Supporting information

Enantioselective Friedel-Crafts Reaction of β-Trifluoromethylated Acrylates with Pyrroles and its Application to Synthesis of Trifluorinated Heliotridane

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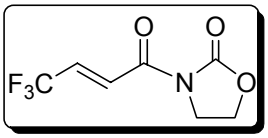
General Methods

All reactions were performed in oven-dried glassware under a nitrogen atmosphere, except where noted. Chemicals and solvents were purchased from commercial suppliers and used as received, excepting as follows. Dichloromethane, THF, ether, and toluene were dried by passing through an activated column. All reactions were monitored by TLC, or ^{19}F NMR. TLC analysis was performed by illumination with a UV lamp (254 nm),

staining with I_2, or PMA [phosphomolybdic acid (5 g) in ethanol (100 ml)] and heating. All flash chromatography was packed with silica-gel (60 N spherical neutral size 63-210 μm) as the stationary phase. ^{1}H NMR (600 MHz) spectra were recorded on a Bruker Avance 600 instrument in $CDCl_3$ (7.26), or CD_2Cl_2 (5.24), and chemical shifts were measured relative to residual solvent peak. Chemical shifts (δ) are expressed in ppm downfield from internal TMS. Data are reported as follows: Chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublet, dt = doublet of triplet, dq = doublet of quartet, m = multiplet, br = broad), coupling constant(s) and integration. ^{13}C NMR (150.9 MHz) spectra were recorded on a Bruker Avance 600 instrument. Chemical shifts are reported in parts per million (ppm) down field from TMS, using the middle resonance of $CDCl_3$ (77.23), or CD_2Cl_2 (53.73) as an internal standard. ^{19}F NMR (188 MHz) was recorded on a Varian Mercury 200 instrument using $CFCl_3$ (0) as an internal standard. HPLC analysis were performed on a JASCO U-2080 plus using 4.6 x 250 mm CHIRALPAK OD-H or CHIRALCEL AD-H column. Optical rotations were measured on a HORIBA SEPA-300. Infrared spectra were recorded on a JASCO FT/IR-200 spectrometer. Mass spectra were recorded on a SHIMADZU GCMS-QP5050A or SHIMADZU LCMS-2010EV. High resolution mass spectra (HRMS) (EI+) were obtained from the Mass Spectrometry Laboratory, Nagoya Institute of Technology, Nagoya.

Synthesis of β–CF_3 Acrylates (1)

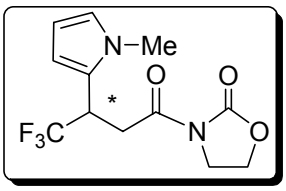


3-[(E)-4,4,4-Trifluorobut-2-enoyl]oxazolidin-2-one (1): The known compound **1** was synthesized according to the reported procedure.[1] ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.91 (dq, 1.8 Hz, 15.6 Hz, 1H), 6.93-6.86 (m, 1H), 4.50 (dt, 7.8 Hz, 0.6 Hz, 2H), 4.12 (dt, 7.8 Hz, 0.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 600 MHz) δ 163.0, 153.4, 132.3 (q, 34.7 Hz), 127.6 (q, 6.2 Hz), 122.5 (q, 270.3 Hz), 62.8, 42.9; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -65.3 (s, 3F).

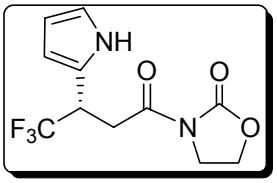
General Catalytic Procedure for the Friedel-Crafts Reactions

To an oven dried 10 mL test tube was added appropriate Lewis acid and 1.1 equiv of (*R, R*)-Ph–dbfox ligand. At N_2 atmosphere, dry CH_2Cl_2 was introduced, followed by stirring at RT for 1 h. 4Å MS and β–CF_3 acrylates were added at RT, then the solution of pyrroles in CH_2Cl_2 was injected by syringe at the reaction temperature. While some Friedel-Crafts products have the same polarity as the starting material on TLC, the reaction would be monitored by ^{19}F NMR. After the starting material disappeared, the residue was directly subjected to the silica-gel column chromatography to afford the title product.

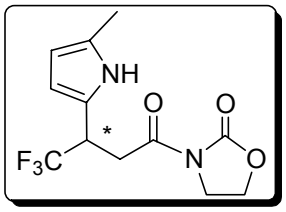
Characterization Data of the Friedel-Crafts Reaction Products



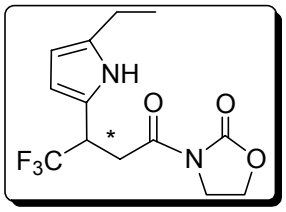
3-[4,4,4-Trifluoro-3-(1-methyl-1H-pyrrol-2-yl)-butyryl]-oxazolidin-2-one (*3a*): At N_2 atmosphere, to 20 mol % (0.010 mmol) of catalyst complex $Zn(NTf_2)_2$/(*R, R*)-Ph-dbfox prepared as described above in 0.2 mL CH_2Cl_2 was sequentially added 4 Å MS (15.0 mg), β-CF_3 acrylates **1a** (10.5 mg, 0.050 mmol), and the solution of N-methyl pyrrole (20.0 mg, 0.250 mmol) in 0.05 mL CH_2Cl_2. The mixture was stirred at -75 ℃ for 24 h, then passed through a plug of silica gel using 3:1 petroleum ether:ethyl acetate to afford the title compound (14.0 mg, 96%) as a clear oil. The enantiomeric purity was determined by HPLC analysis as 98% ee; [Chiralcel OD-H, *n*-hexane/*i*-PrOH = 70/30, flow rate 0.8 mL/min, λ = 232 nm, τ_{min} = 17.9 min, τ_{maj} = 20.6 min]; $[\alpha]_D^{25}$ = -91.6 (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.58 (d, 1.8 Hz, 1H), 6.17-6.15 (m, 1H), 6.08 (t, 3.0 Hz, 1H), 4.43-4.35 (m, 2H), 4.16-4.11 (m, 1H), 3.98-3.89 (m, 2H), 3.81 (dd, 10.8 Hz, 18.0 Hz, 1H), 3.69 (s, 3H), 3.38 (dd, 3.0 Hz, 18.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 169.7, 153.3, 126.0 (q, 279.1 Hz), 125.5, 123.1, 107.9, 107.1, 62.2, 42.4, 36.6 (q, 29.4 Hz), 35.7, 33.9; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.7 (s, 3F); IR (neat) 1781.9, 1701.9, 1489.7, 1397.2, 1338.3, 1315.2, 1267.9, 1225.5, 1159.9, 1103.1, 1039.4, 965.2, 885.1, 760.8, 724.1, 679.8, 664.3, 619.0 cm^{-1}; MS (ESI, *m/z*) 313.050 ($M+Na^+$); HRMS calcd. for $C_{12}H_{13}F_3N_2O_3^+$ 290.0878 found 290.0892.



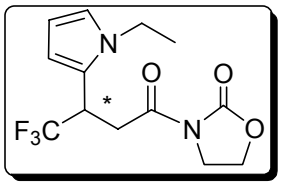
3-[4,4,4-Trifluoro-3-(1H-pyrrol-2-yl)-butyryl]-oxazolidin-2-one (*3b*): At N_2 atmosphere, to 20 mol % (0.010 mmol) of catalyst complex $Zn(NTf_2)_2$/(*R, R*)-Ph–dbfox prepared as described above in 0.2 mL CH_2Cl_2 was sequentially added 4 Å MS (15.0 mg), β-CF_3 acrylates **1a** (10.5 mg, 0.050 mmol), and the solution of pyrrole (17.0 mg, 0.250 mmol) in 0.05 mL CH_2Cl_2. The mixture was stirred at -75 ℃ for 24 h, then passed through a plug of silica gel using 2:1 petroleum ether:ethyl acetate to afford the title compound (13.40 mg, 97%) as a white solid. The enantiomeric purity was determined by HPLC analysis as 99% ee; [Chiralcel OD-H, *n*-hexane/*i*-PrOH = 70/30, flow rate 0.5 mL/min, λ = 232 nm, τ_{maj} = 24.4 min, τ_{min} = 27.1 min]; $[\alpha]_D^{25}$ = +77.8 (*c* 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.46 (br s, 1H), 6.74-6.73 (m, 1H), 6.17-6.14 (m, 2H), 4.42-4.35 (m, 2H), 4.19-4.12 (m, 1H), 3.99-3.89 (m, 2H), 3.72 (dd, 10.2 Hz, 17.4 Hz, 1H), 3.38 (dd, 4.2 Hz, 17.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 170.2, 153.9, 126.5 (q, 279.3 Hz), 124.2, 118.9, 109.1, 108.5, 62.7, 42.9, 39.5 (q, 29.7 Hz), 35.5; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.2 (d, 9.2 Hz, 3F); IR (KBr) 3427.9, 1796.4, 1782.9, 1687.4, 1481.1, 1410.7, 1321.9, 1276.7, 1227.5, 1196.6, 1178.3, 1127.2, 1102.1, 1037.5, 754.0, 731.8, 677.9 cm^{-1}; mp = 150-151 ºC; MS (ESI, *m/z*) 299.050 ($M+Na^+$); HRMS calcd. for $C_{11}H_{11}F_3N_2O_3^+$ 276.0722 found 276.0742.



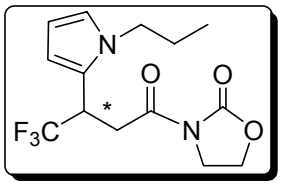
3-[4,4,4-Trifluoro-3-(5-methyl-1H-pyrrol-2-yl)-butyryl]-oxazolidin-2-one (*3c*): At N_2 atmosphere, to 20 mol % (0.010 mmol) of catalyst complex $Zn(NTf_2)_2$/(*R, R*)-Ph-dbfox prepared as described above in 0.2 mL CH_2Cl_2 was sequentially added 4 Å MS (15.0 mg), β-CF_3 acrylates **1a** (10.5 mg, 0.050 mmol), and the solution of pyrrole (20.0 mg, 0.250 mmol) in 0.05 mL CH_2Cl_2. The mixture was stirred at -75 ℃ for 24 h, then passed through a plug of silica gel using 2:1 petroleum ether:ethyl acetate to afford the title compound (14.0 mg, 96%) as a white solid. The enantiomeric purity was determined by HPLC analysis as 97% ee; [Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 232 nm, τ_{maj} = 28.3 min, τ_{min} = 38.0 min]; $[\alpha]_D^{25}$ = -18.1 (*c* 0.33, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.08 (br s, 1H), 6.02-6.01 (m, 1H), 5.81-5.78 (m, 1H), 4.43-4.35 (m, 2H), 4.20-4.10 (m, 1H), 3.97-3.92 (m, 2H), 3.72 (dd, 10.2 Hz, 18.0 Hz, 1H), 3.38 (dd, 4.2 Hz, 18.0 Hz, 1H), 2.23 (s, 3H); ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 169.9, 153.5, 128.5, 126.1 (q, 279.6 Hz), 122.2, 108.4, 106.3, 62.3, 42.5, 39.2 (q, 29.1 Hz), 35.0, 12.9 (d, 3.3 Hz); ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.3 (d, 7.9 Hz, 3F); IR (KBr) 3451.9, 1782.5, 1690.3, 1401.0, 1362.5, 1342.2, 1318.1, 1277.6, 1242.9, 1164.8, 1122.4, 1102.1, 1039.4, 774.3, 754.9, 708.7, 679.8 cm^{-1}; mp = 121-122 ºC; MS (ESI, *m/z*) 313.100 ($M+Na^+$); HRMS calcd. for $C_{12}H_{13}F_3N_2O_3^+$ 290.0878 found 290.0892.



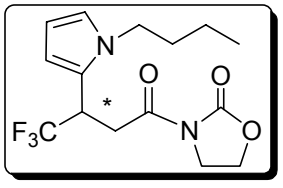
3-[4,4,4-Trifluoro-3-(5-ethyl-1H-pyrrol-2-yl)-butyryl]-oxazolidin-2-one: (*3d*) At N_2 atmosphere, to 20 mol % (0.010 mmol) of catalyst complex $Zn(NTf_2)_2$/(*R, R*)-Ph-dbfox prepared as described above in 0.2 mL CH_2Cl_2 was sequentially added 4 Å MS (15.0 mg), β-CF_3 acrylates **1a** (10.5 mg, 0.050 mmol), and the solution of pyrrole (24.0 mg, 0.250 mmol) in 0.05 mL CH_2Cl_2. The mixture was stirred at -75 ℃ for 24 h, then passed through a plug of silica gel using 2:1 petroleum ether:ethyl acetate to afford the title compound (14.9 mg, 98%) as a white solid. The enantiomeric purity was determined by HPLC analysis as 92% ee; [Chiralcel OD-H, *n*-hexane/*i*-PrOH = 70/30 , flow rate 0.5 mL/min, λ = 232 nm, τ_{maj} = 16.0 min, τ_{min} = 18.9 min]; $[\alpha]_D^{25}$ = -8.0 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.04 (br s, 1H), 6.04-6.03 (m, 1H), 5.83-5.82 (m, 1H), 4.42-4.35 (m, 2H), 4.11-4.07 (m, 1H), 4.01-3.93 (m, 2H), 3.73 (dd, 10.2 Hz, 18.0 Hz, 1H), 3.35 (dd, 4.2 Hz, 18.0 Hz, 1H), 2.59 (t, 7.2 Hz, 2H), 1.22 (dt, 1.2 Hz, 7.2 Hz); ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 169.9, 153.4, 135.0, 126.1 (q, 279.5 Hz), 122.0, 108.1, 104.6, 62.2, 42.5, 39.5 (q, 29.1 Hz), 35.0, 20.8, 13.2; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.2 (d, 9.2 Hz, 3F); IR (KBr) 3386.6, 1790.5, 1780.1, 1682.2, 1389.1, 1385.6, 1270.3, 1185.8, 1160.4, 1125.1, 1110.4, 1038.6, 770.3, 760.9 cm^{-1}; mp = 100-101 ºC; MS (ESI, *m/z*) 327.050 ($M+Na^+$); HRMS calcd. for $C_{13}H_{15}F_3N_2O_3^+$ 304.1035 found 304.1033.



3-[4,4,4-Trifluoro-3-(1-ethyl-1H-pyrrol-2-yl)-butyryl]-oxazolidin-2-one (*3e*): At N_2 atmosphere, to 20 mol % (0.010 mmol) of catalyst complex $Zn(NTf_2)_2$/(*R, R*)-Ph-dbfox prepared as described above in 0.2 mL CH_2Cl_2 was sequentially added 4 Å MS (15.0 mg), β-CF_3 acrylates **1a** (10.5 mg, 0.050 mmol), and the solution of N-ethyl pyrrole (24.0 mg, 0.250 mmol) in 0.05 mL CH_2Cl_2. The mixture was stirred at -75 ℃ for 24 h, then passed through a plug of silica gel using 3:1 petroleum ether:ethyl acetate to afford the title compound (14.6 mg, 96%) as a clear oil. The enantiomeric purity was determined by HPLC analysis as 96% ee; [Chiralcel OD-H, *n*-hexane/*i*-PrOH = 70/30, flow rate 0.8 mL/min, λ = 232 nm, τ_{min} = 12.6 min, τ_{maj} = 17.3 min]; $[\alpha]_D^{25}$ = -79.2 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.67 (d, 1.2 Hz, 1H), 6.18-6.16 (m, 1H), 6.12 (t, 2.4 Hz, 1H), 4.43-4.36 (m, 2H), 4.17-4.13 (m, 1H), 4.08-3.98 (m, 2H), 3.98-3.91 (m, 2H), 3.86 (dd, 10.2 Hz, 18.0 Hz, 1H), 3.38 (dd, 3.6 Hz, 18.0 Hz, 1H), 1.44 (t, 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 169.8, 153.3, 126.0 (q, 279.1 Hz), 124.7, 123.2, 107.9, 107.5, 62.2, 42.5, 41.3, 36.5 (q, 29.3 Hz), 35.8, 16.4; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.5 (d, 7.9 Hz, 3F); IR (neat) 1781.9, 1701.8, 1508.1, 1485.9, 1396.2, 1313.3, 1265.1, 1226.5, 1159.9, 1104.1, 1070.3, 1039.4, 760.8, 722.2, 679.8, 620.0 cm^{-1}; MS (ESI, *m/z*) 327.150 ($M+Na^+$); HRMS calcd. for $C_{13}H_{15}F_3N_2O_3^+$ 304.1035 found 304.1053.

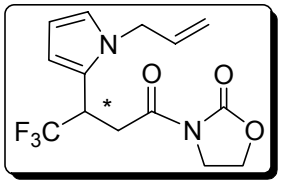


3-[4,4,4-Trifluoro-3-(1-propyl-1H-pyrrol-2-yl)-butyryl]-oxazolidin-2-one (*3f*): At N_2 atmosphere, to 20 mol % (0.010 mmol) of catalyst complex $Zn(NTf_2)_2$/(*R, R*)-Ph-dbfox prepared as described above in 0.2 mL CH_2Cl_2 was sequentially added 4 Å MS (15.0 mg), β-CF_3 acrylates **1a** (10.5 mg, 0.050 mmol), and the solution of N-propyl pyrrole (27.3 mg, 0.250 mmol) in 0.05 mL CH_2Cl_2. The mixture was stirred at -75 ℃ for 24 h, then passed through a plug of silica gel using 3:1 petroleum ether:ethyl acetate to afford the title compound (15.3 mg, 96%) as a clear oil. The enantiomeric purity was determined by HPLC analysis as 95% ee; [Chiralcel OD-H, *n*-hexane/*i*-PrOH = 70/30, flow rate 0.8 mL/min, λ = 232 nm, τ_{min} = 10.5 min, τ_{maj} = 12.7 min]; $[\alpha]_D^{25}$ = -145.8 (*c* 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.65 (t, 1.2 Hz, 1H), 6.18-6.16 (m, 1H), 6.10 (t, 2.4 Hz, 1H), 4.43-4.36 (m, 2H), 4.15-4.13 (m, 1H), 3.99-3.92 (m, 2H), 3.92-3.85 (m, 2H), 3.84 (dd, 10.2 Hz, 18.0 Hz, 1H), 3.38 (dd, 3.6 Hz, 18.0 Hz, 1H), 1.88-1.78 (m, 2H), 0.96 (dt, 1.2 Hz, 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 169.8, 153.3, 126.0 (q, 279.1 Hz), 124.8, 121.9, 107.9, 107.2, 62.2, 48.5, 42.5, 36.6 (q, 29.3 Hz), 35.8, 24.3, 11.3; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.5 (d, 9.2 Hz, 3F);
IR (neat) 1781.9, 1702.8, 1482.0, 1396.2, 1363.4, 1312.3, 1267.9, 1247.7, 1225.5, 1159.9, 1108.9, 1072.2, 963.3, 720.3, 620 cm^{-1}; MS (ESI, *m/z*) 341.100 ($M+Na^+$); HRMS calcd. for $C_{14}H_{17}F_3N_2O_3^+$ 318.1191 found 318.1183.

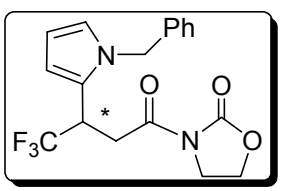


3-[4,4,4-Trifluoro-3-(1-butyl-1H-pyrrol-2-yl)-butyryl]-oxazoli

din-2-one (*3g*): At N_2 atmosphere, to 20 mol % (0.010 mmol) of catalyst complex $Zn(NTf_2)_2$/(*R, R*)-Ph-dbfox prepared as described above in 0.2 mL CH_2Cl_2 was sequentially added 4 Å MS (15.0 mg), β-CF_3 acrylates **1a** (10.5 mg, 0.050 mmol), and the solution of N-butyl pyrrole (30.8 mg, 0.250 mmol) in 0.05 mL CH_2Cl_2. The mixture was stirred at -75 ℃ for 36 h, then passed through a plug of silica gel using 3:1 petroleum ether:ethyl acetate to afford the title compound (15.8 mg, 95%) as a clear oil. The enantiomeric purity was determined by HPLC analysis as 93% ee; [Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 232 nm, τ_{min} = 17.3 min, τ_{maj} = 21.5 min]; $[\alpha]_D^{25}$ = -44.9 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.64 (t, 1.2 Hz, 1H), 6.18-6.16 (m, 1H), 6.10 (t, 2.4 Hz, 1H), 4.43-4.35 (m, 2H), 4.17-4.12 (m, 1H), 4.04-3.88 (m, 4H), 3.84 (dd, 10.2 Hz, 18.0 Hz, 1H), 3.38 (dd, 3.6 Hz, 18.0 Hz, 1H), 1.83-1.74 (m, 2H), 1.40-1.34 (m, 2H), 0.96 (dt, 1.2 Hz, 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 169.8, 153.3, 126.1 (q, 279.3 Hz), 124.8, 121.9, 107.9, 107.2, 62.2, 46.7 (d, 30.9 Hz), 42.5, 36.6 (q, 28.8 Hz), 35.9, 33.1, 20.0, 13.7; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.4 (d, 7.9 Hz, 3F); IR (neat) 1781.9, 1703.8, 1482.0, 1396.2, 1312.3, 1267.0, 1224.6, 1161.9, 1112.7, 1073.2, 1039.4, 961.3, 884.2, 760.8, 719.3 cm^{-1}; MS (ESI, *m/z*) 355.150 ($M+Na^+$); HRMS calcd. for $C_{15}H_{19}F_3N_2O_3^+$ 332.1348 found 332.1361.

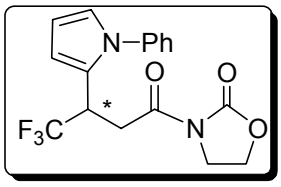


3-[4,4,4-Trifluoro-3-(1-allyl-1H-pyrrol-2-yl)-butyryl]-oxazoli din-2-one (*3h*): At N_2 atmosphere, to 20 mol % (0.010 mmol) of catalyst complex $Zn(NTf_2)_2$/(*R, R*)-Ph-dbfox prepared as described above in 0.2 mL CH_2Cl_2 was sequentially added 4 Å MS (15.0 mg), β-CF_3 acrylates **1a** (10.5 mg, 0.050 mmol), and the solution of N-allyl pyrrole (26.8 mg, 0.250 mmol) in 0.05 mL CH_2Cl_2. The mixture was stirred at -75 ℃ for 36 h, then passed through a plug of silica gel using 3:1 petroleum ether:ethyl acetate to afford the title compound (14.2 mg, 90%) as a clear oil. The enantiomeric purity was determined by HPLC analysis as 95% ee; [Chiralcel OD-H, *n*-hexane/*i*-PrOH = 70/30, flow rate 0.5 mL/min, λ = 232 nm, τ_{min} = 19.7 min, τ_{maj} = 22.8 min]; $[\alpha]_D^{25}$ = -18.5 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.37-6.32 (m, 1H), 6.20-6.19 (m, 1H), 6.13-6.12 (m, 1H), 6.03-5.96 (m, 1H), 5.22-5.20 (m, 1H), 5.12 (dd, 1.2 Hz, 17.4 Hz, 1H), 4.66-4.55 (m, 2H), 4.43-3.36 (m, 2H), 4.17-4.14 (m, 1H), 3.99-3.91 (m, 2H), 3.77 (dd, 10.2 Hz, 18.0 Hz, 1H), 3.41 (dd, 3.6 Hz, 18.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 169.7, 153.3, 134.2, 126.0 (q, 279.5 Hz), 125.2, 122.1, 117.4, 108.4, 107.7, 62.2, 49.4, 42.5, 36.6 (q, 28.8 Hz), 35.9; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.3 (d, 7.9 Hz, 3F); IR (neat) 3442,3, 1718.3, 1419.3, 1363.4, 1293.0, 1255.4, 1191.8, 1161.9, 1110.8, 1032.7, 931.4, 806.1, 742.5, 684.6, 634.5 cm^{-1}; MS (ESI, *m/z*) 339.100 ($M+Na^+$); HRMS calcd. for $C_{14}H_{15}F_3N_2O_3^+$ 316.1035 found 316.1045.

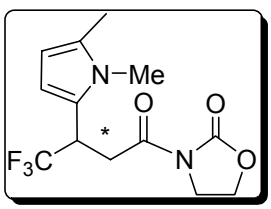


3-[4,4,4-Trifluoro-3-(1-benzyl-1H-pyrrol-2-yl)-butyryl]-oxazo lidin-2-one (*3i*): At N_2 atmosphere, to 20 mol % (0.010 mmol) of catalyst complex $Zn(NTf_2)_2$/(*R, R*)-Ph-dbfox prepared as

described above in 0.2 mL CH_2Cl_2 was sequentially added 4 Å MS (15.0 mg), β-CF_3 acrylates **1a** (10.5 mg, 0.050 mmol), and the solution of N-benzyl pyrrole (39.3 mg, 0.250 mmol) in 0.05 mL CH_2Cl_2. The mixture was stirred at -60 ℃ for 48 h, then passed through a plug of silica gel using 3:1 petroleum ether:ethyl acetate to afford the title compound (17.0 mg, 93%) as a white solid. The enantiomeric purity was determined by HPLC analysis as 86% ee; [Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 232 nm, τ_{maj} = 40.9 min, τ_{min} = 50.4 min]; $[\alpha]_D^{25}$ = -20.0 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.34-7.26 (m, 3H), 7.11 (d, 7.8 Hz, 2H), 6.19-6.14 (m, 1H), 6.25-6.24 (m, 1H), 6.17-6.15 (m, 1H), 5.24 (B of AB, *J* = 16.2 Hz, 1H), 5.15 (A of AB, 16.2 Hz, 1H), 4.39-4.33 (m, 2H), 4.16-4.11 (m, 1H), 3.93-3.87 (m, 2H), 3.68 (ddd, 1.2 Hz, 9.6 Hz, 18.0 Hz, 1H), 3.40 (dd, 3.6 Hz, 18.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 169.6, 153.3, 137.5, 128.7, 127.6, 127.1, 126.9, 126.0 (q, 279.7 Hz), 122.8, 108.7, 107.9, 62.2, 50.5, 42.4, 36.7 (q, 29.0 Hz), 36.1; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.4 (d, 7.9 Hz, 3F); IR (KBr) 1777.1, 1707.7, 1397.2, 1379.8, 1311.4, 1265.1, 1240.9, 1163.8, 1135.8, 1119.5, 754.0, 729.9 cm^{-1}; mp = 92-93 ºC; MS (ESI, *m/z*) 389.100 ($M+Na^+$); HRMS calcd. for $C_{18}H_{17}F_3N_2O_3^+$ 366.1191 found 366.1191.

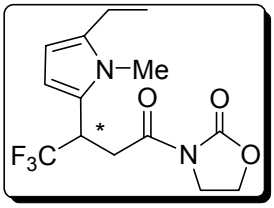


3-[4,4,4-Trifluoro-3-(1-phenyl-1H-pyrrol-2-yl)-butyryl]-oxazolidin-2-one (*3j*): At N_2 atmosphere, to 20 mol % (0.010 mmol) of catalyst complex $Zn(NTf_2)_2$/(*R, R*)-Ph-dbfox prepared as described above in 0.2 mL CH_2Cl_2 was sequentially added 4 Å MS (15.0 mg), β-CF_3 acrylates **1a** (10.5 mg, 0.050 mmol), and the solution of N-phenyl pyrrole (35.8 mg, 0.250 mmol) in 0.05 mL CH_2Cl_2. The mixture was stirred at -20 ℃ for 24 h, then passed through a plug of silica gel using 3:1 petroleum ether:ethyl acetate to afford the title compound (16.6 mg, 94%) as a white solid. The enantiomeric purity was determined by HPLC analysis as 88% ee; [Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 232 nm, τ_{maj} = 21.5 min, τ_{min} = 25.3 min]; $[\alpha]_D^{25}$ = -111.9 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.50-7.41 (m, 5H), 6.79-6.78 (m 1H), 6.34-6.33 (m, 1H), 6.26-6.25 (m, 1H), 4.41-4.38 (m, 2H), 4.09-4.06 (m, 1H), 3.97-3.94 (m, 2H), 3.91 (dd, 11.4 Hz, 18.0 Hz, 1H), 3.29 (dd, 3.6 Hz, 18.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 169.5, 153.4, 139.4, 129.2, 128.0, 127.2, 126.0, 125.8 (q, 279.1 Hz), 123.0, 108.7, 108.4, 62.2, 42.5, 36.6 (q, 29.4 Hz), 35.3; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.6 (s, 3F); IR (KBr) 1773.2, 1717.3, 1703.8, 1597.7, 1502.3, 1393.3, 1321.0, 1267.0, 1152,3, 1113.7, 1037.5, 768.5, 756.9, 736.7 cm^{-1}; mp = 175-176 ºC; MS (ESI, *m/z*) 375.100 ($M+Na^+$); HRMS calcd. for $C_{17}H_{15}F_3N_2O_3^+$ 352.1035 found 352.1035.

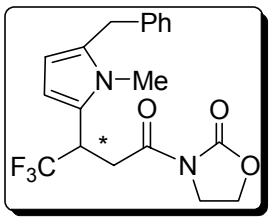


3-[4,4,4-Trifluoro-3-(5-methyl-1-methyl-1H-pyrrol-2-yl)-butyryl]-oxazolidin-2-one (*3k*): At N_2 atmosphere, to 20 mol % (0.010 mmol) of catalyst complex $Zn(NTf_2)_2$/(*R, R*)-Ph-dbfox prepared as described above in 0.2 mL CH_2Cl_2 was sequentially added 4 Å

MS (15.0 mg), β-CF_3 acrylates **1a** (10.5 mg, 0.050 mmol), and the solution of 2-methyl-N-methyl pyrrole (9.6 mg, 0.100 mmol) in 0.05 mL CH_2Cl_2. The mixture was stirred at -75 ℃ for 24 h, then passed through a plug of silica gel using 3:1 petroleum ether:ethyl acetate to afford the title compound (14.7 mg, 97%) as a white solid. The enantiomeric purity was determined by HPLC analysis as 94% ee; [Chiralcel OD-H, *n*-hexane/*i*-PrOH = 70/30, flow rate 0.5 mL/min, λ = 232 nm, τ_{min} = 18.8 min, τ_{maj} = 22.3 min]; $[\alpha]_D^{25}$ = -76.1 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.05 (d, 3.6 Hz, 1H), 5.84 (d, 3.6 Hz, 1H), 4.43-4.35 (m, 2H), 4.17-4.10 (m, 1H), 3.99-3.91 (m, 2H), 3.84 (ddd, 1.2 Hz, 10.8 Hz, 18.0 Hz, 1H), 3.52 (s, 3H), 3.36 (dd, 3.0 Hz, 18.0 Hz, 1H), 2.21 (s, 3H); ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 169.9, 153.3, 129.8, 126.1 (q, 279.5 Hz), 124.7, 106.6, 105.9, 62.2, 42.4, 37.0 (q, 29.0 Hz), 30.2, 12.7; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.7 (d, 7.9 Hz, 3F); IR (KBr) 1776.1, 1698.0, 1413.6, 1333.5, 1316.2, 1260.2, 1227.5, 1160.9, 1116.6, 761.7, 679.9 cm^{-1}; mp = 100-101 ºC; MS (ESI, *m/z*) 327.100 ($M+Na^+$); HRMS calcd. for $C_{13}H_{15}F_3N_2O_3^+$ 304.1035 found 304.1049.

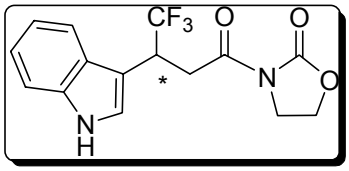


3-[4,4,4-Trifluoro-3-(5-ethyl-1-methyl-1H-pyrrol-2-yl)-butyryl]-oxazolidin-2-one (*3l*): At N_2 atmosphere, to 20 mol % (0.010 mmol) of catalyst complex $Zn(NTf_2)_2$/(*R, R*)-Ph-dbfox prepared as described above in 0.2 mL CH_2Cl_2 was sequentially added 4 Å MS (15.0 mg), β-CF_3 acrylates **1a** (11.0 mg, 0.050 mmol), and the solution of 2-ethyl-N-methyl pyrrole (11.0 mg, 0.100 mmol) in 0.05 mL CH_2Cl_2. The mixture was stirred at -75 ℃ for 48 h, then passed through a plug of silica gel using 3:1 petroleum ether:ethyl acetate to afford the title compound (15.8 mg, 99%) as a white solid. The enantiomeric purity was determined by HPLC analysis as 88% ee; [Chiralcel OD-H, *n*-hexane/*i*-PrOH = 70/30, flow rate 0.5 mL/min, λ = 232 nm, τ_{min} = 18.1 min, τ_{maj} = 21.2 min]; $[\alpha]_D^{25}$ = -55.2 (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.09 (d, 3.6 Hz, 1H), 5.86 (d, 3.6 Hz, 1H), 4.44-4.36 (m, 2H), 4.19-4.14 (m, 1H), 3.99-3.92 (m, 2H), 3.83 (dd, 10.2 Hz, 18.0 Hz, 1H), 3.53 (s, 3H), 3.37 (dd, 3.0 Hz, 18.0 Hz, 1H), 2.58-3.53 (m, 2H), 1.24 (t, 7.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 169.9, 153.4, 136.1, 126.2 (q, 279.5 Hz), 124.9, 106.7, 104.1, 62.3, 42.5, 36.9 (q, 28.4 Hz), 35.7, 30.1, 20.1, 12.6; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.7 (d, 6.6 Hz, 3F); IR (KBr) 1782.9, 1702.8, 1396.2, 1311.4, 1267.0, 1225.5, 1159.9, 1101.1, 1070.3, 1038.5, 960.4, 884.2, 758.9, 678.8 cm^{-1}; mp = 71-72 ºC; MS (ESI, *m/z*) 341.100 ($M+Na^+$); HRMS calcd. for $C_{14}H_{17}F_3N_2O_3^+$ 318.1191 found 318.1182.

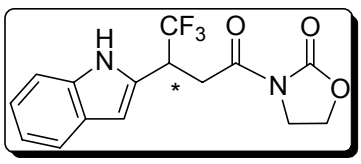


3-[4,4,4-Trifluoro-3-(5-benzyl-1-methyl-1H-pyrrol-2-yl)-butyr yl]-oxazolidin-2-one (*3m*): At N_2 atmosphere, to 20 mol % (0.010 mmol) of catalyst complex $Zn(NTf_2)_2$/(*R, R*)-Ph-dbfox prepared as described above in 0.2 mL CH_2Cl_2 was sequentially added 4 Å MS (15.0 mg), β-CF_3 acrylates **1a** (10.5 mg, 0.050 mmol), and the solution of 2-benzyl-N-methyl pyrrole (17.0 mg,

0.100 mmol) in 0.05 mL CH_2Cl_2. The mixture was stirred at -75 ℃ for 48 h, then passed through a plug of silica gel using 3:1 petroleum ether:ethyl acetate to afford the title compound (18.1 mg, 95%) as a white solid. The enantiomeric purity was determined by HPLC analysis as 76% ee; [Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 232 nm, τ_{maj} = 36.7 min, τ_{min} = 42.9 min]; $[\alpha]_D^{25}$ = -48.5 (*c* 0.43, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.29-7.26 (m, 2H), 7.21-7.19 (m, 1H), 7.10 (d, 7.2 Hz, 2H), 6.10 (d, 3.6 Hz, 1H), 5.836 (d, 3.6 Hz, 1H), 4.43-4.36 (m, 2H), 4.15-4.11 (m, 1H), 3.99-3.91 (m, 4H), 3.83 (dd, 10.8 Hz, 18.0 Hz, 1H), 3.44 (s, 3H), 3.38 (dd, 3.0 Hz, 18.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 169.8, 153.3, 139.1, 132.2, 128.5, 128.4, 128.2, 126.2, 126.1 (q, 279.5 Hz), 125.5, 107.4, 106.7, 62.2, 42.5, 37.0 (q, 29.4 Hz), 35.6, 33.3, 30.5; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.7 (d, 6.6 Hz, 3F); IR (KBr) 1782.9, 1705.7, 1397.2, 1331.6, 1316.2, 1265.1, 1155.2, 1096.3, 757.9, 677.8 cm^{-1}; mp = 153-154 ºC; MS (ESI, *m/z*) 403.100 ($M+Na^+$); HRMS calcd. for $C_{19}H_{19}F_3N_2O_3^+$ 380.1348 found 380.1328.



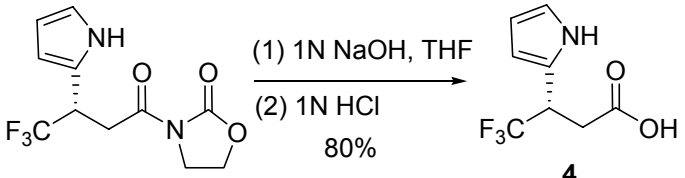
3-[4,4,4-Trifluoro-3-(1H-indole-3-yl)-butyryl]-oxazolidin-2-one (*3n*): At N_2 atmosphere, to 20 mol % (0.010 mmol) of catalyst complex $Zn(NTf_2)_2$/(*R, R*)-Ph-dbfox prepared as described above in 0.2 mL CH_2Cl_2 was sequentially added 4 Å MS (15.0 mg), β-CF_3 acrylates **1a** (10.5 mg, 0.050 mmol), and the solution of indole (11.7 mg, 0.100 mmol) in 0.05 mL CH_2Cl_2. The mixture was stirred at -75 ℃ for 24 h, then passed through a plug of silica gel using 2:1 petroleum ether:ethyl acetate to afford the title compound (16.1 mg, 99%) as a white solid. The enantiomeric purity was determined by HPLC analysis as 99 % ee; [Chiralcel OD-H, *n*-hexane/*i*-PrOH = 70/30, flow rate 0.5 mL/min, λ = 254 nm, τ_{min} = 18.6 min, τ_{maj} = 27.5 min]; $[\alpha]_D^{25}$ = -52.1 (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.21 (br s, 1H), 7.70 (d, 7.8 Hz, 1H), 7.34 (d, 7.8 Hz, 1H), 7.25-7.15 (m, 3H), 4.49-4.45 (m, 1H), 4.35-4.21 (m, 2H), 3.91-3.78 (m, 3H), 3.56 (dd, 4.2 Hz, 17.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 600 MHz) δ 169.8, 153.5, 135.9, 126.9 (q, 279.1 Hz), 126.7, 123.7, 122.5, 120.2, 119.1, 111.3, 109.2, 62.1, 42.5, 37.0 (q, 29.1 Hz), 35.3; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.3 (d, 9.2 Hz, 3F); IR (KBr) 3399.9, 1782.9, 1693.2, 1458.9, 1403.9, 1389.5, 1325.8, 1274.7, 1232.3, 1177.3, 1098.3, 1036.5, 965.2, 741.5 cm^{-1}; mp = 132-133 ºC; MS (ESI, *m/z*) 349.100 ($M+Na^+$); HRMS calcd. $C_{15}H_{13}F_3N_2O_3^+$ for 326.0878 found 326.0905.



3-[4,4,4-Trifluoro-3-(1H-indole-2-yl)-butyryl]-oxazolidin-2-one (*3o*): At N_2 atmosphere, to 20 mol % (0.010 mmol) of catalyst complex $Zn(NTf_2)_2$/(*R, R*)-Ph-dbfox prepared as described above in 0.2 mL CH_2Cl_2 was sequentially added 4 Å MS (15.0 mg), β-CF_3 acrylates **1a** (10.5 mg, 0.050 mmol), and the solution of 4,7-dihydroindole (12.0 mg, 0.100 mmol) in 0.05 mL CH_2Cl_2. After stirring at -75 ℃ for 24 h, the reaction mixture was allowed to warm to RT., and 21.6 mg (2 equiv, 0.200 mmol) of *p*-benzoquinone was added. The reaction was stirred at rt. for 2 h, then passed

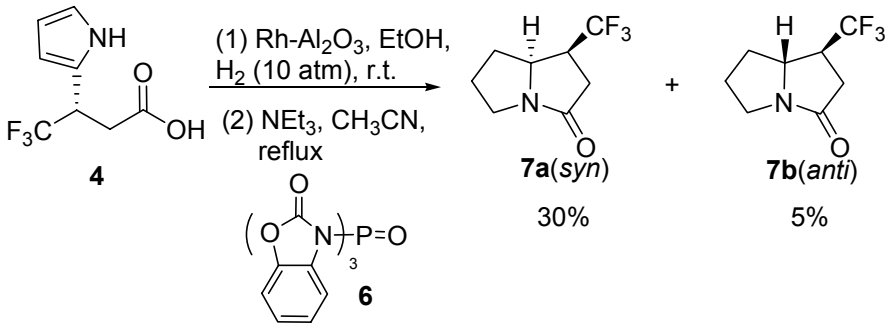
through a plug of silica gel using CH_2Cl_2 to afford the title compound (14.7 mg, 90%) as a yellow solid. The enantiomeric purity was determined by HPLC analysis as 75 % ee; [Chiralcel AD-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 0.5 mL/min, λ = 254 nm, τ_{maj} = 121.8 min, τ_{min} = 146.7 min]; $[\alpha]_D^{25}$ = +1.6 (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.37 (br s, 1H), 7.59 (d, 7.8 Hz, 1H), 7.38 (d, 7.8 Hz, 1H), 7.22 (t, 7.2 Hz, 1H), 7.12 (t, 7.2 Hz, 1H), 6.55 (s, 1H), 4.45-4.28 (m, 3H), 4.00-3.91 (m, 2H), 3.87 (dd, 10.2 Hz, 18.0 Hz, 1H), 3.56 (dd, 3.6 Hz, 18.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 600 MHz) δ 169.5, 153.4, 136.1, 130.8, 127.9, 125.9 (q, 279.6 Hz), 122.6, 120.7, 120.2, 111.0, 102.8, 62.3, 42.5, 39.7 (q, 29.2 Hz), 35.1; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -69.5 (d, 7.9 Hz, 3F); IR (KBr) 3326.6, 1763.6, 1706.7, 1590.9, 1475.3, 1458.9, 1408.7, 1397.2, 1330.6, 1305.6, 1260.3, 1237.1, 1162.9, 1137.8, 1097.3, 1068.4, 1037.5, 789.7, 754.0, 686.5 cm^{-1}; mp = 120-121 ºC; MS (ESI, *m/z*) 349.150 ($M+Na^+$); HRMS calcd. $C_{15}H_{13}F_3N_2O_3^+$ for 326.0878 found 326.0914.

Synthesis of Optically Active Trifluoromethylated Heliotridane

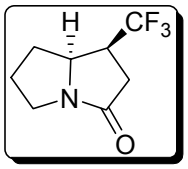


3b **4**

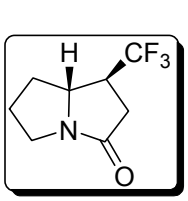
To a solution of (*S*)-**3b** (98% ee, 110.0mg, 0.40 mmol) in THF was added 1 N NaOH (aq., 0.80 mL, 0.80 mmol). After stirring at rt for 1 h, 1 N HCl (aq.) was slowly added to adjust the PH value of the reaction mixture to 1-2. Compound (*S*)-**4** (66.2 mg, 80%) was isolated as a solid by flash column chromatography using 3:1 petroleum ether:ethyl acetate as eluent. $[\alpha]_D^{25}$ = +17.3 (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.26 (br s, 1H), 6.76 (d, 2.4 Hz, 1H), 6.18-6.16 (m, 2H), 3.96-3.91 (m, 1H), 3.01 (dd, 4.2 Hz, 10.8 Hz, 1H), 2.88 (dd, 9.6 Hz, 10.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 176.1, 125.8 (q, 279.5 Hz), 123.2, 118.8, 108.9, 108.1, 39.7 (q, 29.3 Hz), 33.8; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.7 (s, 3F); IR (KBr) 3470.3, 3119.3, 1719.2, 1660.4, 1560.1, 1418.4, 1363.4, 1293.0, 1272.8, 1181.2, 1164.8, 1035.6, 993.2, 930.5, 859.1, 810.9, 680.8 cm^{-1}; mp = 70-71 ºC; MS (ESI, *m/z*) 206.050 ($M-H^-$); HRMS calcd. $C_8H_8F_3NO_2^+$ for 207.0507 found 207.0513.



To a 10 mL test tube was added **4** (66.0 mg, 0.40 mmol), 5% of Rh-Al_2O_3 (8 mg), and 4 mL EtOH. The resulting mixture was put into an autoclave, and purged with H_2 (10 atm). After stirring at rt for 24 h, the catalyst was filtrated through celite, then the solvent was evaporated *in vacuo* to provide the 2-pyrrolidine carboxylic acid as white solid.[2] Without further purification, the compound obtained was heated under reflux with the phosphine oxide **6** (186 mg, 0.41 mmol) and triethyl amine (0.2 mL, 1.43 mmol) in 10 mL acetonitrile. After 6 h, the resulting solution was concentrated, then subjected to column chromatography using ether as eluent. The faster running fractions was determined as **7a** as a colorless oil (23.0 mg, 30%), while the lower fractions was as **7b** a colorless oil (4.0 mg, 5%).[3] The ratio and stereochemistry of the two isomers were identified from ^{19}F NMR spectrum. The value of -67.9 ppm in lower magnetic field due to steric deshielding effect indicates a *cis* arrangement of hydrogen and CF_3 group and thus the structure **7b** for the minor isomer.[4] Hence, the chemical shift value of -71.1 ppm belongs to the major *syn* isomer.

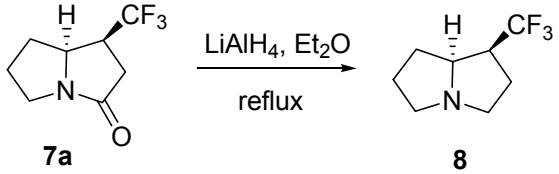


(*syn*)-1-Trifluoromethyl-hexahydropyrrolizin-3-one (7a): $[\alpha]_D^{25}$ = +26.0 (*c* 0.35, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz) δ 3.95 (dt, 6.6 Hz, 9.0 Hz, 1H, 5-H), 3.59 (dt, 8.4 Hz, 11.4 Hz, 1H, 8-H), 3.13-3.09 (m, 1H, 8'-H), 2.91 (dd, 10.2 Hz, 16.2 Hz, 1H, 3-H), 2.87-2.79 (m, 1H, 4-H), 2.67 (dd, 9.0 Hz, 16.2 Hz, 1H, 3'-H), 2.21-2.15 (m, 2H, 6-H, 7-H), 2.12-2.04 (m, 1H, 7'-H), 1.50-1.43 (m, 1H, 6'-H); ^{13}C NMR ($CDCl_3$, 600 MHz) δ 171.1, 126.1 (q, 276.6 Hz), 60.9 (d, 3.2 Hz), 44.8 (q, 29.1 Hz), 41.3, 35.2 (d, 2.26 Hz), 31.6, 26.6; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -71.1 (d, 6.6 Hz, 3F); IR (neat) 2976.6, 2884.9, 1782.9, 1702.8, 1428.0, 1343.2, 1270.9, 1166.7, 1123.3, 1085.7, 688.5 cm^{-1}; MS (ESI, *m/z*) 216.100 ($M+Na^+$); HRMS calcd. $C_8H_{10}F_3NO$ 193.0714 found 193.0756.



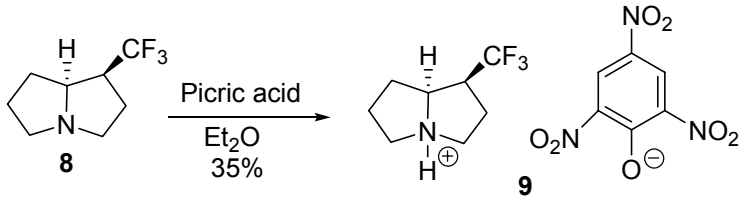
(*anti*)-1-Trifluoromethyl-hexahydropyrrolizin-3-one (7b): $[\alpha]_D^{25}$ = +24.0 (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz) δ 4.04-4.00 (m, 1H, 5-H), 3.57 (dt, 8.4 Hz, 11.4 Hz, 1H, 8-H), 3.23-3.15 (m, 1H, 4-H), 3.14-3.10 (m, 1H, 8'-H), 2.93 (dd, 10.2 Hz, 17.4 Hz, 1H, 3-H), 2.64 (dd, 4.8 Hz, 17.4 Hz, 1H, 3'-H), 2.22-2.17 (m, 1H, 7-H), 2.06-1.98 (m, 1H, 7'-H), 1.96-1.92 (m, 1H, 6-H), 1.75-1.67 (m, 1H, 6'-H); ^{13}C NMR ($CDCl_3$, 600 MHz) δ 172.0, 126.5 (q, 278.5 Hz), 61.1, 41.3, 38.3 (q, 28.5 Hz), 33.9, 29.7, 26.4; ^{19}F NMR

($CDCl_3$, 188 MHz) δ –67.8 (d, 6.6 Hz, 3F); IR (neat) 2926.5, 1779.0, 1684.4, 1484.0, 1428.0, 1392.4, 1294.0, 167.0, 1178.3, 1150.3, 1126.2, 1103.1, 760.8 cm^{-1}; MS (ESI, *m/z*) 216.100 ($M+Na^+$); HRMS calcd. $C_8H_{10}F_3NO$ 193.0714 found 193.0698.



7a **8**

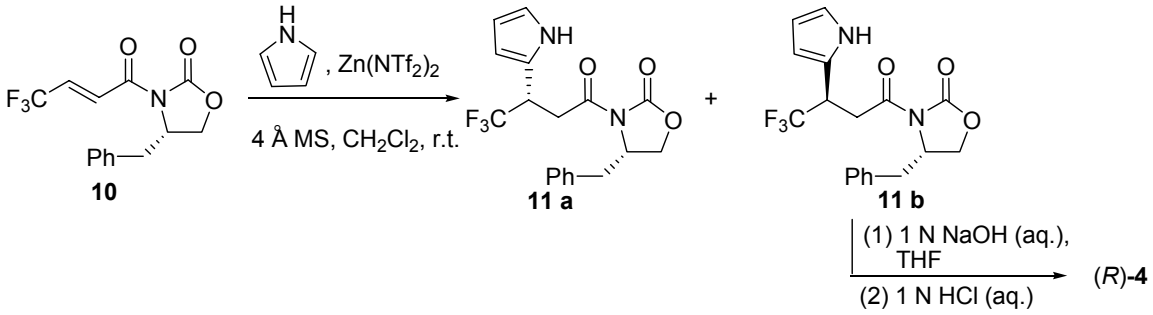
At N_2 atmosphere, to a solution of **7a** (20.0 mg, 0.104 mmol) in ether (2.0 mL) was added $LiAlH_4$ (15.8 mg, 0.416 mmol) directly at 0 ℃. After stirring at 35 ℃ for 6 h, the solution was cooled to rt before $Na_2SO_4{\cdot}10H_2O$ (135.0 mg, 0.416 mmol) was slowly added to the reaction mixture. The resulting solution was stirred at rt for overnight. The solvent was removed by a steady stream of N_2 to obtain slightly yellow oil **8** (10.0 mg, 54% yield).[5] $[\alpha]_D^{25}$ = +20.3 (*c* 0.3, Et_2O); ^1H NMR (CD_2Cl_2, 600 MHz) δ ^1H NMR ($CDCl_3$, 600 MHz) δ 3.41-3.38 (m, 1H, 5-H), 3.04-3.01 (m, 1H, 2-H), 2.83 (dt, 10.2 Hz, 6.6 Hz, 1H, 8-H), 2.54 (dt, 9.6 Hz, 6.6 Hz, 1H, 2'-H), 2.46 (dt, 10.2 Hz, 6.6 Hz, 1H, 8'-H), 2.35-2.29 (m, 1H, 4-H), 2.06-2.00 (m, 1H, 3-H), 1.96-1.85 (m, 2H, 6-H, 3'-H), 1.80-1.73 (m, 1H, 7-H), 1.72-1.65 (m, 1H, 7'-H), 1.54-1.49 (m, 1H, 6'-H); ^{13}C NMR (CD_2Cl_2, 600 MHz) δ 128.1 (q, 277.2 Hz), 64.8(d, 2.3 Hz), 54.7, 54.1, 49.6 (q, 26.1 Hz), 32.2, 27.7 (d, 2.1 Hz), 26.1; ^{19}F NMR (CD_2Cl_2, 188 MHz) δ -70.1 (d, 9.2 Hz, 3F); MS (EI, *m/z*) 179 (M^+); HRMS calcd. $C_8H_{12}F_3N$ for 179.0922 found 179.0941.



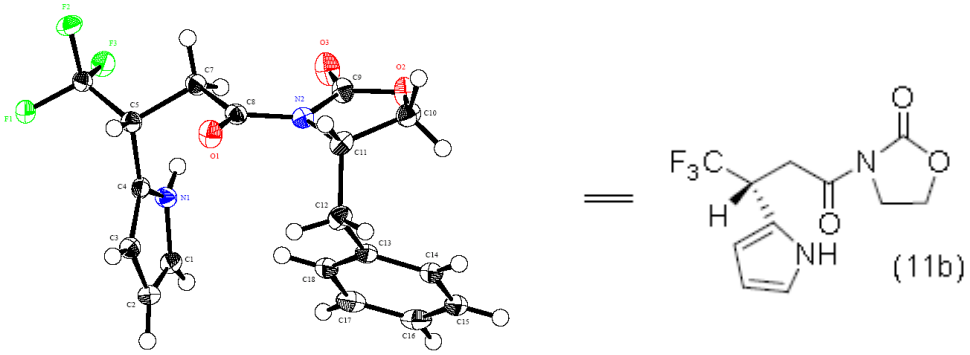
8 **9**

To a solution of **8** (10.0 mg, 0.056 mmol) in 1 mL ether was added the solution of Picric acid (20.0 mg, 0.056 mmol) in 1 mL ether. After stirring for 1h at rt, the precipitate was filtrated as the target compound **9** (8.0 mg, 35% yield). $[\alpha]_D^{25}$ = -5.8 (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz) δ 8.88 (s, 2H, Ar-H), 4.50-4.47 (m, 1H, 5-H), 4.15-4.12 (m, 1H, 2-H), 3.80 (dt, 12.0 Hz, 7.2 Hz, 1H, 8-H), 3.16-3.12 (m, 1H, 8'-H), 3.06 (dt, 10.8 Hz, 6.0 Hz, 1H, 2-H), 2.81-2.75 (m, 1H, 4-H), 2.54-2.46 (m, 2H, 6-H, 3-H), 2.38-2.32 (m, 1H, 7-H), 2.21-2.14 (m, 1H, 7'-H), 2.05-2.00 (m, 1H, 6'-H); ^{13}C NMR ($CDCl_3$, 600 MHz) δ 162.3, 141.6, 128.6, 126.7, 125.2 (q, 277.7 Hz), 67.0 (d, 2.4 Hz), 55.6, 54.9, 48.7 (q, 29.5 Hz), 30.8, 26.7, 25.0; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.0 (d, 6.6 Hz, 3F); IR (KBr) 1716.3, 1637.3, 1557.2, 1489.7, 1434.8, 1329.7, 1276.7, 1162.9, 111.8 cm^{-1}; mp = 181-183 ºC; MS (ESI, *m/z*) 212.200 ($M+Na^+$); Anal. Calcd. (%) for $C_{14}H_{15}F_3N_4O_7$ C, 41.18; H, 3.70; N, 13.72; found C, 41.22; H, 3.90; N, 13.60.

Absolute Stereochemistry Determination



At N_2 atmosphere, to a mixture of (4*S*)-benzyl-3-[(E)-4,4,4-Trifluorobut-2-enoyl]-oxazolidin-2-one **10** (15.0 mg, 0.050 mmol), 4 Å MS (15.0 mg), and 20 mol % of catalyst $Zn(NTf_2)_2$ (6.2 mg, 0.010 mmol) in 0.5 mL CH_2Cl_2 was added pyrrole (17.0 mg, 0.250 mmol). The mixture was stirred at rt for 2 h, then passed through a plug of silica gel using 4:1 petroleum ether:ethyl acetate to afford two diastereoisomers. One diastereoisomer was separated as white solid (13.40 mg, 97%), which was determined as **11b** by single-crystal x-ray analysis. $[\alpha]_D^{25}$ = +81.5 (*c* 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.46 (br s, 1H), 7.29-7.24 (m, 3H), 7.01 (d, 7.2 Hz, 2H), 6.77-6.76 (m, 1H), 6.22-6.17 (m, 2H), 4.67-4.63 (m, 1H), 4.23-4.15 (m, 3H), 3.85 (dd, 10.2 Hz, 17.4 Hz, 1H), 3.31 (dd, 4.2 Hz, 17.4 Hz, 1H), 3.02 (dd, 3.0 Hz, 13.2 Hz, 1H), 2.66 (dd, 9.0 Hz, 13.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 169.8, 153.4, 134.7, 129.4, 129.0, 127.4, 126.1 (q, 279.5 Hz), 123.6, 118.6, 118.6, 108.8, 108.5, 66.2 (d, 3.6 Hz), 39.5 (q, 29.0 Hz), 37.4, 35.1; ^{19}F NMR ($CDCl_3$, 188 MHz) δ -70.1 (d, 9.2 Hz, 3F); IR (KBr) 3387.4, 1776.1, 1692.2, 1441.5, 1401.0, 1358.6, 1302.7, 1262.2, 1218.8, 1195.7, 1163.8, 1153.2, 1132.0, 1101.2, 726.1 cm^{-1}; mp = 150-151 ºC; MS (ESI, *m/z*) 388.850 ($M+Na^+$); HRMS calcd. for $C_{18}H_{17}F_3N_2O_3^+$ 366.1191 found 366.1200.



CIF file of **11b** is available as Supporting Information.

To a solution of **11b** (11.0mg, 0.030 mmol) in THF was added 1 N NaOH (aq., 0.10 mL, 0.10 mmol). After stirring at rt for 1 h, 1N HCl (aq.) was slowly added to adjust the PH

value of the reaction mixture to 1-2. Compound (*R*)-**4** (5.0 mg, 83%) was isolated by flash column chromatography, which has the opposite optical rotation as compound **4** transformed from **3b**. Thus the absolute stereochemistry of compound **3b** was determined as *S*.

References

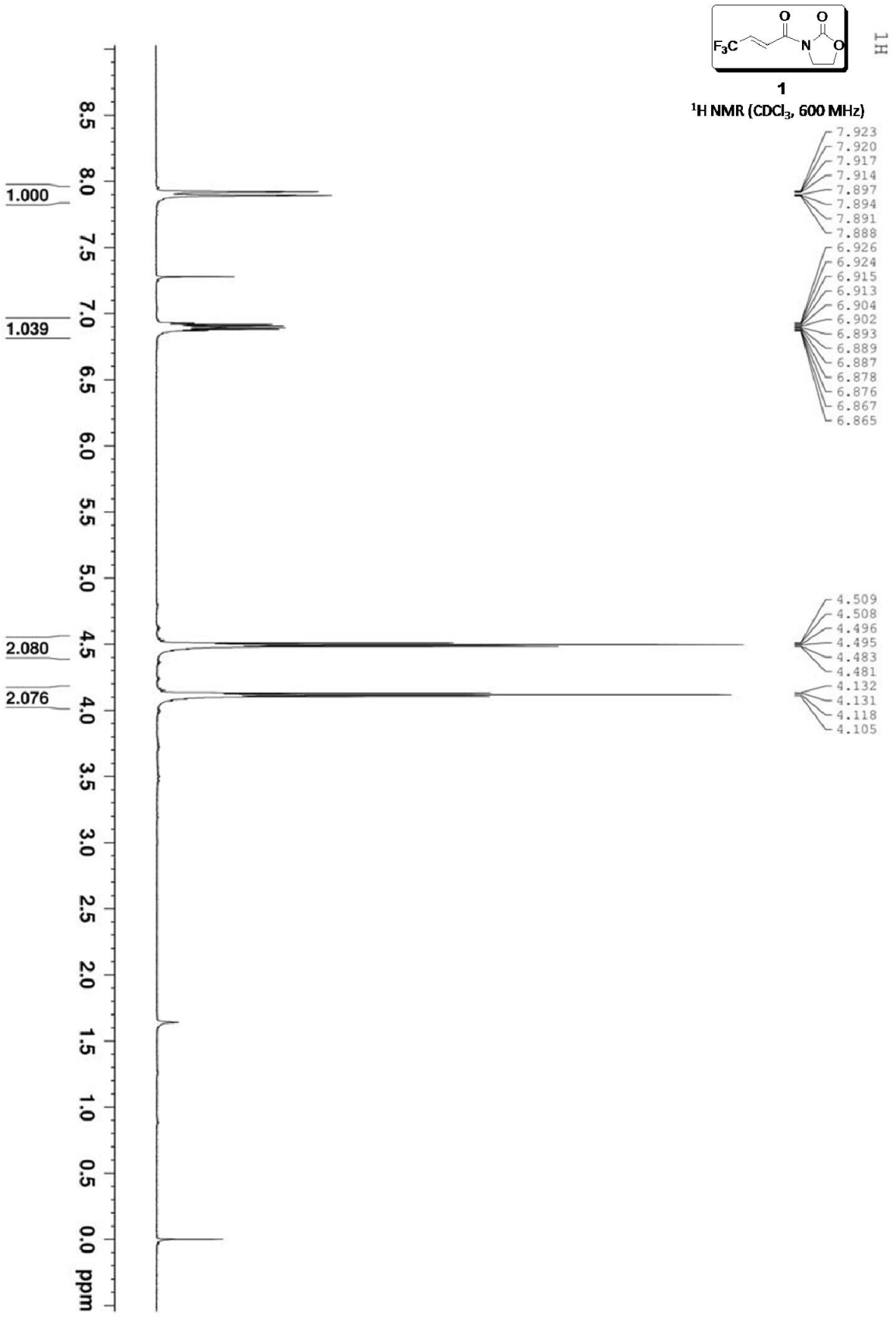
(1) Tamura, K.; Yamazaki, T.; Kitazume, T.; Kubota, T. *J Fluorine Chem.* **2005**, *126*, 918–930.

(2) Evans, D. A.; Fandrick, K. R. *Org. Lett.* **2006**, *8*, 2249-2252.

(3) Gilchrist, T. L.; Lemos, A.; Ottaway, C. J. *J. Chem. Soc. Perkin Trans 1*. **1997**, 3005-3012.

(4) William, R.; Dolbier, JR. *Guide to Fluorine NMR for Organic Chemistry*; WILEY: New Jersey, **2009**; pp 1-256.

(5) Andenson, P. G.; Backvalll, J.-E. *J. Am. Chem. Soc*. **1992,** *114,* 8698-8699.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1
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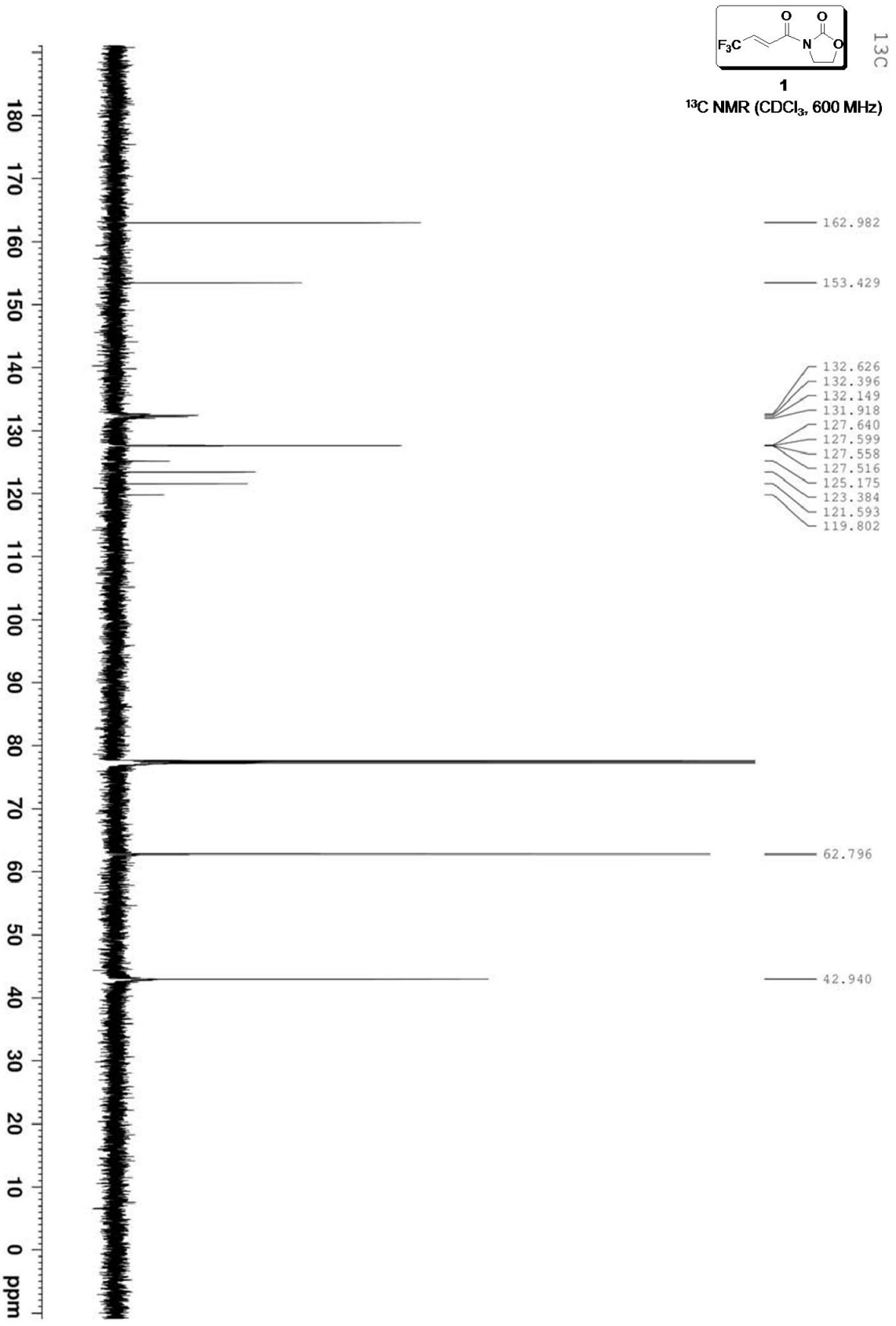
7.920
7.917
7.914
7.897
7.894
7.891
7.888
6.926
6.924
6.915
6.913
6.904
6.902
6.893
6.889
6.887
6.878
6.876
6.867
6.865
4.509
4.508
4.496
4.495
4.483
4.481
4.132
4.131
4.118
4.105
1.000
1.039
2.080
2.076
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


13C
1
13C NMR (CDCl3, 600 MHz)
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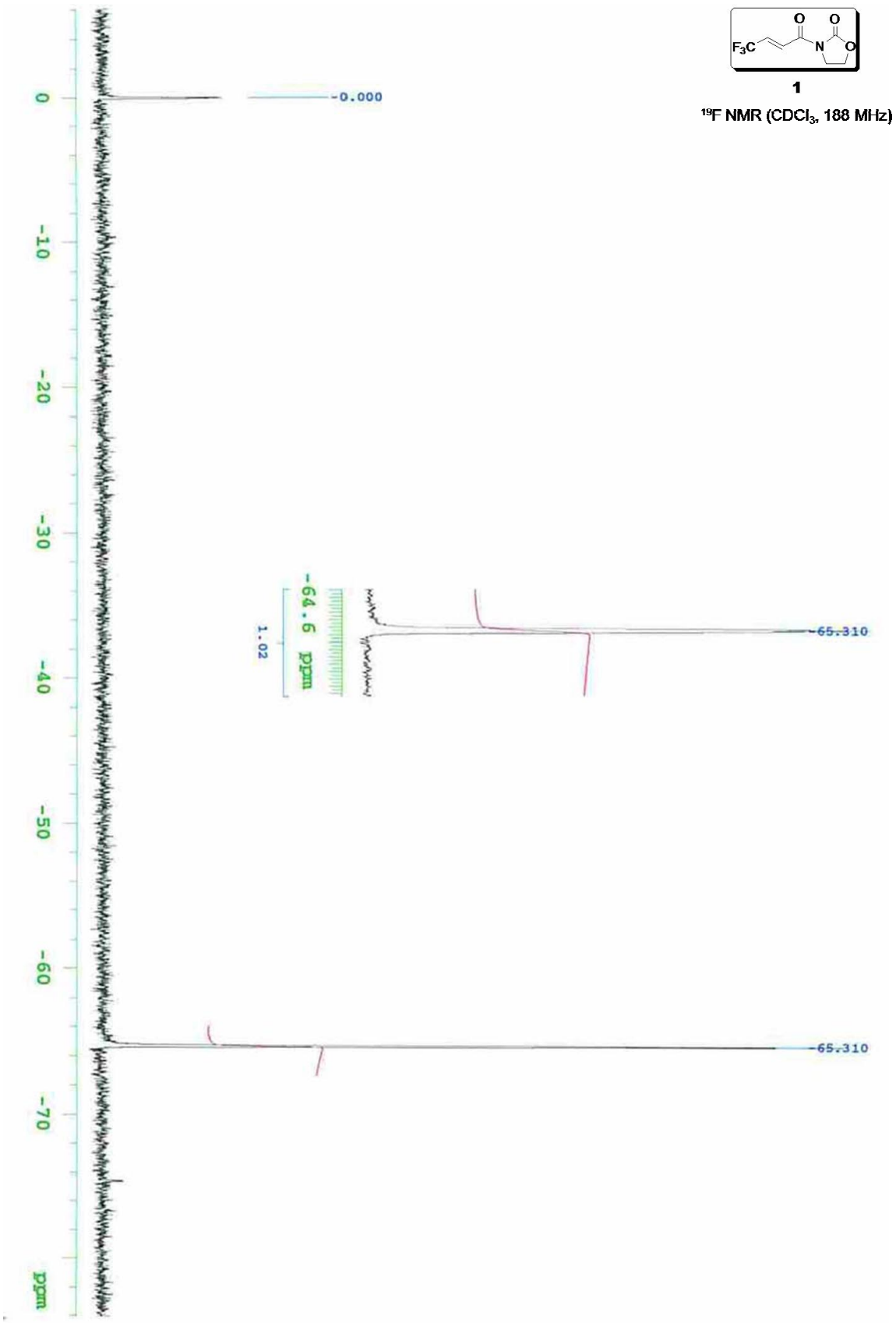
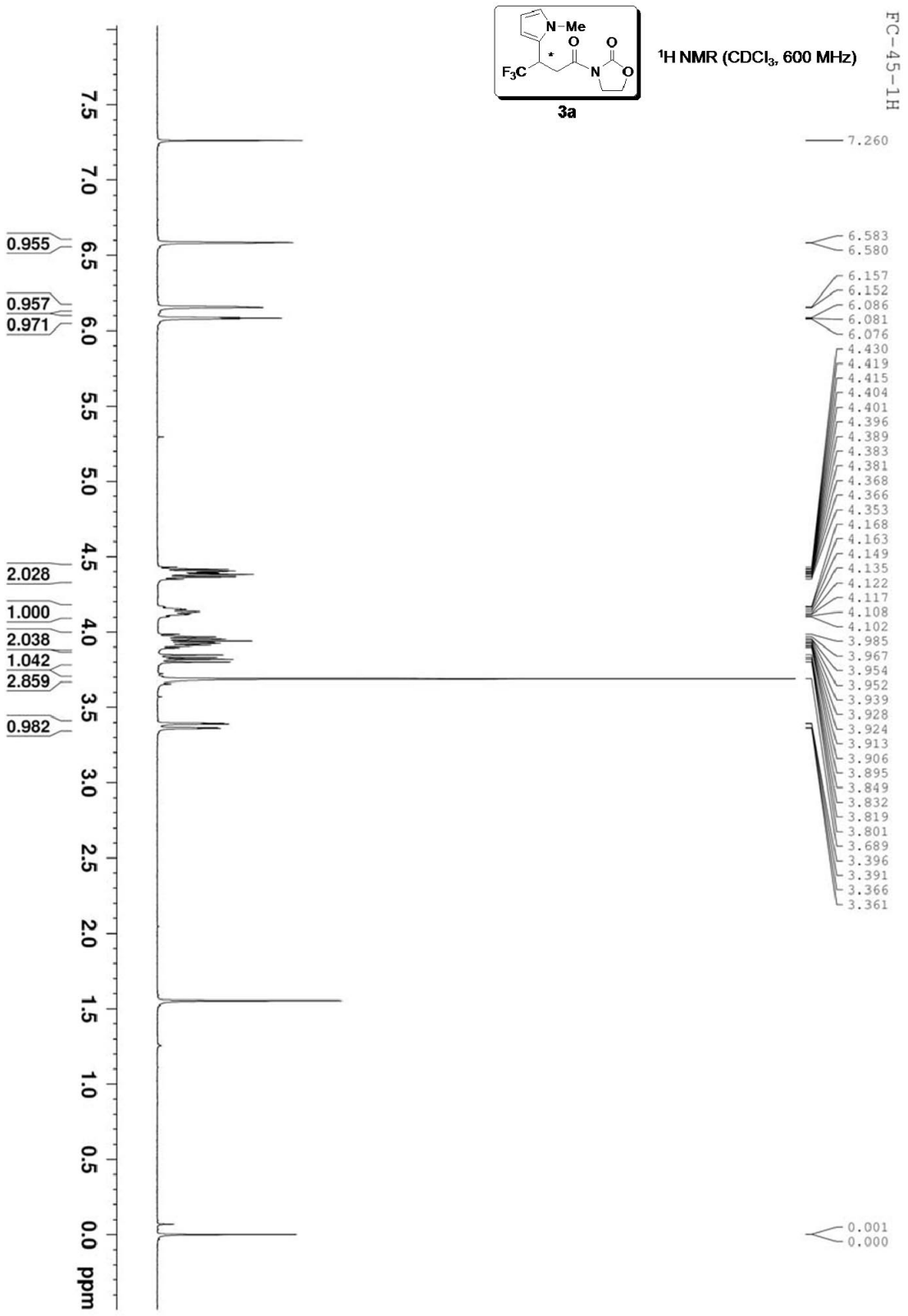
153.429
132.626
132.396
132.149
131.918
127.640
127.599
127.558
127.516
125.175
123.384
121.593
119.802
62.796
42.940
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



1

^{19}F NMR ($CDCl_3$, 188 MHz)


FC-45-1H
N-Me
O
O
F3C
*
N
O
3a
1H NMR (CDCl3, 600 MHz)
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6.583
6.580
6.157
6.152
6.086
6.081
6.076
4.430
4.419
4.415
4.404
4.401
4.396
4.389
4.383
4.381
4.368
4.366
4.353
4.168
4.163
4.149
4.135
4.122
4.117
4.108
4.102
3.985
3.967
3.954
3.952
3.939
3.928
3.924
3.913
3.906
3.895
3.849
3.832
3.819
3.801
3.689
3.396
3.391
3.366
3.361
0.001
0.000
0.955
0.957
0.971
2.028
1.000
2.038
1.042
2.859
0.982
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6.5
6.0
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1.0
0.5
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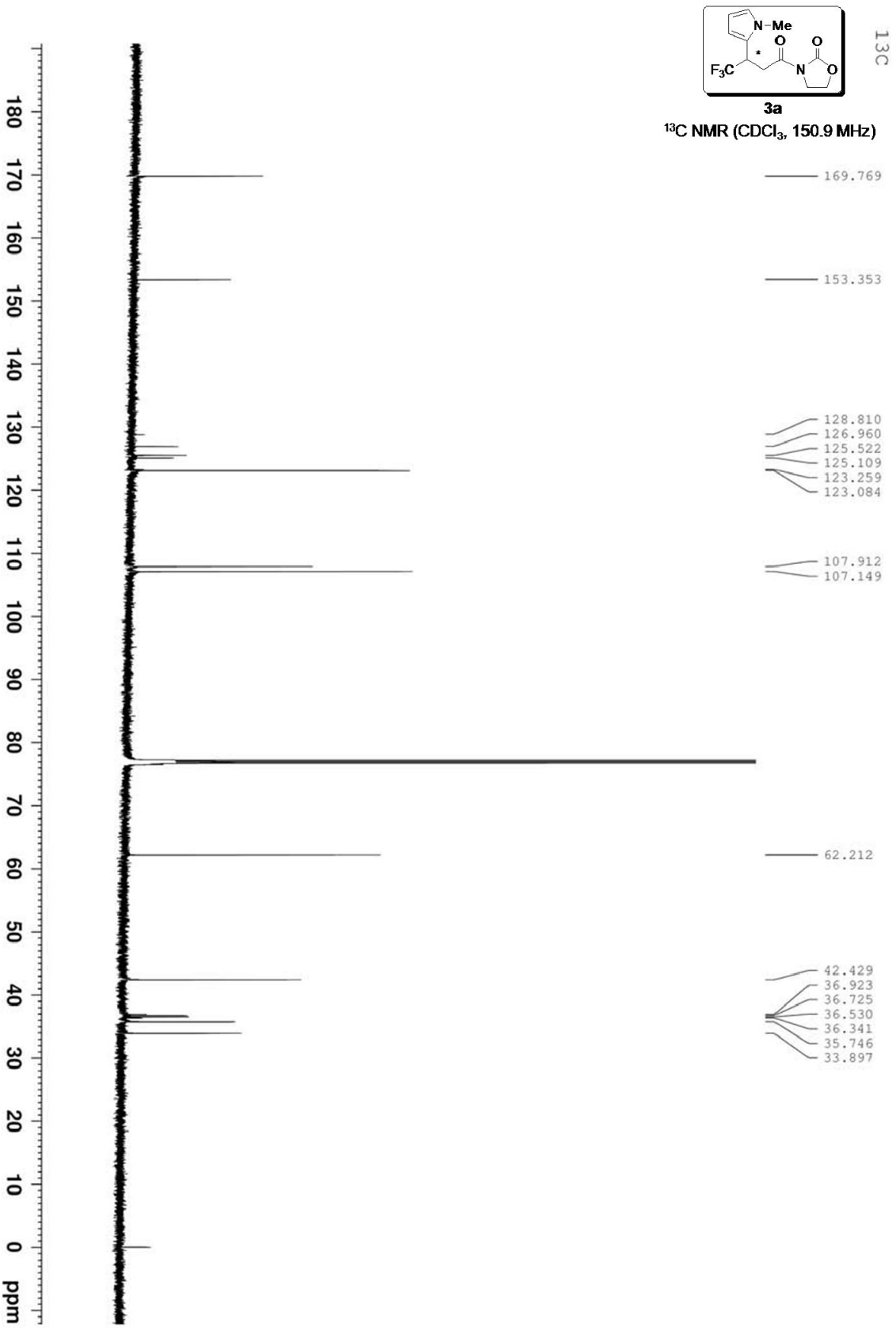
ppm


13C
N-Me
O
O
F3C
*
N
O
3a
13C NMR (CDCl3, 150.9 MHz)
169.769
153.353
128.810
126.960
125.522
125.109
123.259
123.084
107.912
107.149
62.212
42.429
36.923
36.725
36.530
36.341
35.746
33.897
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140
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110
100
90
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70
60
50
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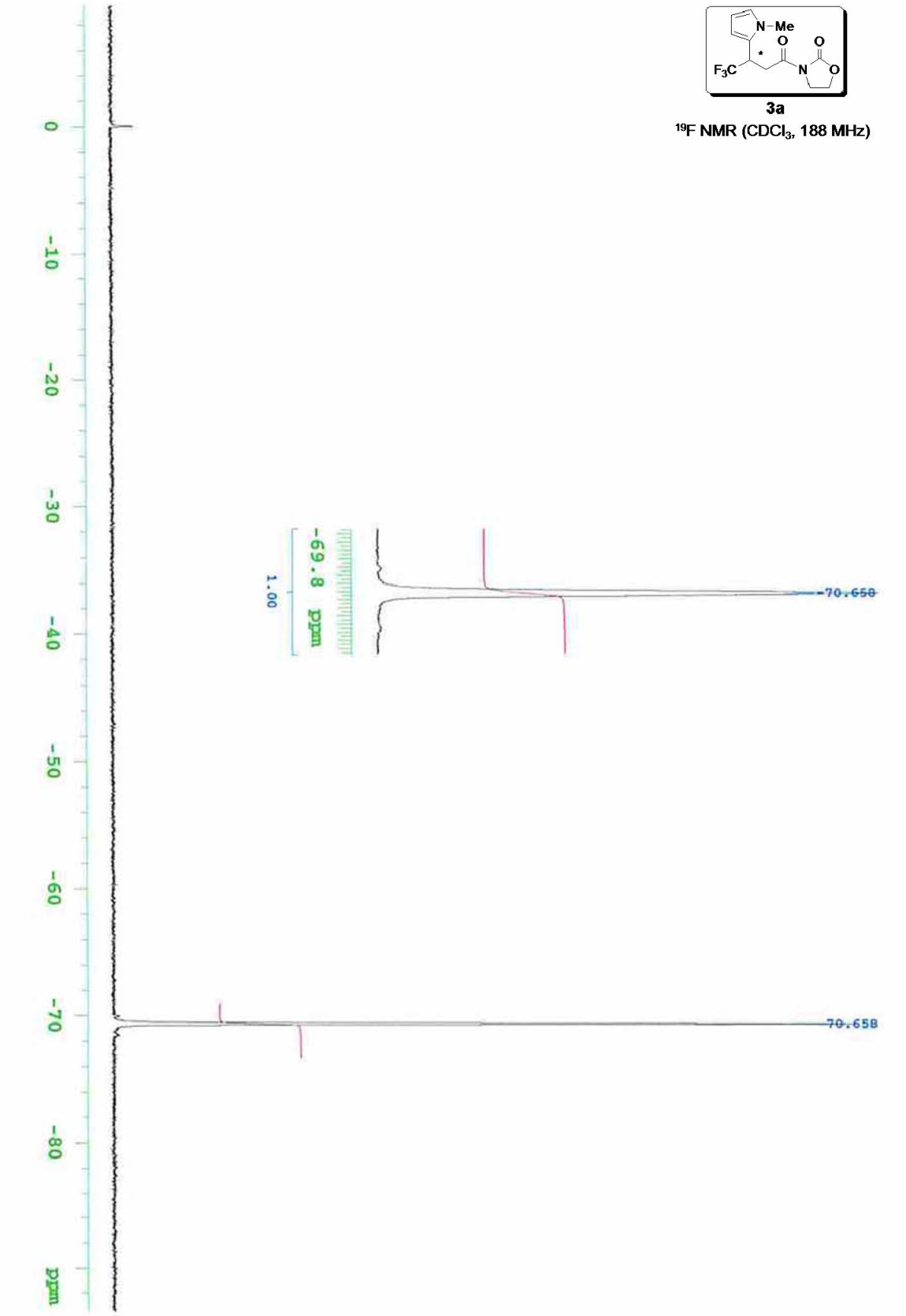
30
20
10
0
ppm


N-Me
O
O
F3C
*
N
O
3a
19F NMR (CDCl3, 188 MHz)
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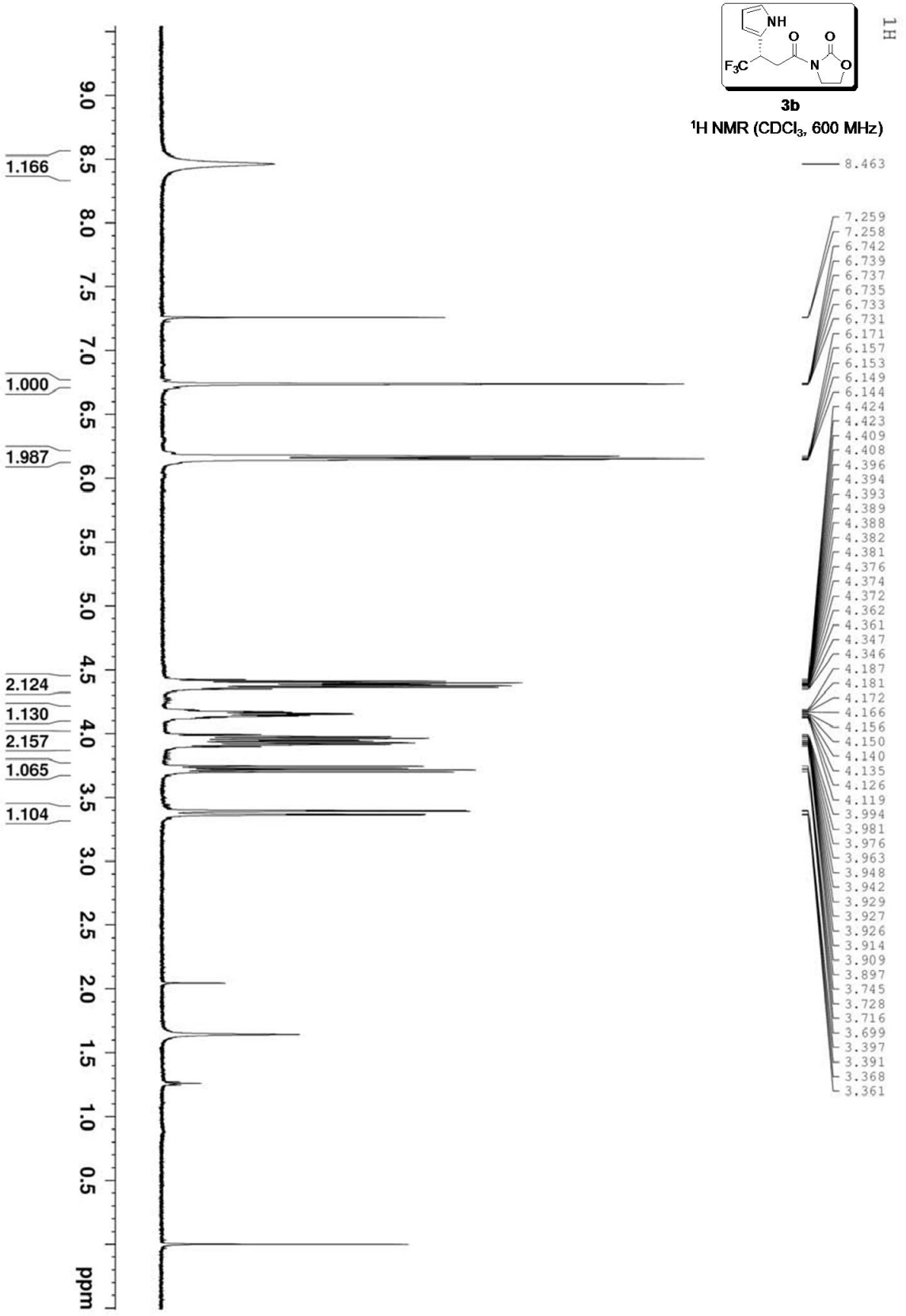
-20
-30
-40
-50
-60
-70
-80
ppm
1.00
-69.8 ppm
-70.658
-70.658


1H
3b
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8.463
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7.258
6.742
6.739
6.737
6.735
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6.731
6.171
6.157
6.153
6.149
6.144
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4.394
4.393
4.389
4.388
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4.376
4.374
4.372
4.362
4.361
4.347
4.346
4.187
4.181
4.172
4.166
4.156
4.150
4.140
4.135
4.126
4.119
3.994
3.981
3.976
3.963
3.948
3.942
3.929
3.927
3.926
3.914
3.909
3.897
3.745
3.728
3.716
3.699
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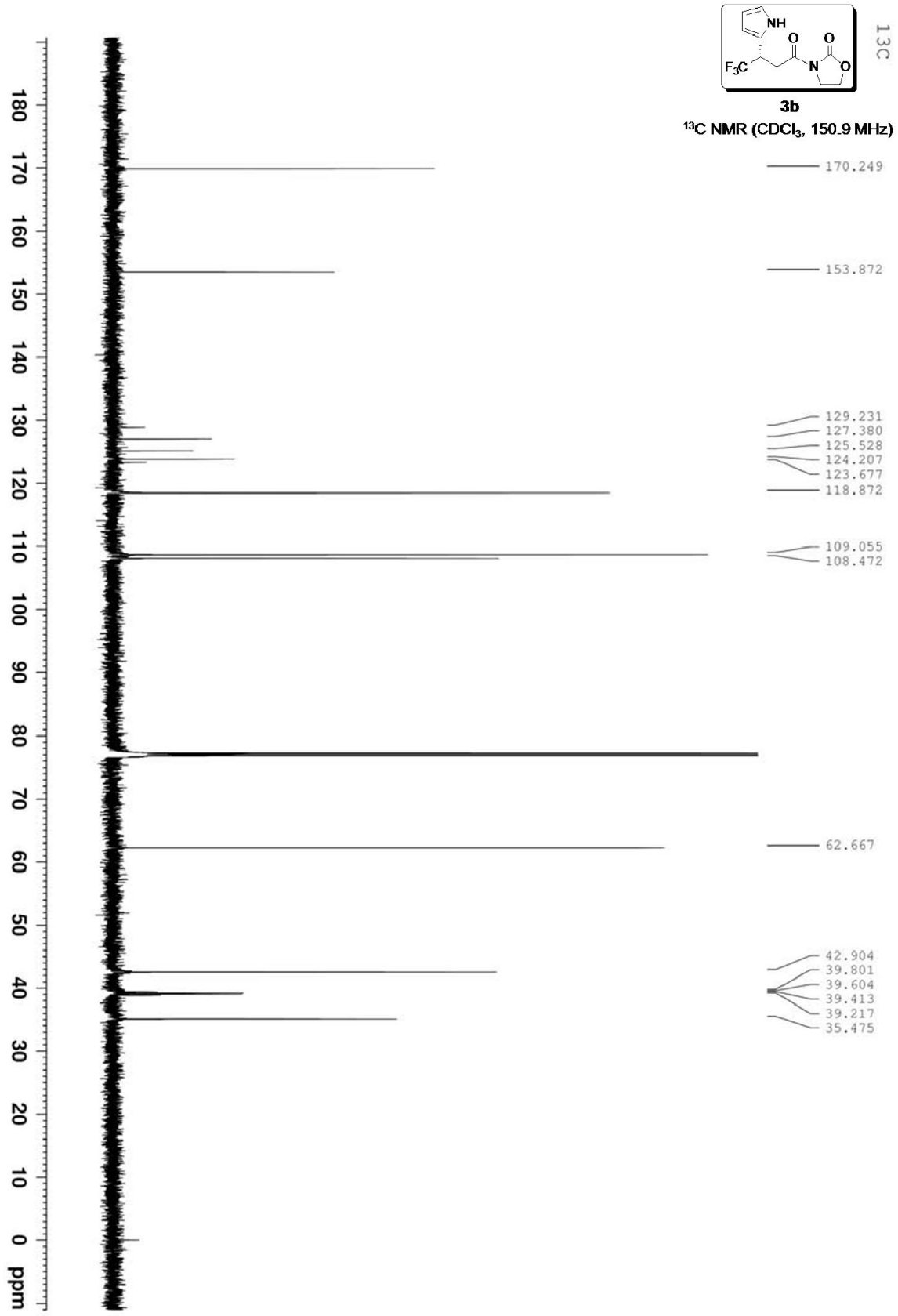
1.104
ppm


13C
3b
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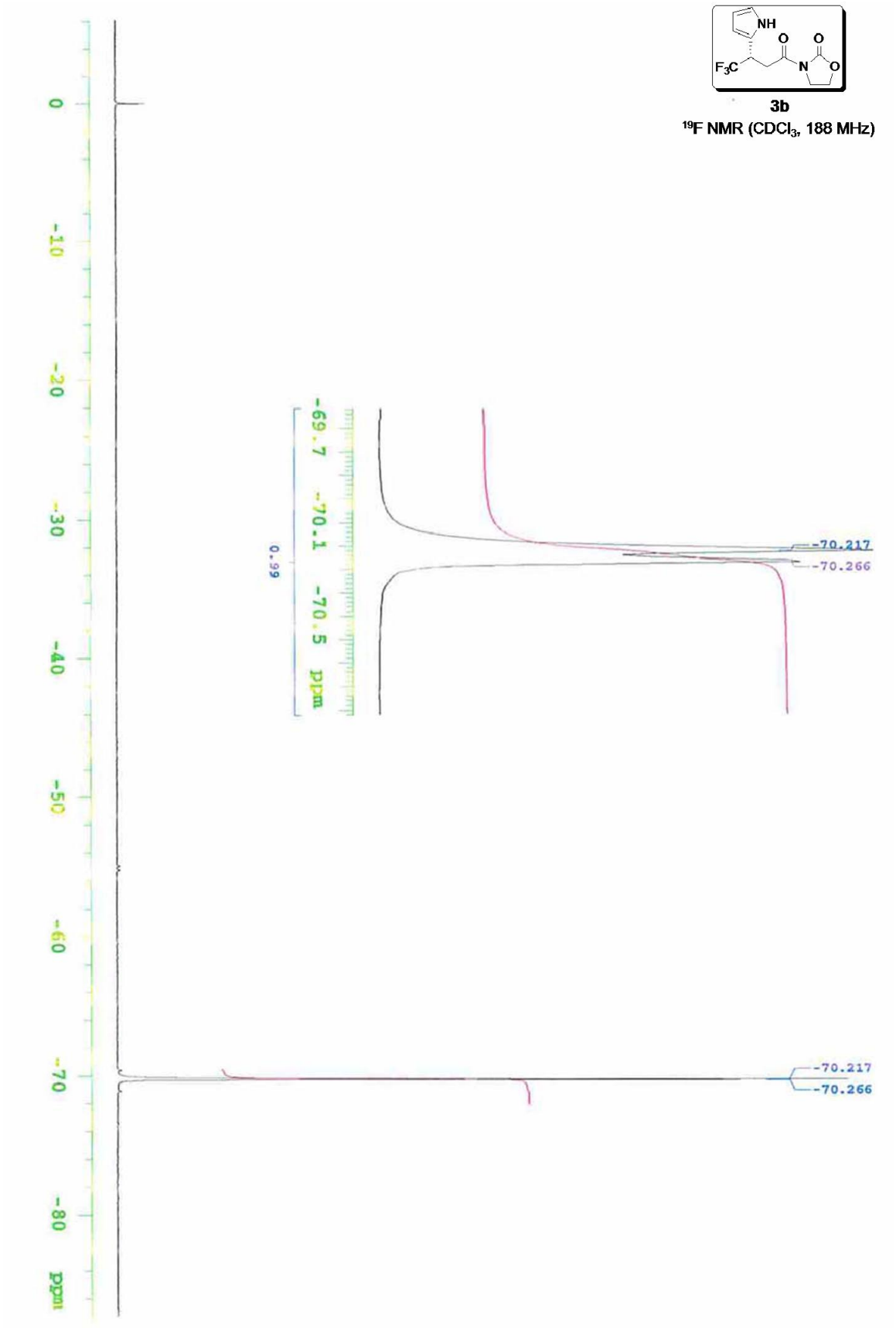
170.249
153.872
129.231
127.380
125.528
124.207
123.677
118.872
109.055
108.472
62.667
42.904
39.801
39.604
39.413
39.217
35.475
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


NH
O
O
F3C
N
O
3b
19F NMR (CDCl3, 188 MHz)
0
-10
-20
-30
-40
-50
-60
-70
-80
ppm
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-70.1
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ppm
0.99
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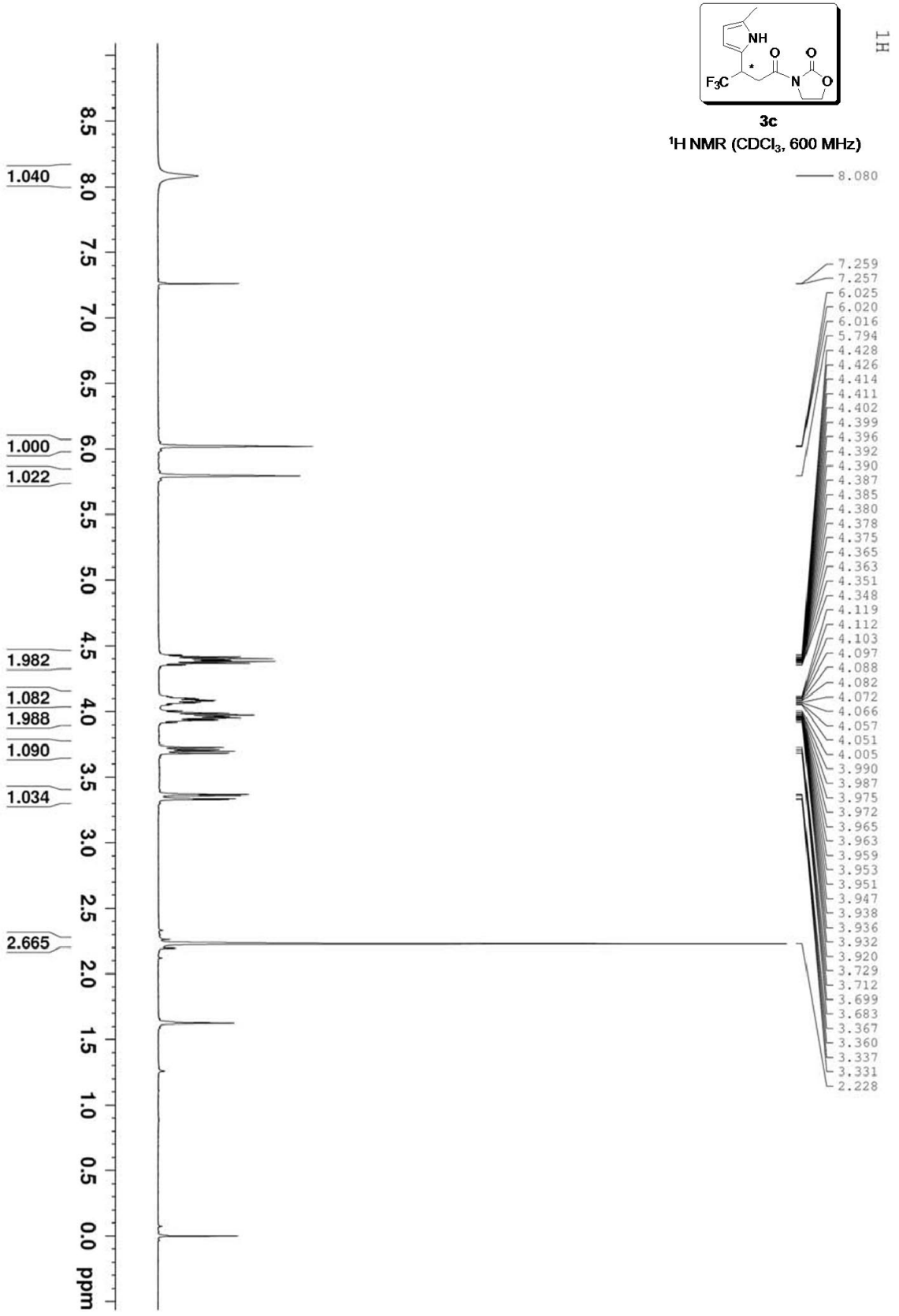
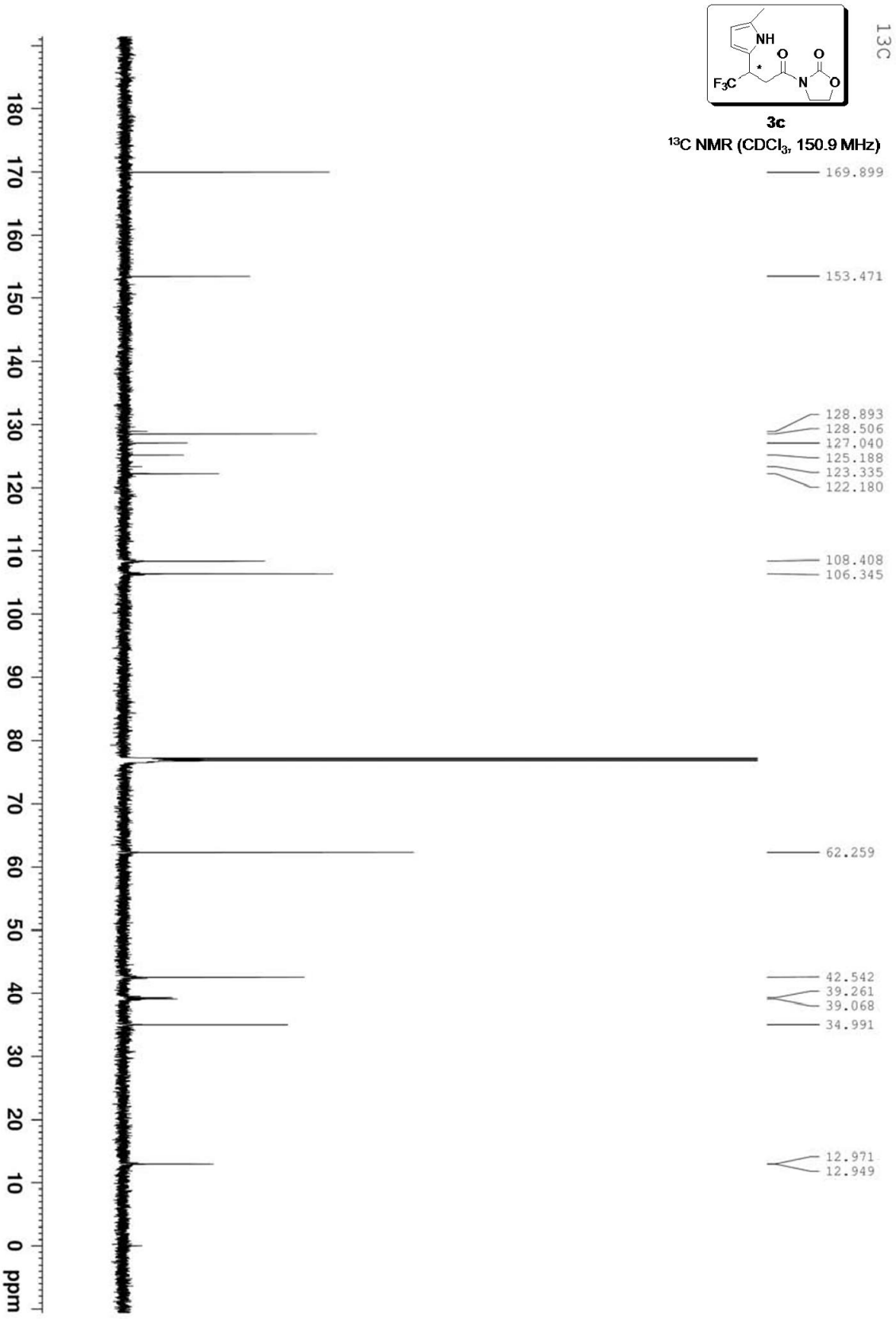
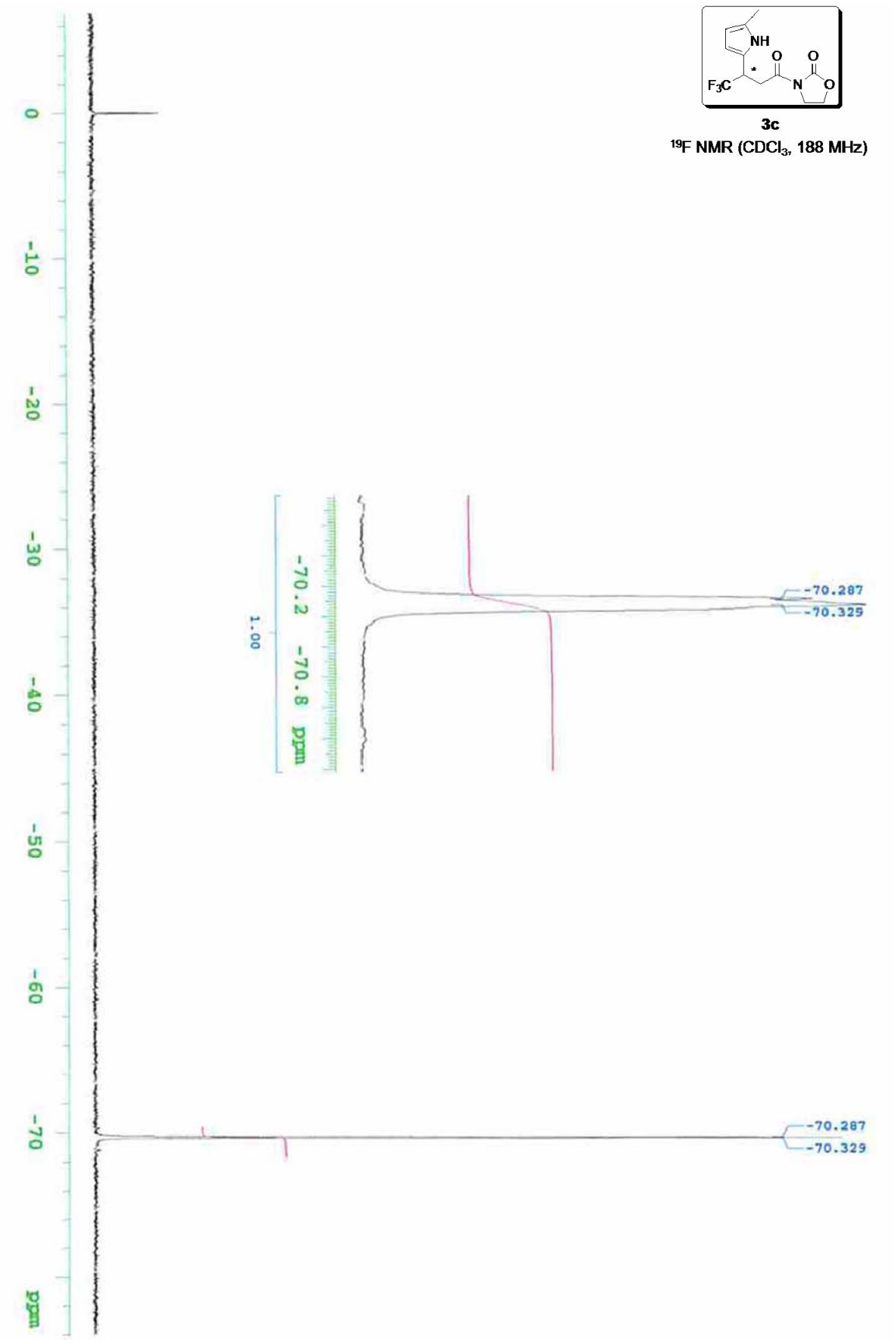
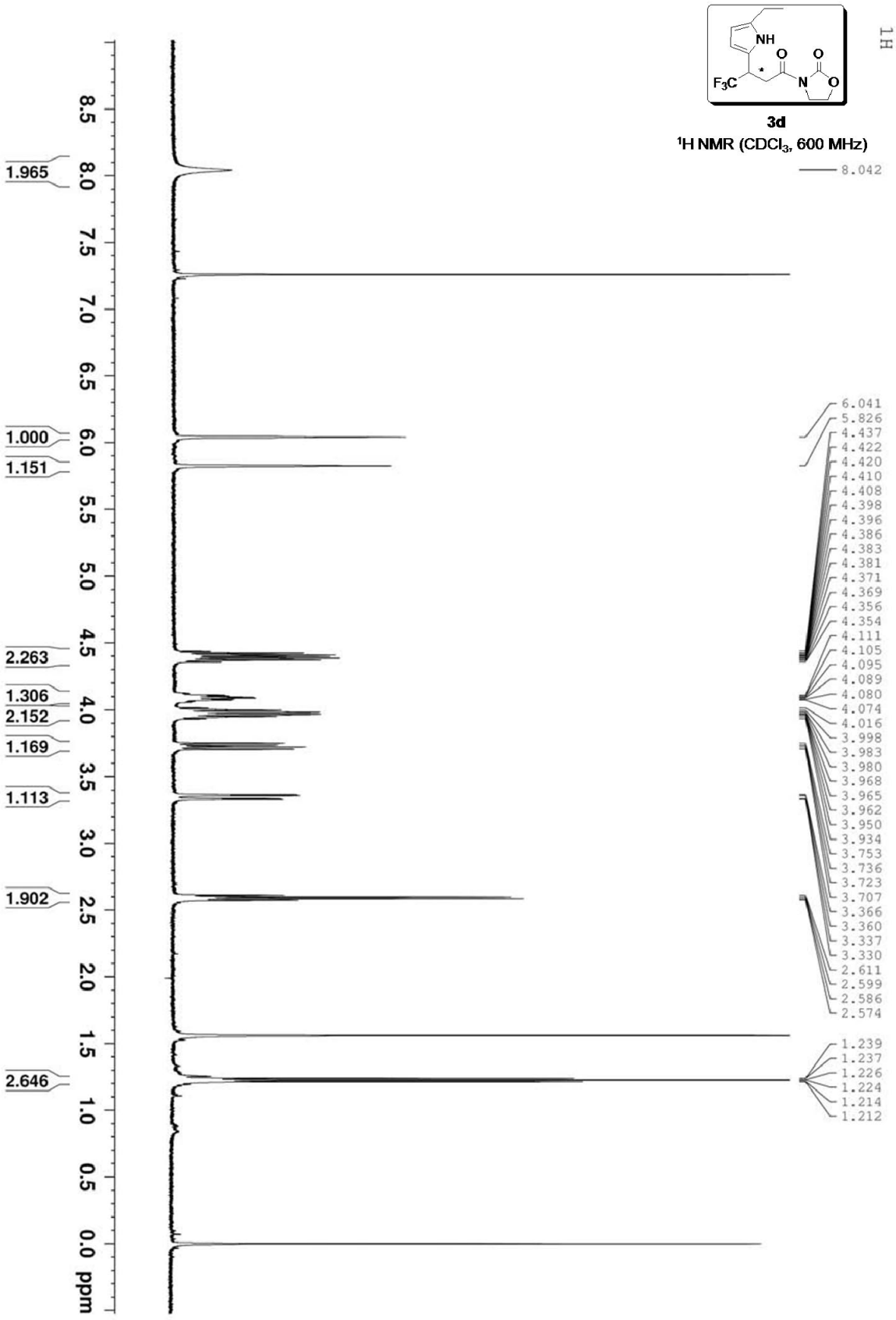
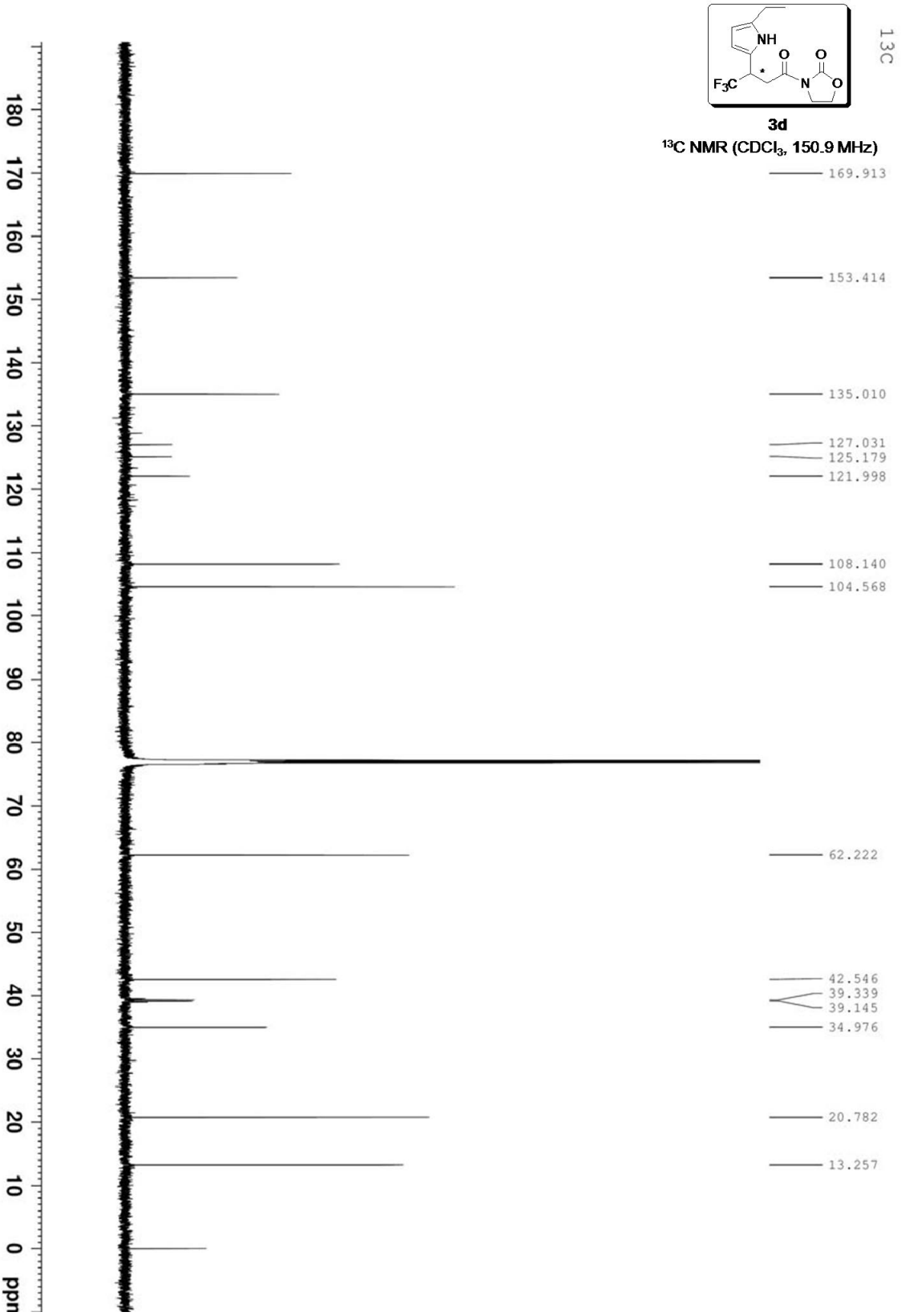
-70.266

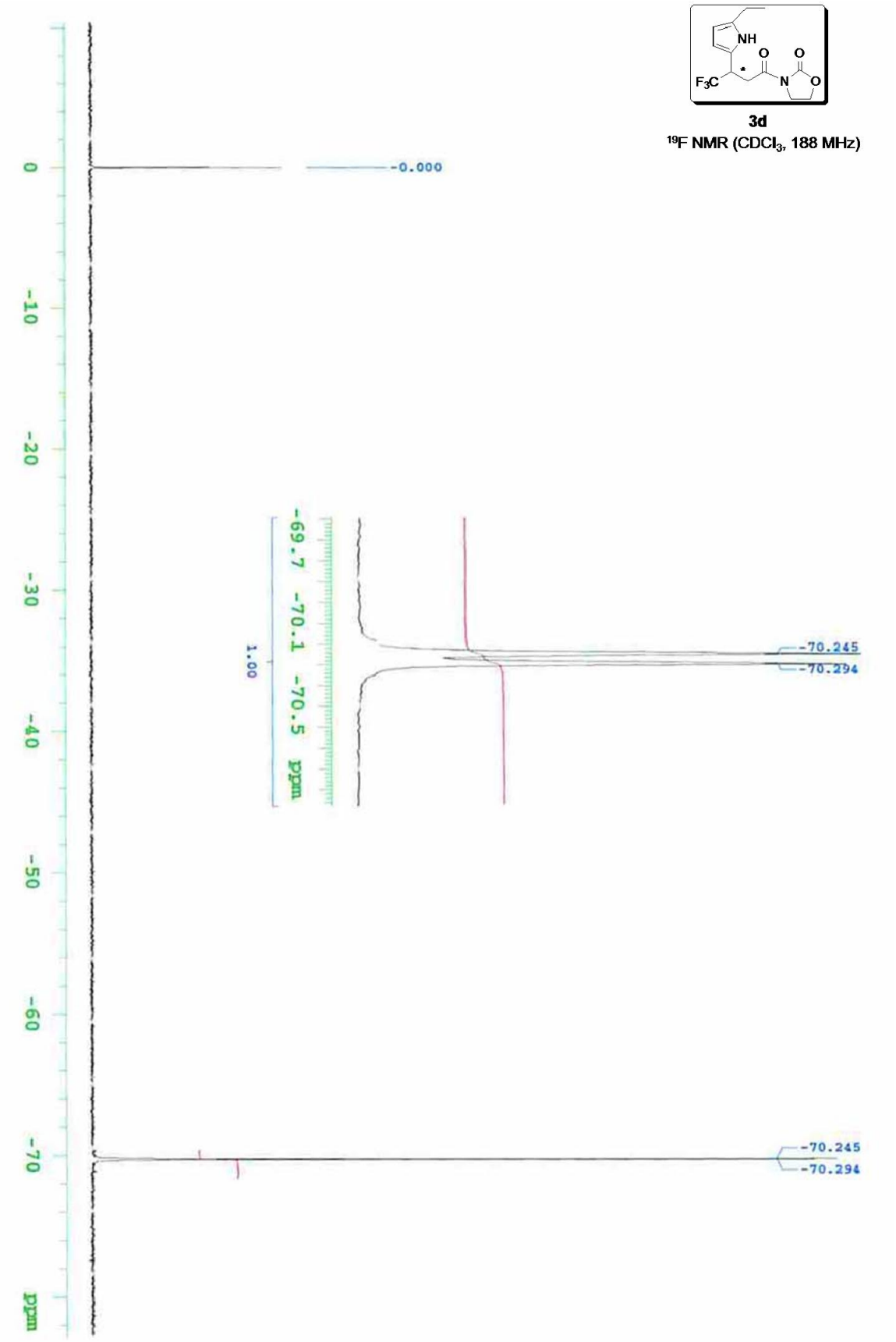

3c
^{1}H NMR ($CDCl_3$, 600 MHz)
1H
8.080
7.259
7.257
6.025
6.020
6.016
5.794
4.428
4.426
4.414
4.411
4.402
4.399
4.396
4.392
4.390
4.387
4.385
4.380
4.378
4.375
4.365
4.363
4.351
4.348
4.119
4.112
4.103
4.097
4.088
4.082
4.072
4.066
4.057
4.051
4.005
3.990
3.987
3.975
3.972
3.965
3.963
3.959
3.953
3.951
3.947
3.938
3.936
3.932
3.920
3.729
3.712
3.699
3.683
3.367
3.360
3.337
3.331
2.228
1.040
1.000
1.022
1.982
1.082
1.988
1.090
1.034
2.665
ppm

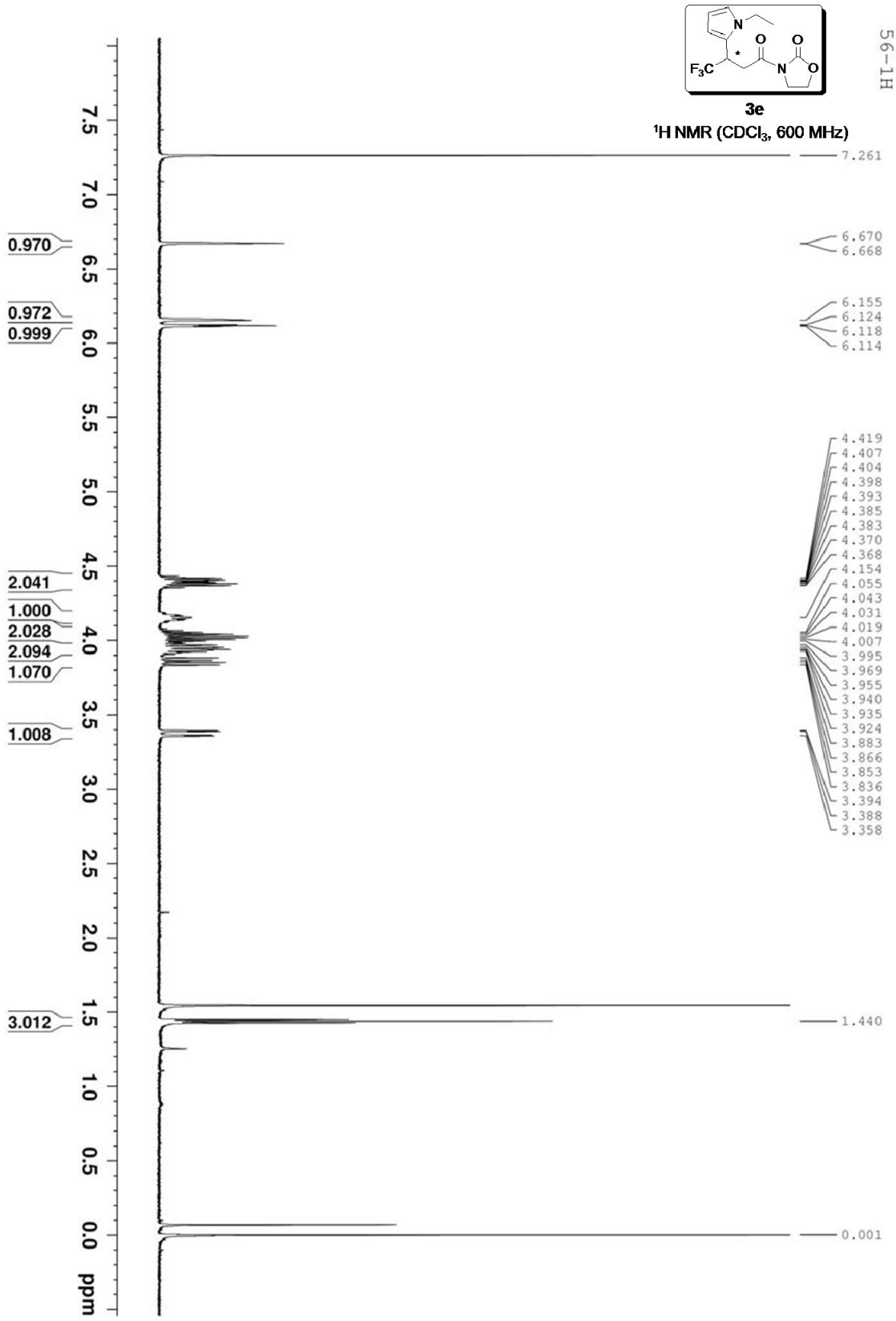

13C
3c
^{13}C NMR ($CDCl_3$, 150.9 MHz)
169.899
153.471
128.893
128.506
127.040
125.188
123.335
122.180
108.408
106.345
62.259
42.542
39.261
39.068
34.991
12.971
12.949
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

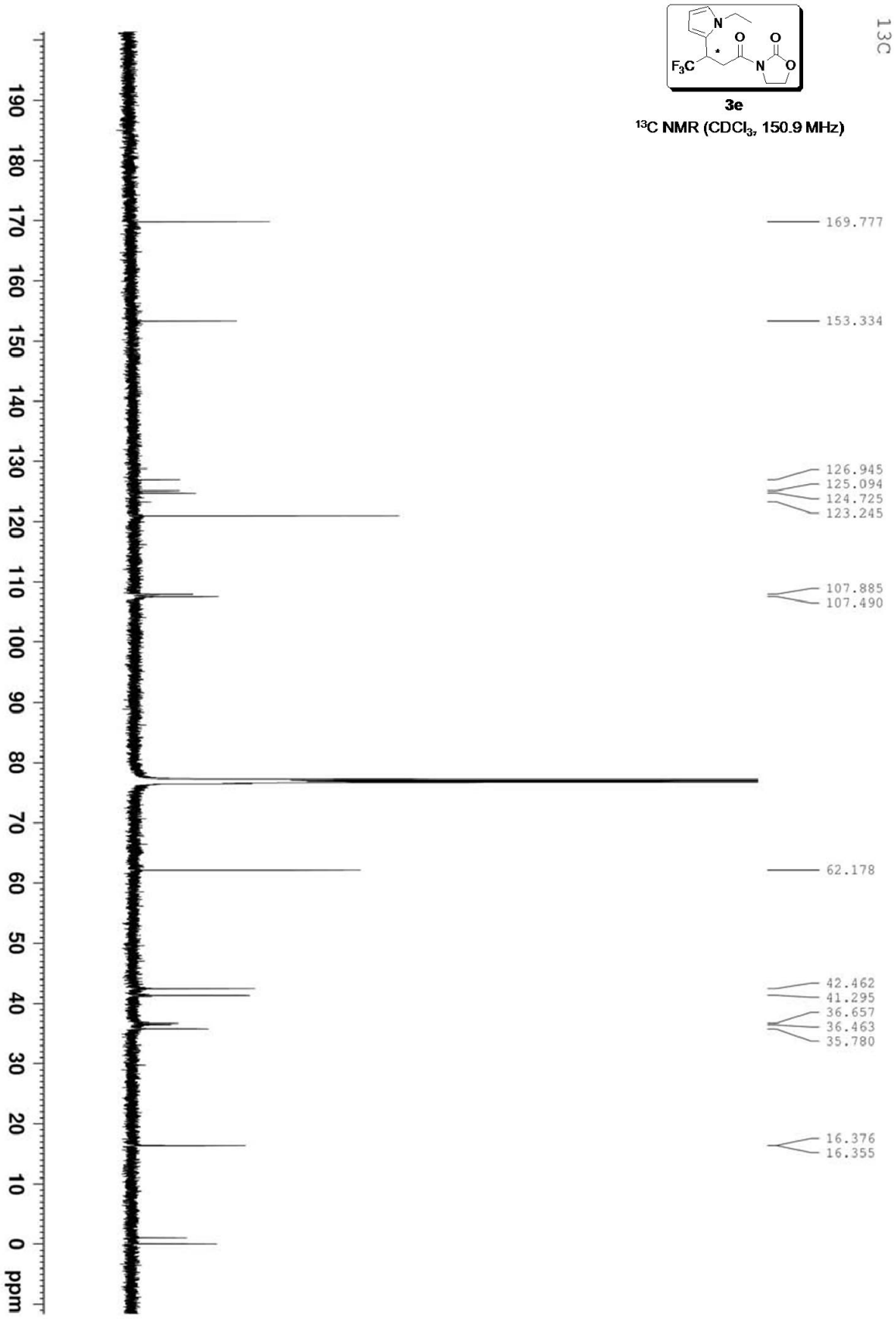

NH
O
O
F3C
N
O
3c
19F NMR (CDCl3, 188 MHz)
0
-10
-20
-30
-40
-50
-60
-70
ppm
-70.287
-70.329
1.00
-70.2
-70.8
ppm
-70.287
-70.329


1H
3d
1H NMR (CDCl3, 600 MHz)
8.042
6.041
5.826
4.437
4.422
4.420
4.410
4.408
4.398
4.396
4.386
4.383
4.381
4.371
4.369
4.356
4.354
4.111
4.105
4.095
4.089
4.080
4.074
4.016
3.998
3.983
3.980
3.968
3.965
3.962
3.950
3.934
3.753
3.736
3.723
3.707
3.366
3.360
3.337
3.330
2.611
2.599
2.586
2.574
1.239
1.237
1.226
1.224
1.214
1.212
1.965
1.000
1.151
2.263
1.306
2.152
1.169
1.113
1.902
2.646
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

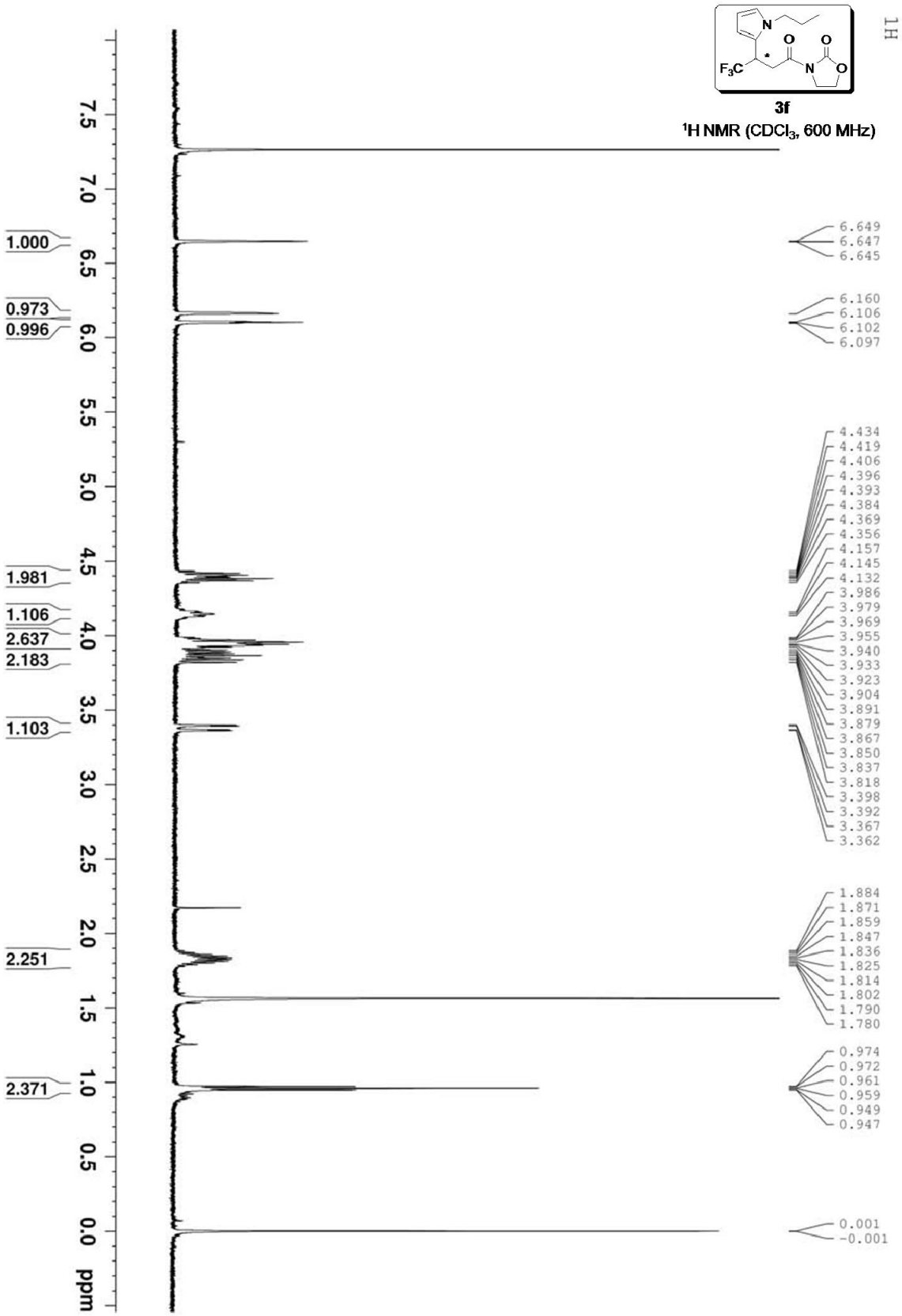

13C
3d
13C NMR (CDCl3, 150.9 MHz)
169.913
153.414
135.010
127.031
125.179
121.998
108.140
104.568
62.222
42.546
39.339
39.145
34.976
20.782
13.257
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

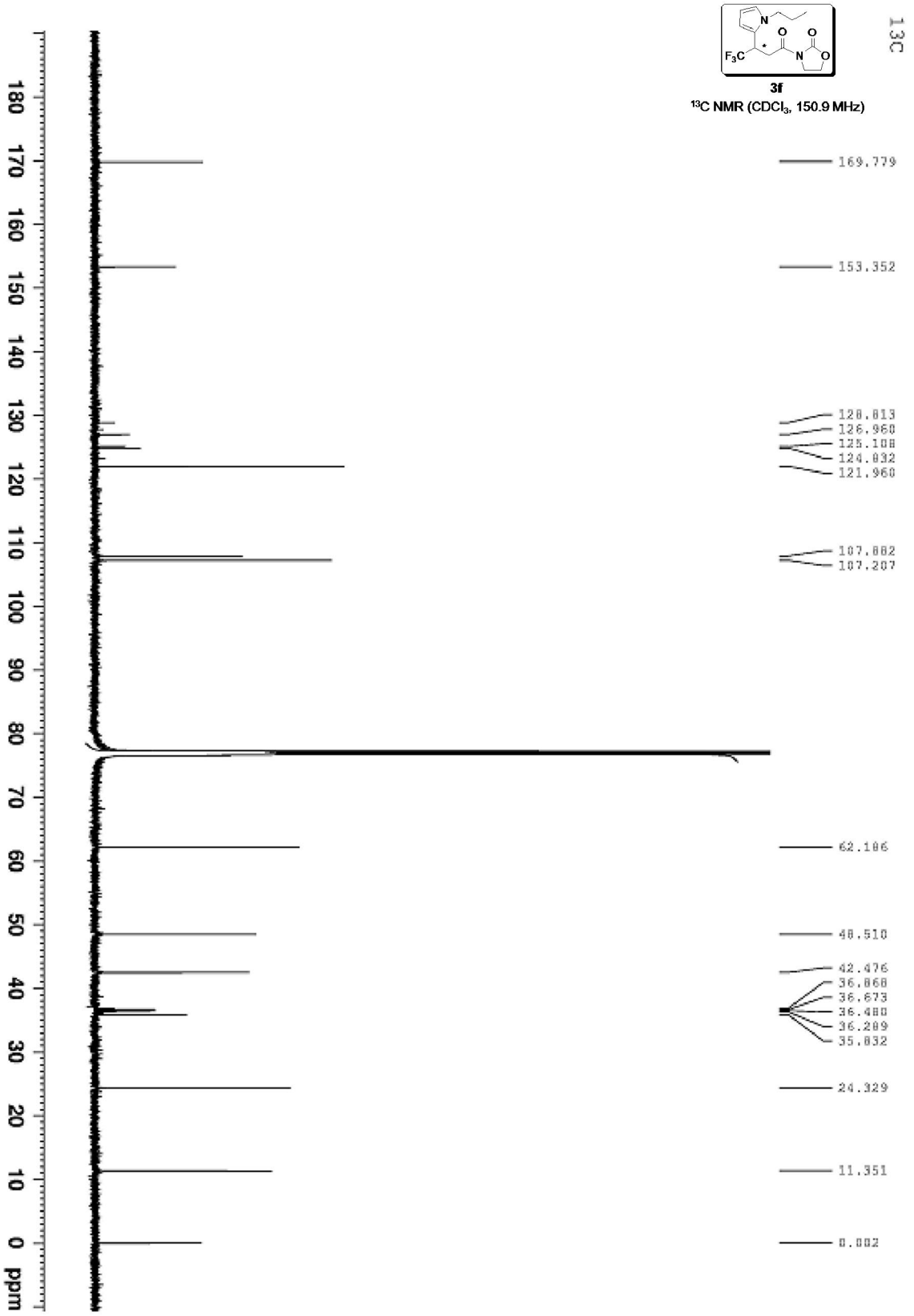

NH
O
O
F3C
N
O
3d
19F NMR (CDCl3, 188 MHz)
-0.000
-70.245
-70.294
-69.7 -70.1 -70.5 ppm
1.00
-70.245
-70.294
0
-10
-20
-30
-40
-50
-60
-70
ppm

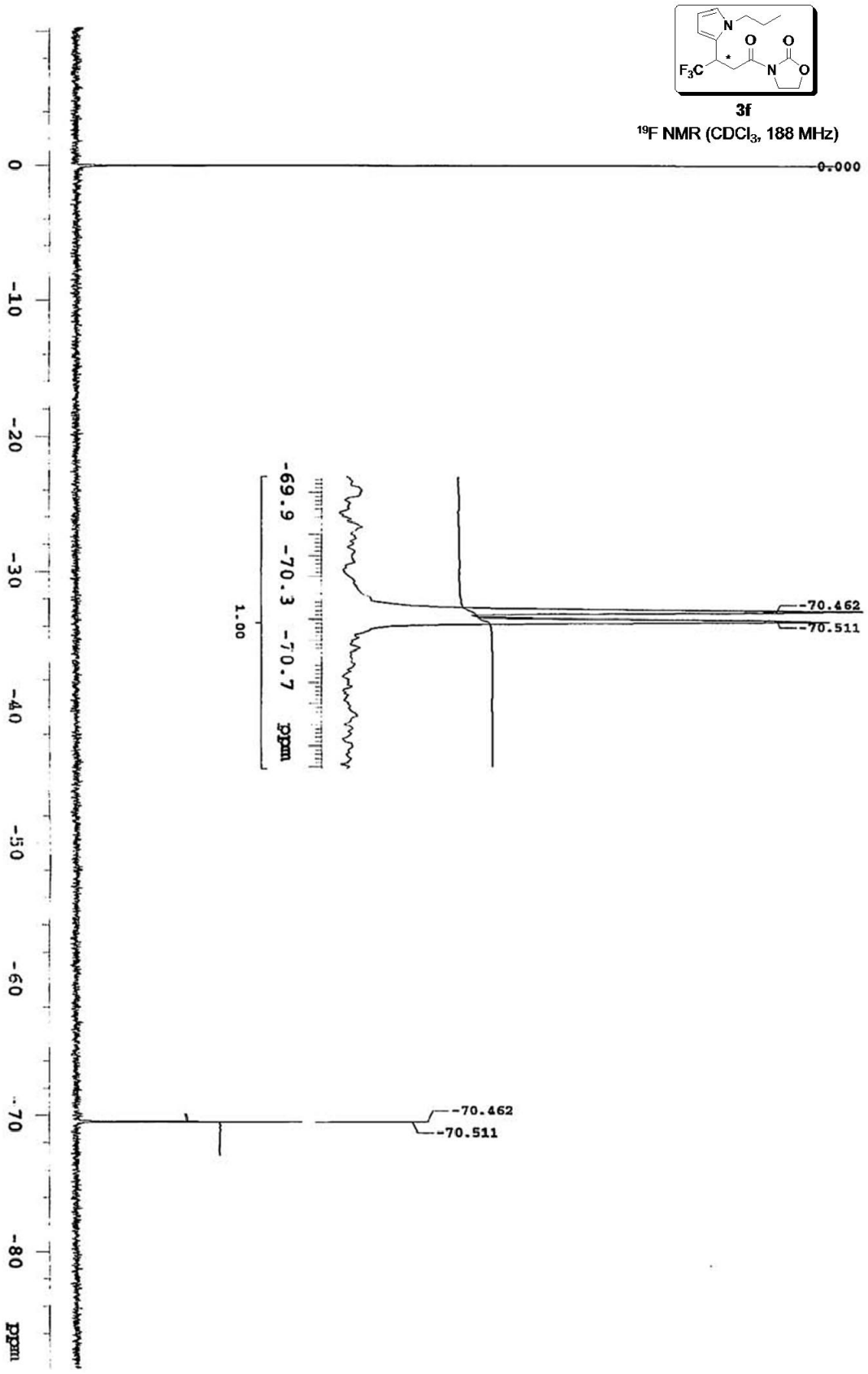

56-1H
3e
1H NMR (CDCl3, 600 MHz)
7.261
6.670
6.668
6.155
6.124
6.118
6.114
4.419
4.407
4.404
4.398
4.393
4.385
4.383
4.370
4.368
4.154
4.055
4.043
4.031
4.019
4.007
3.995
3.969
3.955
3.940
3.935
3.924
3.883
3.866
3.853
3.836
3.394
3.388
3.358
1.440
0.001
0.970
0.972
0.999
2.041
1.000
2.028
2.094
1.070
1.008
3.012
ppm

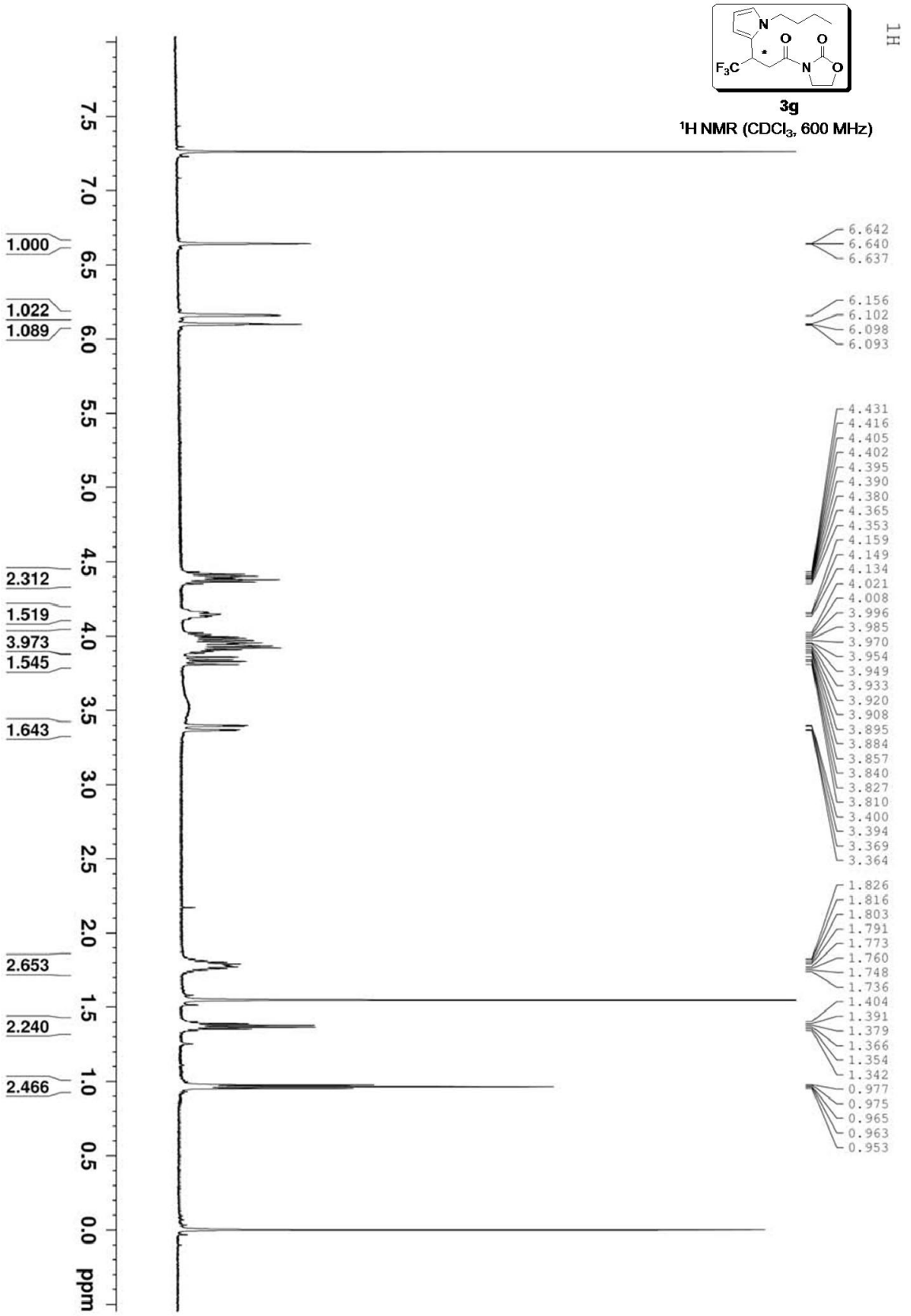

13C
3e
^{13}C NMR ($CDCl_3$, 150.9 MHz)
169.777
153.334
126.945
125.094
124.725
123.245
107.885
107.490
62.178
42.462
41.295
36.657
36.463
35.780
16.376
16.355
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

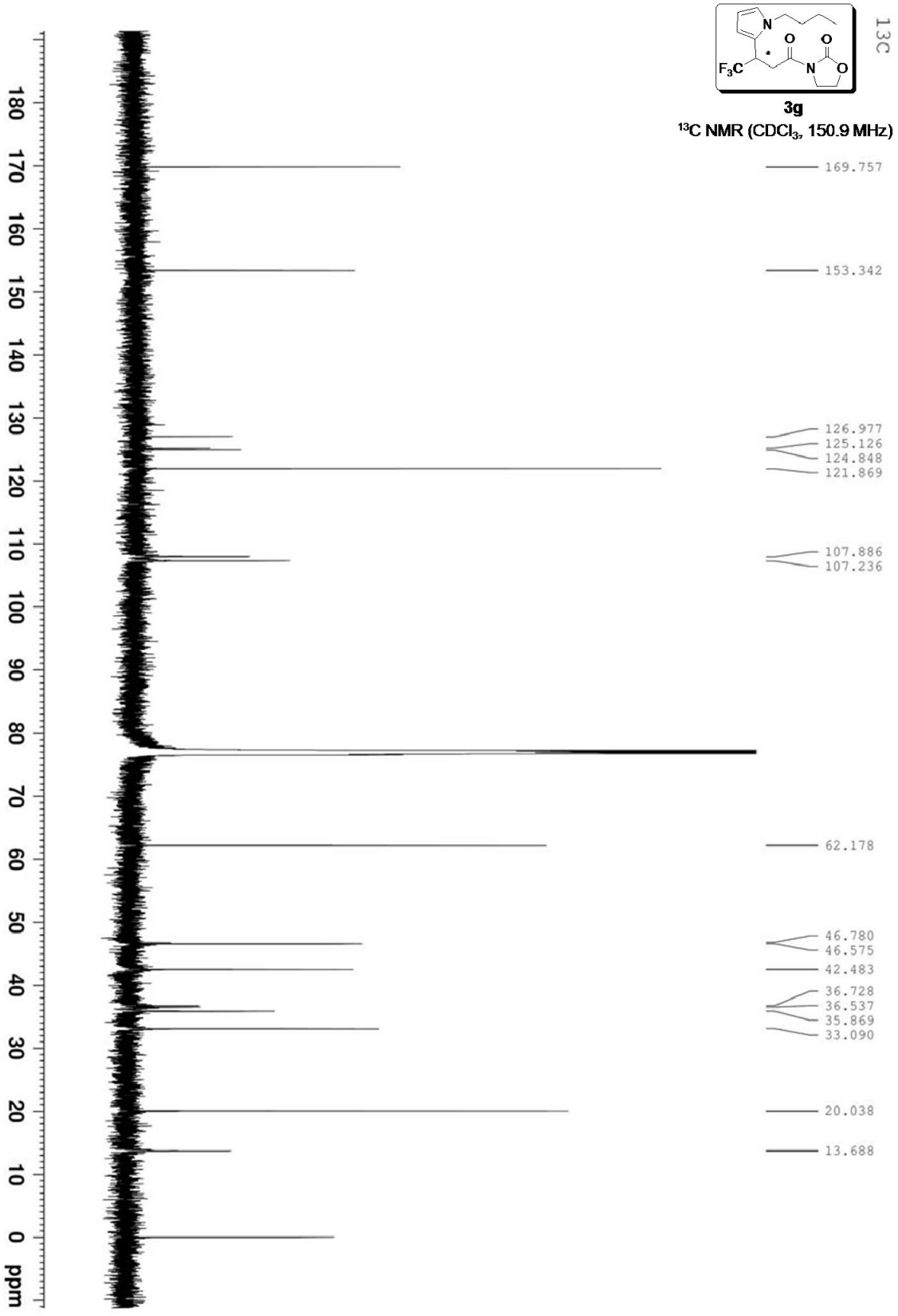

-0.000
3e
19F NMR (CDCl3, 188 MHz)
0
-10
-20
-30
-40
-50
-60
-70
ppm
1.00
-70.0
-70.8
ppm
-70.504
-70.546
-70.504
-70.546

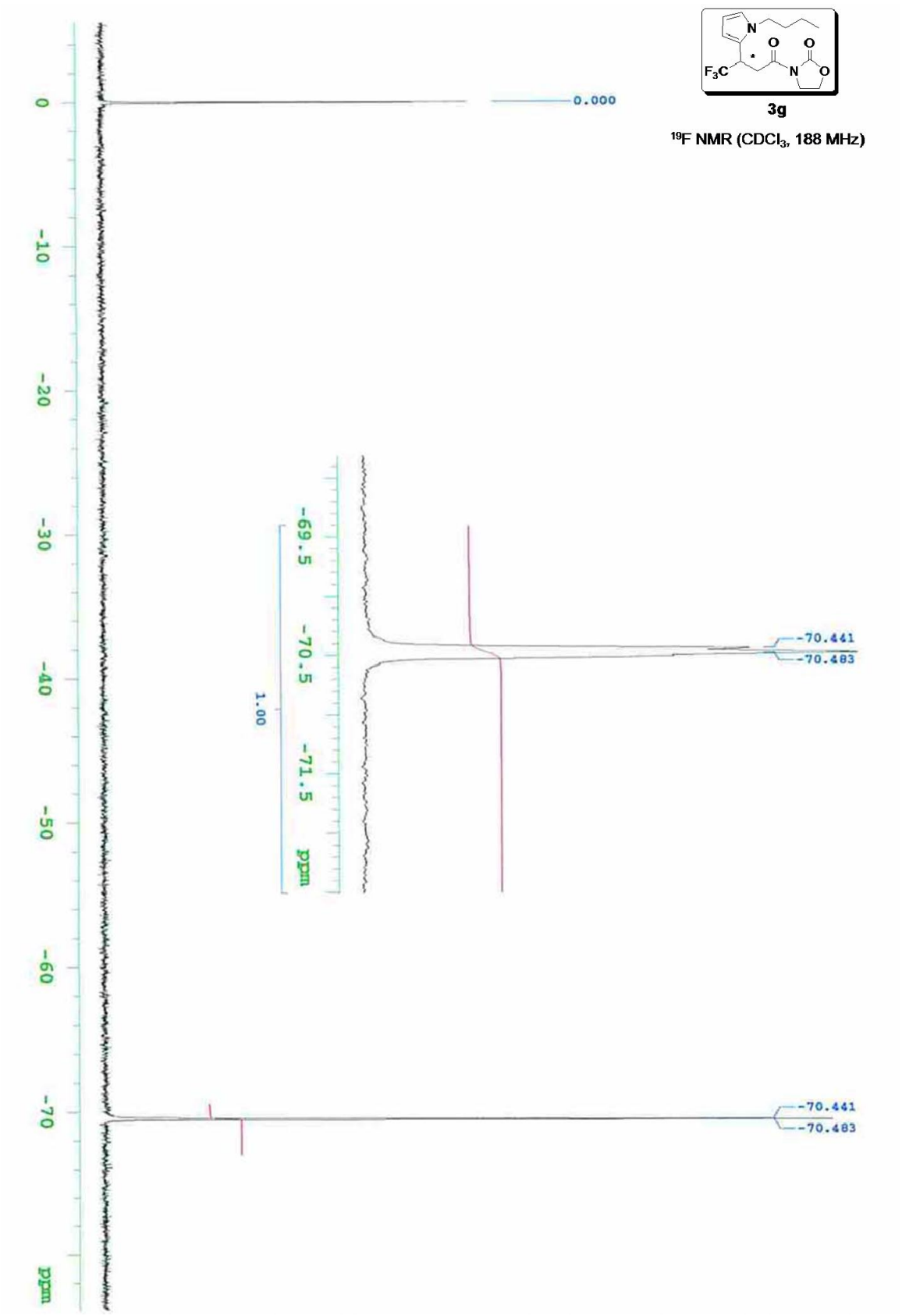

1H
3f
1H NMR (CDCl3, 600 MHz)
6.649
6.647
6.645
6.160
6.106
6.102
6.097
4.434
4.419
4.406
4.396
4.393
4.384
4.369
4.356
4.157
4.145
4.132
3.986
3.979
3.969
3.955
3.940
3.933
3.923
3.904
3.891
3.879
3.867
3.850
3.837
3.818
3.398
3.392
3.367
3.362
1.884
1.871
1.859
1.847
1.836
1.825
1.814
1.802
1.790
1.780
0.974
0.972
0.961
0.959
0.949
0.947
0.001
-0.001
1.000
0.973
0.996
1.981
1.106
2.637
2.183
1.103
2.251
2.371
ppm

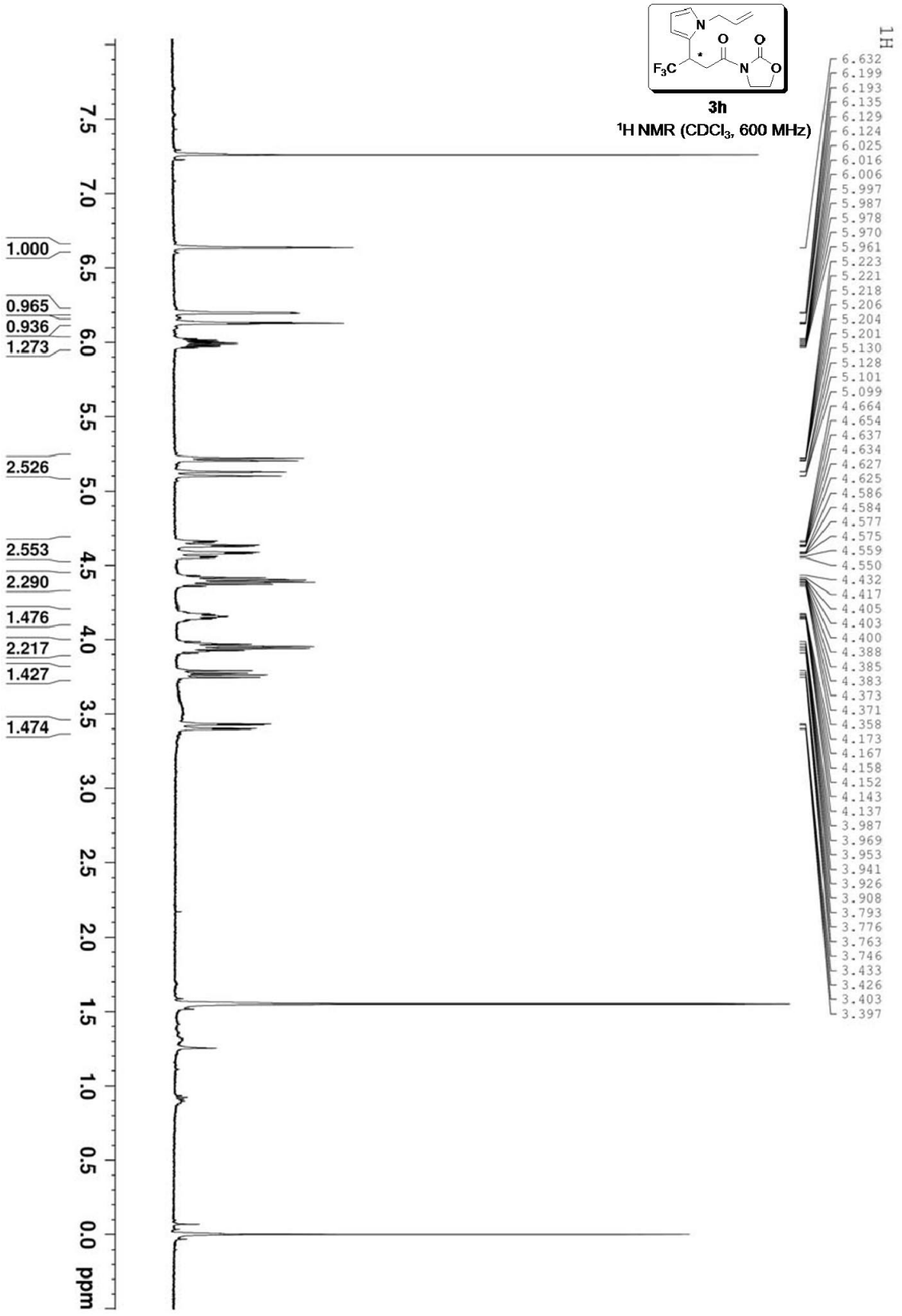

13C
3f
^{13}C NMR ($CDCl_3$, 150.9 MHz)
169.779
153.352
128.813
126.960
125.108
124.032
121.960
107.882
107.207
62.106
48.510
42.476
36.868
36.673
36.480
36.289
35.832
24.329
11.351
0.002
ppm

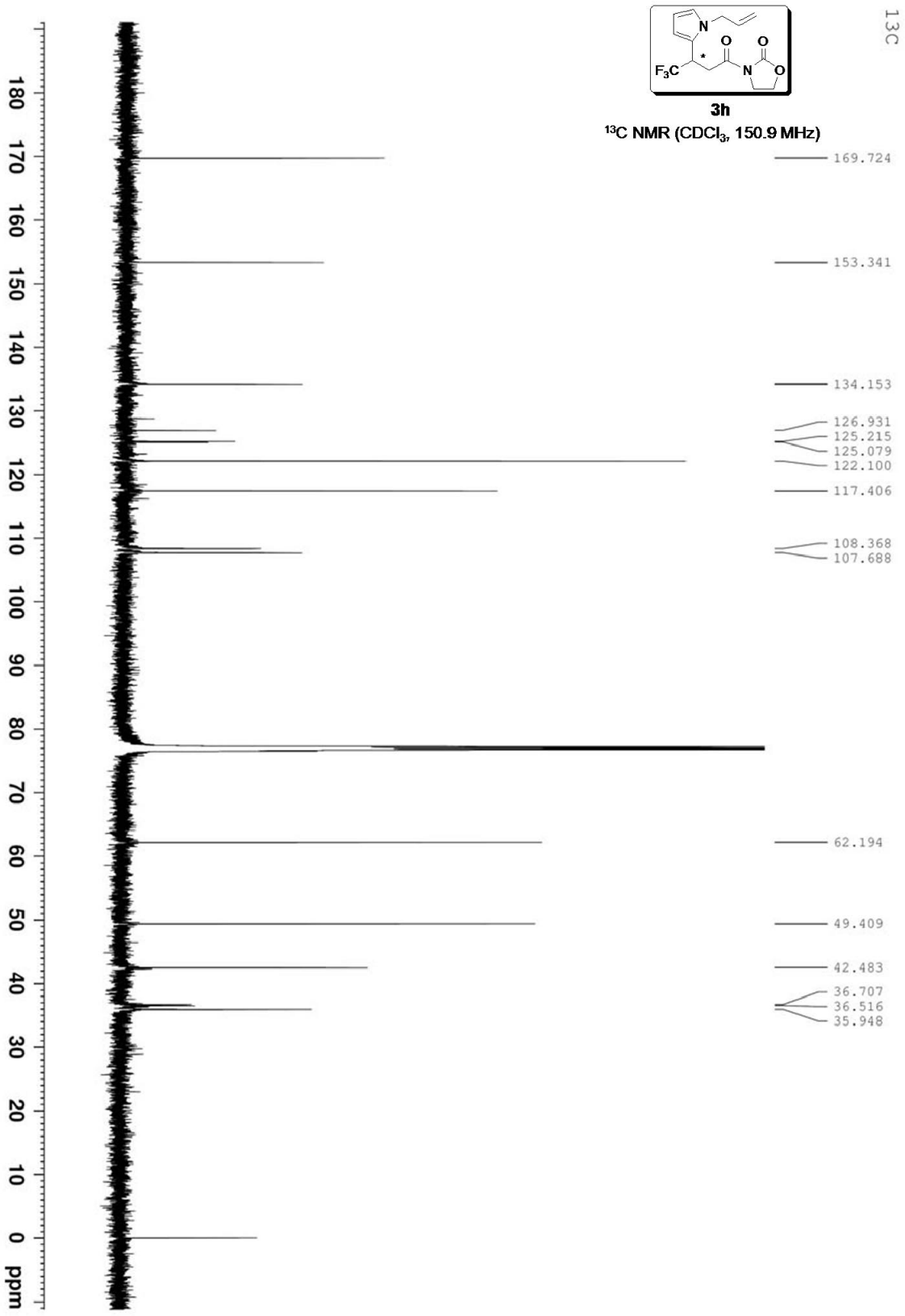

3f
19F NMR (CDCl3, 188 MHz)
0.000
-70.462
-70.511
-69.9 -70.3 -70.7 ppm
1.00
-70.462
-70.511
0
-10
-20
-30
-40
-50
-60
-70
-80
ppm

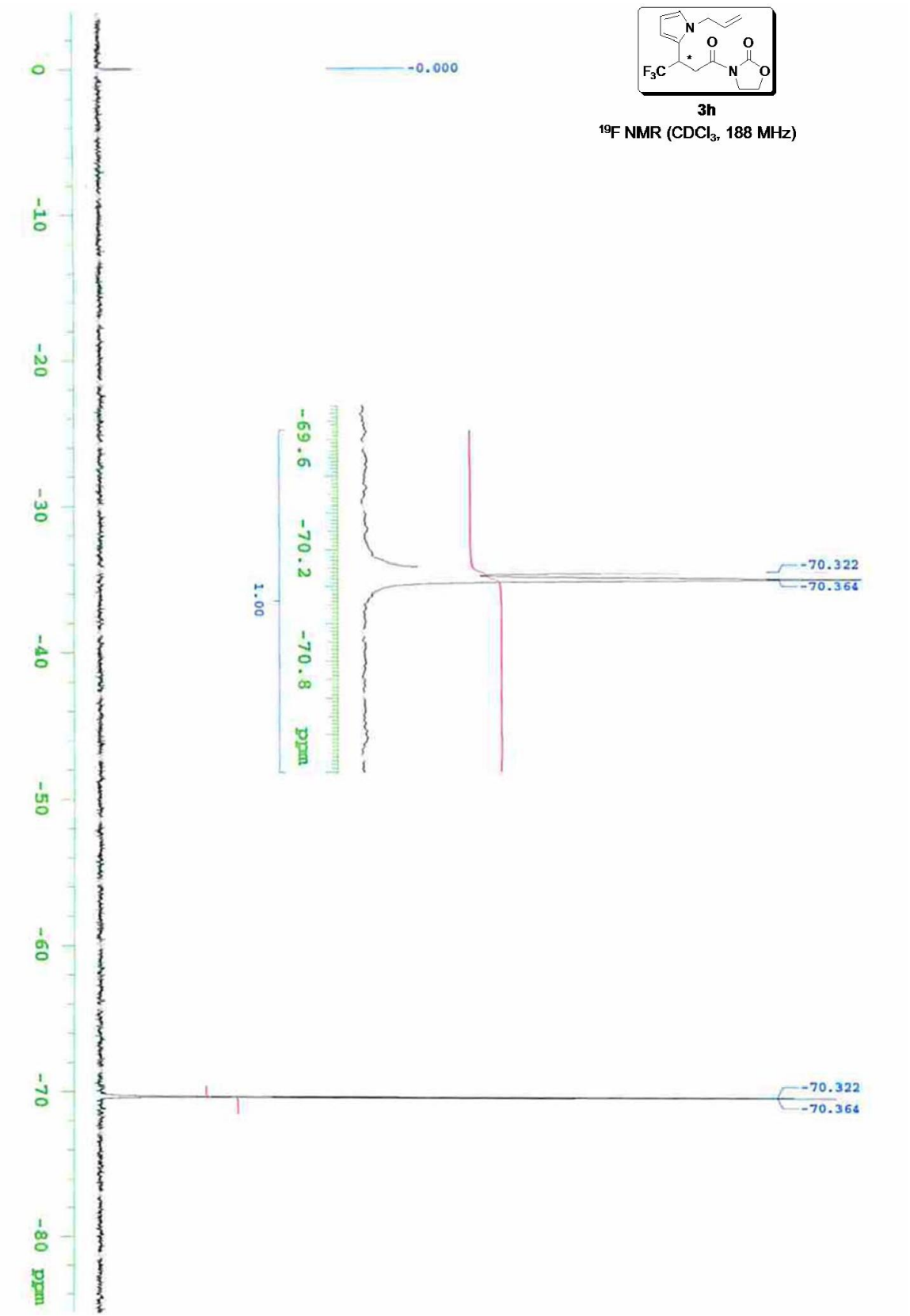

3g
1H NMR (CDCl3, 600 MHz)
1H
1.000
1.022
1.089
2.312
1.519
3.973
1.545
1.643
2.653
2.240
2.466
6.642
6.640
6.637
6.156
6.102
6.098
6.093
4.431
4.416
4.405
4.402
4.395
4.390
4.380
4.365
4.353
4.159
4.149
4.134
4.021
4.008
3.996
3.985
3.970
3.954
3.949
3.933
3.920
3.908
3.895
3.884
3.857
3.840
3.827
3.810
3.400
3.394
3.369
3.364
1.826
1.816
1.803
1.791
1.773
1.760
1.748
1.736
1.404
1.391
1.379
1.366
1.354
1.342
0.977
0.975
0.965
0.963
0.953
ppm


13C
3g
13C NMR (CDCl3, 150.9 MHz)
169.757
153.342
126.977
125.126
124.848
121.869
107.886
107.236
62.178
46.780
46.575
42.483
36.728
36.537
35.869
33.090
20.038
13.688
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


3g
19F NMR (CDCl3, 188 MHz)
0.000
-70.441
-70.483
-70.441
-70.483
1.00
-69.5
-70.5
-71.5
ppm
0
-10
-20
-30
-40
-50
-60
-70
ppm

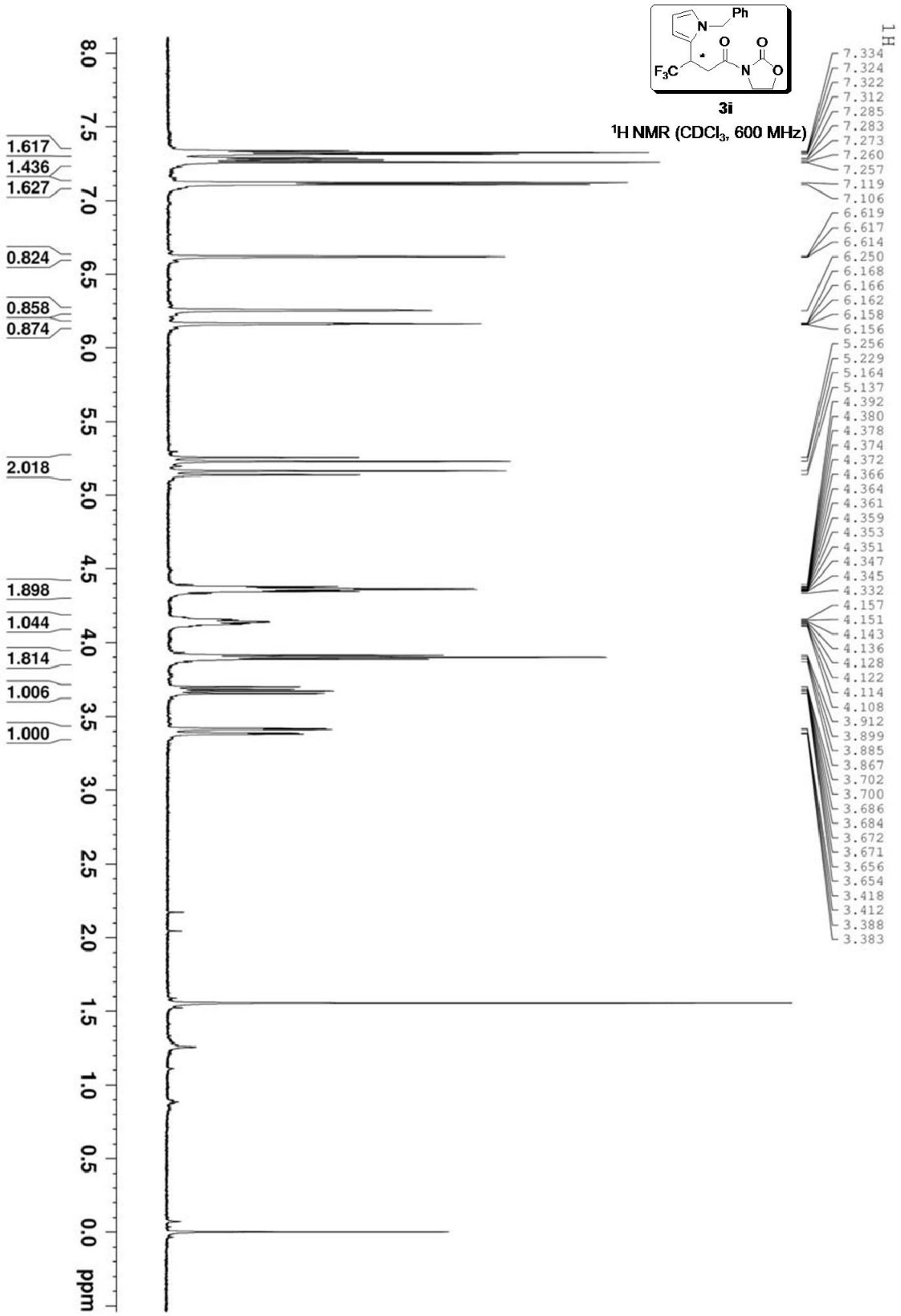

3h
^{1}H NMR ($CDCl_3$, 600 MHz)
1H
6.632
6.199
6.193
6.135
6.129
6.124
6.025
6.016
6.006
5.997
5.987
5.978
5.970
5.961
5.223
5.221
5.218
5.206
5.204
5.201
5.130
5.128
5.101
5.099
4.664
4.654
4.637
4.634
4.627
4.625
4.586
4.584
4.577
4.575
4.559
4.550
4.432
4.417
4.405
4.403
4.400
4.388
4.385
4.383
4.373
4.371
4.358
4.173
4.167
4.158
4.152
4.143
4.137
3.987
3.969
3.953
3.941
3.926
3.908
3.793
3.776
3.763
3.746
3.433
3.426
3.403
3.397
1.000
0.965
0.936
1.273
2.526
2.553
2.290
1.476
2.217
1.427
1.474
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

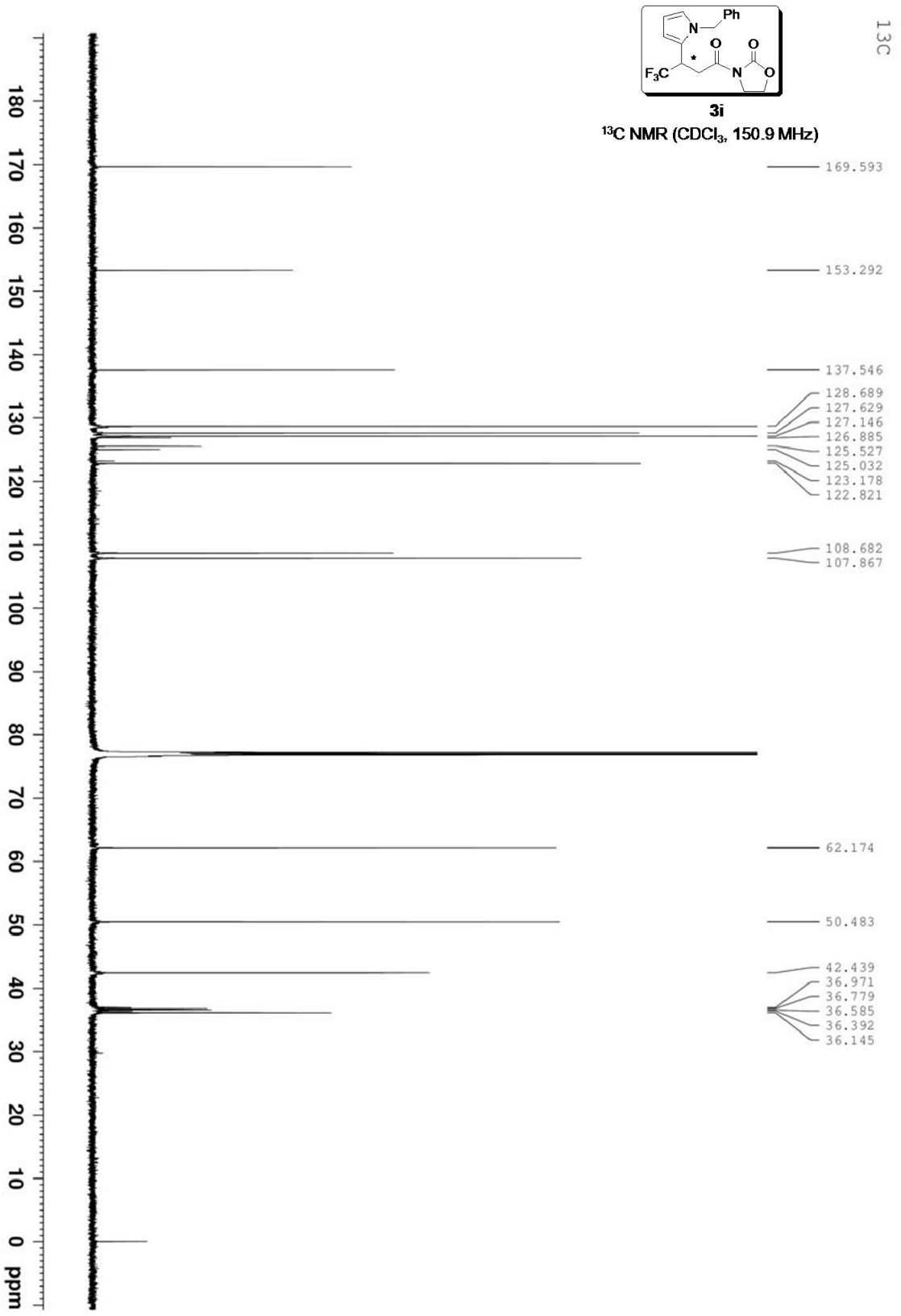

13C
3h
^{13}C NMR ($CDCl_3$, 150.9 MHz)
169.724
153.341
134.153
126.931
125.215
125.079
122.100
117.406
108.368
107.688
62.194
49.409
42.483
36.707
36.516
35.948
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

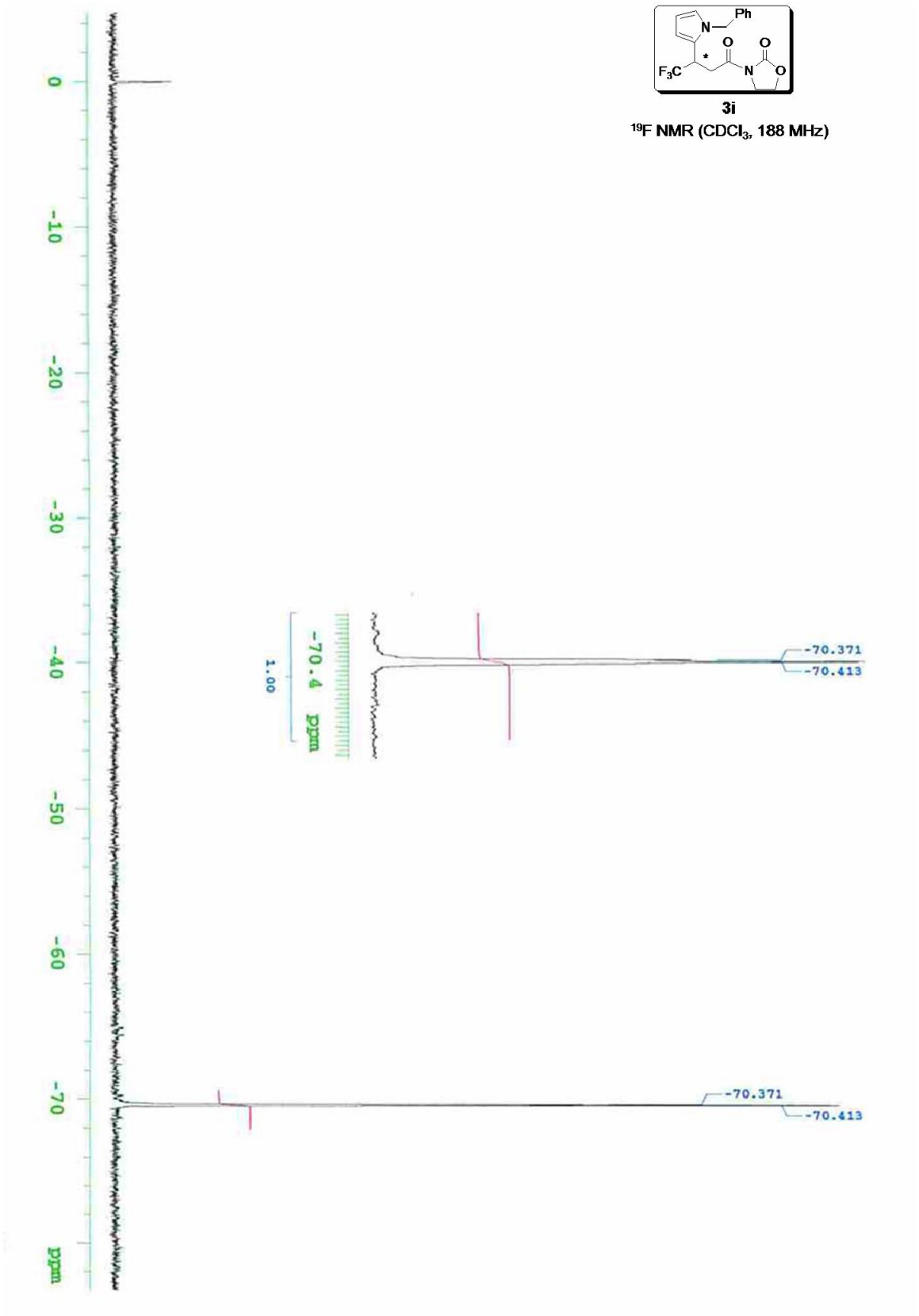


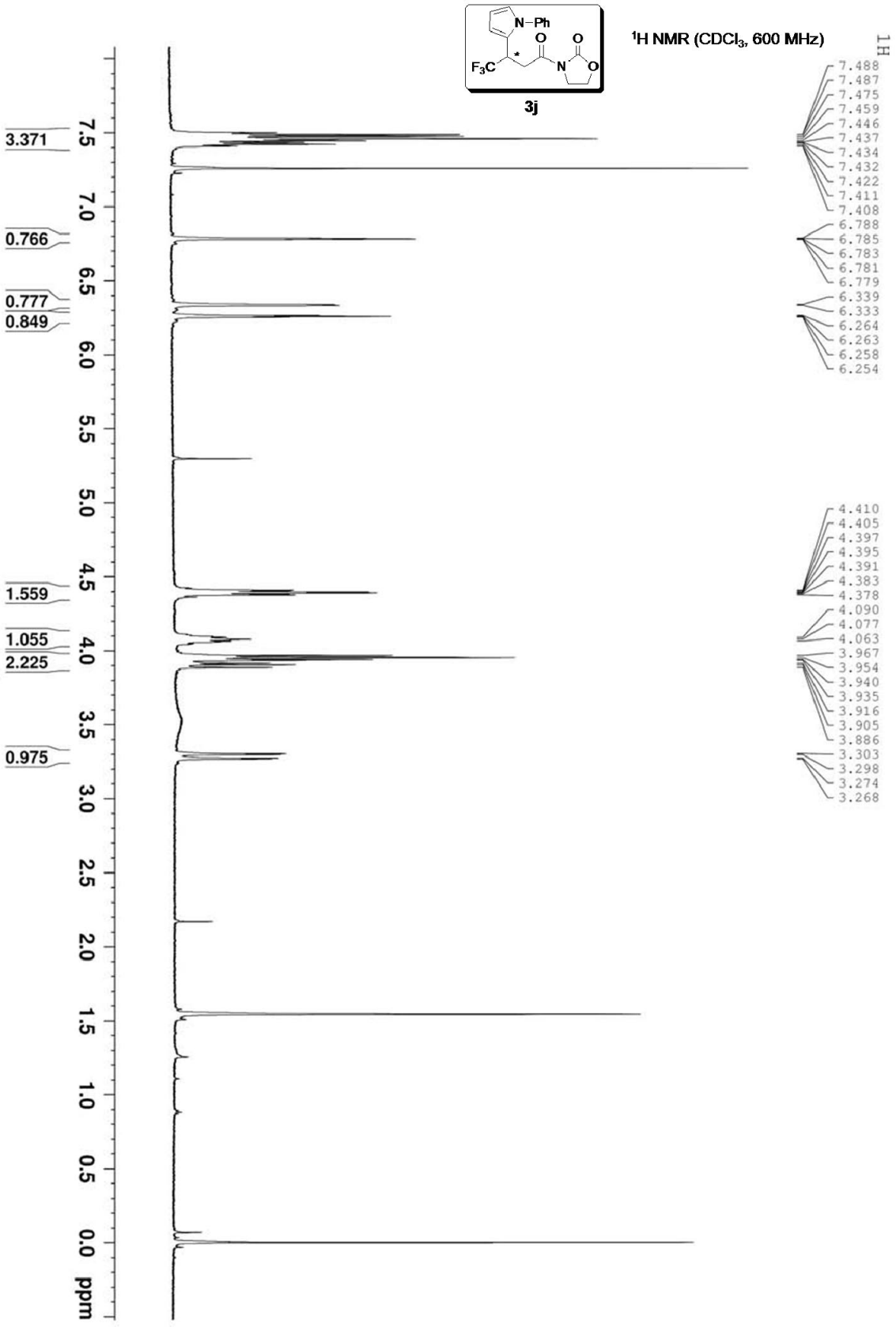
3h

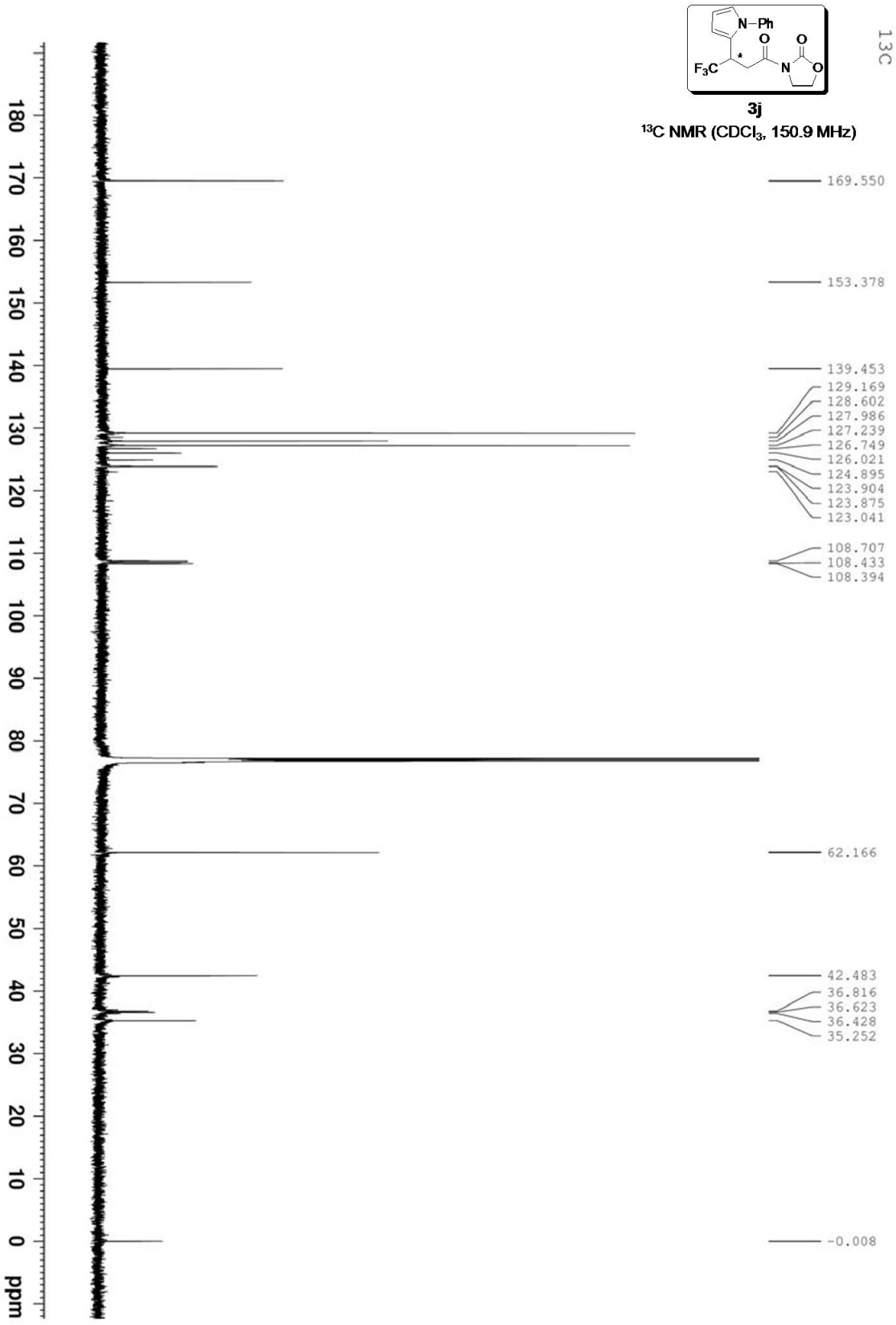
^{19}F NMR ($CDCl_3$, 188 MHz)

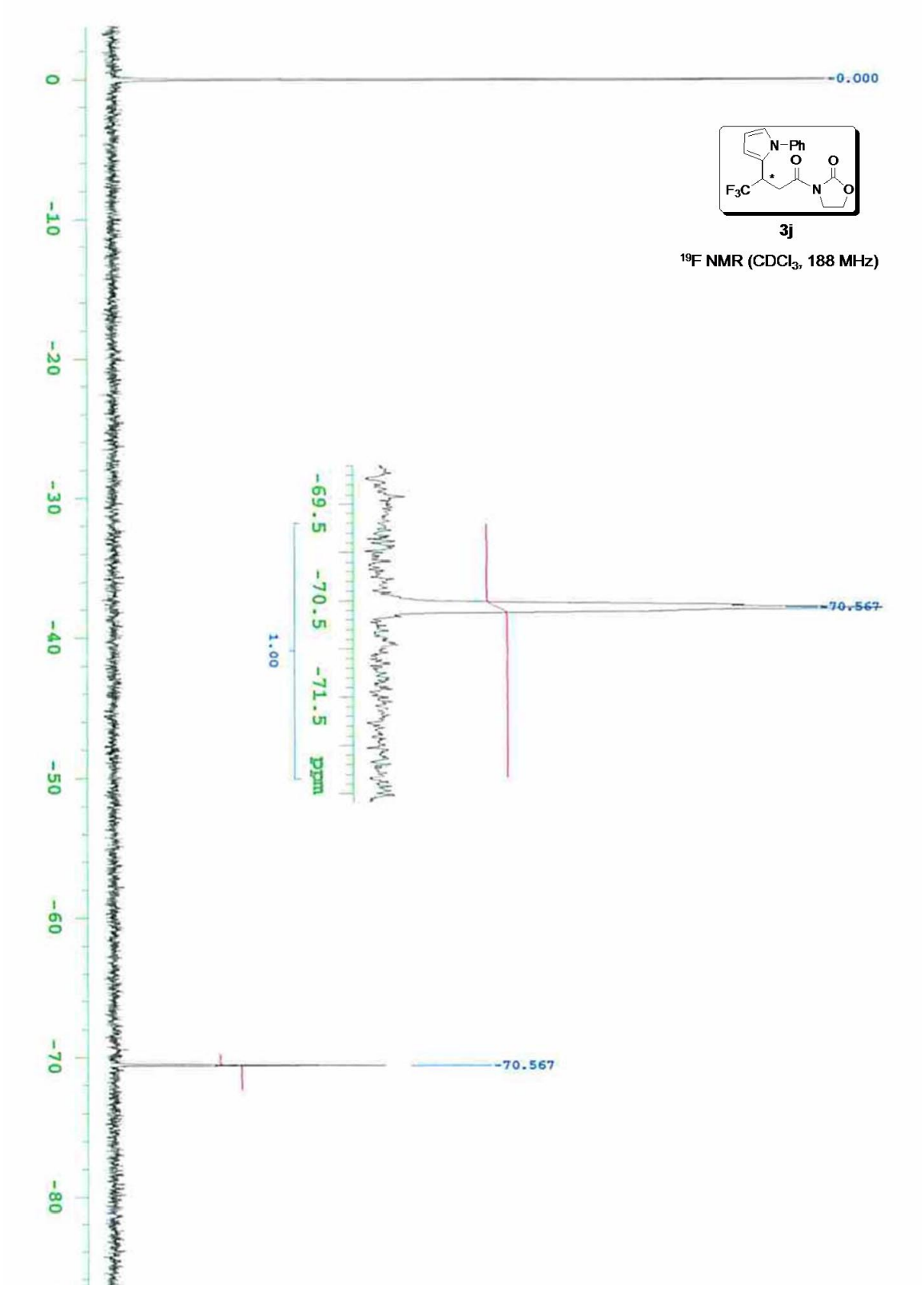

3i
^{1}H NMR ($CDCl_3$, 600 MHz)
1H
7.334
7.324
7.322
7.312
7.285
7.283
7.273
7.260
7.257
7.119
7.106
6.619
6.617
6.614
6.250
6.168
6.166
6.162
6.158
6.156
5.256
5.229
5.164
5.137
4.392
4.380
4.378
4.374
4.372
4.366
4.364
4.361
4.359
4.353
4.351
4.347
4.345
4.332
4.157
4.151
4.143
4.136
4.128
4.122
4.114
4.108
3.912
3.899
3.885
3.867
3.702
3.700
3.686
3.684
3.672
3.671
3.656
3.654
3.418
3.412
3.388
3.383
1.617
1.436
1.627
0.824
0.858
0.874
2.018
1.898
1.044
1.814
1.006
1.000
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


13C
3i
13C NMR (CDCl3, 150.9 MHz)
169.593
153.292
137.546
128.689
127.629
127.146
126.885
125.527
125.032
123.178
122.821
108.682
107.867
62.174
50.483
42.439
36.971
36.779
36.585
36.392
36.145
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


Ph
N
O
O
*
F3C
N
O
3i
19F NMR (CDCl3, 188 MHz)
0
-10
-20
-30
-40
-50
-60
-70
ppm
-70.371
-70.413
1.00
-70.4 ppm
-70.371
-70.413

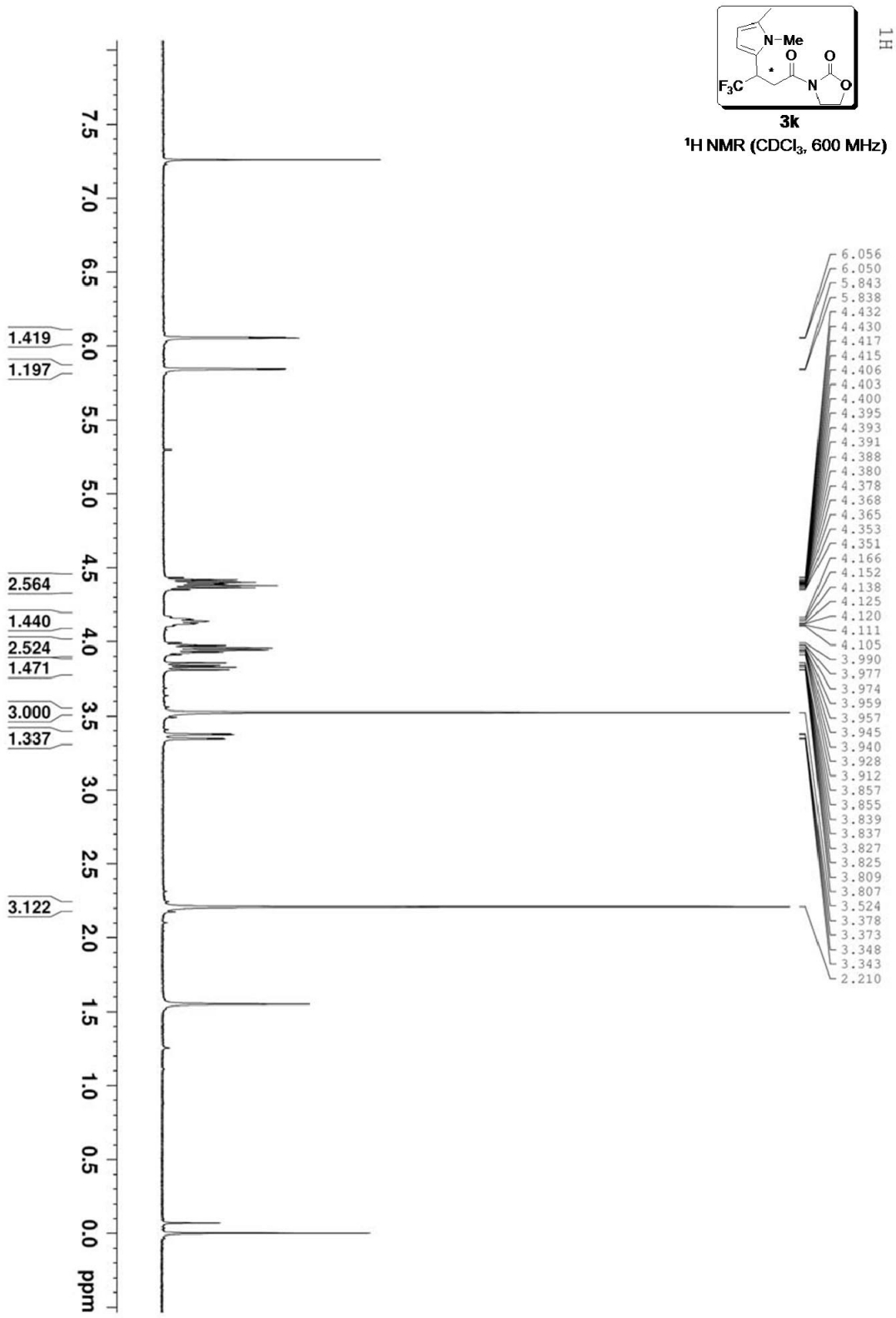

N–Ph
O
O
F3C
*
N
O
3j
1H NMR (CDCl3, 600 MHz)
1H
7.488
7.487
7.475
7.459
7.446
7.437
7.434
7.432
7.422
7.411
7.408
6.788
6.785
6.783
6.781
6.779
6.339
6.333
6.264
6.263
6.258
6.254
4.410
4.405
4.397
4.395
4.391
4.383
4.378
4.090
4.077
4.063
3.967
3.954
3.940
3.935
3.916
3.905
3.886
3.303
3.298
3.274
3.268
3.371
0.766
0.777
0.849
1.559
1.055
2.225
0.975
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

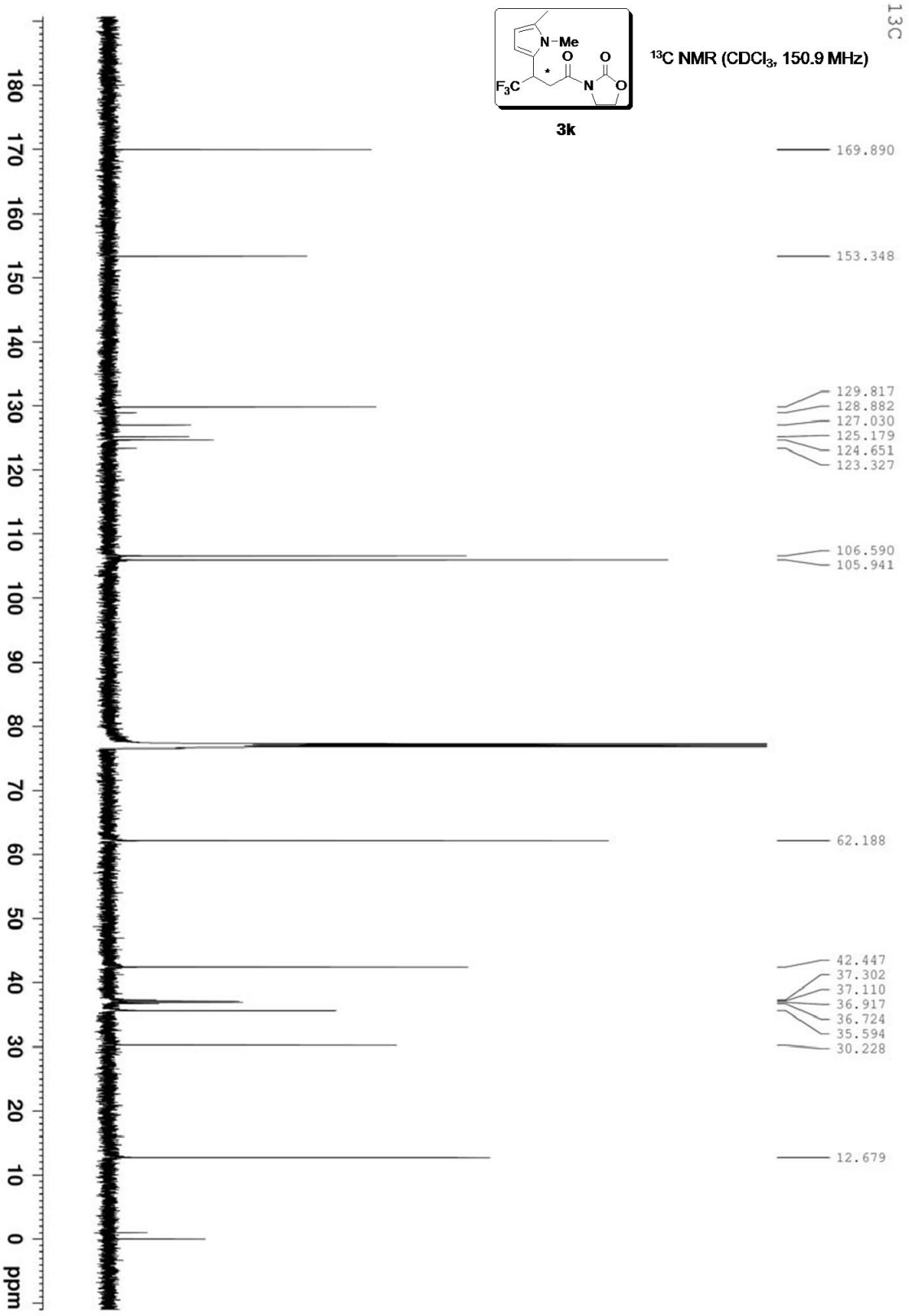

13C
3j
13C NMR (CDCl3, 150.9 MHz)
169.550
153.378
139.453
129.169
128.602
127.986
127.239
126.749
126.021
124.895
123.904
123.875
123.041
108.707
108.433
108.394
62.166
42.483
36.816
36.623
36.428
35.252
-0.008
ppm

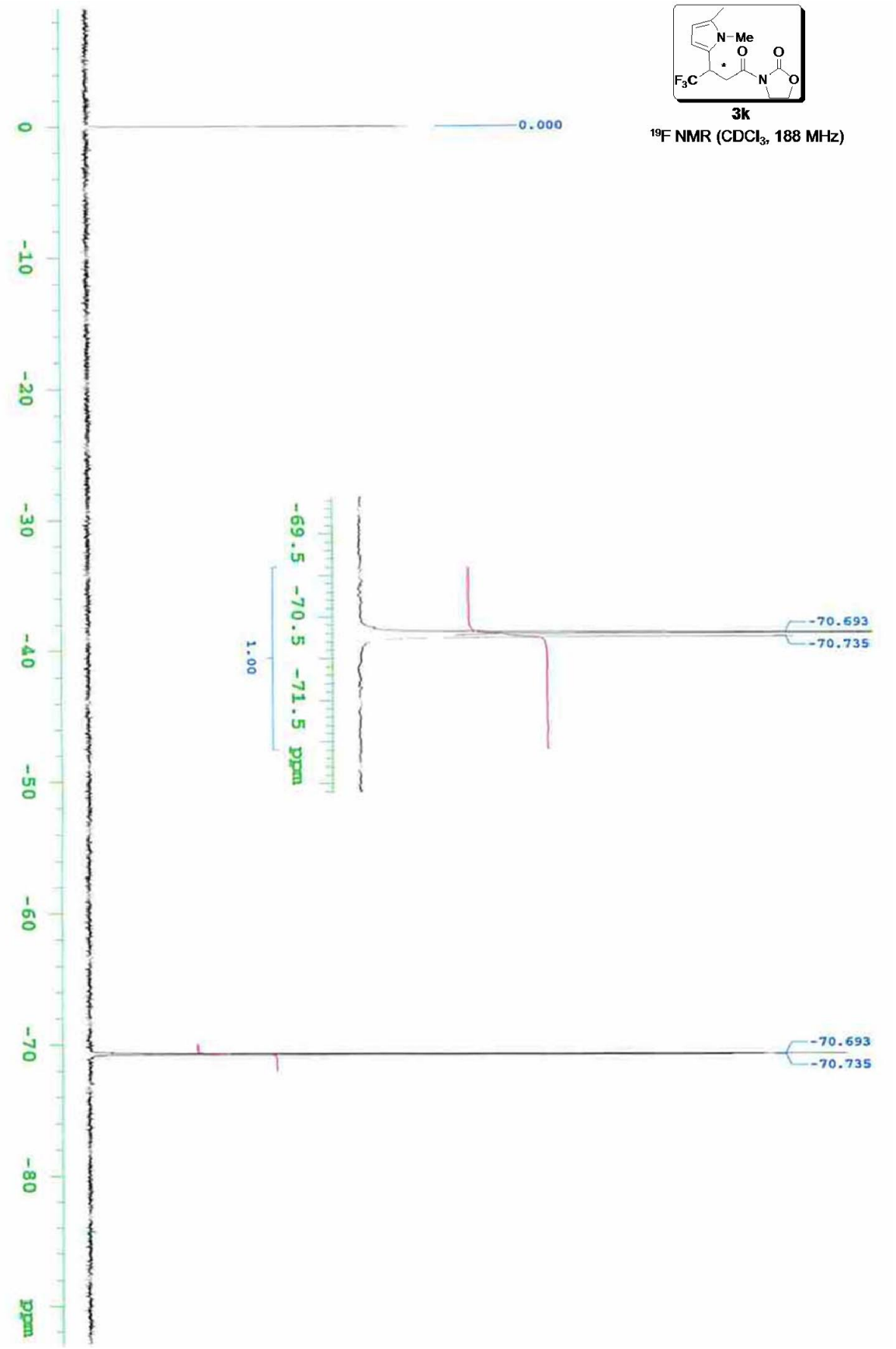


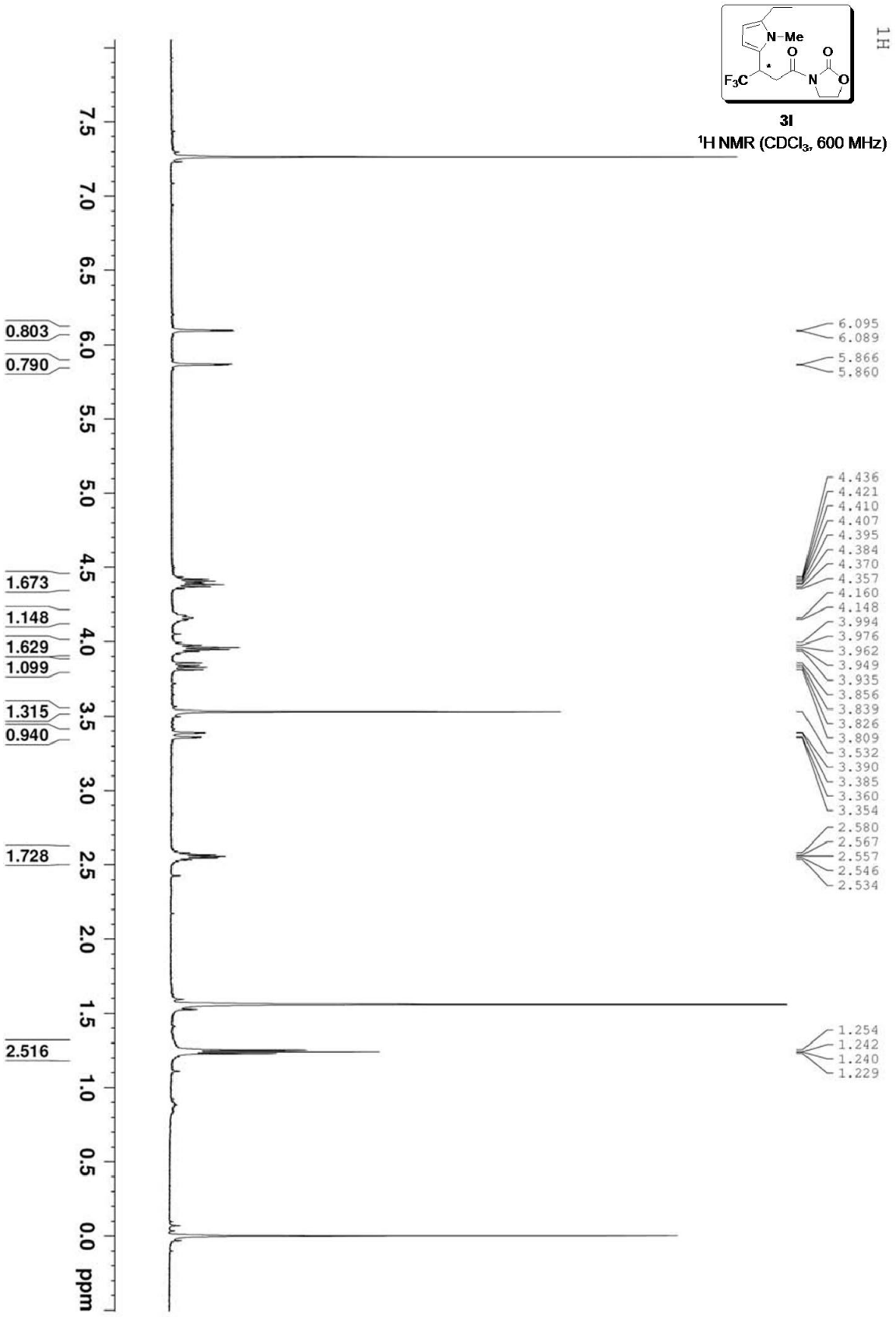
3j

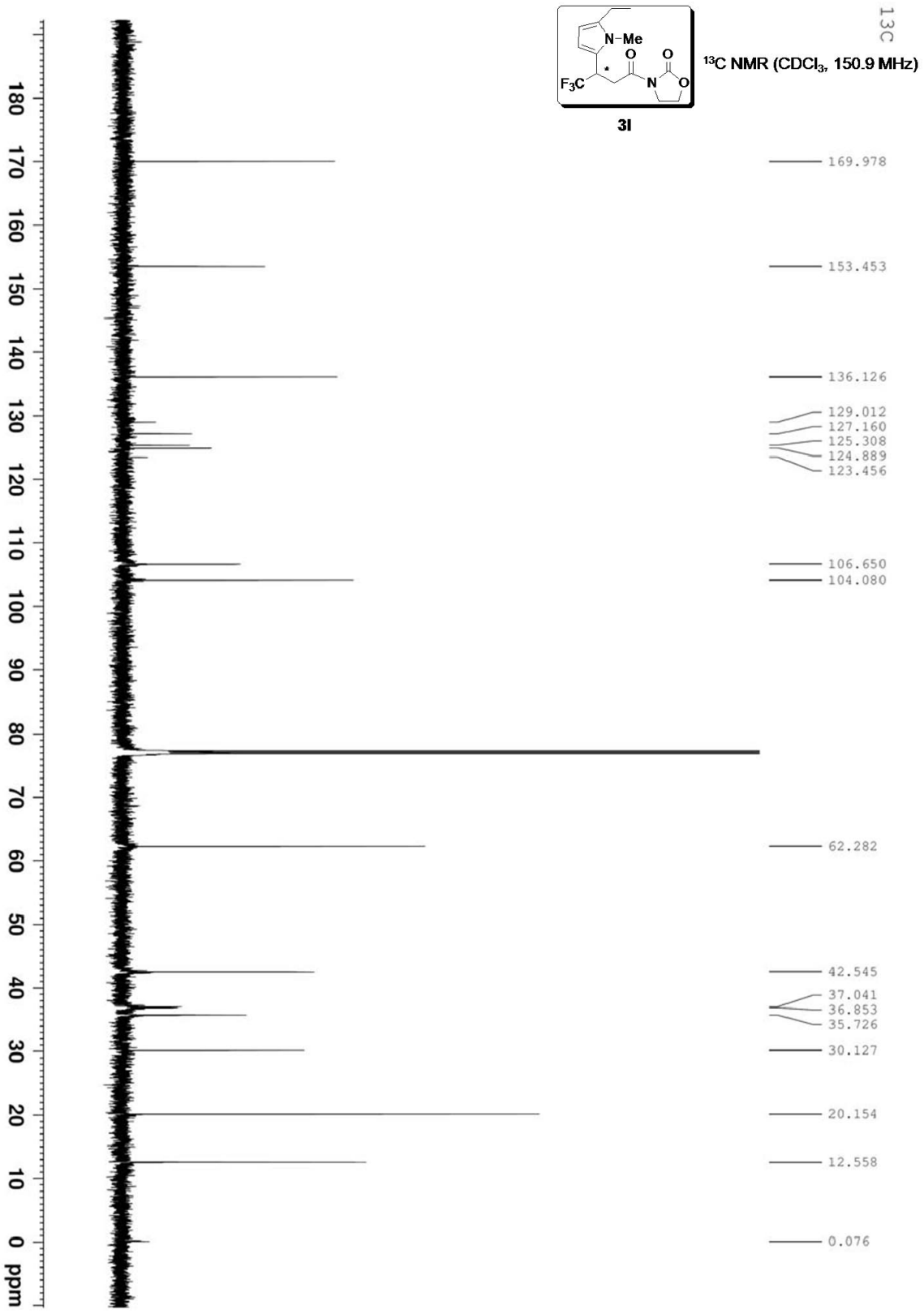
^{19}F NMR ($CDCl_3$, 188 MHz)

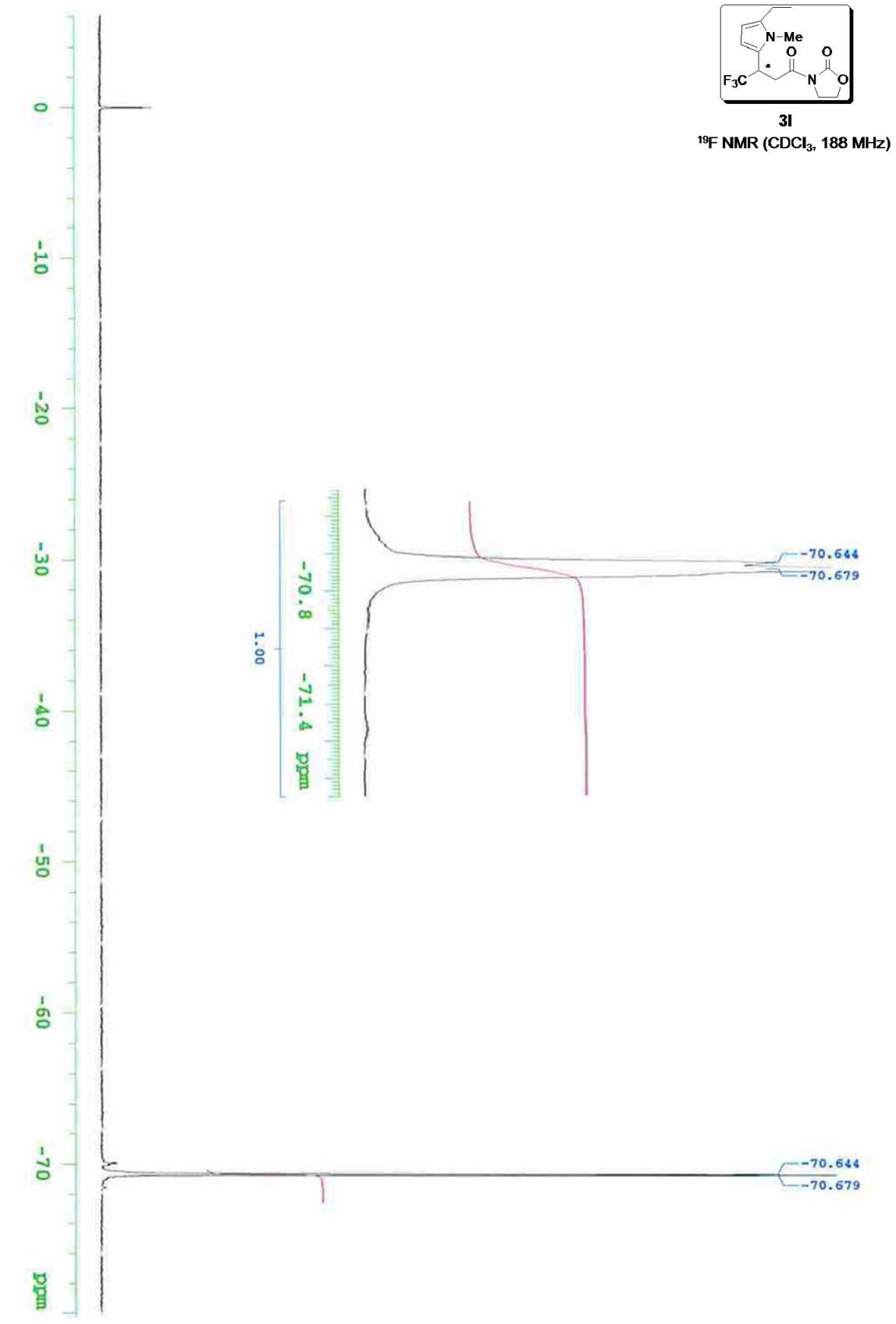

1H
N–Me
O
O
F3C
*
N
O
3k
1H NMR (CDCl3, 600 MHz)
6.056
6.050
5.843
5.838
4.432
4.430
4.417
4.415
4.406
4.403
4.400
4.395
4.393
4.391
4.388
4.380
4.378
4.368
4.365
4.353
4.351
4.166
4.152
4.138
4.125
4.120
4.111
4.105
3.990
3.977
3.974
3.959
3.957
3.945
3.940
3.928
3.912
3.857
3.855
3.839
3.837
3.827
3.825
3.809
3.807
3.524
3.378
3.373
3.348
3.343
2.210
1.419
1.197
2.564
1.440
2.524
1.471
3.000
1.337
3.122
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

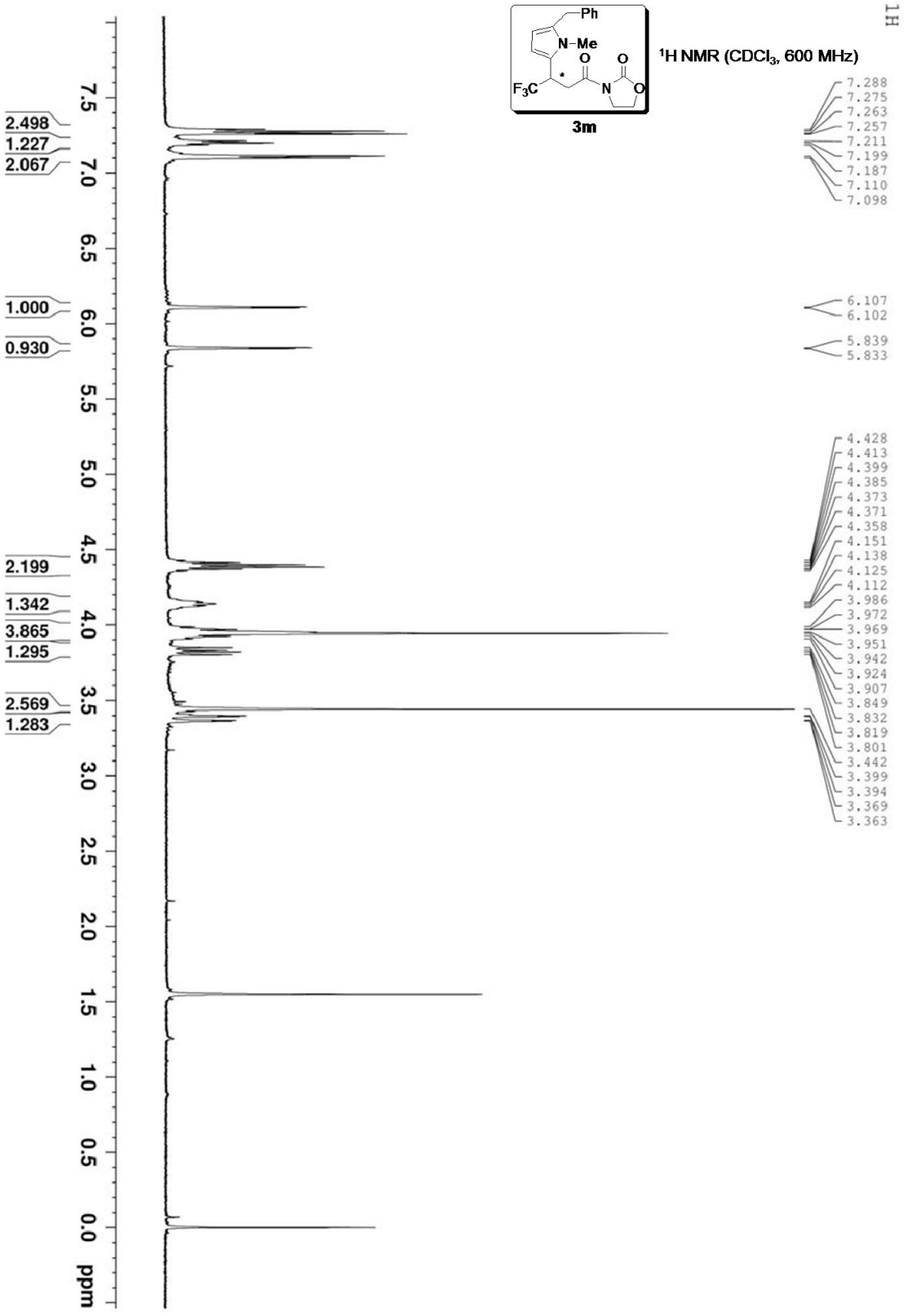

13C
N–Me
O
O
F3C
*
N
O
3k
13C NMR (CDCl3, 150.9 MHz)
169.890
153.348
129.817
128.882
127.030
125.179
124.651
123.327
106.590
105.941
62.188
42.447
37.302
37.110
36.917
36.724
35.594
30.228
12.679
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

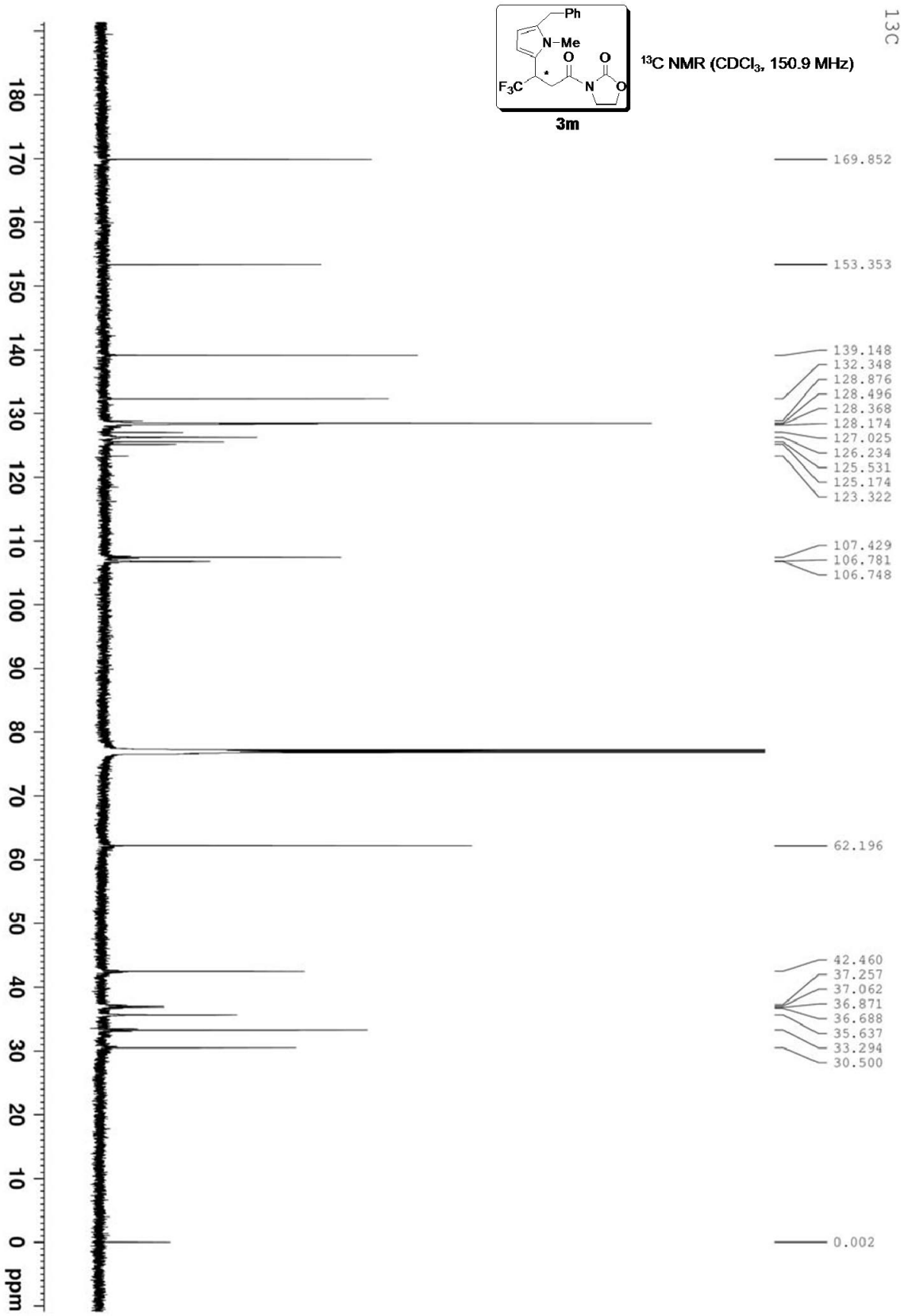

N–Me
O
O
F3C
N
O
3k
19F NMR (CDCl3, 188 MHz)
0.000
-70.693
-70.735
-69.5 -70.5 -71.5 ppm
1.00
-70.693
-70.735
0
-10
-20
-30
-40
-50
-60
-70
-80
ppm


1H
3l
1H NMR (CDCl3, 600 MHz)
6.095
6.089
5.866
5.860
4.436
4.421
4.410
4.407
4.395
4.384
4.370
4.357
4.160
4.148
3.994
3.976
3.962
3.949
3.935
3.856
3.839
3.826
3.809
3.532
3.390
3.385
3.360
3.354
2.580
2.567
2.557
2.546
2.534
1.254
1.242
1.240
1.229
0.803
0.790
1.673
1.148
1.629
1.099
1.315
0.940
1.728
2.516
ppm

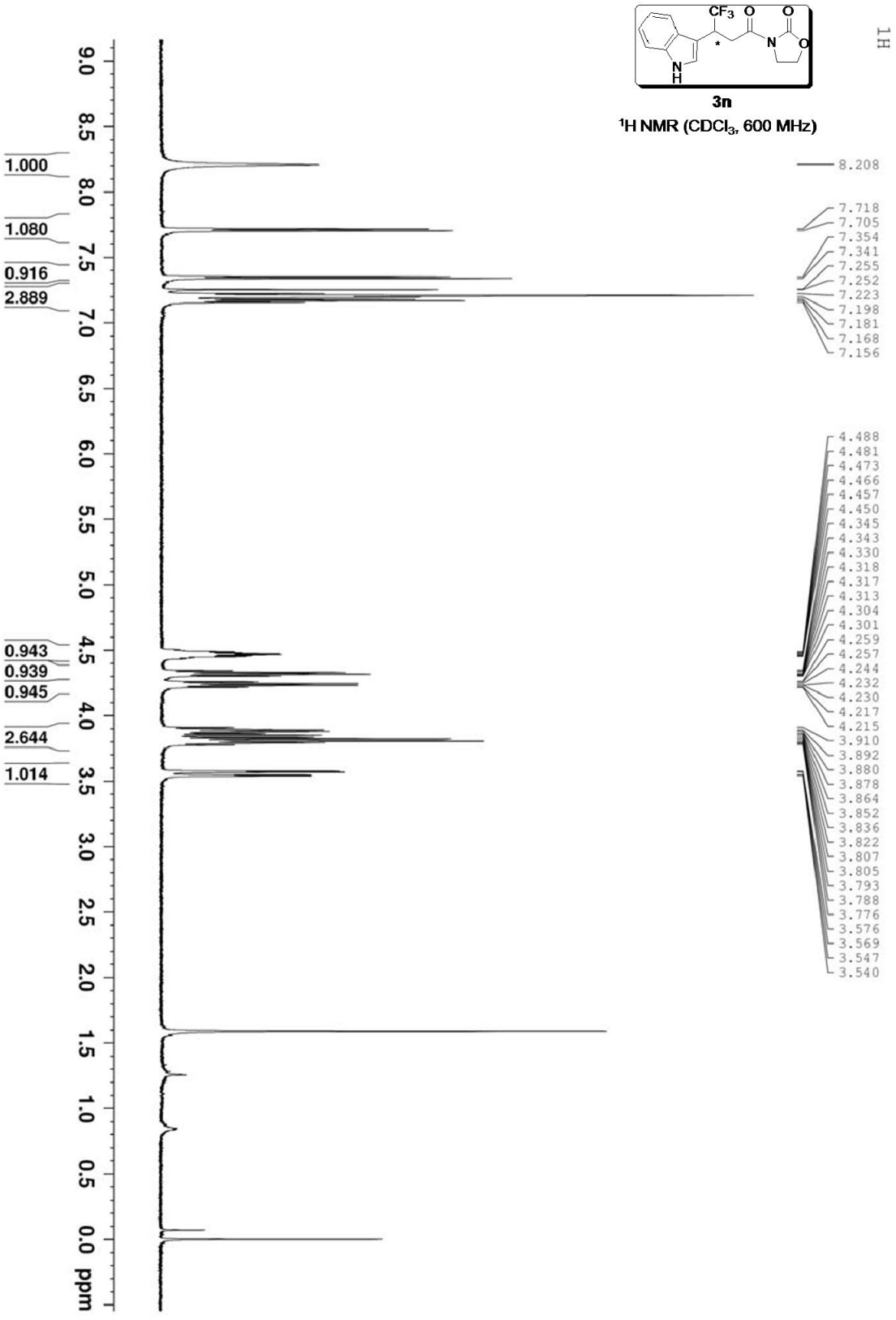

13C
N-Me
O
O
F3C
N
O
3l
13C NMR (CDCl3, 150.9 MHz)
169.978
153.453
136.126
129.012
127.160
125.308
124.889
123.456
106.650
104.080
62.282
42.545
37.041
36.853
35.726
30.127
20.154
12.558
0.076
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

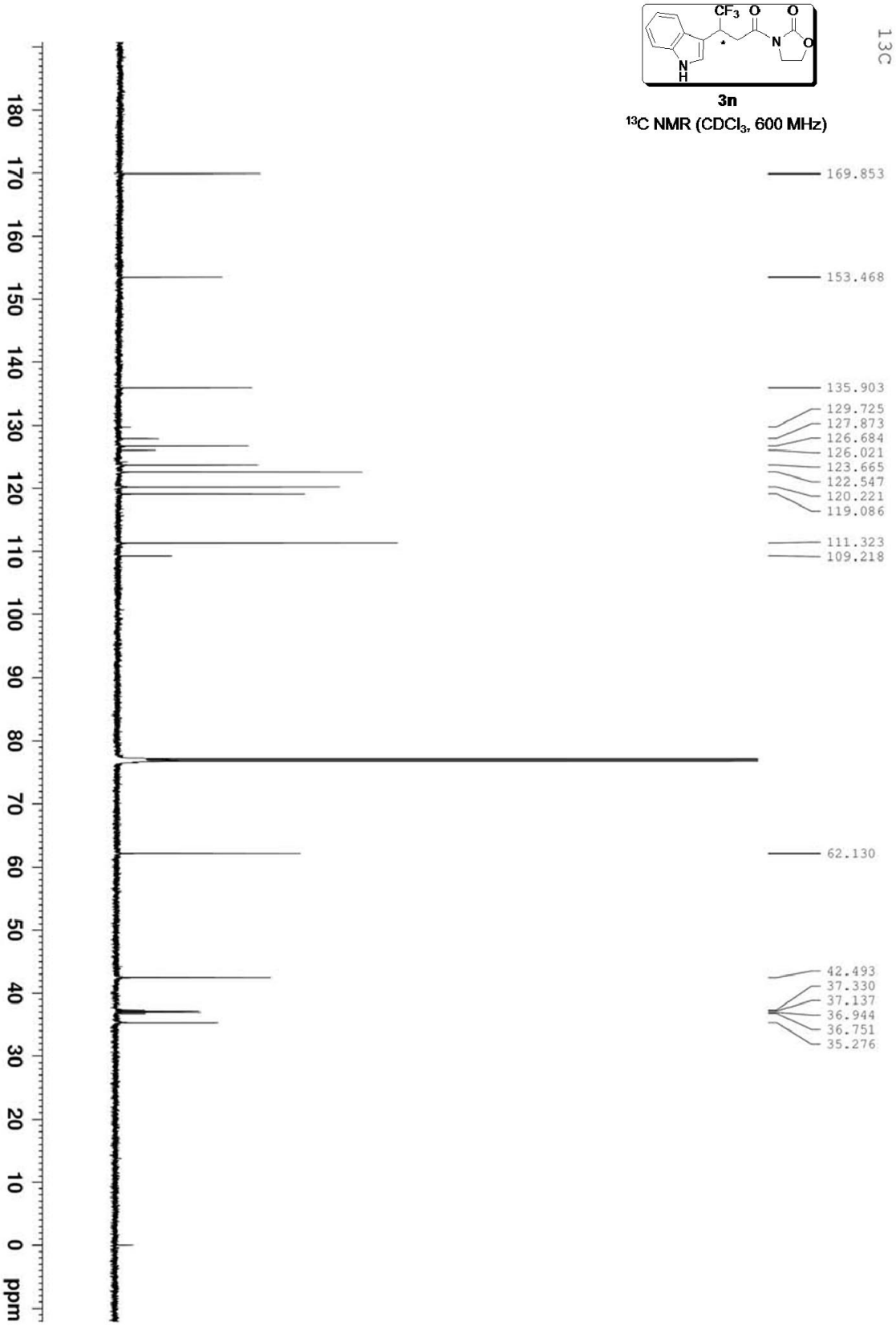

N-Me
O
O
F3C
N
O
3l
19F NMR (CDCl3, 188 MHz)
0
-10
-20
-30
-40
-50
-60
-70
ppm
-70.644
-70.679
1.00
-70.8
-71.4
ppm
-70.644
-70.679

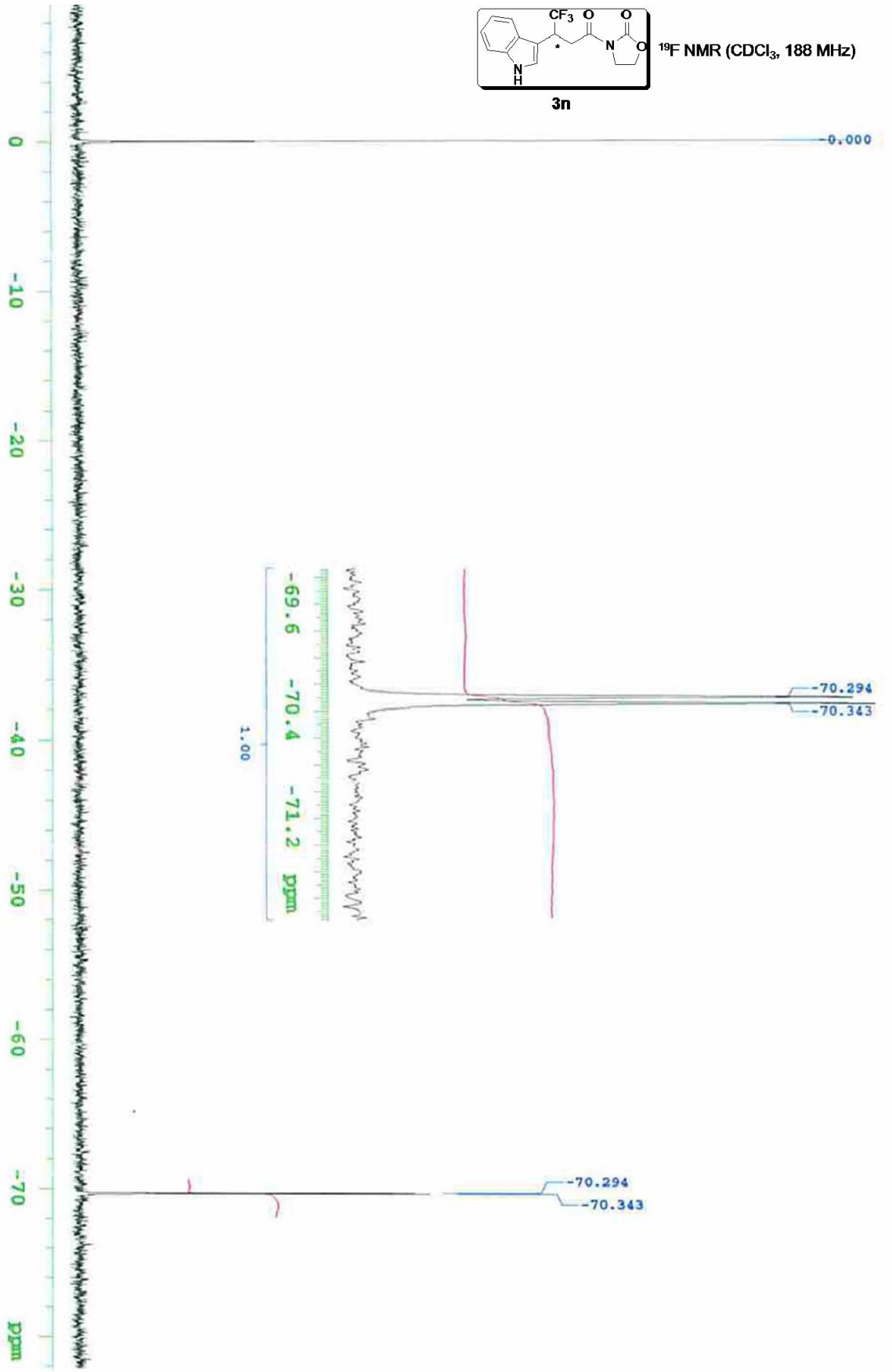

1H
Ph
N–Me
O
O
F3C
N
O
3m
1H NMR (CDCl3, 600 MHz)
7.288
7.275
7.263
7.257
7.211
7.199
7.187
7.110
7.098
6.107
6.102
5.839
5.833
4.428
4.413
4.399
4.385
4.373
4.371
4.358
4.151
4.138
4.125
4.112
3.986
3.972
3.969
3.951
3.942
3.924
3.907
3.849
3.832
3.819
3.801
3.442
3.399
3.394
3.369
3.363
2.498
1.227
2.067
1.000
0.930
2.199
1.342
3.865
1.295
2.569
1.283
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

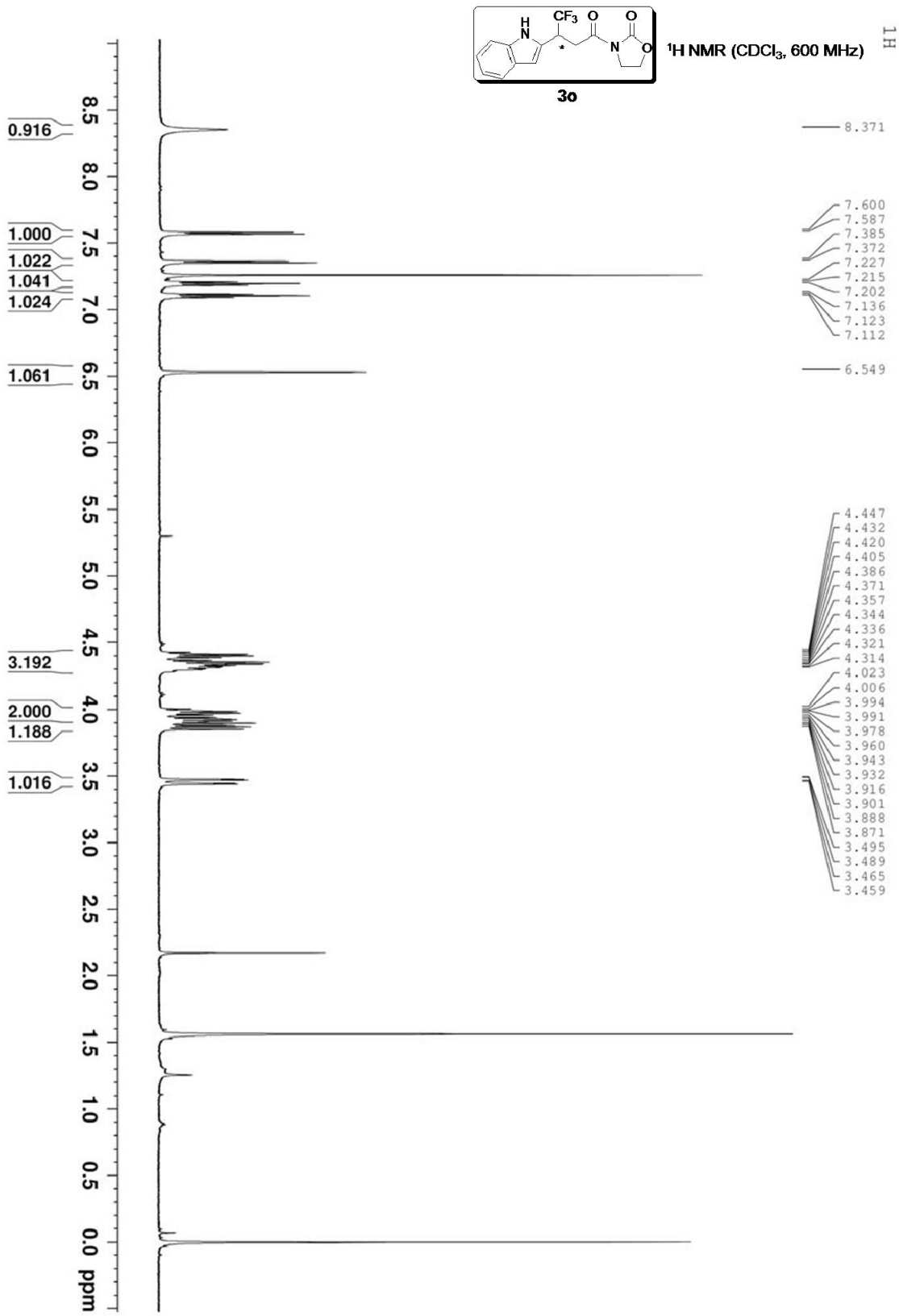

13C
Ph
N–Me
O
O
F3C
N
O
3m
13C NMR (CDCl3, 150.9 MHz)
169.852
153.353
139.148
132.348
128.876
128.496
128.368
128.174
127.025
126.234
125.531
125.174
123.322
107.429
106.781
106.748
62.196
42.460
37.257
37.062
36.871
36.688
35.637
33.294
30.500
0.002
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

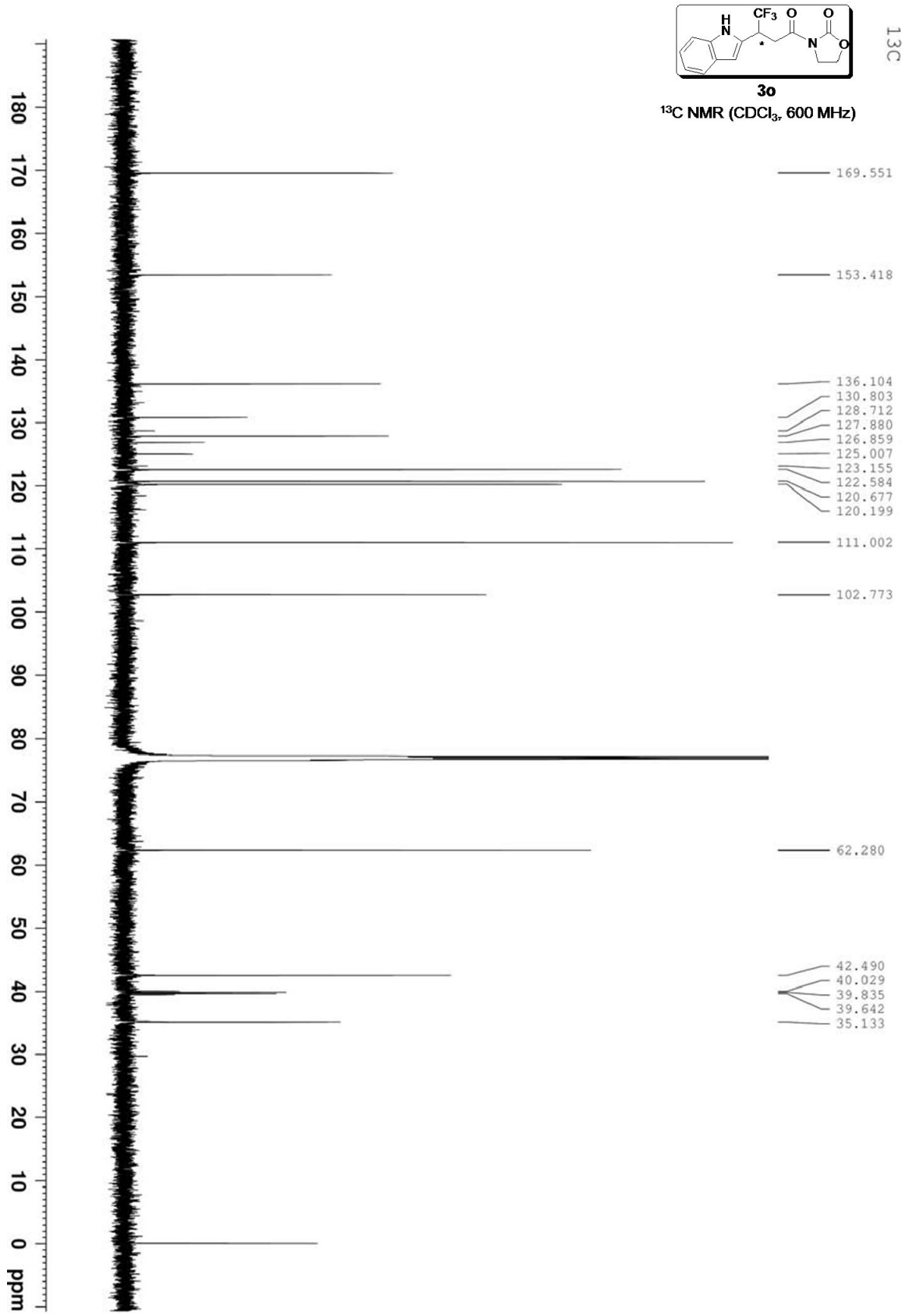

Ph
N–Me
O
O
F3C
*
N
O
3m
19F NMR (CDCl3, 188 MHz)
0.000
-70.665
-70.700
-70.2 ppm
1.00
-70.665
-70.700
0
-10
-20
-30
-40
-50
-60
-70
ppm

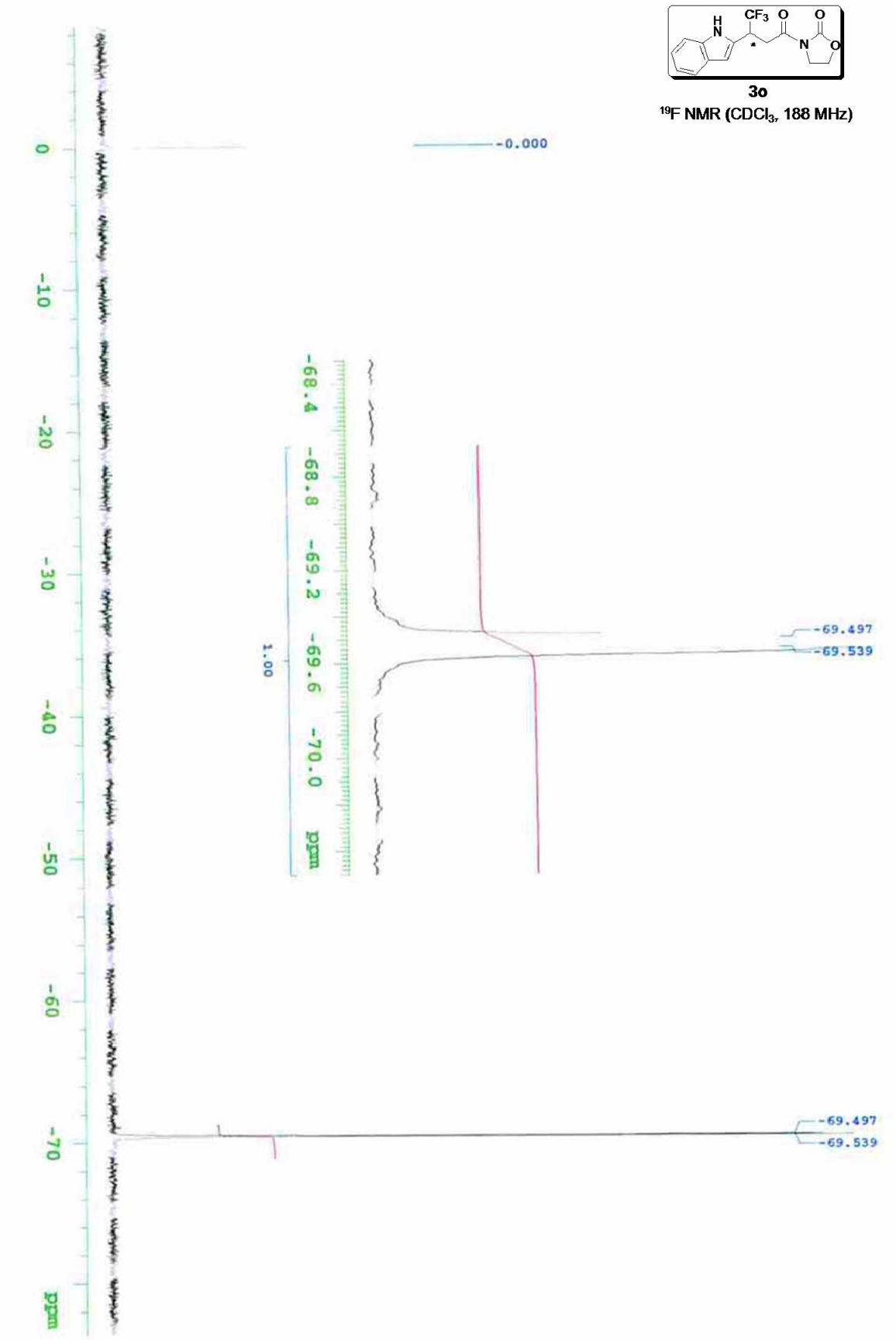

3n
^{1}H NMR ($CDCl_3$, 600 MHz)
1H
1.000
1.080
0.916
2.889
0.943
0.939
0.945
2.644
1.014
8.208
7.718
7.705
7.354
7.341
7.255
7.252
7.223
7.198
7.181
7.168
7.156
4.488
4.481
4.473
4.466
4.457
4.450
4.345
4.343
4.330
4.318
4.317
4.313
4.304
4.301
4.259
4.257
4.244
4.232
4.230
4.217
4.215
3.910
3.892
3.880
3.878
3.864
3.852
3.836
3.822
3.807
3.805
3.793
3.788
3.776
3.576
3.569
3.547
3.540
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

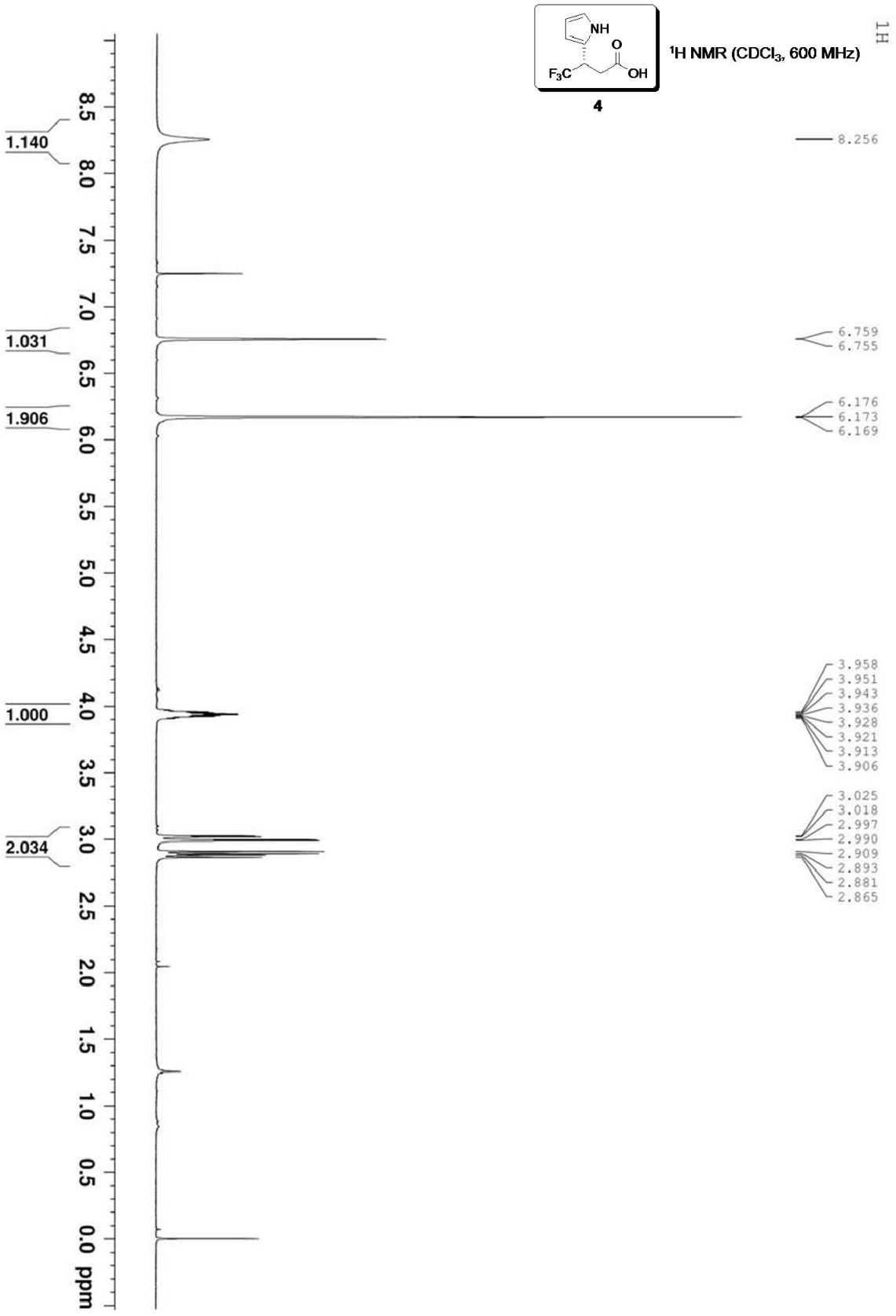

13C
3n
13C NMR (CDCl3, 600 MHz)
169.853
153.468
135.903
129.725
127.873
126.684
126.021
123.665
122.547
120.221
119.086
111.323
109.218
62.130
42.493
37.330
37.137
36.944
36.751
35.276
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

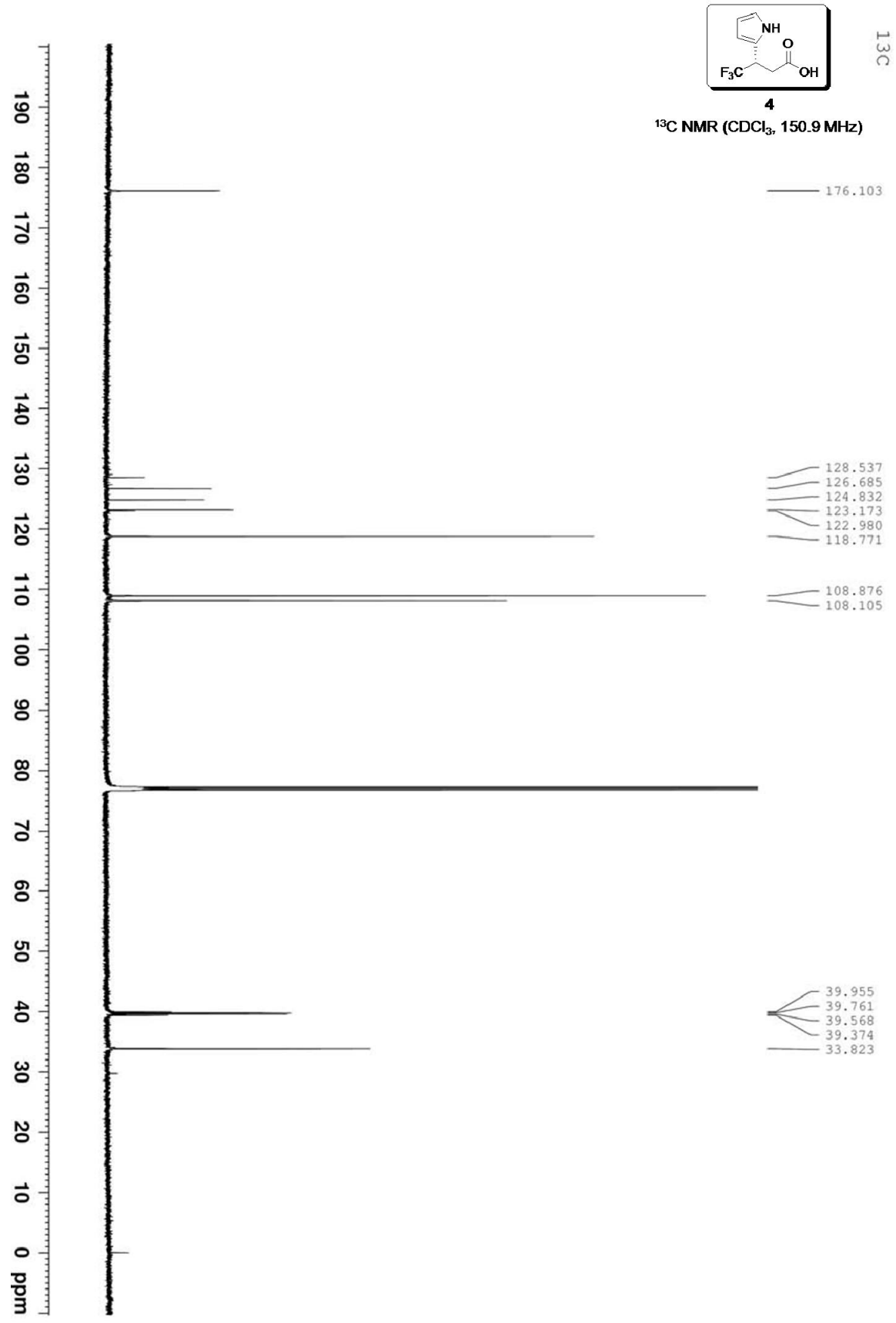

CF3
O
O
N
O
N
H
*
3n
19F NMR (CDCl3, 188 MHz)
0.000
-70.294
-70.343
-69.6
-70.4
-71.2
ppm
1.00
-70.294
-70.343
0
-10
-20
-30
-40
-50
-60
-70
ppm

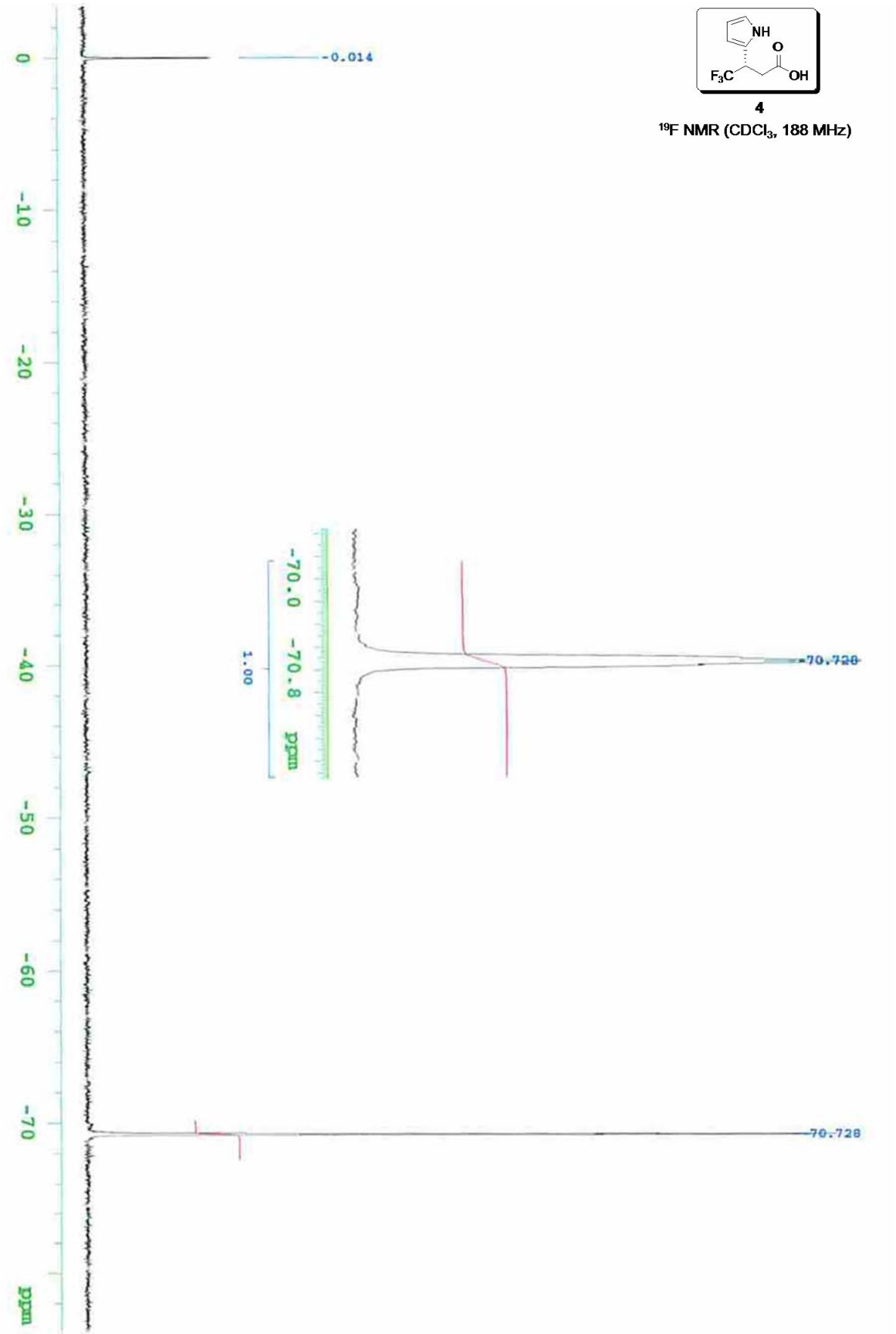

3o
^{1}H NMR ($CDCl_3$, 600 MHz)
1H
0.916
1.000
1.022
1.041
1.024
1.061
3.192
2.000
1.188
1.016
8.371
7.600
7.587
7.385
7.372
7.227
7.215
7.202
7.136
7.123
7.112
6.549
4.447
4.432
4.420
4.405
4.386
4.371
4.357
4.344
4.336
4.321
4.314
4.023
4.006
3.994
3.991
3.978
3.960
3.943
3.932
3.916
3.901
3.888
3.871
3.495
3.489
3.465
3.459
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

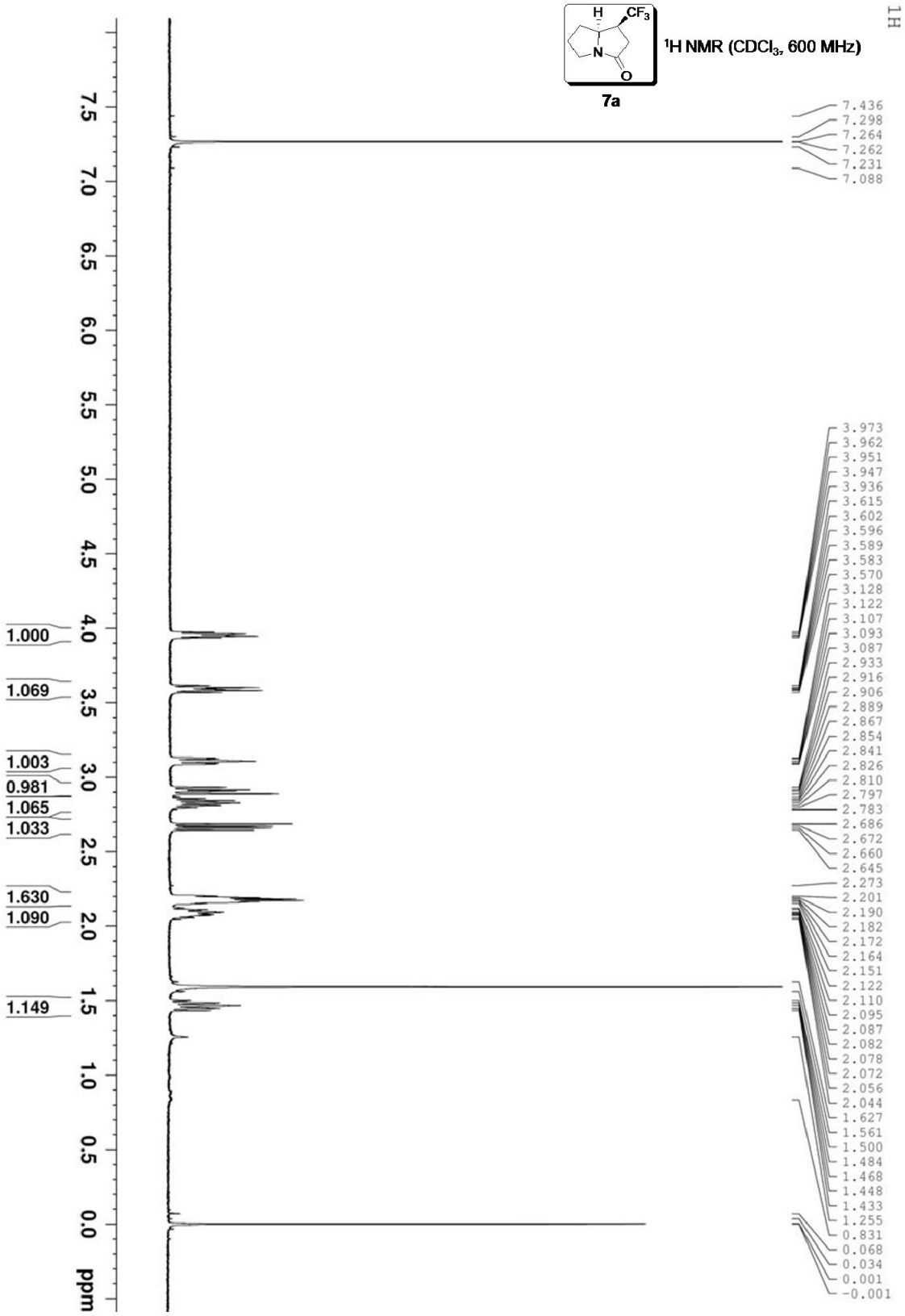

13C
3o
^{13}C NMR ($CDCl_3$, 600 MHz)
169.551
153.418
136.104
130.803
128.712
127.880
126.859
125.007
123.155
122.584
120.677
120.199
111.002
102.773
62.280
42.490
40.029
39.835
39.642
35.133
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

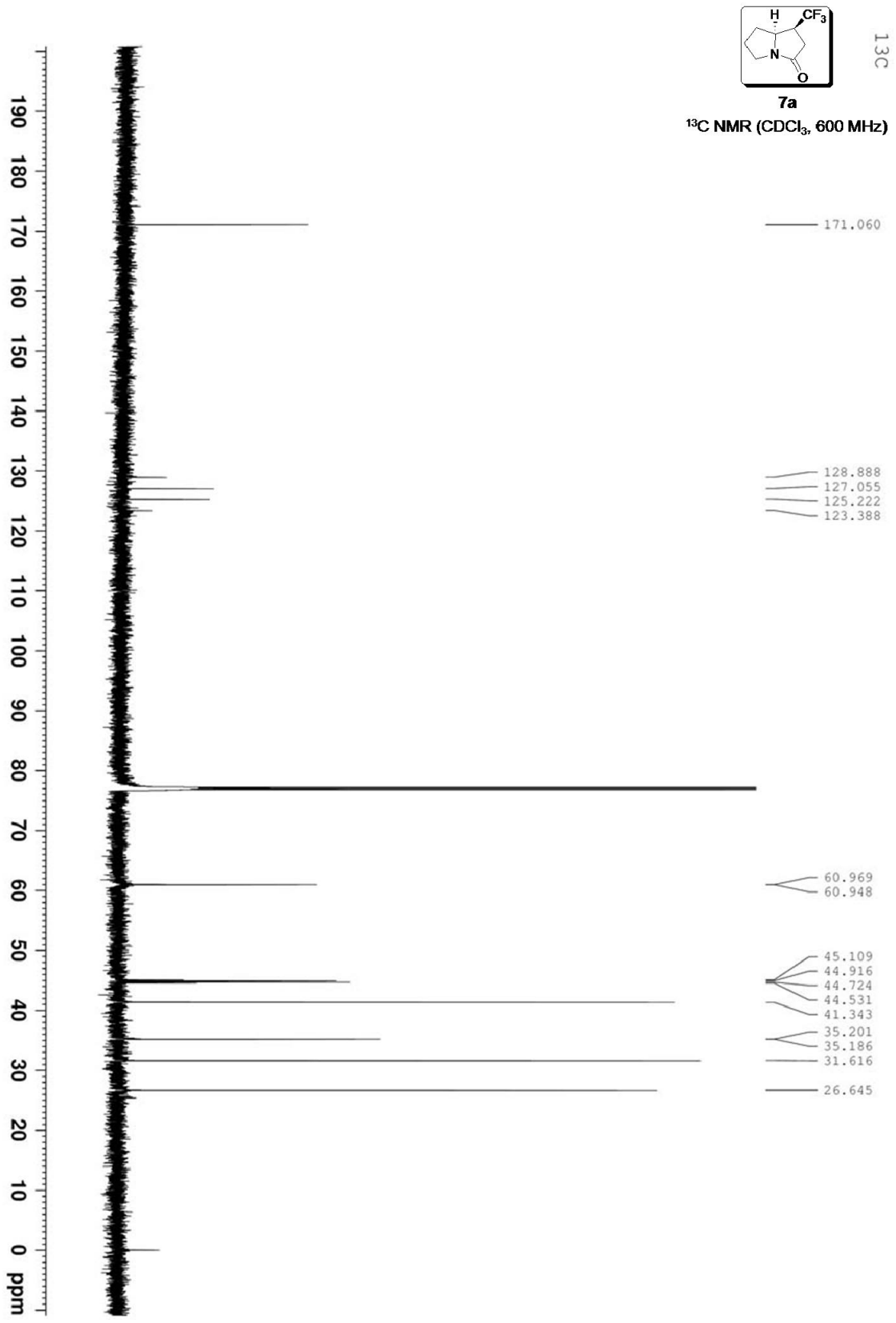

CF3
O
O
H
N
N
O
*
3o
19F NMR (CDCl3, 188 MHz)
-0.000
0
-10
-20
-30
-40
-50
-60
-70
ppm
-68.4
-68.8
-69.2
-69.6
-70.0
ppm
1.00
-69.497
-69.539
-69.497
-69.539

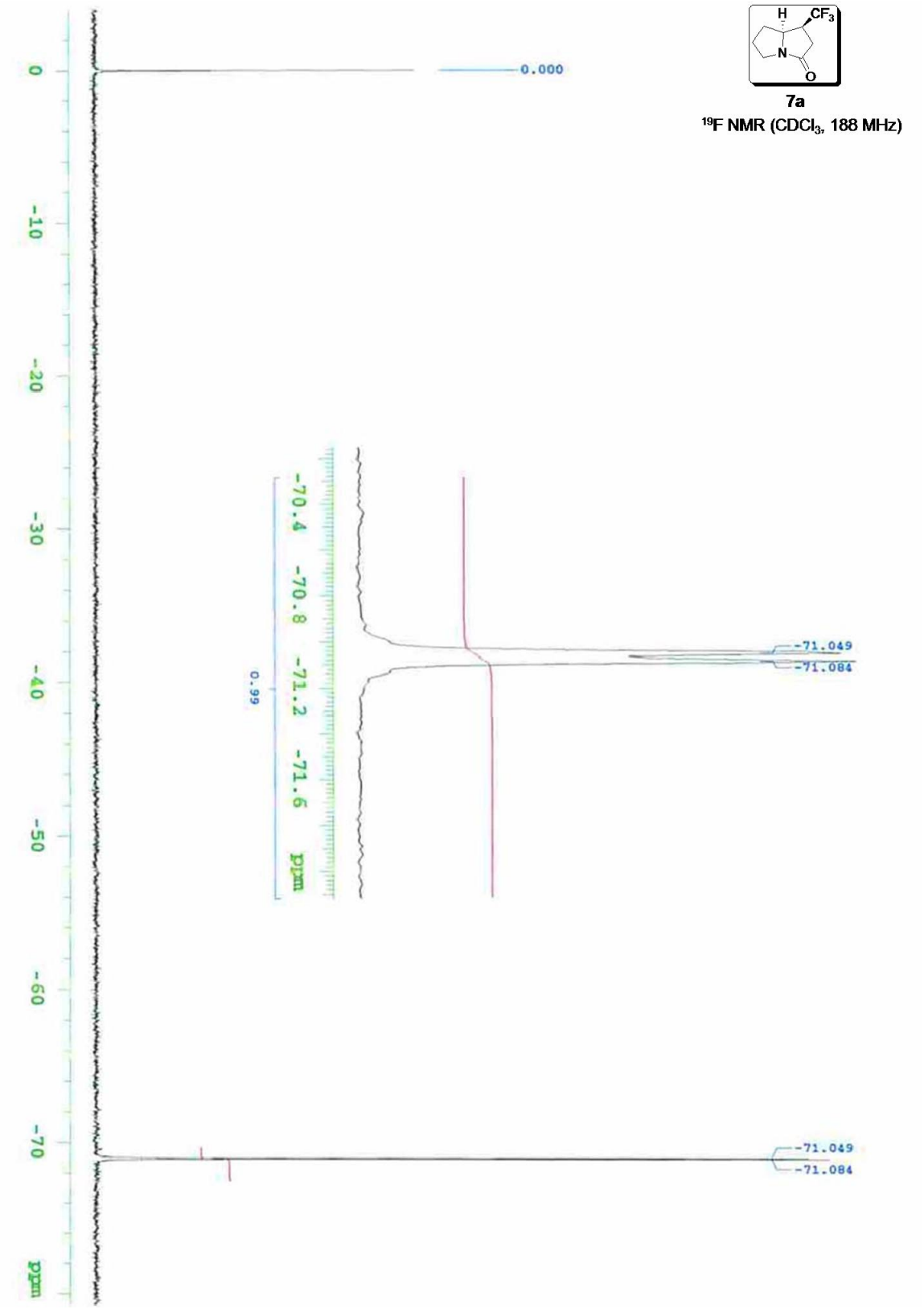

NH
O
F3C
OH
4
1H NMR (CDCl3, 600 MHz)
1H
8.256
6.759
6.755
6.176
6.173
6.169
3.958
3.951
3.943
3.936
3.928
3.921
3.913
3.906
3.025
3.018
2.997
2.990
2.909
2.893
2.881
2.865
1.140
1.031
1.906
1.000
2.034
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


13C
NH
O
OH
F3C
4
13C NMR (CDCl3, 150.9 MHz)
176.103
128.537
126.685
124.832
123.173
122.980
118.771
108.876
108.105
39.955
39.761
39.568
39.374
33.823
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


NH
O
F3C
OH
4
19F NMR (CDCl3, 188 MHz)
-0.014
-70.728
-70.0
-70.8
ppm
1.00
-70.728
0
-10
-20
-30
-40
-50
-60
-70
ppm

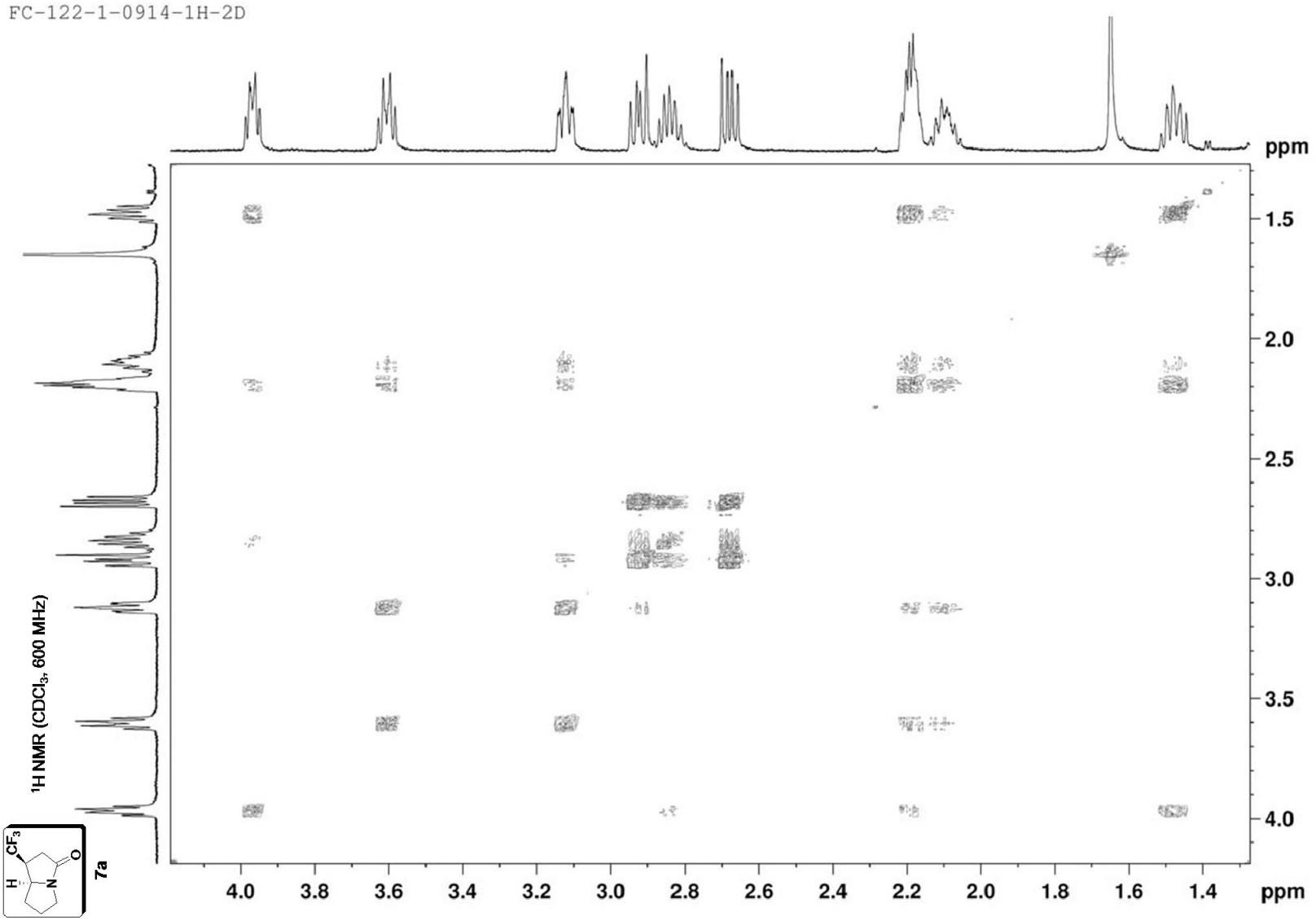

1H
7a
1H NMR (CDCl3, 600 MHz)
7.436
7.298
7.264
7.262
7.231
7.088
3.973
3.962
3.951
3.947
3.936
3.615
3.602
3.596
3.589
3.583
3.570
3.128
3.122
3.107
3.093
3.087
2.933
2.916
2.906
2.889
2.867
2.854
2.841
2.826
2.810
2.797
2.783
2.686
2.672
2.660
2.645
2.273
2.201
2.190
2.182
2.172
2.164
2.151
2.122
2.110
2.095
2.087
2.082
2.078
2.072
2.056
2.044
1.627
1.561
1.500
1.484
1.468
1.448
1.433
1.255
0.831
0.068
0.034
0.001
-0.001
1.000
1.069
1.003
0.981
1.065
1.033
1.630
1.090
1.149
ppm

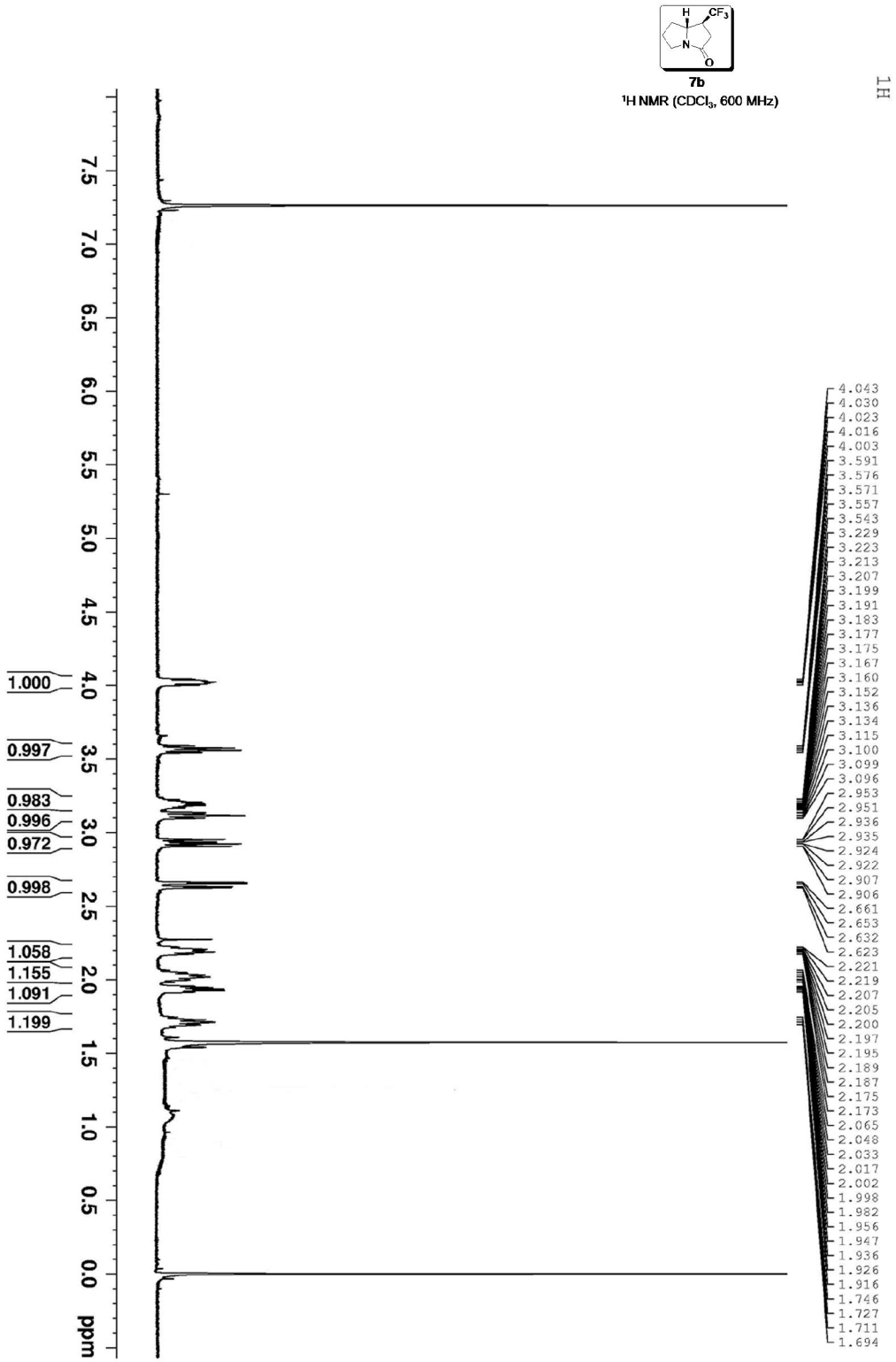

13C
7a
13C NMR (CDCl3, 600 MHz)
171.060
128.888
127.055
125.222
123.388
60.969
60.948
45.109
44.916
44.724
44.531
41.343
35.201
35.186
31.616
26.645
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

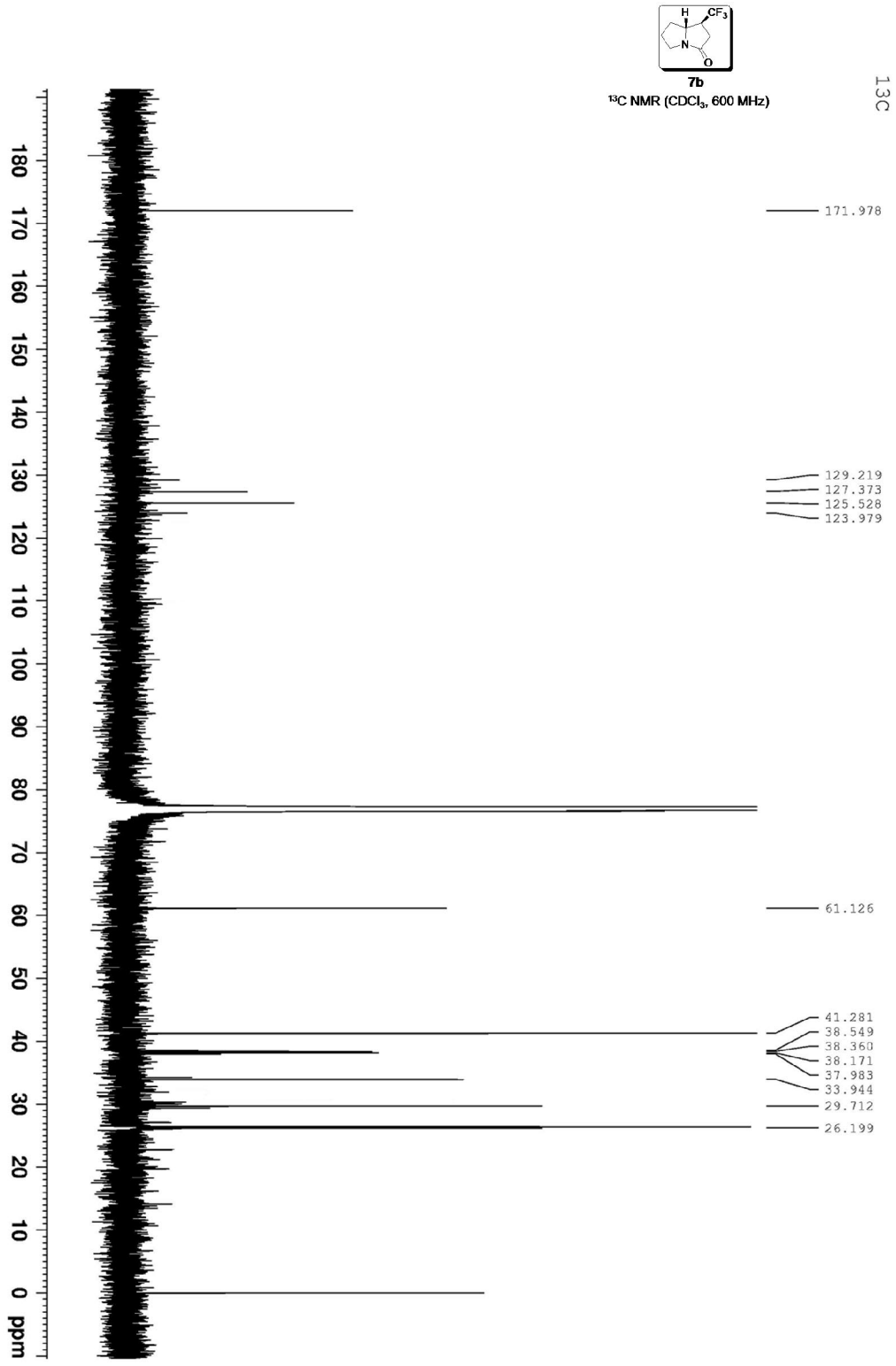


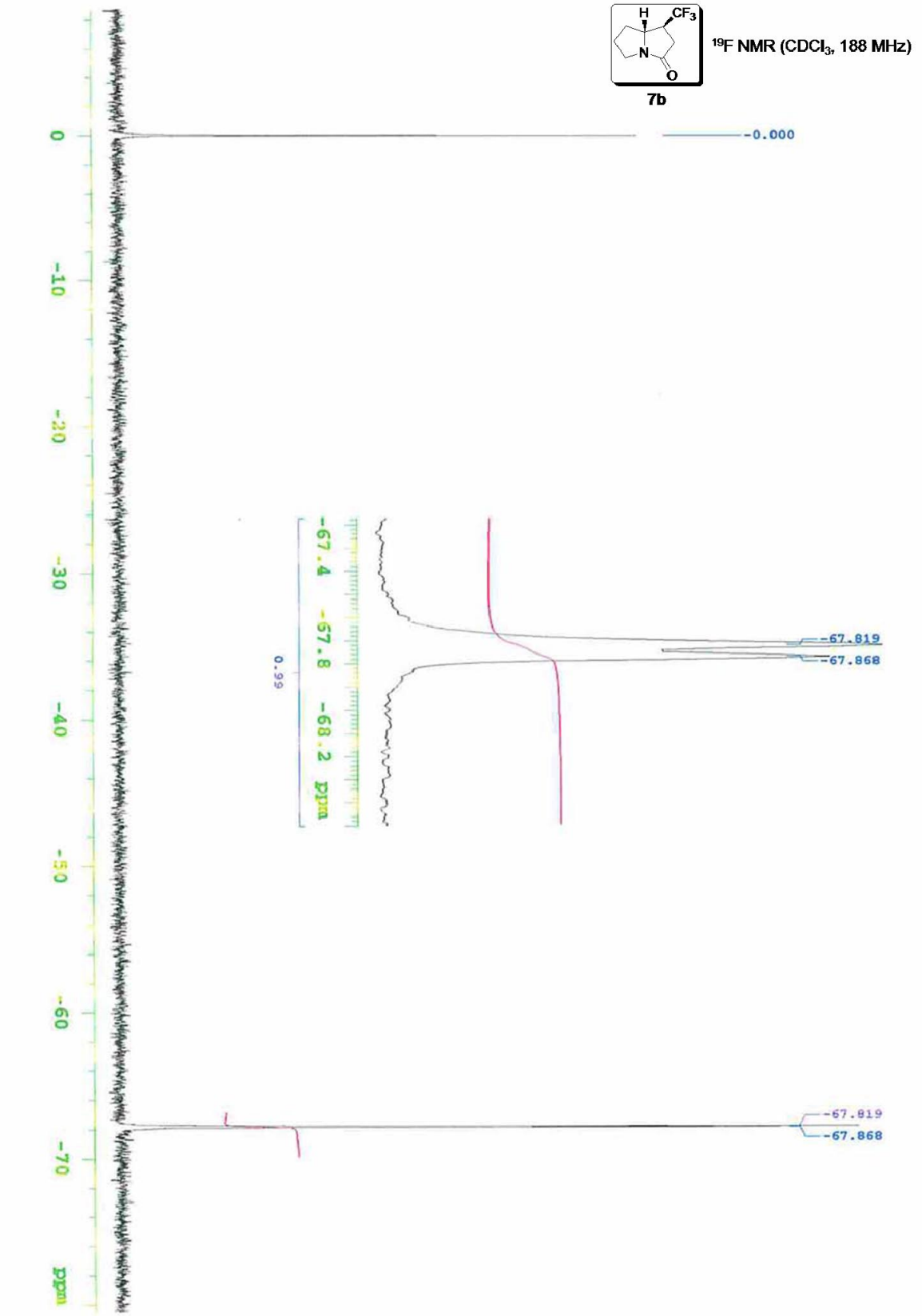
7a

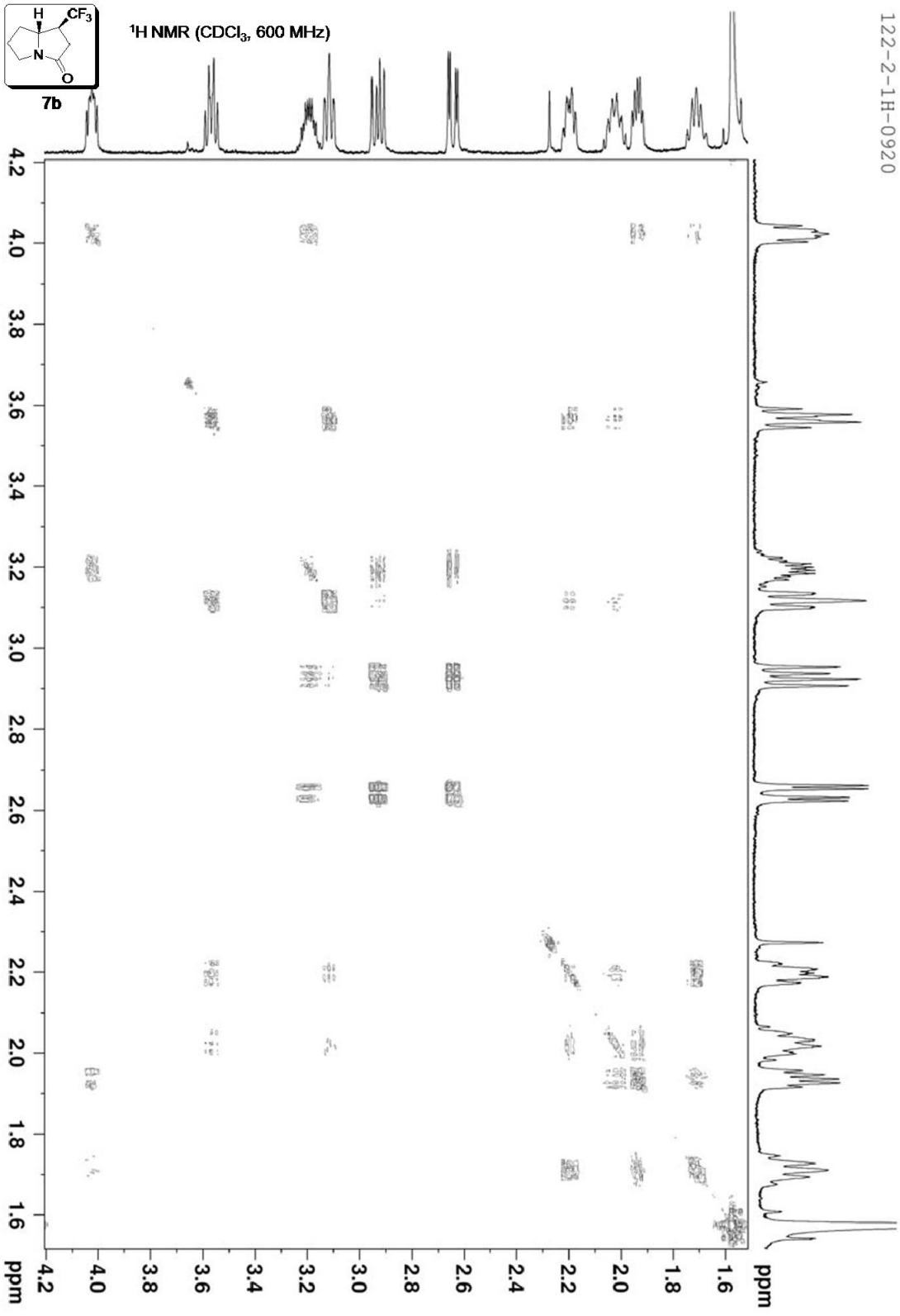
^{19}F NMR ($CDCl_3$, 188 MHz)

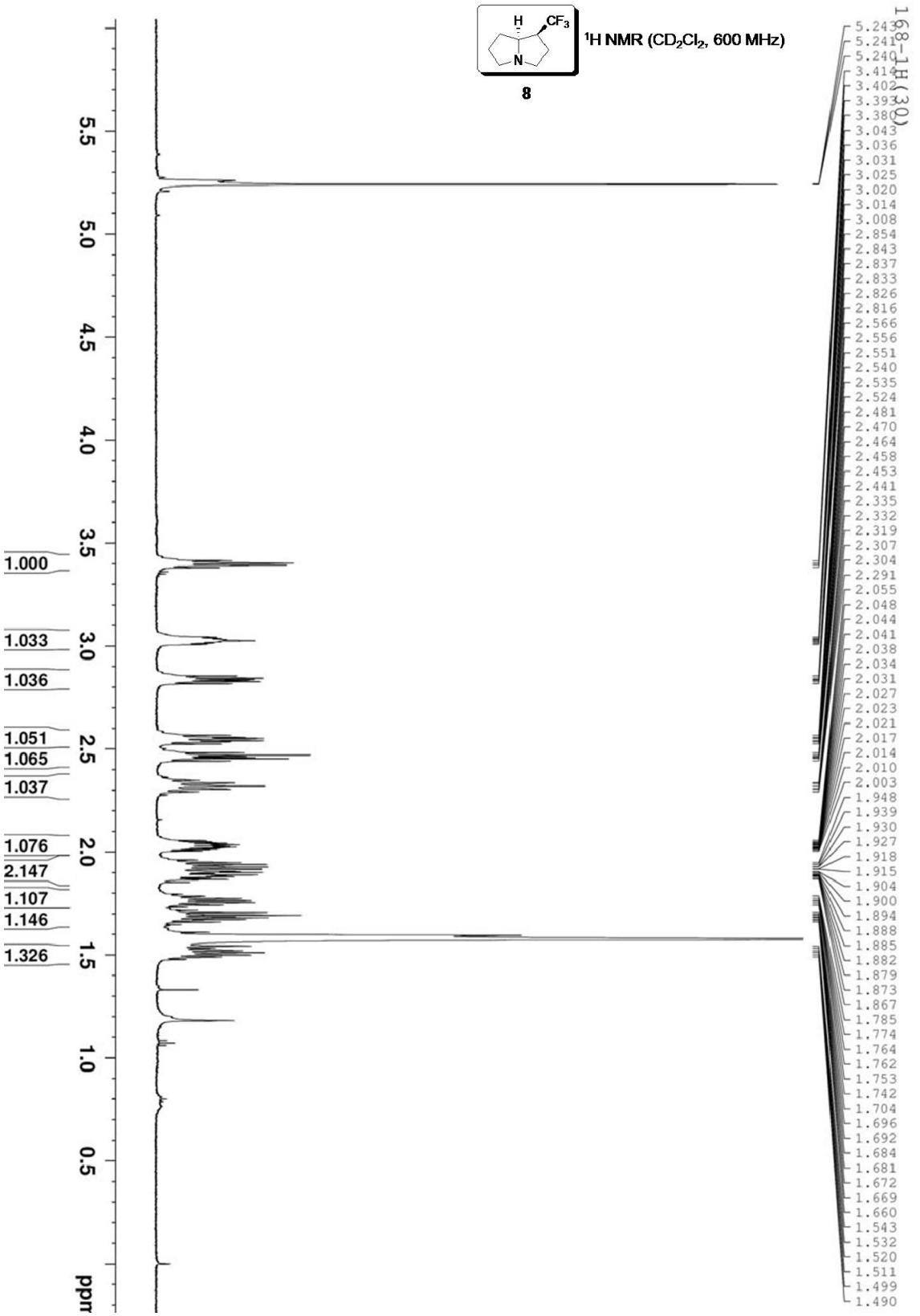

FC-122-1-0914-1H-2D
ppm
1.5
2.0
2.5
3.0
3.5
4.0
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
ppm
^{1}H NMR ($CDCl_3$, 600 MHz)
7a

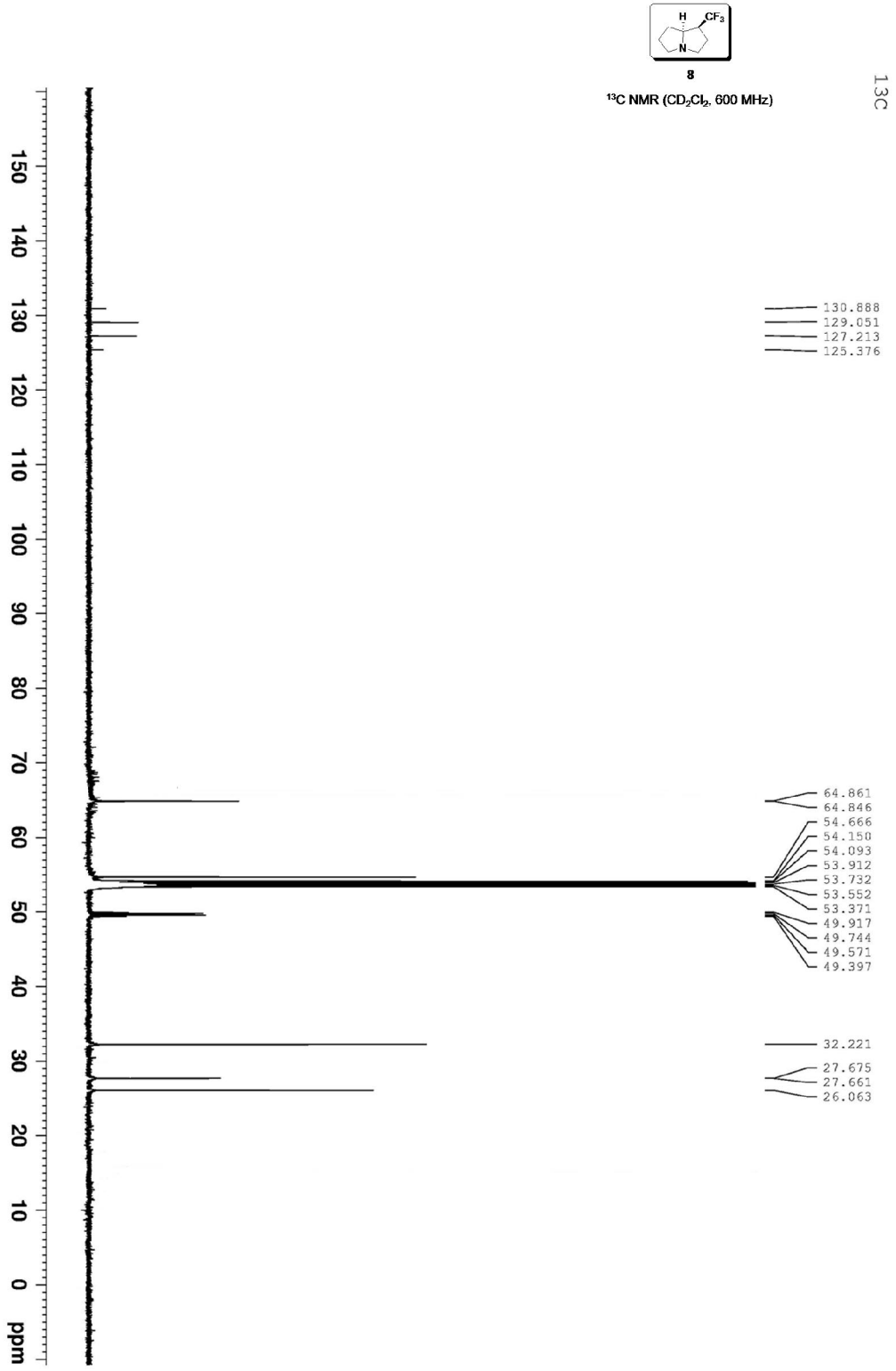

7b
¹H NMR (CDCl₃, 600 MHz)
1H
1.000
0.997
0.983
0.996
0.972
0.998
1.058
1.155
1.091
1.199
ppm
4.043
4.030
4.023
4.016
4.003
3.591
3.576
3.571
3.557
3.543
3.229
3.223
3.213
3.207
3.199
3.191
3.183
3.177
3.175
3.167
3.160
3.152
3.136
3.134
3.115
3.100
3.099
3.096
2.953
2.951
2.936
2.935
2.924
2.922
2.907
2.906
2.661
2.653
2.632
2.623
2.221
2.219
2.207
2.205
2.200
2.197
2.195
2.189
2.187
2.175
2.173
2.065
2.048
2.033
2.017
2.002
1.998
1.982
1.956
1.947
1.936
1.926
1.916
1.746
1.727
1.711
1.694

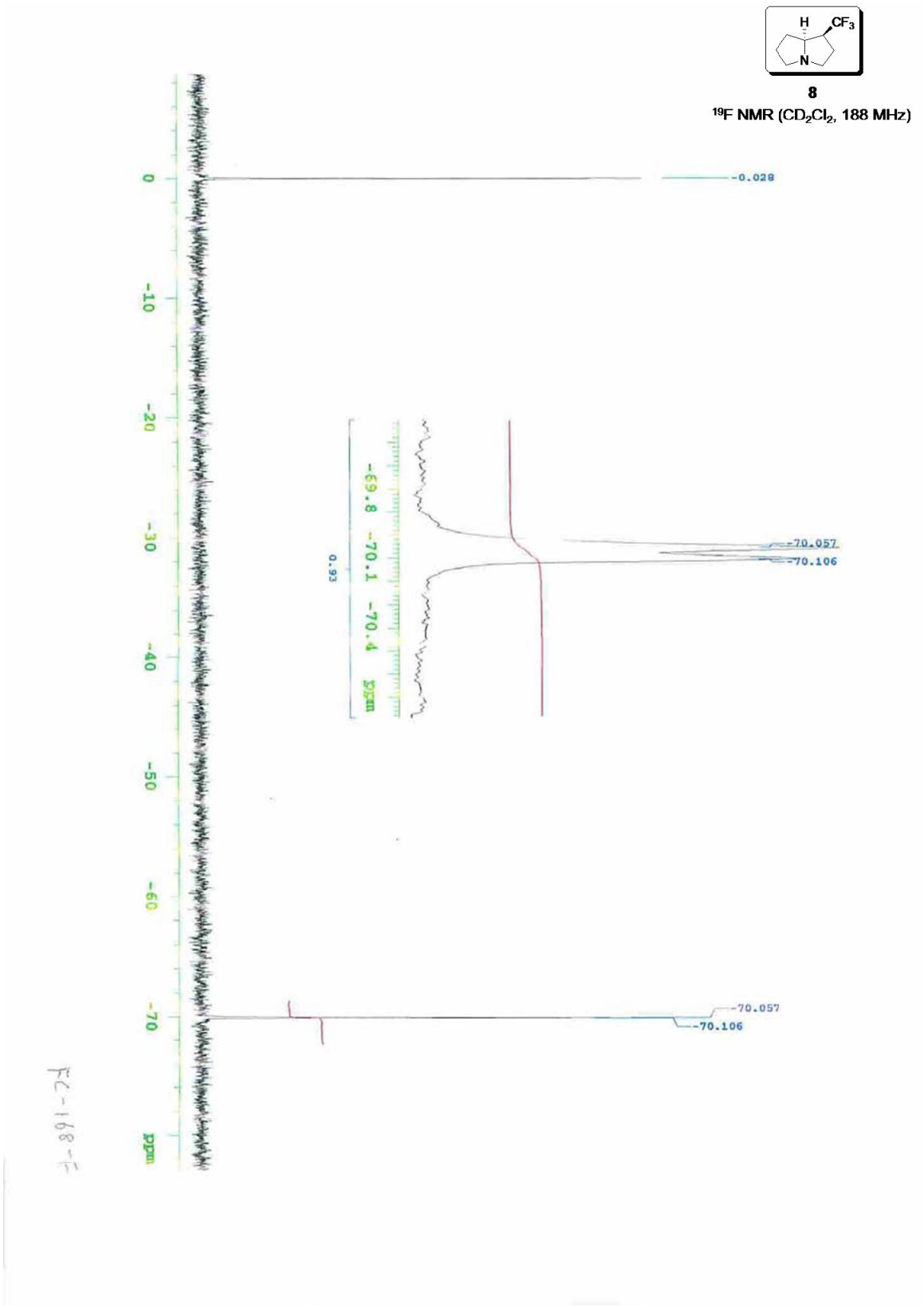

7b
13C NMR (CDCl3, 600 MHz)
13C
171.978
129.219
127.373
125.528
123.979
61.126
41.281
38.549
38.360
38.171
37.983
33.944
29.712
26.199
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


H
CF3
N
O
7b
19F NMR (CDCl3, 188 MHz)
-0.000
-67.819
-67.868
-67.819
-67.868
-67.4 -67.8 -68.2 ppm
0.99
0
-10
-20
-30
-40
-50
-60
-70
ppm

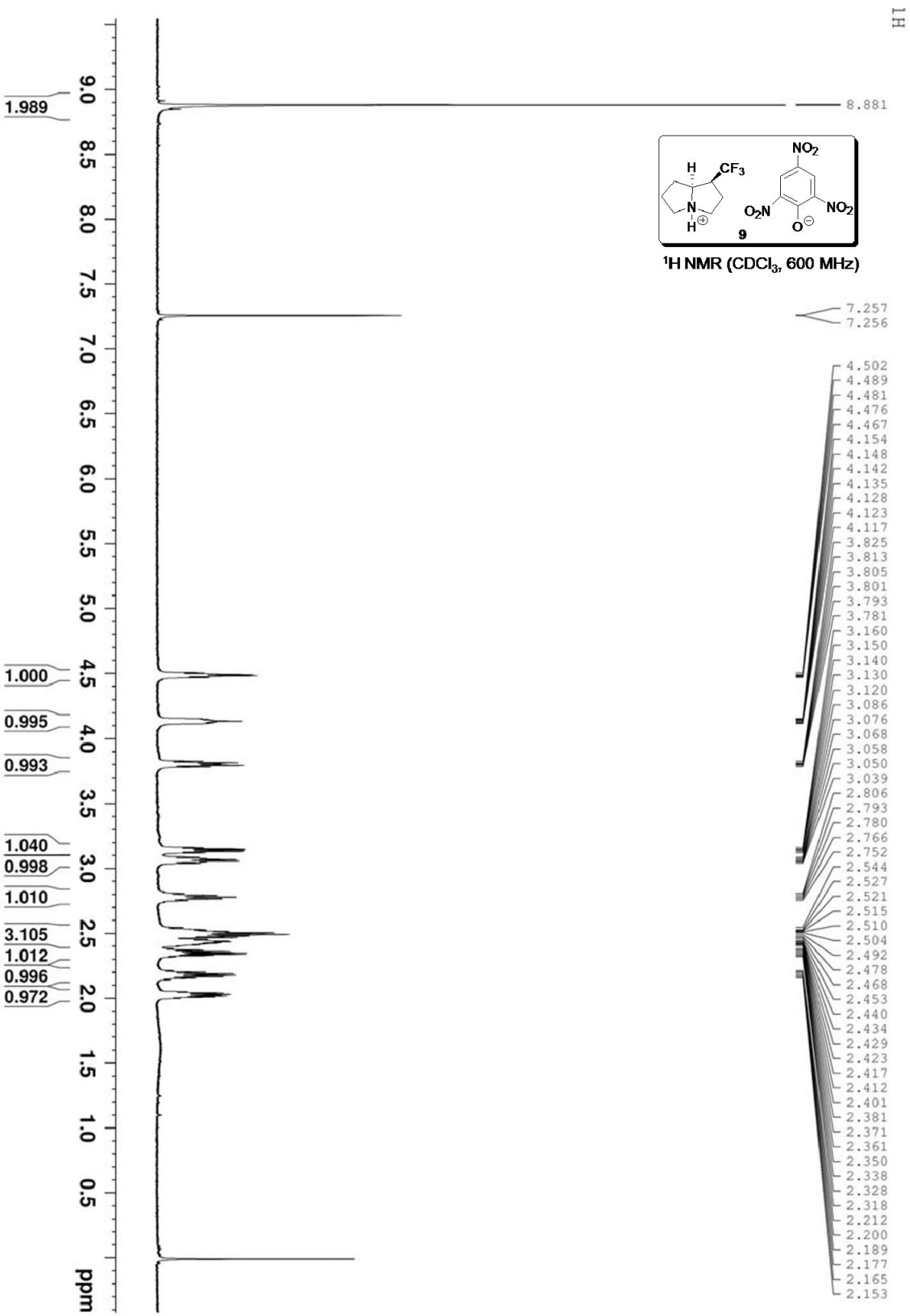

H
CF3
N
O
7b
1H NMR (CDCl3, 600 MHz)
122-2-1H-0920
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
ppm

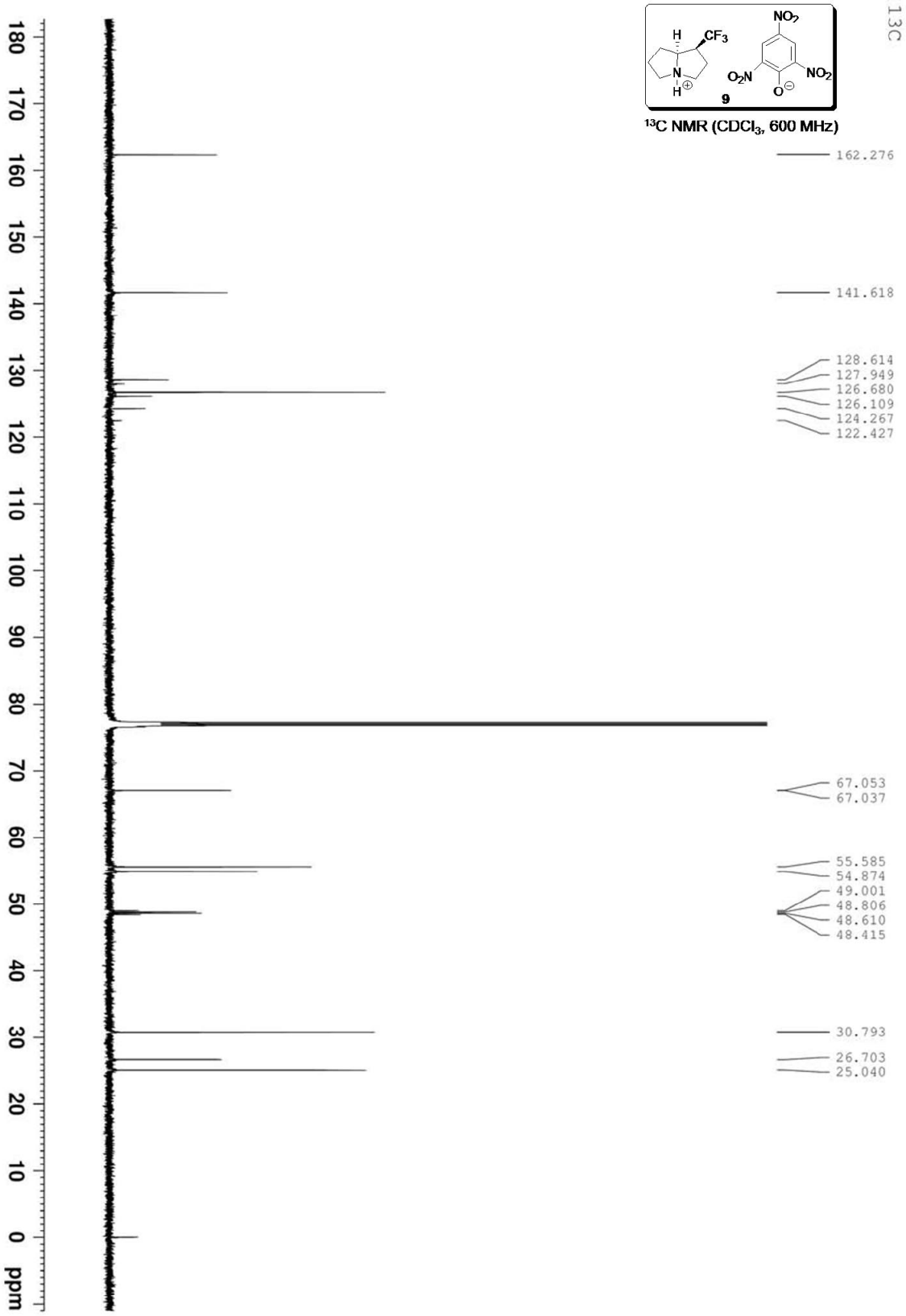

8
^{1}H NMR (CD_2Cl_2, 600 MHz)
168-1H(30)
1.000
1.033
1.036
1.051
1.065
1.037
1.076
2.147
1.107
1.146
1.326
ppm

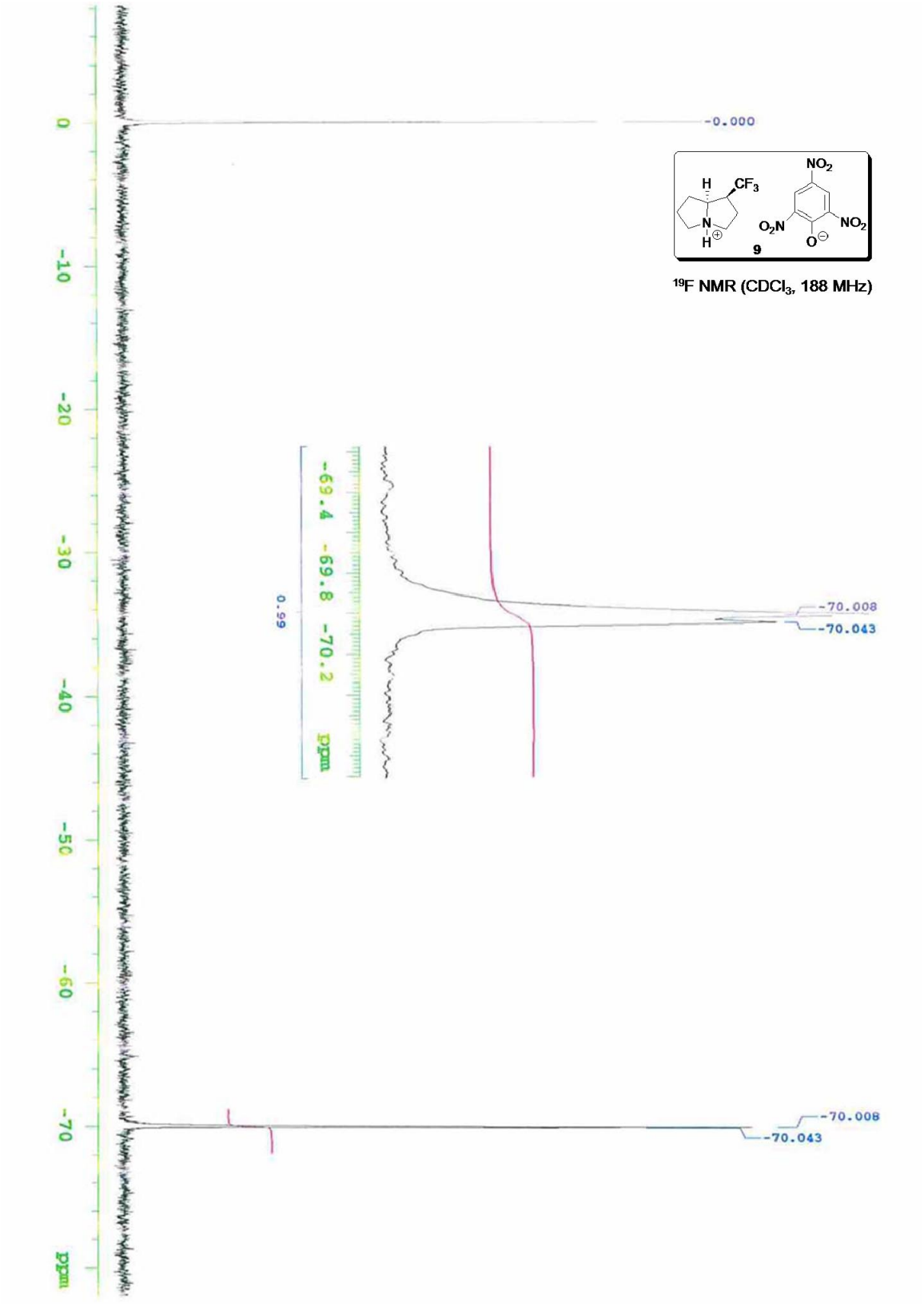

8
^{13}C NMR (CD_2Cl_2, 600 MHz)
13C
130.888
129.051
127.213
125.376
64.861
64.846
54.666
54.150
54.093
53.912
53.732
53.552
53.371
49.917
49.744
49.571
49.397
32.221
27.675
27.661
26.063
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


H
CF3
N
8
19F NMR (CD2Cl2, 188 MHz)
-0.028
-70.057
-70.106
-70.057
-70.106
-69.8
-70.1
-70.4
ppm
0
-10
-20
-30
-40
-50
-60
-70

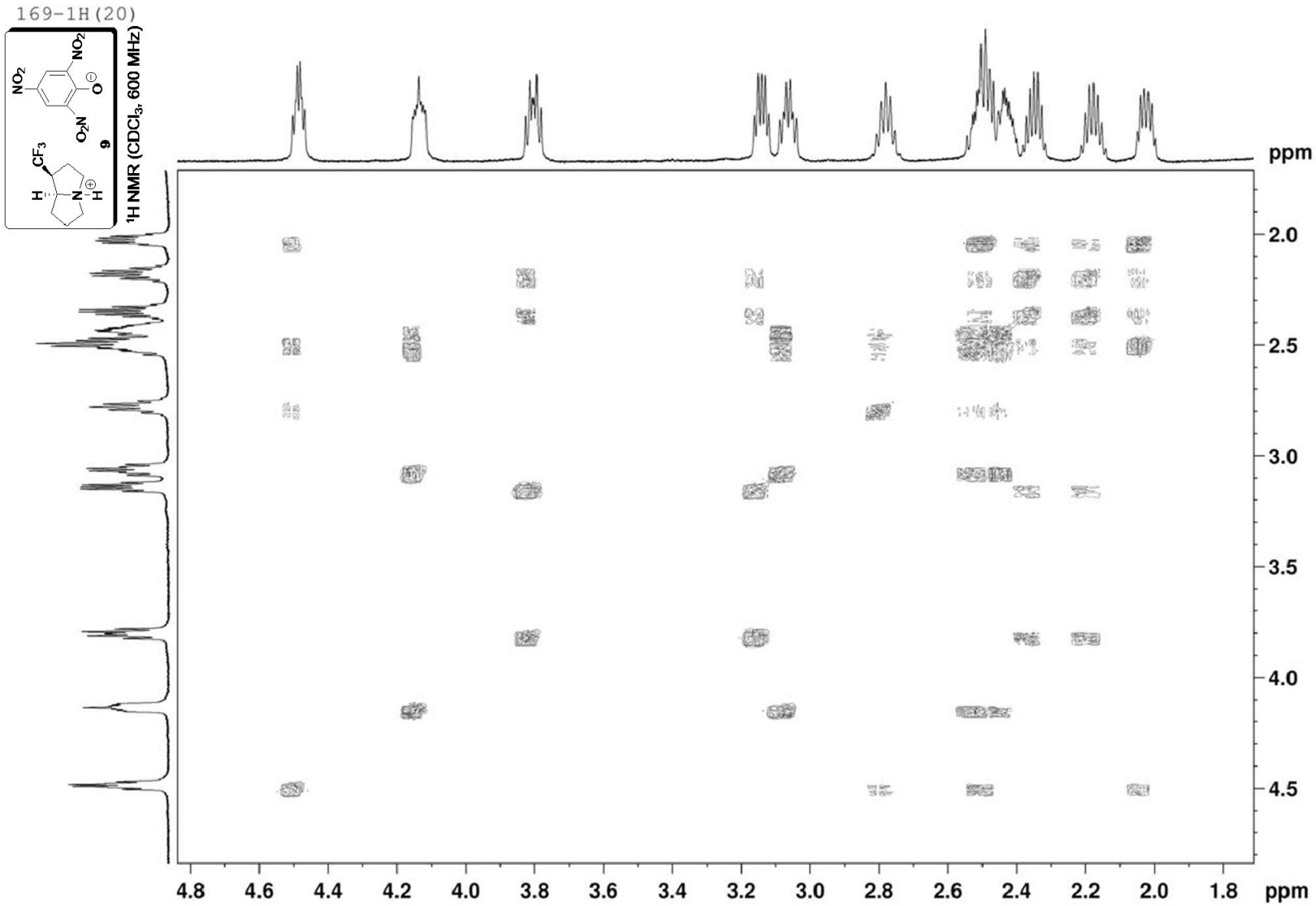
168-1H-2D
H
CF3
N
8
1H NMR (CD2Cl2, 600 MHz)
ppm
3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 ppm
1.6 1.8 2.0 2.2 2.4 2.6 2.8 3.0 3.2 3.4 3.6

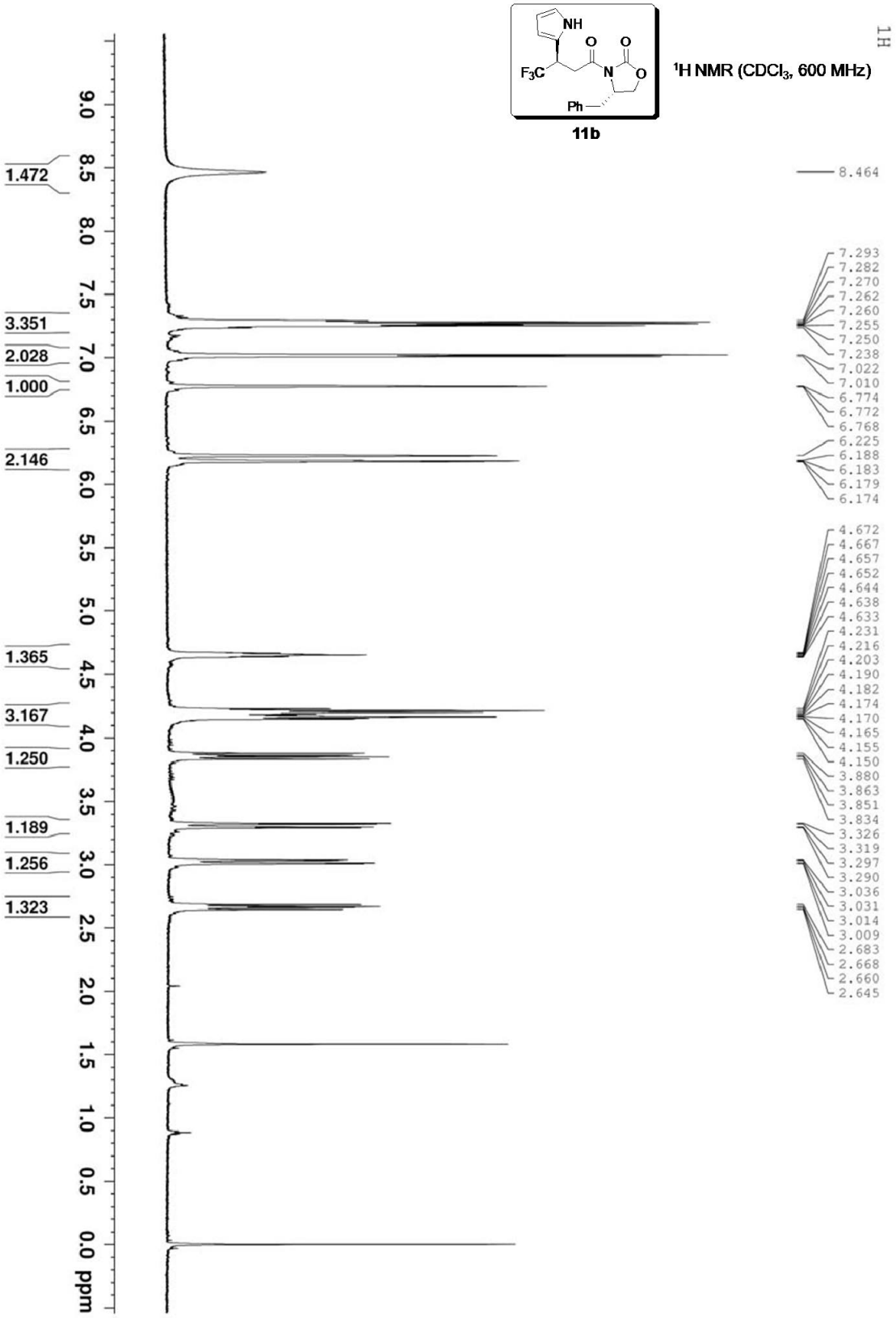

1H
8.881
7.257
7.256
4.502
4.489
4.481
4.476
4.467
4.154
4.148
4.142
4.135
4.128
4.123
4.117
3.825
3.813
3.805
3.801
3.793
3.781
3.160
3.150
3.140
3.130
3.120
3.086
3.076
3.068
3.058
3.050
3.039
2.806
2.793
2.780
2.766
2.752
2.544
2.527
2.521
2.515
2.510
2.504
2.492
2.478
2.468
2.453
2.440
2.434
2.429
2.423
2.417
2.412
2.401
2.381
2.371
2.361
2.350
2.338
2.328
2.318
2.212
2.200
2.189
2.177
2.165
2.153
1.989
1.000
0.995
0.993
1.040
0.998
1.010
3.105
1.012
0.996
0.972
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
9
1H NMR (CDCl3, 600 MHz)

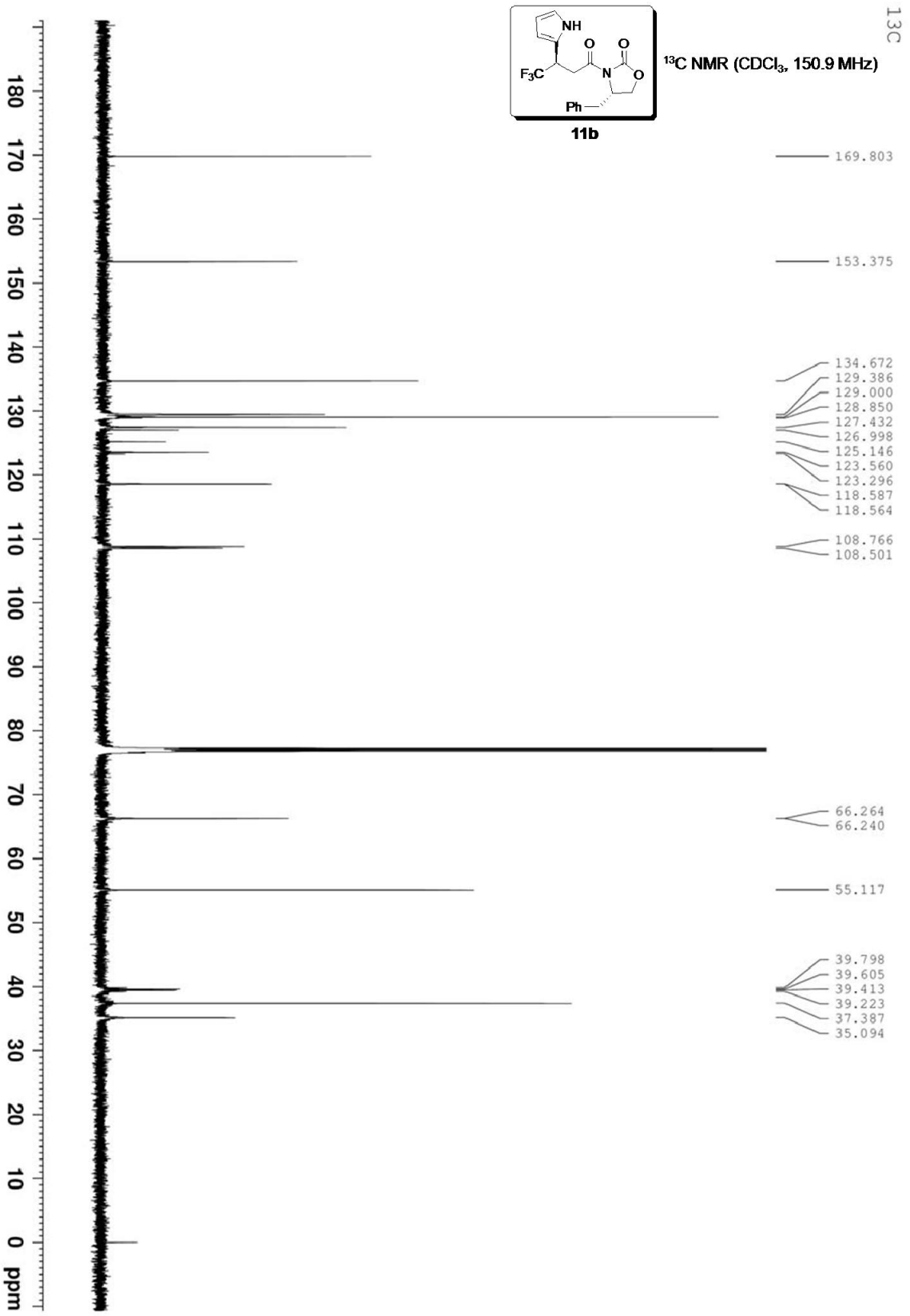

13C
9
13C NMR (CDCl3, 600 MHz)
162.276
141.618
128.614
127.949
126.680
126.109
124.267
122.427
67.053
67.037
55.585
54.874
49.001
48.806
48.610
48.415
30.793
26.703
25.040
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

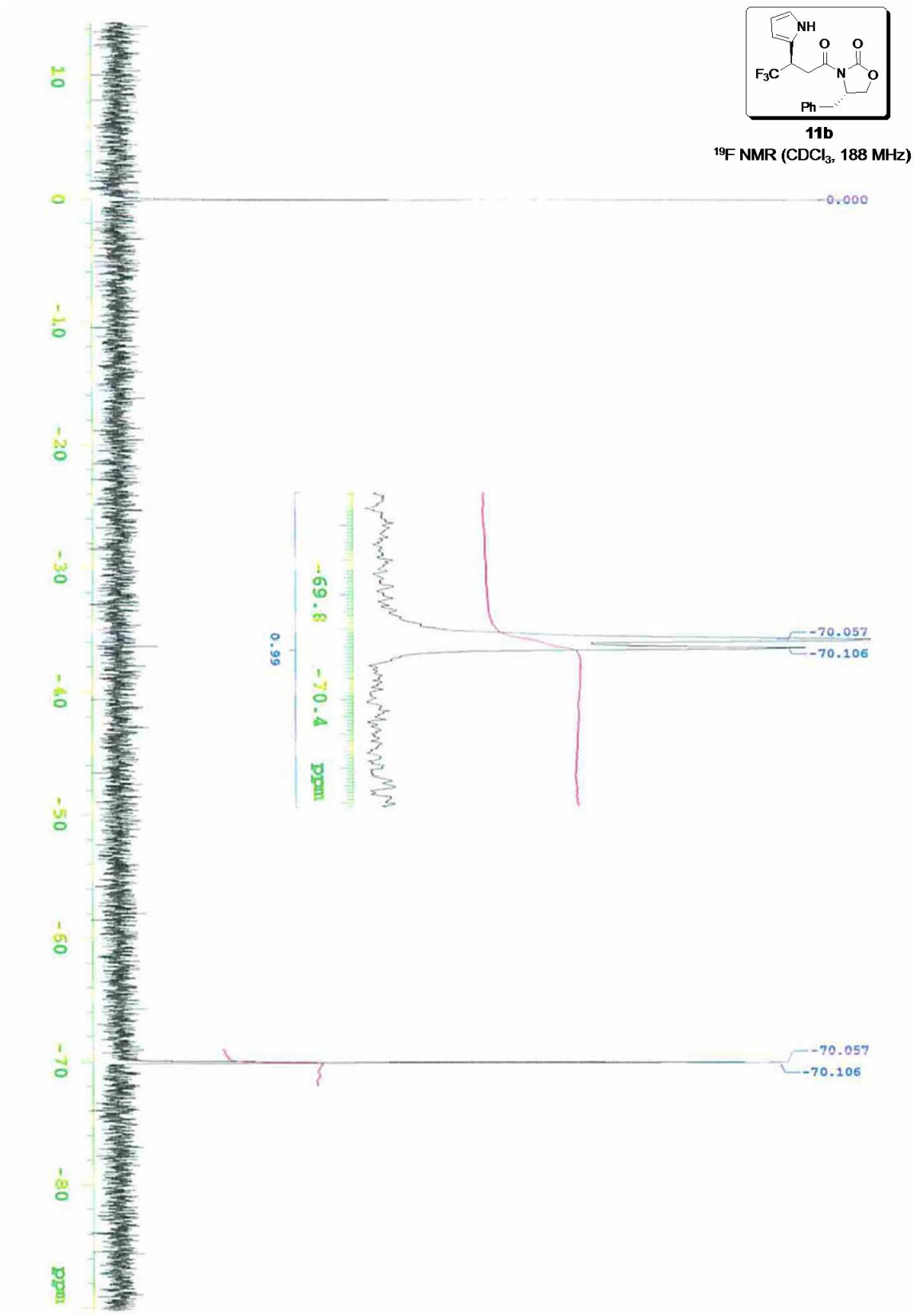


^{19}F NMR ($CDCl_3$, 188 MHz)


169-1H(20)
^{1}H NMR ($CDCl_3$, 600 MHz)
9
ppm
2.0
2.5
3.0
3.5
4.0
4.5
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
ppm

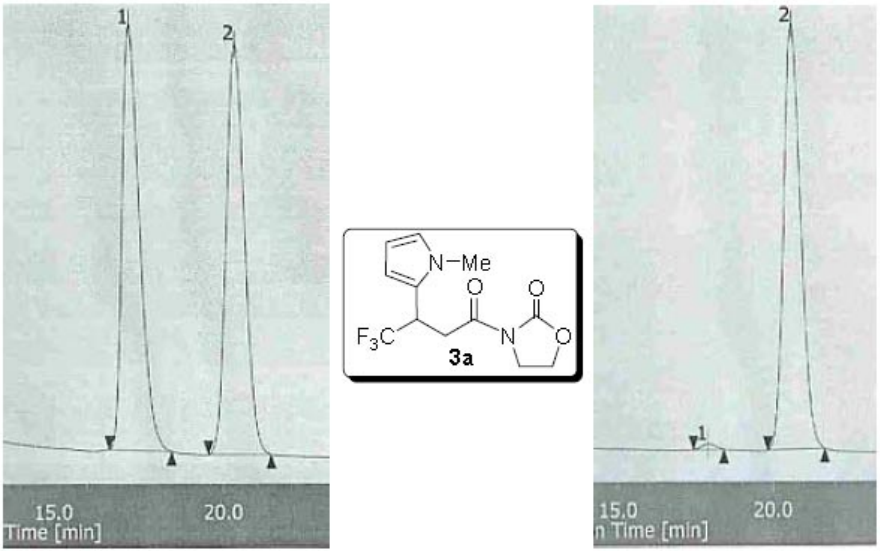

NH
O
O
F3C
N
O
Ph
11b
1H NMR (CDCl3, 600 MHz)
1H
1.472
3.351
2.028
1.000
2.146
1.365
3.167
1.250
1.189
1.256
1.323
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0 ppm
8.464
7.293
7.282
7.270
7.262
7.260
7.255
7.250
7.238
7.022
7.010
6.774
6.772
6.768
6.225
6.188
6.183
6.179
6.174
4.672
4.667
4.657
4.652
4.644
4.638
4.633
4.231
4.216
4.203
4.190
4.182
4.174
4.170
4.165
4.155
4.150
3.880
3.863
3.851
3.834
3.326
3.319
3.297
3.290
3.036
3.031
3.014
3.009
2.683
2.668
2.660
2.645


13C
NH
O
O
F3C
N
O
Ph
11b
13C NMR (CDCl3, 150.9 MHz)
169.803
153.375
134.672
129.386
129.000
128.850
127.432
126.998
125.146
123.560
123.296
118.587
118.564
108.766
108.501
66.264
66.240
55.117
39.798
39.605
39.413
39.223
37.387
35.094
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


NH
O
O
F3C
N
O
Ph
11b
19F NMR (CDCl3, 188 MHz)
0.000
-70.057
-70.106
-69.8
-70.4
ppm
0.99
-70.057
-70.106
10
0
-10
-20
-30
-40
-50
-60
-70
-80
ppm

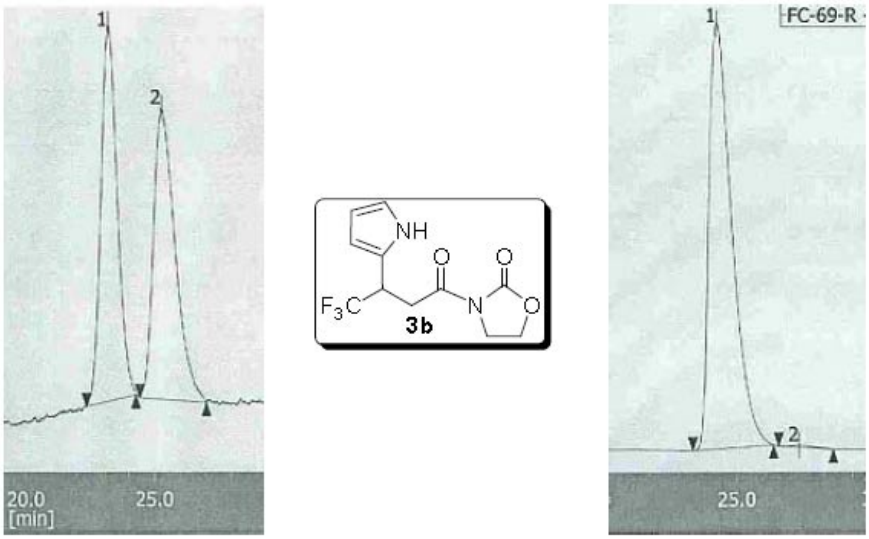
HPLC Charts

3a, 98% ee (OD-H, Hex/i-PrOH = 70/30, flow rate = 0.8 mL/min, λ = 232 nm)



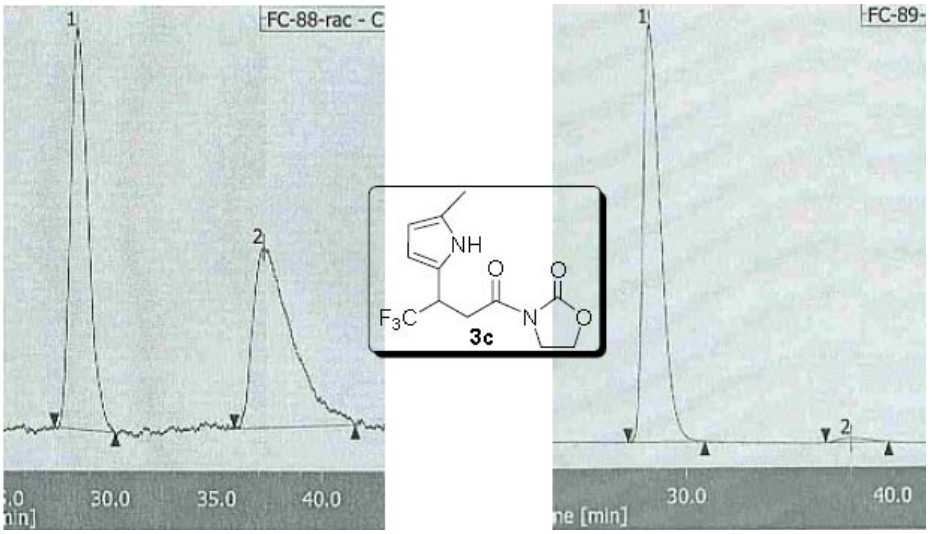
No.	t_R [min]	Area [%]	Height [%]	No.	t_R [min]	Area [%]	Height [%]
1	17.258	49.741	50.959	1	17.917	1.102	1.303
2	20.358	50.259	49.041	2	20.625	98.898	98.697

3b, 99% ee (OD-H, Hex/i-PrOH = 70/30, flow rate = 0.5 mL/min, λ = 232 nm)



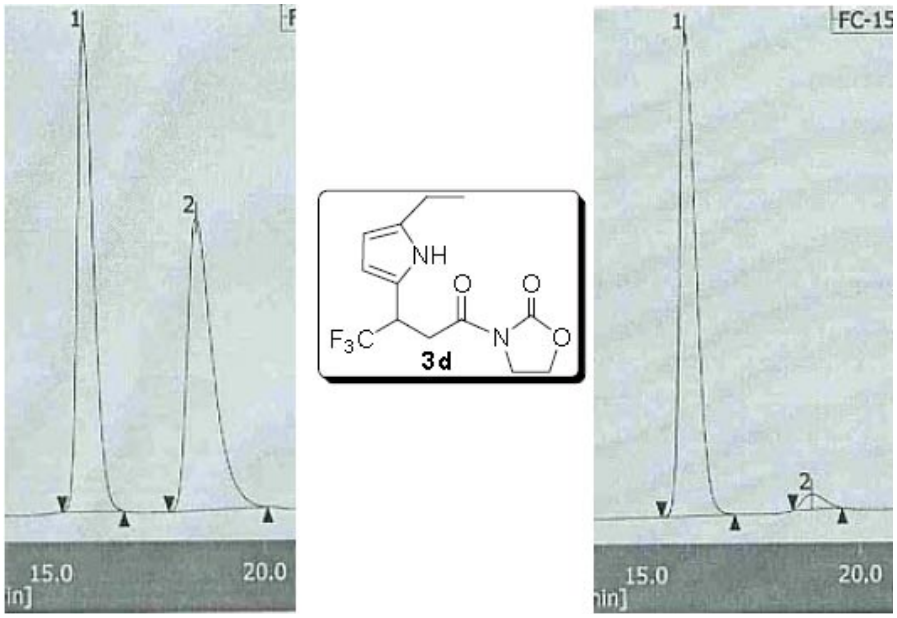
No.	t_R [min]	Area [%]	Height [%]	No.	t_R [min]	Area [%]	Height [%]
1	23.217	49.418	56.370	1	24.375	99.554	99.506
2	25.275	50.582	43.630	2	27.142	0.446	0.494

3c, 97% ee (OD-H, Hex/i-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 232 nm)



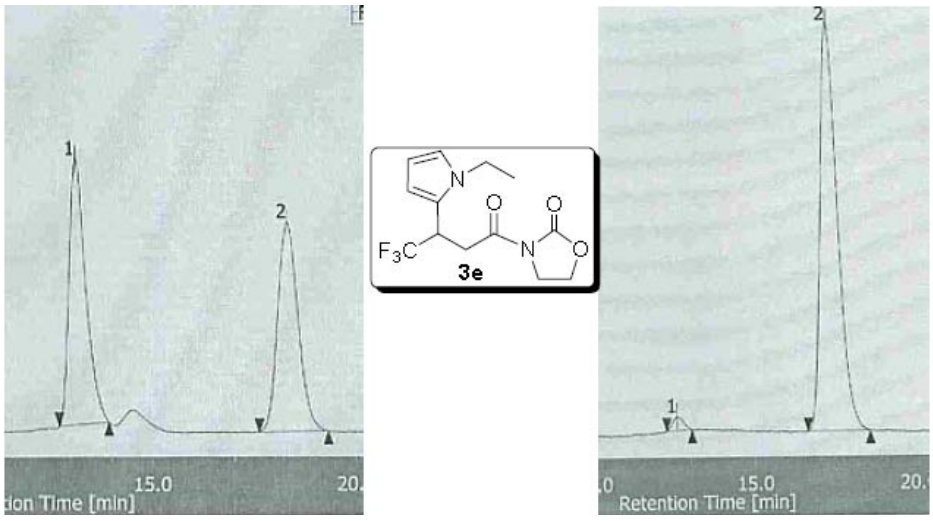
No.	t_R [min]	Area [%]	Height [%]	No.	t_R [min]	Area [%]	Height [%]
1	28.458	50.072	69.127	1	28.342	98.390	99.026
2	37.208	49.928	30.873	2	37.992	1.610	0.974

3d, 92% ee (OD-H, Hex/i-PrOH = 70/30, flow rate = 0.5 mL/min, λ = 232 nm)



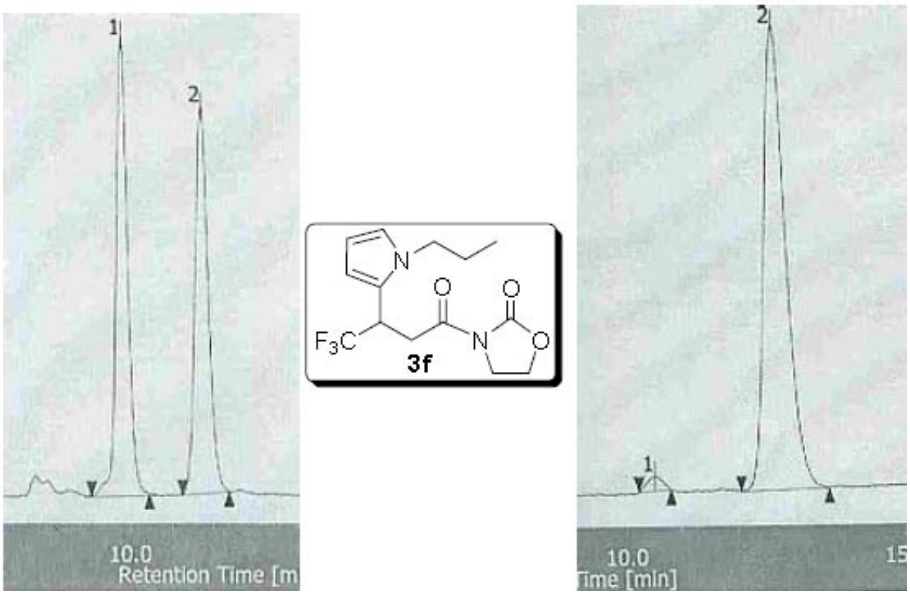
No.	t_R [min]	Area [%]	Height [%]	No.	t_R [min]	Area [%]	Height [%]
1	15.858	50.764	62.289	1	16.033	95.889	96.941
2	18.450	49.236	37.711	2	18.875	4.111	3.059

3e, 96% ee (OD-H, Hex/i-PrOH = 70/30, flow rate = 0.8 mL/min, λ = 232 nm)



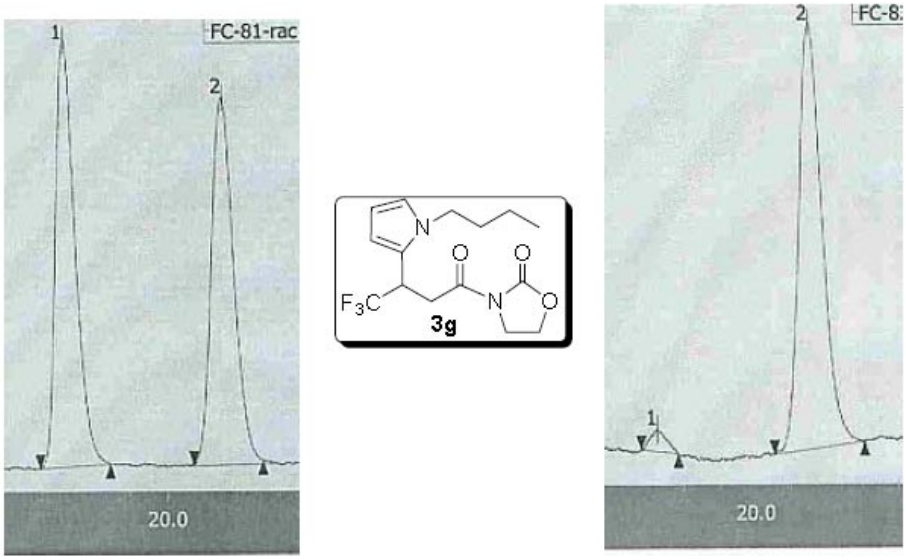
No.	t_R [min]	Area [%]	Height [%]	No.	t_R [min]	Area [%]	Height [%]
1	13.125	51.154	55.999	1	12.583	2.184	3.326
2	18.308	48.846	44.001	2	17.317	97.816	96.674

3f, 95% ee (OD-H, Hex/i-PrOH = 70/30, flow rate = 0.8 mL/min, λ = 232 nm)



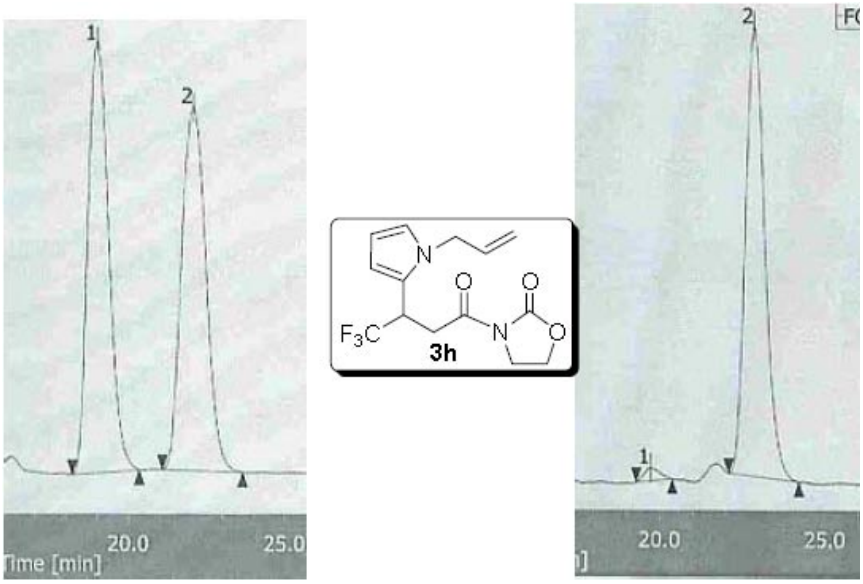
No.	t_R [min]	Area [%]	Height [%]	No.	t_R [min]	Area [%]	Height [%]
1	9.792	50.986	54.311	1	10.508	2.270	3.137
2	11.692	49.014	45.689	2	12.693	97.730	96.863

3g, 93% ee (OD-H, Hex/i-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 232 nm)



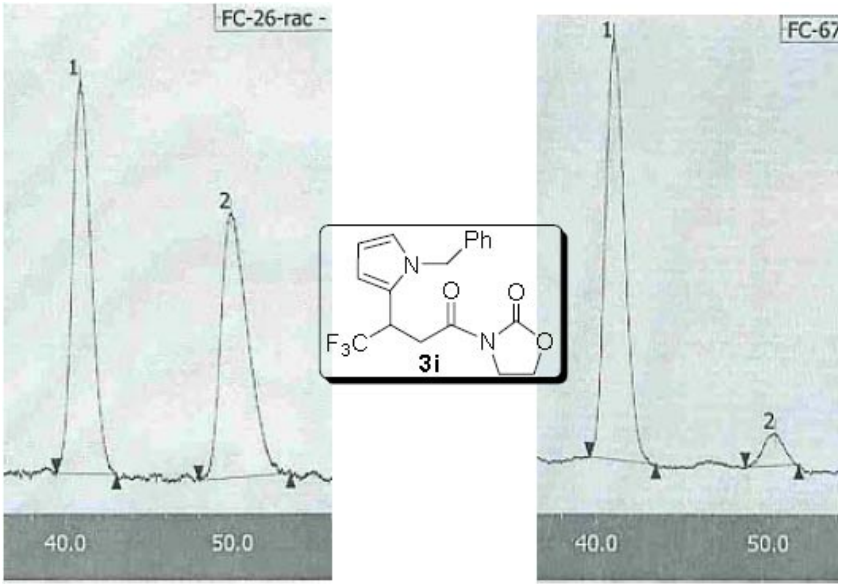
No.	t_R [min]	Area [%]	Height [%]	No.	t_R [min]	Area [%]	Height [%]
1	17.292	50.140	53.772	1	17.275	3.374	4.903
2	21.483	49.860	46.228	2	21.542	96.626	95.097

3h, 95% ee (OD-H, Hex/i-PrOH = 70/30, flow rate = 0.5 mL/min, λ = 232 nm)



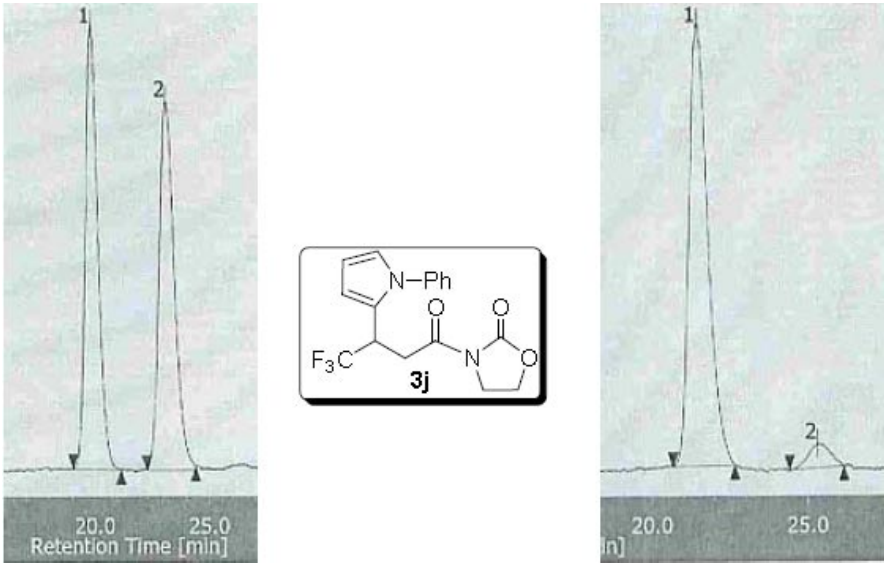
No.	t_R [min]	Area [%]	Height [%]	No.	t_R [min]	Area [%]	Height [%]
1	19.017	50.391	54.310	1	19.725	2.315	2.817
2	22.075	49.609	45.690	2	22.833	97.685	97.183

3i, 85% ee (OD-H, Hex/i-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 232 nm)



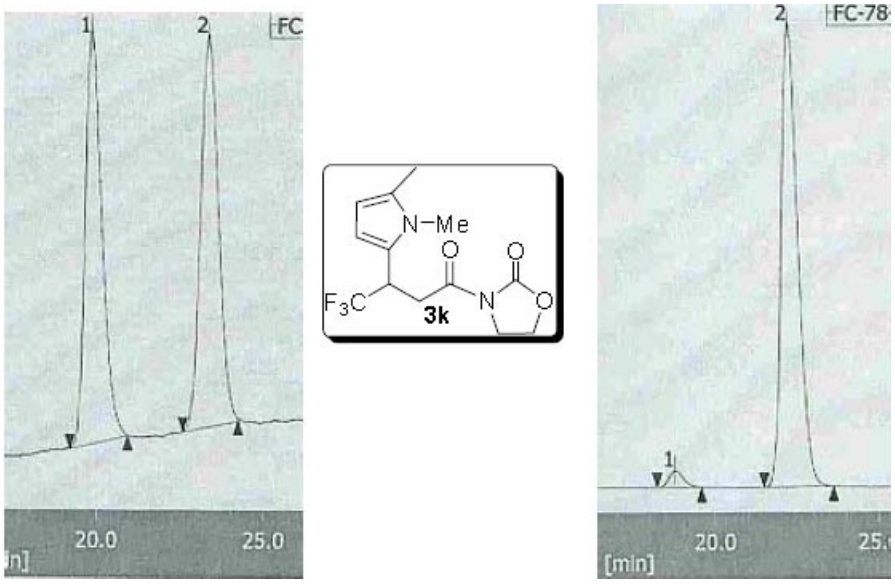
No.	t_R [min]	Area [%]	Height [%]	No.	t_R [min]	Area [%]	Height [%]
1	40.967	50.709	59.833	1	40.975	92.258	92.777
2	49.983	49.291	40.167	2	50.458	7.742	7.223

3j, 88% ee (OD-H, Hex/i-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 232 nm)



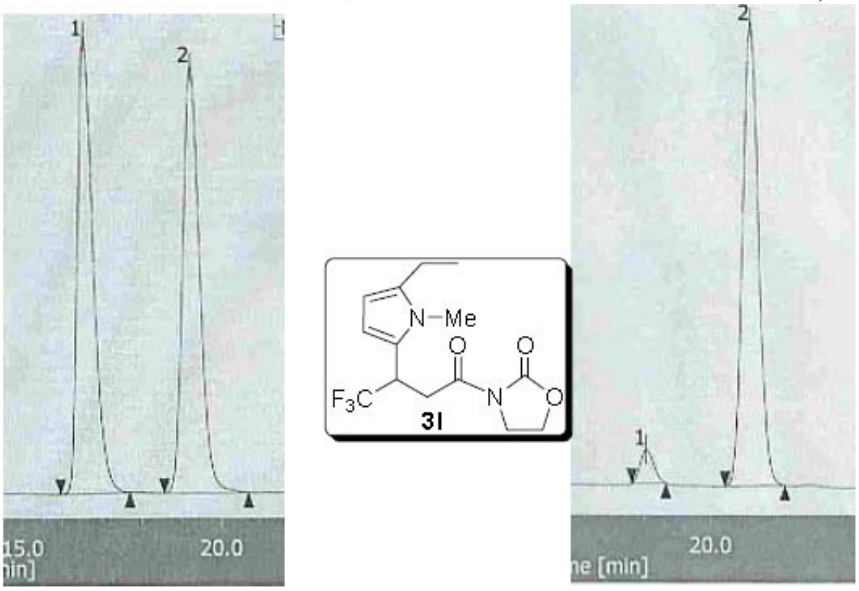
No.	t_R [min]	Area [%]	Height [%]	No.	t_R [min]	Area [%]	Height [%]
1	19.867	49.895	54.713	1	21.508	93.980	94.695
2	23.142	50.105	45.287	2	25.308	6.020	5.305

3k, 94% ee (OD-H, Hex/i-PrOH = 70/30, flow rate = 0.5 mL/min, λ = 232 nm)



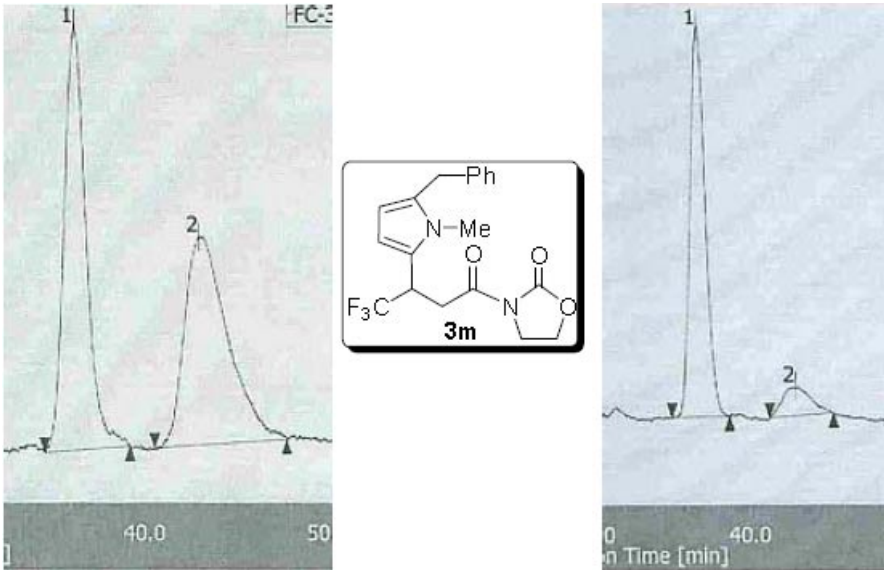
No.	t_R [min]	Area [%]	Height [%]	No.	t_R [min]	Area [%]	Height [%]
1	19.850	49.583	51.266	1	18.783	3.056	3.481
2	23.333	50.417	48.734	2	22.275	96.944	96.519

3l, 88% ee (OD-H, Hex/i-PrOH = 70/30, flow rate = 0.5 mL/min, λ = 232 nm)



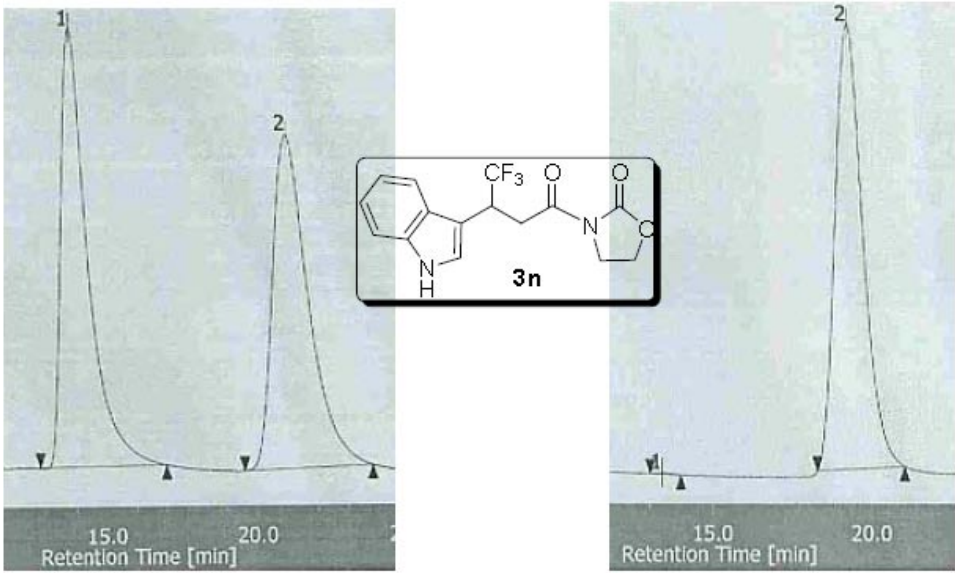
No.	t_R [min]	Area [%]	Height [%]	No.	t_R [min]	Area [%]	Height [%]
1	16.567	49.645	51.767	1	18.067	5.874	6.836
2	19.250	50.355	48.233	2	21.192	94.126	93.164

3m, 76% ee (OD-H, Hex/i-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 232 nm)



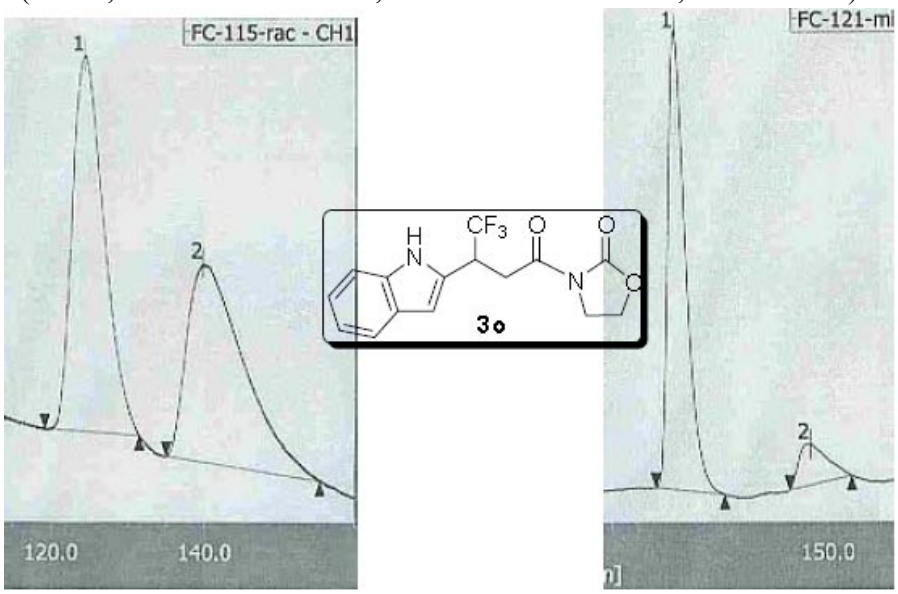
No.	t_R [min]	Area [%]	Height [%]	No.	t_R [min]	Area [%]	Height [%]
1	36.192	50.760	67.263	1	36.725	87.929	93.093
2	42.942	49.240	32.737	2	42.892	12.071	6.907

3n, 99% ee (OD-H, Hex/i-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 232 nm)



No.	t_R [min]	Area [%]	Height [%]	No.	t_R [min]	Area [%]	Height [%]
1	13.842	50.091	56.833	1	13.383	0.147	0.309
2	21.025	49.909	43.167	2	19.192	99.853	99.691

3o, 75% ee (OD-H, Hex/i-PrOH = 90/10, flow rate = 0.5 mL/min, λ = 232 nm)



No.	t_R [min]	Area [%]	Height [%]	No.	t_R [min]	Area [%]	Height [%]
1	124.425	50.937	65.383	1	121.767	87.324	91.777
2	139.817	49.063	34.617	2	146.742	12.676	8.223