Supporting information

The asymmetric construction of CF_3-containing spiro-thiazolone-pyrrolidine compounds via β-ICD catalytic 1,3-dipolar cycloaddition

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1. General Information

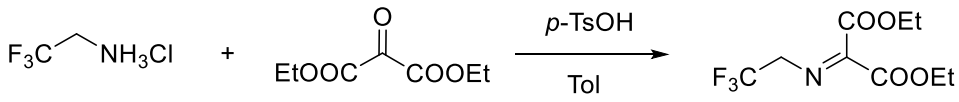
Reactions were monitored by thin layer chromatography (TLC), and compounds were visualized with a UV light at 254 nm. Column chromatography purifications were carried out using silica gel. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on a Bruker (300 MHz) spectrometer in $CDCl_3$, unless otherwise stated, using tetramethylsilane (TMS) as internal standard. Data are presented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constant in Hertz (Hz). Mass peaks are identified by the corresponding *m/z* values. The ee values determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel IA column and Chiracel IC column. Optical rotations were measured on a digital polarimeter and are reported as follows: $[\alpha]_D^T$ (1 g/100 mL, $CHCl_3$).

Catalysts **C1** and **C4** (β-ICD, or β-isocupreidine) were purchased from Daicel Chiral Technologies (China) Co., and catalysts **C2** and **C3** were synthesized according to literature methods. [1]

Reference:

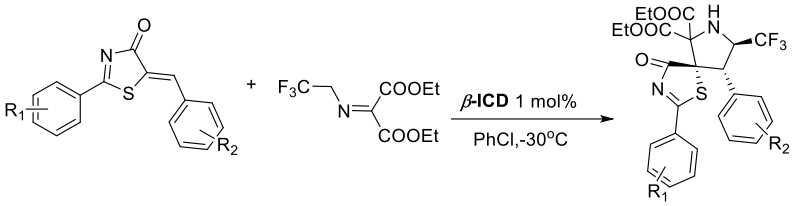
[1] A. Berkessel, S. Mukherjee, T. N. Müller, F. Cleemann, K. Roland, M. Brandenburg, J. M. Neudörfl and J. Lex, *Org. Biomol. Chem.*, 2006, **4**, 4319–4330.

2. Preparation of Substrate 2



Diehyl ketomalonate 13.65 mmol, 2,2,2-trifluoroethylamine hydrochloride (27.00 mmol) and p-toluenesulfonic acid (1.40 mmol) were suspended in toluene (40 mL) in a two-neck flask with a water separator and a condenser. The mixture was then heated to separate the water until complete disappearance of the starting materials, after which it was cooled to room temperature, washed with a small quantity of saturated $NaHCO_3$ solution, extracted with ethyl acetate and washed with brine, dried over anhydrous Na_2SO_4. After an evaporation of the organic solvent, the crude residue was purified by chromatography (silica gel, hexane/ethyl acetate = 4:1).

3. General procedure for the synthesis of Compounds 3a-3y

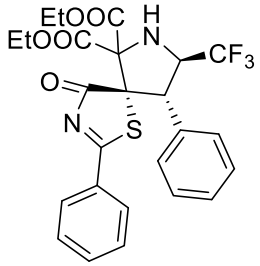


To a solution of β-ICD and (Z)-5-benzylidene-2-phenylthiazol-4(5H)-one **1a** (0.2 mmol) was added **2** (0.3 mmol) in one portion, and the reaction mixture was stirred at -30 °C, which was monitored by TLC inspection. Then the solvent was evaporated under reduced pressure and the crude residue was purified on silica gel flash column chromatography using ethyl acetate/petroleum (1/7) eluent to give the corresponding **3a-3y**.

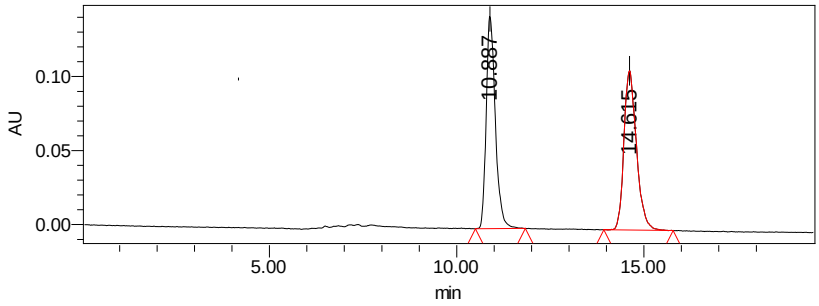
Racemates were prepared following the general procedure by 10 mol% DABCO.

4. Characterization Data of Compounds 3a-3y

Diethyl-(5S,8R,9S)-4-oxo-2,9-diphenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3a)



From 53.0 mg (0.2 mmol) of (Z)-5-benzylidene-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 93.6 mg (90.0% yield) of compound **3a** was obtained as a white solid, $[\alpha]_D^{20}$ = +37 (c = 1.0, $CHCl_3$), Mp. = 48-49 °C. Dr (>20:1) was determined by HPLC analysis. 95% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 10.6 min, t_{minor}= 14.2 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 8.1, 1.2 Hz, 2H), 7.65 - 7.60 (m, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.29 - 7.24 (m, 5H), 4.61 - 4.48 (m, 2H), 4.38 - 4.20 (m, 4H), 3.74 (d, *J* = 9.0 Hz,1H), 1.25 (t, *J* = 7.2Hz, 3H), 1.18 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.0, 191.8, 168.2, 166.6, 135.6, 133.5, 131.3, 129.3, 129.1, 128.7, 128.5, 124.9 (q, J_{C-F} = 277.5 Hz), 80.0, 77.8, 63.3 (q, J_{C-F} = 30.0 Hz), 62.9, 56.8, 13.6, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.9. HRMS (ESI) *m/z* calcd for $C_{25}H_{23}F_3N_2NaO_5S$ $[M+Na]^+$: 543.1172, found 543.1180.



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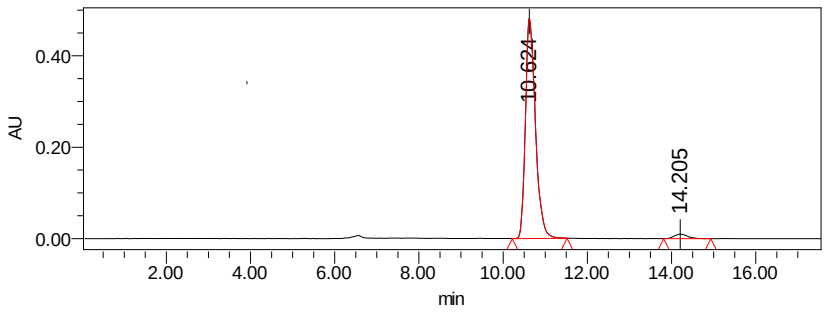

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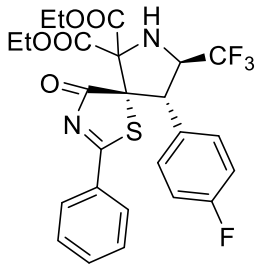
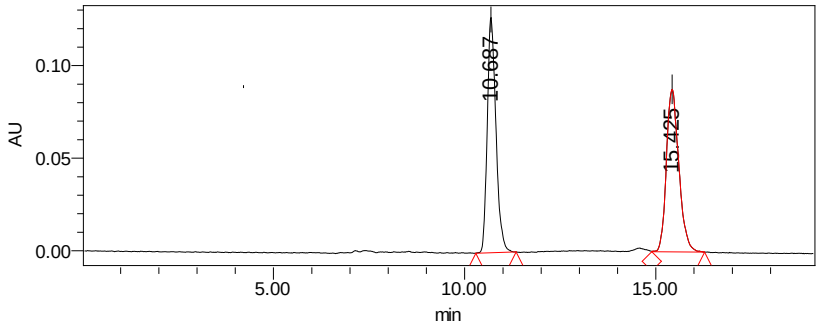
	14.205	215296	2.64	9828	BB	Unknown

Diethyl-(5S,8R,9S)-9-(4-fluorophenyl)-4-oxo-2-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3b)



From 56.6 mg (0.2 mmol) of (Z)-5-(4-fluorobenzylidene)-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 100.0 mg (81.0% yield) of compound **3b** was obtained as a white solid, $[\alpha]_D^{20}$ = +52 (c = 1.0, $CHCl_3$), Mp. = 140-141 °C. Dr (>20:1) was determined by HPLC analysis. 97% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 10.4 min, t_{minor} = 15.0 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 – 7.94 (m, 2H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 2H), 7.32 – 7.27 (m, 2H), 6.97 (t, *J* = 8.6 Hz, 2H), 4.59 (d, *J* = 7.2 Hz, 1H), 4.55 – 4.44 (m, 1H), 4.34 – 4.19 (m, 4H), 3.77 (d, *J* = 9.6Hz, 1H), 1.25 (t, *J* = 7.1Hz, 3H), 1.18 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ195.0, 191.9, 168.2, 166.4, 164.2, 160.9, 135.7, 131.3, 131.2, 131.1, 129.5, 129.5, 129.1, 128.7, 124.7 (q, JC-F = 278.5 Hz), 115.7, 115.4, 80.0, 63.8 (q, JC-F = 29.3 Hz), 62.9, 56.4, 13.6, 13.6. ^{19}F NMR (282 MHz, CDCl3) δ -72.9, -113.1. HRMS (ESI) m/z calcd for $C_{25}H_{22}F_4N_2NaO_5S$ [M+Na]+: 561.1078, found 561.1084.



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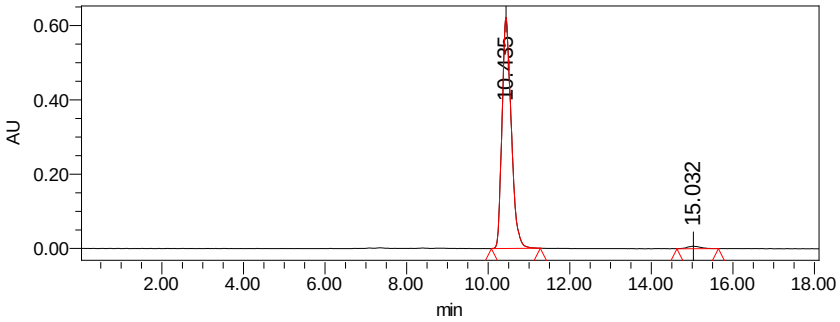

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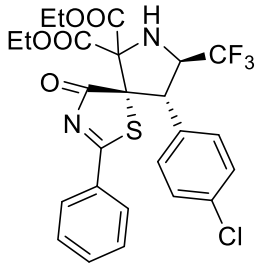
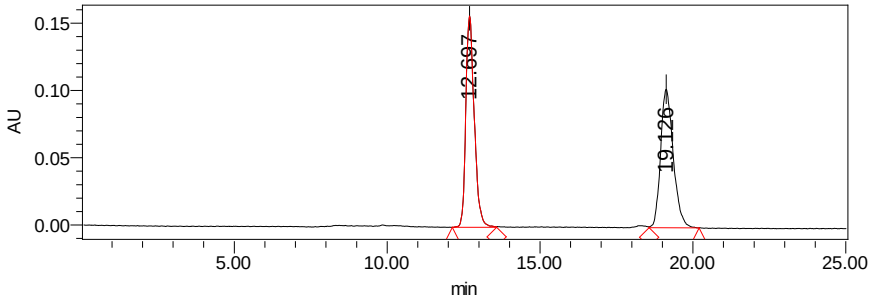
Diethyl-(5S,8R,9S)-9-(4-chlorophenyl)-4-oxo-2-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3c)



From 59.8 mg (0.2 mmol) of (Z)-5-(4-chlorobenzylidene)-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 97.0 mg (88.0% yield) of compound **3c** was obtained as a white solid, $[\alpha]_D^{20}$ = +72 (c = 1.0, $CHCl_3$), Mp. = 139-140 °C. Dr (>20:1) was determined by HPLC analysis. 95% ee was determined by HPLC analysis

(Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 12.6 min, t_{minor} = 19.0 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.1 Hz, 2H), 7.65 (t, *J* = 6.9 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.25 (s, 4H), 4.57 – 4.43 (m, 2H), 4.32 - 4.21 (m, 4H), 3.74 (d, *J* = 6.3 Hz, 1H), 1.26 – 1.16 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ195.0, 192.0, 168.2, 166.3, 135.7, 134.4, 132.3, 131.3, 130.7, 129.2, 128.8, 124.7 (q, J_{C-F} = 278.5 Hz), 80.2, 77.2, 63.7 (q, J_{C-F} = 40.1 Hz) 63.3, 56.5, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -73.0. HRMS (ESI) m/z calcd for $C_{25}H_{22}ClF_3N_2NaO_5S$ $[M+Na]^+$: 577.0782, found 577.0791.



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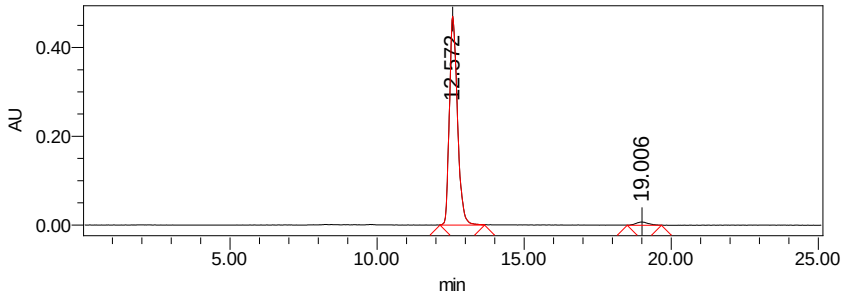
2	19.126	2968012	49.53	103084	VB	Unknown



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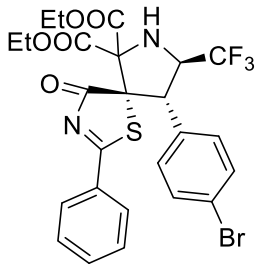
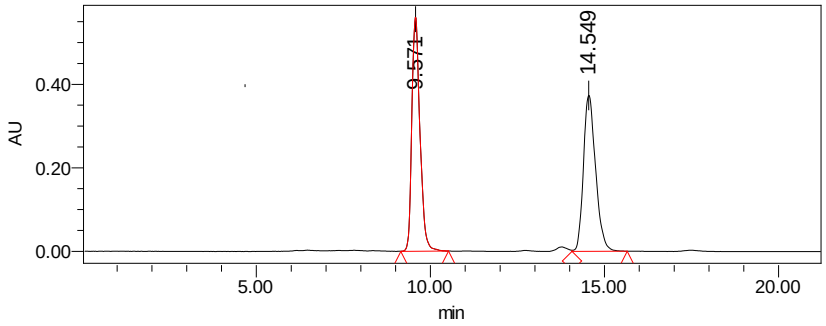
1	12.572	8954201	97.61	470331	VV	Unknown
	19.006	219619	2.39	7392	VV	Unknown

Diethyl-(5S,8R,9S)-9-(4-bromophenyl)-4-oxo-2-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3d)



From 68.6 mg (0.2 mmol) of (Z)-5-(4-bromobenzylidene)-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 112.0 mg (94.0% yield) of compound **3d** was obtained as a white solid, $[\alpha]_D^{20}$ = +66 (c = 1.0, $CHCl_3$), Mp. = 99-100 °C. Dr (>20:1) was determined by HPLC analysis. 97% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 10.2 min, t_{minor} = 15.7 min.. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.5 Hz, 2H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.49 – 7.40 (m, 4H), 7.19 (d, *J* = 7.8 Hz, 2H), 4.56 – 4.44 (m, 2H), 4.33 - 4.20 (m, 4H), 3.77 (d, *J* = 9.0 Hz, 1H), 1.26 – 1.16 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ195.0, 192.0, 168.2, 166.3, 135.8, 132.8, 131.8, 131.2, 131.1, 129.2, 128.8, 124.7 (q, J_{C-F} = 278.3 Hz), 122.7, 80.2, 63.7 (q, J_{C-F} = 30.2 Hz), 63.3, 63.0, 56.5, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.9. HRMS (ESI) m/z calcd for $C_{25}H_{22}BrF_3N_2NaO_5S$ $[M+Na]^+$: 621.0277, found 621.0286.



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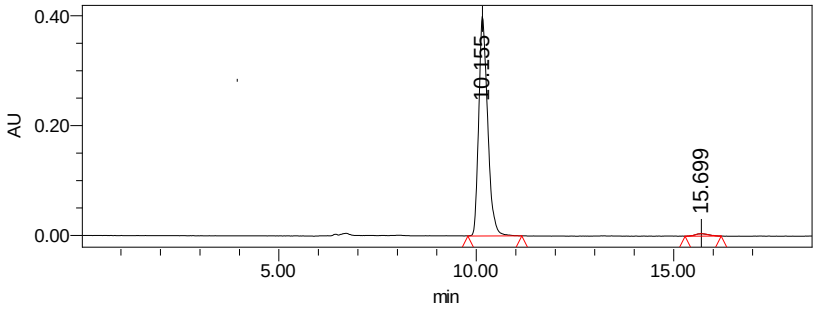
2	14.549	8871726	49.13	370927	bb	Unknown



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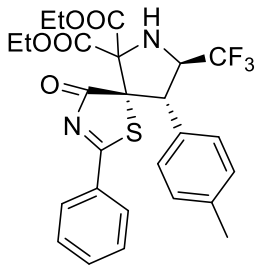
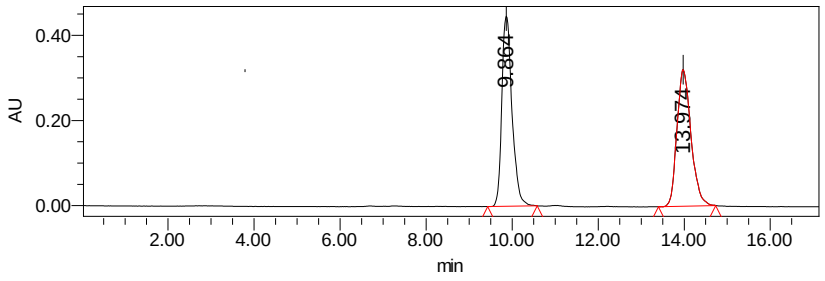
1	10.155	6265466	98.39	399481	BB	Unknown
	15.699	102808	1.61	4287	BB	

Diethyl-(5S,8R,9S)-4-oxo-2-phenyl-9-(p-tolyl)-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3e)



From 55.8 mg (0.2 mmol) of (Z)-5-(4-methylbenzylidene)-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 78.5 mg (74.0% yield) of compound **3e** was obtained as a white solid, $[\alpha]_D^{20}$ = +59 (c = 1.0, $CHCl_3$), Mp. = 114-115 °C. Dr (>20:1) was determined by HPLC analysis. 96% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 9.9 min, t_{minor} = 14.0 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.5 Hz, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.06 (d, *J* = 8.1 Hz, 2H), 4.44 (d, *J* = 7.5 Hz, 1H), 4.54 – 4.46 (m, 1H), 4.32 – 4.19 (m, 4H), 3.74 (d, *J* = 8.7Hz, 1H), 2.25 (s, 3H), 1.25 (t, *J* = 7.2Hz, 3H), 1.17 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ195.0, 192.0, 168.2, 166.6, 138.2, 135.5, 131.5, 130.5, 129.2, 129.2, 129.1, 128.8, 124.9 (q, JC-F = 278.0 Hz), 80.1, 77.8, 63.5 (q, JC-F = 31.3 Hz), 63.2, 56.7, 21.1, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.9. HRMS (ESI) m/z calcd for $C_{26}H_{25}F_3N_2NaO_5S$ $[M+Na]^+$: 557.1328, found 557.1340.



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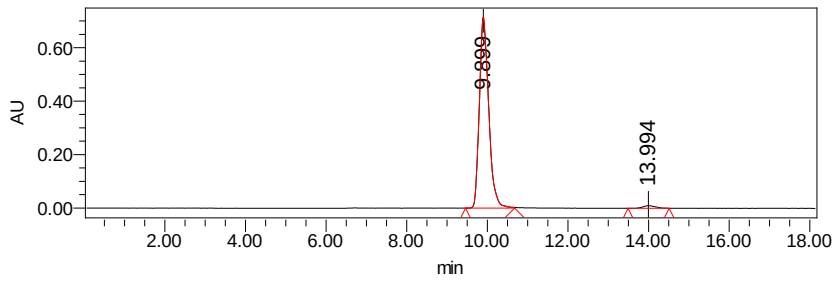

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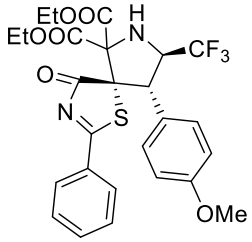
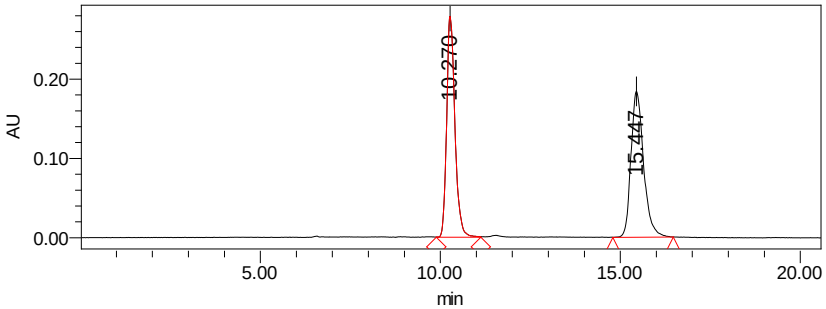
1	9.899	11501141	98.22	715498	BV	Unknown
	13.994	208385	1.78	9482	BB	

Diethyl-(5S,8R,9S)-9-(4-methoxyphenyl)-4-oxo-2-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3f)



From 59.0 mg (0.2 mmol) of (Z)-5-(4-methoxybenzylidene)-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 93.1 mg (85.0% yield) of compound **3f** was obtained as a white solid, $[\alpha]_D^{20}$ = +55 (c = 1.0, $CHCl_3$), Mp. = 109-110 °C. Dr (>20:1) was determined by HPLC analysis. 96% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 10.3 min, t_{minor} = 15.7 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 – 7.93 (m, 2H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.21 (d, *J* = 8.7 Hz, 2H), 6.79 (d, *J* = 8.7 Hz, 2H), 4.57 (d, *J* = 10.5 Hz, 1H), 4.49 – 4.41 (m, 1H), 4.33 – 4.19 (m, 4H), 3.73 (s, 3H), 1.25 (t, *J* = 7.2Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.9, 191.9, 168.2, 166.6, 159.4, 135.5, 131.4, 129.1, 128.7, 125.5, 124.9 (q, J_{C-F} = 279.8 Hz), 113.8, 79.9, 78.0, 63.6 (q, J_{C-F} = 30.0 Hz), 63.1, 62.9, 56.4, 55.1, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.9. HRMS (ESI) m/z calcd for $C_{26}H_{25}F_3N_2NaO_6S$ $[M+Na]^+$: 573.1278, found 573.1289.



	Retention Time	Area	% Area	Height	Int Type	Peak Type
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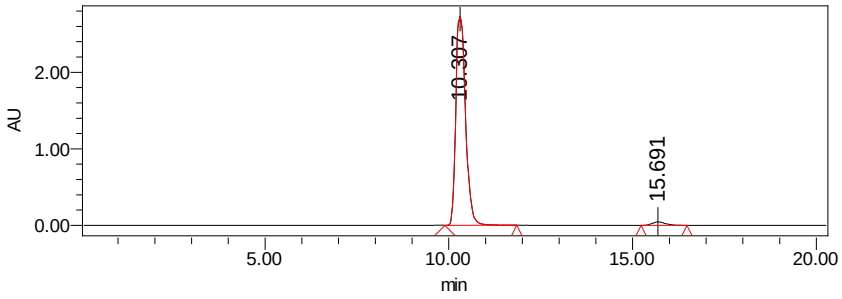
2	15.447	4482622	50.19	184136	BB	Unknown



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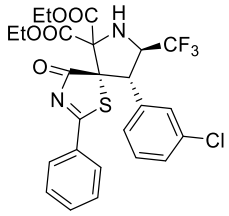
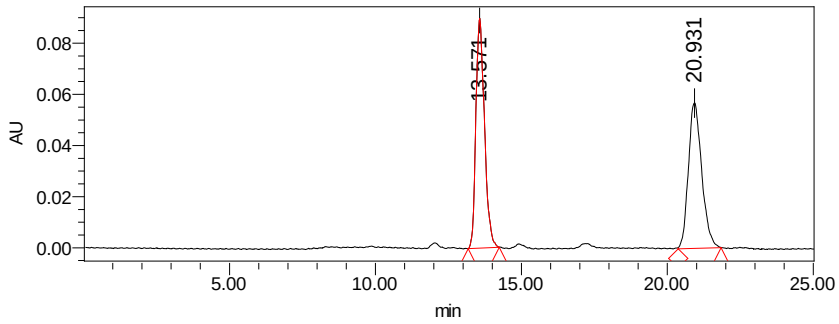
1	10.307	50455963	97.76	2726743	VB	Unknown
2	15.691	1158219	2.24	46241	BB	Unknown

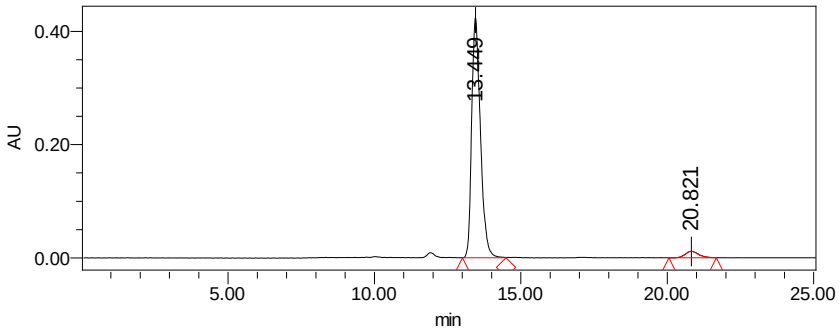
Diethyl-(5S,8R,9S)-9-(3-chlorophenyl)-4-oxo-2-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3g)



From 59.8 mg (0.2 mmol) of (Z)-5-(3-chlorobenzylidene)-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 99.2 mg (90.0% yield) of compound **3g** was obtained as a white solid, $[\alpha]_D^{20}$ = +75 (c = 1.0, $CHCl_3$), Mp. = 122-123 °C. Dr (>20:1) was determined by HPLC analysis. 92% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 13.6 min, t_{minor} = 20.9 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 - 7.95 (m, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.33 (s, 1H), 7.24 - 7.16 (m, 3H), 4.54 - 4.45 (m, 2H), 4.32 - 4.22 (m, 4H), 3.77 (d, *J* = 9.0 Hz, 1H)), 1.25 - 1.18 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ195.1, 192.1, 168.1, 166.3, 135.9, 135.7, 134.4, 131.3, 129.9, 129.3, 129.1, 128.8, 127.8,124.6 (q, J_{C-F} = 278.6 Hz) 80.3, 77.0, 63.9 (q, J_{C-F} = 30.2 Hz), 63.0, 56.8, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -73.0, -119.2. HRMS (ESI) m/z calcd for $C_{25}H_{22}ClF_3N_2NaO_5S$ $[M+Na]^+$: 577.0782, found 577.0792.

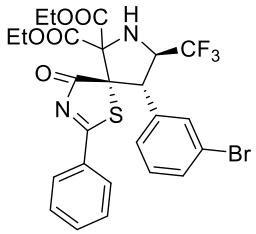


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	13.571	1837679	50.38	89811	BB	Unknown
2	20.931	1809698	49.62	56994	VB	Unknown



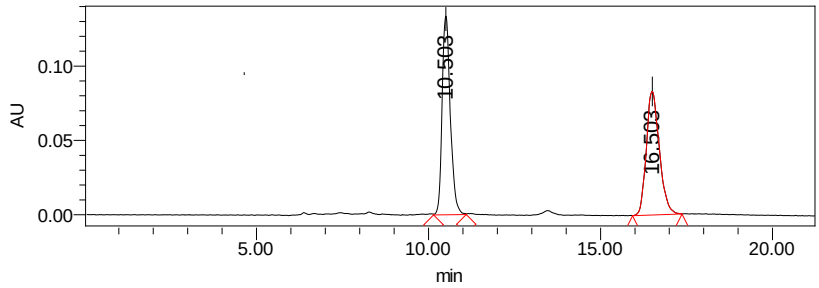
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	13.449	8767854	96.06	423653	BV	Unknown
2	20.821	360035	3.94	11333	BB	Unknown

Diethyl-(5S,8R,9S)-9-(3-bromophenyl)-4-oxo-2-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3h)

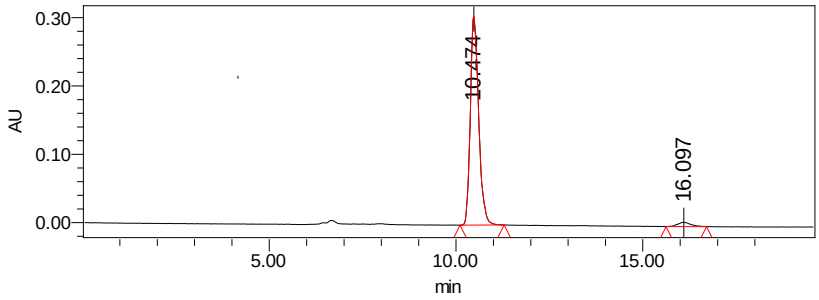


From 68.6 mg (0.2 mmol) of (Z)-5-(3-bromobenzylidene)-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 95.0 mg (79.0% yield) of compound **3h** was obtained as a yellow solid, $[\alpha]_D^{20}$ = +66 (c = 1.0, $CHCl_3$), Mp. = 58-59 °C. Dr (>20:1) was determined by HPLC analysis. 94% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time:

t_{major} = 10.5 min, t_{minor} = 16.1 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (m, 2H), 7.65 (m, 1H), 7.46 (t, *J* = 7.7 Hz, 3H), 7.40 - 7.37 (m, 1H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.15 (t, *J* = 8.0 Hz, 1H), 4.51 - 4.44 (m, *2*H), 4.32 - 4.21 (m, 4H), 3.76 - 3.73 (m, 1H), 1.22 (q, *J* = 7.2 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ195.2, 192.2, 168.2, 166.3, 136.2, 135.7, 132.2, 131.7, 131.3, 129.2, 128.8, 128.2, 124.6 (q, $J_{C\text{-}F}$ = 277.3 Hz), 122.6, 80.3, 77.0, 64.0(q, $J_{C\text{-}F}$ = 30.2 Hz), 63.0, 56.9, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.9. HRMS (ESI) m/z calcd for $C_{25}H_{22}BrF_3N_2NaO_5S$ $[M+Na]^+$: 621.0277, found 621.0284.

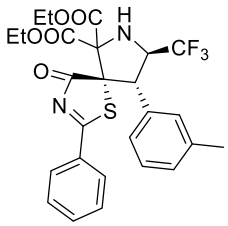


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	10.503	2225652	50.29	133703	VV	Unknown
2	16.503	2199696	49.71	83059	BB	Unknown

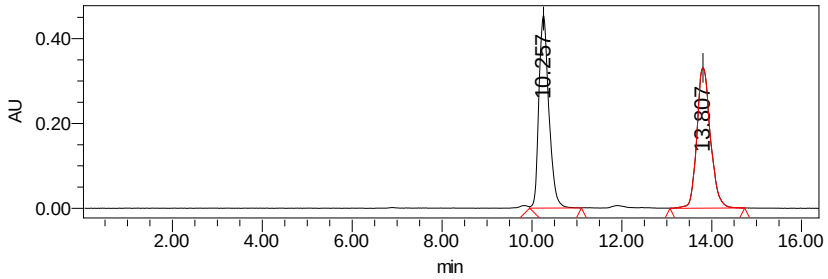


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	10.474	4742702	96.90	305559	BB	Unknown
	16.097	151485	3.10	6215	BB	Unknown

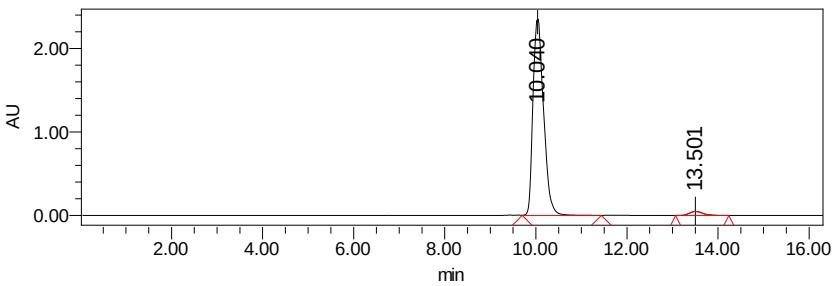
Diethyl-(5S,8R,9S)-4-oxo-2-phenyl-9-(m-tolyl)-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3i)



From 55.8 mg (0.2 mmol) of (Z)-5-(3-methylbenzylidene)-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 105.0 mg (98.0% yield) of compound **3i** was obtained as a yellow solid, $[\alpha]_D^{20}$ = +44 (c = 1.0, $CHCl_3$), Mp. = 120-121 °C. Dr (>20:1) was determined by HPLC analysis. 95% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 10.0 min, t_{minor} = 13.5 min.. ^{1}H NMR (300 MHz, $CDCl_3$) δ7.95 – 7.92 (m, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.19 - 7.10 (m, 2H), 7.03 (d, *J* = 8.7Hz, 2H), 4.32 - 4.20 (m, 4H), 3.76 (d, *J* = 8.4Hz, 1H), 2.26 (s, 3H), 1.24 (t, *J* = 7.1Hz, 3H), 1.18 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ195.1, 192.1, 168.2, 166.6, 138.1, 135.5, 133.5, 131.5, 130.1, 129.3, 129.1, 128.7, 128.3, 126.2, 124.9 (q, J_{C-F} = 277.0 Hz), 80.2, 77.7, 63.6 (q, J_{C-F} = 24.5 Hz), 62.9, 57.0, 21.4, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.9. HRMS (ESI) m/z calcd for $C_{26}H_{25}F_3N_2NaO_5S$ $[M+Na]^+$: 557.1328, found 557.1338.



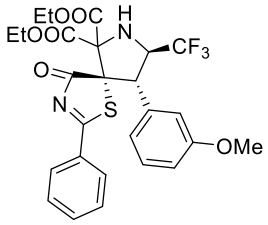
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	10.257	6988377	50.25	454514	VB	Unknown
2	13.807	6917753	49.75	330866	BB	Unknown



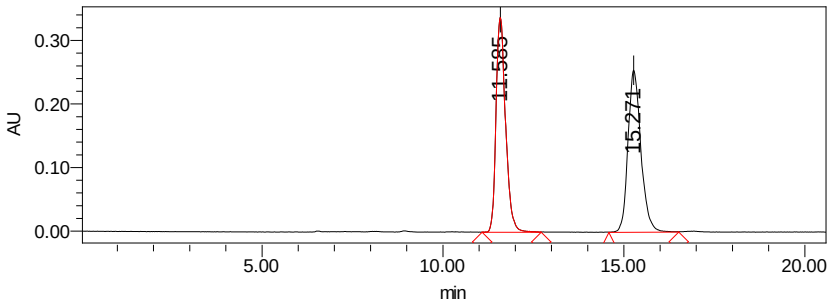
	Retention Time	Area	% Area	Height	Int Type	Peak Type

1	10.040	38363620	97.47	2370763	VV	Unknown
	13.501	997724	2.53	48202	BB	Unknown

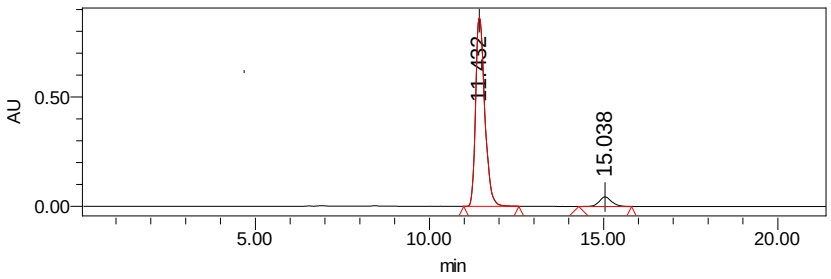
Diethyl-(5S,8R,9S)-9-(3-methoxyphenyl)-4-oxo-2-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3j)



From 59.0 mg (0.2 mmol) of (Z)-5-(3-methoxybenzylidene)-2-phenylthiazol-4(5H)-one (59.0mg, 0.2 mmol) and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 64.6 mg (59.0% yield) of compound **3j** was obtained as a yellow solid, $[\alpha]_D^{20}$ = +57 (c = 1.0, $CHCl_3$), Mp. = 97-98 °C. Dr (>20:1) was determined by HPLC analysis. 87% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 11.4 min, t_{minor} = 15.0 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.5 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 2H), 7.11 (t, *J* = 7.8 Hz, 1H), 6.80 - 6.76 (m, 2H), 6.70 (d, *J* = 8.1Hz, 1H), 4.43 (d, *J* = 1.8 Hz, 2H), 4.24 - 4.12 (m, 4H), 3.66 (s, *3*H), 1.18 - 1.08 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.4, 192.4, 168.2, 166.5, 159.5, 135.5, 135.4, 131.4, 129.5, 129.1, 128.7, 124.8 (q, $J_{C\text{-}F}$ = 278.0 Hz), 121.6, 115.1, 113.7, 80.3, 77.4, 63.8 (q, $J_{C\text{-}F}$ = 28.7 Hz), 62.9, 57.2, 55.2, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -73.0. HRMS (ESI) m/z calcd for $C_{26}H_{25}F_3N_2NaO_6S$ $[M+Na]^+$: 573.1278, found 573.1288.

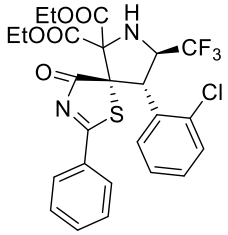


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	11.585	6181484	49.36	337462	VV	Unknown
2	15.271	6341511	50.64	254897	BV	Unknown

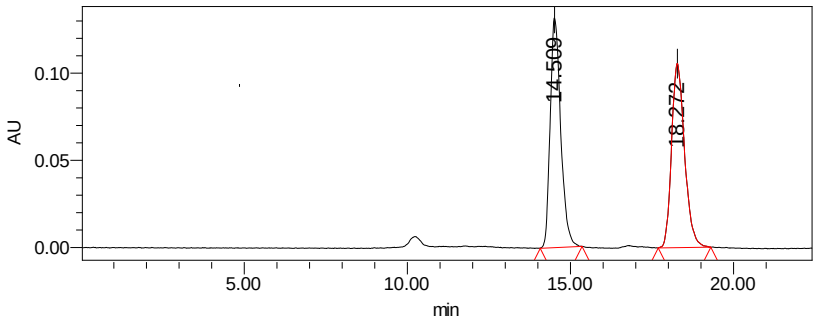


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	11.432	15580514	93.55	863245	BB	Unknown
2	15.038	1073991	6.45	43509	VB	Unknown

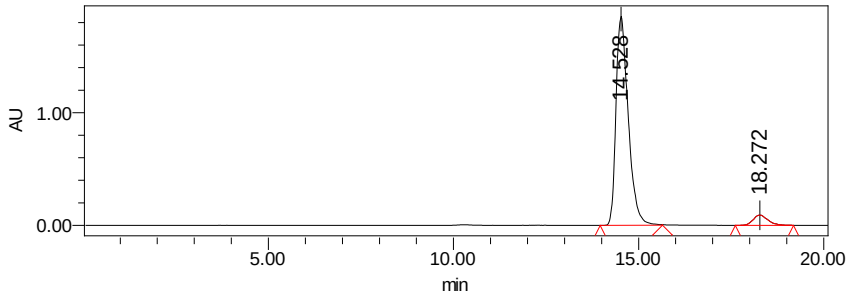
Diethyl-(5S,8R,9S)-9-(2-chlorophenyl)-4-oxo-2-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3k)



From 59.8 mg (0.2 mmol) of (Z)-5-(2-chlorobenzylidene)-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 87 mg (79% yield) of compound **3k** was obtained as a yellow oil, $[\alpha]_D^{20}$ = +42 (c = 1.0, $CHCl_3$), dr (>20:1) was determined by HPLC analysis. 89% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 14.5 min, t_{minor}= 18.3 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.8 Hz, 2H), 7.66 (q, *J* = 8.3 Hz, 2H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.39 - 7.34 (m, 1H), 7.31 – 7.28 (m, 1H), 7.24 – 7.19 (m, 1H), 4.82 (d, *J* = 9.9 Hz, 1H), 4.71 - 4.59 (m, 1H), 4.41 – 4.13 (m, 4H), 3.85 (d, *J* = 11.1Hz, 1H), 1.31 (t, *J* = 7.1Hz, 3H), 1.12 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ196.4, 195.0, 168.5, 165.8, 136.2, 135.4, 133.8, 131.5, 129.6, 129.5, 129.3, 129.0, 128.8, 127.1, 124.5 (q, J_{C-F} = 278.3 Hz), 81.5, 75.0, 64.2 (q, J_{C-F} = 29.5 Hz), 63.5, 62.9, 54.3, 13.8, 13.4. ^{19}F NMR (282 MHz, $CDCl_3$) δ -73.3. HRMS (ESI) *m/z* calcd for $C_{25}H_{22}ClF_3N_2$ NaO_5S $[M+ Na]^+$: 577.0782, found 577.0790.

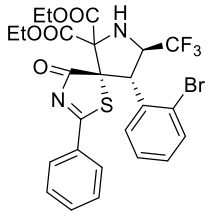


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	14.509	2957120	50.23	131919	BB	Unknown
2	18.272	2930017	49.77	105754	BB	Unknown

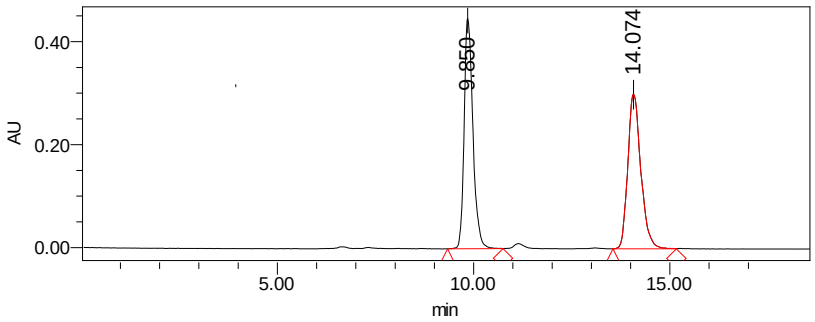


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	14.528	42720203	94.40	1852471	BV	Unknown
2	18.272	2535331	5.60	90825	BB	Unknown

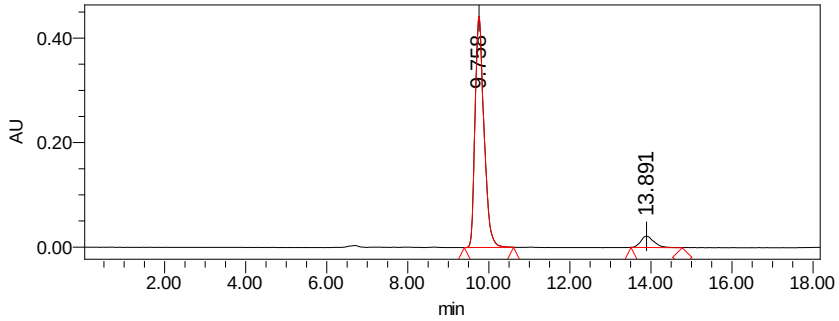
Diethyl-(5S,8R,9S)-9-(2-bromophenyl)-4-oxo-2-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3l)



From 68.6 mg (0.2 mmol) of (Z)-5-(2-bromobenzylidene)-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 91.5 mg (77.0% yield) of compound **3l** was obtained as a white solid, $[\alpha]_D^{20}$ = +41 (c = 1.0, $CHCl_3$), Mp. = 124-125 °C. Dr (>20:1) was determined by HPLC analysis. 87% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 9.8 min, t_{minor}= 13.9 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.5 Hz, 2H), 7.72 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.50 – 7.38 (m, 4H), 7.14 (td, *J* = 7.7, 1.1 Hz, 1H), 4.84 (d, *J* = 9.6Hz, 1H), 4.68 - 4.55 (m, 1H), 4.44 - 4.10 (m, 4H), 3.85 (d, *J* = 11.1 Hz, *3*H), 1.31 (t, *J* = 7.12Hz, 3H), 1.12 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ196.4, 195.0, 168.6, 165.8, 135.7, 135.4, 133.0, 131.6, 129.5, 129.1, 128.8, 127.7, 127.1, 124.6 (q, J_{C-F} = 278.3 Hz), 81.6, 75.0, 63.8 (q, J_{C-F} = 29.8 Hz), 63.5, 62.9, 57.1, 13.8, 13.4. ^{19}F NMR (282 MHz, $CDCl_3$) δ -73.3. HRMS (ESI) *m/z* calcd for $C_{25}H_{22}BrF_3N_2NaO_5S$ $[M+Na]^+$: 621.0277, found 621.0283.

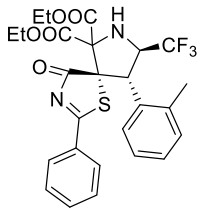


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	9.850	6952061	50.08	447750	BV	Unknown
2	14.074	6931194	49.92	300309	BV	Unknown



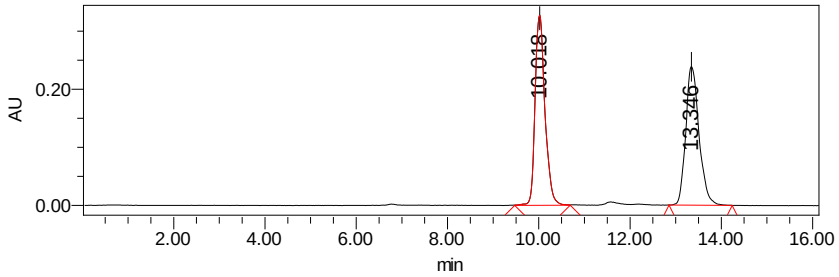
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	9.758	6736930	93.23	441739	BB	Unknown
2	13.891	489575	6.77	21630	BV	Unknown

Diethyl-(5S,8R,9S)-4-oxo-2-phenyl-9-(o-tolyl)-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3m)

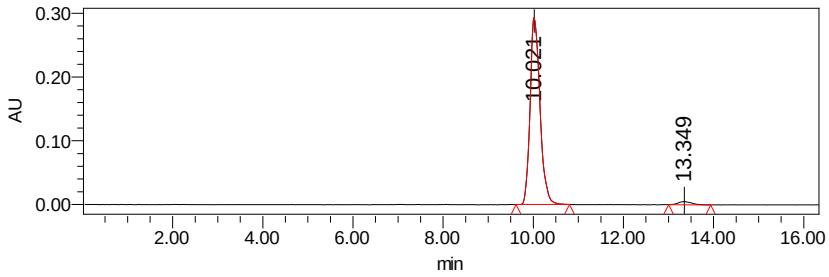


From 55.8 mg (0.2 mmol) of (Z)-5-(2-methylbenzylidene)-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 105 mg (99% yield) of compound **3m** was obtained as a yellow solid, $[\alpha]_D^{20}$ = +50 (c = 1.0, $CHCl_3$), Mp. = 126-127 °C. Dr (>20:1) was determined by HPLC analysis. 95% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 10.0 min, t_{minor}= 13.3 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94

(d, *J* = 7.2 Hz, 2H), 7.80 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 8.0 Hz, 2H), 7.19 – 7.10 (m, 2H), 7.04 (q, *J* = 10.2 Hz, 2H), 4.60 - 4.52 (m, 2H), 4.32 - 4.60 (m, 4H), 3.77 (d, *J* = 7.5 Hz, 1H), 2.26 (s, 3H), 1.24 (t, *J* = 7.1Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ195.1, 192.0, 168.2, 166.6, 138.1, 135.5, 133.5, 131.4, 130.1, 129.3, 129.1, 128.7, 128.3, 126.2, 124.9 (q, J_{C-F} = 278.0 Hz), 80.2, 77.7, 63.5 (q, J_{C-F} = 31.0 Hz), 62.9, 57.0, 21.4, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.9. HRMS (ESI) m/z calcd for $C_{26}H_{25}F_3N_2NaO_5S$ $[M+Na]^+$: 557.1328, found 557.1336.

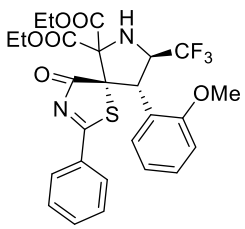


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	10.018	4929020	50.47	327733	VV	Unknown
2	13.346	4836661	49.53	239012	BB	Unknown

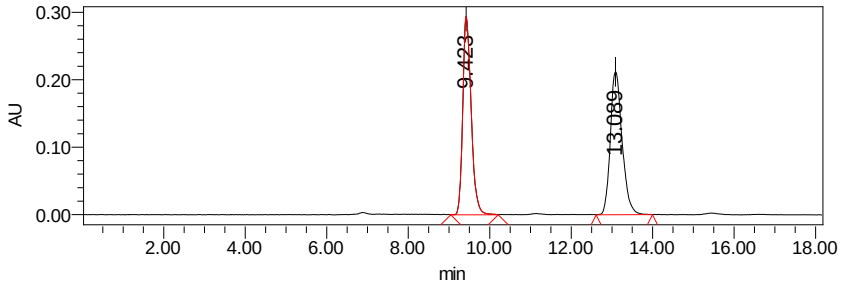


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	10.021	4482319	97.68	293114	BB	Unknown
2	13.349	106462	2.32	5019	BB	Unknown

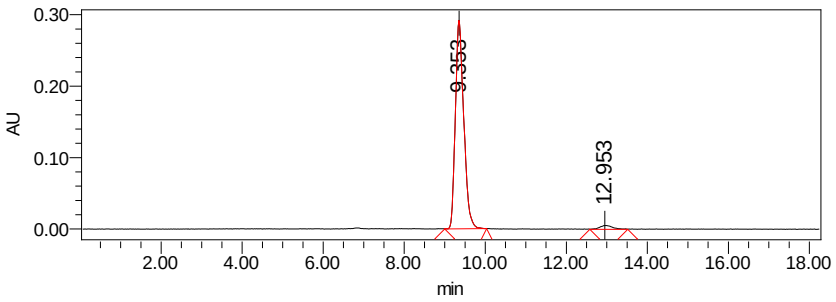
Diethyl-(5S,8R,9S)-9-(2-methoxyphenyl)-4-oxo-2-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3n)



From 59.0 mg (0.2 mmol) of (Z)-5-(2-methoxybenzylidene)-2-phenylthiazol-4(5H)-one (59.0mg, 0.2 mmol) and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 109.0 mg (99.0% yield) of compound **3n** was obtained as a white solid, $[\alpha]_D^{20}$ = -3 (c = 1.0, $CHCl_3$), Mp. = 60-61 °C. Dr (>20:1) was determined by HPLC analysis. 94% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 9.4 min, t_{minor}= 13.0 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ7.99 (d, *J* = 7.8 Hz, 2H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.38 (d, *J* = 6.9 Hz, 1H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.01 (t, *J* = 7.2 Hz, 1H), 6.70 (d, *J* = 8.1 Hz, 1H), 4.80 (d, *J* = 4.5 Hz, 1H), 4.58 (d, *J* = 9.9 Hz, 1H), 4.39 – 4.10 (m, 4H), 3.74 (d, *J* = 10.5 Hz,1H), 3.46 (s, 3H), 1.29 (t, *J* = 6.9Hz, 3H), 1.13 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ196.1, 168.3, 166.1, 158.0, 135.2, 131.8, 129.1, 128.4, 124.8 (q, J_{C-F} = 277.5 Hz), 120.4, 109.6, 80.9, 75.5, 63.3, 62.8, 61.5 (q, J_{C-F} = 29.8 Hz), 54.8, 13.8, 13.4. ^{19}F NMR (282 MHz, $CDCl_3$) δ -73.1. HRMS (ESI) m/z calcd for $C_{26}H_{25}F_3N_2NaO_6S$ $[M+Na]^+$: 573.1278, found 573.1288.

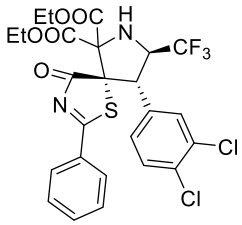


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	9.423	4229083	49.84	294118	VV	Unknown
2	13.089	4256248	50.16	211948	BB	Unknown

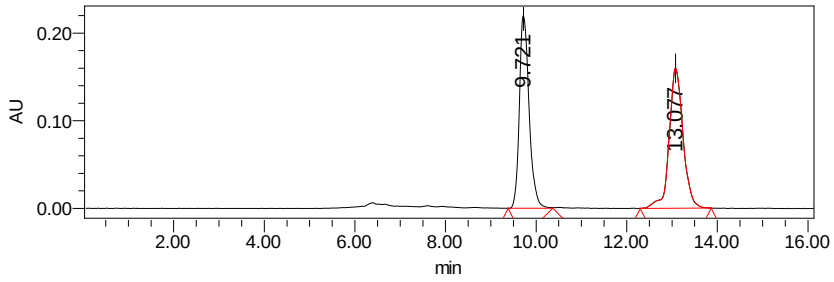


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	9.353	4185738	97.09	291630	VB	Unknown
2	12.953	125617	2.91	5395	VV	Unknown

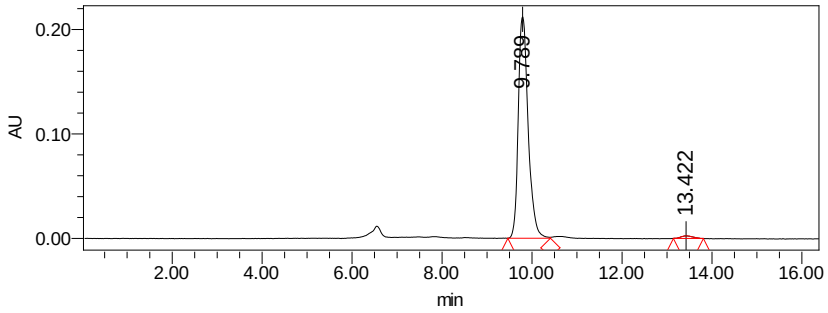
Diethyl-(5S,8R,9S)-9-(3,4-dichlorophenyl)-4-oxo-2-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3o)



From 72.0 mg (0.2 mmol) of (Z)-5-(3,4-dichlorobenzylidene)-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 109.0 mg (93% yield) of compound **3o** was obtained as a white solid, $[\alpha]_D^{20}$ = +72 (c = 1.0, $CHCl_3$), Mp. = 169-170 °C. Dr (>20:1) was determined by HPLC analysis. 97% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 9.8 min, t_{minor} = 13.4 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.2 Hz, 2H), 7.67 (t, *J* = 7.35 Hz, 3H), 7.51 - 7.44 (m, 3H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.18 (dd, *J* = 8.4, 2.1 Hz, 1H), 4.49 - 4.42 (m, 2H), 4.32 - 4.21 (m, 4H), 3.78 (d, *J* = 8.7 Hz, 1H)), 1.25 - 1.18 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ195.1, 192.2, 168.2, 166.2, 135.9, 134.4, 132.8, 132.7, 131.3, 131.2, 130.6, 129.2, 128.9, 124.5 (q, J_{C-F} = 278.5 Hz), 80.4, 64.2 (q, J_{C-F} = 30.2 Hz), 63.4, 63.0, 56.4, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -73.0. HRMS (ESI) m/z calcd for $C_{25}H_{21}Cl_2F_3N_2NaO_5S$ $[M+Na]^+$: 611.0393, found 611.0400.

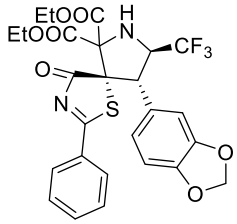


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	9.721	3284888	49.13	220175	BV	Unknown
2	13.077	3401882	50.87	159735	BB	Unknown



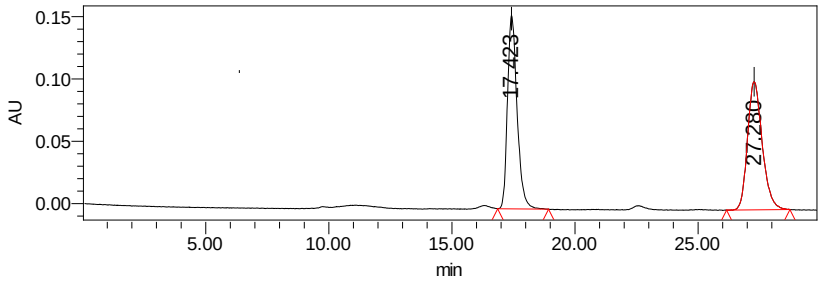
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	9.789	3239095	98.60	211981	BV	Unknown
2	13.422	46074	1.40	2412	BB	Unknown

Diethyl-(5S,8R,9S)-9-(benzo[d][1,3]dioxol-5-yl)-4-oxo-2-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3p)

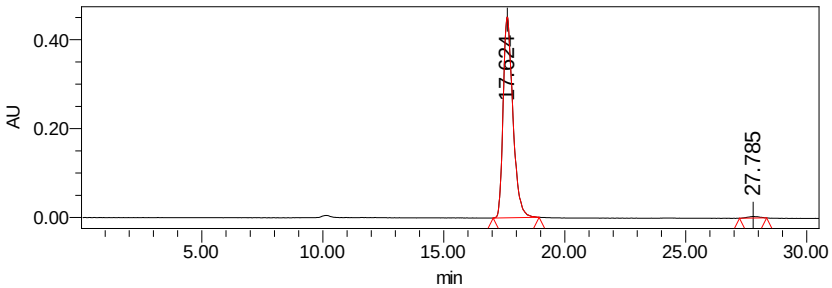


From 61.8 mg (0.2 mmol) of (Z)-5-(benzo[d][1,3]dioxol-5-ylmethylene)-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 98.0 mg (87% yield) of compound **3p** was obtained as a yellow solid, $[\alpha]_D^{20}$ = +94 (c = 1.0, $CHCl_3$), Mp. = 168-169 °C. Dr (>20:1) was determined by HPLC analysis. 98% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1,

1.0 mL/min). Retention time: t_{major} = 17.6 min, t_{minor} = 27.8 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.2 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 2H), 6.86 (s, 1H), 6.73 - 6.66 (m, *2*H), 5.92 (dd, *J* = 6.0, 1.2 Hz, 2H), 4.50 - 4.36 (m, 2H), 3.72 (d, *J* = 9.0 Hz, 1H), 1.25 - 1.16 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.2, 191.2, 167.7, 166.3, 148.1, 142.8, 135.6, 131.5, 129.2, 128.8, 124.6 (q, J_{C-F} = 278.3 Hz), 110.6, 109.7, 79.9, 76.8, 63.2, 62.9, 62.5 (q, J_{C-F} = 31.4 Hz), 50.6, 13.7, 13.5. ^{19}F NMR (282 MHz, $CDCl_3$) δ -73.0. HRMS (ESI) m/z calcd for $C_{26}H_{23}F_3N_2NaO_7S$ $[M+Na]^+$: 587.1070, found 587.1081.

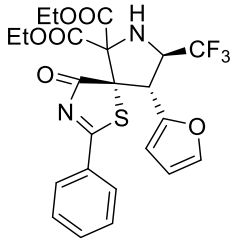


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	17.423	4208189	49.65	155281	bb	Unknown
2	27.280	4267446	50.35	102699	bb	Unknown

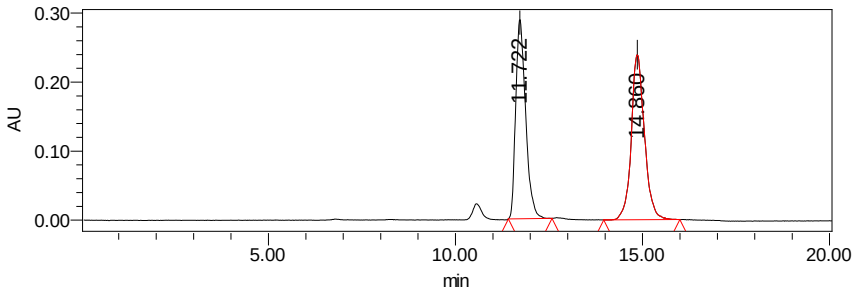


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	17.624	12631699	99.06	451713	BB	Unknown
	27.785	119940	0.94	3503	BB	

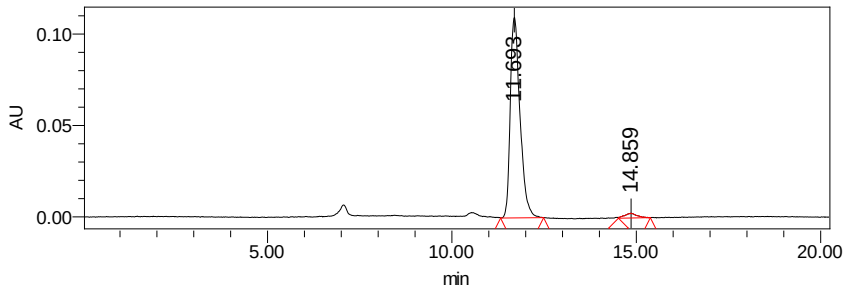
Diethyl-(5S,8R,9R)-9-(furan-2-yl)-4-oxo-2-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3q)



From 51.0 mg (0.2 mmol) of (Z)-5-(furan-2-ylmethylene)-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 84.5 mg (83.0% yield) of compound **3q** was obtained as a yellow solid, $[\alpha]_D^{20}$ = +33 (c = 1.0, $CHCl_3$), Mp. = 71-72 °C. Dr (>20:1) was determined by HPLC analysis. 94% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 11.7 min, t_{minor} = 14.9 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.8 Hz, 2H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 2H), 7.31 (d, *J* = 3.6 Hz, 1H), 6.29 – 6.26 (m, 2H), 4.71 (d, *J* = 9.9 Hz, 1H), 4.62 - 4.49 (m, 1H), 4.32 - 4.19 (m, 4H), 3.74 (d, *J* = 9.6 Hz, 1H), 1.24 (t, *J* = 7.2Hz, 3H), 1.18 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ195.2, 191.2, 167.7, 166.3, 148.1, 142.8, 135.6, 131.5, 129.2, 128.8, 124.6 (q, J_{C-F} = 278.3 Hz), 110.6, 109.7, 79.9, 76.8, 63.2, 62.9, 62.5 (q, J_{C-F} = 31.4 Hz), 50.6, 13.7, 13.5. ^{19}F NMR (282 MHz, $CDCl_3$) δ -73.5. HRMS (ESI) m/z calcd for $C_{23}H_{21}F_3N_2NaO_6S$ [M+Na]`: 533.0965, found 533.0975.



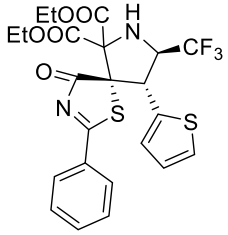
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	11.722	5307224	47.56	288912	bb	Unknown
2	14.860	5850919	52.44	239217	bb	Unknown



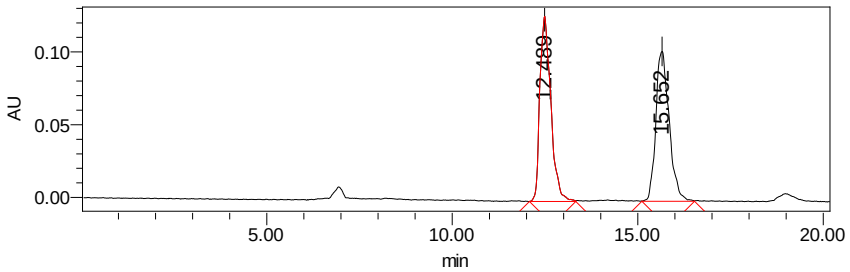
	Retention Time	Area	% Area	Height	Int Type	Peak Type

1	11.693	2013606	97.02	109796	BB	Unknown
2	14.859	61874	2.98	2599	VB	Unknown

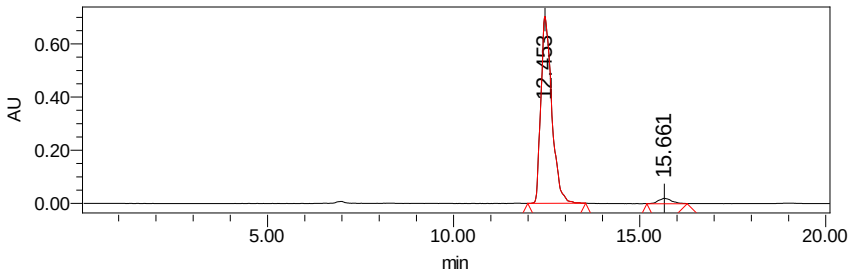
Diethyl-(5S,8R,9R)-4-oxo-2-phenyl-9-(thiophen-2-yl)-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3r)



From 54.2 mg (0.2 mmol) of (Z)-2-phenyl-5-(thiophen-2-ylmethylene)thiazol-4(5H)-one (54.2mg, 0.2 mmol) and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 61.3 mg (58% yield) of compound **3r** was obtained as a yellow oil, $[\alpha]_D^{20}$ = +40 (c = 1.0, $CHCl_3$), dr (>20:1) was determined by HPLC analysis. 93% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 12.5 min, t_{minor} = 15.7 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.0 (d, *J* = 7.2 Hz, 2H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.21 (d, *J* = 5.1 Hz, 1H), 7.0 (d, *J* = 3.0 Hz, 1H), 6.92 - 6.89(m, 1H), 4.92 (d, *J* = 9.9 Hz, 1H), 4.46 – 4.35 (m, 1H), 4.33 – 4.19 (m, 4H), 3.73 (d, *J* = 9.6 Hz,1H), 1.25 (t, *J* = 7.2Hz, 3H), 1.18 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.3, 191.3, 167.9, 166.3, 136.2, 135.7, 131.4, 129.2, 128.8, 128.3, 126.9, 126.2, 124.6 (q, J_{C-F} = 278.5 Hz), 79.8, 77.7, 65.5 (q, J_{C-F} =30.2 Hz), 63.2, 63.0, 52.1, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -73.0. HRMS (ESI) m/z calcd for $C_{23}H_{21}F_3N_2NaO_5S_2$ $[M+Na]^+$: 549.0736, found 549.0749.

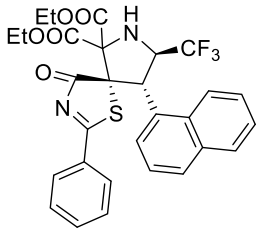


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	12.489	2620159	50.37	127315	VV	Unknown
2	15.652	2581307	49.63	103147	VV	Unknown

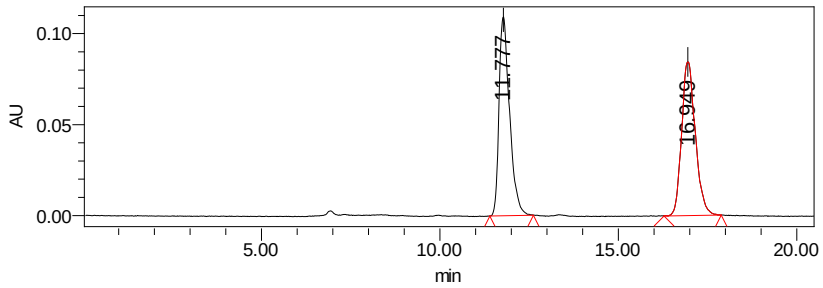


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	12.453	14360701	96.68	706554	BB	Unknown
2	15.661	492607	3.32	19728	BV	Unknown

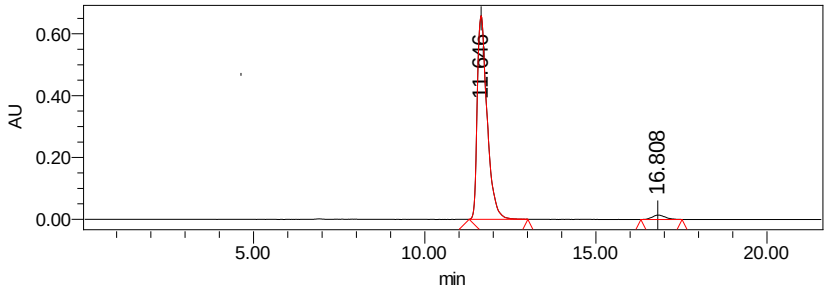
Diethyl-(5S,8R,9S)-9-(naphthalen-1-yl)-4-oxo-2-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3s)



From 63.0 mg (0.2 mmol) of (Z)-5-(naphthalen-1-ylmethylene)-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 97.0 mg (85.0% yield) of compound **3s** was obtained as a yellow solid, $[\alpha]_D^{20}$ = -88 (c = 1.0, $CHCl_3$), Mp. = 159-160 °C. Dr (>20:1) was determined by HPLC analysis. 94% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 11.6 min, t_{minor} = 16.8 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 - 7.73 (m, 6H), 7.56 - 7.45 (m, 2H), 7.42 - 7.24 (m, 4H), 5.27 (d, *J* = 9.9 Hz, 1H), 4.92 - 4.80 (m, 1H), 4.39 – 4.19 (m, 4H), 3.91 (q, *J* = 10.5 Hz, 1H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ197.0, 194.7, 168.5, 166.2, 135.3, 133.7, 132.6, 131.3, 131.3, 128.9, 128.9, 128.9, 128.6, 127.1, 126.4, 125.9, 125.0, 124.8 (q, J_{C-F} = 277.5 Hz), 122.2, 81.4, 76.8, 65.0 (q, J_{C-F} = 29.3 Hz) 63.4, 63.0, 52.4, 13.8, 13.5. ^{19}F NMR (282 MHz, $CDCl_3$) δ -73.2. HRMS (ESI) m/z calcd for $C_{29}H_{25}F_3N_2NaO_5S$ $[M+Na]^+$: 593.1328, found 593.1340.

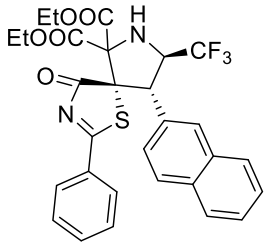


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	11.777	2246758	49.93	109371	BB	Unknown
2	16.949	2252914	50.07	84524	VB	Unknown



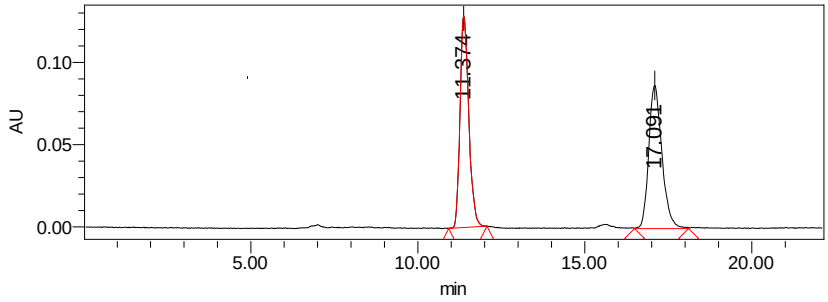
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	11.646	13114842	97.21	658794	VB	Unknown
2	16.808	376281	2.79	14253	BB	Unknown

Diethyl-(5S,8R,9S)-9-(naphthalen-2-yl)-4-oxo-2-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3t)

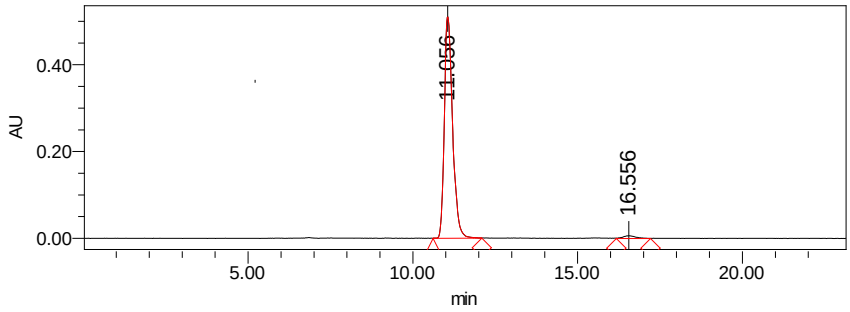


From 63.0 mg (0.2 mmol) of (Z)-5-(naphthalen-2-ylmethylene)-2-phenylthiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 75.0 mg (66.0% yield) of compound **3t** was obtained as a white solid, $[\alpha]_D^{20}$ = +72 (c = 1.0, $CHCl_3$), Mp. = 68-69 °C. Dr (>20:1) was determined by HPLC analysis. 96% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 11.1 min, t_{minor} = 16.6 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86

(d, *J* = 7.2 Hz, 2H), 7.77 - 7.73 (m, 4H), 7.55 - 7.47 (m, 2H), 7.44 - 7.39 (m, 2H), 7.33 (t, *J* = 7.8 Hz, 2H), 4.79 - 4.71 (m, 2H), 4.34 – 4.23 (m, 4H), 3.84 (s, 1H), 1.27 - 1.17 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ195.3, 192.4, 168.3, 166.5, 135.5, 133.1, 133.0, 131.3, 131.3, 129.1, 129.0, 128.8, 128.3, 128.2, 127.6, 126.6, 126.5, 126.3, 124.9 (q, J_{C-F} = 278.0 Hz), 80.5, 77.5, 63.9 (q, J_{C-F} = 30.2 Hz), 63.0, 57.5, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.8. HRMS (ESI) m/z calcd for $C_{29}H_{25}F_3N_2NaO_5S$ $[M+Na]^+$: 593.1328, found 593.1335.

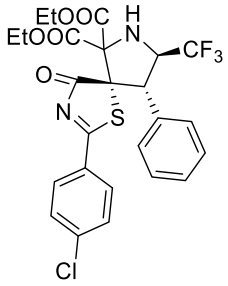


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	11.374	2336615	49.52	128605	BB	Unknown
2	17.091	2382192	50.48	86987	VV	Unknown

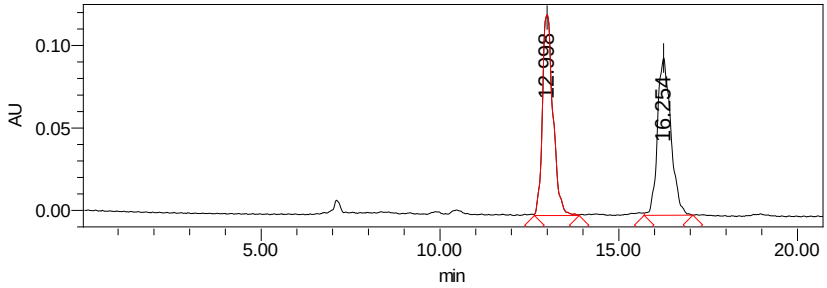


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	11.056	8895112	98.15	510197	BV	Unknown
2	16.556	167606	1.85	6207	VV	Unknown

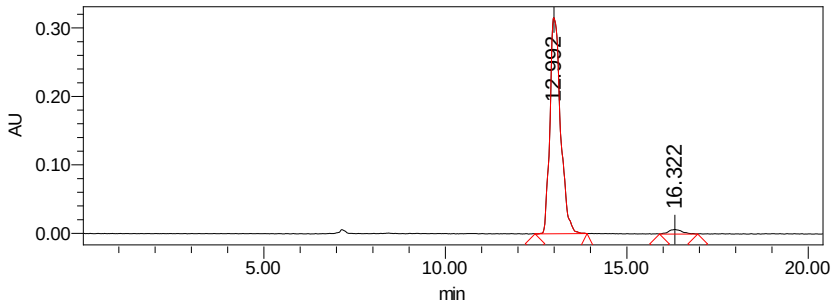
Diethyl-(5S,8R,9S)-2-(4-chlorophenyl)-4-oxo-9-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3u)



From 59.8 mg (0.2 mmol) of (Z)-5-benzylidene-2-(4-chlorophenyl)thiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 84.5 mg (77.0% yield) of compound **3u** was obtained as a yellow solid, $[\alpha]_D^{20}$ = +46 (c = 1.0, $CHCl_3$), Mp. = 169-170 °C. Dr (>20:1) was determined by HPLC analysis. 95% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 13.0 min, t_{minor} = 16.3 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, *J* = 6.9 Hz, 2H), 7.40 (d, *J* = 8.7 Hz, 2H), 7.28 – 7.24 (m, 5H), 4.61 – 4.51 (m, 2H), 4.33 - 4.21 (m, 4H), 3.77 (d, *J* = 8.4 Hz, 1H), 1.27 – 1.17 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.7, 192.0, 168.2, 166.4, 142.1, 133.6, 129.9, 129.8, 129.5, 129.3, 128.6, 124.8 (q, J_{C-F} = 278.3 Hz), 80.1, 77.9, 63.5 (q, J_{C-F} = 29.8 Hz), 63.2, 62.9, 57.3, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.9. HRMS (ESI) m/z calcd for $C_{25}H_{22}ClF_3N_2NaO_5S$ $[M+Na]^+$: 577.0782, found 577.0791.

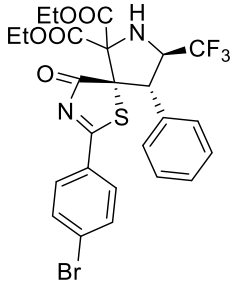


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	12.998	2502824	50.20	121950	VV	Unknown
2	16.254	2483038	49.80	95478	VV	Unknown

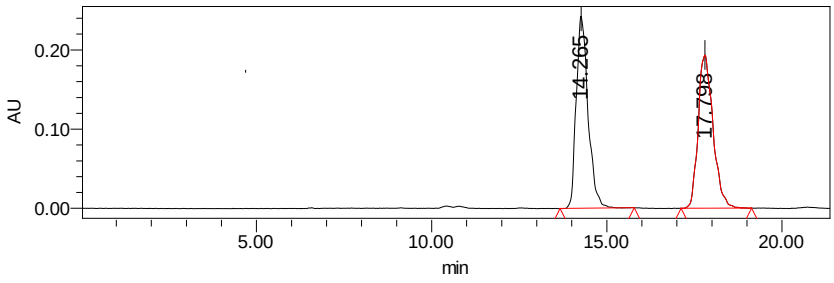


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	12.992	6475526	97.32	316078	VB	Unknown
2	16.322	178637	2.68	6659	VV	Unknown

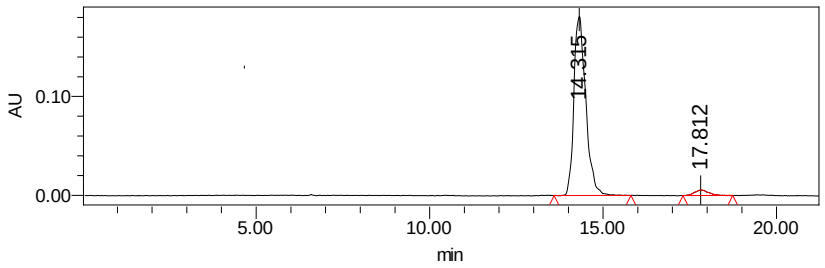
Diethyl-(5S,8R,9S)-2-(4-bromophenyl)-4-oxo-9-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3v)



From 68.6 mg (0.2 mmol) of (Z)-5-benzylidene-2-(4-bromophenyl)thiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 62.6 mg (53.0% yield) of compound **3v** was obtained as a yellow oil, $[\alpha]_D^{20}$ = +57 (c = 1.0, CHCl3), dr (>20:1) was determined by HPLC analysis. 93% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 14.3 min, t_{minor} = 17.8 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.27 (s, 5H), 4.57 – 4.54 (m, 2H), 4.31 - 4.22 (m, 4H), 3.74 (d, *J* = 6.3 Hz, 1H), 1.27 – 1.17 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.9, 192.1, 168.2, 166.4, 133.6, 132.5, 130.9, 130.2, 129.9, 129.3, 128.6, 124.7 (q, J_{C-F} = 277.8 Hz), 80.2, 77.9, 63.6 (q, J_{C-F} = 30.8 Hz), 63.0, 57.4, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.9. HRMS (ESI) m/z calcd for $C_{25}H_{22}BrF_3N_2NaO_5S$ $[M+Na]^+$: 621.0277, found 621.0283.

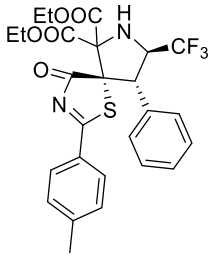


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	14.265	5717492	50.00	242521	bb	Unknown
2	17.798	5717261	50.00	193456	bb	Unknown

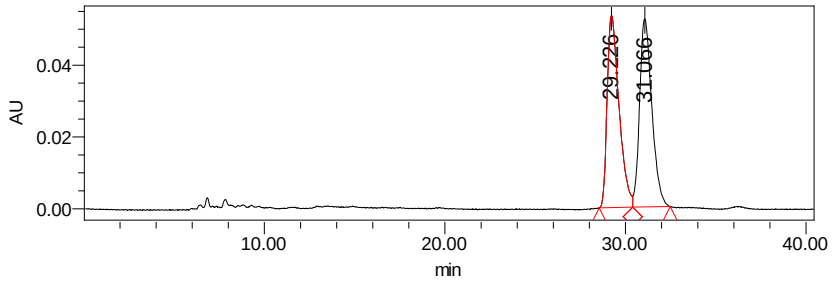


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	14.315	4332020	96.47	181335	bb	Unknown
2	17.812	158438	3.53	5519	bb	Unknown

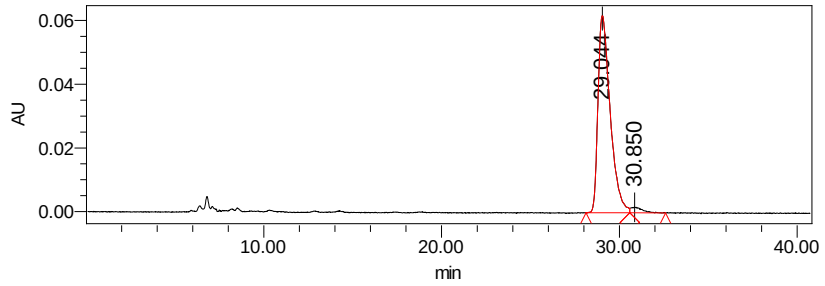
Diethyl-(5*S*,8*R*,9*S*)-2-(4-methyl)-4-oxo-9-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3w)



From 55.8 mg (0.2 mmol) of (*Z*)-5-benzylidene-2-(4-methyl)thiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 102.0 mg (95.0% yield) of compound **3w** was obtained as a white solid, $[\alpha]_D^{20}$ = +36 (c = 1.0, $CHCl_3$), Mp. = 108-109 °C. Dr (>20:1) was determined by HPLC analysis. 95% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 29.0 min, t_{minor} = 30.9 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.4 Hz, 2H), 7.28 - 7.22 (m, 7H), 4.62 (d, *J* = 10.2 Hz, 1H), 4.57 - 4.48 (m, 1H), 4.32 - 4.18 (m, 4H), 3.74 (d, *J* = 9.3 Hz, 1H), 2.40 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.5, 191.9, 168.3, 166.6, 147.2, 133.6, 129.8, 129.3, 128.8, 128.5, 124.8 (q, $J_{C\text{-}F}$ = 278.0 Hz), 80.1, 77.6, 63.5 (q, $J_{C\text{-}F}$ = 30.0 Hz), 62.9, 57.0, 21.9, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.9. HRMS (ESI) m/z calcd for $C_{26}H_{26}F_3N_2O_5S$ $[M+H]^+$: 535.1509, found 535.1515.

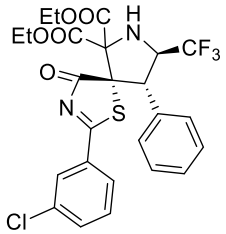


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	29.226	2448473	49.81	53426	BV	Unknown
2	31.066	2466953	50.19	52367	VB	Unknown



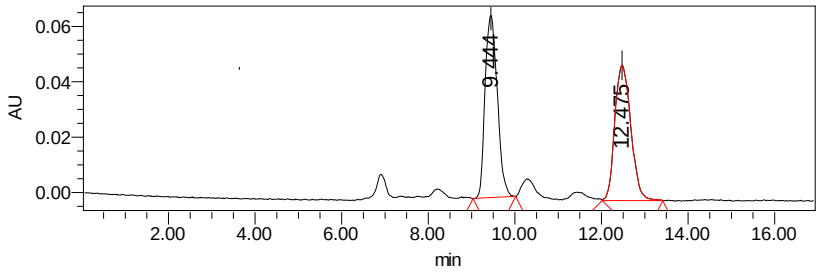
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	29.044	2944670	97.35	61896	bv	Unknown
2	30.850	80070	2.65	1784	vb	Unknown

Diethyl-(5S,8R,9S)-2-(3-chlorophenyl)-4-oxo-9-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3x)

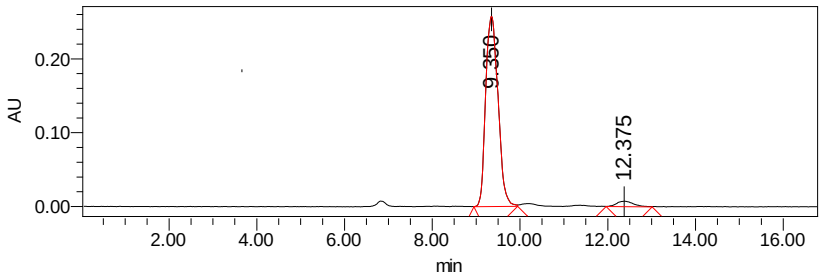


From 59.8 mg (0.2 mmol) of (Z)-5-benzylidene-2-(3-chlorophenyl)thiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 80 mg (48% yield) of compound **3x** was obtained as a yellow solid, $[\alpha]_D^{20}$ = +48 (c = 1.0, $CHCl_3$), Mp. = 107-108 °C. Dr (>20:1) was determined by HPLC analysis. 92% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 9.4 min, t_{minor} = 12.4 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, *J* = 1.8 Hz, 1H), 7.78 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.60-7.56 (m, 1H), 7.38 (t, *J* = 7.95 Hz, 1H), 7.29-

7.25 (m, 5H), 4.58-4.51 (m, 2H), 4.32-4.22 (m, 4H), 3.77-3.74 (m, 1H), 1.27-1.19 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.9, 192.1, 168.2, 166.4, 135.4, 135.2, 133.6, 132.9, 130.4, 129.3, 128.6, 128.4, 126.7, 124.7 (q, J_{C-F} = 278.3 Hz), 80.2, 77.8, 63.6 (q, J_{C-F} = 31.5 Hz), 63.3, 57.4, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -73.0. HRMS (ESI) m/z calcd for $C_{25}H_{22}ClF_3N_2NaO_5S$ $[M+Na]^+$: 577.0782, found 577.0790.

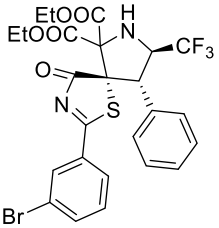


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	9.444	1290790	50.54	65930	bb	Unknown
2	12.475	1263082	49.46	48911	VB	Unknown



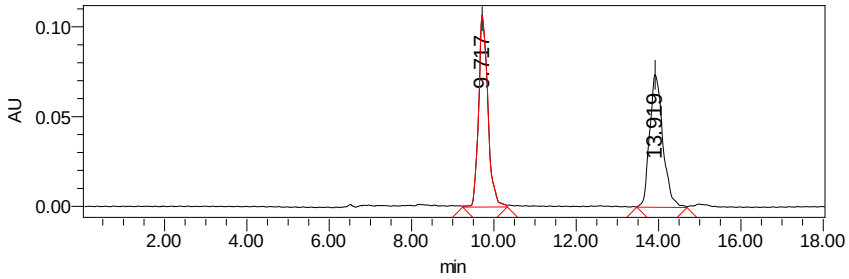
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	9.350	5047581	96.21	257630	BV	Unknown
2	12.375	198664	3.79	7331	VV	Unknown

Diethyl-(5S,8R,9S)-2-(3-bromophenyl)-4-oxo-9-phenyl-8-(trifluoromethyl)-1-thia-3,7-diazaspiro[4.4]non-2-ene-6,6-dicarboxylate (3y)

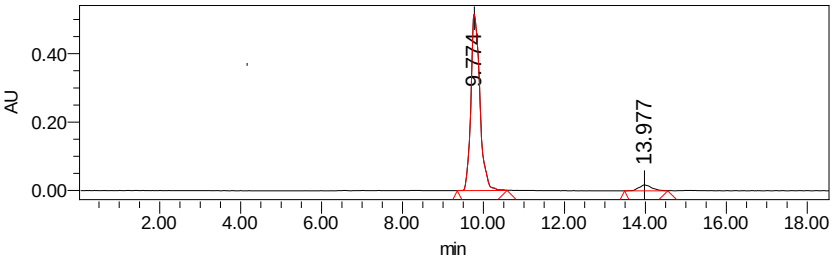


From 68.6 mg (0.2 mmol) of (Z)-5-benzylidene-2-(3-bromophenyl)thiazol-4(5H)-one and 76.6 mg (0.3 mmol, 1.5 equiv) of malonate **2**, 51.0 mg (43.0% yield) of compound **3** was obtained as a yellow oil, $[\alpha]_D^{20}$ = +43 (c = 1.0, $CHCl_3$), dr (>20:1) was determined

by HPLC analysis. 91% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2 -propanol 1:1, 1.0 mL/min). Retention time: t_{major} = 9.8 min, t_{minor} = 14.0 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.4 Hz, 2H), 7.28 – 7.22 (m, 7H), 4.62 (d, *J* = 10.2 Hz, 1H), 4.57 – 4.48 (m, 1H), 4.32 – 4.18 (m, 4H), 3.74 (d, *J* = 9.3Hz, 1H), 2.40 (s, 3H), 1.24 (t, *J* = 7.1Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ193.8, 192.0, 168.2, 166.4, 138.1, 133.6, 133.1, 131.3, 130.6, 129.3, 128.6, 127.2, 124.7 (q, J_{C-F} = 278.0 Hz), 123.2, 80.2, 77.8, 63.6 (q, J_{C-F} = 31.3 Hz), 63.3, 57.4, 13.7, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -73.0. HRMS (ESI) m/z calcd for $C_{25}H_{22}BrF_3N_2NaO_5S$ $[M+Na]^+$: 621.0277, found 621.0285.

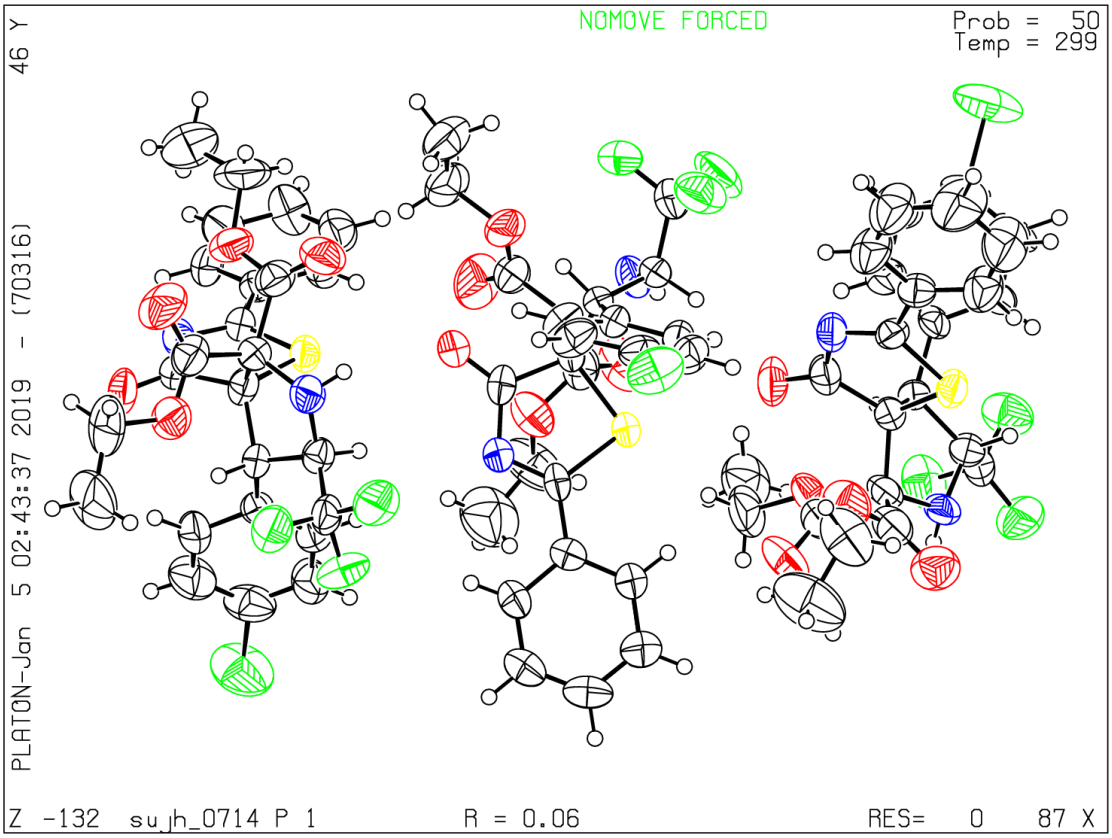


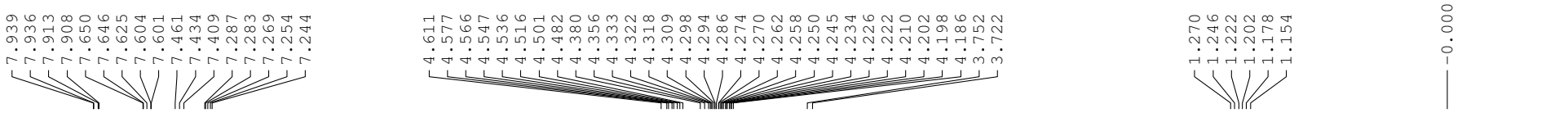
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	9.717	1684029	50.41	107329	VV	Unknown
2	13.919	1656868	49.59	74105	VV	Unknown

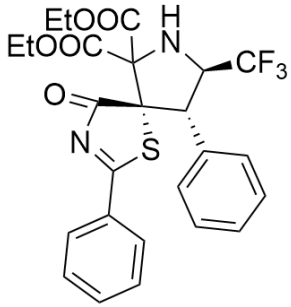


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	9.774	7920593	95.41	516664	BV	Unknown
2	13.977	380735	4.59	16930	BV	Unknown

5. X-ray Structure of Compound 3d

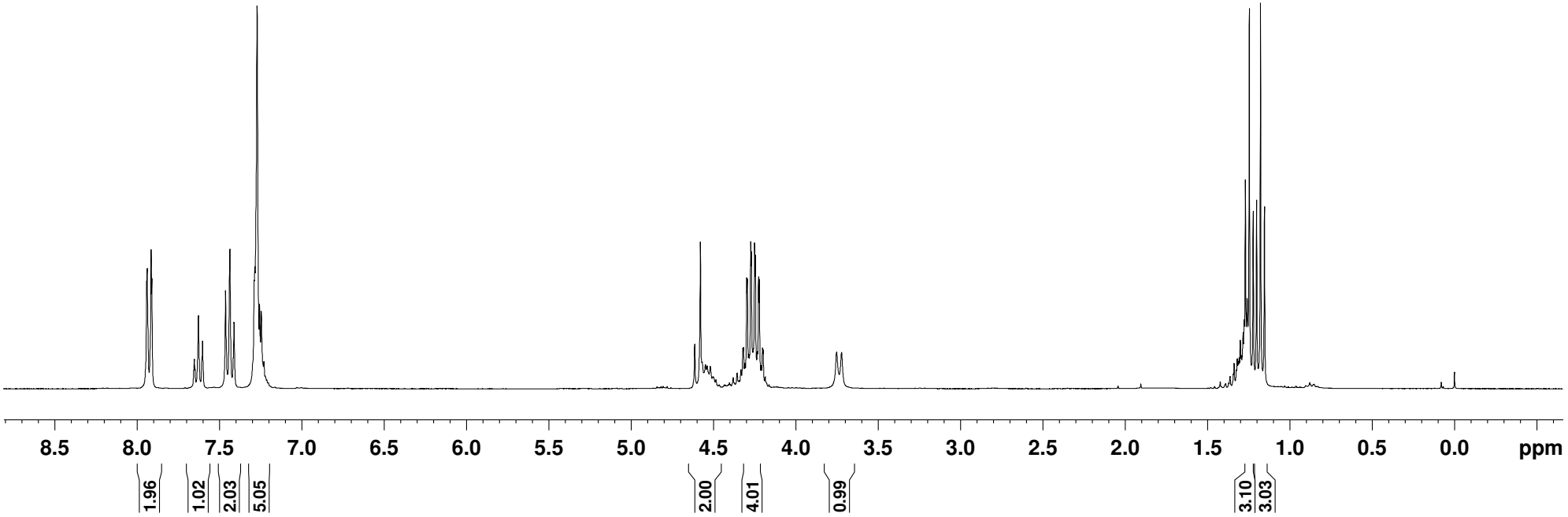


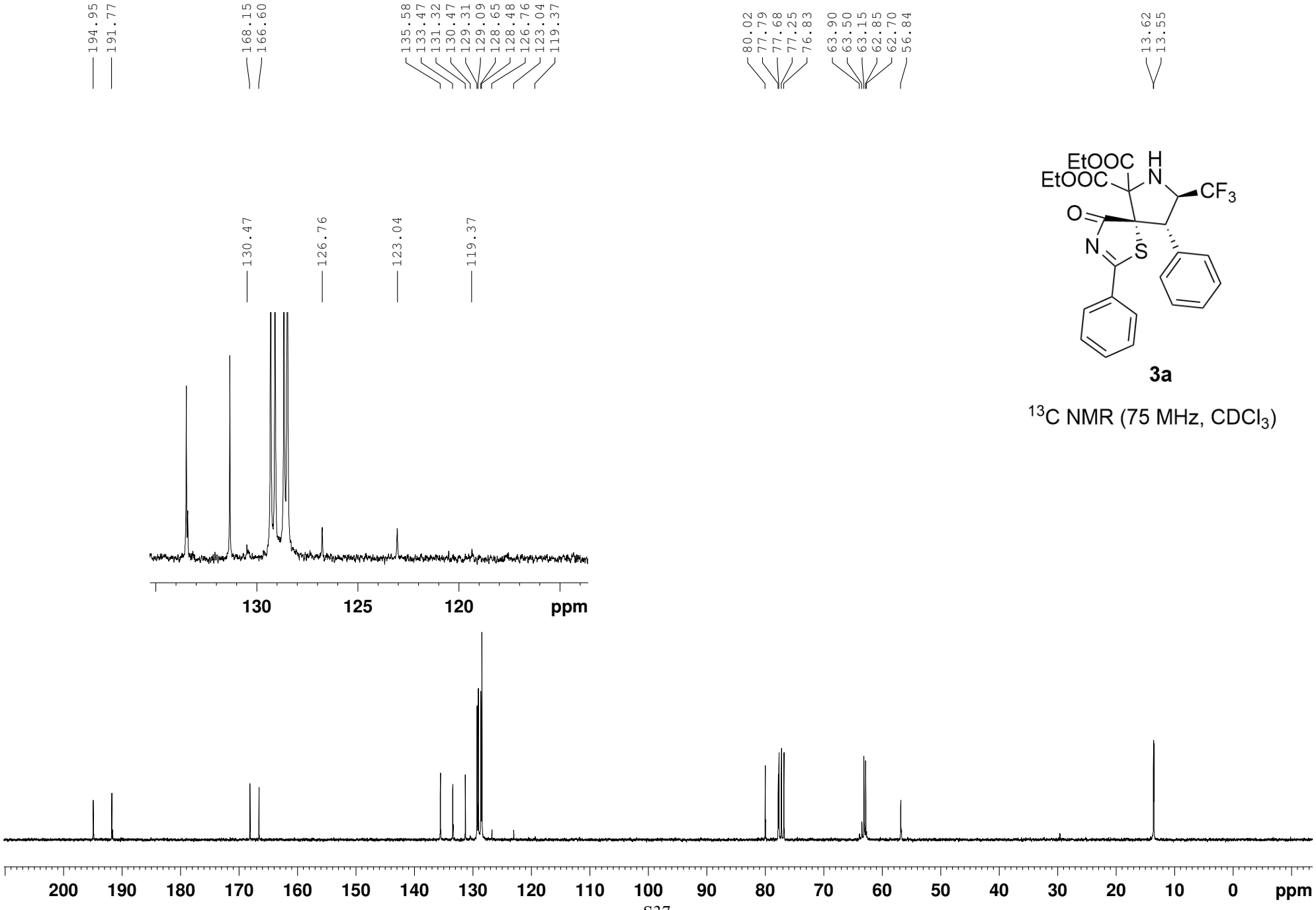




3a

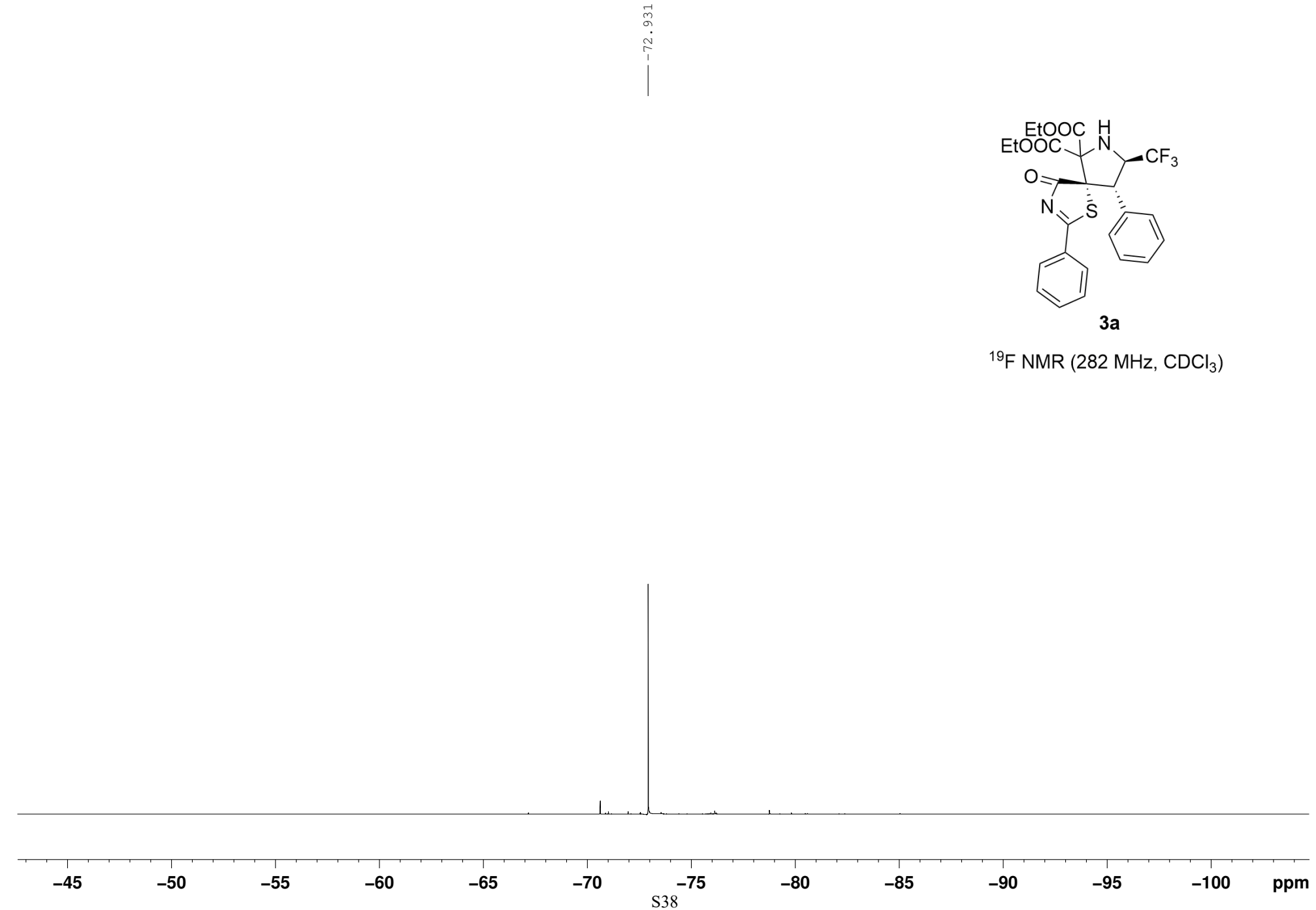
^{1}H NMR (300 MHz, $CDCl_3$)





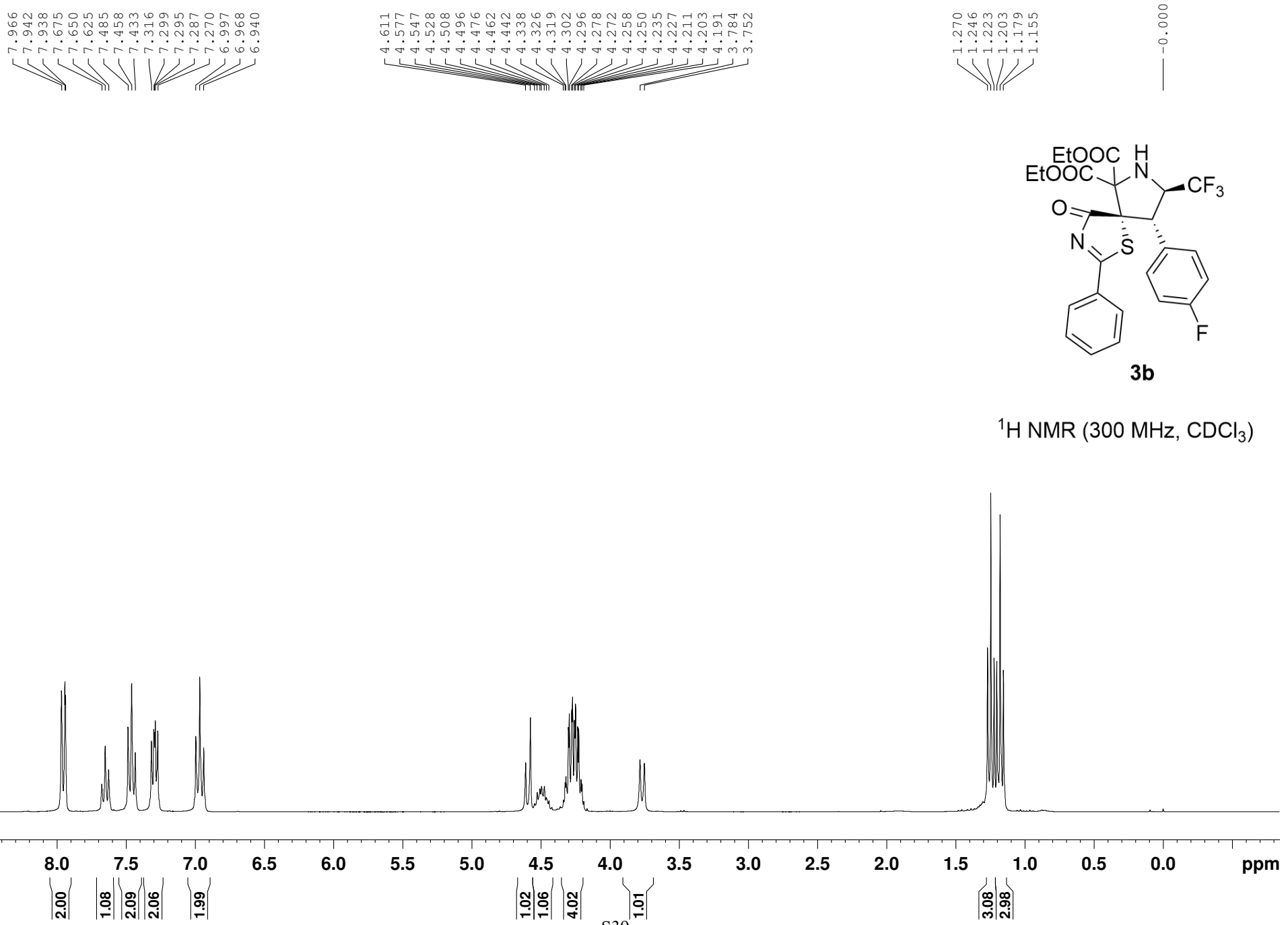
3a

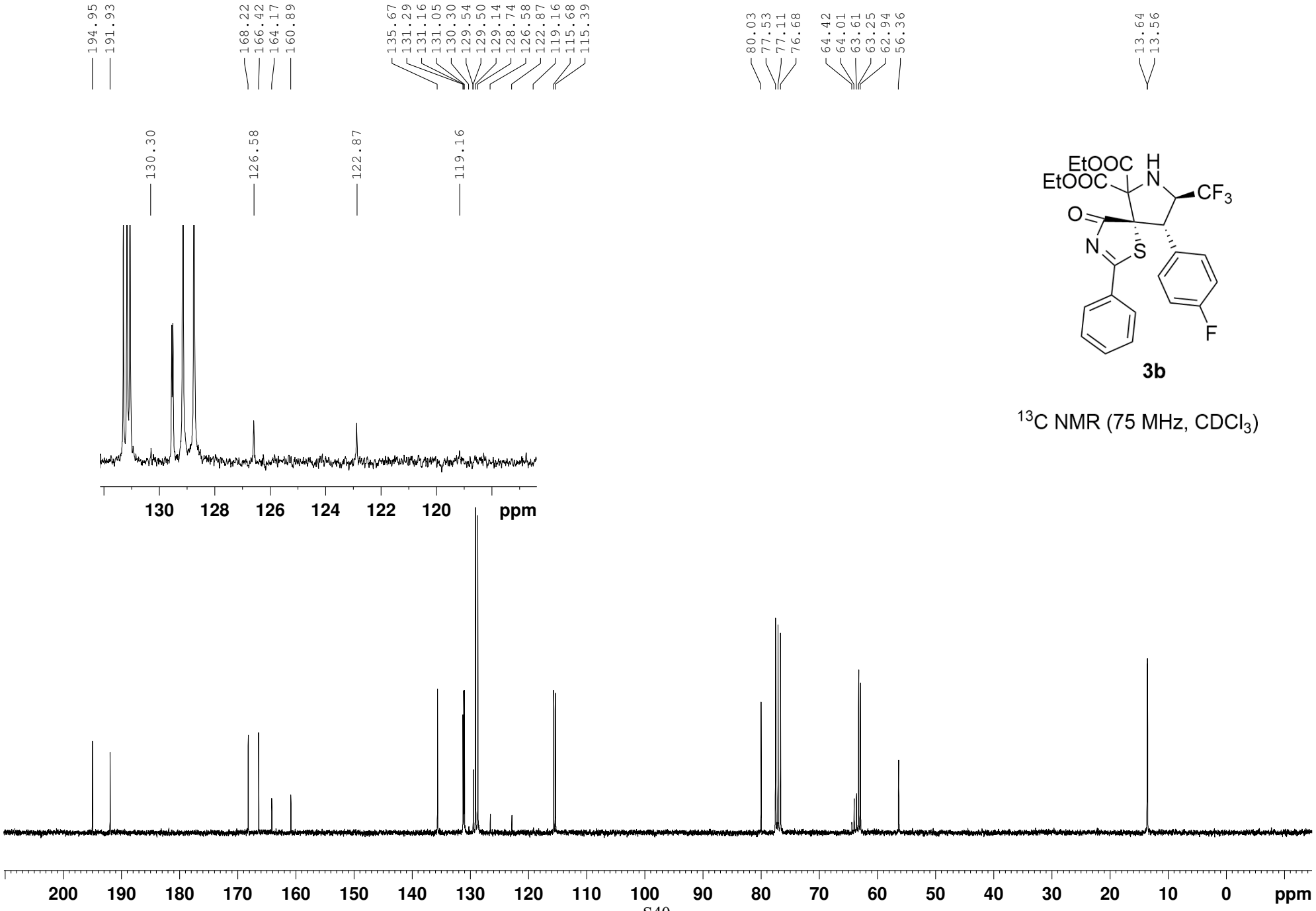
^{13}C NMR (75 MHz, $CDCl_3$)



3a

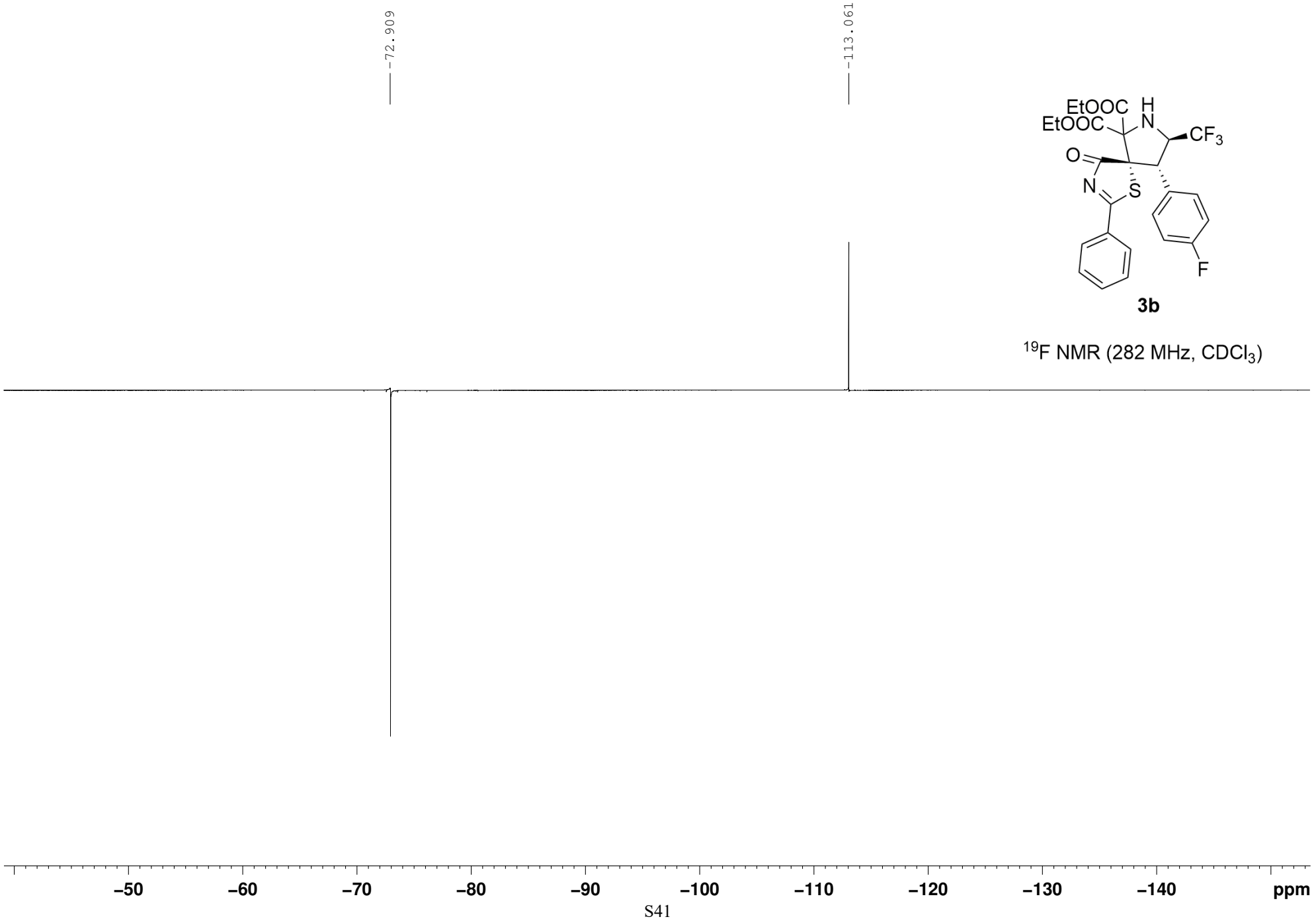
^{19}F NMR (282 MHz, $CDCl_3$)

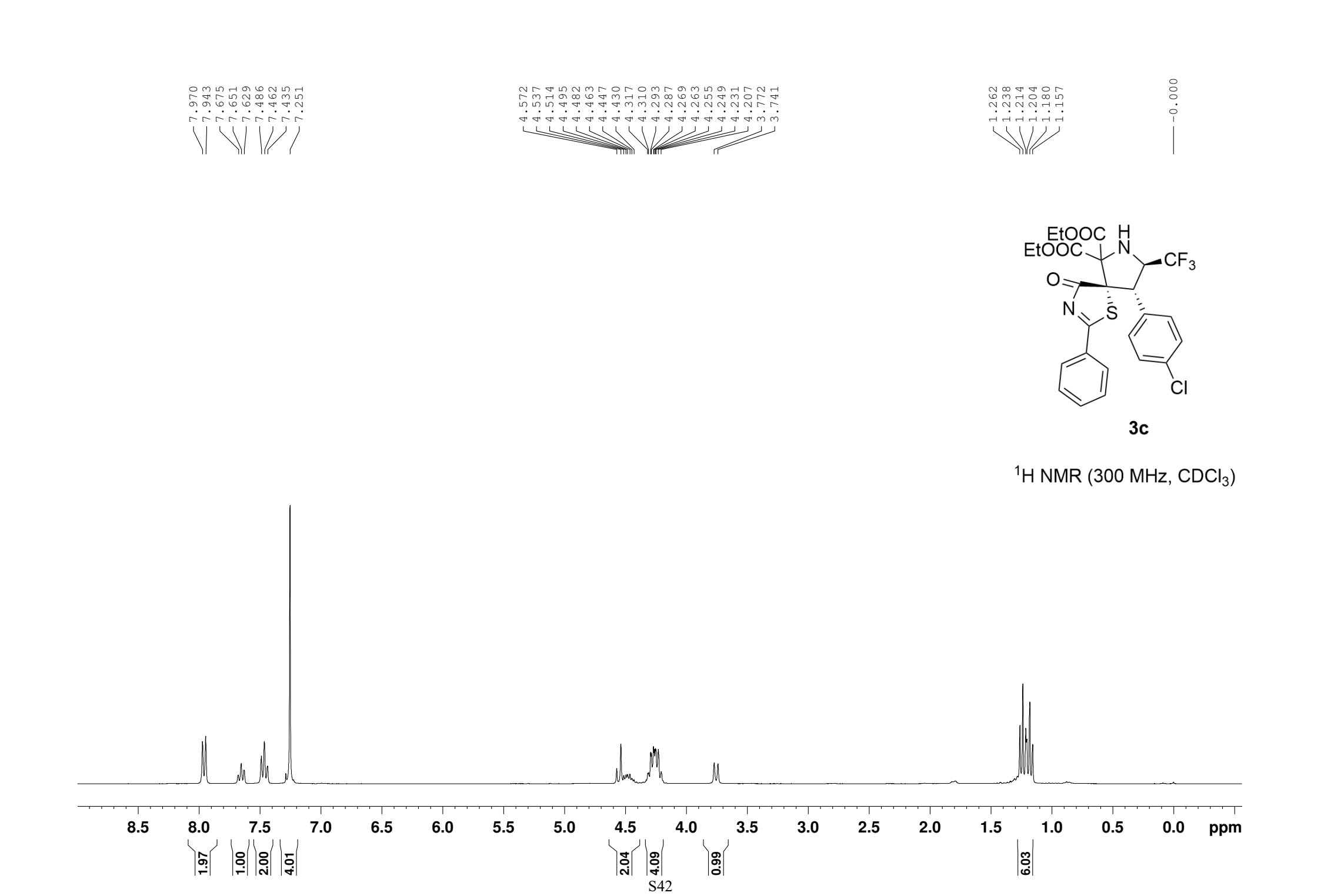

7.966
7.942
7.938
7.675
7.650
7.625
7.485
7.458
7.433
7.316
7.299
7.295
7.287
7.270
6.997
6.968
6.940
4.611
4.577
4.547
4.528
4.508
4.496
4.476
4.462
4.442
4.338
4.326
4.319
4.302
4.296
4.278
4.272
4.258
4.250
4.235
4.227
4.211
4.203
4.191
3.784
3.752
1.270
1.246
1.223
1.203
1.179
1.155
0.000
EtOOC
EtOOC
H
N
CF3
O
N
S
F
3b
1H NMR (300 MHz, CDCl3)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.00
1.08
2.09
2.06
1.99
1.02
1.06
4.02
1.01
3.08
2.98

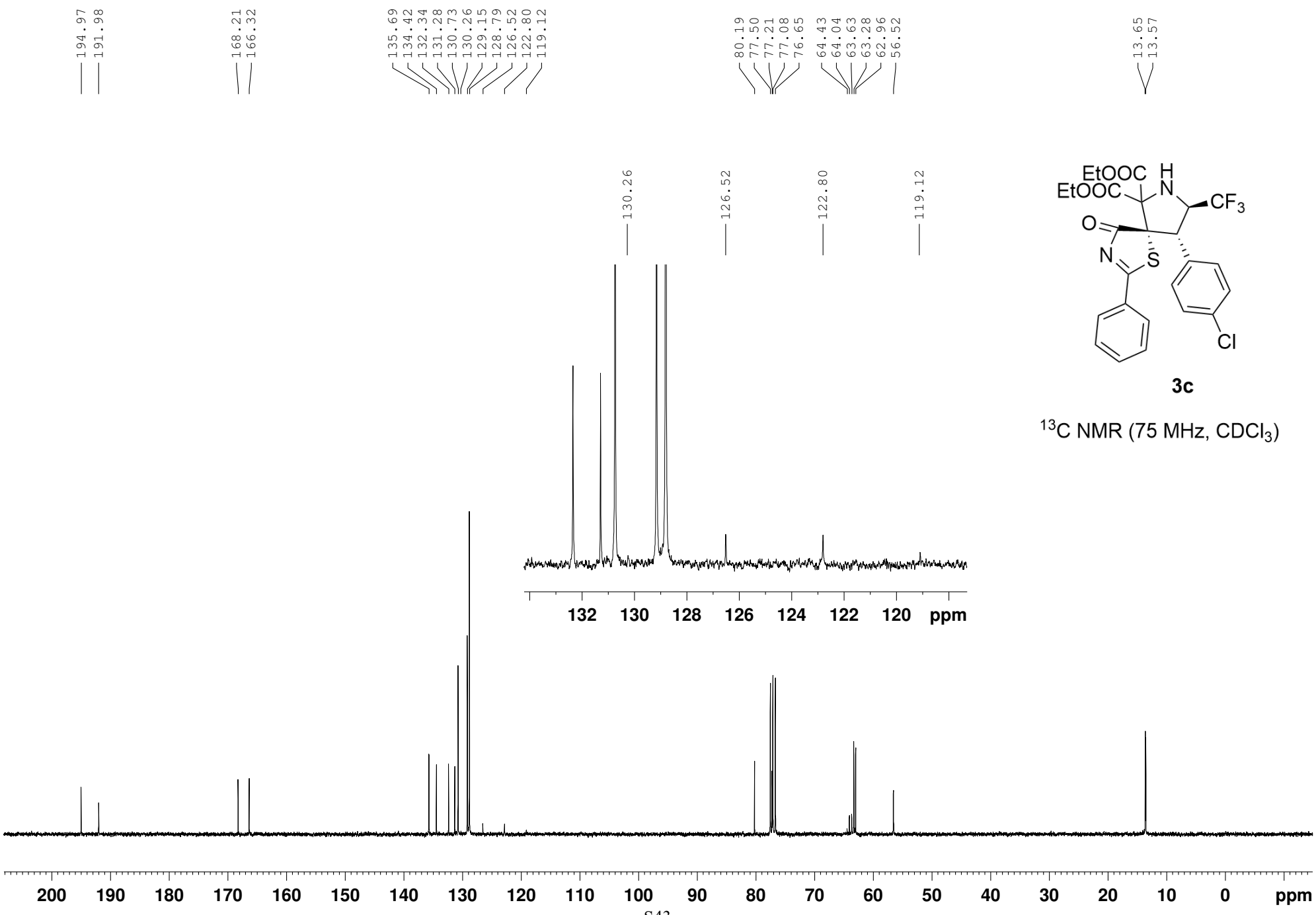


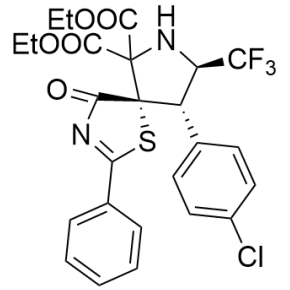
3b

^{13}C NMR (75 MHz, $CDCl_3$)


-72.909
-113.061
EtOOC
EtOOC
H
N
CF3
O
N
S
F
3b
19F NMR (282 MHz, CDCl3)
–50
–60
–70
–80
–90
–100
–110
–120
–130
–140
ppm

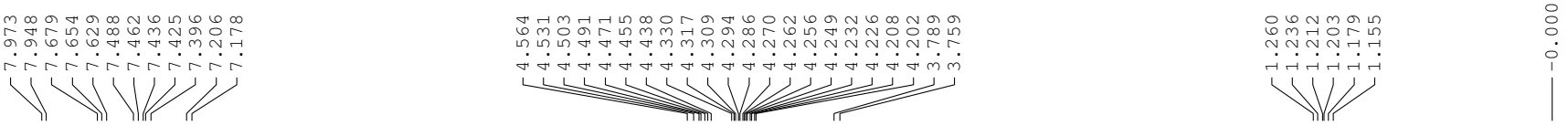

7.970
7.943
7.675
7.651
7.629
7.486
7.462
7.435
7.251
4.572
4.537
4.514
4.495
4.482
4.463
4.447
4.430
4.317
4.310
4.293
4.287
4.269
4.263
4.255
4.249
4.231
4.207
3.772
3.741
1.262
1.238
1.214
1.204
1.180
1.157
0.000
EtOOC
H
N
EtOOC
CF3
O
N
S
Cl
3c
1H NMR (300 MHz, CDCl3)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.97
1.00
2.00
4.01
2.04
4.09
0.99
6.03

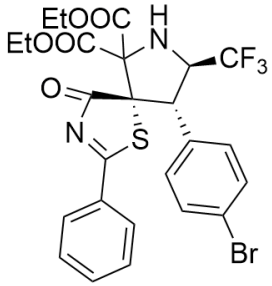

194.97
191.98
168.21
166.32
135.69
134.42
132.34
131.28
130.73
130.26
129.15
128.79
126.52
122.80
119.12
80.19
77.50
77.21
77.08
76.65
64.43
64.04
63.63
63.28
62.96
56.52
13.65
13.57
130.26
126.52
122.80
119.12
132 130 128 126 124 122 120 ppm
EtOOC
EtOOC
H
N
CF3
O
N
S
Cl
3c
13C NMR (75 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



3c

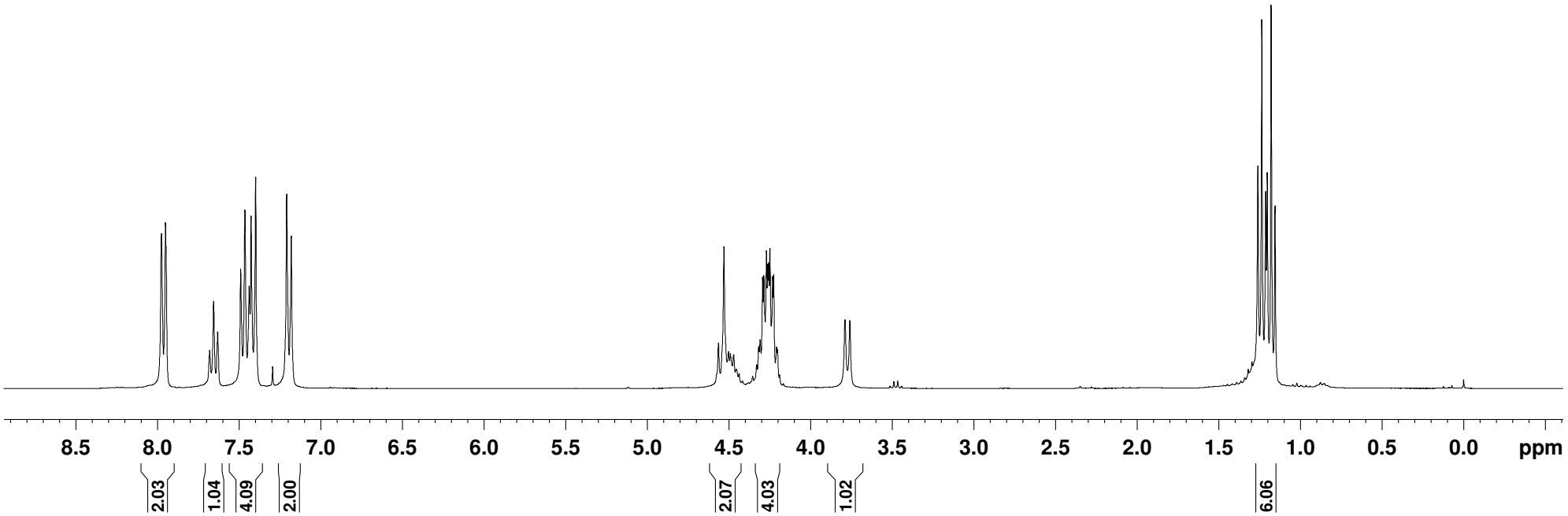
^{19}F NMR (282 MHz, $CDCl_3$)

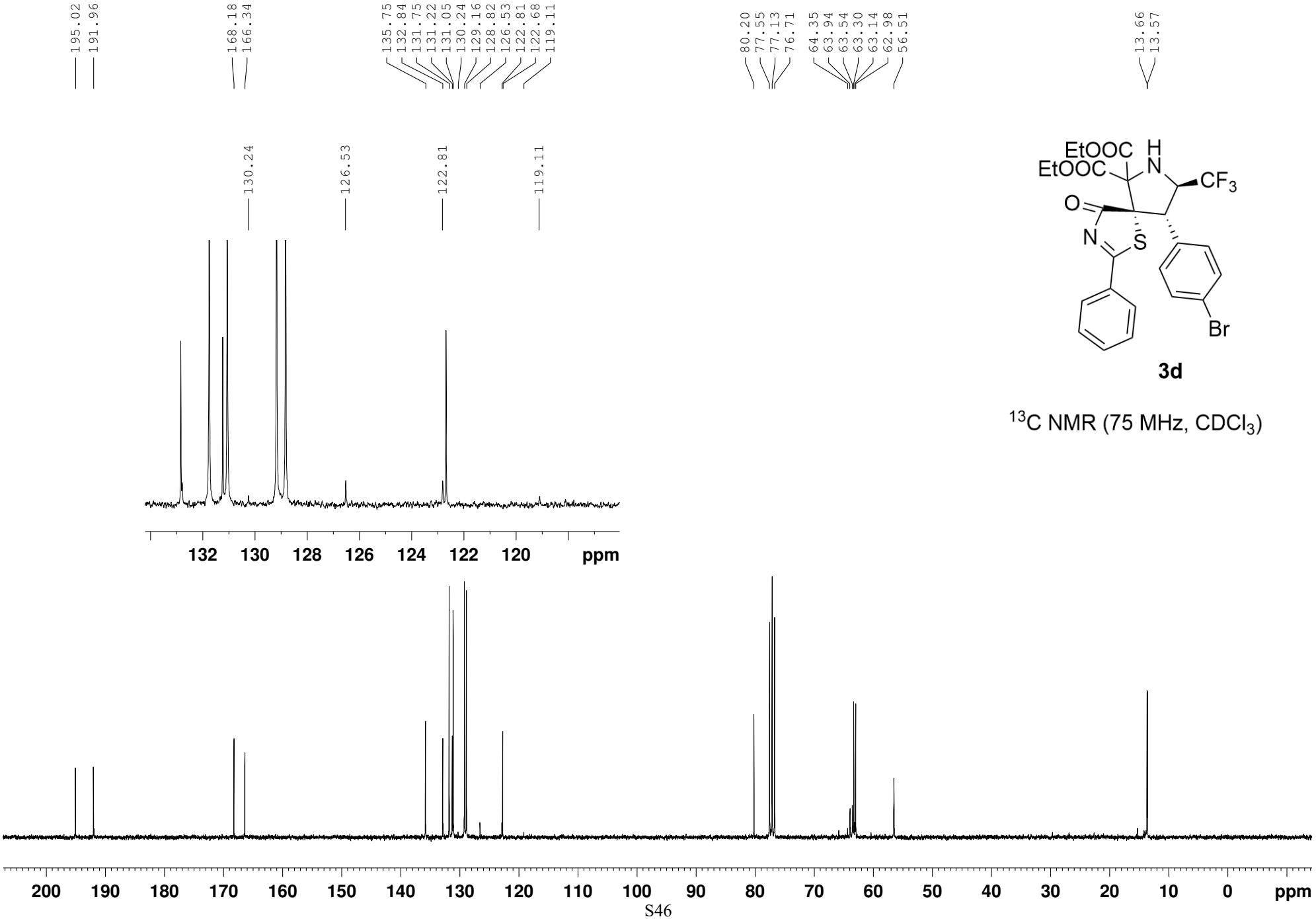


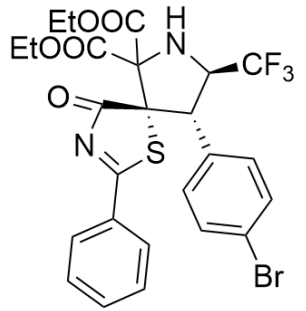


3d

^{1}H NMR (300 MHz, $CDCl_3$)

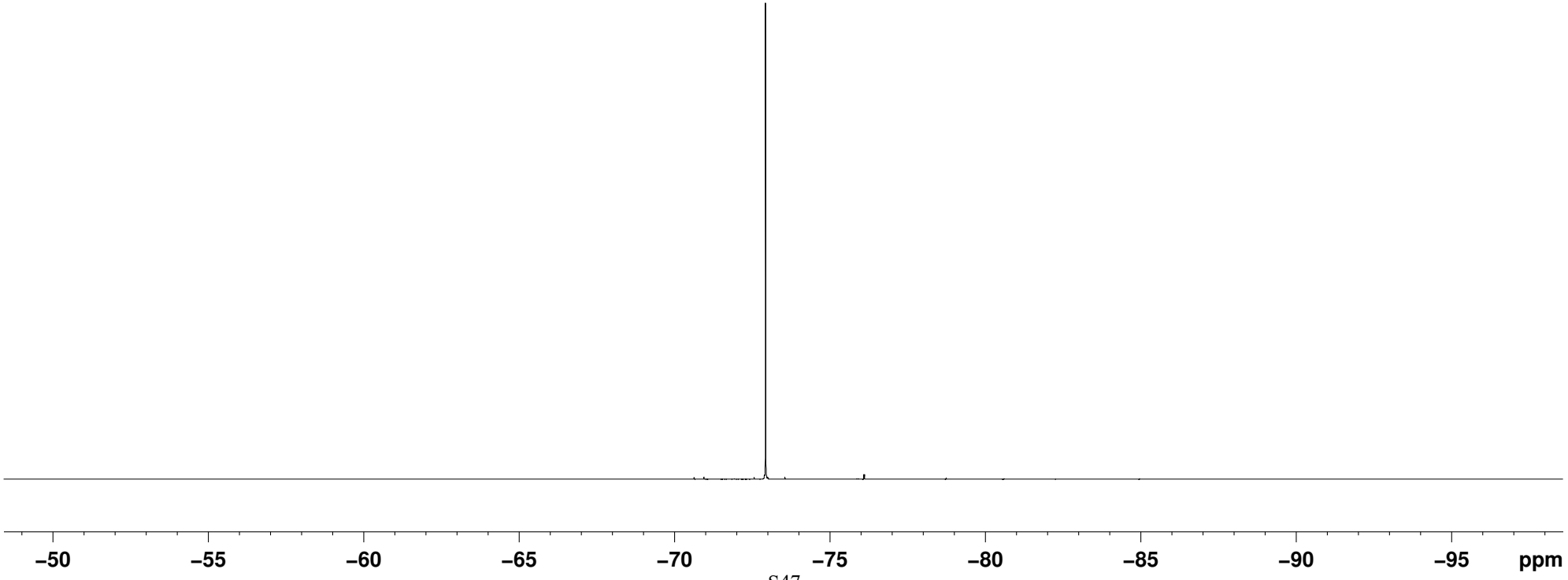


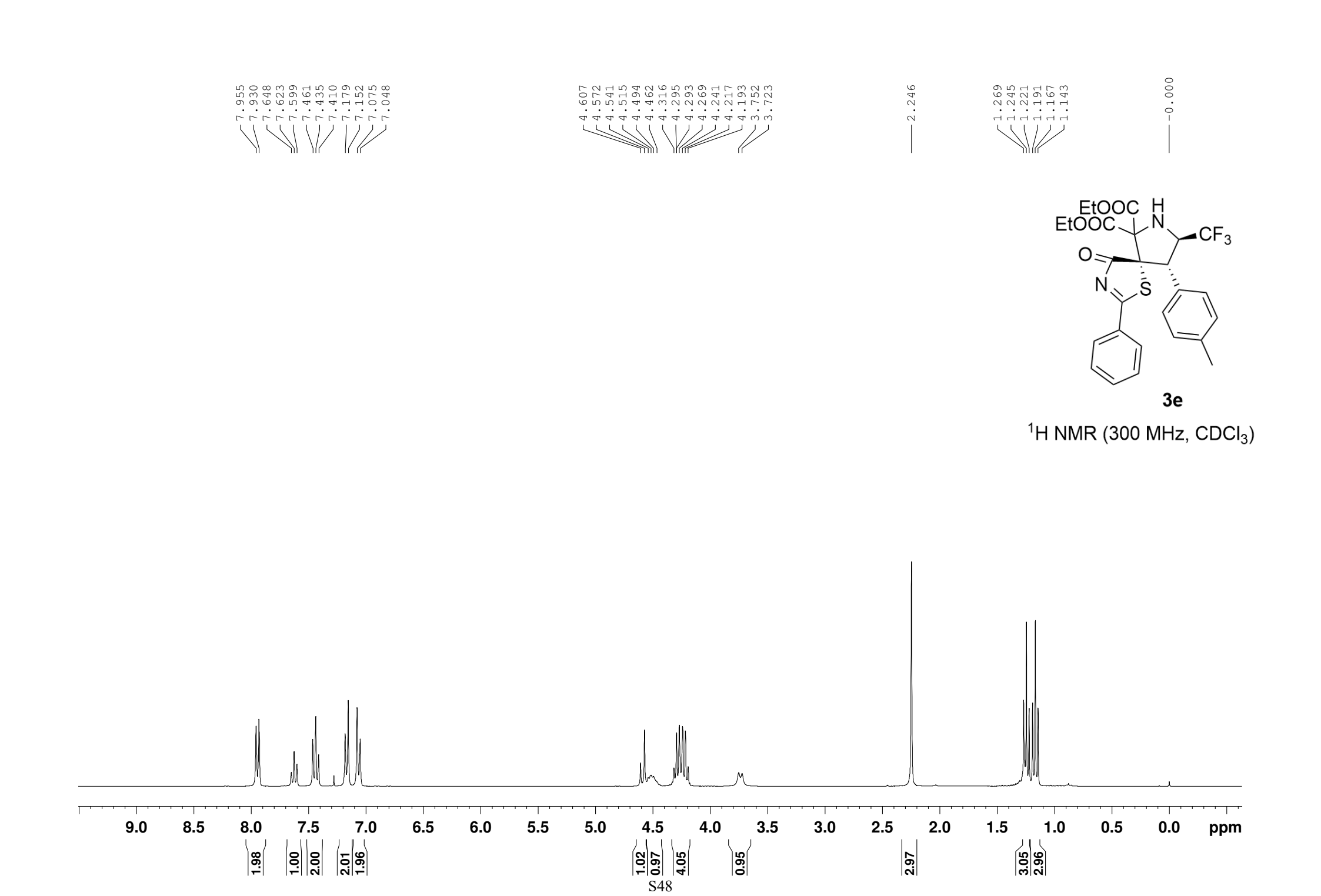

195.02
191.96
168.18
166.34
135.75
132.84
131.75
131.22
131.05
130.24
129.16
128.82
126.53
122.81
122.68
119.11
80.20
77.55
77.13
76.71
64.35
63.94
63.54
63.30
63.14
62.98
56.51
13.66
13.57
EtOOC
EtOOC
H
N
CF3
O
N
S
Br
3d
13C NMR (75 MHz, CDCl3)
ppm

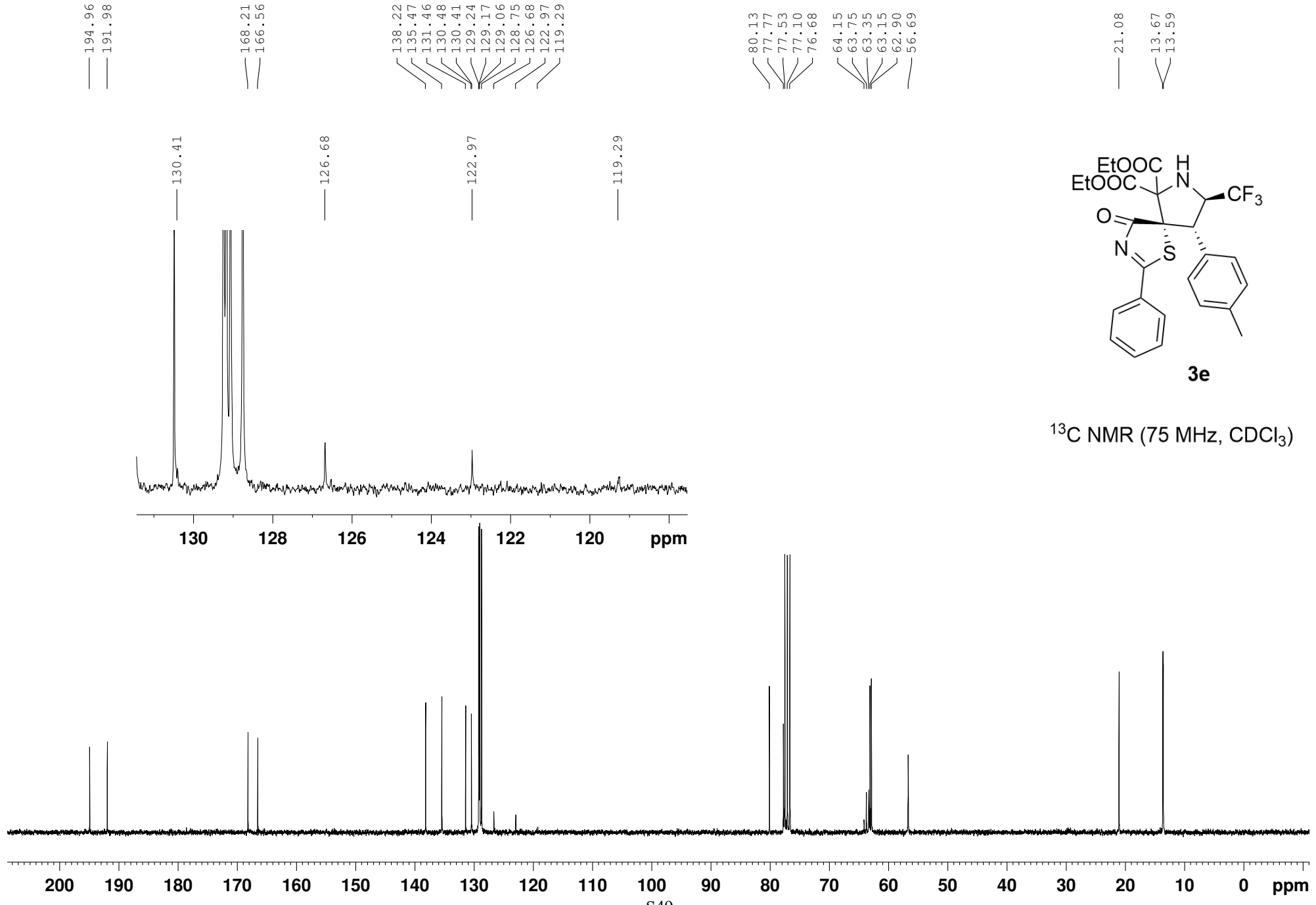


3d

^{19}F NMR (282 MHz, $CDCl_3$)

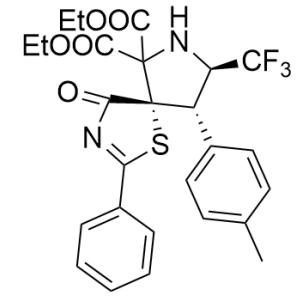



7.955
7.930
7.648
7.623
7.599
7.461
7.435
7.410
7.179
7.152
7.075
7.048
4.607
4.572
4.541
4.515
4.494
4.462
4.316
4.295
4.293
4.269
4.241
4.217
4.193
3.752
3.723
2.246
1.269
1.245
1.221
1.191
1.167
1.143
0.000
EtOOC
EtOOC
H
N
CF3
O
N
S
3e
1H NMR (300 MHz, CDCl3)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.98
1.00
2.00
2.01
1.96
1.02
0.97
4.05
0.95
2.97
3.05
2.96



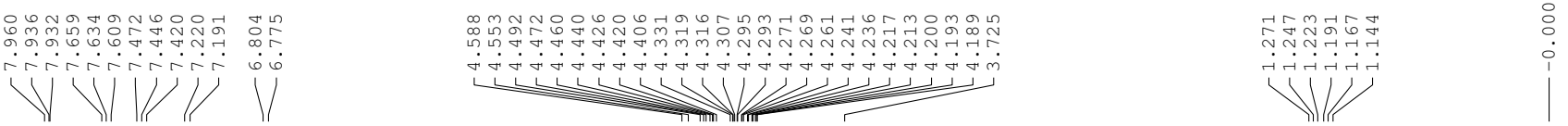
3e

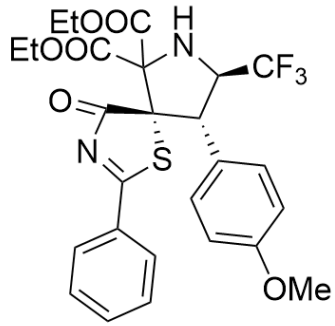
^{13}C NMR (75 MHz, $CDCl_3$)



3e

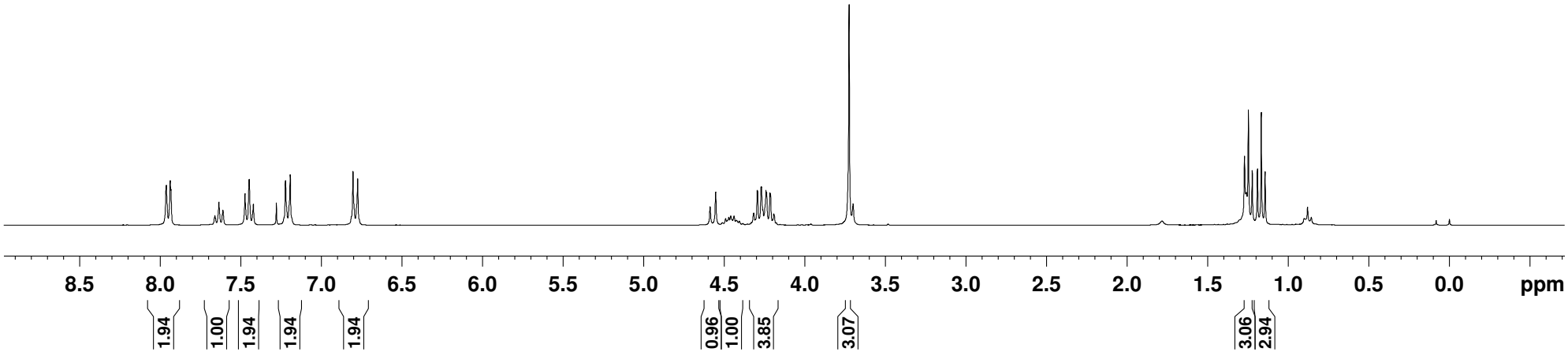
^{19}F NMR (282 MHz, $CDCl_3$)

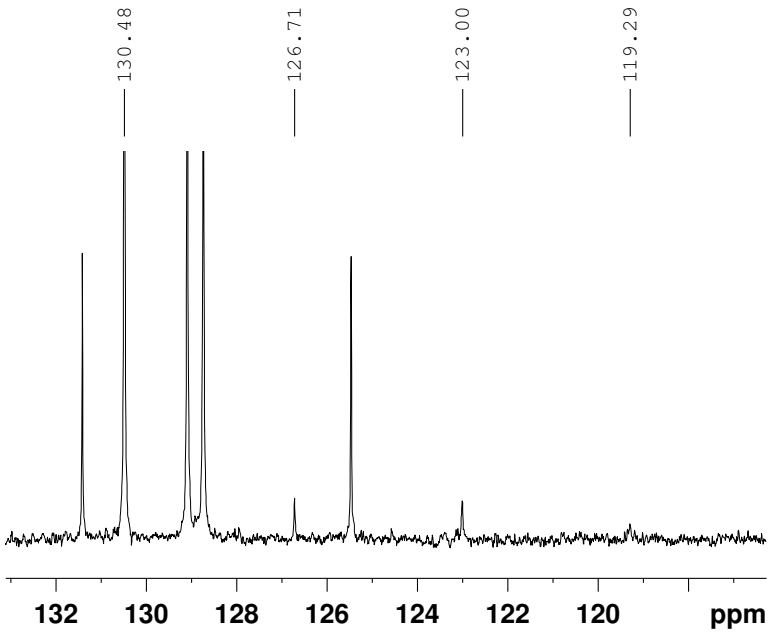


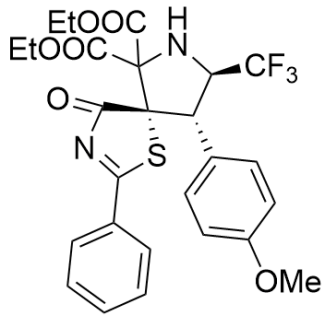


3f

^{1}H NMR (300 MHz, $CDCl_3$)

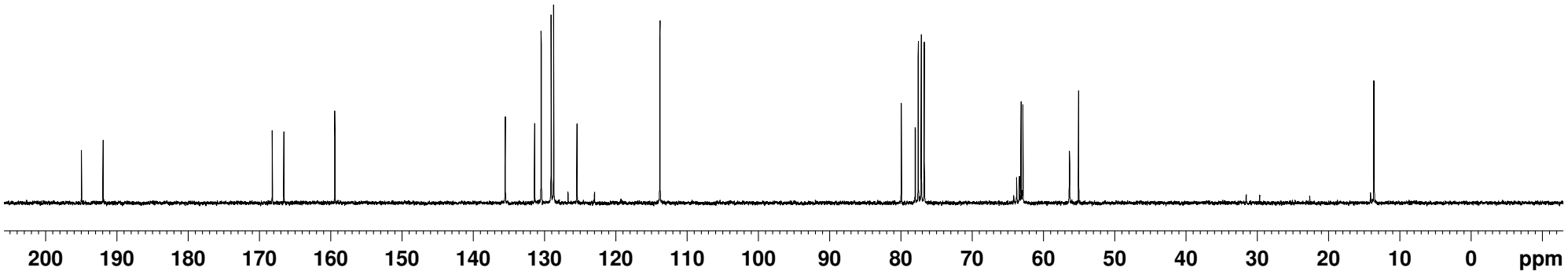


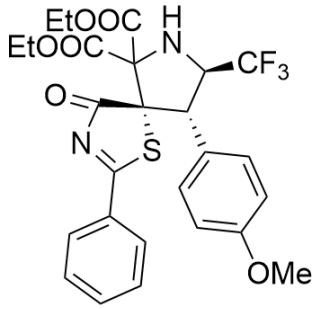




3f

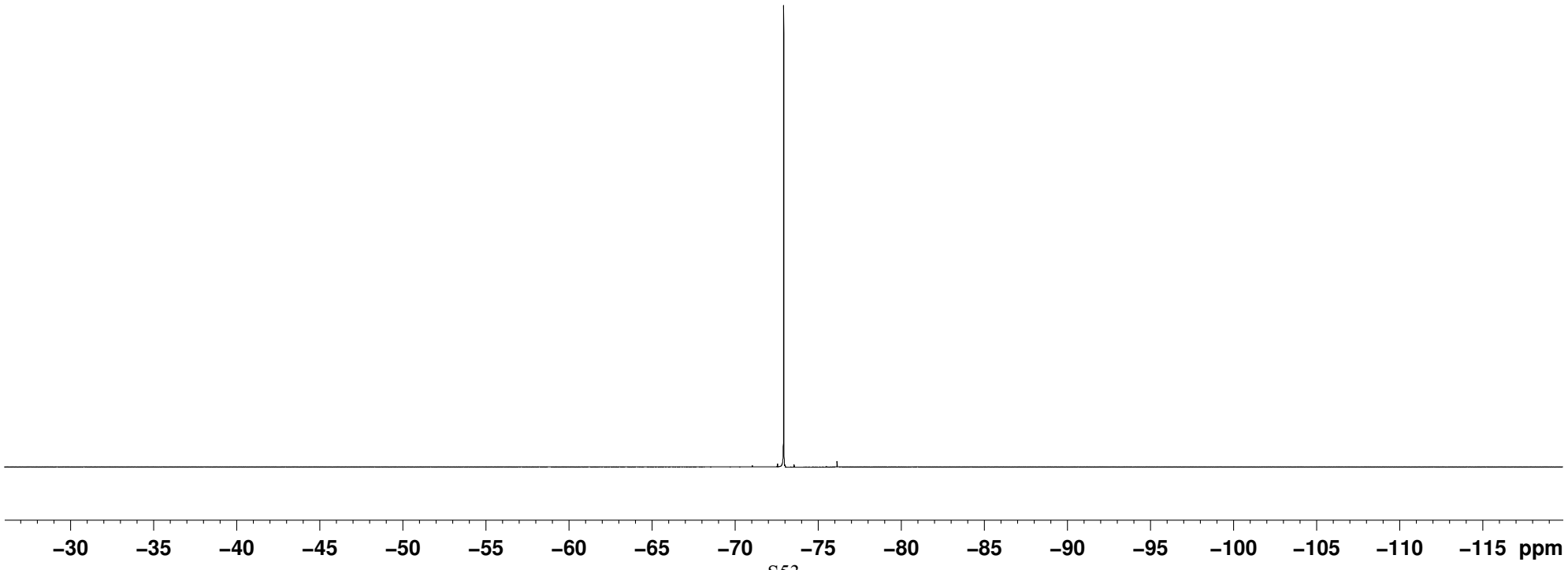
^{13}C NMR (75 MHz, $CDCl_3$)

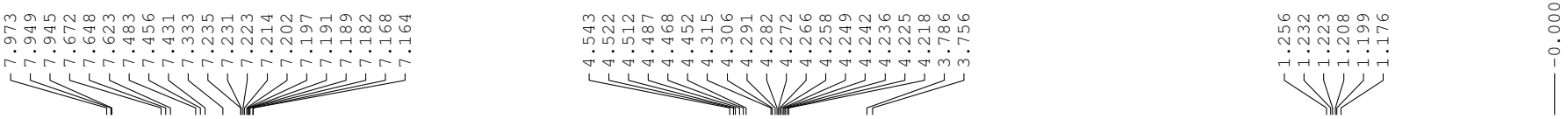


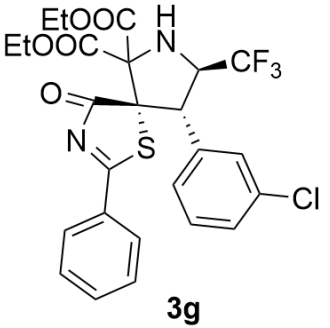


3f

^{19}F NMR (282 MHz, $CDCl_3$)

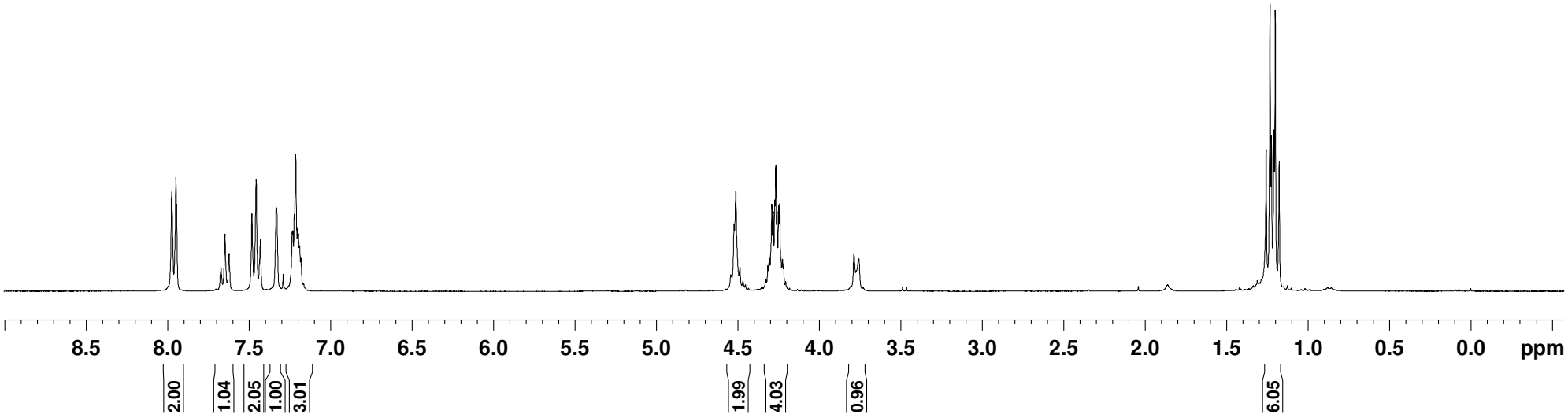


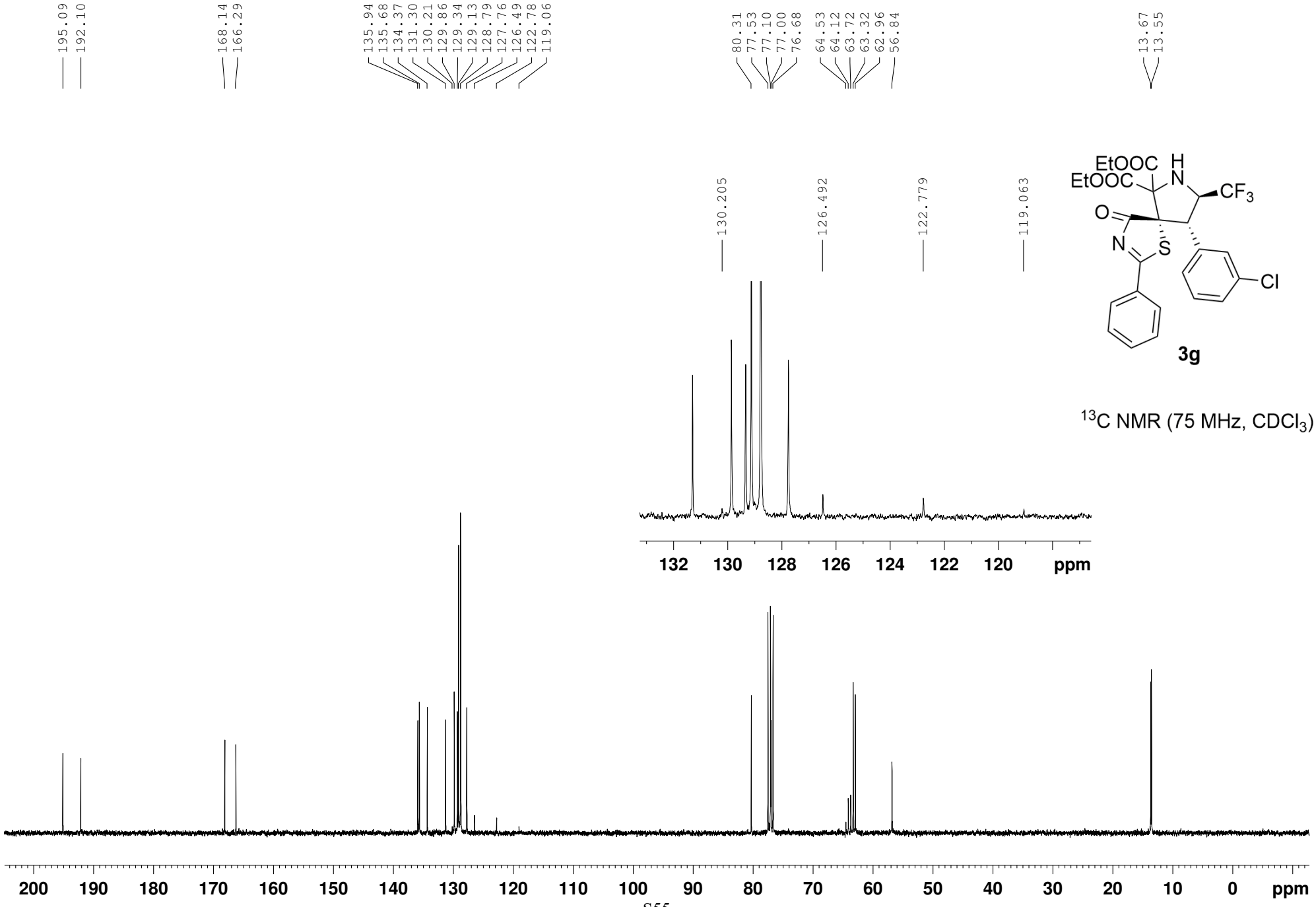




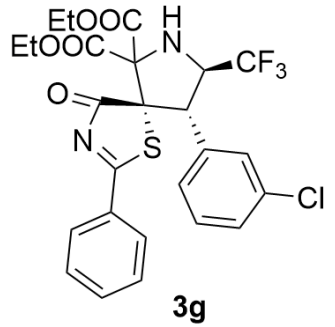
3g

^{1}H NMR (300 MHz, $CDCl_3$)



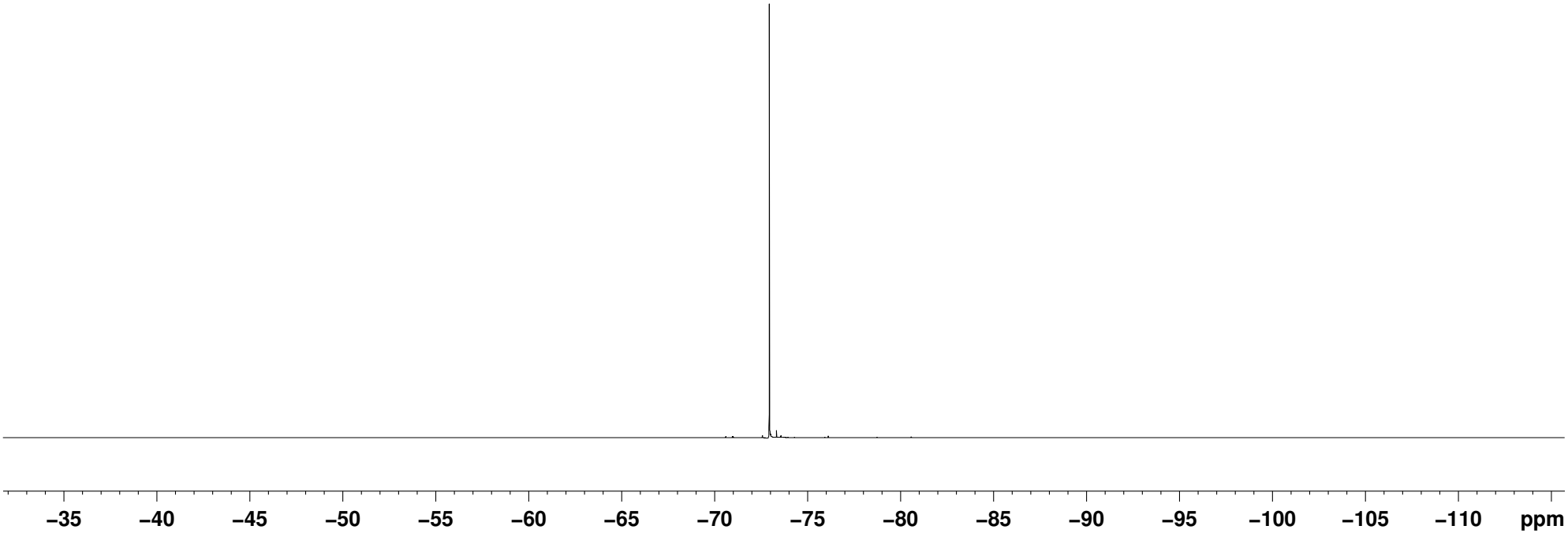


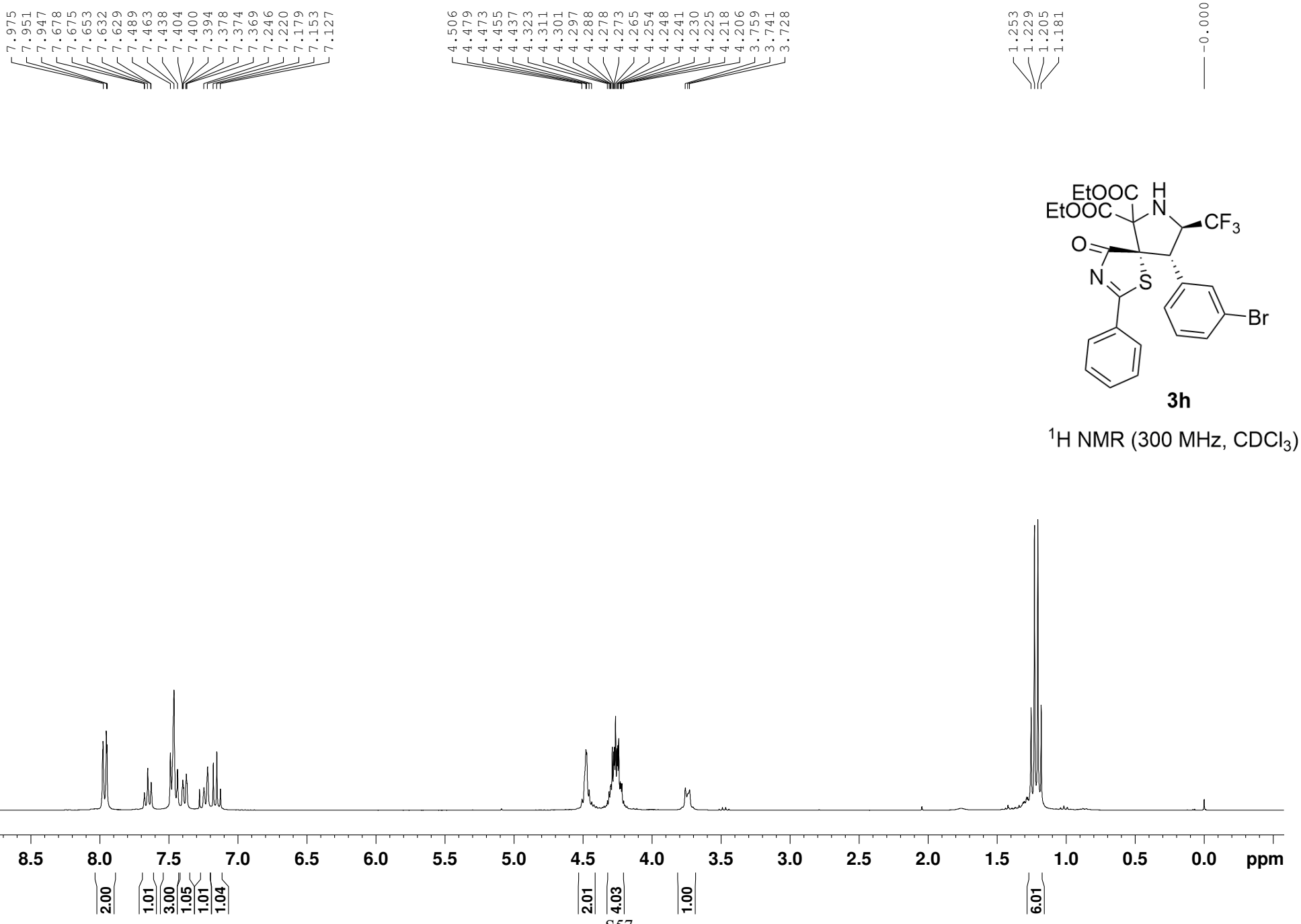
^{13}C NMR (75 MHz, $CDCl_3$)

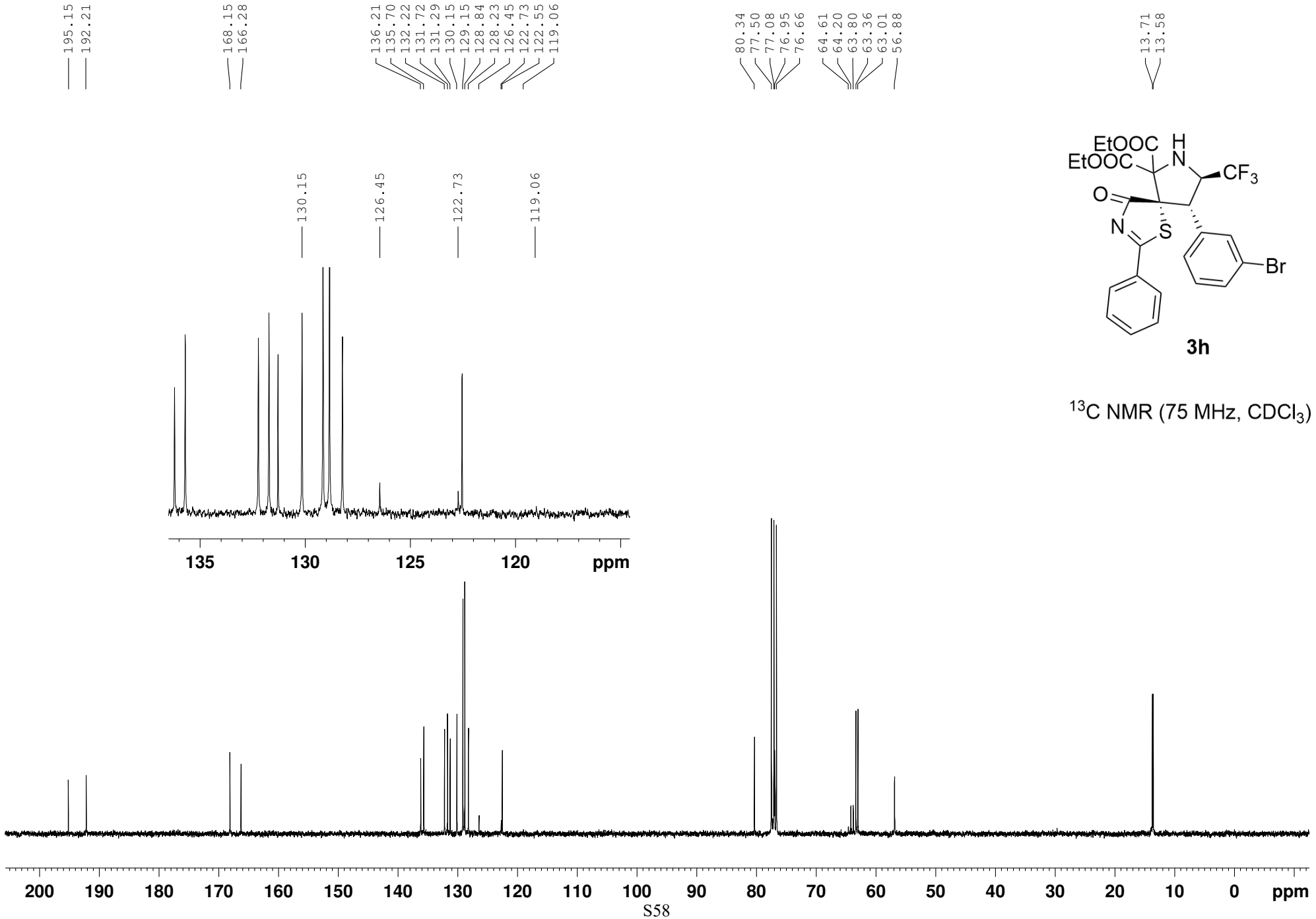


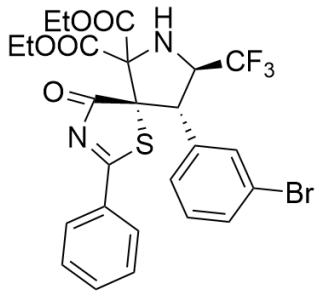
3g

^{19}F NMR (282 MHz, $CDCl_3$)



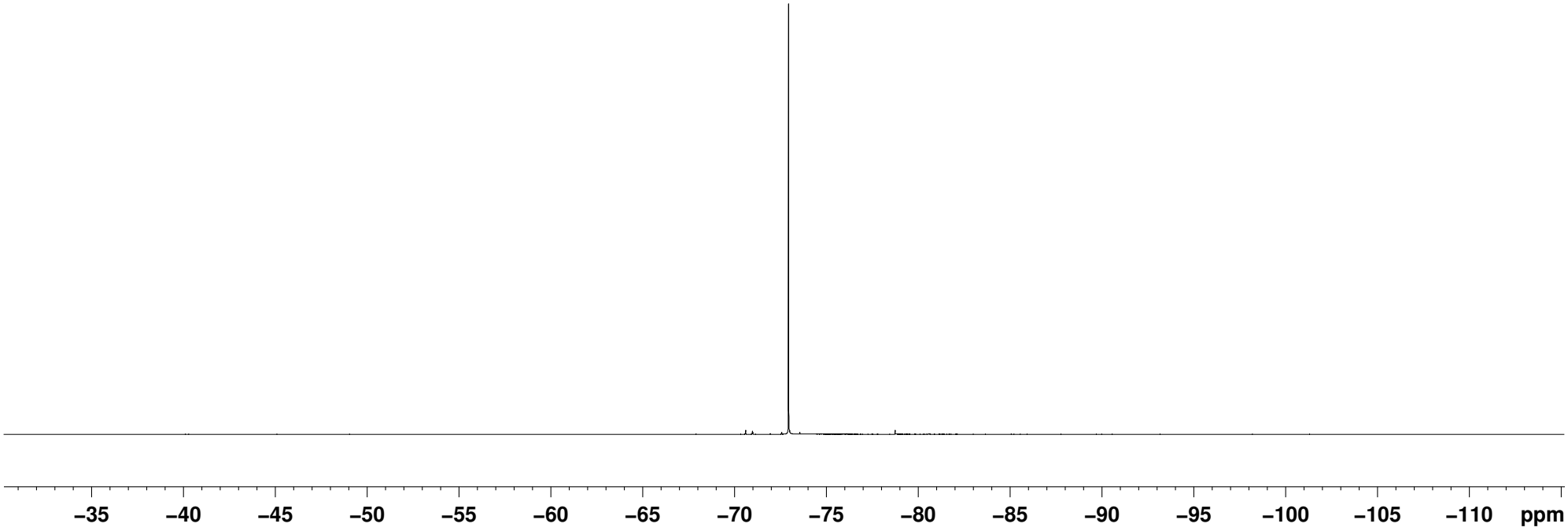

7.975
7.951
7.947
7.678
7.675
7.653
7.632
7.629
7.489
7.463
7.438
7.404
7.400
7.394
7.378
7.374
7.369
7.246
7.220
7.179
7.153
7.127
4.506
4.479
4.473
4.455
4.437
4.323
4.311
4.301
4.297
4.288
4.278
4.273
4.265
4.254
4.248
4.241
4.230
4.225
4.218
4.206
3.759
3.741
3.728
1.253
1.229
1.205
1.181
-0.000
EtOOC
EtOOC
H
N
CF3
O
N
S
Br
3h
1H NMR (300 MHz, CDCl3)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.00
1.01
3.00
1.05
1.01
1.04
2.01
4.03
1.00
6.01

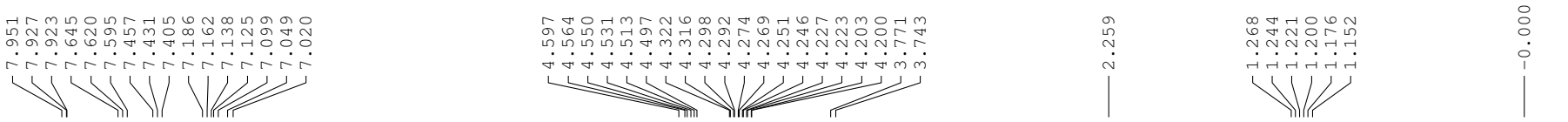

195.15
192.21
168.15
166.28
136.21
135.70
132.22
131.72
131.29
130.15
129.15
128.84
128.23
126.45
122.73
122.55
119.06
80.34
77.50
77.08
76.95
76.66
64.61
64.20
63.80
63.36
63.01
56.88
13.71
13.58
EtOOC
EtOOC
H
N
CF3
O
N
S
Br
3h
13C NMR (75 MHz, CDCl3)
130.15
126.45
122.73
119.06
135
130
125
120
ppm
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

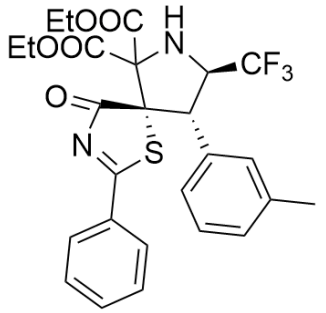


3h

^{19}F NMR (282 MHz, $CDCl_3$)

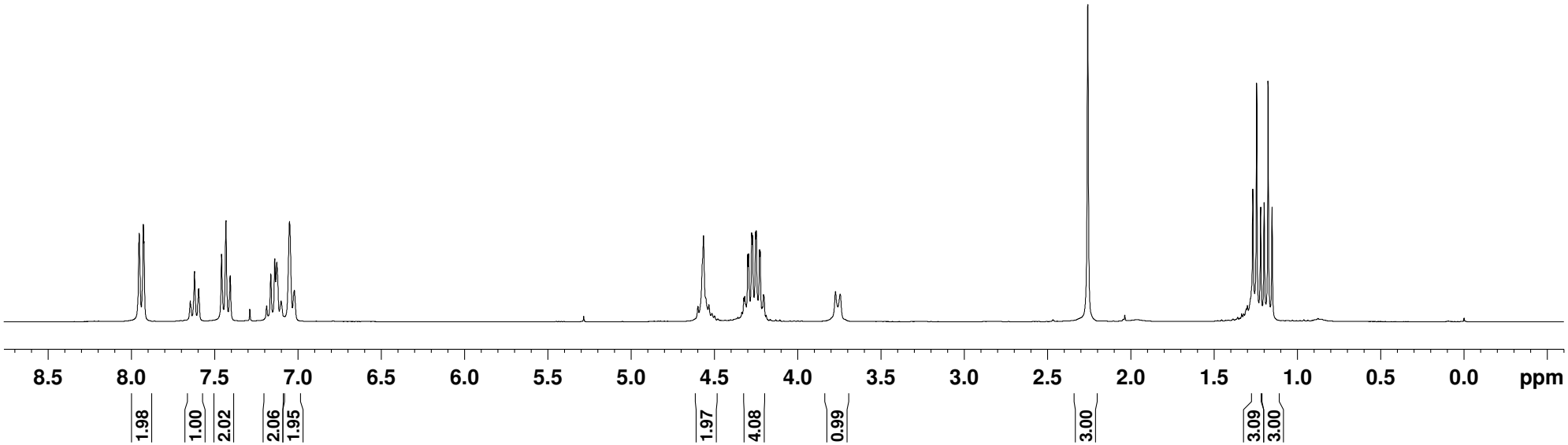


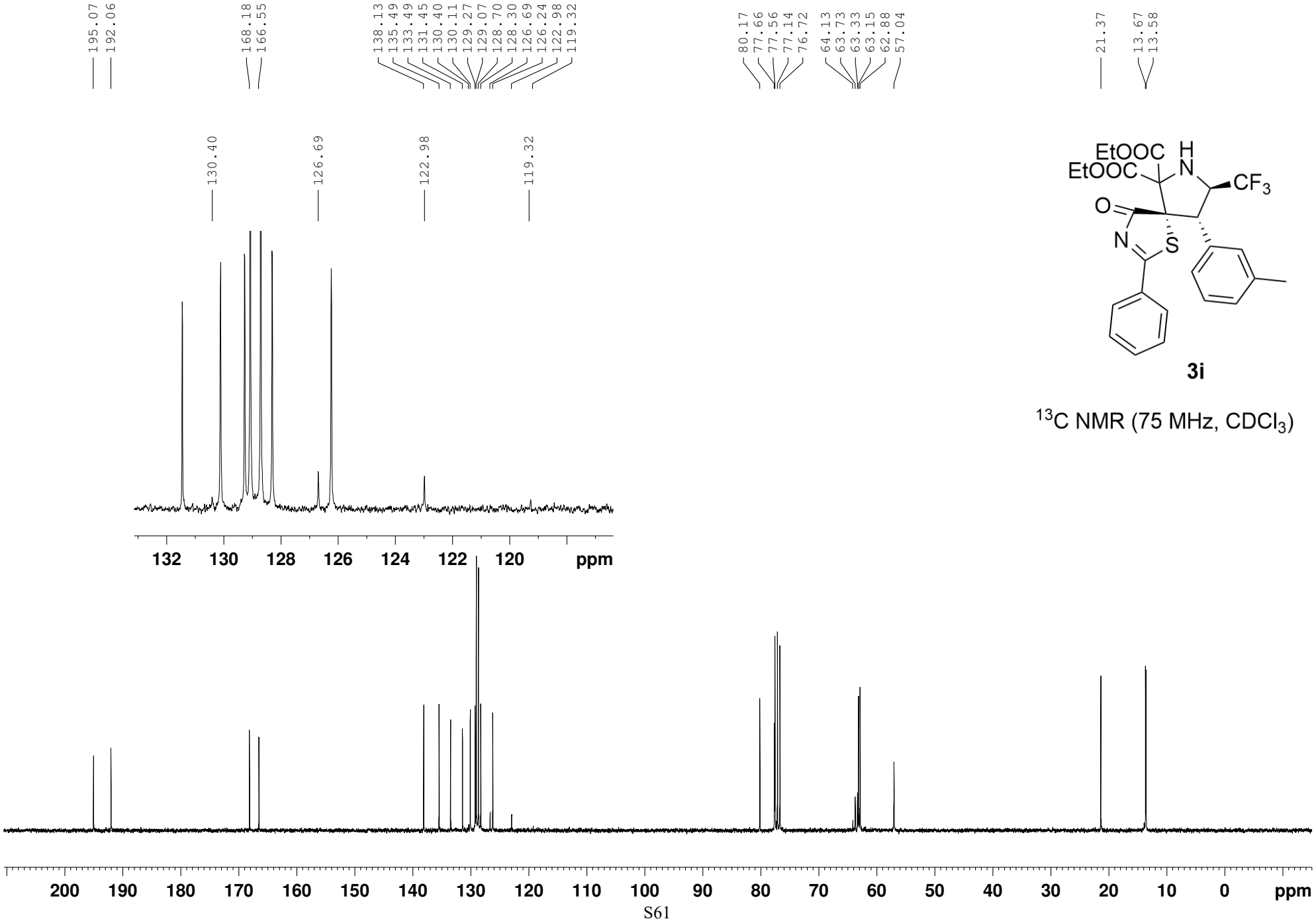




3i

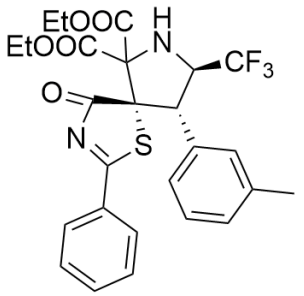
^{1}H NMR (300 MHz, $CDCl_3$)





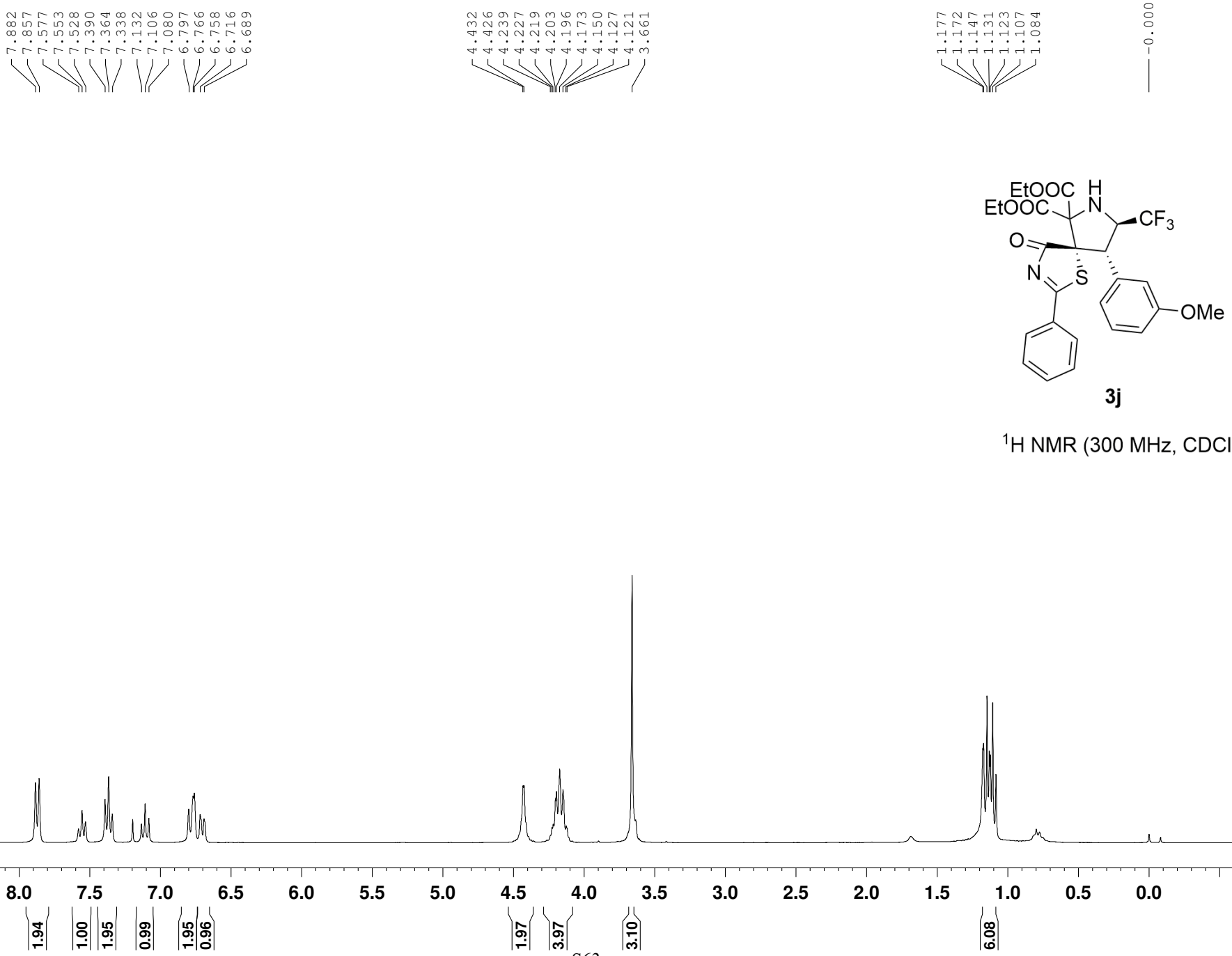
3i

^{13}C NMR (75 MHz, $CDCl_3$)



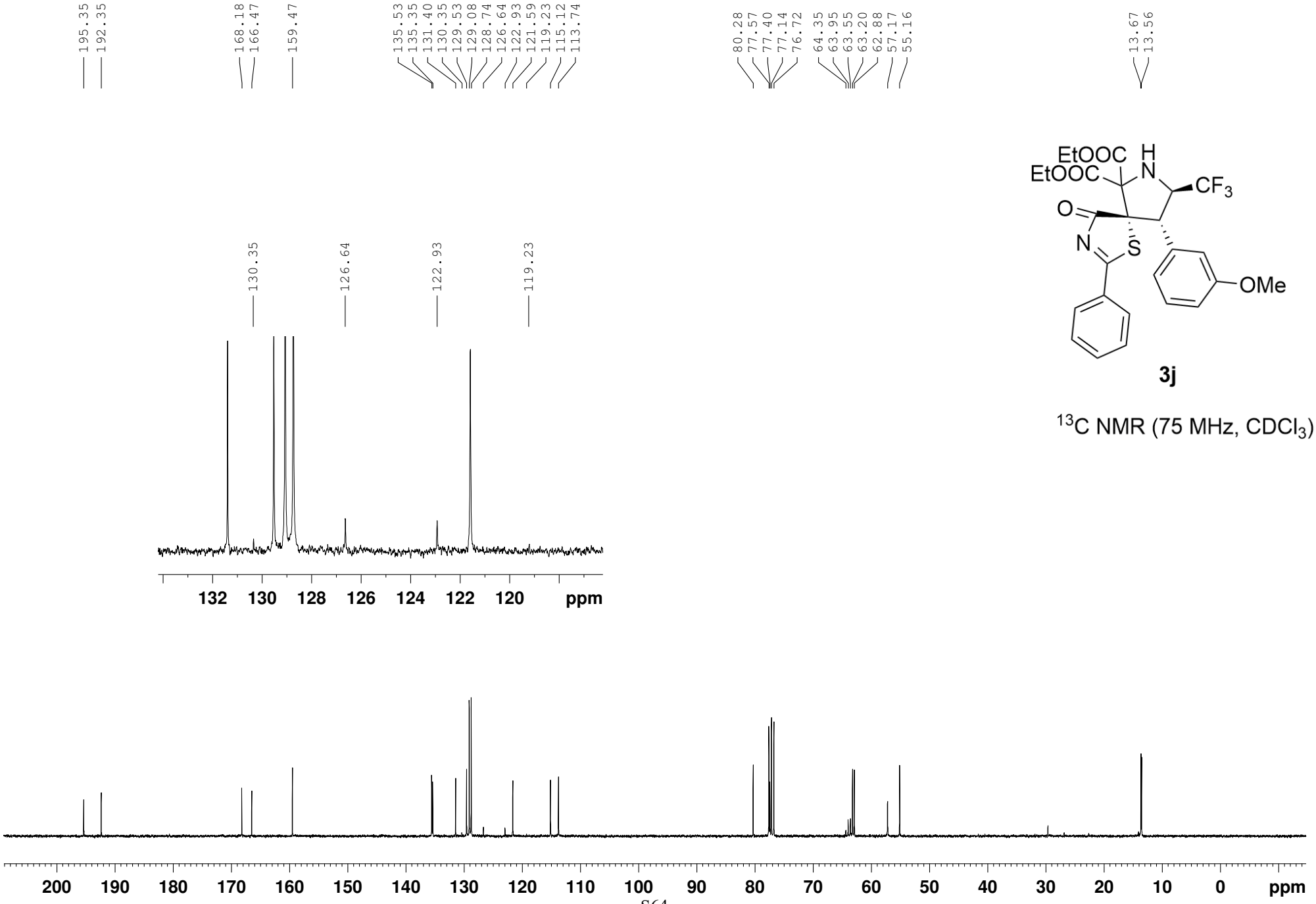
3i

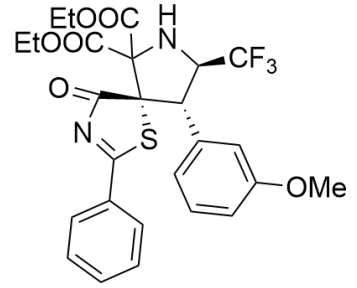
^{19}F NMR (282 MHz, $CDCl_3$)



3j

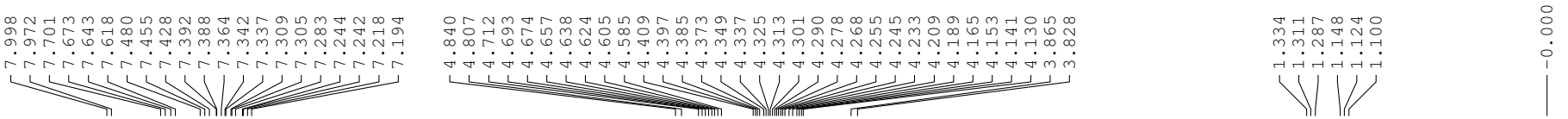
^{1}H NMR (300 MHz, $CDCl_3$)

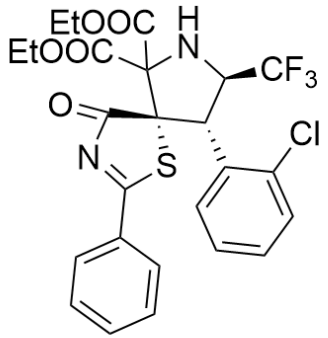

195.35
192.35
168.18
166.47
159.47
135.53
135.35
131.40
130.35
129.53
129.08
128.74
126.64
122.93
121.59
119.23
115.12
113.74
80.28
77.57
77.40
77.14
76.72
64.35
63.95
63.55
63.20
62.88
57.17
55.16
13.67
13.56
130.35
126.64
122.93
119.23
132
130
128
126
124
122
120
ppm
EtOOC
EtOOC
H
N
CF3
O
N
S
OMe
3j
13C NMR (75 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



3j

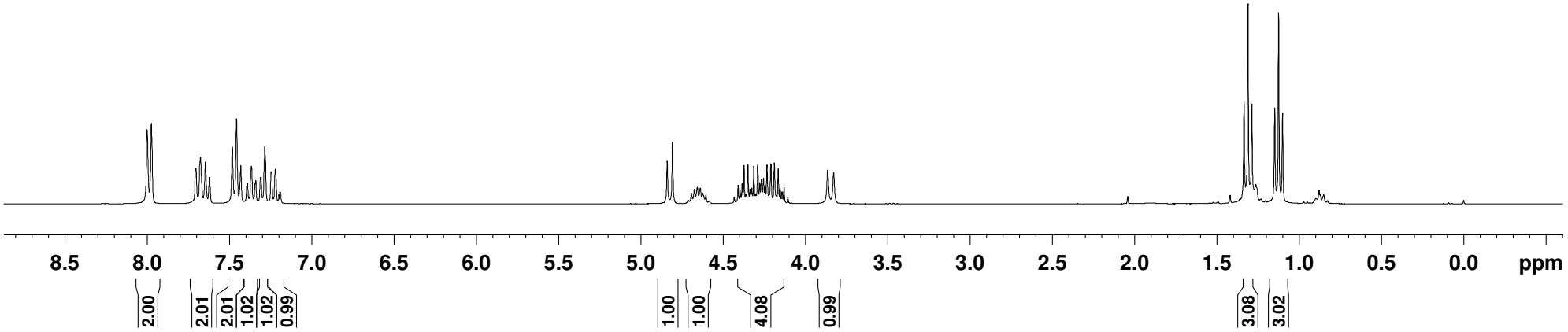
^{19}F NMR (282 MHz, $CDCl_3$)

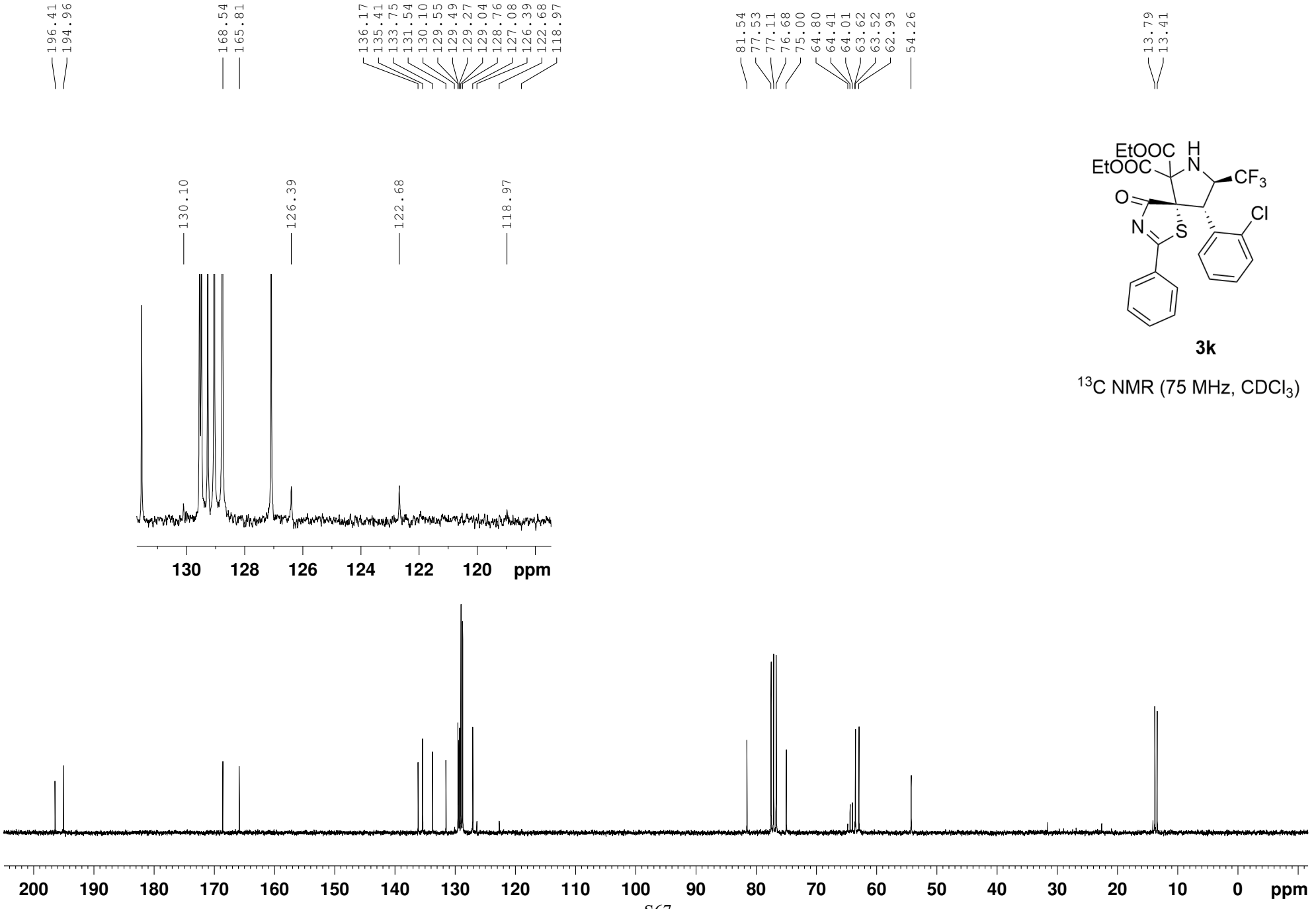




3k

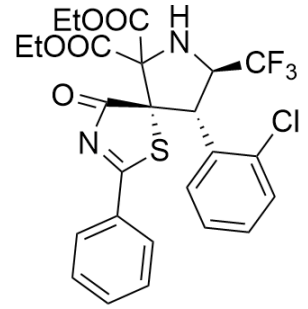
^{1}H NMR (300 MHz, $CDCl_3$)





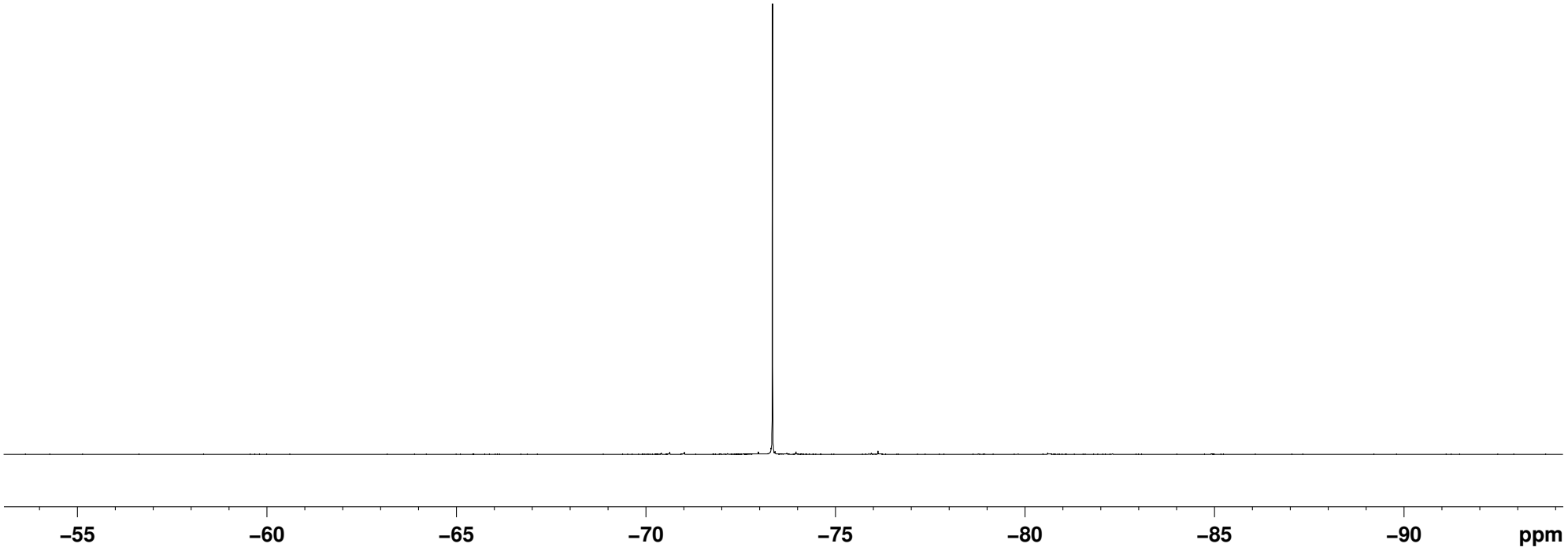
3k

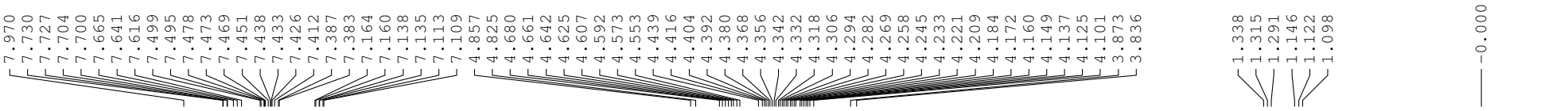
^{13}C NMR (75 MHz, $CDCl_3$)

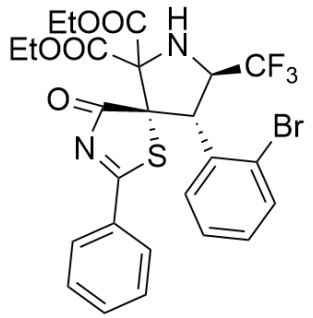


3k

^{19}F NMR (282 MHz, $CDCl_3$)

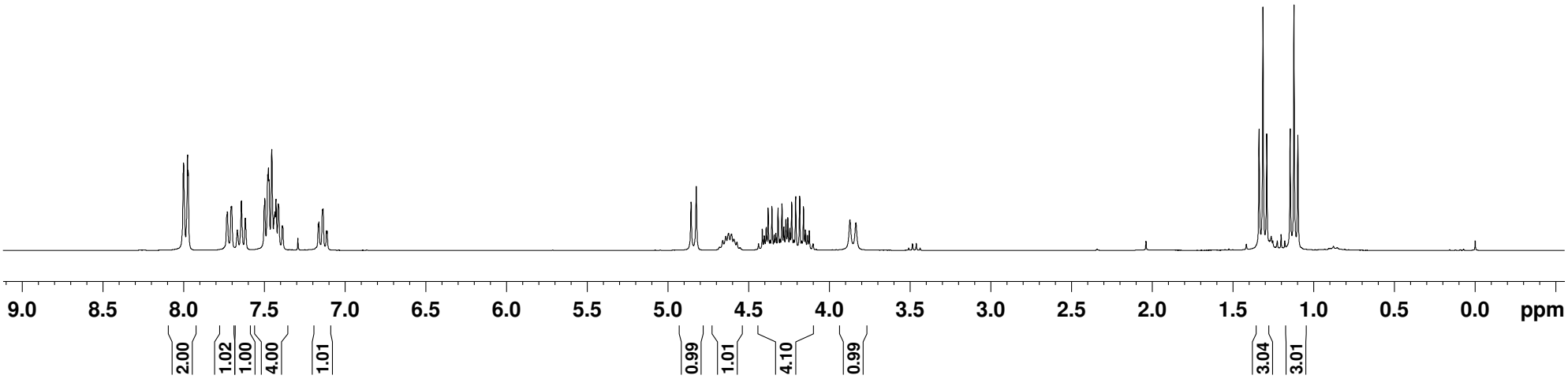


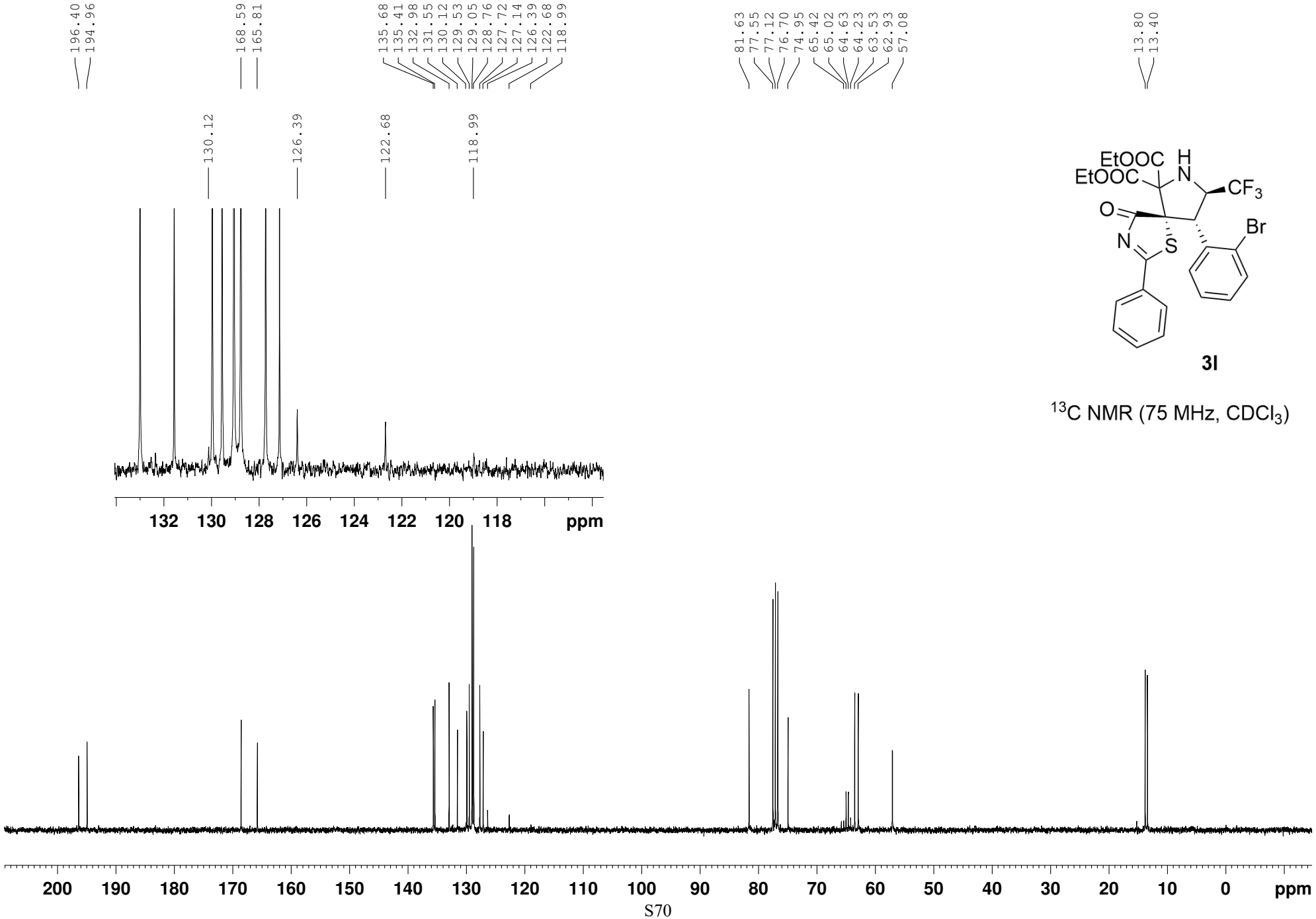




3l

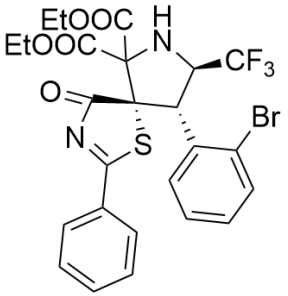
^{1}H NMR (300 MHz, $CDCl_3$)





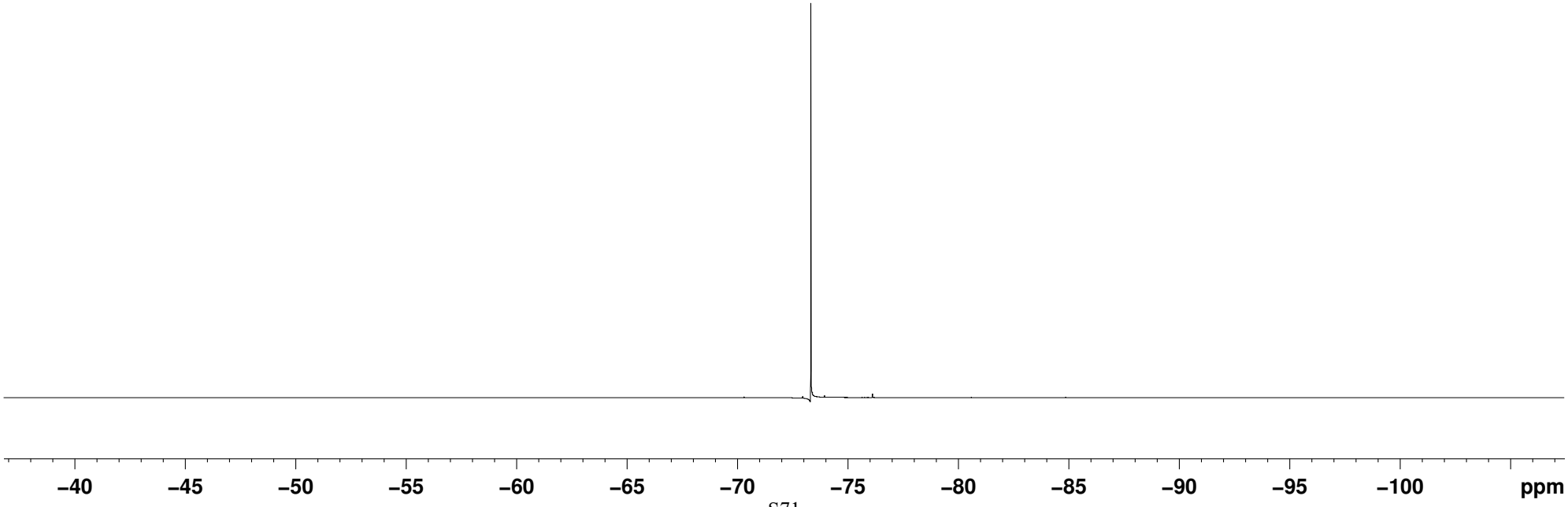
3l

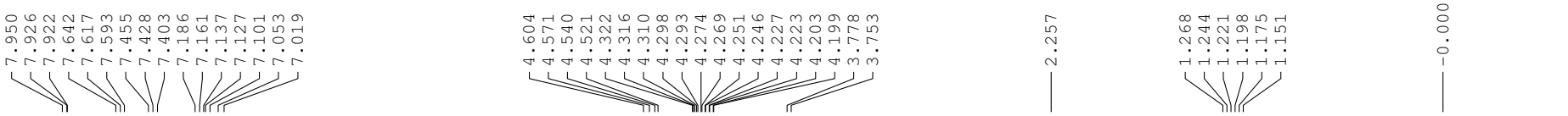
^{13}C NMR (75 MHz, $CDCl_3$)

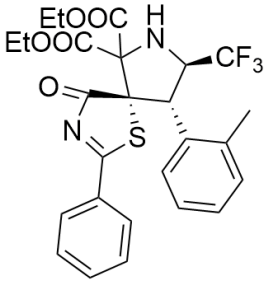


3l

^{19}F NMR (282 MHz, $CDCl_3$)

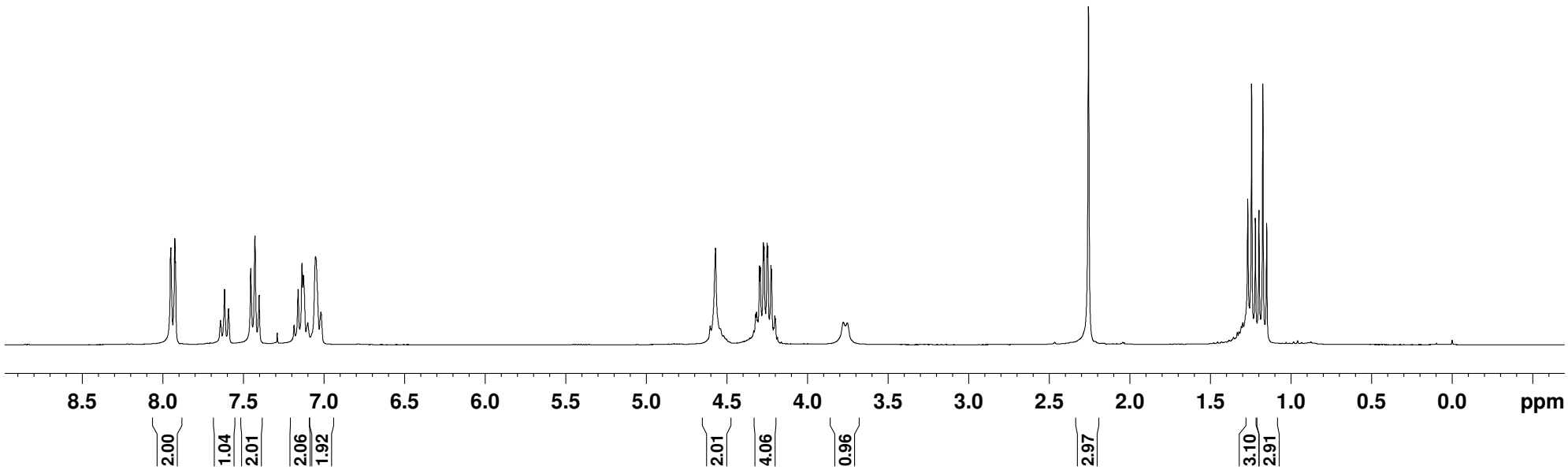


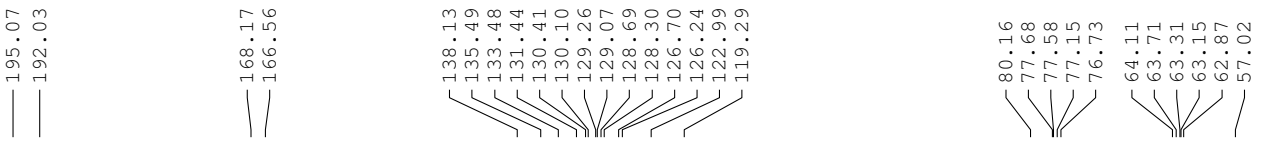


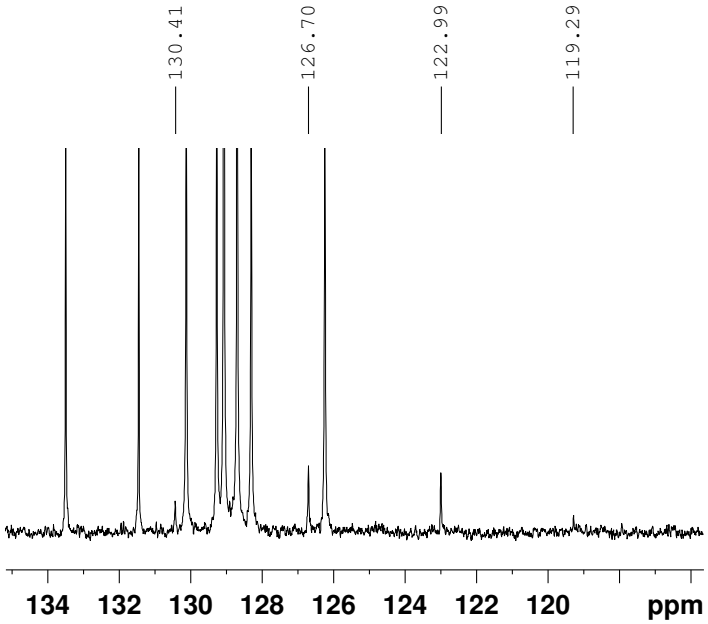


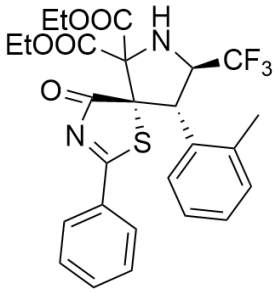
3m

^{1}H NMR (300 MHz, $CDCl_3$)



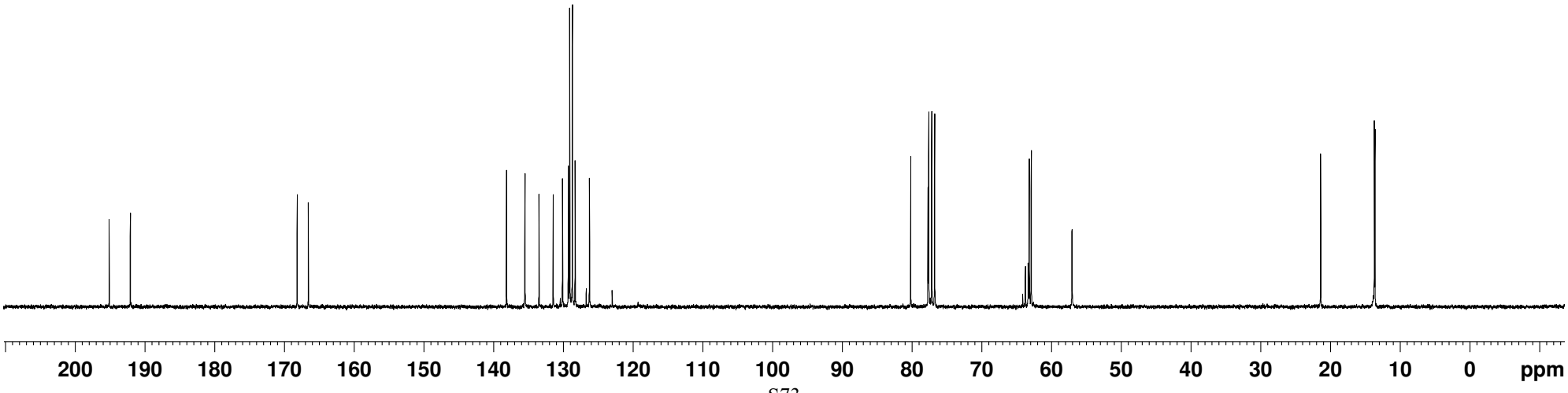


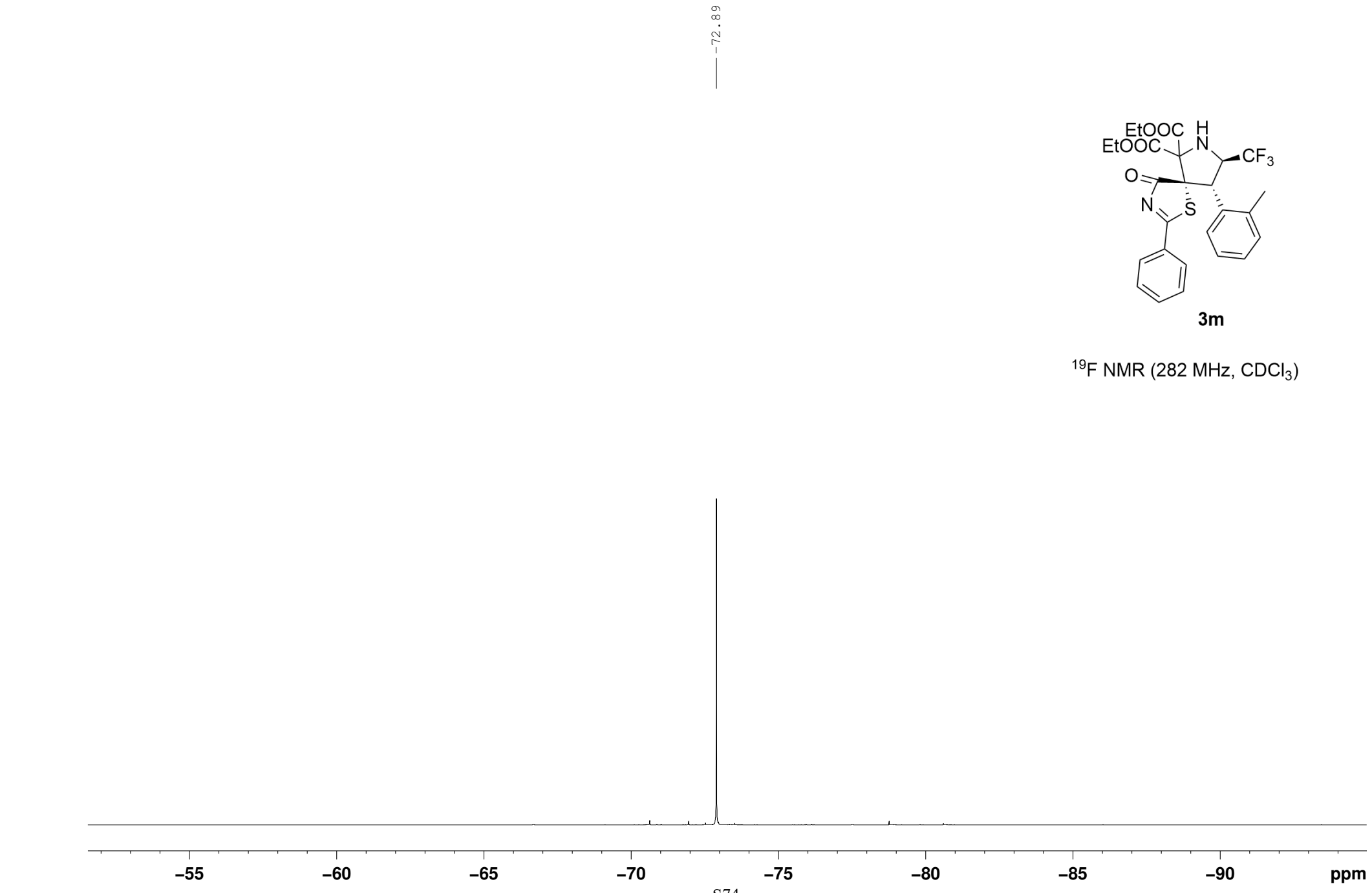


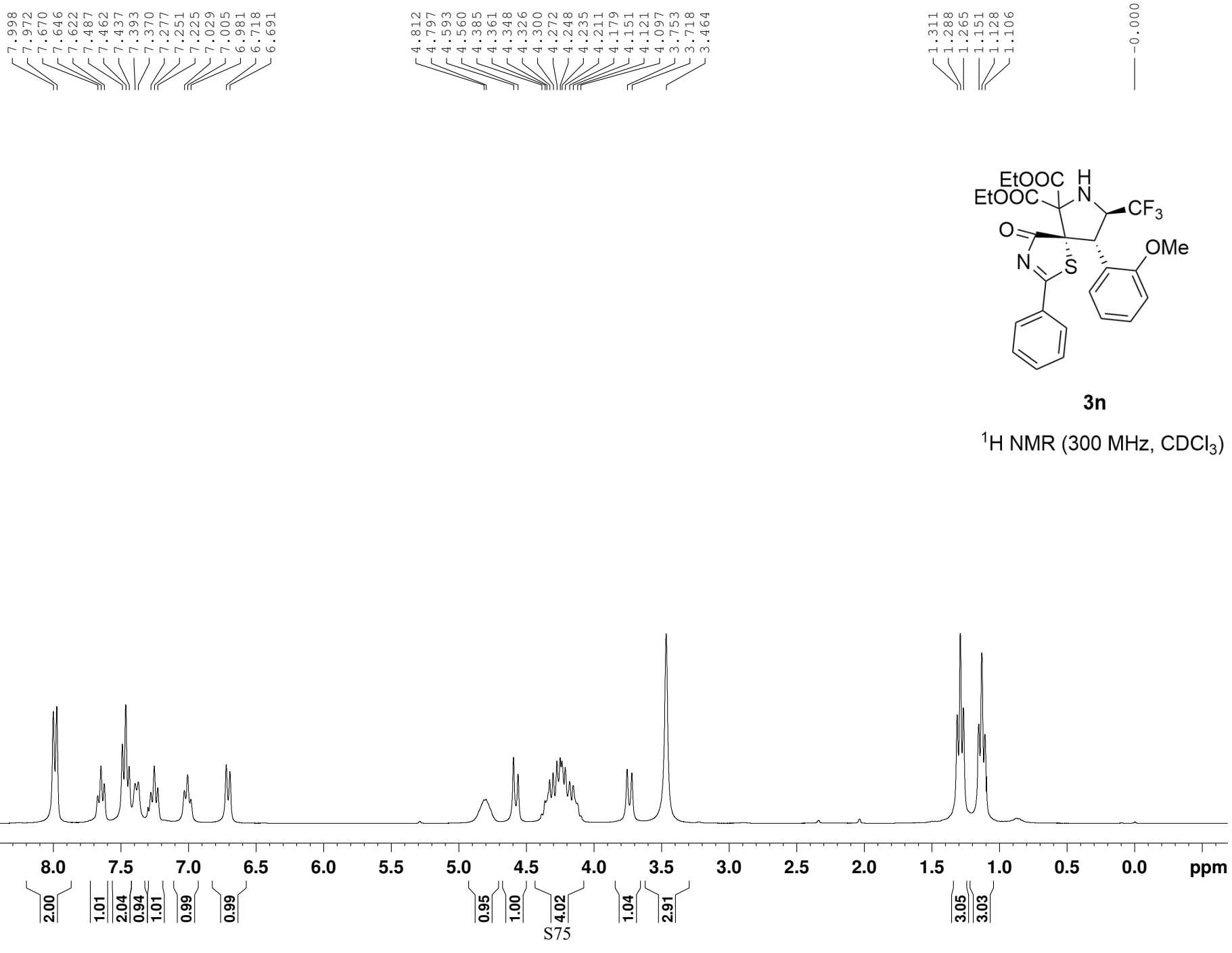


3m

^{13}C NMR (75 MHz, $CDCl_3$)

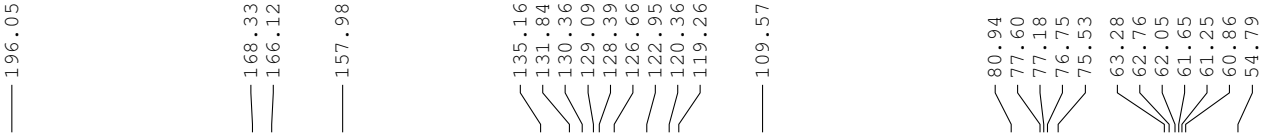


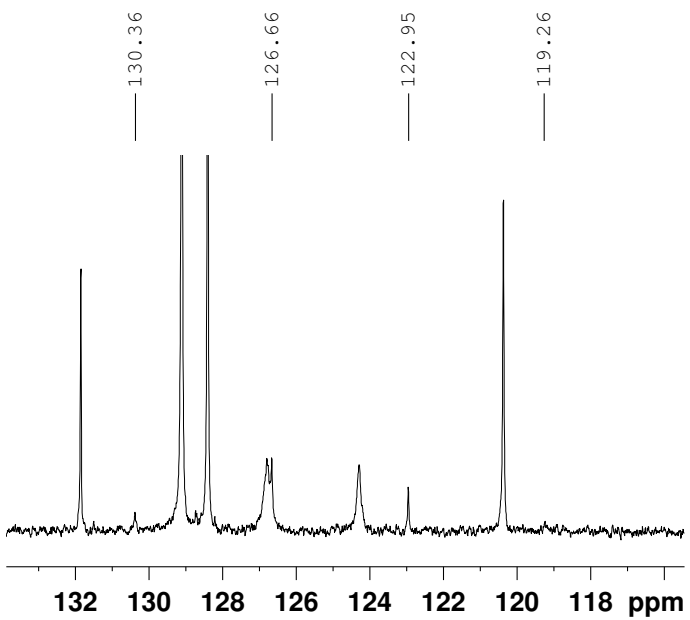

-72.89
EtOOC
EtOOC
H
N
CF3
O
N
S
3m
19F NMR (282 MHz, CDCl3)
–55
–60
–65
–70
–75
–80
–85
–90
ppm

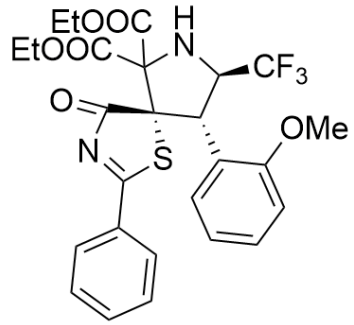


3n

^{1}H NMR (300 MHz, $CDCl_3$)

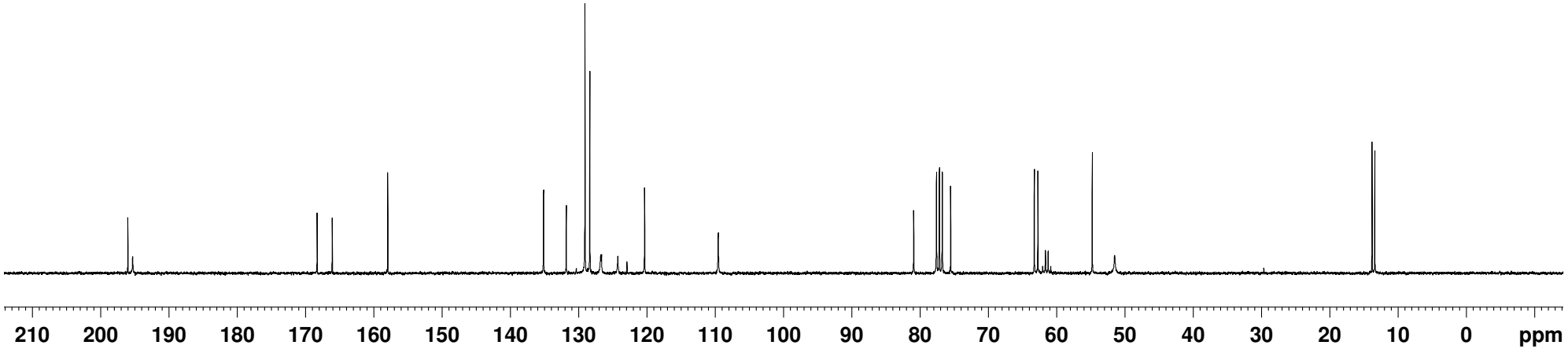


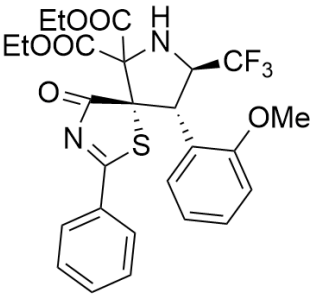




3n

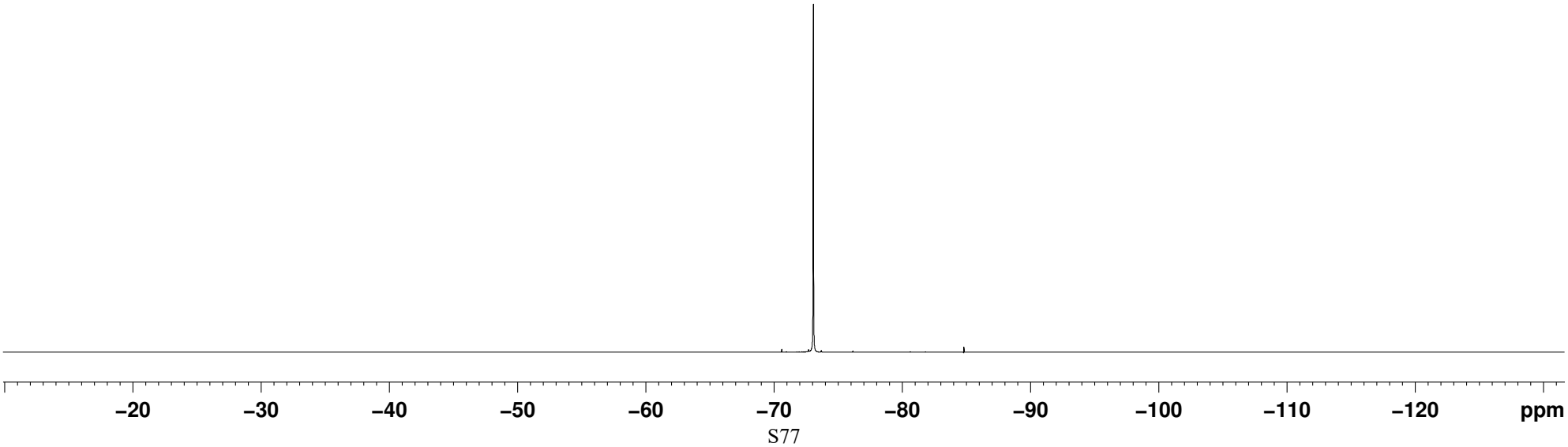
^{13}C NMR (75 MHz, $CDCl_3$)

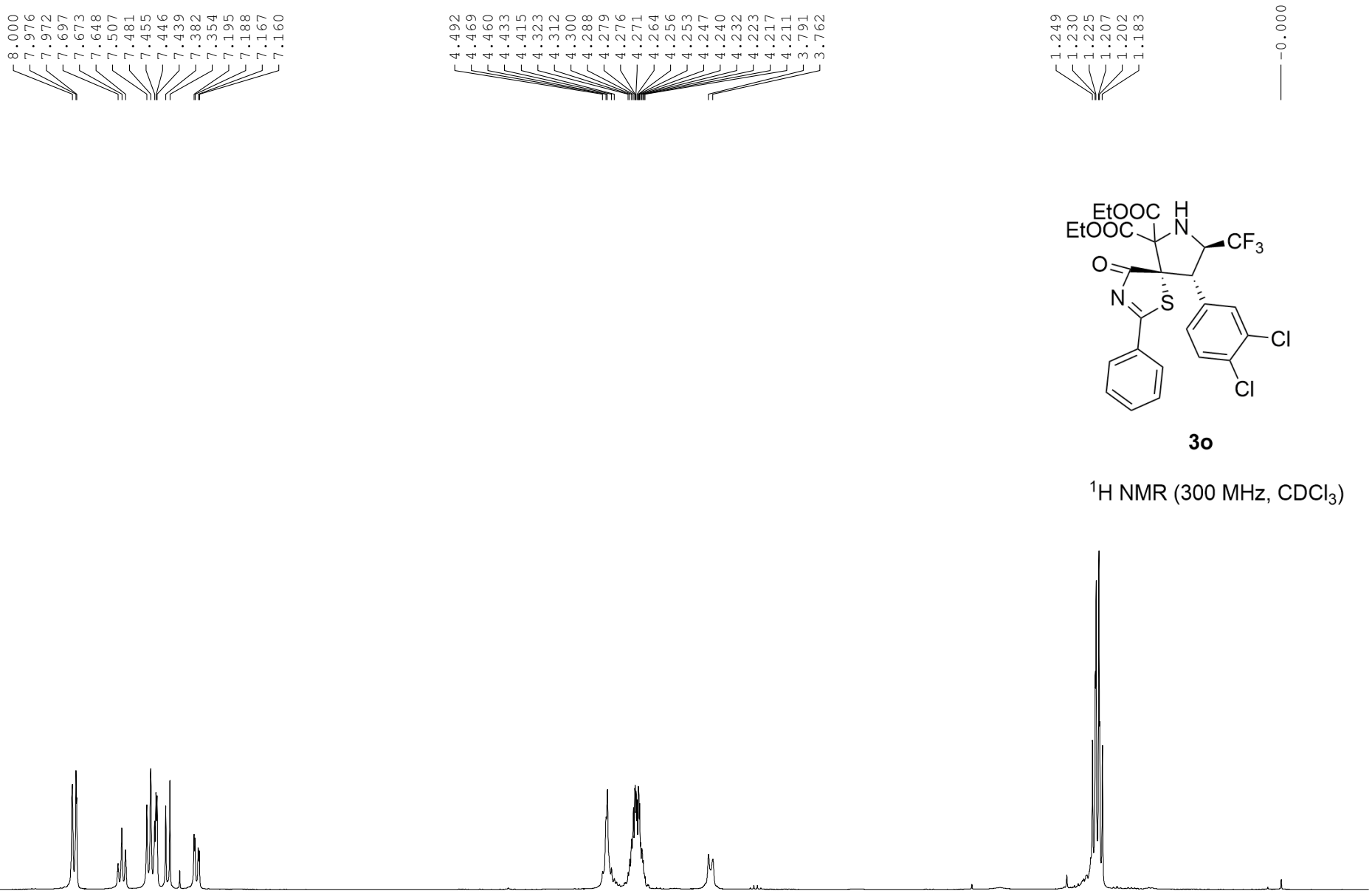




3n

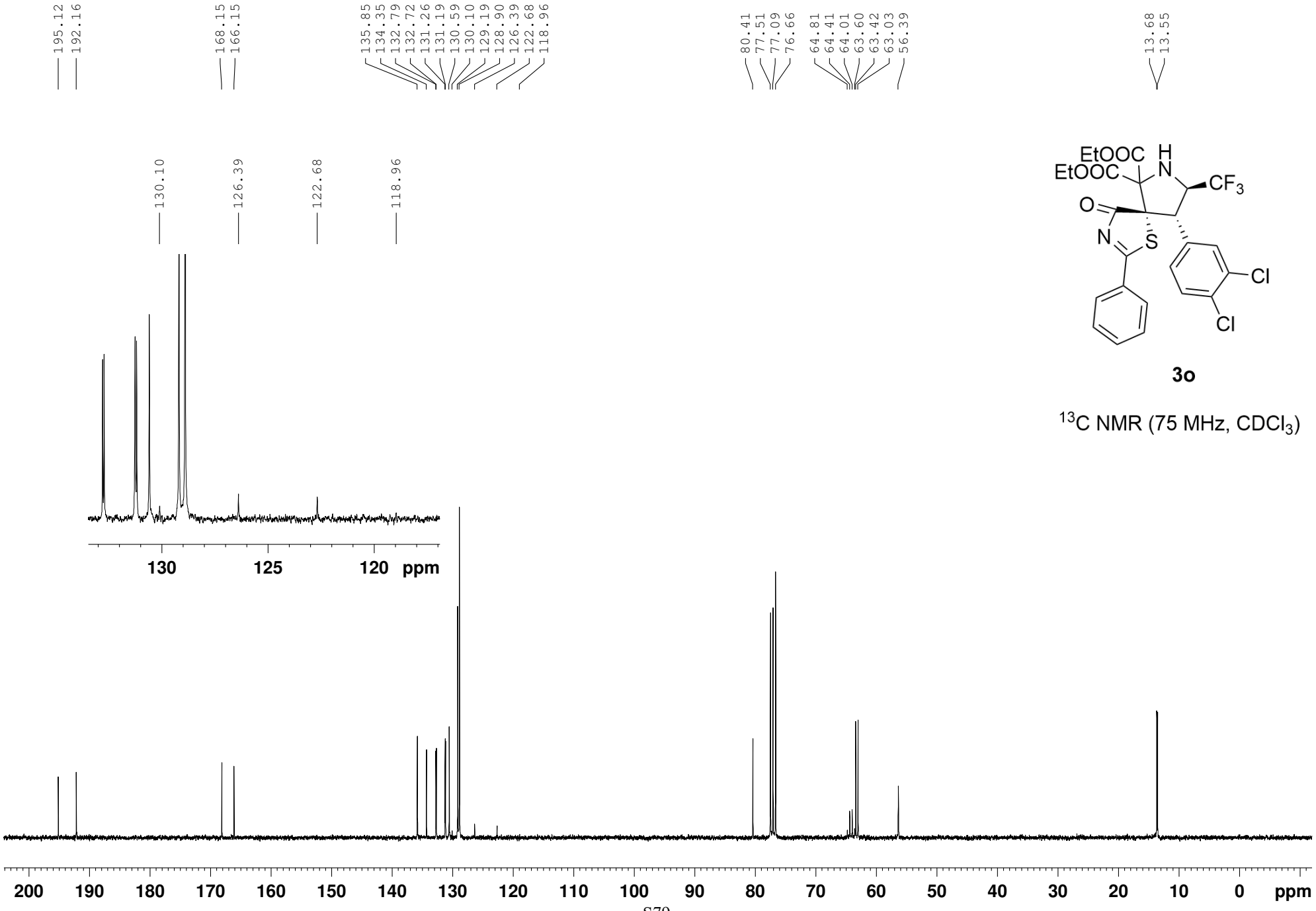
^{19}F NMR (282 MHz, $CDCl_3$)





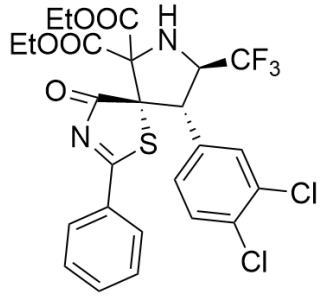
3o

^{1}H NMR (300 MHz, $CDCl_3$)



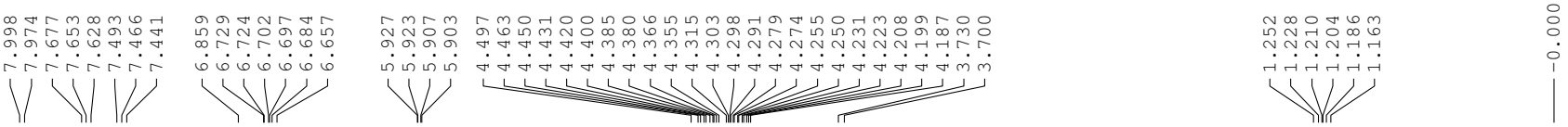
3o

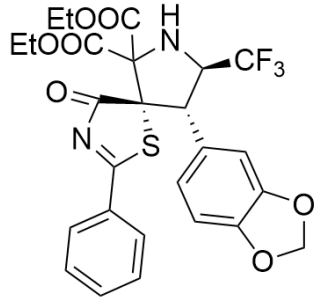
^{13}C NMR (75 MHz, $CDCl_3$)



3o

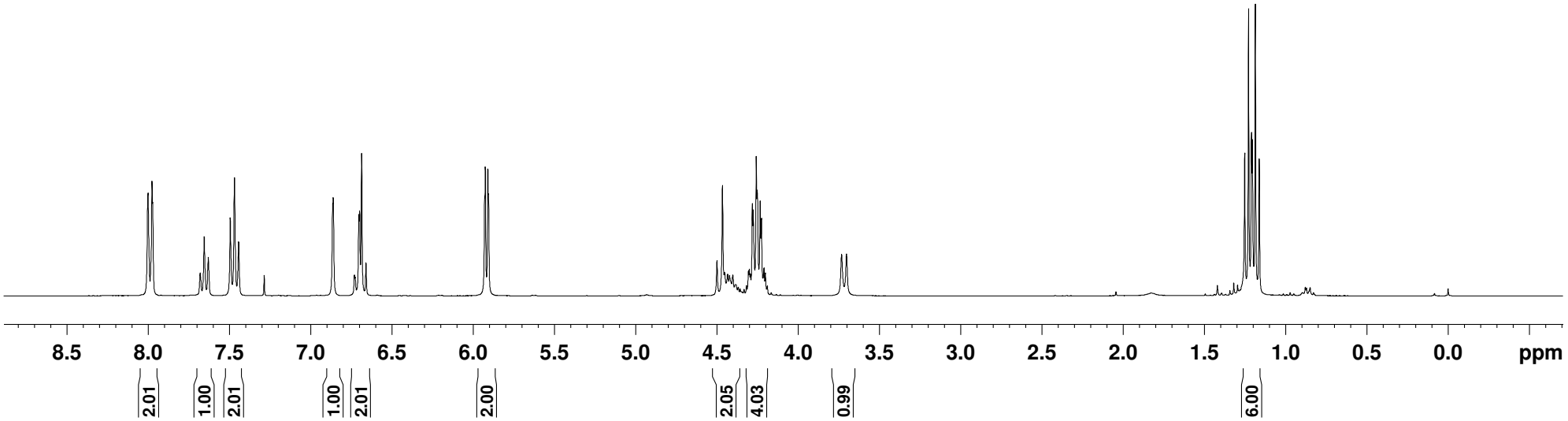
^{19}F NMR (282 MHz, $CDCl_3$)

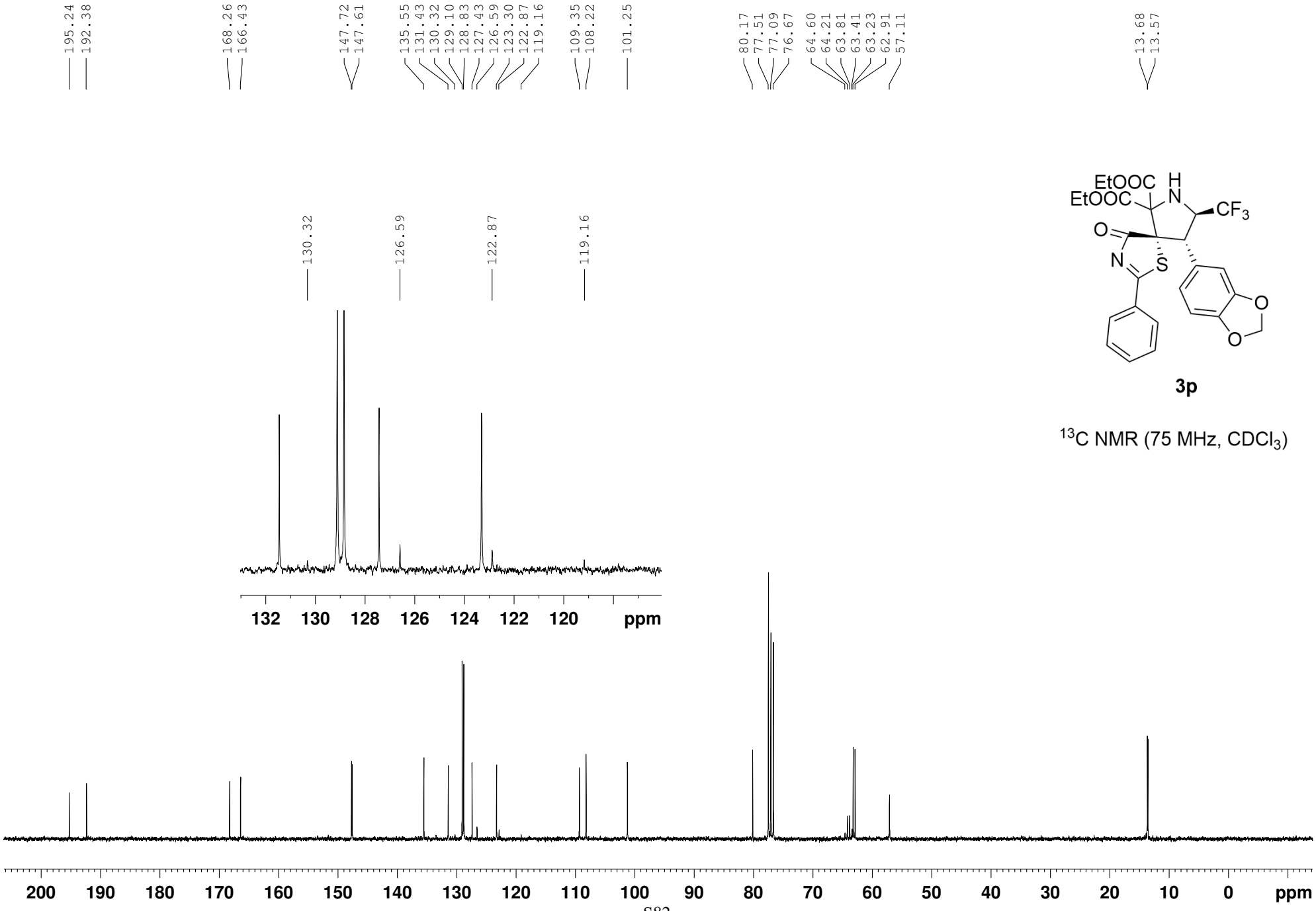




3p

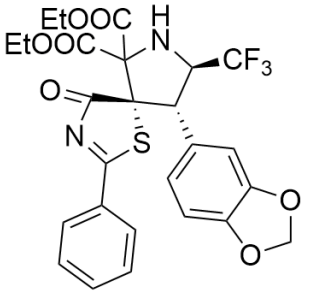
^{1}H NMR (300 MHz, $CDCl_3$)





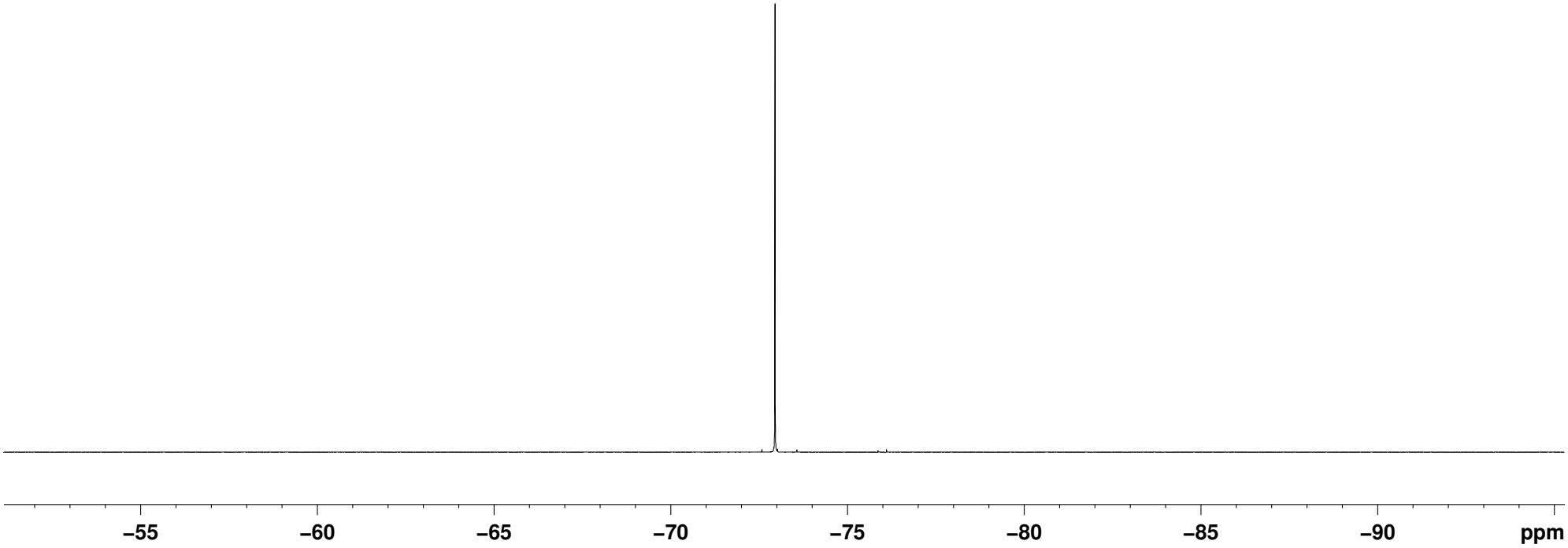
3p

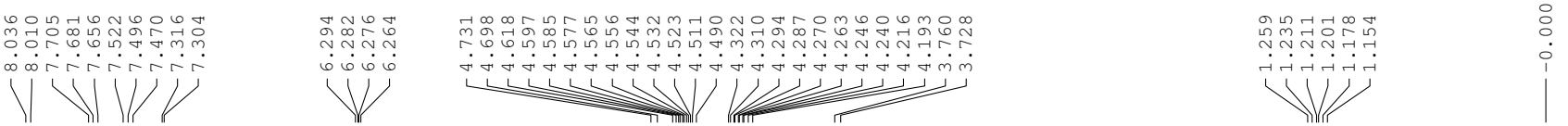
^{13}C NMR (75 MHz, $CDCl_3$)

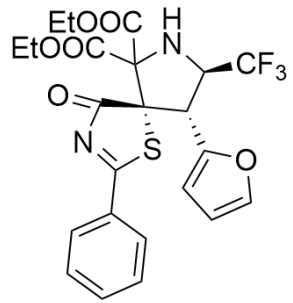


3p

^{19}F NMR (282 MHz, $CDCl_3$)

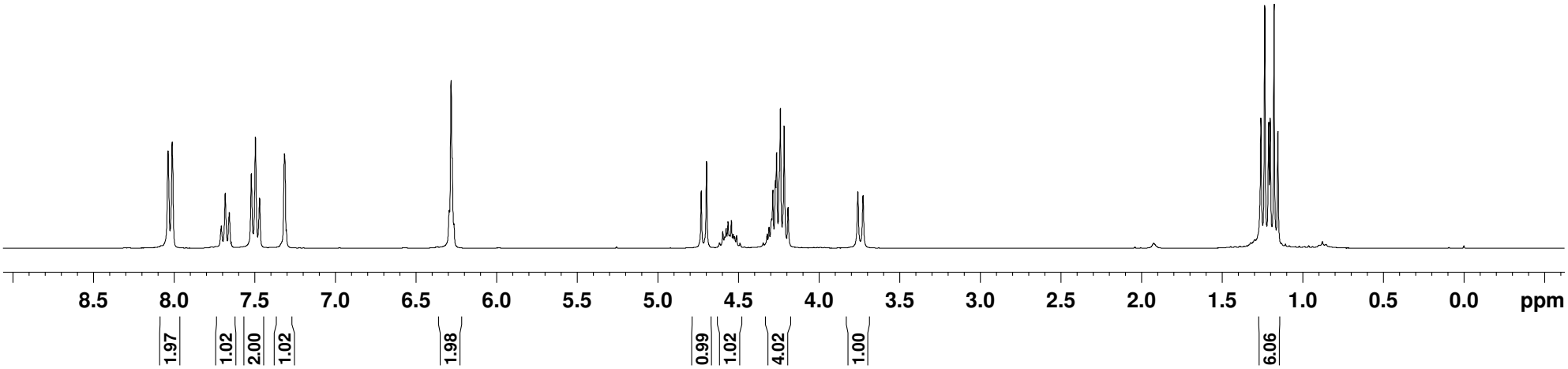


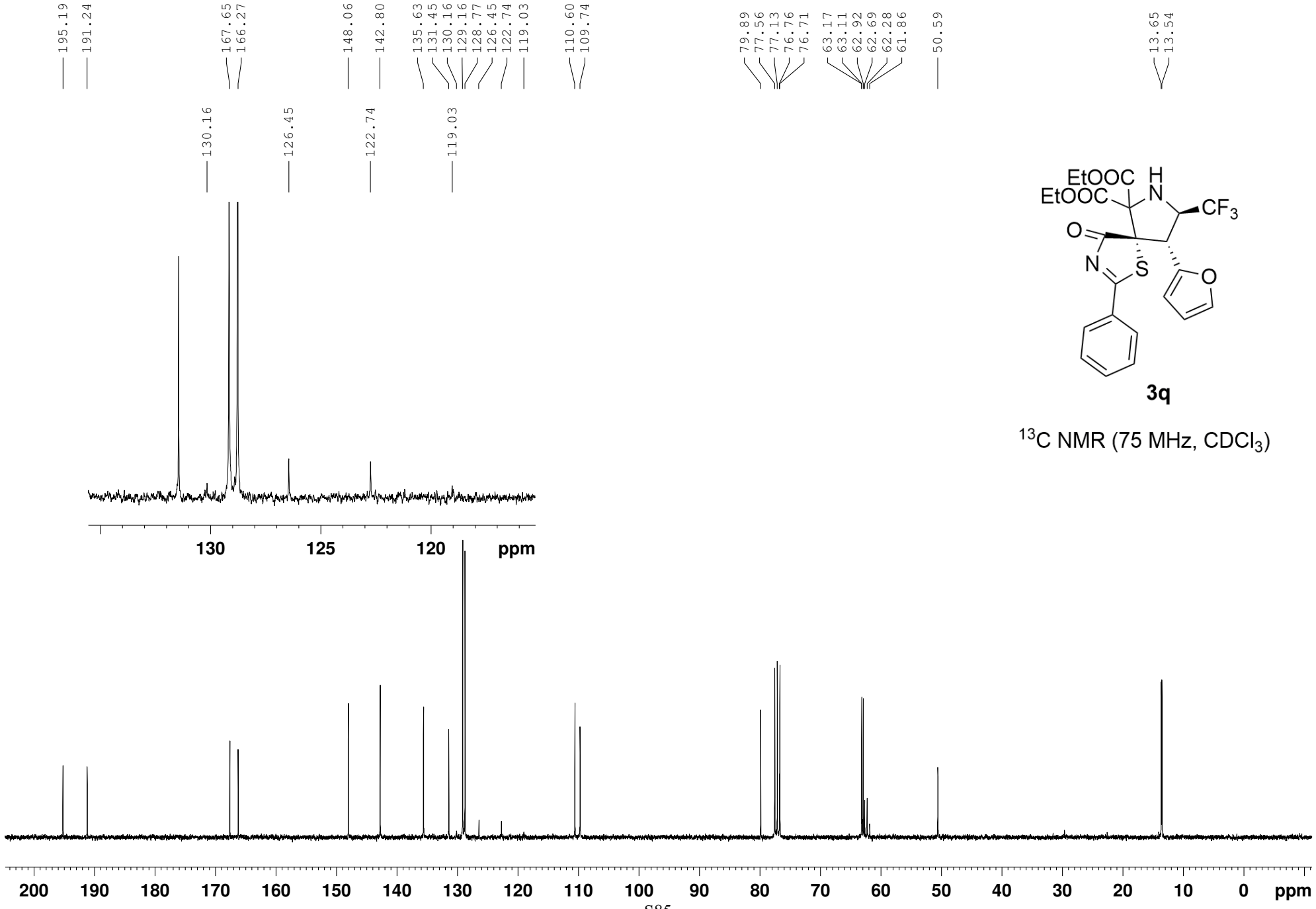




3q

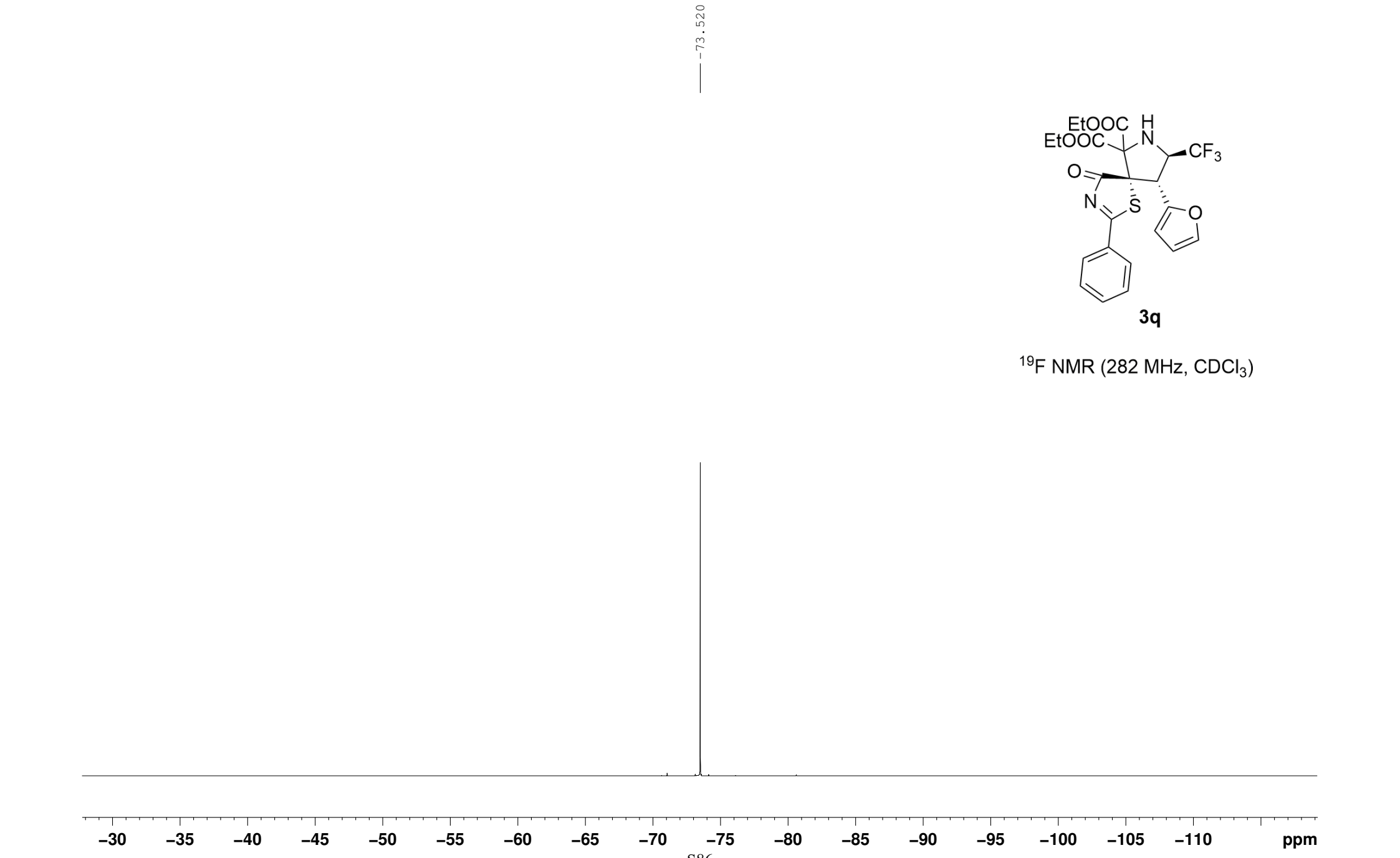
^{1}H NMR (300 MHz, $CDCl_3$)





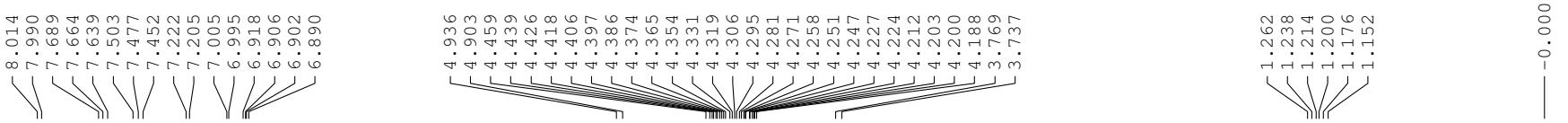
3q

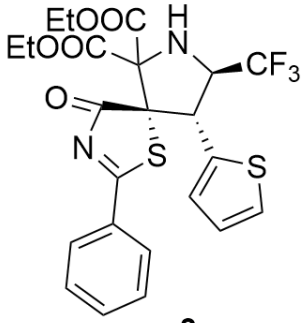
^{13}C NMR (75 MHz, $CDCl_3$)



3q

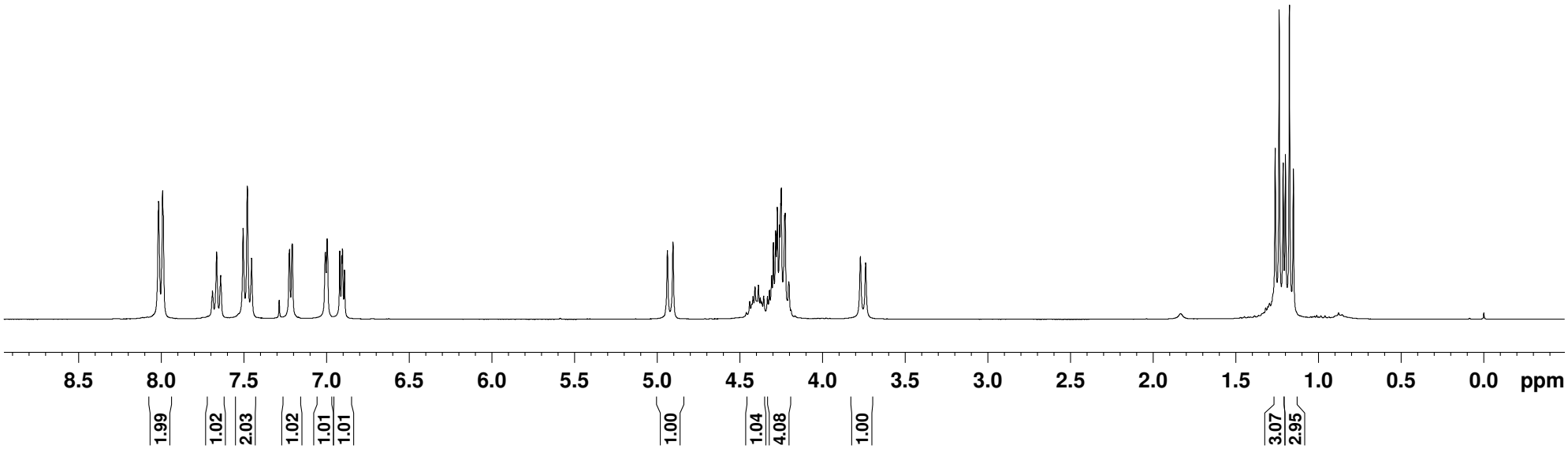
^{19}F NMR (282 MHz, $CDCl_3$)

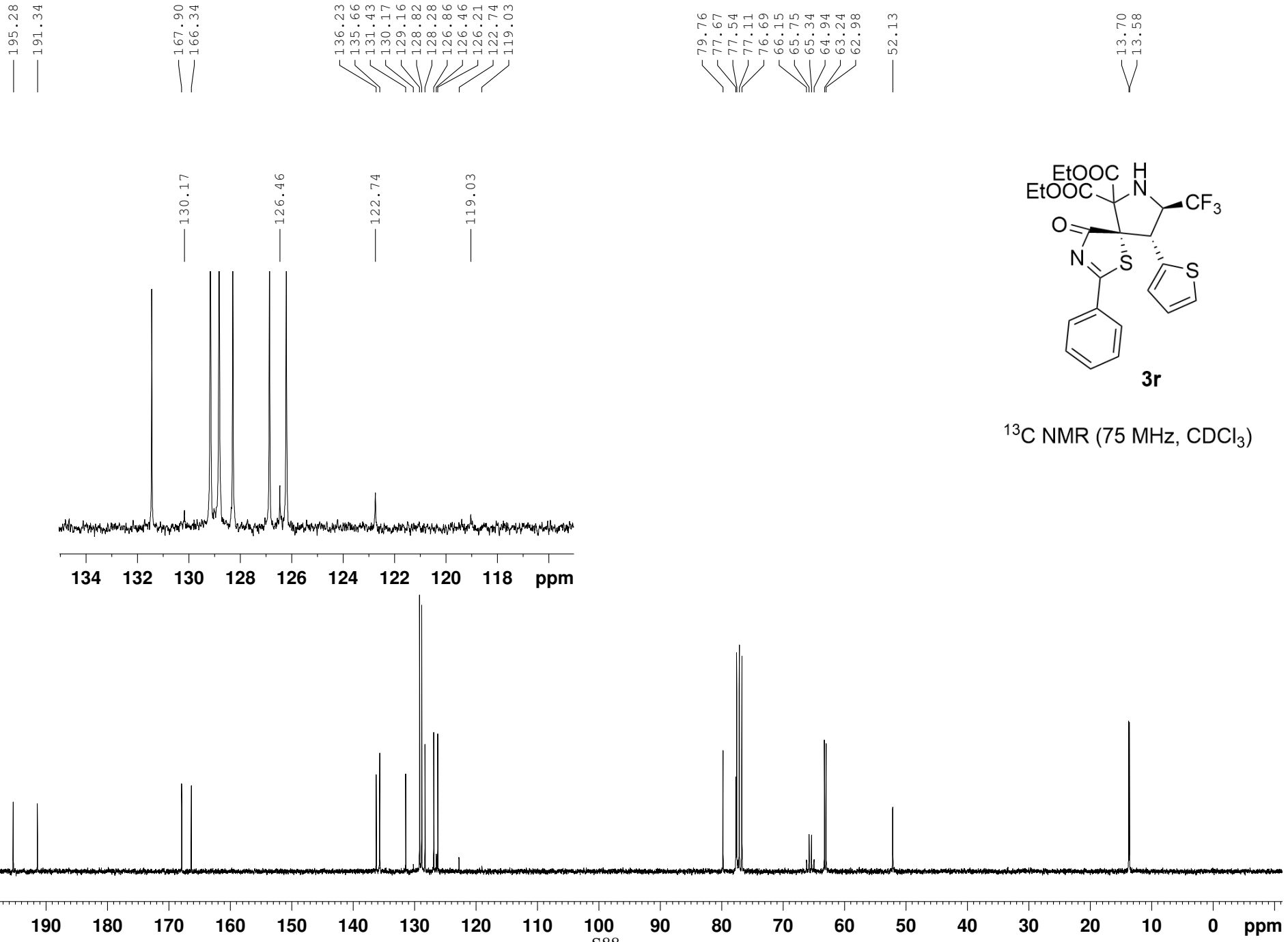


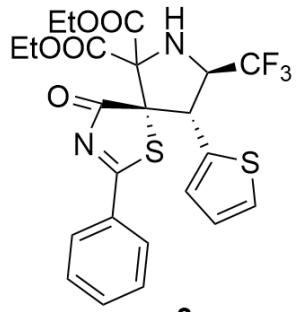


3r

^{1}H NMR (300 MHz, $CDCl_3$)

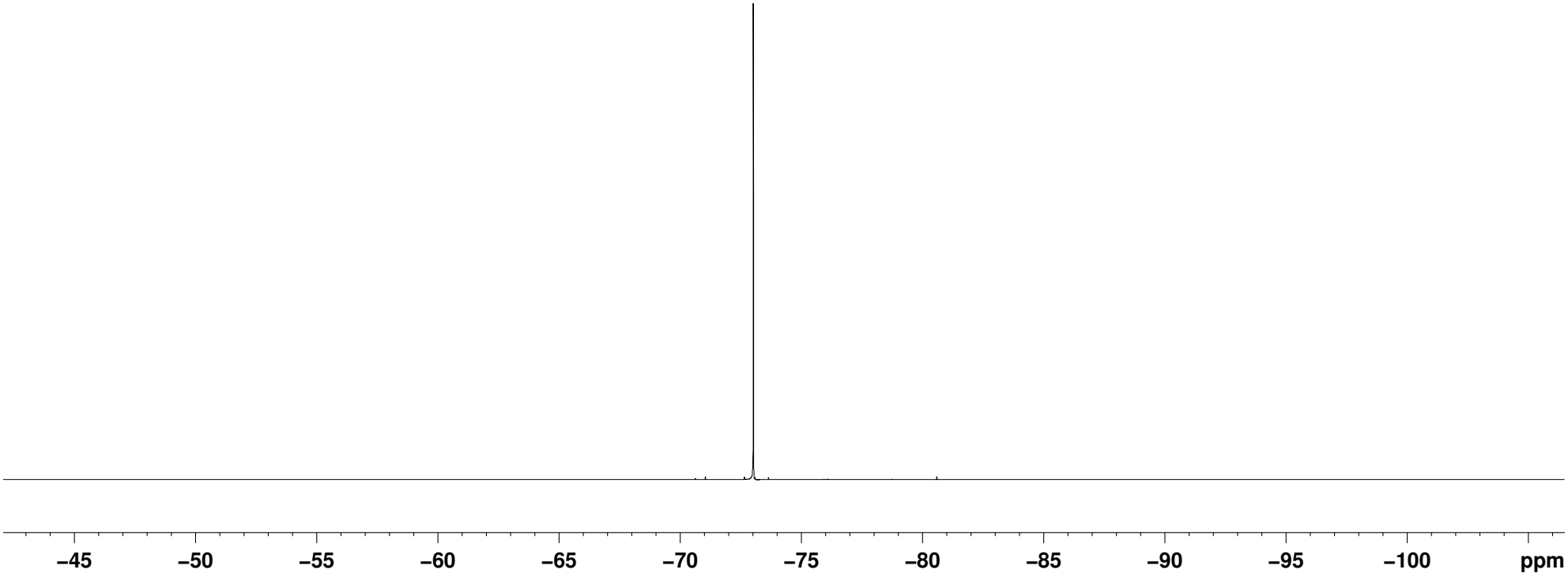


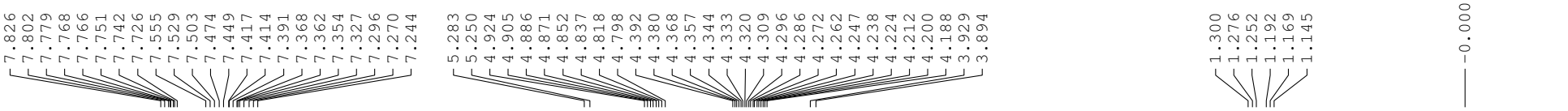

195.28
191.34
167.90
166.34
136.23
135.66
131.43
130.17
129.16
128.82
128.28
126.86
126.46
126.21
122.74
119.03
79.76
77.67
77.54
77.11
76.69
66.15
65.75
65.34
64.94
63.24
62.98
52.13
13.70
13.58
EtOOC
EtOOC
H
N
CF3
O
N
S
S
3r
13C NMR (75 MHz, CDCl3)
134 132 130 128 126 124 122 120 118 ppm
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

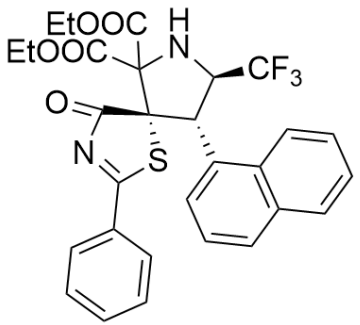


3r

^{19}F NMR (282 MHz, $CDCl_3$)

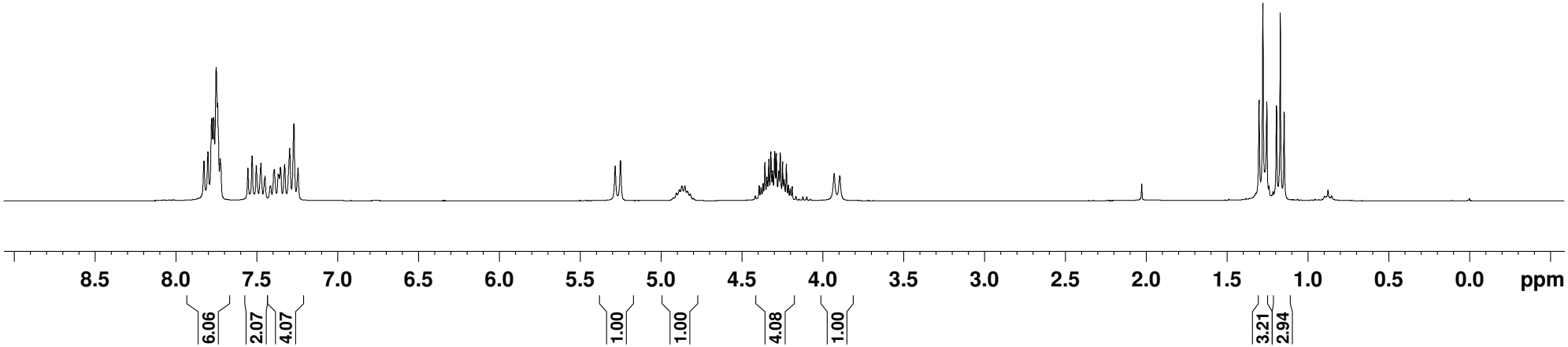


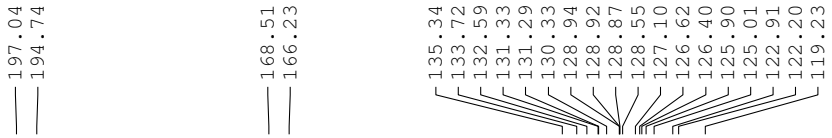


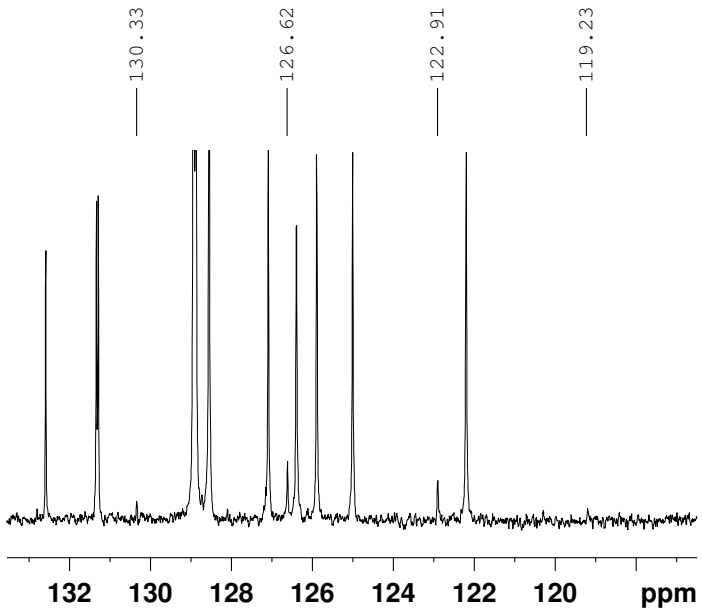


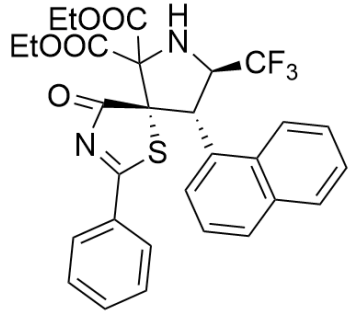
3s

^{1}H NMR (300 MHz, $CDCl_3$)



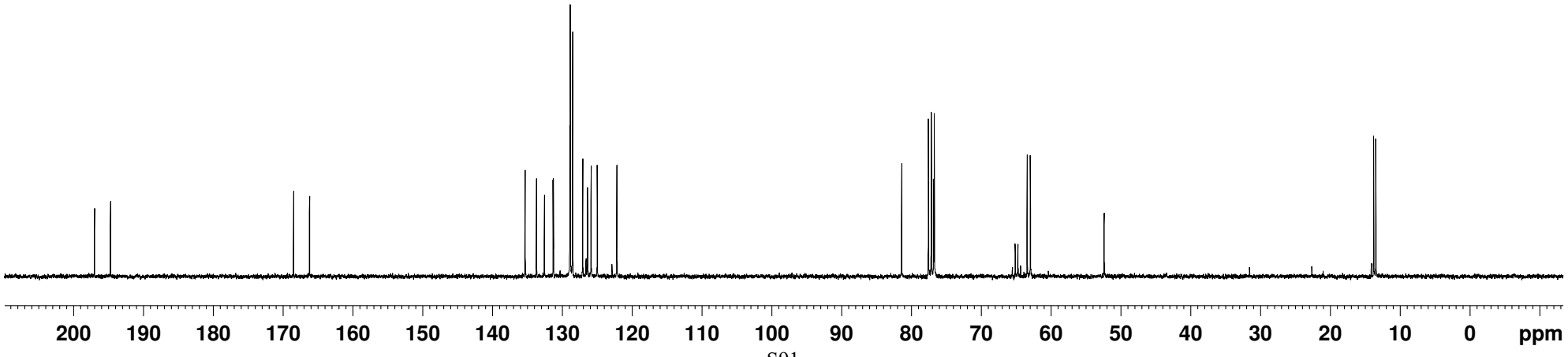


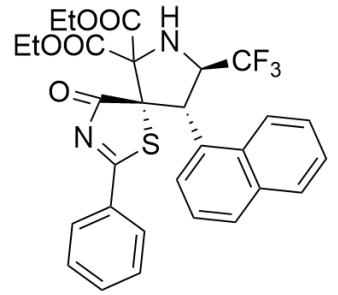




3s

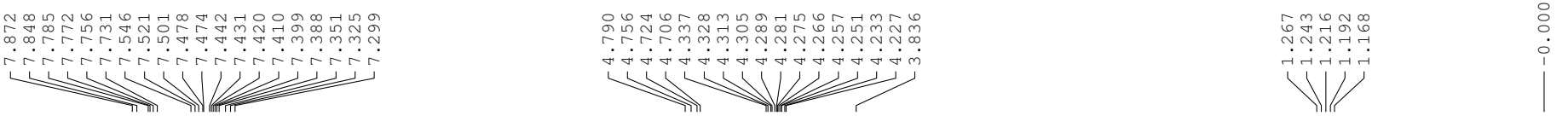
^{13}C NMR (75 MHz, $CDCl_3$)

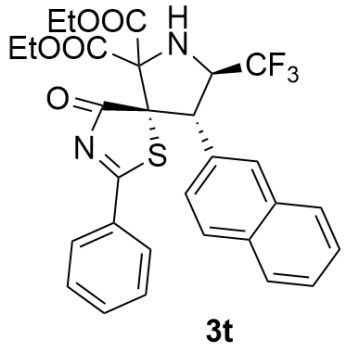




3s

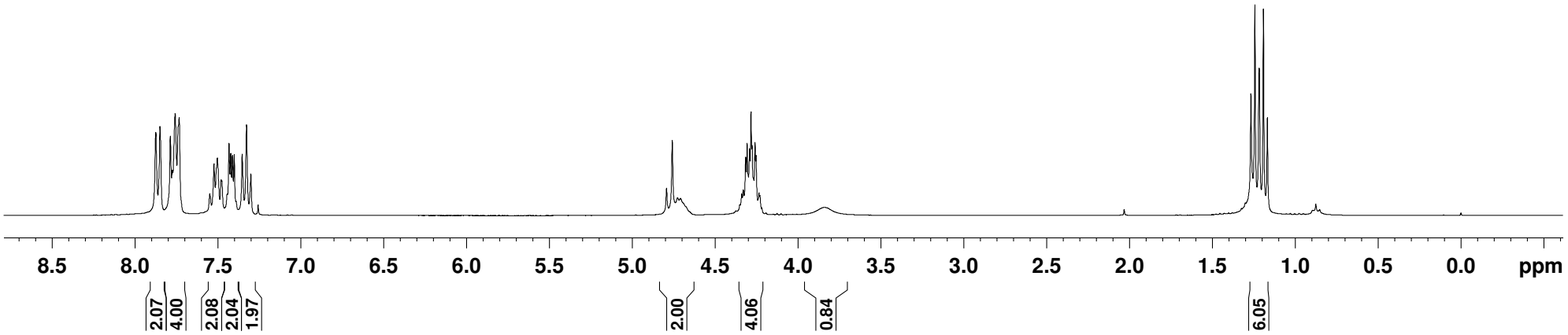
^{19}F NMR (282 MHz, $CDCl_3$)

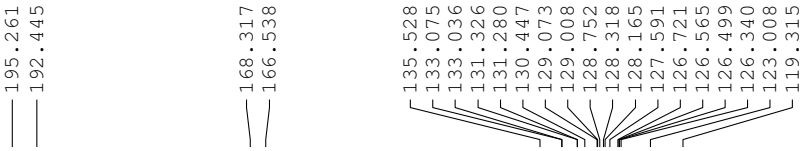


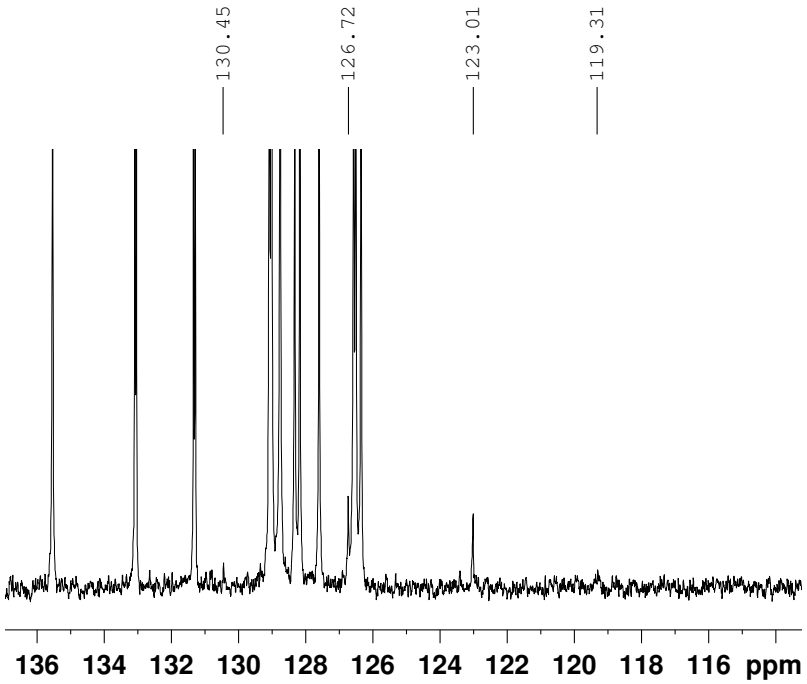


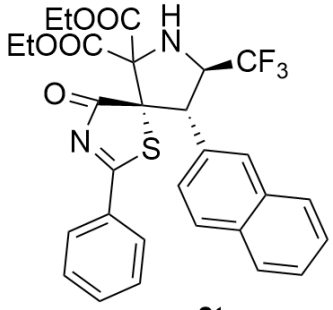
3t

^{1}H NMR (300 MHz, $CDCl_3$)



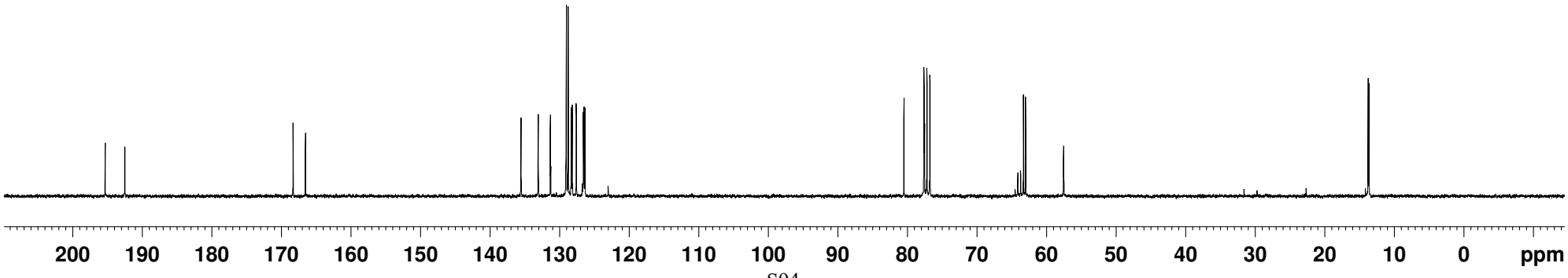


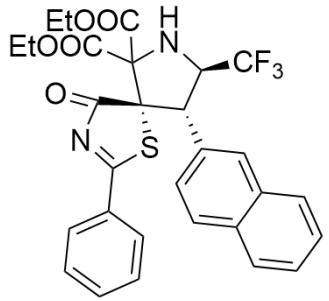




3t

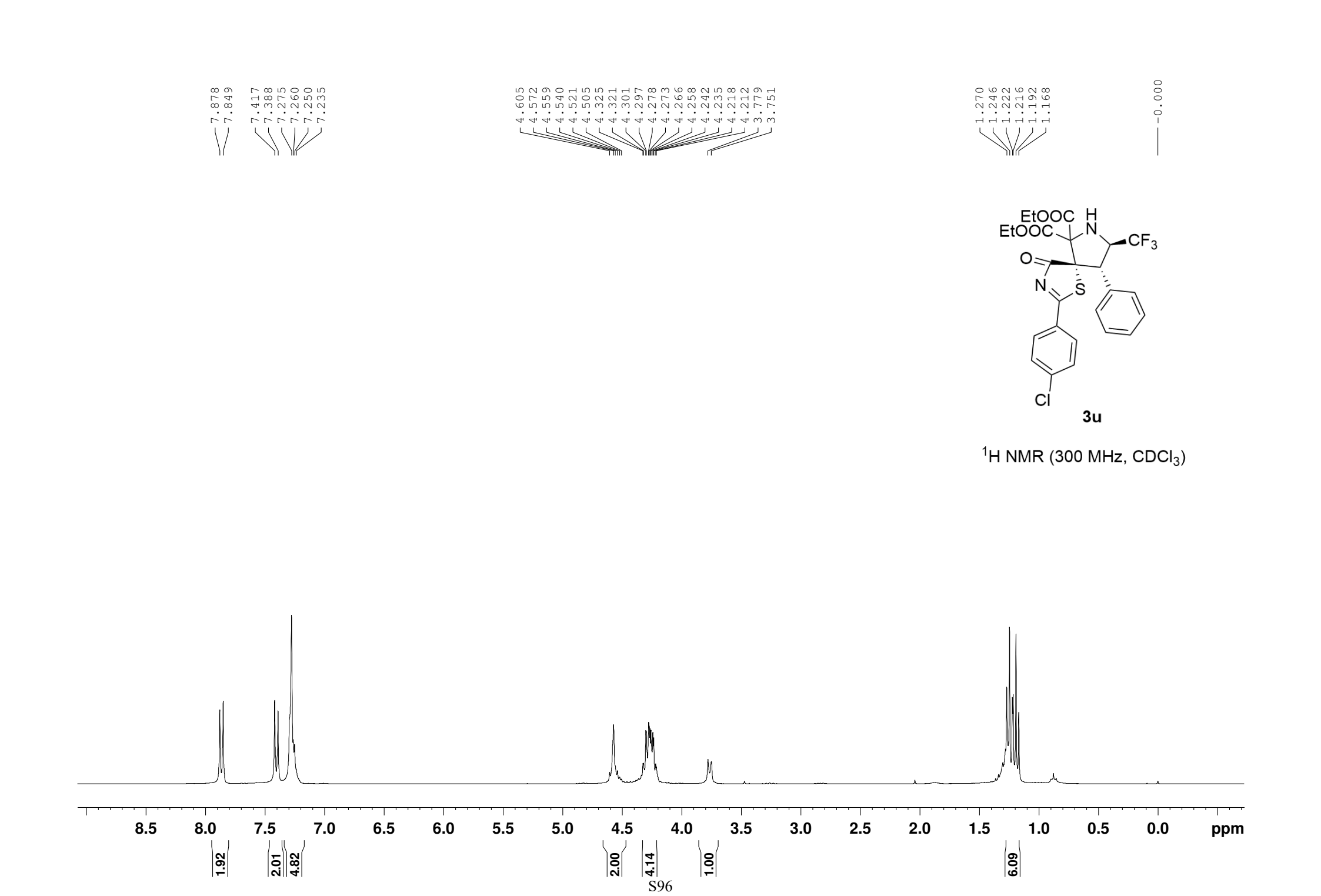
^{13}C NMR (75 MHz, $CDCl_3$)

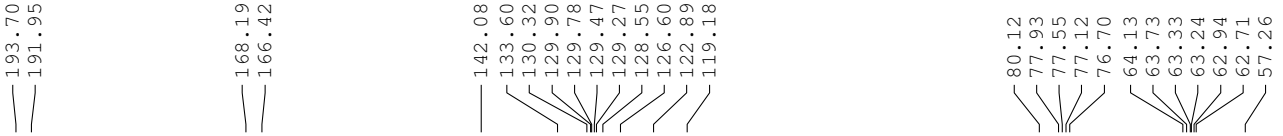


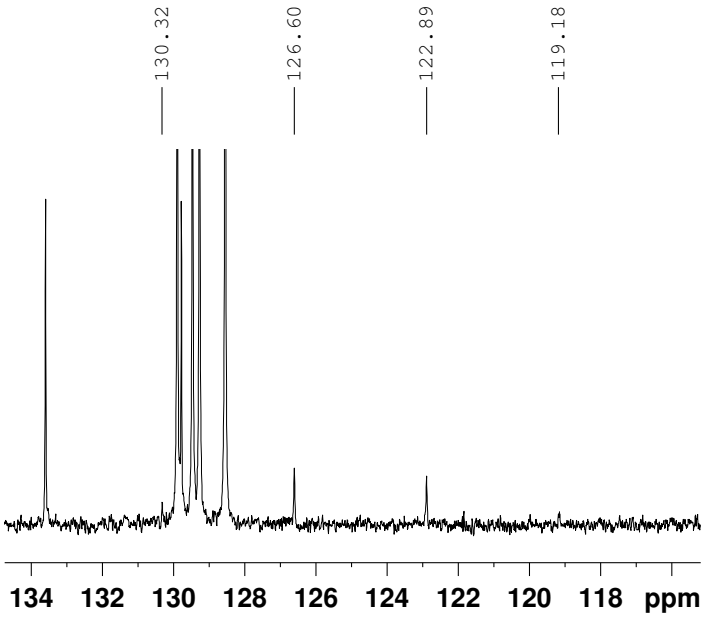


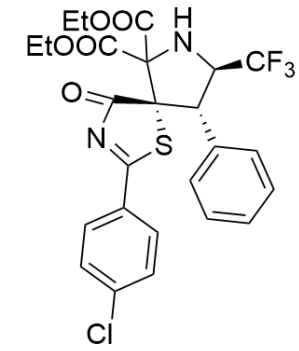
3t

^{19}F NMR (282 MHz, $CDCl_3$)


7.878
7.849
7.417
7.388
7.275
7.260
7.250
7.235
4.605
4.572
4.559
4.540
4.521
4.505
4.325
4.321
4.301
4.297
4.278
4.273
4.266
4.258
4.242
4.235
4.218
4.212
3.779
3.751
1.270
1.246
1.222
1.216
1.192
1.168
0.000
EtOOC
EtOOC
H
N
CF3
O
N
S
Cl
3u
1H NMR (300 MHz, CDCl3)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.92
2.01
4.82
2.00
4.14
1.00
6.09

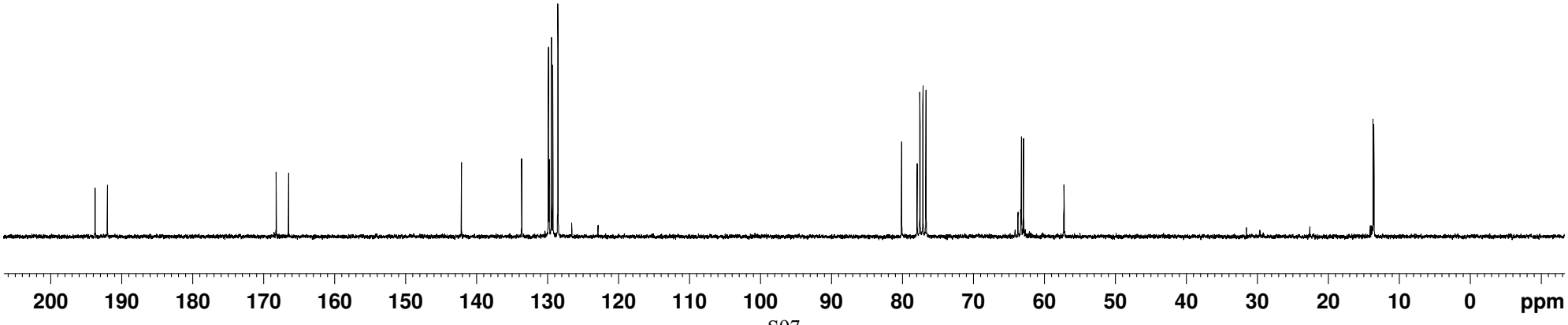


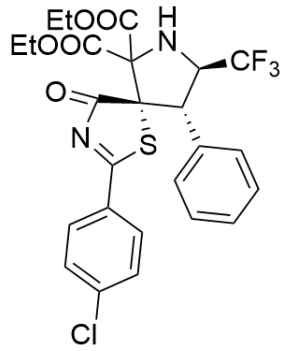




3u

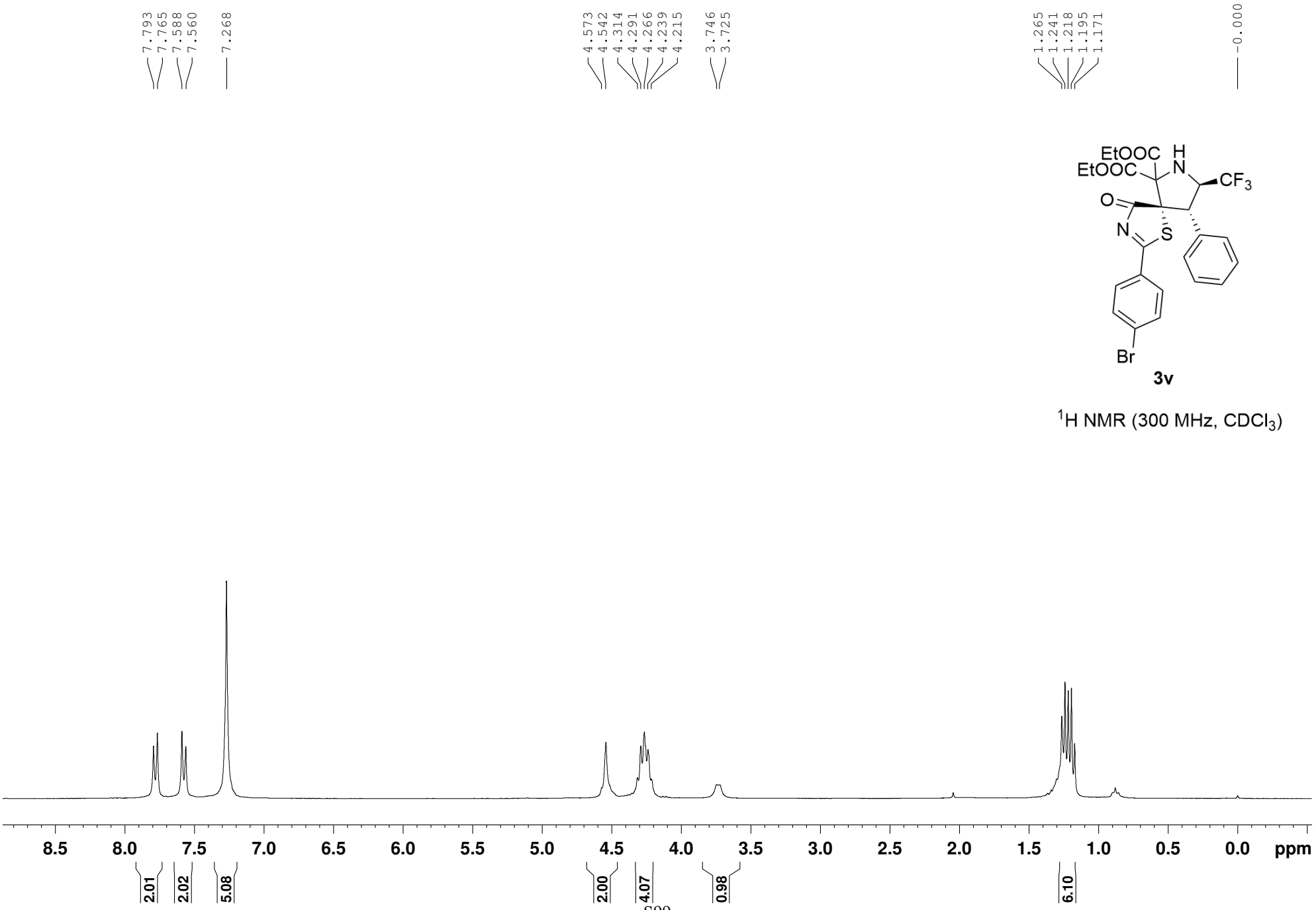
^{13}C NMR (75 MHz, $CDCl_3$)

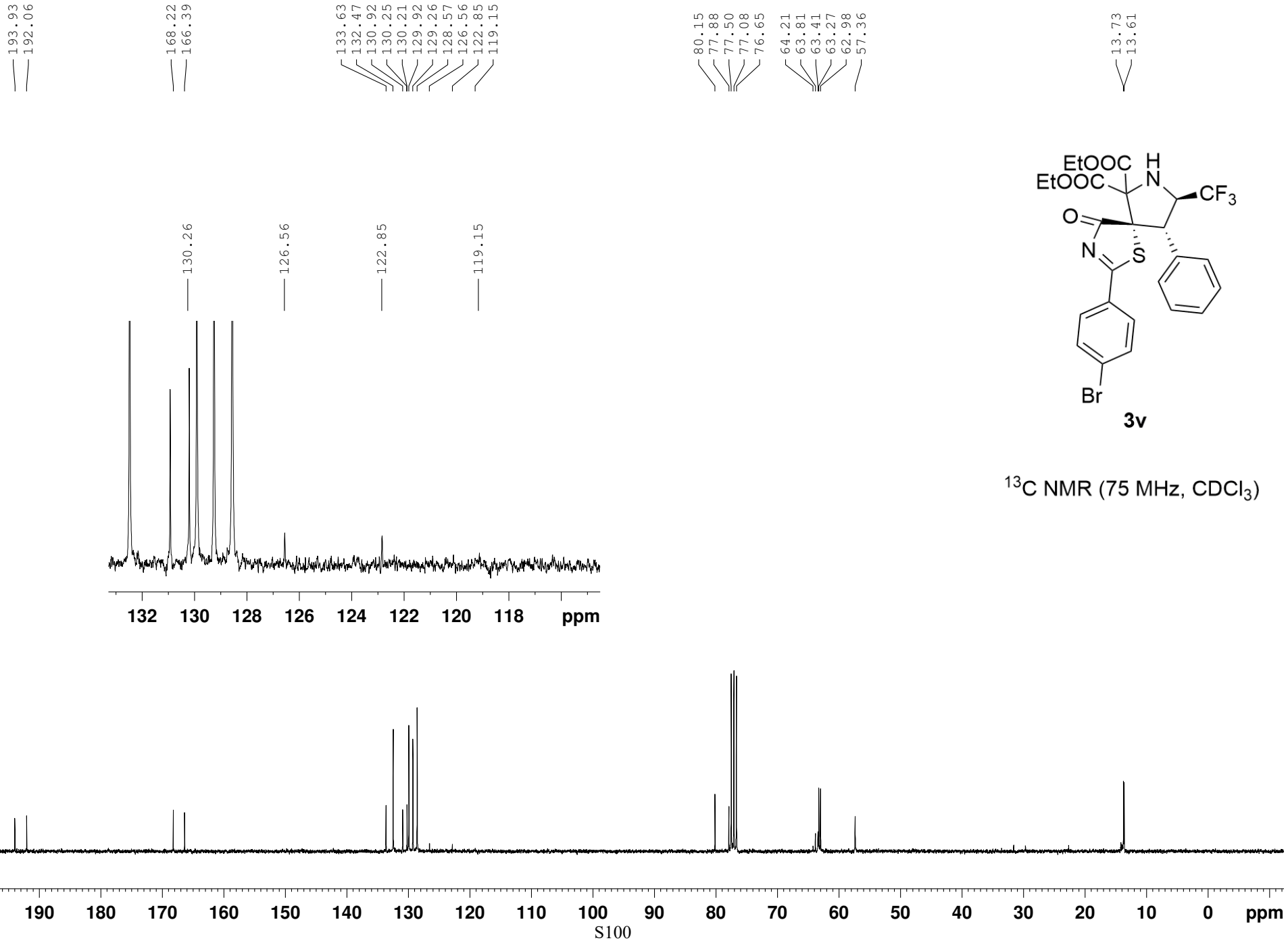




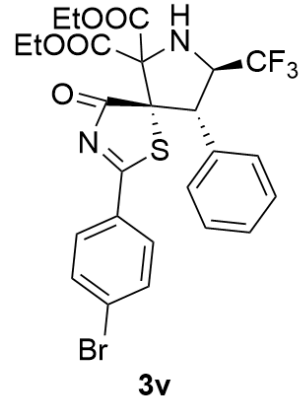
3u

^{19}F NMR (282 MHz, $CDCl_3$)


7.793
7.765
7.588
7.560
7.268
4.573
4.542
4.314
4.291
4.266
4.239
4.215
3.746
3.725
1.265
1.241
1.218
1.195
1.171
0.000
EtOOC
EtOOC
H
N
CF3
O
N
S
Br
3v
1H NMR (300 MHz, CDCl3)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.01
2.02
5.08
2.00
4.07
0.98
6.10

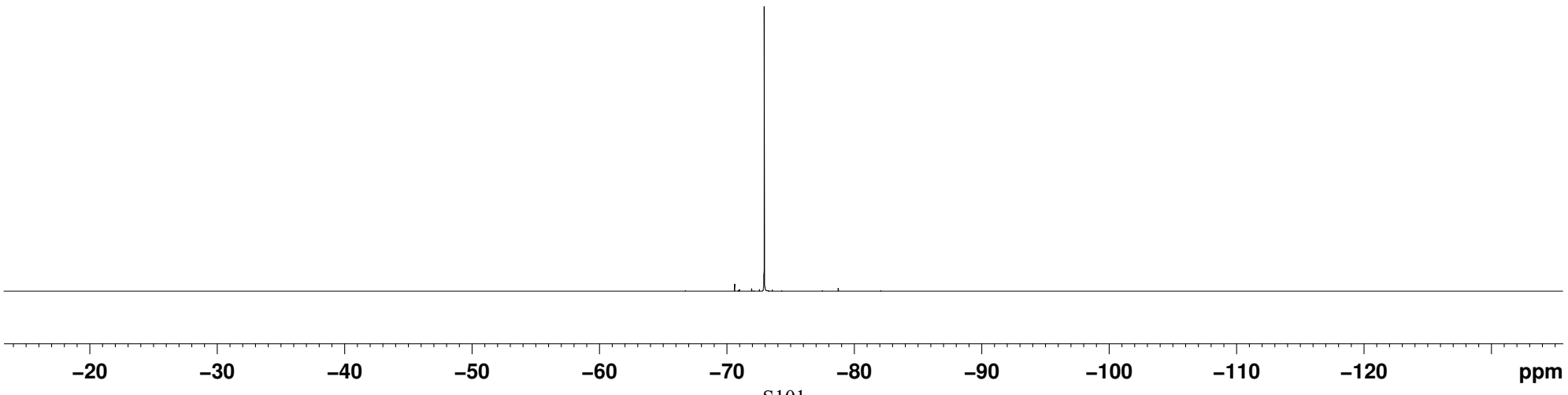


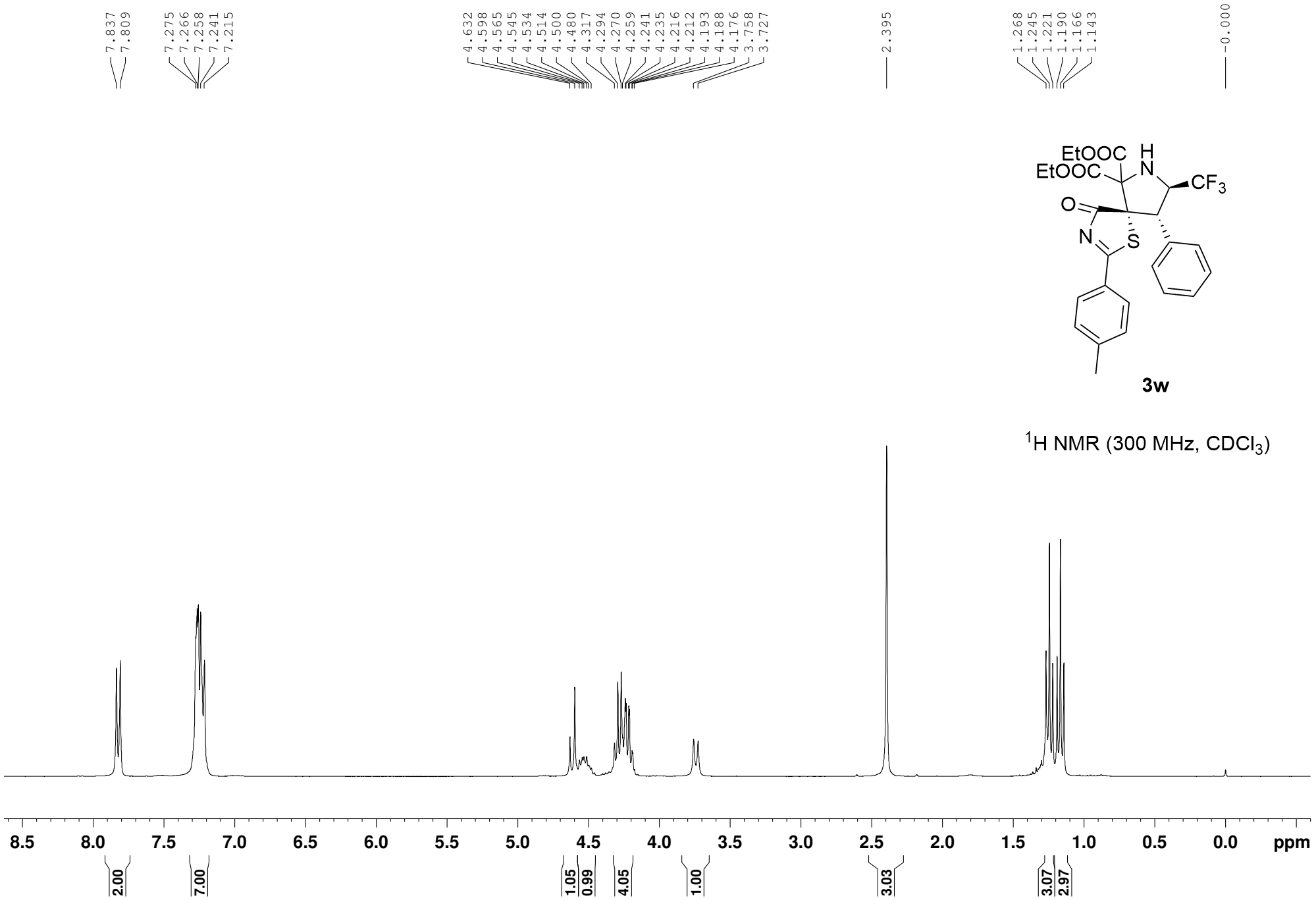
^{13}C NMR (75 MHz, $CDCl_3$)

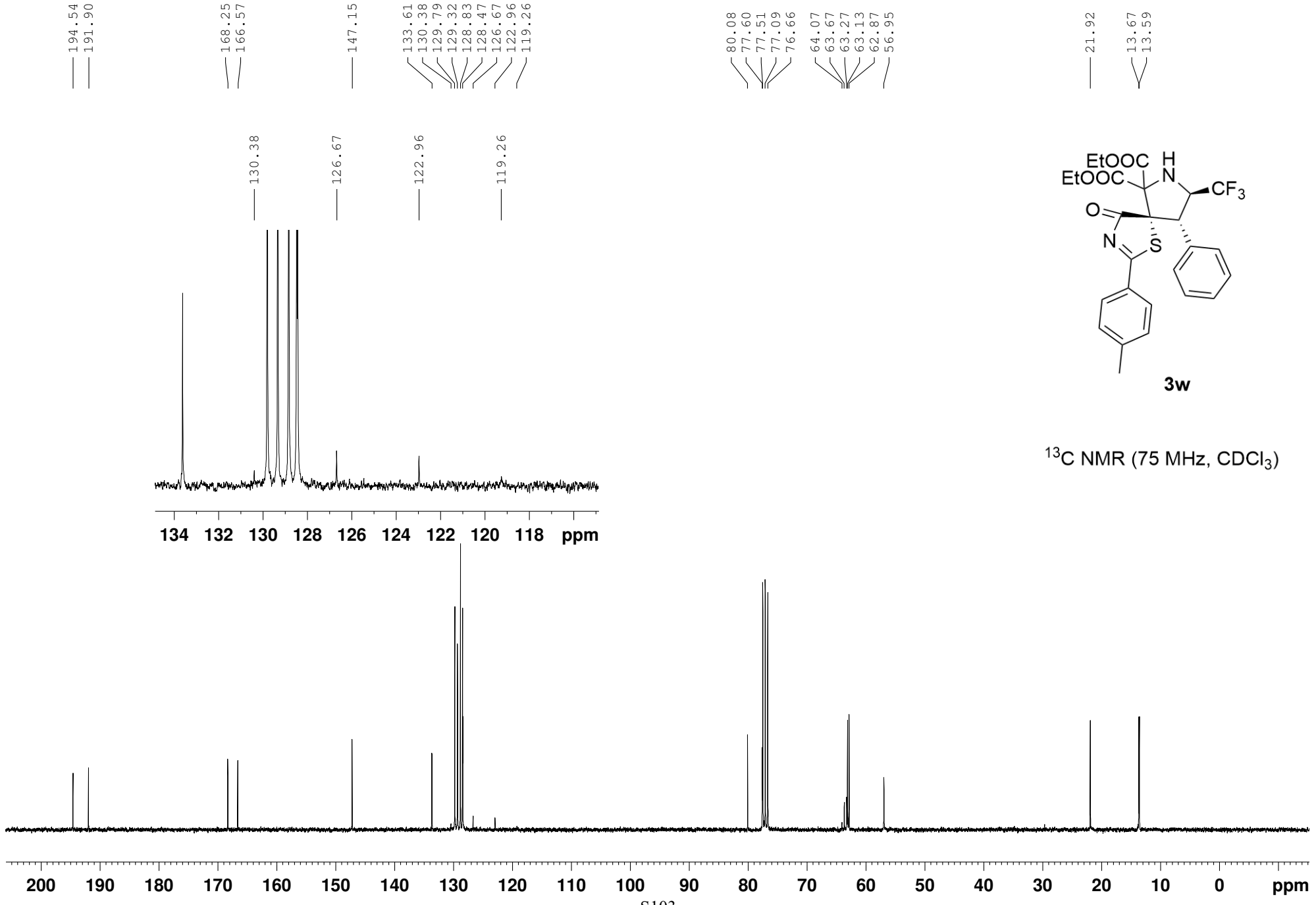


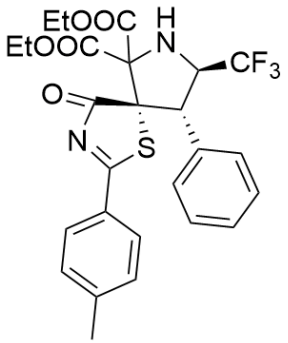
3v

^{19}F NMR (282 MHz, $CDCl_3$)



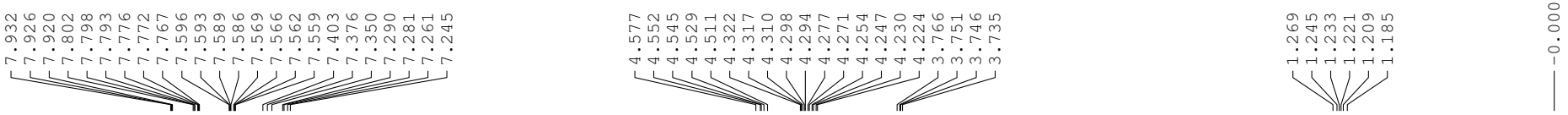

7.837
7.809
7.275
7.266
7.258
7.241
7.215
4.632
4.598
4.565
4.545
4.534
4.514
4.500
4.480
4.317
4.294
4.270
4.259
4.241
4.235
4.216
4.212
4.193
4.188
4.176
3.758
3.727
2.395
1.268
1.245
1.221
1.190
1.166
1.143
-0.000
EtOOC
EtOOC
H
N
CF3
O
N
S
3w
1H NMR (300 MHz, CDCl3)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.00
7.00
1.05
0.99
4.05
1.00
3.03
3.07
2.97

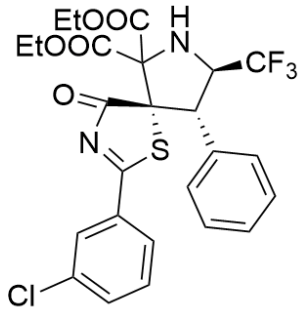

194.54
191.90
168.25
166.57
147.15
133.61
130.38
129.79
129.32
128.83
128.47
126.67
122.96
119.26
80.08
77.60
77.51
77.09
76.66
64.07
63.67
63.27
63.13
62.87
56.95
21.92
13.67
13.59
EtOOC
EtOOC
H
N
CF3
O
N
S
3w
13C NMR (75 MHz, CDCl3)
134 132 130 128 126 124 122 120 118 ppm
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



3w

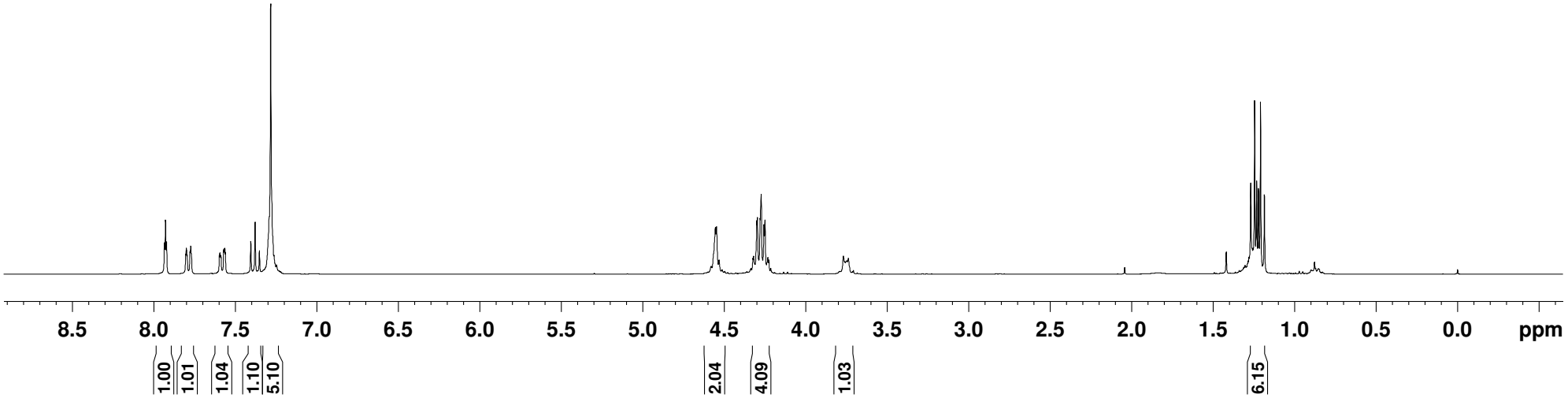
^{19}F NMR (282 MHz, $CDCl_3$)

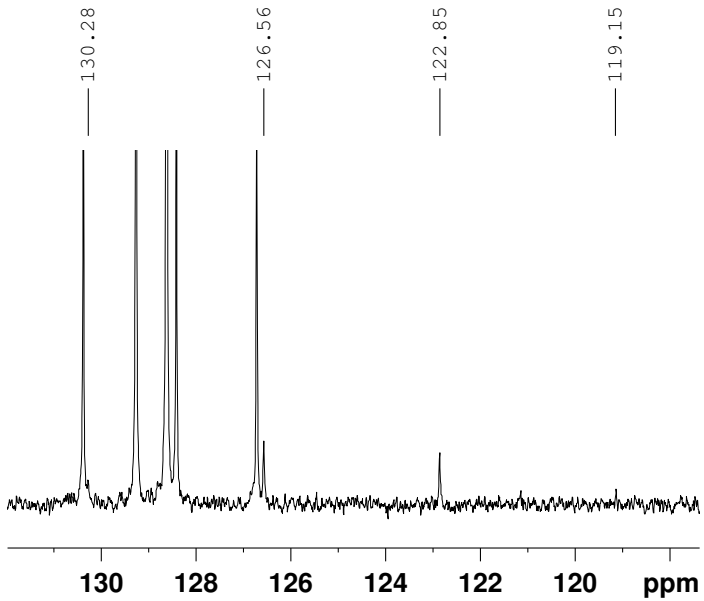


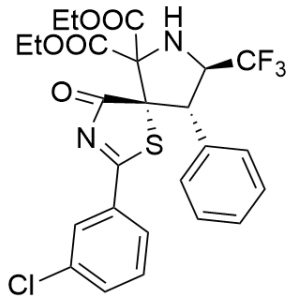


3x

^{1}H NMR (300 MHz, $CDCl_3$)

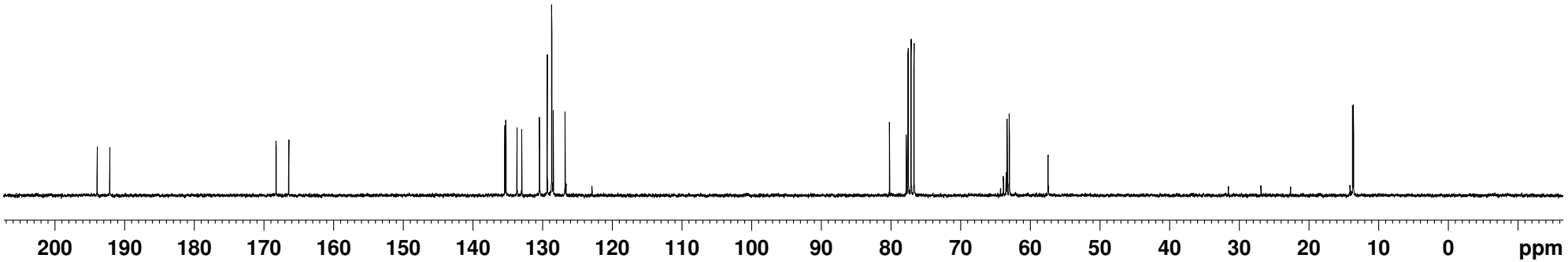


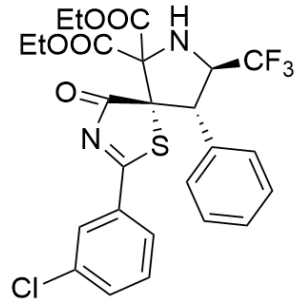




3x

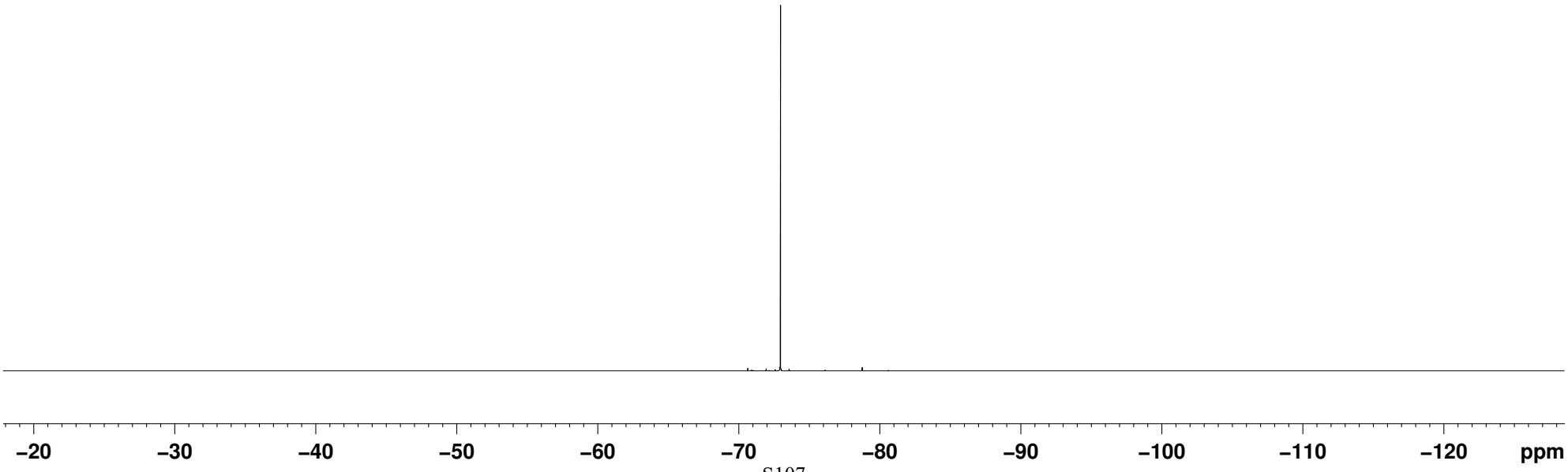
^{13}C NMR (75 MHz, $CDCl_3$)

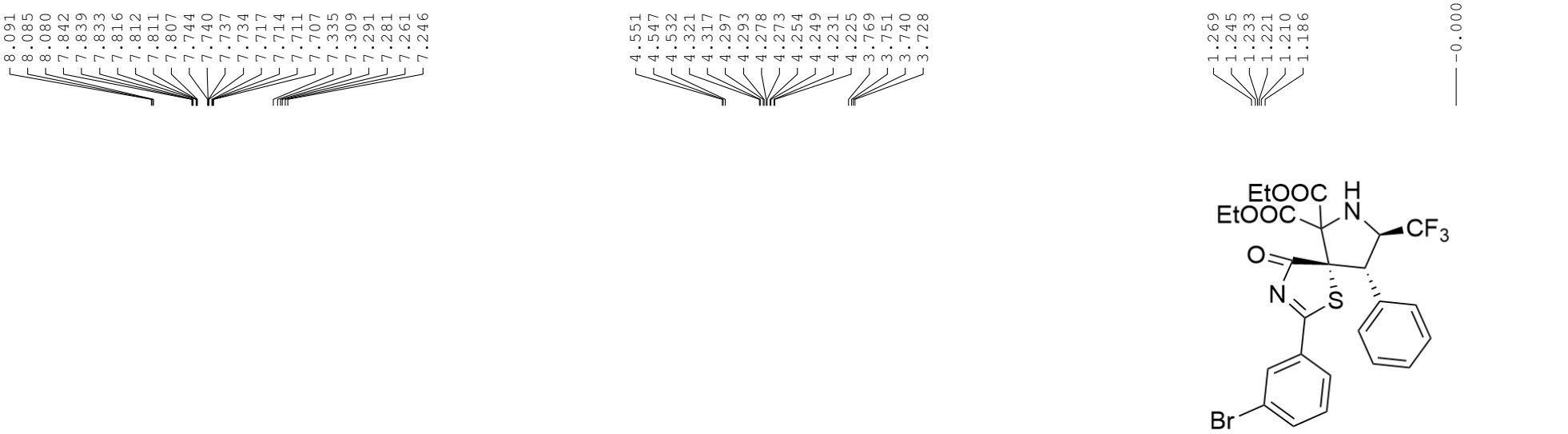




3x

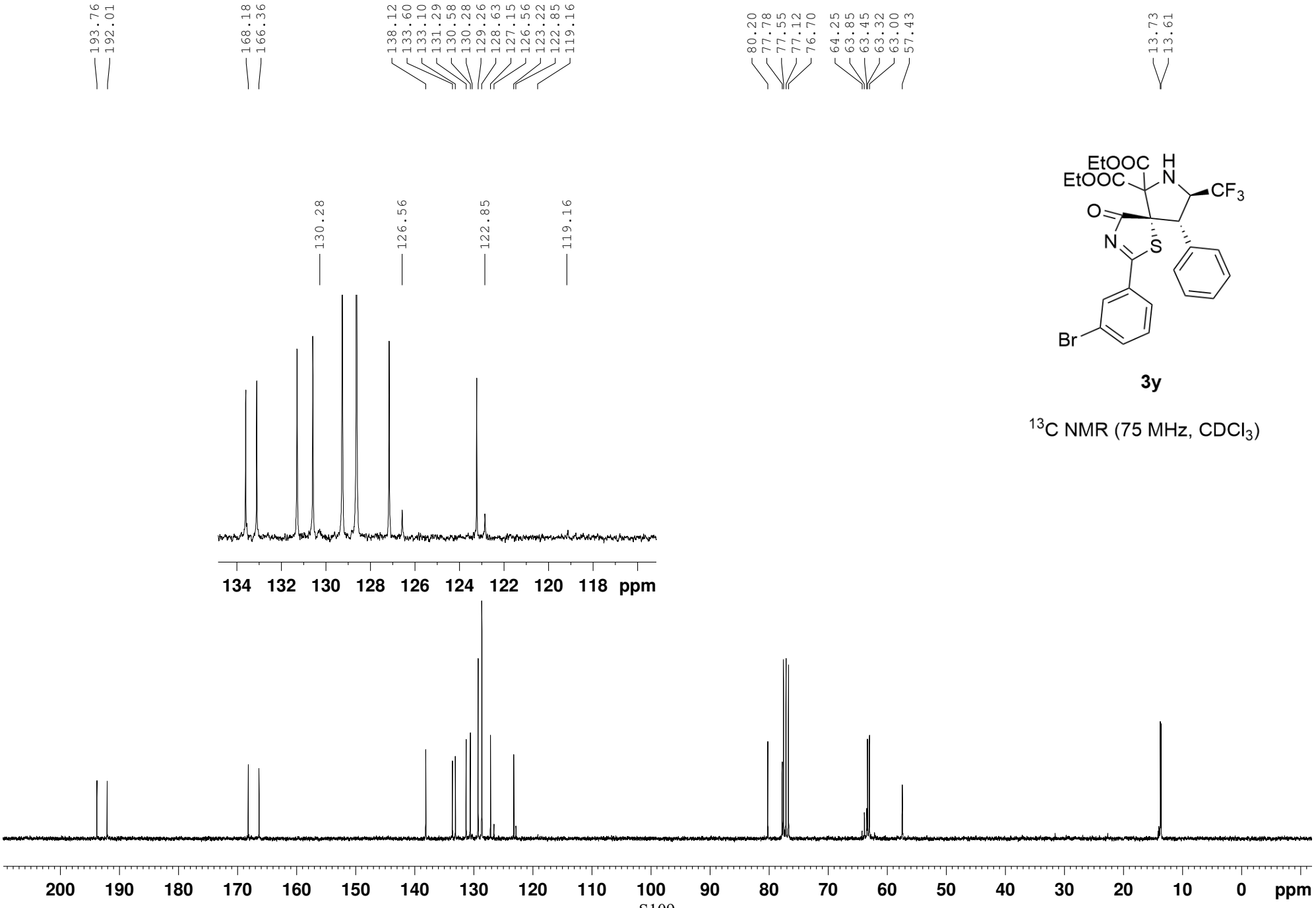
^{19}F NMR (282 MHz, $CDCl_3$)

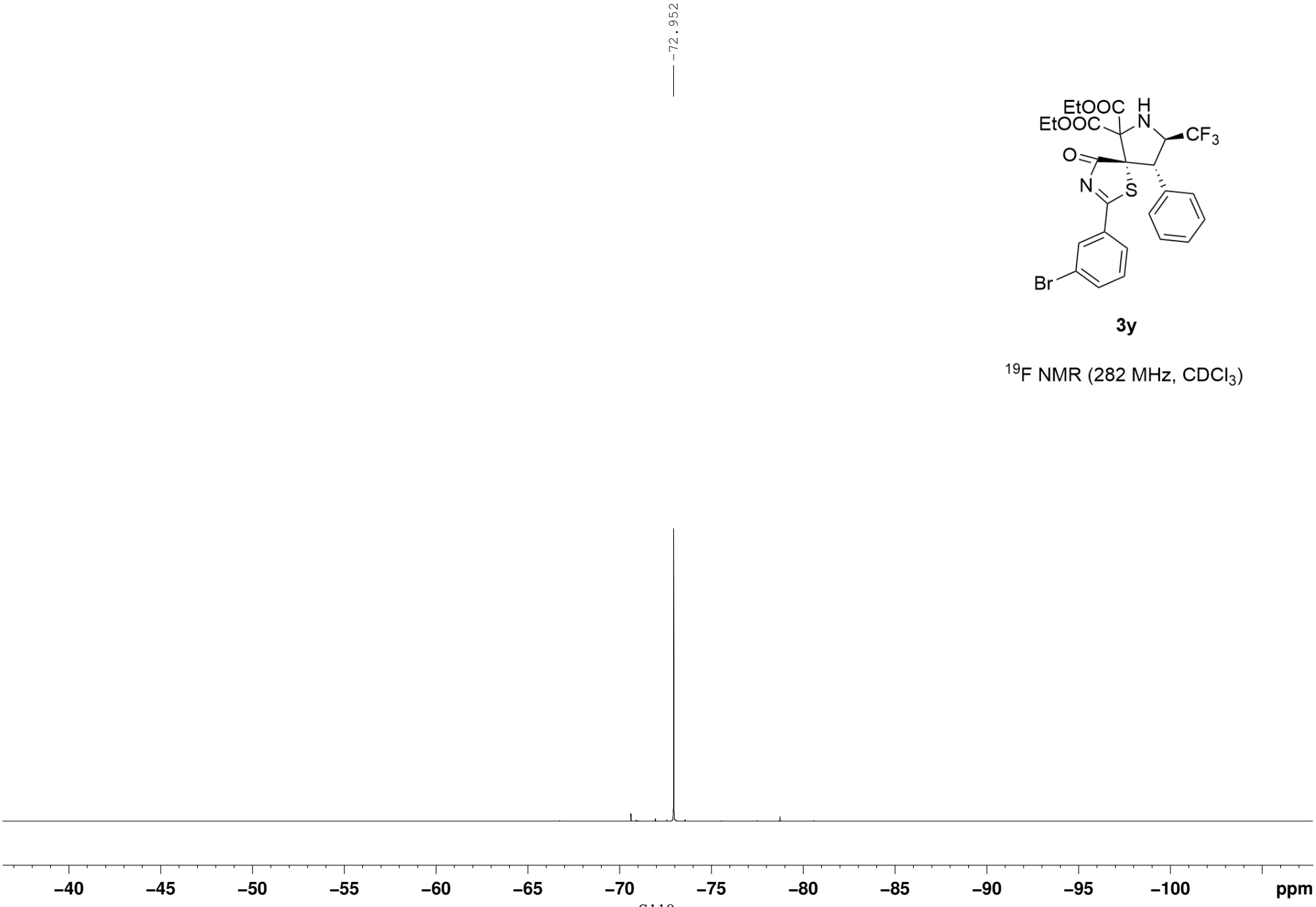




3y

^{1}H NMR (300 MHz, $CDCl_3$)


193.76
192.01
168.18
166.36
138.12
133.60
133.10
131.29
130.58
130.28
129.26
128.63
127.15
126.56
123.22
122.85
119.16
80.20
77.78
77.55
77.12
76.70
64.25
63.85
63.45
63.32
63.00
57.43
13.73
13.61
EtOOC
EtOOC
H
N
CF3
O
N
S
Br
3y
13C NMR (75 MHz, CDCl3)
134 132 130 128 126 124 122 120 118 ppm
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



3y

^{19}F NMR (282 MHz, $CDCl_3$)