The preparation of difluoromethylated indoles via electrochemical oxidation under catalyst- and oxidant-free conditions

Dong Zhang [a, *], Wenqiao Chang [a], Yun Li [a], Songying Zhan [a], Junjie Pan [a], Shunhui Cai [a], Na Li [a], Xiaoqin Yang [a], Zheng Fang [b]

[a] School of Pharmacy, Yancheng Teachers University, Yancheng 224007, China.

[b] College of Biotechnology and Pharmaceutical Engineering, Nanjing Tech University, Nanjing 211816, China.

*Corresponding Author(s): Dong Zhang, E-mail: zhangd@yctu.edu.cn

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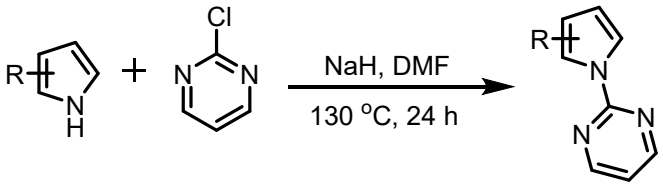
1. General Information

All reactions were carried out with magnetic stirring and in dried glassware. Standard syringe techniques were applied for transfer of dry solvents. Unless otherwise indicated, all commercially available chemicals were used without purification. ^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz), and ^{19}F NMR (376 MHz) were measured on a 400 M spectrometer. The chemical shifts are given in parts per million (ppm) on the delta (δ) scale. ^{1}H NMR chemical shifts were determined relative to internal tetramethylsilane (TMS) at δ 7.26 ppm. ^{13}C NMR chemical shifts were determined relative to $CDCl_3$ at δ 77.16 ppm. The following abbreviations are used to explain multiplicities: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, td=triplet of doublet, q = quartet, m = multiplet, and br = broad. Analytical thin-layer chromatography (TLC) was performed on 0.2 mm coated silica gel plates, and the course of the reactions were visualized using a UV light 254 nm. High-resolution mass spectra (HRMS) were obtained on an Agilent mass spectrometer using electrospray ionization-time-of-flight (ESI-TOF).

2. Experimental Section

2.1 Synthesis of starting material [1]



In an oven-dried flask (100 mL), NaH (60% dispersion in mineral oil, 11 mmol) was added in portions at 0 °C to a stirred solution of the corresponding indoles or pyrrole (10 mmol) in DMF (25 mL). After stirring for 30min at 0 °C, 2-chloropyrimidine (12 mmol) was added and the mixture was stirred at 130 °C for 24 h. Then, the reaction mixture was cooled to room temperature, poured into H_2O (300 mL) and extracted with EtOAc (4×50 mL). The combined organic phase was dried over Na_2SO_4. The filtrate was concentrated in vacuo and the crude product was purified by column chromatography on silica gel (n-hexane/EtOAc) to give the desired product.

2.2 Experimental device

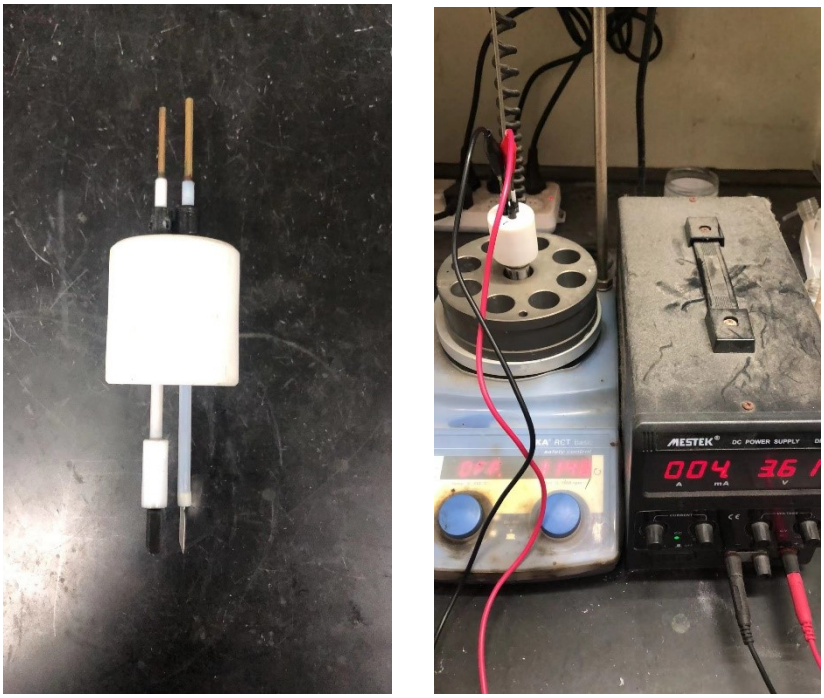
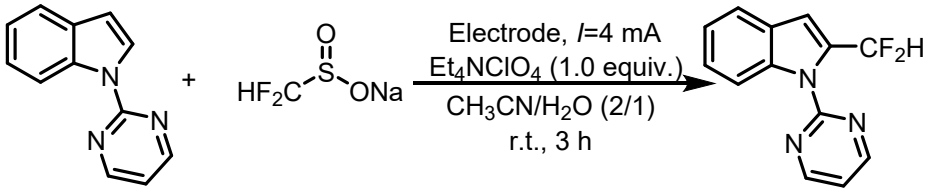


Figure S1. Experimental device

2.3 Optimization of other Reaction Conditions

Table S1. Screen the loading of **2** and electrode [a, b]

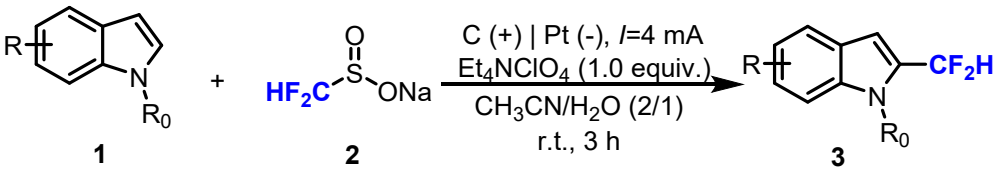


1a **2** **3a**

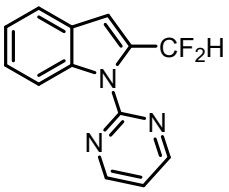
Entry	HF_2CSO_2Na (equiv.)	electrode	Yield (%) [b]
1	2.0	C (+) | Pt (-)	73
2	1.0	C (+) | Pt (-)	44
3	1.5	C (+) | Pt (-)	57
4	3.0	C (+) | Pt (-)	71
5	2.0	C (+) | C (-)	15
6	2.0	Pt (+) | Pt (-)	0
7	2.0	Pt (+) | C (-)	0

[a] Reaction conditions: undivided cell, electrode, 4 mA, **1a** (0.2 mmol, 1.0 equiv.), **2** (equiv.), Et_4NClO_4 (1.0 equiv.), CH_3CN/H_2O (6 mL, v/v = 2/1), stirred under air in an open tube at room temperature for 3 h. [b] Isolated yield.

2.4 General procedures for the synthesis of difluoromethylated indoles via electrochemical oxidation

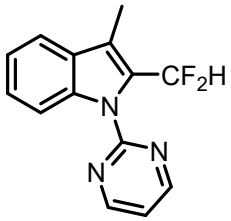


A 50 mL vial was charged with substrate **1** (0.2 mmol, 1.0 equiv.), **2** (0.4 mmol, 2.0 equiv.), Et_4NClO_4 (0.2 mmol, 1.0 equiv.), CH_3CN/H_2O (6 mL, v/v = 2/1) and a magnetic stir bar. The vial was equipped with a graphite electrode as an anode and platinum electrode (10 mm × 10 mm × 0.1 mm) as cathode. The whole cell was an undivided cell. The reaction mixture was stirred and electrolyzed at a constant current of 4 mA without a reference electrode under room temperature for 3 h (2.24 F mol^{-1}). After completion of the reaction, it was monitored with TLC, the reaction mixture was diluted with EtOAc (10 mL) and filtered through a silica gel pad. The vial and silica gel were washed with an additional volume of EtOAc (20 mL). The filtrate was concentrated in vacuo, and the resulting residue was purified by flash column chromatography using EtOAc/*n*-hexane as an eluent to afford the product **3**. It should be noted that only moderate yields were obtained for most case mostly due to the system voltage increasing with the consumption of electrolyte. The substrates and products would be decomposed quickly at a high voltage, which made the yield hard to improve.



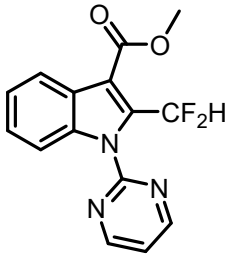
2-(Difluoromethyl)-1-(pyrimidin-2-yl)-1*H*-indole (**3a**)

White solid, ^1H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.6 Hz, 2H), 8.69 (d, *J* = 8.2 Hz, 1H), 7.96 – 7.64 (m, 2H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.29 (t, *J* = 7.1 Hz, 1H), 7.15 (s, 1H), 7.11 (t, *J* = 4.6 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.77 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.18, 157.73, 137.45, 133.30 (t, *J* = 28.9 Hz), 128.20, 125.37, 122.84, 121.78, 117.15, 115.92, 110.79 (t, *J* = 234.8 Hz), 109.29 (t, *J* = 6.3 Hz). HRMS (ESI-TOF) m/z Calcd for $C_{13}H_9F_2N_3$ $[M+H]^+$: 246.0837, found: 246.0829.



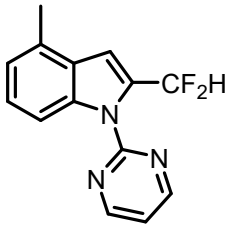
2-(Difluoromethyl)-3-methyl-1-(pyrimidin-2-yl)-1*H*-indole (**3b**)

White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.3 Hz, 2H), 8.52 (d, *J* = 8.1 Hz, 1H), 7.81 (t, *J* = 53.8 Hz, 1H), 7.65 (d, *J* = 7.4 Hz, 1H), 7.39 (t, *J* = 7.7 Hz, 1H), 7.30 (t, *J* = 7.2 Hz, 1H), 7.13 (t, *J* = 4.8 Hz, 1H), 2.56 (t, *J* = 3.3 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.48 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.29, 157.88, 136.53, 129.96, 128.45 – 127.18 (m), 125.65, 122.47, 119.91 (t, *J* = 2.5 Hz), 119.65, 117.00, 115.26, 112.09 (t, *J* = 234.3 Hz), 9.40 (t, *J* = 2.9 Hz). HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{11}F_2N_3$ $[M+H]^+$: 260.0994, found: 260.0979.



Methyl 2-(difluoromethyl)-1-(pyrimidin-2-yl)-1*H*-indole-3-carboxylate (**3c**)

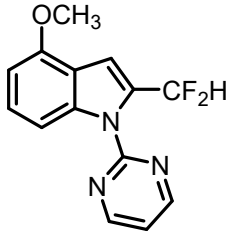
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, *J* = 4.8 Hz, 2H), 8.22 (d, *J* = 7.0 Hz, 1H), 7.96 – 7.51 (m, 2H), 7.47 – 7.29 (m, 3H), 4.01 (s, 4H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.58 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.71, 158.90, 157.01, 136.91, 135.25 (t, *J* = 23.4 Hz), 126.03, 125.52, 123.74, 122.64, 119.96, 112.85, 112.40 (t, *J* = 5.4 Hz), 109.03 (t, *J* = 238.3 Hz), 51.94. HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{11}F_2N_3O_2$ $[M+H]^+$: 304.0892, found: 304.0883.



2-(Difluoromethyl)-4-methyl-1-(pyrimidin-2-yl)-1*H*-indole (**3d**)

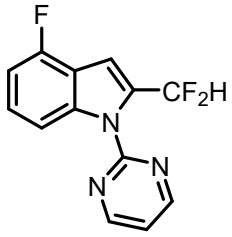
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, *J* = 4.6 Hz, 2H), 8.50 (d, *J* = 8.1 Hz, 1H), 7.81 (t, *J* = 55.9 Hz, 1H), 7.36 – 7.27 (m, 1H), 7.19 (s, 1H), 7.13 (t, *J* = 4.8 Hz, 1H), 7.09 (d, *J* = 7.0 Hz, 1H), 2.59 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.49 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$)

δ 158.20, 157.79, 137.29, 132.67 (t, *J* = 28.3 Hz), 131.24, 127.93, 125.47, 123.15, 117.14, 113.38, 110.88 (t, *J* = 236.6 Hz), 107.70 (t, *J* = 6.7 Hz), 18.62. HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{11}F_2N_3$ $[M+H]^+$: 260.0994, found: 260.0978.



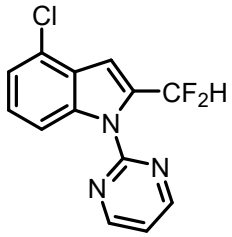
2-(Difluoromethyl)-4-methoxy-1-(pyrimidin-2-yl)-1*H*-indole (**3e**)

White solid, ^1H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.8 Hz, 2H), 8.24 (d, *J* = 8.1 Hz, 1H), 7.77 (t, *J* = 56.5 Hz, 1H), 7.30 (m, 2H), 7.13 (t, *J* = 4.8 Hz, 1H), 6.69 (d, *J* = 7.6 Hz, 1H), 3.97 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.54 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.19, 157.79, 153.64, 138.69, 131.78 (t, *J* = 28.8 Hz), 126.27, 118.84, 117.23, 110.78 (t, *J* = 236.1 Hz), 108.79, 106.44 (t, *J* = 7.3 Hz), 102.74, 55.56. HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{11}F_2N_3O$ $[M+H]^+$: 276.0943, found: 260.0928.



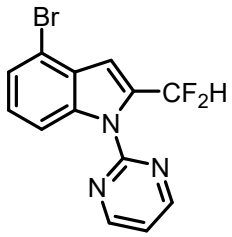
2-(Difluoromethyl)-4-fluoro-1-(pyrimidin-2-yl)-1*H*-indole (**3f**)

White solid, ^1H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.6 Hz, 2H), 8.44 (d, *J* = 8.3 Hz, 1H), 7.77 (t, *J* = 55.3 Hz, 1H), 7.34 – 7.29 (m, 1H), 7.23 (s, 1H), 7.18 (t, *J* = 4.8 Hz, 1H), 7.01 – 6.87 (m, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.18 (s, 2F), -121.75 (s, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.30, 157.64 (d, *J* = 4.8 Hz), 155.19, 139.47 (d, *J* = 9.1 Hz), 133.37 (t, *J* = 29.3 Hz), 126.01 (d, *J* = 7.6 Hz), 117.60, 117.34, 111.99 (d, *J* = 3.9 Hz), 110.48 (t, *J* = 237.2 Hz), 107.81 (d, *J* = 18.2 Hz), 104.83 (t, *J* = 7.2 Hz). HRMS (ESI-TOF) m/z Calcd for $C_{13}H_8F_3N_3$ $[M+H]^+$: 264.0743, found: 264.0729.



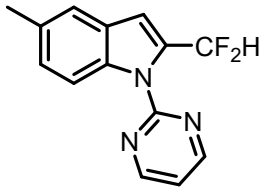
4-Chloro-2-(difluoromethyl)-1-(pyrimidin-2-yl)-1*H*-indole (**3g**)

White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.6 Hz, 2H), 8.56 (d, *J* = 7.3 Hz, 1H), 7.77 (t, *J* = 55.3 Hz, 1H), 7.33 – 7.27 (m, 2H), 7.25 (s, 1H), 7.17 (t, *J* = 4.6 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.25 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.29, 157.49, 138.02, 133.88 (t, *J* = 29.1 Hz), 127.05, 126.95, 125.93, 122.57, 117.63, 114.58, 110.48 (t, *J* = 237.3 Hz), 107.36 (t, *J* = 7.1 Hz). HRMS (ESI-TOF) m/z Calcd for $C_{13}H_8ClF_2N_3$ [M+H] $^{+}$: 280.0448, found: 280.0425.



4-Bromo-2-(difluoromethyl)-1-(pyrimidin-2-yl)-1*H*-indole (**3h**)

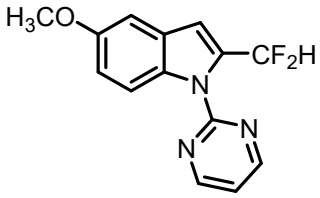
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.5 Hz, 2H), 8.62 (d, *J* = 8.1 Hz, 1H), 7.78 (t, *J* = 55.8 Hz, 1H), 7.44 (d, *J* = 7.4 Hz, 1H), 7.25 – 7.14 (m, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.25 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.32, 157.57, 137.69, 133.93 (t, *J* = 29.3 Hz), 128.93, 126.21, 125.79, 117.66, 115.59, 115.11, 110.50 (t, *J* = 237.3 Hz), 109.14 (t, *J* = 7.1 Hz). HRMS (ESI-TOF) m/z Calcd for $C_{13}H_8BrF_2N_3$ [M+H] $^{+}$: 323.9942, found: 323.9923.



2-(Difluoromethyl)-5-methyl-1-(pyrimidin-2-yl)-1*H*-indole (**3i**)

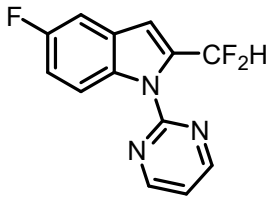
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 4.8 Hz, 2H), 8.56 (d, *J* = 8.4 Hz, 1H), 7.79 (t, *J* = 56.2 Hz, 1H), 7.45 (s, 1H), 7.21 (d, *J* = 8.6 Hz, 1H), 7.11 (t, *J* = 4.8 Hz, 1H), 7.06 (s, 1H), 2.47 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.65 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.14, 157.84, 135.80, 133.35 (t, *J* = 28.9 Hz), 132.32, 128.50, 126.90, 121.50, 116.91, 115.74, 110.84 (t, *J* = 236.9 Hz), 109.11 (t, *J* = 7.0 Hz). HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{11}F_2N_3$ [M+H]

$^{+}$: 260.0994, found: 260.0975.



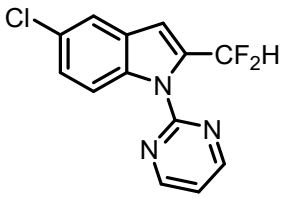
2-(Difluoromethyl)-5-methoxy-1-(pyrimidin-2-yl)-1*H*-indole (**3j**)

White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 4.8 Hz, 2H), 8.60 (d, *J* = 8.9 Hz, 1H), 7.79 (t, *J* = 55.9 Hz, 1H), 7.14 – 7.08 (m, 2H), 7.06 (s, 1H), 7.02 (dd, *J* = 9.1, 2.3 Hz, 1H), 3.88 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.44 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.14, 157.70, 155.94, 134.31 – 133.08 (m), 132.35, 128.99, 117.13, 116.91, 114.90, 110.74 (t, *J* = 236.4 Hz), 109.15 (t, *J* = 7.1 Hz), 103.32, 55.79. HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{11}F_2N_3O$ [M+H] $^{+}$: 276.0943, found: 260.0927.



2-(Difluoromethyl)-5-fluoro-1-(pyrimidin-2-yl)-1*H*-indole (**3k**)

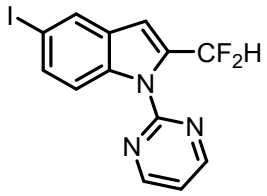
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.8 Hz, 2H), 8.66 (dd, *J* = 9.2, 4.6 Hz, 1H), 7.78 (t, *J* = 55.9 Hz, 1H), 7.31 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.16 (t, *J* = 4.7 Hz, 1H), 7.14 – 7.06 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.11 (s, 2F), -120.91 (s, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.43, 158.25, 157.82 (d, *J* = 47.7 Hz), 134.82 (t, *J* = 29.2 Hz), 133.90, 128.94 (d, *J* = 10.1 Hz), 117.34, 117.26, 113.45 (d, *J* = 25.2 Hz), 110.55 (t, *J* = 236.8 Hz), 109.06 – 108.88 (m), 106.79 (d, *J* = 23.6 Hz). HRMS (ESI-TOF) m/z Calcd for $C_{13}H_8F_3N_3$ [M+H] $^{+}$: 264.0743, found: 264.0729.



5-Chloro-2-(difluoromethyl)-1-(pyrimidin-2-yl)-1*H*-indole (**3l**)

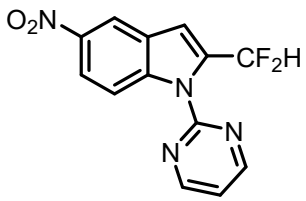
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.8 Hz, 2H), 8.63 (d, *J* = 9.1 Hz, 1H), 7.94 – 7.61 (m, 2H), 7.33 (dd, *J* = 9.1, 2.1 Hz, 1H), 7.18 (t, *J* = 4.8 Hz, 1H), 7.07 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.45 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.29, 157.53, 135.82, 134.60

(t, J = 29.1 Hz), 129.35, 128.40, 125.59, 121.16, 117.47, 117.28, 110.50 (t, J = 236.9 Hz), 108.57 (t, J = 6.9 Hz). HRMS (ESI-TOF) m/z Calcd for $C_{13}H_8ClF_2N_3$ $[M+H]^+$: 280.0448, found: 280.0426.



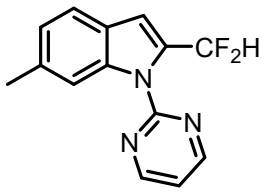
2-(Difluoromethyl)-5-iodo-1-(pyrimidin-2-yl)-1*H*-indole (**3m**)

White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 4.8 Hz, 2H), 8.46 (d, J = 8.7 Hz, 1H), 8.00 (s, 1H), 7.93 – 7.55 (m, 2H), 7.18 (t, J = 4.8 Hz, 1H), 7.04 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.21 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.28, 157.48, 136.65, 134.50 – 133.77 (m), 133.74, 130.50, 128.93, 118.02, 117.49, 110.43 (t, J = 238.4 Hz), 108.16 (t, J = 7.1 Hz), 86.66. HRMS (ESI-TOF) m/z Calcd for $C_{13}H_8IF_2N_3$ $[M+H]^+$: 371.9804, found: 371.9813.



2-(Difluoromethyl)-5-nitro-1-(pyrimidin-2-yl)-1*H*-indole (**3n**)

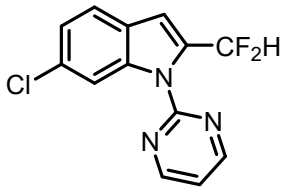
Light yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, J = 4.8 Hz, 2H), 8.79 (d, J = 9.3 Hz, 1H), 8.62 (d, J = 2.2 Hz, 1H), 8.28 (dd, J = 9.3, 2.3 Hz, 1H), 7.80 (t, J = 55.5 Hz, 1H), 7.34 – 7.27 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.79 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.55, 157.15, 143.73, 140.25, 136.43, 127.80, 120.41, 118.41, 118.30, 116.32, 110.13 (t, J = 237.7 Hz), 109.91 (t, J = 6.9 Hz). HRMS (ESI-TOF) m/z Calcd for $C_{13}H_8F_2N_4O_2$ $[M+H]^+$: 291.0688, found: 291.0675.



2-(Difluoromethyl)-6-methyl-1-(pyrimidin-2-yl)-1*H*-indole (**3o**)

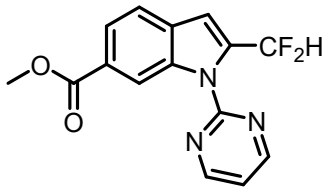
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 4.8 Hz, 2H), 8.48 (s, 1H), 7.78 (t, J = 56.3 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.18 – 7.02 (m, 3H), 2.53 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.76 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.19, 157.78, 137.83, 135.48, 132.68 (t, J = 28.9 Hz), 125.98, 124.48, 121.36, 117.04, 115.72, 110.87 (t, J = 236.4 Hz), 109.23 (t, J = 6.9

Hz). HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{11}F_2N_3$ [M+H] $^+$: 260.0994, found: 260.0975.



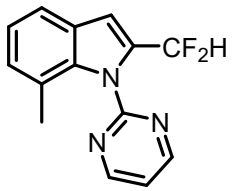
6-Chloro-2-(difluoromethyl)-1-(pyrimidin-2-yl)-1*H*-indole (**3p**)

White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.8 Hz, 2H), 8.75 (d, *J* = 1.6 Hz, 1H), 7.77 (t, *J* = 55.9 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.30 – 7.23 (m, 1H), 7.18 (t, *J* = 4.8 Hz, 1H), 7.10 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.12 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.30, 157.46, 137.68, 133.98 (t, *J* = 29.1 Hz), 131.27, 126.69, 123.55, 122.49, 117.50, 116.23, 110.53 (t, *J* = 236.7 Hz), 109.05 (t, *J* = 6.9 Hz). HRMS (ESI-TOF) m/z Calcd for $C_{13}H_8ClF_2N_3$ [M+H] $^+$: 280.0448, found: 280.0427.



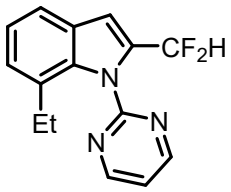
Methyl 2-(difluoromethyl)-1-(pyrimidin-2-yl)-1*H*-indole-6-carboxylate (**3q**)

White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.35 (s, 1H), 8.82 (d, *J* = 4.8 Hz, 2H), 8.01 – 7.62 (m, 3H), 7.21 (t, *J* = 4.8 Hz, 1H), 7.16 (s, 1H), 3.97 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.29 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.90, 158.46, 157.42, 136.85, 136.10 (t, *J* = 29.1 Hz), 131.74, 126.99, 123.80, 121.52, 118.08, 117.71, 110.42 (t, *J* = 237.0 Hz), 108.86 (t, *J* = 6.8 Hz), 52.35. HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{11}F_2N_3O_2$ [M+H] $^+$: 304.0892, found: 304.0881.



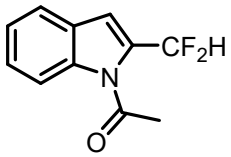
2-(Difluoromethyl)-7-methyl-1-(pyrimidin-2-yl)-1*H*-indole (**3r**)

White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (d, *J* = 4.8 Hz, 2H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.39 – 7.30 (m, 1H), 7.23 – 7.05 (m, 3H), 7.04 (s, 1H), 2.09 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.44 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.66, 157.79, 137.05, 133.18 (t, *J* = 27.9 Hz), 128.40, 127.86, 123.28, 122.45, 119.92, 119.32, 110.32 (t, *J* = 236.2 Hz), 107.37 (t, *J* = 5.8 Hz), 20.88. HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{11}F_2N_3$ [M+H] $^+$: 260.0994, found: 260.0979.



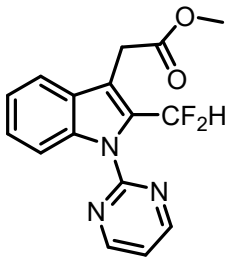
2-(Difluoromethyl)-7-ethyl-1-(pyrimidin-2-yl)-1*H*-indole (**3s**)

White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (d, *J* = 4.8 Hz, 2H), 7.57 – 7.55 (m, 1H), 7.34 (d, *J* = 4.7 Hz, 1H), 7.32 – 7.17 (m, 3H), 7.06 (d, *J* = 6.1 Hz, 1H), 2.47 (q, *J* = 7.5 Hz, 2H), 0.98 (t, *J* = 7.5 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.56 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.69, 158.18, 136.32, 133.34 (t, *J* = 28.0 Hz), 129.49, 128.63, 125.68, 122.59, 119.96, 119.42, 110.35 (t, *J* = 236.1 Hz), 107.49 (t, *J* = 5.9 Hz), 26.46, 13.80. HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{13}F_2N_3$ $[M+H]^+$: 274.1150, found: 274.1132.



1-(2-(Difluoromethyl)-1*H*-indol-1-yl) ethan-1-one (**3t**)

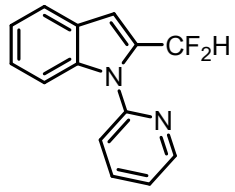
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.5 Hz, 1H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.54 – 7.22 (m, 3H), 7.12 (s, 1H), 2.85 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.55 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.37, 136.19, 134.31 (t, *J* = 28.9 Hz), 128.96, 126.23, 123.81, 122.88, 114.39, 111.73 (t, *J* = 7.3 Hz), 110.16 (t, *J* = 236.8 Hz), 27.05. HRMS (ESI-TOF) m/z Calcd for $C_{11}H_9F_2NO$ $[M+H]^+$: 210.0725, found: 210.0709.



Methyl 2-(2-(difluoromethyl)-1-(pyrimidin-2-yl)-1*H*-indol-3-yl) acetate (**3u**)

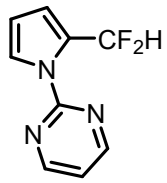
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.8 Hz, 2H), 8.53 (d, *J* = 8.5 Hz, 1H), 7.86 (t, *J* = 54.4 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.40 (t, *J* = 8.3 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 4.8 Hz, 1H), 4.08 (t, *J* = 2.1 Hz, 2H), 3.72 (s, 38H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.19 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.49, 158.32, 157.64, 136.43, 129.79 – 128.47 (m), 125.82, 122.85, 119.53, 117.44, 115.81 (t, *J* = 2.5 Hz), 115.36, 111.87 (t, *J* = 235.9 Hz), 52.31,

30.22 (t, J = 3.3 Hz). HRMS (ESI-TOF) m/z Calcd for $C_{16}H_{13}F_2N_3O_2$ $[M+H]^+$: 318.1049, found: 318.1033.



2-(Difluoromethyl)-1-(pyridin-2-yl)-1*H*-indole (**3v**)

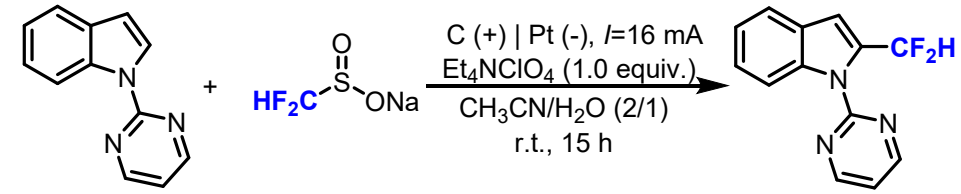
Light yellow oily substance, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 3.4 Hz, 1H), 8.44 – 8.26 (m, 1H), 7.87 (td, J = 8.1, 1.9 Hz, 1H), 7.80 (d, J = 3.5 Hz, 1H), 7.50 (d, J = 8.2 Hz, 1H), 7.37 – 7.31 (m, 2H), 7.23 (dd, J = 7.1, 5.1 Hz, 1H), 6.96 (t, J = 56.0 Hz, 1H), 6.93 (d, J = 2.8 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.52 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.10, 148.93, 138.75, 135.60, 127.21, 126.01 (t, J = 22.4 Hz), 122.63, 121.43, 120.62, 119.93 – 118.13 (m), 115.70, 115.45 (t, J = 237.5 Hz),114.94, 103.75. HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{10}F_2N_2$ $[M+H]^+$: 245.0885, found: 245.0876.



2-(2-(Difluoromethyl)-1*H*-pyrrol-1-yl) pyrimidine (**3w**)

White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, J = 4.8 Hz, 2H), 7.91 (d, J = 1.1 Hz, 1H), 7.66 (s, 1H), 7.13 (t, J = 4.8 Hz, 1H), 6.75 (s, 1H), 6.32 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.61 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.45, 156.53, 127.50, 123.35, 117.85, 114.95 – 113.86 (m), 110.47 (t, J = 232 Hz), 110.46. HRMS (ESI-TOF) m/z Calcd for $C_9H_7F_2N_3$ $[M+H]^+$: 196.0681, found: 196.0673.

2.5 Scale-up synthesis of 3a

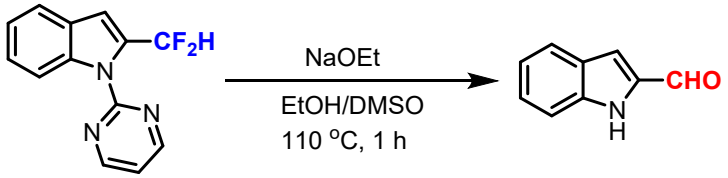


1a (4 mmol, 0.78 g) **2** (2 equiv.) **3a** (58%, 0.57 g)

A 250 mL three-necked bottle was charged with substrate **1a** (4 mmol, 0.78 g), **2** (8 mmol, 1.10 g), Et_4NClO_4 (4 mmol, 0.92 g), CH_3CN/H_2O (120 mL, v/v = 2/1) and a magnetic stir bar. The

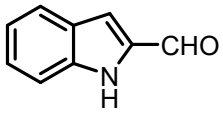
bottle was equipped with platinum electrodes (20 mm × 20 mm × 0.1 mm) as a cathode and a graphite rod (Φ6 mm × 90 mm) as an anode. The whole cell was an undivided cell. The reaction mixture was stirred and electrolyzed at a constant current of 16 mA without a reference electrode under room temperature for 15 h. After completion of the reaction, it was monitored with TLC. Then, then reaction mixtures were washed by H_2O and extracted with DCM (3×30 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*, and the resulting residue was purified by flash column chromatography using EtOAc/*n*-hexane (1:4) as the eluent to afford the product **3a** in 58% yield.

2.6 Derivatization of product 3a



3a **3aa** (71%)

To a solution of 2-(difluoromethyl)-1-(pyrimidin-2-yl)-1*H*-indole **3a** (0.5 mmol, 1.0 eq) in DMSO (2.0 mL) was added NaOEt (1.5 mmol, 3.0 eq) (20% wt. in EtOH) at room temperature under Ar atmosphere. After the mixture was stirred at 110 °C for 1 h, saturated aq. NH_4Cl was added at room temperature. Then the reaction mixture was diluted with EtOAc (15 mL) and washed with H_2O (3× 15 mL). The aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by flash column chromatography using EtOAc/hexanes (1:10) as eluent to afford the desired product **3aa** in 71% yield.



1*H*-indole-2-carbaldehyde (**3aa**)

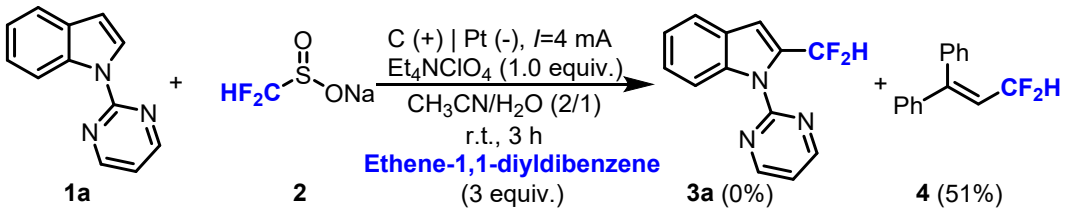
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (s, 1H), 9.38 (s, 1H), 7.76 (d, J = 8.7 Hz, 1H), 7.48 (d, J = 9.1 Hz, 1H), 7.41 (d, J = 7.1 Hz, 1H), 7.30 (s, 1H), 7.19 (t, J = 8.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.36, 138.18, 136.03, 127.49, 127.41, 123.56, 121.38, 115.14, 112.64. HRMS (ESI-TOF) m/z Calcd for C_9H_8NO $[M+H]^+$: 146.0600, found: 146.0612.

2.7 Cyclic voltammetry (CV) experiments

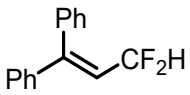
Cyclic voltammograms of **1a**, **2** and **BHT** were performed in a three-electrode cell connected

to a schlenk line under nitrogen at room temperature. The working electrode was a steady glassy carbon disk electrode while the counter electrode was a platinum wire. The reference was an Ag/AgCl electrode submerged in saturated aqueous KCl solution. (1) **1a** (0.2 mmol) and a mixed solvent CH_3CN/H_2O (6 mL, v/v=2/1) containing Et_4NClO_4 (0.2 mmol) were poured into the electrochemical cell in cyclic voltammetry experiments. The scan rate was 0.10 V/s, ranging from 0 V to 2.5 V. (2) **2** (0.4 mmol) and a mixed solvent CH_3CN/H_2O (6 mL, v/v=2/1) containing Et_4NClO_4 (0.2 mmol) were poured into the electrochemical cell in cyclic voltammetry experiments. The scan rate was 0.10 V/s, ranging from 0 V to 2.5 V. (3) **BHT** (0.6 mmol) and a mixed solvent CH_3CN/H_2O (6 mL, v/v=2/1) containing Et_4NClO_4 (0.2 mmol) were poured into the electrochemical cell in cyclic voltammetry experiments. The scan rate was 0.10 V/s, ranging from 0 V to 2.5 V. (4) **TEMPO** (0.6 mmol) and a mixed solvent CH_3CN/H_2O (6 mL, v/v=2/1) containing Et_4NClO_4 (0.2 mmol) were poured into the electrochemical cell in cyclic voltammetry experiments. The scan rate was 0.10 V/s, ranging from 0 V to 2.5 V. (5) A mixed solvent CH_3CN/H_2O (6 mL, v/v=2/1) containing Et_4NClO_4 (0.2 mmol) were poured into the electrochemical cell in cyclic voltammetry experiments. The scan rate was 0.10 V/s, ranging from 0 V to 2.5 V.

2.8 Free radical trapping experiment



A 50 mL vial was charged with substrate **1a** (0.2 mmol, 1.0 equiv.), **2** (0.4 mmol, 2.0 equiv.), Et_4NClO_4 (0.2 mmol, 1.0 equiv.), Ethene-1,1-diyldibenzene (0.6 mmol, 3.0 equiv.), CH_3CN/H_2O (6 mL, v/v = 2/1) and a magnetic stir bar. The vial was equipped with a graphite rod (Φ 6 mm) as an anode and platinum electrodes (10 mm × 10 mm × 0.1 mm) as cathode. The whole cell was an undivided cell. The reaction mixture was stirred and electrolyzed at a constant current of 4 mA without a reference electrode under room temperature for 3 h (2.24 F mol^{-1}). The whole reaction process was monitored with TLC. The results showed that the formation of **3a** was complete inhibited, and the difluoromethyl radical was captured by ethene-1,1-diyldibenzene to form the compound **4** in 51% yield.



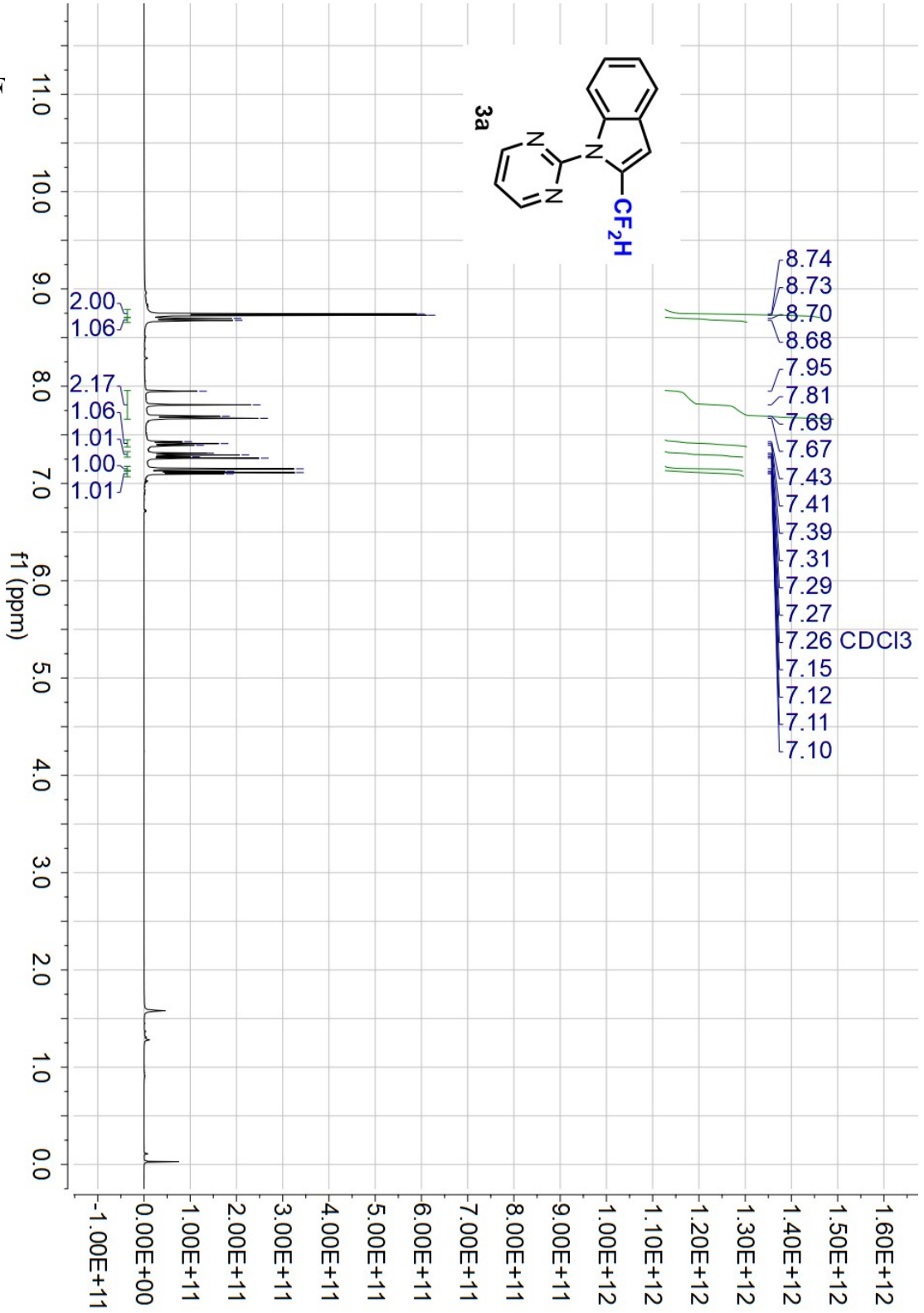
(3,3-Difluoroprop-1-ene-1,1-diyl) dibenzene (**4**)

Light yellow oily substance, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (q, *J* = 3.7 Hz, 3H), 7.37 – 7.31 (m, 3H), 7.31 – 7.27 (m, 2H), 7.26 – 7.19 (m, 2H), 6.35 – 5.76 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.65. ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.78 (t, *J* = 12.9 Hz), 140.18, 137.37, 129.94, 129.17, 128.82, 128.60, 128.56, 128.16, 120.19 (t, *J* = 26.7 Hz), 113.88 (t, *J* = 229.4 Hz). HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{12}F_2$ $[M+Na]^+$: 253.0799, found: 253.0787.

3. Reference

[1] L. Ackermann and A. V. Lygin, *Org. Lett.*, 2011, **13**, 3332-3335.

4. ^{1}H NMR, ^{19}F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8.68
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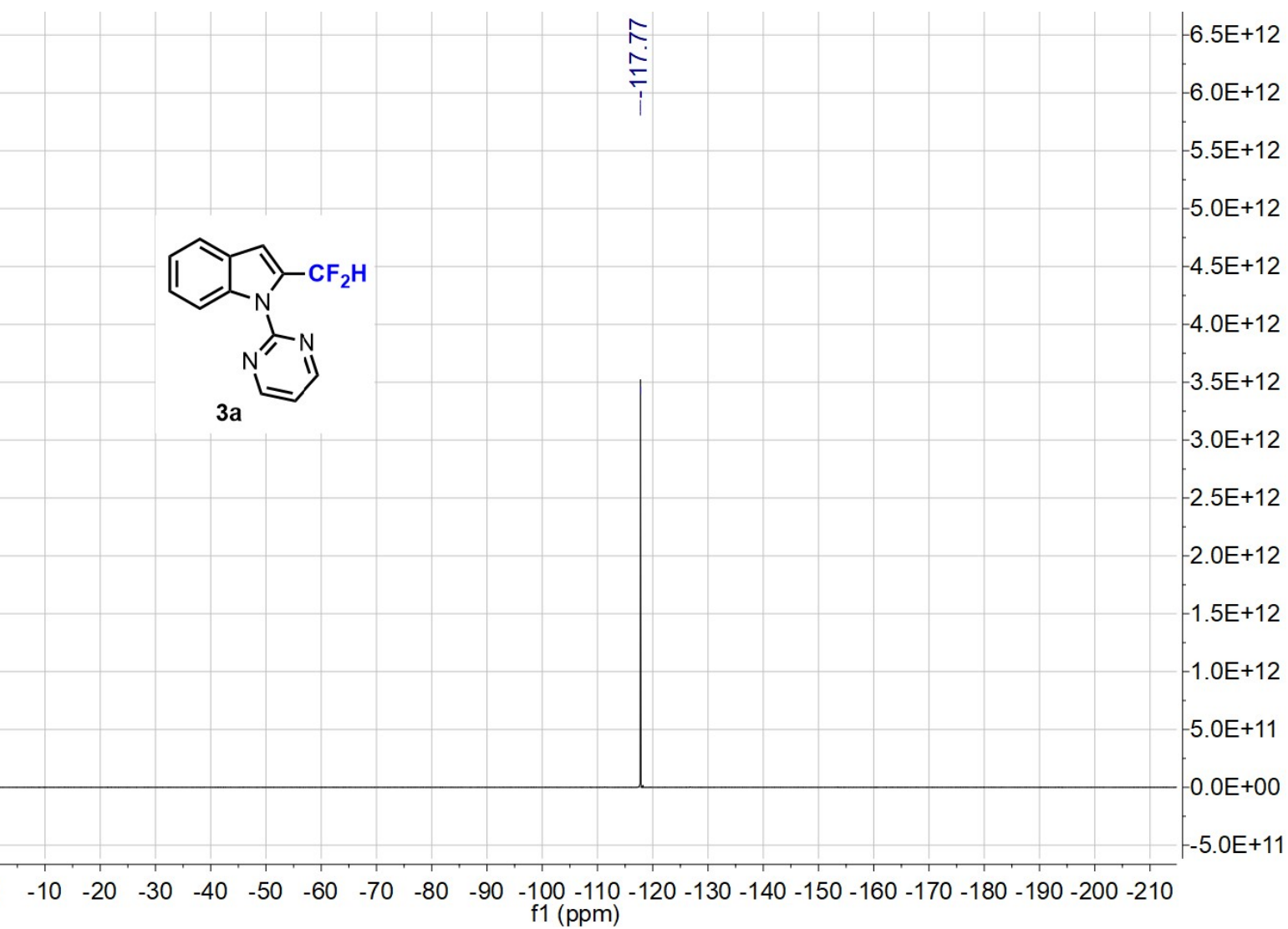
7.69
7.67
7.43
7.41
7.39
7.31
7.29
7.27
7.26 CDCl3
7.15
7.12
7.11
7.10
2.00
1.06
2.17
1.06
1.01
1.00
1.01
f1 (ppm)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CF2H
N
N
N
3a
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4.0E+12
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
5.0E+11
0.0E+00
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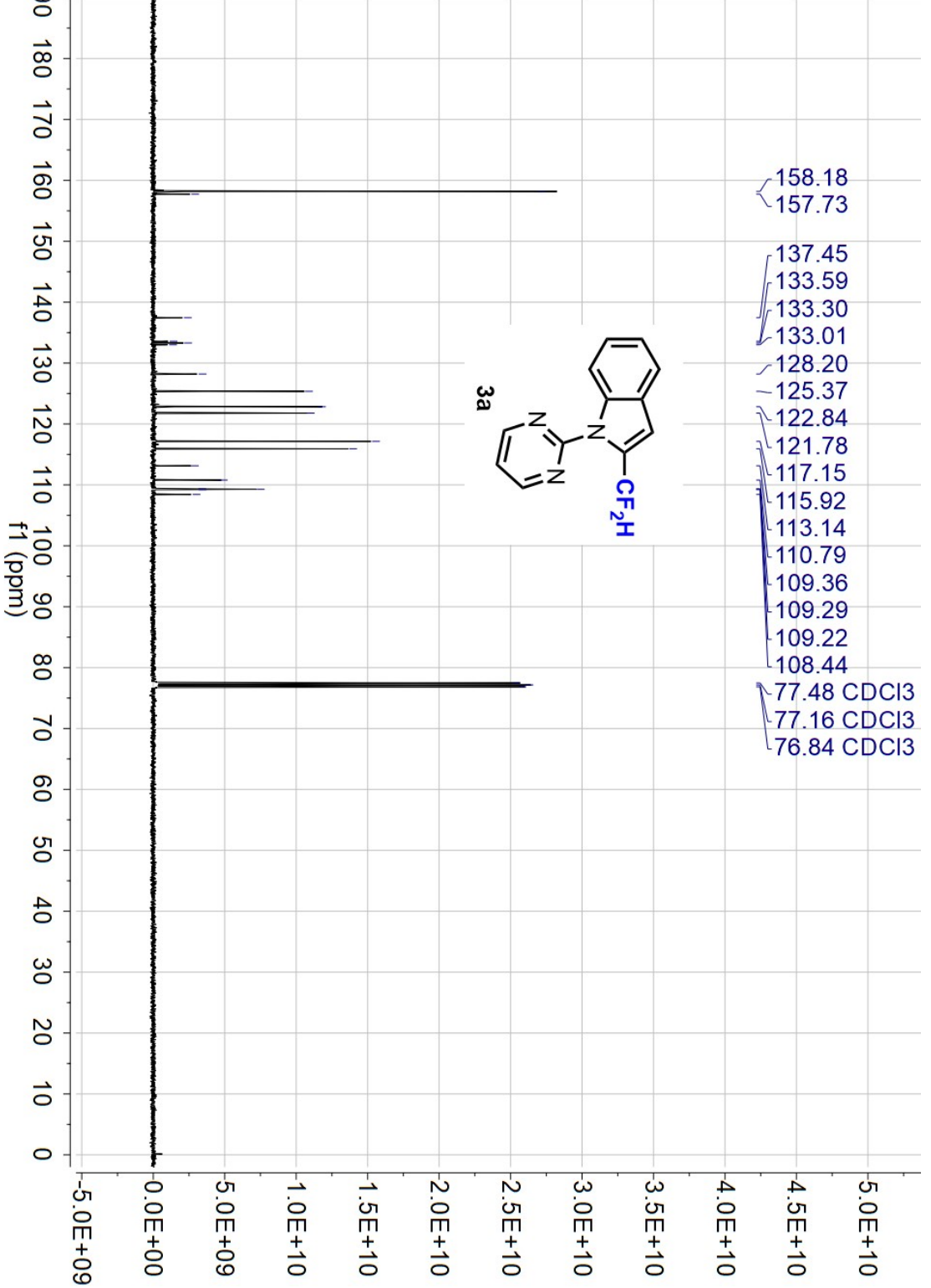
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)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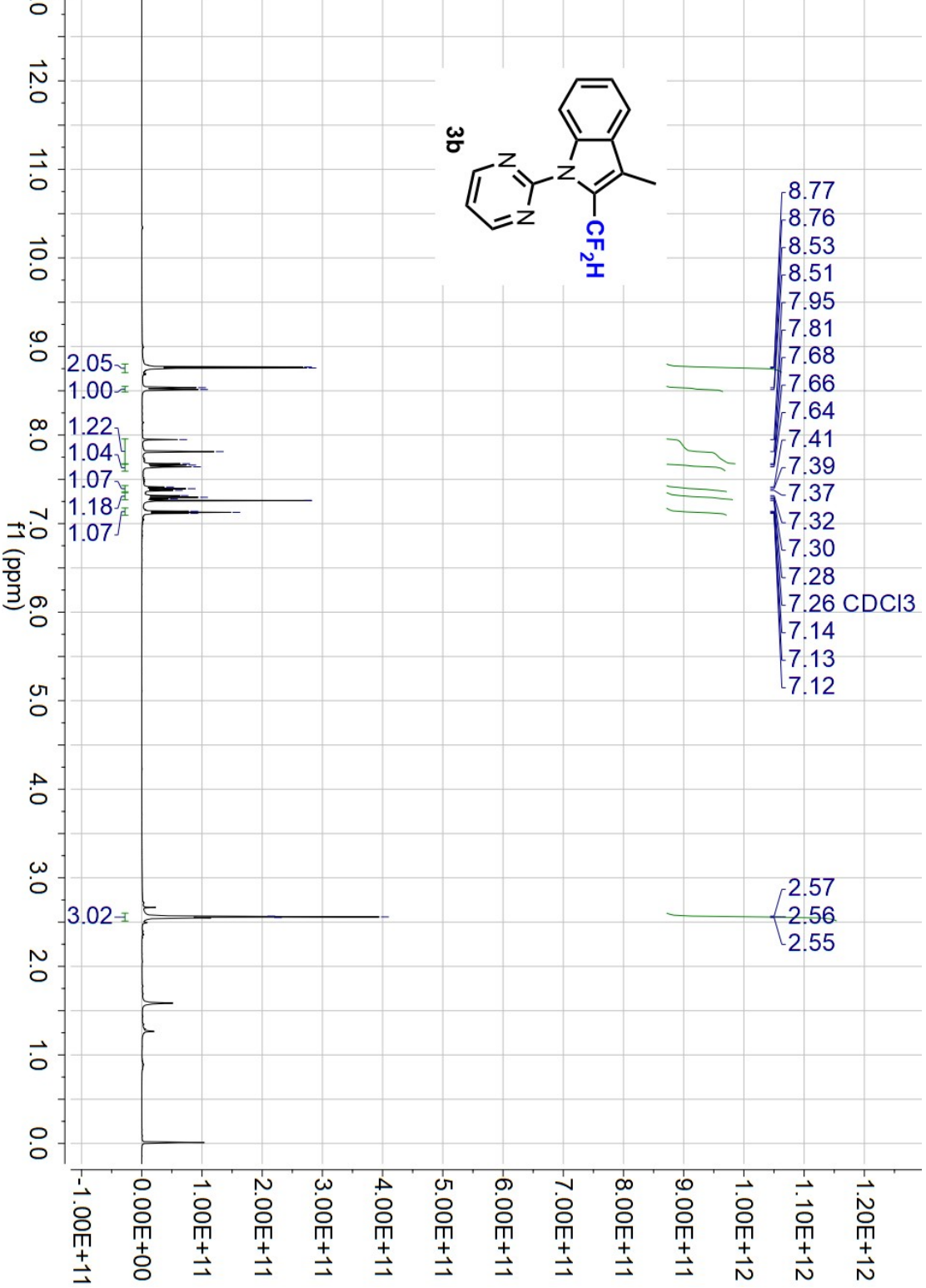
76.84 CDCl3
3a
CF2H
f1 (ppm)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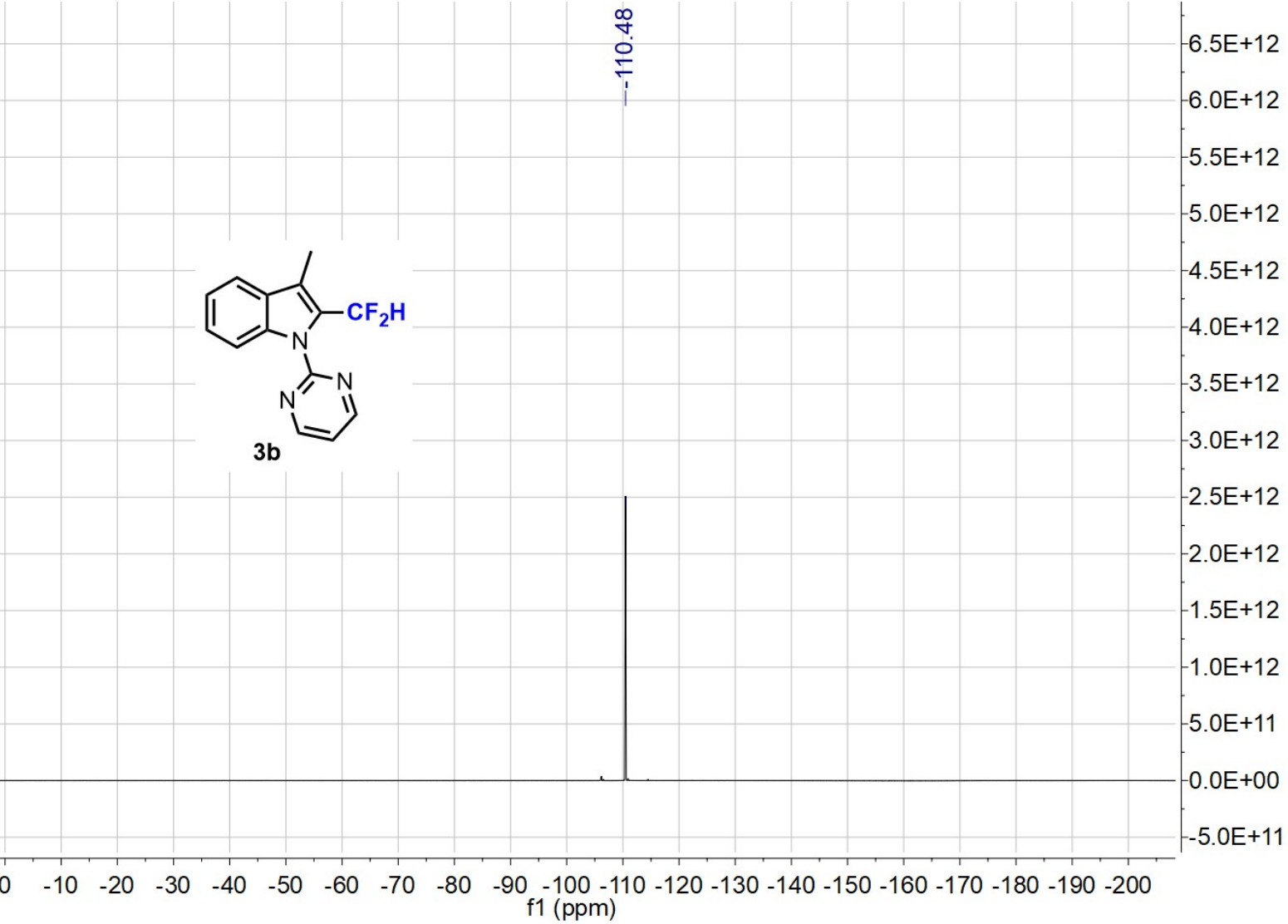
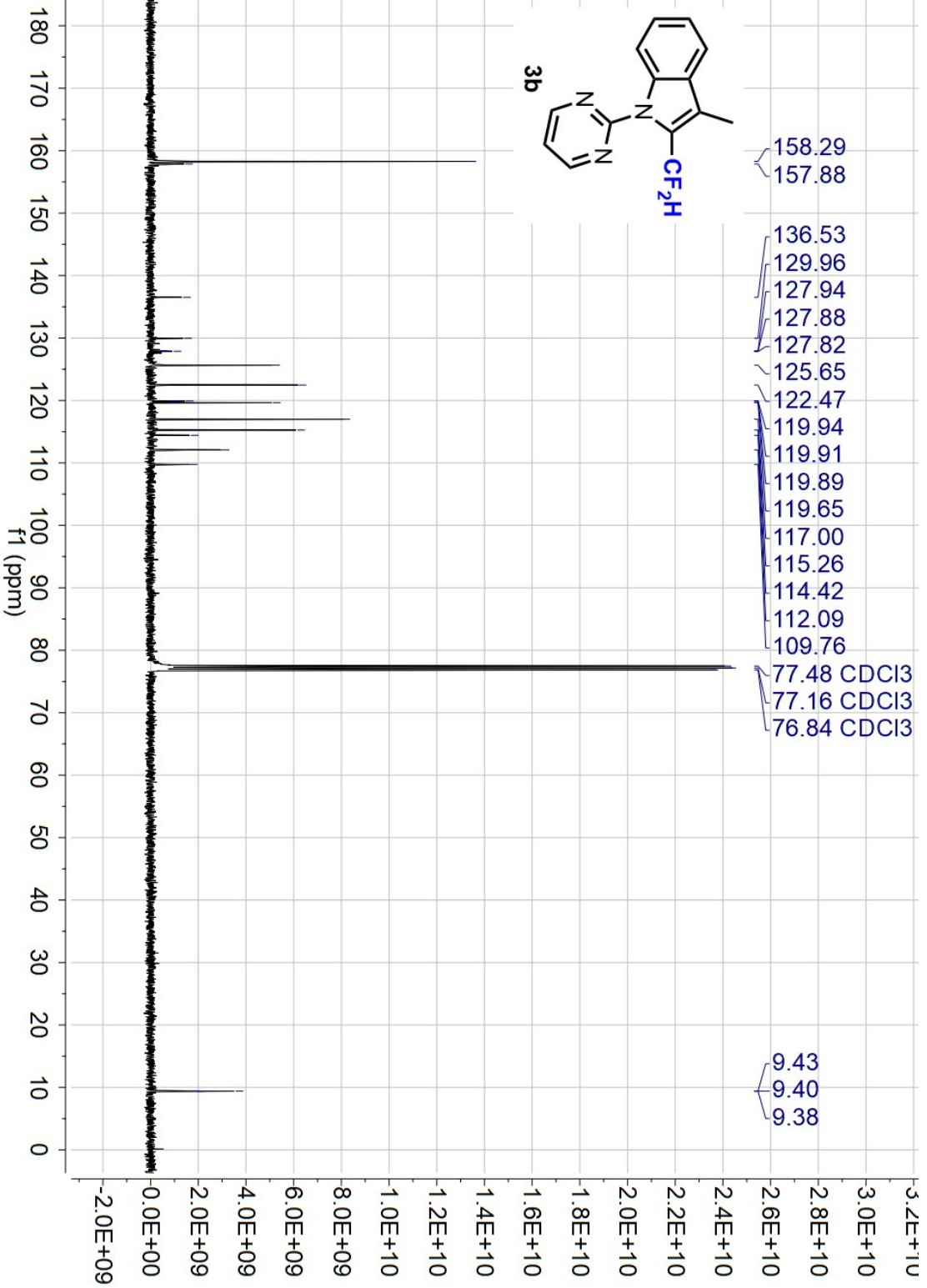
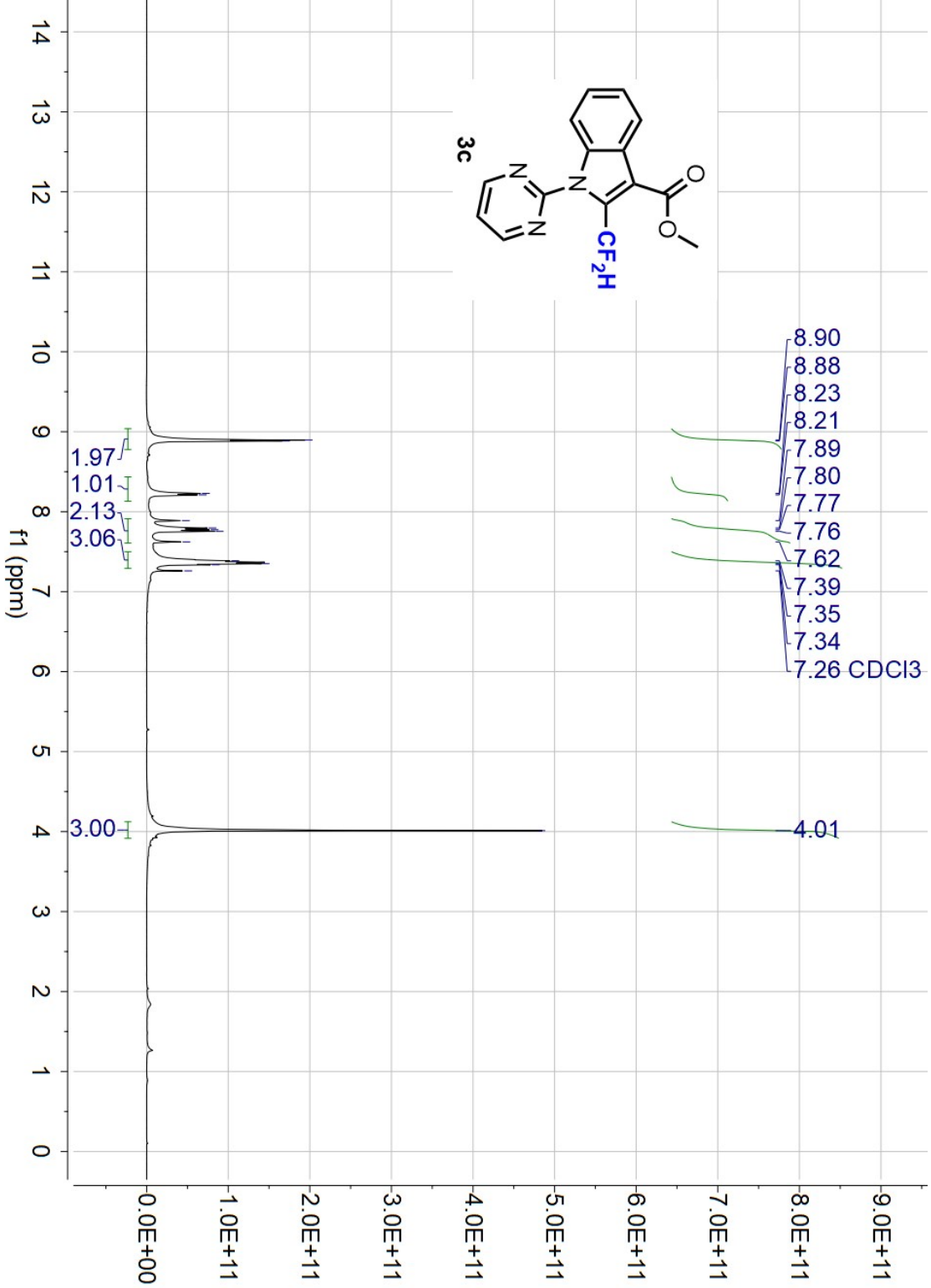
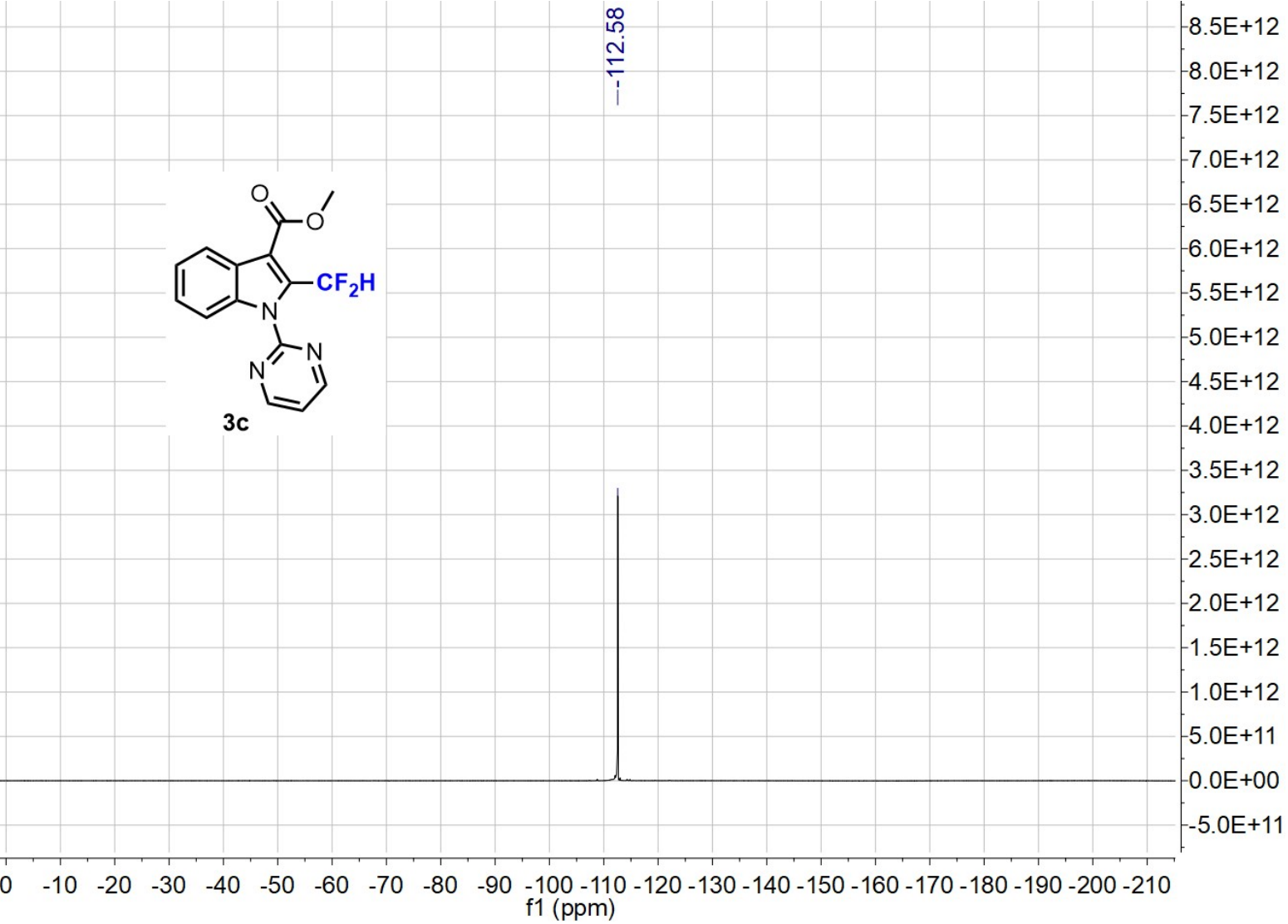
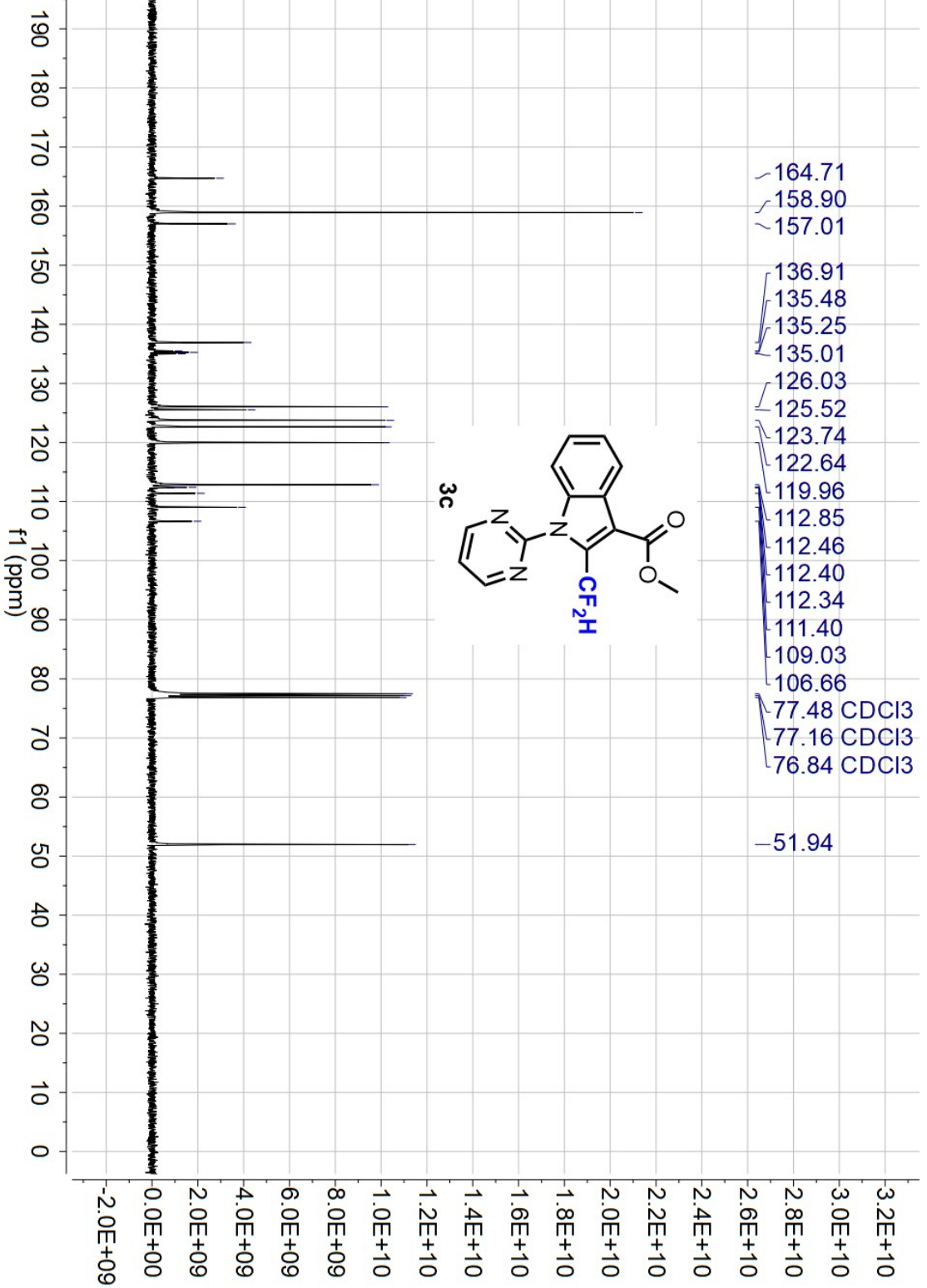
7.37
7.32
7.30
7.28
7.26 CDCl3
7.14
7.13
7.12
2.57
2.56
2.55
2.05
1.00
1.22
1.04
1.07
1.18
1.07
3.02
f1 (ppm)

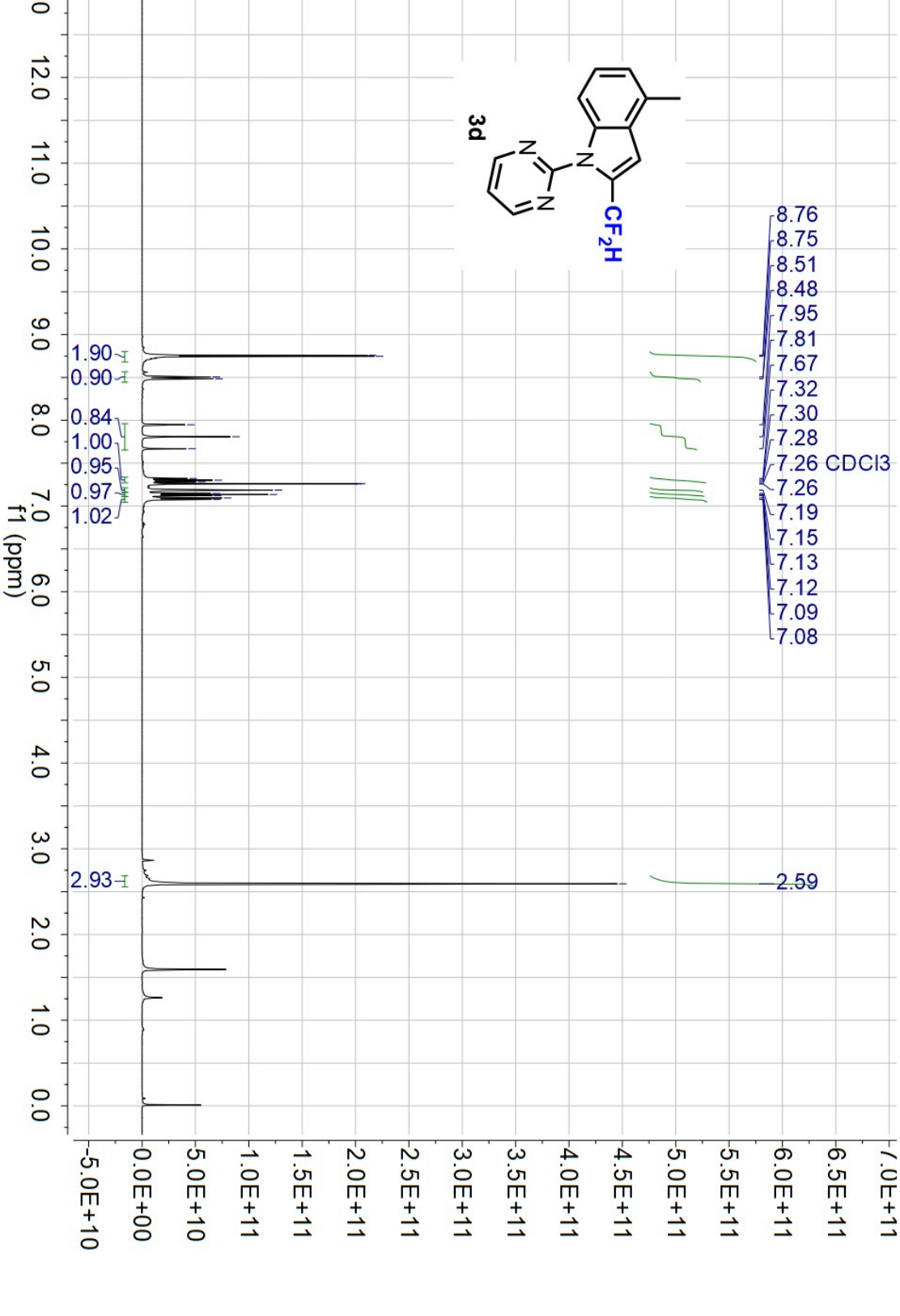

-110.48
6.5E+12
6.0E+12
5.5E+12
5.0E+12
4.5E+12
4.0E+12
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
5.0E+11
0.0E+00
-5.0E+11
CF2H
N
N
N
3b
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

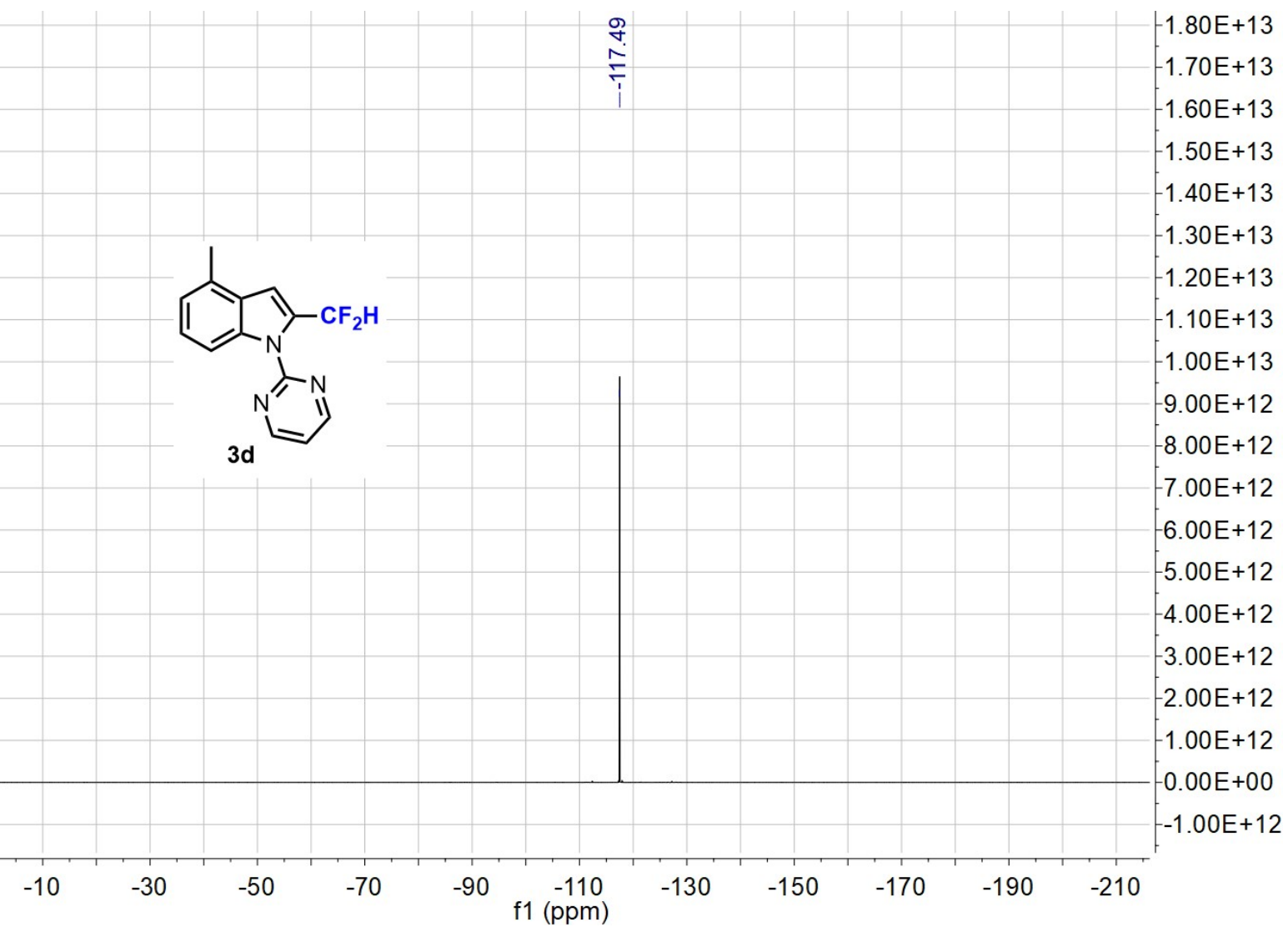

3b
CF2H
158.29
157.88
136.53
129.96
127.94
127.88
127.82
125.65
122.47
119.94
119.91
119.89
119.65
117.00
115.26
114.42
112.09
109.76
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
9.43
9.40
9.38
f1 (ppm)

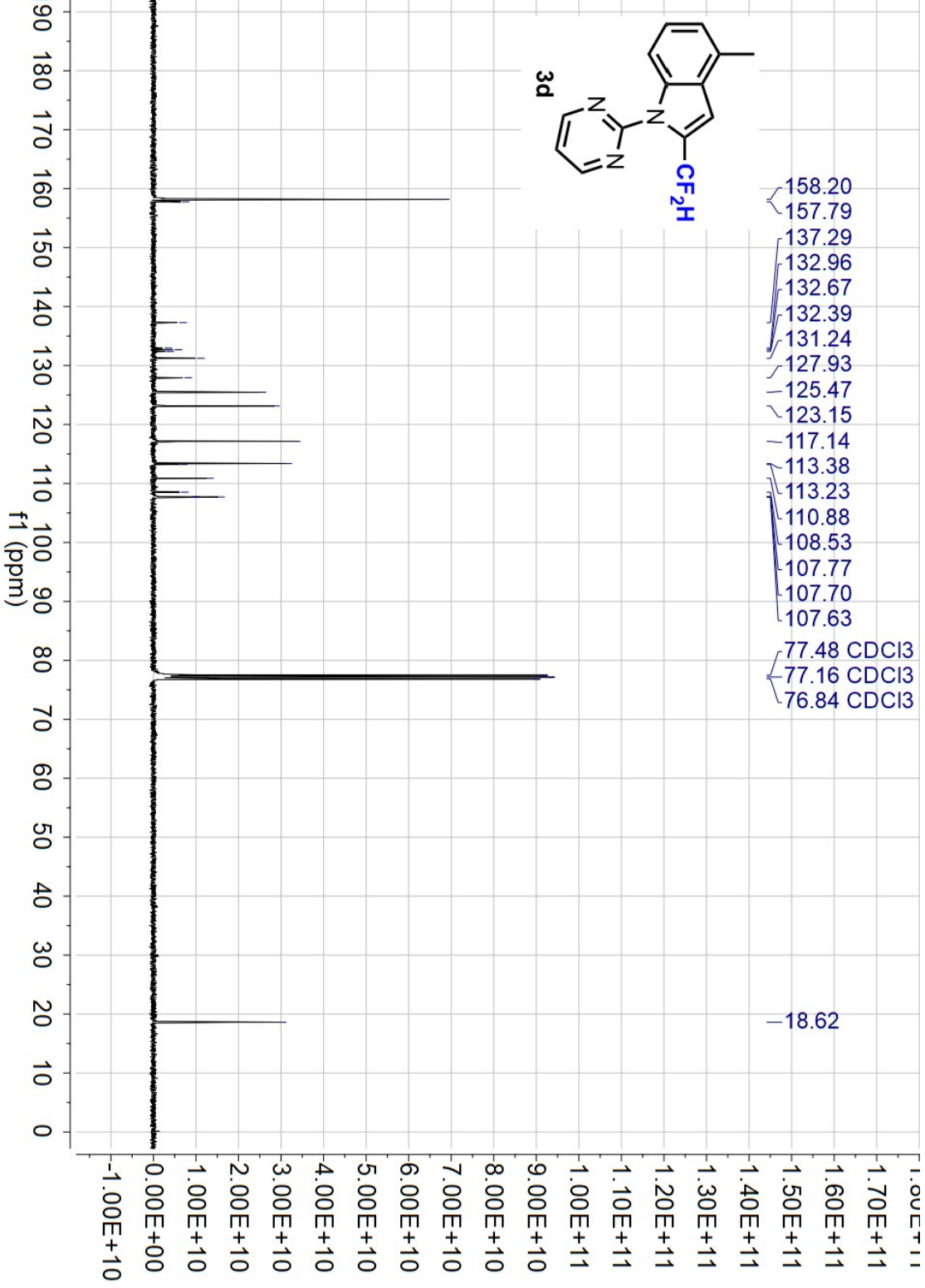

3c
CF2H
8.90
8.88
8.23
8.21
7.89
7.80
7.77
7.76
7.62
7.39
7.35
7.34
7.26 CDCl3
4.01
1.97
1.01
2.13
3.06
3.00
f1 (ppm)

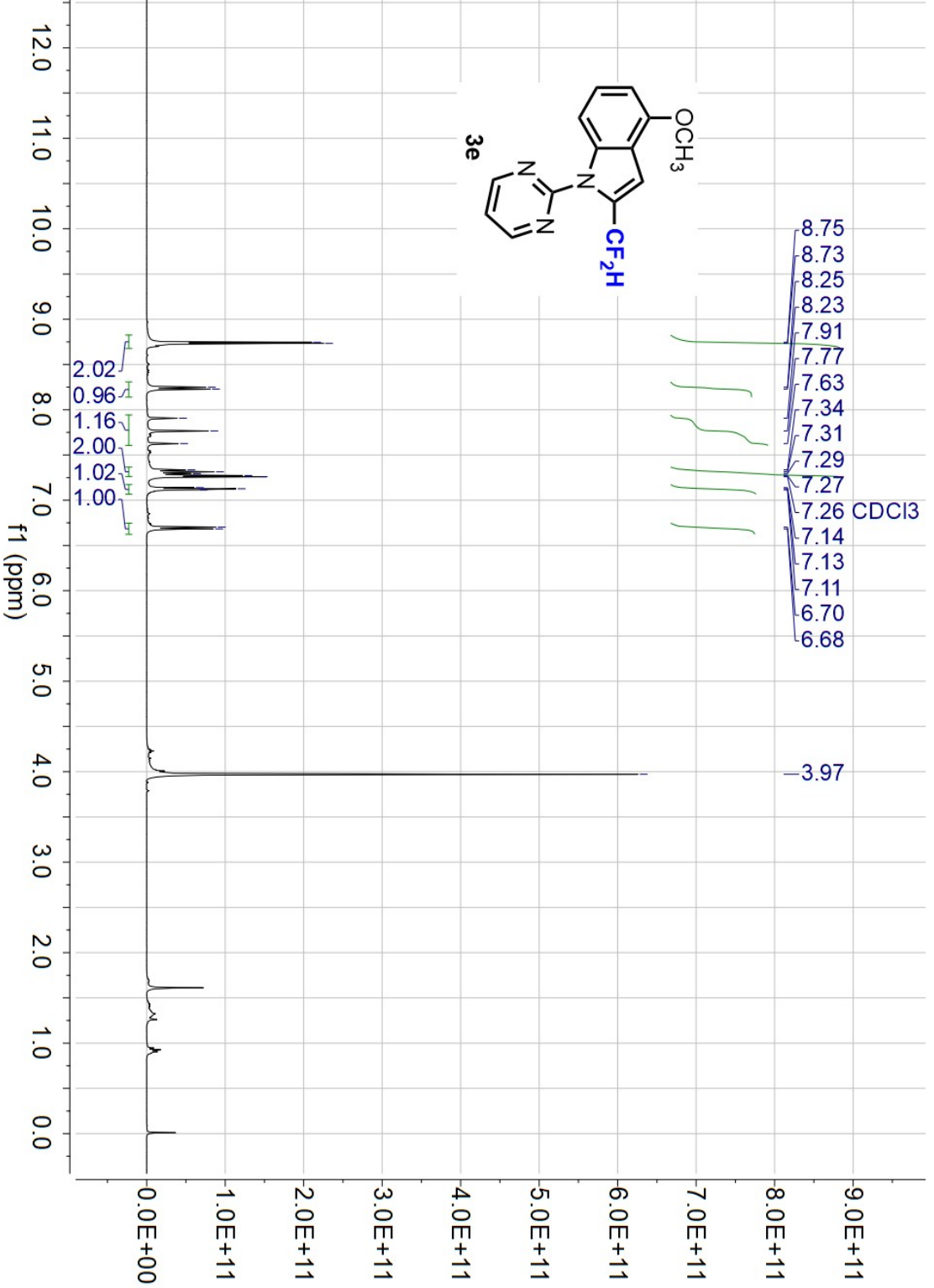

-112.58
3c
8.5E+12
8.0E+12
7.5E+12
7.0E+12
6.5E+12
6.0E+12
5.5E+12
5.0E+12
4.5E+12
4.0E+12
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
5.0E+11
0.0E+00
-5.0E+11
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

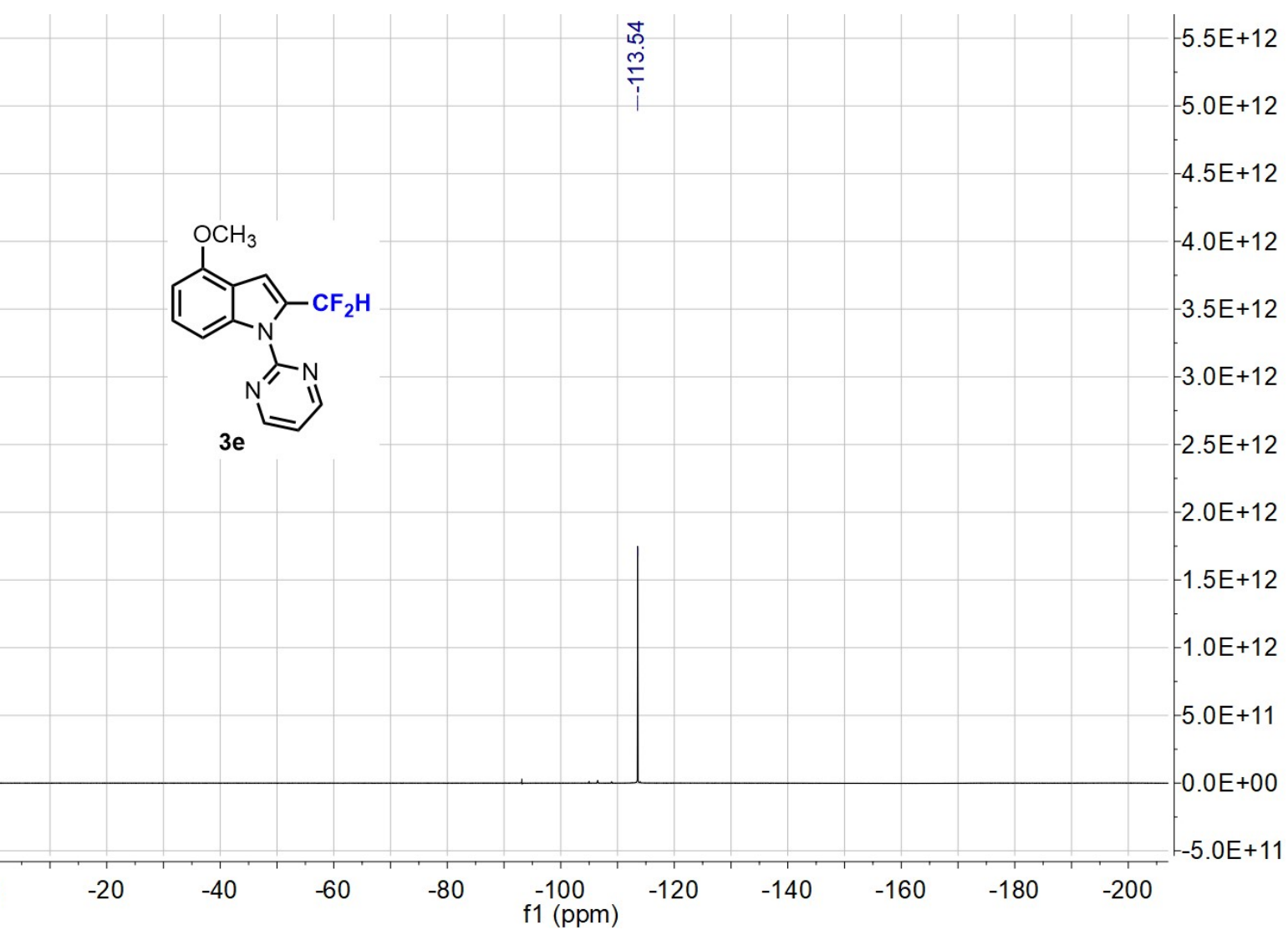

164.71
158.90
157.01
136.91
135.48
135.25
135.01
126.03
125.52
123.74
122.64
119.96
112.85
112.46
112.40
112.34
111.40
109.03
106.66
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
51.94
3c
CF2H
f1 (ppm)

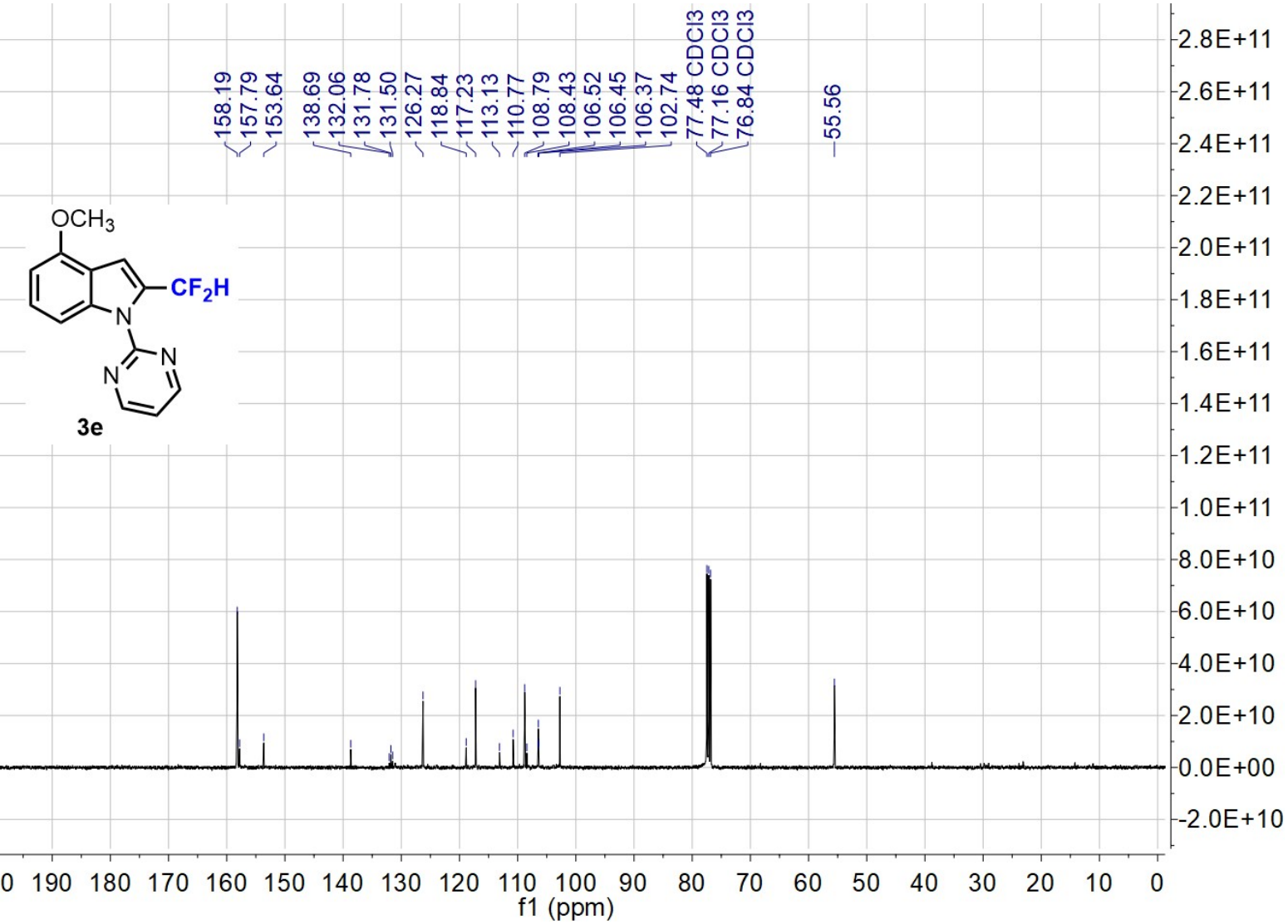

3d
CF2H
8.76
8.75
8.51
8.48
7.95
7.81
7.67
7.32
7.30
7.28
7.26 CDCl3
7.26
7.19
7.15
7.13
7.12
7.09
7.08
1.90
0.90
0.84
1.00
0.95
0.97
1.02
2.93
2.59
f1 (ppm)

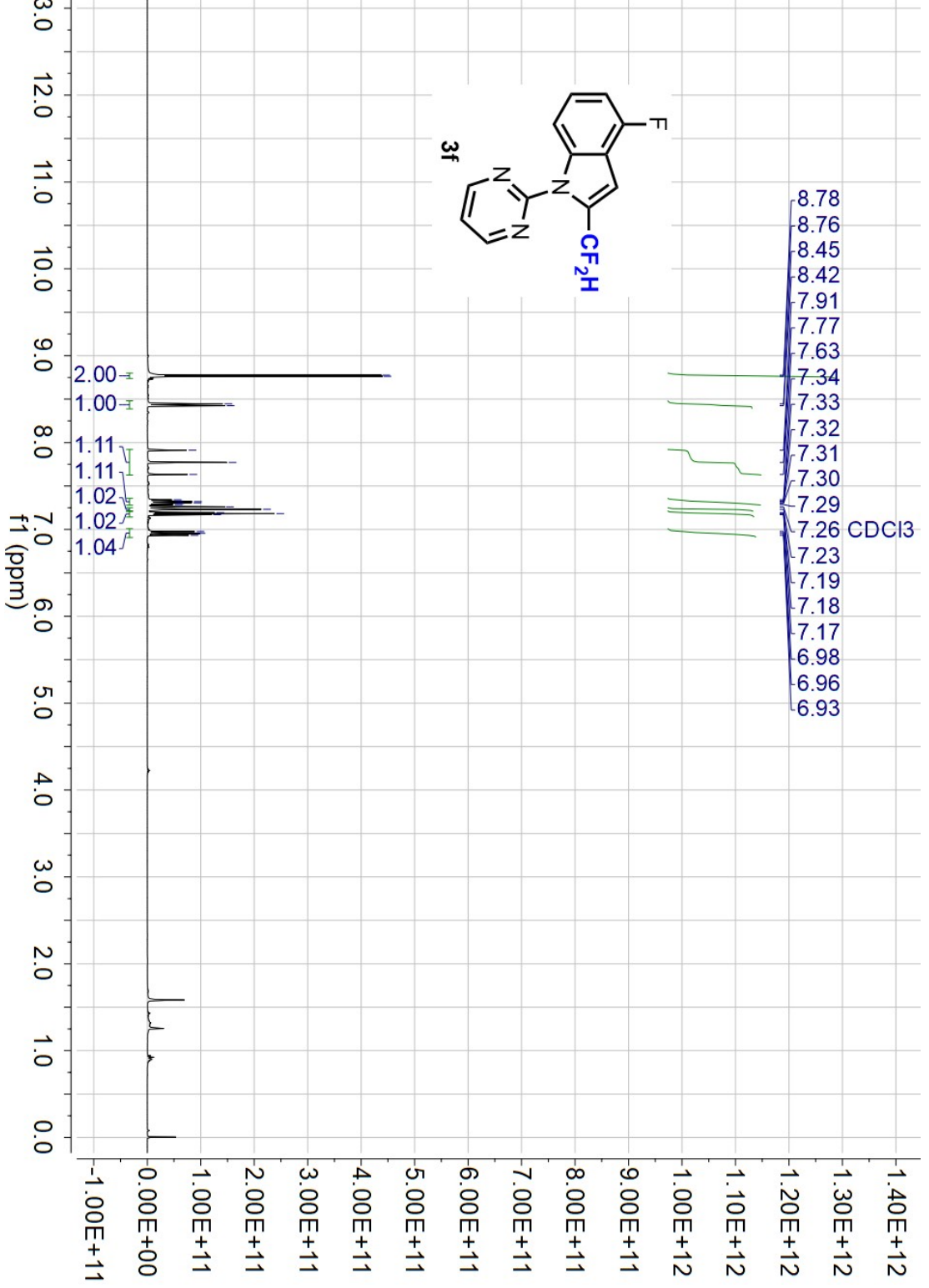

-117.49
CF2H
N
N
N
3d
1.80E+13
1.70E+13
1.60E+13
1.50E+13
1.40E+13
1.30E+13
1.20E+13
1.10E+13
1.00E+13
9.00E+12
8.00E+12
7.00E+12
6.00E+12
5.00E+12
4.00E+12
3.00E+12
2.00E+12
1.00E+12
0.00E+00
-1.00E+12
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

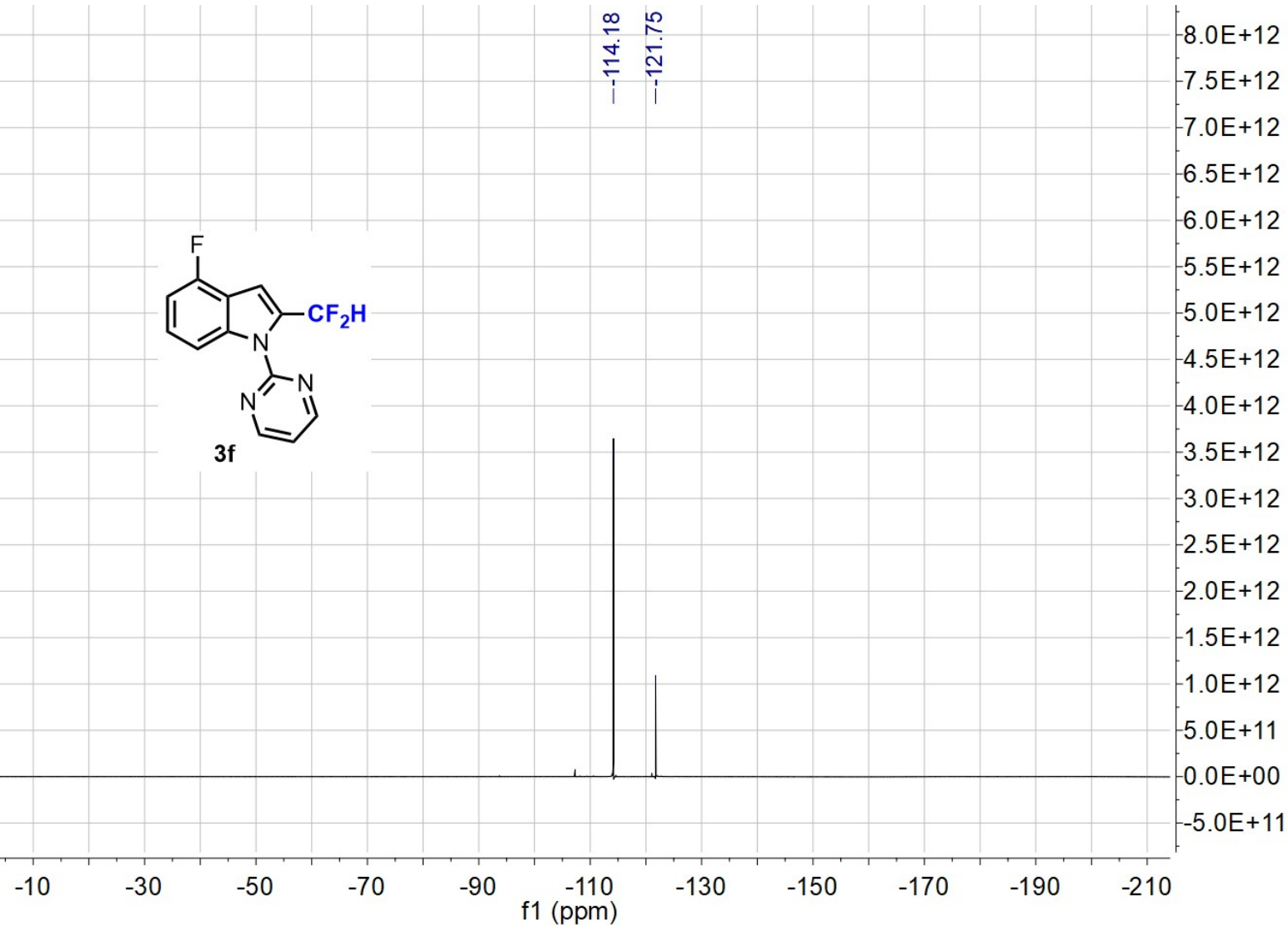

3d
CF2H
158.20
157.79
137.29
132.96
132.67
132.39
131.24
127.93
125.47
123.15
117.14
113.38
113.23
110.88
108.53
107.77
107.70
107.63
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
18.62
f1 (ppm)

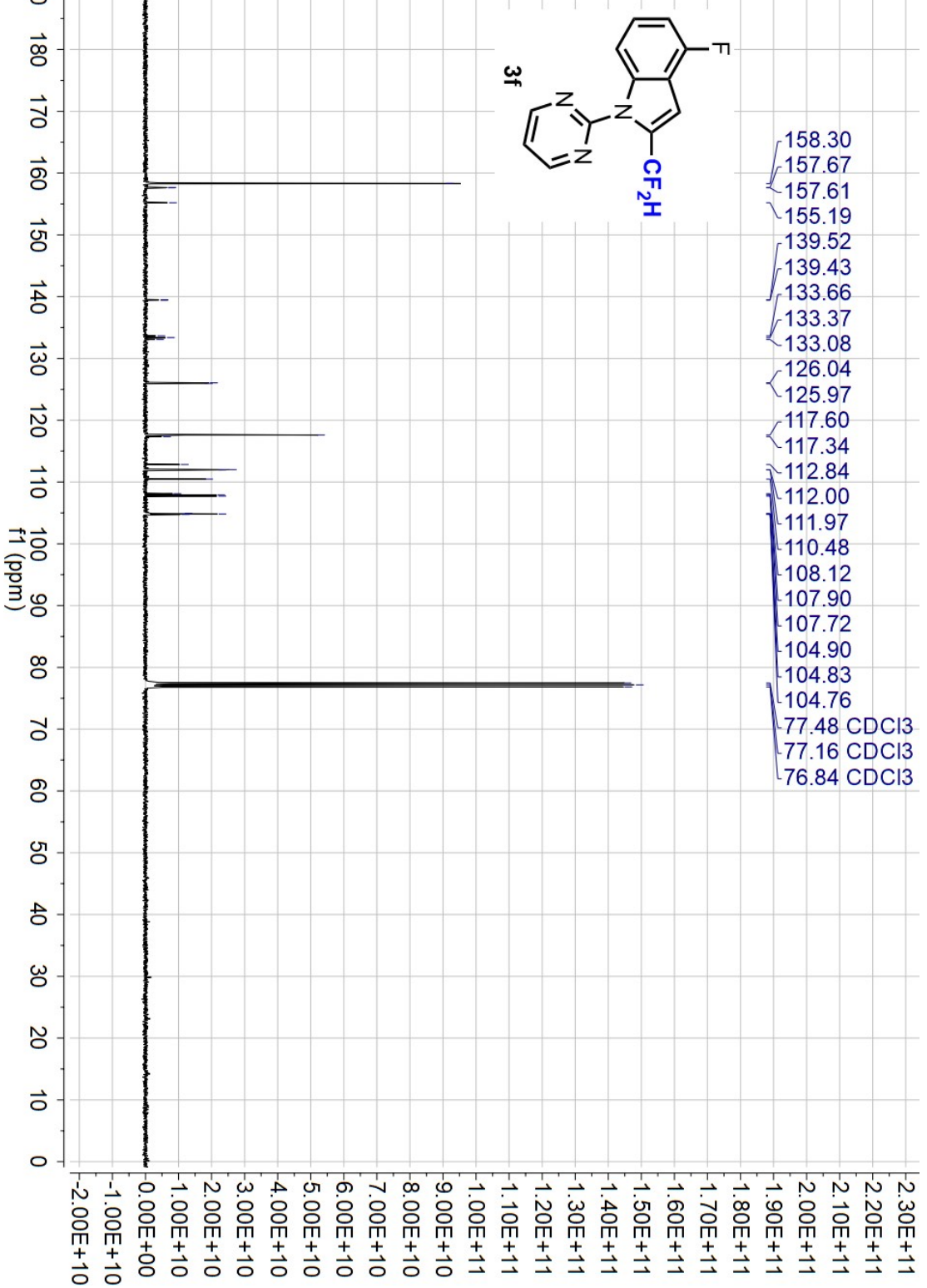

3e
OCH3
CF2H
N
N
N
8.75
8.73
8.25
8.23
7.91
7.77
7.63
7.34
7.31
7.29
7.27
7.26 CDCl3
7.14
7.13
7.11
6.70
6.68
3.97
2.02
0.96
1.16
2.00
1.02
1.00
f1 (ppm)
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
0.0E+00
1.0E+11
2.0E+11
3.0E+11
4.0E+11
5.0E+11
6.0E+11
7.0E+11
8.0E+11
9.0E+11

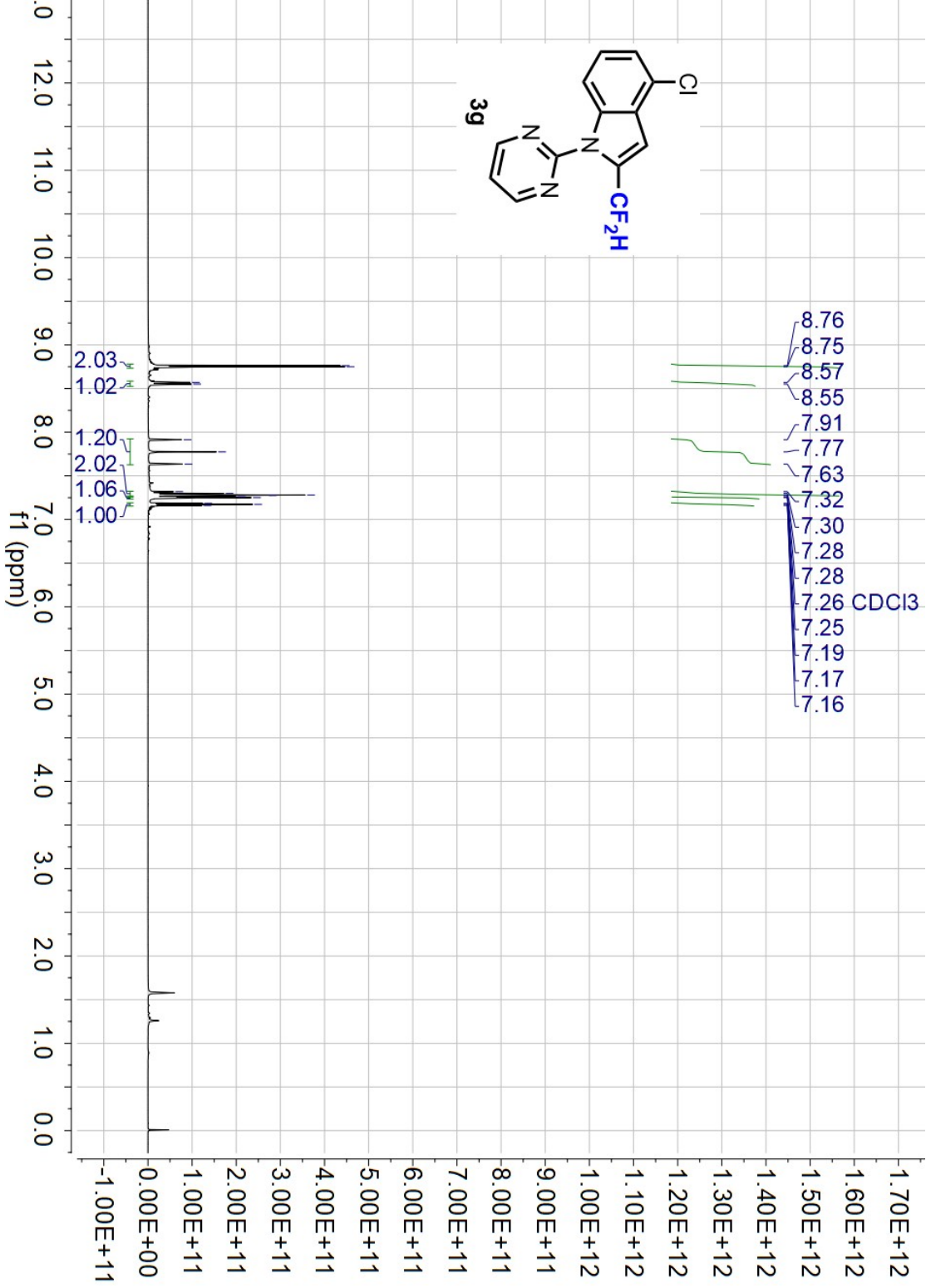

-113.54
OCH3
CF2H
N
N
N
3e
5.5E+12
5.0E+12
4.5E+12
4.0E+12
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
5.0E+11
0.0E+00
-5.0E+11
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

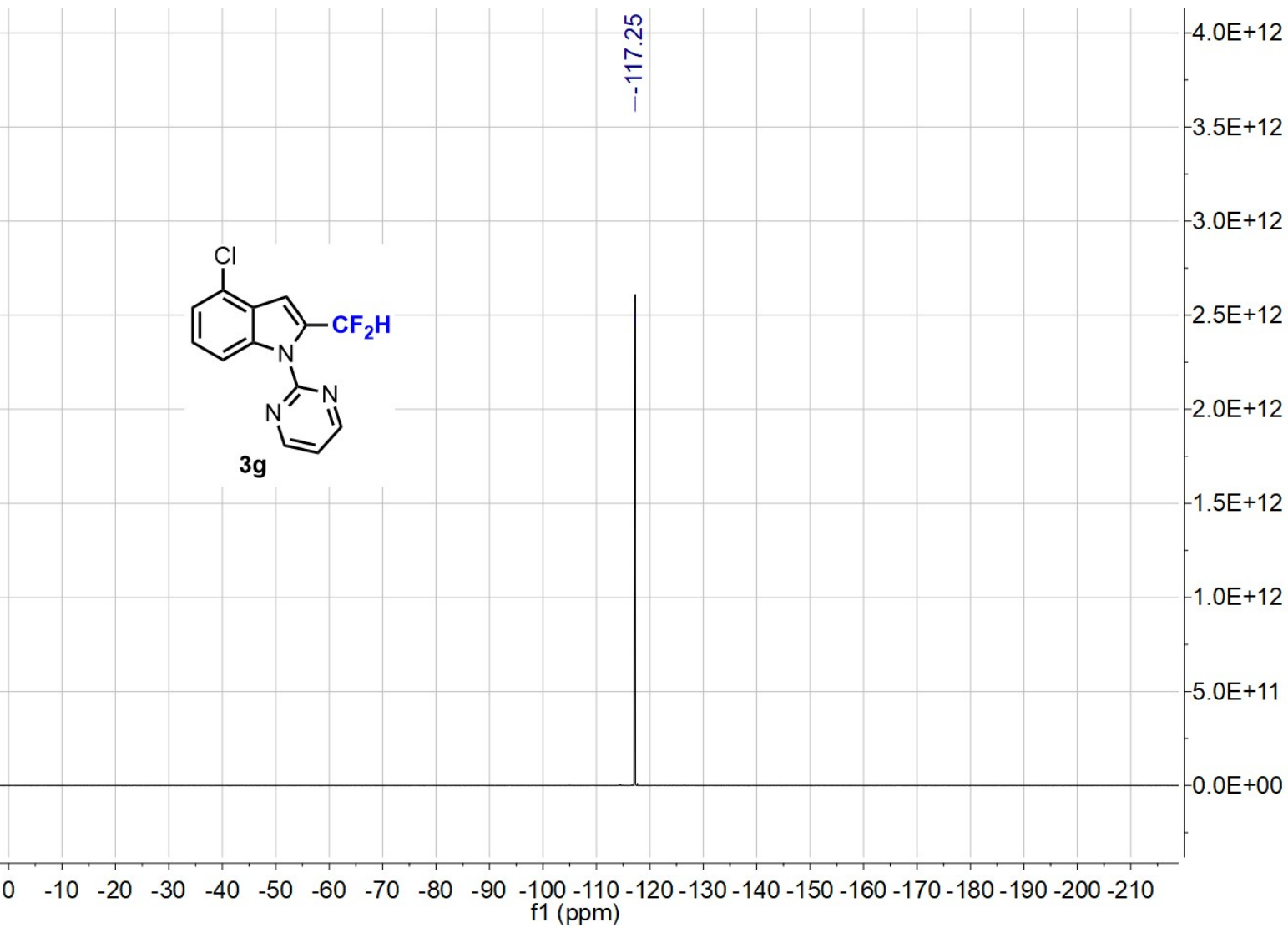

158.19
157.79
153.64
138.69
132.06
131.78
131.50
126.27
118.84
117.23
113.13
110.77
108.79
108.43
106.52
106.45
106.37
102.74
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.56
OCH3
CF2H
N
N
N
3e
2.8E+11
2.6E+11
2.4E+11
2.2E+11
2.0E+11
1.8E+11
1.6E+11
1.4E+11
1.2E+11
1.0E+11
8.0E+10
6.0E+10
4.0E+10
2.0E+10
0.0E+00
-2.0E+10
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

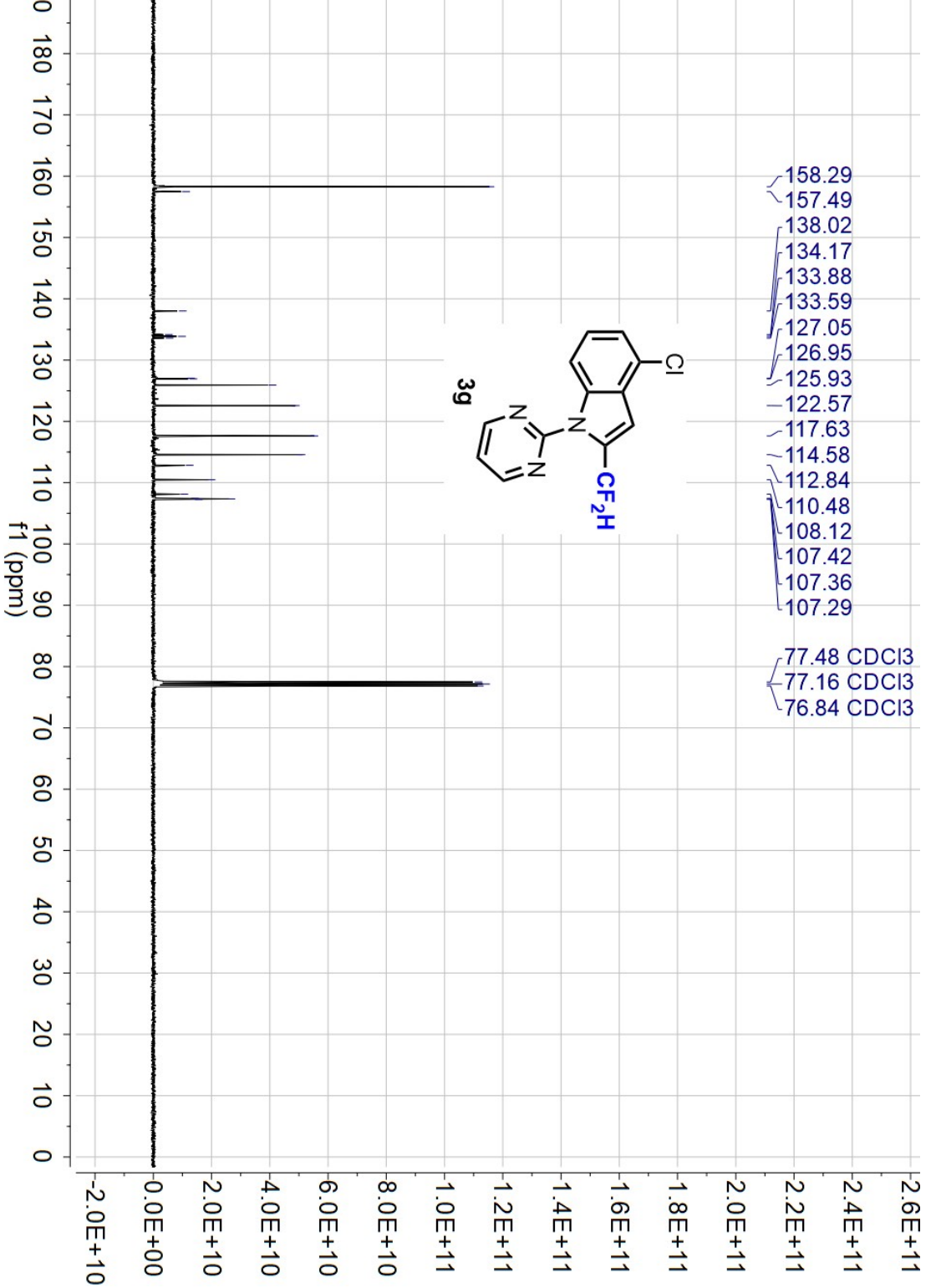

3f
F
N
N
N
CF2H
8.78
8.76
8.45
8.42
7.91
7.77
7.63
7.34
7.33
7.32
7.31
7.30
7.29
7.26 CDCl3
7.23
7.19
7.18
7.17
6.98
6.96
6.93
2.00
1.00
1.11
1.11
1.02
1.02
1.04
f1 (ppm)

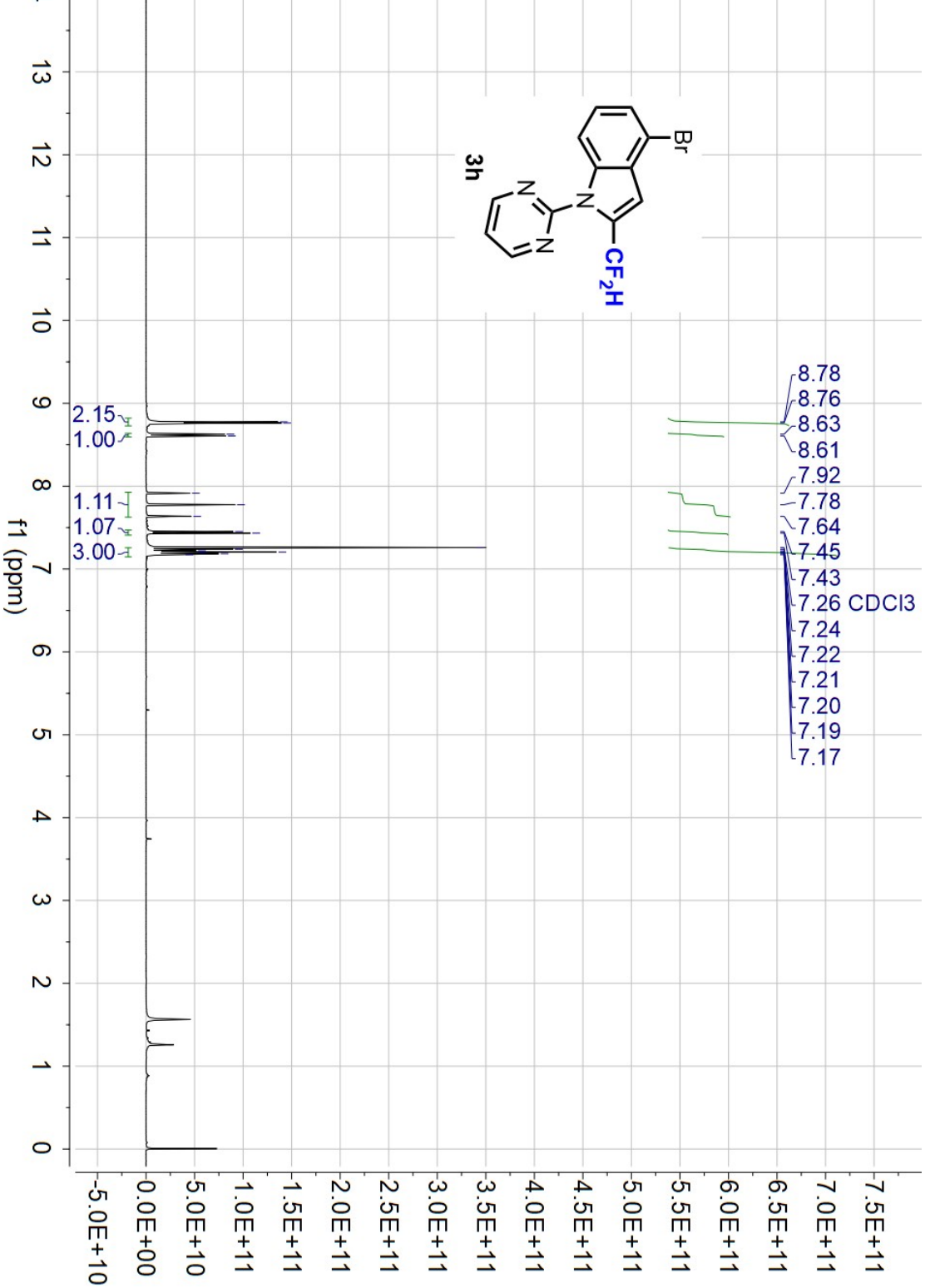

-114.18
-121.75
F
CF2H
N
N
N
3f
8.0E+12
7.5E+12
7.0E+12
6.5E+12
6.0E+12
5.5E+12
5.0E+12
4.5E+12
4.0E+12
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
5.0E+11
0.0E+00
-5.0E+11
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

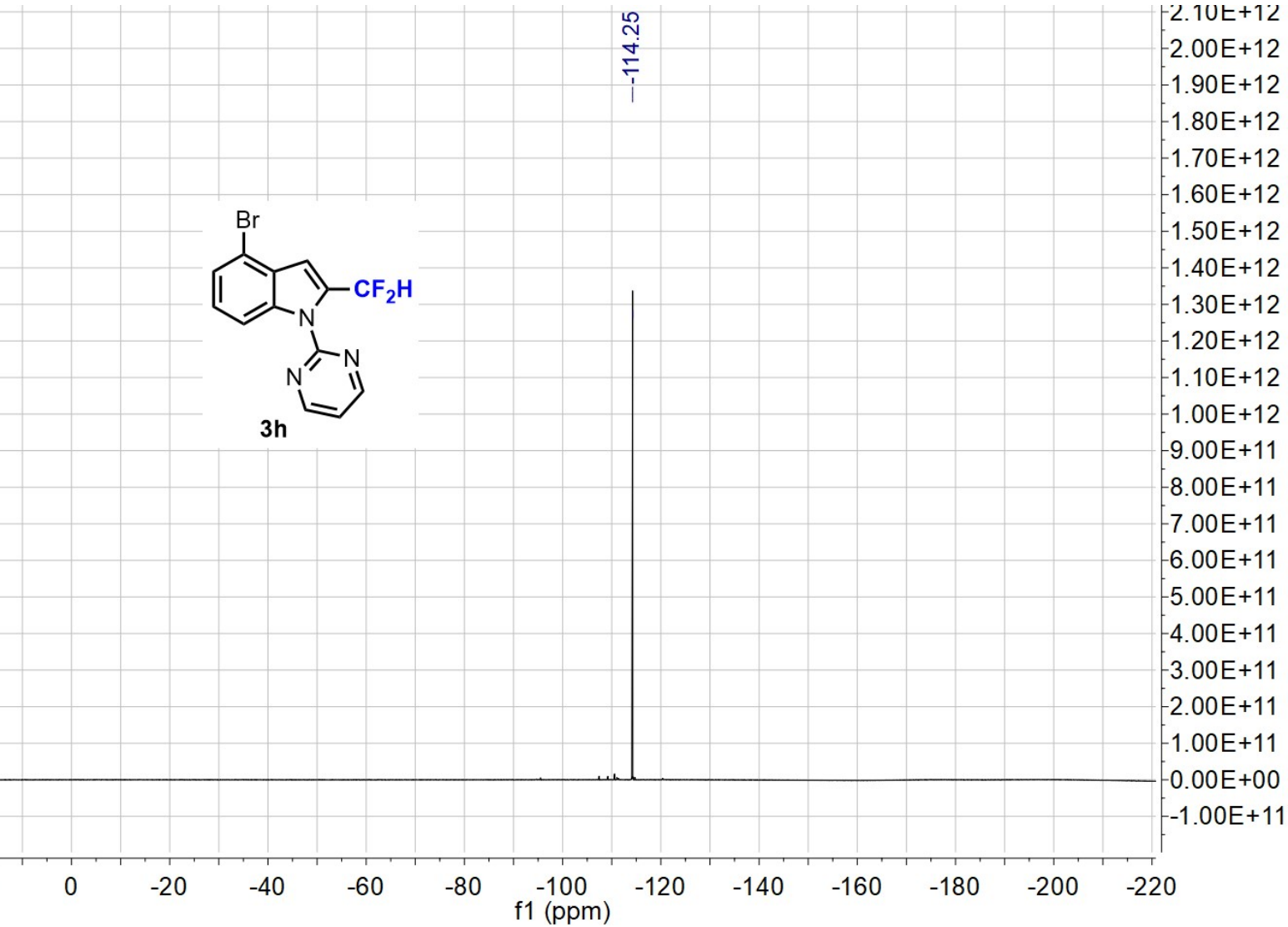

3f
F
N
N
N
CF2H
158.30
157.67
157.61
155.19
139.52
139.43
133.66
133.37
133.08
126.04
125.97
117.60
117.34
112.84
112.00
111.97
110.48
108.12
107.90
107.72
104.90
104.83
104.76
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
f1 (ppm)

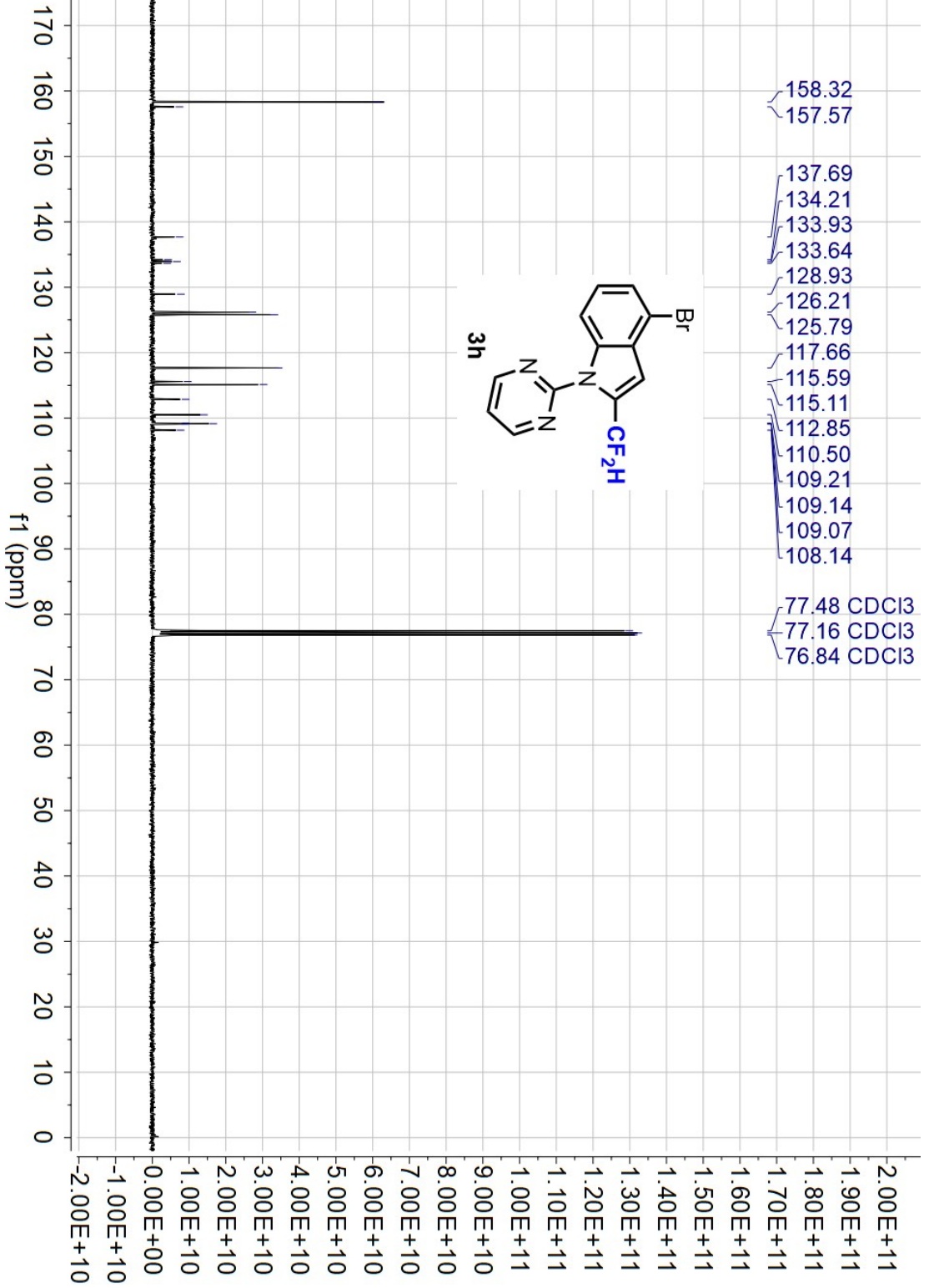

3g
Cl
N
N
N
CF2H
8.76
8.75
8.57
8.55
7.91
7.77
7.63
7.32
7.30
7.28
7.28
7.26 CDCl3
7.25
7.19
7.17
7.16
2.03
1.02
1.20
2.02
1.06
1.00
f1 (ppm)

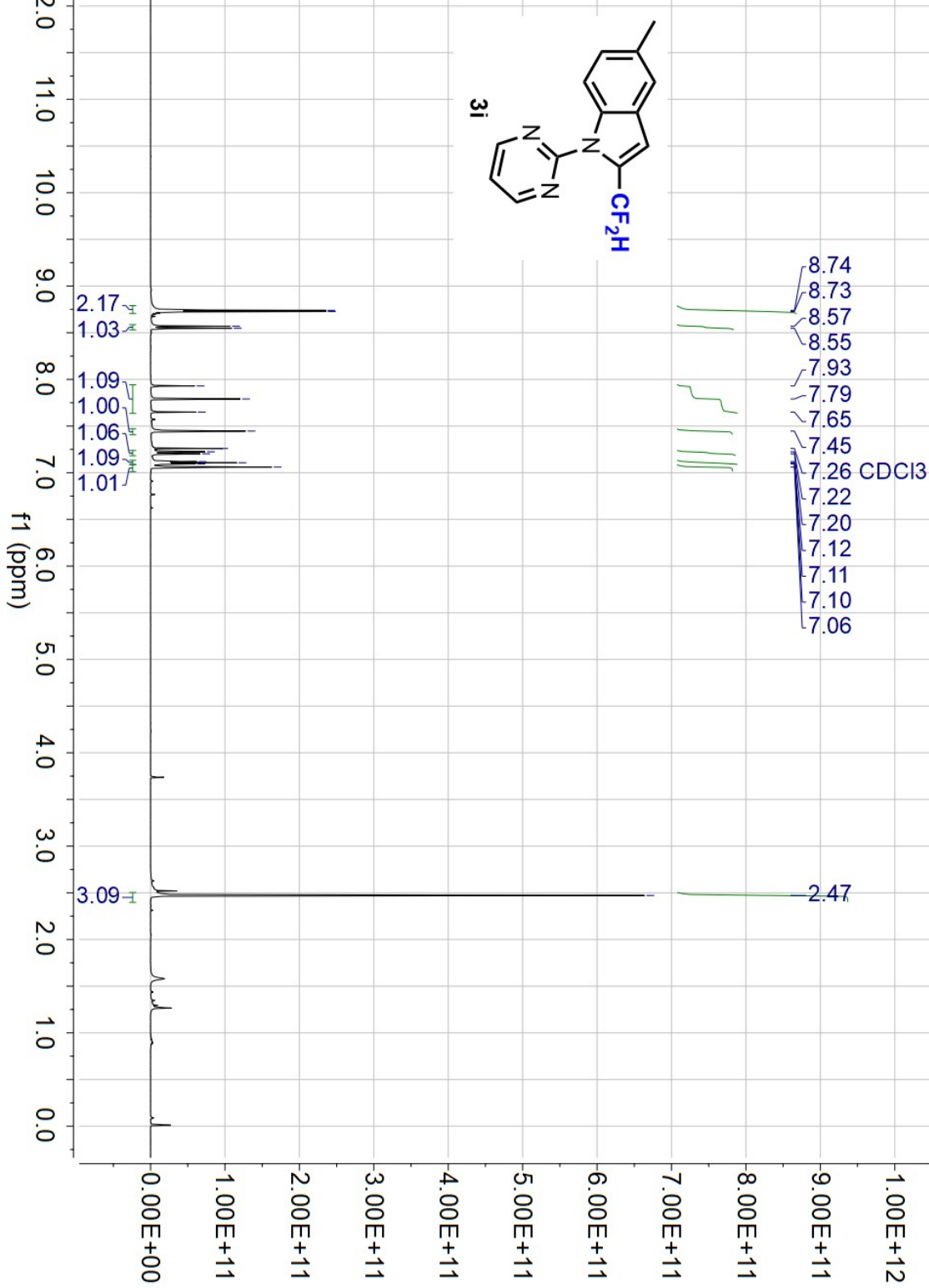

-117.25
Cl
CF2H
N
N
N
3g
4.0E+12
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
5.0E+11
0.0E+00
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

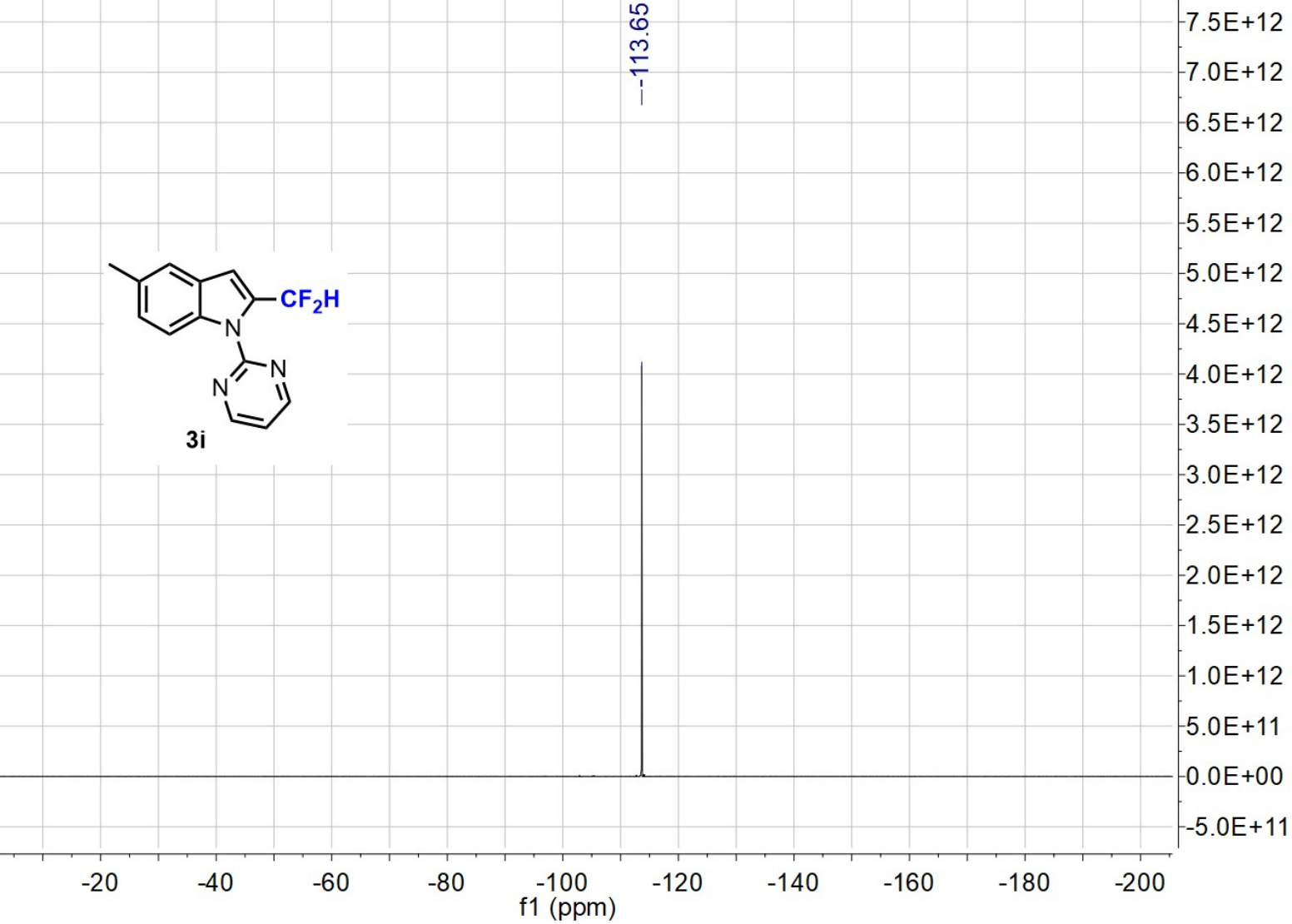

158.29
157.49
138.02
134.17
133.88
133.59
127.05
126.95
125.93
122.57
117.63
114.58
112.84
110.48
108.12
107.42
107.36
107.29
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
3g
Cl
CF2H
f1 (ppm)

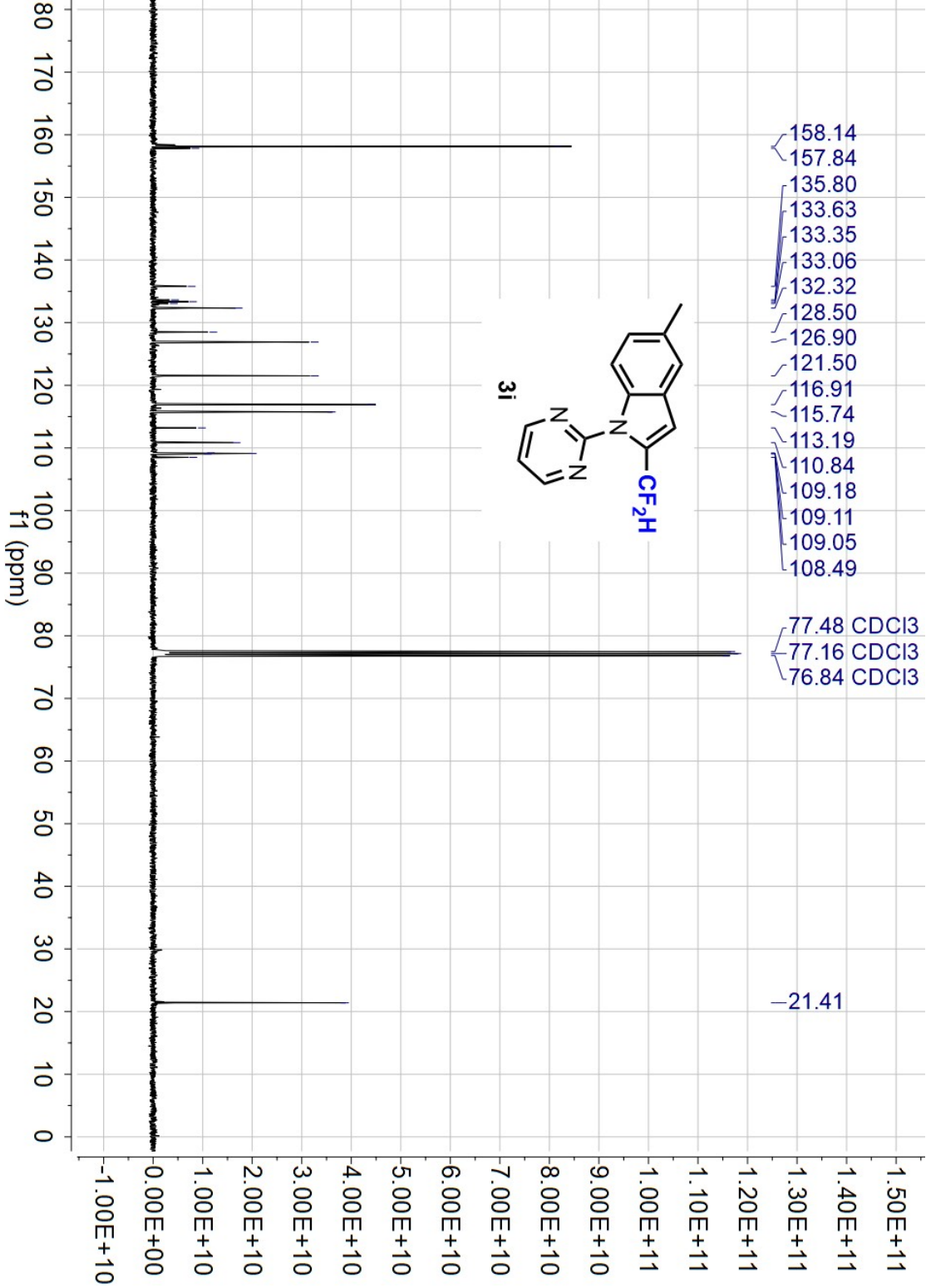

3h
Br
N
N
N
CF2H
8.78
8.76
8.63
8.61
7.92
7.78
7.64
7.45
7.43
7.26 CDCl3
7.24
7.22
7.21
7.20
7.19
7.17
2.15
1.00
1.11
1.07
3.00
f1 (ppm)

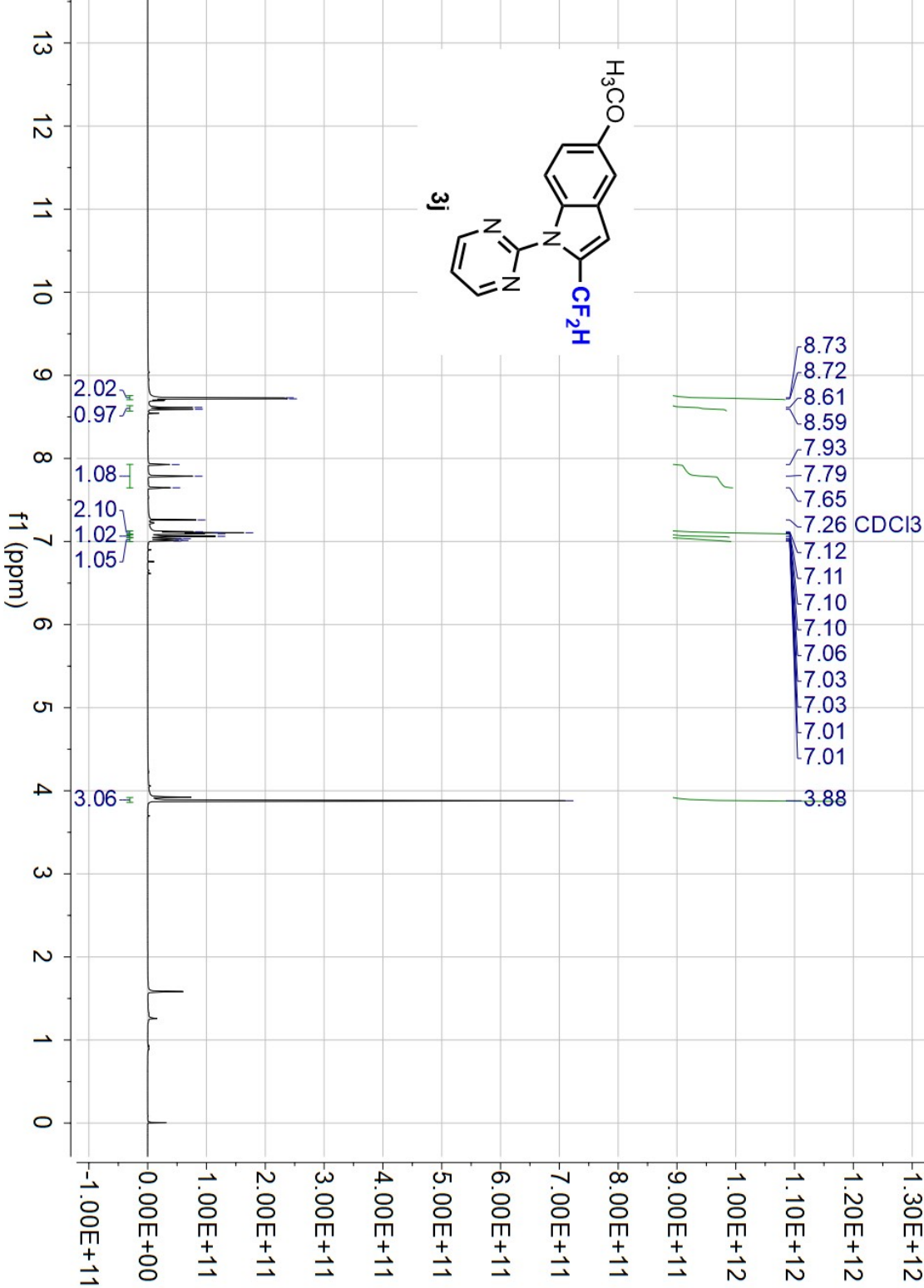

-114.25
Br
CF2H
N
N
N
3h
2.10E+12
2.00E+12
1.90E+12
1.80E+12
1.70E+12
1.60E+12
1.50E+12
1.40E+12
1.30E+12
1.20E+12
1.10E+12
1.00E+12
9.00E+11
8.00E+11
7.00E+11
6.00E+11
5.00E+11
4.00E+11
3.00E+11
2.00E+11
1.00E+11
0.00E+00
-1.00E+11
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
f1 (ppm)

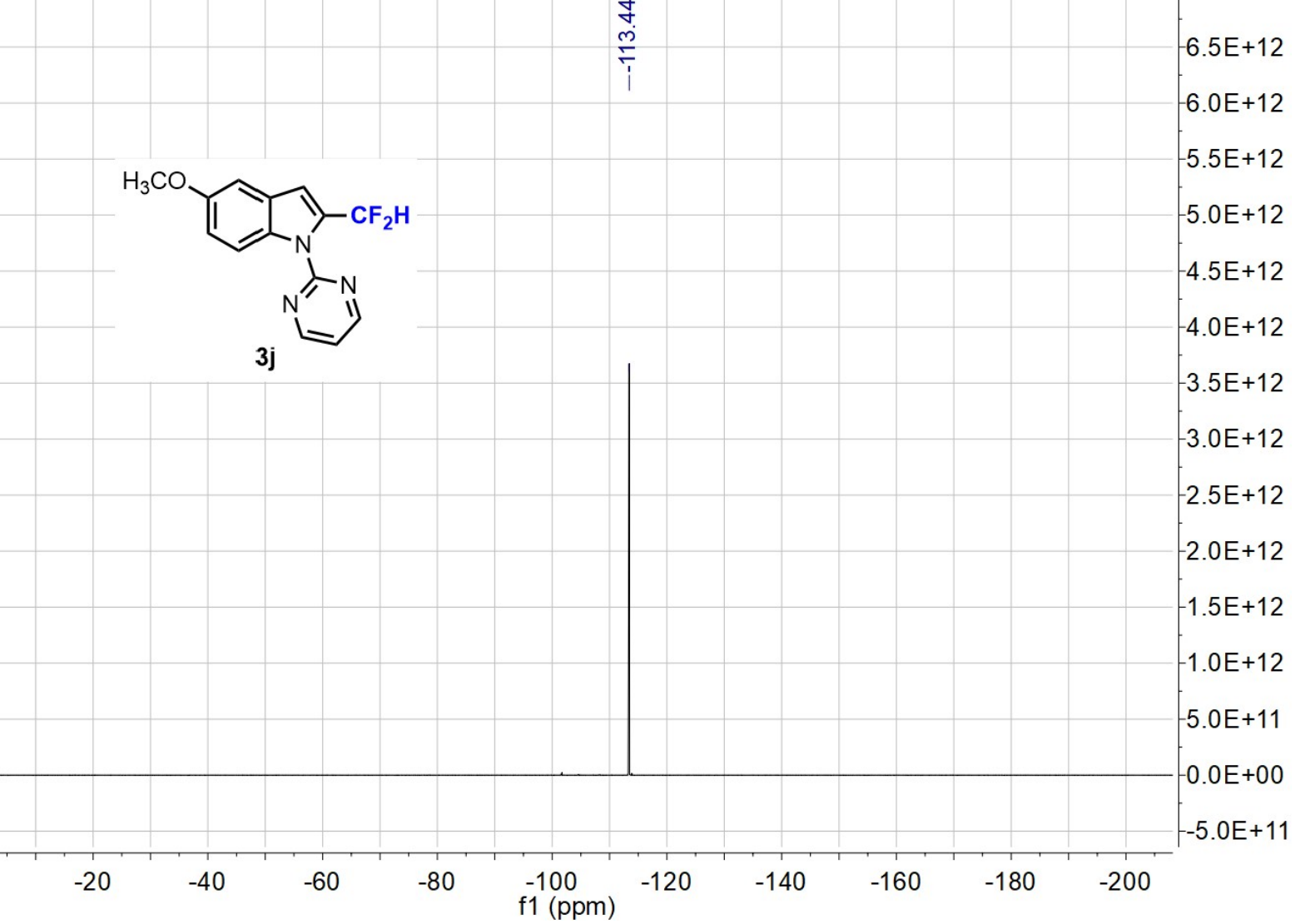

158.32
157.57
137.69
134.21
133.93
133.64
128.93
126.21
125.79
117.66
115.59
115.11
112.85
110.50
109.21
109.14
109.07
108.14
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
3h
Br
CF2H
f1 (ppm)

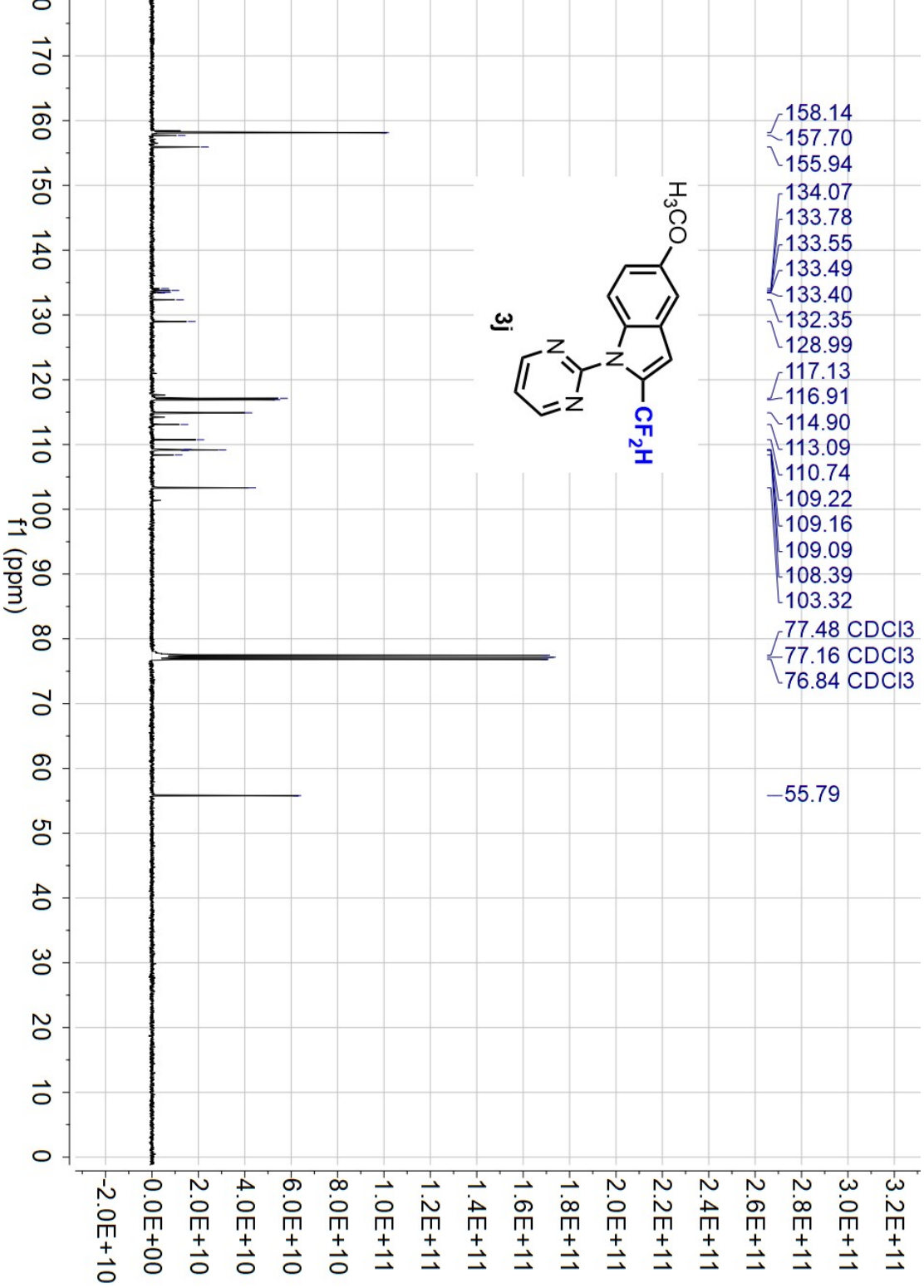

3i
CF2H
8.74
8.73
8.57
8.55
7.93
7.79
7.65
7.45
7.26 CDCl3
7.22
7.20
7.12
7.11
7.10
7.06
2.17
1.03
1.09
1.00
1.06
1.09
1.01
3.09
2.47
f1 (ppm)

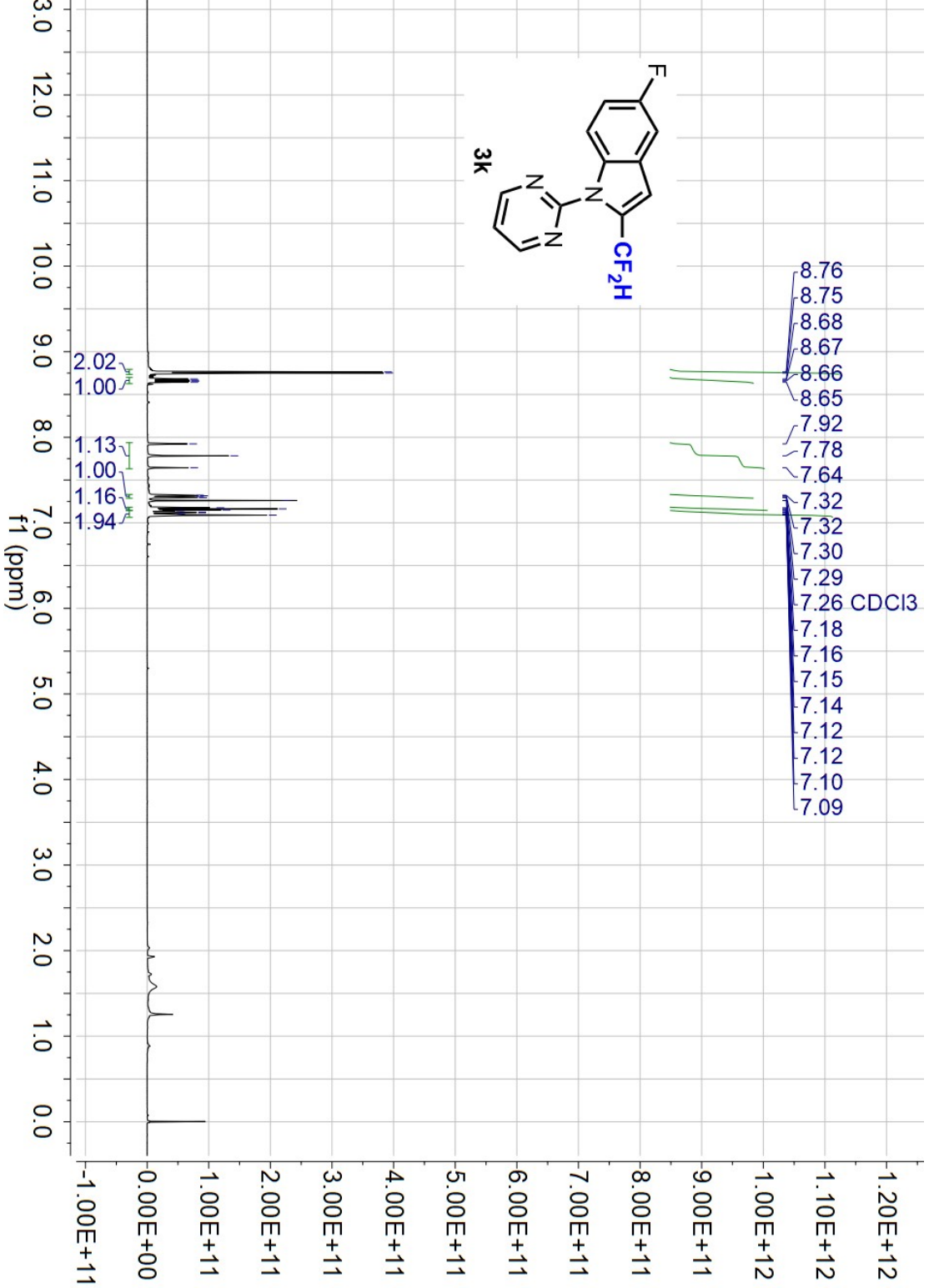

-113.65
CF2H
N
N
N
3i
7.5E+12
7.0E+12
6.5E+12
6.0E+12
5.5E+12
5.0E+12
4.5E+12
4.0E+12
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
5.0E+11
0.0E+00
-5.0E+11
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

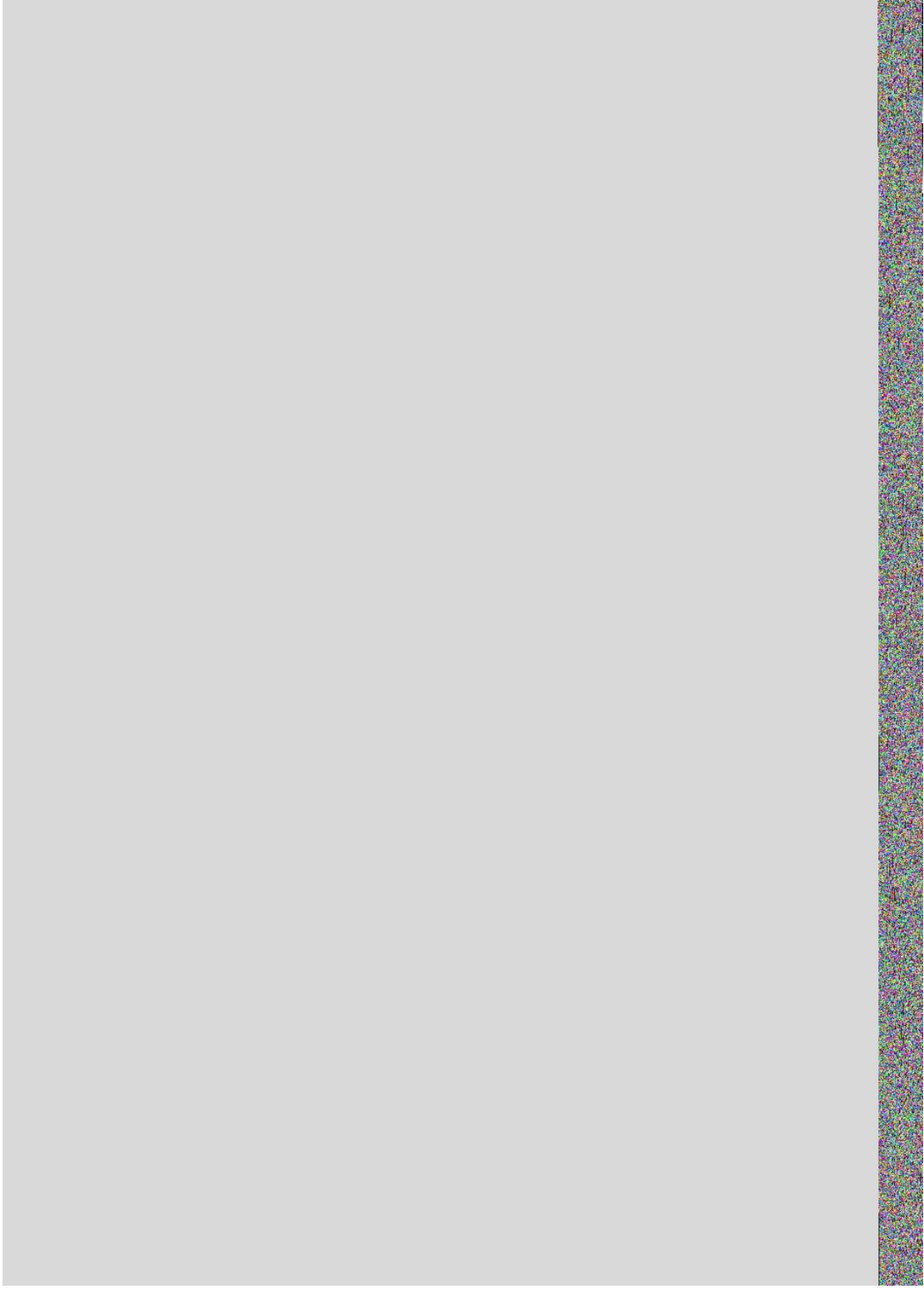

158.14
157.84
135.80
133.63
133.35
133.06
132.32
128.50
126.90
121.50
116.91
115.74
113.19
110.84
109.18
109.11
109.05
108.49
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
21.41
3i
CF2H
f1 (ppm)

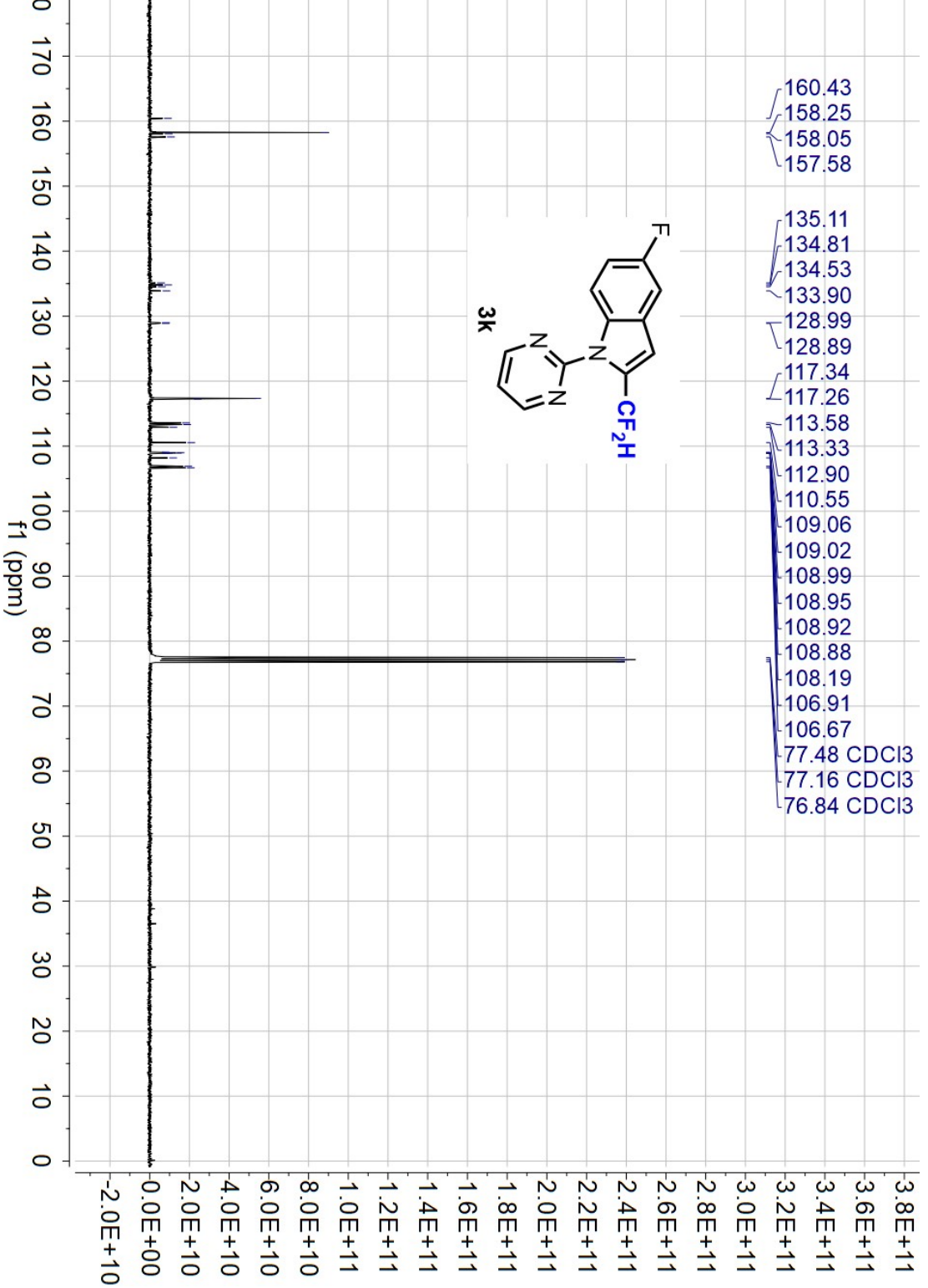

3j
H3CO
CF2H
f1 (ppm)
2.02
0.97
1.08
2.10
1.02
1.05
3.06
8.73
8.72
8.61
8.59
7.93
7.79
7.65
7.26 CDCl3
7.12
7.11
7.10
7.10
7.06
7.03
7.03
7.01
7.01
3.88

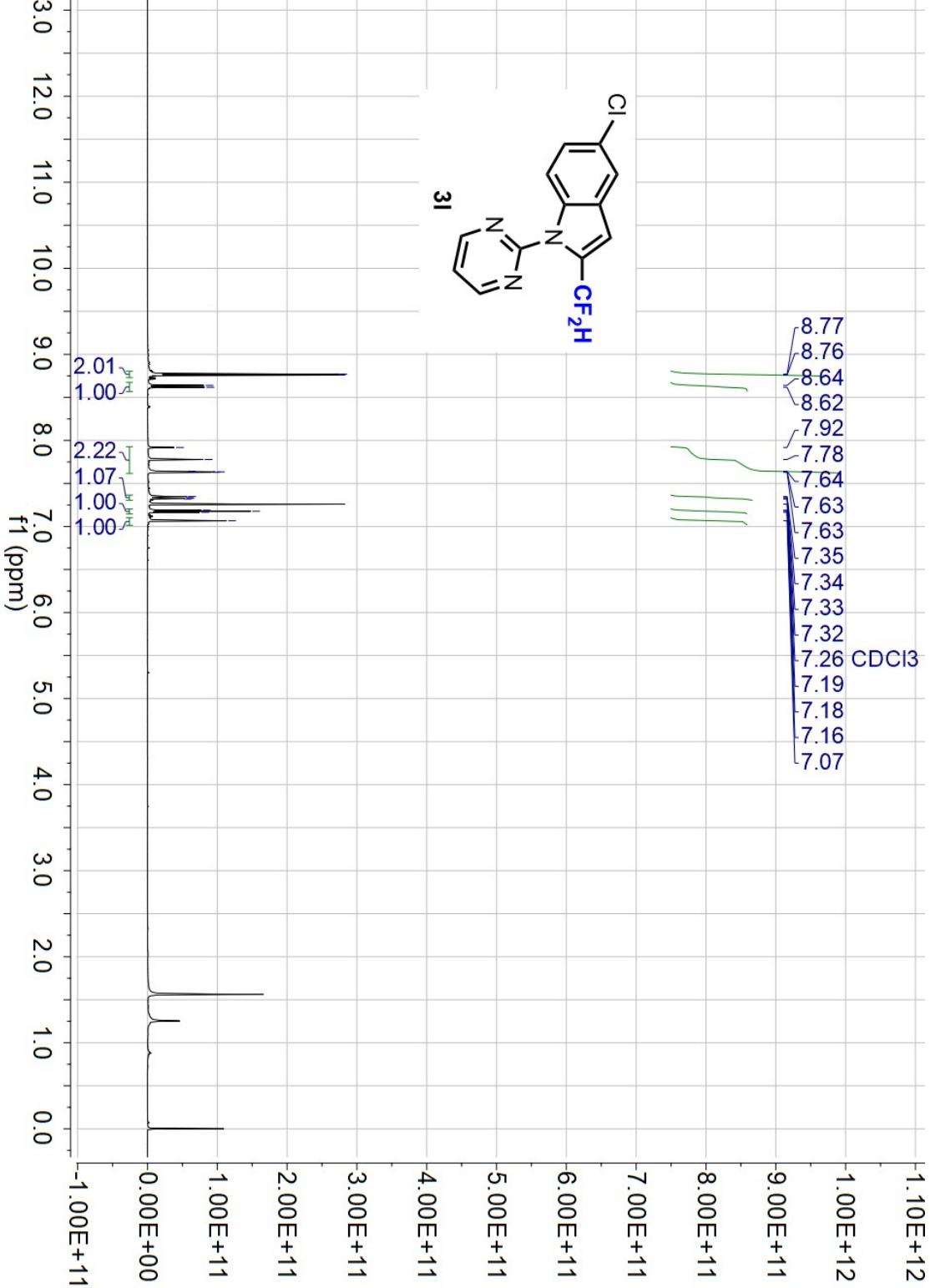

-113.44
H3CO
CF2H
N
N
N
3j
6.5E+12
6.0E+12
5.5E+12
5.0E+12
4.5E+12
4.0E+12
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
5.0E+11
0.0E+00
-5.0E+11
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

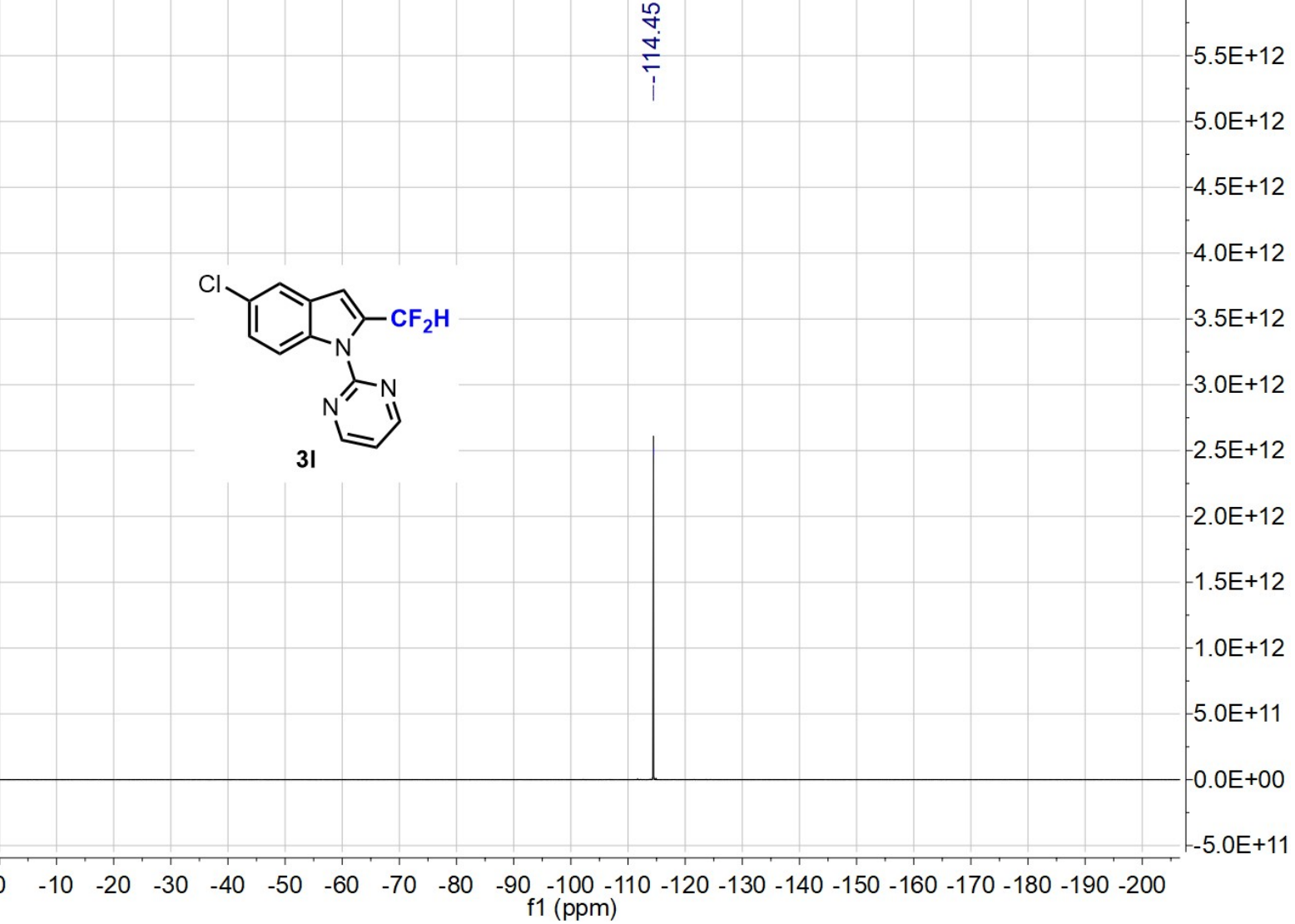

158.14
157.70
155.94
134.07
133.78
133.55
133.49
133.40
132.35
128.99
117.13
116.91
114.90
113.09
110.74
109.22
109.16
109.09
108.39
103.32
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.79
H3CO
CF2H
3j
f1 (ppm)

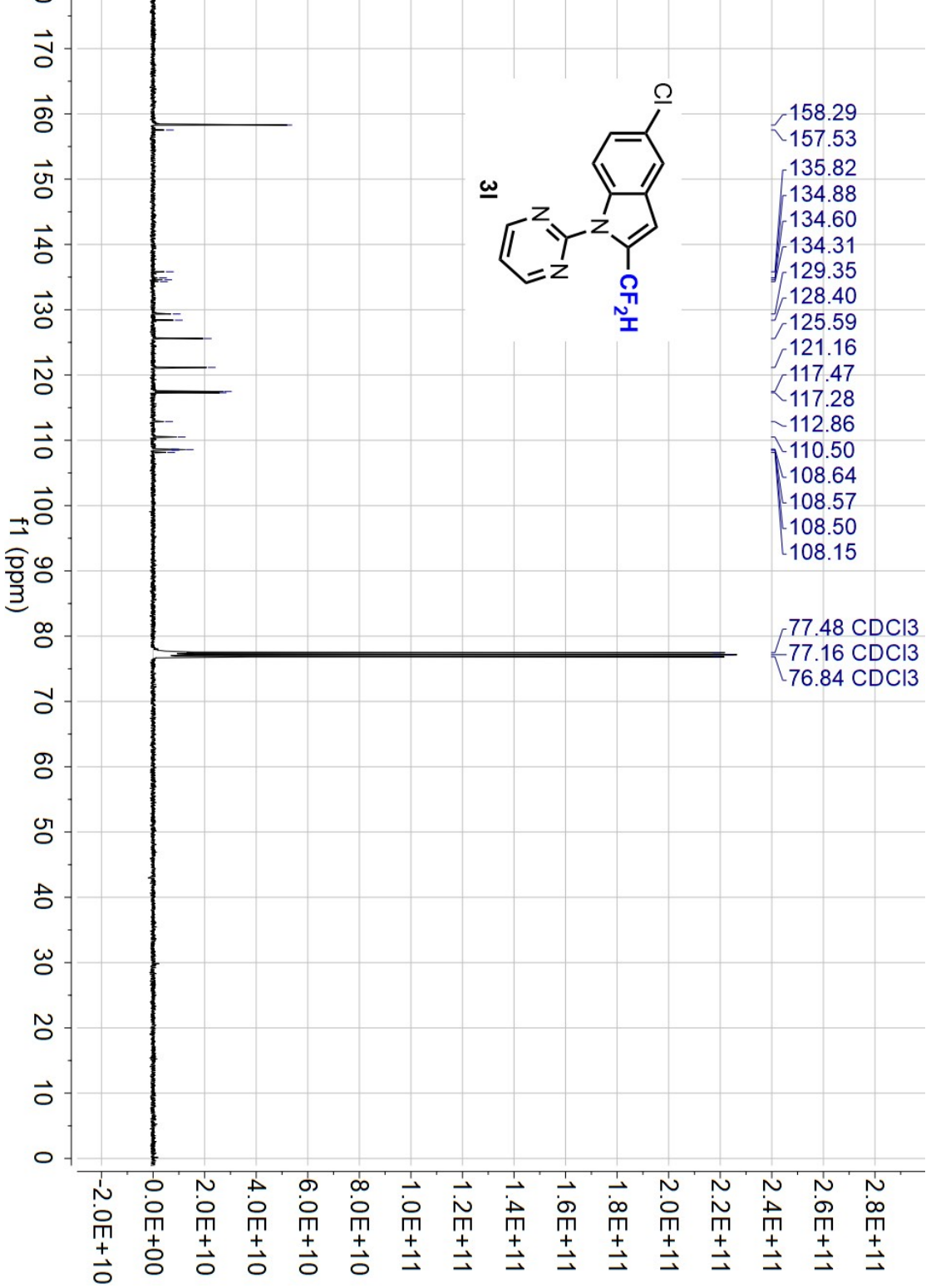

3k
F
N
N
N
CF2H
8.76
8.75
8.68
8.67
8.66
8.65
7.92
7.78
7.64
7.32
7.32
7.30
7.29
7.26 CDCl3
7.18
7.16
7.15
7.14
7.12
7.12
7.10
7.09
2.02
1.00
1.13
1.00
1.16
1.94
f1 (ppm)

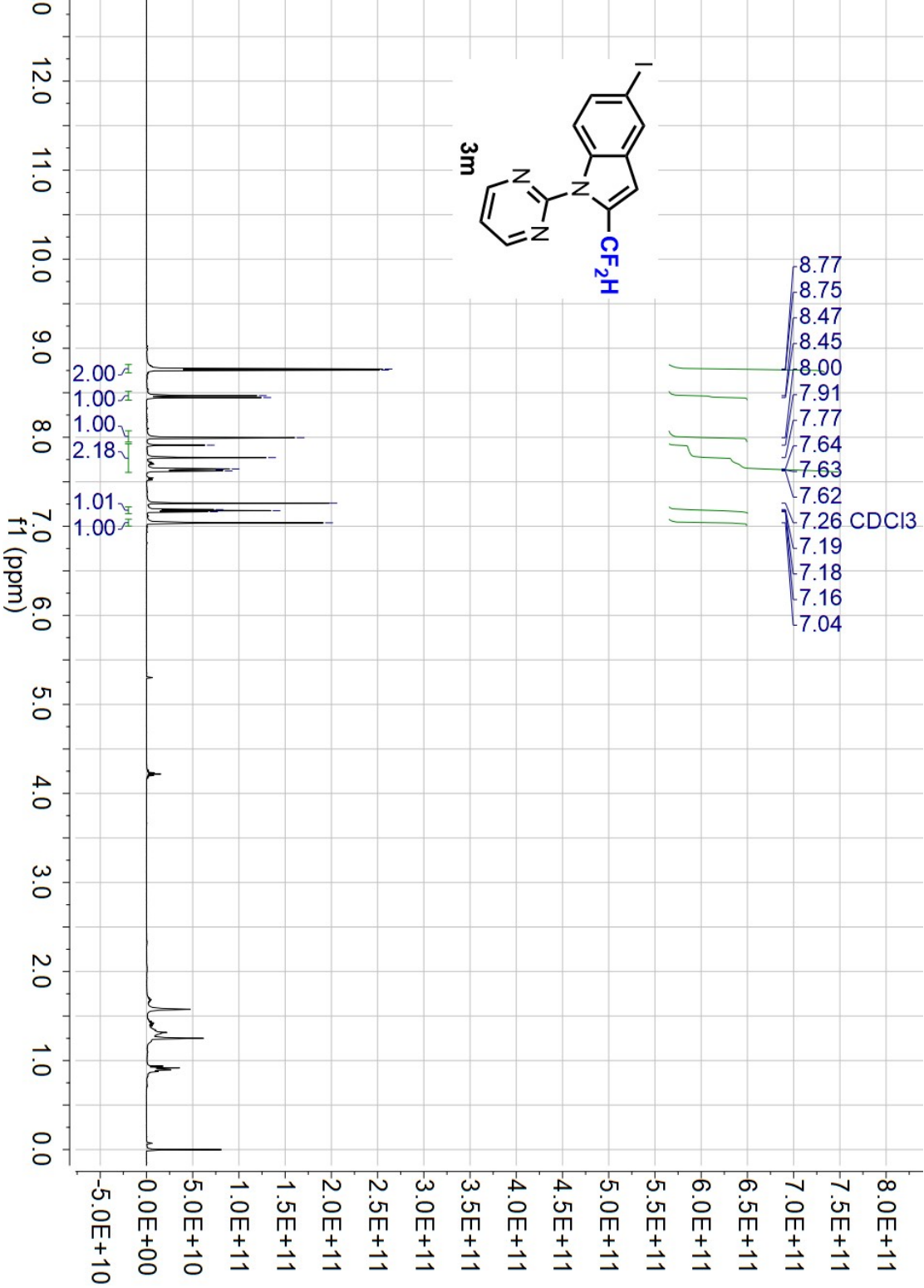


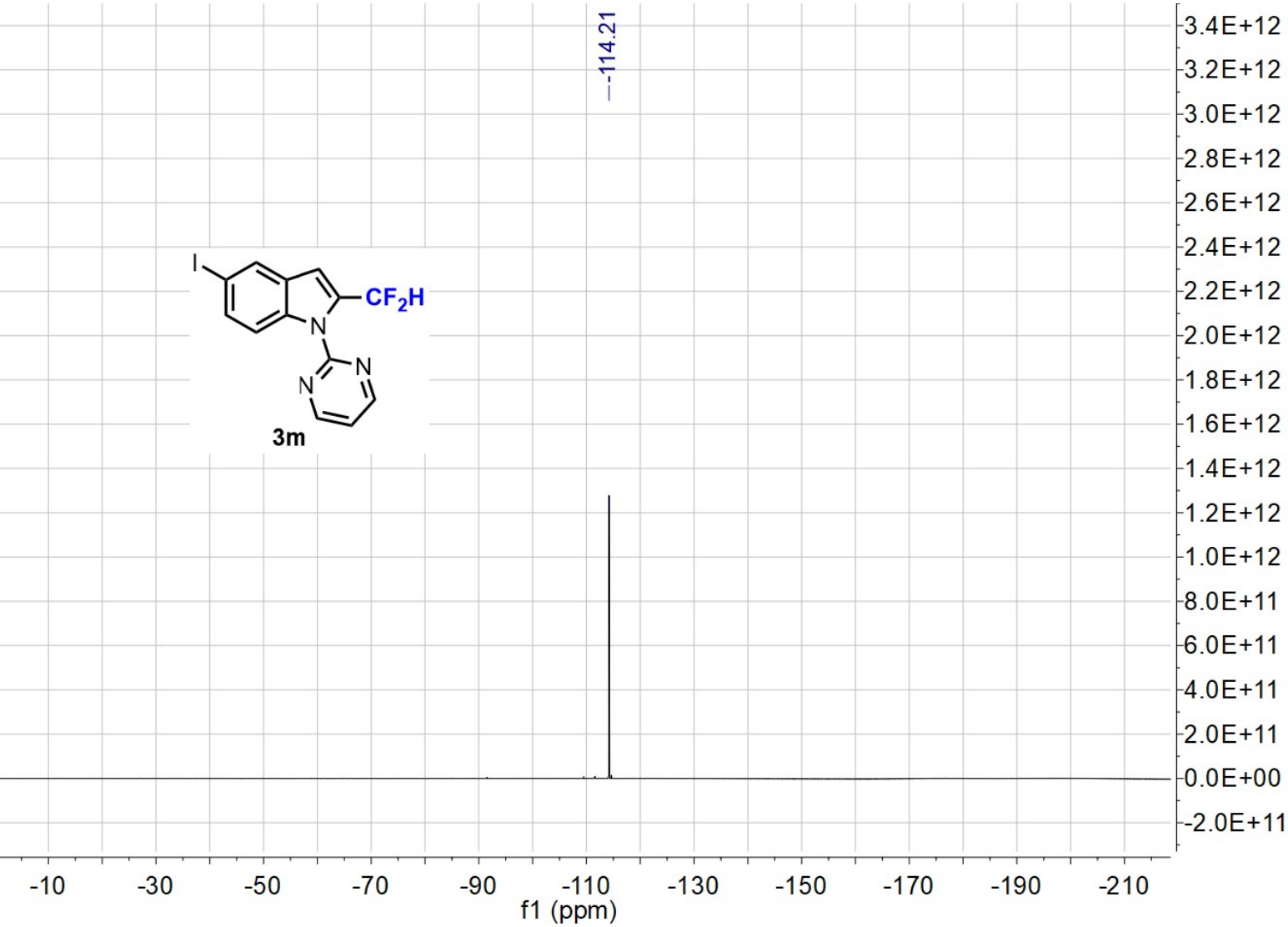

160.43
158.25
158.05
157.58
135.11
134.81
134.53
133.90
128.99
128.89
117.34
117.26
113.58
113.33
112.90
110.55
109.06
109.02
108.99
108.95
108.92
108.88
108.19
106.91
106.67
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
3k
F
N
N
N
CF2H
f1 (ppm)

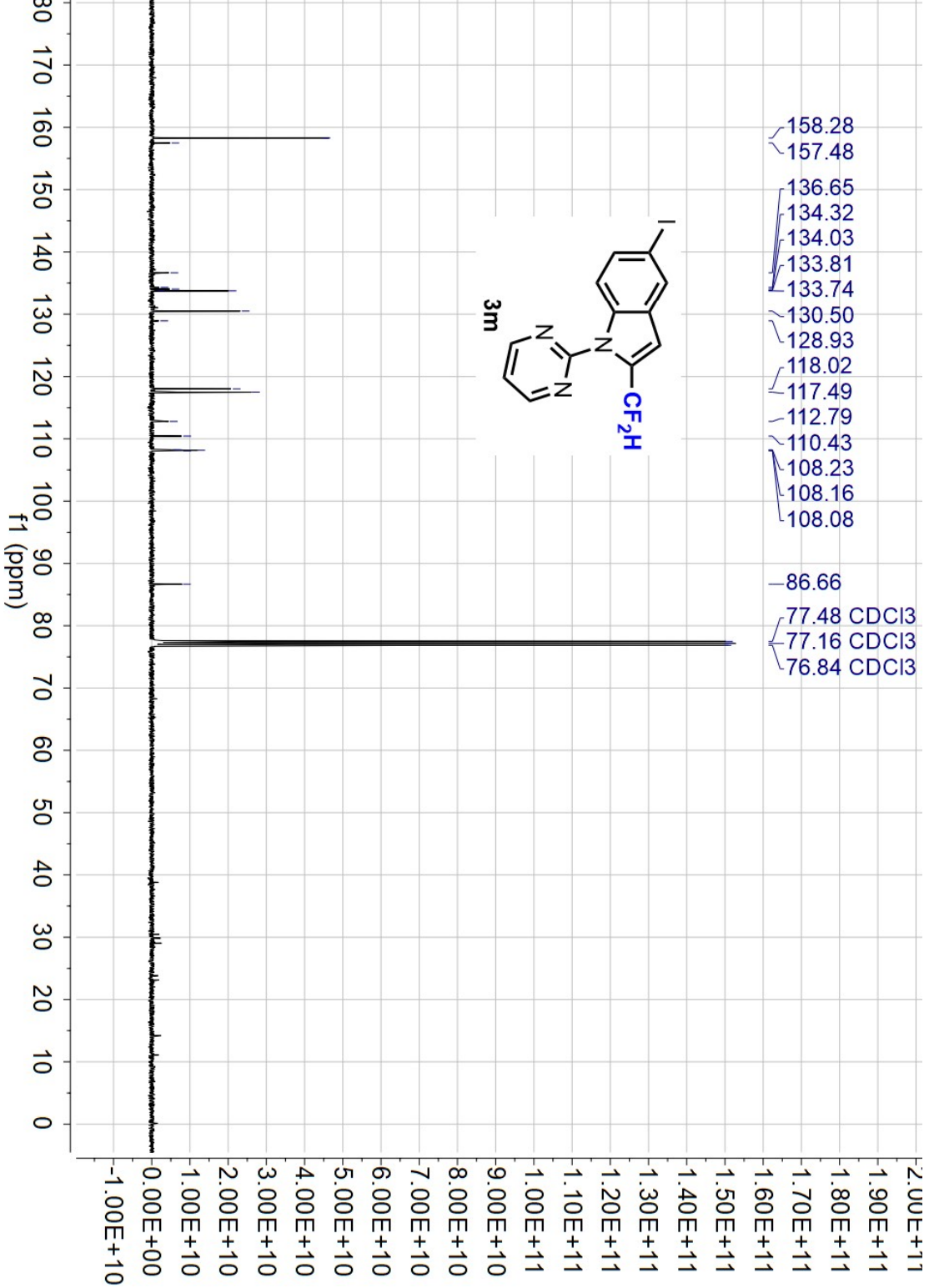

3l
Cl
N
N
N
CF2H
8.77
8.76
8.64
8.62
7.92
7.78
7.64
7.63
7.63
7.35
7.34
7.33
7.32
7.26 CDCl3
7.19
7.18
7.16
7.07
2.01
1.00
2.22
1.07
1.00
1.00
f1 (ppm)

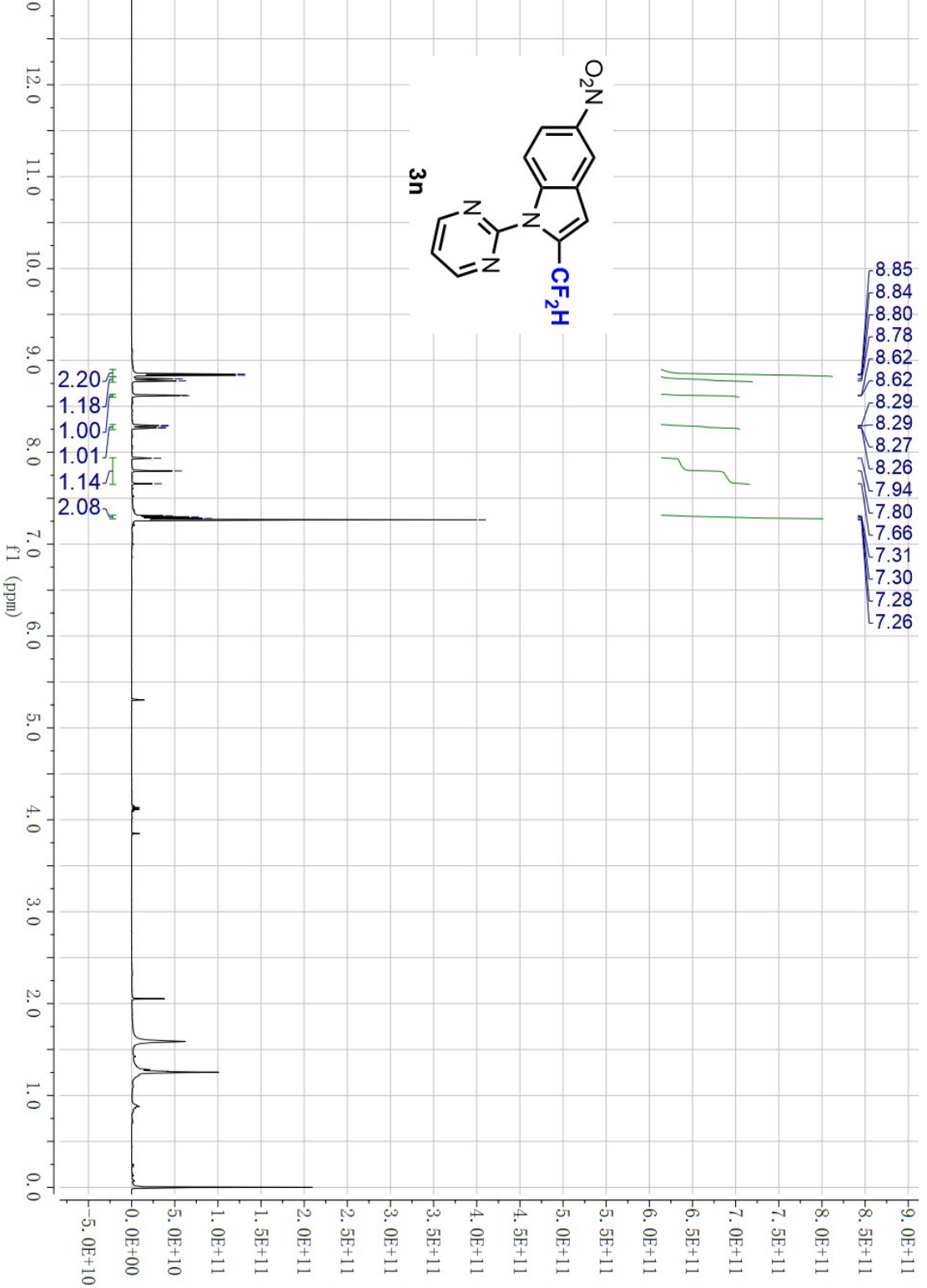

-114.45
Cl
CF2H
N
N
N
3l
5.5E+12
5.0E+12
4.5E+12
4.0E+12
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
5.0E+11
0.0E+00
-5.0E+11
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

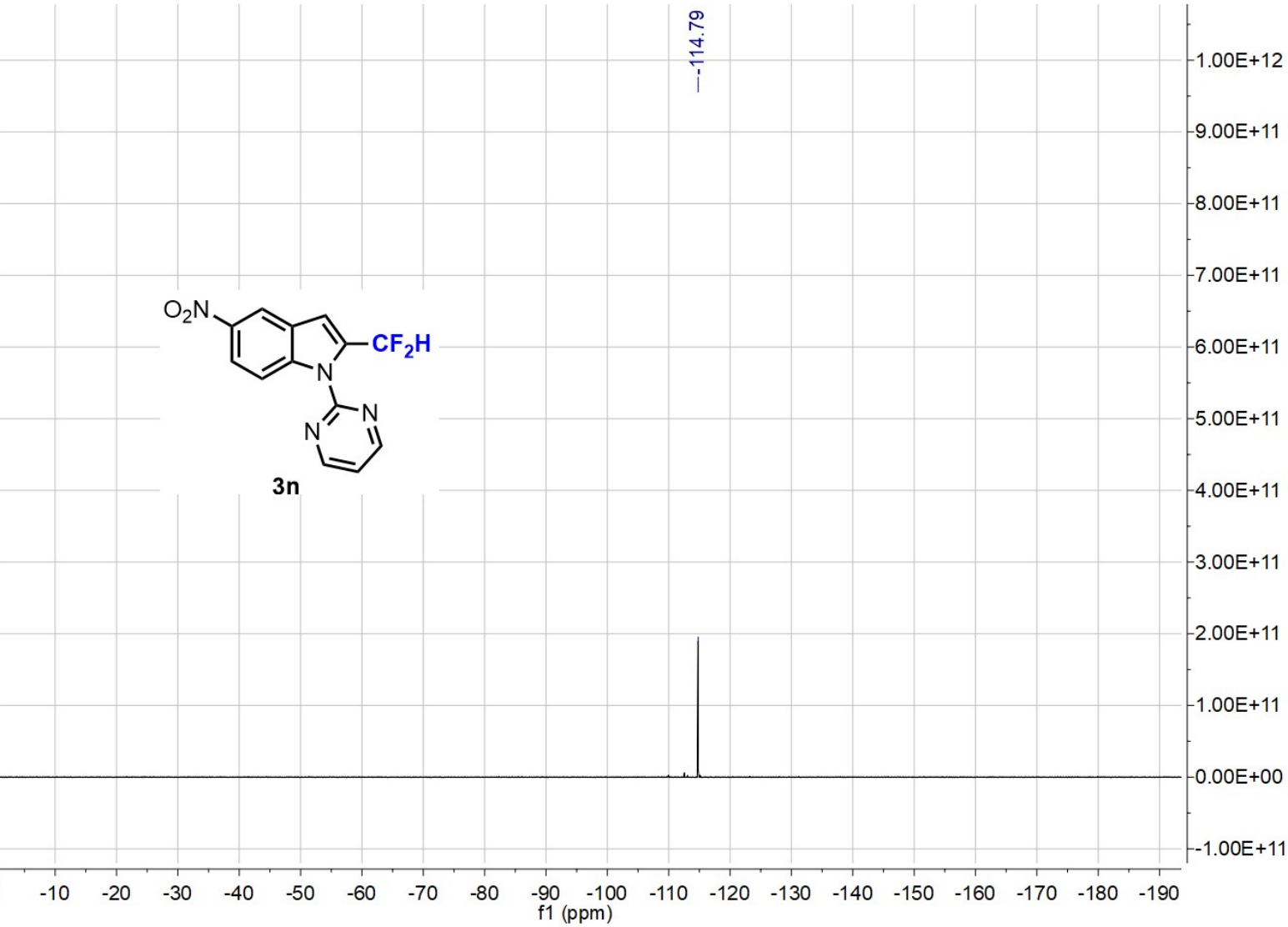

3l
Cl
N
N
CF2H
158.29
157.53
135.82
134.88
134.60
134.31
129.35
128.40
125.59
121.16
117.47
117.28
112.86
110.50
108.64
108.57
108.50
108.15
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
f1 (ppm)

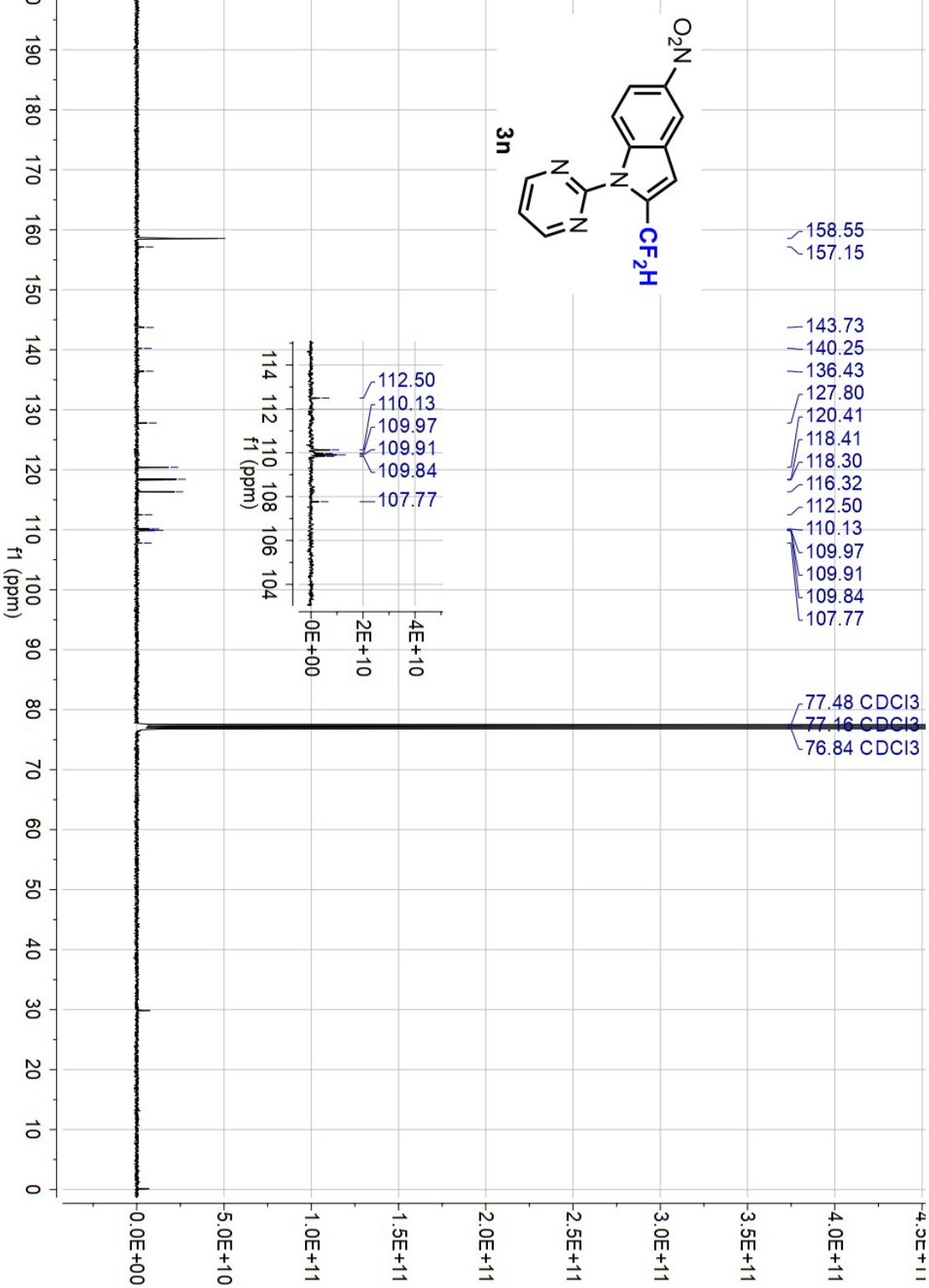

3m
I
N
N
N
CF2H
8.77
8.75
8.47
8.45
8.00
7.91
7.77
7.64
7.63
7.62
7.26 CDCl3
7.19
7.18
7.16
7.04
2.00
1.00
1.00
2.18
1.01
1.00
f1 (ppm)

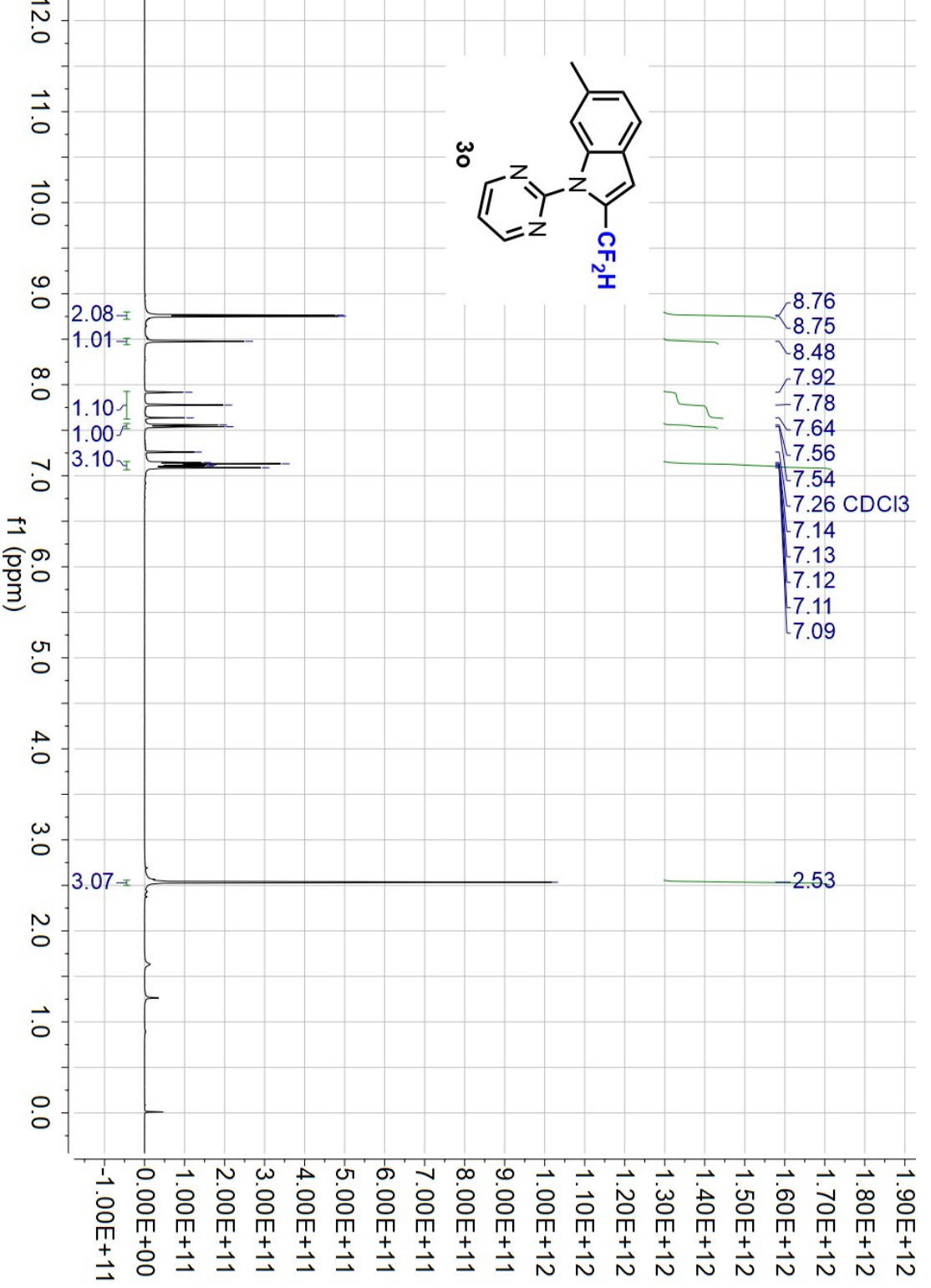

-114.21
3.4E+12
3.2E+12
3.0E+12
2.8E+12
2.6E+12
2.4E+12
2.2E+12
2.0E+12
1.8E+12
1.6E+12
1.4E+12
1.2E+12
1.0E+12
8.0E+11
6.0E+11
4.0E+11
2.0E+11
0.0E+00
-2.0E+11
I
CF2H
N
N
N
3m
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

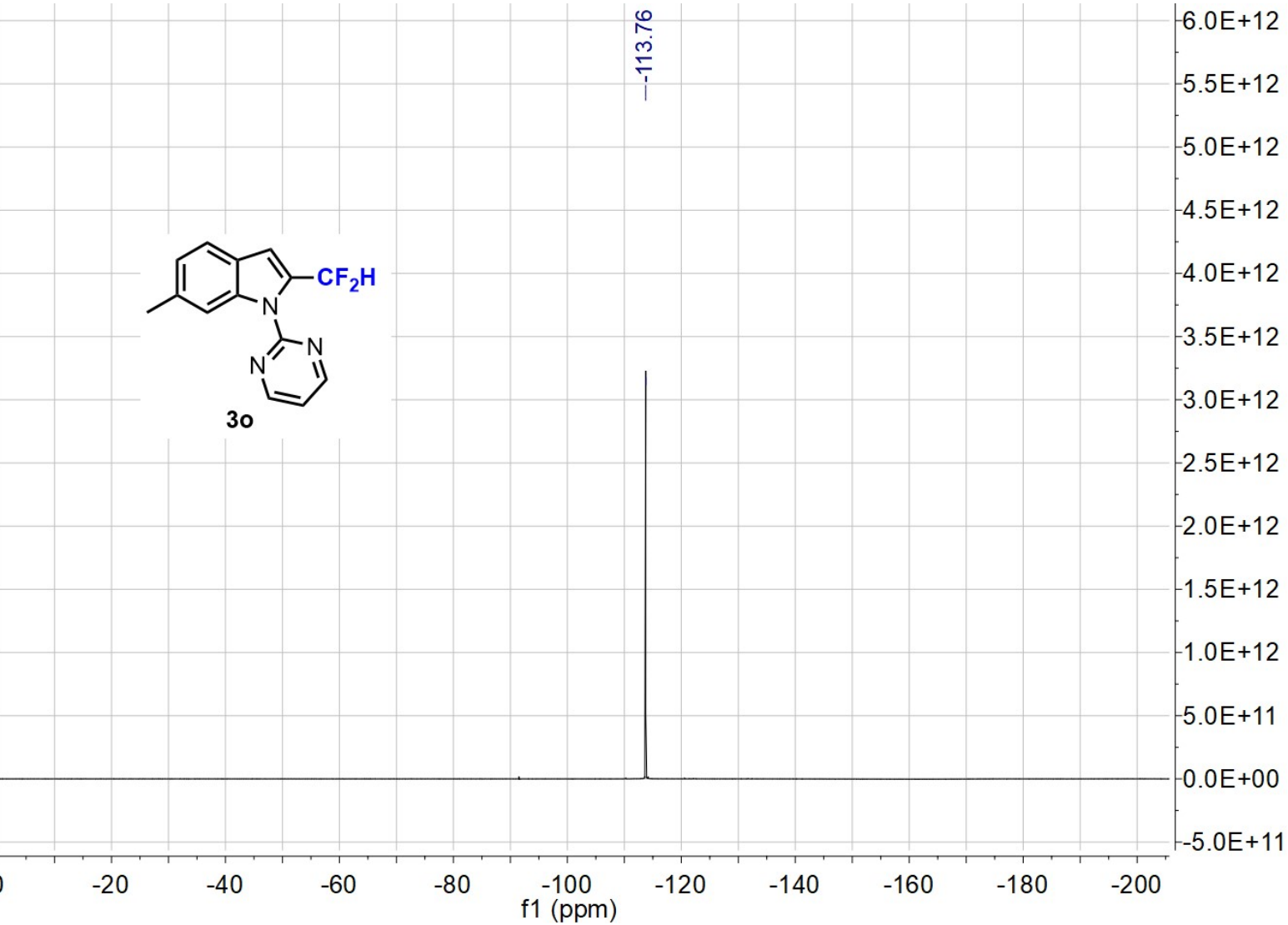

158.28
157.48
136.65
134.32
134.03
133.81
133.74
130.50
128.93
118.02
117.49
112.79
110.43
108.23
108.16
108.08
86.66
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
3m
CF2H
f1 (ppm)

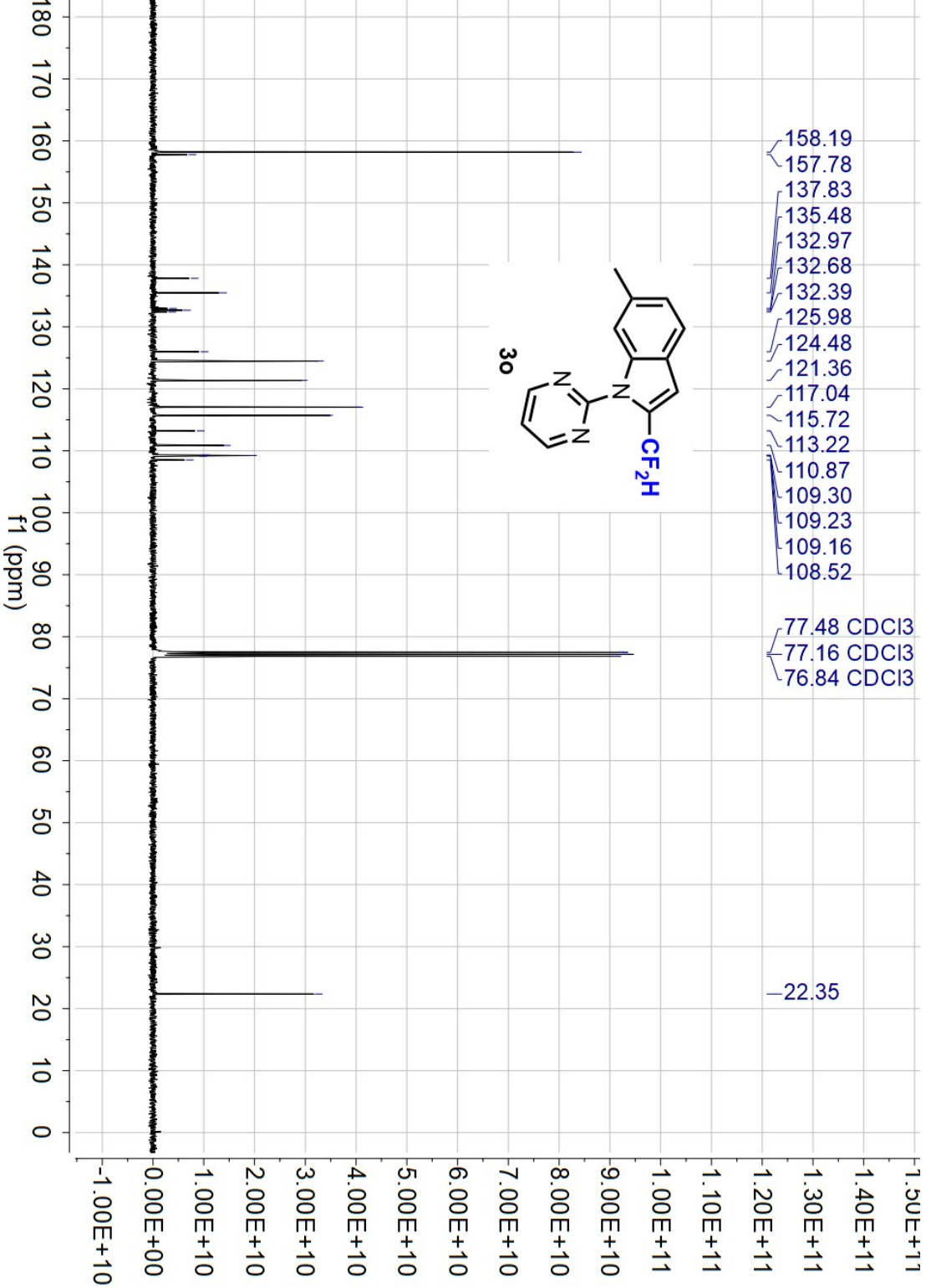

3n
O_2N
N
N
N
CF_2H
2.20
1.18
1.00
1.01
1.14
2.08
8.85
8.84
8.80
8.78
8.62
8.62
8.29
8.29
8.27
8.26
7.94
7.80
7.66
7.31
7.30
7.28
7.26
f1 (ppm)

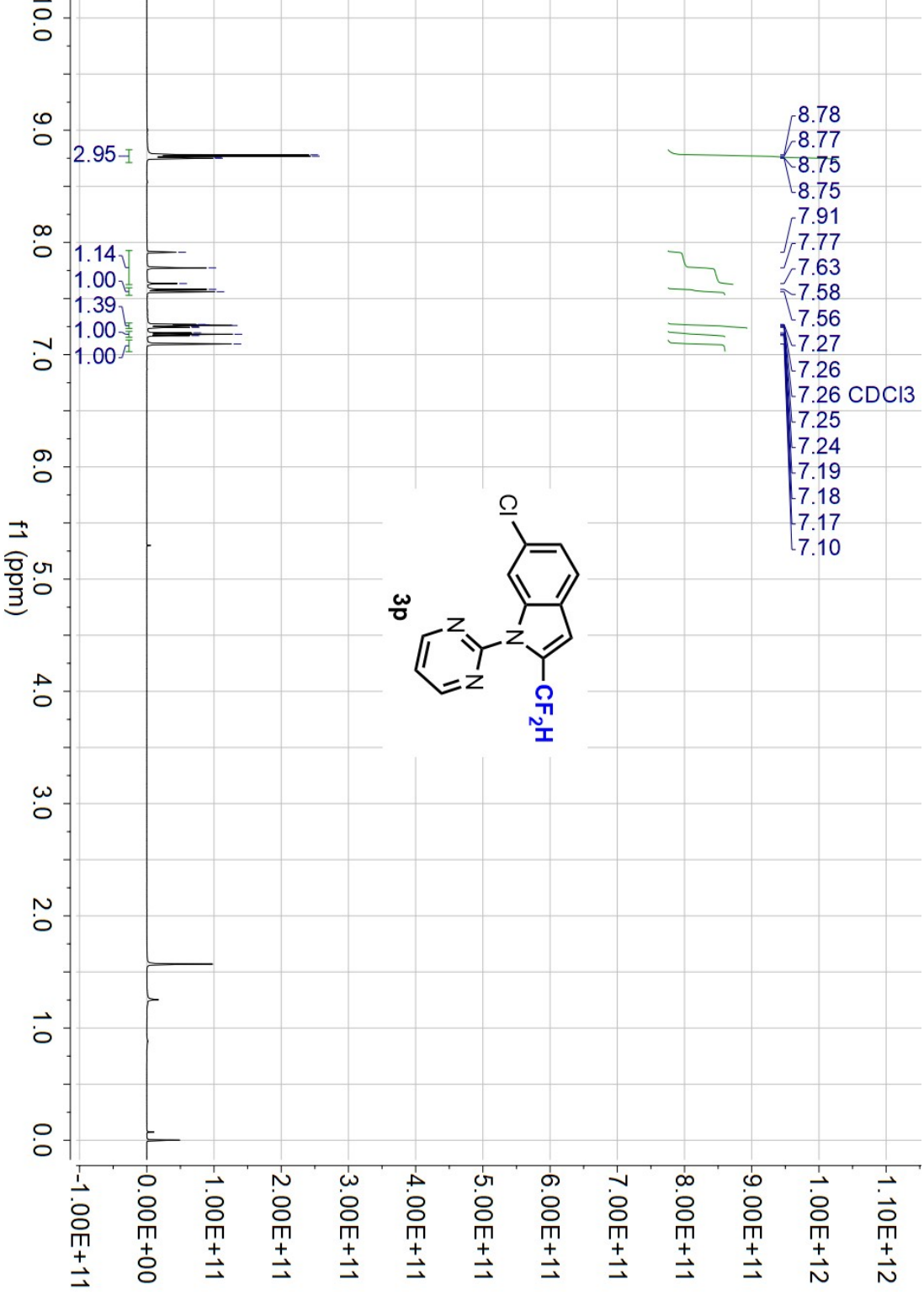

-114.79
1.00E+12
9.00E+11
8.00E+11
7.00E+11
6.00E+11
5.00E+11
4.00E+11
3.00E+11
2.00E+11
1.00E+11
0.00E+00
-1.00E+11
O2N
CF2H
N
N
N
3n
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

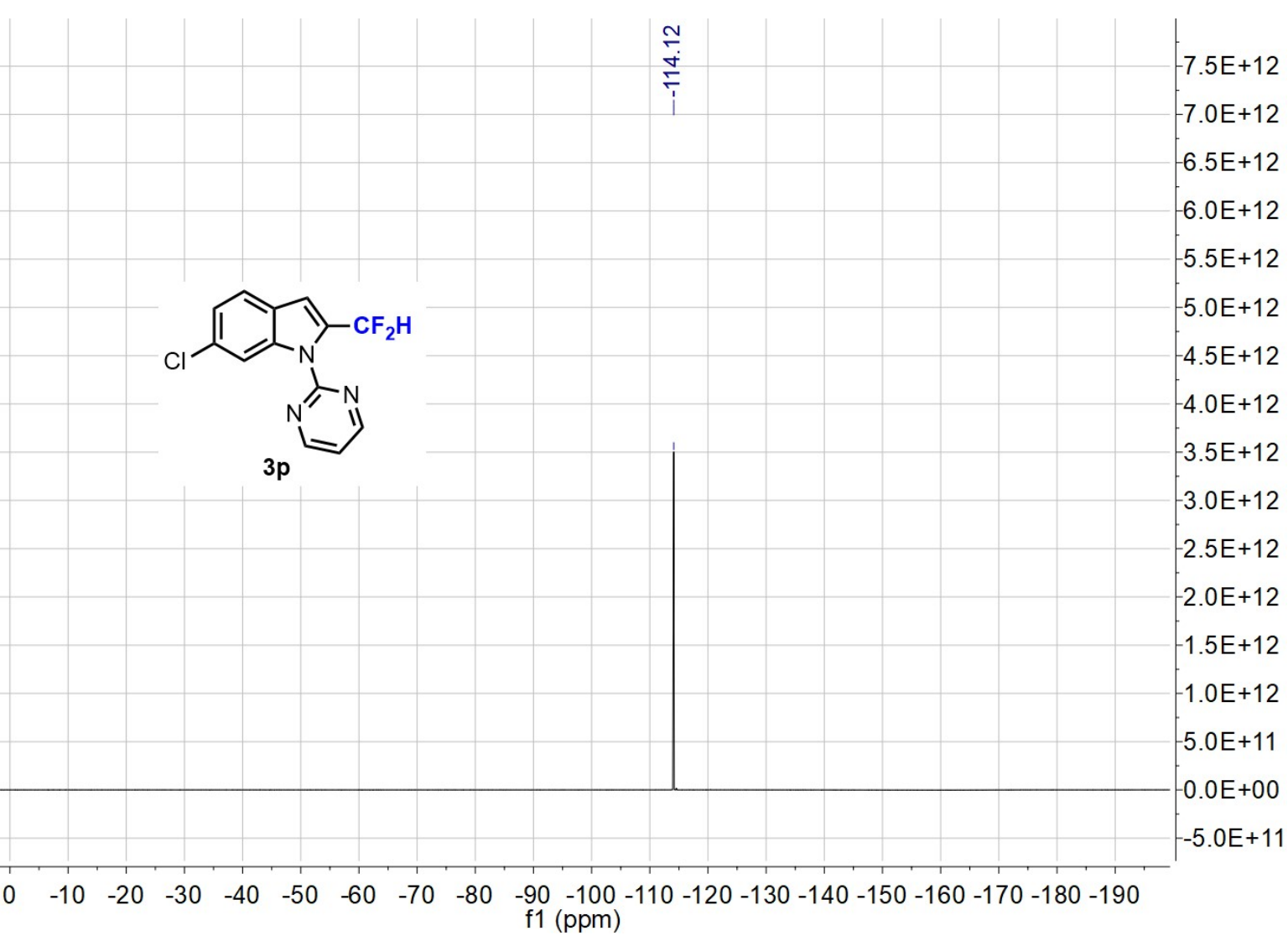

3n
O2N
N
N
N
CF2H
158.55
157.15
143.73
140.25
136.43
127.80
120.41
118.41
118.30
116.32
112.50
110.13
109.97
109.91
109.84
107.77
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
f1 (ppm)

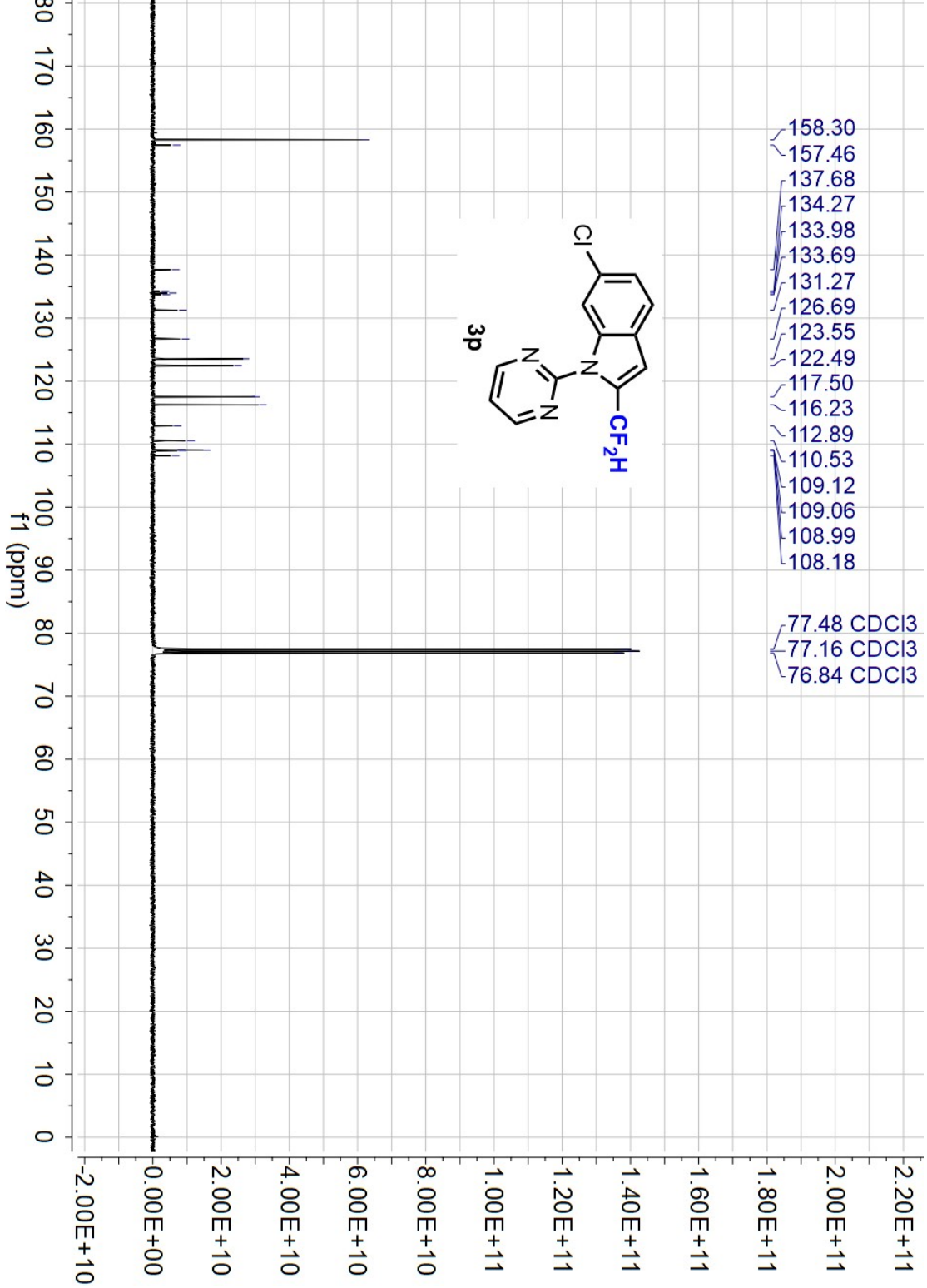

3o
CF2H
N
N
N
2.08
1.01
1.10
1.00
3.10
3.07
8.76
8.75
8.48
7.92
7.78
7.64
7.56
7.54
7.26 CDCl3
7.14
7.13
7.12
7.11
7.09
2.53
f1 (ppm)

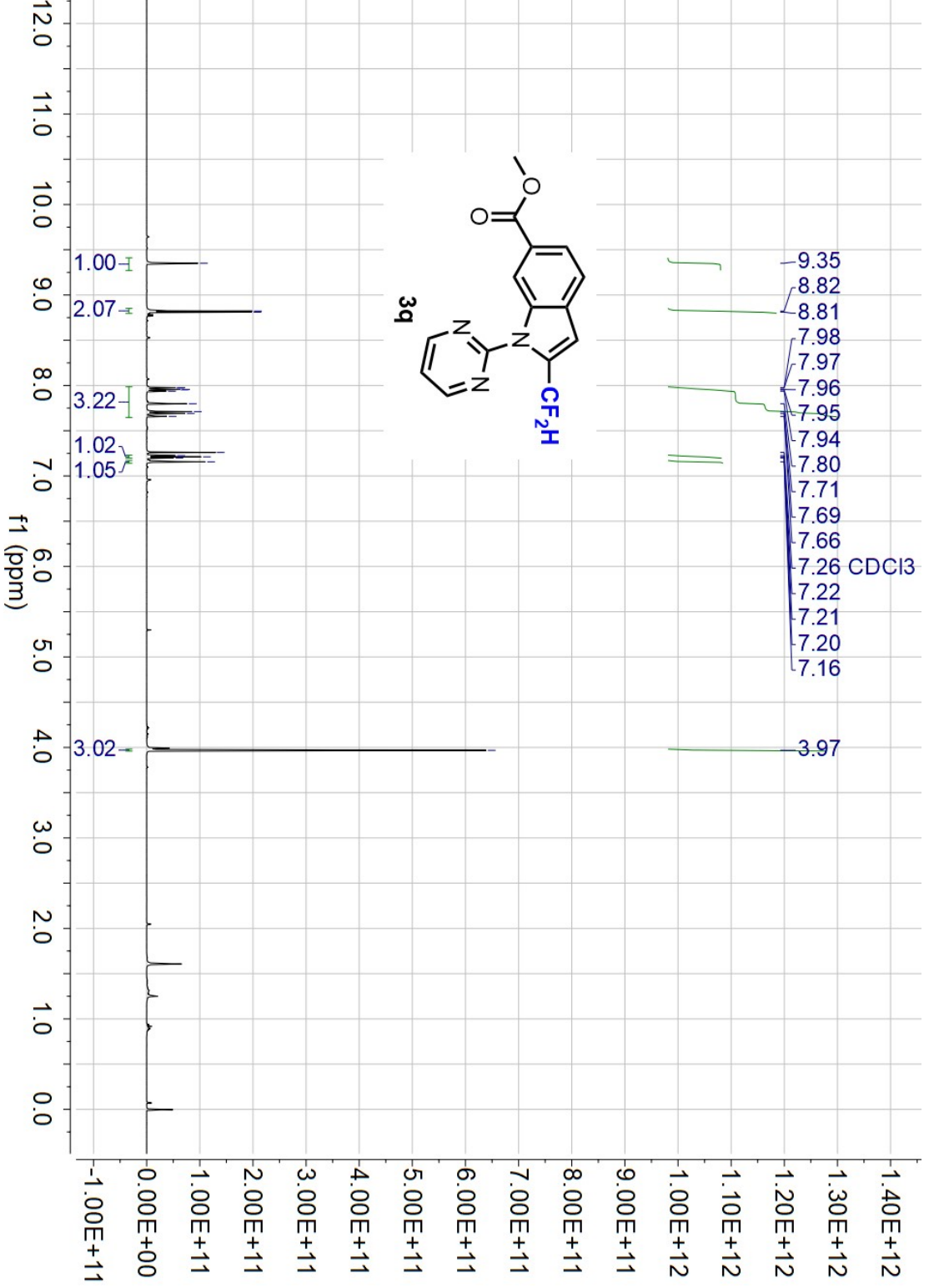

-113.76
6.0E+12
5.5E+12
5.0E+12
4.5E+12
4.0E+12
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
5.0E+11
0.0E+00
-5.0E+11
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)
CF2H
N
N
N
3o

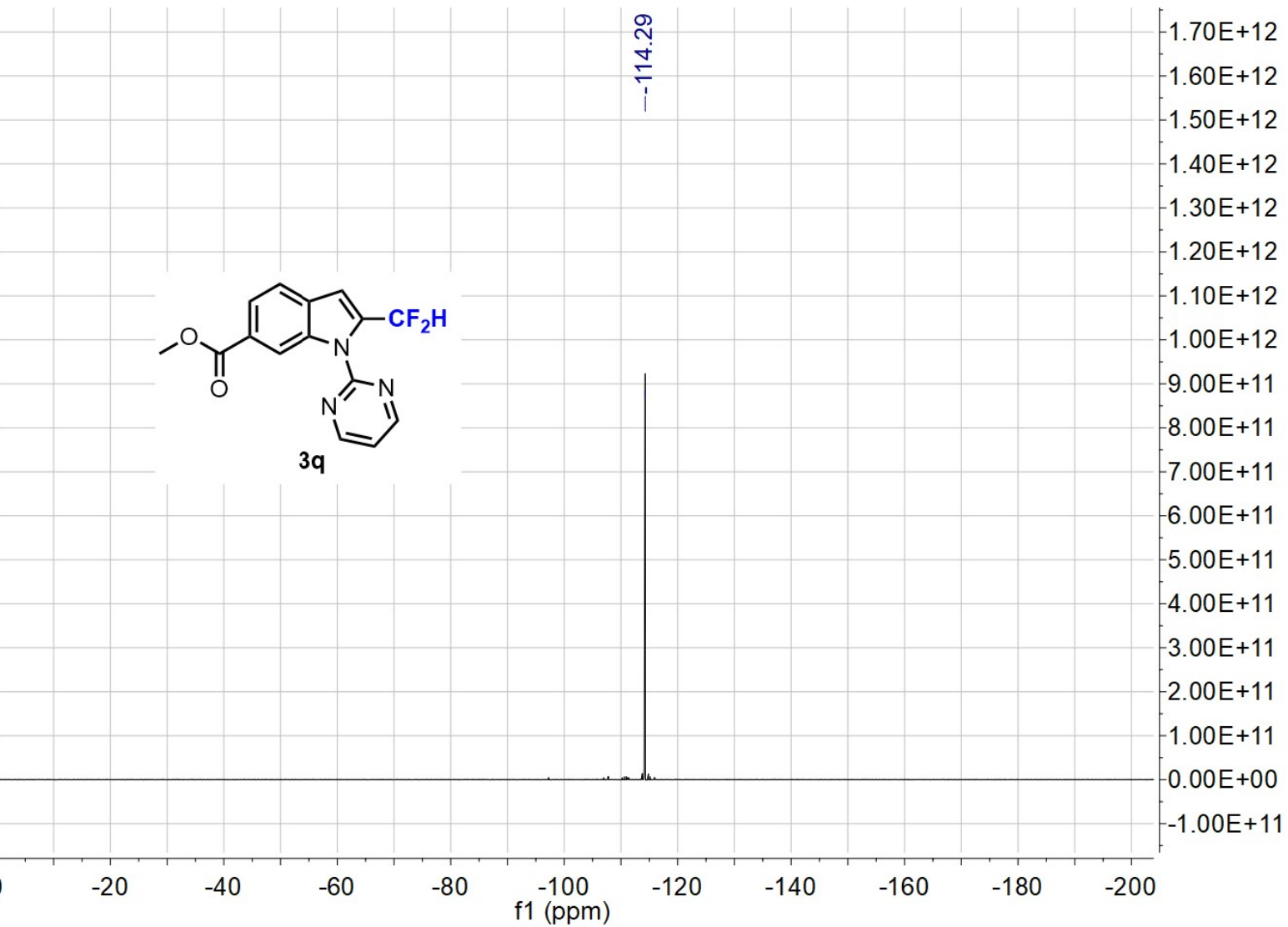

158.19
157.78
137.83
135.48
132.97
132.68
132.39
125.98
124.48
121.36
117.04
115.72
113.22
110.87
109.30
109.23
109.16
108.52
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
22.35
3o
CF2H
f1 (ppm)

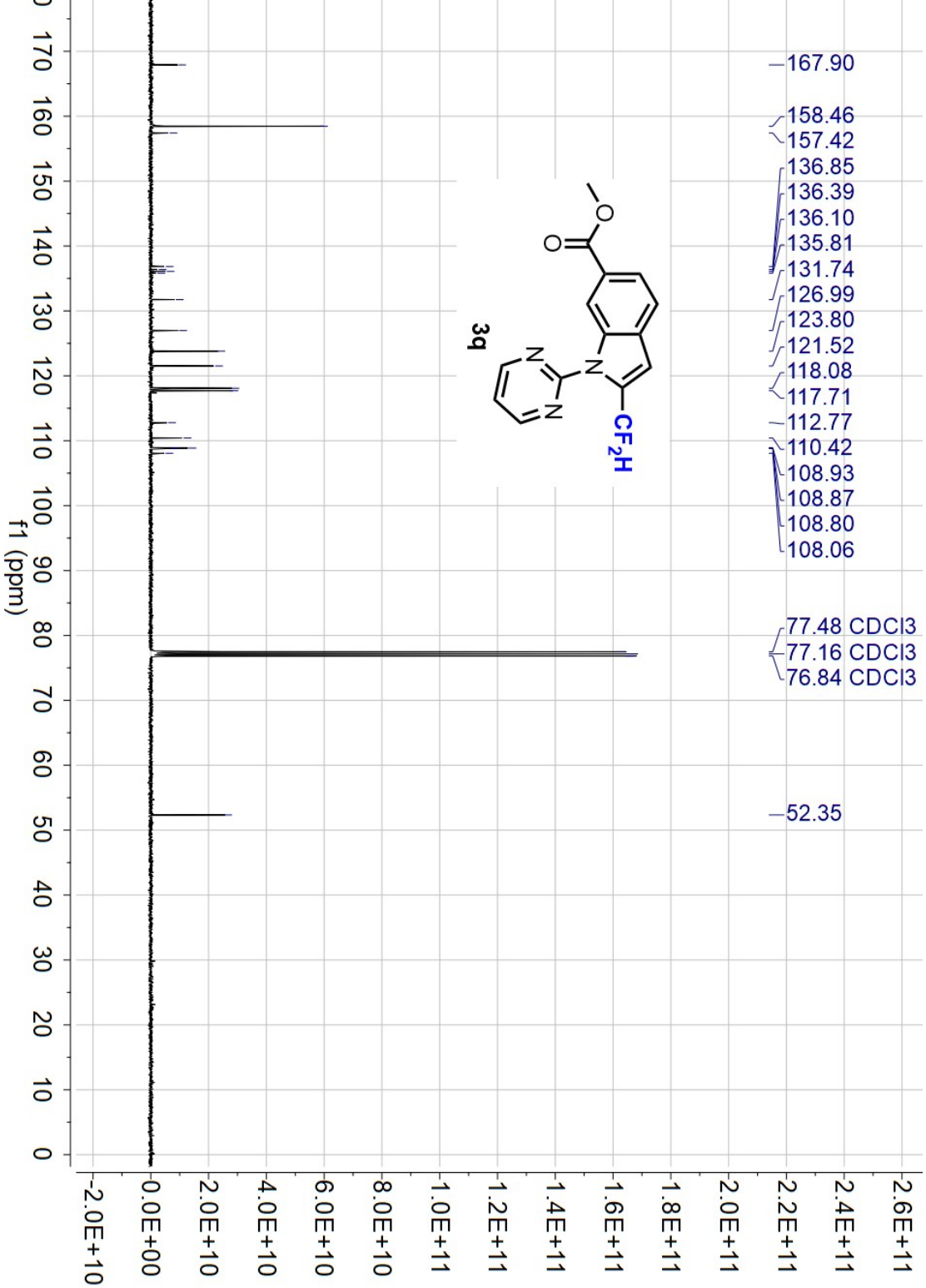

8.78
8.77
8.75
8.75
7.91
7.77
7.63
7.58
7.56
7.27
7.26
7.26 CDCl3
7.25
7.24
7.19
7.18
7.17
7.10
2.95
1.14
1.00
1.39
1.00
1.00
Cl
N
N
N
CF2H
3p
f1 (ppm)

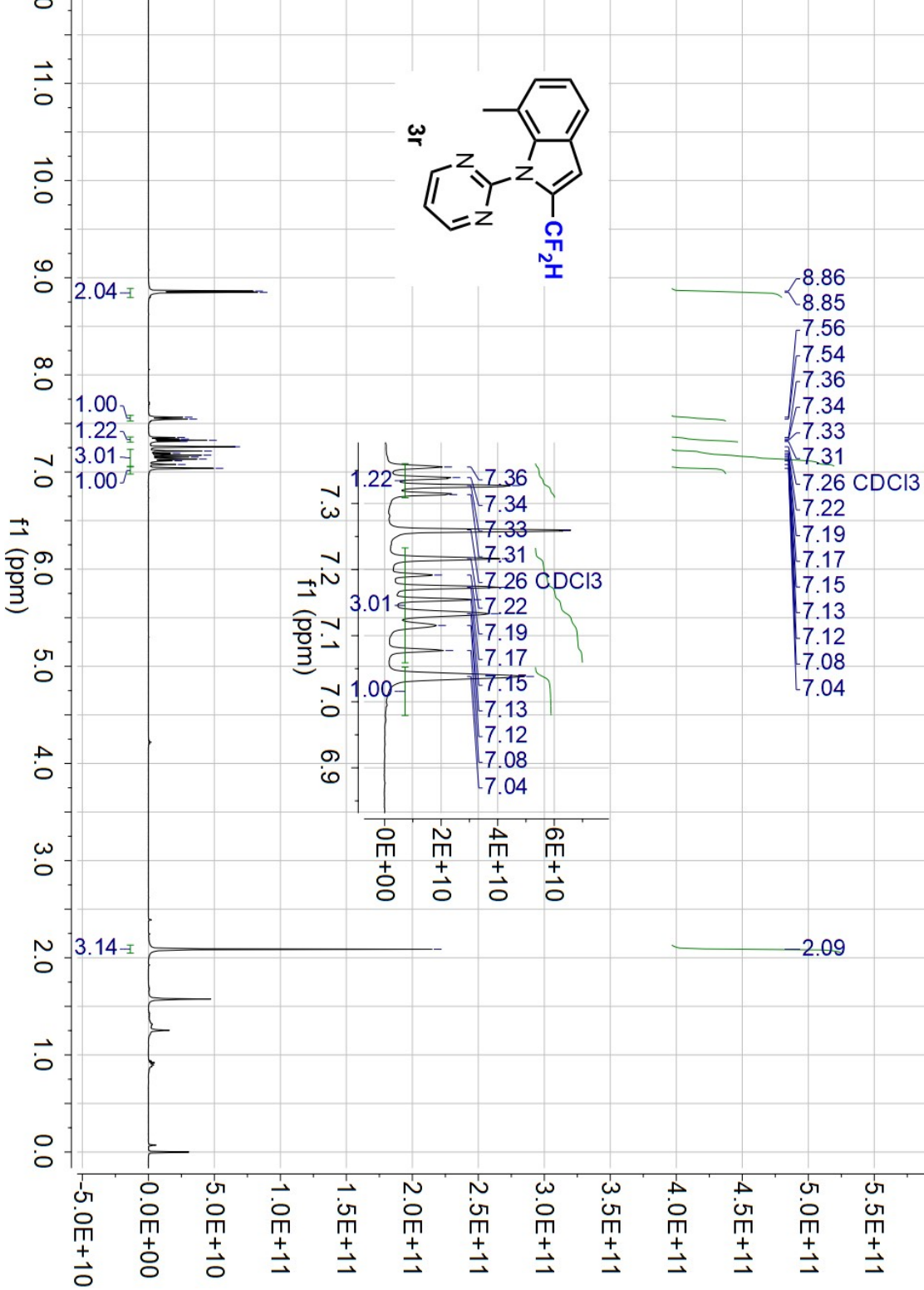

-114.12
7.5E+12
7.0E+12
6.5E+12
6.0E+12
5.5E+12
5.0E+12
4.5E+12
4.0E+12
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
5.0E+11
0.0E+00
-5.0E+11
Cl
N
N
N
CF2H
3p
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

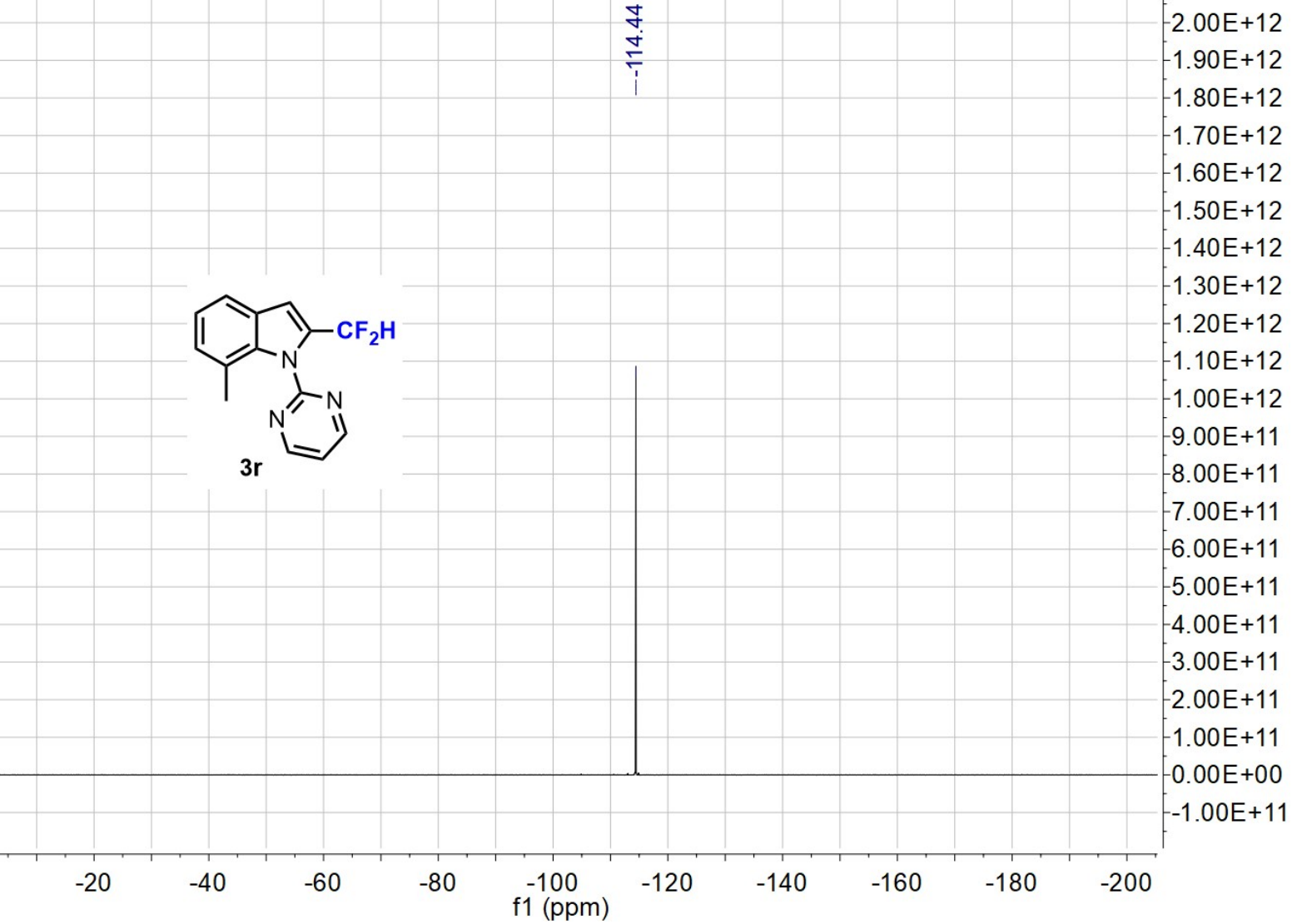

158.30
157.46
137.68
134.27
133.98
133.69
131.27
126.69
123.55
122.49
117.50
116.23
112.89
110.53
109.12
109.06
108.99
108.18
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
3p
Cl
N
N
N
CF2H
f1 (ppm)

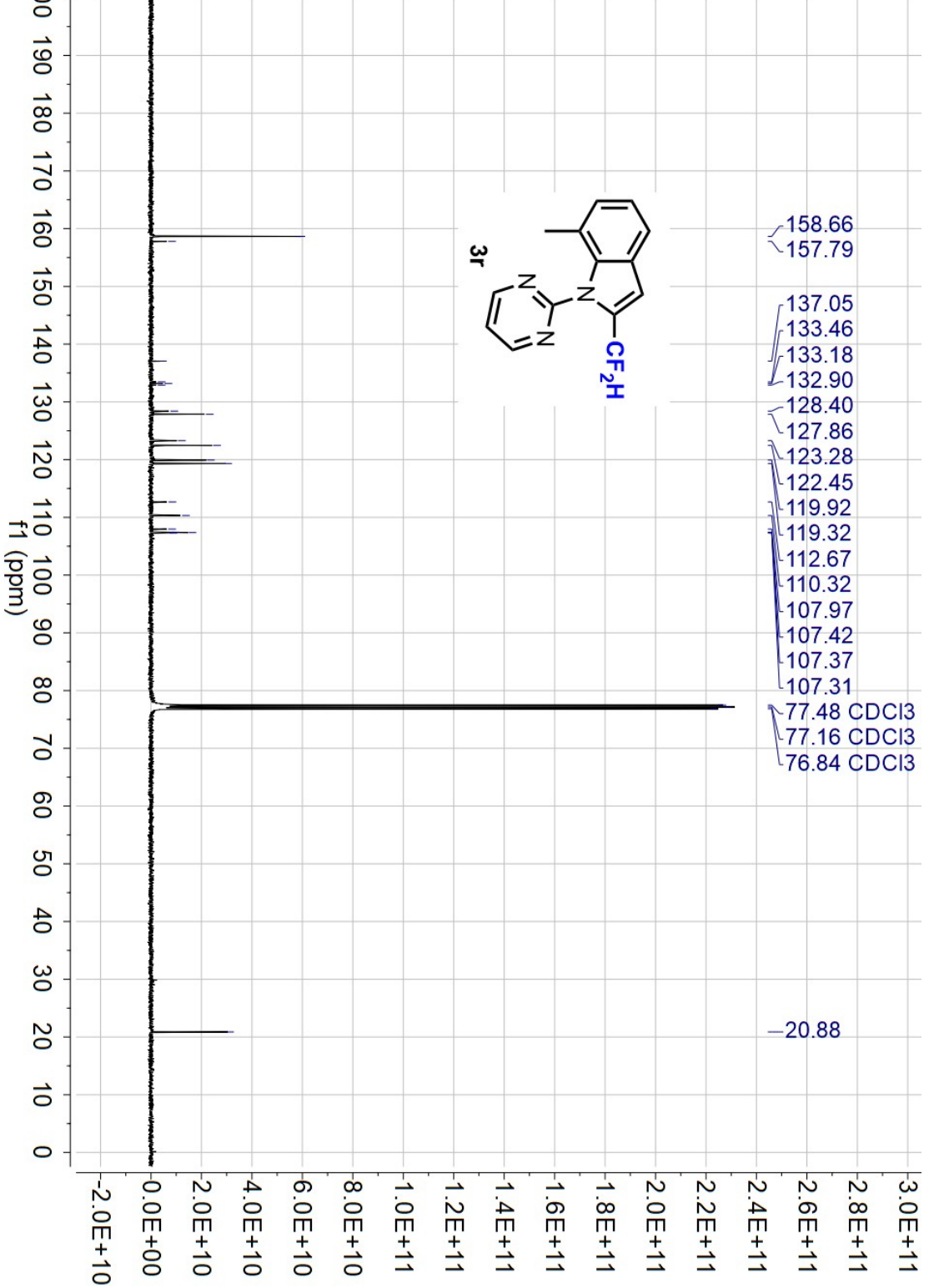

3q
CF2H
1.00
2.07
3.22
1.02
1.05
3.02
9.35
8.82
8.81
7.98
7.97
7.96
7.95
7.94
7.80
7.71
7.69
7.66
7.26 CDCl3
7.22
7.21
7.20
7.16
3.97
f1 (ppm)

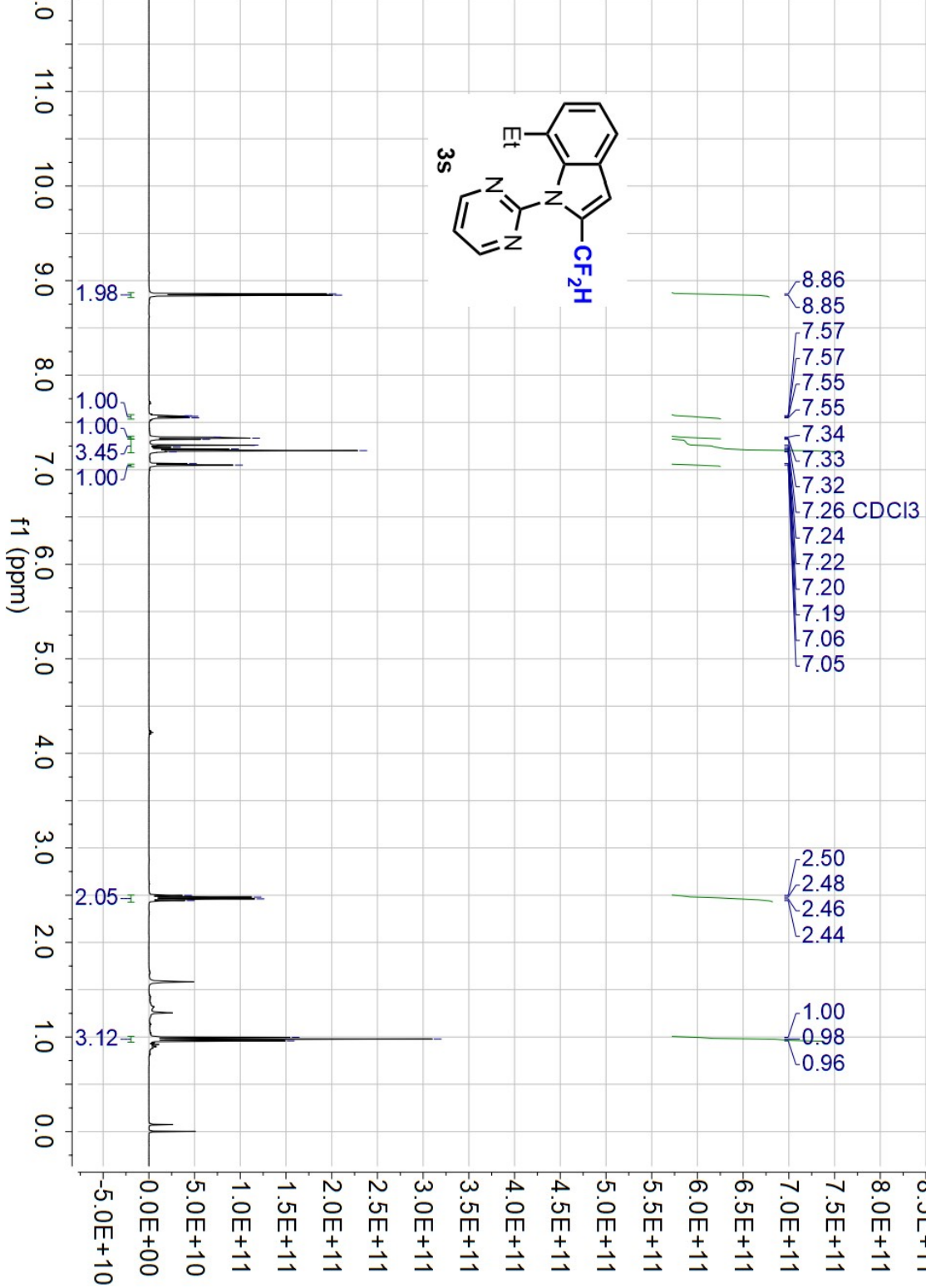

-114.29
CF2H
O
O
N
N
N
3q
1.70E+12
1.60E+12
1.50E+12
1.40E+12
1.30E+12
1.20E+12
1.10E+12
1.00E+12
9.00E+11
8.00E+11
7.00E+11
6.00E+11
5.00E+11
4.00E+11
3.00E+11
2.00E+11
1.00E+11
0.00E+00
-1.00E+11
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

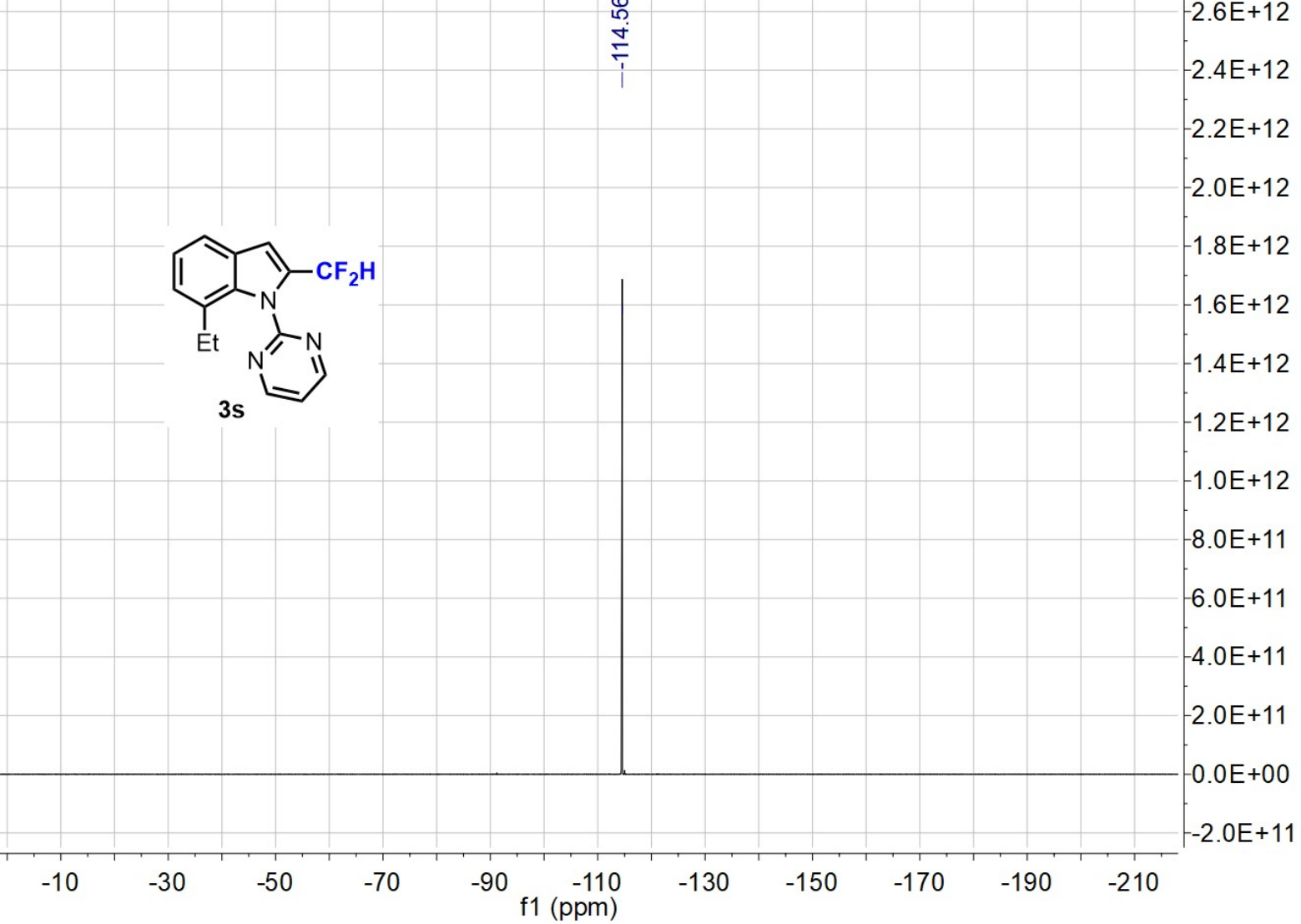

167.90
158.46
157.42
136.85
136.39
136.10
135.81
131.74
126.99
123.80
121.52
118.08
117.71
112.77
110.42
108.93
108.87
108.80
108.06
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
52.35
3q
CF2H
f1 (ppm)

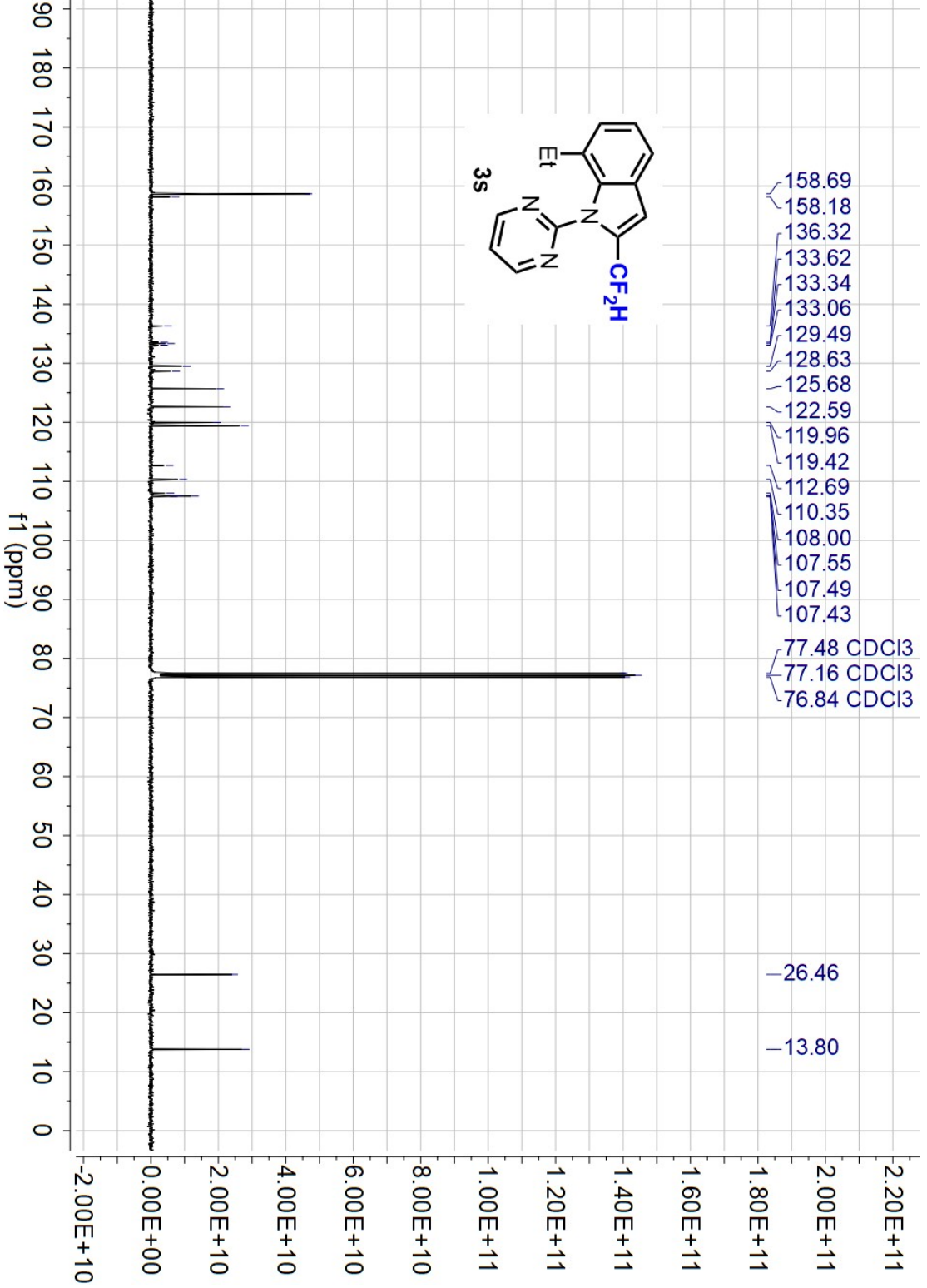

3r
CF2H
2.04
1.00
1.22
3.01
1.00
3.14
8.86
8.85
7.56
7.54
7.36
7.34
7.33
7.31
7.26 CDCl3
7.22
7.19
7.17
7.15
7.13
7.12
7.08
7.04
2.09
f1 (ppm)

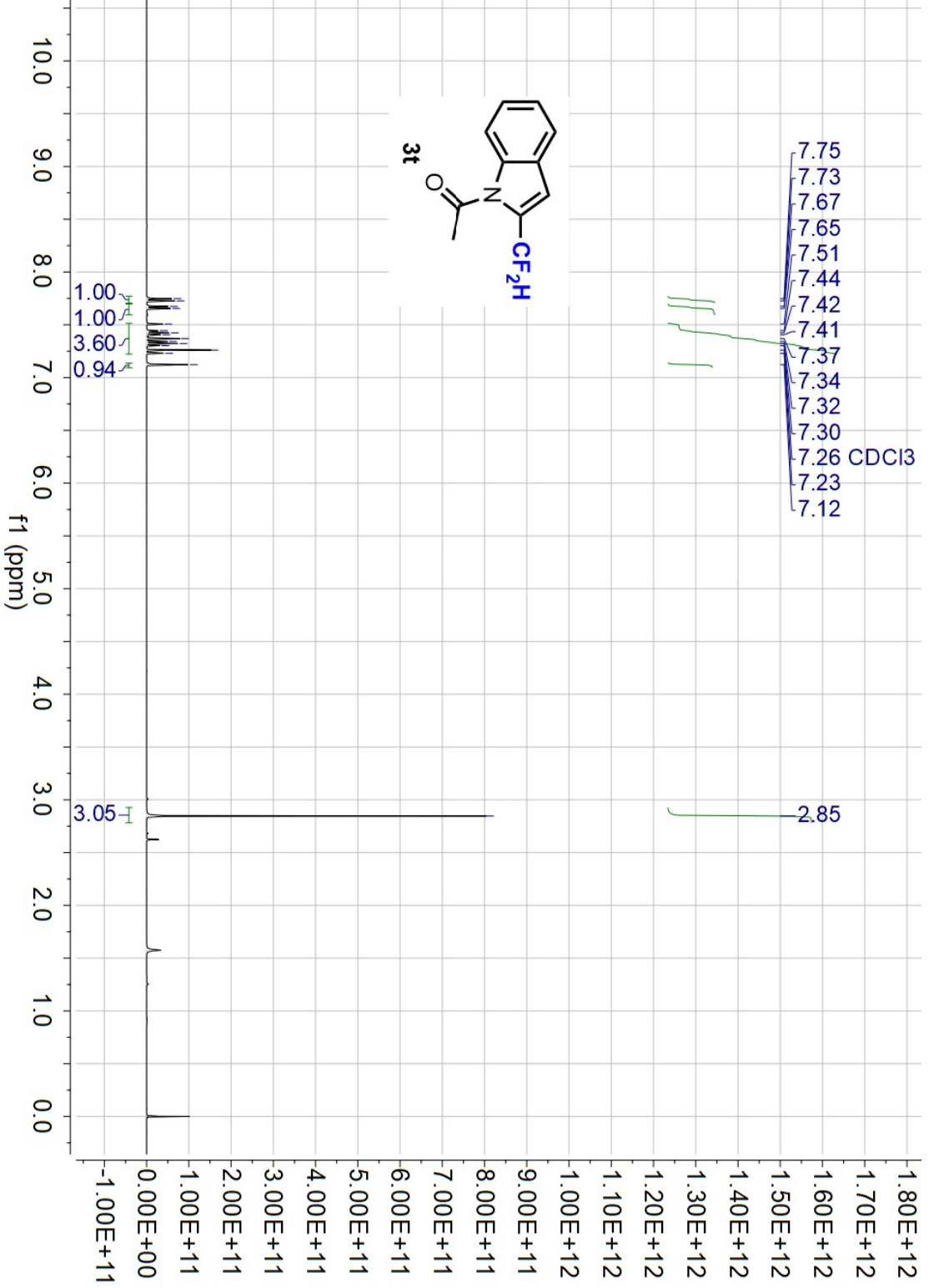

-114.44
CF2H
N
N
N
3r
2.00E+12
1.90E+12
1.80E+12
1.70E+12
1.60E+12
1.50E+12
1.40E+12
1.30E+12
1.20E+12
1.10E+12
1.00E+12
9.00E+11
8.00E+11
7.00E+11
6.00E+11
5.00E+11
4.00E+11
3.00E+11
2.00E+11
1.00E+11
0.00E+00
-1.00E+11
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

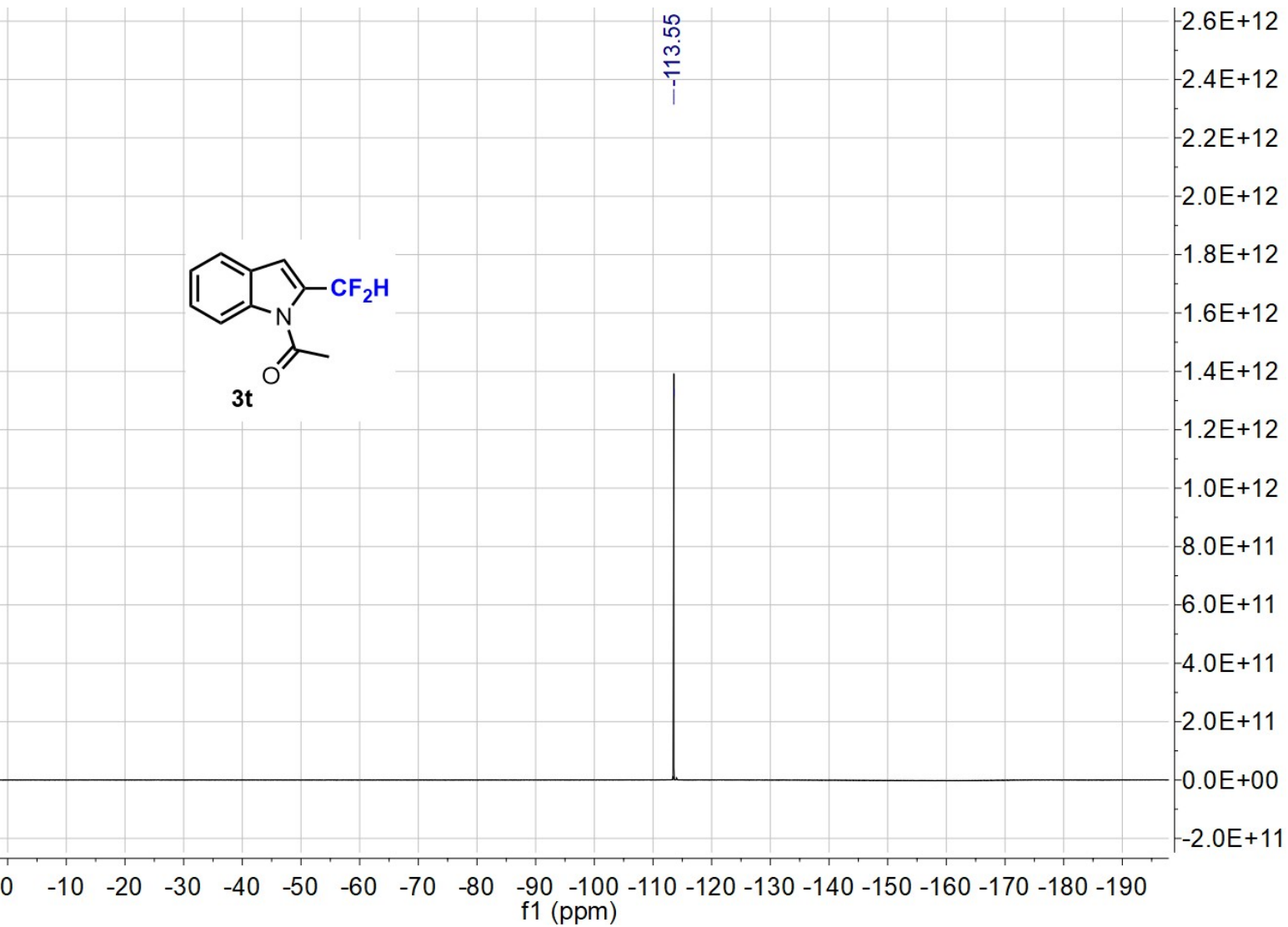

3r
CF2H
158.66
157.79
137.05
133.46
133.18
132.90
128.40
127.86
123.28
122.45
119.92
119.32
112.67
110.32
107.97
107.42
107.37
107.31
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
20.88
f1 (ppm)

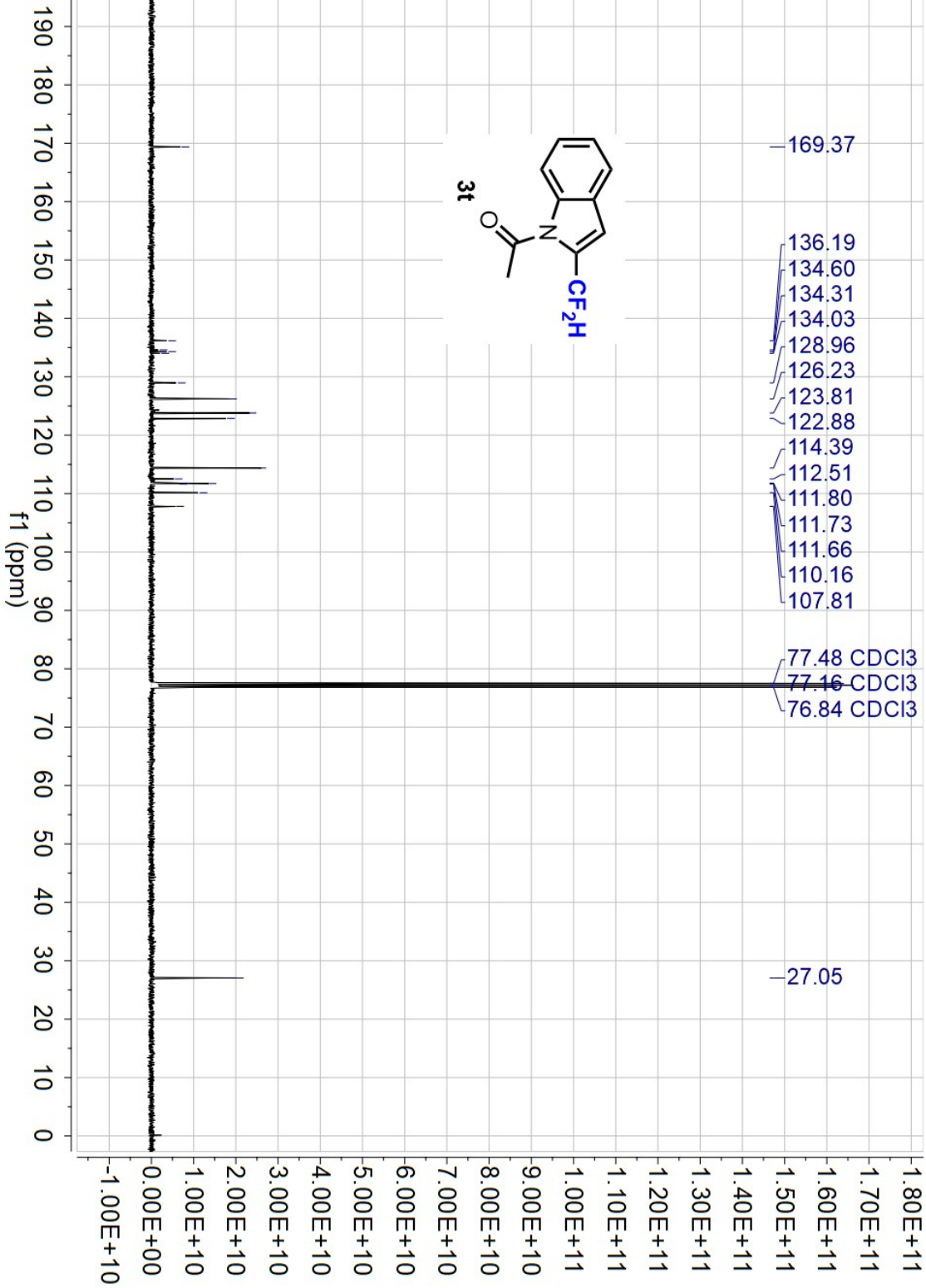

3s
Et
N
N
N
CF2H
1.98
1.00
1.00
3.45
1.00
2.05
3.12
8.86
8.85
7.57
7.57
7.55
7.55
7.34
7.33
7.32
7.26 CDCl3
7.24
7.22
7.20
7.19
7.06
7.05
2.50
2.48
2.46
2.44
1.00
0.98
0.96
f1 (ppm)

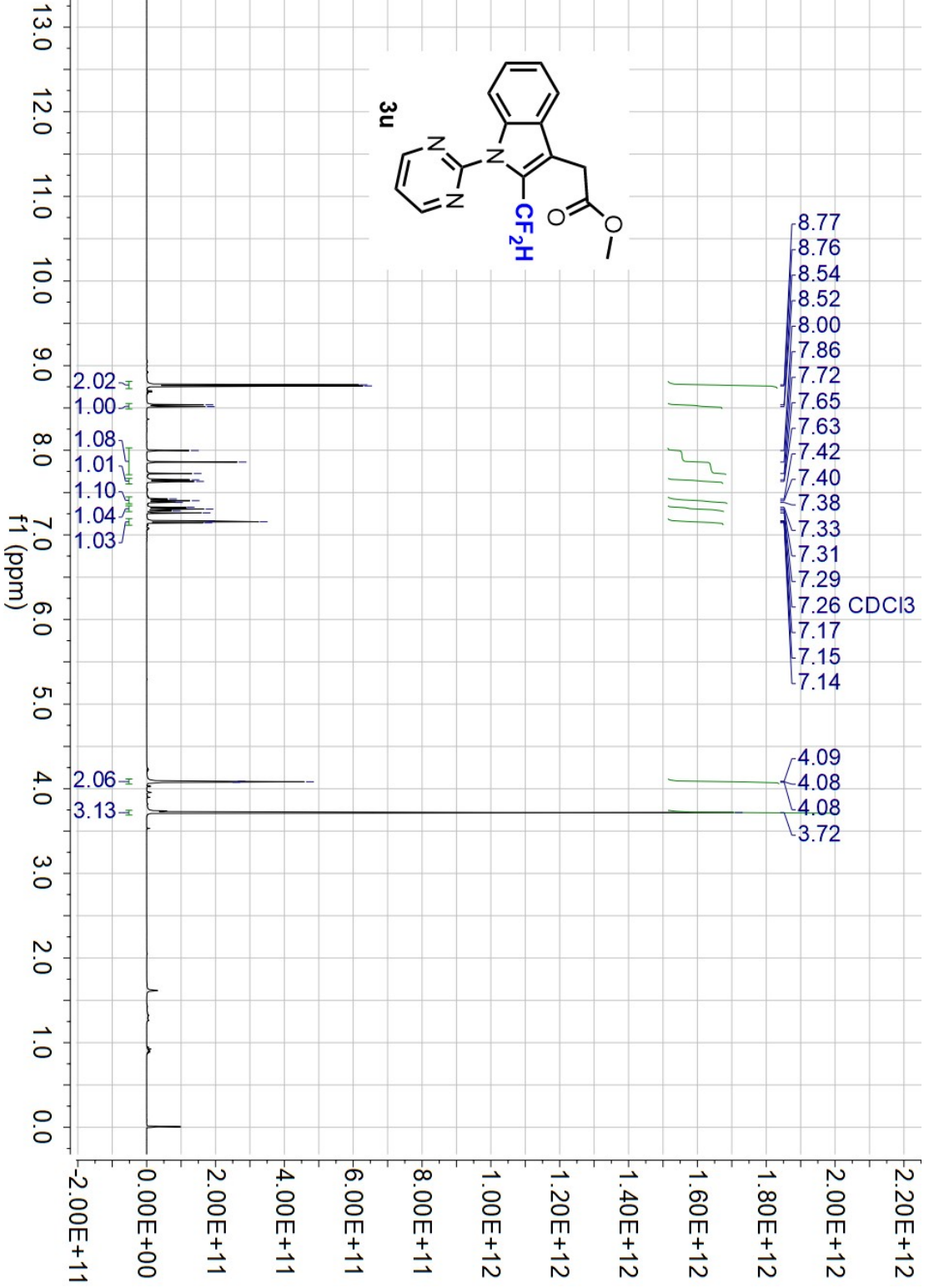

-114.56
2.6E+12
2.4E+12
2.2E+12
2.0E+12
1.8E+12
1.6E+12
1.4E+12
1.2E+12
1.0E+12
8.0E+11
6.0E+11
4.0E+11
2.0E+11
0.0E+00
-2.0E+11
CF2H
N
Et
N
N
3s
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

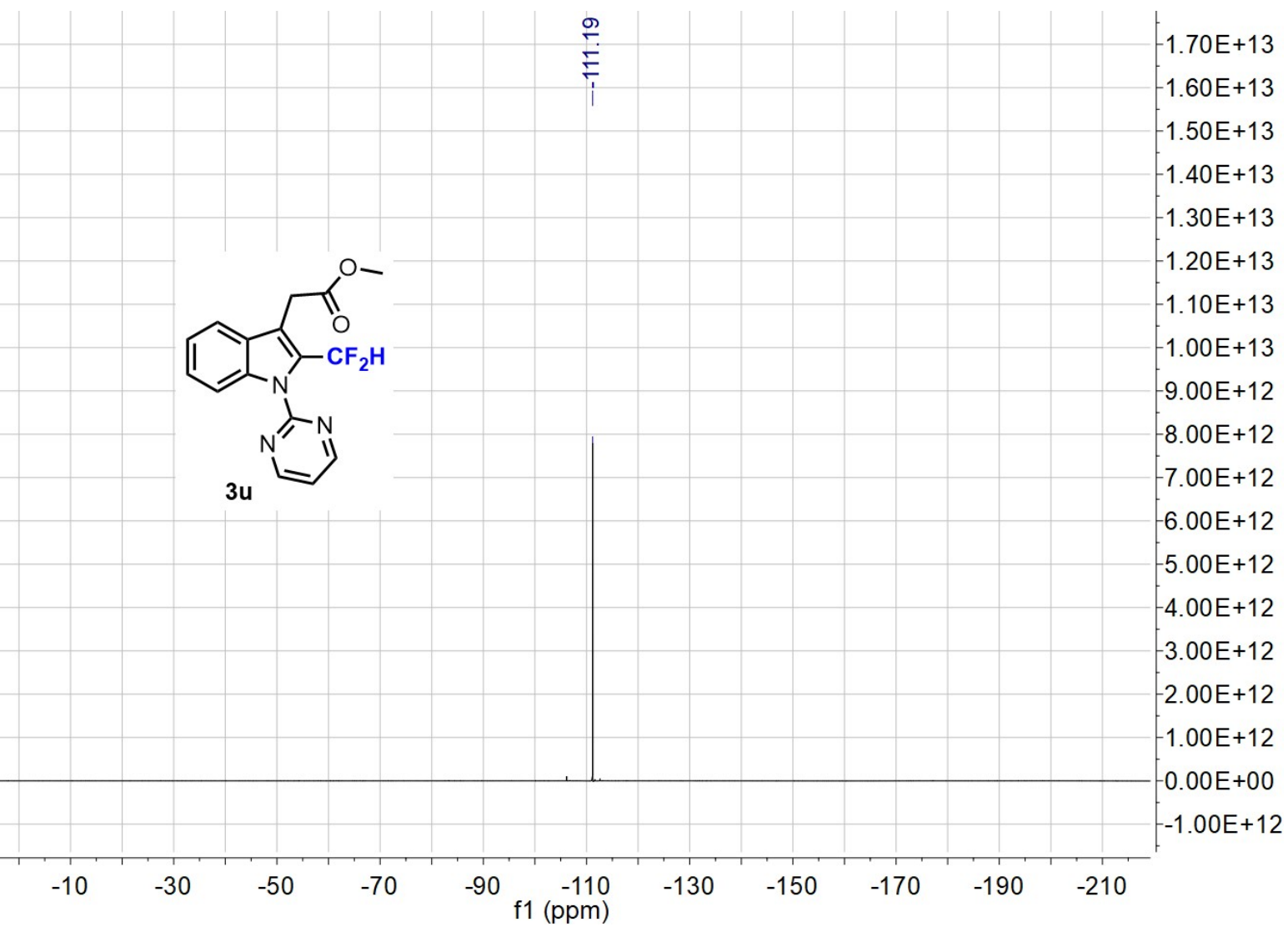

Et
3s
CF2H
158.69
158.18
136.32
133.62
133.34
133.06
129.49
128.63
125.68
122.59
119.96
119.42
112.69
110.35
108.00
107.55
107.49
107.43
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
26.46
13.80
f1 (ppm)

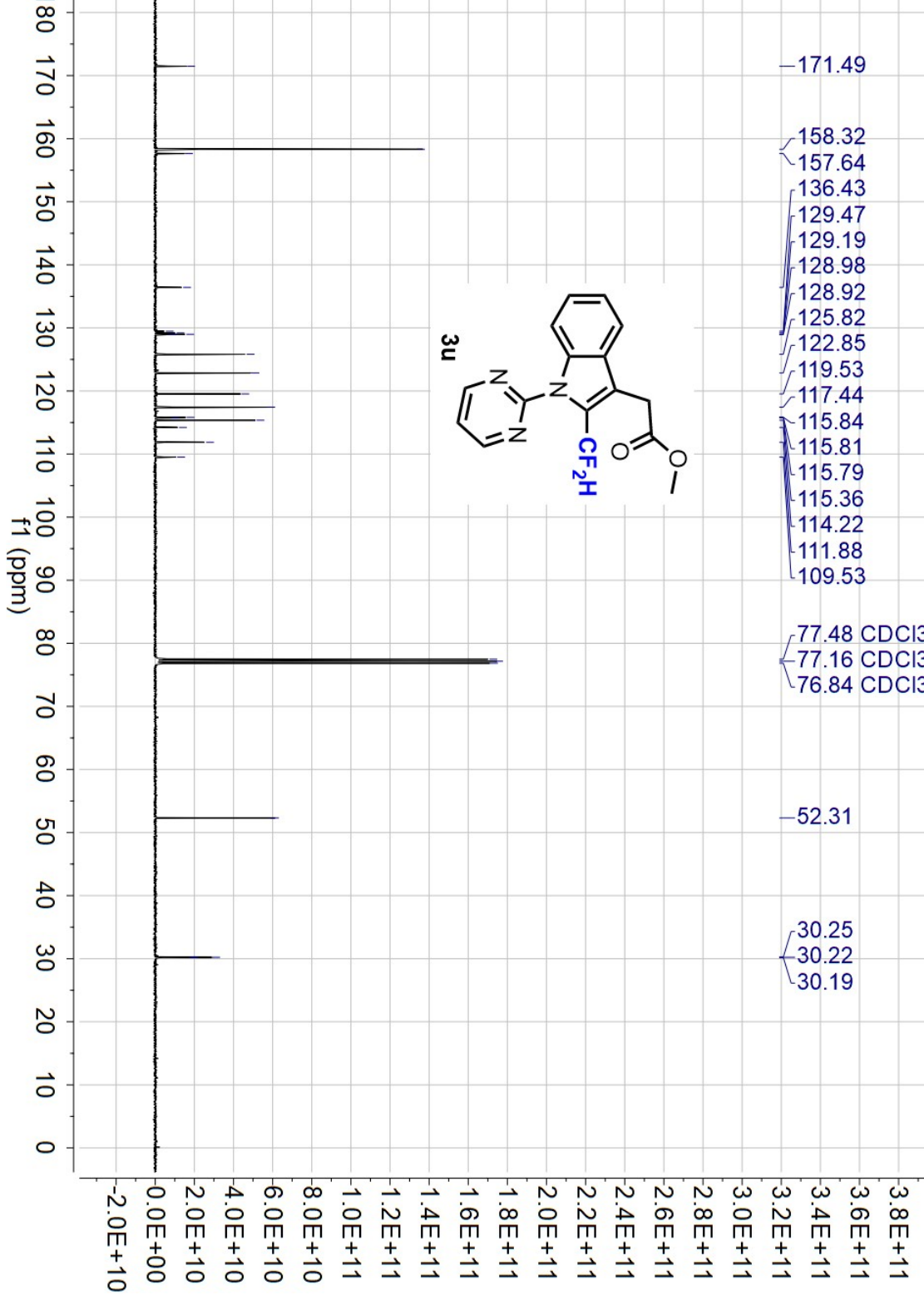

3t
CF2H
7.75
7.73
7.67
7.65
7.51
7.44
7.42
7.41
7.37
7.34
7.32
7.30
7.26 CDCl3
7.23
7.12
1.00
1.00
3.60
0.94
3.05
2.85
f1 (ppm)

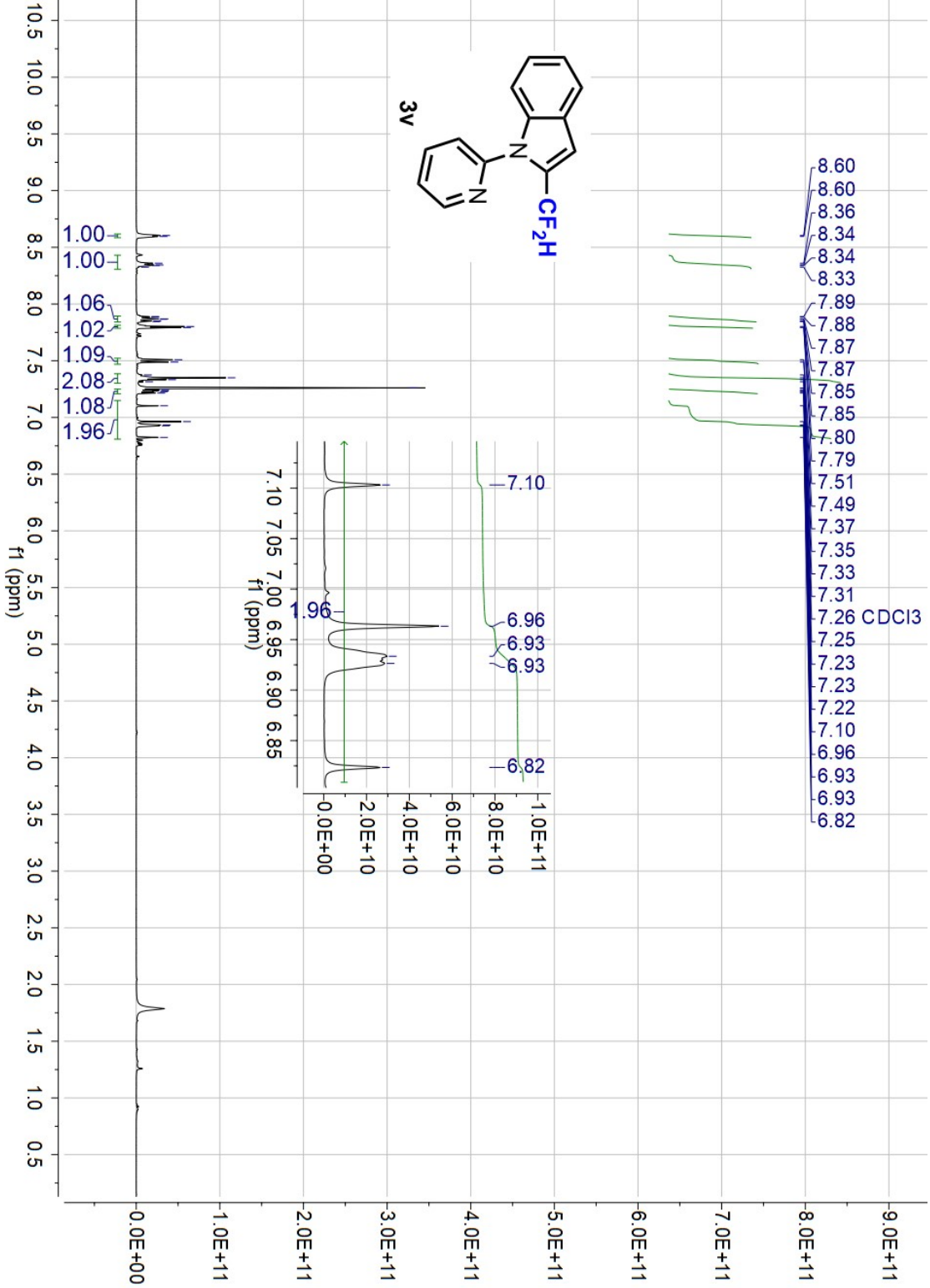

-113.55
CF2H
N
O
3t
2.6E+12
2.4E+12
2.2E+12
2.0E+12
1.8E+12
1.6E+12
1.4E+12
1.2E+12
1.0E+12
8.0E+11
6.0E+11
4.0E+11
2.0E+11
0.0E+00
-2.0E+11
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

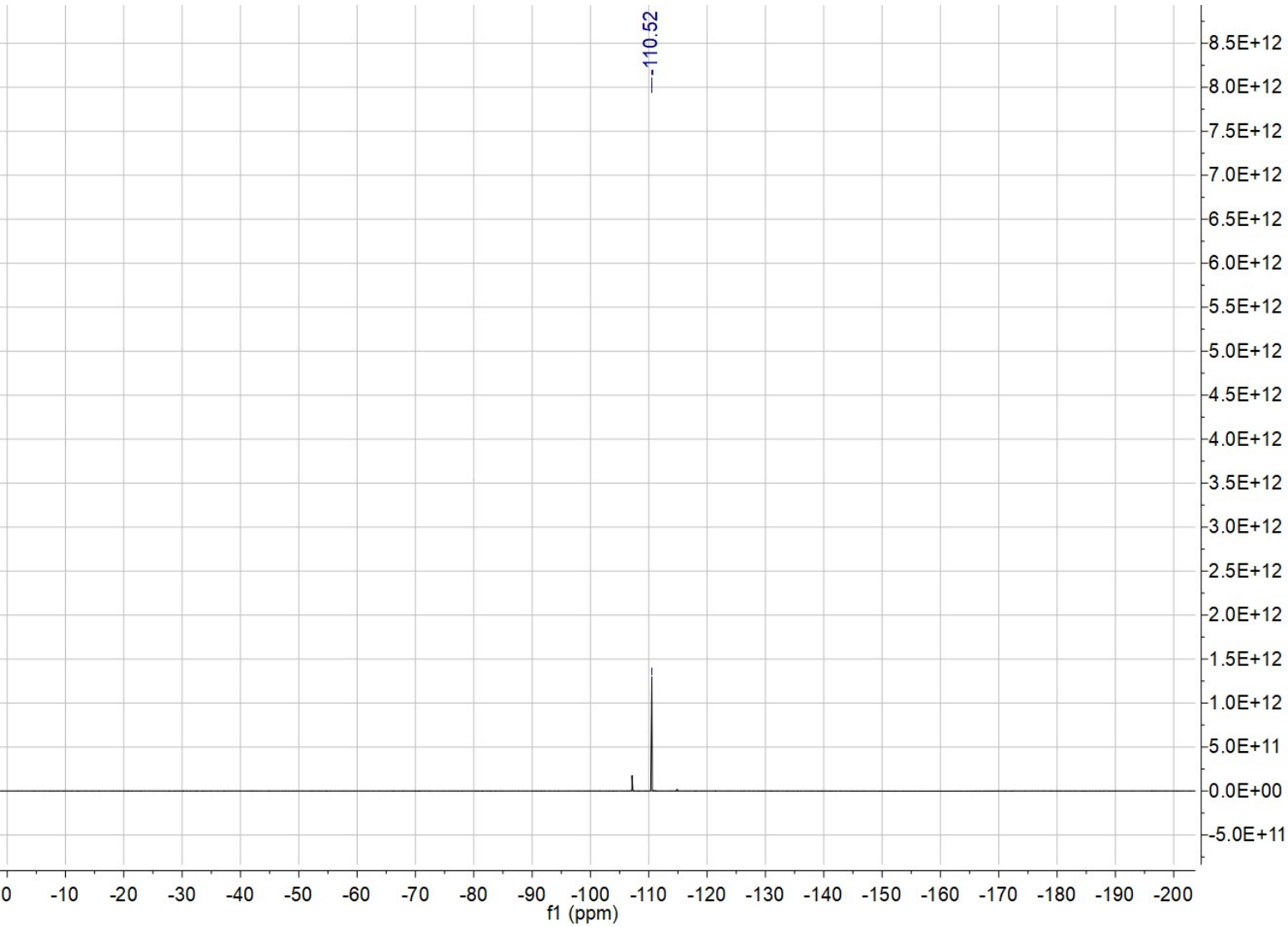

3t
CF2H
169.37
136.19
134.60
134.31
134.03
128.96
126.23
123.81
122.88
114.39
112.51
111.80
111.73
111.66
110.16
107.81
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
27.05
f1 (ppm)

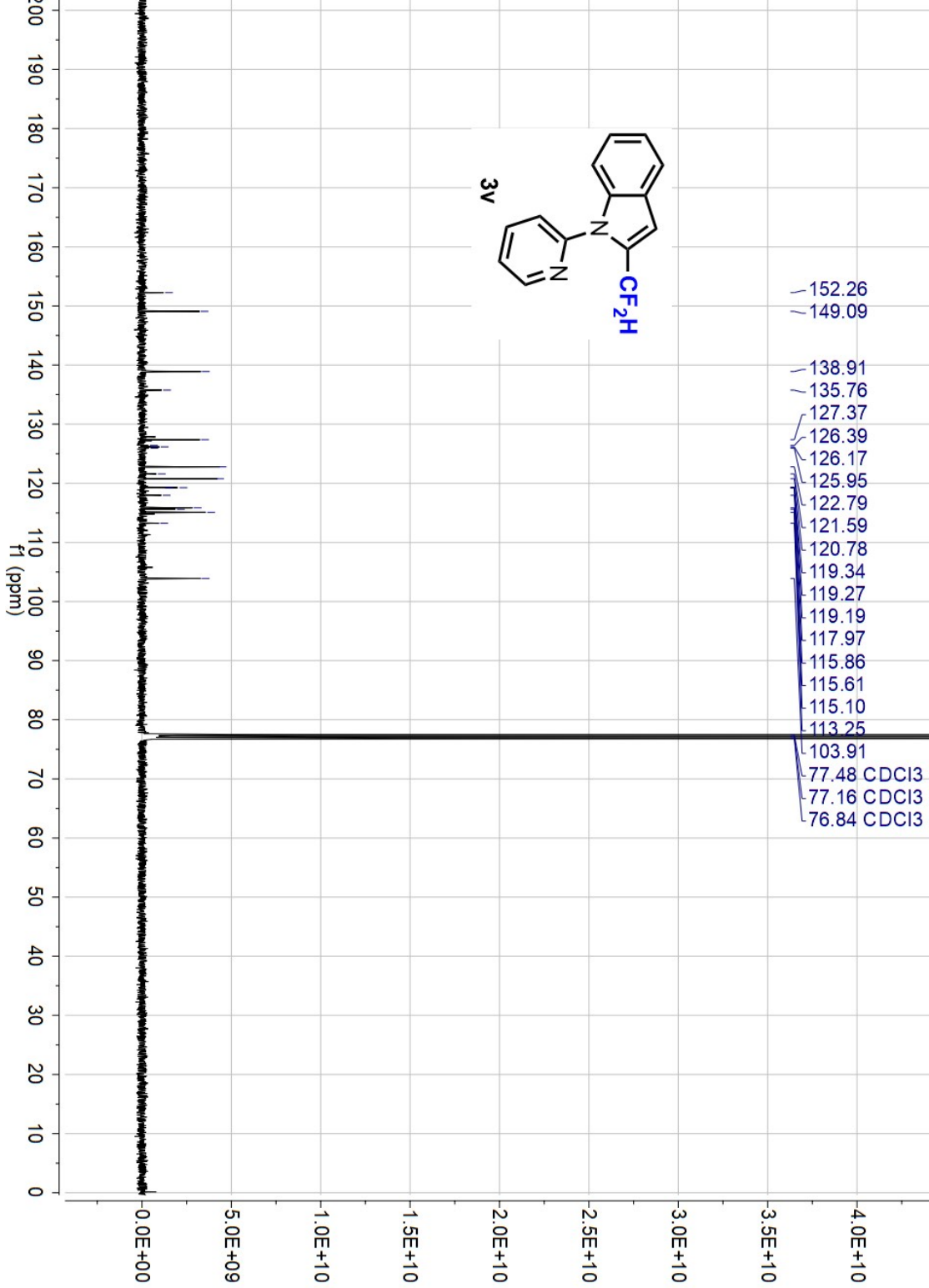

3u
CF2H
8.77
8.76
8.54
8.52
8.00
7.86
7.72
7.65
7.63
7.42
7.40
7.38
7.33
7.31
7.29
7.26 CDCl3
7.17
7.15
7.14
4.09
4.08
4.08
3.72
2.02
1.00
1.08
1.01
1.10
1.04
1.03
2.06
3.13
f1 (ppm)

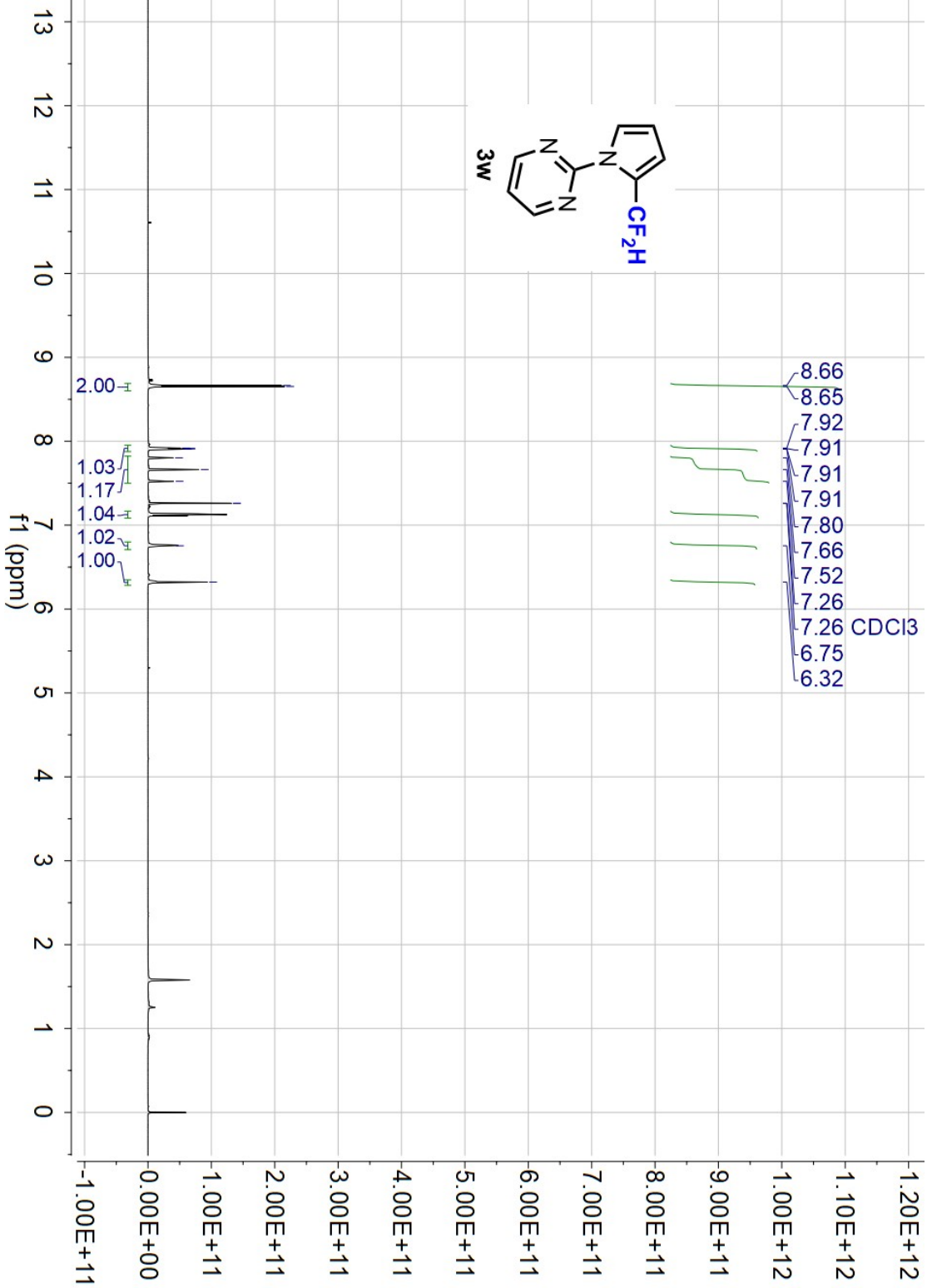

-111.19
1.70E+13
1.60E+13
1.50E+13
1.40E+13
1.30E+13
1.20E+13
1.10E+13
1.00E+13
9.00E+12
8.00E+12
7.00E+12
6.00E+12
5.00E+12
4.00E+12
3.00E+12
2.00E+12
1.00E+12
0.00E+00
-1.00E+12
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)
O
O
CF2H
N
N
N
3u

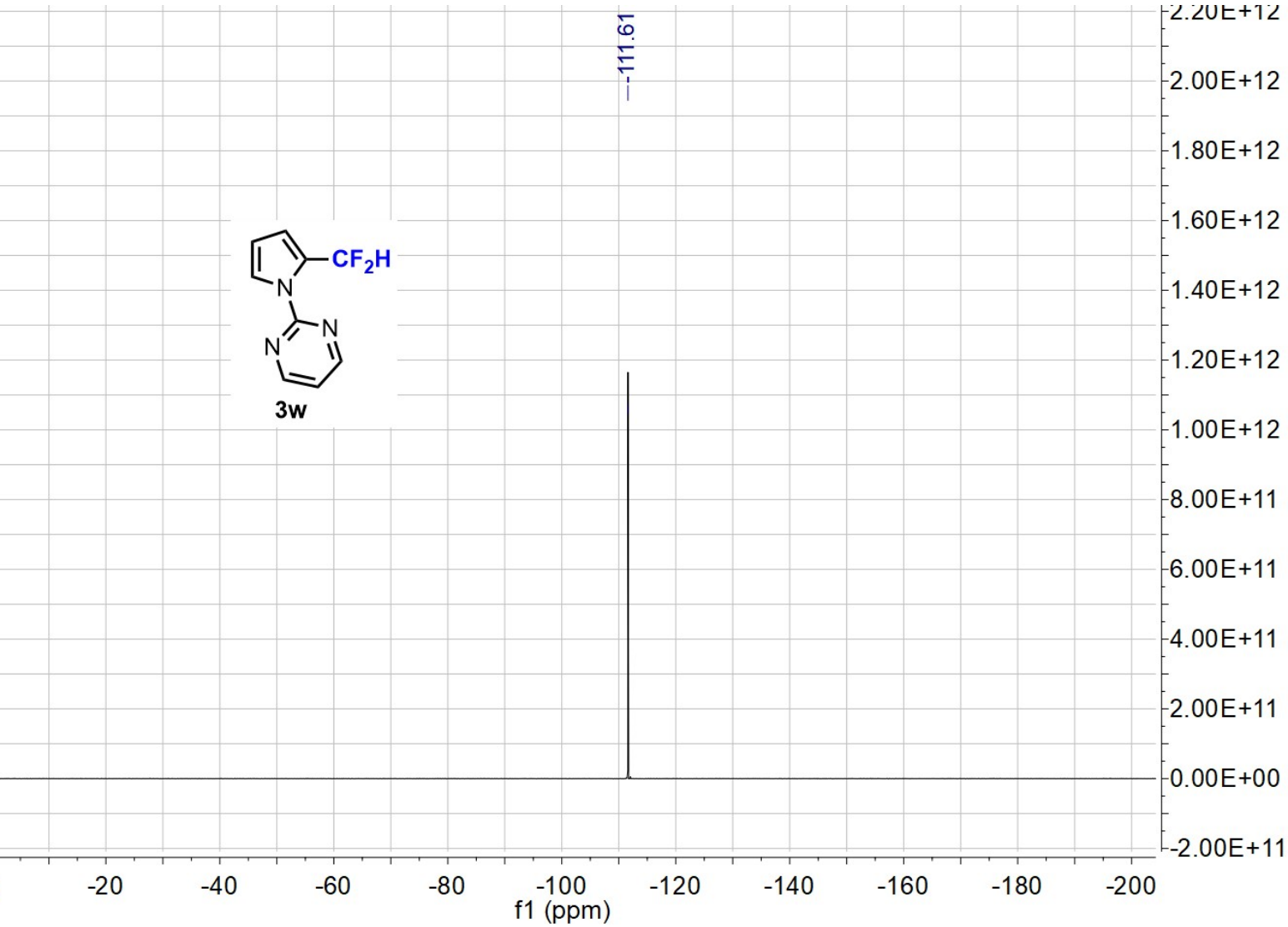

3u
CF2H
171.49
158.32
157.64
136.43
129.47
129.19
128.98
128.92
125.82
122.85
119.53
117.44
115.84
115.81
115.79
115.36
114.22
111.88
109.53
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
52.31
30.25
30.22
30.19
f1 (ppm)

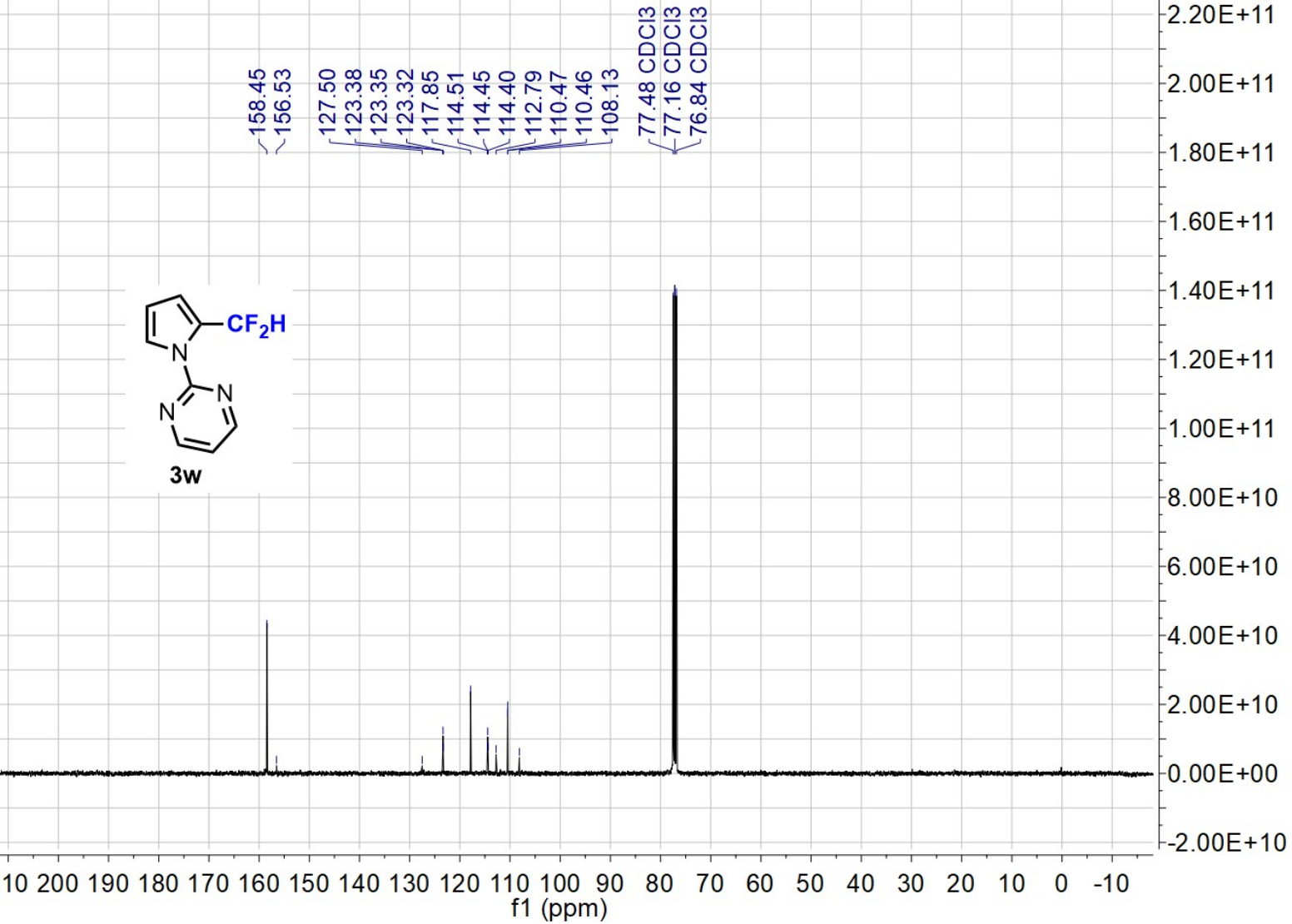

3v
CF2H
1.00
1.00
1.06
1.02
1.09
2.08
1.08
1.96
8.60
8.60
8.36
8.34
8.34
8.33
7.89
7.88
7.87
7.87
7.85
7.85
7.80
7.79
7.51
7.49
7.37
7.35
7.33
7.31
7.26 CDCl3
7.25
7.23
7.23
7.22
7.10
6.96
6.93
6.93
6.82
7.10
6.96
6.93
6.93
6.82
1.96
f1 (ppm)

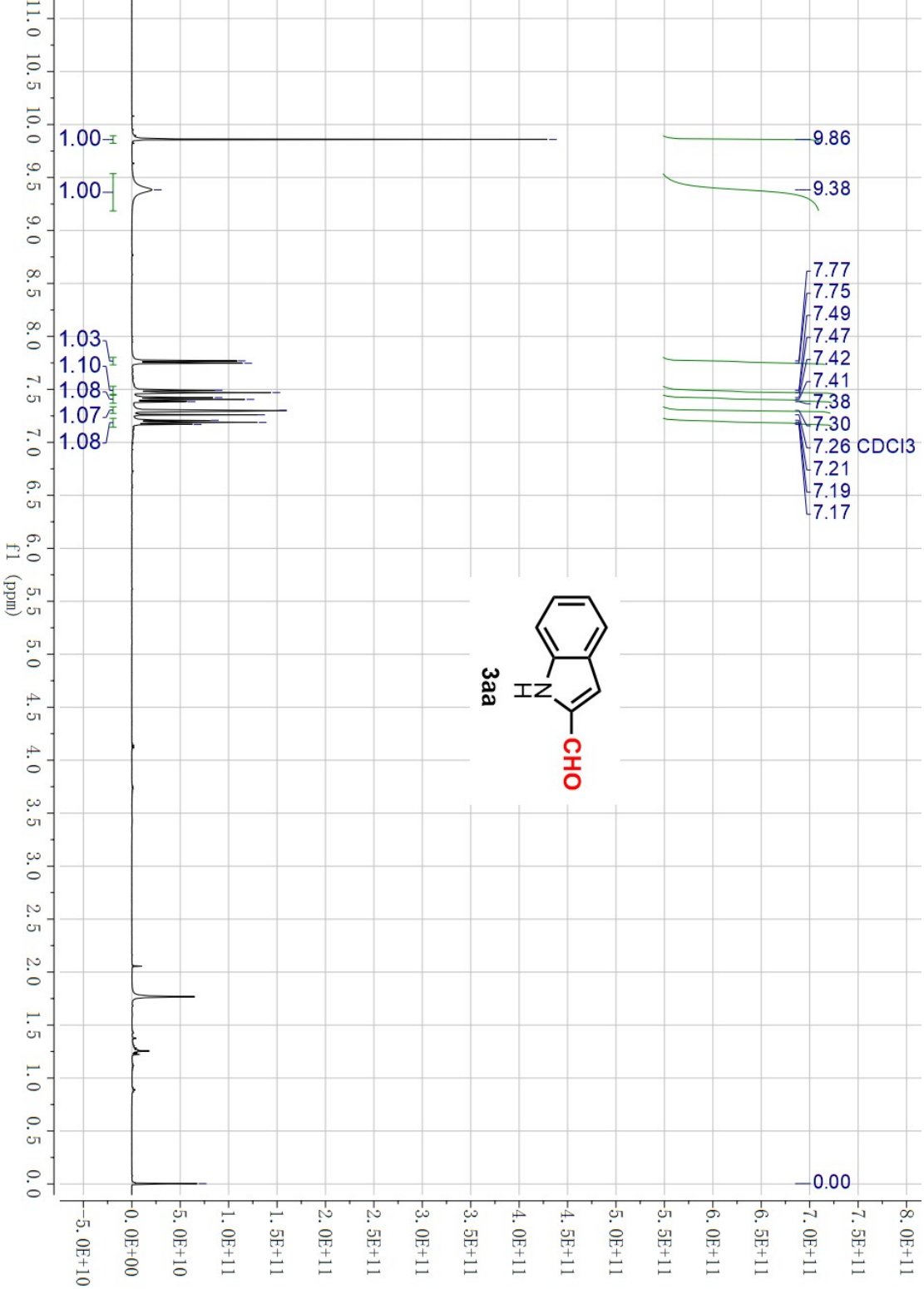

-110.52
8.5E+12
8.0E+12
7.5E+12
7.0E+12
6.5E+12
6.0E+12
5.5E+12
5.0E+12
4.5E+12
4.0E+12
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
5.0E+11
0.0E+00
-5.0E+11
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

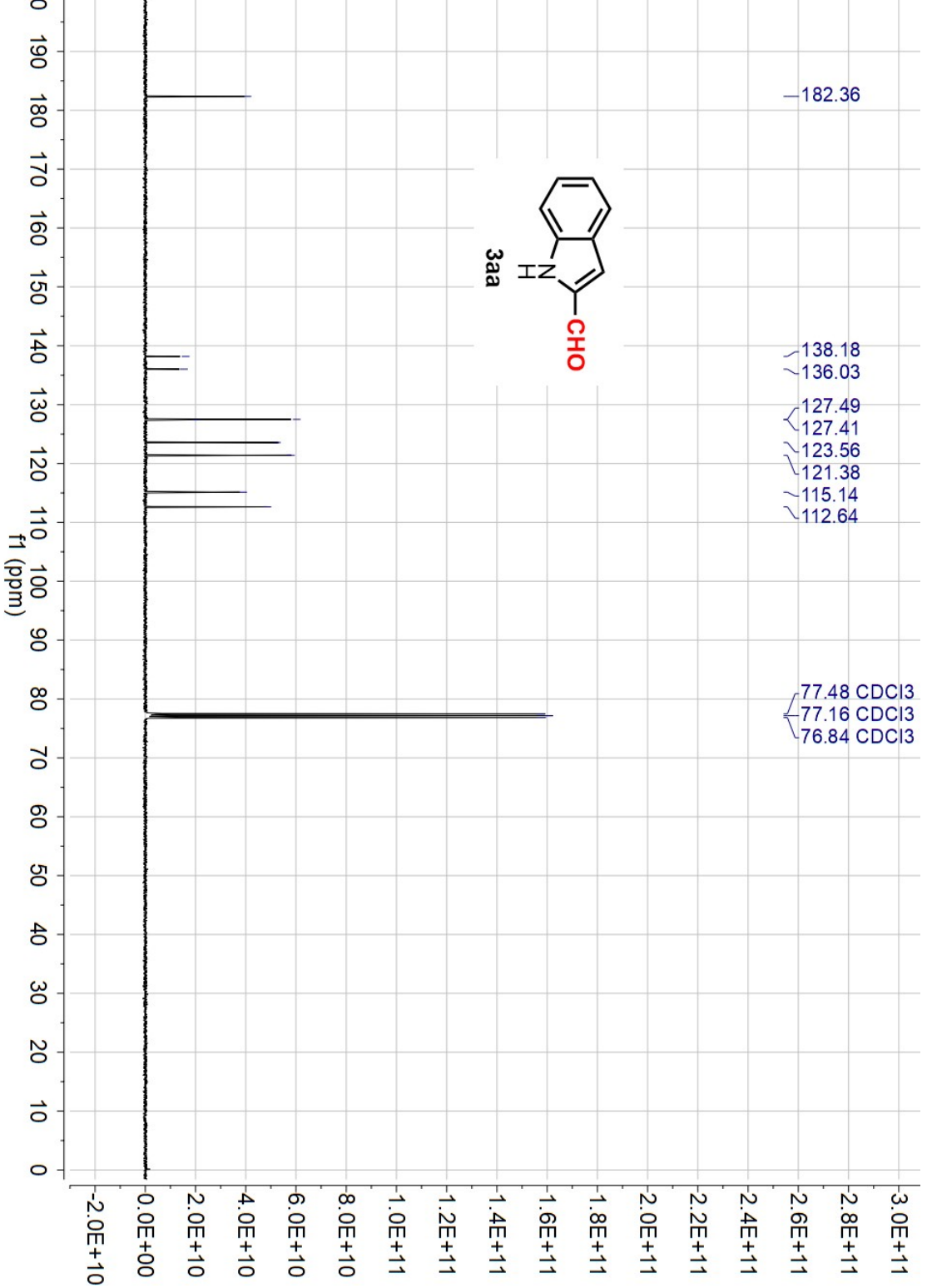

3v
CF2H
N
N
152.26
149.09
138.91
135.76
127.37
126.39
126.17
125.95
122.79
121.59
120.78
119.34
119.27
119.19
117.97
115.86
115.61
115.10
113.25
103.91
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
0.0E+00
5.0E+09
1.0E+10
1.5E+10
2.0E+10
2.5E+10
3.0E+10
3.5E+10
4.0E+10

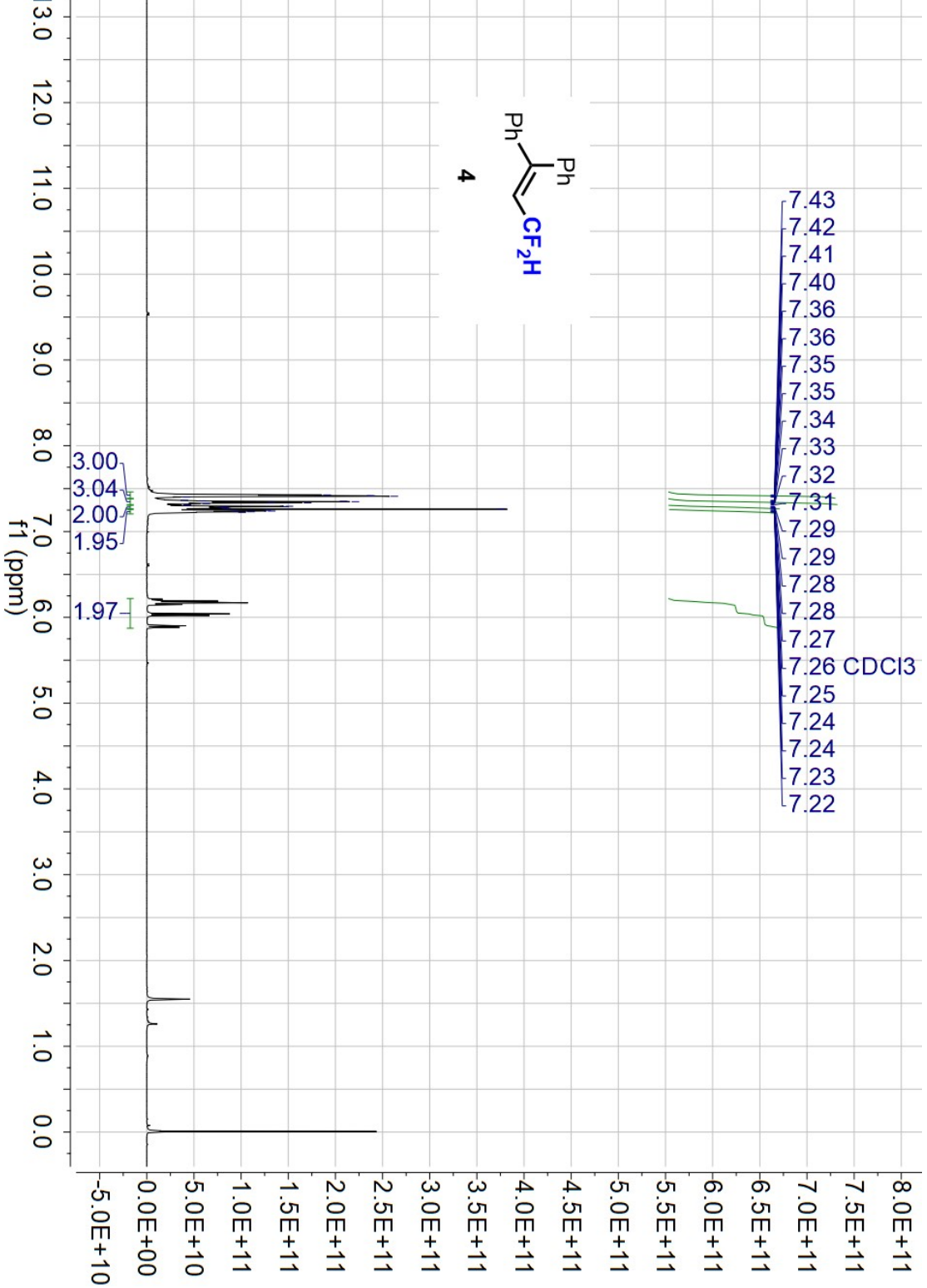

3w
CF2H
8.66
8.65
7.92
7.91
7.91
7.91
7.80
7.66
7.52
7.26
7.26 CDCl3
6.75
6.32
2.00
1.03
1.17
1.04
1.02
1.00
f1 (ppm)

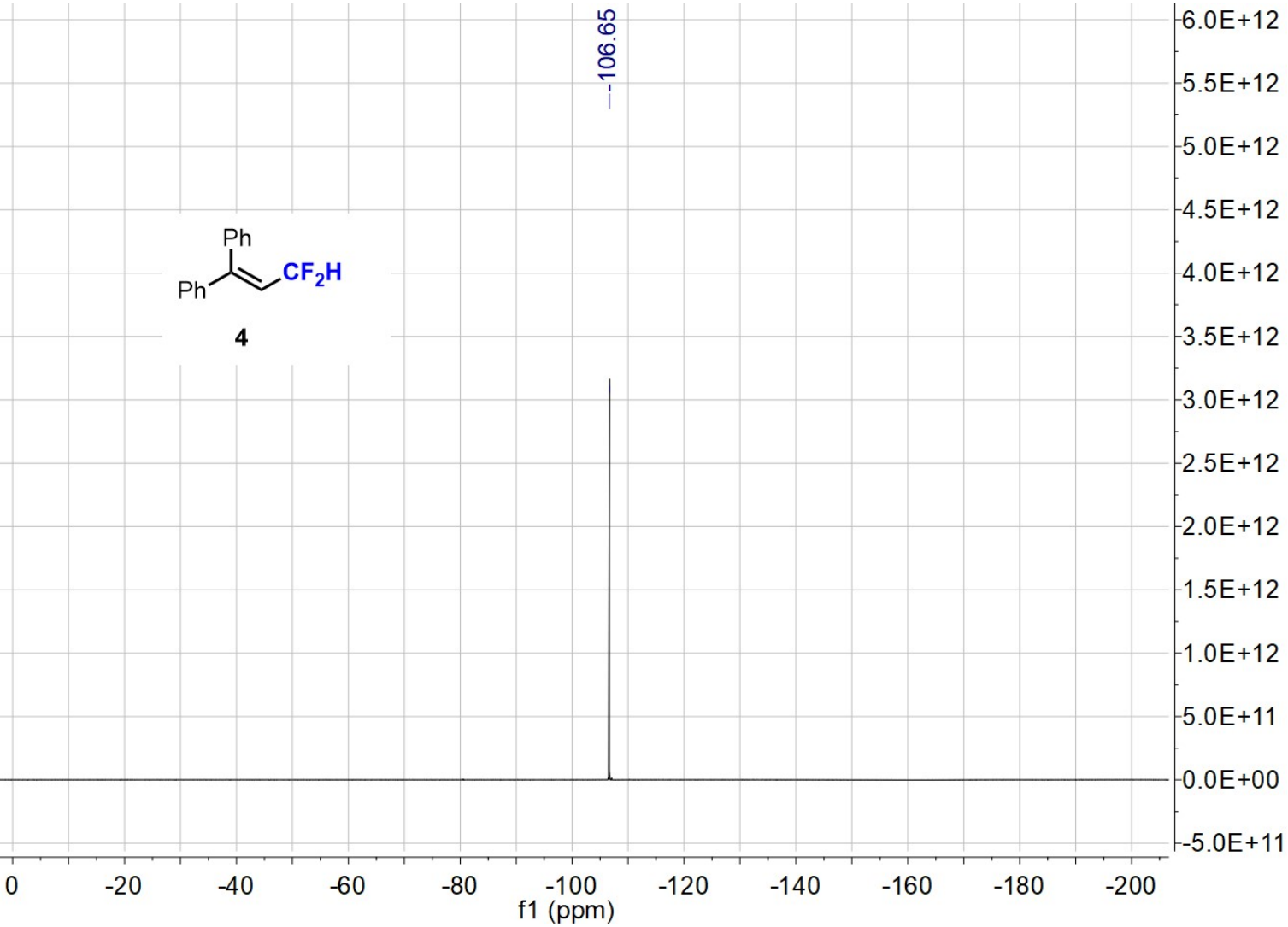

-111.61
CF2H
N
N
N
3w
2.20E+12
2.00E+12
1.80E+12
1.60E+12
1.40E+12
1.20E+12
1.00E+12
8.00E+11
6.00E+11
4.00E+11
2.00E+11
0.00E+00
-2.00E+11
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

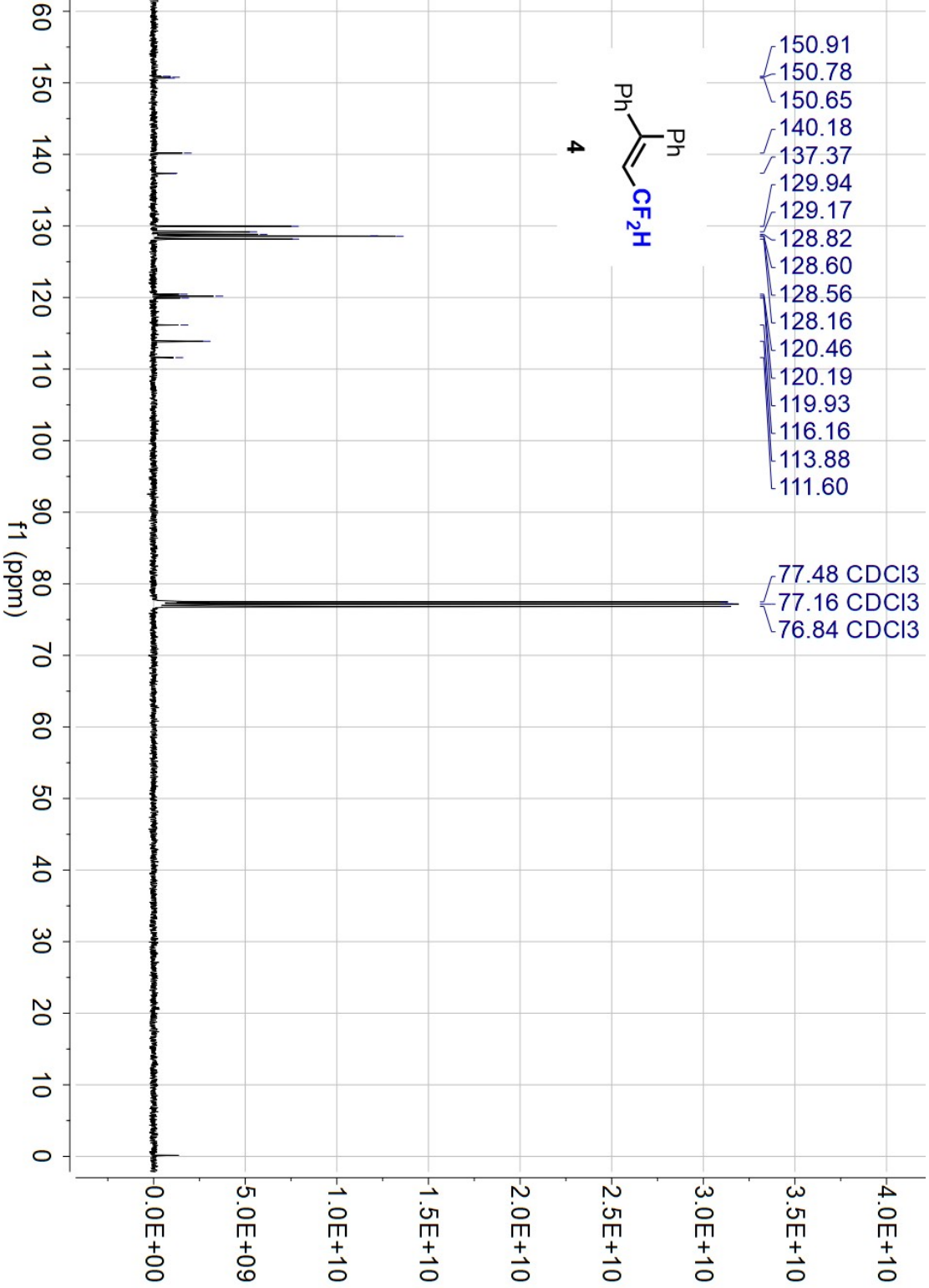

158.45
156.53
127.50
123.38
123.35
123.32
117.85
114.51
114.45
114.40
112.79
110.47
110.46
108.13
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
CF2H
3w
2.20E+11
2.00E+11
1.80E+11
1.60E+11
1.40E+11
1.20E+11
1.00E+11
8.00E+10
6.00E+10
4.00E+10
2.00E+10
0.00E+00
-2.00E+10
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


1.00
1.00
1.03
1.10
1.08
1.07
1.08
9.86
9.38
7.77
7.75
7.49
7.47
7.42
7.41
7.38
7.30
7.26 CDCl3
7.21
7.19
7.17
0.00
3aa
CHO
f1 (ppm)


182.36
138.18
136.03
127.49
127.41
123.56
121.38
115.14
112.64
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
3aa
CHO
N
H
f1 (ppm)


Ph
Ph
CF2H
4
7.43
7.42
7.41
7.40
7.36
7.36
7.35
7.35
7.34
7.33
7.32
7.31
7.29
7.29
7.28
7.28
7.27
7.26 CDCl3
7.25
7.24
7.24
7.23
7.22
3.00
3.04
2.00
1.95
1.97
f1 (ppm)


-106.65
Ph
Ph
CF2H
4
6.0E+12
5.5E+12
5.0E+12
4.5E+12
4.0E+12
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
5.0E+11
0.0E+00
-5.0E+11
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)


150.91
150.78
150.65
140.18
137.37
129.94
129.17
128.82
128.60
128.56
128.16
120.46
120.19
119.93
116.16
113.88
111.60
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
Ph
Ph
CF2H
4
f1 (ppm)