In Situ Generated CF_3CHN_2 with 3-Ylideneoxindoles to Access CF_3-Containing Pyrazolo[1,5-*c*]quinazolines Derivatives

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Supporting Information

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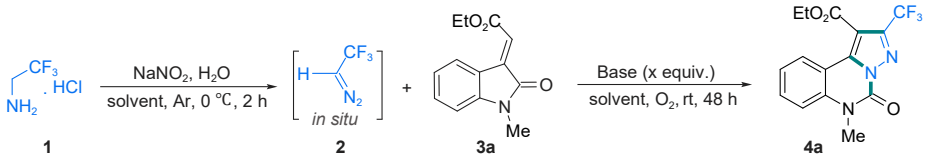
1. General experimental information

Unless otherwise specified, all commercially available reagents are utilized without the need for further purification. Silica gel column chromatography (300–400 mesh) is employed. ^{1}H, ^{19}F, and ^{13}C NMR spectra were measured on 400, 376, and 100 MHz spectrometers, respectively. $CDCl_3$ was used as a solvent, chemical shifts were reported in ppm (δ) from tetramethylsilane (TMS) with the solvent resonance as the internal standard. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, dd = doublet of doublets, td = triplet of doublets, ddd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, m = multiplet), coupling constants (Hz) and integration. High-resolution mass spectra HRMS measurements were obtained on a TOF analyzer.

Preparation of 3-ylideneoxindoles (**3a–w**) was conducted following the previously reported and all reagents used for the reaction were purchased from Biddepharm (China), Tansoole (China), or Innochem (China).

2. Optimization of the reaction conditions for the construction of 4a[a]



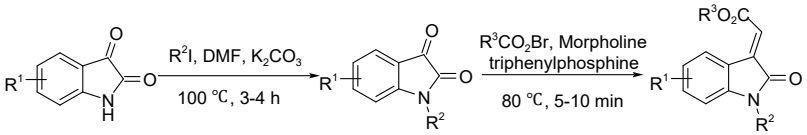
1 2 3a 4a

Entry	Solvent	Temperature (°C)	Base (x equiv.)	Yield (%)[b]
1[c]	Et_2O	rt	DBU (0.5)	40
2[c]	1,4-dioxane	rt	DBU (0.5)	N.R.
3[c]	THF	rt	DBU (0.5)	N.R.
4[c]	DCM	rt	DBU (0.5)	33
5	**PhMe**	rt	**DBU (0.5)**	**78**
6[d]	PhMe	rt	DBU (0.5)	39
7[e]	PhMe	rt	DBU (0.5)	55
8[f]	PhMe	rt	DBU (0.5)	68
9	PhMe	rt	Cs_2CO_3 (0.5)	N.R.
10	PhMe	rt	K_2CO_3 (0.5)	N.R.
11	PhMe	rt	Et_3N (0.5)	N.R.
12	PhMe	rt	NaOH (0.5)	N.R.
13	PhMe	rt	^{t}-BuOK (0.5)	N.R.
14	PhMe	rt	DBN (0.5)	50
15	PhMe	rt	DBU (0.25)	60
16	PhMe	rt	DBU (0.75)	60
17	PhMe	rt	DBU (1.0)	50
18	PhMe	-10	DBU (0.5)	66
19	PhMe	0	DBU (0.5)	59
20	PhMe	40	DBU (0.5)	46
21[g]	PhMe	rt	DBU (0.5)	35
22[h]	PhMe	rt	DBU (0.5)	42
23[i]	PhMe	rt	DBU (0.5)	65

[a]Standard conditions: performed with $CF_3CH_2NH_2$·HCl (1.5mmol, 6.0 equiv.), $NaNO_2$ (1.65 mmol, 6.6 equiv.) 0.2 mL H_2O at 0 °C for 2 h. The mixture is then dried with Sodium sulfate anhydrous, then **3a** (0.25 mmol, 1.0 equiv.), DBU (0.5 equiv.) and 5 mL of drying solvent were added at room temperature under O_2 atmosphere (balloon) for 48 h. [b]Isolated yields based on **3a** are given. [c] The reaction was performed for 120 h. [d]The reaction was performed in 3 mL of dry solvent. [e]The reaction was performed in 10 mL of dry solvent. [f]The reaction was performed in 15 mL of dry solvent. [g]2.0 equiv. of $CF_3CH_2NH_2$·HCl was used. [h]4.0 equiv. of $CF_3CH_2NH_2$·HCl was used. [i]10.0 equiv. of $CF_3CH_2NH_2$·HCl was used.

3. Synthetic methods of substrates

3.1 Synthesis of 3-ylideneoxindoles **3a–w**

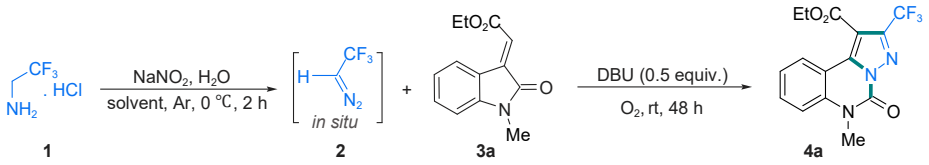


3a–w

Select a 150 mL double-mouth bottle, add the stirring agent, isatin (15 mmol, 1.0 equiv.), K_2CO_3 (30 mmol, 2.0 equiv.) and dissolve in 10 mL DMF. The reaction was vigorously stirred in an oil bath at 100 °C for 5 min and CH_3I (30 mmol, 2.0 equiv.) was added for reflux reaction for 5 h. After the reaction was complete, ice water was added to the reaction mixture, standing for 30 min, and the crude product 1-methylindole-2, 3-dione was filtered.

A clean nightshade bottle with a capacity of 100 mL was chosen next for further steps in the process. Into this reaction vessel, 1-methylindole-2, 3-dione is weighed (6.0 mmol, 1.0 equiv.), ethyl bromoacetate (6.6 mmol, 1.1 equiv.), triphenylphosphine (6.6 mmol, 1.1 equiv.), and morpholine (6.0 mmol, 1.0 equiv.) were precisely measured out and added sequentially at a temperature maintained at around 80 °C for about 10 min duration. The progress of this subsequent reaction step also underwent monitoring via the TLC method. Following completion, the target compound series labeled as "**3a–w**" was purified through column chromatography (using a solvent system of petroleum ether/ethyl acetate = 10:1).[1]

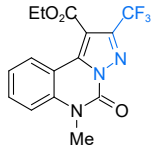
4. Representative procedure for the synthesis of compound 4a



1 **2** **3a** **4a**

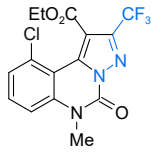
$CF_3CH_2NH_2$·HCl (1.5mmol, 6.0 equiv.), $NaNO_2$ (1.65 mmol, 6.6 equiv.), 0.2 mL H_2O at 0 °C for 2 h.[2] The mixture was then dried with anhydrous sodium sulfate and then added with **3a** (0.25 mmol, 1.0 equiv.), DBU (0.5 equiv.) and stirred at room temperature in 5 mL of drying solvent under O_2 atmosphere (balloon) for 48 h. Finally, the mixture was concentrated under reduced pressure and then purified by silica gel flash column chromatography (using a solvent system of petroleum ether/ethyl acetate = 10:1) to obtain the target compound **4a** (65.9 mg, yield 78%).

5. Characterization data of compounds 4a–w



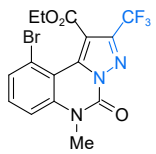
Scheme 2, 4a

Ethyl 6-methyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4a): White solid, 65.9 mg, 78% yield, m.p. 161.5 – 162.6 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 9.06 (dd, J = 8.4, 1.6 Hz, 1H), 7.72 – 7.68 (m, 1H), 7.44 – 7.40 (m, 2H), 4.46 (q, J = 7.2 Hz, 2H), 3.86 (s, 3H), 1.44 (t, J = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 162.09, 146.23 (q, J = 38.1 Hz), 144.54, 141.81, 136.56, 132.79, 127.72, 124.33, 120.30 (q, J = 269.5 Hz), 114.87, 112.28, 108.88, 62.27, 31.93, 13.83; **^{19}F NMR:** (376 MHz, $CDCl_3$) δ - 61.66 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{15}H_{12}F_3N_3O_3$ $[M+H]^+$ 340.0909, found 340.0904.



Scheme 2, 4b

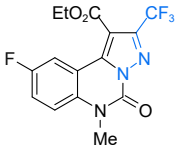
Ethyl 10-chloro-6-methyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4b): White solid, 42.1 mg, 45% yield, m.p. 124.1 – 125.5 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.58 (t, J = 8.4 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 8.8 Hz, 1H), 4.38 (q, J = 7.2 Hz, 2H), 3.81 (s, 3H), 1.34 (t, J = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 162.53, 145.08 (q, J = 38.7 Hz), 144.12, 138.49, 137.26, 132.28, 132.16, 126.57, 120.16 (q, J = 269.8 Hz), 113.77, 112.74, 111.55, 62.44, 32.56, 13.90; **^{19}F NMR:** (376 MHz, $CDCl_3$) δ - 62.03 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{15}H_{11}ClF_3N_3O_3$ $[M+Na]^+$ 396.0339, found 396.0342.



Scheme 2, 4c

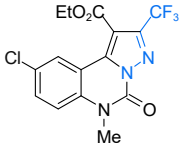
Ethyl 10-bromo-6-methyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4c): Yellow solid, 40.1 mg, 38% yield, m.p. 156.3 – 157.8 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.0 Hz, 1H), 7.50 (t, J = 8.4 Hz, 1H), 7.38 (d, J = 8.4 Hz, 1H), 4.39 (q, J = 6.8 Hz, 2H), 3.80

(s, 2H), 1.33 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) *δ* 162.28, 145.24 (q, *J* = 38.6 Hz), 144.13, 139.33, 138.85, 132.39, 130.26, 121.18, 120.15 (q, *J* =269.8 Hz), 114.25, 113.17, 112.50, 62.44, 32.52, 13.86; **^{19}F NMR:** (376 MHz, $CDCl_3$) *δ* - 62.07 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{15}H_{11}BrF_3N_3O_3$ $[M+Na]^+$ 439.9834, found 439.9832.



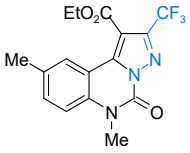
Scheme 2, 4d

Ethyl 9-fluoro-6-methyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4d): Purple solid, 54.6 mg, 61% yield, m.p. 201.7 – 202.8 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) *δ* 8.93 (dd, *J* = 9.6, 2.4 Hz, 1H), 7.43 – 7.36(m, 2H), 4.46 (q, *J* = 7.2 Hz, 2H), 3.84 (s, 3H), 1.43 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) *δ* 161.78, 158.67 (d, *J* = 243.4 Hz), 146.42(q, *J* = 38.3 Hz), 144.20, 141.12, 133.19,120.39 (d, *J* = 23.4 Hz), 120.21 (q, *J* = 269.6 Hz), 116.62 (d, *J* = 8.5 Hz), 114.22 (d, *J* = 26.9 Hz), 113.43 (d, *J* = 10.0 Hz), 109.49, 62.45, 32.30, 13.81; **^{19}F NMR:** (376 MHz, $CDCl_3$) *δ* - 61.69 (s, 3F, CF_3), *δ* - 115.77 (s, 1F); **HRMS-ESI (m/z):** calcd for $C_{15}H_{12}F_3N_3O_3$ $[M+H]^+$ 358.0815, found 358.0808.



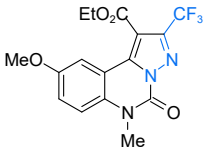
Scheme 2, 4e

Ethyl 9-chloro-6-methyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4e): White solid, 51.3 mg, 55% yield, m.p.206.8 – 207.1 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) *δ* 9.19 (d, *J* = 2.4 Hz, 1H), 7.67 – 7.64 (m, 1H), 7.35 (d, *J* = 8.8 Hz, 1H), 4.49 (q, *J* = 7.2 Hz, 2H), 3.85 (s, 3H), 1.45 (t, *J* = 7.2Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) *δ* 161.78, 146.60 (d, *J* = 38.0 Hz), 144.25, 140.83, 135.26, 132.79, 130.19, 127.53, 120.22 (q, *J* = 270.0 Hz), 116.32, 113.55, 109.59, 63.98, 34.06, 15.14; **^{19}F NMR:** (376 MHz, $CDCl_3$) *δ* - 61.71 (s, 3F, CF_3); HRMS-ESI (m/z): calcd for $C_{15}H_{11}ClF_3N_3O_3$ $[M+H]^+$ 374.0519, found 374.0512.



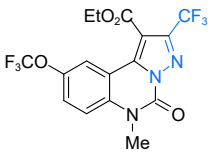
Scheme 2, 4f

Ethyl 6,9-dimethyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4f): White solid, 65.8 mg, 75% yield, m.p. 167.7 – 168.8 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 8.80 (d, J = 0.8 Hz, 1H), 7.49 (dd, J = 8.8, 2.0 Hz,1H), 7.28 (s, 1H), 4.49 (q, J = 7.2 Hz,2H), 3.83 (s, 3H), 2.49 (s, 3H), 1.46 (t, J = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 162.15, 146.18 (q, J = 37.7 Hz), 144.54, 141.75, 134.48, 134.30, 133.79, 127.49, 120.37 (q, J = 269.5 Hz), 114.73, 112.16, 108.69, 62.24, 31.88, 21.06, 13.87; **^{19}F NMR:** (376 MHz, $CDCl_3$) δ - 61.63 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{16}H_{15}F_3N_3O_3$ $[M+H]^+$ 354.1066, found 354.1060.



Scheme 2, 4g

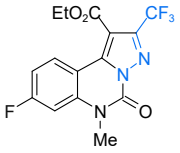
Ethyl 9-methoxy-6-methyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4g): White solid, 57.1 mg, 62% yield, m.p. 172.5 – 173.1 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 8.71 (d, J = 2.8 Hz, 1H), 7.28 – 7.21 (m, 2H), 4.44 (q, J = 7.2 Hz, 2H), 3.89 (s, 3H), 3.80 (s, 3H), 1.42 (t, J = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 162.15, 156.02, 146.27 (q, J = 37.8 Hz), 144.33, 141.88, 130.59, 121.04, 120.35 (q, J = 270.0 Hz), 116.06, 113.04, 110.17, 108.79, 62.25, 55.95, 32.01, 13.84; **^{19}F NMR:** (376 MHz, $CDCl_3$) δ - 61.58 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{16}H_{14}F_3N_3O_4$ $[M+H]^+$ 370.1015, found 370.1007.



Scheme 2, 4h

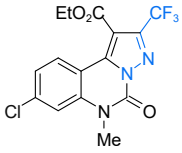
Ethyl 6-methyl-5-oxo-9-(trifluoromethoxy)-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4h): White solid, 69.6 mg, 66% yield, m.p. 191.3 – 191.6 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 9.21 (d, J = 1.6 Hz, 1H), 7.57 (dd, J = 9.2, 2.4 Hz, 1H), 7.45 (d, J = 8.8 Hz, 1H), 4.48 (q, J = 7.2 Hz, 2H), 3.87 (s, 3H), 1.44 (t, J = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 161.73,

146.64 (d, *J* = 38.3 Hz), 145.12, 144.21, 141.02, 135.16, 125.57,120.55 (q, *J* = 257.2 Hz), 120.51, 120.16 (q, *J* = 270.0 Hz), 116.44, 113.40, 109.77, 62.55, 32.33, 13.80; **^{19}F NMR:** (376 MHz, $CDCl_3$) *δ* - 58.20 (s, 3F, CF_3), δ - 61.74 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{16}H_{11}F_6N_3O_4$ $[M+H]^+$ 424.0732, found 424.0727.



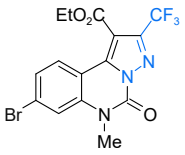
Scheme 2, 4i

Ethyl 8-fluoro-6-methyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4i): Purple solid, 76.4 mg, 86% yield, m.p. 175.4 – 176.1 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) *δ* 9.20 (dd, *J* = 8.8, 6.0 Hz, 1H), 7.14 – 7.07 (m, 2H), 4.44 (q, *J* = 7.2 Hz, 2H), 3.81 (s, 3H), 1.42 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $cdcl_3$) *δ* 164.80 (d, *J* = 253.4 Hz), 161.93, 146.44 (q, *J* = 38.0 Hz), 144.29, 141.59, 138.76 (d, *J* = 10.9 Hz), 130.68 (d, *J* = 10.0 Hz), 120.17 (q, *J* = 269.8 Hz), 112.01 (d, *J* = 21.9 Hz), 108.83 (d, *J* = 2.7 Hz), 108.46, 102.43 (d, *J* = 27.7 Hz), 62.27, 32.15, 13.77; **^{19}F NMR:** (376 MHz, $CDCl_3$) *δ* - 61.74 (s, 3F, CF_3), *δ* - 102.47 (s, 1F); **HRMS-ESI (m/z):** calcd for $C_{15}H_{11}F_4N_3O_3$ $[M+H]^+$ 358.0815, found 358.0807.



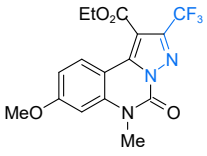
Scheme 2, 4j

Ethyl 8-chloro-6-methyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4j): White solid, 67.5 mg, 72% yield, m.p. 203.7 – 204.2 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) *δ* 9.10 (d, *J* = 8.8 Hz, 1H), 7.40 – 7.34 (m, 2H), 4.45 (q, *J* = 7.2 Hz, 2H), 3.83 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) *δ* 161.94, 146.56 (q, *J* =38.0 Hz), 144.28, 141.46, 139.05, 137.70, 129.34, 124.66, 120.19 (q, *J* = 269.9 Hz), 115.11, 110.88, 109.08, 62.38, 32.14, 13.82; **^{19}F NMR:** (376 MHz, $CDCl_3$) *δ* - 61.72 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{15}H_{11}ClF_3N_3O_3$ $[M+H]^+$ 374.0519, found 374.0514.



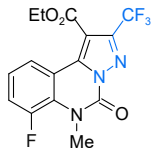
Scheme 2, 4k

Ethyl 8-bromo-6-methyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4k): White solid, 67.9 mg, 65% yield, m.p. 189.7 – 190.3 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 9.01 (d, *J* = 8.8 Hz, 1H), 7.55 – 7.49 (m, 2H), 4.45 (q, *J* = 7.2 Hz, 2H), 3.83 (s, 3H), 1.42 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 161.92, 146.56 (d, *J* = 38.3 Hz), 144.22, 141.50, 137.61, 129.27, 127.54, 127.33, 120.18 (q, *J* = 269.9 Hz), 118.05, 111.23, 109.17, 62.39, 32.14, 13.81; **^{19}F NMR:** (376 MHz, $CDCl_3$) δ - 61.72 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{15}H_{11}BrF_3N_3O_3$ $[M+H]^+$ 418.0014, found 418.0008.



Scheme 2, 4l

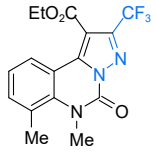
Ethyl 8-methoxy-6-methyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4l): White solid, 59.8 mg, 65% yield, m.p. 202.1 – 203 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 9.10 (d, *J* = 9.2 Hz, 1H), 6.94 (dd, *J* = 9.2, 2.4 Hz, 1H), 6.80 (d, *J* = 2.4 Hz, 1H), 4.44 (q, *J* = 7.2 Hz, 2H), 3.95 (s, 3H), 3.80 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 163.00, 162.23, 146.39 (d, *J* = 37.2 Hz), 144.74, 142.40, 138.67, 129.91, 120.40 (q, *J* = 269.5 Hz), 110.11, 107.30, 105.75, 100.37, 62.03, 55.91, 31.92, 13.86; **^{19}F NMR:** (376 MHz, $CDCl_3$) δ - 61.75 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{16}H_{14}F_3N_3O_4$ $[M+H]^+$ 370.1015, found 370.1010.



Scheme 2, 4m

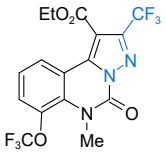
Ethyl 7-fluoro-6-methyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4m): Purple solid, 54.6 mg, 61% yield, m.p. 180.2 – 181.1 °C; **^{1}H NMR:** (400 MHz, CDCl3) δ 8.80 – 8.78 (m, 1H), 7.44 – 7.38 (m, 1H), 7.36 – 7.31 (m, 1H), 4.46 (q, *J* = 7.2 Hz, 2H), 4.02 (d, *J* = 9.2 Hz, 3H), 1.43 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 162.01, 150.63 (d, *J* = 246.9

Hz), 146.55 (q, *J* = 38.3 Hz), 144.81, 140.97, 125.84 (d, *J* = 7.2 Hz), 125.21 (d, *J* = 8.6 Hz), 123.46 (d, *J* = 3.9 Hz), 120.48 (d, *J* = 23.1 Hz), 120.18 (q, *J* = 270.1 Hz), 114.84 (d, *J* = 1.9 Hz), 109.48, 62.49, 36.44, 13.83; **^{19}F NMR:** (376 MHz, $CDCl_3$) *δ* - 61.69 (s, 3F, CF_3), *δ* - 119.36 (s, 1F); **HRMS-ESI (m/z):** calcd for $C_{15}H_{11}F_4N_3O_3$ $[M+H]^+$ 358.0815, found 358.0810.



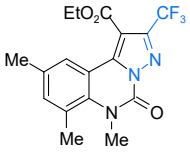
Scheme 2, 4n

Ethyl 6,7-dimethyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-c]quinazoline-1-carboxylate (4n): White solid, 32.5 mg, 35% yield, m.p. 119.7 – 120.6 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) *δ* 8.74 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.30 – 7.26 (m, 1H), 4.45 (q, *J* = 7.6 Hz, 2H), 3.85 (s, 1H), 2.67 (s, 3H), 1.42 (t, *J* = 7.2 Hz, 2H); **^{13}C NMR:** (100 Hz, $CDCl_3$) δ 162.29, 146.43 (q, *J* = 37.3 Hz), 146.24, 142.05, 137.75, 136.99, 126.55, 125.20, 124.84, 120.33 (q, *J* = 269.4 Hz), 114.53, 108.92, 62.31, 39.73, 23.27, 13.85; **^{19}F NMR:** (376 MHz, $CDCl_3$) *δ* - 61.72 (s, 3F, CF_3); **HRMS-ESI (m/z)**: calcd for $C_{16}H_{11}F_6N_3O_4$ $[M+Na]^+$ 376.0885, found 376.0890.



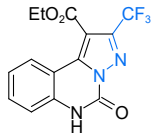
Scheme 2, 4o

Ethyl 6-methyl-5-oxo-7-(trifluoromethoxy)-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4o): White solid, 43.5 mg, 43% yield, m.p. 135.1 – 136.2 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) *δ* 9.01 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.61 – 7.58 (m, 1H), 7.57 – 7.40 (m, 1H), 4.47 (q, *J* = 7.2 Hz, 2H), 3.95 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR:** (100 Hz, $CDCl_3$) *δ* 162.00, 146.75 (d, *J* = 38.2 Hz), 145.16, 140.80, 136.83, 130.95, 127.06, 126.66, 125.17, 120.60 (q, *J* = 258.6 Hz), 120.14 (q, *J* = 269.9 Hz), 115.56, 109.73, 62.57, 38.05, 13.84; **^{19}F NMR:** (376 MHz, $CDCl_3$) *δ* - 57.63 (s, 3F, CF_3), *δ* - 61.73 (s, 3F, CF_3); **HRMS-ESI (m/z)**: calcd for $C_{16}H_{11}F_6N_3O_4$ $[M+H]^+$ 424.0732, found 424.0727.



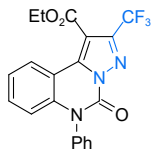
Scheme 2, 4p

Ethyl 6,7,9-trimethyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4p): White solid, 51.8 mg, 57% yield, m.p. 57.1 – 57.7 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.28 (s, 1H), 4.47 (q, J = 7.2 Hz, 1H), 3.83 (s, 3H), 2.64 (s, 3H), 2.41 (s, 3H), 1.43 (t, J = 7.6 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 162.28, 146.30 (q, J = 38.0 Hz), 146.22, 141.98, 138.09, 135.54, 134.60, 126.27, 124.99, 120.32 (q, J = 269.8 Hz), 114.31, 108.65, 62.26, 39.61, 23.17, 20.83, 13.85; **^{19}F NMR:** (376 MHz, $CDCl_3$) δ - 61.69 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{17}H_{16}F_3N_3O_3$ $[M+H]^+$ 368.1222, found 368.1214.



Scheme 2, 4q

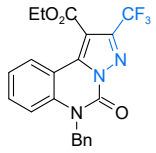
Ethyl 5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4q): White solid, 28.6 mg, 37% yield, m.p. 121.5 – 122.4 °C; **^{1}H NMR:** (400 MHz, DMSO-d_6) δ 12.48 (s, 1H), 8.71 – 8.69 (m, 1H), 7.65 – 7.61 (m, 1H), 7.38 – 7.29 (m, 2H), 4.40 (q, J = 7.2 Hz, 2H), 1.34 (t, J = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, DMSO-d_6) δ 161.77,143.92 (d, J = 37.0 Hz), 143.55, 143.34, 136.33, 132.80, 126.44, 123.60, 120.92 (q, J = 268.8 Hz), 116.54, 111.43, 107.91, 62.16, 14.01; **^{19}F NMR:** (376 MHz, DMSO-d_6) δ - 60.11 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{14}H_{10}F_3N_3O_3$ $[M+H]^+$ 326.0753, found 326.0746.



Scheme 2, 4r

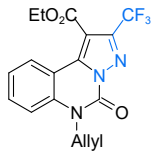
Ethyl 5-oxo-6-phenyl-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4r): White solid, 67.7 mg, 68% yield, m.p. 216.7 – 217.2 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 9.05 (dd, J = 8.0, 1.2 Hz, 1H), 7.68 – 7.59 (m, 3H), 7.48 – 7.43 (m, 1H), 7.40 – 7.36 (m, 3H), 6.70 (dd, J = 8.4, 1.2 Hz, 1H), 4.49 (q, J = 7.2 Hz, 2H), 1.46 (t, J = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 162.18,

146.51 (d, *J* = 38.1 Hz), 144.04, 142.34, 138.08, 135.86, 132.32, 130.78, 130.15, 128.87, 127.44, 124.47, 120.32 (q, *J* = 269.8 Hz), 116.88, 112.18, 109.23, 62.35, 13.88; **^{19}F NMR:** (376 MHz, $CDCl_3$) *δ* - 61.68 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{20}H_{14}F_3N_3O_3$ $[M+H]^+$ 402.1066, found 402.1058.



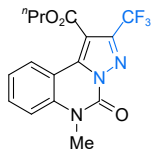
Scheme 2, 4s

Ethyl 6-benzyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4s): White solid, 79.7 mg, 77% yield, m.p. 151.6 – 152.4 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) *δ* 9.03 (d, *J* = 8.4 Hz, 1H), 7.56 - 7.52(m, 1H), 7.37 – 7.28 (m, 7H), 5.62 (s, 2H), 4.48 (q, *J* = 6.8 Hz, 2H), 1.44 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) *δ* 162.15, 146.56 (d, *J* = 38.2 Hz), 145.13, 142.02, 135.92, 134.65, 132.75, 129.22, 128.16, 127.85, 126.72, 124.42,121.65, 114.23 (q, *J* = 325.4 Hz), 62.34, 48.39, 13.87; **^{19}F NMR:** (376 MHz, $CDCl_3$) *δ* - 61.70 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{21}H_{16}F_3N_3O_3$ $[M+H]^+$ 416.1222, found 416.1217.



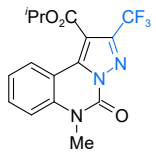
Scheme 2, 4t

Ethyl 6-allyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4t): White solid, 63.5 mg, 65% yield, m.p. 191.3 – 192.6 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) *δ* 9.04 (d, *J* = 8.0 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.41 – 7.37 (m, 2H), 6.03 – 5.93 (m, 1H), 5.34 – 5.23 (m, 2H), 5.02 (d, *J* = 4.8 Hz, 2H), 4.47 (q, *J* = 7.2 Hz, 2H), 1.44 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) *δ* 162.18, 146.45 (d, *J* = 38.1 Hz), 144.40, 141.95, 135.89, 132.71, 130.34, 127.86, 124.37,120.32 (q, *J* = 269.9 Hz), 118.79, 115.62, 112.52, 108.98, 62.33, 46.98, 13.88; **^{19}F NMR:** (376 MHz, $CDCl_3$) *δ* - 61.69 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{17}H_{14}F_3N_3O_3$ $[M+H]^+$ 366.1066, found 366.1060.



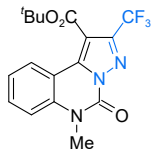
Scheme 2, 4u

Propyl 6-methyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4u): White solid, 38.5 mg, 44% yield, m.p. 143.4 – 144.3 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 9.03 (d, J = 8.4 Hz, 1H), 7.71 – 7.67 (m, 1H), 7.42 – 7.38 (m, 2H), 4.36 (t, J = 6.8 Hz, 2H), 3.85 (s, 3H), 1.83 (q, J = 7.2 Hz, 2H), 1.04 (t, J = 7.6 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 162.30, 146.17 (d, J = 38.0 Hz), 144.58, 141.87, 136.60, 132.81, 127.79, 124.37, 120.30 (q, J = 270.0 Hz), 114.89, 112.36, 108.91, 68.05, 31.97, 21.78, 10.51; **^{19}F NMR:** (376 MHz, $CDCl_3$) δ - 61.71 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{16}H_{14}F_3N_3O_3$ $[M+H]^+$ 354.1066, found 354.1060.



Scheme 2, 4v

Isopropyl 6-methyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4v): White solid, 37.8 mg, 43% yield, m.p. 176.1 – 177.3 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 9.05 (d, J = 8.0 Hz, 1H), 7.71 – 7.66 (m, 1H), 7.42 – 7.39 (m, 2H), 5.36 – 5.29 (m, 1H), 3.85 (s, 3H), 1.42 (d, J = 6.4 Hz, 6H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 161.49, 146.00 (q, J = 37.8 Hz), 144.44, 141.58, 136.41, 132.64, 127.56, 124.19, 120.28 (q, J = 269.5 Hz), 114.77, 112.19, 109.26, 70.32, 31.83, 21.50; **^{19}F NMR:** (376 MHz, $CDCl_3$) δ - 61.34 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{16}H_{14}F_3N_3O_3$ $[M+H]^+$ 354.1066, found 354.1057.



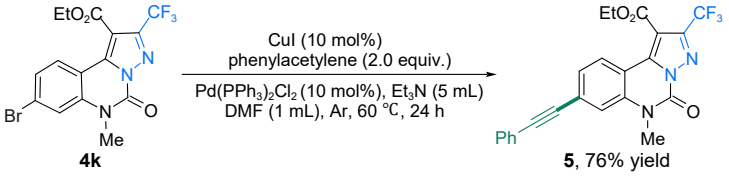
Scheme 2, 4w

Tert-butyl 6-methyl-5-oxo-2-(trifluoromethyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline-1-carboxylate (4w): White solid, 76.1 mg, 69% yield, m.p. 181.3 – 182.3 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 8.94 (dd, J = 8.0, 1.6 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.40 – 7.52 (m, 2H), 3.83 (s, 3H), 1.64 (s, 9H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 161.33, 145.96 (q, J = 37.7 Hz), 144.61, 141.27, 136.44, 132.54, 127.49, 124.29, 120.37 (q, J = 269.8 Hz), 114.84, 112.44, 110.59, 83.91, 31.90, 27.97; **^{19}F NMR:**

(376 MHz, $CDCl_3$) δ - 61.25 (s, 3F, CF_3); **HRMS-ESI (m/z):** calcd for $C_{17}H_{16}F_3N_3O_3$ $[M+H]^+$ 368.1222, found 368.1213.

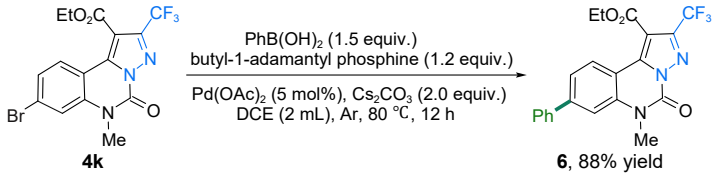
6. Transformation of 4k into 5–10 (Scheme 4)

6.1 Synthesis of **5** from **4k**.



To a 25 mL flame-dried vial with a magnetic stir bar, **4k** (83.6 mg, 0.2 mmol), phenylacetylene (40.8 mg, 0.4 mmol), $Pd(PPh_3)_2Cl_2$ (14.0 mg, 0.02 mmol), CuI (4.0 mg, 0.02 mmol), Et_3N (5 mL), and DMF (1 mL) were added under argon atmosphere at 60 °C for 24 h. After the completion of the reaction, it was diluted with water, and extracted with dichloromethane (15 mL × 3). The combined organic phase was concentrated and purified by flash column chromatography to afford the desired product **5** (66.4 mg, 76% yield).[3] White solid, m.p. 170.7 – 171.5 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 9.07 (d, J = 8.8 Hz, 1H), 7.60 – 7.53 (m, 2H), 7.50 (d, J = 6.8 Hz, 2H), 7.39 (dd, J = 5.3, 1.8 Hz, 3H), 4.46 (q, J = 7.2 Hz, 2H), 3.86 (s, 3H), 1.43 (t, J = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 162.01, 146.46 (q, J = 38.3 Hz), 144.46, 141.56, 136.73, 131.95, 129.36, 128.68, 127.90, 127.23, 122.20, 120.29 (q, J = 269.5 Hz), 117.59, 111.84, 109.13, 93.59, 88.20, 62.33, 32.03, 13.83; **HRMS-ESI (m/z):** calcd for $C_{23}H_{16}F_3N_3O_3$ $[M+H]^+$ 440.1222, found 440.1228.

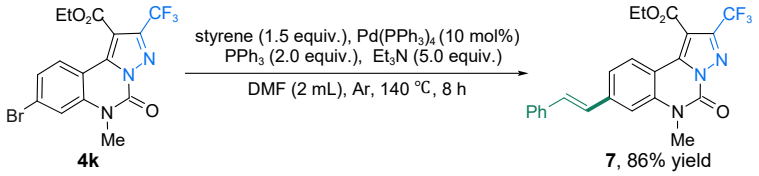
6.2 Synthesis of **6** from **4k**.



To a 5 mL flame-dried vial with a magnetic stir bar, **4k** (83.6 mg, 0.2 mmol), phenylboronic acid (36.6 mg, 0.3 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), Cs_2CO_3 (65.2 mg, 0.4 mmol), butyl-1-adamantyl phosphine (4.4 mg, 0.24 mmol), and DCE (2.0 mL) were added under argon atmosphere at 80 °C for 12 h. After the completion of the reaction, it was concentrated and purified by flash column chromatography to afford the desired product **6** (72.2 mg, 88% yield).[3] m.p. 144.9 –

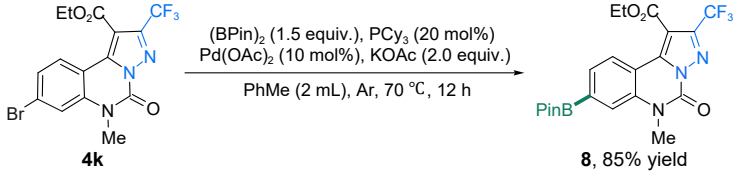
145.1°C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 9.14 (d, J = 8.8 Hz, 1H), 7.66 – 7.61 (m, 3H), 7.54 – 7.44 (m, 4H), 4.48 (q, J = 7.2 Hz, 2H), 3.90 (s, 3H), 1.44 (t, J = 7.2 Hz, 3H); **^{13}C NMR:** δ 162.14,146.42 (d, J = 38.0 Hz), 145.84, 144.70, 141.93, 139.40, 137.19, 129.34, 129.00, 128.40, 127.47, 123.30,120.34 (q, J = 269.7 Hz), 113.22, 111.25, 108.78, 62.25, 32.02, 13.86; **HRMS-ESI (m/z):** calcd for $C_{21}H_{16}F_3N_3O_3$ $[M+Na]^+$ 438.1041, found 438.1041.

6.3 Synthesis of **7** from **4k**.



To a 5 mL flame-dried vial with a magnetic stir bar, **4k** (83.6 mg, 0.2 mmol), styrene (41.7 mg, 0.4 mmol), $Pd(PPh_3)_4$ (25 mg, 0.02 mmol), PPh_3 (0.6 mg, 0.002 mmol) and Et_3N (101.1 mg, 1 mmol) in DMF (2 mL) was stirred at 140°C under Ar for 8 hours. After cooling to room temperature, the mixture was diluted with H_2O and extracted with EtOAc. The combined organic layer was washed with brine and dried over Na_2SO_4. Then the filtrate was concentrated and purified by column chromatography to give the desired product **7** (69.8 mg, 81% yield).[4] m.p. 182.1 – 182.9 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 9.05 (d, J = 8.4 Hz, 1H), 7.56 (d, J = 8.0 Hz, 3H), 7.42 – 7.30 (m, 4H), 7.26 – 7.14 (m, 2H), 4.47 (q, J = 7.2 Hz, 2H), 3.89 (s, 3H), 1.44 (t, J = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 162.16, 146.43 (d, J = 37.7 Hz), 144.71, 141.94, 137.26, 136.28, 132.76, 129.04, 128.93, 128.23, 127.09, 126.94, 122.04,120.36 (q, J = 269.7 Hz), 112.64, 111.29, 108.61, 62.23, 31.98, 13.87; **HRMS-ESI (m/z):** calcd for $C_{23}H_{18}F_3N_3O_3$ $[M+H]^+$ 442.1379, found 442.1378.

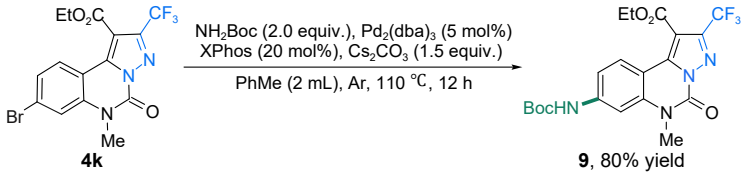
6.4 Synthesis of **8** from **4k**.



To a 5 mL flame-dried vial with a magnetic stir bar, **4k** (83.6 mg, 0.2 mmol), $(BPin)_2$ (76.2 mg, 0.3 mmol), KOAc (40.0 mg, 0.4 mmol), PCy_3 (11.3 mg, 20 mol%), $Pd(OAc)_2$ (4.5 mg, 10 mol%), and PhMe (2.0 mL) were added under argon atmosphere, and the mixture was stirred at 70 ˚C for 2 h. After the completion of the reaction, it was purified by flash column chromatography on silica S32 gel (petroleum ether/ethyl acetate = 10:1) to afford the desired product **8** (76.7 mg, 85% yield).[3]

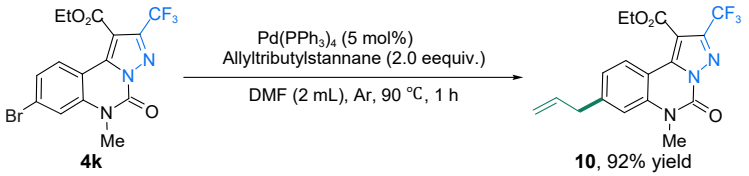
White solid, m.p. 137.6 – 138.5 ˚C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 8.97 (d, J = 8.0 Hz, 1H), 7.81 – 7.79 (m, 2H), 4.47 (q, J = 7.2 Hz, 2H), 3.91 (s, 3H), 1.43 (t, J = 7.2 Hz, 3H), 1.38 (s, 12H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 162.09, 146.29 (d, J = 38.3 Hz),144.67, 141.64, 135.87, 130.25, 126.69, 120.95, 120.33 (q, J = 269.9 Hz), 114.31, 109.41, 84.81, 62.32, 32.15, 25.02, 13.87; **HRMS-ESI (m/z):** calcd for $C_{21}H_{23}F_3N_3O_5B$ $[M+Na]^+$ 488.1581, found 488.1583.

6.5 Synthesis of **9** from **4k**.



To a 5 mL flame-dried vial with a magnetic stir bar, **4k** (83.6 mg, 0.2 mmol), NH_2Boc (35.2 mg, 0.3 mmol), $Pd_2(dba)_3$ (9.2 mg, 5 mol%), XPhos (19.1 mg, 20 mol%), Cs_2CO_3 (97.7 mg, 3 mmol), and PhMe (2.0 mL) were added under argon atmosphere, and the mixture was stirred at 110 ˚C for 12 h. After the completion of the reaction, it was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 15:1 - 4:1) to afford the desired product **9** (73.5 mg, 80% yield). Yellow solid, m.p. 110.3 – 110.9 ˚C; **^{1}H NMR:** (400 MHz, DMSO-d_6) δ 9.97 (s, 1H), 8.73 – 8.70 (m, 1H), 7.81 (s, 1H), 7.39 – 7.37 (m, 1H), 4.38 (q, J = 6.4 Hz, 2H), 3.63 (s, 3H), 1.52 (s, 9H), 1.33 (t, J = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 162.25, 152.23, 146.42 (d, J = 38.5 Hz), 144.85, 142.79, 142.26, 138.26, 128.87, 120.43 (d, J = 260.0 Hz), 113.91, 107.58, 107.04, 103.20, 81.98, 62.04, 32.10, 28.35, 13.83; **HRMS-ESI (m/z):** calcd for $C_{20}H_{21}F_3N_4O_5$ $[M+Na]^+$ 477.1362, found 477,1366.

6.6 Synthesis of **10** from **4k**.



To a 5 mL flame-dried vial with a magnetic stir bar, **4k** (83.6 mg, 0.2 mmol), $Pd(PPh_3)_4$ (11.6 mg, 5 mol%), allyltributylstannane (124.0 µL, 0.4 mmol), and DMF (2.0 mL) were added under argon atmosphere, and the mixture was stirred at 90 ˚C for 1 h. After the completion of the reaction, it was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to afford the desired product **10** (69.8 mg, 92% yield).[3] White solid, m.p. 83.2 – 84.5˚C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 8.92 (d, J = 8.0 Hz, 1H), 7.21 – 7.16 (m, 2H), 6.01 – 5.91 (m, 1H), 5.17 – 5.12 (m,

2H), 4.43 (q, *J* = 7.2 Hz, 2H), 3.80 (s, 2H), 3.52 (d, *J* = 6.8 Hz, 2H), 1.41 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 162.05, 146.16 (q, *J* = 37.9 Hz), 144.58, 141.93, 136.81, 135.63, 127.78, 124.90, 120,32 (q, *J* = 269.5 Hz), 117.60, 114.66, 110.36, 108.34, 62.12, 40.48, 31.84, 13.80; **HRMS-ESI (m/z):** calcd for $C_{18}H_{16}F_3N_3O_3$ $[M+Na]^+$ 402.1041, found 402.1045.

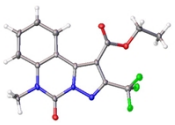
7. Reference

1. J. Azizian, M. R. Mohammadizadeh, Z. Kazemizadeh, N. Karimi, A. A. Mohammadi, A. R.

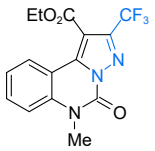
Karimi, A. Alizadeh, *Lett. Org. Chem*. 2006, **3**, 56–57.

2. T.-R. Li, S.-W. Duan, W Ding, Y.-Y. Liu, J.-R. Chen, L.-Q. Lu, W.-J. Xiao, *J. Org. Chem*. 2014, **79**, 2296–2302.
3. Y.-C. Fang, J.-H. Chen, R.-F. Xiu, L.-R. Zhang, F.-H. Zheng, Y.-Z. Chen, Z.-W. Gao, W.-Y. Han, *Org. Chem. Front*. 2023, **10**, 3752–3759.
4. D. Arora, H. Kumar, D. Malhotra, M Malhotra, *Pharmacologyonline* 2011, **3**, 659–668.

8. X-ray crystallographic data of 4a



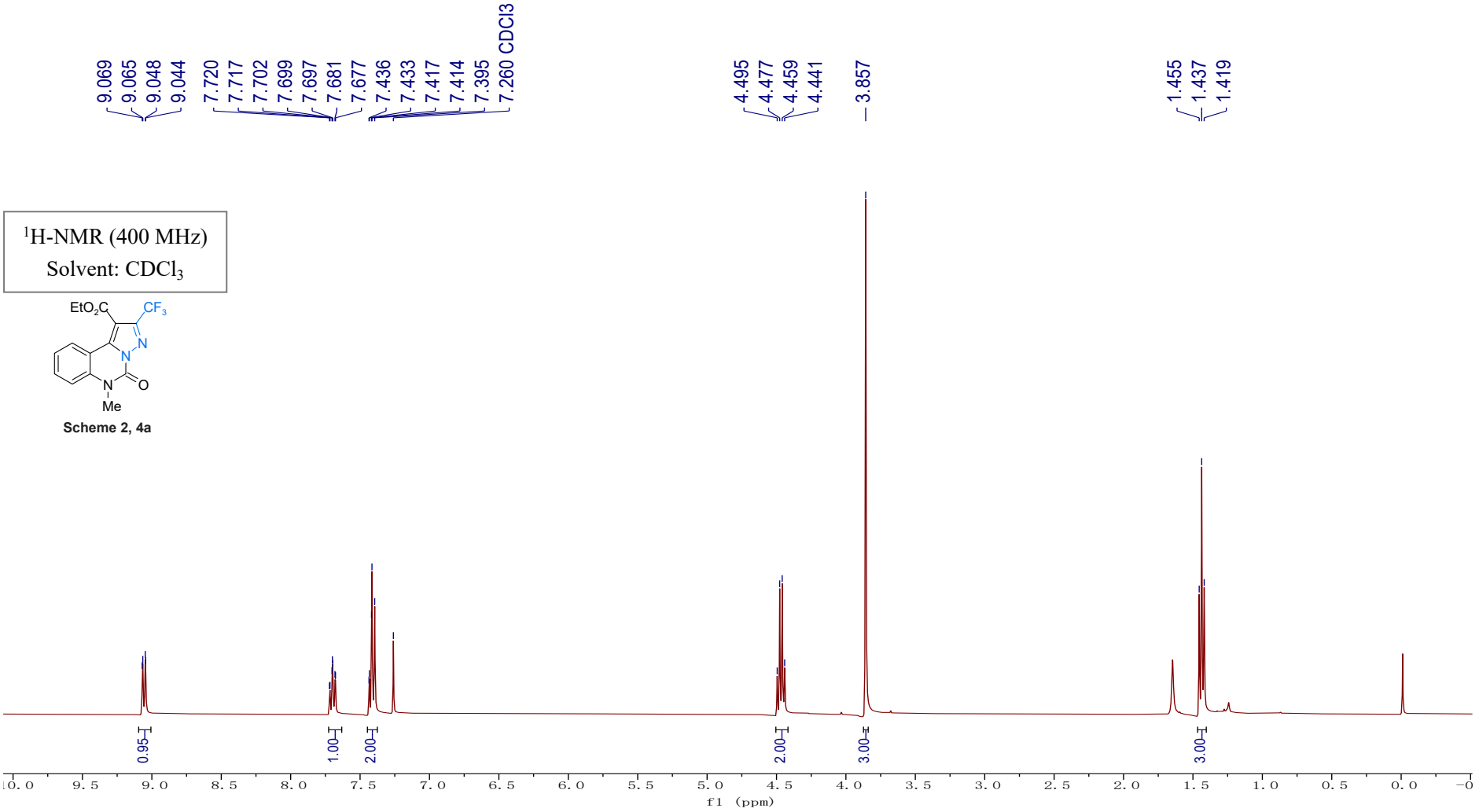
X-ray of **4a**
(CCDC: 2349912)

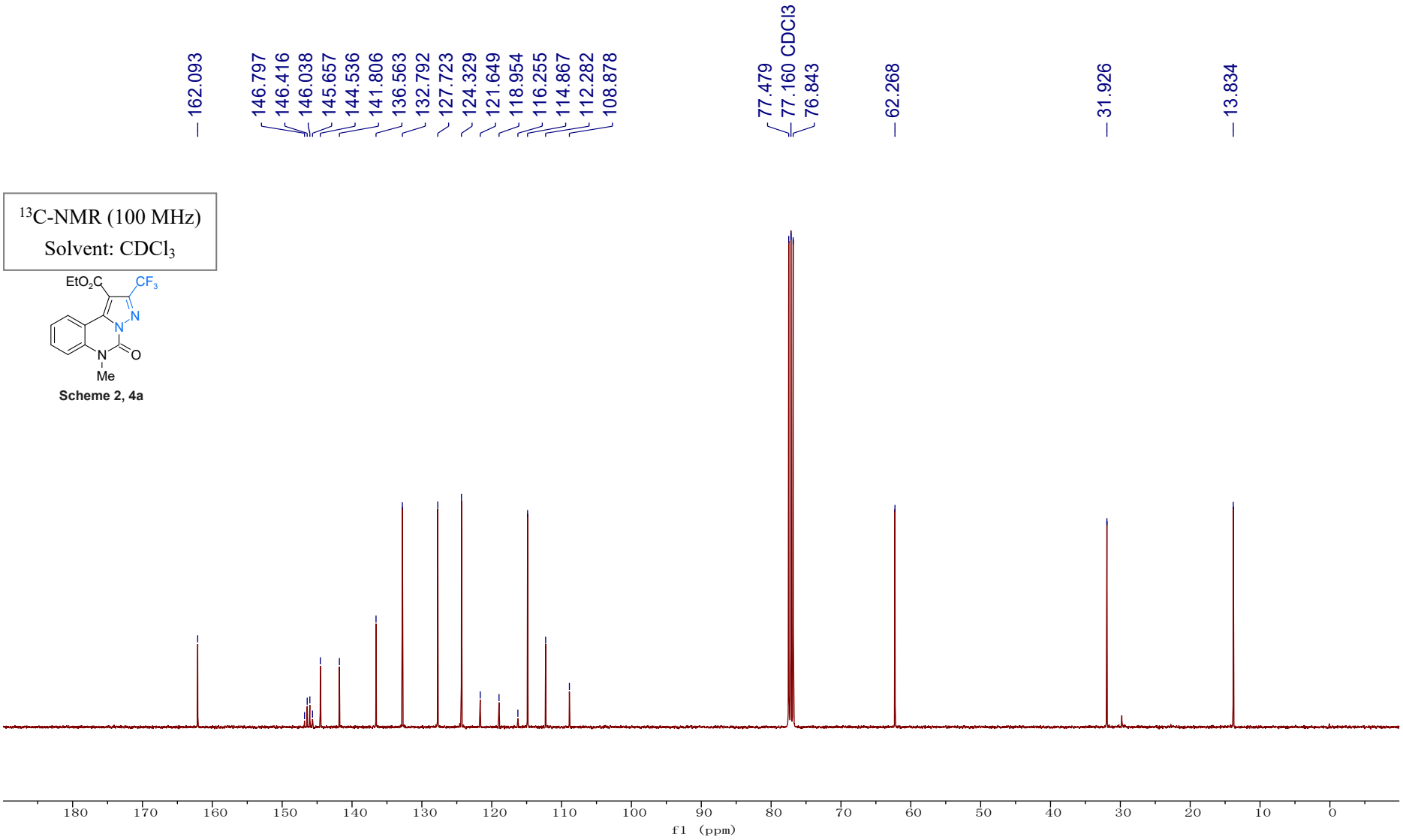


4a

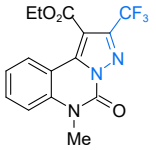
Empirical formula	$C_{15}H_{12}F_3N_3O_3$
Formula weight	339.28
Temperature/K	99.97(15)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	25.8074(13)
b/Å	4.65278(14)
c/Å	26.1585(13)
α/°	90
β/°	116.535(6)
γ/°	90
Volume/Å^3	2810.1(3)
Z	8
ρ_{calc}g/cm^3	1.604
μ/mm^{-1}	1.219
F(000)	1392.0
Crystal size/mm^3	0.16 × 0.13 × 0.11
Radiation	Cu Kα (λ = 1.54184)
2 θ range for data collection/°	6.468 to 148.592
Index ranges	-31 ≤ h ≤ 28, -5 ≤ k ≤ 5, -4 ≤ l ≤ 32
Reflections collected	5524
Independent reflections	5524 [R_{int} = 0.0388, R_{sigma} = 0.0435]
Data/restraints/parameters	5524/0/438
Goodness-of-fit on F^2	1.108
Final R indexes [I>=2σ (I)]	R_1 = 0.1144, wR_2 = 0.3068
Final R indexes [all data]	R_1 = 0.1181, wR_2 = 0.3085
Largest diff. peak/hole / e Å^{-3}	1.21/-0.68

8. ^{1}H, ^{13}C and ^{19}F NMR spectra of 4a–w and 5–10

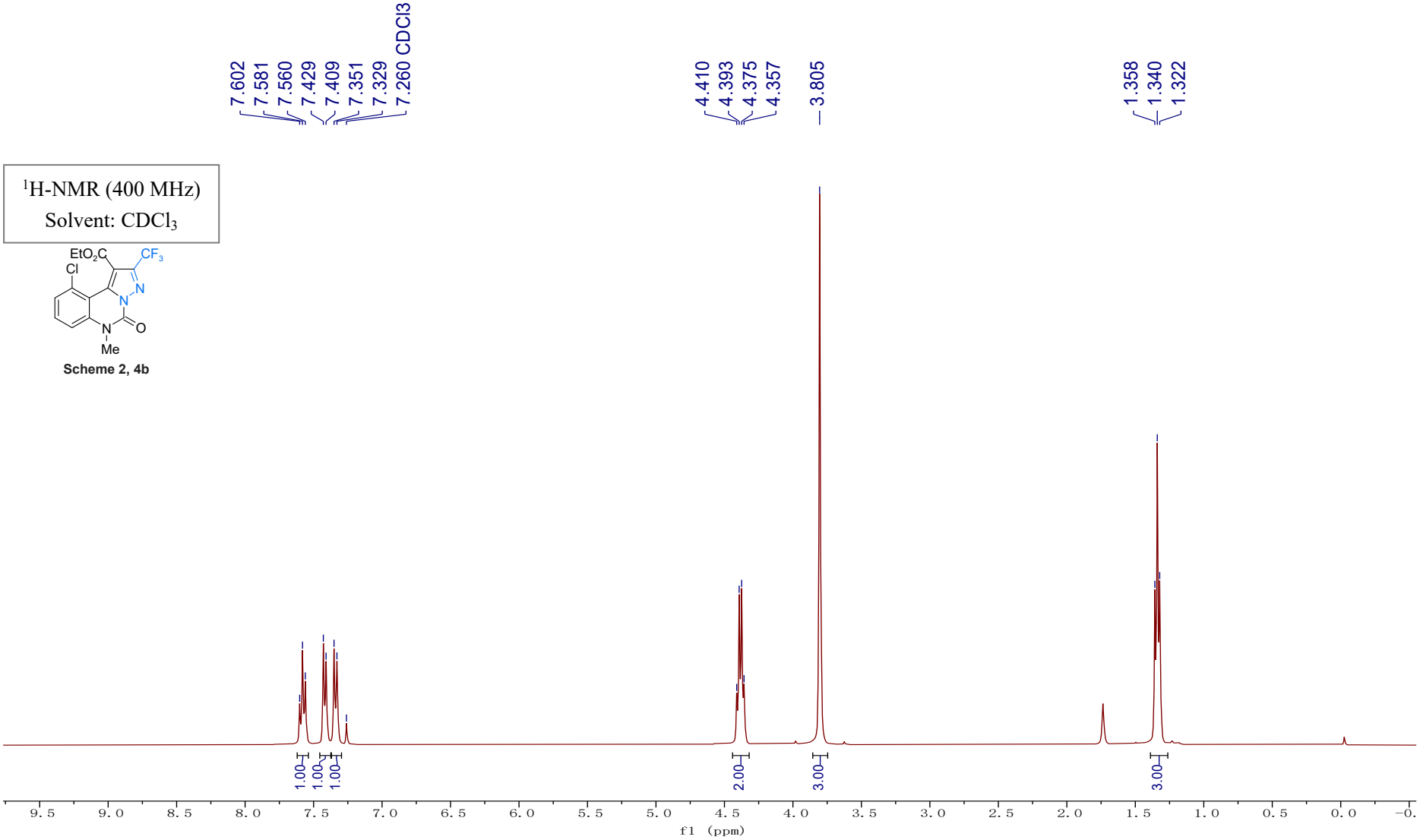

9.069
9.065
9.048
9.044
7.720
7.717
7.702
7.699
7.697
7.681
7.677
7.436
7.433
7.417
7.414
7.395
7.260 CDCl3
4.495
4.477
4.459
4.441
3.857
1.455
1.437
1.419
^{1}H-NMR (400 MHz)
Solvent: $CDCl_3$
EtO_2C
CF_3
N
N
O
Me
Scheme 2, 4a
0.95
1.00
2.00
2.00
3.00
3.00
f1 (ppm)

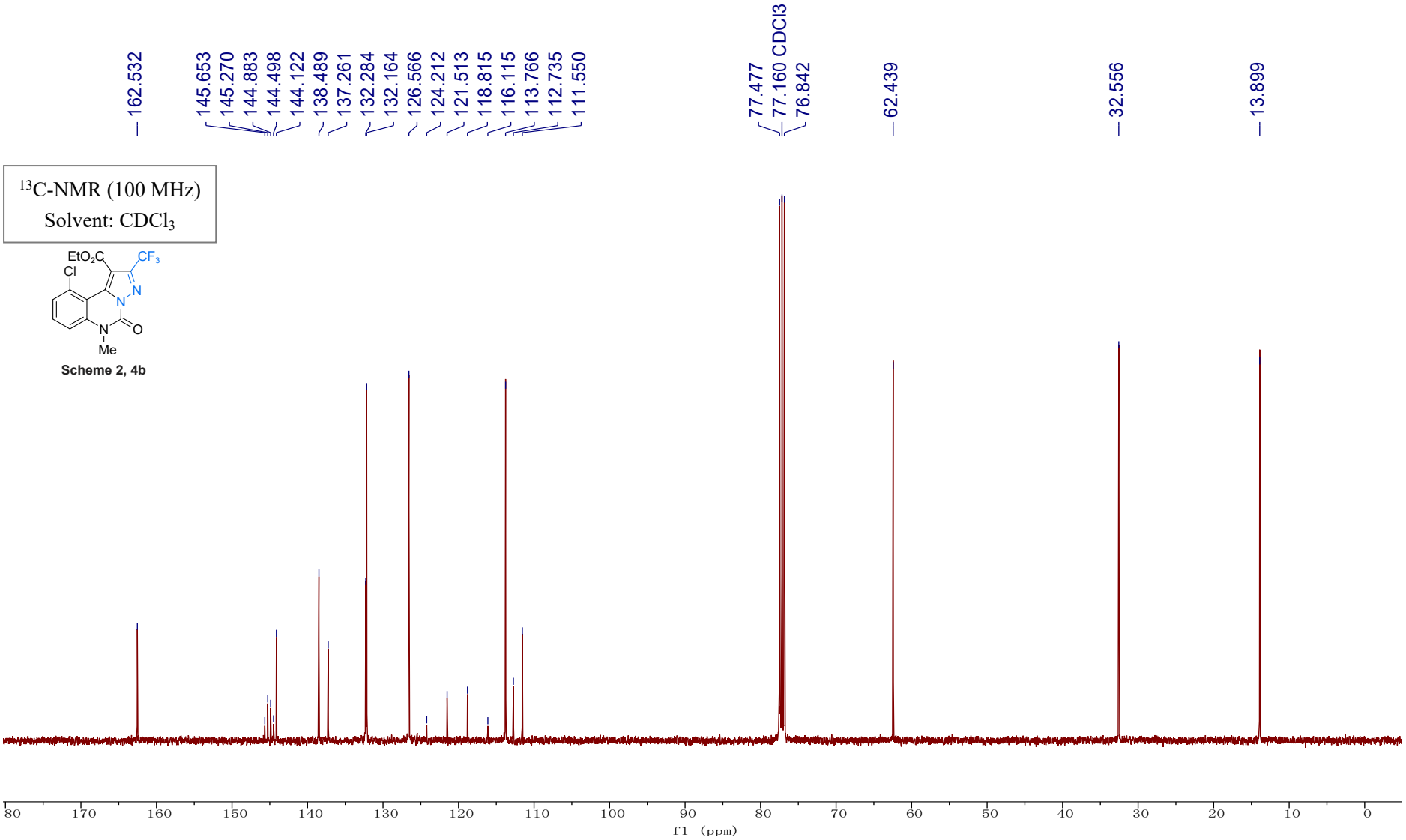

162.093
146.797
146.416
146.038
145.657
144.536
141.806
136.563
132.792
127.723
124.329
121.649
118.954
116.255
114.867
112.282
108.878
77.479
77.160 CDCl3
76.843
62.268
31.926
13.834
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
O
N
Me
Scheme 2, 4a
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

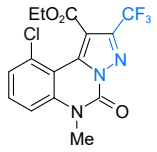


Scheme 2, 4a

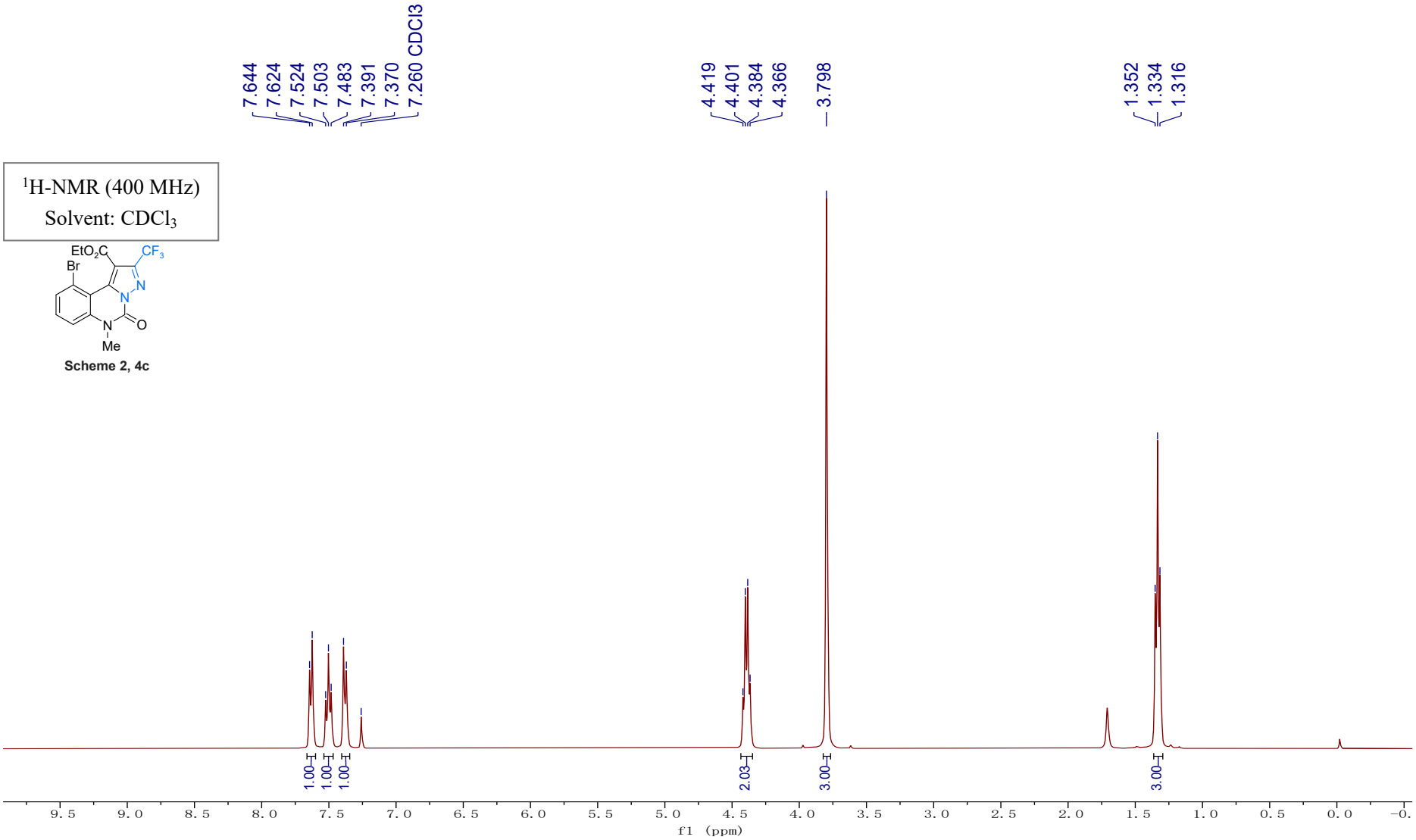

7.602
7.581
7.560
7.429
7.409
7.351
7.329
7.260 CDCl3
4.410
4.393
4.375
4.357
3.805
1.358
1.340
1.322
1H-NMR (400 MHz)
Solvent: CDCl3
EtO2C
CF3
Cl
N
N
O
N
Me
Scheme 2, 4b
1.00
1.00
1.00
2.00
3.00
3.00
f1 (ppm)

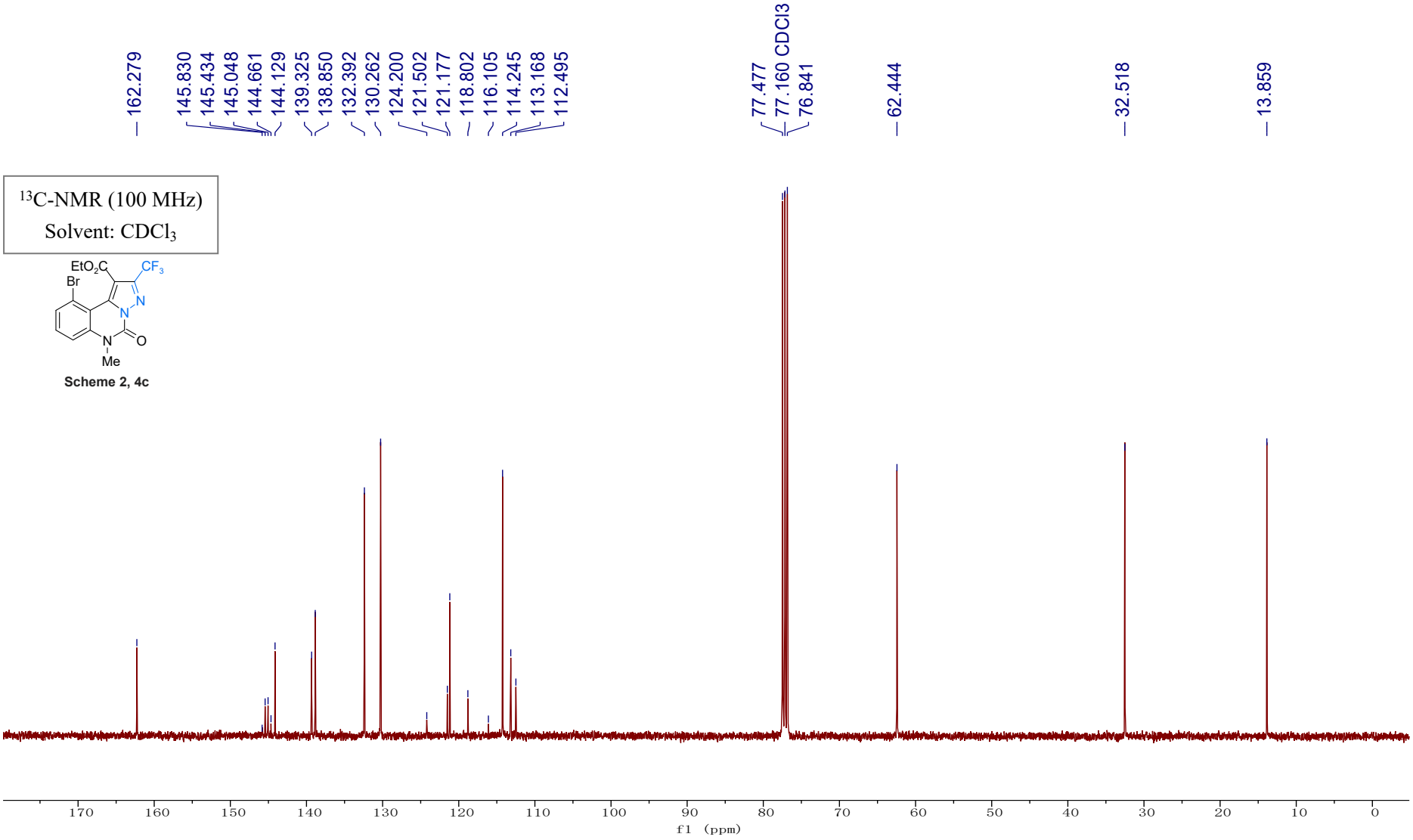

162.532
145.653
145.270
144.883
144.498
144.122
138.489
137.261
132.284
132.164
126.566
124.212
121.513
118.815
116.115
113.766
112.735
111.550
77.477
77.160 CDCl3
76.842
62.439
32.556
13.899
^{13}C-NMR (100 MHz)
Solvent: $CDCl_3$
EtO_2C
CF_3
Cl
N
N
O
N
Me
Scheme 2, 4b
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

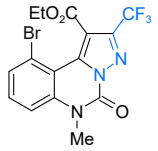


Scheme 2, 4b

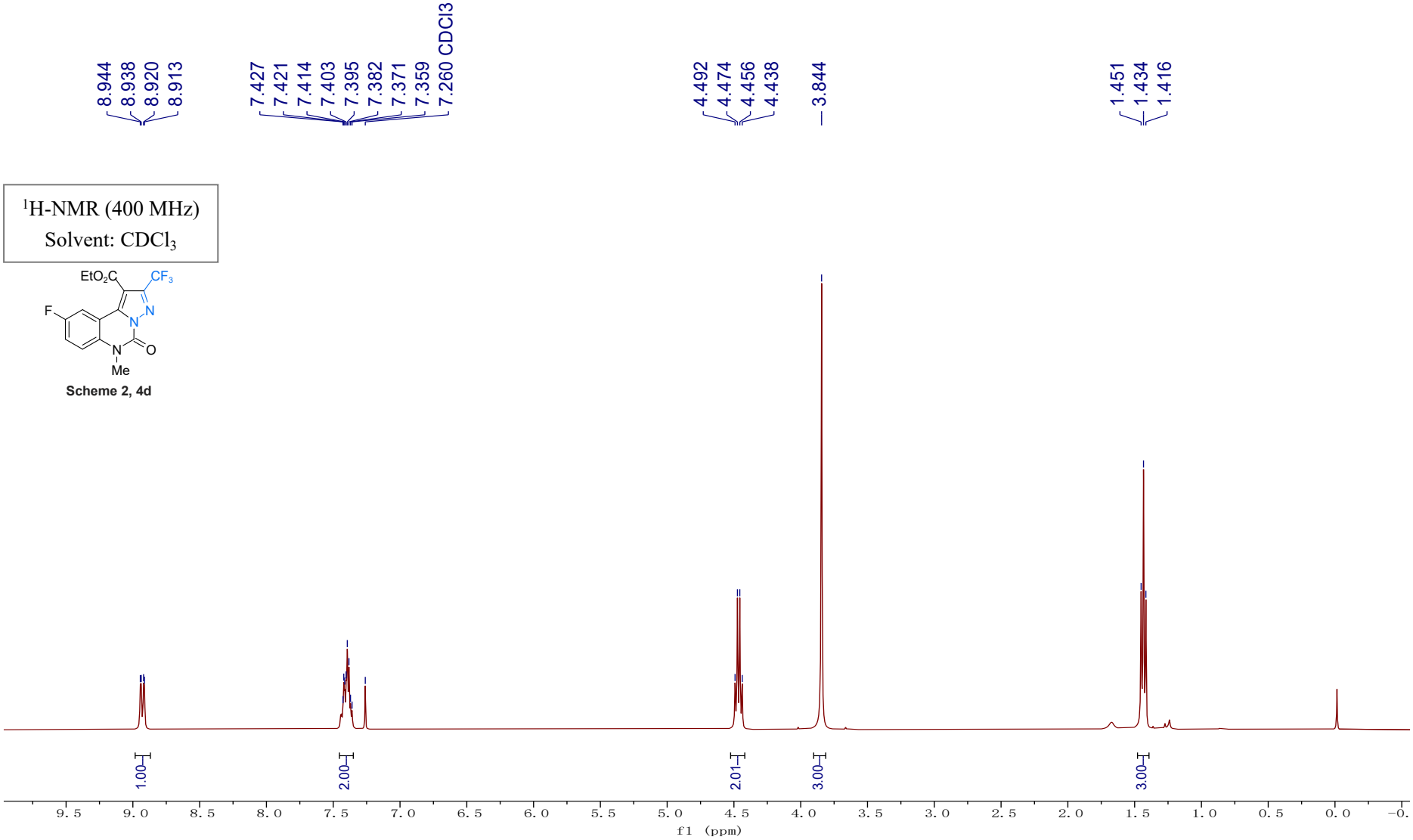

7.644
7.624
7.524
7.503
7.483
7.391
7.370
7.260 CDCl3
4.419
4.401
4.384
4.366
3.798
1.352
1.334
1.316
1H-NMR (400 MHz)
Solvent: CDCl3
EtO2C
CF3
Br
N
N
N
O
Me
Scheme 2, 4c
1.00
1.00
1.00
2.03
3.00
3.00
f1 (ppm)

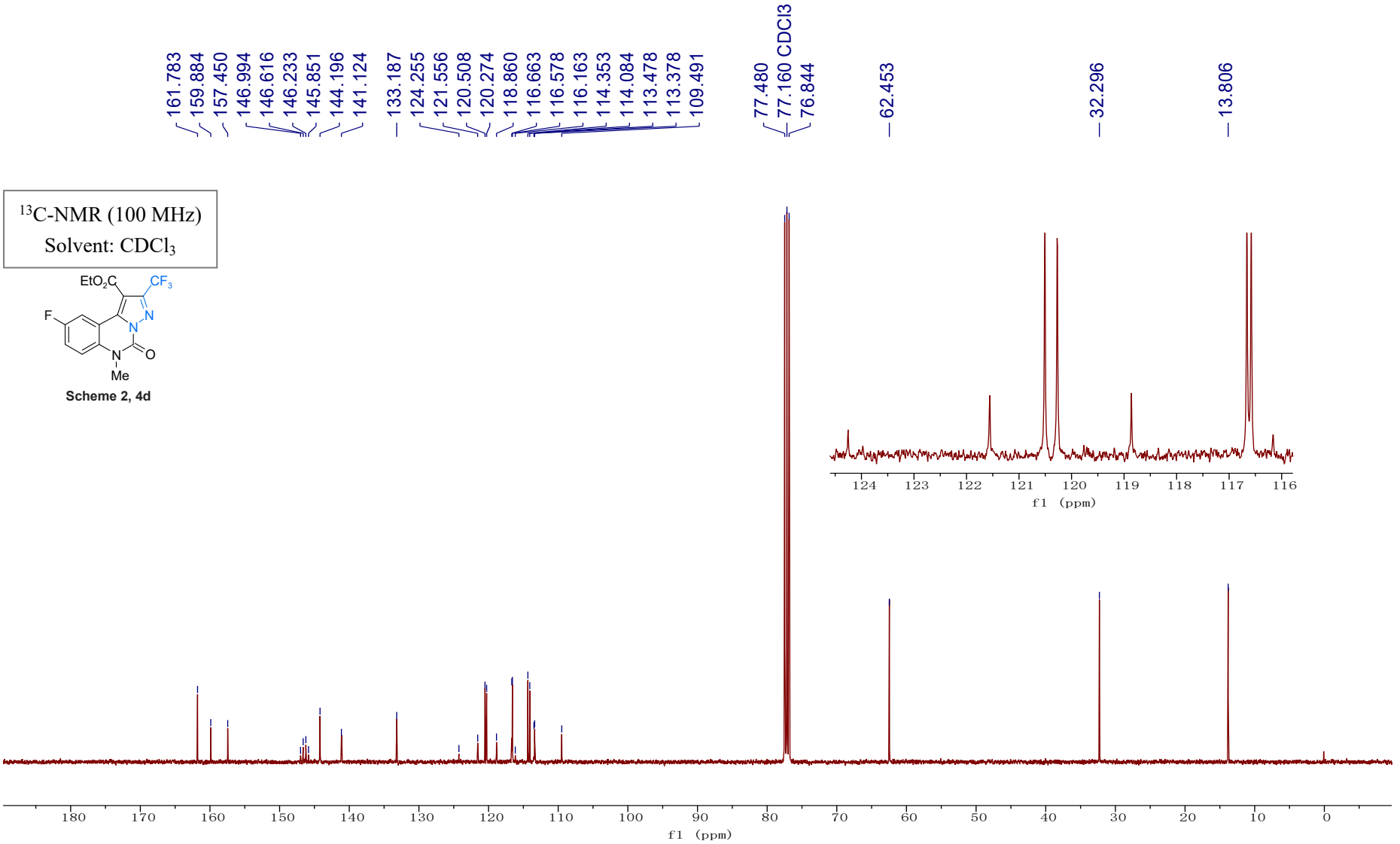

162.279
145.830
145.434
145.048
144.661
144.129
139.325
138.850
132.392
130.262
124.200
121.502
121.177
118.802
116.105
114.245
113.168
112.495
77.477
77.160 CDCl3
76.841
62.444
32.518
13.859
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
Br
N
N
N
O
Me
Scheme 2, 4c
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

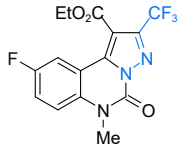


Scheme 2, 4c

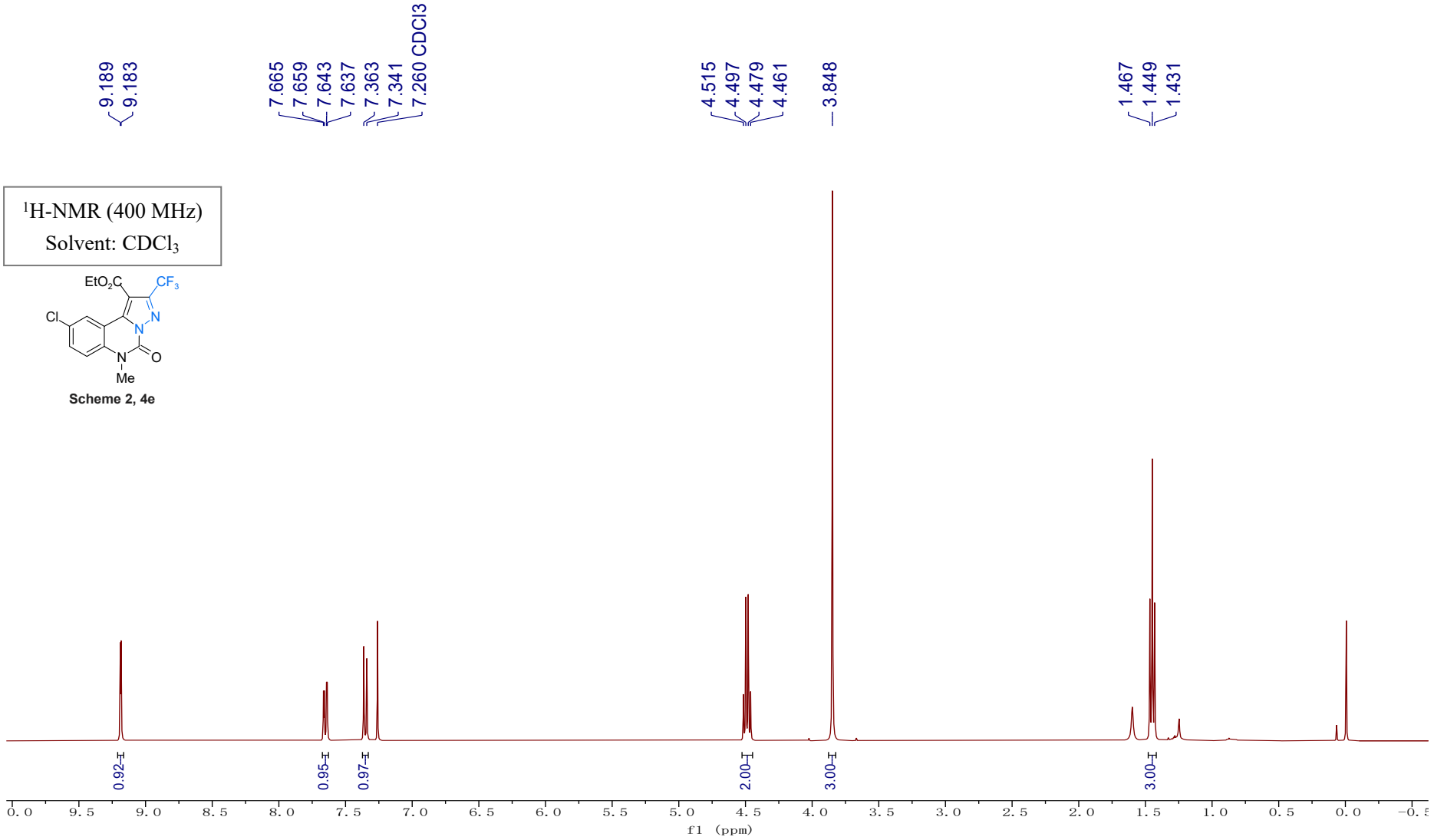

8.944
8.938
8.920
8.913
7.427
7.421
7.414
7.403
7.395
7.382
7.371
7.359
7.260 CDCl3
4.492
4.474
4.456
4.438
3.844
1.451
1.434
1.416
1H-NMR (400 MHz)
Solvent: CDCl3
EtO2C
CF3
F
N
N
O
N
Me
Scheme 2, 4d
1.00
2.00
2.01
3.00
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.
f1 (ppm)

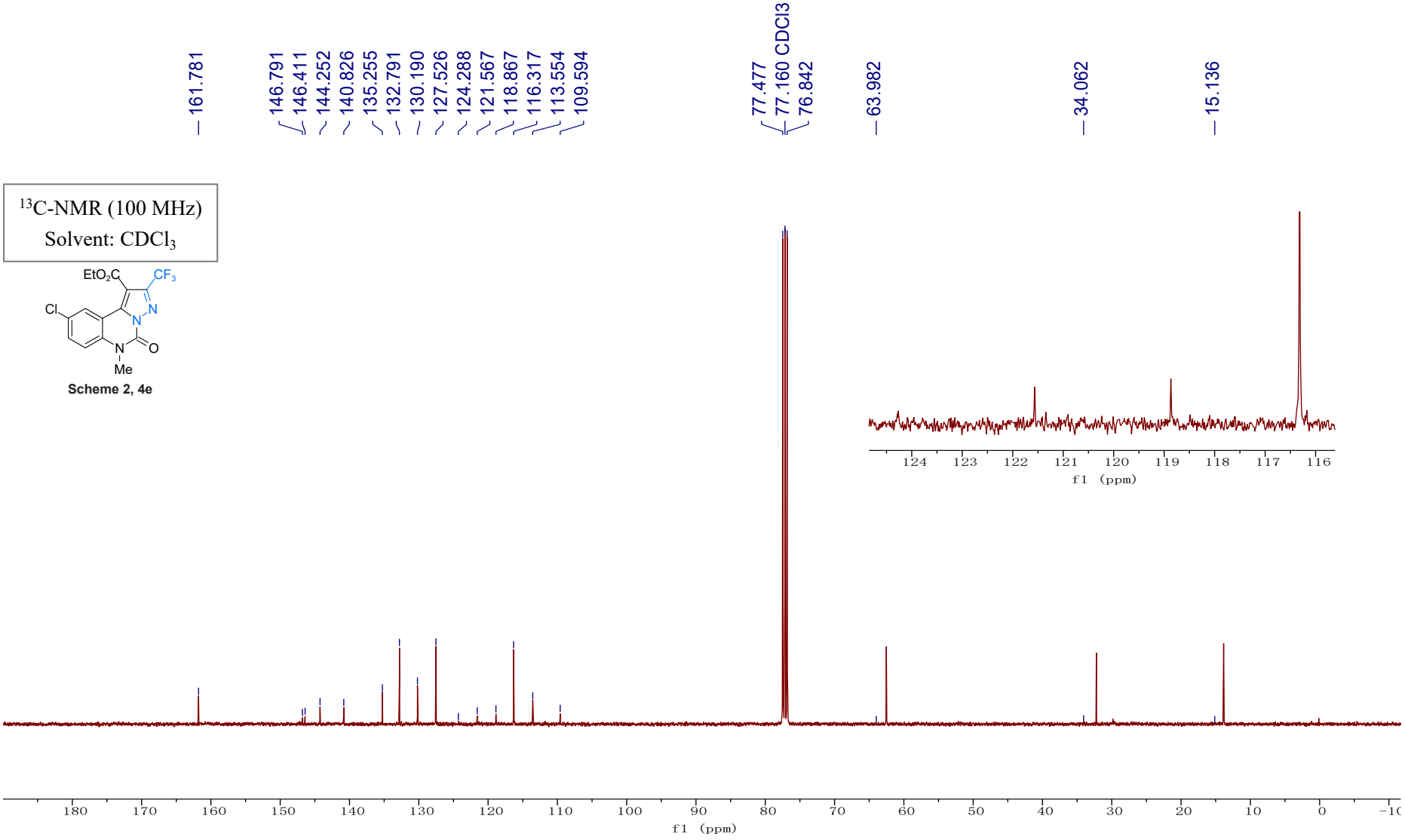

161.783
159.884
157.450
146.994
146.616
146.233
145.851
144.196
141.124
133.187
124.255
121.556
120.508
120.274
118.860
116.663
116.578
116.163
114.353
114.084
113.478
113.378
109.491
77.480
77.160 CDCl3
76.844
62.453
32.296
13.806
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
F
N
N
N
O
Me
Scheme 2, 4d
f1 (ppm)
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

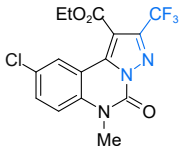


Scheme 2, 4d

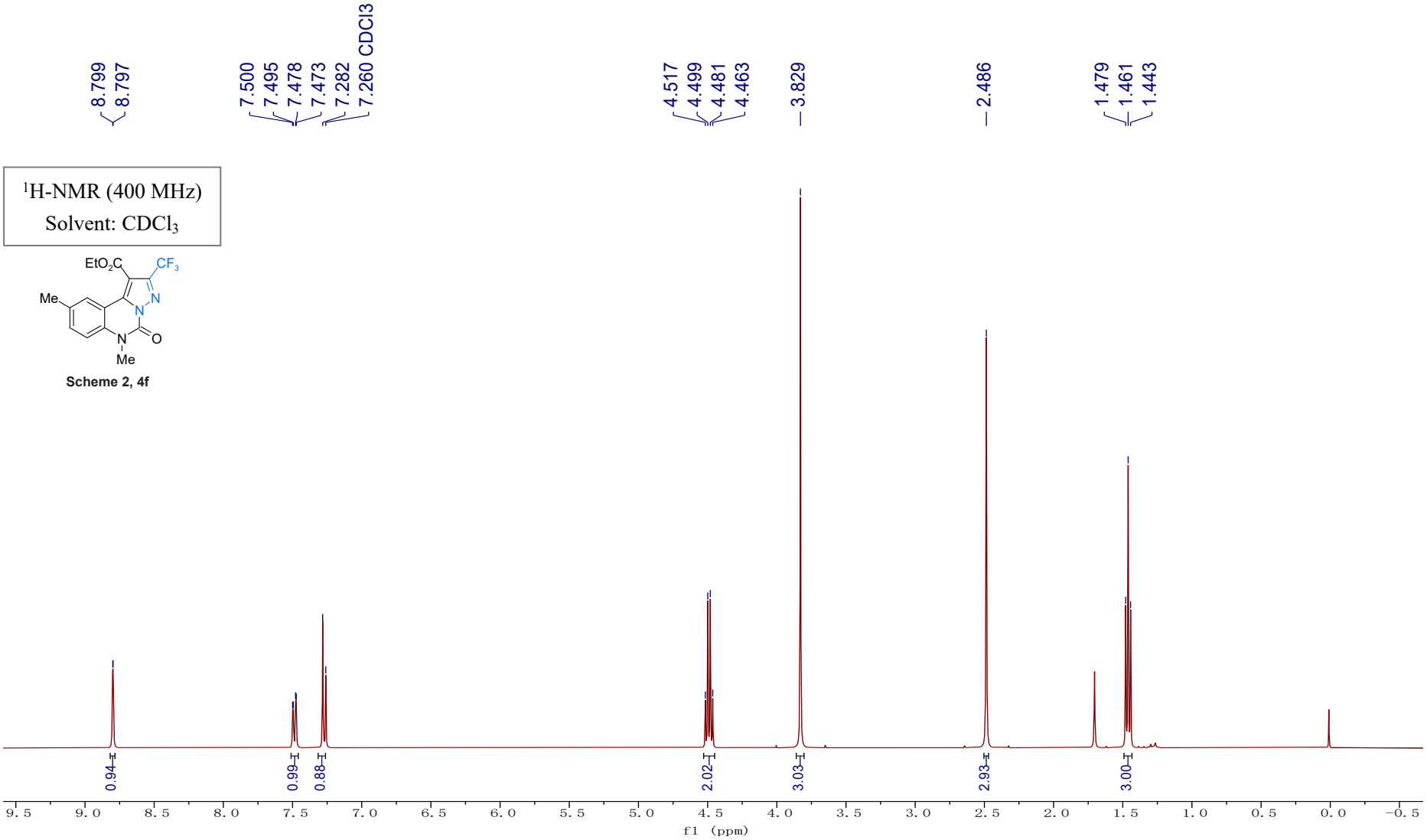

9.189
9.183
7.665
7.659
7.643
7.637
7.363
7.341
7.260 CDCl3
4.515
4.497
4.479
4.461
3.848
1.467
1.449
1.431
^{1}H-NMR (400 MHz)
Solvent: $CDCl_3$
EtO_2C
CF_3
Cl
N
N
N
O
Me
Scheme 2, 4e
0.92
0.95
0.97
2.00
3.00
3.00
f1 (ppm)

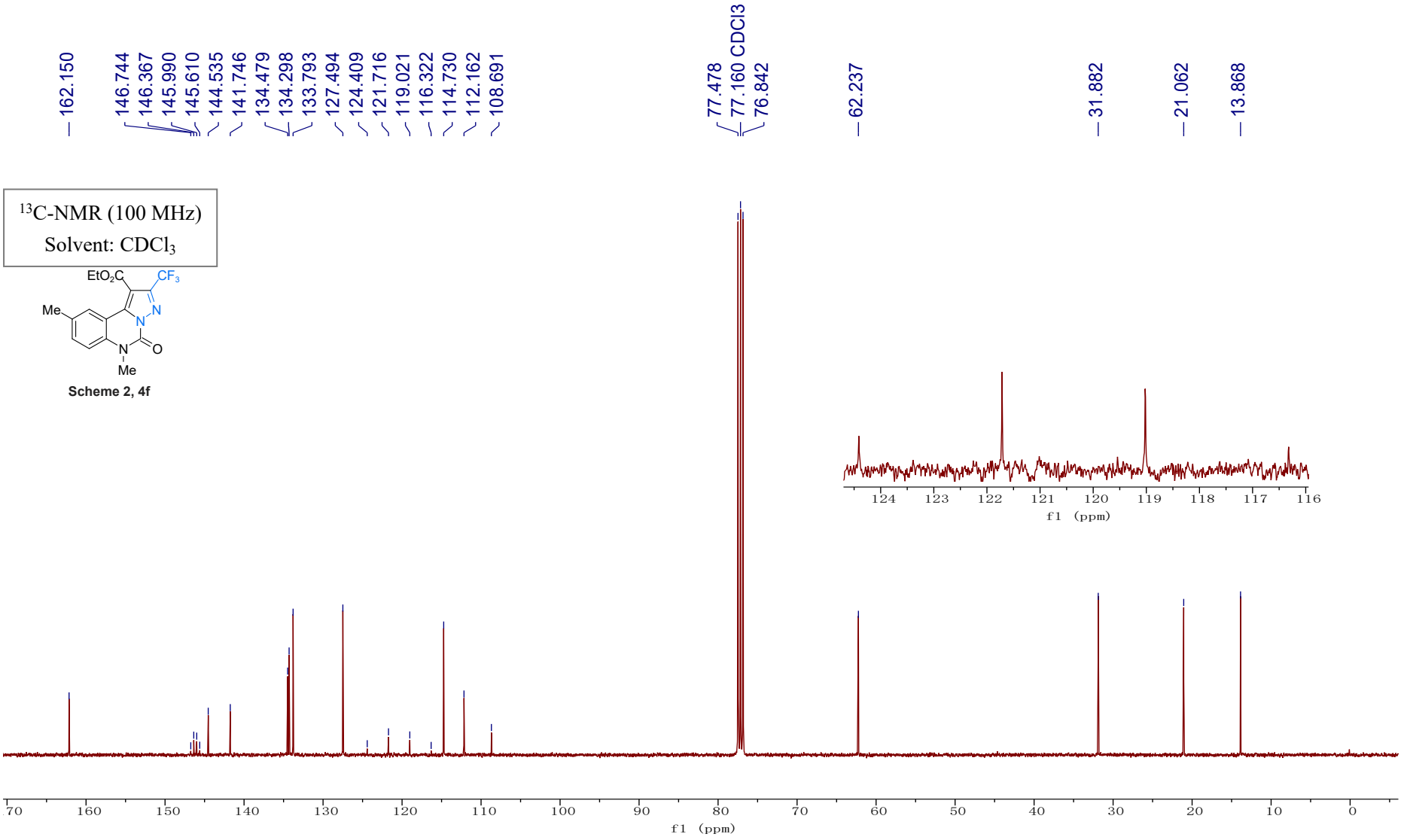

161.781
146.791
146.411
144.252
140.826
135.255
132.791
130.190
127.526
124.288
121.567
118.867
116.317
113.554
109.594
77.477
77.160 CDCl3
76.842
63.982
34.062
15.136
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
Cl
N
N
O
Me
Scheme 2, 4e
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

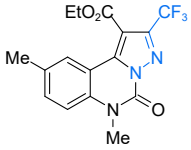


Scheme 2, 4e

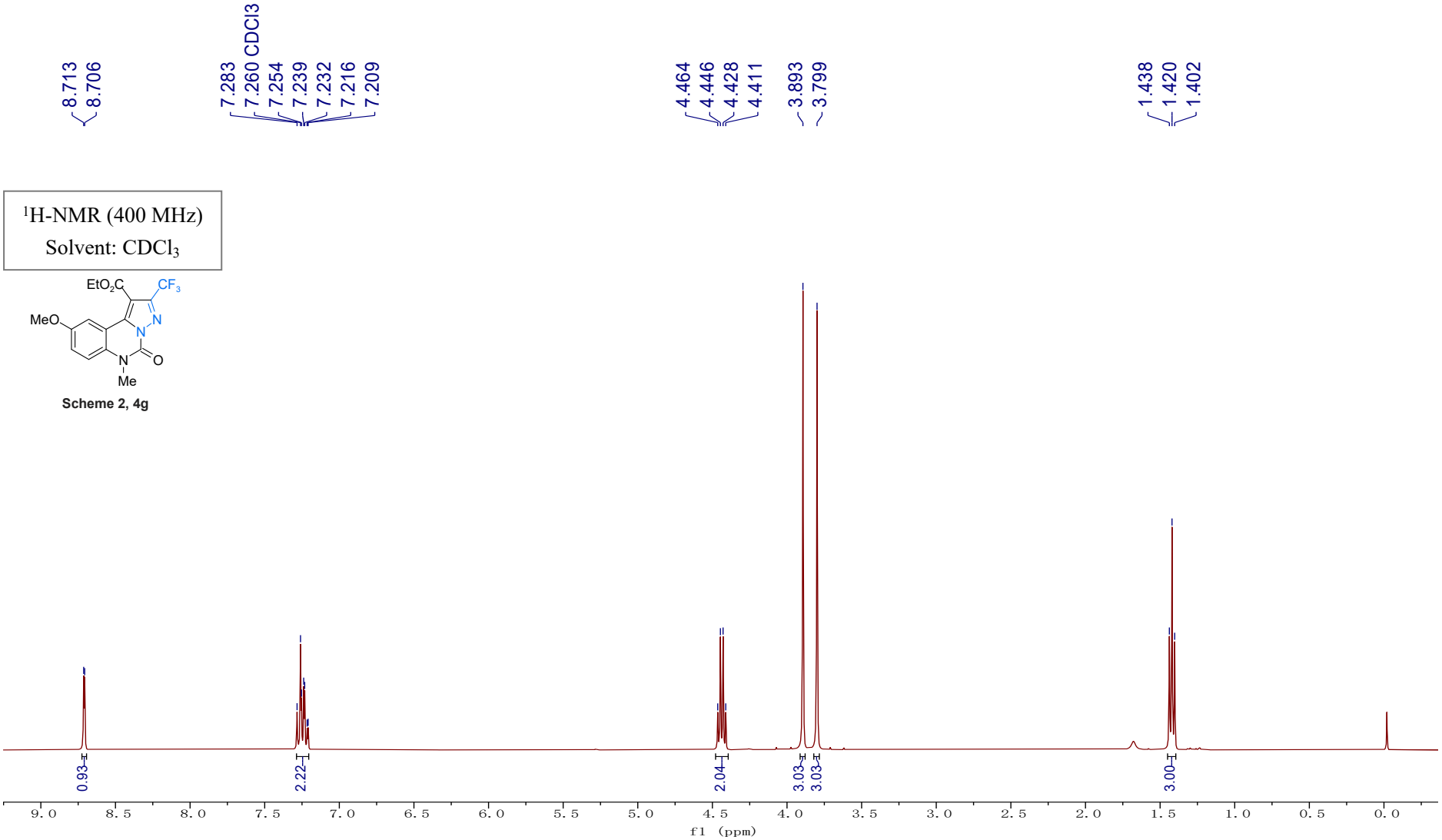

8.799
8.797
7.500
7.495
7.478
7.473
7.282
7.260 CDCl3
4.517
4.499
4.481
4.463
3.829
2.486
1.479
1.461
1.443
1H-NMR (400 MHz)
Solvent: CDCl3
EtO2C
CF3
Me
N
N
O
Me
Scheme 2, 4f
0.94
0.99
0.88
2.02
3.03
2.93
3.00
f1 (ppm)

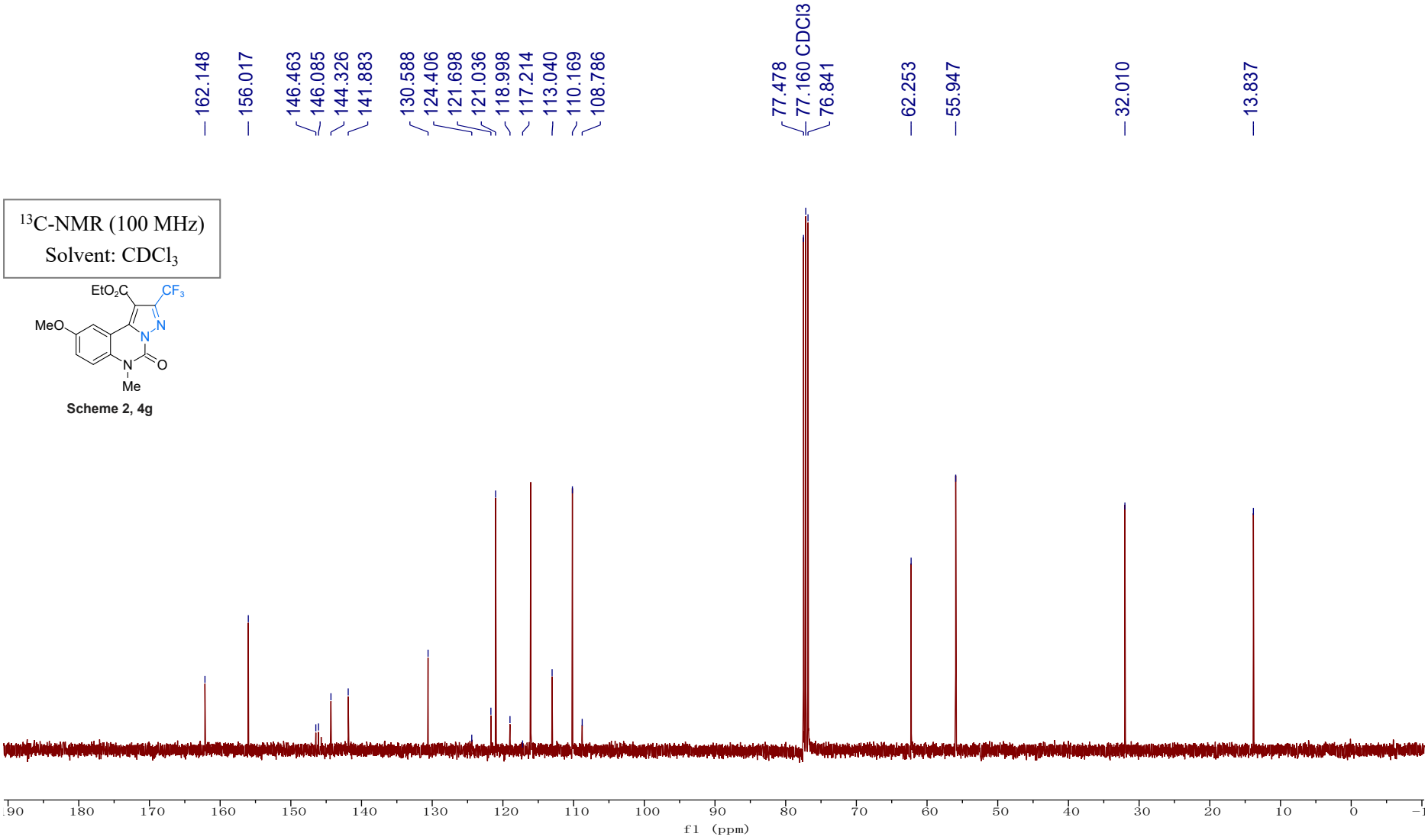

162.150
146.744
146.367
145.990
145.610
144.535
141.746
134.479
134.298
133.793
127.494
124.409
121.716
119.021
116.322
114.730
112.162
108.691
77.478
77.160 CDCl3
76.842
62.237
31.882
21.062
13.868
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
Me
N
N
O
N
Me
Scheme 2, 4f
f1 (ppm)
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

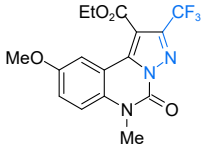


Scheme 2, 4f

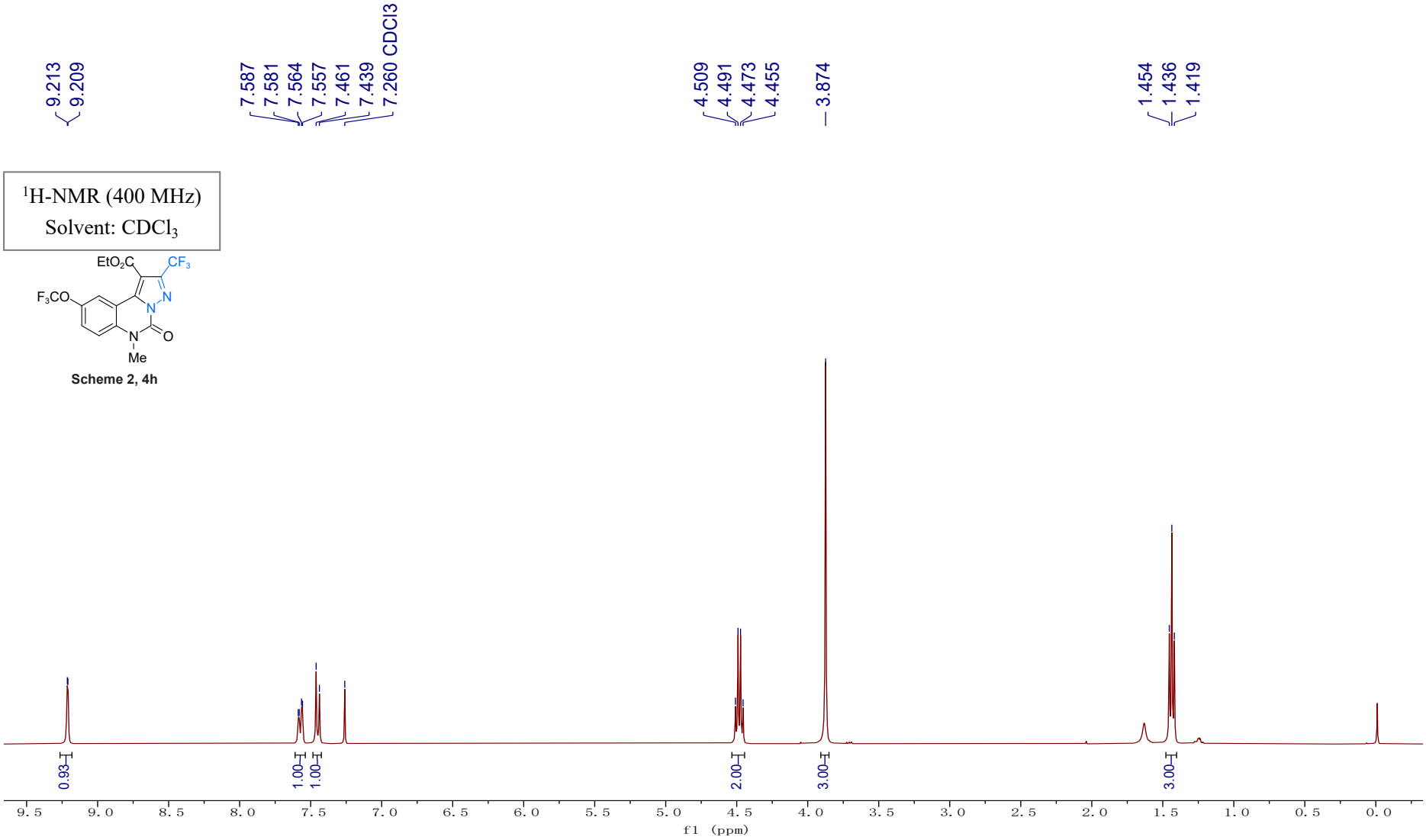

8.713
8.706
7.283
7.260 CDCl3
7.254
7.239
7.232
7.216
7.209
4.464
4.446
4.428
4.411
3.893
3.799
1.438
1.420
1.402
1H-NMR (400 MHz)
Solvent: CDCl3
EtO2C
CF3
MeO
N
N
O
Me
Scheme 2, 4g
0.93
2.22
2.04
3.03
3.03
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

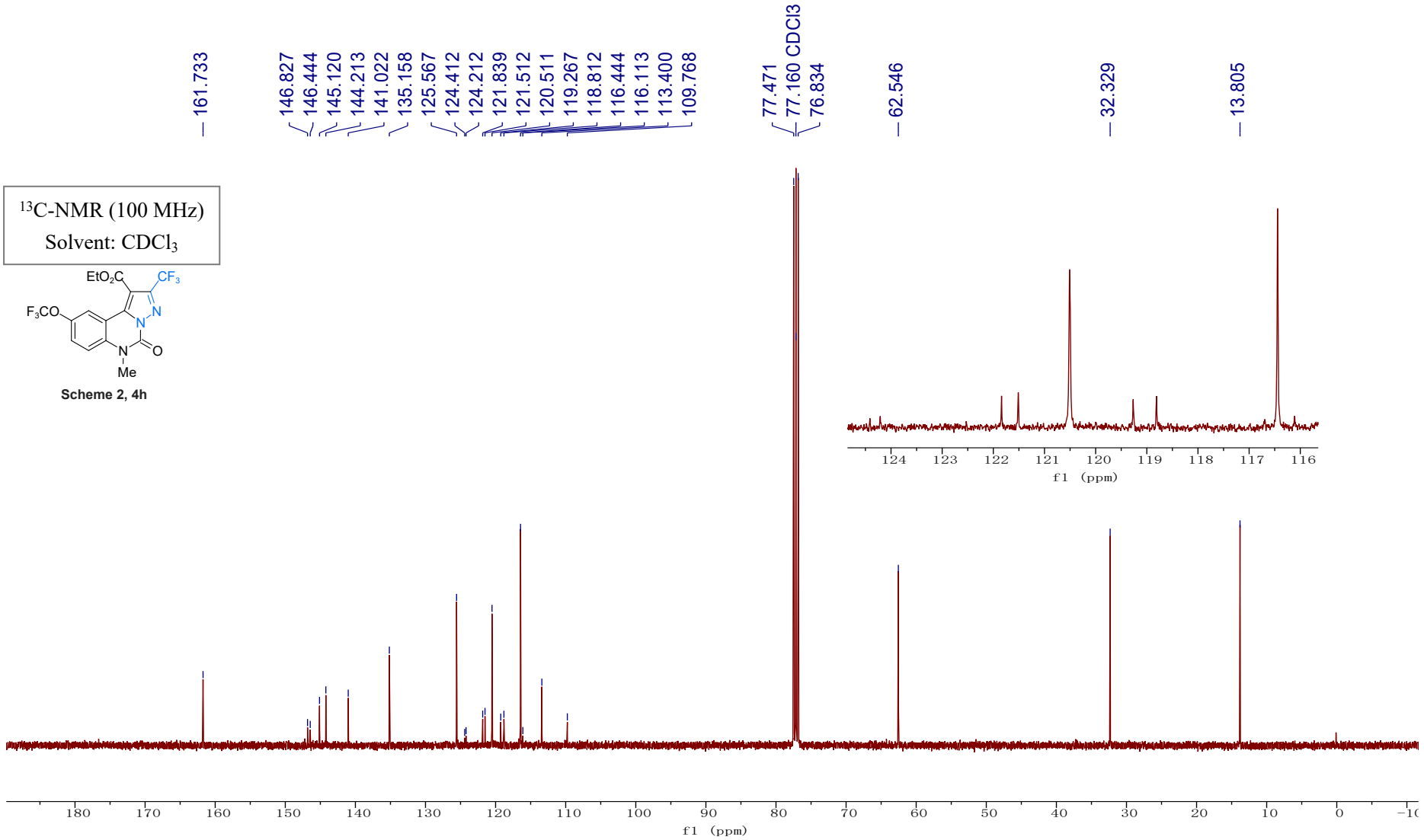

162.148
156.017
146.463
146.085
144.326
141.883
130.588
124.406
121.698
121.036
118.998
117.214
113.040
110.169
108.786
77.478
77.160 CDCl3
76.841
62.253
55.947
32.010
13.837
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
MeO
N
N
O
Me
Scheme 2, 4g
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

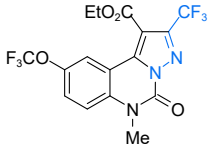


Scheme 2, 4g

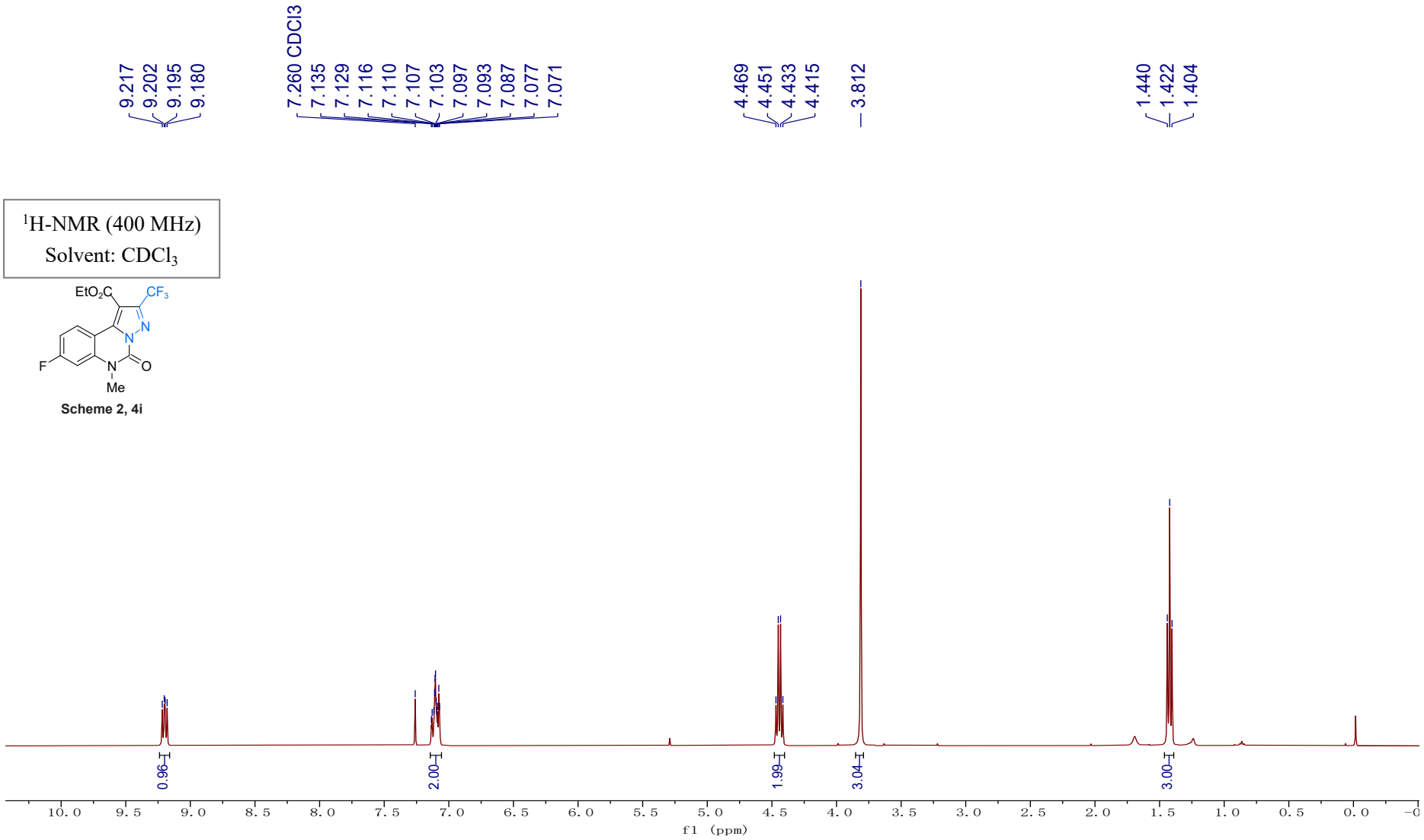

9.213
9.209
7.587
7.581
7.564
7.557
7.461
7.439
7.260 CDCl3
4.509
4.491
4.473
4.455
3.874
1.454
1.436
1.419
1H-NMR (400 MHz)
Solvent: CDCl3
EtO2C
CF3
F3CO
N
N
O
Me
Scheme 2, 4h
0.93
1.00
1.00
2.00
3.00
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

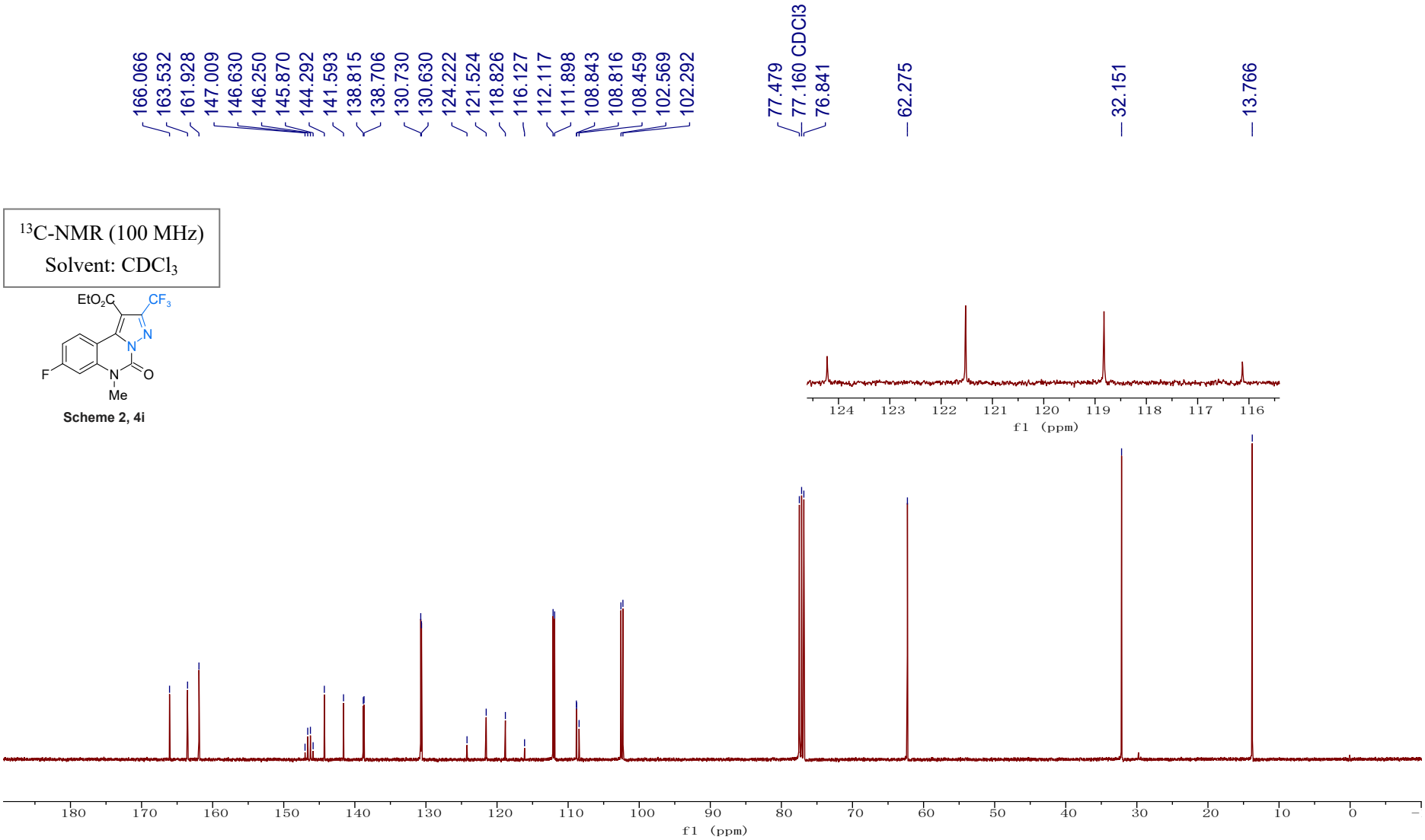

161.733
146.827
146.444
145.120
144.213
141.022
135.158
125.567
124.412
124.212
121.839
121.512
120.511
119.267
118.812
116.444
116.113
113.400
109.768
77.471
77.160 CDCl3
76.834
62.546
32.329
13.805
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
F3CO
N
N
O
Me
Scheme 2, 4h
f1 (ppm)
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

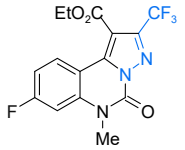


Scheme 2, 4h

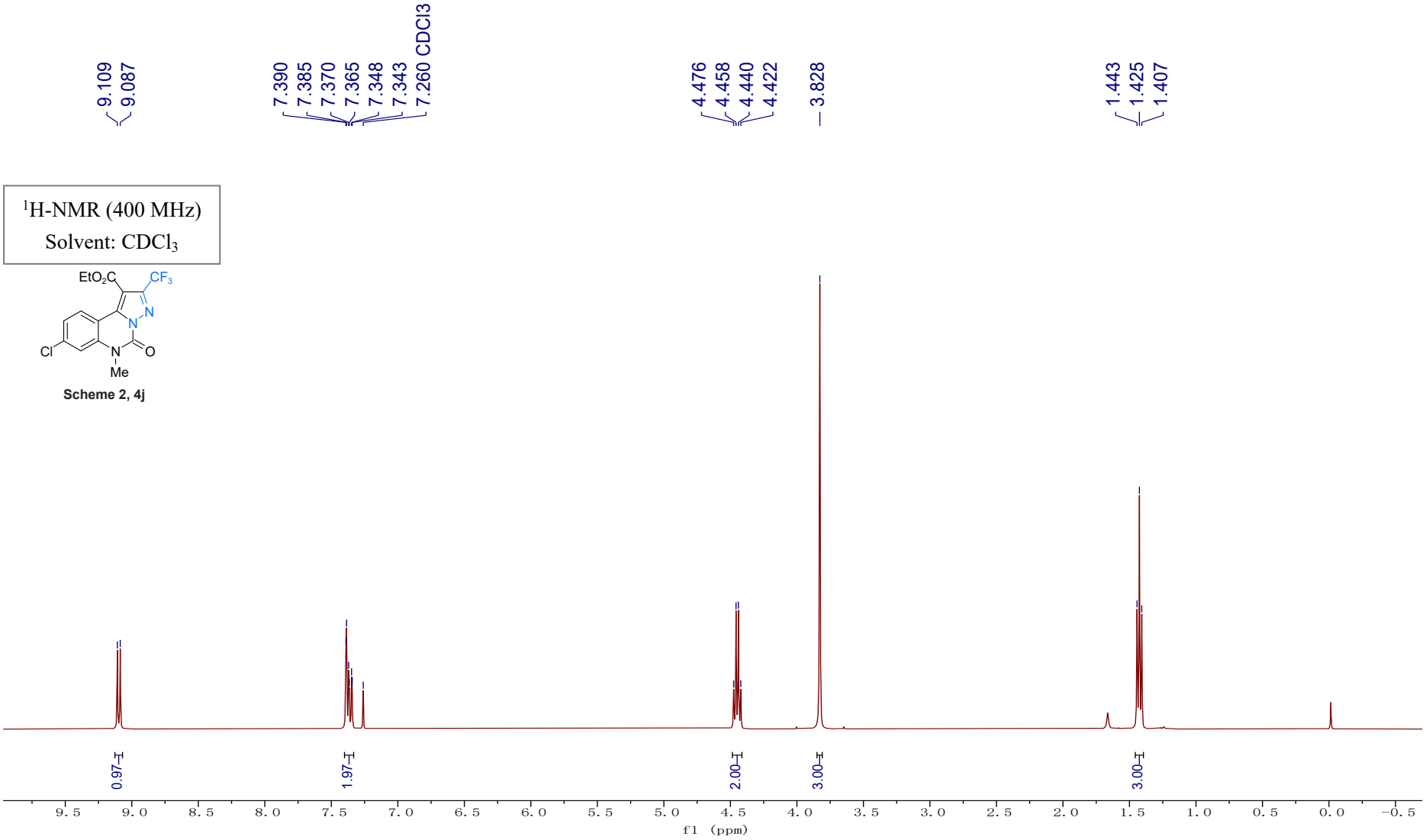

9.217
9.202
9.195
9.180
7.260 CDCl3
7.135
7.129
7.116
7.110
7.107
7.103
7.097
7.093
7.087
7.077
7.071
4.469
4.451
4.433
4.415
3.812
1.440
1.422
1.404
1H-NMR (400 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
F
N
O
Me
Scheme 2, 4i
0.96
2.00
1.99
3.04
3.00
f1 (ppm)

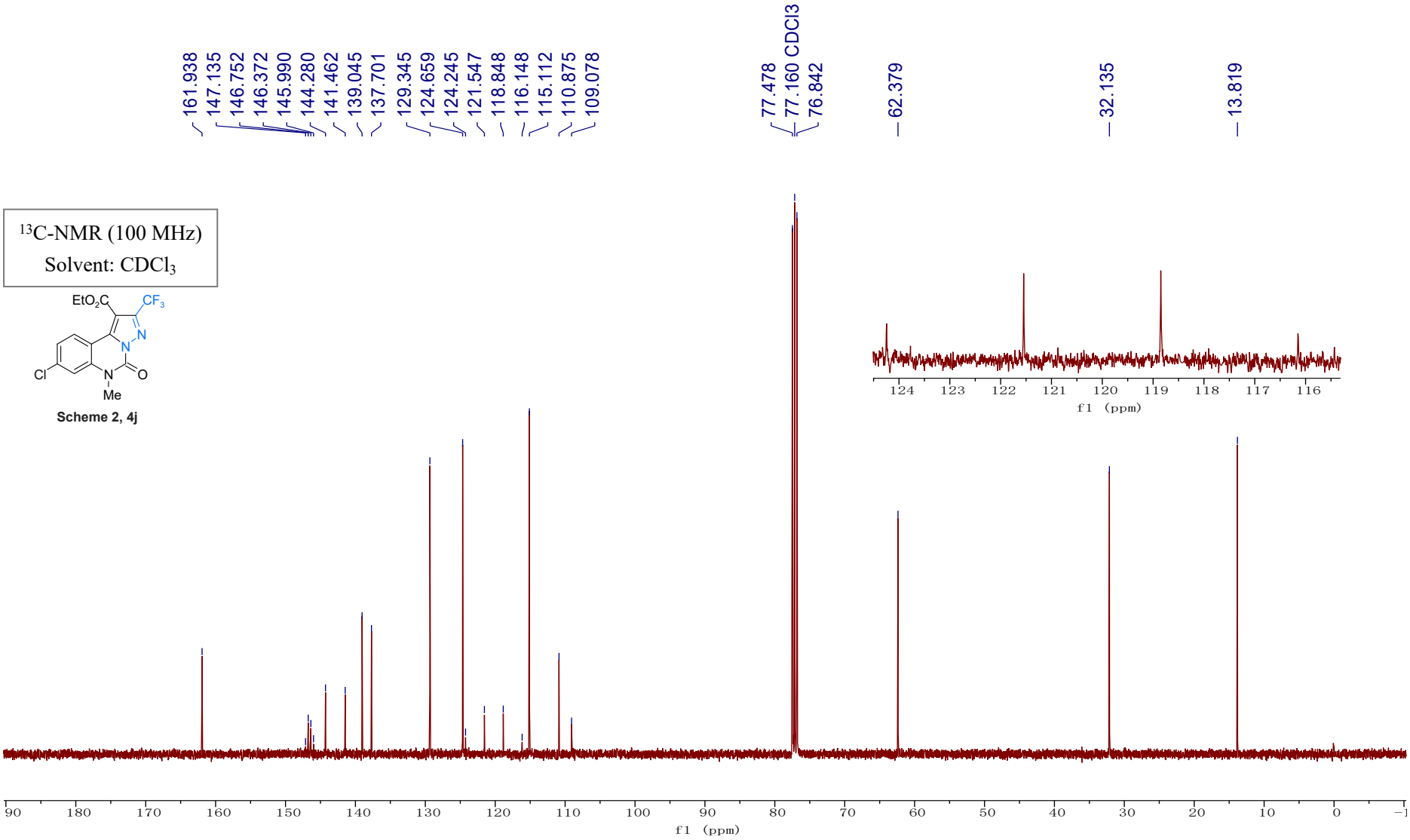

166.066
163.532
161.928
147.009
146.630
146.250
145.870
144.292
141.593
138.815
138.706
130.730
130.630
124.222
121.524
118.826
116.127
112.117
111.898
108.843
108.816
108.459
102.569
102.292
77.479
77.160 CDCl3
76.841
62.275
32.151
13.766
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
F
N
O
Me
Scheme 2, 4i
f1 (ppm)
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

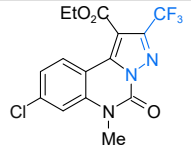


Scheme 2, 4i

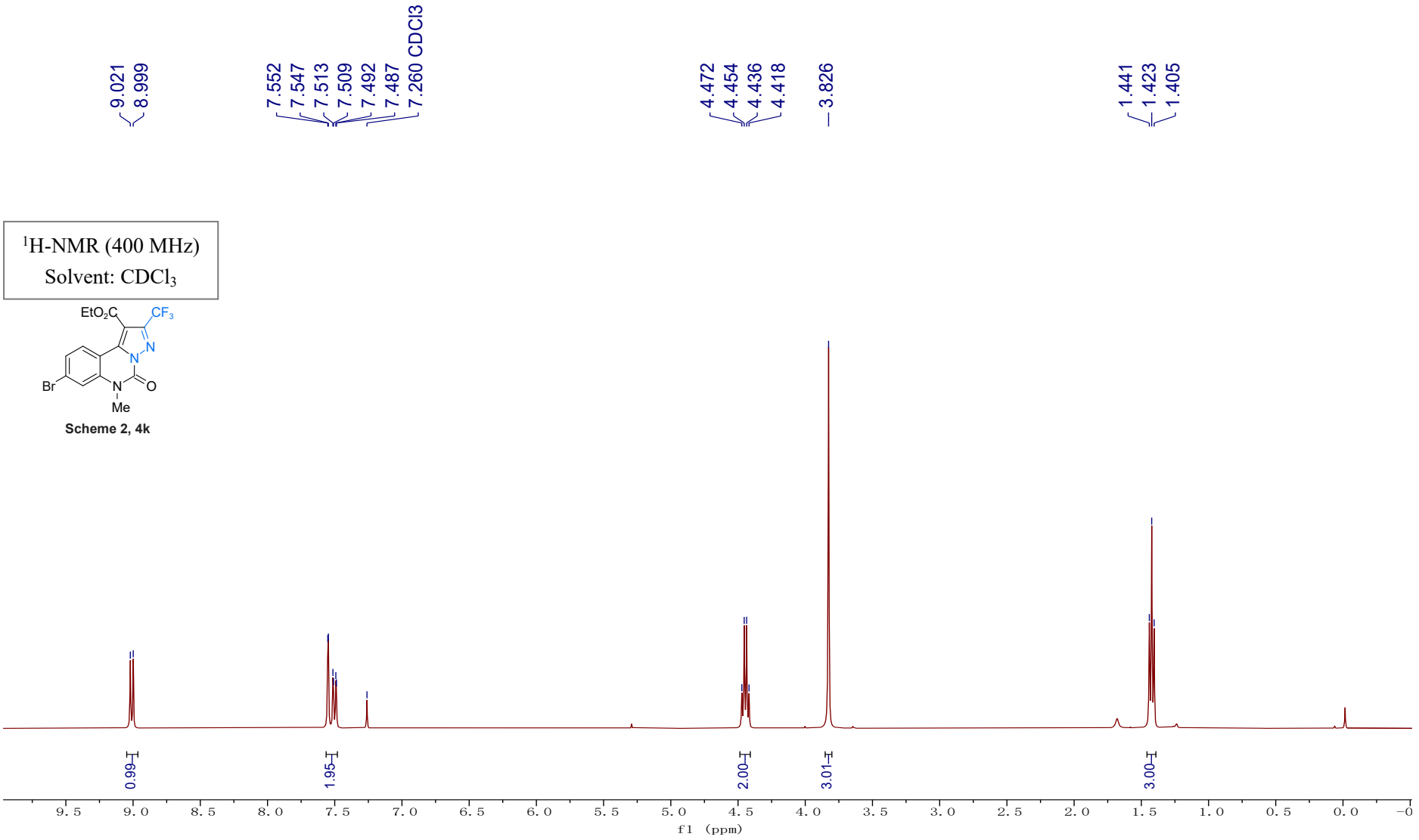

9.109
9.087
7.390
7.385
7.370
7.365
7.348
7.343
7.260 CDCl3
4.476
4.458
4.440
4.422
3.828
1.443
1.425
1.407
^{1}H-NMR (400 MHz)
Solvent: $CDCl_3$
EtO_2C
CF_3
N
N
Cl
N
O
Me
Scheme 2, 4j
0.97
1.97
2.00
3.00
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)

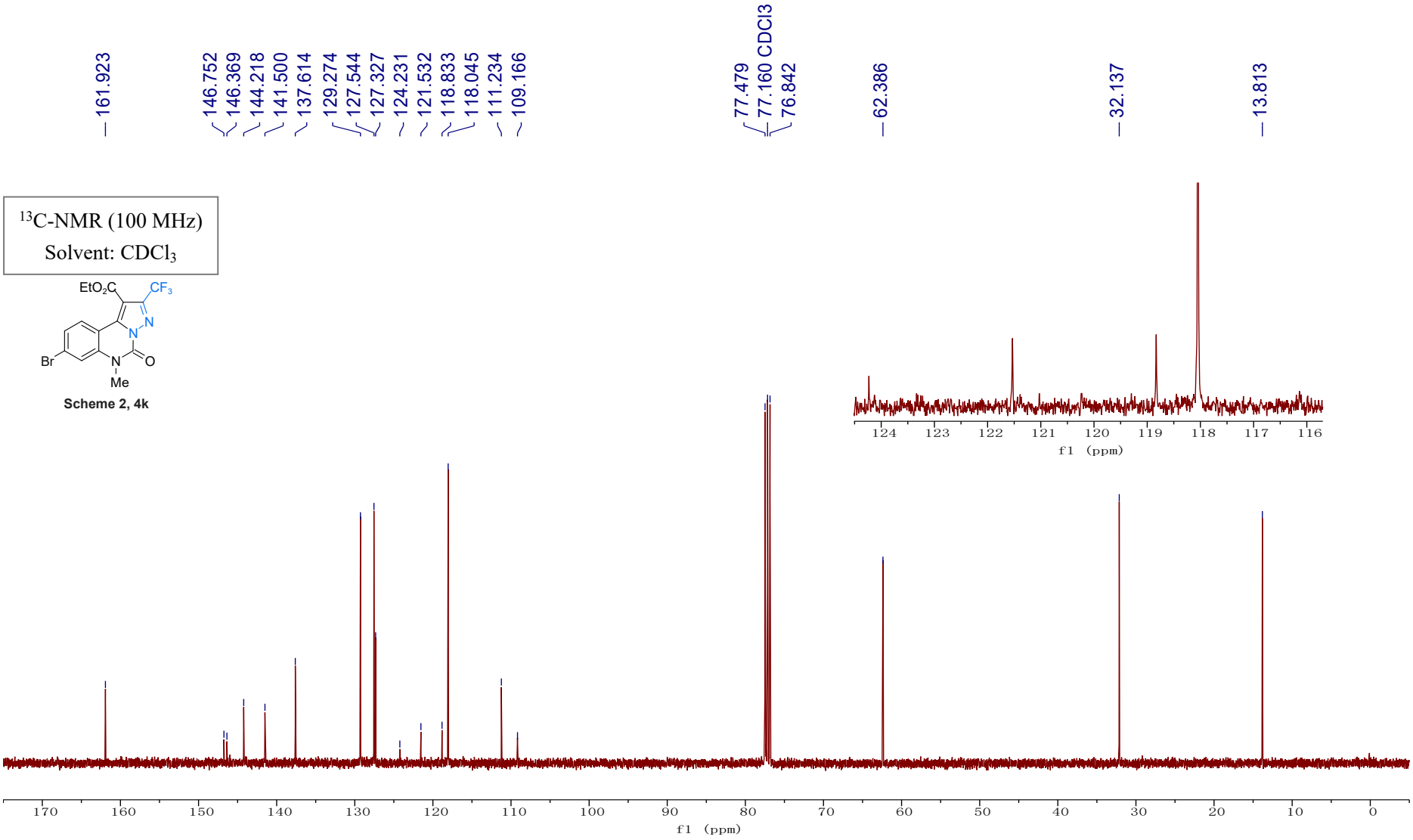

161.938
147.135
146.752
146.372
145.990
144.280
141.462
139.045
137.701
129.345
124.659
124.245
121.547
118.848
116.148
115.112
110.875
109.078
77.478
77.160 CDCl3
76.842
62.379
32.135
13.819
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
Cl
N
O
Me
Scheme 2, 4j
f1 (ppm)
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

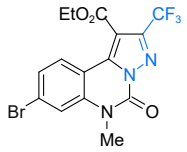


Scheme 2, 4j

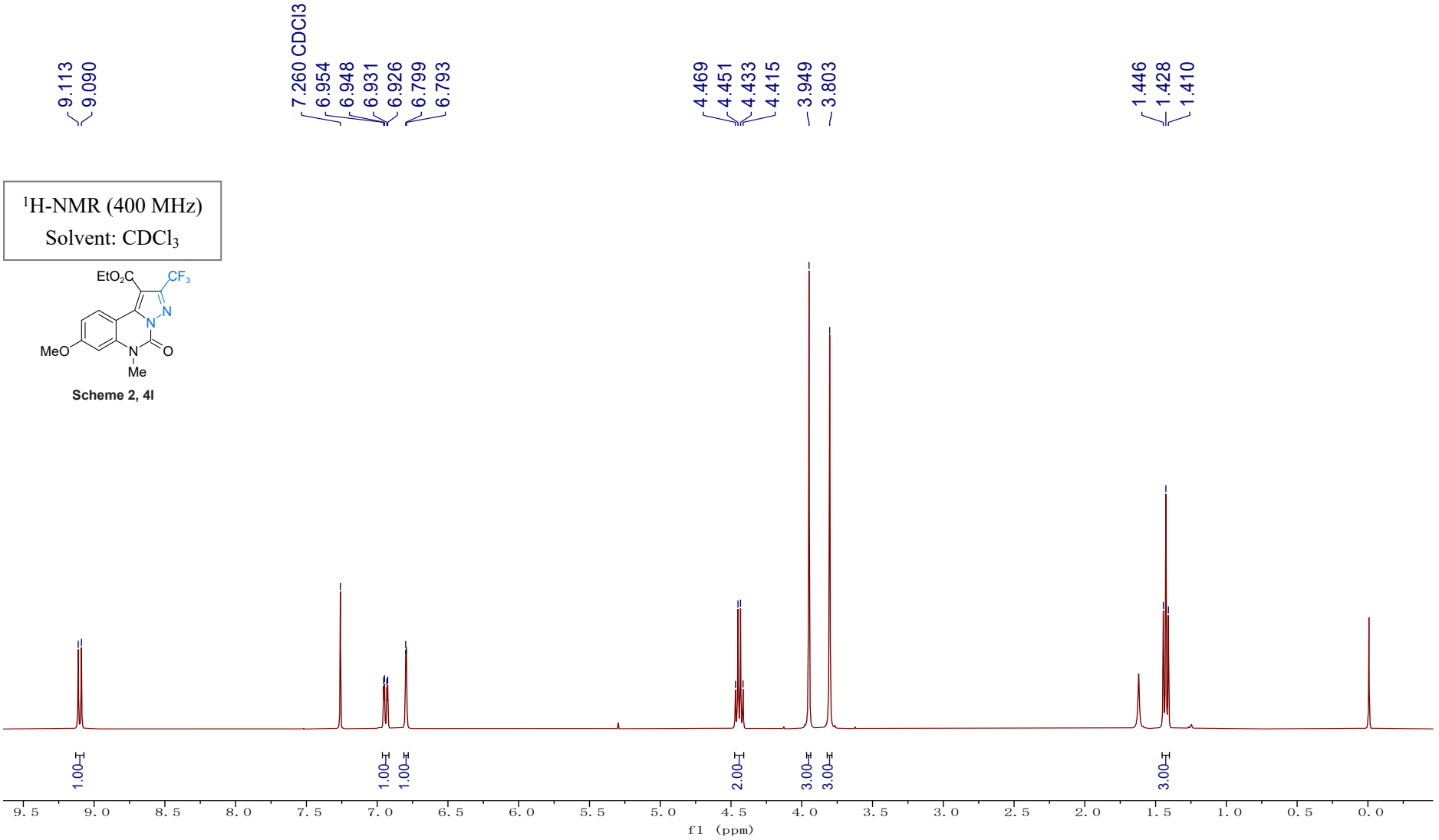

9.021
8.999
7.552
7.547
7.513
7.509
7.492
7.487
7.260 CDCl3
4.472
4.454
4.436
4.418
3.826
1.441
1.423
1.405
^{1}H-NMR (400 MHz)
Solvent: $CDCl_3$
EtO_2C
CF_3
N
N
Br
N
O
Me
Scheme 2, 4k
0.99
1.95
2.00
3.01
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0
f1 (ppm)

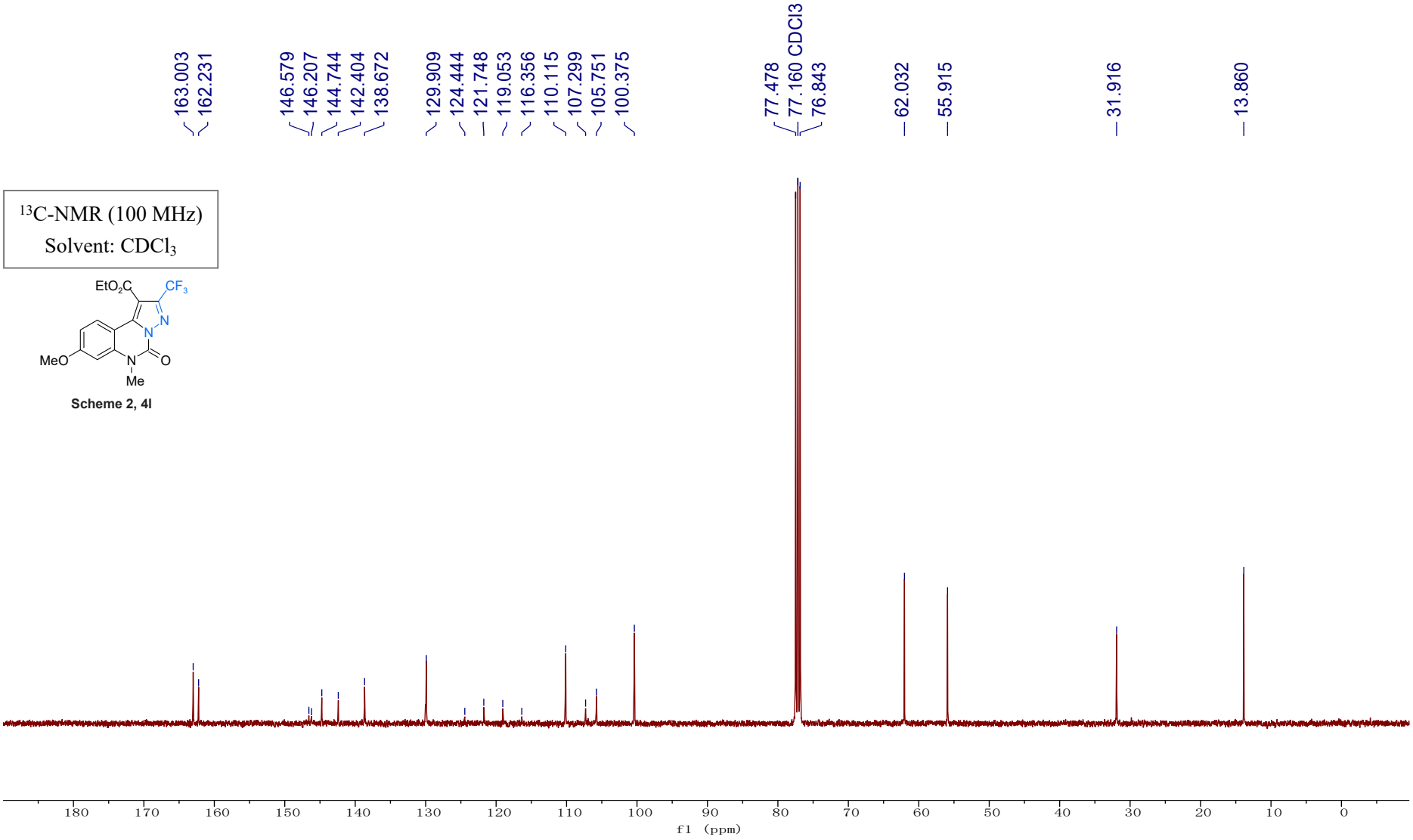

161.923
146.752
146.369
144.218
141.500
137.614
129.274
127.544
127.327
124.231
121.532
118.833
118.045
111.234
109.166
77.479
77.160 CDCl3
76.842
62.386
32.137
13.813
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
Br
N
O
Me
Scheme 2, 4k
f1 (ppm)
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

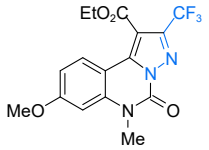


Scheme 2, 4k

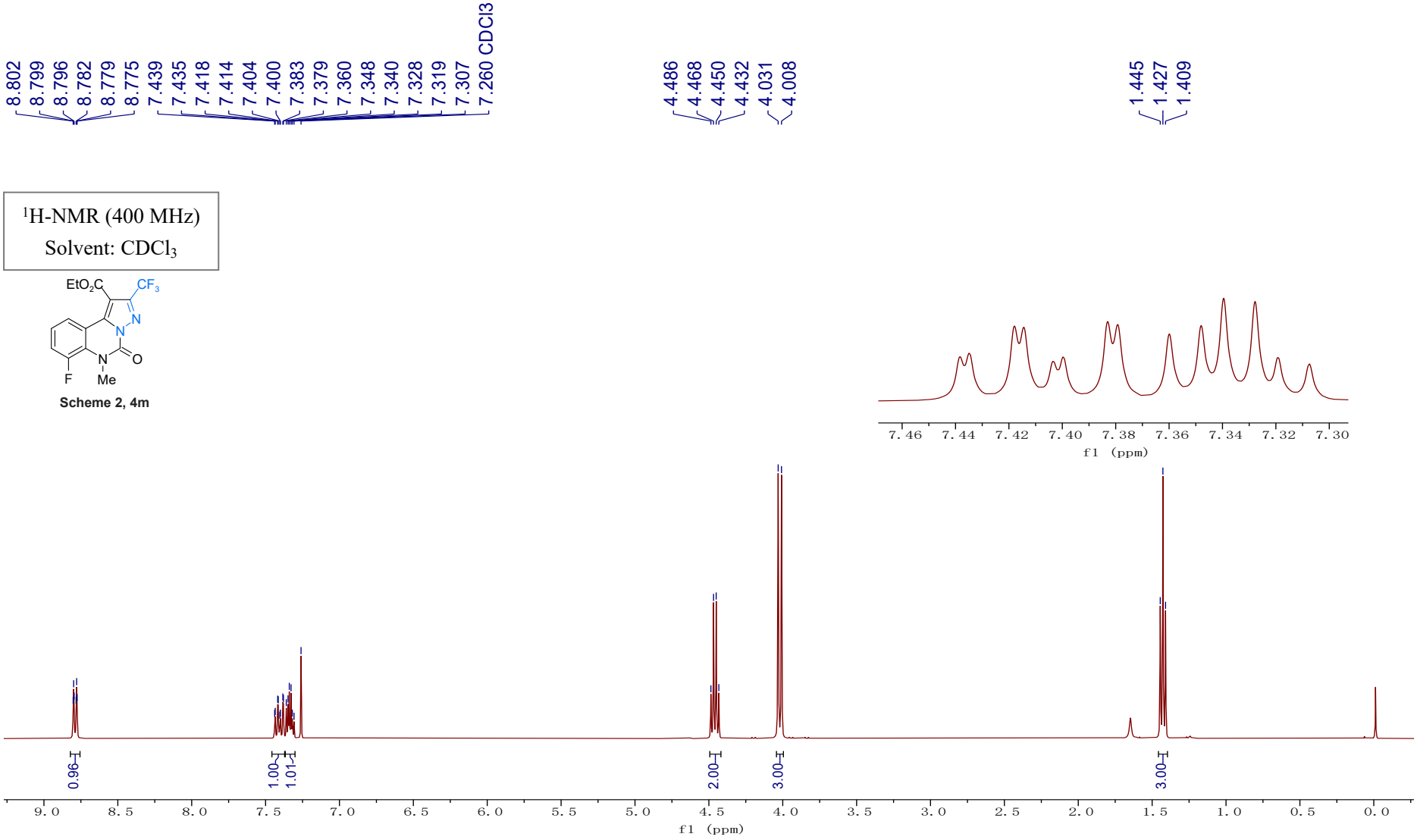

9.113
9.090
7.260 CDCl3
6.954
6.948
6.931
6.926
6.799
6.793
4.469
4.451
4.433
4.415
3.949
3.803
1.446
1.428
1.410
1H-NMR (400 MHz)
Solvent: CDCl3
EtO2C
CF3
MeO
N
O
Me
Scheme 2, 4l
1.00
1.00
1.00
2.00
3.00
3.00
3.00
f1 (ppm)

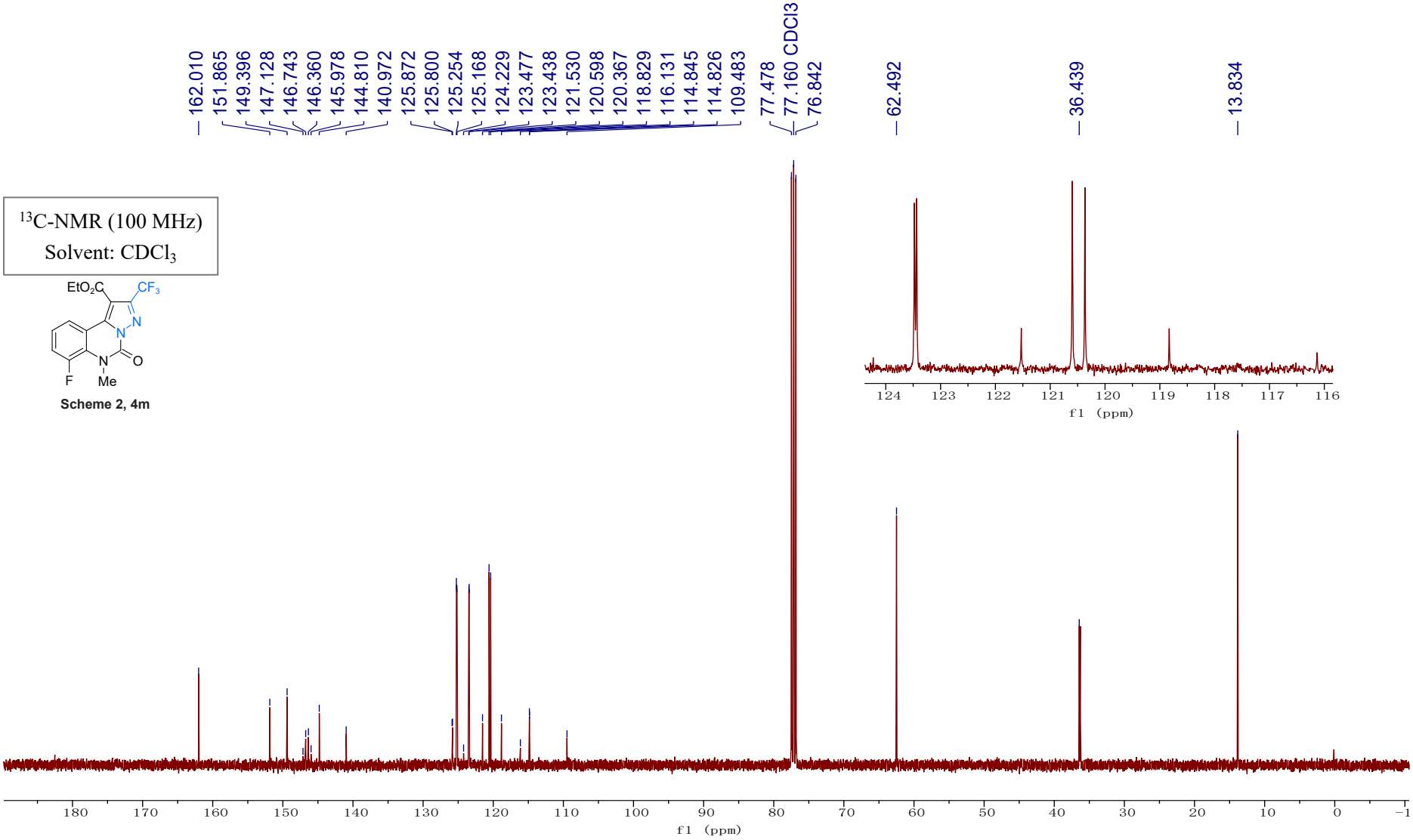

163.003
162.231
146.579
146.207
144.744
142.404
138.672
129.909
124.444
121.748
119.053
116.356
110.115
107.299
105.751
100.375
77.478
77.160 CDCl3
76.843
62.032
55.915
31.916
13.860
^{13}C-NMR (100 MHz)
Solvent: $CDCl_3$
EtO_2C
CF_3
N
N
MeO
N
O
Me
Scheme 2, 4l
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

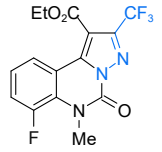


Scheme 2, 4l

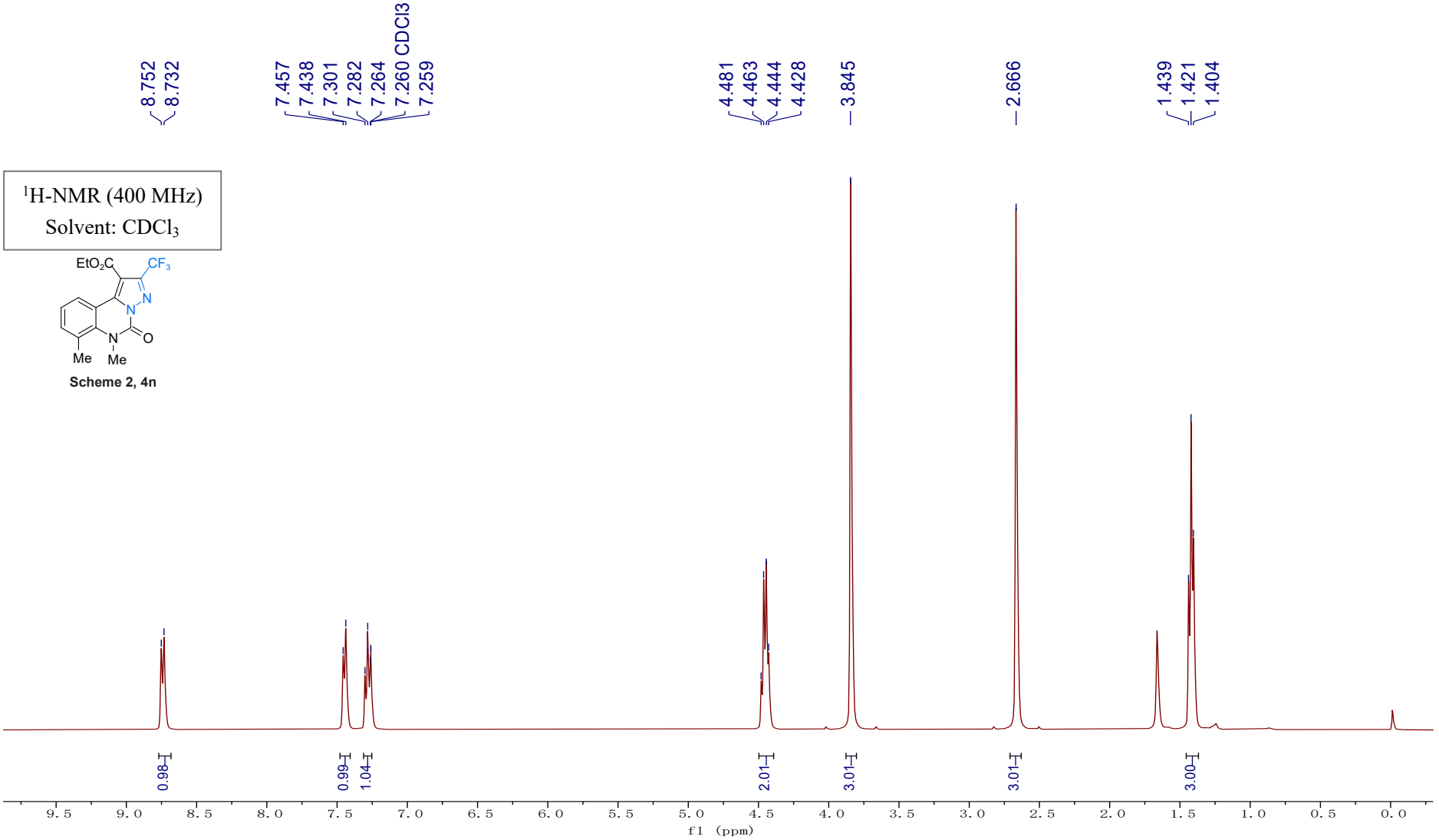

8.802
8.799
8.796
8.782
8.779
8.775
7.439
7.435
7.418
7.414
7.404
7.400
7.383
7.379
7.360
7.348
7.340
7.328
7.319
7.307
7.260 CDCl3
4.486
4.468
4.450
4.432
4.031
4.008
1.445
1.427
1.409
[1]H-NMR (400 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
N
O
F
Me
Scheme 2, 4m
7.46
7.44
7.42
7.40
7.38
7.36
7.34
7.32
7.30
f1 (ppm)
0.96
1.00
1.01
2.00
3.00
3.00
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
f1 (ppm)


162.010
151.865
149.396
147.128
146.743
146.360
145.978
144.810
140.972
125.872
125.800
125.254
125.168
124.229
123.477
123.438
121.530
120.598
120.367
118.829
116.131
114.845
114.826
109.483
77.478
77.160 CDCl3
76.842
62.492
36.439
13.834
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
N
O
F
Me
Scheme 2, 4m
f1 (ppm)
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

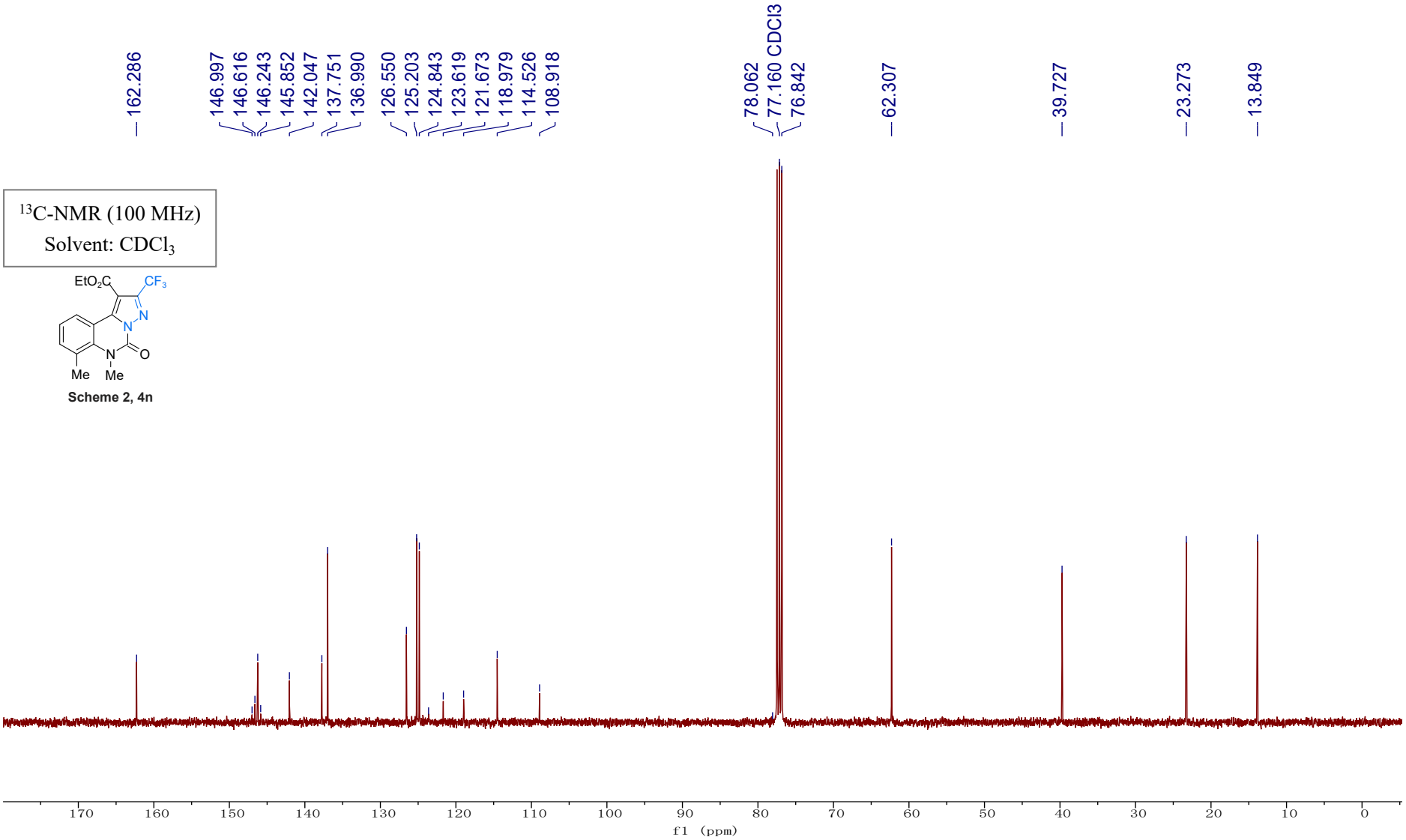


Scheme 2, 4m

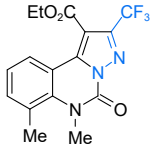


^{1}H-NMR (400 MHz)
Solvent: $CDCl_3$

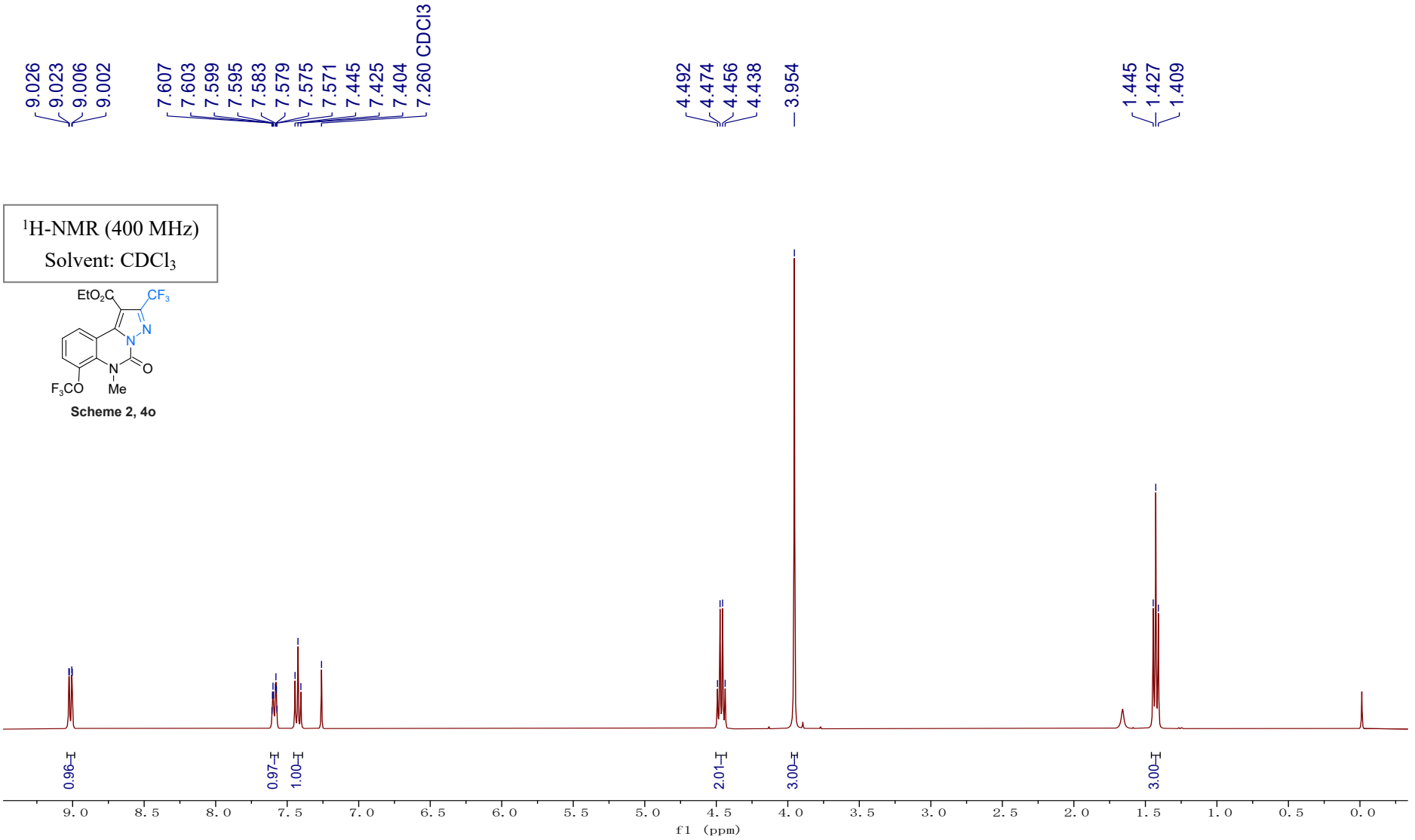
Scheme 2, 4n

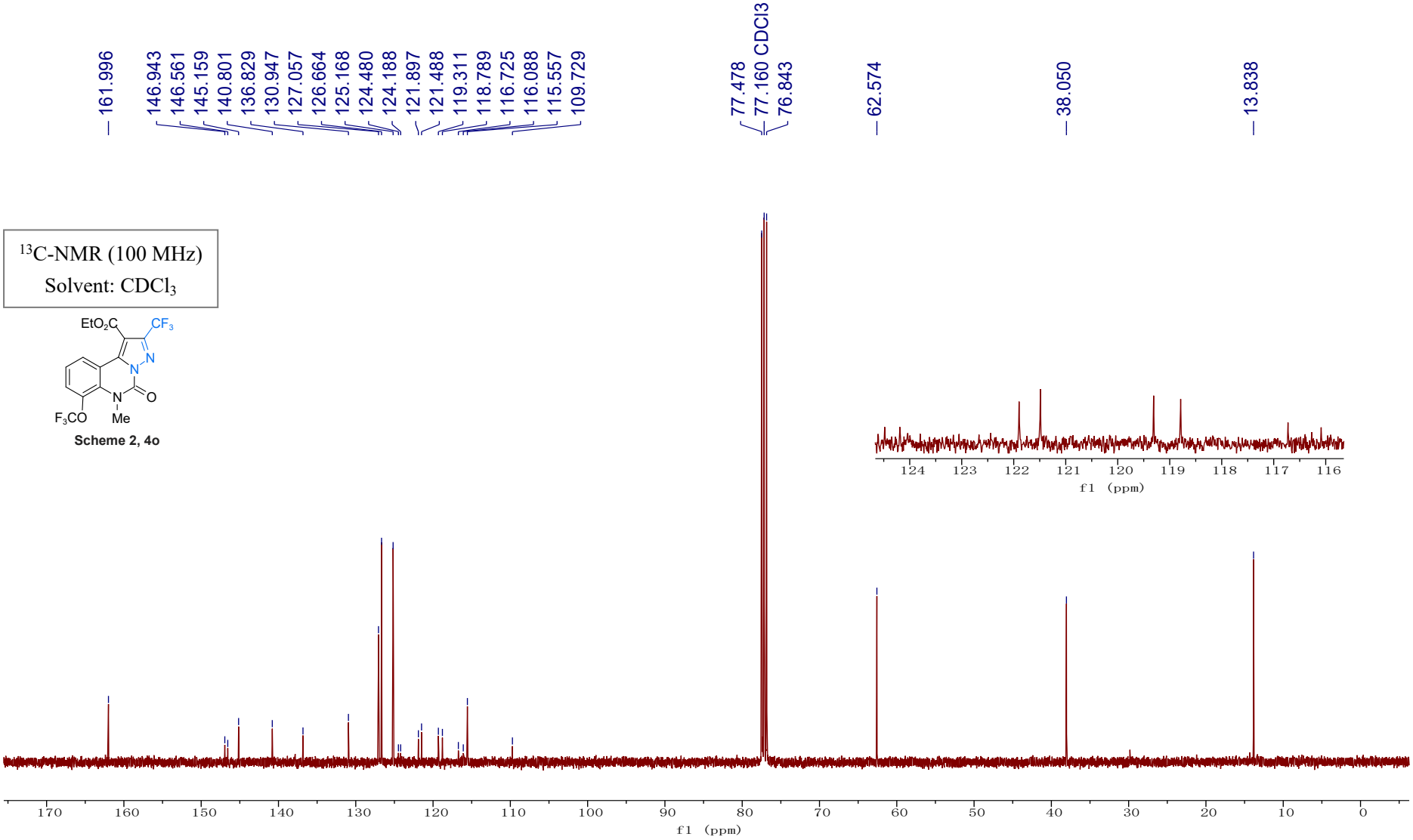

162.286
146.997
146.616
146.243
145.852
142.047
137.751
136.990
126.550
125.203
124.843
123.619
121.673
118.979
114.526
108.918
78.062
77.160 CDCl3
76.842
62.307
39.727
23.273
13.849
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
N
O
Me
Me
Scheme 2, 4n
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

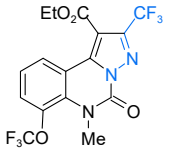


Scheme 2, 4n

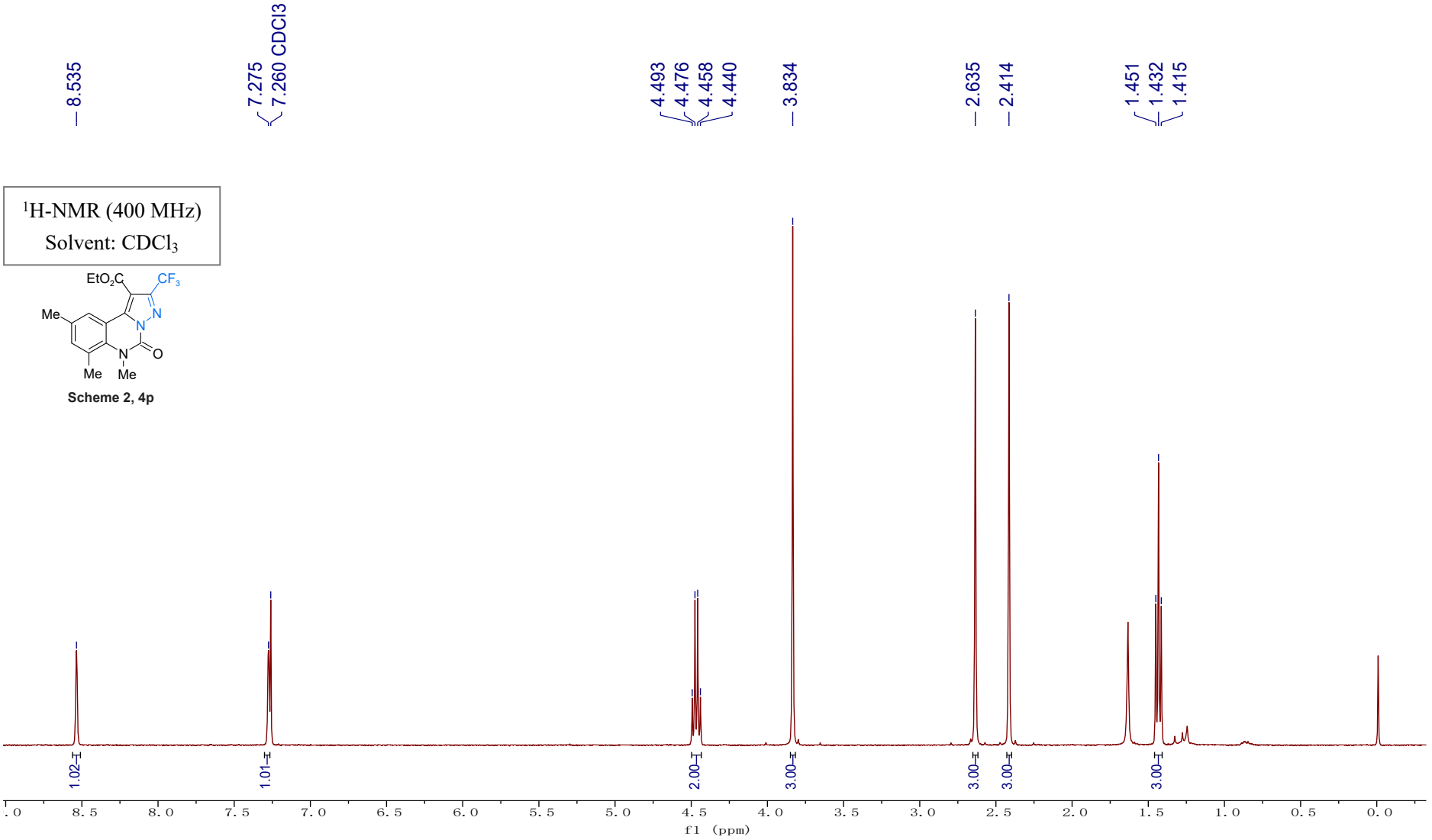

9.026
9.023
9.006
9.002
7.607
7.603
7.599
7.595
7.583
7.579
7.575
7.571
7.445
7.425
7.404
7.260 CDCl3
4.492
4.474
4.456
4.438
3.954
1.445
1.427
1.409
^{1}H-NMR (400 MHz)
Solvent: $CDCl_3$
EtO_2C
CF_3
N
N
O
N
Me
F_3CO
Scheme 2, 4o
0.96
0.97
1.00
2.01
3.00
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

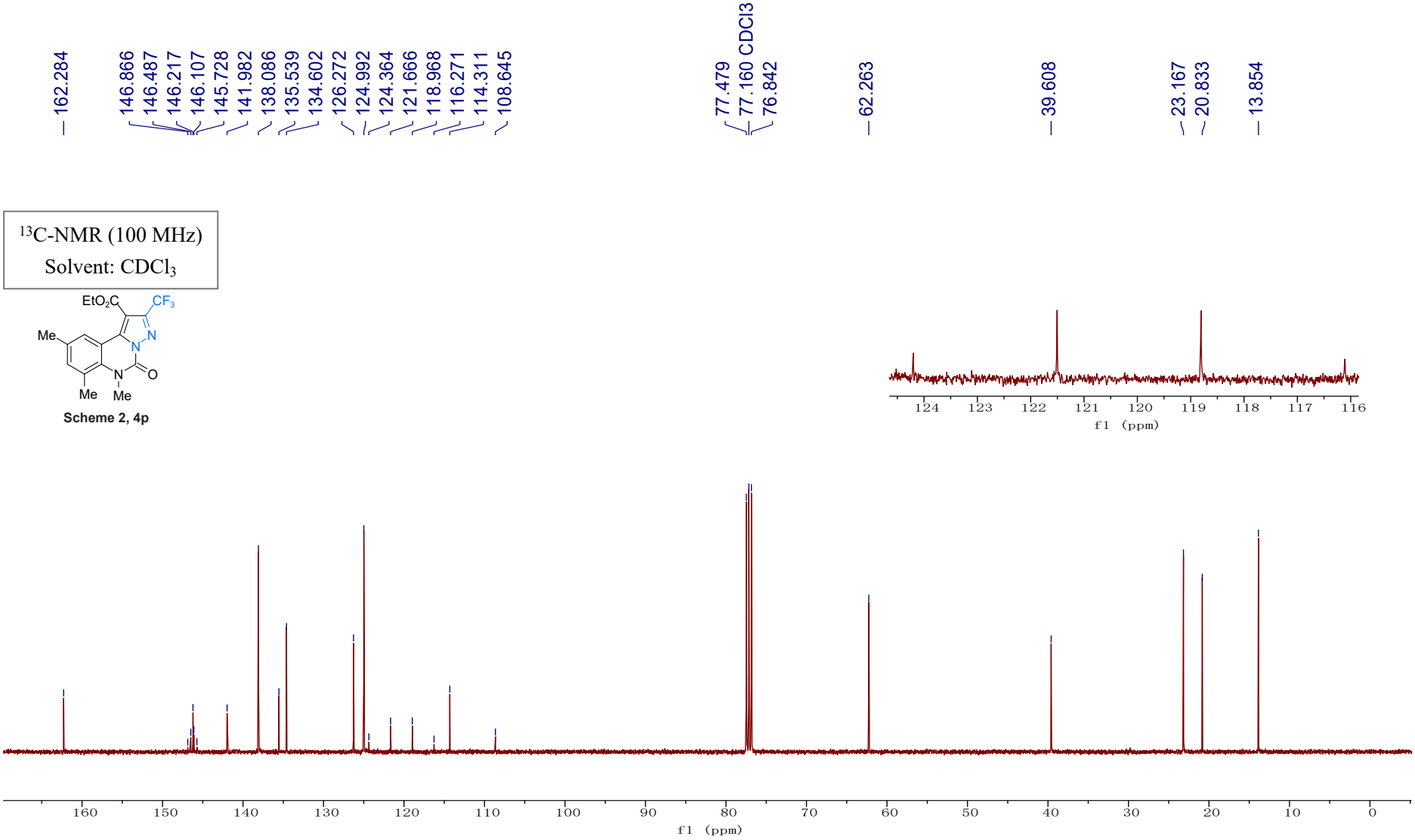

161.996
146.943
146.561
145.159
140.801
136.829
130.947
127.057
126.664
125.168
124.480
124.188
121.897
121.488
119.311
118.789
116.725
116.088
115.557
109.729
77.478
77.160 CDCl3
76.843
62.574
38.050
13.838
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
O
N
F3CO
Me
Scheme 2, 4o
124
123
122
121
120
119
118
117
116
f1 (ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

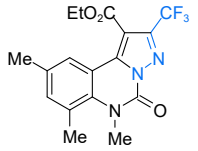


Scheme 2, 4o

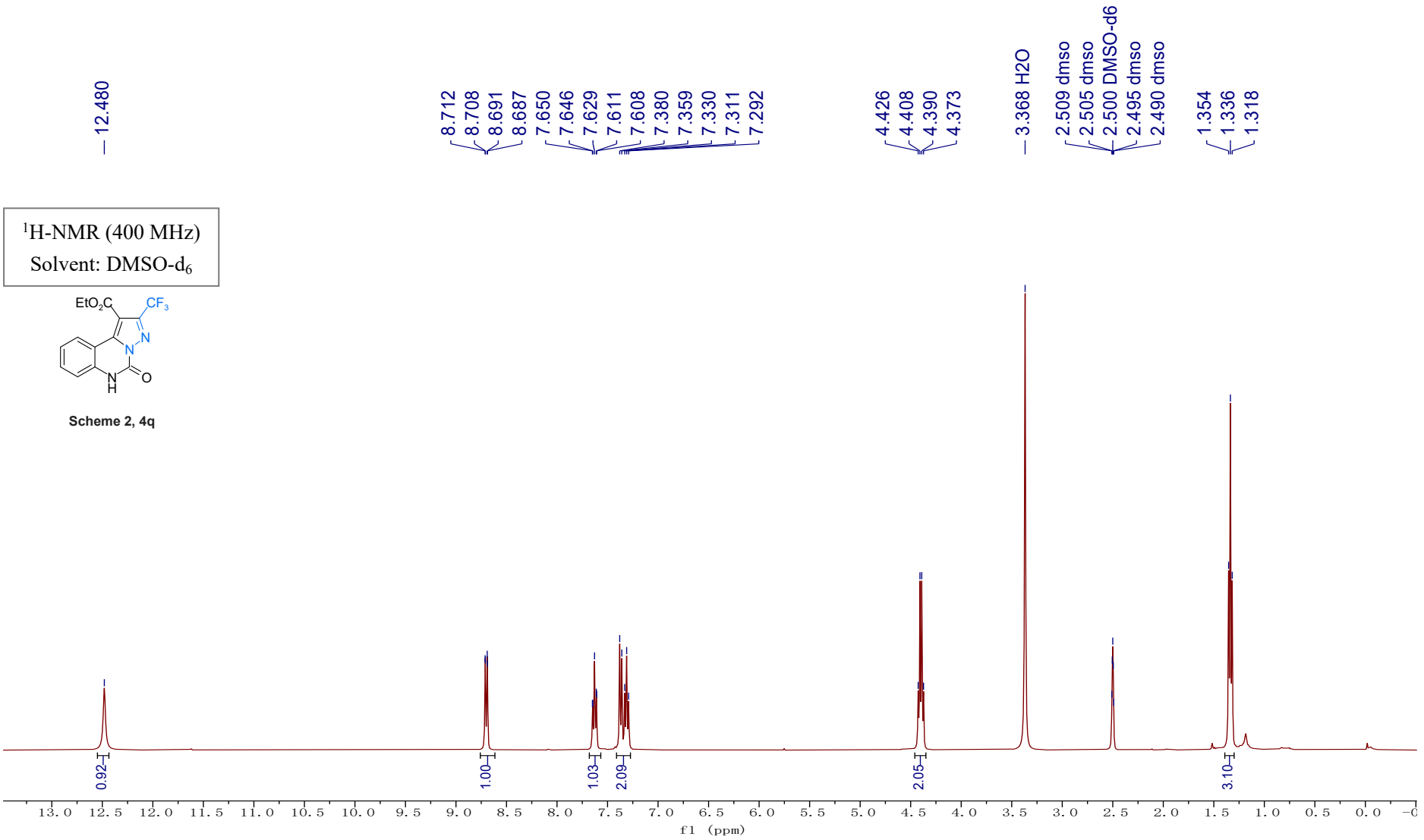

8.535
7.275
7.260 CDCl3
4.493
4.476
4.458
4.440
3.834
2.635
2.414
1.451
1.432
1.415
1H-NMR (400 MHz)
Solvent: CDCl3
EtO2C
CF3
Me
N
N
O
Me
Me
Scheme 2, 4p
1.02
1.01
2.00
3.00
3.00
3.00
3.00
f1 (ppm)


162.284
146.866
146.487
146.217
146.107
145.728
141.982
138.086
135.539
134.602
126.272
124.992
124.364
121.666
118.968
116.271
114.311
108.645
77.479
77.160 CDCl3
76.842
62.263
39.608
23.167
20.833
13.854
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
Me
N
N
O
Me
Me
Scheme 2, 4p
124
123
122
121
120
119
118
117
116
f1 (ppm)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

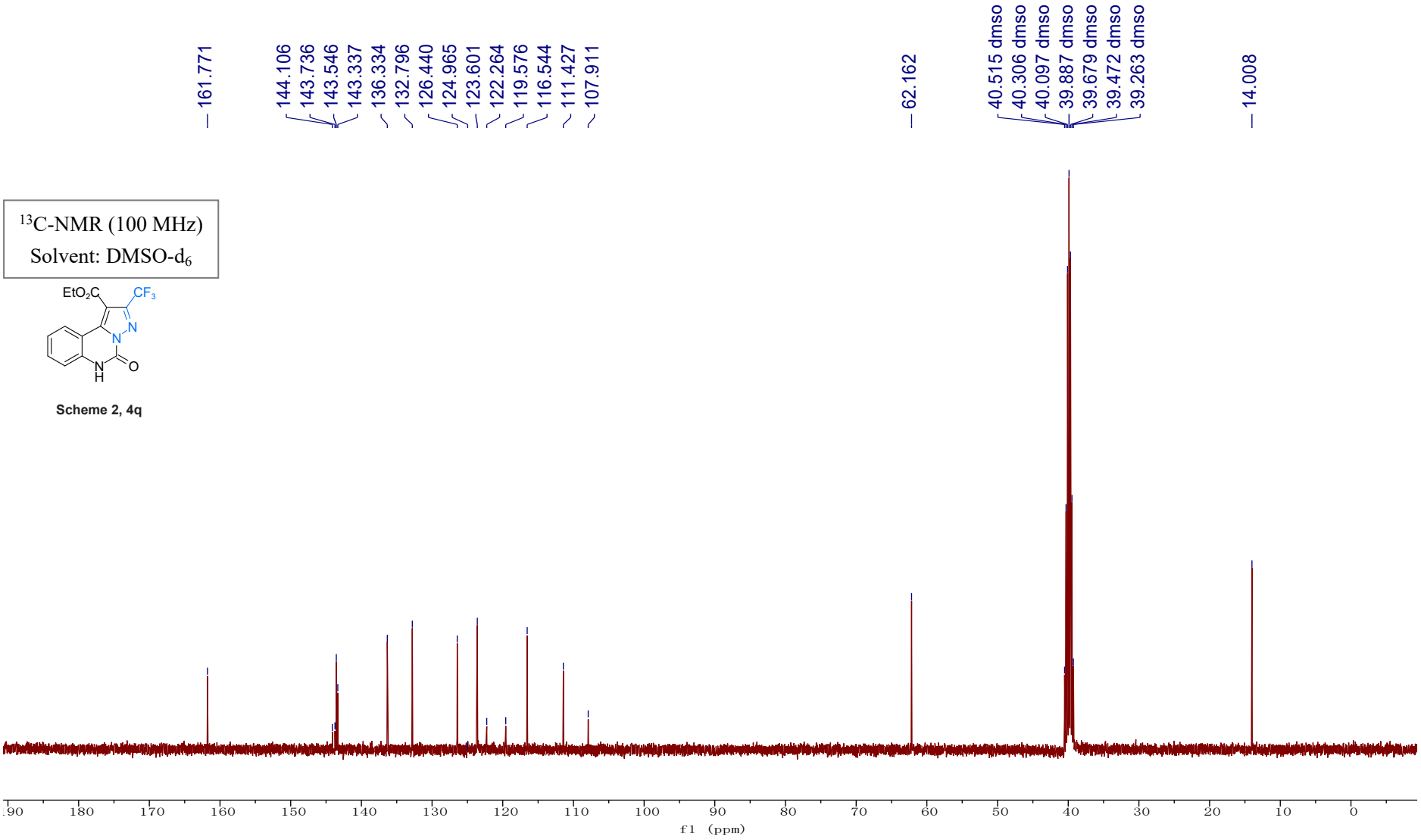


Scheme 2, 4p

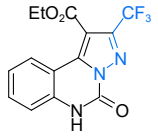


^{1}H-NMR (400 MHz)
Solvent: DMSO-d_6

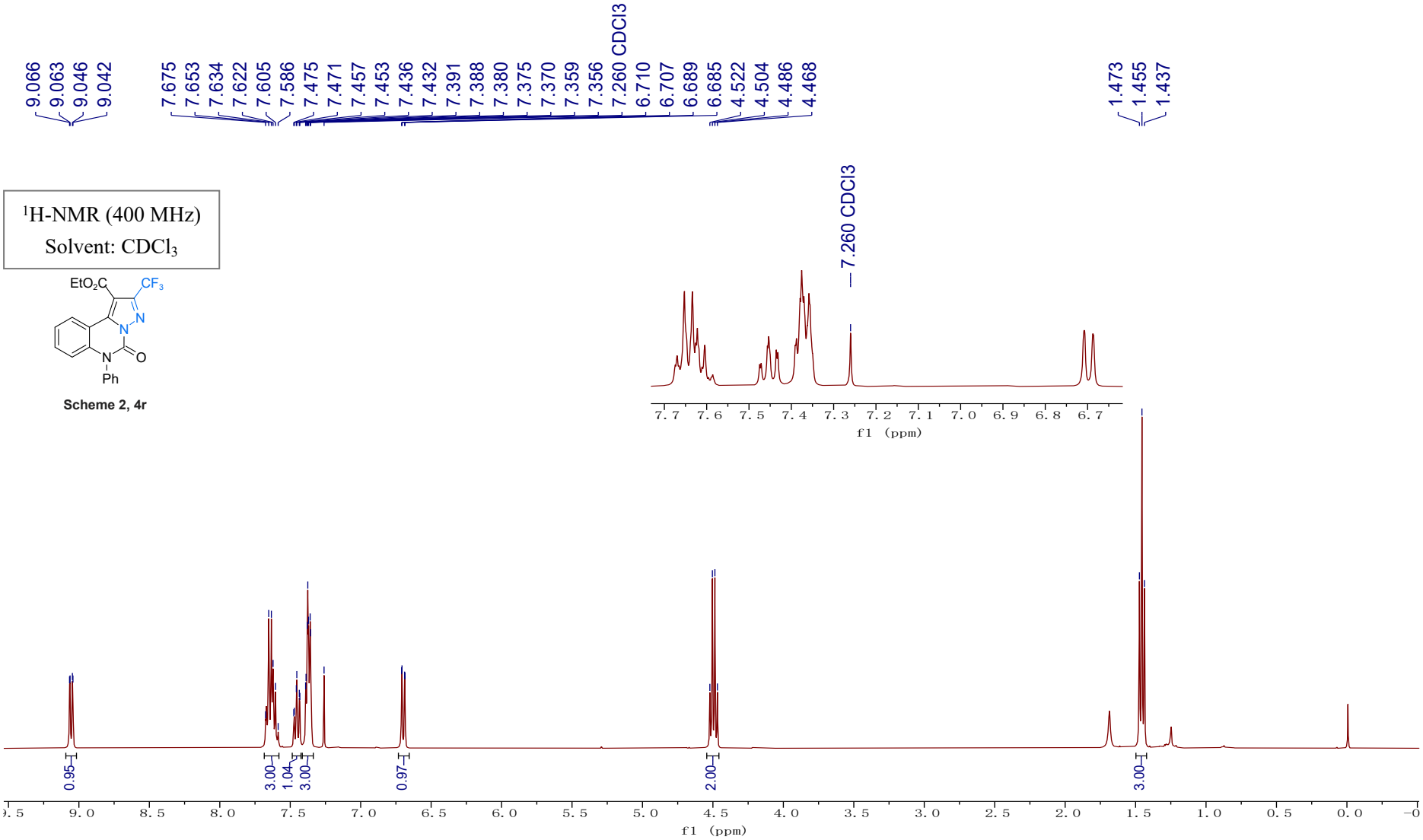
Scheme 2, 4q

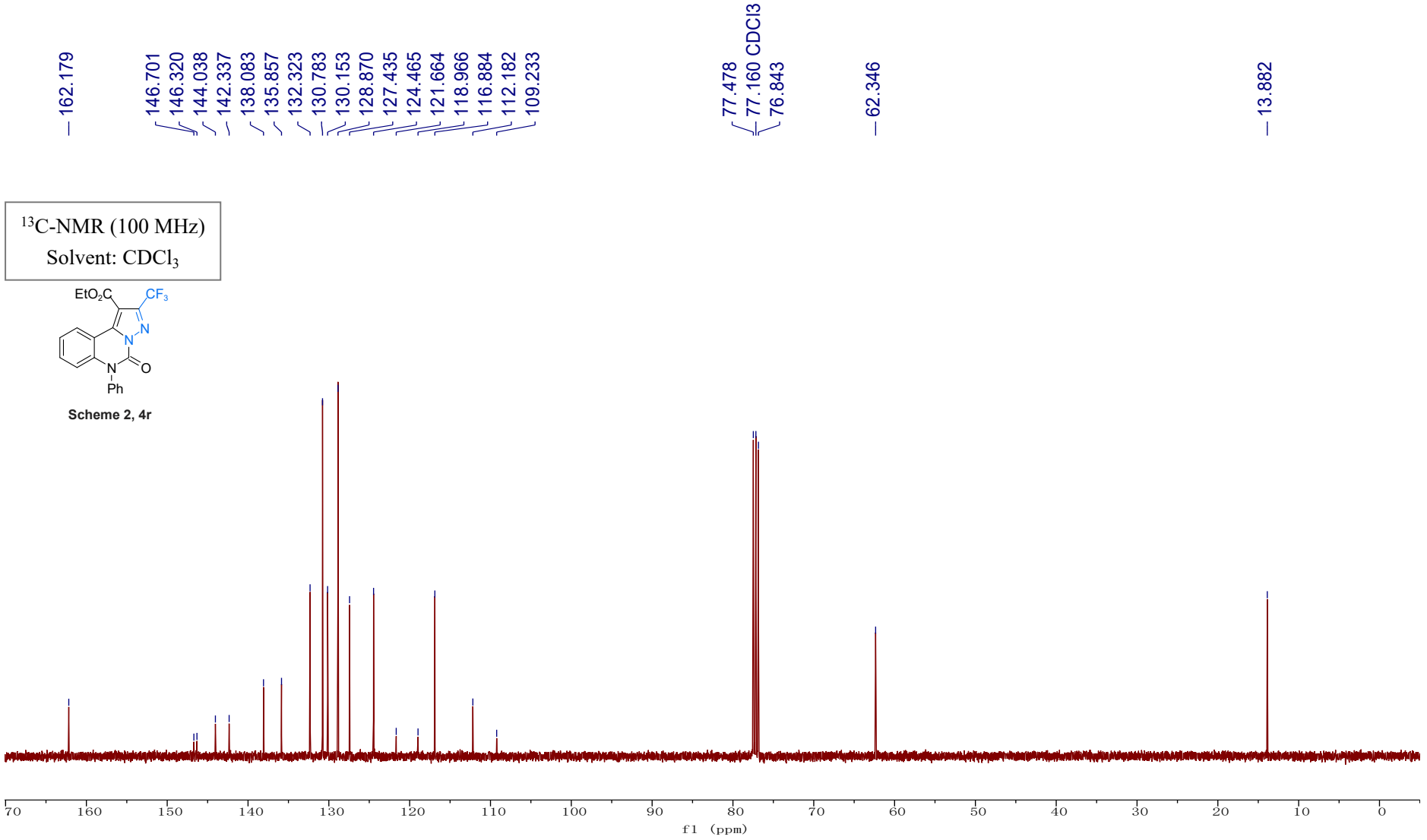

161.771
144.106
143.736
143.546
143.337
136.334
132.796
126.440
124.965
123.601
122.264
119.576
116.544
111.427
107.911
62.162
40.515 dmso
40.306 dmso
40.097 dmso
39.887 dmso
39.679 dmso
39.472 dmso
39.263 dmso
14.008
13C-NMR (100 MHz)
Solvent: DMSO-d6
EtO2C
CF3
N
N
N
H
O
Scheme 2, 4q
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: DMSO-d_6

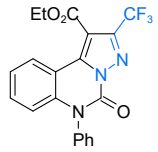


Scheme 2, 4q

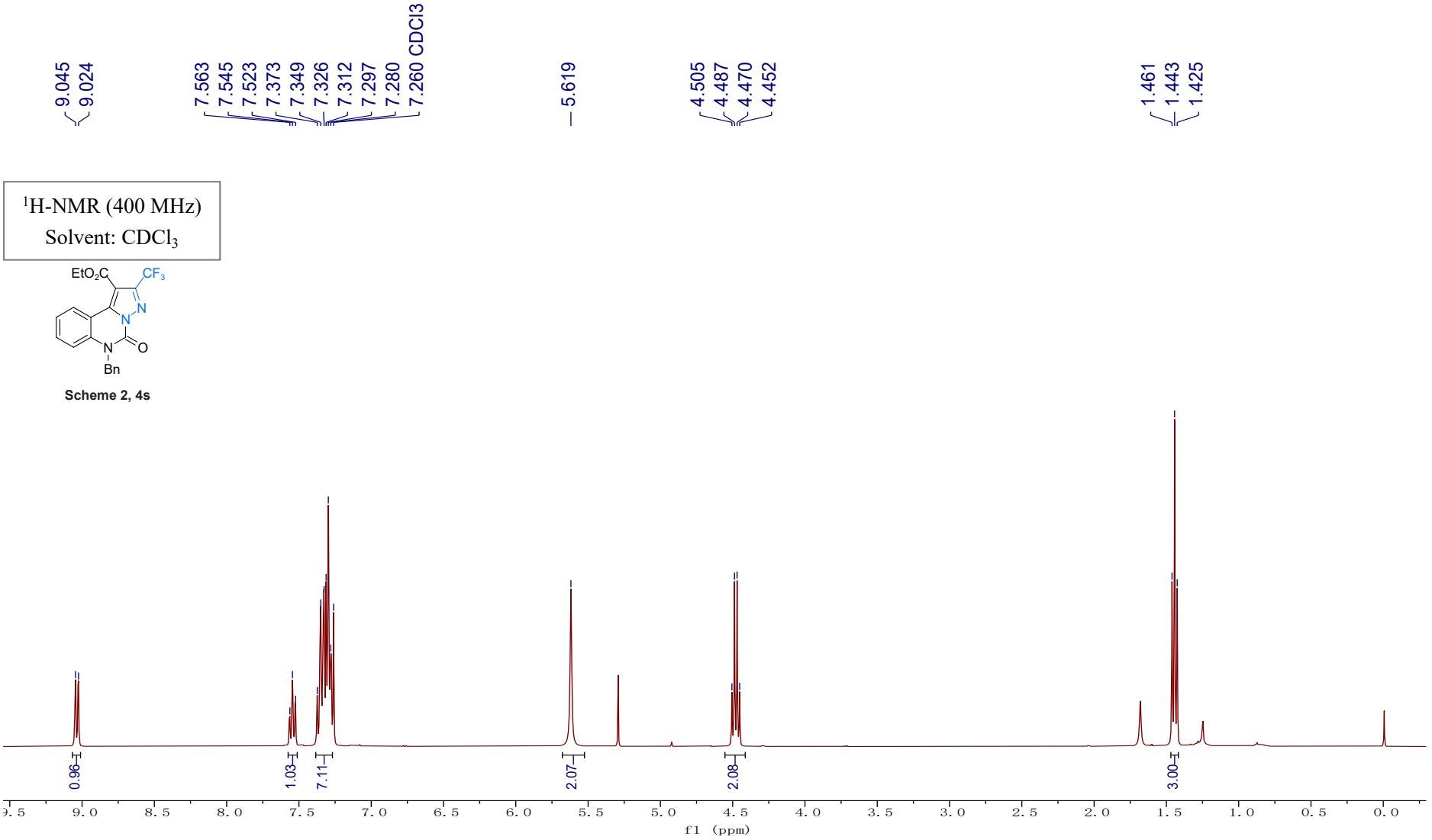

9.066
9.063
9.046
9.042
7.675
7.653
7.634
7.622
7.605
7.586
7.475
7.471
7.457
7.453
7.436
7.432
7.391
7.388
7.380
7.375
7.370
7.359
7.356
7.260 CDCl3
6.710
6.707
6.689
6.685
4.522
4.504
4.486
4.468
1.473
1.455
1.437
[1]H-NMR (400 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
O
Ph
Scheme 2, 4r
7.260 CDCl3
f1 (ppm)
0.95
3.00
1.04
3.00
0.97
2.00
3.00
f1 (ppm)


162.179
146.701
146.320
144.038
142.337
138.083
135.857
132.323
130.783
130.153
128.870
127.435
124.465
121.664
118.966
116.884
112.182
109.233
77.478
77.160 CDCl3
76.843
62.346
13.882
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
O
Ph
Scheme 2, 4r
f1 (ppm)

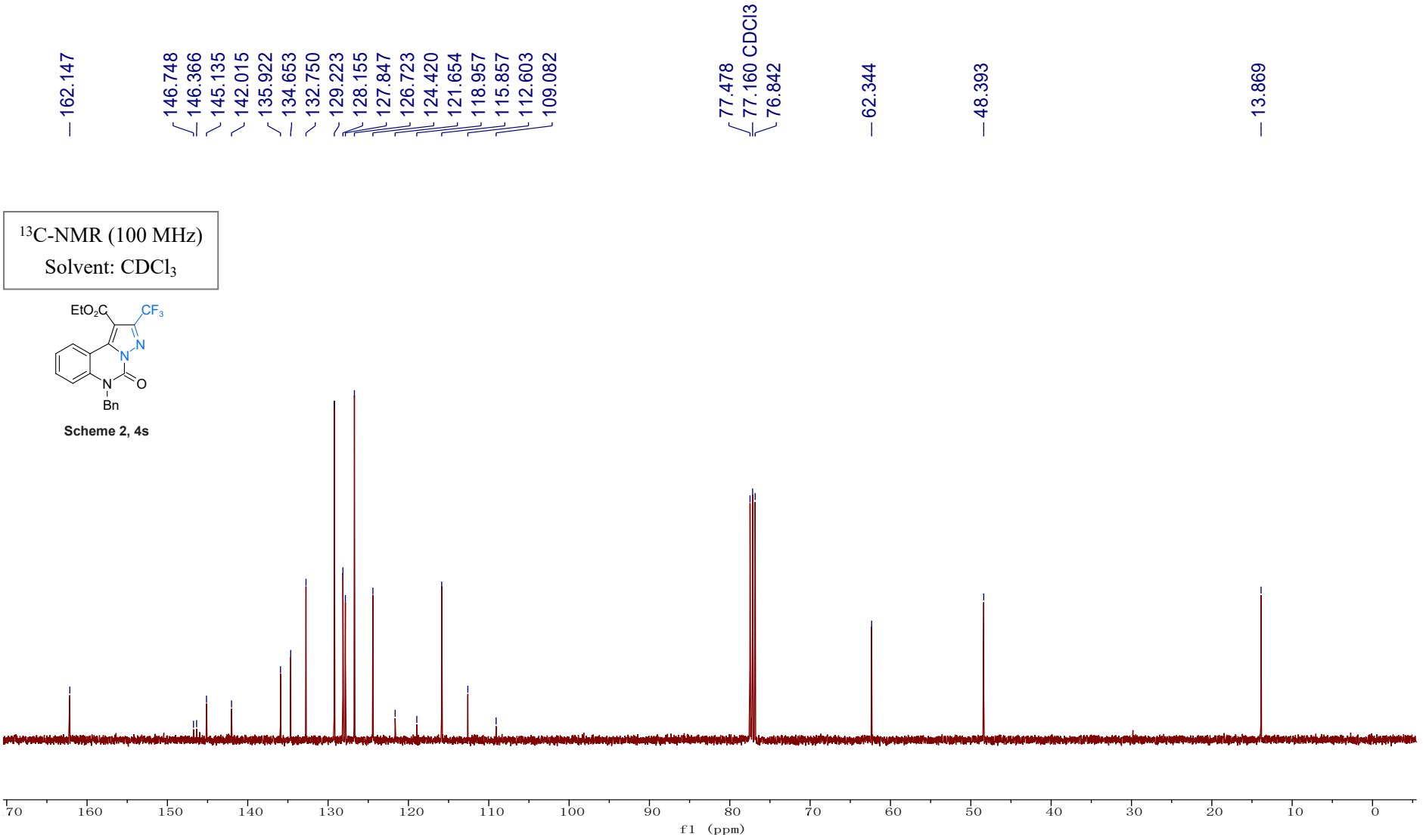
^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$



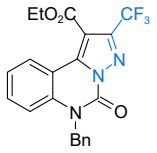
Scheme 2, 4r


9.045
9.024
7.563
7.545
7.523
7.373
7.349
7.326
7.312
7.297
7.280
7.260 CDCl3
5.619
4.505
4.487
4.470
4.452
1.461
1.443
1.425
1H-NMR (400 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
O
N
Bn
0.96
1.03
7.11
2.07
2.08
3.00
f1 (ppm)

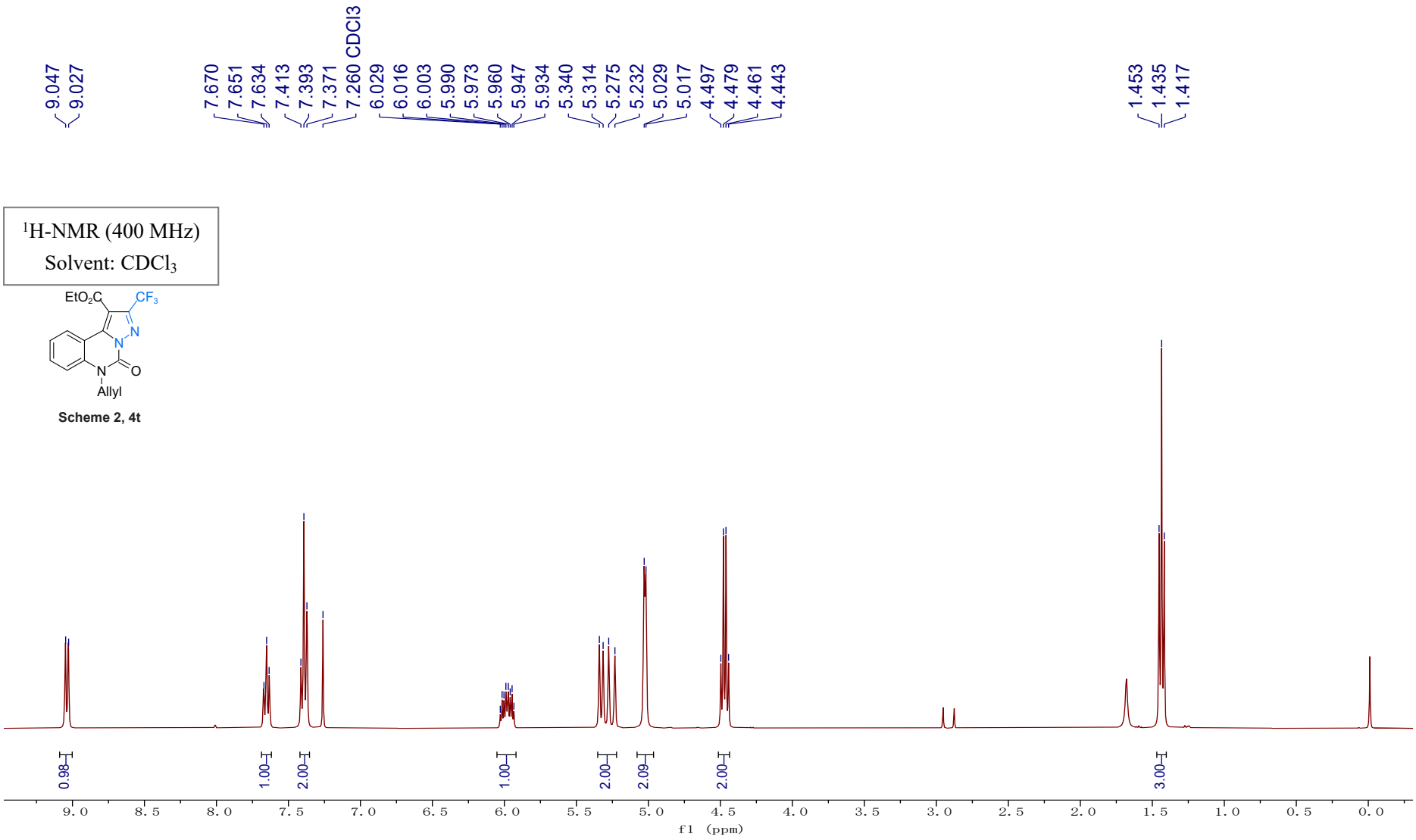
Scheme 2, 4s

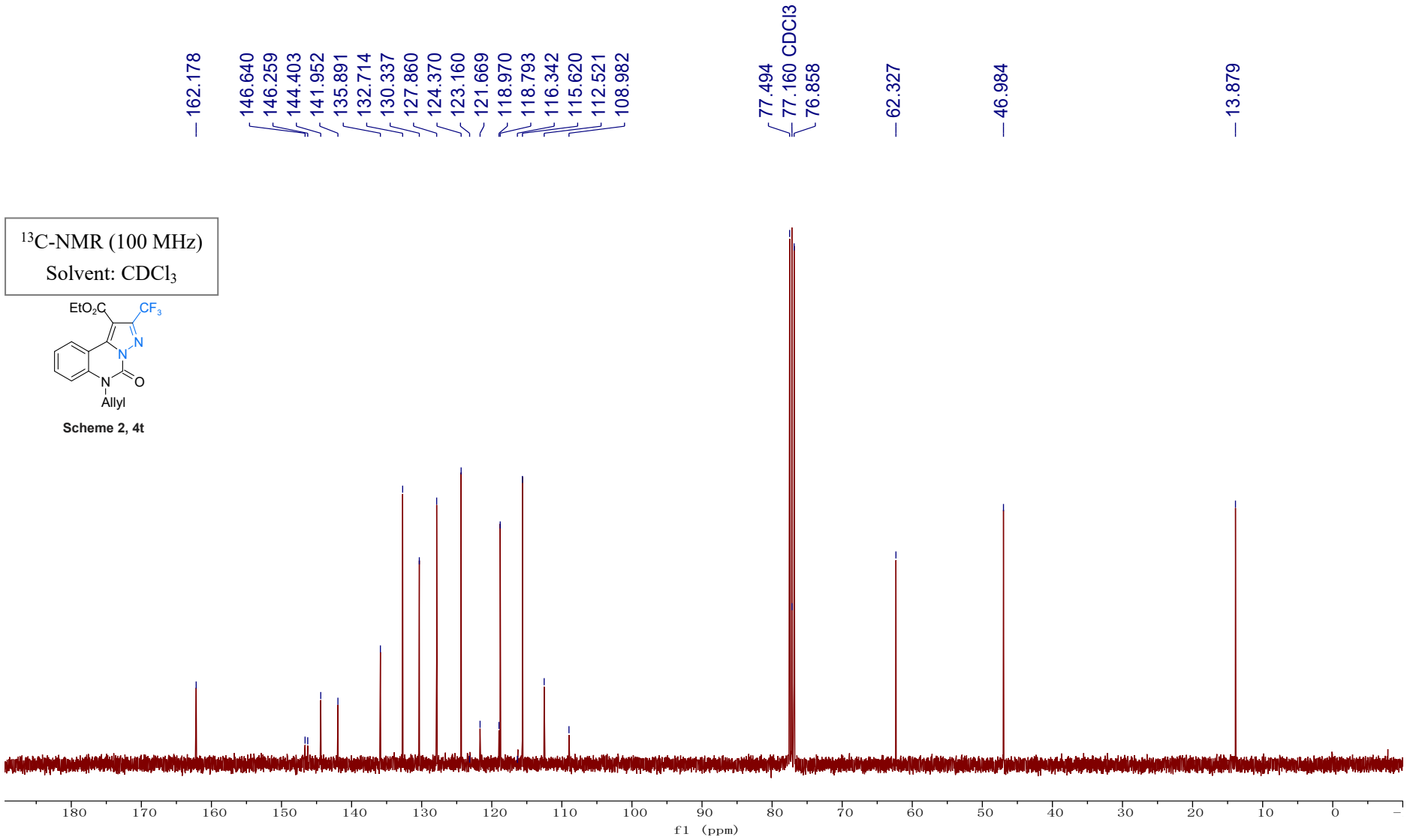

162.147
146.748
146.366
145.135
142.015
135.922
134.653
132.750
129.223
128.155
127.847
126.723
124.420
121.654
118.957
115.857
112.603
109.082
77.478
77.160 CDCl3
76.842
62.344
48.393
13.869
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
N
O
Bn
Scheme 2, 4s
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

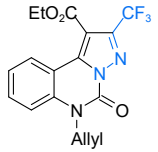


Scheme 2, 4s

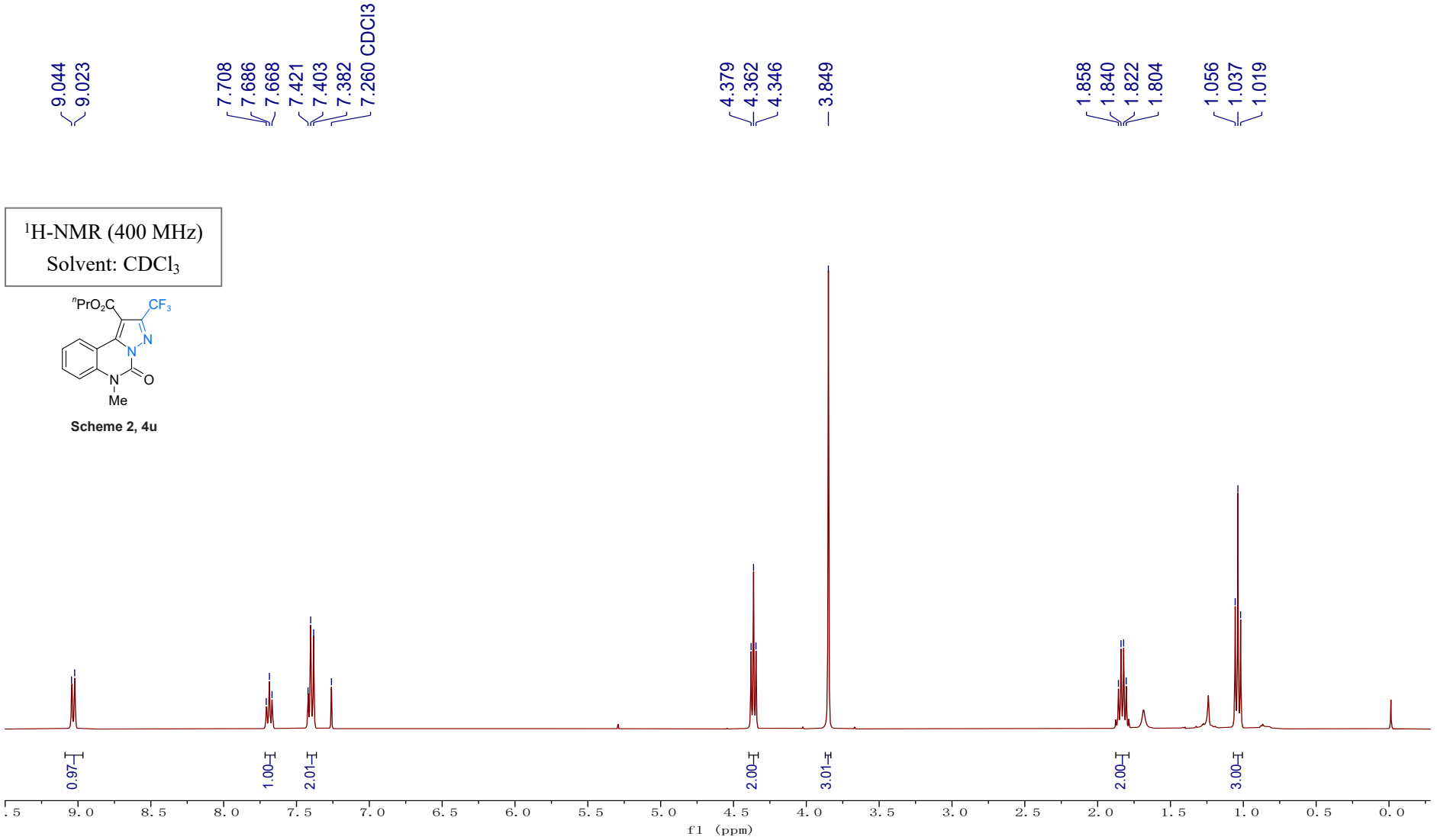

9.047
9.027
7.670
7.651
7.634
7.413
7.393
7.371
7.260 CDCl3
6.029
6.016
6.003
5.990
5.973
5.960
5.947
5.934
5.340
5.314
5.275
5.232
5.029
5.017
4.497
4.479
4.461
4.443
1.453
1.435
1.417
^{1}H-NMR (400 MHz)
Solvent: $CDCl_3$
EtO_2C
CF_3
N
N
N
O
Allyl
Scheme 2, 4t
0.98
1.00
2.00
1.00
2.00
2.09
2.00
3.00
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
f1 (ppm)

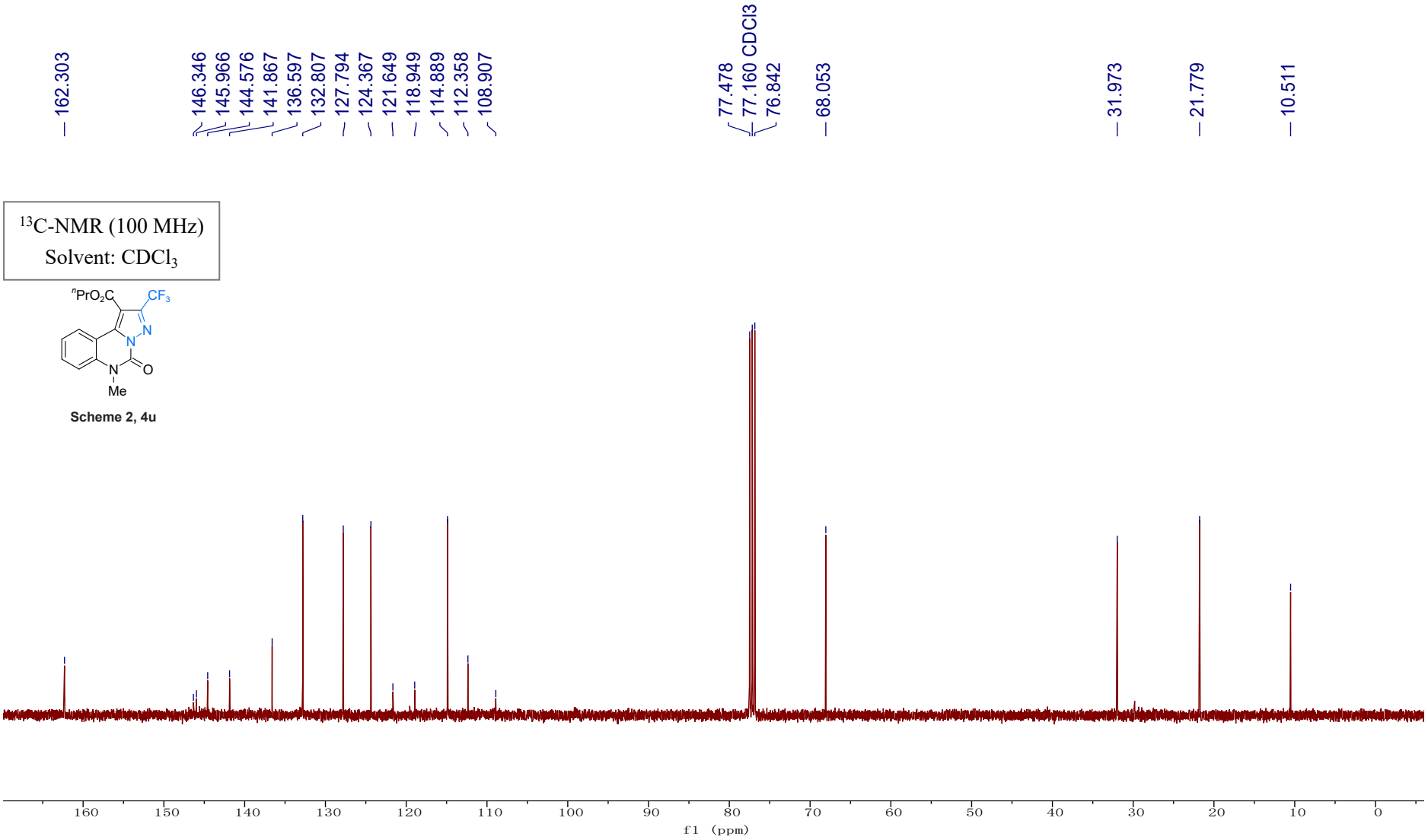

162.178
146.640
146.259
144.403
141.952
135.891
132.714
130.337
127.860
124.370
123.160
121.669
118.970
118.793
116.342
115.620
112.521
108.982
77.494
77.160 CDCl3
76.858
62.327
46.984
13.879
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
N
O
Allyl
Scheme 2, 4t
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

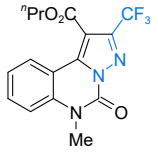


Scheme 2, 4t

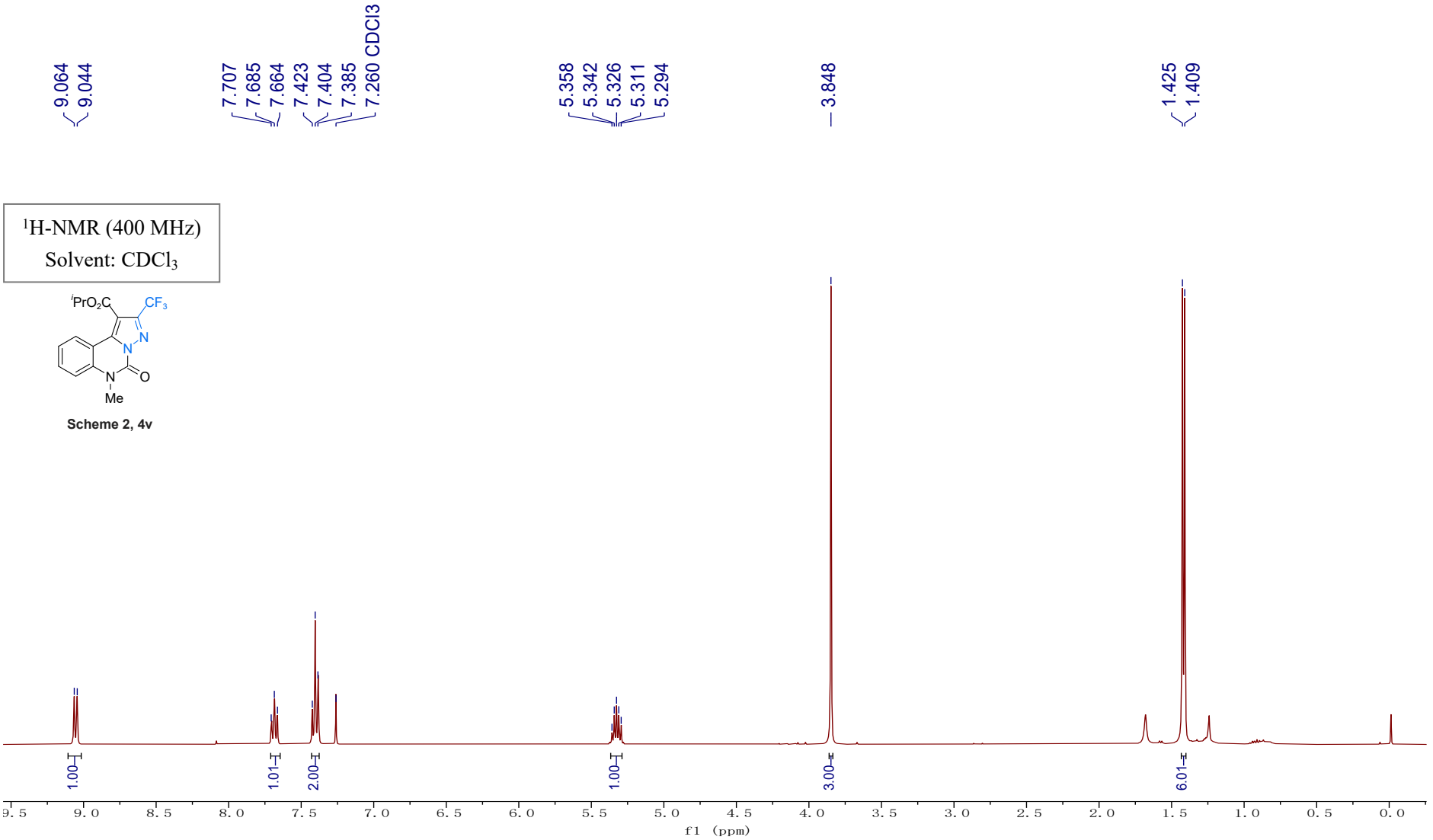

9.044
9.023
7.708
7.686
7.668
7.421
7.403
7.382
7.260 CDCl3
4.379
4.362
4.346
3.849
1.858
1.840
1.822
1.804
1.056
1.037
1.019
1H-NMR (400 MHz)
Solvent: CDCl3
nPrO2C
CF3
N
N
N
O
Me
Scheme 2, 4u
0.97
1.00
2.01
2.00
3.01
2.00
3.00
f1 (ppm)

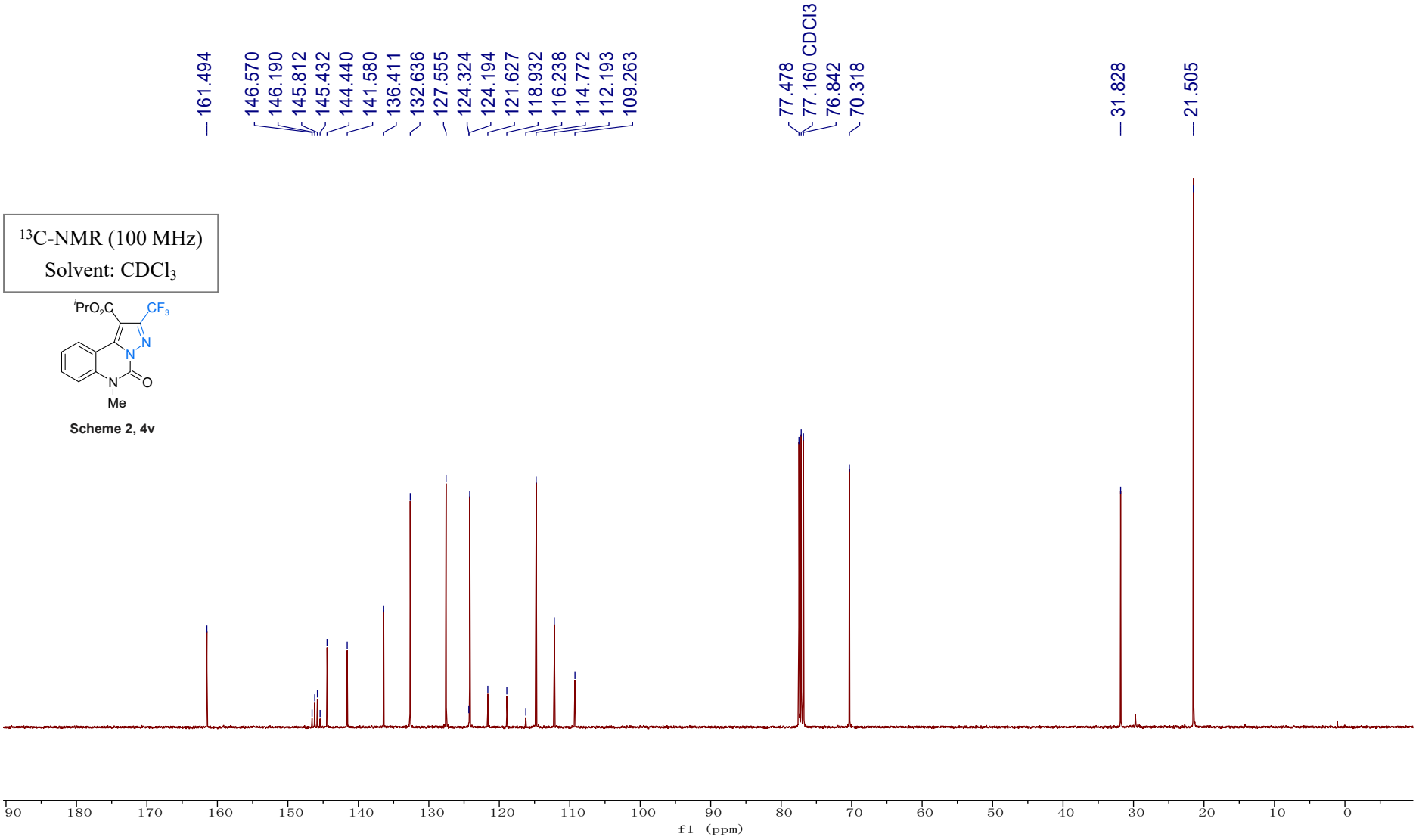

162.303
146.346
145.966
144.576
141.867
136.597
132.807
127.794
124.367
121.649
118.949
114.889
112.358
108.907
77.478
77.160 CDCl3
76.842
68.053
31.973
21.779
10.511
13C-NMR (100 MHz)
Solvent: CDCl3
nPrO2C
CF3
N
N
N
O
Me
Scheme 2, 4u
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

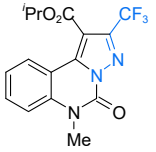


Scheme 2, 4u

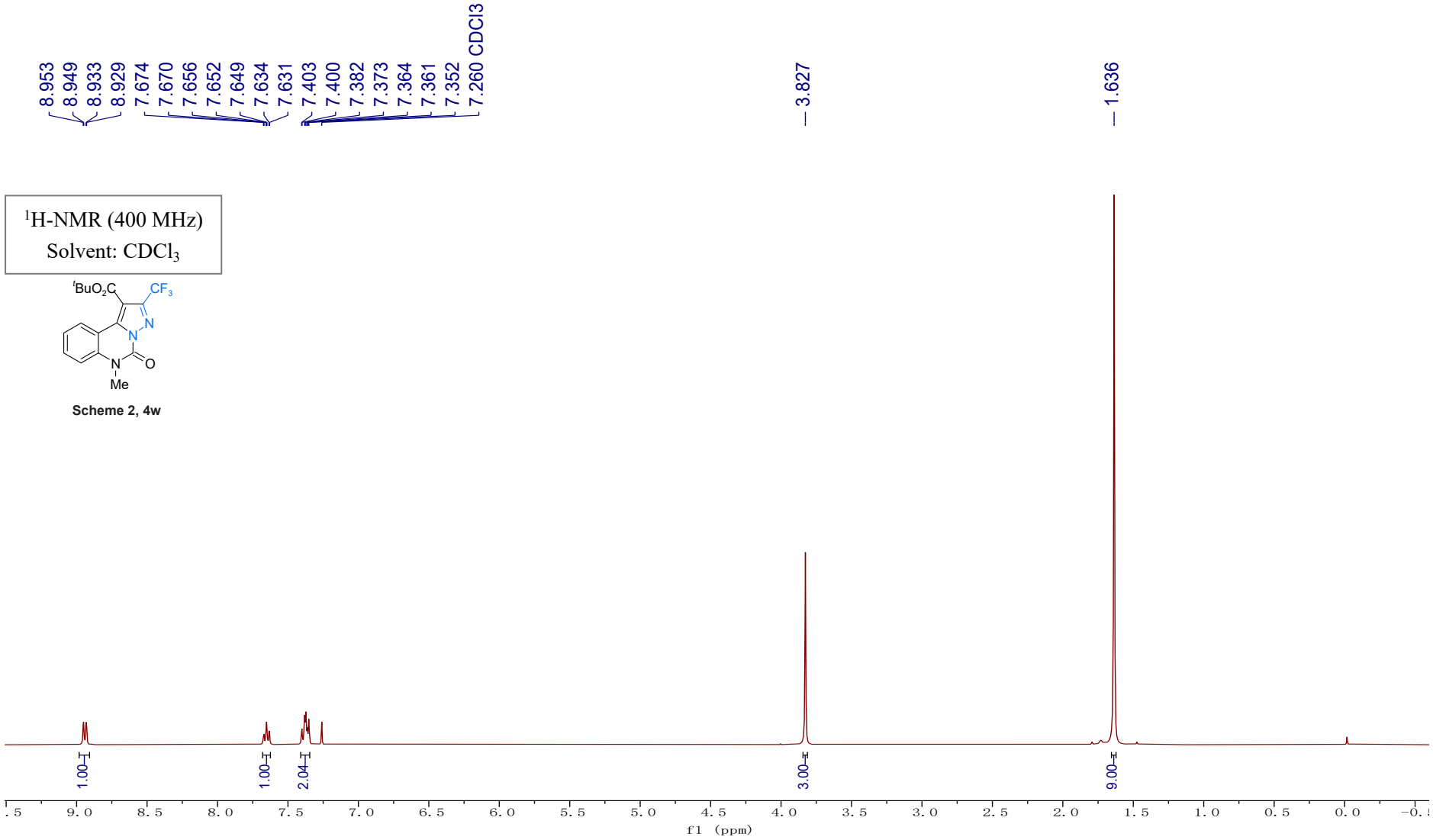

9.064
9.044
7.707
7.685
7.664
7.423
7.404
7.385
7.260 CDCl3
5.358
5.342
5.326
5.311
5.294
3.848
1.425
1.409
1H-NMR (400 MHz)
Solvent: CDCl3
iPrO2C
CF3
N
N
N
O
Me
Scheme 2, 4v
1.00
1.01
2.00
1.00
3.00
6.01
f1 (ppm)

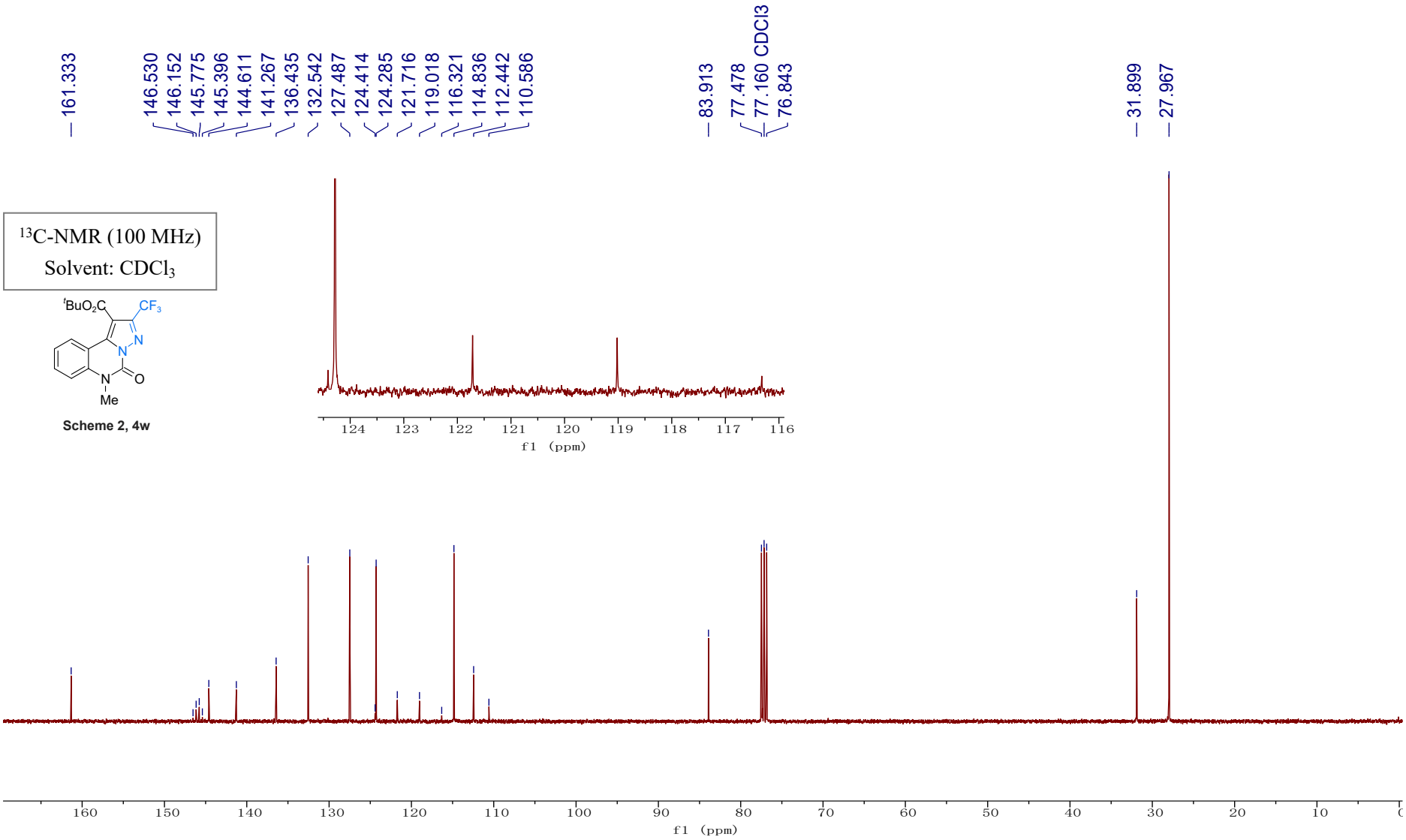

161.494
146.570
146.190
145.812
145.432
144.440
141.580
136.411
132.636
127.555
124.324
124.194
121.627
118.932
116.238
114.772
112.193
109.263
77.478
77.160 CDCl3
76.842
70.318
31.828
21.505
13C-NMR (100 MHz)
Solvent: CDCl3
iPrO2C
CF3
N
N
N
O
Me
Scheme 2, 4v
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$

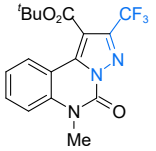


Scheme 2, 4v

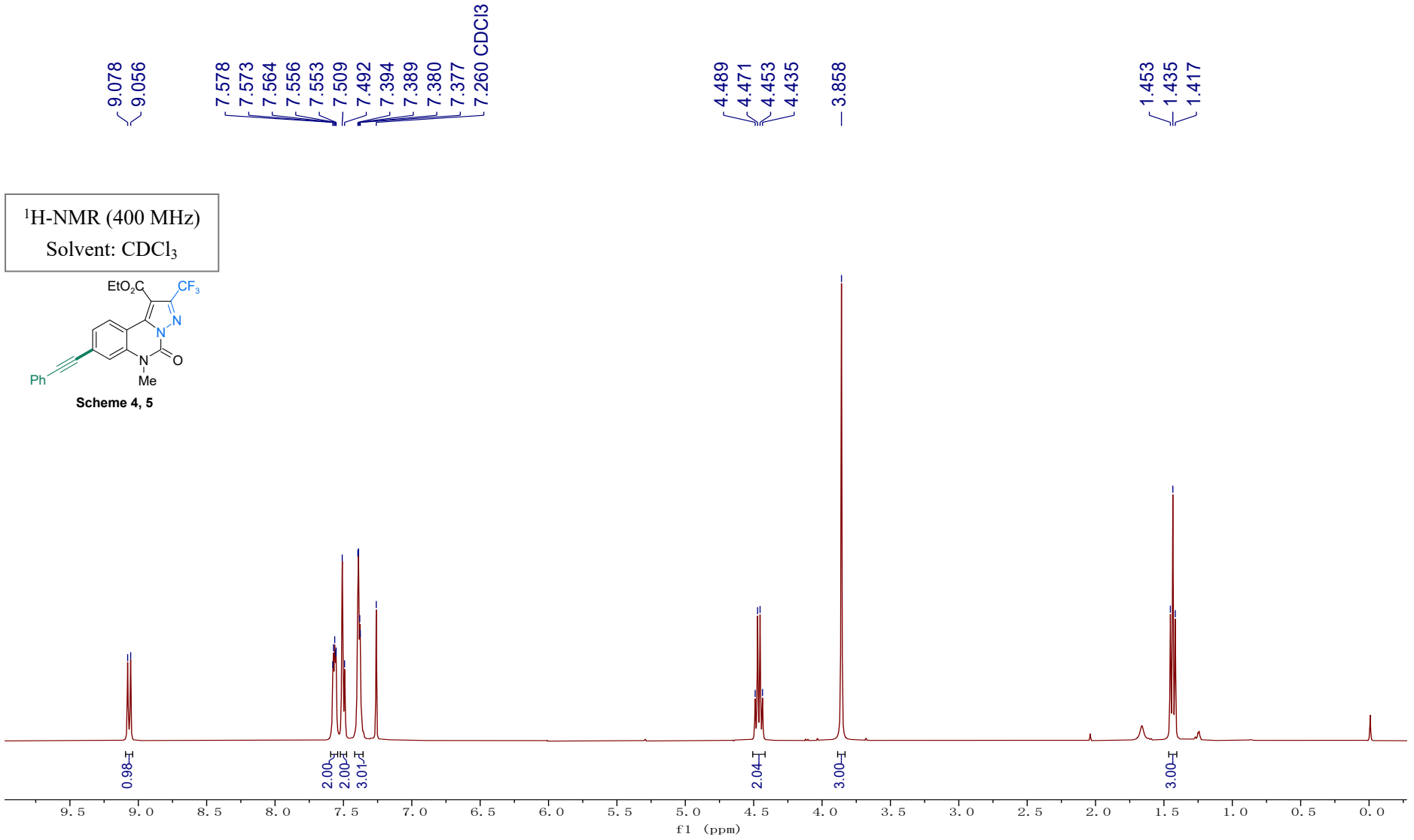

8.953
8.949
8.933
8.929
7.674
7.670
7.656
7.652
7.649
7.634
7.631
7.403
7.400
7.382
7.373
7.364
7.361
7.352
7.260 CDCl3
3.827
1.636
1H-NMR (400 MHz)
Solvent: CDCl3
tBuO2C
CF3
N
N
N
O
Me
Scheme 2, 4w
1.00
1.00
2.04
3.00
9.00
f1 (ppm)

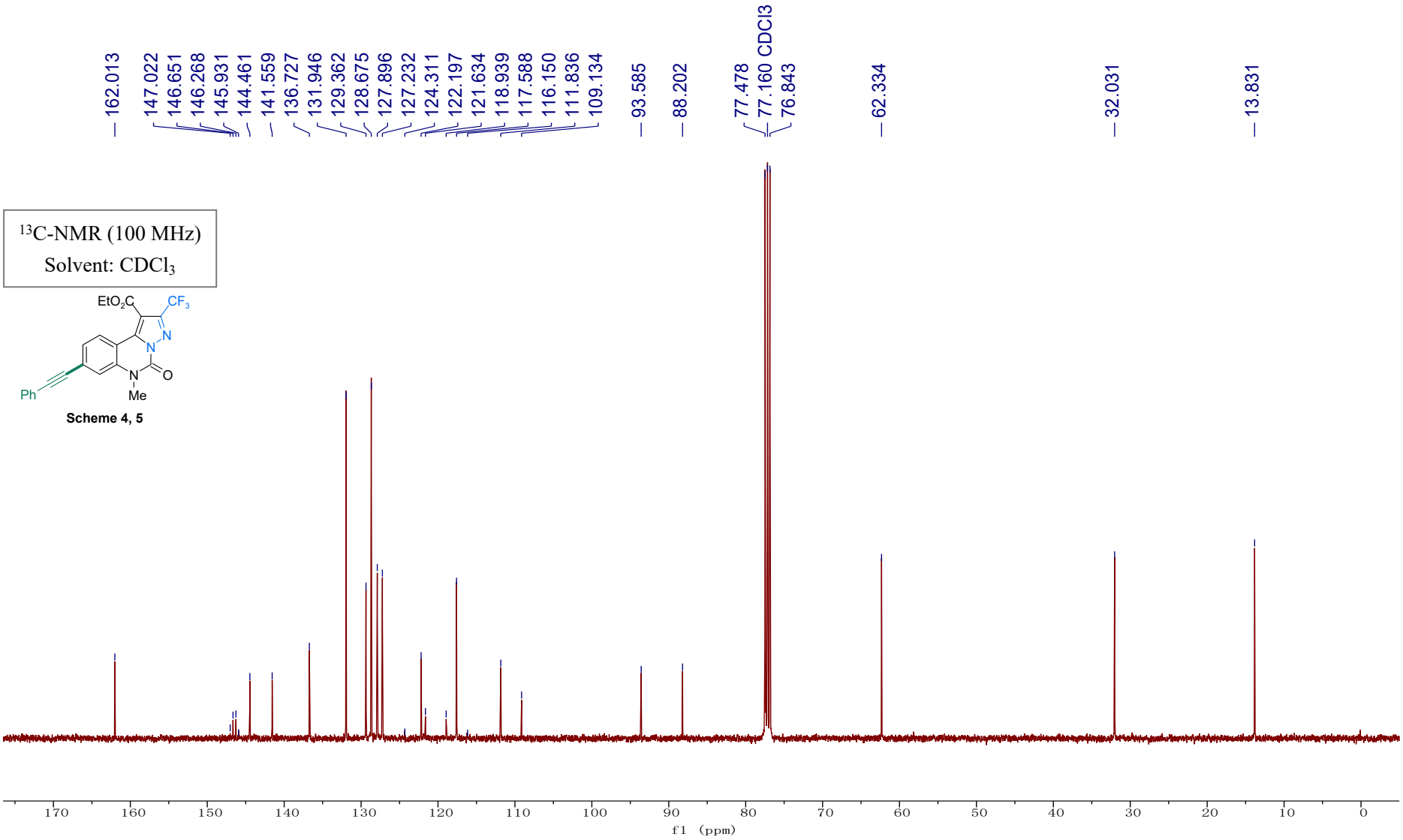

161.333
146.530
146.152
145.775
145.396
144.611
141.267
136.435
132.542
127.487
124.414
124.285
121.716
119.018
116.321
114.836
112.442
110.586
83.913
77.478
77.160 CDCl3
76.843
31.899
27.967
13C-NMR (100 MHz)
Solvent: CDCl3
tBuO2C
CF3
N
N
N
O
Me
Scheme 2, 4w
124
123
122
121
120
119
118
117
116
f1 (ppm)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

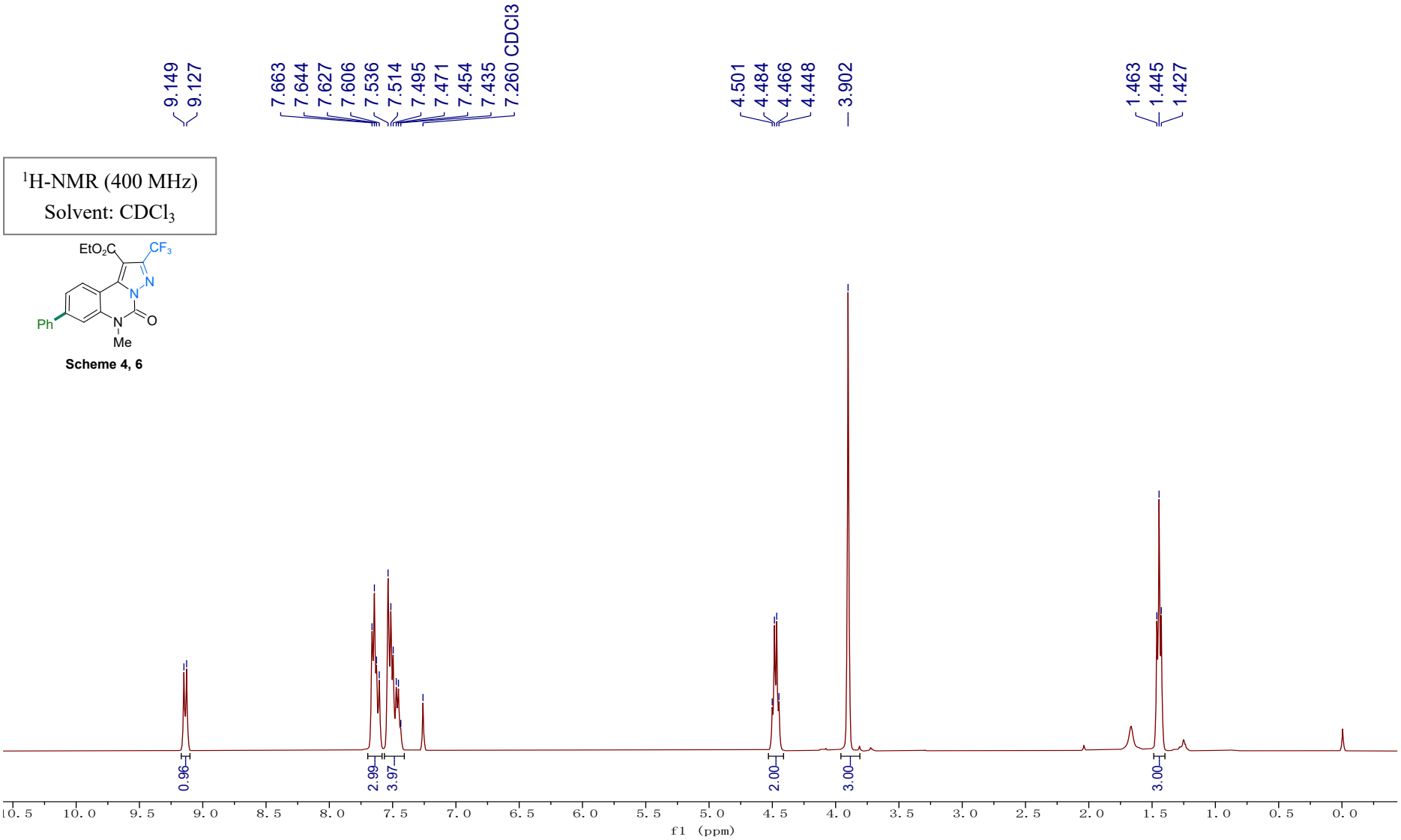
^{19}F-NMR (376 MHz)
Solvent: $CDCl_3$



Scheme 2, 4w

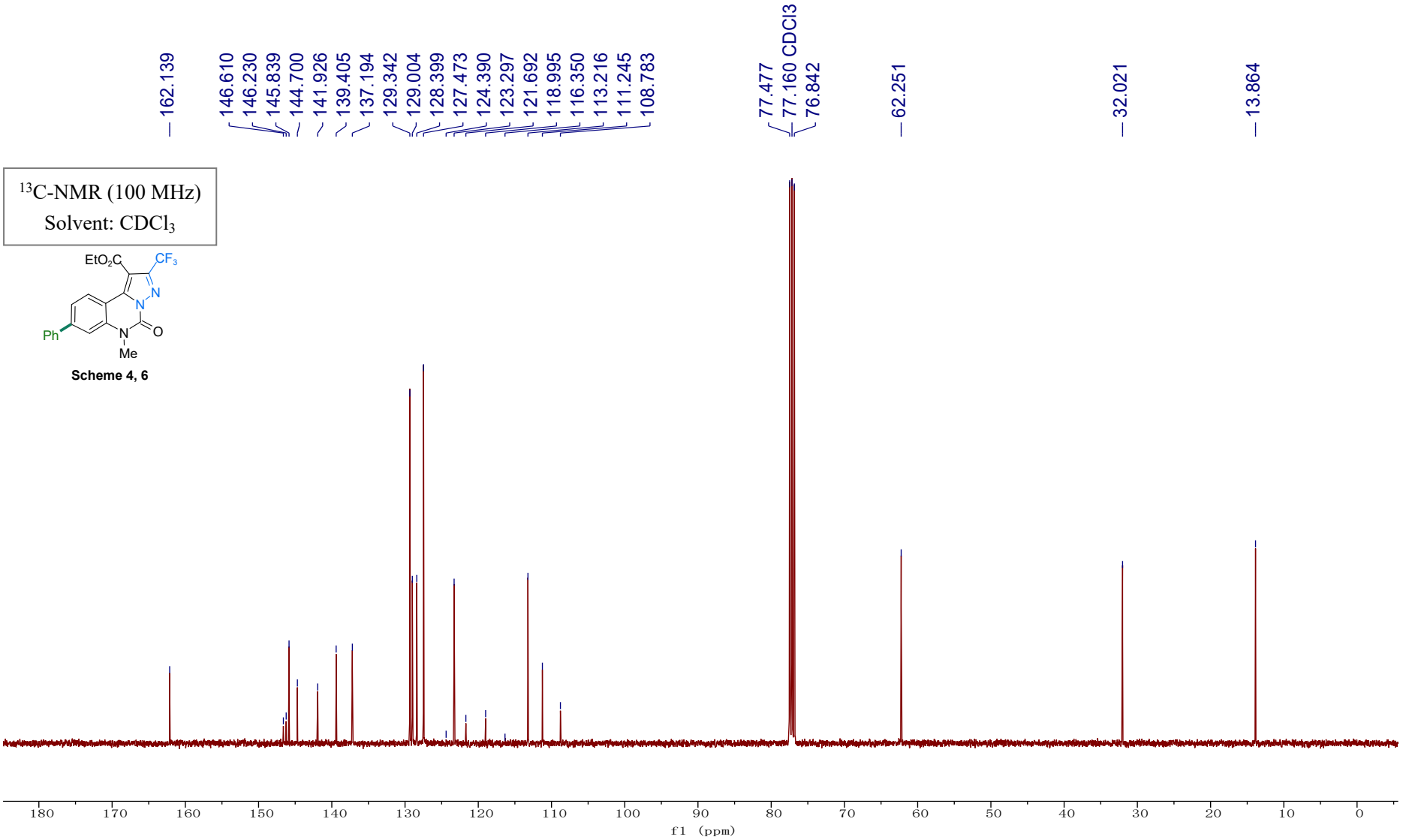

9.078
9.056
7.578
7.573
7.564
7.556
7.553
7.509
7.492
7.394
7.389
7.380
7.377
7.260 CDCl3
4.489
4.471
4.453
4.435
3.858
1.453
1.435
1.417
1H-NMR (400 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
N
O
Me
Ph
Scheme 4, 5
0.98
2.00
2.00
3.01
2.04
3.00
3.00
f1 (ppm)

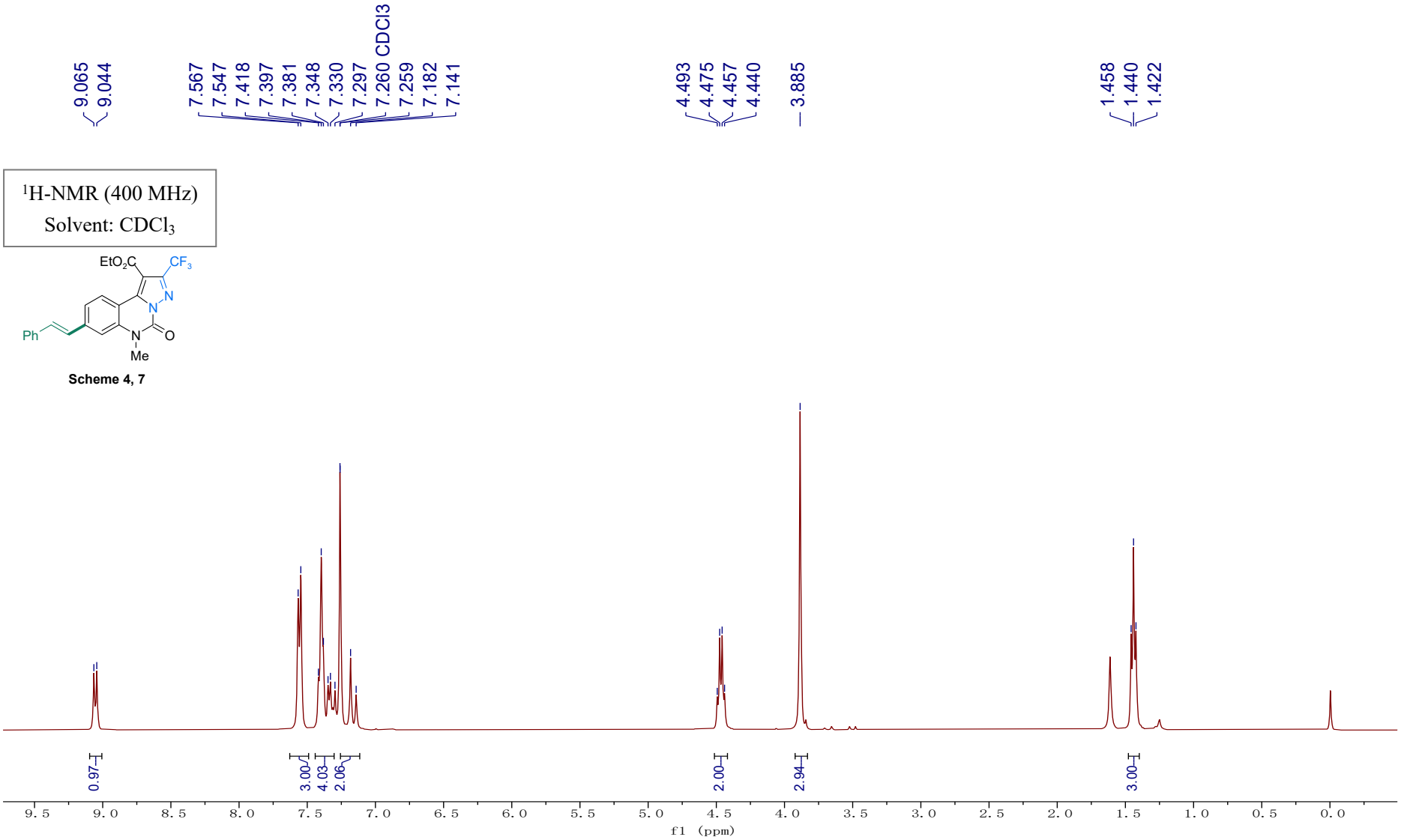

162.013
147.022
146.651
146.268
145.931
144.461
141.559
136.727
131.946
129.362
128.675
127.896
127.232
124.311
122.197
121.634
118.939
117.588
116.150
111.836
109.134
93.585
88.202
77.478
77.160 CDCl3
76.843
62.334
32.031
13.831
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
N
O
Me
Ph
Scheme 4, 5
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

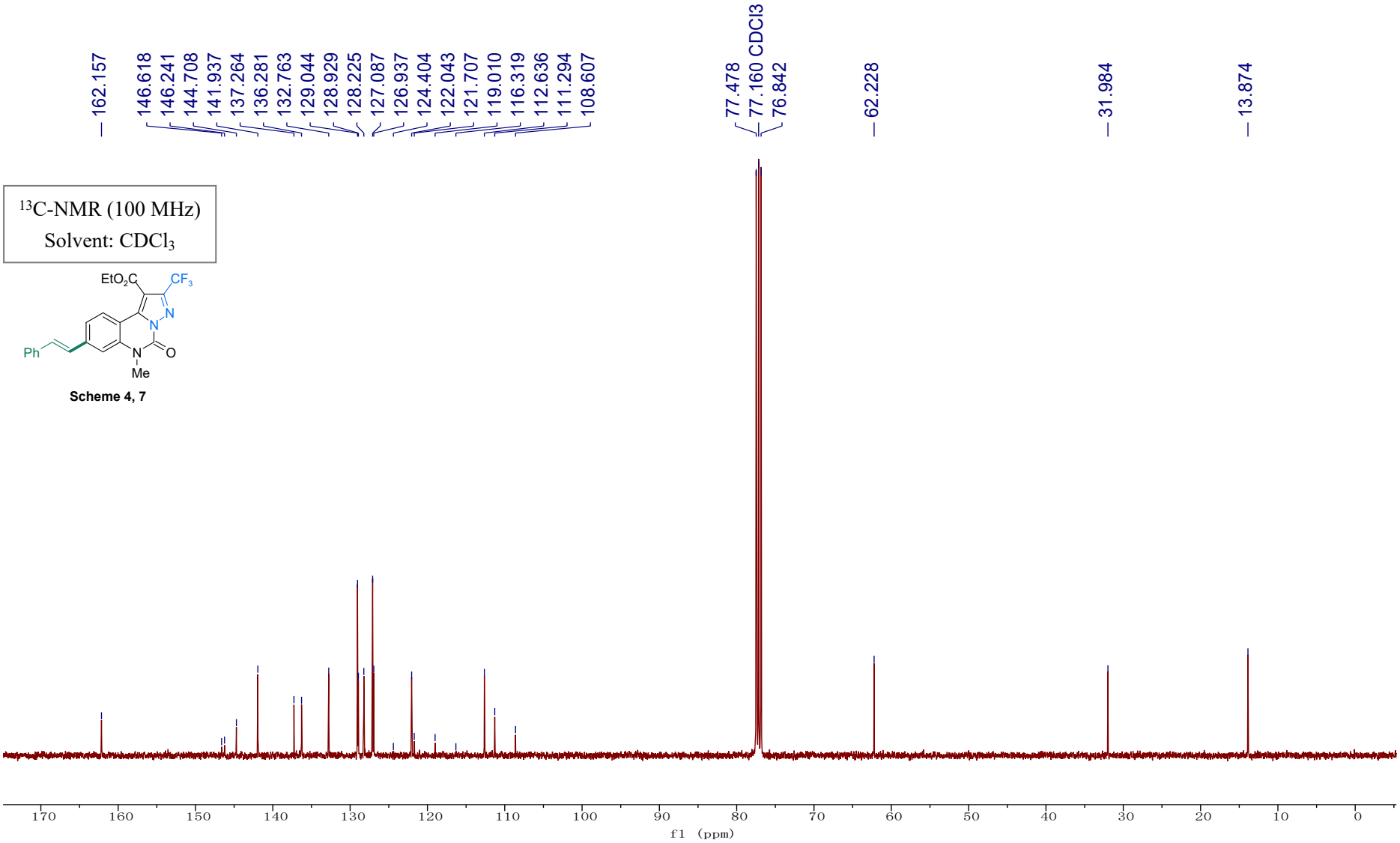


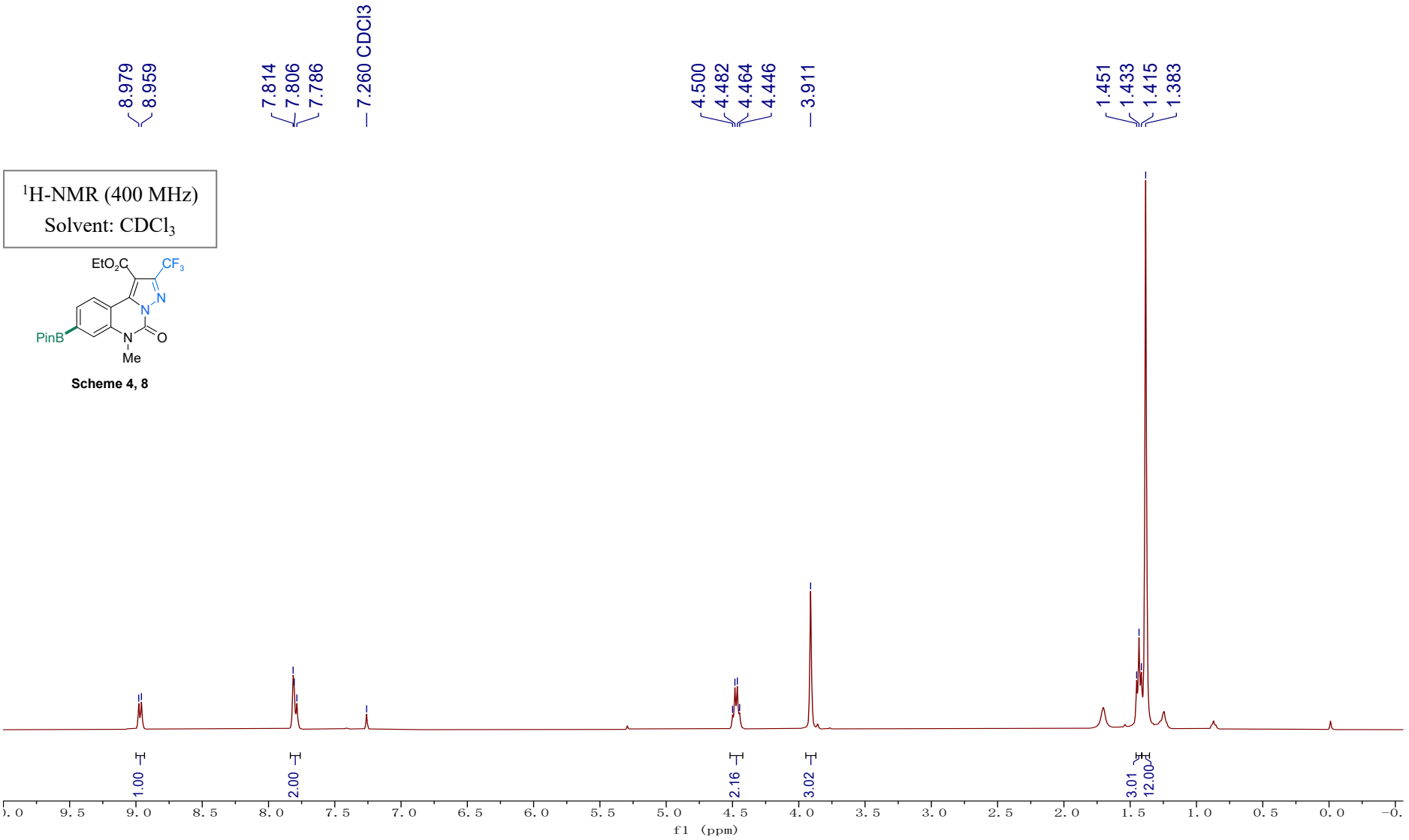
^{1}H-NMR (400 MHz)
Solvent: $CDCl_3$

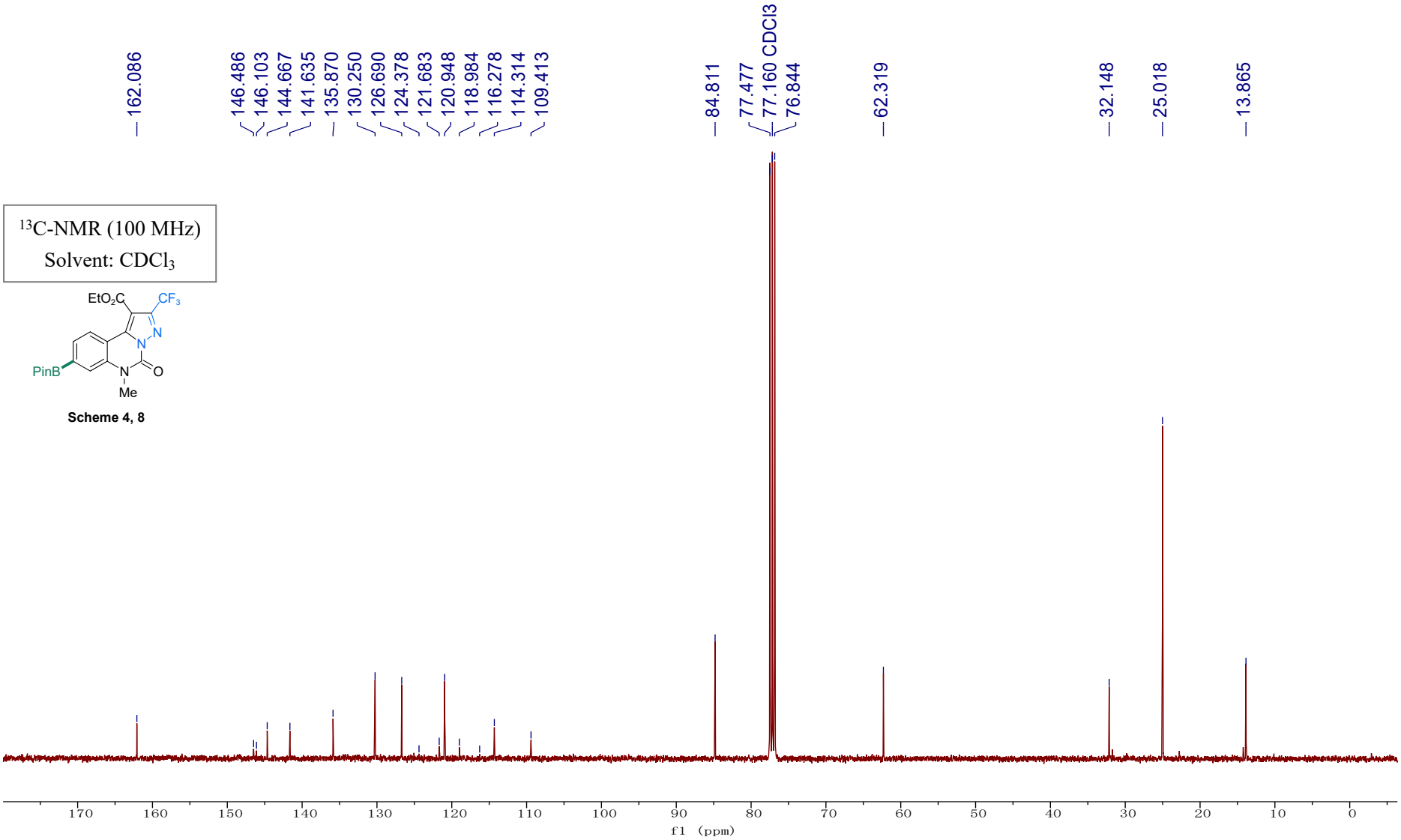
Scheme 4, 6

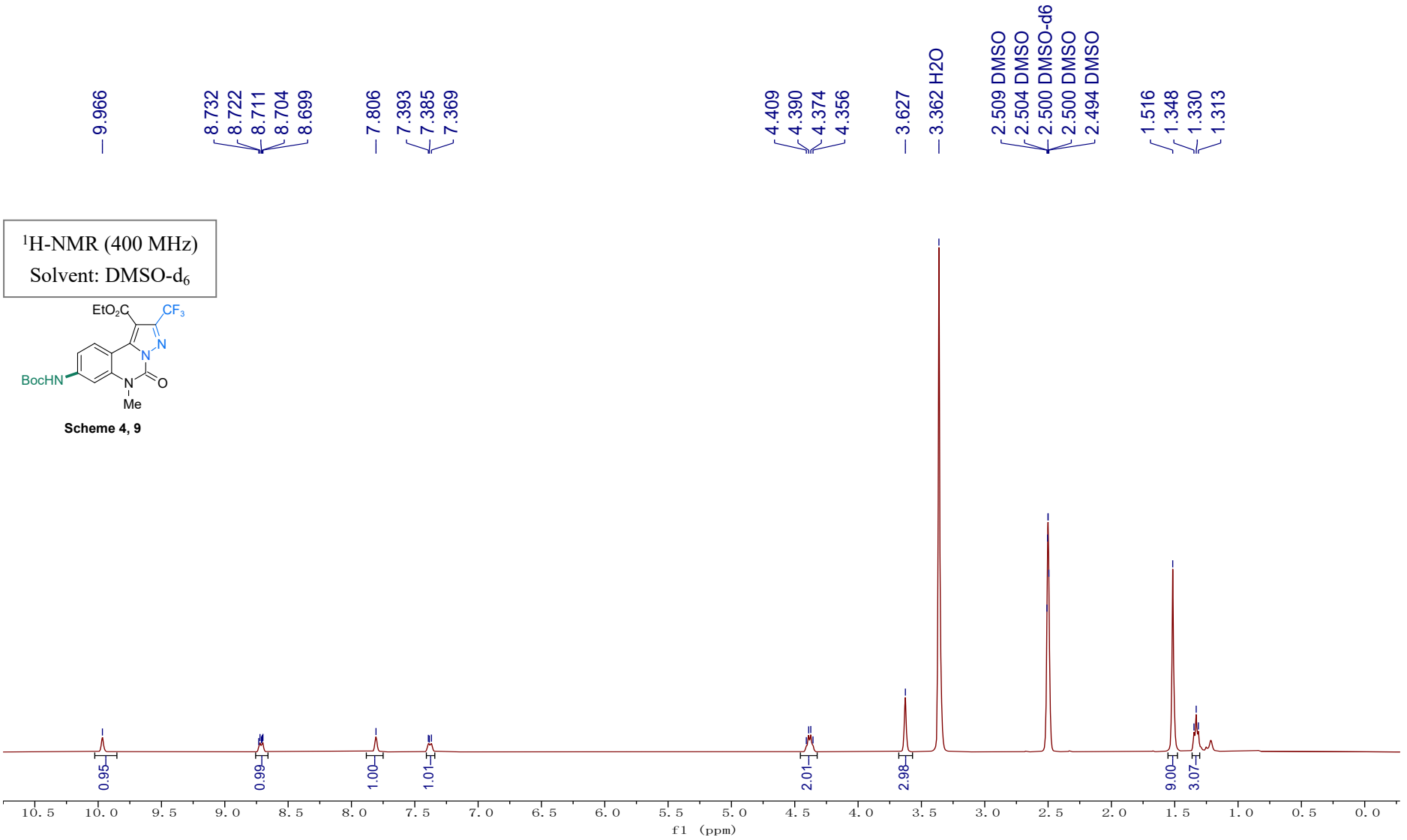

162.139
146.610
146.230
145.839
144.700
141.926
139.405
137.194
129.342
129.004
128.399
127.473
124.390
123.297
121.692
118.995
116.350
113.216
111.245
108.783
77.477
77.160 CDCl3
76.842
62.251
32.021
13.864
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
O
Ph
N
Me
Scheme 4, 6
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.065
9.044
7.567
7.547
7.418
7.397
7.381
7.348
7.330
7.297
7.260 CDCl3
7.259
7.182
7.141
4.493
4.475
4.457
4.440
3.885
1.458
1.440
1.422
1H-NMR (400 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
Ph
N
O
Me
Scheme 4, 7
0.97
3.00
4.03
2.06
2.00
2.94
3.00
9.5 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
f1 (ppm)


162.157
146.618
146.241
144.708
141.937
137.264
136.281
132.763
129.044
128.929
128.225
127.087
126.937
124.404
122.043
121.707
119.010
116.319
112.636
111.294
108.607
77.478
77.160 CDCl3
76.842
62.228
31.984
13.874
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
Ph
N
O
Me
Scheme 4, 7
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

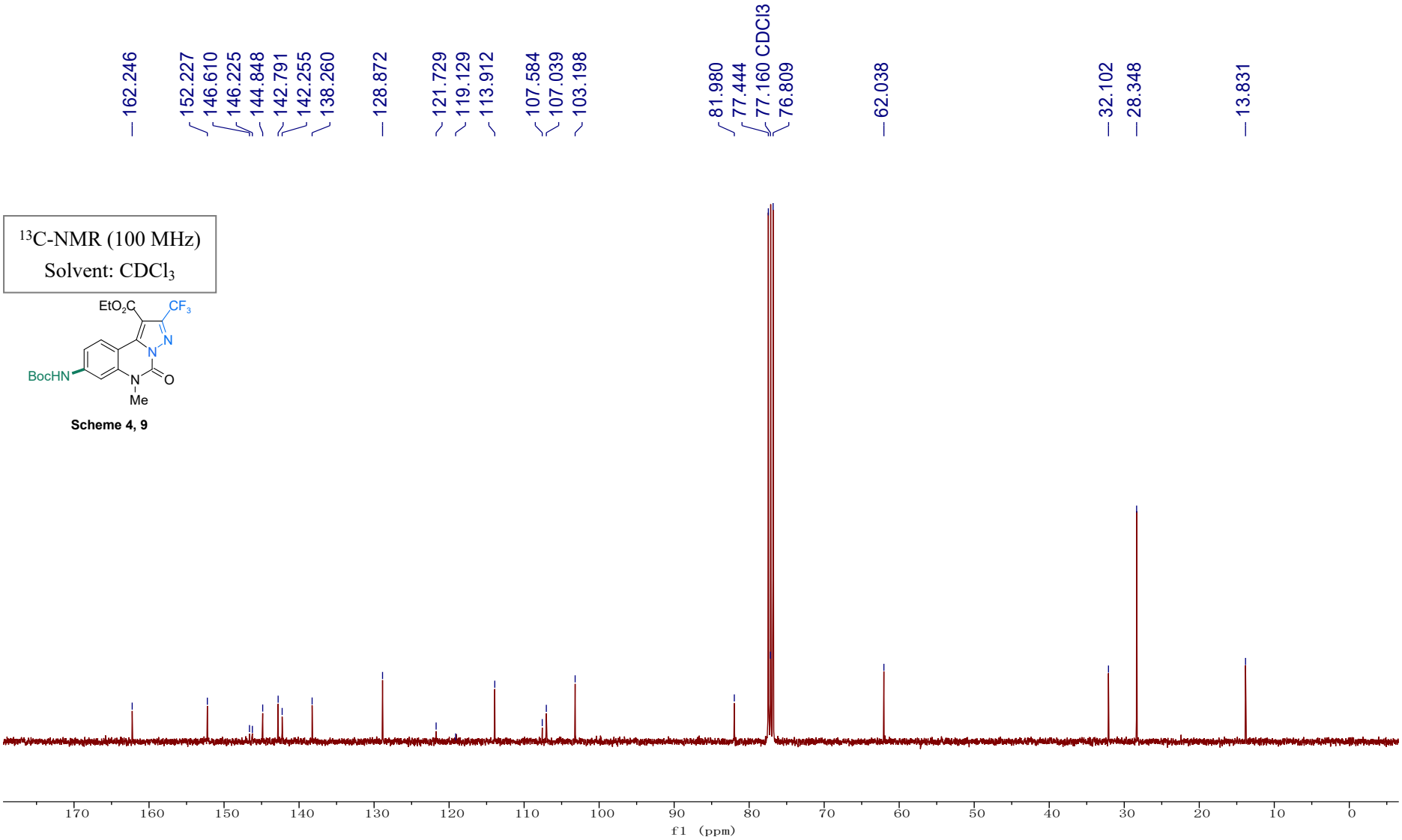

8.979
8.959
7.814
7.806
7.786
7.260 CDCl3
4.500
4.482
4.464
4.446
3.911
1.451
1.433
1.415
1.383
1H-NMR (400 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
PinB
N
O
Me
Scheme 4, 8
1.00
2.00
2.16
3.02
3.01
12.00
f1 (ppm)

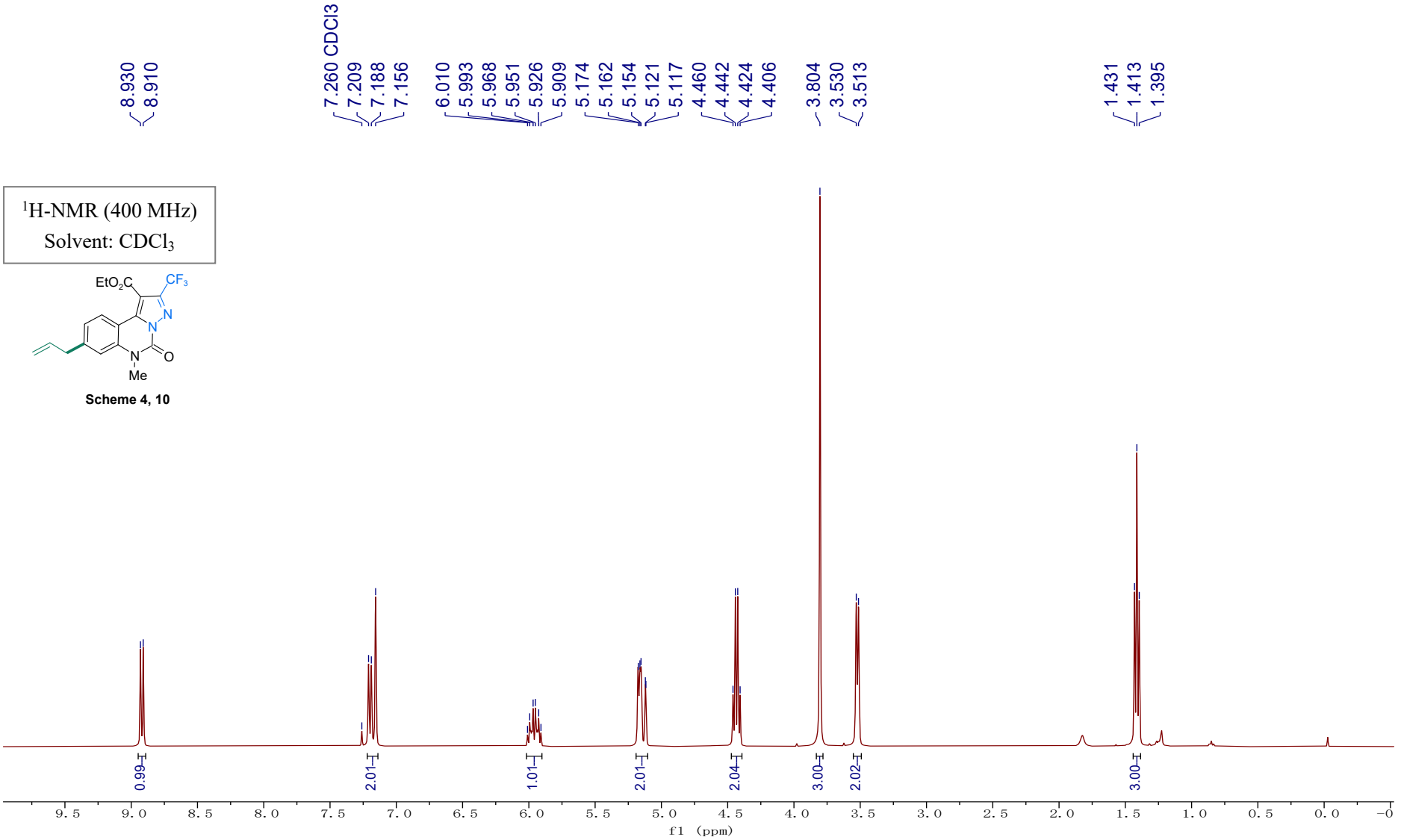

162.086
146.486
146.103
144.667
141.635
135.870
130.250
126.690
124.378
121.683
120.948
118.984
116.278
114.314
109.413
84.811
77.477
77.160 CDCl3
76.844
62.319
32.148
25.018
13.865
^{13}C-NMR (100 MHz)
Solvent: $CDCl_3$
EtO_2C
CF_3
N
N
PinB
N
O
Me
Scheme 4, 8
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



^{1}H-NMR (400 MHz)
Solvent: DMSO-d_6

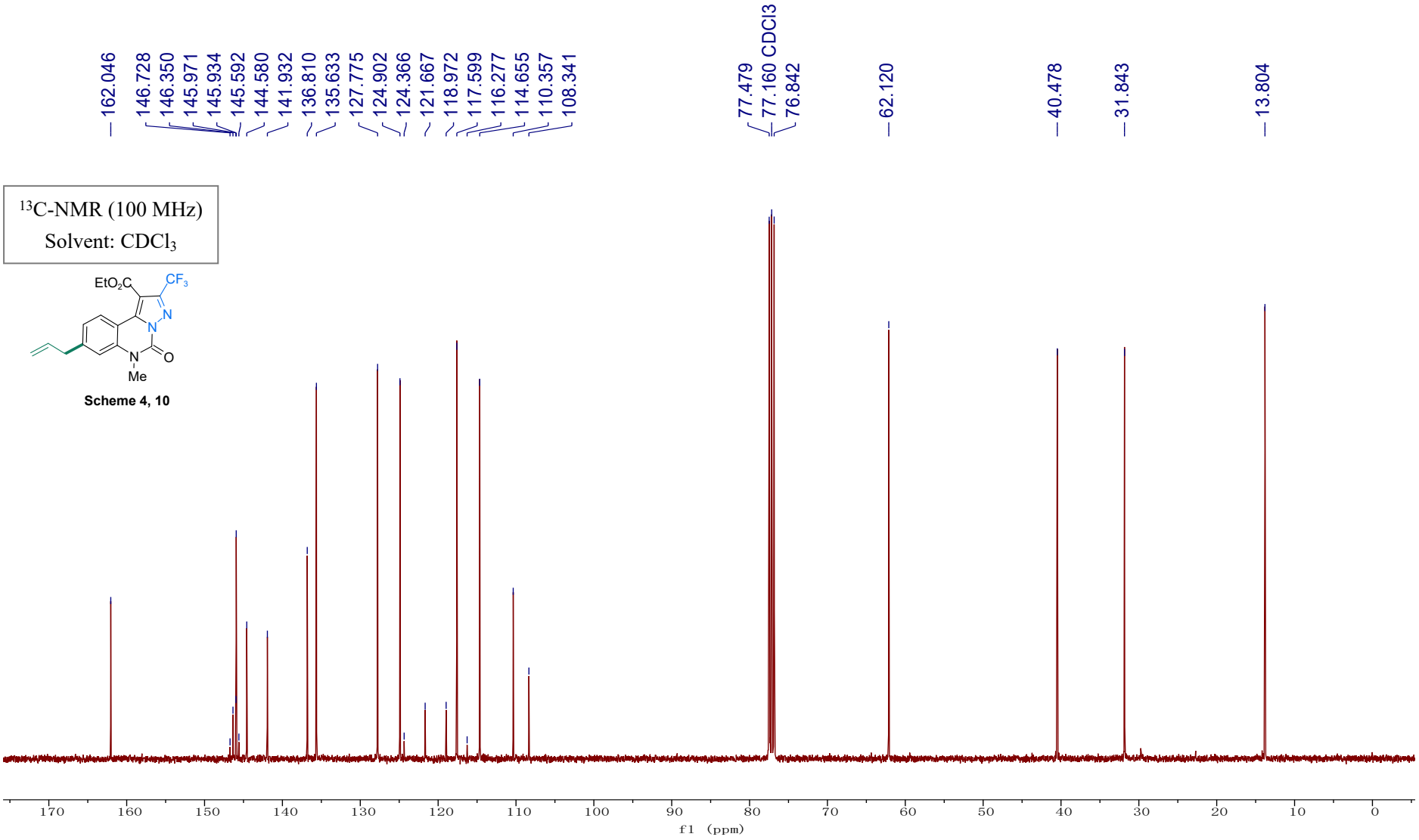
Scheme 4, 9


162.246
152.227
146.610
146.225
144.848
142.791
142.255
138.260
128.872
121.729
119.129
113.912
107.584
107.039
103.198
81.980
77.444
77.160 CDCl3
76.809
62.038
32.102
28.348
13.831
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
BocHN
N
O
Me
Scheme 4, 9
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



^{1}H-NMR (400 MHz)
Solvent: $CDCl_3$

Scheme 4, 10


162.046
146.728
146.350
145.971
145.934
145.592
144.580
141.932
136.810
135.633
127.775
124.902
124.366
121.667
118.972
117.599
116.277
114.655
110.357
108.341
77.479
77.160 CDCl3
76.842
62.120
40.478
31.843
13.804
13C-NMR (100 MHz)
Solvent: CDCl3
EtO2C
CF3
N
N
N
O
Me
Scheme 4, 10
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)