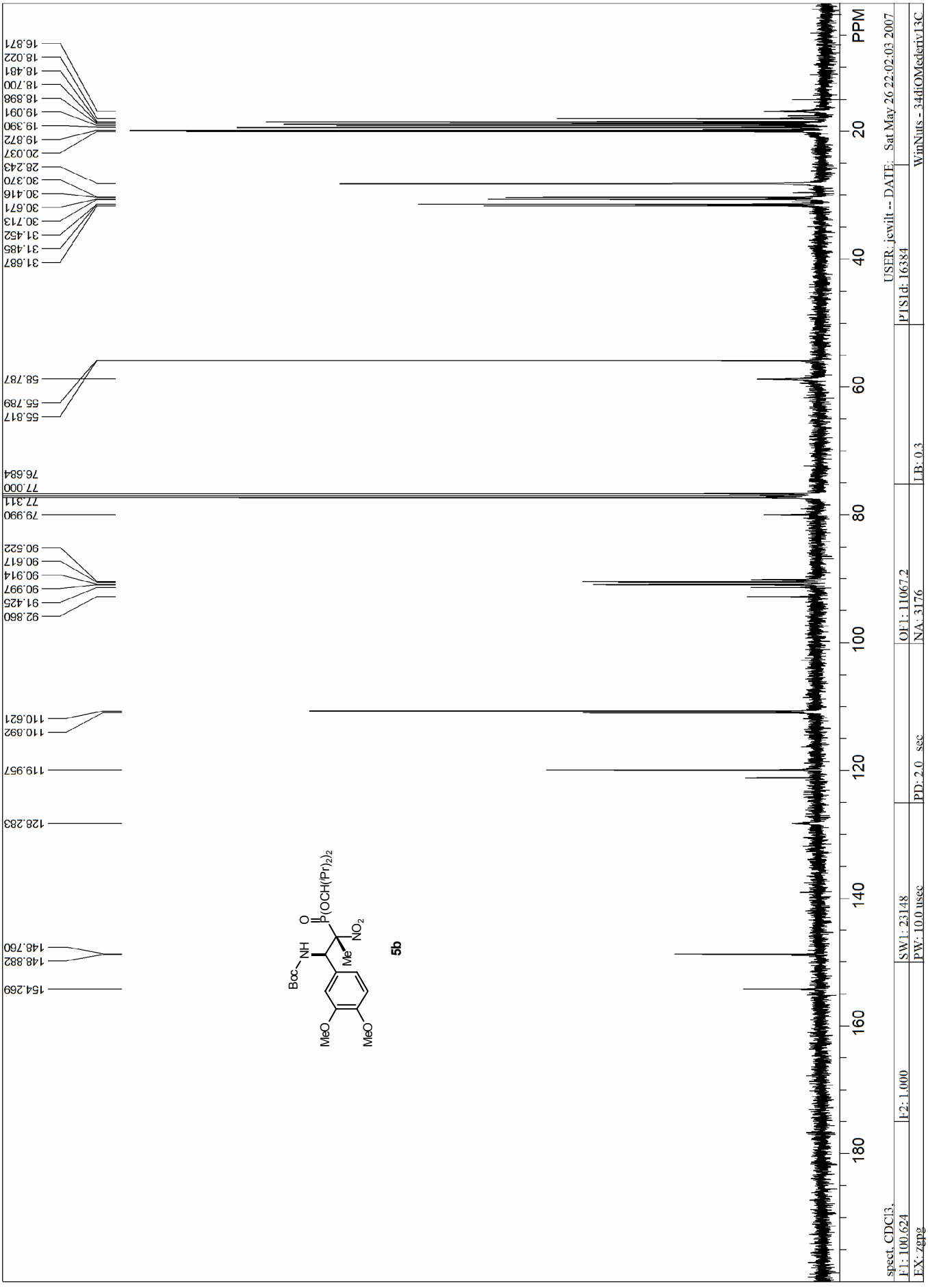
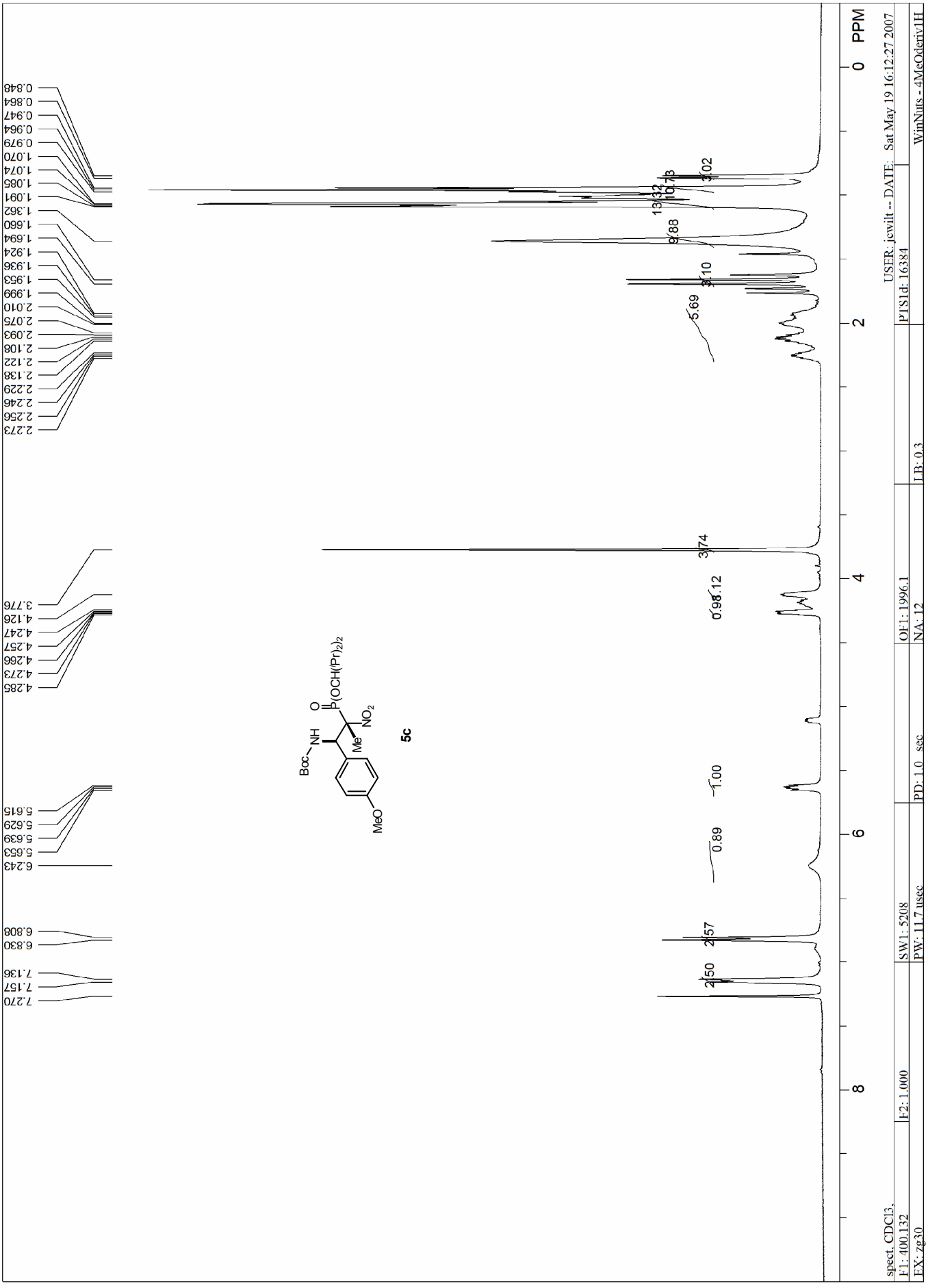
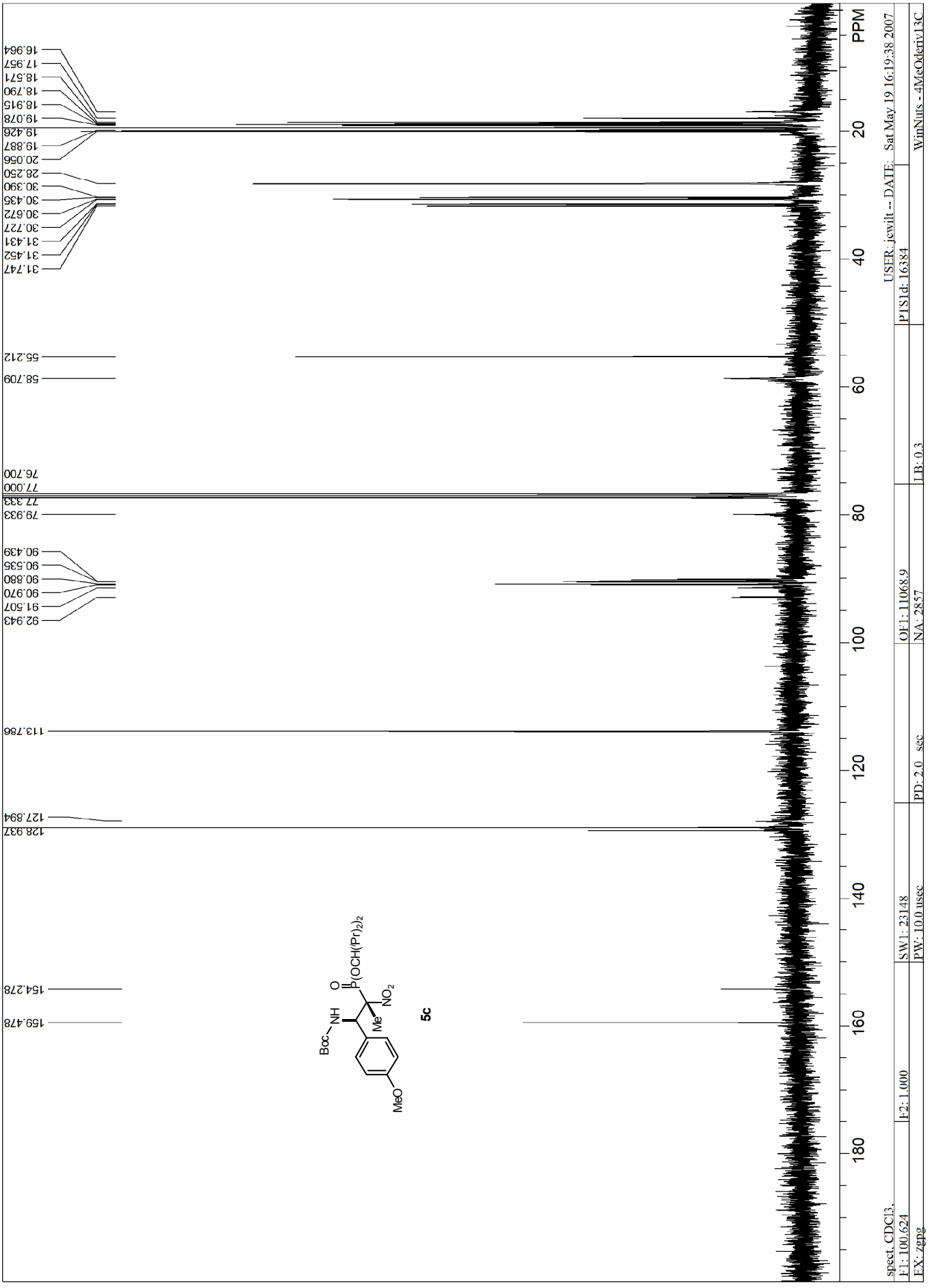
LB: 0.3
USER: jcwilt -- DATE: Sat May 19 20:06:54 2007
P1S1d: 16384
WinNuts - 4Clderiv1H

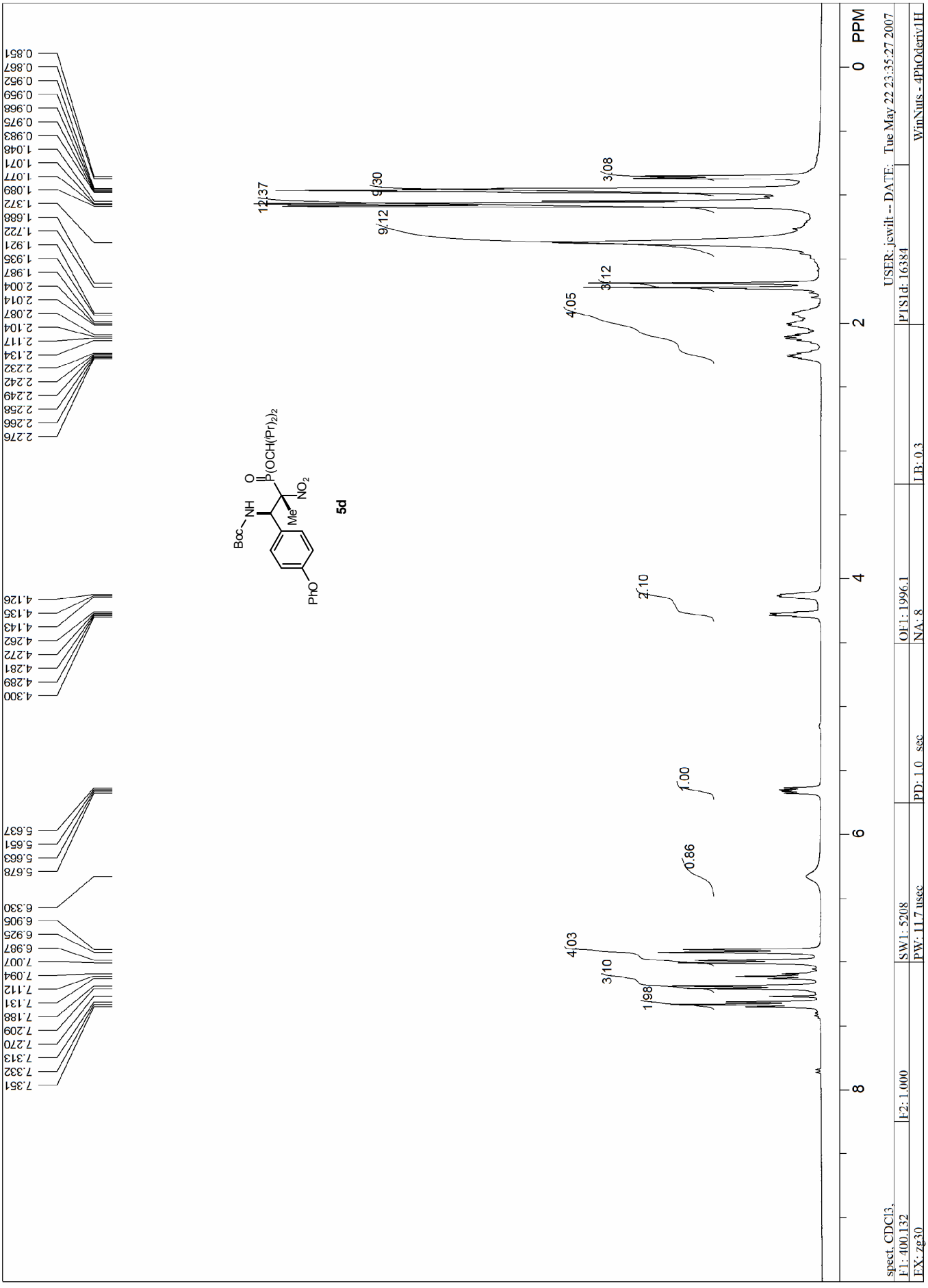


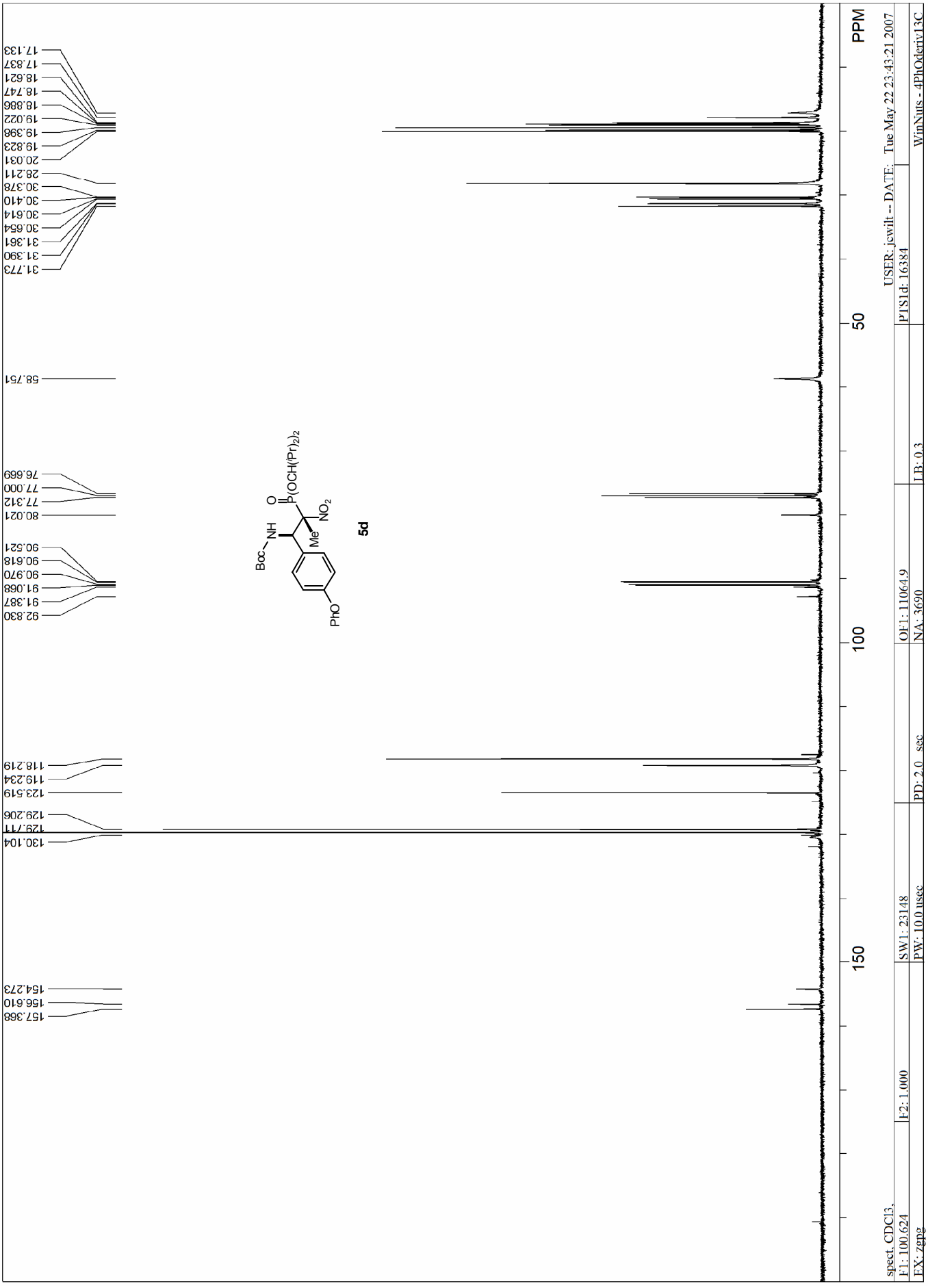


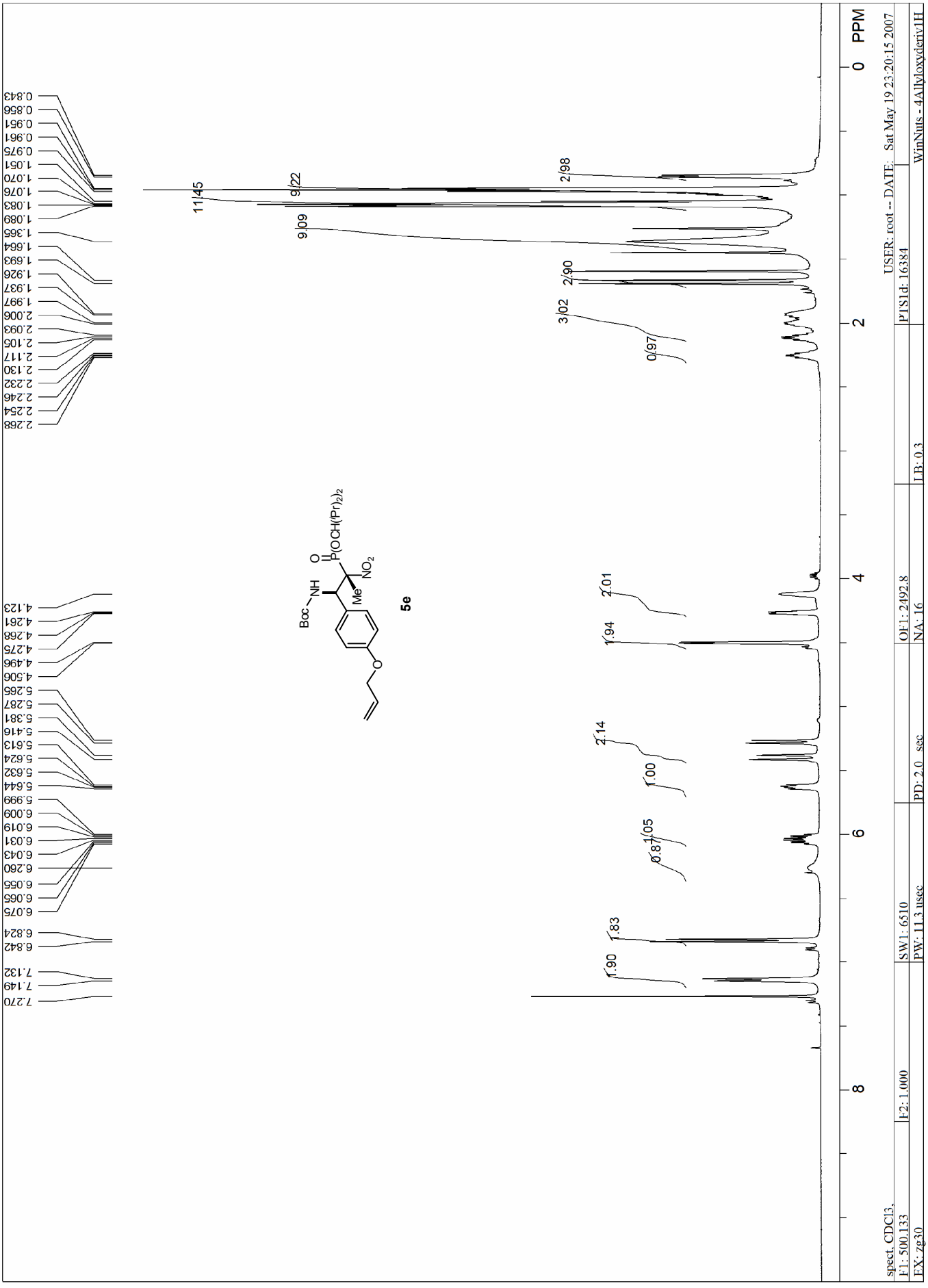


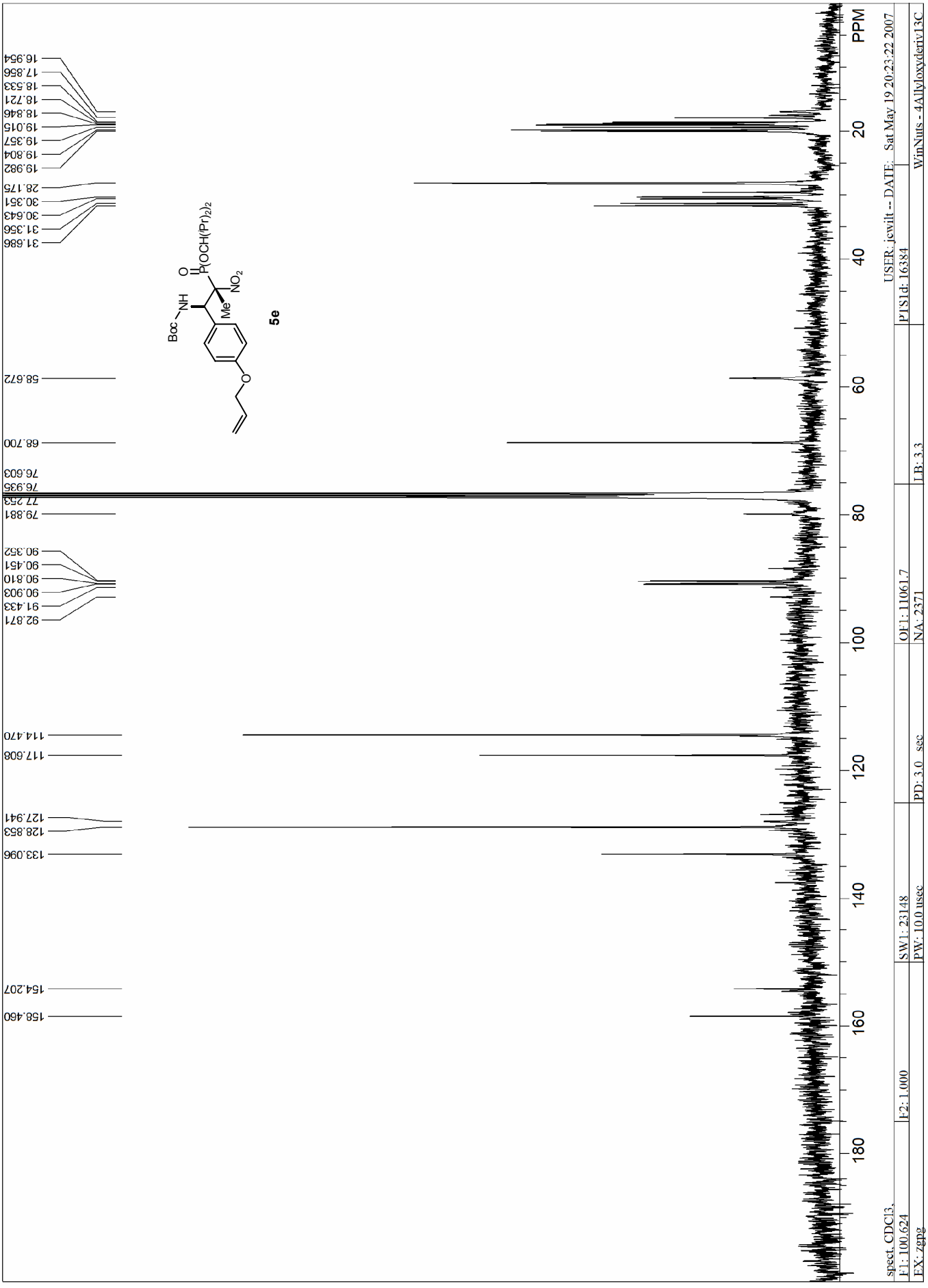


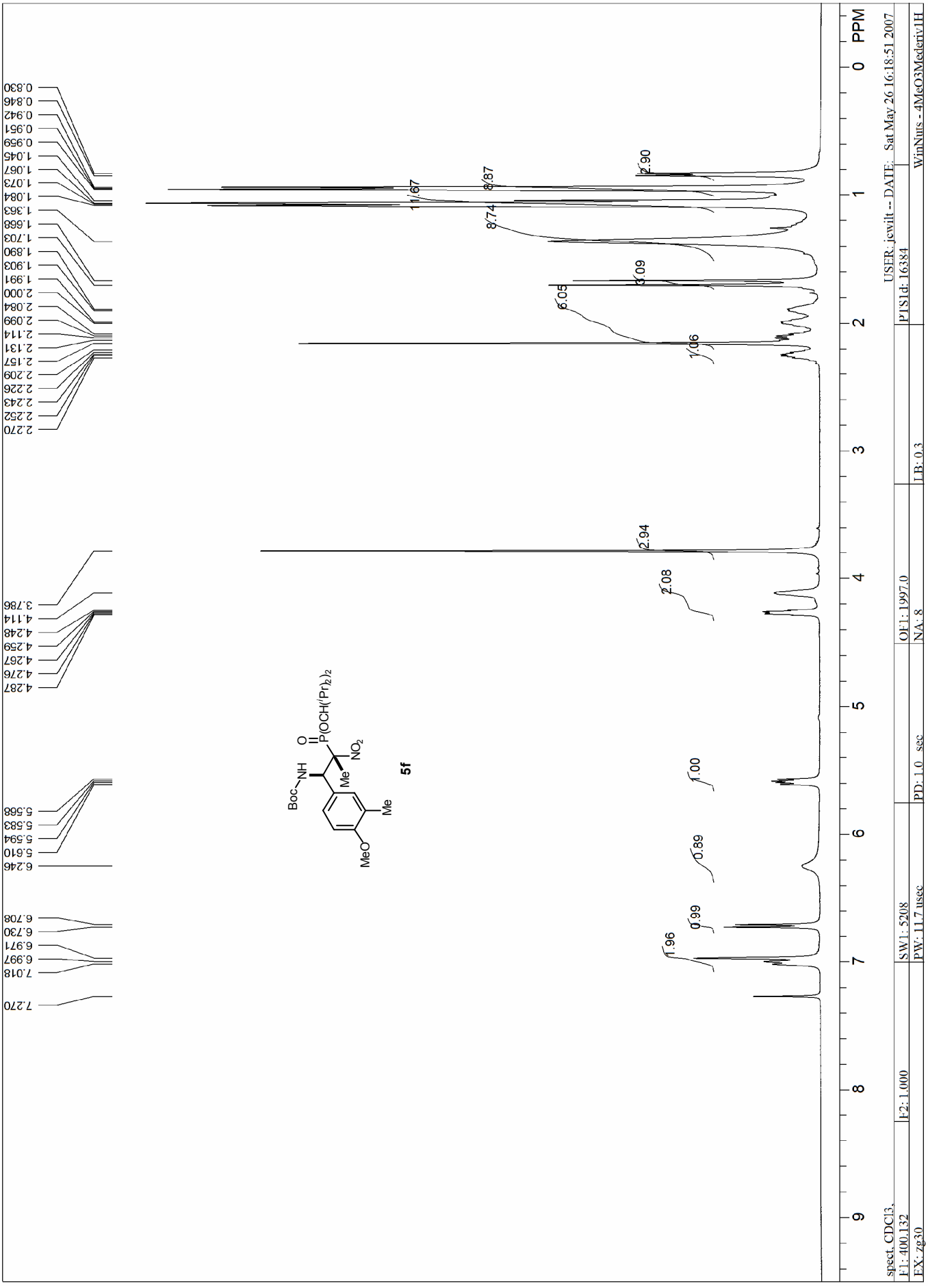








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6.246
6.708 6.730 6.971 6.997
7.018
7.270
1.67 8.87 8.74 2.90 3.09 6.05 1.06 2.94 2.08 1.00 0.89 0.99 1.96
Boc NH O P(OCH(iPr)2)2 Me NO2 Me MeO
5f
USER: jcwilt -- DATE: Sat May 26 16:18:51 2007
spect. CDCl3.
F1: 400.132 | F2: 1.000 | SW1: 5208 | OF1: 1997.0 | P1S1d: 16384
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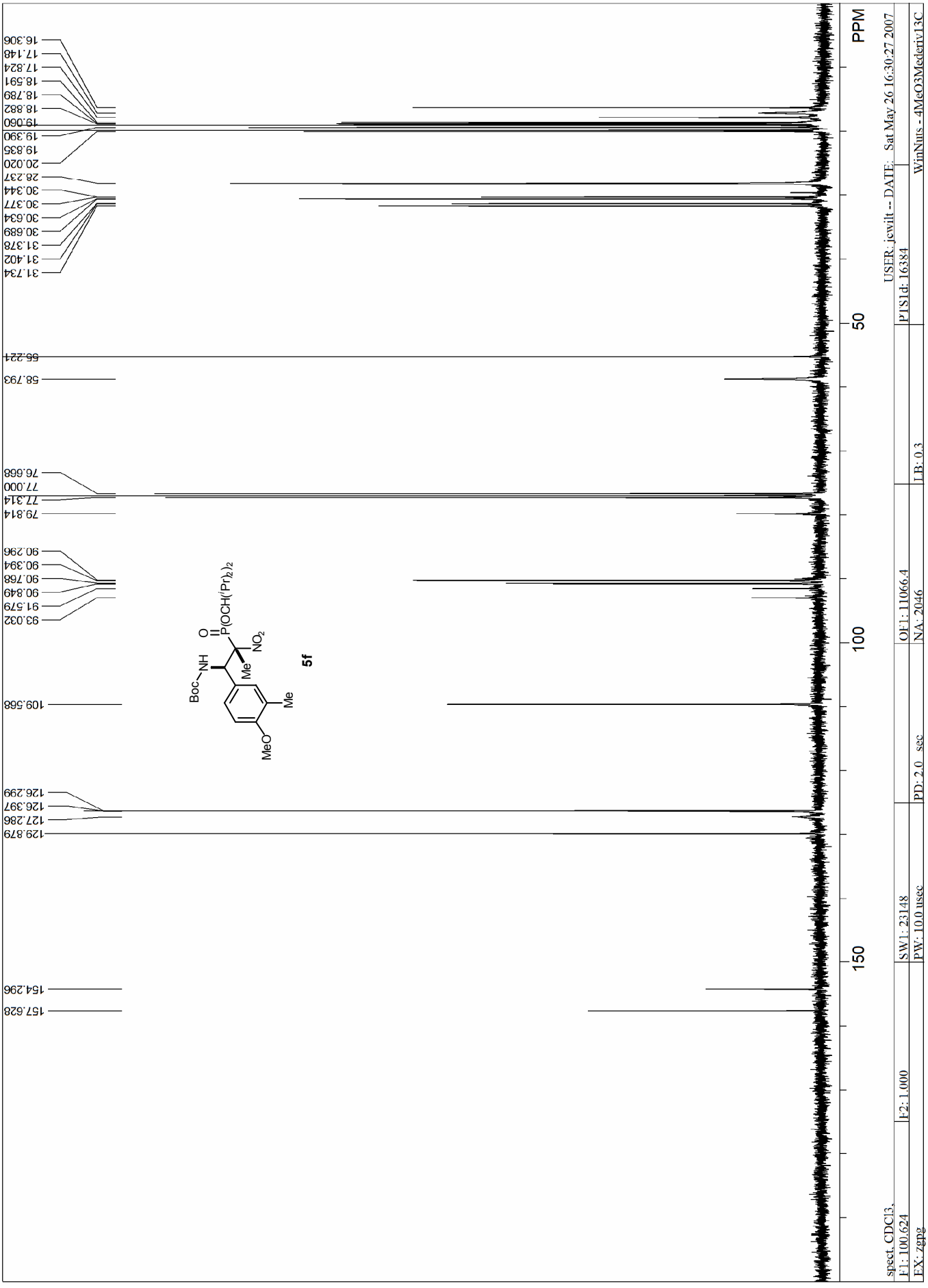

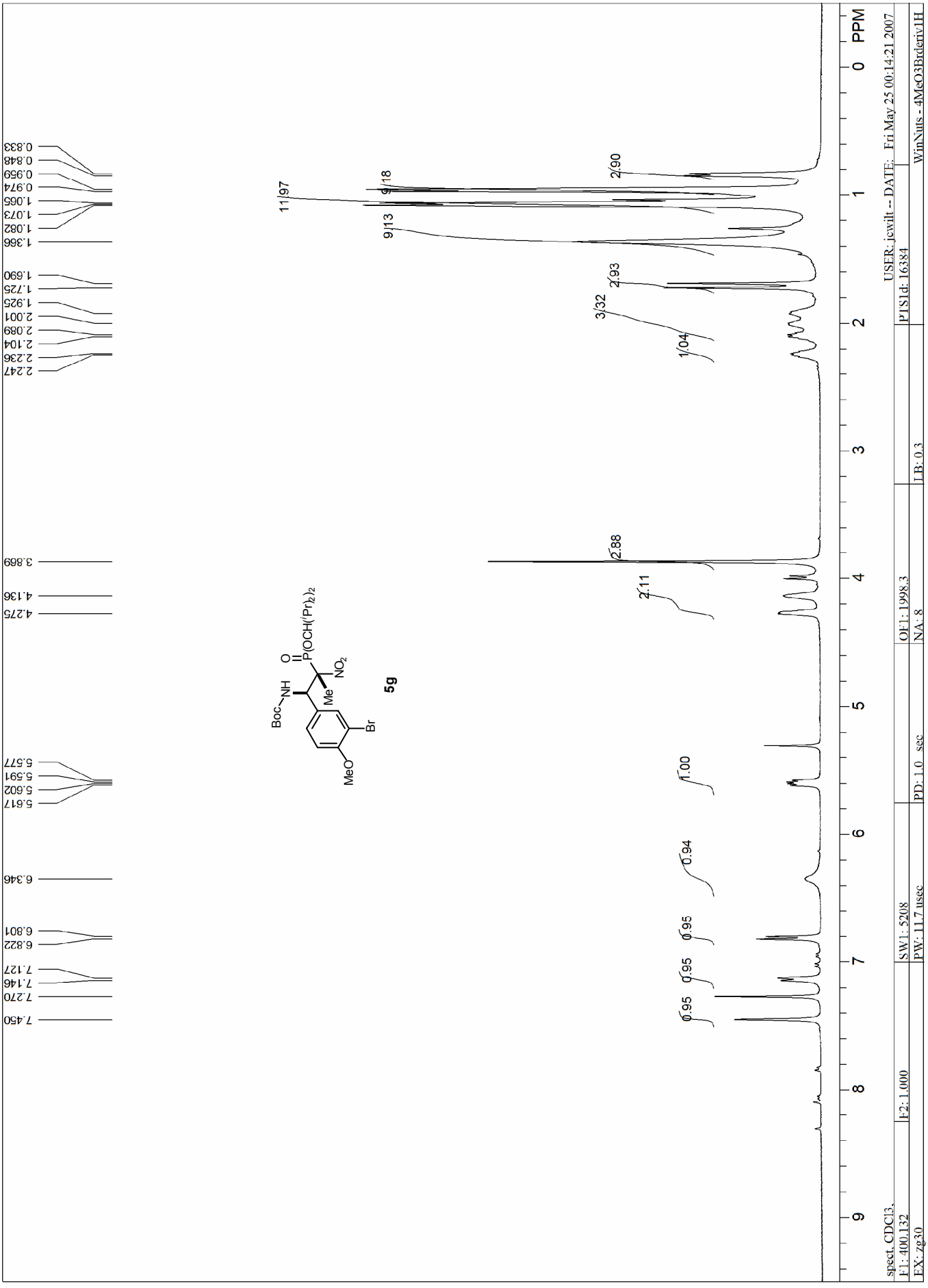

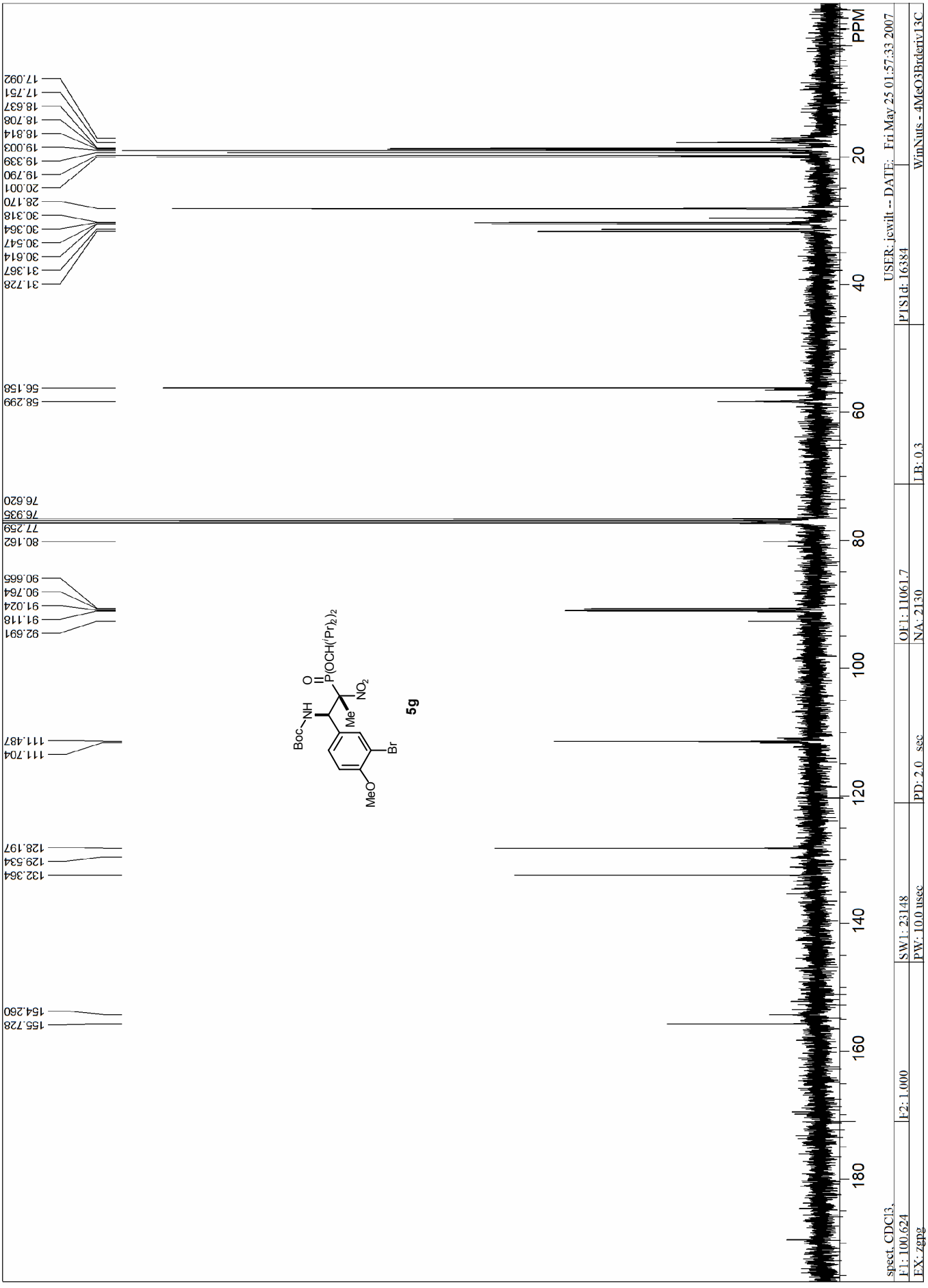

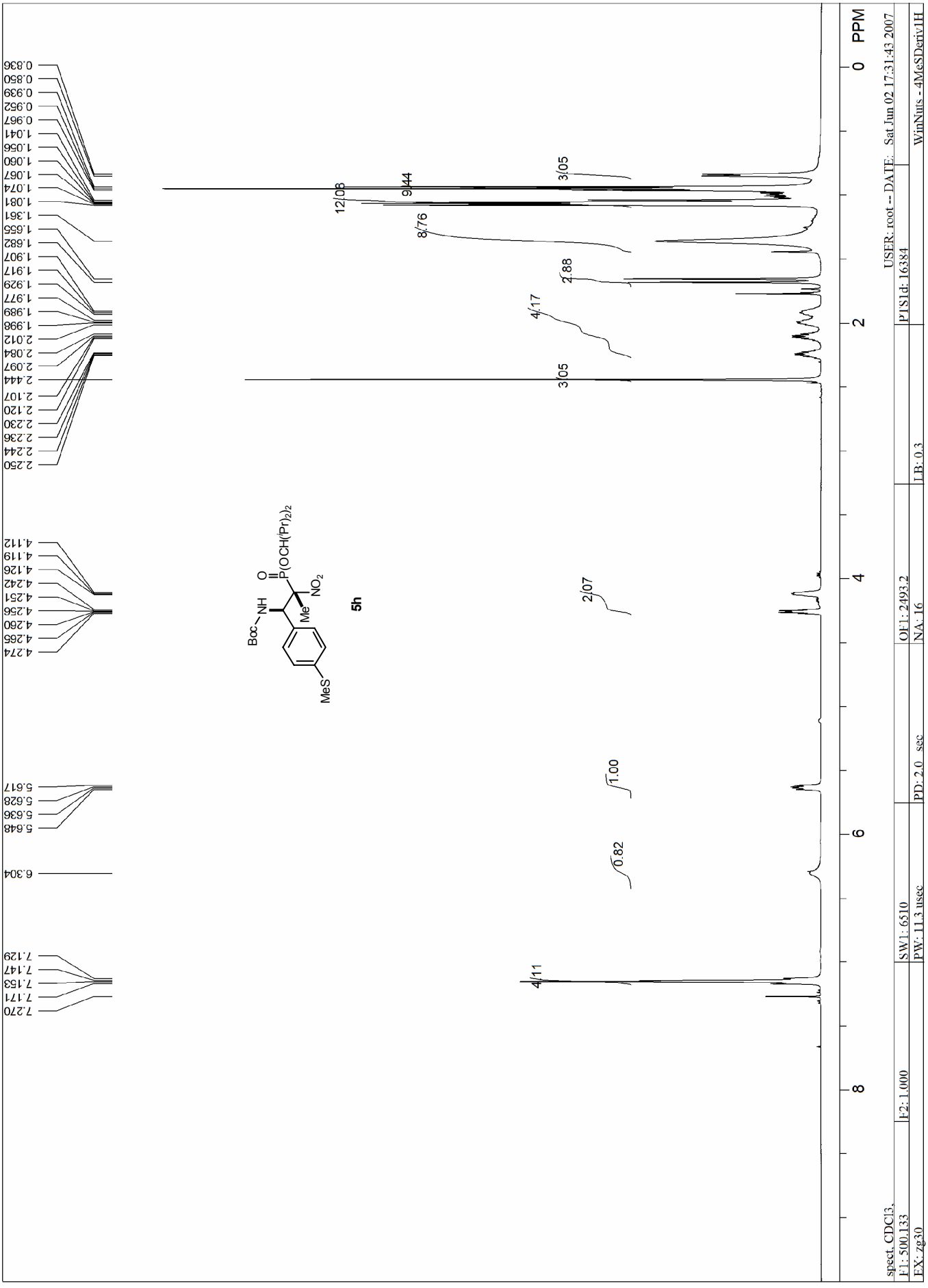

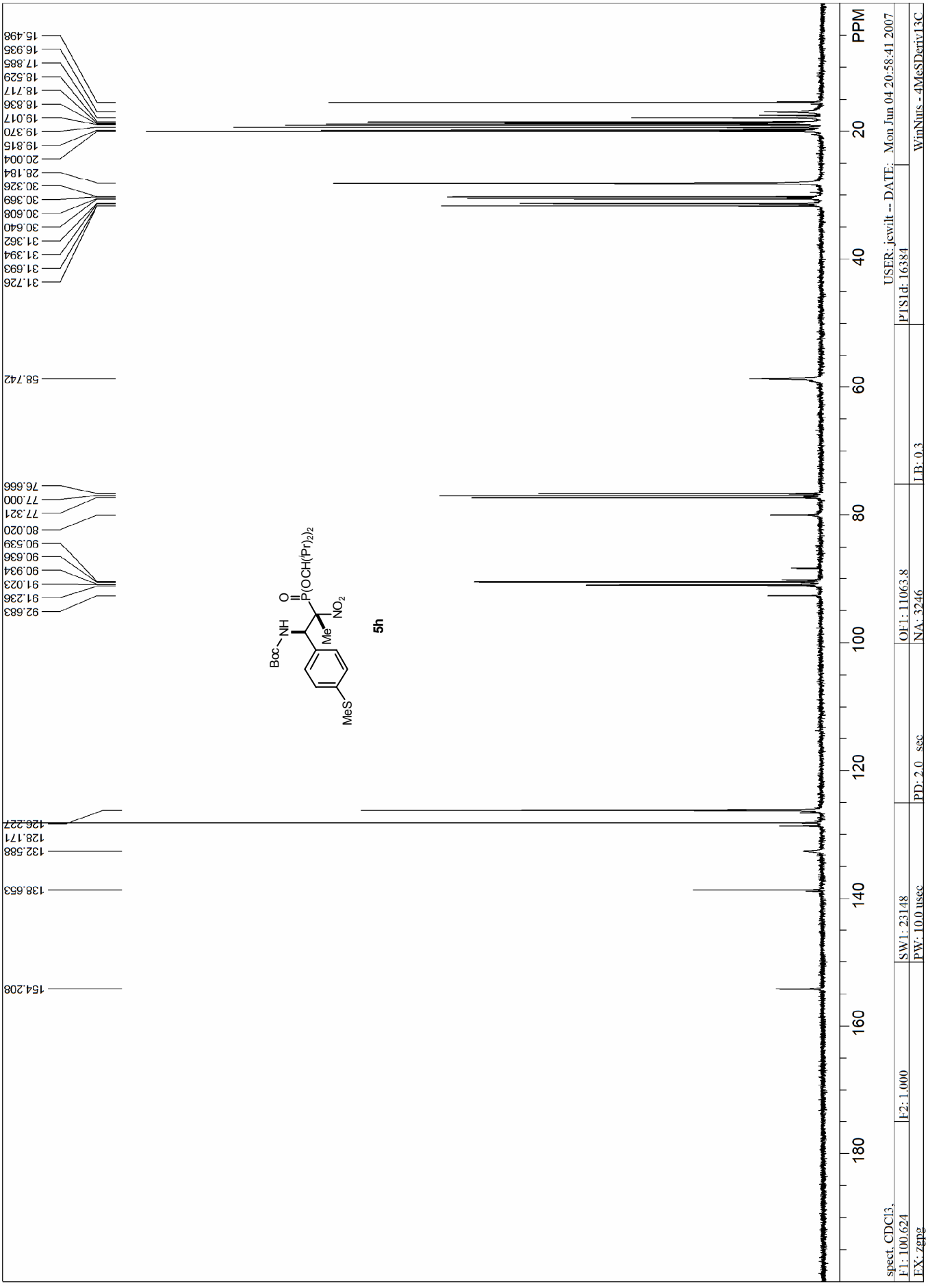

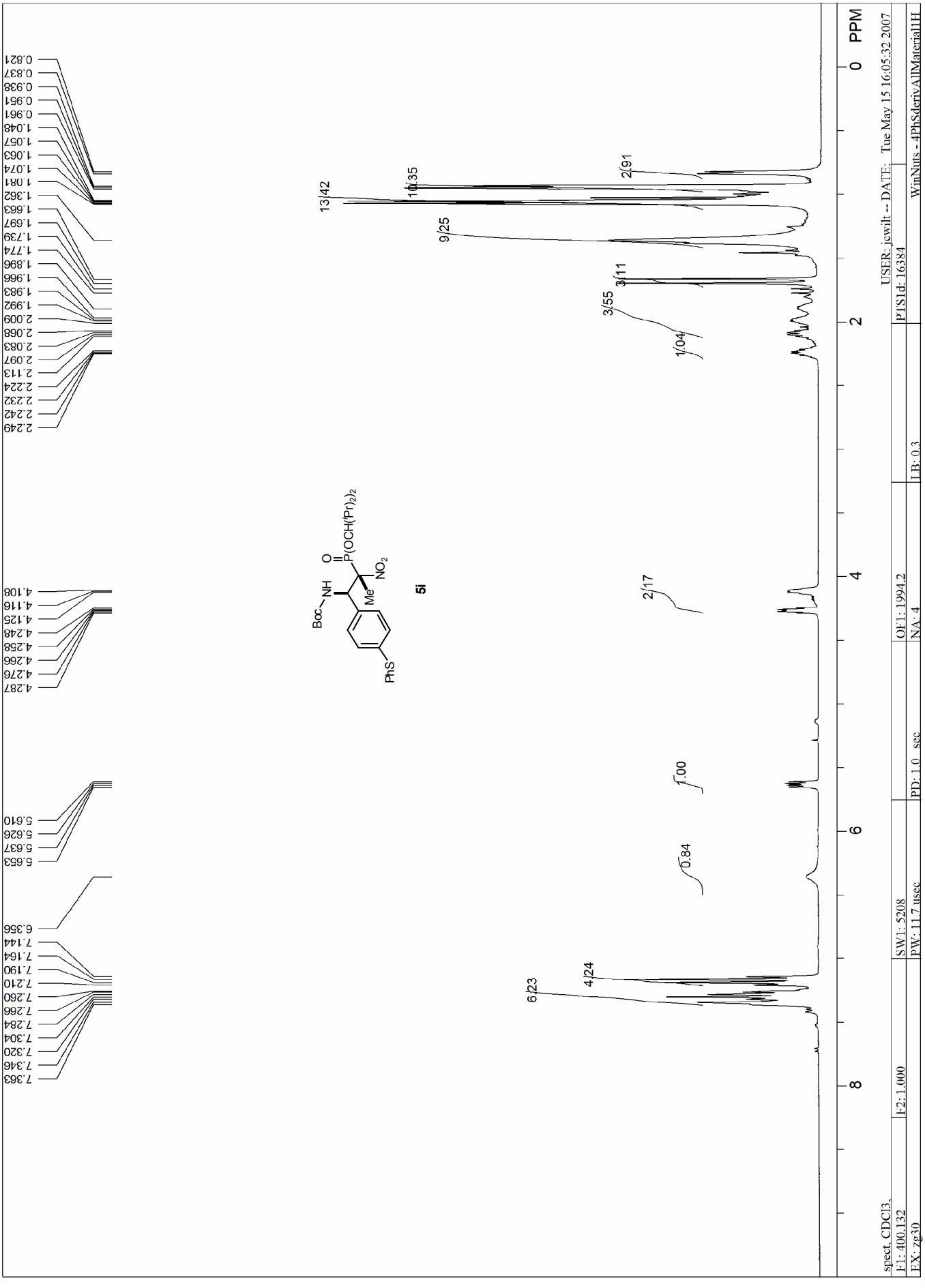

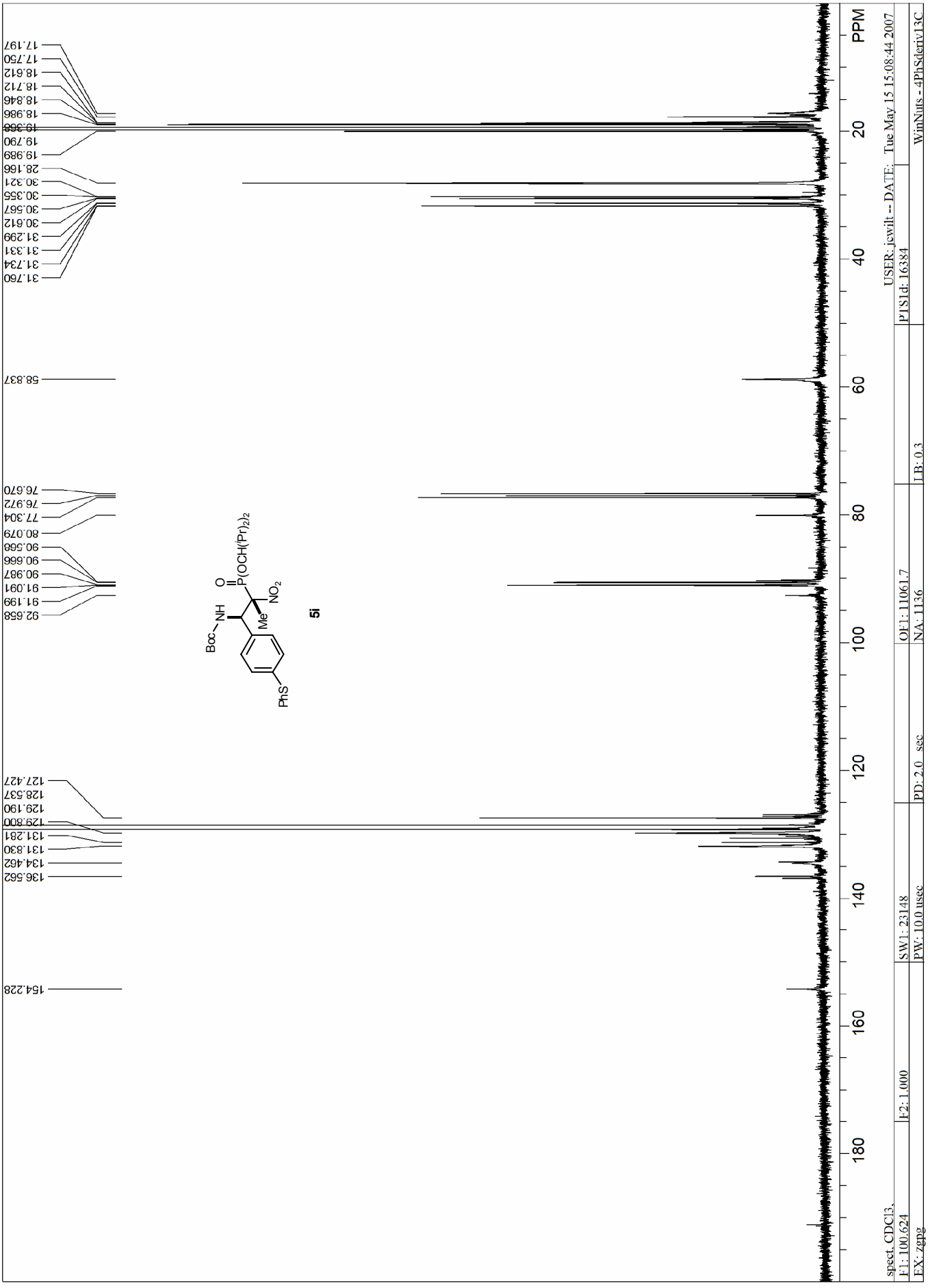

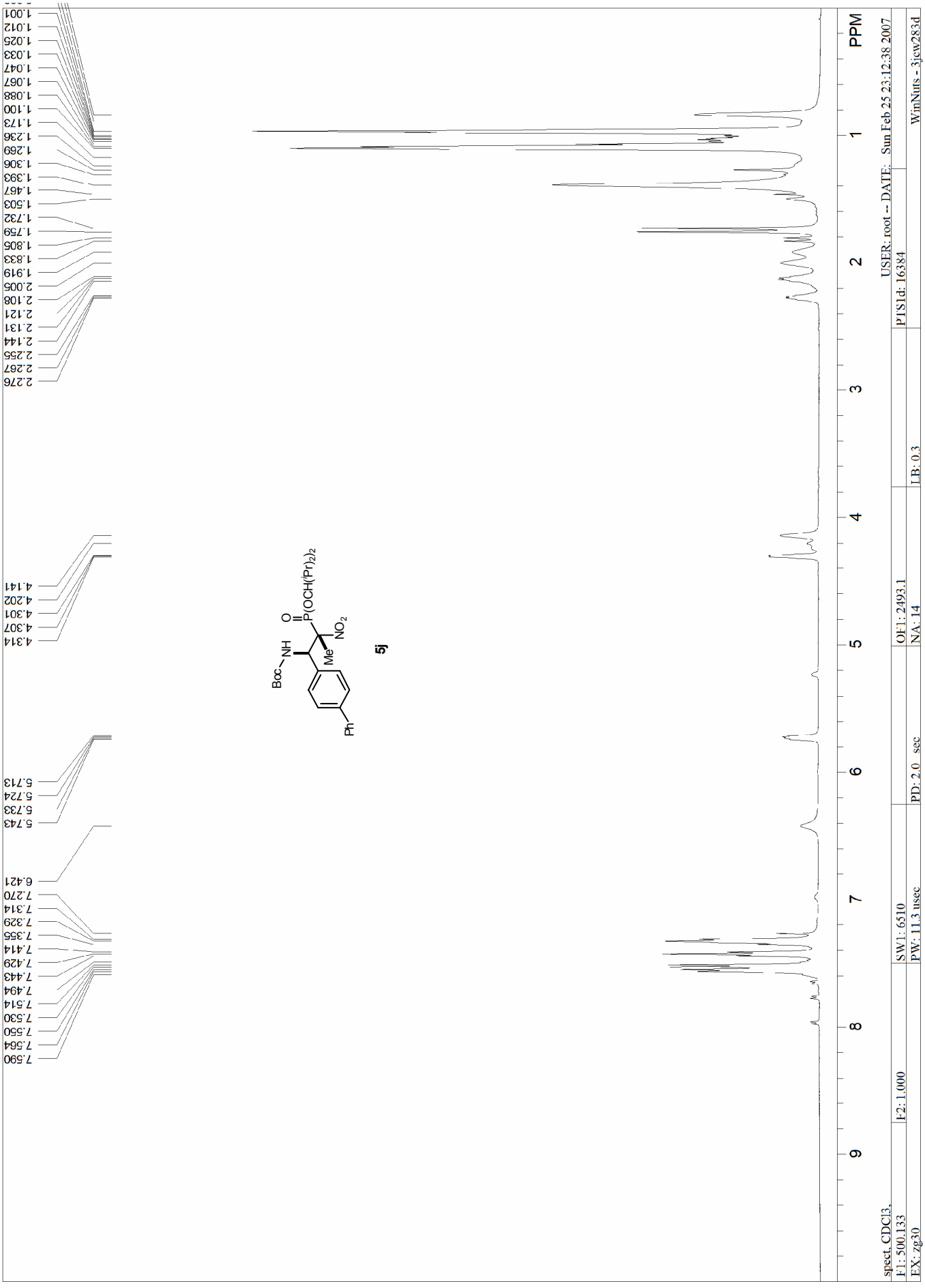

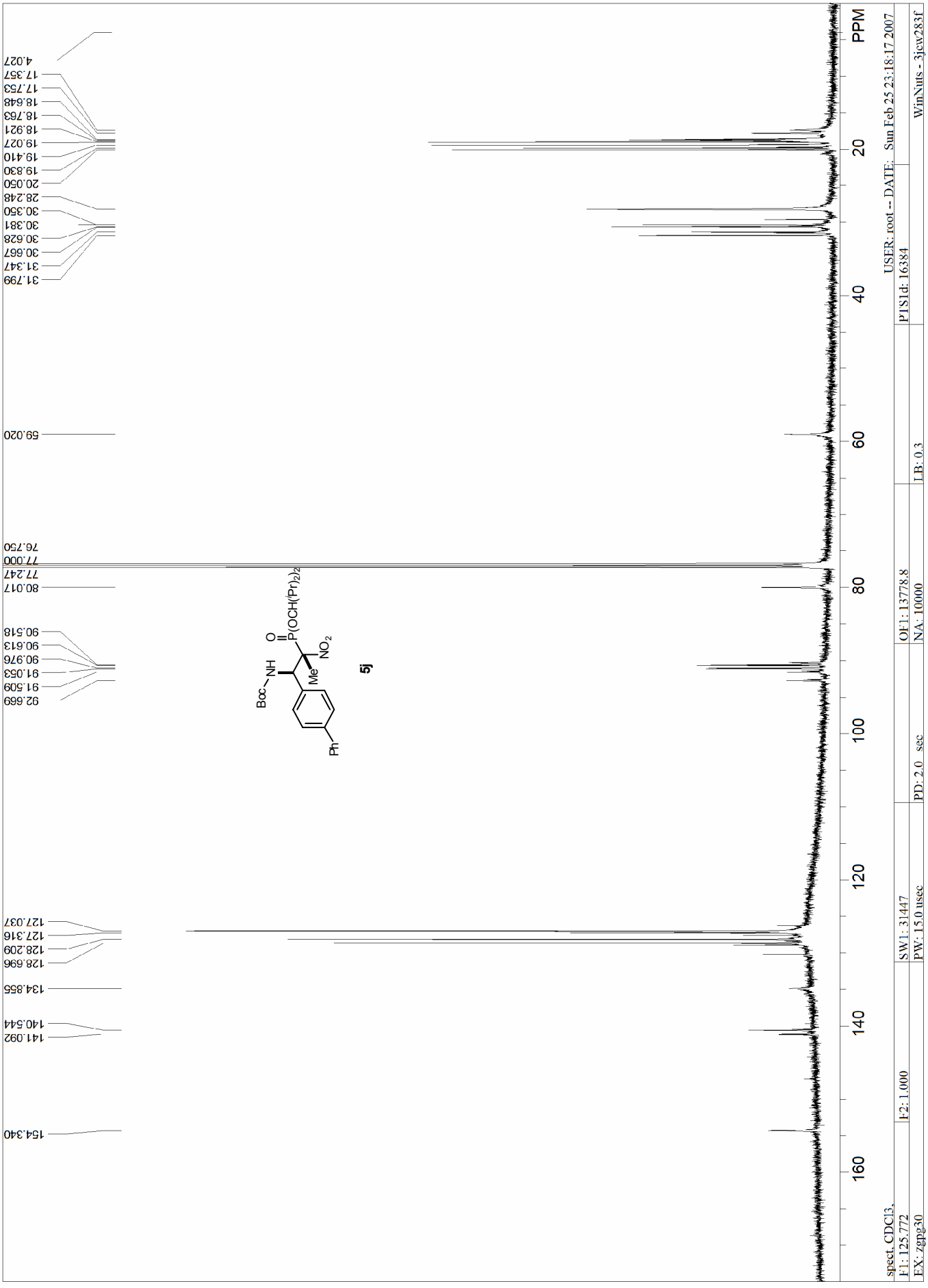

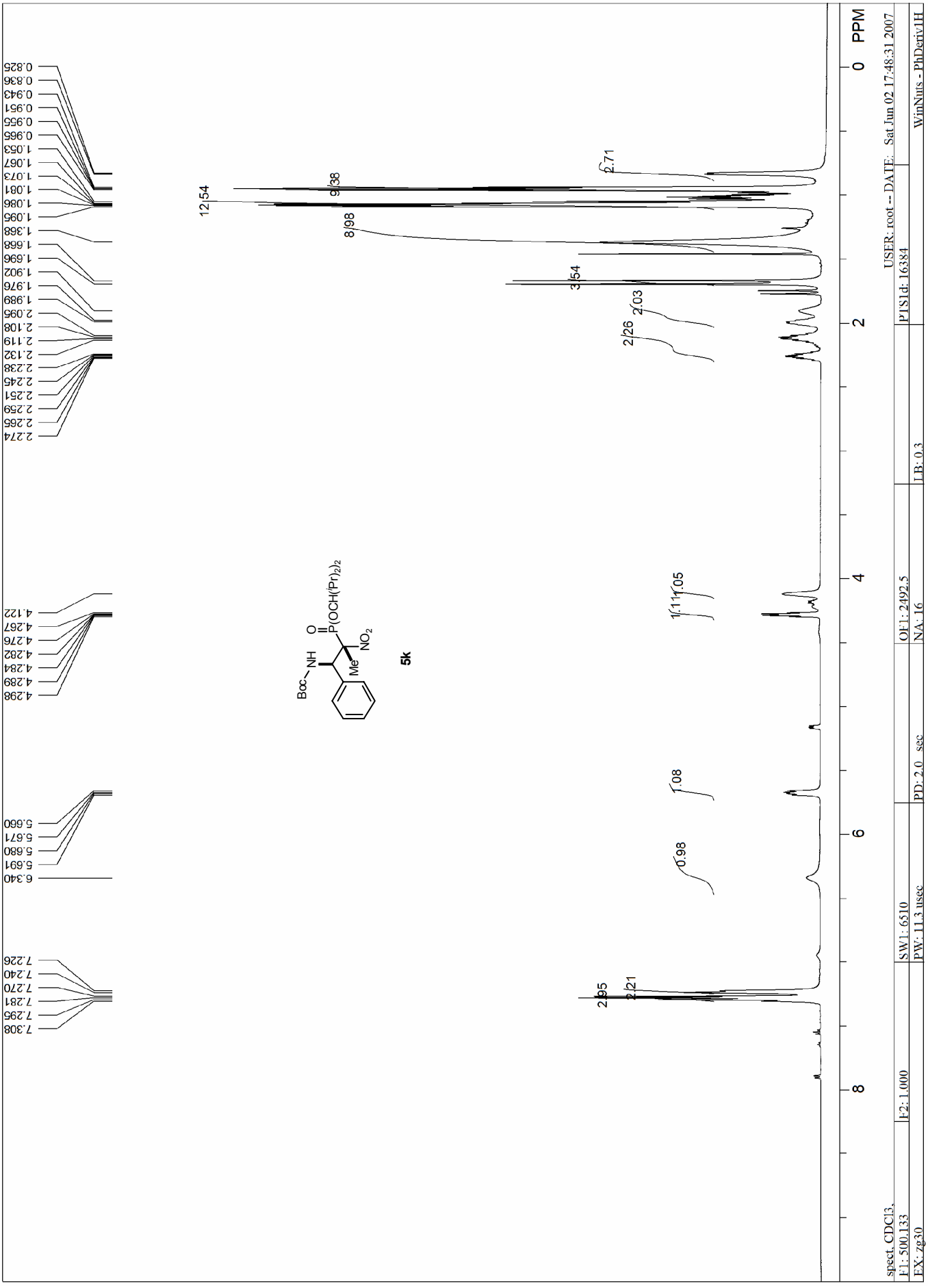

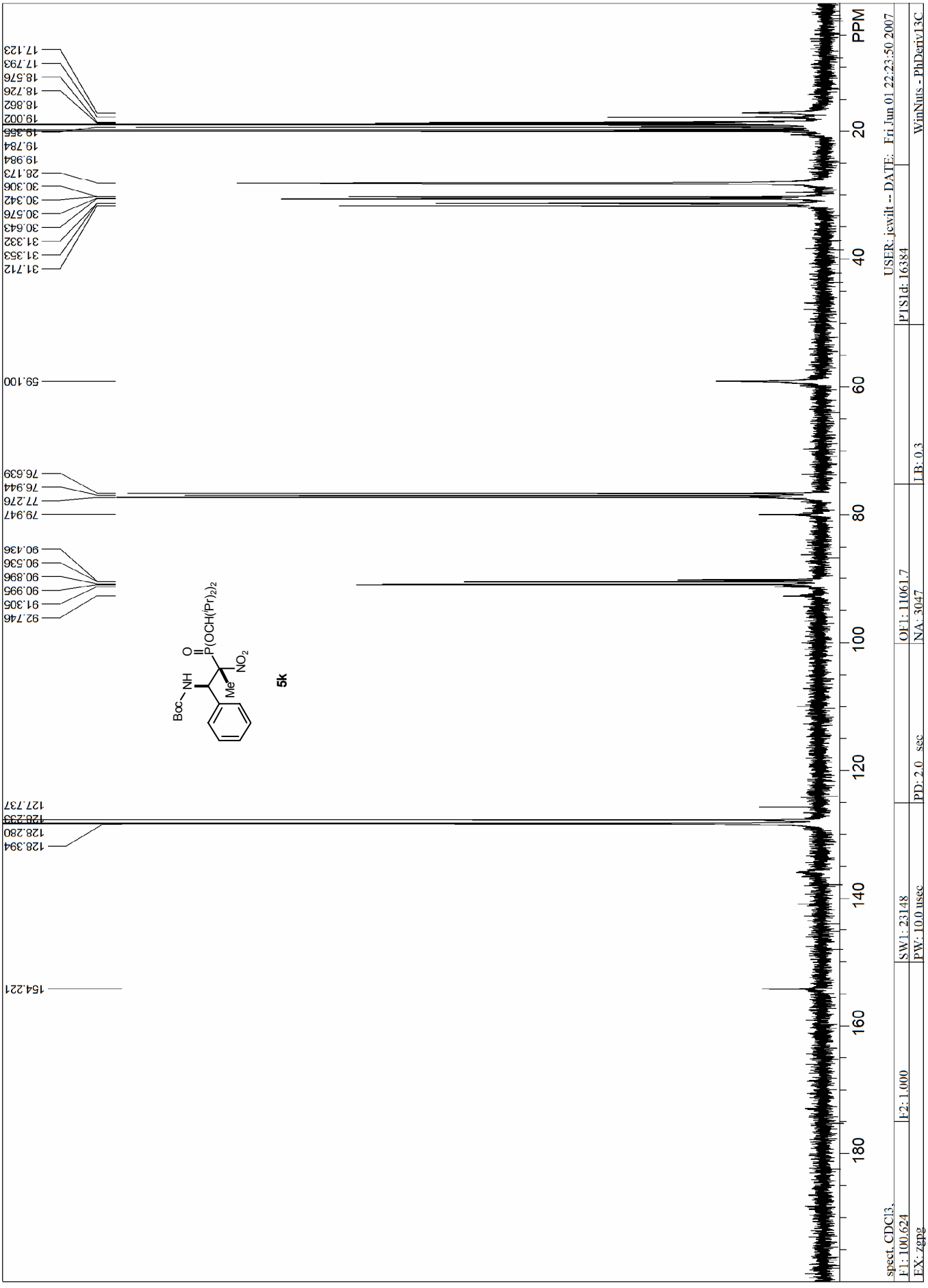

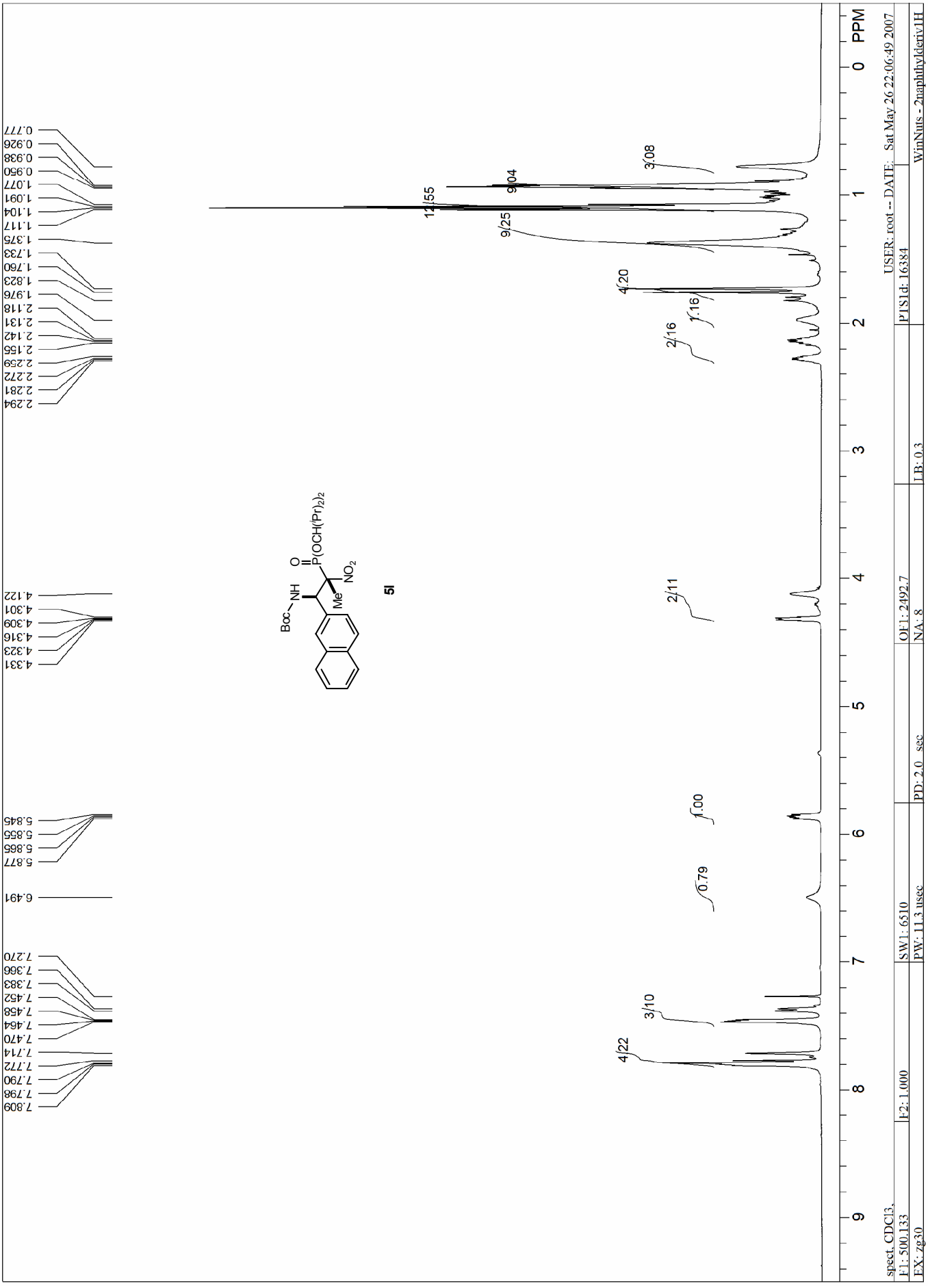

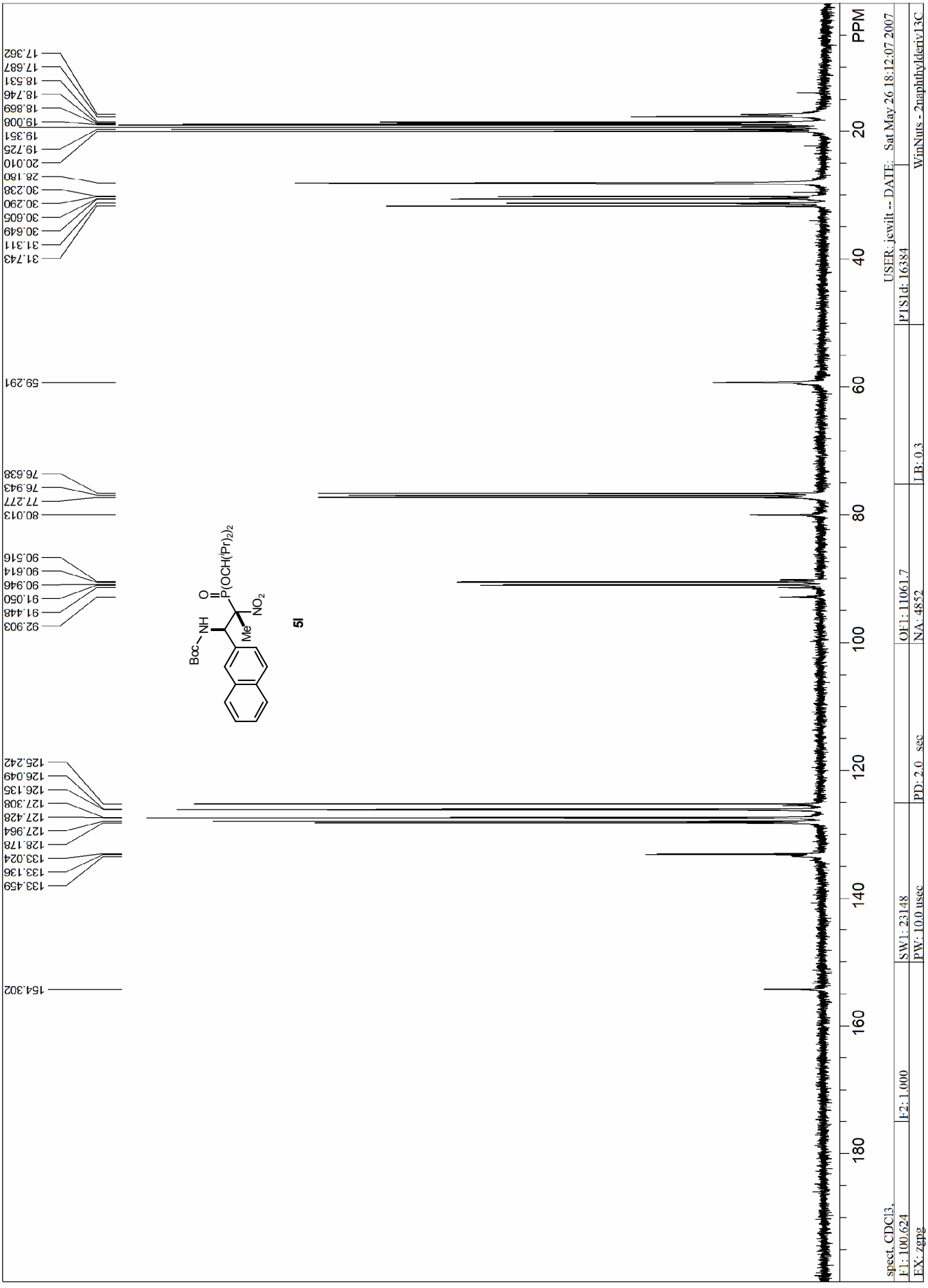

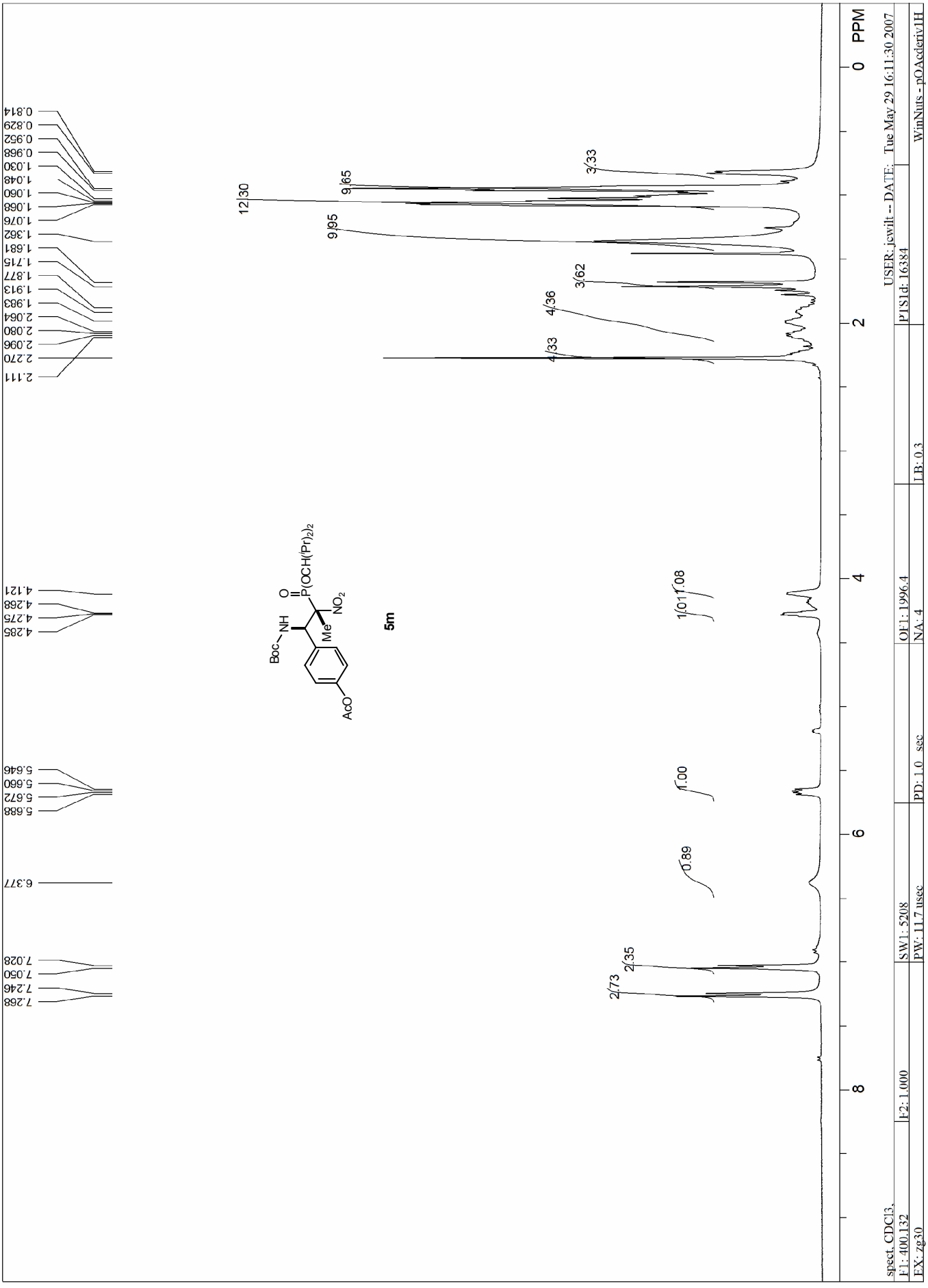

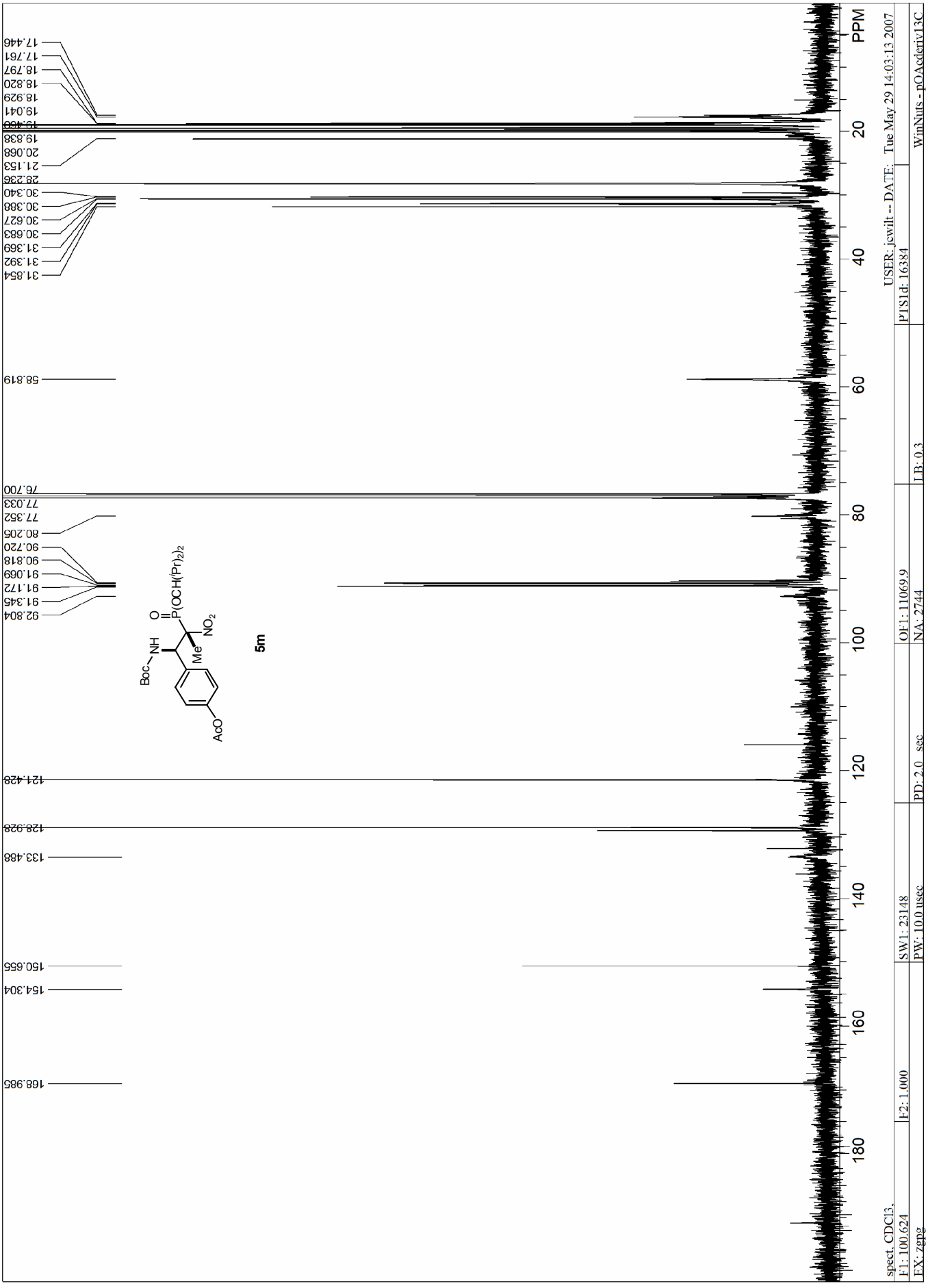

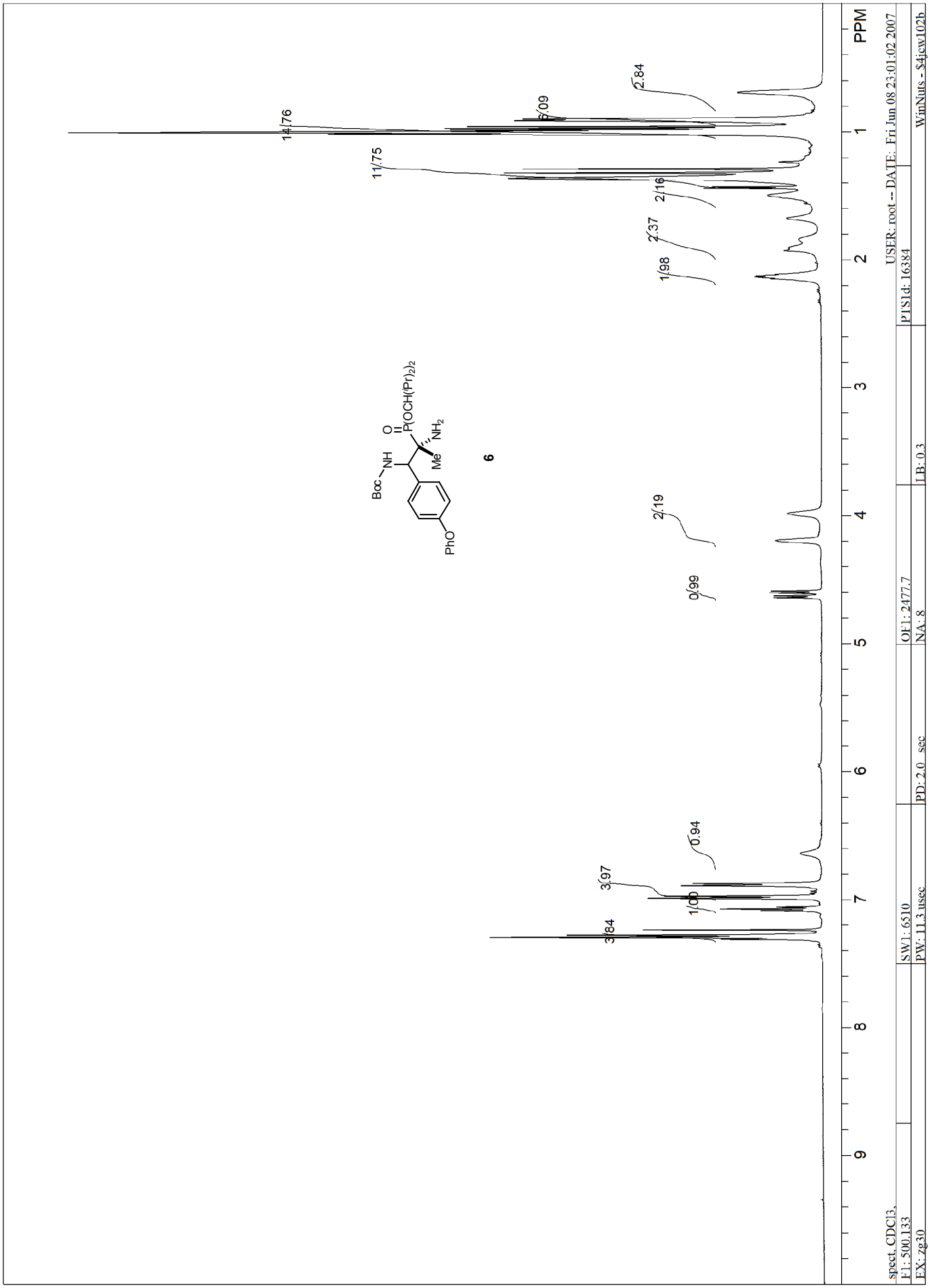
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PhO
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