

Supporting Information

A New Method for Aromatic Difluoromethylation: Copper-Catalyzed Cross-Coupling and Decarboxylation Sequence from Aryl Iodides

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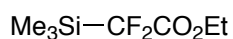
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General Remarks:

All reactions were carried out under a nitrogen atmosphere in flame-dried glassware. Syringes which were used to transfer anhydrous solvents or reagents were purged with argon prior to use. Starting materials, reagents, and dry solvent were purchased from commercial suppliers and used without further purification. ^1H NMR spectra were recorded using Me_4Si as an internal standard (δ 0 ppm). ^{19}F NMR spectra were recorded using hexafluorobenzene (C_6F_6) as an internal standard (δ 0 ppm). Splitting patterns were reported as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad.

Typical Procedure for Preparation of α -Silyldifluoroacetates 5

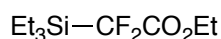
Ethyl 2,2-Difluoro-2-(trimethylsilyl)acetate (**5a**)¹



5a

To the suspension of Mg (972 mg, 40 mmol) and chlorotrimethylsilane (8.69 g, 80 mmol) in anhydrous DMF (60 mL) were added ethyl chlorodifluoroacetate (793 mg, 20 mmol) at 0 °C under a nitrogen atmosphere. And then the reaction mixture was stirred for additional 90 min at rt and quenched with water. The aqueous layer was extracted with Et_2O . Then, the combined organic phase was washed with water, dried over anhydrous Na_2SO_4 . Evaporation of the filtrate and bulb-to-bulb distillation (91 mmHg, 110 °C) provided **5a** as a pale yellow oil (2.73 g, 70%); IR (neat) 1760 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 4.32 (q, $J = 7.0$ Hz, 2H), 1.35 (t, $J = 7.0$ Hz, 3H), 0.24 (s, 9H); ^{19}F NMR (376 MHz, CDCl_3) δ 38.5 (s, 2F); EI-MS m/z (%) 181 (M- CH_3 , 6), 153 (10), 125 (6), 103 (8), 77 (26), 73 (100).

Ethyl 2,2-Difluoro-2-(triethylsilyl)acetate (**5b**)

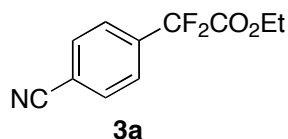


5b

By a procedure similar to that for **5a**, the title compound was obtained using Et_3SiCl as a pale yellow oil (64%); IR (neat) 1763 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 4.31 (q, $J = 7.1$ Hz, 2H), 1.35 (t, $J = 7.1$ Hz, 3H), 1.02 (t, $J = 8.0$ Hz, 9H), 0.77 (q, $J = 8.0$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.2 (t, $^2J_{\text{CF}} = 25.3$ Hz), 121.7 (t, $^1J_{\text{CF}} = 268$ Hz), 61.9, 13.8, 6.4, 0.8 (t, $^3J_{\text{CF}} = 2.0$ Hz); ^{19}F NMR (376 MHz, CDCl_3) δ 42.9 (s, 2F); EI-MS m/z (%) 209 (M- C_2H_5 , 120), 131 (12), 115 (38), 87 (100). Anal. Calcd for $\text{C}_{10}\text{H}_{20}\text{O}_2\text{F}_2\text{Si}$: C, 50.39; H, 8.46. Found: C, 50.25; H, 8.57.

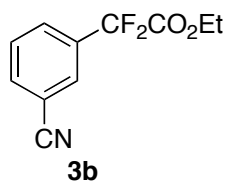
Typical Procedure of Cu(I)-Promoted Cross-Coupling of Aryl Iodides with α -Trimethylsilyldifluoroacetate **5a (Stoichiometric in Copper).**

Ethyl 2-(4-Cyanophenyl)-2,2-difluoroacetate (3a**)**²



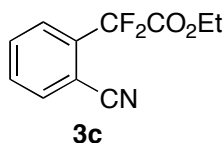
To a mixture of CuI (57.1 mg, 0.30 mmol), KF (20.9 mg, 0.36 mmol), 4-iodobenzonitrile (**1a**, 68.7 mg, 0.3 mmol), and DMSO (0.6 mL) was added ethyl 2,2-difluoro-2-(trimethylsilyl)acetate (**5a**, 70.7 mg, 0.36 mmol) at room temperature. The reaction mixture was stirred at 60 °C in an atmosphere of nitrogen for 15 h and quenched with water. The aqueous layer was extracted with ethyl acetate. Then, the combined organic phase was washed with water, dried over anhydrous Na₂SO₄. Purification by column chromatography on silica gel (hexane/ethyl acetate = 50/1) gave 48.3 mg (0.21 mmol, 71%) of ethyl 2-(4-cyanophenyl)-2,2-difluoroacetate (**3a**) as a colorless oil; IR (neat) 2245, 1764 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, J = 8.8 Hz, 2H), 7.74 (d, J = 8.8 Hz, 2H), 4.34 (q, J = 7.0 Hz, 2H), 1.31 (t, J = 7.0 Hz, 3H); ¹⁹F NMR (376 MHz, CDCl₃) δ 56.8 (s, 2F); EI-MS m/z (%) 225 (M⁺, 2), 181 (2), 152 (100), 126 (4), 102 (8), 75 (4).

Ethyl 2-(3-Cyanophenyl)-2,2-difluoroacetate (3b**)**



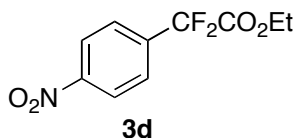
By a procedure similar to that for **3a**, the title compound was obtained from **1b** as a colorless oil (69% isolated yield); IR (neat) 2250, 1778 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.92 (s, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.80 (d, J = 7.8 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H), 4.33 (t, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 163.4 (t, ² J_{CF} = 34.4 Hz), 134.7, 134.5 (t, ² J_{CF} = 26.7 Hz), 130.1 (t, ³ J_{CF} = 6.2 Hz), 129.9, 129.6 (t, ³ J_{CF} = 6.2 Hz), 117.8, 113.2, 112.3 (t, ¹ J_{CF} = 252 Hz), 63.9, 14.0; ¹⁹F NMR (376 MHz, CDCl₃) δ 57.2 (s, 2F); EI-MS m/z (%) 225 (M⁺, 1), 181 (4), 153 (50), 152 (100), 126 (8), 102 (10), 75 (5). Anal. Calcd for C₁₁H₉NO₂F₂: C, 58.67; H, 4.03; N, 6.22. Found: C, 58.30; H, 3.95; N, 6.17.

Ethyl 2-(2-Cyanophenyl)-2,2-difluoroacetate (3c)



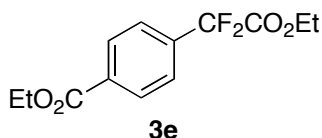
By a procedure similar to that for **3a**, the title compound was obtained from **1c** as a colorless oil (44% isolated yield); IR (neat) 2248, 1780 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.85-7.60 (m, 3H), 7.66-7.57 (m, 1H), 4.38 (t, $J = 7.1$ Hz, 2H), 1.36 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 162.5 (t, $^2J_{\text{CF}} = 33.9$ Hz), 135.3 (t, $^2J_{\text{CF}} = 25.1$ Hz), 134.7, 132.9, 131.5, 127.0 (t, $^3J_{\text{CF}} = 7.2$ Hz), 116.1, 112.2 (t, $^1J_{\text{CF}} = 253$ Hz), 110.3 (t, $^3J_{\text{CF}} = 3.6$ Hz), 63.9, 13.7; ^{19}F NMR (470 MHz, CDCl_3) δ 60.1 (s, 2F); EI-MS m/z (%) 181 (5), 154 (8), 153 (99), 153 (100), 133 (12), 126 (18), 102 (11). HRMS Calculated for $\text{C}_{11}\text{H}_9\text{NO}_2\text{F}_2$ (M+H): 226.06796; Found: 226.06831.

Ethyl 2,2-Difluoro-2-(4-nitrophenyl)acetate (3d)³



The title compound was obtained from **1d** according to the general procedure and purified by column chromatography (hexane/ethyl acetate = 50/1) to give colorless solids (29% isolated yield); mp 48.0-49.0 $^\circ\text{C}$; IR (KBr) 1773, 1532, 1355 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.33 (d, $J = 9.0$ Hz, 2H), 7.82 (d, $J = 9.0$ Hz, 2H), 4.33 (q, $J = 7.0$ Hz, 2H), 1.32 (t, $J = 7.0$ Hz, 3H); ^{19}F NMR (376 MHz, CDCl_3) δ 57.2 (s, 2F); EI-MS m/z (%) 172 (100), 156 (16), 142 (16), 126 (42), 107 (5), 75 (4).

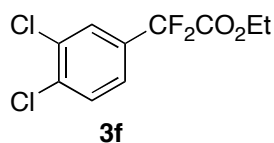
Ethyl 4-(2-Ethoxy-1,1-difluoro-2-oxoethyl)benzoate (3e)⁴



The title compound was obtained from **1e** according to the general procedure and purified by column chromatography (hexane/ethyl acetate = 50/1) to give a colorless oil (73% isolated yield); IR (neat)

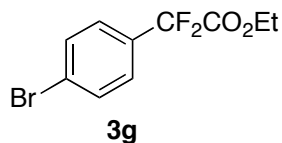
1783, 1740 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.13 (d, $J = 8.2$ Hz, 2H), 7.68 (d, $J = 8.2$ Hz, 2H), 4.41 (q, $J = 7.2$ Hz, 2H), 4.30 (q, $J = 7.2$ Hz, 2H), 1.41 (t, $J = 7.2$ Hz, 3H), 1.30 (t, $J = 7.2$ Hz, 3H); ^{19}F NMR (376 MHz, CDCl_3) δ 57.2 (s, 2F); EI-MS m/z (%) 272 (M^+ , 2), 227 (15), 199 (100), 171 (34), 126 (14).

Ethyl 2-(3,4-Dichlorophenyl)-2,2-difluoroacetate (**3f**)⁵



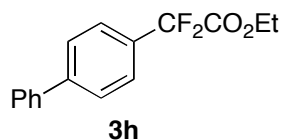
The title compound was obtained from **1f** according to the general procedure and purified by column chromatography (hexane/ethyl acetate = 100/1) to give a colorless oil (73% isolated yield); IR (neat) 1777 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.71 (d, $J = 2.1$ Hz, 1H), 7.54 (d, $J = 8.4$ Hz, 1H), 7.44 (dd, $J = 8.4, 2.1$ Hz, 1H), 4.31 (q, $J = 7.1$ Hz, 2H), 1.32 (t, $J = 7.1$ Hz, 3H); ^{19}F NMR (376 MHz, CDCl_3) δ 57.6 (s, 2F); EI-MS m/z (%) 270 ($\text{M}+2$, 7), 269 ($\text{M}+1$, 1), 268 (M^+ , 12), 199 (10), 198 (5), 197 (59), 196 (11), 195 (100), 160 (7), 125 (10), 75 (4).

Ethyl 2-(4-Bromophenyl)-2,2-difluoroacetate (**3g**)⁶



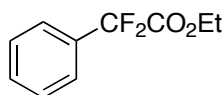
The title compound was obtained from **1g** according to the general procedure and purified by column chromatography (hexane/ethyl acetate = 50/1) to give a colorless oil (54% isolated yield); IR (neat) 1775 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.60 (d, $J = 8.6$ Hz, 2H), 7.48 (d, $J = 8.6$ Hz, 2H), 4.30 (q, $J = 7.2$ Hz, 2H), 1.31 (t, $J = 7.2$ Hz, 3H); ^{19}F NMR (376 MHz, CDCl_3) δ 57.6 (s, 2F); EI-MS m/z (%) 280 ($\text{M}+2$, 12), 278 (M^+ , 12), 207 (94), 205 (100), 126 (32), 75 (8).

Ethyl 2-(Biphenyl-4-yl)-2,2-difluoroacetate (**3h**)⁷



The title compound was obtained from **1h** according to the general procedure and purified by column chromatography (hexane/ethyl acetate = 50/1) to give colorless solids (68% isolated yield); mp 24.5-26.0 °C; IR (KBr) 1780 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.38-7.70 (m, 9H), 4.35 (q, *J* = 7.2 Hz, 2H), 1.33 (t, *J* = 7.2 Hz, 3H); ¹⁹F NMR (376 MHz, CDCl₃) δ 58.3 (s, 2F); EI-MS *m/z* (%) 276 (M⁺, 21), 203 (100), 183 (6), 152 (6).

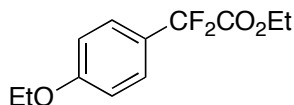
Ethyl 2,2-Difluoro-2-phenylacetate (**3i**)⁸



3i

The title compound was obtained from **1i** according to the general procedure and purified by column chromatography (hexane/ethyl acetate = 50/1) to give a colorless oil (40% isolated yield); IR (neat) 1776 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.61 (d, *J* = 9.2 Hz, 2H) 7.44-7.52 (m, 3H), 4.30 (q, *J* = 7.2 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 3H); ¹⁹F NMR (376 MHz, CDCl₃) δ 57.8 (s, 2F); EI-MS *m/z* (%) 200 (M⁺, 8), 127 (100), 77 (6).

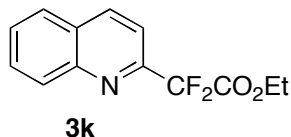
Ethyl 2-(4-Ethoxyphenyl)-2,2-difluoroacetate (**3j**)



3j

The title compound was obtained from **1g** according to the general procedure and purified by column chromatography (hexane/ethyl acetate = 50/1) to give a colorless oil (72% isolated yield); IR (neat) 1780 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.52 (d, *J* = 8.8 Hz, 2H), 6.93 (d, *J* = 8.8 Hz, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 4.06 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 164.3 (t, ²*J*_{CF} = 35.7 Hz), 160.9, 126.9, 124.5 (t, ²*J*_{CF} = 26.0 Hz), 114.3, 113.5 (t, ¹*J*_{CF} = 250 Hz), 63.5, 62.8, 14.5, 13.7; ¹⁹F NMR (376 MHz, CDCl₃) δ 59.2 (s, 2F); EI-MS *m/z* (%) 244 (M⁺, 12), 171 (98), 143 (100), 126 (4). Anal. Calcd for C₁₂H₁₄O₃F₂: C, 53.84; H, 4.09. Found: C, 54.10; H, 4.13.

Ethyl 2,2-Difluoro-2-(quinolin-2-yl)acetate (**3k**)⁹

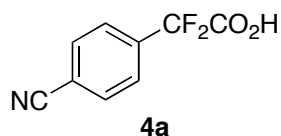


The title compound was obtained from **1k** according to the general procedure and purified by column chromatography (hexane/ethyl acetate = 50/1) to give a pale yellow oil (87% isolated yield); IR (neat) 1778 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.37 (d, $J = 8.6$ Hz, 1H), 8.17 (d, $J = 8.6$ Hz, 1H), 7.93-7.64 (m, 4H), 4.46 (q, $J = 7.2$ Hz, 2H), 1.39 (t, $J = 7.2$ Hz, 3H); ^{19}F NMR (376 MHz, CDCl_3) δ 57.4 (s, 2F); EI-MS m/z (%) 252 ($\text{M}+1$, 3), 251 (M^+ , 24), 206 (5), 179 (54), 178 (100), 128 (48). Anal. Calcd for $\text{C}_{13}\text{H}_{11}\text{NO}_2\text{F}_2$: C, 62.15; H, 4.41; N, 5.58. Found: C, 61.91; H, 4.43; N, 5.43.

Typical Procedure of Cu(I)-Catalyzed Cross-Coupling of Aryl Iodides with α -Trimethylsilyldifluoroacetate **5b** (*Catalytic in Copper*).

To a mixture of CuI (11.4 mg, 0.06 mmol), CsF (54.7 mg, 0.36 mmol), 4-iodobenzonitrile (**1a**, 68.7 mg, 0.3 mmol), and DME (0.6 mL) was added ethyl 2,2-difluoro-2-(triethylsilyl)acetate (**5b**, 85.7 mg, 0.36 mmol) at room temperature. The reaction mixture was stirred at 60 $^\circ\text{C}$ in an atmosphere of nitrogen for 15 h. Aryldifluoroacetate **3a** was formed in 71% NMR yield, which was calculated by ^{19}F NMR integration of product **3a** relative to the 2,2,2-trifluoroethanol internal standard.

Typical Procedure of Hydrolysis of Ethyl Ester **3**. 2-(4-Cyanophenyl)-2,2-difluoroacetic Acid (**4a**)

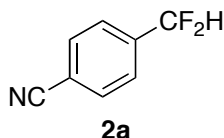


To a methanol (12 mL) solution of **3a** (900.8 mg, 4.0 mmol) was added 1N K_2CO_3 (12 mL) at room temperature. The mixture was stirred at 25 $^\circ\text{C}$ for 18 h and poured into 5% HCl, and successively extracted with ethyl acetate. The combined organic phase was washed with brine and dried over anhydrous Na_2SO_4 . After removal of the solvents in vacuo, the residue was purified by silica-gel column chromatography (hexane/ethyl acetate = 20/1) to give **4a** (754.7 mg, 96%) as colorless solids; mp >143 $^\circ\text{C}$ (decomp); IR (KBr) 3500-2700 (br), 2270, 1782 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.80 (d, $J = 9.2$ Hz, 2H), 7.77 (d, $J = 9.2$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 166.2 (t, $^2J_{\text{CF}} = 36.6$ Hz), 136.8 (t, $^2J_{\text{CF}} = 25.7$ Hz), 132.8, 126.7 (t, $^3J_{\text{CF}} = 6.2$ Hz), 117.7, 115.4 (t, $^4J_{\text{CF}} = 2.1$ Hz), 112.3 (t, $^1J_{\text{CF}} =$

252 Hz); ^{19}F NMR (376 MHz, CDCl_3) δ 56.3 (s, 2F); EI-MS m/z (%) 197 (M^+ , 6), 152 (100). Anal. Calcd for $\text{C}_9\text{H}_5\text{NO}_2\text{F}_2$: C, 54.83; H, 2.56; N, 7.11. Found: C, 55.22; H, 2.71; N, 7.26.

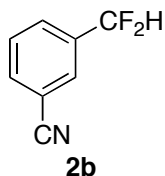
Typical Procedure for Hydrolysis of Ethyl Esters **3** and Decarboxylation.

4-(Difluoromethyl)benzonitrile (**2a**)¹⁰



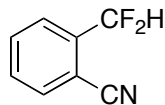
To a methanol (6.0 mL) solution of **3a** (450.4 mg, 2.0 mmol) was added 1 N K_2CO_3 (6.0 mL) at room temperature. The mixture was stirred at 25 °C for 2 h and poured into 5% HCl, and successively extracted with ethyl acetate. The combined organic phase was washed with brine and dried over anhydrous Na_2SO_4 . After removal of the solvents in vacuo, the residue (**4a**) and KF (581.1 mg, 10.0 mmol) were dissolved in 8.0 mL of DMF. The reaction mixture was stirred at 170 °C in an atmosphere of nitrogen for 2 h. After cooling to room temperature, water (3.0 mL) was added to the reaction mixture. Organic materials were extracted for three times with ethyl acetate and the combined organic layer were washed with brine and dried over Na_2SO_4 . After removal of the solvent under reduced pressure, the residue was purified by silica-gel column chromatography (hexane/ethyl acetate = 50/1) to give **2a** (256.6 mg, 84%) as a pale yellow oil; IR (neat) 2250 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.78 (d, $J = 8.2$ Hz, 2H), 7.64 (d, $J = 8.2$ Hz, 2H), 6.69 (t, $J_{\text{HF}} = 57.4$ Hz, 1H); ^{19}F NMR (376 MHz, CDCl_3) δ 48.6 (d, $J_{\text{HF}} = 57.4$ Hz, 2F); EI-MS m/z (%) 152 (M^+ , 70), 152 (100), 134 (12), 103 (36).

3-(Difluoromethyl)benzonitrile (**2b**)¹¹



The title compound was obtained from **3b** according to the general procedure and purified by column chromatography (hexane/ethyl acetate = 50/1) to give a pale yellow oil (57% isolated yield); IR (neat) 2247 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.82-7.74 (m, 3H), 7.61 (t, $J = 7.7$ Hz, 1H), 6.68 (t, $J_{\text{HF}} = 55.9$ Hz, 1H); ^{19}F NMR (470 MHz, CDCl_3) δ 49.2 (d, $J_{\text{HF}} = 55.9$ Hz, 2F); EI-MS m/z (%) 154 (M^+ , 6), 153 (M^+ , 68), 152 (100), 134 (10), 125 (6), 103 (33), 76 (9).

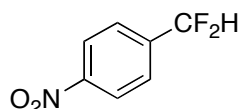
2-(Difluoromethyl)benzonitrile (**2c**)^{11,12}



2c

The title compound was obtained from **3c** according to the general procedure and purified by column chromatography (hexane/ethyl acetate = 30/1) to give a pale yellow oil (67% isolated yield); IR (neat) 2250 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.81-7.70 (m, 3H), 7.62 (t, $J = 7.4$ Hz, 1H), 6.94 (t, $J_{\text{HF}} = 54.6$ Hz, 1H); ^{19}F NMR (470 MHz, CDCl_3) δ 49.6 (d, $J_{\text{HF}} = 54.6$ Hz, 2F); EI-MS m/z (%) 154 ($\text{M}+1$, 8), 153 (M^+ , 96), 152 (100), 134 (12), 126 (22), 125 (12), 103 (47), 76 (14).

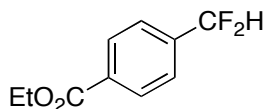
1-Nitro-4-(difluoromethyl)benzene (**2d**)^{10d,13}



2d

The title compound was obtained from **3d** according to the general procedure and purified by column chromatography (hexane/ethyl acetate = 50/1) to give a pale yellow oil (81% isolated yield); IR (neat) 1539, 1360 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.16 (d, $J = 8.0$ Hz, 1H), 7.91 (d, $J = 8.0$ Hz, 1H), 7.79 (t, $J = 8.0$ Hz, 1H), 7.69 (t, $J = 8.0$ Hz, 1H), 7.40 (t, $J_{\text{HF}} = 55.8$ Hz, 1H); ^{19}F NMR (376 MHz, CDCl_3) δ 46.7 (d, $J_{\text{HF}} = 55.8$ Hz, 2F); EI-MS m/z (%) 173 (M^+ , 12), 156 (30), 143 (63), 127 (100), 95 (54), 77 (23).

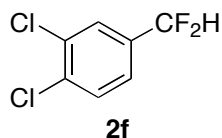
Ethyl 4-(Difluoromethyl)benzoate (**2e**)¹⁴



2e

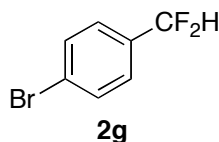
The title compound was obtained from **3e** according to the general procedure and purified by column chromatography (hexane/ethyl acetate = 50/1) to give a colorless oil (74% isolated yield); IR (neat) 1725 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.13 (d, $J = 7.8$ Hz, 2H), 7.59 (d, $J = 7.8$ Hz, 2H), 6.69 (t, $J_{\text{HF}} = 56.0$ Hz, 1H), 4.41 (q, $J = 7.1$ Hz, 2H), 1.41 (t, $J = 7.1$ Hz, 3H); ^{19}F NMR (376 MHz, CDCl_3) δ 49.6 (d, $J_{\text{HF}} = 56.0$ Hz, 2F); EI-MS m/z (%) 200 (M^+ , 14), 172 (37), 155 (100), 127 (39).

1,2-Dichloro-4-(difluoromethyl)benzene (**2f**)¹⁵



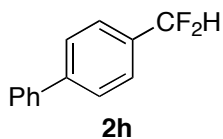
The title compound was obtained from **3f** according to the general procedure and purified by column chromatography (hexane) to give a colorless oil (77% isolated yield); ¹H NMR (300 MHz, CDCl₃) δ 7.61 (s, 1H), 7.55 (d, *J* = 8.2 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 1H), 6.61 (t, *J*_{HF} = 56.1 Hz, 1H); ¹⁹F NMR (470 MHz, CDCl₃) δ 50.1 (d, *J*_{HF} = 56.1 Hz, 2F); EI-MS *m/z* (%) 200 (M+4, 8), 198 (M+2, 38), 196 (M⁺, 60), 195 (26), 177 (10), 163 (30), 161 (100), 75 (12).

1-Bromo-4-(difluoromethyl)benzene (**2g**)¹⁶



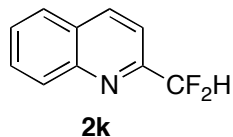
The title compound was obtained from **3g** according to the general procedure and purified by column chromatography (hexane) to give a colorless oil (59% isolated yield); ¹H NMR (300 MHz, CDCl₃) δ 7.60 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 6.61 (t, *J*_{HF} = 56.2 Hz, 1H); ¹⁹F NMR (376 MHz, CDCl₃) δ 50.6 (d, *J*_{HF} = 56.2 Hz, 2F); EI-MS *m/z* (%) 208 (M+2, 66), 206 (M⁺, 71), 189 (11), 187 (11), 158 (7), 156 (7), 127 (100), 107 (15).

4-(Difluoromethyl)biphenyl (**2h**)¹⁷



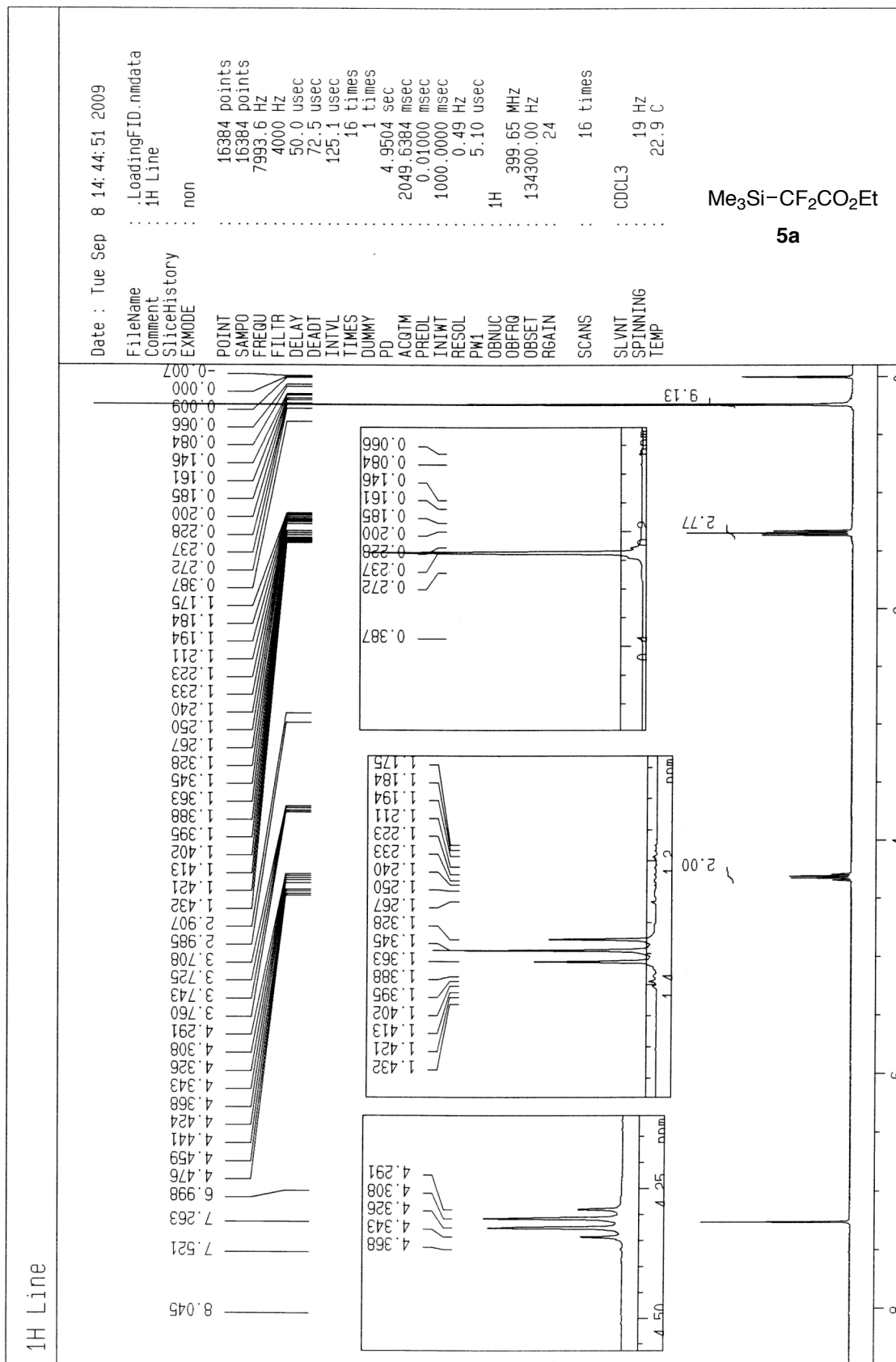
The title compound was obtained from **3h** according to the general procedure and purified by column chromatography (hexane/ethyl acetate = 50/1) to give colorless solids (62% isolated yield); mp 77.0-77.5 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.69-7.37(m, 9H), 6.70 (t, *J*_{HF} = 56.4 Hz, 1H); ¹⁹F NMR (376 MHz, CDCl₃) δ 51.3 (d, *J*_{HF} = 56.4 Hz, 2F); EI-MS *m/z* (%) 204 (M⁺, 100), 183 (17), 152 (17), 127 (8).

2-(Difluoromethyl)quinoline (2k)¹⁸

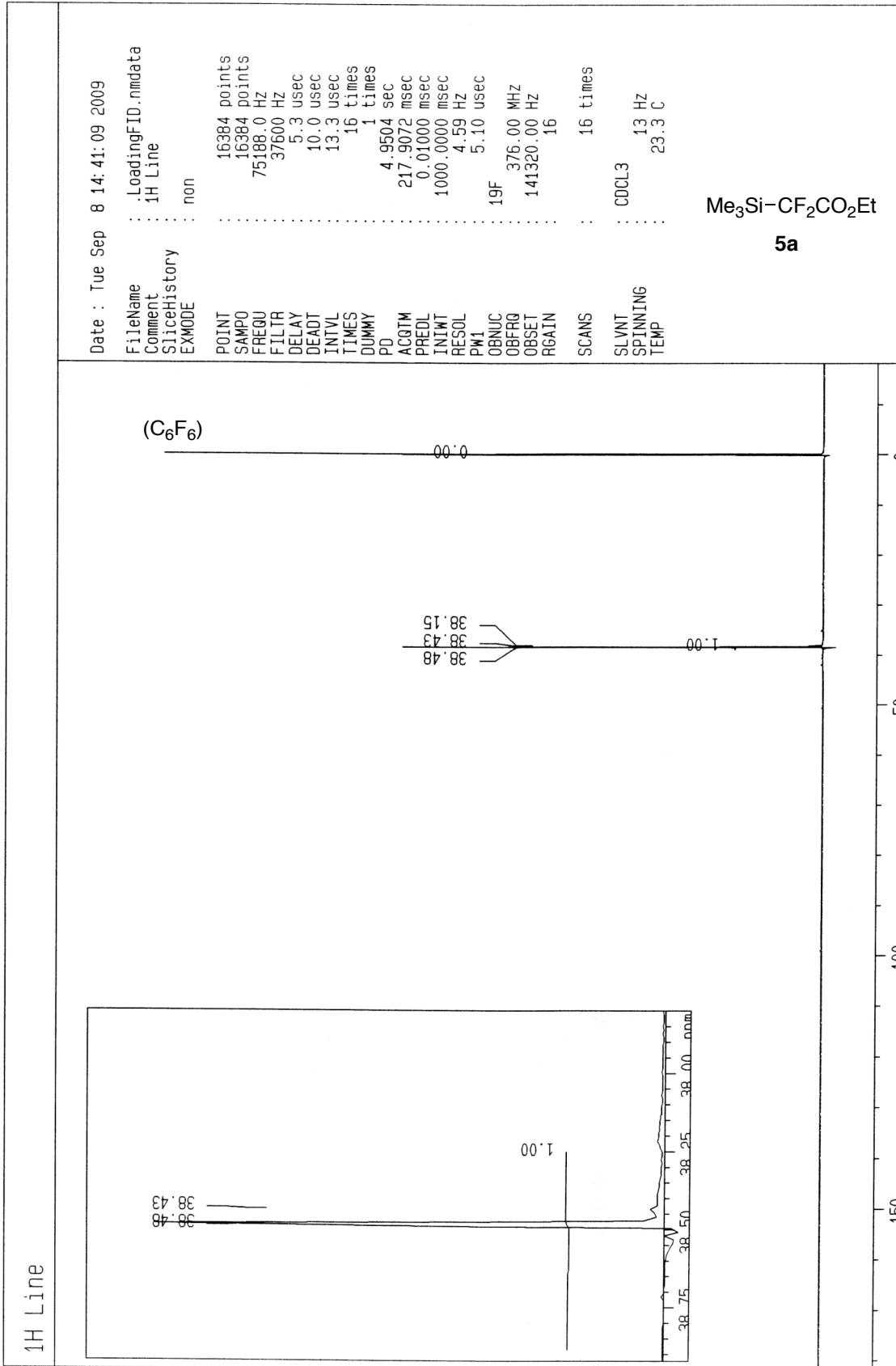


The title compound was obtained from **3k** according to the general procedure and purified by column chromatography (hexane/ethyl acetate = 50/1) to give a yellow oil (89% isolated yield); ¹H NMR (500 MHz, CDCl₃) δ 8.34 (d, *J* = 8.5 Hz, 1H), 8.15 (d, *J* = 8.5 Hz, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.80 (dd, *J* = 8.5 Hz, 6.9 Hz, 1H), 7.74 (d, *J* = 8.5 Hz, 1H), 7.65 (dd, *J* = 8.1 Hz, 6.9 Hz, 1H), 6.79 (t, *J*_{HF} = 55.4 Hz, 1H); ¹⁹F NMR (470 MHz, CDCl₃) δ 51.7 (d, *J*_{HF} = 55.4 Hz, 2F); EI-MS *m/z* (%) 180 (M+1, 11), 179 (M⁺, 100), 129 (26), 128 (58), 101 (17).

¹H NMR Spectrum of Compound 5a



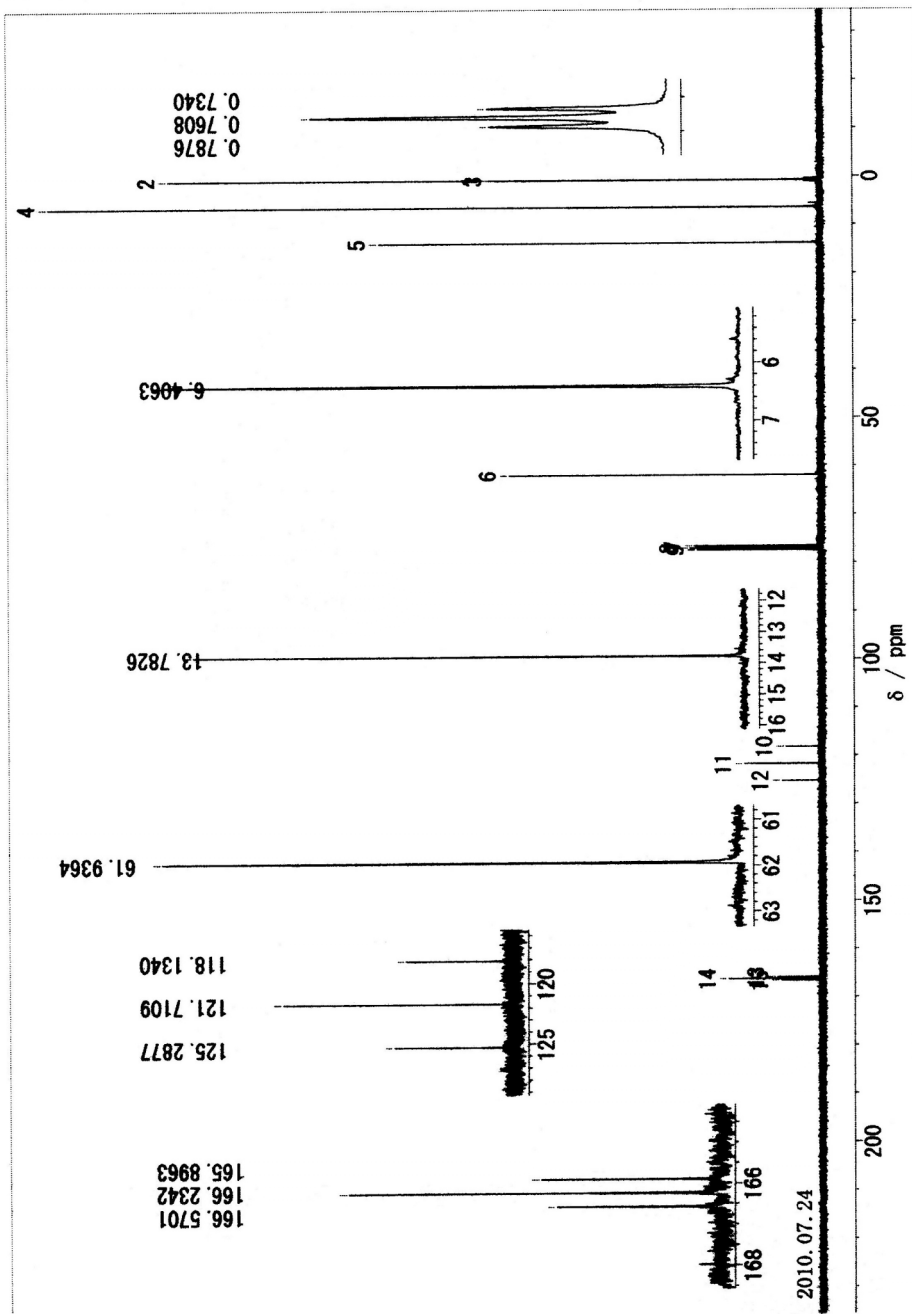
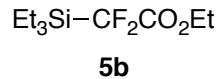
¹⁹F NMR Spectrum of Compound 5a



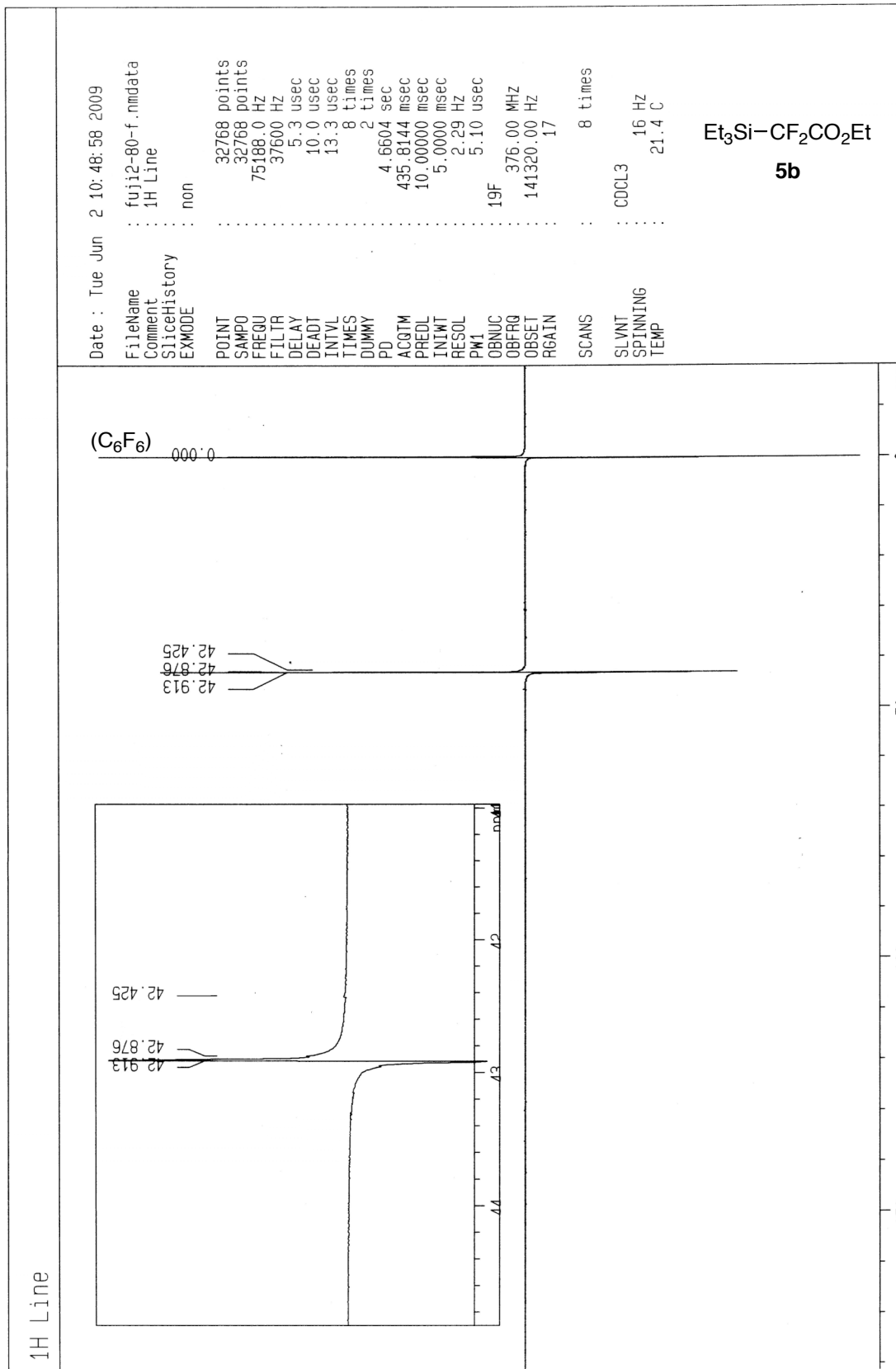
¹³C NMR Spectrum of Compound 5b

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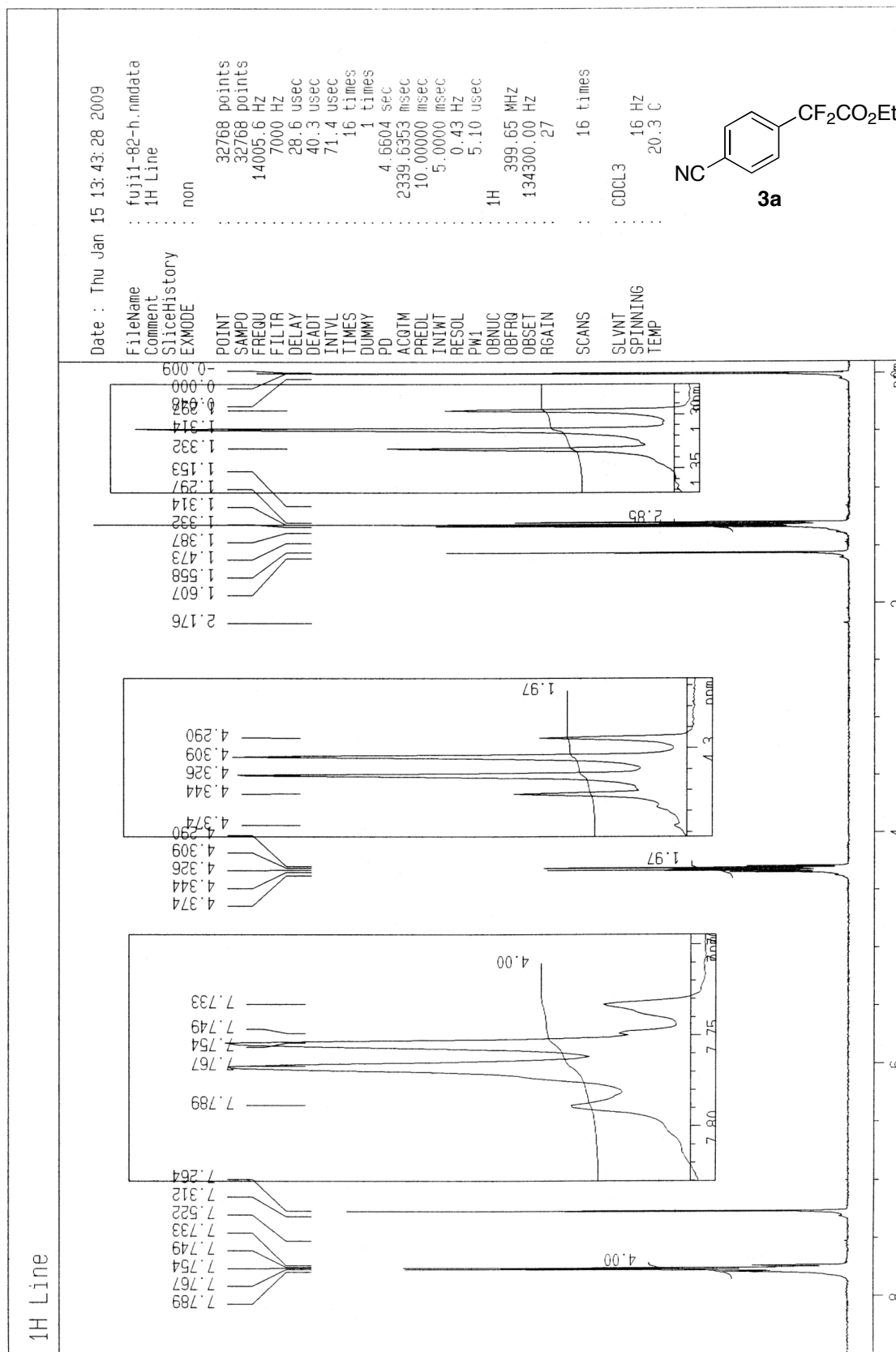
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 ObsFine 1840.0 Hz
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 Pulse2 10.0 μs
 Pulse3 10.0 μs
 P11 1.0 ms
 P12 1.0 ms
 P13 1.0 ms
 Loop1 1
 Point 131072(ZeroFill
 : ×4)
 Scan 1024
 DummyScan 1
 Frequency (Span) 20408.1 Hz
 AcqTime 1.6056 s
 PD 1.394 s
 RGain 24
 Broad.Factor 0.3114 Hz
 ExMode BCM
 IrrNuc ¹H
 IrrFreq 300.4 MHz
 IrrSet 130.0 kHz
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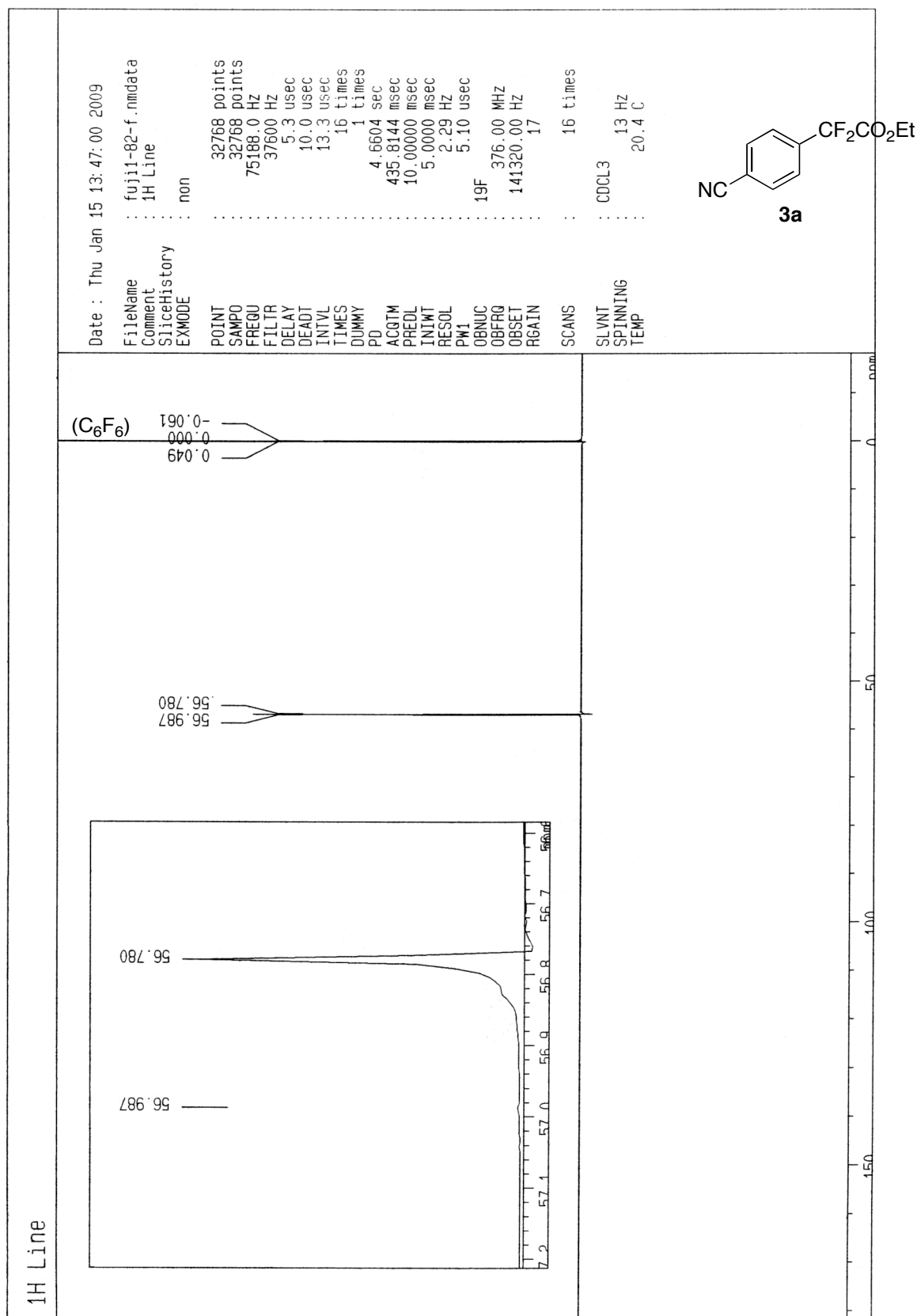
¹⁹F NMR Spectrum of Compound **5b**



¹H NMR Spectrum of Compound 3a



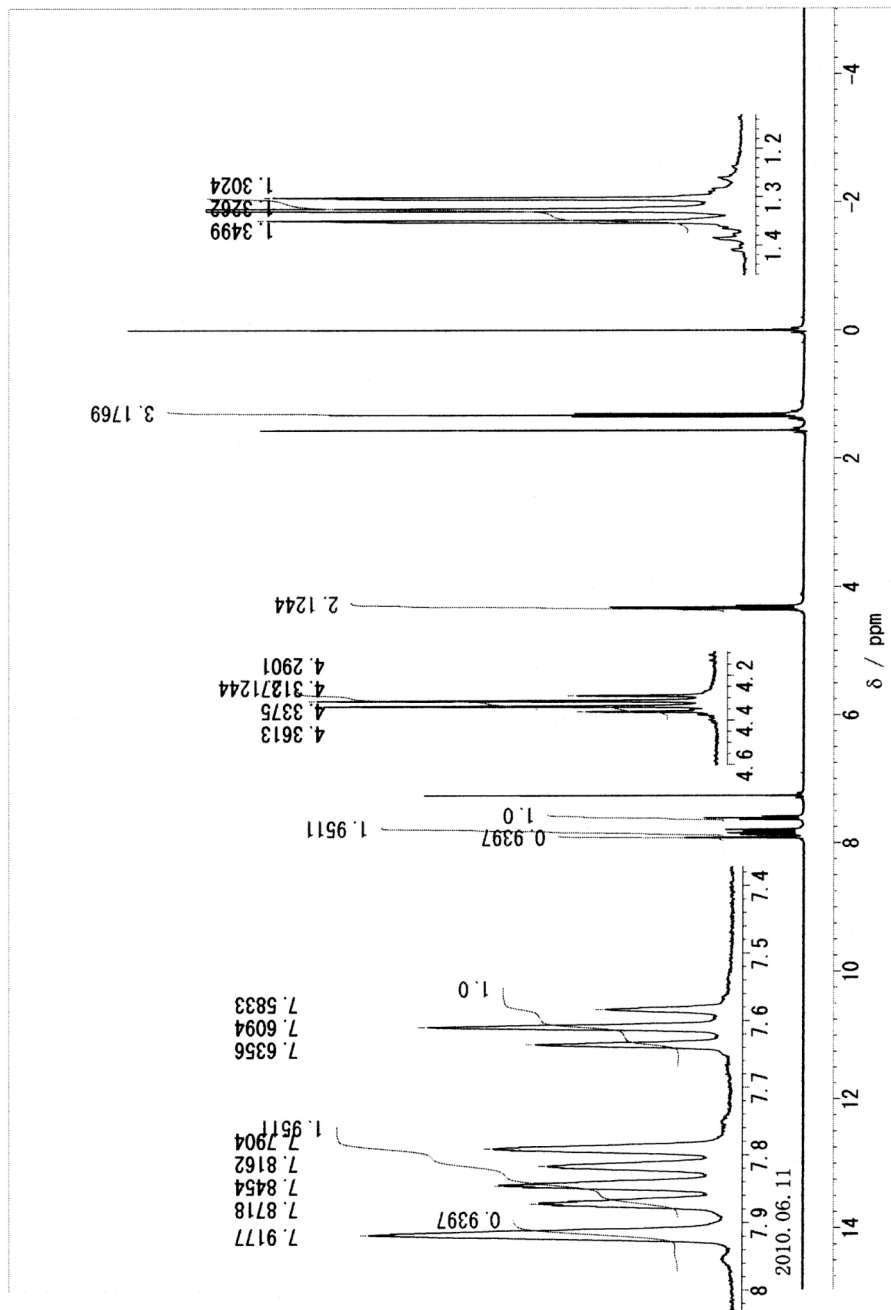
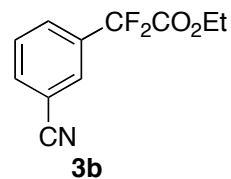
¹⁹F NMR Spectrum of Compound **3a**



¹H NMR Spectrum of Compound **3b**

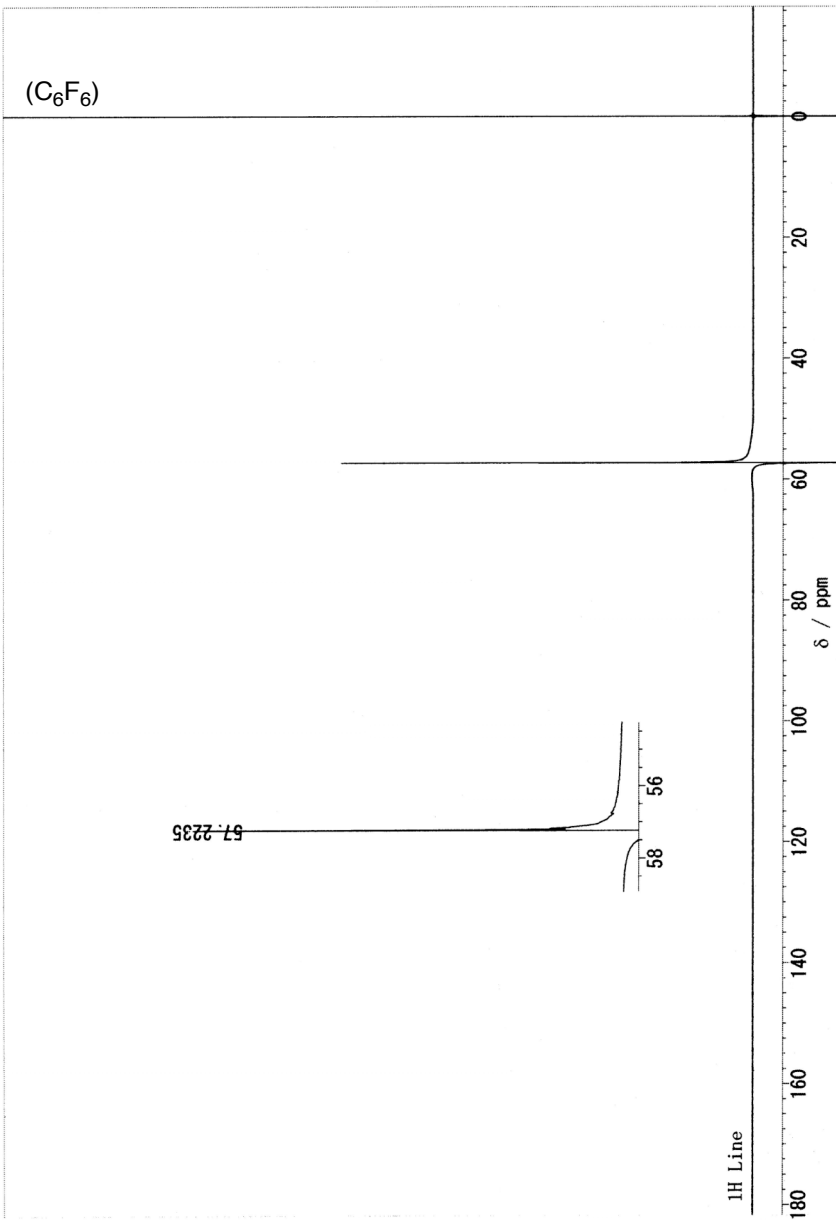
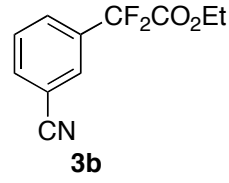
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Date 11/Jun/2010 21:36:02
Comment: 2010.06.11

¹H
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ObsFreq 130.0 kHz
ObsSet 1150.0 Hz
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Pulse2 10.0 μs
Pulse3 10.0 μs
PI1 1.0 ms
PI2 1.0 ms
PI3 1.0 ms
Loop1 1
Point 131072(ZeroFill
: X4)
Scan 16
DummyScan 1
Frequency (Span) 6002.4 Hz
AcqTime 5.4592 s
PD 1.547 s
RGain 20
Broad. Factor 0.0916 Hz
ExMode NON
IrrNuc ¹H
IrrFreq 300.4 MHz
IrrSet 130.0 kHz
IrrFine 1150.0 Hz
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Spinning 13.0 Hz
Temperature 22.1 °C
Printed 2010/Nov/25 20:52:59



¹⁹F NMR Spectrum of Compound **3b**

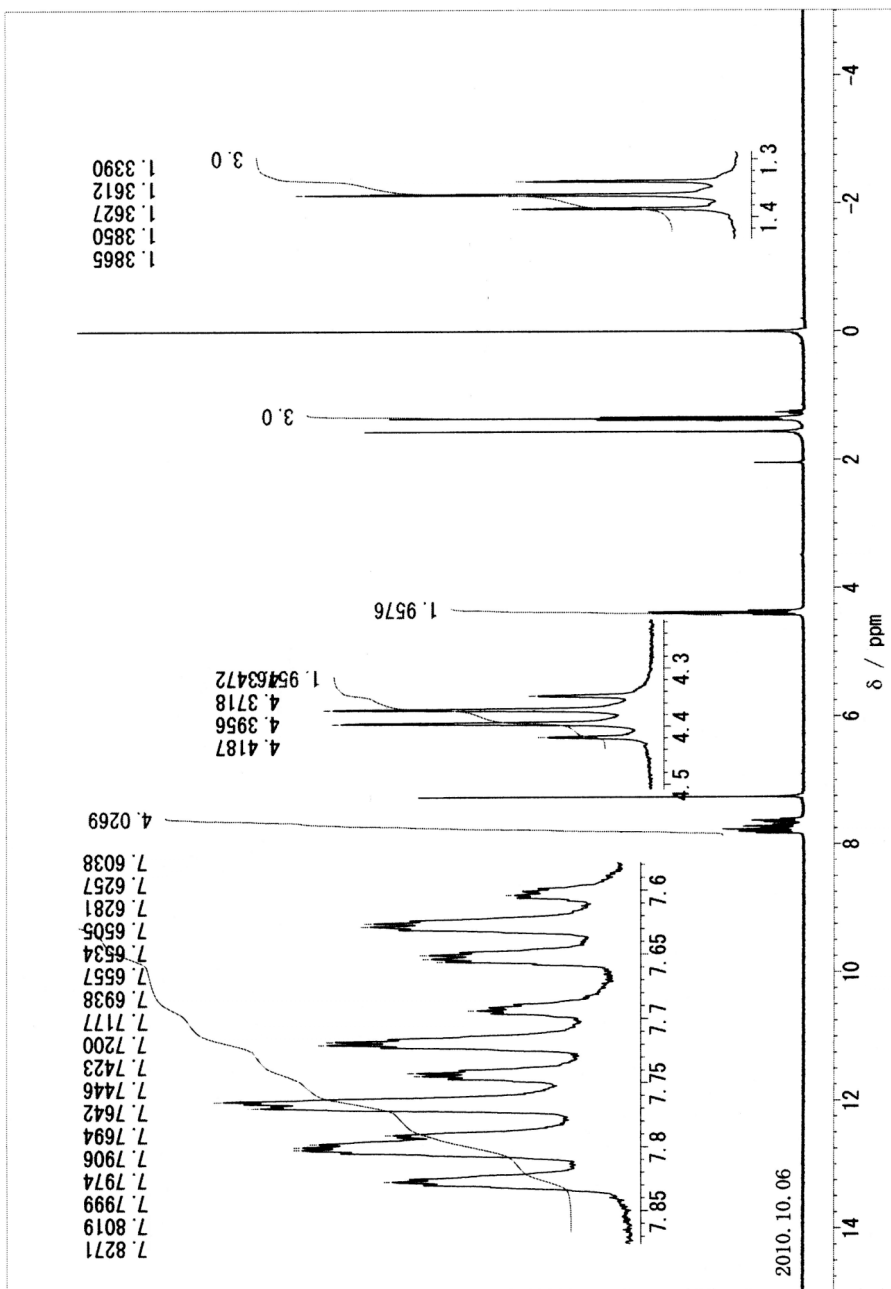
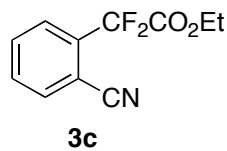
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mdata
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¹⁹F
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ObsSet: 141.0 kHz
ObsFine: 320.0 Hz
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Pulse2: 12.0 μs
Pulse3: 10.0 μs
P11: 0.25 ms
P12: 0.25 ms
P13: 1.0 ms
Loop1: 0
Point: 16384
Scan: 16
DummyScan: 1
Frequency (Span): 75187.97 Hz
AcqTime: 0.2179 s
PD: 4.9504 s
RGain: 17
Broad. Factor: 0.25 Hz
ExMode: non
IrrNuc: ¹H
IrrFreq: 399.65 MHz
IrrSet: 134.0 kHz
IrrFine: 300.0 Hz
IrrPulse: 50 μs
IrrAttn: 0
Spinning: 14.0 Hz
Temperature: 19.2 °C
Printed: 2010/dec/03 13:48:32



¹H NMR Spectrum of Compound 3c

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 Comment: 2010.10.06

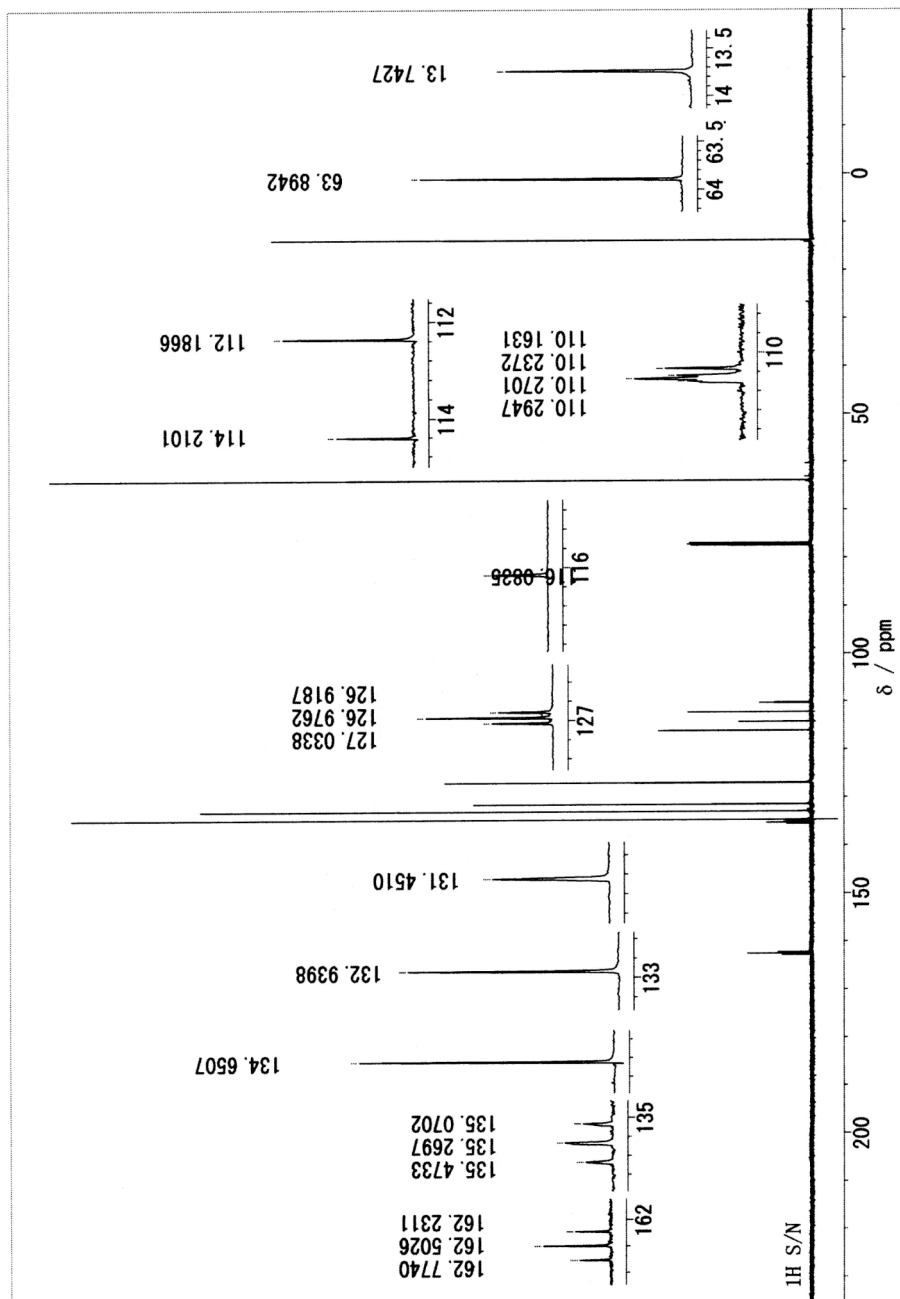
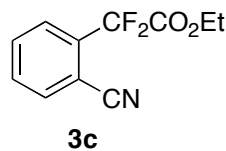
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 ObsFine 1150.0 Hz
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 Pulse2 10.0 μs
 Pulse3 10.0 μs
 P11 1.0 ms
 P12 1.0 ms
 P13 1.0 ms
 Loop1 1
 Point 131072(ZeroFill
 : X4)
 Scan 16
 DummyScan 1
 Frequency(Span) 6002.4 Hz
 AcqTime 5.4592 s
 PD 1.547 s
 RGain 23
 Broad. Factor 0.0916 Hz
 ExMode NON
 IrrNuc ¹H
 IrrFreq 300.4 MHz
 IrrSet 130.0 kHz
 IrrFine 1150.0 Hz
 IrrPulse 50 μs
 IrrAttn 511
 Spinning 13.0 Hz
 Temperature 21.2 °C
 Printed 2010/Nov/25 21:53:53



¹³C NMR Spectrum of Compound 3c

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 3-13C\FUJ15-13-13C.nmdata
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Comment: 1H S/N
¹³C
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 ObsFreq 128.0 kHz
 ObsSet -42.0 Hz
 ObsFine 4.0 μs
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 Pulse2 10.0 μs
 Pulse3 2.324 ms
 P11 0.25 ms
 P12 1.0 ms
 P13 0
 Loop1 32768
 Point 512
 Scan 4
 DummyScan
 Frequency(Span) 33898.3 Hz
 AcqTime 0.9667 s
 PD 2.0333 s
 RGain 29
 Broad. Factor 0.25 Hz
 ExMode bcm
 IrrNuc ¹H
 IrrFreq 500.0 MHz
 IrrSet 162.0 kHz
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 Spinning 10.0 Hz
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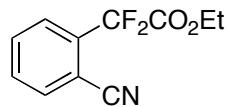
¹⁹F NMR Spectrum of Compound 3c

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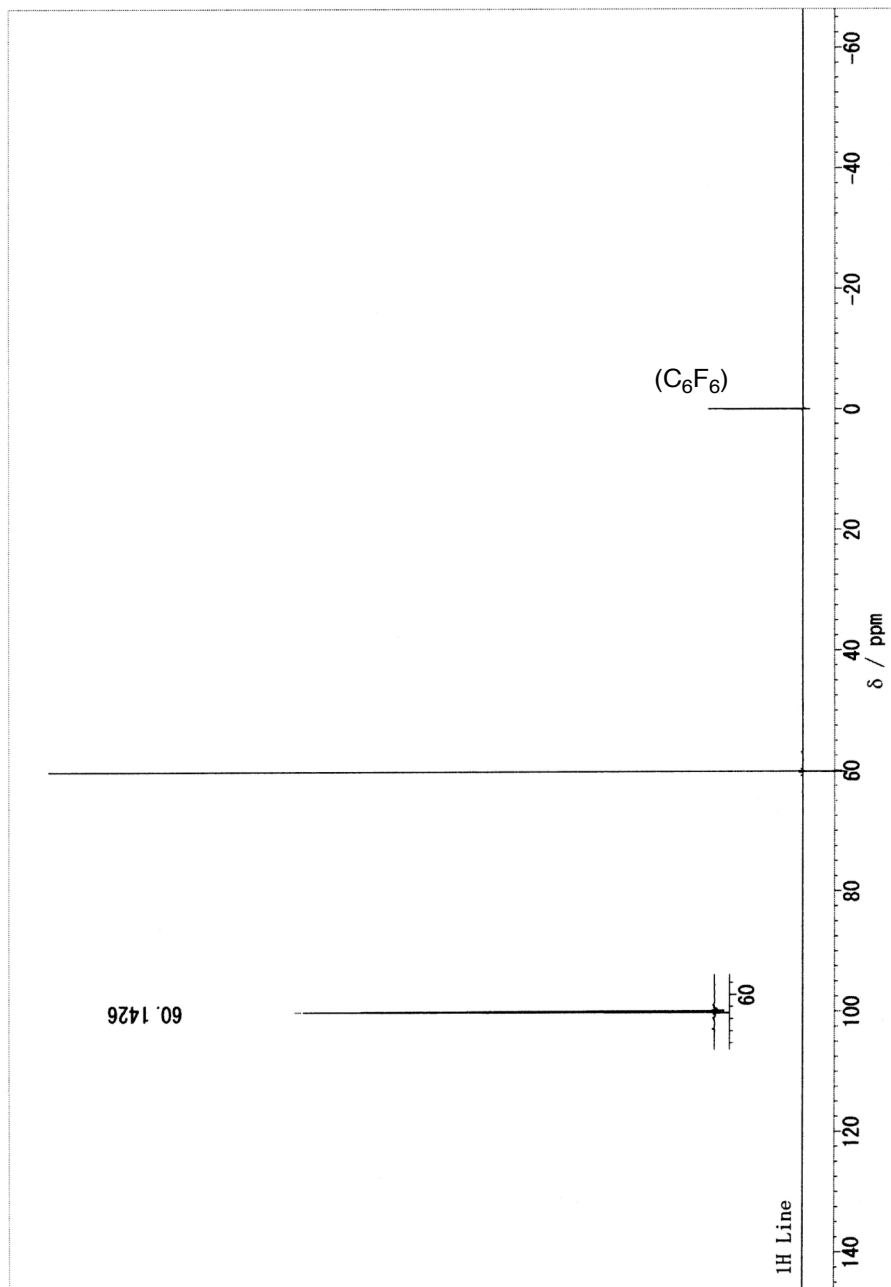
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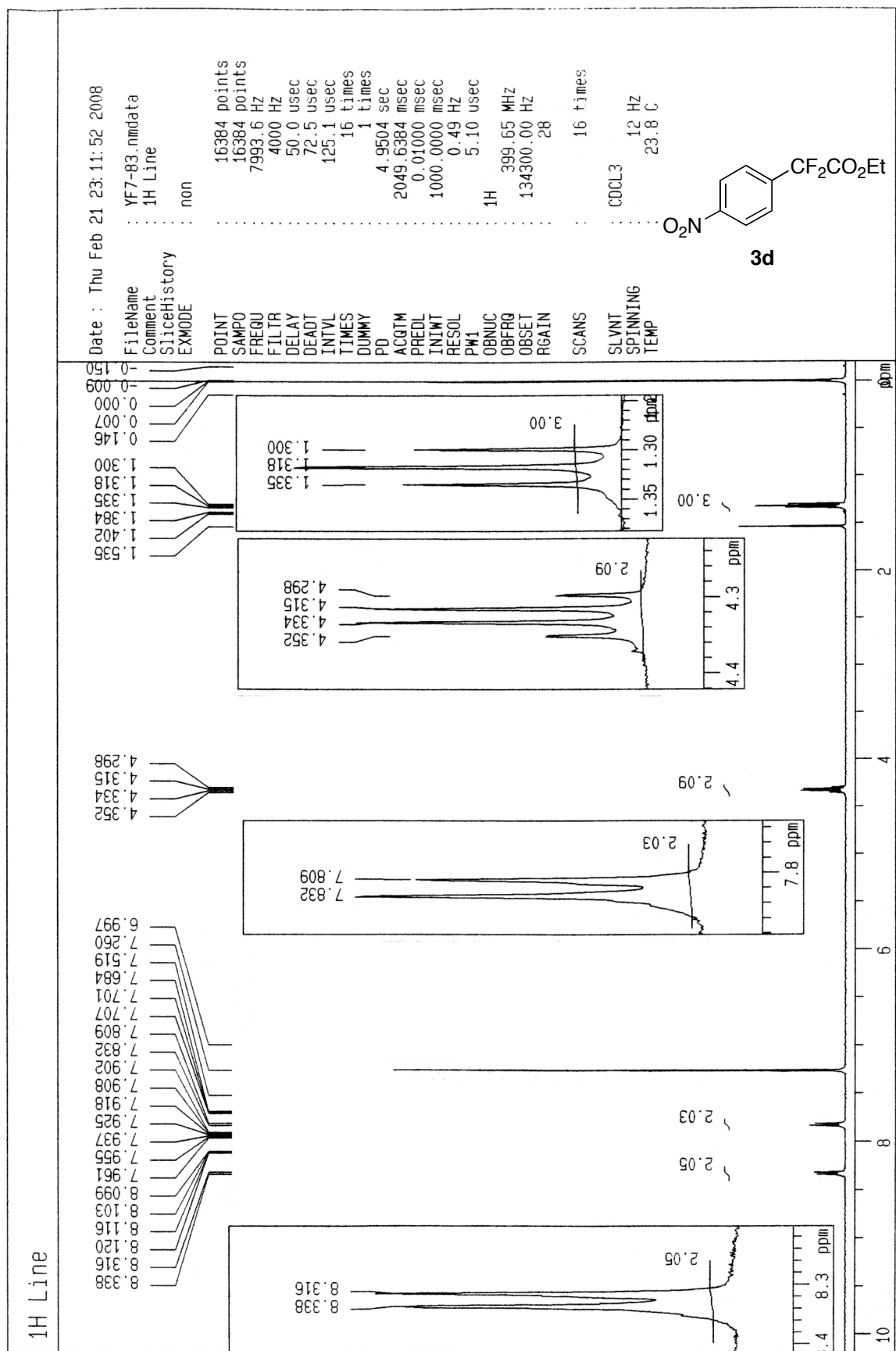
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PI2 0.05 ms
PI3 1.0 ms
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DummyScan 4
Frequency (Span) 100000.0 Hz
AcqTime 0.3277 s
PD 5.6893 s
RGain 23
Broad. Factor 0.25 Hz
ExMode non
IrrNuc ¹H
IrrFreq 500.0 MHz
IrrSet 162.0 kHz
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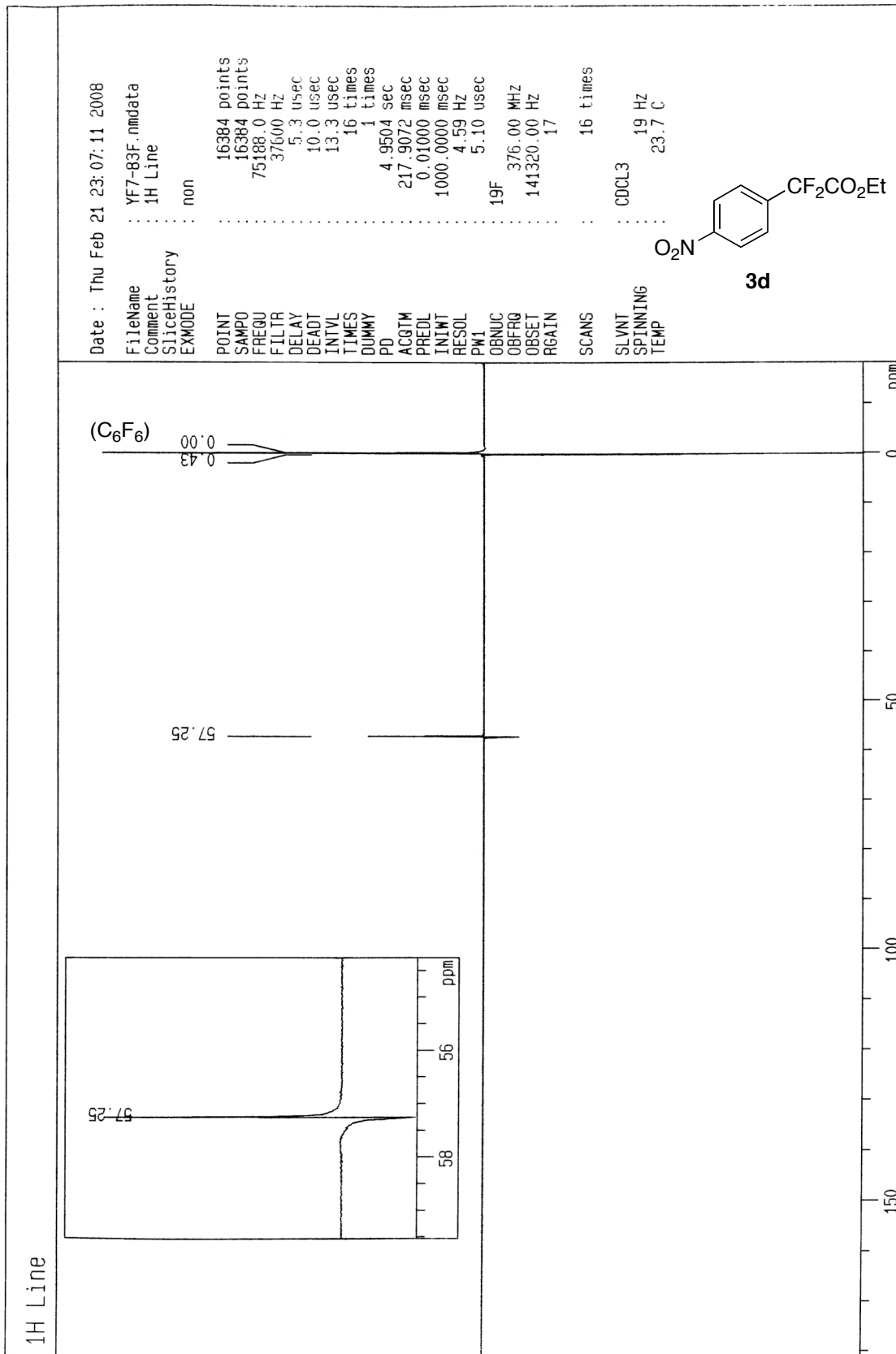
3c



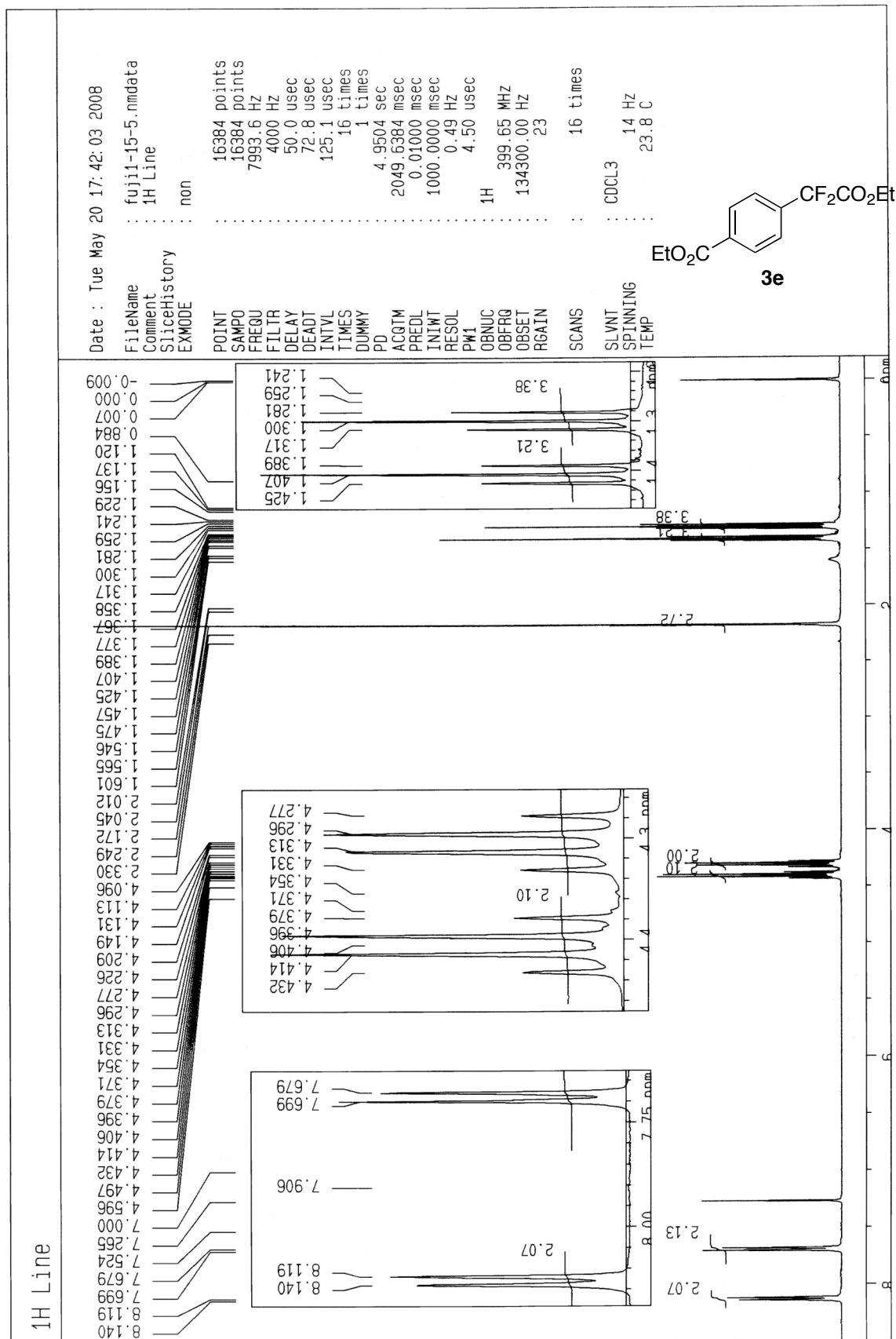
¹H NMR Spectrum of Compound 3d



¹⁹F NMR Spectrum of Compound **3d**

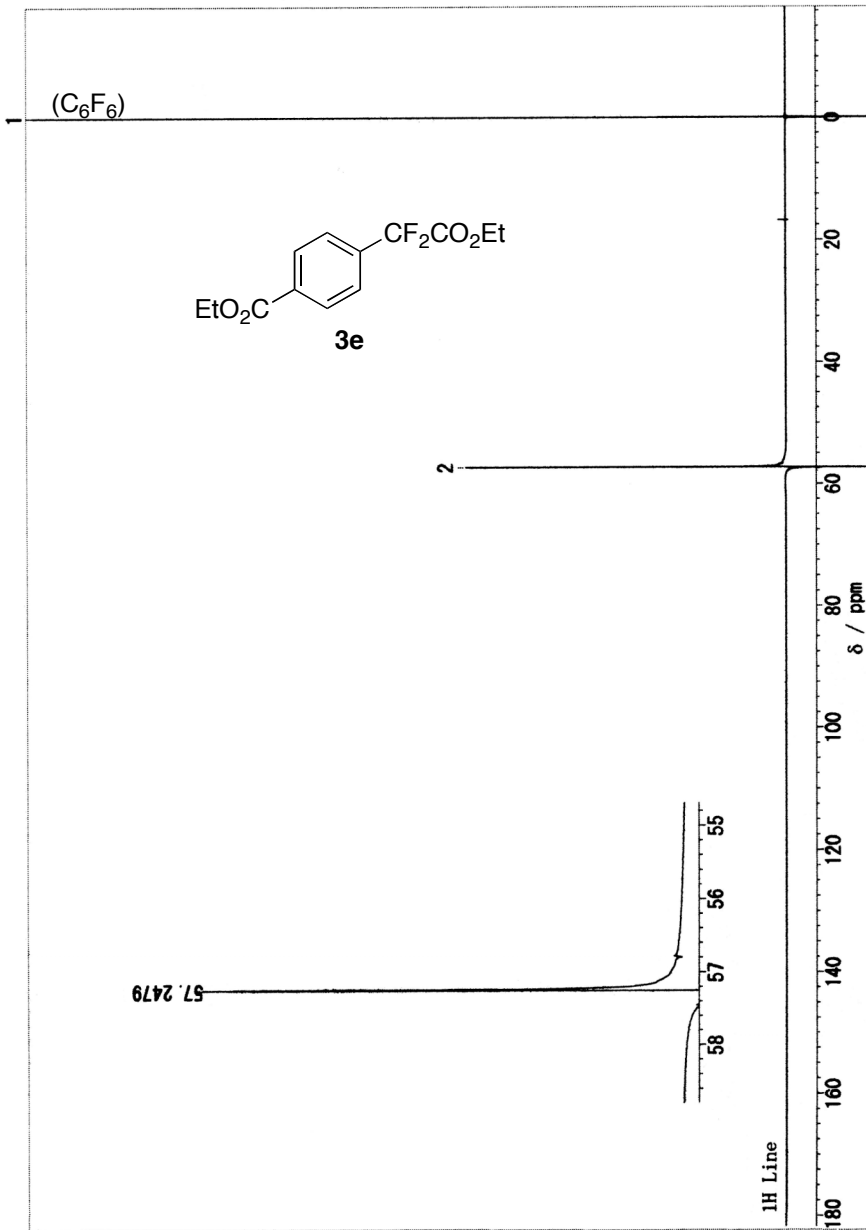


¹H NMR Spectrum of Compound 3e



¹⁹F NMR Spectrum of Compound 3e

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ObsSet 320.0 Hz
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Pulse2 10.0 μs
Pulse3 0.25 ms
PI1 0.25 ms
PI2 1.0 ms
PI3 0
Loop1 16384
Point 16
Scan 1
DummyScan 1
Frequency (Span) 75187.97 Hz
AcqTime 0.2179 s
PD 4.9504 s
RGain 16
Broad.Factor 0.25 Hz
ExMode non
IrrNuc ¹H
IrrFreq 399.65 MHz
IrrSet 134.0 kHz
IrrFine 300.0 Hz
IrrPulse 50 μs
IrrAttn 0
Spinning 15.0 Hz
Temperature 24.0 °C
Printed 2010/Aug/23 09:48:02



No.	δ/ppm	Height
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¹H NMR Spectrum of Compound 3f

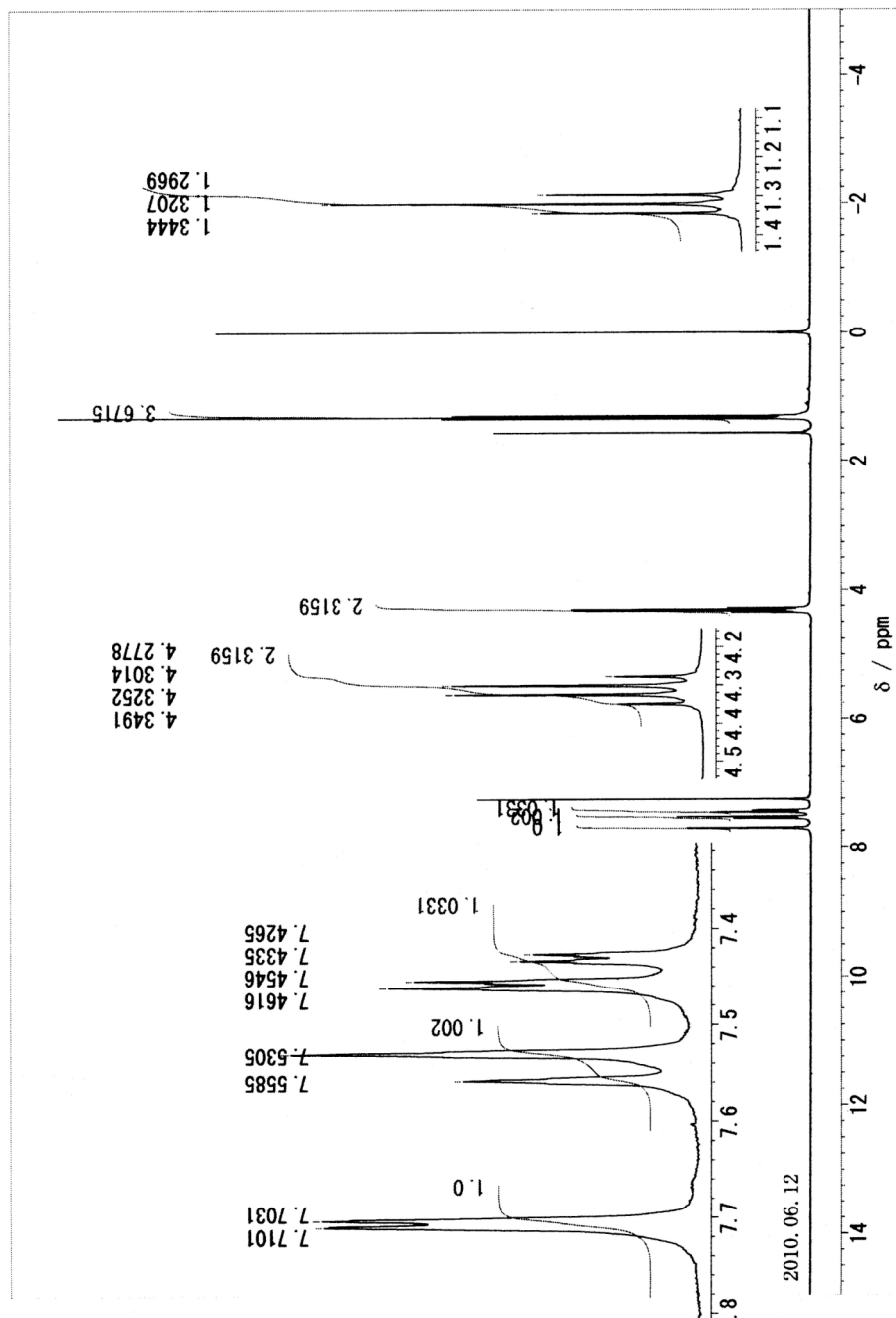
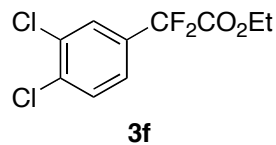
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 Comment: 2010.06.12

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 ObsSet 130.0 kHz
 ObsFine 1150.0 Hz
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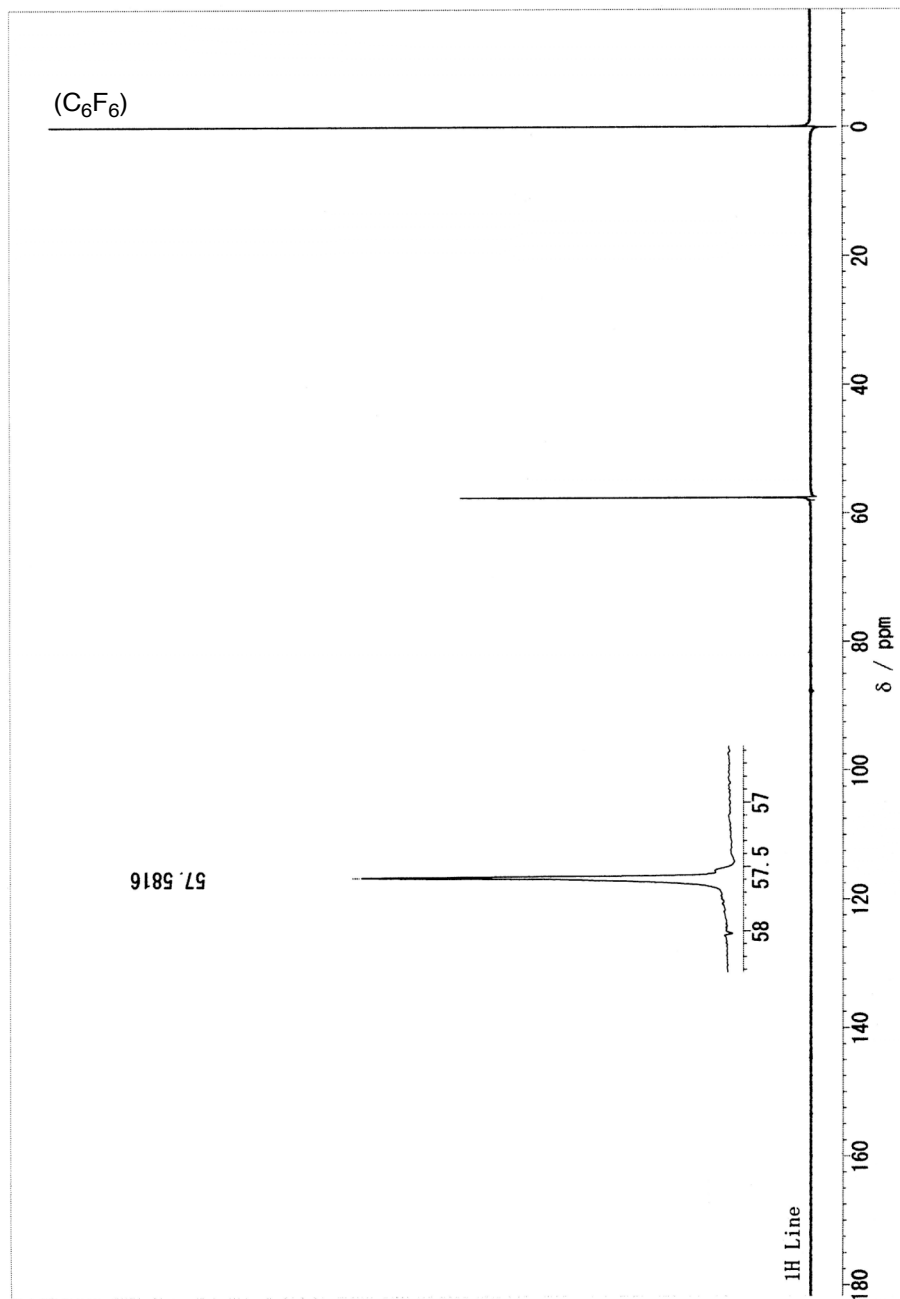
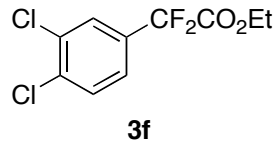
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 RGain 19
 Broad.Factor 0.0916 Hz
 ExMode NON
 IrrNuc 1H
 IrrFreq 300.4 MHz
 IrrSet 130.0 kHz
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 Spinning 14.0 Hz
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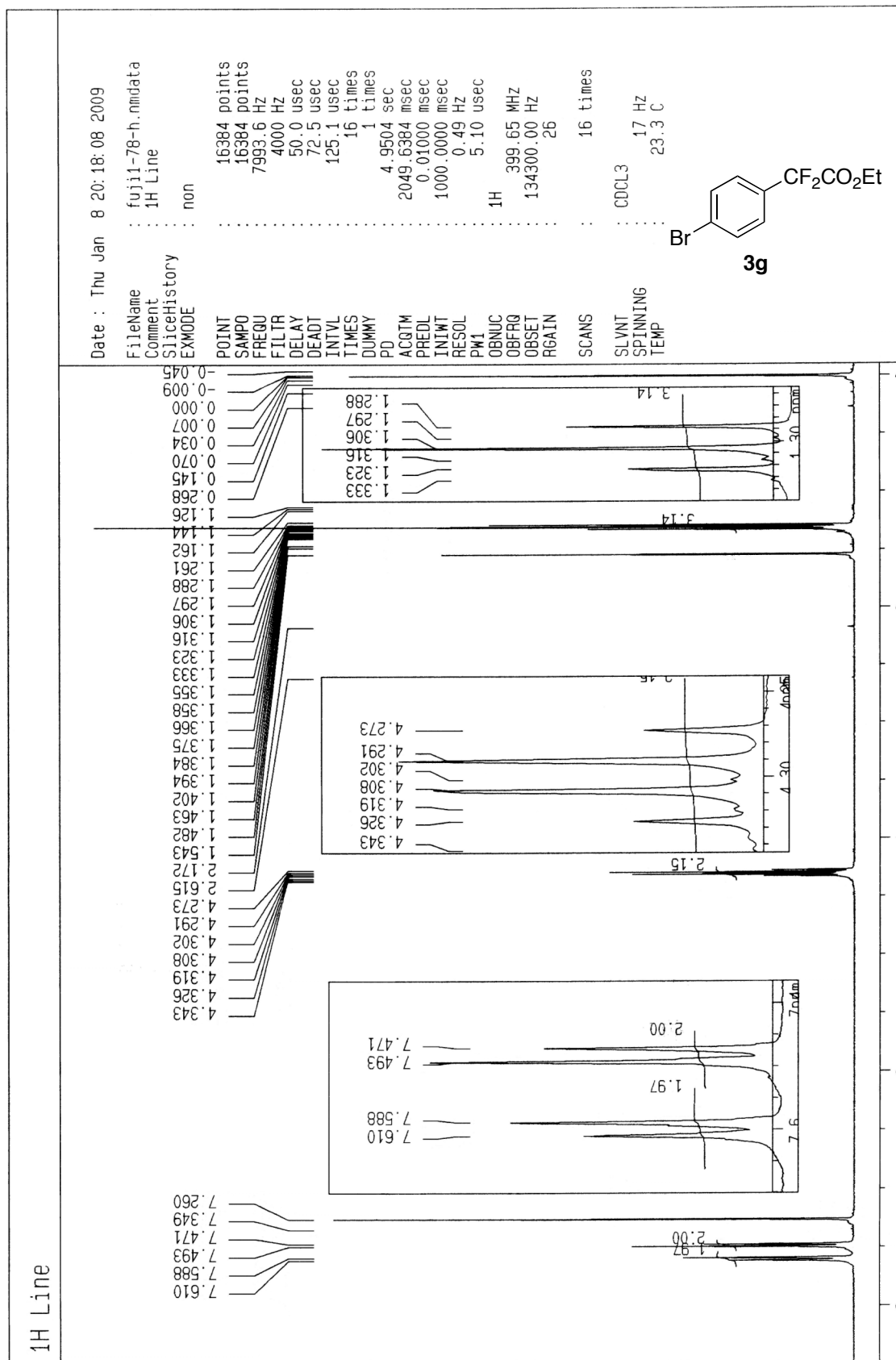


¹⁹F NMR Spectrum of Compound **3f**

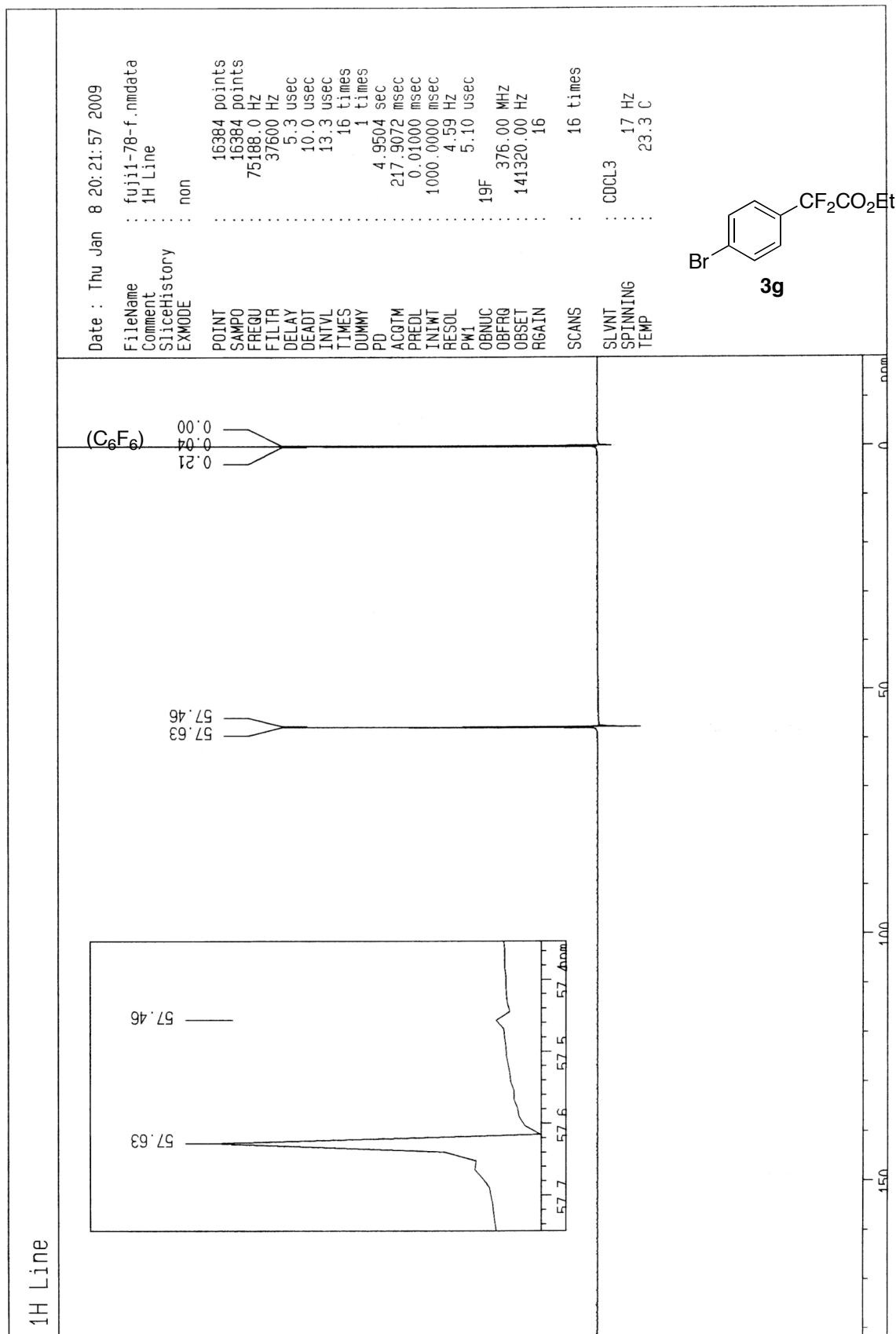
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 Date 14/Feb/2010 21:10:19
 Comment: 1H Line
 19F
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 ObsFreq 141.0 kHz
 ObsSet 320.0 Hz
 ObsFine 5.1 μs
 Pulse1 12.0 μs
 Pulse2 10.0 μs
 Pulse3 0.25 ms
 P11 0.25 ms
 P12 1.0 ms
 P13 0
 Loop1 16384
 Point 16
 Scan 1
 DummyScan 75187.97 Hz
 Frequency (Span) 0.2179 s
 AcqTime 4.9504 s
 PD 17
 RGain 0.25 Hz
 Broad.Factor non
 ExMode .H
 IrrNuc 399.65 MHz
 IrrFreq 134.0 kHz
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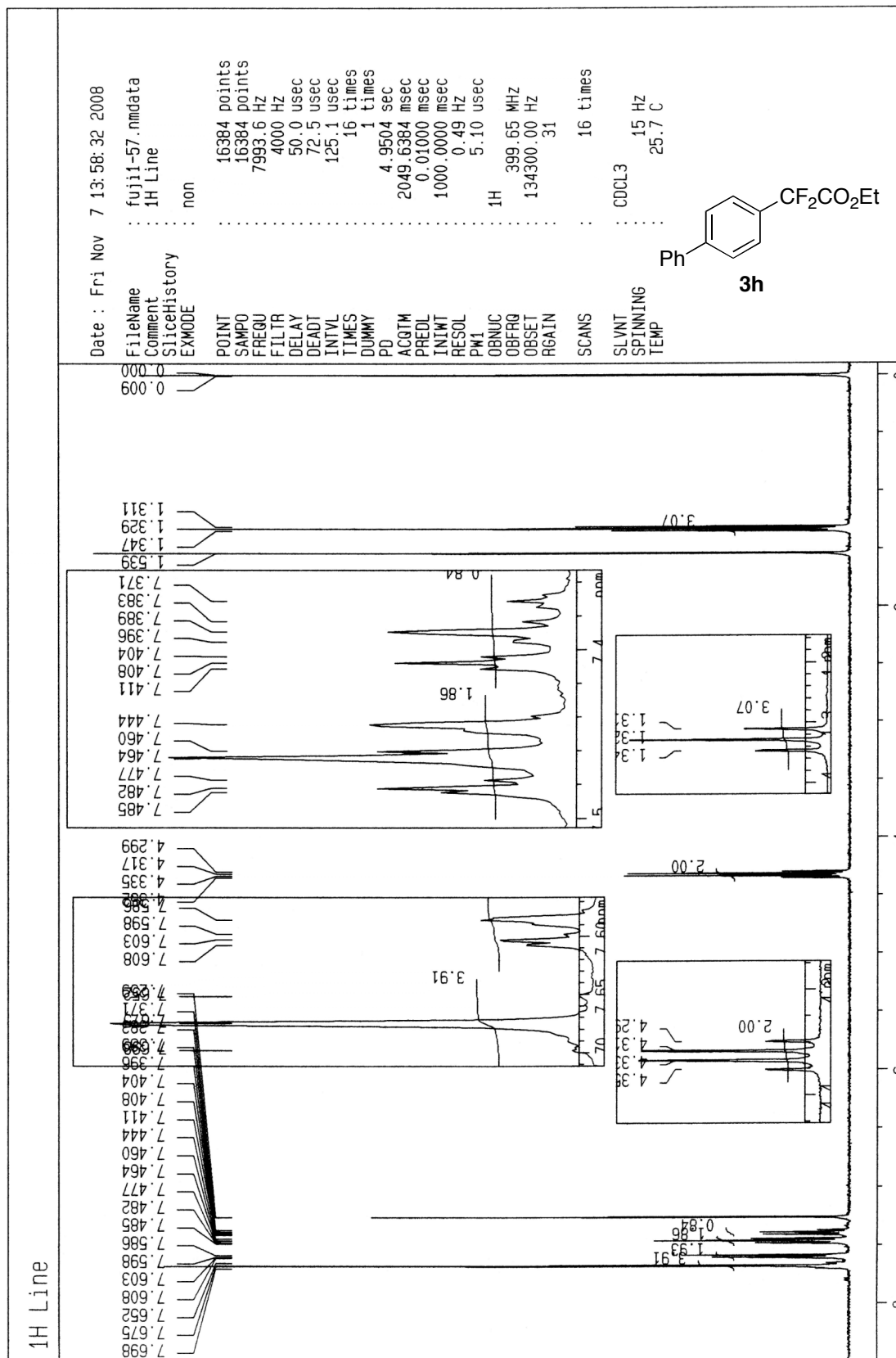
¹H NMR Spectrum of Compound 3g



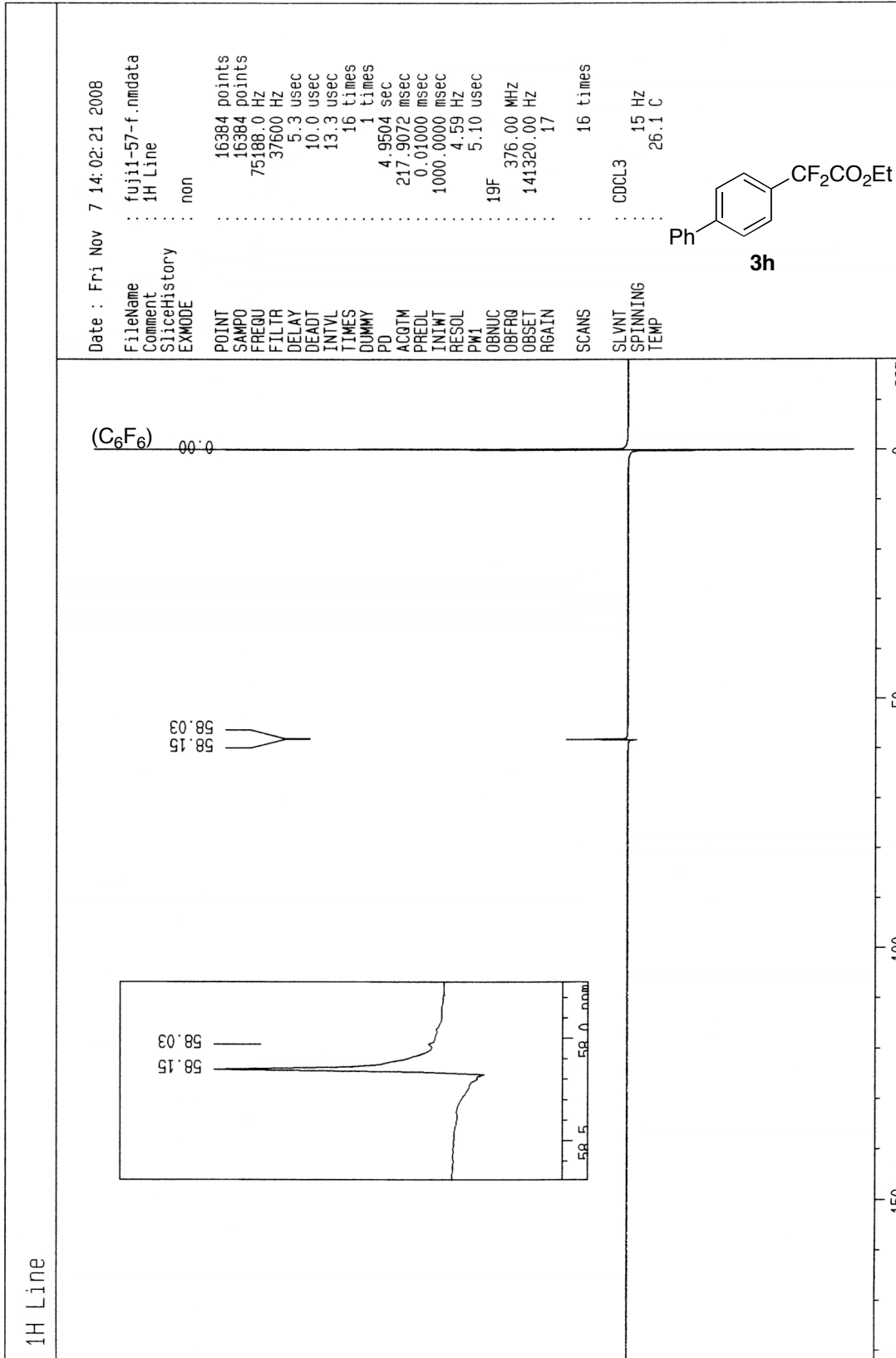
¹⁹F NMR Spectrum of Compound **3g**



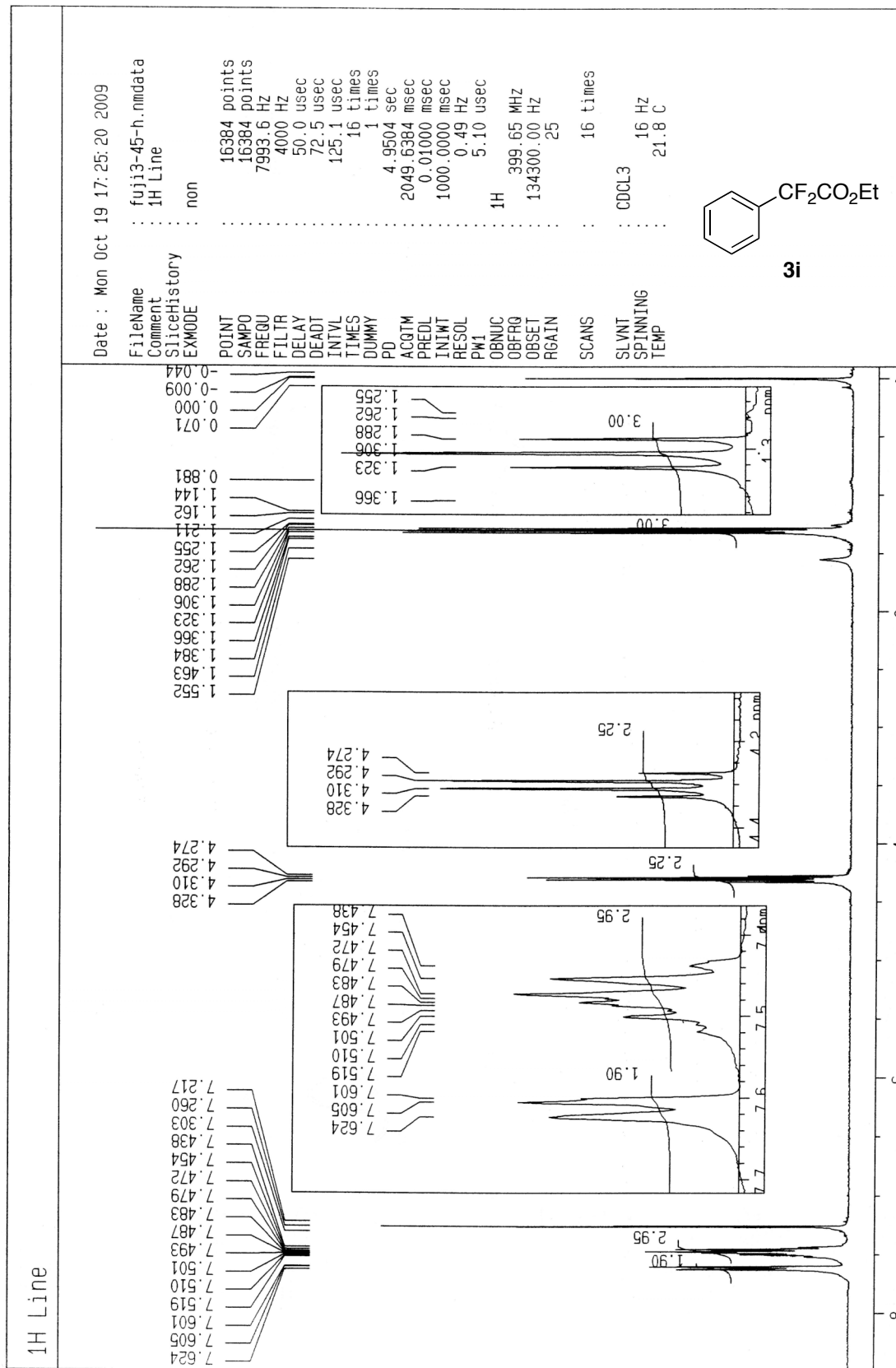
¹H NMR Spectrum of Compound 3h



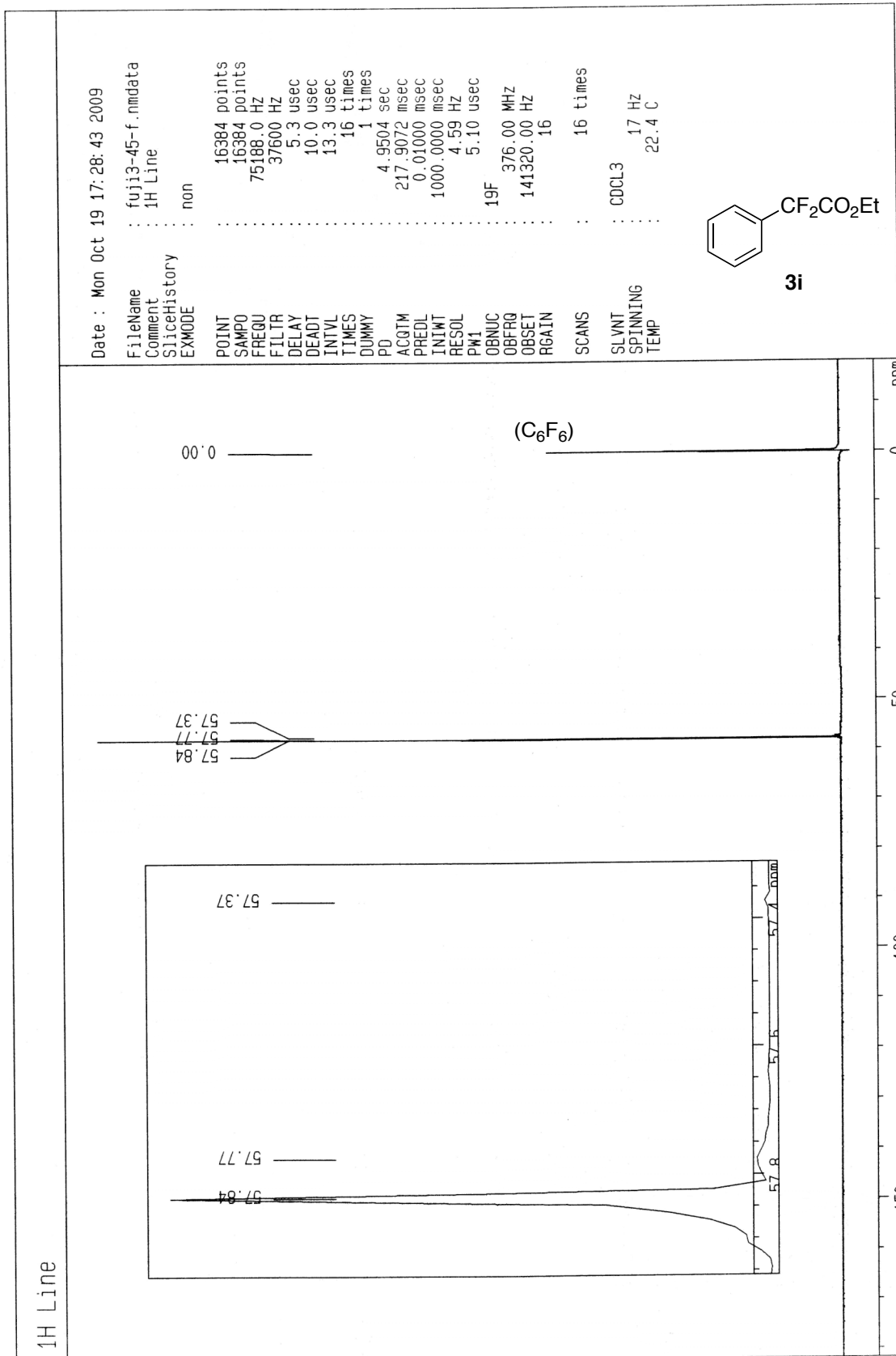
¹⁹F NMR Spectrum of Compound **3h**



¹H NMR Spectrum of Compound 3i

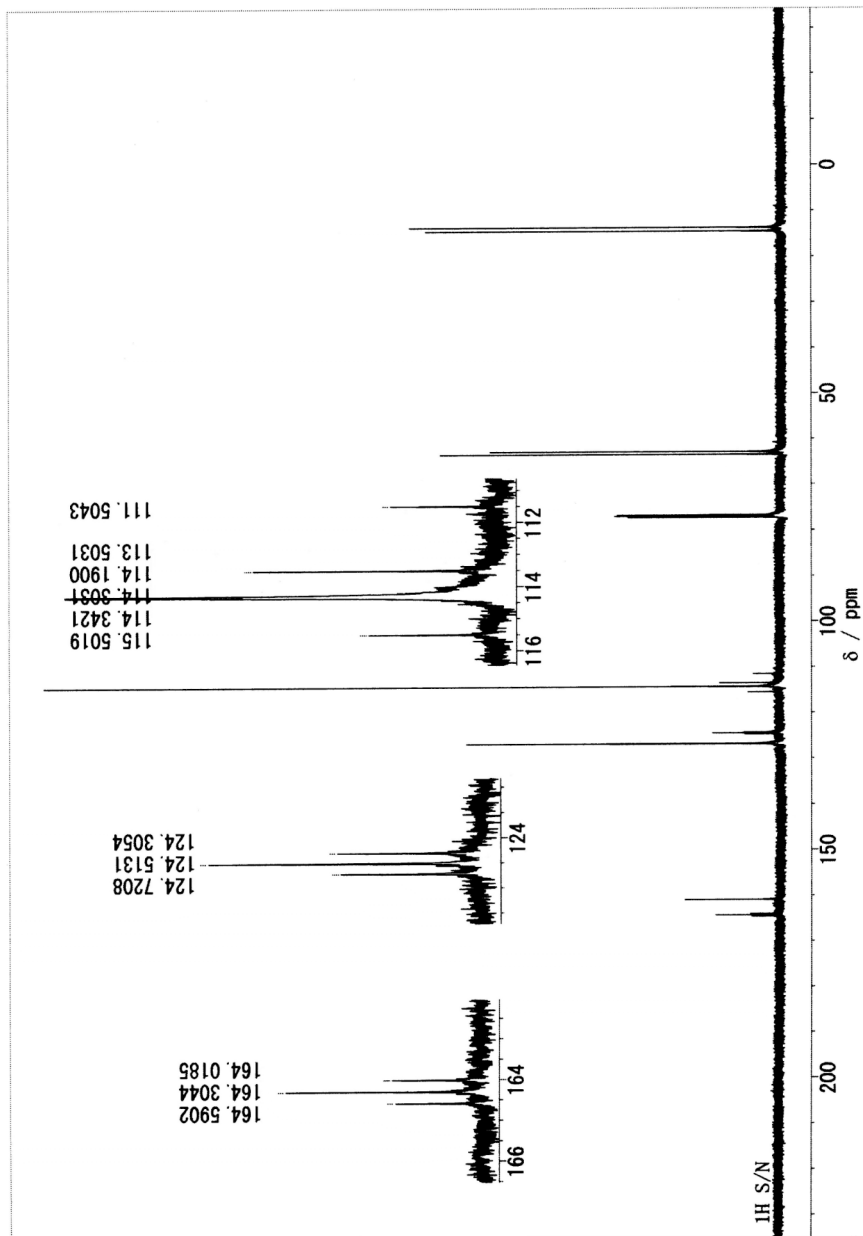
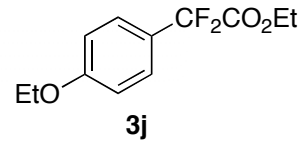


¹⁹F NMR Spectrum of Compound 3i

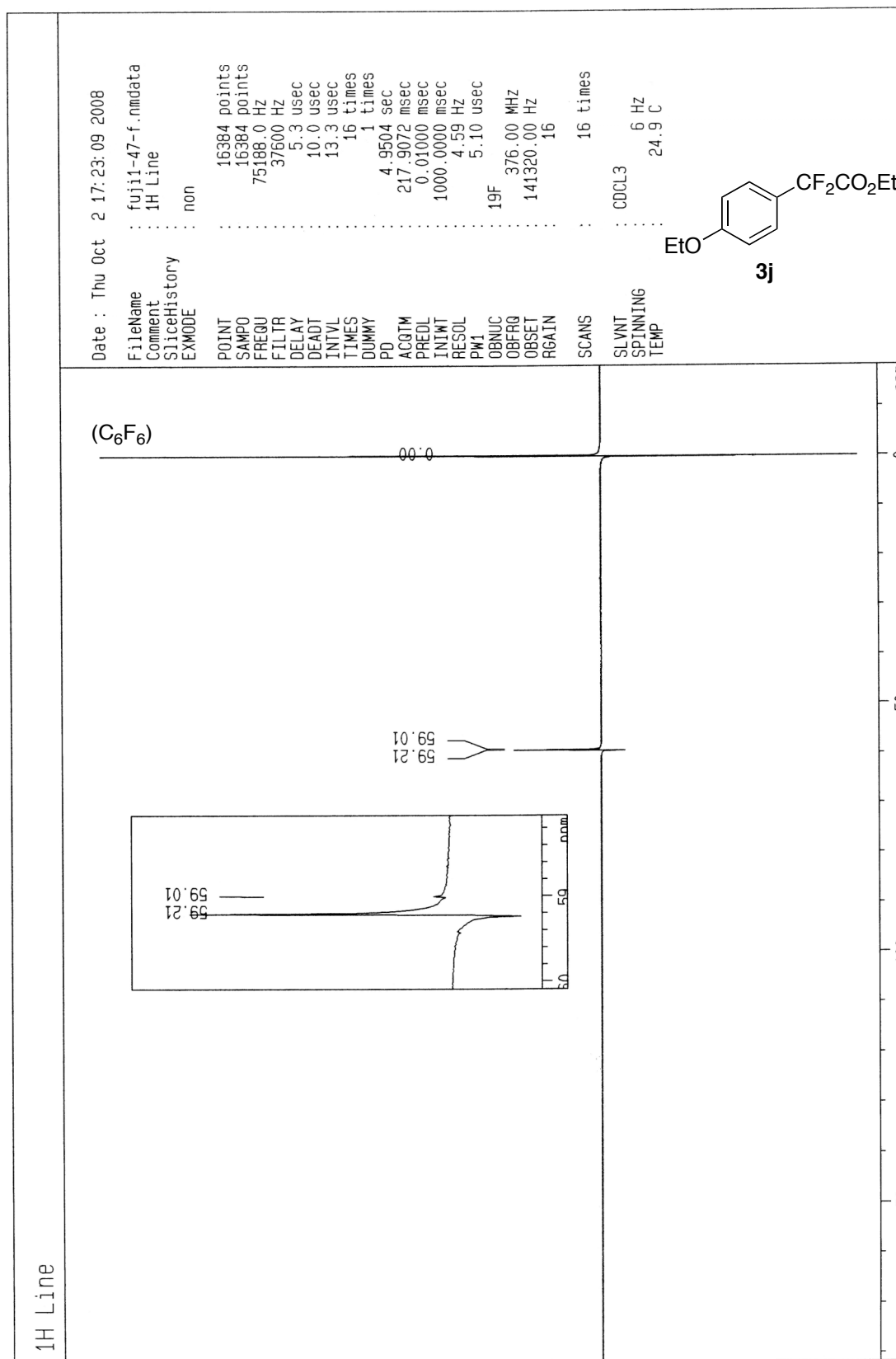


¹³C NMR Spectrum of Compound 3j

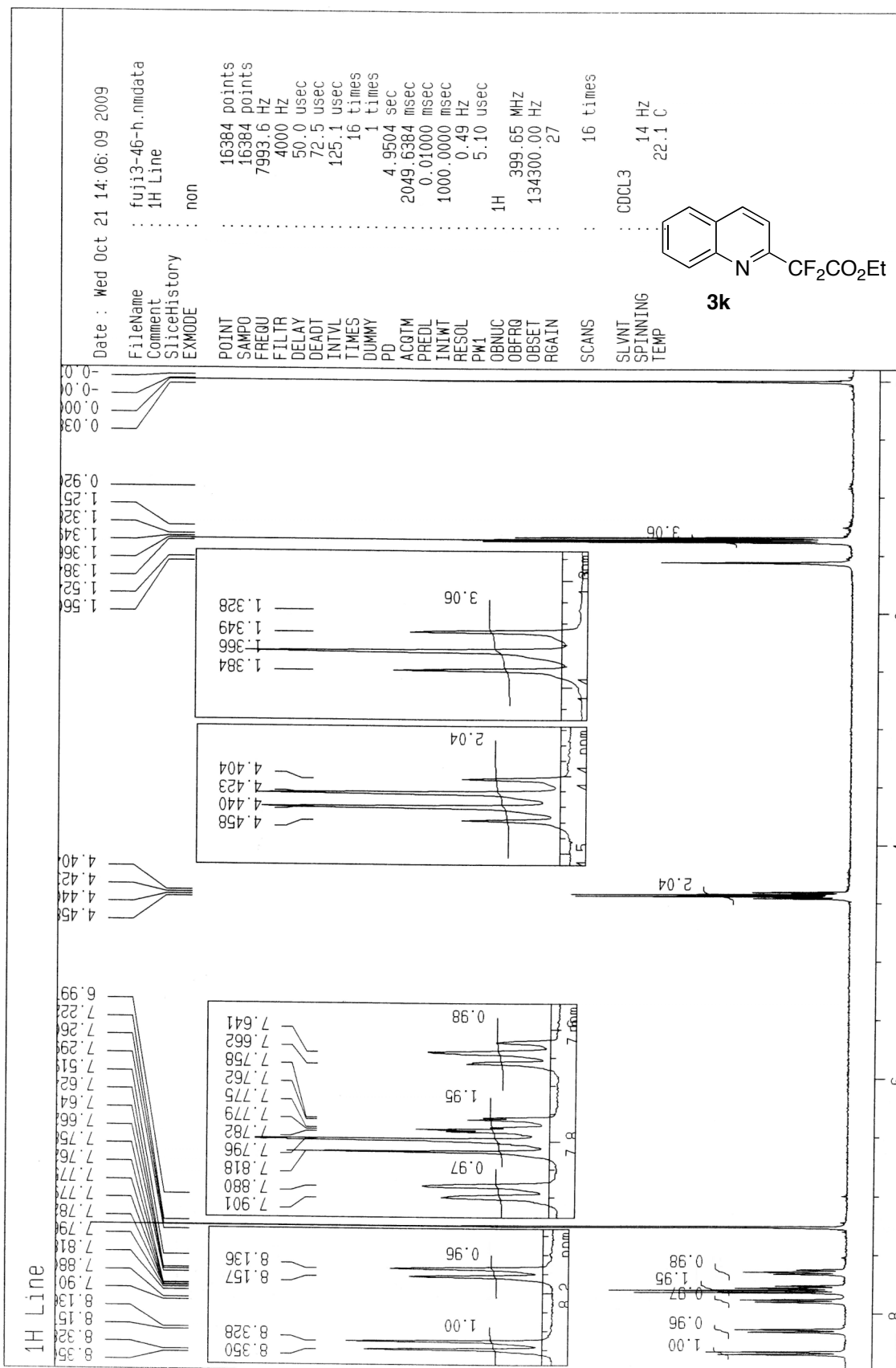
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Pulse 2.0333 s
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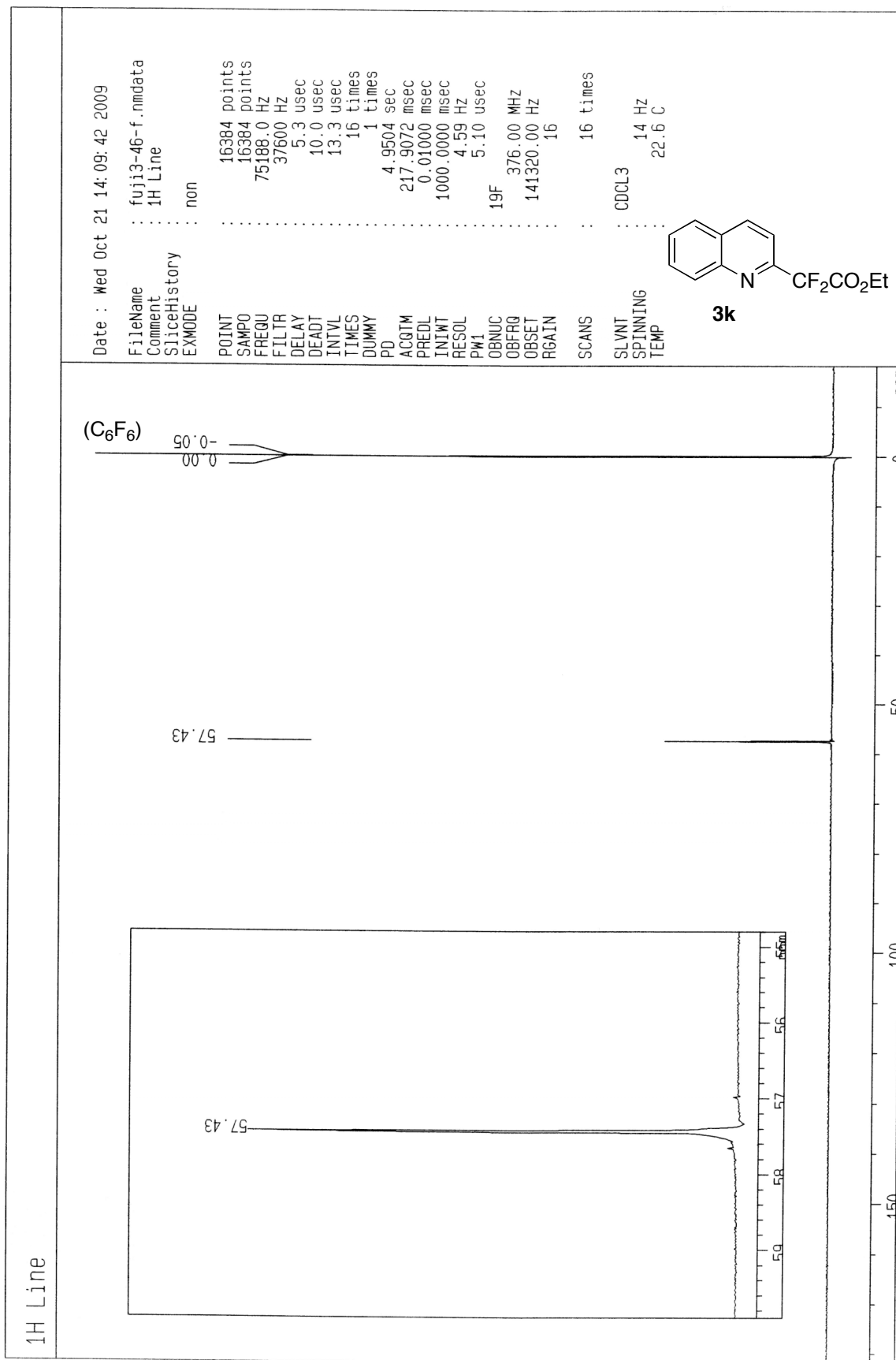
¹⁹F NMR Spectrum of Compound 3j



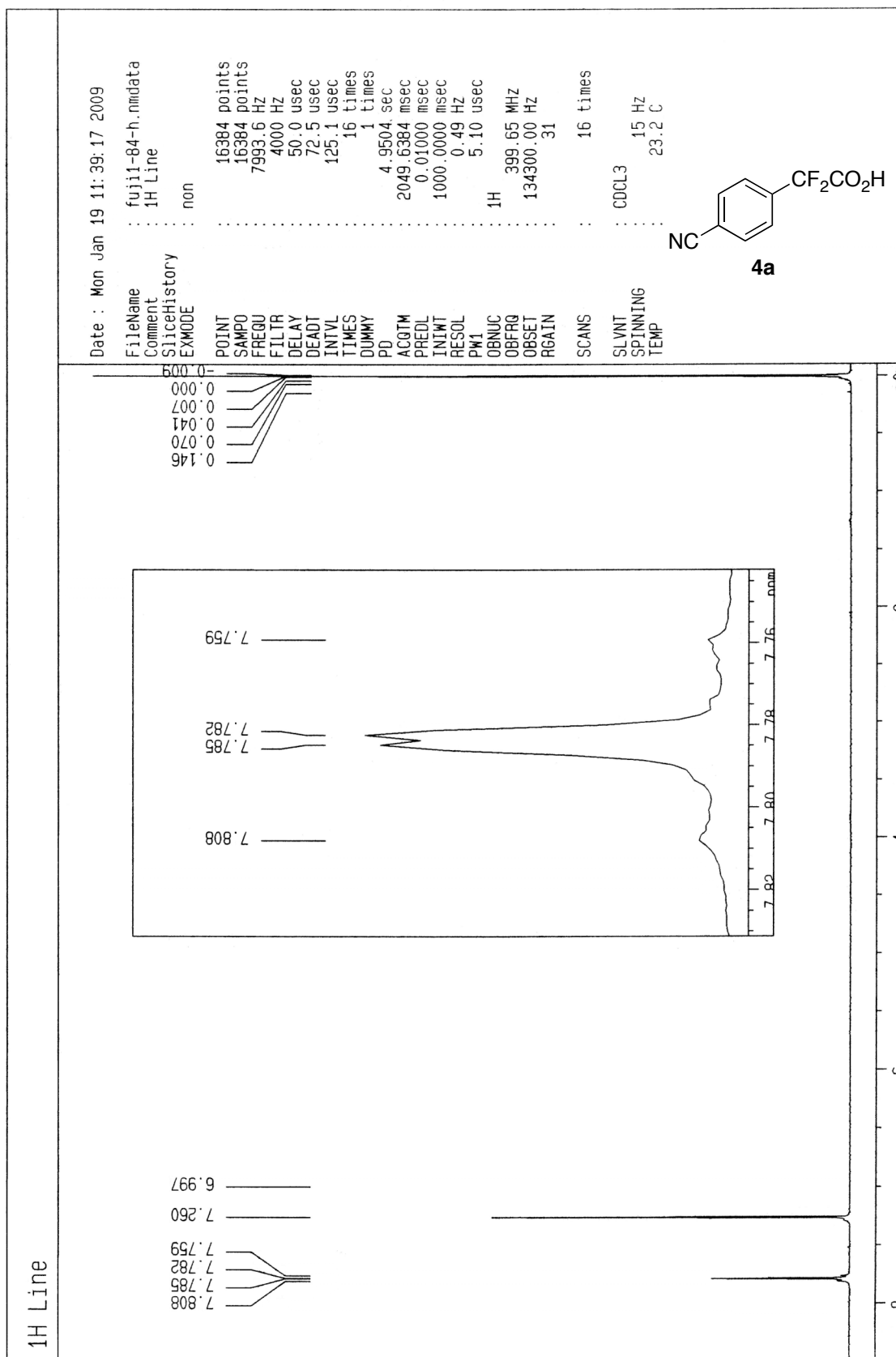
¹H NMR Spectrum of Compound 3k



¹⁹F NMR Spectrum of Compound 3k

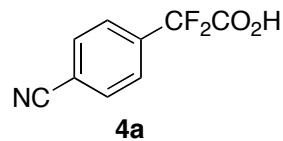
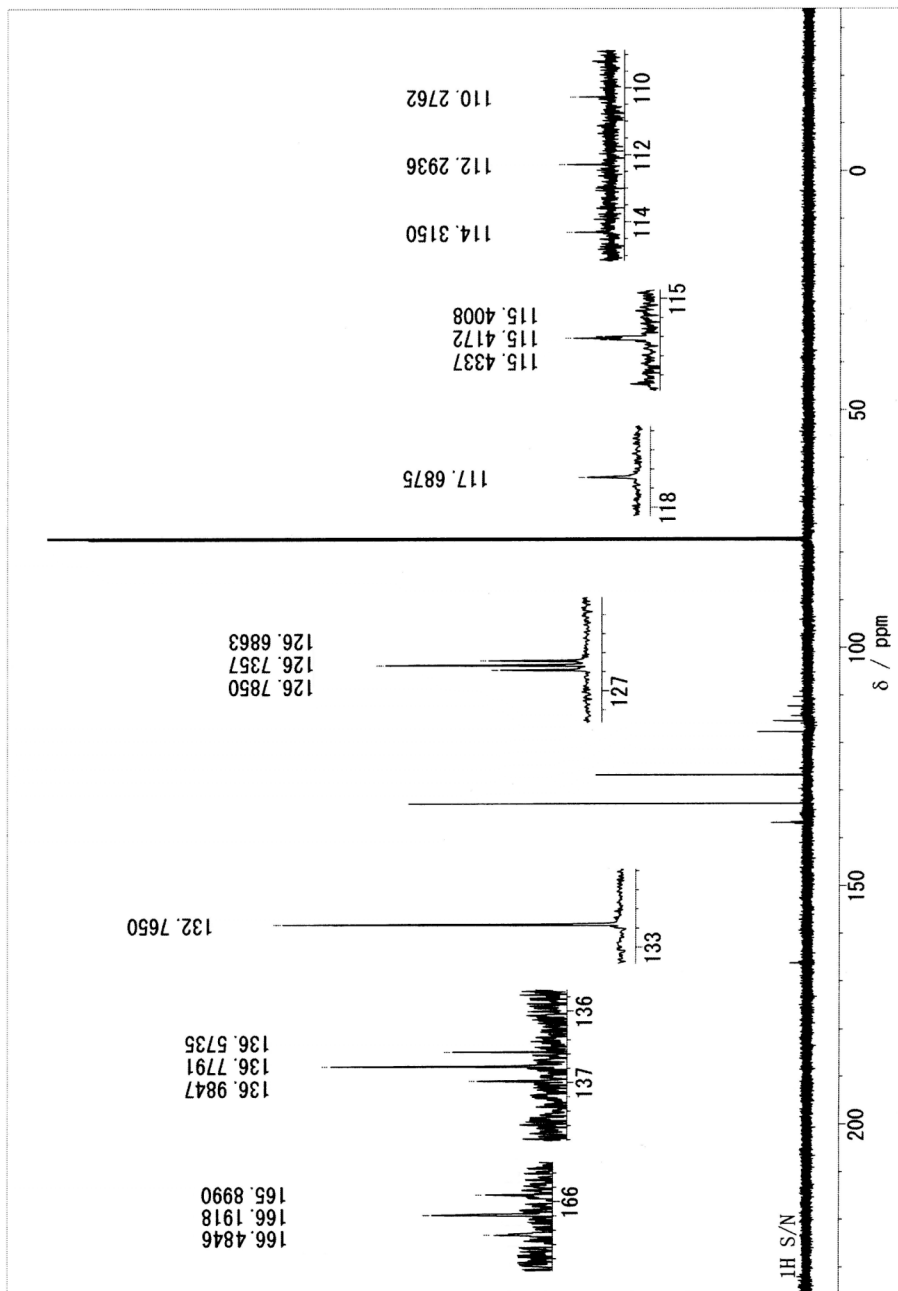


¹H NMR Spectrum of Compound 4a

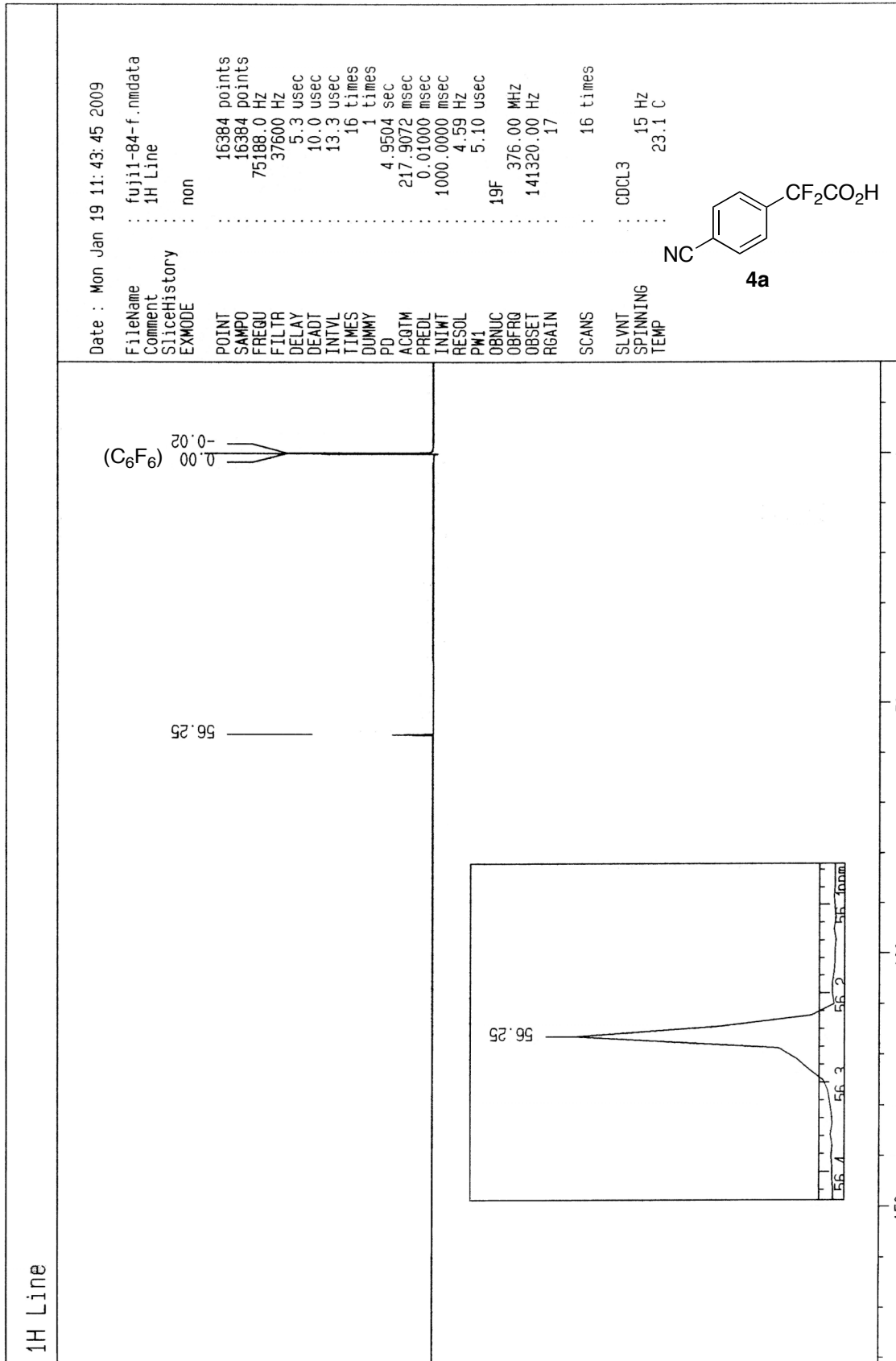


¹³C NMR Spectrum of Compound 4a

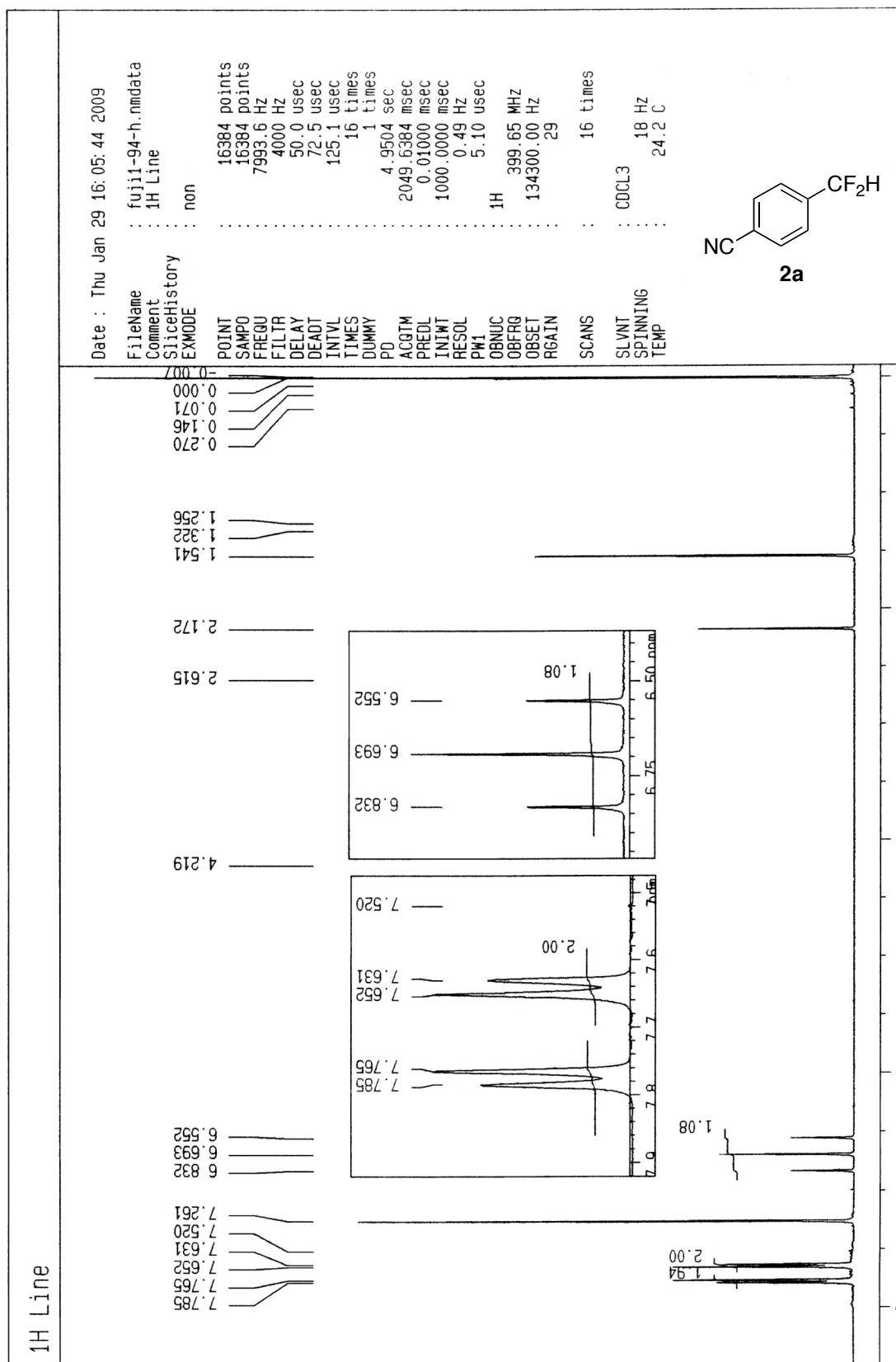
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 Pulse3 2.324 ms
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 P12 1.0 ms
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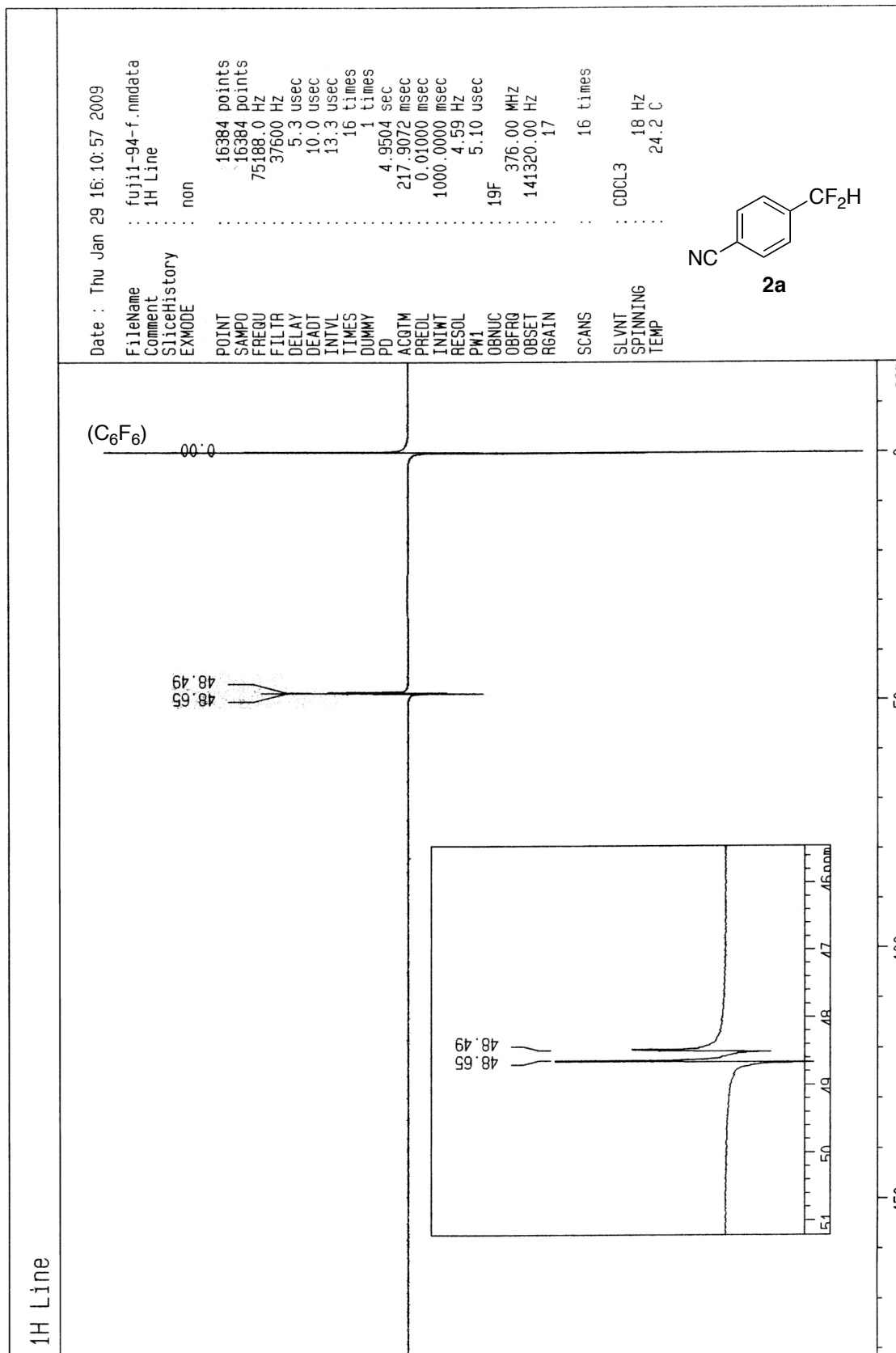
¹⁹F NMR Spectrum of Compound 4a



¹H NMR Spectrum of Compound 2a

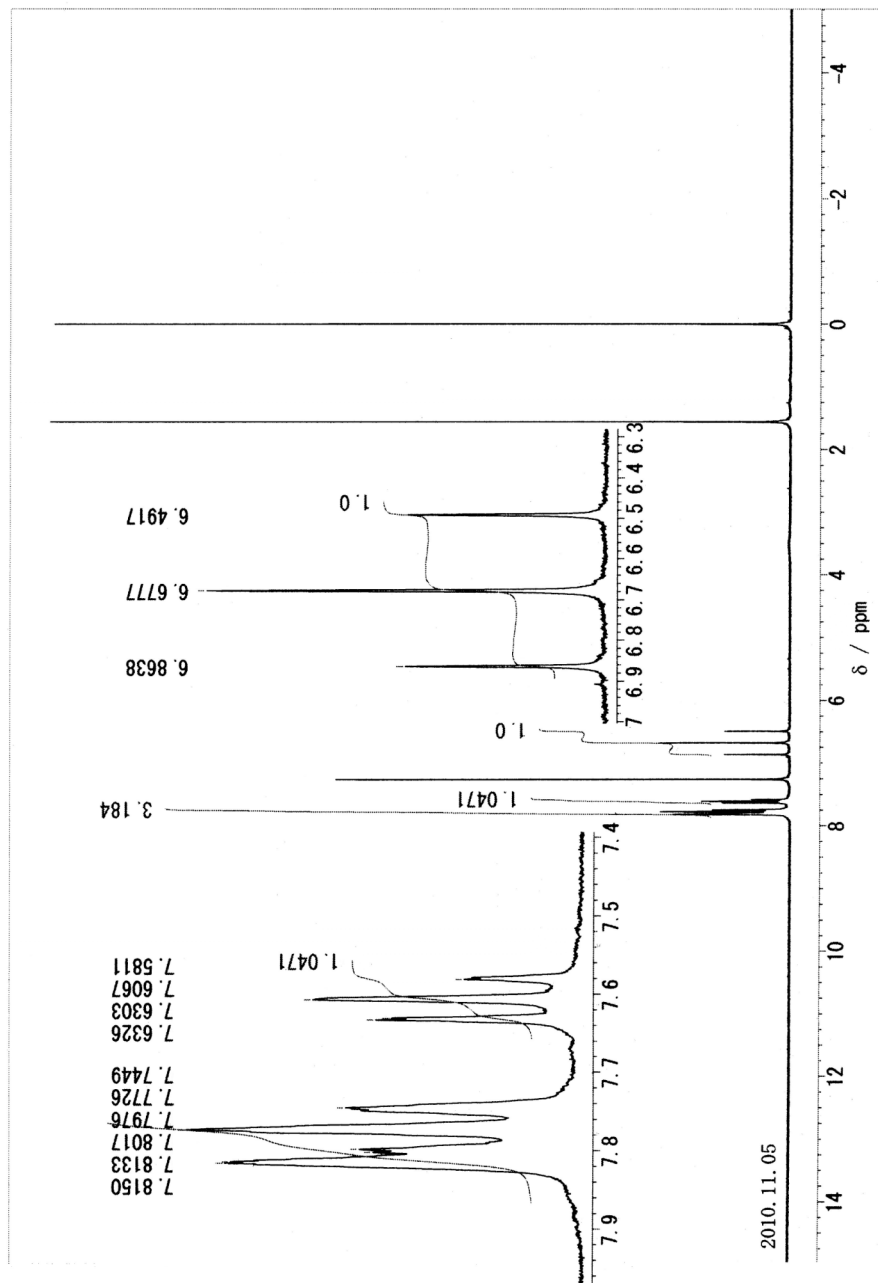
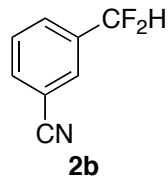


¹⁹F NMR Spectrum of Compound 2a



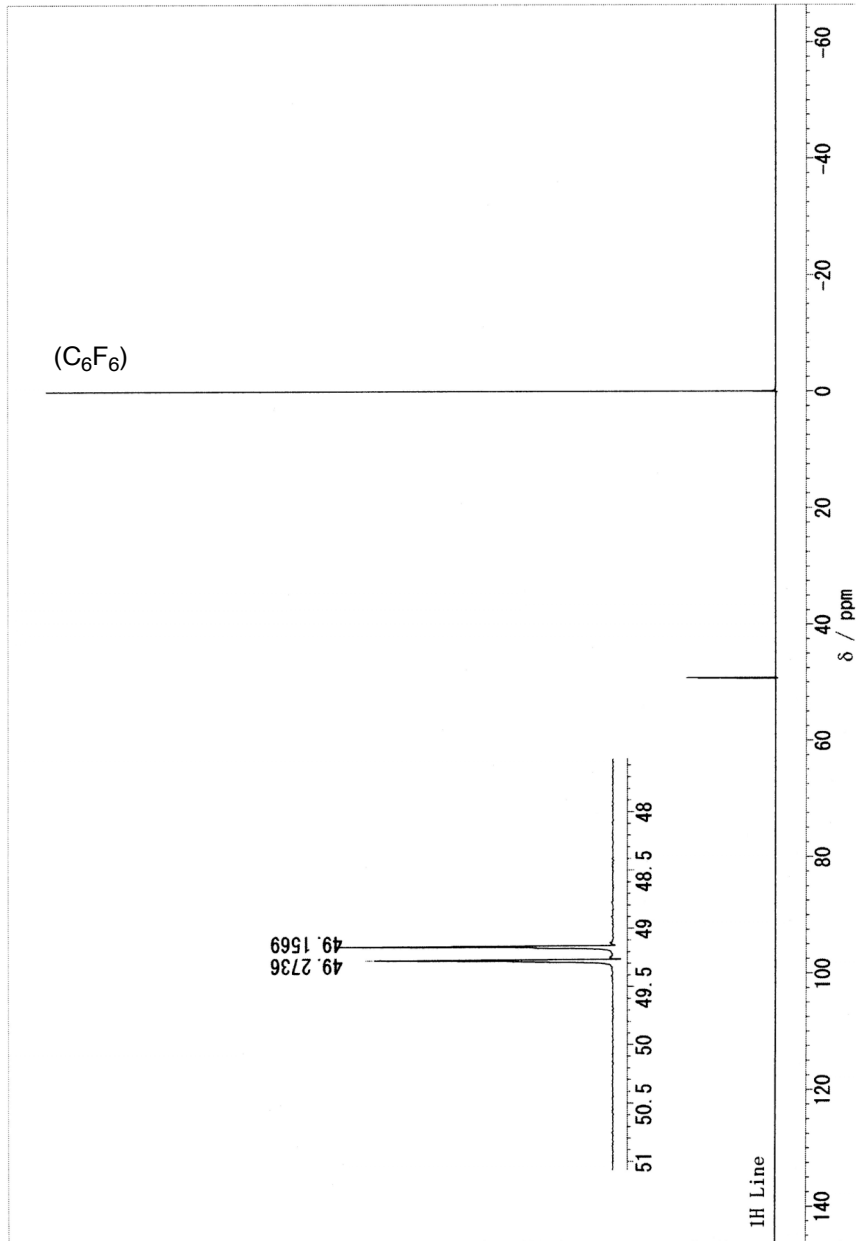
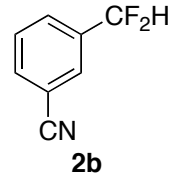
¹H NMR Spectrum of Compound **2b**

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 ObsNuc ¹H
 ObsFreq 300.4 MHz
 ObsSet 130.0 kHz
 ObsFine 1150.0 Hz
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 Pulse2 10.0 μs
 Pulse3 10.0 μs
 P11 1.0 ms
 P12 1.0 ms
 P13 1.0 ms
 Loop1 1
 Point 131072(ZeroFill
 :×4)
 Scan 16
 DummyScan 1
 Frequency(Span) 6002.4 Hz
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 PD 1.547 s
 RGain 24
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¹⁹F NMR Spectrum of Compound **2b**

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Pulse2 12.0 μs
Pulse3 10.0 μs
P11 600.0 ms
P12 0.05 ms
P13 1.0 ms
Loop1 0
Point 32768
Scan 16
DummyScan 2
Frequency (Span) 100000.0 Hz
AcqTime 0.3277 s
PD 5.6893 s
RGain 22
Broad. Factor 0.25 Hz
ExMode non
IrrNuc ¹H
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IrrSet 162.0 kHz
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¹H NMR Spectrum of Compound 2c

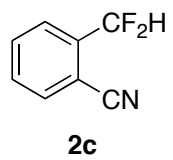
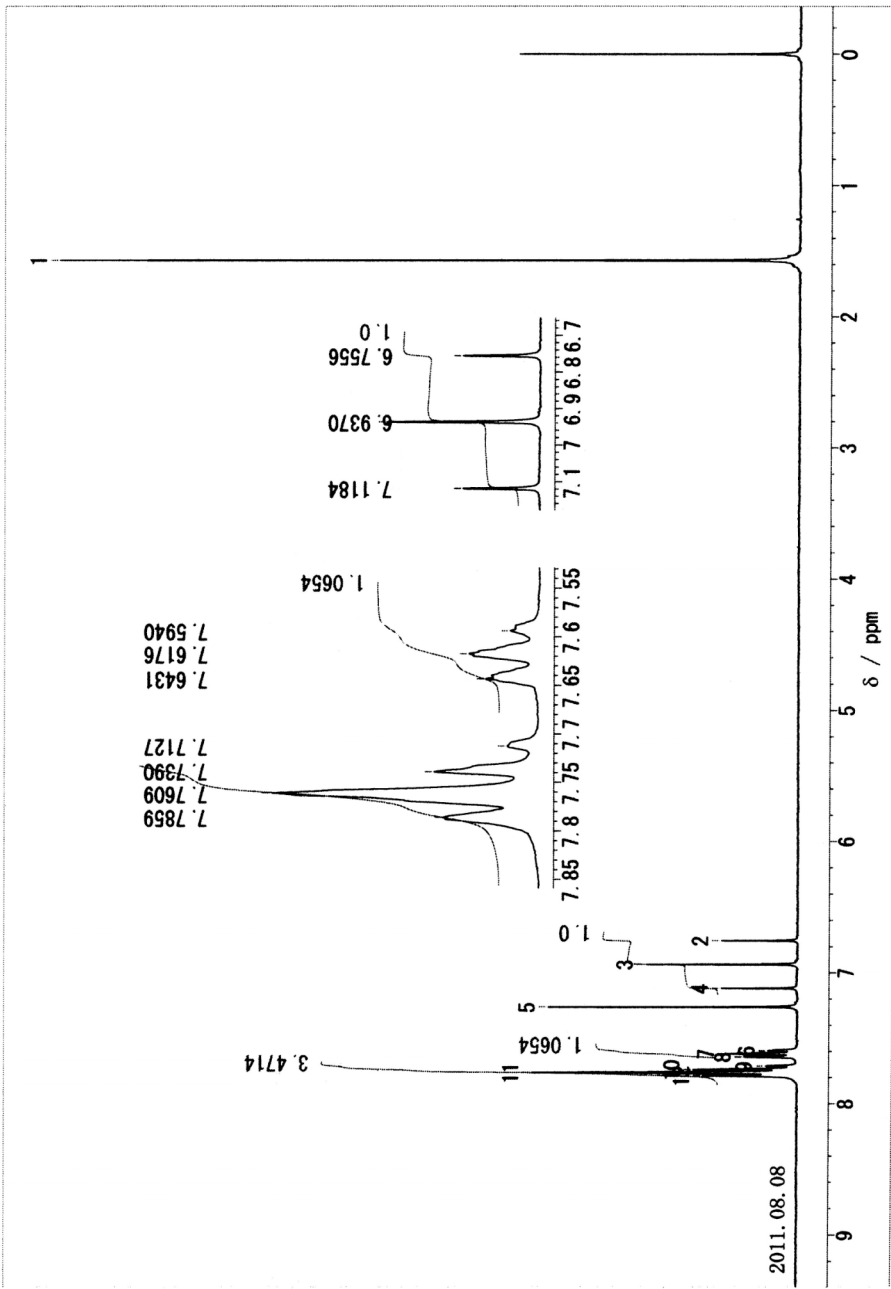
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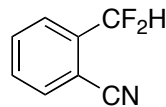
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PI1 1.0 ms
PI2 1.0 ms
PI3 1.0 ms
Loop1 1
Point 131072(Zerofill
: ×4)

Scan 16
DummyScan 1
Frequency 6009.6 Hz
AcqTime 5.4526 s
PD 1.547 s
RGain 21
Broad.Factor 0.0917 Hz
ExMode NON
IrrNuc ¹H
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IrrSet 130.0 kHz
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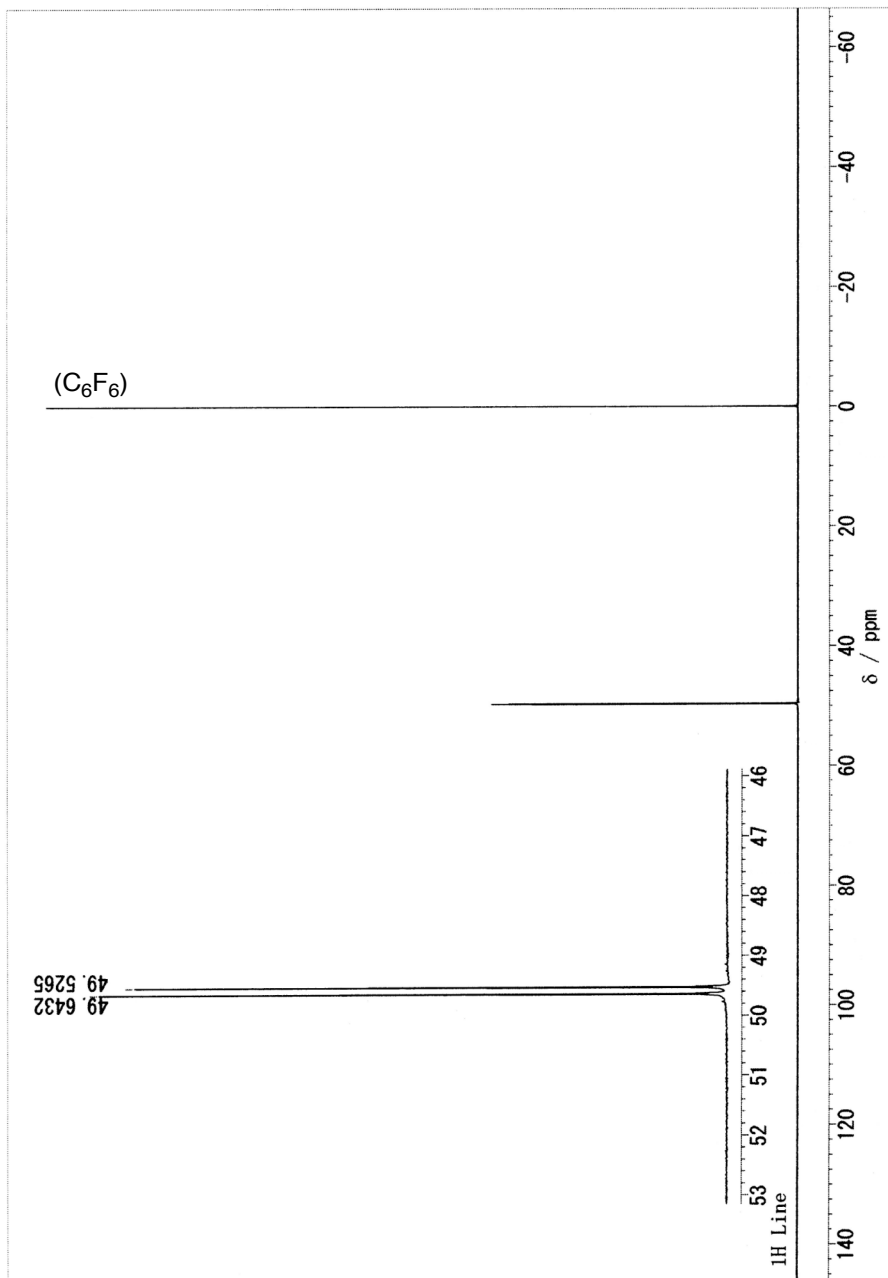


¹⁹F NMR Spectrum of Compound 2c

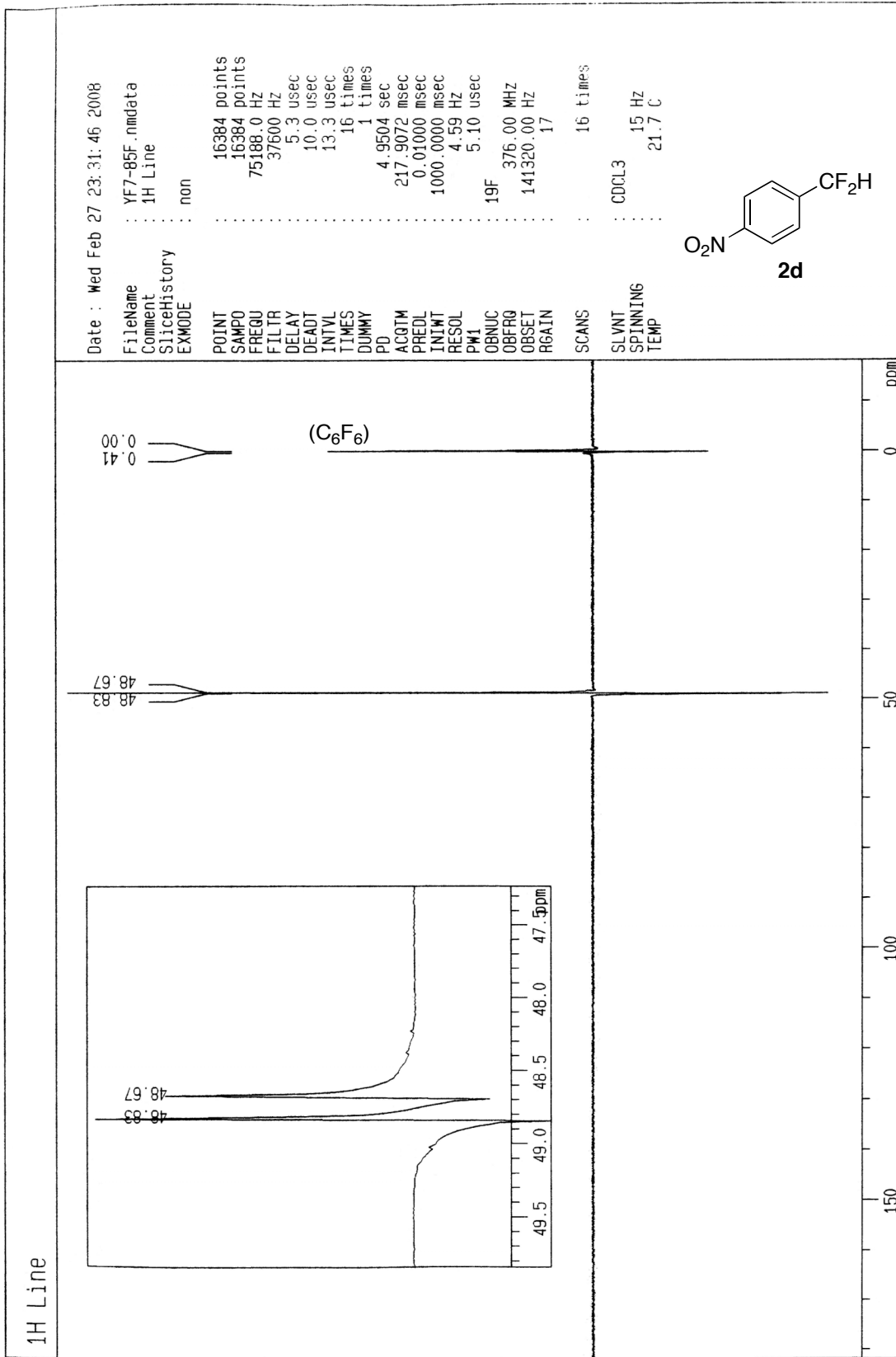
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 Pulse1 6.08 μs
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 Pulse3 10.0 μs
 P11 600.0 ms
 P12 0.05 ms
 P13 1.0 ms
 Loop1 0
 Point 32768
 Scan 16
 DummyScan 2
 Frequency (Span) 100000.0 Hz
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 PD 5.6893 s
 RGain 22
 Broad_Factor 0.25 Hz
 ExMode non
 IrrNuc 1H
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 Spinning 11.0 Hz
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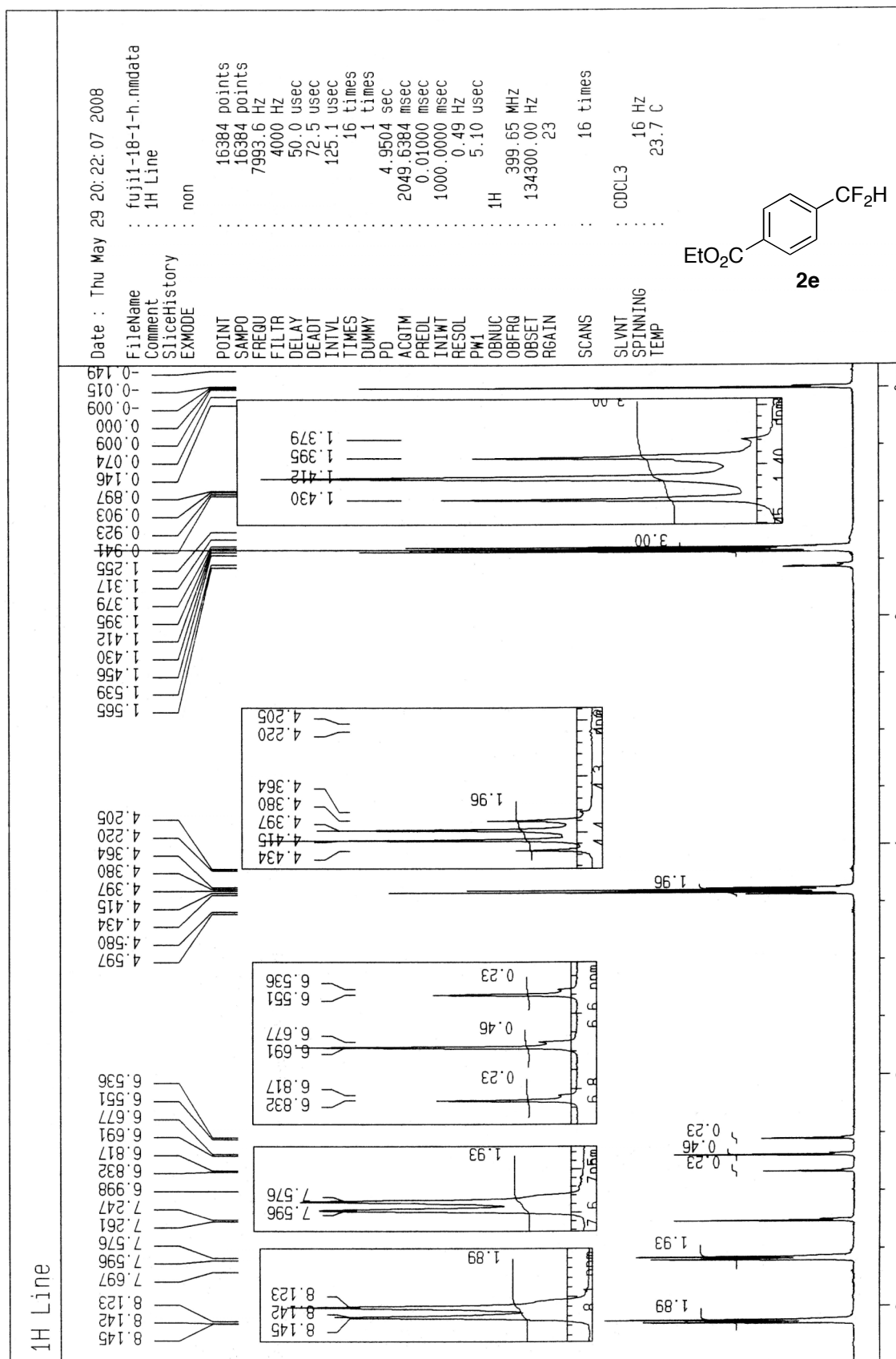
2c



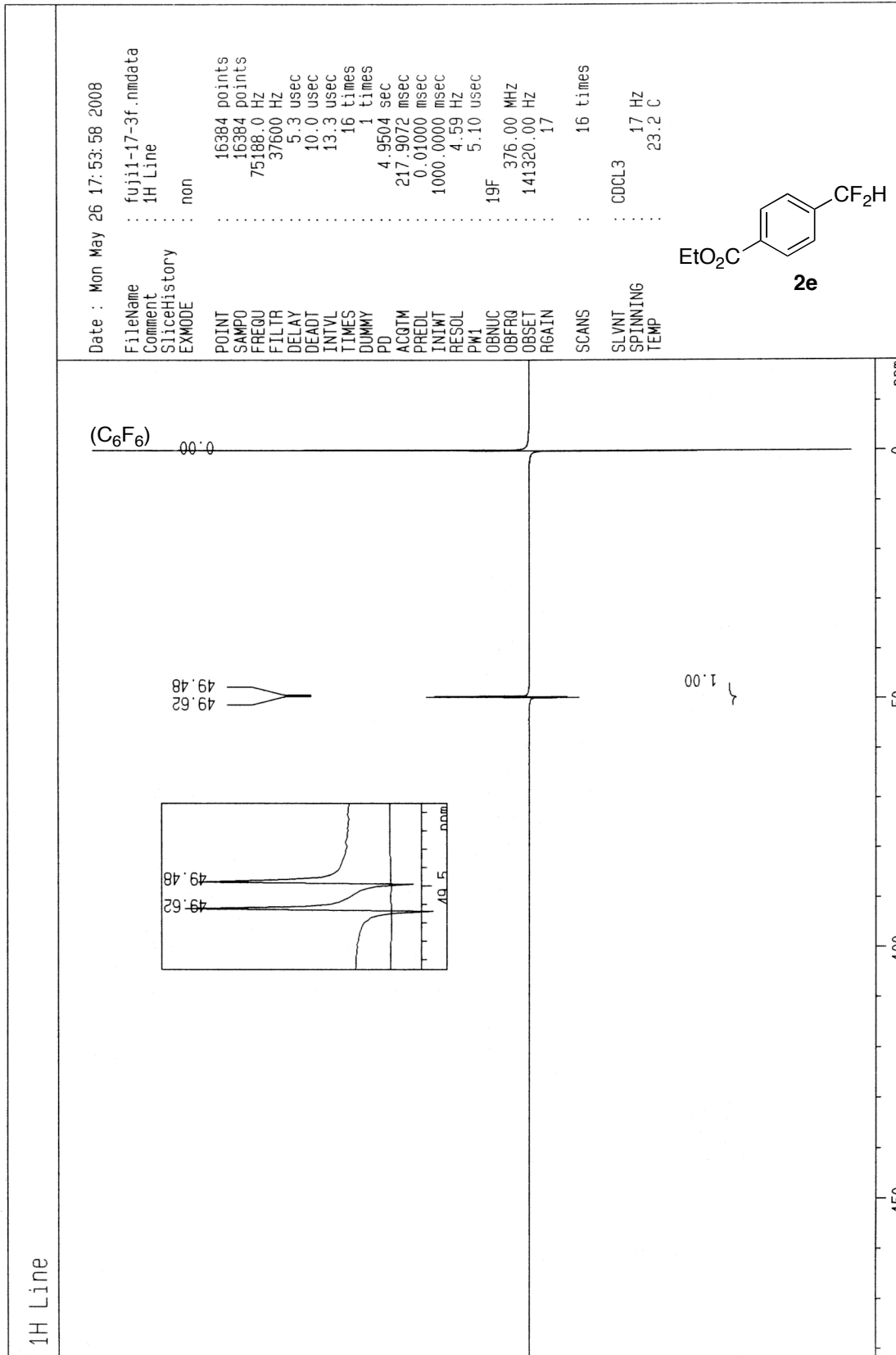
¹⁹F NMR Spectrum of Compound **2d**



¹H NMR Spectrum of Compound 2e

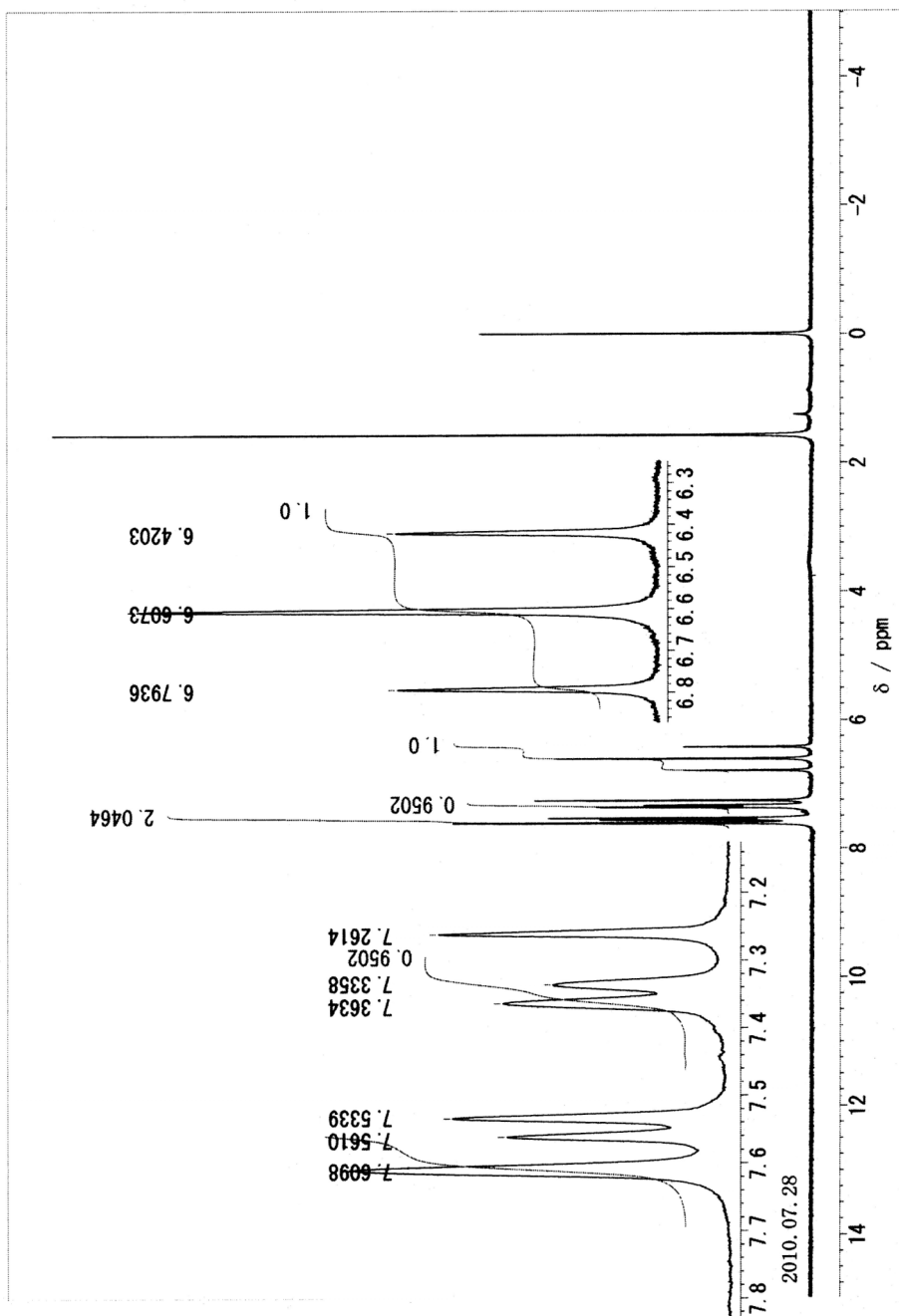
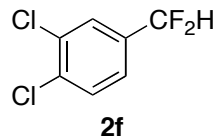


¹⁹F NMR Spectrum of Compound 2e



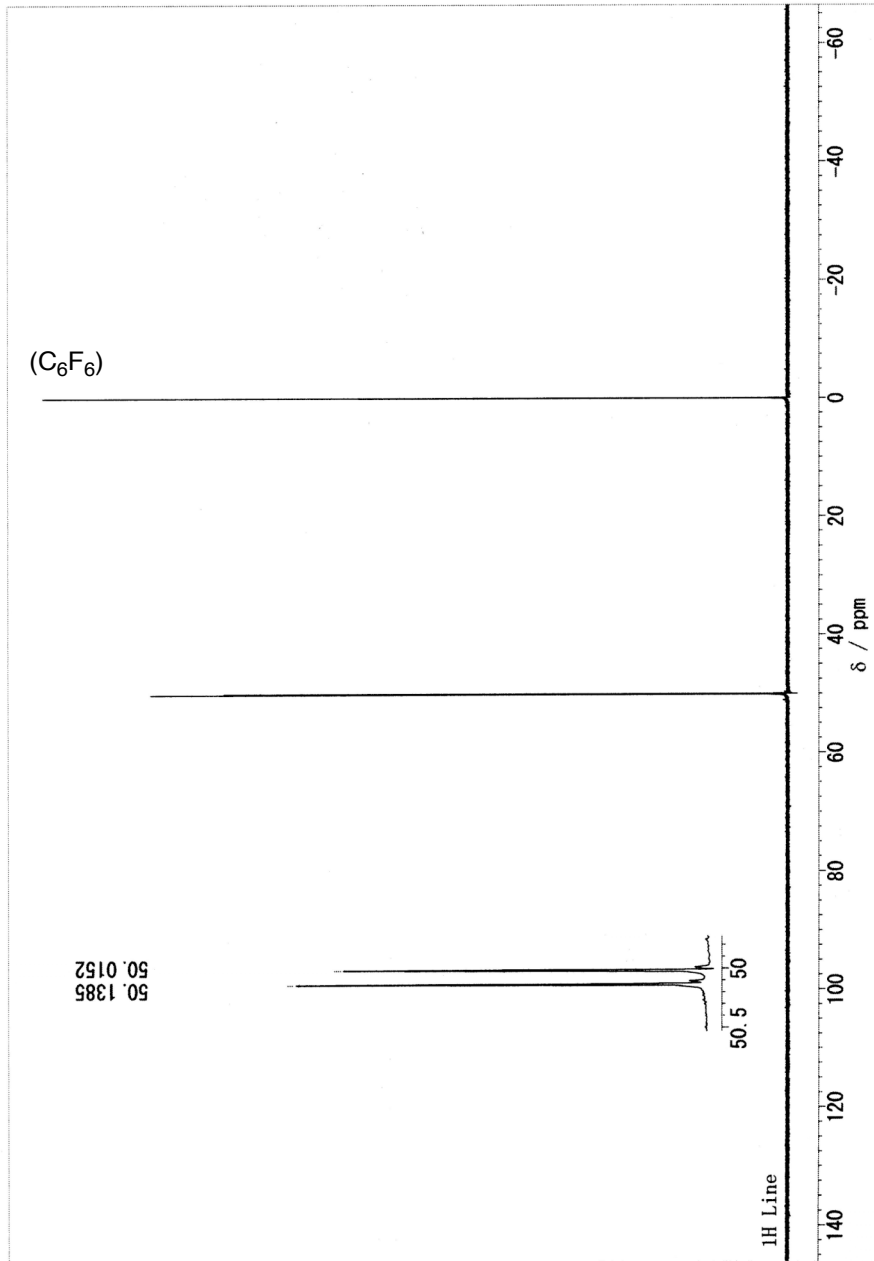
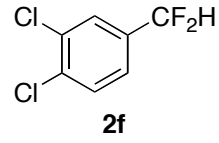
¹H NMR Spectrum of Compound 2f

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Pulse3 10.0 μs
PI1 1.0 ms
PI2 1.0 ms
PI3 1.0 ms
Loop1 1
Point 131072(ZeroFill
Scan 16
DummyScan 1
Frequency (Span) 6009.6 Hz
AcqTime 5.4526 s
PD 1.547 s
RGain 19
Broad.Factor 0.0917 Hz
ExMode NON
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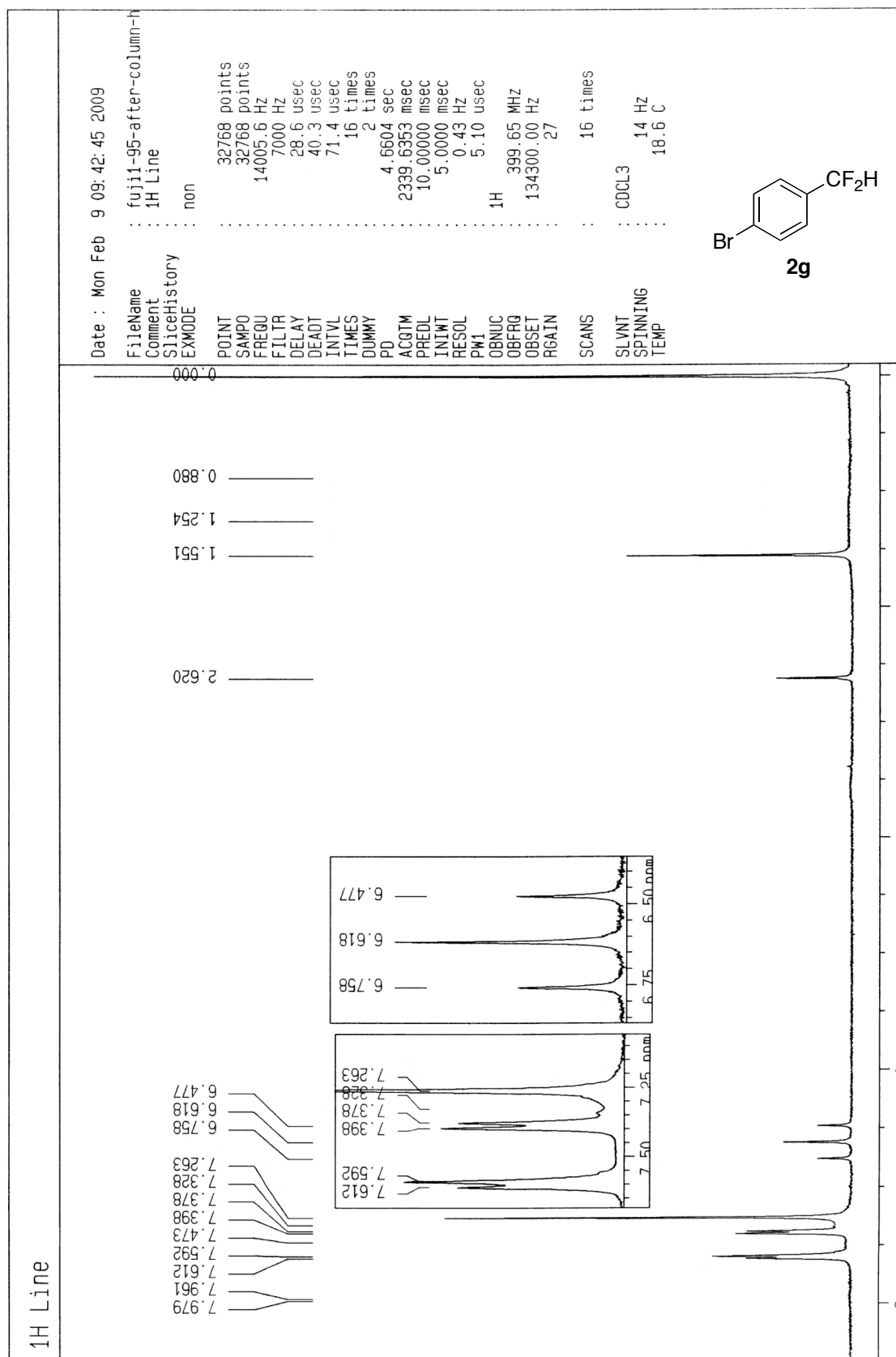


¹⁹F NMR Spectrum of Compound 2f

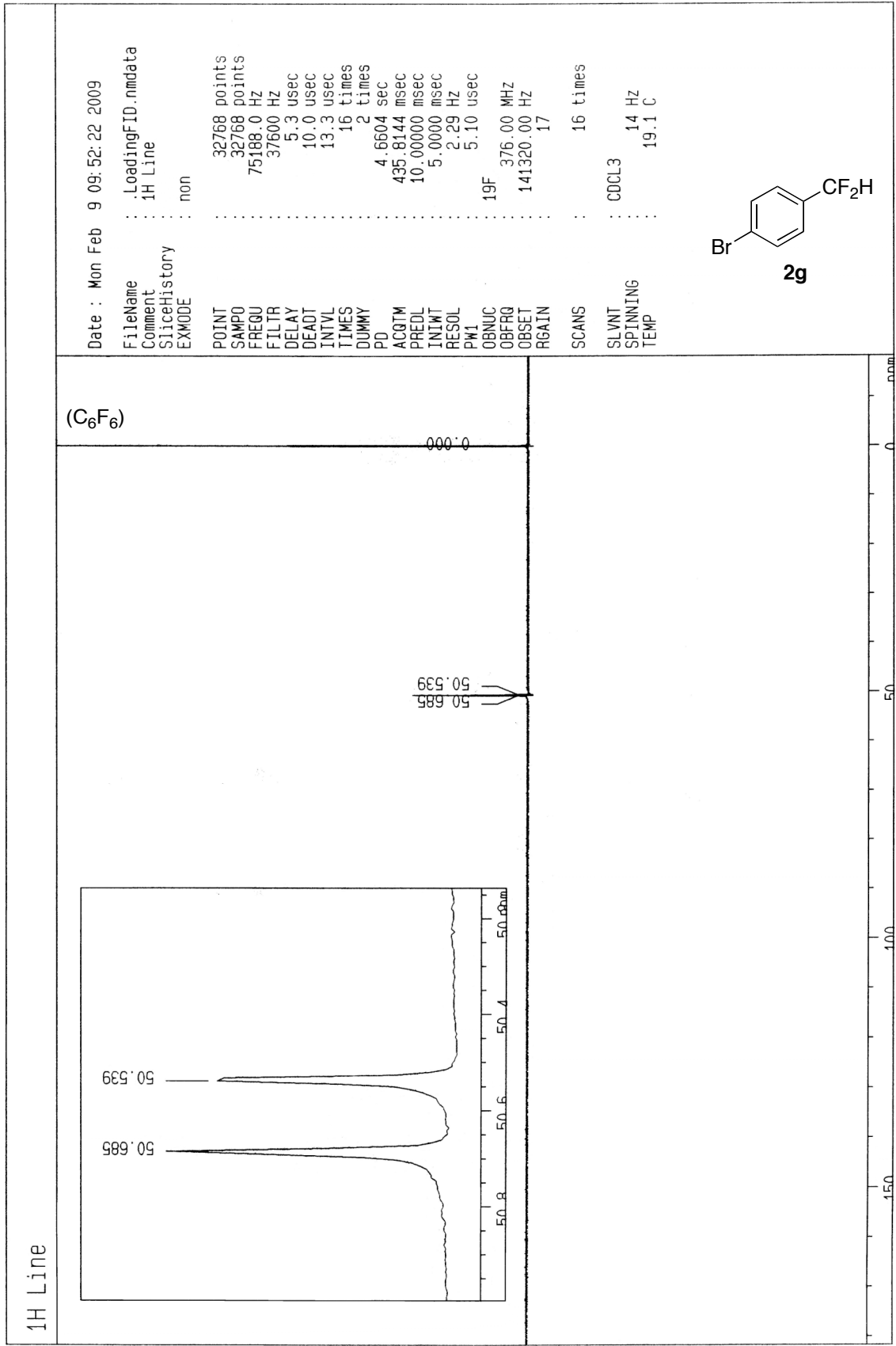
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P13 1.0 ms
Loop1 0
Point 32768
Scan 8
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Frequency (Span) 100000.0 Hz
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Broad. Factor 0.25 Hz
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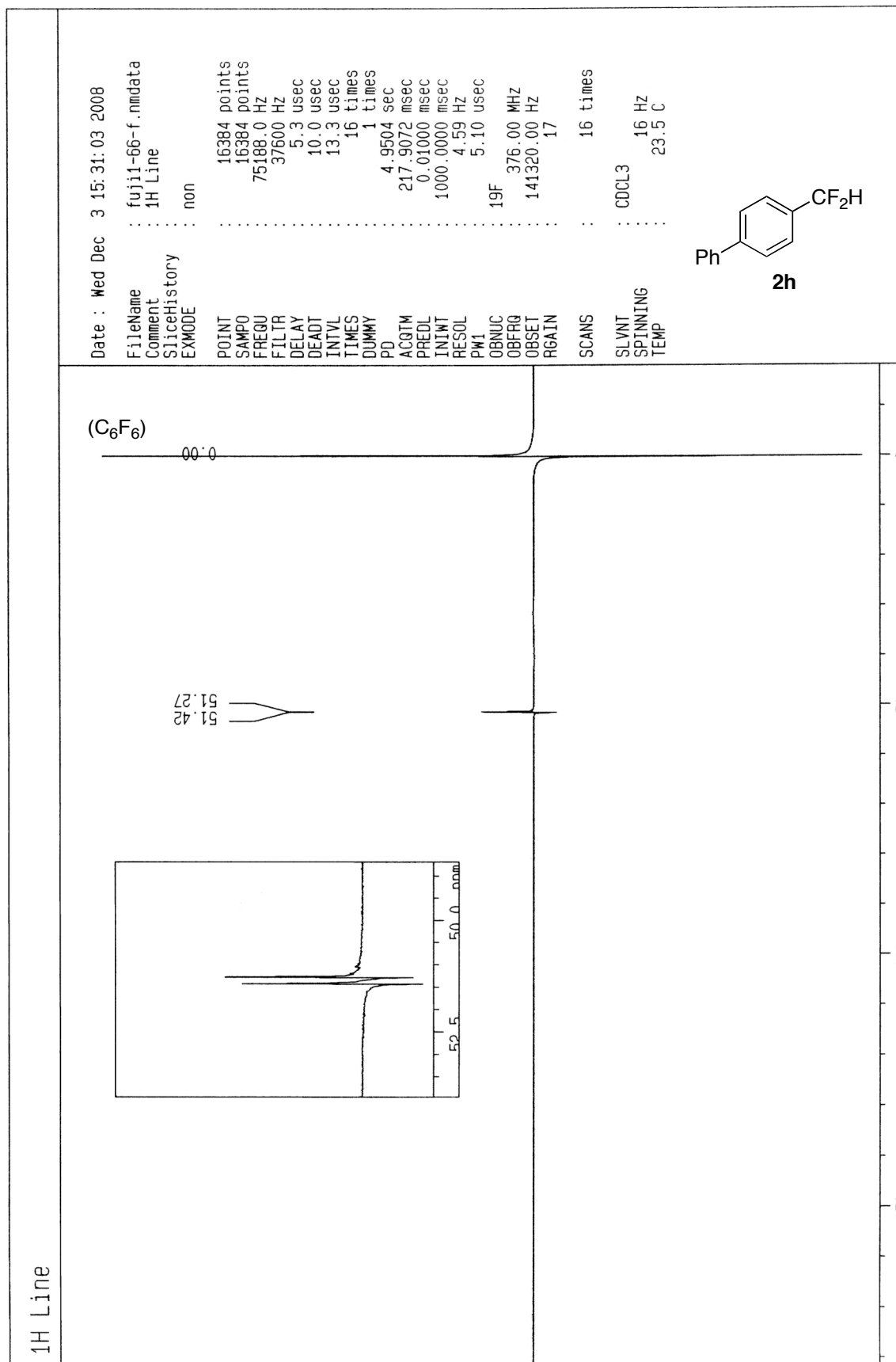
¹H NMR Spectrum of Compound **2g**



¹⁹F NMR Spectrum of Compound 2g



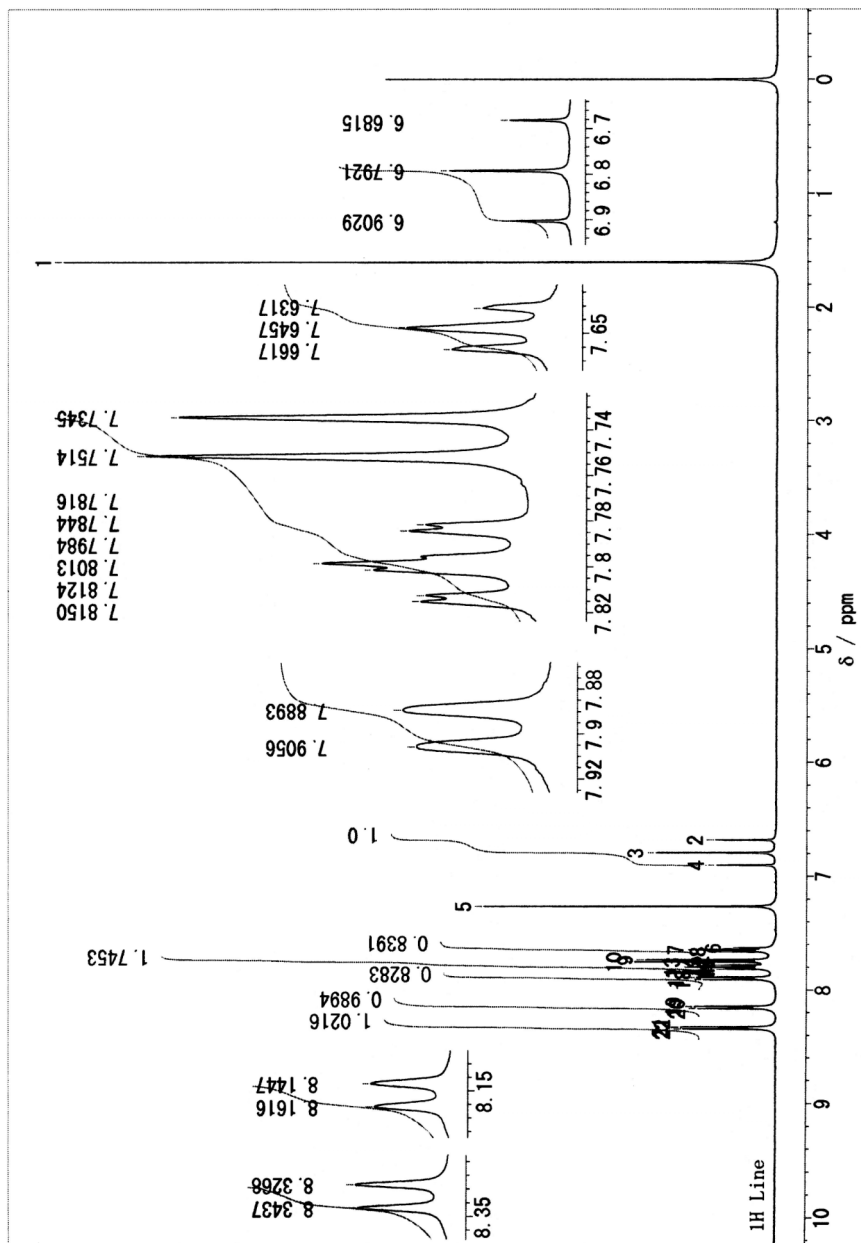
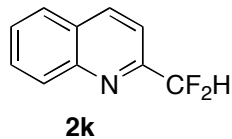
¹⁹F NMR Spectrum of Compound **2h**



¹H NMR Spectrum of Compound 2k

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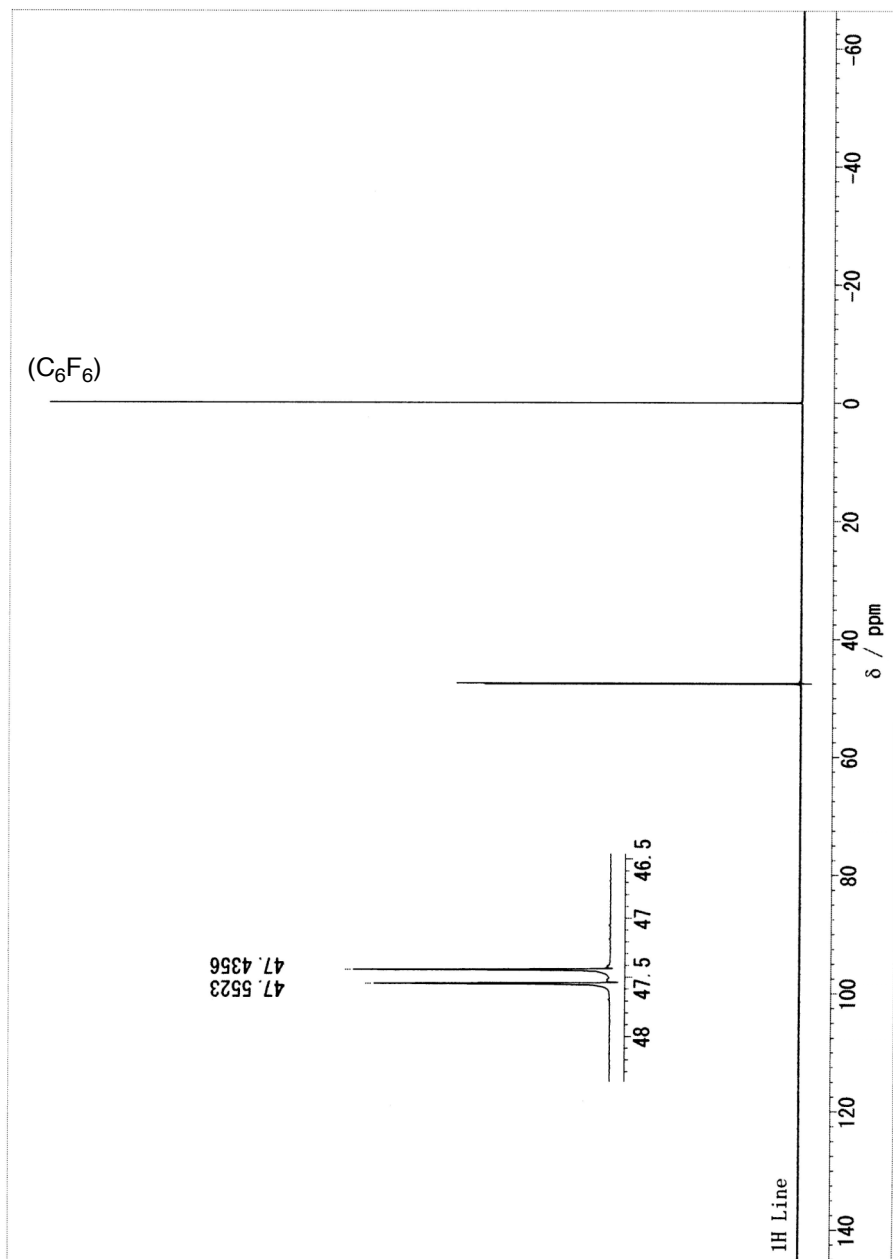
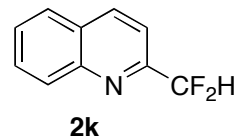
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 P13 1.0 ms
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¹⁹F NMR Spectrum of Compound 2k

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