Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Enantioselective synthesis of α-perfluoroalkylated prolines, their 6,7-membered homologues and derivatives

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Contents

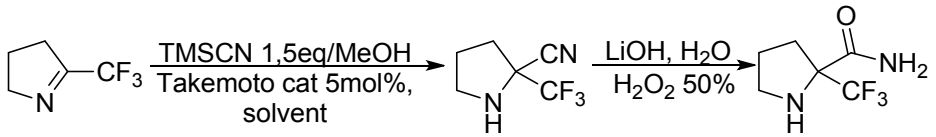
General method

^{1}D NMR (^{1}H, ^{19}F, and ^{13}C) spectra were obtained with Bruker AV-400, and Agilent 400-MR spectrometers. Chemical shifts for 1H NMR spectroscopic data were referenced to internal tetramethylsilane (δ = 0.0 ppm); chemical shifts for ^{13}C NMR spectroscopic data were referenced to $CDCl_3$ (δ = 77.0 ppm); chemical shifts for ^{19}F NMR spectroscopic data were referenced to $PhCF_3$ (δ = –63.90 ppm). Enantiomeric excess (*ee*) were determined by HPLC («Stayer» by Akvilon). TLC was carried out on precoated silica plates (Silufol UV-254), which were visualized with UV light and/or staining with ninhydrine solution or aqueous $Ce(SO_4)_2$ solution with phosphomolybdic and sulfuric acids. Flash chromatography was carried out using MP Silica 60 (320–630 mesh) with the solvents indicated. Starting cyclic imines were synthesized according to the following procedure[1]. 1-(3,5-Bis(trifluoromethyl)phenyl)-3-((1R,2R)-(-)-2-9dimethylamino)cyclohexyl)thiourea (Takemoto catalyst) was purchased from abcr.

Reaction optimization

The model reactions in several protic (i-PrOH, MeOH), polar aprotic (CH_2Cl_2, $C_2H_4Cl_2$, Et_2O, DMF, DMSO, CH_3CN, THF) and nonpolar (benzene, xylene, toluene, hexane) solvents were investigated. It was found out that the reaction in protic solvents resulted in racemic **3a** and proceeded more rapidly (4 days for *i*-PrOH and 1 day for MeOH). Low conversion (10-12% accordingly ^{19}F NMR monitoring) after two months was observed in DMF, DMSO, THF and Et_2O. Others solvents (CH_2Cl_2, $C_2H_4Cl_2$, CH_3CN, benzene, xylene, toluene, hexane) demonstrated up to 99% ee, however the reaction in $C_2H_4Cl_2$ proceeded in reasonable time (4 days) to give after hydrolysis of **2a** amide **3**a in the highest yield (88%).

Table 1. Solvent optimization

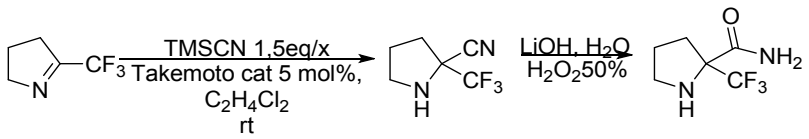


Solvent	1st step time	1st step yield	2st step	$[\alpha]_D^{20}$	*ee*, %

	reaction, days	(^{19}F NMR spectra), %	yield, %		
i-PrOH	5	98	81	0	0
MeOH	1	100	82	0	0
Benzene	18	97	68	-81.0	>99
Xylene	12	95	86	-81.4	>99
Toluene	6	95	74	-69.0	95
Hexene	10	95	87	-81.2	>99
$C_2H_4Cl_2$	4	98	88	-82.2	>99
CH_2Cl_2	7	94	82	-50.6	-
$CHCl_3$	6	97	68	-81.2	>99
CH_3CN	48	92	69	-50.8	-
Et_2O	8	4	-	-	-
THF	4	4	-	-	-
DMF	5	7	-	-	-
DMSO	30	80	-	-	-

Also to finding an optimal reaction condition different addictive ($CF_3CH(OH)CF_3$, CF_3CH_2OH, *i*-PrOH) for producing HCN were investigated. However use of addictive other than methanol lead to decrease of reaction enantioselectivity.

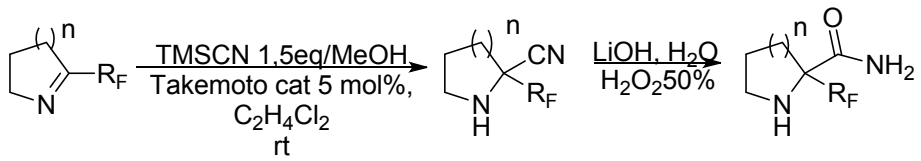
Table 2. Additives optimization



x	1st step time reaction, days	1st step yield (^{19}F NMR spectra),	2st step yield, %	*ee*, %
-	14	16	-	-
MeOH	6	100	85	>99
$CF_3CH(OH)CF_3$	6	98	71	84
CF_3CH_2OH	6	96	68	86
i-PrOH	9	95	57	82

After finding the optimal conditions for obtaining pure enantiomer 2-trifluoromethyl-pyrrolidyne carboxyamide (**3a**) (99% *ee*) those were applied for others imines **b-e**. The reaction was very sensitive to the ring size and substituent at α-position of starting imine. Pentafluoroethyl-substituted imines (**1b, 1d**) reacted very slowly (about two months) with low enantioselectivity (42 % *ee* for **1b** and 11% *ee* for **1d**). The most difficult situation was observed in the case of 6-membered imine **1d** bearing pentafluoroethyl group. We believe that these results can be explained by much higher steric bulkiness of C_2F_5 group over CF_3 moiety as well as significant difference in geometry of starting imines. In cases of hydrocyanation of trifluoromethylated imines **1c** and **1e** reasonably high enantioselectivity was achieved - 79 and 80% *ee* correspondingly.

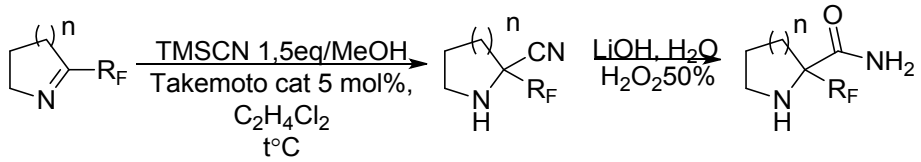
Table 3. Influence of substituent and ring size on reaction enantioselectivity



n	R	1st step time reaction, days	1st step yield (^{19}F NMR spectra)	2st step yield, %	*ee*, %
1	CF_3	4	100	88	>99
1	C_2F_5	10	74	64	42
2	CF_3	12	92	67	79
2	C_2F_5	24	92	78	11
3	CF_3	18	100	87	80

To improve enantioselectivity of the reaction with imines **1c** and **1e** hydrocyanation under decreased temperature was studied. . Imines with pentafluoroethyl substituents (**1b, 1d**) were not used for temperature optimization due to long reaction time. The enantiomeric excess for amide **3c** obtained from imine **1c** reached 90% *ee* at -20°C. In the case of amide **3e** the improvement of enantioselectivity was lower than expected (from 80% *ee* to 83% *ee* at 0°C and 81% *ee* at -20°C).

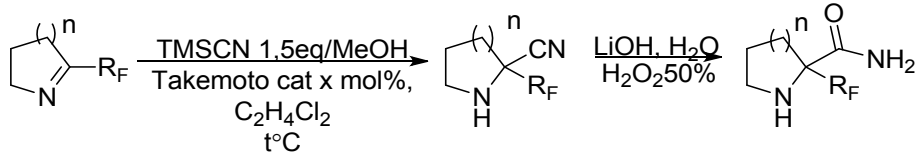
Table 4. Temperature optimization for imines **1c** and **1e**



n	R_F	t°C	1st step time reaction, days	1st step yield (^{19}F NMR spectra)	2st step yield, %	*ee*, %
2	CF_3	0	13	70	65	81
		-20	9	96	93	90
3	CF_3	0	4	100	90	80
		-20	4	95	85	83

Increasing the amount of Takemoto catalyst (15 mol %) resolved this problem and enantioselectivity of Strecker reaction was improved significantly to provide 95-96% ee for both imines **1c** and **1e**. Using 20% of catalyst the reaction with **1b** also gave appropriate 90% *ee* for amide **3b** in 85% isolated yield (**Table 5).**

Table 5. Optimal condition for enantioselective Strecker reaction with cyclic imines **1a-e**



Imine	n	R_f	Cat, mol%	T, °C	1st step reac-tion time, days	Yield of **3**, (%)	*ee*, %
1a	1	CF_3	5	rt	4	82	99
1b	1	C_2F_5	20	rt	90	85	90
1c	2	CF_3	15	-20	6	97	96
1d	2	C_2F_5	5	rt	90	89	11
1e	3	CF_3	15	0	6	98	95

Synthesis

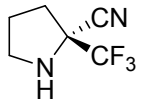
Procedure for synthesis of cyclic nitriles **2a-e**

A. For racemic products

In a screw-capped vial cyclic imine (1mmol) and TMSCN (1.5 mmol, 0.215mL) was added. Reaction mixture was dissolved by MeOH (about 5mL) as solvent and stay for a night. After reaction complete, the solvent was carefully removed under vacuum (volatile product) and crude products were let into the next transformation without purification.

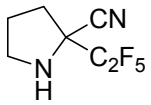
B. For asymmetric products

In a screw-capped vial cyclic imine (1mmol) was dissolved in dichloroethane (2mL). To the solution cat Takemoto (0.05mmol for 1a, 0.15 mmol for 1c,e, 0.2mmol for 1b), TMSCN (1.5 mmol, 0.215mL), MeOH (1.5 mmol, 0.05mL) were added. Reaction was monitoring by ^{19}F spectra. After reaction complete, the solvent was carefully removed under vacuum (volatile product) and the residue was purified by silica gel chromatography (CH_2Cl_2).



(R)-2-(trifluoromethyl)pyrrolidine-2-carbonitrile **(2a)**, According to NMR ^{19}F - 100 %, after evaporation – 97%, colorless volatile liquid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.87-2.04 (2H, m), 2.24-2.36 (2H, m), 2.53 (1H, bs, NH), 3.13-3.16 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.0, 33.0 (**C**H_2-C_q), 46.3 (CH_2-N), 62.1 (q, J_{CF} = 33.1 Hz, **C**-CF_3), 117.7 (CN), 123.3 (q, J_{CF} = 281.2 Hz, CF_3). ^{19}F NMR (280 MHz, $CDCl_3$): δ -79.1 (3F, s, CF_3). IR(KBr): 3465 (bs), 3273 (bs), 1309, 1189, 1057, 953 cm^{-1}. HRMS (ESI): calcd. for $C_6H_8F_3N_2$ $[M+H]^+$ 165.0640, found 165.0636.

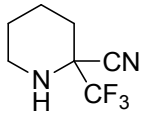
Optical rotation $[\alpha]^{20}_D$ = +12.0 (c = 0.5, MeOH).



2-(Pentafluoroethyl)pyrrolidine-2-carbonitrile **(2b)**, According to NMR ^{19}F - 100 %, after evaporation – 99%, , colorless volatile liquid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.98-2.10 (2H, m), 2.26 (1H, bs, NH), 2.36-2.45 (2H, m, CH_2), 3.24-3.27 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.9, 33.4 (**C**H_2-C_q), 46.3 (CH_2-N), 61.7 (t, J_{CF} = 26.5 Hz, **C**-CF_2), 112.2 (tq, J_{CF} = 260.6 Hz, J_{CF} = 36.1 Hz, CF_2),

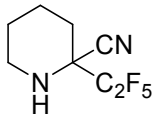
117.7 (CN), 118.9 (qt, J_{CF} = 287.9 Hz, J_{CF} = 35.8 Hz, CF_3). ^{19}F NMR (280 MHz, $CDCl_3$): δ -79.1 (3F, s, CF_3), -119.8 (1F, d, J_{FF} = 271.3 Hz, CF_2), -123.8 (1F, d, J_{FF} = 271.3 Hz, CF_2). IR(KBr): 3361 (bs), 2237, 1346, 1209, 1169, 1111, 1049, 742 cm^{-1}. HRMS (ESI): calcd. for $C_7H_8F_5N_2$ $[M+H]^+$ 215.0608, found 215.0606.

Optical rotation $[\alpha]^{20}_D$ = +7.6 (c = 0.5, MeOH).

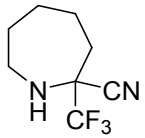


2-(trifluoromethyl)piperidine-2-carbonitrile **(2c)**, According to NMR ^{19}F - 100 %, after evaporation –73 %, colorless volatile liquid, ^1H NMR (400 MHz, $CDCl_3$): δ 1.47-1.54 (1H, m), 1.64-1.82 (3H, m), 1.89-1.91 (1H, m), 2.00-2.03 (1H, m), 2.15 (1H, bs, NH), 2.92-2.97 (1H, m, N-**C**$\mathbf{H_2}$), 3.12-3.14 (1H, m, N-**C**$\mathbf{H_2}$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.1, 23.8, 28.3 (**C**H_2-C_q), 42.6 (CH_2-N), 60.7 (q, J_{CF} = 30.2 Hz, **C**-CF_3), 115.3 (CN), 122.8 (q, J_{CF} = 282.0 Hz, CF_3). ^{19}F NMR (280 MHz, $CDCl_3$): δ -80.2 (3F, s, CF_3). IR(KBr): 3334 (bs), 1311, 1203, 1194, 1176, 1128 cm^{-1}. HRMS (ESI): calcd. for $C_7H_9F_3N_2$ $[M+H]^+$ 179.0796, found 179.0801.

Optical rotation $[\alpha]^{20}_D$ = +40.8 (c = 0.5, CH_2Cl_2).



2-(Perfluoroethyl)piperidine-2-carbonitrile **(2d)**, According to NMR ^{19}F - 100 %, after evaporation – 63 %, colorless volatile liquid, ^1H NMR (400 MHz, $CDCl_3$): δ 1.42-1.54 (1H, m), 1.63-1.75 (2H, m), 1.81-1.92 (2H, m), 1.99-2.03 (1H, m), 2.10 (1H, bs, NH), 2.93-2.99 (1H, m, N-**C**$\mathbf{H_2}$), 3.11-3.14 (1H, m, N-**C**$\mathbf{H_2}$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.3, 23.8, 28.2 (**C**H_2-C_q), 42.7 (CH_2-N), 61.1 (t, J_{CF} = 23.4 Hz, **C**-CF_2), 112.2 (tq, J_{CF} = 262.1 Hz, J_{CF} = 36.5 Hz, CF_2), 114.8 (CN), 118.7 (qt, J_{CF} = 287.9 Hz, J_{CF} = 35.4 Hz, CF_3). ^{19}F NMR (280 MHz, $CDCl_3$): δ -78.2 (3F, s, CF_3), -121.9 (1F, d, J_{FF} = 278.3 Hz, CF_2), -122.8 (1F, d, J_{FF} = 278.3 Hz, CF_2). IR(KBr): 3461 (bs), 3257 (bs), 1338, 1310, 1216, 1058 cm^{-1}. HRMS (ESI): calcd. for $C_8H_{10}F_5N_2$ $[M+H]^+$ 229.0764, found 229.0762.

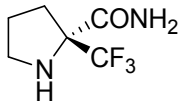


2-(trifluoromethyl)azepane-2-carbonitrile **(2e)**, According to NMR ^{19}F - 100 %, after evaporation –95 %, colorless volatile liquid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.56-1.69 (4H, m), 1.70-1.80 (1H, m), 1.84-1.93 (1H, m), 2.09-2.17 (2H, m), 2.28 (1H, bs, NH), 2.90-3.03 (2H, m, N-**CH_2**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.4, 28.5, 30.6, 32.3 (**C**H_2-C_q), 43.5 (CH_2-N), 62.5 (q, J_{CF} = 28.8 Hz, **C**-CF_3), 117.3 (CN), 123.4 (q, J_{CF} = 284.9 Hz, CF_3). ^{19}F NMR (280 MHz, $CDCl_3$): δ -79.2 (3F, s, CF_3). IR(KBr): 3356 (bs), 1269, 1194, 1180, 1119 cm^{-1}. HRMS (ESI): calcd. for $C_7H_{11}F_3N$ $[M - CN]^+$ 166.0844, found 166.0846.

Optical rotation $[\alpha]^{20}_D$ = +32.1 (c = 1.83, MeOH).

Procedure for synthesis of amides **3a-e**

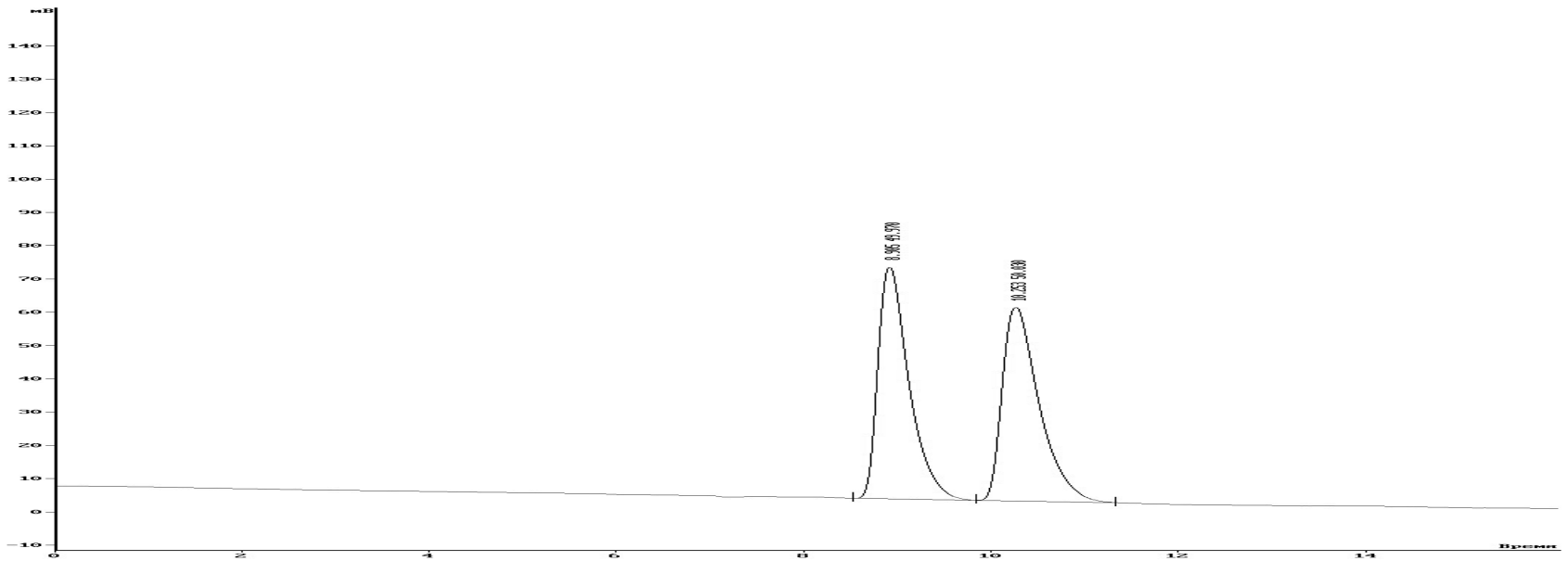
To a solution of aminonitile 2 (1mmol) in MeOH (3mL) LiOH*H_2O (0.21 g, 3.5 mmol), H_2O (1 mL), H_2O_2 30% (0.5 mL) were added and mixture was stirred at rt for 1.5-2 hours. After that, water was added and solution was extracted with EtOAc. Organic lay was dried on Na_2SO_4 and concentrated under reduced pressure to obtain crude amide, which was purified by silica gel chromatography (EtOac/Hex = 2/1).



(R)-2-(trifluoromethyl)pyrrolidine-2-carboxamide **(3a)**, 88 %, 99 % *ee*, white solid, mp 108-110ºC ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.71-1.87 (2H, m), 2.18-2.22 (2H, m), 3.04-3.07 (2H, m), 6.83 (1H, bs, **NH_2**CO), 7.31 (1H, bs, **NH_2**CO). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.3, 32.2 (**C**H_2-C_q), 47.5 (CH_2-N), 70.7 (q, J_{CF} = 26.2 Hz, **C**-CF_3), 125.9 (q, J_{CF} = 283.4 Hz, CF_3), 173.0 ($CONH_2$). ^{19}F NMR (280 MHz, DMSO): δ -74.1 (3F, s, CF_3). IR(KBr): 1703, 1171 cm^{-1}. HRMS (ESI): calcd. for $C_6H_9F_3N_2O$ $[M+H]^+$ 183.0740, found 183.0747.

Optical rotation $[\alpha]^{20}_D$ = -88.2 (c = 0.5, MeOH).

HPLC condition: Chiral column Chiracel OJ (250×4.6 mm), heptane/*i*-PrOH = 9/1, flow rate = 1 mL/min, wavelength = 206 nm. $t_{r\ minor}$ = 8.983 min (0.455), $t_{r\ major}$ = 10.122 min (99.545)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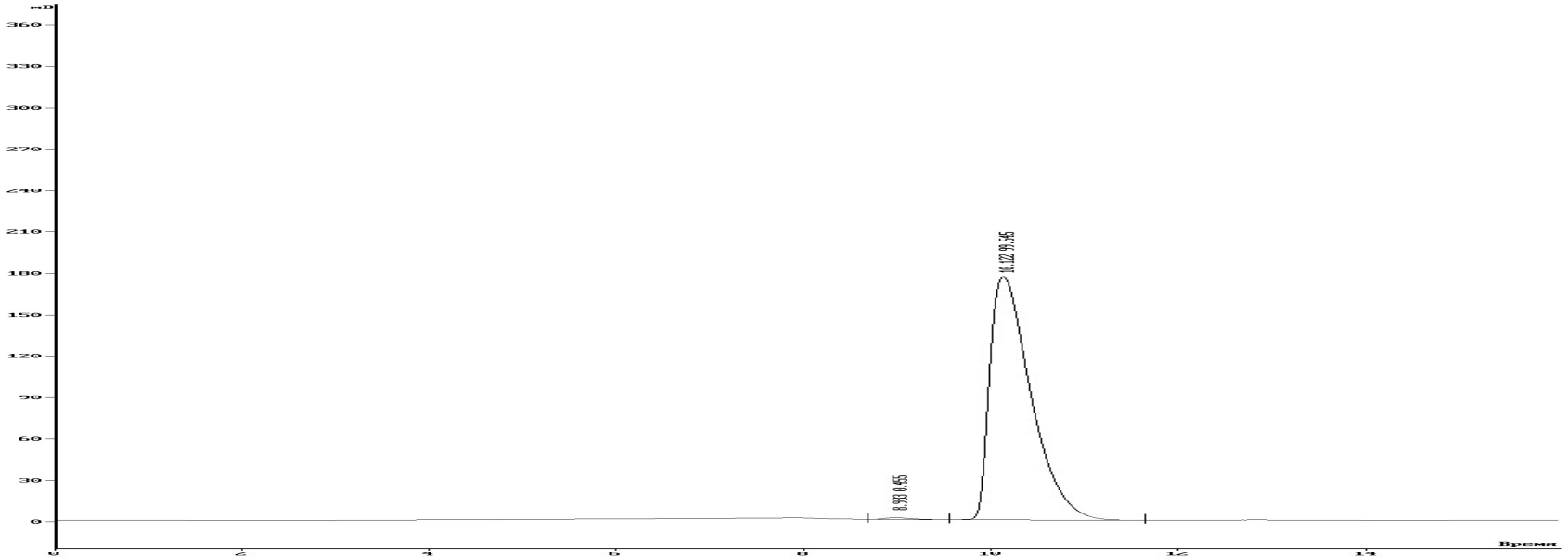
10.253 50.630
Время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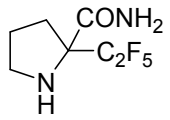
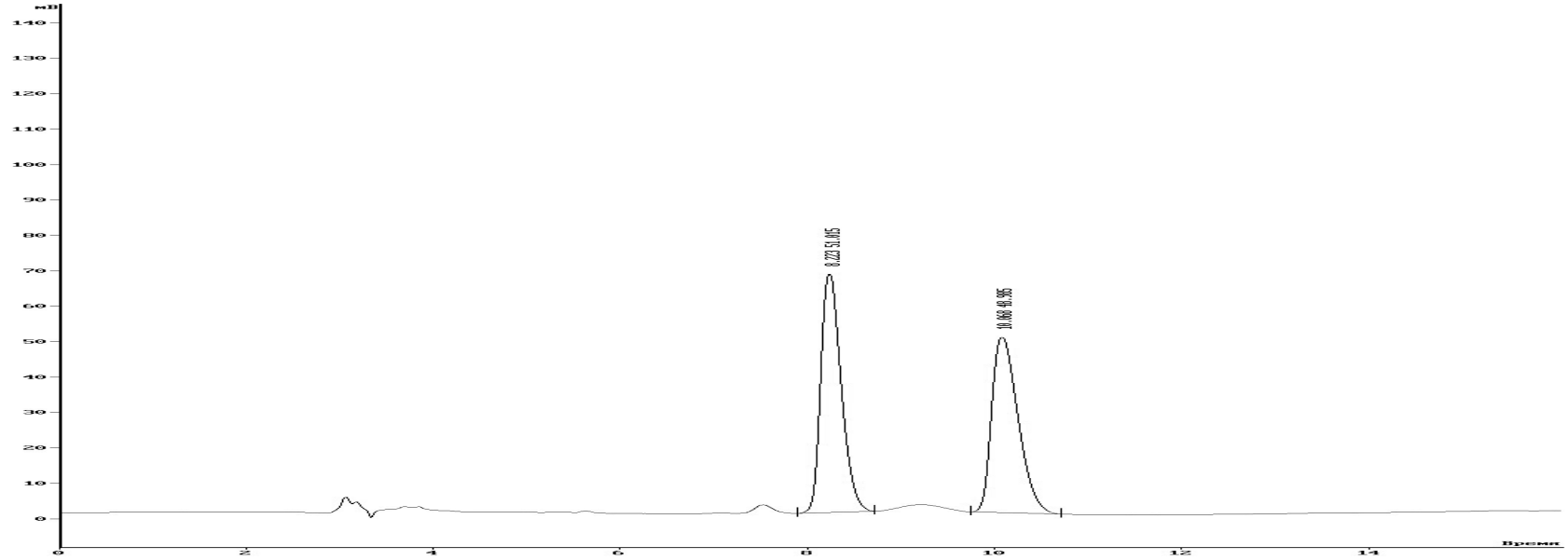


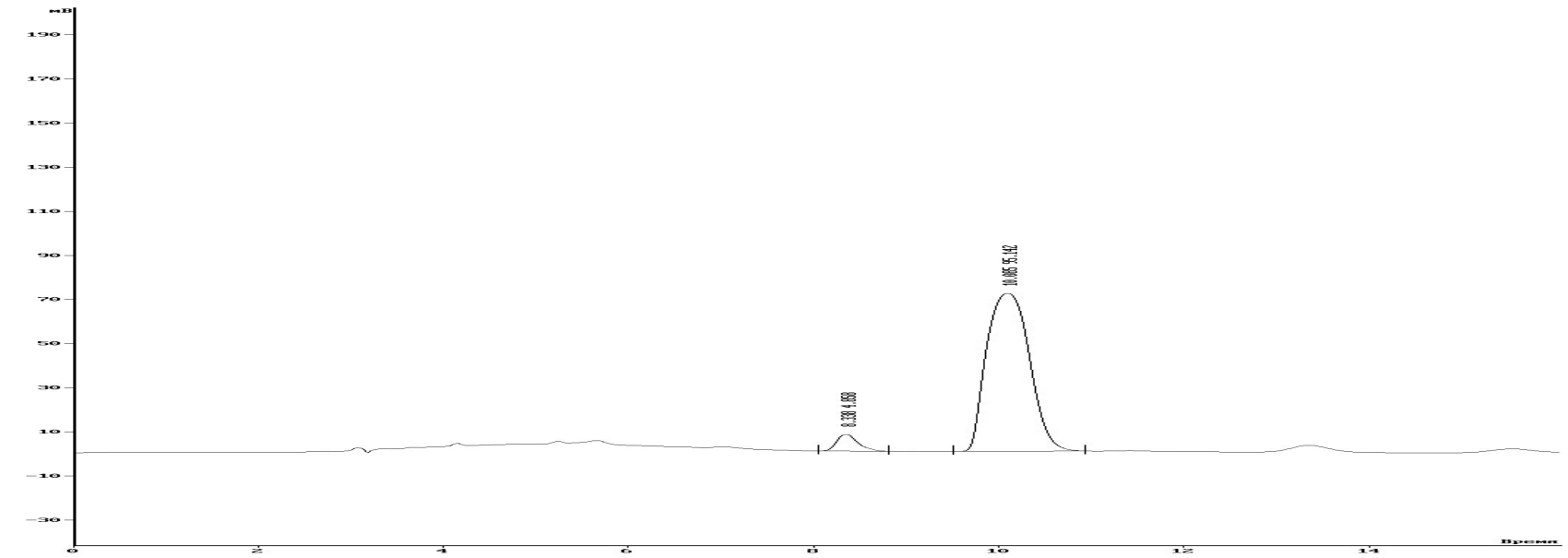
2-(pentafluoroethyl)prolinamide **(3b)**, 85 %, 90 % *ee*, white solid, mp 41-43ºC ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.68-1.91 (2H, m), 2.23-2.38 (2H, m, **CH_2**-C_q), 2.62 (1H, bs, **NH**), 3.03-3.05 (2H, m, **CH_2**-N), 6.77 (1H, bs, **NH_2**CO), 7.14 (1H, bs, **NH_2**CO). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.1, 32.6 (**C**H_2-C_q), 47.8 (CH_2-N), 70.7 (t, J_{CF} = 21.6 Hz, **C**-CF_2), 114.7 (tq, J_{CF} = 262.4 Hz, J_{CF} = 35.8 Hz, CF_2), 119.0 (qt, J_{CF} = 287.9 Hz, J_{CF} = 36.5 Hz, CF_3), 172.7 (d, J_{CF} = 4.8 Hz, $CONH_2$).

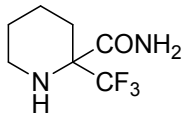
^{19}F NMR (280 MHz, $CDCl_3$): δ -79.4 (3F, s, CF_3), -115.6 (1F, d, J_{FF} = 276.8 Hz, CF_2), -120.8 (1F, d, J_{FF} = 276.8 Hz, CF_2). IR(KBr): 1691, 1213 cm^{-1}. HRMS (ESI): calcd. for $C_7H_9F_5N_2O$ $[M+H]^+$ 233.0708, found 233.0714.

Optical rotation $[\alpha]^{20}_D$ = -33.2 (c = 1, MeOH).

HPLC condition: Chiral column CHIRALPAK AS-H (250×4.6 mm), heptane/*i*-PrOH = 9/1, flow rate = 1 mL/min, wavelength = 206 nm. $t_{r\ minor}$ = 8.338 min (4.858), $t_{r\ major}$ = 10.085 min (95.142)



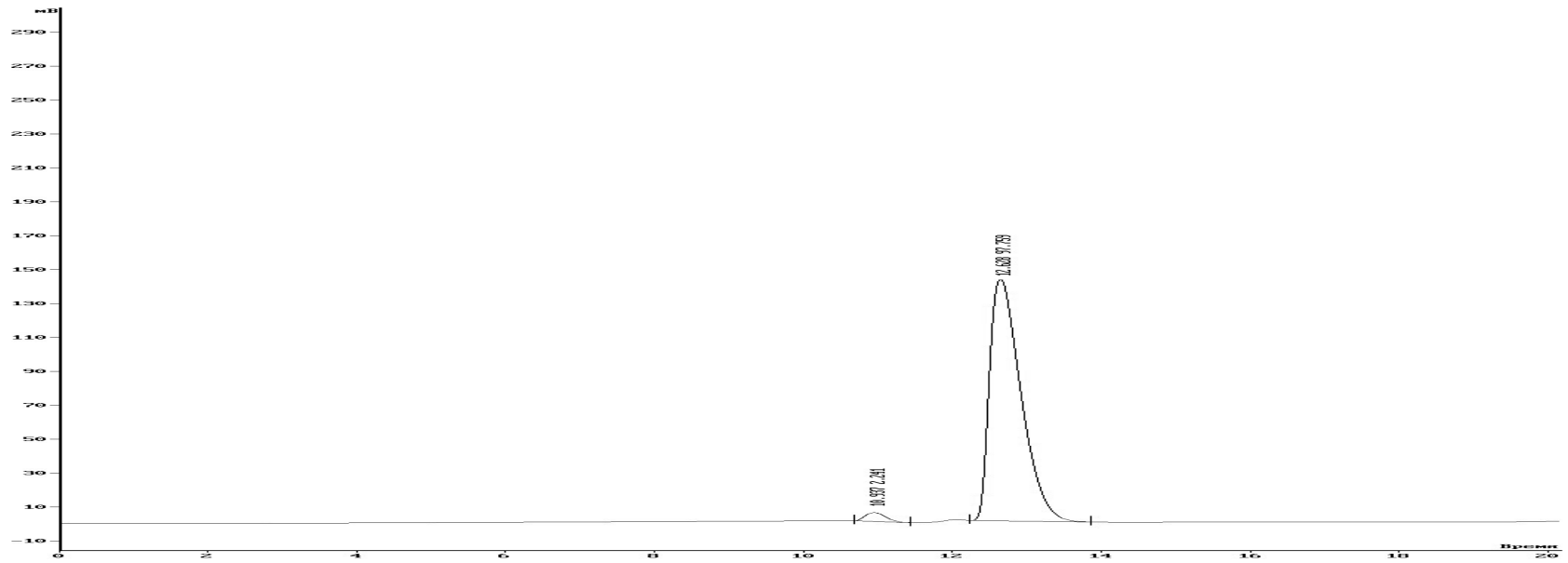




2-(trifluoromethyl)piperidine-2-carboxamide **(3c)**, 97 %, 96% *ee*, white solid, mp 128-130ºC ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24-1.60 (4H, m), 1.74-1.82 (2H, m), 2.40-2.44 (1H, m), 2.68-2.75 (1H, m, **CH_2**-C_q), 3.02-3.05 (1H, m, **CH_2**-C_q), 6.05 (1H, bs, CO**NH_2**), 7.18 (1H, bs, CO**NH_2**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.3, 25.3, 26.3 (**C**H_2-C_q), 42.4 (CH_2-N), 64.7 (q, J_{CF} = 24.7 Hz, **C**-CF_3), 124.7 (q, J_{CF} = 284.2 Hz, CF_3), 169.6 ($CONH_2$). ^{19}F NMR (280 MHz, $CDCl_3$): δ -76.8 (3F, s, CF_3). IR(KBr): 3396 (NH), 3307 (NH), 3217 (NH), 1697 (CO), 1674 (CO), 1184 cm^{-1}. HRMS (ESI): calcd. for $C_7H_{11}F_3N_2O$ $[M+H]^+$ 197.0896, found 197.0892.

Optical rotation $[\alpha]^{20}_D$ = +3.2 (c = 0.5, MeOH).

HPLC condition: Chiral column CHIRALPAK AS-H (250×4.6 mm), heptane/*i*-PrOH = 9/1, flow rate = 1 mL/min, wavelength = 206 nm. $t_{r\ minor}$ = 10.937 min (2.241), $t_{r\ major}$ = 12.628 min (97.759)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230
210
190
170
150
130
110
90
70
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30
10
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6
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10
12
14
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18
20
Время
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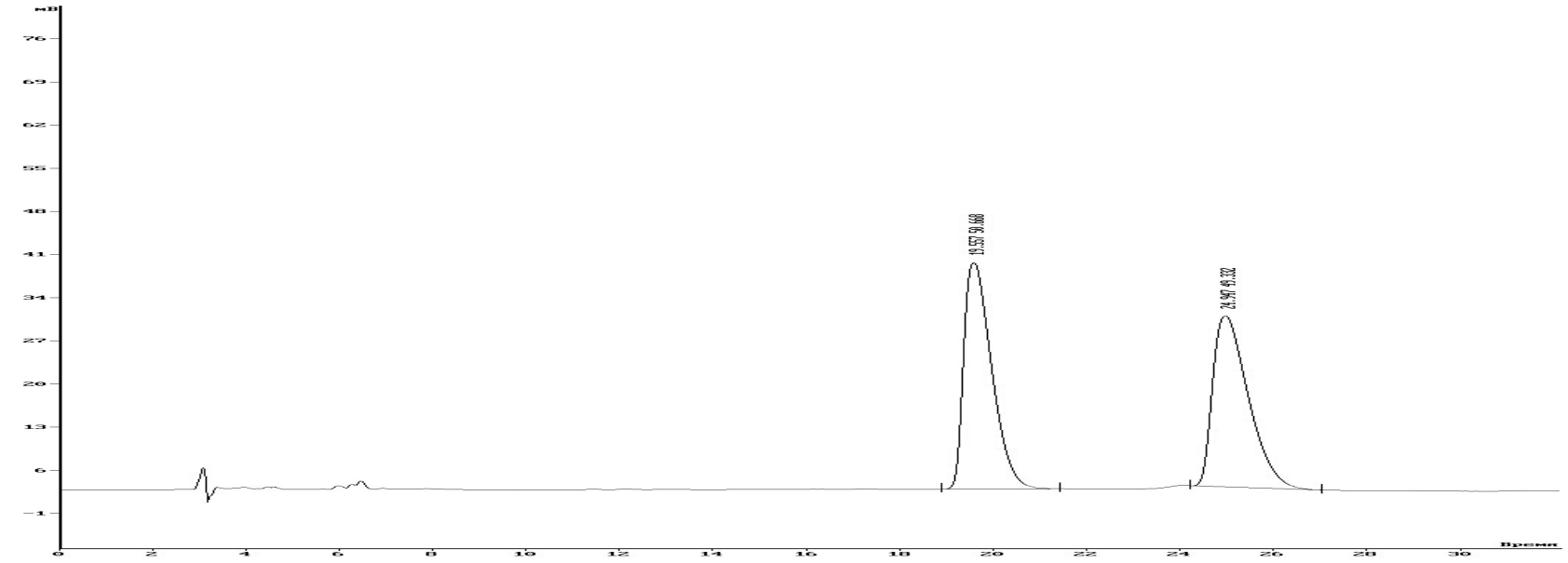
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Время
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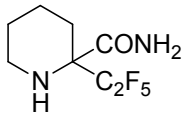
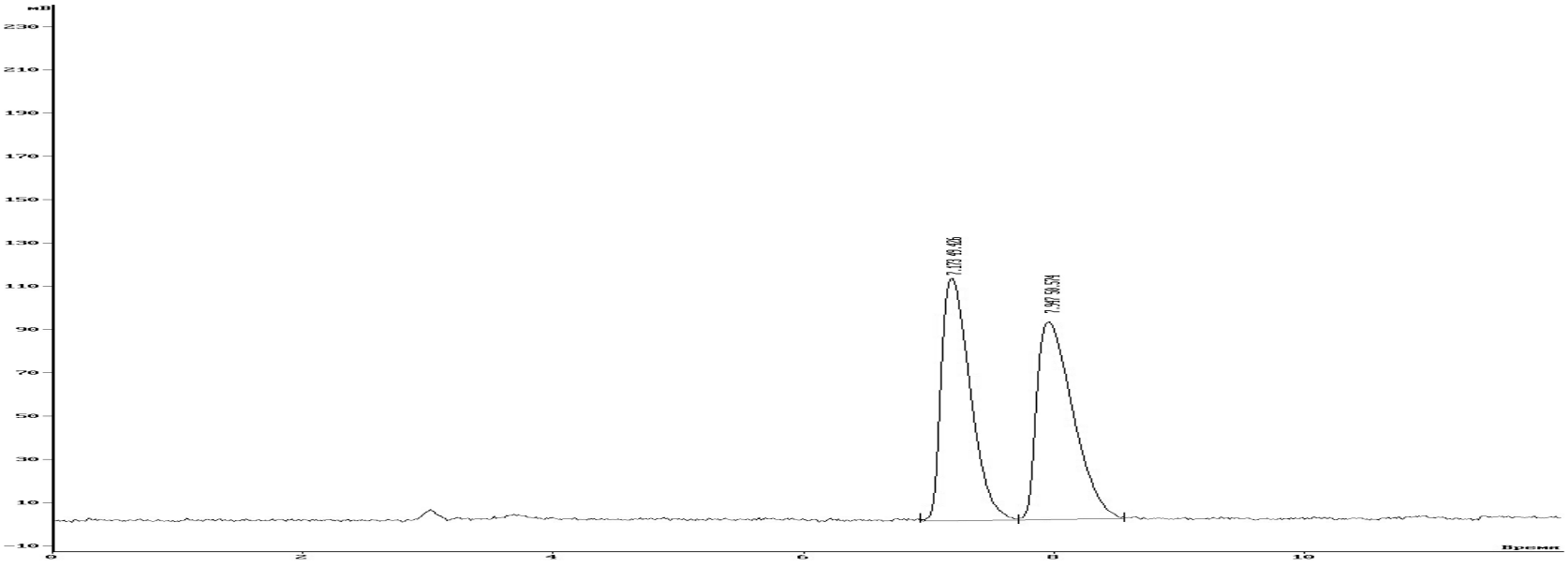
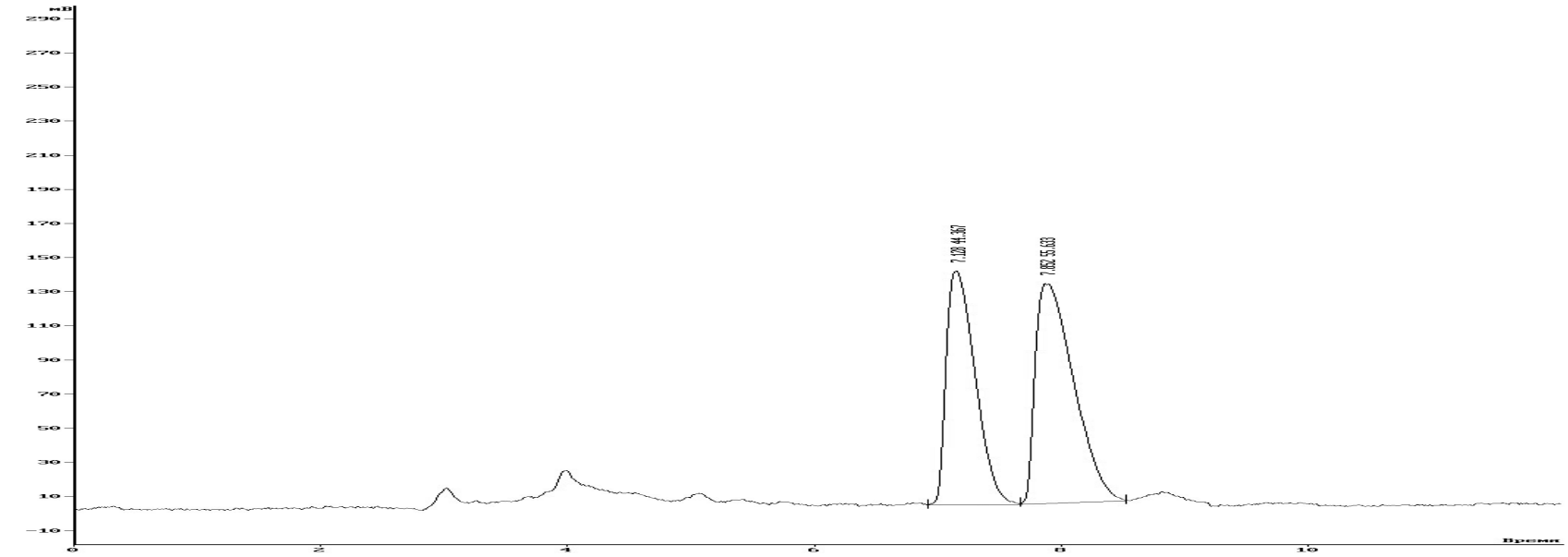


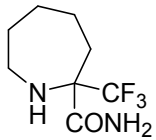
2-(Perfluoroethyl)piperidine-2-carboxamide **(3d)**, 89 %, 11 % *ee*, white solid, mp 72-74ºC ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22-1.64 (4H, m), 1.78-1.81 (1H, m, **CH$_2$**-C$_q$), 2.39-2.43 (1H, m, **CH$_2$**-C$_q$), 2.68-2.76 (1H, m, **CH$_2$**-NH), 2.98-3.02 (1H, m, **CH$_2$**-NH), 6.69 (1H, bs, CO**NH$_2$**), 7.15 (1H, bs, CO**NH$_2$**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.4, 25.2, 26.2 (**C**H$_2$-C$_q$), 42.4 (**C**H$_2$-N), 65.2 (t, J_{CF} = 20.1 Hz, **C**-CF$_2$), 114.0 (tq, J_{CF} = 262.4 Hz, J_{CF} = 36.5 Hz, **C**F$_2$), 119.1 (qt, J_{CF} = 287.9 Hz, J_{CF} = 36.7 Hz, **C**F$_3$), 169.6 (CONH$_2$). ^{19}F NMR (280 MHz, $CDCl_3$): δ -78.8 (3F, s, CF$_3$), -121.6 (1F, d, J_{FF} = 278.8 Hz, CF$_2$), -122.5 (1F, d, J_{FF} = 278.8 Hz, CF$_2$). IR(KBr): 1693, 1678, 1119, 1099, 1059 cm^{-1}. HRMS (ESI): calcd. for $C_8H_{11}F_5N_2O$ [M+H]$^+$ 247.0864, found 247.0870.

HPLC condition: Chiral column CHIRALPAK AS-H (250×4.6 mm), heptane/*i*-PrOH = 9/1, flow rate = 1 mL/min, wavelength = 206 nm.

$t_{r\ \mathrm{minor}}$ = 7.128 min (44.367), $t_{r\ \mathrm{major}}$ = 7.852 min (55.633)



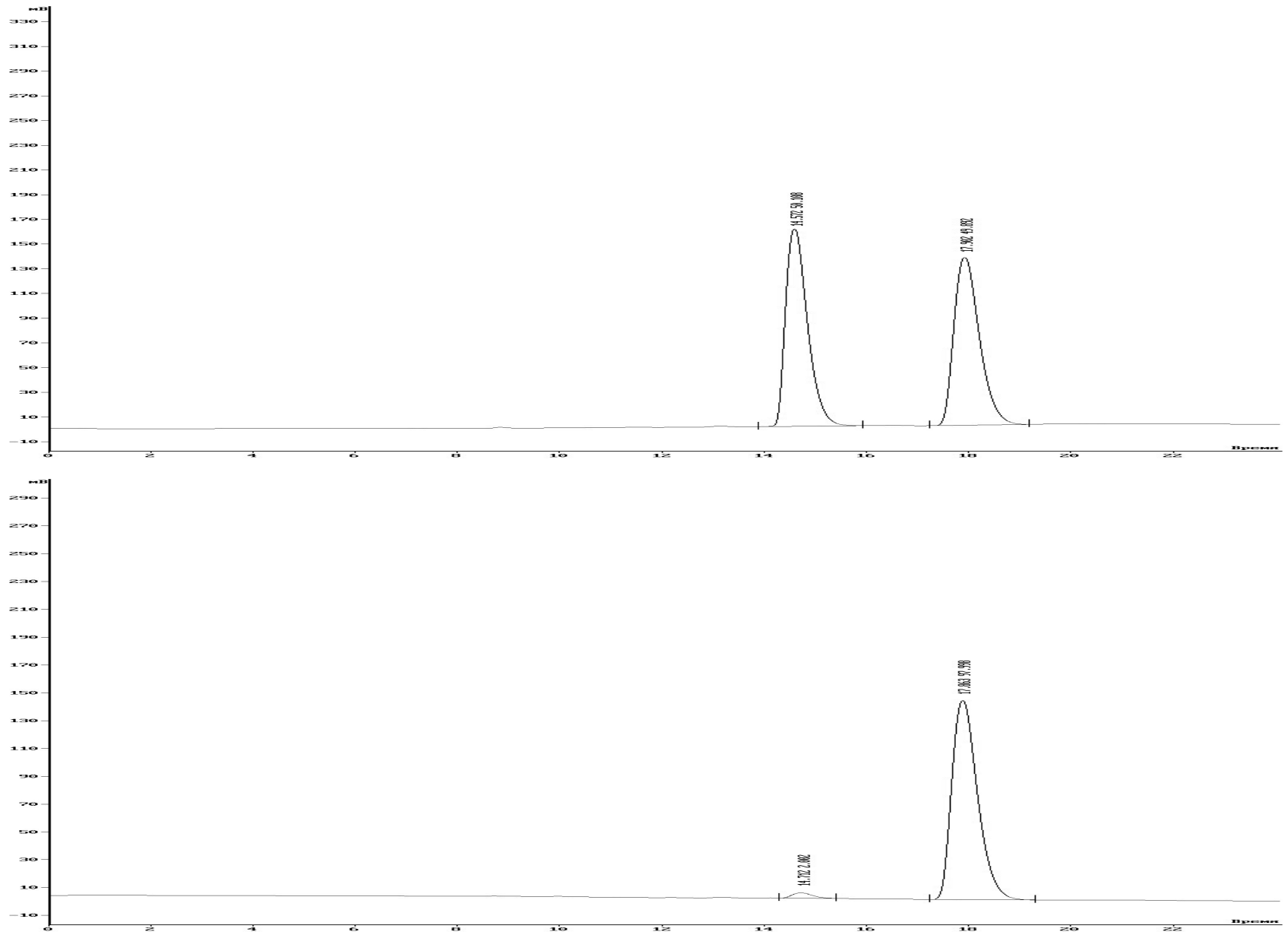




2-(Trifluoromethyl)azepane-2-carboxamide **(3e)**, 99 %, 96 % *ee*, white solid, mp 72-73ºC ^{1}H NMR (400 MHz, DMSO): δ 1.13-1.40 (3H, m), 1.69-1.71 (3H, m), 1.79-1.85 (1H, m), 2.27-2.33 (1H, m), 2.82-2.92 (2H, m, **CH_2**-N), 7.02 (1H, bs, **NH_2**CO), 7.62 (1H, bs, **NH_2**CO). ^{13}C NMR (100 MHz, DMSO): δ 22.7, 29.6, 30.3, 33.0 (**C**H_2-C_q), 43.7 (CH_2-N), 68.1 (q, J_{CF} = 24.0 Hz, **C**-CF_3), 126.4 (q, J_{CF} = 288.2 Hz, CF_3), 173.5 (**CO**NH_2). ^{19}F NMR (280 MHz, DMSO): δ -75.1 (3F, s, CF_3). IR(KBr): 3421 (NH), 3361 (NH), 3250 (bs, NH), 3192 (bs, NH), 1693 (CO), 1171 cm^{-1}. HRMS (ESI): calcd. for $C_8H_{13}F_3N_2O$ $[M+H]^+$ 211.1053, found 211.1053.

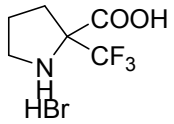
Optical rotation $[\alpha]^{20}_D$ = -21.2 (c = 0.5, MeOH).

HPLC condition: Chiral column 3-AmyCoat (150×4.6 mm), heptane/*i*-PrOH = 98/2, flow rate = 1 mL/min, wavelength = 206 nm. $t_{r\ minor}$ = 14.712 min (2.002), $t_{r\ major}$ = 17.863 min (97.998)



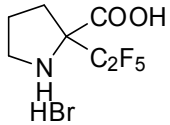
Procedure for synthesis of aminoacids **4a-e**

Amide 2 (1 mmol) was dissolved in HBr (HI) (4 mL) and was heated to reflux. Reaction was monitoring by NMR ^{19}F spectra. After reaction complete solution concentrated under reduced pressure. Residue was recrystallized with methanol and concentrated to obtain salt of aminoacid.



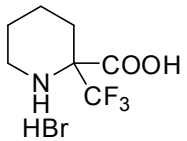
2-(trifluoromethyl)pyrrolidine-2-carboxylic acid hydrobromide (**4a)** 99 %, white solid, degradation over 200°C. ^{1}H NMR (400 MHz, D_2O): δ 1.82-2.08 (2H, m), 2.27-2.39 (2H, m), 2.92-2.98 (1H, m), 3.25-3.31 (1H, m). ^{13}C NMR (100 MHz, D_2O): δ 25.9, 32.1, 47.4 (CH_2-N), 71.9 (q, J_{CF} = 25.0 Hz, **C**-CF_3), 126.5 (q, J_{CF} = 281.6 Hz, CF_3), 175.3 (**C**OOH). ^{19}F NMR (280 MHz, D_2O): δ -73.1 (3F, s, CF_3). IR(KBr): 3389 cm^{-1} (OH), 2970 cm^{-1}(NH^+), 1712 cm^{-1} (CO), 1200 cm^{-1} (CF), 1185 cm^{-1}(CF). HRMS (ESI): calcd. for $C_6H_9F_3NO_2$ $[M+H]^+$ 184.0585, found 184.0576.

Optical rotation $[\alpha]^{20}_D$ = -21.2 (c = 0.5, MeOH).



2-(perfluoroethyl)pyrrolidine-2-carboxylic acid hydrobromide (**4b)**, 98 %, white solid, degradation over 200°C. ^{1}H NMR (400 MHz, D_2O): δ 1.7-1.99 (2H, m), 2.32-2.50 (2H, m), 3.27-3.37 (2H, m). ^{13}C NMR (100 MHz, D_2O): δ 22.0, 30.3, 47.4, 72.2 (t, J_{CF} = 29.4 Hz, **C**-CF_3), 111.6 (tq, J_{CF} = 262.1 Hz, J_{CF} = 39.1 Hz, **C**F_2), 117.5 (qt, J_{CF} = 286.4 Hz, J_{CF} = 35.4 Hz, **C**F_3), 166.1 (**C**OOH). ^{19}F NMR (280 MHz, D_2O): δ -80.97 (s, CF_3), -117.78 (q, J_{CF} = 285.4 Hz, CF_2). IR(KBr): 2870 cm^{-1} (OH), 2750 cm^{-1} (NH^+), 1760 cm^{-1} (CO), 1220 cm^{-1} (CF), 1110 cm^{-1} (CF). HRMS (ESI): calcd. for $C_7H_9F_5NO_2$ $[M+H]^+$ 234.0548 found 234.0548.

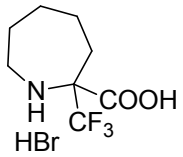
Optical rotation $[\alpha]^{20}_D$ = -18.4 (c = 0.5, MeOH).



2-(trifluoromethyl)piperidine-2-carboxylic acid hydrobromide (**4c)**, 98 %, brown solid, 255-257°C. ^{1}H NMR (400 MHz, D_2O): δ 1.20-1.31 (1H, m), 1.43-1.53 (1H, m), 1.67-1.77 (3H, m), 2.32 (1H, d, J = 14.5 Hz), 3.09 (1H, dt, $J_{H,H}$ = 13.0 Hz, $J_{H,H}$ = 3.1 Hz),

3.28 (1H, d, J = 12.8 Hz). ^{13}C NMR (100 MHz, D_2O): δ 17.7, 20.1, 42.9, 66.0 (q, J_{CF} = 28.4 Hz, **C**-CF_3), 121.9 (q, J_{CF} = 284.9 Hz, CF_3), 164.5 (**C**OOH). ^{19}F NMR (280 MHz, D_2O): δ -75.8 (s, CF_3). IR(KBr): 3096 cm^{-1} (OH), 2830 cm^{-1} (NH^+), 1751 cm^{-1} (CO), 1215 cm^{-1} (CF), 1146 cm^{-1} (CF). HRMS (ESI): calcd. for $C_7H_{11}F_5NO_2$ $[M+H]^+$ 198.0737 found 198.0737.

Optical rotation $[\alpha]^{20}_D$ = +5.9 (c = 1, MeOH).

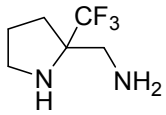


2-(trifluoromethyl)azepane-2-carboxylic acid hydrobromide (**4e)**, 99 %, brown oil. ^{1}H NMR (400 MHz, D_2O): δ 1.18-1.38 (2H, m), 1.44-1.79 (4H, m), 2.01-2.08 (1H, m), 2.26-2.32 (1H, m), 3.14-3.26 (2H, m). ^{13}C NMR (100 MHz, D_2O): δ 21.6, 25.6, 26.4, 27.7, 45.5, 70.2 (q, J_{CF} = 23.9 Hz, **C**-CF_3), 122.6 (q, J_{CF} = 285.3 Hz, CF_3), 166.2 (**C**OOH). ^{19}F NMR (280 MHz, D_2O): δ -73.6 (s, CF_3). IR(KBr): 3097 cm^{-1} (OH), 2834 cm^{-1} (NH^+), 1747 cm^{-1} (CO), 1251 cm^{-1} (CF), 1186 cm^{-1} (CF). HRMS (ESI): calcd. for $C_8H_{13}F_3NO_2$ $[M+H]^+$ 212.0893 found 212.0900.

Optical rotation $[\alpha]^{20}_D$ = -1.9 (c = 0.73, MeOH).

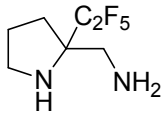
Procedure for synthesis of diamines **5a-e**

To a stirred solution of cyclic nitrile **2a-c,e** (2 mmol) in MeOH (5 mL) NH_3 aq (3 mL), Ni-Ra were added and reaction was vacuumed and carried out in H_2 atmosphere. Mixture was stirred during two days after that, filtered over celite, rinsed by water and concentrated to half volume. Residue extracted with Et_2O, organic lay dried over Na_2SO_4 and concentrated under reduced pressure to obtain pure product.



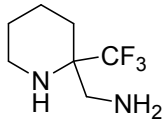
*(2-(Trifluoromethyl)pyrrolidin-2-yl)methanamine (***5a)**, 90 %, yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54-1.73 (5H, m), 1.80-1.96 (2H, m), 2.63 (1H, dd, J_1 = 0.8 Hz, J_2 = 13.3 Hz), 2.89-3.04 (3H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.9, 30.0, 44.9 (**C**H_2-C_q), 47.3 (CH_2-N), 67.2 (q, J_{CF} = 24.7 Hz, **C**-CF_3), 128.3 (q, J_{CF} = 284.5 Hz, CF_3). ^{19}F NMR (280 MHz, $CDCl_3$): δ -78.2 (3F, s, CF_3). IR(KBr): 3299 (bs, NH), 3414 (bs, NH),1167 (C-F), 1151 (C-F) cm^{-1}. HRMS (ESI): calcd. for $C_6H_{11}F_3N_2$ $[M+H]^+$ 169.0947, found 169.0954.

Optical rotation $[\alpha]^{20}_D$ = -5.2 (c = 0.5, MeOH).



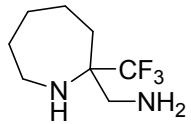
1-[2-(Pentafluoroethyl)pyrrolidin-2-yl]methanamine **(5b)**, 78 %, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.56-1.81 (6H, m), 1.96-2.04 (1H, m), 2.57 (1H, d, J = 13.5 Hz, **C**$\mathbf{H_2}$-NH_2), 2.84-2.91 (2H, m including 2.86, d, J = 13.5 Hz, **C**$\mathbf{H_2}$-NH_2), 2.95-3.00 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.6, 30.2, 45.2, 47.1, 67.6 (t, J_{CF} = 19.2 Hz, **C**-C_2F_5), 116.9 (tq, J_1 = 257.3 Hz, J_2 = 35.0 Hz, CF_2), 119.5 (qt, J_1 = 287.5 Hz, J_2 = 37.2 Hz, CF_3). ^{19}F NMR (280 MHz, $CDCl_3$): δ -119.6 (2F, CF_2), -79.2 (3F, s, CF_3). IR(ATR, ZnSe): 3322 (bs), 2960, 1336, 1191, 1159, 1043, 736 cm^{-1}. HRMS (ESI): calcd. for $C_7H_{12}F_5N_2$ $[M+H]^+$ 219.0915, found 219.0925.

Optical rotation $[\alpha]^{20}_D$ = +2.4 (c = 0.5, CH_2Cl_2).



(2-(Trifluoromethyl)piperidin-2-yl)methanamine **(5c)**, 82 %, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39-1.62 (9H, m), 2.63-2.66 (1H, m, **C**$\mathbf{H_2}$-NH), 2.70 (2H, s, **C**$\mathbf{H_2}$-NH_2), 2.79-2.80 (1H, m, **C**$\mathbf{H_2}$-NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.5, 24.5, 25.4 (**C**H_2-C_q), 40.7 (CH_2-N), 42.8 (CH_2-N), 58.0 (q, J_{CF} = 22.8 Hz, **C**-CF_3), 128.1 (q, J_{CF} = 288.6 Hz, CF_3). ^{19}F NMR (280 MHz, $CDCl_3$): δ -75.8 (3F, s, CF_3). IR(KBr): 3305 (bs, NH), 1156 (C-F), 1130 (C-F) cm^{-1}. HRMS (ESI): calcd. for $C_7H_{13}F_3N_2$ $[M+H]^+$ 183.1104, found 187.1108.

Optical rotation $[\alpha]^{20}_D$ = -0.8 (c = 1, CH_2Cl_2).

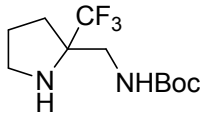


1-[2-(Trifluoromethyl)azepan-2-yl]methanamine **(5e)**, 79 %, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23-1.47 (5H, m), 1.59-1.76 (5H, m), 2.57-2.61 (1H, m), 2.76-2.82 (3H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.6, 30.5, 30.9, 33.6, 43.1, 46.3, 61.5 (q, J_{CF} = 22.1 Hz, **C**-CF_3), 128.9 (q, J_{CF} = 290.4 Hz, CF_3). ^{19}F NMR (280 MHz, $CDCl_3$): δ -76.9 (3F, s, CF_3). IR(neat): 3350 (bs), 1160 cm^{-1}. HRMS (ESI): calcd. for $C_8H_{16}F_3N_2$ $[M+H]^+$ 197.1260, found 197.1262.

Optical rotation $[\alpha]^{20}_D$ = -6.4 (c = 0.5, CH_2Cl_2).

Procedure for synthesis of Boc-protected diamines **6a-e**

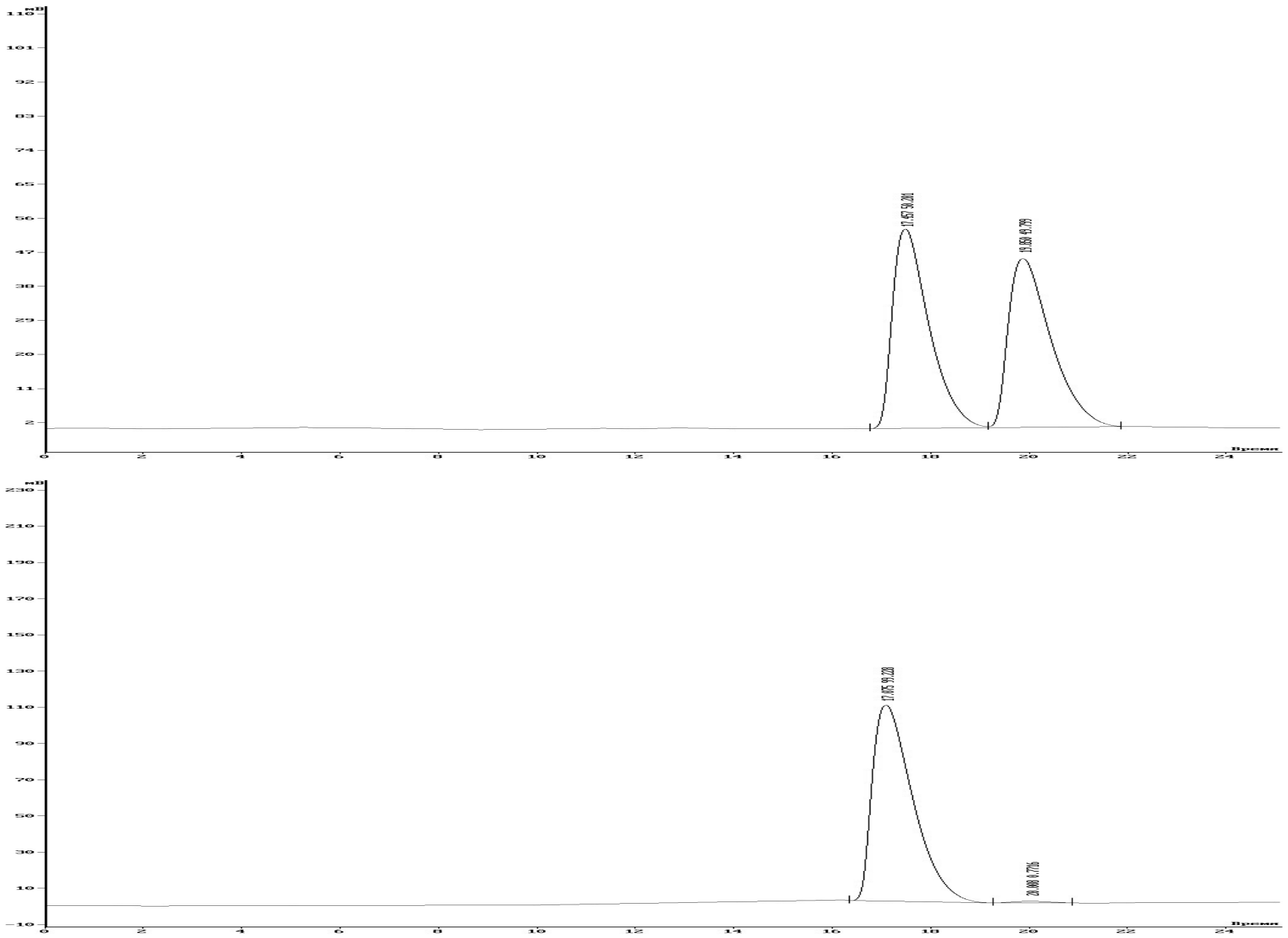
To a solution of diamines 4 (1 mmol) in CH_2Cl_2 Boc_2O (1.1 mmol) and Et_3N (1.5 mmol) were added. Mixture was stirred over night. After that, reaction was concentrated under reduced pressure and purified with silica gel chromatography (CH_2Cl_2/MeOH = 100/1).



tert-butyl ((2-(trifluoromethyl)pyrrolidin-2-yl)methyl)carbamate **(6a)**, 99 %, 98% *ee*, white solid, mp 90-92°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (9H, s), 1.68-1.80 (2H, m), 1.84-1.90 (1H, m), 1.95-1.99 (1H, m), 2.10 (1H, bs, NH), 2.96-3.05 (2H, m), 3.28-3.40 (2H, m), 4.97 (1H, bs, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.7, 28.2, 29.9, 43.6, 47.2, 66.9 (q, J_{CF} = 24.7 Hz, **C**-CF_3), 79.8, 127.9 (q, J_{CF} = 284.5 Hz), 156.7. ^{19}F NMR (280 MHz, $CDCl_3$): δ -78.0 (s, CF_3). IR(KBr): 3230 (bs), 2987, 1698, 1554, 1369, 1282, 1164, 946 cm^{-1}. HRMS (ESI): calcd. for $C_{11}H_{20}F_3N_2O_2$ $[M+H]^+$ 269.1472, found 219269.1473.

Optical rotation $[\alpha]^{20}_D$ = -4.0 (c = 0.5, MeOH).

HPLC condition: Chiral column CHIRALCEL OD (250×4.6 mm), heptane/*i*-PrOH = 99.5/0.5, flow rate = 1 mL/min, wavelength = 206 nm. $t_{r\ minor}$ = 20.008 min (0.7716), $t_{r\ major}$ = 17.075 min (99.228).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19.658 49.799
Время
mV
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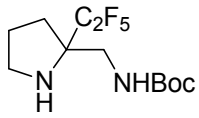
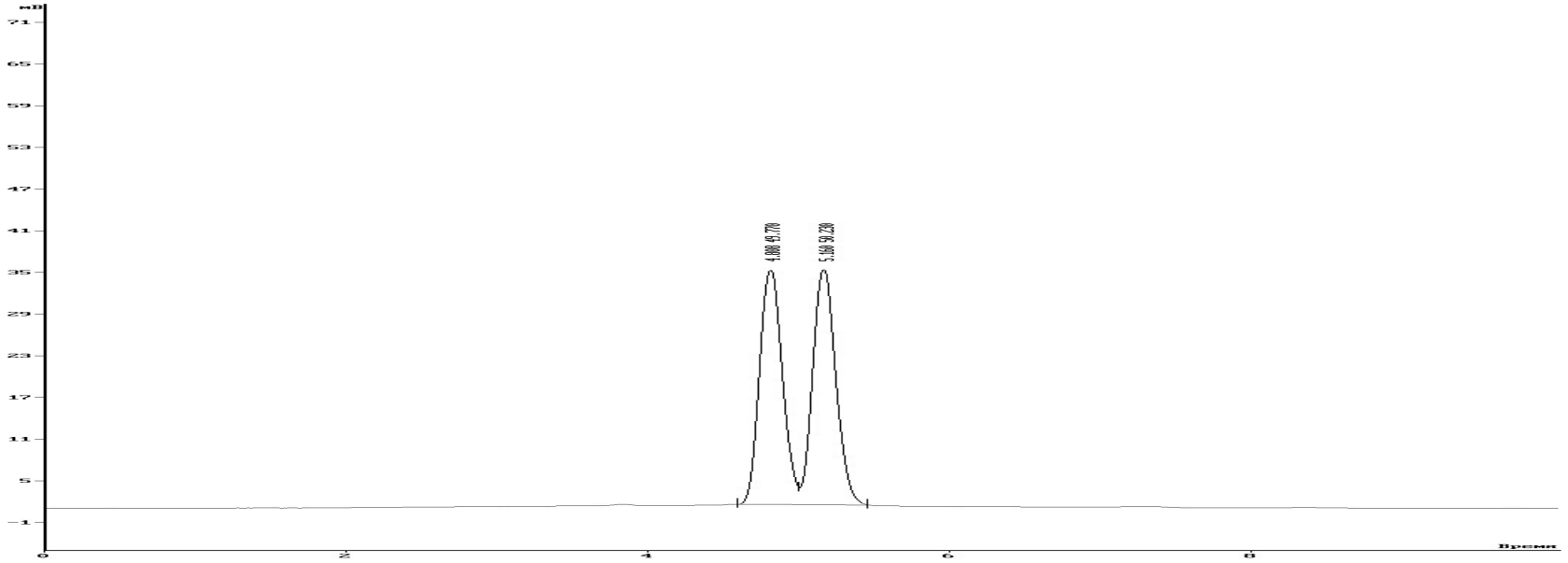
Время

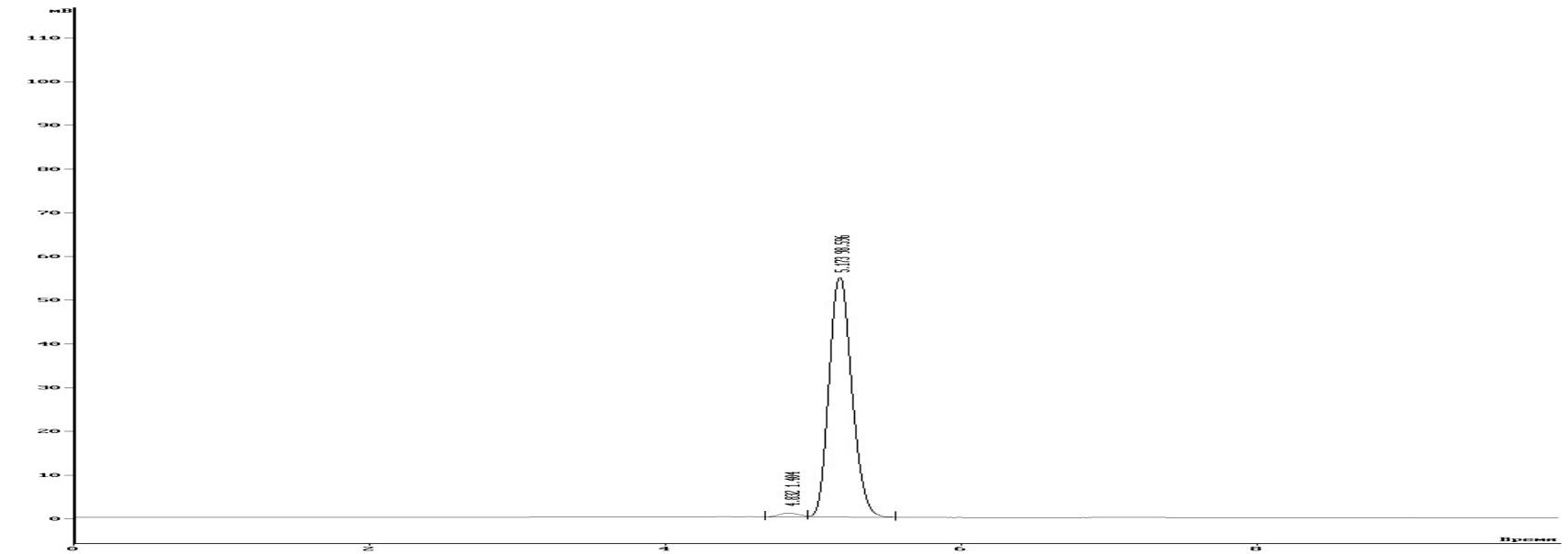


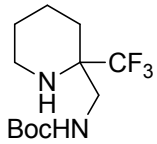
tert-butyl ((2-(perfluoroethyl)pyrrolidin-2-yl)methyl)carbamate **(6b)**, 99 %, 97% *ee*, colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (9H, s), 1.71-1.87 (3H, m), 2.07-2.13 (2H, m), 2.93-3.09 (2H, m), 3.26-3.40 (2H, m), 5.00 (1H, bs, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.6, 28.2, 30.0, 43.8, 47.3, 67.5 (t, J_{CF} = 19.9 Hz, **C**-CF_2), 79.8, 116.5 (tq, J_1 = 222.2 Hz, J_2 = 35.0 Hz, CF_2), 119.5 (qt, J_1 = 287.5 Hz, J_2 = 37.0 Hz, CF_3). 156.8. ^{19}F NMR (280 MHz, $CDCl_3$): δ -120.5 (2F, s, CF_2), -78.9 (3F, s, CF_3). IR(KBr): 3282, 2979, 1698, 1558, 1371, 1172, 950, 728 cm^{-1}. HRMS (ESI): calcd. for $C_{12}H_{20}F_5N_2O_2$ $[M+H]^+$ 319.1440, found 319.1440.

Optical rotation $[\alpha]^{20}_D$ = +2.4 (c = 0.5, CH_2Cl_2).

HPLC condition: Chiral column 3-AmyCoat (150×4.6 mm), heptane/*i*-PrOH = 98/, flow rate = 1 mL/min, wavelength = 206 nm. $t_{r\ minor}$ = 4.832 min (1.404), $t_{r\ major}$ = 5.173 min (98.596).



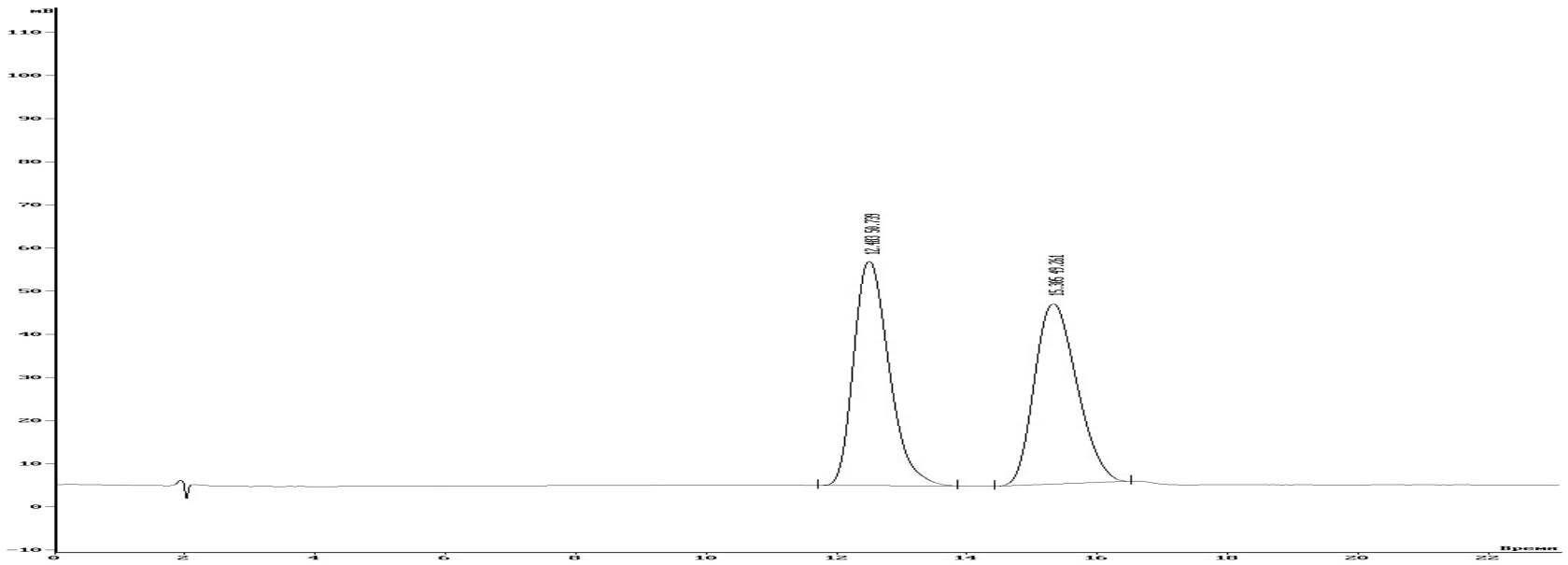




tert-butyl ((2-(trifluoromethyl)piperidin-2-yl)methyl)carbamate **(6c)**, 99%, 95% *ee*, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39 (9H, s), 1.44-1.72 (7H, m), 2.78-2.87 (2H, m), 3.10 (1H, dd, J_1 = 4.3 Hz, J_2 = 14.5 Hz), 3.53-3.59 (1H, m), 4.88 (1H, bs, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.4, 24.5, 25.3, 28.2, 40.8, 41.1, 58.0 (q, J_{CF} = 23.6 Hz, **C**-CF_3), 79.5, 127.7 (q, J_{CF} = 287.5 Hz), 156.0. ^{19}F NMR (280 MHz, $CDCl_3$): δ -77.2 (s, CF_3). IR(KBr): 33230 (bs), 2952, 1716, 1544, 1265, 1172, 744, 651 cm^{-1}. HRMS (ESI): calcd. for $C_{12}H_{22}F3N_2O_2$ $[M+H]^+$ 283.1628, found 283.1628.

Optical rotation $[\alpha]^{20}_D$ = -2.2 (c = 2.1, MeOH).

HPLC condition: Chiral column 3-AmyCoat (150×4.6 mm), heptane/*i*-PrOH = 98/2, flow rate = 1 mL/min, wavelength = 206 nm. $t_{r\ \text{minor}}$ =12.522 min (2.383), $t_{r\ \text{major}}$ = 14.905 min (97.617).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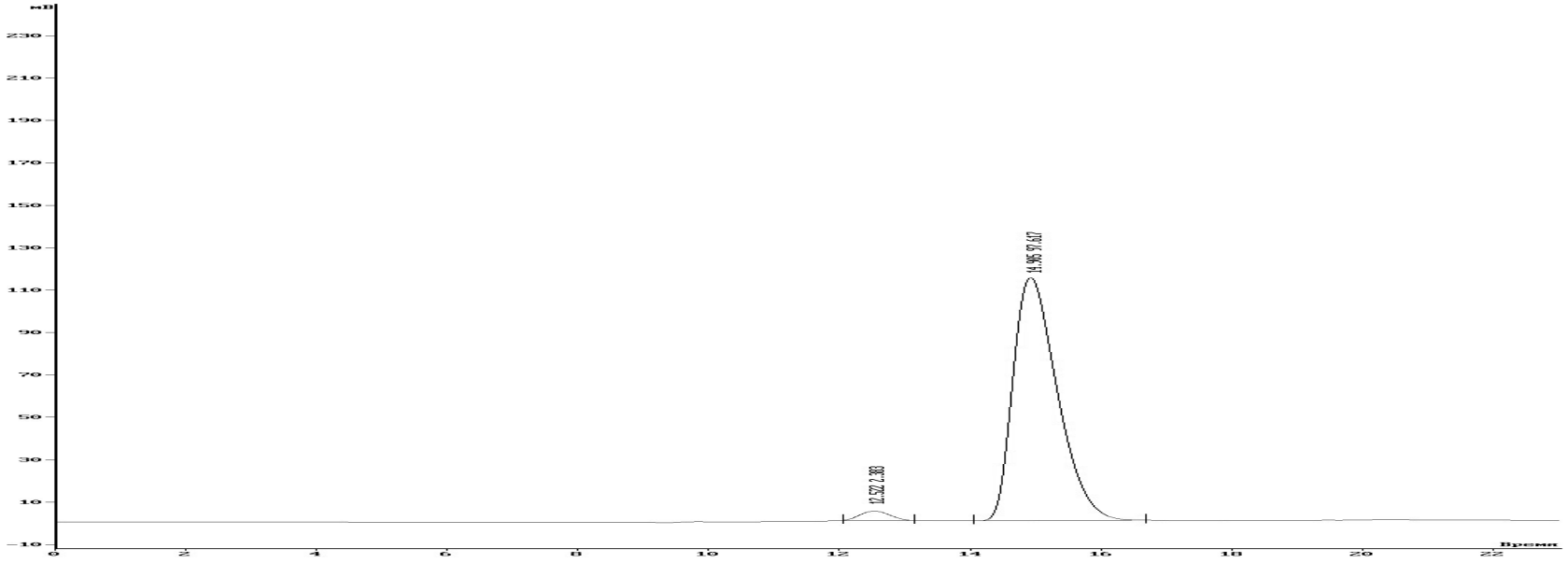
Время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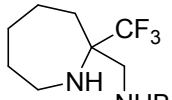
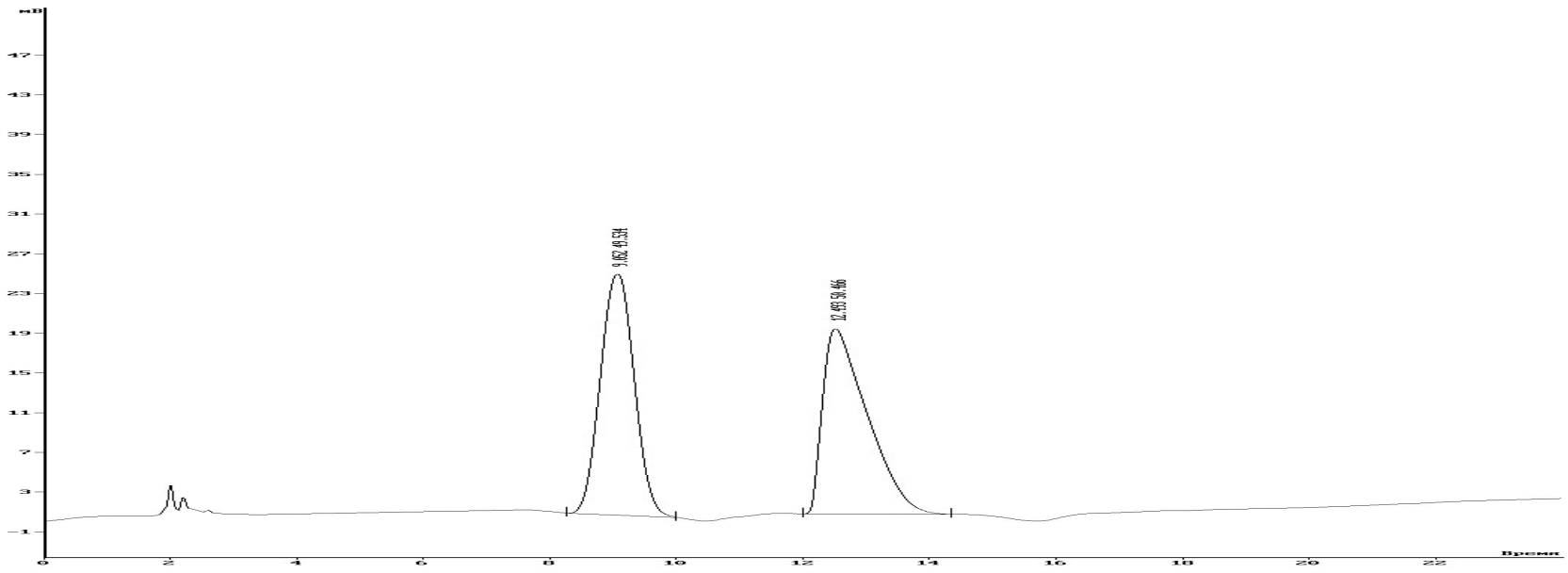
Время

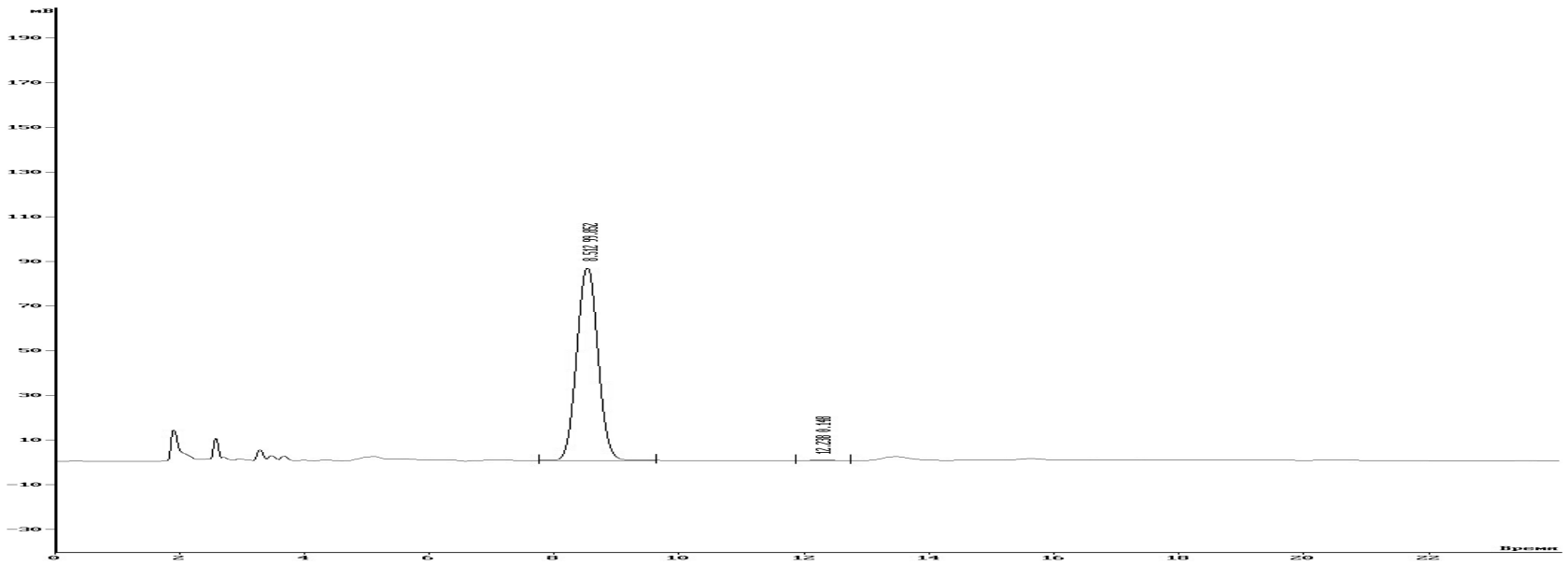


tert-butyl ((2-(trifluoromethyl)azepan-2-yl)methyl)carbamate **(6e)**, 99%, >99% *ee*, white solid, mp 82-84°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29-1.34 (2H, m), 1.40 (9H, s), 1.55-1.81 (7H, m), 2.77-2.87 (2H, m), 3.16-3.21 (1H, m), 3.30-3.36 (1H, m), 4.82 (1H, bs, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.7, 28.2, 30.5, 30.9, 33.6, 43.4, 44.2, 61.7 (q, J_{CF} = 22.2 Hz, **C**-CF_3), 79.6, 128.4 (q, J_{CF} = 289.0 Hz), 156.2. ^{19}F NMR (280 MHz, $CDCl_3$): δ-77.9 (s, CF_3). IR(KBr): 3268 (bs), 2953, 1687, 1367, 1255, 1162, 1058, 781 cm^{-1}. HRMS (ESI): calcd. for $C_{12}H_{22}F3N_2O_2$ $[M+H]^+$ 297.1785, found 297.1785.

Optical rotation $[\alpha]^{20}_D$ = -1.4 (c = 1, CH_2Cl_2).

HPLC condition: Chiral column Kromasil-3-AmyCoat (150x4.6 мм), heptane/*i*-PrOH = 95.5/0.5, flow rate = 1 mL/min, wavelength = 206 nm. $t_{r\ \mathrm{minor}}$ = 12.238 min (0.148), $t_{r\ \mathrm{major}}$ = 8.512 min (99.852)

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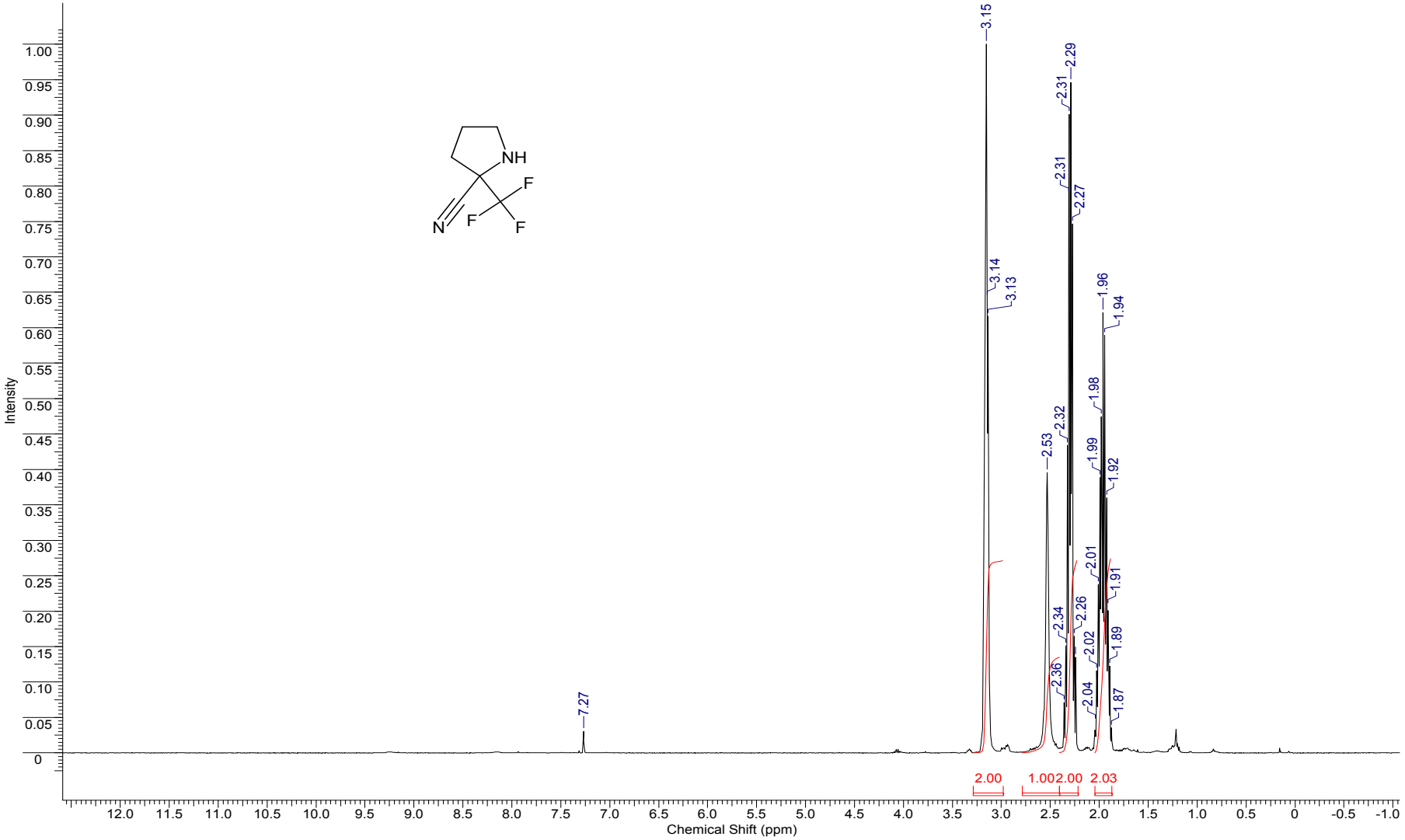
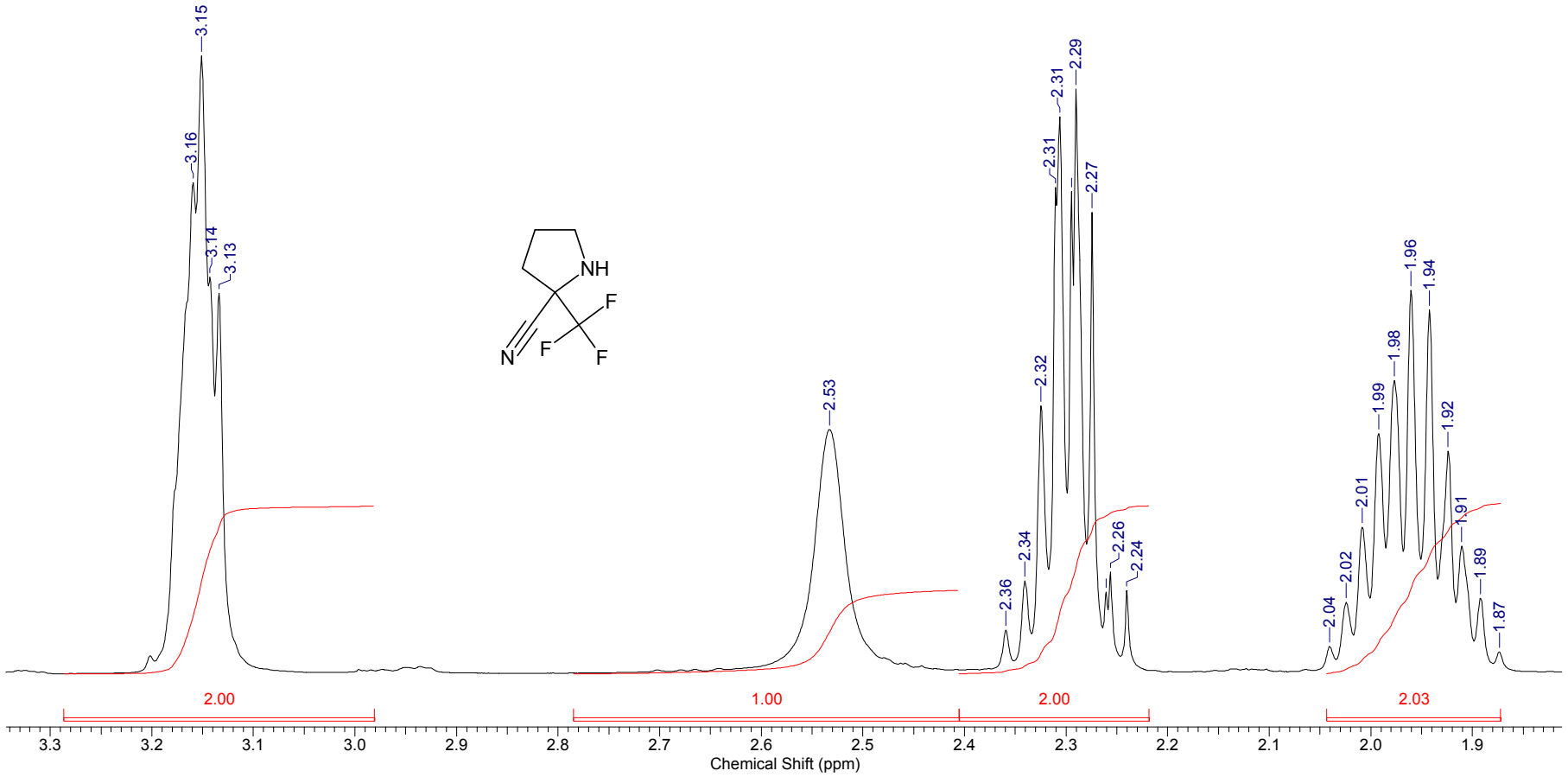
20
22
Время

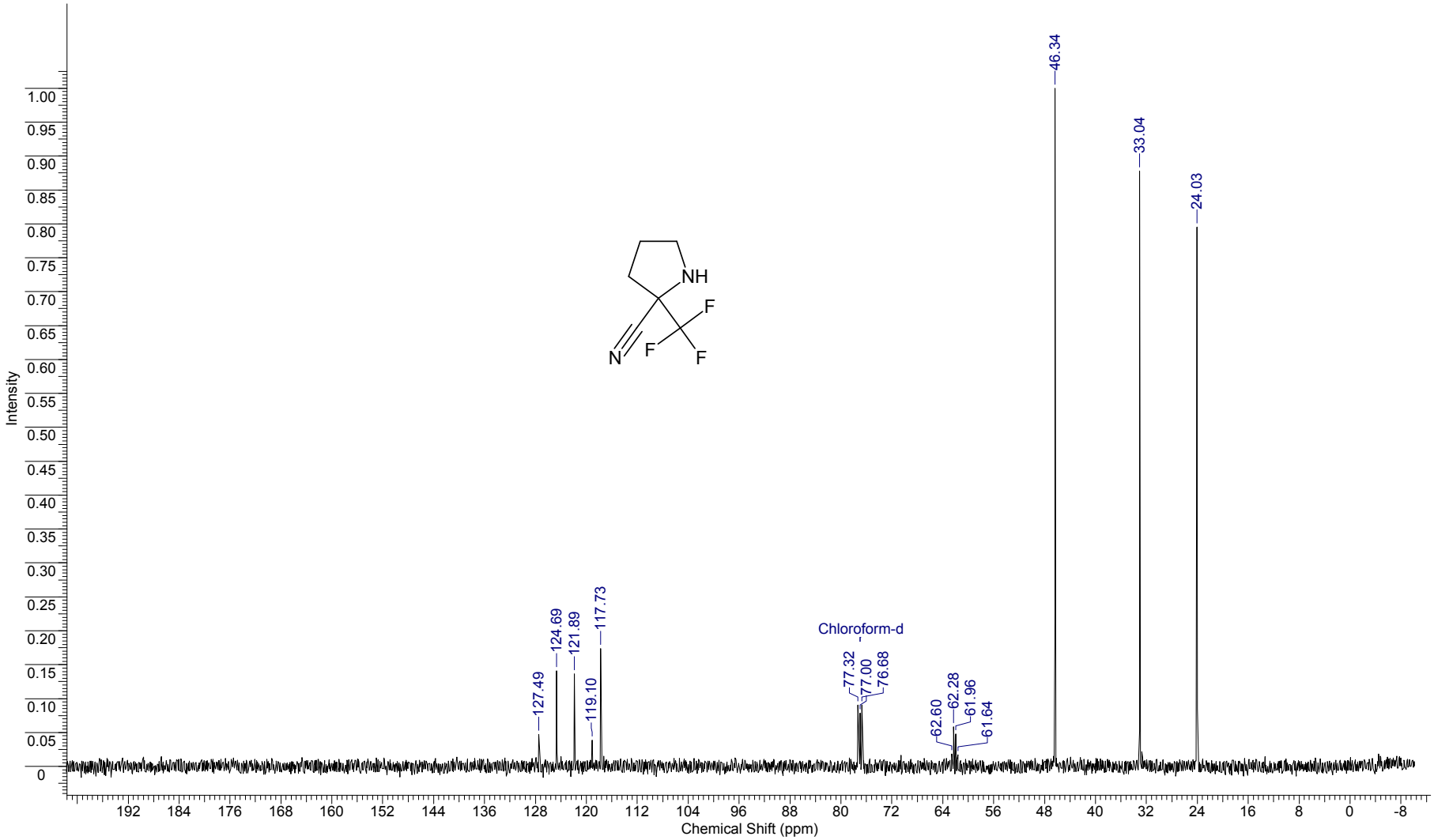
NMR spectra



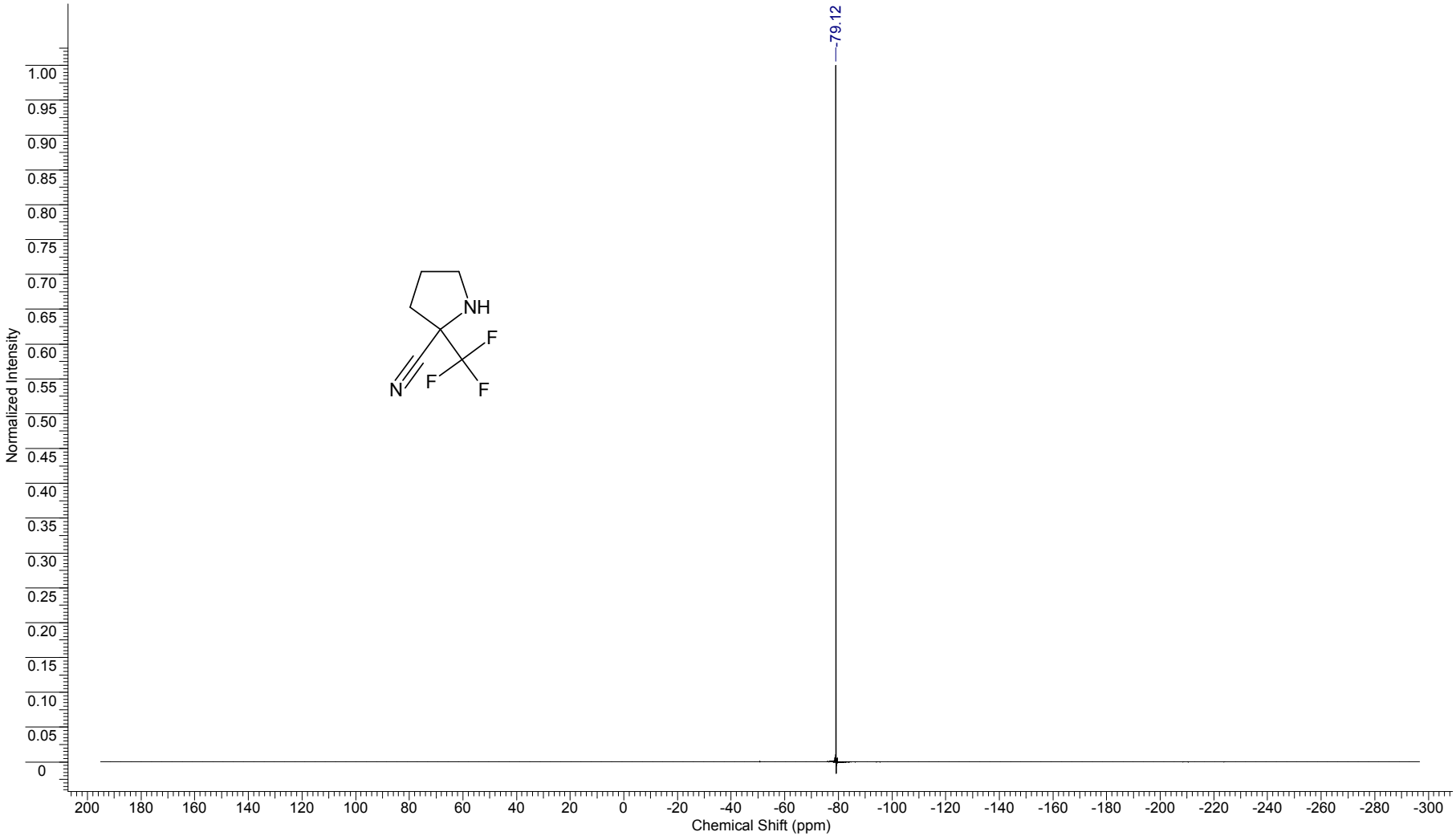
^{1}H NMR (400 MHz, $CDCl_3$) for compound **2a**



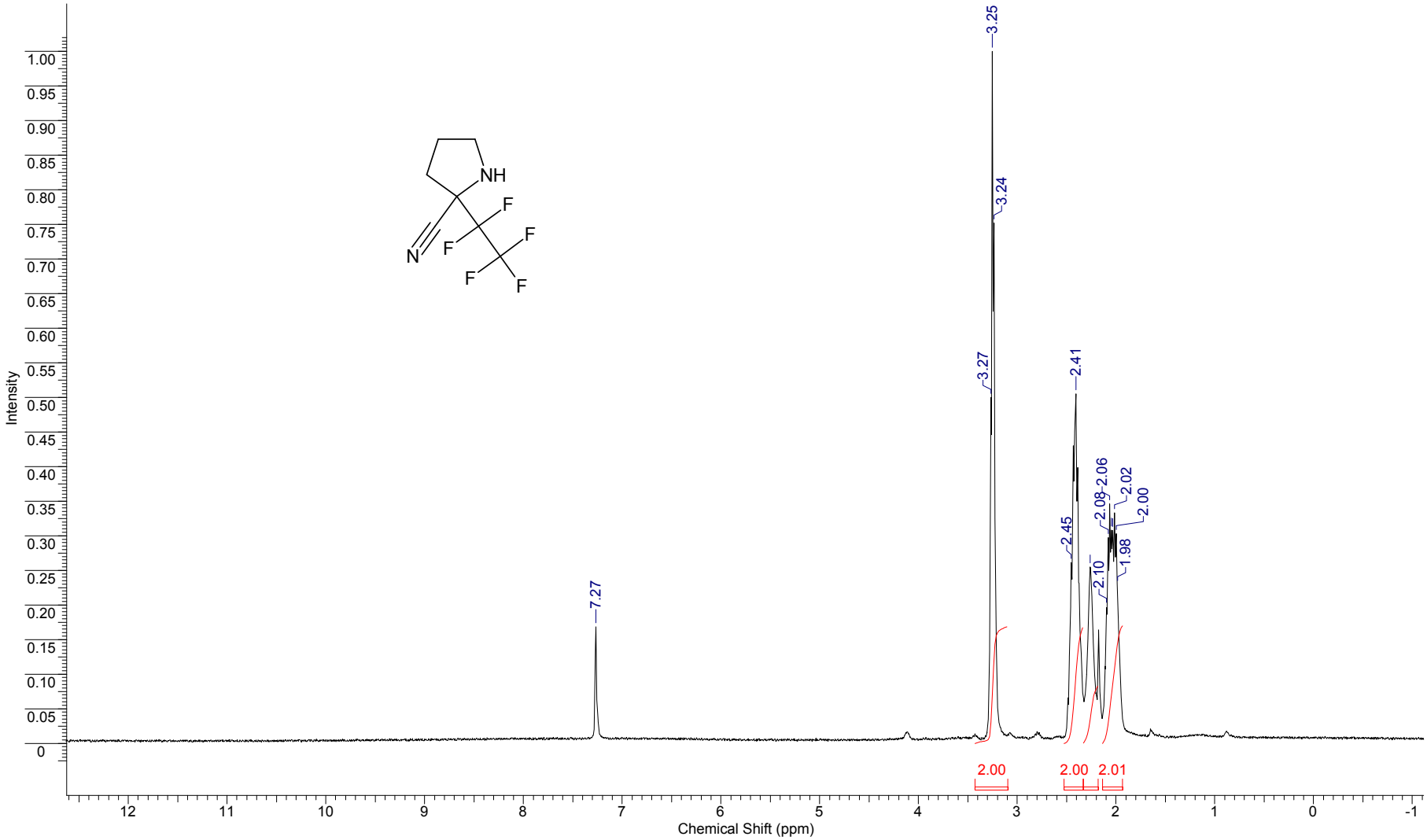
^{1}H NMR (400 MHz, $CDCl_3$) for compound **2a** aliphatic region



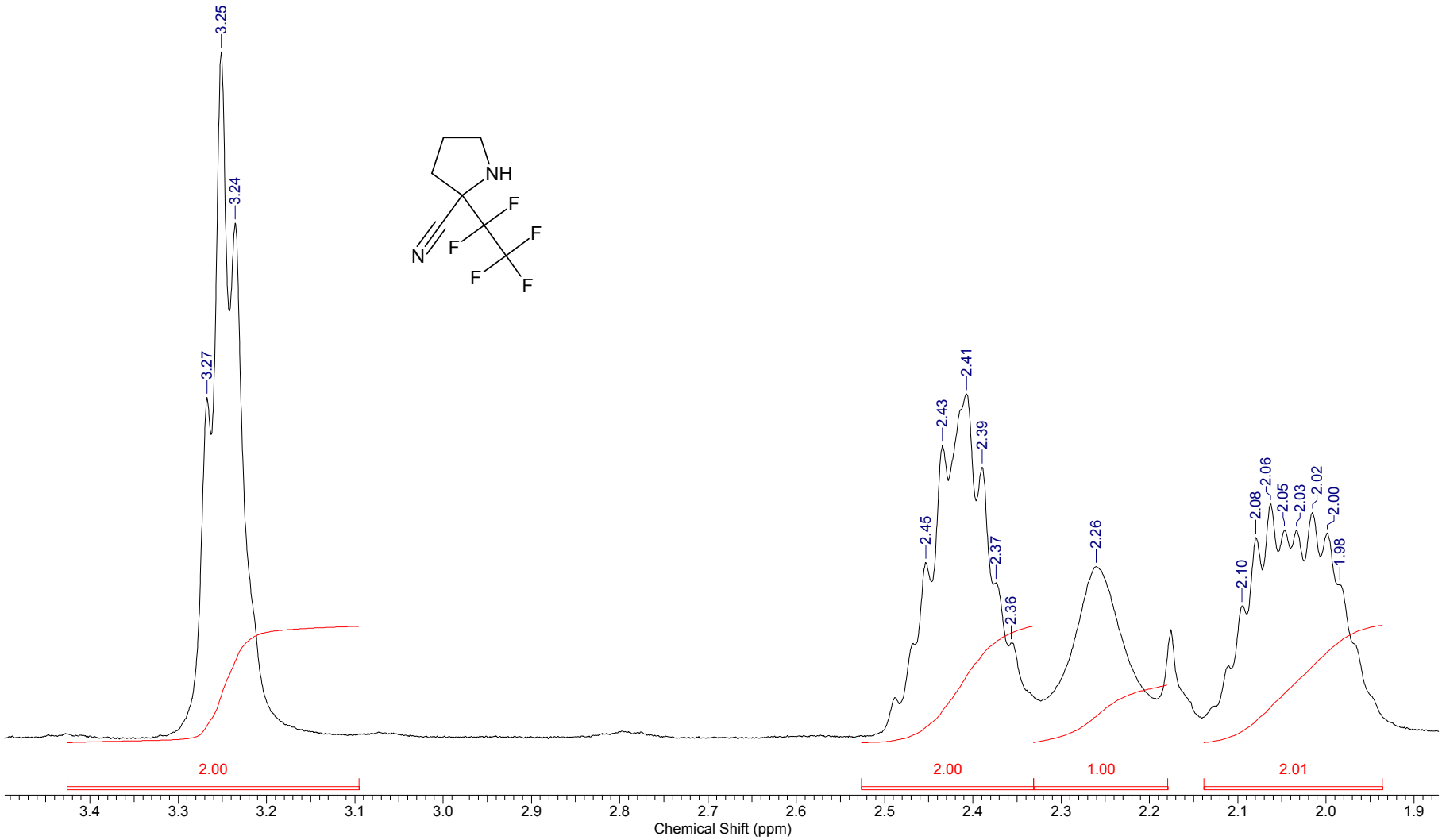
^{13}C NMR (100 MHz, $CDCl_3$) for compound **2a**



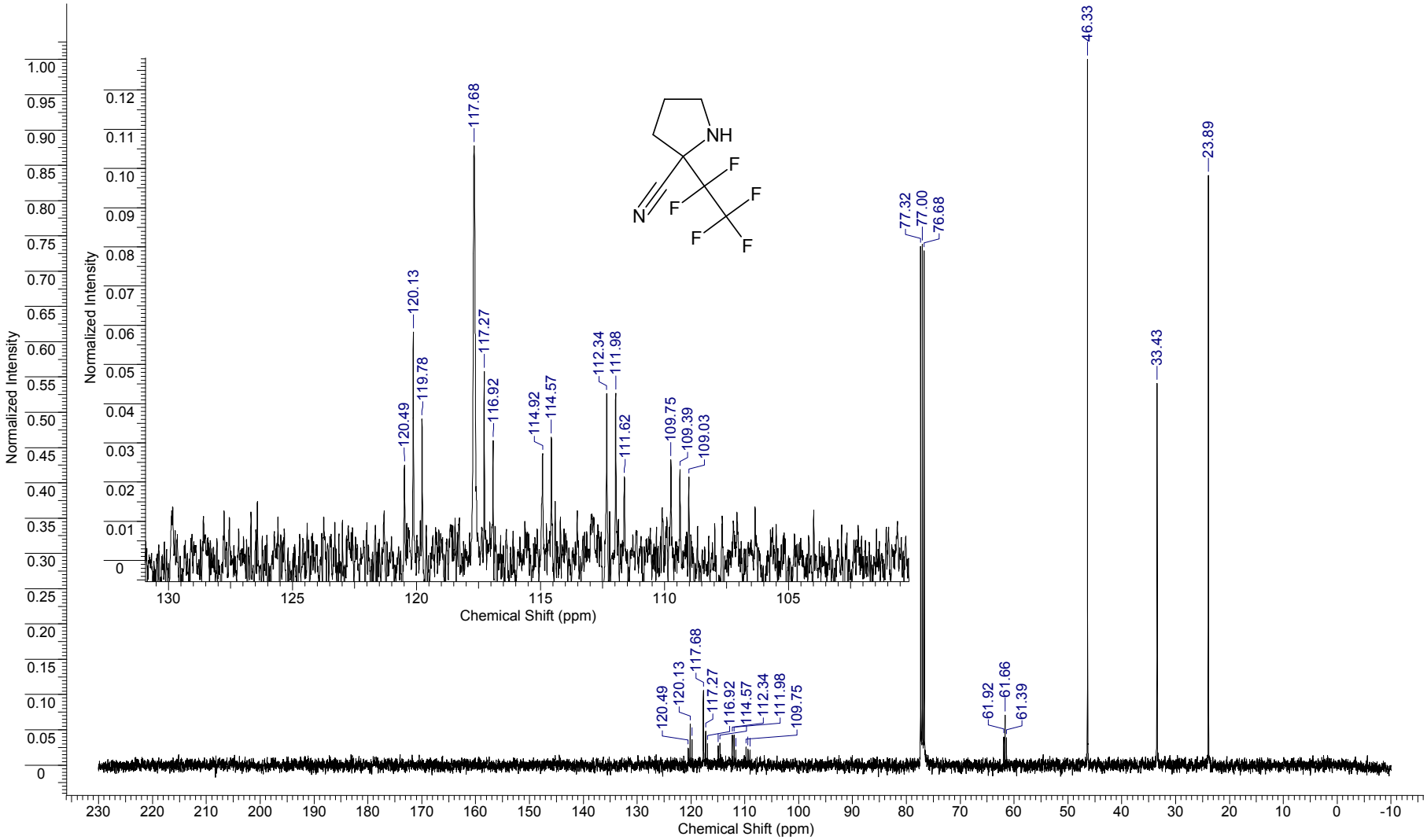
^{19}F NMR (280 MHz, $CDCl_3$) for compound **2a**



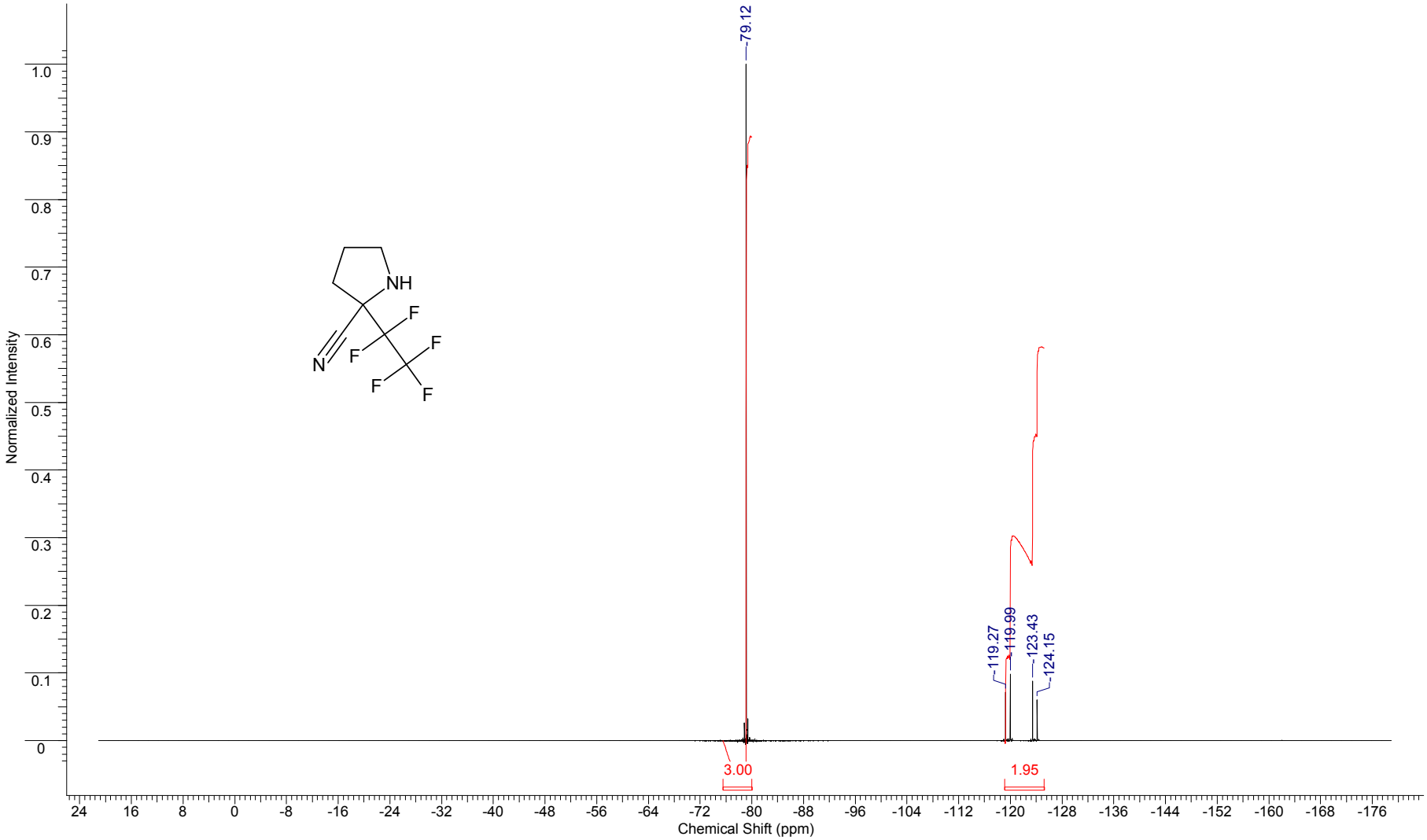
^{1}H NMR (400 MHz, $CDCl_3$) for compound **2b**



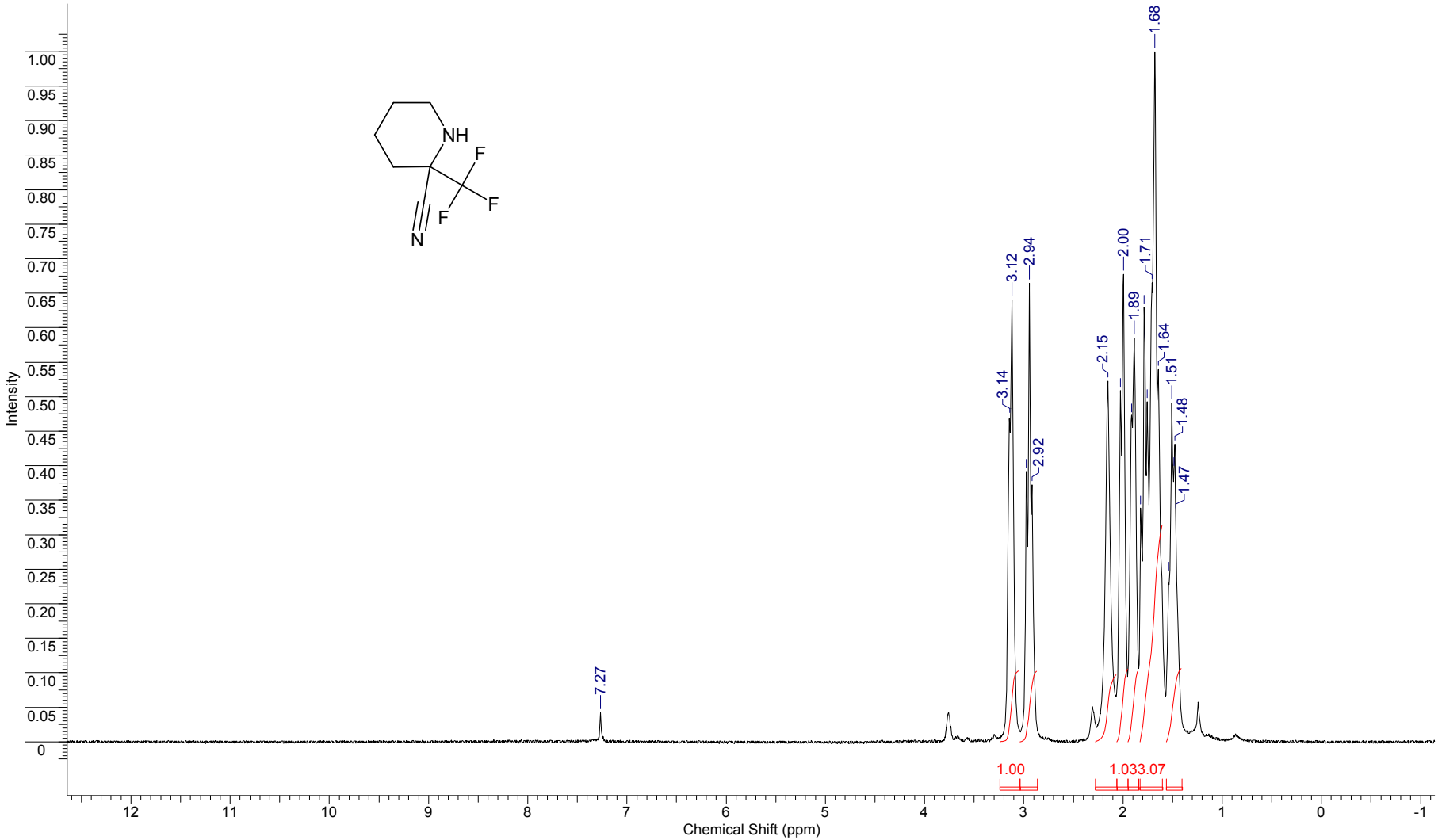
^{1}H NMR (400 MHz, $CDCl_3$) for compound **2b** aliphatic region



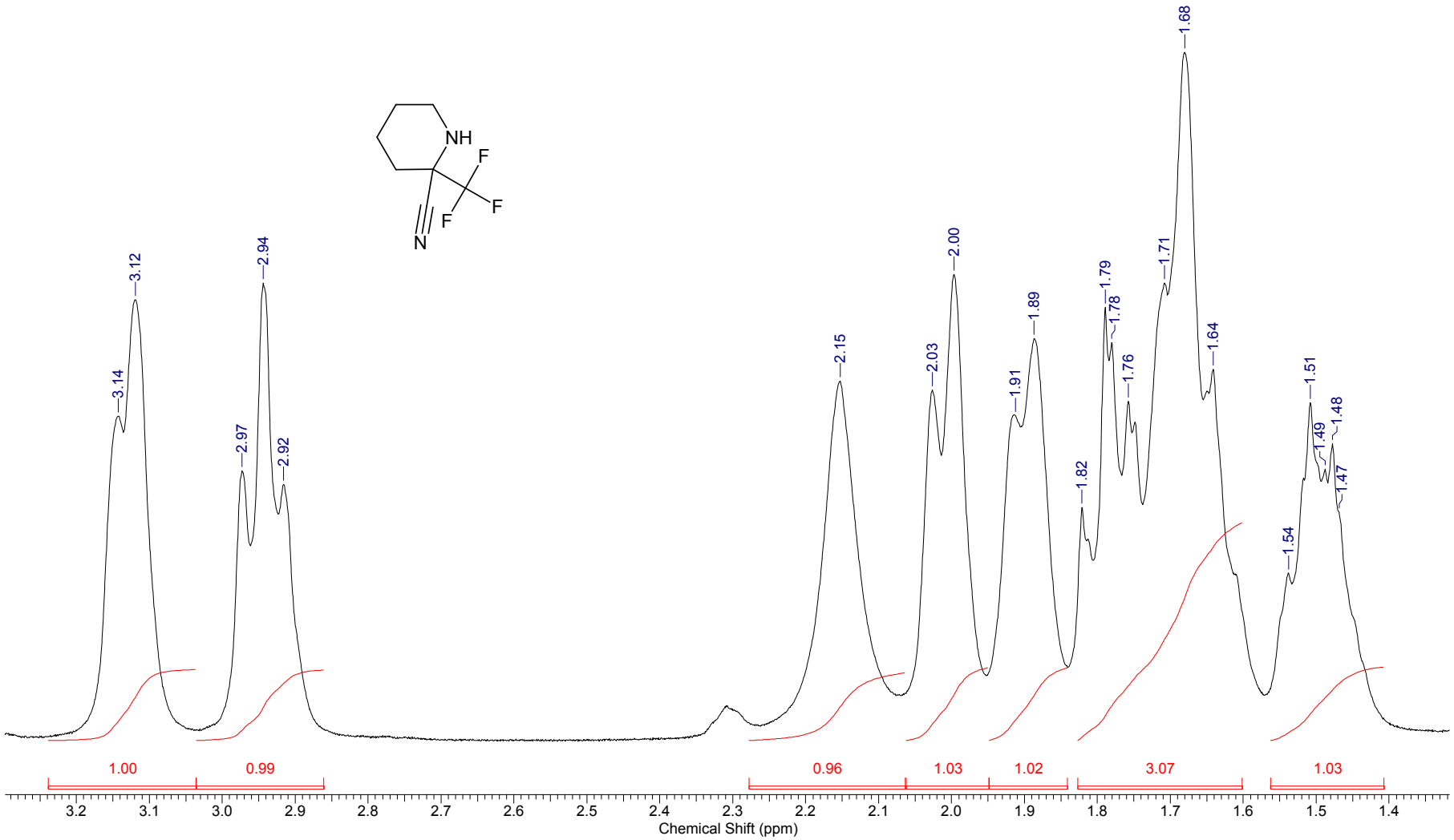
^{13}C NMR (100 MHz, $CDCl_3$) for compound **2b**



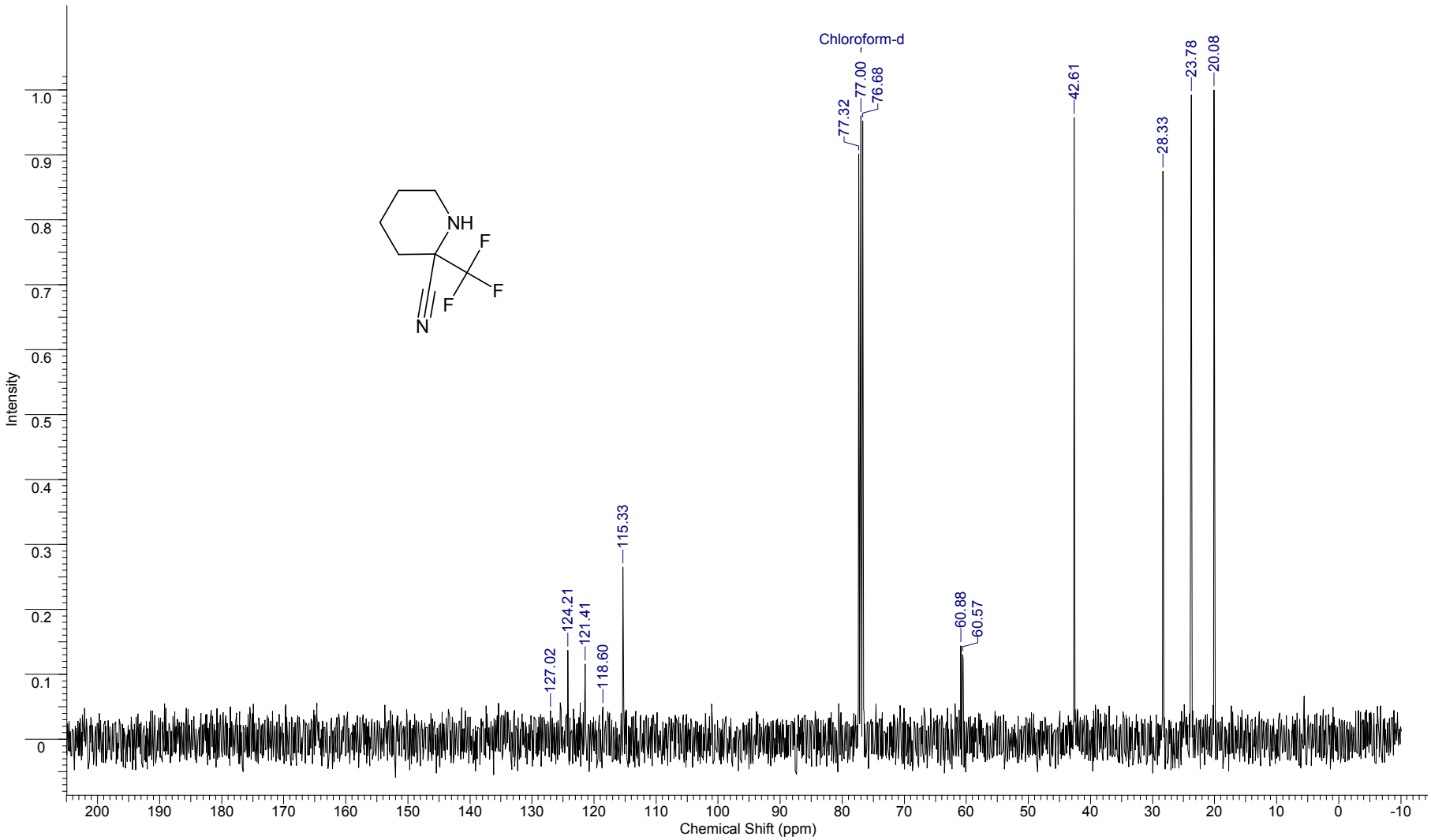
^{19}F NMR (280 MHz, $CDCl_3$) for compound **2b**



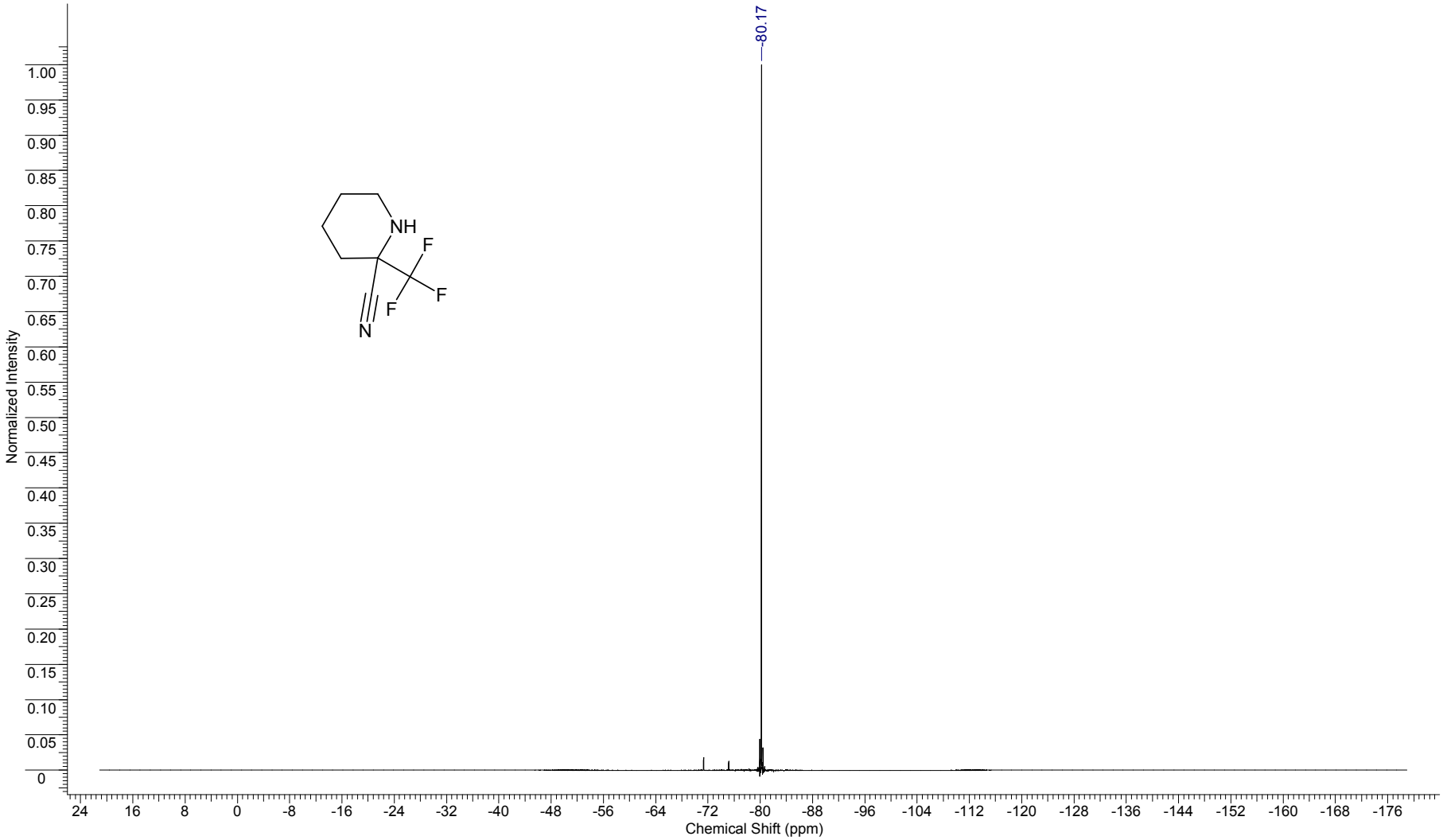
^{1}H NMR (400 MHz, $CDCl_3$) for compound **2c**



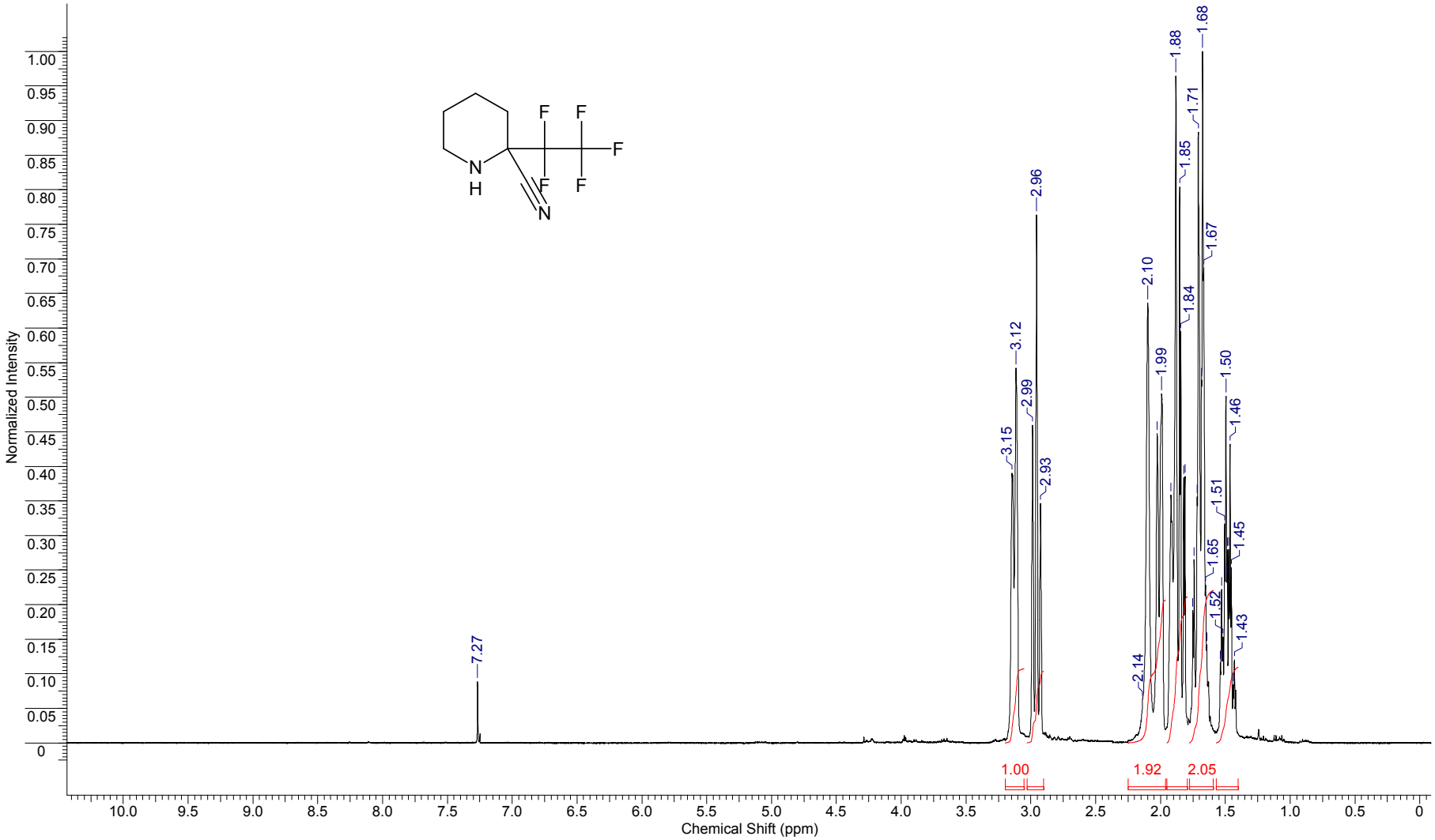
^{1}H NMR (400 MHz, $CDCl_3$) for compound **2c** aliphatic region



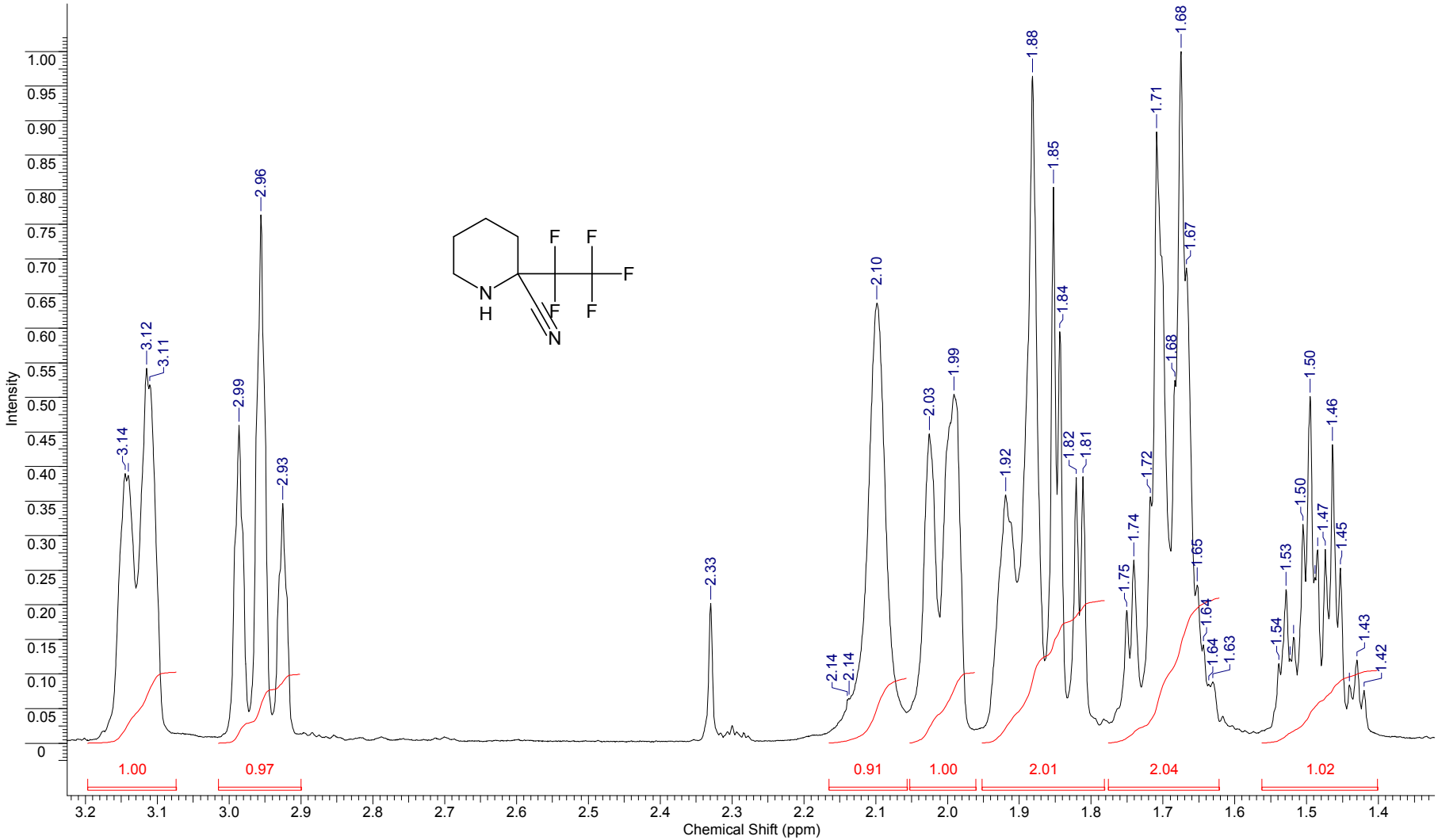
^{13}C NMR (100 MHz, $CDCl_3$) for compound **2c**



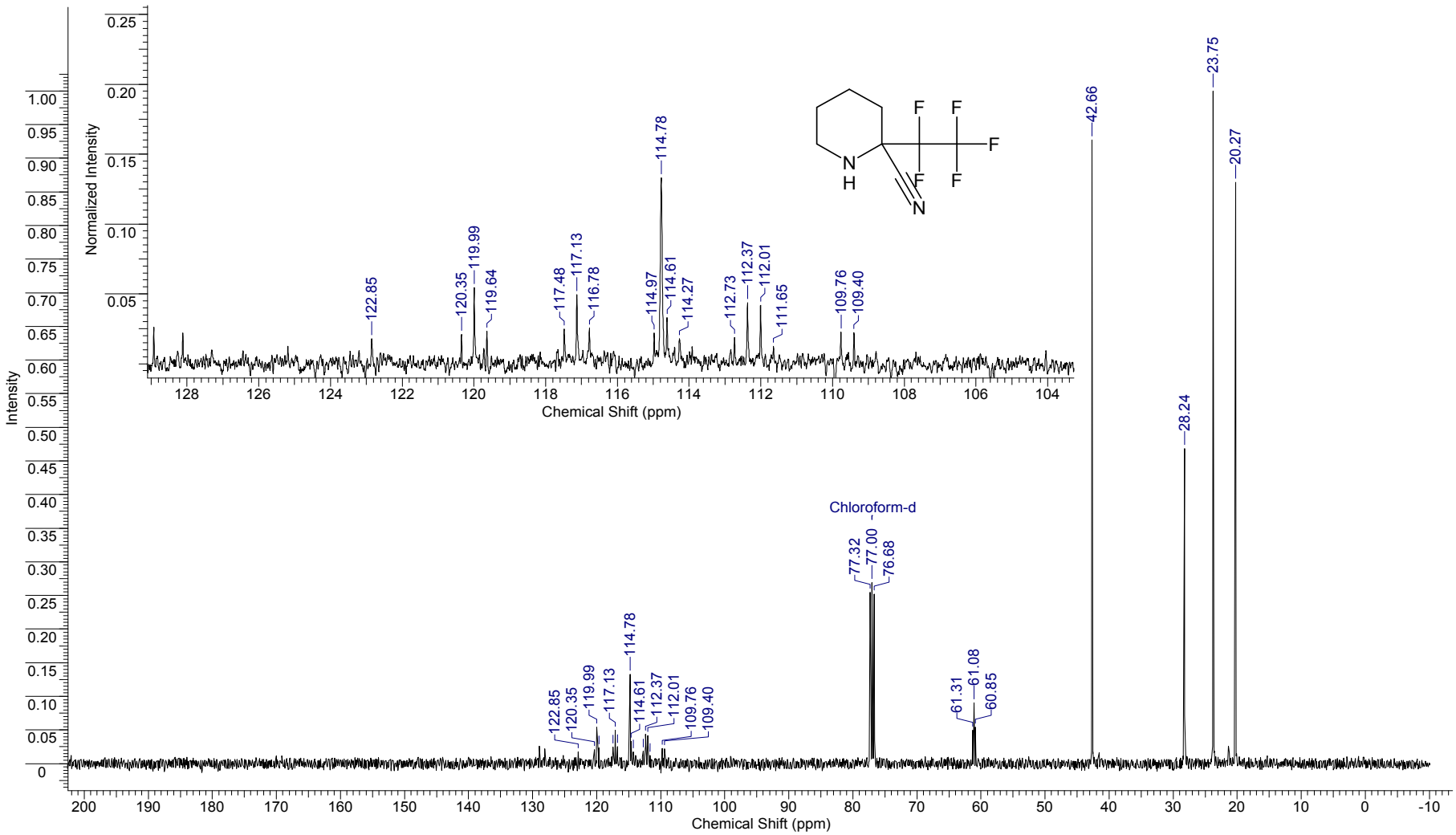
^{19}F NMR (280 MHz, $CDCl_3$) for compound **2c**



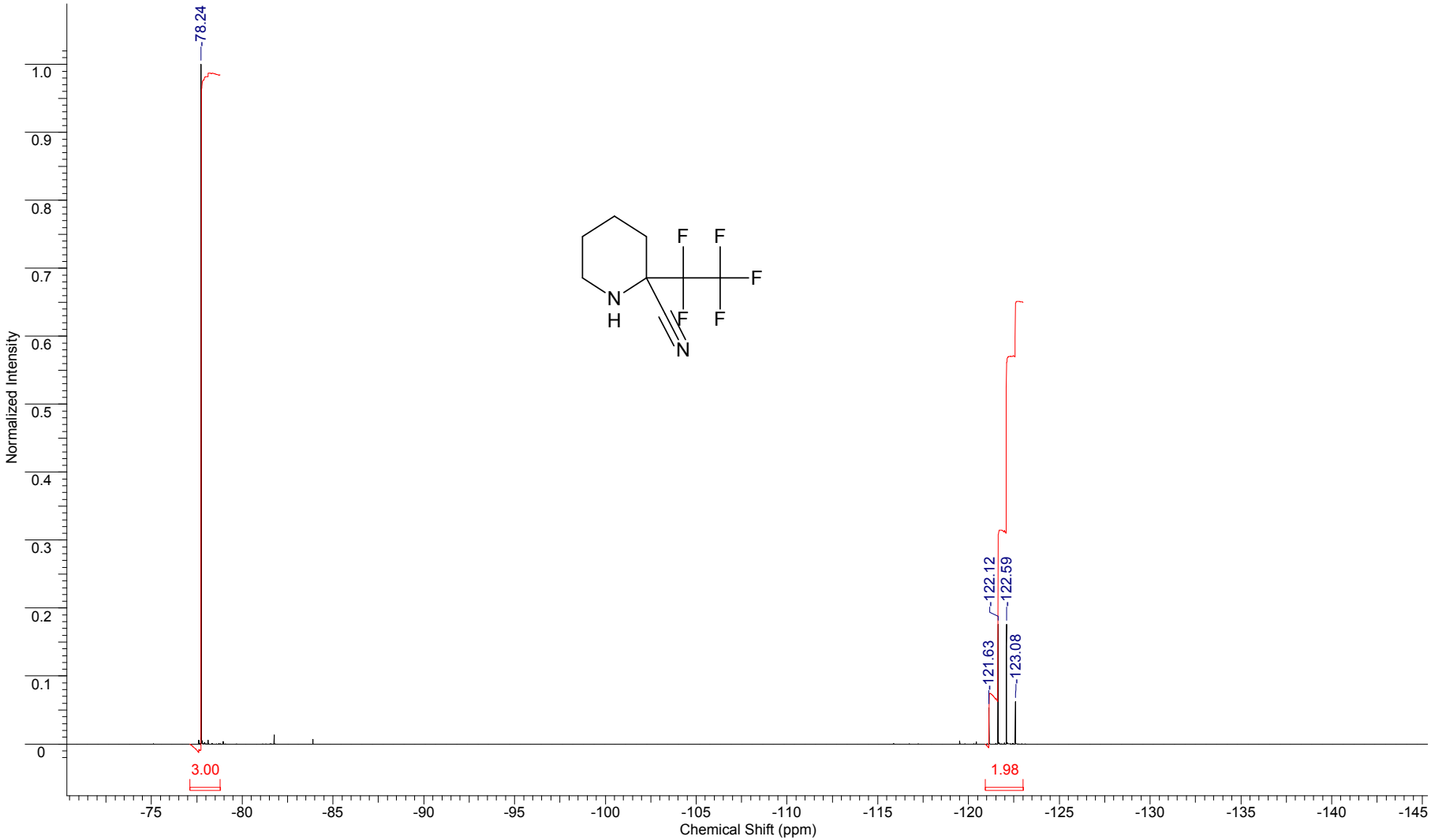
^{1}H NMR (400 MHz, $CDCl_3$) for compound **2d**



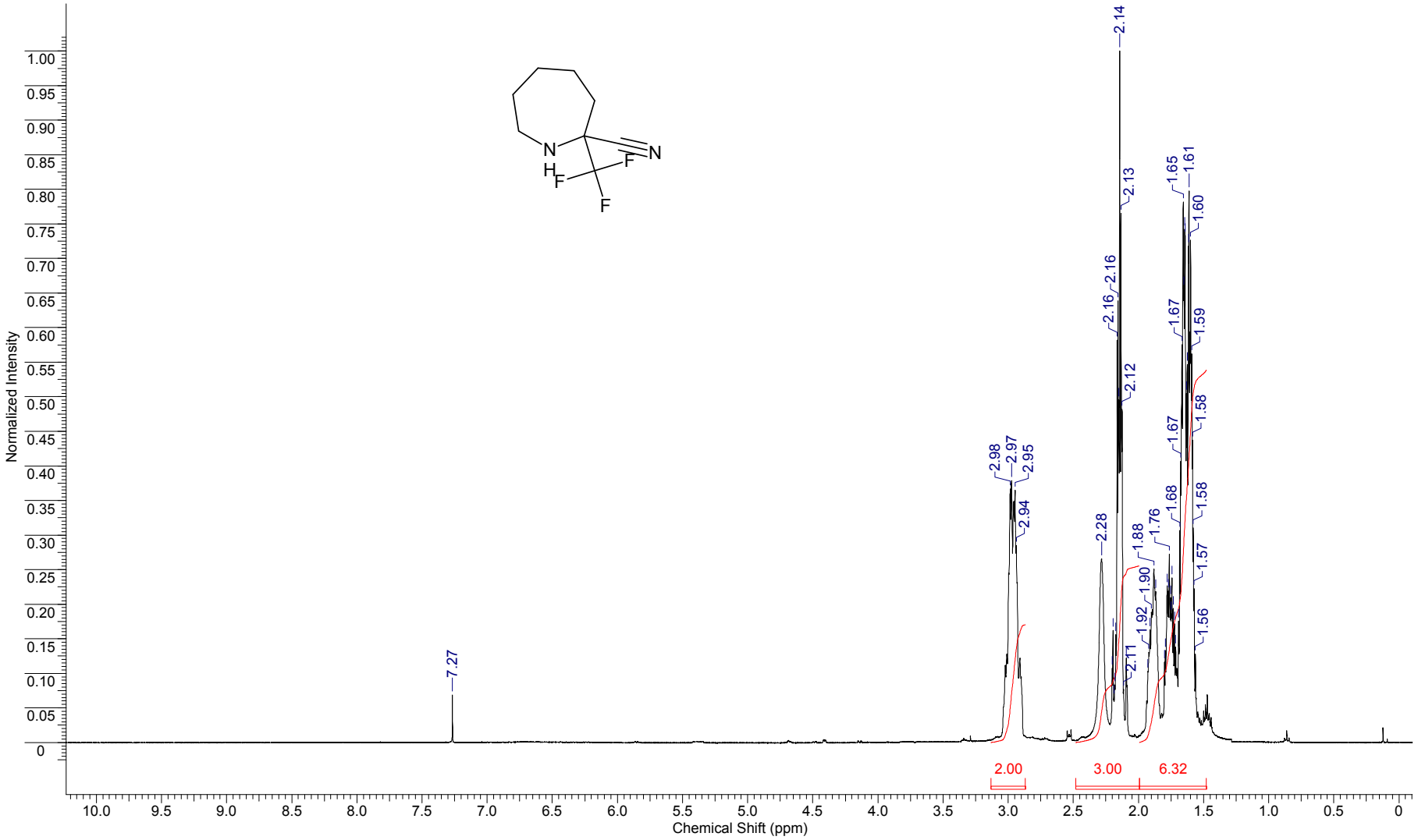
^{1}H NMR (400 MHz, $CDCl_3$) for compound **2d** aliphatic region



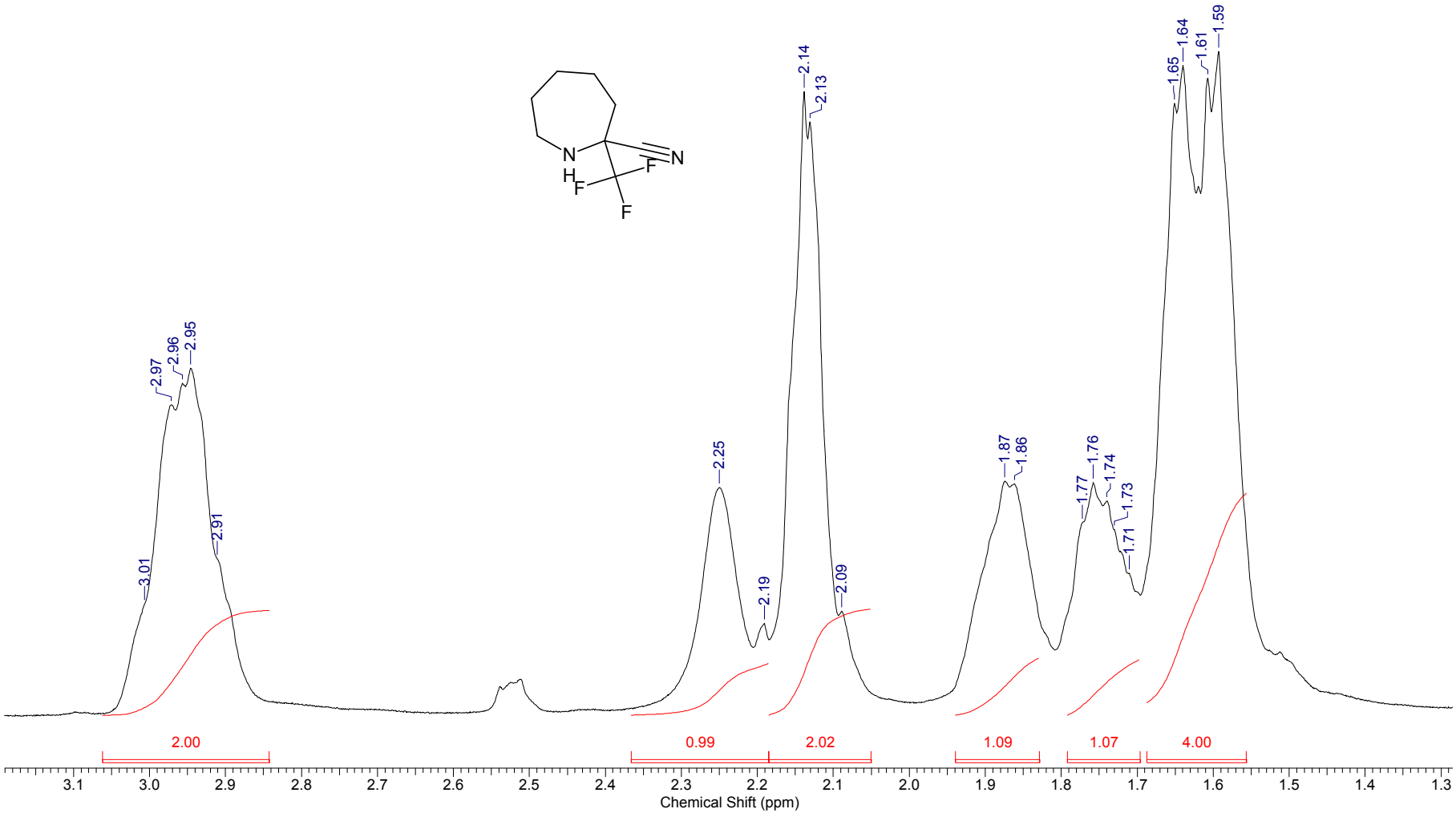
^{13}C NMR (100 MHz, $CDCl_3$) for compound **2d**



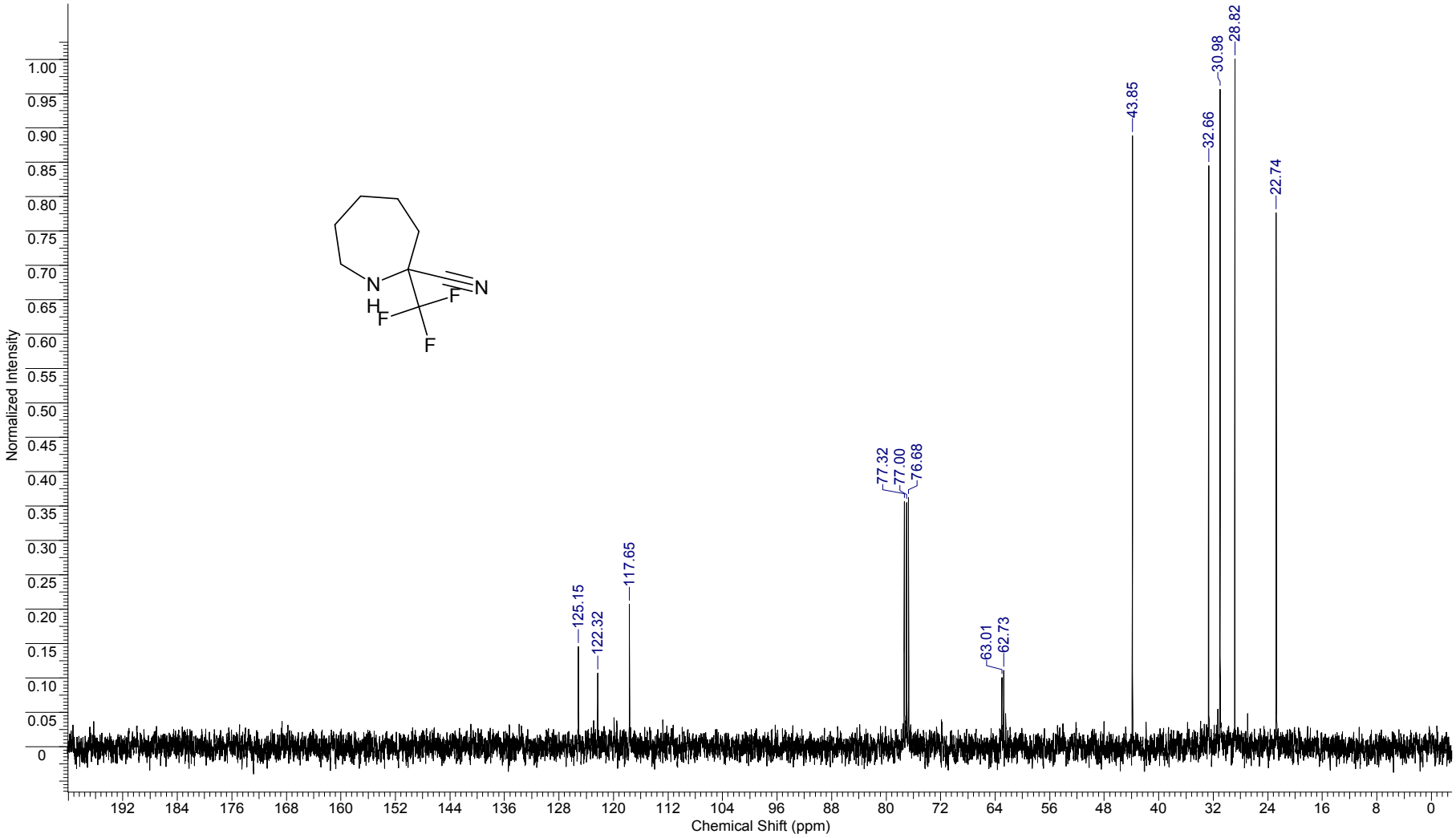
^{19}F NMR (280 MHz, $CDCl_3$) for compound **2d**



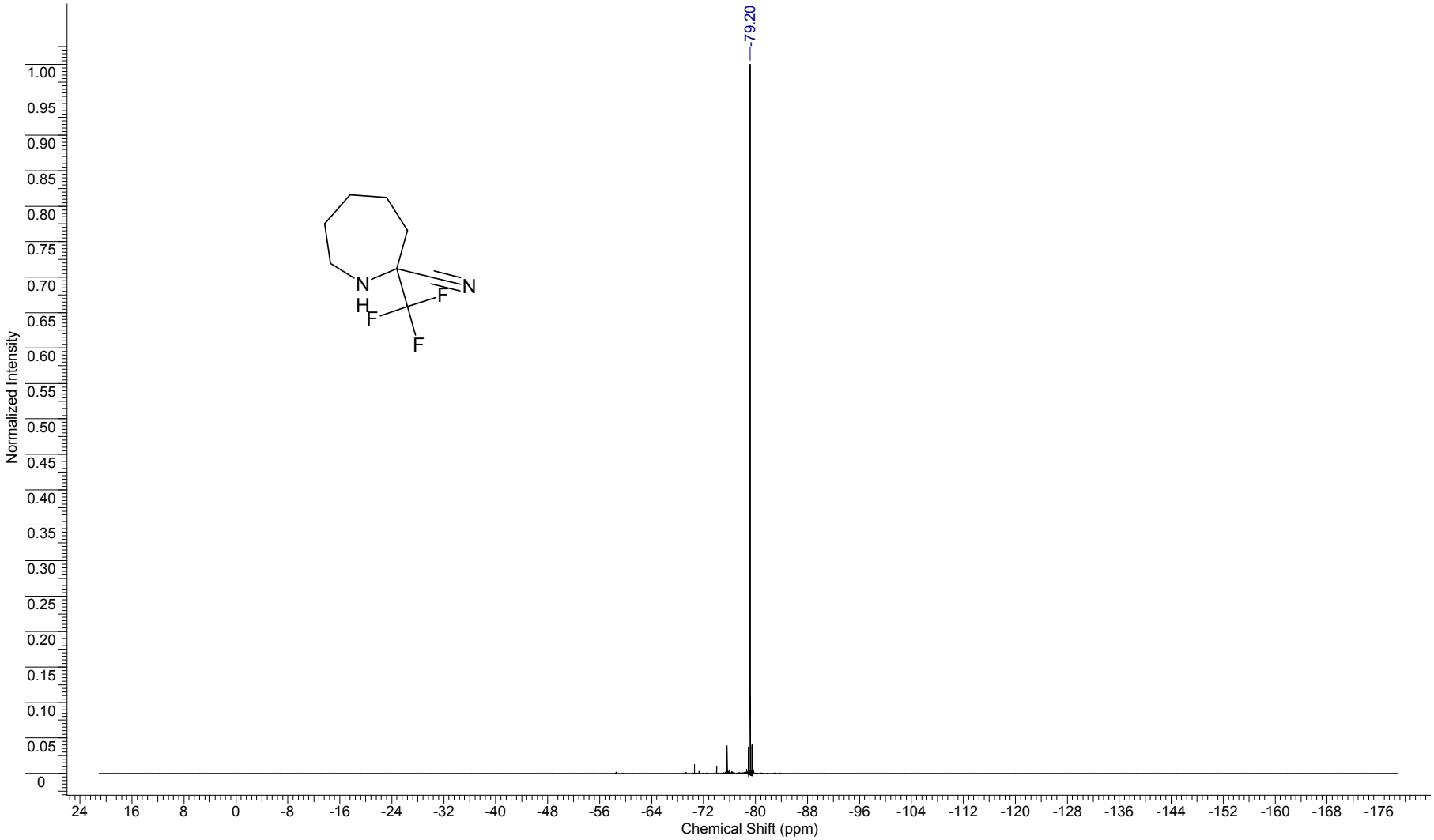
^{1}H NMR (400 MHz, $CDCl_3$) for compound **2e**



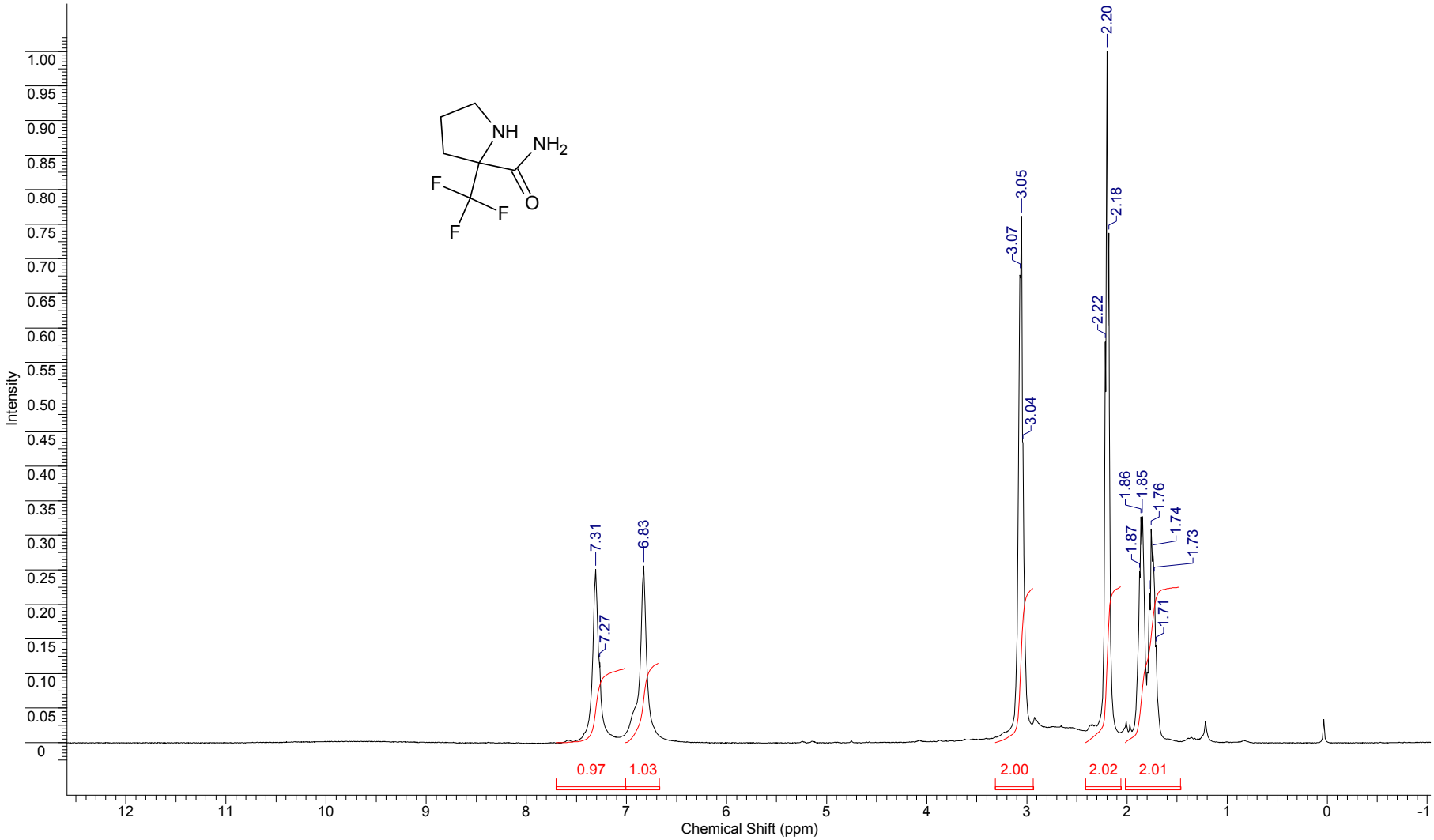
^{1}H NMR (400 MHz, $CDCl_3$) for compound **2e** aliphatic region



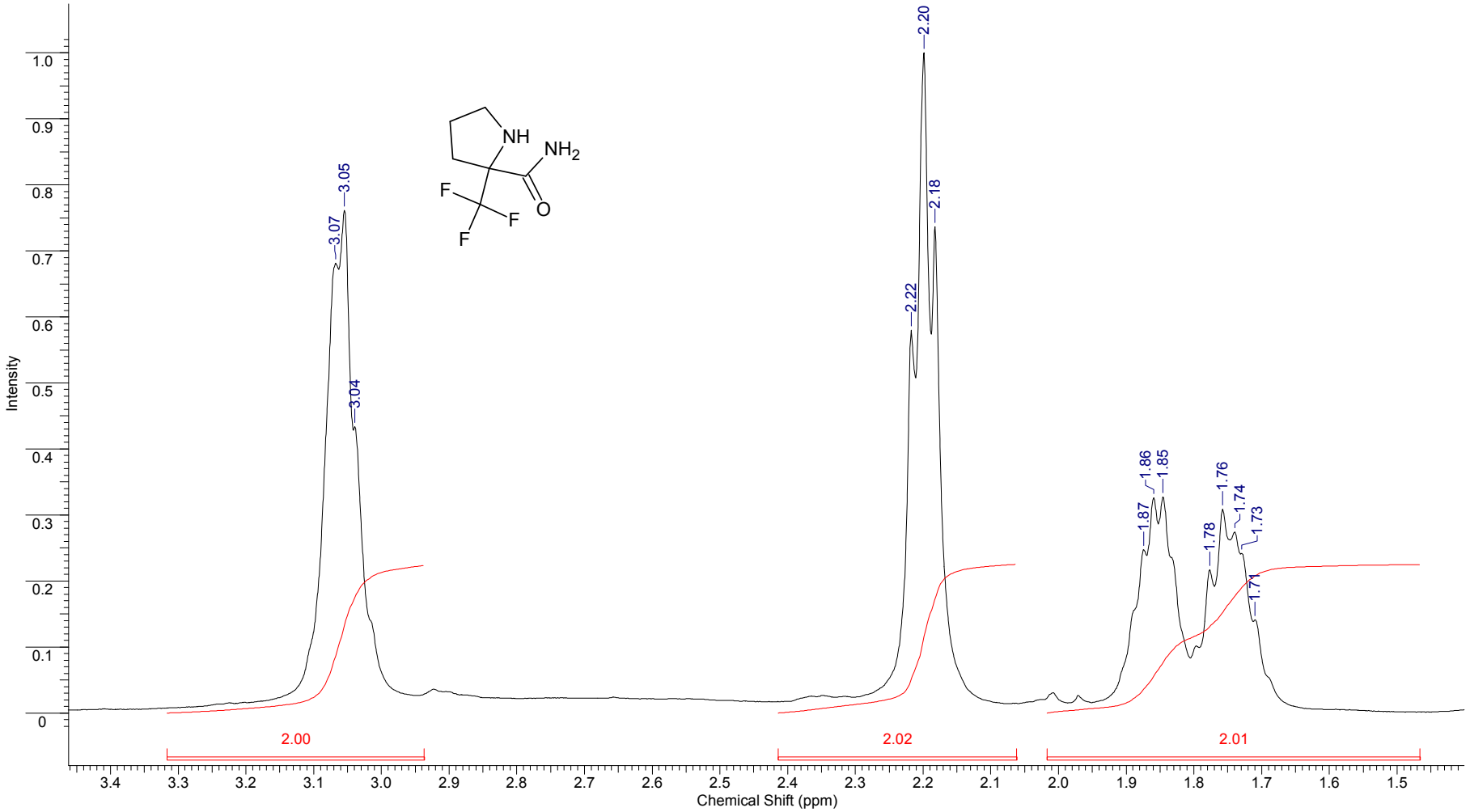
^{13}C NMR (100 MHz, $CDCl_3$) for compound **2e**



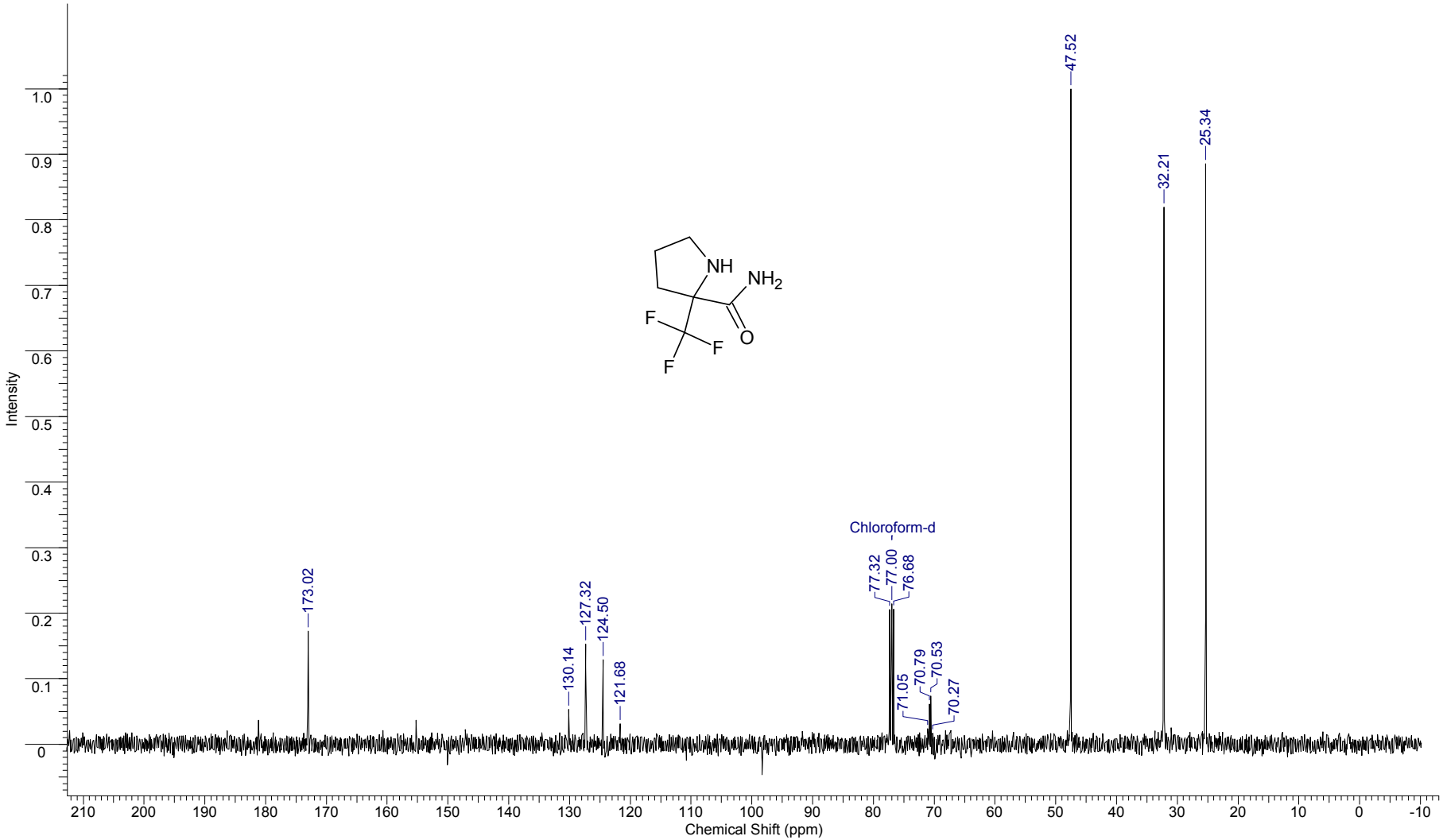
^{19}F NMR (280 MHz, $CDCl_3$) for compound **2e**



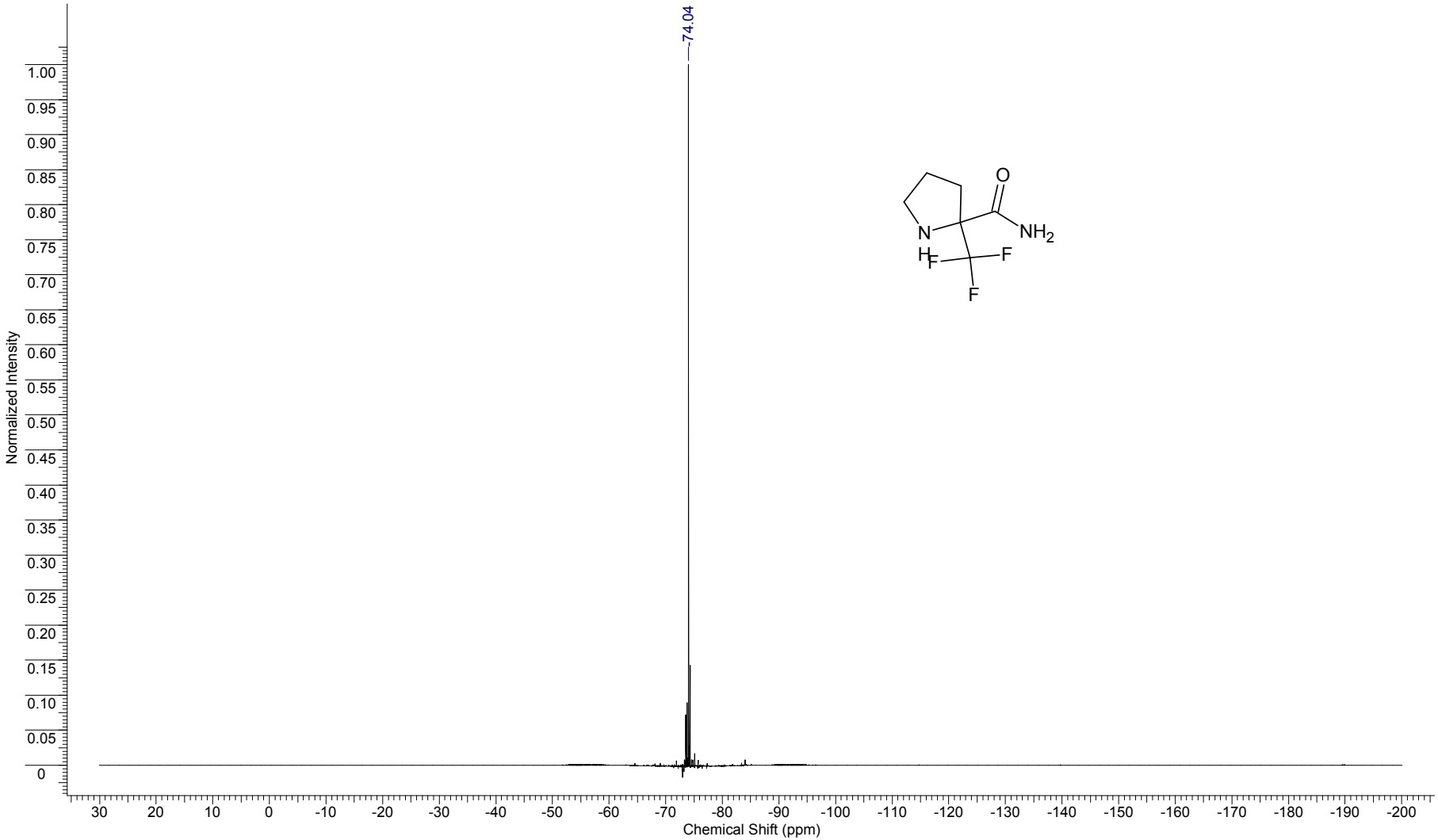
^{1}H NMR (400 MHz, $CDCl_3$) for compound **3a**



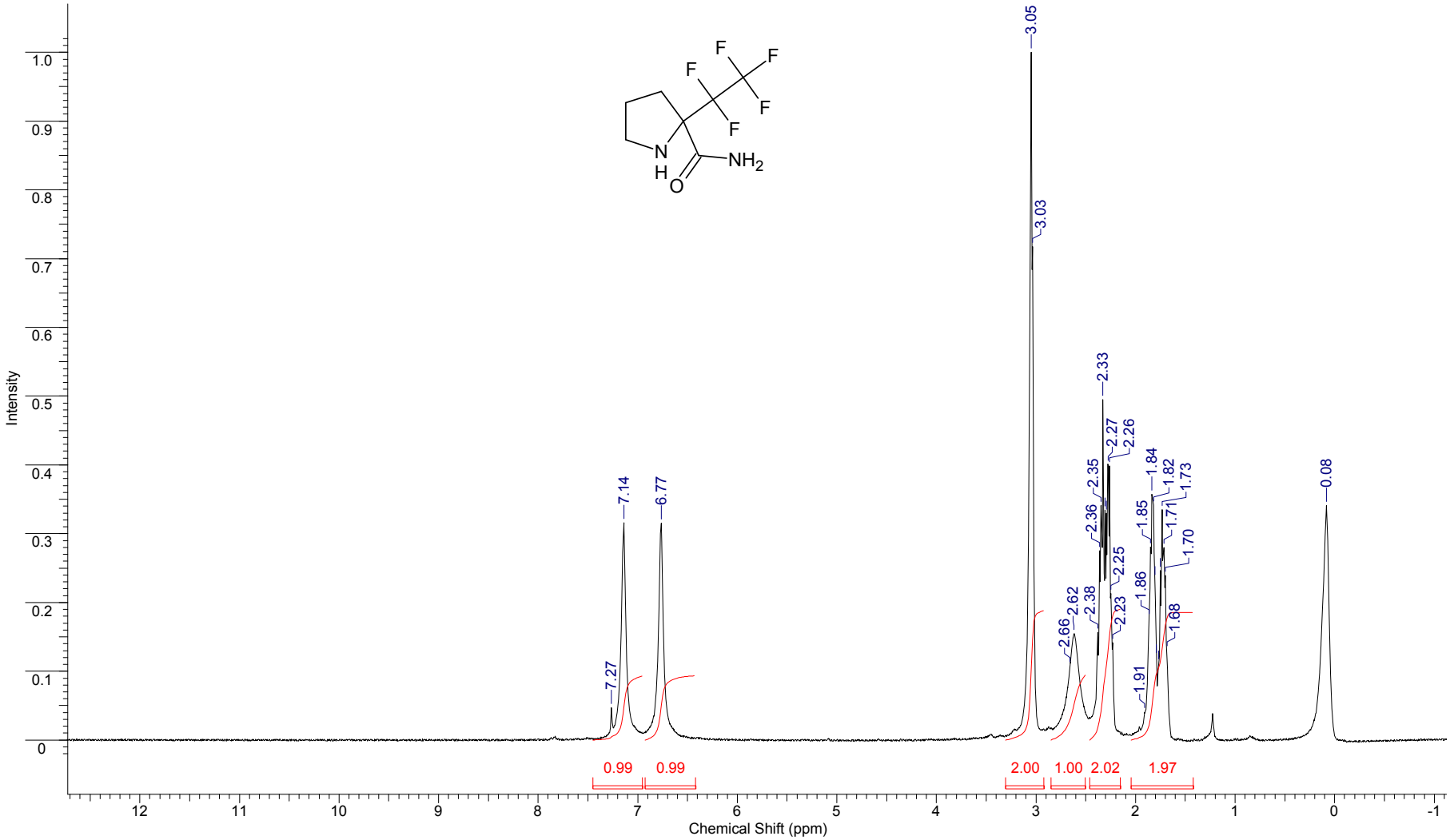
^{1}H NMR (400 MHz, $CDCl_3$) for compound **3a** aliphatic region



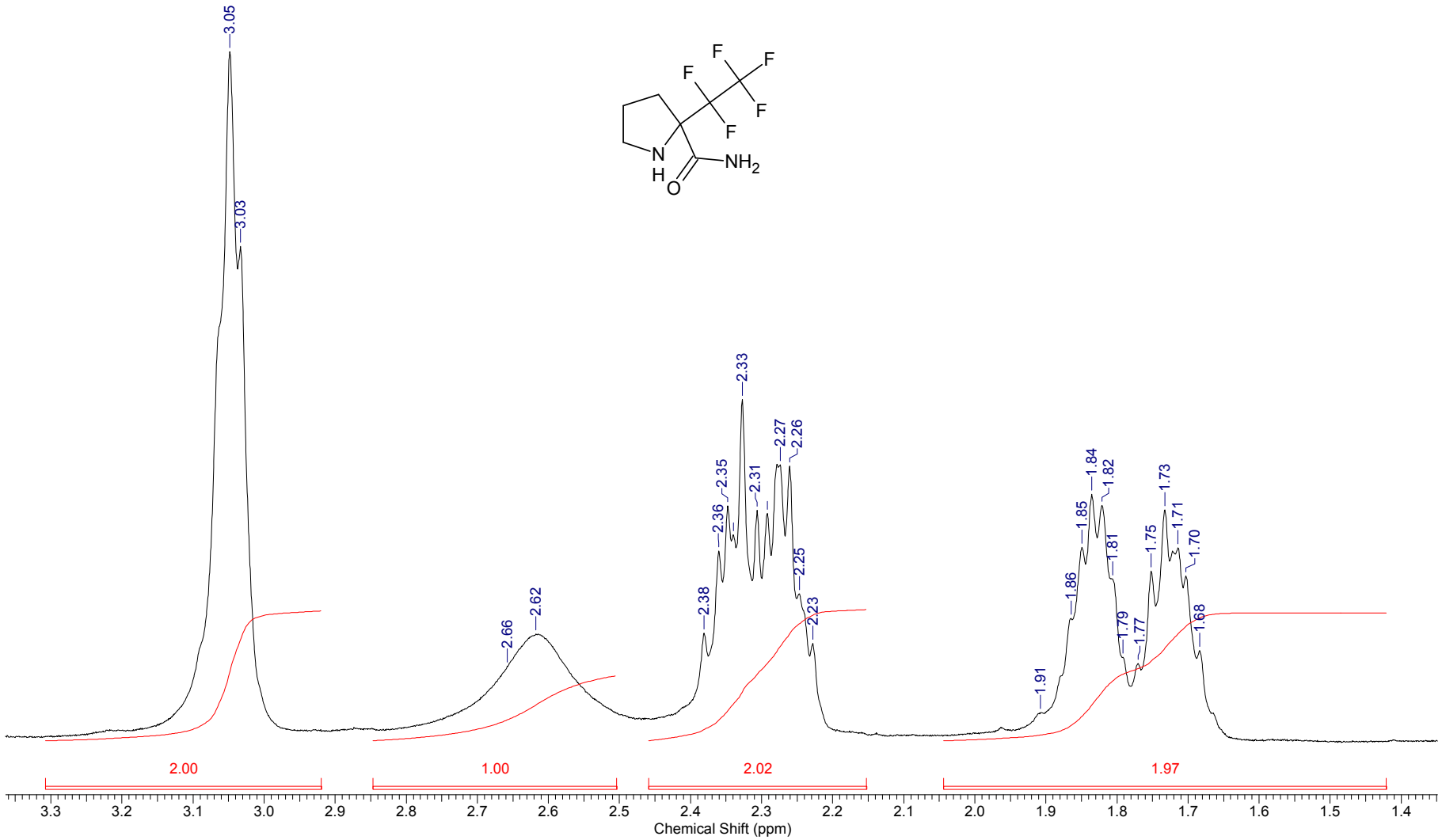
^{13}C NMR (100 MHz, $CDCl_3$) for compound **3a**



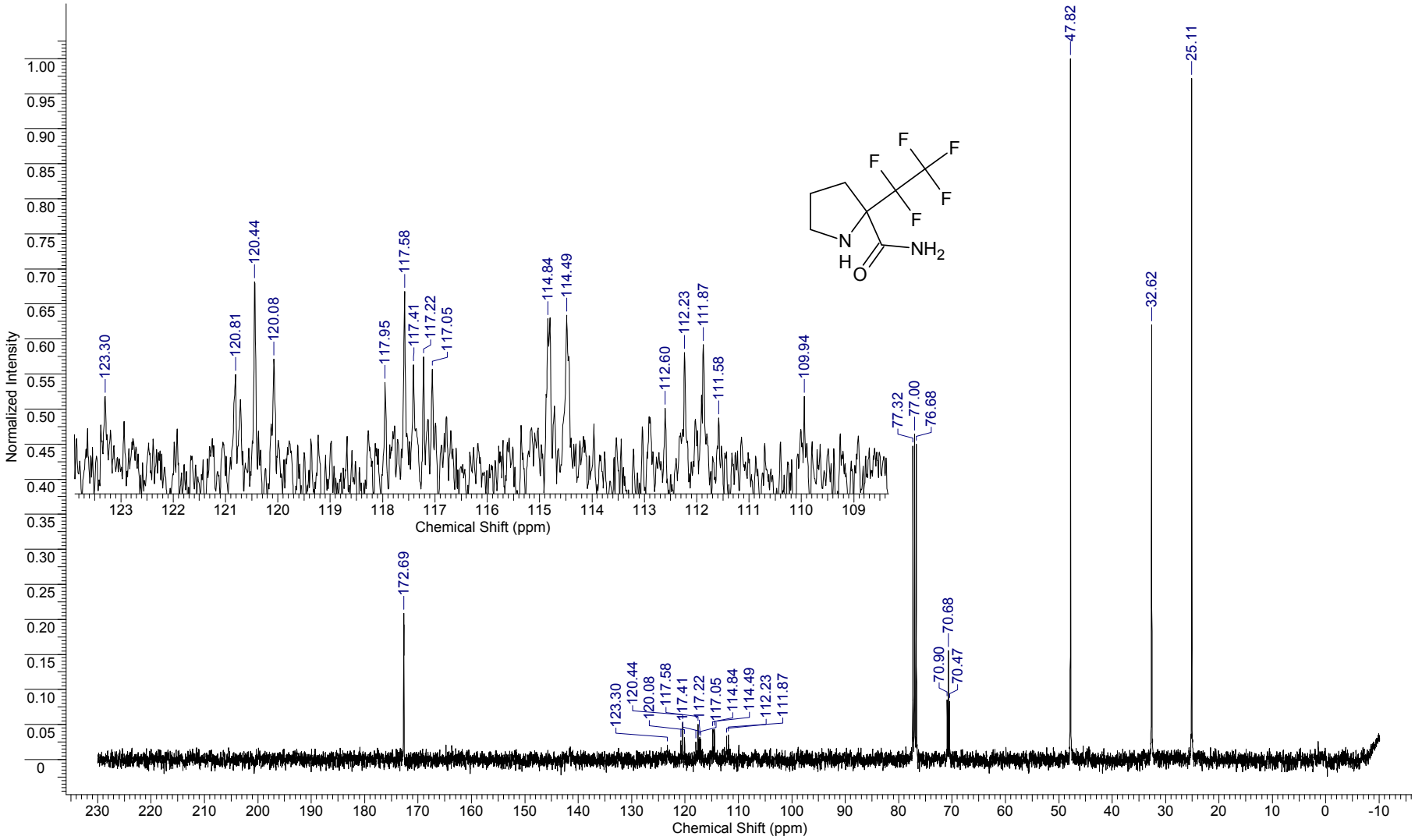
^{19}F NMR (280 MHz, $CDCl_3$) for compound **3a**



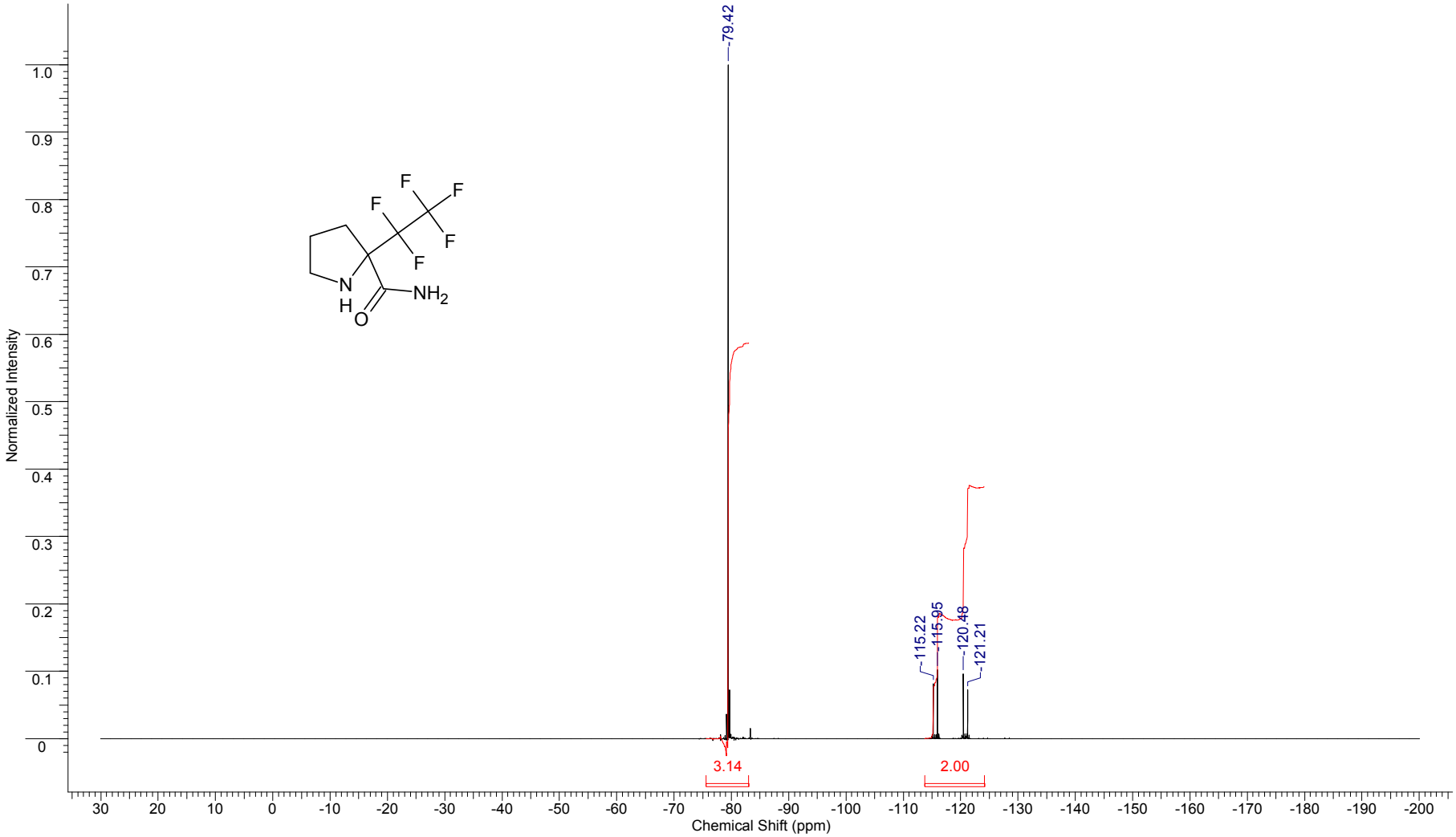
^{1}H NMR (400 MHz, $CDCl_3$) for compound **3b**



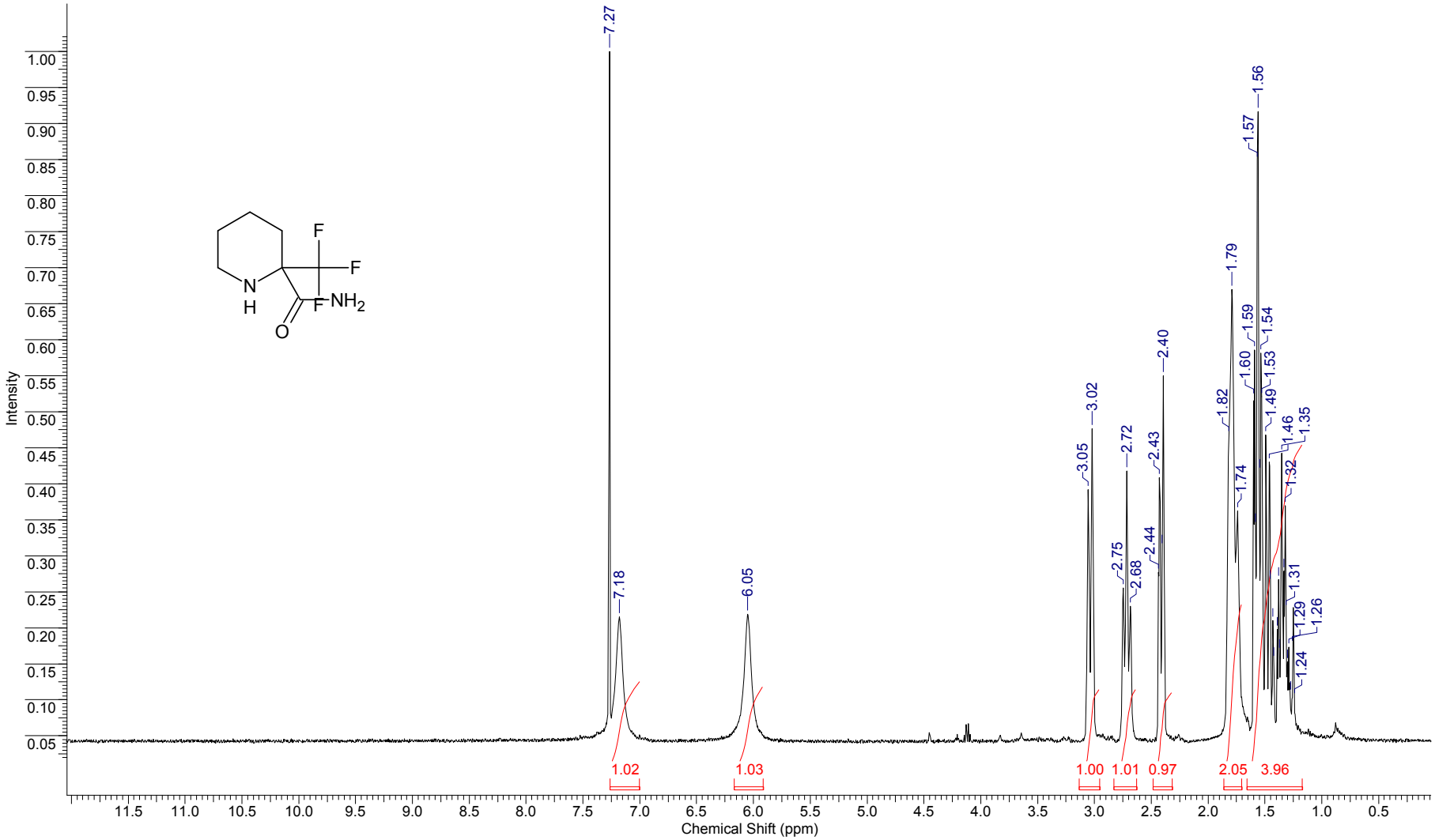
^{1}H NMR (400 MHz, $CDCl_3$) for compound **3b** aliphatic region



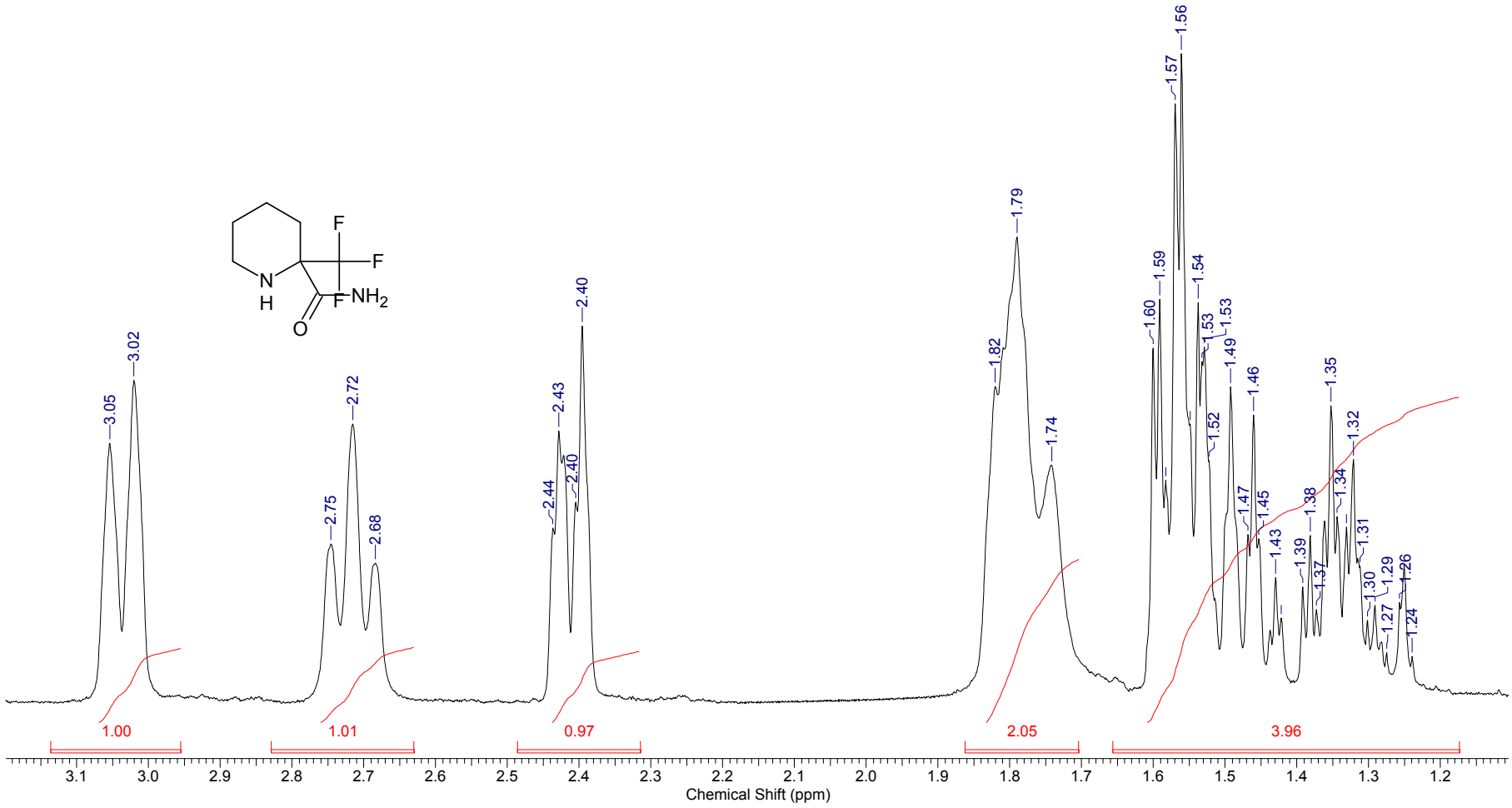
^{13}C NMR (100 MHz, $CDCl_3$) for compound **3b**



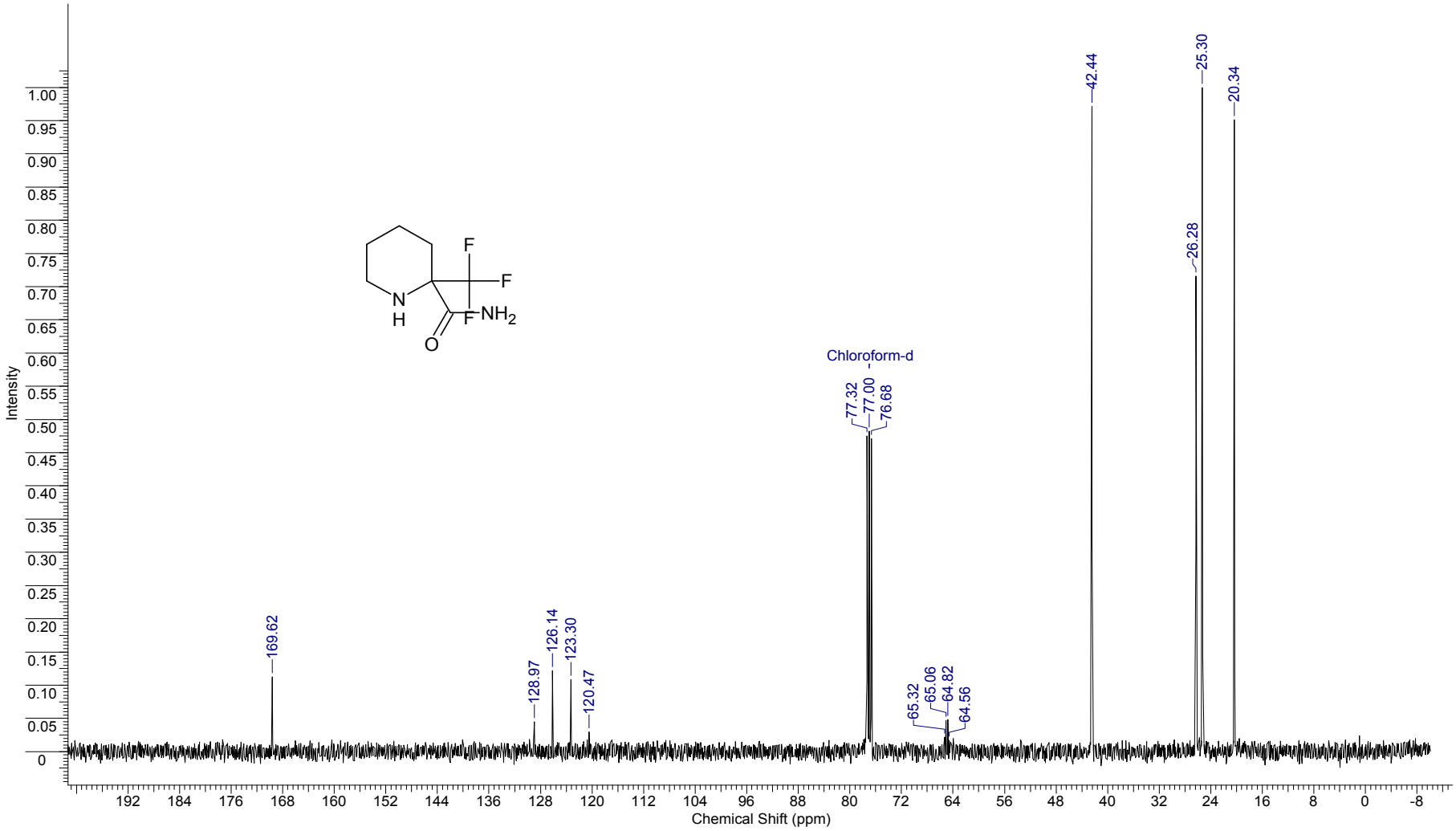
^{19}F NMR (280 MHz, $CDCl_3$) for compound **3b**



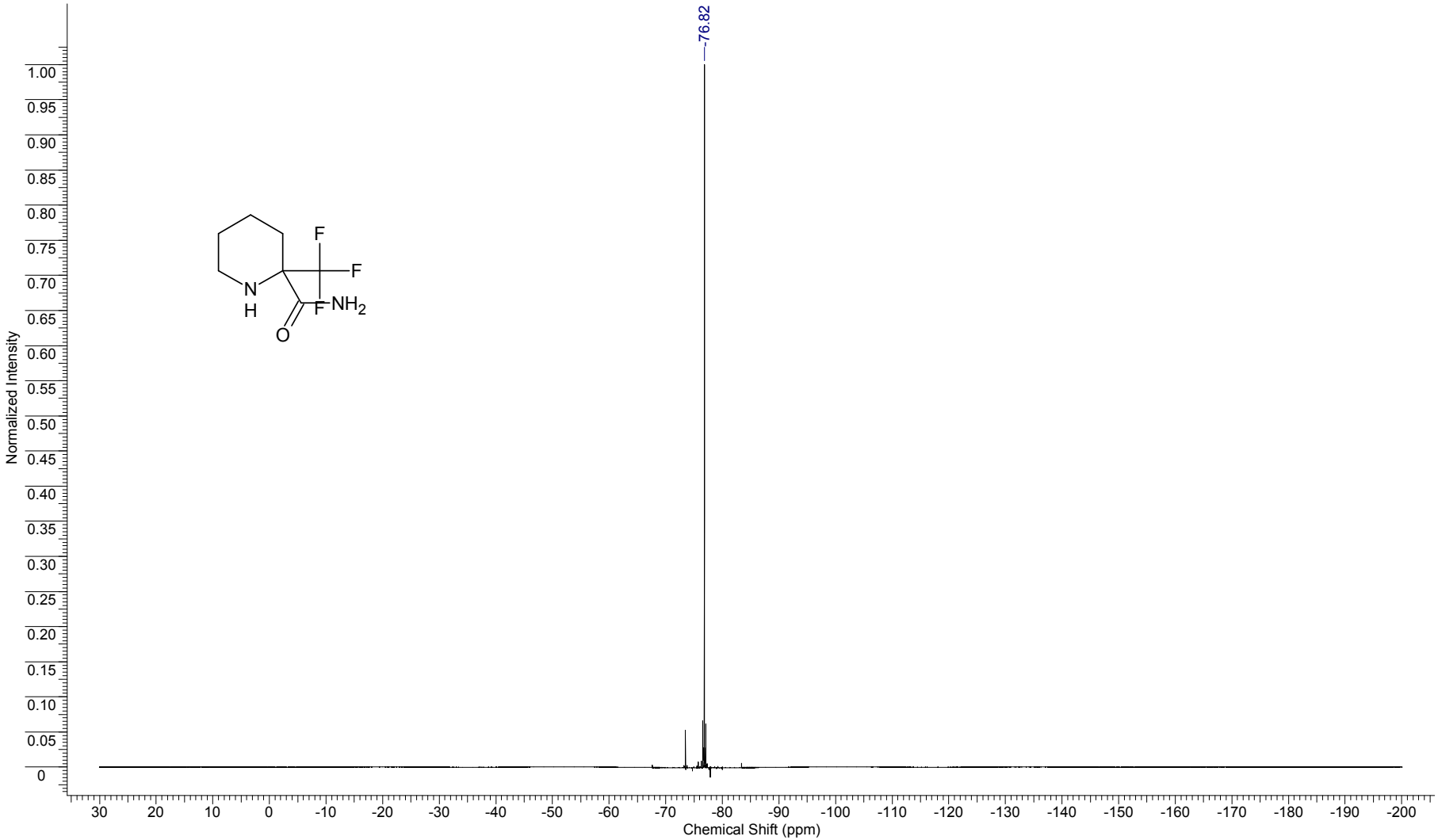
^{1}H NMR (400 MHz, $CDCl_3$) for compound **3c**



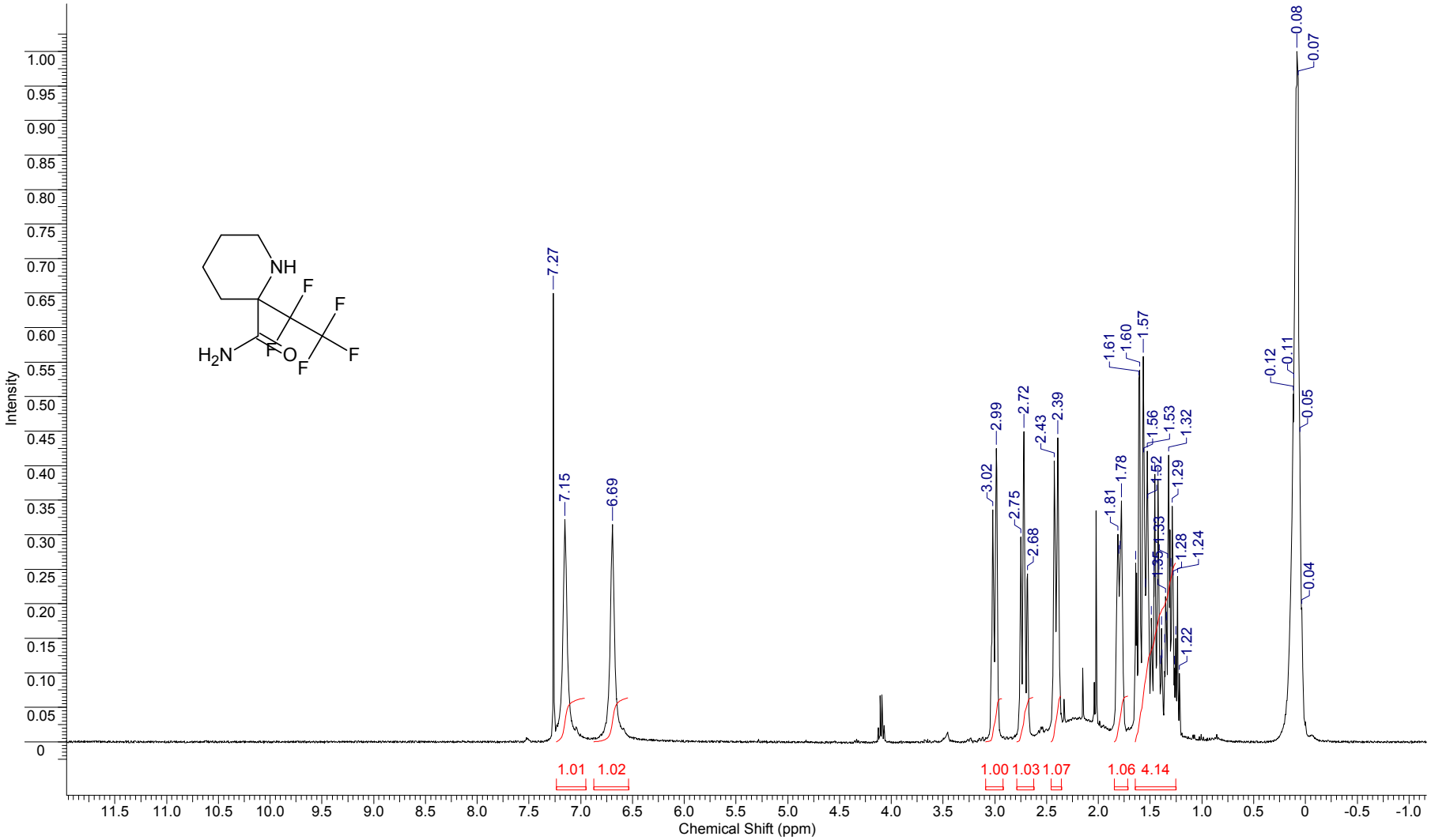
^{1}H NMR (400 MHz, $CDCl_3$) for compound **3c** aliphatic region



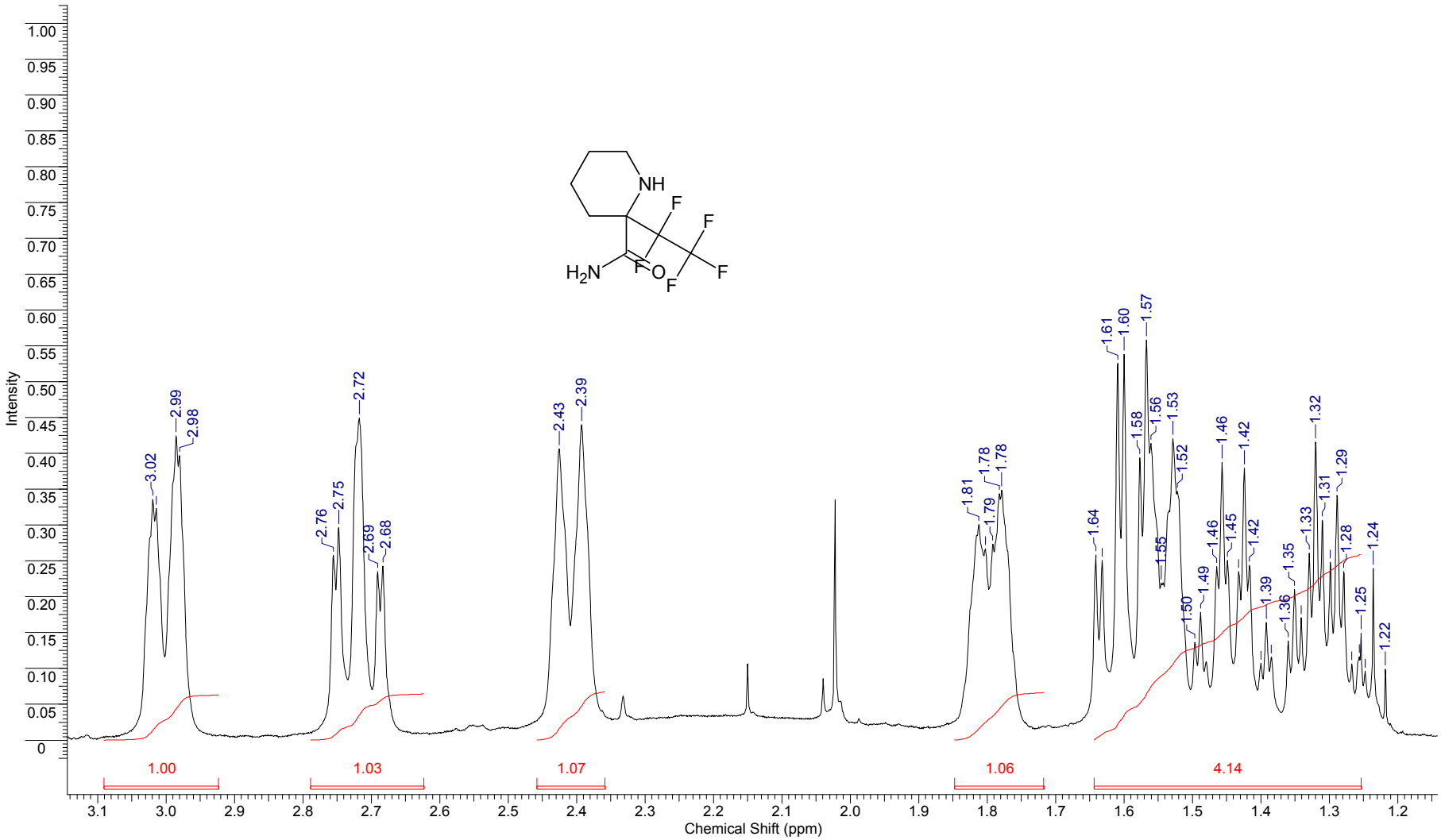
^{13}C NMR (100 MHz, $CDCl_3$) for compound **3c**



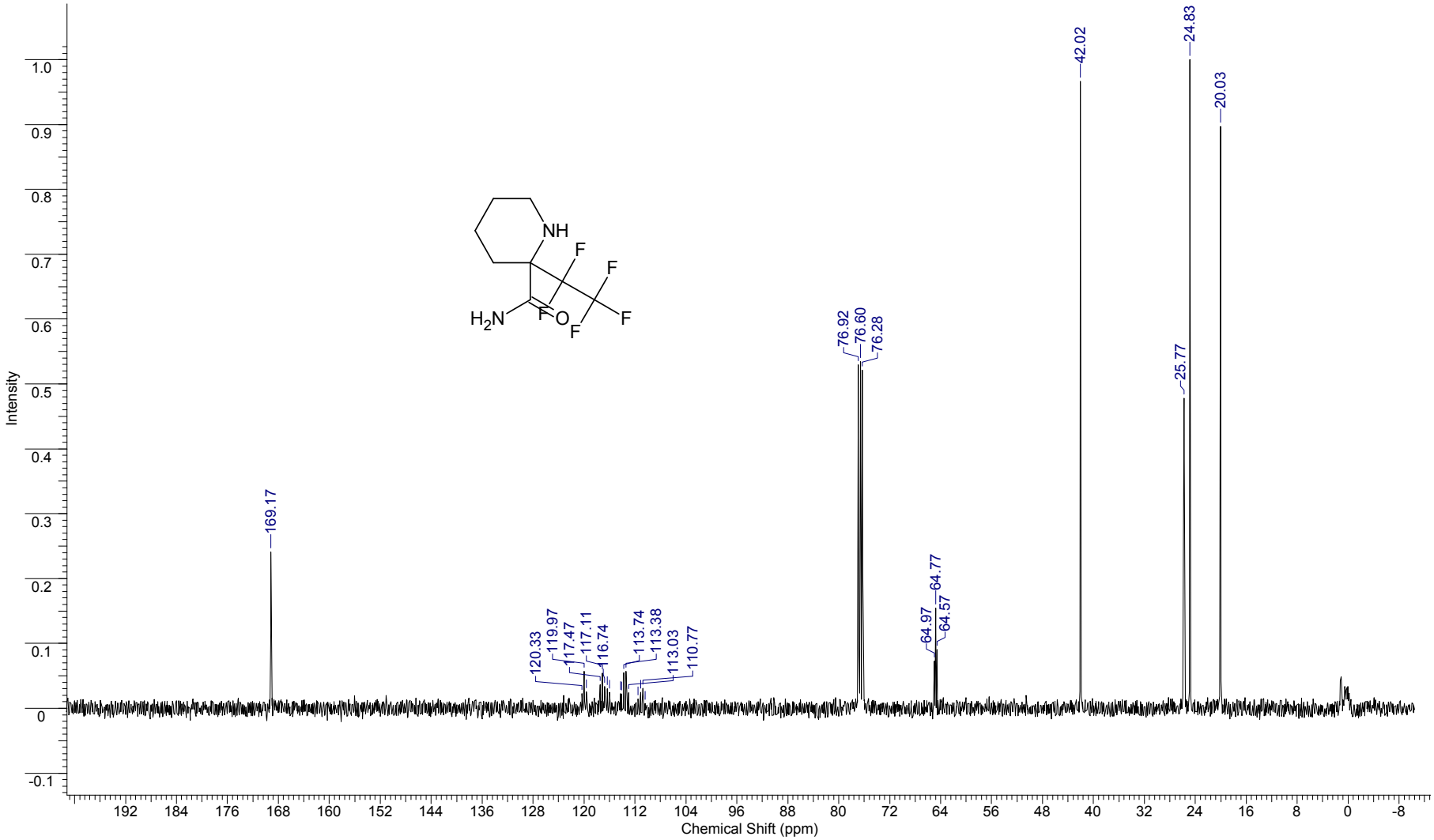
^{19}F NMR (280 MHz, $CDCl_3$) for compound **3c**



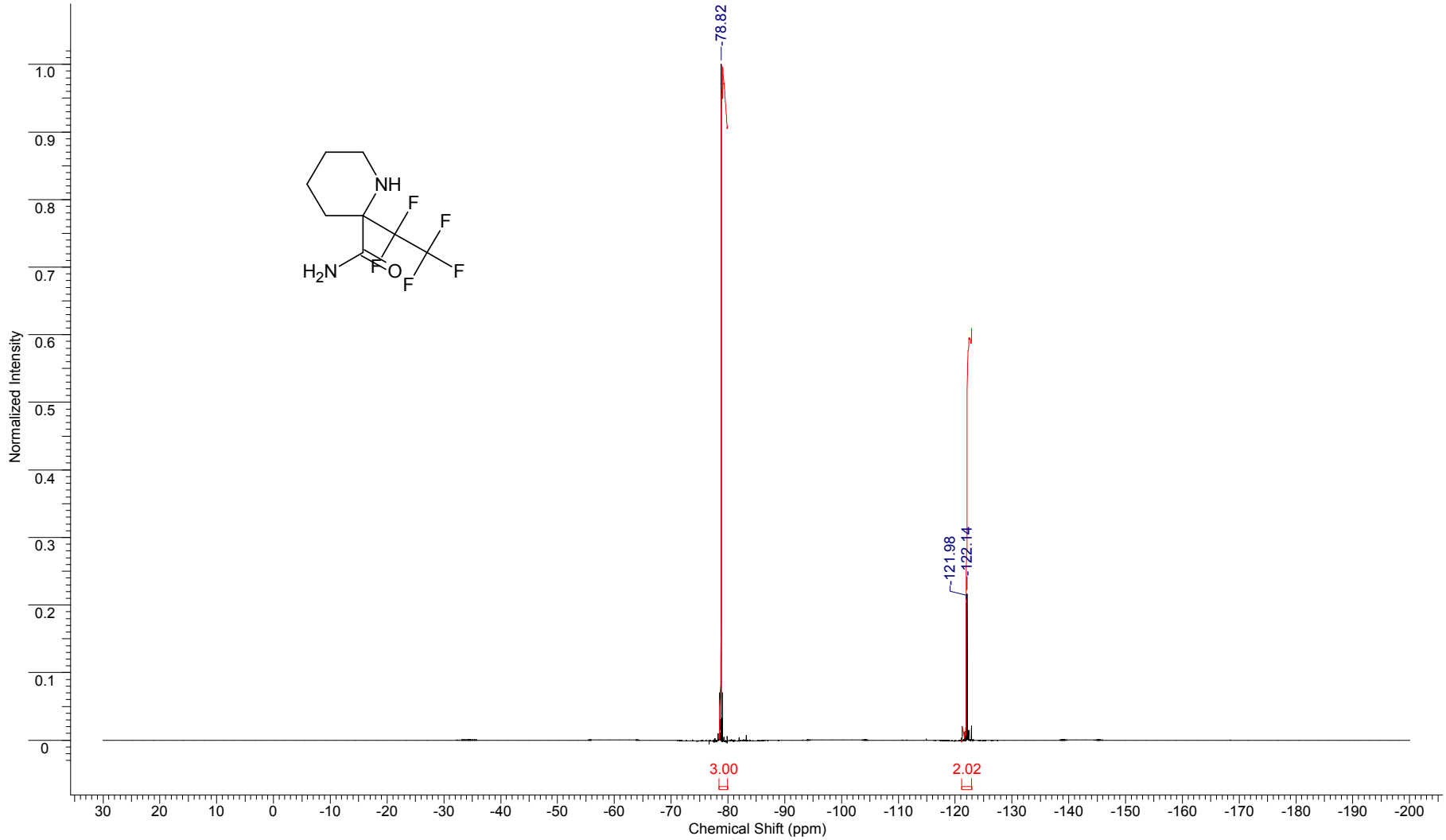
^{1}H NMR (400 MHz, $CDCl_3$) for compound **3d**



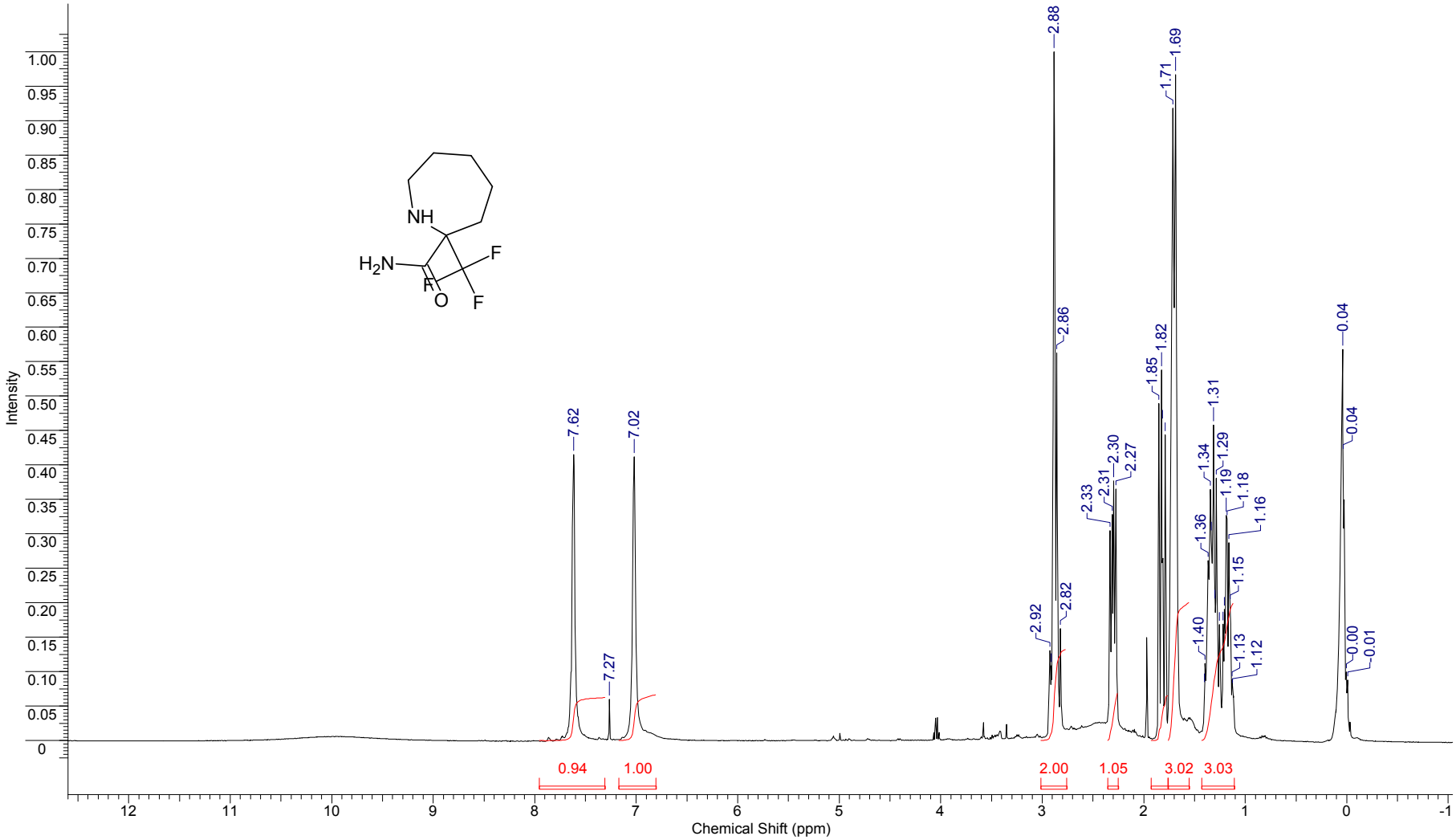
^{1}H NMR (400 MHz, $CDCl_3$) for compound **3d** aliphatic region



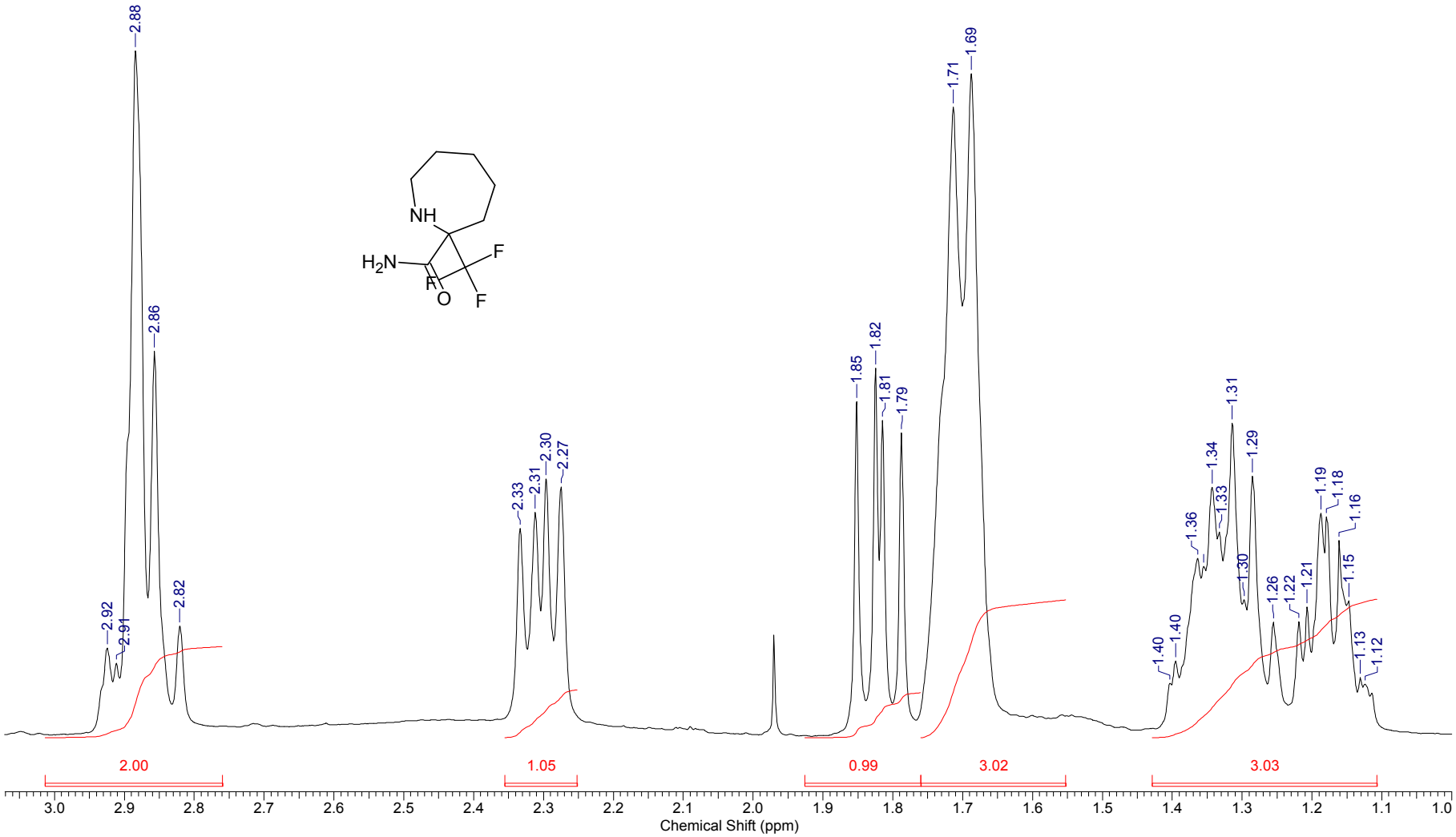
^{13}C NMR (100 MHz, $CDCl_3$) for compound **3d**



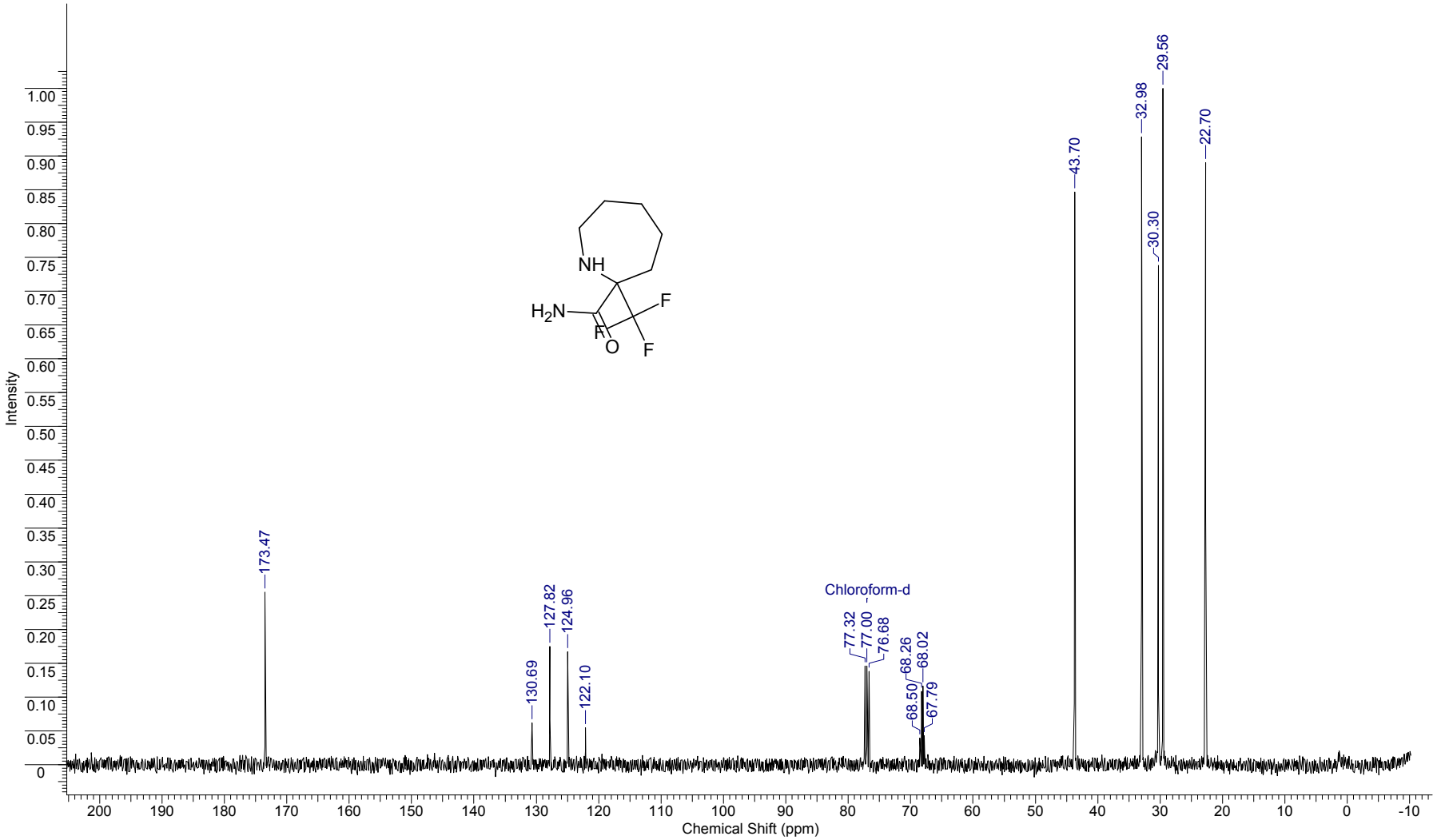
^{19}F NMR (280 MHz, $CDCl_3$) for compound **3d**



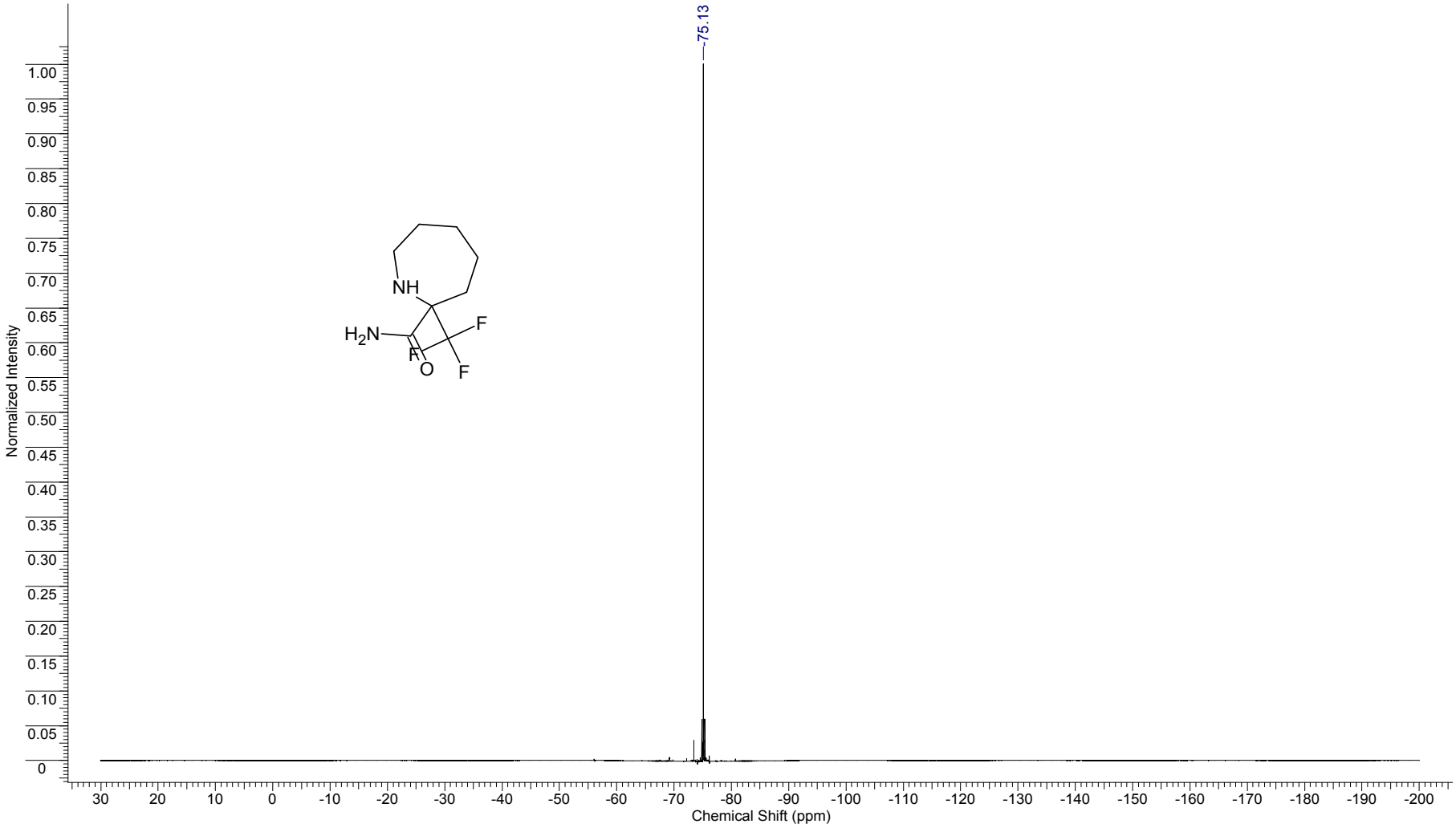
^{1}H NMR (400 MHz, $CDCl_3$) for compound **3e**



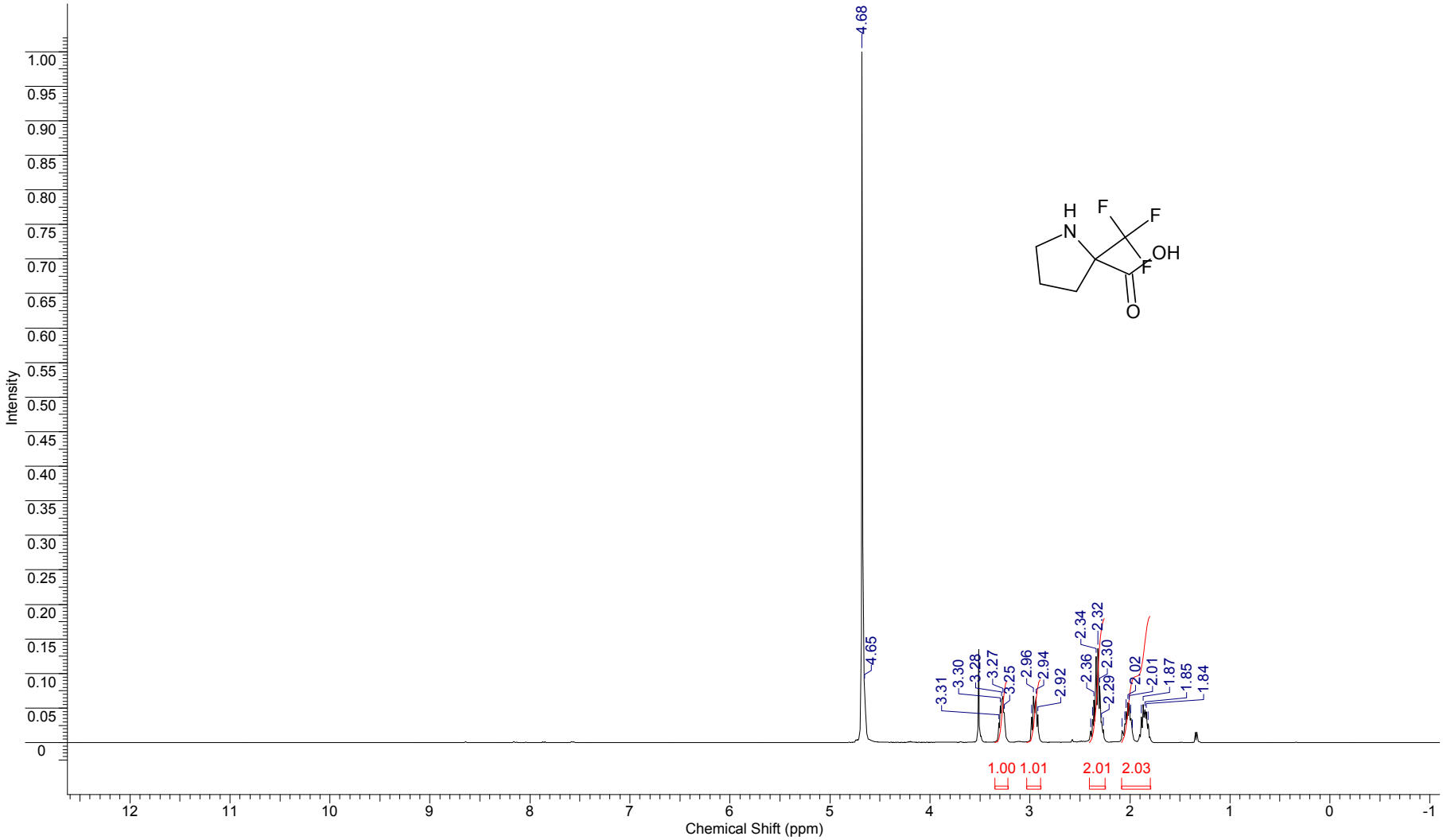
^{1}H NMR (400 MHz, $CDCl_3$) for compound **3e** aliphatic region



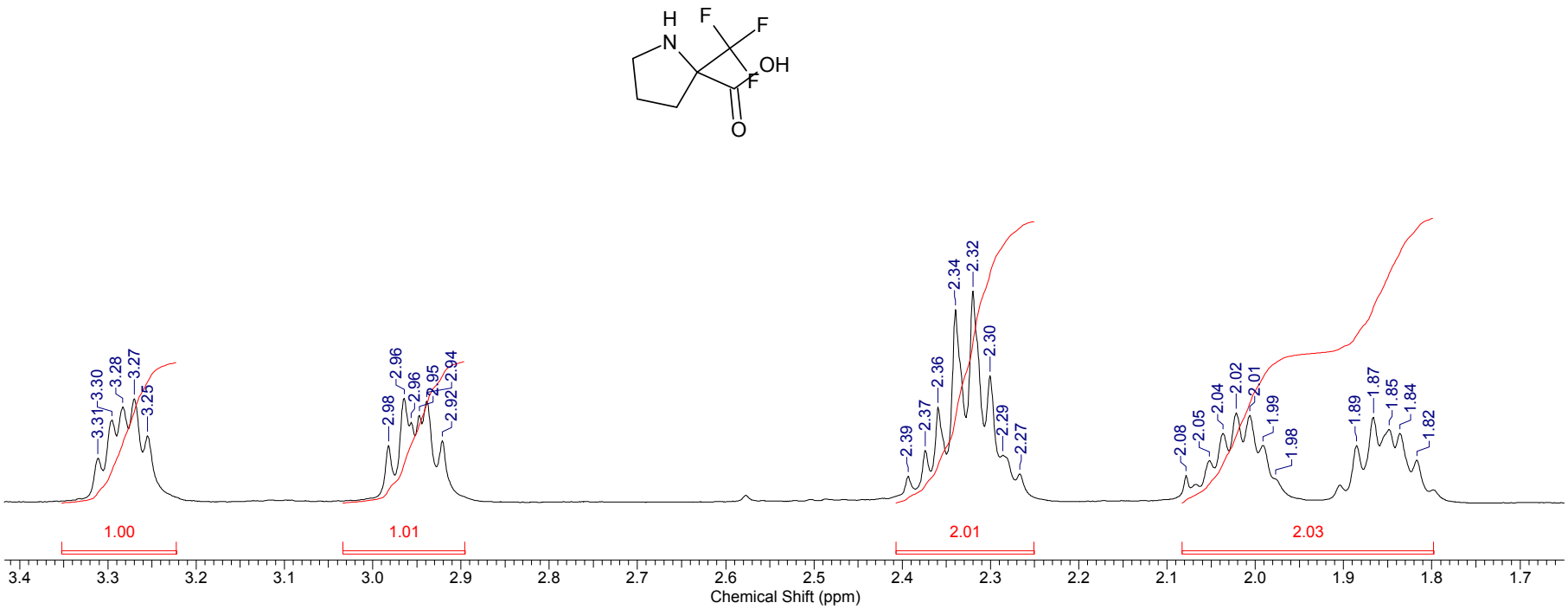
^{13}C NMR (100 MHz, $CDCl_3$) for compound **3e**



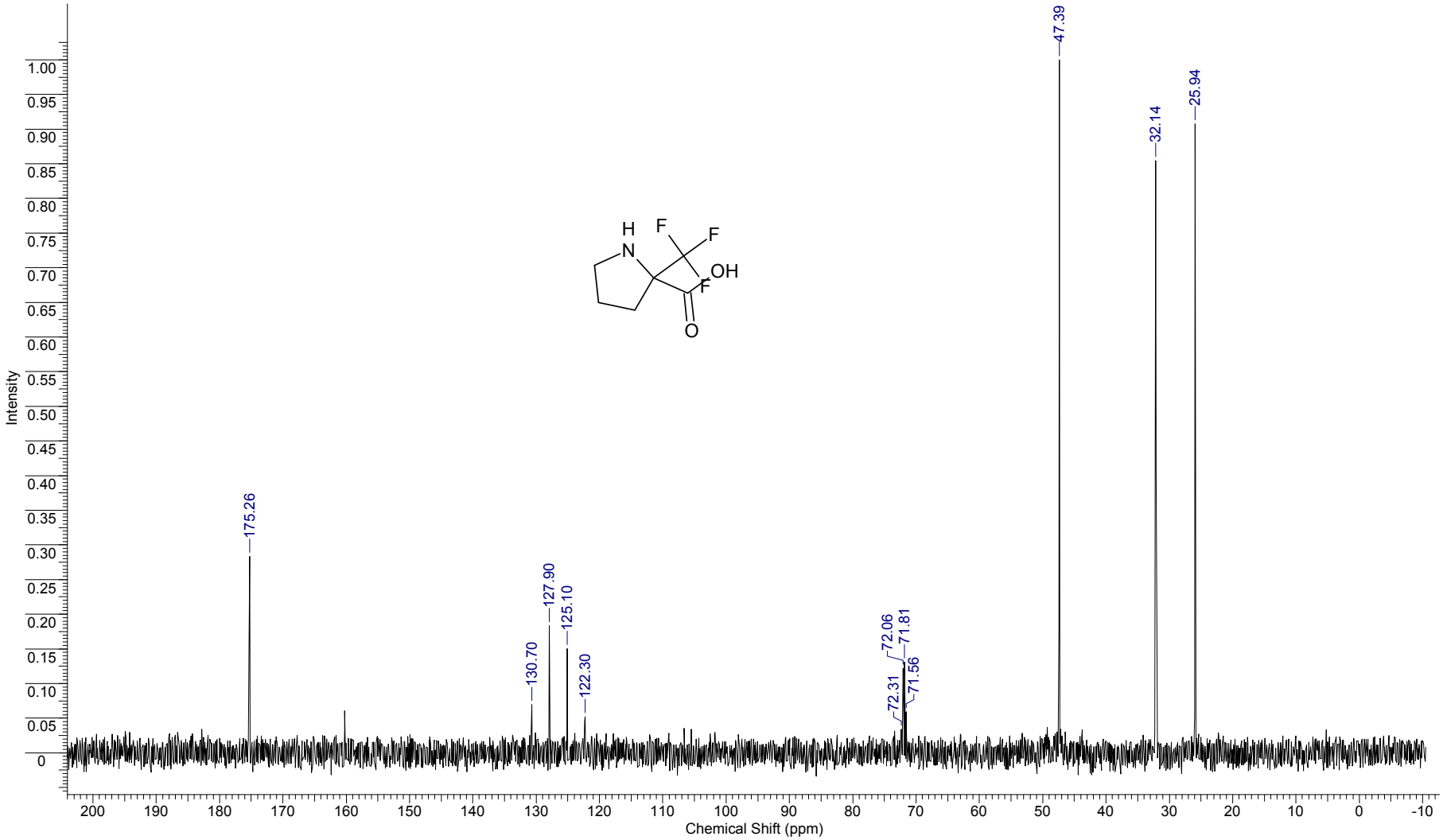
^{19}F NMR (280 MHz, $CDCl_3$) for compound **3e**



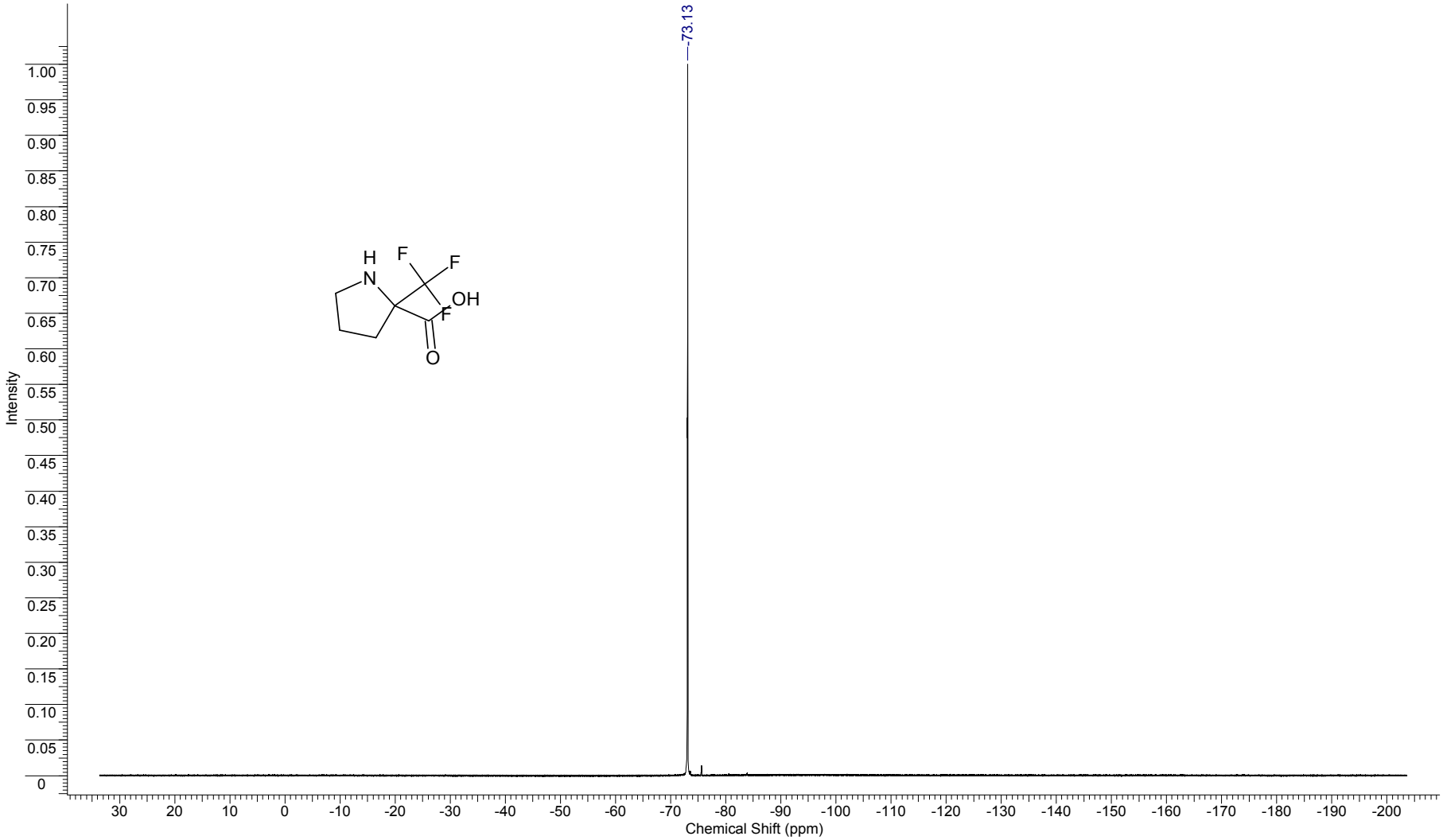
^{1}H NMR (400 MHz, D_2O) for compound **4a**



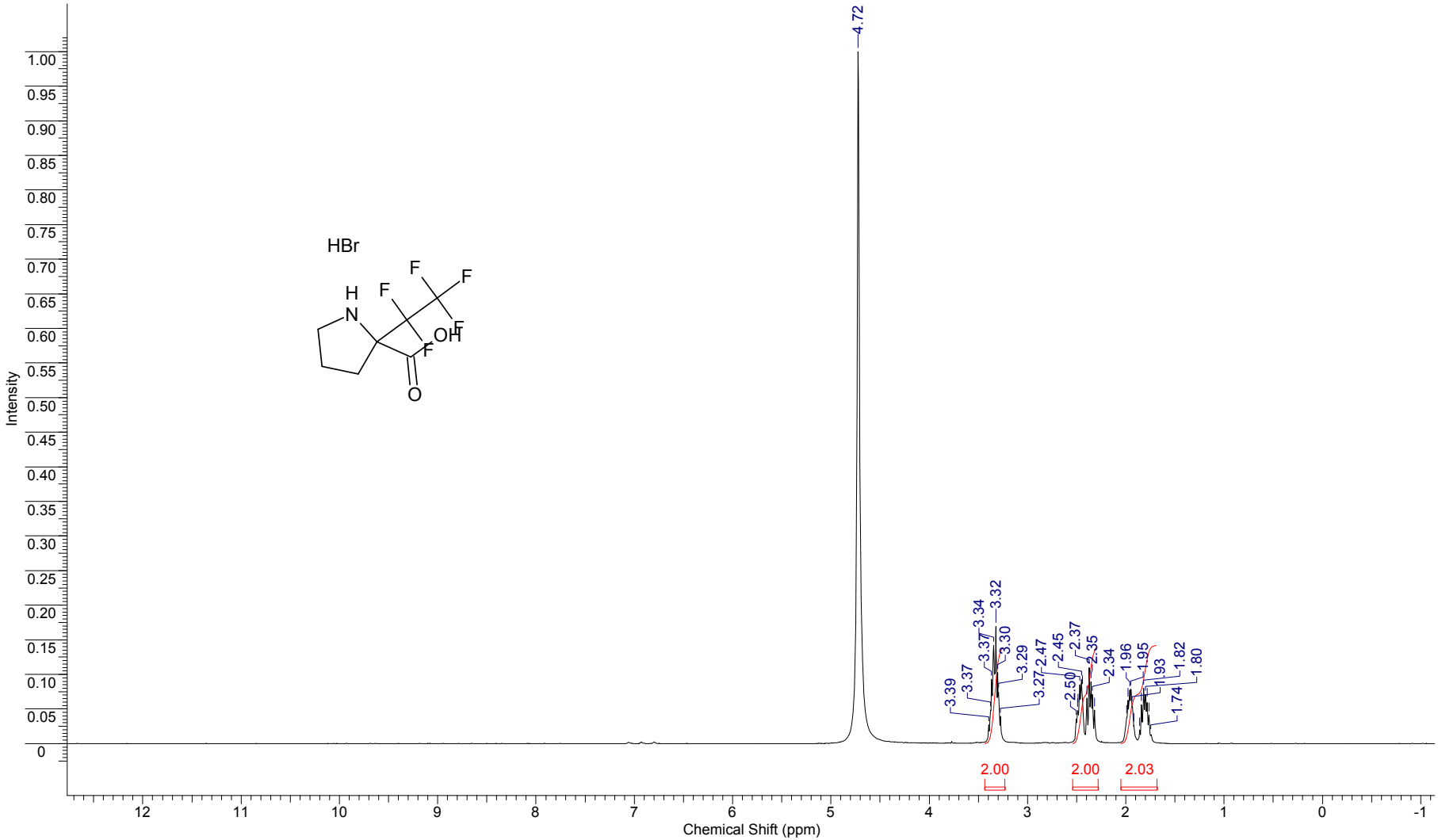
^{1}H NMR (400 MHz, D_2O) for compound **4a** aliphatic region



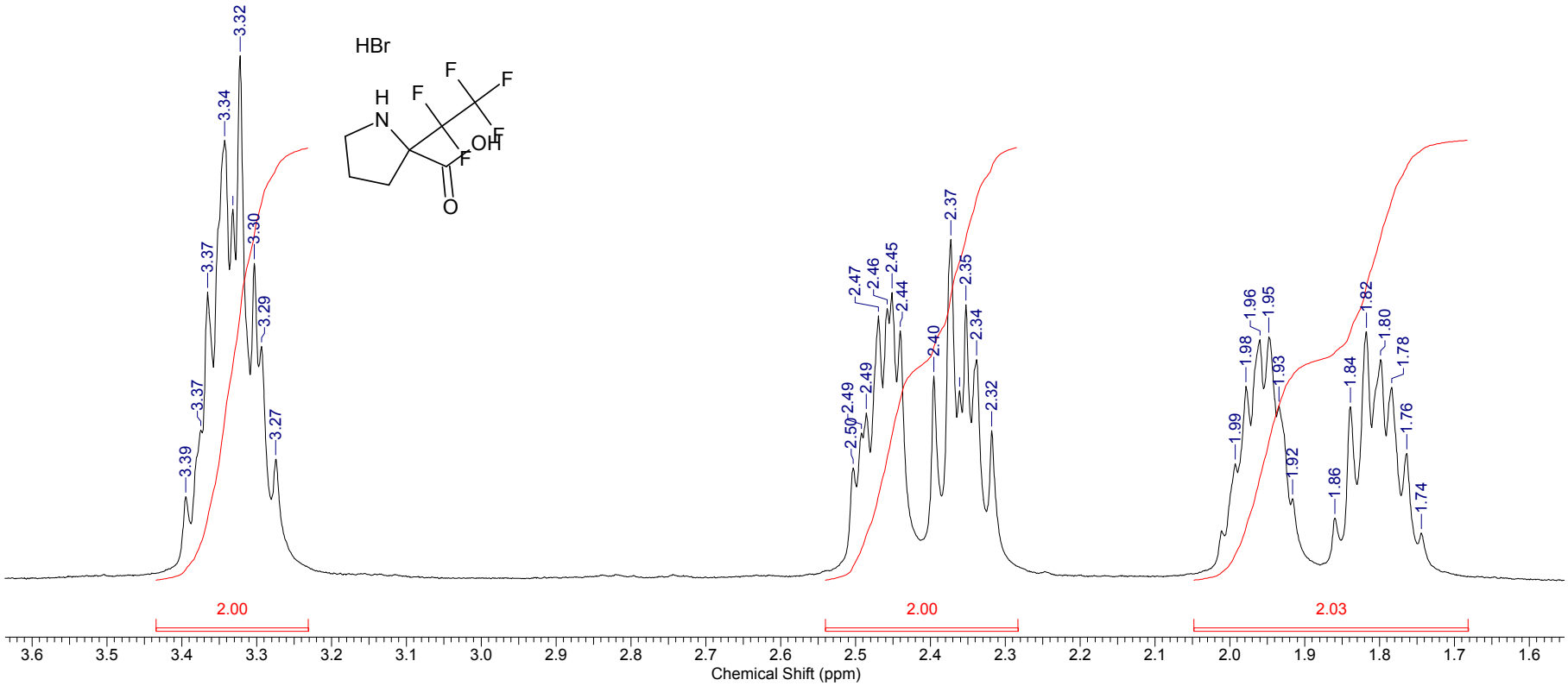
^{13}C NMR (100 MHz, D_2O) for compound **4a**



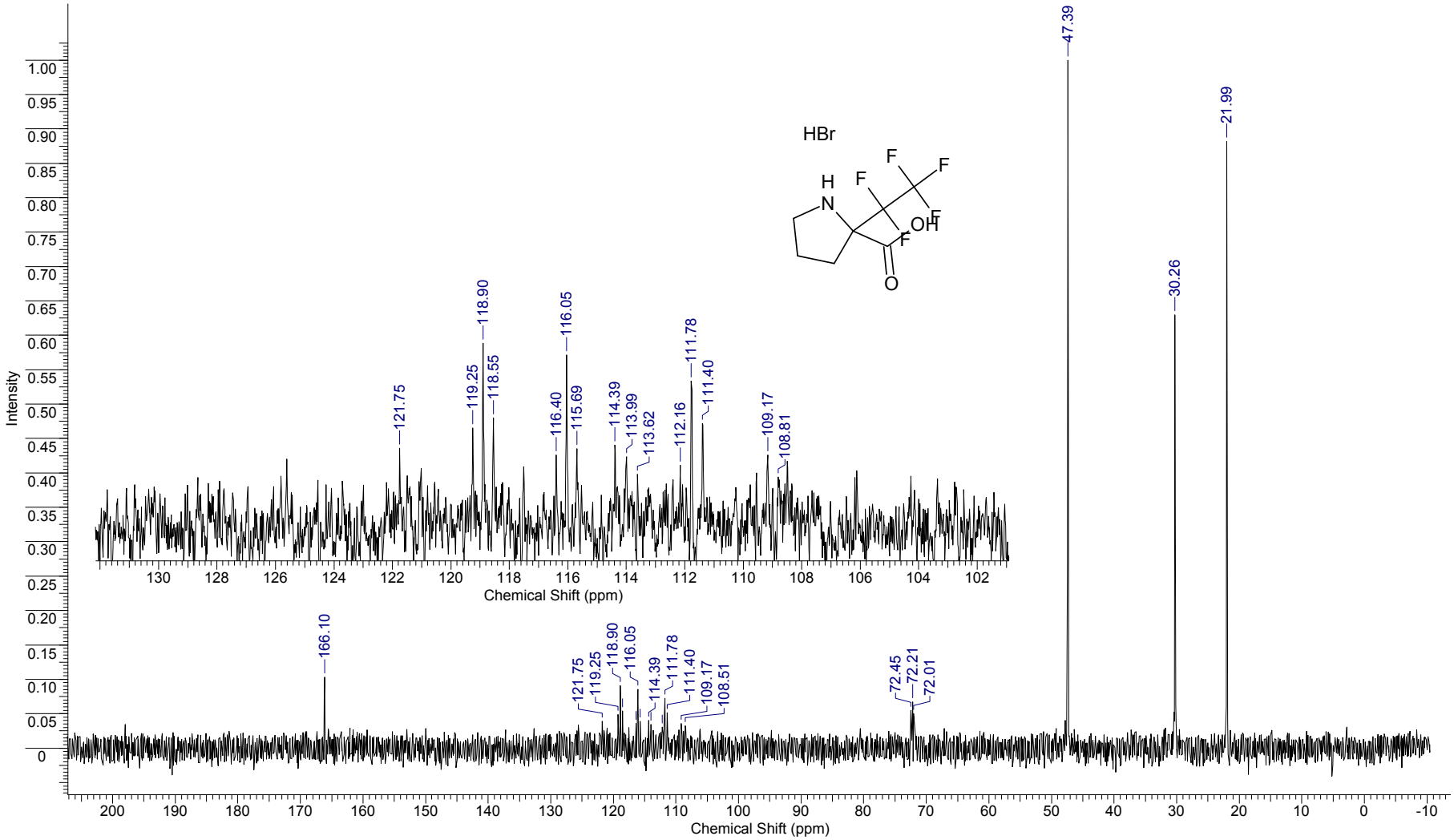
^{19}F NMR (280 MHz, D_2O) for compound **4a**



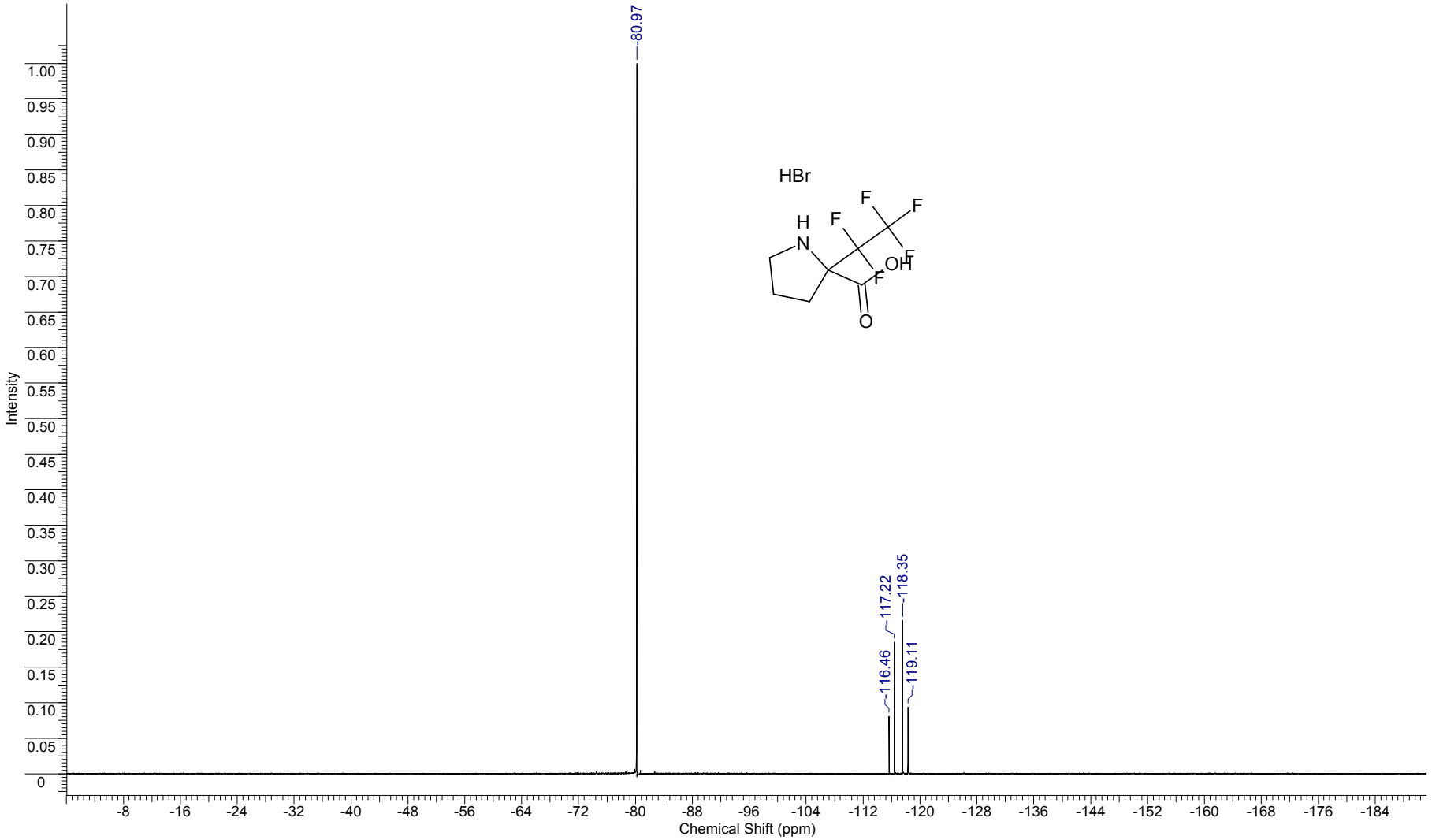
^{1}H NMR (400 MHz, D_2O) for compound **4b**



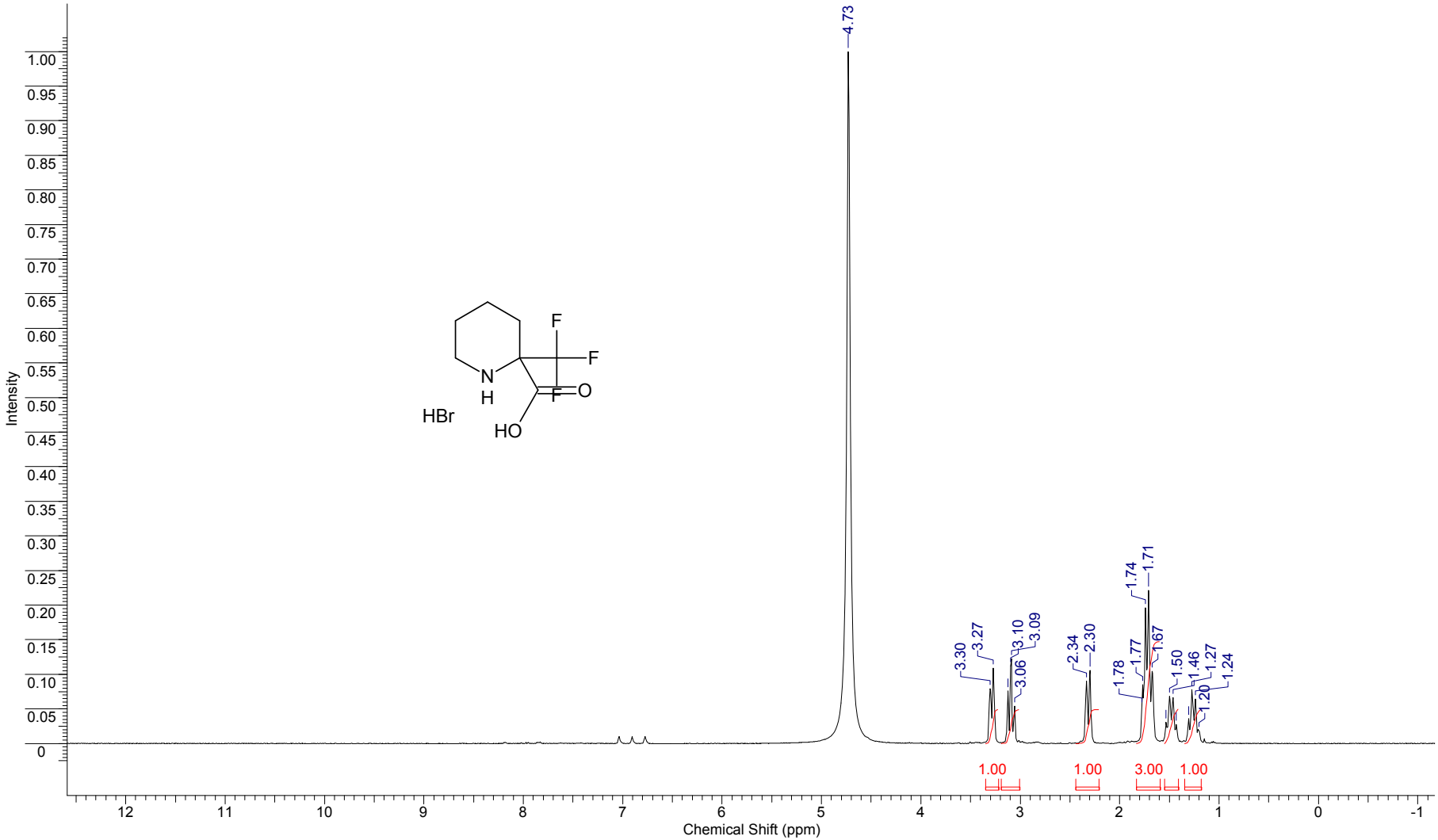
^{1}H NMR (400 MHz, D_2O) for compound **4b** aliphatic region



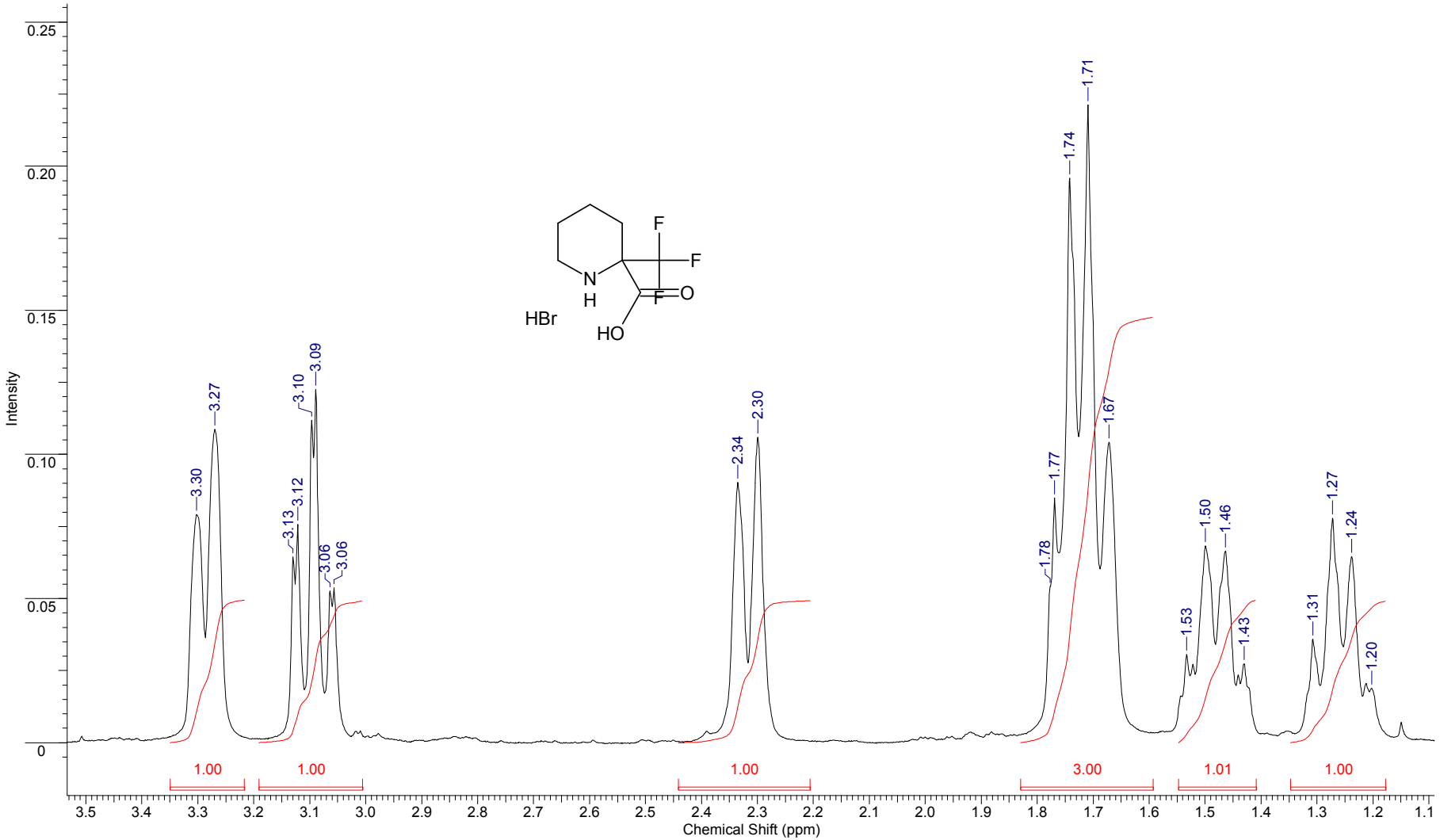
^{13}C NMR (100 MHz, D_2O) for compound **4b**



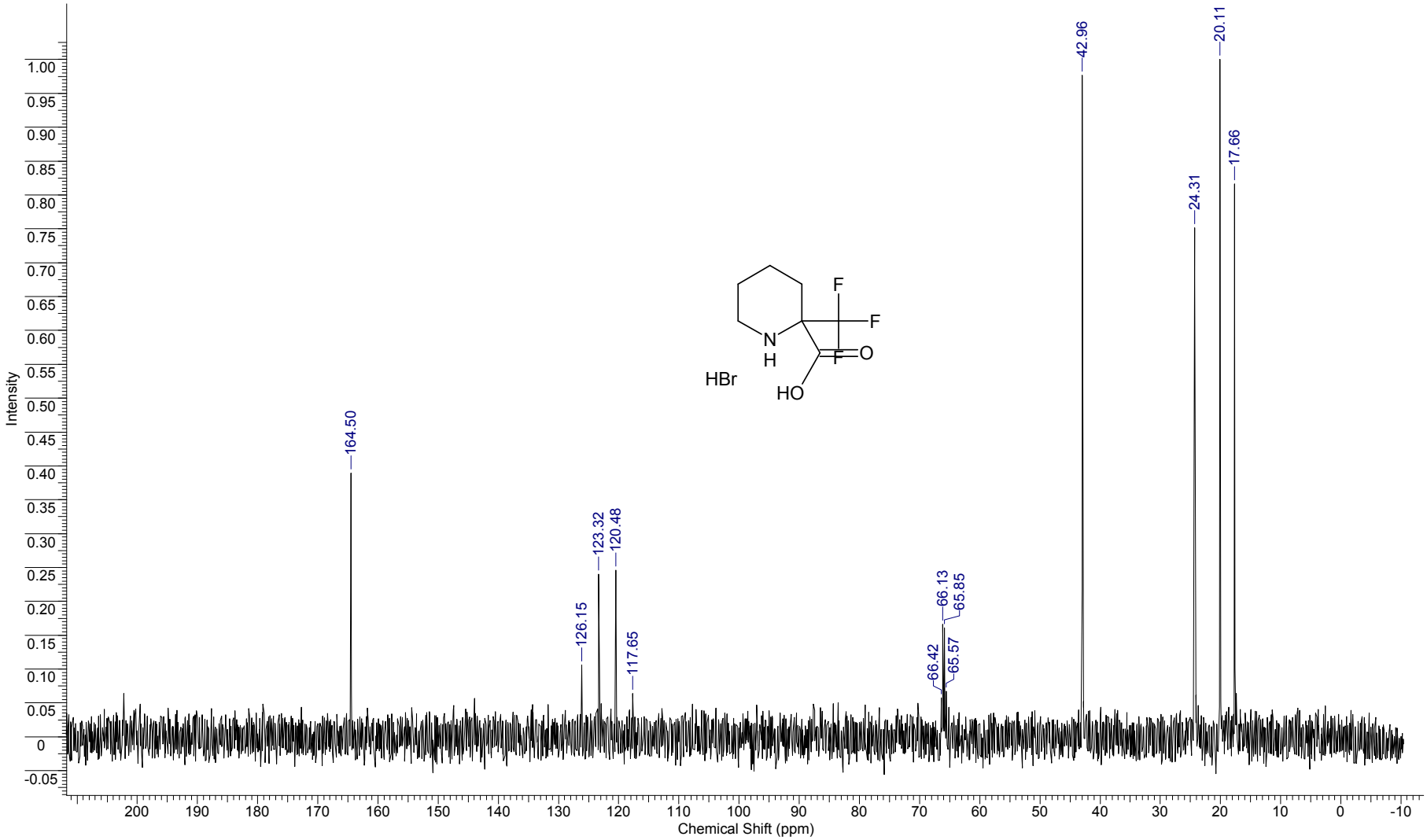
^{19}F NMR (280 MHz, D_2O) for compound **4b**



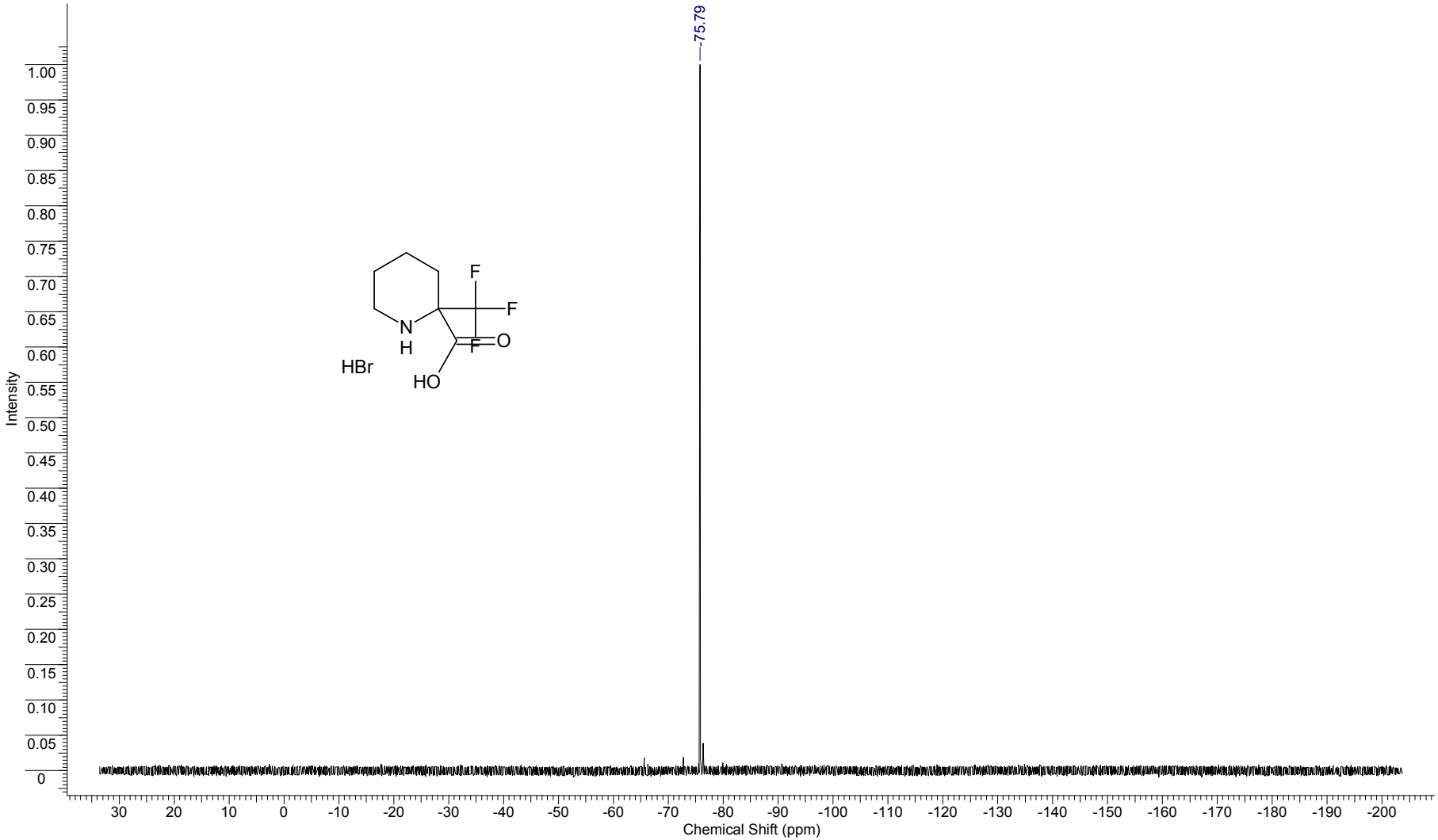
^{1}H NMR (400 MHz, D_2O) for compound **4c**



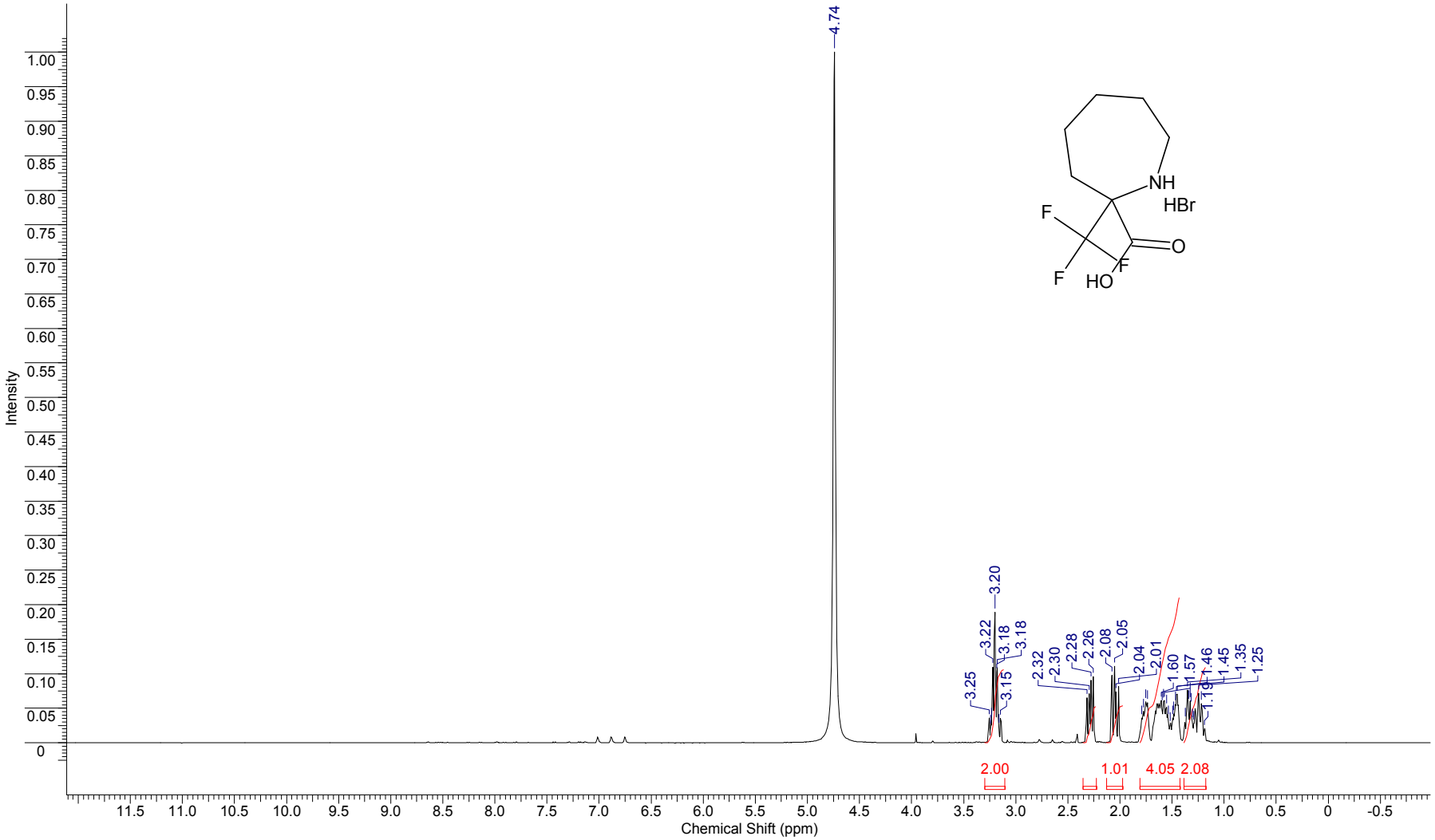
^{1}H NMR (400 MHz, D_2O) for compound **4c** aliphatic region



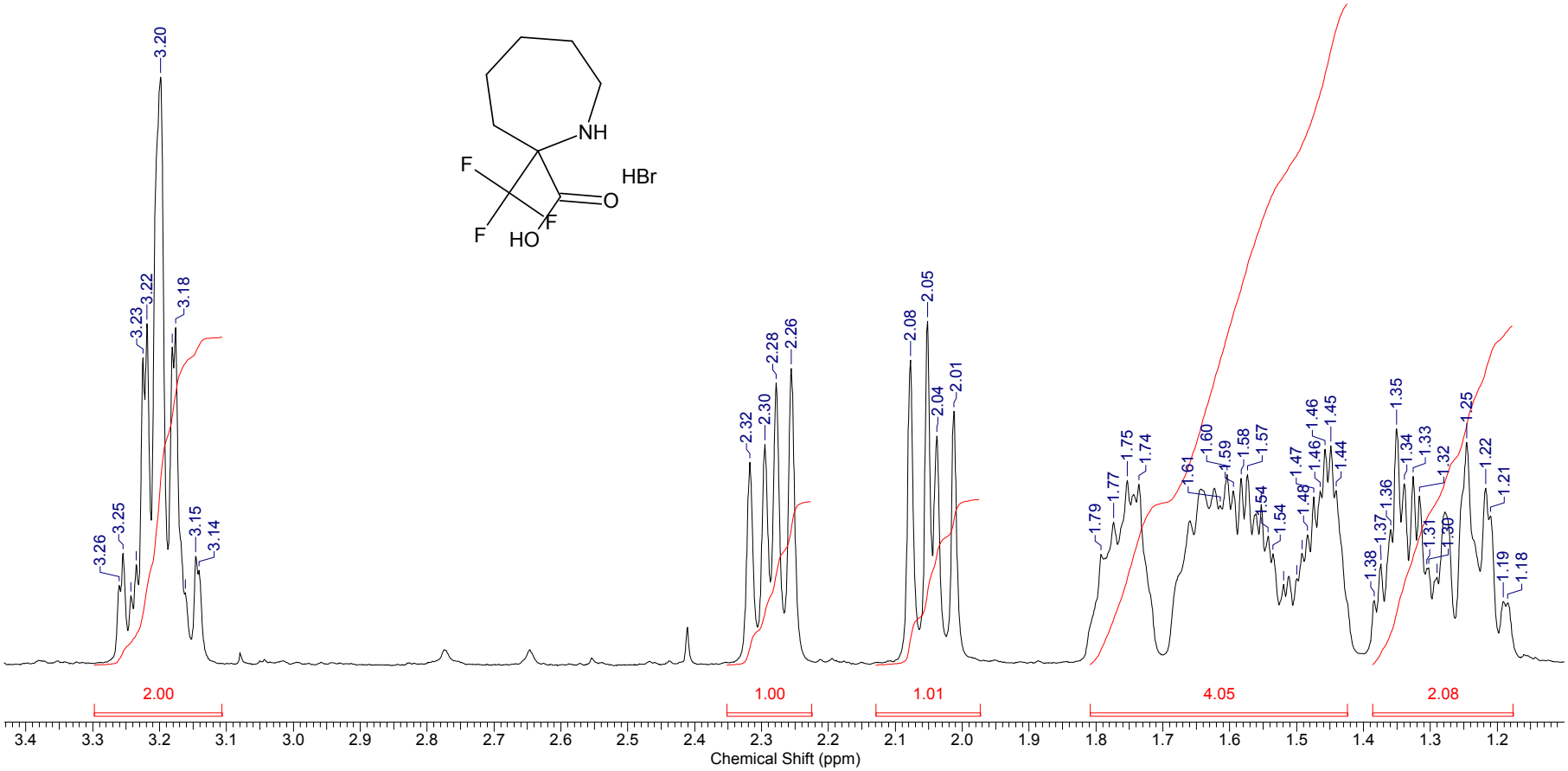
^{13}C NMR (100 MHz, D_2O) for compound **4c**



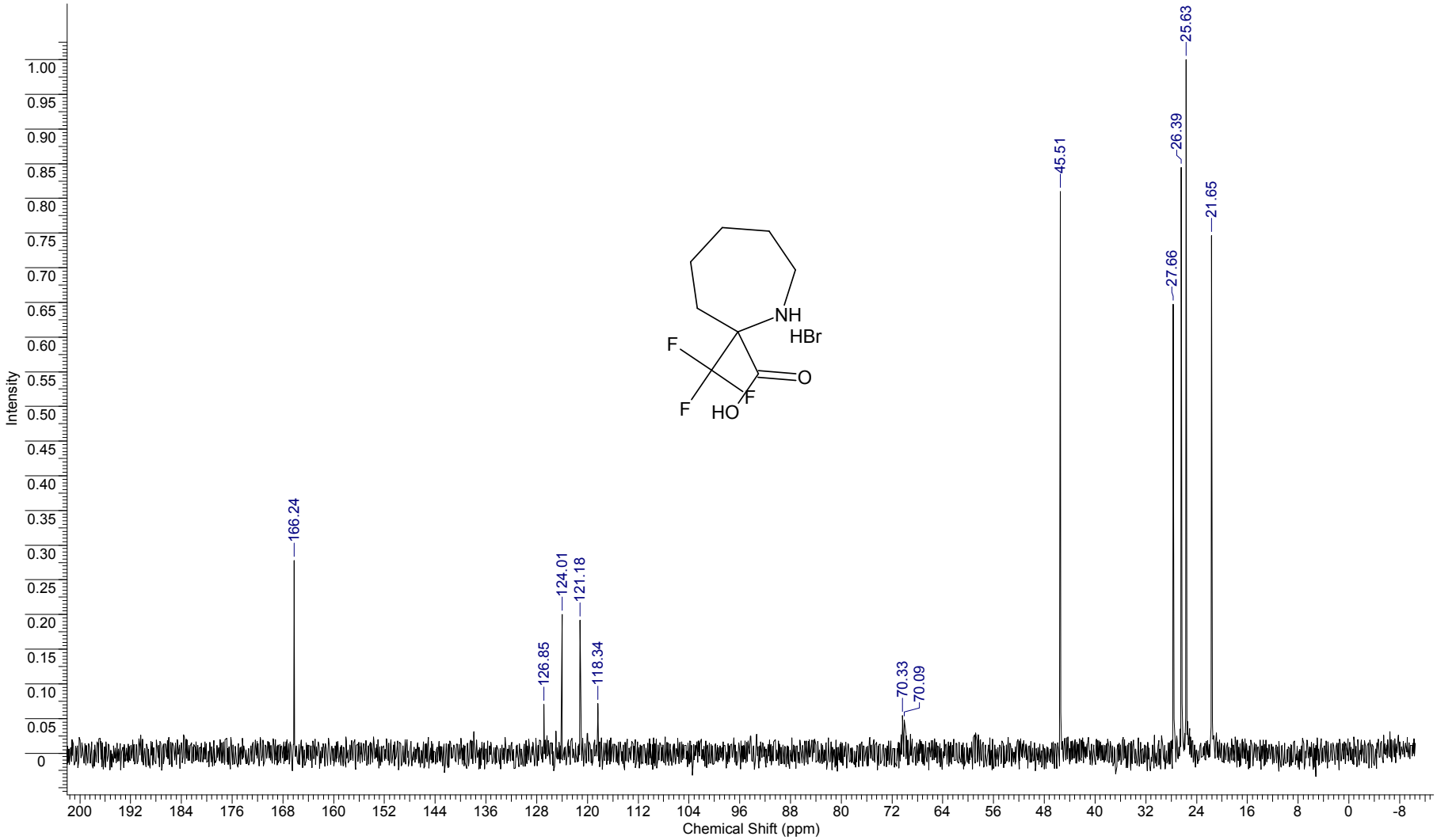
^{19}F NMR (280 MHz, D_2O) for compound **4c**



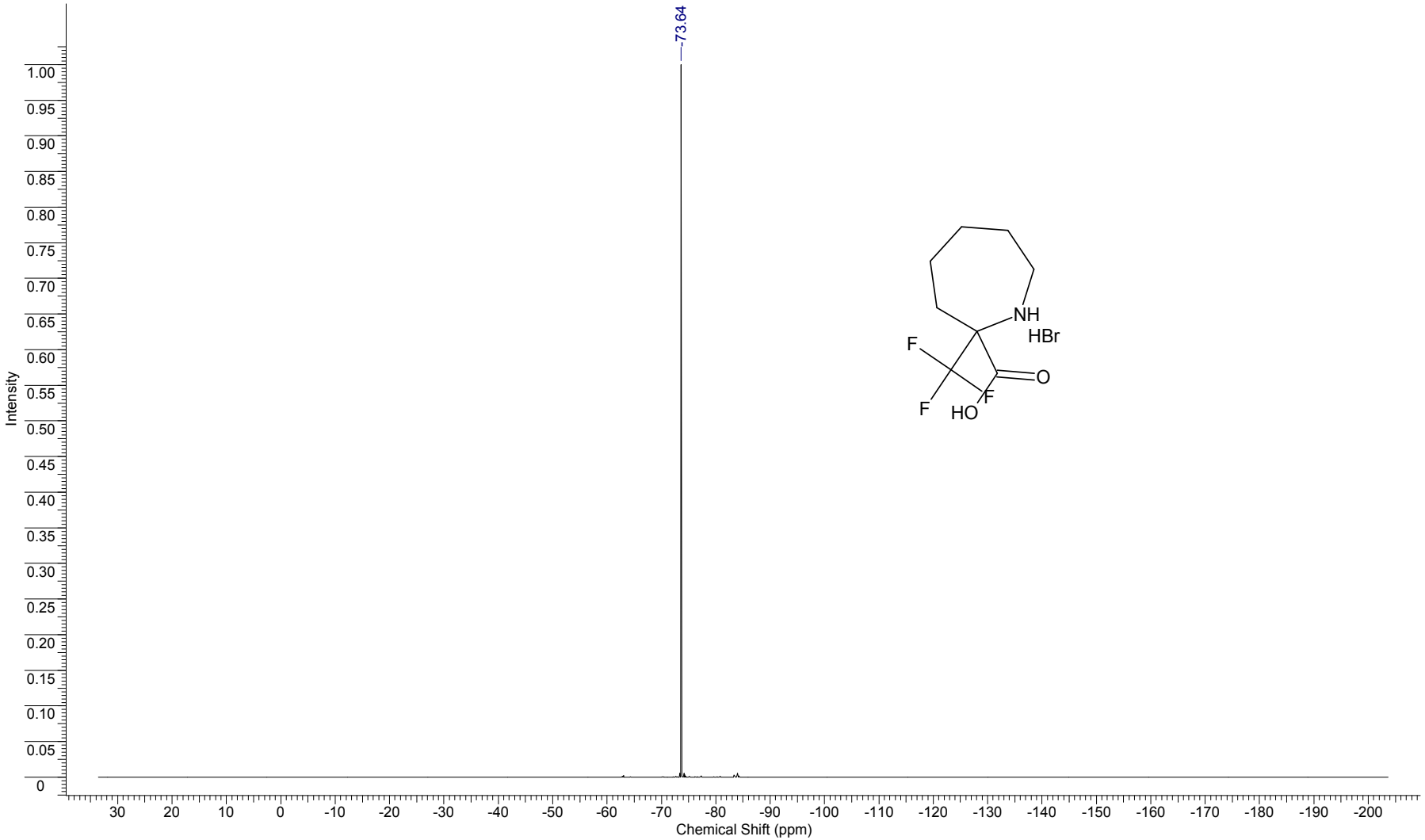
^{1}H NMR (400 MHz, D_2O) for compound **4e**



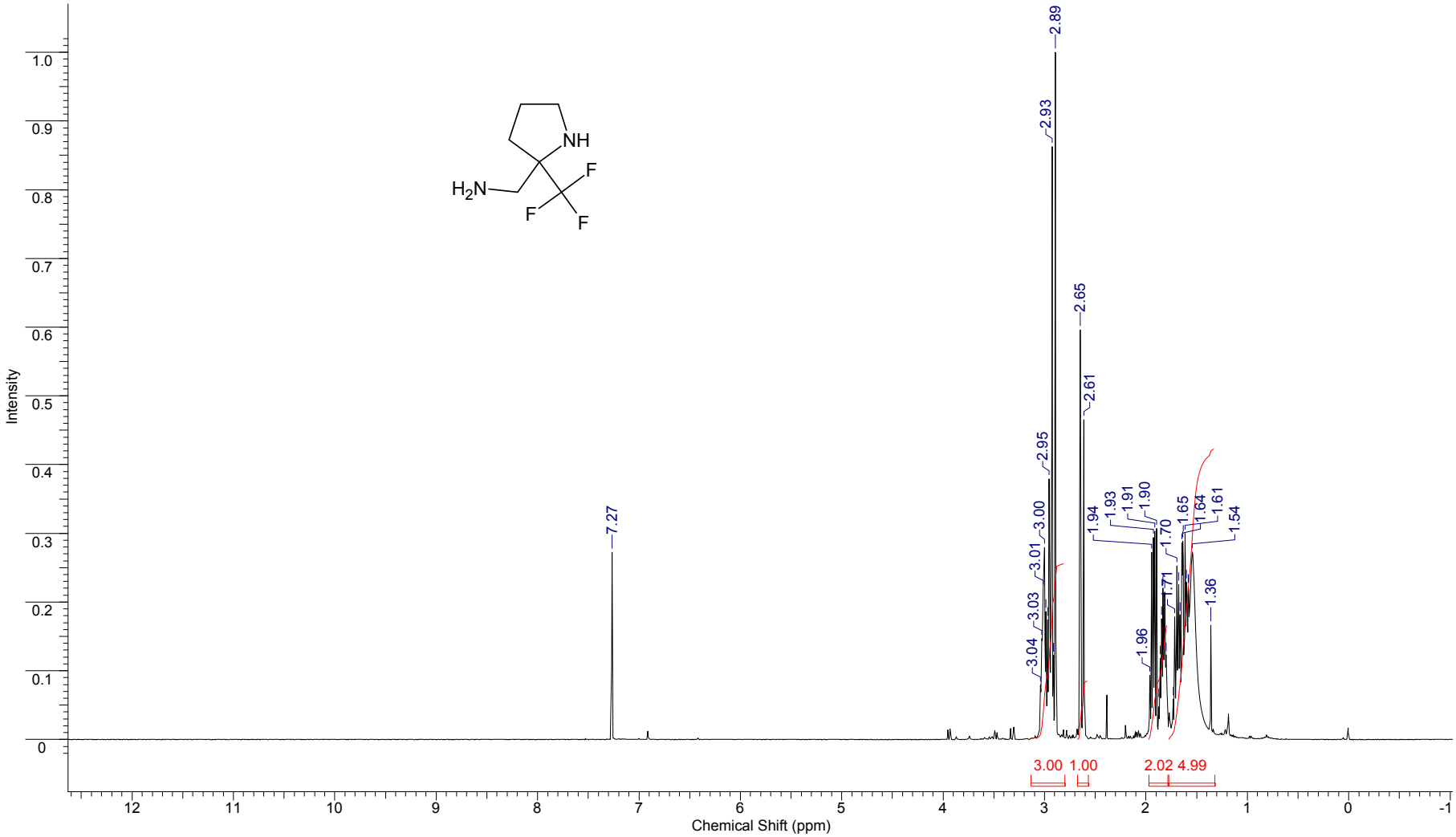
^{1}H NMR (400 MHz, D_2O) for compound **4e** aliphatic region



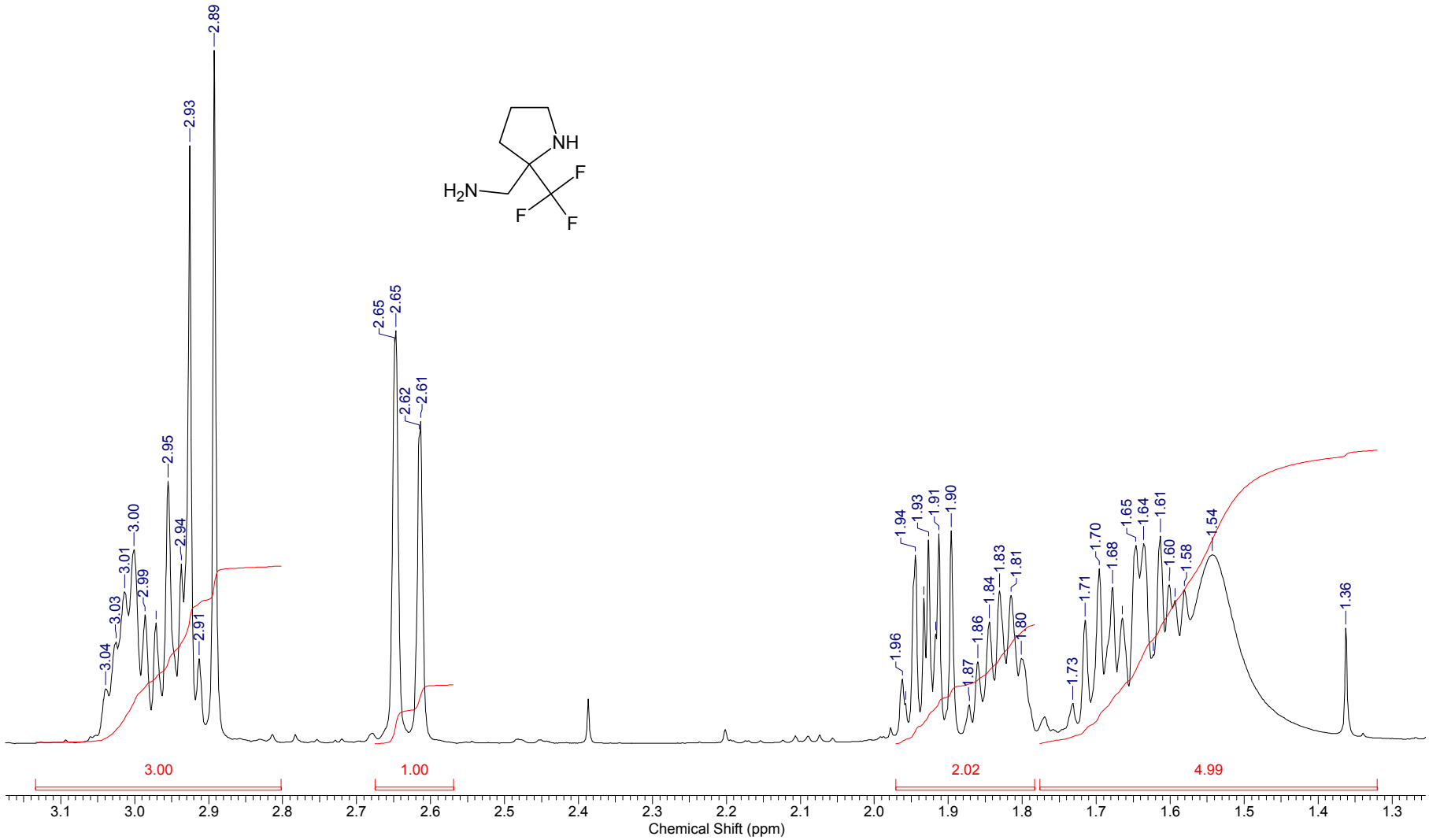
^{13}C NMR (100 MHz, D_2O) for compound **4e**



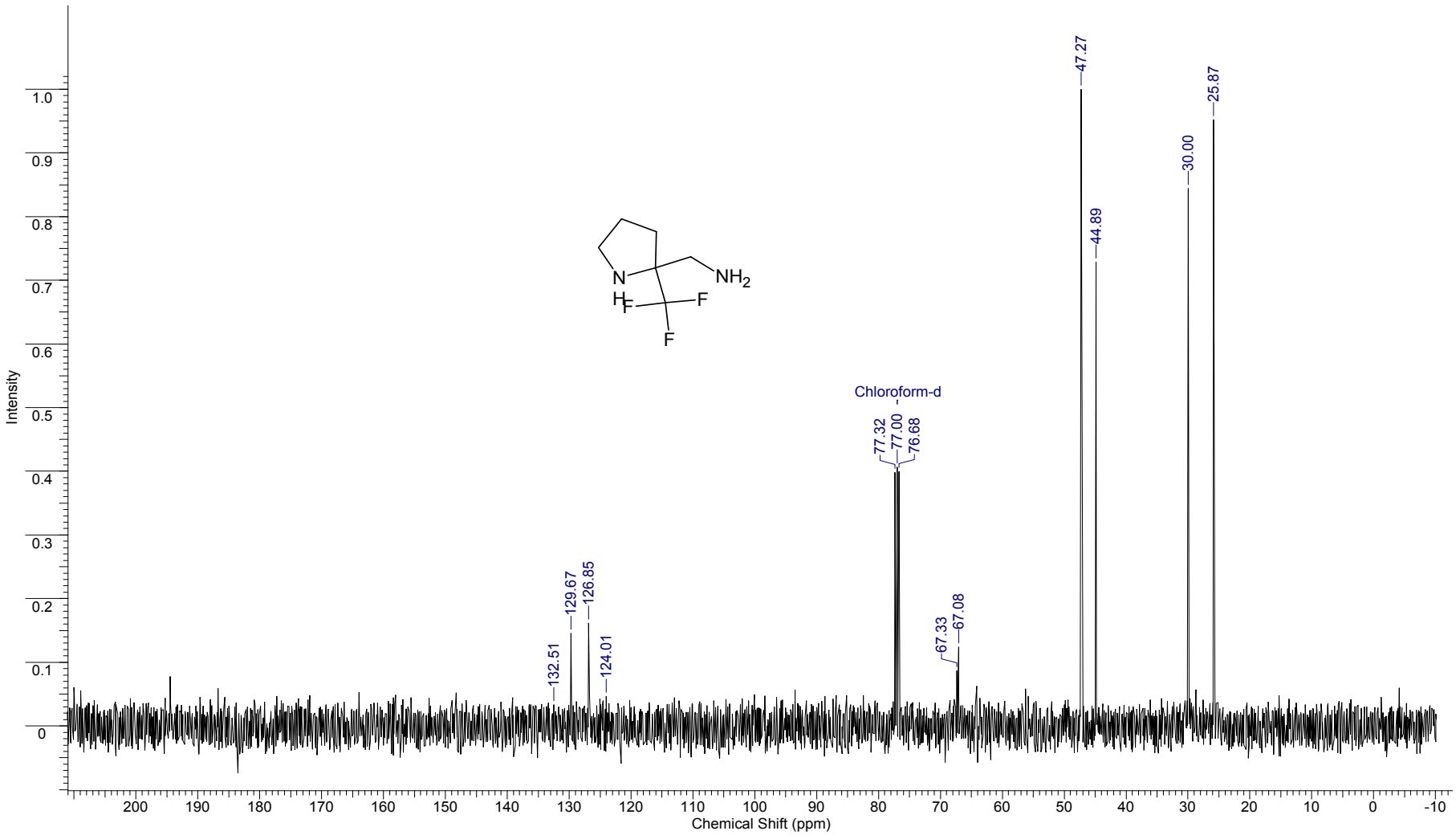
^{19}F NMR (280 MHz, D_2O) for compound **4e**



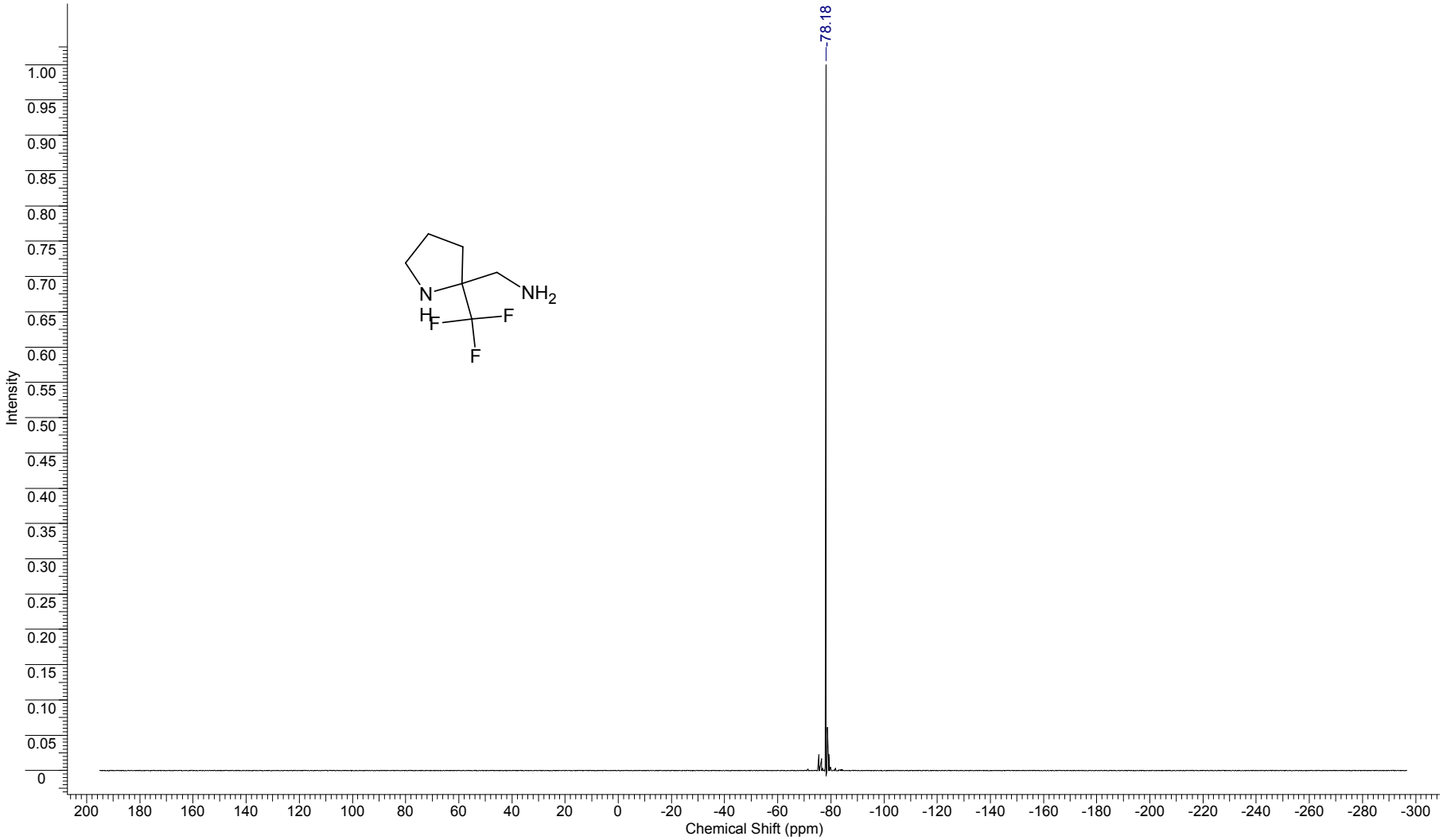
^{1}H NMR (400 MHz, $CDCl_3$) for compound **4a**



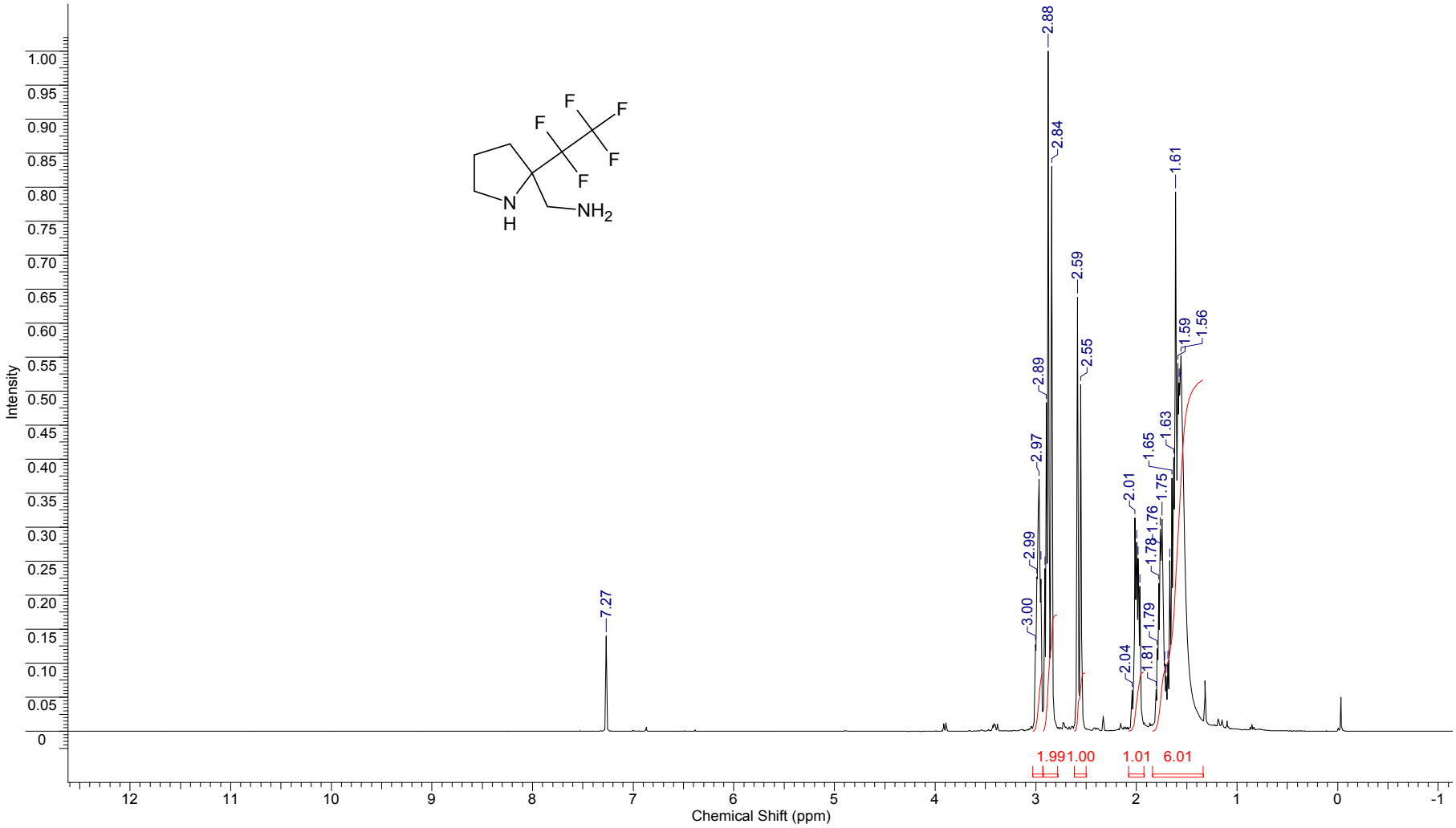
^{1}H NMR (400 MHz, $CDCl_3$) for compound **5a** aliphatic region



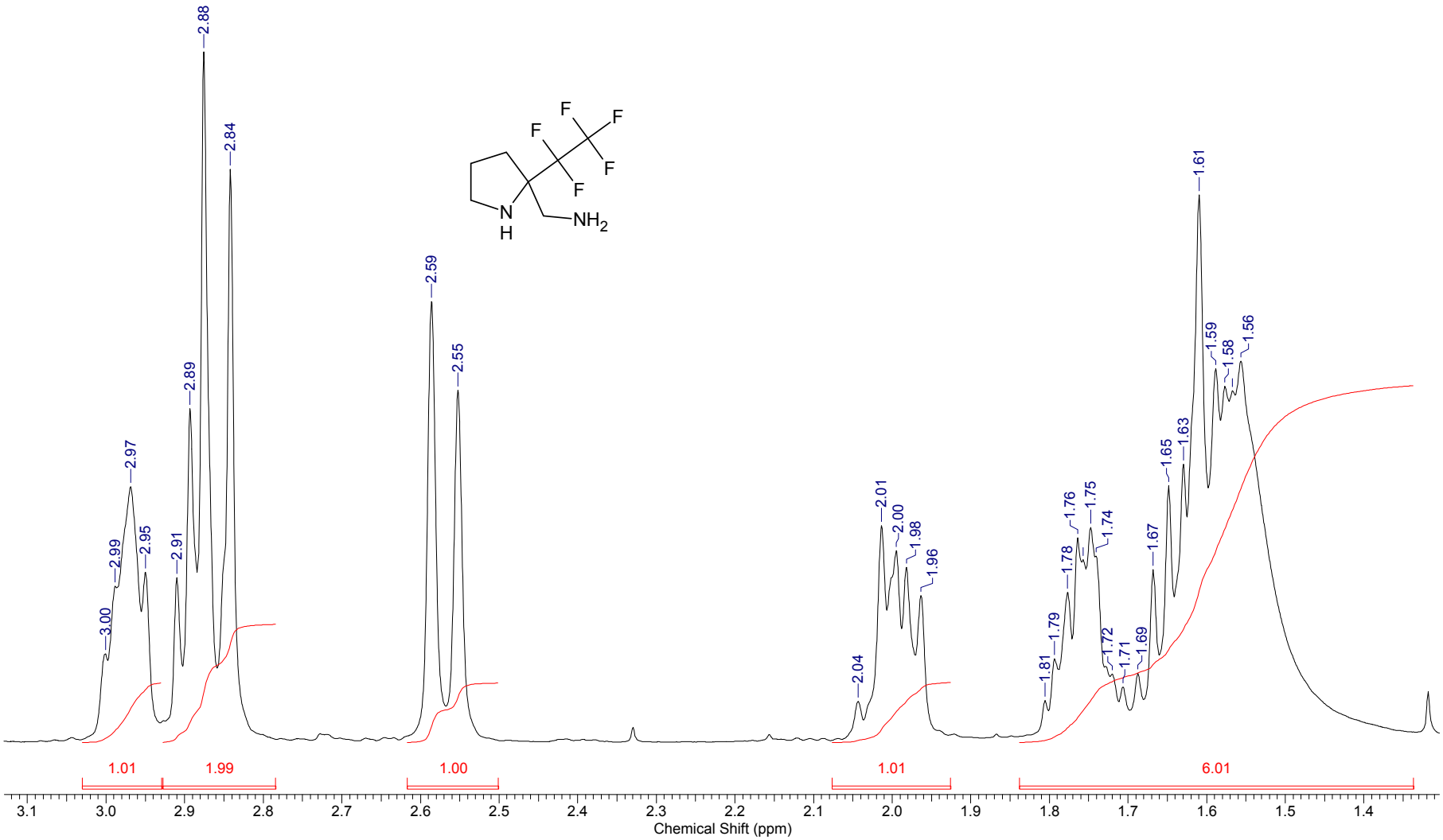
^{13}C NMR (100 MHz, $CDCl_3$) for compound **5a**



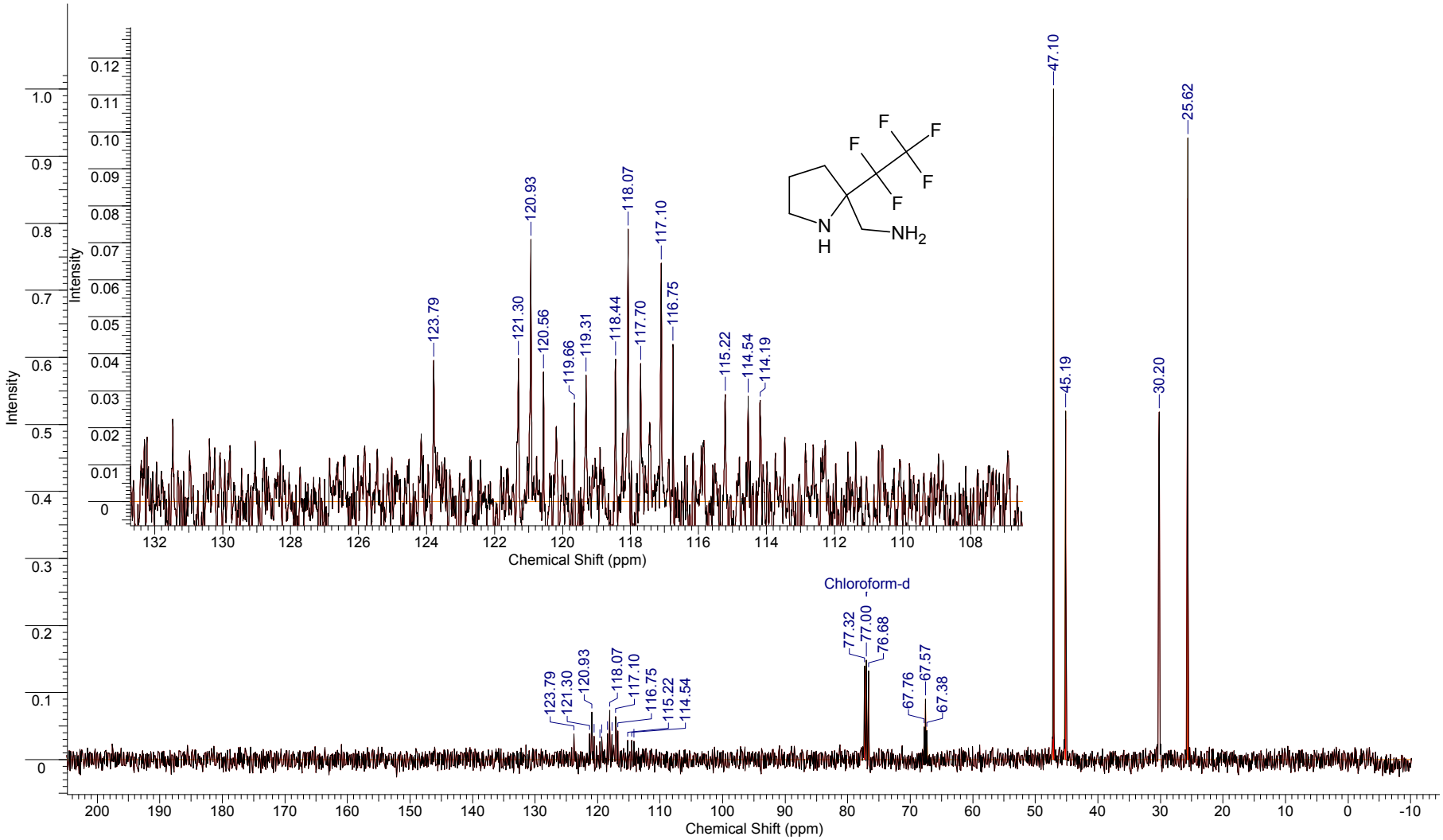
^{19}F NMR (280 MHz, $CDCl_3$) for compound **5a**



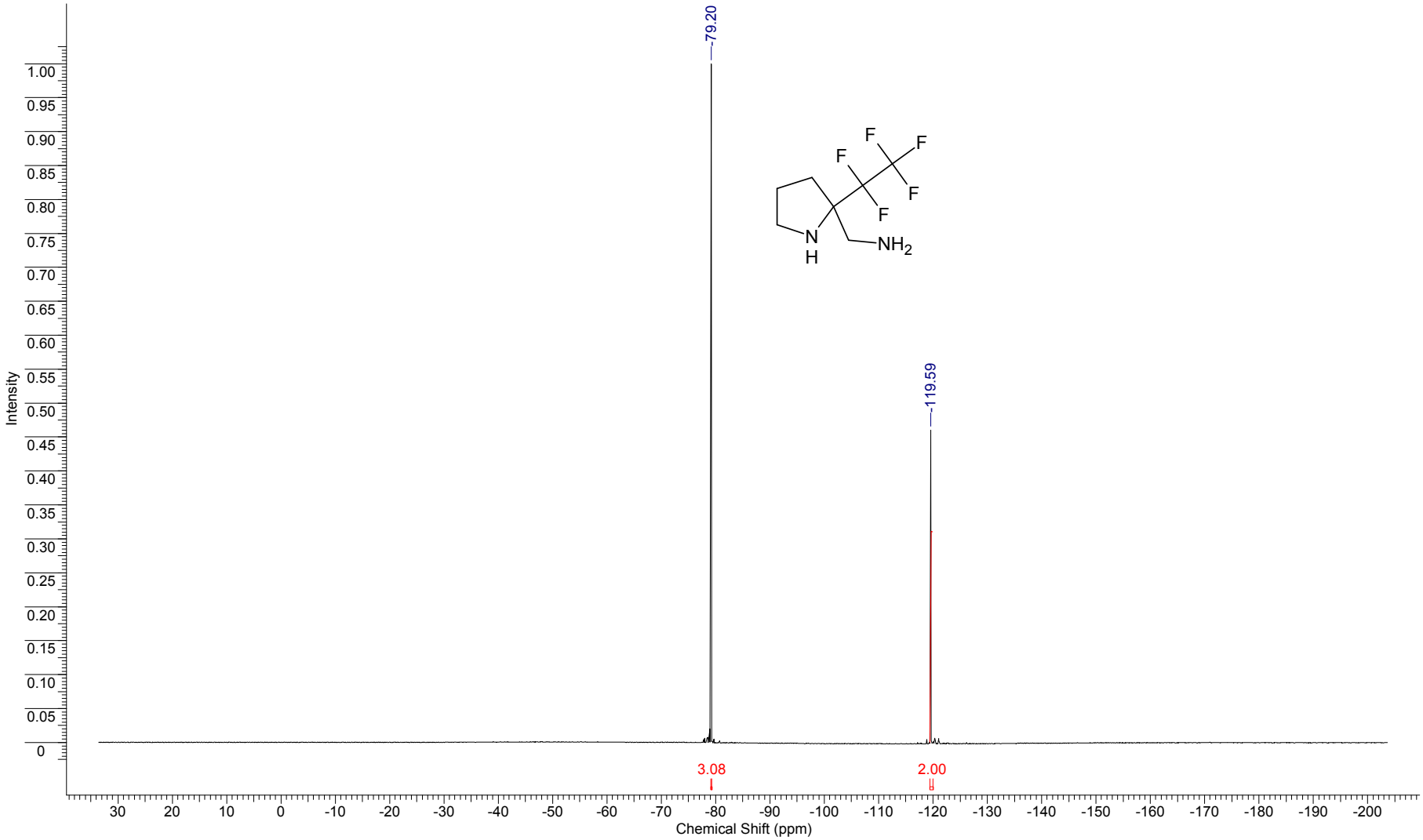
^{1}H NMR (400 MHz, $CDCl_3$) for compound **5b**



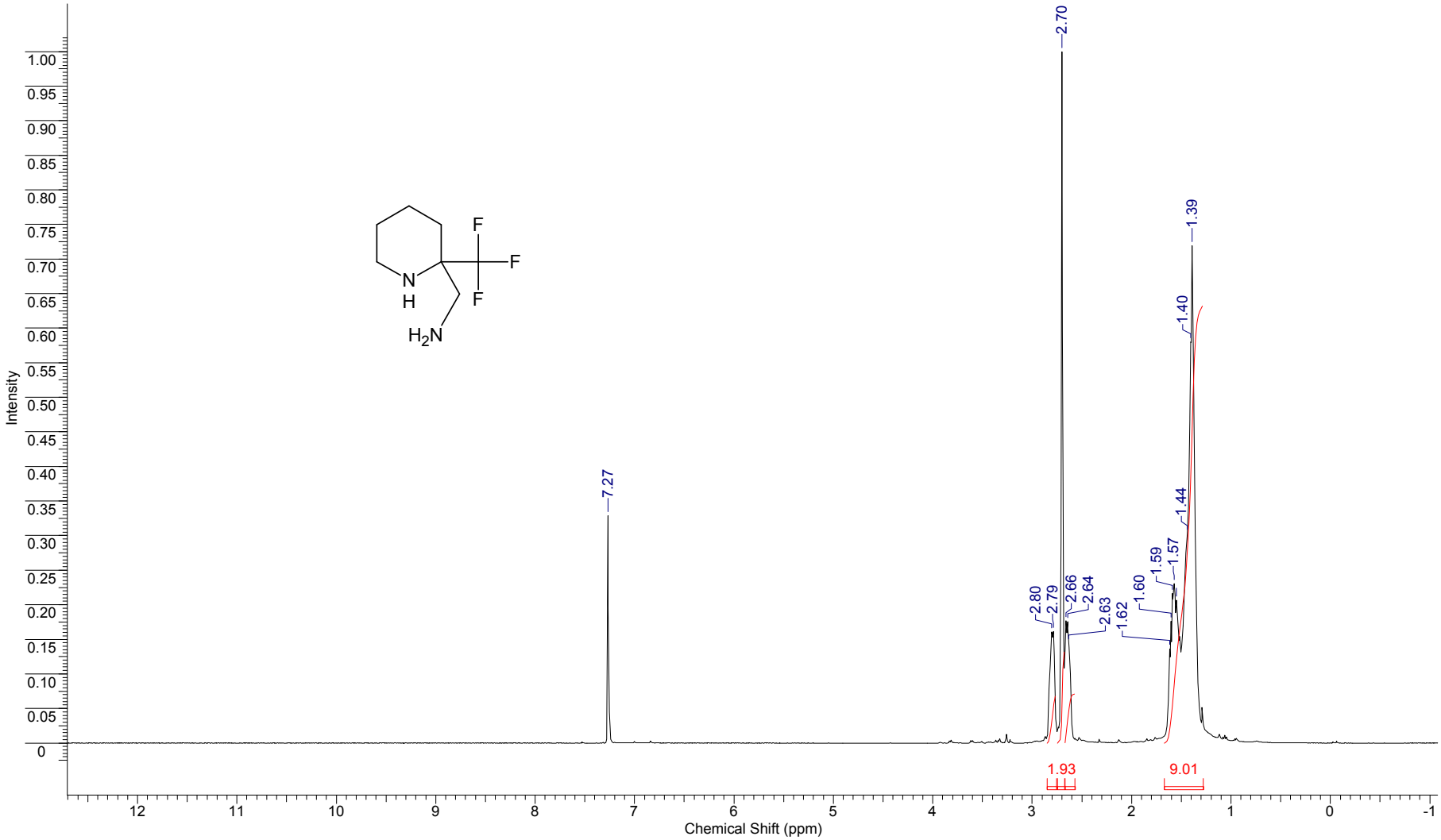
^{1}H NMR (400 MHz, $CDCl_3$) for compound **5b** aliphatic region



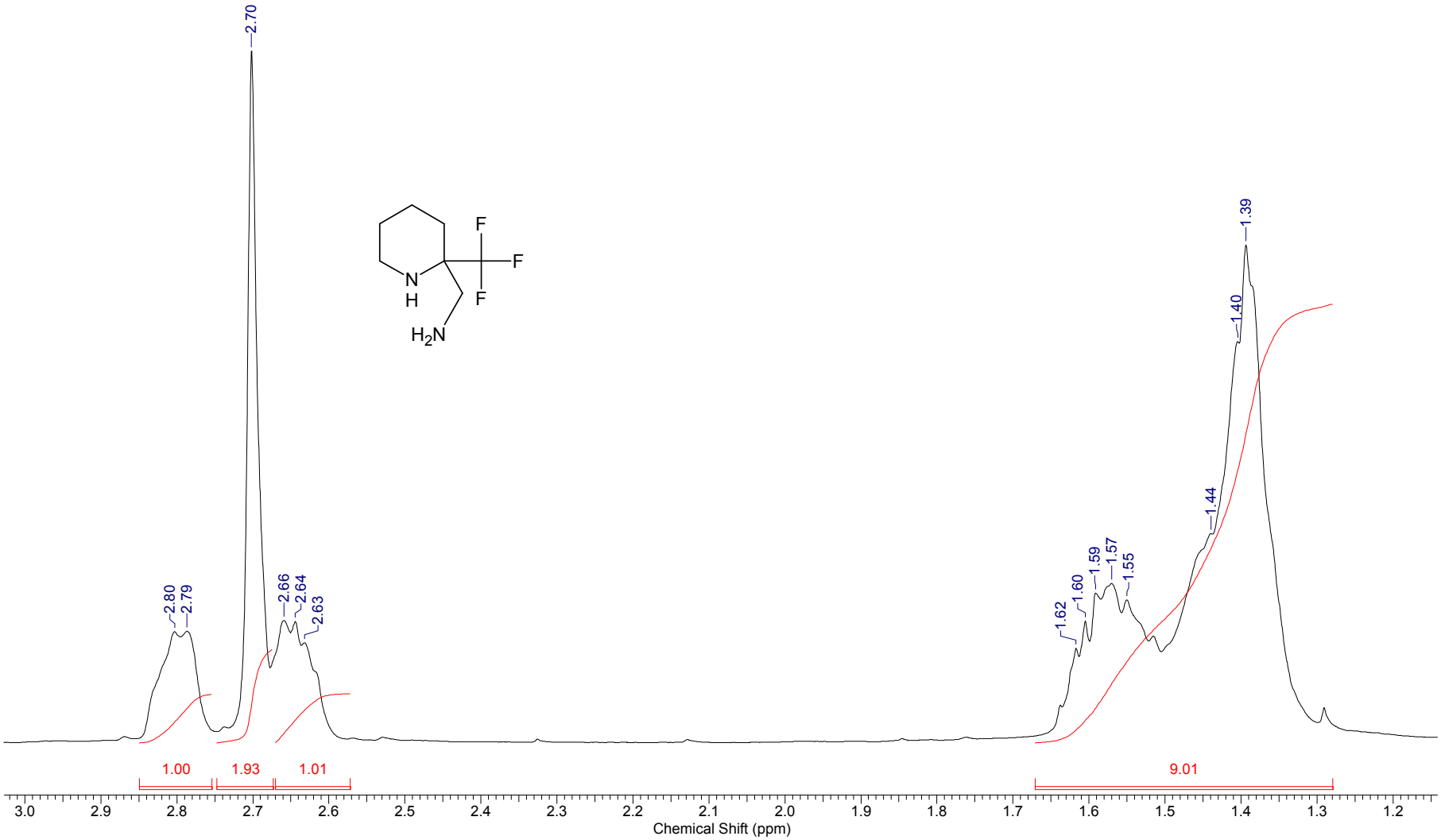
^{13}C NMR (100 MHz, $CDCl_3$) for compound **5b**



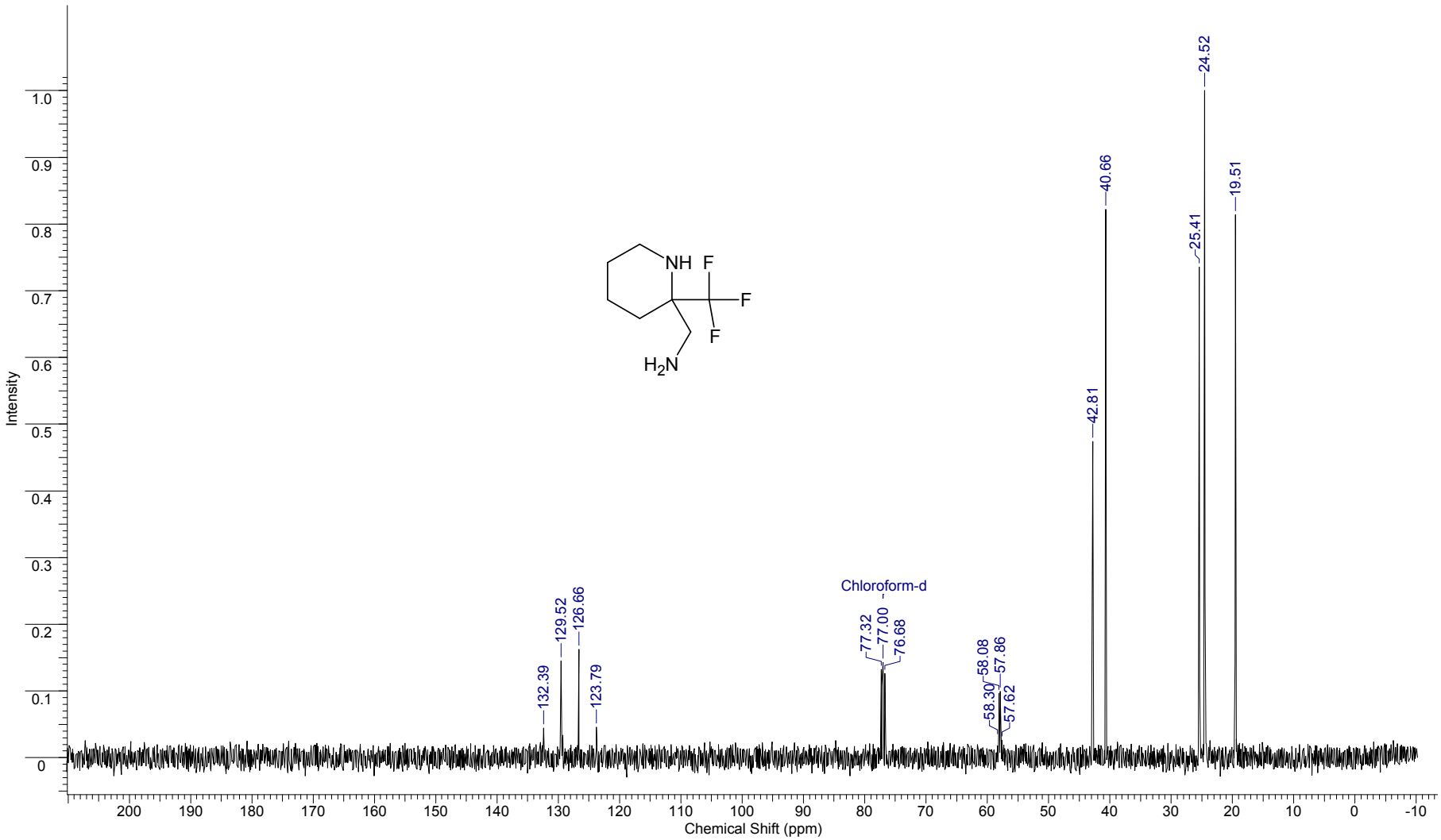
^{19}F NMR (280 MHz, $CDCl_3$) for compound **5b**



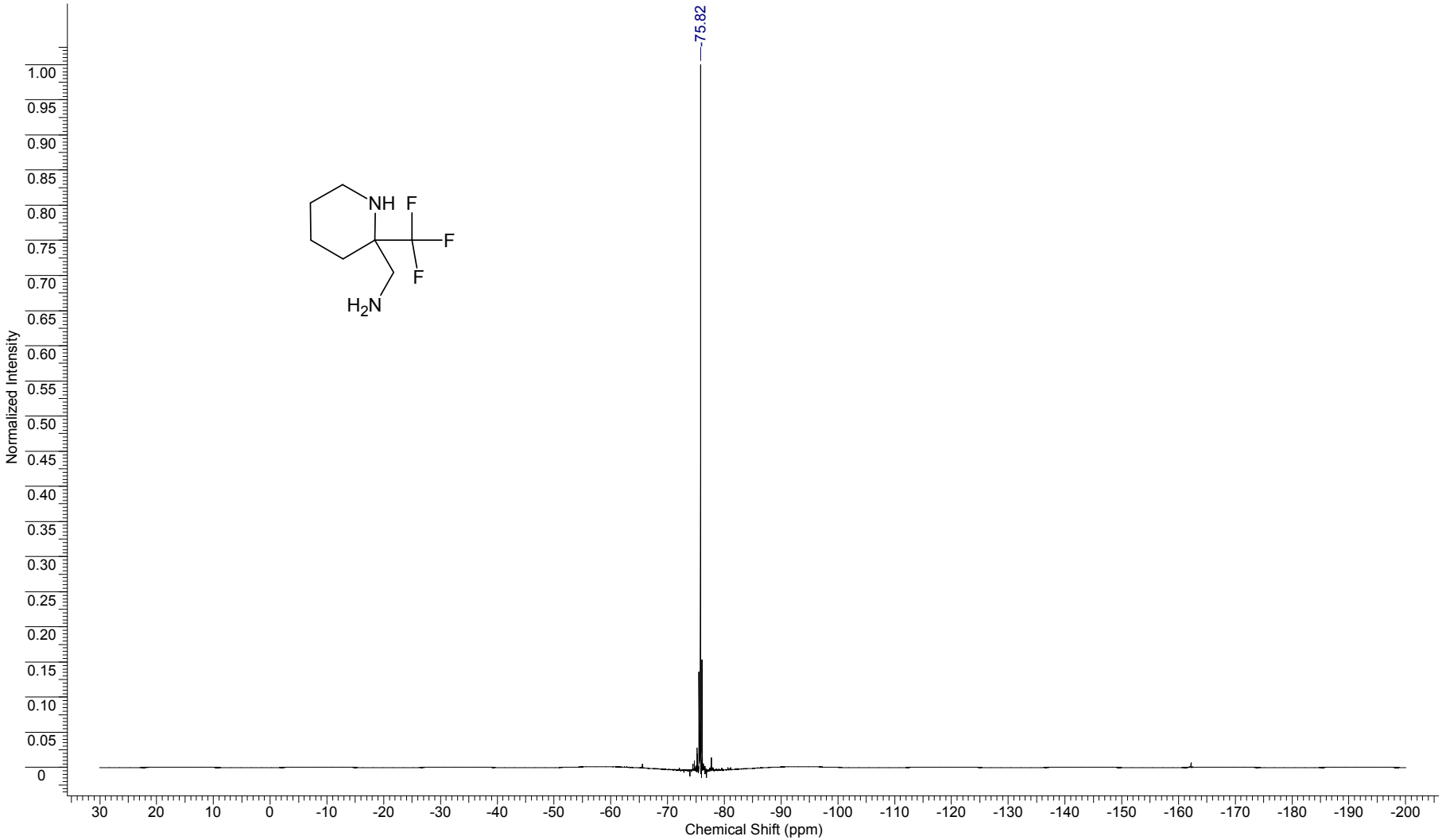
^{1}H NMR (400 MHz, $CDCl_3$) for compound **5c**



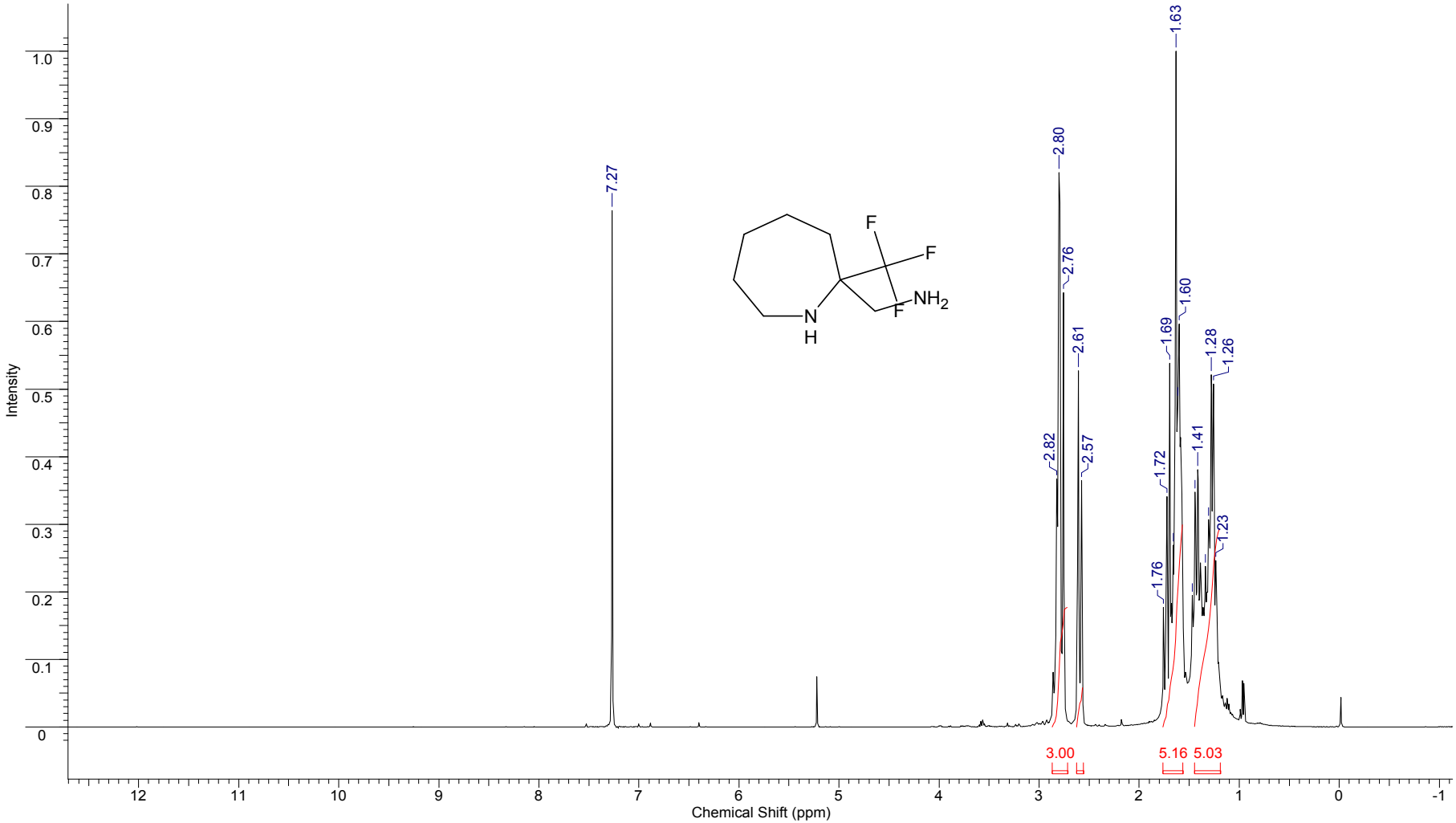
^{1}H NMR (400 MHz, $CDCl_3$) for compound **5c** aliphatic region



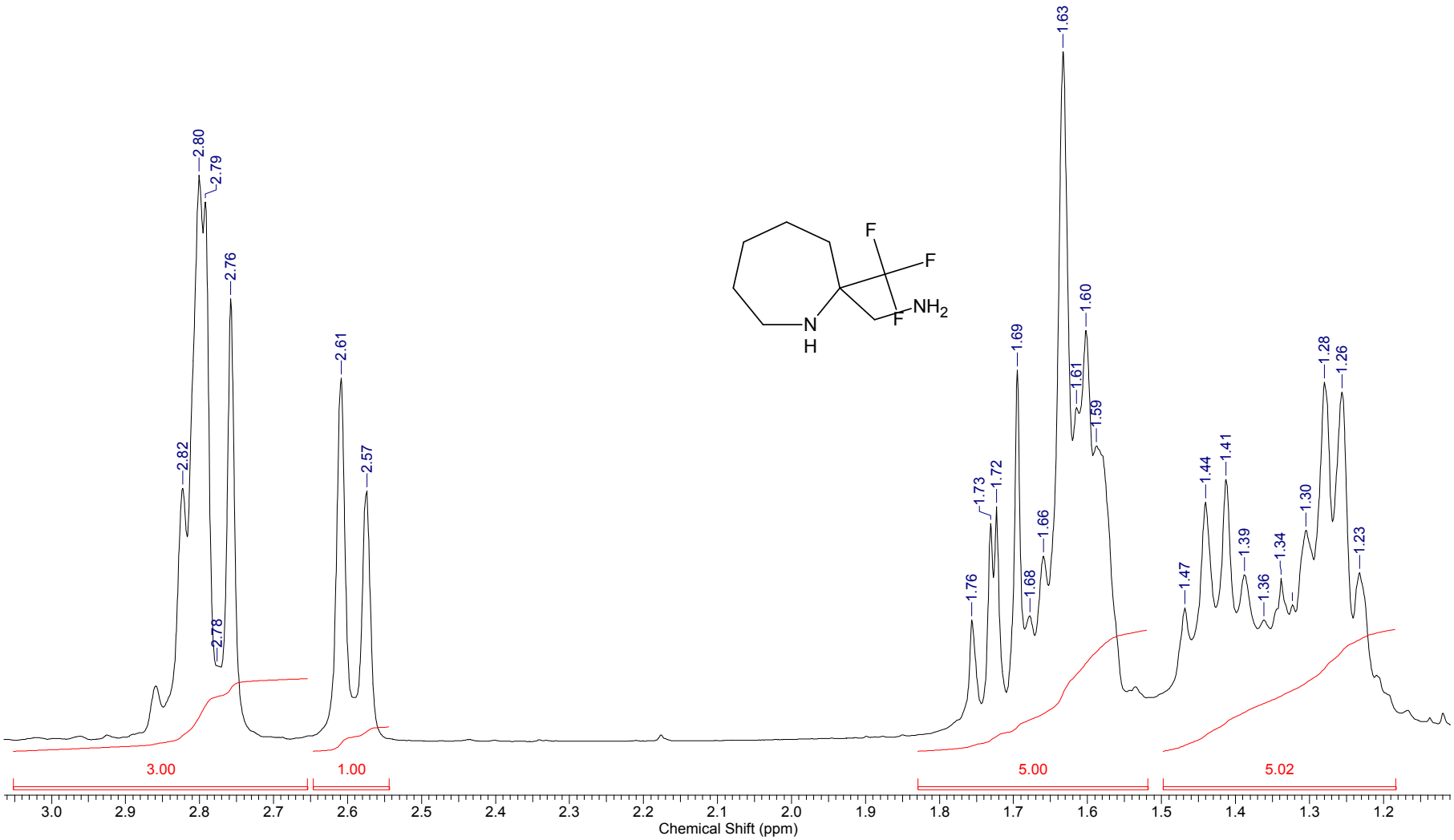
^{13}C NMR (100 MHz, $CDCl_3$) for compound **5c**



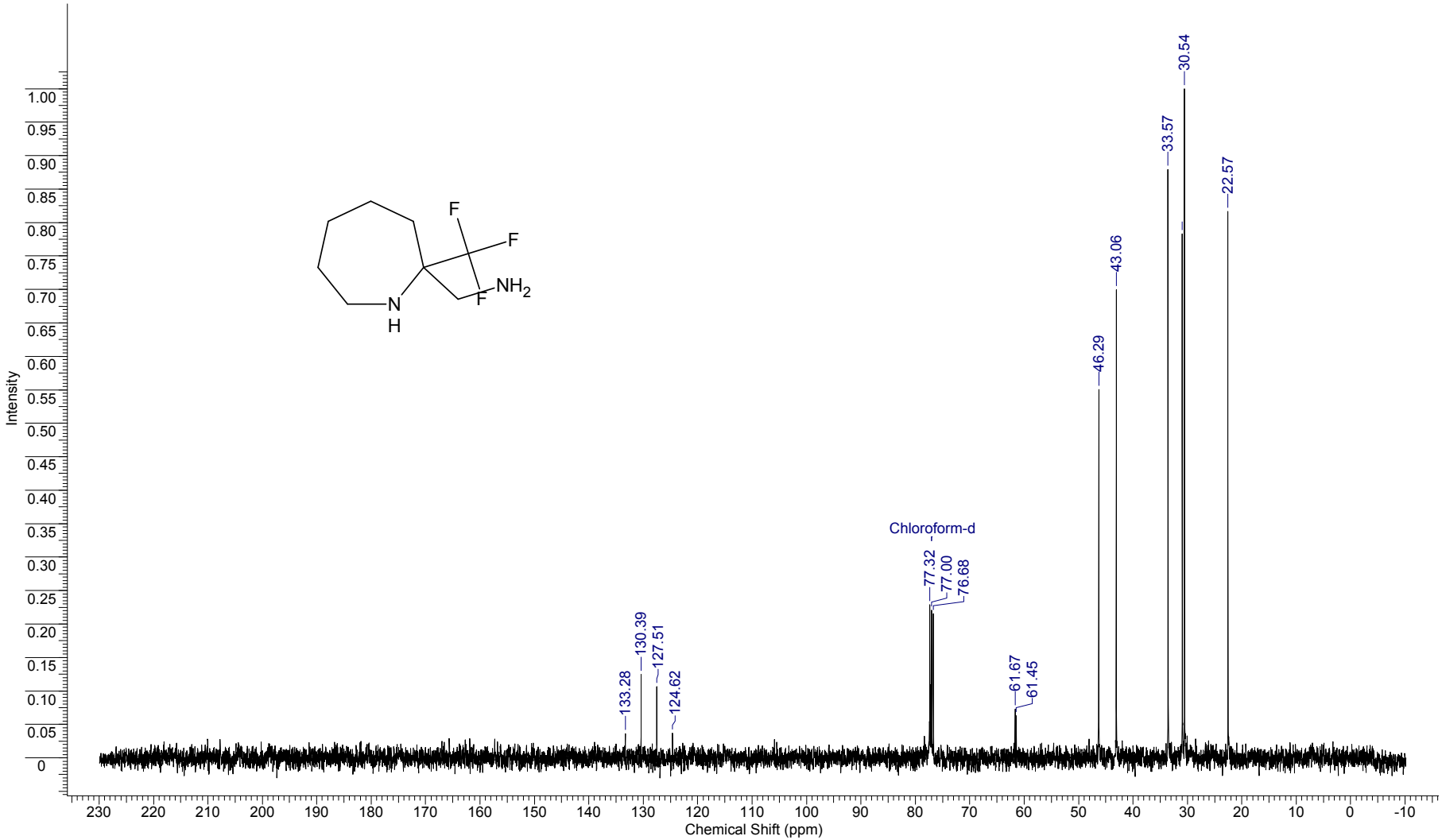
^{19}F NMR (280 MHz, $CDCl_3$) for compound **5c**



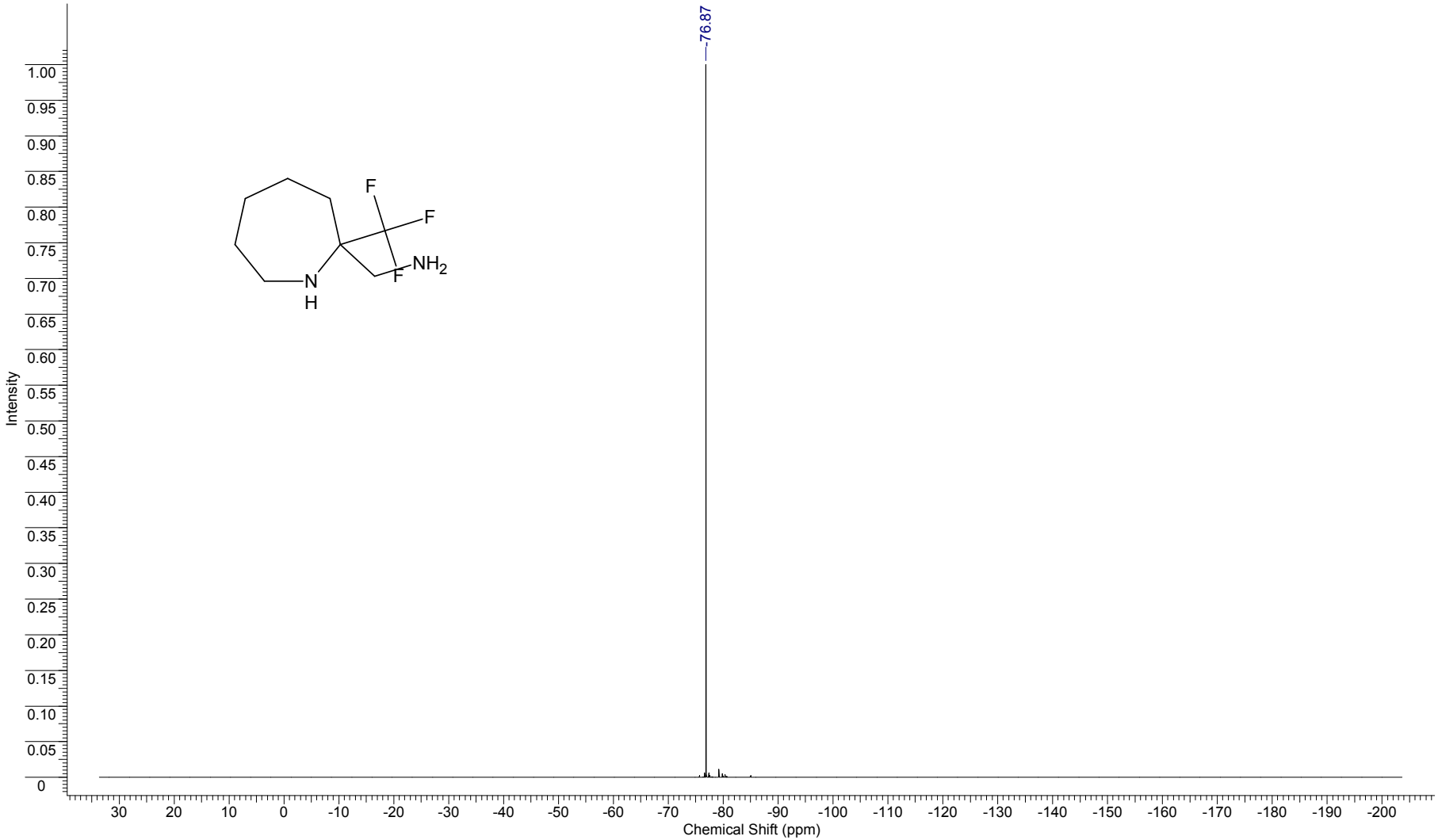
^{1}H NMR (400 MHz, $CDCl_3$) for compound **5e**



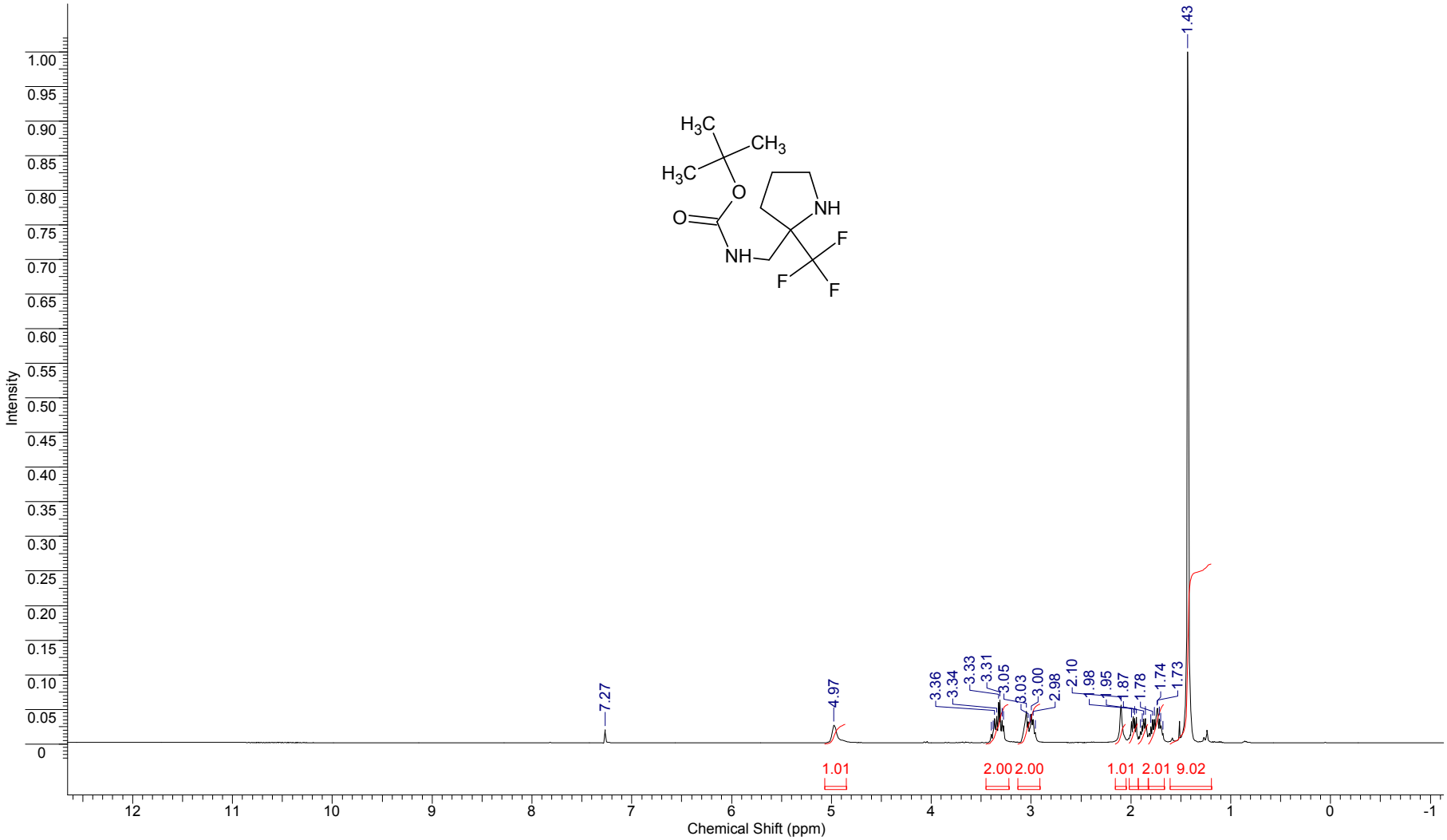
^{1}H NMR (400 MHz, $CDCl_3$) for compound **5e** aliphatic region



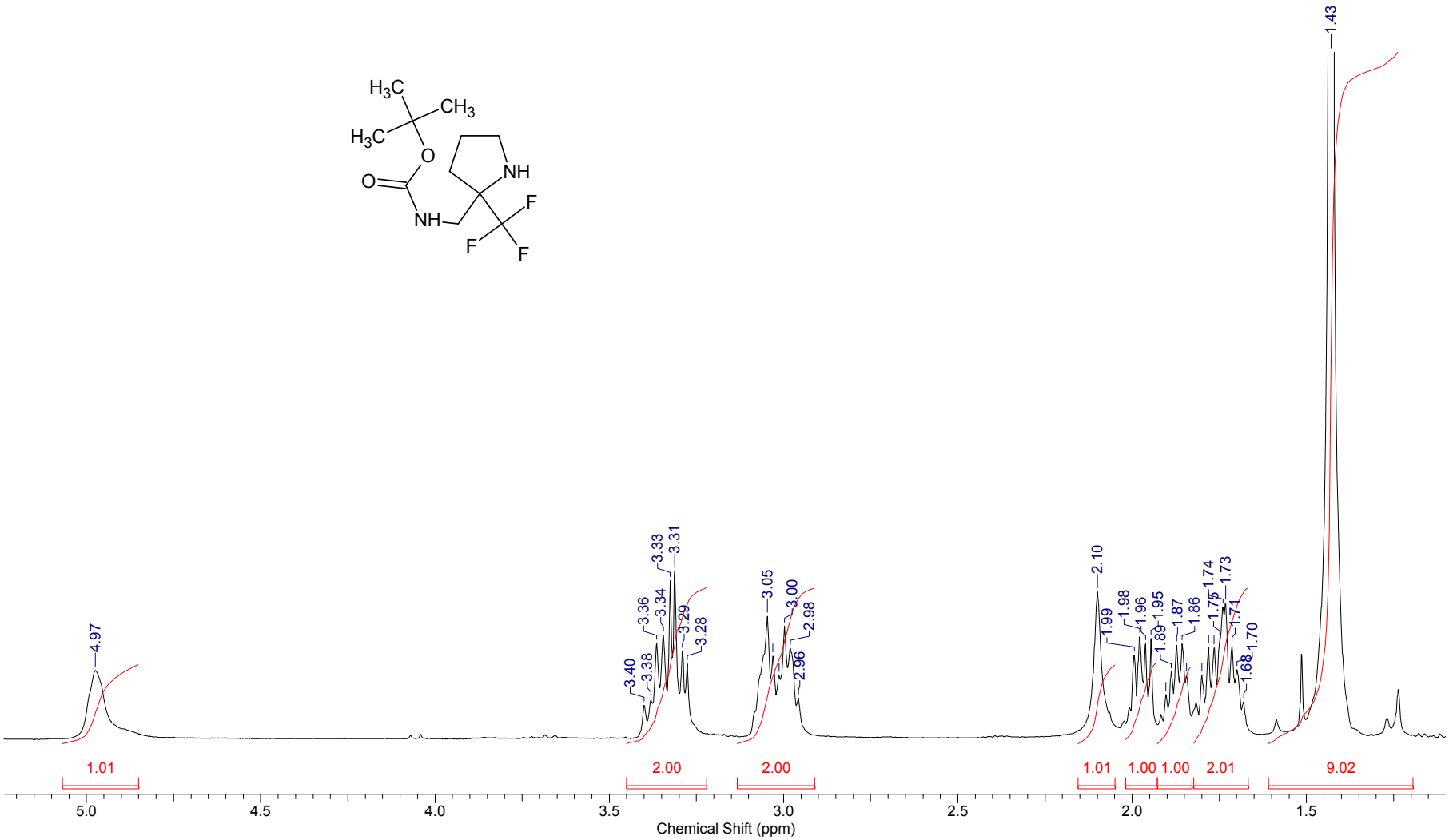
^{13}C NMR (100 MHz, $CDCl_3$) for compound **5e**



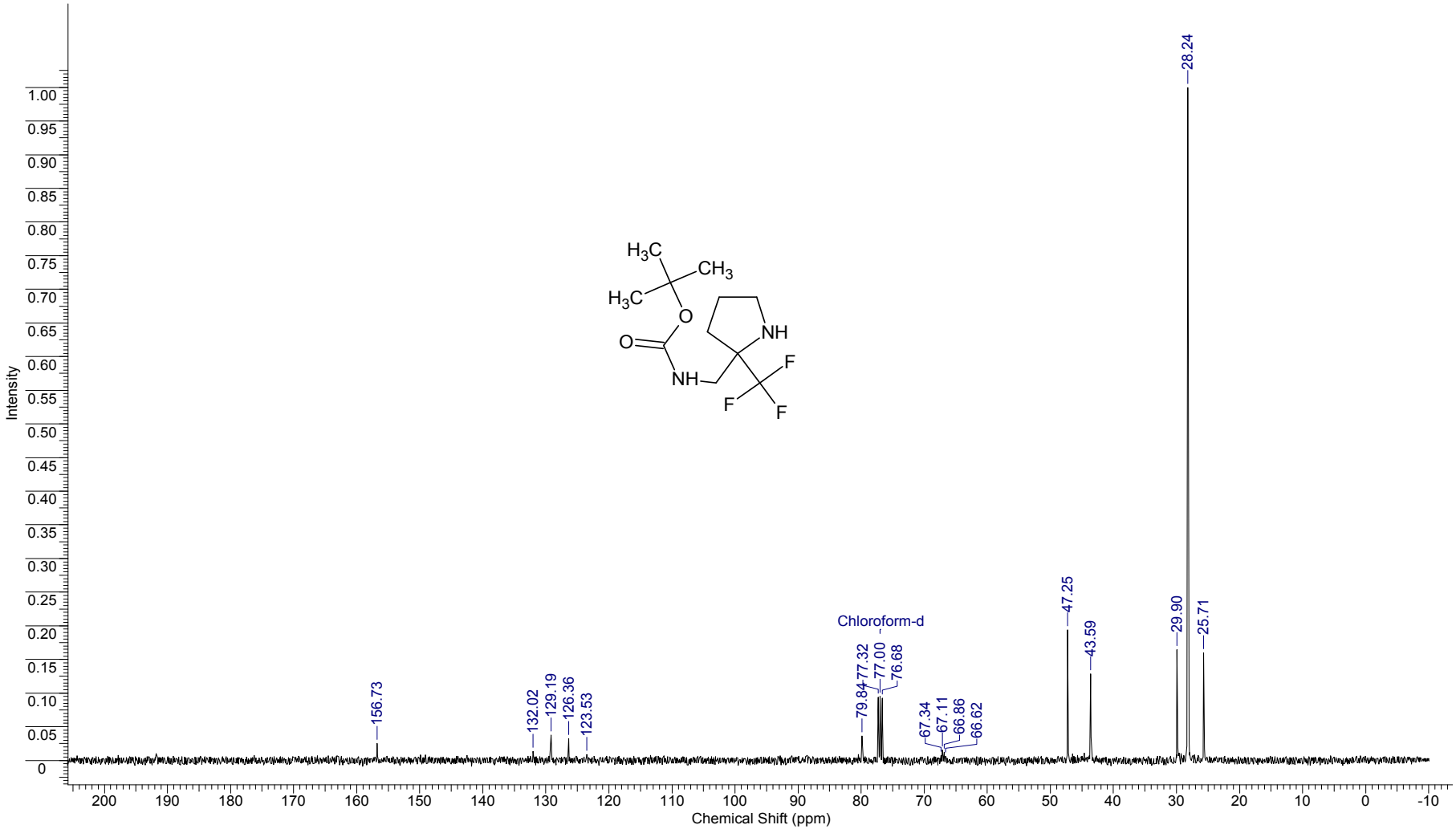
^{19}F NMR (280 MHz, $CDCl_3$) for compound **5e**



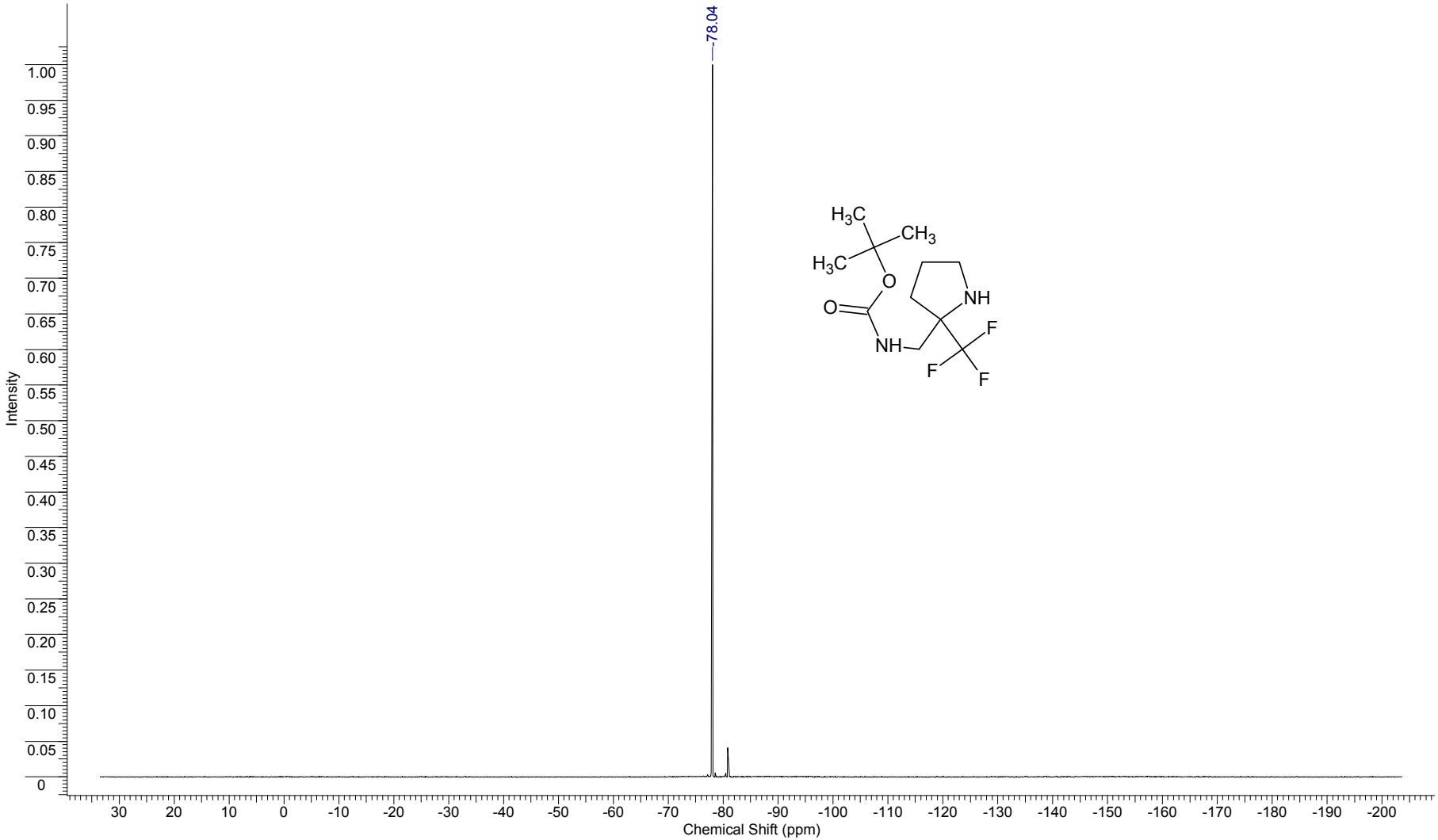
^{1}H NMR (400 MHz, $CDCl_3$) for compound **6a**



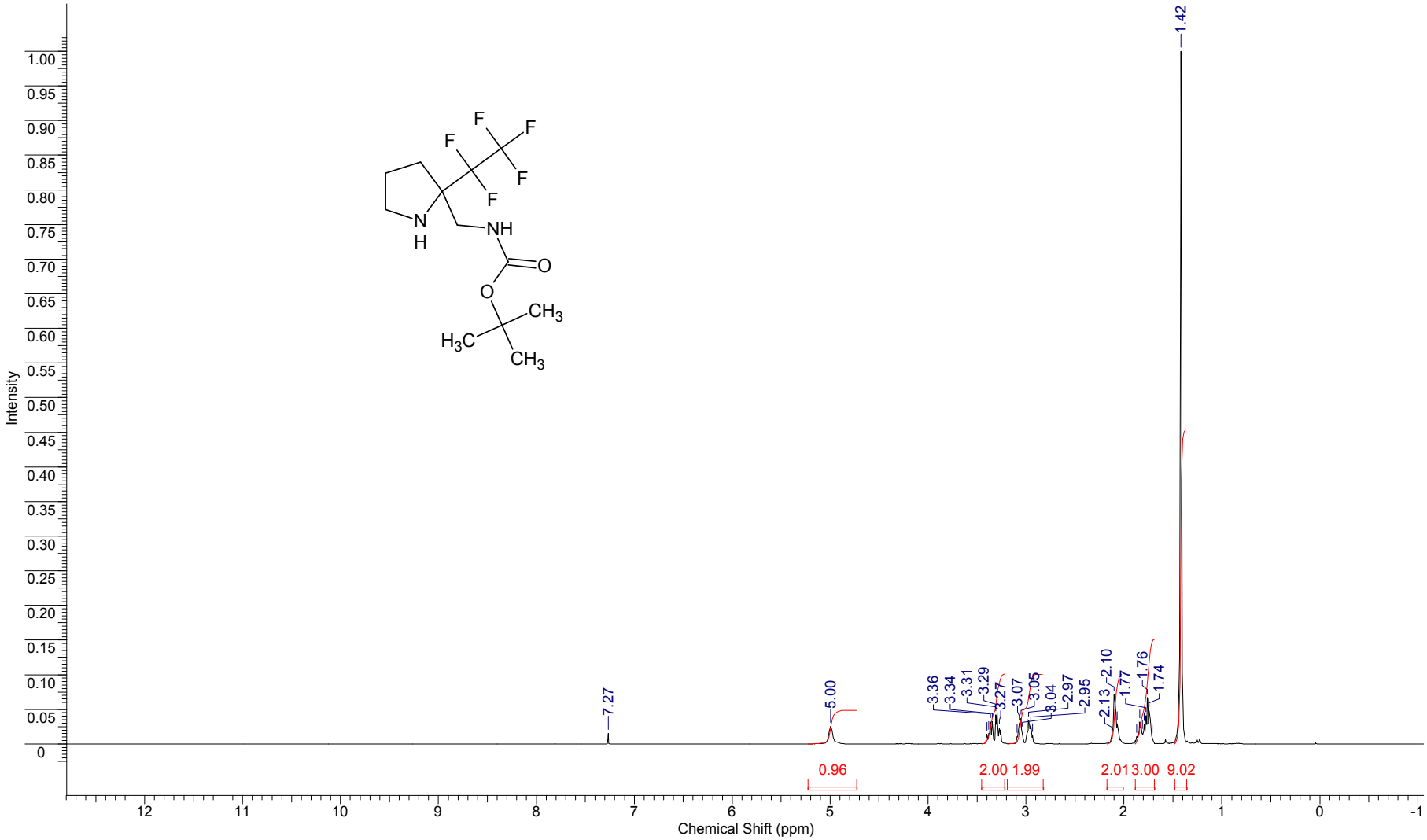
^{1}H NMR (400 MHz, $CDCl_3$) for compound **6a** aliphatic region



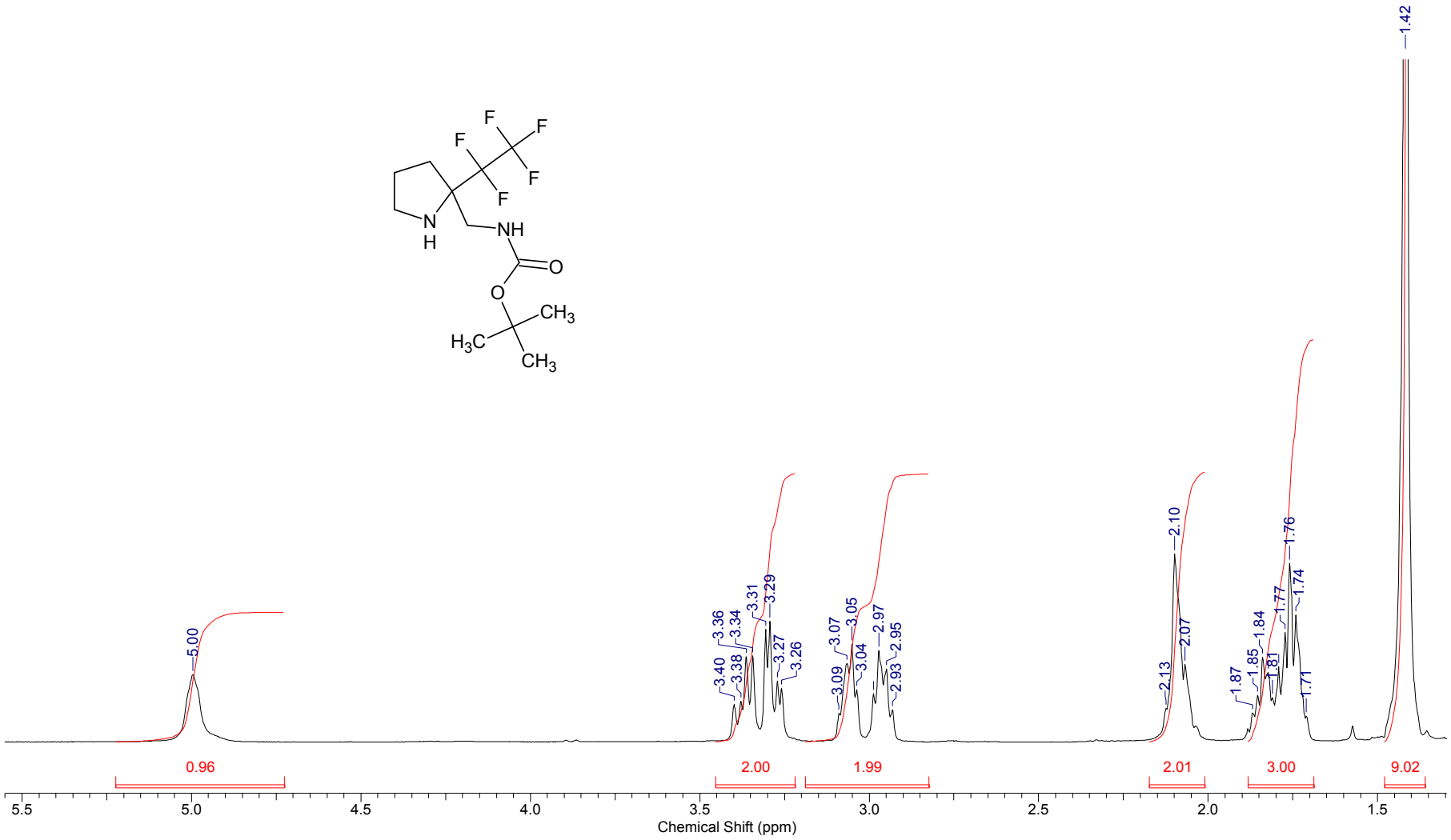
^{13}C NMR (100 MHz, $CDCl_3$) for compound **6a**



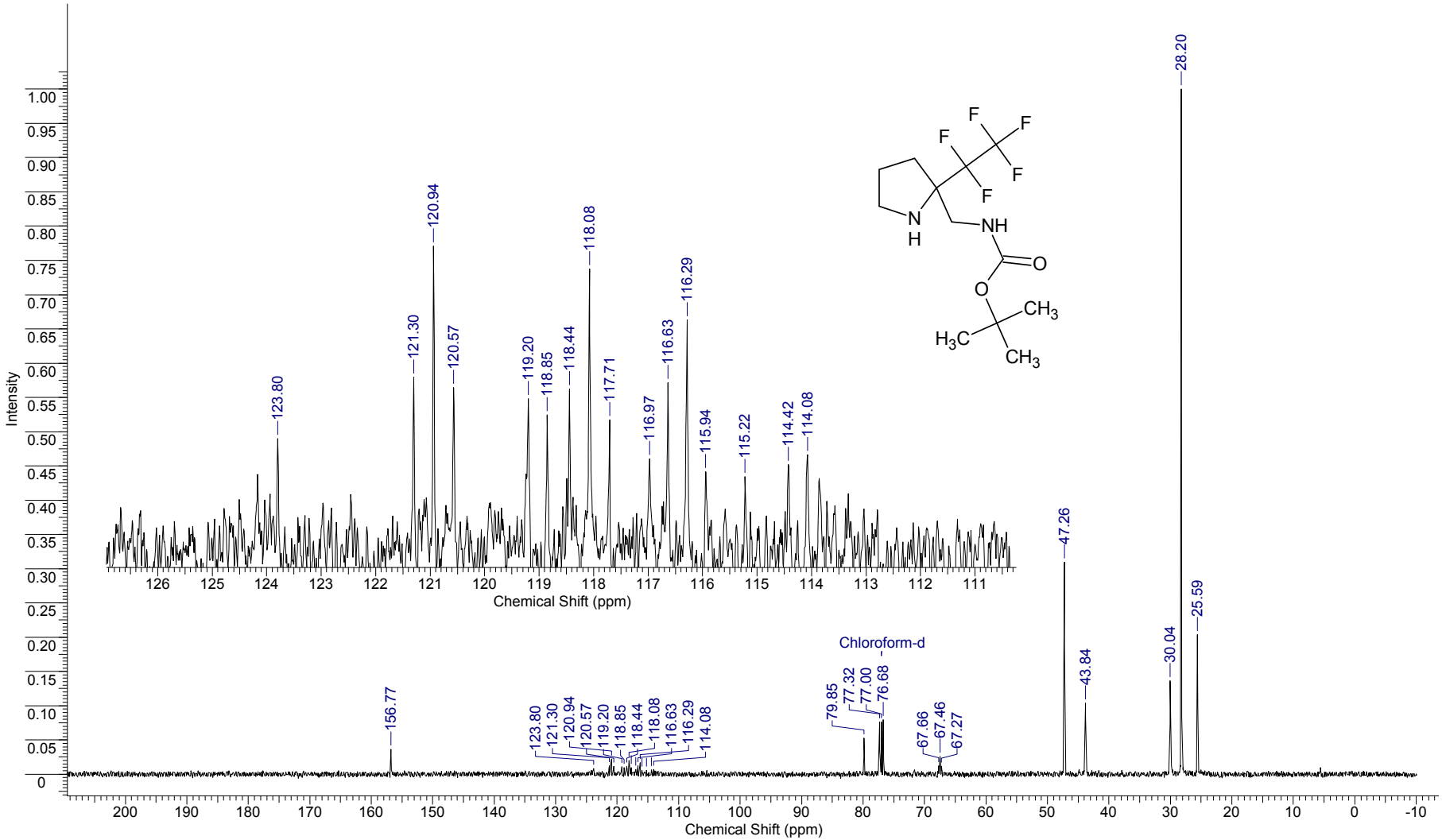
^{19}F NMR (280 MHz, $CDCl_3$) for compound **6a**



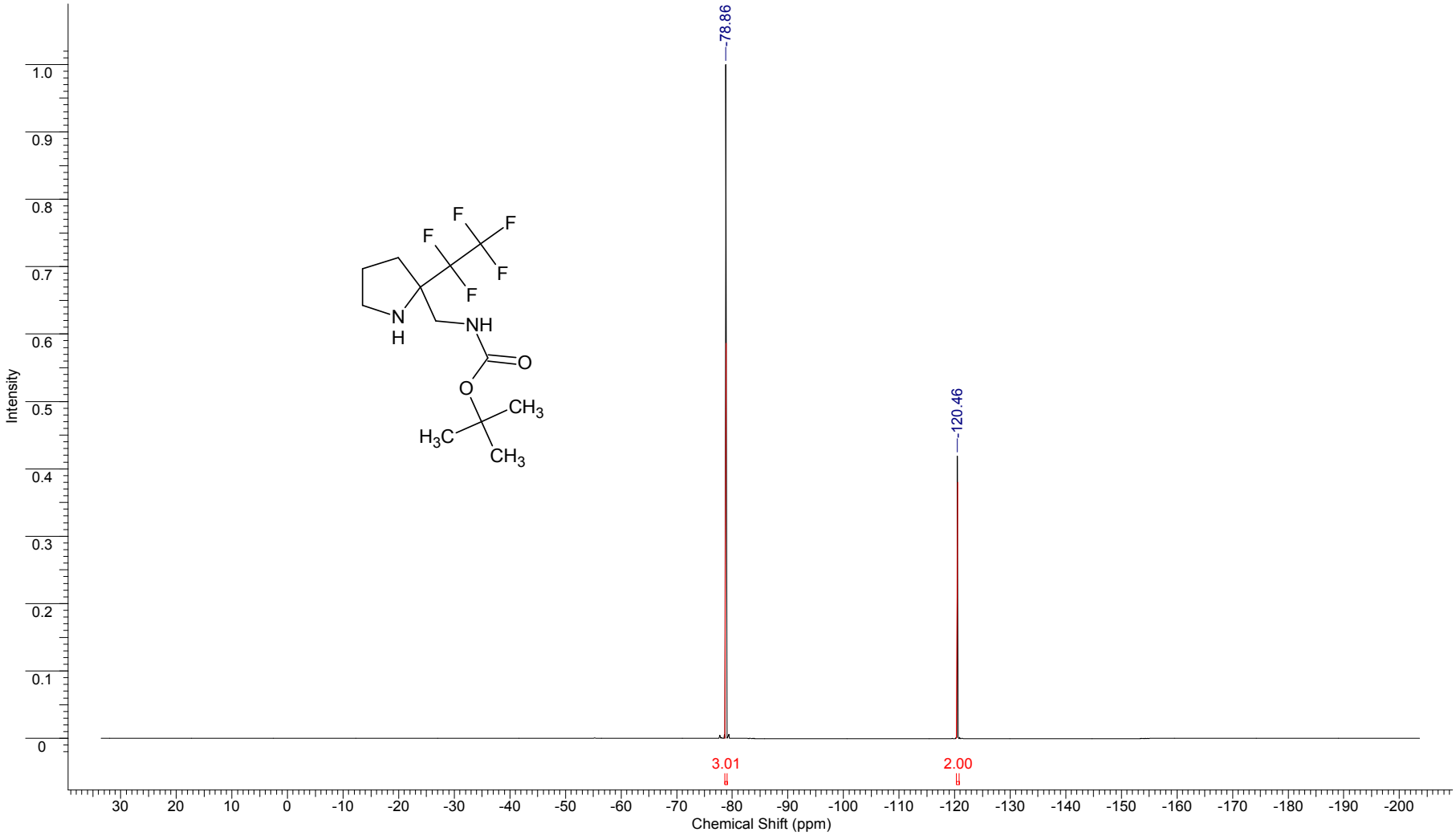
^{1}H NMR (400 MHz, $CDCl_3$) for compound **6b**



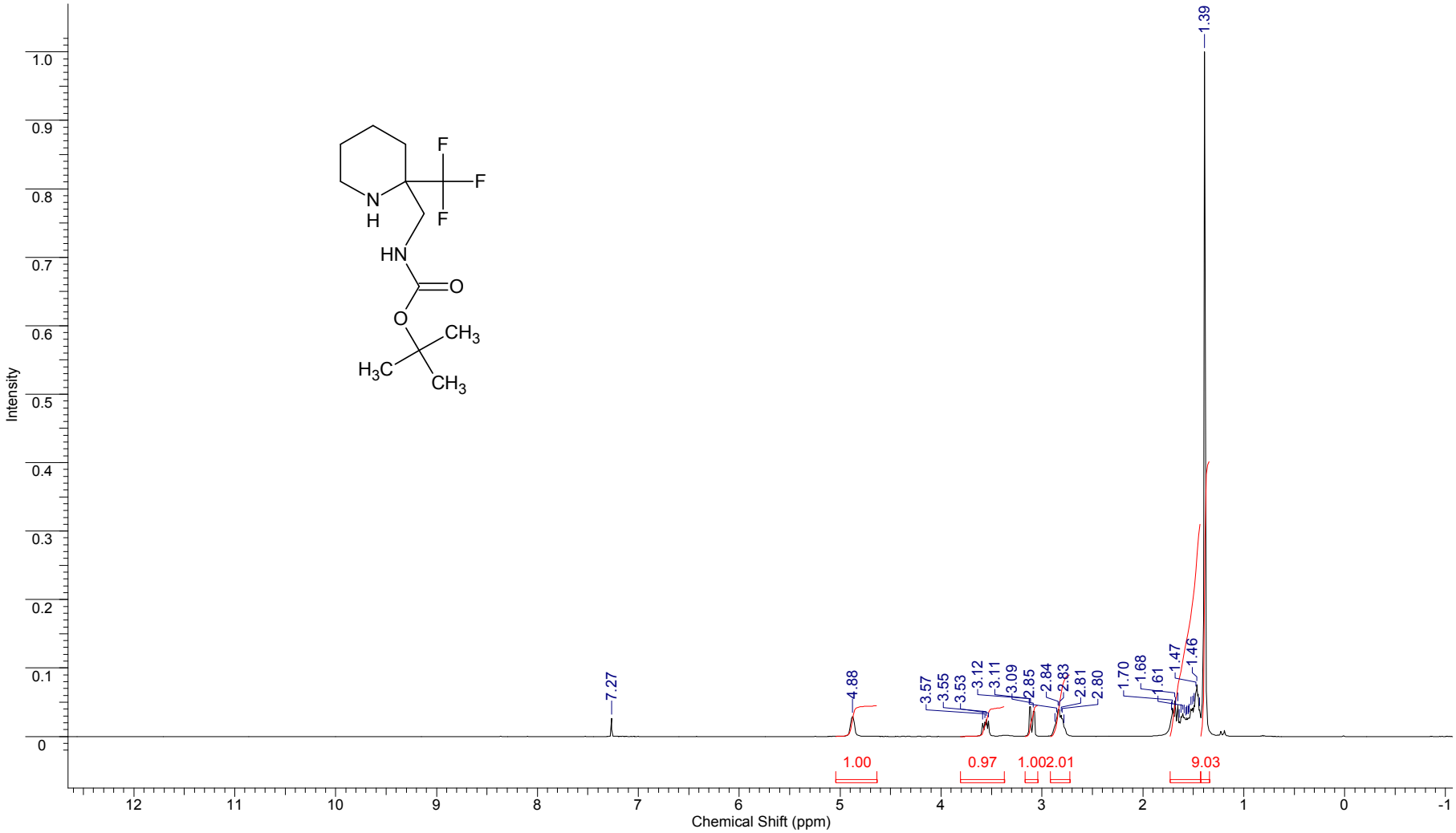
^{1}H NMR (400 MHz, $CDCl_3$) for compound **6b** aliphatic region



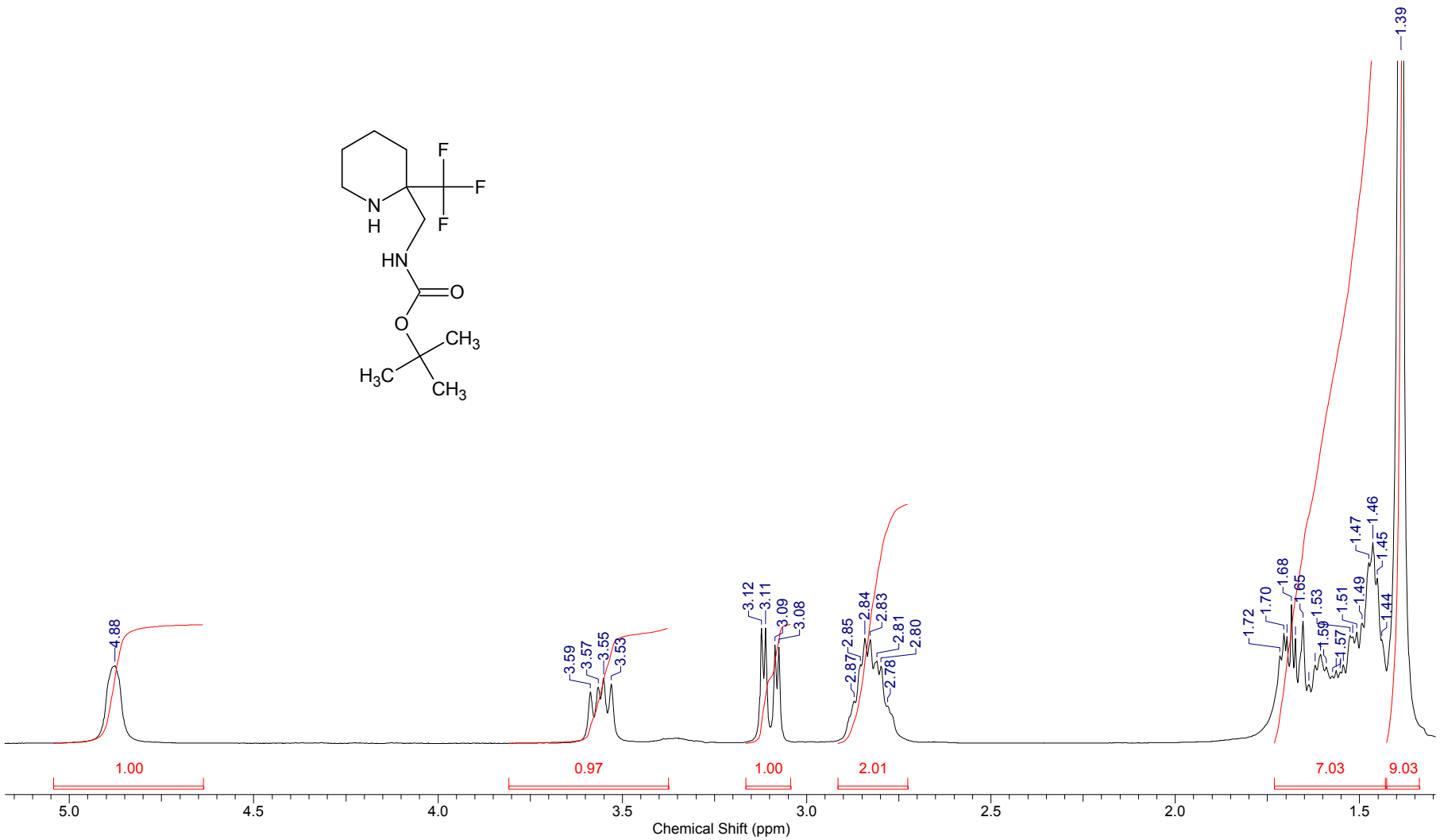
^{13}C NMR (100 MHz, $CDCl_3$) for compound **6b**



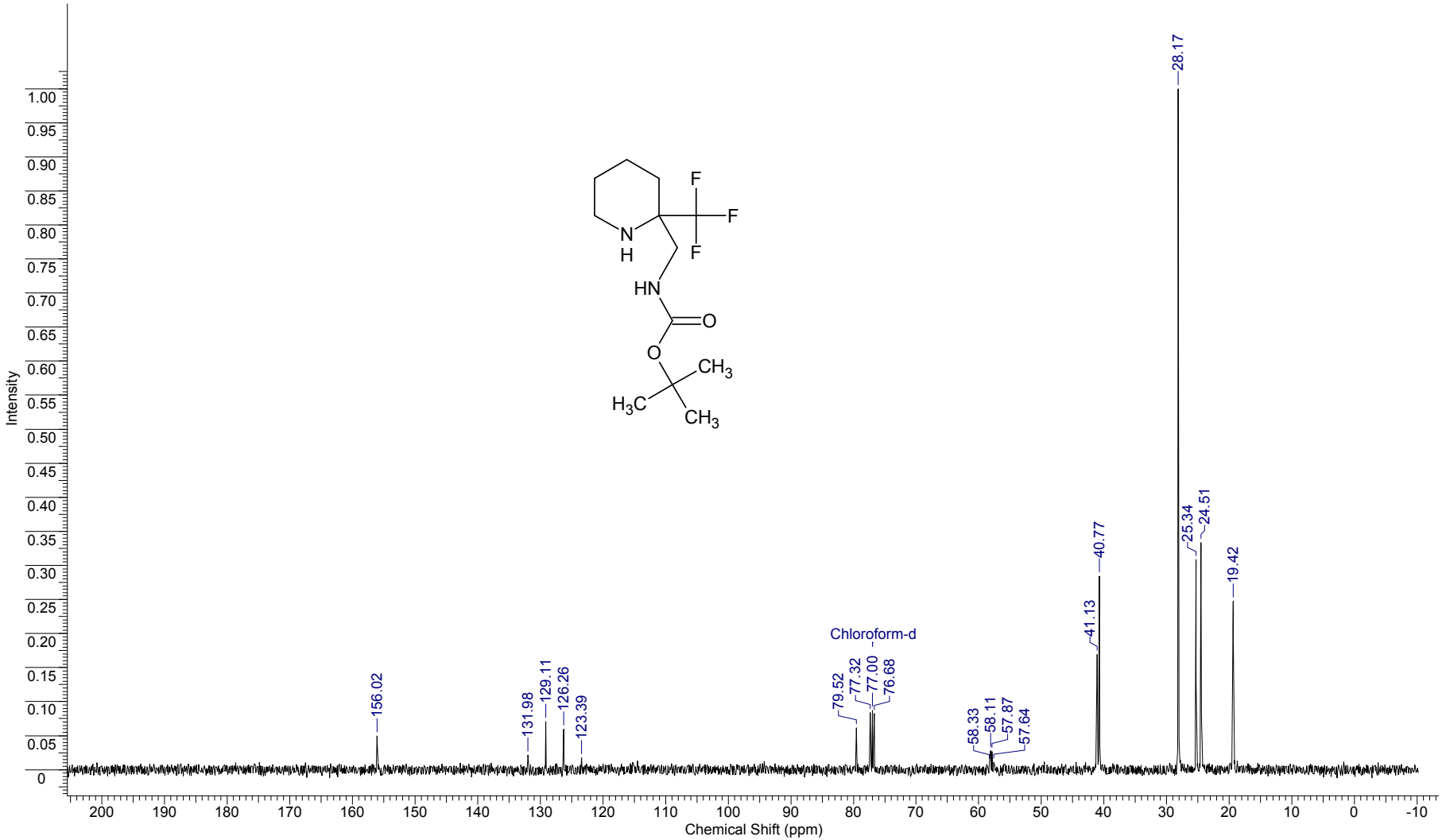
^{19}F NMR (280 MHz, $CDCl_3$) for compound **6b**



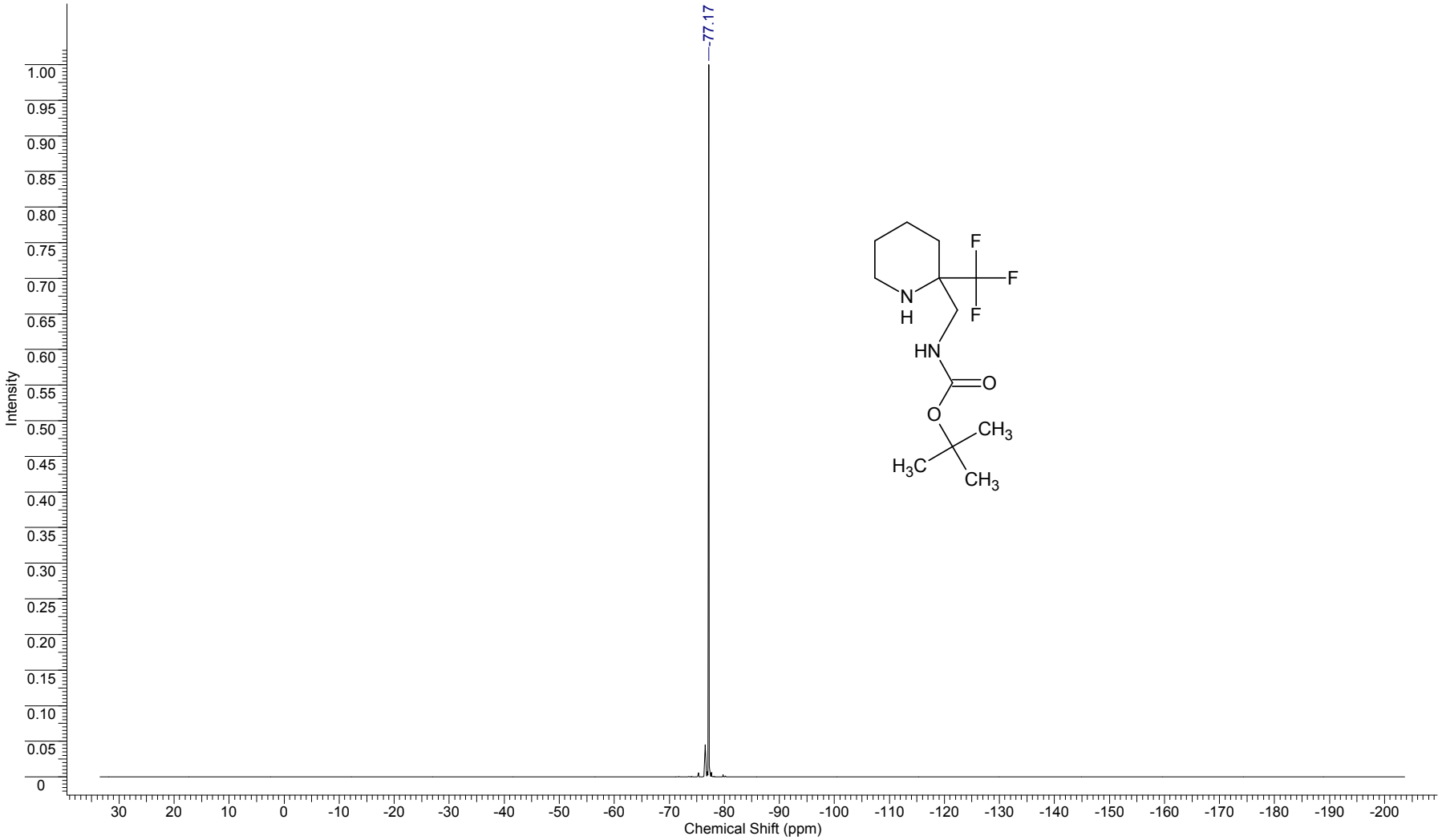
^{1}H NMR (400 MHz, $CDCl_3$) for compound **6c**



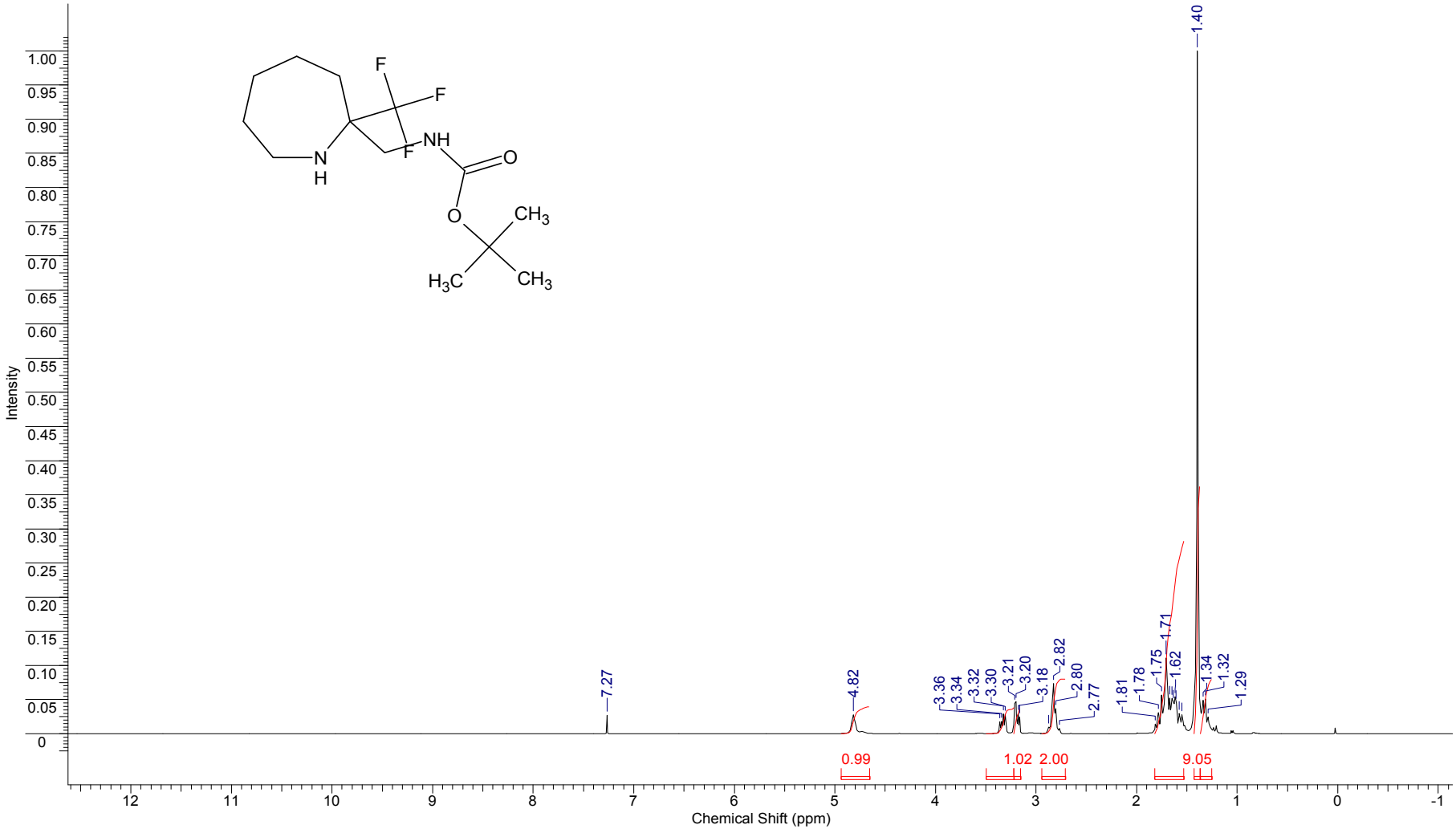
^{1}H NMR (400 MHz, $CDCl_3$) for compound **6c** aliphatic region



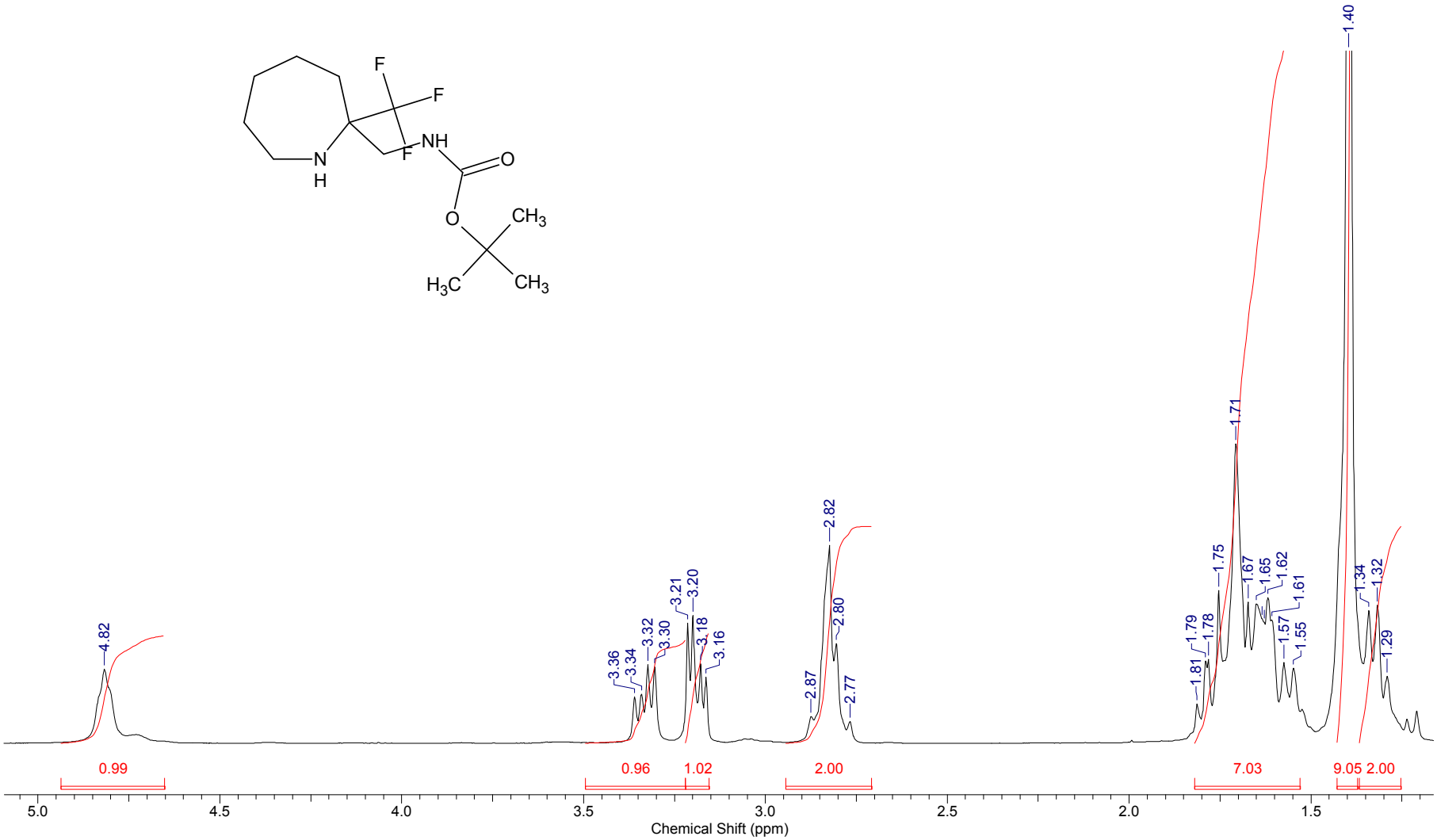
^{13}C NMR (100 MHz, $CDCl_3$) for compound **6c**



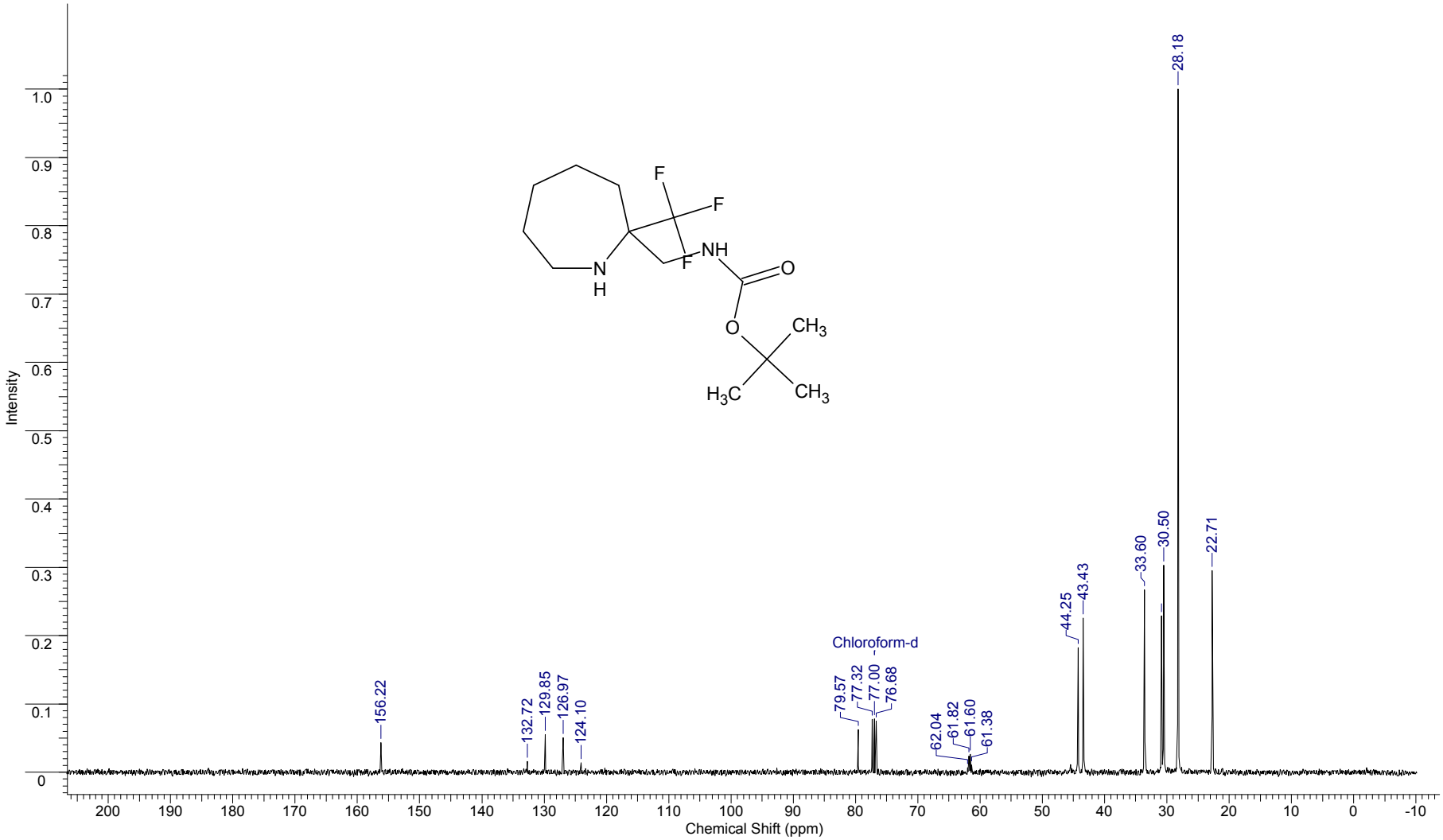
^{19}F NMR (280 MHz, $CDCl_3$) for compound **6c**



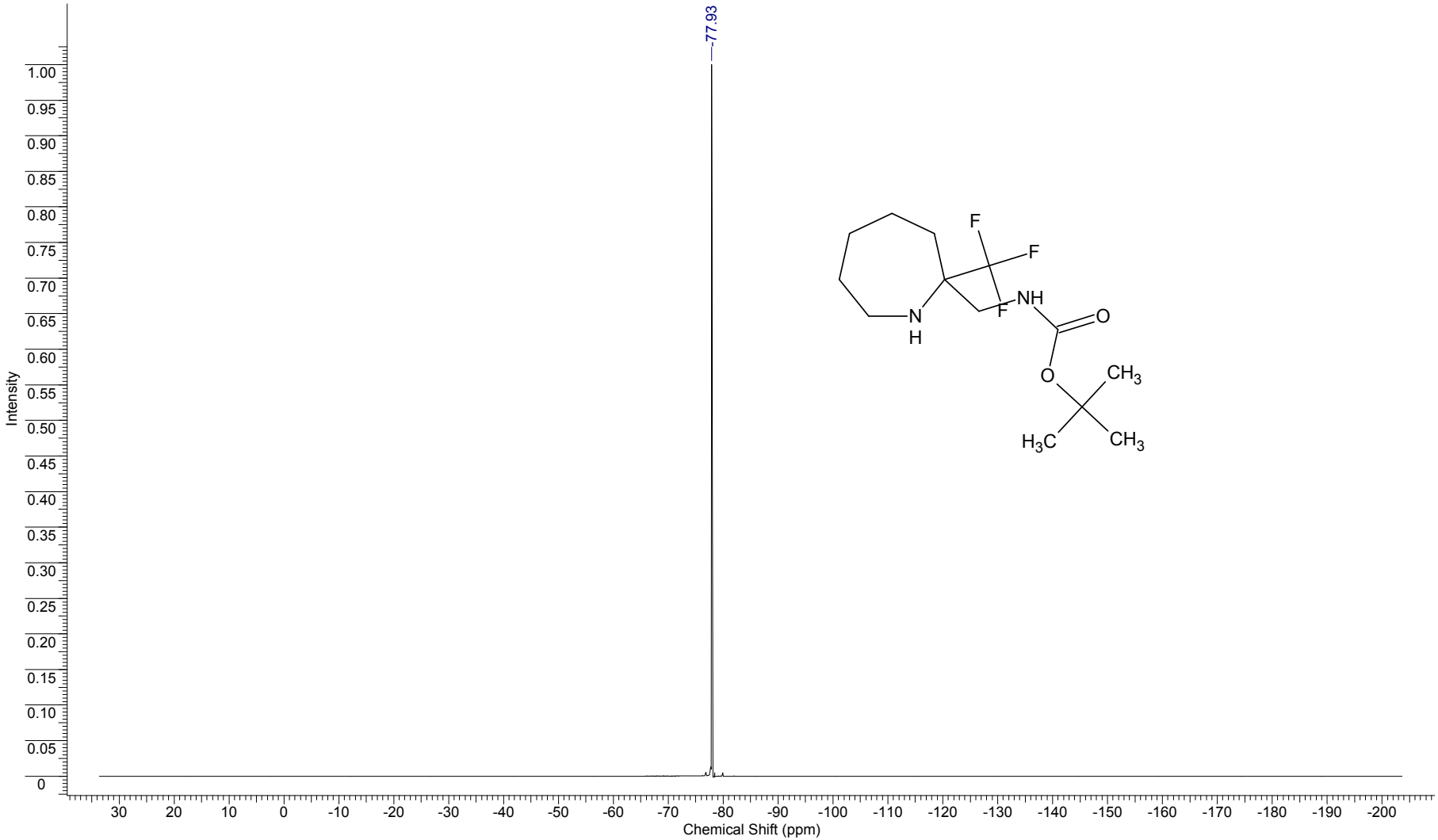
^{1}H NMR (400 MHz, $CDCl_3$) for compound **6e**



^{1}H NMR (400 MHz, $CDCl_3$) for compound **6e** aliphatic region



^{13}C NMR (100 MHz, $CDCl_3$) for compound **6e**



^{19}F NMR (280 MHz, $CDCl_3$) for compound **6e**

References

(1) a) A. V. Gulevich, N., E. Shevchenko, E. S. Balenkova, G.-V. Röschenthaler, V. G. Nenajdenko, *Synlett,* 2009, **3**, 0403 b) E. N. Shevchenko, E. S. Balenkova, G.-V. Röschenthaler, V. G. Nenajdenko, *Synthesis,* 2010, **1**, 0120.