

B(C₆F₅)₃-Catalyzed Metal-Free Hydrogenation of 3,6-Diarylpyridazines

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Supporting Information

General information: All air-sensitive compounds were handled under an atmosphere of argon or in a nitrogen-filled glovebox. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker AV 400 at ambient temperature with CDCl_3 and $\text{DMSO}-d_6$ as solvent and TMS as internal standard. Chemical shifts (δ) were given in ppm, referenced to the residual proton resonance of TMS (0), to the carbon resonance of the CDCl_3 (77.23). Coupling constants (J) were given in Hertz (Hz). IR spectrums were recorded on Perkin-Elmer-983 spectrometer. Column chromatography was performed on silica gel (200-300 mesh) or on basic alumina (200-300 mesh). All solvents were purified by conventional methods, distilled before use. Commercially available reagents were used without further purification.

Typical procedure for the synthesis of 3,6-disubstituted pyridazines: To an argon flushed glass pressure tube were added $\text{Pd}_2(\text{dba})_3$ (0.25 mmol), 2-dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl (S-Phos) (1.0 mmol), 3,6-dichloropyridazine (10 mmol), arylboronic acid (20 mmol), and K_3PO_4 (30 mmol), followed by dry 1,4-dioxane (20 mL). The tube was closed by a teflon screw cap and the reaction mixture was stirred at 100 °C for 36 h. The mixture was then cooled to room temperature and diluted with water (10 mL) and dichloromethane (50 mL). The layers were separated and the aqueous layer was extracted with dichloromethane (50 mL x 2). The combined organic layers were dried with anhydrous sodium sulphate, filtered, and the solvent was evaporated. The residue was purified by column on silica gel using petroleum ether/ dichloromethane as the eluent to afford 3,6-disubstituted pyridazines.

P. Ehlers, A. Petrosyan, T. V. Ghochikyan, A. S. Saghyan, A. Neubauer, S. Lochbrunner and P. Langer, *Synlett*, 2013, **24**, 359.

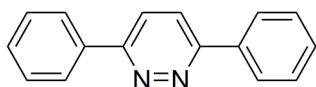
Procedure for the synthesis of pyridazines (1h, 1i, 1t): see the reference: J. Nakayama, T. Konishi, A. Ishii and M. Hoshino, *Bull. Chem. Soc. Jpn.*, 1989, **62**, 2608.

Procedure for the synthesis of pyridazines 1q: A mixture of 4-methoxyacetophenone (10.0 mmol), 1,3-diphenylpropane-1,3-dione (10.0 mmol), iodine (11.0 mmol), and copper oxide (11.0 mmol) in dimethyl sulfoxide (30 mL) was stirred at 70 °C for 12 h until nearly completed conversion of the substrates by TLC analysis and then extracted with ethyl acetate (40 mL x 2). The extract was washed with 10 %

sodium thiosulfate solution (w/w) (50 mL). After drying over anhydrous sodium sulphate and evaporation, hydrazine hydrate (150.0 mmol) was added and the mixture was stirred at reflux in *t*-BuOH (50 mL) for 3 h. After the reaction complete (as monitored by TLC), the solvent was removed under reduced pressure, and water (100 mL) was added to the residue, and then the mixture was extracted with ethyl acetate (50 mL x 3). The extract was dried over anhydrous sodium sulphate and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using petroleum ether/ dichloromethane to afford the product **1q** (1.5739 g, 60% yield).

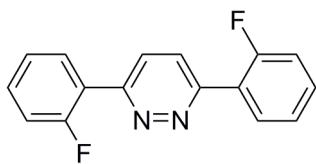
Q.-H. Gao, Y.-P. Zhu, M. Lian, M.-C. Liu, J.-J. Yuan, G.-D. Yin and A.-X. Wu, *J. Org. Chem.*, 2012, **77**, 9865.

Representative procedure for hydrogenation of pyridazines (Table 2, entry 1): To a glass test tube (10 mL) was added $B(C_6F_5)_3$ (0.0128 g, 0.025 mmol), 3,6-diphenylpyridazine (**1a**) (0.0581 g, 0.25 mmol) and dry toluene (0.50 mL) in a nitrogen atmosphere glovebox. The tube was then moved to a stainless-steel autoclave. After being sealed, the autoclave was purged three times with H_2 and the final pressure of hydrogen was adjusted to 20 bar. The reaction mixture was stirred at 120 °C for 6 h. After cooling to ambient temperature, the solvent was removed under reduced pressure. The crude residue was purified by column chromatography on basic alumina using petroleum ether/dichloromethane as the eluent to afford 3,6-diphenyl-1,4,5,6-tetrahydropyridazine (**2a**) as a light yellow solid 0.0561 g (95% yield).

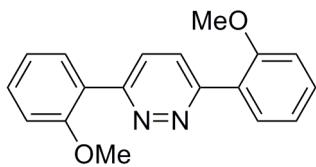


1a, 1.97 g (85 % yield), white solid; 1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.24-8.12 (m, 4H), 7.94 (s, 2H), 7.62-7.47 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 157.8, 136.3, 130.3, 129.3, 127.2, 124.4.

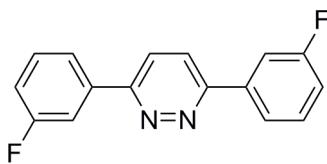
Q.-H. Gao, Y.-P. Zhu, M. Lian, M.-C. Liu, J.-J. Yuan, G.-D. Yin and A.-X. Wu, *J. Org. Chem.*, 2012, **77**, 9865.



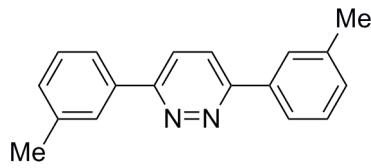
1b, 2.25 g (84 % yield), white solid, m.p. 157-158 °C; IR (film): 1616, 1573, 1488, 1216 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 8.29 (ddd, *J* = 8.0, 8.0, 2.0 Hz, 2H), 8.04 (s, 2H), 7.53-7.44 (m, 2H), 7.36 (d, *J* = 7.6 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 161.1 (d, *J*_{C-F} = 249.0 Hz), 154.8 (d, *J*_{C-F} = 2.0 Hz), 131.9 (d, *J*_{C-F} = 8.0 Hz), 131.1 (d, *J*_{C-F} = 2.0 Hz), 127.4 (d, *J*_{C-F} = 10.0 Hz), 125.1 (d, *J*_{C-F} = 3.0 Hz), 124.5 (d, *J*_{C-F} = 11.0 Hz), 116.5 (d, *J*_{C-F} = 23.0 Hz); ¹⁹F NMR (564 MHz, CDCl₃, ppm) δ -117.1; HRMS (ESI) Calcd. for C₁₆H₁₁N₂F₂ (M+H): 269.0885, Found: 269.0881.



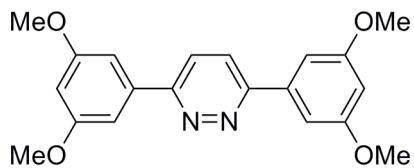
1c, 2.13 g (73 % yield), white solid; ¹H NMR (400 MHz, CDCl₃, ppm): δ 8.07 (dd, *J* = 7.6, 2.0 Hz, 2H), 8.03 (s, 2H), 7.49-7.42 (m, 2H), 7.15 (ddd, *J* = 7.6, 7.6, 2.0 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 2H), 3.90 (s, 6H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 157.5, 156.7, 131.5, 131.1, 127.5, 126.3, 121.5, 111.5, 55.8. S.-J. Lin, Z.-D. Liu and , Y.-H. Hu, *J. Comb. Chem.*, 2007, **9**, 742.



1d, 2.38 g (89 % yield), white solid, m.p. 195-196 °C; IR (film): 1588, 1507, 1442 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.94 (s, 2H), 7.92 (d, *J* = 7.6 Hz, 4H), 7.56-7.47 (m, 2H), 7.25-7.17 (m, 2H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 163.6 (d, *J*_{C-F} = 245.0 Hz), 157.1 (d, *J*_{C-F} = 3.0 Hz), 138.4 (d, *J*_{C-F} = 8.0 Hz), 130.9 (d, *J*_{C-F} = 8.0 Hz), 124.5, 122.8 (d, *J*_{C-F} = 2.0 Hz), 117.3 (d, *J*_{C-F} = 21.0 Hz), 114.2 (d, *J*_{C-F} = 23.0 Hz); ¹⁹F NMR (564 MHz, CDCl₃, ppm) δ -111.9; HRMS (ESI) Calcd. for C₁₆H₁₁N₂F₂ (M+H): 269.0885, Found: 269.0882.



1e, 2.21 g (85 % yield), white solid, m.p. 134-136 °C; IR (film): 1602, 1588, 1409 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 8.02 (s, 2H), 7.92 (d, *J* = 7.2 Hz, 2H), 7.91 (s, 2H), 7.43 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.32 (d, *J* = 7.6 Hz, 2H), 2.48 (s, 6H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 157.9, 139.0, 136.3, 131.0, 129.1, 127.9, 124.4, 124.2, 21.8; HRMS (ESI) Calcd. for C₁₈H₁₇N₂ (M+H): 261.1386, Found: 261.1383.

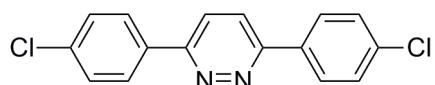


1f, 2.81 g (80 % yield), white solid, m.p. 158-160 °C; IR (film): 1595, 1457, 1428 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.91 (s, 2H), 7.35 (d, *J* = 2.0 Hz, 4H), 6.63-6.59 (m, 2H), 3.90 (s, 12H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 161.5, 157.6, 138.1, 124.5, 105.2, 102.7, 55.8; HRMS (ESI) Calcd. for C₂₀H₂₁O₄N₂ (M+H): 353.1496, Found: 353.1491.



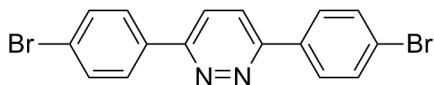
1g, 2.41 g (90 % yield), white solid; ¹H NMR (400 MHz, CDCl₃, ppm): δ 8.21-8.12 (m, 4H), 7.89 (s, 2H), 7.26-7.19 (m, 4H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 164.5 (d, *J*_{C-F} = 249.0 Hz), 156.9, 132.4 (d, *J*_{C-F} = 3.0 Hz), 129.1 (d, *J*_{C-F} = 9.0 Hz), 124.2, 116.4 (d, *J*_{C-F} = 21.0 Hz); ¹⁹F NMR (564 MHz, CDCl₃, ppm) δ -111.0.

R. Singht and A. S. Hay, *Macromolecules*, 1992, **25**, 1025.



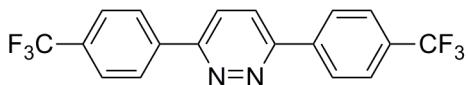
1h, 1.50 g (50 % yield), light yellow solid; ¹H NMR (400 MHz, CDCl₃, ppm): δ 8.11 (d, *J* = 8.0 Hz, 4H), 7.91 (s, 2H), 7.53 (d, *J* = 8.0 Hz, 4H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 157.0, 136.8, 134.6, 129.6, 128.4, 124.2.

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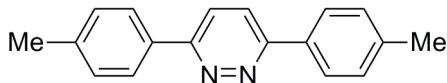


1i, 1.87 g (48 % yield), light yellow solid; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 8.04 (d, $J = 8.8$ Hz, 4H), 7.91 (s, 2H), 7.69 (d, $J = 8.8$ Hz, 4H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 157.1, 135.1, 132.6, 128.7, 125.2, 124.2.

J. Nakayama, T. Konishi, A. Ishii and M. Hoshino, *Bull. Chem. Soc. Jpn.*, 1989, **62**, 2608.

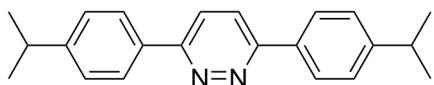


1j, 3.31 g (90 % yield), white solid, m.p. >250 °C; IR (film): 1616, 1589, 1329 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 8.30 (d, $J = 8.0$ Hz, 4H), 8.03 (s, 2H), 7.83 (d, $J = 8.0$ Hz, 4H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$, ppm): δ 156.5, 139.5, 130.2 (q, $J_{\text{C-F}} = 31.0$ Hz), 127.7, 126.8 (q, $J_{\text{C-F}} = 271.0$ Hz), 125.9 (q, $J_{\text{C-F}} = 3.7$ Hz), 125.6; ^{19}F NMR (564 MHz, CDCl_3 , ppm) δ -62.8; HRMS (ESI) Calcd. for $\text{C}_{18}\text{H}_{11}\text{N}_2\text{F}_6$ ($\text{M}+\text{H}$): 369.0821, Found: 369.0815.



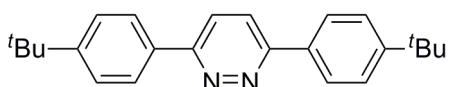
1k, 2.31 g (89 % yield), light yellow solid; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 8.05 (d, $J = 8.0$ Hz, 4H), 7.87 (s, 2H), 7.34 (d, $J = 7.6$ Hz, 4H), 2.44 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 157.5, 140.3, 133.6, 130.0, 126.9, 124.0, 21.6.

J. Nakayama, T. Konishi, A. Ishii and M. Hoshino, *Bull. Chem. Soc. Jpn.*, 1989, **62**, 2608.



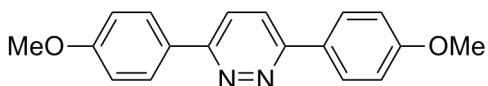
1l, 2.65 g (84 % yield), light yellow solid, m.p. 229-231 °C; IR (film): 1609, 1585, 1428 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 8.09 (d, $J = 8.0$ Hz, 4H), 7.88 (s, 2H), 7.40 (d, $J = 8.0$ Hz, 4H), 3.00 (hept, $J =$

7.2 Hz, 2H), 1.31 (d, J = 7.2 Hz, 12H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 157.6, 151.3, 134.0, 127.4, 127.1, 124.1, 34.2, 24.1; HRMS (ESI) Calcd. for $\text{C}_{22}\text{H}_{25}\text{N}_2$ ($\text{M}+\text{H}$): 317.2012, Found: 317.2008.



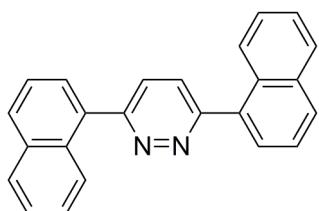
1m, 2.92 g (85 % yield), white solid; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 8.10 (d, J = 8.4 Hz, 4H), 7.89 (s, 2H), 7.56 (d, J = 8.4 Hz, 4H), 1.38 (s, 18H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 157.5, 153.5, 133.5, 126.8, 126.2, 124.1, 35.0, 31.5.

S.-J. Lin, Z.-D. Liu and , Y.-H. Hu, *J. Comb. Chem.*, 2007, **9**, 742.

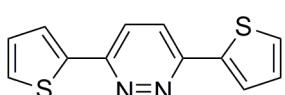


1n, 2.33 g (80 % yield), light yellow solid; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 8.12 (d, J = 8.8 Hz, 4H), 7.83 (s, 2H), 7.06 (d, J = 8.8 Hz, 4H), 3.89 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 161.4, 156.9, 129.0, 128.4, 123.6, 114.7, 55.6.

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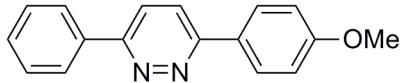


1o, 2.99 g (90 % yield), white solid, m.p. 199-201 °C; IR (film): 1593, 1536, 1508 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 8.28-8.17 (m, 2H), 8.22 (d, J = 8.0 Hz, 2H), 8.01-7.96 (m, 2H), 7.91 (s, 2H), 7.82 (d, J = 6.8 Hz, 2H), 7.66 (dd, J = 7.6, 7.6 Hz, 2H), 7.62-7.50 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 160.0, 135.4, 134.2, 131.3, 130.2, 128.8, 128.6, 128.3, 127.2, 126.5, 125.6, 125.5; HRMS (ESI) Calcd. for $\text{C}_{24}\text{H}_{17}\text{N}_2$ ($\text{M}+\text{H}$): 333.1386, Found: 333.1381.



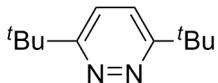
1p, 1.90 g (78 % yield), yellow solid; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.75 (s, 2H), 7.66 (d, J = 2.8 Hz, 2H), 7.49 (d, J = 4.8 Hz, 2H), 7.16 (dd, J = 4.8, 2.8 Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 153.6, 140.9, 129.4, 128.3, 126.2, 122.7.

J. Nakayama, T. Konishi, A. Ishii and M. Hoshino, *Bull. Chem. Soc. Jpn.* 1989, **62**, 2608.



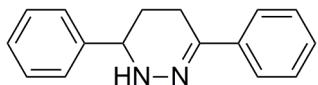
1q, 1.57 g (60 % yield), gray solid; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 8.22-8.09 (m, 4H), 7.95-7.84 (m, 2H), 7.61-7.46 (m, 3H), 7.06 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 161.6, 157.4, 157.3, 136.5, 130.1, 129.2, 128.8, 128.5, 127.0, 124.3, 123.7, 114.7, 55.6.

Q.-H. Gao, Y.-P. Zhu, M. Lian, M.-C. Liu, J.-J. Yuan, G.-D. Yin and A.-X. Wu, *J. Org. Chem.*, 2012, **77**, 9865.



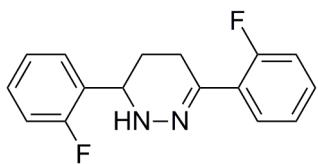
1t, 0.86 g, (45 % yield), white solid; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.44 (s, 2H), 1.55 (s, 18H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 167.8, 123.4, 36.7, 30.2.

J. Nakayama, T. Konishi, A. Ishii and M. Hoshino, *Bull. Chem. Soc. Jpn.* 1989, **62**, 2608.

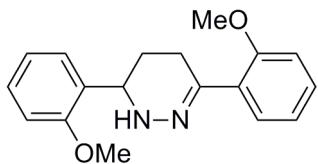


2a, 0.0561 g (95 % yield), white solid; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.69 (d, J = 7.2 Hz, 2H), 7.46-7.21 (m, 8H), 5.82 (s, 1H), 4.18 (d, J = 8.4 Hz, 1H), 2.86-2.74 (m, 1H), 2.74-2.59 (m, 1H), 2.29-2.08 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 143.4, 142.3, 138.8, 128.9, 128.5, 128.1, 128.0, 127.2, 124.7, 56.6, 28.8, 23.7.

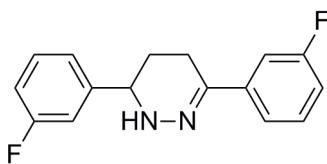
Z.-I. Yoshida, T. Harada and Y. Tamaru, *Tetrahedron Lett.*, 1976, **42**, 3823.



2b, 0.0613 g (90 % yield), yellow solid, m.p. 112-114 °C; IR (film): 3287, 1491, 1457, 1234 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.62 (ddd, *J* = 8.0, 8.0, 1.6 Hz, 1H), 7.50 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H), 7.34-7.22 (m, 2H), 7.21-7.11 (m, 2H), 7.11-7.00 (m, 2H), 5.86 (s, 1H), 4.61 (dd, *J* = 9.2, 2.4 Hz, 1H), 2.96-2.83 (m, 1H), 2.68-2.58 (m, 1H), 2.29-2.19 (m, 1H), 2.19-2.07 (m, 1H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 160.7 (d, *J*_{C-F} = 247.0 Hz), 160.6 (d, *J*_{C-F} = 244.0 Hz), 142.3 (d, *J*_{C-F} = 3.0 Hz), 129.5 (d, *J*_{C-F} = 8.0 Hz), 129.3 (d, *J*_{C-F} = 9.0 Hz), 129.1 (d, *J*_{C-F} = 4.0 Hz), 128.1 (d, *J*_{C-F} = 4.0 Hz), 127.3 (d, *J*_{C-F} = 12.0 Hz), 124.7 (d, *J*_{C-F} = 3.0 Hz), 124.3 (d, *J*_{C-F} = 3.0 Hz), 116.3 (d, *J*_{C-F} = 22.0 Hz), 115.7 (d, *J*_{C-F} = 21.0 Hz), 49.2 (d, *J*_{C-F} = 2.0 Hz), 26.8, 26.0 (d, *J*_{C-F} = 7.0 Hz); ¹⁹F NMR (564 MHz, CDCl₃, ppm) δ -115.0, -119.8; HRMS (ESI) Calcd. for C₁₆H₁₅N₂F₂ (M+H): 273.1198, Found: 273.1195.

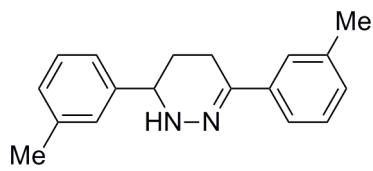


2c, 0.0629 g (85 % yield), light yellow solid, m.p. 172-174 °C; IR (film): 3292, 1614, 1260 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.46 (d, *J* = 7.6 Hz, 1H), 7.40 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.28-7.21 (m, 2H), 7.02-6.93 (m, 2H), 6.93-6.86 (m, 2H), 5.77 (s, 1H), 4.59 (d, *J* = 7.2 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 2.96-2.82 (m, 1H), 2.62-2.53 (m, 1H), 2.21-2.12 (m, 1H), 2.12-2.02 (m, 1H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 157.5, 157.1, 146.9, 130.4, 129.7, 129.5, 129.2, 128.6, 127.2, 121.1, 121.0, 111.3, 110.5, 55.7, 55.6, 49.6, 26.8, 26.4; HRMS (ESI) Calcd. for C₁₈H₂₁O₂N₂ (M+H): 297.1595, Found: 297.1598.

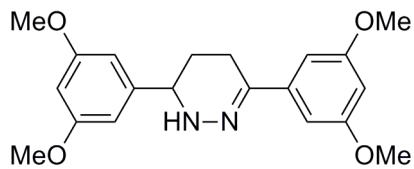


2d, 0.0593 g (87 % yield), white solid, m.p. 130-132 °C; IR (film): 3300, 1614, 1582, 1448, 1272 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.47-7.37 (m, 2H), 7.37-7.27 (m, 2H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.12

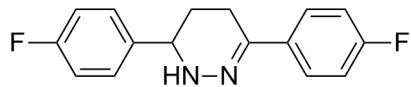
(d, $J = 9.6$ Hz, 1H), 7.07-6.94 (m, 2H), 5.88 (s, 1H), 4.18 (d, $J = 8.0$ Hz, 1H), 2.82-2.67 (m, 1H), 2.67-2.57 (m, 1H), 2.28-2.17 (m, 1H), 2.17-2.07 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 163.28 (d, $J_{\text{C}-\text{F}} = 246.0$ Hz), 163.26 (d, $J_{\text{C}-\text{F}} = 242.0$ Hz), 144.7 (d, $J_{\text{C}-\text{F}} = 7.0$ Hz), 141.8 (d, $J_{\text{C}-\text{F}} = 1.3$ Hz), 141.0 (d, $J_{\text{C}-\text{F}} = 7.0$ Hz), 130.5 (d, $J_{\text{C}-\text{F}} = 9.0$ Hz), 129.8 (d, $J_{\text{C}-\text{F}} = 8.0$ Hz), 122.7 (d, $J_{\text{C}-\text{F}} = 1.6$ Hz), 120.2 (d, $J_{\text{C}-\text{F}} = 1.5$ Hz), 115.0 (d, $J_{\text{C}-\text{F}} = 21.0$ Hz), 114.8 (d, $J_{\text{C}-\text{F}} = 22.0$ Hz), 114.0 (d, $J_{\text{C}-\text{F}} = 22.0$ Hz), 111.5 (d, $J_{\text{C}-\text{F}} = 23.0$ Hz), 56.0, 28.5, 23.2; ^{19}F NMR (564 MHz, CDCl_3 , ppm) δ -112.5, -113.5; HRMS (ESI) Calcd. for $\text{C}_{16}\text{H}_{15}\text{N}_2\text{F}_2$ ($\text{M}+\text{H}$): 273.1198, Found: 273.1193.



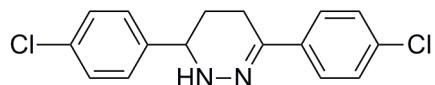
2e, 0.0627 g (95 % yield), white solid, m.p. 106-108 °C; IR (film): 3350, 1682, 1254, cm^{-1} ; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.53 (s, 1H), 7.46 (d, $J = 7.6$ Hz, 1H), 7.32-7.17 (m, 4H), 7.17-7.07 (m, 2H), 5.78 (s, 1H), 4.59 (dd, $J = 10.0, 3.2$ Hz, 1H), 2.86-2.73 (m, 1H), 2.73-2.62 (m, 1H), 2.37 (s, 6H), 2.25-2.07 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 143.7, 142.3, 138.8, 138.6, 138.0, 128.81, 128.79, 128.4, 127.9, 125.4, 124.3, 121.9, 56.6, 28.8, 23.8, 21.7, 21.6; HRMS (ESI) Calcd. for $\text{C}_{18}\text{H}_{21}\text{N}_2$ ($\text{M}+\text{H}$): 265.1699, Found: 265.1696.



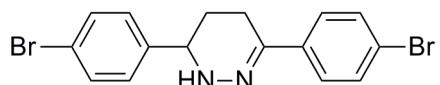
2f, 0.0837 g (94 % yield), white solid, m.p. 156-157 °C; IR (film): 3355, 1596, 1457, 1205, 1153 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 6.86 (s, 2H), 6.57 (s, 2H), 6.42 (s, 2H), 5.82 (s, 1H), 4.09 (d, $J = 8.8$ Hz, 1H), 3.82 (s, 6H), 3.80 (s, 6H), 2.83-2.69 (m, 1H), 2.69-2.58 (m, 1H), 2.26-2.16 (m, 1H), 2.16-2.06 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 161.2, 160.9, 144.7, 142.9, 140.9, 105.0, 102.8, 100.4, 100.0, 56.7, 55.5, 28.7, 23.7; HRMS (ESI) Calcd. for $\text{C}_{20}\text{H}_{25}\text{O}_4\text{N}_2$ ($\text{M}+\text{H}$): 357.1809, Found: 357.1804.



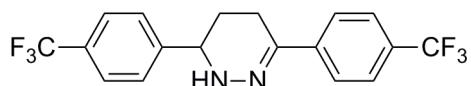
2g, 0.0646 g (95 % yield), white solid, m.p. 194-196 °C; IR (film): 3293, 1730, 1508 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.64 (dd, *J* = 5.6, 5.6 Hz, 2H), 7.35 (dd, *J* = 5.6, 5.6 Hz, 2H), 7.06-6.95 (m, 4H), 5.72 (s, 1H), 4.10 (dd, *J* = 10.4, 2.4 Hz, 1H), 2.82-2.68 (m, 1H), 2.68-2.58 (m, 1H), 2.25-2.04 (m, 2H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 163.2 (d, *J*_{C-F} = 246.0 Hz), 162.6 (d, *J*_{C-F} = 244.0 Hz), 142.6, 137.9 (d, *J*_{C-F} = 3.0 Hz), 134.9 (d, *J*_{C-F} = 3.0 Hz), 128.8 (d, *J*_{C-F} = 8.0 Hz), 126.4 (d, *J*_{C-F} = 8.0 Hz), 115.8 (d, *J*_{C-F} = 21.0 Hz), 115.3 (d, *J*_{C-F} = 22.0 Hz), 55.9, 28.9, 23.7; ¹⁹F NMR (564 MHz, CDCl₃, ppm) δ -114.39, -114.42; HRMS (ESI) Calcd. for C₁₆H₁₅N₂F₂ (M+H): 273.1198, Found: 273.1195.



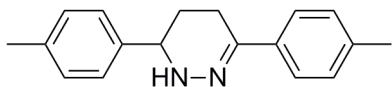
2h, 0.0710 g (93 % yield), light brown solid, m.p. 237-239 °C; IR (film): 3302, 1682, 1591, 1265 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.61 (d, *J* = 8.4 Hz, 2H), 7.43-7.25 (m, 6H), 5.80 (s, 1H), 4.13 (d, *J* = 8.8 Hz, 1H), 2.83-2.64 (m, 1H), 2.64-2.48 (m, 1H), 2.21-2.18 (m, 1H), 2.18-2.02 (m, 1H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 142.2, 140.6, 137.1, 133.9, 129.2, 128.6, 128.5, 125.9, 55.9, 28.6, 23.3; HRMS (ESI) Calcd. for C₁₆H₁₅N₂Cl₂ (M+H): 305.0607, Found: 305.0602.



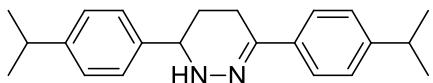
2i, 0.0886 g (90 % yield), light brown solid, m.p. >250 °C; IR (film): 3288, 1615, 1486 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.58-7.43 (m, 6H), 7.27 (d, *J* = 7.2 Hz, 2H), 5.81 (s, 1H), 4.12 (dd, *J* = 10.4, 2.8 Hz, 1H), 2.79-2.68 (m, 1H), 2.67-2.57 (m, 1H), 2.25-2.18 (m, 1H), 2.18-2.07 (m, 1H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 142.2, 141.1, 137.5, 132.4, 131.6, 128.9, 126.2, 122.2, 122.0, 55.9, 28.5, 23.2; HRMS (ESI) Calcd. for C₁₆H₁₅N₂Br₂ (M+H): 392.9597, Found: 392.9597.



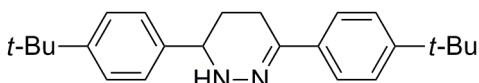
2j, 0.0865 g (93 % yield), yellow solid, m.p. 215-217 °C; IR (film): 3297, 1602, 1327, 1115, 1070 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 2H), 6.00 (s, 1H), 4.28 (dd, *J* = 10.0, 2.8 Hz, 1H), 2.85-2.74 (m, 1H), 2.71-2.61 (m, 1H), 2.32-2.22 (m, 1H), 2.22-2.10 (m, 1H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 146.0, 141.8, 141.5, 130.2 (q, *J*_{C-F} = 32.0 Hz), 127.5, 127.2 (q, *J*_{C-F} = 271.2 Hz), 127.0 (q, *J*_{C-F} = 271.5 Hz), 126.0 (q, *J*_{C-F} = 3.5 Hz), 125.5 (q, *J*_{C-F} = 3.5 Hz), 124.8, 56.0, 28.4, 23.0; ¹⁹F NMR (564 MHz, CDCl₃, ppm) δ -62.5, -62.6; HRMS (ESI) Calcd. for C₁₈H₁₅N₂F₆ (M+H): 373.1134, Found: 373.1129.



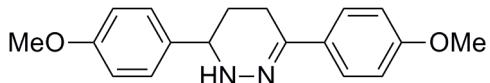
2k, 0.0627 g (95 % yield), white solid, m.p. 225-227 °C; IR (film): 3289, 1514, 1106 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.57 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.8 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 5.73 (s, 1H), 4.10 (dd, *J* = 10.0, 3.6 Hz, 1H), 2.83-2.72 (m, 1H), 2.71-2.61 (m, 1H), 2.36 (s, 6H), 2.22-2.08 (m, 2H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 143.7, 139.3, 137.8, 137.7, 136.1, 129.6, 129.2, 127.1, 124.6, 56.4, 28.8, 23.8, 21.4, 21.3; HRMS (ESI) Calcd. for C₁₈H₂₁N₂ (M+H): 265.1699, Found: 265.1698.



2l, 0.0753 g (94 % yield), light gray solid, m.p. 198-200 °C; IR (film): 3293, 1506, 1361 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 7.6 Hz, 2H), 7.23 (d, *J* = 7.2 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 5.74 (s, 1H), 4.11 (dd, *J* = 10.0, 2.8 Hz, 1H), 2.92 (heptet, *J* = 6.8 Hz, 2H), 2.84-2.73 (m, 1H), 2.72-2.65 (m, 1H), 2.25-2.08 (m, 2H), 1.26 (d, *J* = 6.8 Hz, 6H), 1.25 (d, *J* = 6.8 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 148.9, 148.7, 143.7, 139.7, 136.5, 127.2, 126.9, 126.5, 124.7, 56.4, 34.1, 28.8, 24.21, 24.20, 24.1, 23.8; HRMS (ESI) Calcd. for C₂₂H₂₉N₂ (M+H): 321.2325, Found: 321.2323.

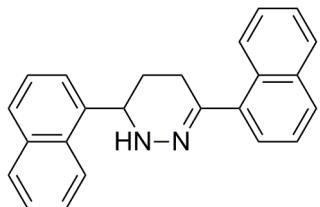


2m, 0.0827 g (95 % yield), white solid, m.p. 187-189 °C. IR (film): 3355, 1607, 1508 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.61 (d, *J* = 8.4 Hz, 2H), 7.48-7.28 (m, 6H), 5.75 (s, 1H), 4.11 (dd, *J* = 10.0, 2.0 Hz, 1H), 2.85-2.72 (m, 1H), 2.72-2.61 (m, 1H), 2.25-2.10 (m, 2H), 1.33 (s, 18H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 151.1, 151.0, 143.6, 139.3, 136.1, 126.9, 125.8, 125.4, 124.4, 56.3, 34.8, 31.6, 31.5, 28.8, 23.7; HRMS (ESI) Calcd. for C₂₄H₃₃N₂ (M+H): 349.2638, Found: 349.2634.

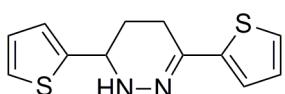


2n, 0.0644 g (87 % yield), light brown solid; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.62 (d, *J* = 8.8 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 5.65 (s, 1H), 4.07 (dd, *J* = 10.0 Hz, 3.6 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 2.83-2.72 (m, 1H), 2.72-2.65 (m, 1H), 2.22-2.07 (m, 2H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 159.7, 159.5, 143.7, 134.3, 131.6, 128.4, 126.0, 114.3, 113.8, 56.1, 55.52, 55.51, 28.9, 24.0.

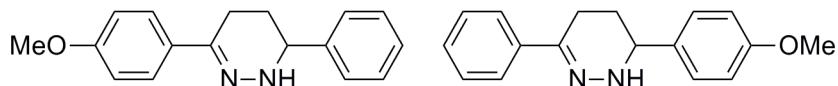
Y. Tamaru, T. Harada and Z. Yoshida, *J. Org. Chem.*, 1978, **43**, 3371.



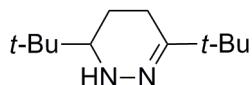
2o, 0.0799 g (95 % yield), white solid, m.p. 146-148 °C; IR (film): 3352, 1596 1508 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 8.41 (d, *J* = 8.4 Hz, 1H), 8.22 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 7.6 Hz, 1H), 7.91-7.82 (m, 3H), 7.80 (d, *J* = 7.2 Hz, 1H), 7.62-7.46 (m, 7H), 6.04 (s, 1H), 5.13 (dd, *J* = 9.2 Hz, 3.6 Hz, 1H), 3.03-2.90 (m, 1H), 2.78-2.68 (m, 1H), 2.56-2.39 (m, 2H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 146.5, 137.9, 137.8, 134.3, 134.2, 131.3, 131.0, 129.4, 128.6, 128.5, 128.4, 126.6, 126.5, 126.01, 126.96, 126.95, 125.4, 125.3, 124.0, 122.9, 52.6, 28.1, 27.9; HRMS (ESI) Calcd. for C₂₄H₂₁N₂ (M+H): 337.1699, Found: 337.1695.



2p, 0.0528 g (85 % yield), yellow solid, m.p. 158-160 °C; IR (film): 3287, 1646, 1466 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.27-7.26 (m, 1H), 7.21 (d, *J* = 5.4 Hz, 1H), 7.07-7.04 (m, 2H), 7.01-6.97 (m, 2H), 5.77 (s, 1H), 4.48 (dd, *J* = 10.0, 2.8 Hz, 1H), 2.78-2.73 (m, 2H), 2.30-2.27 (m, 1H), 2.26-2.17 (m, 1H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 145.0, 144.3, 141.3, 127.2, 126.9, 125.5, 125.0, 124.8, 123.3, 52.3, 29.3, 23.8; HRMS (ESI) Calcd. for C₁₂H₁₃N₂S₂ (M+H): 249.0515, Found: 249.0512.



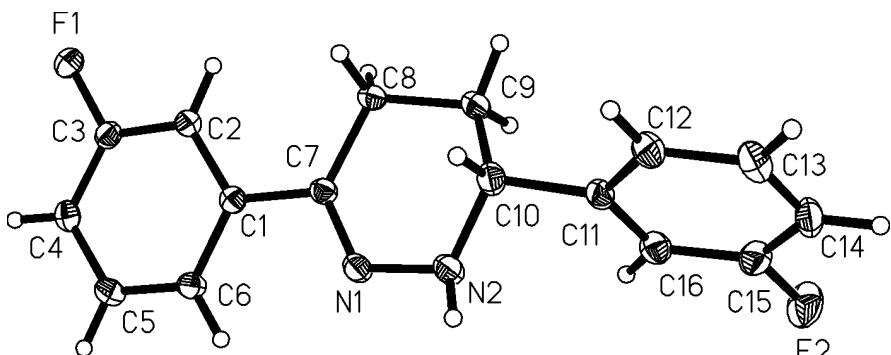
2q and **2q'** (ca.1:1), 0.0619 g (93 % yield), white solid, m.p. 160-162 °C; IR (film): 3298, 1612, 1513, 1254 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.68 (d, *J* = 8.8 Hz, 2H), 7.63 (d, *J* = 8.8 Hz, 2H), 7.44-7.28 (m, 10H), 6.97-6.93 (m, 4H), 5.75 (brs, 2H), 4.11 (ddd, *J* = 9.6, 3.2, 3.2 Hz, 2H), 3.83 (s, 3H), 3.82 (s, 3H), 2.85-2.73 (m, 2H), 2.73-2.60 (m, 2H), 2.26-2.08 (m, 4H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 159.8, 159.5, 143.8, 143.5, 142.3, 138.8, 134.2, 131.6, 128.9, 128.5, 128.3, 128.04, 128.02, 127.2, 126.0, 124.7, 114.3, 113.8, 55.7, 55.1, 55.52, 55.50, 28.9, 28.8, 23.9, 23.8.



2t, 0.0378g (77 % yield), colourless oil; ¹H NMR (400 MHz, CDCl₃, ppm): δ 5.22 (s, 1H), 2.51 (dd, *J* = 11.2, 2.7 Hz, 1H), 2.34-2.17 (m, 2H), 1.89-1.80 (m, 1H), 1.66-1.52 (m, 1H), 1.09 (s, 9H), 0.93 (s, 9H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 156.2, 60.4, 37.3, 32.5, 28.4, 26.3, 21.9, 21.5. HRMS (ESI) Calcd. for C₁₂H₂₅N₂ (M+H): 197.2012, Found: 197.2012.

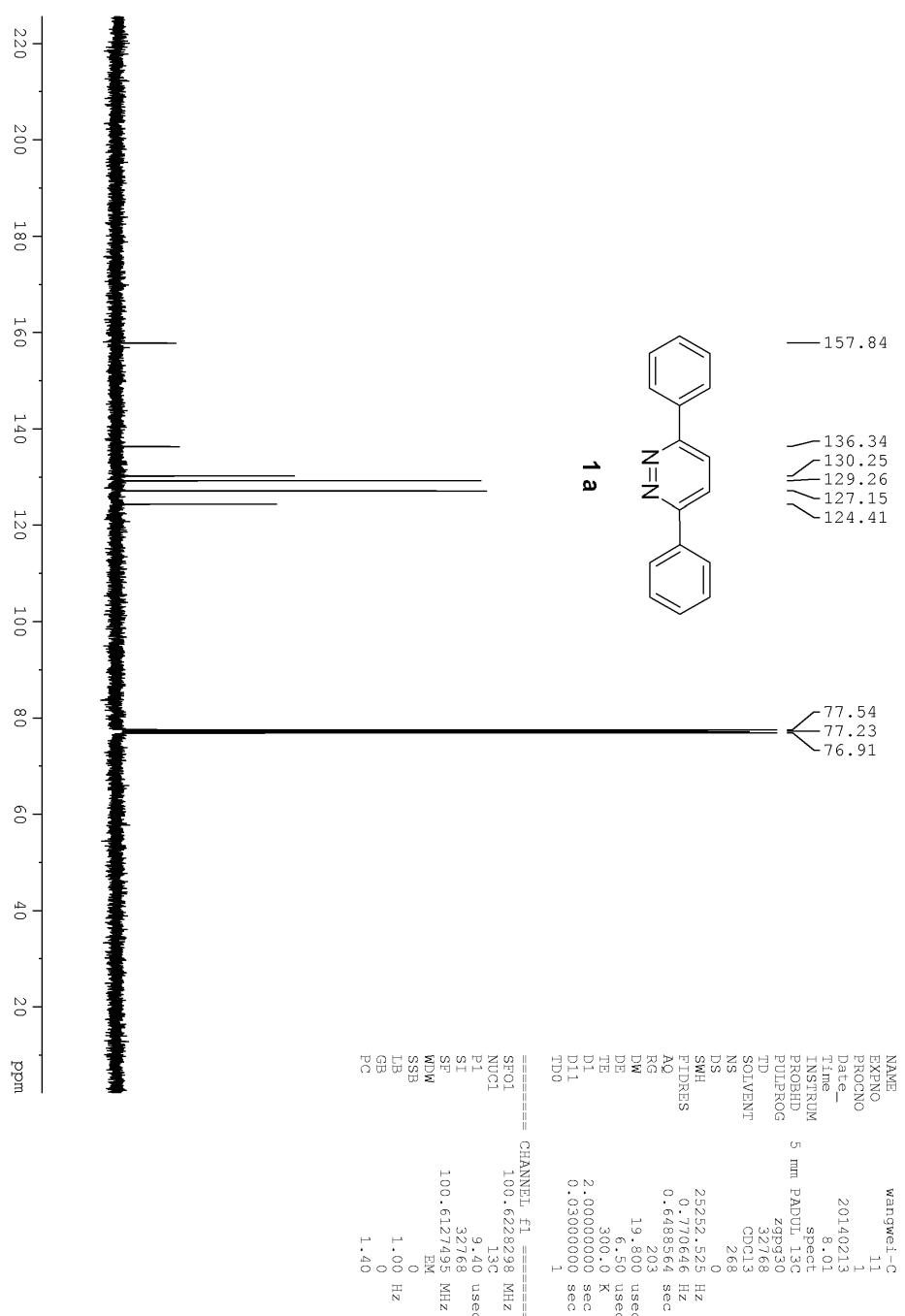
Table 1. Crystal data and structure refinement for compound **2d**.

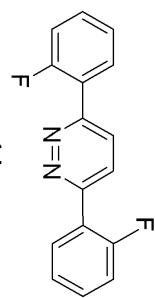
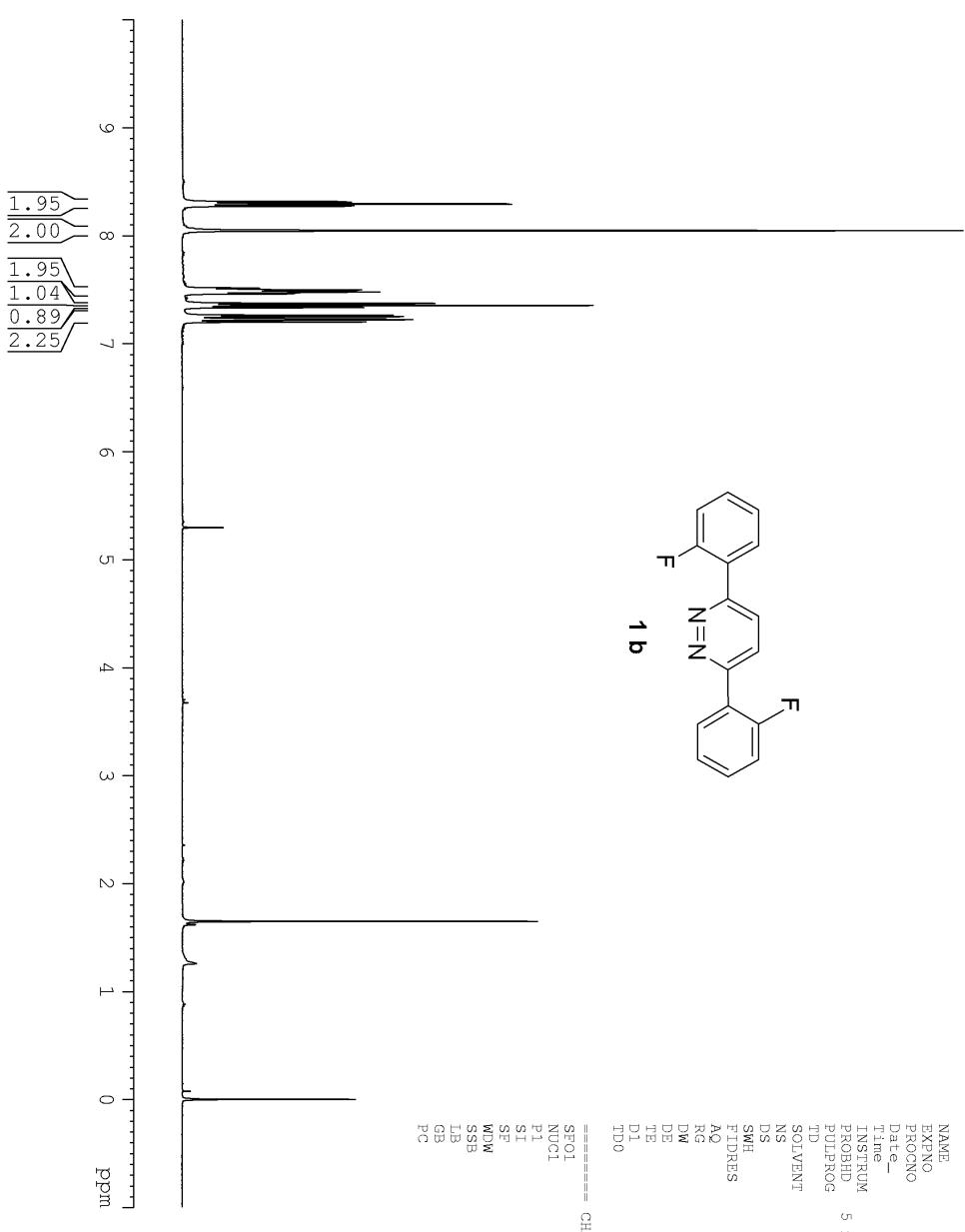
Identification code	sa3599	
Empirical formula	C16 H14 F2 N2	
Formula weight	272.29	
Temperature	173.1500 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 5.633(2) Å b = 10.581(4) Å c = 11.330(5) Å	$\alpha = 97.097(6)^\circ$. $\beta = 103.762(8)^\circ$. $\gamma = 92.953(4)^\circ$.
Volume	648.6(5) Å ³	
Z	2	
Density (calculated)	1.394 Mg/m ³	
Absorption coefficient	0.103 mm ⁻¹	
F(000)	284	
Crystal size	0.23 x 0.16 x 0.11 mm ³	
Theta range for data collection	1.869 to 27.483°.	
Index ranges	-7<=h<=7, -13<=k<=13, -14<=l<=13	
Reflections collected	8212	
Independent reflections	2970 [R(int) = 0.0345]	
Completeness to theta = 26.000°	99.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.8049	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	2970 / 0 / 195	
Goodness-of-fit on F ²	1.148	
Final R indices [I>2sigma(I)]	R1 = 0.0603, wR2 = 0.1423	
R indices (all data)	R1 = 0.0678, wR2 = 0.1488	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.317 and -0.206 e.Å ⁻³	

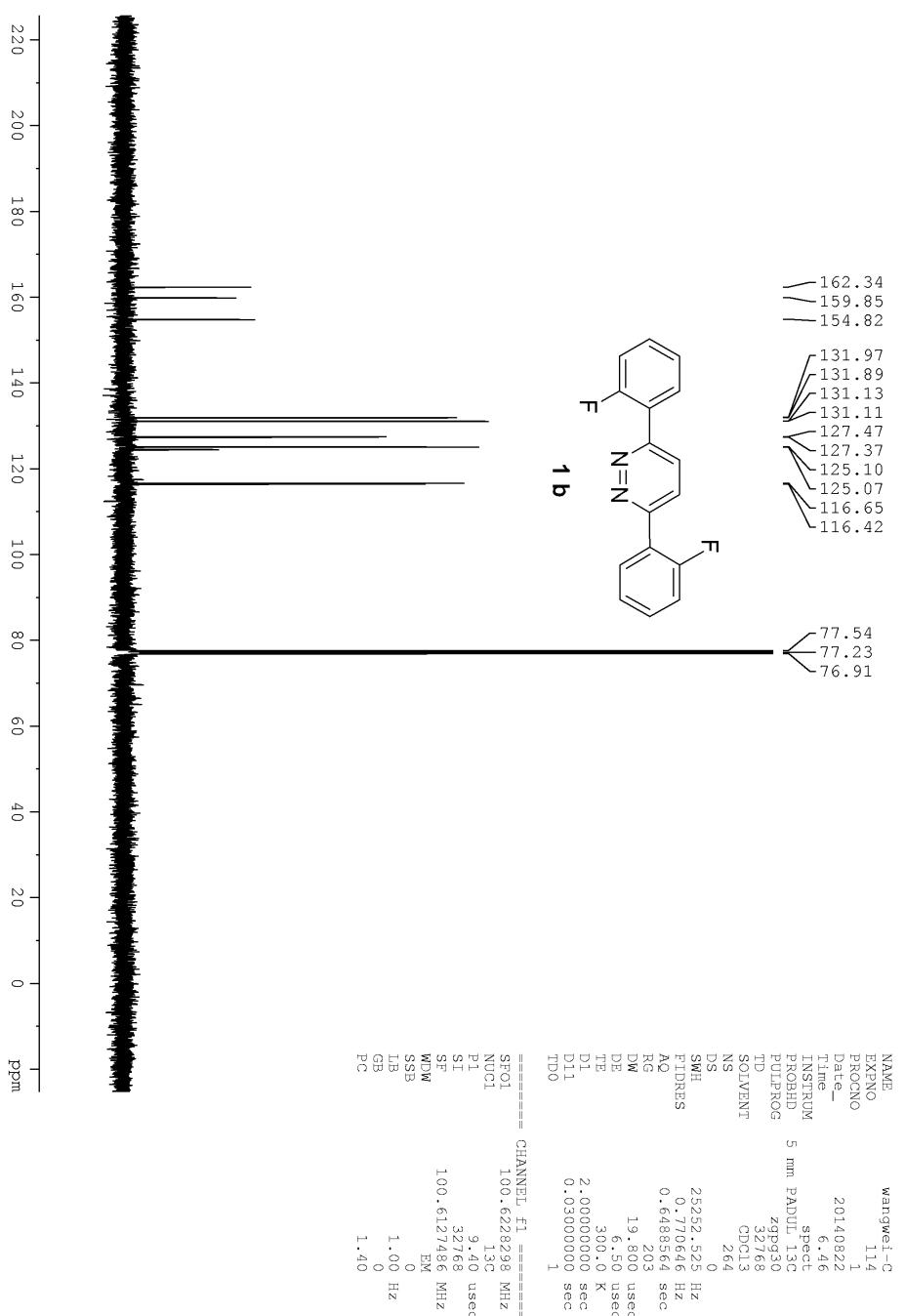


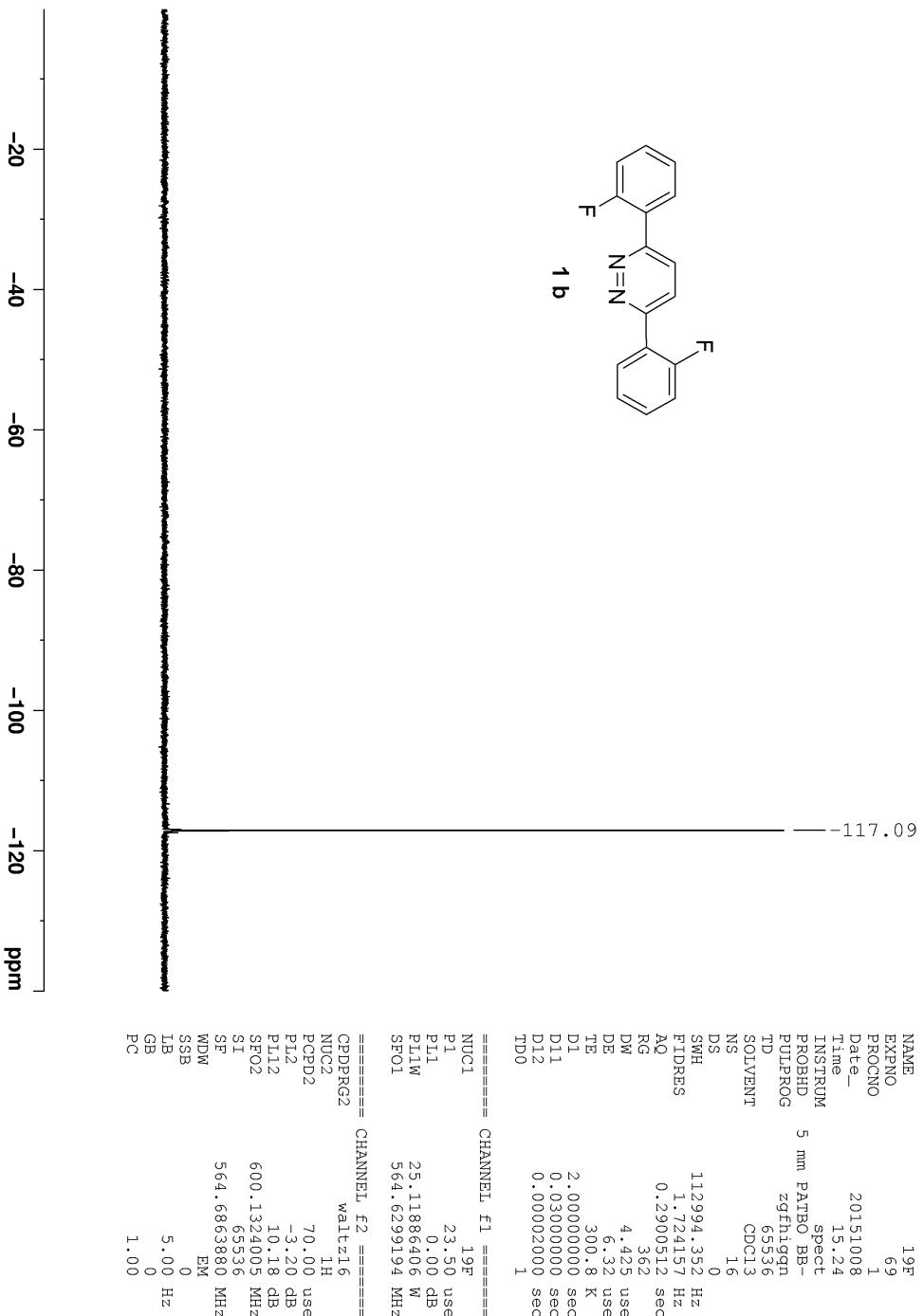
NMR spectra for the substrates and products.

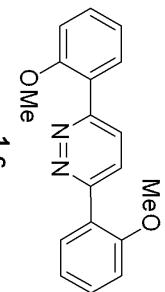
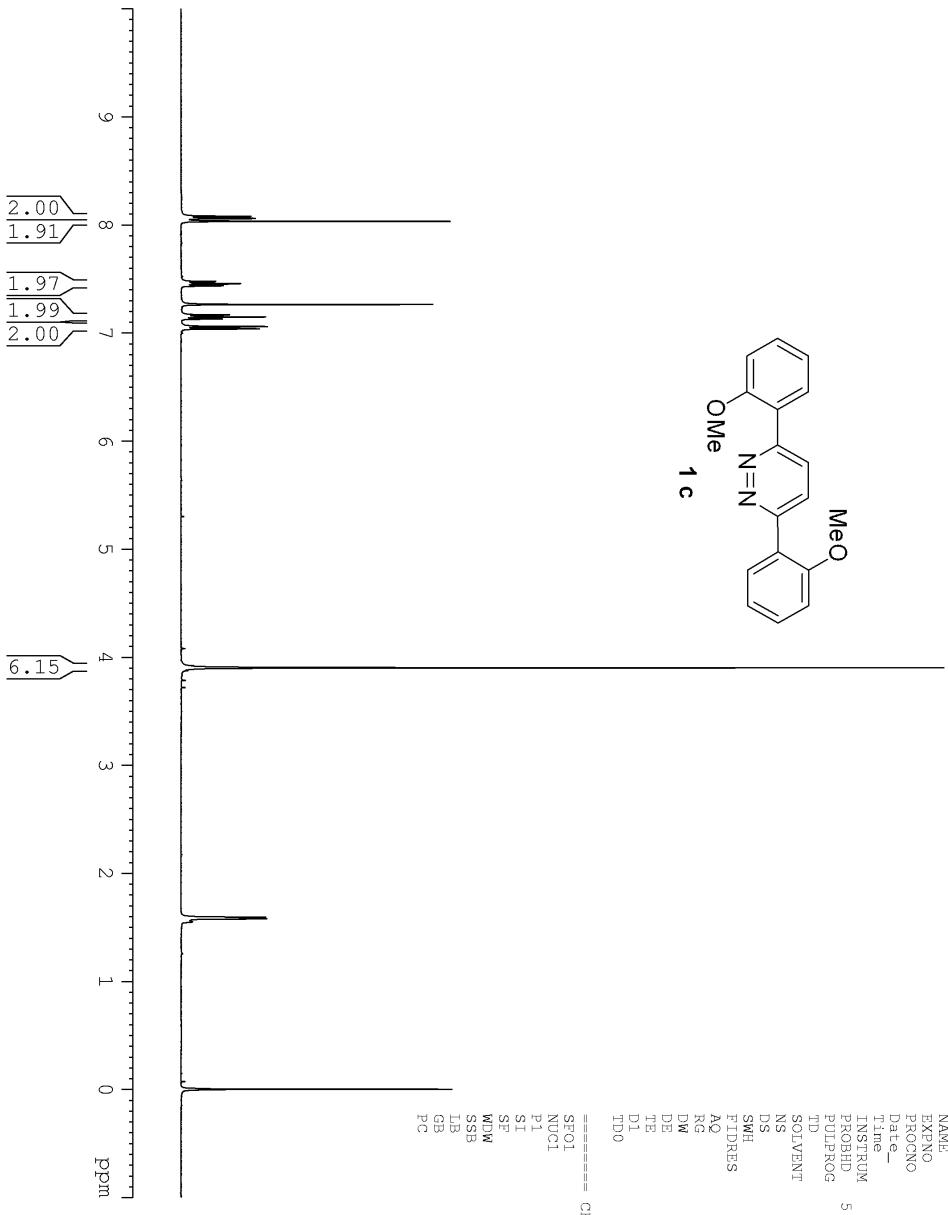




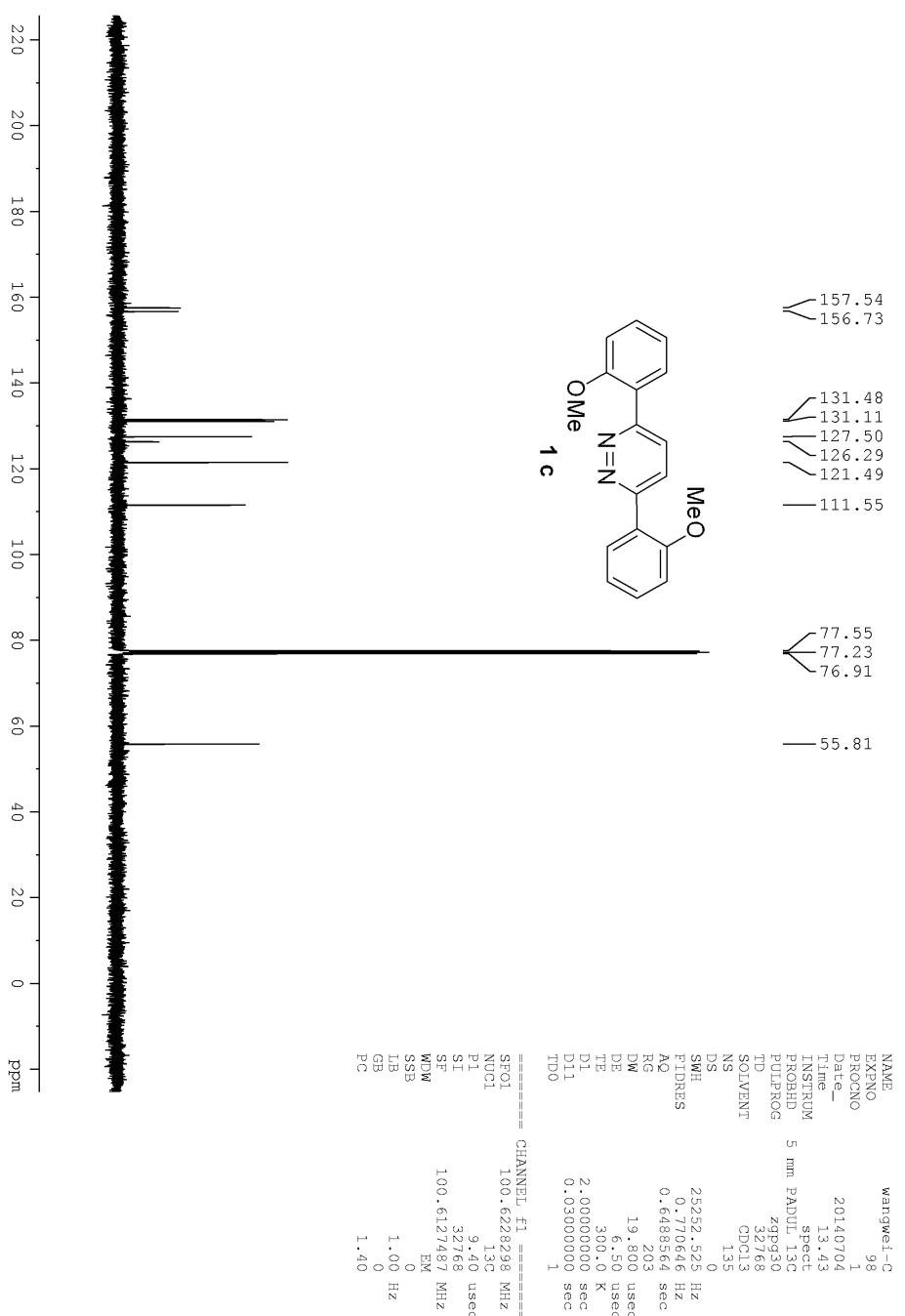


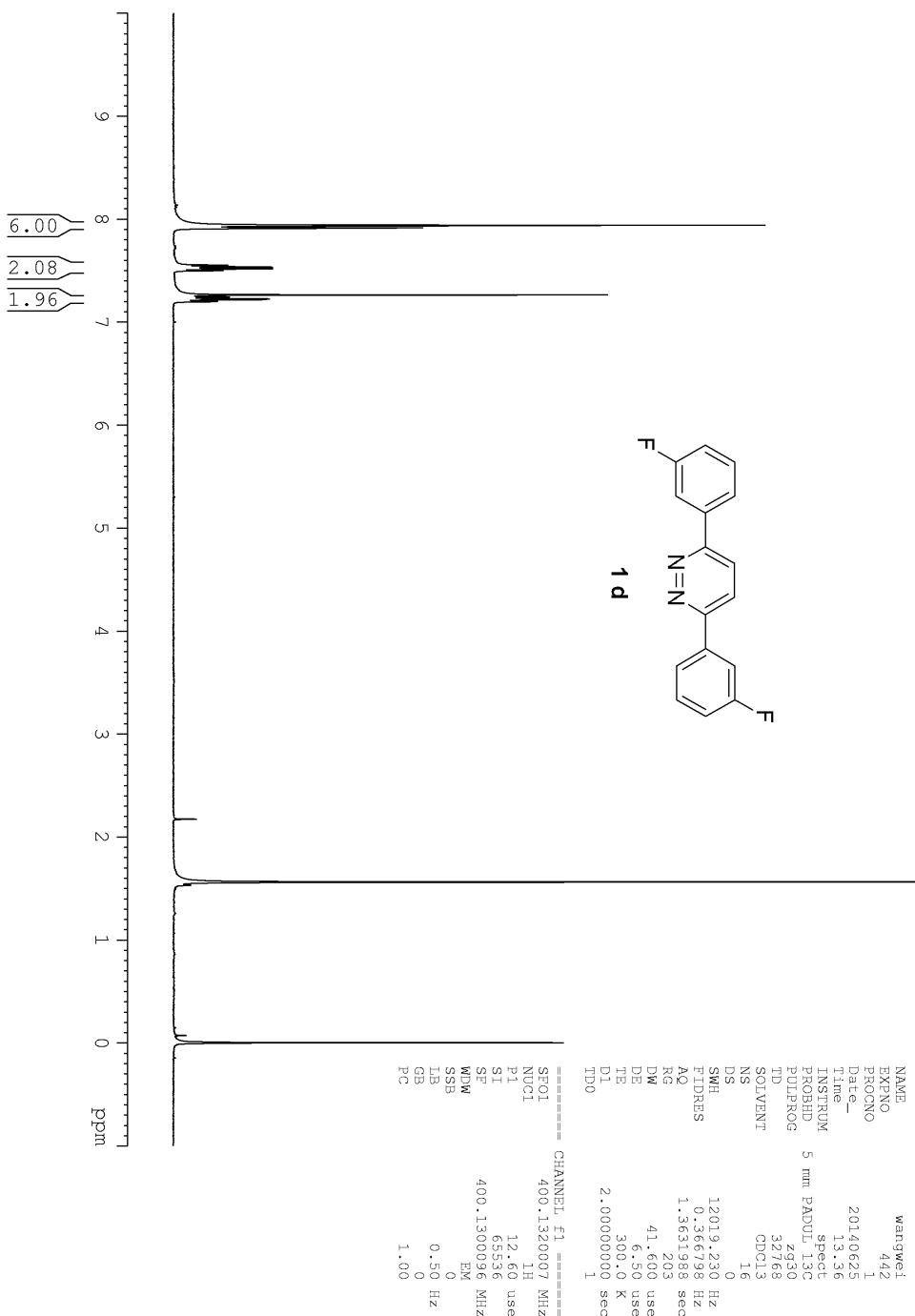


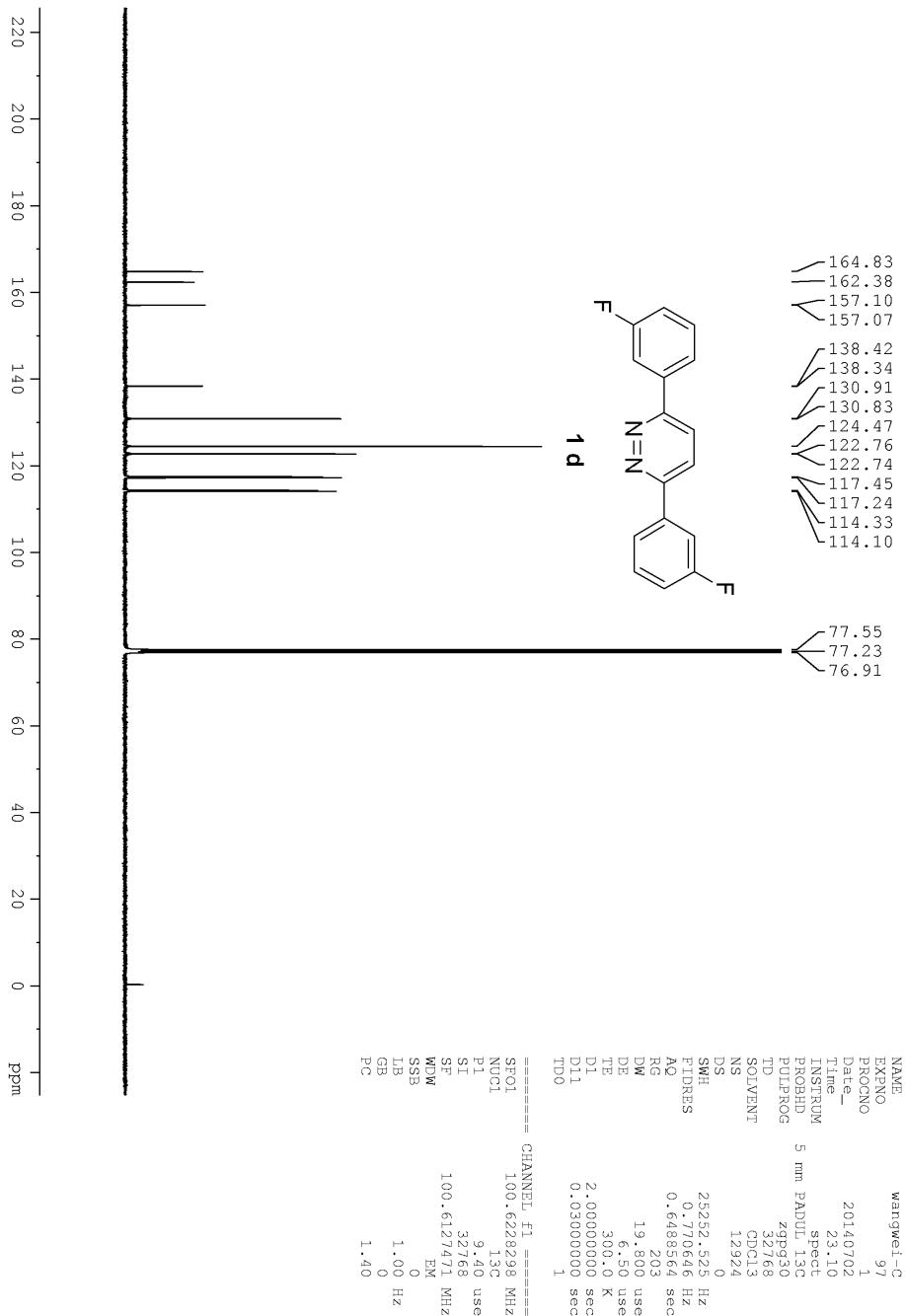


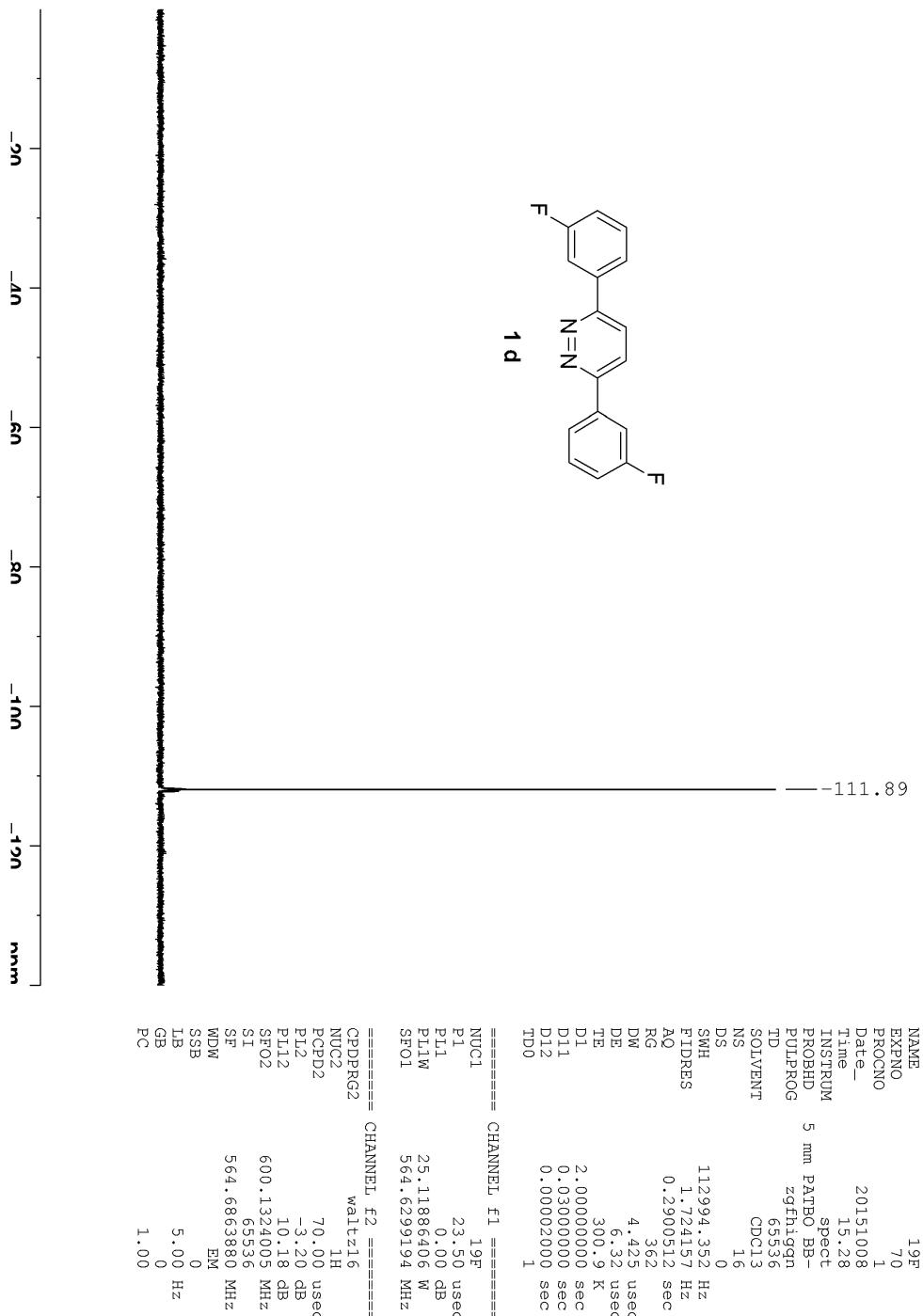


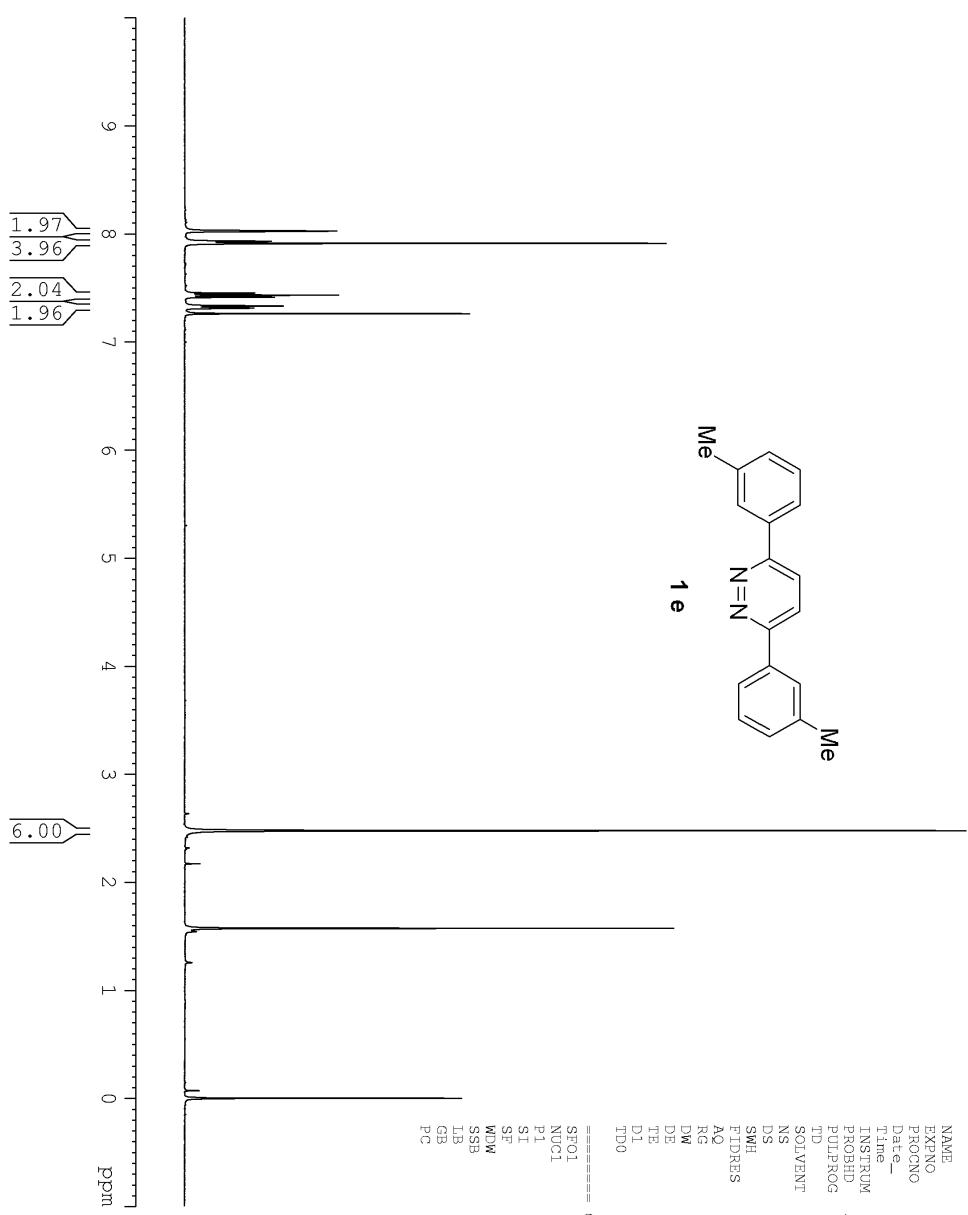
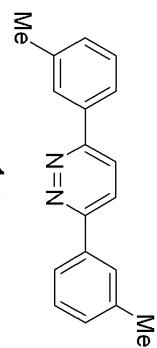
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EXPO	460	
PROCMO	1	
Date_	20140704	
Time	9.39	
INSTRIUM	5 mm PADUL.13C	
SPECTRUM		
PULLPROG	z930	
TD	32768	
SOLVENT	CDCl3	
NS	16	
DS	0	
SWH	1.2019-1.230 Hz	
FIDRES	0.366793 sec	
AQ	1.3633198 sec	
RG	2.003	
DW	41.600 usec	
DE	6.500 usec	
TE	300.0 K	
D1	2.0000000 sec	
TDO	1	
==== CHANNEL f1 =====		
SF01	400.1320007 MHz	
NUCL	1H	
P1	12.60 usec	
SI	655.535	
SP	400.1300093 MHz	
WW	EMX	

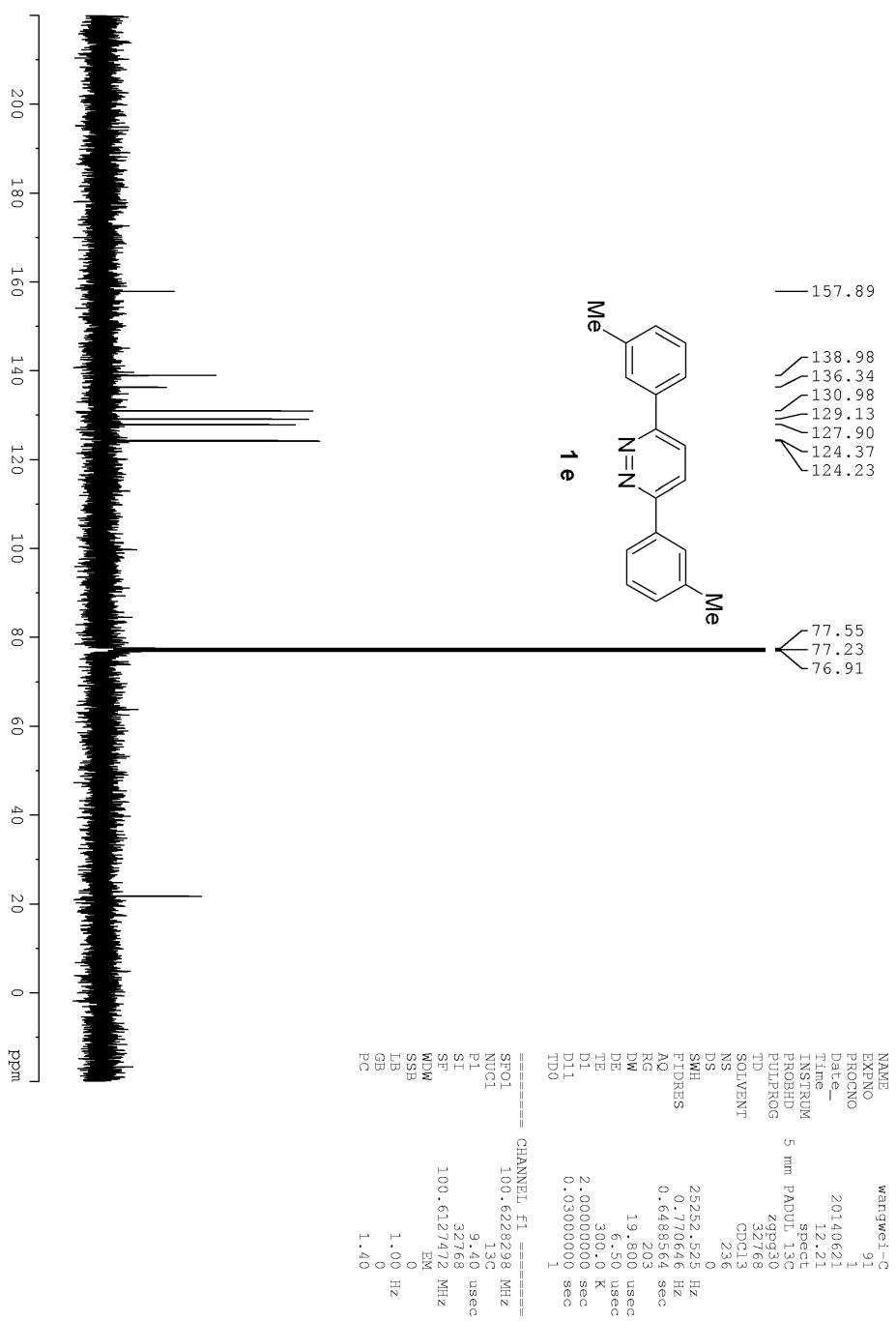


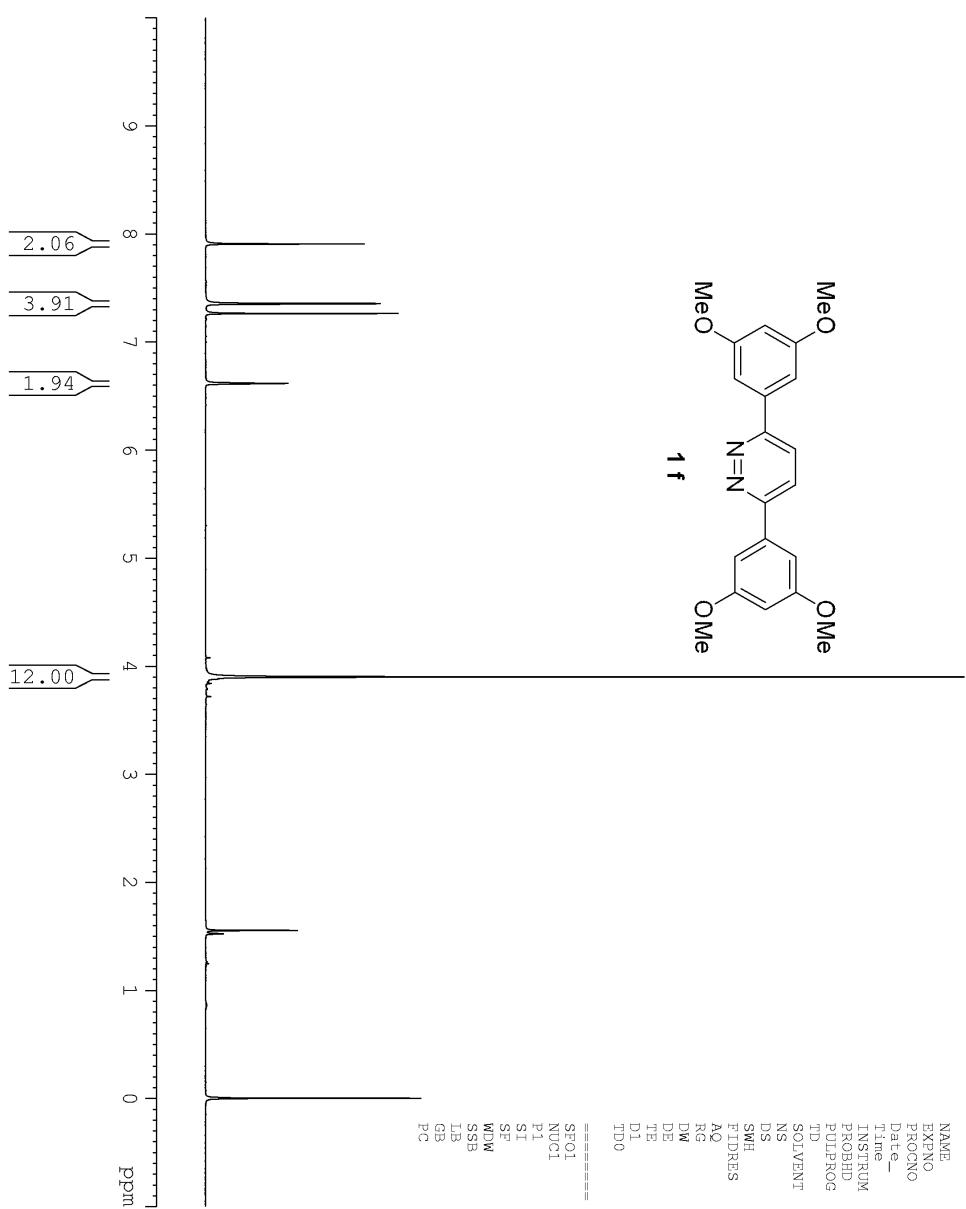
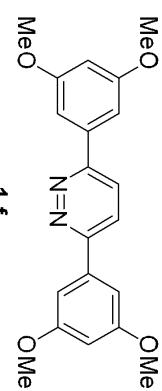










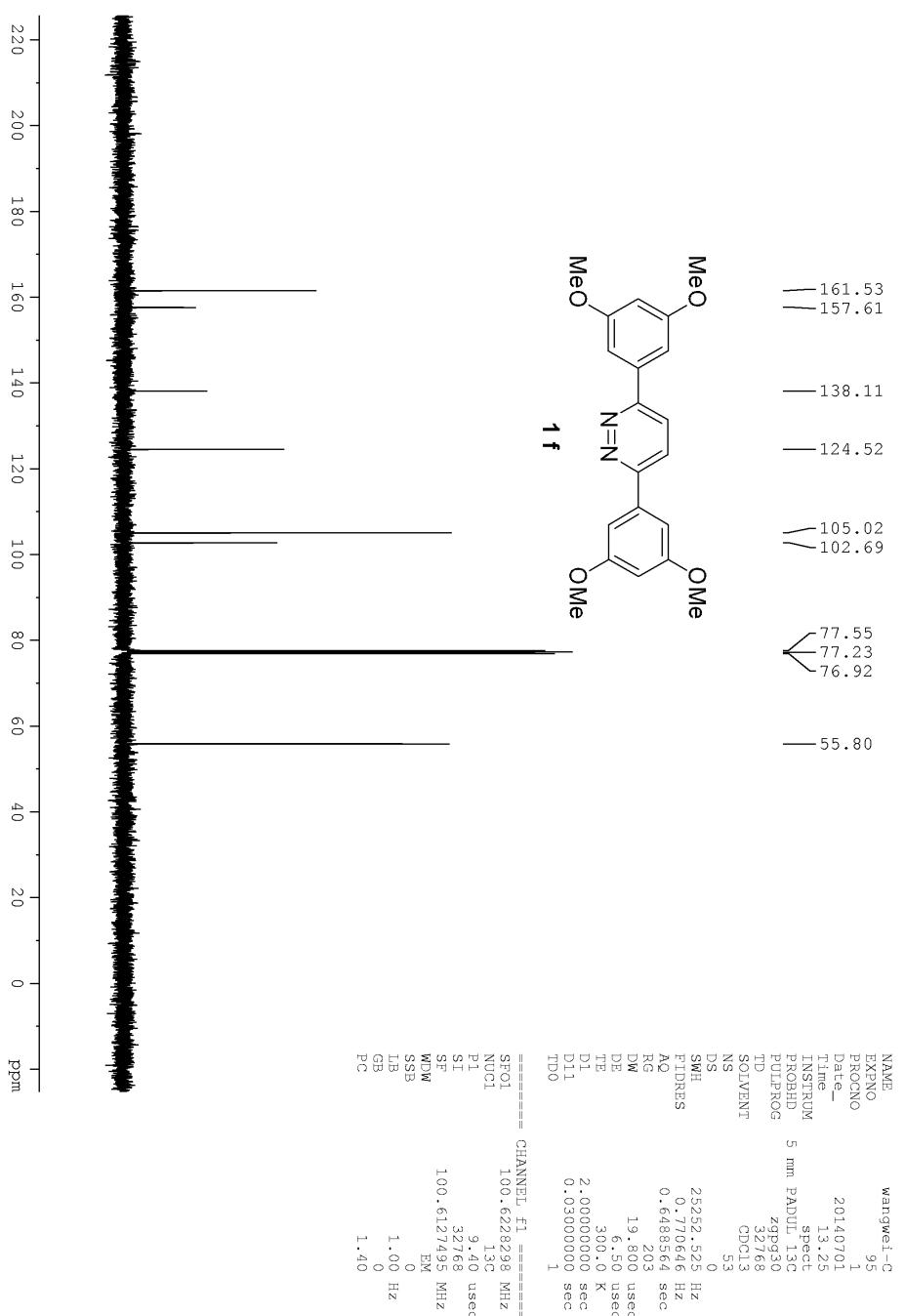


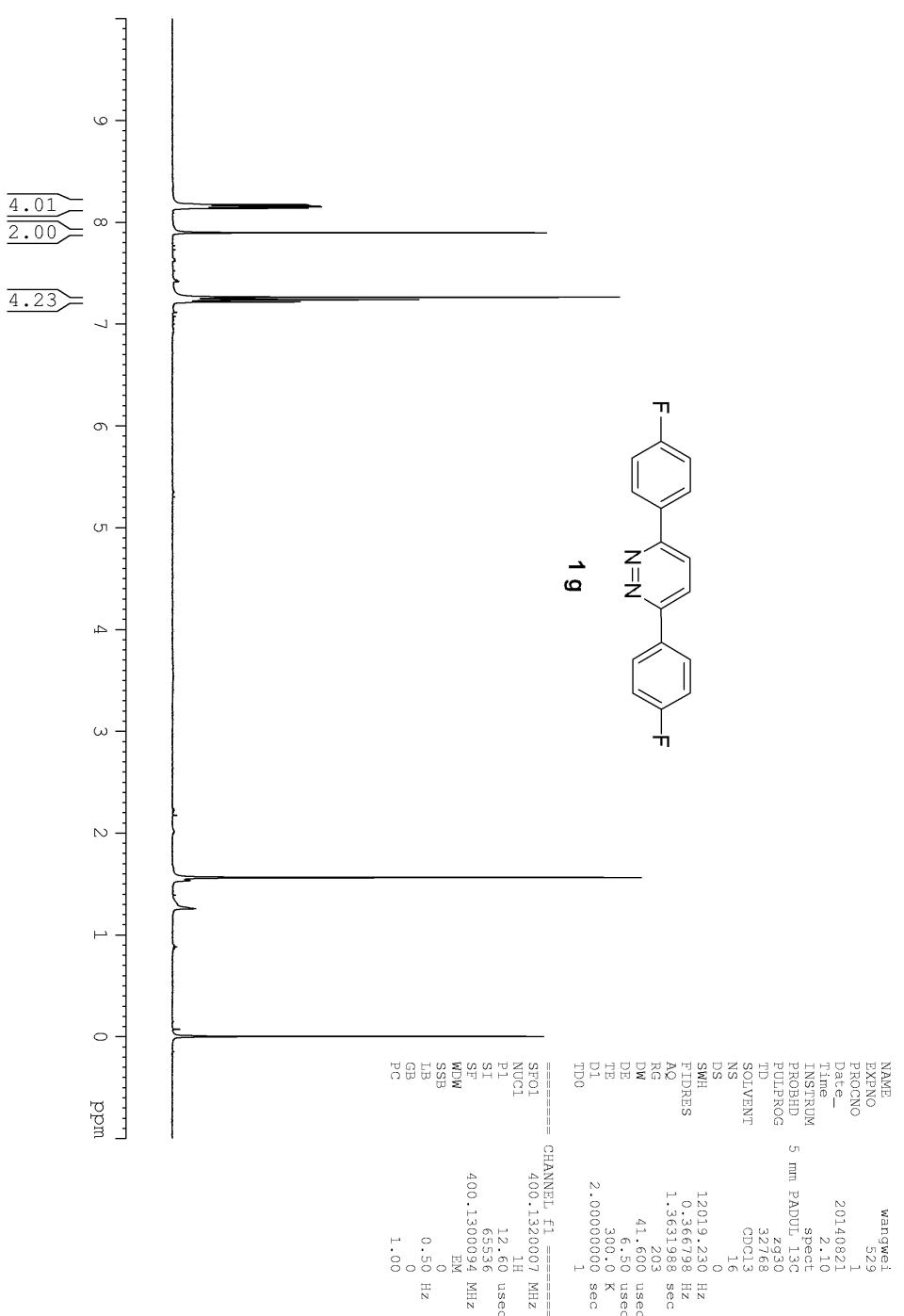
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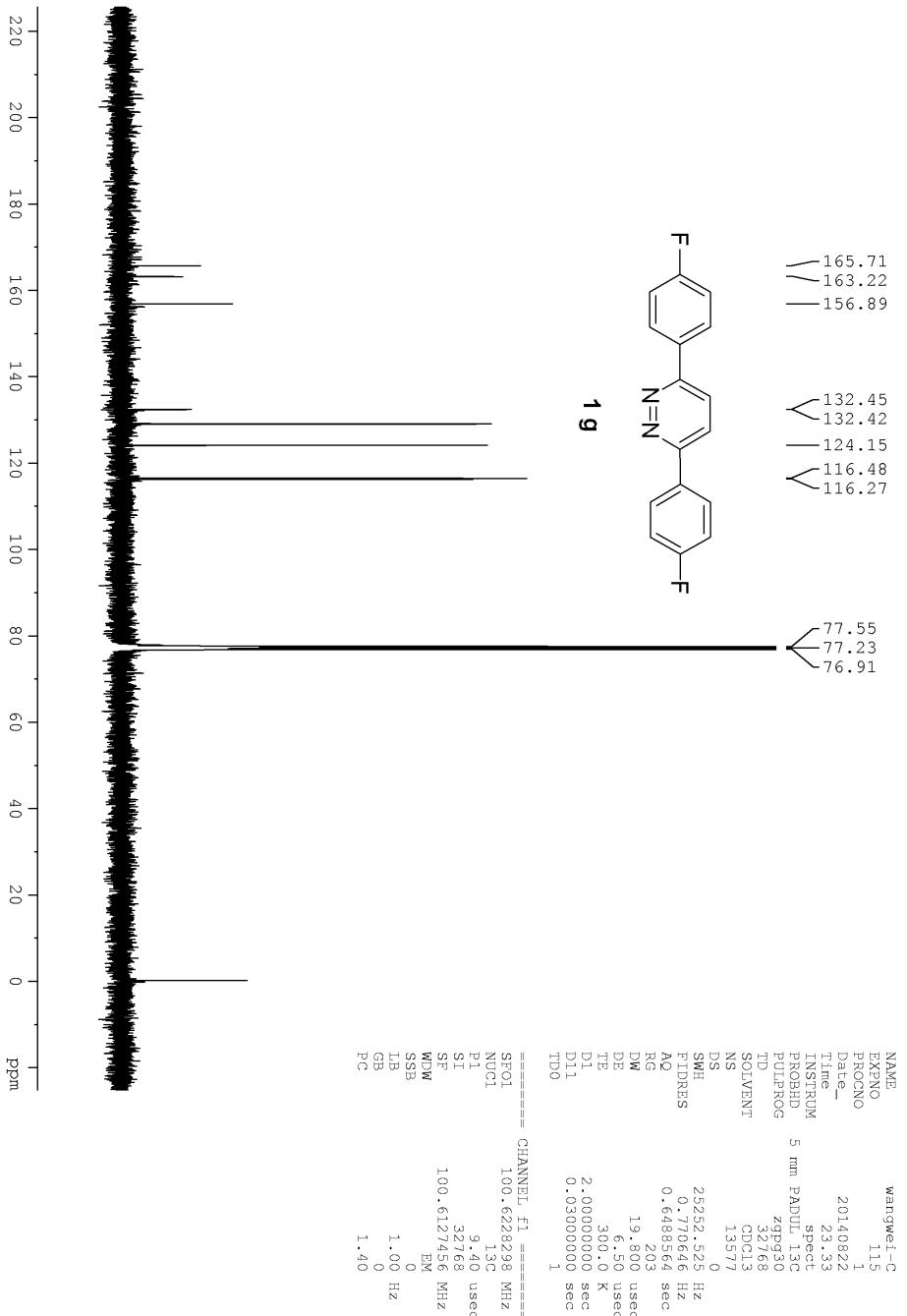
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EXNO         455
PROCNO        1
Date_      20140701
Time       13.09
INSTRUM     spect
PROBHD      5 mm PADUL 13C
PULPROG    zg30
TD        32768
SOLVENT      CDCl3
NS           16
DS            0
SWH        12019.230 Hz
SFH        0.366798 Hz
FIDRES     1.3631988 sec
AQ           2.03
RG           41.600 usec
DW           6.50 usec
DE           300.0 K
TE           2.0000000 sec
D1             1
TDO          1

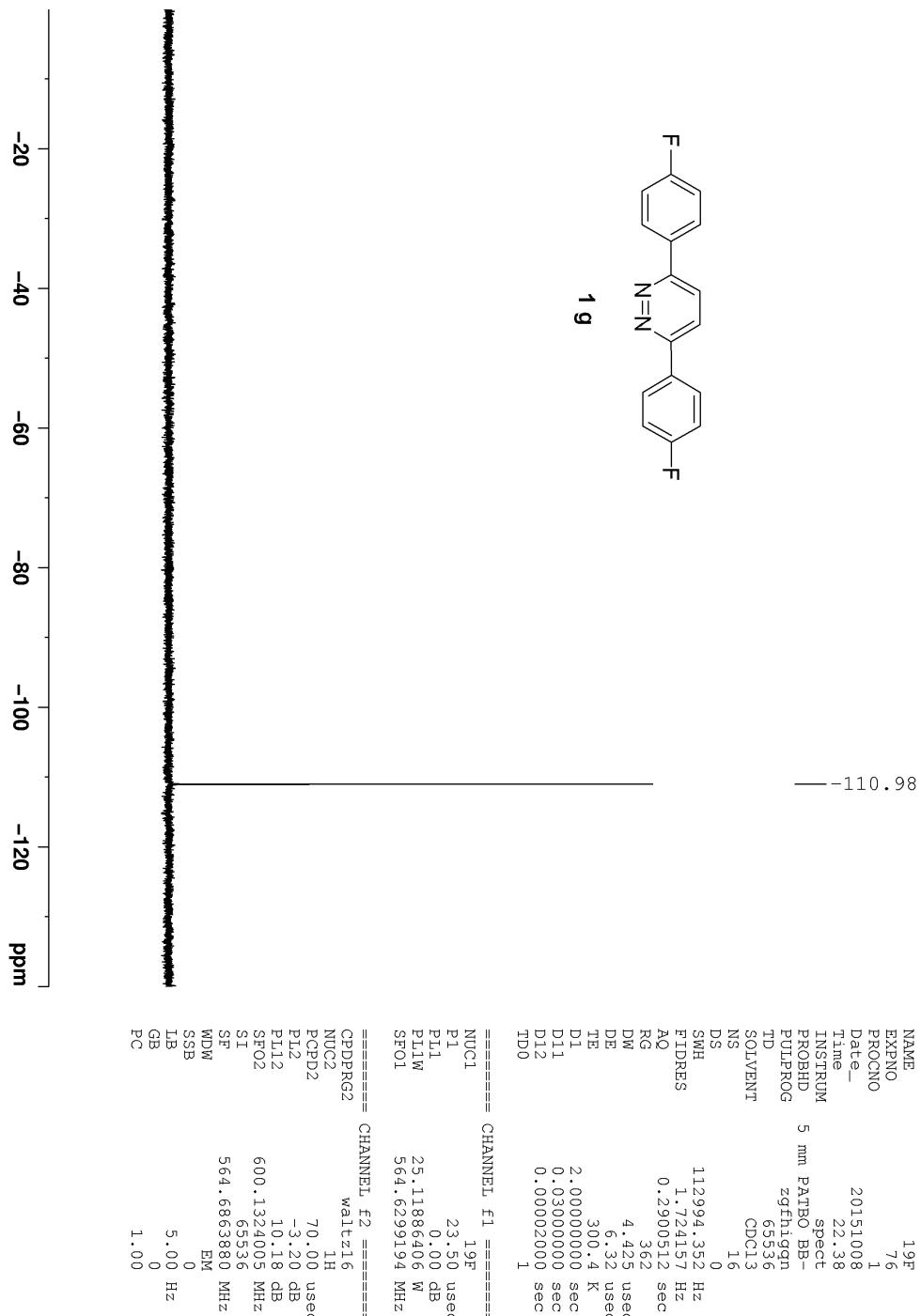
===== CHANNEL f1 =====
SF01      400.132007 MHz
NUC1          1H
P1           12.60 usec
SI            65536
SF        400.1300098 MHz
WDW         EM
SSB          0
LB          0.50 Hz
GB          0
PC           1.00

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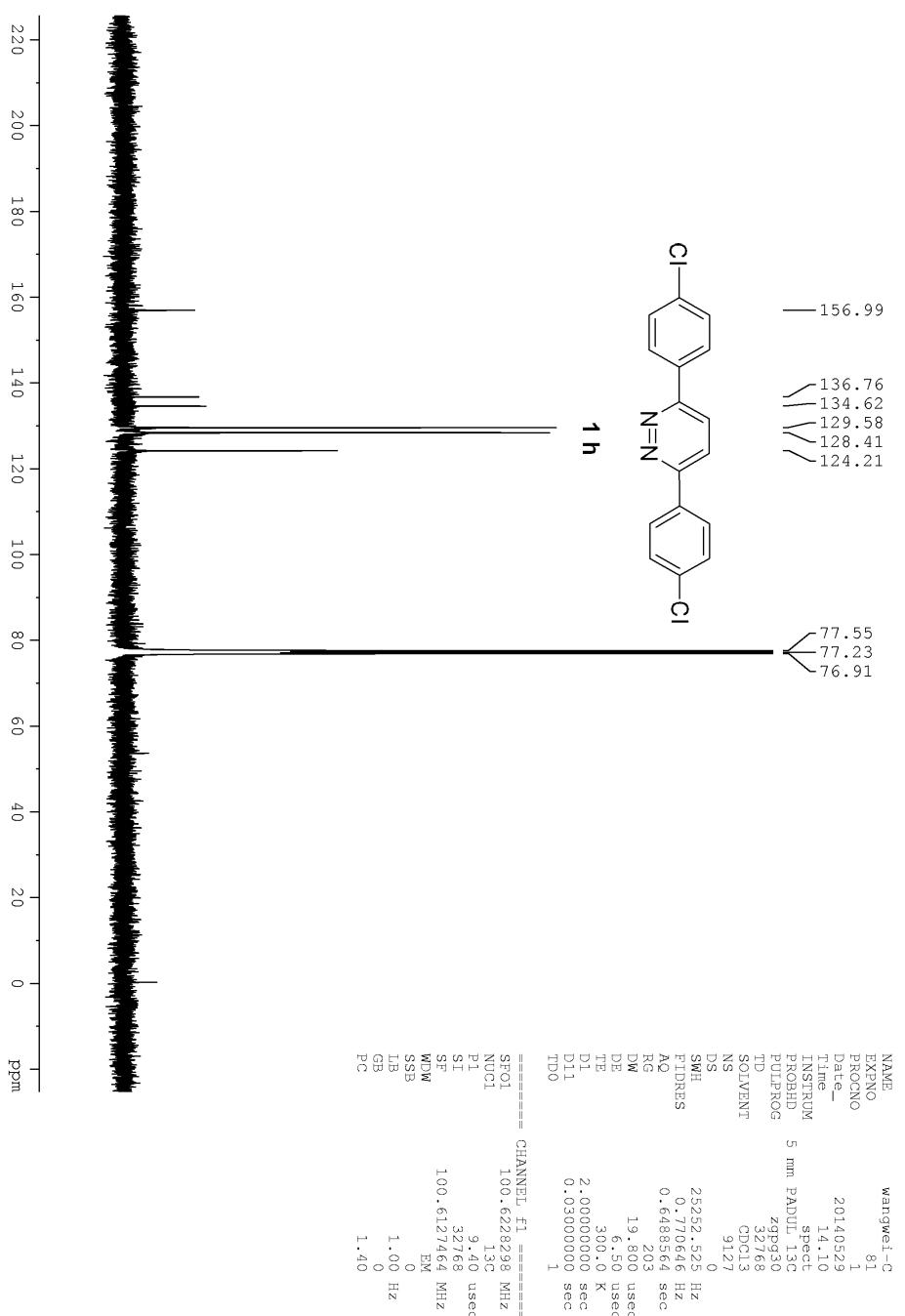


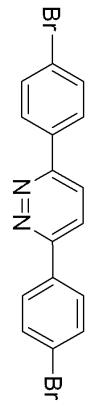




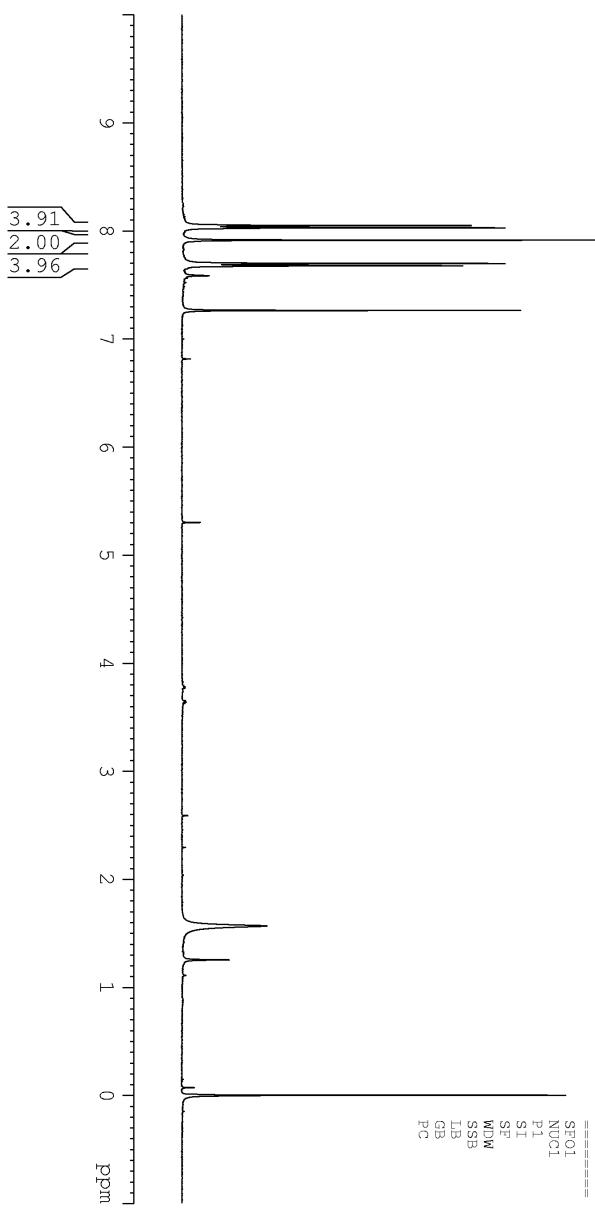








1i

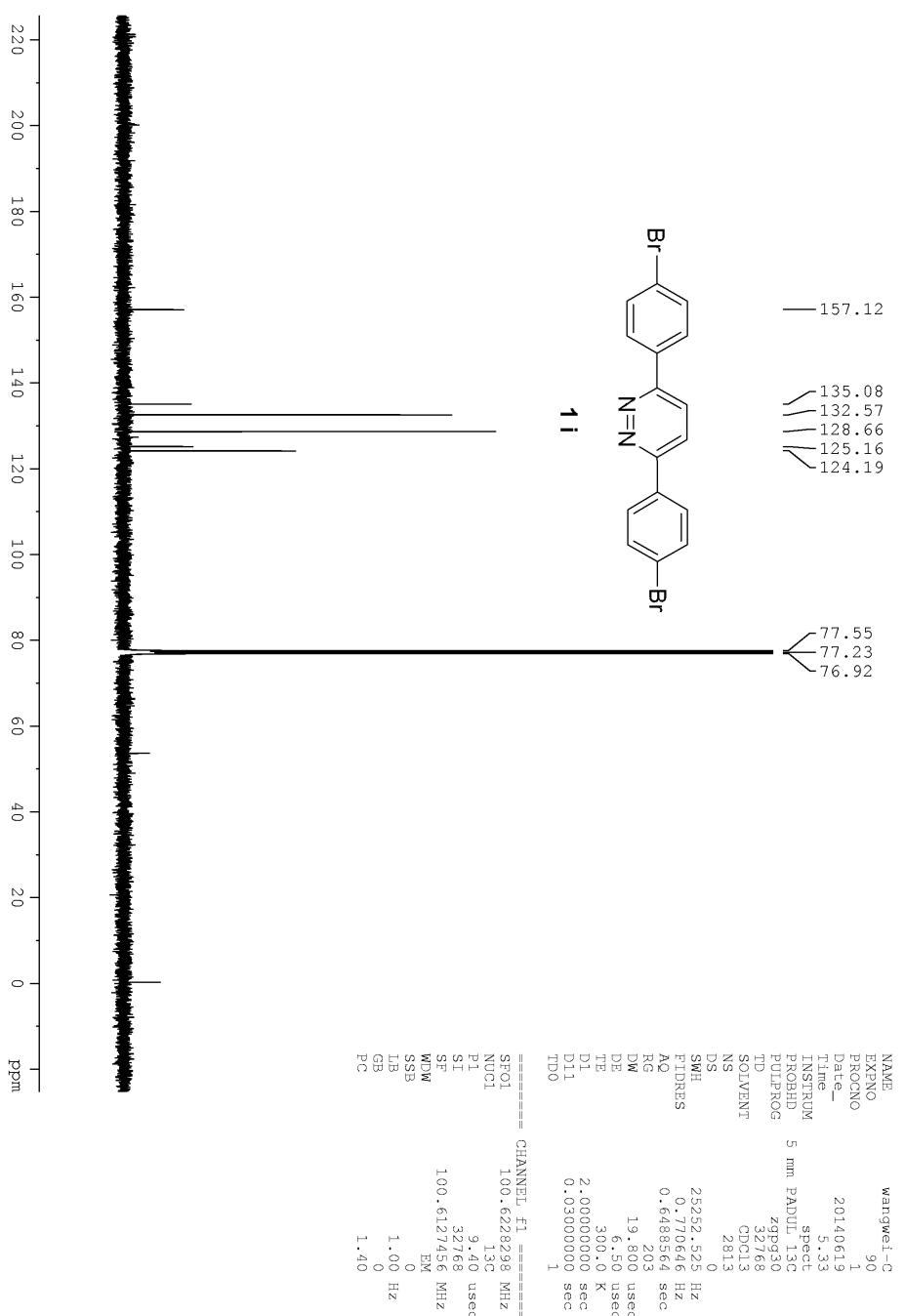


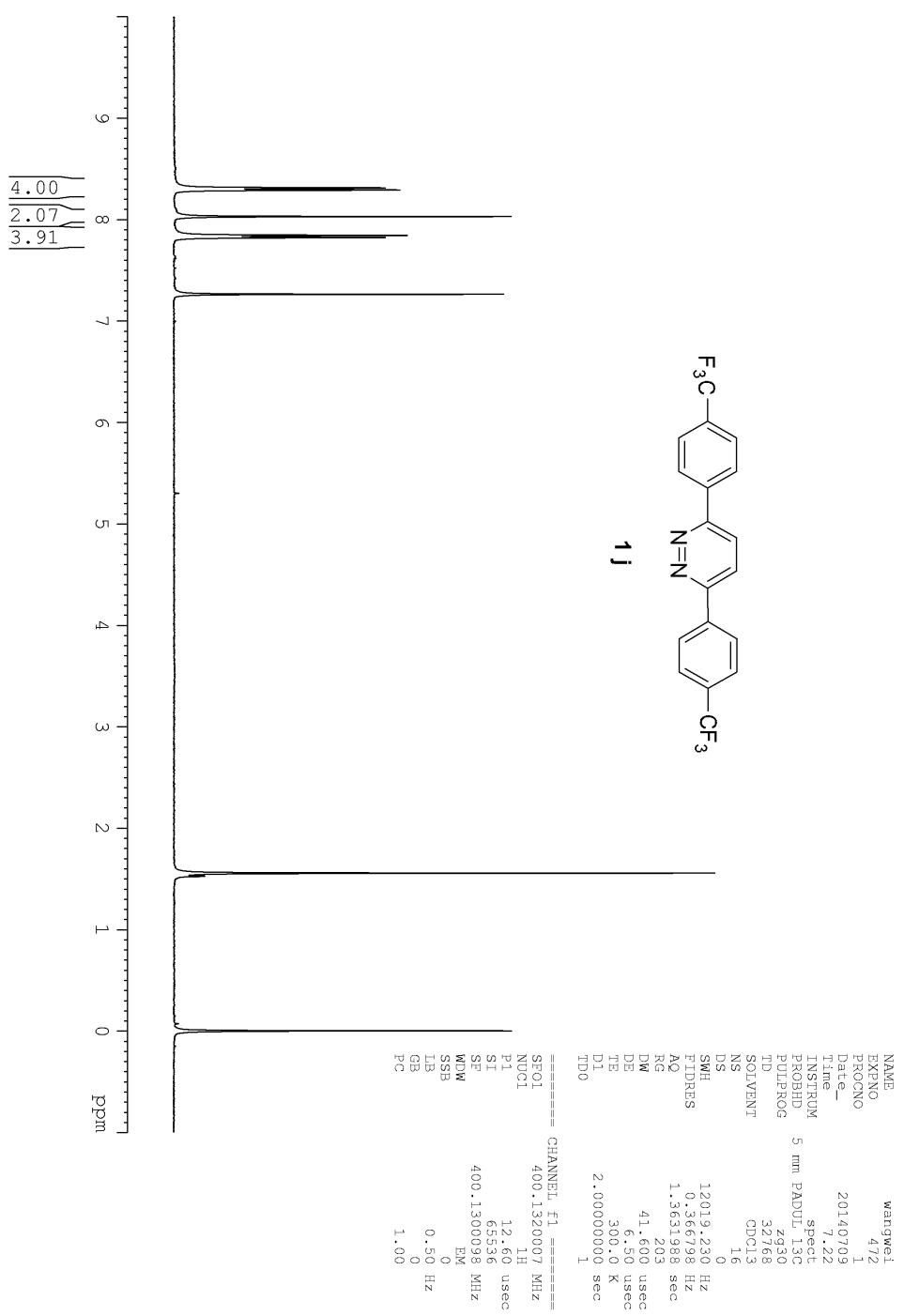
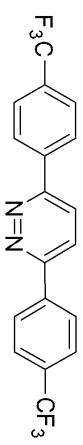
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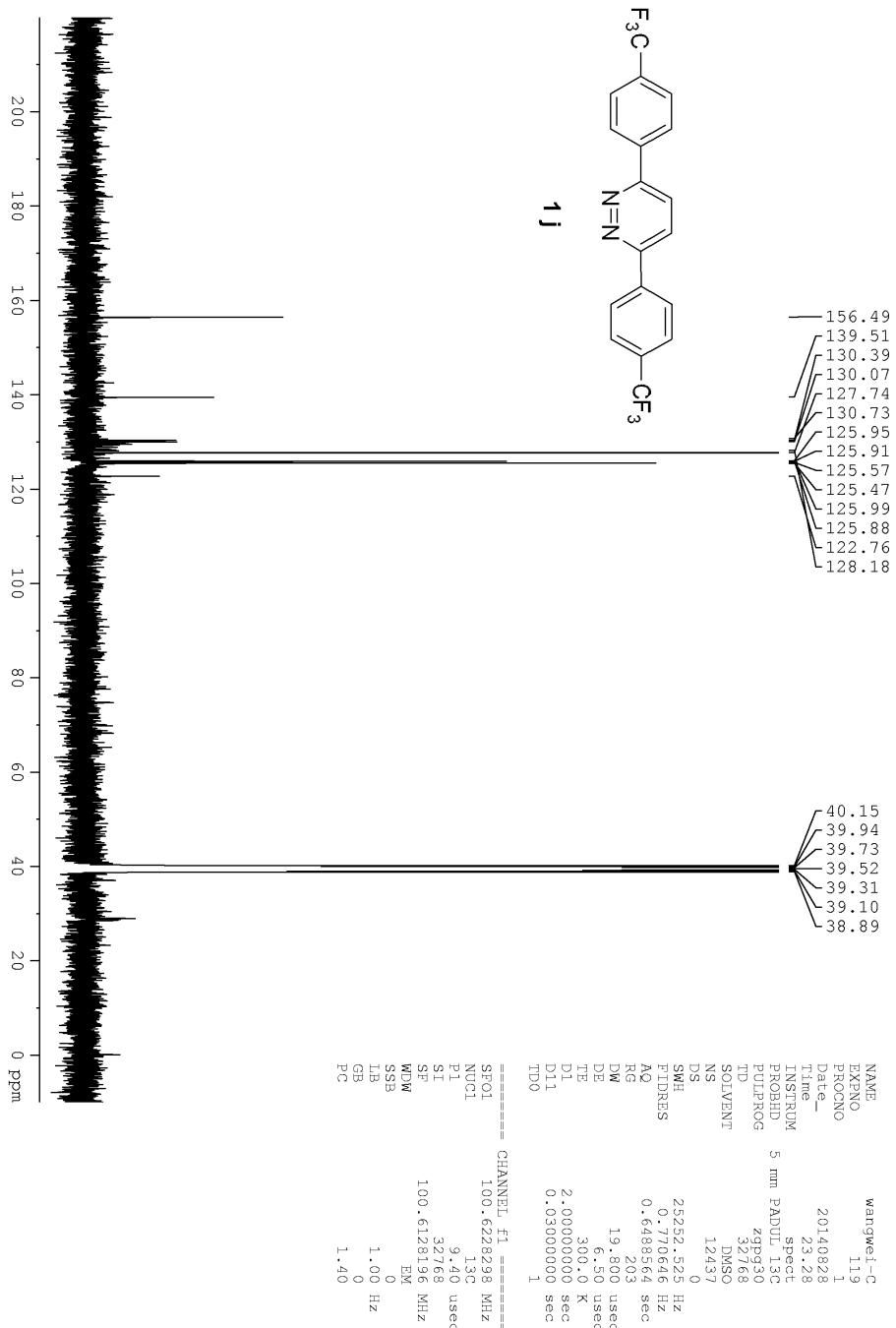
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EXNO         431
PROCNO      1
PROBHD     5 mm PADUL 13C
PULPROG    zg30
TD          32768
SOLVENT     CDCl3
NS           16
DS            0
SWH        12019.230 Hz
SFH        0.366798 Hz
TDRES      1.3631988 sec
AQ           2.03
RG           41.600 usec
DW           6.50 usec
DE           300.0 K
TE           2.0000000 sec
D1          1
TDO          1

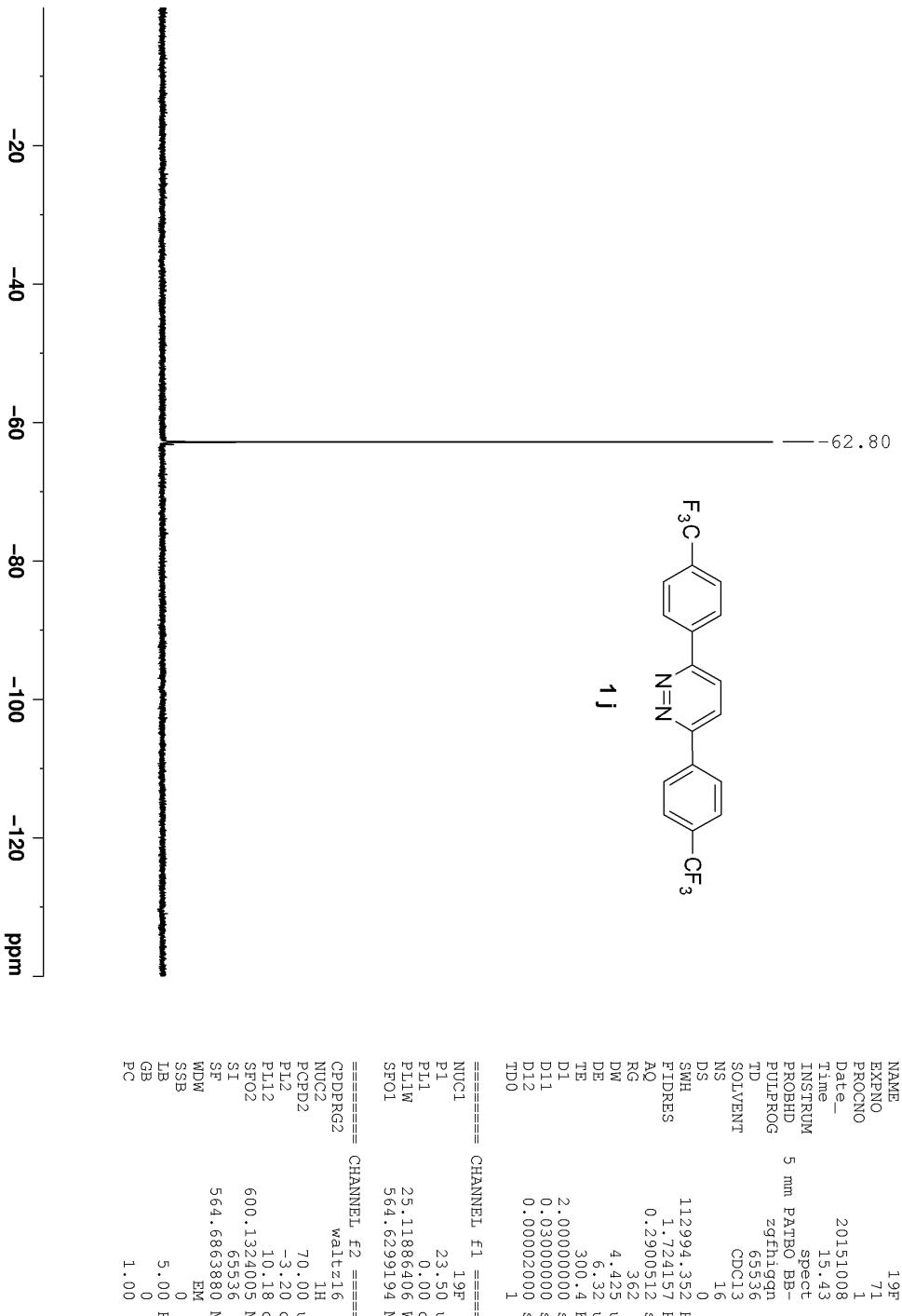
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CHANNEL f1 =====
SF01       400.132007 MHz
NUCL1      1H
P1          12.60 usec
SI           65536
SF          400.1300094 MHz
WDW        EM
SSB          0
LB          0.50 Hz
GB          0
PC          1.00

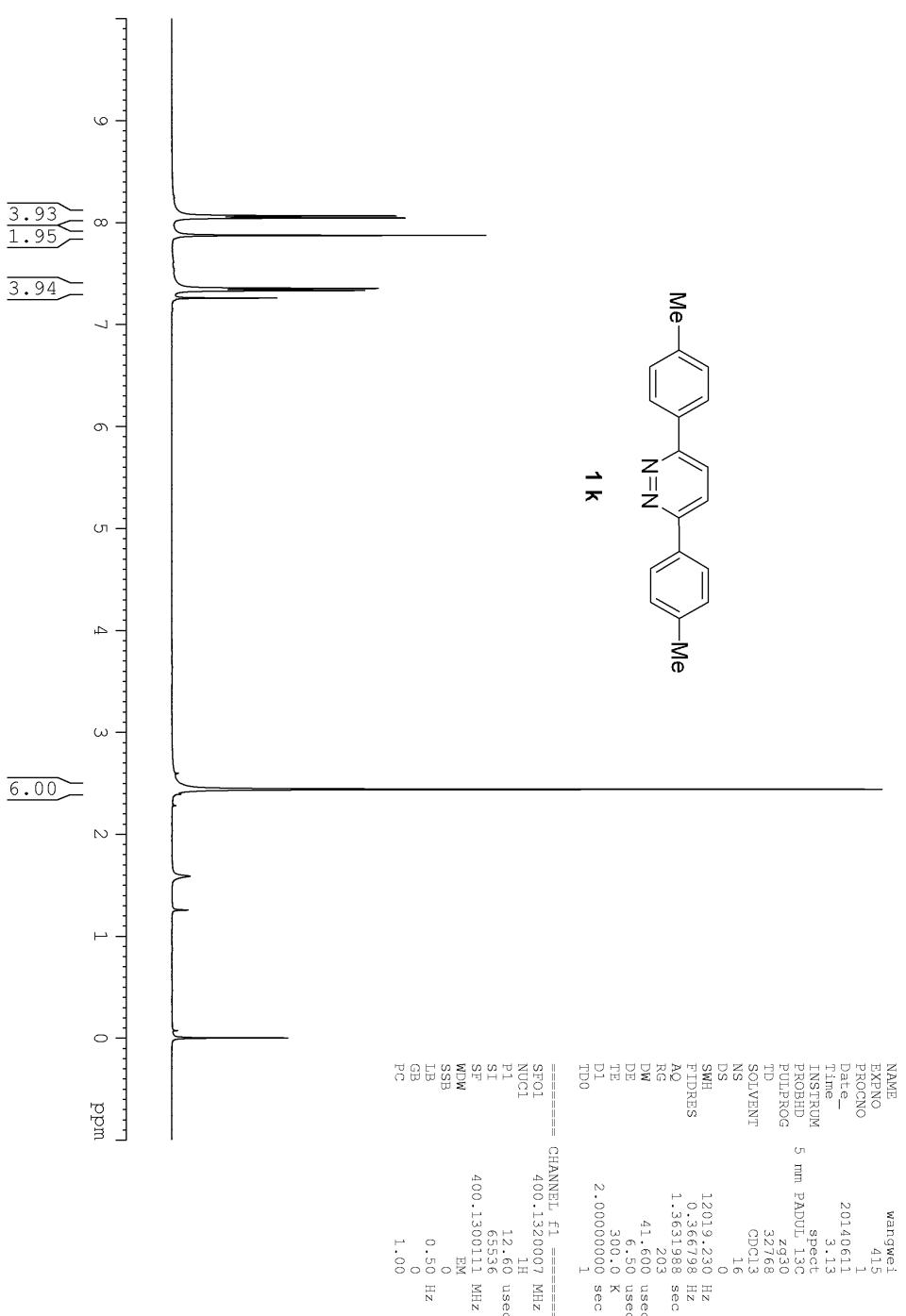
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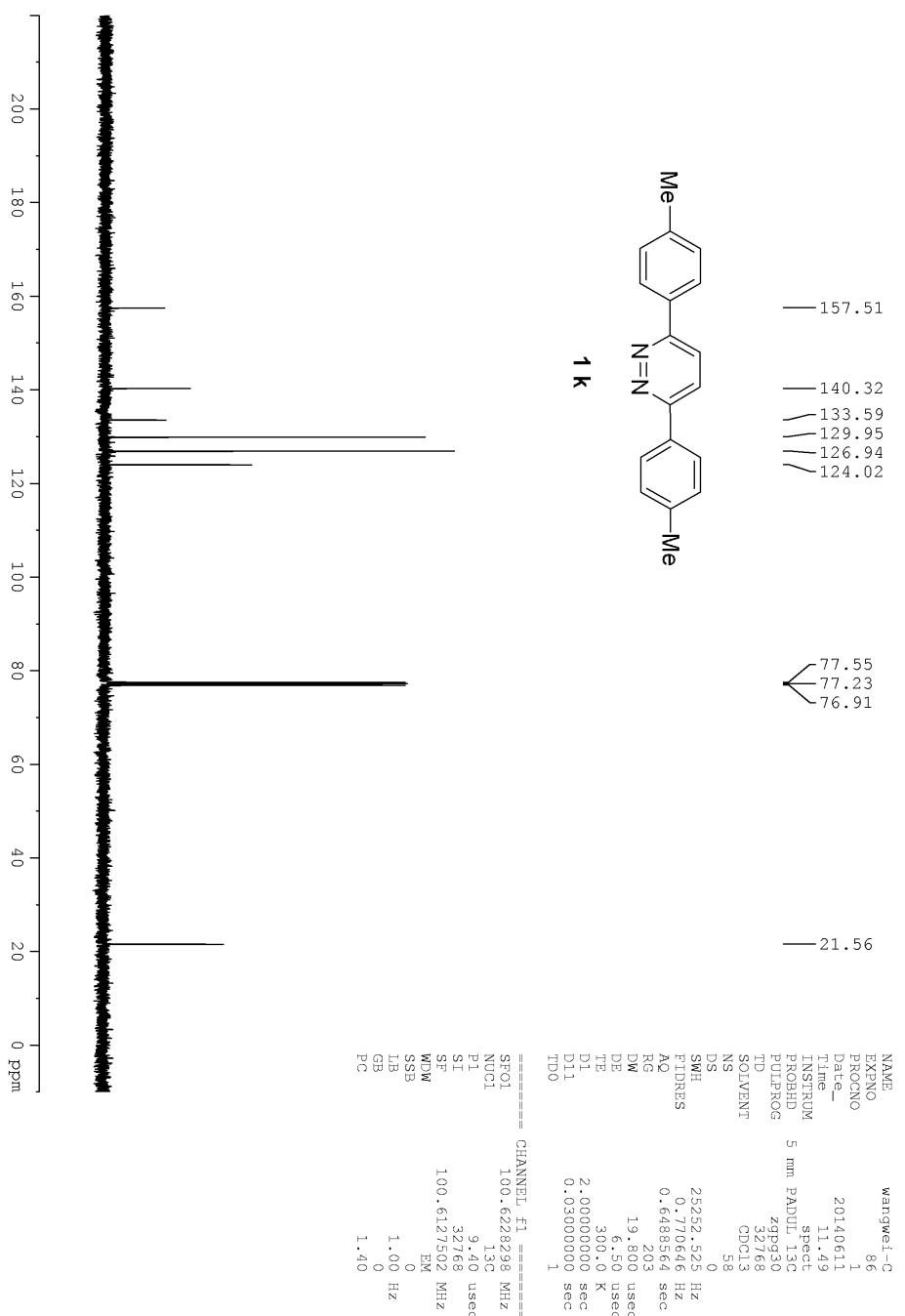


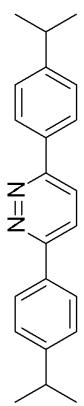


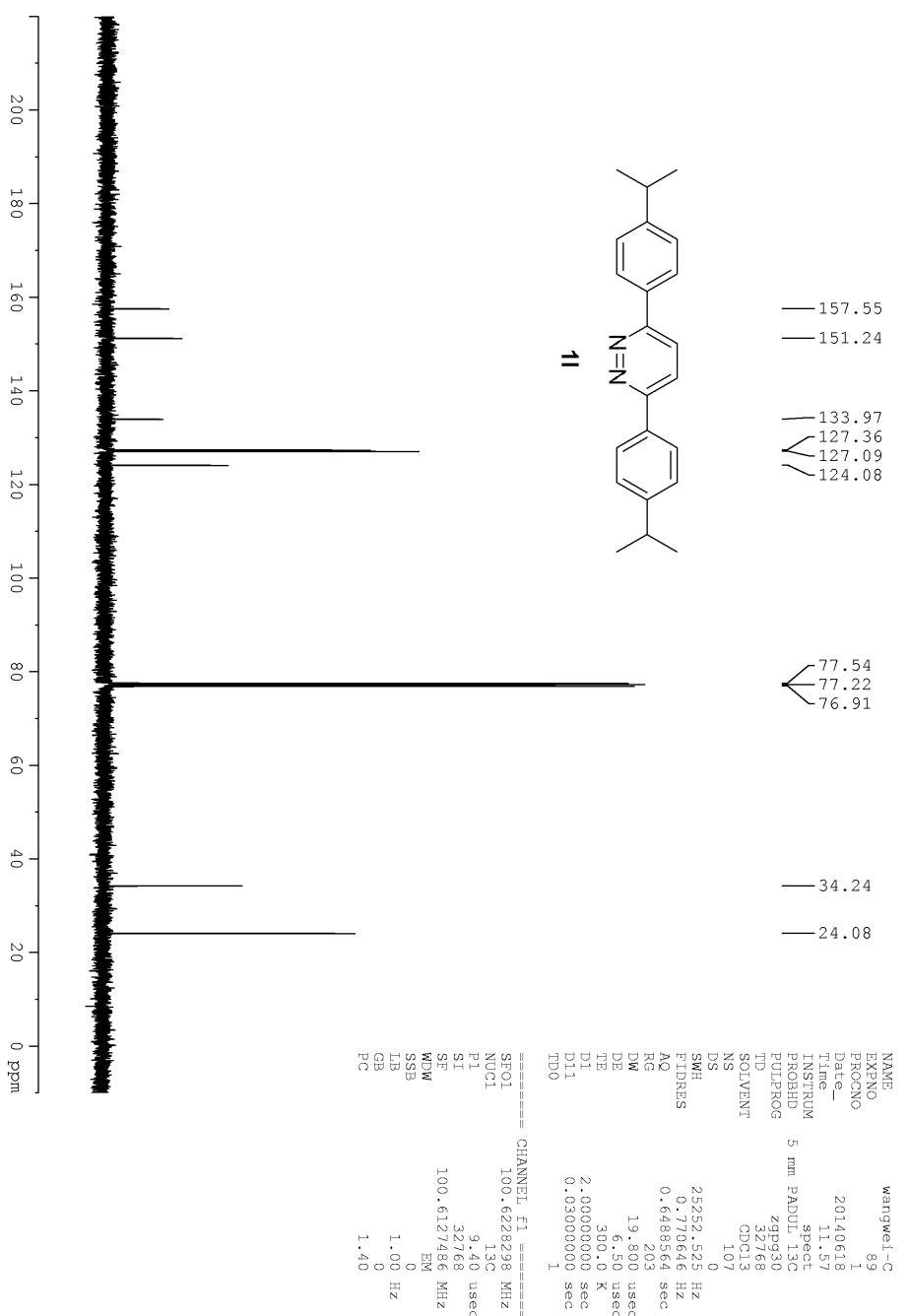


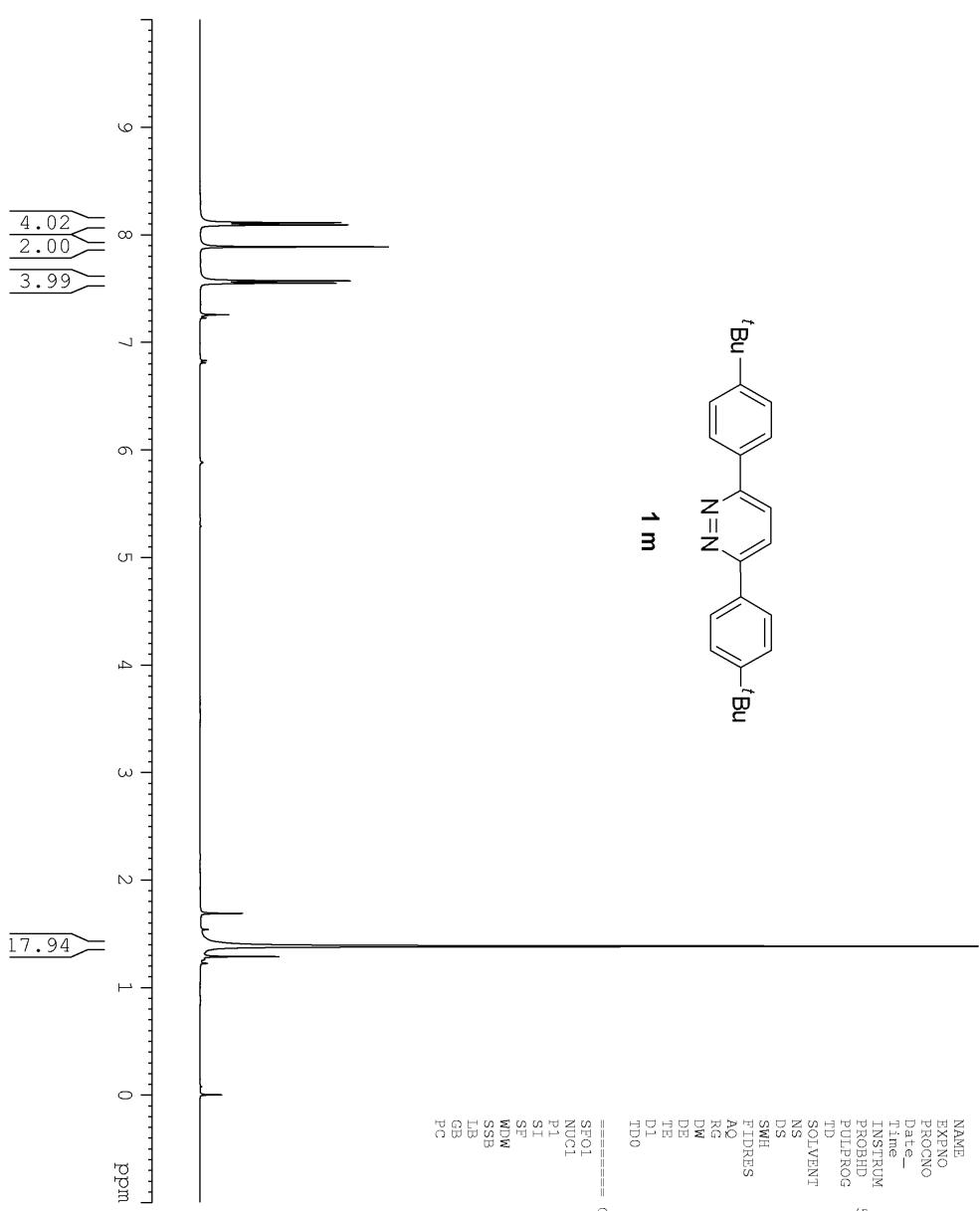


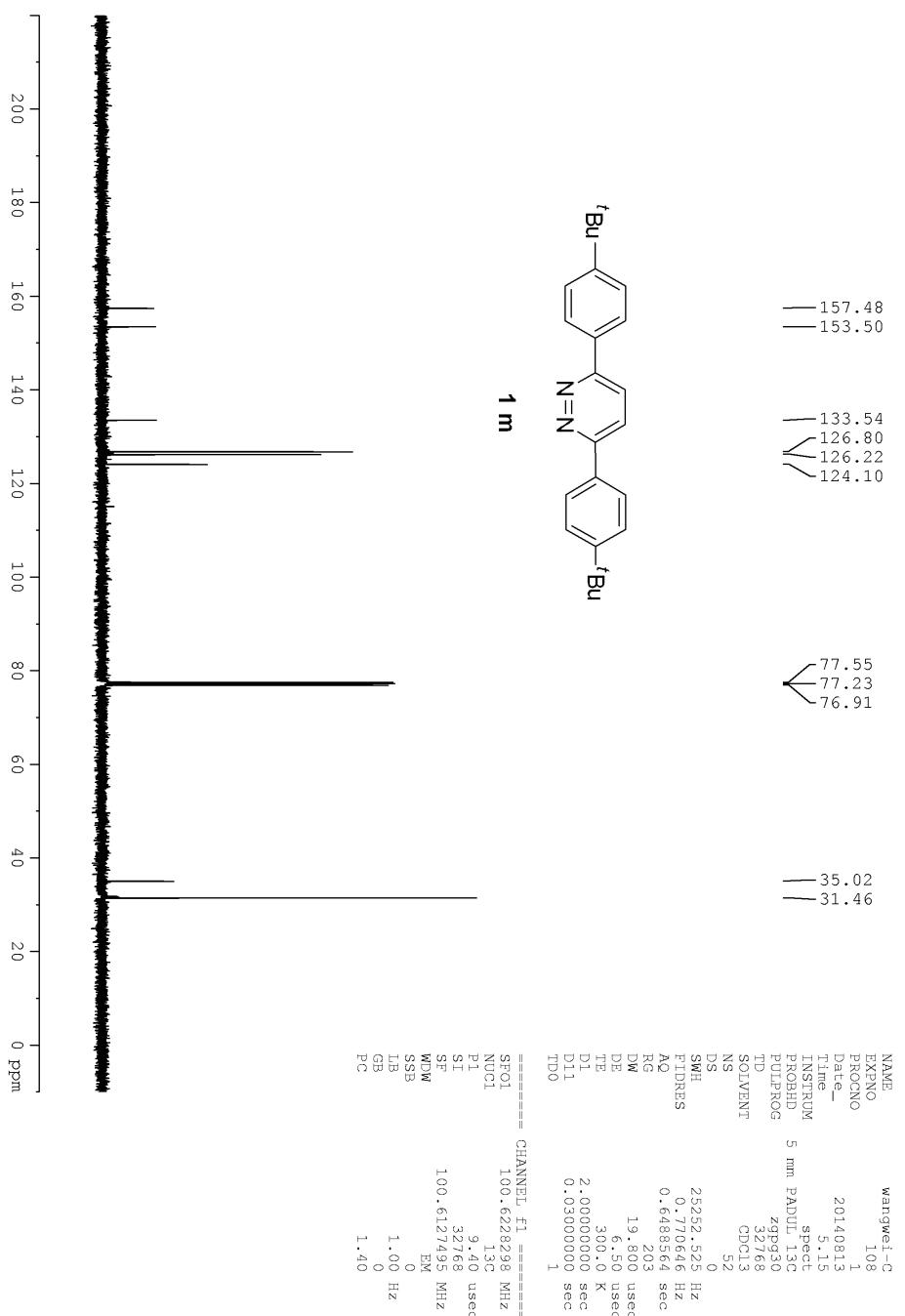


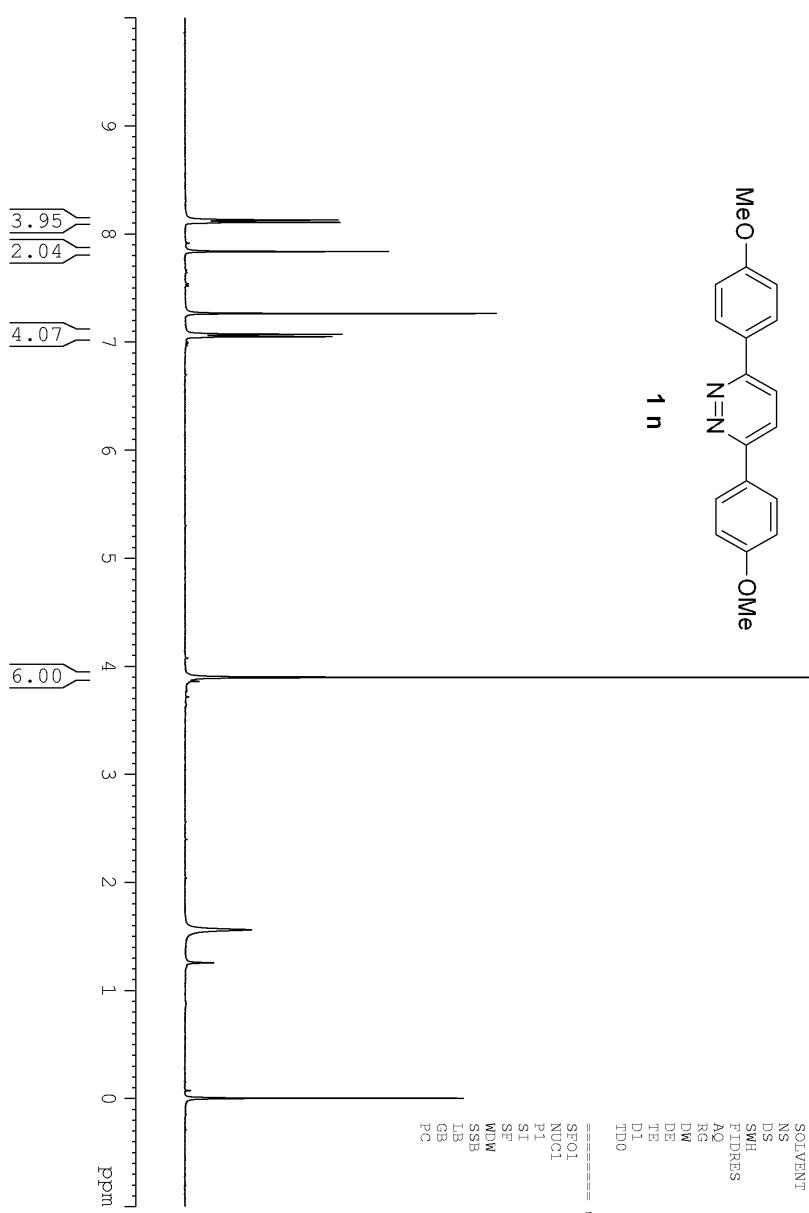
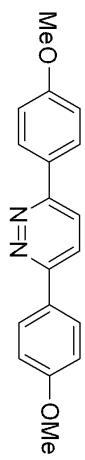


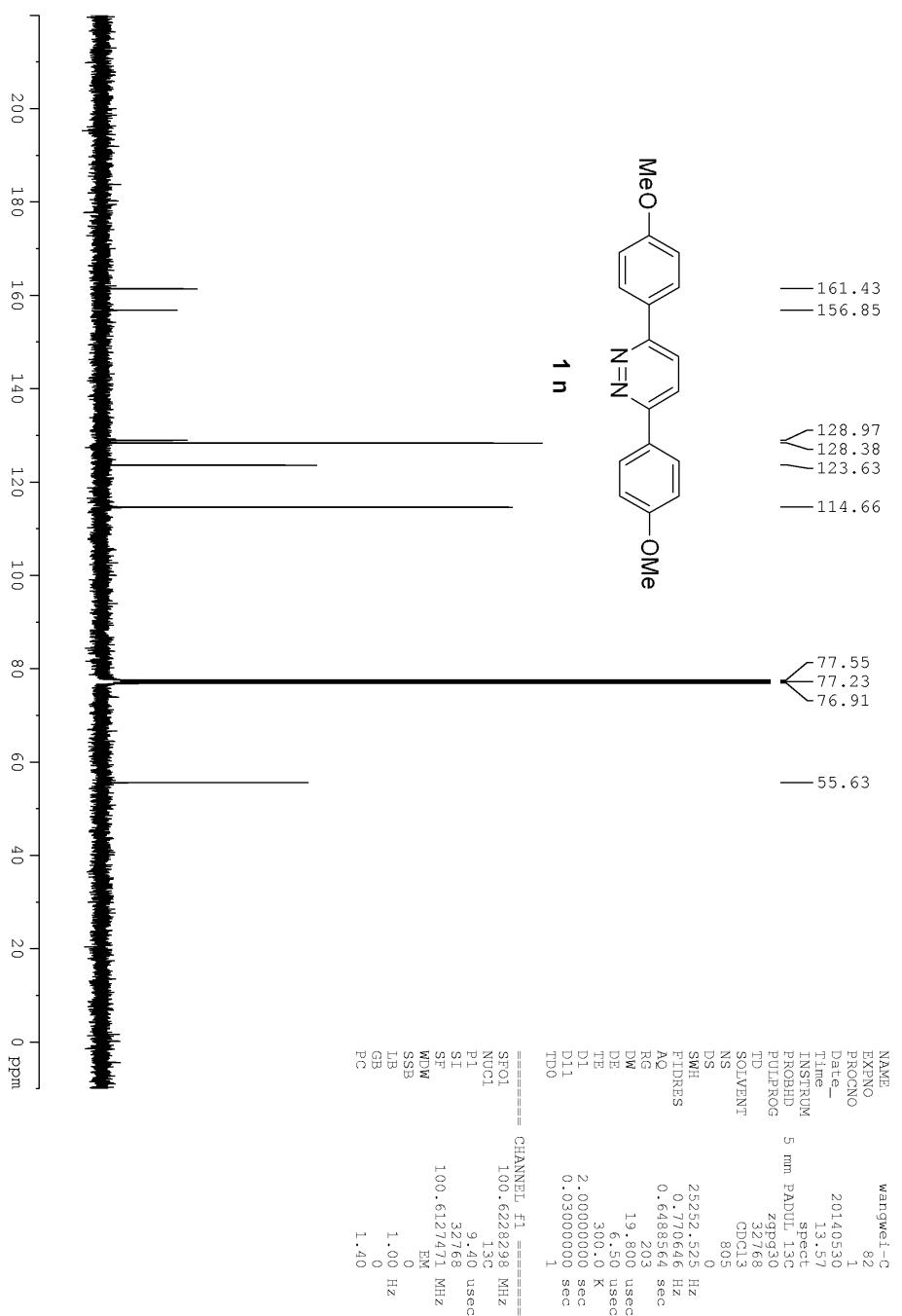


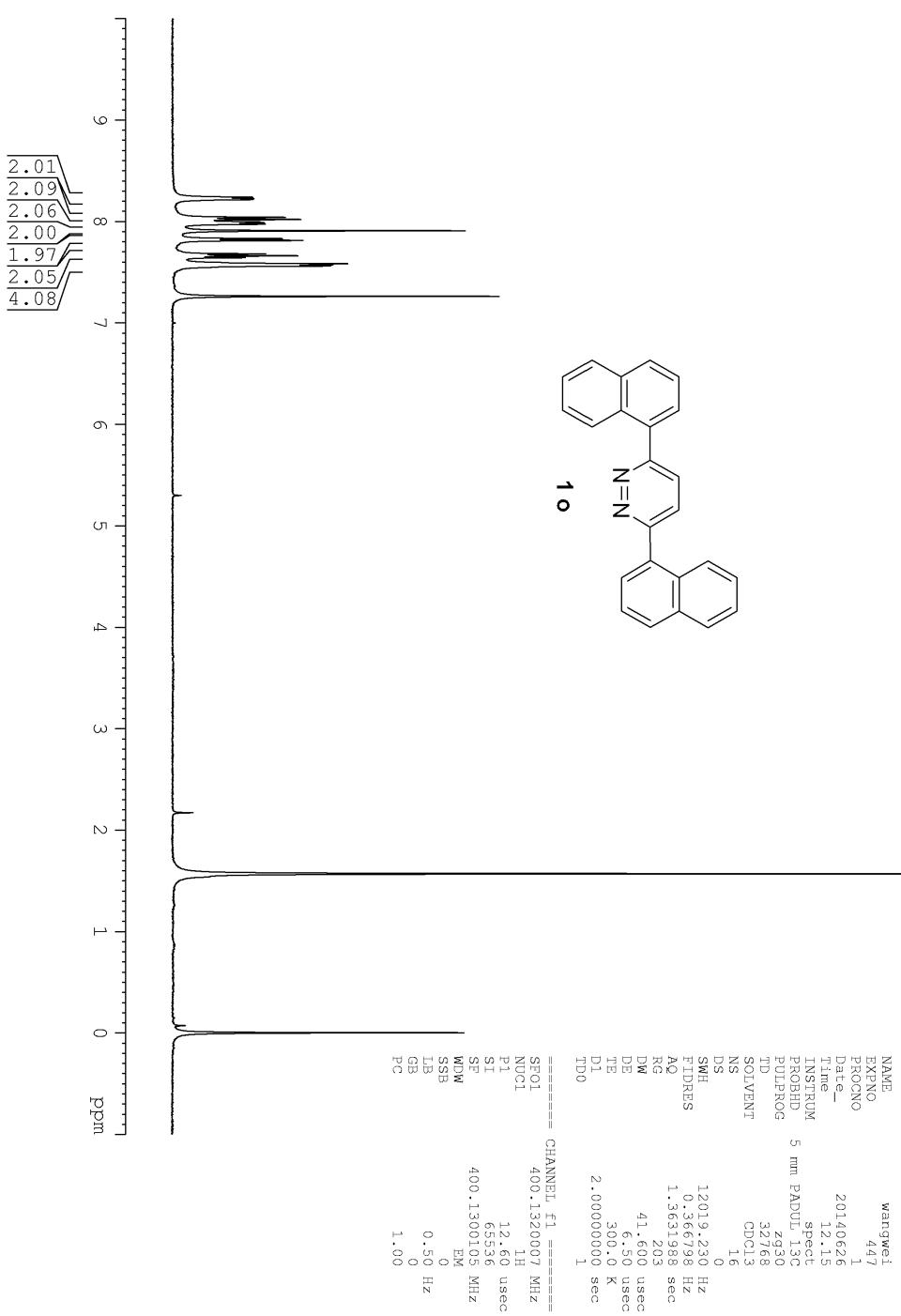


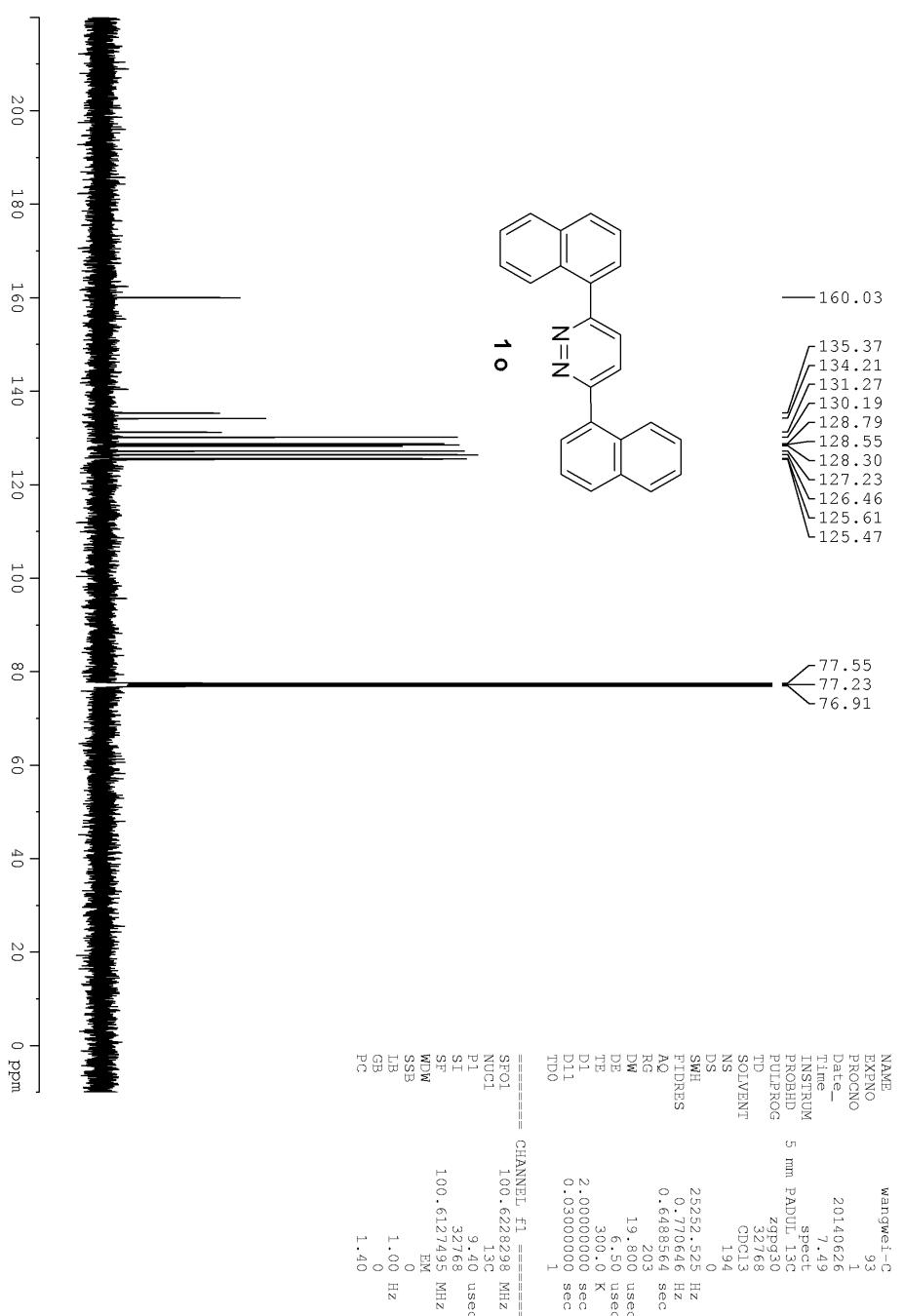


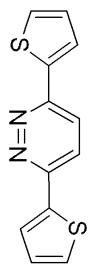












1p

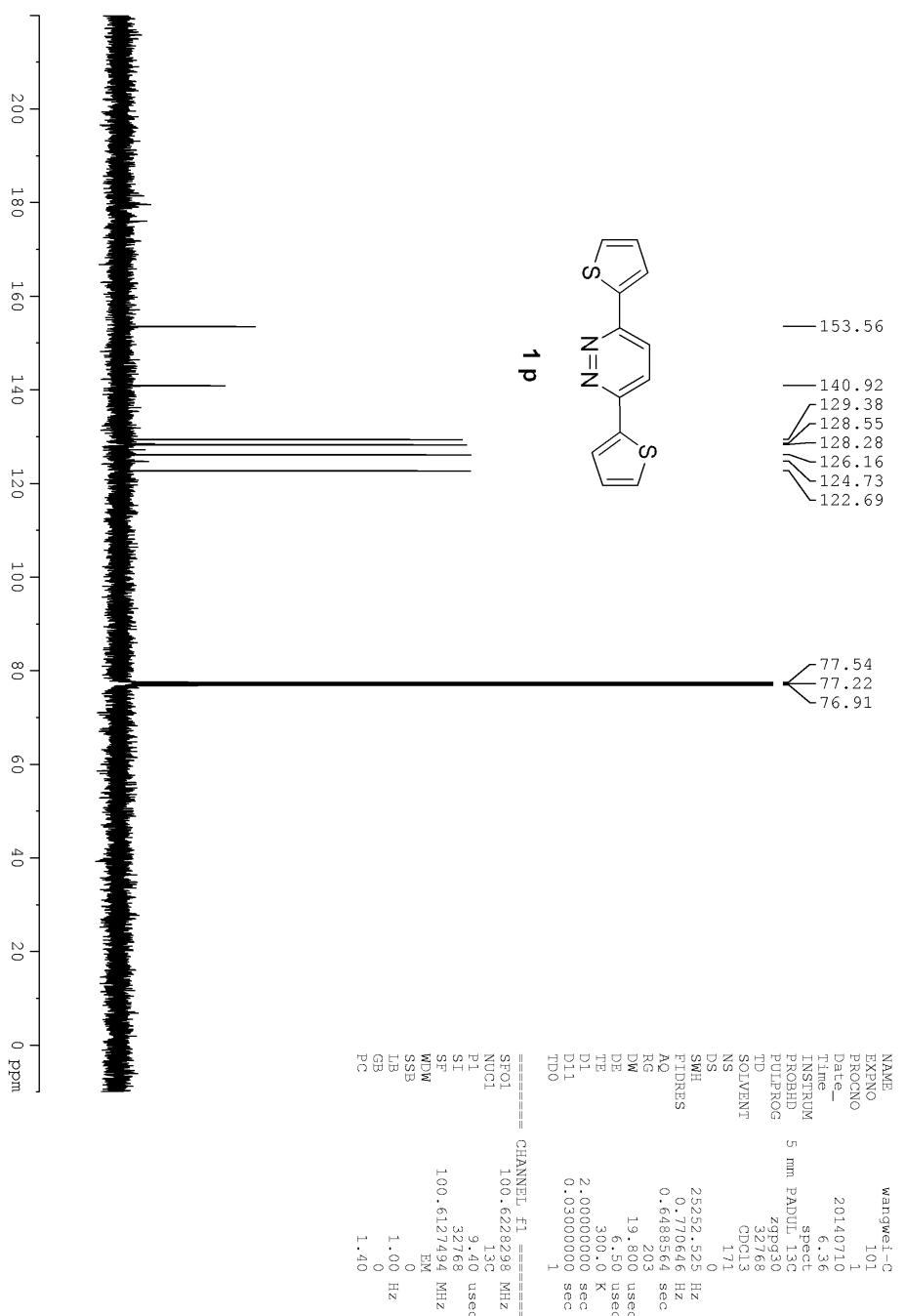


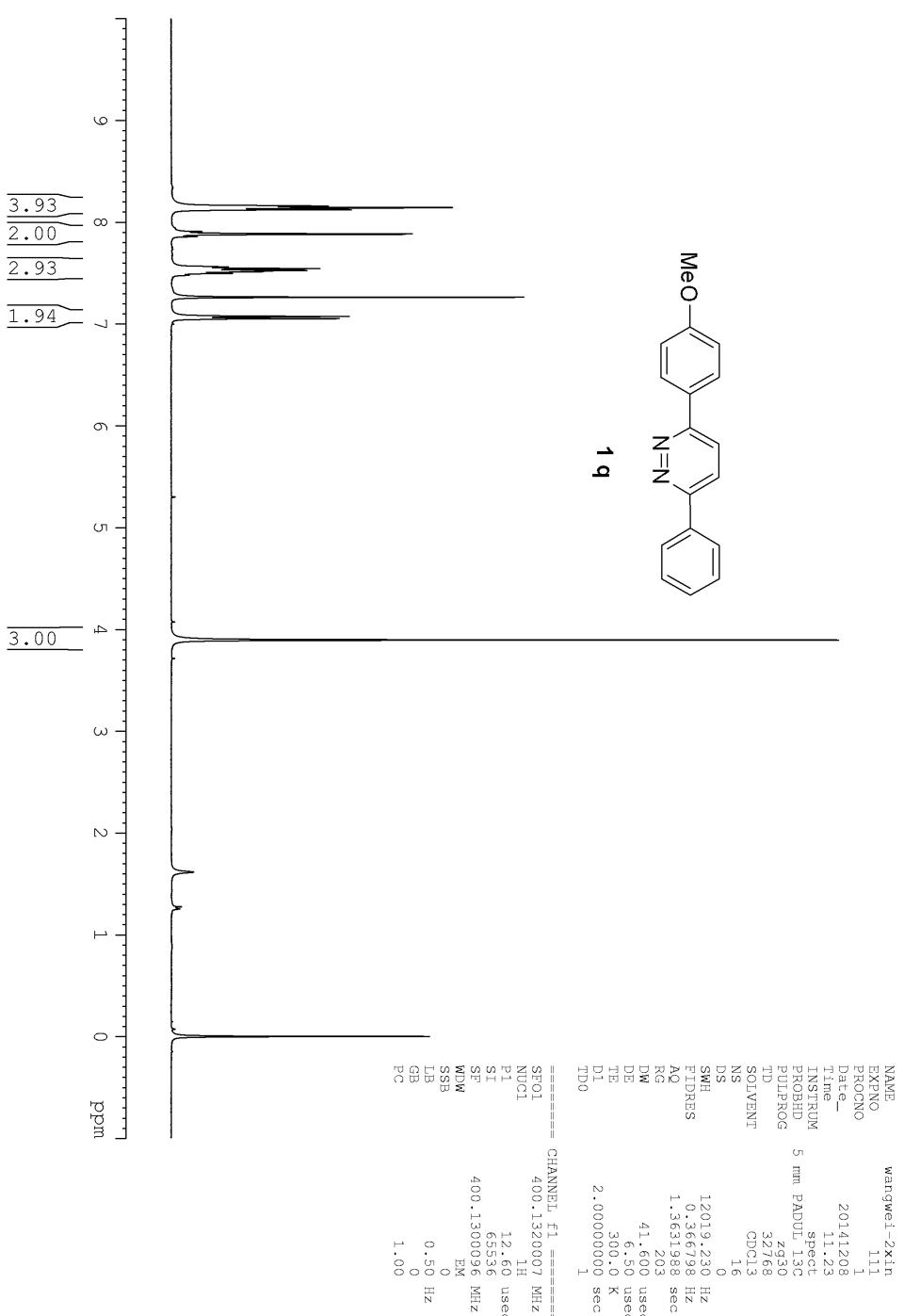
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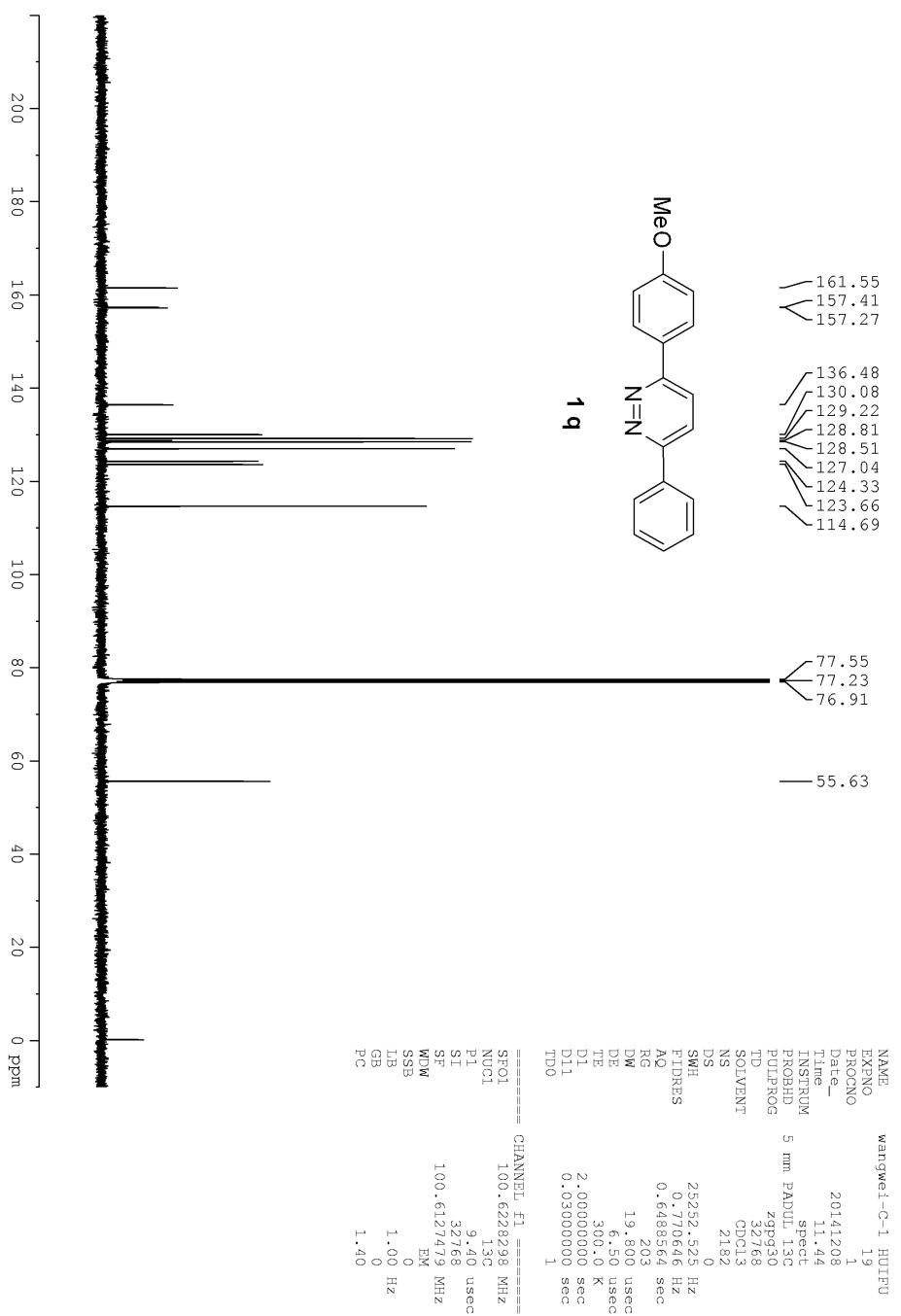
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EXNO          474
PROCNO        1
Date_         20140710
Time          6.33
INSTRUM       spect
PROBHD       5 mm PADUL 13C
PULPROG      zg30
TD           32768
SOLVENT       CDCl3
NS            16
DS            0
SWH          12019.230 Hz
SFH          0.366798 Hz
FIDRES       1.3631988 sec
AQ            2.03
RG            41.600 usec
DW            6.50 usec
TE            300.0 K
D1           2.0000000 sec
TDO          1

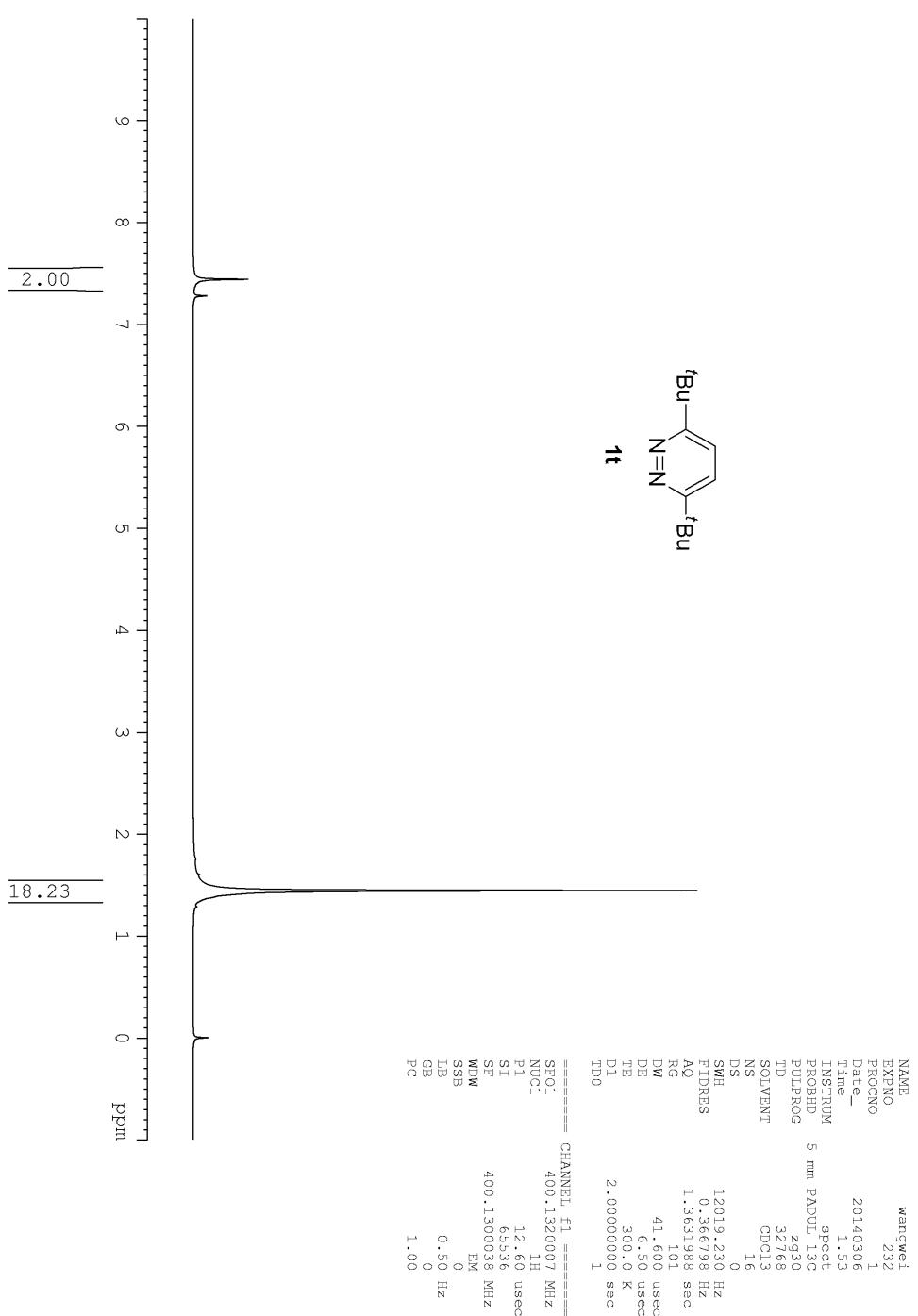
=====
CHANNEL f1 =====
SFO1        400.132007 MHz
NUC1         1H
P1           12.60 usec
SI            65536
SF          400.1300096 MHz
WDW         EM
SSB          0
LB           0.50 Hz
GB           0
PC           1.00

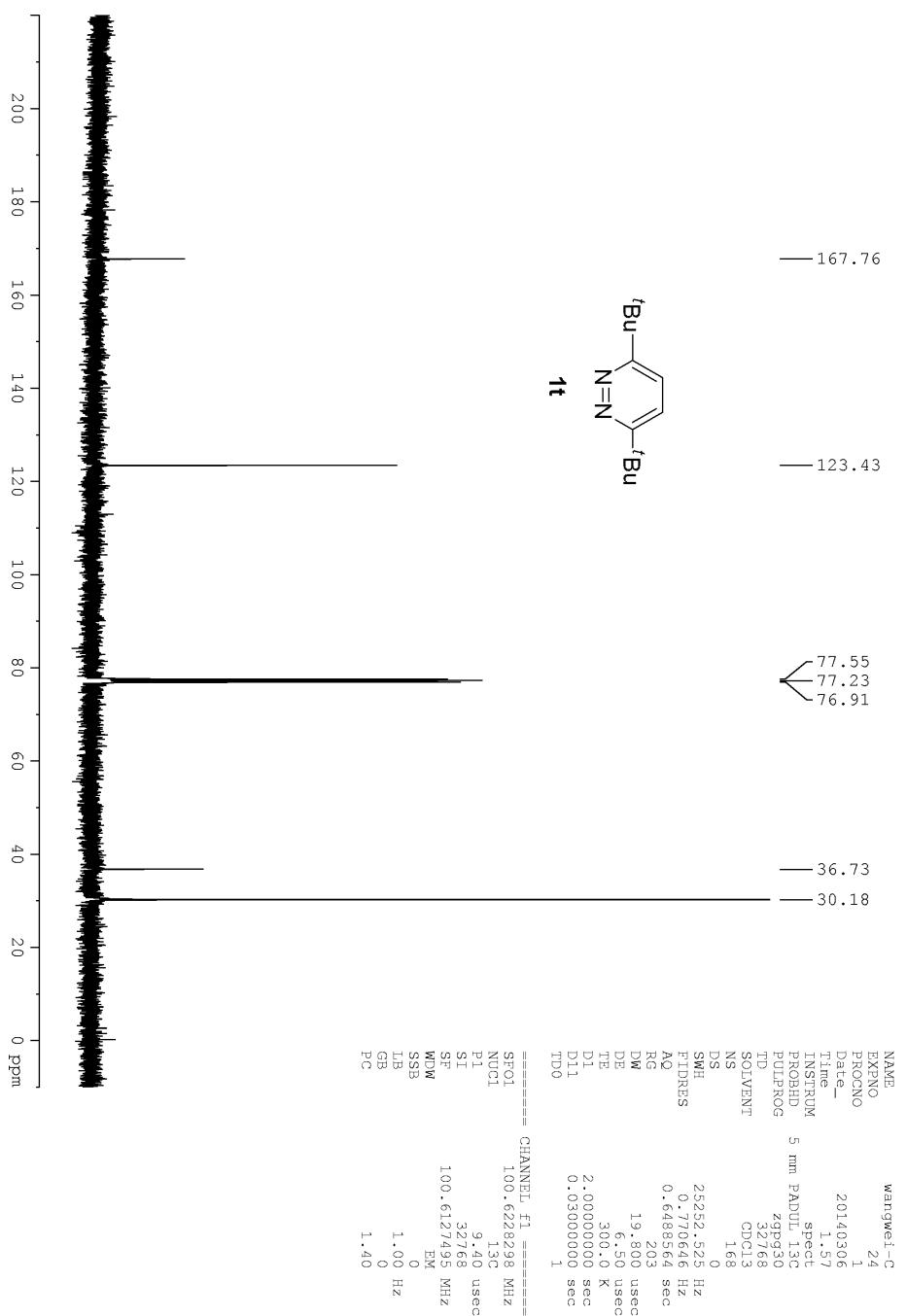
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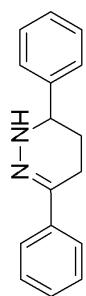




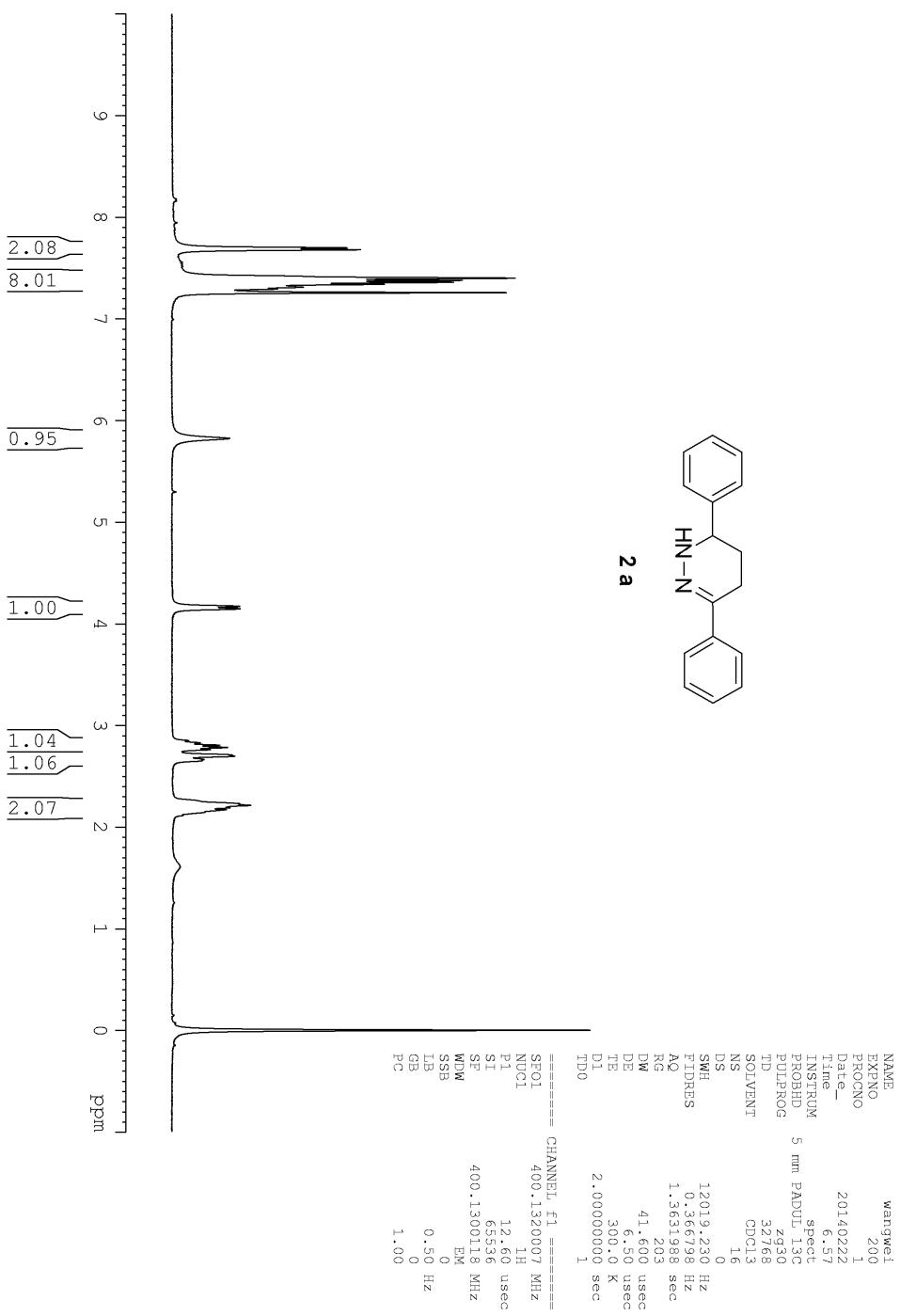


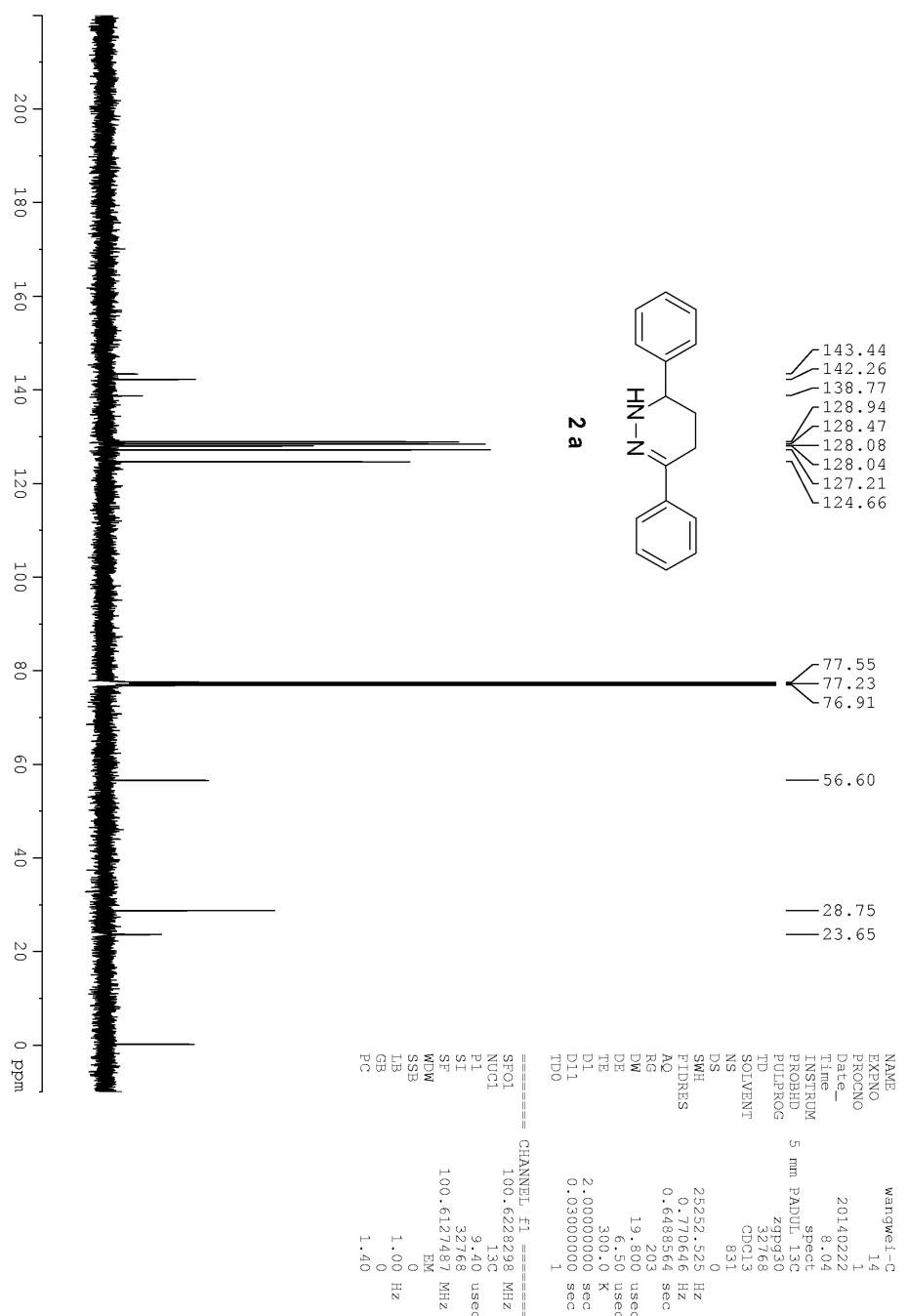


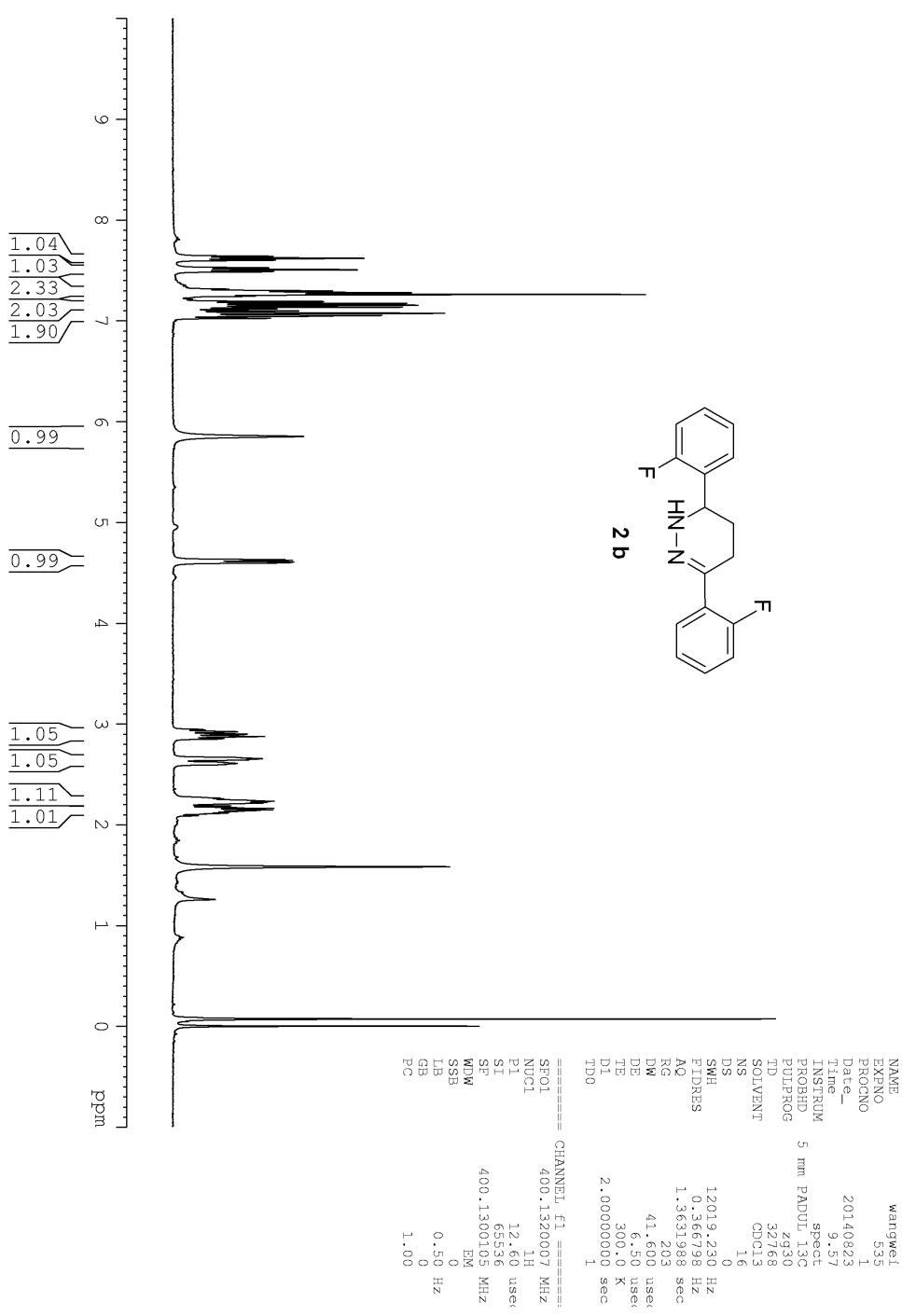


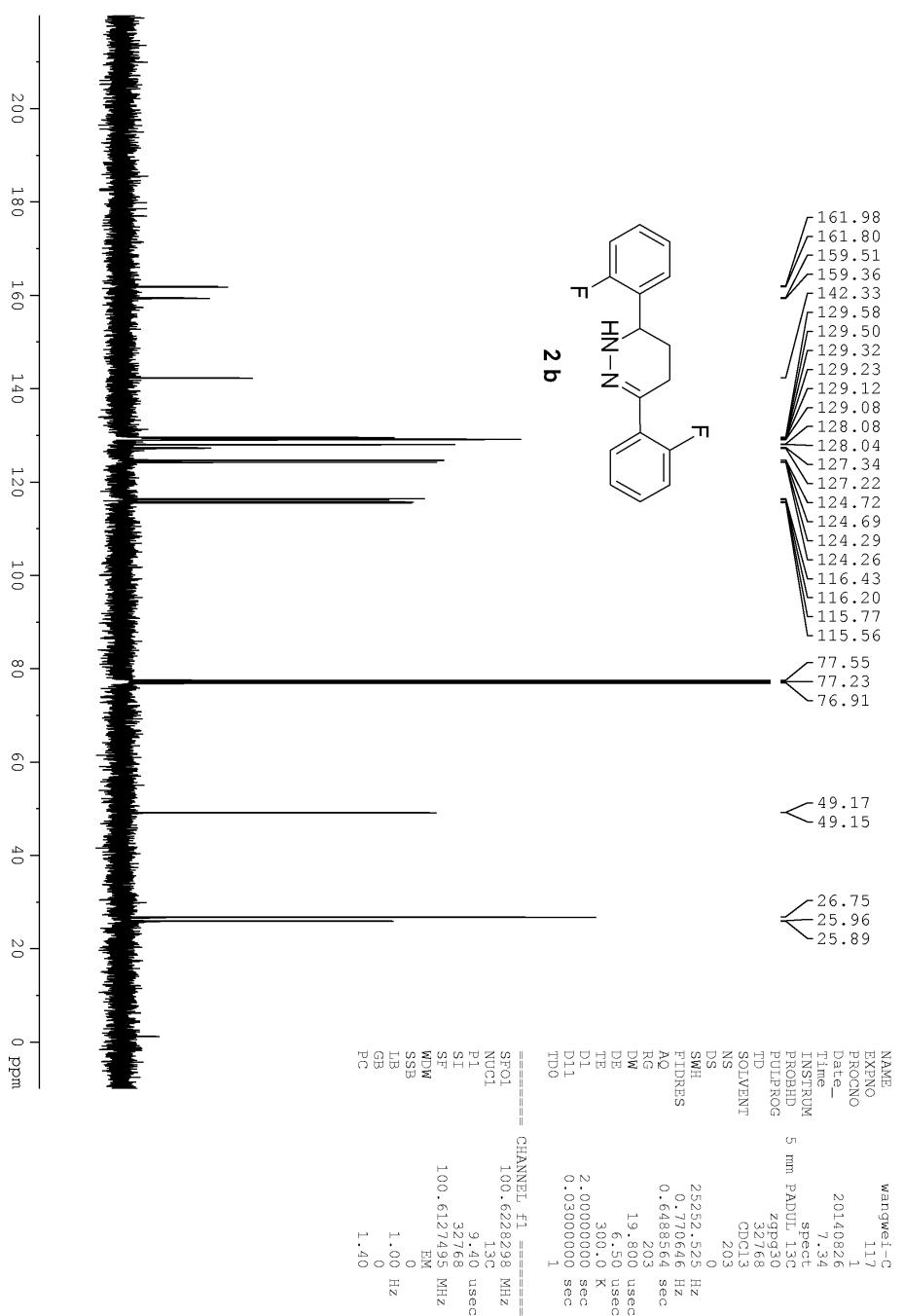


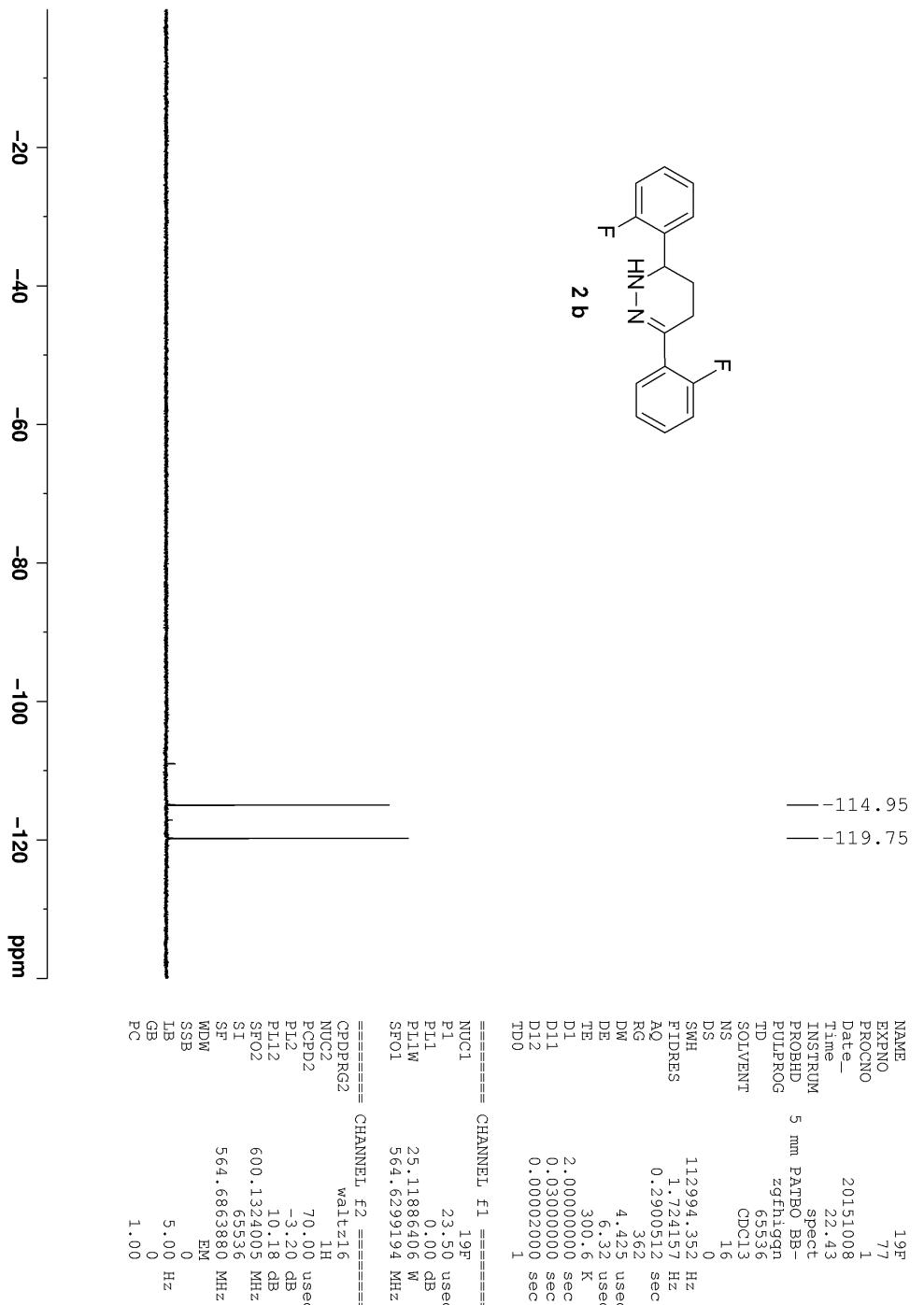
2 a

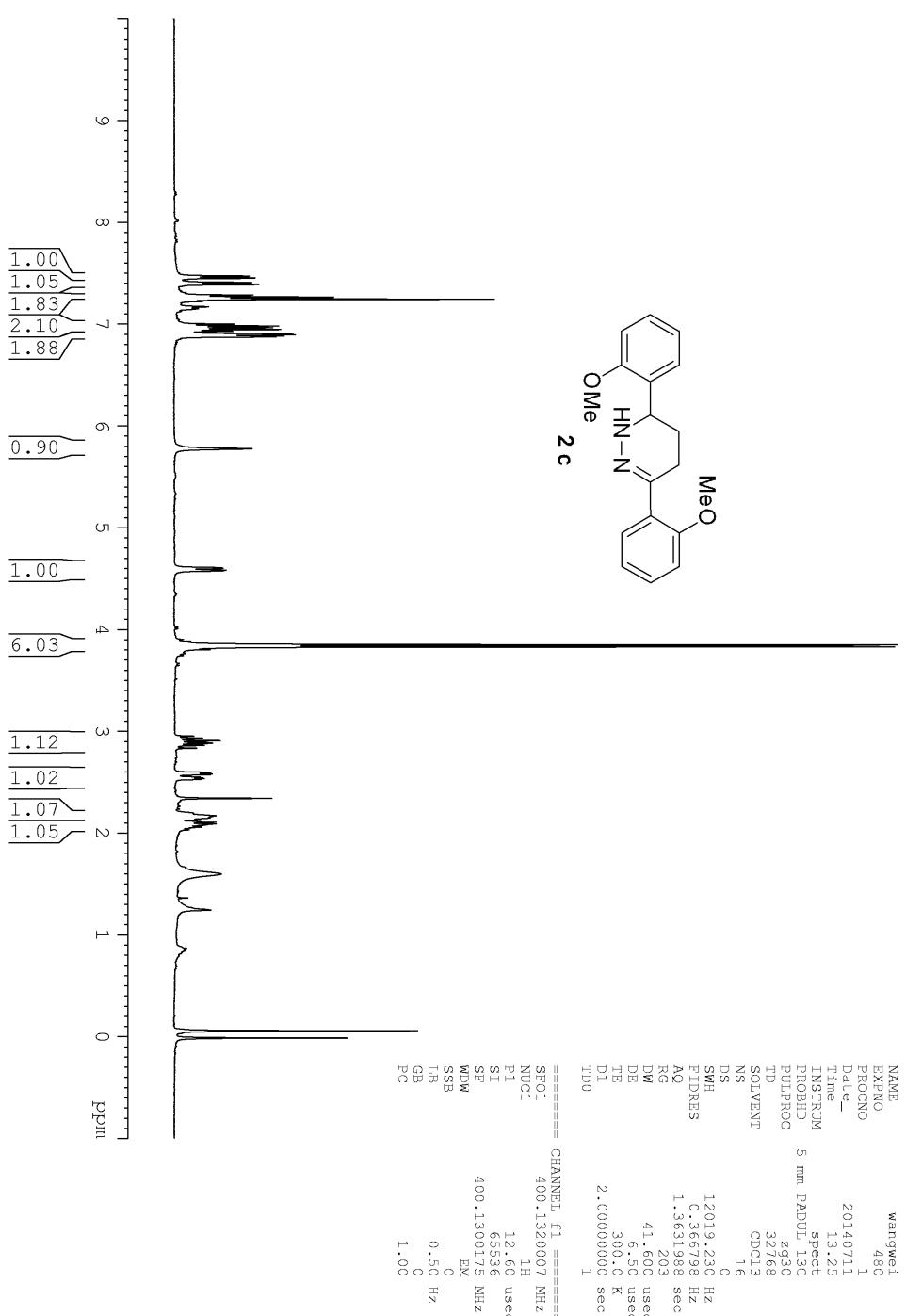


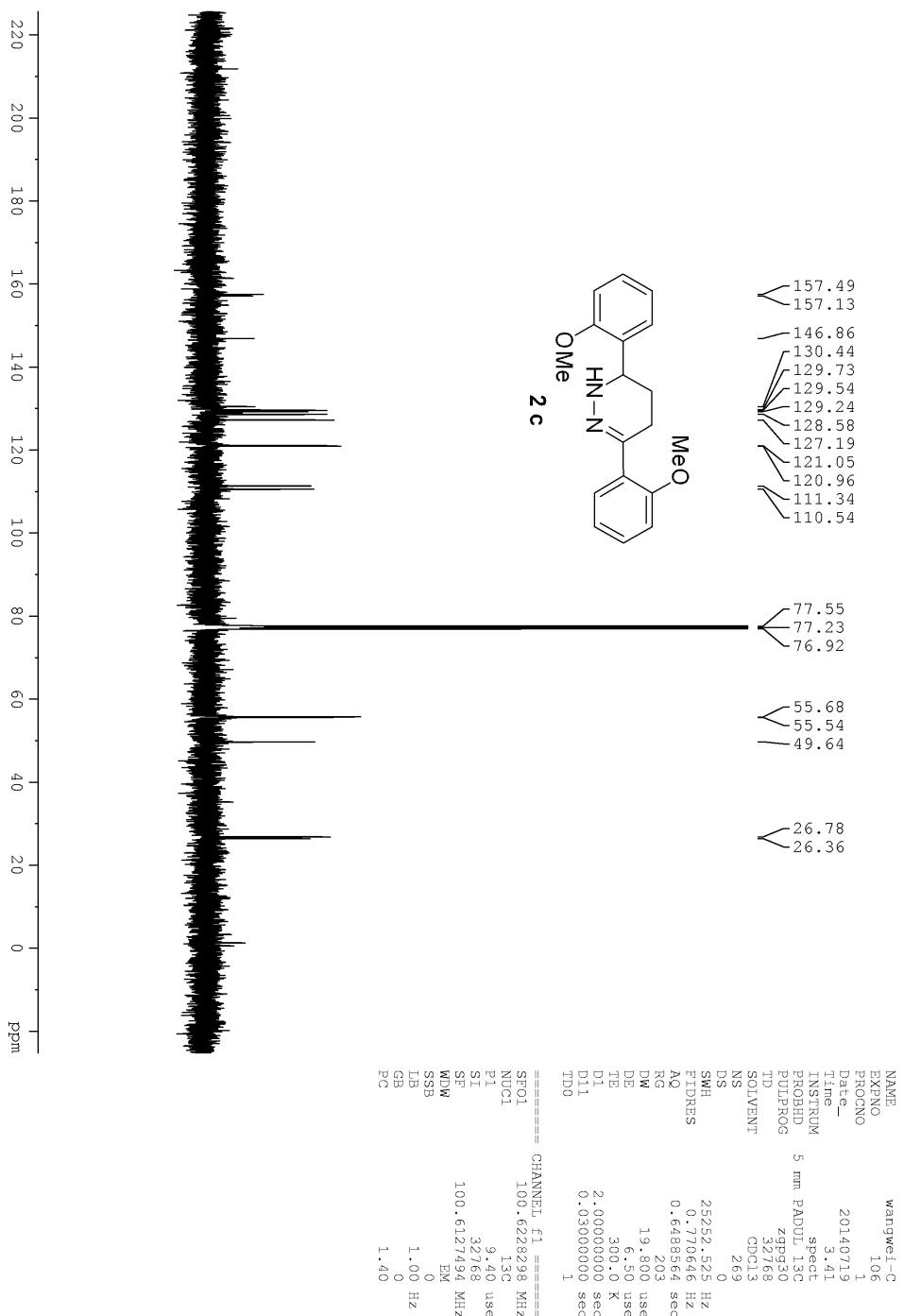


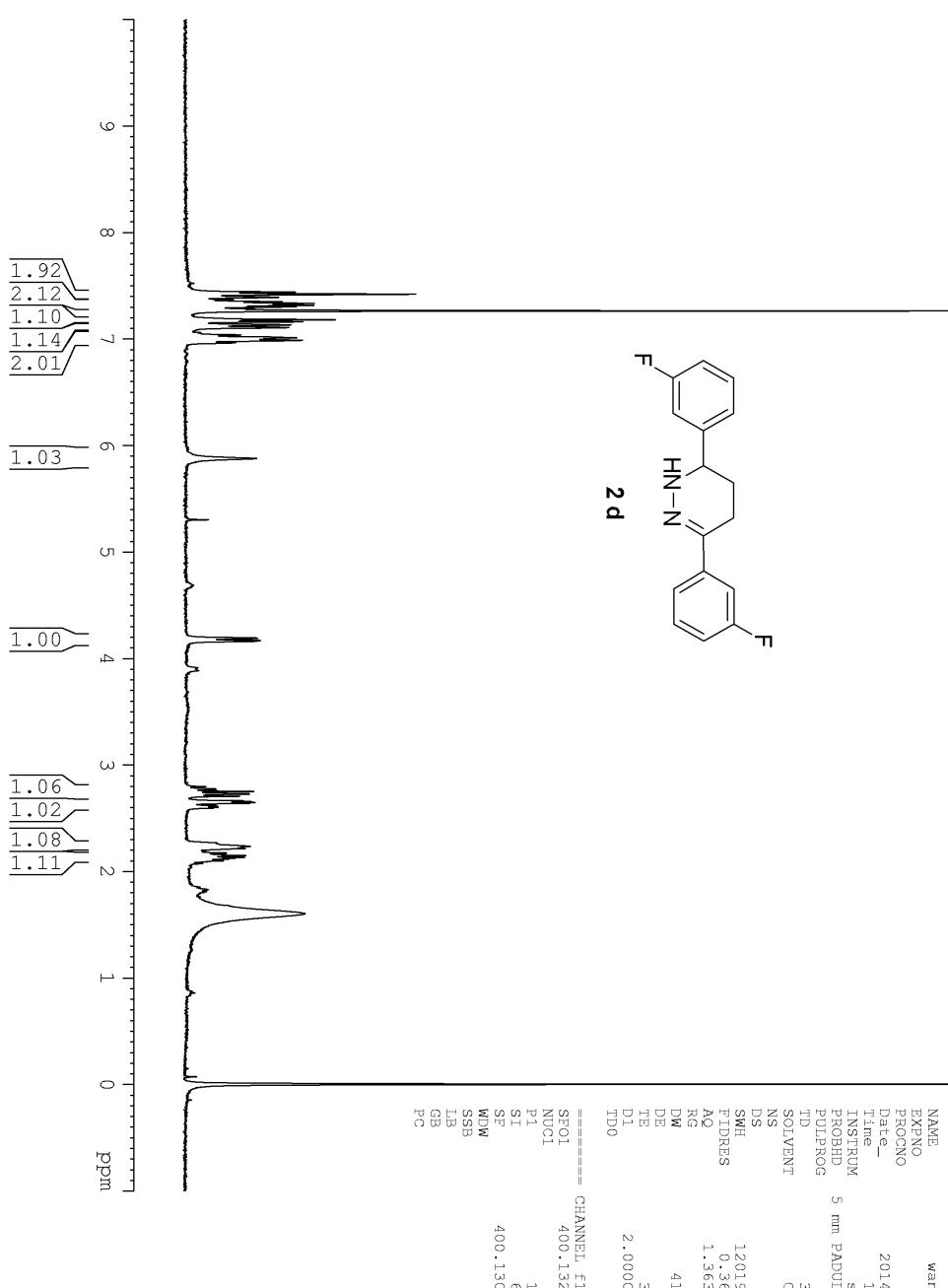


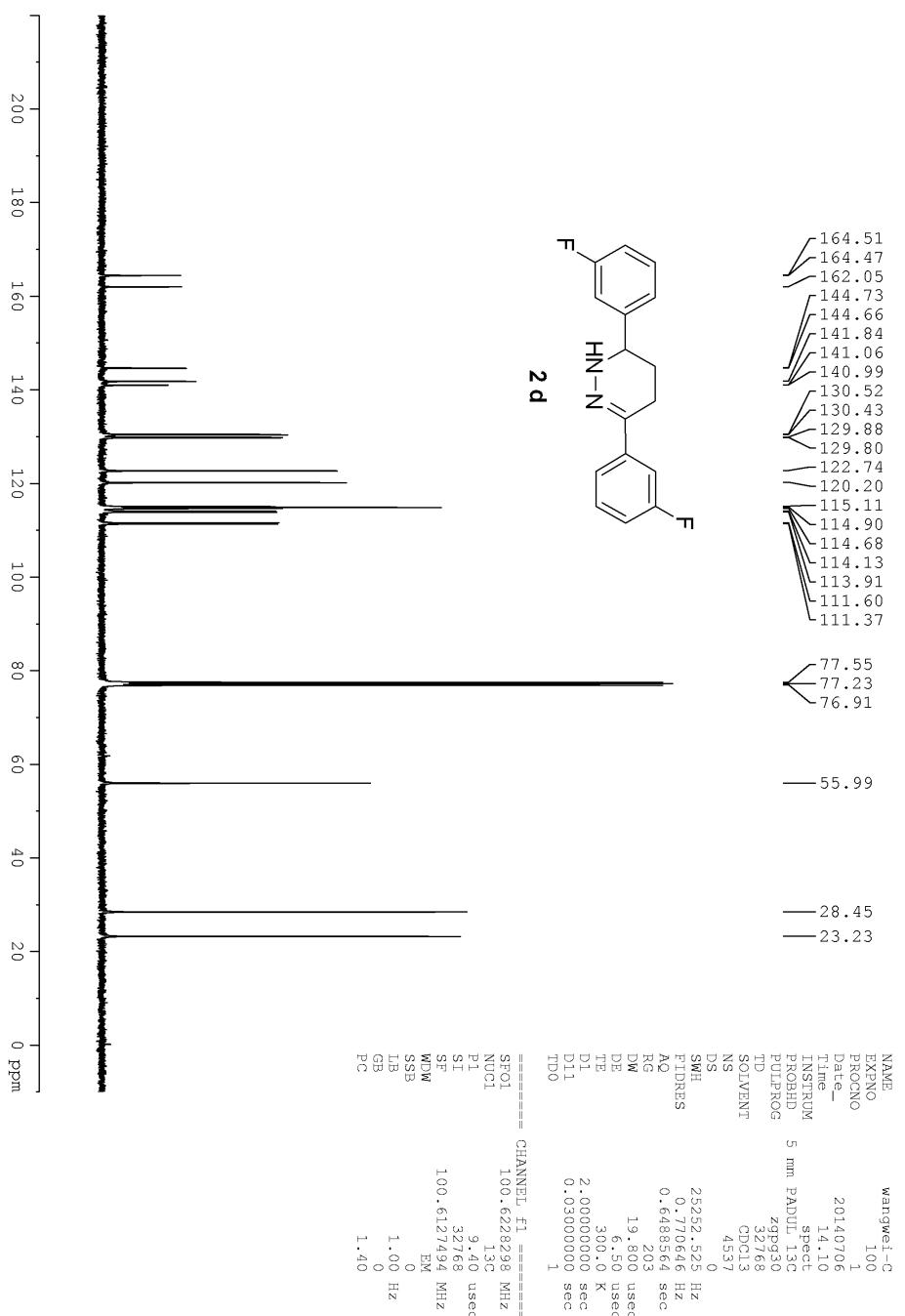


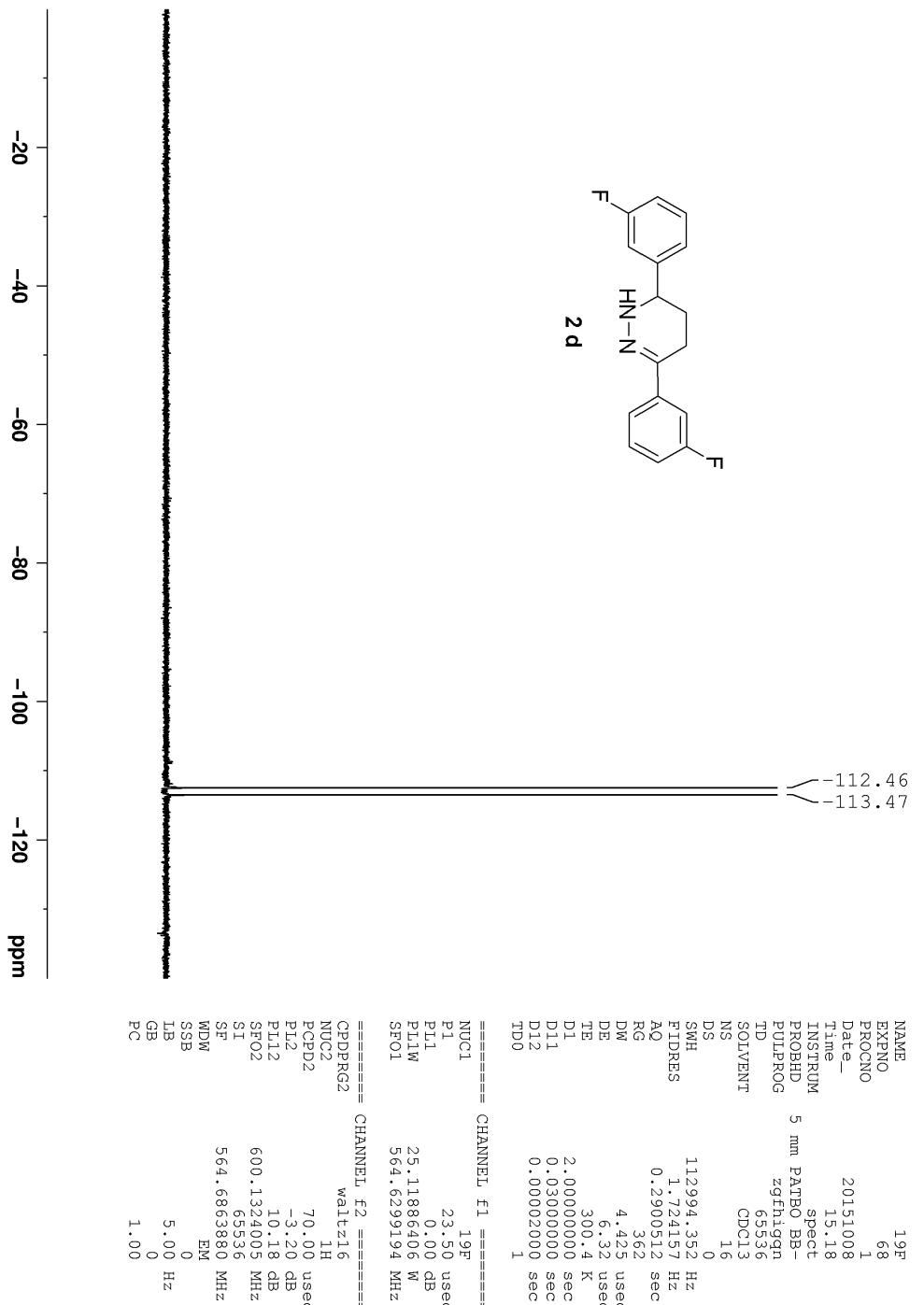


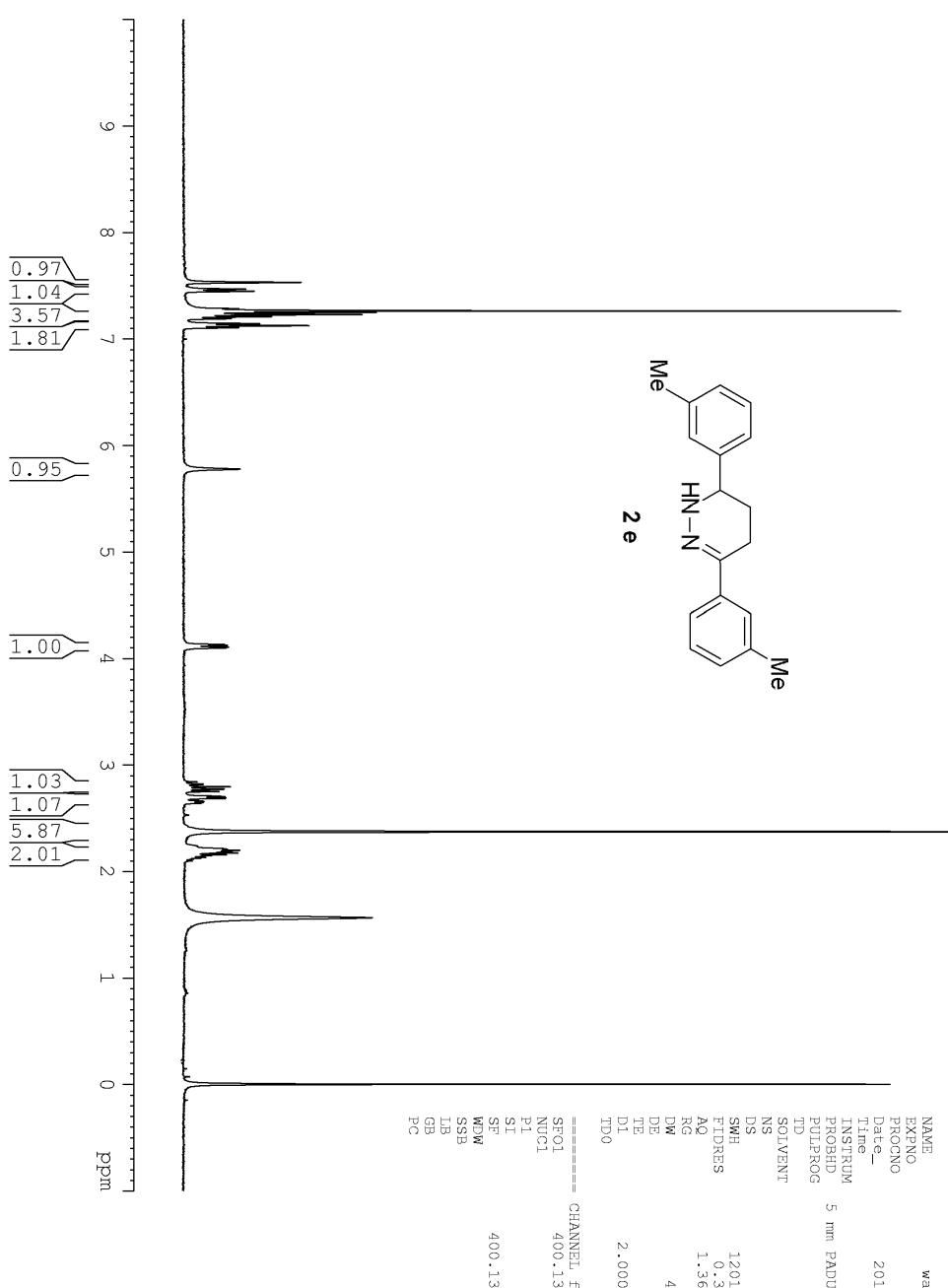


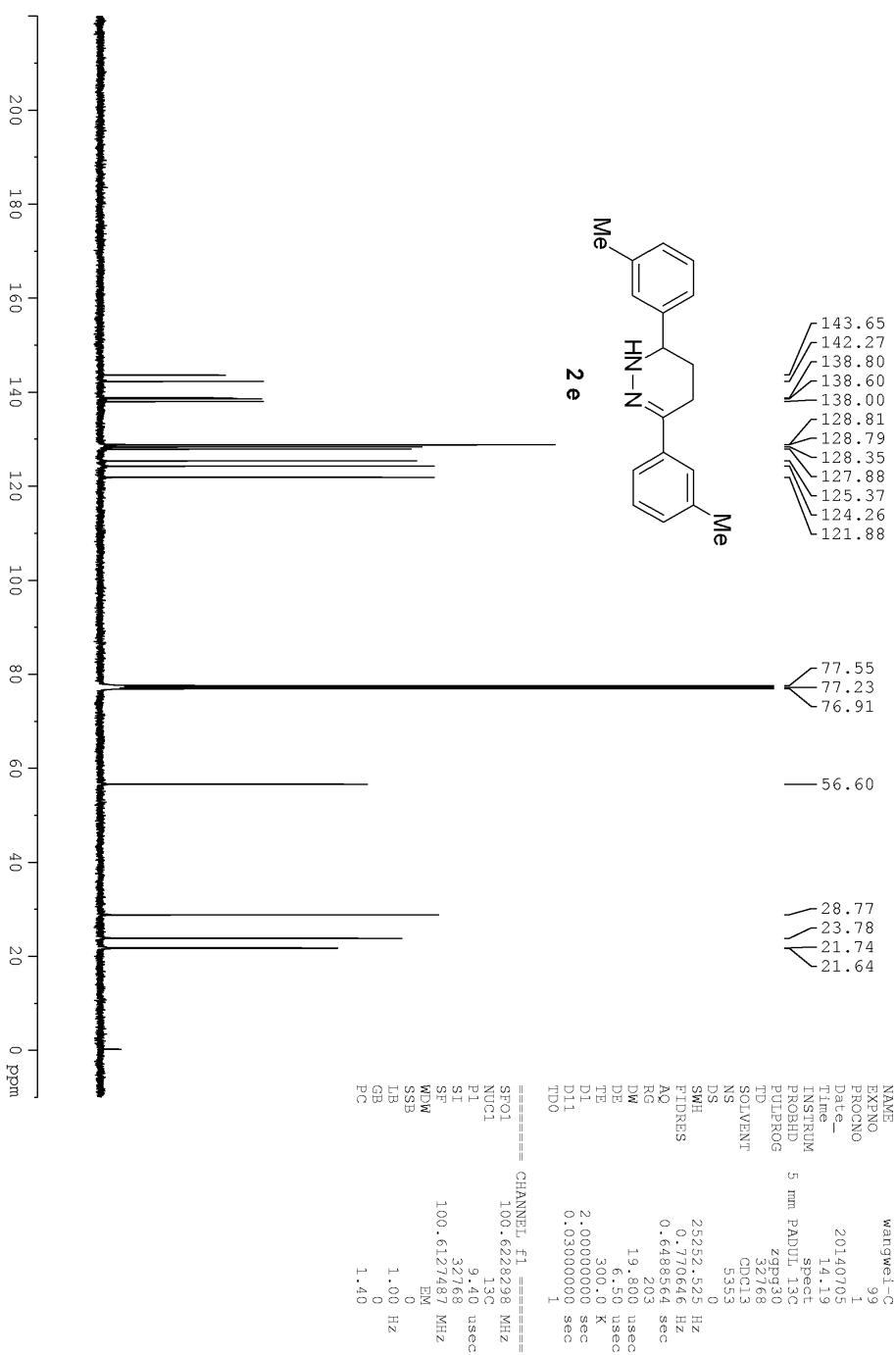




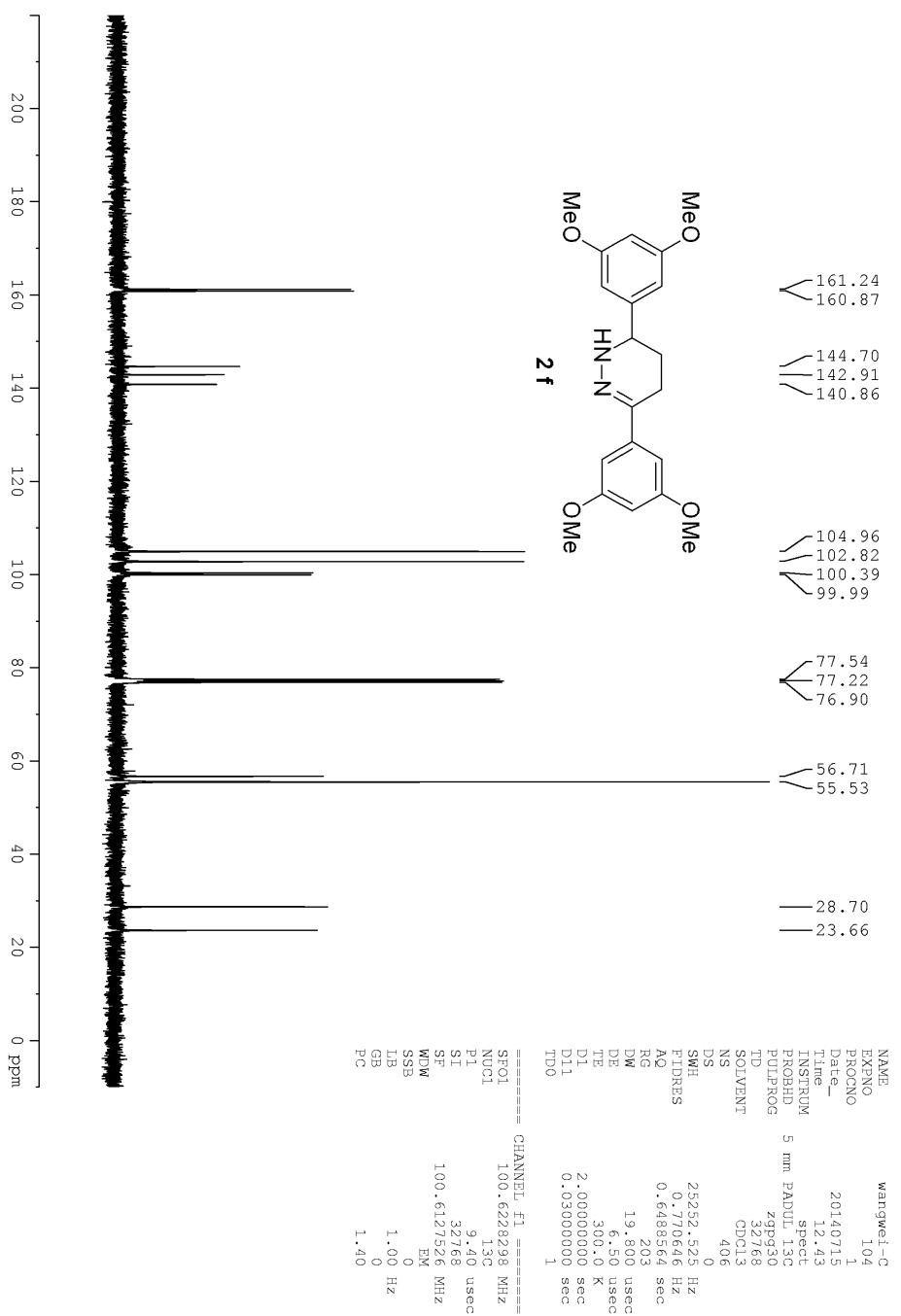


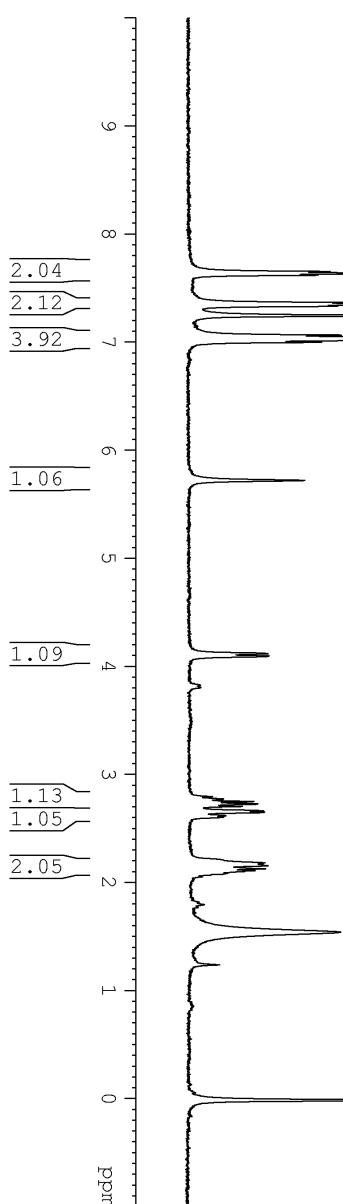
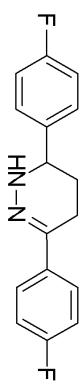












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NAME          wangwei
EXNNO         539
PROGNO        1
Date_         20140826
Time          9.25
INSTRUM       Spect
PROBHD        5 mm PADUL 13C
PULPROG      z930
TD            32768
SOLVENT       CDCl3
NS            16
DS            0
SWH           12019.230 Hz
SFH           0.366798 Hz
FIRES        1.3631988 sec
AQ            2.03
RG            41.600 usec
DW            6.50 usec
DE            300.0 K
TE            2.0000000 sec
D1            1
TDO           1

===== CHANNEL f1 =====
SFO1          400.132007 MHz
NUCL1         1H
P1             12.60 usec
SI              65536
SF             400.1300175 MHz
WDW           EM
SSB           0
LB            0.50 Hz
GB            0
PC            1.00

```

