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Synthesis of 4-trifluoromethyl-2*H*-chromenes via the reaction of 2-(trifluoroacetyl)phenols with vinyltriphenylphosphonium chloride

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Supporting Information

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I General Information

^{1}H NMR and ^{13}C{^{1}H} NMR spectra were run on a Bruker Avance^{TM} 400 instrument (working frequency of 400.13 MHz and 100.925 MHz, respectively). The proton chemical shifts were measured relative to the residual solvent signal δ ($CDCl_3$) 7.28 and δ (DMSO-d_6) 2.50 and recalculated from the $SiMe_4$ signal. Chemical shifts for ^{13}C nuclei were determined with respect to the signal for $CDCl_3$ (77.0 ppm) and recalculated from the $SiMe_4$ signal. ^{19}F NMR and ^{19}F{^{1}H} NMR spectra were recorded on a Bruker Avance^{TM} 400 instrument (working frequency of 376.50 MHz). The ^{19}F NMR shifts were measured relative to trifluoroacetic acid (an external standard) and referenced to $CFCl_3$.

Mass spectra were obtained on a Finnigan Polaris Q instrument (ion trap, 70 eV, the direct insertion probe procedure or a GCMS method were used for the sample injection).

IR absorption spectra were recorded on a Bruker Tensor 37 FT-IR spectrometer (KBr pellets) in the 4000—400 cm^{-1} range.

Elemental analysis was performed in the Laboratory of Elemental Analysis of A.N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences.

Silica gel with the particle size of 0.06—0.20 mm (Merck Kieselgel 60) was used for column chromatography. Reaction monitoring was performed using Merck Kieselgel 60 F254 TLC plates.

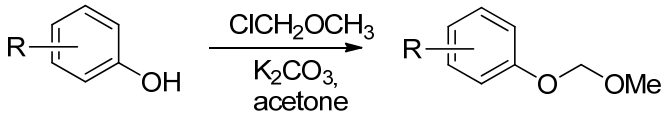
Tetrahydrofuran, diethyl ether, and dioxane were refluxed over sodium metal in the presence of benzophenone until a persistent dark blue color appeared followed by distillation under argon. *N*-Butyllithium (1.6 *M* solution in hexane) was purchased from «Acros». The lithiation reactions were performed under argon.

N,N-Dimethylformamide and dimethylsulfoxide (both from «Catrosa») were distilled under reduced pressure over CaH_2 before use. Toluene and acetonitrile (both from «Catrosa») were distilled over CaH_2 before use. Petroleum ether (PE, bp 40-70^{o}C), ethyl acetate (EtOAc), and methylene chloride were distilled over $CaCl_2$ before use.

Chloromethyl methyl ether (MOM-Cl) was prepared from dimethoxymethane and benzoyl chloride according to M. Reggelin and S. Doerr.[1]

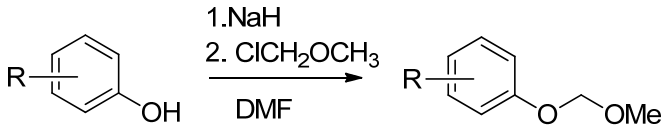
II Synthesis and characterization of starting compounds

Procedure 1 for MOM protection of substituted phenols[2]



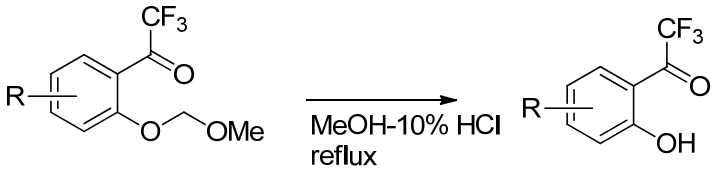
K_2CO_3 (40 mmol) and MOM-Cl (30 mmol) were added to a solution of substituted phenol or substituted 2-bromophenol (20 mmol) in dry acetone. The reaction mixture was stirred at 40-45 ^oC for 2 h, concentrated by evaporation, poured into a large excess of cold water, and extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4, and rotary evaporated. The residue was purified by column chromatography on silica gel or by distillation.

Procedure 2 for MOM protection of substituted phenols



NaH (45 mmol) was added portionwise to a solution of substituted phenol (40 mmol) in 100 ml of DMF in an atmosphere of inert gas at 0 °C. The addition usually took 30-40 min. The solution was warmed to 20 °C, stirred for 1 h, and cooled to 0 °C. MOM-Cl (4.83 g, 60 mmol) was added to the phenolate solution at 0 °C. The reaction was warmed to 20 °C, stirred for 16 h, poured into ice water, and extracted with EtOAc (30 ml x 3). The combined organic phases were washed with saturated K_2CO_3 solution, brine, dried with Na_2SO_4, and rotary evaporated.

MOM deprotection procedure



A MOM protected substituted phenol (20-40 mmol) or a MOM protected substituted 2-bromophenol (30 mmol) underwent a lithiation reaction followed by trifluoroacetylation of an aryllithium intermediate. After quenching with aqueous HCl or ammonium chloride, a MOM-protected 2-trifluoroacetylphenol was dissolved in a mixture of methanol (30 ml) and 10% aqueous HCl (6 ml). The solution was refluxed for 5 hours. Methanol was rotary evaporated.

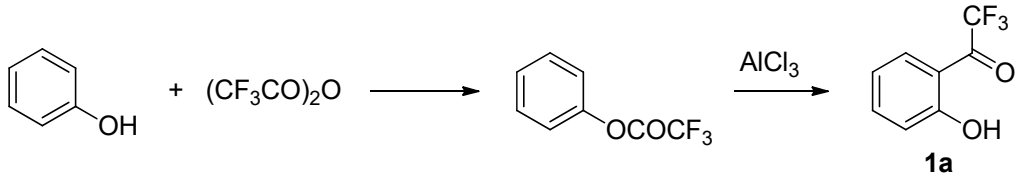
The residue was treated with diethyl ether (50 ml). The organic layer was separated, washed with saturated NaCl solution, dried over Na_2SO_4, and rotary evaporated.

Synthesis of 2-(trifluoroacetyl)phenols (1a-s).

Some of 2-(trifluoroacetyl)phenols used throughout this work are commercially available but expensive to purchase as any fluoroorganics.

Several synthetic approaches were used for obtaining 2-(trifluoroacetyl)phenols throughout this work. Phenols **1a**, **1g**, **1h**, **1i**, **1p, 1s** were prepared by Fries rearrangement of the corresponding aryl trifluoroacetates usually followed by purification through a copper salt according to the literature precedents.[3-5] Phenols **1b** and **1d** were prepared by lithiation with *n*-BuLi of MOM-protected 4-chloro-2-bromophenol and MOM-protected 4-methoxy-2-bromophenol, respectively, followed by trifluoroacylation with ethyl trifluoroacetate. Phenols **1e**, **1k**, **1l**, **1m**, **1o, 1q**, and **1t** were synthesized by lithiation of the corresponding MOM-protected phenols with *n*-BuLi followed by trifluoroacylation with ethyl trifluoroacetate or difluoroacylation with ethyl difluoroacetate (for **1s**). Features of the lithiation reaction of MOM-protected phenols for the synthesis of a specific 2-(trifluoroacetyl)phenol (in particular, the use of TMEDA or 2,2,6,6-tetramethylpiperidine, the temperature regimes of lithiation reactions) are taken from the literature for the synthesis of the corresponding salicylaldehydes,[6,7] salicylic acid[8] or 3,3′-di(trifluoroacetyl)-1,1′-binaphthol [9] and are given below. Phenol **1j** was obtained by trifluoroacylation of 3-acetoxy-*N*,*N*-diethylbenzene with trifluoroacetic anhydride followed by deprotection of the acetyl group.[10] Phenols **1c** and **1n** were synthesized by bromination with *N*-bromosuccinimide of phenol **1a** and phenol **1c**, respectively. Nitration of phenol **1a** with 70% nitric acid in acetic acid gives a mixture of phenols **1f** and **1r** in a ratio of 3:2, from which phenol **1f** was isolated by crystallization. Phenol **1r** was obtained by a multistage synthesis from 3-nitrosalicylaldehyde using the Ruppert-Prakash reagent and the Swern oxidation.

Synthesis of 1-(2-hydroxyphenyl)-2,2,2-trifluoroethan-1-one (1a)

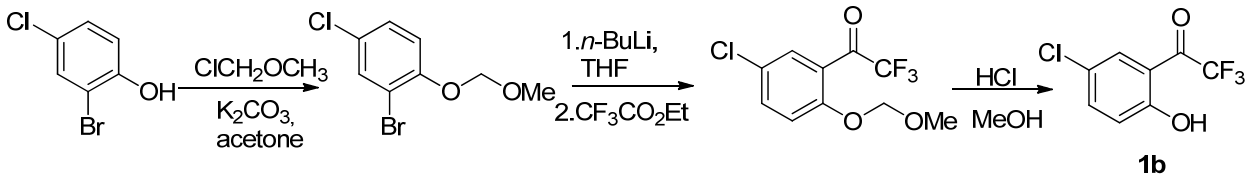


1a

Phenyl 2,2,2-trifluoroacetate was obtained from phenol and trifluoroacetic anhydride according to the procedure described in the literature.[4]

1-(2-Hydroxyphenyl)-2,2,2-trifluoroethan-1-one (1a) was obtained from phenyl 2,2,2-trifluoroacetate by Fries rearrangement in the presence of $AlCl_3$ according to the procedure described in the literature.[4] ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.09 (s, 1H), 7.91 – 7.80 (m, 1H), 7.73 – 7.58 (m, 1H), 7.11 (d, *J* = 8.5 Hz, 1H), 7.08 – 6.98 (m, 1H). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -70.33 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.4 (q, *J* = 35.4 Hz), 164.6, 139.0, 130.7 (q, *J* = 3.7 Hz), 120.0, 119.1, 116.4 (q, *J* = 289.9 Hz), 113.9. The ^{1}H, ^{13}C, and ^{19}F NMR spectra of phenol **1a** fully correspond to the spectral characteristics given in the literature.[4,11]

Synthesis of 1-(5-chloro-2-hydroxyphenyl)-2,2,2-trifluoroethan-1-one (1b)



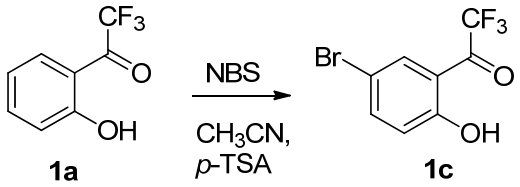
1b

2-Bromo-4-chloro-1-(methoxymethoxy)benzene was obtained from 2-bromo-4-chlorophenol (10.37 g, 50.0 mmol) and MOM-Cl (6.04 g, 75 mmol) in the presence of K_2CO_3 (13.82 g, 100.0 mmol) in acetone (100 ml) according to procedure 1 for MOM protection of phenols. The residue after evaporation of ethyl acetate was distilled to give the product (11.36 g, 90.4%) as a colorless liquid, bp 101-103 °C/1 Torr. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, *J* = 2.5 Hz, 1H), 7.27 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.14 (d, *J* = 8.8 Hz, 1H), 5.28 (s, 2H), 3.57 (s, 3H). The ^{1}H NMR spectrum of the product corresponds to the spectral characteristics given in the literature.[12]

1-(5-Chloro-2-hydroxyphenyl)-2,2,2-trifluoroethan-1-one (1b). To 2-bromo-4-chloro-1-(methoxymethoxy)benzene (7.54 g, 30 mmol) in THF (80 ml) was added *n*-BuLi (18.8 ml of a 1.6 M solution in hexane, 30 mmol) at -75 °C. Upon completion of the addition, the reaction mixture was stirred for 30 min and ethyl trifluoroacetate (6.0 g, 42 mmol) was added dropwise at a temperature below -70 °C. The reaction was warmed gradually to 0 °C and made distinctly acidic with 5% aq. HCl. The organic layer was separated; the aqueous layer was extracted with ether (2 x 40 ml). The combined organic phases were rotary evaporated to give 8.7 g of a pale yellow liquid. After the MOM deprotection step, 5.25 g of a pale yellow liquid was isolated. This liquid was purified by column chromatography on silica gel (eluent: PE/CH_2Cl_2 = 2/1) to give 4.3 g of compound **1b**. Further purification by distillation gave pure phenol **1b** (3.8 g, 56%) as a pale yellow liquid with bp 80-83 °C/10 Torr which slowly solidified into pale yellow crystals with mp

39-40 °C (from PE). The ^{1}H, ^{13}C, and ^{19}F NMR spectra fully correspond to the spectral characteristics given in the literature.[11] Found: C, 42.77; H, 1.98. Calcd. for $C_8H_4ClF_3O_2$: C, 42.79; H, 1.80%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.05 (s, 1H), 7.92 – 7.75 (m, 1H), 7.64 (dd, *J* = 9.1, 2.5 Hz, 1H), 7.13 (d, *J* = 9.1 Hz, 1H). $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.55 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.8 (q, *J* = 36.0 Hz), 163.1, 139.0, 129.5 (q, *J* = 4.0 Hz), 124.9, 120.7, 116.11 (q, *J* = 289.8 Hz), 114.30. EIMS 70 eV, *m/z*: 224 (M^+, 8%), 155 (100, M–CF_3), 127 (24, M–CF_3–CO), 99 (38, M–CF_3–2CO).

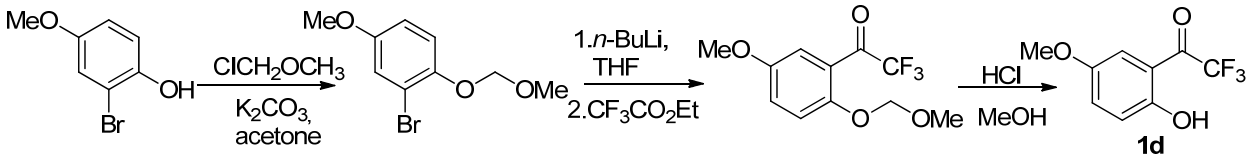
Synthesis of 1-(5-bromo-2-hydroxyphenyl)-2,2,2-trifluoroethan-1-one (1c)



1a **1c**

1-(5-Bromo-2-hydroxyphenyl)-2,2,2-trifluoroethan-1-one (1c). To a solution of 1-(2-hydroxyphenyl)-2,2,2-trifluoroethan-1-one **1a** (4.0 г, 21 ммоль) in 100 ml of acetonitrile was added *N*-bromosuccinimide (5.6 g, 31.5 mmol) and *p*-toluenesulfonic acid monohydrate (2.0 g, 10.5 mmol) at rt. The reaction mixture was stirred for 60 h. Acetonitrile was evaporated, the residue was dissolved in chloroform (50 ml), washed with water, saturated NaCl solution, dried with Na_2SO_4, and rotary evaporated. The residue (~6.0 g) was purified by column chromatography on silica gel (eluent: PE/CH_2Cl_2 = 2/1) to give 3.2 g of a pale yellow liquid which contained about 95% of compound **1c**. Recrystallization from PE afforded pure phenol **1c** (2.5 g, 44%) as pale yellow crystals, mp 35-36 °C (from PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.02 (s, 1H), 8.00 – 7.86 (m, 1H), 7.73 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.04 (d, *J* = 9.0 Hz, 1H). $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.45 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.7 (q, *J* = 36.0 Hz), 163.5, 141.7, 132.6 (q, *J* = 4.1 Hz), 121.1, 116.1 (q, *J* = 289.7 Hz), 115.0, 111.7. The ^{1}H and ^{19}F NMR spectra of phenol **1c** fully correspond to the spectral characteristics given in the literature.[4,13]

Synthesis of 2,2,2-trifluoro-1-(2-hydroxy-5-methoxyphenyl)ethan-1-one (1d)

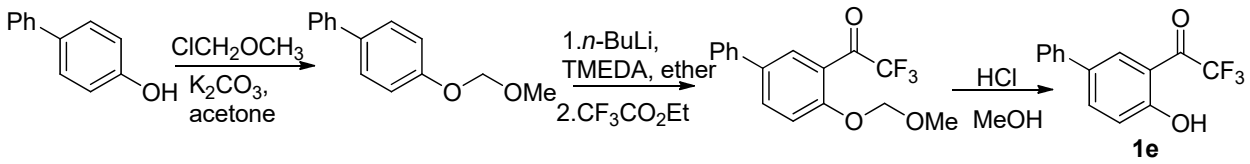


1d

2-Bromo-4-methoxy-1-(methoxymethoxy)benzene was obtained from 2-bromo-4-methoxyphenol (15.0 g, 73.9 mmol) and MOM-Cl (8.86 g, 110 mmol) in the presence of K_2CO_3 (20.45 g, 148.0 mol) in acetone (100 ml) according to procedure 1 for MOM protection of phenols. The residue after evaporation of ethyl acetate was distilled to give the product (15.05 g, 82.5%) as a colorless liquid with bp 108-110 °C/1 Torr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, *J* = 3.0 Hz, 1H), 7.10 (d, *J* = 9.0 Hz, 1H), 6.82 (dd, *J* = 9.0, 3.0 Hz, 1H), 5.18 (s, 2H), 3.78 (s, 3H), 3.55 (s, 3H). The ^{1}H NMR spectrum of the product corresponds to the spectral characteristics given in the literature.[14]

2,2,2-Trifluoro-1-(2-hydroxy-5-methoxyphenyl)ethan-1-one (1d) was obtained from 2-bromo-4-methoxy-1-(methoxymethoxy)benzene (7.41 g, 30 mmol) by lithiation with *n*-BuLi (18.8 ml of a 1.6 M solution in hexane, 30 mmol) in THF (80 ml) at -75 °C followed by trifluoroacetylation with ethyl trifluoroacetate (6.0 g, 42 mmol) at the temperature below -70 °C and MOM deprotection with a mixture of methanol and 10% aq. HCl. The procedure is analogous to the synthesis of 1-(5-chloro-2-hydroxyphenyl)-2,2,2-trifluoroethan-1-one **1b**. The residue after the MOM deprotection step (5.32 g of a pale yellow liquid) was purified by column chromatography on silica gel (eluent: PE/CH_2Cl_2 = 1/1) to give 4.6 g of compound **1d** which slowly solidified into pale yellow crystals. Recrystallization from PE afforded pure compound **1d** (3.9 g, 59%) as pale yellow crystals, mp 39-40 °C (from PE). Found: C, 49.14; H, 3.38. Calcd. for $C_9H_7F_3O_3$: C, 49.10; H, 3.20%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.83 (s, 1H), 7.30 (dd, *J* = 9.1, 2.9 Hz, 1H), 7.21 (s, 1H), 7.05 (d, *J* = 9.2 Hz, 1H), 3.83 (s, 3H). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -70.47 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.8 (q, *J* = 35.2 Hz), 159.6, 152.2, 128.2, 120.1, 116.4 (q, *J* = 289.9 Hz), 113.1, 111.3 (q, *J* = 3.9 Hz), 55.8.

Synthesis of 2,2,2-trifluoro-1-(4-hydroxy-[1,1'-biphenyl]-3-yl)ethan-1-one (1e)



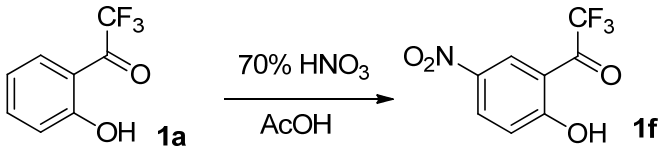
4-(Methoxymethoxy)-1,1`-biphenyl was obtained from 4-phenylphenol (5.11 g, 30 mmol) and MOM-Cl (4.03 g, 50 mmol) in the presence of K_2CO_3 (12.43 g, 90 mmol) in 100 ml of acetone according to procedure 1 for MOM protection of phenols. The residue after evaporation of ethyl acetate was purified by silica gel column chromatography (eluent: PE/EA = 10/1) to give 6.22 g (89%) of the product as white crystals, mp 41-42 °C (from PE/EtOAc). ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.62 – 7.51 (m, 4H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.3 Hz, 1H), 7.15 (d, *J* = 8.8 Hz, 2H), 5.25 (s, 2H), 3.54 (s, 3H). The ^{1}H NMR spectrum of the product corresponds to the spectral characteristics given in the literature.[15]

2,2,2-Trifluoro-1-(4-hydroxy-[1,1'-biphenyl]-3-yl)ethan-1-one 1e. To a solution of 4-(methoxymethoxy)-1,1`-biphenyl (4.3 g, 20 mmol) in ether (80 ml) was added TMEDA (2.8 g, 24 mmol). The reaction mixture was cooled to -20 °C, and *n*-BuLi (15 ml of a 1.6 N solution, 24 mmol) was added dropwise. The reaction mixture was stirred for 2 hours at -20 – 0 °C. The resulting orange suspension was cooled to -50 °C and a solution of ethyl trifluoroacetate (5.68 g, 40 mmol) in ether (20 ml) was added dropwise. The reaction was warmed to 0 °C and made distinctly acidic with 5% aq. HCl. The organic layer was separated; the aqueous layer was extracted with ether (2x30 ml). The combined organic phases were rotary evaporated. The residue (6.41 g) underwent the MOM deprotection procedure to give oily crystals (5.31 g). Further purification by column chromatography on silica gel (eluent: PE/CH_2Cl_2 = 3/1) afforded pure phenol **1e** (3.2 g, 60%) as yellow crystals, mp 58-59 °C (from PE). Found: C, 63.17; H, 3.55. Calcd. for $C_{14}H_9F_3O_2$: C, 63.16; H, 3.41%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.09 (s, 1H), 8.05 – 7.99 (m, 1H), 7.90 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.59 – 7.53 (m, 2H), 7.53 – 7.46 (m, 2H), 7.42 (t, *J* = 7.2 Hz, 1H), 7.21 (d, *J* = 8.8 Hz, 1H). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -70.11 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.5 (q, *J* = 35.4 Hz), 164.0, 139.1, 138.0, 133.5, 129.1, 128.7 (q, *J* = 3.7 Hz), 127.7, 126.7, 119.5, 116.5 (q, *J* = 290.0 Hz), 114.0.

Synthesis of 2,2,2-trifluoro-1-(2-hydroxy-5-nitrophenyl)ethan-1-one (1f)

Method 1.

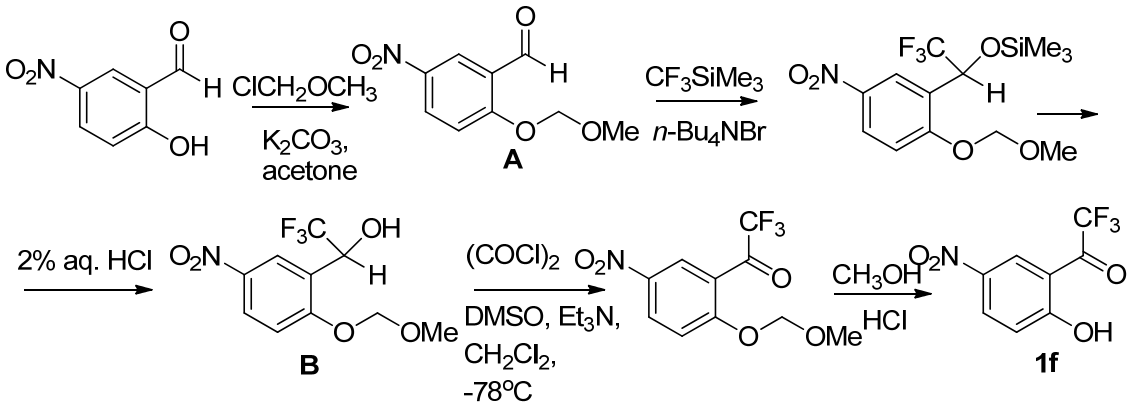


To a solution of 1-(2-hydroxyphenyl)-2,2,2-trifluoroethan-1-one **1a** (9.51 g, 50 mmol) in 100 ml of glacial acetic acid was added dropwise 70% nitric acid (5.0 g, 3.55 ml, 55 mmol). The reaction mixture was stirred for 24 h, poured into 300 ml of water, and extracted with ethyl acetate (3x80 ml). The combined organic phases were dried with Na_2SO_4 and rotary evaporated. The residue was distilled to give 8.3 g of a light yellow liquid with bp 90-100 °C/1 Torr. According to the ^{1}H NMR spectrum, it consisted of 2,2,2-trifluoro-1-(2-hydroxy-5-nitrophenyl)ethan-1-one **1f** (about 55%), 2,2,2-trifluoro-1-(2-hydroxy-3-nitrophenyl)ethan-1-one **1r** (about 35%) and 2-

nitrophenol. This phenolic mixture was dissolved in a mixture of 6 ml of PE and 6 ml of EA. The solution was kept in the refrigerator at -18 °C. The crystalline mass was filtered cold and recrystallized from a mixture of PE and EtOAc to give pure phenol **1f** (1.57 g, 13%) as pale yellow crystals, mp 70-71 °C (from PE/EtOAc). Found: C, 40.85; H, 1.84; N, 6.07. Calcd. for $C_8H_4F_3NO_4$: C, 40.87; H, 1.71; N, 5.96%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.53 (s, 1H), 8.83 (s, 1H), 8.53 (dd, *J* = 9.3, 2.6 Hz, 1H), 7.28 (d, *J* = 9.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.3 (q, *J* = 36.8 Hz), 168.4, 140.3, 133.2, 127.2 (q, *J* = 4.1 Hz), 120.4, 115.9 (q, *J* = 289.6 Hz), 112.7. ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -70.52 (s, CF_3). EIMS 70 eV, *m/z*: 235 (M^+, 2%), 166 (100, M–CF_3), 120 (73, M–CF_3–NO_2), 92 (34, M–CF_3–NO_2–CO).

According to the ^{1}H and ^{19}F NMR spectroscopy data as well as chromato-mass spectrometry analysis, the combined mother liquors contained over 50% of 2,2,2-trifluoro-1-(2-hydroxy-3-nitrophenyl)ethan-1-one **1r**. However, we failed to isolate phenol **1r** from this mixture. For a method of the synthesis of phenol **1r** see below. NMR spectra of phenol **1r** from a mixture with phenol **1f** and 2-nitrophenol are as follows. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.67 (s, 1H), 8.41 (dd, *J* = 8.3, 1.6 Hz, 1H), 8.10 (d, *J* = 7.9 Hz, 1H), 7.21 (t, *J* = 8.1 Hz, 1H). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -72.74 (s, CF_3).

Method 2. 2,2,2-Trifluoro-1-(2-hydroxy-5-nitrophenyl)ethan-1-one **1f** was also obtained from 2-hydroxy-5-nitrobenzaldehyde. The reaction sequence included MOM-protection of 2-hydroxy-5-nitrobenzaldehyde to give compound **A**, CF_3-group introduction into the aldehyde function using Ruppert-Prakash reagent CF_3SiMe_3, oxygen desilylation with 2% aq. HCl to give compound **B**, Swern oxidation of the 2,2,2-trifluoroethanolic fragment into the trifluoroacetyl group, and MOM deprotection to obtain phenol **1f**.



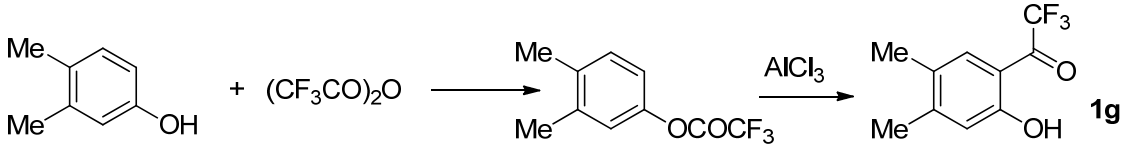
2-(Methoxymethoxy)-5-nitrobenzaldehyde (compound A) was obtained from 2-hydroxy-5-nitrobenzaldehyde and MOM-Cl in the presence of K_2CO_3 in acetone according to procedure 1

for MOM protection of phenols. Yield 79%. White crystals with mp 65-66 °C (from PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.51 (s, 1H), 8.73 (d, *J* = 2.9 Hz, 1H), 8.42 (dd, *J* = 9.2, 2.9 Hz, 1H), 7.41 (d, *J* = 9.2 Hz, 1H), 5.45 (s, 2H), 3.58 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.5, 163.5, 142.2, 130.4, 125.1, 124.3, 115.6, 95.1, 57.0. ^{1}H NMR spectrum corresponds to the spectral characteristics given in the literature.[16]

2,2,2-Trifluoro-1-[2-(methoxymethoxy)-5-nitrophenyl]ethan-1-ol (compound B) was obtained by treatment of compound **A** with CF_3SiMe_3 in the presence of catalytic amounts of *n*-Bu_4NF in THF followed by oxygen desilylation with 2% aq. HCl in THF. Yield 98%. Off-white crystals with mp 56-57 °C (from PE/EtOAc). Found: C, 42.95; H, 2.98; N, 5.07. Calcd. for $C_{10}H_8F_3NO_5$: C, 43.02; H, 2.89; N, 5.02%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 2.6 Hz, 1H), 8.28 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.31 (d, *J* = 9.2 Hz, 1H), 5.59 – 5.54 (m, 1H), 5.37 (d, *J* = 7.0 Hz, 1H), 5.34 (d, *J* = 7.0 Hz, 1H), 3.52 (s, 3H), 3.07 (d, *J* = 5.6 Hz, 1H). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -78.35 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 142.01, 126.4, 124.9, 124.3, 124.1 (q, *J* = 282.6 Hz), 113.9, 94.7, 66.4 (q, *J* = 33.5 Hz), 56.7.

2,2,2-Trifluoro-1-(2-hydroxy-5-nitrophenyl)ethan-1-one (**1f).** To a solution of oxalyl chloride (0.51 g, 4 mmol) in CH_2Cl_2 (10 ml) was added DMSO (0.55 g, 7 mmol) in CH_2Cl_2 (5 ml) at -60 °C. After 15 min, compound **B** (0.56 g, 2 mmol) was added at the same temperature. The reaction mixture was stirred for 30 min and cooled to -75 °C before Et_3N (1.21 g, 12 mmol) was added. The reaction was stirred for 2 h, warmed to 0 °C, and quenched with 20 ml of water. The organic layer was separated, washed with water, and rotary evaporated. The residue (0.51 g of yellow crystals) underwent the MOM deprotection procedure to give 0.36 g of beige crystals. Further purification by sublimation gave pure phenol **1f** (0.29 g, 62%). Its physico-chemical and NMR spectral data were in full accordance with those of phenol **1f** obtained by nitration of 1-(2-hydroxyphenyl)-2,2,2-trifluoroethanone **1a.**

Synthesis of 2,2,2-trifluoro-1-(2-hydroxy-4,5-dimethylphenyl)ethan-1-one (1g)

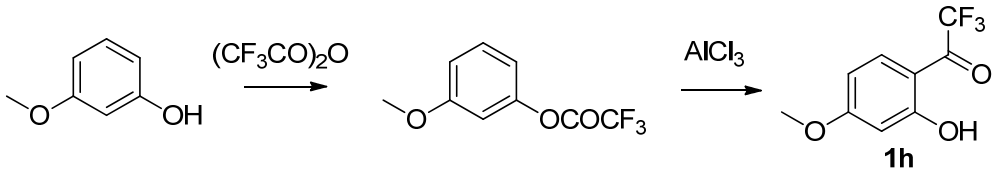


3,4-Dimethylphenyl 2,2,2-trifluoroacetate was obtained from 3,4-dimethylphenol and trifluoroacetic anhydride by analogy with the method for obtaining phenyl trifluoroacetate[4]. Light yellow liquid, bp 77-80 °C/10 Torr. Yield 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.2

Hz, 1H), 7.00 (d, *J* = 2.3 Hz, 1H), 6.96 (dd, *J* = 8.2, 2.3 Hz, 1H), 2.31 (s, 3H), 2.30 (s, 3H). $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -74.78 (s, CF_3).

2,2,2-Trifluoro-1-(2-hydroxy-4,5-dimethylphenyl)ethan-1-one (1g). $AlCl_3$ **(**33.2 g, 0.25 mol) was loaded into a 1-liter three-necked flask equipped with a mechanical stirrer, a dropping funnel and a reflux condenser. The flask was placed in an oil bath which was heated to 75 °C. At this temperature, 48.6 g (0.22 mol) of 3,4-dimethylphenyl trifluoroacetate was added dropwise with vigorous stirring. The release of HCl was observed from the resulting mushy mass. After about 30 minutes, gas evolution ceased. At this point, the temperature of the oil bath was raised to 85 °C. The reaction was heated until gas evolution has ceased, then the temperature of the oil bath was raised to 95 °C and finally to 110 °C. Heating at this temperature was continued until gas evolution has ceased. The solid black reaction mass was cooled to 20 °C and 10% aq. HCl was added carefully. After the end of gas evolution, 150 ml of methylene chloride was added. The organic layer was separated; the aqueous was extracted with methylene chloride (2x50 ml). The combined organic phases were filtered, washed with brine, dried over Na_2SO_4, and the solvent was rotary evaporated. The residue was distilled to afford 32.5 g of liquid-crystalline mass, which was a mixture of phenol **1g** and 3,4-dimethylphenol in a ratio of 4:1. The separation of the product from 3,4-dimethylphenol was carried out by treatment of the resulting mixture with an ammonia-ethanol solution of $Cu(OAc)_2xH_2O$ (for the procedure, see lit.[4]). The brown-green complex was collected by filtration on a Buchner funnel, washed with water, dried, and treated with conc. aq HCl until complete dissolution of the copper complex. After extraction with methylene chloride (3x50 ml), the combined organic phases were washed with brine and dried over Na_2SO_4. The solvent was rotary evaporated, and the residue was distilled to give compound **1g** (20.8 g, 42.8%) as a pale yellow liquid which slowly solidified into pale yellow crystals with mp 50-51 °C (from pentane). Found: C, 54.87; H, 4.29. Calcd. for $C_{10}H_9F_3O_2$: C, 55.05; H, 4.16%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.00 (s, 1H), 7.53 (s, 1H), 6.90 (s, 1H), 2.33 (s, 3H), 2.26 (s, 3H). $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.18 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.5 (q, *J* = 35.0 Hz), 163.2, 150.6, 130.1 (q, *J* = 3.6 Hz), 128.6, 119.4, 116.6 (q, *J* = 289.9 Hz), 111.8, 20.8, 18.9.

Synthesis of 2,2,2-trifluoro-1-(2-hydroxy-4-methoxyphenyl)ethan-1-one (1h)

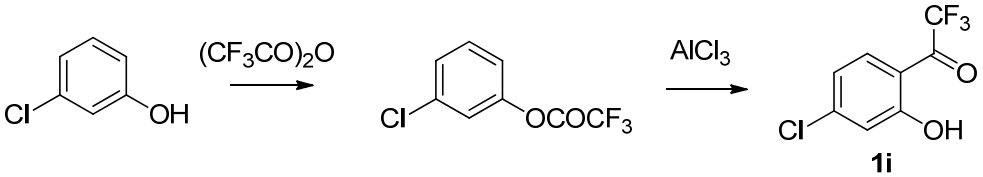


1h

3-Methoxyphenyl 2,2,2-trifluoroacetate. Trifluoroacetic anhydride (17.9 g, 85 mmol) was added in one portion to a solution of 3-methoxyphenol (9.9 g, 80 mmol) in 20 ml of methylene chloride at 10 °C. The reaction mixture was refluxed for 6 h and rotary evaporated. The residue was distilled to give 17.2 g (98%) of 3-methoxyphenyl 2,2,2-trifluoroacetate as a colorless liquid, bp 81-82 ^{o}C/10 Torr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (t, *J* = 8.3 Hz, 1H), 6.90 (dd, *J* = 8.4, 2.2 Hz, 1H), 6.83 (dd, *J* = 8.1, 2.2 Hz, 1H), 6.77 (t, *J* = 2.2 Hz, 1H), 3.85 (s, 3H). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -74.71 (s, CF_3).

2,2,2-Trifluoro-1-(2-hydroxy-4-methoxyphenyl)ethan-1-one (1h). A solution of 3-methoxyphenyl 2,2,2-trifluoroacetate (6.6 g, 30 mmol) in 10 ml of carbon disulfide was added dropwise to a suspension of $AlCl_3$ (4.4 g, 33 mmol) in 20 ml of carbon disulfide. The reaction mixture was heated for 24 hours at 45 °C. Heating leads to the gradual formation of a highly viscous phase. The reaction was cooled to room temperature, carefully treated with 10% aq. HCl, extracted with CH_2Cl_2 (3x50 ml). The combined organic phases were washed with brine, dried over Na_2SO_4, and rotary evaporated. The residue was purified by column chromatography on silica gel (eluent: PE/EtOAc = 8/1). The fraction with R_f 0.45 was collected to afford phenol **1h** (1.5 g, 22.7%) as white crystals with mp 65-66 ^{o}C (from PE/EtOAc) (lit.,[17] mp 62-64 ^{o}C). Found: C, 49.05; H, 3.29. Calcd. for $C_9H_7F_3O_3$: C, 49.10; H, 3.20%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.60 (s, 1H), 7.72 (dq, *J* = 9.1, 2.1 Hz, 1H), 6.54 (dd, *J* = 9.2, 2.5 Hz, 1H), 6.50 (d, *J* = 2.5 Hz, 1H), 3.90 (s, 3H). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -70.14 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.2 (q, *J* = 35.1 Hz), 168.2, 168.0, 132.3 (q, *J* = 3.8 Hz), 116.7 (q, *J* = 289.6 Hz), 109.6, 108.0, 101.1, 55.9.

Synthesis of 2,2,2-trifluoro-1-(2-hydroxy-4-chlorophenyl)ethan-1-one (1i)



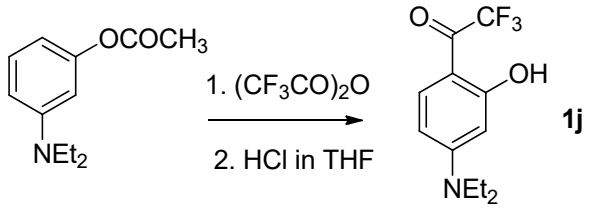
1i

3-Chlorophenyl 2,2,2-trifluoroacetate was obtained from 3-chlorophenol and trifluoroacetic anhydride by analogy with the method for obtaining phenyl 2,2,2-trifluoroacetate.[4] Colorless

liquid with bp 67 °C/10 Torr. Yield 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (t, *J* = 8.1 Hz, 1H), 7.36 (ddd, *J* = 8.1, 2.0, 1.1 Hz, 1H), 7.30 (t, *J* = 2.0 Hz, 1H), 7.16 (ddd, *J* = 8.1, 2.0, 1.1 Hz, 1H). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -74.67 (s, CF_3).

2,2,2-Trifluoro-1-(2-hydroxy-4-chlorophenyl)ethan-1-one (1i) was obtained from 3-chlorophenyl 2,2,2-trifluoroacetate by Fries rearrangement in the presence of $AlCl_3$ according to a procedure similar to the preparation of 2,2,2-trifluoro-1-(2-hydroxy-4-methoxyphenyl)ethan-1-one **1h**. Purification by column chromatography on silica gel, (eluent: PE/CH_2Cl_2 = 3/1). A pale yellow liquid or pale yellow crystals with mp 26-27 °C. Yield 33%. Found: C, 42.76; H, 1.97. Calcd. for $C_8H_4ClF_3O_2$: C, 42.79; H, 1.80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.19 (s, 1H), 7.78 (dq, *J* = 8.8, 2.0 Hz, 1H), 7.14 (d, *J* = 2.0 Hz, 1H), 7.02 (dd, *J* = 8.8, 2.0 Hz, 1H). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -70.53 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.75 (q, *J* = 35.8 Hz), 165.1, 145.5, 131.6 (q, *J* = 3.8 Hz), 120.9, 119.2, 116.3 (q, *J* = 289.7 Hz), 112.4. EIMS 70 eV, *m/z*: 224 (M^+, 6%), 155 (100, M–CF_3), 127 (16, M–CF_3–CO), 99 (37, M–CF_3–2CO).

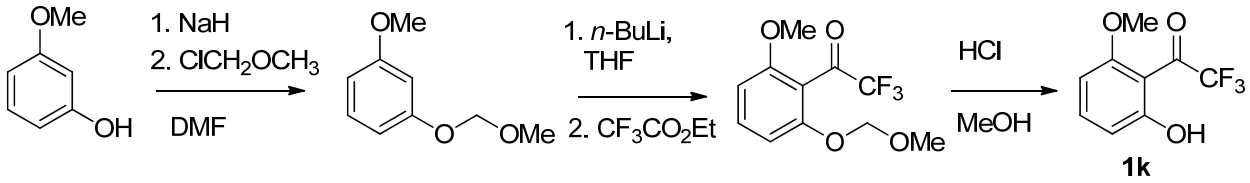
Synthesis of 1-(4-(diethylamino)-2-hydroxyphenyl)-2,2,2-trifluoroethan-1-one (1j)



1j

1-(4-(Diethylamino)-2-hydroxyphenyl)-2,2,2-trifluoroethan-1-one (1j) was obtained according to the procedure described in the literature.[10] Yield 54%. Mp 49-50 °C (lit.,[10] mp 51-52 °C). The ^{1}H, ^{13}C, and ^{19}F NMR spectra fully correspond to the spectral characteristics given in the literature.[18] ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.86 (s, 1H), 7.59 (dq, *J* = 9.5, 2.2 Hz, 1H), 6.29 (dd, *J* = 9.5, 2.6 Hz, 1H), 6.13 (d, *J* = 2.6 Hz, 1H), 3.46 (q, *J* = 7.1 Hz, 4H), 1.25 (t, *J* = 7.1 Hz, 6H). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -69.42 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.2 (q, *J* = 33.9 Hz), 167.3, 155.2, 132.4 (q, *J* = 3.6 Hz), 117.4 (q, *J* = 289.3 Hz), 105.4, 104.2, 97.0, 44.9, 12.5.

Synthesis of 2,2,2-trifluoro-1-(2-hydroxy-6-methoxyphenyl)ethan-1-one (1k)

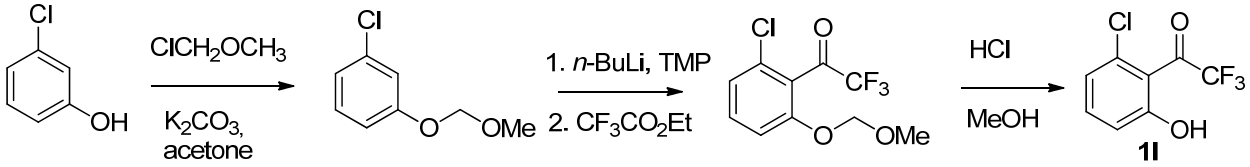


1k

1-Methoxy-3-(methoxymethoxy)benzene was obtained from sodium 3-methoxyphenolate and MOM-Cl in DMF according to procedure 2 for MOM protection of phenols. Yield 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (t, *J* = 8.2 Hz, 1H), 6.67 (ddd, *J* = 8.2, 2.3, 0.8 Hz, 1H), 6.64 (t, *J* = 2.3 Hz, 1H), 6.60 (ddd, *J* = 8.2, 2.4, 0.8 Hz, 1H), 5.19 (s, 2H), 3.82 (s, 3H), 3.51 (s, 3H). ^{1}H NMR spectrum corresponds to the spectral characteristics given in the literature.[19]

2,2,2-Trifluoro-1-(2-hydroxy-6-methoxyphenyl)ethan-1-one (1k). To a solution of 1-methoxy-3-(methoxymethoxy)benzene (6.59 g, 40.0 mmol) in THF (80 ml) was added dropwise *n*-BuLi (34.2 ml of a 1.6 N solution, 54.7 mmol) at 0 °C. The reaction mixture was stirred for 2.5 h at 0 - +5 °C and for 0.5 h at 10 °C. The resulting pale yellow solution was cooled to -40 °C, and a solution of ethyl trifluoroacetate (11.37 g, 80 mmol) in THF (20 ml) was added dropwise. The reaction mixture was stirred for 0.5 h at -40 °C, warmed to 0 °C, and made distinctly acidic with 5% aq. HCl. The organic layer was separated; the aqueous layer was extracted with ether (2 x 30 ml). The combined organic phases were washed with brine, dried over Na_2SO_4, and rotary evaporated. The residue was distilled in vacuo, the fraction with bp 100-120 °C/2 Torr (8.0 g) was collected. It contained 83% of 2,2,2-trifluoro-1-(2-methoxy-6-(methoxymethoxy)phenyl)ethan-1-one [^{1}H NMR spectrum (400 MHz, C_6D_6) δ 7.01 (t, *J* = 8.4 Hz, 1H), 6.75 (d, *J* = 8.5 Hz, 1H), 6.11 (d, *J* = 8.4 Hz, 1H), 4.74 (s, 2H), 3.17 (s, 3H), 3.11 (s, 3H), ^{19}F{^{1}H} NMR spectrum (376 MHz, C_6D_6) δ -77.15 (s, CF_3)], 7% of 2,2,2-trifluoro-1-(4-methoxy-2-(methoxymethoxy)phenyl)ethan-1-one and ~10% of the starting 1-methoxy-3-(methoxymethoxy)benzene. This mixture underwent the MOM deprotection procedure. The residue was purified by silica gel column chromatography (eluent: PE/EtOAc = 8/1) to give pure phenol **1k** (5.11 g, 59%) as a yellow liquid or yellow crystals with mp 23-24^{o}C. Found: C, 49.27; H, 3.31. Calcd. for $C_9H_7F_3O_3$: C, 49.10; H, 3.20%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.02 (s, 1H), 7.50 (t, *J* = 8.4 Hz, 1H), 6.65 (dd, *J* = 8.4, 0.9 Hz, 1H), 6.46 (d, *J* = 8.3 Hz, 1H), 3.92 (s, 3H). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -74.38 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.0 (q, *J* = 38.1 Hz), 164.9, 161.2, 139.0, 116.6 (q, *J* = 287.5 Hz), 110.6, 107.8, 102.1, 56.0. ^{1}H NMR spectroscopy data correspond to the spectral characteristics given in the literature.[20]

Synthesis of 1-(2-chloro-6-hydroxyphenyl)-2,2,2-trifluoroethan-1-one (1l)

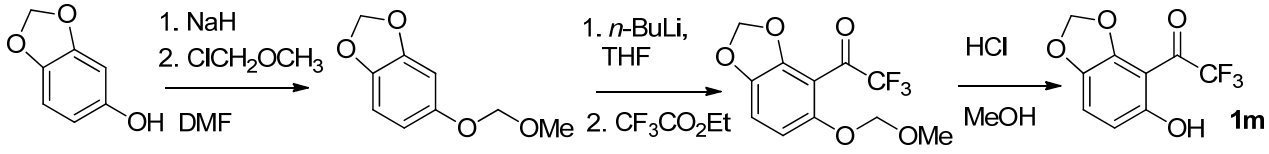


1-Chloro-3-(methoxymethoxy)benzene was obtained from 3-chlorophenol and MOM-Cl in the presence of K_2CO_3 in acetone according to procedure 1 for MOM protection of phenols. Colorless liquid, bp 59-61 °C/10 Torr. Yield 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (t, *J* = 8.1 Hz, 1H), 7.09 (t, *J* = 2.1 Hz, 1H), 7.01 (dd, *J* = 7.9, 1.6 Hz, 1H), 6.95 (dd, *J* = 8.3, 2.3 Hz, 1H), 5.19 (s, 2H), 3.50 (s, 3H). ^{1}H NMR spectrum corresponds to the spectral characteristics given in the literature.[21]

1-(2-Chloro-6-hydroxyphenyl)-2,2,2-trifluoroethan-1-one (1l). The synthesis was carried out by analogy with the Schlosser method[8] for the synthesis of 6-chloro-2-hydroxybenzoic acid.

To a solution of *n*-BuLi (16 ml of a 1.6 M solution in hexane, 25.6 mmol) in THF (50 ml) were added successively 2,2,6,6-tetramethylpiperidine (3.53 g, 25 mmol) and 1-chloro-3-(methoxymethoxy)benzene (4.3 g, 25 mmol) at -75 °C. The reaction mixture was stirred for 2 h at -75 °C before ethyl trifluoroacetate (5.68 g, 40 mmol) in THF (15 ml) was added maintaining the temperature below -65 °C. The reaction mixture was slowly warmed to 0 °C and made distinctly acidic with 5% aq. HCl. The organic layer was separated; the aqueous layer was extracted with ether (2 x 40 ml). The combined organic phases were washed with brine, dried over Na_2SO_4, and rotary evaporated. The residue (7.7 g) was distilled to give a liquid (4.8 g) with bp 82-90 °C/2 Torr. It underwent the MOM deprotection procedure. The residue (3.8 g) was distilled to obtain phenol **1l** (2.9 g, 52%) as a pale yellow liquid, bp 112-115 °C/15 Torr. It crystallized upon storage in the refrigerator. White crystals, mp 42-43°C (from PE/EtOAc). Found: C, 42.74; H, 1.97. Calcd. for $C_8H_4ClF_3O_2$: C, 42.79; H, 1.80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.40 (t, *J* = 8.2 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -73.84 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.0 (q, *J* = 39.1 Hz), 157.7, 134.6, 133.0, 122.6, 119.9, 115.7, 115.4 (q, *J* = 290.3 Hz).

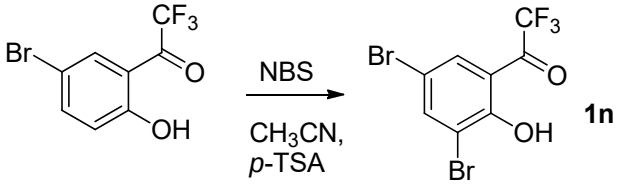
Synthesis of 2,2,2-trifluoro-1-(5-hydroxybenzo[d][1,3]dioxol-4-yl)ethan-1-one (1m)



5-(Methoxymethoxy)benzo[*d*][1,3]dioxole was obtained from sesamol (benzo[d][1,3]dioxol-5-ol) (5.42 g, 39.3 mmol), NaH (1.88 g of a 60% suspension, 47.1 mmol), and MOM-Cl (4.83 g, 60 mmol) in 100 ml of DMF according to procedure 2 for MOM protection of phenols. The residue after evaporation of ethyl acetate (7.5 g) was distilled to give 6.3 g (88.2%) of the product as a colorless liquid, bp 107-110°C/1 Torr (lit.,[22] 103 °C/0.35 Torr). ^{1}H NMR (400 MHz, C_6D_6) δ 6.88 (d, *J* = 2.4 Hz, 1H), 6.68 (d, *J* = 8.4 Hz, 1H), 6.62 (dd, *J* = 8.4, 2.3 Hz, 1H), 5.40 (s, 2H), 4.86 (s, 2H), 3.22 (s, 3H).

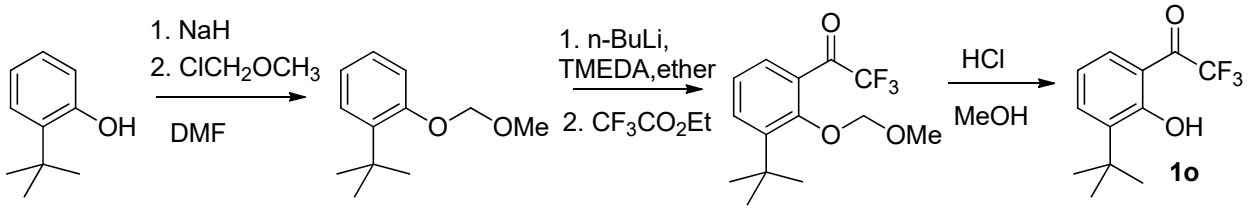
2,2,2-Trifluoro-1-(5-hydroxybenzo[*d*][1,3]dioxol-4-yl)ethan-1-one (1m). To a solution of 5-(methoxymethoxy)benzo[*d*][1,3]dioxole (3.64 g, 20 mmol) in THF (50 ml) was added *n*-BuLi (15.6 ml of a 1.6 M solution in hexane, 25 mmol) at -5 – 0 °C. As *n*-BuLi was added, the color of the solution turned to yellow and then to red. The reaction mixture was stirred at 0 °C for 40 min. The resulting burgundy-red solution was cooled to -40 °C, and ethyl trifluoroacetate (5.68 g, 40 mmol) was added. The reaction mixture was stirred for 1 h at -40 °C, warmed up gradually to 0 °C. At this moment 40 ml of a saturated NH_4Cl solution was added. The resulting upper organic layer was separated; the aqueous layer was diluted with 50 ml of water and extracted with diethyl ether (3 x 30 ml). The combined organic phases were rotary evaporated. The residue (5.4 g of burgundy-red liquid) underwent the MOM deprotection procedure to afford red oily crystals (4.7 g). Purification by column chromatography on silica gel (eluent: PE/EtOAc = 8/1) gave phenol **1m** (3.15 g, 67%) as red crystals, mp 94-95 °C (from PE/EtOAc). Found: C, 46.13; H, 2.19. ^{1}H Calcd. for $C_9H_5F_3O_4$: C, 46.17; H, 2.15%. NMR (400 MHz, $CDCl_3$) δ 10.61 (s, 1H), 7.10 (d, *J* = 8.7 Hz, 1H), 6.51 (d, *J* = 8.7 Hz, 1H), 6.11 (s, 2H). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -76.18 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.1 (q, *J* = 39.6 Hz), 157.7, 148.2, 140.7, 118.5, 116.0 (q, *J* = 287.6 Hz), 109.1, 102.5, 101.6.

Synthesis of 1-(3,5-dibromo-2-hydroxyphenyl)-2,2,2-trifluoroethan-1-one (1n)



1-(3,5-Dibromo-2-hydroxyphenyl)-2,2,2-trifluoroethan-1-one (1n). To a solution of 1-(5-bromo-2-hydroxyphenyl)-2,2,2-trifluoroethan-1-one **1c** (2.1 g, 7.8 mmol) in 20 mL of acetonitrile were added *N*-bromosuccinimide (1.6 g, 9.0 mmol) and *p*-toluenesulfonic acid monohydrate (0.76 g, 4.0 mmol) at rt. The reaction mixture was stirred for 24 h. Acetonitrile was rotary evaporated, the residue was dissolved in chloroform (30 ml), washed with water, brine, dried with Na_2SO_4, and rotary evaporated. The residue was purified by column chromatography on silica gel (eluent: PE/CH_2Cl_2 = 2/1) to afford phenol **1n** (1.9 g, 70%) as yellow crystals, mp 72-73 °C (from PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.59 (s, 1H), 8.05 (d, *J* = 2.1 Hz, 1H), 7.98 – 7.85 (m, 1H). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -70.20 (s, CF_3). ^{13}C NMR (101 MHz, CDCl3) δ 183.67 (q, *J* = 36.7 Hz), 159.92, 144.1, 131.9 (q, *J* = 4.1 Hz), 115.9 (q, *J* = 289.7 Hz), 115.3, 114.0, 111.7. The ^{1}H, ^{13}C, and ^{19}F NMR spectroscopy data fully correspond to the spectral characteristics given in the literature.[23]

Synthesis of 2,2,2-trifluoro-1-(2-hydroxy-3-t-butylphenyl)ethan-1-one (1o)

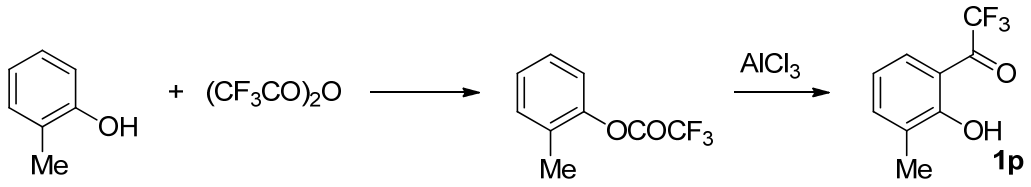


2-*tert*-Butyl-1-(methoxymethoxy)benzene was obtained from 2-*tert*-butylphenol (6.0 g, 40 mmol), NaH (1.15 g of 60% suspension, 48 mmol), and MOM-Cl (4.83 g, 60 mmol) in DMF (100 ml) according to procedure 2 for MOM protection of phenols. The residue after evaporation of ethyl acetate was purified by column chromatography on silica gel (eluent: PE/CH_2Cl_2 = 1/1) to provide the product (7.38 g, 95%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.22 – 7.16 (m, 1H), 7.13 (dd, *J* = 8.1, 1.2 Hz, 1H), 6.97 (td, *J* = 7.7, 1.4 Hz, 1H), 5.27 (s, 2H), 3.53 (s, 3H), 1.43 (s, 9H). The ^{1}H NMR spectroscopy data fully correspond to the spectral characteristics given in the literature.[24]

2,2,2-Trifluoro-1-(2-hydroxy-3-*t*-butylphenyl)ethan-1-one (1o). To a solution of TMEDA (5.24 g, 45 mmol) in ether (100 ml) was added *n*-BuLi (28 ml of a 1.6 M solution in hexane, 45 mmol) at 0 °C followed by 2-*tert*-butyl-1-(methoxymethoxy)benzene (7.38 g, 38 mmol). The reaction mixture was allowed to reach room temperature and stirred for 5 hours. The resulting yellow solution was cooled to -40 °C, and ethyl trifluoroacetate (7.4 g, 52 mmol) was added. The reaction mixture was stirred for 1 h at -40 °C, warmed up gradually to 0 °C. At this moment 40

ml of a saturated NH_4Cl solution was added. The upper organic layer was separated; the aqueous layer was diluted with 50 ml of water and extracted with diethyl ether (2x30 ml). The combined organic phases were rotary evaporated. The residue underwent the MOM deprotection procedure to afford a yellow liquid which consisted of phenol **1o** and 2-*tert*-butylphenol. The separation of the product from 2-*tert*-butylphenol was carried out by treating the mixture with an ammonia-ethanol solution of $Cu(OAc)_2xH_2O$ (for the procedure, see lit.[4]). The brown-yellow complex was filtered on a Buchner funnel, washed with water, dried and treated with conc. aq. HCl until complete dissolution of the copper complex. After extraction with methylene chloride (3 x 30 ml), the combined organic phases were washed with brine, dried over Na_2SO_4, and rotary evaporated. The residue was purified by column chromatography on silica (eluent: PE/CH_2Cl_2 = 4/1) to afford phenol **1o** (2.67 g, 28%) as a pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.99 (s, 1H), 7.75 – 7.69 (m, 1H), 7.65 (d, *J* = 7.6 Hz, 1H), 6.95 (t, *J* = 7.9 Hz, 1H), 1.45 (s, 9H). $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -69.70 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.0 (q, *J* = 34.9 Hz), 164.5, 139.5, 136.2, 128.6 (q, *J* = 3.8 Hz), 119.2, 116.6 (q, *J* = 289.9 Hz), 113.8, 35.1, 29.1. ^{1}H NMR spectroscopy data correspond to the spectral characteristics given in the literature.[25]

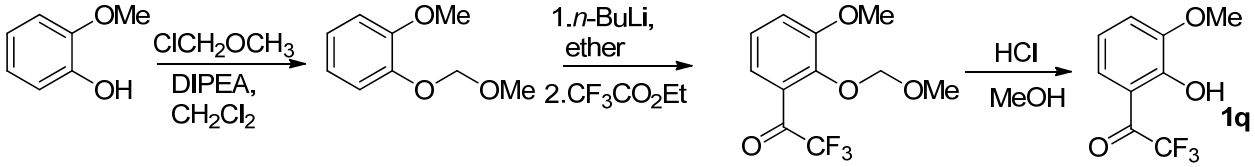
Synthesis of 2,2,2-trifluoro-1-(2-hydroxy-3-methylphenyl)ethan-1-one (1p)



o-Tolyl 2,2,2-trifluoroacetate was obtained from o-cresol and trifluoroacetic anhydride by analogy with the method for obtaining phenyl 2,2,2-trifluoroacetate[4]. Pale yellow liquid, bp 64-65 ^{o}C/10 Torr. Yield 93%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 – 7.26 (m, 3H), 7.24 – 7.11 (m, 1H), 2.28 (s, 3H).

2,2,2-Trifluoro-1-(2-hydroxy-3-methylphenyl)ethan-1-one (1p) was obtained from *o*-tolyl 2,2,2-trifluoroacetate by Fries rearrangement in the presence of $AlCl_3$ according to a procedure similar to the preparation of 2,2,2-trifluoro-1-(2-hydroxy-4,5-dimethylphenyl)ethan-1-one **1g**. Yield 21%. Yellow liquid, bp 80-81 ^{o}C/12 Torr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.41 (s, 1H), 7.70 (d, *J* = 8.3 Hz, 1H), 7.51 (d, *J* = 7.2 Hz, 1H), 6.93 (t, *J* = 7.8 Hz, 1H), 2.32 (s, 3H). $^{19}F\{^1H\}$ NMR (282 MHz, $CDCl_3$) δ -70.03 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.6 (q, *J* = 35.3 Hz), 163.2, 139.6, 128.3, 128.2 (q, *J* = 3.8 Hz), 119.3, 116.6 (q, *J* = 289.9 Hz), 113.2, 15.5.

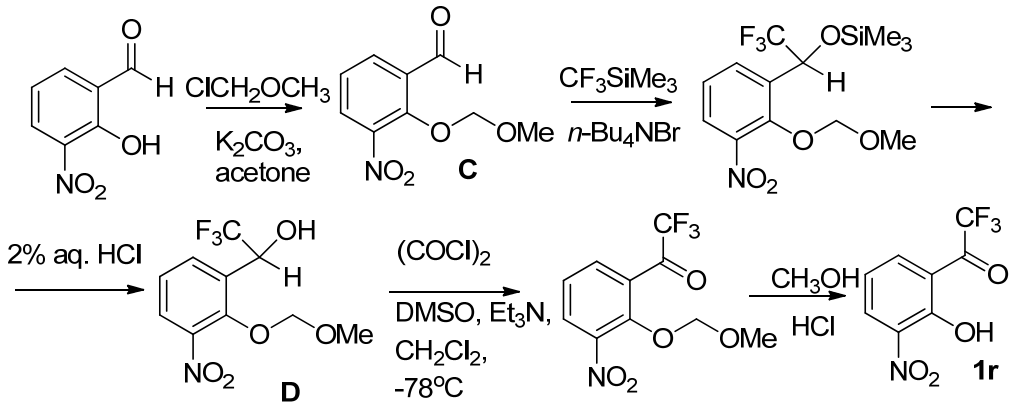
Synthesis of 2,2,2-trifluoro-1-(2-hydroxy-3-methoxyphenyl)ethan-1-one (1q)



1-Methoxy-2-(methoxymethoxy)benzene was prepared according to the method described in the literature.[26] From 10.0 g (80 mmol) of guaiacol and *N*,*N*-diisopropylethylamine (15.5 g, 120 mmol), it was obtained 9.4 g (69.4%) of 1-methoxy-2-(methoxymethoxy)benzene as a colorless liquid, bp 108-109 °C/15 Torr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, *J* = 7.9 Hz, 1H), 7.02 (t, *J* = 7.0 Hz, 1H), 6.96 – 6.86 (m, 1H), 5.26 (s, 2H), 3.90 (s, 3H), 3.55 (s, 3H).

2,2,2-Trifluoro-1-(2-hydroxy-3-methoxyphenyl)ethan-1-one (1q). *n*-BuLi (37.5 ml of a 1.6 M solution in hexane, 60 mmol) was added dropwise to 1-methoxy-2-(methoxymethoxy)benzene (5.04 g, 30 mmol) in 100 ml of Et_2O at 0 °C. The reaction mixture was allowed to reach room temperature and stirred for 2.5 hours, while the formation of a thick suspension was observed. To dissolve the suspension and to stir properly the reaction mixture, THF (50 ml) was added. The reaction was cooled to -40 °C. A solution of ethyl trifluoroacetate (8.52 g, 60 mmol) in 10 ml of Et_2O was added, maintaining the temperature at -40 °C. After adding 4/5 volume of ethyl trifluoroacetate solution, the precipitate dissolved to form a yellow solution. The reaction was warmed to 0 °C and 5% aq. HCl was added until the solution was distinctly acidic. The pale yellow organic layer was separated; the aqueous layer was extracted with ether (2 x 30 ml). The combined organic phases were rotary evaporated. The resulting yellow liquid (7.7 g) underwent the MOM deprotection procedure. The residue (6.25 g of oily yellow crystals) was purified by recrystallization from PE/EtOAc to obtain phenol **1q** (5.15 g, 78%) as yellow crystals, mp 65-66 °C (from PE/EtOAc). Found: C, 49.17; H, 3.22. Calcd. for $C_9H_7F_3O_3$: C, 49.10; H, 3.20%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.25 (s, 1H), 7.40 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 6.94 (t, *J* = 8.2 Hz, 1H), 3.92 (s, 3H). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -70.41 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.7 (q, *J* = 35.7 Hz), 155.1, 149.1, 121.4 (q, *J* = 3.8 Hz), 119.5, 119.1, 116.3 (q, *J* = 289.7 Hz), 113.9, 56.2.

Synthesis of 2,2,2-trifluoro-1-(2-hydroxy-3-nitrophenyl)ethan-1-one (1r)



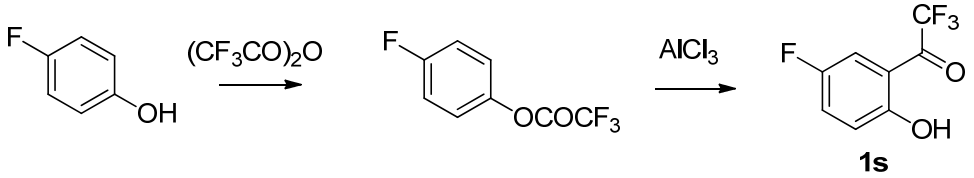
2-(Methoxymethoxy)-3-nitrobenzaldehyde (compound C) was obtained from 2-hydroxy-3-nitrobenzaldehyde and MOM-Cl in the presence of K_2CO_3 in acetone according to procedure 1 for MOM protection of phenols. Yield 77%. White crystals with mp 57-58 °C (from PE/EtOAc). Found: C, 51.17; H, 4.31; N, 6.56. Calcd. for $C_9H_9NO_5$: C, 51.19; H, 4.30; N, 6.63%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.39 (s, 1H), 8.14 (dd, *J* = 7.9, 1.5 Hz, 1H), 8.12 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.43 (t, *J* = 7.9 Hz, 1H), 5.25 (s, 2H), 3.61 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.3, 153.3, 144.8, 133.1, 132.0, 130.5, 124.9, 102.9, 58.2.

2,2,2-Trifluoro-1-(2-(methoxymethoxy)-3-nitrophenyl)ethan-1-ol (compound D) was obtained by treatment of compound **C** with CF_3SiMe_3 in the presence of catalytic amounts of *n*-Bu_4NF in THF followed by oxygen desilylation reaction with 2% aq. HCl in THF. Yield 90%. Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.0 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 5.70 – 5.54 (m, 1H), 5.22 (d, *J* = 6.4 Hz, 1H), 5.11 (d, *J* = 6.4 Hz, 1H), 3.63 (s, 3H), 3.47 (s, 1H). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -76.82 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.6, 144.2, 133.5, 131.6, 126.5, 125.1, 124.2 (q, *J* = 282.1 Hz), 102.1, 66.3 (q, *J* = 33.0 Hz), 57.9.

2,2,2-Trifluoro-1-(2-hydroxy-3-nitrophenyl)ethan-1-one (1r) was obtained by Swern oxidation of compound **D** as described earlier for 2,2,2-trifluoro-1-(2-hydroxy-5-nitrophenyl)ethan-1-one **1f.** The residue after the MOM deprotection procedure was distilled to give a yellow liquid with bp 103-105 °C/ 2 Torr. Yield 63%. Found: C, 40.72; H, 1.87. Calcd. for $C_8H_4F_3NO_4$: C, 40.87; H, 1.71. ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.68 (s, 1H), 8.41 (d, *J* = 8.2 Hz, 1H), 8.09 (dq, *J* = 7.7, 0.4 Hz, 1H), 7.20 (t, *J* = 8.0 Hz, 1H). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -72.74 (s, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.2 (q, *J* = 37.6 Hz), 156.0, 137.8 (q, *J* = 2.3 Hz), 136.2, 132.2, 120.8, 119.8, 115.8 (q, *J* = 290.3 Hz). EIMS 70 eV, *m/z*: 235 (M^+, 1%), 166 (100, M–CF_3), 149 (24, M–CF_3–OH), 120 (76, M–CF_3–NO_2), 92 (39, M–CF_3–NO_2–CO). NMR spectral data of so obtained phenol **1r** were in full

accordance with those of phenol **1r** from the nitration reaction of 1-(2-hydroxyphenyl)-2,2,2-trifluoroethan-1-one **1a** (see above).

Synthesis of 2,2,2-trifluoro-1-(2-hydroxy-4-fluorophenyl)ethan-1-one (1s)

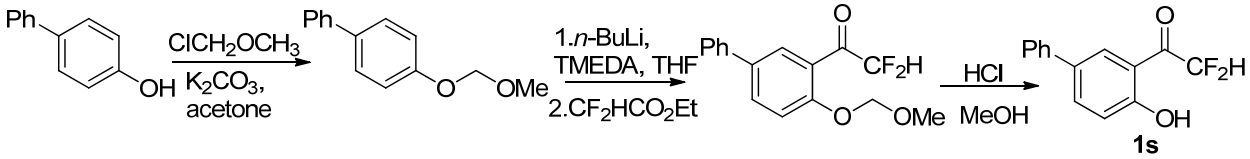


1s

4-Fluorophenyl 2,2,2-trifluoroacetate was obtained from 4-fluorophenol and trifluoroacetic anhydride by analogy with the method for obtaining phenyl 2,2,2-trifluoroacetate.[4] Colorless liquid with bp 67 ^{o}C/15 Torr. Yield 86%.

2,2,2-Trifluoro-1-(2-hydroxy-4-fluorophenyl)ethan-1-one (1s) was obtained from 4-fluorophenyl 2,2,2-trifluoroacetate by Fries rearrangement in the presence of $AlCl_3$ according to the procedure described in the literature.[4] Purification by treatment of 4-fluorophenol – phenol **1s** mixture with an ammonia-ethanol solution of $Cu(OAc)_2xH_2O$ (for the procedure, see lit.[4]) gave phenol **1s**. Phenol **1s** is a volatile pale yellow liquid. To avoid the heavy losses, a methylene chloride solution of compound **1s** after aq. HCl treatment and the following extraction is recommended to evaporate under atmospheric pressure. Phenol **1s** was isolated as a mixture with 4-fluorophenol (~10%) and was used as such. Yield 23%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.88 (s, 1H), 7.56 – 7.47 (m, 1H), 7.42 (ddd, *J* = 9.3, 7.6, 3.0 Hz, 1H), 7.10 (dd, *J* = 9.3, 4.5 Hz, 1H). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -70.71 (s, 3F, CF_3), -121.74 (s, 1F, F_{ar}).

Synthesis of 2,2-difluoro-1-(4-hydroxy-[1,1'-biphenyl]-3-yl)ethan-1-one (1t)



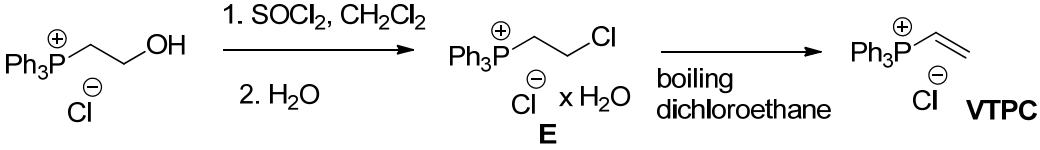
1s

TMEDA (2.8 g, 24 mmol) was added to a solution of 4-(methoxymethoxy)-1,1`-biphenyl (4.3 g, 20 mmol) in THF (60 mL). The solution was cooled to -75°C and *n*-BuLi (15 ml of a 1.6 N solution, 24 mmol) was added dropwise. The reaction mixture was stirred for 0.5 h at -75 °C, warmed to 0 °C, cooled again to -75 °C, and a solution of ethyl difluoroacetate (3.72 g, 30 mmol) in 10 ml of THF was added dropwise. The reaction mixture was warmed to 0 °C for 1 h, a 5% aq. HCl was added until the solution was distinctly acidic. The organic layer was separated; the aqueous layer was extracted with ether (2 x 30 ml). The combined organic phases were rotary

evaporated. The residue underwent the MOM deprotection procedure. The residue (4.81 g as a yellow oil) was purified by silica gel column chromatography (eluent: PE/EtOAc = 8/1) followed by crystallization from PE/EtOAc in the refrigerator at -18 °C to give phenol **1t** (2.8 g, 56%) as yellow crystals, mp 37-38 °C (from PE/EtOAc). Found: C, 67.81; H, 4.04. Calcd. for $C_{14}H_{10}F_2O_2$: C, 67.74; H, 4.06%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.31 (s, 1H), 8.10 (m, 1H), 7.86 (dd, *J* = 8.8, 2.3 Hz, 1H), 7.56 (d, *J* = 7.2 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.18 (d, *J* = 8.8 Hz, 1H), 6.40 (t, *J* = 53.2 Hz, 1H). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -120.86 (s, CF_2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.8 (t, *J* = 25.0 Hz), 163.4, 139.3, 137.3, 133.1, 129.1, 128.5 (t, *J* = 4.2 Hz), 127.6, 126.8, 119.3, 115.5, 110.9 (t, *J* = 253.3 Hz).

Synthesis of vinyltriphenylphosphonium chloride

Vinyltriphenylphosphonium chloride (VTPC) is available via a convenient, multigram synthesis.[27] We have modified this synthetic procedure in order to obtain the reagent of high purity. The treatment with water after chlorination of 2-(hydroxyethyl)triphenylphosphonium chloride with thionyl chloride provided 2-(chloroethyl)triphenylphosphonium chloride hydrate **E** of high purity. A solution of phosphonium salt **E** in 1,2-dichloroethane was boiled under a heavy reflux in the presence of 4Å molecular sieves to give VTPC.



2-(Hydroxyethyl)triphenylphosphonium chloride was obtained from triphenylphosphine and 2-chloroethanol according to the known procedure.[27] Mp 240-242 °C (lit.,[27] 240-242 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 - 7.78 (m, 9H), 7.77 - 7.68 (m, 6H), 4.14 (dt, *J* = 18.4, 6.0 Hz, 2H), 3.84 (dt, *J* = 11.9, 6.0 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.82 (d, *J* = 2.8 Hz), 133.66 (d, *J* = 10.3 Hz), 130.19 (d, *J* = 12.8 Hz), 118.48 (d, *J* = 86.5 Hz), 55.25 (d, *J* = 4.7 Hz), 26.83 (d, *J* = 50.4 Hz). ^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$) δ 24.11 (s).

2-(Chloroethyl)triphenylphosphonium chloride hydrate (phosphonium salt E). A 1-liter three-necked flask equipped with a mechanical stirrer, an addition funnel, and a reflux condenser was charged with 2-(hydroxyethyl)triphenylphosphonium chloride (102.8 g, 0.3 mol), methylene chloride (300 ml) and 5 drops of DMF. Thionyl chloride (47.6 g, 0.4 mol) was added dropwise to the resulting suspension under vigorous stirring and cooling with ice water. Addition of thionyl chloride caused a violent reaction accompanied by gas evolution and gradual homogenization

of the reaction mixture. By the end of the addition (after about 1 h), the reaction mixture became completely homogeneous. The reaction was stirred for 3 hours and left overnight. The next morning the reaction mixture was rotary evaporated at a temperature not exceeding 40 °C. The residue was dissolved in 300 ml of cold water. The resulting solution was extracted with methylene chloride (5 x 100 ml). The combined organic phases were dried with Na_2SO_4 and rotary evaporated. The residue was crystallized with acetone to afford phosphonium salt **E** (85.2 g, 74.9%) as off-white crystals. Mp 117-119 ^{o}C (decomp.). Found: C, 63.19; Cl, 18.79; H, 5.67. Calcd. for $C_{20}H_{21}Cl_2OP$: C, 63.34; Cl, 18.70; H, 5.58%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.76 (m, 9H), 7.75 - 7.65 (m, 6H), 4.56 (dt, *J* = 11.9, 6.0 Hz, 2H), 4.04 (dt, *J* = 21.6, 6.0 Hz, 2H), 3.92 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.23 (d, *J* = 2.8 Hz), 133.81 (d, *J* = 10.3 Hz), 130.43 (d, *J* = 12.7 Hz), 117.52 (d, *J* = 86.6 Hz), 37.31 (d, *J* = 5.4 Hz), 26.78 (d, *J* = 53.7 Hz). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 23.06 (s).

Vinyltriphenylphosphonium chloride (VTPC). The initial suspension of phosphonium salt **E** (85.2 g, 0.22 mol) in 350 ml of 1,2-dichloroethane was dissolved upon heating to form a clear solution. The solution was boiled for 36 h in the standard Soxhlet extraction apparatus, with 4Å molecular sieves (40 g) being placed in the thimble to perform the continuous removal of water from 1,2-dichloroethane. Thereafter, the solution was boiled additionally for 36 h under a heavy reflux. The solvent was rotary evaporated. The crystalline residue was suspended in 300 ml of dry ethyl acetate, heated at reflux for 1 h, cooled to RT, collected by filtration and dried in vacuum to afford VTPC (65.6 g, 89.9%) as grey crystals. Mp 130-132 ^{o}C (lit.,[27] 125-130 ^{o}C). Found: C, 73.92; Cl, 11.07; H, 5.58. Calcd. for $C_{20}H_{18}ClP$: C, 73.96; Cl, 10.92; H, 5.59%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (ddd, *J* = 25.0, 17.7, 12.4 Hz, 1H), 7.90 - 7.79 (m, 3H), 7.78 - 7.64 (m, 12H), 7.17 (dd, *J* = 50.4, 12.3 Hz, 1H), 6.15 (dd, *J* = 25.3, 17.8 Hz, 1H). ^{1}H{^{31}P} NMR (400 MHz, $CDCl_3$) δ 8.60 – 8.43 (m, 1H), 7.85 – 7.79 (m, 3H), 7.75 – 7.65 (m, 12H), 7.23 (d, *J* = 11.6 Hz, 1H), 6.15 (d, *J* = 17.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.22, 135.41 (d, *J* = 2.8 Hz), 133.82 (d, *J* = 10.5 Hz), 130.52 (d, *J* = 12.9 Hz), 119.01 (d, *J* = 80.2 Hz), 117.08 (d, *J* = 90.5 Hz). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 20.15 (s).

III X-ray diffraction experiment

Single crystal X-ray diffraction experiment for compound **2g** was carried out using SMART APEX2 CCD diffractometer (λ(Mo-Kα) = 0.71073 Å, graphite monochromator, ω-scans) at 120 K. Collected data were processed by the SAINT and SADABS programs incorporated into

the APEX2 program package.[28] The structure was solved by the direct methods and refined by the full-matrix least-squares procedure against F^2 in anisotropic approximation. The refinement was carried out with the SHELXTL program.[29] The CCDC number 2169359 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

Crystallographic data for **2g**: $C_{12}H_{11}F_3O$ are monoclinic, space group $P2_1/c$: a = 9.7631(12) Å, b = 10.2430(14) Å, c = 10.4343(13) Å, β = 92.382(4)°, V = 1042.6(2) Å^3, Z = 4, M = 228.21, d_{cryst} = 1.454 g·cm^{-3}. $wR2$ = 0.1141 calculated on F^2_{hkl} for all 2108 independent reflections with $2\theta <$ 52.8°, (*GOF* = 1.010, R = 0.0408 calculated on F_{hkl} for 1414 reflections with $I > 2\sigma(I)$).

IV References

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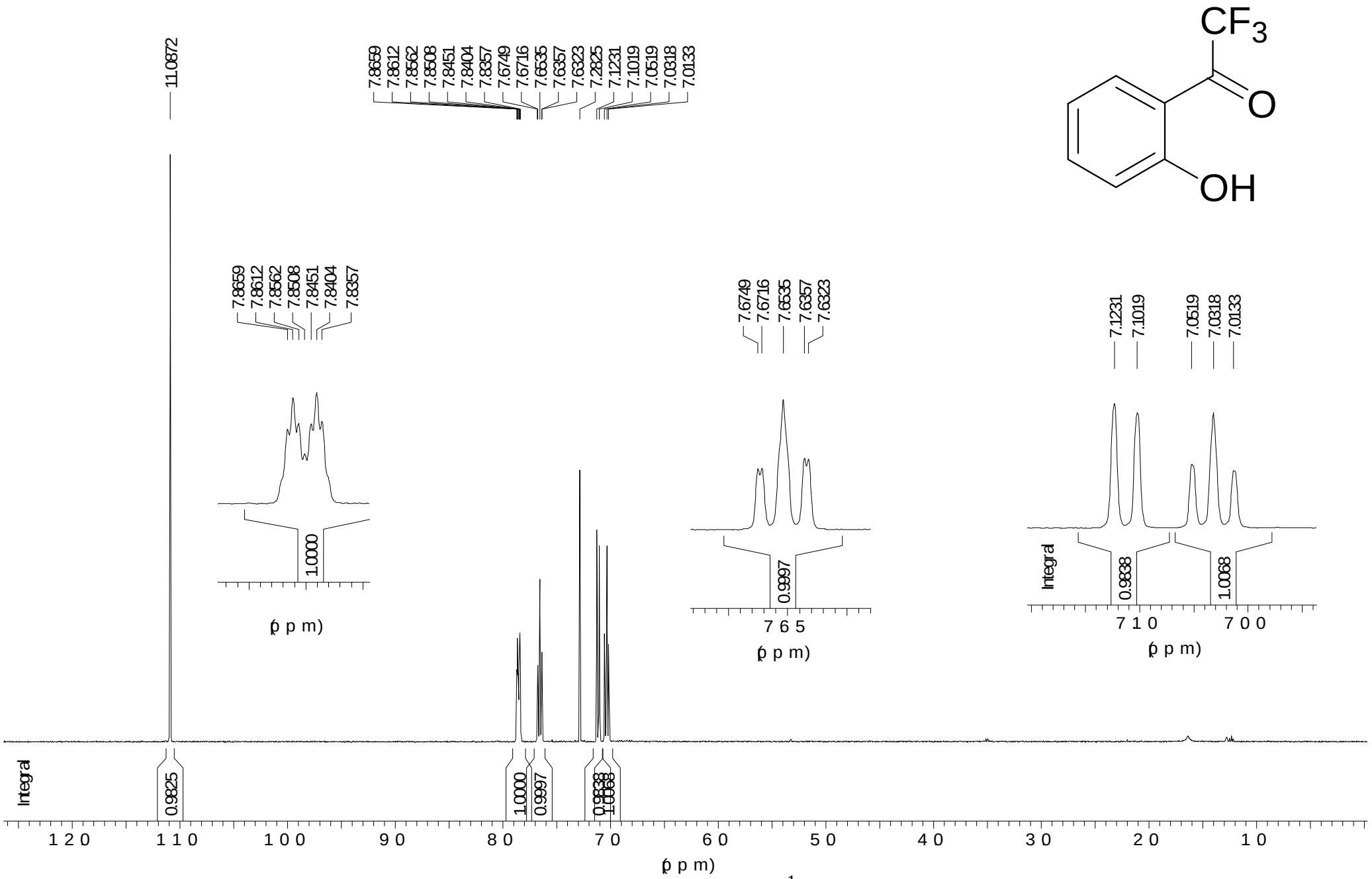
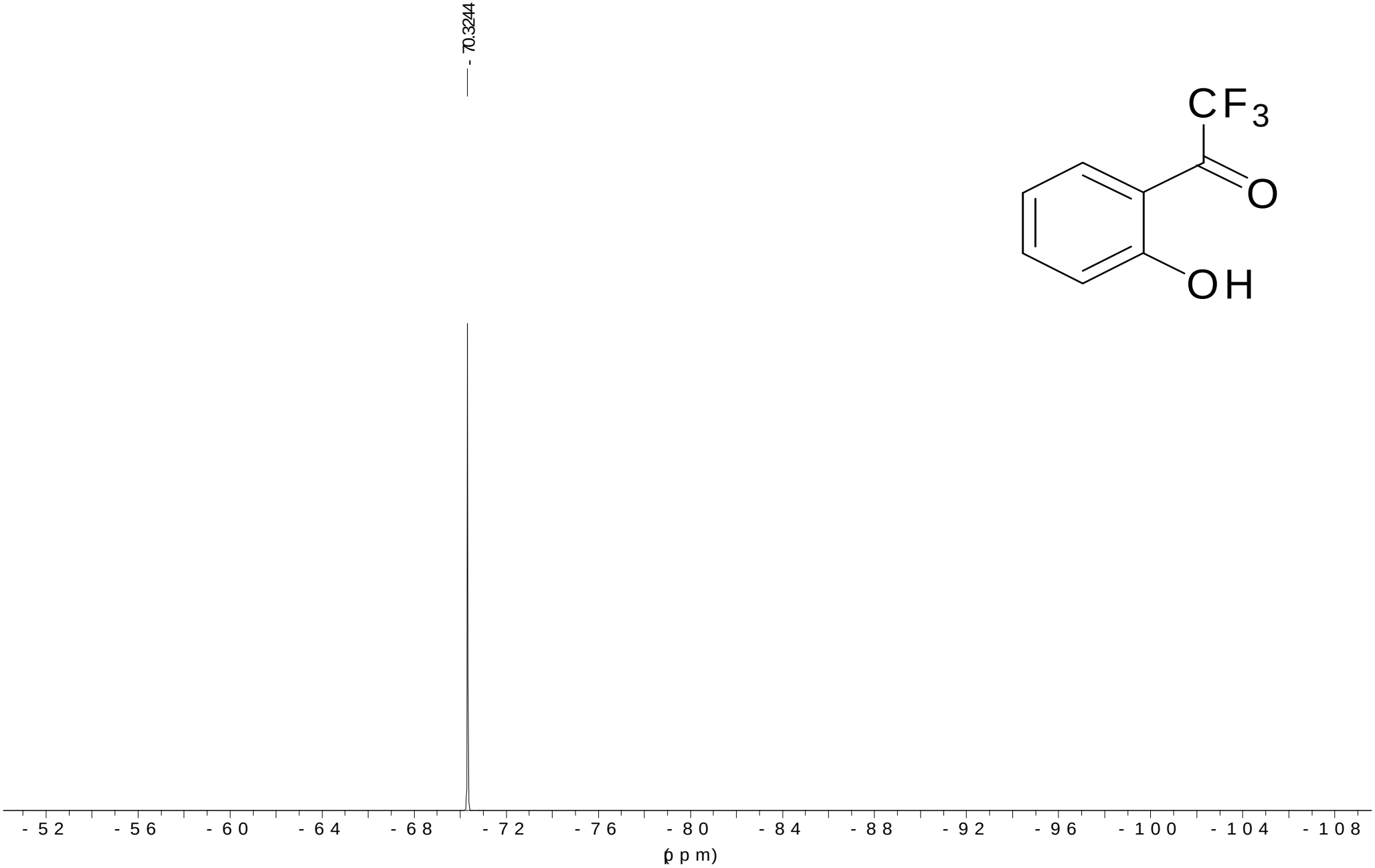


Compound **1a** spectrum NMR ^{1}H in $CDCl_3$



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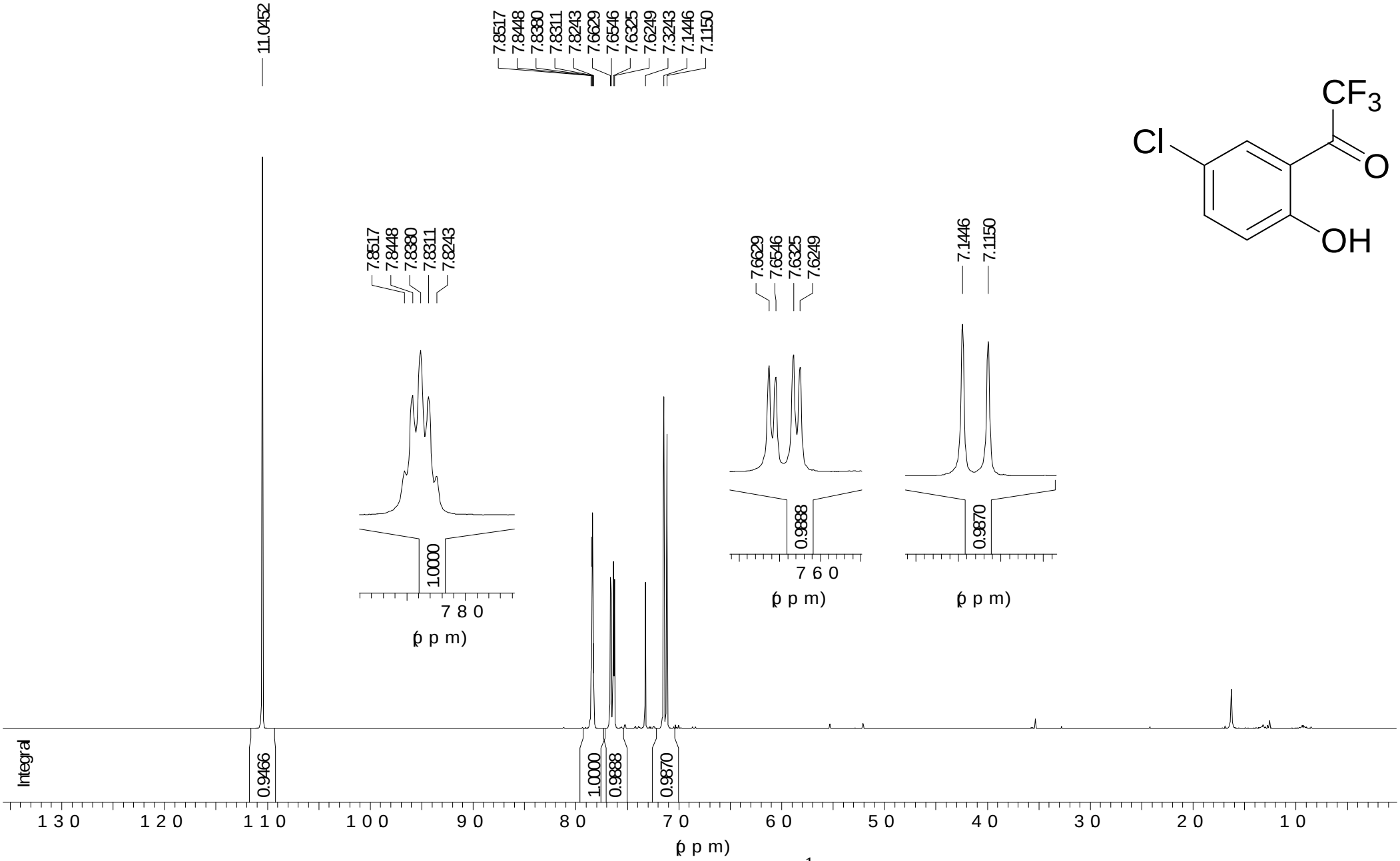

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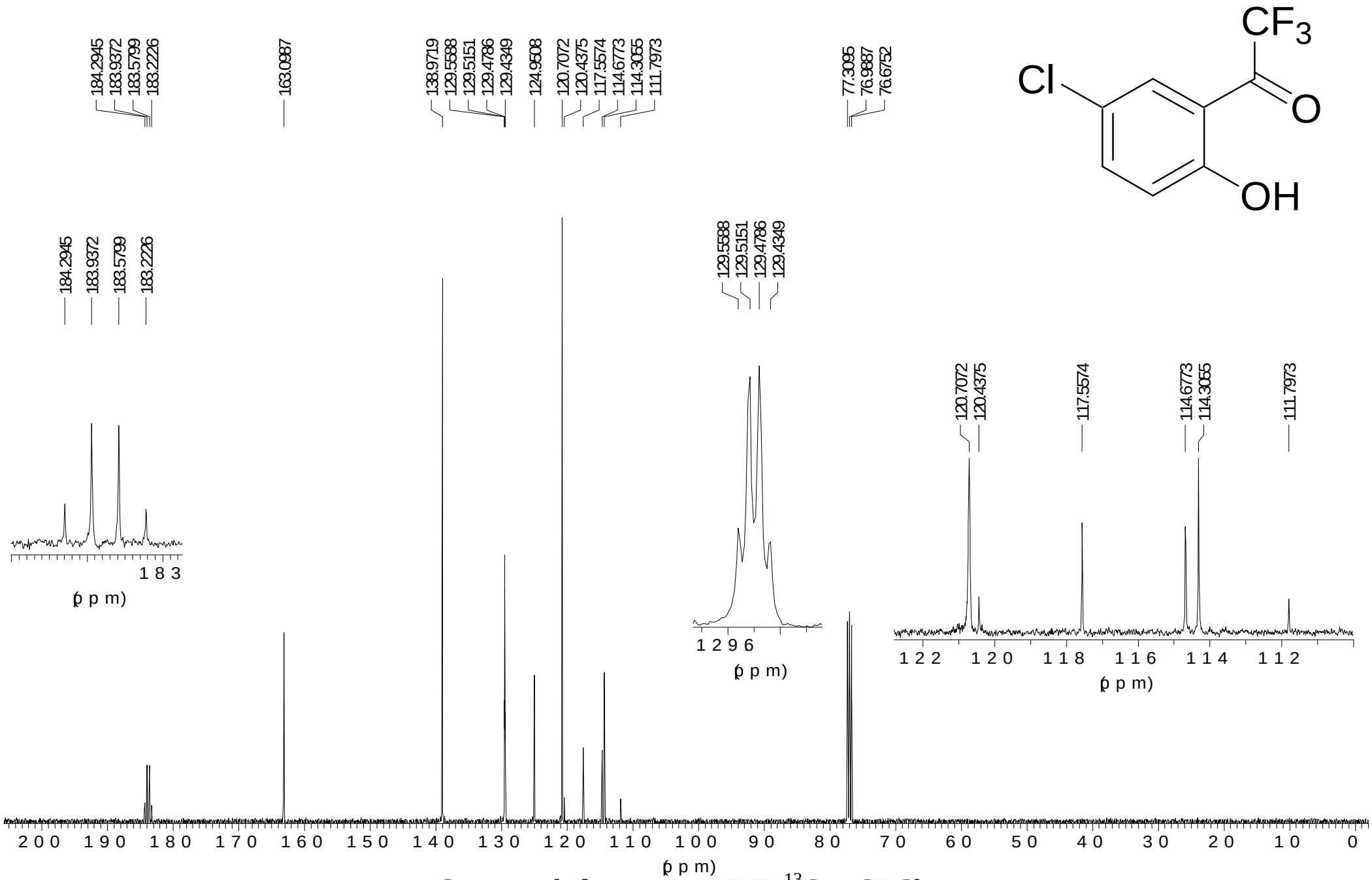

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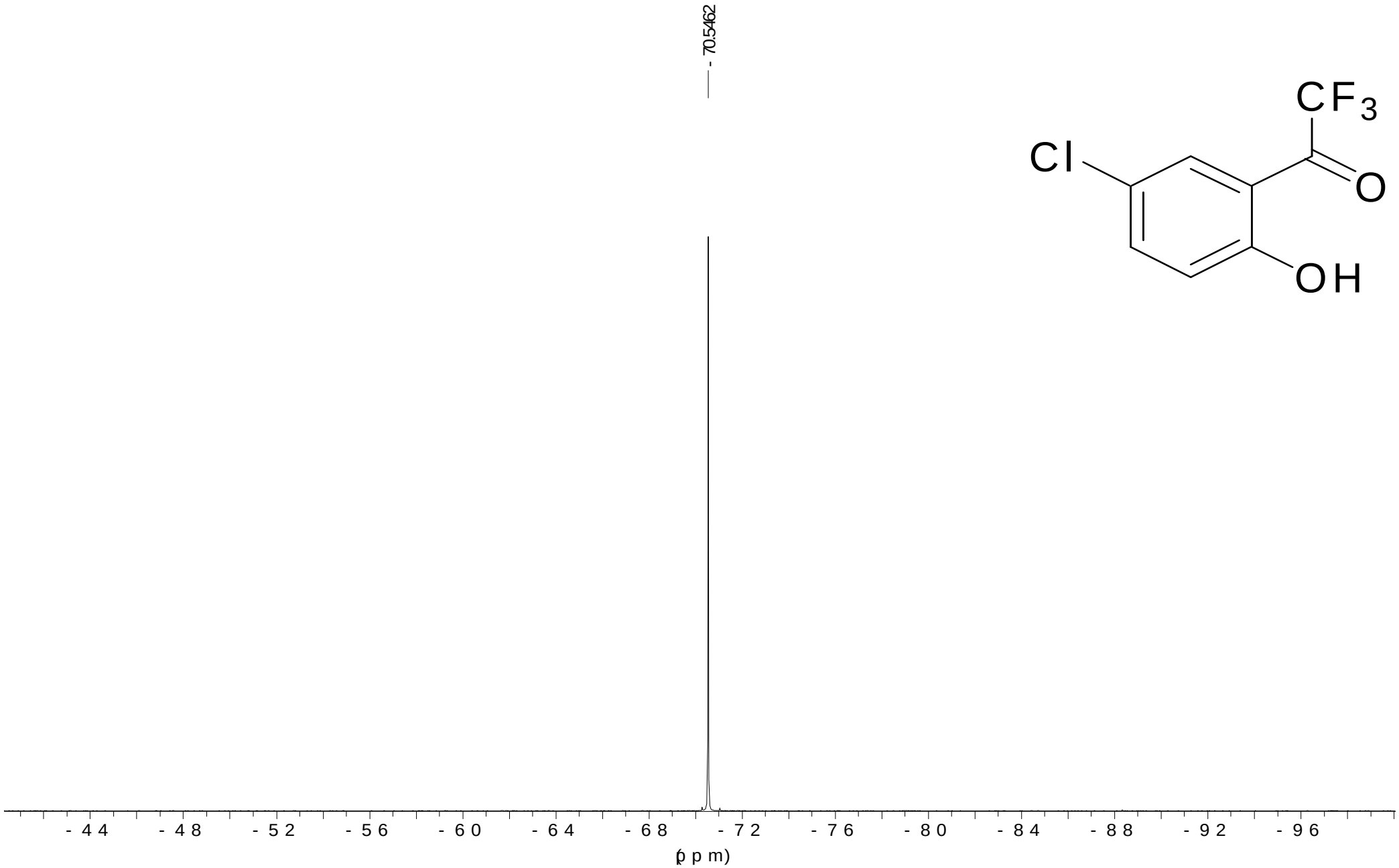

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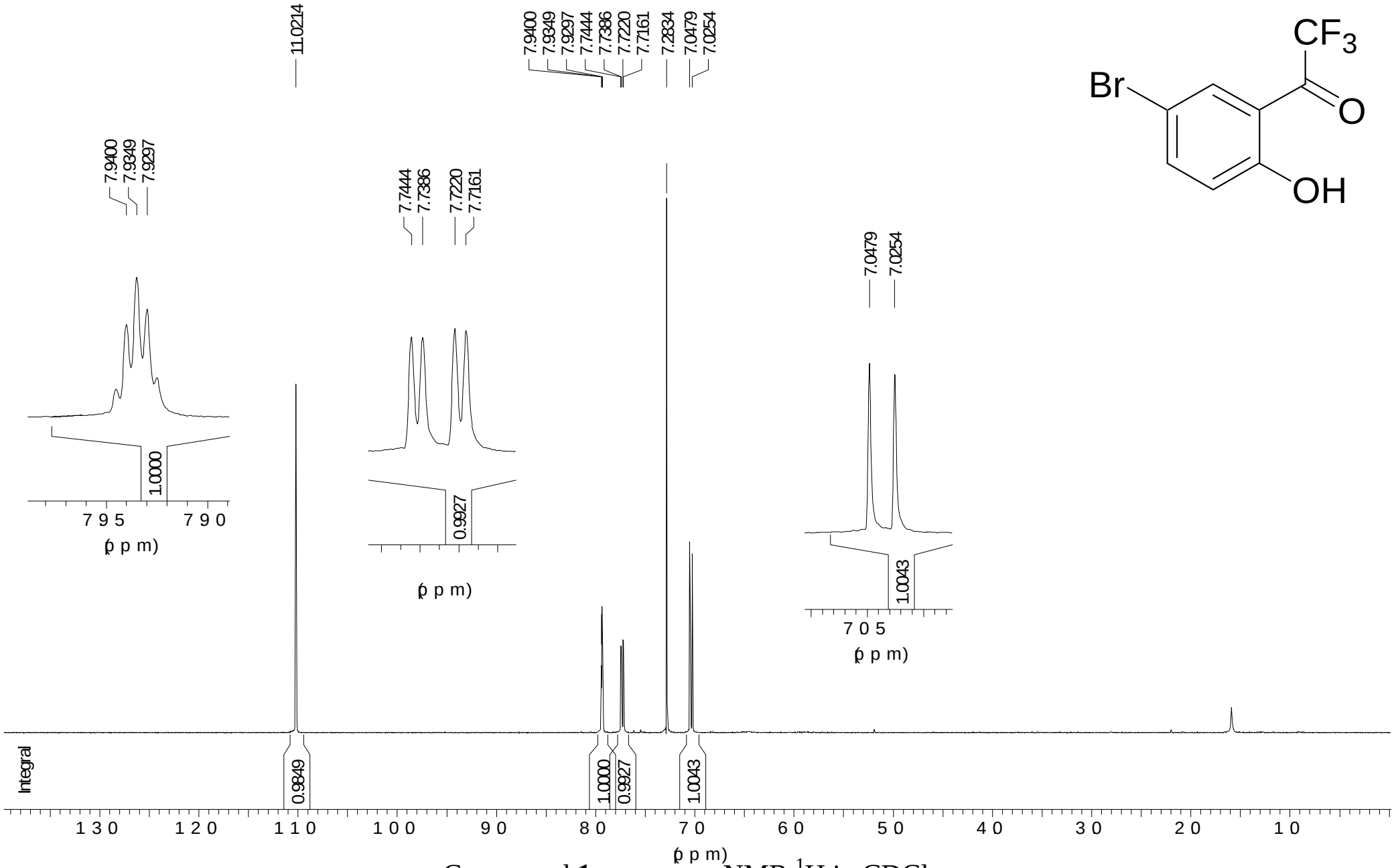

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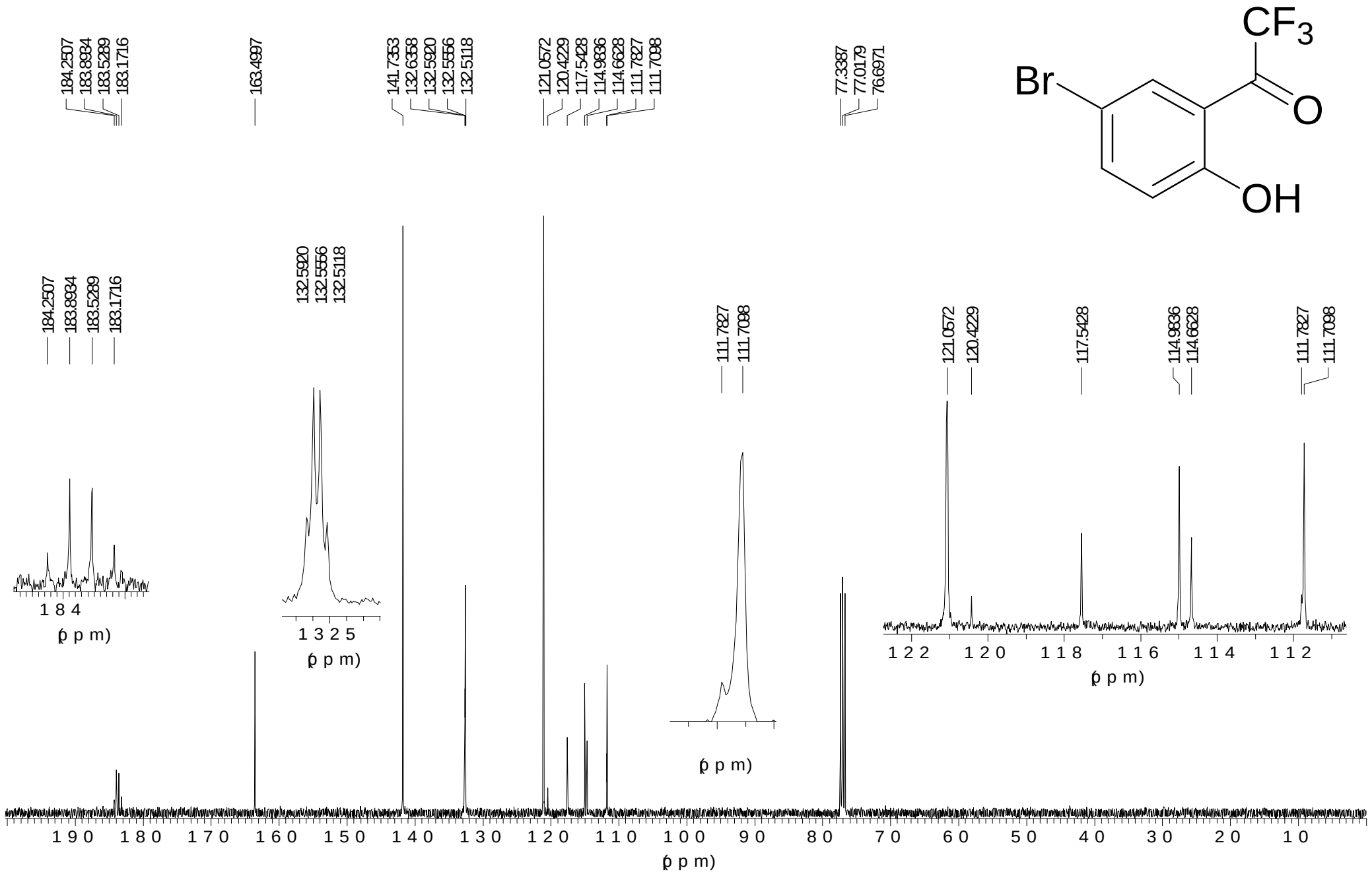

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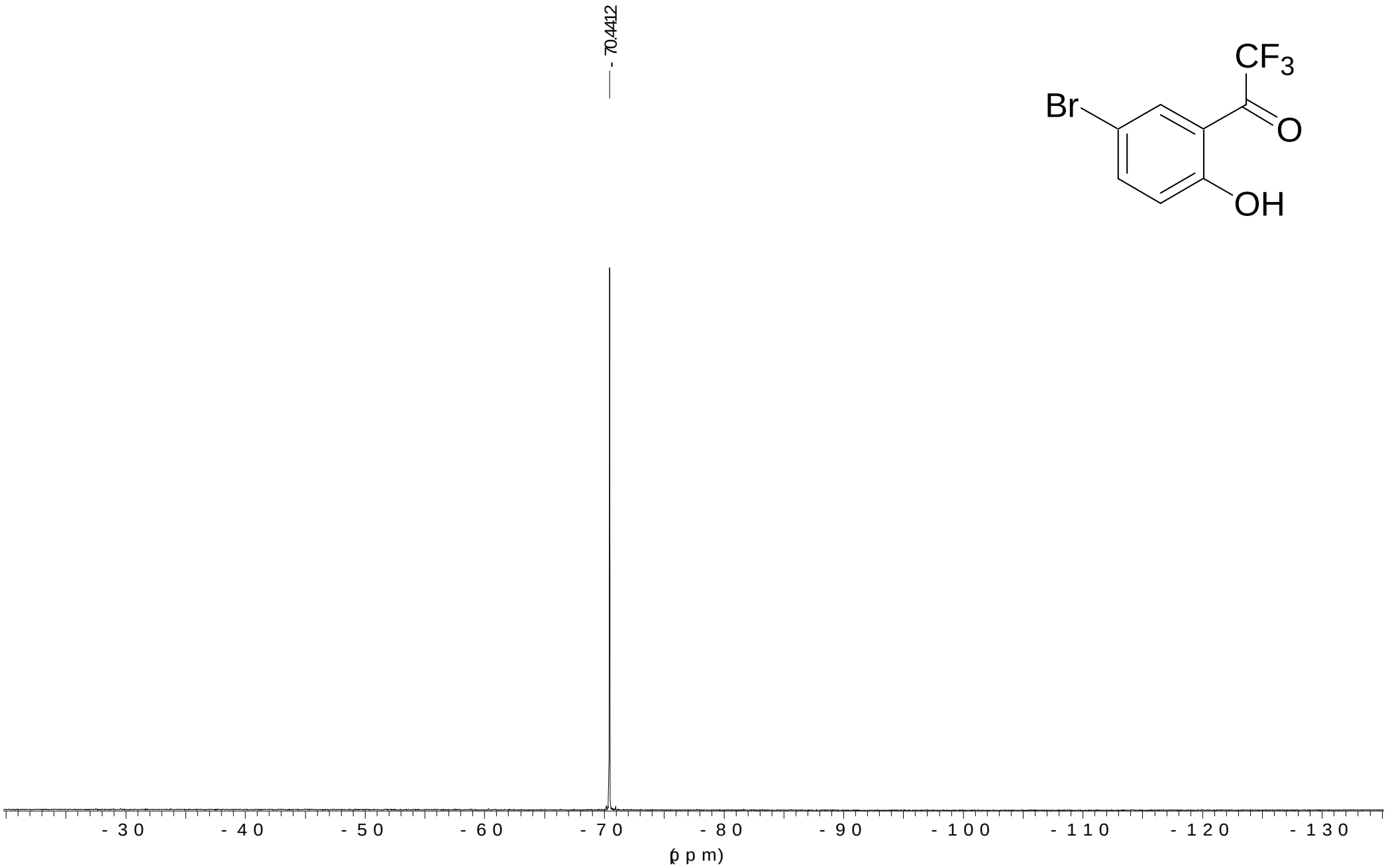

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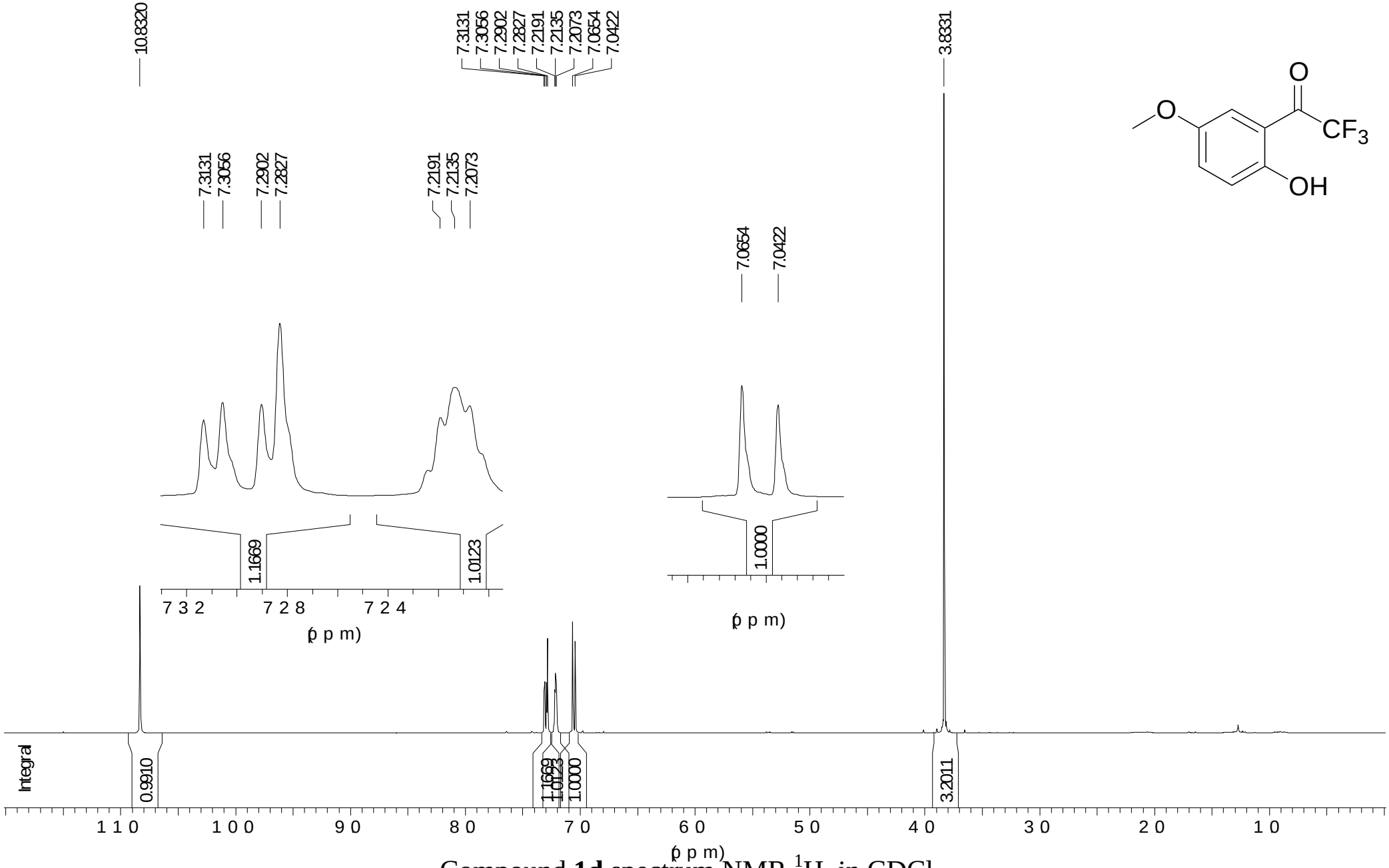

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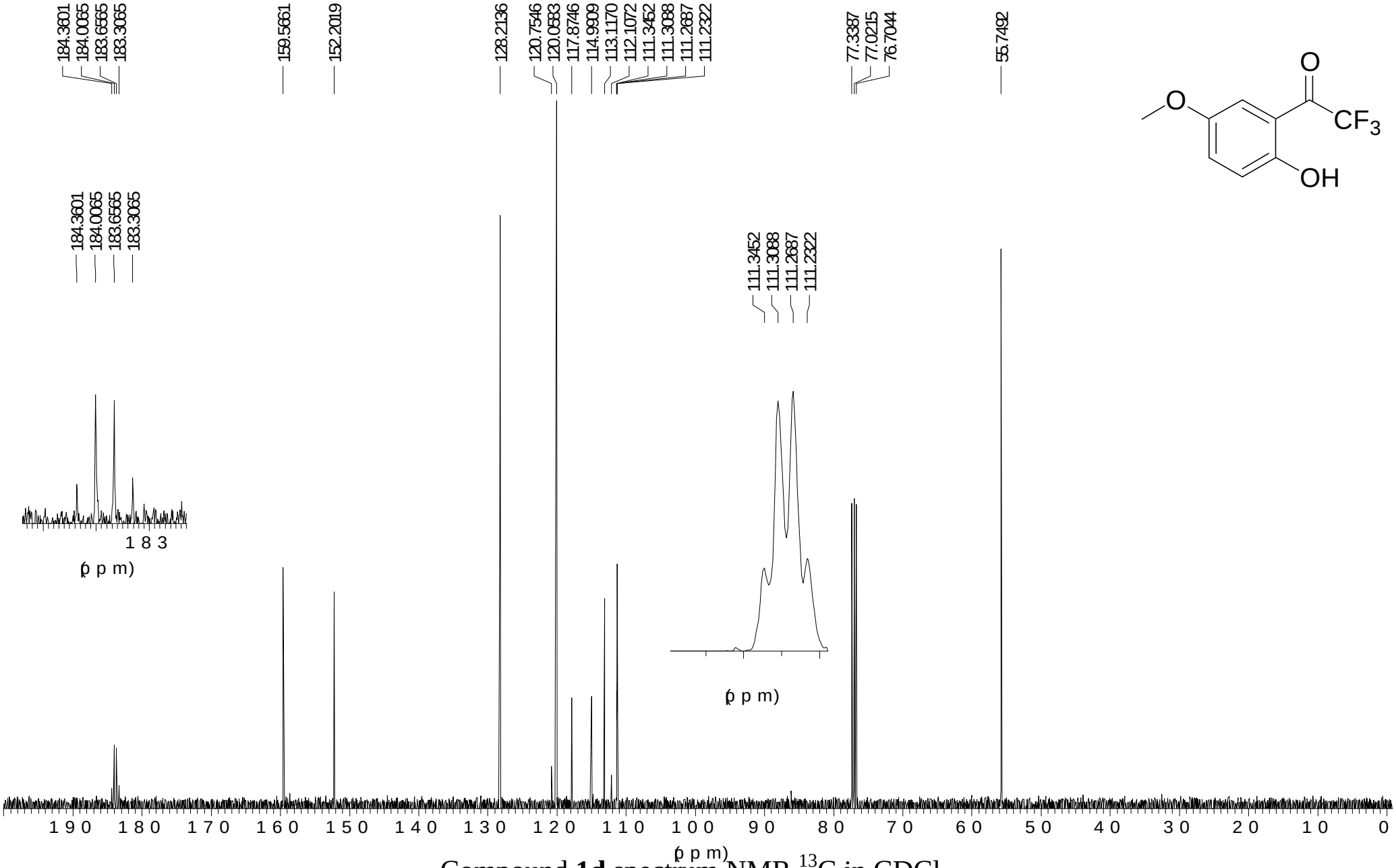
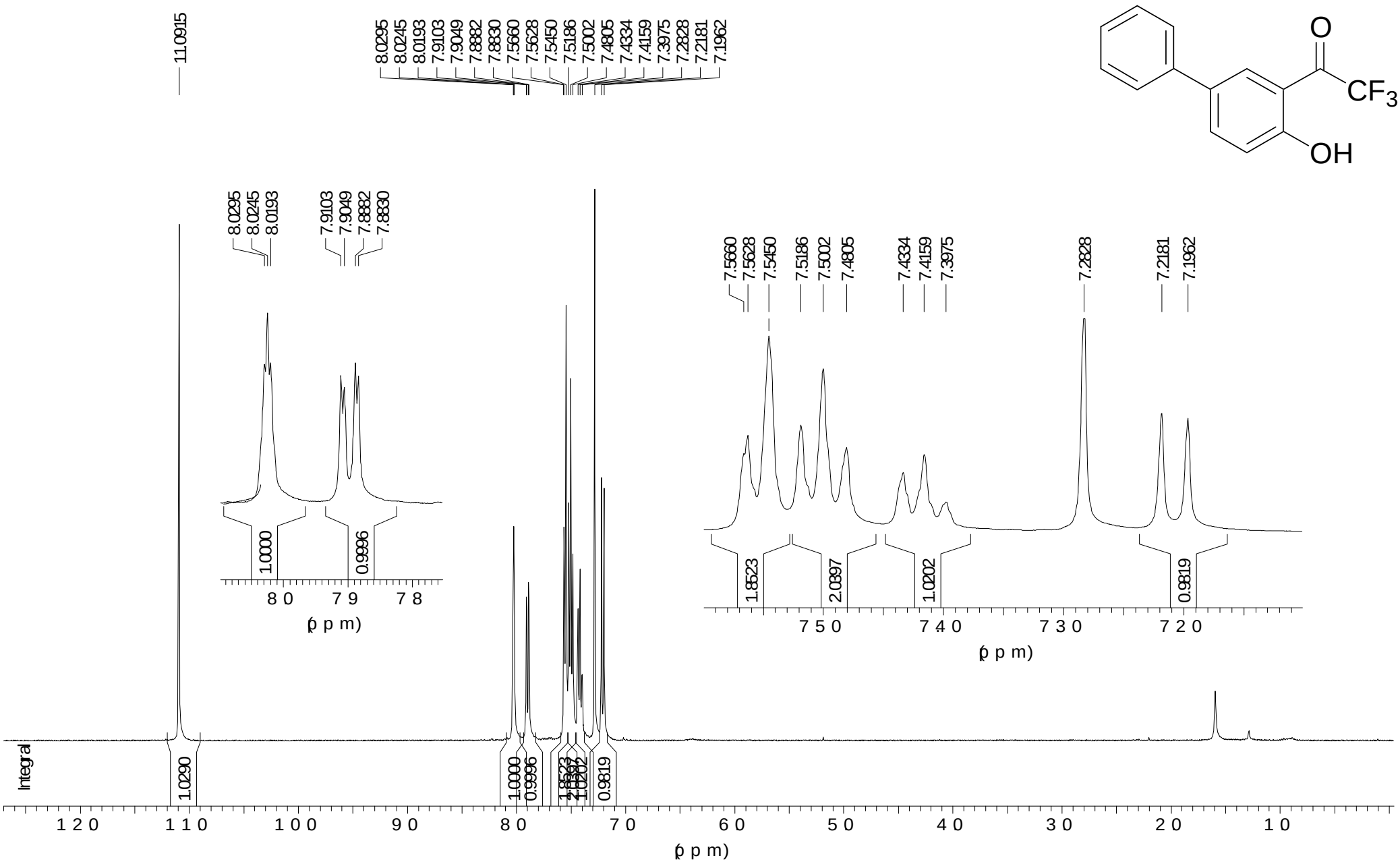


Compound **1d** spectrum NMR ^{13}C in $CDCl_3$

Compound **1d** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



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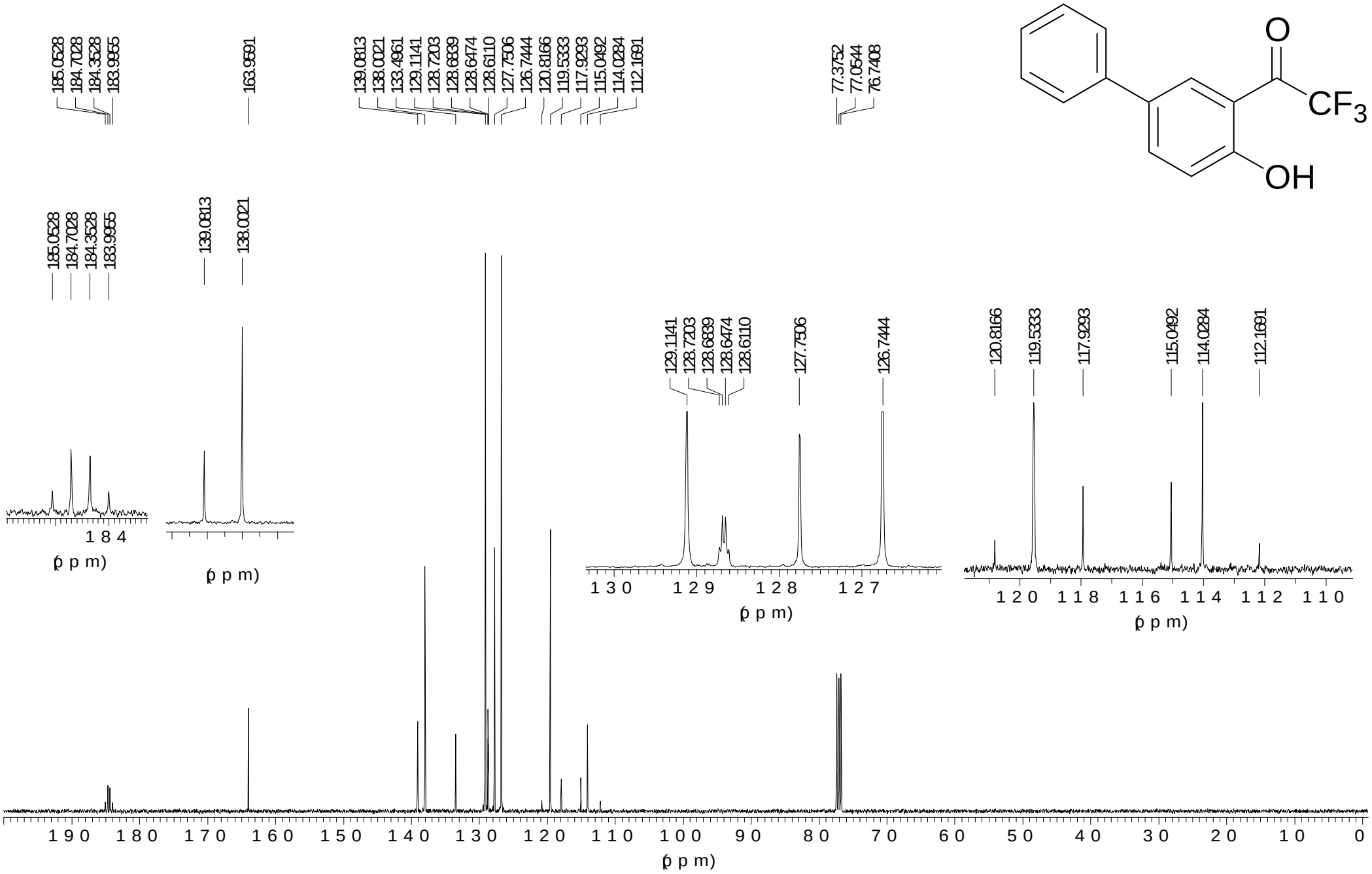

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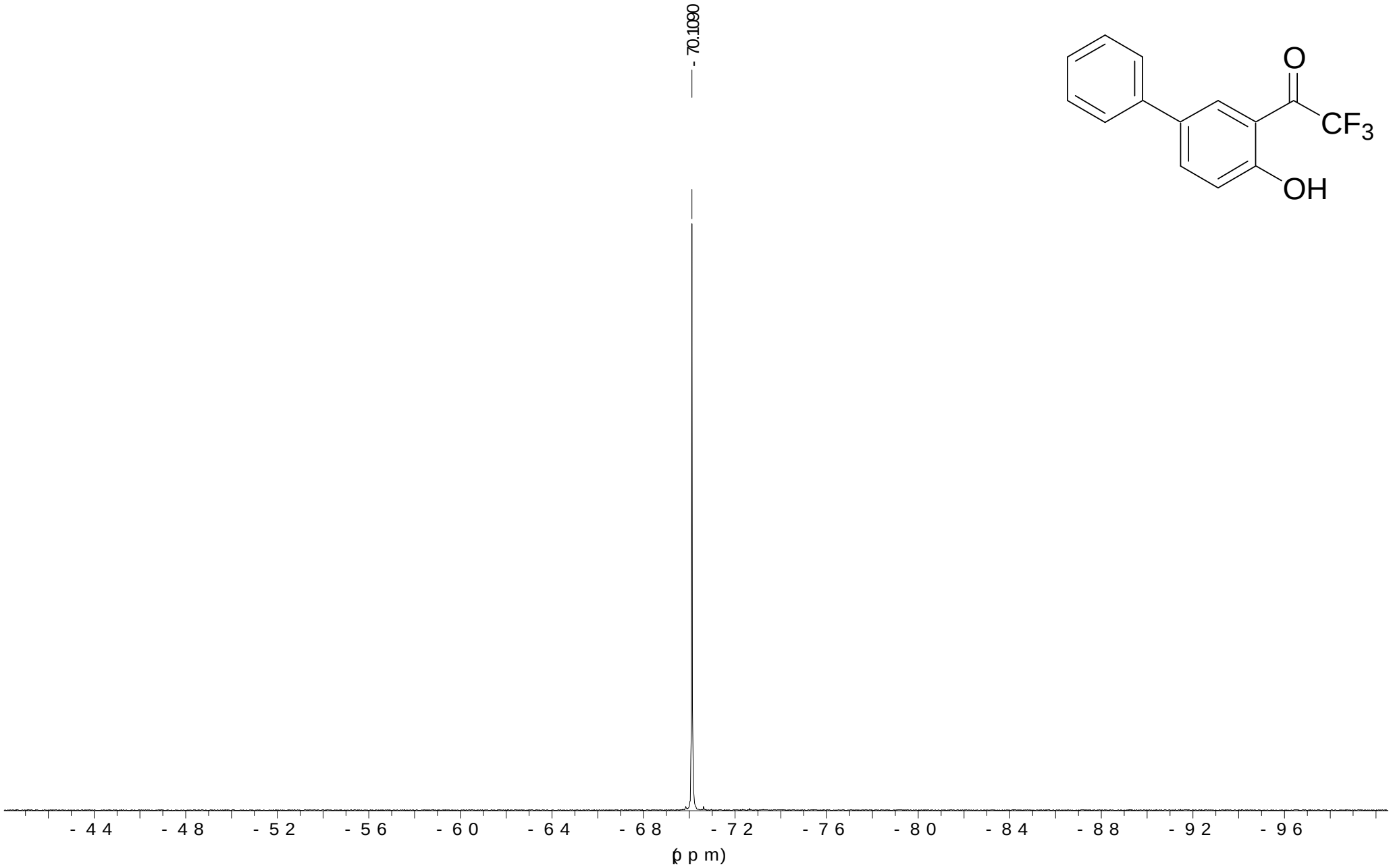

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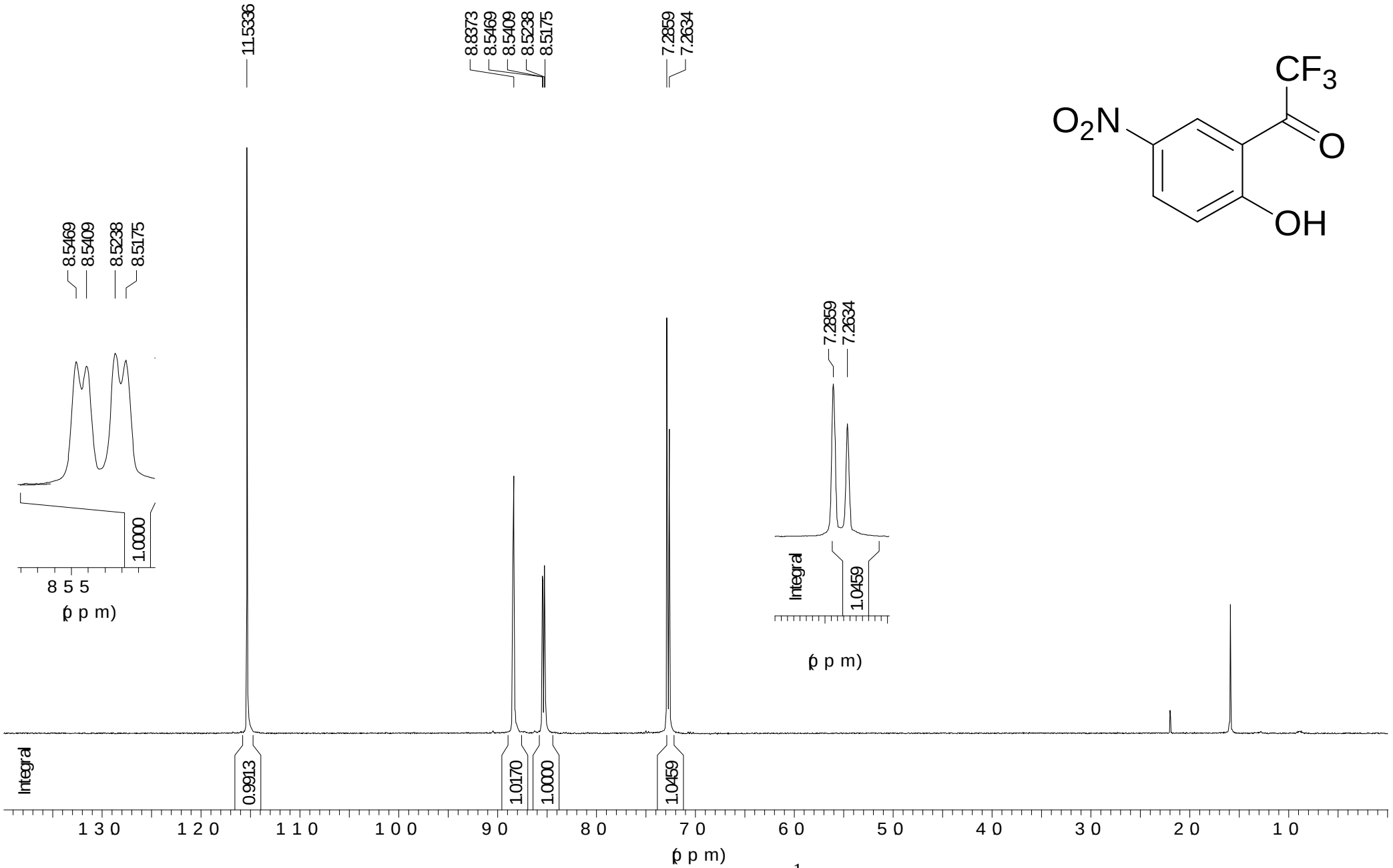

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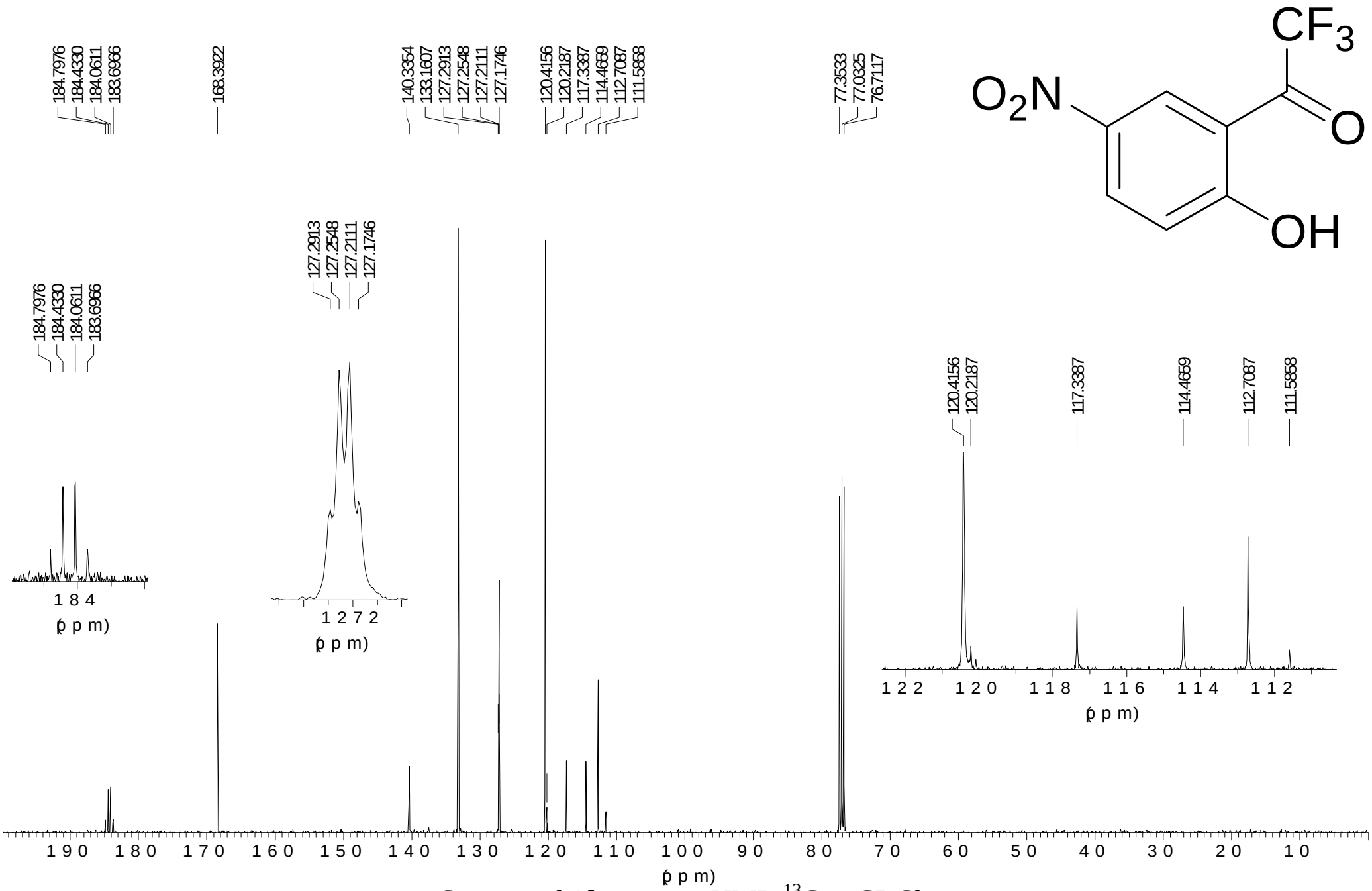

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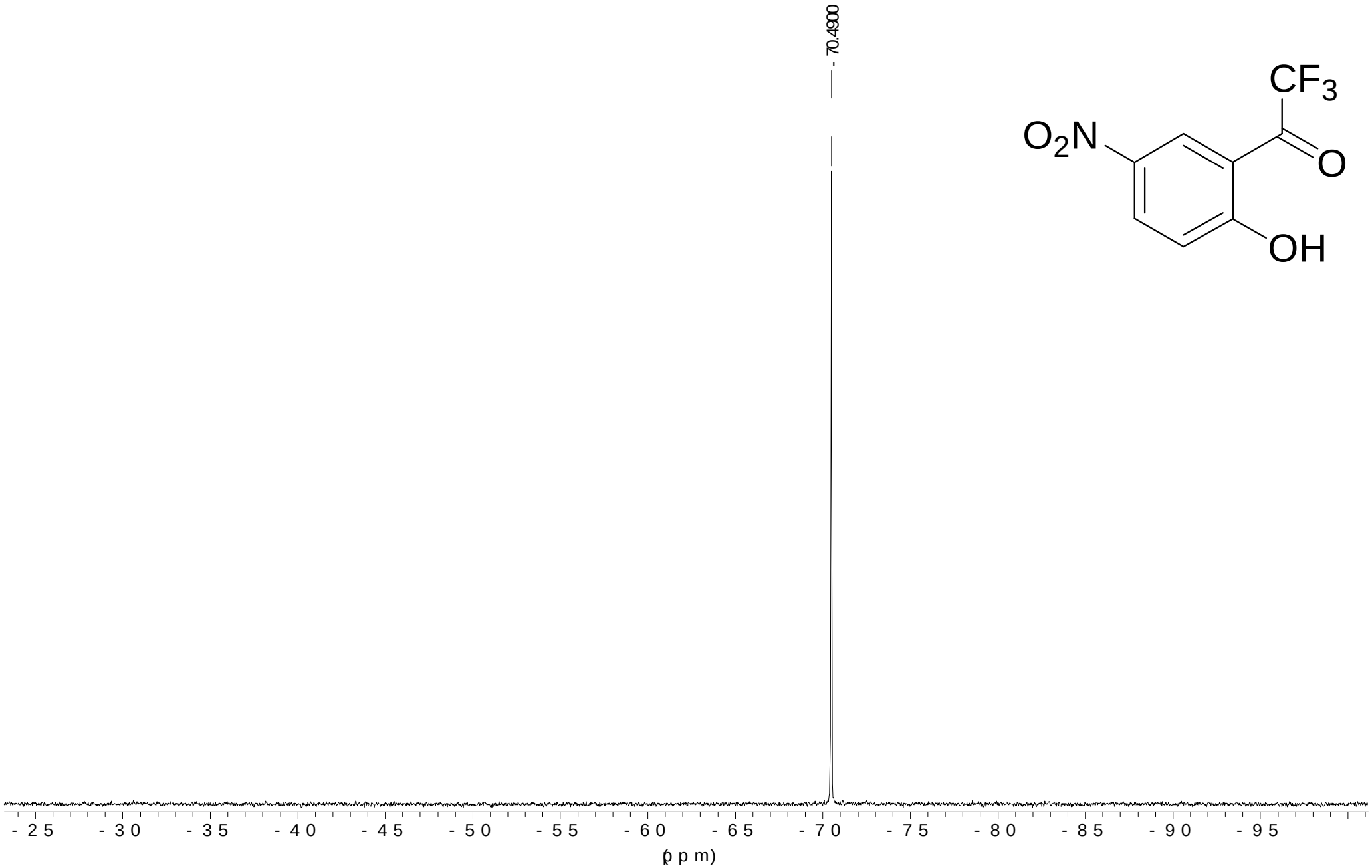

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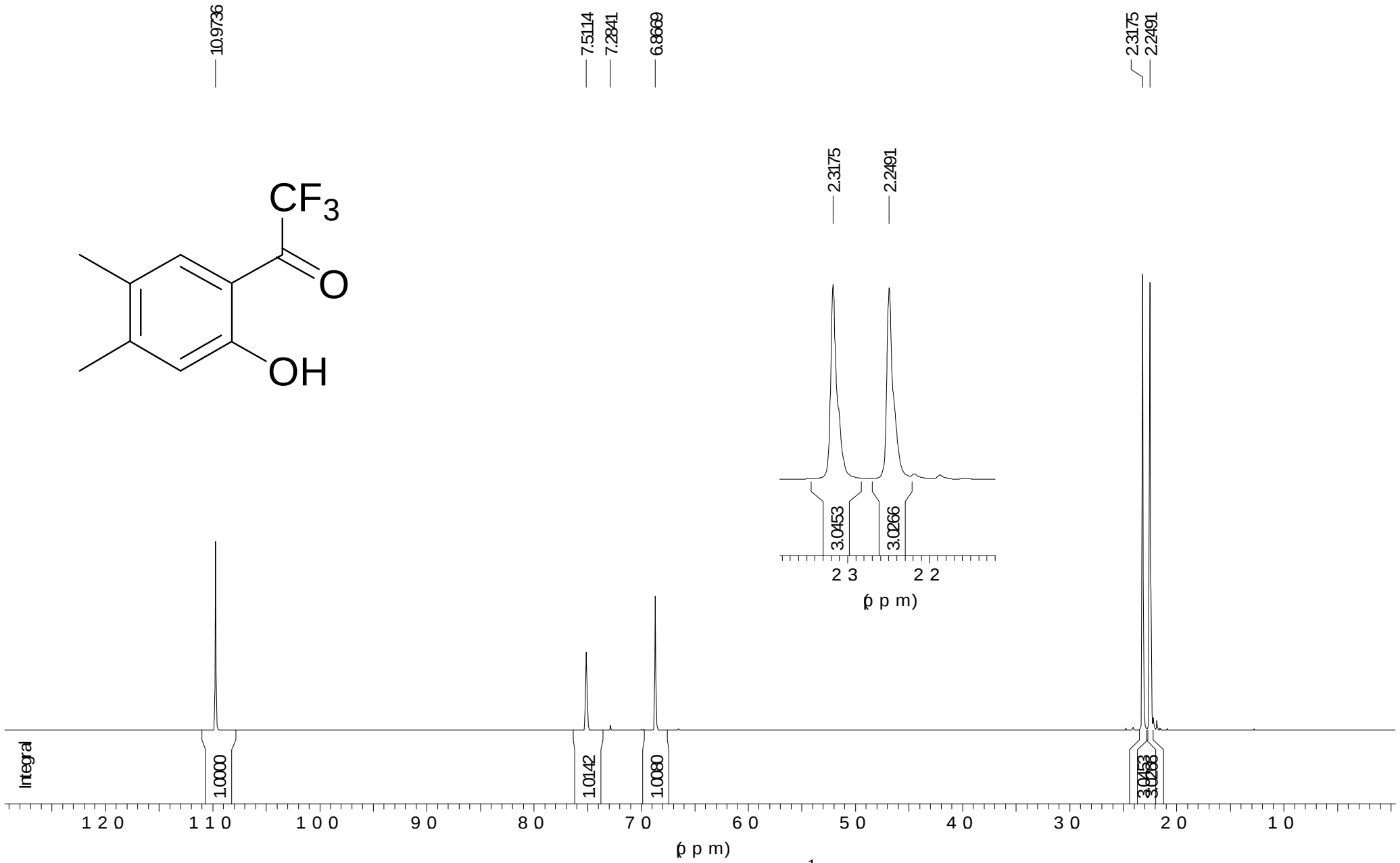

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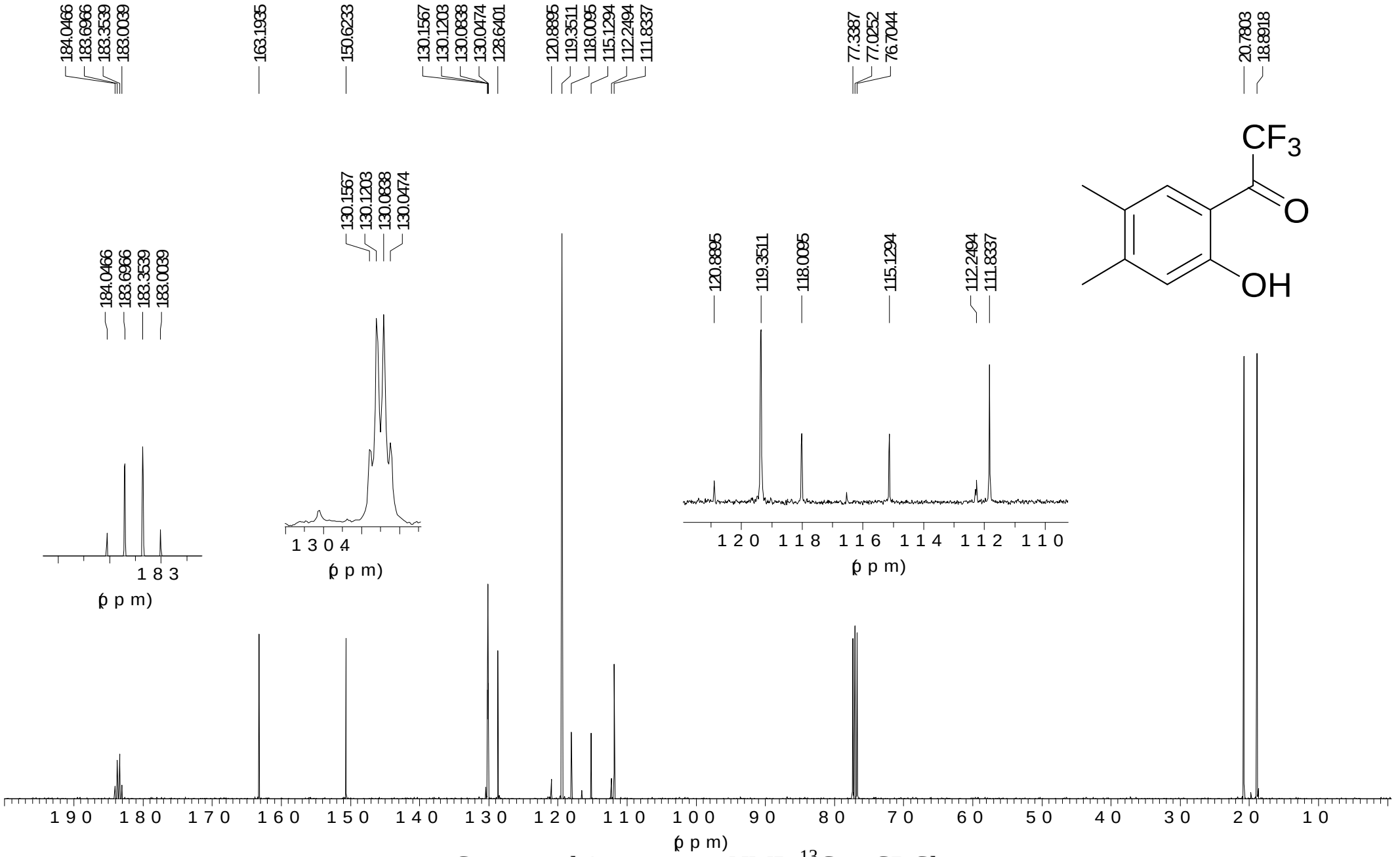

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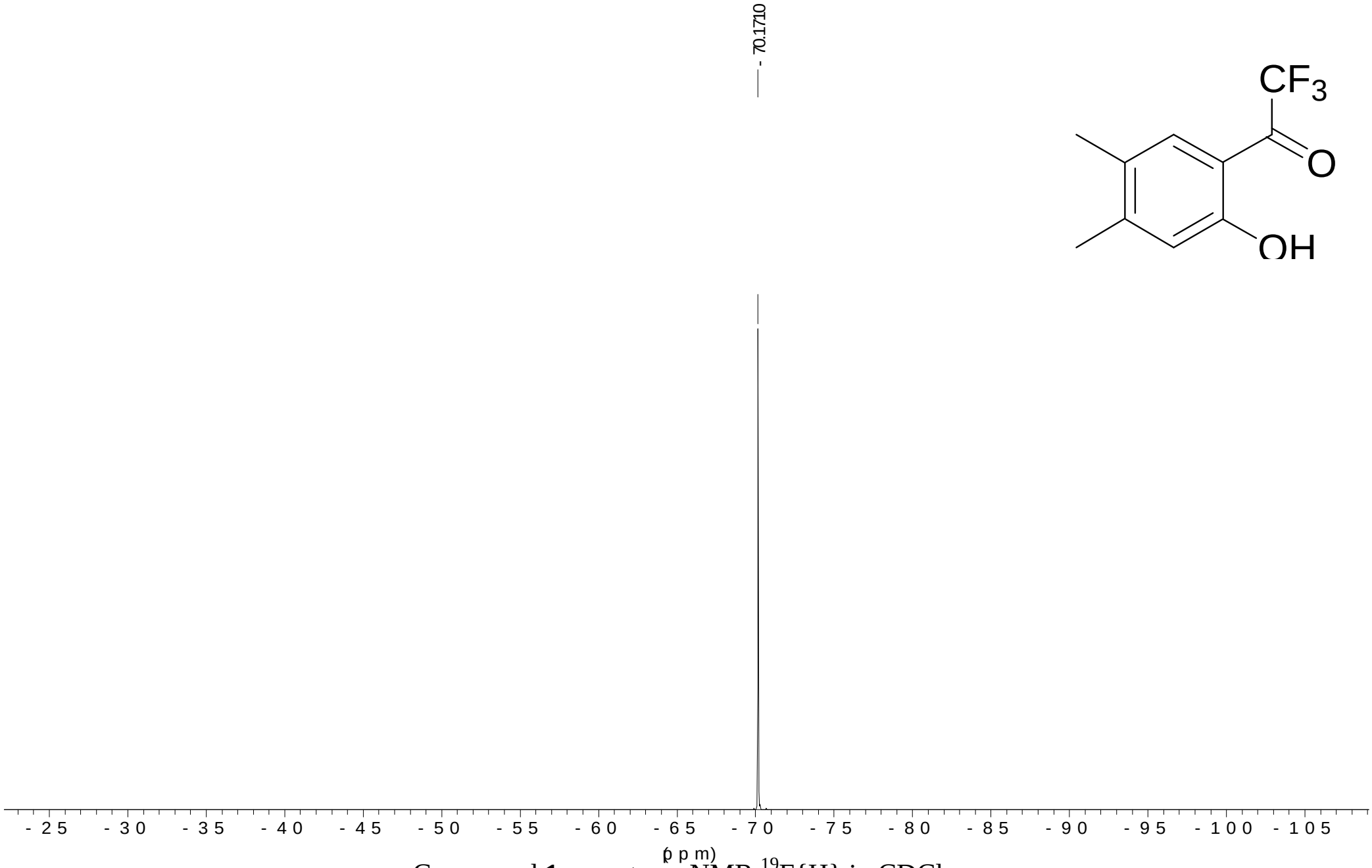

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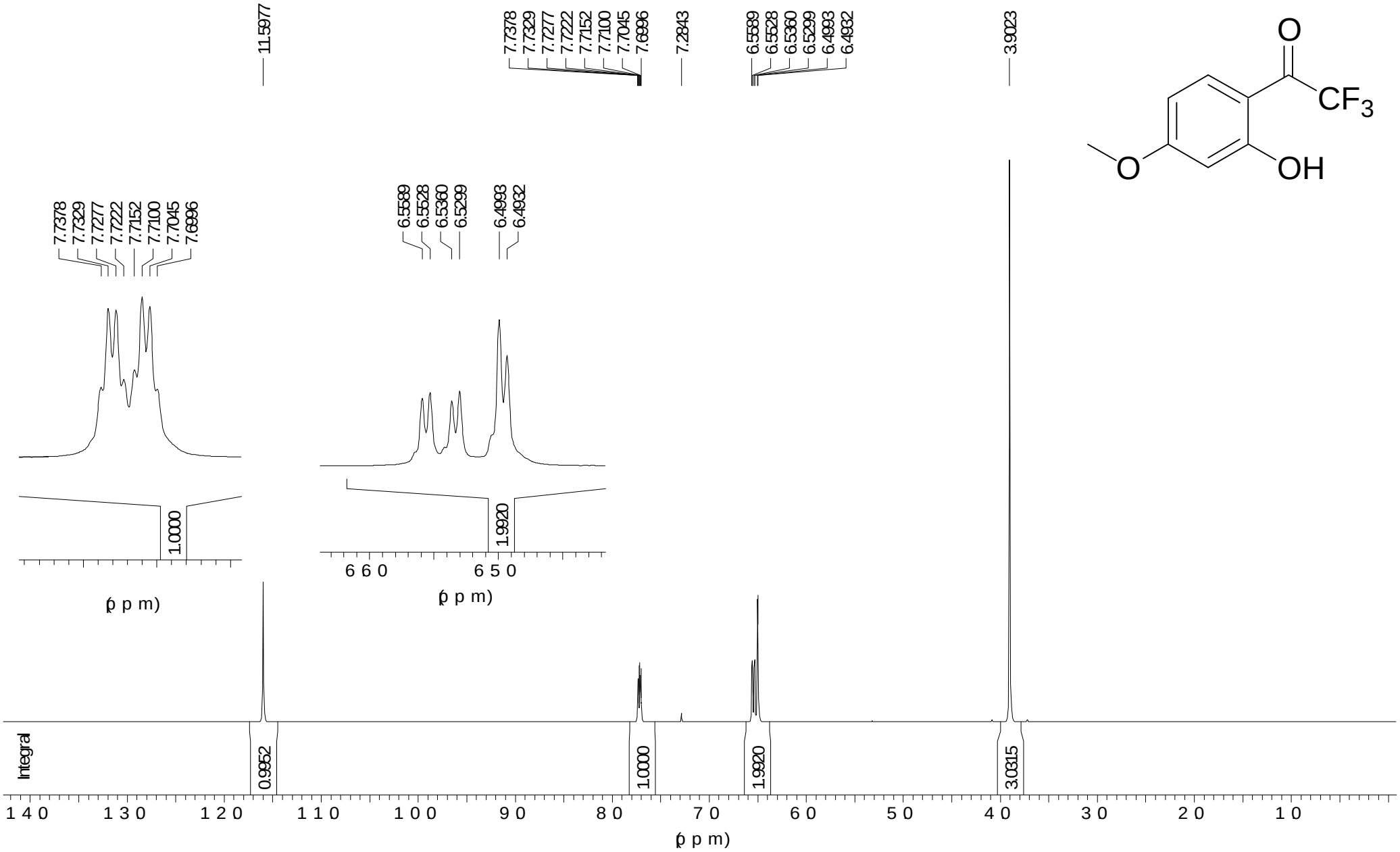

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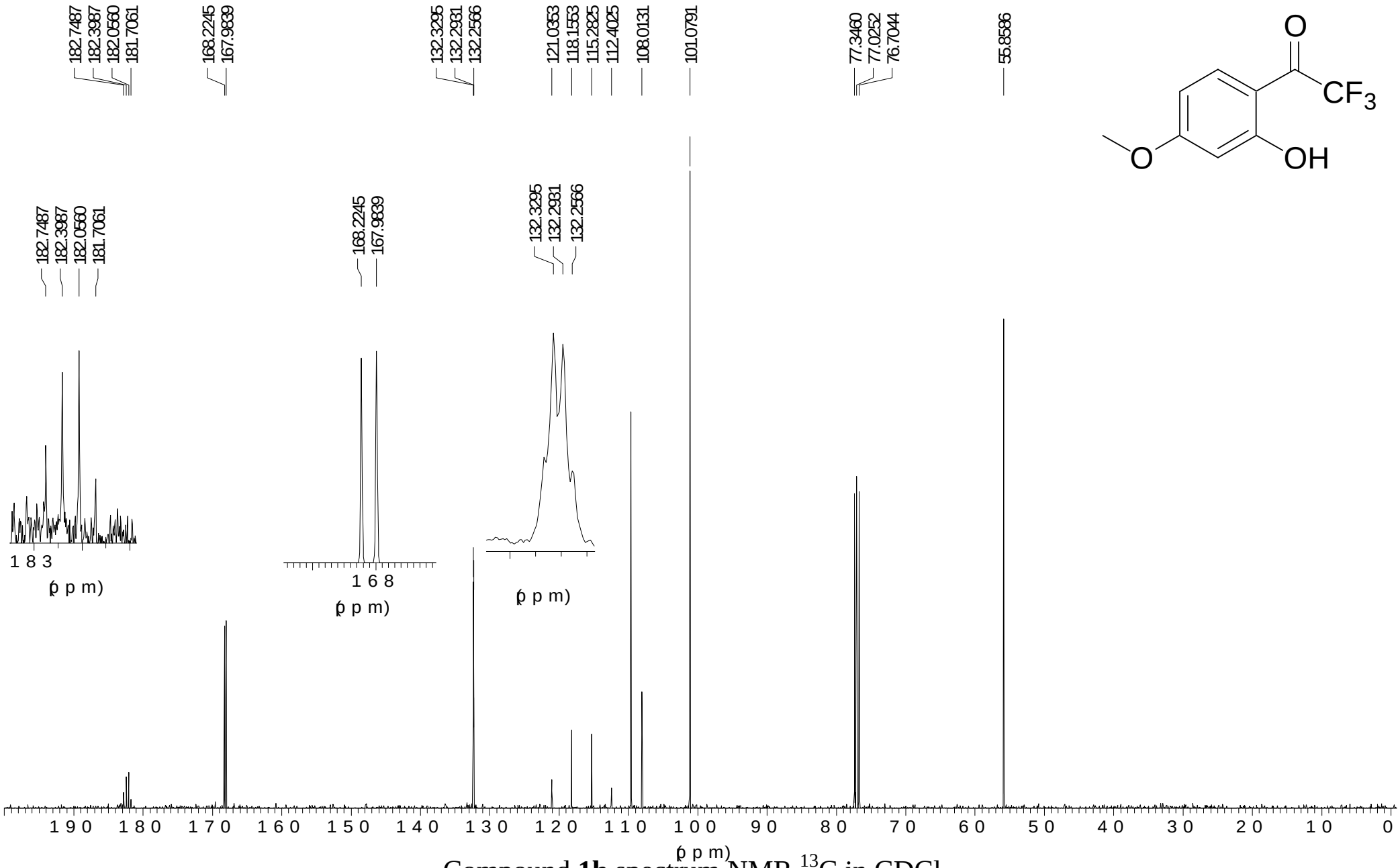

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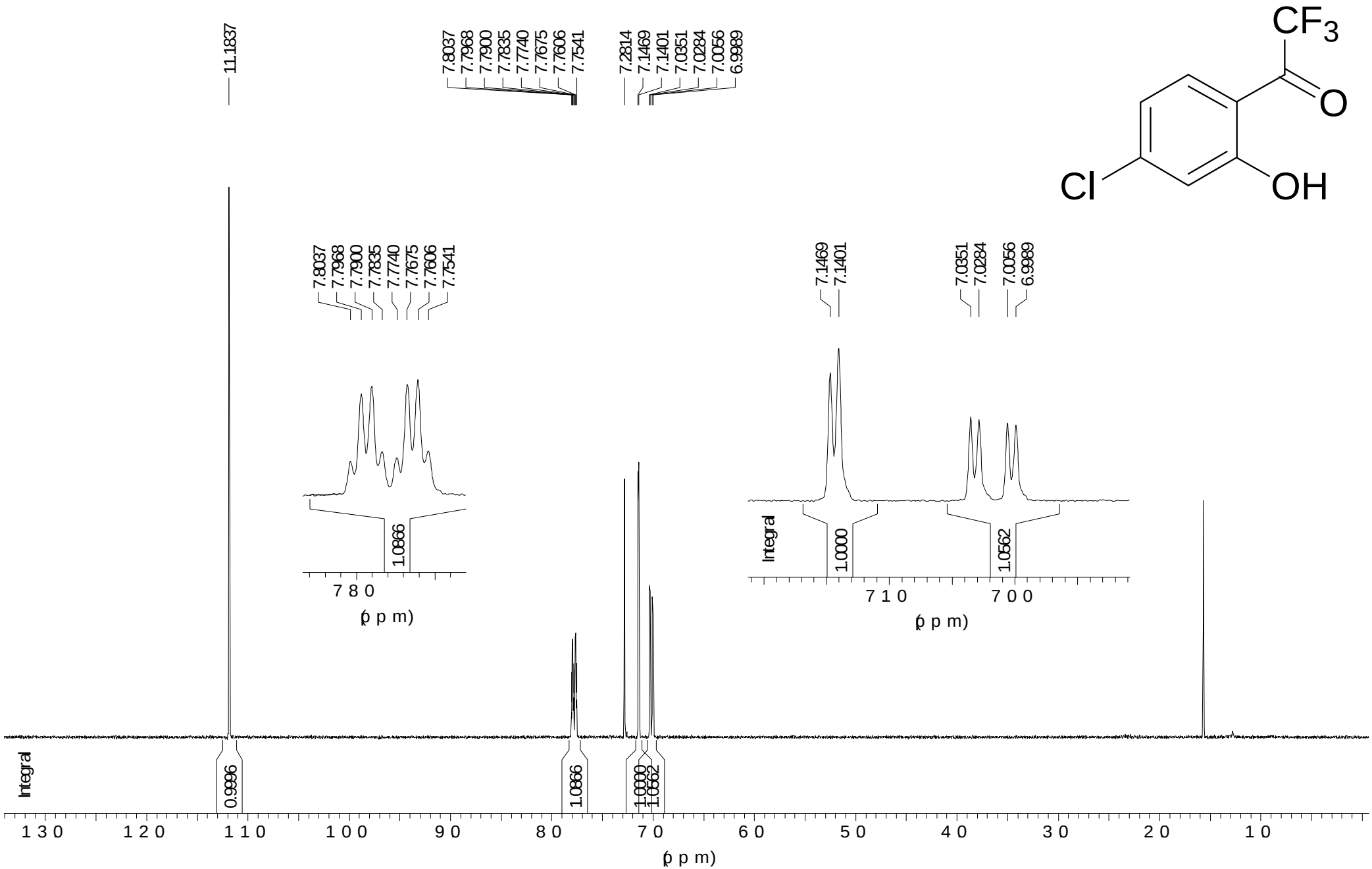

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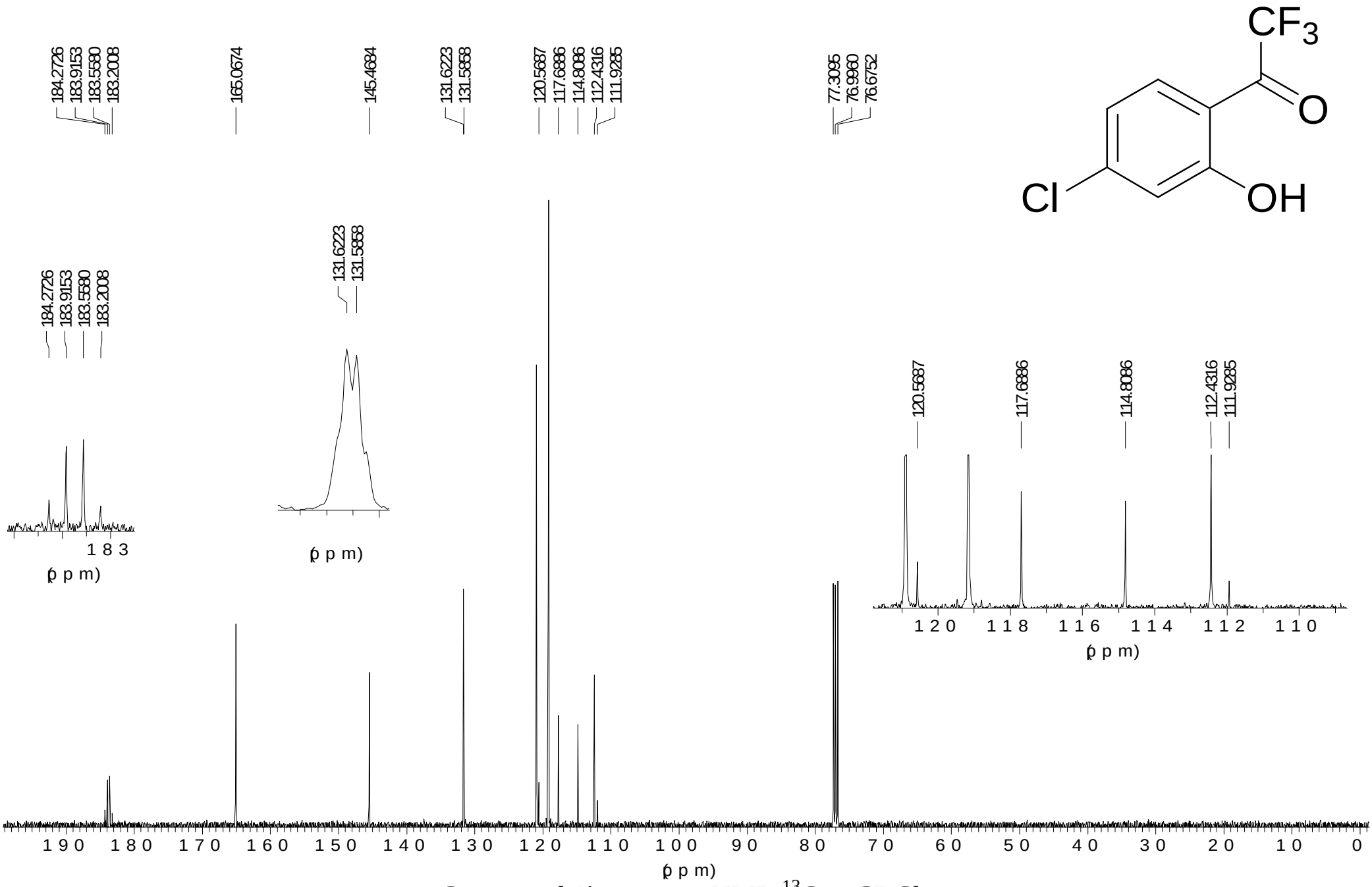

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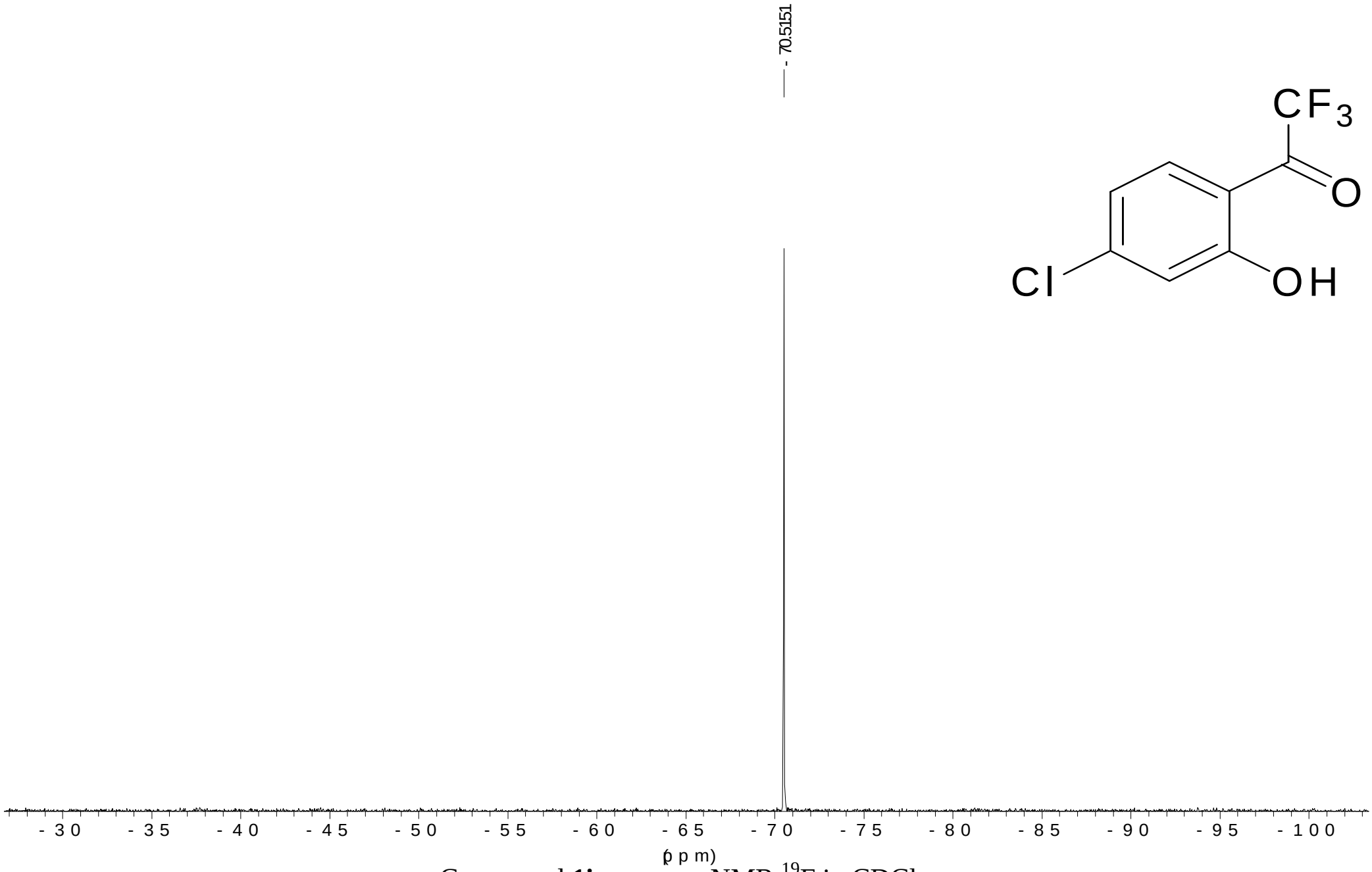

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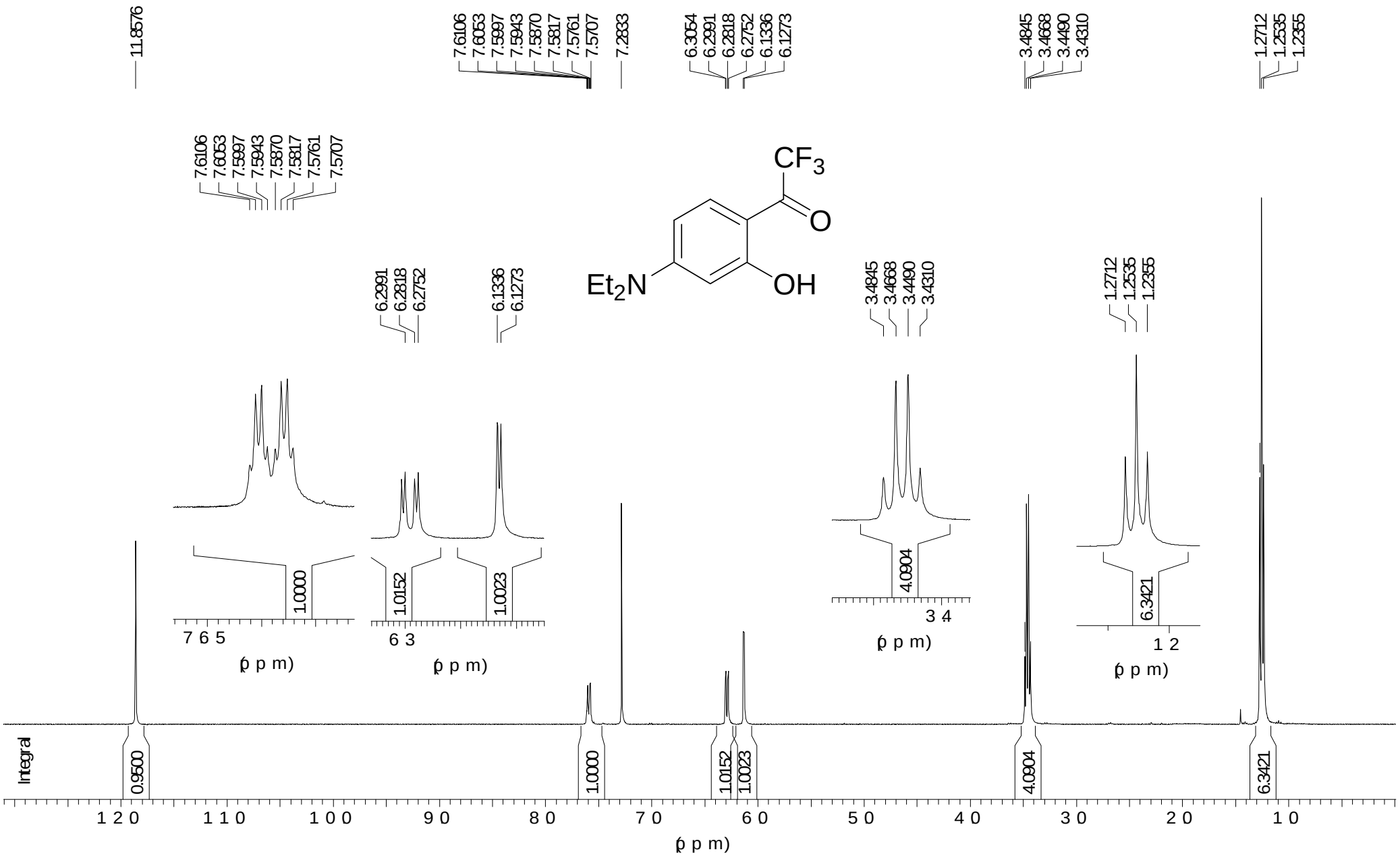

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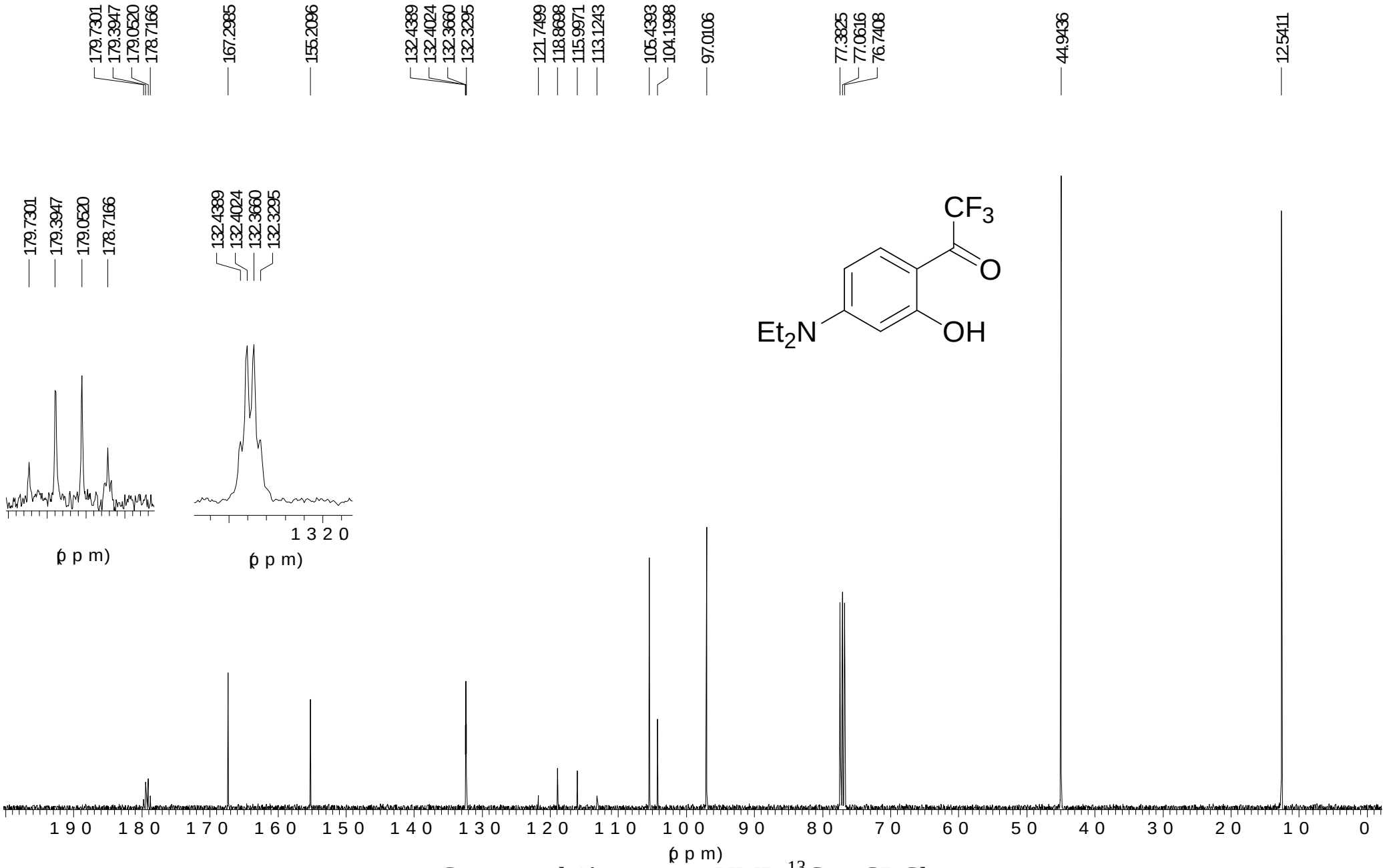

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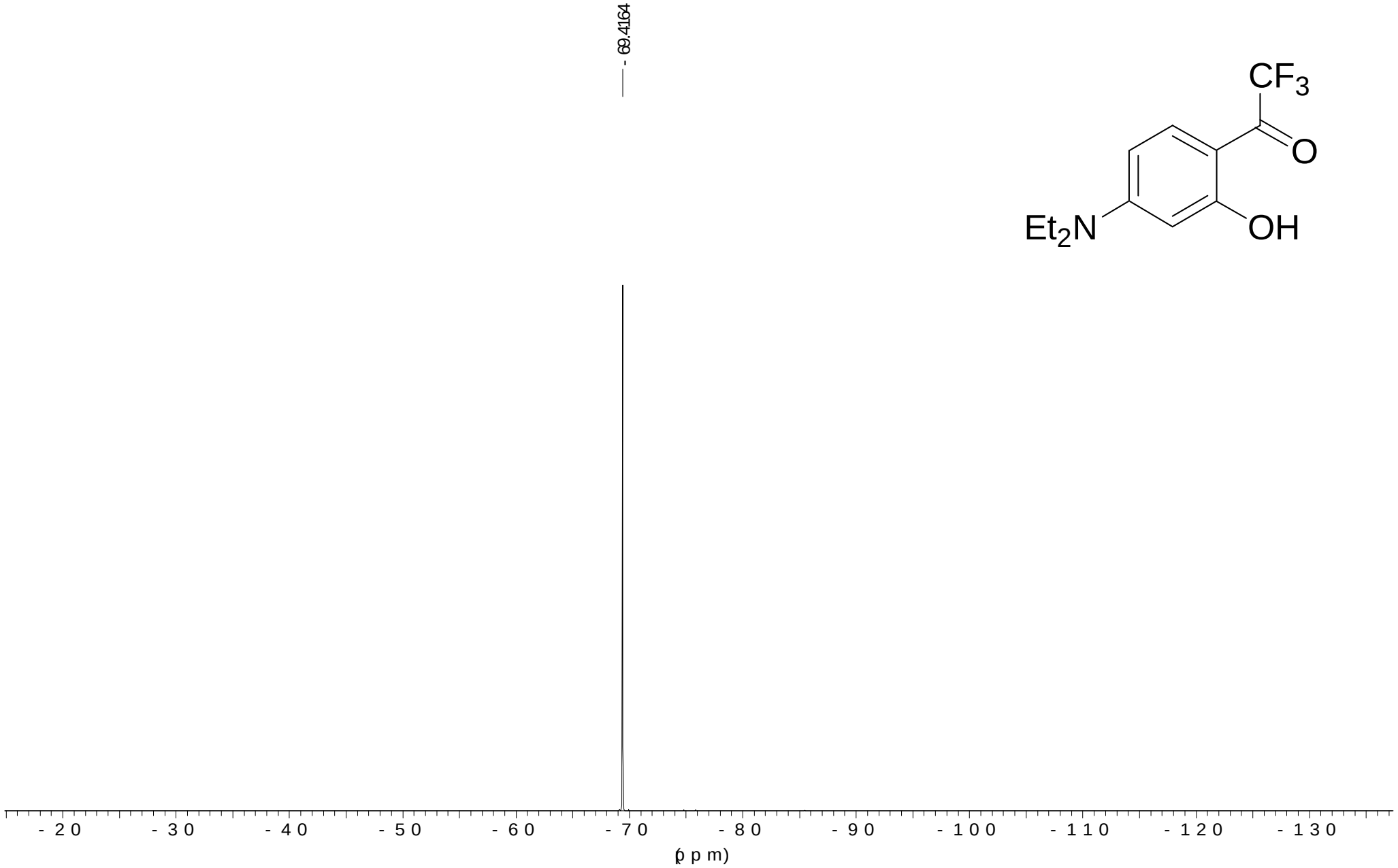

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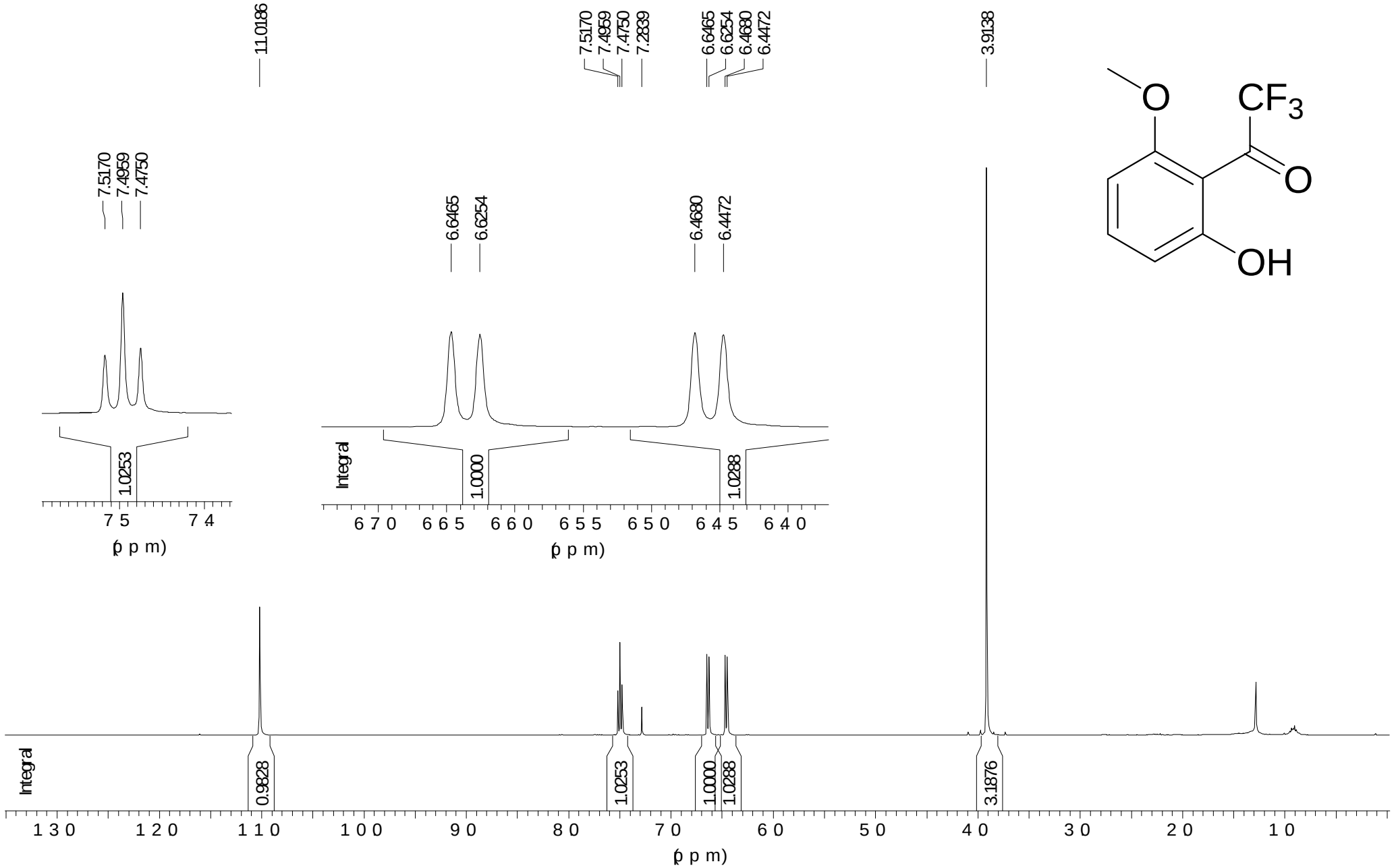

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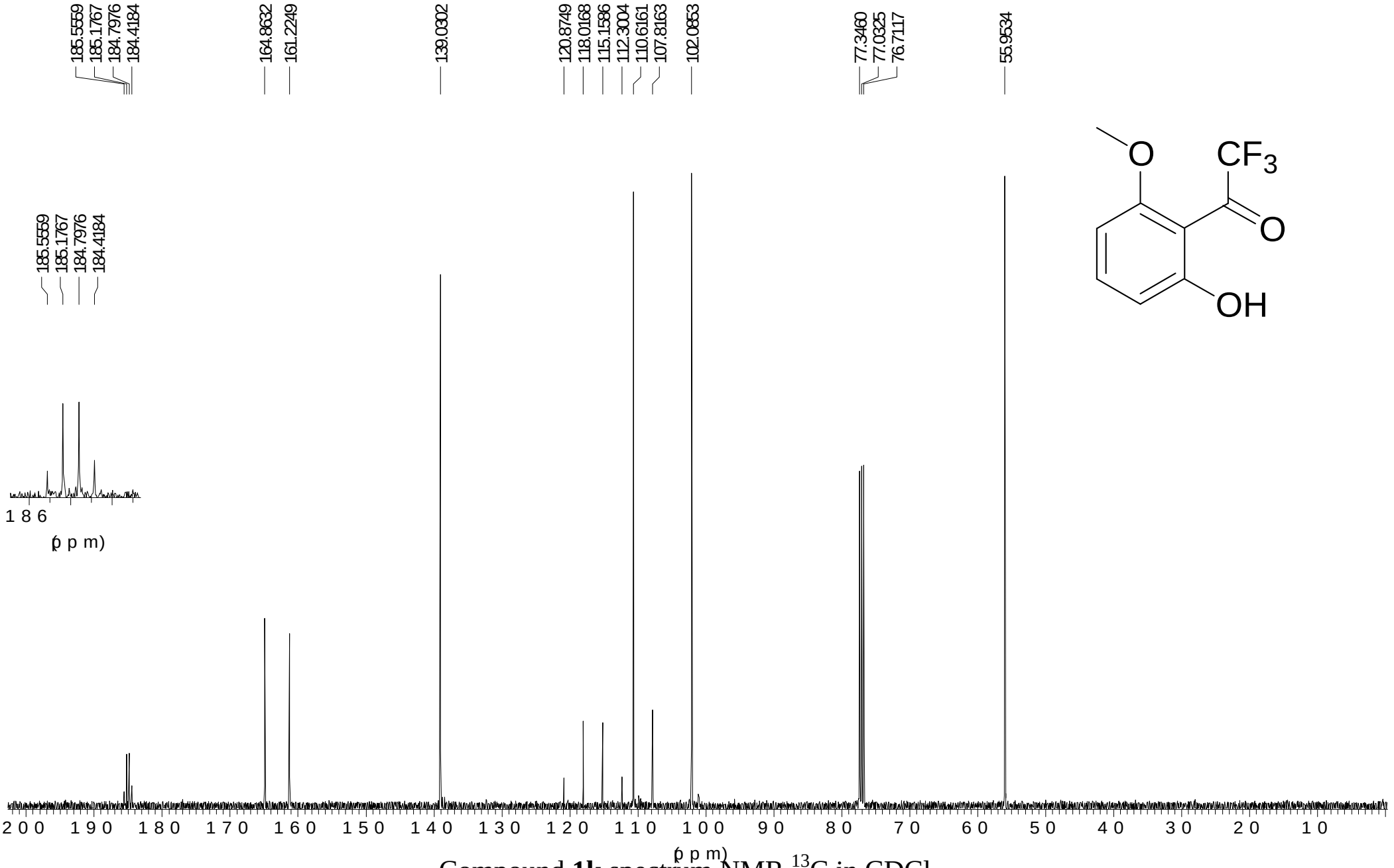

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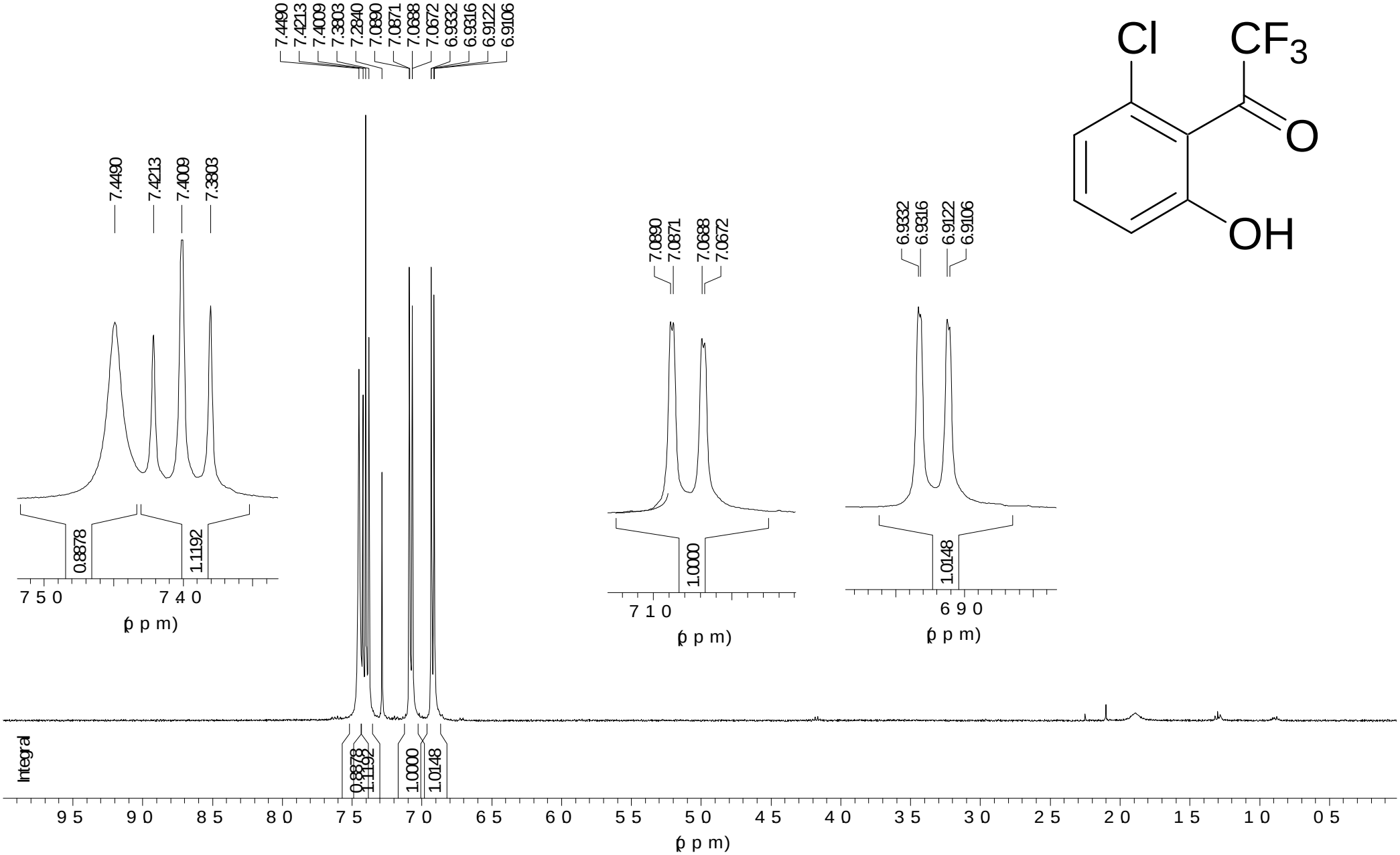

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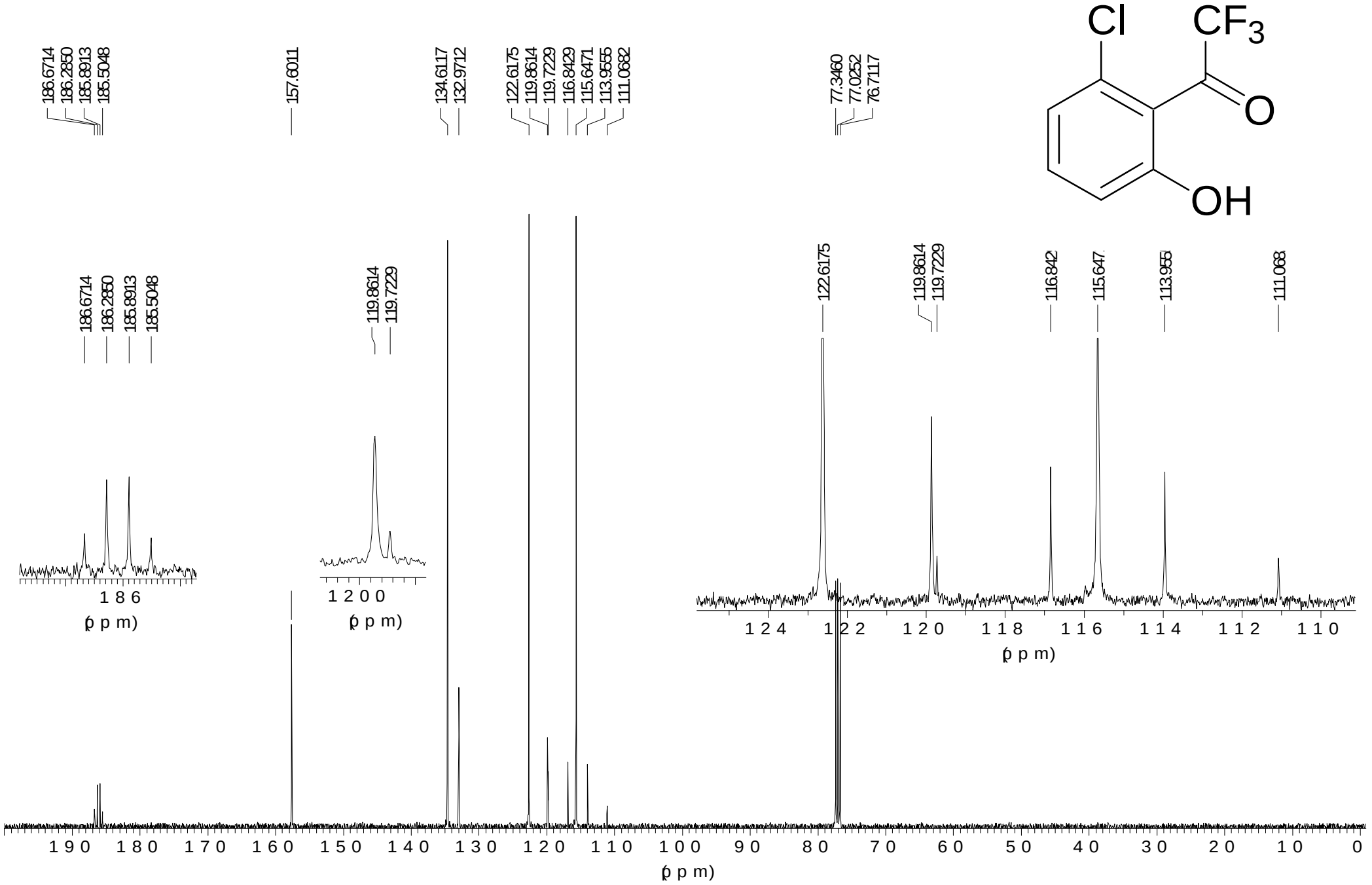

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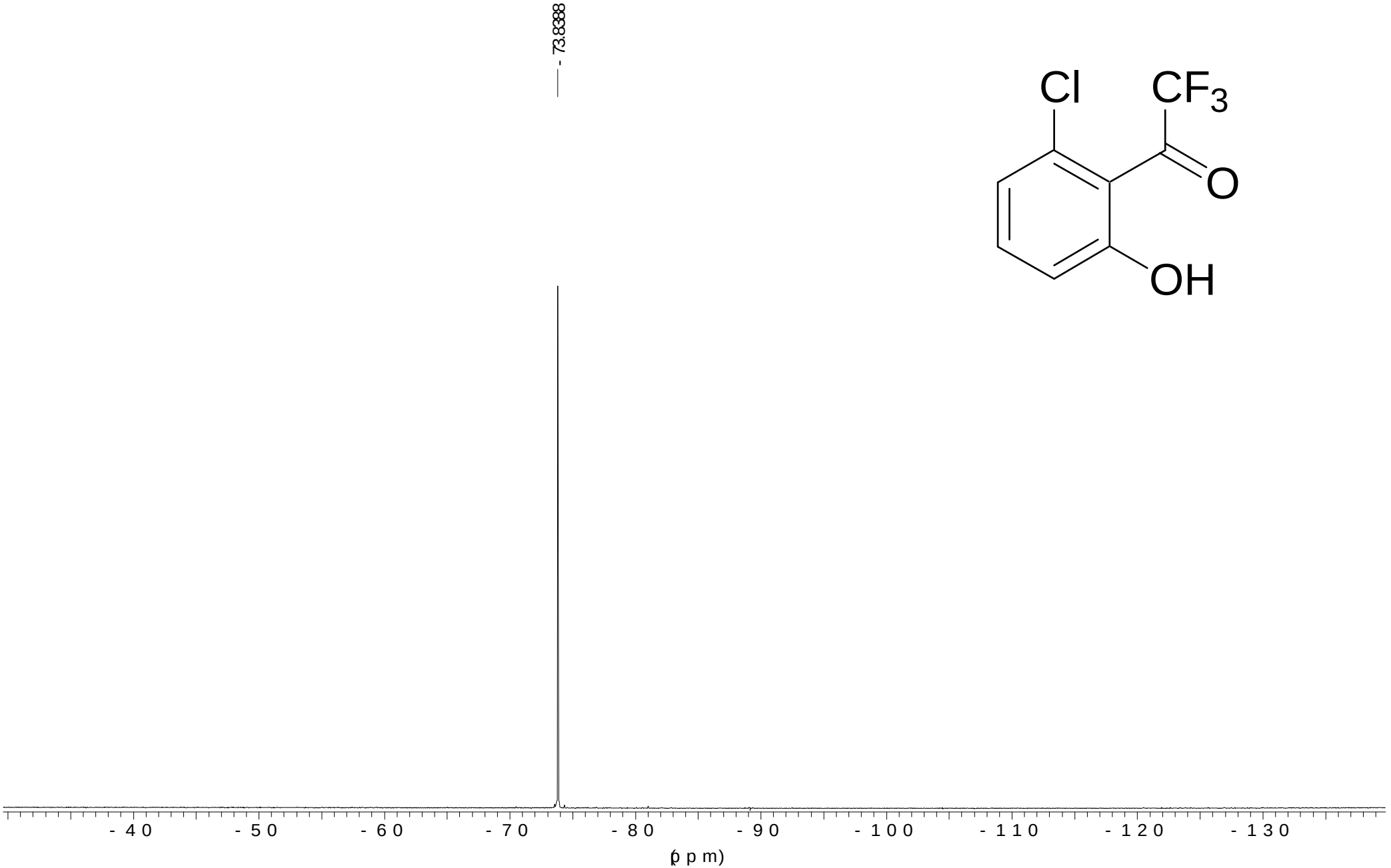

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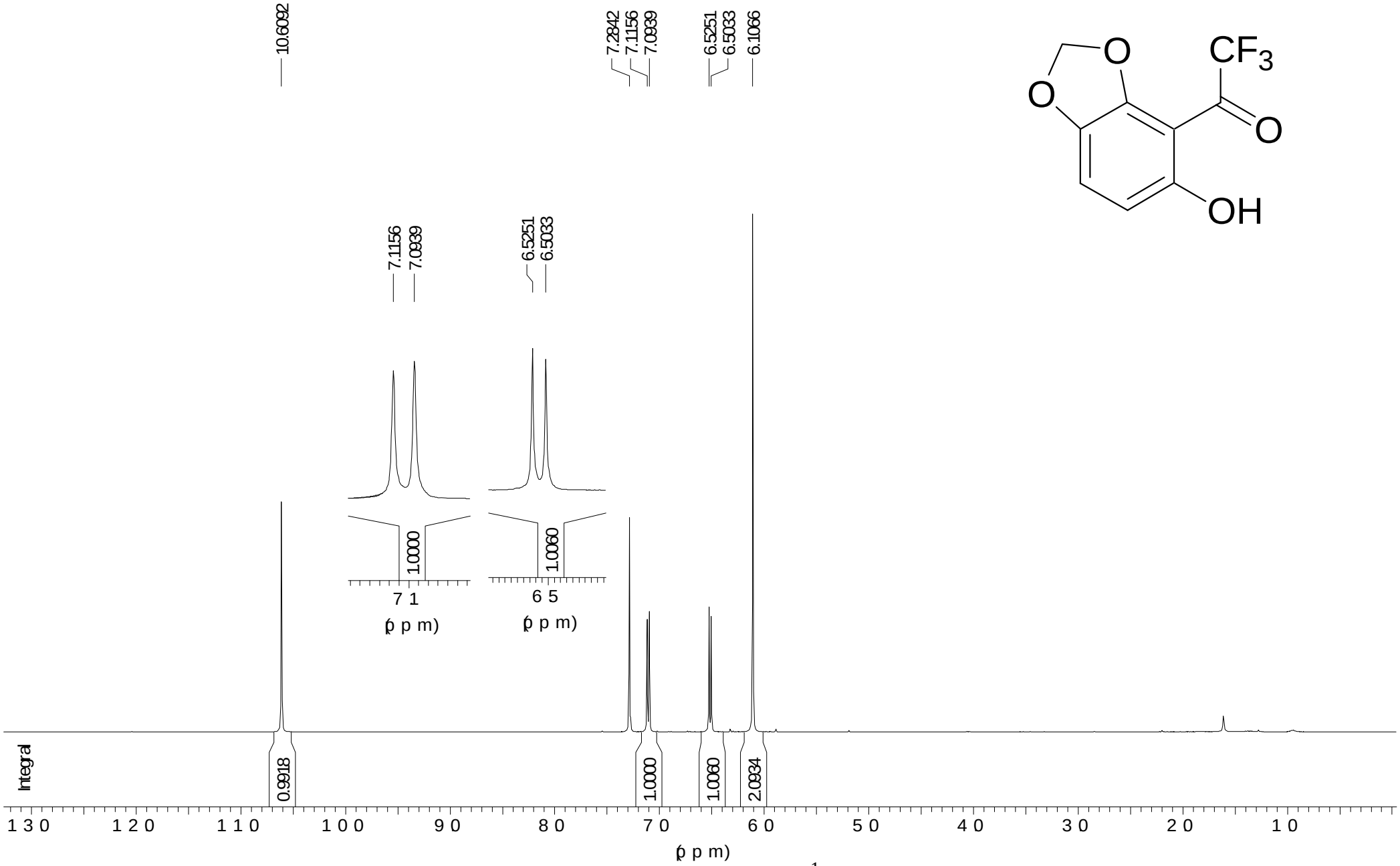

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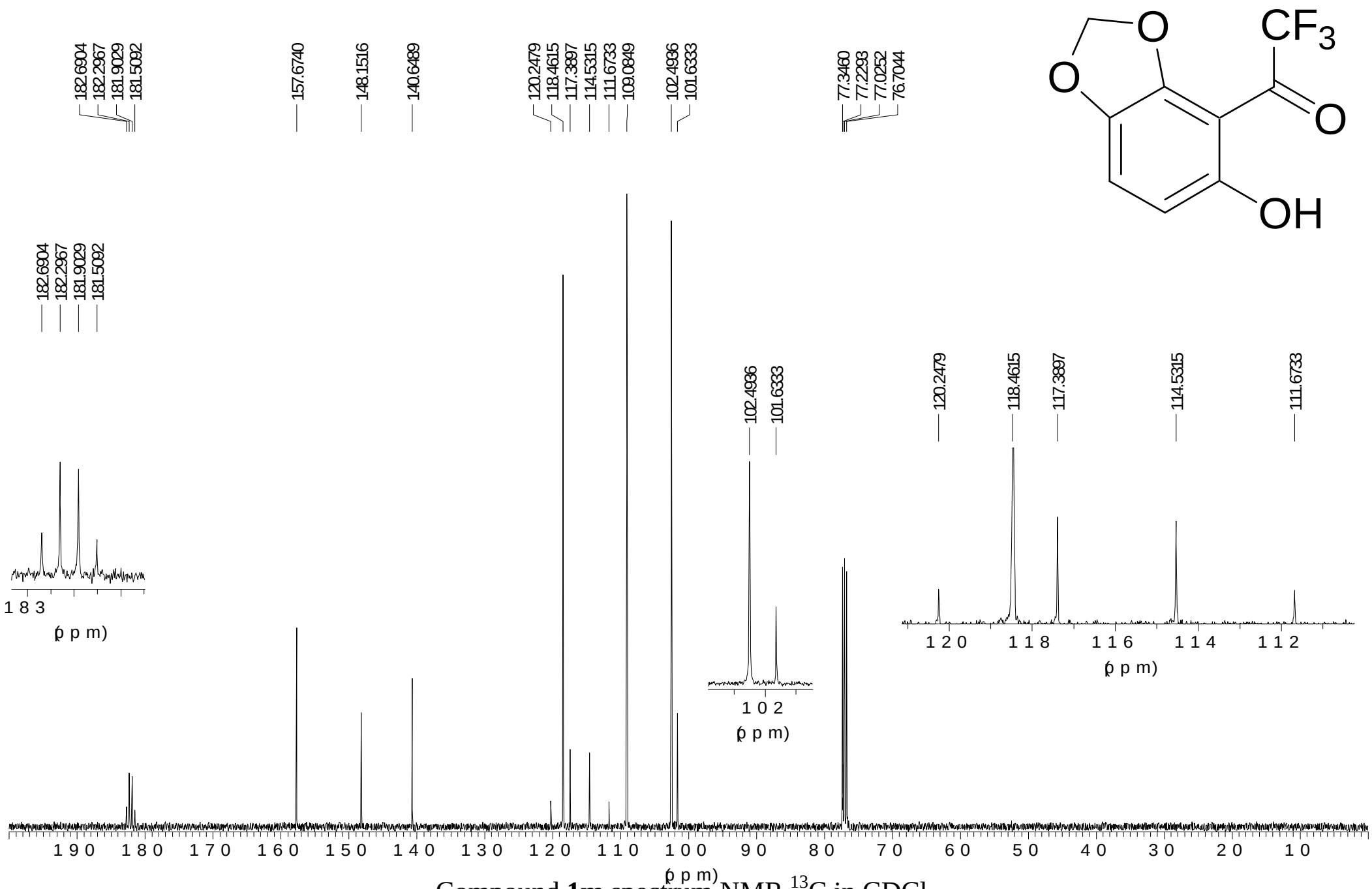

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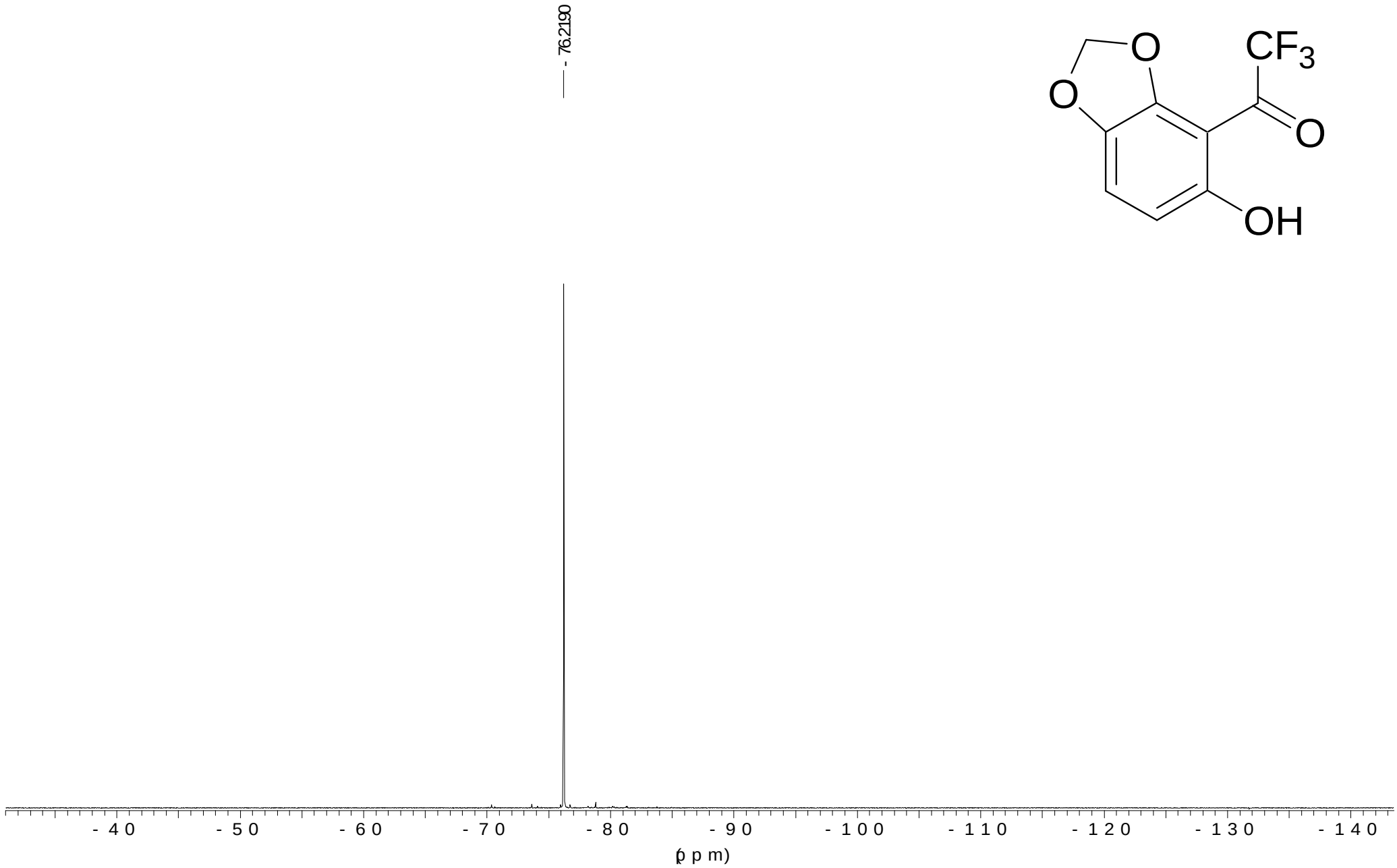

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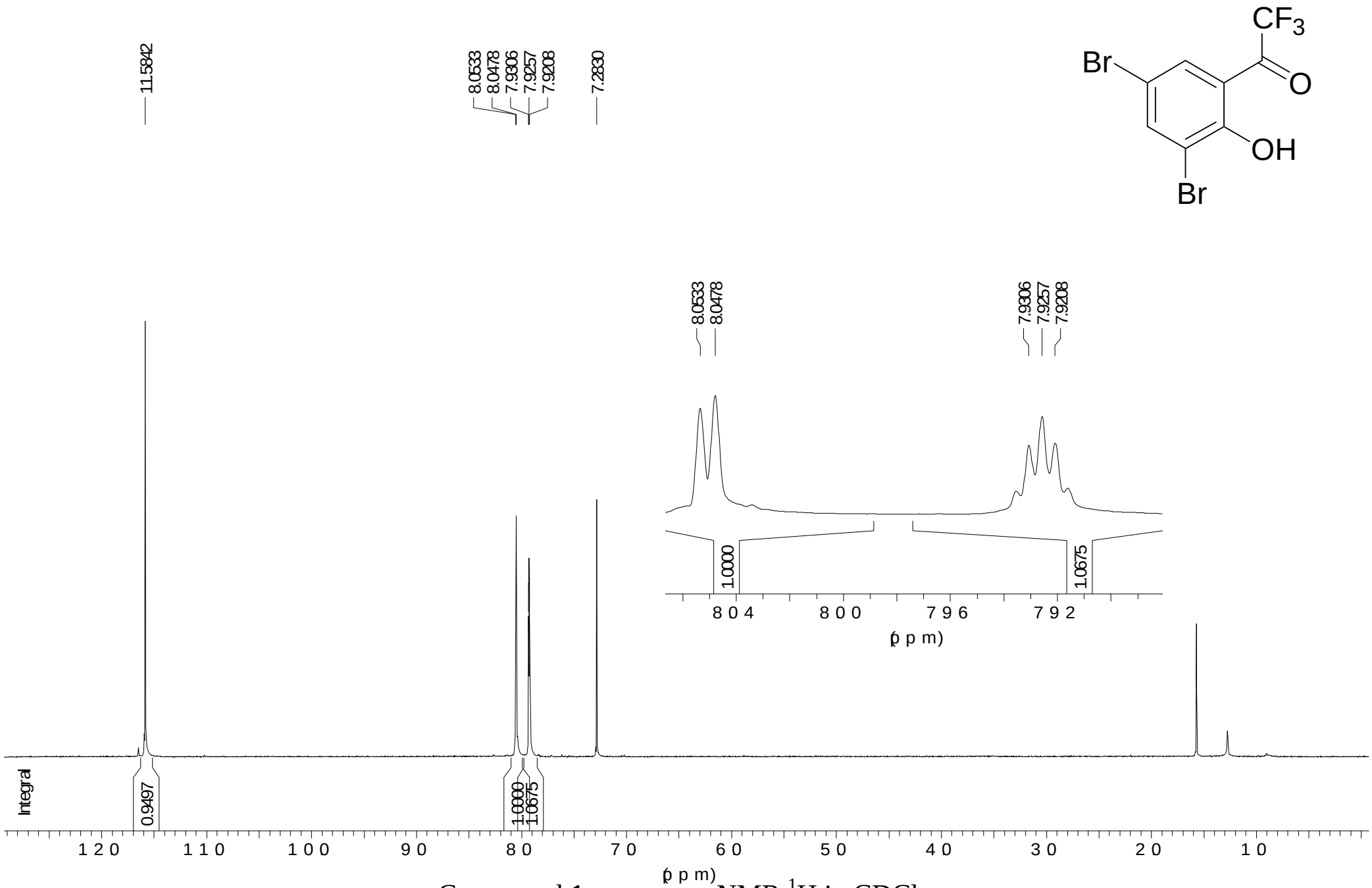

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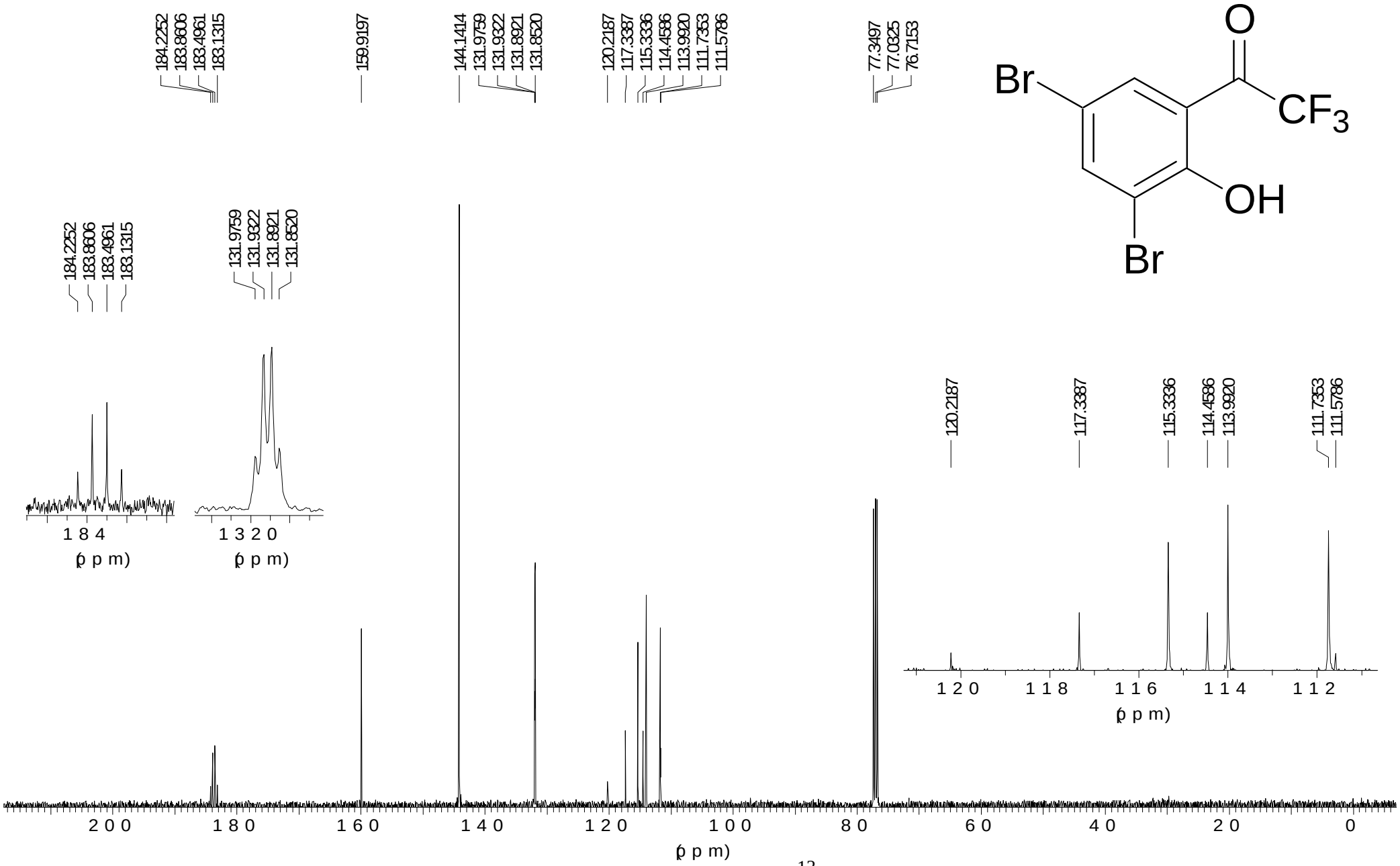

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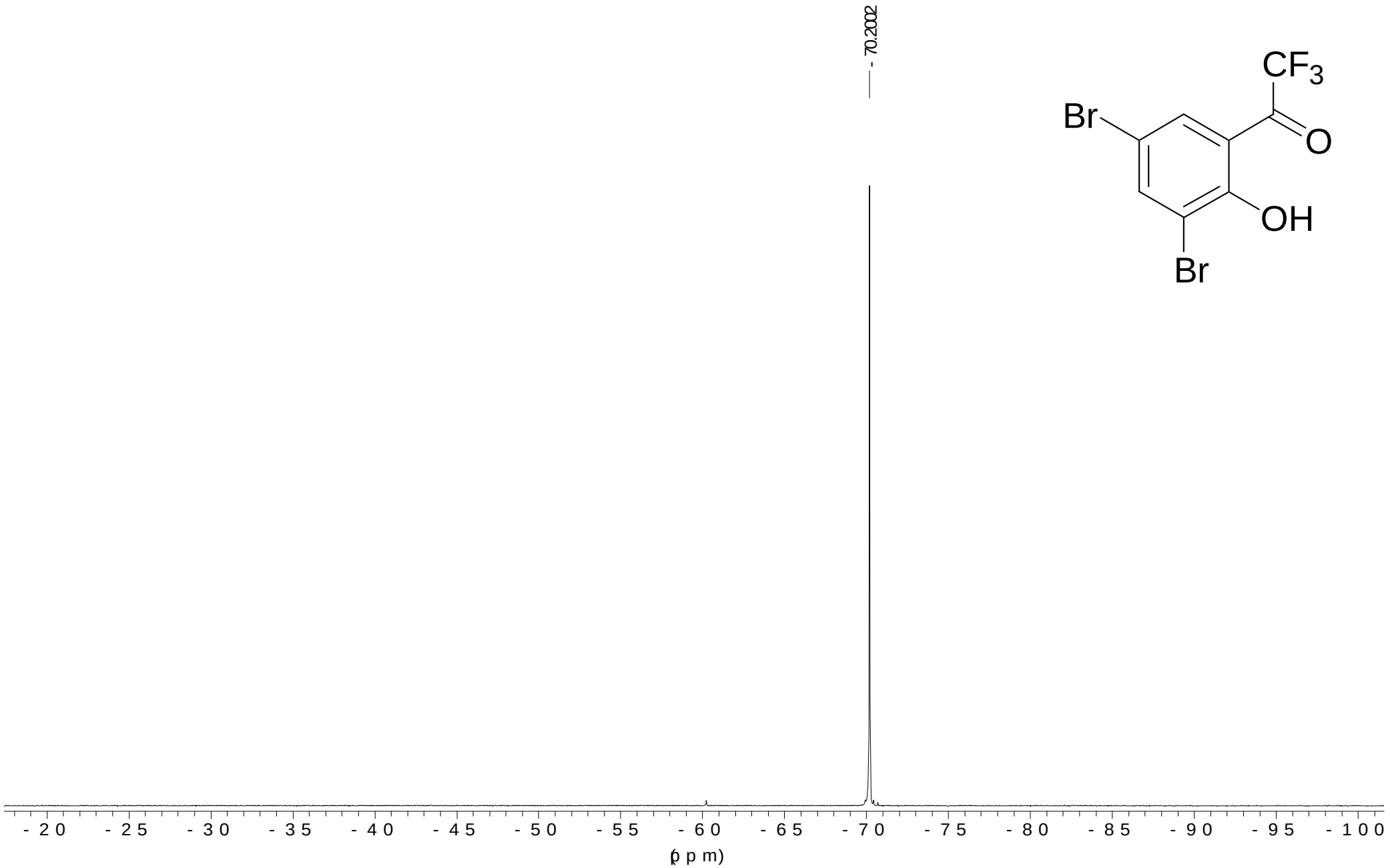

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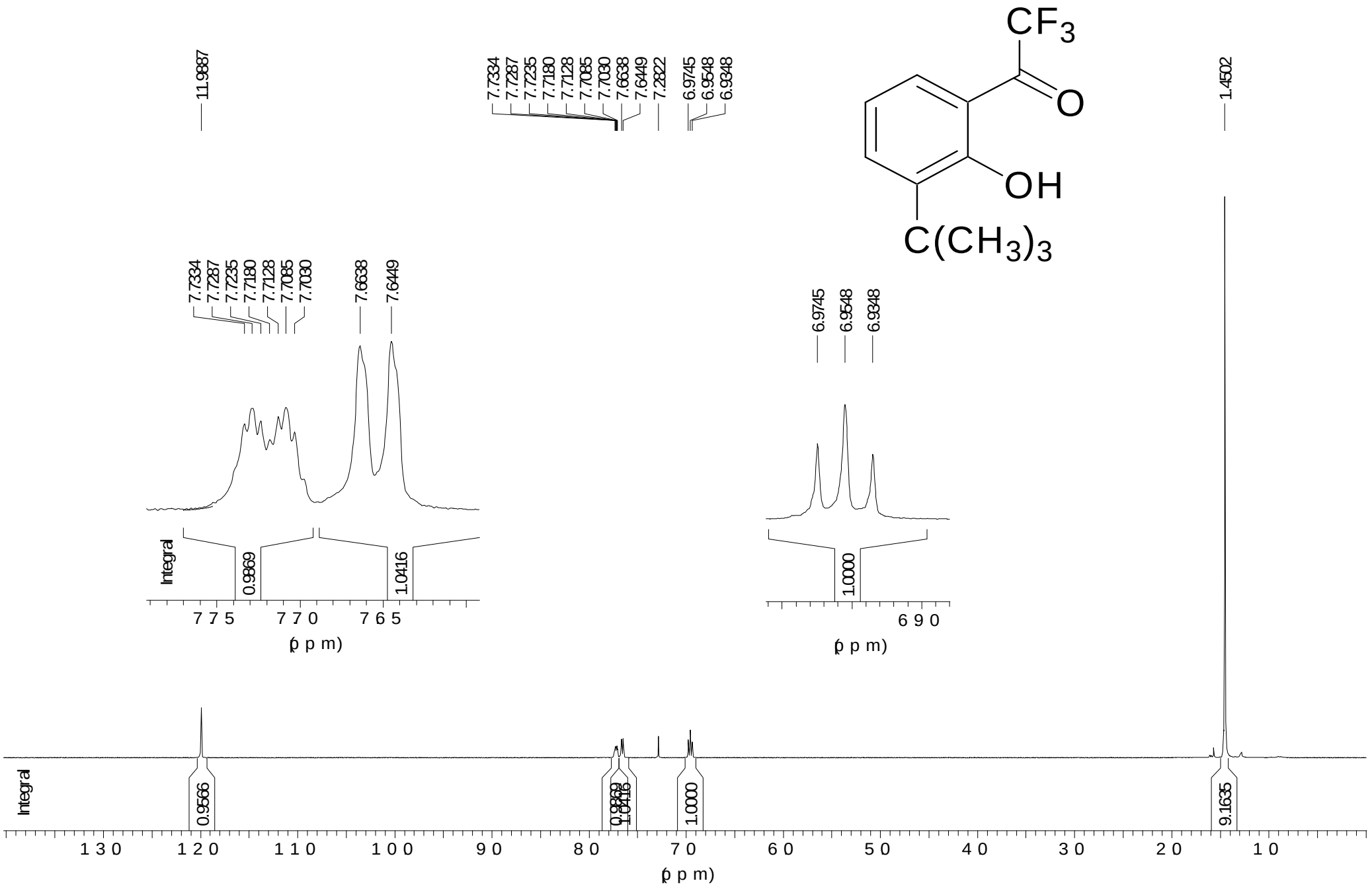

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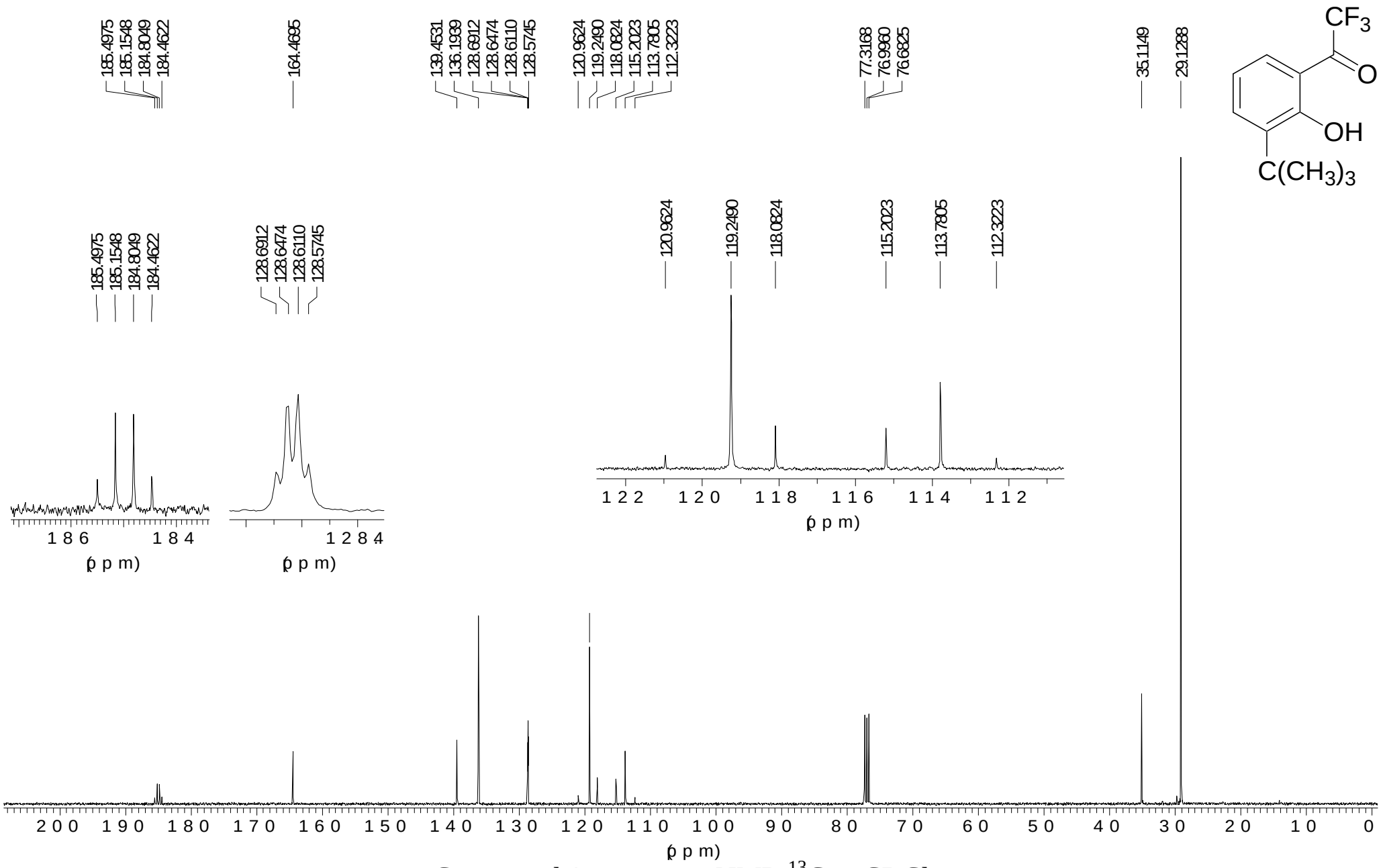

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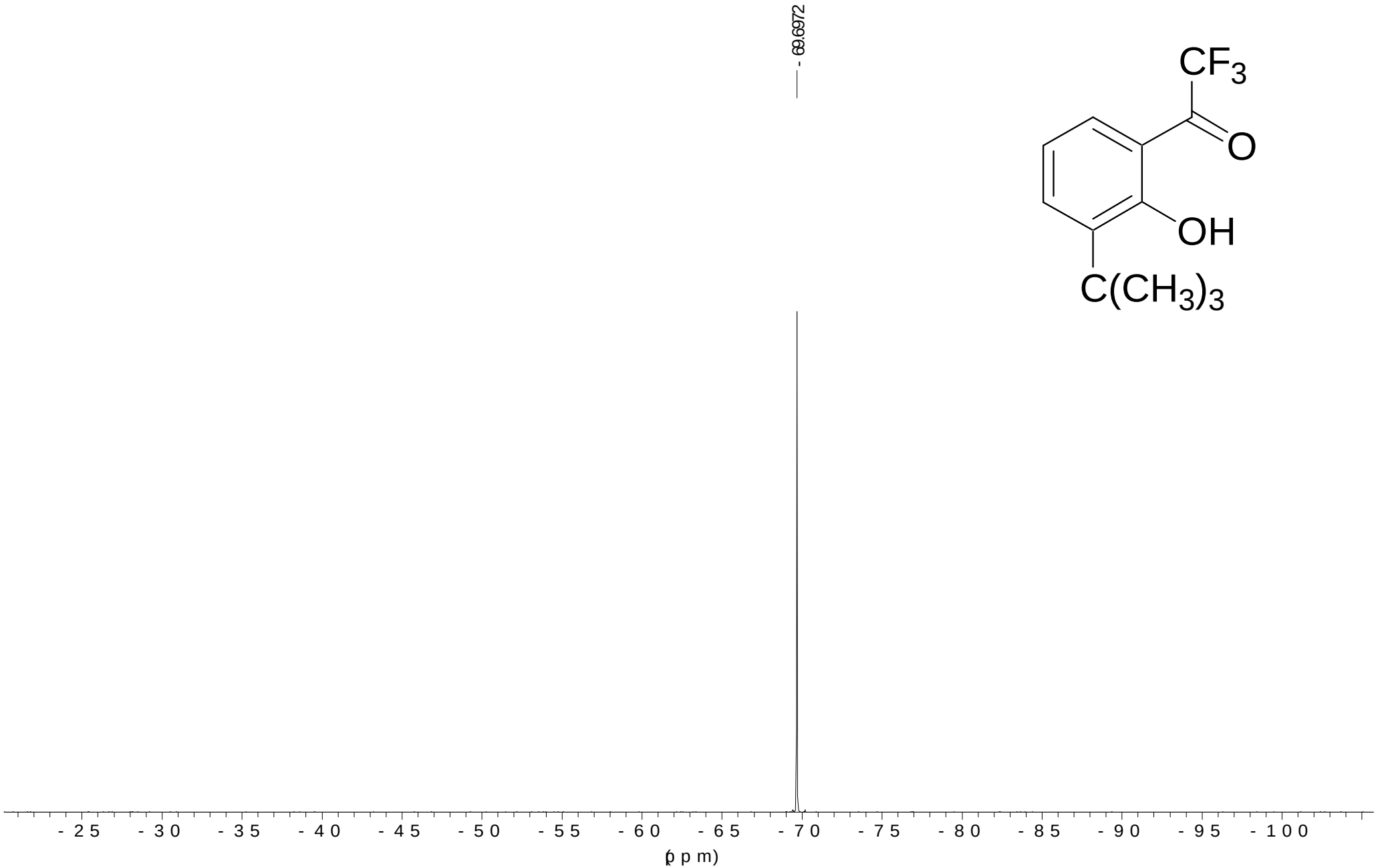

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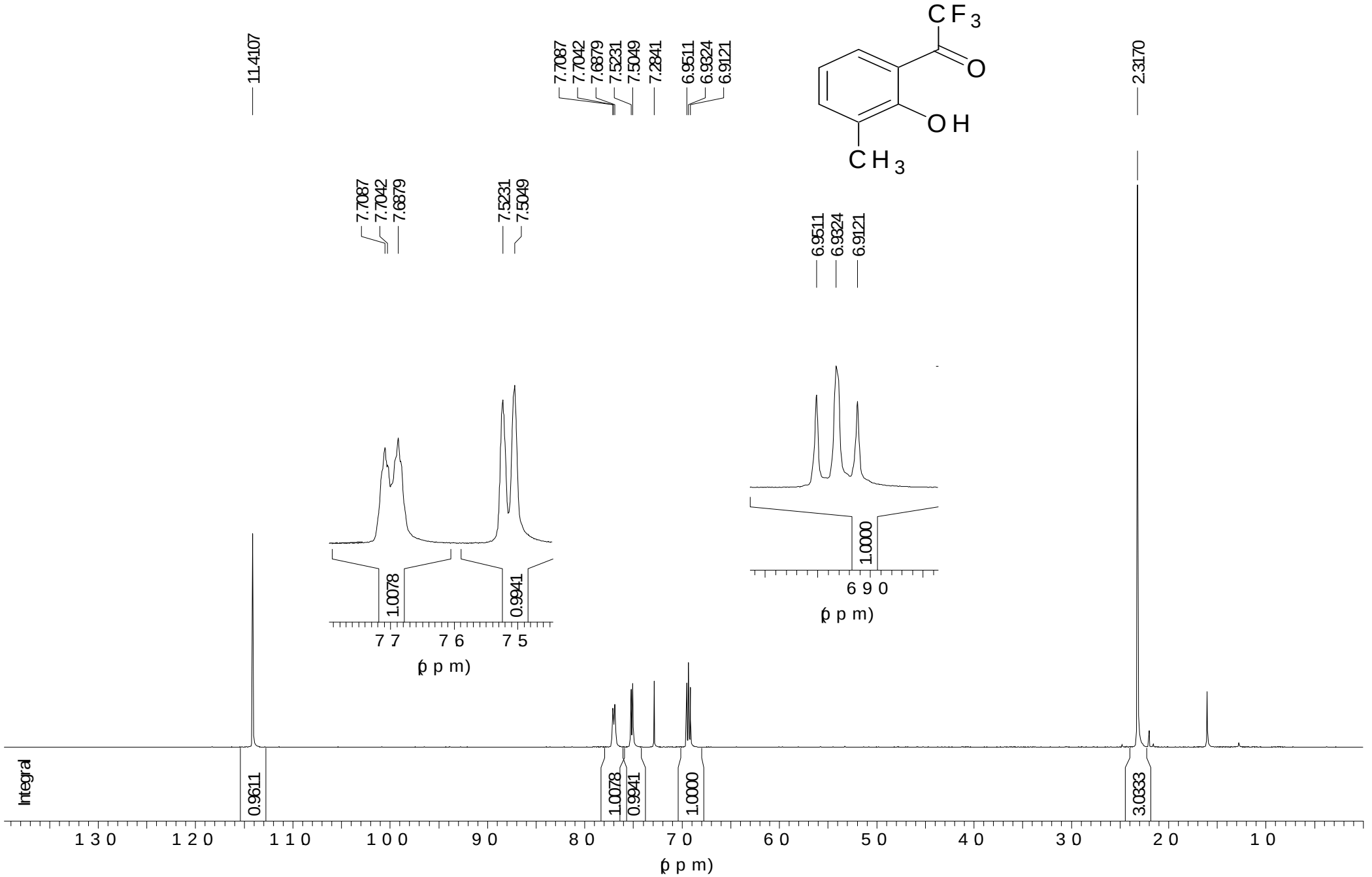

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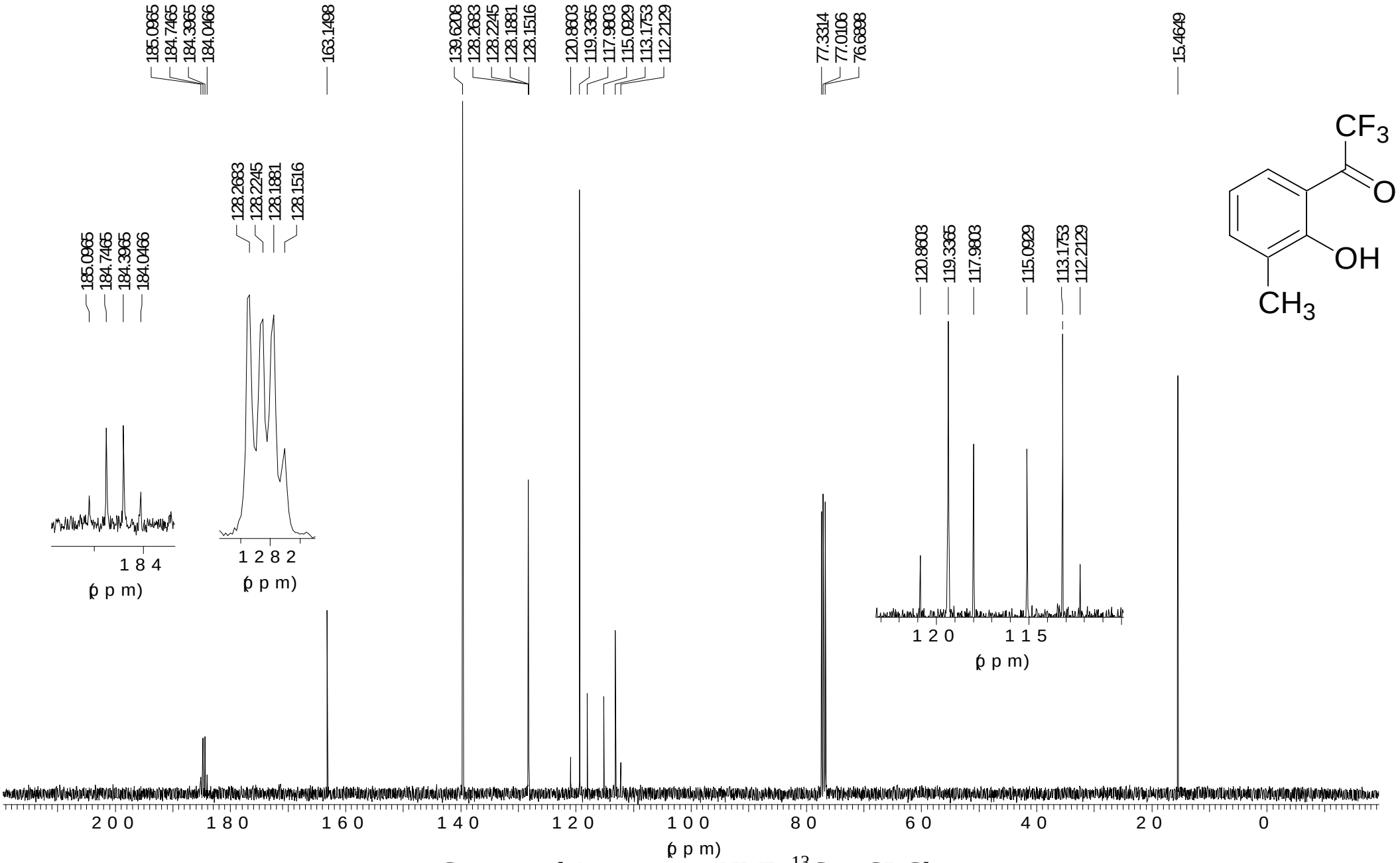
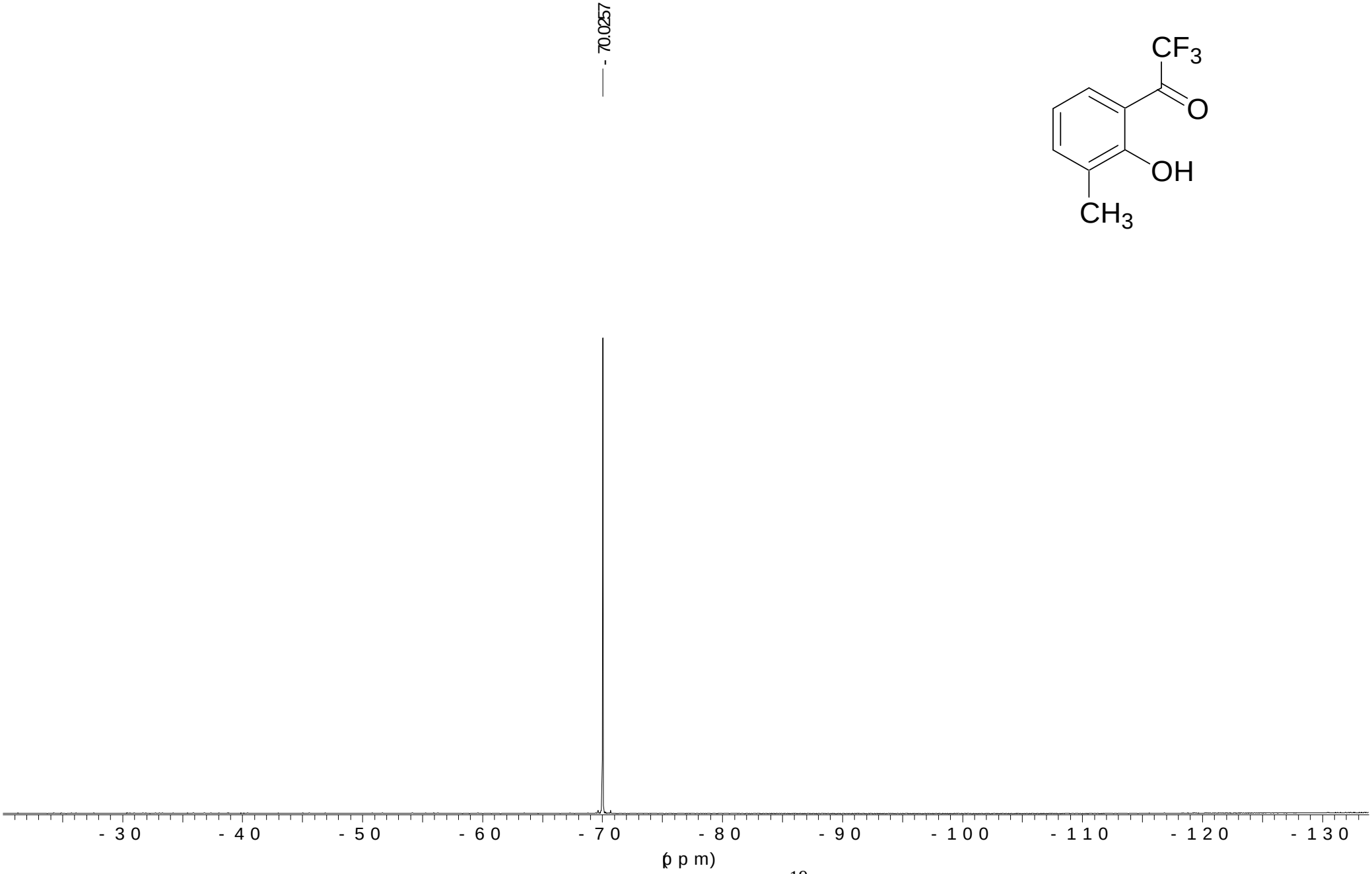
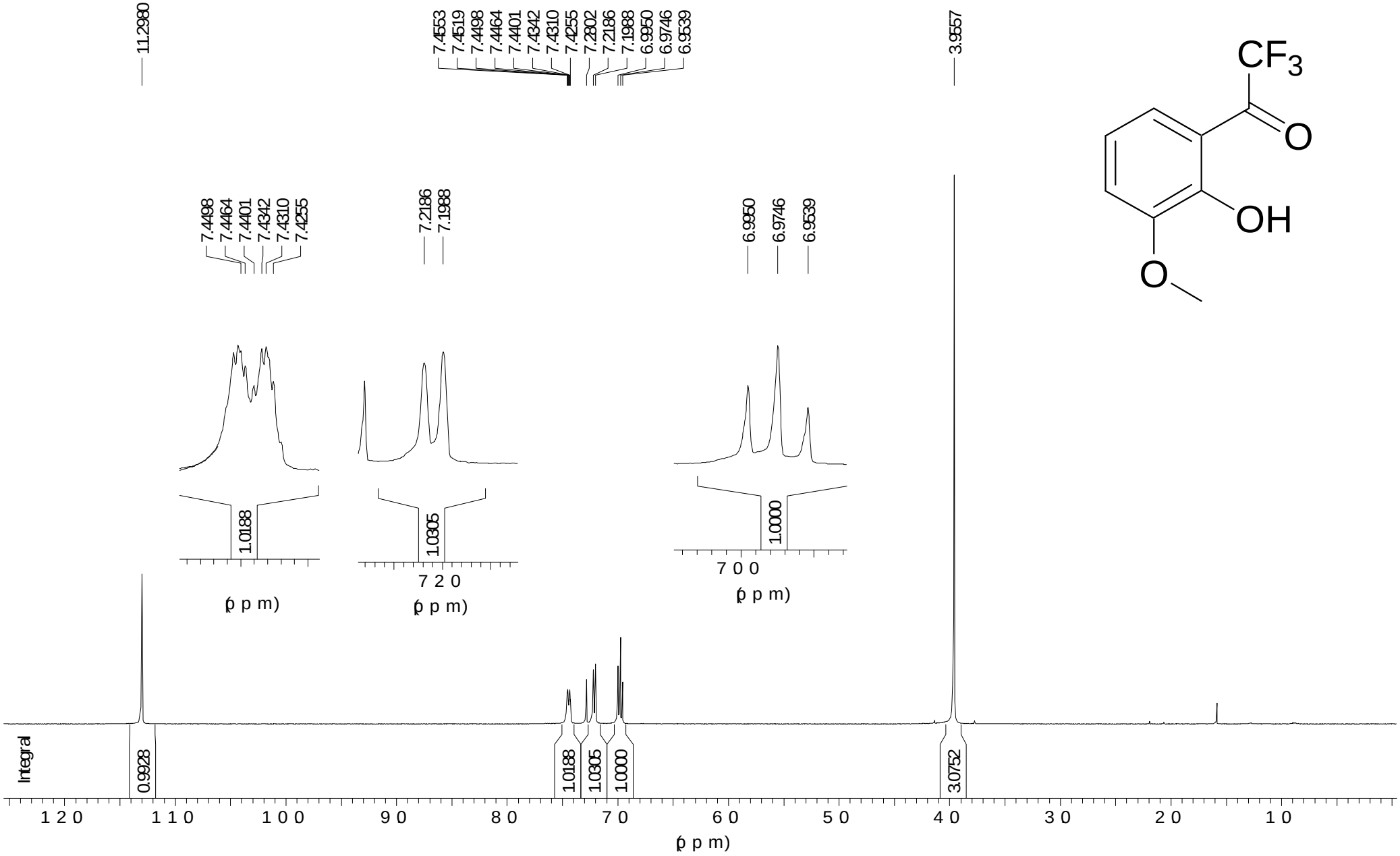


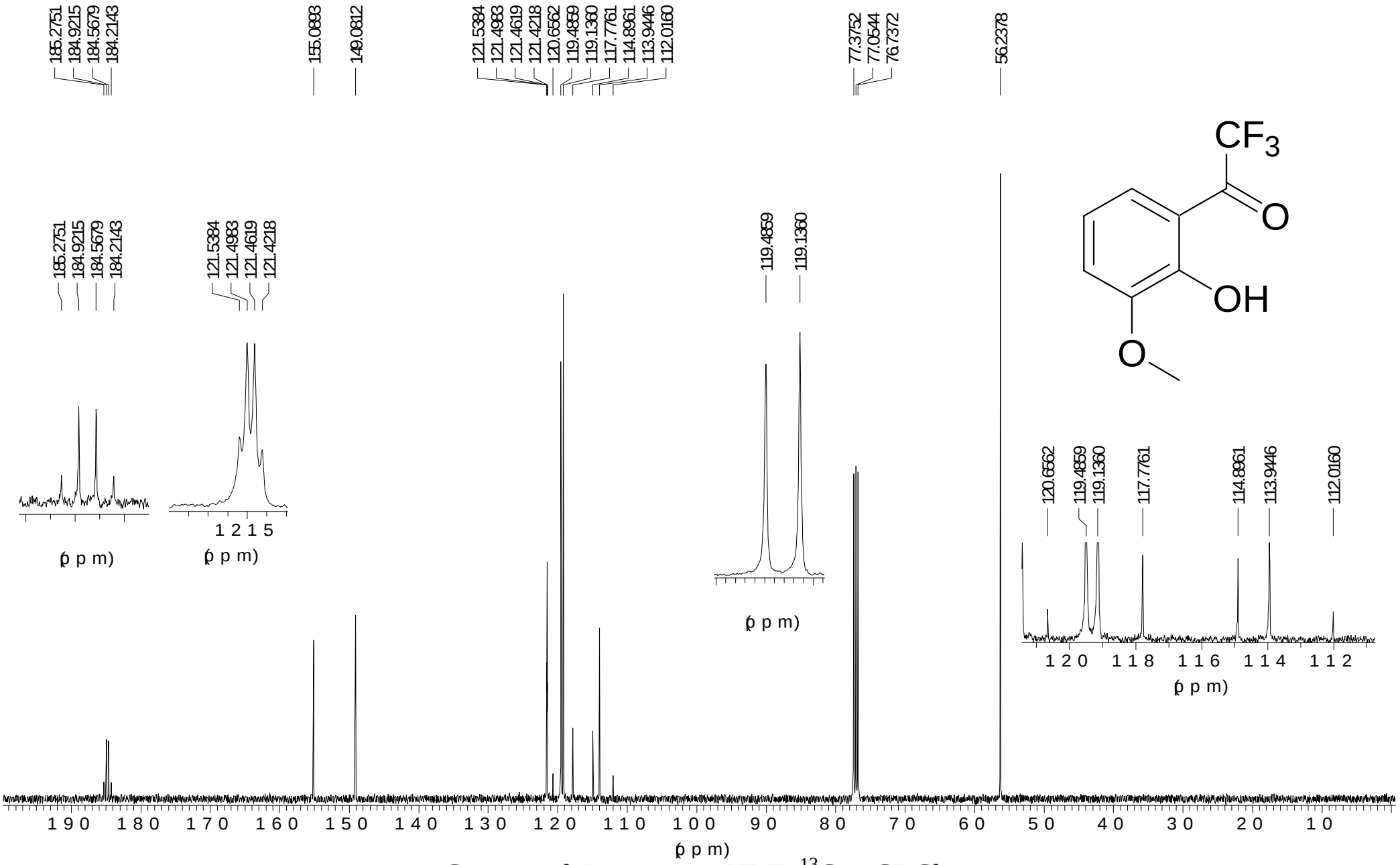
Compound **1p** spectrum NMR ^{13}C in $CDCl_3$



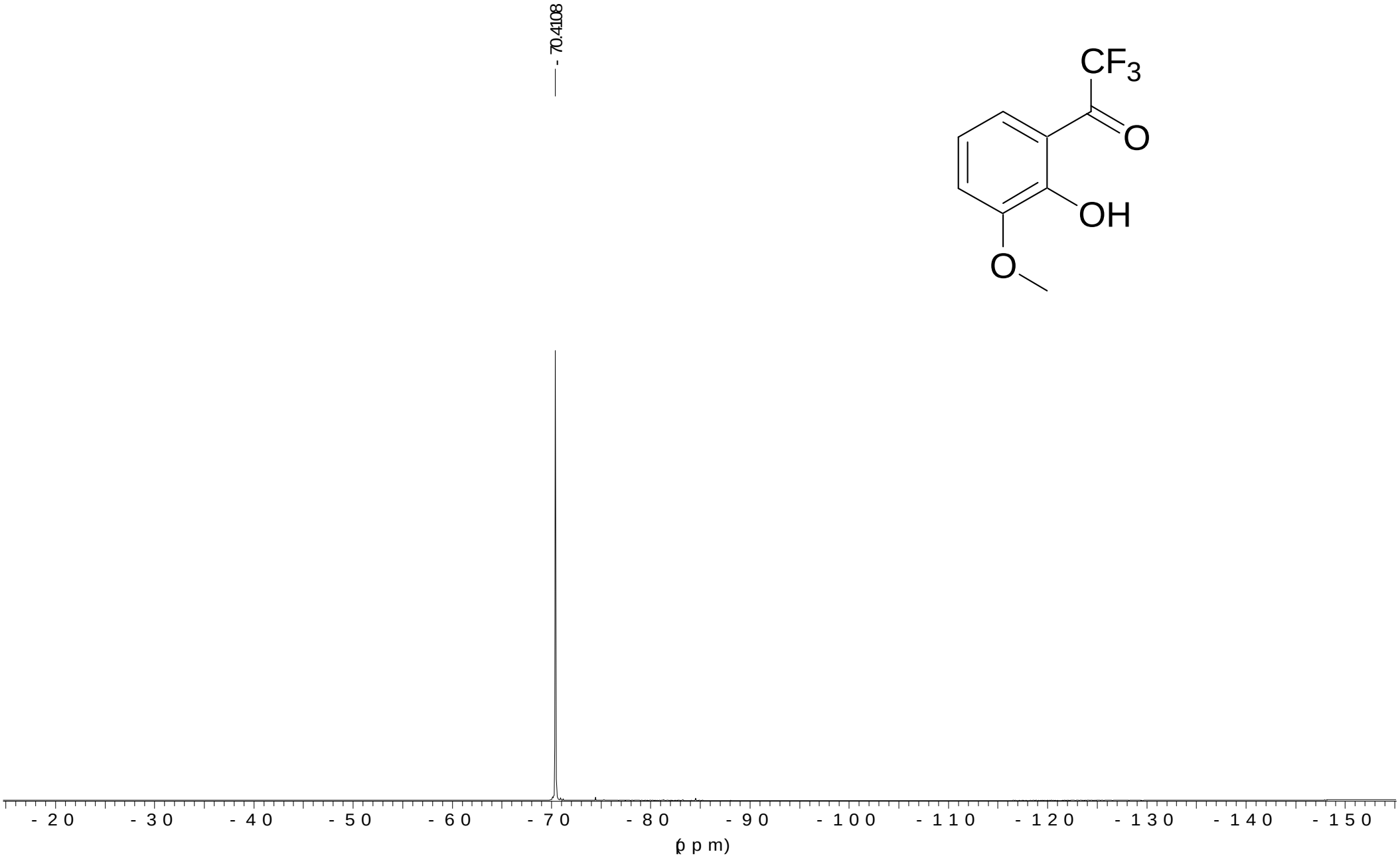
Compound **1p** spectrum NMR ^{19}F in $CDCl_3$



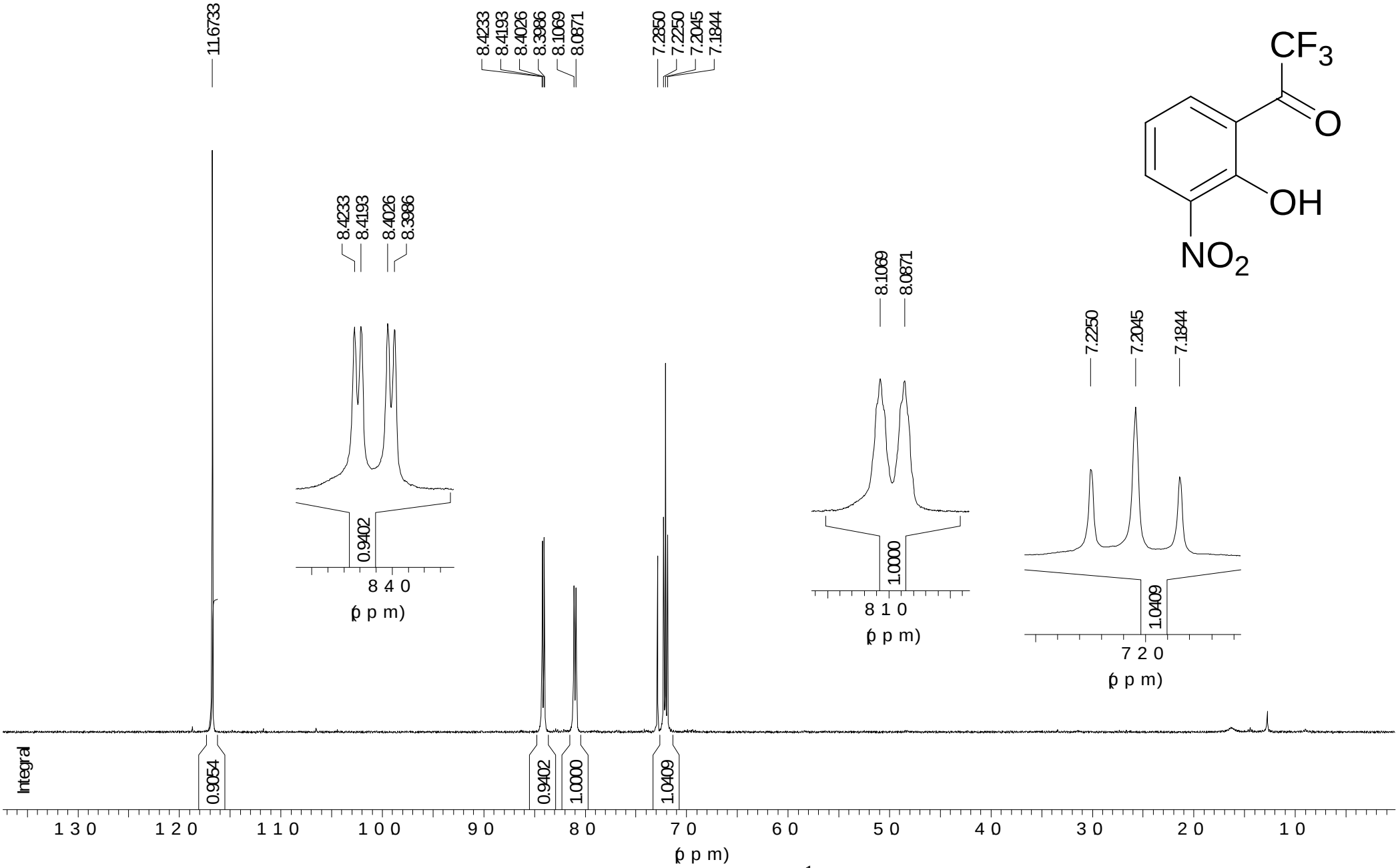
Compound **1q** spectrum NMR ^{1}H in $CDCl_3$



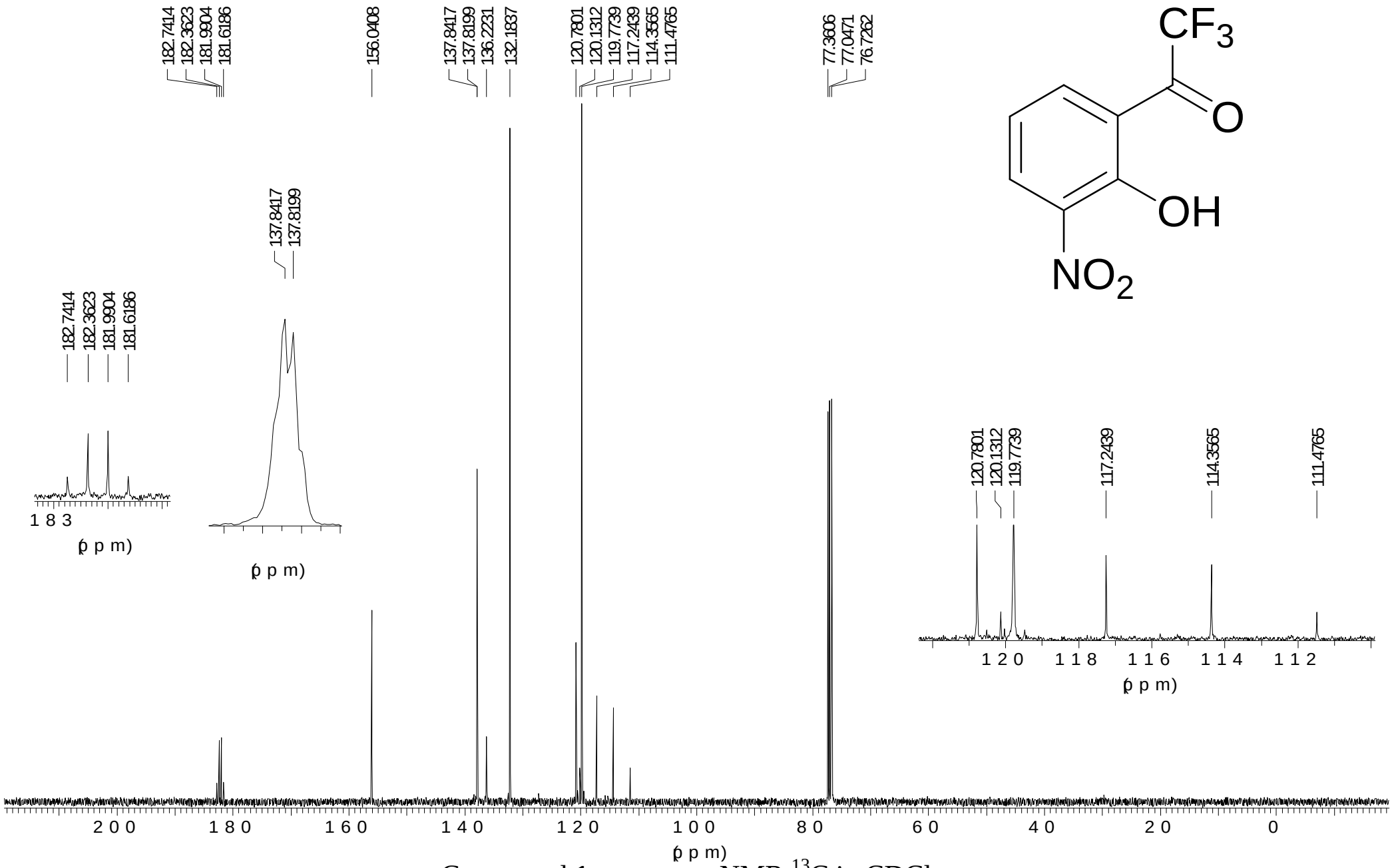
Compound **1q** spectrum NMR ^{13}C in $CDCl_3$



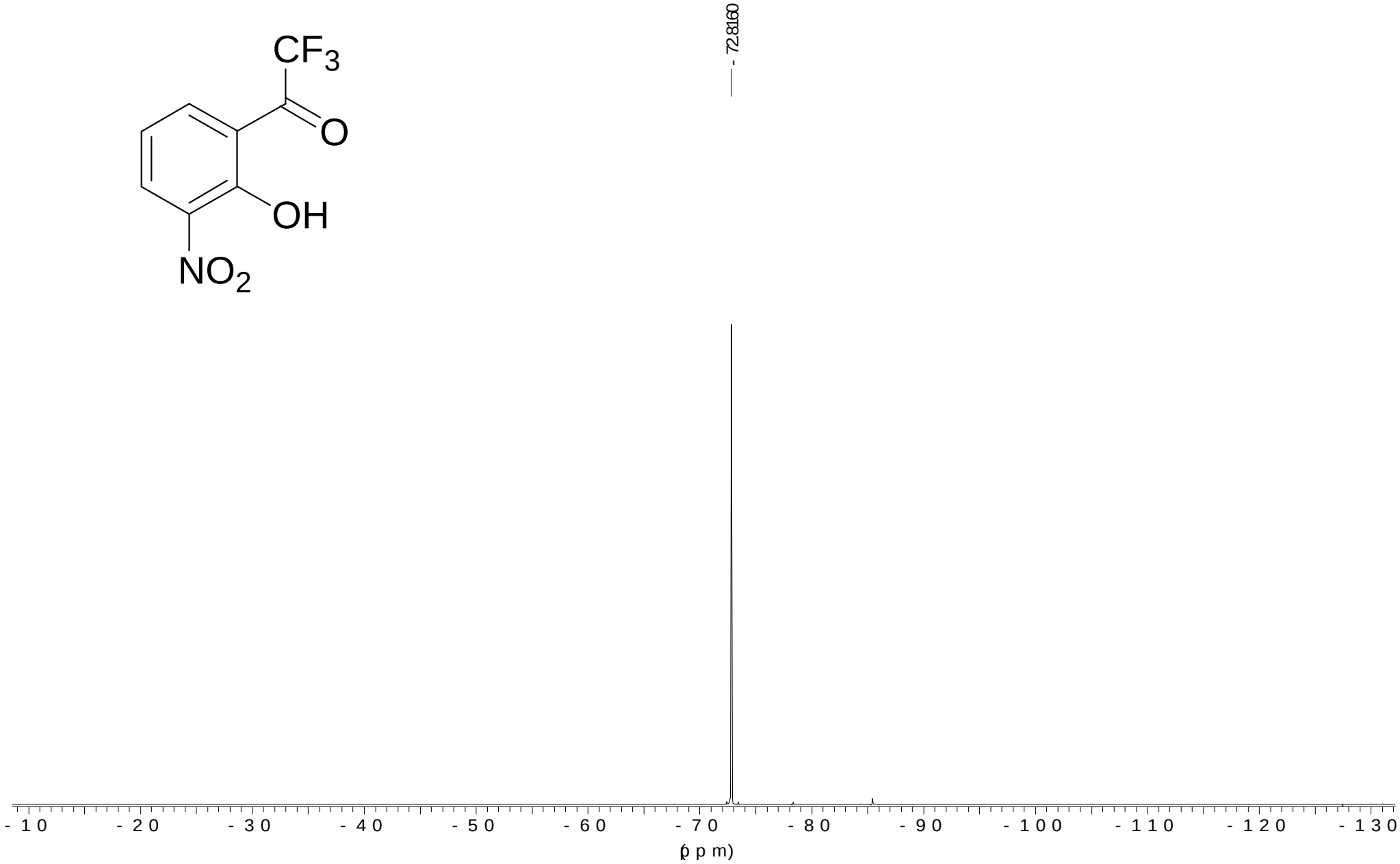
Compound **1q** spectrum NMR ^{19}F in $CDCl_3$



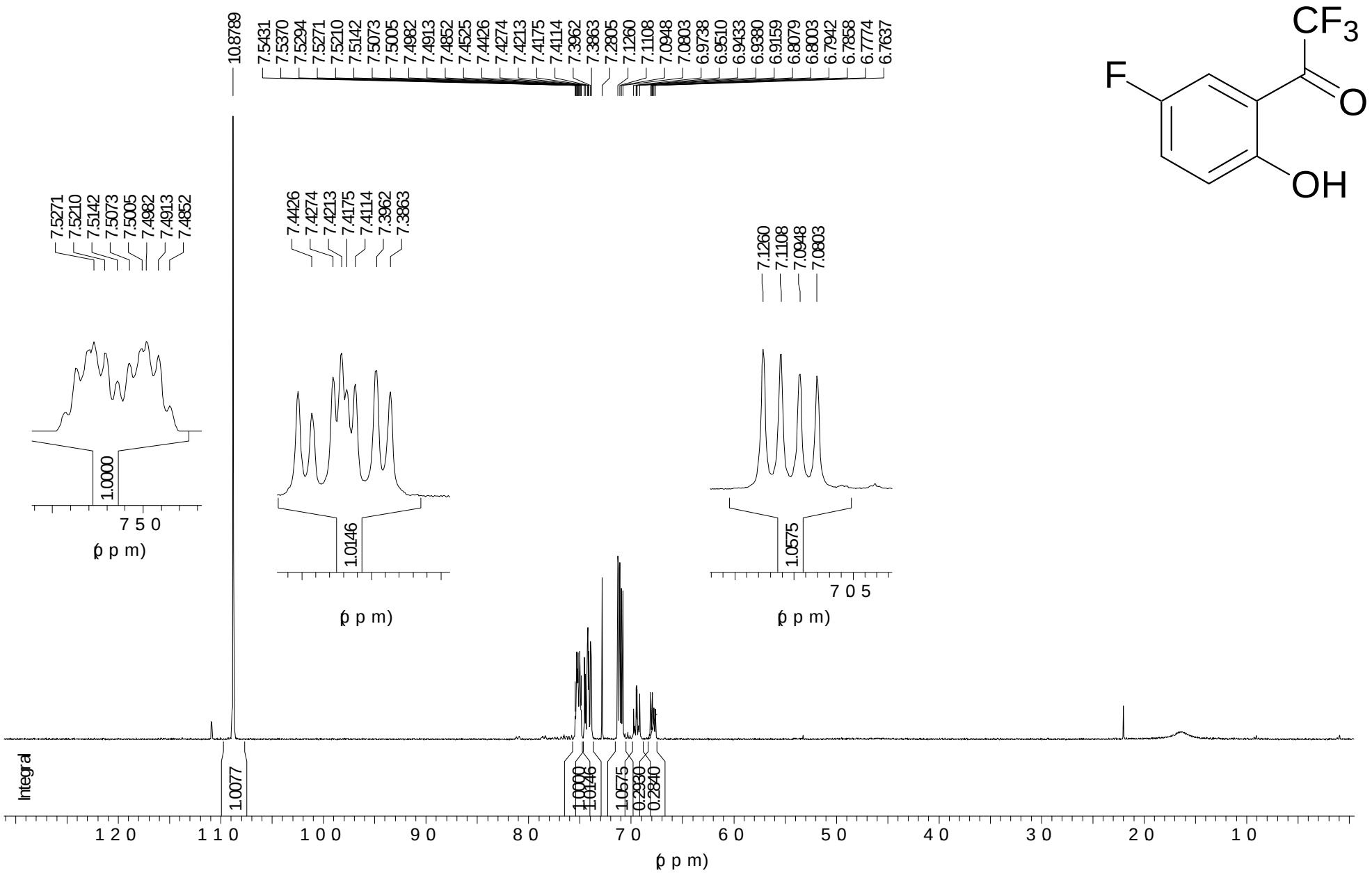
Compound **1r** spectrum NMR ^{1}H in $CDCl_3$



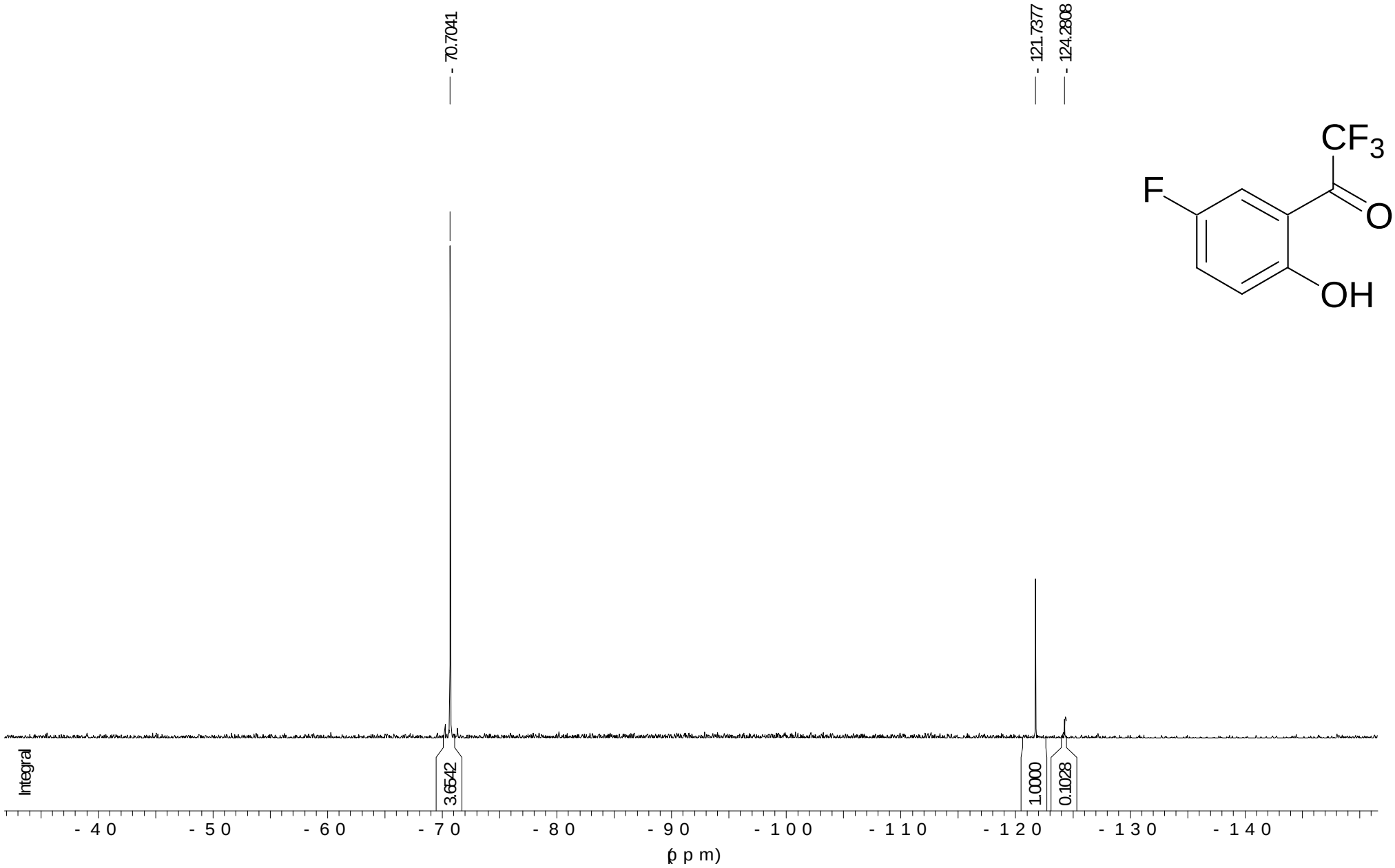
Compound **1r** spectrum NMR ^{13}C in $CDCl_3$



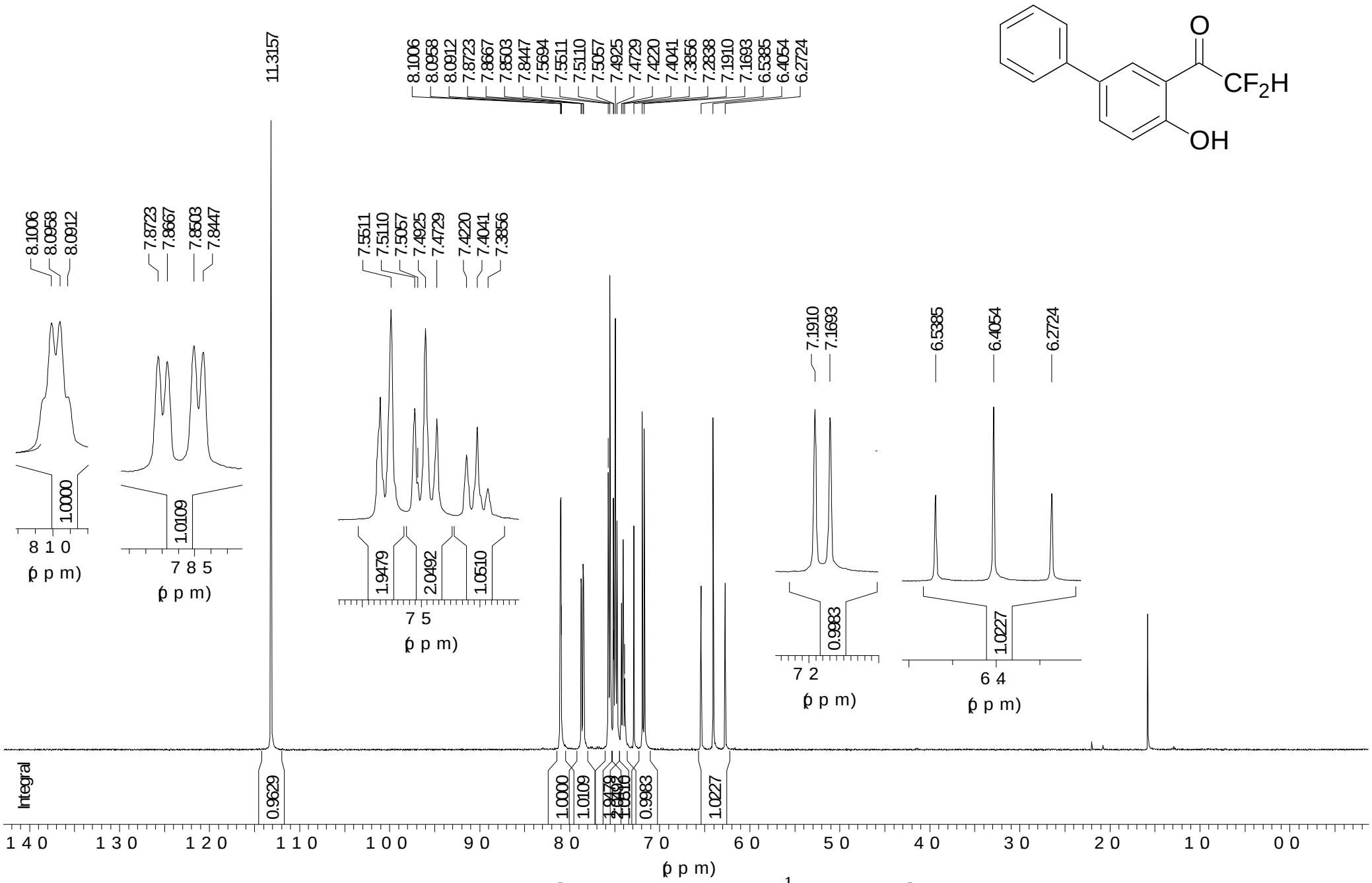
Compound **1r** spectrum NMR ^{19}F in $CDCl_3$



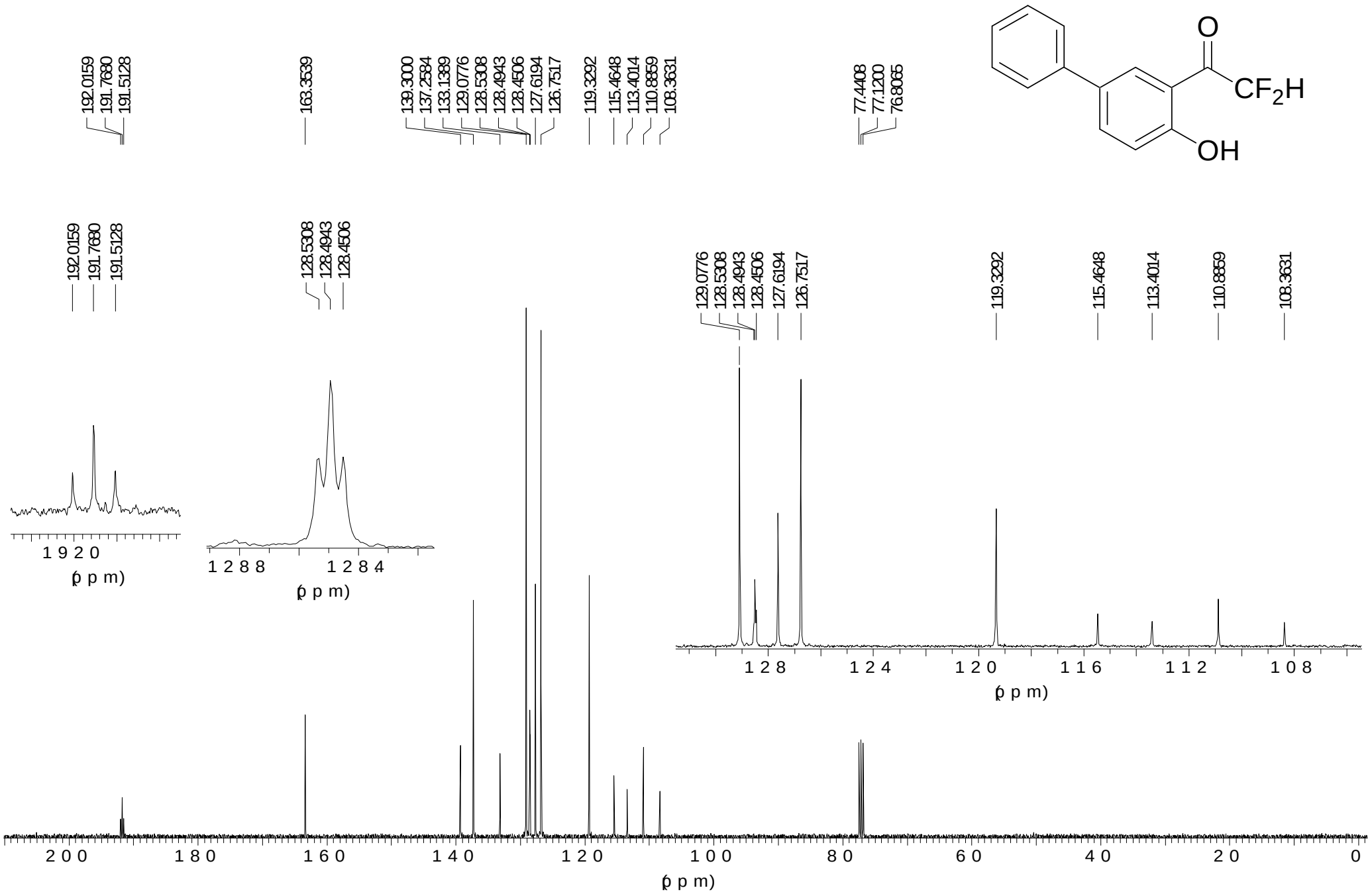
Compound **1s** (+ ~ 10% of 4-fluorophenol) spectrum NMR ^{1}H in $CDCl_3$



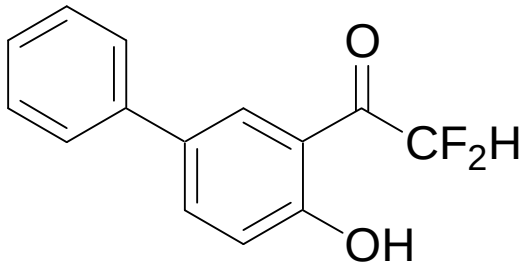
Compound **1s** (with ~10% of 4-fluorophenol) spectrum NMR ^{19}F in $CDCl_3$



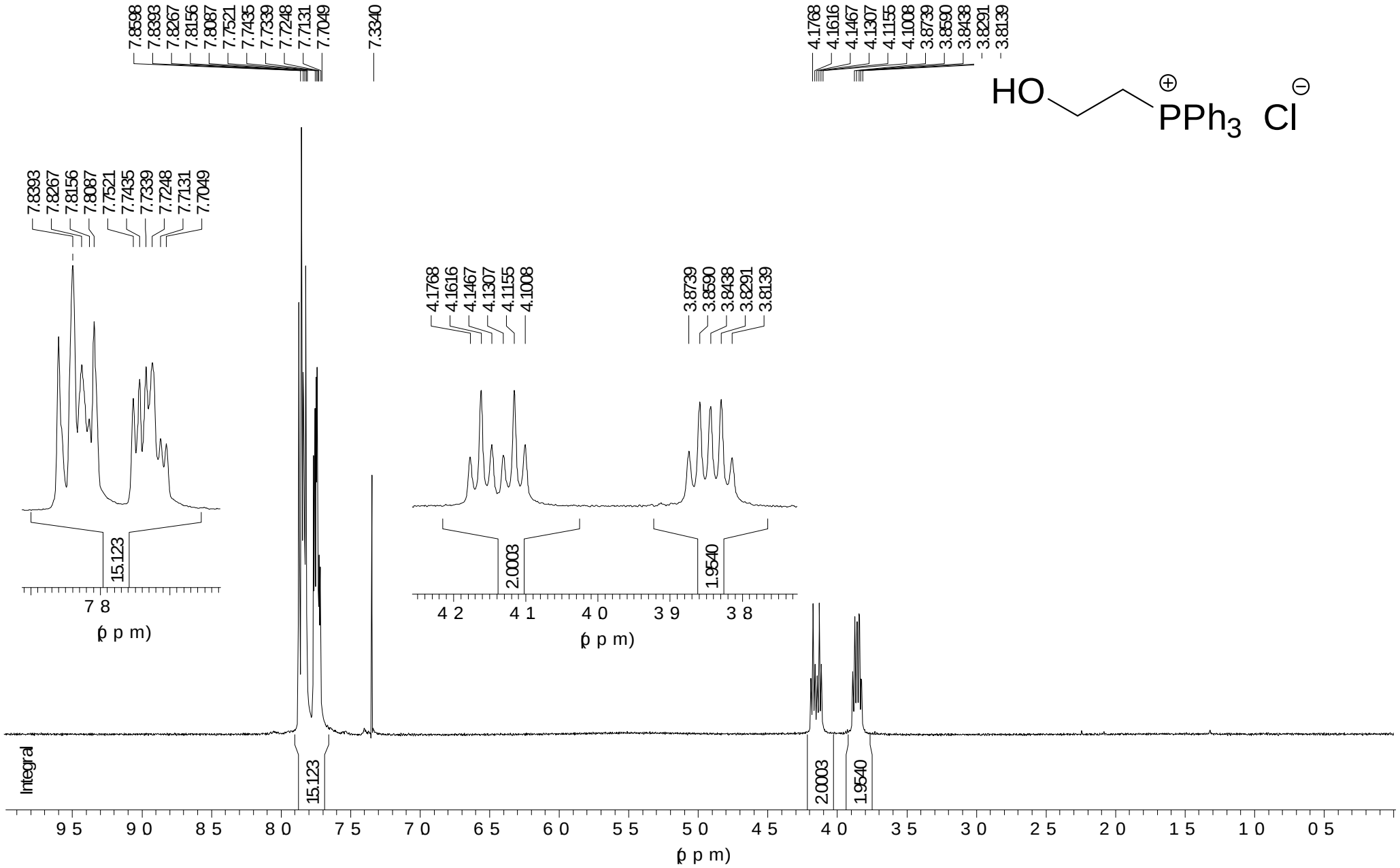
Compound **1t** spectrum NMR ^{1}H in $CDCl_3$



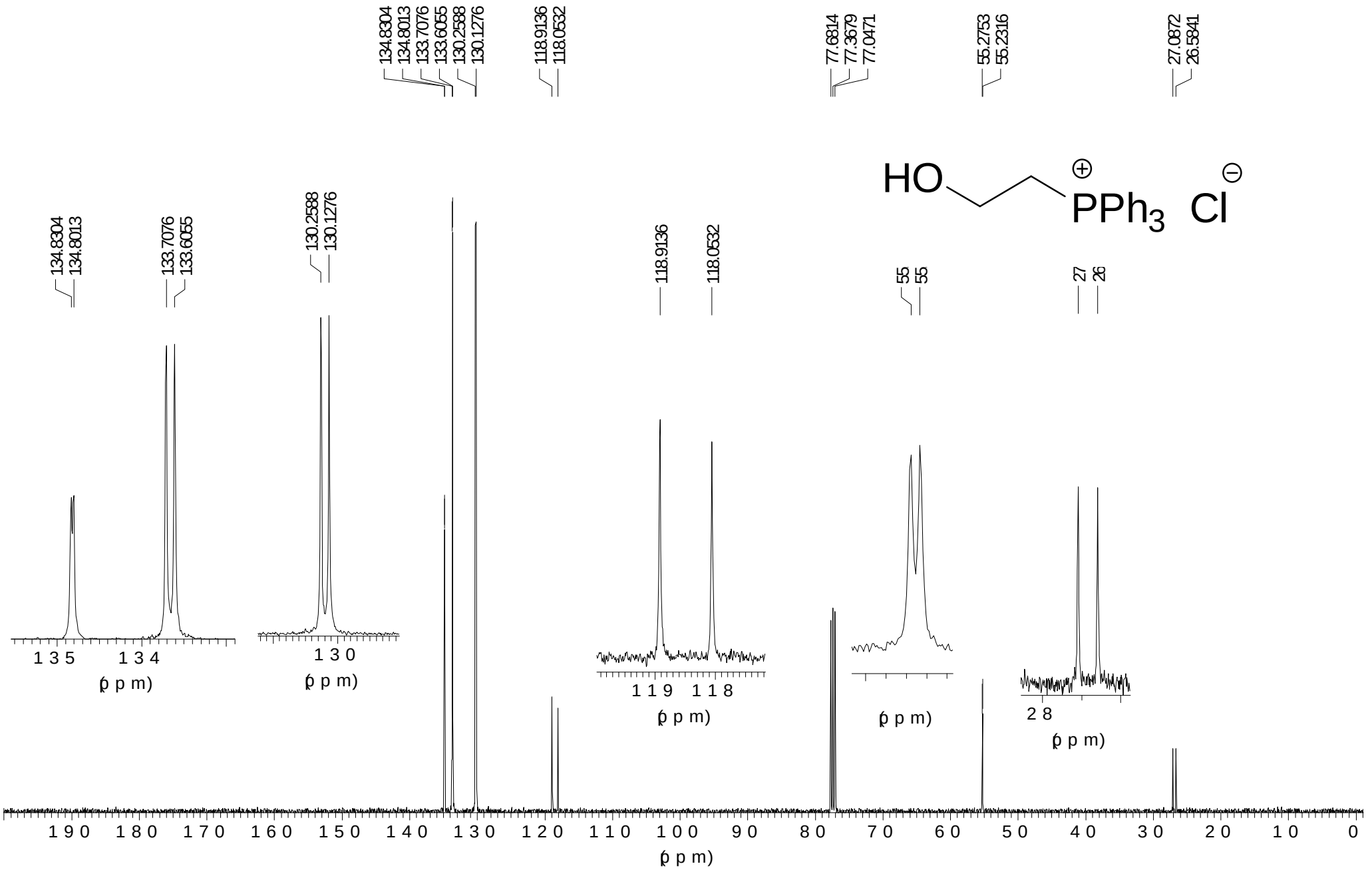
Compound **1t** spectrum NMR ^{13}C in $CDCl_3$



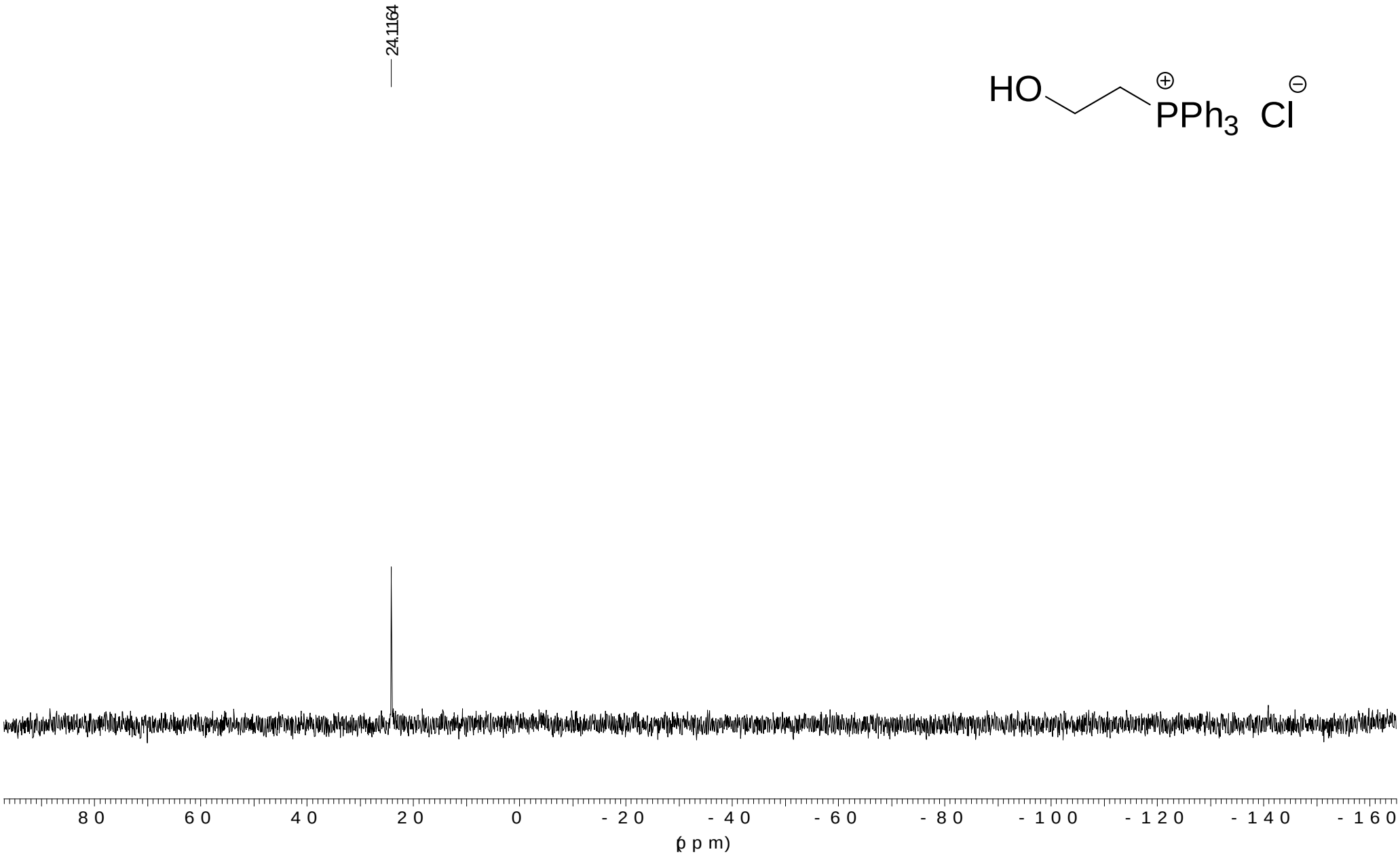
Compound **1t** spectrum NMR ^{19}F in $CDCl_3$



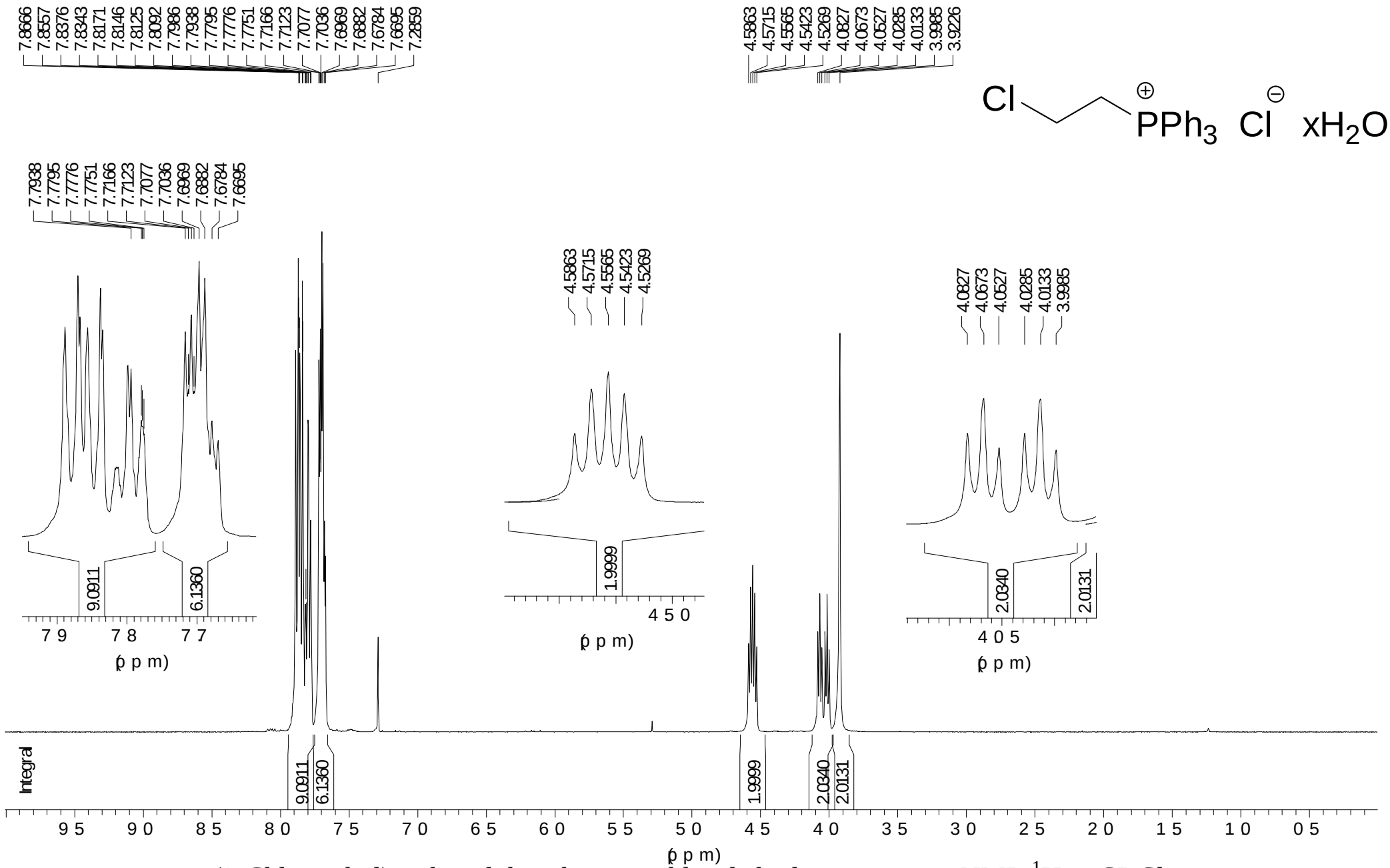
(2-Hydroxyethyl)triphenylphosphonium chloride spectrum NMR ^{1}H in $CDCl_3$



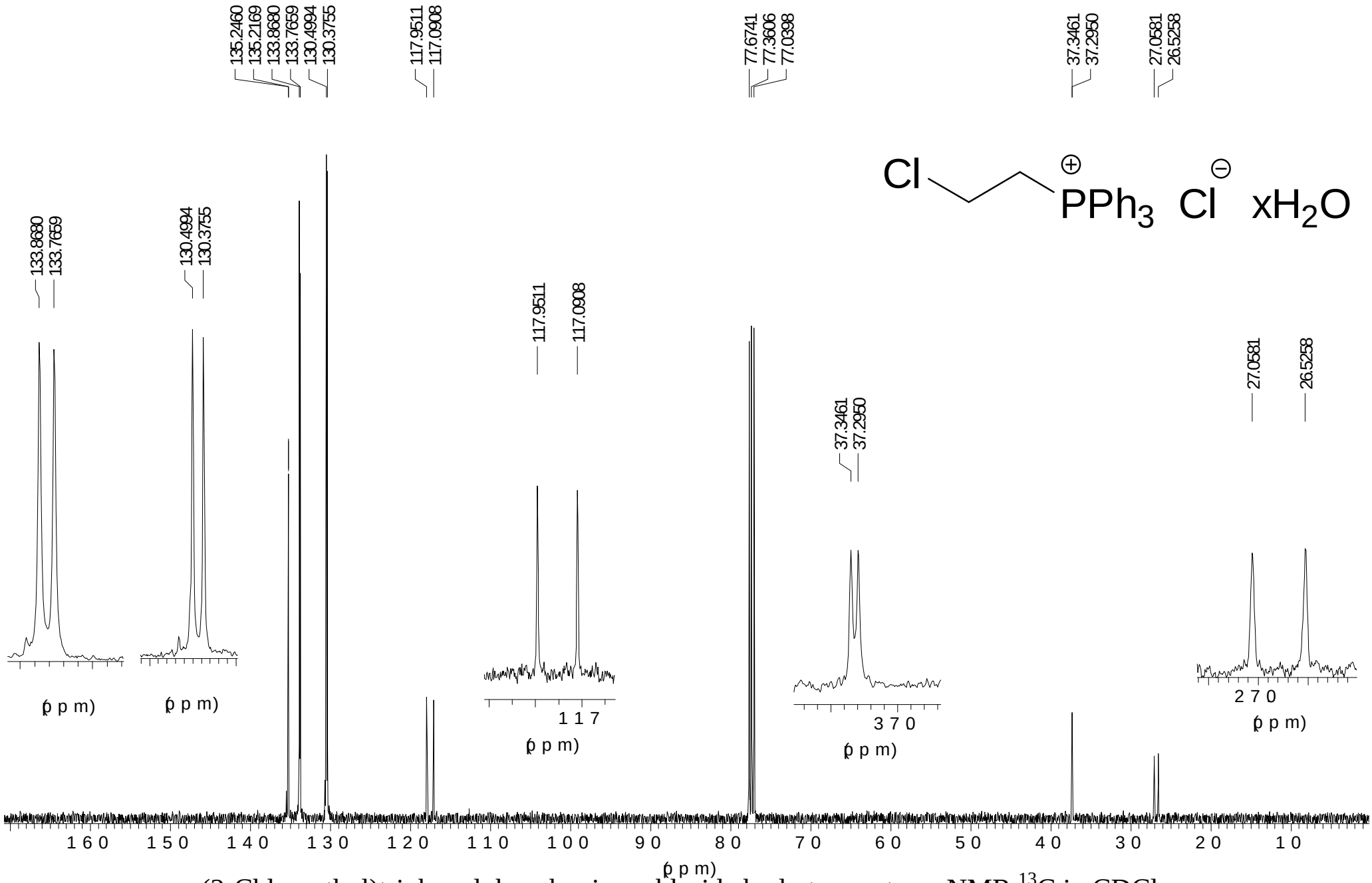
(2-Hydroxyethyl)triphenylphosphonium chloride spectrum NMR ^{13}C in $CDCl_3$



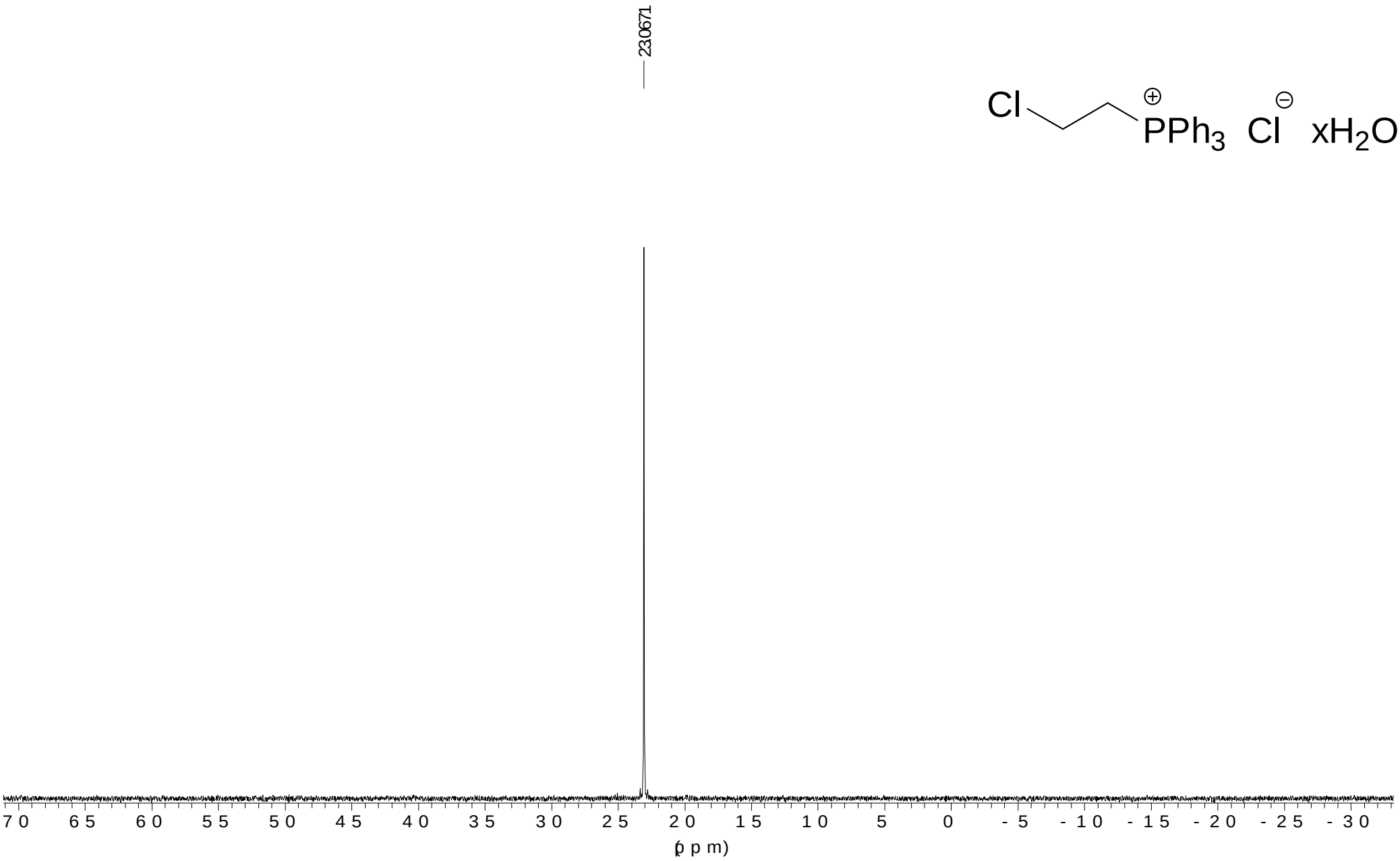
(2-Hydroxyethyl)triphenylphosphonium chloride spectrum NMR ^{31}P in $CDCl_3$



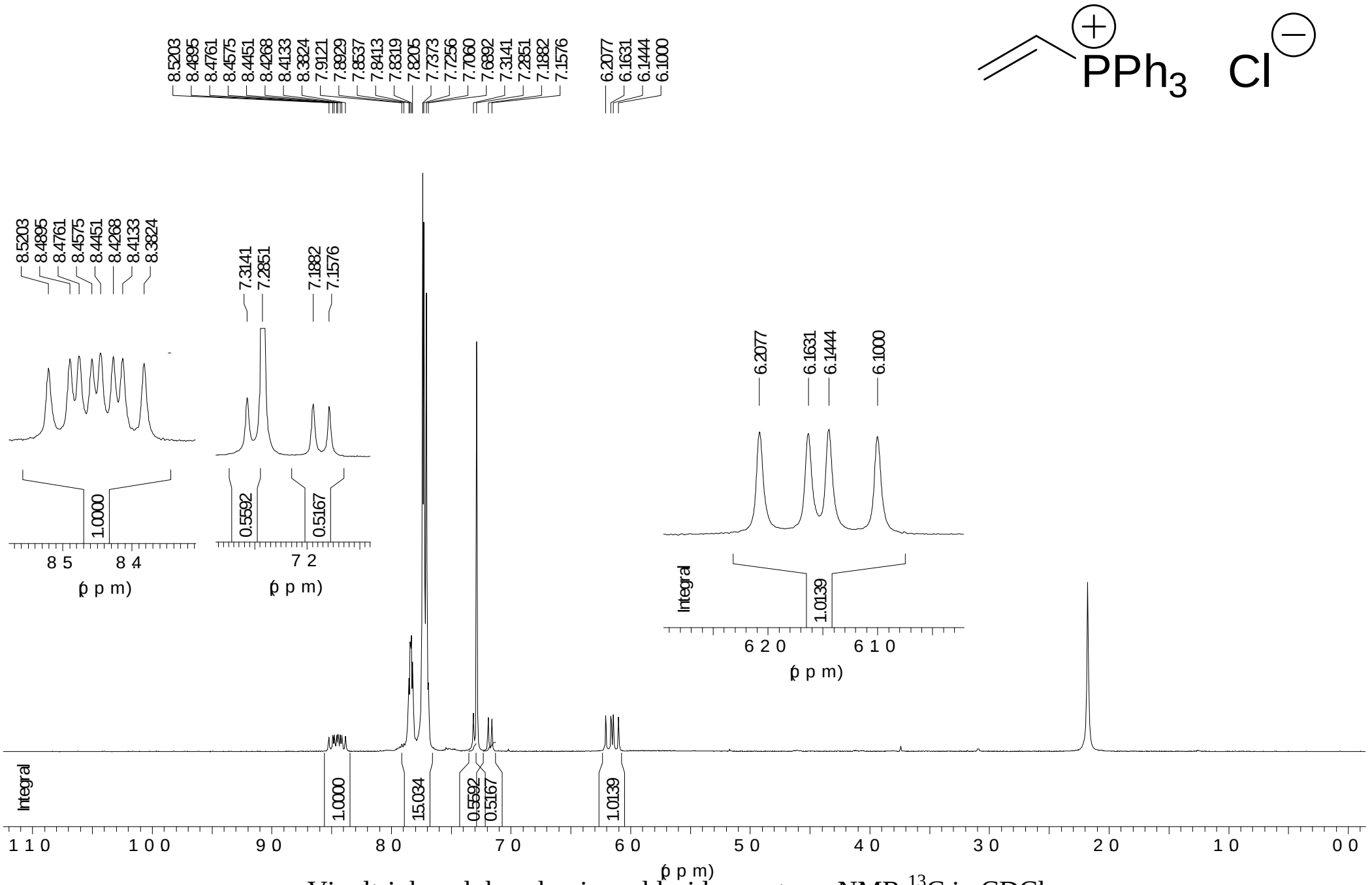
(2-Chloroethyl)triphenylphosphonium chloride hydrate spectrum NMR ^{1}H in $CDCl_3$



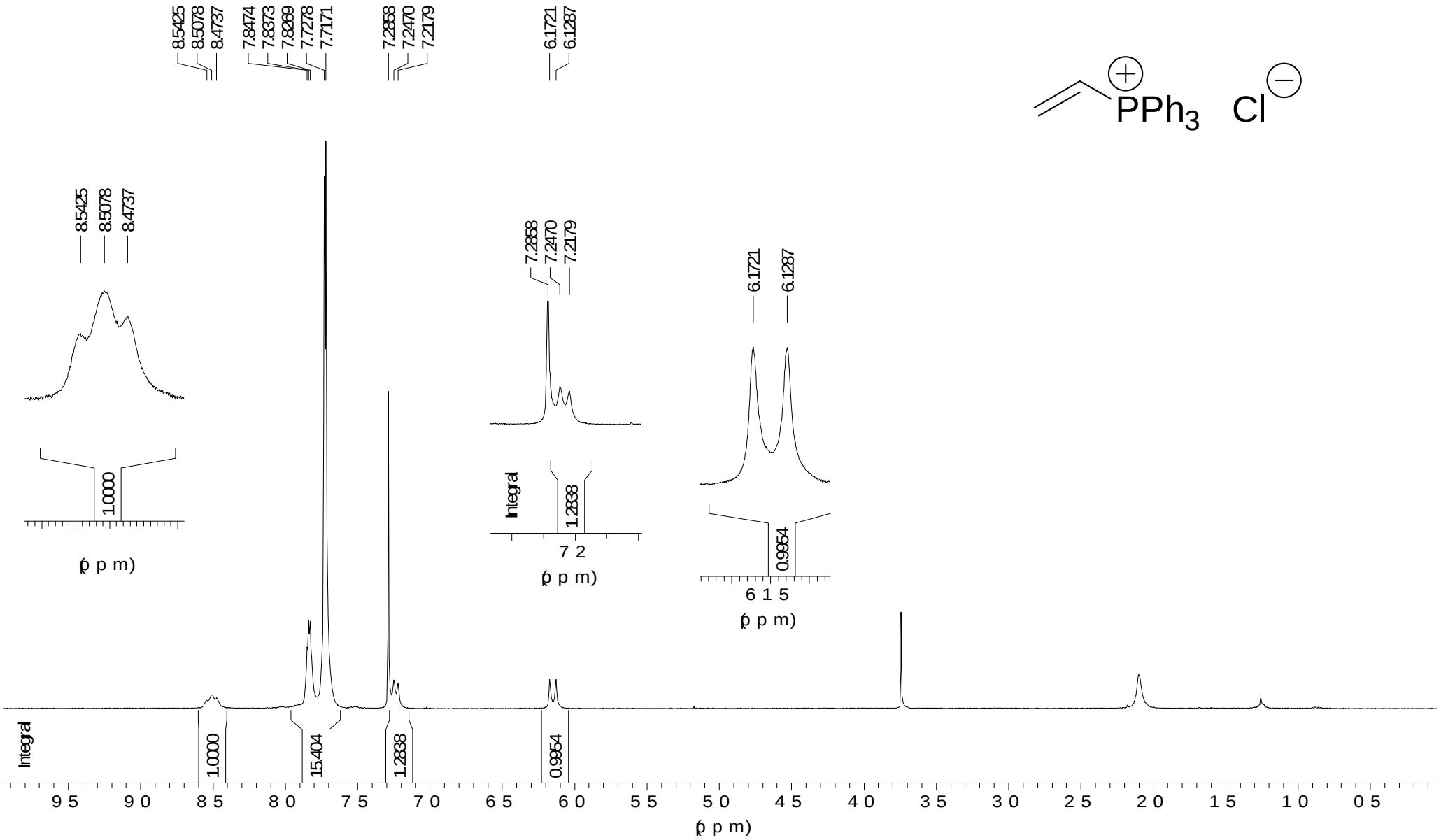
(2-Chloroethyl)triphenylphosphonium chloride hydrate spectrum NMR ^{13}C in $CDCl_3$



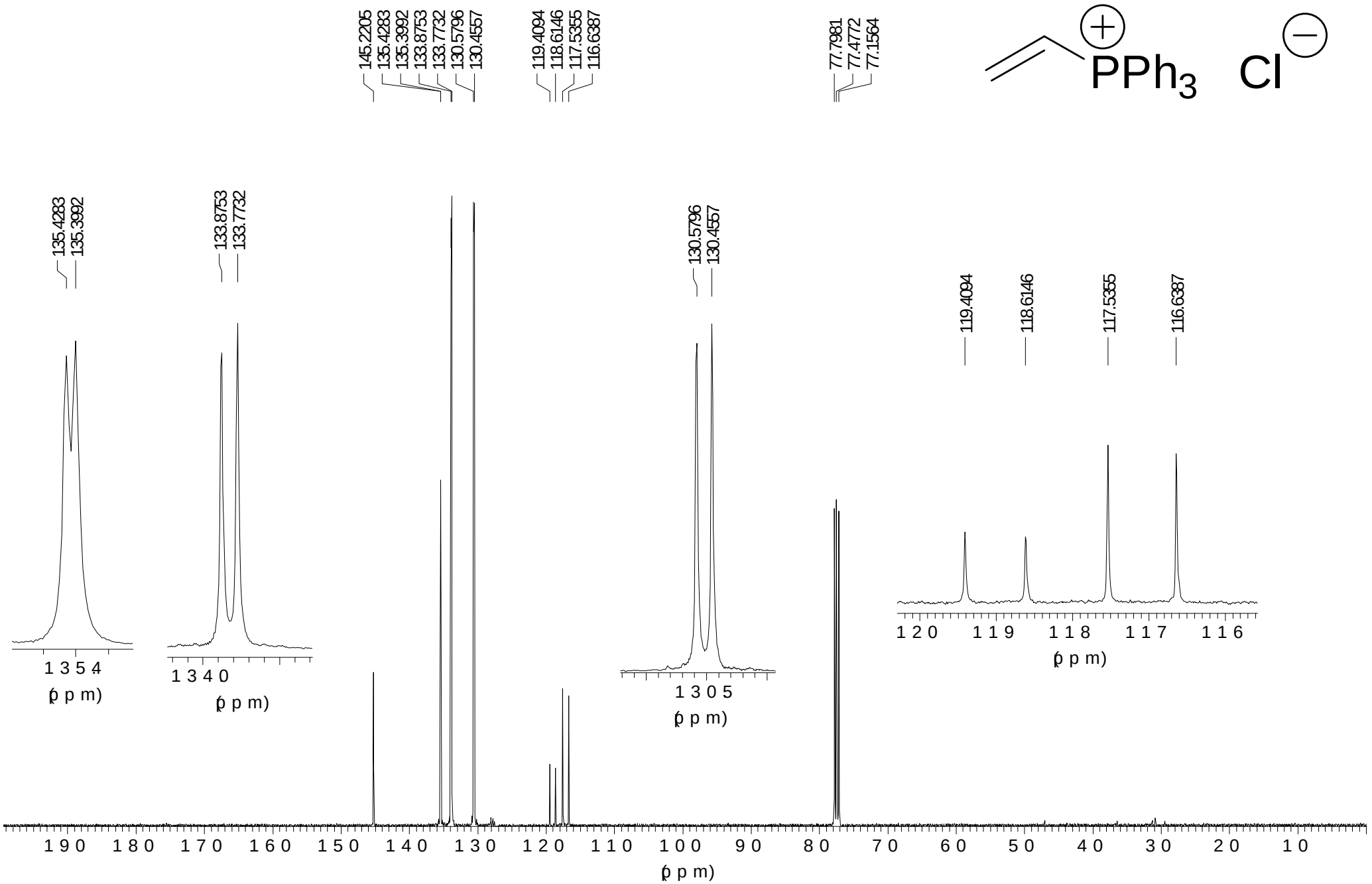
(2-Chloroethyl)triphenylphosphonium chloride hydrate spectrum NMR ^{31}P in $CDCl_3$



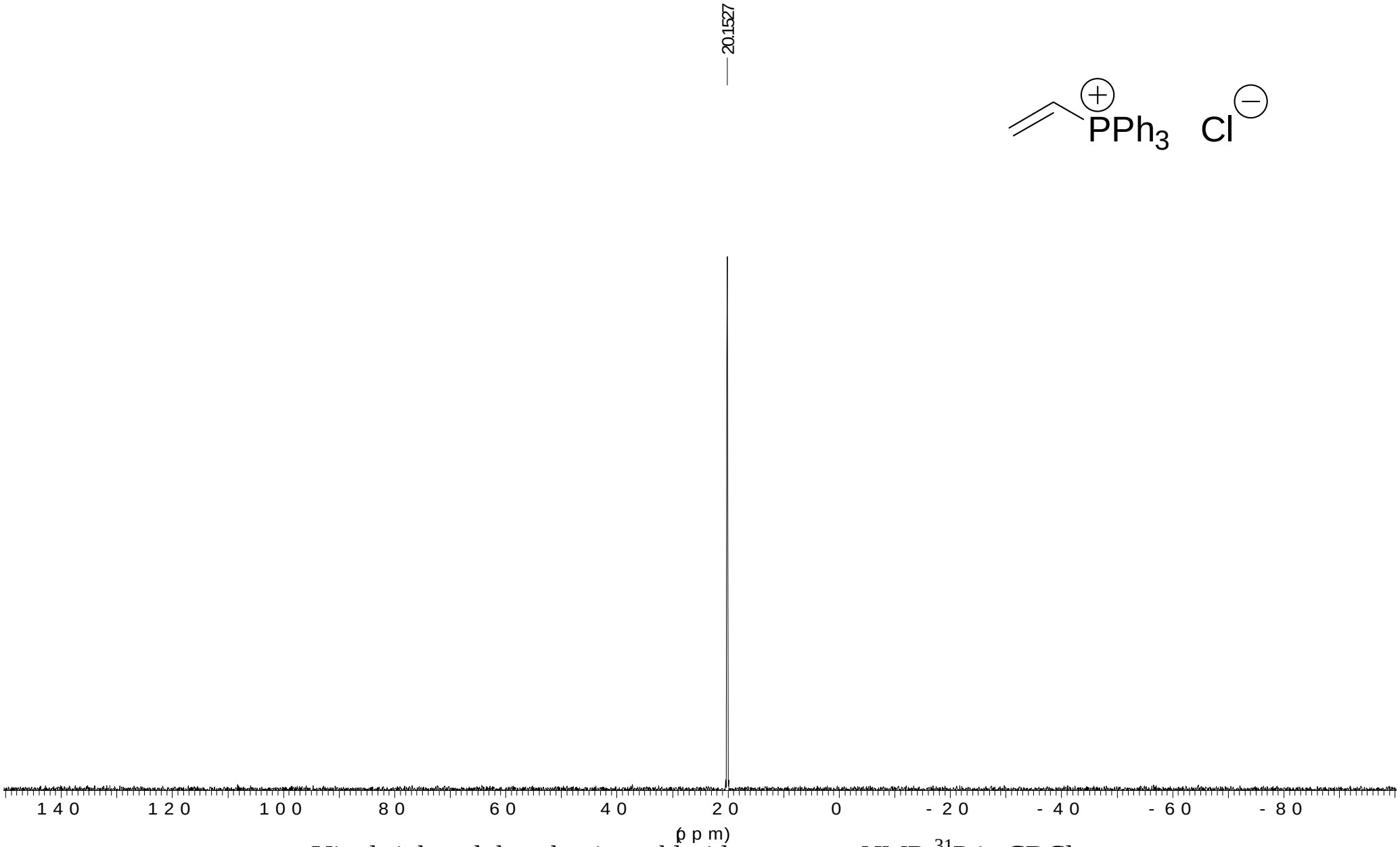
Vinyltriphenylphosphonium chloride spectrum NMR ^{13}C in $CDCl_3$



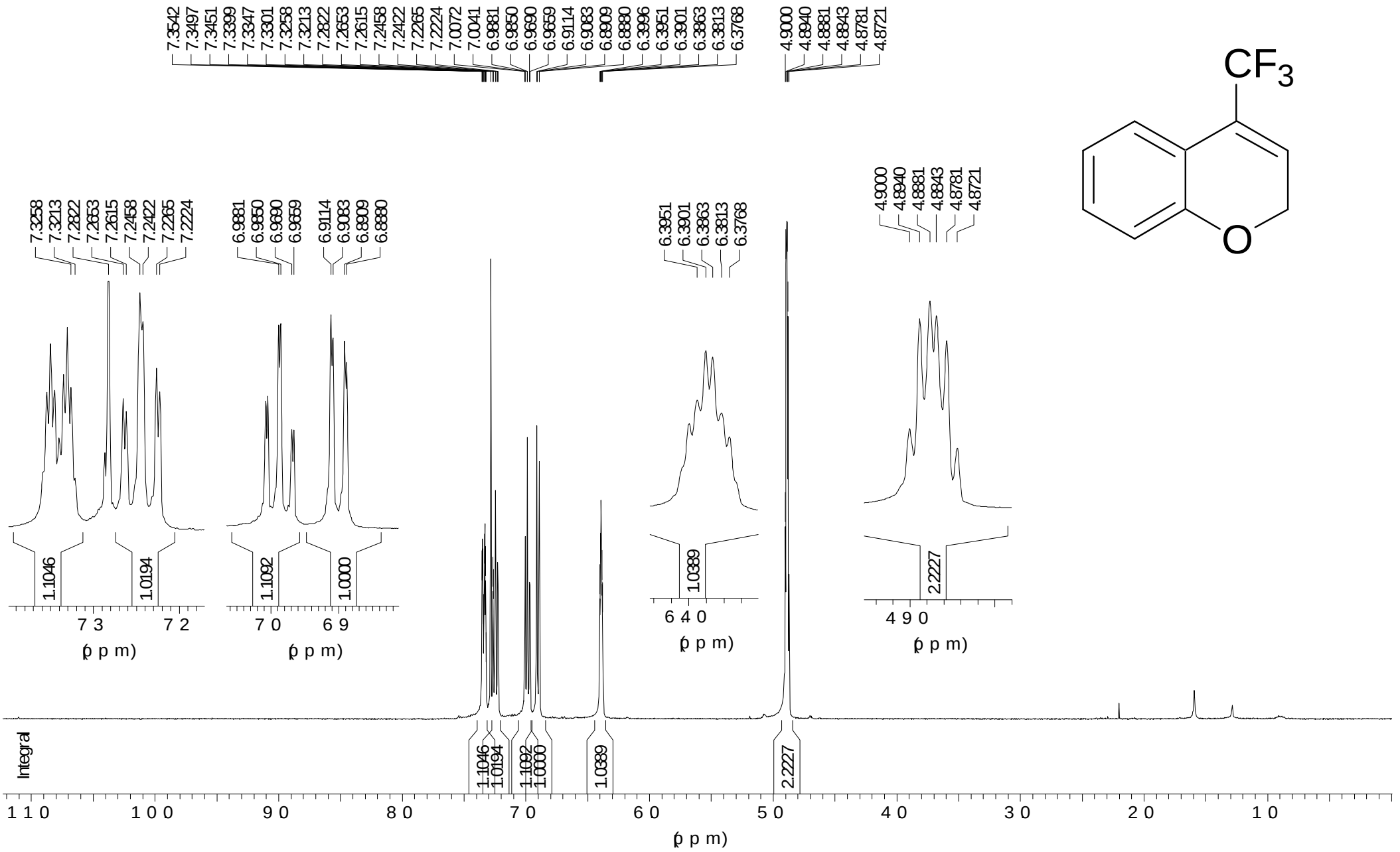
Vinyltriphenylphosphonium chloride spectrum NMR $^{1}H\{^{31}P\}$ in $CDCl_3$



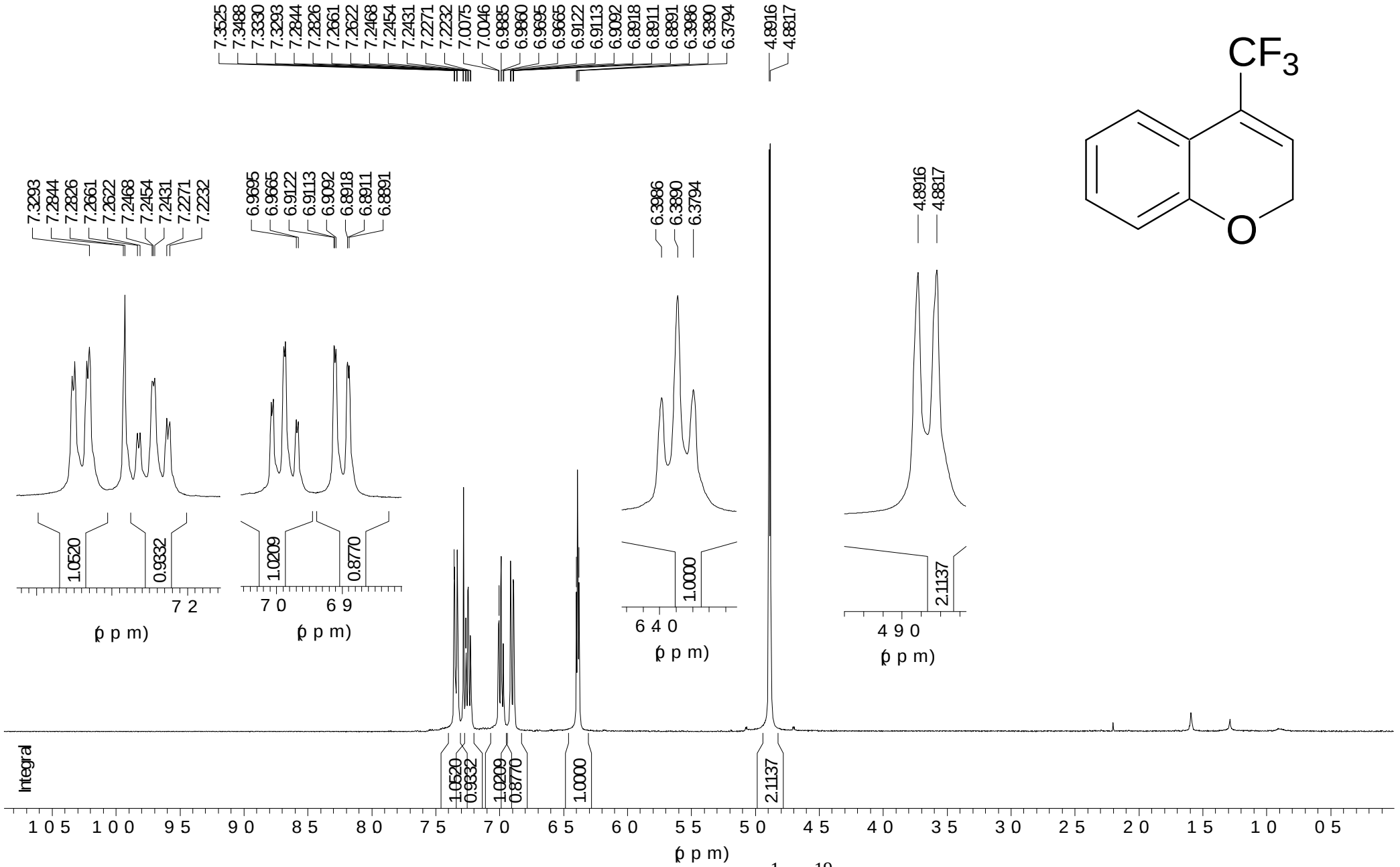
Vinyltriphenylphosphonium chloride spectrum NMR ^{13}C in $CDCl_3$



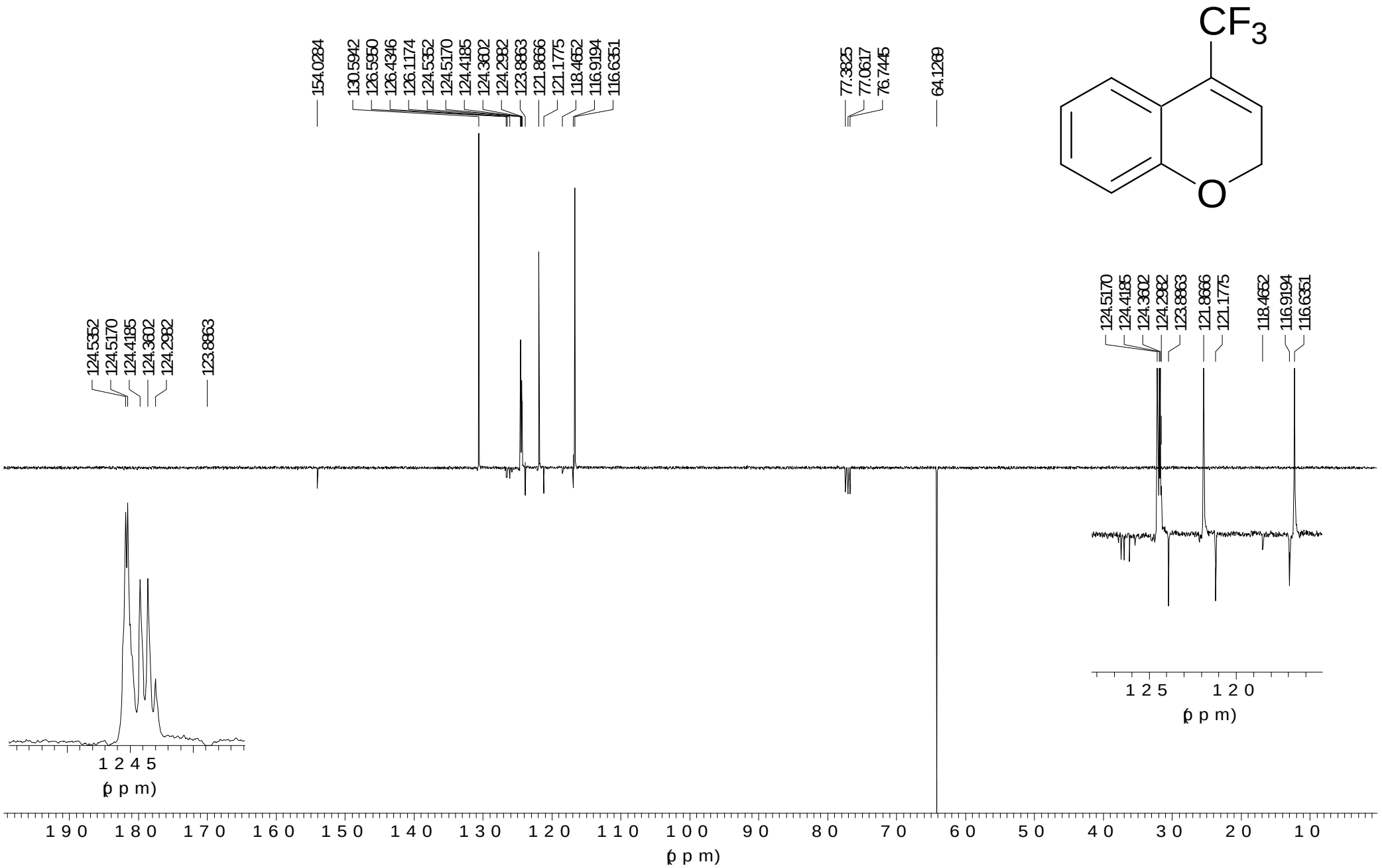
Vinyltriphenylphosphonium chloride spectrum NMR ^{31}P in $CDCl_3$



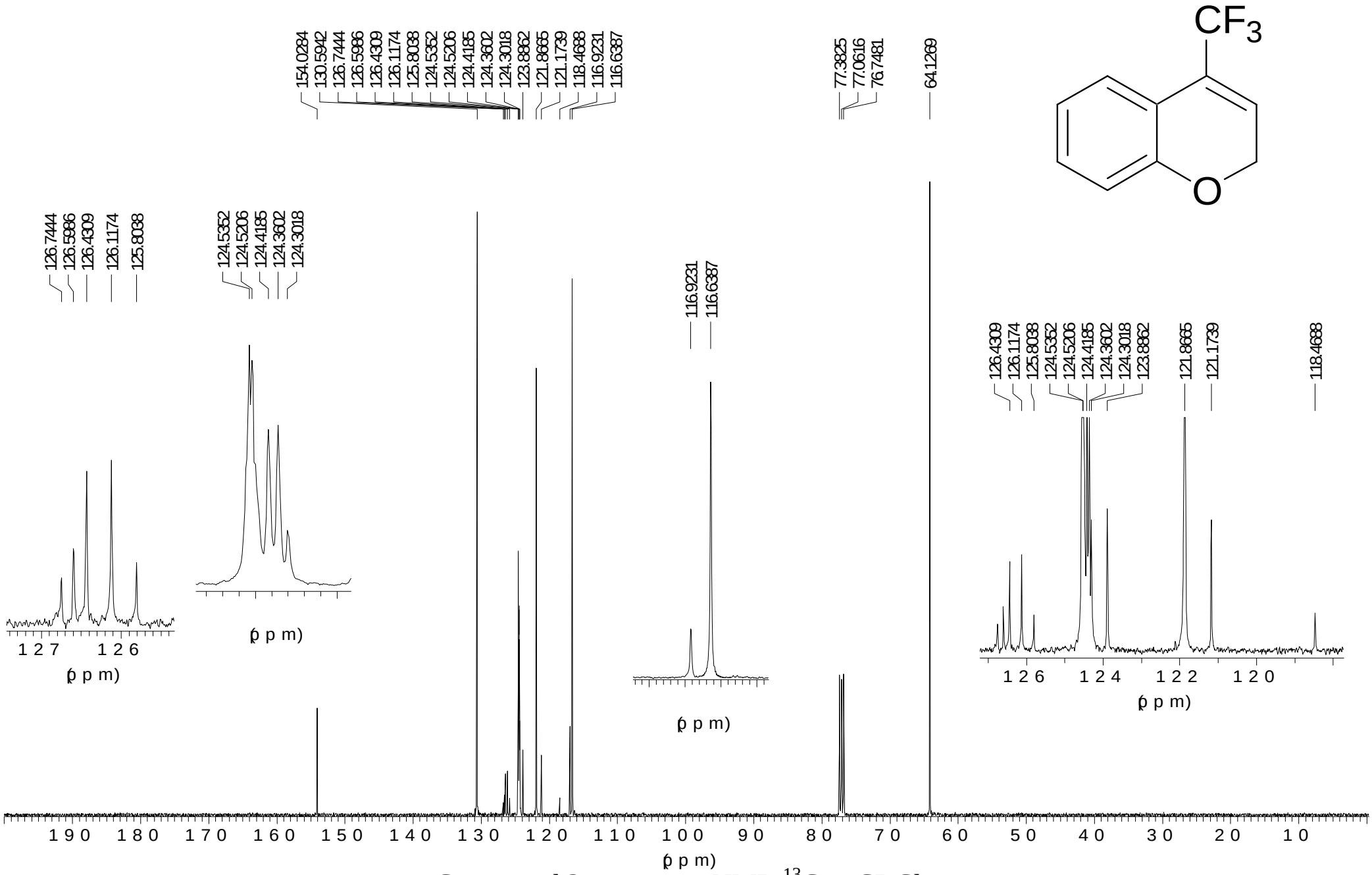
Compound **2a** spectrum NMR ^{1}H in $CDCl_3$



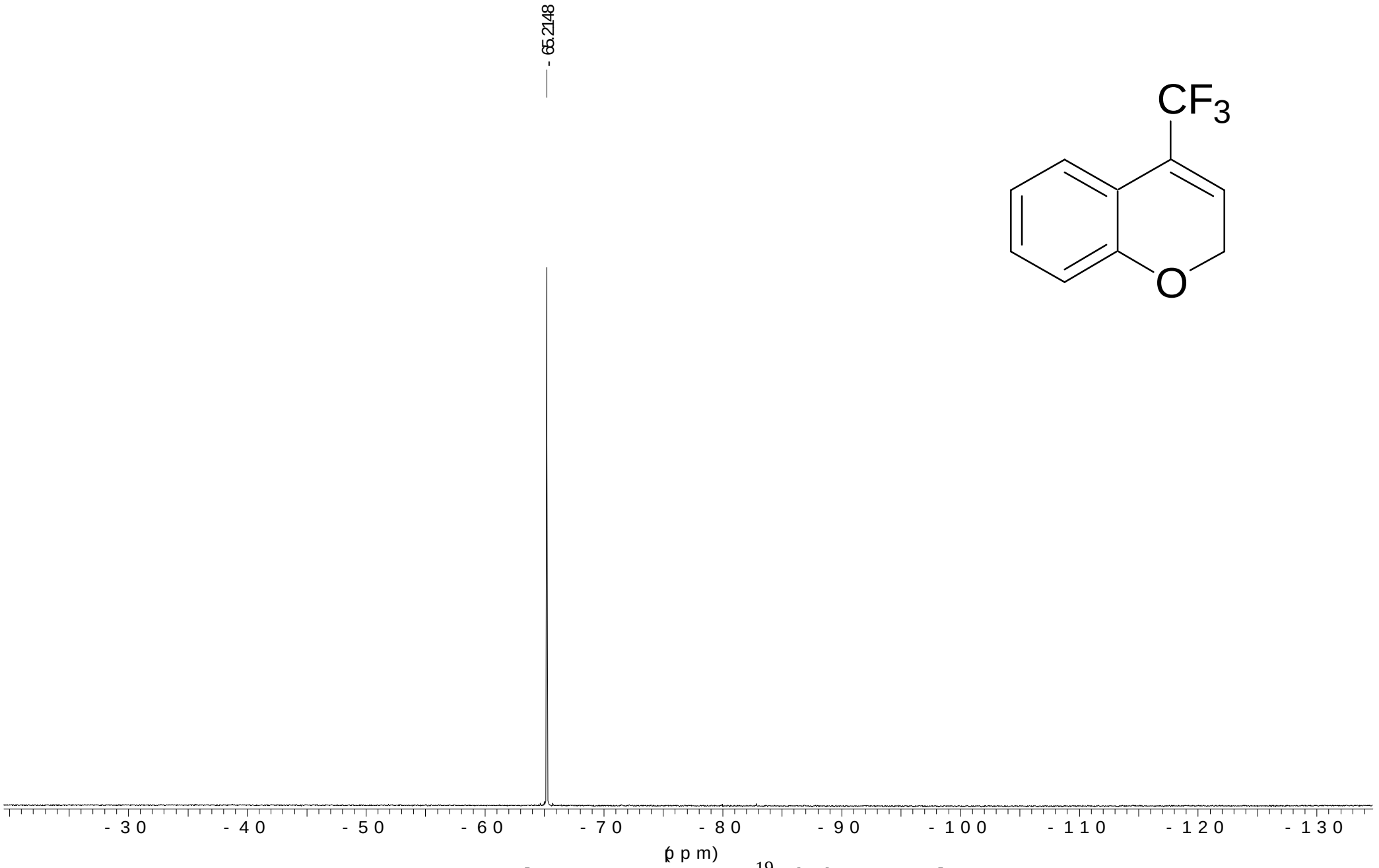
Compound **2a** spectrum NMR $^{1}H\{^{19}F\}$ in $CDCl_3$



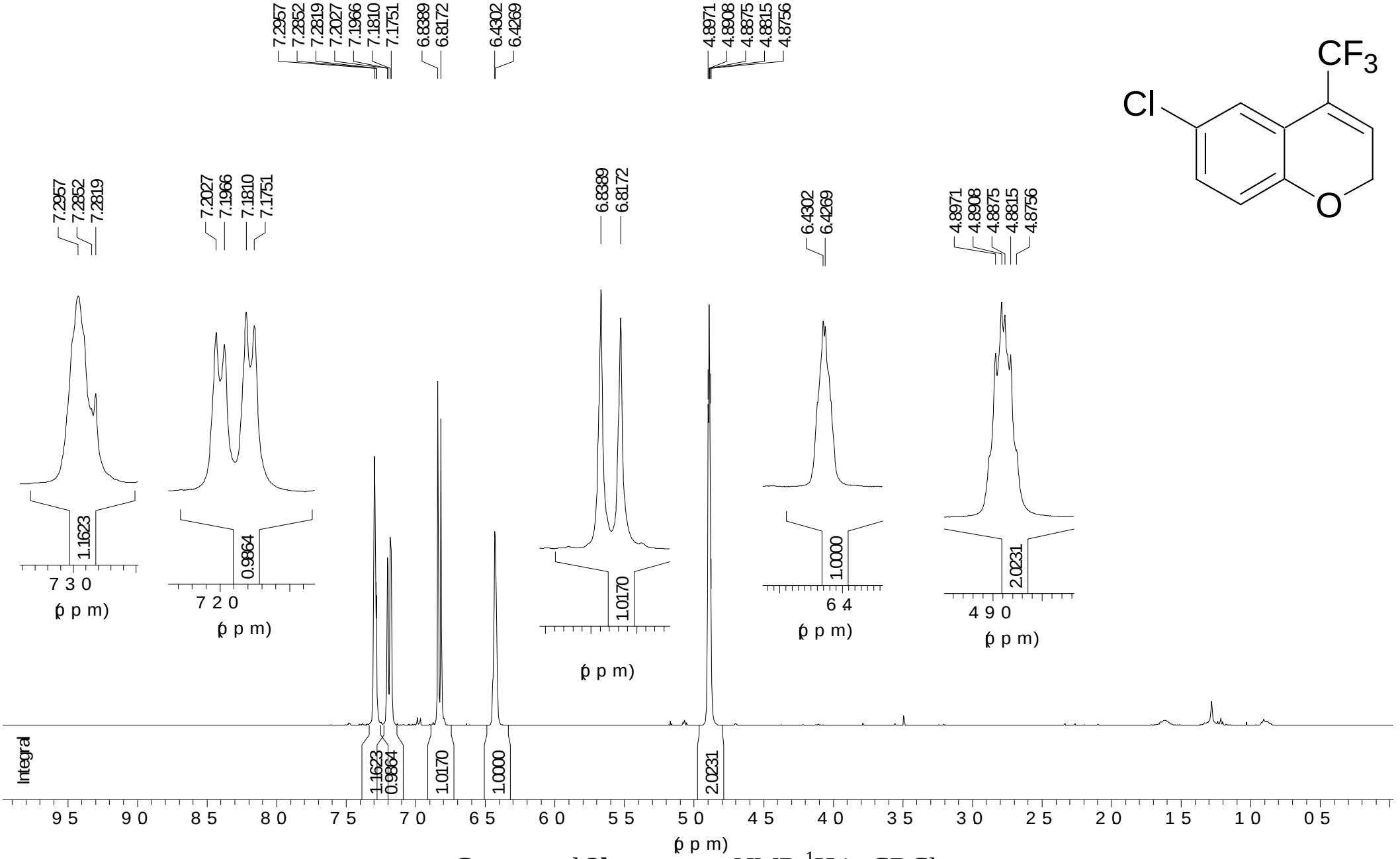
Compound **2a** spectrum NMR ^{13}C DEPT in $CDCl_3$



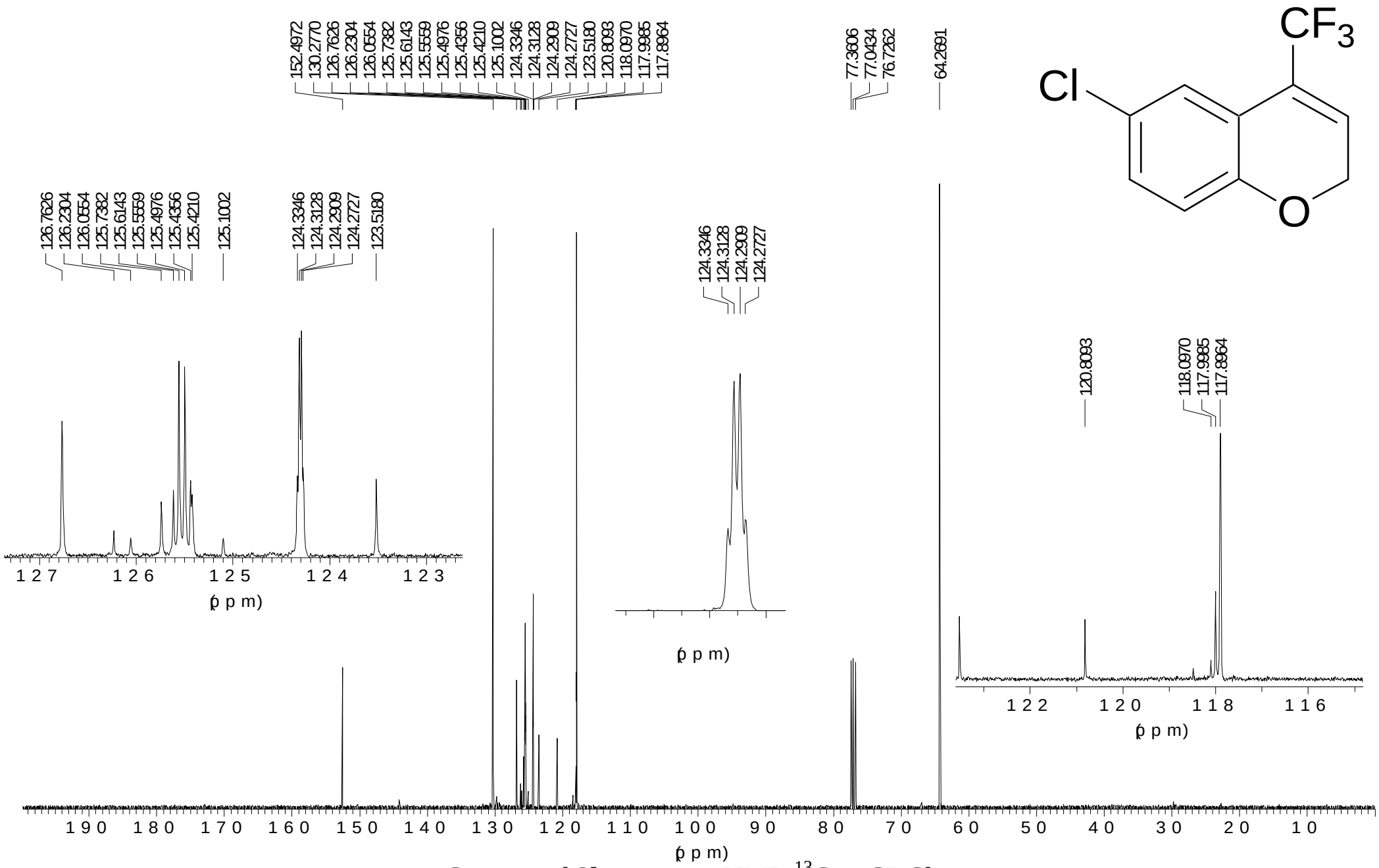
Compound **2a** spectrum NMR ^{13}C in $CDCl_3$



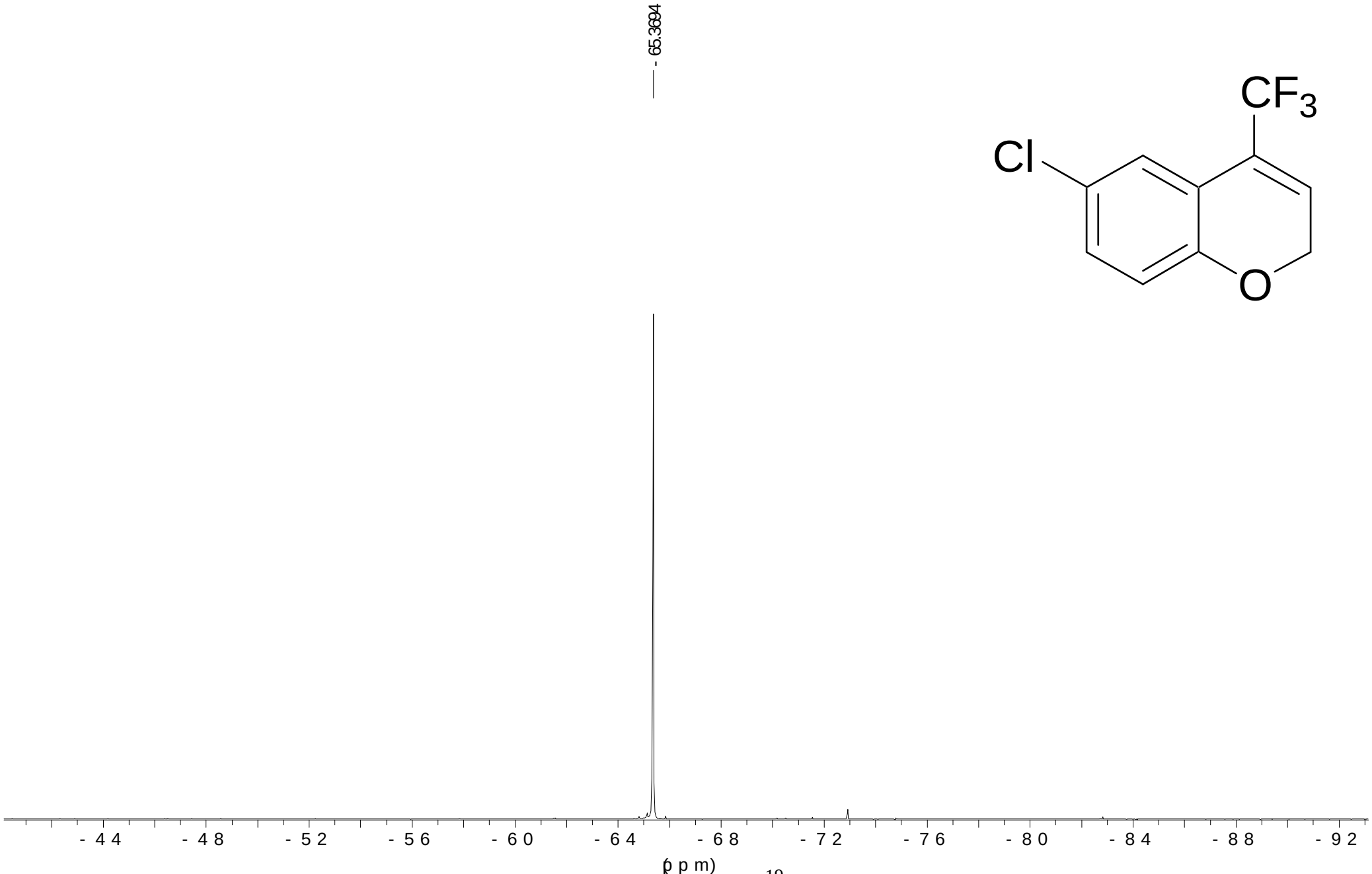
Compound **2a** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



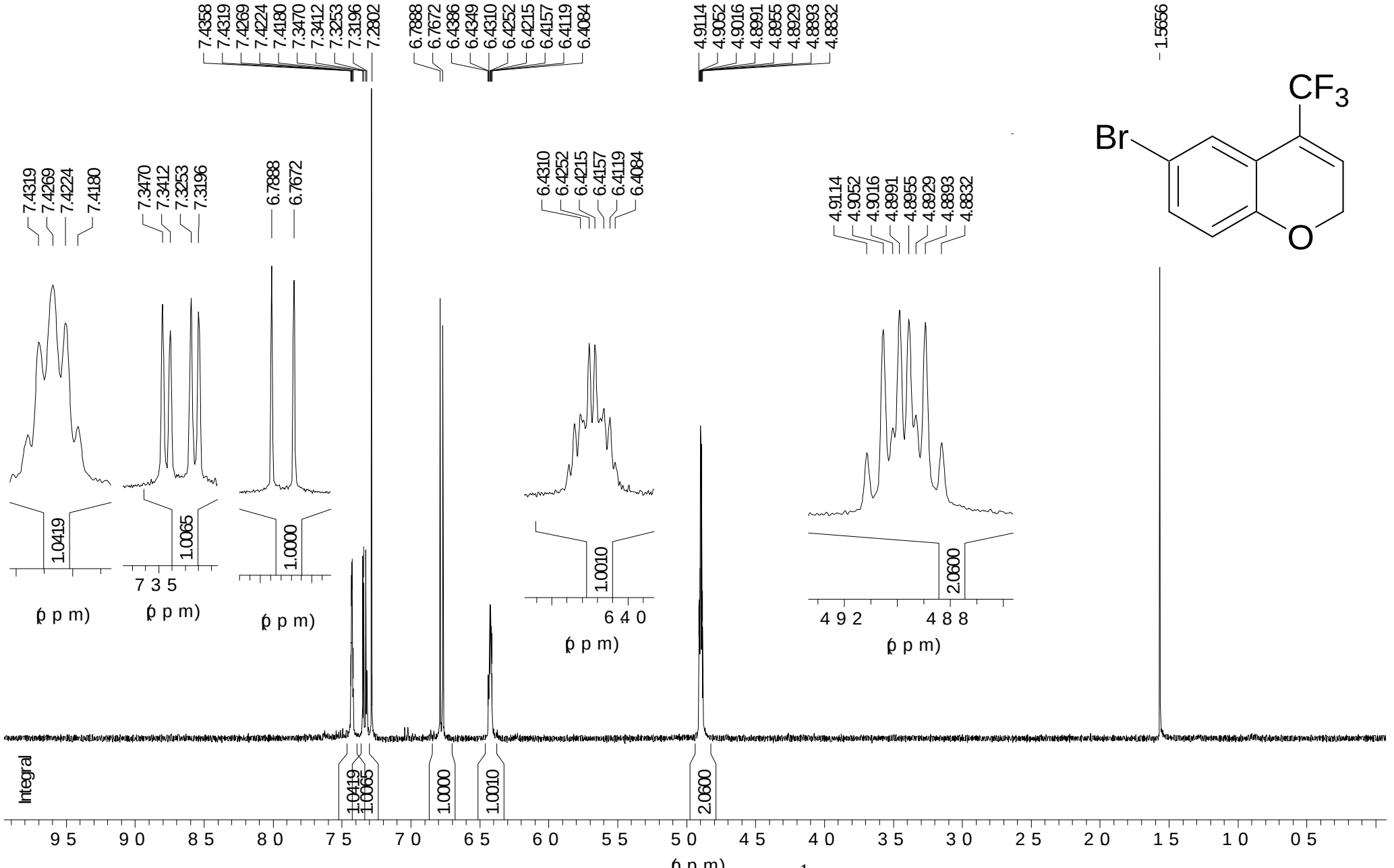
Compound **2b** spectrum NMR ^{1}H in $CDCl_3$



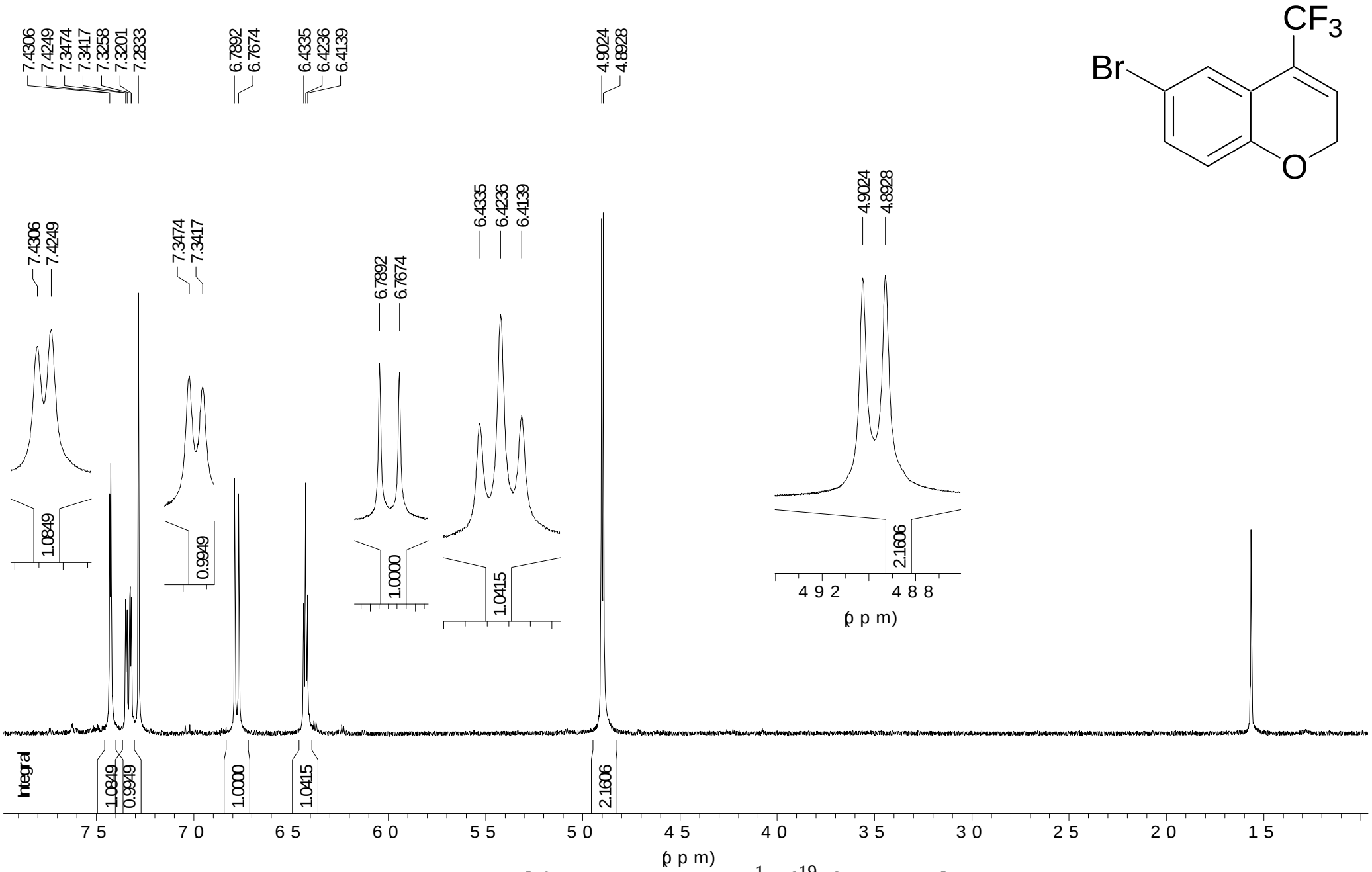
Compound **2b** spectrum NMR ^{13}C in $CDCl_3$



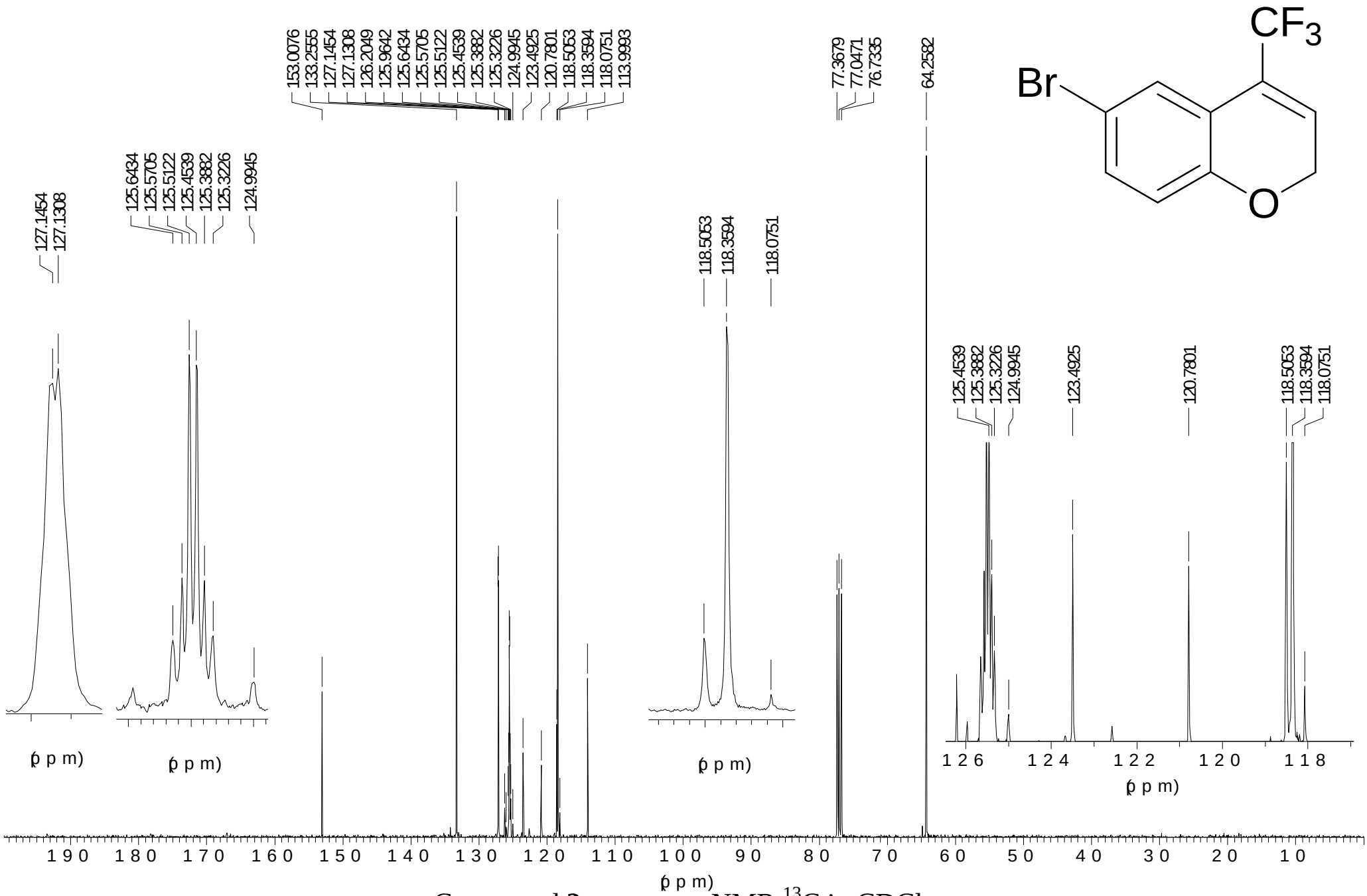
Compound **2b** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



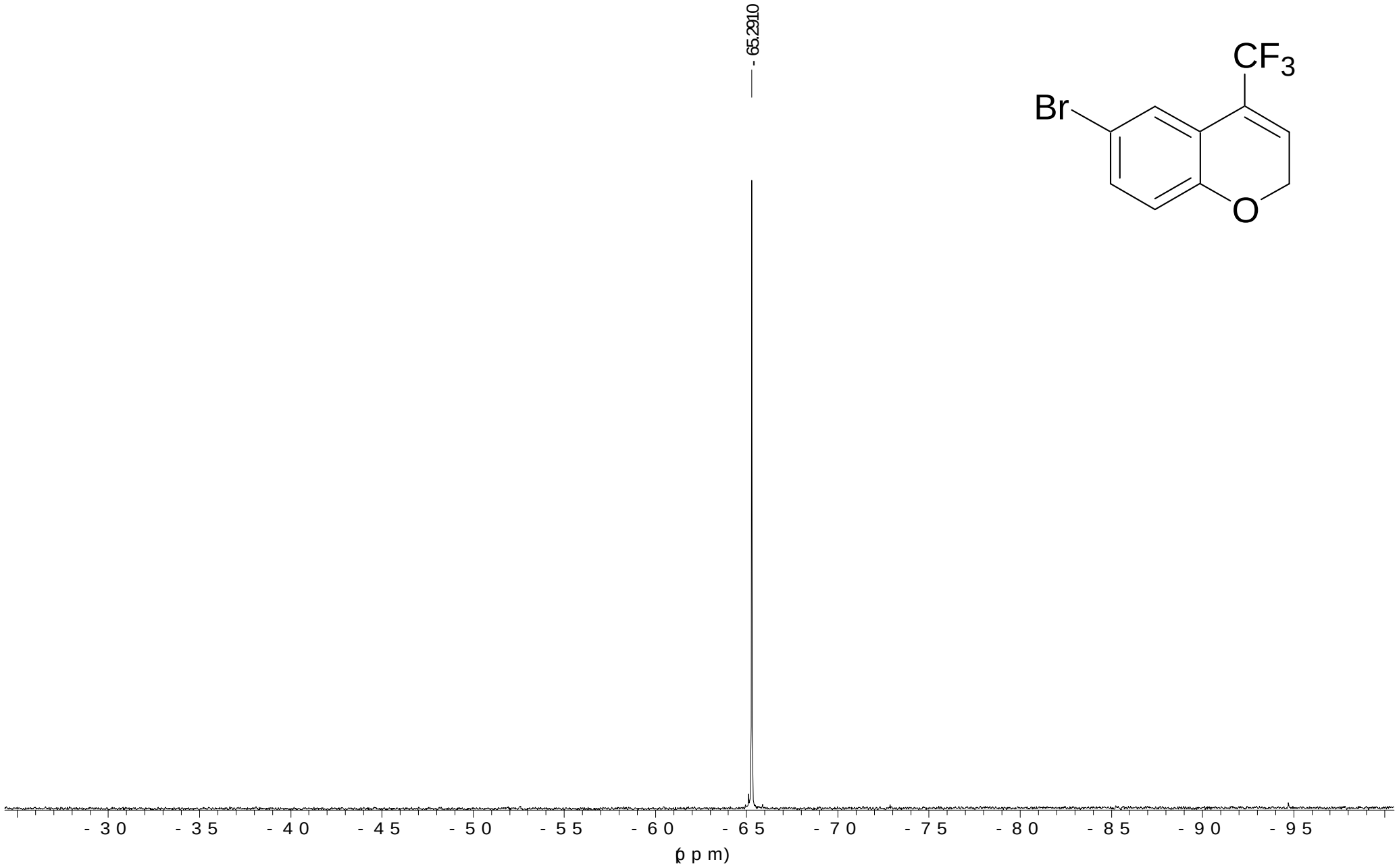
Compound **2c** spectrum NMR ^{1}H in $CDCl_3$



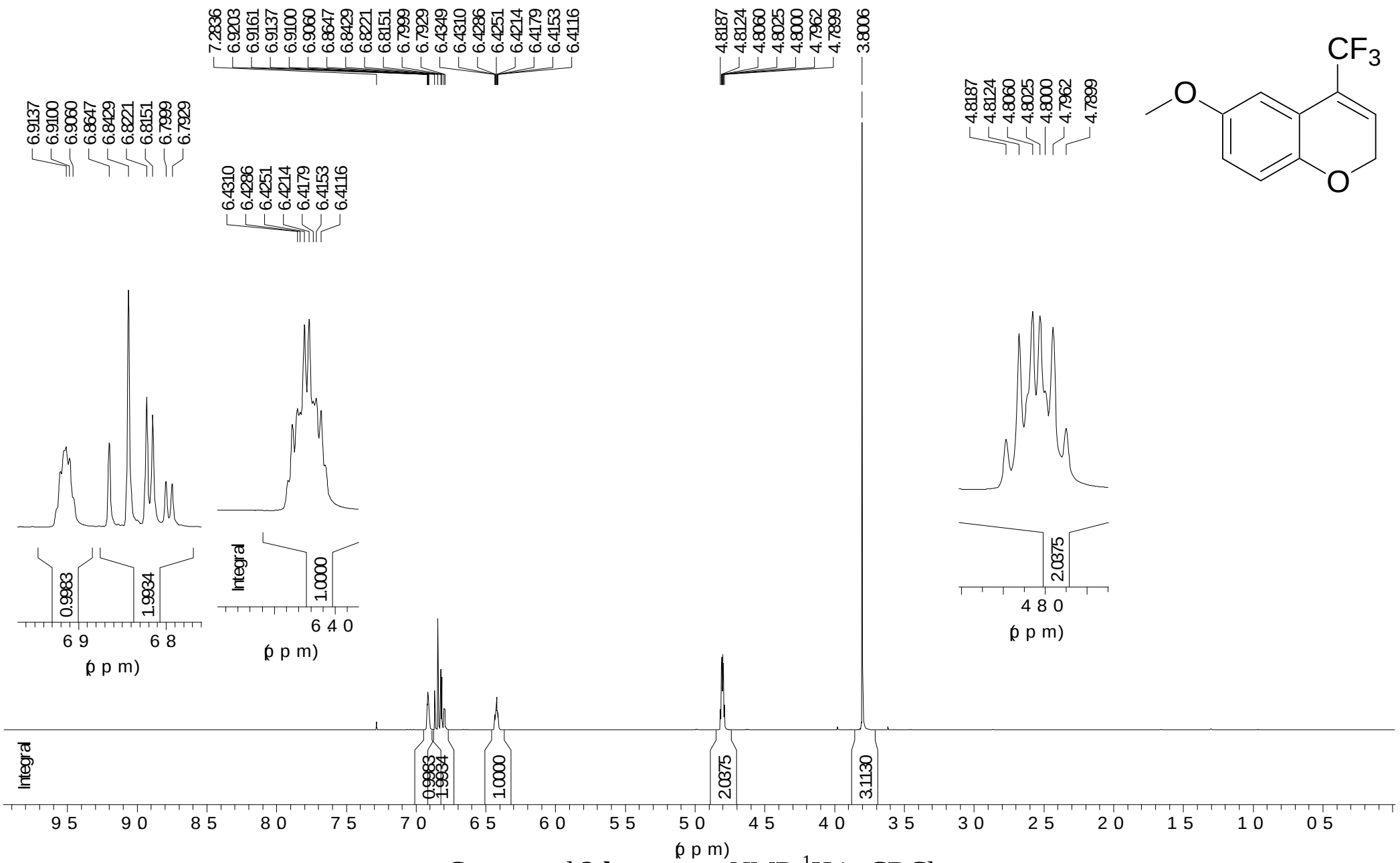
Compound **2c** spectrum NMR $^{1}H\{^{19}F\}$ in $CDCl_3$



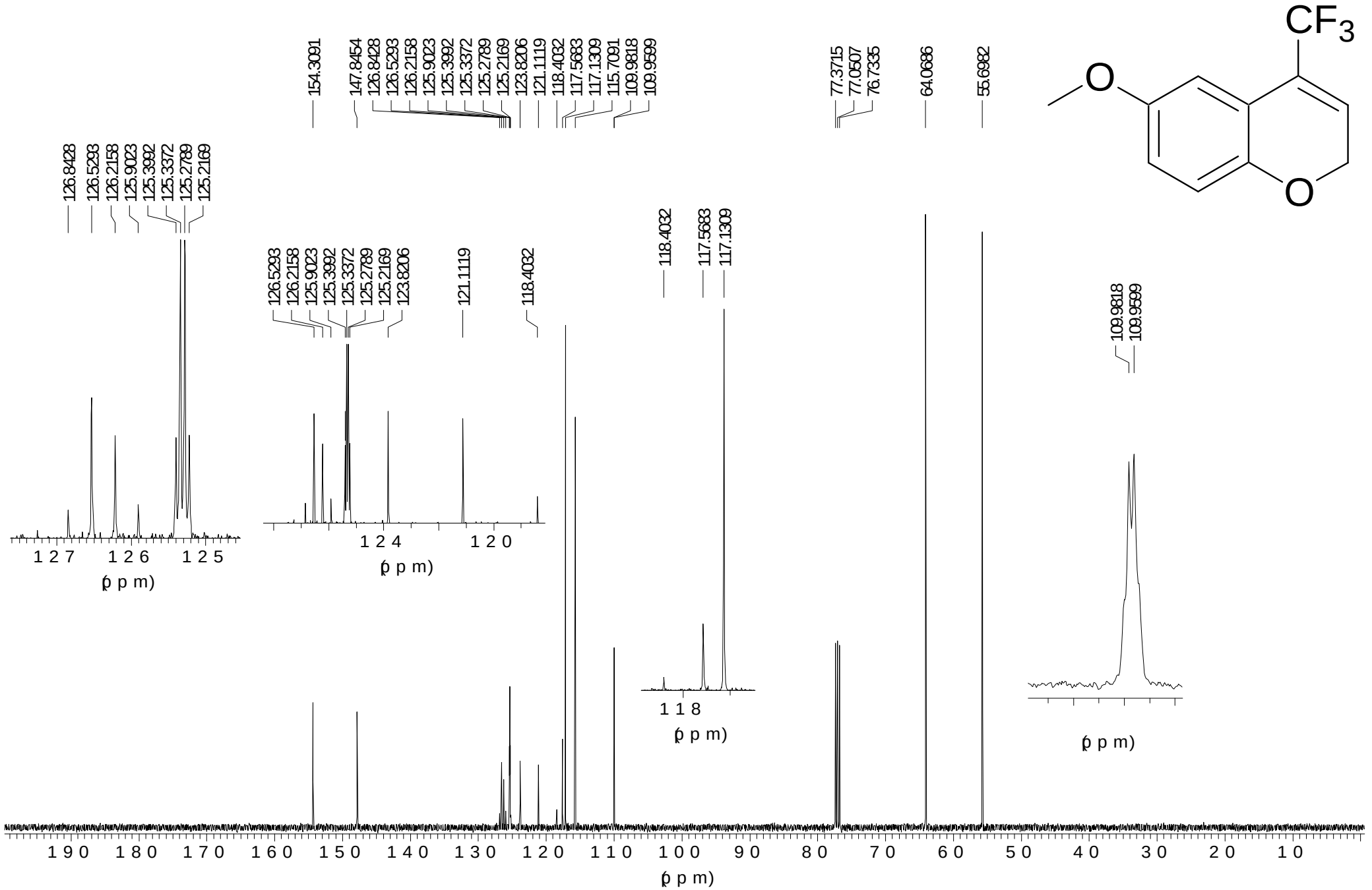
Compound **2c** spectrum NMR ^{13}C in $CDCl_3$



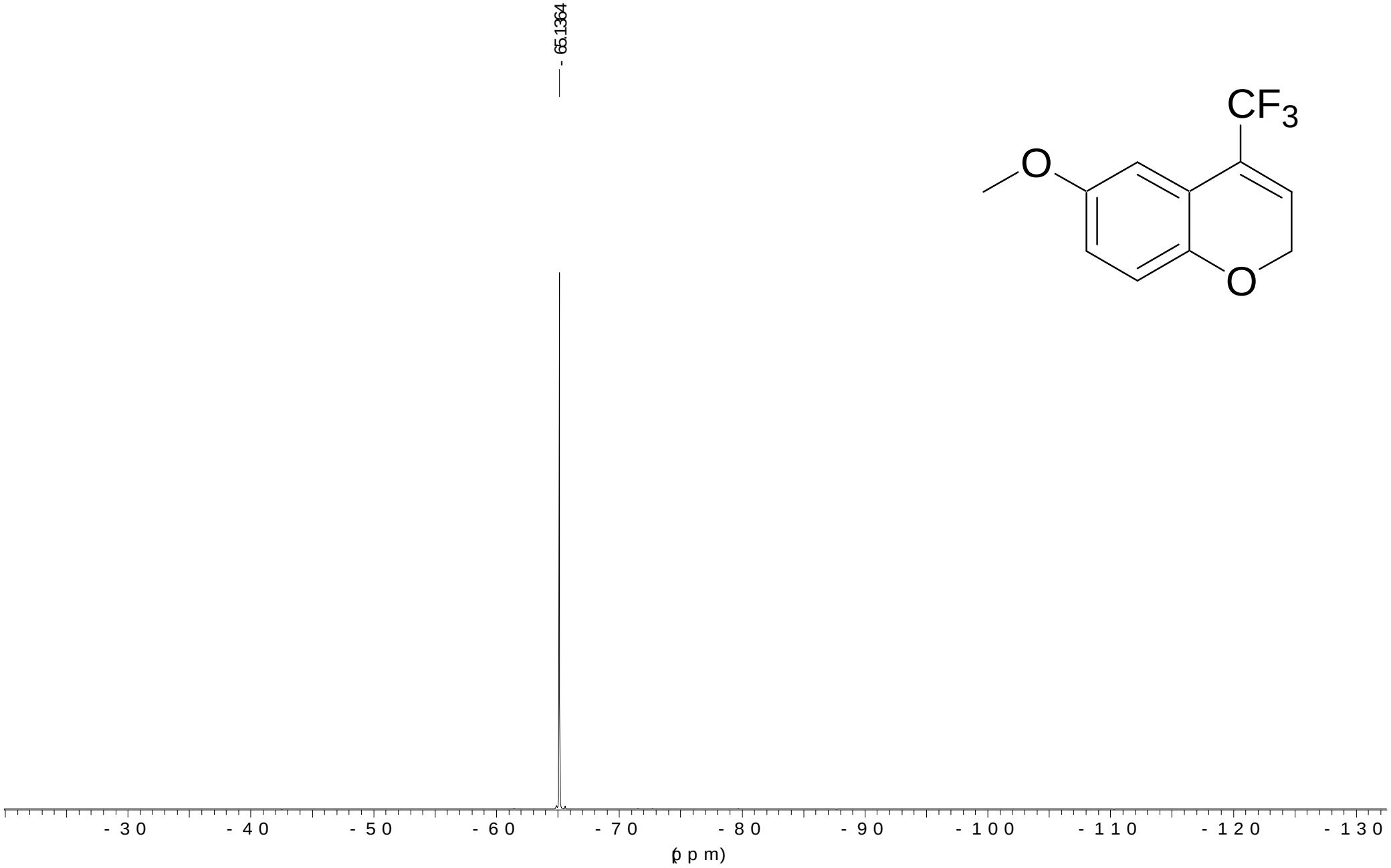
Compound **2c** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



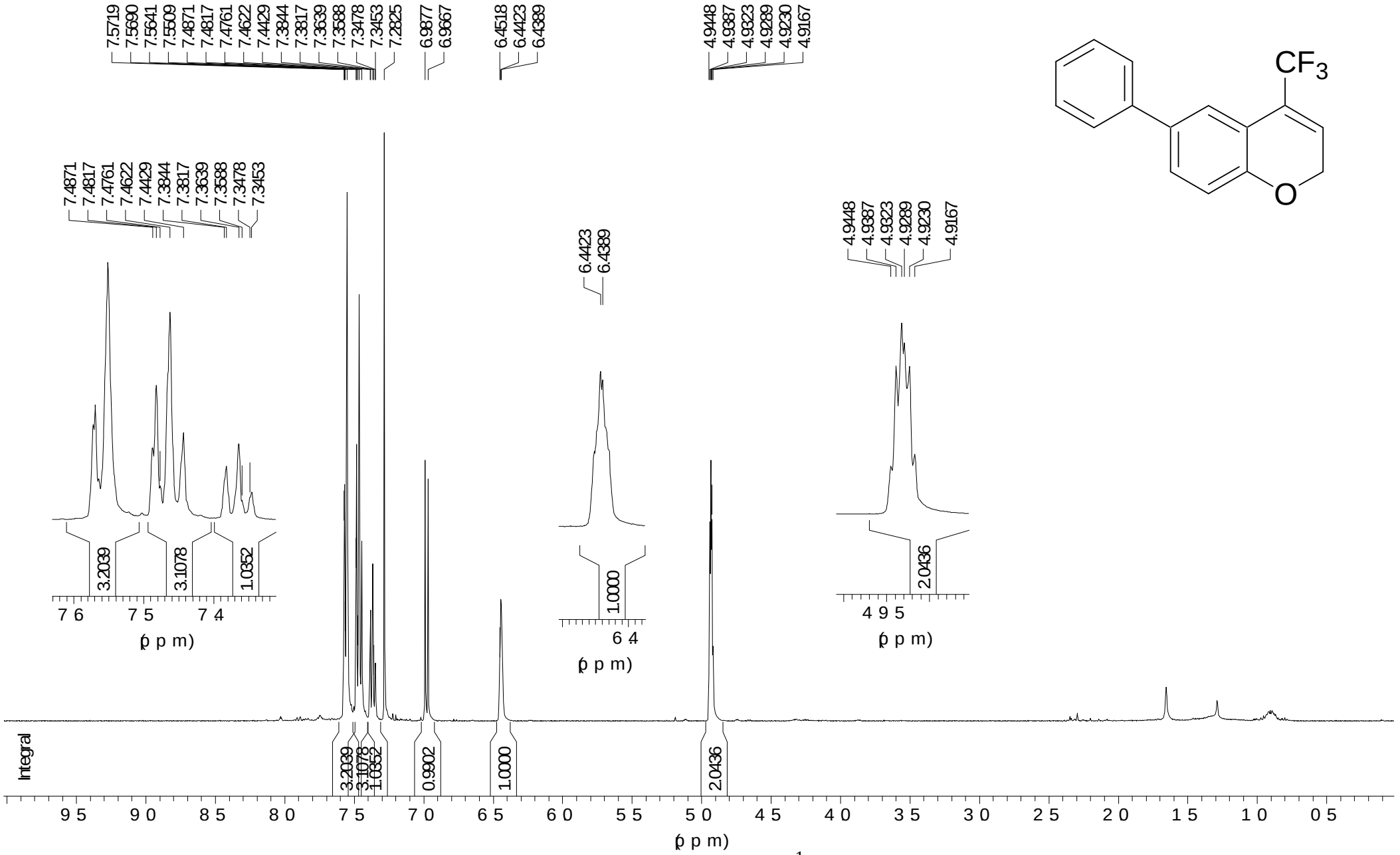
Compound **2d** spectrum NMR ^{1}H in $CDCl_3$



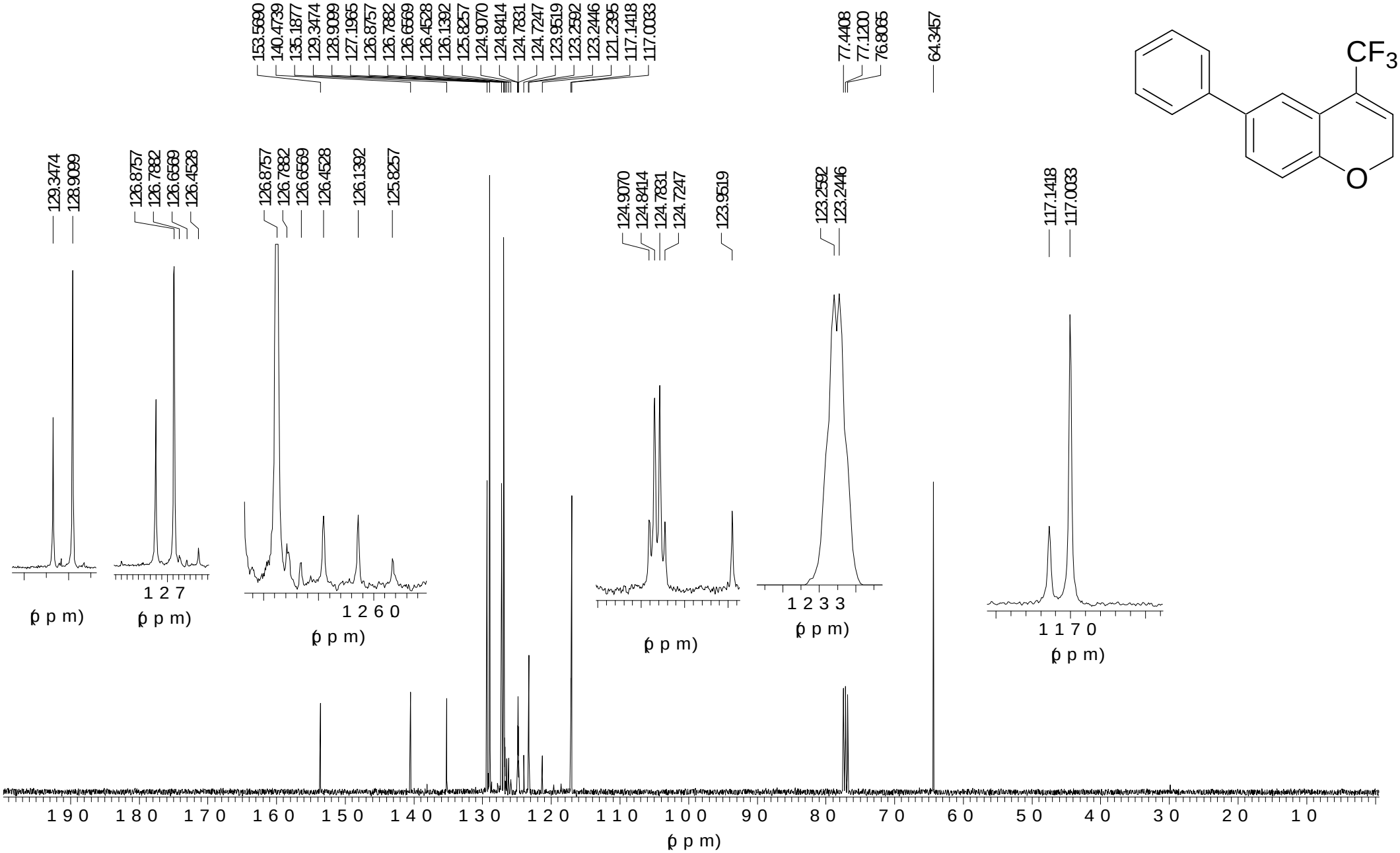
Compound **2d** spectrum NMR ^{13}C in $CDCl_3$



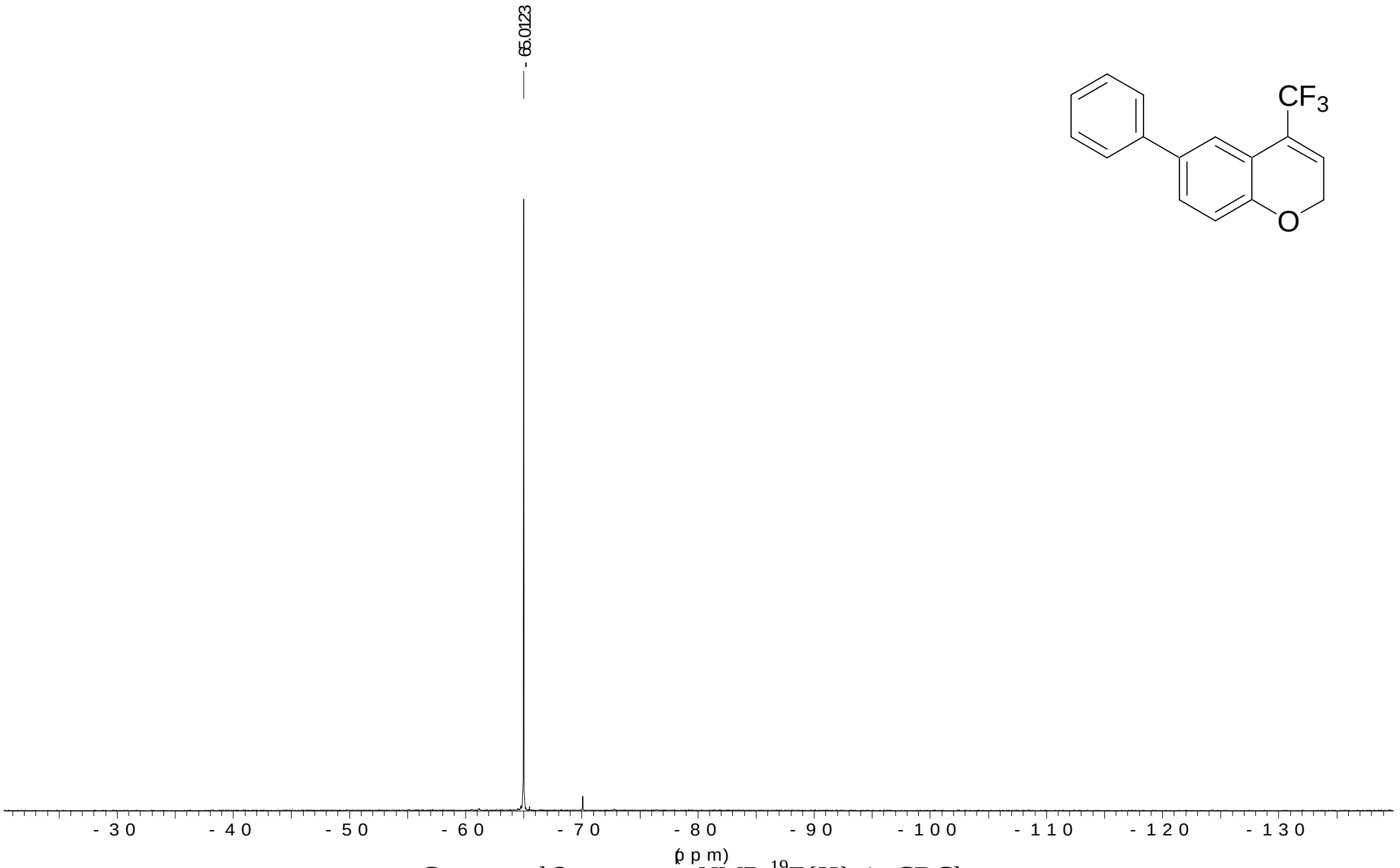
Compound **2d** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



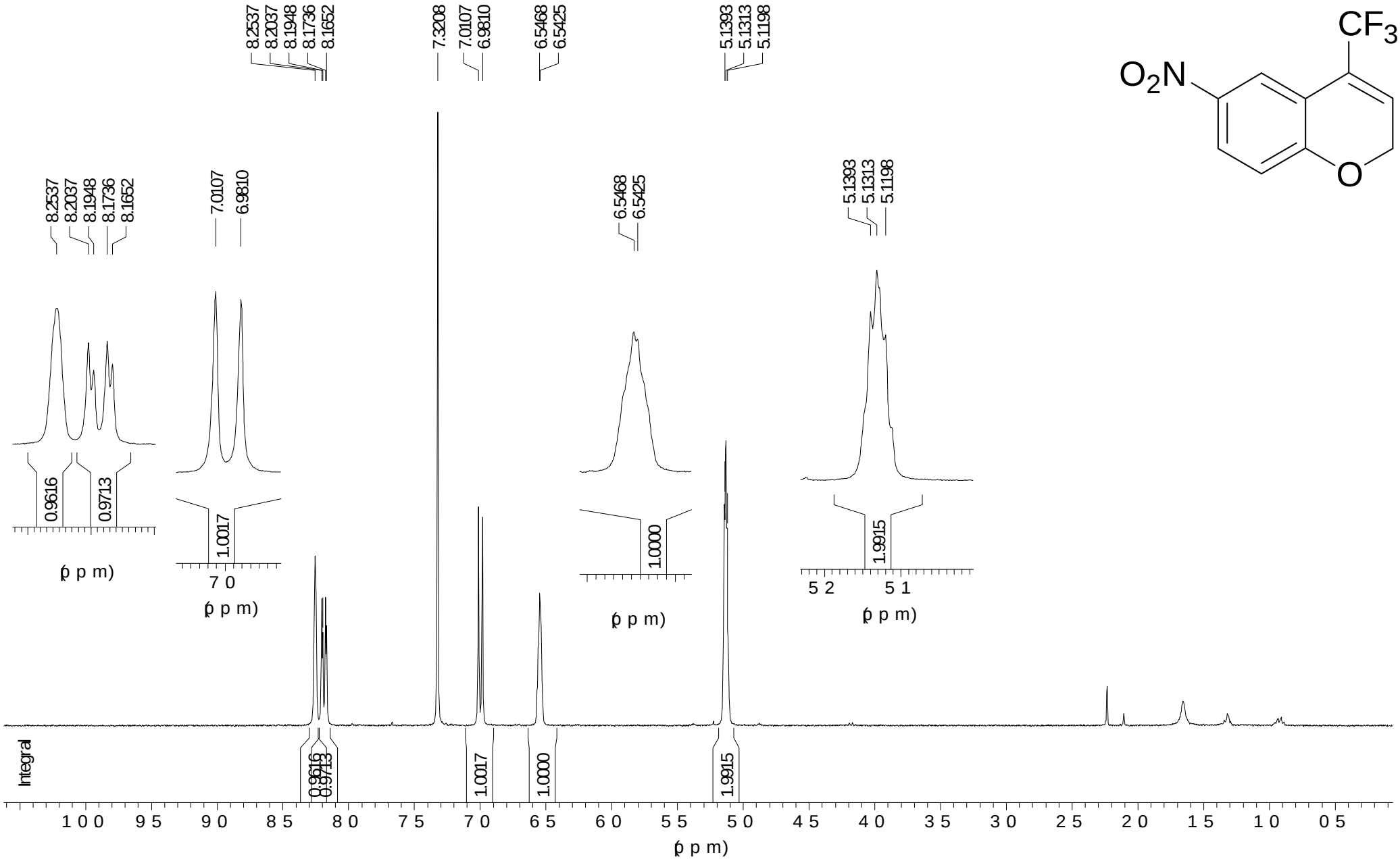
Compound **2e** spectrum NMR ^{1}H in $CDCl_3$



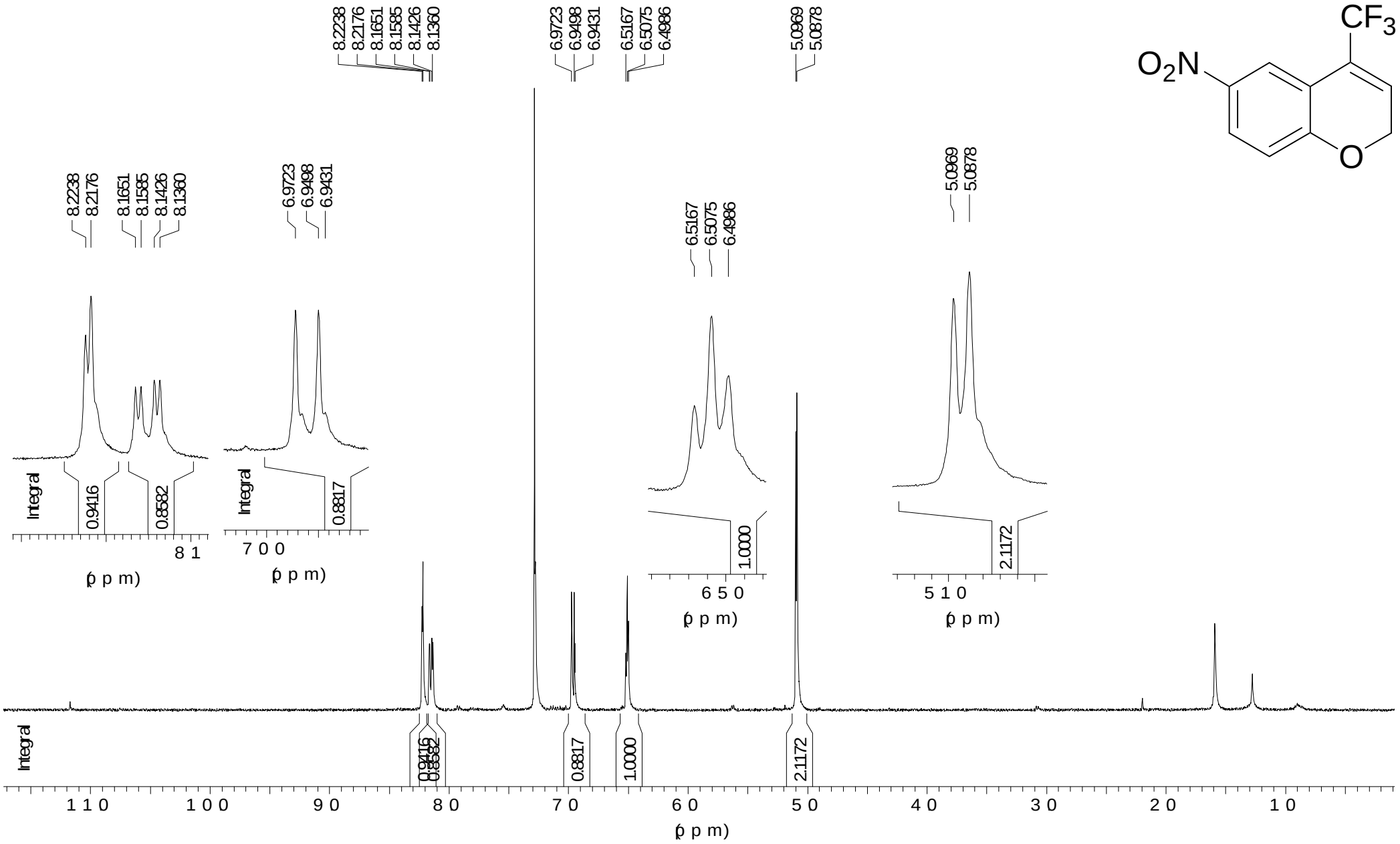
Compound **2e** spectrum NMR ^{13}C in $CDCl_3$



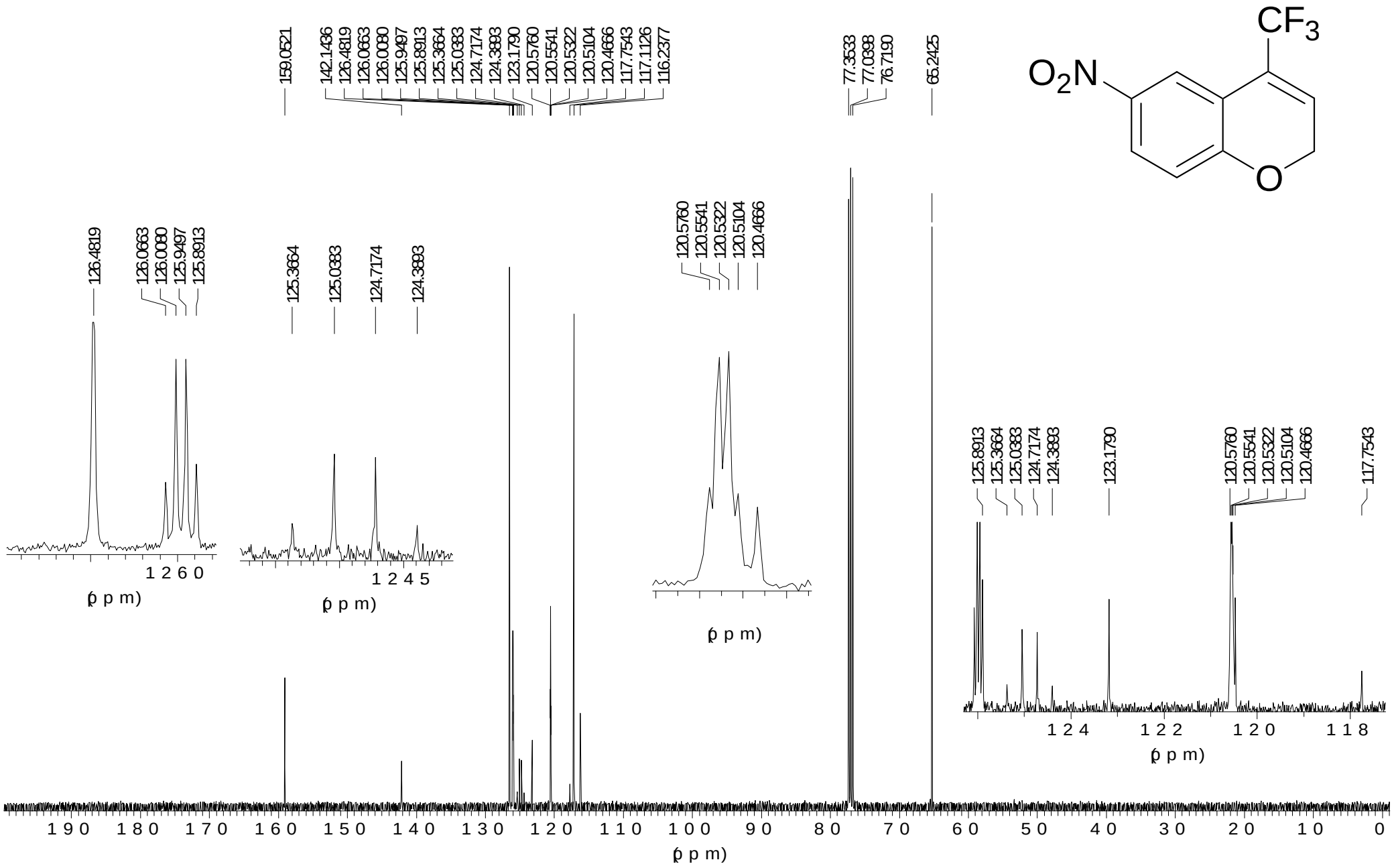
Compound **2e** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



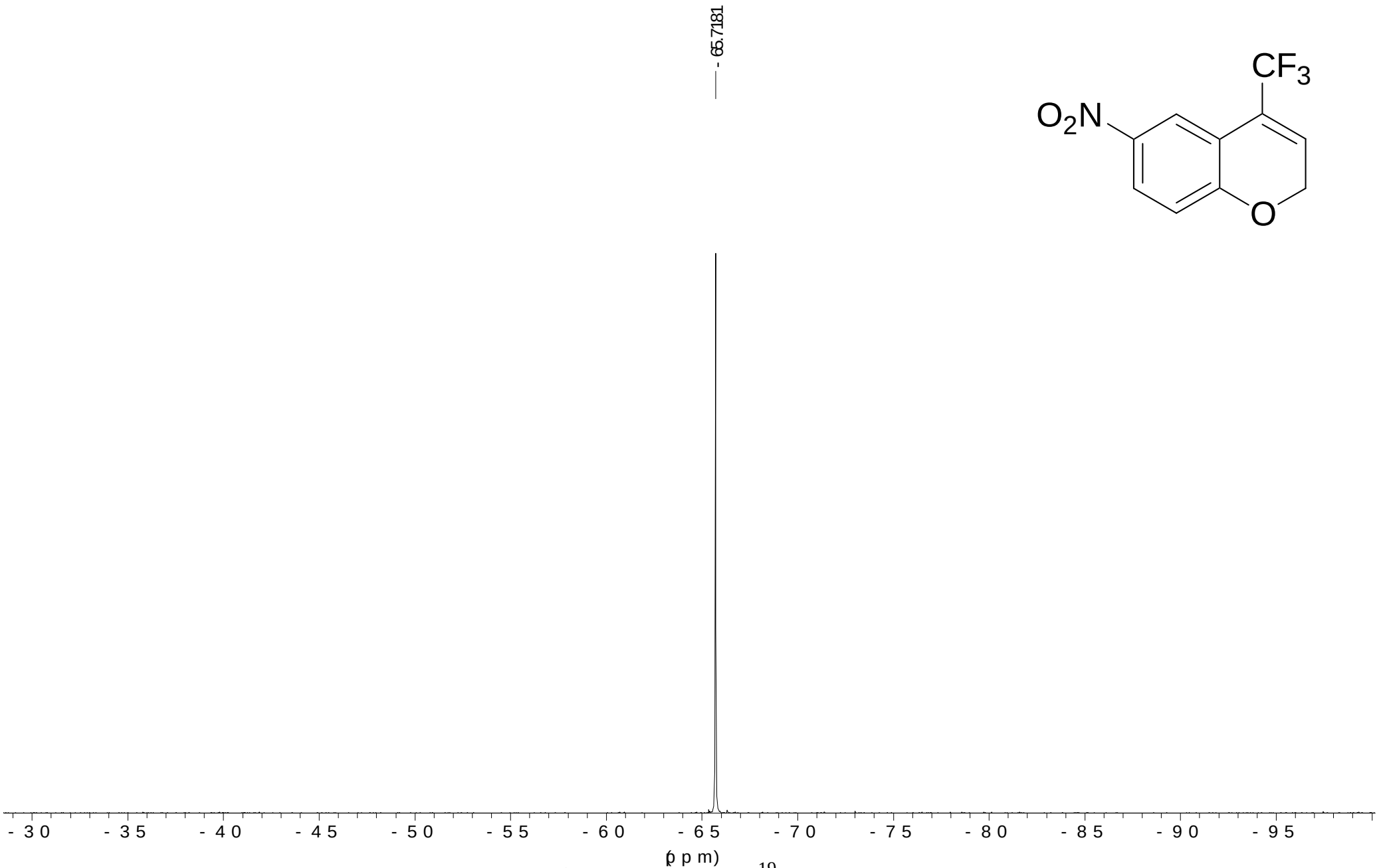
Compound **2f** spectrum NMR ^{1}H in $CDCl_3$



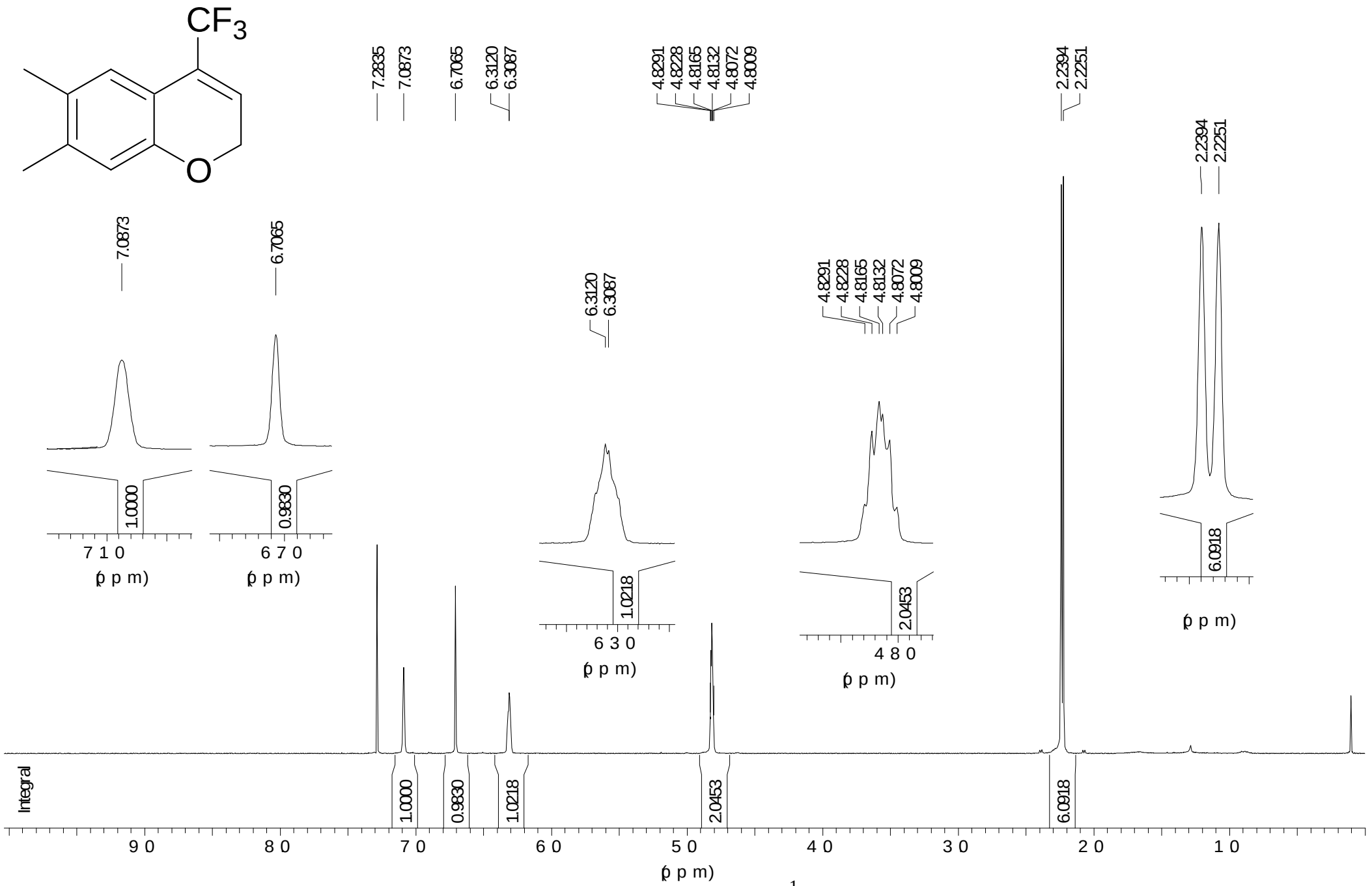
Compound **2f** spectrum NMR $^{1}H\{^{19}F\}$ in $CDCl_3$



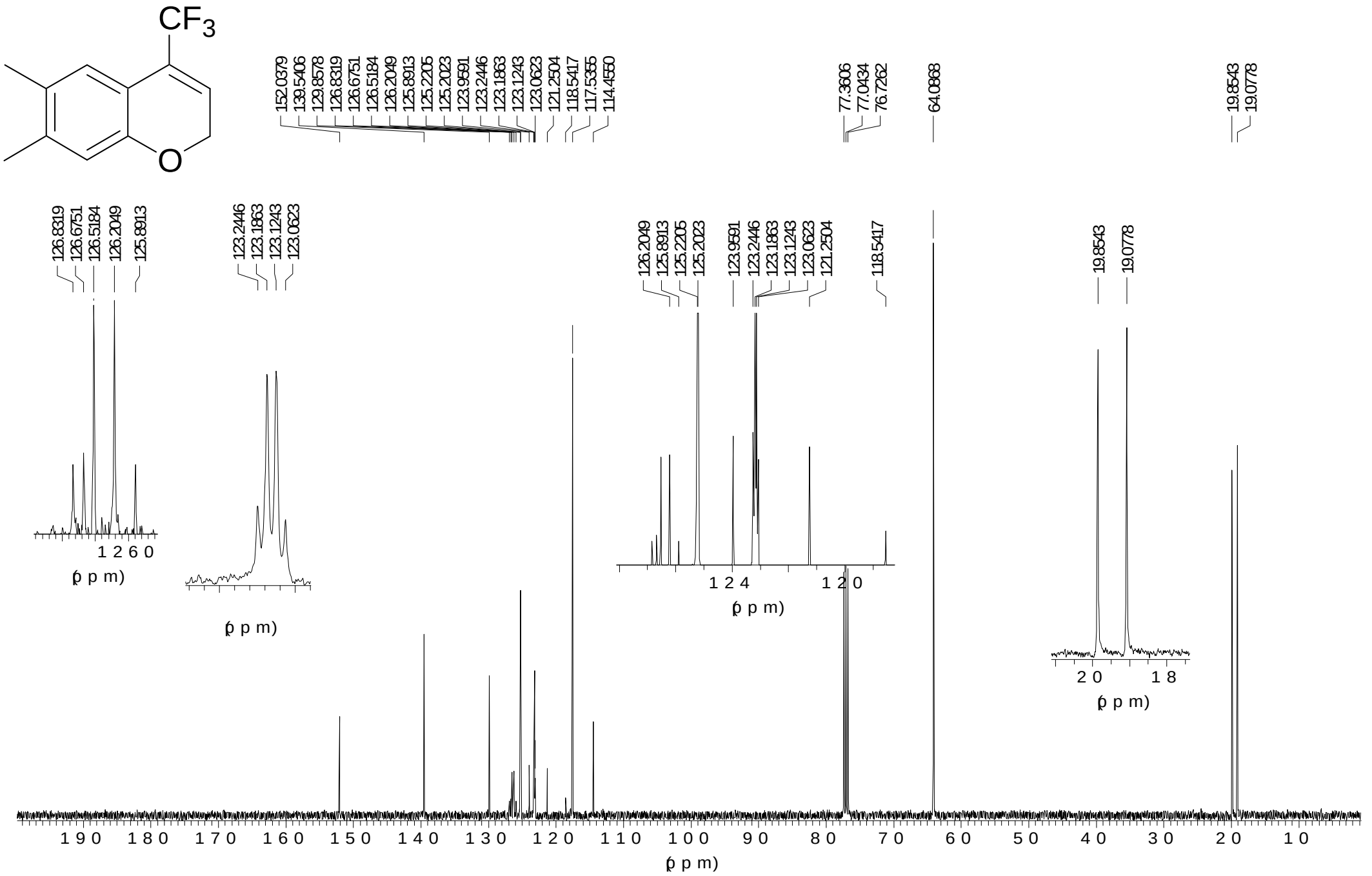
Compound **2f** spectrum NMR ^{13}C in $CDCl_3$



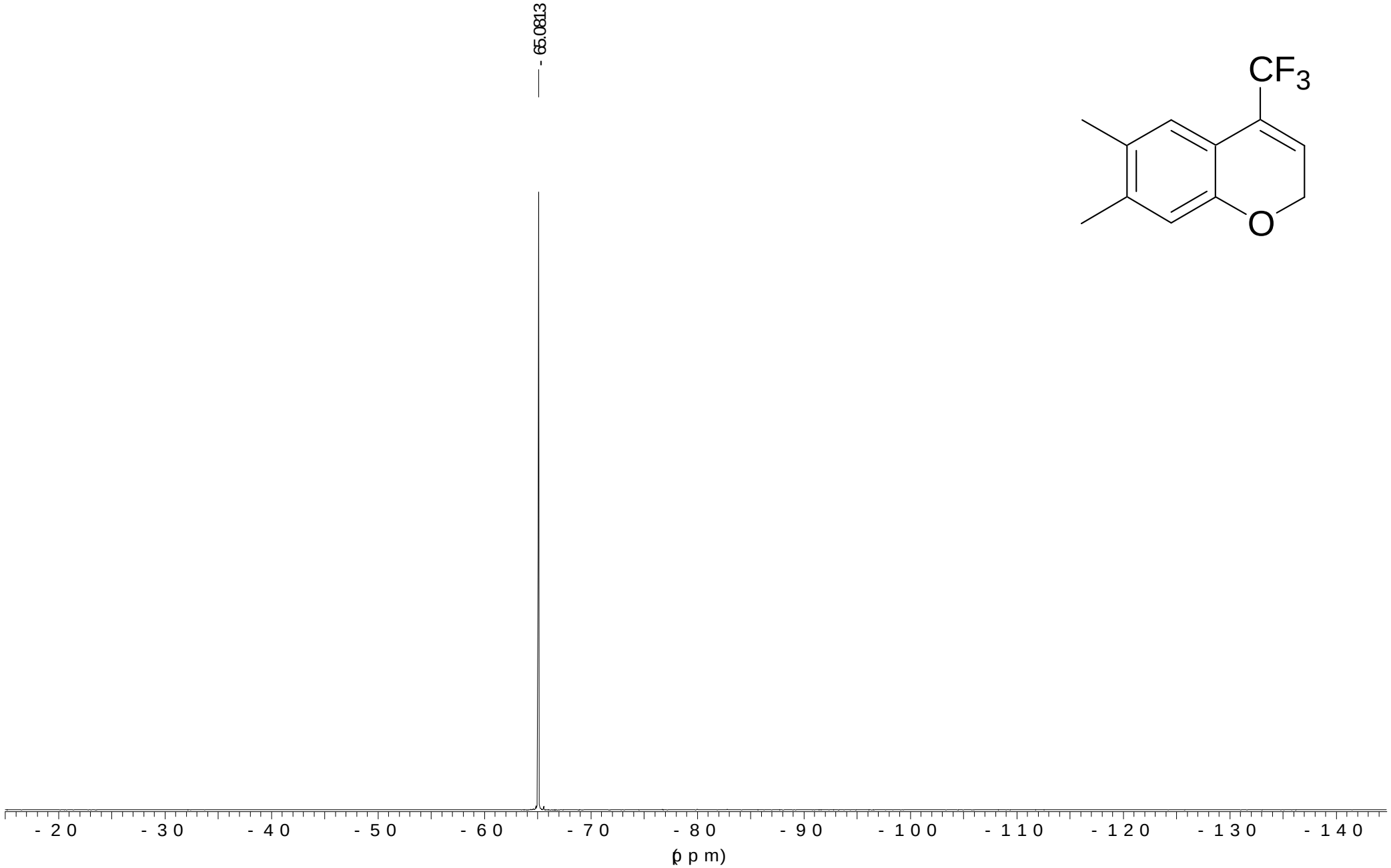
Compound **2f** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



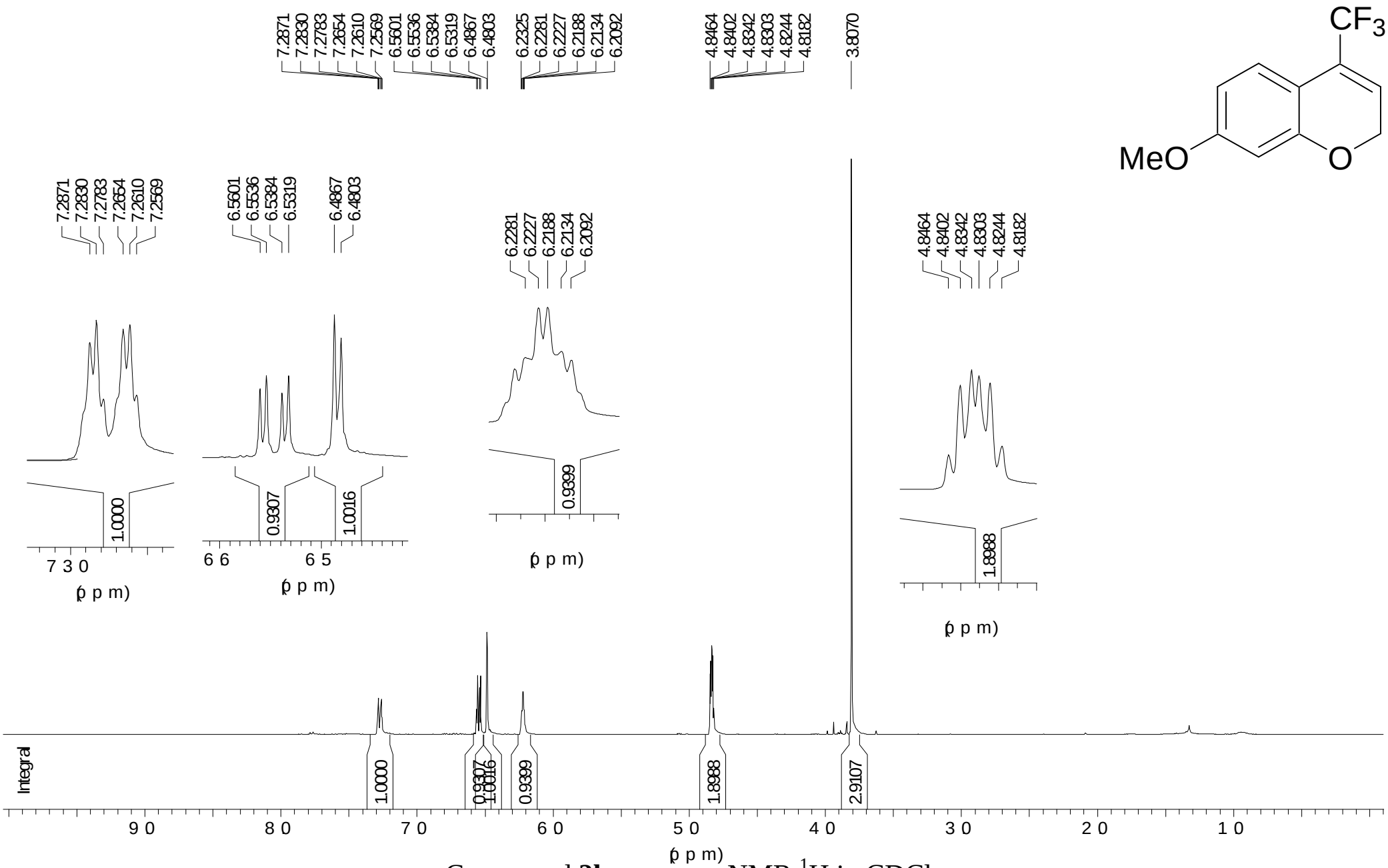
Compound **2g** spectrum NMR ^{1}H in $CDCl_3$



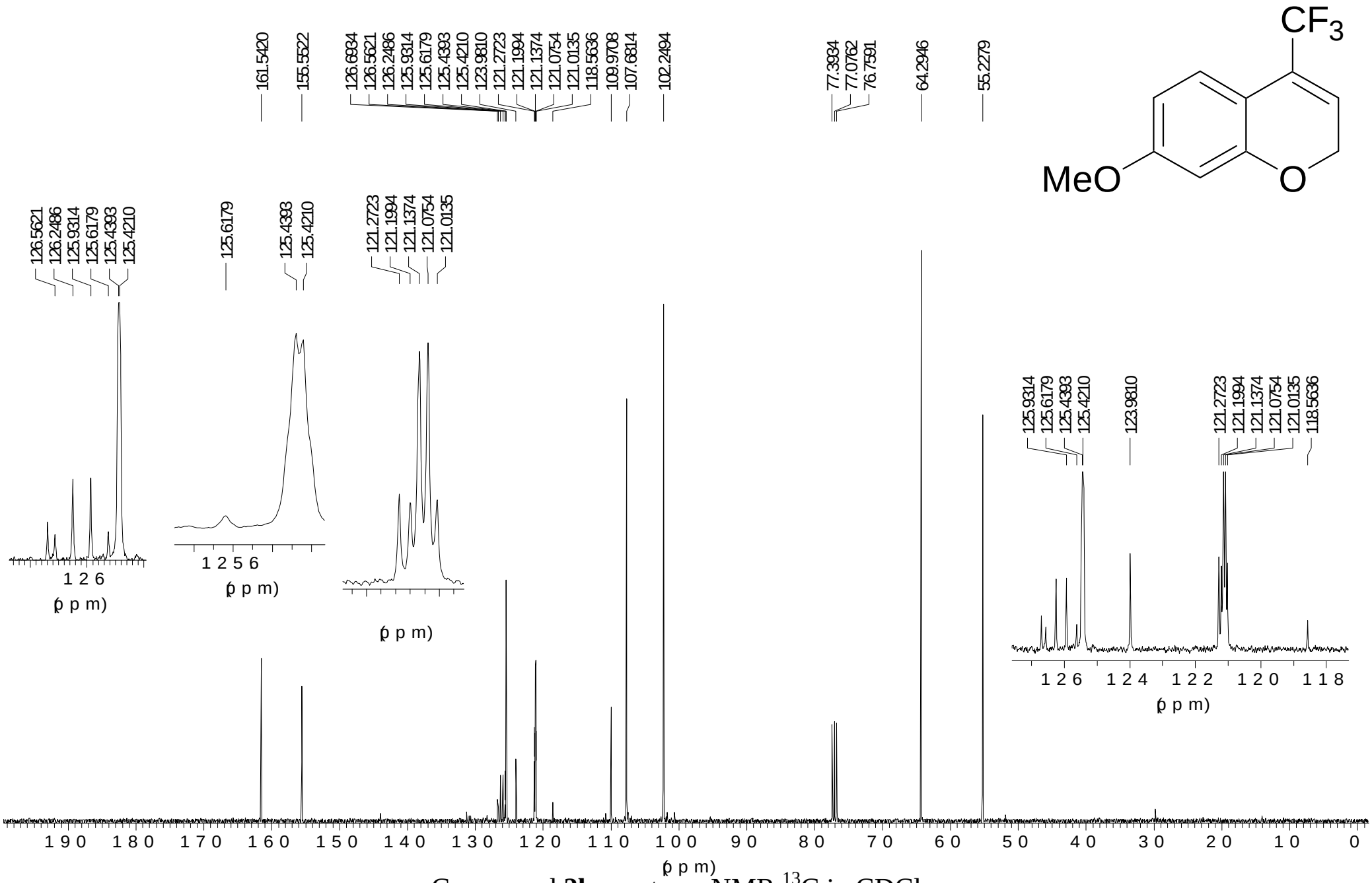
Compound **2g** spectrum NMR ^{13}C in $CDCl_3$



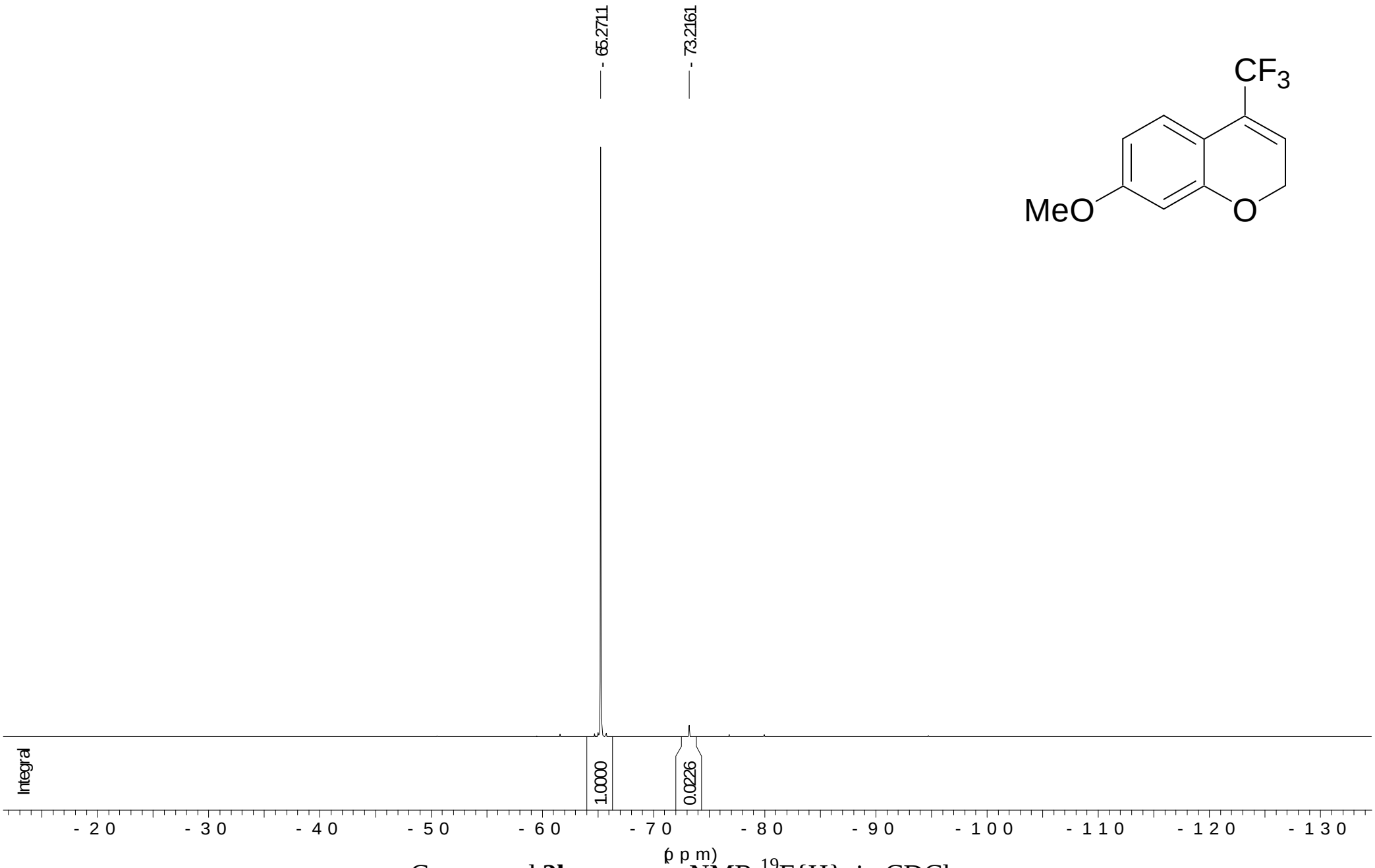
Compound **2g** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



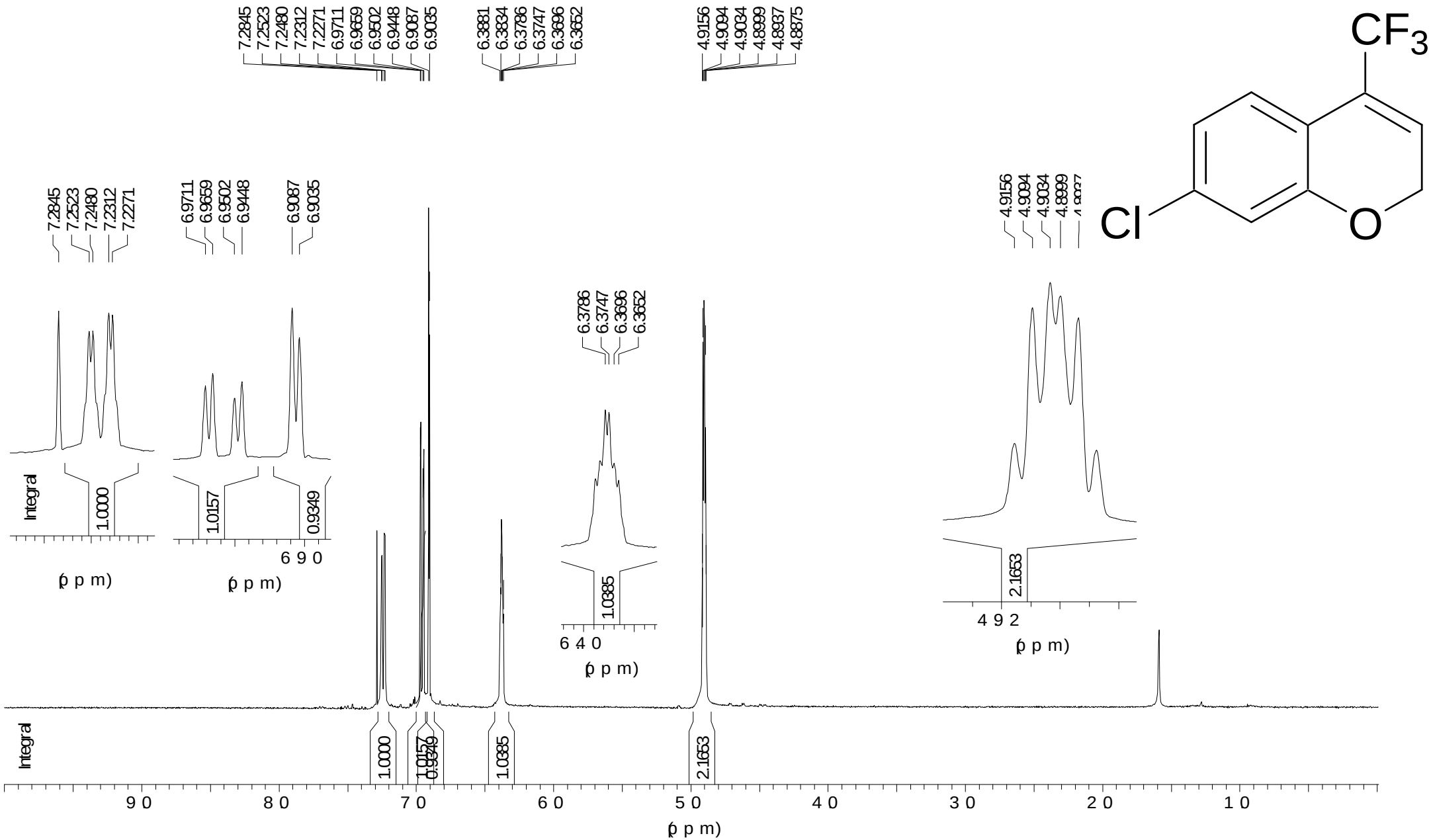
Compound **2h** spectrum NMR ^{1}H in $CDCl_3$



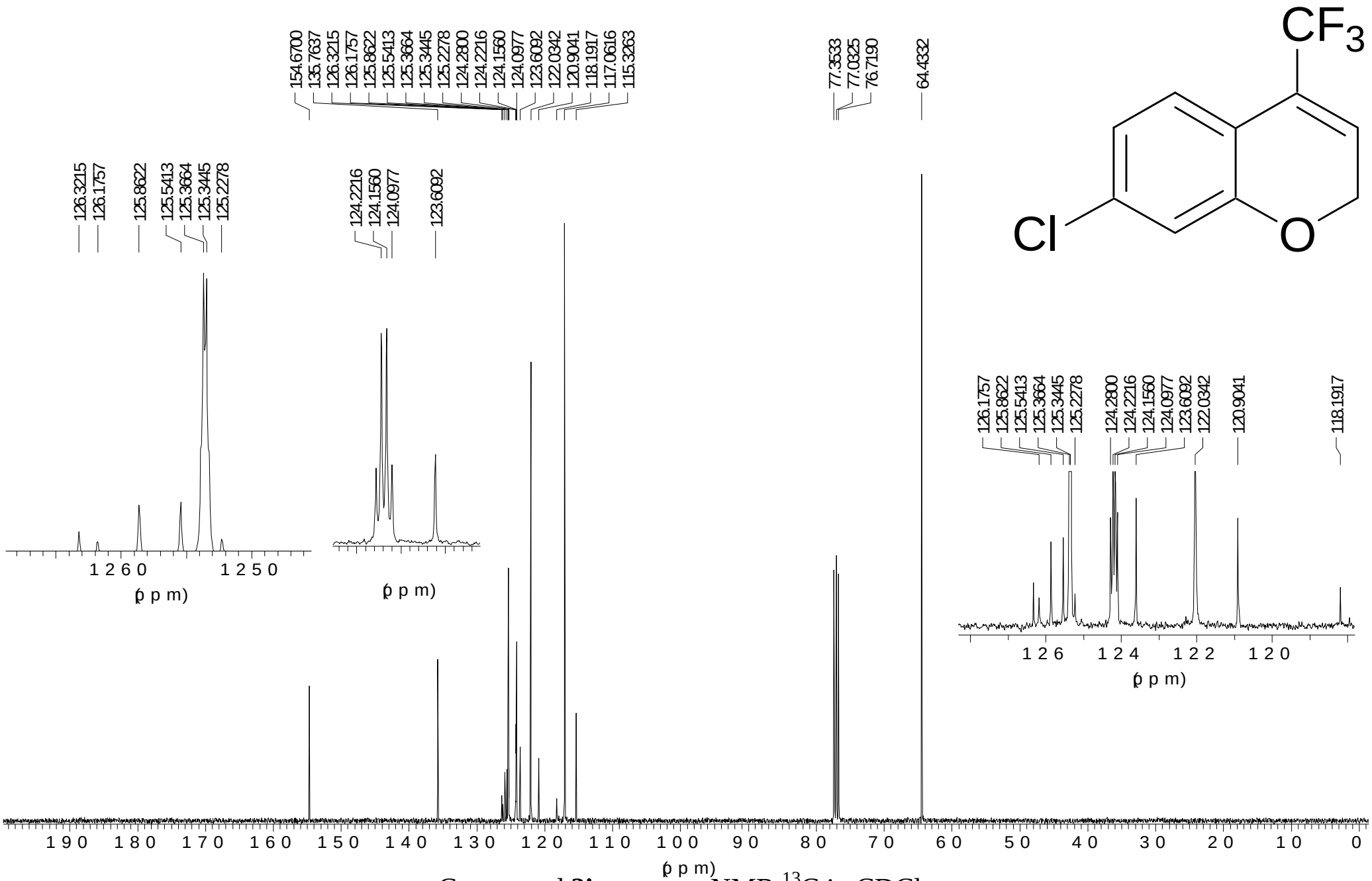
Compound **2h** spectrum NMR ^{13}C in $CDCl_3$



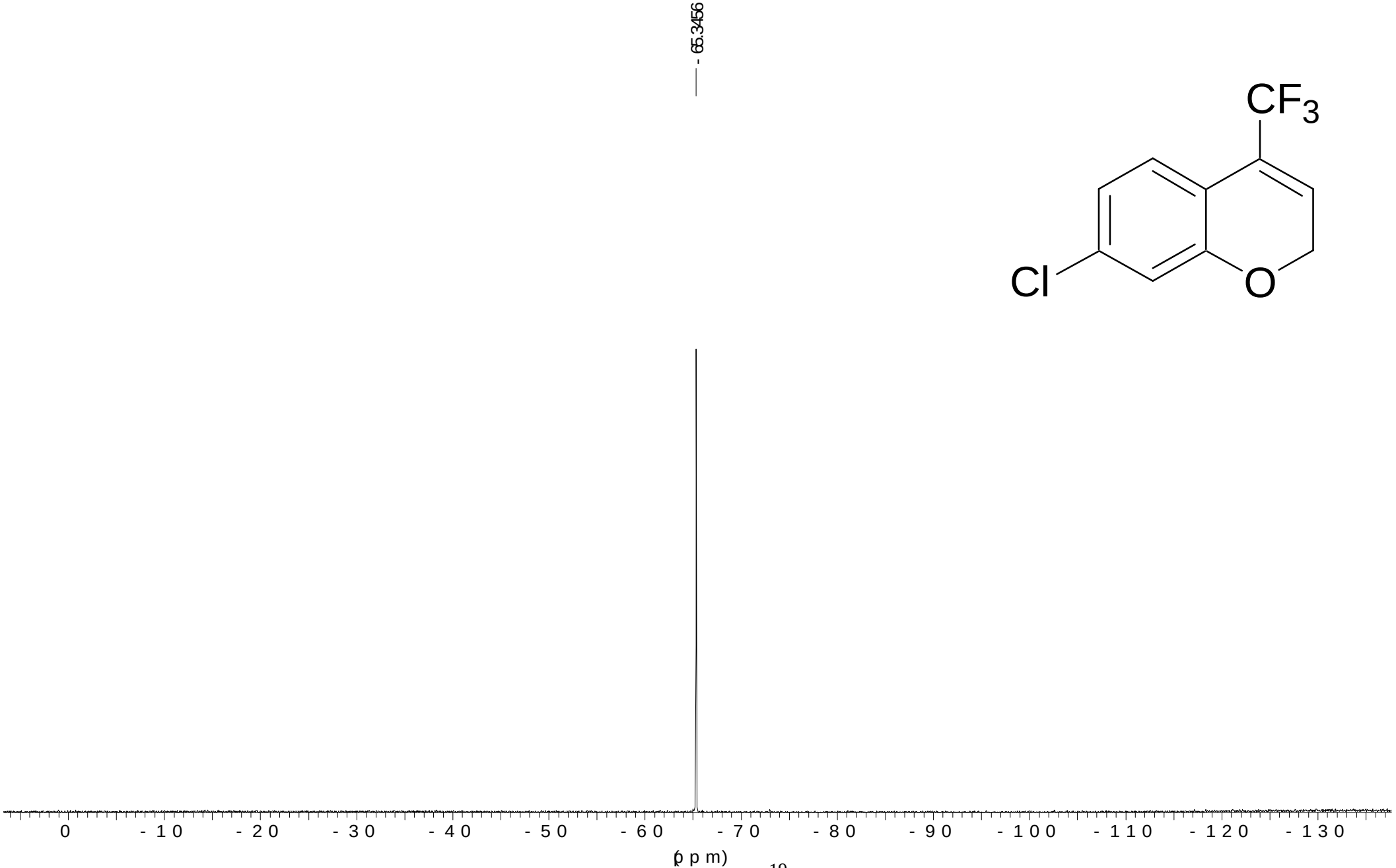
Compound **2h** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



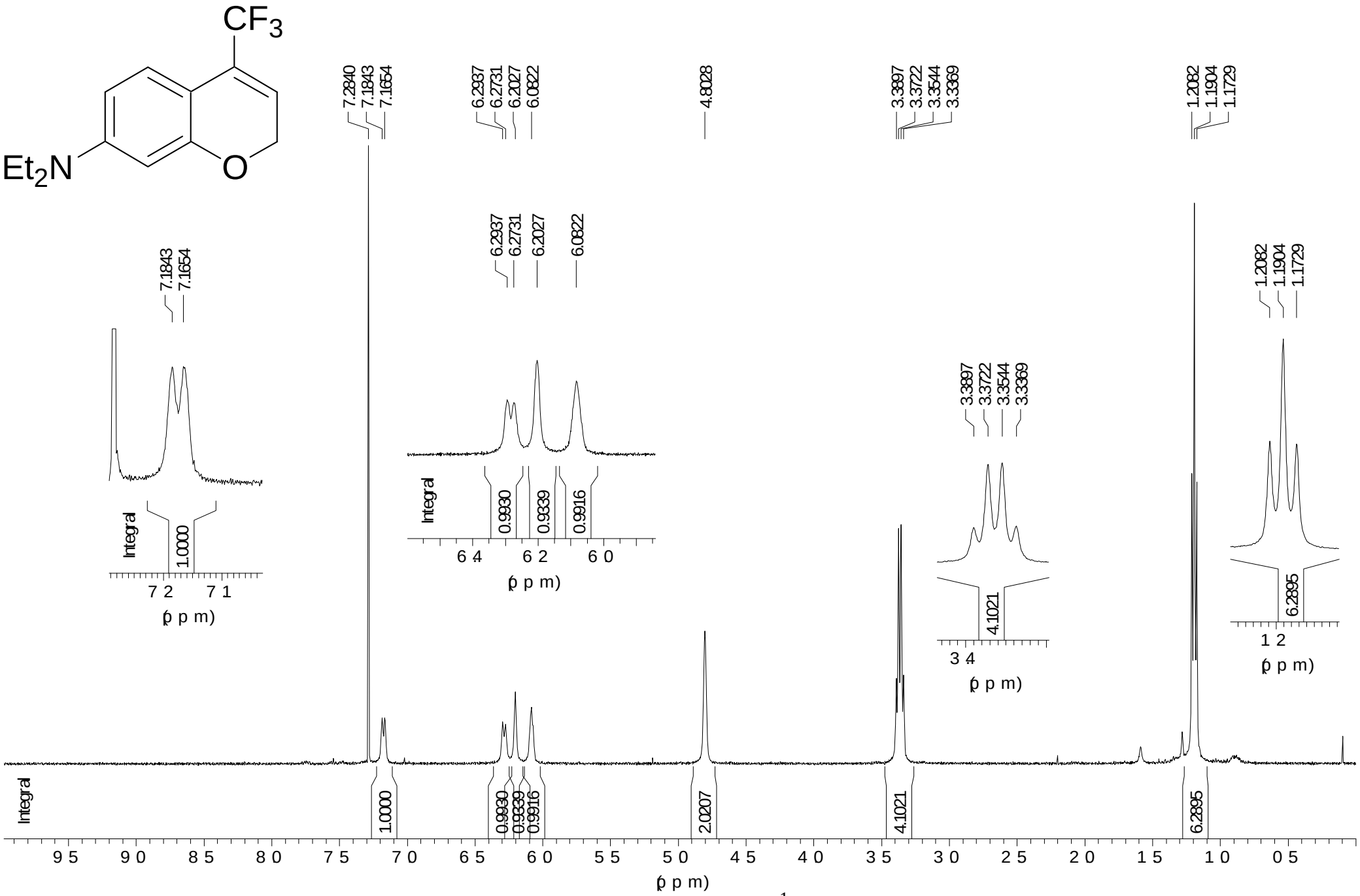
Compound **2i** spectrum NMR ^{1}H in $CDCl_3$



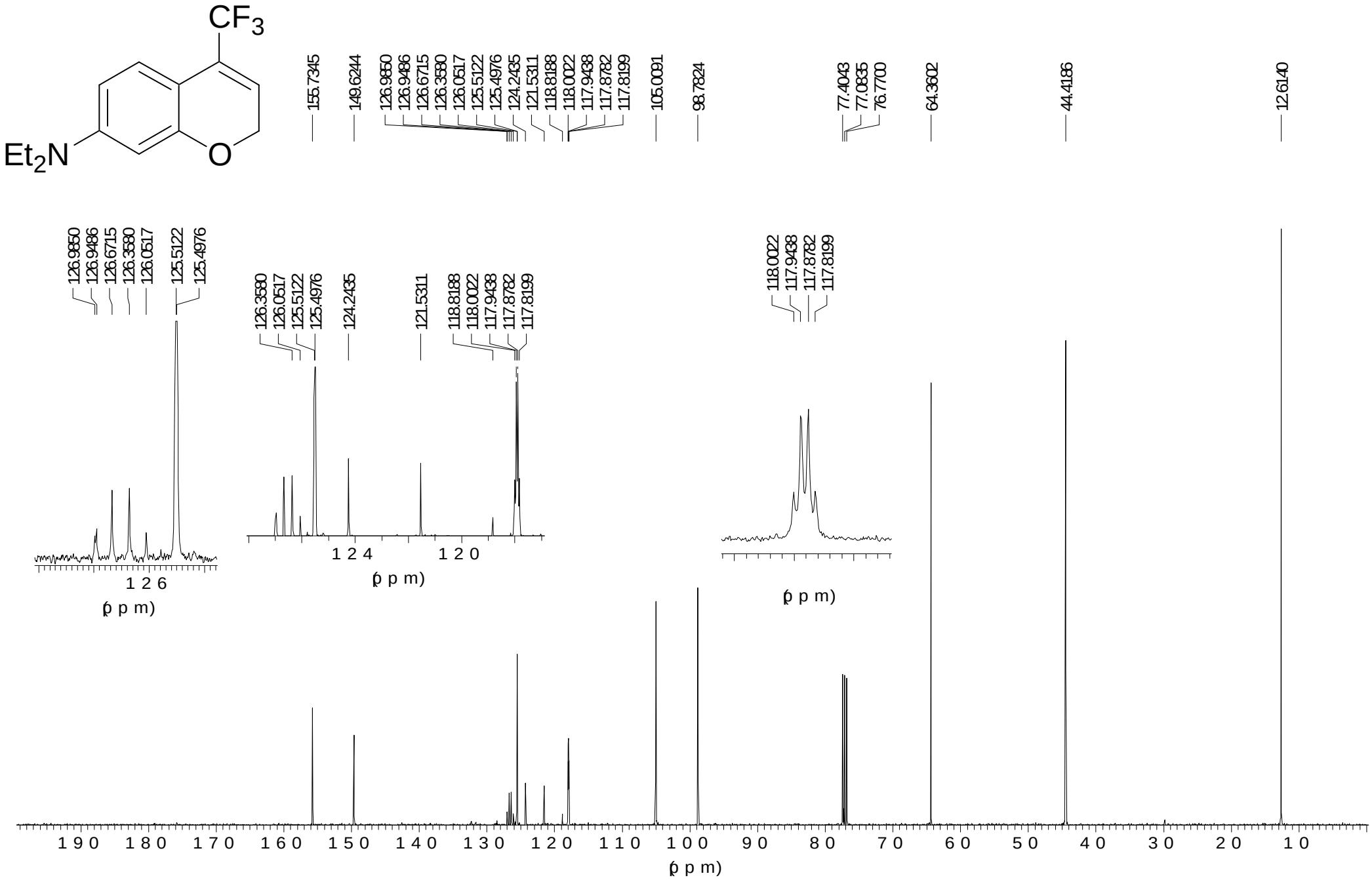
Compound **2i** spectrum NMR ^{13}C in $CDCl_3$



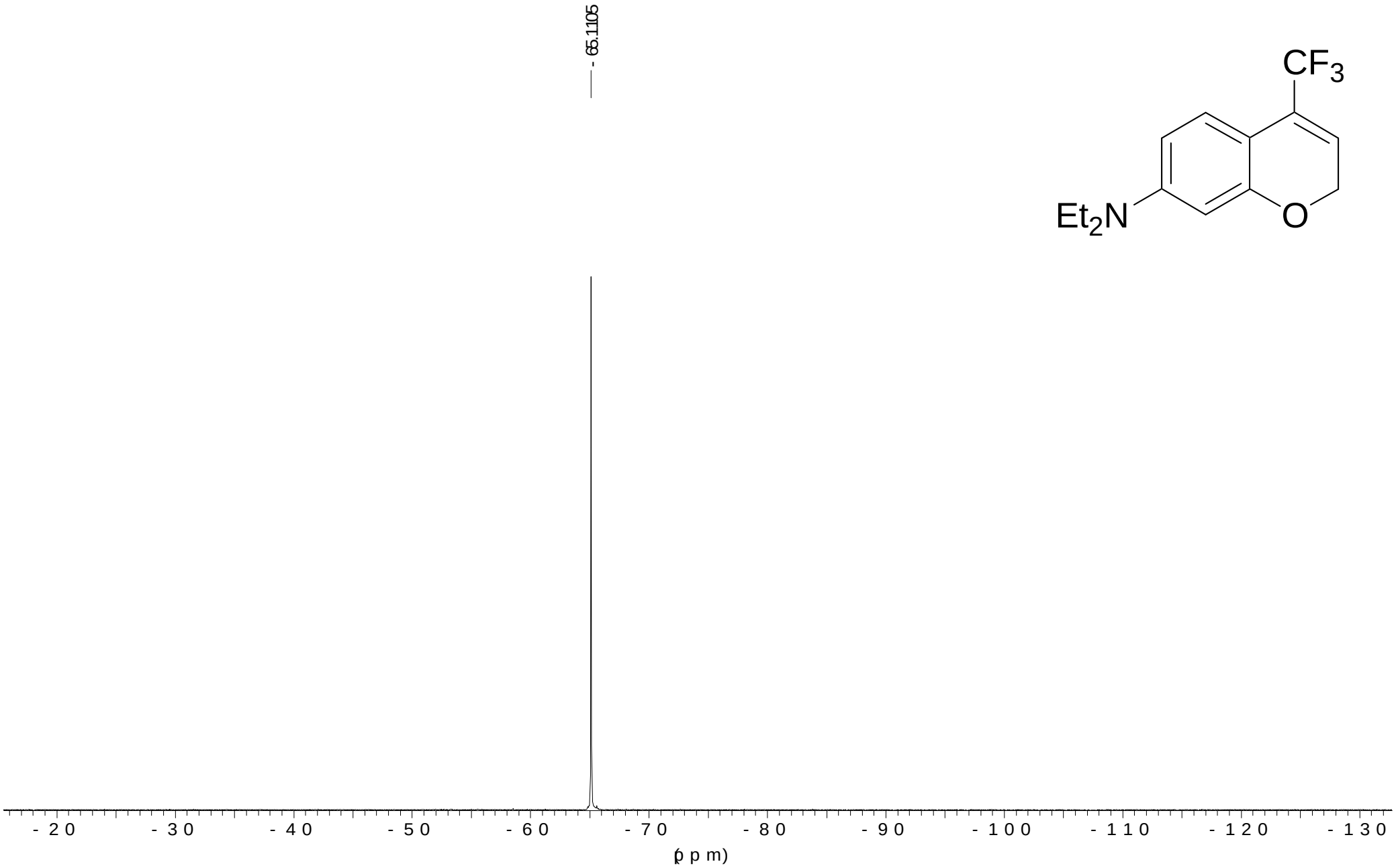
Compound **2i** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



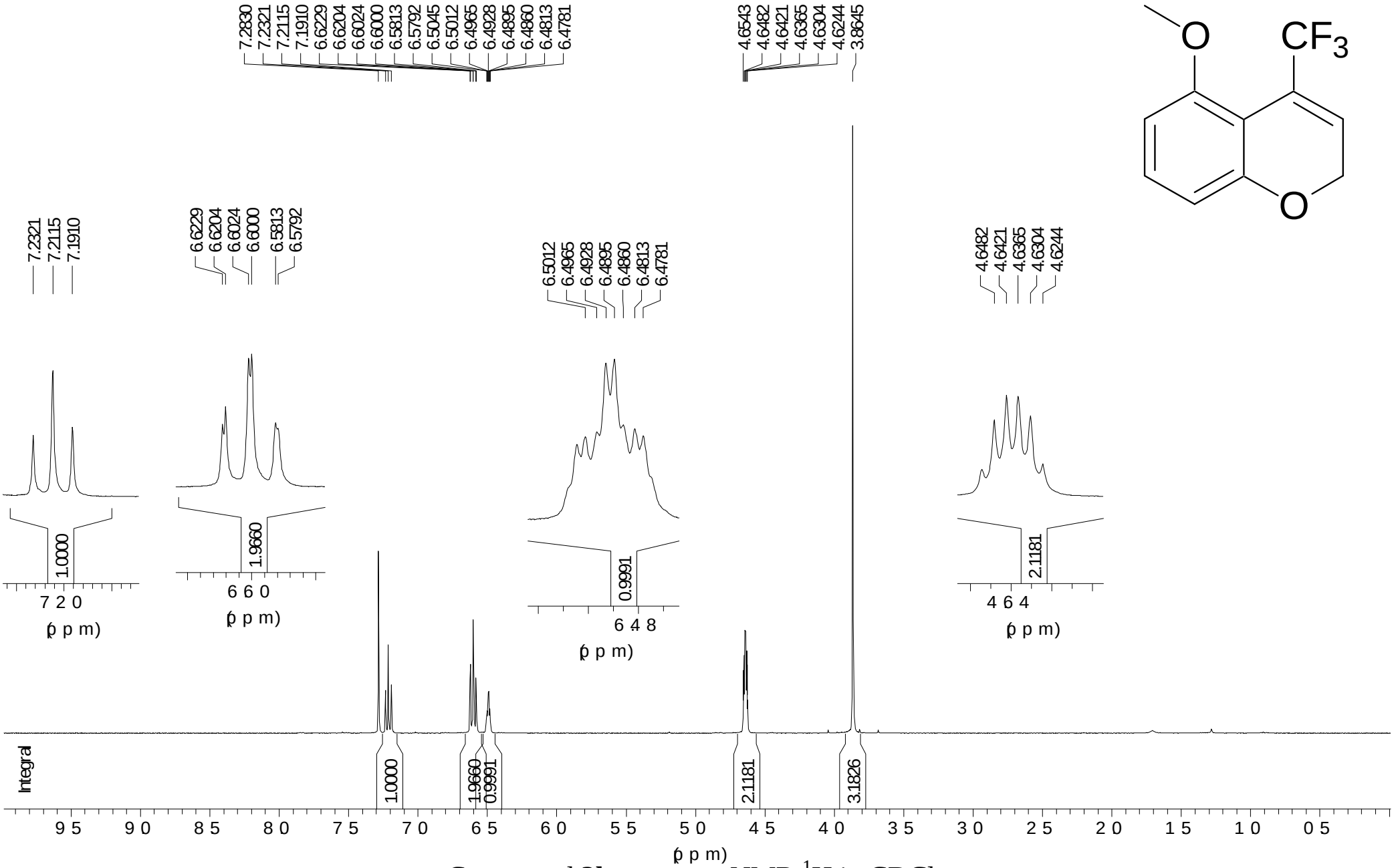
Compound **2j** spectrum NMR ^{1}H in $CDCl_3$



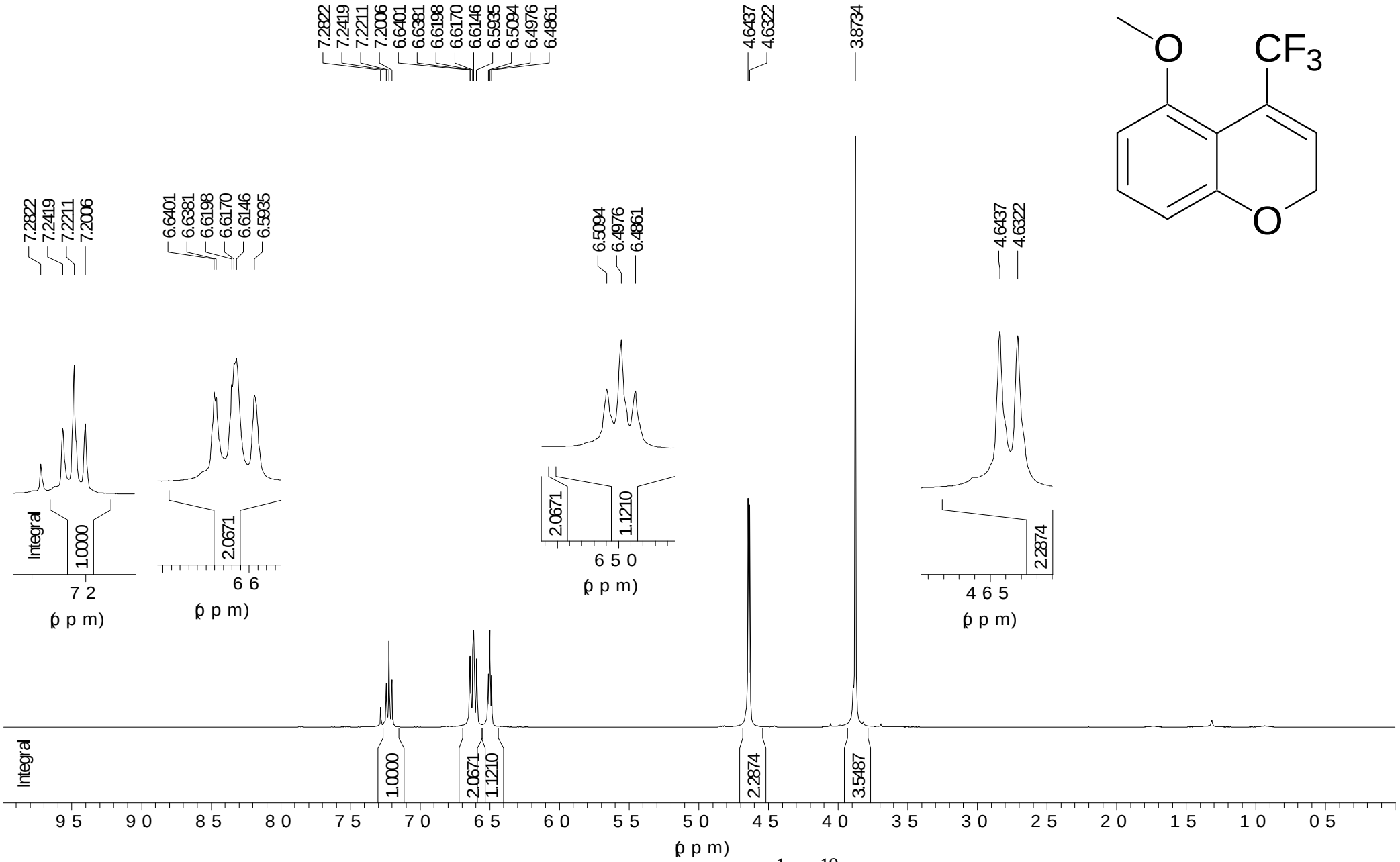
Compound **2j** spectrum NMR ^{13}C in $CDCl_3$



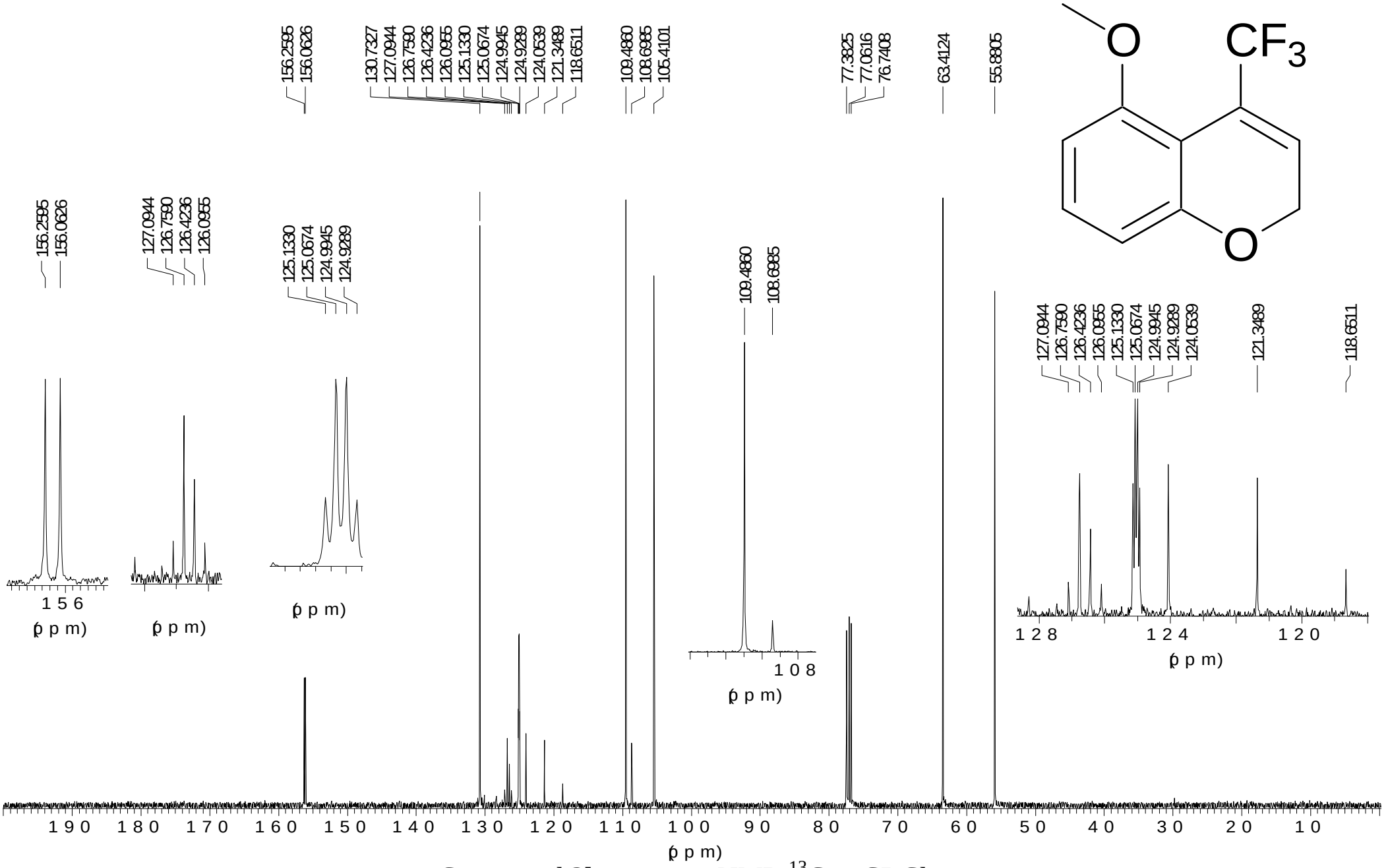
Compound **2j** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



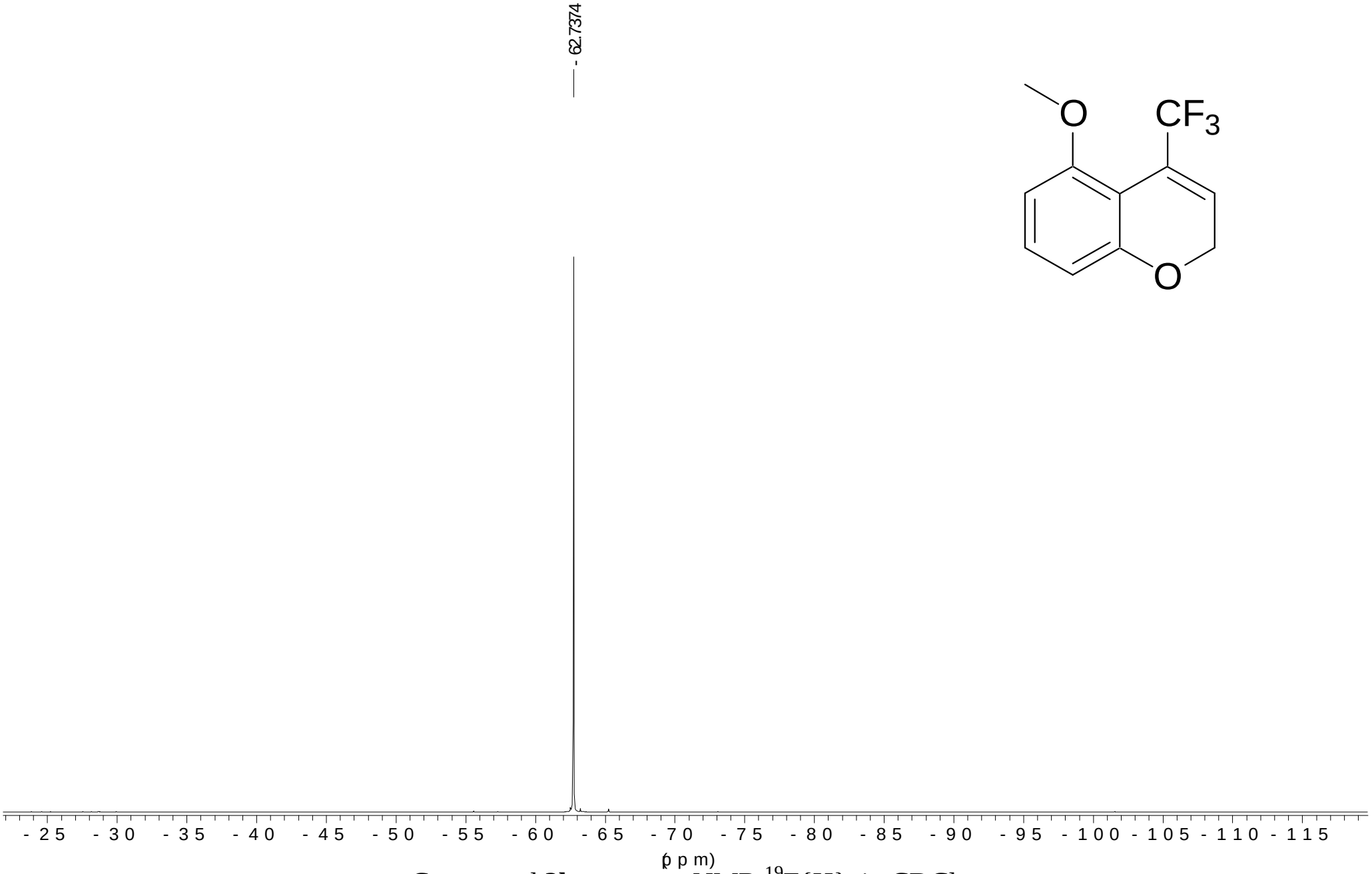
Compound **2k** spectrum NMR ^{1}H in $CDCl_3$



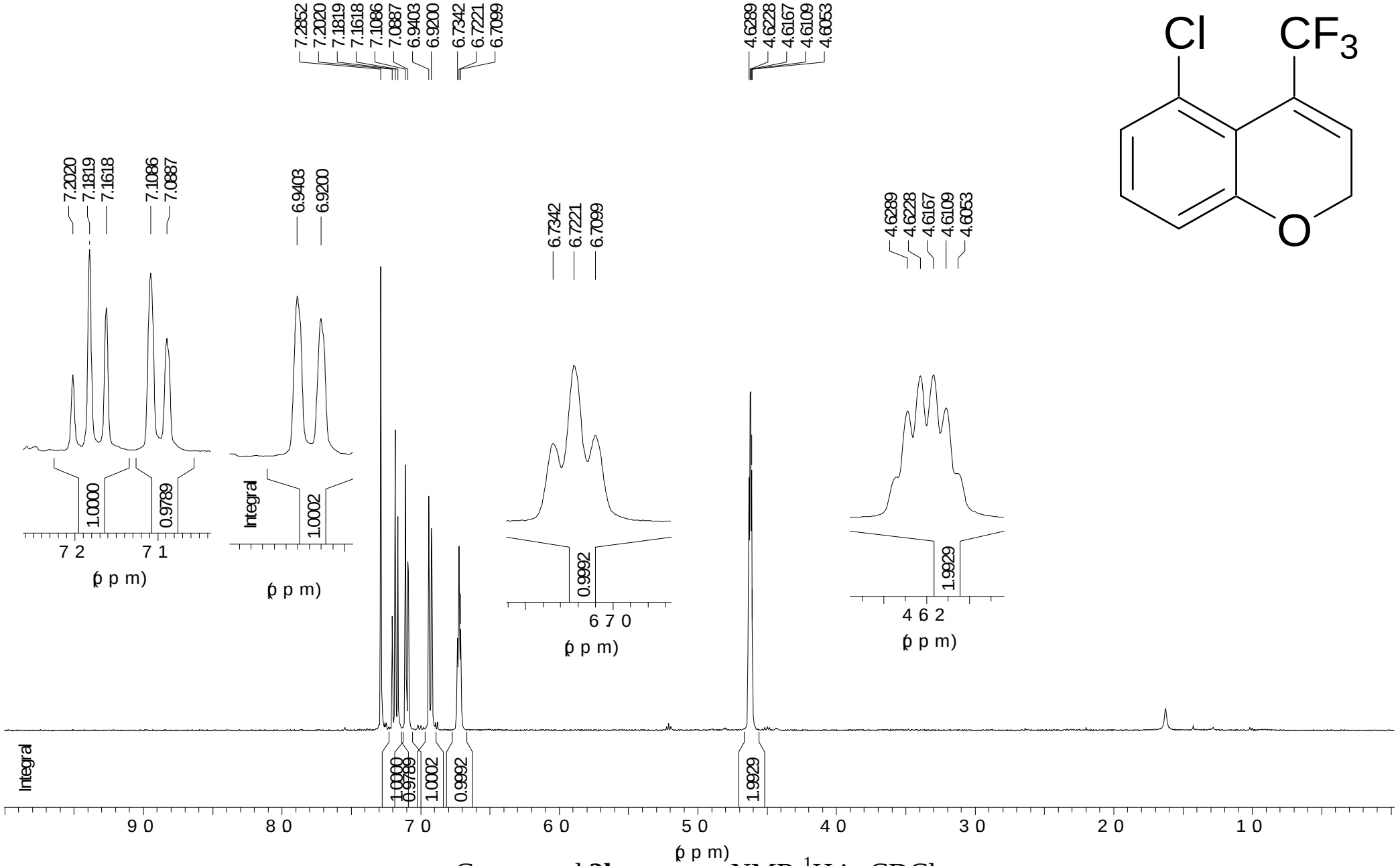
Compound **2k** spectrum NMR $^{1}H\{^{19}F\}$ in $CDCl_3$



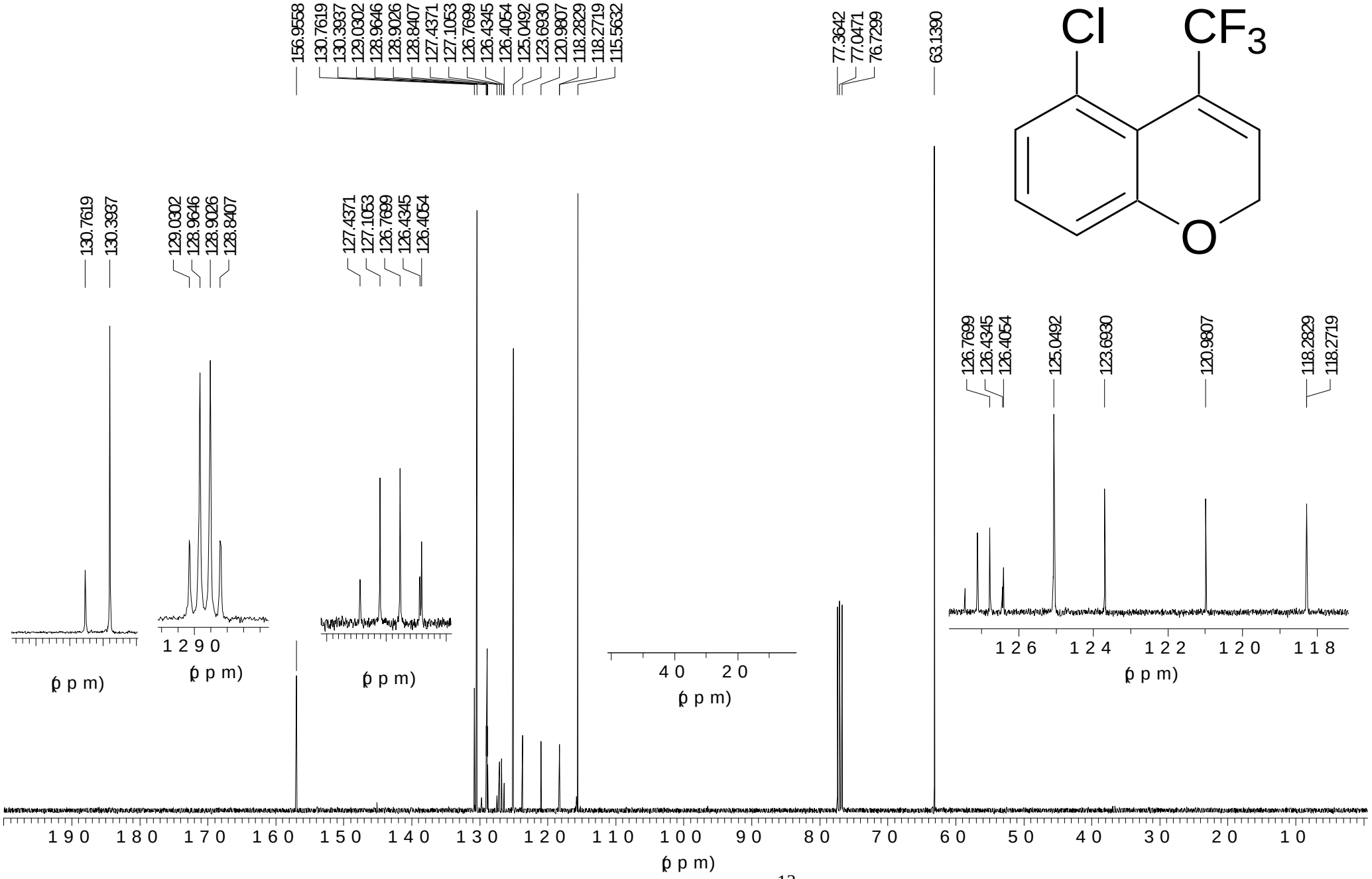
Compound **2k** spectrum NMR ^{13}C in $CDCl_3$



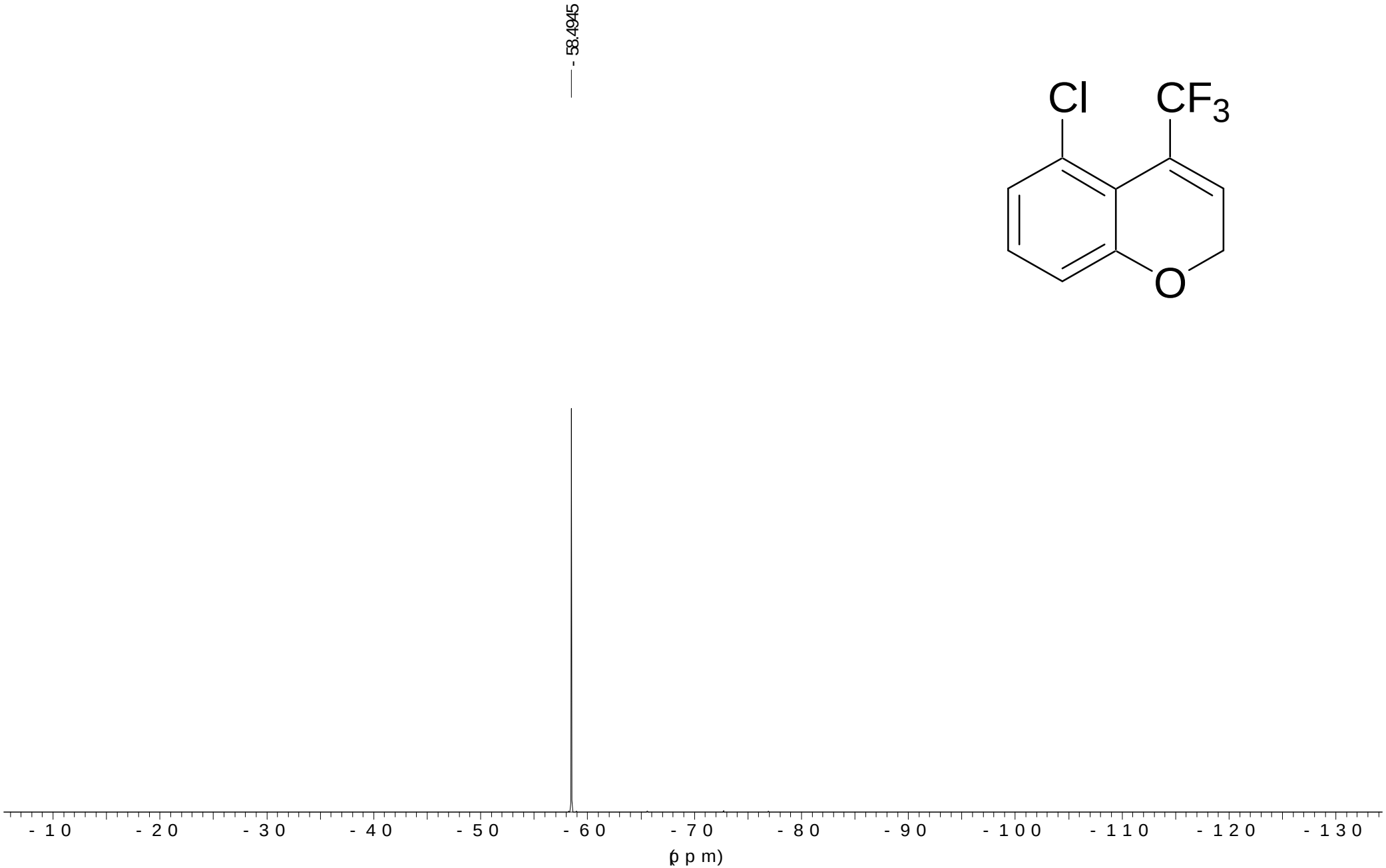
Compound **2k** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



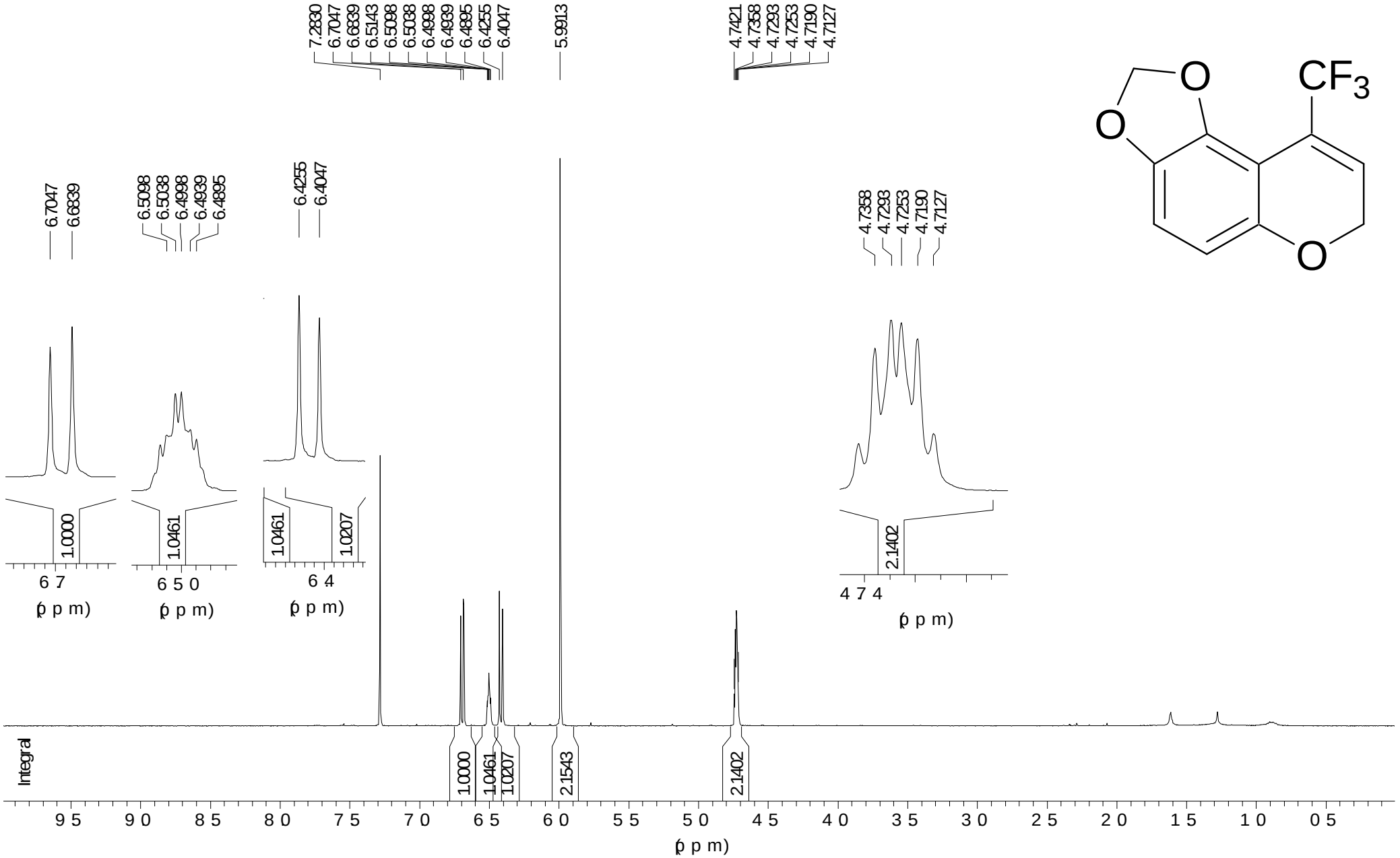
Compound **2l** spectrum NMR ^{1}H in $CDCl_3$



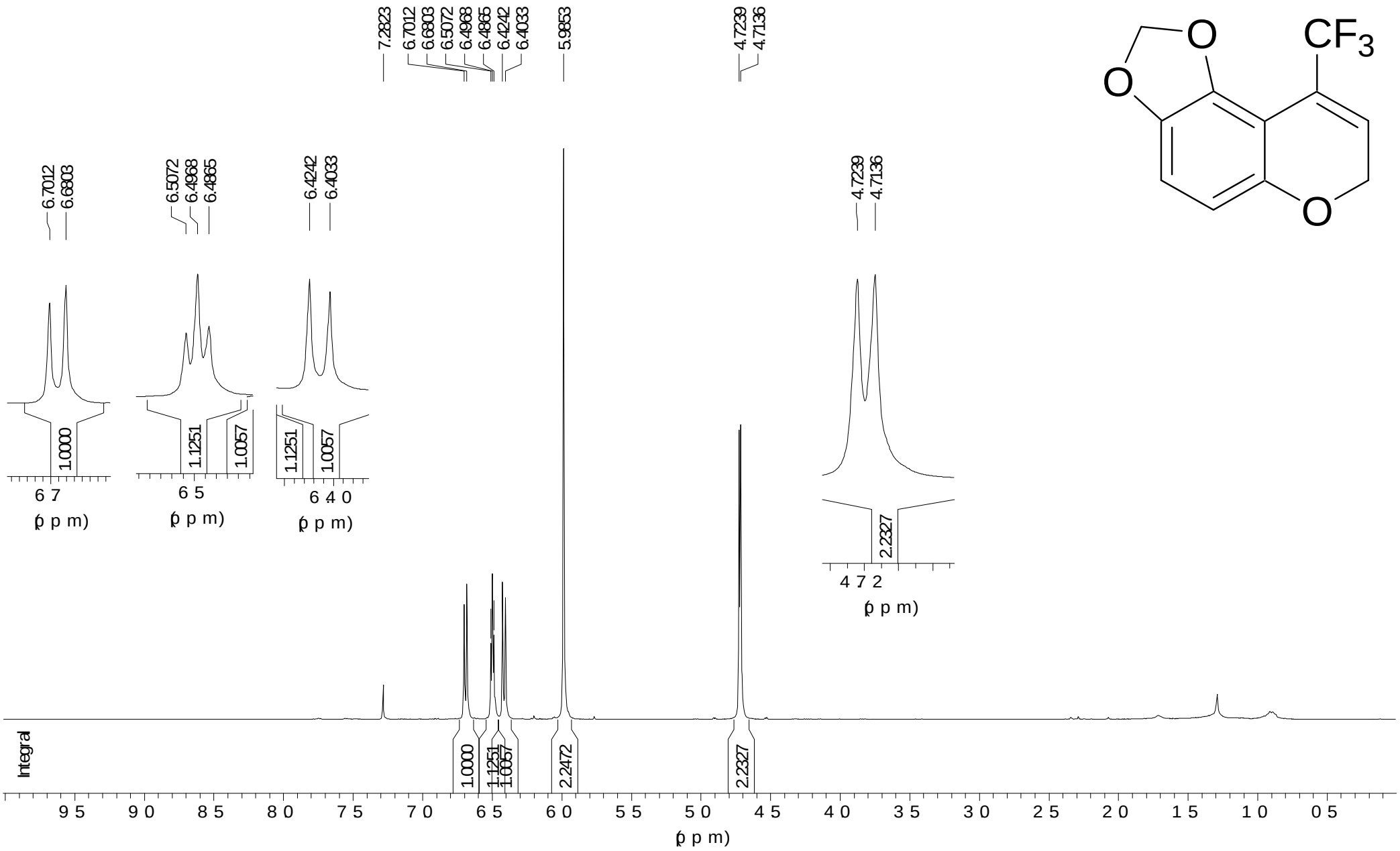
Compound **2l** spectrum NMR ^{13}C in $CDCl_3$



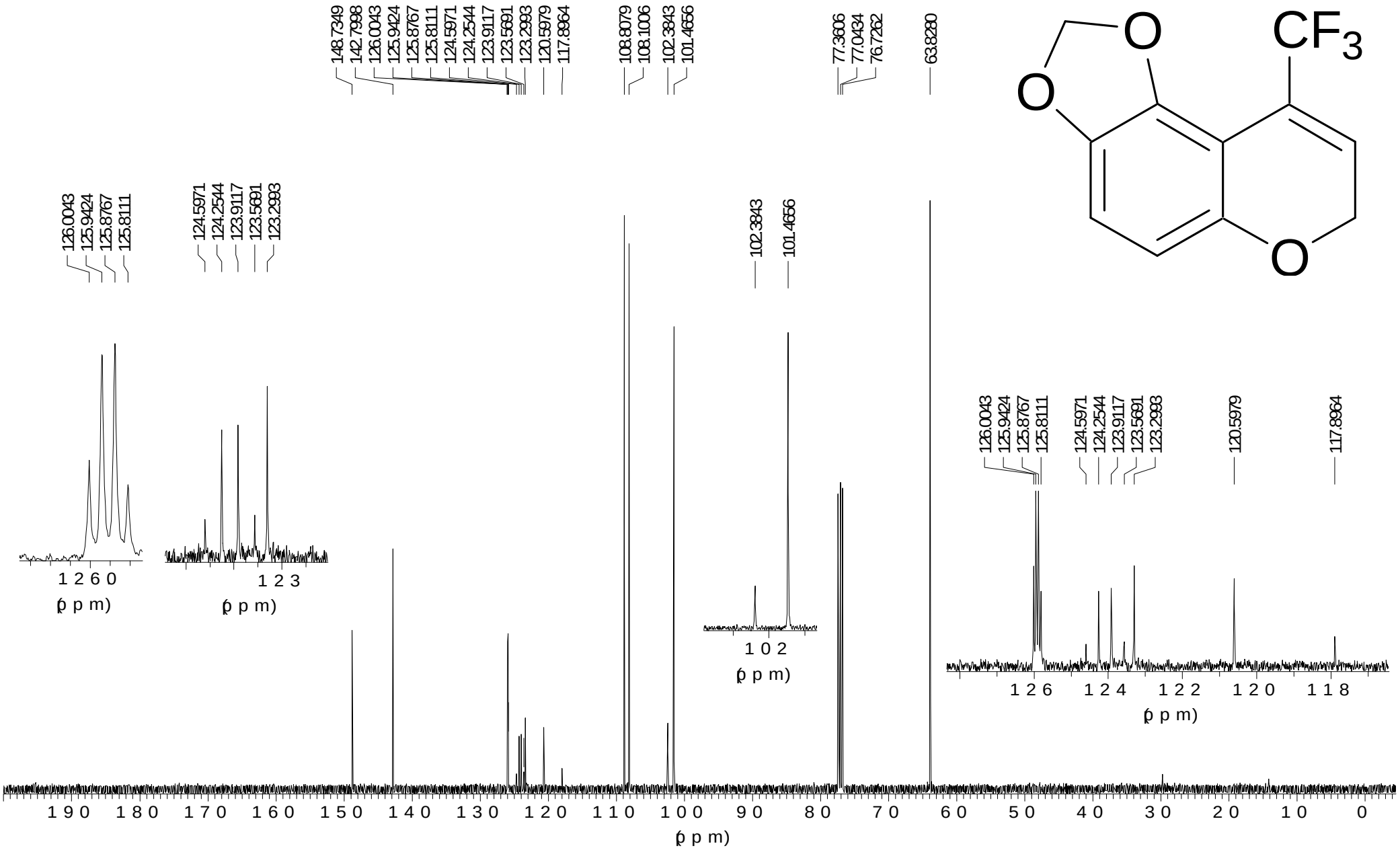
Compound **2l** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



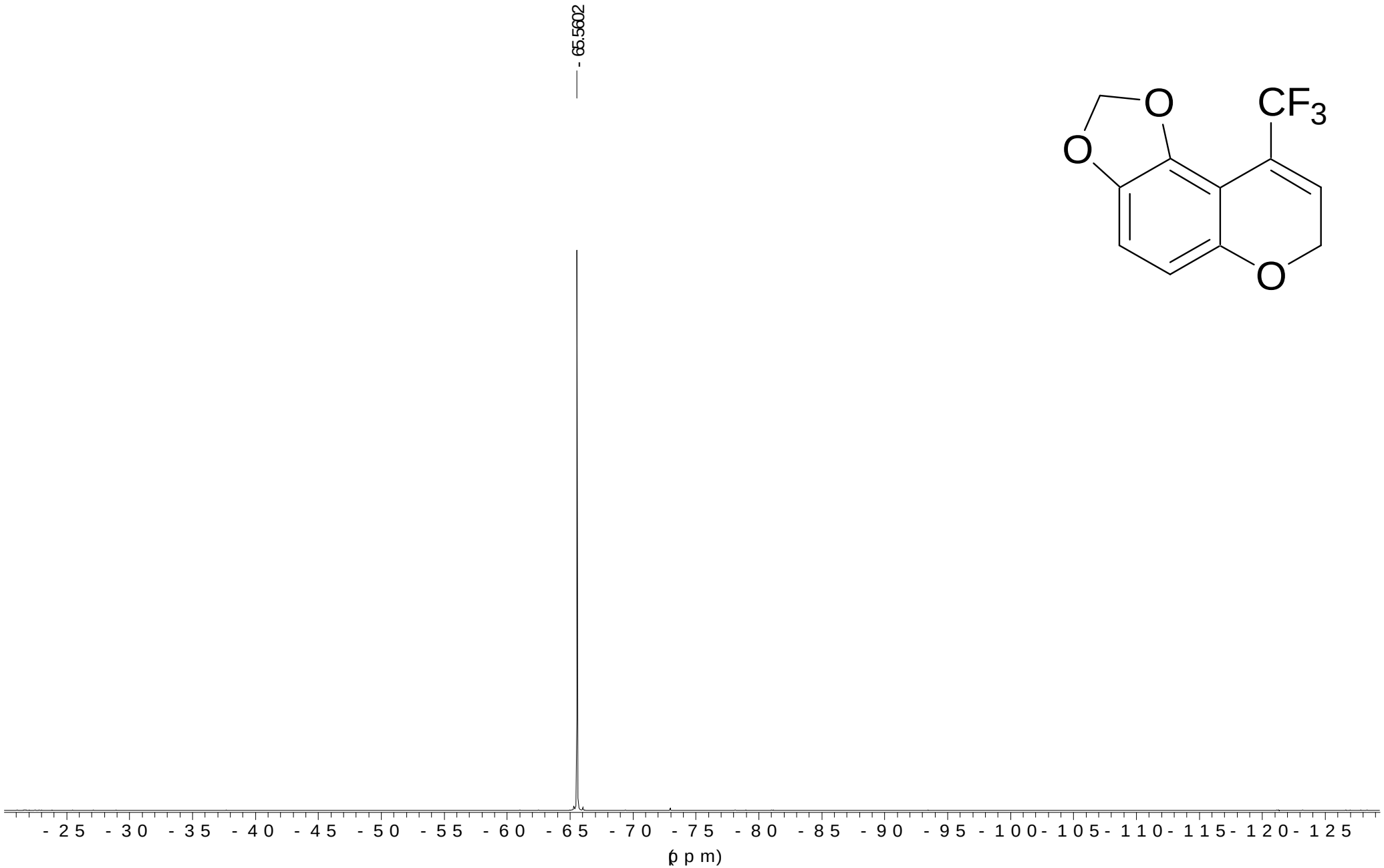
Compound **2m** spectrum NMR ^{1}H in $CDCl_3$



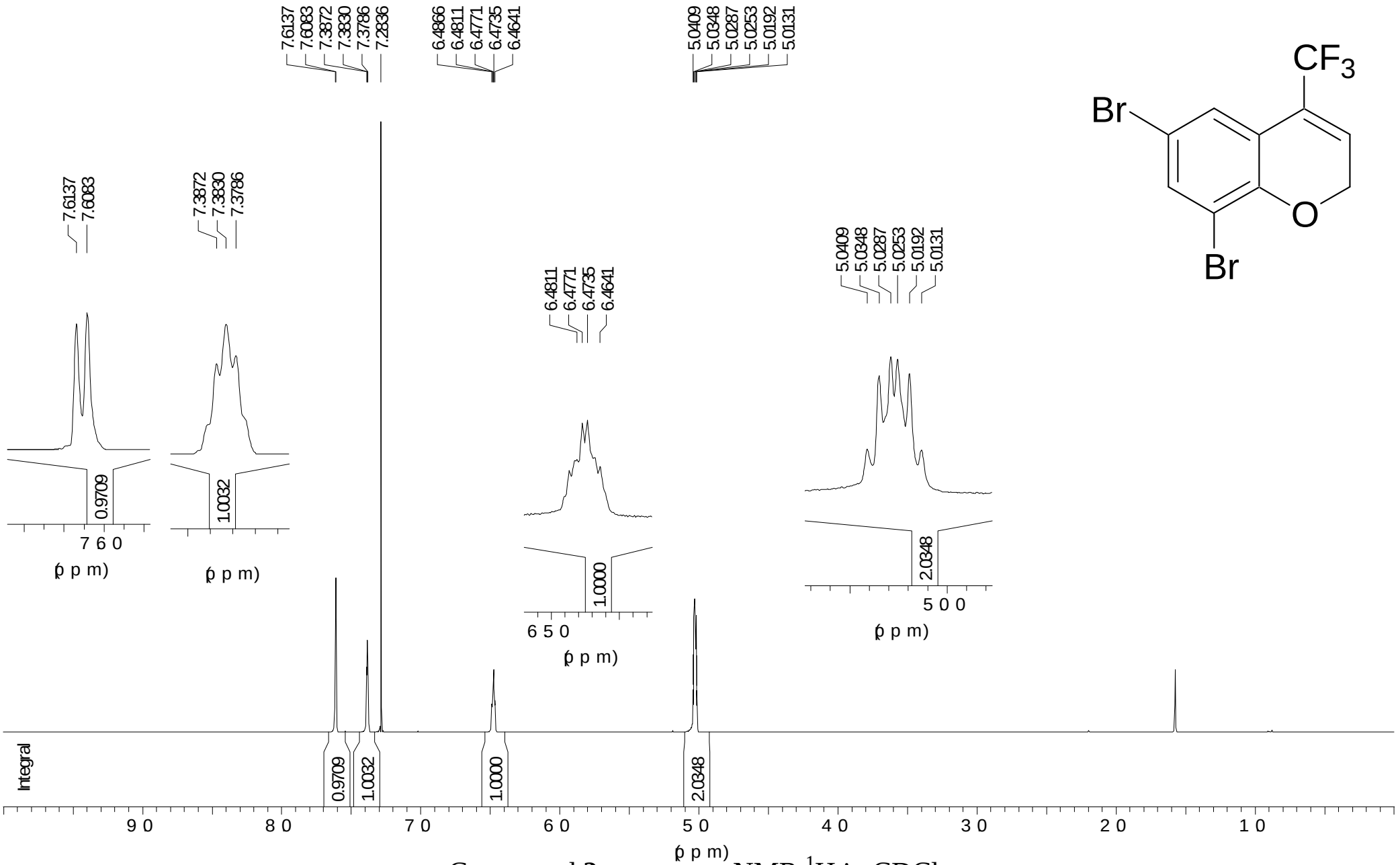
Compound **2m** spectrum NMR $^{1}H\{^{19}F\}$ in $CDCl_3$



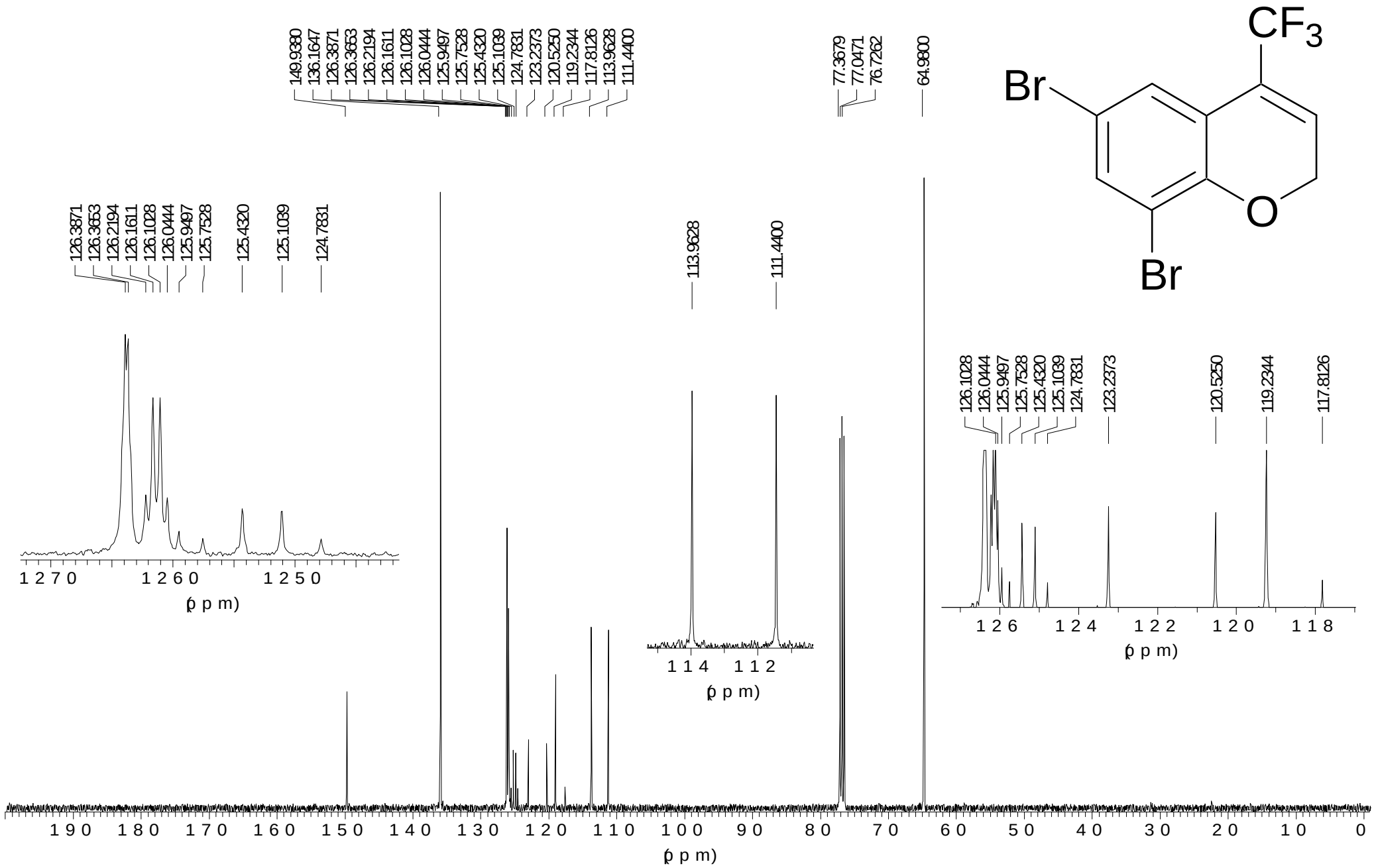
Compound **2m** spectrum NMR ^{13}C in $CDCl_3$



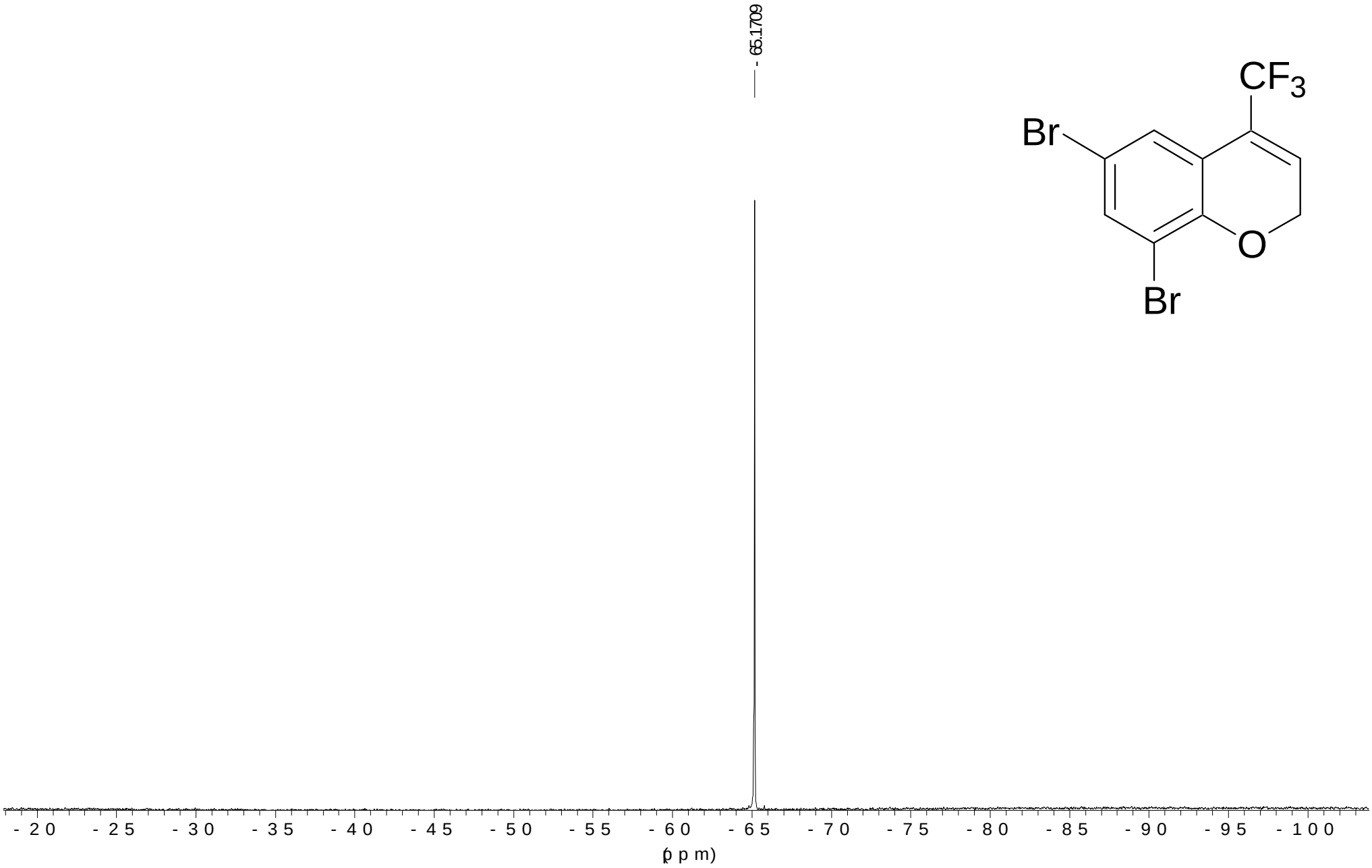
Compound **2m** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



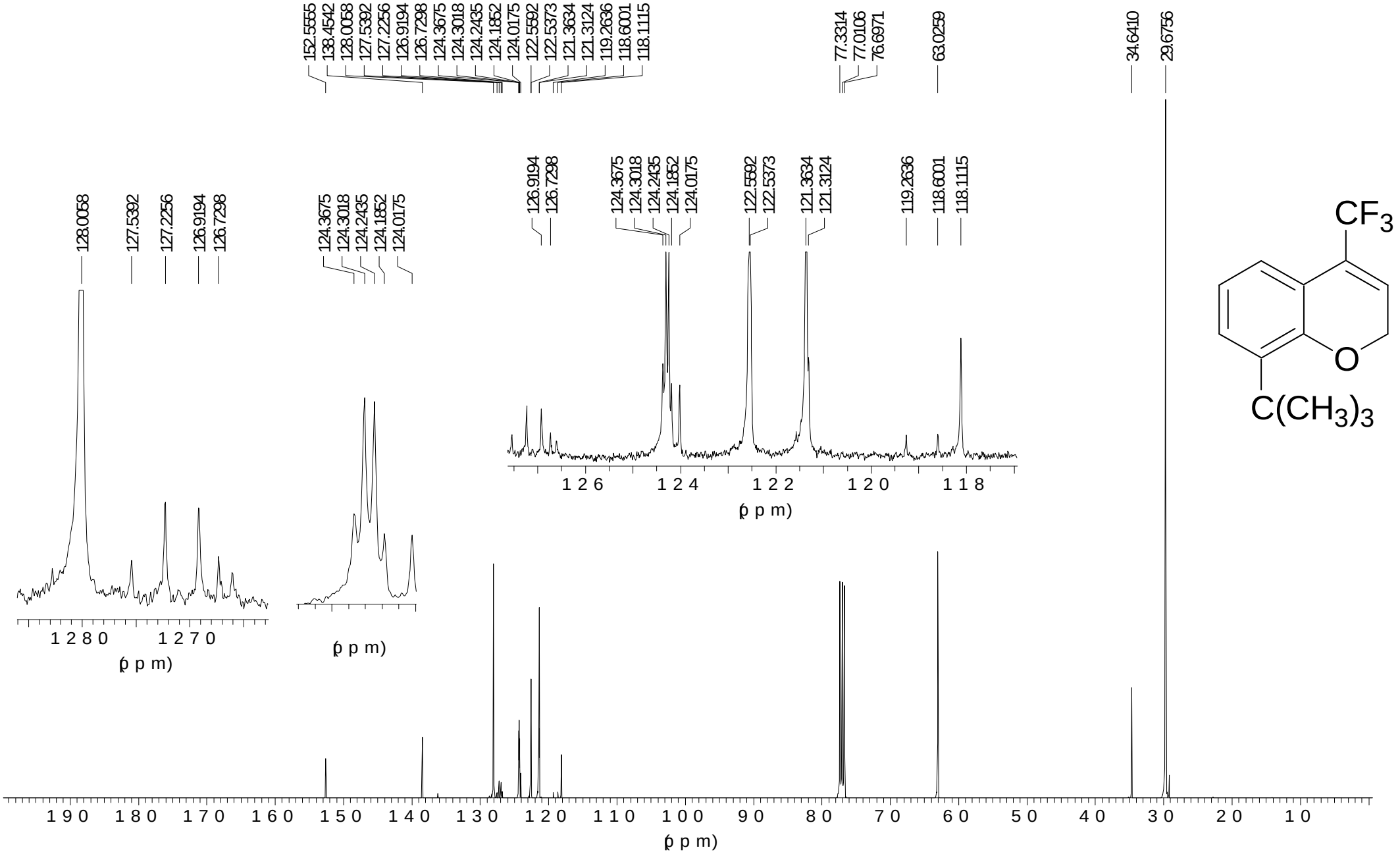
Compound **2n** spectrum NMR ^{1}H in $CDCl_3$



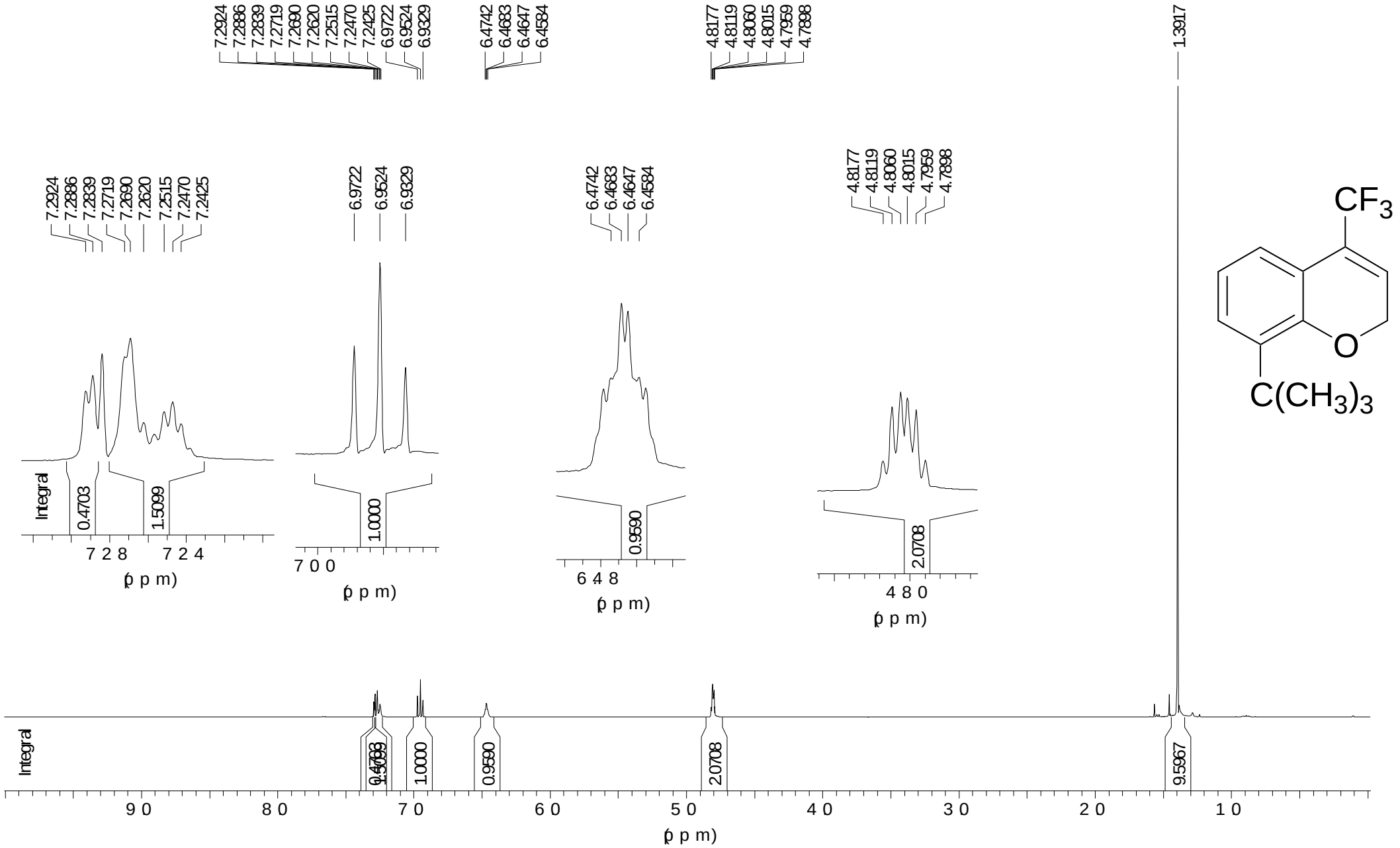
Compound **2n** spectrum NMR ^{13}C in $CDCl_3$



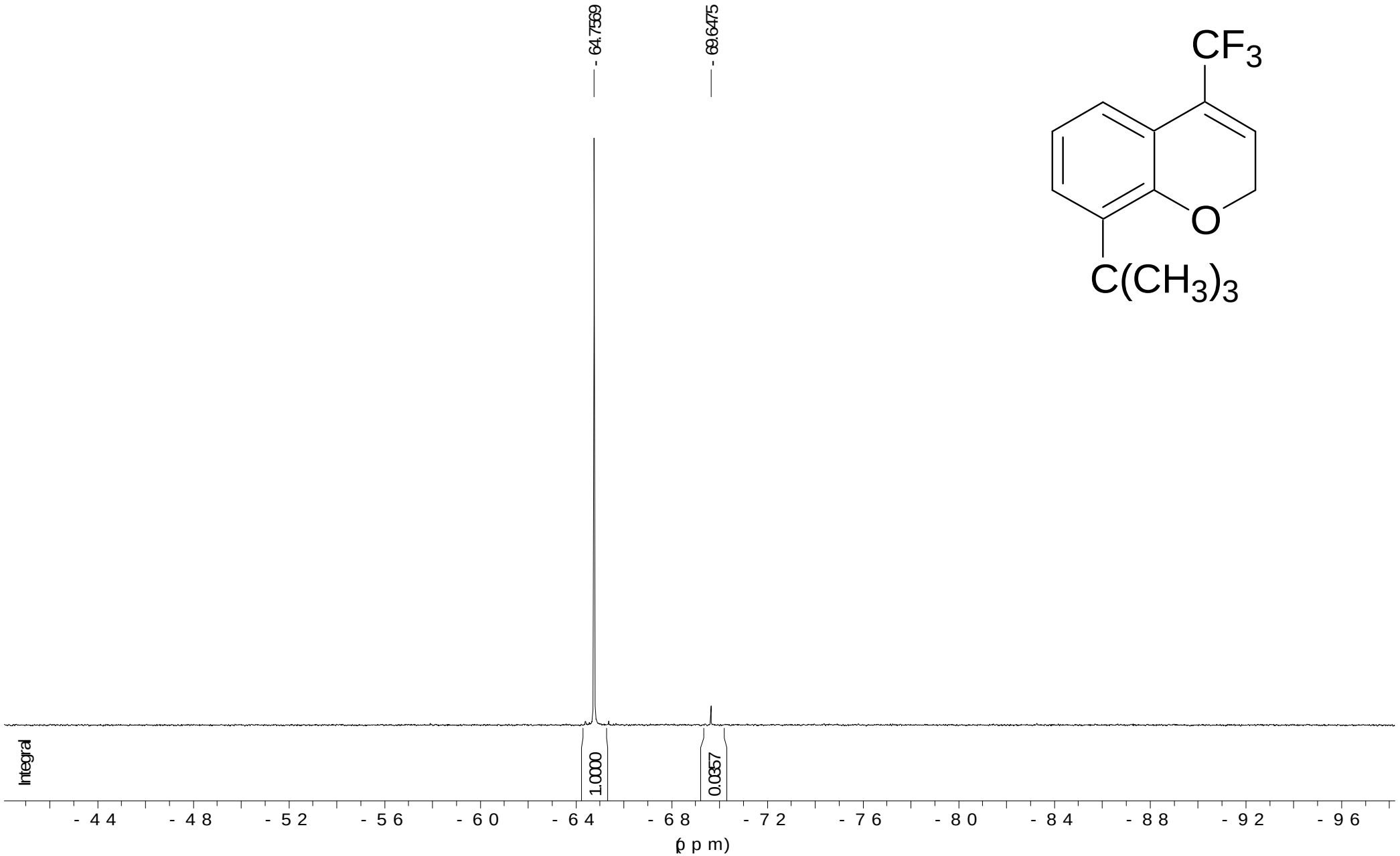
Compound **2n** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



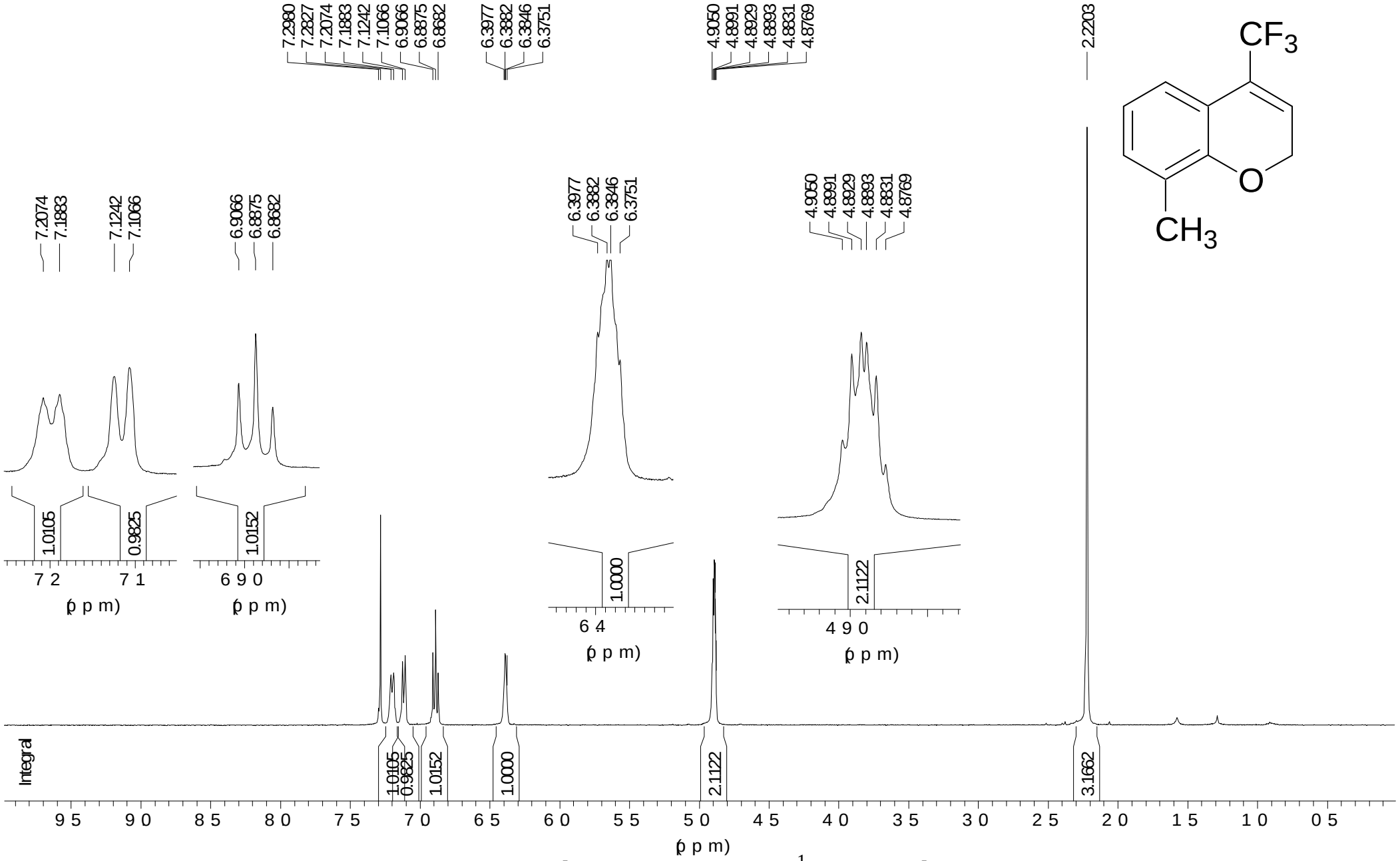
Compound **2o** spectrum NMR ^{13}C in $CDCl_3$



Compound **2o** spectrum NMR ^{1}H in $CDCl_3$



Compound **2o** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



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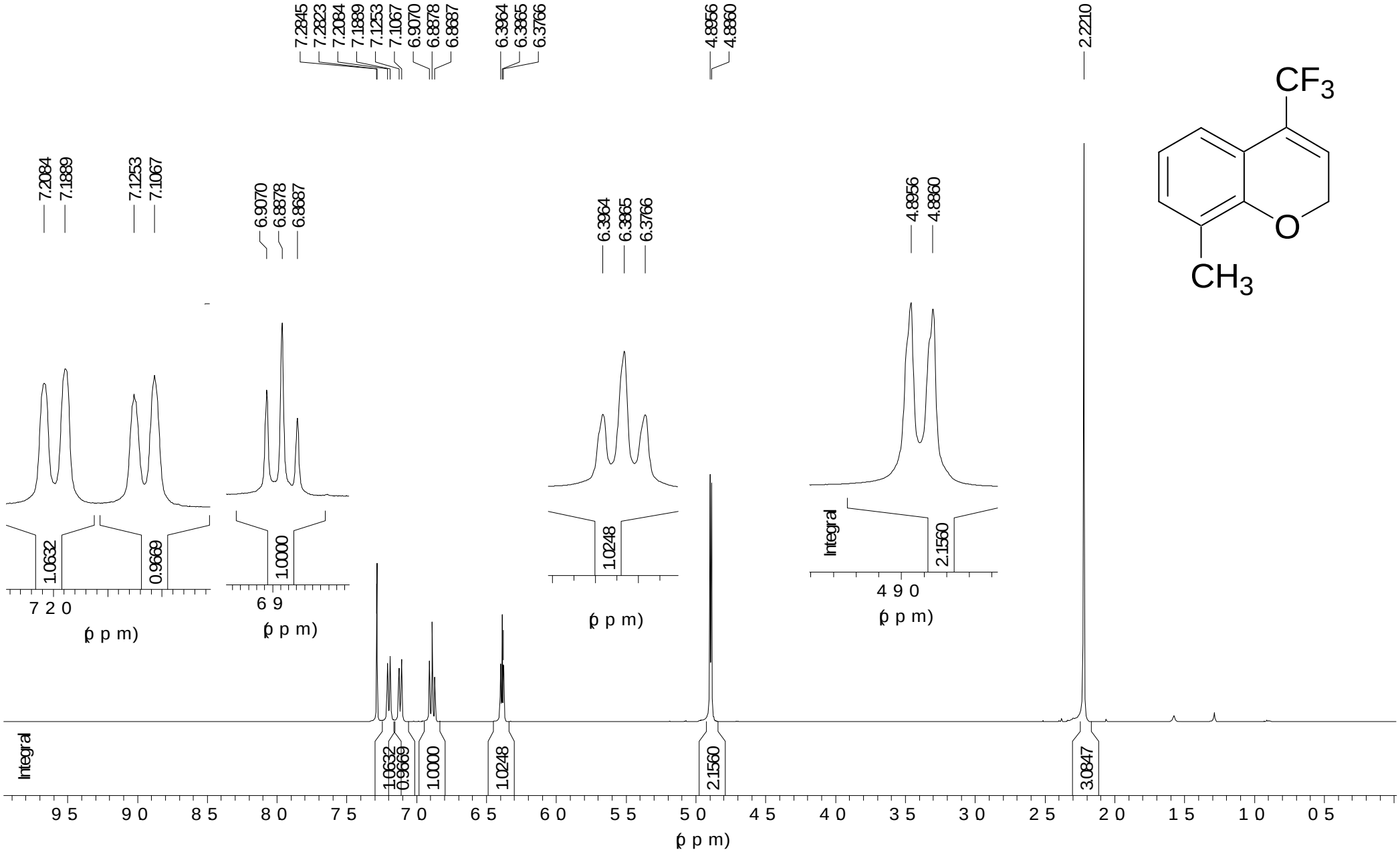
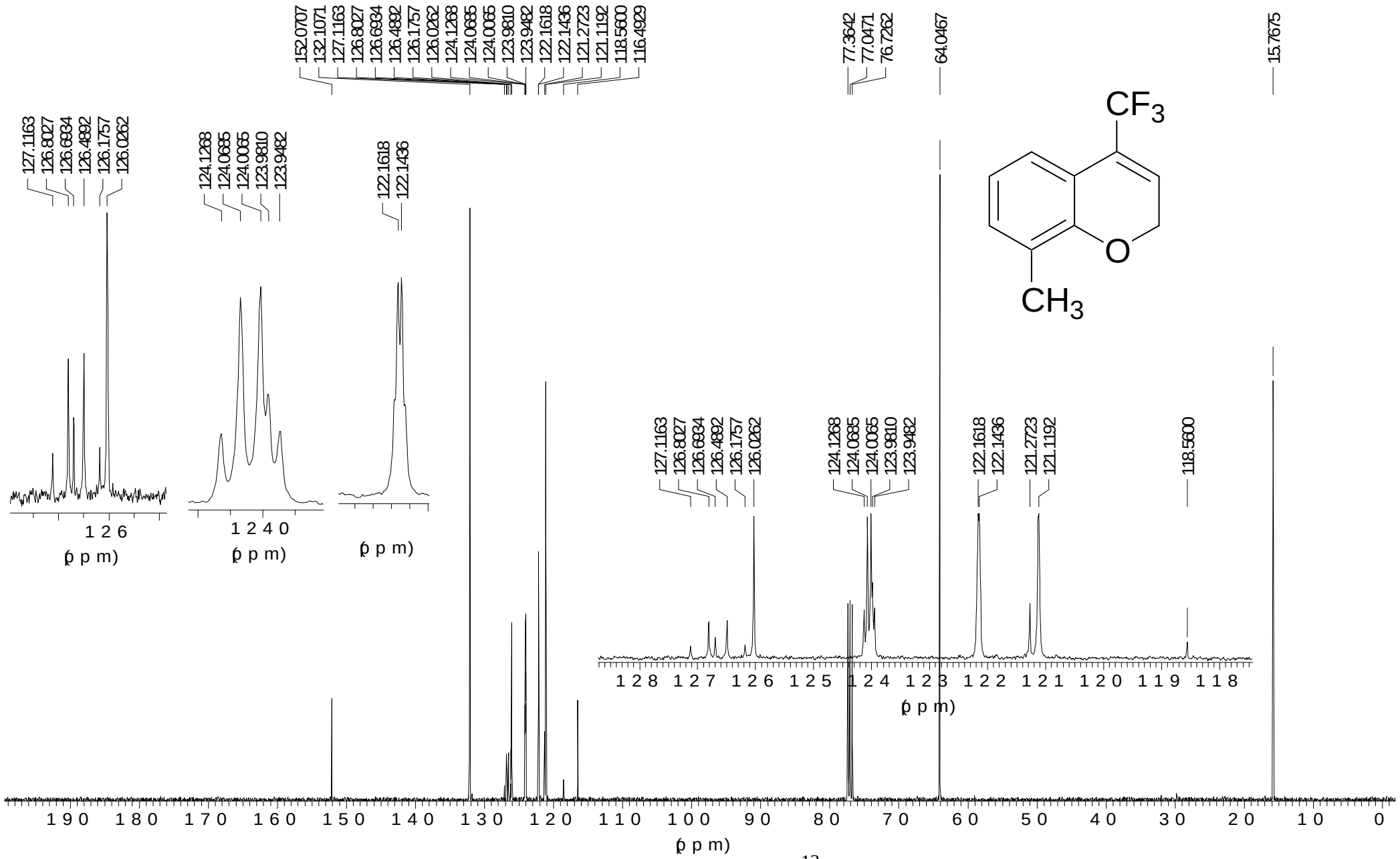
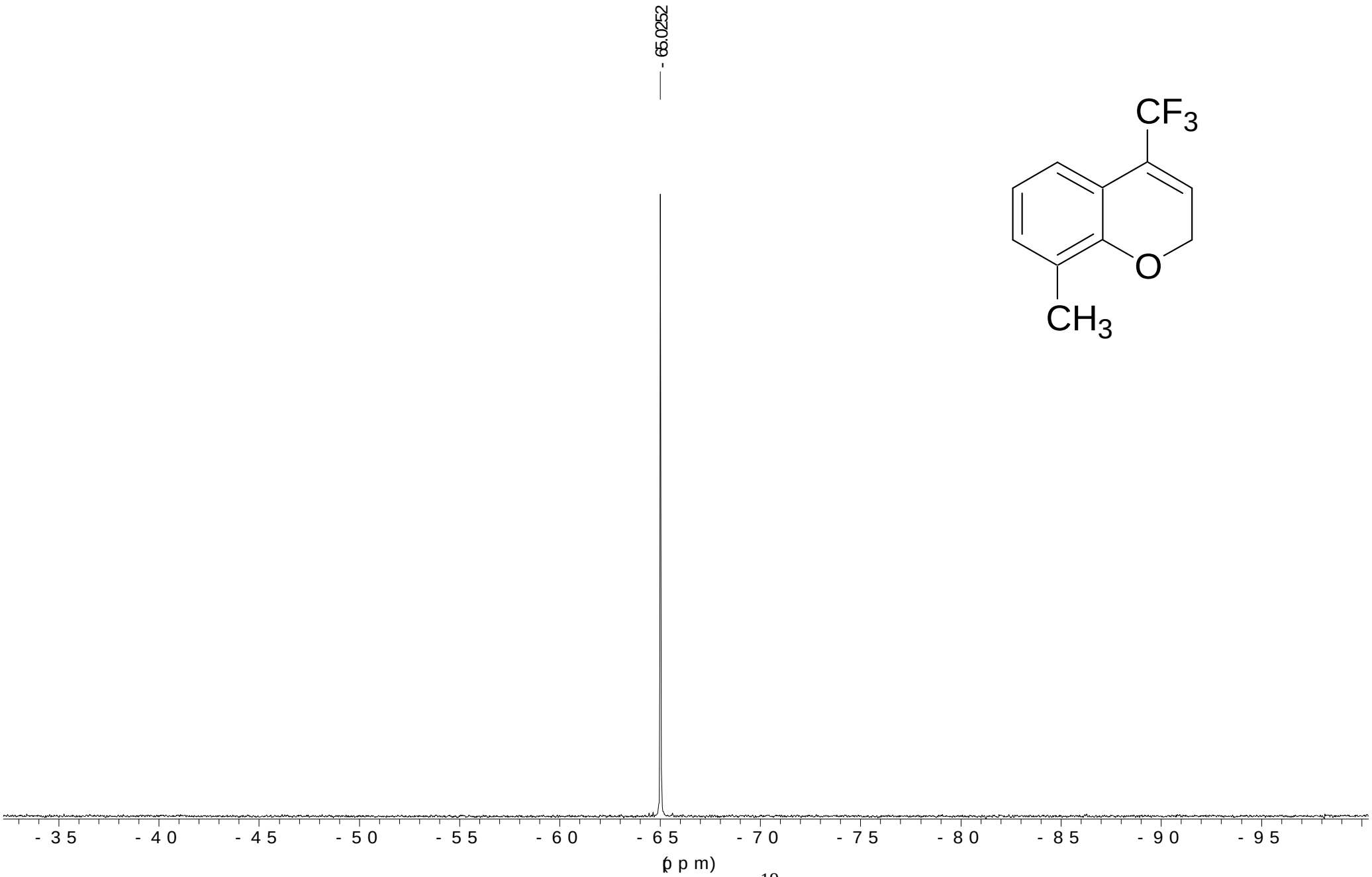


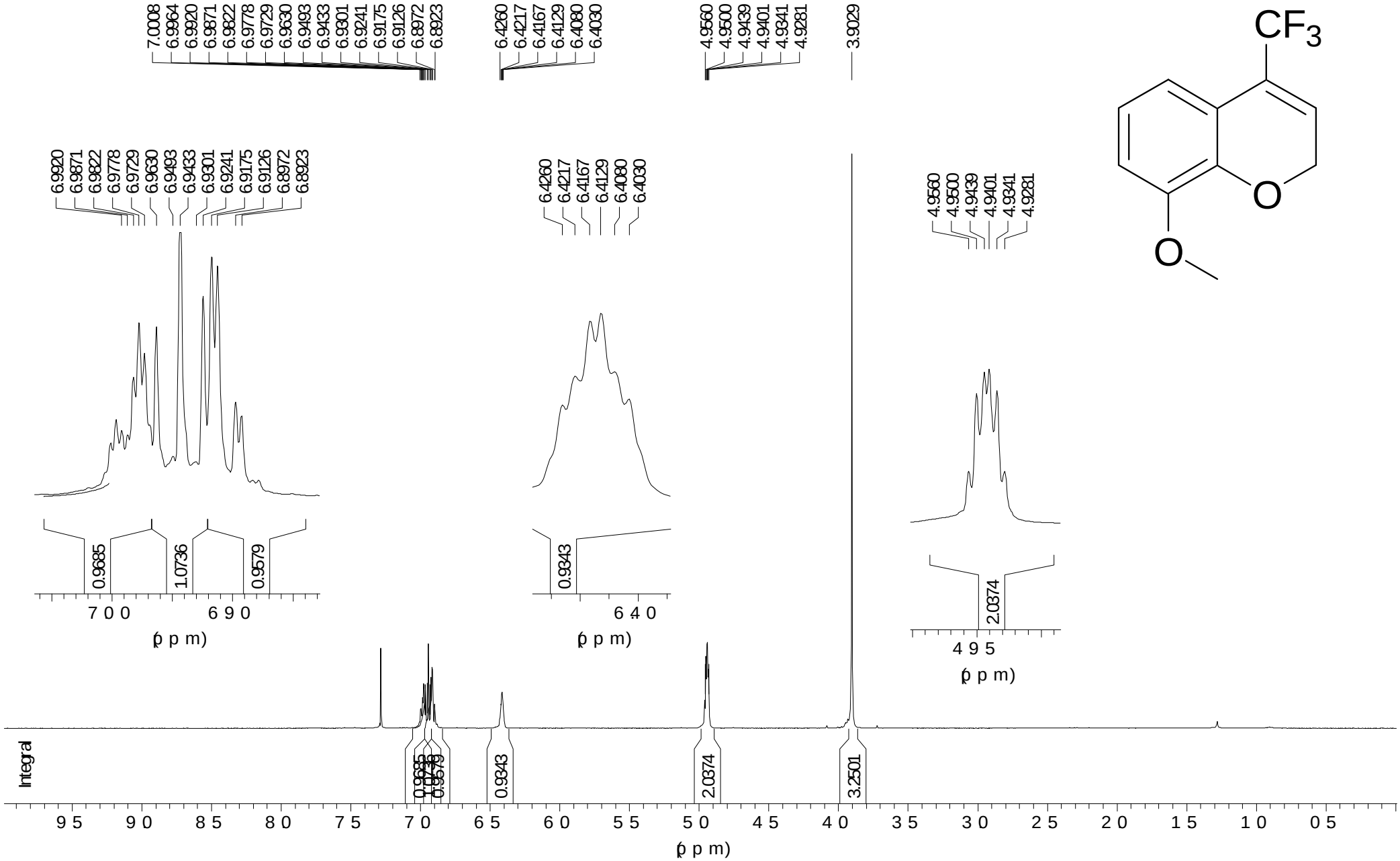
Compound **2p** spectrum NMR $^{1}H\{^{19}F\}$ in $CDCl_3$



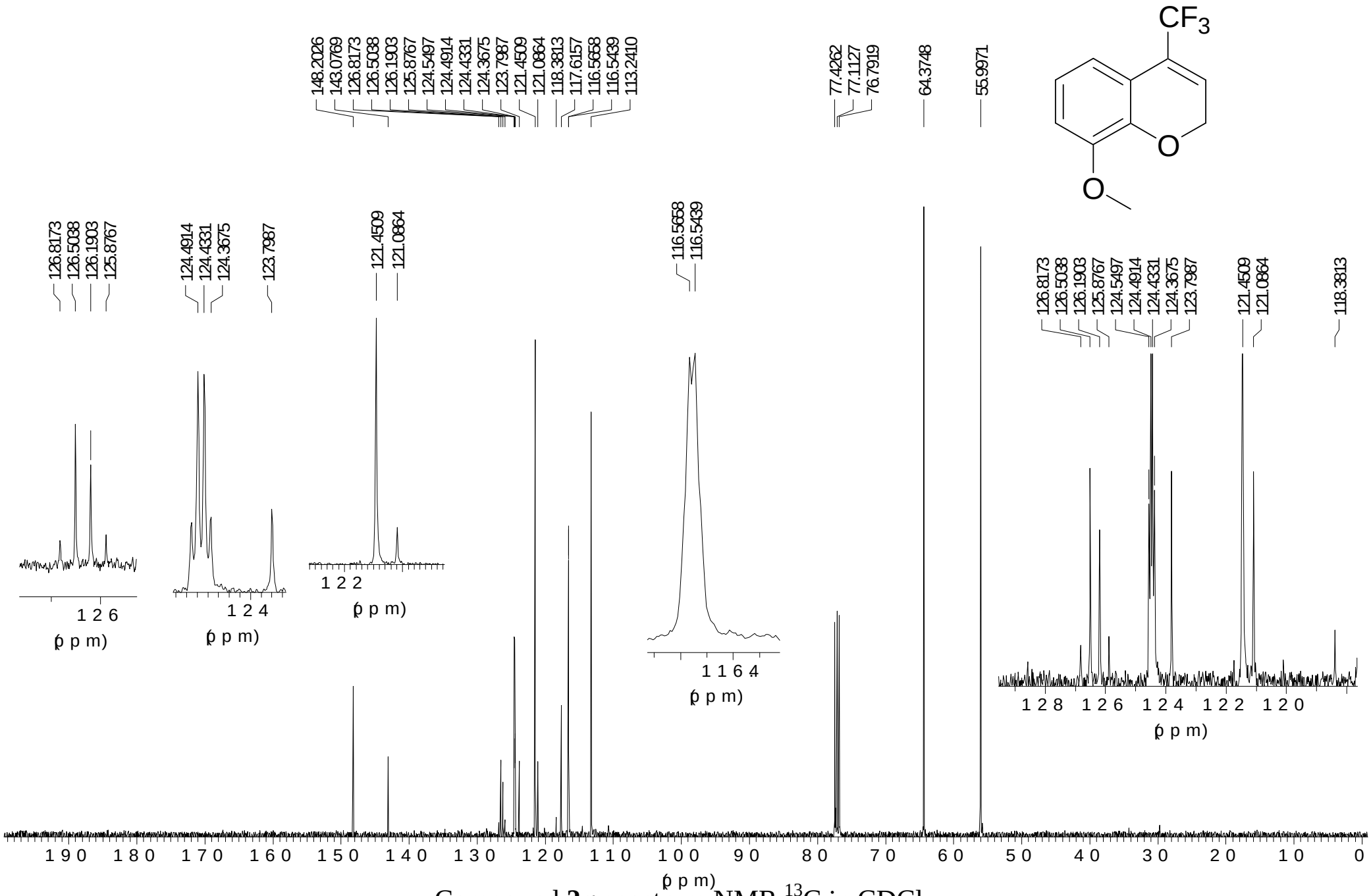
Compound **2p** spectrum NMR ^{13}C in $CDCl_3$



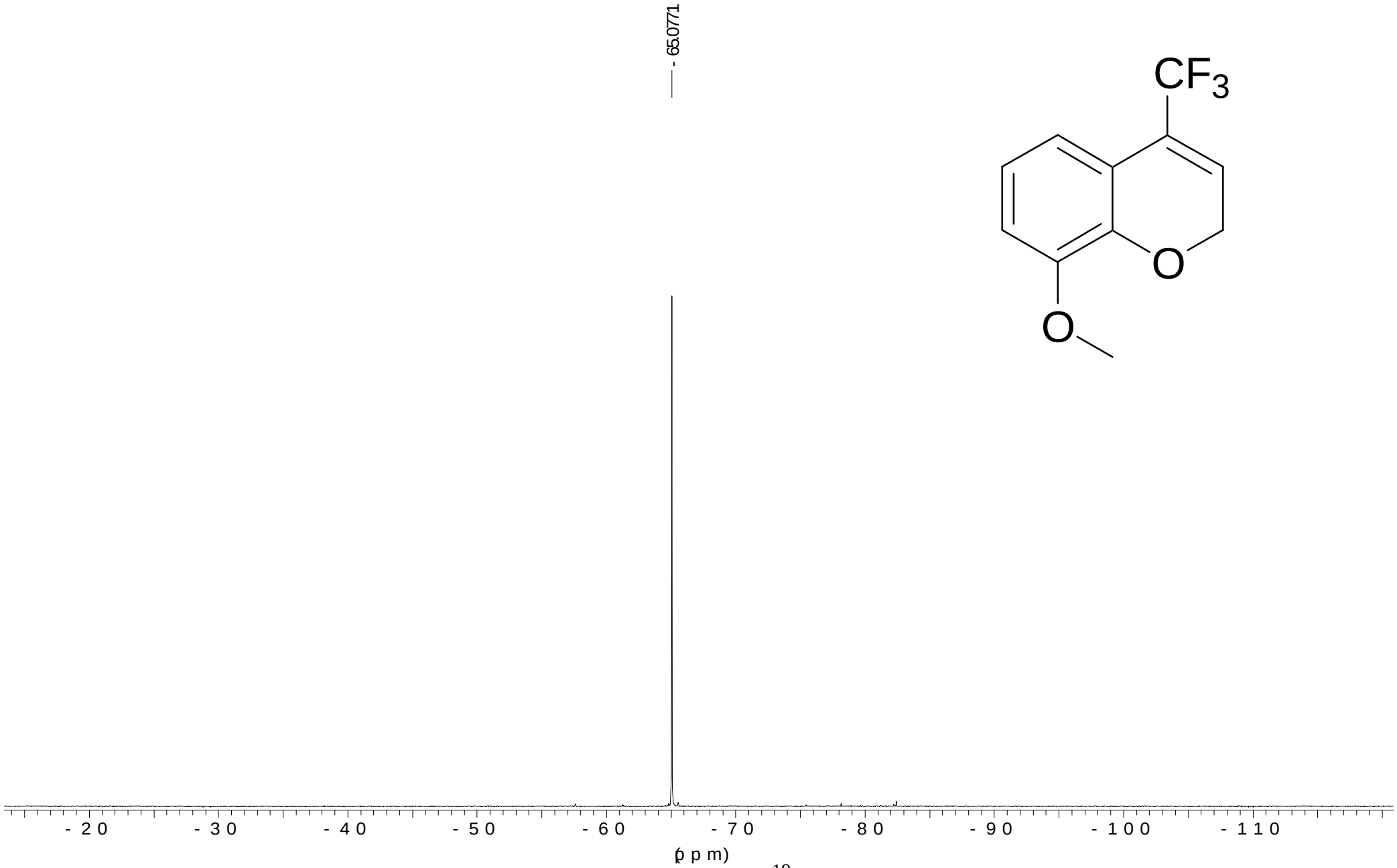
Compound **2p** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



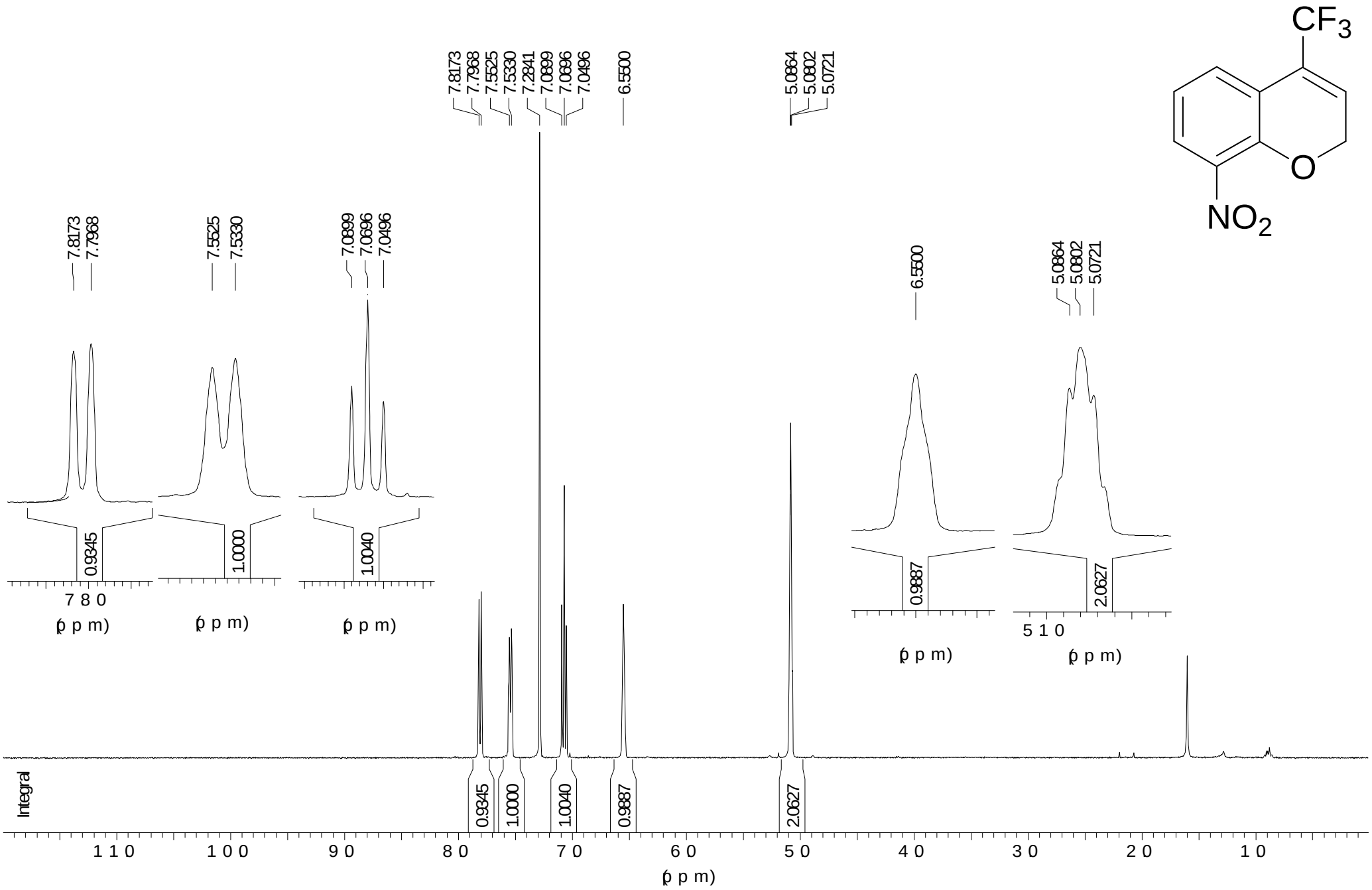
Compound **2q** spectrum NMR ^{1}H in $CDCl_3$



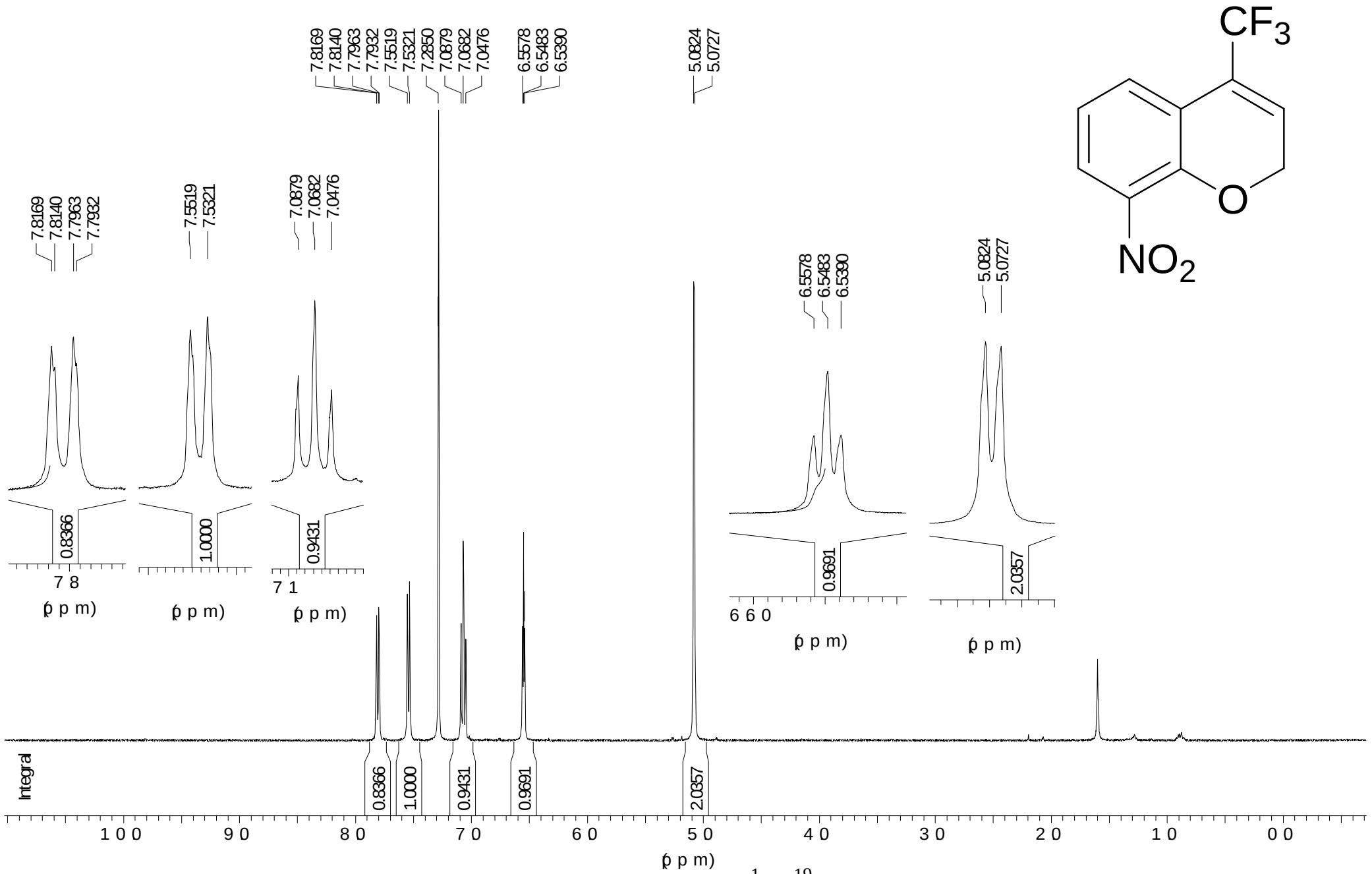
Compound **2q** spectrum NMR ^{13}C in $CDCl_3$



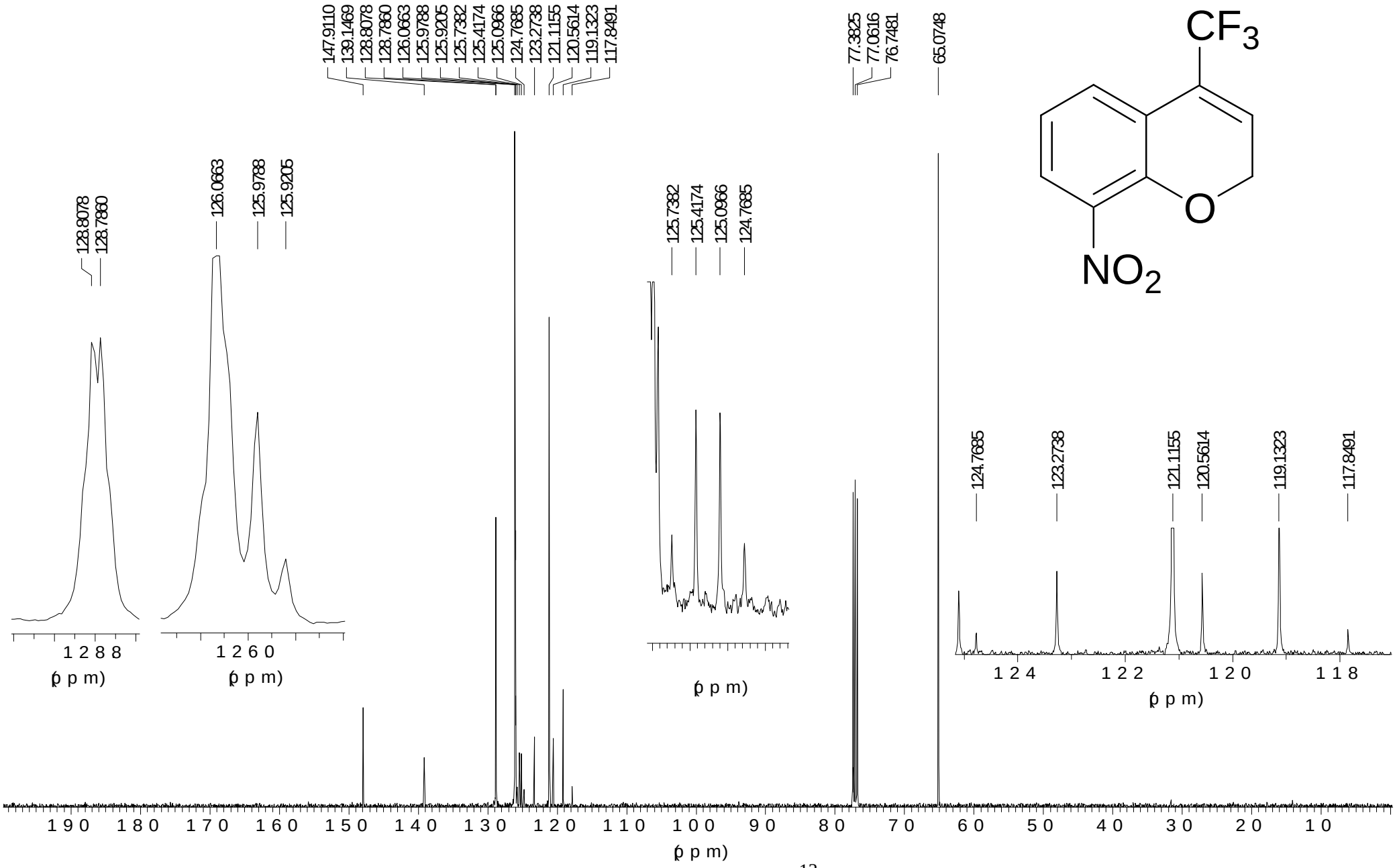
Compound **2q** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



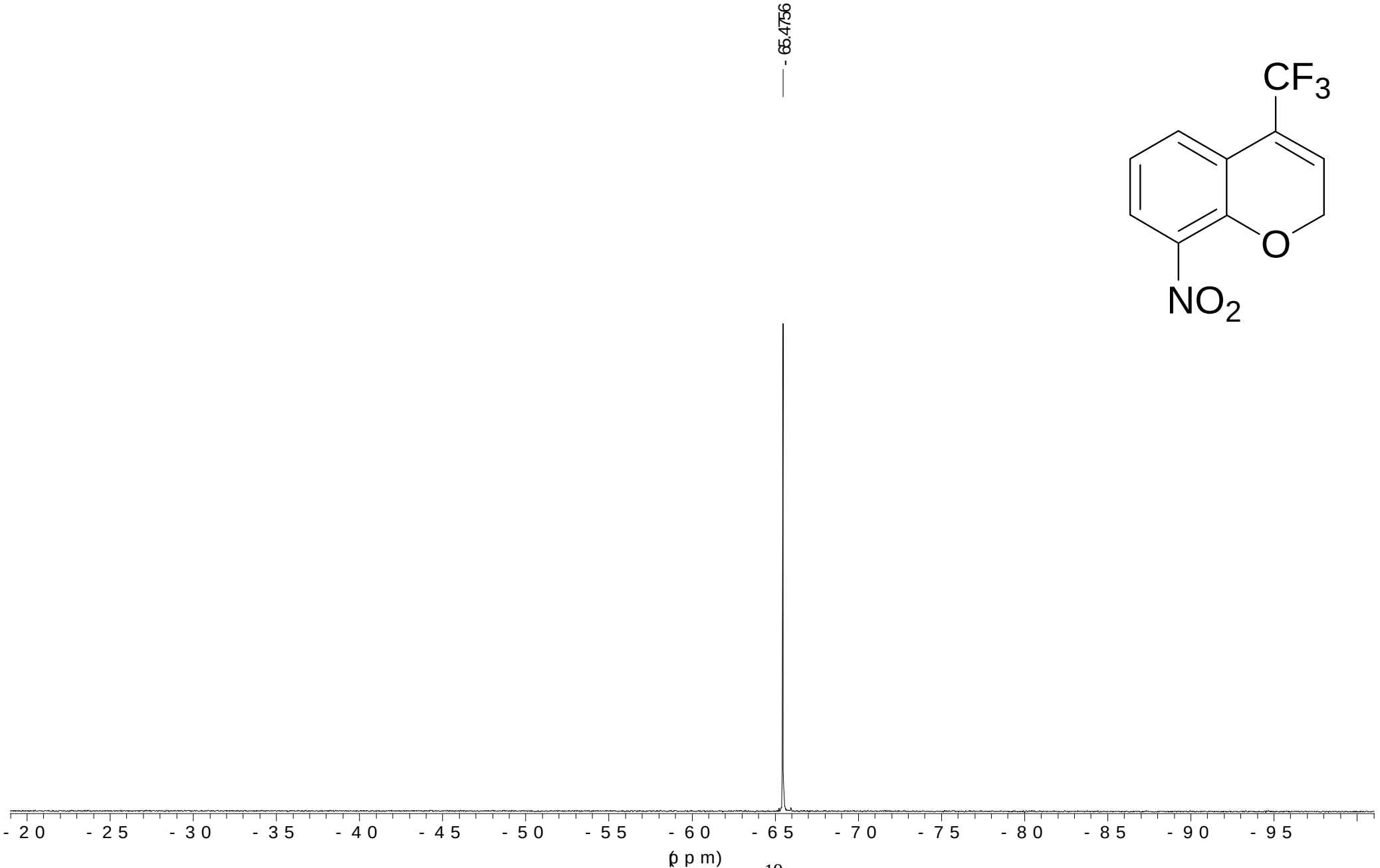
Compound **2r** spectrum NMR ^{1}H in $CDCl_3$



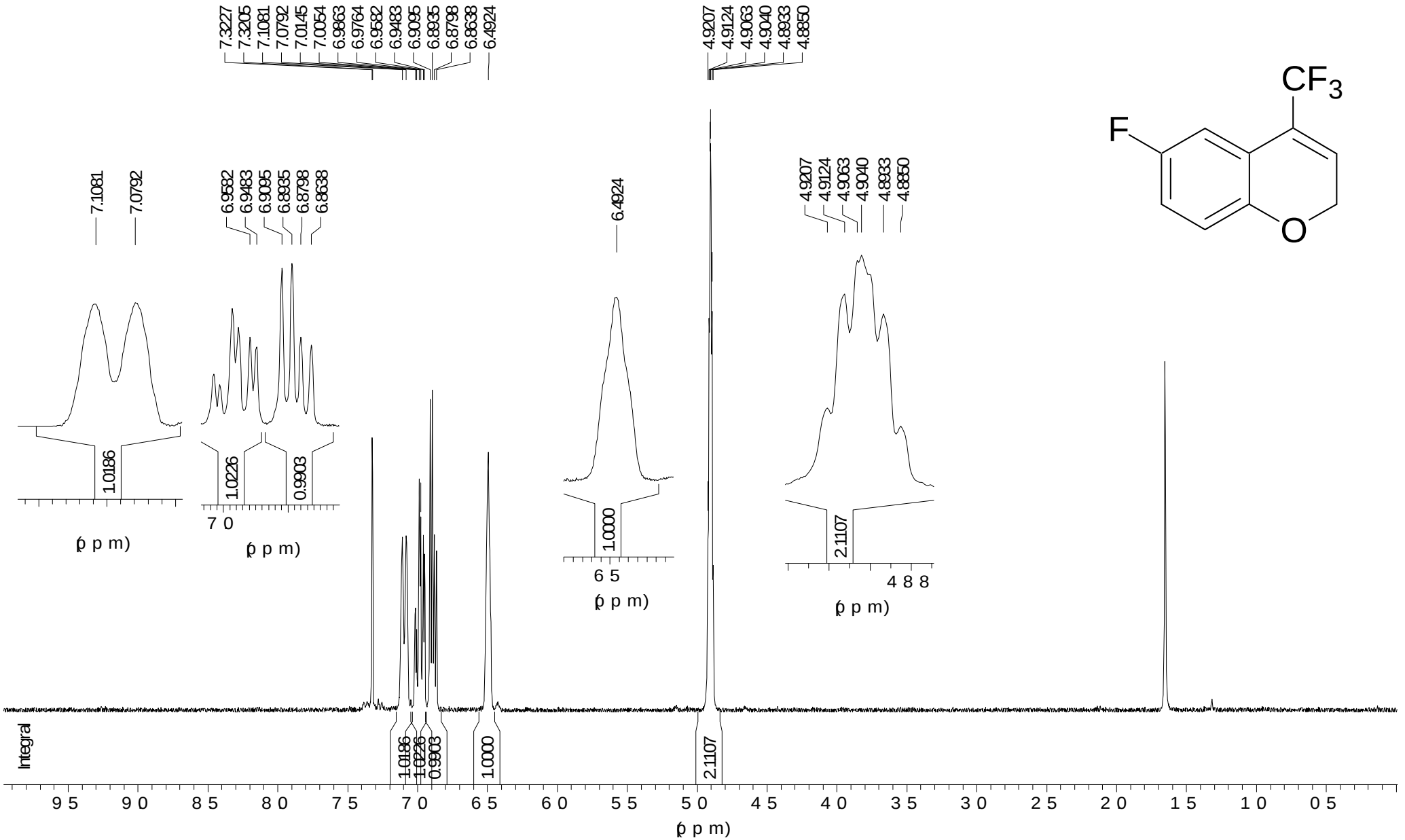
Compound **2r** spectrum NMR $^{1}H\{^{19}F\}$ in $CDCl_3$



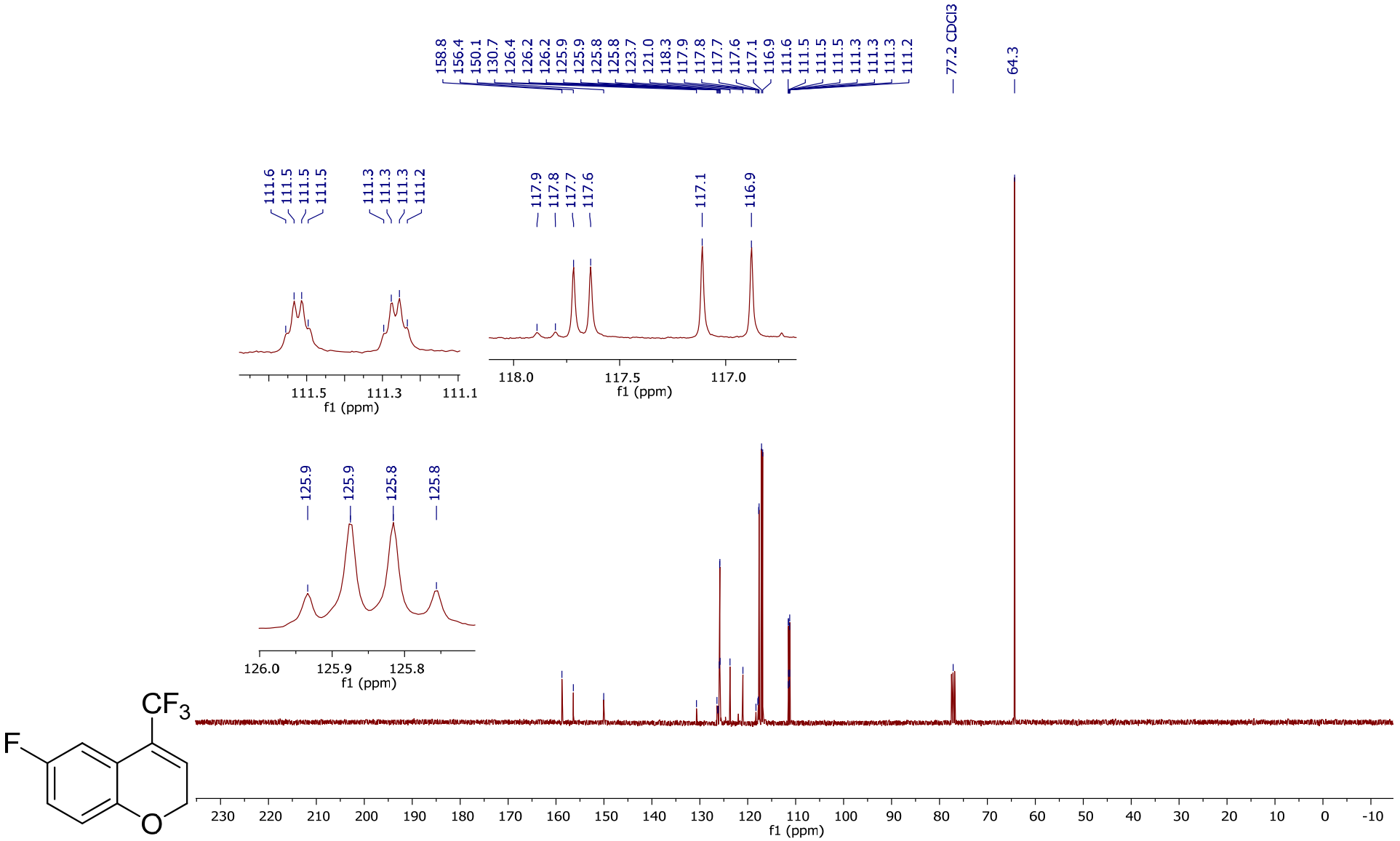
Compound **2r** spectrum NMR ^{13}C in $CDCl_3$



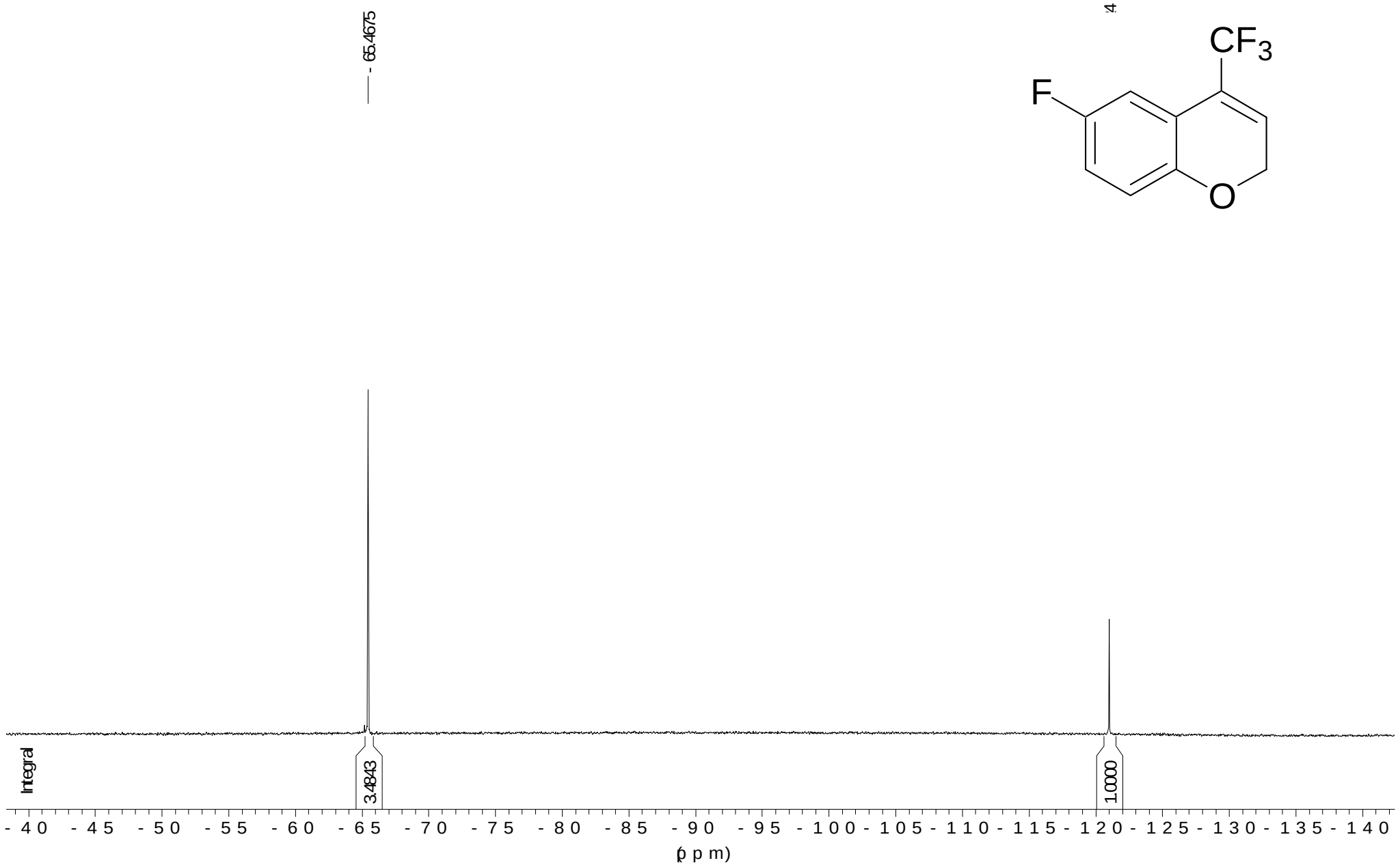
Compound **2r** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



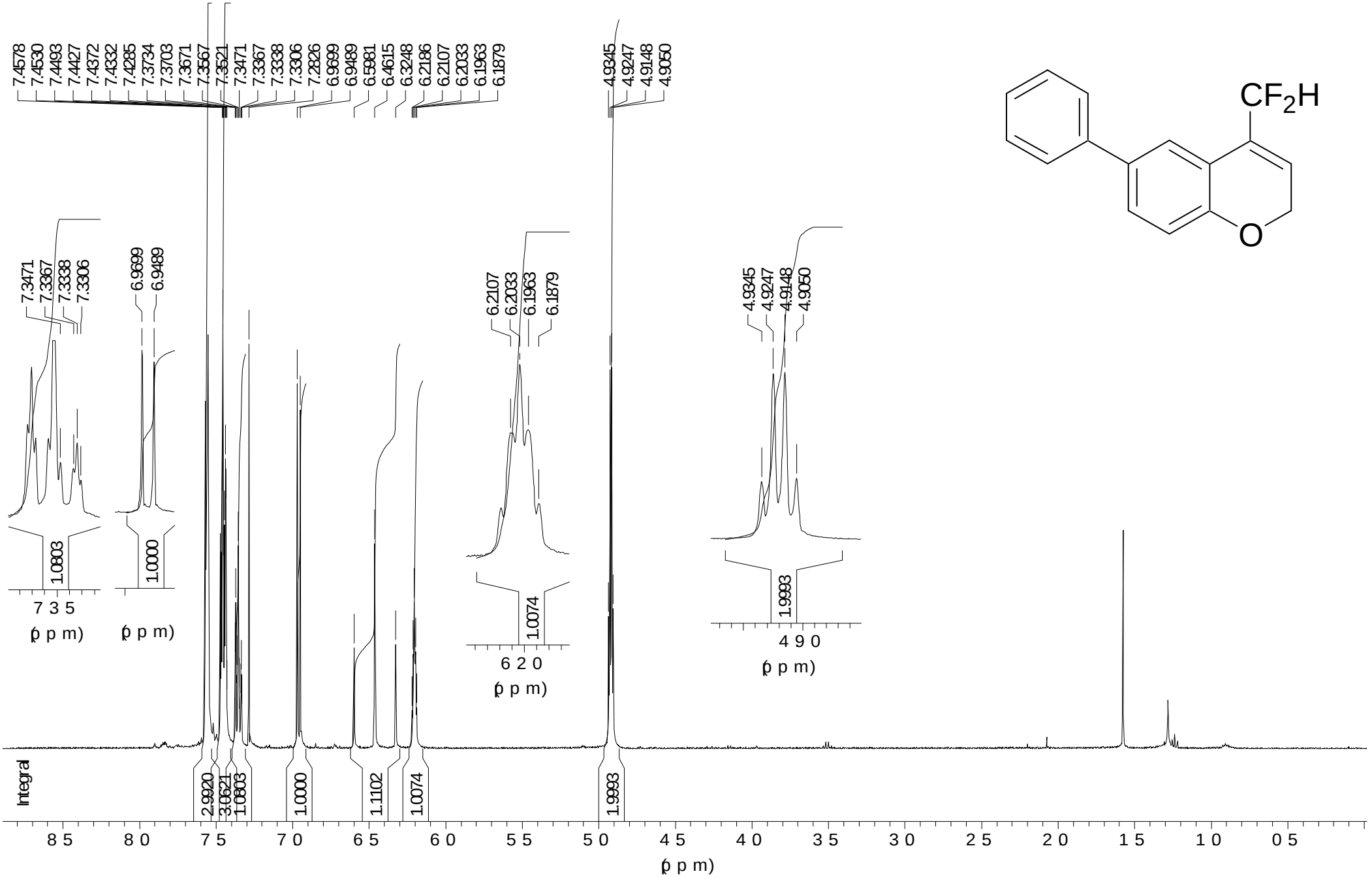
Compound **2s** spectrum NMR ^{1}H in $CDCl_3$



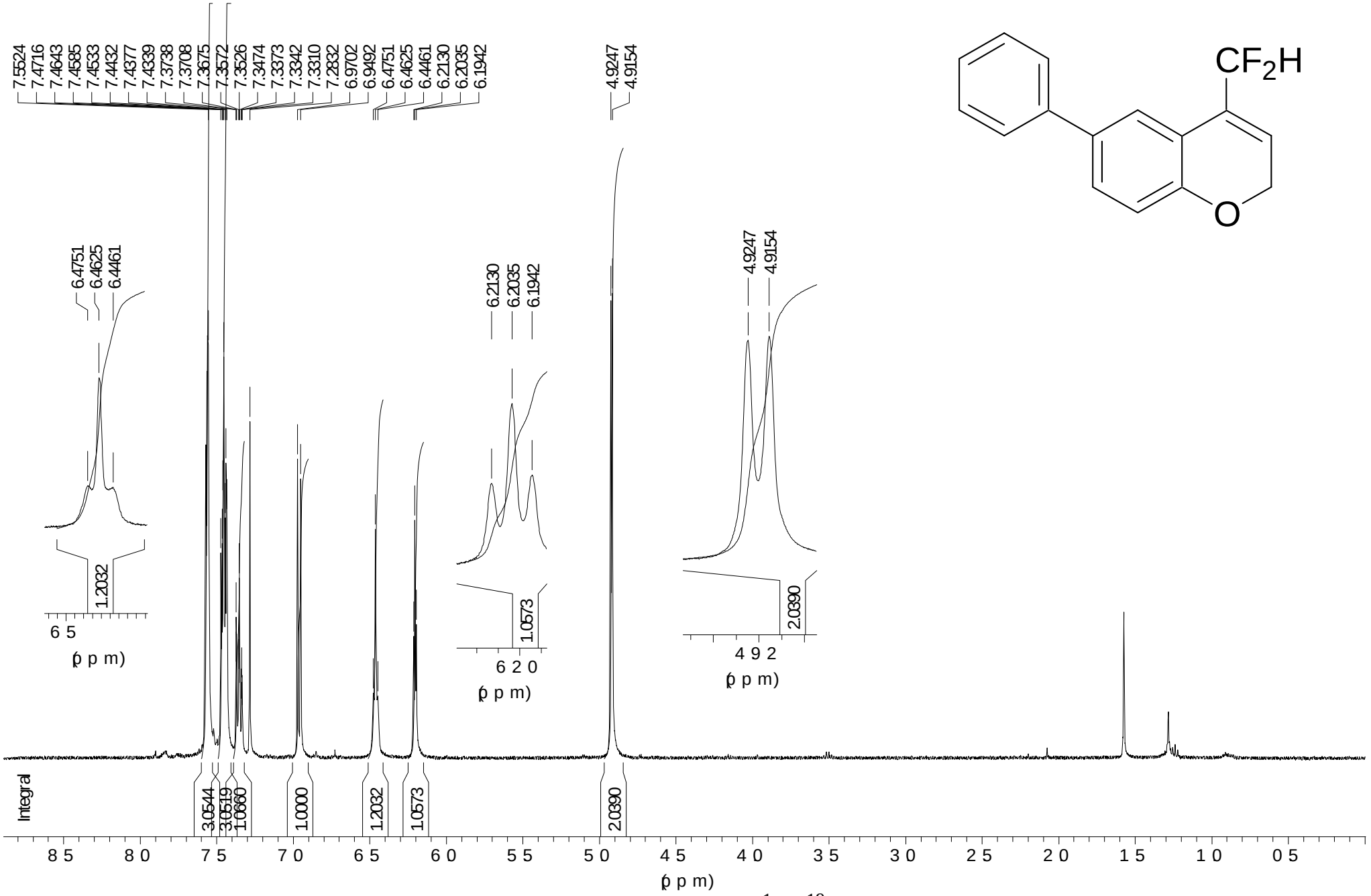
Compound **2s** spectrum NMR ^{13}C in $CDCl_3$



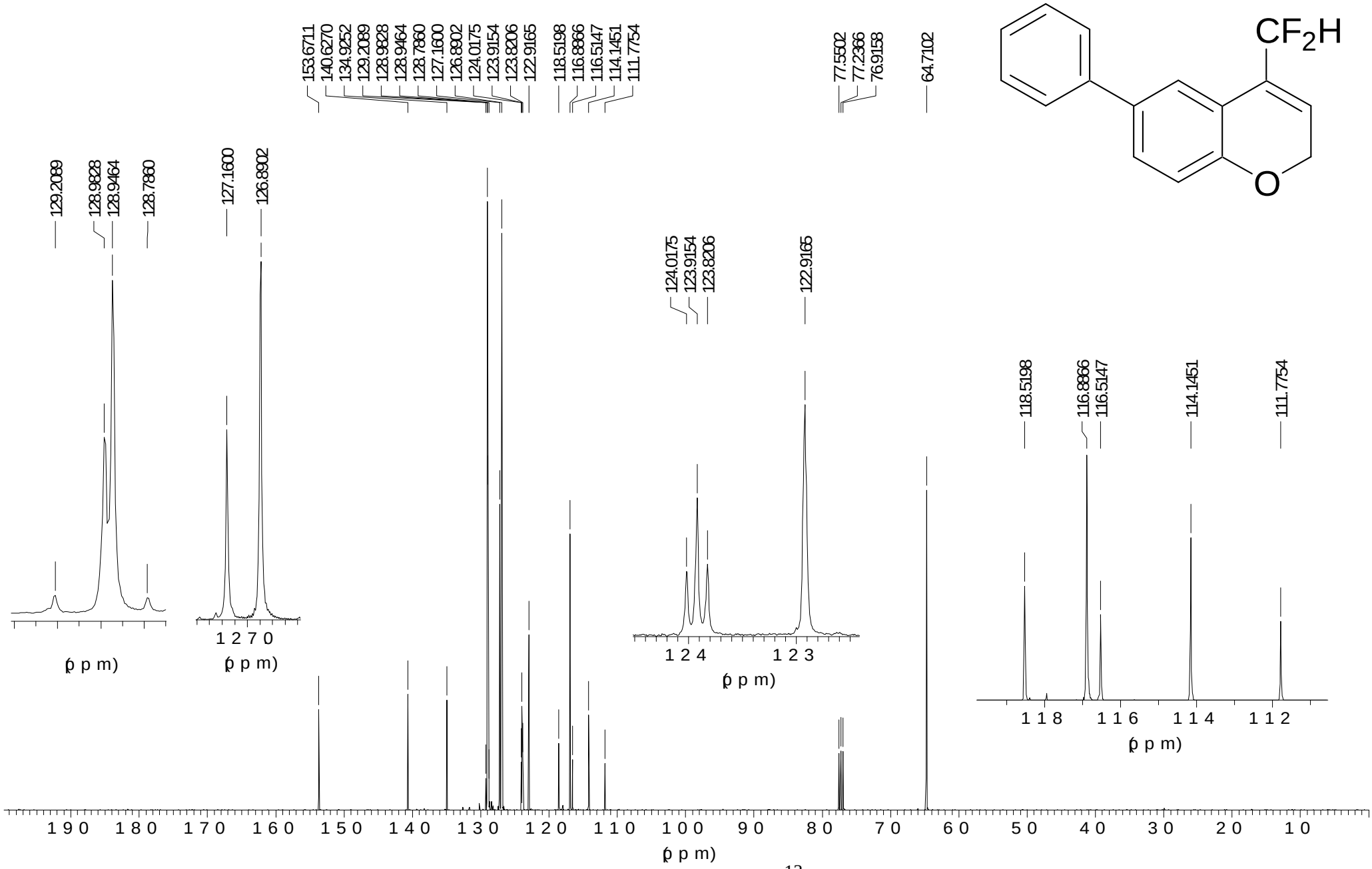
Compound **2s** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



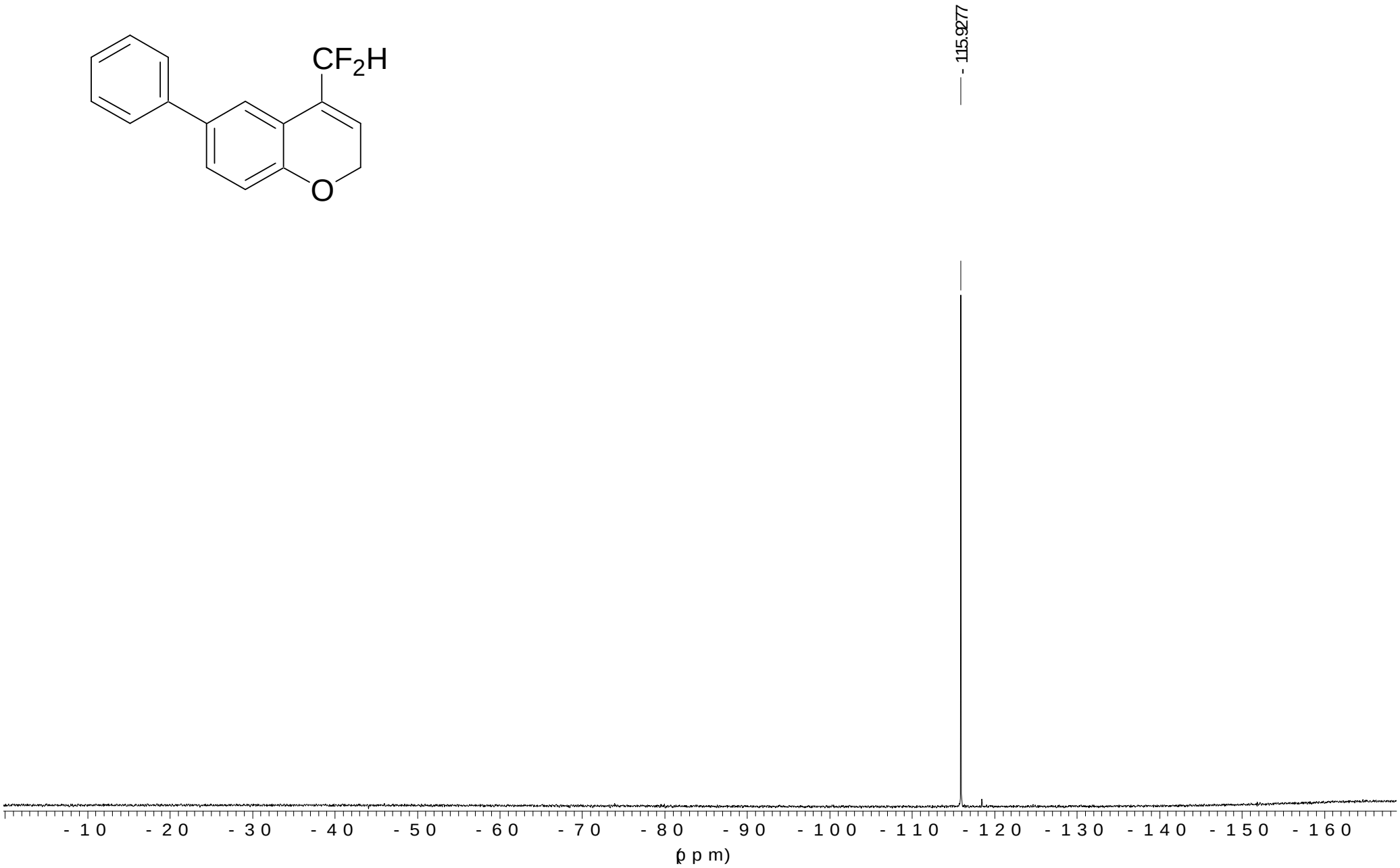
Compound **2t** spectrum NMR ^{1}H in $CDCl_3$



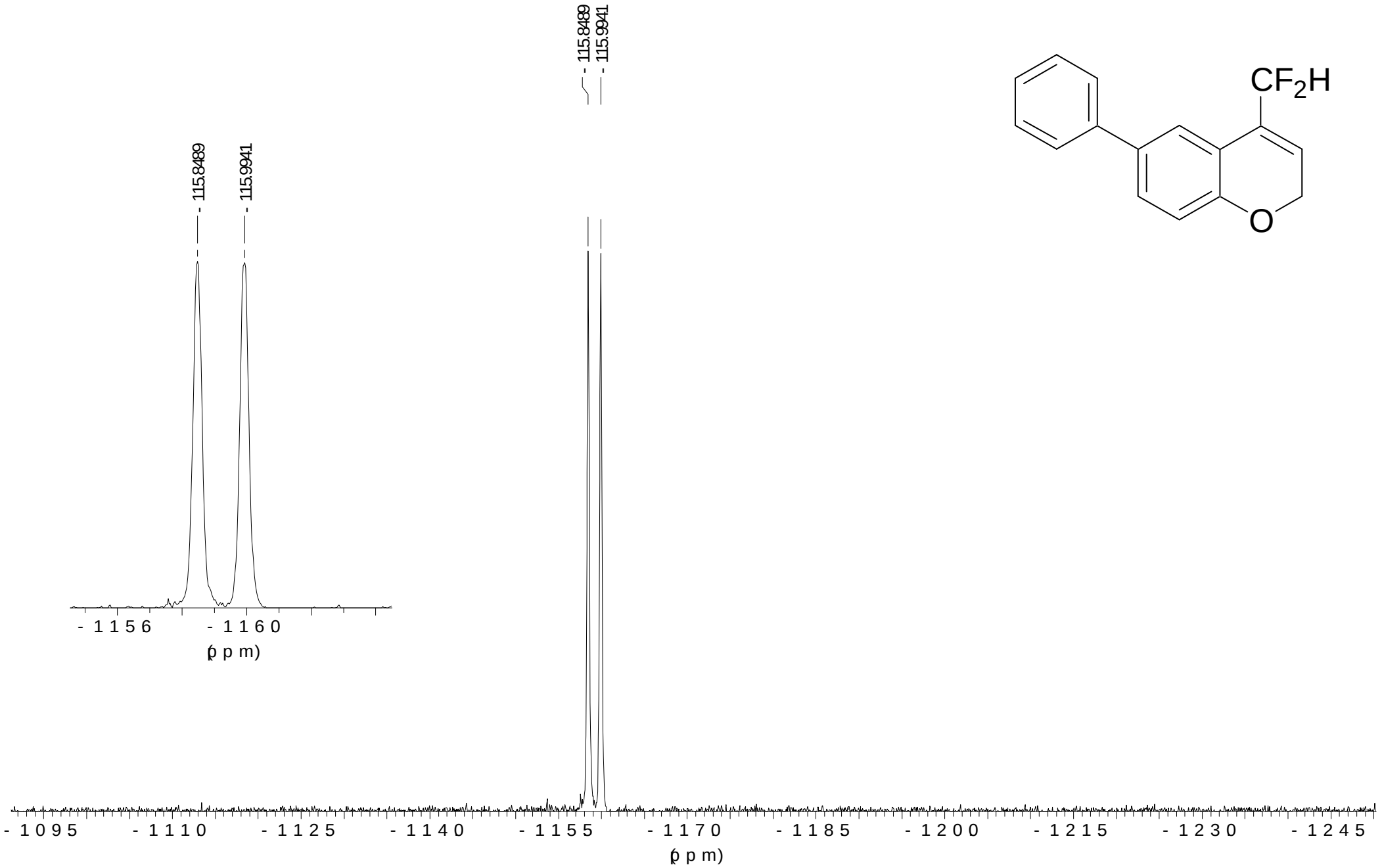
Compound **2t** spectrum NMR $^{1}H\{^{19}F\}$ in $CDCl_3$



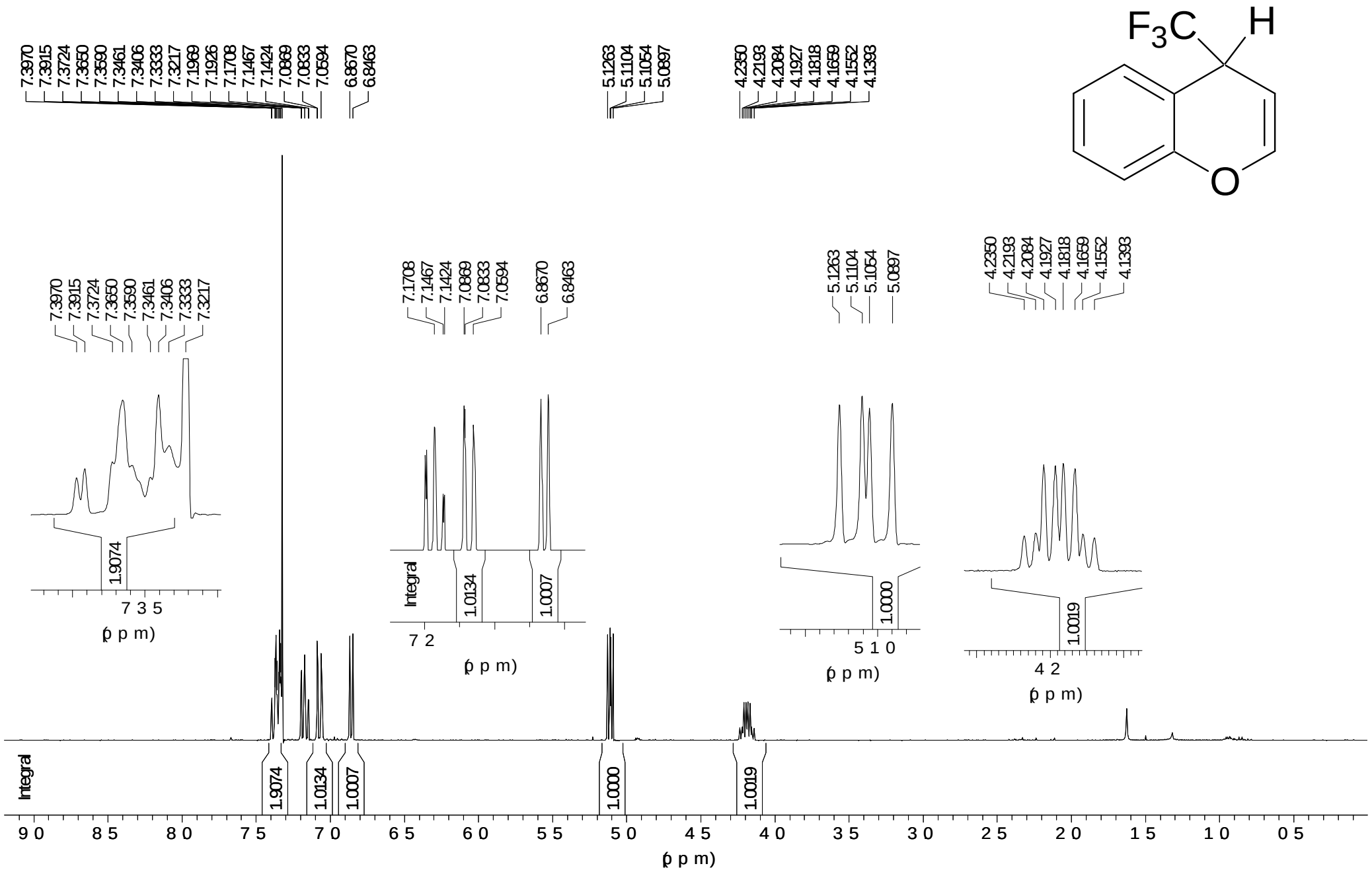
Compound **2t** spectrum NMR ^{13}C in $CDCl_3$



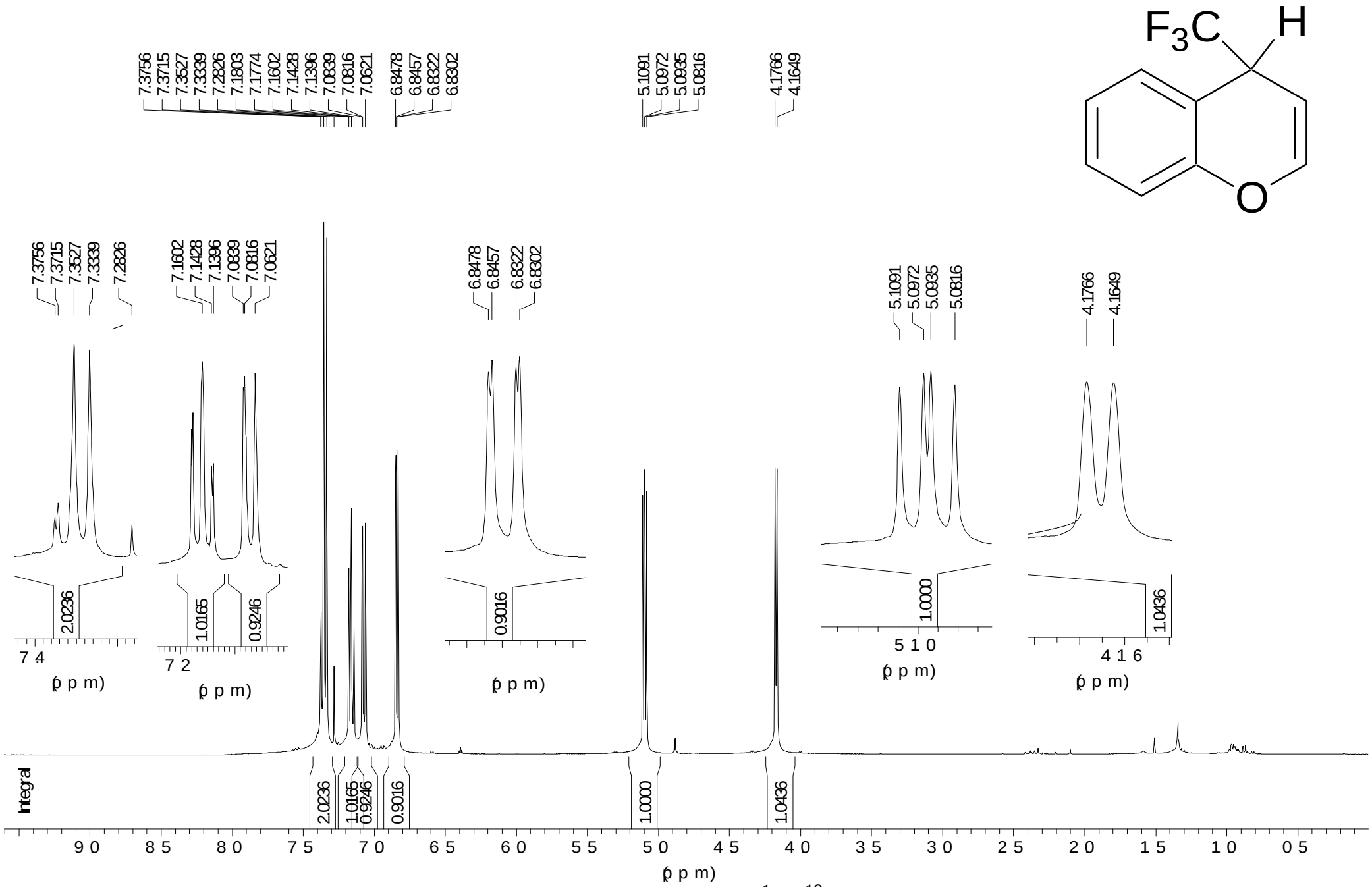
Compound **2t** spectrum NMR $^{19}F\{H\}$ in $CDCl_3$



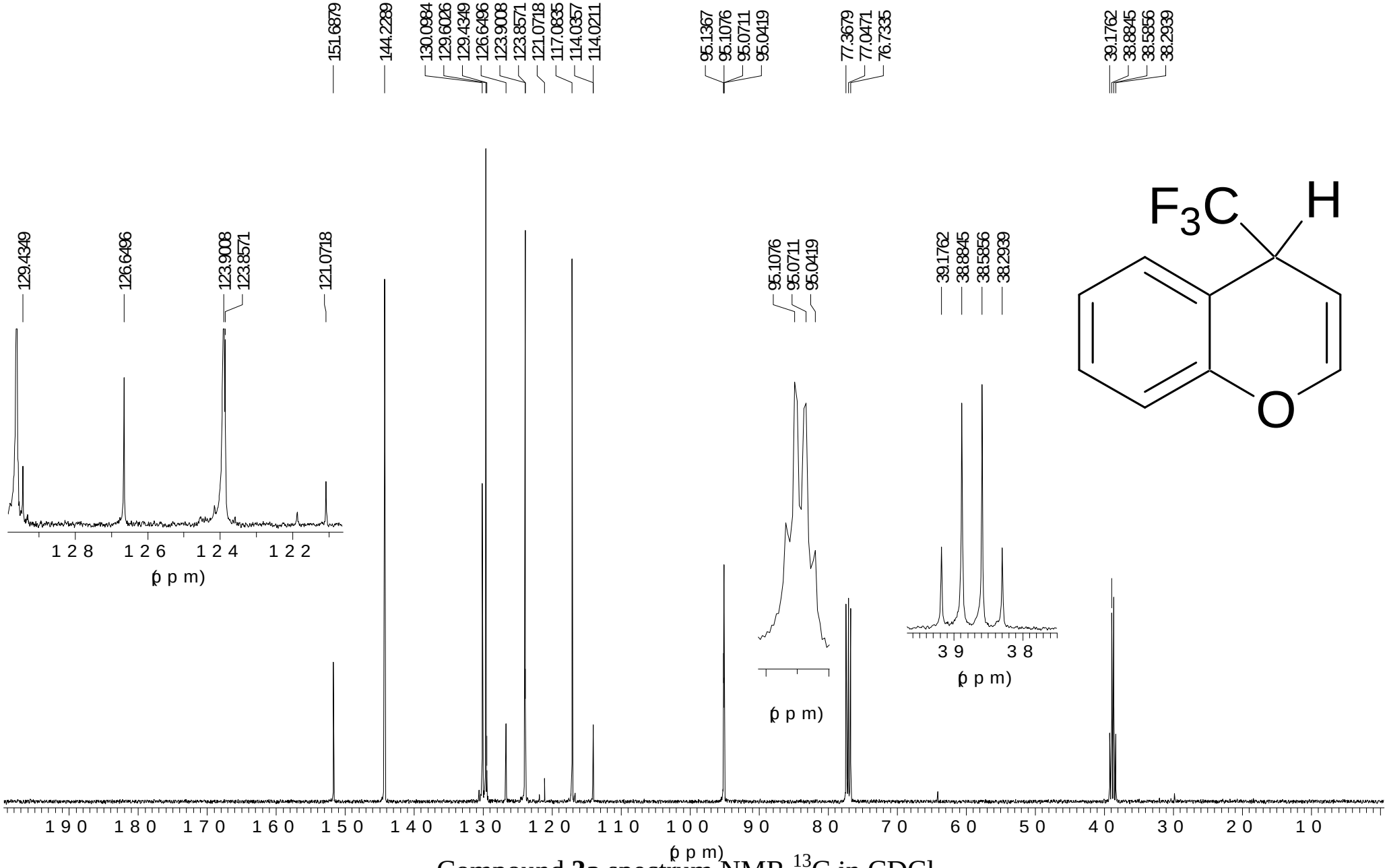
Compound **2t** spectrum NMR ^{19}F in $CDCl_3$



Compound **3a** spectrum NMR ^{1}H in $CDCl_3$

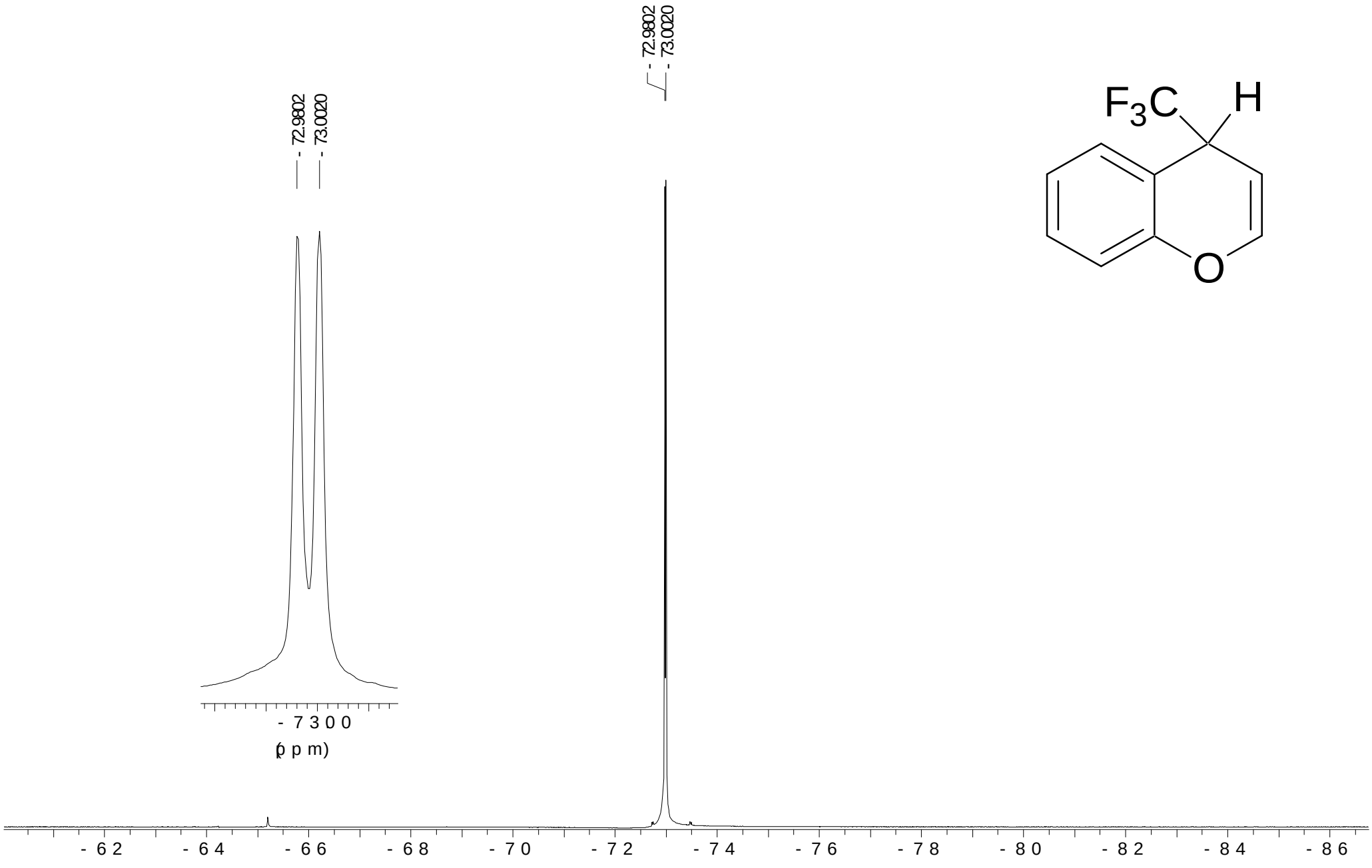


Compound **3a** spectrum NMR $^{1}H\{^{19}F\}$ in $CDCl_3$

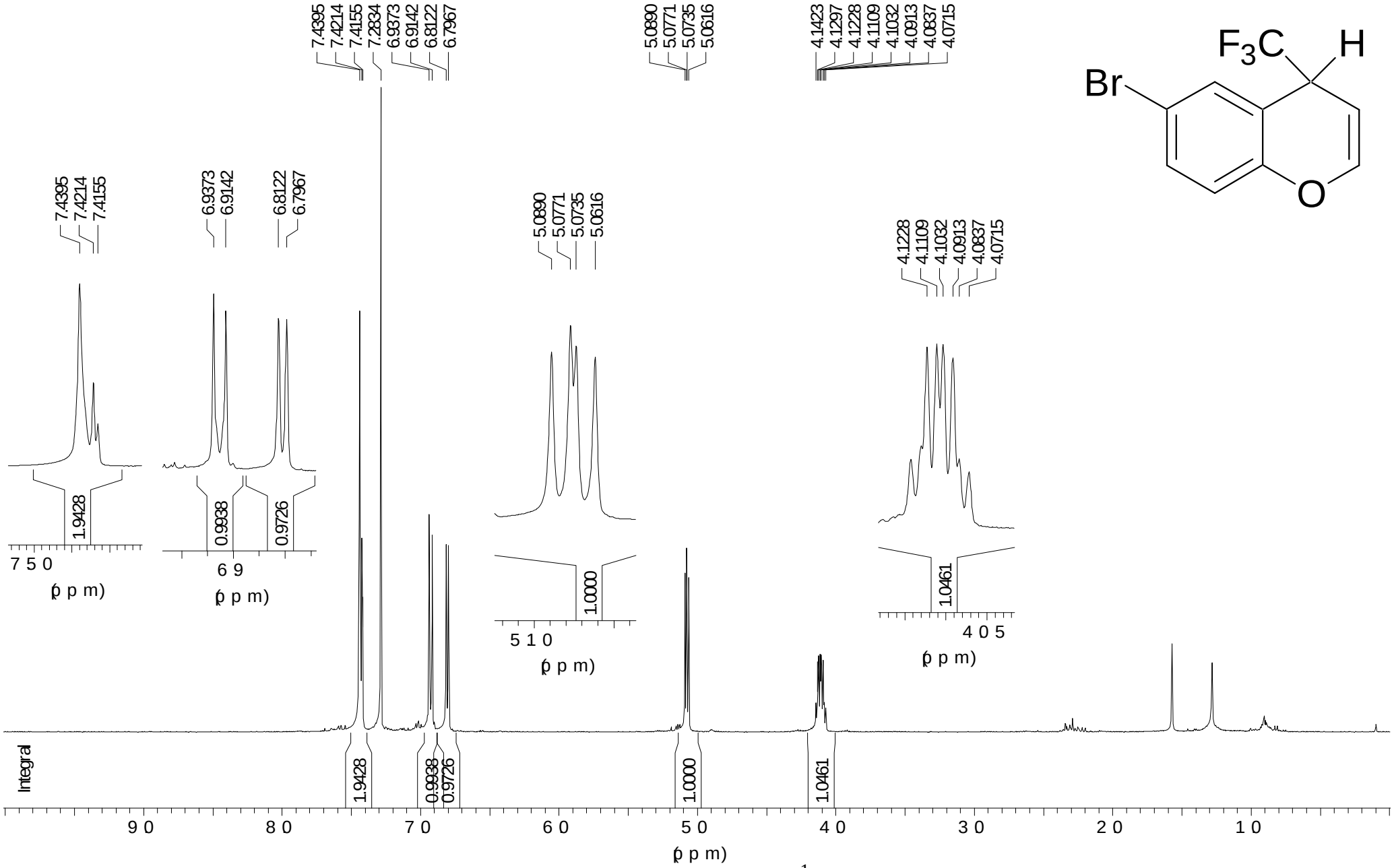


Compound **3a** spectrum NMR ^{13}C in $CDCl_3$

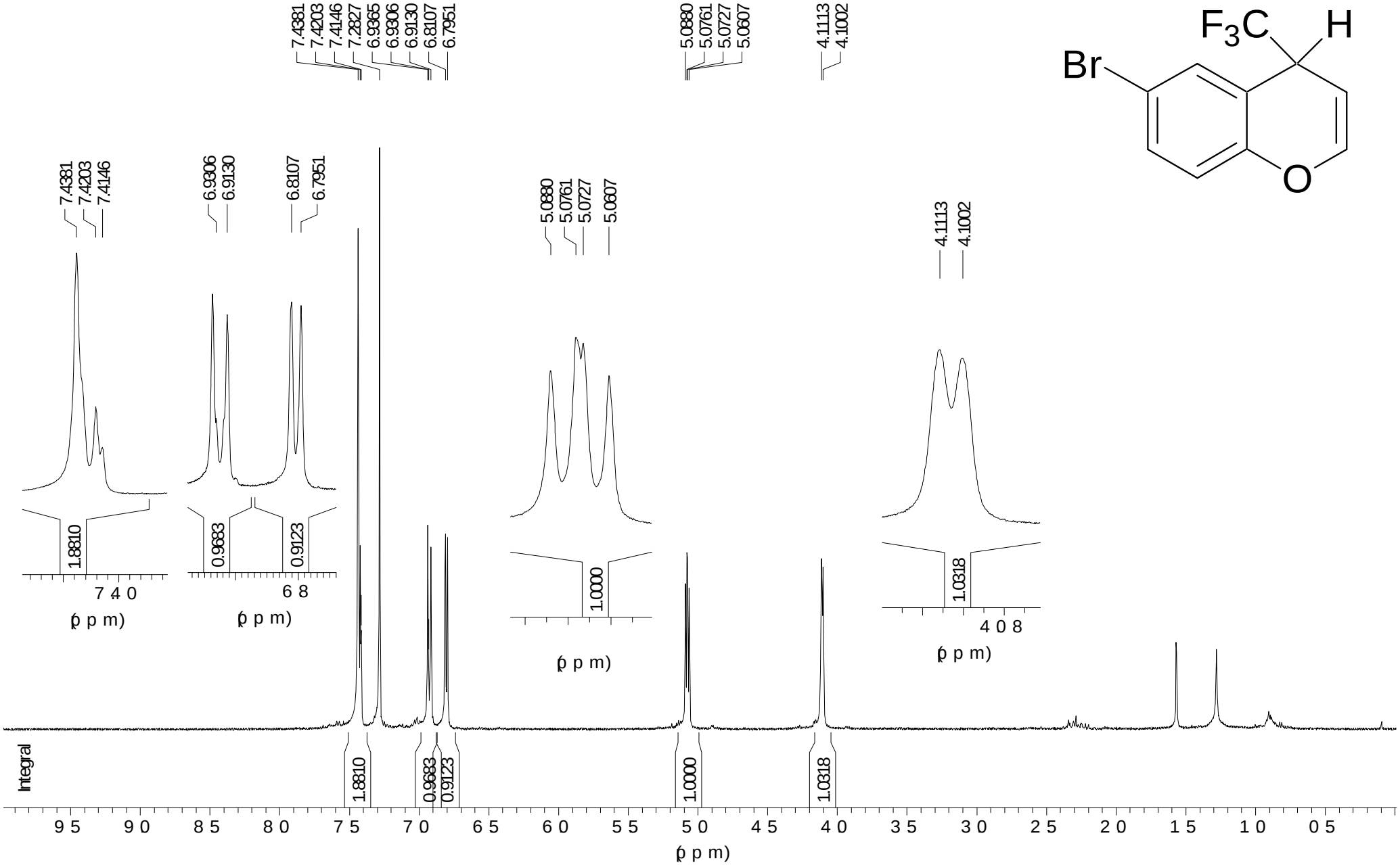
Compound **3a** spectrum NMR ^{19}F in $CDCl_3$



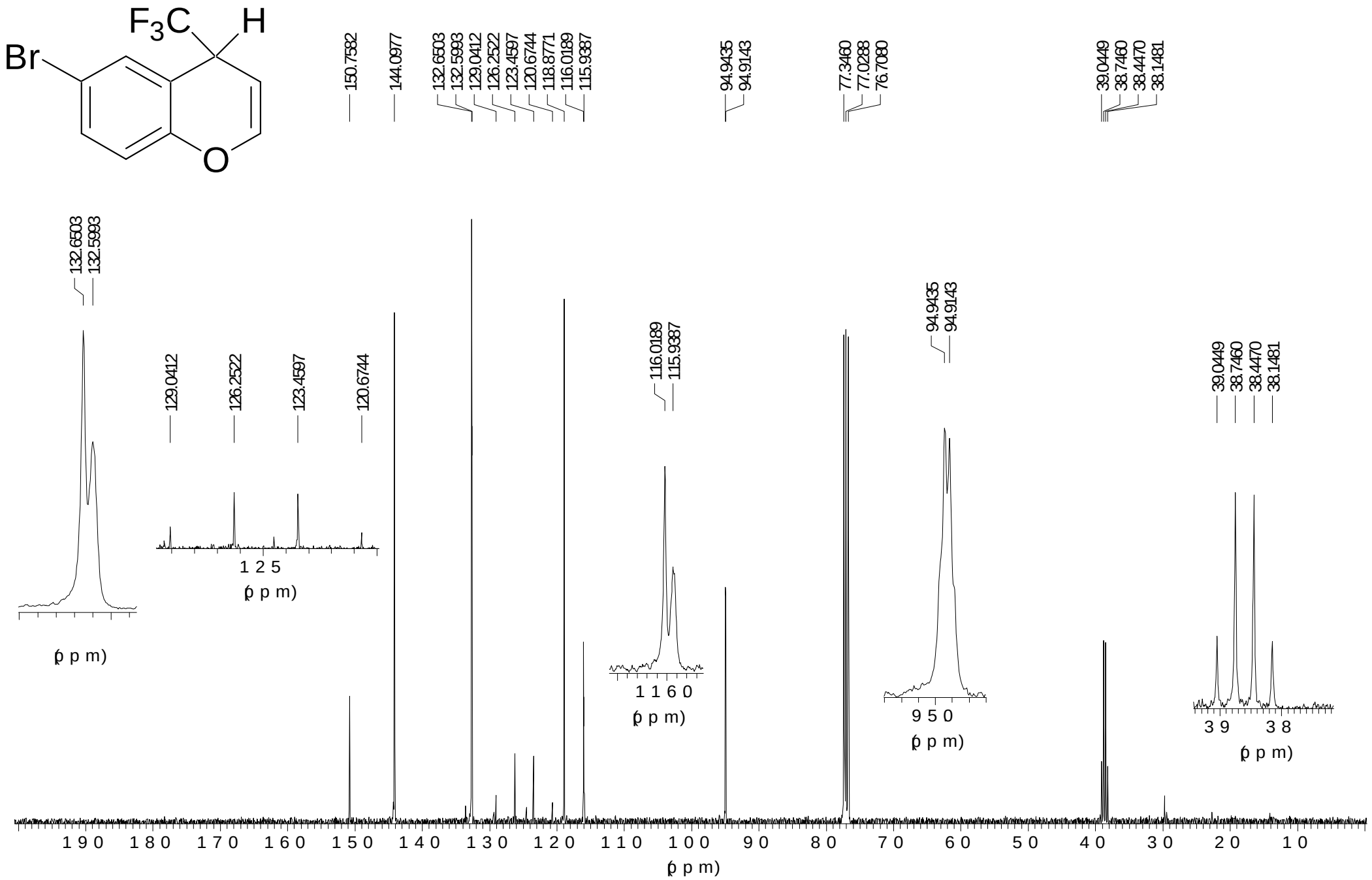
Compound **3a** spectrum NMR ^{19}F without ^{1}H decoupling in $CDCl_3$



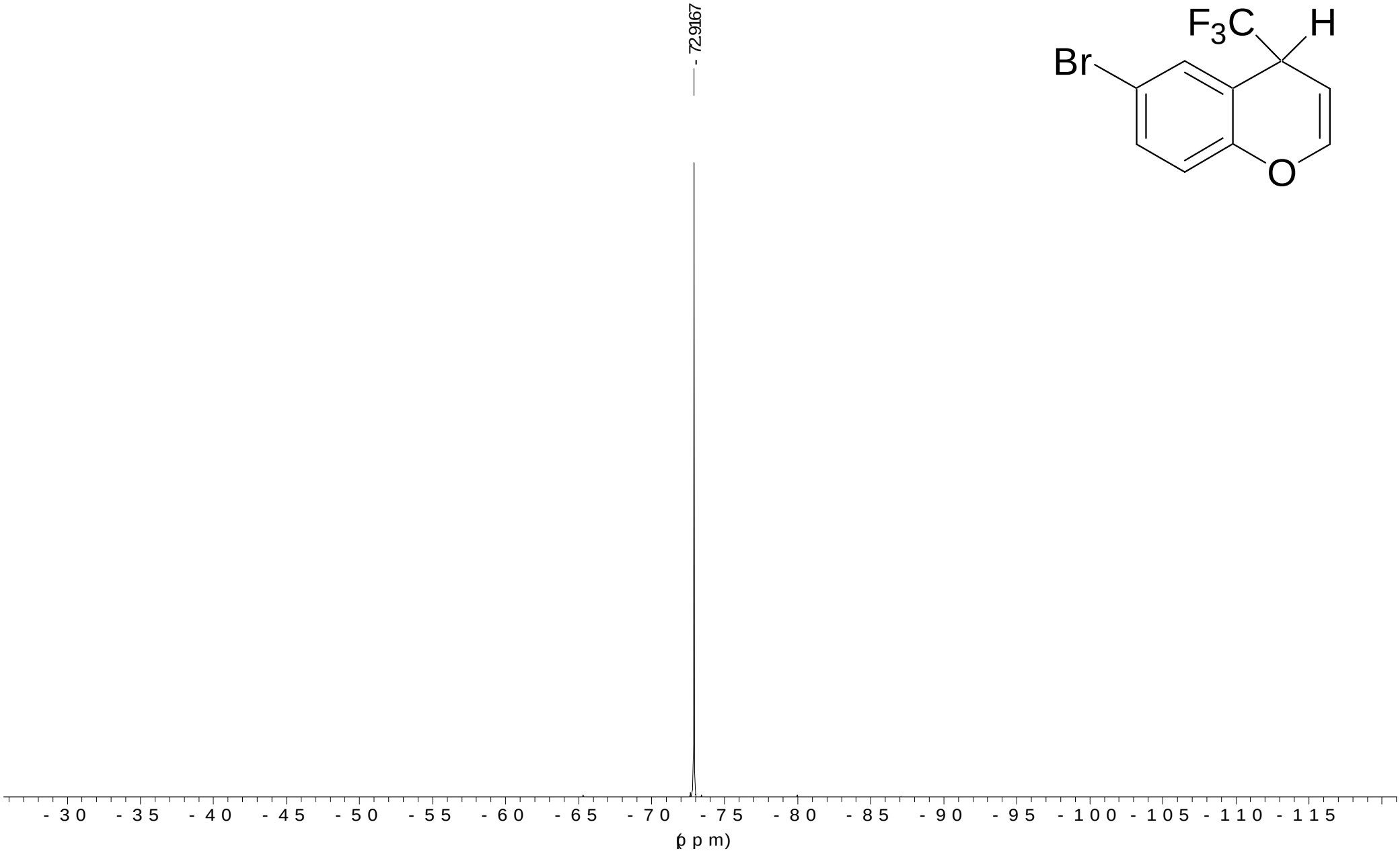
Compound **3c** spectrum NMR ^{1}H in $CDCl_3$



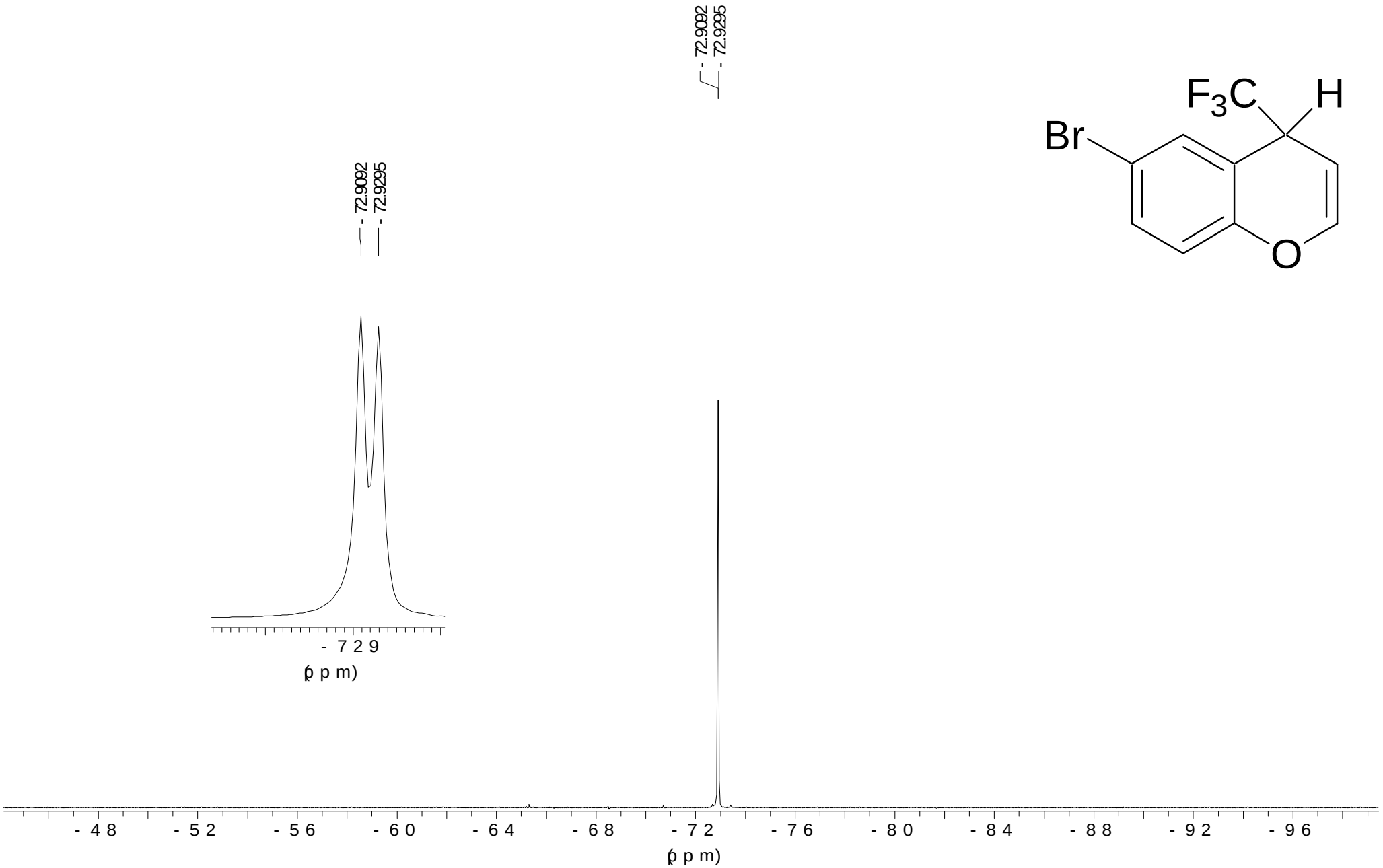
Compound **3c** spectrum NMR $^{1}H\{^{19}F\}$ in $CDCl_3$



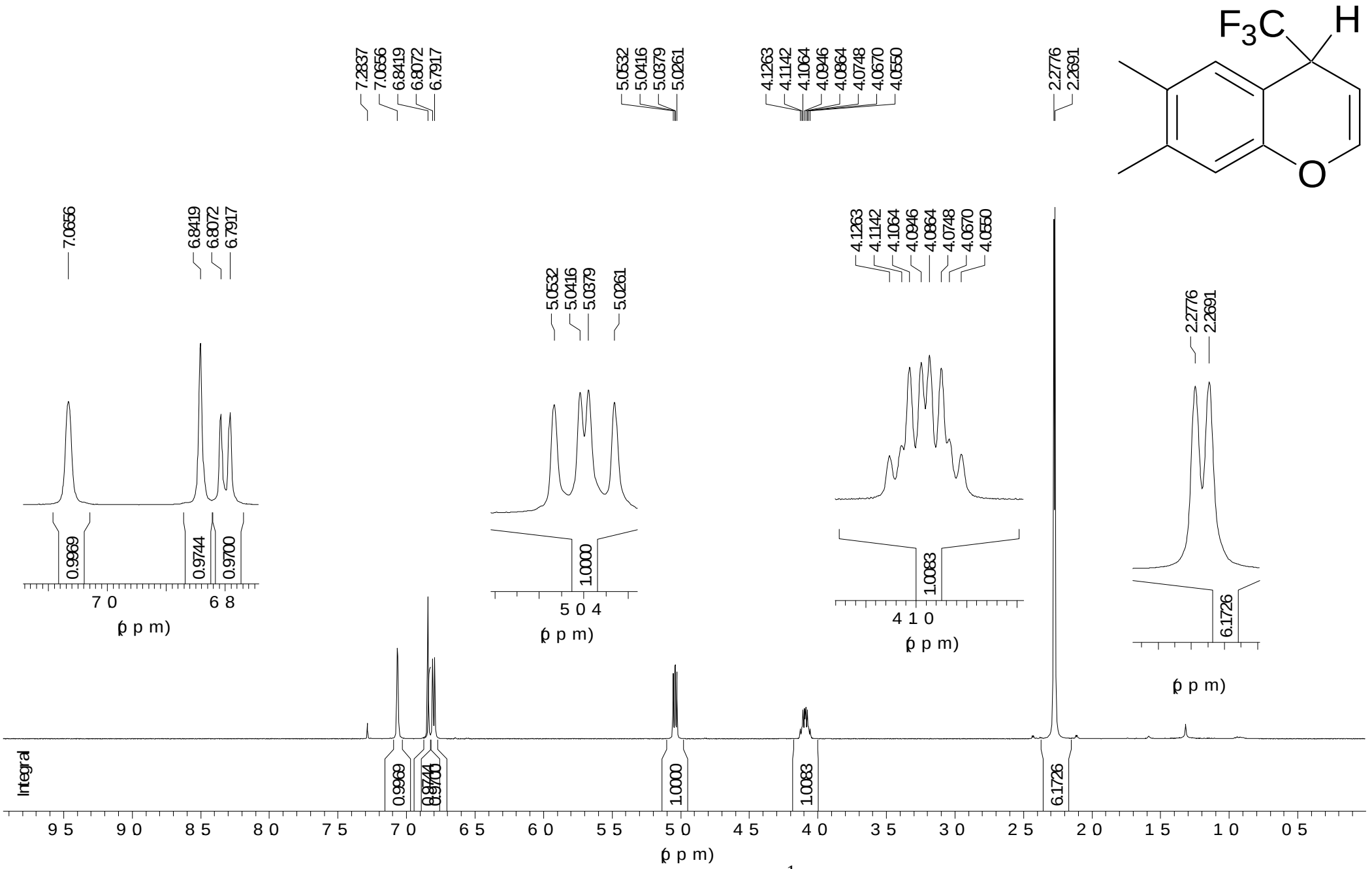
Compound **3c** spectrum NMR ^{13}C in $CDCl_3$



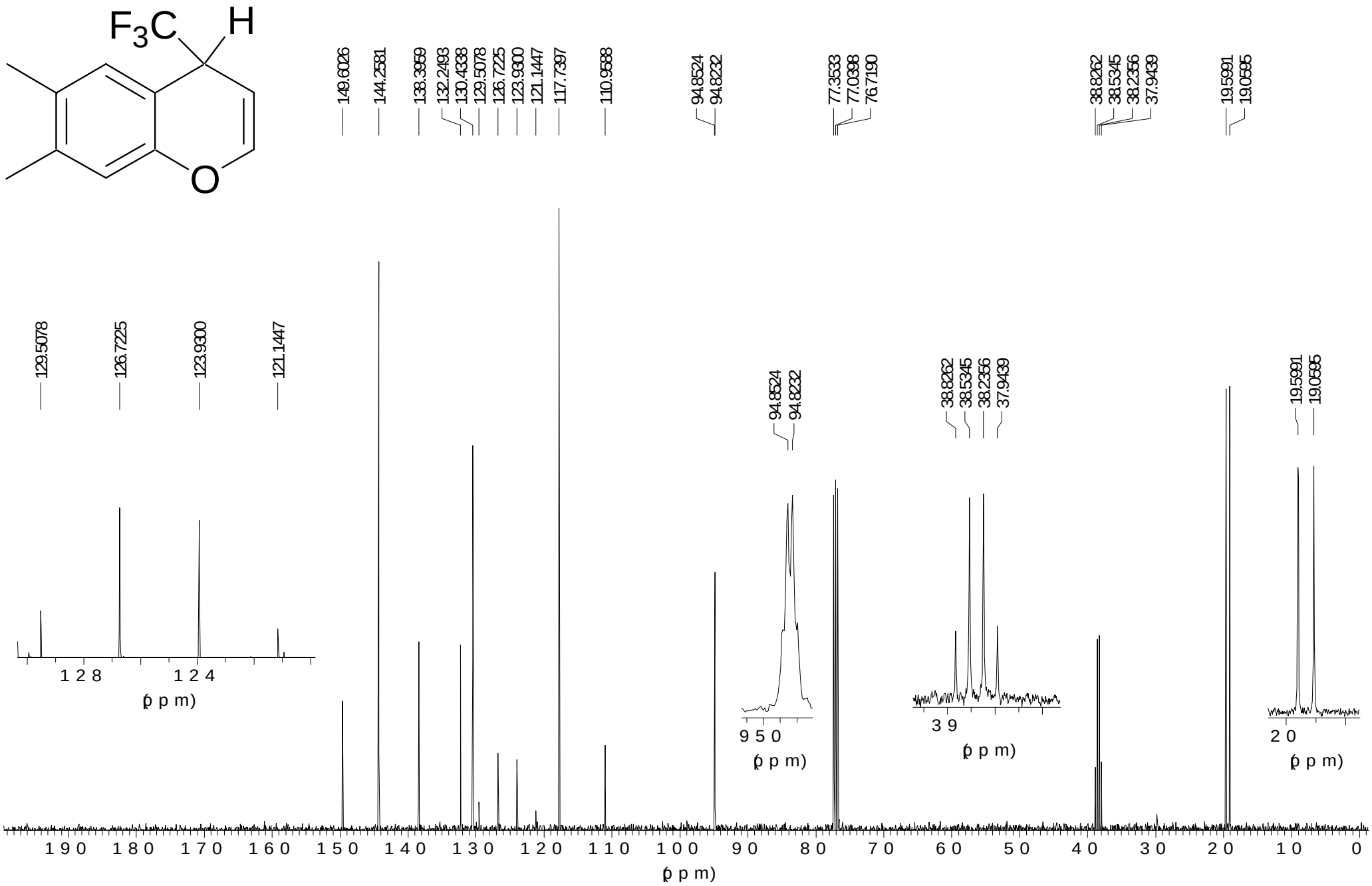
Compound **3c** spectrum NMR ^{19}F in $CDCl_3$



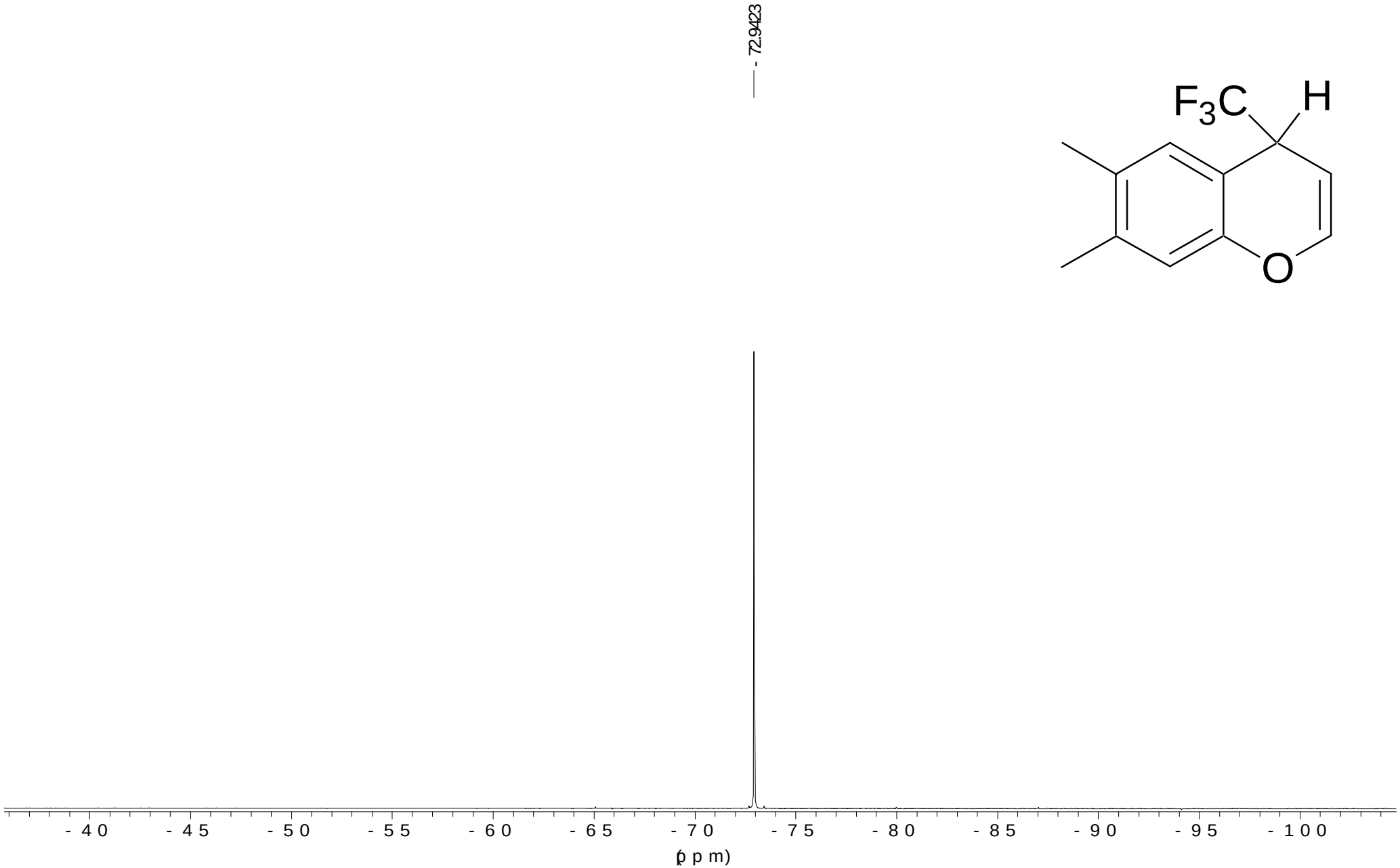
Compound **3c** spectrum NMR ^{19}F without ^{1}H decoupling in $CDCl_3$



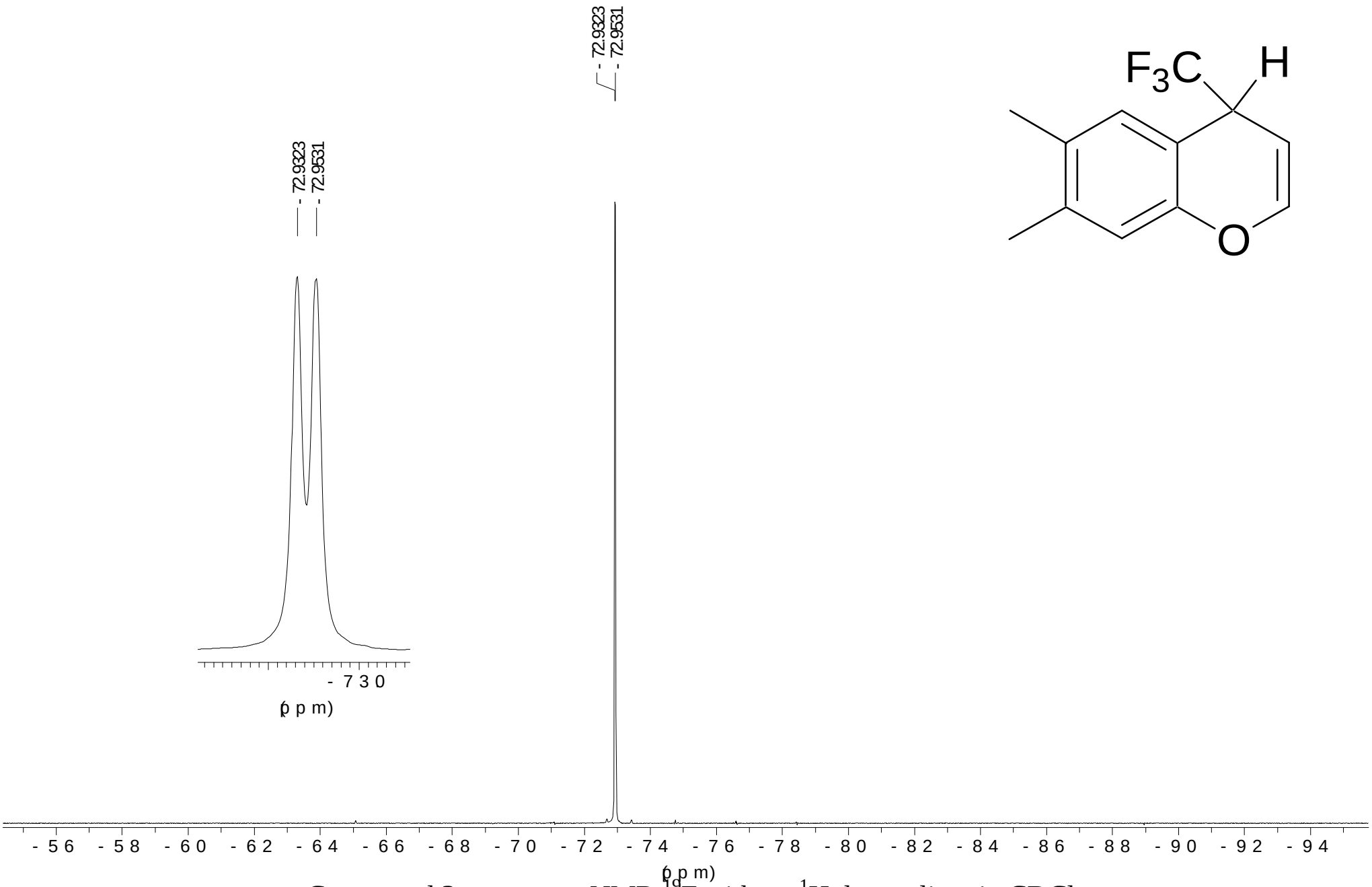
Compound **3g** spectrum NMR ^{1}H in $CDCl_3$



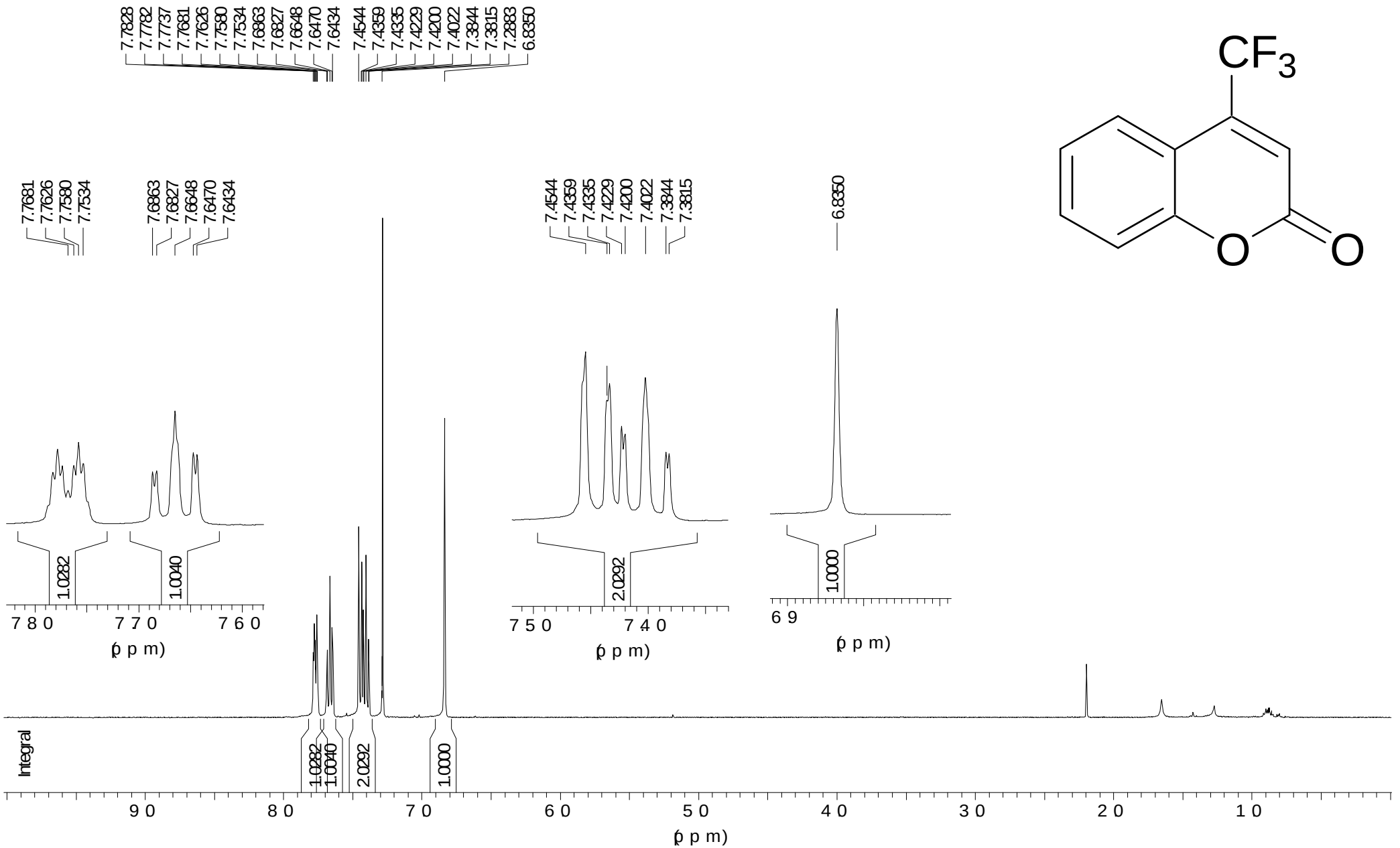
Compound **3g** spectrum NMR ^{13}C in $CDCl_3$



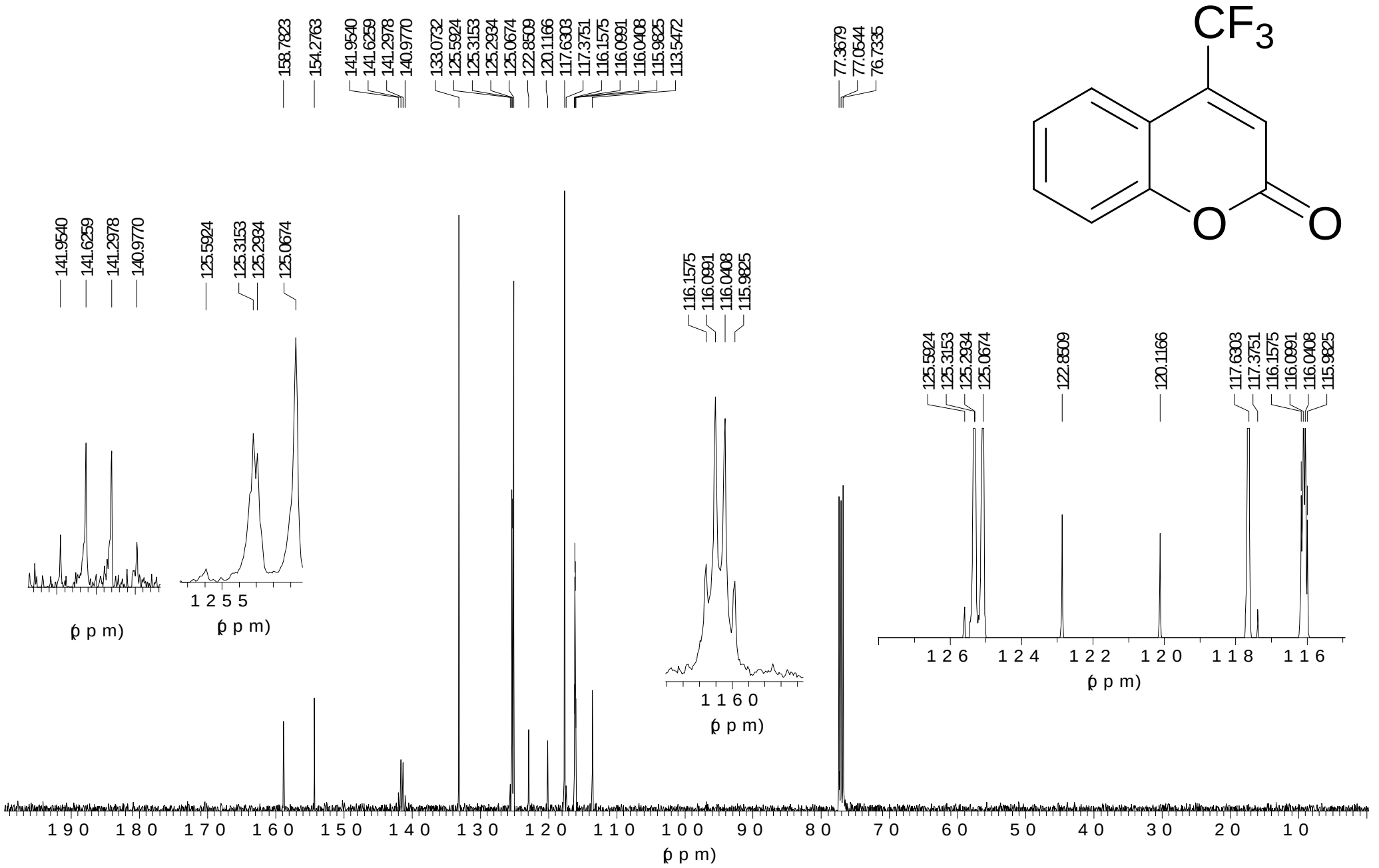
Compound **3g** spectrum NMR ^{19}F in $CDCl_3$



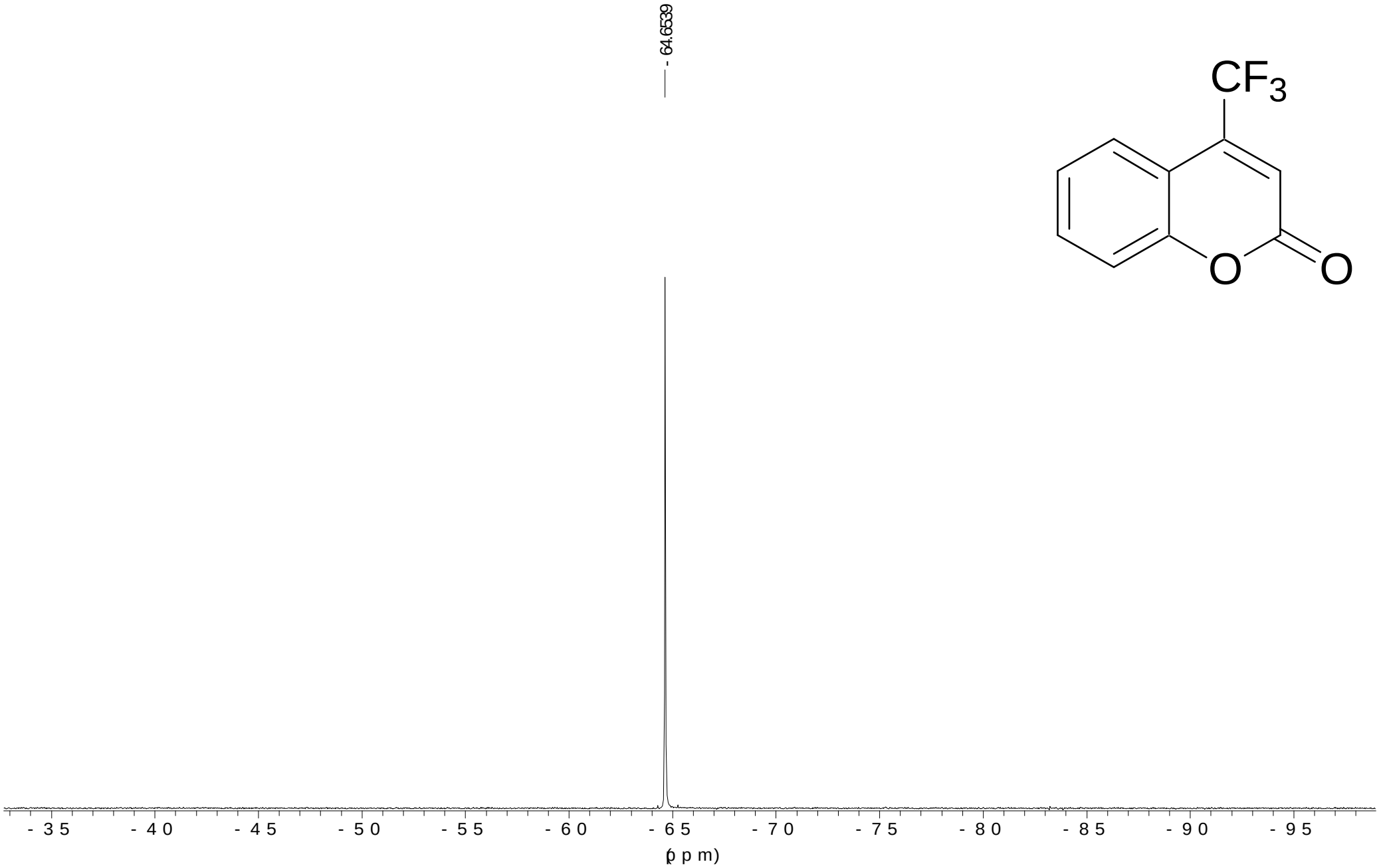
Compound **3g** spectrum NMR ^{19}F without ^{1}H decoupling in $CDCl_3$



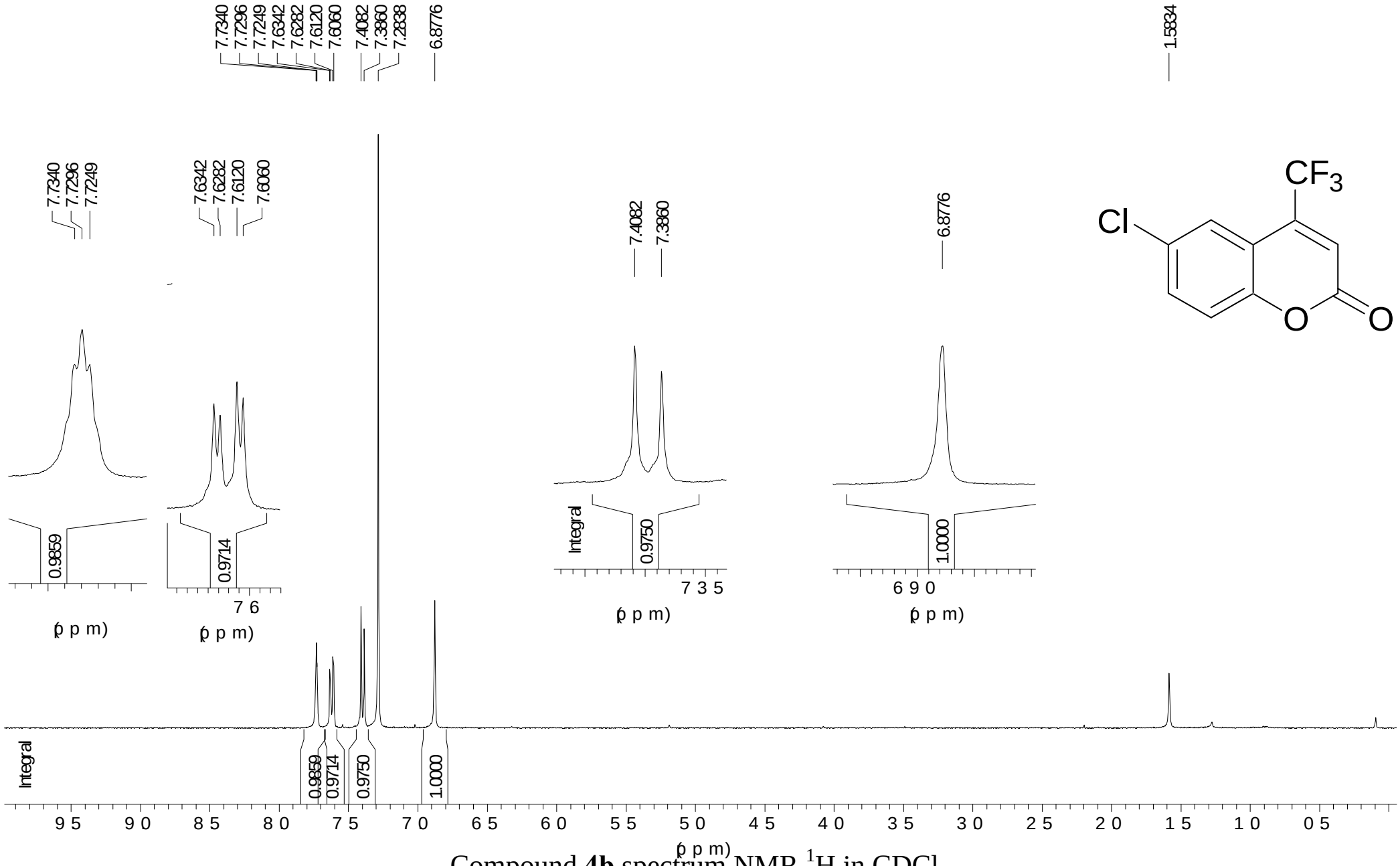
Compound **4a** spectrum NMR ^{1}H in $CDCl_3$



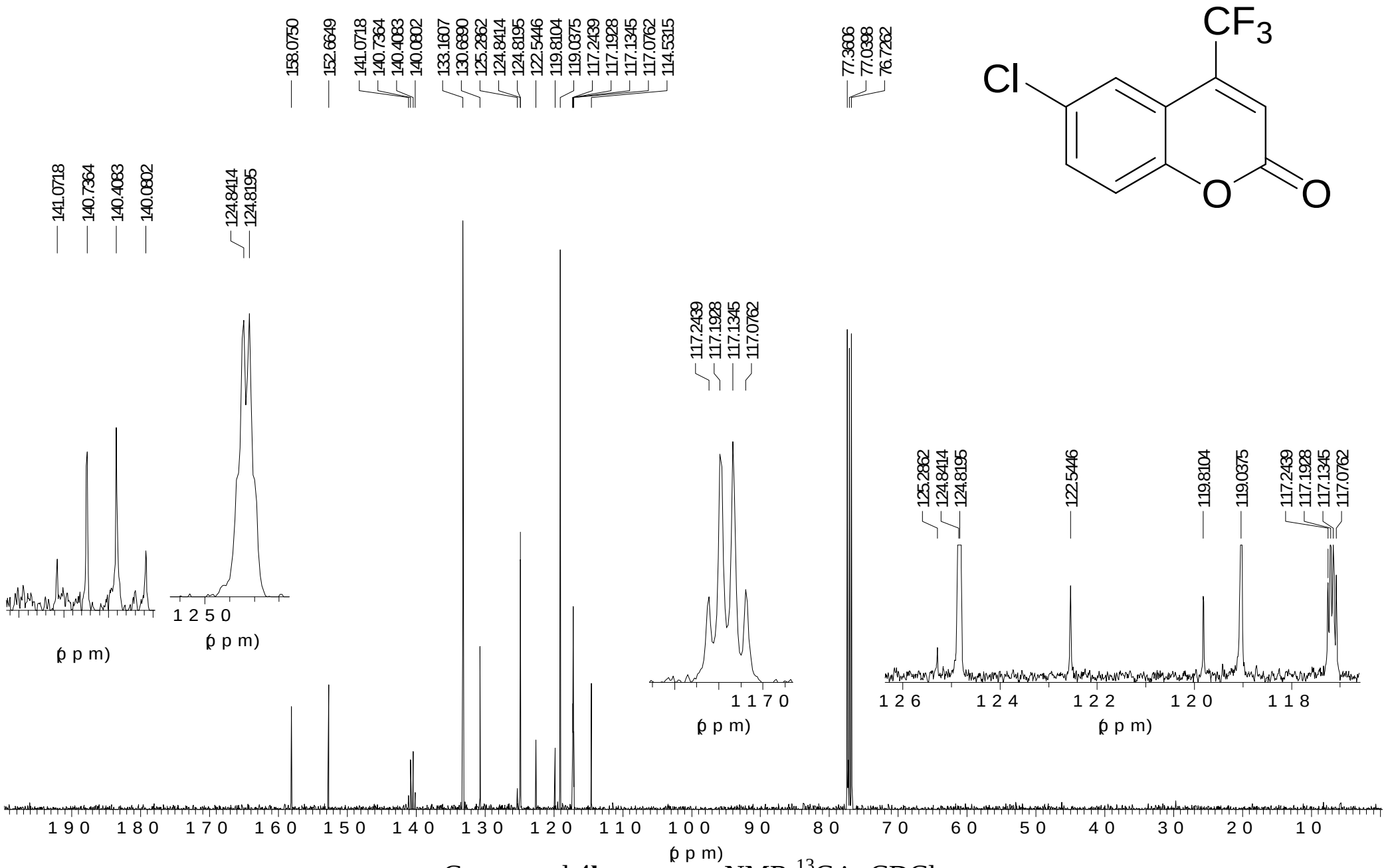
Compound **4a** spectrum NMR ^{13}C in $CDCl_3$



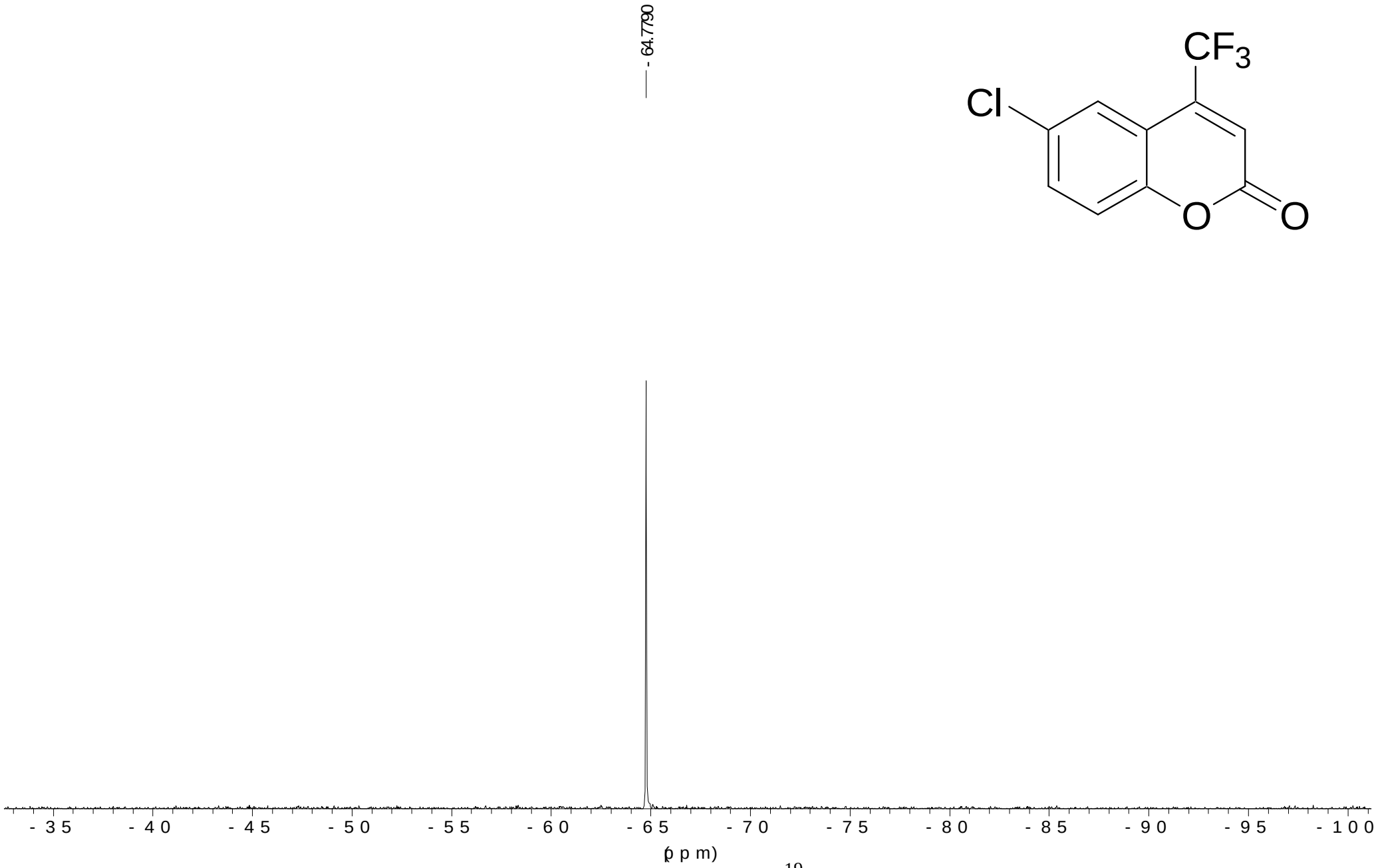
Compound **4a** spectrum NMR ^{19}F in $CDCl_3$



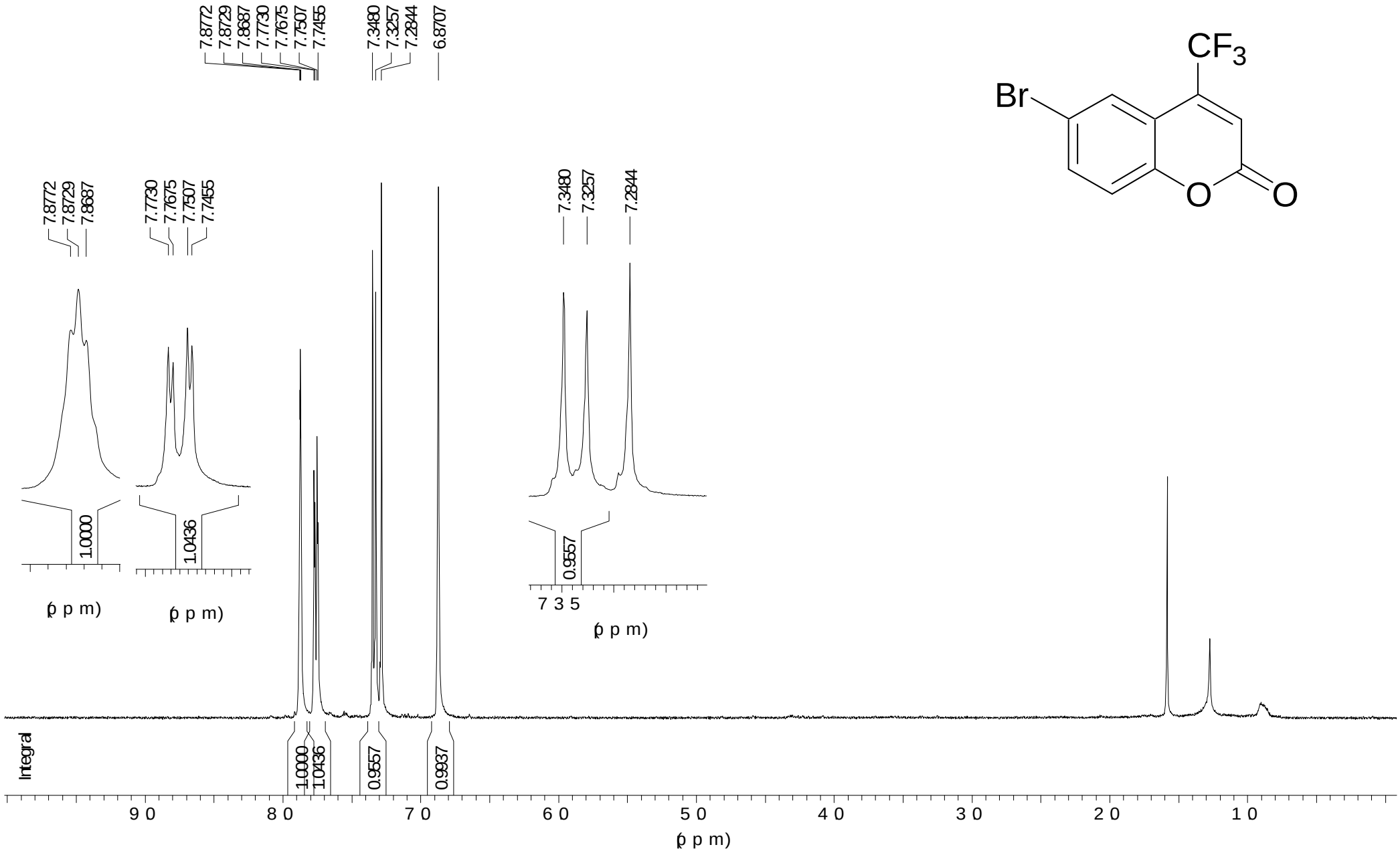
Compound **4b** spectrum NMR ^{1}H in $CDCl_3$



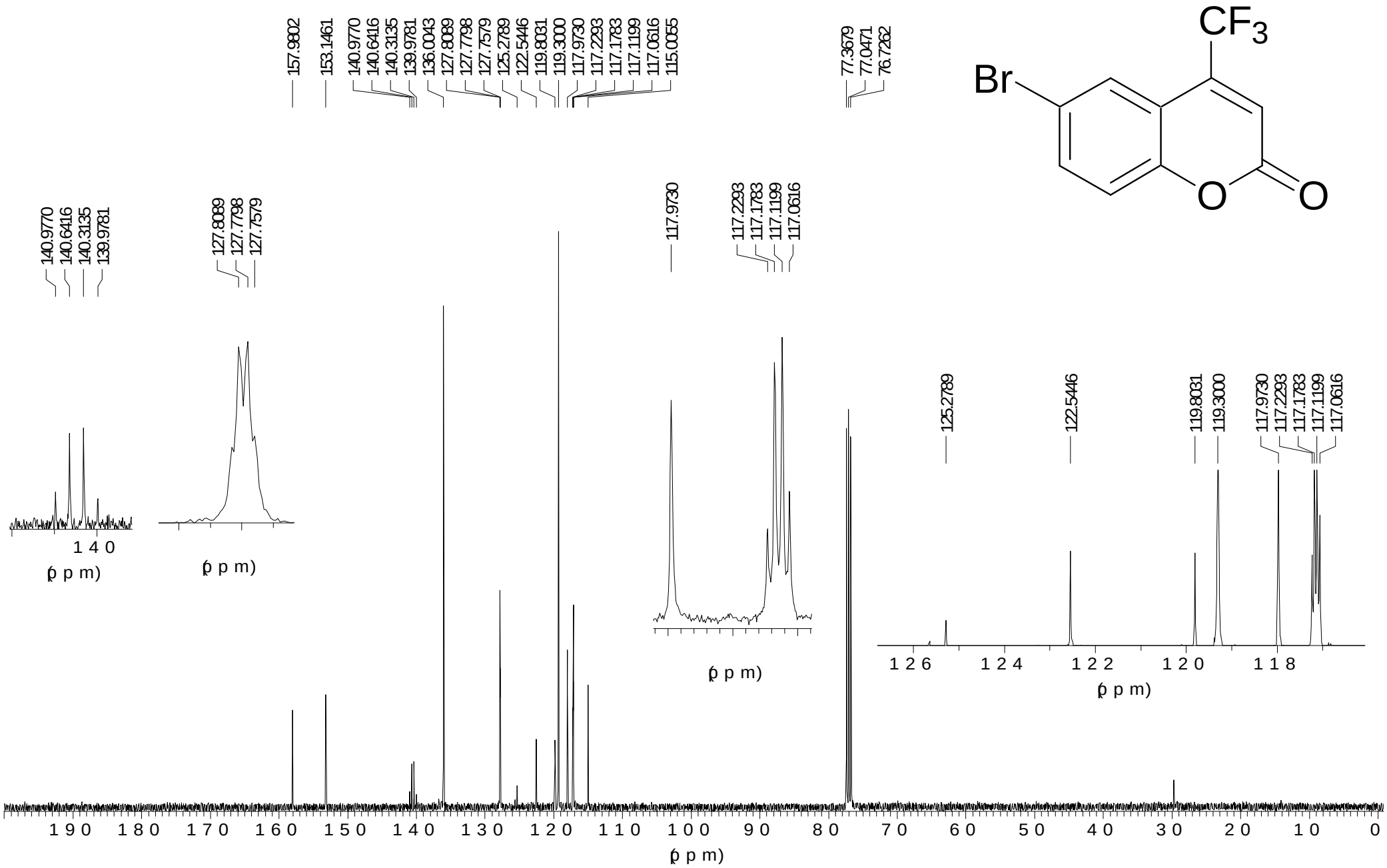
Compound **4b** spectrum NMR ^{13}C in $CDCl_3$



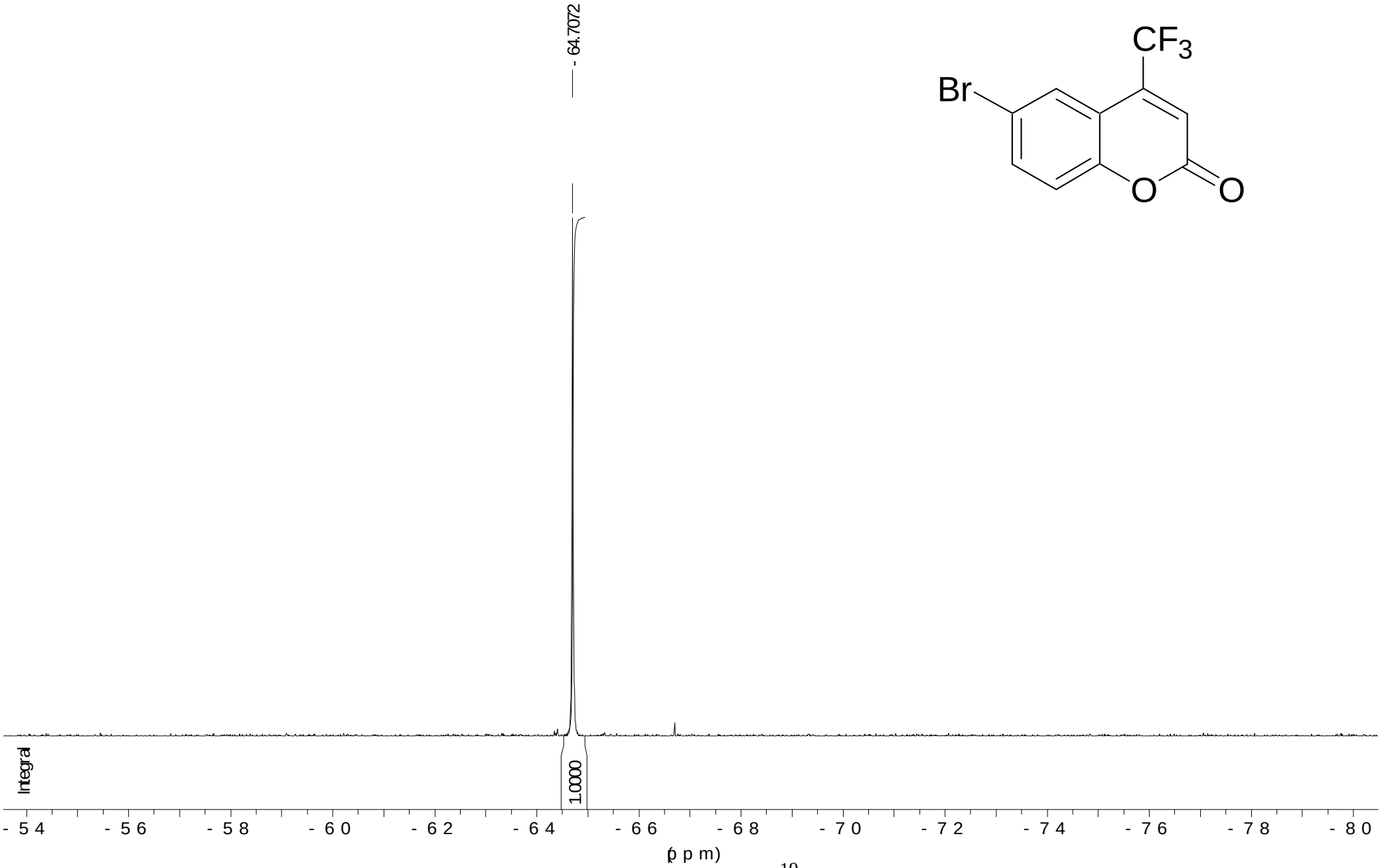
Compound **4b** spectrum NMR ^{19}F in $CDCl_3$



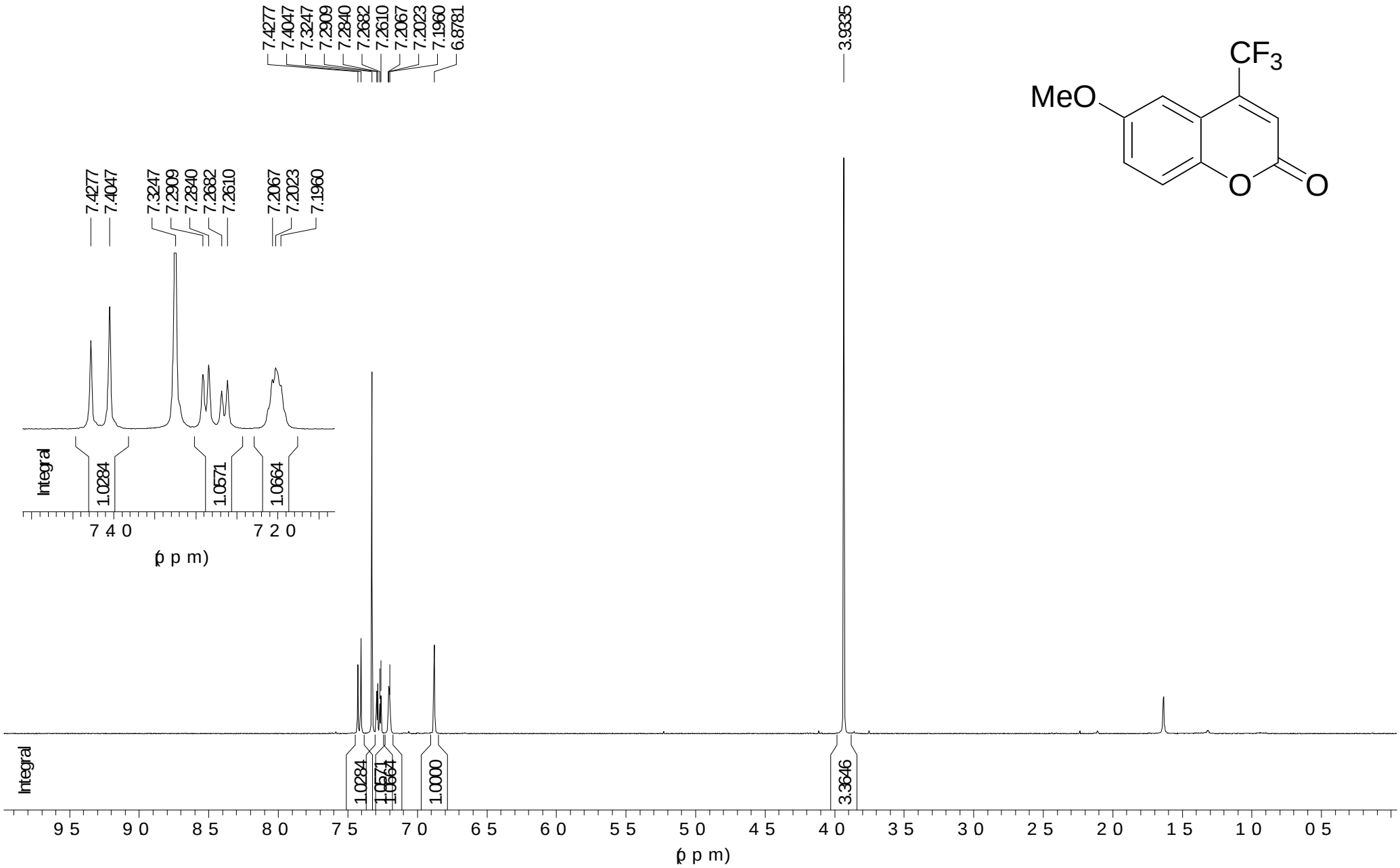
Compound **4c** spectrum NMR ^{1}H in $CDCl_3$



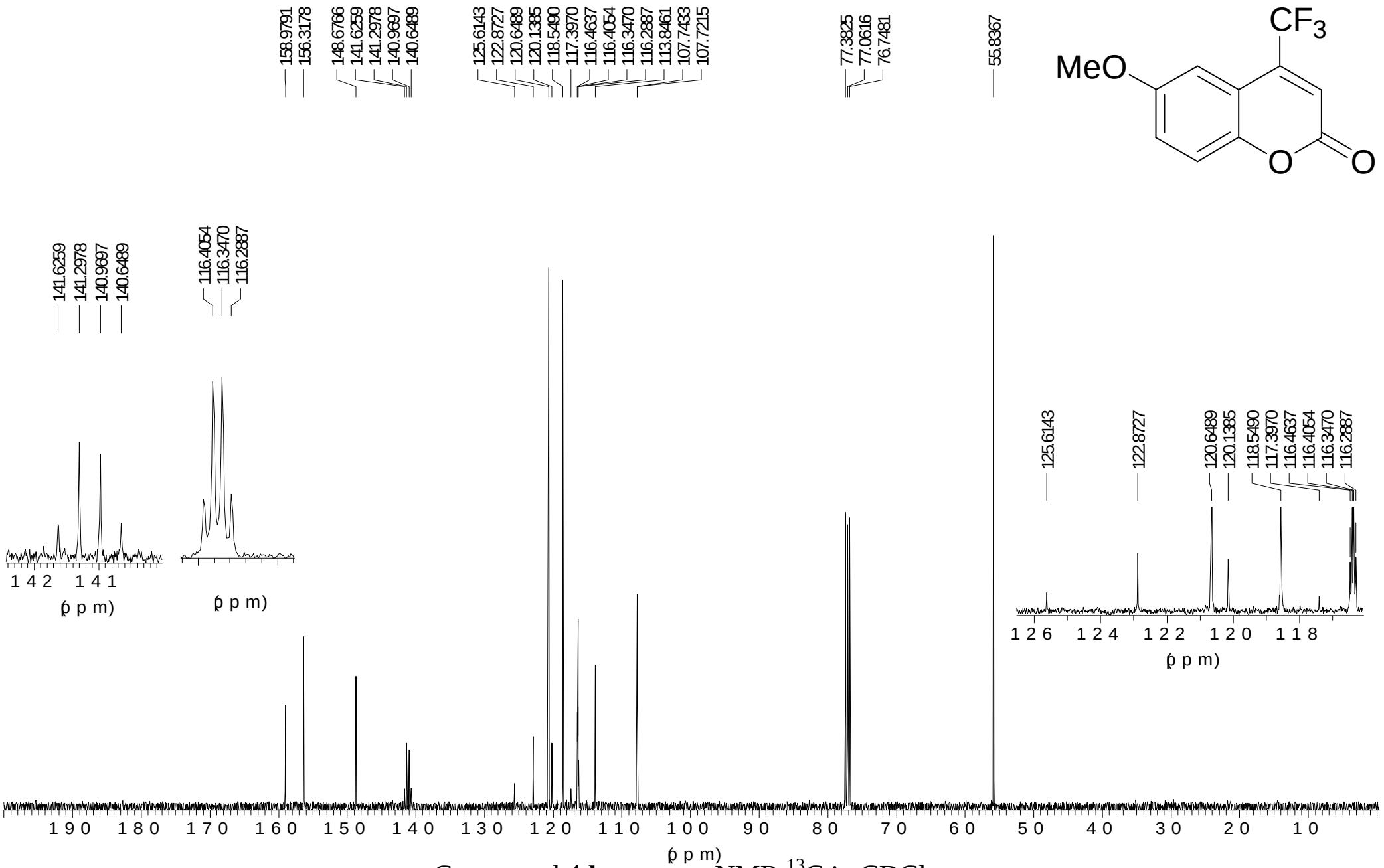
Compound **4c** spectrum NMR ^{13}C in $CDCl_3$



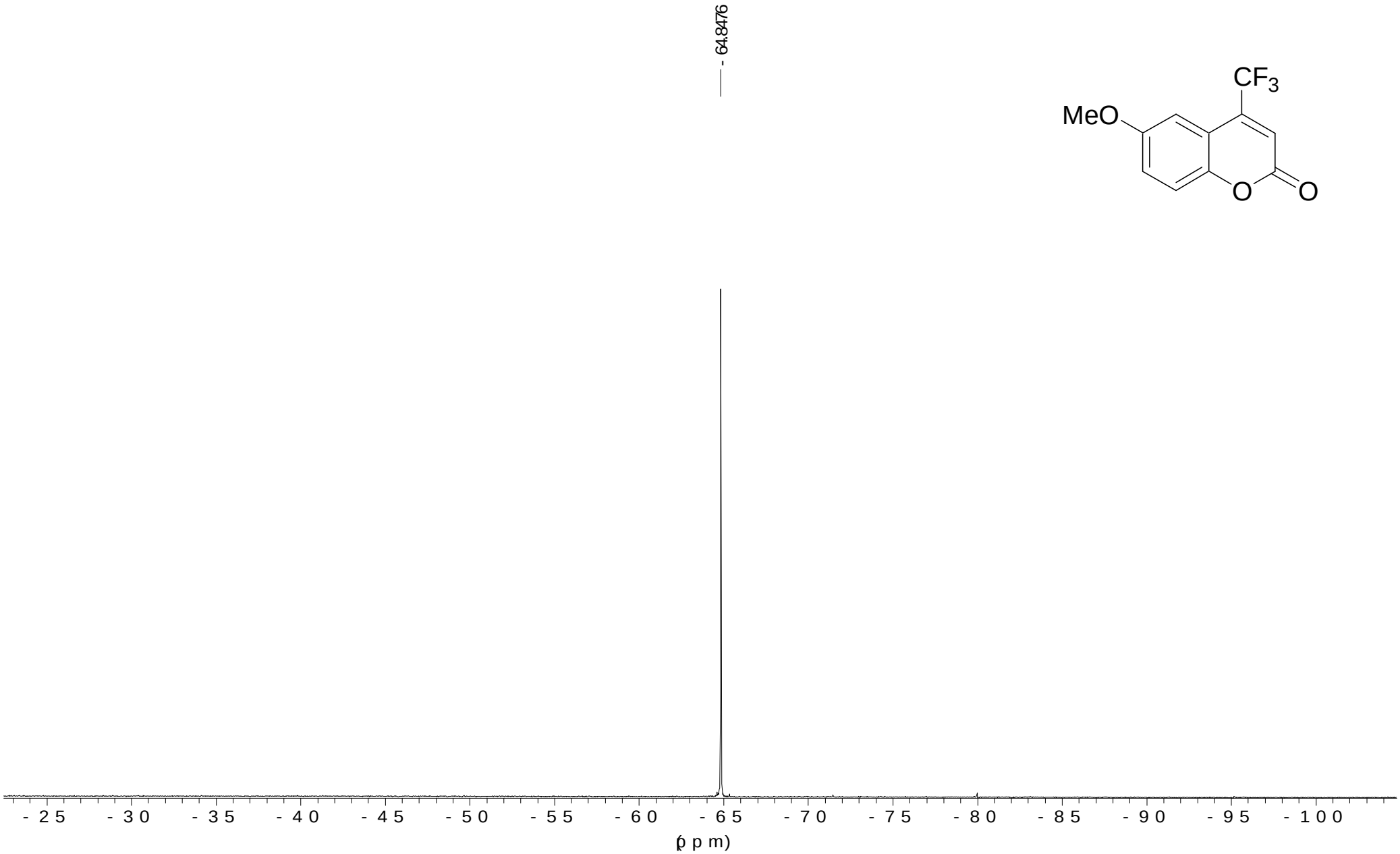
Compound **4c** spectrum NMR ^{19}F in $CDCl_3$



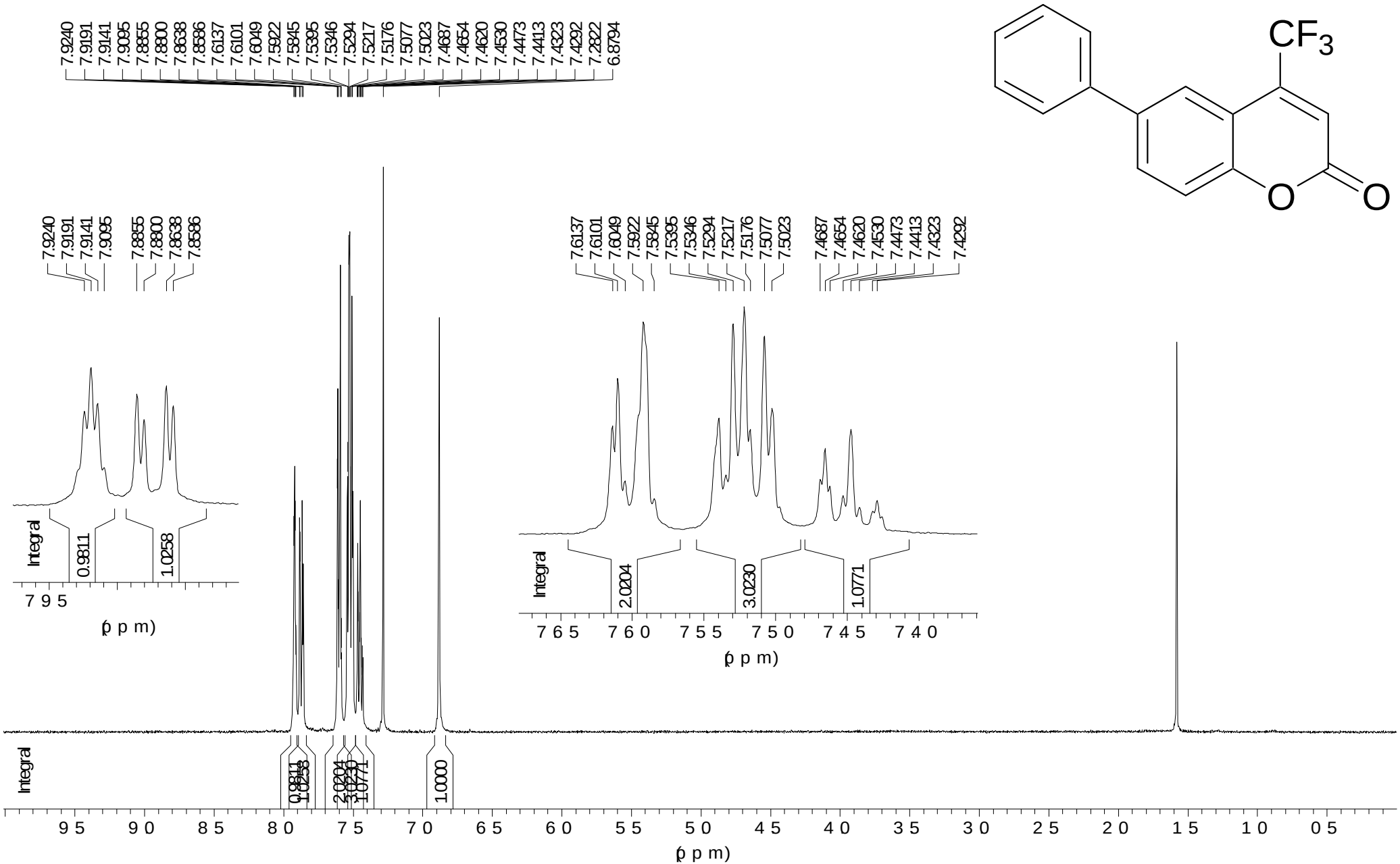
Compound **4d** spectrum NMR ^{1}H in $CDCl_3$



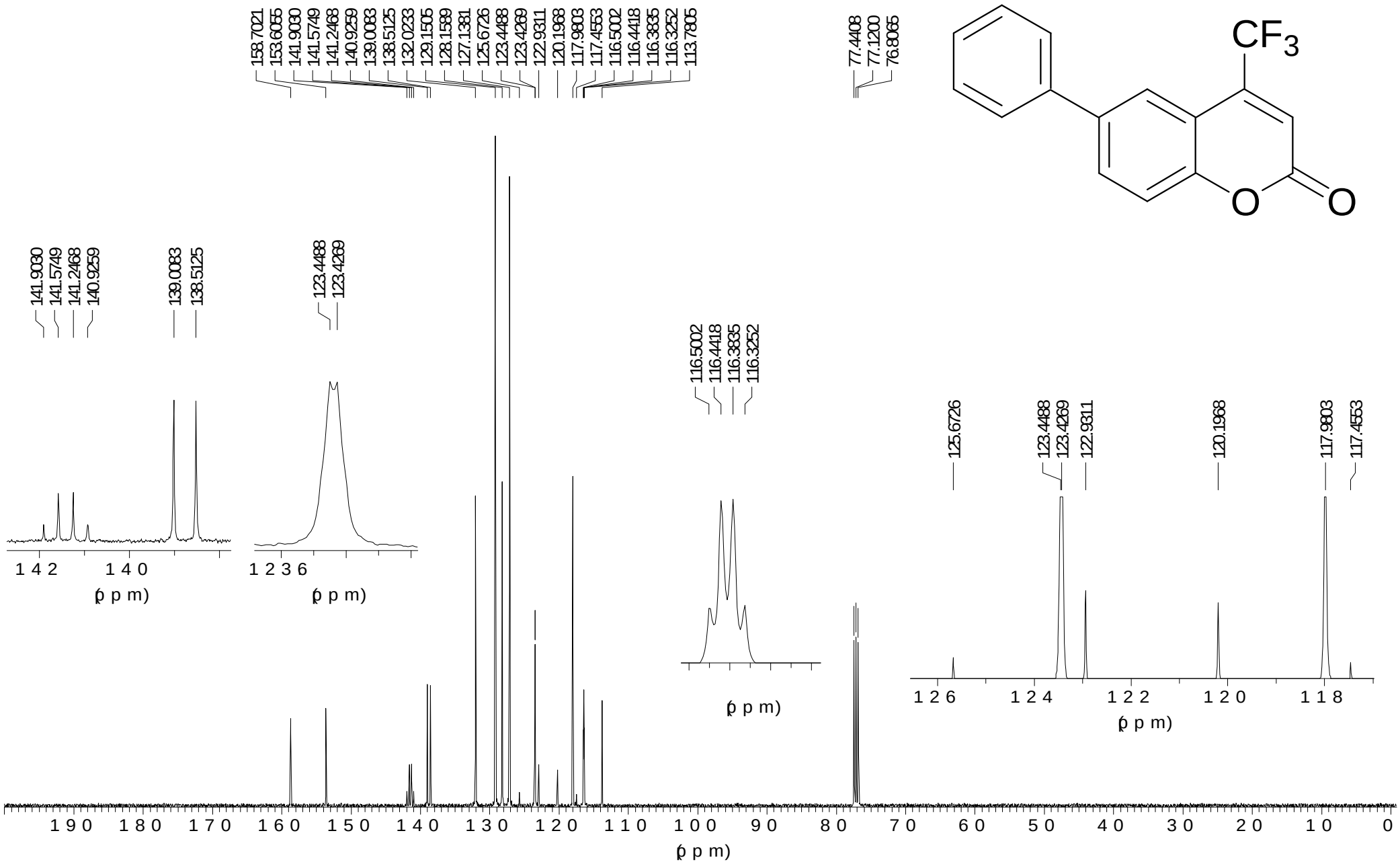
Compound **4d** spectrum NMR ^{13}C in $CDCl_3$



Compound **4d** spectrum NMR ^{19}F in $CDCl_3$

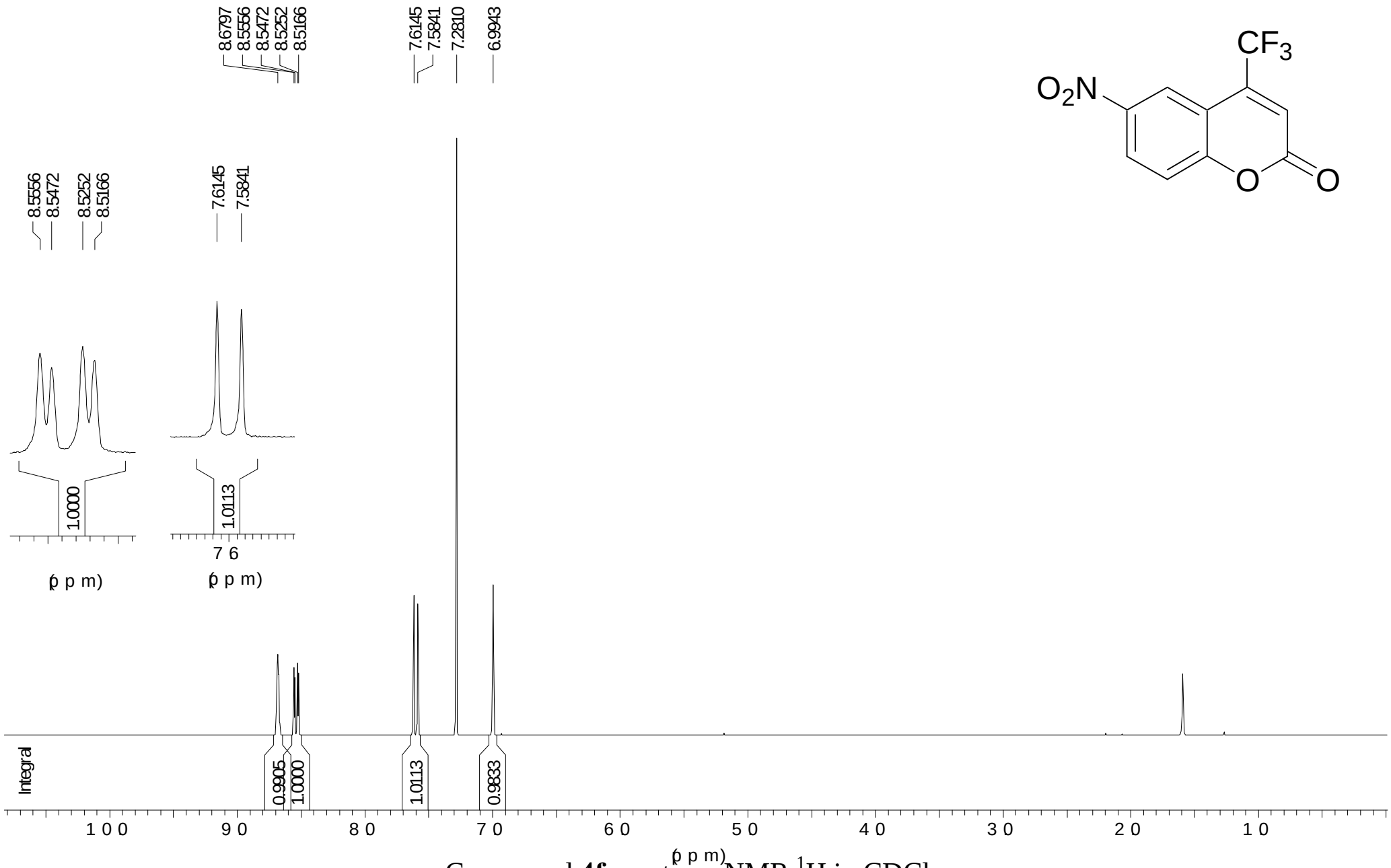


Compound **4e** spectrum NMR ^{1}H in $CDCl_3$

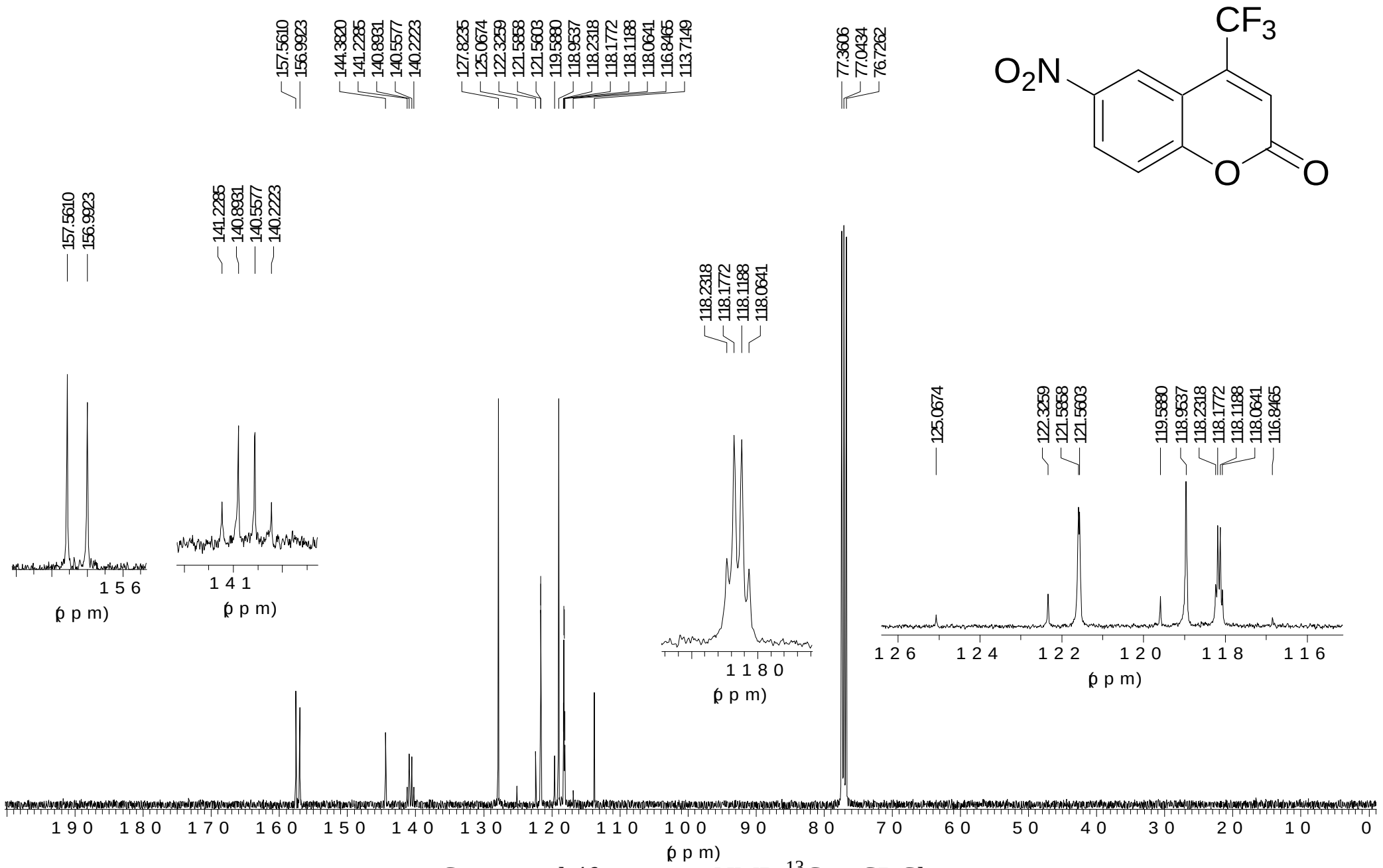


Compound **4e** spectrum NMR ^{13}C in $CDCl_3$

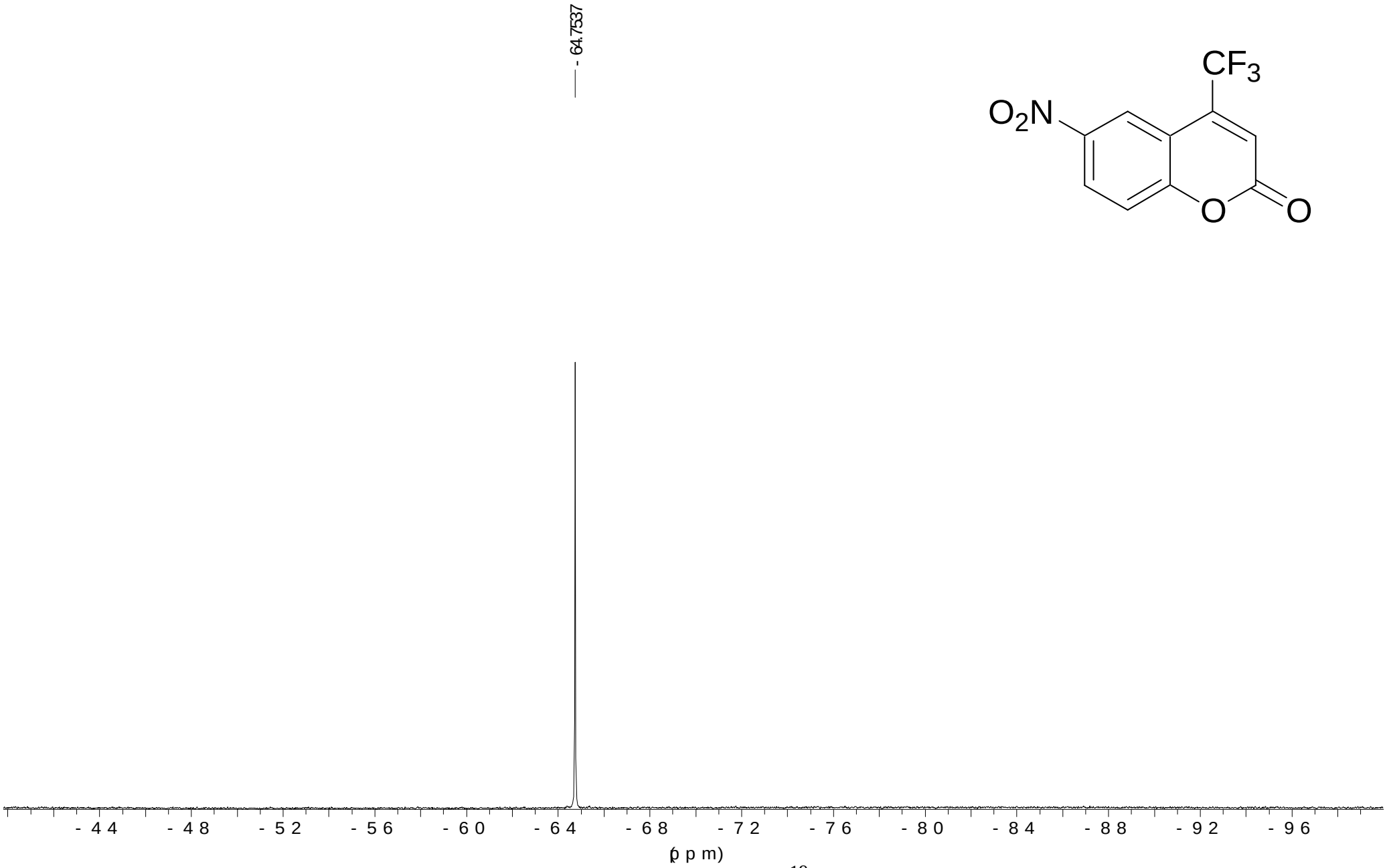
Compound **4e** spectrum NMR ^{19}F in $CDCl_3$



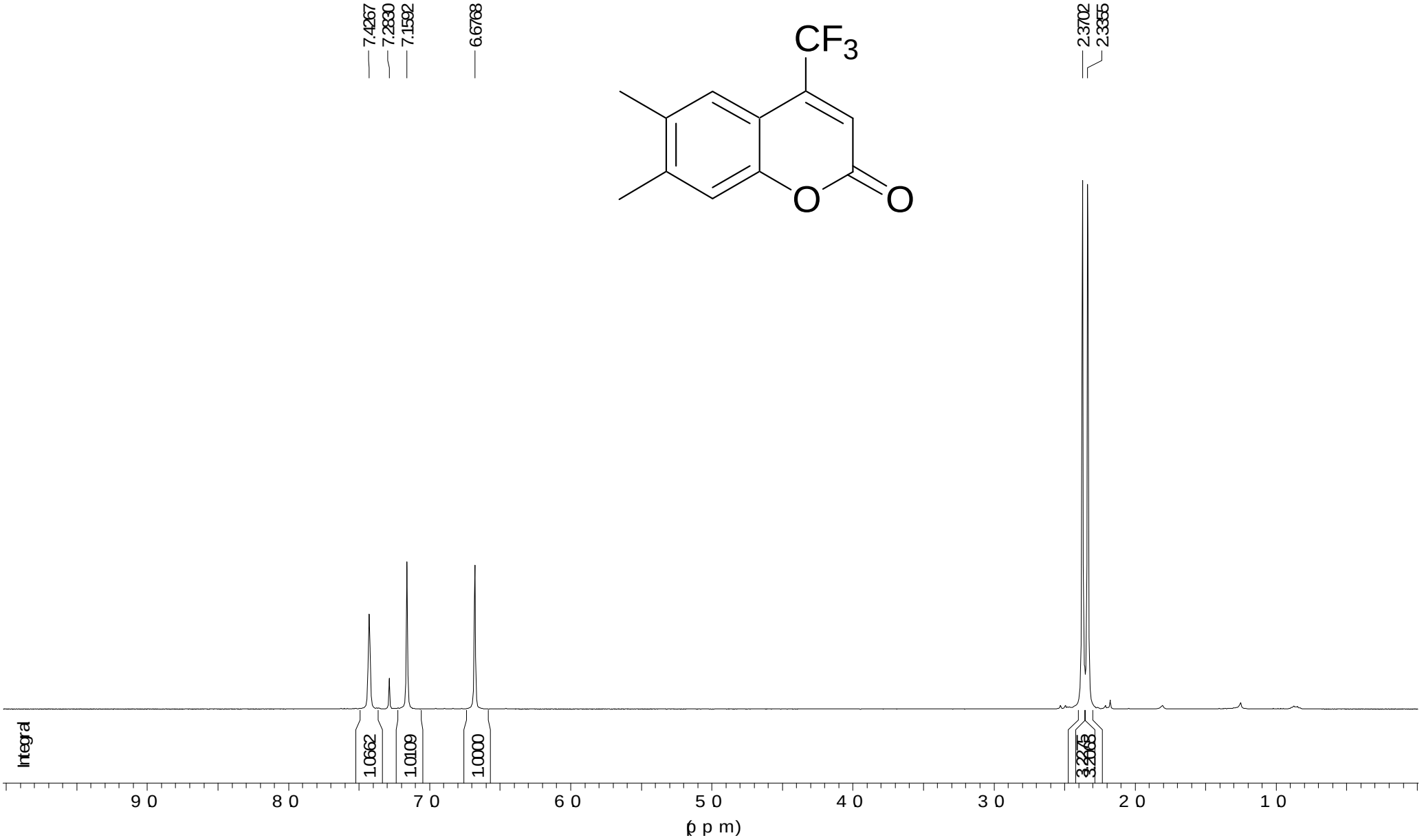
Compound **4f** spectrum NMR ^{1}H in $CDCl_3$



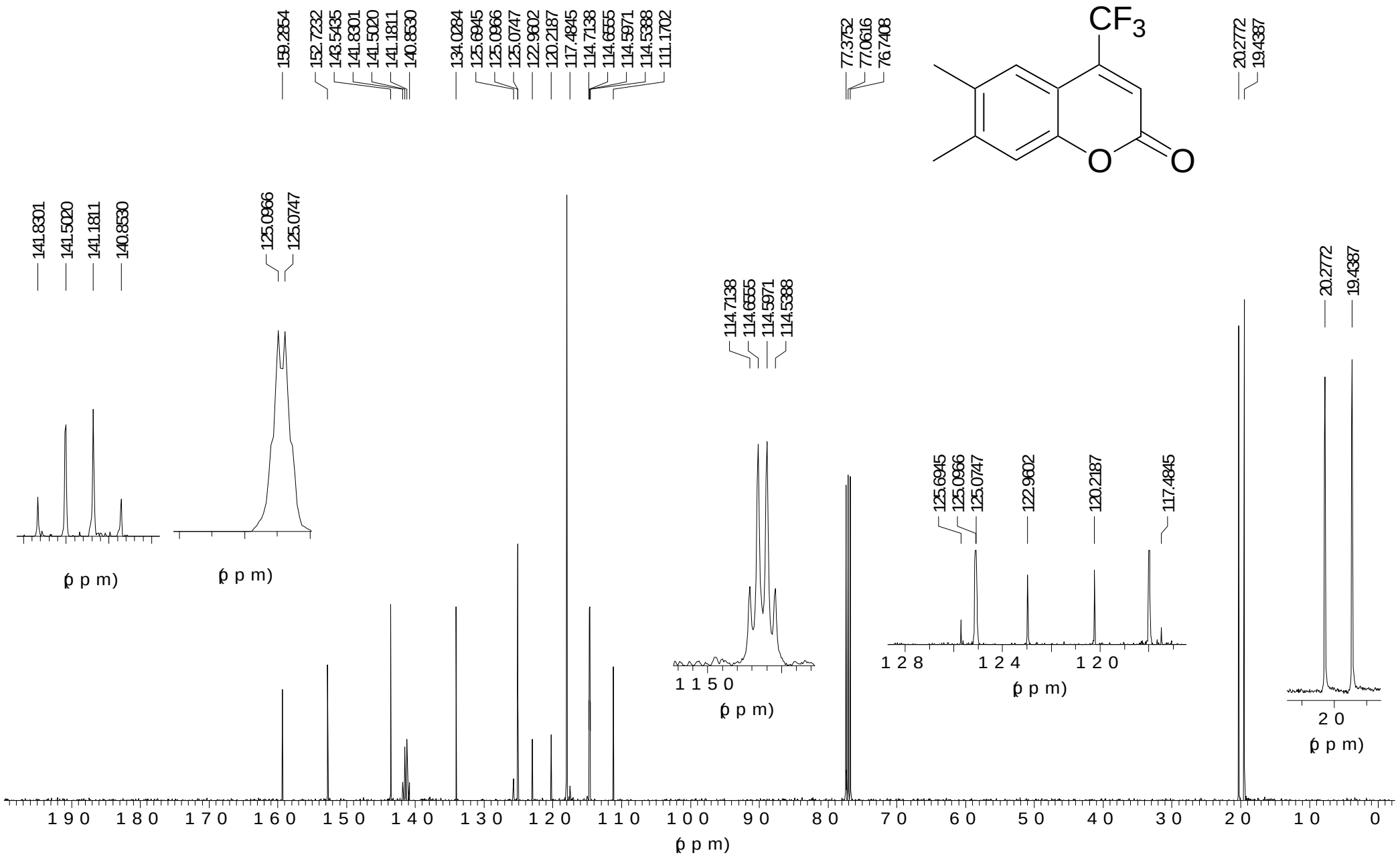
Compound **4f** spectrum NMR ^{13}C in $CDCl_3$



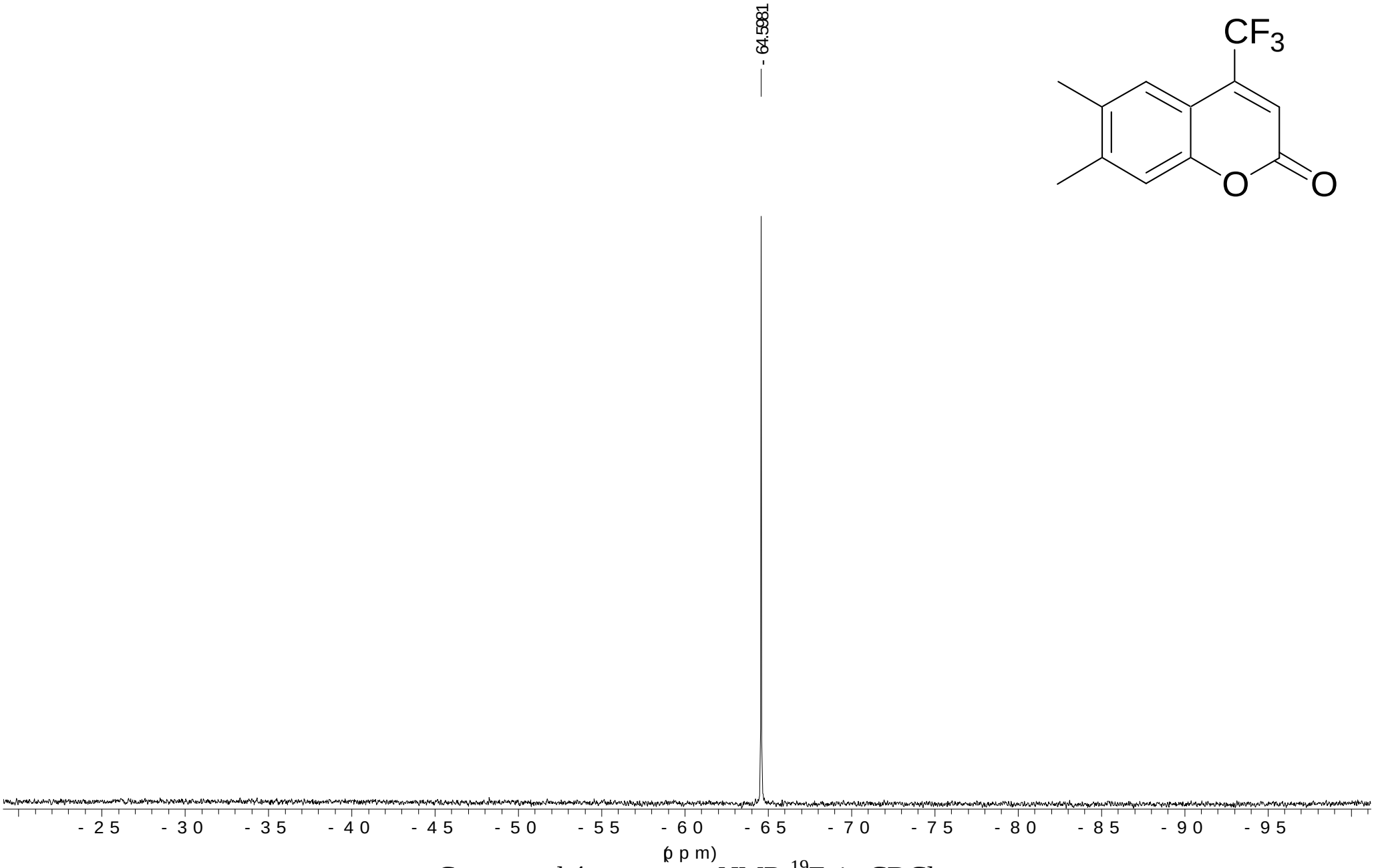
Compound **4f** spectrum NMR ^{19}F in $CDCl_3$



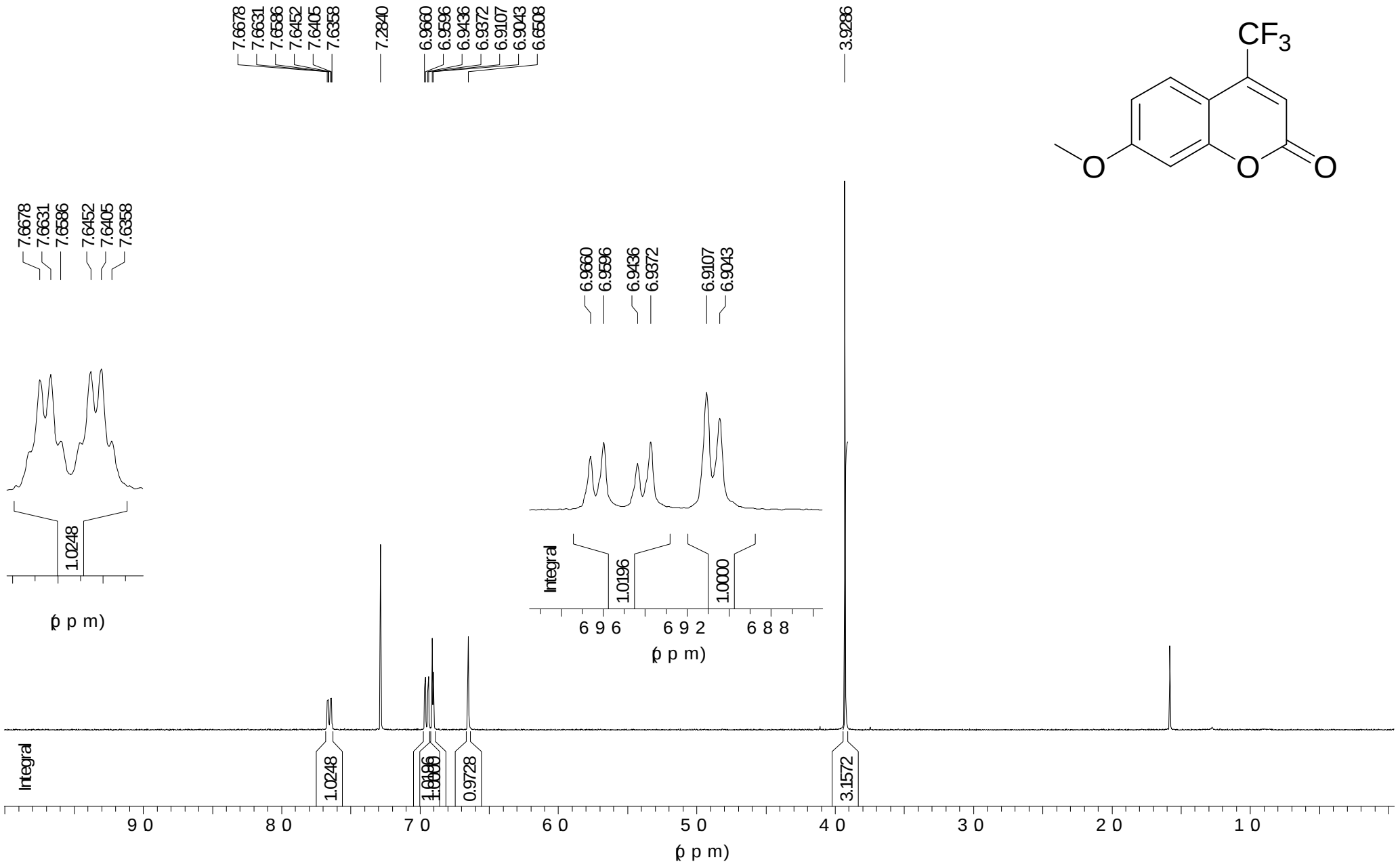
Compound **4g** spectrum NMR ^{1}H in $CDCl_3$



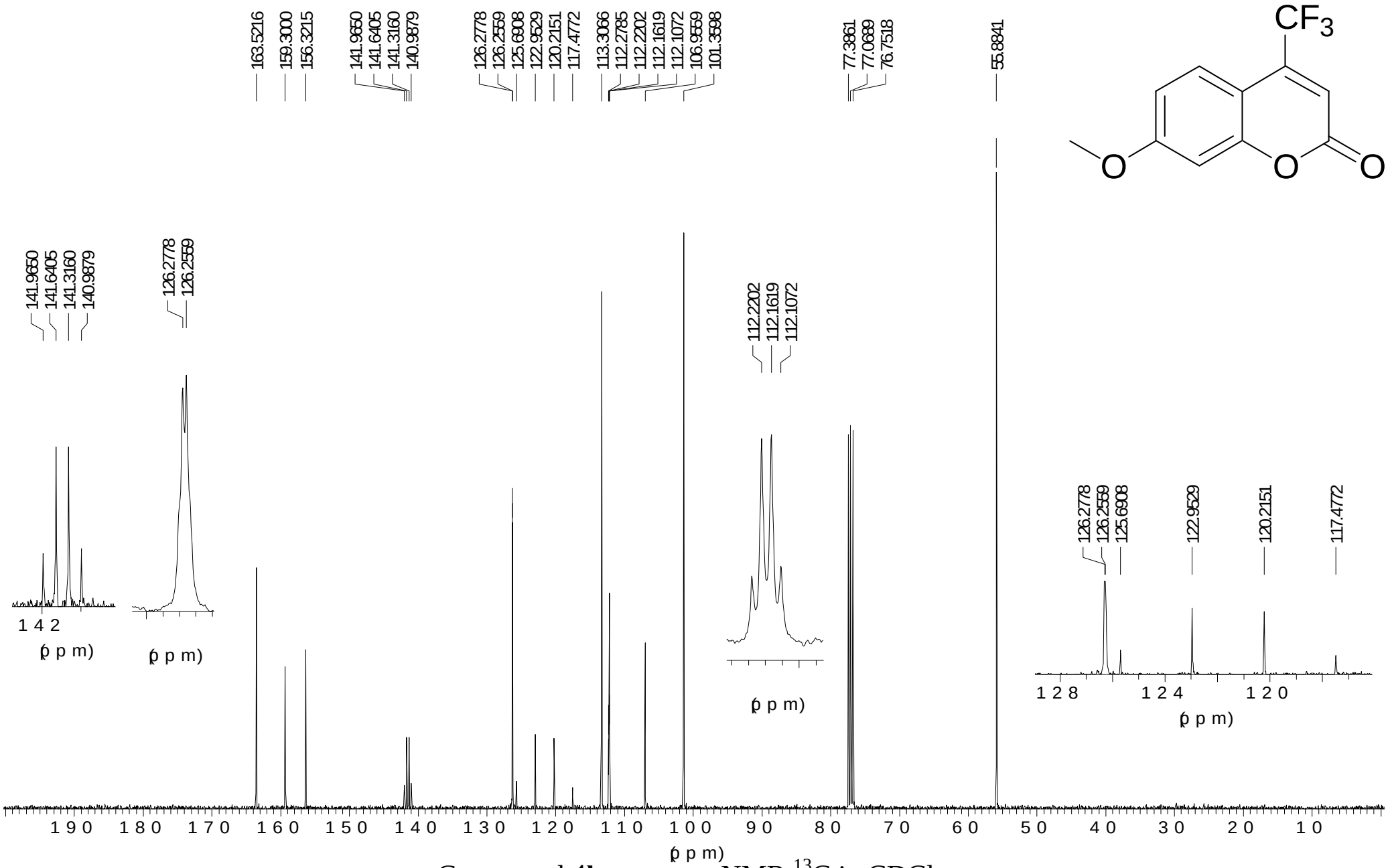
Compound **4g** spectrum NMR ^{13}C in $CDCl_3$



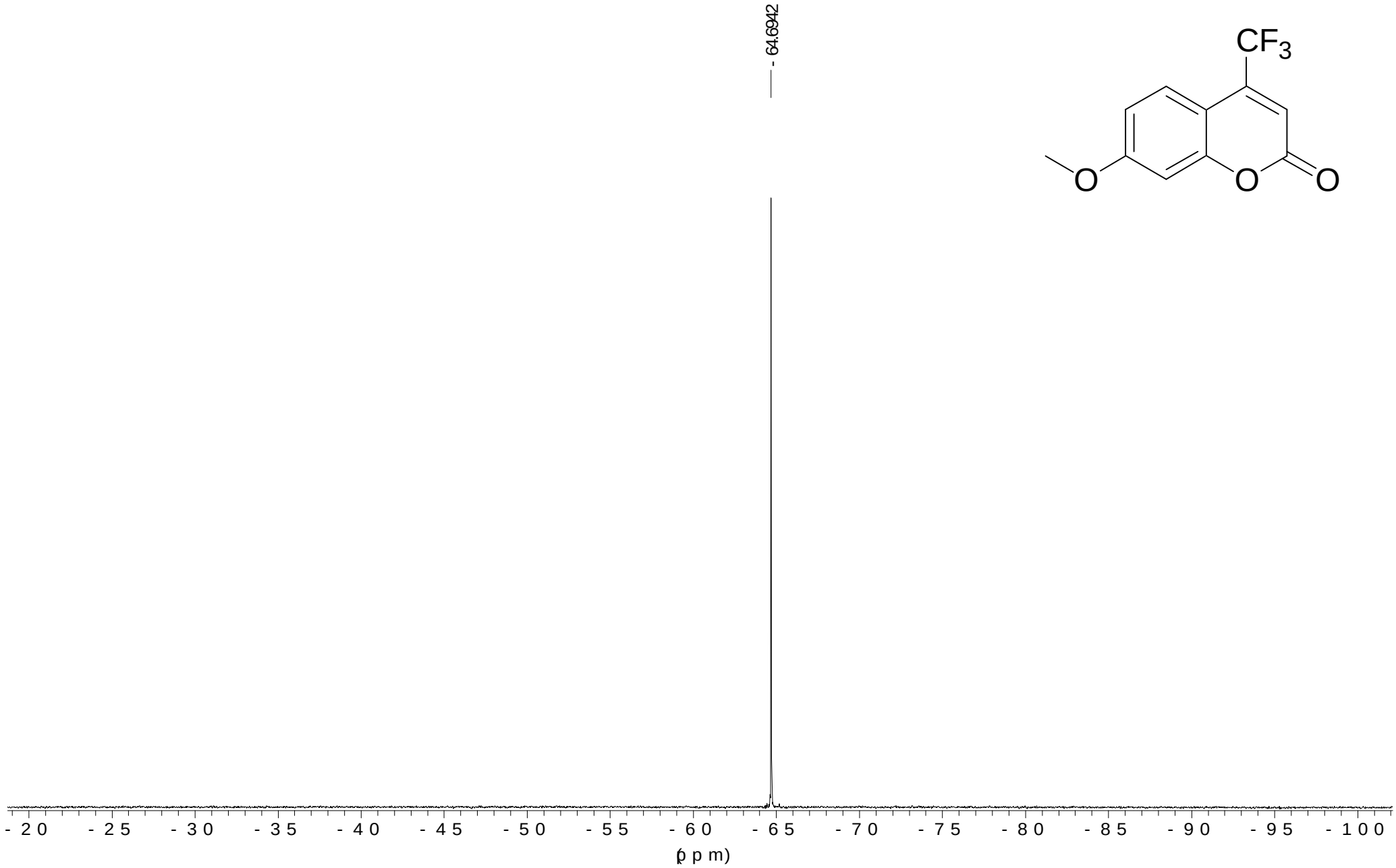
Compound **4g** spectrum NMR ^{19}F in $CDCl_3$



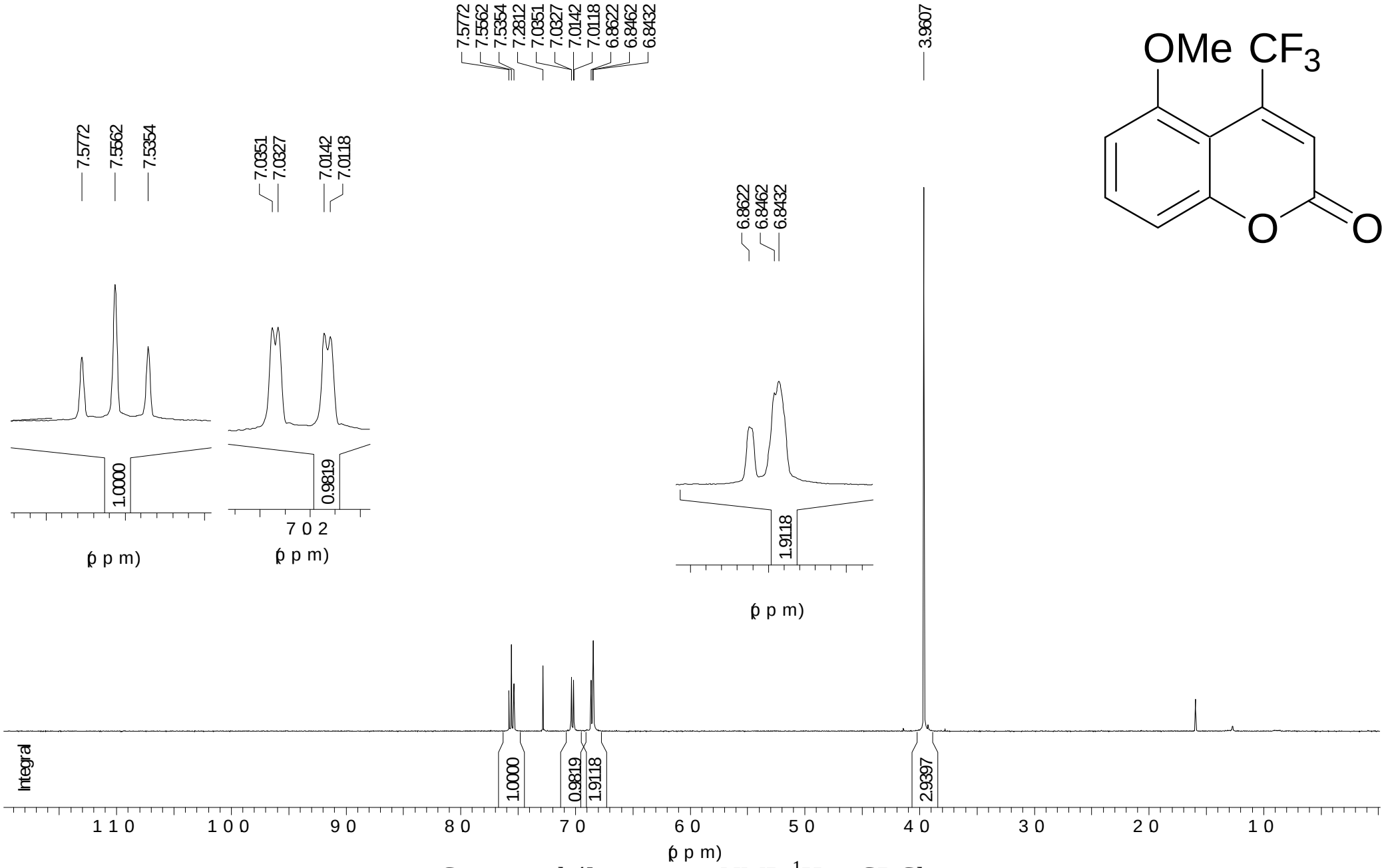
Compound **4h** spectrum NMR ^{1}H in $CDCl_3$



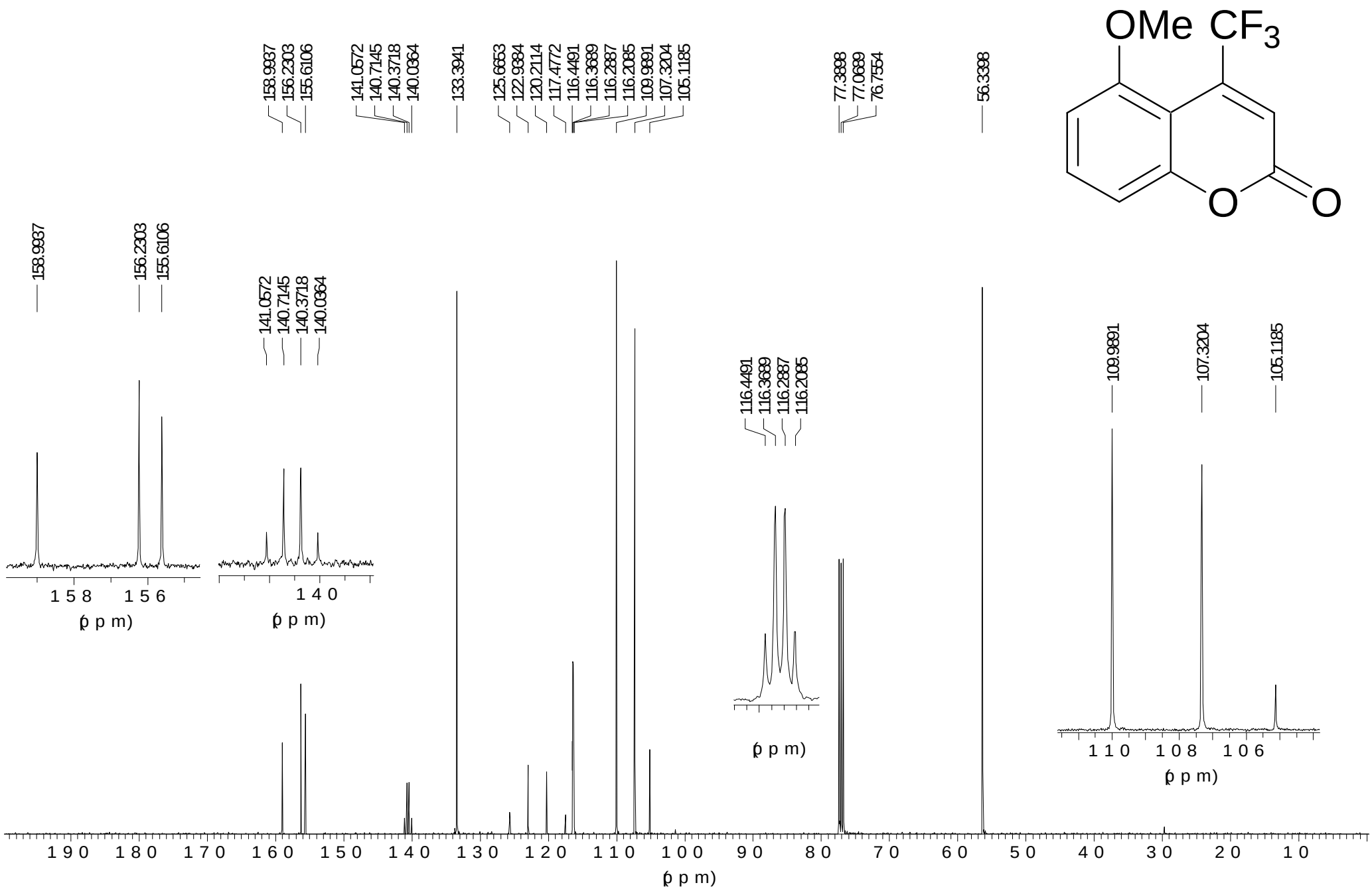
Compound **4h** spectrum NMR ^{13}C in $CDCl_3$



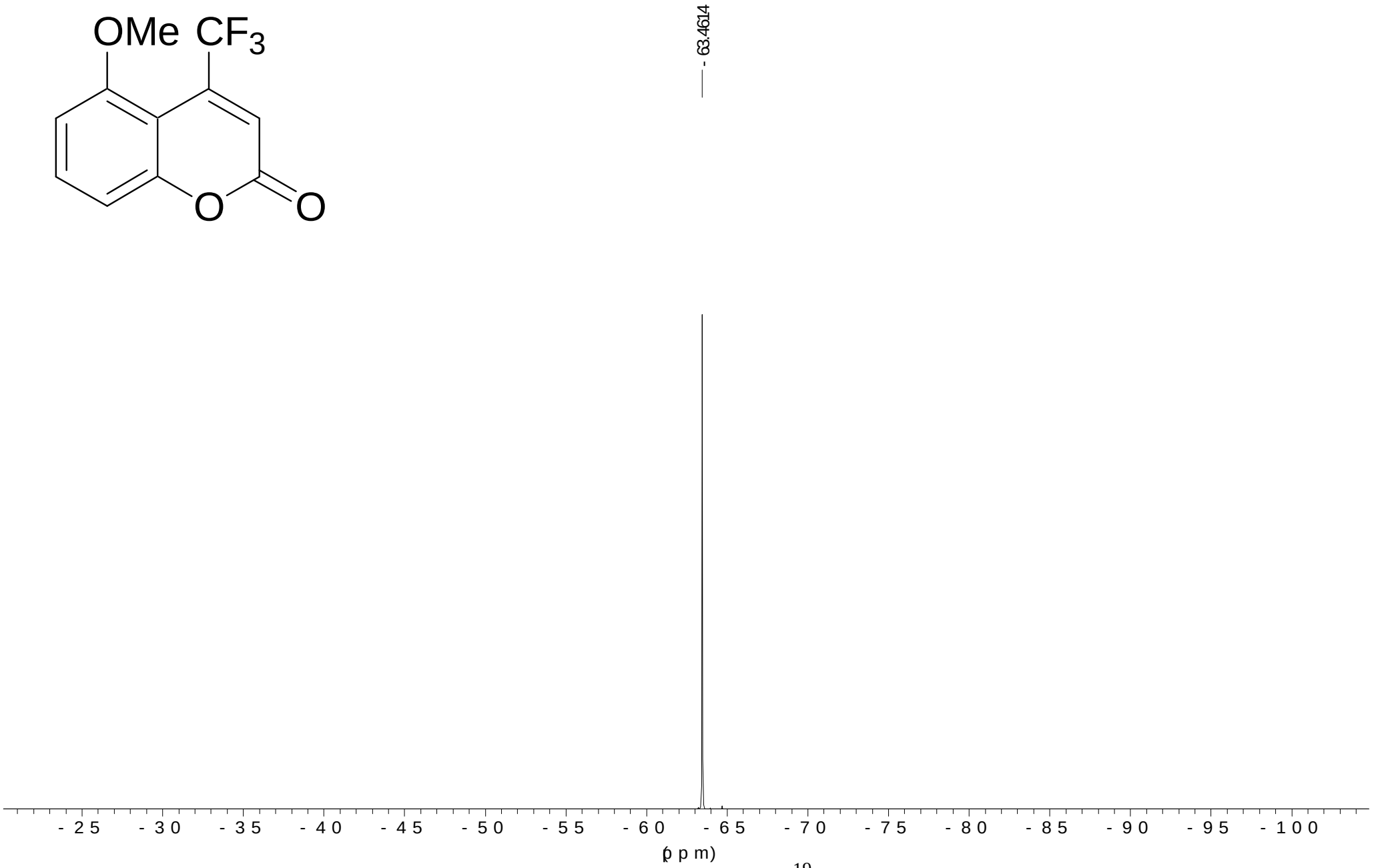
Compound **4h** spectrum NMR ^{19}F in $CDCl_3$



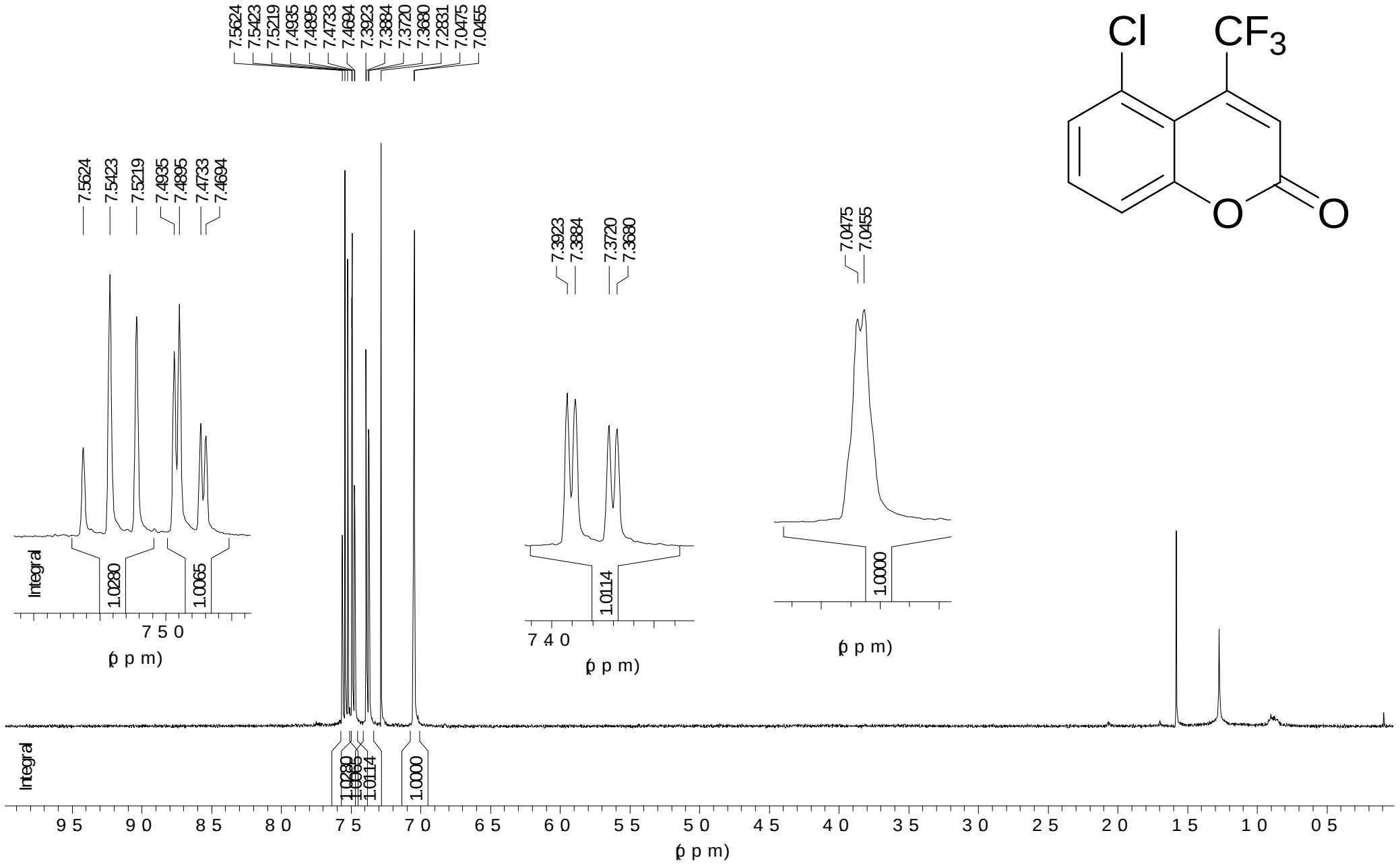
Compound **4k** spectrum NMR ^{1}H in $CDCl_3$



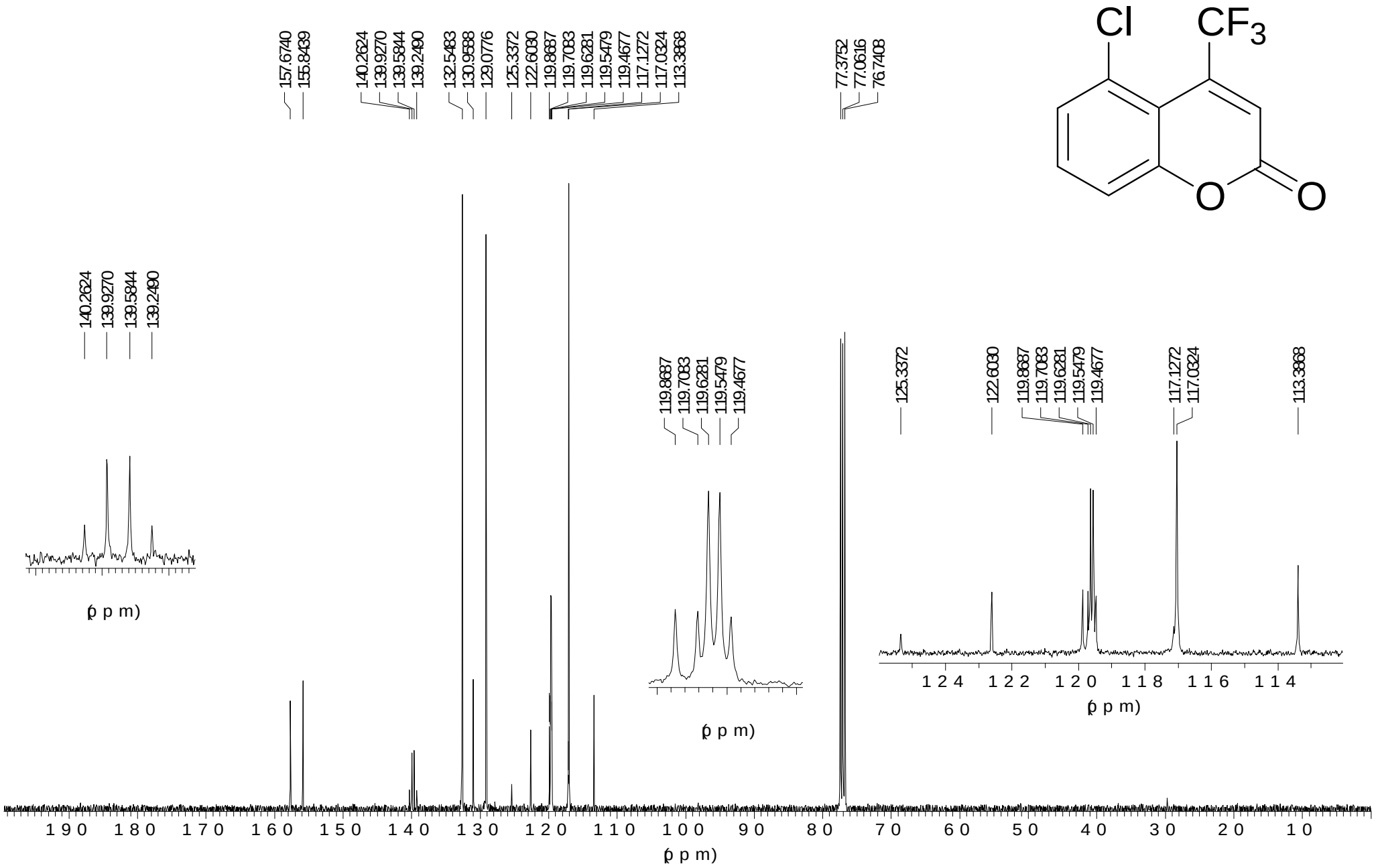
Compound **4k** spectrum NMR ^{13}C in $CDCl_3$



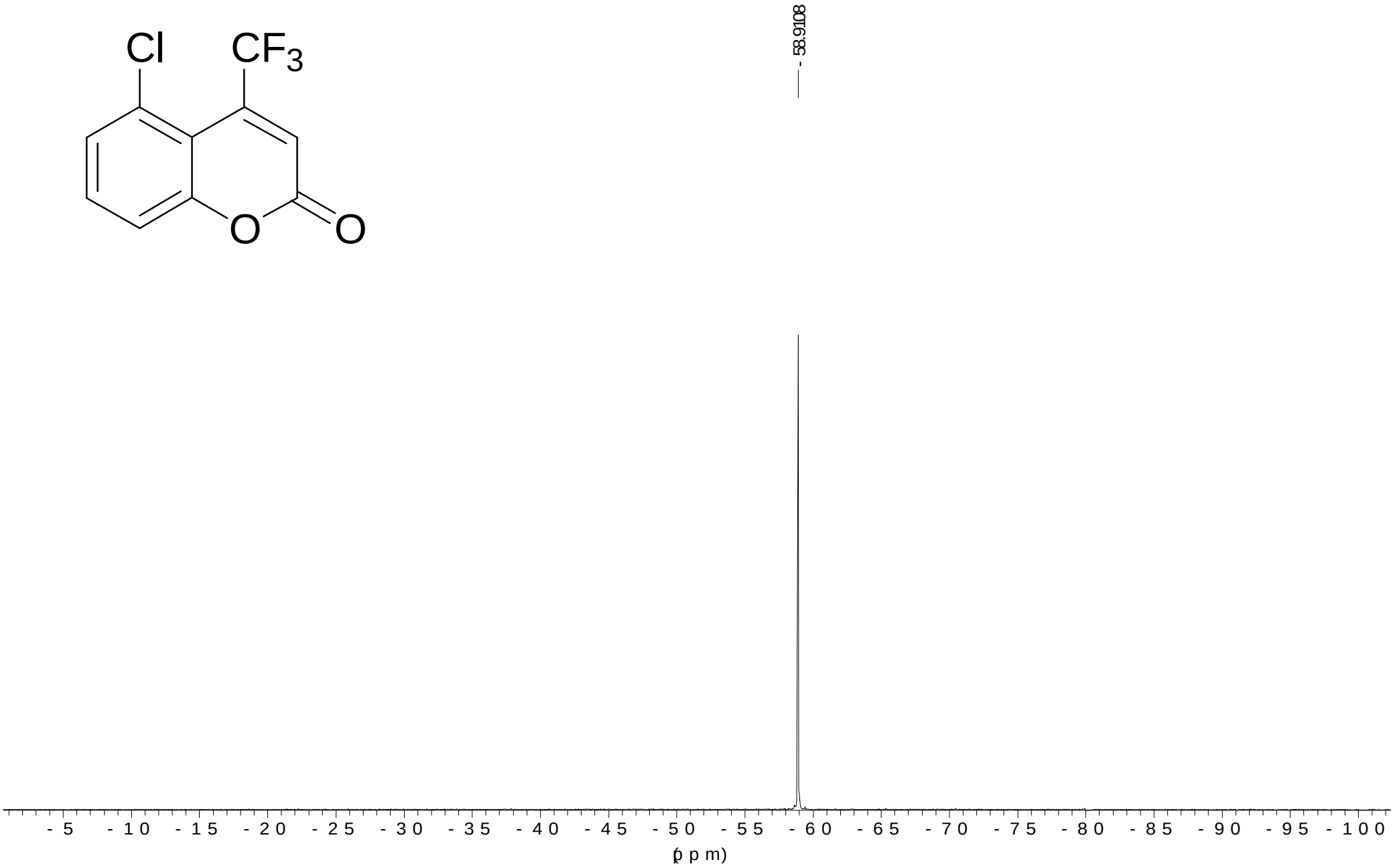
Compound **4k** spectrum NMR ^{19}F in $CDCl_3$



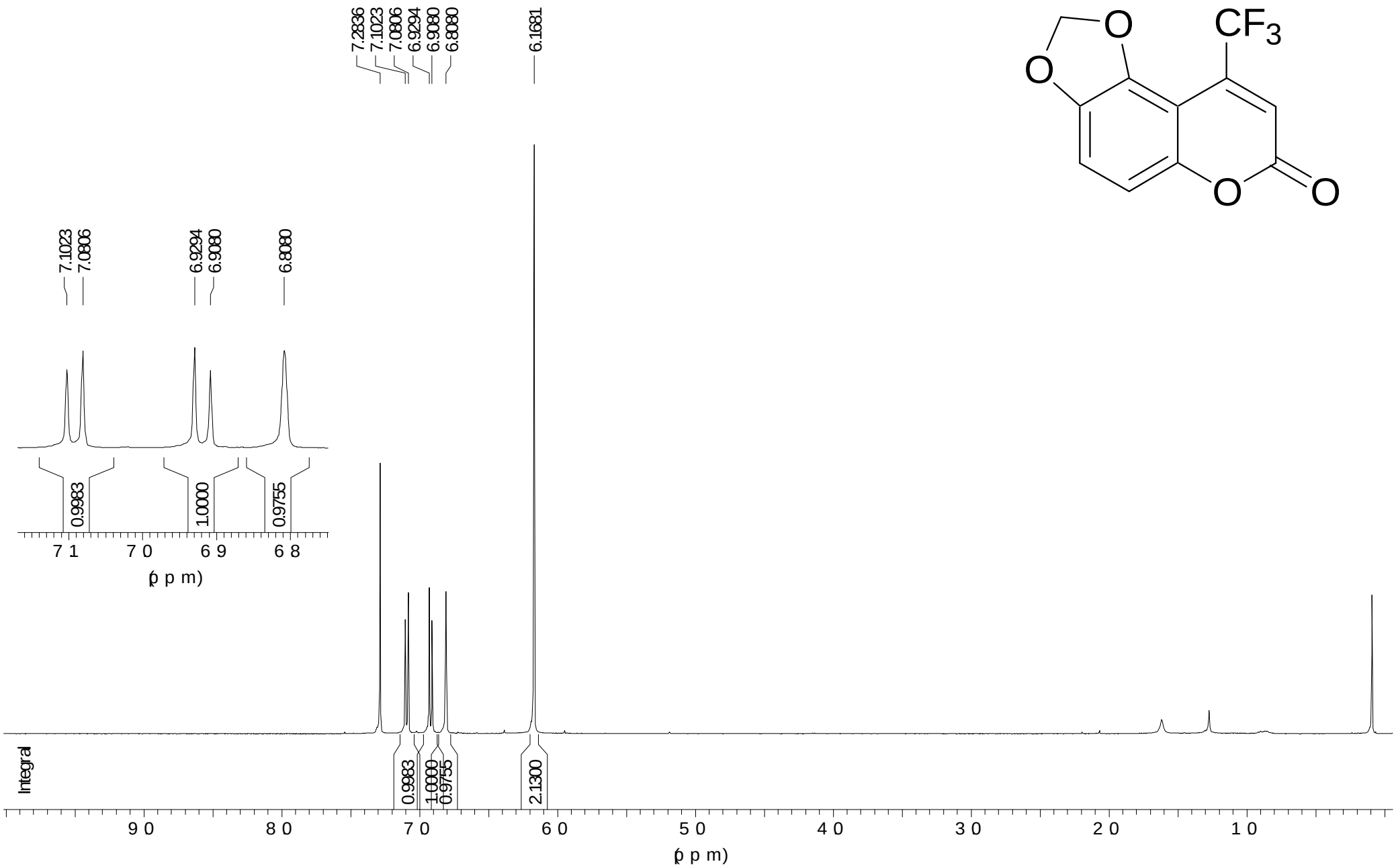
Compound **4l** spectrum NMR ^{1}H in $CDCl_3$



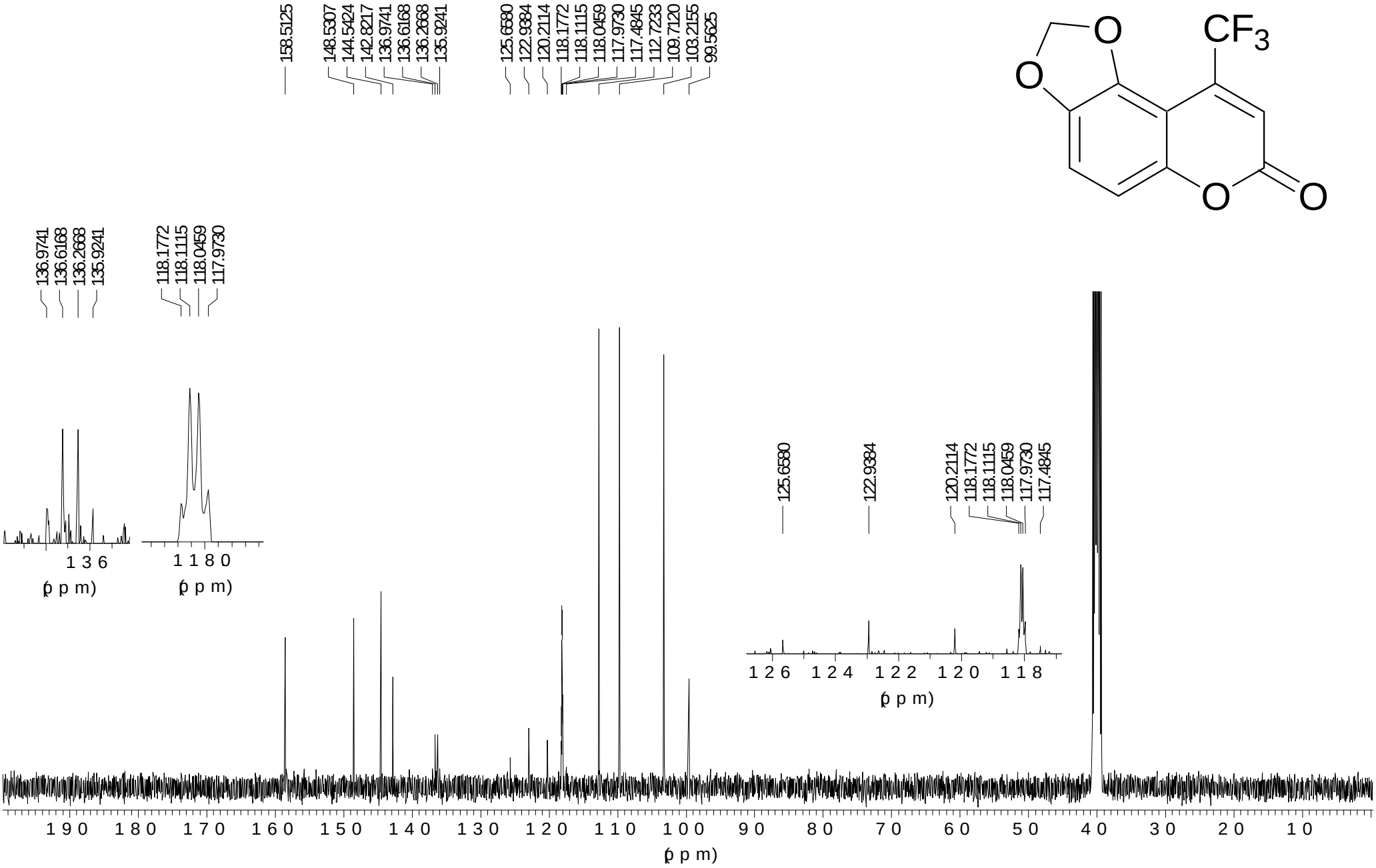
Compound **4l** spectrum NMR ^{13}C in $CDCl_3$



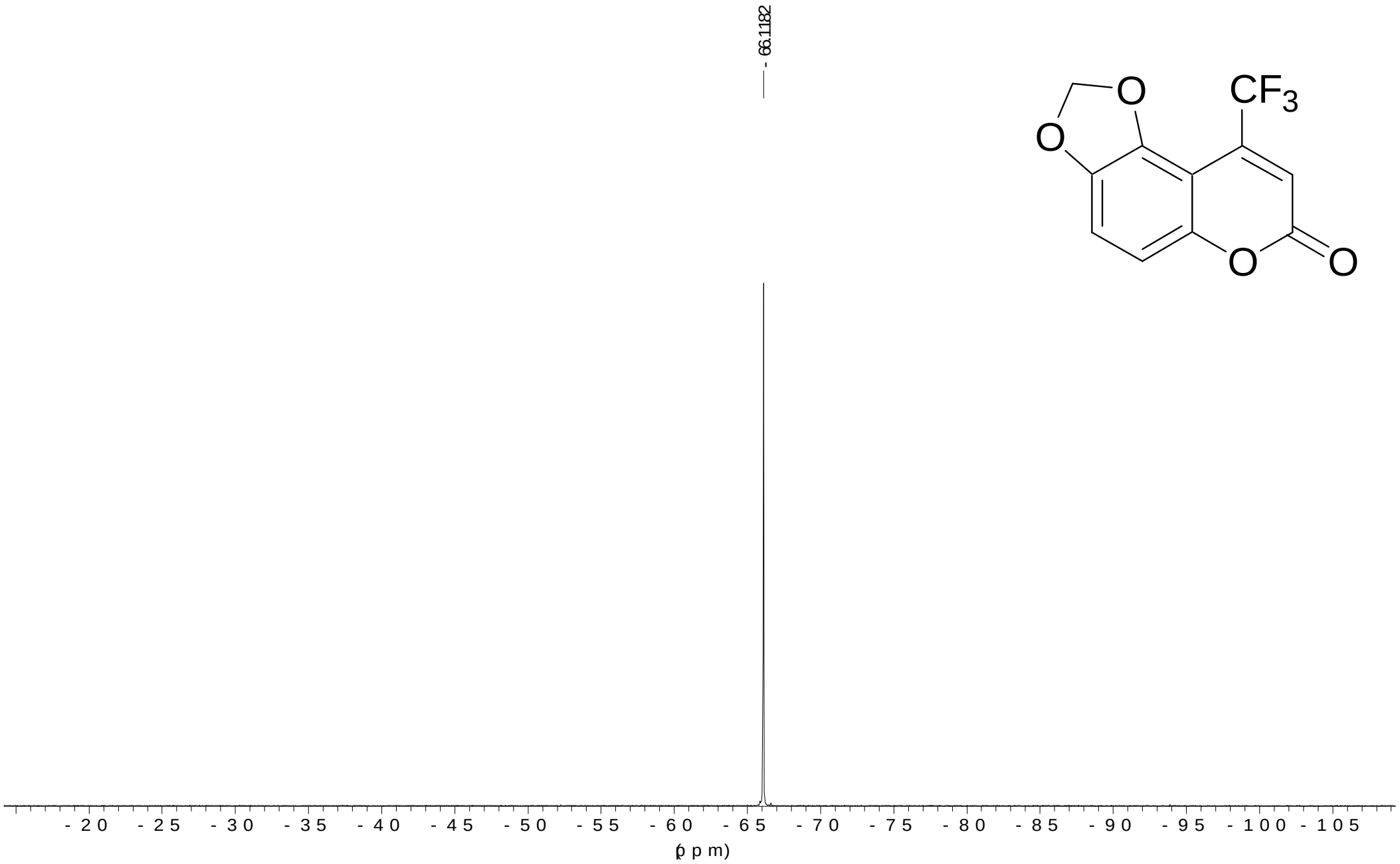
Compound **4l** spectrum NMR ^{19}F in $CDCl_3$



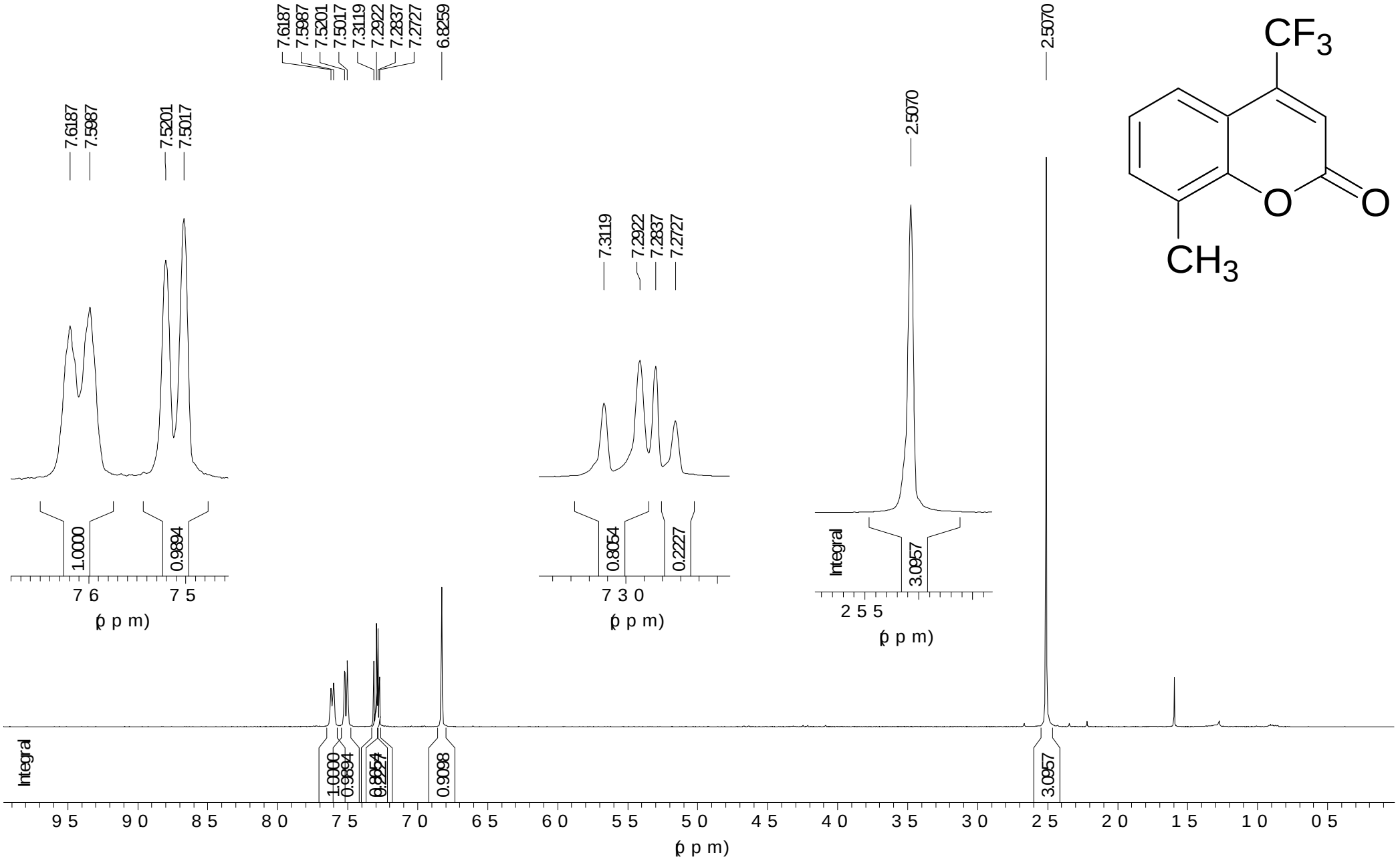
Compound **4m** spectrum NMR ^{1}H in $CDCl_3$



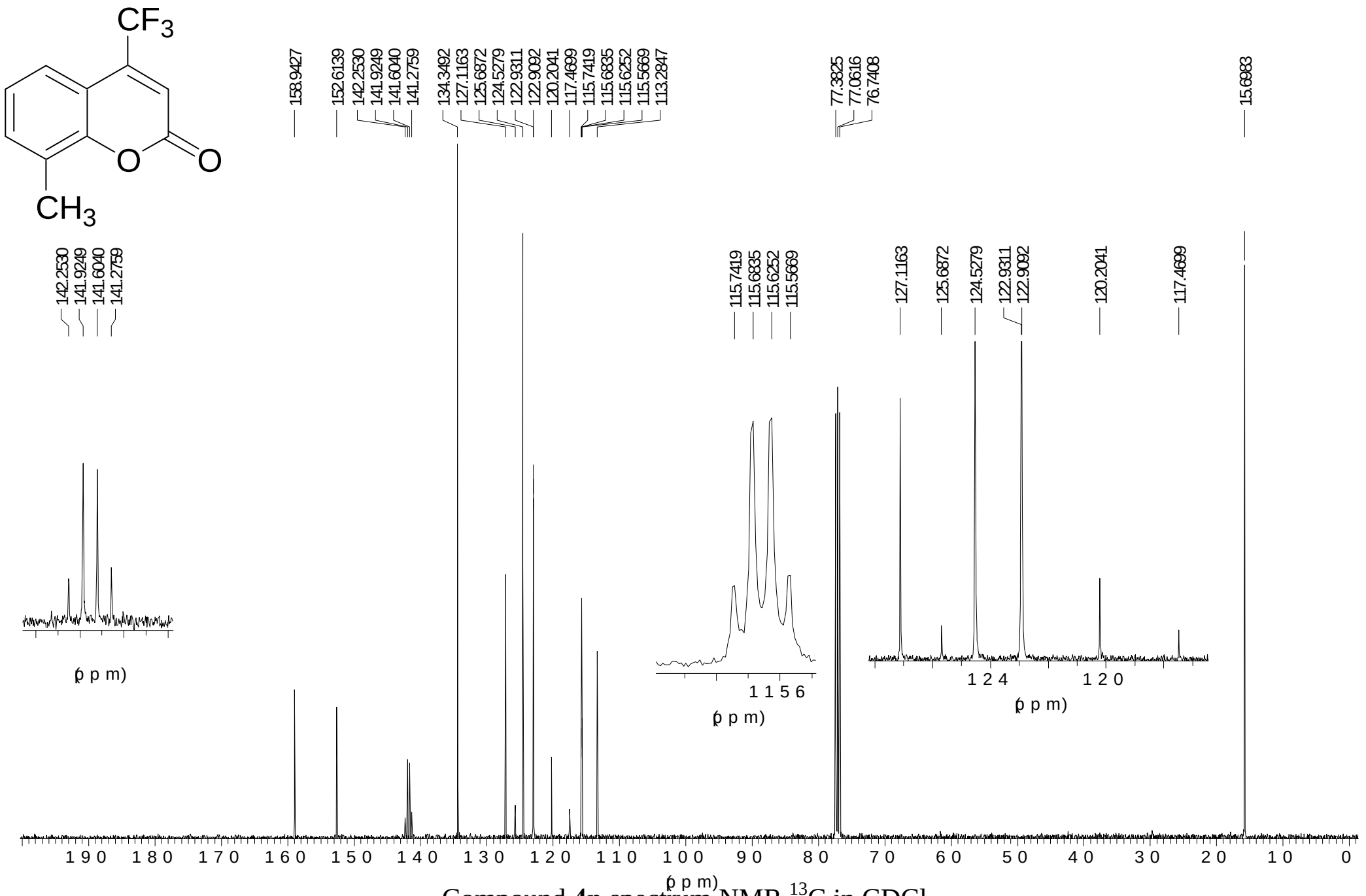
Compound **4m** spectrum NMR ^{13}C in d_6-DMSO



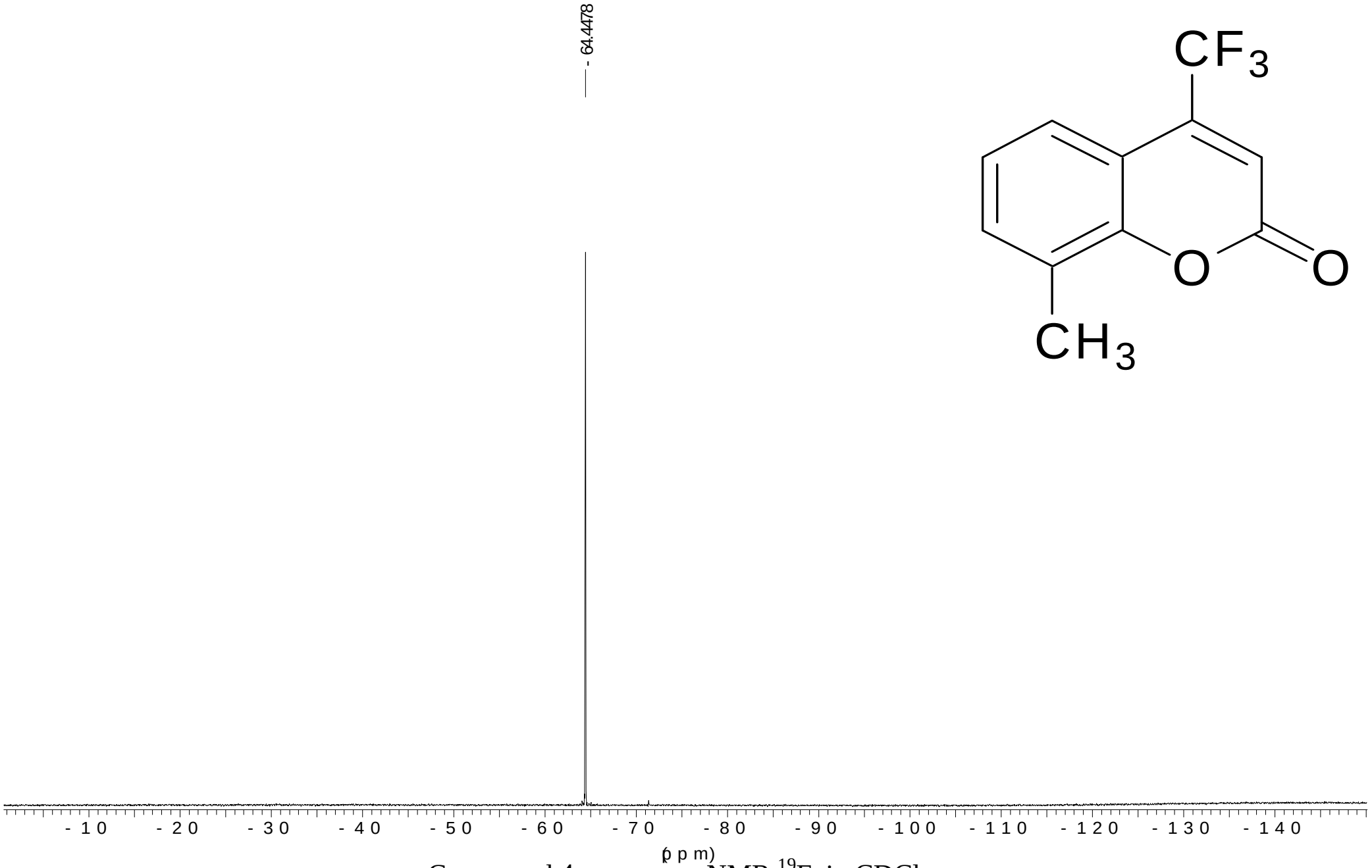
Compound **4m** spectrum NMR ^{19}F in $CDCl_3$



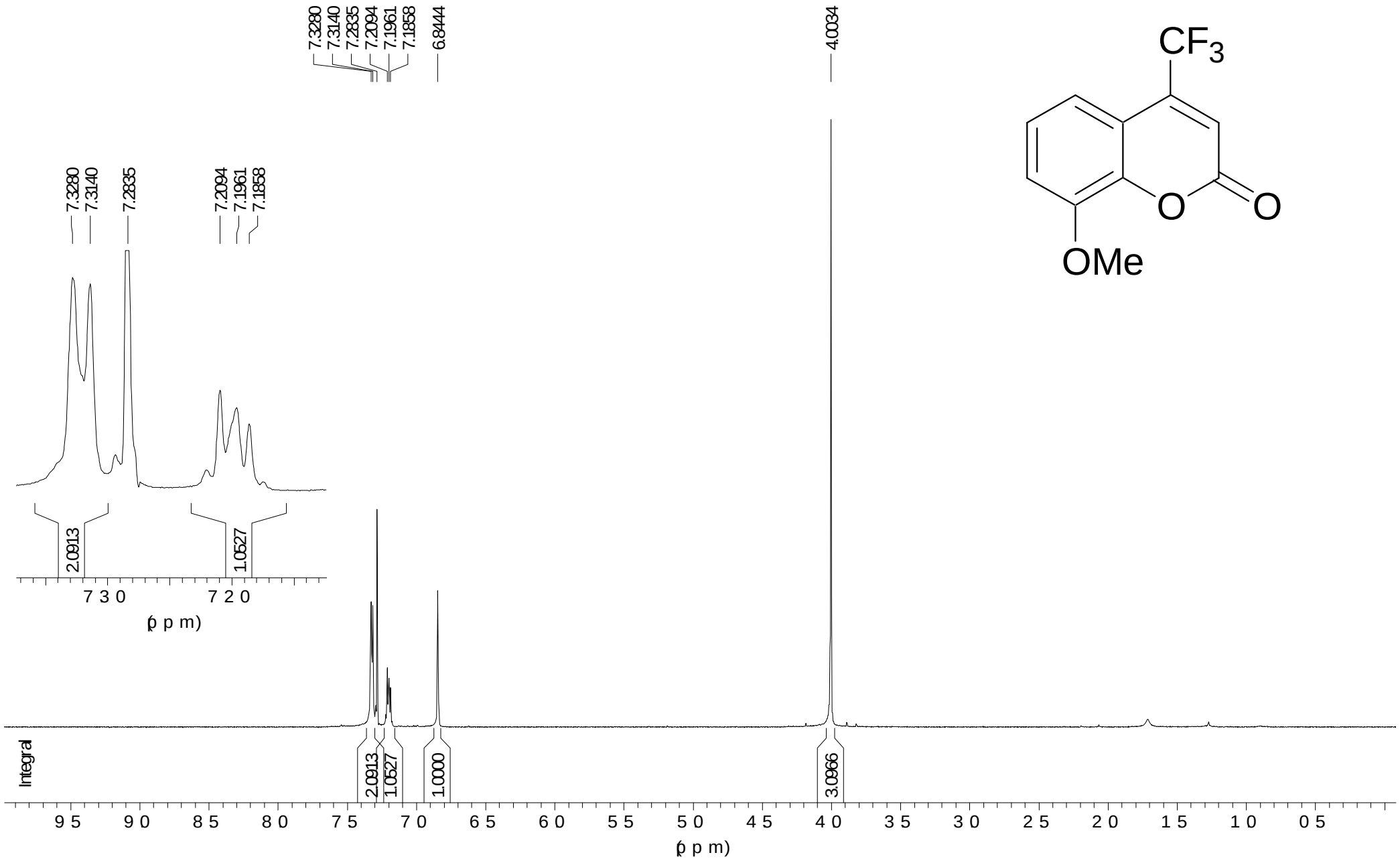
Compound **4p** spectrum NMR ^{1}H in $CDCl_3$



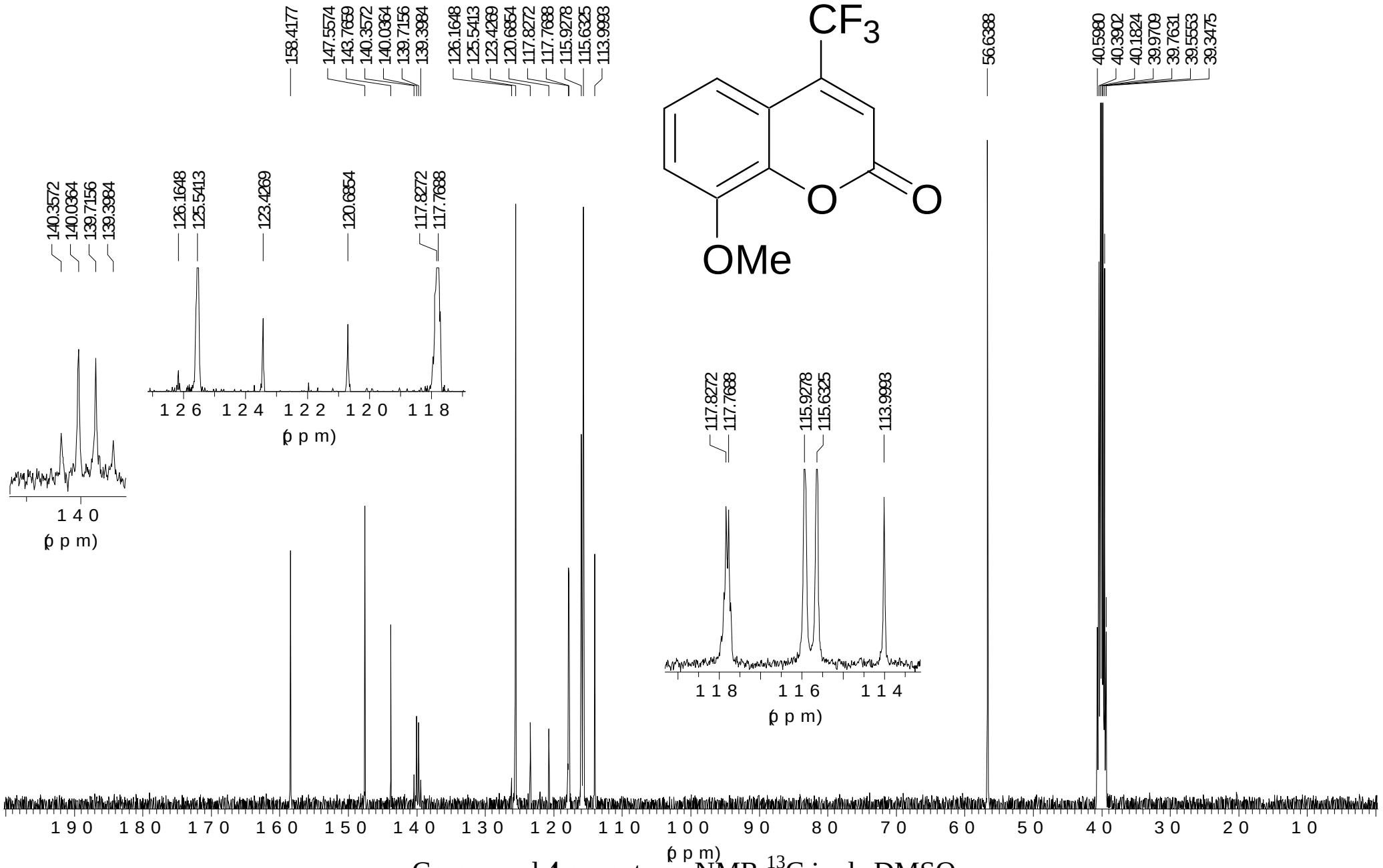
Compound **4p** spectrum NMR ^{13}C in $CDCl_3$



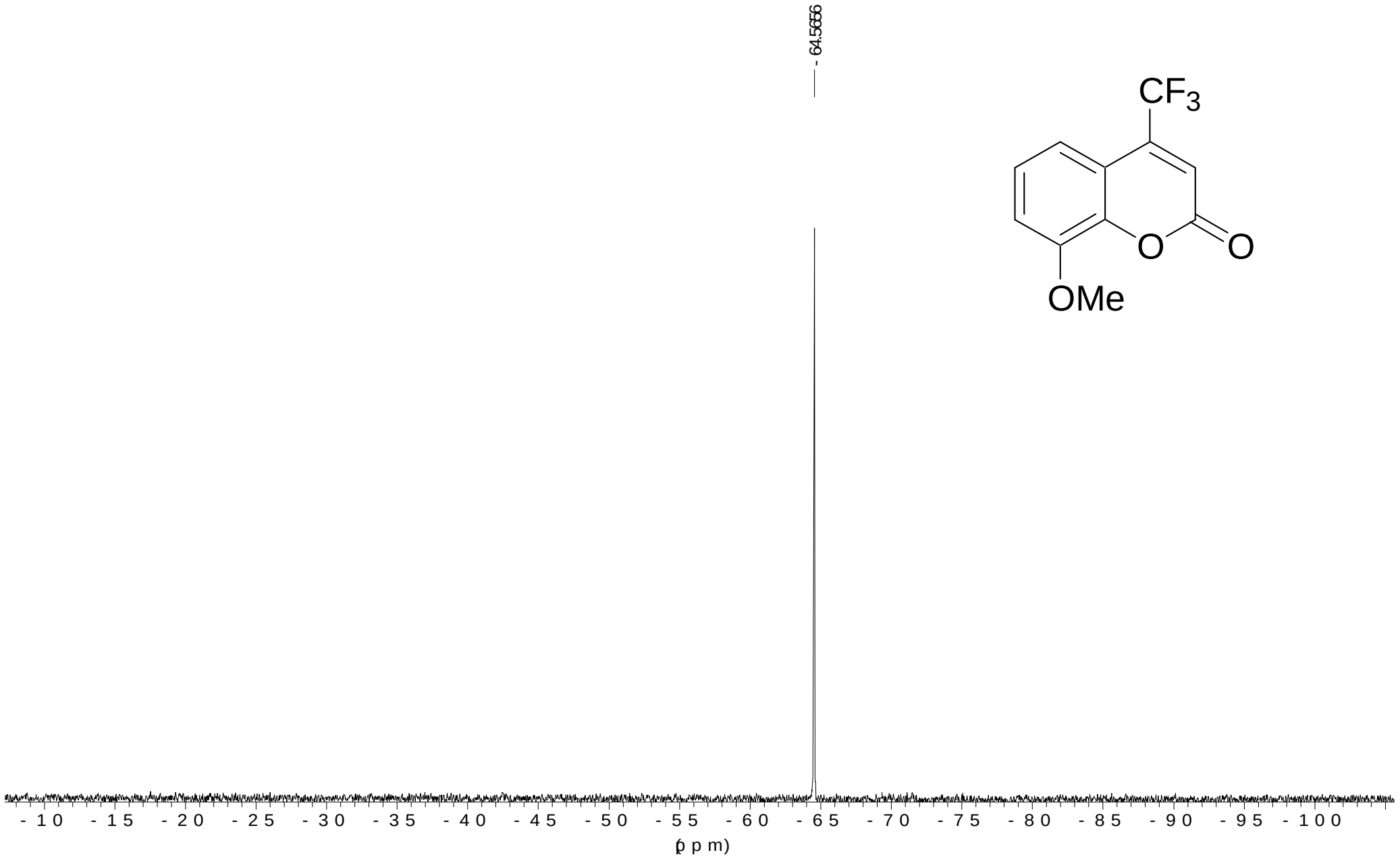
Compound **4p** spectrum NMR ^{19}F in $CDCl_3$



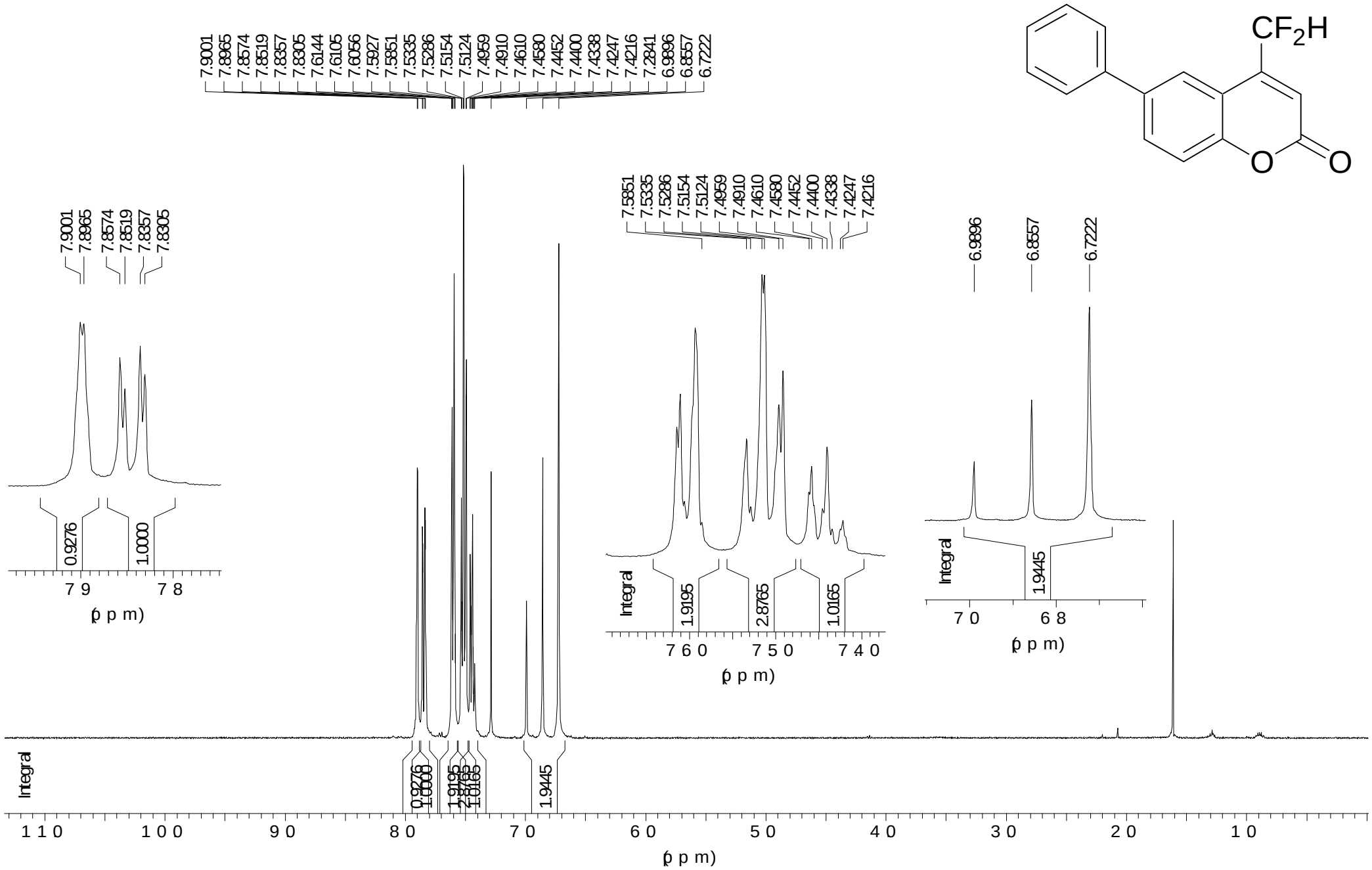
Compound **4q** spectrum NMR ^{1}H in $CDCl_3$



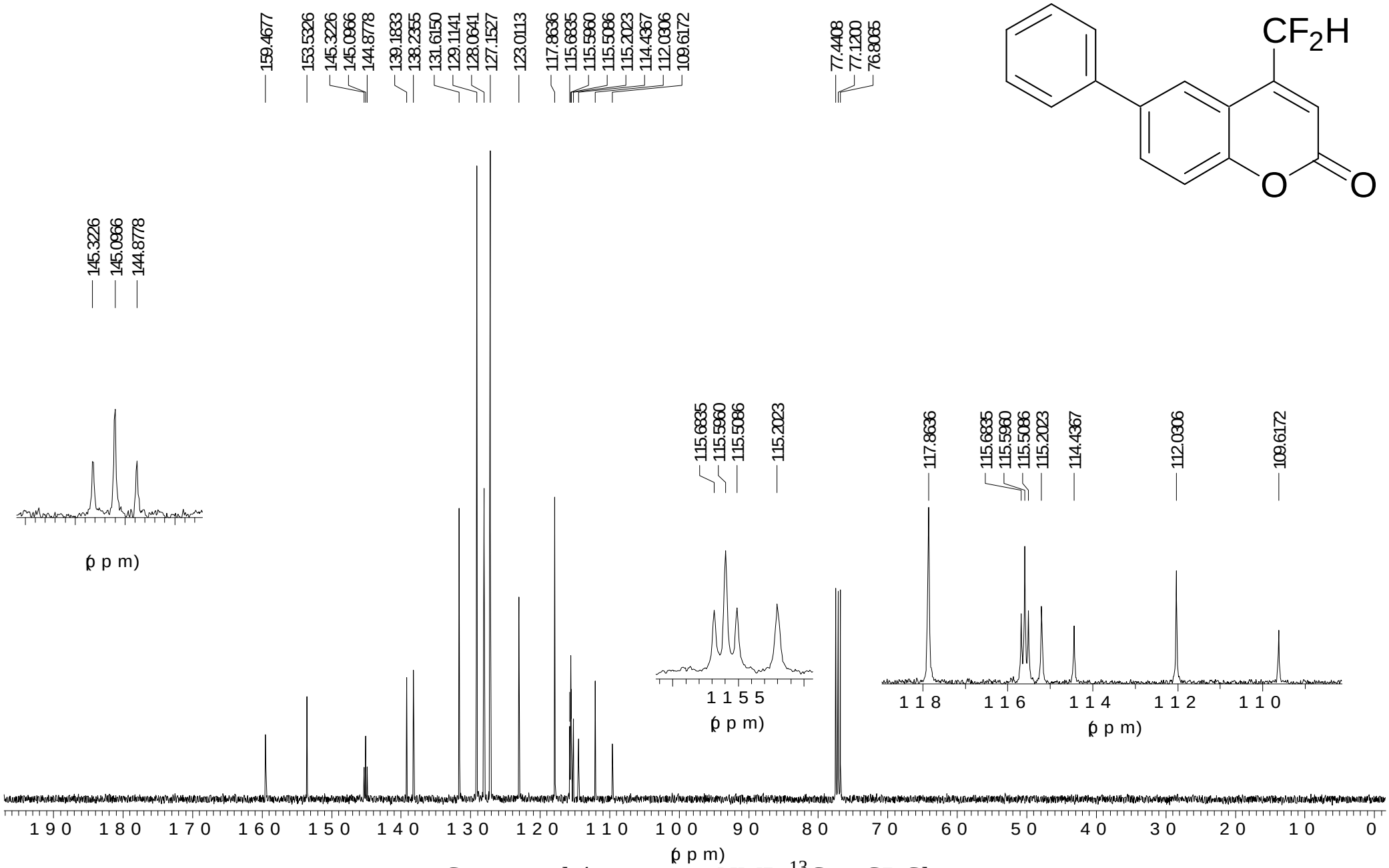
Compound **4q** spectrum NMR ^{13}C in d_6-DMSO



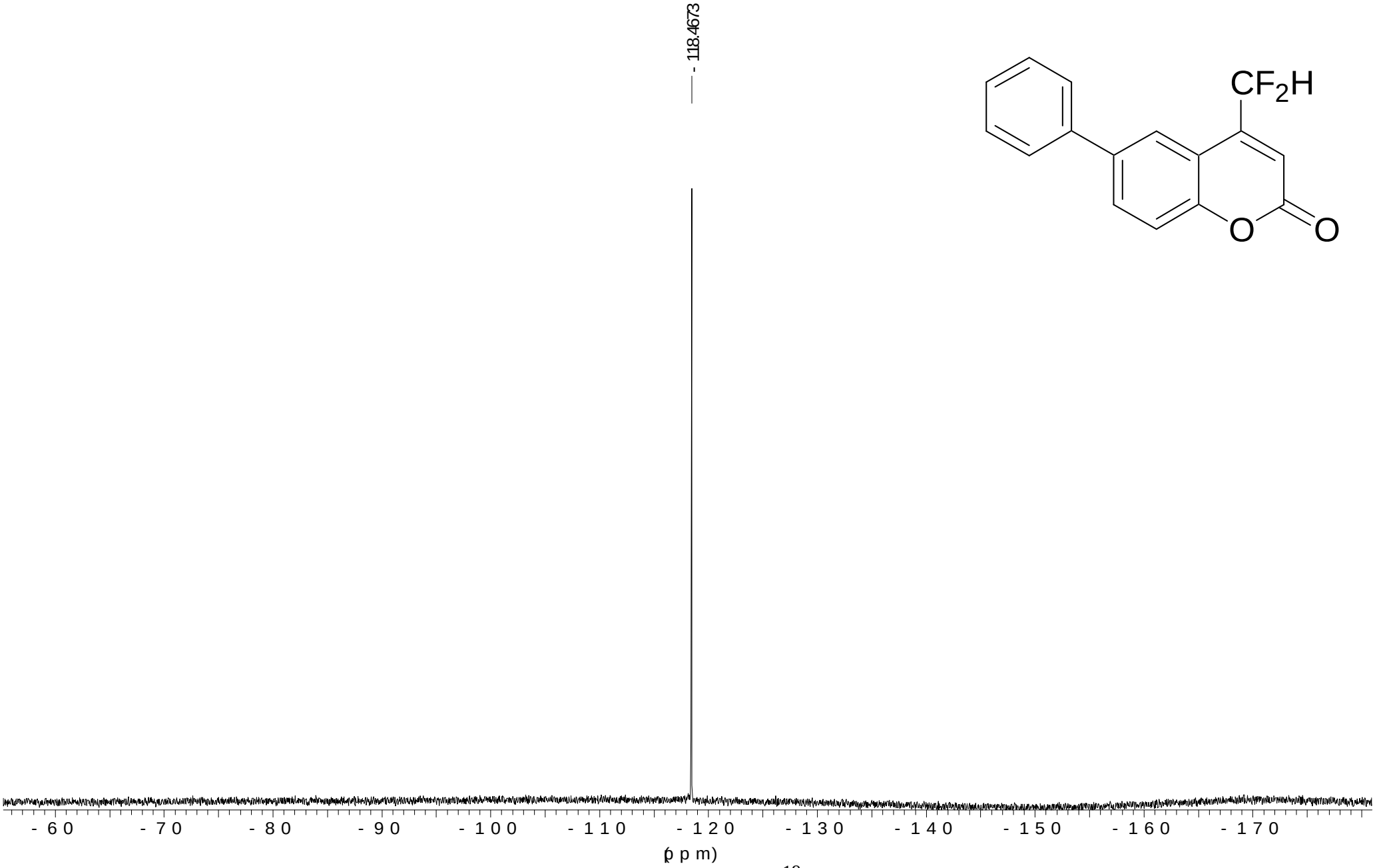
Compound **4q** spectrum NMR ^{19}F in $CDCl_3$



Compound **4t** spectrum NMR ^{1}H in $CDCl_3$



Compound **4**t spectrum NMR ^{13}C in $CDCl_3$



Compound **4t** spectrum NMR ^{19}F in $CDCl_3$