Supplementary Information for

Late-Stage (Radio)Fluorination of Alkyl Phosphonates *via* Electrophilic Activation

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1 Supplementary Notes

1.1 General reagent information

Commercially available reagents were procured from Energy Chemical (China) and Sigma-Aldrich (Switzerland) and utilized as received unless specified otherwise. Anhydrous *N*,*N*-dimethylformamide (DMF), anhydrous tetrahydrofuran (THF), anhydrous dimethyl sulfoxide (DMSO), all stored over molecular sieves, were purchased from Energy Chemical. Additional common solvents were procured from Sinopharm (China) and employed without further treatment. Deuterated solvents including $CDCl_3$, D_2O, CD_3OD, CH_3OD, and DMSO-d_6 were obtained from Energy Chemical; CD_2Cl_2 was procured from Cambridge Isotope Laboratories (United States). Ultra-pure water was obtained from an ELGA PURELAB flex system (UK).

The compounds (**S16**−**S36**, E[c(RGDyK)]$_2$) were procured from commercial suppliers and employed as reagents in the direct fluorination of alkyl phosphonates *via* electrophilic activation.

1.2 General analytical information

All fluorination reactions were carried out with magnetic agitation in oven-dried glass-bottomed vessels. Subsequent concentration of organic solutions was performed under reduced pressure using a Heidolph rotary evaporator (Hei-VAP Value, Germany). The reaction progress was tracked *via* thin-layer chromatography (TLC) on aluminum plates (2.5 cm × 5 cm) coated with silicone GF254, supplied by Energy Chemical, or on polyamide film plates sourced from Lu Qiao Si-Jia Biochemistry Plastics Company (China). Chromatographic visualization utilized a 254 nm ultraviolet fluorescence quenching technique, alkaline potassium permanganate staining, or iodine staining.

^{1}H, ^{13}C, ^{31}P and ^{19}F nuclear magnetic resonance (NMR) spectra were recorded on a Zhongke-Niujin AS 400 MHz or Bruker AVANCE 600 MHz NMR spectrometer (China) at room temperature. All the chemical shifts (δ) for protons were reported in ppm downfield from tetramethylsilane (TMS) and were referenced to residual protium in the deuterated solvents (^{1}H NMR: CD_3OD at 3.31 ppm, $CDCl_3$ at 7.26 ppm). Chemical shifts for carbon signals were reported in ppm and were referenced to the carbon resonances of the solvent peak (^{13}C NMR: CD_3OD at 49.00 ppm, $CDCl_3$ at 77.00 ppm). Multiplicity was described with singlet (s), doublet (d) and multiplet (m). Coupling constants (*J*) were given in Hertz (Hz). High resolution mass spectrometry (HRMS)

data is recorded on a Waters Xevo G2-XS Tof mass Spectrometer (USA) or Thermo Q-Exactive Mass Spectrometer (USA). High-performance liquid chromatography (HPLC) analysis was performed using a NanoChrom C18 column (5 μm, 4.6 × 250 mm, China). HPLC purification was carried out on a SEP Basic-C18 semi-preparative column (120A 5μm 10 × 250 mm China).

1.3 General radiochemistry information

Activation of the Sep-Pak® Plus Short C18 cartridge (Waters, Part No. WAT020515): Using a 10 mL syringe, extract 5 mL of methanol and slowly wash the C18 column. Then, push 10 mL of air through the column to remove any remaining methanol. Next, wash the C18 column with 10 mL of pure water. Finally, push 10 mL of air through the column to complete the activation process.

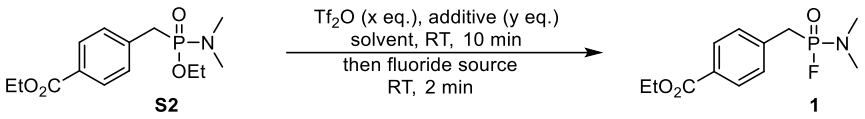
Activation of the Sep-Pak® light QMA cartridge (Waters, USA): The QMA column was activated using a 10 mL syringe to draw 5 mL of a pre-prepared 0.5 M K_2CO_3 solution, which was slowly washed through the column. Subsequently, 10 mL of air flushed the column to remove the liquid. Next, a wash with 10 mL of pure water was performed on the QMA column. Finally, an additional 10 mL of air completed the activation process.

HPLC analysis was performed using two Thermo Fisher Dionex ultra-mate 3000 instruments (United States) denoted as HPLC 1# and HPLC 2#, both equipped with an SPD-20A UV detector and an Elysia Raytest Gabi Star γ-radiation detector from Hungary, interconnected in series. In both HPLC 1# and 2#, the retention times of the radio peaks and the corresponding UV peaks were observed to shift by 0.10 to 0.20 min and 0.50 to 0.80 min, respectively, due to the distance between the UV detector (254 nm) and the radiation detector. Radio-TLC were acquired using an Eckert & Ziegler MS-1000F scanner from the United States, which was equipped with Mini-Scan and Flow-Count functionalities. All phosphonate fluorination precursors are now numbered as **S1**–**S57**, and the resulting fluorinated phosphonates are numbered **1**–**46**, with '[^{18}F]' added before the corresponding Arabic numerals to indicate the ^{18}F-products. Intermediates in the synthesis of phosphonate precursors are labeled as **i-1** to **i-10**, and unstable intermediates in mechanistic studies are represented as **INT-1** to **INT-5**." The bases in the additive screening are represented by the letter '**a**' and superscript Arabic numerals from 1 to 11 (**a^{1}**-**a^{11}**).

2. Supplementary Methods

2.1 Condition optimization for fluorination of alkyl phosphonates

Table S1: Selected optimization table for alkyl phosphonates fluorination[a]



Entry	Tf_2O/x eq.	Additive/ y eq.	Solvnet[b]	Fluoride source	Conversion (%)[c]
1	1.0	Pyridine/1.0	CH_2Cl_2	TBAF	11 ± 6
2	1.0	Pyridine/1.5	CH_2Cl_2	TBAF	36 ± 3
3	1.5	Pyridine/1.0	CH_2Cl_2	TBAF	6 ± 2
4	2.0	Pyridine/1.5	CH_2Cl_2	TBAF	19 ± 3
5	2.0	Pyridine/2.0	CH_2Cl_2	TBAF	27 ± 5
6	1.5	Pyridine/2.0	CH_2Cl_2	TBAF	47 ± 1
7	1.5	Diphenylsulfane/2.0	CH_2Cl_2	TBAF	0
8	1.5	Pyridine/2.0	CH_2Cl_2	$Et_3N{\cdot}3HF$	93 ± 3
9[d]	TFAA, 1.5 eq.	Pyridine/2.0	CH_2Cl_2	$Et_3N{\cdot}3HF$	trace
10	1.5	Pyridine/2.0	THF	$Et_3N{\cdot}3HF$	trace
11	1.5	Pyridine/2.0	Toluene	$Et_3N{\cdot}3HF$	11 ± 2
12	1.5	Pyridine/2.0	CH_3CN	$Et_3N{\cdot}3HF$	35 ± 2
13	1.5	Pyridine/2.0	1,4-Dioxane	$Et_3N{\cdot}3HF$	3 ± 1

[a] Reactions were performed using 0.2 mmol **16**, tetrabutylammonium fluoride (TBAF 1.2 eq.)/$Et_3N{\cdot}3HF$ (0.5 eq.) in solvent (0.2 M).

[b] CH_2Cl_2: dichloromethane; THF: tetrahydrofuran; CH_3CN: acetonitrile.

[c] Conversions determined by ^{31}P NMR.

[d] Replace Tf_2O with trifluoroacetic anhydride (TFAA).

2.2 General synthetic procedures and characterization

General compounds information

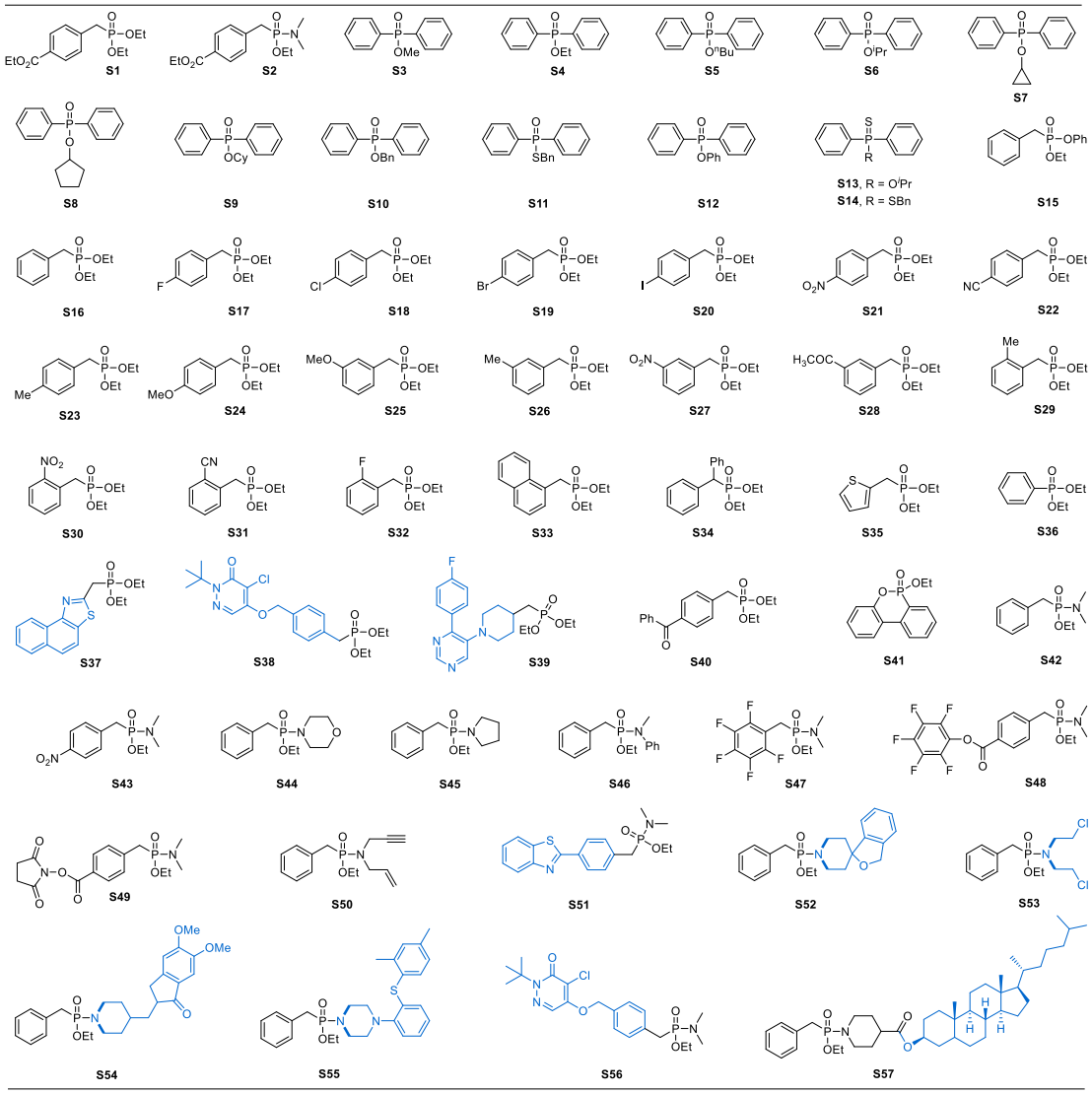


Fig. S1: An Overview of ethyl phosphonates (**S1**–**S57**) was discussed in this work.

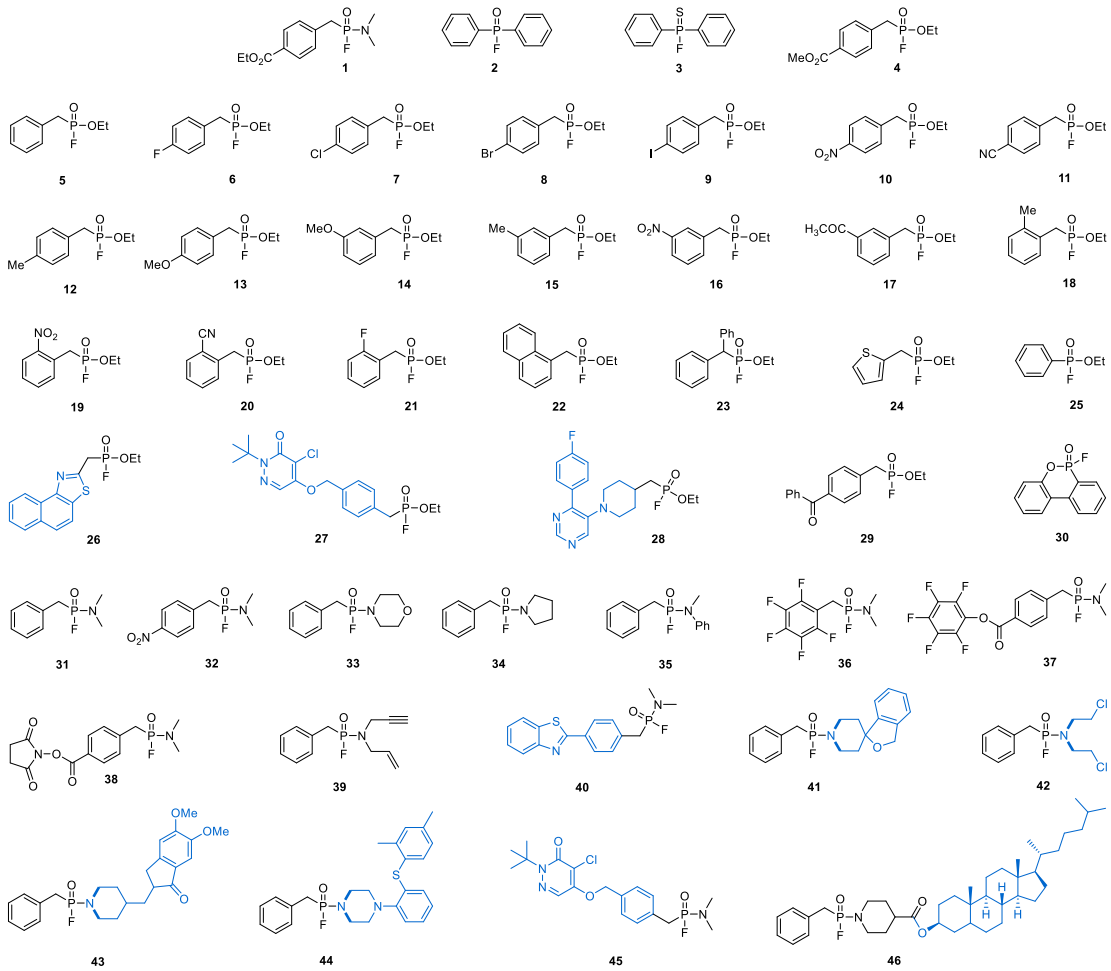
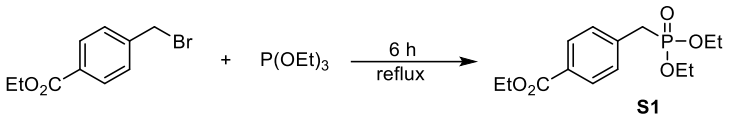


Fig. S2: An Overview of fluorophosphines (**1**–**46**) was discussed in this work.

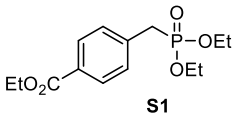
2.2.1 General synthetic procedures for substrates

Procedure A for the formation of S1



4-(Bromomethyl)benzoic acid ethyl ester (1.1 eq.) and triethyl phosphite (1.0 eq.) were initially stirred at room temperature without additional solvent and subsequently heated to 150 ℃ for refluxing over a period of 3−6 h[1]. The progress of the reaction was carefully monitored using thin-layer chromatography (TLC) or ^{31}P NMR. Once the reaction reached completion, any residual unreacted triethyl phosphite was removed through vacuum distillation. The resulting crude product was then subjected to purification by silica gel column chromatography with a mixture of petroleum ether and ethyl acetate as the eluent in a ratio of 3:1, effectively removing the solvent and yielding the purified compound S**1**.

Ethyl 4-((diethoxyphosphoryl)methyl)benzoate (S1)



Colorless oil, yield: 73%.

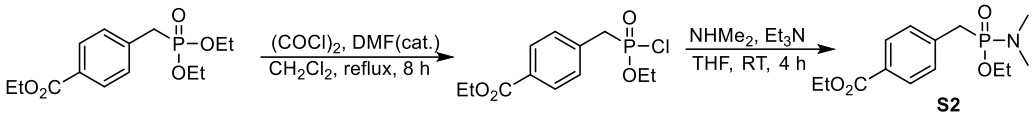
^{1}H NMR (400 MHz, CDCl$_3$): δ 7.95 (d, *J* = 7.6 Hz, 2H), 7.3 (d, *J* = 7.6 Hz, 2H), 4.33 (q, *J* = 6.8 Hz, 2H), 3.98 (t, *J* = 7.2 Hz, 4H), 3.17 (d, *J* = 22.4 Hz, 2H), 1.35 (t, *J* = 7.2 Hz, 3H), 1.21 (t, *J* = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, CDCl$_3$): δ 166.3, 136.9 (d, *J* = 9.2 Hz), 129.7, 129.6, 129.0 (d, *J* = 3.5 Hz), 62.2 (d, *J* = 6.7 Hz), 60.8, 33.9 (d, *J* = 136.8 Hz), 16.3 (d, *J* = 5.8 Hz), 14.2.

^{31}P NMR (162 MHz, CDCl$_3$): δ 25.2 (s, 1P).

HRMS (m/z) calculated for $C_{14}H_{22}O_5P^+$ ($[M+H]^+$): 301.1199, found: 301.1201.

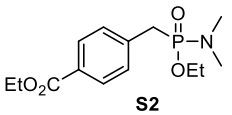
Procedure B for the formation of S2



Step 1: Under ambient conditions, a 2 M solution of oxalyl chloride (2 eq.) was gradually added dropwise to the ethyl 4-((diethoxyphosphoryl)methyl)benzoate (**S1**) (1.0 eq.). Next, 2 drops of DMF were introduced as a catalyst. The reaction mixture was then heated to 60 ℃ and refluxed for 8 h[2]. The reaction progress was monitored using ^{31}P NMR, as the P^{v}−Cl compound typically exhibits a chemical shift around 35−45 ppm. While TLC is ineffective in detecting the reaction process of unstable intermediates, ^{31}P NMR enables clear product identification and quantification of conversion. Upon completion of the reaction, the solvent and excess oxalyl chloride were removed under reduced pressure. The resulting product can be utilized directly in the subsequent step without requiring further purification.

Step 2: The initial product was dissolved in tetrahydrofuran, followed by the slow addition of a mixture of $NHMe_2$ and Et_3N, both dissolved in THF, under ice bath conditions. Subsequently, the reaction mixture was allowed to warm up to RT and react for 2 h, with the progress of the reaction monitored by TLC. After the reaction was complete, the precipitate was filtered, and the solvent was removed under reduced pressure. The crude product was then purified using silica gel column chromatography to eliminate the solvent and obtain the purified compounds **S2**.

Ethyl 4-(((dimethylamino)(ethoxy)phosphoryl)methyl)benzoate (S2)



White solid, yield: 65%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 6.4 Hz, 2H), 4.30 (q, *J* = 7.2 Hz, 2H), 3.79−4.01 (m, 2H), 3.04−3.19 (m, 2H), 2.48 (t, *J* = 8 Hz, 6H), 1.32 (t, *J* = 7.2 Hz, 3H), 1.32 (t, *J* = 7.2 Hz, 3H).

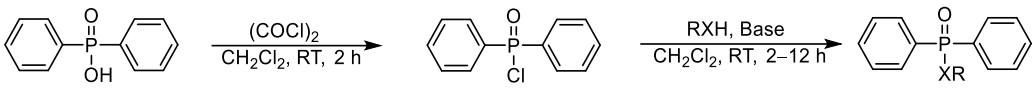
^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 137.9 (d, *J* = 8.1 Hz), 129.6, 129.5, 128.7 (d, *J* = 3.2 Hz), 60.7, 59.6 (d, *J* = 6.8 Hz), 36.2 (d, *J* = 3.9 Hz), 33.9 (d, *J* = 123.8 Hz), 16.1

(d, J = 6.5 Hz), 14.2.

^{31}P NMR (162 MHz, $CDCl_3$): δ 29.9 (s, 1P).

HRMS (m/z) calculated for $C_{14}H_{23}NO_4P^+$ ($[M+H]^+$): 300.1359; found: 300.1351.

General procedure C for the formation of diphenylphosphinate (S3−S12).

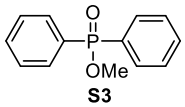


S3–S12

Step 1: The diphenylphosphinic acid was dissolved in a small amount of dichloromethane, and then oxalyl chloride (1.5 eq. 2 M in CH_2Cl_2) was slowly added dropwise with vigorous stirring. The reaction was conducted at room temperature for 2 h[3], and its progress was monitored using ^{31}P NMR. After the reaction was completed, the solvent and residual oxalyl chloride were removed by vacuum evaporation without the need for purification.

Step 2: The reaction mixture from the previous step was then dissolved in CH_2Cl_2. A mixture of RXH and base (base = 2.0 eq. Et_3N for R = Ar/Bn; base = 1.2 eq. NaH for R = Alkyl) was gradually added dropwise under an ice bath, and the reaction was continued at room temperature for 2−12 h[3]. The advancement of the reaction was monitored by TLC. Upon completion of the reaction, the organic layer was extracted, and the collected organic phase was dried and concentrated. Subsequently, the crude product was purified using silica gel column chromatography with a petroleum ether: ethyl acetate eluent in a ratio of 3:2 to 1:1, to remove the solvent and obtain the purified compounds **S3**−**S12**.

Methyl diphenylphosphinate (S3)



S3

Colorless oil, yield: 87%.

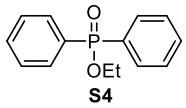
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.74 (d, J = 11.2 Hz, 3H), 7.40−7.44 (m, 4H), 7.47−7.51 (m, 2H), 7.76−7.81 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 132.2 (d, J = 2.6 Hz), 131.6 (d, J = 10 Hz), 130.3, 128.6 (d, J = 13.1 Hz), 51.53 (d, J = 6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 33.3 (s, 1P).

HRMS (m/z) calculated for $C_{13}H_{14}O_2P^+$ ([M+H]$^+$): 233.0726; found: 233.0733.

Ethyl diphenylphosphinate (S4)



S4

Colorless oil, yield: 64%.

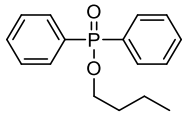
^{1}H NMR (400 MHz, CDCl$_3$): δ 7.79 (dd, *J* = 12 Hz, 8 Hz, 4H), 7.45−7.49 (m, 2H), 7.38−7.43 (m, 4H), 4.04−4.11 (m, 2H), 1.33 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): δ 131.9 (d, *J* = 10.4 Hz), 131.5 (d, *J* = 40.4 Hz), 131.4 (d, *J* = 137 Hz), 128.4 (d, *J* = 52 Hz), 61.1 (d, *J* = 23.6 Hz), 16.3 (d, *J* = 26 Hz).

^{31}P NMR (162 MHz, CDCl$_3$): δ 31.5 (s, 1P).

HRMS (m/z) calculated for $C_{14}H_{16}O_2P^+$ ([M+H]$^+$): 247.0882; found: 247.0890.

Butyl diphenylphosphinate (S5)



S5

White solid, yield: 77%.

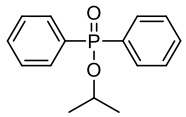
^{1}H NMR (400 MHz, CDCl$_3$): δ 7.78−7.83 (m, 4H), 7.48−7.52 (m, 2H), 7.41−7.46 (m, 4H), 4.02 (q, *J* = 6.8 Hz, 2H), 1.67−1.74 (m, 2H), 1.38−1.48 (m, 2H), 0.91 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): δ 132.0 (d, *J* = 2.6 Hz), 133.7 (d, *J* = 136 Hz), 131.6 (d, *J* = 10 Hz), 128.5 (d, *J* = 13 Hz), 64.7 (d, *J* = 6 Hz), 32.6 (d, *J* = 6.5 Hz), 18.8, 13.6.

^{31}P NMR (162 MHz, CDCl$_3$): δ 31.1 (s, 1P).

HRMS (m/z) calculated for $C_{16}H_{20}O_2P^+$ ([M+H]$^+$): 275.1195; found: 275.1208.

Isopropyl diphenylphosphinate (S6)



S6

White solid, yield: 52%.

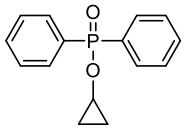
^{1}H NMR (400 MHz, CDCl$_3$): δ 7.78−7.83 (m, 4H), 7.47−7.50 (m, 2H), 7.40−7.44 (m, 4H), 4.63−4.70 (m, 1H), 1.33 (d, *J* = 6.4 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 24.3 (d, *J* = 4 Hz), 70.2 (d, *J* = 6 Hz), 128.4 (d, *J* = 13 Hz), 131.6 (d, *J* = 10 Hz), 131.9 (d, *J* = 2.6 Hz), 132.4 (d, *J* = 136 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 29.7 (s, 1P).

HRMS (m/z) calculated for $C_{15}H_{18}O_2P^+$ ($[M+H]^+$): 261.1039; found: 261.1044.

Cyclopropyl diphenylphosphinate (S7)



S7

Colorless oil, yield: 37%.

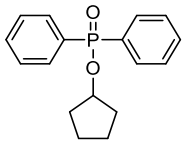
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75−7.80 (m, 4H), 7.45−7.49 (m, 2H), 7.38−7.43 (m, 4H), 3.86−3.91 (m, 1H), 0.82−0.83 (m, 2H), 0.51−0.55 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 132.1, 131.3 (d, *J* = 137 Hz), 131.5 (d, *J* = 10.2 Hz), 128.4 (d, *J* = 13.1 Hz), 49.8 (d, *J* = 6 Hz), 5.7 (d, *J* = 4.1 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 32.4 (s, 1P).

HRMS (m/z) calculated for $C_{15}H_{16}O_2P^+$ ($[M+H]^+$): 259.0882; found: 259.0886.

Cyclopentyl diphenylphosphinate (S8)



S8

White solid, yield: 75%.

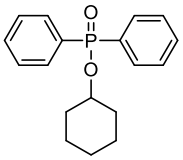
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76−7.81 (m, 4H), 7.45−7.50 (m, 2H), 7.41−7.43 (m, 4H), 4.88 (m, 1H), 1.79−1.89 (m, 6H), 1.56 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 132.4 (d, *J* = 137 Hz), 131.8 (d, *J* = 2.4 Hz), 131.6 (d, *J* = 10 Hz), 128.4 (d, *J* = 13 Hz), 78.7 (d, *J* = 6.3 Hz), 34.28 (d, *J* = 4.1 Hz), 23.0.

^{31}P NMR (162 MHz, $CDCl_3$): δ 29.9 (s, 1P).

HRMS (m/z) calculated for $C_{17}H_{20}O_2P^+$ ($[M+H]^+$): 287.1195; found: 287.1201.

Cyclohexyl diphenylphosphinate (S9)



S9

White solid, yield: 69%.

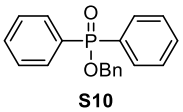
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78−7.83 (m, 4H), 7.48−7.50 (m, 2H), 7.42−7.44 (m, 4H), 4.40−4.42 (m, 1H), 1.87−1.88 (m, 2H), 1.70−1.72 (m, 2H), 1.59−1.61 (m, 2H), 1.37−1.47 (m, 1H), 1.26−1.36 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 132.6 (d, J = 136 Hz), 131.8 (d, J = 2.4 Hz), 131.5 (d, J = 10 Hz), 128.6 (d, J = 13 Hz), 74.9 (d, J = 6.1 Hz), 33.9 (d, J = 3.5 Hz), 25.1, 23.5.

^{31}P NMR (162 MHz, $CDCl_3$): δ 29.7 (s, 1P).

HRMS (m/z) calculated for $C_{18}H_{22}O_2P^+$ ($[M+H]^+$): 301.1352; found: 301.1359.

Benzyl diphenylphosphinate (S10)



S10

White solid, yield: 81%.

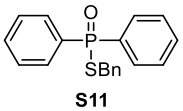
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81−7.86 (m, 4H), 7.51−7.53 (m, 2H), 7.41−7.46 (m, 4H), 7.29−7.37 (m, 5H), 5.07 (d, J = 6.8 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 136.3 (d, J = 7.4 Hz), 132.1 (d, J = 2.6 Hz), 131.6 (d, J = 10.2 Hz), 131.9, 130.6, 128.5 (d, J = 7.9 Hz), 128.1 (d, J = 63.9 Hz), 128.2, 66.2 (d, J = 5.5 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 32.3 (s, 1P).

HRMS (m/z) calculated for $C_{19}H_{18}O_2P^+$ ($[M+H]^+$): 309.1039; found: 309.1042.

***S*-benzyl diphenylphosphinothioate (S11)**



S11

White solid, yield: 78%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84−7.89 (m, 4H), 7.45−7.52 (m, 6H), 7.39−7.45 (m, 4H), 7.20−7.23 (m, 5H), 4.02 (d, J = 2.3 Hz, 2H).

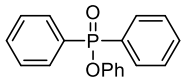
^{13}C NMR (100 MHz, $CDCl_3$): δ 136.8 (d, J = 5.3 Hz), 133.1 (d, J = 106 Hz), 132.3 (d, J = 2.8 Hz), 131.5 (d, J = 10.4 Hz), 128.9, 128.7, 128.53 (d, J = 2.4 Hz), 127.4, 33.1 (d,

J = 1.7 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 42.7 (s, 1P).

HRMS (m/z) calculated for $C_{19}H_{18}OPS^+$ ($[M+H]^+$): 325.0810; found: 325.0816.

Phenyl diphenylphosphinate (S12)



S12

White solid, yield: 65%.

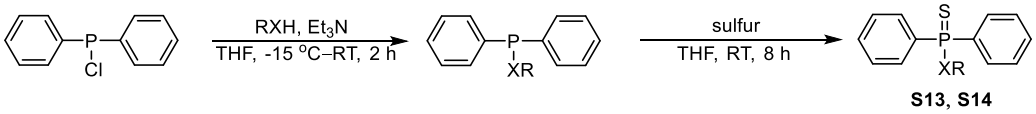
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11 (t, J = 3.4 Hz, 1H), 7.24−7.31 (m, 4H), 7.48−7.52 (m, 4H), 7.55−7.59 (m, 2H), 7.91−7.97 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 150.9 (d, J = 8.3 Hz), 132.4 (d, J = 2.7 Hz), 131.8 (d, J = 10.3 Hz), 130.9 (d, J = 137 Hz), 129.6, 128.5 (d, J = 13.4 Hz), 124.5, 120.7 (d, J = 4.7 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 30.4 (s, 1P).

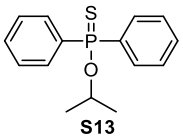
HRMS (m/z) calculated for $C_{18}H_{16}O_2P^+$ ($[M+H]^+$): 295.0882; found: 295.0894.

General procedure D for the formation of diphenylphosphinothioate (S13, S14)



Chlorodiphenylphosphane (1.1 equiv.) was dissolved in THF, and the temperature was lowered to −15 ℃. Then, a mixture of 1.0 eq. RXH (propane-2-alcohol/phenyl methylmercaptan) and 1.2 eq Et_3N was slowly added dropwise. The reaction mixture was then allowed to warm up to room temperature (RT) and react for 2 h[4]. After the completion of the reaction, sulfur (5.0 eq.) was added to the reaction system, and the reaction was continued at RT for 8 h. The progress of the reaction was monitored by TLC. Upon completion of the reaction, the reaction mixture was extracted, and the organic phase was collected, dried, and concentrated under reduced pressure. Subsequently, the crude product was purified using silica gel column chromatography to remove the solvent and obtain the purified compounds **S13**, **S14**.

***O*-Isopropyl diphenylphosphinothioate (S13)**



White solid, yield: 43%.

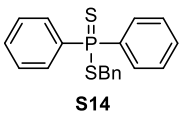
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86−7.92 (m, 4H), 7.38−7.44 (m, 6H), 4.86−4.95 (m, 1H), 1.30 (d, *J* = 6.4 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 133.1, 131.9 (d, *J* = 2.6 Hz), 131.6 (d, *J* = 10 Hz), 128.4 (d, *J* = 13 Hz), 70.3 (d, *J* = 6 Hz), 24.3 (d, *J* = 4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 42.1 (s, 1P).

HRMS (m/z) calculated for $C_{15}H_{18}OPS^+$ ($[M+H]^+$): 277.0810; found: 277.0816.

Benzyl diphenylphosphinodithioate (S14)



White solid, yield: 21%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96−7.81 (m, 4H), 7.51−7.54 (m, 6H), 7.30−7.32 (m,

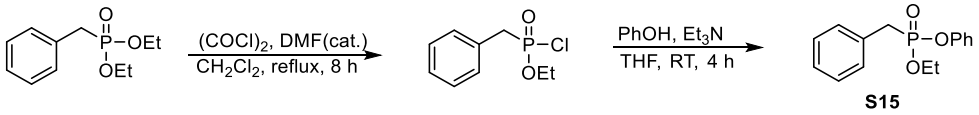
2H), 7.19−7.27 (m, 3H), 4.22 (d, J = 3 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 136.7 (d, J = 5.7 Hz), 134.1 (d, J = 84 Hz), 133.8 (d, J = 3 Hz), 131.5 (d, J = 11.3 Hz), 129.3, 128.6, 128.5 (d, J = 4.1 Hz), 127.44, 35.9 (d, J = 1.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 64.1 (s, 1P).

HRMS (m/z) calculated for $C_{19}H_{18}PS_2^+$ ($[M+H]^+$): 341.0582; found: 341.0588.

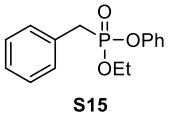
General procedure E for the formation of S15



Step 1: The synthesis method employs **Step 1** of **Procedure B**.

Step 2: The initial product was dissolved in tetrahydrofuran, followed by the slow addition of a mixture of PhOH and Et_3N, both dissolved in THF, under ice bath conditions. Subsequently, the reaction mixture was allowed to warm up to RT and react for 2 h, with the progress of the reaction monitored by TLC. After the reaction was complete, the precipitate was filtered, and the solvent was removed under reduced pressure. The crude product was then purified using silica gel column chromatography to eliminate the solvent and obtain the purified compounds **S15**.

Phenyl benzylphosphonate (S15)



S15

Colorless oil, yield: 54%.

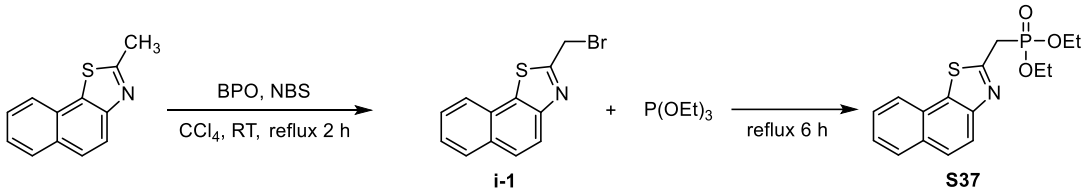
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.21 (m, 7H), 7.15–7.06 (m, 3H), 4.13–3.98 (m, 2H), 3.31 (dd, J = 21.7, 2.6 Hz, 2H), 1.19 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5 (d, J = 8.8 Hz), 130.9 (d, J = 9.4 Hz), 129.9 (d, J = 6.8 Hz), 129.6, 128.6 (d, J = 3.2 Hz), 127.0 (d, J = 3.7 Hz), 124.8, 120.4 (d, J = 4.3 Hz), 63.0 (d, J = 7.2 Hz), 33.7 (d, J = 138.9 Hz), 16.2 (d, J = 5.9 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 23.3 (s, 1P).

HRMS (m/z) calculated for $C_{15}H_{18}O_3P^+$ ($[M+H]^+$): 277.0988; found: 277.0982.

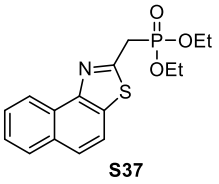
Procedure F for the formation of S37



Step 1: 2-methylnaphtho[2,1-*d*]thiazole (4 mmol, 1.0 eq.) and *N*-bromosuccinimide (NBS, 1.0 eq.) were introduced into the reaction flask, succeeded by the addition of the dibenzoyl peroxide (BPO, 0.05 eq.) in 50 mL CCl_4, while maintaining constant stirring. Elevate the mixture's temperature to 80 ℃ and maintain reflux for a duration of 2 h[5]. The reaction's progression was monitored using TLC. After the completion of the reaction, allow it to cool to RT, filter the mixture, and remove CCl_4 under reduced pressure. For column chromatography purification of the residue, a mixture of petroleum ether and ethyl acetate (3:2−1:1) was employed as the elution, resulting in the isolation of the purified bromine compound **i-1**.

Step 2: The synthesis method employs **Procedure A**.

Ethyl (naphtho[1,2-*d*]thiazol-2-ylmethyl)phosphonofluoridate (S37)



Colorless oil, yield: 74%.

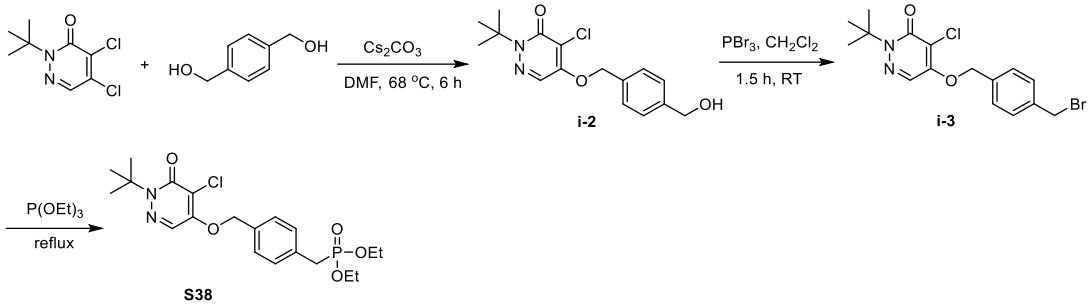
^{1}H NMR (600 MHz, $CDCl_3$): δ 8.76 (d, *J* = 8.3 Hz, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.84 (d, *J* = 7.4 Hz, 1H), 7.78 (d, *J* = 8.8 Hz, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.56 (t, *J* = 7.2 Hz, 1H), 4.22–4.13 (m, 4H), 3.84 (d, *J* = 20.0 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 159.8 (d, *J* = 9.8 Hz), 149.2, 132.6, 131.9, 128.5, 128.1, 127.0, 126.1, 125.9, 123.8, 118.8, 63.0 (d, *J* = 6.6 Hz), 33.5, 16.4 (d, *J* = 5.7 Hz).

^{31}P NMR (243 MHz, $CDCl_3$): δ 21.2 (s, 1P).

HRMS (m/z) calculated for $C_{16}H_{18}NNaO_3PS^+$ ($[M+Na]^+$): 358.0637; found: 358.0630.

Procedure G for the formation of S38

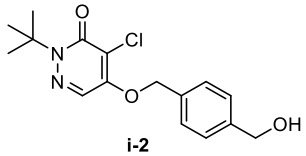


Step 1: 2-(*tert*-Butyl)-4,5-dichloropyridazin-3(2H)-one (4.53 mmol) was dissolved in 15 mL dry DMF. 1,4-phenylene dimethanol (3.2 g, 23.16 mmol) and Cs_2CO_3 (6.0 g, 18.41 mmol) were added, and the mixture was stirred at 68 ℃ for 6 h, then cooled. The product was extracted with EtOAc, dried under vacuum, and purified by column chromatography to yield compound **i-2** as a white solid[6].

Step 2: Compound **i-2** (0.91 g, alcoholic) was dissolved in 15 ml of dry dichloromethane. PBr_3 (0.14 ml) was then introduced dropwise into the solution. The reaction was performed at room temperature for approximately 1.5 h. The crude product was isolated by extraction with water (30 mL) and dried under vacuum. The resulting white solid product **i-3** was obtained in a quantitative yield, ready for the subsequent step without further purification.

Step 3: The synthesis of compound **S38** was completed according to the synthesis **Procedure A** of this study.

2-(*Tert*-butyl)-4-chloro-5-((4-(hydroxymethyl)benzyl)oxy)pyridazin-3(2*H*)-one (i-2)



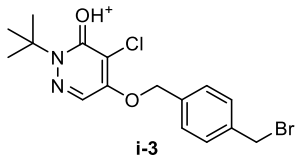
White solid, yield: 76%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (s, 1H), 7.40 (d, *J* = 1.6 Hz, 4H), 5.30 (s, 2H), 4.71 (s, 2H), 1.61 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 159.0, 153.7, 141.7, 134.0, 127.4, 127.3, 125.1, 118.2, 71.6, 66.4, 64.7, 27.8.

HRMS (m/z) calculated for $C_{16}H_{20}ClN_2O_3^+$ ($[M+H]^+$): 323.1157; found: 323.1151.

5-((4-(Bromomethyl)benzyl)oxy)-2-(tert-butyl)-4-chloropyridazin-3(2*H*)-one (i-3)



i-3

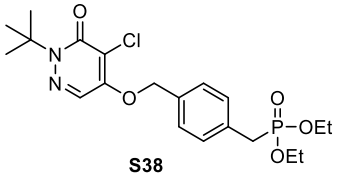
White solid, yield: 96%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (s, 1H), 7.43 (d, *J* = 7.6 Hz, 2H), 7.39 (d, *J* = 7.6 Hz, 2H), 5.30 (s, 2H), 4.49 (s, 2H), 1.62 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 153.5, 138.4, 135.0, 129.6, 127.4, 124.9, 118.2, 71.3, 66.4, 32.7, 27.8.

HRMS (m/z) calculated for $C_{16}H_{19}BrClN_2O_2^+$ ($[M+H]^+$): 385.0313; found: 385.0318.

Diethyl (4-(((1-(*tert*-butyl)-5-chloro-6-oxo-1,6-dihydropyridazin-4-yl)oxy)methyl)benzyl)phosphonate (S38)



S38

White solid, yield: 69%.

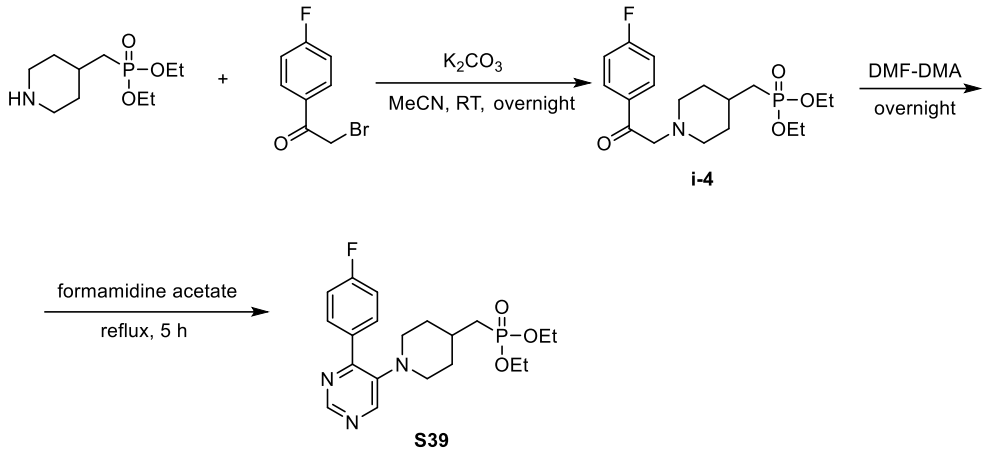
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (s, 1H), 7.29−7.32 (s, 4H), 5.26 (d, *J* = 1.6 Hz, 2H), 3.96−3.99 (m, 4H), 3.12 (d, *J* = 21.6 Hz, 2H), 1.58 (s, 9H), 1.19, (t, *J* = 7.2 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 153.5, 133.4 (d, *J* = 3.9 Hz), 132.3 (d, *J* = 9.0 Hz), 130.2 (d, *J* = 6.5 Hz), 127.2 (d, *J* = 2.9 Hz), 125.0, 118.1, 71.4, 66.3, 62.1 (d, *J* = 6.7 Hz), 33.4 (d, *J* = 137.5 Hz), 27.7, 16.2 (d, *J* = 5.9 Hz).

^{31}P NMR (162 MHz, $DMSO_{d6}$): δ 25.9 (1P).

HRMS (m/z) calculated for $C_{20}H_{29}ClN_2O_5P^+$ ($[M+H]^+$): 443.1497; found: 443.1492.

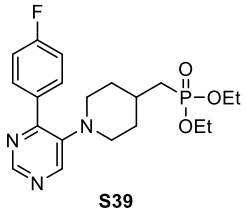
Procedure H for the formation of S39



To a solution of diethyl (piperidin-4-ylmethyl)phosphonate (5.8 g, 25.0 mmol) and K_2CO_3 (4.33 g, 31.3 mmol) in acetonitrile (50 mL), 2-bromo-1-(4-fluorophenyl)ethanone (4.91 g, 22.7 mmol) dissolved in acetonitrile (30 mL) was added dropwise at room temperature. The reaction mixture was stirred overnight at the same temperature. Following this, the mixture was concentrated under reduced pressure, diluted with water, and extracted with ethyl acetate. The organic phase was washed with brine, dried over sodium sulfate, filtered, and then concentrated in vacuo. The resulting pale yellow solid, **i-4** (7.42 g, 88%), was used directly in the subsequent reaction without additional purification.

A solution of **i-4** (3.71 g, 10 mmol) and DMF-DMA (18.2 mL, 130 mmol) was heated to reflux overnight. After cooling, the mixture was concentrated under reduced pressure. The residue was then dissolved in *n*-butanol (10 mL) and diisopropylethylamine (DIPEA, 10 mL). Formamidine acetate (3.6 g, 35 mmol) was added, and the resulting mixture was stirred at 100 °C overnight. The reaction mixture was then diluted with water and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel to afford **S39** (1.75 g, 43%) as a dark brown oil.

Diethyl ((1-(4-(4-fluorophenyl)pyrimidin-5-yl)piperidin-4-yl)methyl)phosphonate (S39)



S39

Dark brown oil, yield: 43%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.88 (s, 1H), 8.40 (s, 1H), 8.06–8.19 (m, 2H), 7.13–7.19 (m, 2H), 4.06–4.13 (m, 4H), 3.18 (d, *J* = 10.1 Hz, 2H), 2.62–2.68 (m, 2H), 2.04–2.07 (m, 2H), 1.82–1.90 (m, 3H), 1.69–1.78 (m, 2H), 1.32 (t, *J* = 7.2 Hz, 6H).

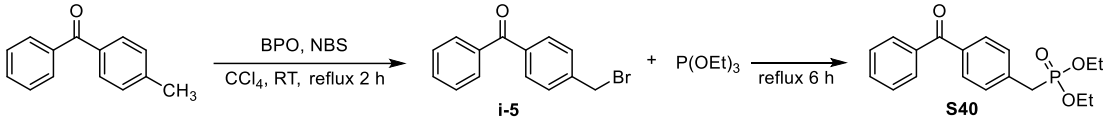
^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 162.7, 156.5, 152.4, 147.1, 144.0, 134.0, 130.2 (d, *J* = 8.3 Hz), 115.4 (d, *J* = 21.2 Hz), 61.5 (d, *J* = 6.6 Hz), 50.7, 33.1 (d, *J* = 11.0 Hz), 32.7, 31.8, 30.3 (d, *J* = 4.3 Hz), 16.4 (d, *J* = 5.7 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 30.5 (s, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -110.5 (s, 1F).

HRMS (m/z) calculated for $C_{20}H_{27}FN_3NaO_3P^+$ ($[M+Na]^+$): 430.1666; found: 430.1660.

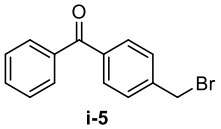
Procedure I for the formation of S40



Step 1: Phenyl(*p*-tolyl)methanone (4 mmol, 1.0 eq.) and *N*-bromosuccinimide (NBS, 1.0 eq.) were introduced into the reaction flask, succeeded by the addition of the dibenzoyl peroxide (BPO, 0.05 eq.) in 50 mL CCl_4, while maintaining constant stirring. Elevate the mixture's temperature to 80 ℃ and maintain reflux for a duration of 2 h[7]. The reaction's progression was monitored using TLC. After the completion of the reaction, allow it to cool to RT, filter the mixture, and remove CCl_4 under reduced pressure. For column chromatography purification of the residue, a mixture of petroleum ether and ethyl acetate (3:2−1:1) was employed as the elution, resulting in the isolation of the purified compound **i-5**.

Step 2: The synthesis method employs **Procedure A**.

Diethyl (4-benzoylbenzyl)phosphonate (i-5)



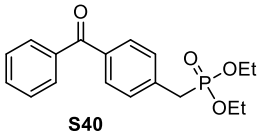
White solid, yield: 93%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77−7.80 (m, 4H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.47−7.51 (m, 4H), 4.53 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 195.9, 142.1, 137.4, 132.5, 130.5, 129.9, 128.9, 128.3, 32.2.

HRMS (m/z) calculated for $C_{14}H_{12}BrO^+$ ($[M+H]^+$): 275.0066; found: 275.0061.

Diethyl (4-benzoylbenzyl)phosphonate (S40)



White solid, yield: 77%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (t, *J* = 6.0 Hz, 4H), 7.58 (t, *J* = 6.8 Hz, 1H), 7.47

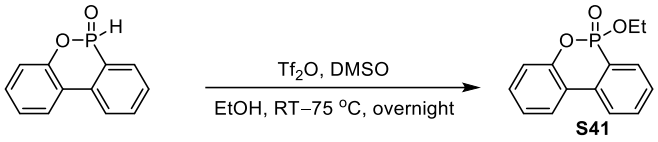
(t, *J* = 6.8 Hz, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 4.01−4.09 (m, 4H), 3.22 (d, *J* = 22.4 Hz, 2H), 1.26 (t, *J* = 7.2 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 196.2, 137.6, 136.7 (d, *J* = 9.1 Hz), 136.1 (d, *J* = 3.4 Hz), 132.3, 130.3 (d, *J* = 2.8 Hz), 129.9, 129.7 (d, *J* = 6.3 Hz), 128.3, 62.3 (d, *J* = 6.7 Hz), 33.9 (d, *J* = 137 Hz), 16.4 (d, *J* = 5.8 Hz).

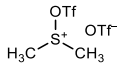
^{31}P NMR (162 MHz, $CDCl_3$): δ 25.2 (s, 1P).

HRMS (m/z) calculated for $C_{18}H_{22}O_4P^+$ ($[M+H]^+$): 333.1250; found: 333.1256.

Procedure J for the formation of S41

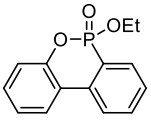


The mixture of the dibenzo[*c*,*e*][1,2]oxaphosphinine 6-oxide (0.2 mmol, 40.4 mg, 1.0 eq.), Tf_2O (0.6 mmol, 169.3 mg, 3.0 eq.), and DMSO (0.4 mmol, 31.2 mg, 2.0 eq.) was dissolved in 1.0 mL of EtOH under a N_2 atmosphere. (Tf_2O and DMSO form an *in situ*



active intermediate to initiate the reaction.) Subsequently, the reaction mixture was heated in a round-bottom flask in a 75 °C oil bath overnight[8]. The progress of the reaction was monitored using TLC. After the completion of the reaction, water was added to quench it, and then the organic phase was extracted and dried under reduced pressure. Finally, the crude product was purified using silica gel column chromatography with petroleum ether/ethyl acetate (4:1−3:1) as the eluent to obtain the purified compound **S41**.

6-Ethoxydibenzo[*c*,*e*][1,2]oxaphosphinine 6-oxide (S41)



S41

Colorless oil, yield: 77%.

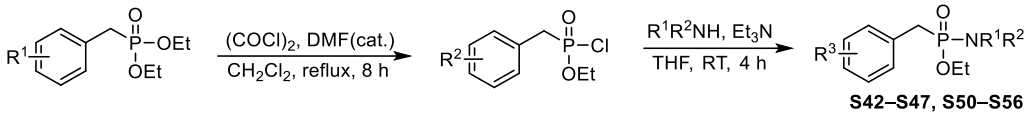
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94−8.02 (m, 3H), 7.72 (t, *J* = 7.6 Hz, 1H), 7.51−7.55 (m, 1H), 7.40 (t, *J* = 15.2 Hz, 1H), 7.24−7.30 (m, 2H), 4.19−4.27 (m, 2H), 1.29 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 149.8 (d, *J* = 7.7 Hz), 136.9 (d, *J* = 7 Hz), 133.4 (d, *J* = 2.2 Hz), 130.4, 130.0 (d, *J* = 9.1 Hz), 128.2 (d, *J* = 15.3 Hz), 125.2, 124.6, 123.9 (d, *J* = 12 Hz), 123.3 (d, *J* = 181 Hz), 122.5 (d, *J* = 12 Hz), 120.1, (d, *J* = 6.6 Hz), 62.9 (d, *J* = 6.6 Hz), 16.2 (d, *J* = 5.7 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 10.2 (1P).

HRMS (m/z) calculated for $C_{14}H_{14}O_3P^+$ ($[M+H]^+$): 261.0675; found: 261.0673.

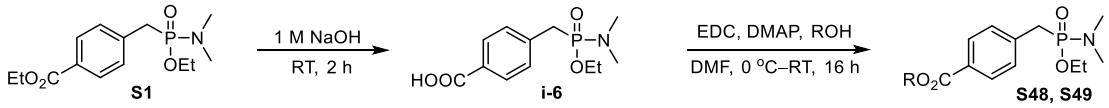
General procedure K for the formation of S42−S47, S50−S56,



Step 1: Under ambient conditions, a 2 M solution of oxalyl chloride (2.0 eq.) was gradually added dropwise to the desired benzyl phosphonate diethyl compound (1.0 eq.). Next, 2 drops of DMF were introduced as a catalyst. The reaction mixture was then heated to 60 °C and refluxed for 8 h[9]. The reaction progress was monitored using ^{31}P-NMR (the P−Cl compound typically exhibits a chemical shift around 35−45 ppm). Upon completion of the reaction, the solvent and excess oxalyl chloride were removed under reduced pressure. The resulting product can be utilized directly in the subsequent step without requiring further purification.

Step 2: The initial product was dissolved in tetrahydrofuran, followed by the slow addition of a mixture of R^1R^2NH and Et_3N, both dissolved in THF, under ice bath conditions. Subsequently, the reaction mixture was allowed to warm up to RT and react for 2 h, with the progress of the reaction monitored by TLC. After the reaction was complete, the precipitate was filtered, and the solvent was removed under reduced pressure. The crude product was then purified using silica gel column chromatography to eliminate the solvent and obtain the purified compounds **S42**−**S47**, **S50**−**S56**.

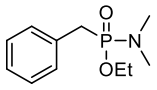
General procedure L for the formation of S48, S49



Step 1: Compound ethyl 4-(((ethoxyphosphoryl)oxy)methyl)benzoate **S1** (1.0 eq.) was dissolved in a 1 M NaOH aqueous solution (3.0 eq.) and stirred at RT for 2 h. The progress of the reaction was monitored by TLC until the reaction mixture became clear. After the reaction was complete, the mixture was extracted once with CH_2Cl_2, and the aqueous phase was acidified with 1 M HCl. Subsequently, CH_2Cl_2 was added for three extractions, and the organic layer was collected, dried, and concentrated to obtain the carboxylated compound **i-6** resulting from the hydrolysis, which was directly used in the next reaction without purification.

Step 2: The carboxylated compound **i-6** (1.0 eq.) was dissolved in CH_2Cl_2, and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI, 1.5 eq.) and 4-dimethylaminopyridine (DMAP, 2.0 eq.) were added at 0 ℃. Subsequently, the hydroxyl-containing compound (*N*-hydroxysuccinimide or pentafluorophenol) dissolved in CH_2Cl_2 was slowly added dropwise to the reaction mixture. After the addition was complete, the reaction was allowed to proceed at room temperature for 16 h[10], and the progress of the reaction was monitored by TLC. Upon completion of the reaction, water was added to quench the reaction, and then the mixture was extracted with CH_2Cl_2. The organic layer was collected, dried, and concentrated to remove the organic solvent. Finally, the crude product was purified using silica gel column chromatography (petroleum ether: ethyl acetate = 1:1−2:3) to obtain the purified compounds **S48** and **S49**.

Ethyl *P*-benzyl-*N*,*N*-dimethylphosphonamidate (S42)



S42

Yellowish solid, yield: 79%.

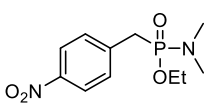
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27−7.31 (m, 5H), 3.85−4.07 (m, 2H), 3.04−3.19 (m, 2H), 2.52 (d, *J* = 8.8 Hz, 6H), 1.28 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 132.2 (d, *J* = 8.0 Hz), 129.5 (d, *J* = 6.2 Hz), 128.2 (d, *J* = 2.7 Hz), 126.3 (d, *J* = 3.3 Hz), 59.5 (d, *J* = 7.0 Hz), 36.2 (d, *J* = 3.9 Hz), 33.6 (d, *J* = 124.9 Hz), 16.0 (d, *J* = 6.5 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 31.3 (1P).

HRMS (m/z) calculated for $C_{11}H_{19}NO_2P^+$ ($[M+H]^+$): 228.1148; found: 228.1141.

Ethyl *N*,*N*-dimethyl-*P*-(4-nitrobenzyl)phosphonamidate (S43)



S43

Yellowish solid, yield: 87%.

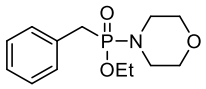
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23 (t, *J* = 7.2 Hz, 6H), 2.55 (d, *J* = 8.8 Hz, 2H), 3.82−4.02 (m, 2H), 7.39−7.42 (m, 2H), 8.10 (d, *J* = 8.4 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 16.0 (d, *J* = 6.5 Hz), 33.7 (d, *J* = 123.7 Hz), 36.2 (d, *J* = 4 Hz), 123.5 (d, *J* = 2.7 Hz), 59.9 (d, *J* = 6.9 Hz), 130.4 (d, *J* = 6.0 Hz), 140.6 (d, *J* = 8.2 Hz), 146.7 (d, *J* = 3.6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 29.0 (1P).

HRMS (m/z) calculated for $C_{11}H_{18}N_2O_4P^+$ ($[M+H]^+$): 273.0999; found: 273.1006.

Ethyl benzyl(morpholino)phosphinate (S44)



S44

White solid, yield: 72%.

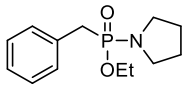
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (t, *J* = 14 Hz, 3H), 2.85−2.96 (m, 4H), 3.08−3.27 (m, 2H), 3.48−3.55 (m, 4H), 4.12−4.18 (m, 2H), 7.26−7.37 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 131.9 (d, *J* = 7.7 Hz), 129.8 (d, *J* = 6.4 Hz), 128.5 (d, *J* = 2.4 Hz), 126.8 (d, *J* = 3.8 Hz), 67.1 (d, *J* = 4.8 Hz), 59.9 (d, *J* = 7.3 Hz), 44.2, 34.1 (d, *J* = 126 Hz), 16.3 (d, *J* = 6.7 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 28.5 (1P).

HRMS (m/z) calculated for $C_{13}H_{21}NO_3P^+$ ($[M+H]^+$): 270.1254; found: 270.1250.

Ethyl benzyl(pyrrolidin-1-yl)phosphinate (S45)



S45

Colorless oil, yield: 70%.

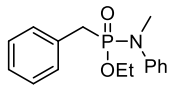
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (t, *J* = 6.8 Hz, 3H), 1.69−1.75 (m, 4H), 3.07−3.09 (m, 2H), 2.95−2.97 (m, 2H), 3.15 (dd, *J* = 28 Hz, 8.8 Hz, 2H), 3.88−4.09 (m, 2H), 7.21−7.24 (m, 1H), 7.29 (d, *J* = 4.4 Hz, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3 (d, *J* = 6.5 Hz), 26.2 (d, *J* = 7.7 Hz), 33.7 (d, *J* = 125 Hz), 46.5 (d, *J* = 4.2 Hz), 59.7 (d, *J* = 6.8 Hz), 126.5 (d, *J* = 3.2 Hz), 128.3 (d, *J* = 2.5 Hz), 129.6 (d, *J* = 6.2 Hz), 132.5 (d, *J* = 8 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 28.5 (1P).

HRMS (m/z) calculated for $C_{13}H_{21}NO_2P^+$ ($[M+H]^+$): 254.1304; found: 254.1308.

Ethyl *P*-benzyl-*N*-methyl-*N*-phenylphosphonamidate (S46)



S46

Yellow oil, yield: 26%.

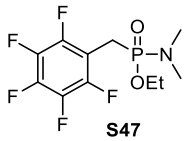
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21−7.30 (m, 5H), 7.11−7.16 (m, 4H), 7.05−7.08 (m, 1H), 3.94−4.19 (m, 2H), 3.24 (d, *J* = 20 Hz, 2H), 3.0 (d, J = 7.6 Hz, 3H), 1.29 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 144.3 (d, *J* = 4.6 Hz), 131.5 (d, *J* = 8.2 Hz), 129.8 (d, *J* = 6.4 Hz), 128.9, 128.3 (d, *J* = 2.9 Hz), 126.7 (d, *J* = 3.5 Hz), 123.4, 121.8 (d, *J* = 3.4 Hz), 60.4 (d, *J* = 7.0 Hz), 36.2 (d, *J* = 3.8 Hz), 33.7 (d, *J* = 125.6 Hz), 16.1 (d, *J* = 6.7 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 28.4 (1P).

HRMS (m/z) calculated for $C_{16}H_{21}NO_2P^+$ ($[M+H]^+$): 290.1304; found: 290.1309.

Ethyl *N*,*N*-dimethyl-*P*-((perfluorophenyl)methyl)phosphonamidate (S47)



S47

Colorless oil, yield: 36%.

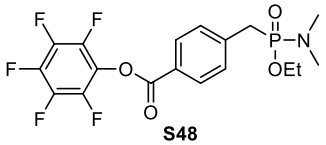
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (t, *J* = 6.8 Hz, 3H), 2.64 (d, *J* = 9.2 Hz, 6H), 3.10−3.17 (m, 2H), 3.88−4.09 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 145.1 (d, *J* = 245.7 Hz), 143.8 (m), 141.2 (m), 138.7 (m), 136.2(m), 107.5 (m), 60.2 (d, *J* = 6.7 Hz), 35.9 (d, *J* = 4.2 Hz), 20.7 (d, *J* = 128.6 Hz), 15.9 (d, *J* = 6.7 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 26.1 (1P). ^{19}F NMR (376 MHz, $CDCl_3$): δ -141.8 (2F), -156.3 (1F), -162.3 (2F).

HRMS (m/z) calculated for $C_{11}H_{14}F_5NO_2P^+$ ($[M+H]^+$): 318.0677; found: 318.0671.

Perfluorophenyl 4-(((dimethylamino)(ethoxy)phosphoryl)methyl)benzoate (S48)



S48

White solid, yield: 43%.

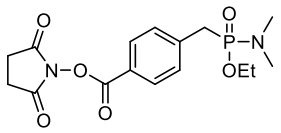
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, *J* = 7.6 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 2H), 3.88−4.09 (m, 2H), 3.12−3.29 (m, 2H), 2.60 (d, *J* = 8.8 Hz, 6H), 1.30 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 162.4, 140.5 (d, *J* = 8.1 Hz), 139.2, 138.2, 136.7, 130.8 (d, *J* = 2.5 Hz), 130.3 (d, *J* = 6 Hz), 125.2 (d, *J* = 3.4 Hz), 59.9 (d, *J* = 6.9 Hz), 36.4 (d, *J* = 4 Hz), 34.1 (d, *J* = 123.6 Hz), 16.2 (d, *J* = 6.6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 24.1 (1P).

HRMS (m/z) calculated for $C_{18}H_{18}F_5NO_4P^+$ ($[M+H]^+$): 438.0888; found: 438.0893.

2,5-Dioxopyrrolidin-1-yl 4-(((dimethylamino)(ethoxy)phosphoryl)methyl)benzoate (S49)



S49

White solid, yield: 55%.

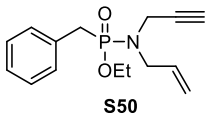
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.14 (t, *J* = 7.2 Hz, 3H), 2.43 (d, *J* = 8.8 Hz, 6H) 2.75 (s, 4H), 3.07 (dd, *J* = 22 Hz, 8.8 Hz, 2H), 3.73−3.93 (m, 2H), 7.31 (d, *J* = 7.2 Hz, 2H), 7.92 (d, *J* = 8.0 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.1, 161.4, 140.5 (d, *J* = 8.1 Hz), 130.2 (d, *J* = 2.4 Hz), 129.9 (d, *J* = 5.9 Hz), 122.9 (d, *J* = 3.1 Hz), 59.5 (d, *J* = 6.8 Hz), 35.9 (d, *J* = 3.9 Hz), 33.8 (d, *J* = 123.3 Hz), 25.3, 15.8 (d, *J* = 6.5 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 29.3 (1P).

HRMS (m/z) calculated for $C_{16}H_{22}N_2O_6P^+$ ($[M+H]^+$): 369.1210; found: 369.1213.

Ethyl *N*-allyl-*P*-benzyl-*N*-(prop-2-yn-1-yl)phosphonamidate (S50)



S50

White solid, yield: 56%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27−7.32 (m, 4H), 7.21−7.23 (m, 1H), 5.45−5.55 (m, 1H), 5.16 (dd, *J* = 22.8 Hz, 17.2Hz, 2H), 3.89−4.10 (m, 2H), 3.51−3.80 (m, 4H), 3.08−3.23 (m, 2H), 1.27 (t, *J* = 7.2 Hz, 3H), 2.20 (s, 1H).

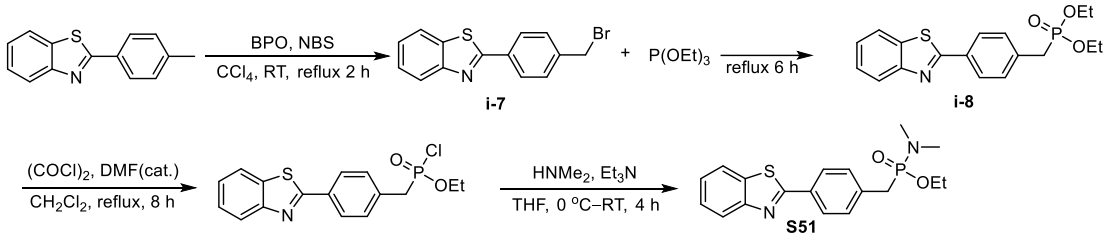
^{13}C NMR (100 MHz, $CDCl_3$): δ 133.5 (d, *J* = 3.1 Hz), 132.0 (d, *J* = 8.7 Hz), 129.9 (d, *J* = 6.3 Hz), 128.4 (d, *J* = 2.8 Hz), 126.6 (d, *J* = 3.4 Hz), 118.5, 79.7, 71.9, 60.14 (d, *J*

= 7 Hz), 47.5 (d, *J* = 3.6 Hz), 34.8 (d, *J* = 126 Hz), 34.0, (d, *J* = 5.3 Hz), 16.1 (d, *J* = 6.9 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 30.3 (1P).

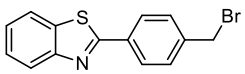
HRMS (m/z) calculated for $C_{15}H_{21}NO_2P^+$ ([M+H]$^+$): 278.1304; found: 278.1307.

Procedure M for the formation of S51



The synthesis methods for preparing **i-7** and **i-8** in **Steps 1** and **2**, respectively, utilize **Procedure A**. The synthesis method for preparing compound **S51** in **Steps 3** and **4** employs **Procedure E**.

2-(4-(Bromomethyl)phenyl)benzo[*d*]thiazole (i-7)



i-7

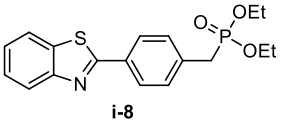
White solid, yield: 97%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07−8.09 (m, 3H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 3H), 7.40 (t, *J* = 7.2 Hz, 1H), 4.54 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 154.0, 140.6, 135.0, 133.6, 129.7, 127.9, 126.4, 125.4, 123.3, 121.6, 32.5.

HRMS (m/z) calculated for $C_{14}H_{11}BrNS^+$ ([M+H]$^+$): 303.9790; found: 303.9793.

Diethyl (benzo[*d*]thiazol-2-ylmethyl)phosphonate (i-8)



i-8

White solid, yield: 77%.

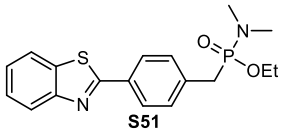
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (t, *J* = 7.6 Hz, 3H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.40−7.44 (m, 2H), 7.38 (t, *J* = 7.6 Hz, 1H), 4.00−4.08 (m, 4H), 3.22 (d, *J* = 22.0 Hz, 2H), 1.26 (t, *J* = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 154.0, 134.9 (d, *J* = 2.4 Hz), 134.8, 132.3 (d, *J* = 3.5 Hz), 130.4 (d, *J* = 6.5 Hz), 127.7 (d, *J* = 3.0 Hz), 126.3, 125.2, 123.1, 121.6, 62.3 (d, *J* = 6.7 Hz), 33.8 (d, *J* = 137.0 Hz), 16.4 (d, *J* = 6.0 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 25.5 (1P).

HRMS (m/z) calculated for $C_{18}H_{21}NO_3PS^+$ ($[M+H]^+$): 362.0974; found: 362.0970.

Ethyl *P*-benzyl-*N*,*N*-bis(2-chloroethyl)phosphonamidate (S51)



S51

White solid, yield: 64%.

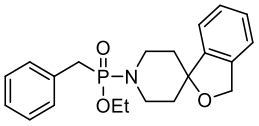
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02−8.07 (m, 3H), 7.88 (t, *J* = 8.0 Hz, 1H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.35−7.42 (m, 3H), 3.87−4.09 (m, 2H), 3.11−3.25 (m, 2H), 2.57 (d, *J* = 8.8 Hz, 6H), 1.29 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 153.9, 136.0 (d, *J* = 8.2 Hz), 134.9, 131.9 (d, *J* = 3.5 Hz), 130.3 (d, *J* = 6.0 Hz), 127.6 (d, *J* = 2.4 Hz), 126.3, 125.1, 123.0, 121.6, 59.8 (d, *J* = 6.8 Hz), 36.4 (d, *J* = 3.7 Hz), 33.9 (d, *J* = 124.3 Hz),16.2 (d, *J* = 6.1 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 30.2 (1P).

HRMS (m/z) calculated for $C_{18}H_{22}N_2O_2PS^+$ ($[M+H]^+$): 361.1134; found: 361.1139.

Ethyl benzyl(3*H*-spiro[isobenzofuran-1,4'-piperidin]-1'-yl)phosphinate (S52)



S52

White solid, yield: 78%.

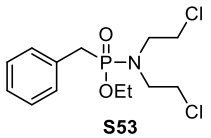
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30−7.36 (m, 4H), 7.22−7.25 (m, 3H), 7.15−7.18 (m, 1H), 6.93−6.95 (m, 1H), 5.0 (s, 2H), 3.92−4.12 (m, 2H), 3.37−3.43 (m, 2H), 2.93−3.09 (m, 4H), 2.51 (d, *J* = 8.8 Hz, 1H), 1.56−1.64 (m, 3H), 1.31 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 145.2, 138.7, 132.5 (d, *J* = 7.7 Hz), 129.8, 128.5, 127.7, 127.3, 126.7, 120.8 (d, *J* = 51.3 Hz), 84.5, 70.7, 59.7 (d, *J* = 6.8 Hz), 40.8 (d, *J* = 20.9 Hz), 36.5 (d, *J* = 8.9 Hz), 34.2 (d, *J* = 126.5 Hz), 16.3 (d, *J* = 6.5 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 29.7 (1P).

HRMS (m/z) calculated for $C_{21}H_{27}NO_3P^+$ ($[M+H]^+$): 372.1723; found: 372.1728.

Ethyl *P*-benzyl-*N*,*N*-bis(2-chloroethyl)phosphonamidate (S53)



S53

White solid, yield: 54%.

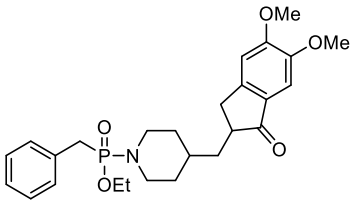
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25−7.33 (m, 5H), 3.91−4.15 (m, 2H), 3.40 (d, *J* = 6.8 Hz, 4H), 3.08−3.32 (m, 6H), 1.28 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): 16.2 (d, *J* = 6.6 Hz), 34.3 (d, *J* = 125.4 Hz), 42.17, 48.7 (d, *J* = 4 Hz), 60.5 (d, *J* = 6.8 Hz), 126.9 (d, *J* = 3.4 Hz), 128.6 (d, *J* = 2.7 Hz), 129.7 (d, *J* = 6.4 Hz), δ 131.7 (d, *J* = 8 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 31.0 (1P).

HRMS (m/z) calculated for $C_{13}H_{21}Cl_2NO_2P^+$ ($[M+H]^+$): 324.0681; found: 324.0688.

Ethyl benzyl(4-((5,6-dimethoxy-1-oxo-2,3-dihydro-1*H*-inden-2-yl)methyl)piperidin-1-yl)phosphinate (S54)



S54

White solid, yield: 69%.

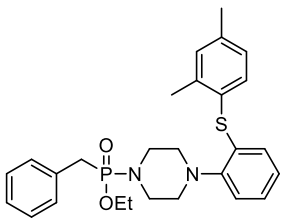
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27−7.33 (m, 5H), 7.18 (s, 1H), 6.87 (s, 1H), 3.98 (s, 3H), 3.92 (s, 3H), 3.48−3.51 (m, 2H), 3.20−3.26 (m, 2H), 3.05−3.15 (m, 1H), 2.67 (d, *J* = 14.4 Hz, 2H), 2.59−2.61 (m, 1H), 2.38−2.48 (m, 2H), 1.84−1.87 (m, 1H), 1.59−1.70 (m, 3H), 1.28−1.34 (m, 5H), 0.96−1.12 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 207.4, 155.5, 149.4, 148.6, 132.4 (d, *J* = 7.8 Hz), 129.8, (d, *J* = 6.1 Hz), 129.1, 128.3, 126.5, 107.3, 104.4, 59.6 (d, *J* = 6.8 Hz), 56.1 (d, *J* = 12.3 Hz), 44.9 (d, *J* = 5.4 Hz), 44.3 (d, *J* = 10.4 Hz), 38.8 (d, *J* = 10.5 Hz), 34.3, (d, *J* = 126 Hz), 34.4, (d, *J* = 7.8 Hz), 33.2, (d, *J* = 7.1 Hz), 32.1, 16.2 (d, *J* = 6.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 29.2 (1P).

HRMS (m/z) calculated for $C_{26}H_{35}NO_5P^+$ ($[M+H]^+$): 472.2247; found: 472.2245.

Ethyl benzyl(4-(2-((2,4-dimethylphenyl)thio)phenyl)piperazin-1-yl)phosphinate (S55)



S55

White solid, yield: 51%.

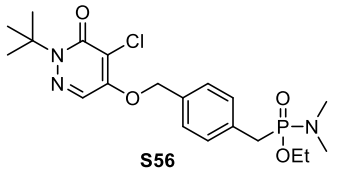
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29−7.39 (m, 6H), 7.18 (d, *J* = 7.2 Hz, 1H), 7.04−7.128 (m, 2H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.87−6.92 (m, 1H), 6.54 (t, *J* = 7.2 Hz, 1H), 3.99−4.21 (m, 2H), 3.11−3.26 (m, 6H), 2.88−2.93 (m, 4H), 2.36 (dd, J_1 = 24.4 Hz, J_2 = 7.6 Hz, 6H), 1.34−1.39 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 142.3, 139.2, 136.1, 134.6, 131.3 (d, *J* = 8.1 Hz), 131.6, 129.9 (d, *J* = 6.0 Hz), 128.5, 127.8, 126.7, 126.2, 125.4, 124.5, 119.9, 59.8 (d, *J* = 6.6 Hz), 53.4, 52.1, 44.5, 34.3 (d, *J* = 125.8 Hz), 20.8 (d, *J* = 61.1 Hz), 16.3 (d, *J* = 6.3 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 29.9 (1P).

HRMS (m/z) calculated for $C_{27}H_{34}N_2O_2PS^+$ ($[M+H]^+$): 481.2073; found: 481.2073.

Ethyl *P*-(4-(((1-(tert-butyl)-5-chloro-6-oxo-1,6-dihydropyridazin-4-yl)oxy)methyl)benzyl)-*N*,*N*-dimethylphosphonamidate (S56)



S56

White solid, yield: 49%.

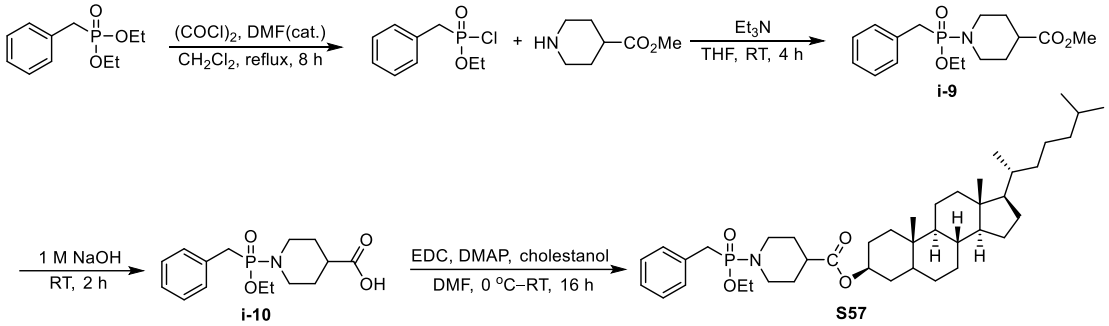
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (s, 1H), 7.31−7.36 (m, 4H), 5.29 (s, 2H), 3.84−4.03 (m, 2H), 3.08−3.17 (m, 2H), 2.55 (d, *J* = 8.8 Hz, 6H), 1.62 (s, 9H), 1.28, (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 159.0, 153.6, 133.3 (d, *J* = 8.1 Hz), 133.2 (d, *J* = 3.7 Hz), 130.3 (d, *J* = 6.1 Hz), 127.3 (d, *J* = 2.8 Hz), 125.1, 118.3, 71.6, 66.4, 59.7 (d, *J* = 7.0 Hz), 36.4 (d, *J* = 3.9 Hz), 33.4 (d, *J* = 124.9 Hz), 27.8, 16.2 (d, *J* = 6.6 Hz).

^{31}P NMR (162 MHz, $DMSO_{d6}$): δ 30.8 (1P).

HRMS (m/z) calculated for $C_{20}H_{30}ClN_3O_4P^+$ ($[M+H]^+$): 442.1657; found: 442.1655.

Procedure N for the formation of S57

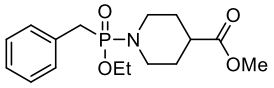


The synthetic methods for preparing **i-9** in **steps 1** and **2** are consistent with the aforementioned "General **procedure B** for the formation of **S2**.

Step 3: Compound **i-9** (1.0 eq.), which is 1-(benzyloxycarbonyl) piperidine-4-carboxylic acid methyl ester, was dissolved in a 1 M NaOH aqueous solution (3.0 eq.) and stirred at RT for 2 h. The progress of the reaction was monitored using TLC until the reaction mixture became clear. Upon completion of the reaction, the mixture was subjected to a single extraction with dichloromethane, and the resulting aqueous phase was acidified using 1 M HCl. Then, CH_2Cl_2 was added for three extractions, and the organic layer was collected, dried, and concentrated to obtain the carboxylated compound **i-10** through hydrolysis.

Step 4: Compound **i-10** (1.0 eq.) carboxylate was dissolved in DMF, and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI 1.5 eq.) and DMAP (2.0 eq.) were added at 0 ℃. Then, the hydroxyl-containing compound cholestane was slowly added to the reaction mixture dissolved in DMF. After the addition was complete, the reaction was allowed to proceed at room temperature for 16 h, and the progress of the reaction was monitored by TLC. Upon completion of the reaction, the organic solvent was removed under reduced pressure, and the residue was purified using silica gel column chromatography with a mixture of petroleum ether and ethyl acetate (1:1−2:3) as the eluent to remove the solvent and obtain the purified compound **S57**.

Methyl 1-(benzyl(ethoxy)phosphoryl)piperidine-4-carboxylate (i-9)



i-9

White solid, yield: 86%.

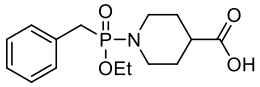
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (t, *J* = 7.2 Hz, 3H), 1.39−1.54 (m, 2H), 1.78 (t, *J* = 11.6 Hz, 2H), 2.31−2.65 (m, 3H), 3.03−3.23 (m, 2H), 3.37−3.47 (m, 2H), 3.67 (s, 3H), 4.05−4.11 (m, 2H), 7.24−7.30 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.8, 132.2 (d, *J* = 7.9 Hz), 129.7 (d, *J* = 6.4 Hz), 128.3 (d, *J* = 2.4 Hz), 126.6 (d, *J* = 3.2 Hz), 59.7 (d, *J* = 6.9 Hz), 51.6, 43.5, 40.9, 34.2 (d, *J* = 125.6 Hz), 28.4 (dd, *J* = 8.3 Hz, 3.9 Hz), 16.2 (d, *J* = 6.5 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 29.1 (1P).

HRMS (m/z) calculated for $C_{16}H_{25}NO_4P^+$ ($[M+H]^+$): 326.1516; found: 326.1511.

1-(Benzyl(ethoxy)phosphoryl)piperidine-4-carboxylic acid (i-10)



i-10

White solid, yield: 82%.

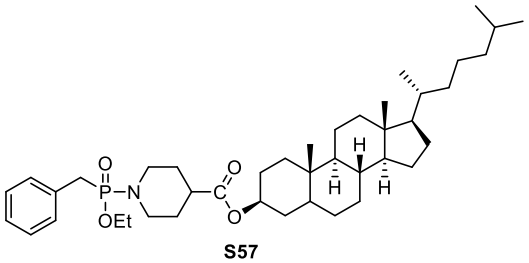
^{1}H NMR (400 MHz, MeOD): δ 7.22−7.27 (m, 5H), 6.04 (s, 1H), 3.88−4.11 (m, 2H), 3.34−3.45 (m, 2H), 3.04−3.23 (m, 2H), 2.29−2.64 (m, 3H), 1.79 (t, *J* = 11.2 Hz, 2H), 1.40−1.52 (m, 2H), 1.28 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, MeOD): δ 177.8, 131.9 (d, *J* = 8.1 Hz), 129.8 (d, *J* = 6.4 Hz), 128.4 (d, *J* = 2.6 Hz), 126.7 (d, *J* = 3.2 Hz), 60.2 (d, *J* = 7.0 Hz), 43.6, 40.8, 34.3 (d, *J* = 125.9 Hz), 28.3 (dd, *J* = 10.4 Hz, 3.7 Hz), 16.2 (d, *J* = 6.5 Hz).

^{31}P NMR (162 MHz, MeOD): δ 29.7 (1P).

HRMS (m/z) calculated for $C_{15}H_{23}NO_4P^+$ ($[M+H]^+$): 312.1359; found: 312.1361.

(3*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-Dimethyl-17-((*R*)-6-methylheptan-2-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl 1-(benzyl(ethoxy)phosphoryl)piperidine-4-carboxylate (S57)



S57

White solid, yield: 40%.

^{1}H NMR (400 MHz, $DMSO_{d6}$): δ 7.27−7.29 (m, 4H), 7.22−7.23 (m, 1H), 4.04−4.09

(m, 1H), 3.34−3.50 (m, 2H), 3.01−3.21 (m, 1H), 2.24−2.64 (m, 2H), 1.91−2.04 (m, 2H), 1.61−1.83 (m, 8H), 1.46−1.53 (m, 6H), 1.21−1.42 (m, 15H), 0.97−1.04 (m, 11H), 0.90 (d, J = 6.4 Hz, 3H), 0.86 (d, J = 6.4 Hz, 6H), 0.81 (s, 3H), 0.64 (s, 3H).

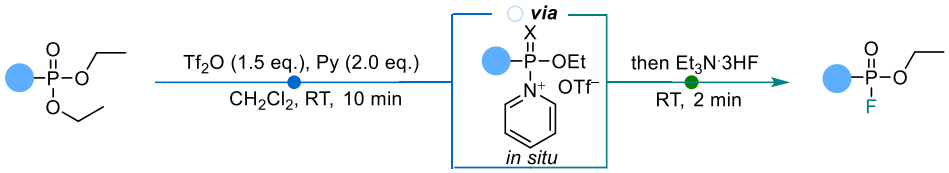
^{13}C NMR (100 MHz, DMSO$_{d6}$): δ 174.1, 132.3 (d, J = 7.8 Hz), 129.8 (d, J = 6.3 Hz), 128.4 (d, J = 2.7 Hz), 126.7 (d, J = 3.3 Hz), 73.7, 59.7 (d, J = 6.9 Hz), 56.3 (d, J = 13.6 Hz), 54.2, 48.9, 44.6, 43.6, 42.6, 41.3, 39.9, 39.5, 36.7, 36.1, 35.8, 35.4 (d, J = 2.1 Hz), 34.3 (d, J = 125.3 Hz), 33.9, 31.9, 28.6, 28.5, 28.4 (d, J = 3.5 Hz), 28.2, 27.9, 27.4, 25.6, 24.9, 24.2, 23.8, 22.6 (d, J = 25.1 Hz), 21.2, 18.6, 16.3 (d, J = 6.6 Hz), 12.1 (d, J = 16.1 Hz).

^{31}P NMR (162 MHz, DMSO$_{d6}$): δ 29.0 (1P).

HRMS (m/z) calculated for $C_{42}H_{69}NO_4P^+$ ($[M+H]^+$): 682.4959; found: 682.4953.

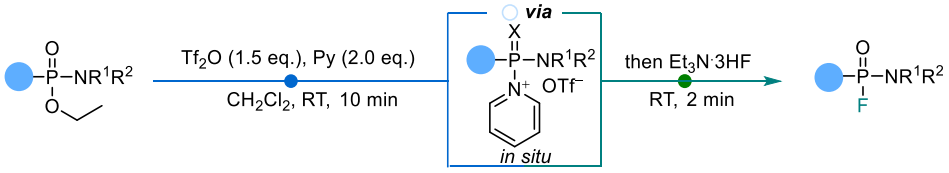
2.2.2 Representative procedure for the fluorination of alkyl phosphonates

General procedure for the synthesis of ethyl phosphorofluoridate



The diethyl phosphonate compound (0.2 mmol) was dissolved in 1 mL of CH_2Cl_2 at RT, and then Tf_2O (0.3 mmol, 50.5 μL, 1.5 eq.) was added to the reaction mixture for 5 min, followed by Py (0.4 mmol, 32 μL, 2.0 eq.) for an additional 5 min. Following this, the fluorinating reagent $Et_3N{\cdot}3HF$ (0.5 eq.) was introduced into the system. The progress of the reaction was monitored using TLC or ^{31}P NMR, and after 2 min, the reaction was completed. The reaction mixture, with a volume of approximately 1 mL, underwent direct purification through silica gel column chromatography to afford the desired products **4**–**30**.

General procedure for the synthesis of fluorophosphoramidate



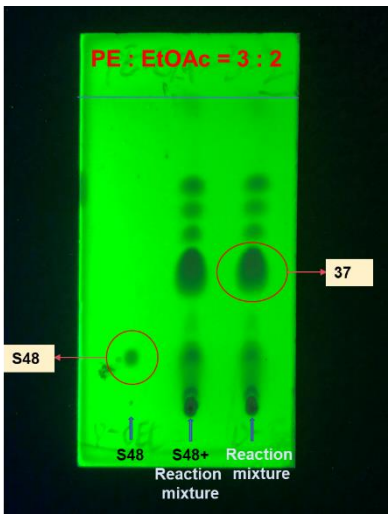
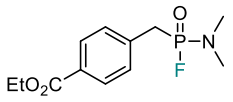


Fig. S3: Thin Layer Chromatography (TLC) analysis of the synthesis of fluorophosphoramidate (**37**) from phosphonamide ethyl ester (**S43**).

The phosphonic acid monoethyl ester compound (0.2 mmol) was dissolved in 1 mL of CH_2Cl_2 at RT. Subsequently, Tf_2O (0.3 mmol, 50.5 μL, 1.5 eq.) was added dropwise,

and the reaction proceeded for 5 min. Following this, Py (0.4 mmol, 32 μL, 2.0 eq.) was slowly introduced to the reaction mixture, and the reaction was allowed to continue for an additional 5 min. Then, the fluorinating reagent $Et_3N{\cdot}3HF$ (0.5 eq.) was incorporated into the system. The progress of the reaction was monitored using TLC or ^{31}P NMR, and after 2 min, the reaction reached completion. The reaction mixture, with an approximate volume of 1 mL, underwent direct purification through silica gel column chromatography to eliminate the solvent and obtain the purified compounds **1**, **31**−**46**.

Ethyl 4-(((dimethylamino)fluorophosphoryl)methyl)benzoate (1)



1

White solid, yield: 92%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 2.0 Hz, 2H), 7.32 (d, *J* = 2.4 Hz, 2H), 4.31−4.36 (m, 2H), 3.23−3.38 (m, 2H), 2.60 (dd, *J* = 2.4 Hz, 10.0 Hz), 1.35 (t, *J* = 7.2 Hz, 3H).

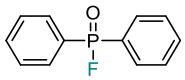
^{13}C NMR (100 MHz, $CDCl_3$): δ 166.1, 135.7 (dd, *J* = 2.4 Hz, 8.6 Hz), 129.9 (d, *J* = 2.9 Hz), 129.5, 129.4, 60.9, 35.8, 32.7 (dd, *J* = 32.9 Hz, 129.0 Hz), 14.2.

^{31}P NMR (162 MHz, $CDCl_3$): δ 32.64 (d, *J* = 1050.9 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -66.37 (d, *J* = 1049.8 Hz, 1F).

HRMS (m/z) calculated for $C_{12}H_{18}NFO_3P^+$ ($[M+H]^+$): 274.1003, found 274.1007.

Diphenylphosphinic fluoride (2)



2

Colorless oil, yield: 68%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26−7.58 (m, 6H), 7.78−7.83 (m, 4H).

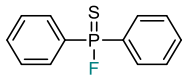
^{13}C NMR (100 MHz, $CDCl_3$): δ 133.2 (d, *J* = 7 Hz), 131.3 (d, *J* = 11.2 Hz), 128.7 (d, *J* = 14 Hz), 128.6 (dd, *J* = 140.4 Hz, 22.1 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 40.8 (d, *J* = 1020 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -75.1 (d, *J* = 1020 Hz, 1F).

HRMS (m/z) calculated for $C_{12}H_{10}FNaOP^+$ ($[M+Na]^+$): 243.0346; found: 243.0340.

Diphenylphosphinothioic fluoride (3)



3

Colorless oil, yield: 83%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84−7.89 (m, 4H), 7.56−7.59 (m, 2H), 7.47−7.52 (m, 4H).

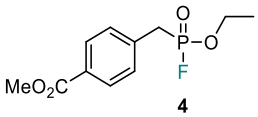
^{13}C NMR (100 MHz, $CDCl_3$): δ 132.8 (d, *J* = 2.6 Hz), 131.0 (d, *J* = 12.3 Hz), 128.7 (d, *J* = 14.1 Hz), 53.4.

^{31}P NMR (162 MHz, $CDCl_3$): δ 102.2 (d, *J* = 1022 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -82.6 (d, *J* = 1022 Hz, 1F).

HRMS (m/z) calculated for $C_{12}H_{10}FNaPS^+$ ($[M+Na]^+$): 259.0117; found: 259.0113.

Methyl 4-((ethoxyfluorophosphoryl)methyl)benzoate (4)



4

Colorless oil, yield: 42%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 6.8 Hz, 2H), 4.17−4.24 (m, 2H), 3.92 (s, 3H), 3.36 (d, *J* = 23.2 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H).

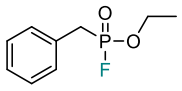
^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 134.7 (d, *J* = 10.6 Hz), 130.1 (d, *J* = 2.7 Hz), 129.8, 129.7, 64.2 (d, *J* = 7.4 Hz), 52.1 (d, *J* = 20.5 Hz), 32.4 (dd, *J* = 141.7 Hz, 25 Hz), 16.2 (d, *J* = 5.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 23.7 (d, *J* = 1078 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -65.4 (d, *J* = 1077 Hz, 1F).

HRMS (m/z) calculated for $C_{11}H_{15}FO_4P^+$ ($[M+H]^+$): 261.0687; found: 261.0683.

Ethyl benzylphosphonofluoridate (5)



5

Colorless oil, yield: 73%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.28 (t, *J* =7.2 Hz, 3H), 3.30 (d, *J* = 22.4 Hz, 2H), 4.15−4.23 (m, 2H), 7.29−7.36 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 129.7 (d, *J* = 7 Hz), 129.4 (d, *J* = 9.8 Hz), 128.8 (d, *J*

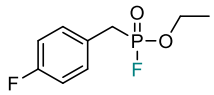
= 2.9 Hz), 127.5 (d, *J* = 3.6 Hz), 63.9 (d, *J* = 7.3 Hz), 32.2 (d, *J* = 141.7 Hz, 24.6 Hz), 16.2 (d, *J* = 5.5 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 25.1 (d, *J* = 1077 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -64.3 (d, *J* = 1076 Hz, 1F).

HRMS (m/z) calculated for $C_9H_{13}FO_2P^+$ ($[M+H]^+$): 203.0632; found: 203.0638.

Ethyl (4-fluorobenzyl)phosphonofluoridate (6)



6

Colorless oil, yield: 91%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (t, *J* =7.2 Hz, 3H), 3.28 (d, *J* = 22.4 Hz, 2H), 4.17−4.24 (m, 2H), 7.03 (t, *J* =8.4 Hz, 2H), 7.26−7.27 (m, 2H).

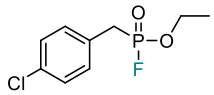
^{13}C NMR (100 MHz, $CDCl_3$): δ 162.3 (dd, *J* = 245 Hz, 4 Hz), 131.2 (t, *J* = 7.7 Hz), 125.1 (d, *J* = 35.1 Hz), 115.8 (dd, *J* = 21.6 Hz, 2.9 Hz), 63.9 (d, *J* = 7.3 Hz), 31.3 (dd, *J* = 142.7 Hz, 24.8 Hz), 16.2 (d, *J* = 5.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ -64.5 (d, *J* = 1078 Hz, 1F), -114.7 (d, *J* = 5.3 Hz, 1F).

^{31}P NMR (162 MHz, $CDCl_3$): δ 24.5 (d, *J* = 1078 Hz, 1P).

HRMS (m/z) calculated for $C_9H_{12}F_2O_2P^+$ ($[M+H]^+$): 221.0537; found: 221.0535.

Ethyl (4-chlorobenzyl)phosphonofluoridate (7)



7

Colorless oil, yield: 77%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (t, *J* =6.8 Hz, 3H), 3.26 (d, *J* = 22.8 Hz, 2H), 4.16−4.24 (m, 2H), 7.21−7.24 (m, 2H), 7.31 (d, *J* = 8.4 Hz, 2H).

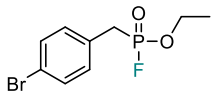
^{13}C NMR (100 MHz, $CDCl_3$): δ 16.2 (d, *J* = 5.3 Hz), 31.6 (dd, *J* = 142.5 Hz, 24.9 Hz), 64.1 (d, *J* = 7.4 Hz), 127.9 (d, *J* = 9.9 Hz), 129.0 (d, *J* = 3 Hz), 130.9 (d, *J* = 7.1 Hz), 133.6 (d, *J* = 4.5 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 24.2 (d, *J* = 1078 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -64.1 (d, *J* = 1077 Hz, 1F).

HRMS (m/z) calculated for $C_9H_{12}ClFO_2P^+$ ($[M+H]^+$): 237.0242; found: 237.0245.

Ethyl (4-bromobenzyl)phosphonofluoridate (8)



8

Colorless oil, yield: 87%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (t, *J* =7.2 Hz, 3H), 3.25 (d, *J* = 22.8 Hz, 2H), 4.16−4.24 (m, 2H), 7.16−7.18 (m, 2H), 7.46 (d, *J* = 8.4 Hz, 2H).

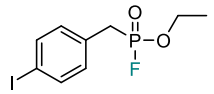
^{13}C NMR (100 MHz, $CDCl_3$): δ 132.0 (d, *J* = 2.8 Hz), 131.3 (d, *J* = 7.1 Hz), 128.5 (d, *J* = 9.8 Hz), 121.7 (d, *J* = 4.8 Hz), 64.1 (d, *J* = 7.3 Hz), 31.6 (dd, *J* = 142.3 Hz, 24.8 Hz), 16.2 (d, *J* = 5.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ -64.1 (d, *J* = 1077 Hz, 1F).

^{31}P NMR (162 MHz, $CDCl_3$): δ 24.2 (d, *J* = 1078 Hz, 1P).

HRMS (m/z) calculated for $C_9H_{12}BrFO_2P^+$ ($[M+H]^+$): 280.9737; found: 280.9731.

Ethyl (4-iodobenzyl)phosphonofluoridate (9)



9

Colorless oil, yield: 76%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (t, *J* =6.8 Hz, 3H), 3.23 (d, *J* = 21.6 Hz, 2H), 4.16−4.24 (m, 2H), 7.04 (d, *J* = 8 Hz, 2H), 7.66 (d, *J* = 7.2 Hz, 2H).

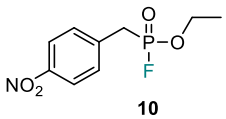
^{13}C NMR (100 MHz, $CDCl_3$): δ 137.9 (d, *J* = 2.7 Hz), 131.5 (d, *J* = 6.9 Hz), 129.2 (d, *J* = 9.5 Hz), 93.1 (d, *J* = 5 Hz), 64.0 (d, *J* = 7.4 Hz), 31.8 (dd, *J* = 142.2 Hz, 24.7 Hz), 16.2 (d, *J* = 5.3 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 23.9 (d, *J* = 1078 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -63.9 (d, *J* = 1078 Hz, 1F).

HRMS (m/z) calculated for $C_9H_{12}FIO_2P^+$ ($[M+H]^+$): 328.9598; found: 328.9593.

Ethyl (4-nitrobenzyl)phosphonofluoridate (10)



10

Colorless oil, yield: 55%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.31 (t, *J* = 6.8 Hz, 3H), 3.41 (d, *J* = 23.6 Hz, 2H), 4.19−4.27 (m, 2H), 7.48 (dd, *J* = 8.8 Hz, 2.4 Hz, 2H), 8.20 (d, *J* = 8.4 Hz, 2H).

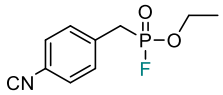
^{13}C NMR (100 MHz, $CDCl_3$): δ 16.2 (d, *J* = 5.4 Hz), 32.2 (dd, *J* = 141.7 Hz, 25.4 Hz), 64.4 (d, *J* = 7.3 Hz), 123.9 (d, *J* = 2.7 Hz), 130.6 (d, *J* = 6.8 Hz), 137.2 (d, *J* = 9.7 Hz), 147.4 (d, *J* = 3.9 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 22.5 (d, *J* = 1078 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -62.9 (d, *J* = 1077 Hz, 1F).

HRMS (m/z) calculated for $C_9H_{12}FNO_4P^+$ ($[M+H]^+$): 248.0482; found: 248.0486.

Ethyl (4-cyanobenzyl)phosphonofluoridate (11)



11

Colorless oil, yield: 74%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (t, *J* = 7.2 Hz, 3H), 3.36 (d, *J* = 23.6 Hz, 2H), 4.19−4.27 (m, 2H), 7.42 (d, *J* = 7.6 Hz, 2H), 7.64 (d, *J* = 7.6 Hz, 2H).

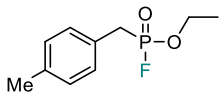
^{13}C NMR (100 MHz, $CDCl_3$): δ 16.2 (d, *J* = 5.4 Hz), 32.5 (dd, *J* = 142 Hz, 25.3 Hz), 64.3 (d, *J* = 7.2 Hz), 111.7 (d, *J* = 3.9 Hz), 118.3, 130.5 (d, *J* = 7 Hz), 132.6 (d, *J* = 2.9 Hz), 135.1 (d, *J* = 9.6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 22.8 (d, *J* = 1078 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -65.0 (d, *J* = 1078 Hz, 1F).

HRMS (m/z) calculated for $C_{10}H_{12}FNO_2P^+$ ($[M+H]^+$): 228.0584; found: 228.0587.

Ethyl (4-methylbenzyl)phosphonofluoridate (12)



12

Colorless oil, yield: 89%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (t, *J* =7.2 Hz, 3H), 2.33 (s, 3H), 3.26 (d, *J* = 22.4 Hz, 2H), 4.15−4.22 (m, 2H), 7.13−7.19 (m, 4H).

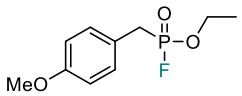
^{13}C NMR (100 MHz, $CDCl_3$): δ 137.2 (d, *J* = 3.9 Hz), 129.5, 129.4, 126.2 (d, *J* = 9.9 Hz), 63.8 (d, *J* = 7.3 Hz), 31.7 (dd, *J* = 141.7 Hz, 24.3 Hz), 21.0, 16.2 (d, *J* = 5.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 25.4 (d, *J* = 1078 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -64.7 (d, *J* = 1076 Hz, 1F).

HRMS (m/z) calculated for $C_{10}H_{15}FO_2P^+$ ($[M+H]^+$): 217.0788; found: 217.0782.

Ethyl (4-methoxybenzyl)phosphonofluoridate (13)



13

Colorless oil, yield: 43%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24−7.31 (m, 2H), 6.89−6.92 (m, 2H), 4.20−4.22 (m, 2H), 3.80 (s, 3H), 3.23−3.30 (m, 2H), 1.30−1.34 (m, 3H).

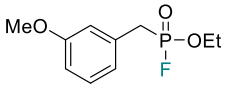
^{13}C NMR (100 MHz, $CDCl_3$): δ 159.0, 130.7, 121.1, 114.3, 63.8, 55.2, 31.2 (dd, J = 143.1 Hz, 25.1 Hz), 16.2.

^{31}P NMR (162 MHz, $CDCl_3$): δ 25.4 (d, J = 1078 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -65.0 (d, J = 1078 Hz, 1F).

HRMS (m/z) calculated for $C_{10}H_{15}FO_3P^+$ ($[M+H]^+$): 233.0737; found: 233.0733.

Ethyl (3-methoxybenzyl)phosphonofluoridate (14)



14

Colorless oil, yield: 76%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22–7.26 (m, 1H), 6.86–6.89 (m, 1H), 6.81–6.84 (m, 2H), 4.15–4.23 (m, 2H), 3.8 (s, 3H), 3.23–3.30 (m, 2H), 1.3 (t, J = 7.1 Hz, 3H).

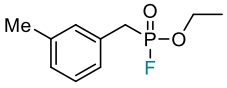
^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8 (d, J = 3.2 Hz), 130.7 (d, J = 9.8 Hz), 129.8 (d, J = 3.4 Hz), 122.0 (d, J = 7.2 Hz), 115.3 (d, J = 7.1 Hz), 113.0 (d, J = 3.8 Hz), 63.9 (d, J = 7.4 Hz), 55.2, 32.2 (dd, J = 142.4, 24.4 Hz), 16.2 (d, J = 5.6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 24.9 (d, J = 1076.6 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -64.2 (d, J = 1076.1 Hz, 1F).

HRMS (m/z) calculated for $C_{10}H_{15}FO_3P^+$ ($[M+H]^+$): 233.0737; found: 233.0728.

Ethyl (3-methylbenzyl)phosphonofluoridate (15)



15

Colorless oil, yield: 74%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20−7.26 (m, 1H), 7.11 (s, 3H), 4.15−4.23 (m, 2H), 3.26 (dd, J = 22.4 Hz, 2 Hz, 2H), 2.34 (s, 3H), 1.27−1.29 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 138.5 (d, J = 3 Hz), 130.4 (d, J = 7 Hz), 129.2 (d, J =

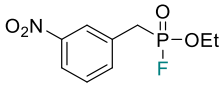
9.8 Hz), 128.5 (dd, *J* = 40.4Hz, 2.7 Hz), 126.7 (d, *J* = 7 Hz), 63.9 (d, *J* = 7.2 Hz), 32.1 (dd, *J* = 141.6 Hz, 24.2 Hz), 21.3, 16.2 (d, *J* = 5.3 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 25.3 (d, *J* = 1077 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -64.3 (d, *J* = 1077 Hz, 1F).

HRMS (m/z) calculated for $C_{10}H_{15}FO_2P^+$ ($[M+H]^+$): 217.0788; found: 217.0781.

Ethyl (3-nitrobenzyl)phosphonofluoridate (16)



16

Colorless oil, yield: 77%.

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.19–8.15 (m, 1H), 7.66–7.67 (m, 1H), 7.54 (t, *J* = 8.0 Hz, 1H), 4.22–4.28 (m, 1H), 3.41 (d, *J* = 23.2 Hz, 1H), 1.32 (t, *J* = 7.1 Hz, 2H).

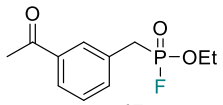
^{13}C NMR (151 MHz, $CDCl_3$): δ 148.5, 135.7 (d, *J* = 6.6 Hz), 131.7 (d, *J* = 9.5 Hz), 129.9 (d, *J* = 3.3 Hz), 124.6 (d, *J* = 7.6 Hz), 122.7 (d, *J* = 3.3 Hz), 64.4 (d, *J* = 7.6 Hz), 31.9 (dd, *J* = 143.7, 25.6 Hz), 16.2 (d, *J* = 5.6 Hz).

^{31}P NMR (243 MHz, $CDCl_3$): δ 22.9 (d, *J* = 1077.1 Hz, 1P).

^{19}F NMR (565 MHz, $CDCl_3$): δ -63.3 (d, *J* = 1078.6 Hz, 1F).

HRMS (m/z) calculated for $C_9H_{12}FNO_4P^+$ ($[M+H]^+$): 248.0482; found: 248.0487.

Ethyl (3-acetylbenzyl)phosphonofluoridate (17)



17

Colorless oil, yield: 47%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.9 (s, 2H), 7.5 (d, *J* = 8.0 Hz, 1H), 7.4 (t, *J* = 7.8 Hz, 1H), 4.17–4.25 (m, 2H), 3.4 (d, *J* = 22.9 Hz, 2H), 2.6 (s, 3H), 1.3 (t, *J* = 7.6 Hz, 3H).

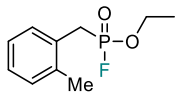
^{13}C NMR (100 MHz, $CDCl_3$): δ 191.1, 133.0 (d, *J* = 7.8 Hz), 130.7 (d, *J* = 10.7 Hz), 129.4 (d, *J* = 3.9 Hz), 128.4 (d, *J* = 8.2 Hz), 126.4 (d, *J* = 4.5 Hz), 124.9, 64.2 (d, *J* = 8.3 Hz), 32.1 (dd, *J* = 143.1, 25.7 Hz), 29.6, 16.2 (d, *J* = 6.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 23.8 (d, *J* = 1077.3 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -63.8 (d, *J* = 1077.3 Hz, 1F).

HRMS (m/z) calculated for $C_{11}H_{15}FO_3P^+$ ($[M+H]^+$): 245.0737; found: 245.0731.

Ethyl (2-methylbenzyl)phosphonofluoridate (18)



18

Colorless oil, yield: 66%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21 (t, *J* =6.8 Hz, 3H), 2.31 (s, 3H), 3.23 (d, *J* = 22.8 Hz, 2H), 4.07−4.15 (m, 2H), 7.11−7.12 (m, 3H), 7.16−7.19 (m, 2H).

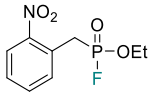
^{13}C NMR (100 MHz, $CDCl_3$): δ 16.2 (d, *J* = 5.5 Hz), 19.8, 29.5 (dd, *J* = 141.4 Hz, 24.2 Hz), 63.8 (d, *J* = 7.4 Hz), 126.3 (d, *J* = 3.4 Hz), 127.7 (d, *J* = 3.9 Hz), 130.5 (d, *J* = 5.9 Hz), 130.7 (d, *J* = 3.2 Hz), 137.0 (d, *J* = 2.7 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 25.3 (d, *J* = 1079 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -63.5 (d, *J* = 1079 Hz, 1F).

HRMS (m/z) calculated for $C_{10}H_{15}FO_2P^+$ ($[M+H]^+$): 217.0788; found: 217.0791.

Ethyl (2-nitrobenzyl)phosphonofluoridate (19)



19

Colorless oil, yield: 32%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, *J* = 8.4 Hz, 1H), 7.58−7.62 (m, 1H), 7.47−7.50 (m, 2H), 4.18−4.25 (m, 2H), 3.77−3.97 (m, 2H), 1.29 (t, *J* = 7.2 Hz, 3H).

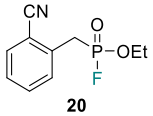
^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 133.5 (d, *J* = 4.2 Hz), 133.1 (d, *J* = 7.3 Hz), 128.8 (d, *J* = 4.5 Hz), 125.6 (d, *J* = 3.9 Hz), 125.3 (d, *J* = 11.0 Hz), 64.4 (d, *J* = 8.1 Hz), 29.4 (dd, *J* = 143.5, 26.2 Hz), 16.1 (d, *J* = 6.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 22.3 (d, *J* = 1079.1, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -62.7 (d, *J* = 1077.7 Hz, 1F).

HRMS (m/z) calculated for $C_9H_{12}FNO_4P^+$ ($[M+H]^+$): 248.0482; found: 248.0485.

Ethyl (2-cyanobenzyl)phosphonofluoridate (20)



20

Colorless oil, yield: 43%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66−7.68 (m, 1H), 7.52−7.61 (m, 2H), 7.39−7.42 (m, 1H), 4.24−4.28 (m, 2H), 3.56 (d, *J* = 23.6 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 3H).

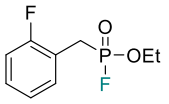
^{13}C NMR (100 MHz, $CDCl_3$): δ 133.6 (d, *J* = 10.2 Hz), 133.1 (d, *J* = 6.1 Hz), 133.0 (d, *J* = 6.5 Hz), 130.9 (d, *J* = 6.5 Hz), 128.2 (d, *J* = 4.5 Hz), 117.2 (d, *J* = 3.1 Hz), 113.5 (d, *J* = 8.6 Hz), 64.5 (d, *J* = 8.0 Hz), 30.8 (dd, *J* = 143.7, 26.6 Hz), 16.1 (d, *J* = 6.5 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 21.8 (d, *J* = 1078.5 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -62.9 (d, *J* = 1078.1 Hz, 1F).

HRMS (m/z) calculated for $C_{10}H_{12}FNO_2P^+$ ($[M+H]^+$): 228.0584; found: 228.0567.

Ethyl (2-fluorobenzyl)phosphonofluoridate (21)



21

Colorless oil, yield: 81%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27−7.38 (m, 1H), 7.27−7.31 (m, 1H), 7.06−7.15 (m, 2H), 4.19−4.26 (m, 2H), 3.36 (dd, *J* = 22.8, 3.2 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 3H).

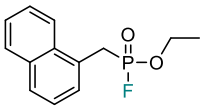
^{13}C NMR (100 MHz, $CDCl_3$): δ 160.8 (dd, *J* = 247.4, 7.8 Hz), 131.6 (dd, *J* = 5.9, 3.2 Hz), 129.5 (dd, *J* = 8.0, 3.9 Hz), 124.4 (t, *J* = 3.7 Hz), 117.0 (dd, *J* = 15.5, 10.1 Hz), 115.7 (dd, *J* = 21.8, 3.2 Hz), 64.1 (d, J = 7.2 Hz), 25.1 (ddd, *J* = 145.6, 26.5, 3.5 Hz), 16.2 (d, *J* = 5.6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 23.7 (d, *J* = 1077.9, 5.18 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -64.0 (d, *J* = 1076.1 Hz, 1F), -116.8 (s, 1F).

HRMS (m/z) calculated for $C_9H_{12}F_2O_2P^+$ ($[M+H]^+$): 221.0537; found: 221.0531.

Ethyl (naphthalen-1-ylmethyl)phosphonofluoridate (22)



22

Colorless oil, yield: 70%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.19 (t, *J* = 7.2 Hz, 3H), 3.78 (dd, *J* = 23.2 Hz, 2.4 Hz, 2H), 4.09−4.16 (m, 2H), 7.43−7.53 (m, 3H), 7.57 (t, *J* = 7.2 Hz, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.87 (d, *J* = 8 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H).

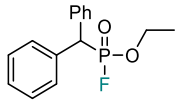
^{13}C NMR (100 MHz, $CDCl_3$): δ 133.9 (d, *J* = 2.8 Hz), 131.7 (d, *J* = 5.5 Hz), 128.8, 128.6 (d, *J* = 8.1 Hz), 128.5 (d, *J* = 4.4 Hz), 126.5, 125.9, 125.8 (d, *J* = 10.8 Hz), 125.3 (d, *J* = 4.2 Hz), 123.8, 64.0 (d, *J* = 7.3 Hz), 29.2 (dd, *J* = 142.6 Hz, 24.9 Hz), 16.1(d, *J* = 4.3 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 24.8 (d, *J* = 1081 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -62.9 (d, *J* = 1080 Hz, 1F).

HRMS (m/z) calculated for $C_{13}H_{15}FO_2P^+$ ($[M+H]^+$): 253.0788; found: 253.0781.

Ethyl benzhydrylphosphonofluoridate (23)



23

Colorless oil, yield: 42%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.19 (t, *J* = 6.8 Hz, 3H), 4.06−4.21 (m, 2H), 4.60 (d, *J* = 27.2 Hz, 2H), 7.30 (d, *J* = 6.4 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 4H), 7.50 (d, *J* = 7.2 Hz, 4H).

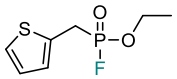
^{13}C NMR (100 MHz, $CDCl_3$): δ 16.0 (d, *J* = 4.3 Hz), 49.9 (dd, *J* = 141.3 Hz, 22.9 Hz), 64.6 (d, *J* = 6.9 Hz), 127.7, 128.9, 129.2 (dd, *J* = 18 Hz, 8.5 Hz), 134.9 (d, *J* = 3.7 Hz.

^{31}P NMR (162 MHz, $CDCl_3$): δ 23.4 (d, *J* = 1094 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -64.2 (d, *J* = 1094 Hz, 1F).

HRMS (m/z) calculated for $C_{15}H_{17}FO_2P^+$ ($[M+H]^+$): 279.0945; found: 279.0947.

Ethyl (thiophen-2-ylmethyl)phosphonofluoridate (24)



24

Colorless oil, yield: 51%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15−7.19 (m, 1H), 6.90−6.95 (m, 2H), 4.14−4.22 (m, 2H), 3.45 (dd, *J* = 21.2 Hz, 6.4 Hz, 2H), 1.24 (t, *J* = 7.2 Hz, 3H).

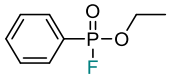
^{13}C NMR (100 MHz, $CDCl_3$): δ 129.6 (d, *J* = 11.3 Hz), 127.9 (d, *J* = 8.8 Hz), 127.3, 125.5, 64.3 (d, *J* = 7.1 Hz), 26.6 (dd, *J* = 148 Hz, 27.5 Hz), 16.2 (d, *J* = 4.3 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 22.6 (d, *J* = 1080 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -64.8 (d, *J* = 1080 Hz, 1F).

HRMS (m/z) calculated for $C_7H_{11}FO_2PS^+$ ($[M+H]^+$): 209.0196; found: 209.0197.

Ethyl phenylphosphonofluoridate (25)



25

Colorless oil, yield: 59%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (t, *J* = 7.2 Hz, 3H), 4.30−4.38 (m, 2H), 7.52 (dd, *J* = 12.4 Hz, 7.2 Hz, 2H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.85 (dd, *J* = 14.4 Hz, 8 Hz, 2H).

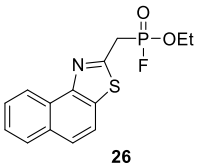
^{13}C NMR (100 MHz, $CDCl_3$): δ 133.6 (d, *J* = 2.7 Hz), 131.7 (d, *J* = 10.8 Hz), 128.7 (d, *J* = 16.3 Hz), 123.8 (d, *J* = 29.9 Hz), 63.9 (d, *J* = 6.1 Hz), 16.3 (d, *J* = 5.7 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 17.1 (d, *J* = 1043 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -63.9 (d, *J* = 1042 Hz, 1F).

HRMS (m/z) calculated for $C_8H_{11}FO_2P^+$ ($[M+H]^+$): 189.0475; found: 189.0471.

Ethyl (naphtho[1,2-*d*]thiazol-2-ylmethyl)phosphonofluoridate (26)



26

Colorless oil, yield: 45%.

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.78 (d, *J* = 8.2 Hz, 1H), 7.95 (d, *J* = 8.1 Hz, 1H), 7.87 (d, *J* = 8.8 Hz, 1H), 7.83 (d, *J* = 8.8 Hz, 1H), 7.68 (t, *J* = 7.2 Hz, 1H), 7.59 (t, *J* = 7.2 Hz, 1H), 4.33–4.40 (m, 2H), 4.00 (dd, *J* = 22.9, 2.3 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H).

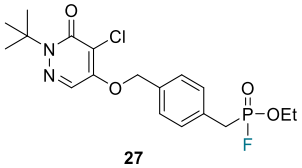
^{13}C NMR (151 MHz, $CDCl_3$): δ 156.9 (dd, *J* = 9.7, 1.9 Hz), 149.3 (d, *J* = 1.9 Hz), 132.6 (d, *J* = 1.9 Hz), 132.0, 128.5, 128.1, 127.2, 126.4, 126.3, 123.8, 118.6, 65.0 (d, *J* = 7.4 Hz), 31.6 (dd, *J* = 146.0, 27.7 Hz), 16.3 (d, *J* = 5.9 Hz).

^{31}P NMR (243 MHz, $CDCl_3$): δ 19.5 (d, *J* = 1073.7 Hz, 1P).

^{19}F NMR (565 MHz, $CDCl_3$): δ -61.6 (d, *J* = 1075.0 Hz, 1F).

HRMS (m/z) calculated for $C_{14}H_{14}FNO_2PS^+$ ($[M+H]^+$): 310.0461; found: 310.0455.

Ethyl (4-(((1-(tert-butyl)-5-chloro-6-oxo-1,6-dihydropyridazin-4-yl)oxy)methyl) benzyl)phosphonofluoridate (27)



27

Colorless oil, yield: 57%.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.71 (s, 1H), 7.38 (d, *J* = 7.9 Hz, 2H), 7.33–7.35 (m, 2H), 5.29 (s, 2H), 4.17–4.22 (m, 2H), 3.28–3.30 (m, 2H), 1.61 (s, 9H), 1.28 (t, *J* = 7.1 Hz, 3H).

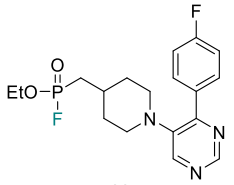
^{13}C NMR (151 MHz, $CDCl_3$): δ 159.0, 153.6, 134.3 (d, *J* = 4.3 Hz), 130.2 (d, *J* = 6.8 Hz), 130.1 (d, *J* = 10.0 Hz), 127.5 (d, *J* = 3.8 Hz), 125.0, 118.3, 71.4, 66.4, 64.0 (d, *J* = 7.6 Hz), 31.9 (dd, *J* = 142.7, 24.4 Hz), 27.8, 16.2 (d, *J* = 5.5 Hz).

^{31}P NMR (243 MHz, $CDCl_3$): δ 24.5 (d, *J* = 1077.4 Hz, 1P).

^{19}F NMR (565 MHz, $CDCl_3$): δ -64.0 (d, *J* = 1077.9 Hz, 1F).

HRMS (m/z) calculated for $C_{18}H_{24}ClFN_2O_4P^+$ ($[M+H]^+$): 417.1141; found: 417.1146.

Ethyl ((1-(4-(4-fluorophenyl)pyrimidin-5-yl)piperidin-4-yl)methyl)phosphonofluoridate (28)



28

Colorless oil, yield: 50%.

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.89 (s, 1H), 8.40 (s, 1H), 8.09–8.11 (m, 2H), 7.15 (t, *J* = 8.7 Hz, 2H), 4.23–4.31 (m, 2H), 3.16–3.21 (m, 2H), 2.67 (t, *J* = 11.4 Hz, 2H), 1.91–1.93 (m, 1H), 1.87–1.90 (m, 3H), 1.67 (s, 3H), 1.38 (t, *J* = 7.0 Hz, 3H).

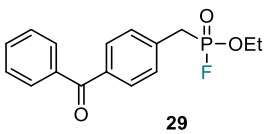
^{13}C NMR (151 MHz, $CDCl_3$): δ 164.4, 162.8, 156.6, 152.7, 147.3, 143.9, 134.0, 130.3 (d, *J* = 7.9 Hz), 115.5 (d, *J* = 22.0 Hz), 63.2 (d, *J* = 7.6 Hz), 50.7, 46.7, 32.9 (d, *J* = 11.5 Hz), 31.1 (dd, *J* = 142.4, 21.3 Hz), 29.7, 16.3 (d, *J* = 5.5 Hz).

^{31}P NMR (243 MHz, $CDCl_3$): δ 29.7 (d, *J* = 1072.0 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -60.3 (d, *J* = 1072.9 Hz, 1F), -110.4 (s, 1F).

HRMS (m/z) calculated for $C_{18}H_{23}F_2N_3O_2P^+$ ($[M+H]^+$): 382.1490; found: 382.1483.

Ethyl (4-benzoylbenzyl)phosphonofluoridate (29)



29

Colorless oil, yield: 78%.

^{1}H NMR (400 MHz, $DMSO_{d6}$): δ 7.78 (d, *J* = 8.0 Hz, 4H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.48 (t, *J* = 7.2 Hz, 2H), 7.42 (d, *J* = 6.8 Hz, 2H), 4.20−4.28 (m, 2H), 3.39 (d, *J* = 23.6 Hz, 2H), 1.32 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $DMSO_{d6}$): δ 196.0, 137.3, 136.8, 134.2 (d, *J* = 9.7 Hz), 132.5, 130.6 (d, *J* = 2.7 Hz), 129.9, 129.6 (d, *J* = 20.0 Hz), 128.3 (d, *J* = 14.5 Hz), 64.2 (d, *J* =

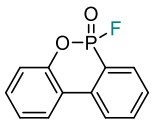
7.5Hz), 32.44 (dd, J_1 = 141.5 Hz, J_2 = 25.0 Hz), 16.2.

^{31}P NMR (162 MHz, DMSO$_{d6}$): δ 23.8 (d, *J* = 1077 Hz, 1P).

^{19}F NMR (376 MHz, CDCl$_3$): δ -63.43 (d, *J* = 1077 Hz, 1F).

HRMS (m/z) calculated for $C_{16}H_{17}FO_3P^+$ ([M+H]$^+$): 307.0894; found: 307.0899.

6-Fluorodibenzo[*c*,*e*][1,2]oxaphosphinine 6-oxide (30)



30

Colorless oil, yield: 67%.

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.29−7.36 (m, 2H), 7.44 (t, *J* = 3.9 Hz, 1H), 7.56−7.61 (m, 1H), 7.82 (t, *J* = 8 Hz, 1H), 7.97−8.12 (m, 3H).

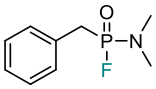
^{13}C NMR (100 MHz, CDCl$_3$): δ 149.3 (d, *J* = 8.3 Hz), 137.5 (d, *J* = 7.9 Hz), 134.9, 131.0 (t, *J* = 4.6 Hz), 128.6 (d, *J* = 16.4 Hz), 125.6, 125.3, 124.3 (d, *J* = 13 Hz), 121.7 (d, *J* = 12.7 Hz), 120.3 (d, *J* = 7.3 Hz), 119.5 (d, *J* = 28.9 Hz), 117.7, (d, *J* = 29 Hz).

^{31}P NMR (162 MHz, CDCl$_3$): δ 7.3 (d, *J* = 1074 Hz, 1P).

^{19}F NMR (376 MHz, CDCl$_3$): δ -55.4 (d, *J* = 1073 Hz, 1F).

HRMS (m/z) calculated for $C_{12}H_9FO_2P^+$ ([M+H]$^+$): 235.0319; found: 235.0325.

***P*-benzyl-*N*,*N*-dimethylphosphonamidic fluoride (31)**



31

Colorless oil, yield: 67%.

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.32−7.37 (m, 5H), 3.24−3.38 (m, 2H), 2.65 (d, *J* = 9.6, 6H).

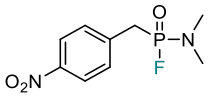
^{13}C NMR (100 MHz, CDCl$_3$): δ 130.4 (dd, *J* = 8.6, 2.2 Hz), 129.4 (d, *J* = 6.6 Hz), 128.7, 127.2, 35.74 (d, *J* = 4.1 Hz), 32.5 (dd, *J* = 32.0, 129.4 Hz).

^{31}P NMR (162 MHz, CDCl$_3$): δ 34.1 (d, *J* = 1049 Hz, 1P).

^{19}F NMR (376 MHz, CDCl$_3$): δ -67.3 (d, *J* = 1049 Hz, 1F).

HRMS (m/z) calculated for $C_9H_{14}FNOP^+$ ([M+H]$^+$): 202.0792; found: 202.0797.

***N*,*N*-Dimethyl-*P*-(4-nitrobenzyl)phosphonamidic fluoride (32)**



32

Yellowish solid, yield: 65%.

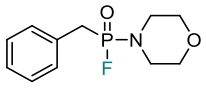
^{1}H NMR (400 MHz, CDCl$_3$): δ 8.18 (d, *J* = 8 Hz, 2H), 7.47 (d, *J* = 7.6 Hz, 2H), 3.29−3.45 (m, 2H), 2.68 (d, *J* = 9.6 Hz, 6H).

^{13}C NMR (100 MHz, CDCl$_3$): δ 147.2 (d, *J* = 3.5 Hz), 138.4 (d, *J* = 8.5 Hz), 130.4 (d, *J* = 6.5 Hz), 123.9 (d, *J* = 2.4 Hz), 35.8 (d, *J* = 3.8 Hz), 32.5 (dd, *J* = 129.2 Hz, 33.7 Hz). **^{31}P NMR (162 MHz, CDCl$_3$)**: δ 31.5 (d, *J* = 1053 Hz, 1P).

^{19}F NMR (376 MHz, CDCl$_3$): δ -68.1 (d, *J* = 1050 Hz, 1F).

HRMS (m/z) calculated for $C_{12}H_9FO_2P^+$ ($[M+H]^+$): 247.0642; found: 247.0644.

Benzyl(morpholino)phosphinic fluoride (33)



33

White solid, yield: 61%.

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.33−7.40 (m, 5H), 3.56−3.60 (m, 4H), 3.25−3.43 (m, 2H), 3.07−3.16 (m, 4H).

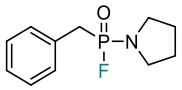
^{13}C NMR (100 MHz, CDCl$_3$): δ 130.1 (d, *J* = 8.6 Hz), 129.6 (d, *J* = 6.8 Hz), 128.9 (d, *J* = 2.7 Hz), 127.5 (d, *J* = 3.5 Hz), 66.9 (d, *J* = 4.1 Hz), 43.9, 38.9 (dd, *J* = 129.9 Hz, 31.3 Hz).

^{31}P NMR (162 MHz, CDCl$_3$): δ 31.0 (d, *J* = 1055 Hz, 1P).

^{19}F NMR (376 MHz, CDCl$_3$): δ -65.5 (d, *J* = 1055 Hz, 1F).

HRMS (m/z) calculated for $C_{12}H_9FO_2P^+$ ($[M+H]^+$): 244.0897; found: 244.0906.

Benzyl(pyrrolidin-1-yl)phosphinic fluoride (34)



34

White solid, yield: 51%.

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.27−7.33 (m, 5H), 3.13−3.39 (m, 6H), 1.74−1.79 (m, 4H).

^{13}C NMR (100 MHz, CDCl$_3$): δ 130.6 (d, *J* = 8.2 Hz), 129.5 (d, *J* = 6.5 Hz), 128.7 (d,

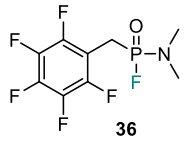
J = 2 Hz), 127.1 (d, *J* = 1 Hz), 46.4 (d, *J* = 4 Hz), 33.1 (dd, *J* = 128.6 Hz, 31.1 Hz), 26.1 (d, *J* = 8.1 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 31.3 (d, *J* = 1044 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -64.4 (d, *J* = 1045 Hz, 1F).

HRMS (m/z) calculated for $C_{12}H_9FO_2P^+$ $[M+H]^+$: 228.0948; found: 228.0941.

_N_,_N_-Dimethyl-_P_-((perfluorophenyl)methyl)phosphonamidic fluoride (36)



36

Light yellow oil, yield: 43%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.25−3.41 (m, 2H), 2.64 (d, *J* = 10.0 Hz, 6H).

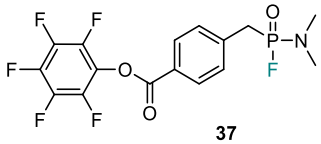
^{13}C NMR (100 MHz, $CDCl_3$): δ 179.9, 144.9 (d, *J* = 250 Hz), 140.0 (d, *J* = 278 Hz), 62.5 (d, *J* = 6.5 Hz), 20.9 (d, *J* = 142 Hz), 16.2 (d, *J* = 6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 28.1 (d, *J* = 1054 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -65.3 (d, *J* = 1053 Hz, 2F), -141.5 (2F), -154.4 (1F), -161.2 (2F).

HRMS (m/z) calculated for $C_9H_9F_6NOP^+$ ($[M+H]^+$): 292.0320; found: 292.0324.

Perfluorophenyl 4-(((dimethylamino)fluorophosphoryl)methyl)benzoate (37)



37

White solid, yield: 66%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.70 (dd, *J* = 10.0 Hz, 2.0 Hz, 6H), 3.33−3.49 (m, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 8.17 (d, *J* = 8.0 Hz, 2H).

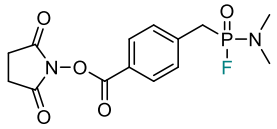
^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2, 142.6 (d, *J* = 8.5 Hz), 140.1 (m), 139.2 (m), 137.9 (m), 136.7 (m), 131.2 (d, *J* = 2.5 Hz), 130.1 (d, *J* = 6.5 Hz), 126.1 (d, *J* = 3.4 Hz), 35.8 (d, *J* = 4.2 Hz), 32.8 (dd, *J* = 32.7 Hz, 129.3 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 32.0 (*J* = 1052 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -65.8 (d, *J* = 1052 Hz, 1F), -152.4 (d, *J* = 17.7 Hz, 2F), -157.8 (t, *J* = 21.1 Hz, 1F), -162.2 (t, *J* = 21.8 Hz, 2F).

HRMS (m/z) calculated for $C_{16}H_{13}F_6NO_3P^+$ ($[M+H]^+$): 412.0532; found: 412.0537.

2,5-Dioxopyrrolidin-1-yl 4-(((dimethylamino)fluorophosphoryl)methyl)benzoate (38)



38

White solid, yield: 45%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.65 (dd, *J* = 9.6 Hz, 1.6 Hz, 6H), 2.90 (s, 4H), 3.30−3.46 (m, 2H), 7.46 (d, *J* = 6.4 Hz, 2H), 8.10 (d, *J* = 8.0 Hz, 2H).

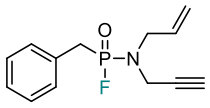
^{13}C NMR (100 MHz, $CDCl_3$): δ 169.2, 161.5, 138.5 (d, *J* = 6.2 Hz), 131,0 (d, *J* = 2.8 Hz), 130.1 (d, *J* = 6.6 Hz), 124.2 (d, *J* = 3.4 Hz), 35.9 (d, *J* = 4.1 Hz), 33.0 (dd, *J* = 129.1 Hz, 33.7 Hz), 25.6.

^{31}P NMR (162 MHz, $CDCl_3$): δ 31.9 (d, *J* = 1052 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -65.7 (d, *J* = 1051 Hz, 1F).

HRMS (m/z) calculated for $C_{14}H_{17}FN_2O_5P^+$ ($[M+H]^+$): 343.0854; found: 343.0856.

***N*-Allyl-*P*-benzyl-*N*-(prop-2-yn-1-yl)phosphonamidic fluoride (39)**



39

White solid, yield: 63%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26−7.33 (m, 5H), 5.52−5.59 (m, 1H), 5.19−5.25 (m, 2H), 3.68−3.91 (m, 2H), 3.61−3.64 (m, 2H), 3.27−3.42 (m, 2H), 2.23 (s, 1H).

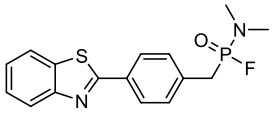
^{13}C NMR (100 MHz, $CDCl_3$): δ 133.5 (d, *J* = 2 Hz), 129.9 (d, *J* = 8.6 Hz), 129.8 (d, *J* = 6.7 Hz), 128.8 (d, *J* = 2 Hz), 127.4 (d, *J* = 3.2 Hz), 119.4, 78.6, 72.6, 47.6 (d, *J* = 3.2 Hz), 34.0 (d, *J* = 5.4 Hz), 33.7 (d, *J* = 128.5 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 33.1 (d, *J* = 1058 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -65.4 (d, *J* = 1057 Hz, 1F).

HRMS (m/z) calculated for $C_{13}H_{16}FNOP^+$ ($[M+H]^+$): 252.0948; found: 252.0940.

***P*-(4-(benzo[*d*]thiazol-2-yl)benzyl)-*N*,*N*-dimethylphosphonamidic fluoride (40)**



40

White solid, yield: 47%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, *J* = 8.0 Hz, 3H), 7.91 (d, *J* = 7.7 Hz, 1H), 7.48–7.52 (m, 1H), 7.38–7.45 (m, 3H), 3.29–3.45 (m, 2H), 2.68 (dd, *J* = 9.7, 2.2 Hz, 6H).

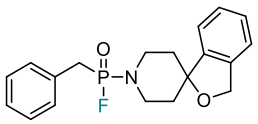
^{13}C NMR (100 MHz, $CDCl_3$): δ 154.1, 135.0, 132.8, 130.2 (d, *J* = 6.8 Hz), 127.9 (d, *J* = 3.0 Hz), 127.8, 127.5, 126.4, 125.3, 123.2, 121.6, 35.9 (d, *J* = 4.2 Hz, 4H), 30.8 (dd, *J* = 43.9 Hz, 125.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 32.9 (d, *J* = 1052 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -66.4 (d, *J* = 1051 Hz, 1F).

HRMS (m/z) calculated for $C_{16}H_{17}FN_2OPS^+$ ($[M+H]^+$): 335.0778; found: 335.0772.

Benzyl(3*H*-spiro[isobenzofuran-1,4'-piperidin]-1'-yl)phosphinic fluoride (41)



41

White solid, yield: 63%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23–7.32 (m, 5H), 7.18–7.19 (m, 2H), 7.10–7.12 (m, 1H), 6.88–6.90 (m, 1H), 4.95 (s, 2H), 3.35–3.45 (m, 2H), 3.17–3.54 (m, 2H), 3.03–3.12 (m, 2H), 1.51–1.61 (m, 4H).

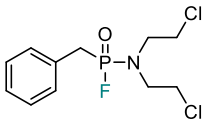
^{13}C NMR (100 MHz, $CDCl_3$): δ 144.9, 138.6, 130.7 (d, *J* = 2.4 Hz), 130.6 (d, *J* = 2.3 Hz), 129.6 (d, *J* = 6.8 Hz), 128.9, 127.8, 127.4, 127.3, 120.9 (d, *J* = 54.5 Hz), 84.3, 70.9, 40.8 (d, *J* = 3.1 Hz), 36.4, 32.9 (dd, *J* = 131.0 Hz, 32.6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 32.1 (d, *J* = 1052 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -64.6 (dd, *J* = 5.64 Hz, 1051 Hz, 1F).

HRMS (m/z) calculated for $C_{19}H_{22}FNO_2P^+$ ($[M+H]^+$): 346.1367; found: 346.1368.

***P*-benzyl-*N*,*N*-bis(2-chloroethyl)phosphonamidic fluoride (42)**



42

White solid, yield: 71%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.38 (m, 5H), 3.35−3.47 (m, 8H), 3.23−3.31 (m, 2H).

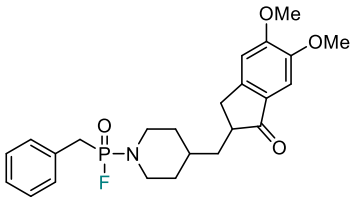
^{13}C NMR (100 MHz, $CDCl_3$): δ 129.7, 129.6, 129.1, 127.7 (d, *J* = 15.4 Hz), 48.0 (d, *J* = 3.9 Hz), 41.6, 33.0 (dd, *J* = 128.7 Hz, 30.1 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 34.0 (d, *J* = 1062 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -62.9 (d, *J* = 1061 Hz, 1F).

HRMS (m/z) calculated for $C_{11}H_{16}Cl_2FNOP^+$ ($[M+H]^+$): 298.0325; found: 298.0331.

Benzyl(4-((5,6-dimethoxy-1-oxo-2,3-dihydro-1*H*-inden-2-yl)methyl)piperidin-1-yl)phosphinic fluoride (43)



43

White solid, yield: 76%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.46 (m, 5H),7.36 (s, 1H) 6.95 (s, 1H), 4.06 (s, 3H), 4.00 (s, 3H), 3.58–3.66 (m, 2H), 3.42–3.48 (m, 1H), 3.29–3.83 (m, 2H), 2.74–2.77 (m, 3H), 1.88–1.93 (m, 3H), 1.70–1.75 (m, 3H), 1.11–1.22 (m, 2H).

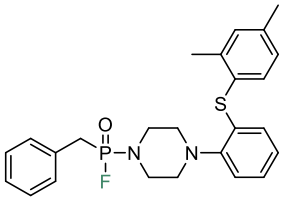
^{13}C NMR (100 MHz, $CDCl_3$): δ 206.9, 155.3, 149.2, 148.3, 130.3 (d, *J* = 8.3 Hz), 129.3, 128.8, 128.4, 126.9, 107.1 (d, *J* = 6.1 Hz), 104.1 (d, *J* = 10.5 Hz), 55.8 (d, *J* = 15.9 Hz), 44.5, 43.8 (d, *J* = 6.7 Hz), 38.4, 33.8, 33.3, 32.4 (dd, *J* = 131.7 Hz, 38.5 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 31.9 (d, *J* = 1052 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -65.1 (dd, *J* = 1052 Hz, 25.5Hz, 1F).

HRMS (m/z) calculated for $C_{24}H_{30}FNO_4P^+$ ($[M+H]^+$): 446.1891; found: 446.1897.

Benzyl(4-(2-((2,4-dimethylphenyl)thio)phenyl)piperazin-1-yl)phosphinic fluoride (44)



44

White solid, yield: 56%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30−7.39 (m, 6H), 7.15 (s, 1H), 7.02−7.08 (m, 2H), 6.95 (d, *J* = 8.0 Hz, 1H), 6.88 (t, *J* = 7.6 Hz, 1H), 3.24−3.43 (m, 6H), 2.92 (s, 4H), 2.33 (d, *J* = 25.6 Hz, 6H).

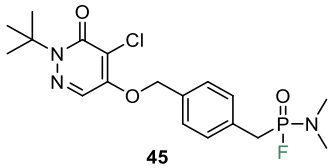
^{13}C NMR (100 MHz, $CDCl_3$): δ 148.7, 142.3, 139.3, 136.1, 134.7, 131.7, 130.4 (d, *J* = 8.7 Hz), 129.7 (d, *J* = 6.8 Hz), 128.9 (d, *J* = 2.5 Hz), 127.8, 127.6, 127.4 (d, *J* = 3.2 Hz), 126.3, 125.5, 124.8, 120.0, 51.9 (d, *J* = 3.8 Hz), 44.3, 33.0 (dd, *J* = 130.4 Hz, 32 Hz), 21.2, 20.5.

^{31}P NMR (162 MHz, $CDCl_3$): δ 31.6 (d, *J* = 1055 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -64.6 (d, *J* = 1054 Hz, 1F).

HRMS (m/z) calculated for $C_{25}H_{29}FN_2OPS^+$ ($[M+H]^+$): 455.1717; found: 455.1713.

***P*-(4-(((1-(*tert*-butyl)-5-chloro-6-oxo-1,6-dihydropyridazin-4-yl)oxy)methyl)benzyl)-*N*,*N*-dimethylphosphonamidic fluoride (45)**



45

White solid, yield: 51%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 4.5 Hz, 1H), 7.36 (dd, *J* = 3.3 Hz, 13.1 Hz, 4H), 5.30 (d, *J* = 2.4 Hz, 2H), 3.23–3.36 (m, 2H), 2.64–2.68 (m, 6H), 1.63 (d, *J* = 4.5 Hz, 9H).

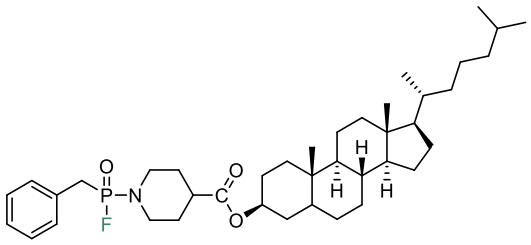
^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 153.6, 133.9 (d, *J* = 3.6 Hz), 131.3 (d, *J* = 8.8 Hz), 130.1 (d, *J* = 6.6 Hz), 127.6 (d, *J* = 2.8 Hz), 125.0, 118.3, 71.4, 66.4, 35.8 (d, *J* = 4.1 Hz), 32.2 (dd, *J* = 32.5 Hz, 130.5 Hz), 27.8 (s, 21H).

^{31}P NMR (162 MHz, $CDCl_3$): δ 33.5 (d, *J* = 1051 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -66.7 (d, *J* = 1051 Hz, 1F).

HRMS (m/z) calculated for $C_{18}H_{25}ClFN_3O_3P^+$ ($[M+H]^+$): 416.1301; found: 416.1306.

(3*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-Dimethyl-17-((*R*)-6-methylheptan-2-yl)hexade-cahydro-1*H*-cyclopenta[a]phenanthren-3-yl 1-(benzylfluorophosphoryl) -piperidi-ne-4-carboxylate (46)



46

White solid, yield: 50%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30−7.35 (m, 5H), 3.38−3.43 (m, 1H), 3.19−3.31 (m, 1H), 2.72−2.77 (m, 1H), 2.32−2.37 (m, 1H), 1.96 (d, *J* = 12 Hz, 1H), 1.71−1.81 (m, 4H), 1.64−1.67 (m, 2H), 1.43−1.58 (m, 8H), 1.22−1.38 (m, 14H), 1.04−1.15 (m, 6H), 0.94−0.99 (m, 3H), 0.85−0.90 (m, 10H), 0.81 (s, 3H), 0.64 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 130.4 (d, *J* = 1 0.7 Hz), 129.6 (d, *J* = 6.8 Hz), 128.8 (d, *J* = 2.7 Hz), 127.4 (d, *J* = 3.4 Hz), 73.9, 56.3 (d, *J* = 13.5 Hz), 54.2, 44.6, 43.3, 42.6, 40.9, 39.9, 39.5, 36.7, 36.2, 35.8, 35.5, 34.0, 33.8, 33.5, 32.6, 32.2, 30.0, 29.7, 31.9, 28.6, 28.2 (d, *J* = 6.6 Hz), 28.0, 27.4, 24.2, 23.8, 22.7 (d, *J* = 25.3 Hz), 21.2, 18.7, 12.1 (d, *J* = 16.3 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ 31.7 (d, *J* = 1055 Hz, 1P).

^{19}F NMR (376 MHz, $CDCl_3$): δ -65.4 (d, *J* = 1054 Hz, 1F).

HRMS (m/z) calculated for $C_{40}H_{64}FNO_3P^+$ ($[M+H]^+$): 656.4602; found: 656.4606.

2.3 Experimental Procedures for Radiochemistry

2.3.1 General procedure for the preparation of [^{18}F]TBAF, [^{18}F]CsF, [^{18}F]KF/K_{222}, [^{18}F]KF/18-cr-6

[^{18}F]F^- was produced through the $^{18}O(p, n)^{18}F$ reaction using the IBA 18/9 cyclotron (Belgium) and was delivered in [^{18}O]H_2O. The [^{18}F] fluoride ([^{18}F]F^-) was extracted from the [^{18}O]-enriched water using QMA and then introduced into a glass vial reactor with a pre-configured eluent (**Table S2**). The resulting solution was co-evaporated and dried at 110 ℃, and this process was repeated three times using clean glass vials (300 μL acetonitrile × 3) for subsequent utilization.

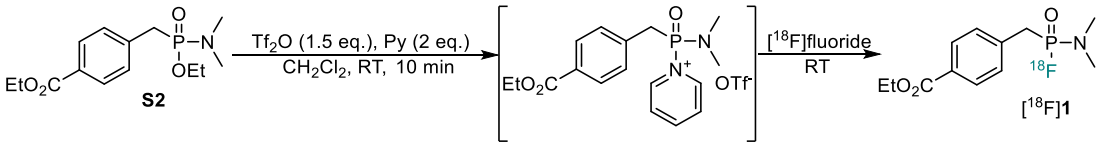
Table S2: Detailed formulas of eluent

Entry	[^{18}F]fluoride	Eluent
1	[^{18}F]TBAF	6.0 mg nBu$_4$N$^+$OH$^-$ in 100 μL CH_3CN
2	[^{18}F]CsF	7.5 mg Cs_2CO_3 in 100 μL CH_3CN
3	[^{18}F]KF/K_{222}	8.0 mg K_{222}, 1.0 mg K_2CO_3 in CH_3CN/H_2O (4/1, v/v, 0.5 mL)
4	[^{18}F]KF/18-cr-6	6.0 mg 18-crown-6, 1.0 mg K_2CO_3 in CH_3CN/H_2O (4/1, v/v, 0.5 mL)

2.3.2 Optimization studies for alkyl phosphonates ^{18}F-fluorination

The reaction conditions for ^{18}F-fluorination were reevaluated in comparison to fluorination. Initially, the conditions were kept consistent with those used for non-radioactive in order to screen suitable [^{18}F]fluoride. The precursor **S2** underwent conversion into a pyridinium salt intermediate within a 10 min period. Subsequently, the intermediate was introduced into a glass vial reactor, where a previously prepared dry 37−55.5 MBq [^{18}F]fluoride was present, and the mixture was incubated at RT with continuous shaking for 5−10 min. After the completion of the reaction, 9900 μL of water was added to quench the reaction and radiochemical conversion (RCC) was assessed using radio-TLC by dividing the area under the curve (AUC) of the radioactive peak of interest by the total AUC of all radioactive peaks. The radiochemical yield (RCY) is based on the ratio of the final isolated product to that of the initial radioactivity, with all amounts decay corrected to the same time[11]. In all ^{18}F-labeling reaction systems, due to the presence of acidic and water-soluble impurities in the reaction mixture, a simple purification step using a C18 cartridge is typically performed prior to HPLC analysis to remove these impurities.

Table S3: Optimization for alkyl phosphonates ^{18}F-fluorination



Entry	Precursor load /μmol	[^{18}F]fluoride	Reaction time /min	RCC$_{TLC}$ (%)[a]
1	20	[^{18}F]TBAF	5	10 ± 5
2	20	[^{18}F]CsF	5	37 ± 1
3	20	[^{18}F]KF/K$_{222}$	5	58 ± 5
4	20	[^{18}F]KF/18-cr-6	5	5 ± 1
5	20	[^{18}F]KF/K$_{222}$	10	78 ± 5
6	2	[^{18}F]KF/K$_{222}$	10	67 ± 5
7	1	[^{18}F]KF/K$_{222}$	10	62 ± 3
8	0.2	[^{18}F]KF/K$_{222}$	10	16 ± 6
9	0.02	[^{18}F]KF/K$_{222}$	10	5 ± 2

[a] RCC$_{TLC}$s determined by radio-TLC.

2.3.3 Radio$_{TLC}$ and radio-HPLC analysis of ^{18}F-labeled compounds

All ^{18}F-labeling reactions were performed following the specified protocol: 3 μmol of precursor were dissolved in 300 μL CH_2Cl_2. Then, 2 eq. of Tf_2O were added for 5 min, followed by the addition of 1.5 eq. of pyridine for another 5 min. The resulting intermediate solution was subsequently divided into three equal portions and introduced into separate glass vial reactors, each containing pre-prepared 37−55.5 MBq dried [^{18}F]KF/K_{222}. The reactors were continuously oscillated at room temperature for 10 minutes. Upon completion of the reaction, 9900 μL of water was added to quench the reaction. The RCCs of the reaction were determined using radio-TLC with methanol as the developing agent (n = 3). Additionally, the RCY and co-injection were measured using a radio-HPLC.

S15, as a precursor, undergoes highly selective ^{18}F-fluorination to yield an unstable phenyl benzylphosphonofluoridate, which, as reported in the literature[12], is prone to hydrolysis and cannot be isolated due to its instability, spontaneously converting into benzylphosphonofluoridic acid. The results demonstrated a high selectivity for the alkyl phosphonate esters, aligning with our expectations.

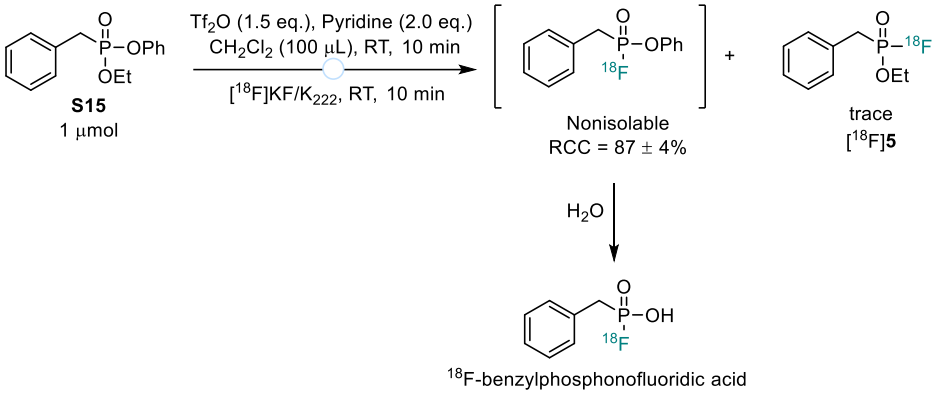


Fig. S4: The selectivity of the reaction was verified by ^{18}F-fluorination.

Table S4: Average radiochemical conversion for ^{18}F-benzylphosphonofluoridic acid

Run	1	2	3	Average
RCC_{TLC} (%)	77	76	80	78 ± 2

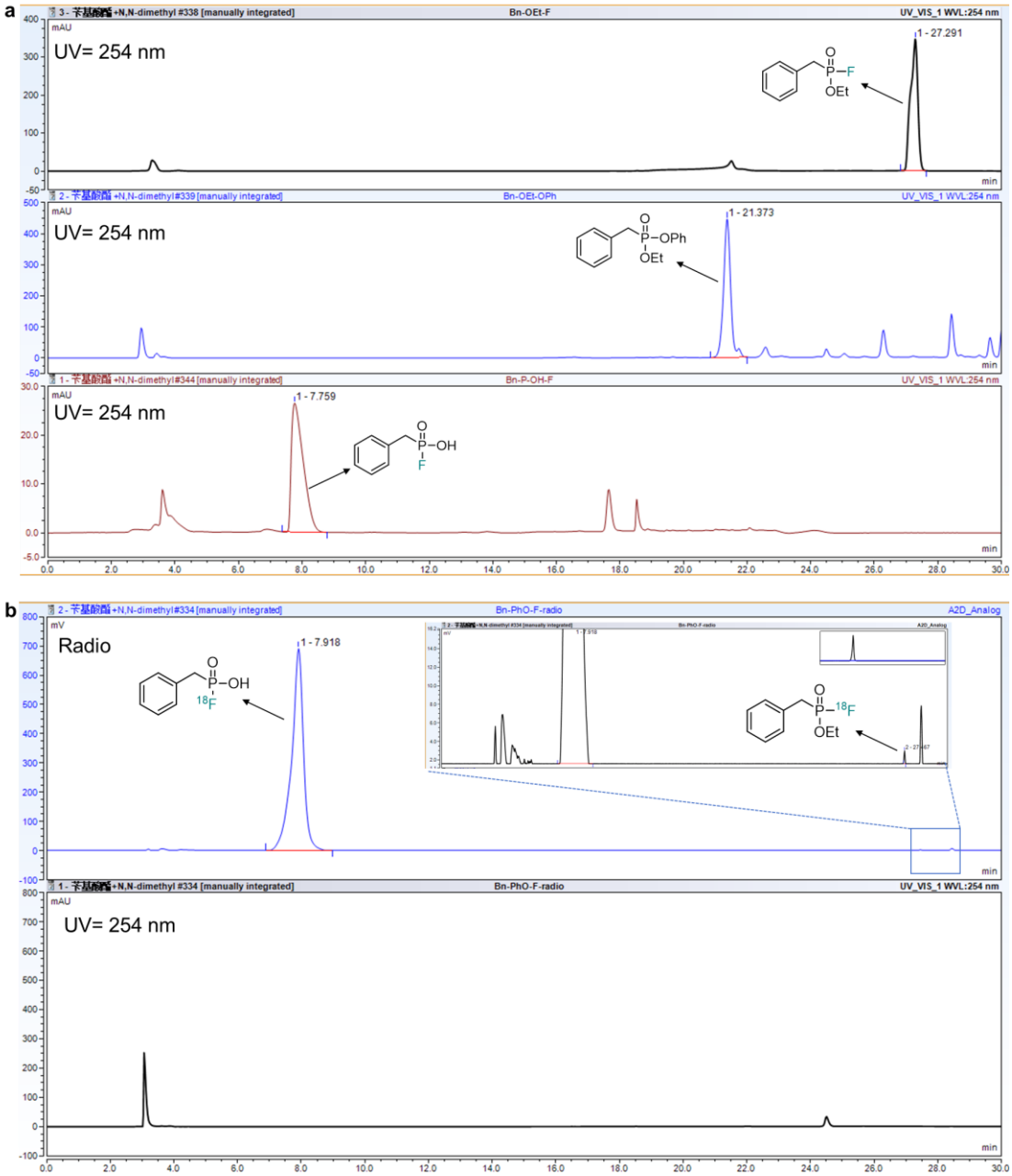


Fig. S5: a. HPLC traces of precursor and reference compounds; **b.** HPLC traces of crude ^{18}F-labeled products. 1# HPLC conditions; NanoChrom C18 column (5 μm, 4.6 × 250 mm); isocratic elution, 0−10 min, 10% of CH_3CN and 90% of water containing 0.1%TFA, 10−30 min, from 10% of CH_3CN and 90% of water containing 0.1%TFA to 70% of CH_3CN and 30% of water containing 0.1%TFA; flow rate: 1.0 mL/min.

Preparation of [^{18}F]1

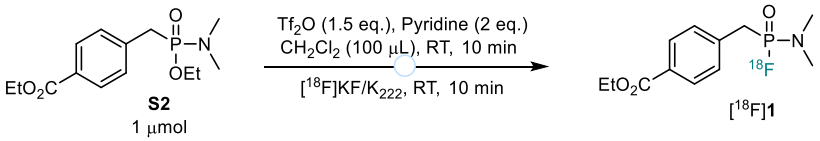


Table S5: Average radiochemical conversion for [^{18}F]**1**

Run	1	2	3	Average
RCC_{TLC} (%)	63	66	59	62 ± 3

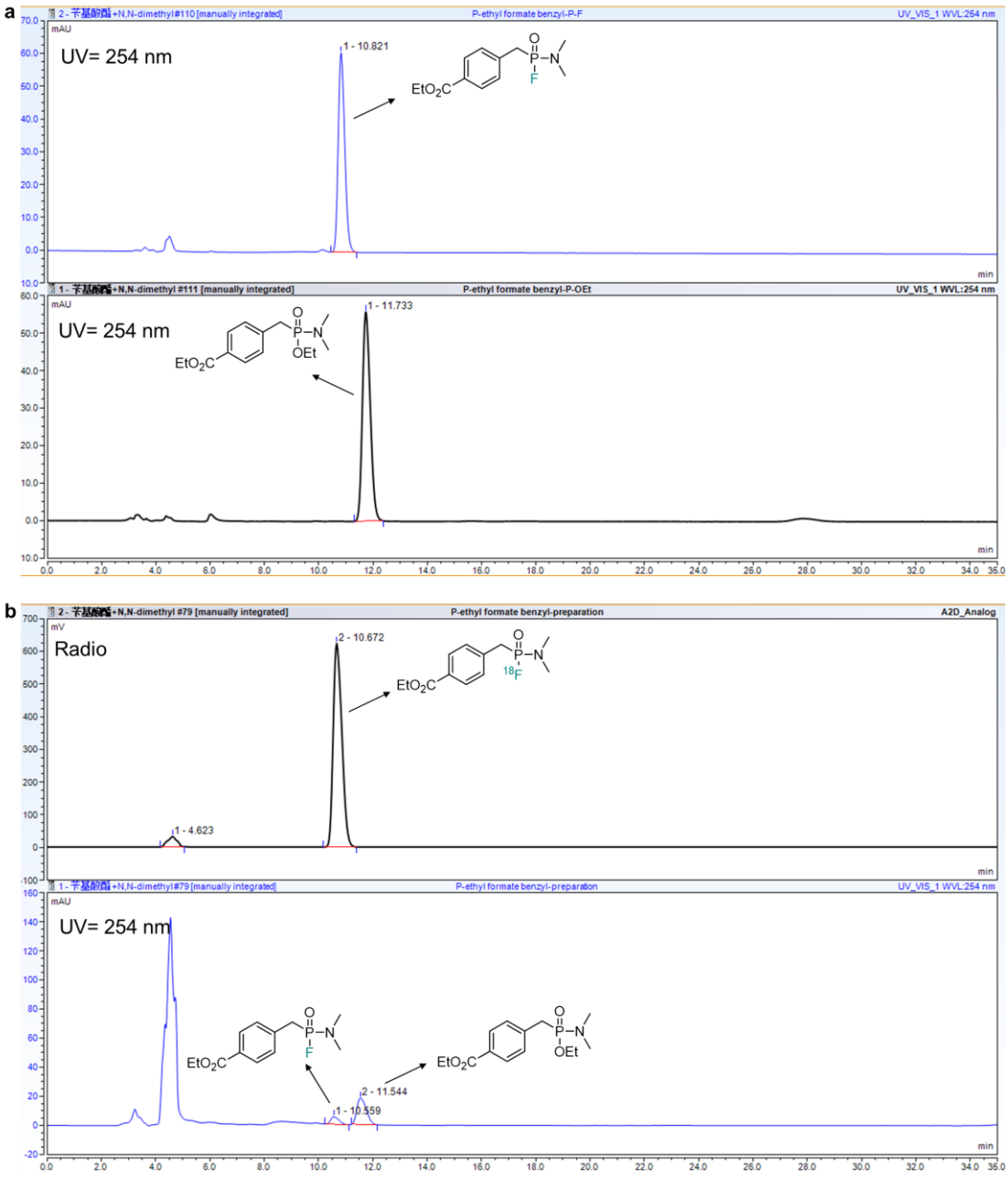


Fig. S6: a. HPLC traces of precursor and reference compounds; **b.** HPLC traces of crude ^{18}F-labeled products. 1# HPLC conditions; SEP Basic-C18 semi-preparative column (120A 5μm 10 × 250 mm); isocratic elution, 0−10 min, from 50% of CH_3CN and 50% of water containing 0.1%TFA to 40% of CH_3CN and 60% of water containing 0.1%TFA; 10−25 min, from 40% of CH_3CN and 60% of water containing 0.1%TFA to 35% of CH_3CN and 65%

of water containing 0.1%TFA; 25−35 min, 35% of CH_3CN and 65% of water containing 0.1%TFA; flow rate: 3.0 mL/min.

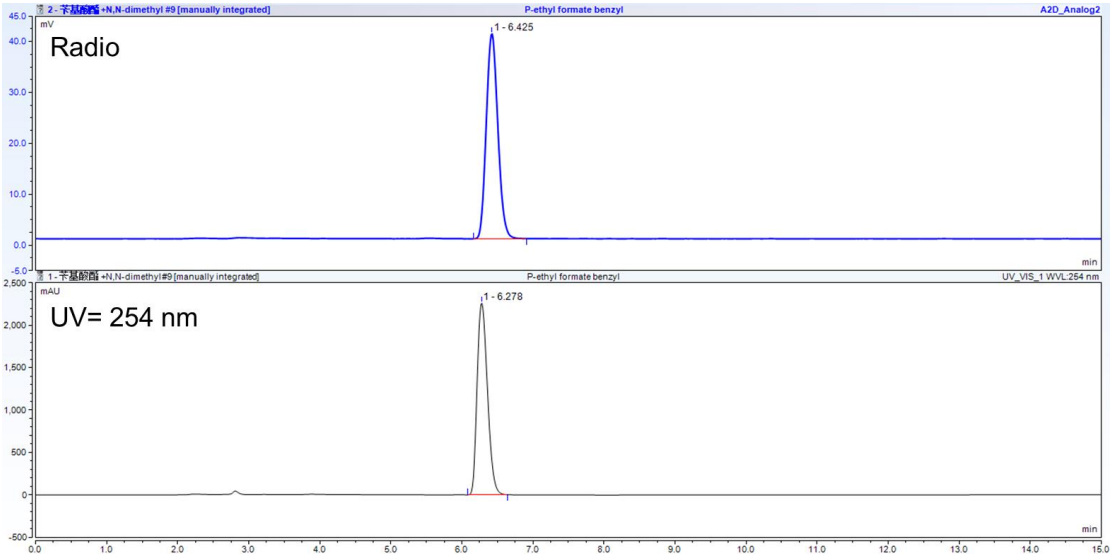


Fig. S7: Co-injection for [^{18}F]**1**. 1# HPLC conditions; NanoChrom C18 column (5 μm, 4.6 × 250 mm); isocratic elution, H_2O/CH_3CN = 50/50, and the flow rate was 1.0 mL/min for 15 min. The RCP was > 99%. (The HPLC trace of the co-injection represents the results of the purified ^{18}F-product mixed with the corresponding reference compound, allowing confirmation of radiochemical purity (RCP) from the co-injection HPLC trace.)

Preparation of [^{18}F]36

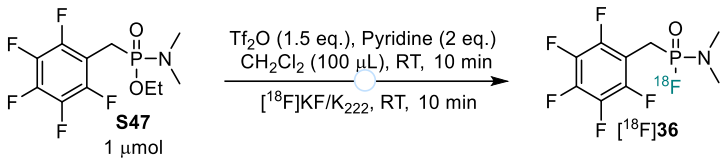


Table S6: Average radiochemical conversion for [^{18}F]**36**

Run	1	2	3	Average
RCC_{TLC} (%)	75	84	69	76 ± 7

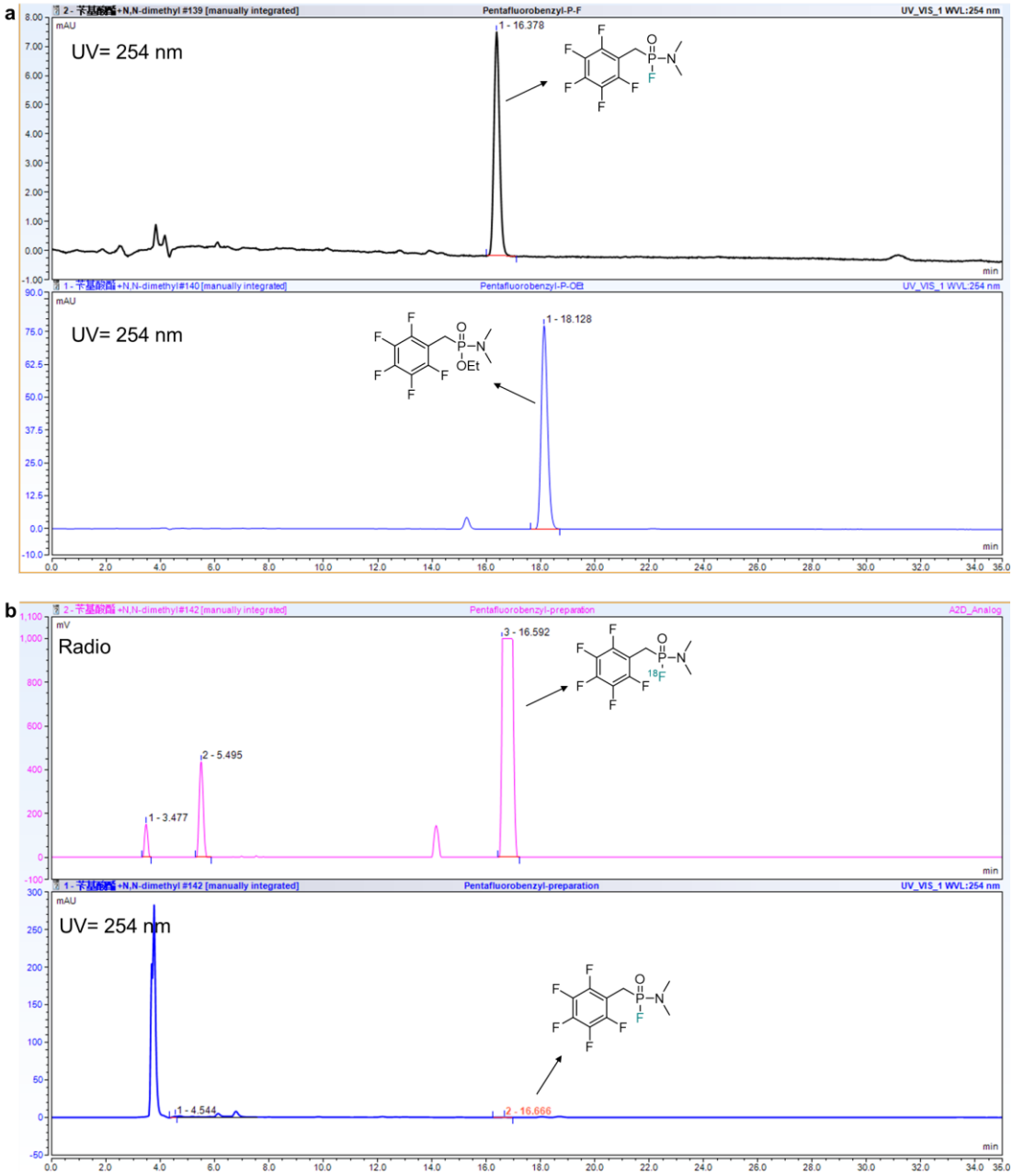


Fig. S8: a. HPLC traces of precursor and reference compounds; **b.** HPLC traces of crude ^{18}F-labeled products. 1# HPLC conditions; SEP Basic-C18 semi-preparative column (120A 5μm 10 × 250mm); isocratic elution, 0−10 min, from 40% of CH_3CN and 60% of water containing 0.1%TFA to 50% of CH_3CN and 50% of water containing 0.1%TFA; 10−20 min, 50% of CH_3CN and 50% of water containing 0.1%TFA; 20−35 min, from 50% of CH_3CN and 50% of water containing 0.1%TFA to 55% of CH_3CN and 45% of water containing 0.1%TFA; flow rate: 3.0 mL/min.

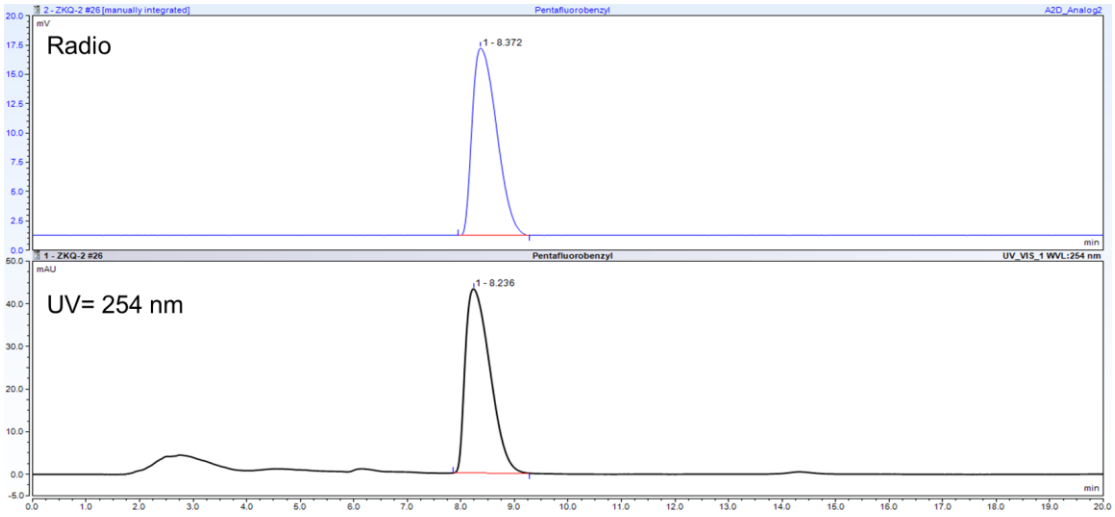


Fig. S9: Co-injection for [^{18}F]**36**. 1# HPLC condition; NanoChrom C18 column (5 μm, 4.6 × 250 mm); isocratic elution, H_2O/CH_3CN = 50/50, and the flow rate was 1.0 mL/min for 20 min. The RCP was > 99%.

Preparation of [^{18}F]37

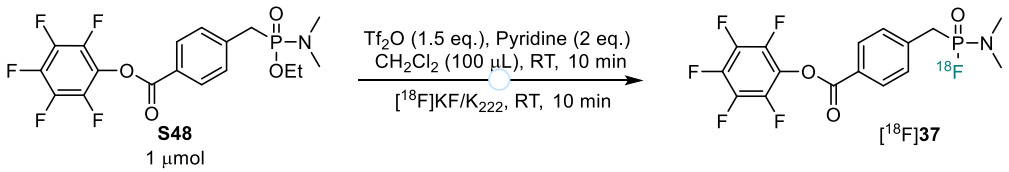


Table S7: Average radiochemical conversion for [^{18}F]**37**

Run	1	2	3	Average
RCC_{TLC} (%)	70	67	77	71 ± 5

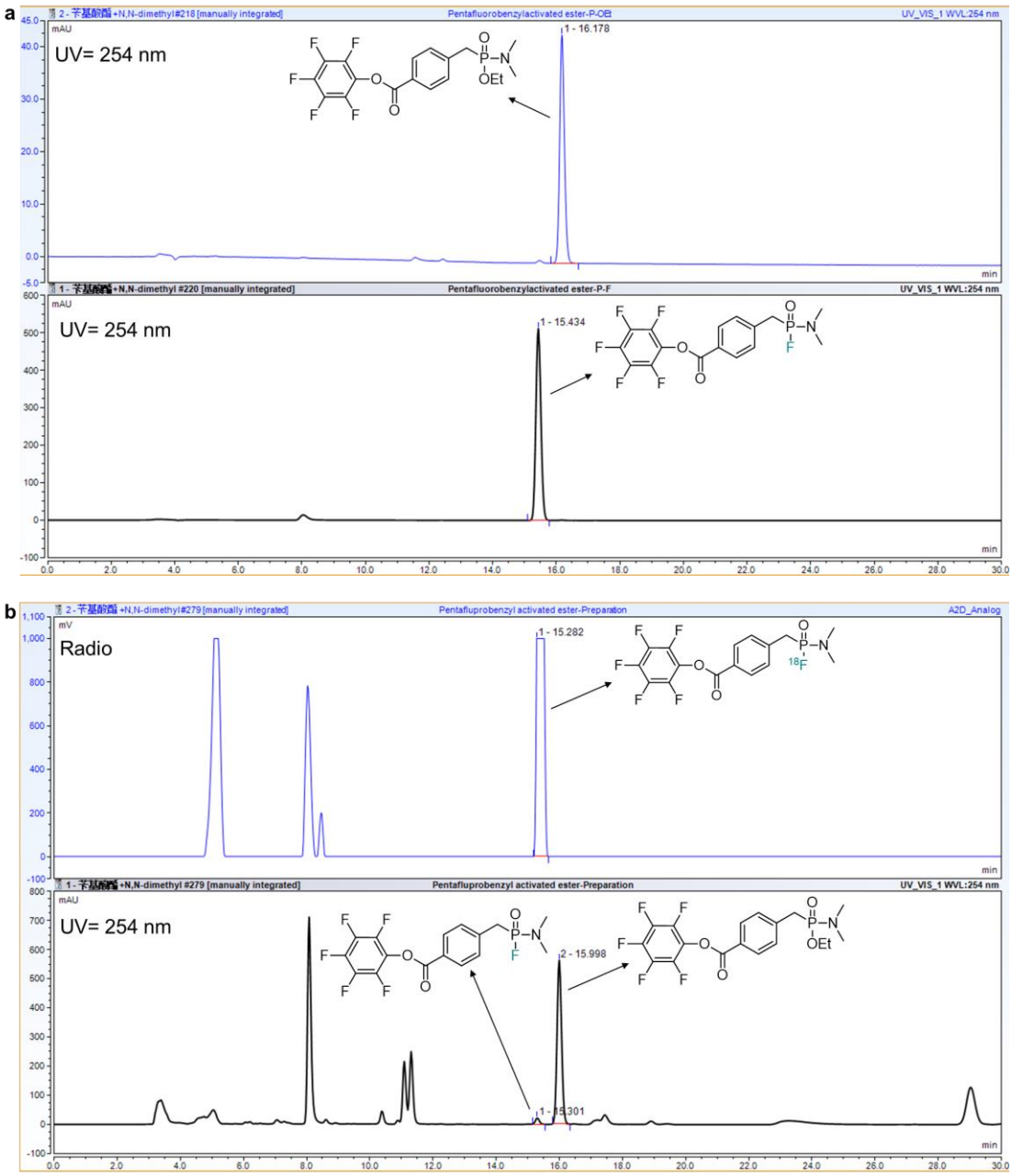


Fig. S10: a. HPLC traces of precursor and reference compounds; **b.** HPLC traces of crude ^{18}F-labeled products. 1# HPLC conditions; SEP Basic-C18 semi-preparative column (120A 5μm 10 × 250mm); isocratic elution, 0−10 min, from 50% of CH_3CN and 50% of water containing 0.1%TFA to 70% of CH_3CN and 30% of water containing 0.1%TFA; 10−30 min, from 70% of CH_3CN and 30% of water containing 0.1%TFA to 75% of CH_3CN and 25% of water containing 0.1%TFA; flow rate: 3.0 mL/min.

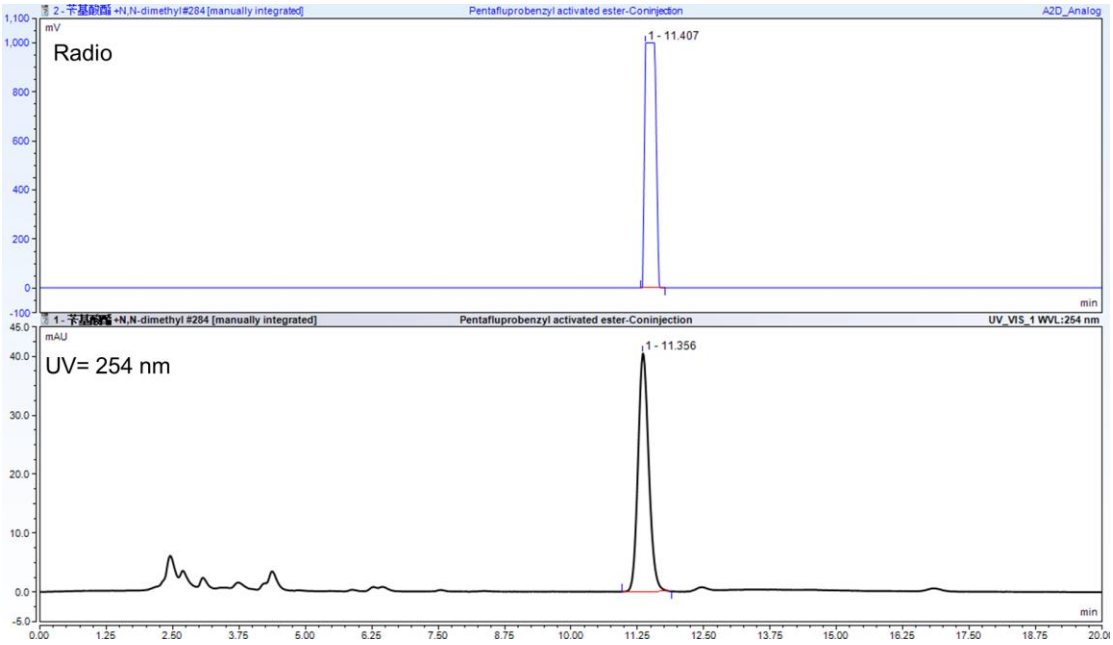


Fig. S11: Co-injection for [^{18}F]**37**. 2# HPLC condition; NanoChrom C18 column (5 μm, 4.6 × 250 mm), isocratic elution, water containing 0.1%TFA/CH_3CN = 40/60, and the flow rate was 1.0 mL/min for 20 min. The RCP was > 99%.

Preparation of [^{18}F]38

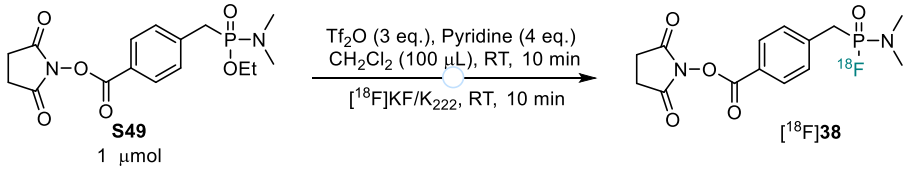


Table S8: Average radiochemical conversion for [^{18}F]**38**

Run	1	2	3	Average
RCC_{TLC} (%)	90	88	85	88 ± 3

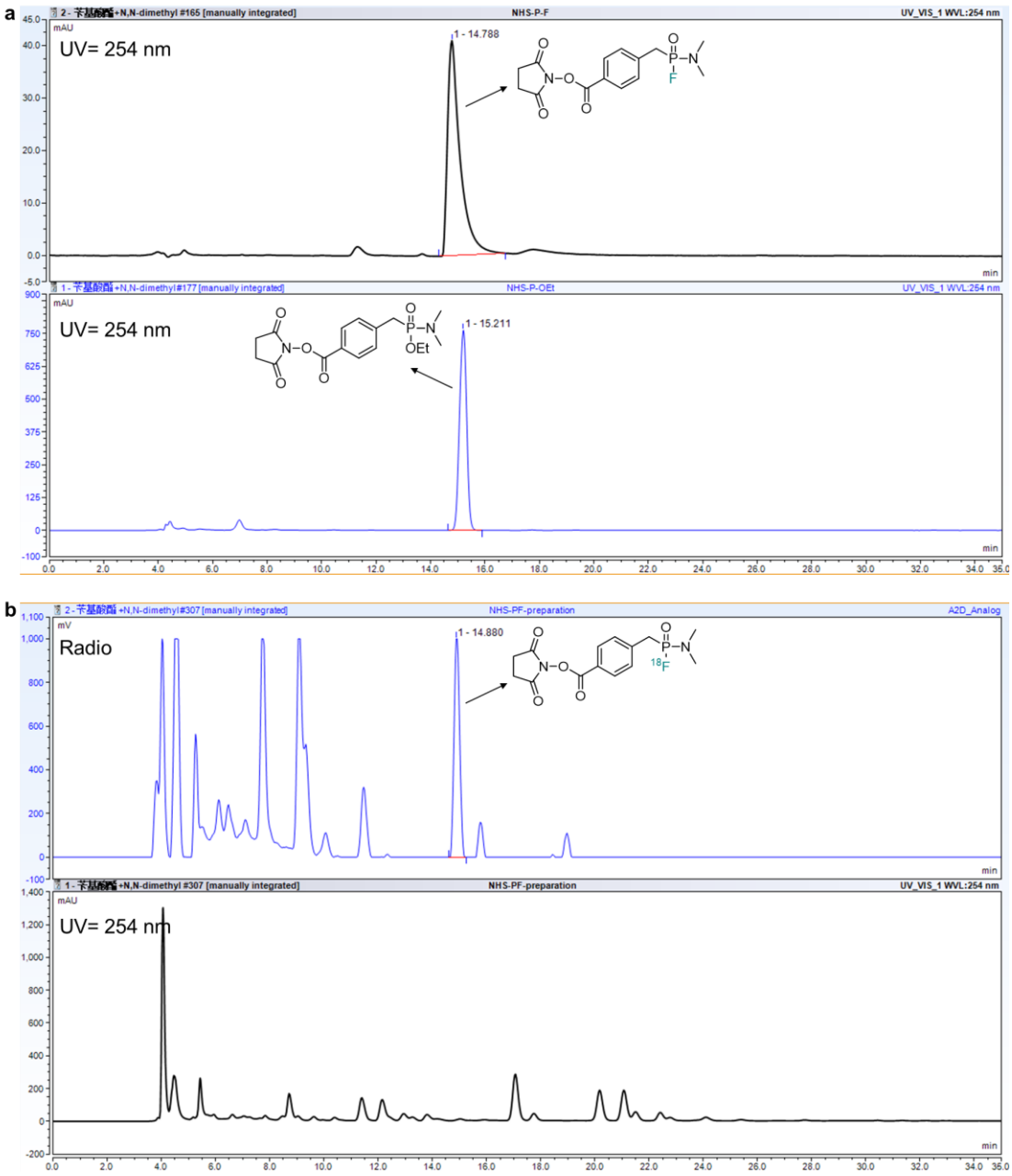


Fig. S12: a. HPLC traces of precursor and reference compounds; **b.** HPLC traces of crude ^{18}F-labeled products. 1# HPLC conditions; SEP Basic-C18 semi-preparative column (120A 5μm 10 × 250mm); isocratic elution, 0−20 min, from 30% of CH_3CN and 70% of water containing 0.1%TFA to 40% of CH_3CN and 60% of water containing 0.1%TFA; from 40% of CH_3CN and 60% of water containing 0.1%TFA to 50% of CH_3CN and 50% of water containing 0.1%TFA; flow rate: 3.0 mL/min.

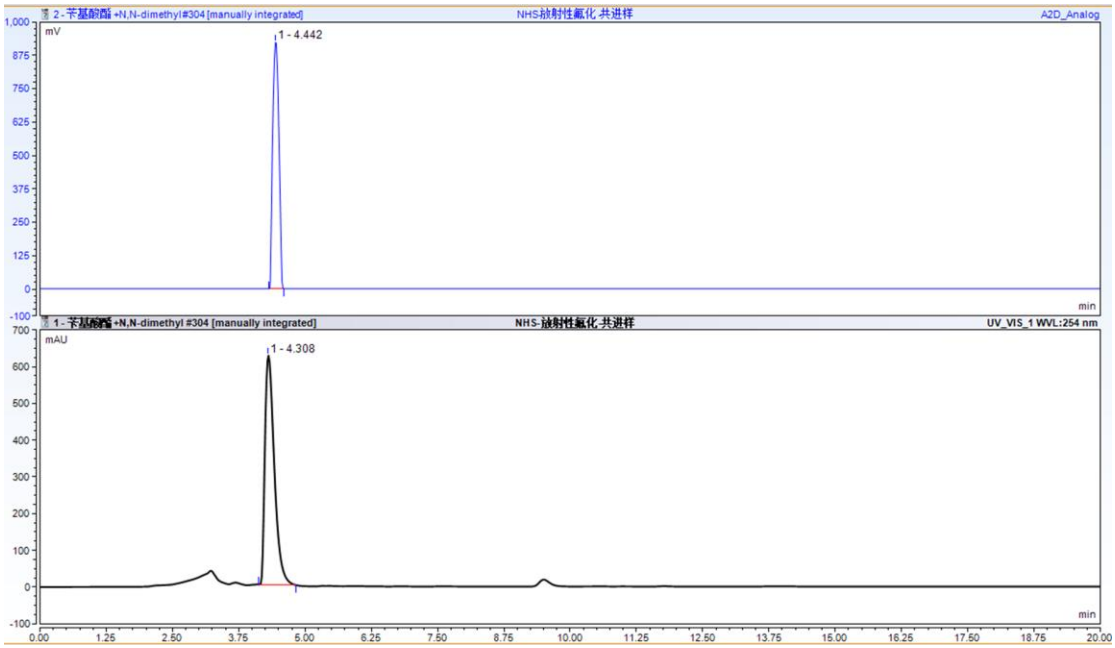


Fig. S13: Co-injection for [^{18}F]**38**. 1# HPLC condition; NanoChrom C18 column (5 μm, 4.6 × 250 mm), isocratic elution, water containing 0.1%TFA/CH_3CN = 45/55, and the flow rate was 1 mL/min for 20 min. The RCP was > 99%.

Preparation of [^{18}F]39

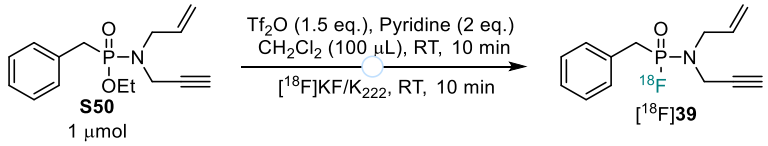


Table S9. Average radiochemical conversion for [^{18}F]**39**

Run	1	2	3	Average
RCC_{TLC} (%)	73	85	72	77 ± 7

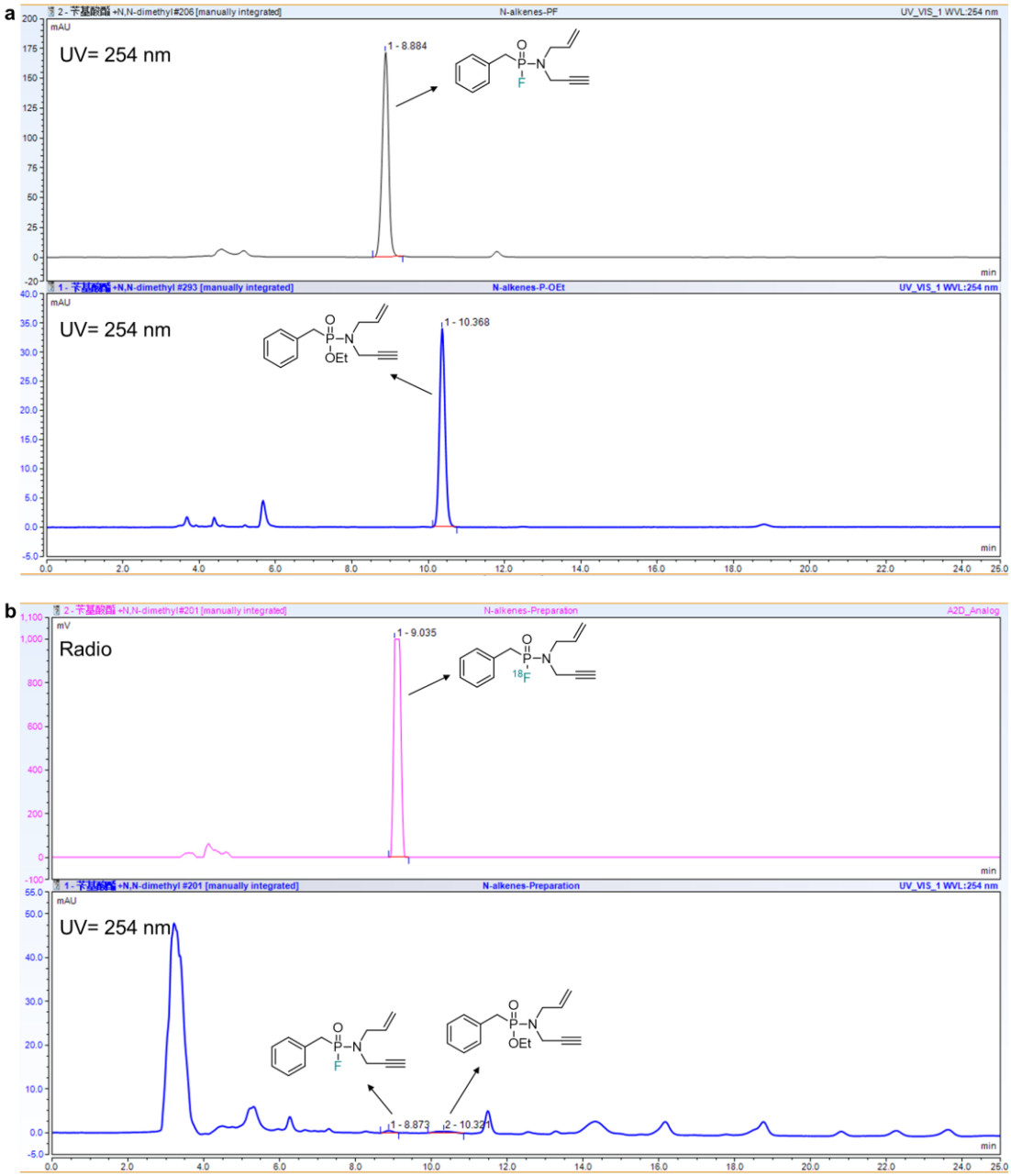


Fig. S14: a. HPLC traces of precursor and reference compounds; **b.** HPLC traces of crude ^{18}F-labeled products. 1# HPLC conditions; SEP Basic-C18 semi-preparative column (120A 5μm 10 × 250mm); isocratic elution, 0−10 min, from 50% of CH_3CN and 50% of water containing 0.1%TFA to 65% of CH_3CN and 35% of water containing 0.1%TFA; from 65% of CH_3CN and 35% of water containing 0.1%TFA to 70% of CH_3CN and 30% of water containing 0.1%TFA; flow rate: 3.0 mL/min.

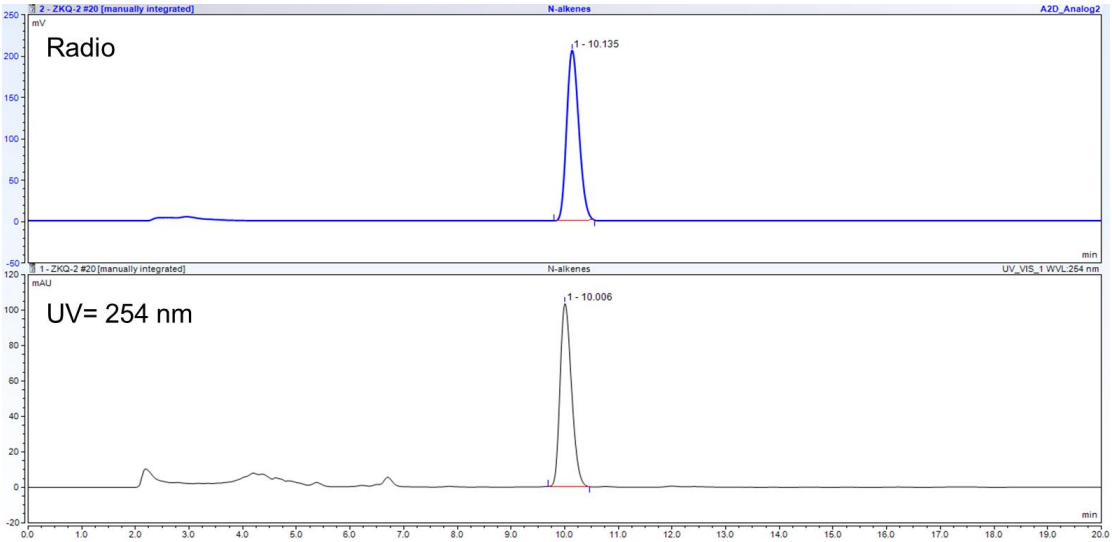


Fig. S15: Co-injection for [^{18}F]**39**. 1# HPLC condition; NanoChrom C18 column (5 μm, 4.6 × 250 mm), isocratic elution, water containing 0.1%TFA/CH_3CN = 50/50, and the flow rate was 1 mL/min for 20 min. The RCP was >97%.

Preparation of [^{18}F]40

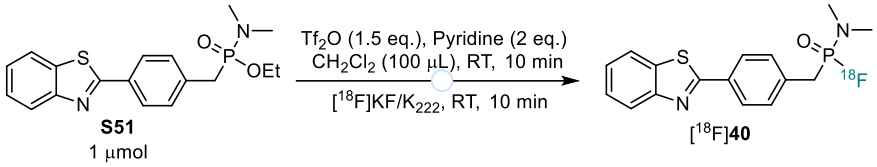


Table S10. Average radiochemical conversion for [^{18}F]**40**

Run	1	2	3	Average
RCC_{TLC} (%)	61	59	55	58 ± 3

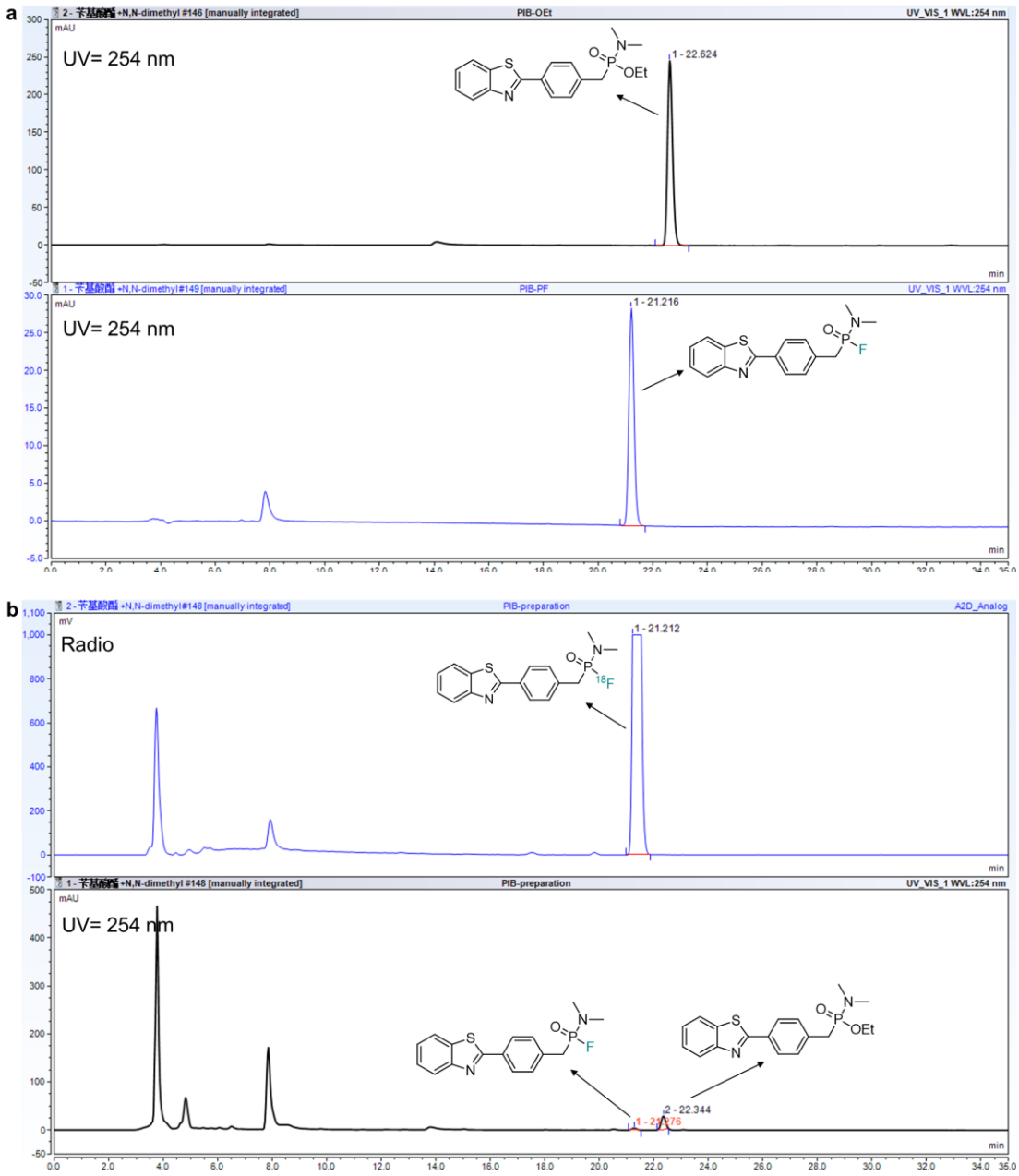


Fig. S16: a. HPLC traces of precursor and reference compounds; **b.** HPLC traces of crude ^{18}F-labeled products. 1# HPLC conditions; SEP Basic-C18 semi-preparative column (120A 5μm 10 × 250mm); isocratic elution, 0−10 min, from 40% of CH_3CN and 60% of water containing 0.1%TFA to 50% of CH_3CN and 50% of water containing 0.1%TFA; 10−15 min, from 50% of CH_3CN and 50% of water containing 0.1%TFA to 55% of CH_3CN and 45% of water containing 0.1%TFA; 15−18 min, from 55% of CH_3CN and 45% of water containing 0.1%TFA to 60% of CH_3CN and 40% of water containing 0.1%TFA; 18−35 min, 60% of CH_3CN and 40% of water containing 0.1%TFA; flow rate: 3.0 mL/min.

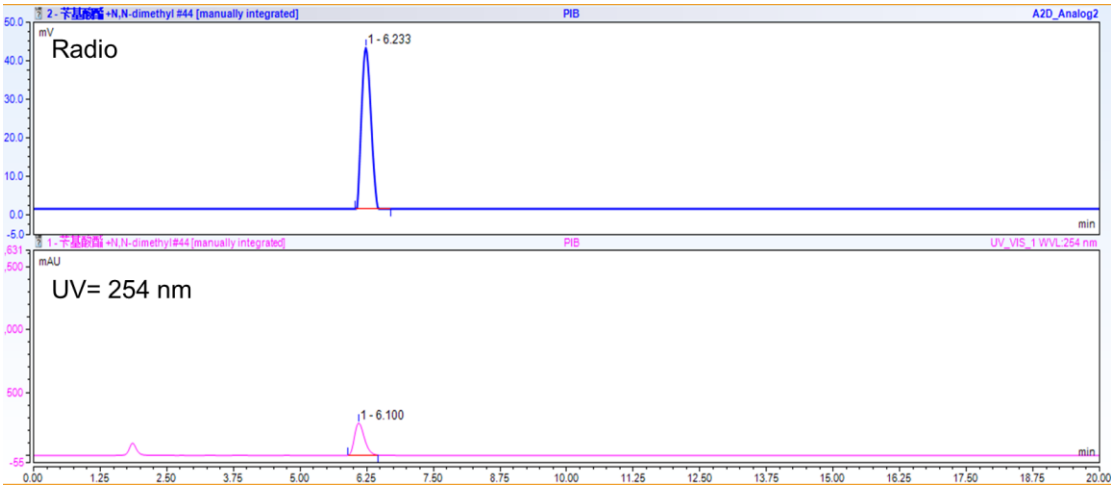


Fig. S17: Co-injection for [^{18}F]**40**. 1# HPLC condition; NanoChrom C18 column (5 μm, 4.6 × 250 mm), isocratic elution, H_2O/CH_3CN = 50/50, and the flow rate was 1 mL/min for 20 min. The RCP was >99%.

Preparation of [^{18}F]41

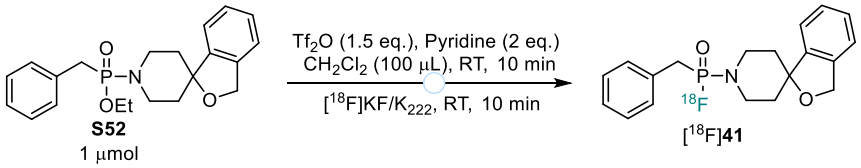


Table S11: Average radiochemical conversion for [^{18}F]**41**

Run	1	2	3	Average
RCC_{TLC} (%)	38	58	57	51 ± 11

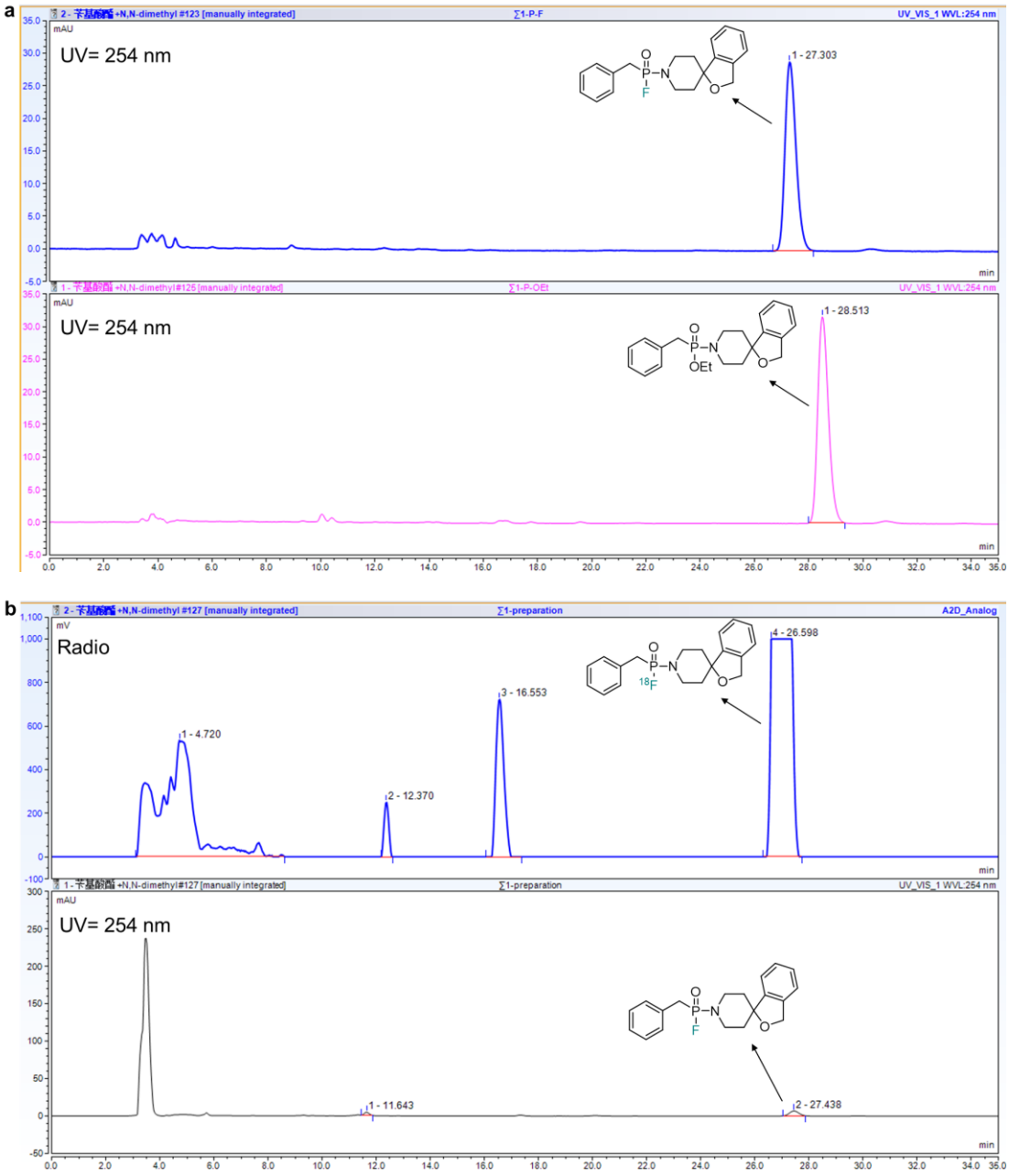


Fig. S18: a. HPLC traces of precursor and reference compounds; **b.** HPLC traces of crude ^{18}F-labeled products. 1# HPLC conditions; SEP Basic-C18 semi-preparative column (120A 5μm 10 × 250mm); isocratic elution, 0−10 min, from 40% of CH_3CN and 60% of water containing 0.1%TFA to 50% of CH_3CN and 50% of water containing 0.1%TFA; 10−20 min, 50% of CH_3CN and 50% of water containing 0.1%TFA for 10 min; 20−35 min, from 50% of CH_3CN and 50% of water containing 0.1%TFA to 55% of CH_3CN and 45% of water containing 0.1%TFA; flow rate: 3.0 mL/min.

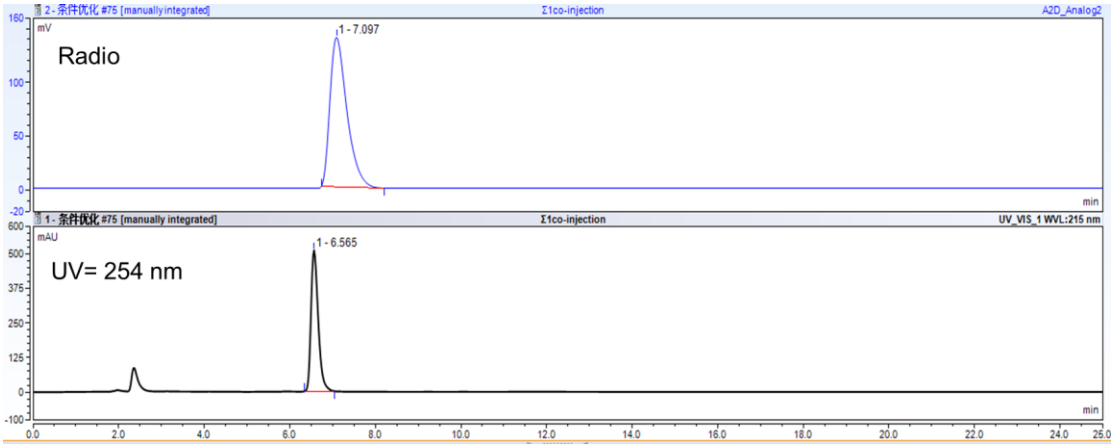


Fig. S19: Co-injection for [^{18}F]**41**. 2# HPLC condition; NanoChrom C18 column (5 μm, 4.6 × 250 mm), isocratic elution, H_2O/CH_3CN = 35/65, and the flow rate was 1 mL/min for 25 min. The RCP was > 99%.

Preparation of [^{18}F]42

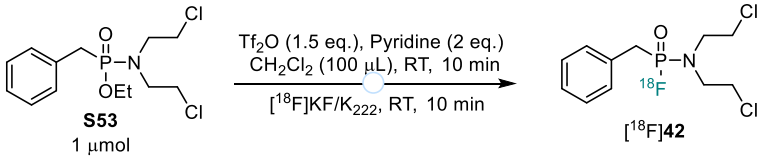
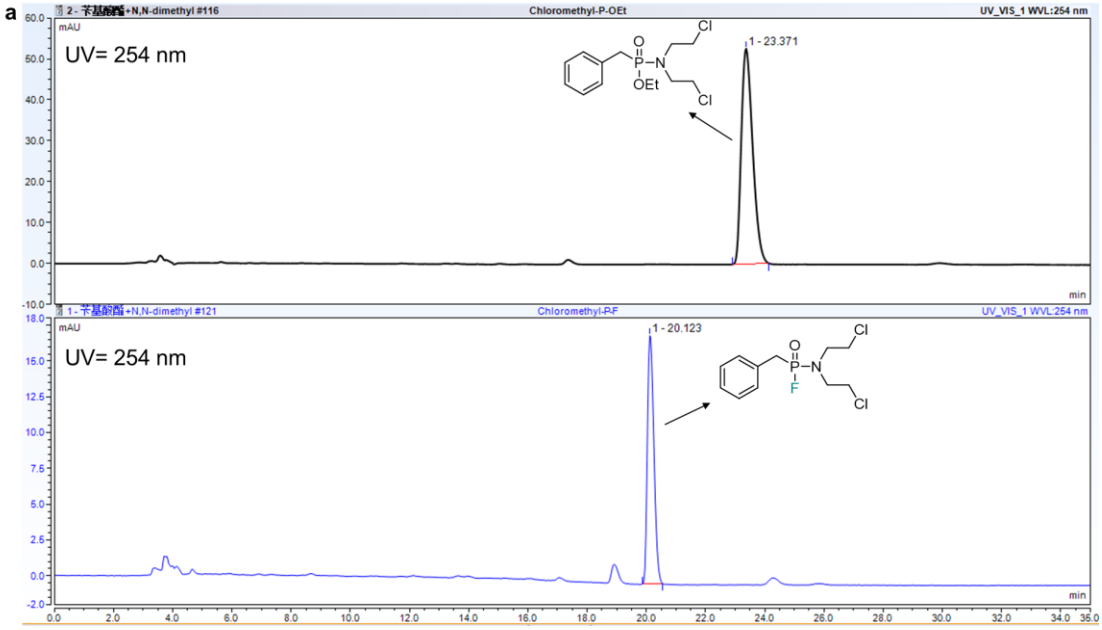


Table S12: Average radiochemical conversion for [^{18}F]**42**

Run	1	2	3	Average
RCC_{TLC} (%)	86	62	77	75 ± 12



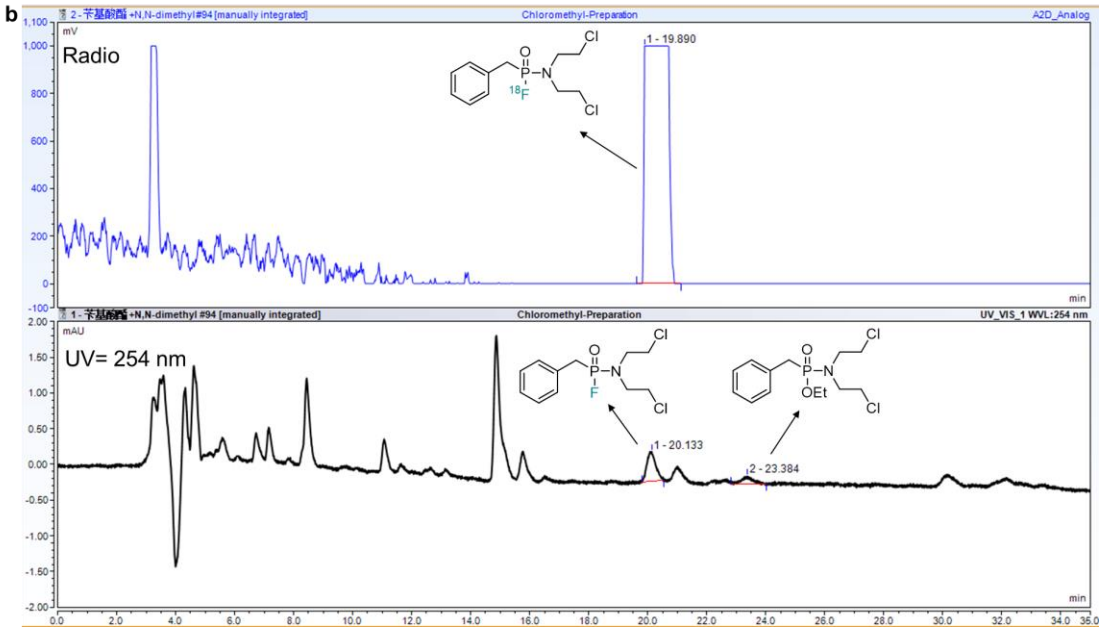


Fig. S20: a. HPLC traces of precursor and reference compounds; **b.** HPLC traces of crude ^{18}F-labeled products. 1# HPLC conditions; SEP Basic-C18 semi-preparative column (120A 5μm 10 × 250mm); isocratic elution, 0−10 min, from 40% of CH_3CN and 60% of water containing 0.1%TFA to 50% of CH_3CN and 50% of water containing 0.1%TFA; 10−20 min, 50% of CH_3CN and 50% of water containing 0.1%TFA; 20−35 min, from 50% of CH_3CN and 50% of water containing 0.1%TFA to 55% of CH_3CN and 45% of water containing 0.1%TFA; flow rate: 3.0 mL/min.

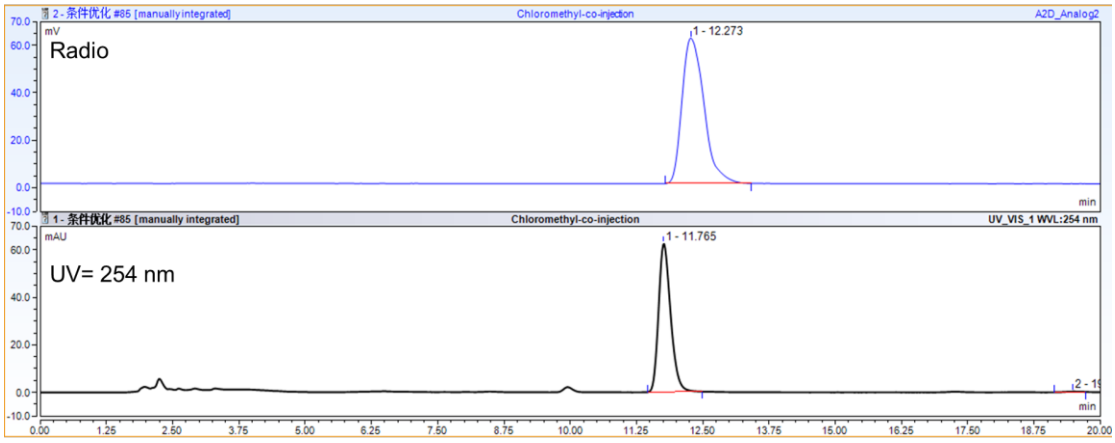


Fig. S21: Co-injection for [^{18}F]**42**. 2# HPLC condition: NanoChrom C18 column (5 μm, 4.6 × 250 mm), isocratic elution, H_2O/CH_3CN = 50/50, and the flow rate was 1 mL/min for 20 min. The RCP was > 99%.

Preparation of [^{18}F]43

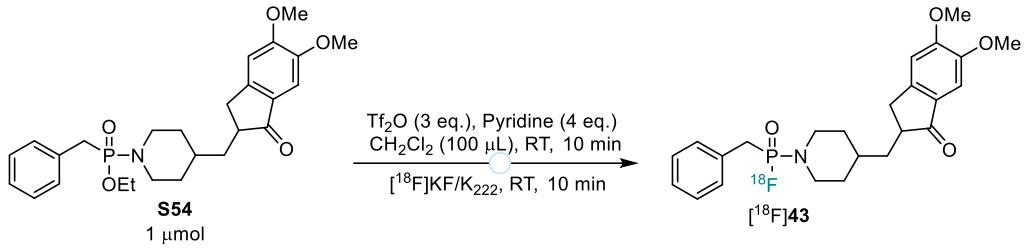
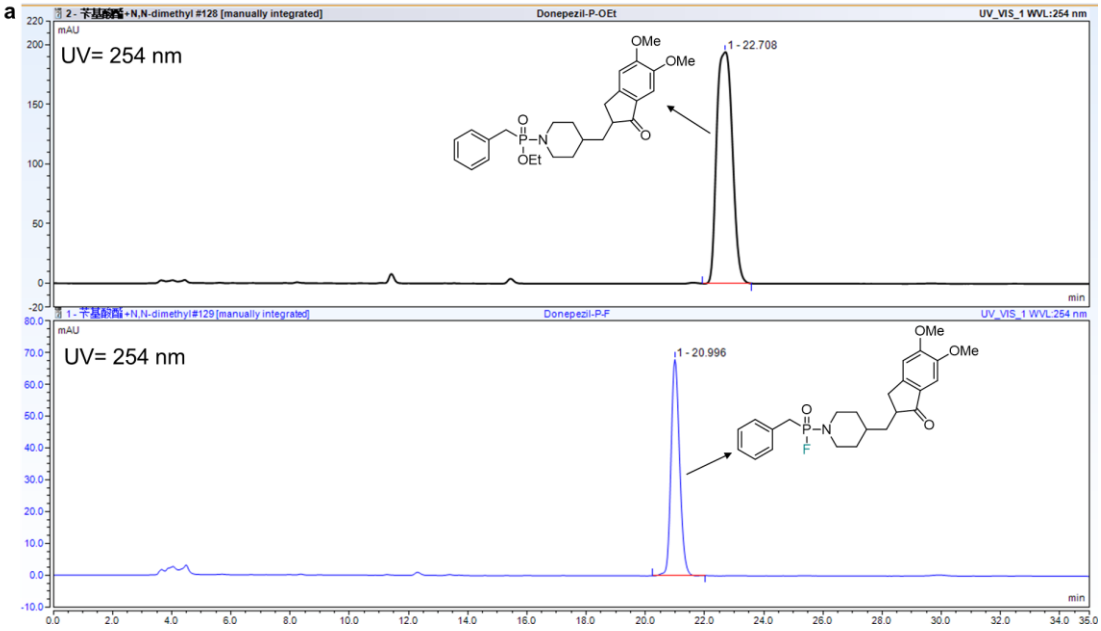


Table S13: Average radiochemical conversion for [^{18}F]**43**

Run	1	2	3	Average
RCC_{TLC} (%)	63	57	64	61 ± 4

a



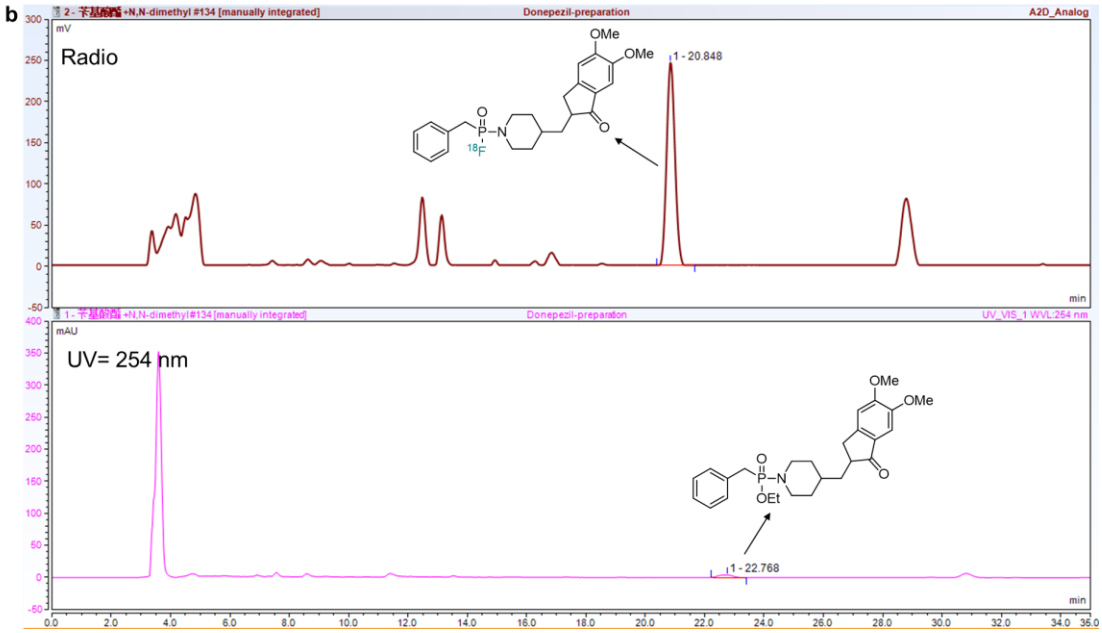


Fig. S22: a. HPLC traces of precursor and reference compounds; **b.** HPLC traces of crude ^{18}F-labeled products. 1# HPLC conditions; SEP Basic-C18 semi-preparative column (120A 5μm 10 × 250mm); isocratic elution, 0−10 min, from 40% of CH_3CN and 60% of water containing 0.1%TFA to 50% of CH_3CN and 50% of water containing 0.1%TFA; 10−20 min, 50% of CH_3CN and 50% of water containing 0.1%TFA; 20−35 min, from 50% of CH_3CN and 50% of water containing 0.1%TFA to 55% of CH_3CN and 45% of water containing 0.1%TFA; flow rate: 3.0 mL/min.

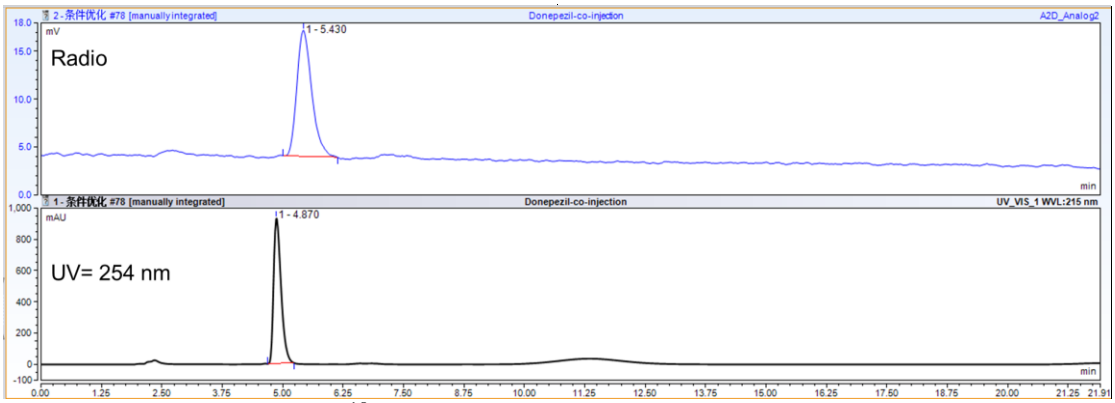


Fig. S23: Co-injection for [^{18}F]**43**. 2# HPLC condition; NanoChrom C18 column (5 μm, 4.6 × 250 mm), isocratic elution, H_2O/CH_3CN = 35/65, and the flow rate was 1 mL/min for 20 min. The RCP was > 97%.

Preparation of [^{18}F]44

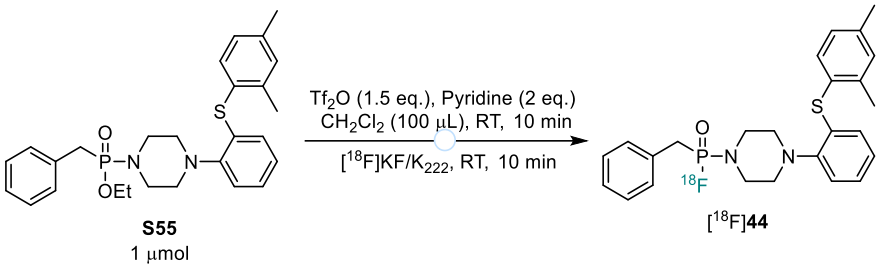
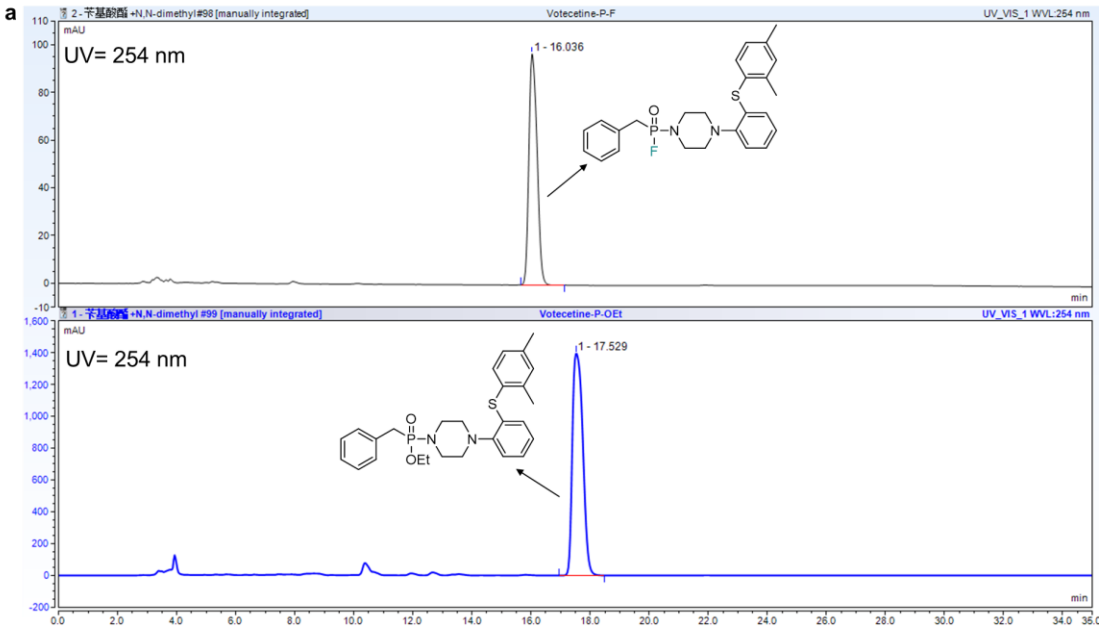


Table S14: Average radiochemical conversion for [^{18}F]**44**

Run	1	2	3	Average
RCC_{TLC} (%)	67	66	71	68 ± 2



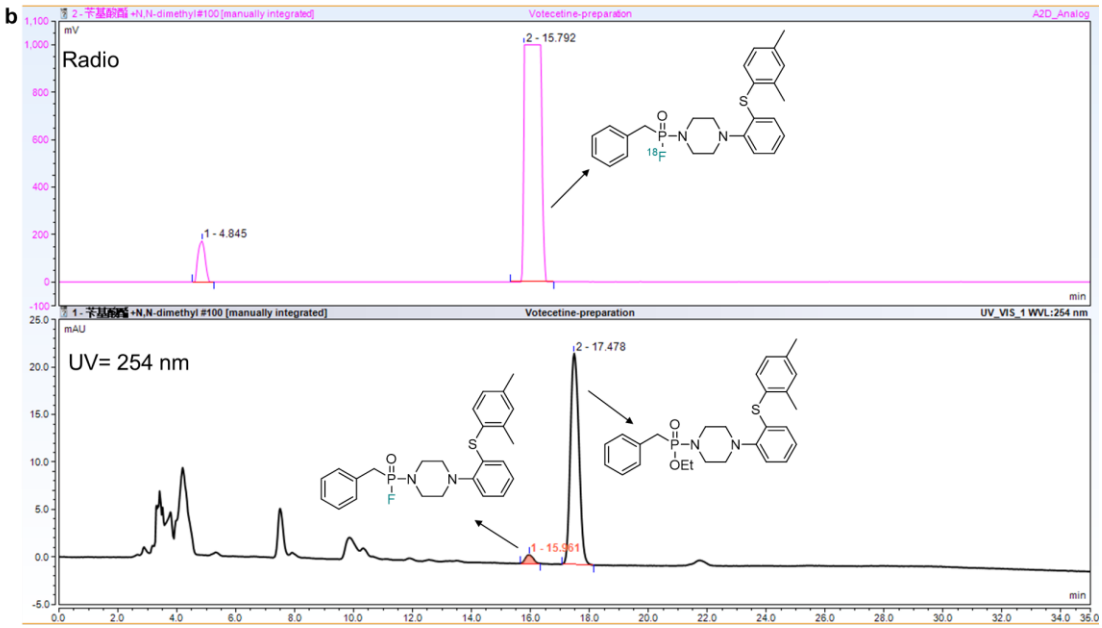


Fig. S24: a. HPLC traces of precursor and reference compounds; **b.** HPLC traces of crude ^{18}F-labeled products. 1# HPLC conditions; SEP Basic-C18 semi-preparative column (120A 5μm 10 × 250mm); isocratic elution, 0−15 min, from 80% of CH_3CN and 20% of water containing 0.1%TFA to 85% of CH_3CN and 15% of water containing 0.1%TFA; 15−25 min, 85% of CH_3CN and 15% of water containing 0.1%TFA; 25−35 min, from 85% of CH_3CN and 15% of water containing 0.1%TFA to 90% of CH_3CN and 10% of water containing 0.1%TFA; flow rate: 3.0 mL/min.

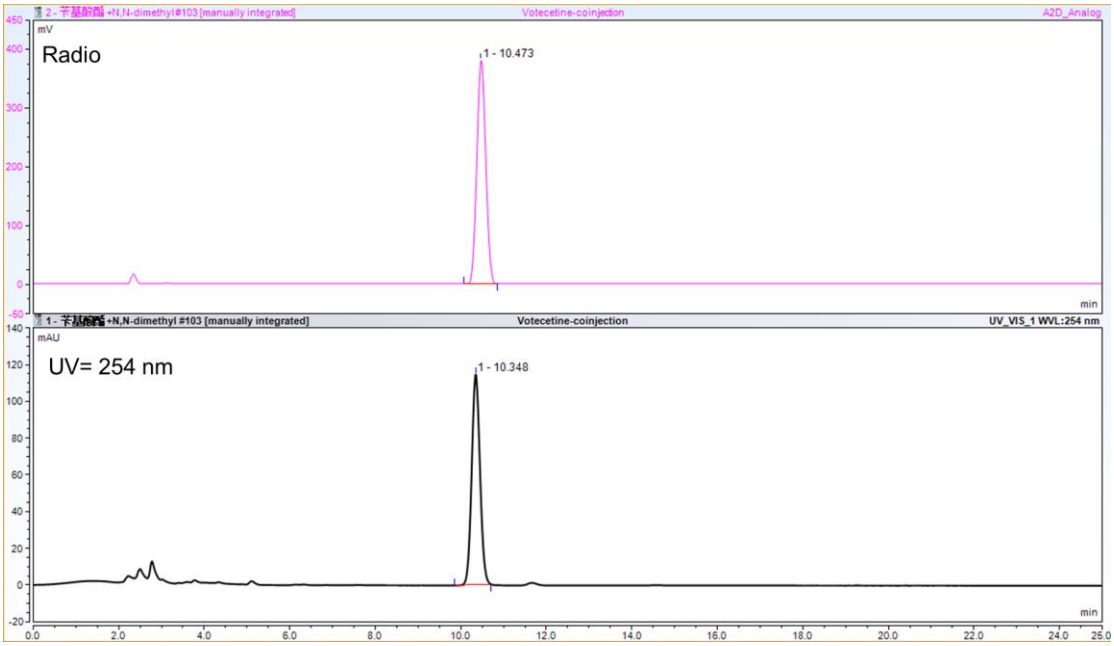


Fig. S25: Co-injection for [^{18}F]**44**. 1# HPLC condition: NanoChrom C18 column (5 μm, 4.6 × 250 mm), isocratic elution, water containing 0.1%TFA/CH_3CN = 50/50, and the flow

rate was 1 mL/min for 20 min. The RCP was > 98%.

Preparation of [^{18}F]45

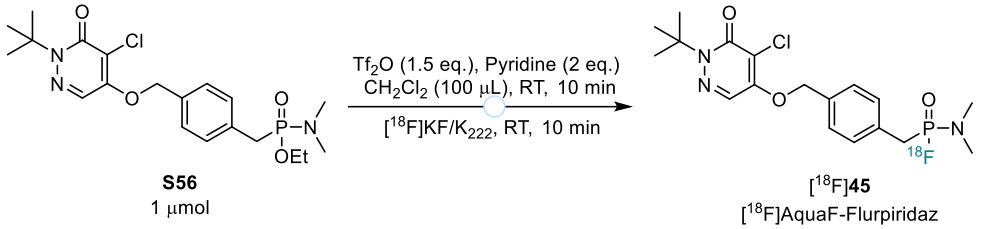
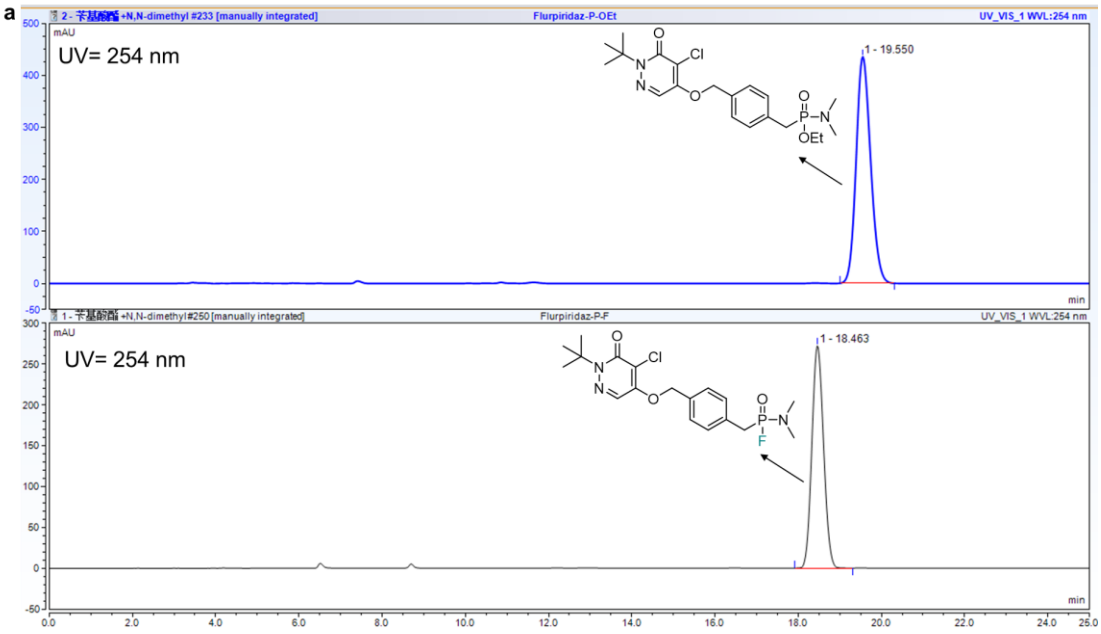


Table S15. Average radiochemical conversion for [^{18}F]**45**

Run	1	2	3	Average
RCC_{TLC} (%)	65	59	47	57 ± 9

a



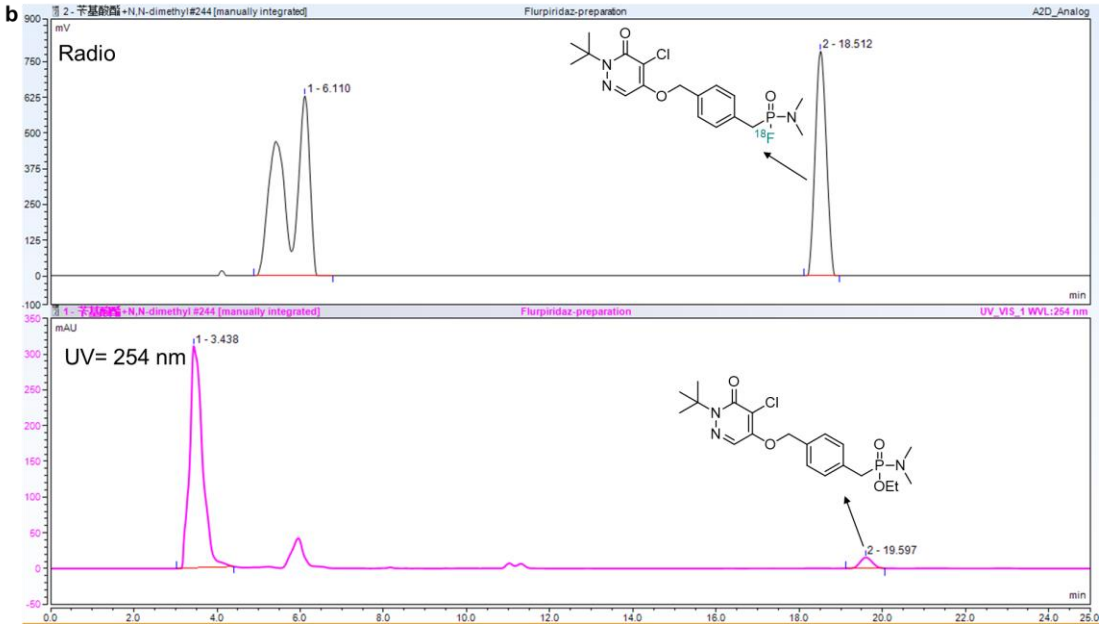


Fig. S26: a. HPLC traces of precursor and reference compounds; **b.** HPLC traces of crude ^{18}F-labeled products. 1# HPLC conditions; SEP Basic-C18 semi-preparative column (120A 5μm 10 × 250mm); elution: isocratic elution, water containing 0.1%TFA/CH_3CN = 50/50, and the flow rate was 3 mL/min for 25 min.

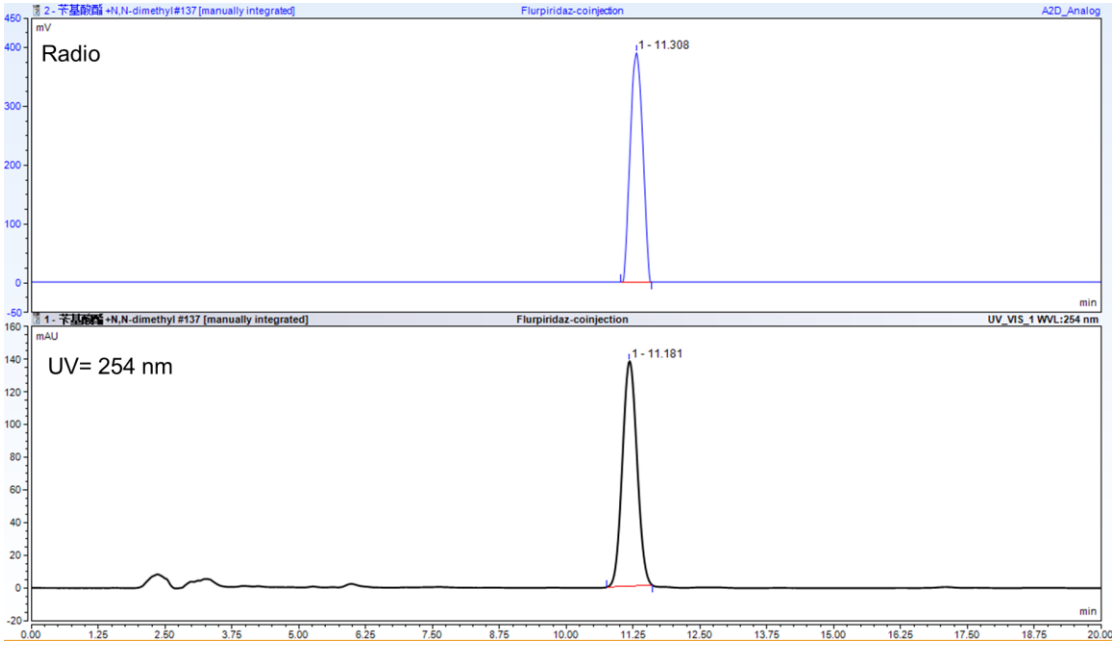


Fig. S27: Co-injection for [^{18}F]**45**. 1# HPLC condition: NanoChrom C18 column (5 μm, 4.6 × 250 mm), isocratic elution, H_2O/CH_3CN = 50/50, and the flow rate was 1 mL/min for 20 min. The RCP was >98%.

Preparation of BFPA-E[c(RGDyK)]$_2$

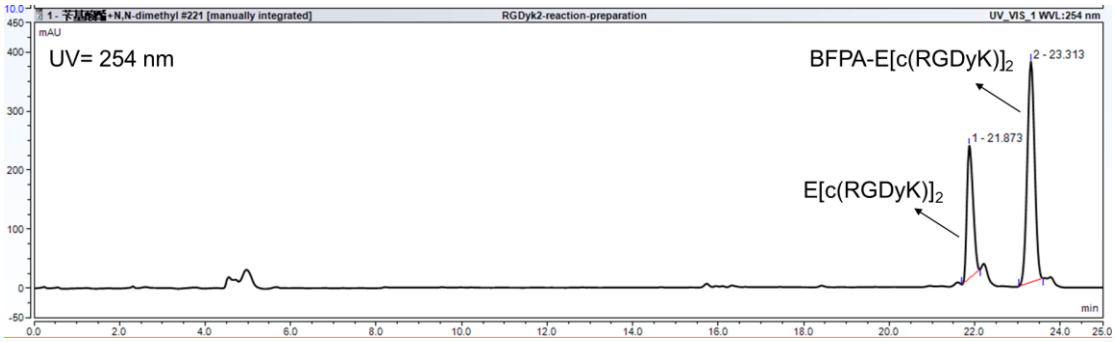
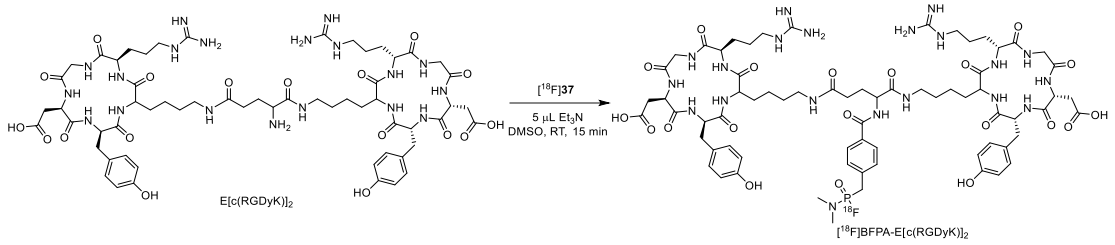


Fig. S28: HPLC traces of crude products. 1# HPLC conditions: SEP Basic-C18 semi-preparative column (120A 5μm 10 × 250mm); gradient elution, 0−10 min, from 10% of CH_3CN and 90% of water containing 0.1%TFA to 20% of CH_3CN and 80% of water containing 0.1%TFA; 10−25 min, from 20% of CH_3CN and 80% of water containing 0.1%TFA to 30% of CH_3CN and 70% of water containing 0.1%TFA; flow rate: 3.0 mL/min.

Preparation of [^{18}F]BFPA-E[c(RGDyK)]$_2$



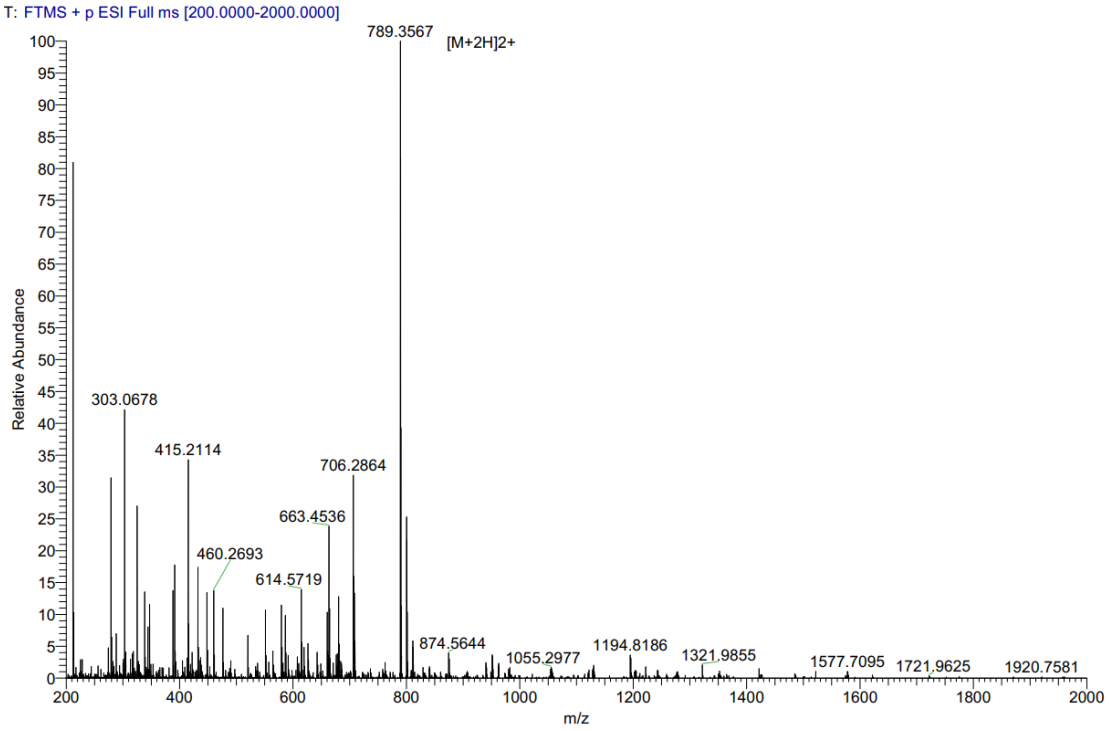


Fig. S29: Mass spectrometry identification of standards. **HRMS (m/z)** calculated for $C_{69}H_{99}FN_{20}O_{20}P^{2+}$ ($[M+2H]^{2+}$): 789.3567 found: 789.3567.

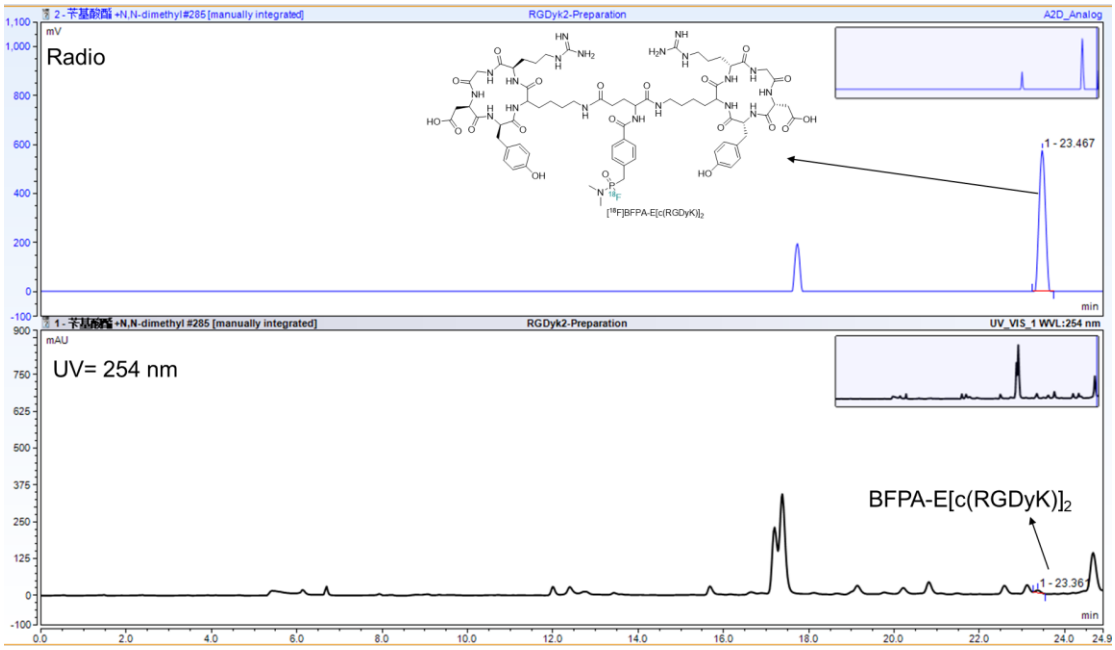


Fig. S30: HPLC traces of crude ^{18}F-labeled products. 1# HPLC conditions: SEP Basic-C18 semi-preparative column (120A 5μm 10 × 250mm); gradient elution, 0−10 min, from 10% of CH_3CN and 90% of water containing 0.1%TFA to 20% of CH_3CN and 80% of water containing 0.1%TFA; 10−25 min, from 20% of CH_3CN and 80% of water containing 0.1%TFA to 30% of CH_3CN and 70% of water containing 0.1%TFA; flow rate: 3.0 mL/min.

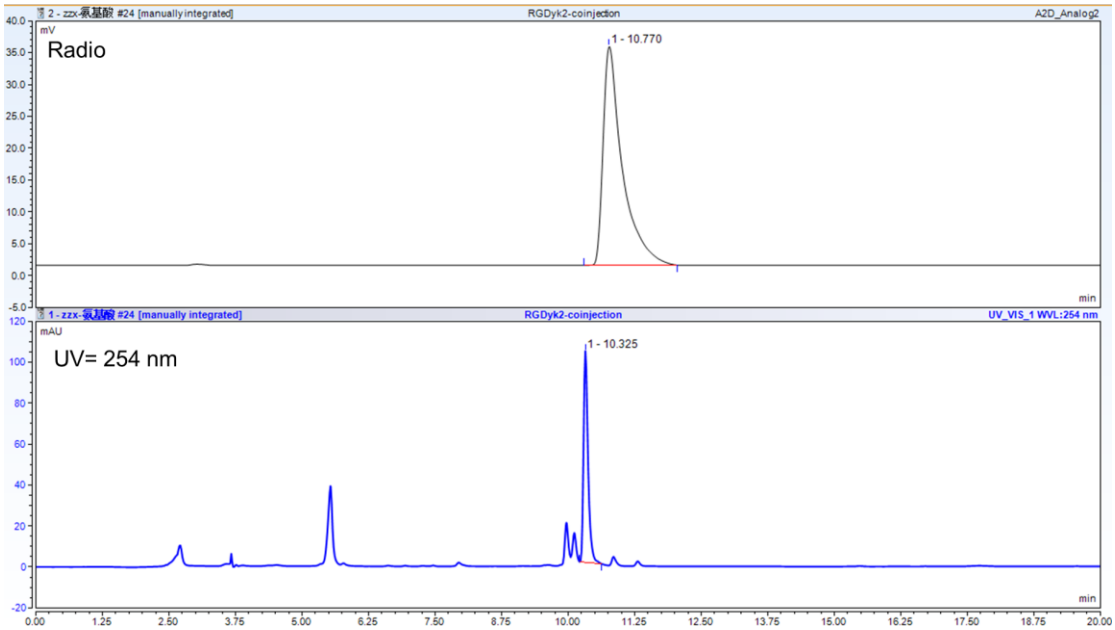
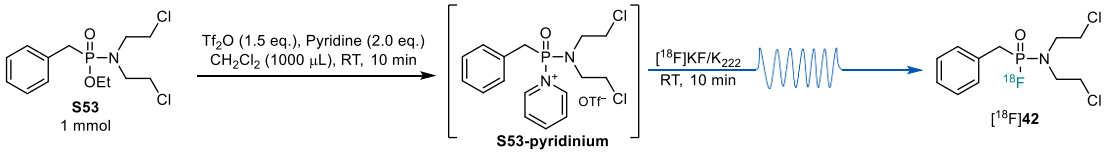


Fig. S31: Co-injection for [^{18}F]BFPA-E[c(RGDyK)]$_2$. 2# HPLC condition: NanoChrom C18 column (5 μm, 4.6 × 250 mm), gradient elution, from 10% of CH_3CN and 90% of water containing 0.1%TFA to 50% of CH_3CN and 50% of water containing 0.1%TFA, and the flow rate was 1 mL/min for 20 min. The RCP was > 99%.

2.4 Automated radiosynthesis

2.4.1 Synthesizing [^{18}F]42 on an Allinone module



The automated synthesis of [^{18}F]**42** was performed on an AllinOne module (Trasis, Ans, Belgium) following this stepwise procedure, and the resultant module program was edited in Trasis-AllinOne 2.3.4.

The Sep-Pak® Plus Short C18 cartridge and Sep-Pak® Light QMA cartridge utilized in the experiment were pre-activated and subsequently loaded into the cartridge as detailed in section **1.3** of this report. Slot 2 was filled with a solution containing 8.0 mg of K_{222}, 1.0 mg of K_2CO_3 in CH_3CN/H_2O (4/1, v/v, 0.5 mL) as the eluent. Slot 3 was filled with an anhydrous CH_2Cl_2 (1.0 mL) solution of the precursor 1-(benzyl(bis(2-chloroethyl)amino)phosphoryl)pyridin-1-ium. The solvent reservoirs (slot 14 and 15) were filled with anhydrous EtOH (~10 mL) and CH_3CN (~20 mL), respectively, and a water bag was placed in slot 16. During liquid transmission, the dead volume of the corresponding pipeline should be cleared based on the actual situation to ensure the precision of the liquid dosage.

The [^{18}F]fluoride obtained from the [^{18}O]H_2O supplied by the cyclotron is captured on the QMA located in slot 5. Subsequently, the QMA is purged with air, followed by the elution of [^{18}F]fluoride from the QMA into the reactor using the eluent from slot 2. 1 mL of CH_3CN is added and then dried under an airflow at 110 ℃. Once the drying process is completed and the reactor temperature returns to room temperature, the precursor solution from slot 3 is transferred into the reactor. The resulting mixture is agitated and thoroughly mixed using a syringe in slot 3, with this step repeated twice for homogenization. Subsequently, the loop is purged with 3 mL of air, and the reaction mixture is allowed to proceed at room temperature for 10 min. After the completion of the reaction, 9 mL of water is added to the reactor to dilute the reaction mixture. Subsequently, the organic compounds in the mixture are trapped on the C18 in slot 9. Using a syringe, 10 mL of water is slowly injected into the C18 for washing, followed by air blowing to remove fluoride ions and acidic impurities. Finally, the crude product is eluted with 0.5 mL of CH_3CN into a transfer vial, and then injected into the HPLC

system for separation. The crude reaction mixture is purified using reverse-phase semi-preparative HPLC (120A 5μm 10 × 250mm). Receive the CH_3CN/H_2O mixed solution separated by HPLC in another transfer vial, dilute it with water (10 mL), then concentrate the product on the C18 in slot 13. Dry the captured product with air blowing, then elute the desired [^{18}F]**42** into a product vial using 0.5 mL of EtOH. Subsequently, take an appropriate amount for the determination of A_m.

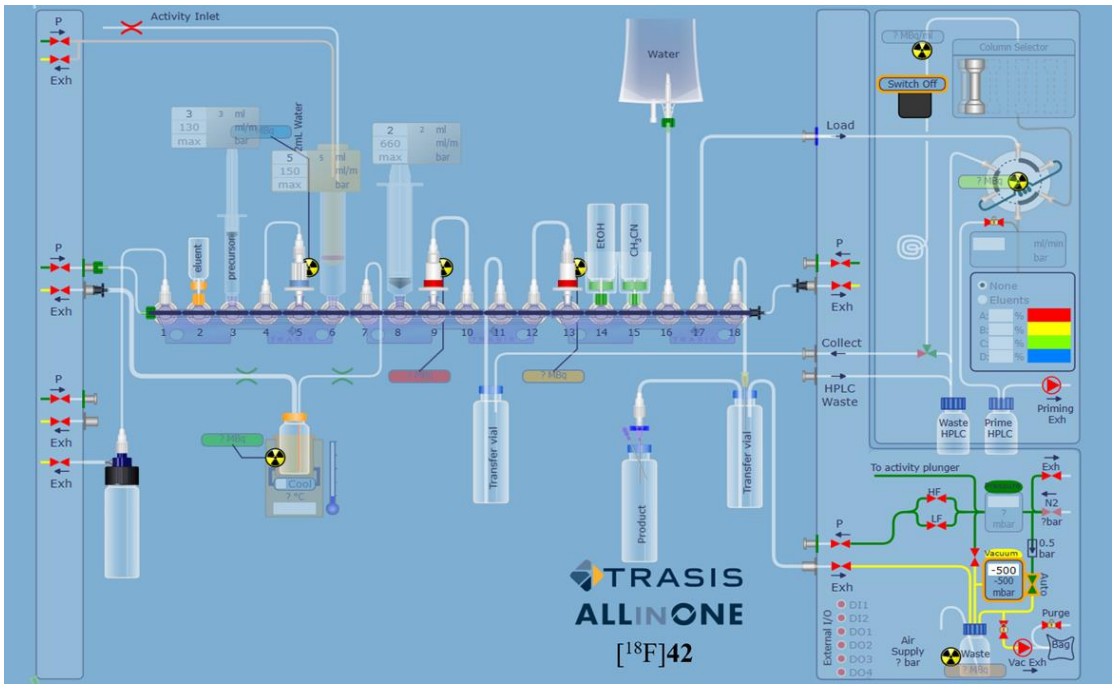


Fig. S32: Graphical representation of the cassette designed for the automated synthesis of [^{18}F]**42** on a Trasis AllinOne synthesizer.

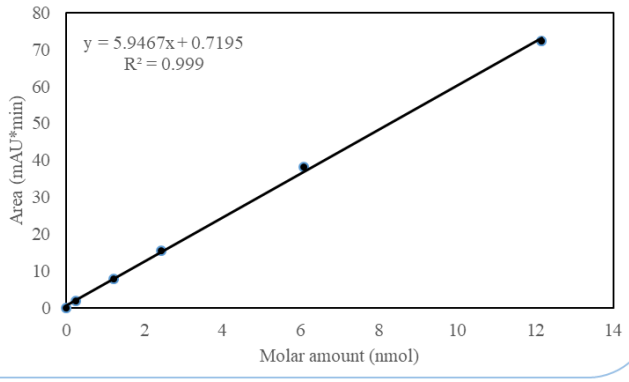
2.4.2 Molar activity calculations

A_m values were determined with the separated chemically and radiochemically pure samples > 99% purity samples. The sample was injected into HPLC to record the injection activity and injection time, respectively. Subsequently, the UV signal corresponding to the desired radioactive fluorination product was integrated, the chemical amount of the sample is calculated by the standard curve, and then A_m is calculated.

Molar activity calculation of [^{18}F]37

The standard curve (**Fig. S33**) of HPLC peak area (UV, 254 nm) versus molar amount of **37** was plotted.

Molar amount of **37** (nmol)	Area (mAU*min)
0	0
12.16	72.2557
6.08	38.2970
2.432	15.5376
1.216	7.9405
0.2432	1.8951



Standard curve equation: $y = 5.9467x + 0.7195$

Fig. S33: Standard curve acquired with **37** at 254 nm

Table S16: Molar activity calculation of [^{18}F]**37**

Measurement	Activity injected （MBq, d.c.）	Peak area (mAU*min)	Molar amount (μmol)	A_m (GBq/μmol)
1	0.402	0.785	1.10×10^{-5}	36.5
2	2.459	1.028	5.19×10^{-5}	47.4

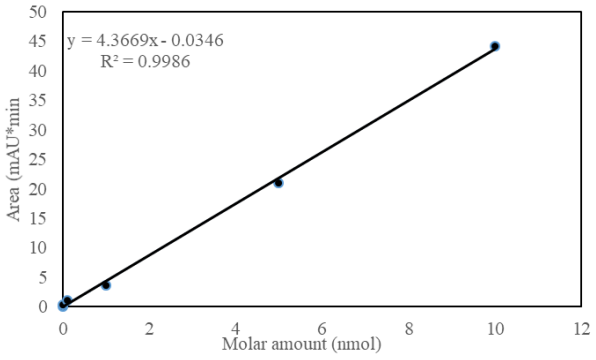
"d.c." means decay correction.

The isolated [^{18}F]**37** has an average A_m of 42 ± 7 GBq/μmol (n = 2).

Molar activity calculation of [^{18}F]40

The standard curve (**Fig. S34**) of HPLC peak area (UV, 254 nm) versus molar amount of **40** was plotted.

Molar amount of **40** (nmol)	Area (mAU*min)
0	0
0.01	0.3104
0.1	0.2958
1	3.6245
5	20.9223
10	44.1360



Standard curve equation: $y = 4.33669x - 0.0346$

Fig. S34: Standard curve acquired with [^{18}F]**40** at 254 nm

Table S17: Molar activity calculation of [^{18}F]**40**

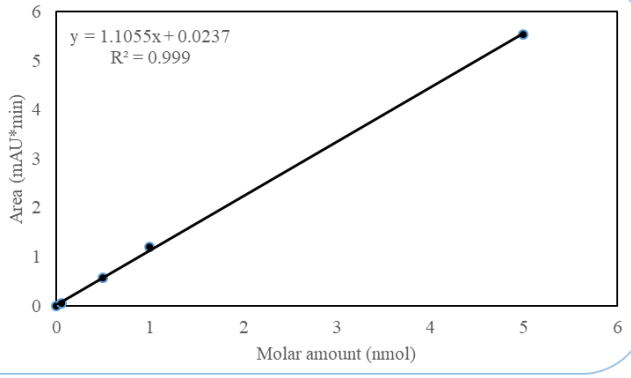
Measurement	Activity injected (MBq, d.c.)	Peak area (mAU*min)	Molar amount (µmol)	A_m (GBq/µmol)
1	2.64	0.0852	2.74×10^{-5}	95
2	3.88	0.1118	3.35×10^{-5}	115.8

The isolated [^{18}F]**40** has an average A_m of 105 ± 14 GBq/µmol (n = 2).

Molar activity calculation of [^{18}F]42

The standard curve (**Fig. S35**) of HPLC peak area (UV, 254 nm) versus molar amount of **42** was plotted.

Molar amount of **42** (nmol)	Area (mAU*min)
0	0
0.05	0.0506
0.5	0.5669
1	1.2046
5	5.5372



Standard curve equation: $y = 1.1055x + 0.0237$

Fig. S35: Standard curve acquired with **42** at 254 nm

Table S18: Molar activity calculation of [^{18}F]**42**

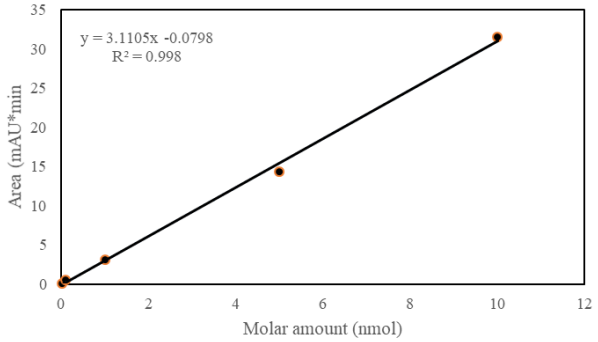
Measurement	Activity injected (MBq, d.c.)	Peak area (mAU*min)	Molar amount (µmol)	A_m (GBq/µmol)
1	7.08	0.0544	2.778×10^{-5}	254.9
2	8.03	0.0271	3.076×10^{-5}	261.1
3	7.41	0.0582	3.121×10^{-5}	237.4

The isolated [^{18}F]**42** has an average A_m of 251 ± 12 GBq/µmol (n = 3).

Molar activity calculation of [^{18}F]43

The standard curve (**Fig. S36**) of HPLC peak area (UV, 254 nm) versus molar amount of **43**was plotted.

Molar amount of **43** (nmol)	Area (mAU*min)
0	0
0.01	0.0702
0.1	0.549
1	3.168
5	14.359
10	31.565



Standard curve equation: $y = 3.1105x - 0.0798$

Fig. S36: Standard curve acquired with **43** at 254 nm

Table S19: Molar activity calculation of [^{18}F]**43**

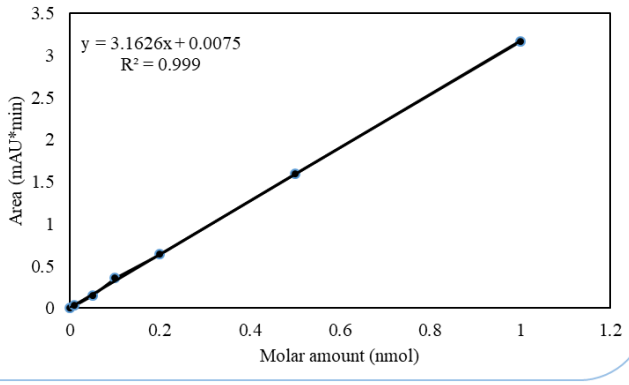
Measurement	Activity injected （MBq, d.c.）	Peak area (mAU*min)	Molar amount (μmol)	A_m (GBq/μmol)
1	2.98	0.0982	5.72×10^{-5}	52.1
2	7.322	0.2550	10.76×10^{-5}	68

The isolated [^{18}F]**37** has an average A_m of 60 ± 11 GBq/μmol (n = 2).

Molar activity calculation of [^{18}F]45

The standard curve (**Fig. S37**) of HPLC peak area (UV, 254 nm) versus molar amount of **45** was plotted.

Molar amount of **45** (nmol)	Area (mAU*min)
0	0
0.01	0.0301
0.05	0.1489
0.1	0.3545
0.2	0.6422
0.5	1.5951
1	3.1644



Standard curve equation: $y = 3.1626x + 0.0075$

Fig. S37: Standard curve acquired with **45** at 254 nm

Table S20: Molar activity calculation of [^{18}F]**45**

Measurement	Activity injected (MBq, d.c.)	Peak area (mAU*min)	Molar amount (μmol)	A_m (GBq/μmol)
1	2.891	0.0863	2.492×10^{-5}	116

The isolated [^{18}F]**45** has an average A_m of 116 GBq/μmol.

2.5 From Stability to Interaction

2.5.1 Stability evaluation

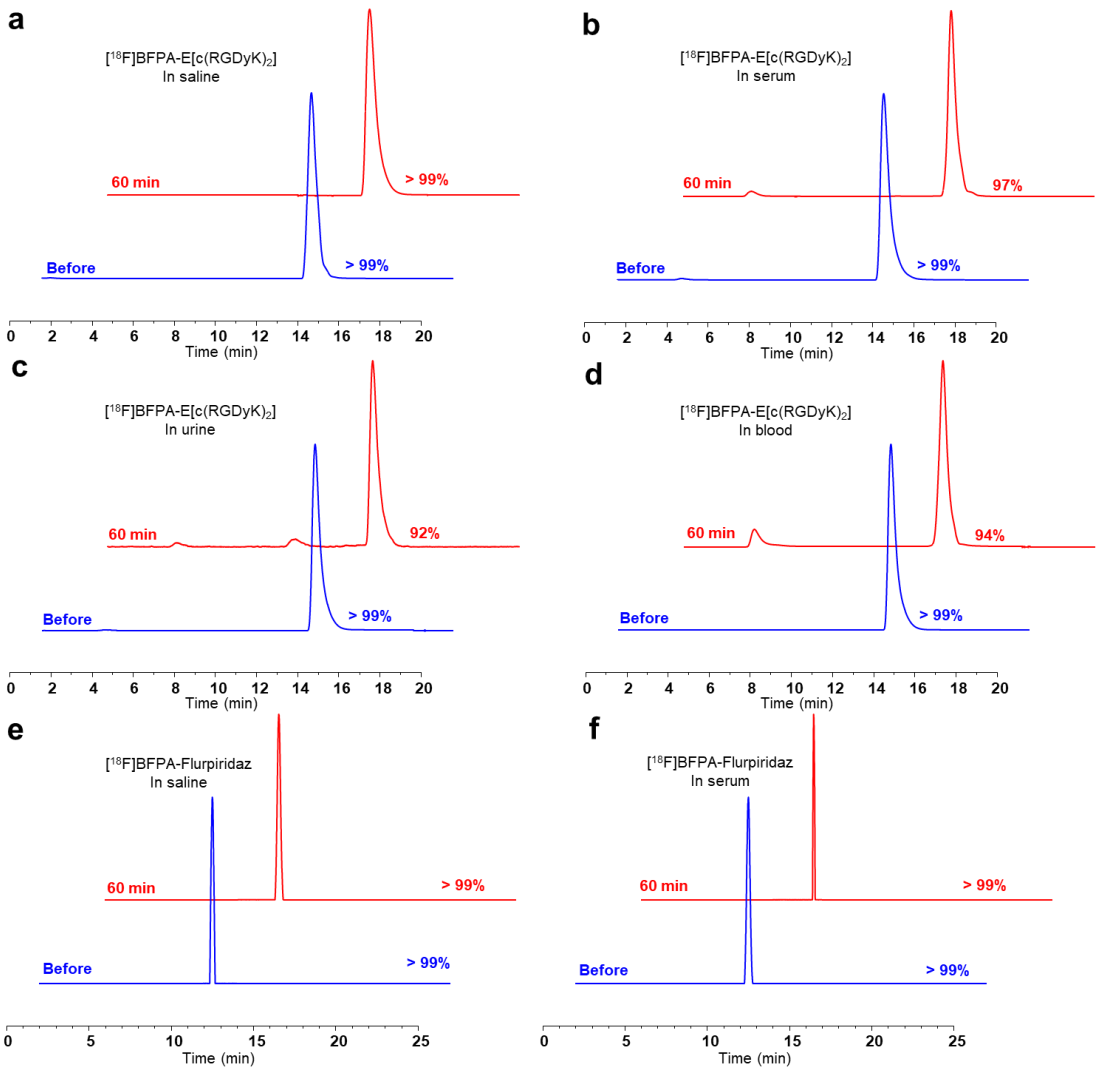


Fig. S38: Stability of radiotracer in *vivo* and *vitro* for 60 min. (**a**, **b**) Radio-HPLC analysis

demonstrated that the stability of [^{18}F]BFPA-E[c(RGDyK)]$_2$ in saline > 99% and serum > 97% *in vitro*. 1# HPLC conditions: NanoChrom C18 column (5 μm, 4.6 × 250 mm), gradient elution, from 10% of CH_3CN and 90% of water containing 0.1%TFA to 50% of CH_3CN and 55% of water containing 0.1%TFA, and the flow rate was 1 mL/min for 20 min. (**c**, **d**) Radio-HPLC analysis demonstrated that [^{18}F]BFPA-E[c(RGDyK)]$_2$ remains stable at over 92% in urine and over 94% in blood *in vivo*. (**e**, **f**) Radio-HPLC analysis also confirmed that [^{18}F]BFPA-Flurpiridaz exhibited stability of over 99% in both saline and serum *in vitro*. HPLC conditions were consistent with **Fig. S27**.

2.5.2 IC_{50} determination *via* cell competitive binding assay

The IC_{50} value for [^{18}F]BFPA-Flurpiridaz was found to be 148.0 nM, which is significantly lower than the IC_{50} of 248.2 nM for the parent compound Flurpiridaz. This suggests that the modified with fluorophosphine moiety tracer exhibits enhanced binding affinity.

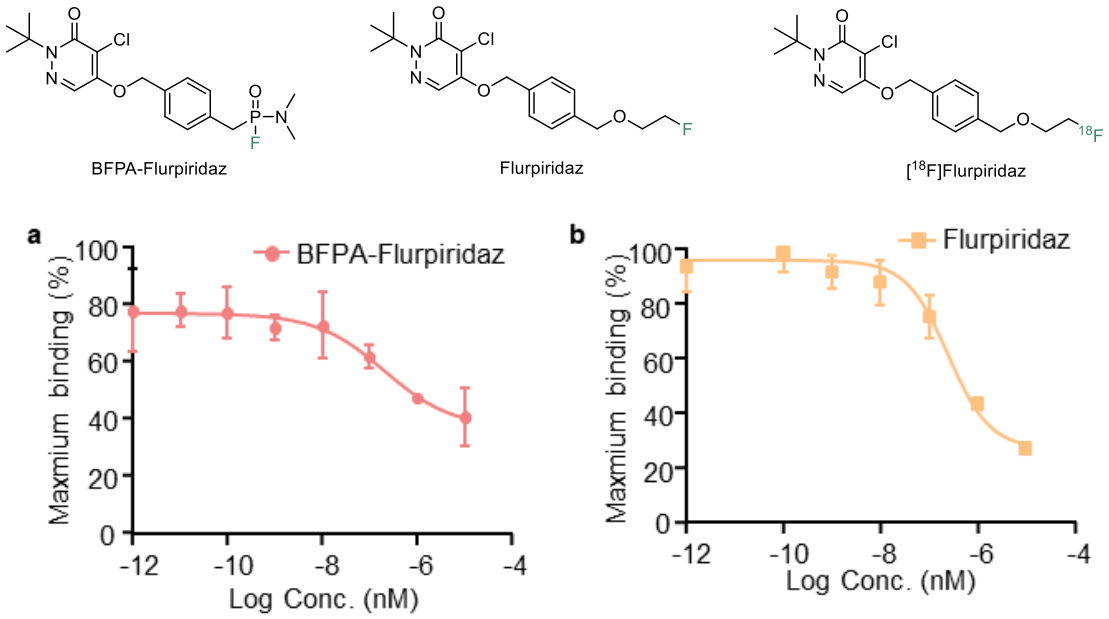
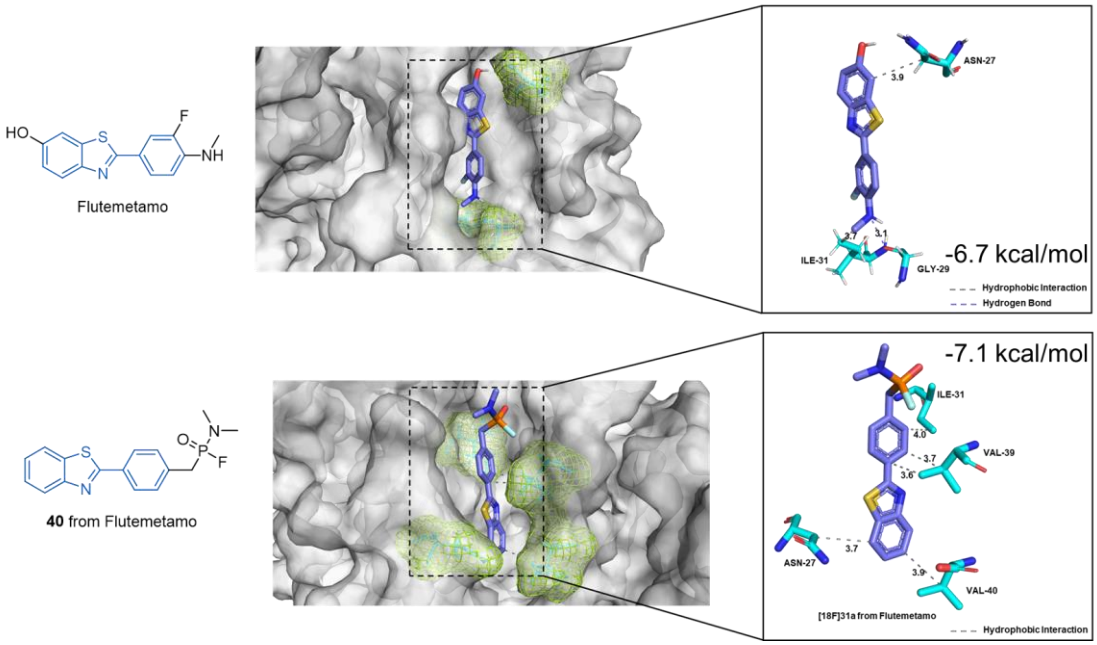


Fig. S39: IC_{50} curves of BFPA-Flurpiridaz (**a**) and Flurpiridaz (**b**) inhibiting [^{18}F]Flurpiridaz.

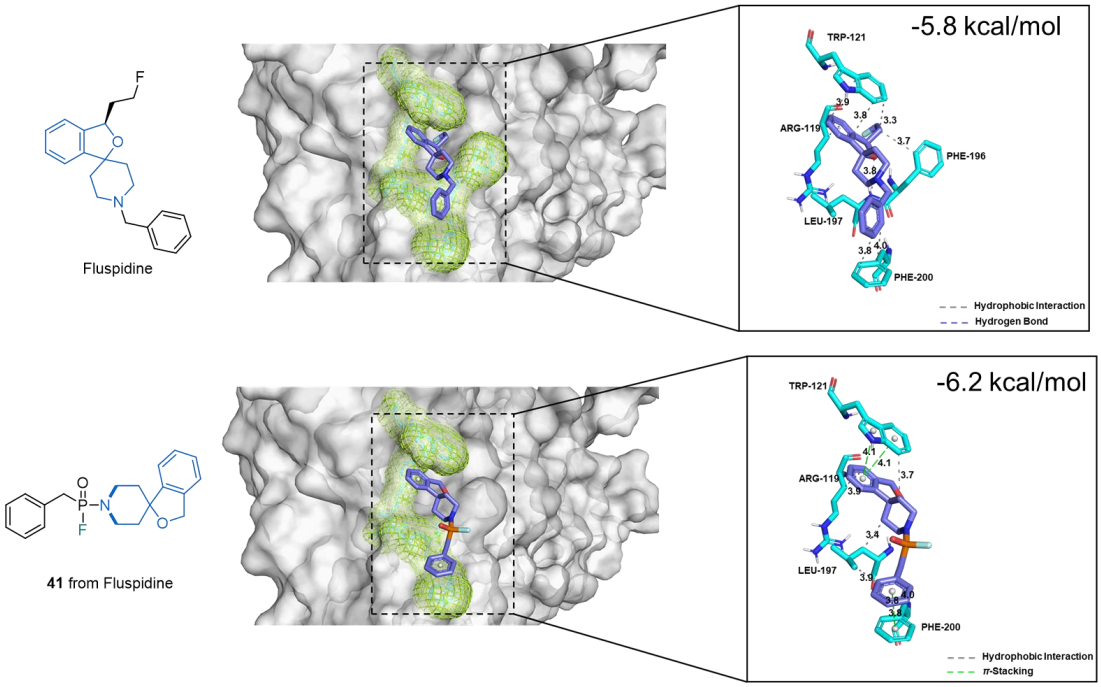
2.5.3 Molecular Docking

The docking results revealed that the binding modes of the parent drug and the BFPA-modified derivative were nearly identical, indicating that the modification did not impair the drug's binding affinity or interaction with the protein. Notably, in certain cases, the BFPA-modified derivatives were able to form an additional hydrogen bond (the additional hydrogen bond donor is from the P=O), which may enhance the overall binding interaction with the target protein.[13-15]

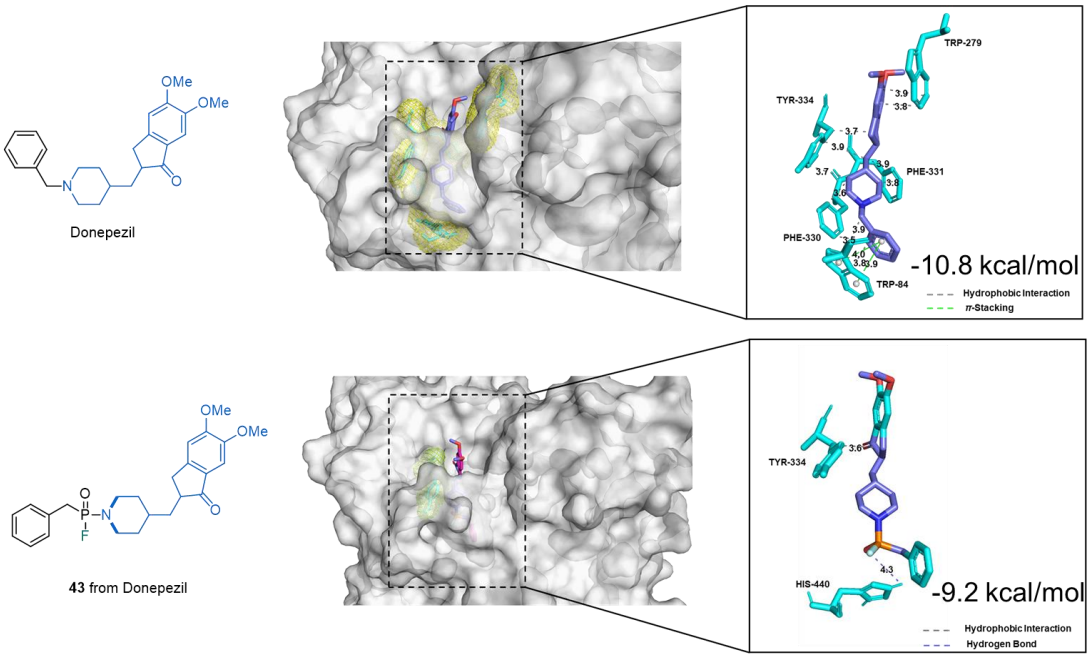
a. Docking Flutemetamo and **40** to Aβ. (PDB: 2LMO)



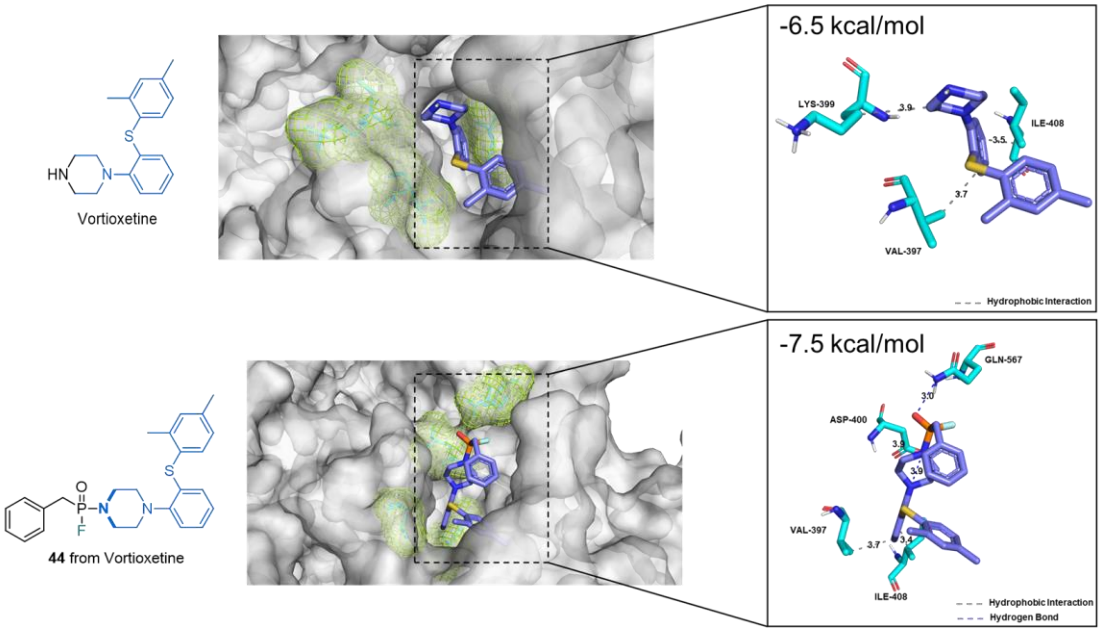
b. Docking Fluspidine and **41** to σ1. (PDB: 5HK1)



c. Docking Donepezil and **43** to AChE. (PDB: 1EVE)



d. Docking Vortioxetine and **44** to SERT. (PDB: 6ZDV)



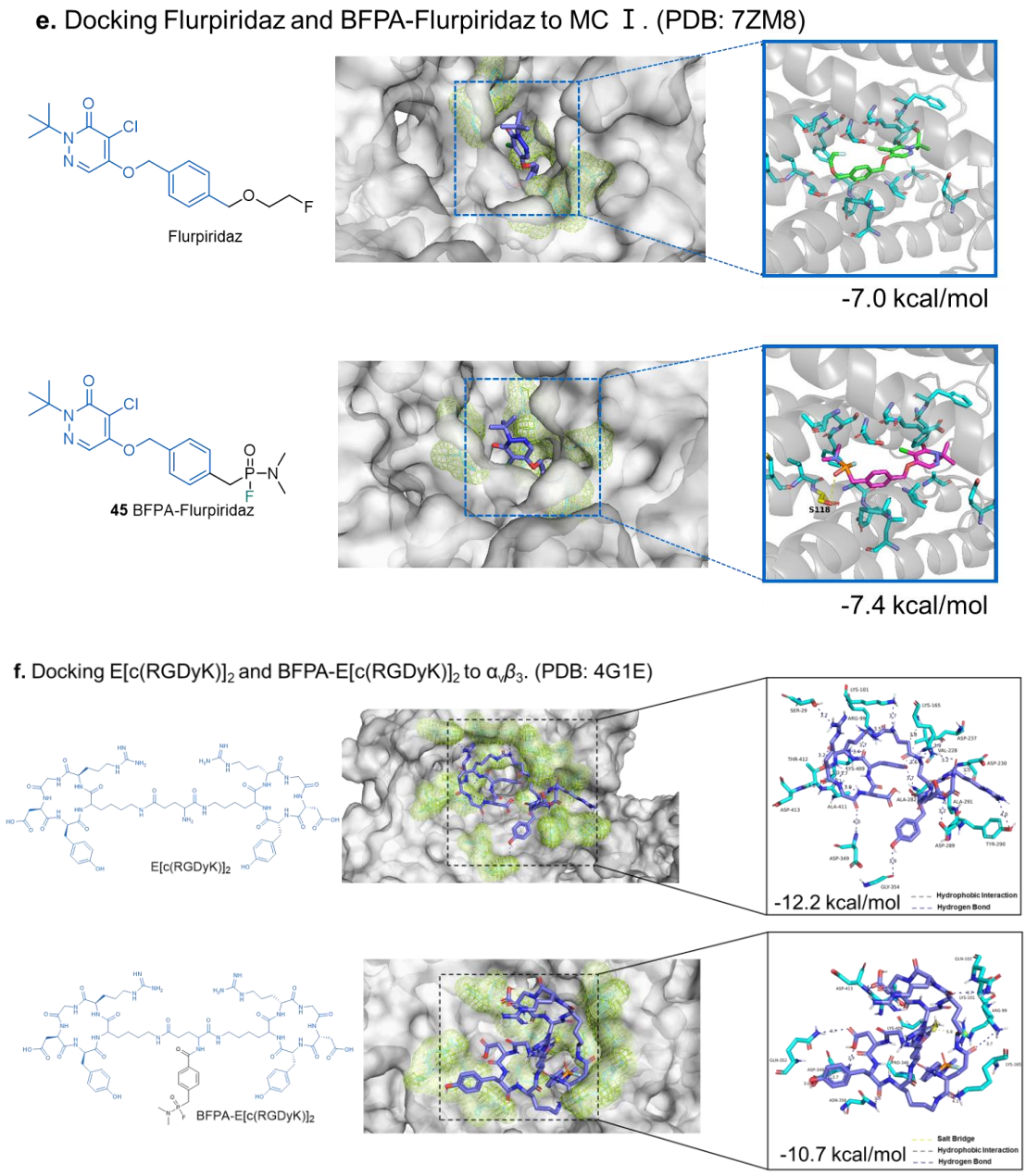
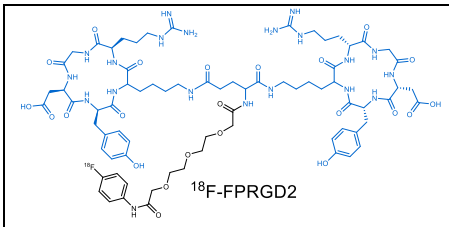
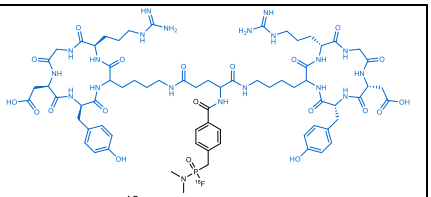
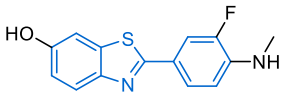
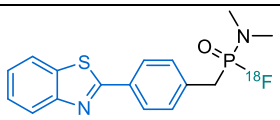
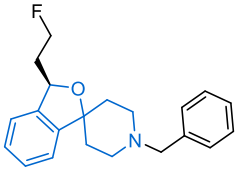
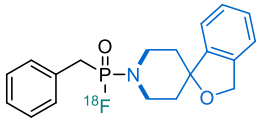
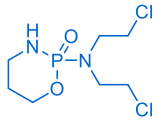
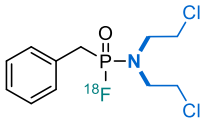
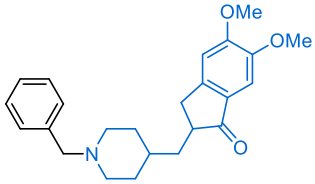
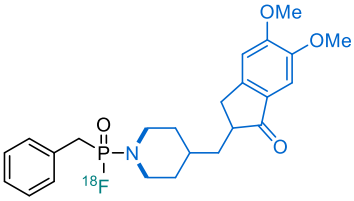
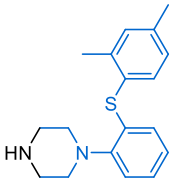
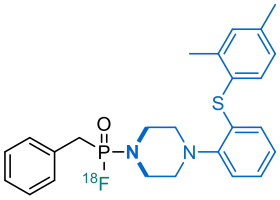


Fig. S40: Ligand−protein docking. All protein structures are sourced from the Protein Data Bank (PDB, http://www.rcsb.org/).

Table S21: Physicochemical Properties Analysis: cLog *P* and Log *D*

Log $D_{7.4}$ of original molecule	Trend	Log $D_{7.4}$ of BFPA-modified
Flurpiridaz Log $P = 2.73$[16]		[^{18}F]BFPA-Flurpiridaz ([^{18}F]**45**) Log $D_{7.4} = 2.06 \pm 0.01$

 ^{18}F-FPRGD2 Log P = -2.28 ± 0.05[17]		 [^{18}F]BFPA-E[c(RGDyK)]$_2$ Log $D_{7.4}$ = -2.05 ± 0.04
cLog P of original molecule	Trend	cLog P of BFPA-modified
 Flutemetamo cLog P = 4.16		 [^{18}F]**40** from Flutemetamo cLog P = 3.09
 Fluspidine cLog P = 4.08		 [^{18}F]**41** from Fluspidine cLog P = 2.89
 Cyclophosphamide cLog P = 0.76		 [^{18}F]**42** from cyclophosphamide cLog P = 2.64
 Donepezil cLog P = 4.14		 [^{18}F]**43** from Donepezil cLog P = 3.93
 Vortioxetine cLog P = 4.51		 [^{18}F]**44** from Vortioxetine cLog P = 5.40

2.6 Positron emission tomography imaging

2.6.1 Animal models. All animal procedures were conducted in accordance with the Guide for the Care and Use of Laboratory Animals and approved by the Animal Care and Use Committee of Xiamen University (240506 XMULAC20240099).

2.6.2 *In vivo* MicroPET imaging of [^{18}F]BFPA-E[c(RGDyK)]$_2$ was conducted in U87MG glioma xenografts in male nude mice.

All MicroPET/CT images were acquired using an Inveon MicroPET/CT scanner (Siemens) and subsequently analyzed with the Inveon Research Workplace Software (Siemens).

For the MicroPET imaging study, an U87MG tumor-bearing male nude mice received a bolus tail-vein injection of a solution of [^{18}F]BFPA-E[RGDyk]$_2$ (~3.7 MBq) dissolved in 0.9% saline (100 μL). The mouse was anesthetized using inhaled 2% isoflurane 25 min after injection and then placed on the MicroPET/CT scanner bed. A 5 min PET scan was performed at 30 min after injection.

2.6.3 Blocking study

A male nude mice with an U87MG tumor was administered a bolus tail-vein injection of a solution containing [^{18}F]BFPA-E[RGDyk]$_2$ (~3.7 MBq) and E[c(RGDyK)]$_2$ (200 μg), dissolved in 0.9% saline (100 μL). The mice was anesthetized with 2% inhaled isoflurane 25 min after injection and then carefully positioned on the MicroPET/CT scanner bed. Subsequently, a 5 min MicroPET scan was performed at 30 min post-injection to assess the imaging results.

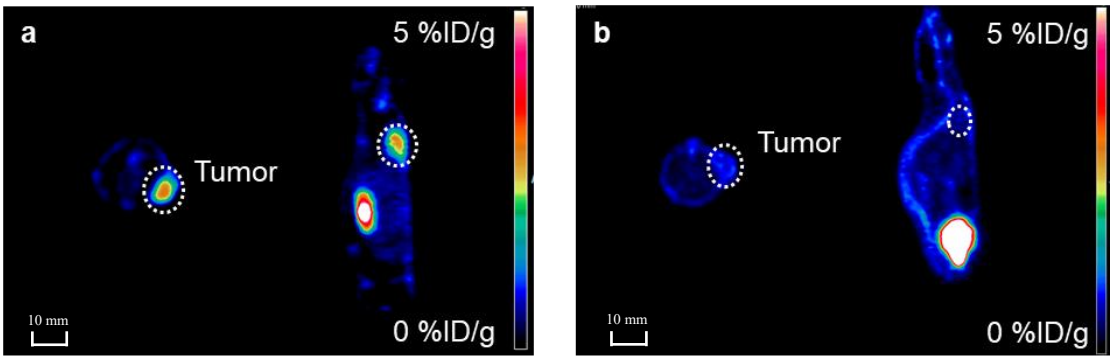


Fig. S41: a MicroPET images of [^{18}F]BFPA-E[c(RGDyK)]$_2$ in U87MG xenograft mice at 30 min after tail vein injection. **b** MicroPET images of U87MG xenograft mice at 30 min after simultaneous injection of [^{18}F]BFPA-E[c(RGDyK)]$_2$ and E[c(RGDyK)]$_2$ (200 μg).

2.7 Mechanism proposal and computational study

2.7.1 Research mechanisms: NMR and MS

The possible compounds in the reaction system were estimated by ^{1}HNMR, ^{19}F NMR and ^{31}P NMR *in situ*.

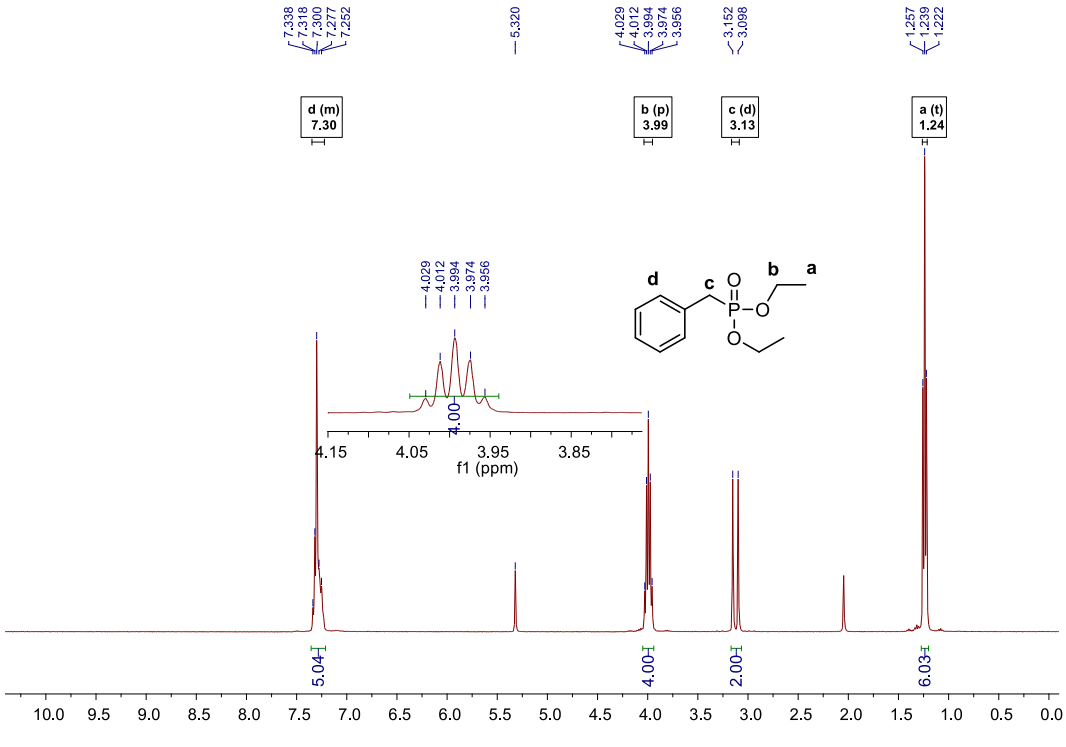
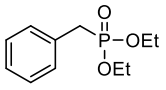


Fig. S42: ^{1}H NMR of  in CD_2Cl_2, 400 MHz.

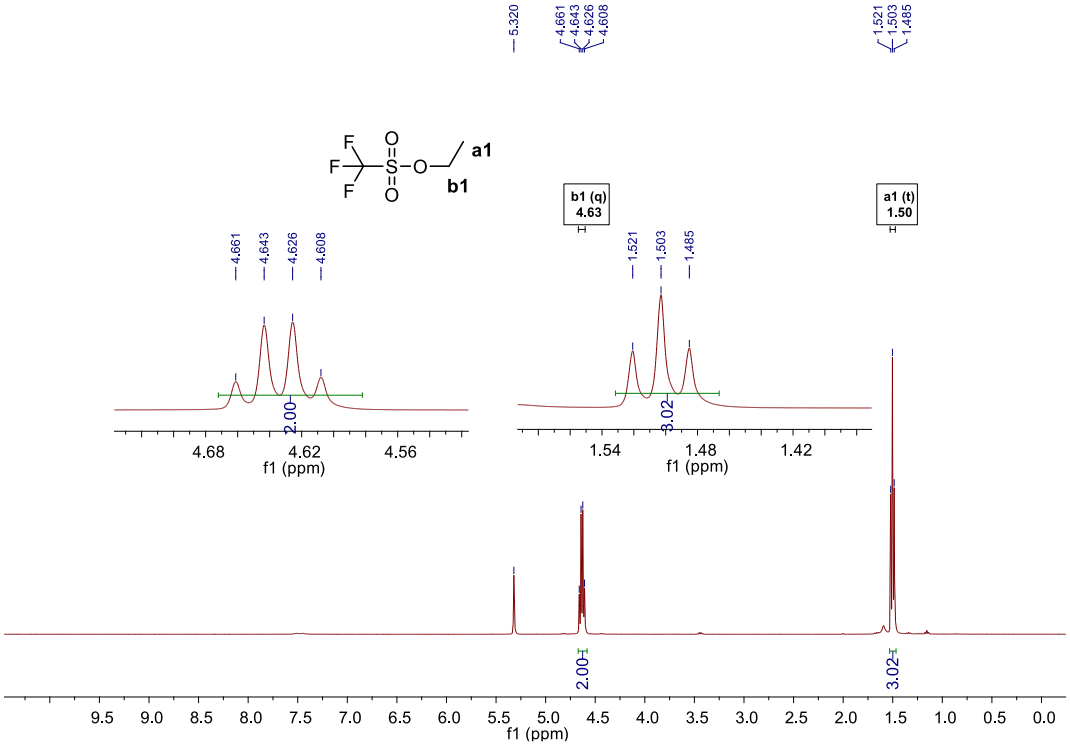


Fig. S43: ^{1}H NMR of TfOEt in CD_2Cl_2, 400 MHz.

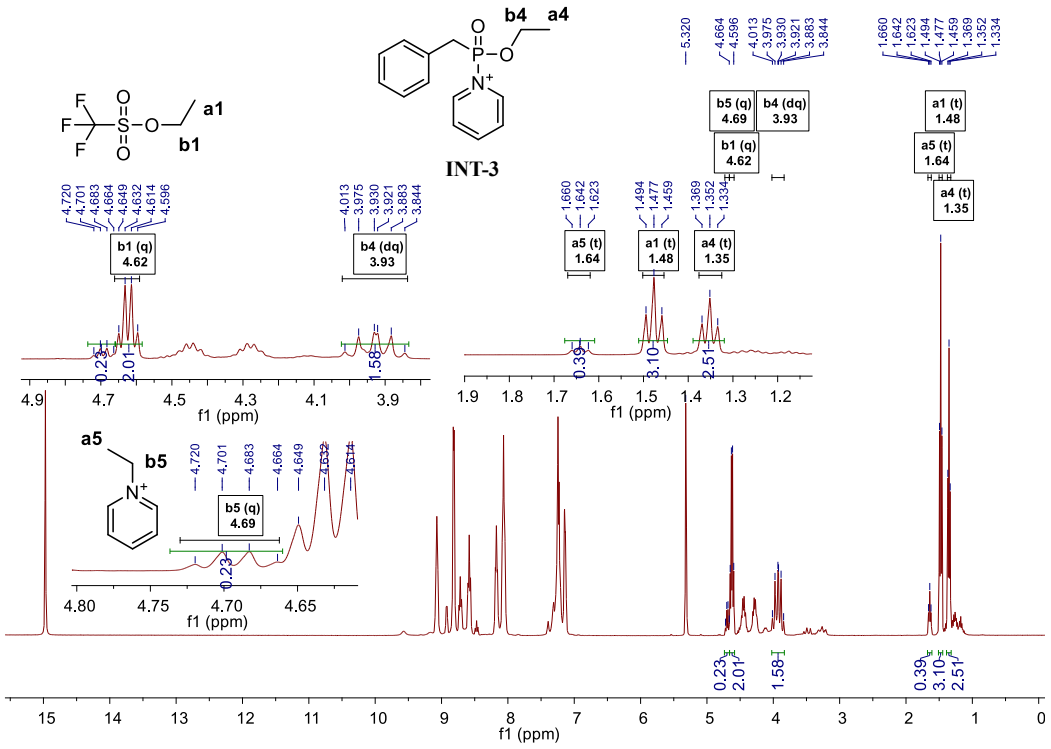
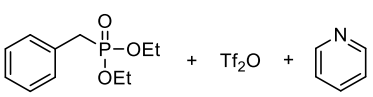


Fig. S44: Crude ^{1}H NMR of  in CD_2Cl_2, 400 MHz.

In the reaction system, 1-ethylpyridin-1-ium detected may be the product of the reaction between pyridine and TfOEt.

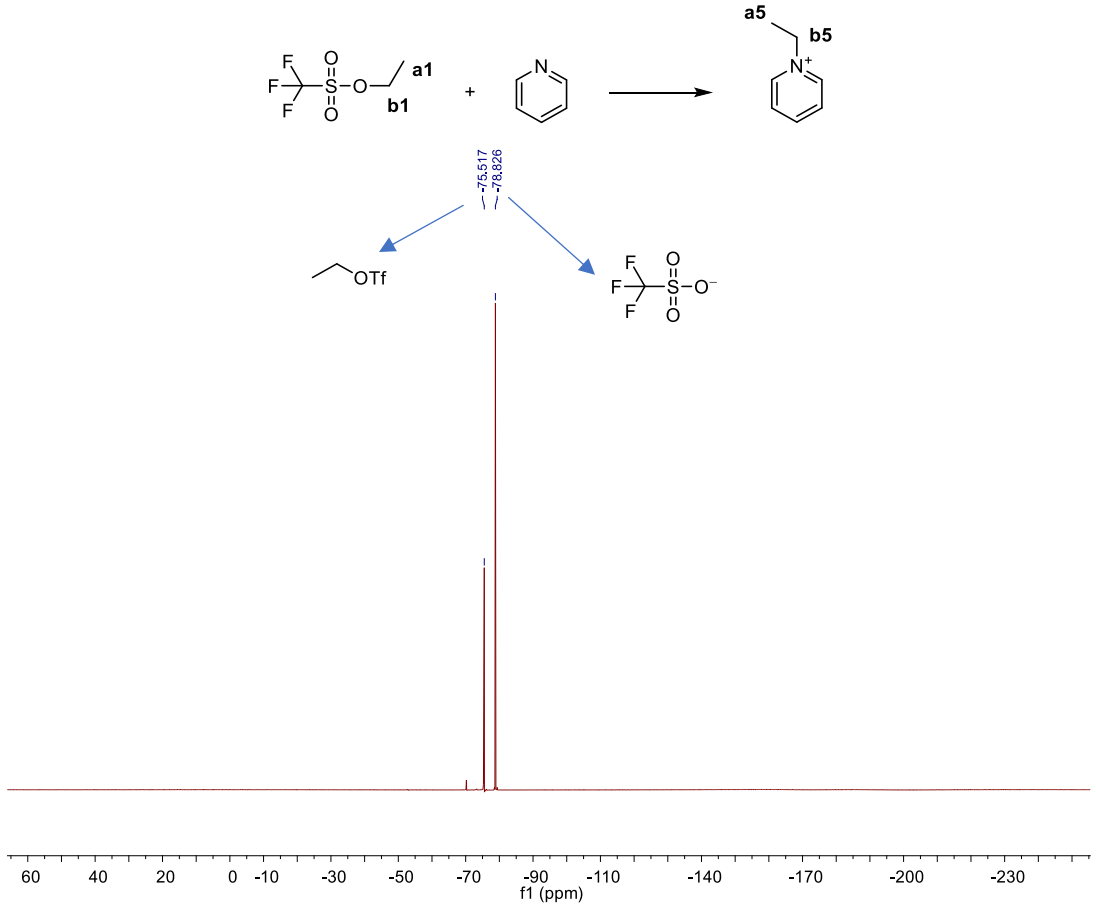
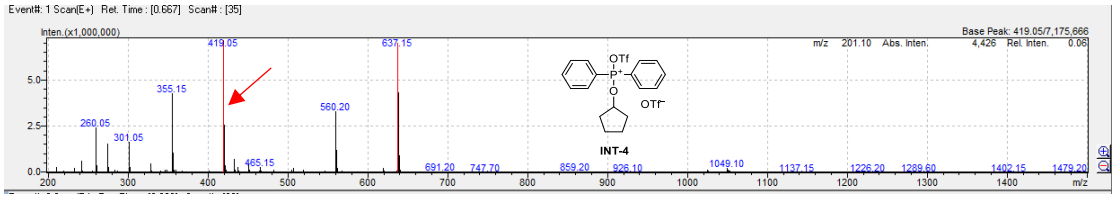


Fig. S45: Crude ^{19}F NMR of + Tf_2O + in CD_2Cl_2, 162 MHz.

INT-4: MS (m/z) calculated for $C_{18}H_{19}F_3O_4PS^+$ $[M+H]^+$: 419.0688; found: 419.05.



INT-5: MS (m/z) calculated for $C_{23}H_{24}F_3NO_4PS^+$ $[M+H]^+$: 498.1110; found: 498.10.

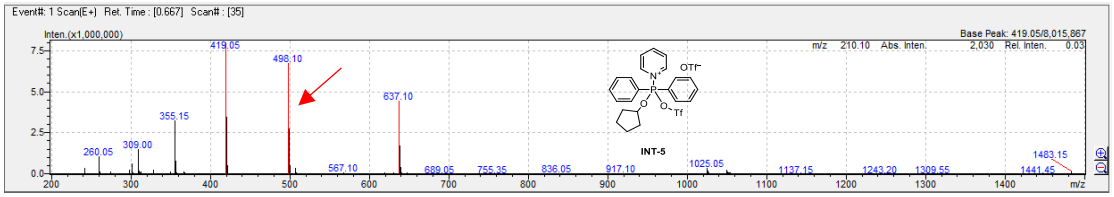


Fig. S46: MS determination of fluorination of compound **S8** *in situ*.

2.7.2 Reaction pathways and free-energy profiles

Computational Details:

Calculations were carried out using the Gaussian 09 programme. Geometries were optimized using the M06 density functional method[18] and 6-31G* basis set. Solvation effect was treated by the default PCM method[19]. Then, frequency analyses were performed at the same level of theory. Single-point energy calculations were performed using the 6-311++G** basis set with the same density functional method and solvation model.

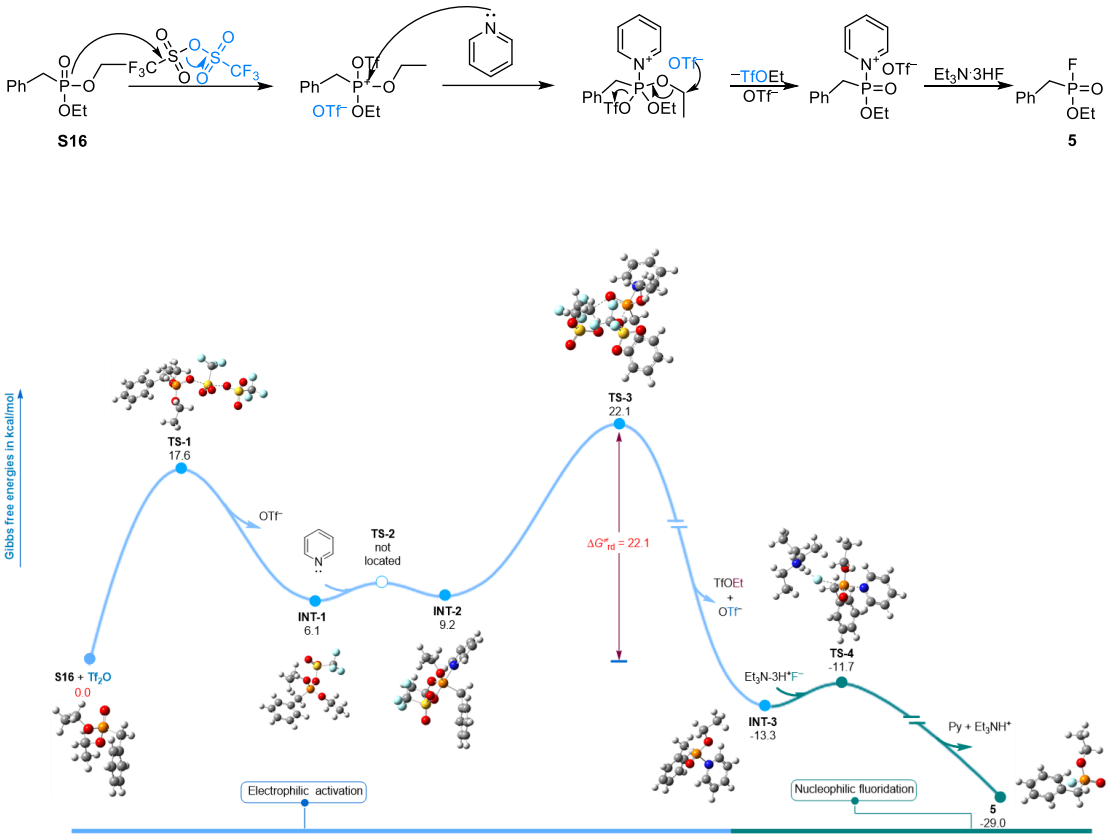


Fig.. S47: Using the Gaussian 09 program, DFT calculations at the m06+GD3/6-311++G** level of theory were employed to predict activation energy barriers for the mechanistic proposal for fluorination of alkyl phosphonates, along with reaction pathways and free-energy profiles. Gaussview 5.0 is used for data analysis.

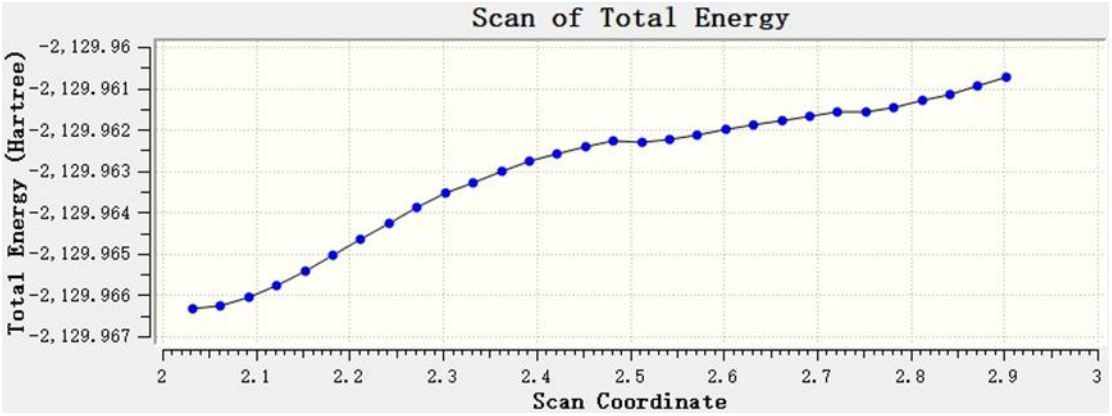


Fig. S48: Scan of total energy with respect to the P···N distance from 2.03 to 2.95 Å indicates that transition state between B and C may not exist.

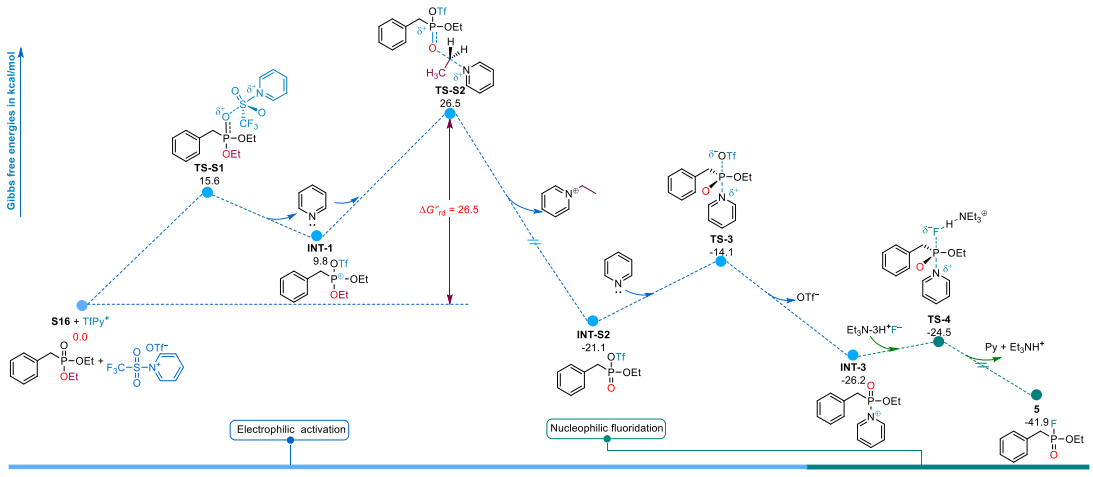


Fig. S49: The energy distribution of alkyl phosphonate (**S16**) activated by Tf_2O for fluorination at a less likely alternative pathway.

3. Supplementary Figures

3.1 Radio-TLC traces of RCCs

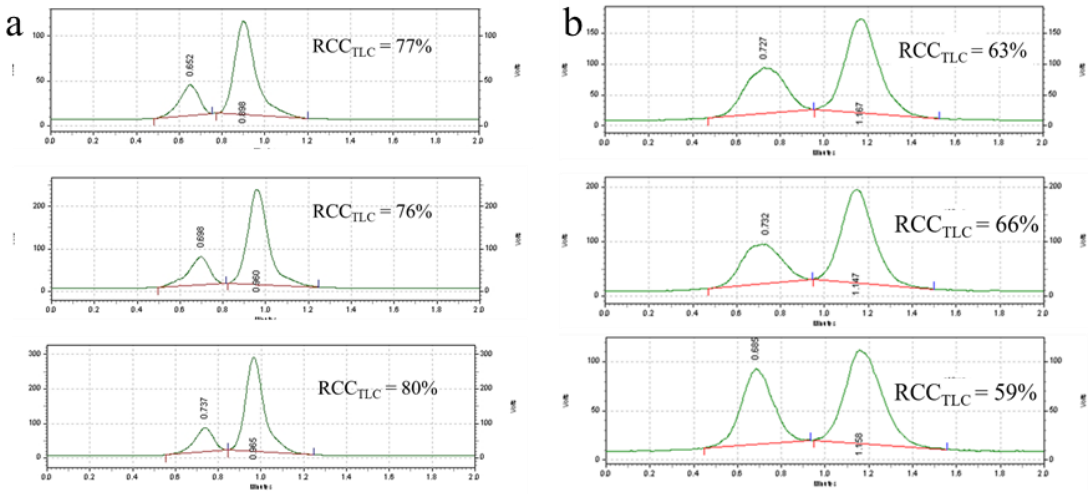


Fig. A1: Radio-TLC traces of (**a**) ^{18}F-benzylphosphonofluoridic acid (RCC = 78 ± 2%) and (**b**) [^{18}F]**1** (RCC = 62 ± 3%). Developing solvent: MeOH.

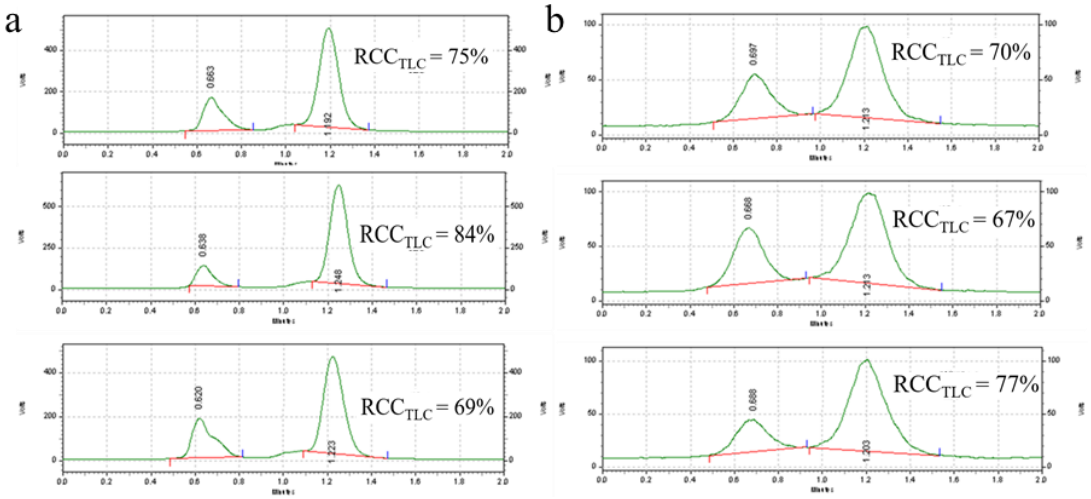


Fig. A2: Radio-TLC traces of (**a**) [^{18}F]**36** (RCC = 76 ± 7%) and (**b**) [^{18}F]**37** (RCC = 71 ± 5%). Developing solvent: MeOH.

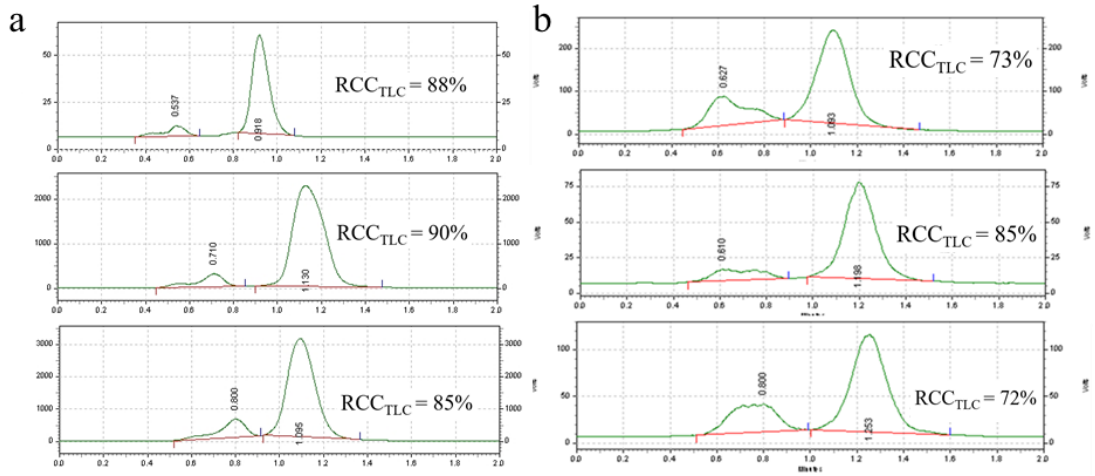


Fig. A3: Radio-TLC traces of (**a**) [^{18}F]**38** (RCC = 88 ± 3%) and (**b**) [^{18}F]**39** (RCC = 77 ± 7%). Developing solvent: MeOH.

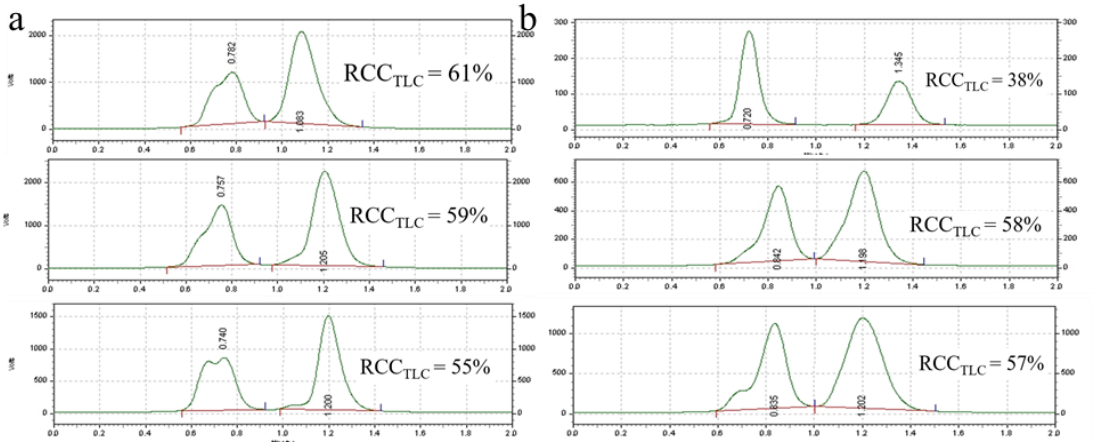


Fig. A4: Radio-TLC traces of (**a**) [^{18}F]**40** (RCC = 58 ± 3%) and (**b**) [^{18}F]**41** (RCC = 51 ± 11%). Developing solvent: MeOH.

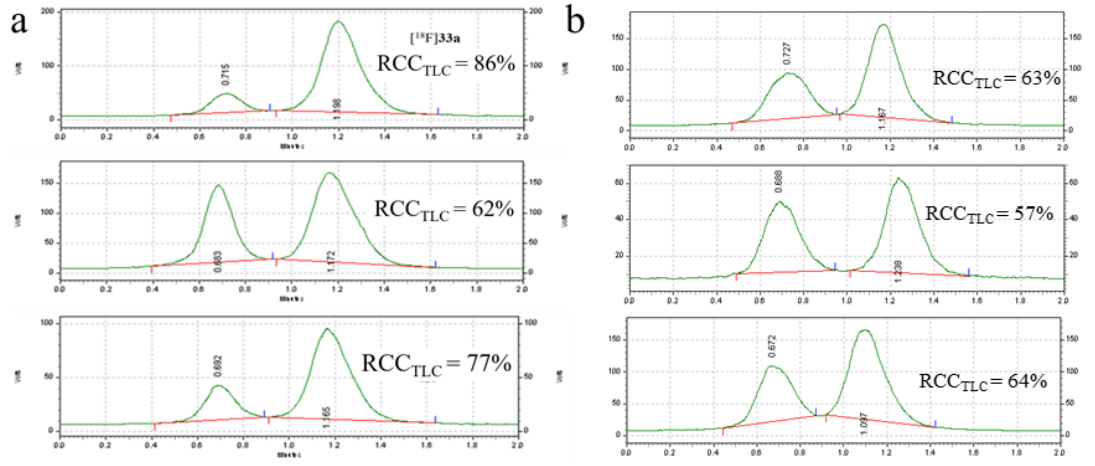


Fig. A5: Radio-TLC traces of (**a**) [^{18}F]**42** (RCC = 75 ± 12%) and (**b**) [^{18}F]**43** (RCC = 61 ± 4%). Developing solvent: MeOH.

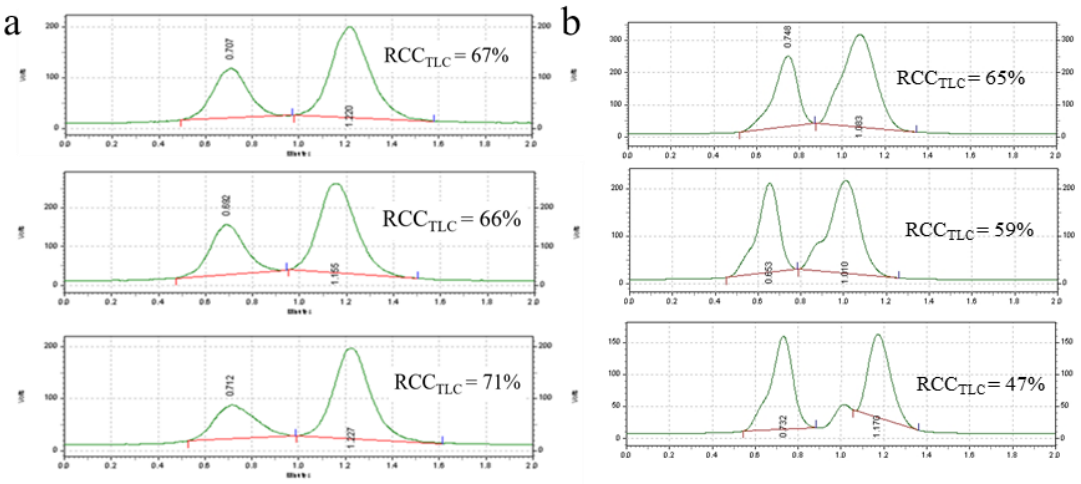
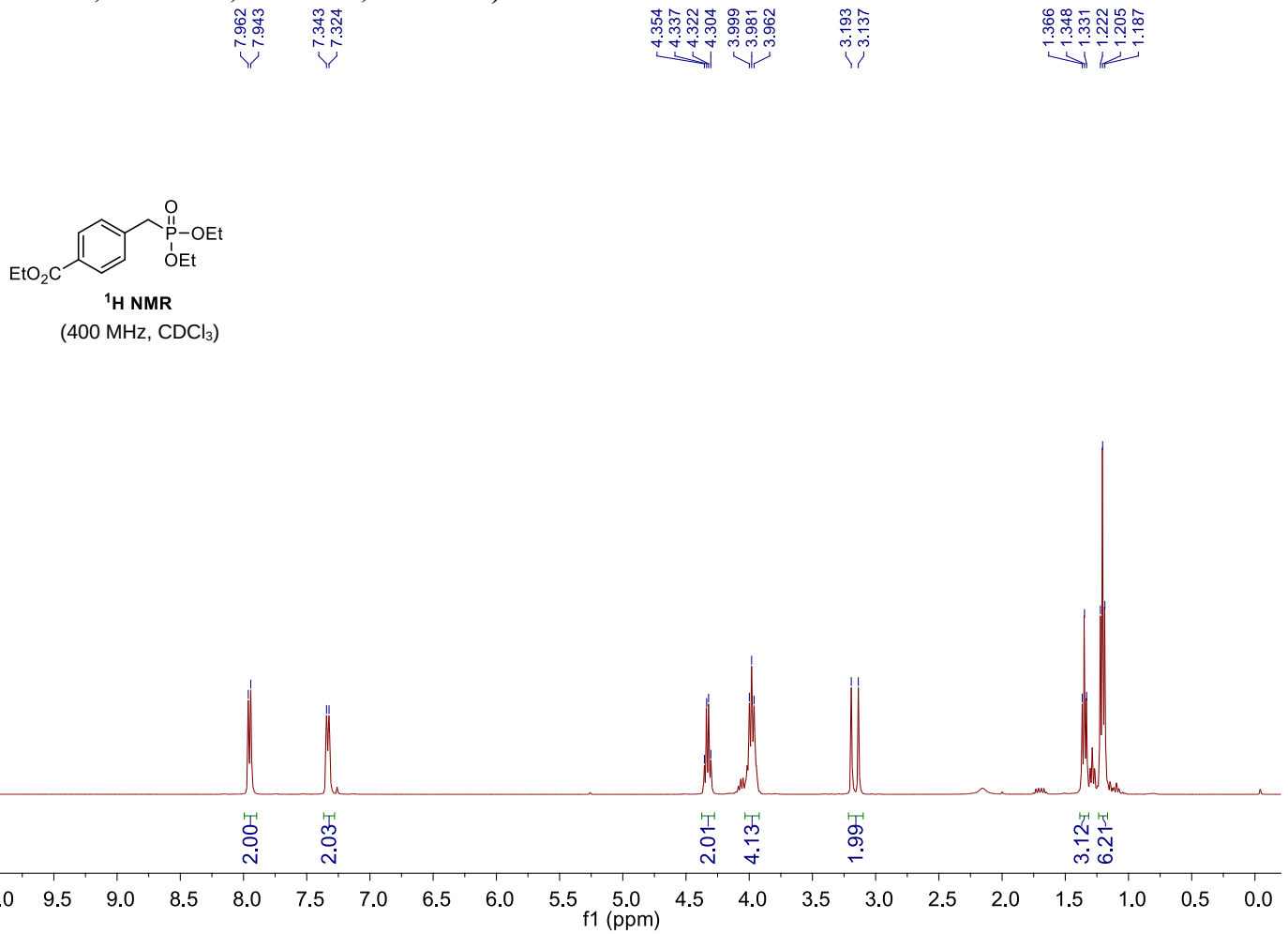


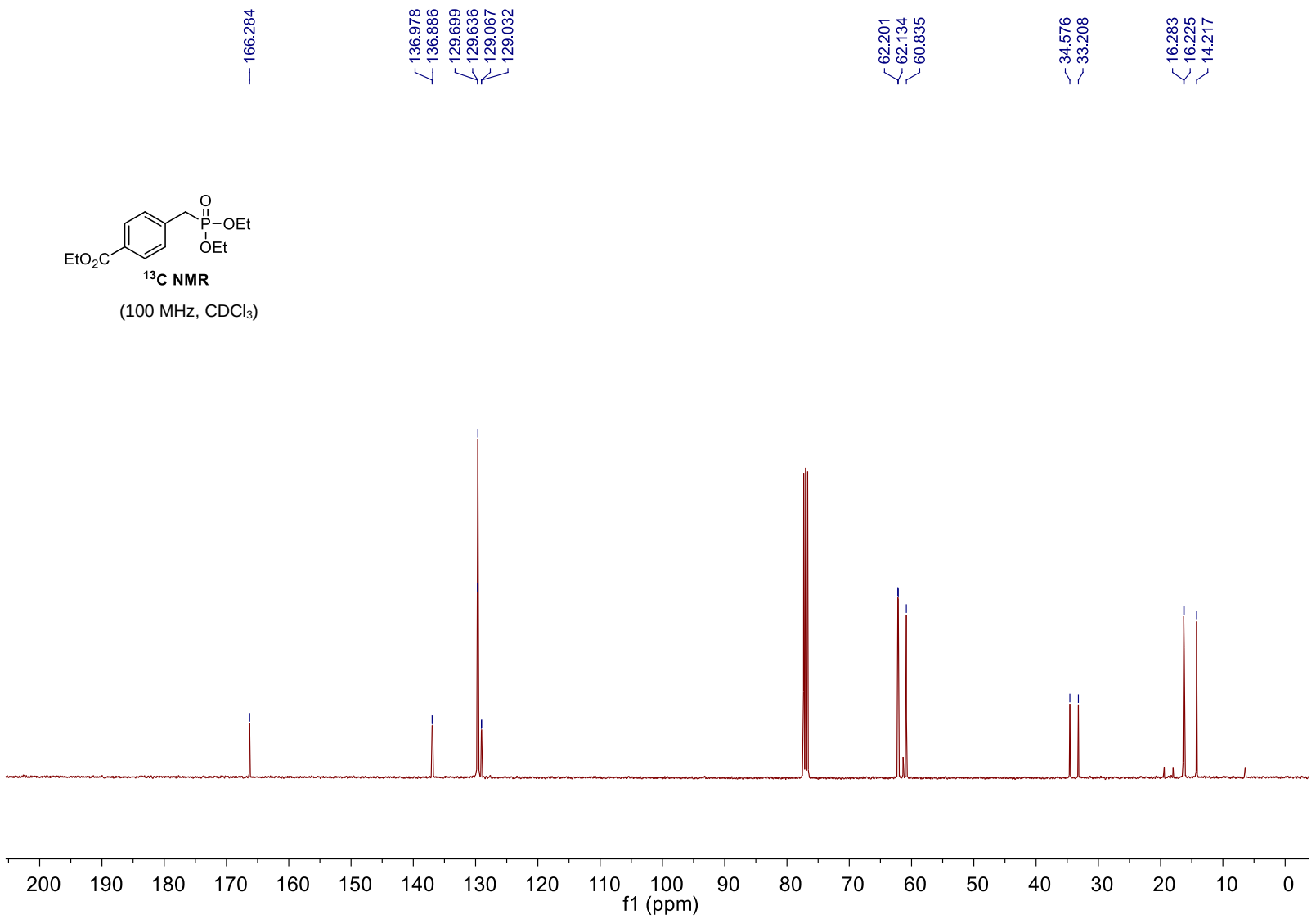
Fig. A6: Radio-TLC traces of (a) [^{18}F]**44** (RCC = 68 ± 2%) and (b) [^{18}F]**45** (RCC = 57 ± 9%). Developing solvent: MeOH.

3.2 NMR spectra (^{1}H NMR, ^{13}C NMR, ^{31}P NMR, ^{19}F NMR)



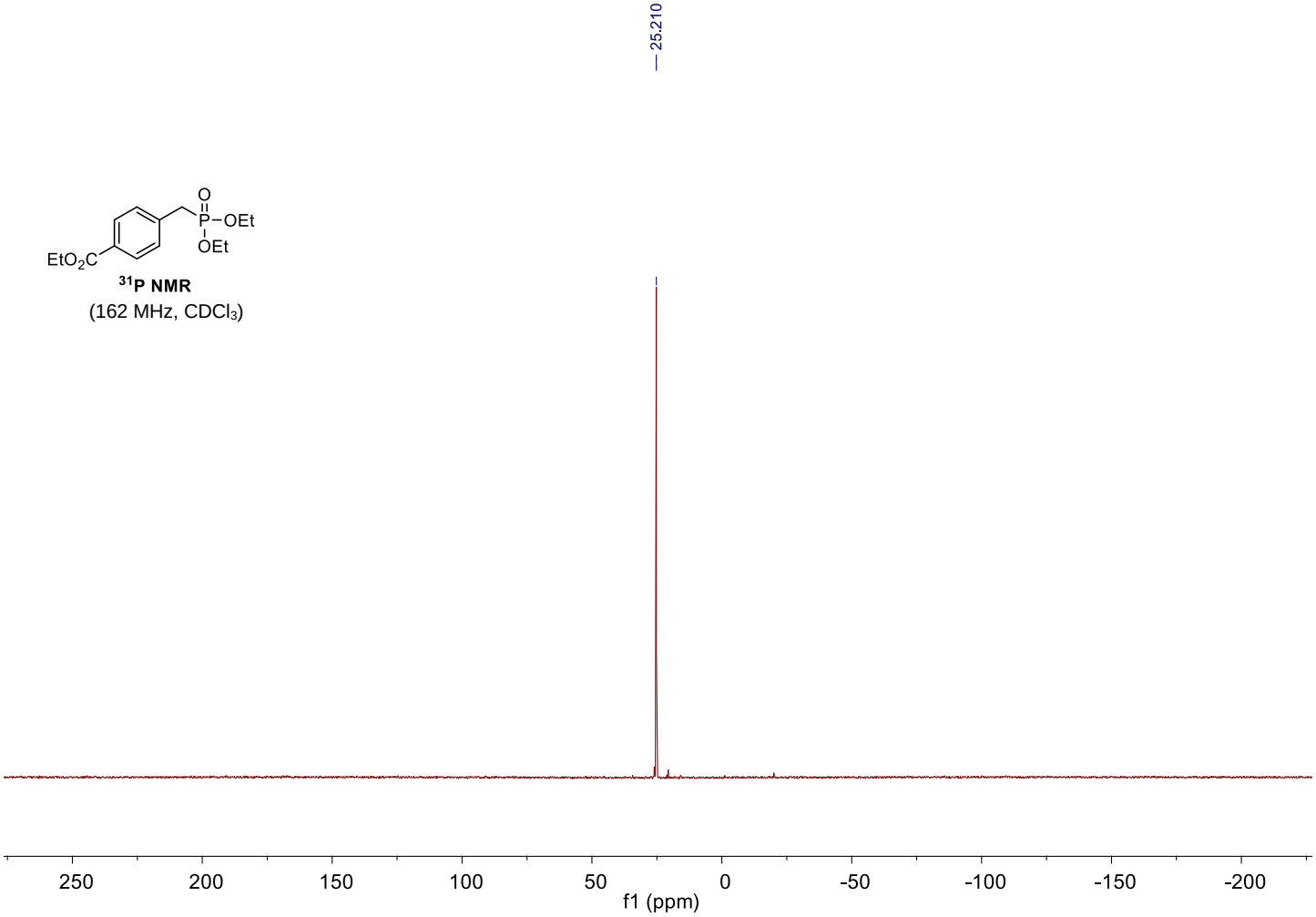
^{1}H NMR

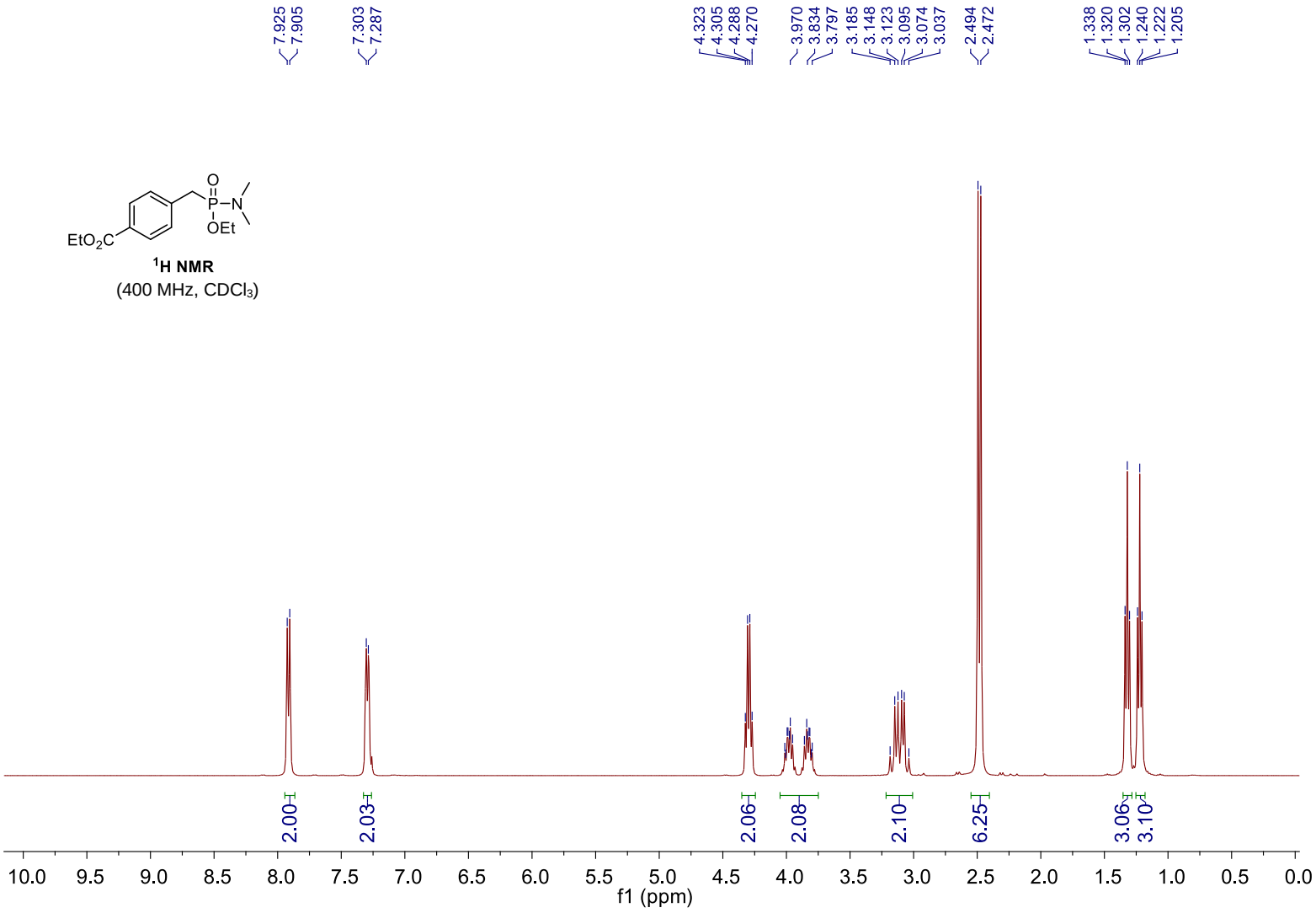
(400 MHz, $CDCl_3$)

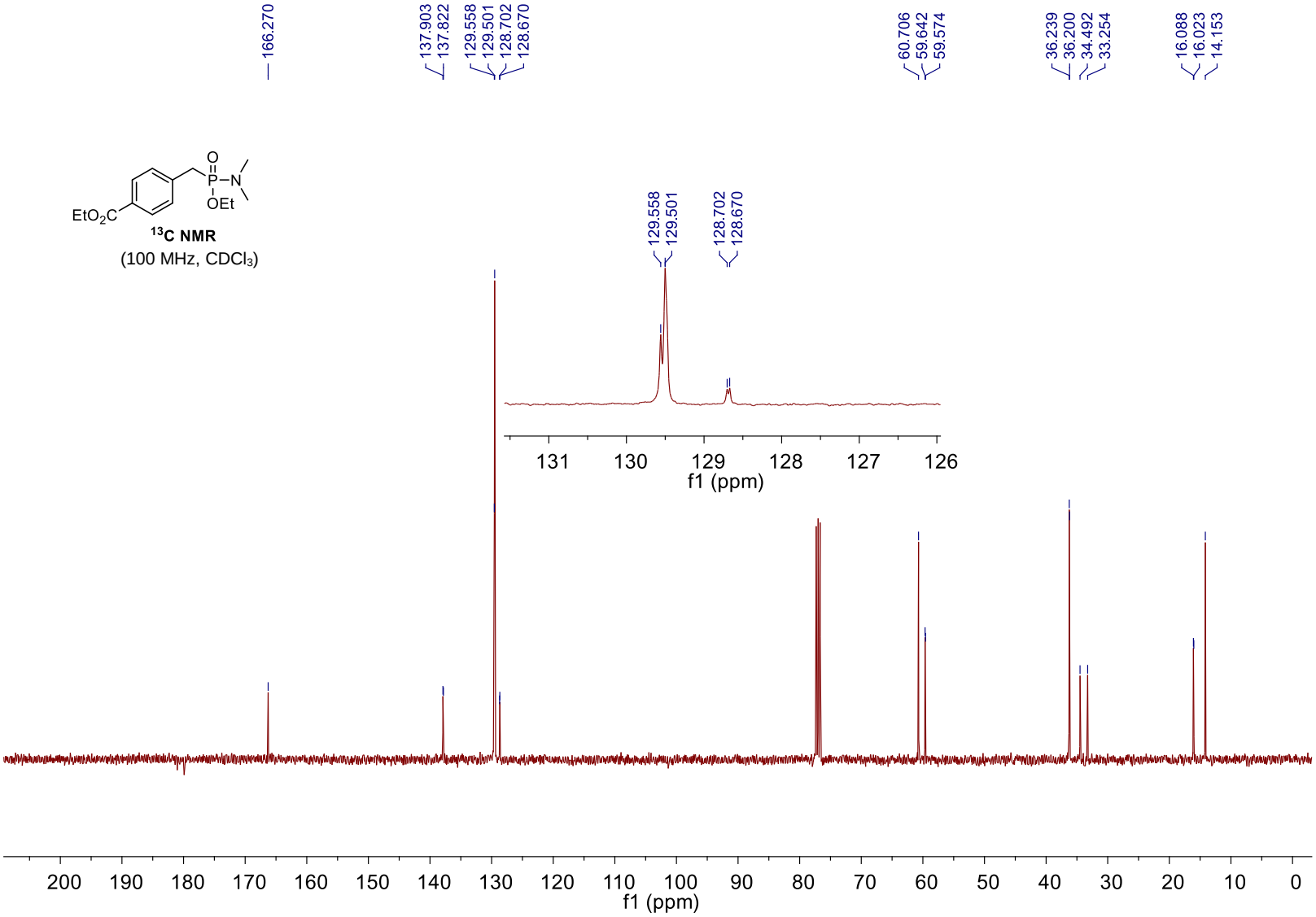


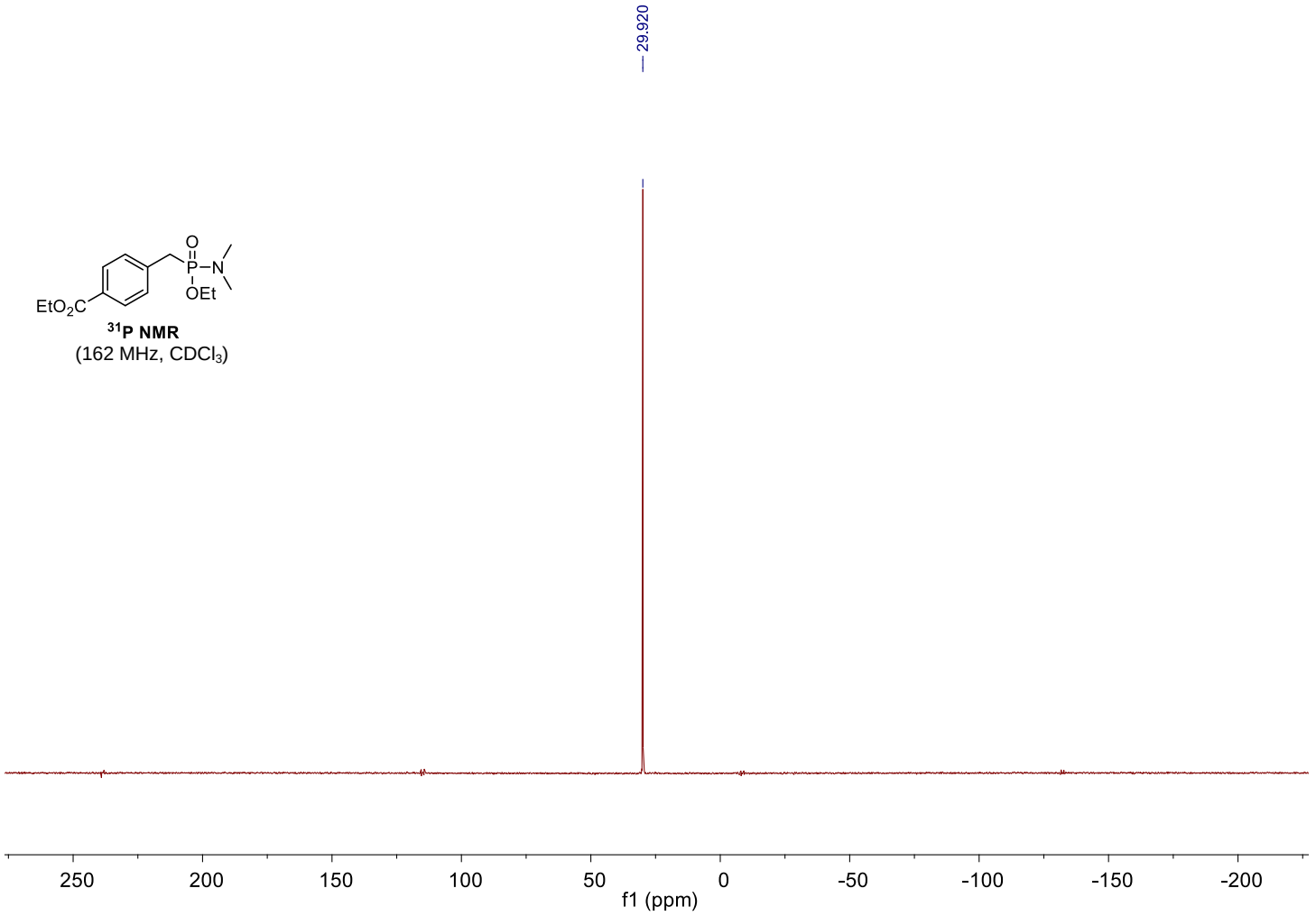
^{13}C NMR

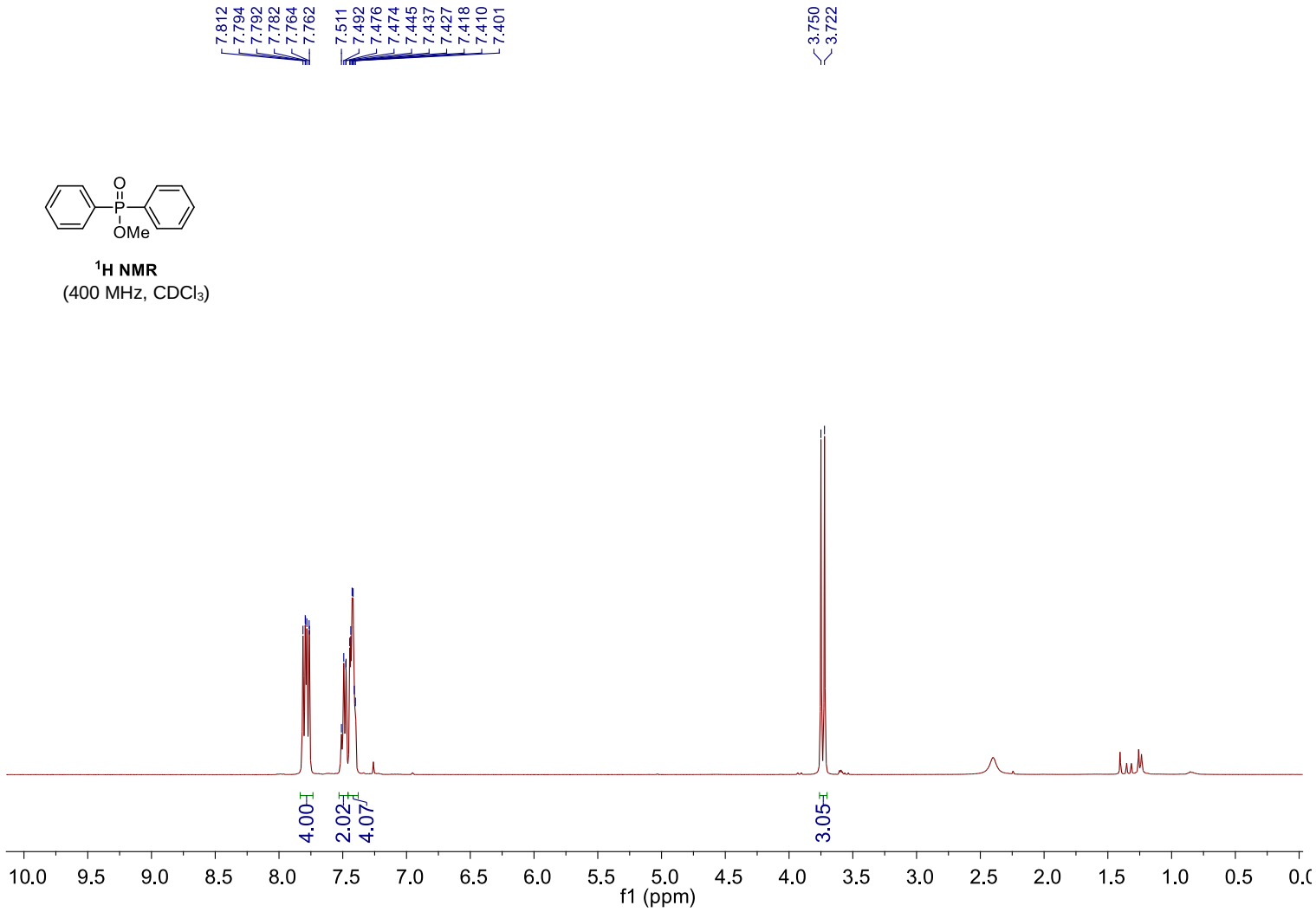
(100 MHz, $CDCl_3$)


25.210
O
P–OEt
OEt
EtO2C
31P NMR
(162 MHz, CDCl3)
250
200
150
100
50
0
-50
-100
-150
-200
f1 (ppm)

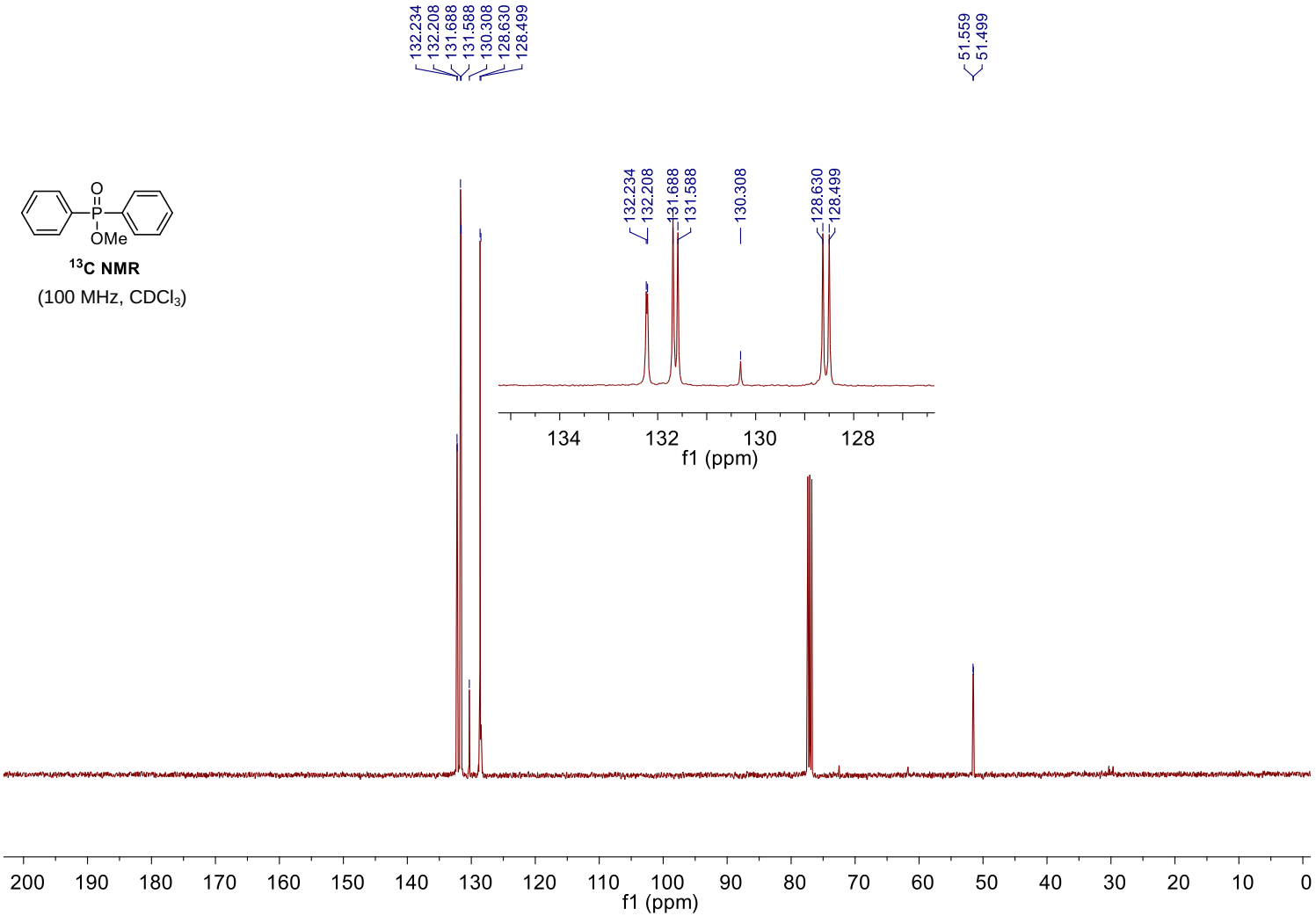

7.925
7.905
7.303
7.287
4.323
4.305
4.288
4.270
3.970
3.834
3.797
3.185
3.148
3.123
3.095
3.074
3.037
2.494
2.472
1.338
1.320
1.302
1.240
1.222
1.205
EtO2C
O
P
N
OEt
1H NMR
(400 MHz, CDCl3)
2.00
2.03
2.06
2.08
2.10
6.25
3.06
3.10
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

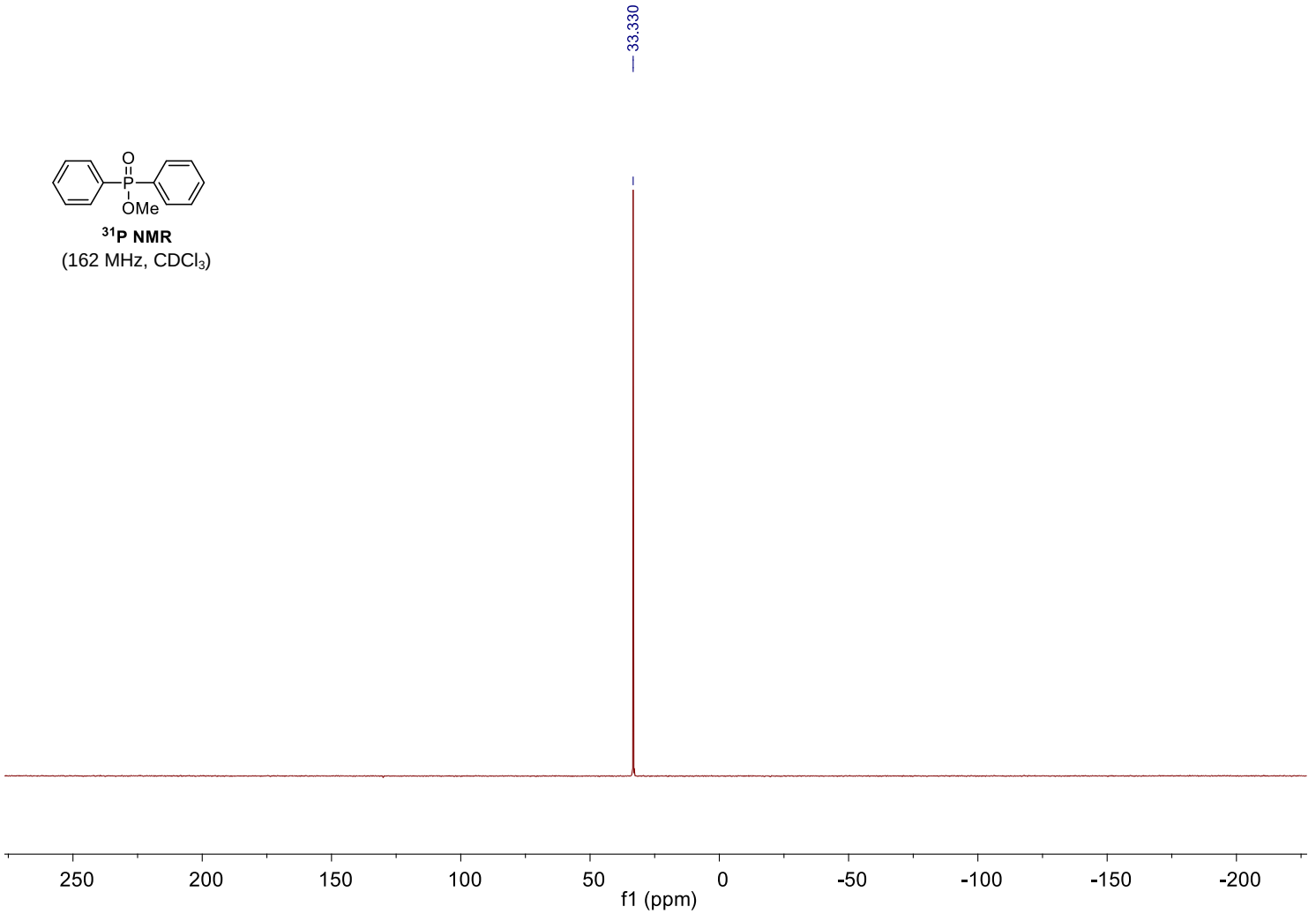

166.270
137.903
137.822
129.558
129.501
128.702
128.670
60.706
59.642
59.574
36.239
36.200
34.492
33.254
16.088
16.023
14.153
EtO2C
O
P
N
OEt
13C NMR
(100 MHz, CDCl3)
129.558
129.501
128.702
128.670
131
130
129
128
127
126
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


29.920
O
P
N
OEt
EtO2C
31P NMR
(162 MHz, CDCl3)
250
200
150
100
50
0
-50
-100
-150
-200
f1 (ppm)

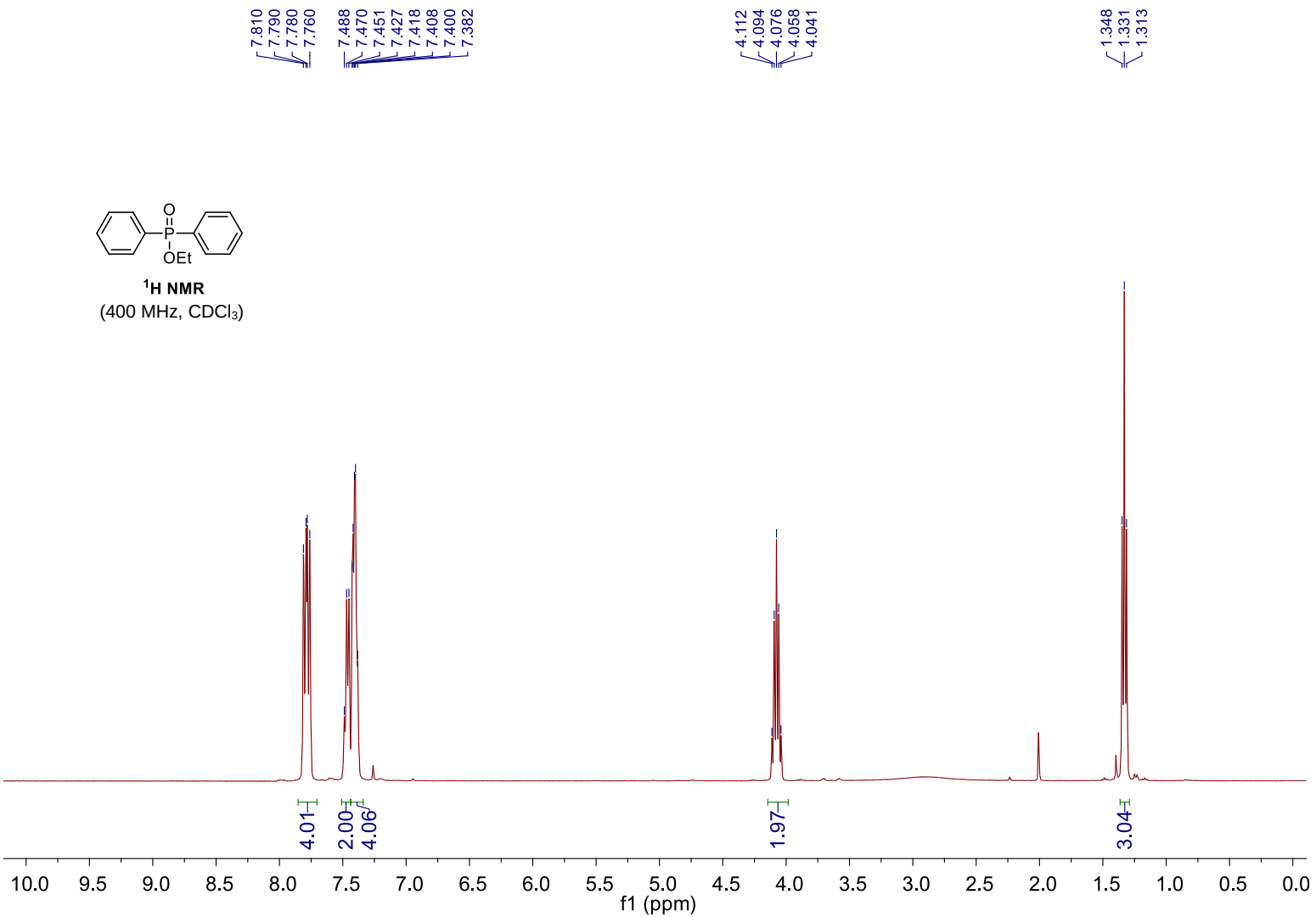


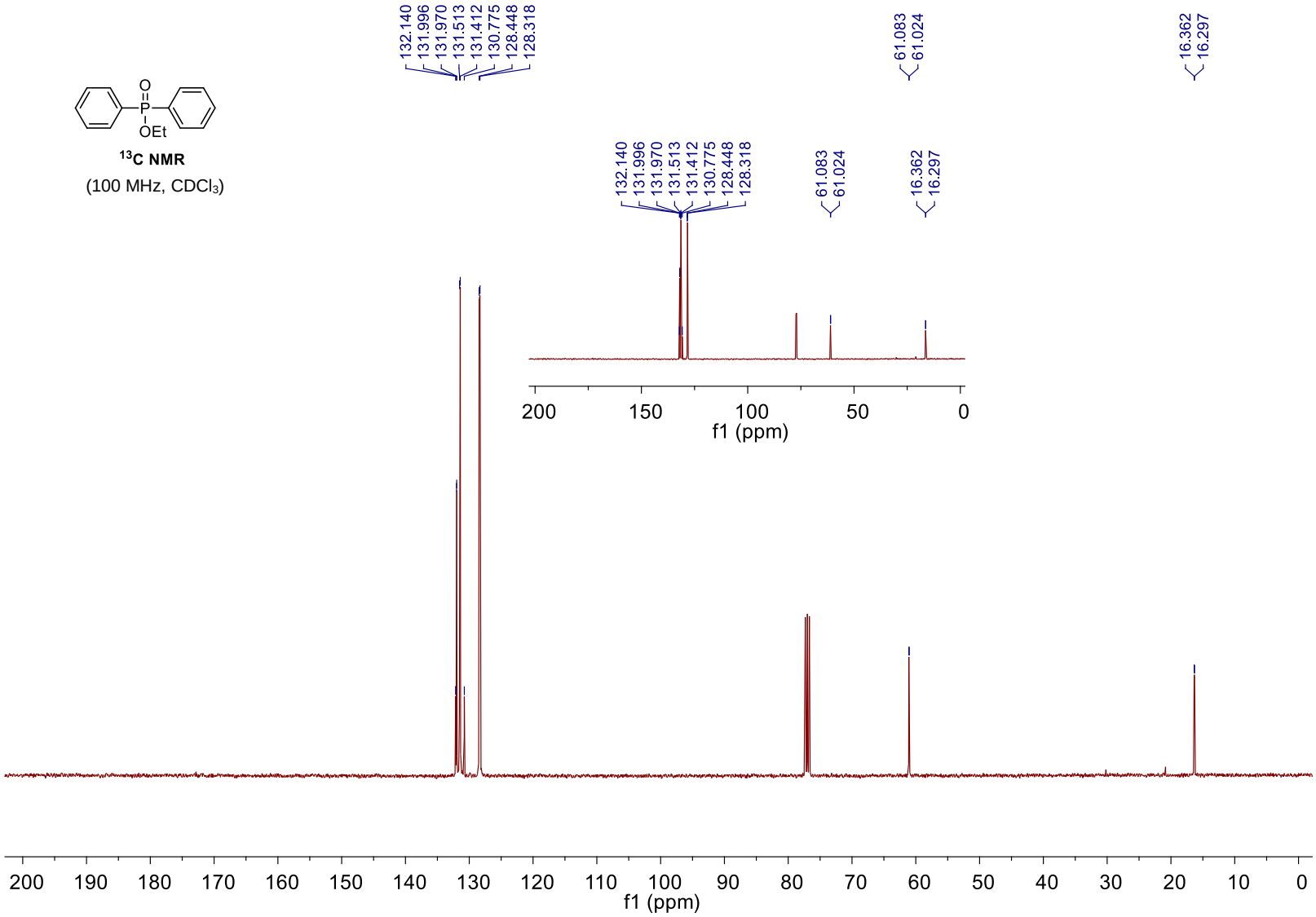
^{1}H NMR
(400 MHz, $CDCl_3$)

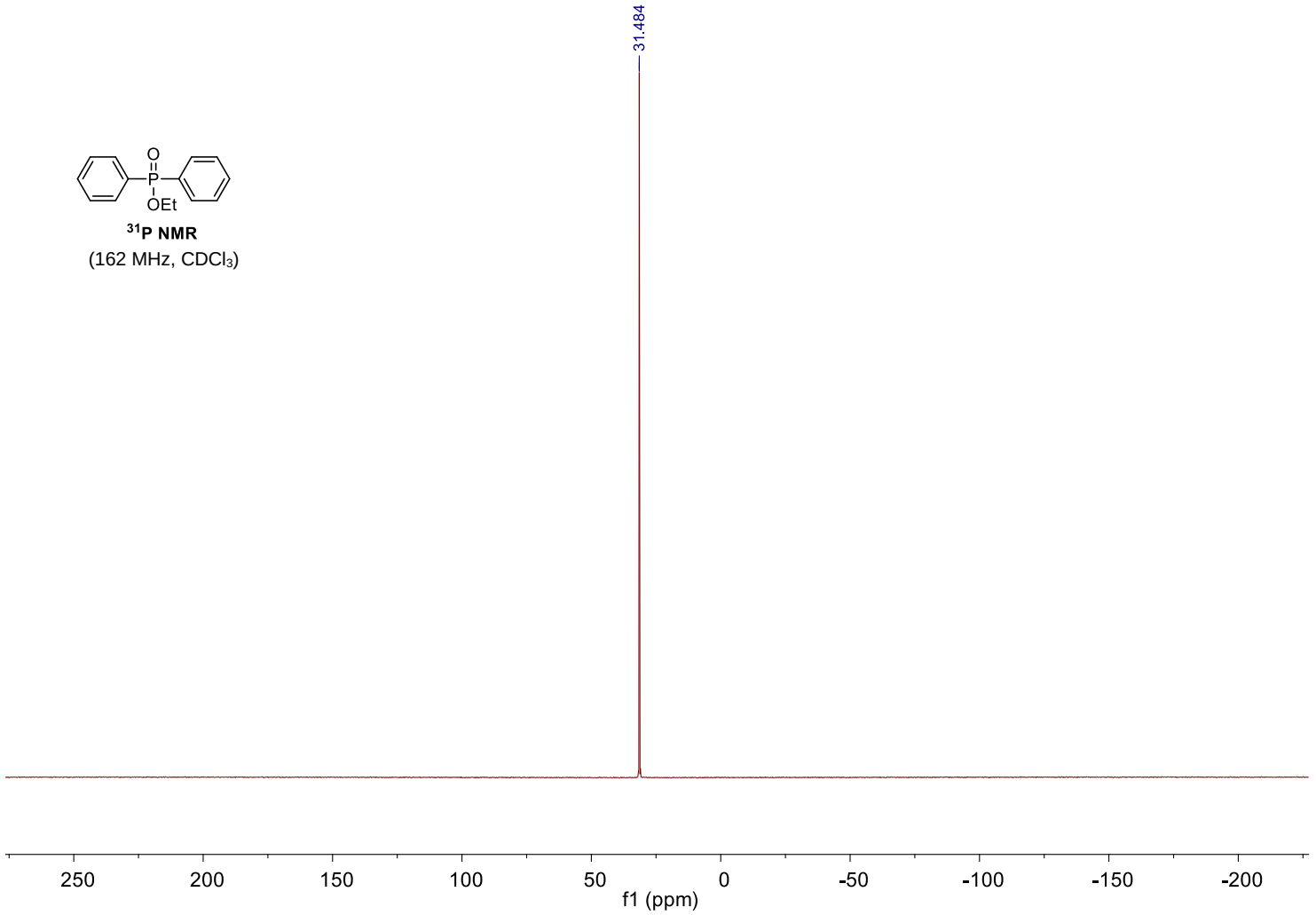

132.234
132.208
131.688
131.588
130.308
128.630
128.499
51.559
51.499
O
P
OMe
13C NMR
(100 MHz, CDCl3)
f1 (ppm)
f1 (ppm)



^{31}P NMR
(162 MHz, $CDCl_3$)

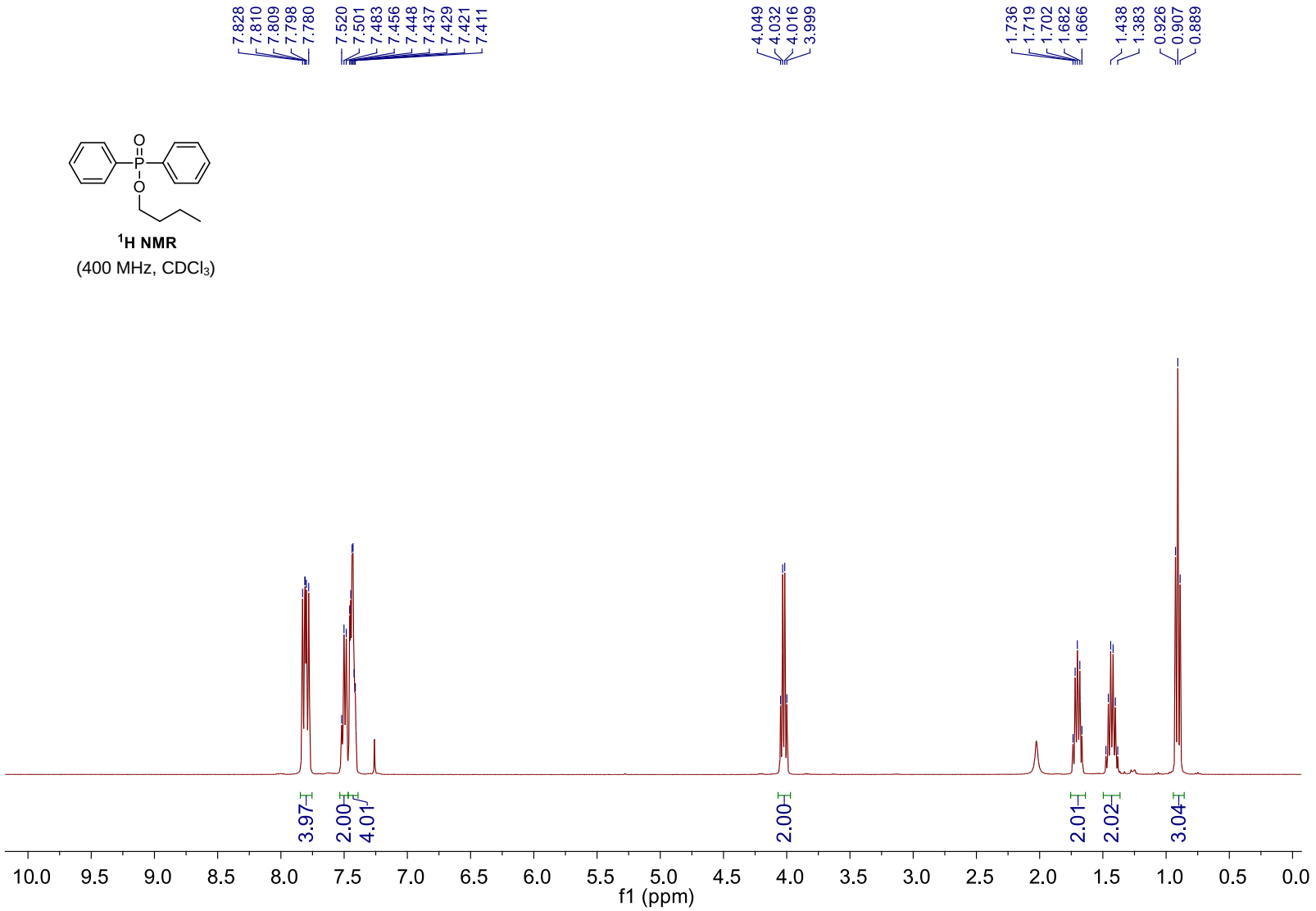

7.810
7.790
7.780
7.760
7.488
7.470
7.451
7.427
7.418
7.408
7.400
7.382
4.112
4.094
4.076
4.058
4.041
1.348
1.331
1.313
O
P
OEt
1H NMR
(400 MHz, CDCl3)
4.01
2.00
4.06
1.97
3.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

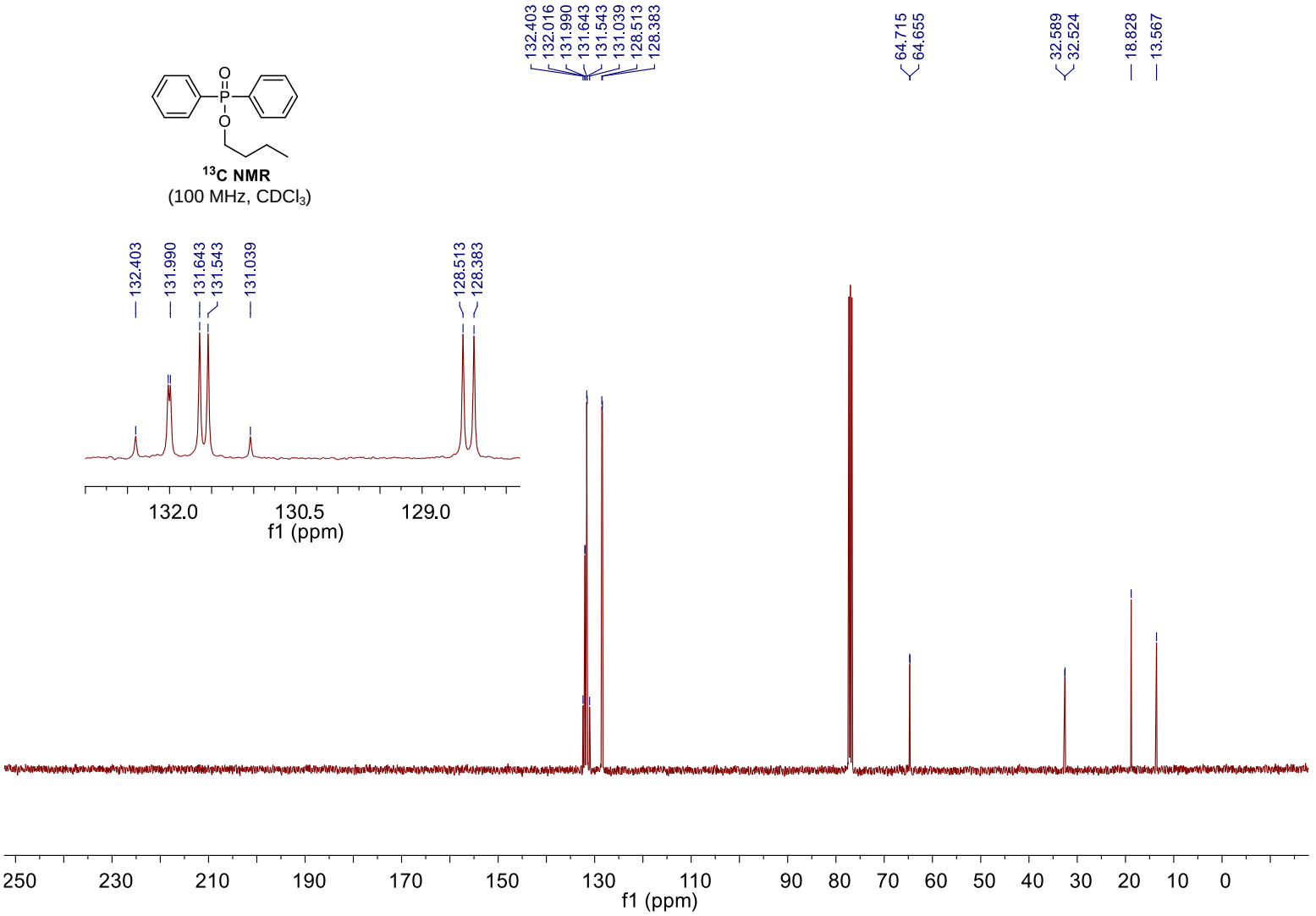

132.140
131.996
131.970
131.513
131.412
130.775
128.448
128.318
61.083
61.024
16.362
16.297
O
P
OEt
13C NMR
(100 MHz, CDCl3)
200
150
100
50
0
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

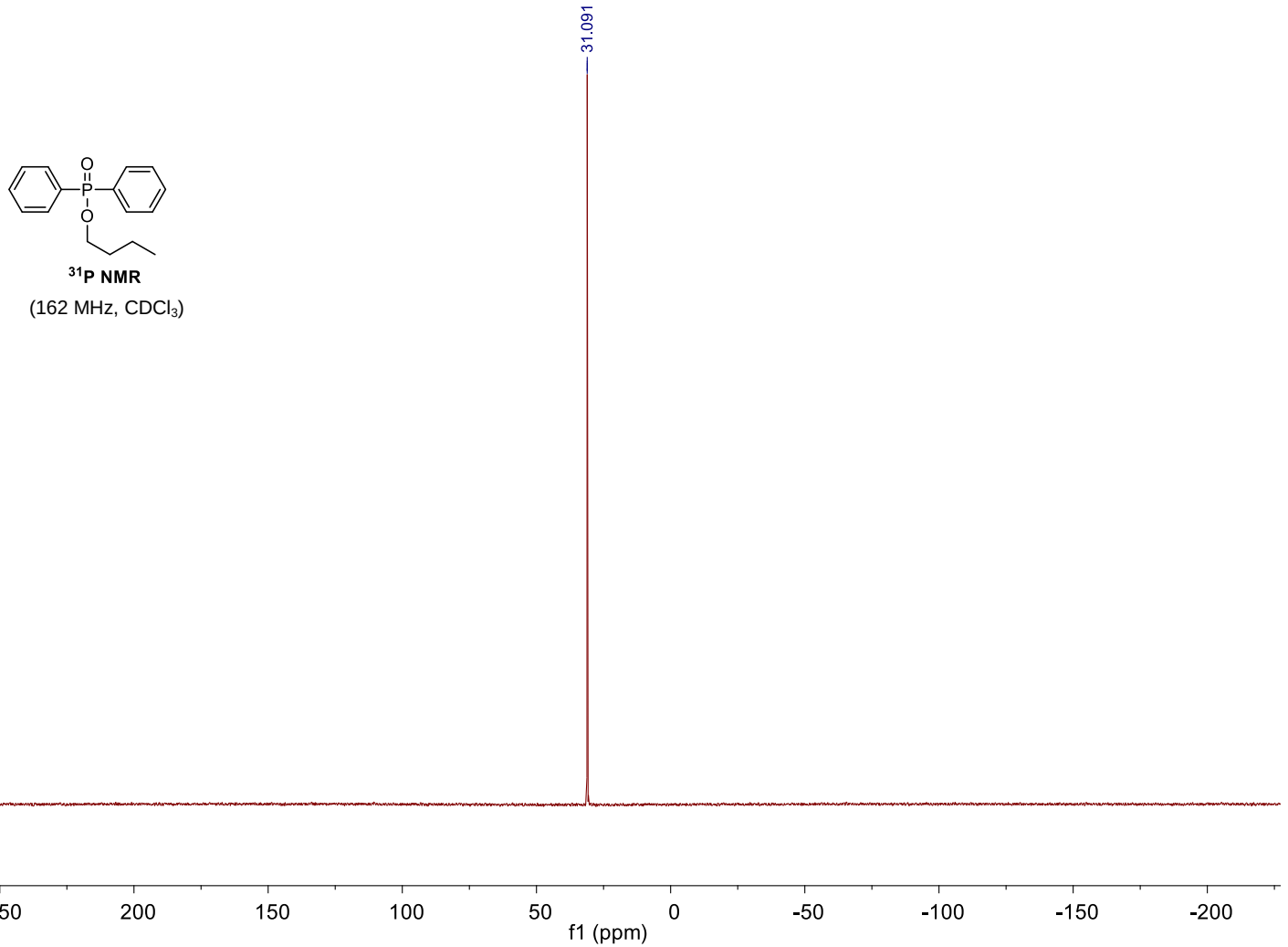


^{31}P NMR

(162 MHz, $CDCl_3$)

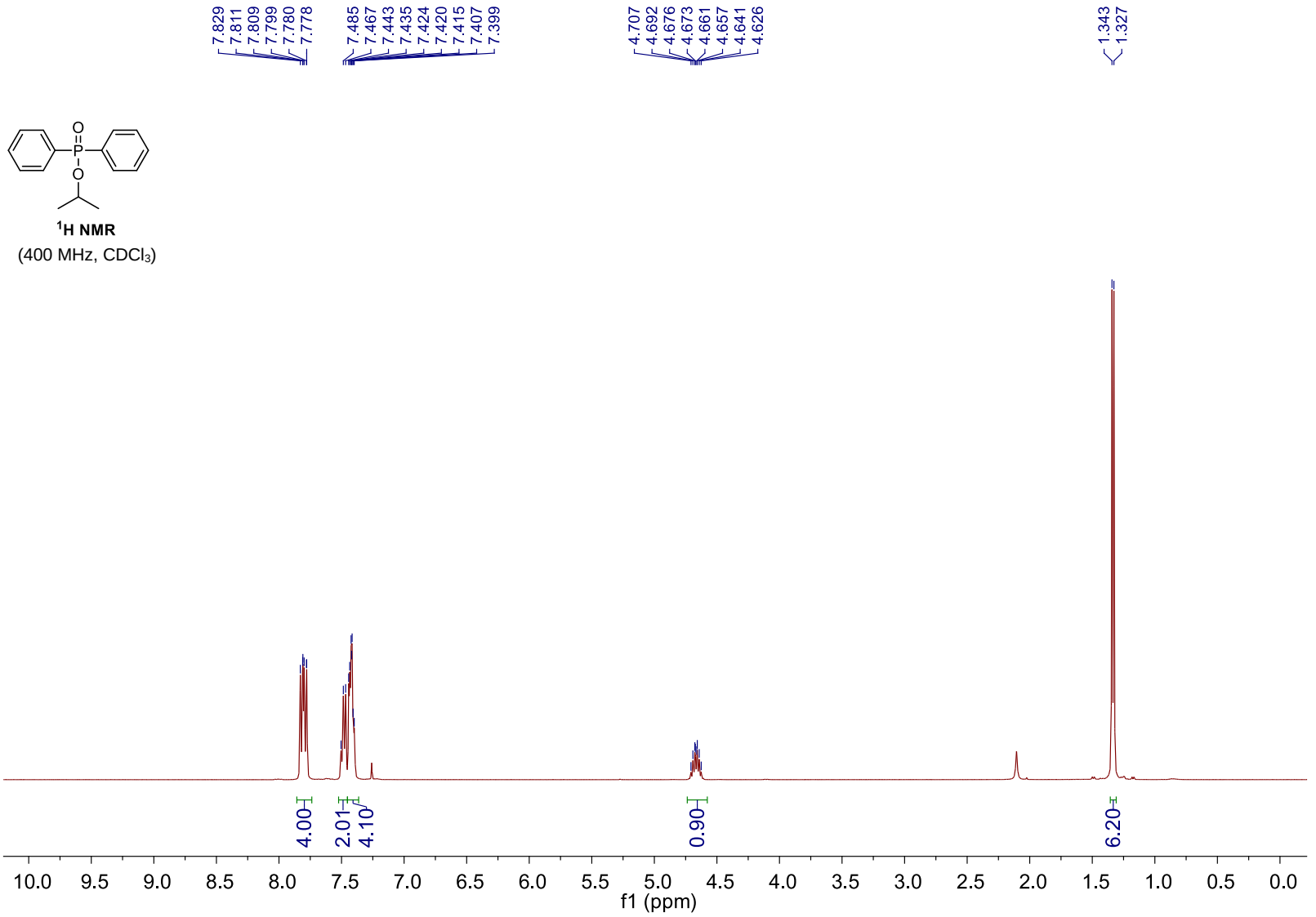

7.828
7.810
7.809
7.798
7.780
7.520
7.501
7.483
7.456
7.448
7.437
7.429
7.421
7.411
4.049
4.032
4.016
3.999
1.736
1.719
1.702
1.682
1.666
1.438
1.383
0.926
0.907
0.889
O
P
O
1H NMR
(400 MHz, CDCl3)
3.97
2.00
4.01
2.00
2.01
2.02
3.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

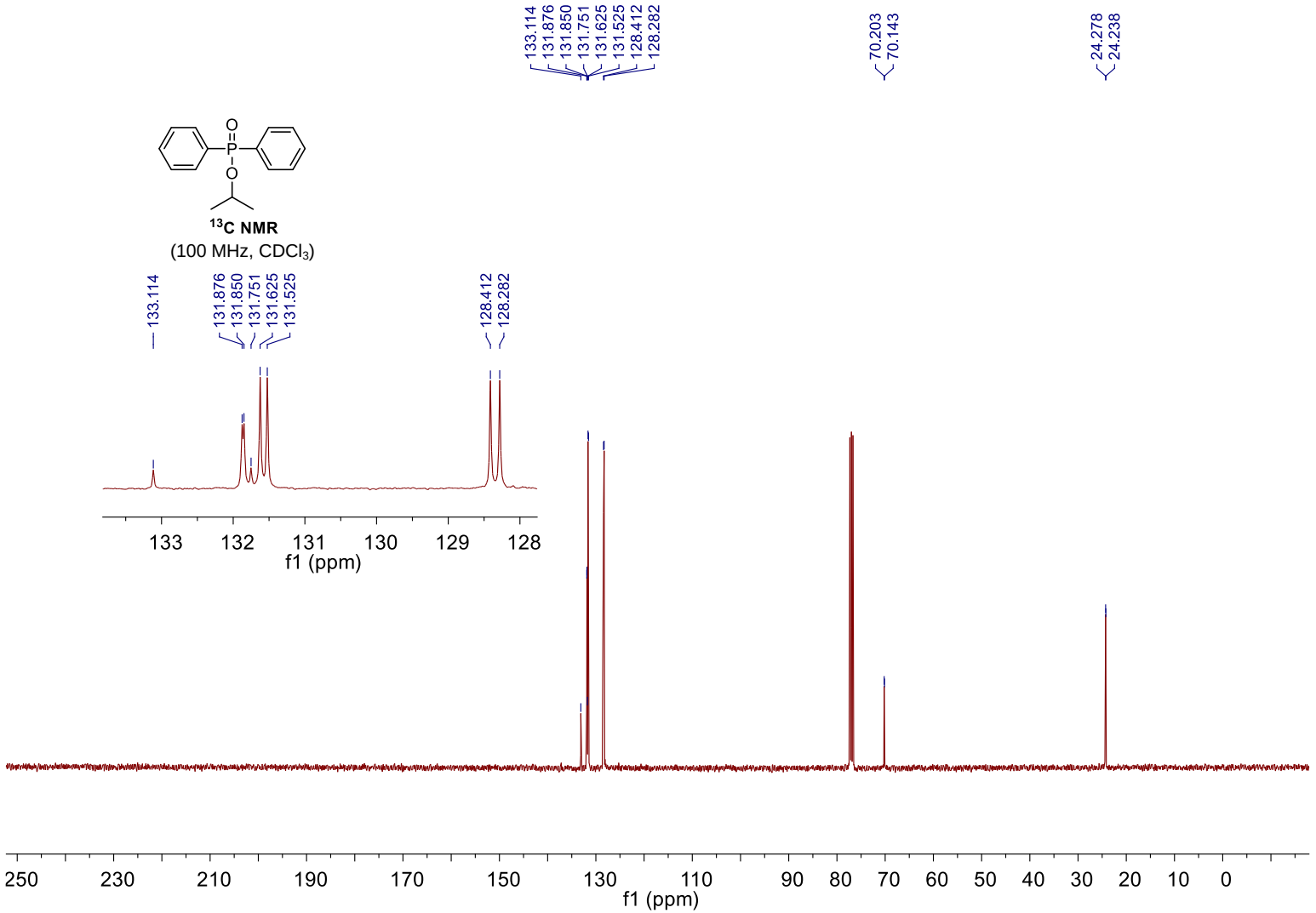

132.403
132.016
131.990
131.643
131.543
131.039
128.513
128.383
64.715
64.655
32.589
32.524
18.828
13.567
^{13}C NMR
(100 MHz, CDCl$_3$)
f1 (ppm)
f1 (ppm)

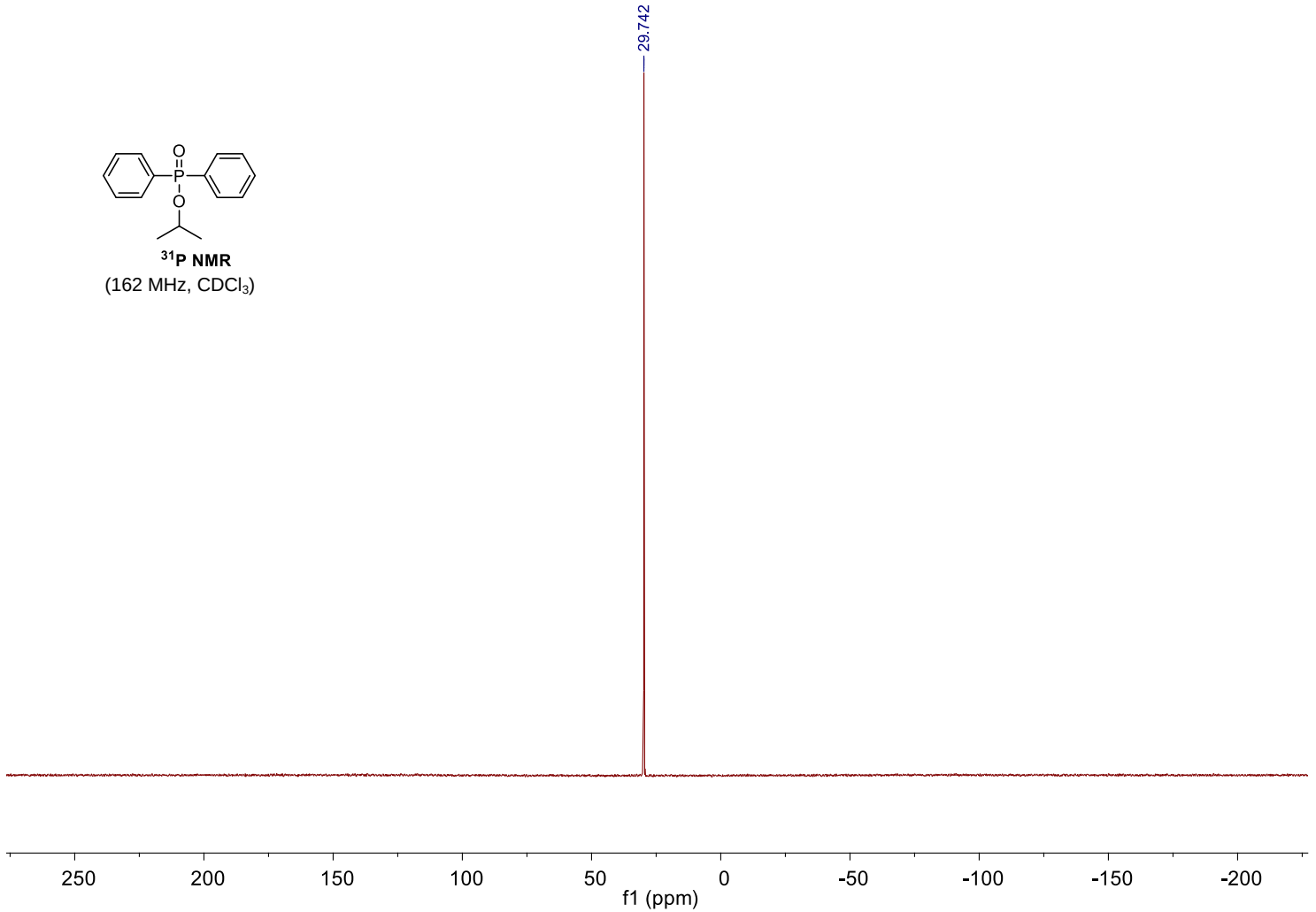


^{31}P NMR

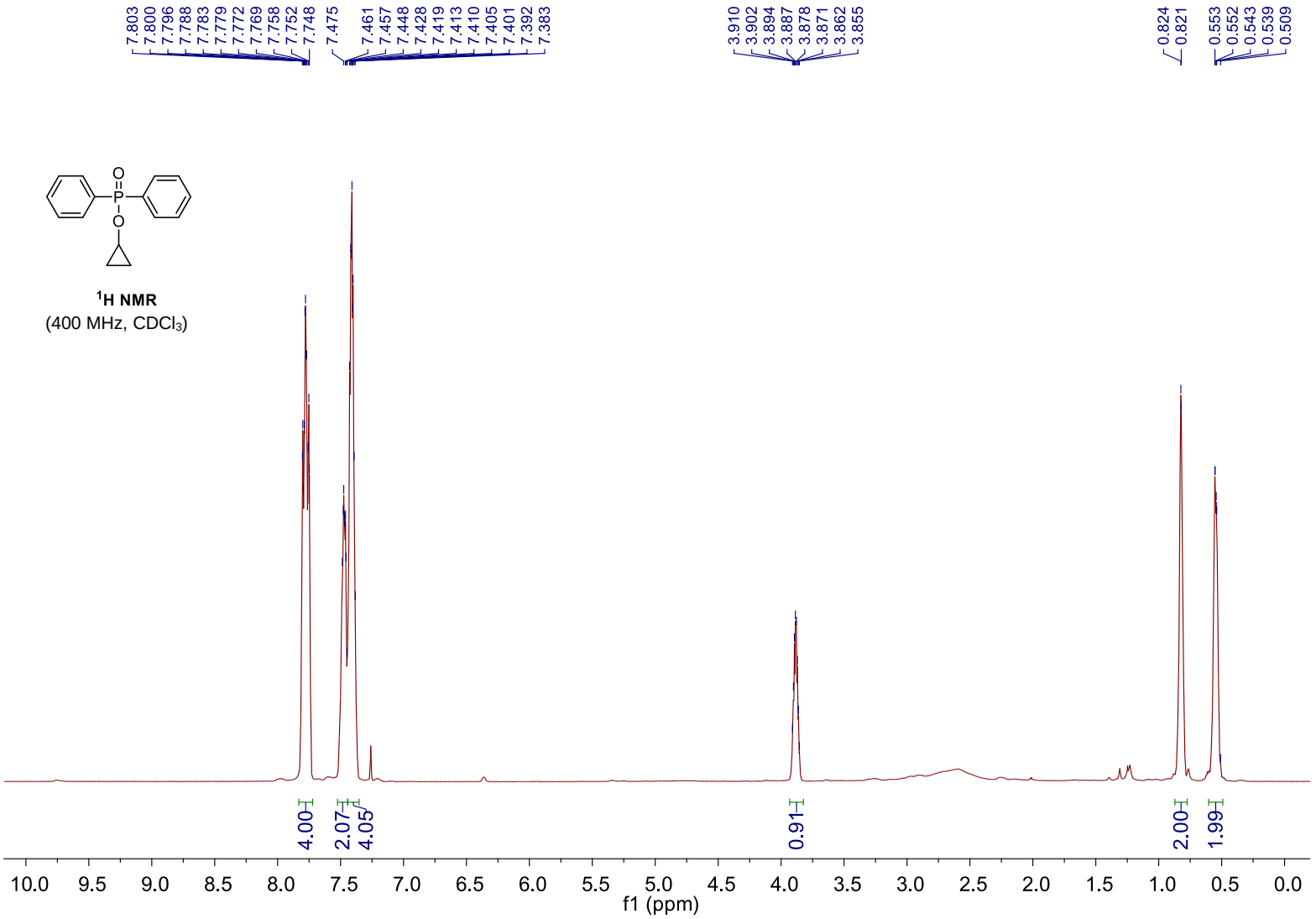
(162 MHz, $CDCl_3$)

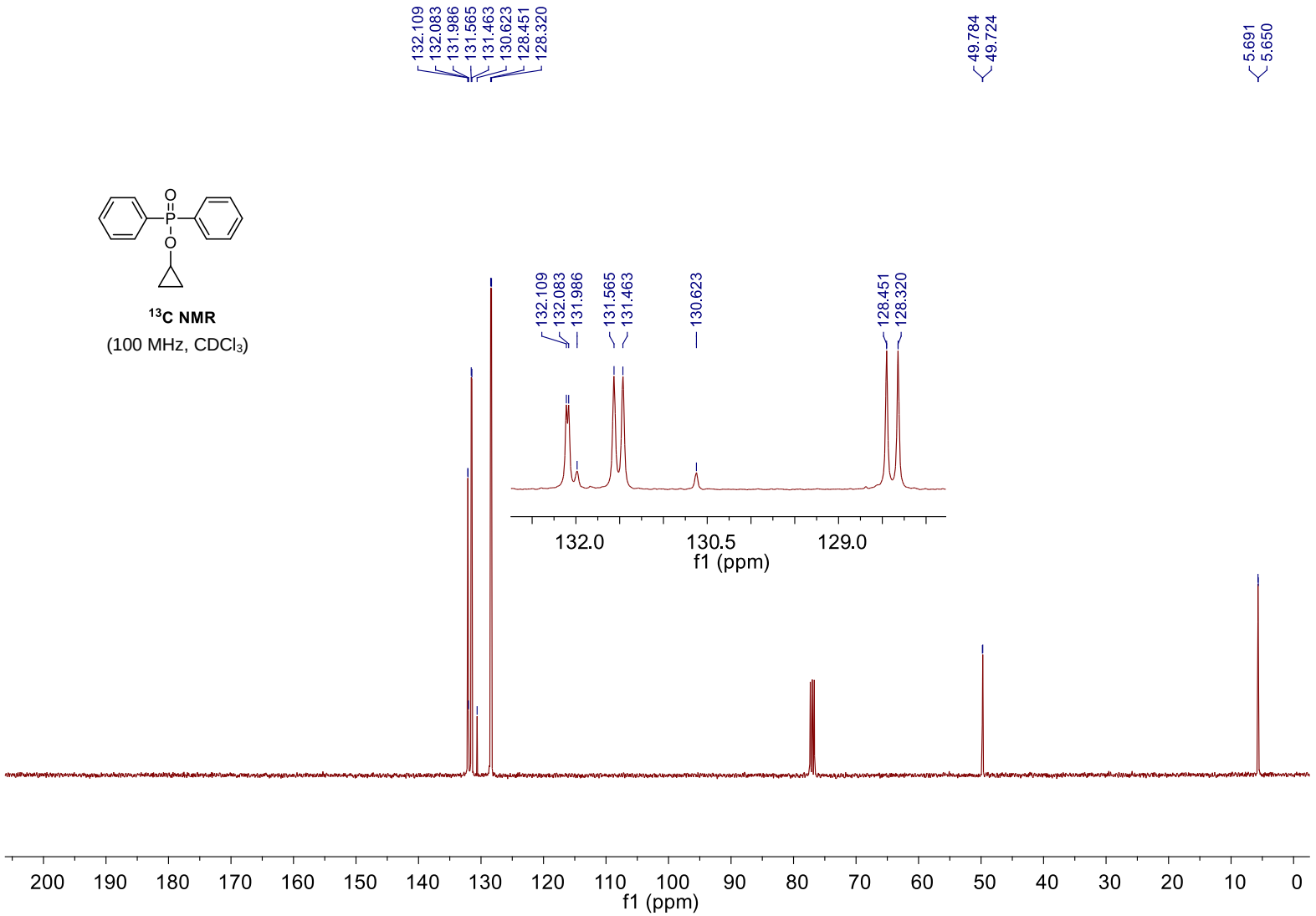

7.829
7.811
7.809
7.799
7.780
7.778
7.485
7.467
7.443
7.435
7.424
7.420
7.415
7.407
7.399
4.707
4.692
4.676
4.673
4.661
4.657
4.641
4.626
1.343
1.327
O
P
O
¹H NMR
(400 MHz, CDCl₃)
4.00
2.01
4.10
0.90
6.20
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

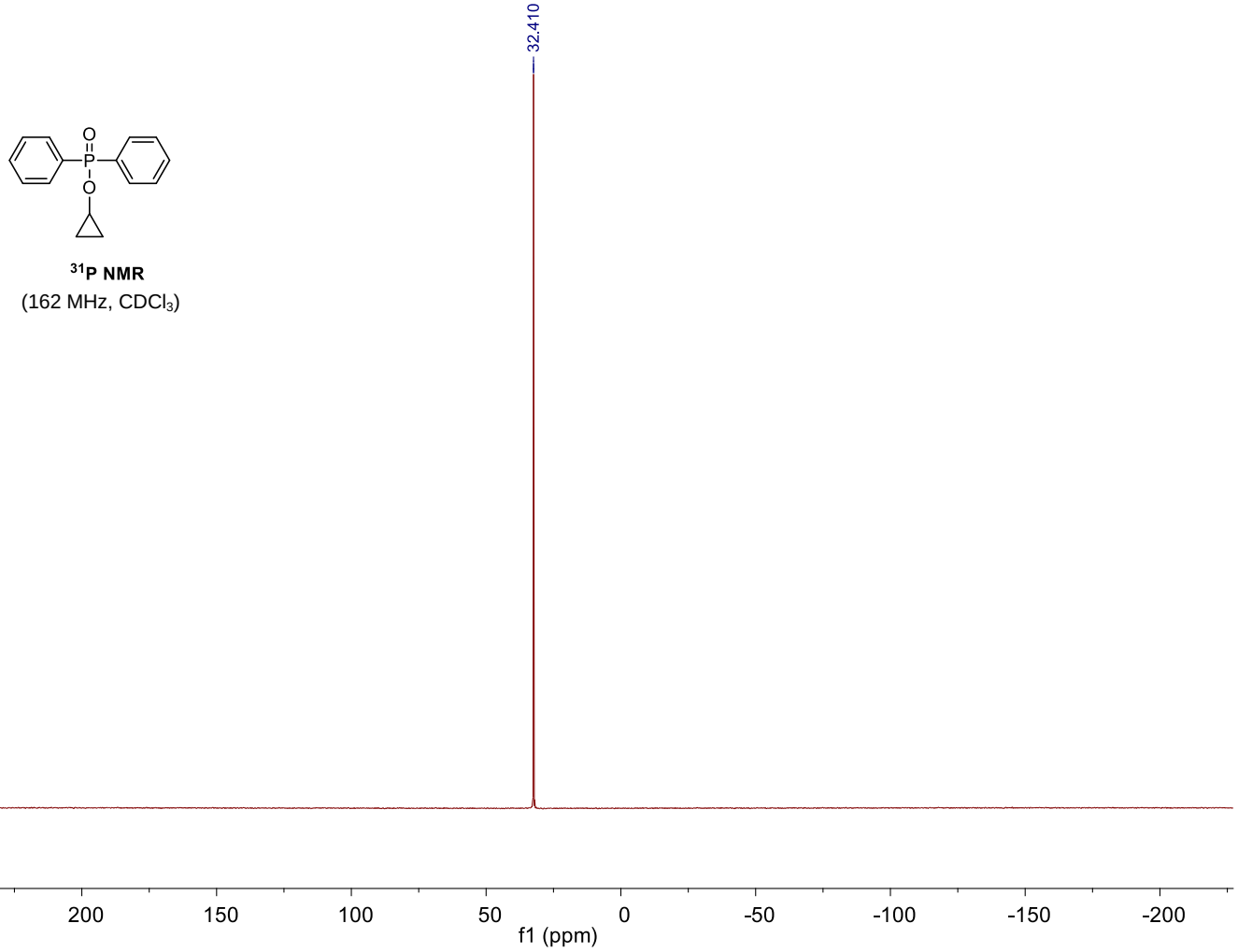

133.114
131.876
131.850
131.751
131.625
131.525
128.412
128.282
70.203
70.143
24.278
24.238
^{13}C NMR
(100 MHz, $CDCl_3$)
f1 (ppm)
f1 (ppm)



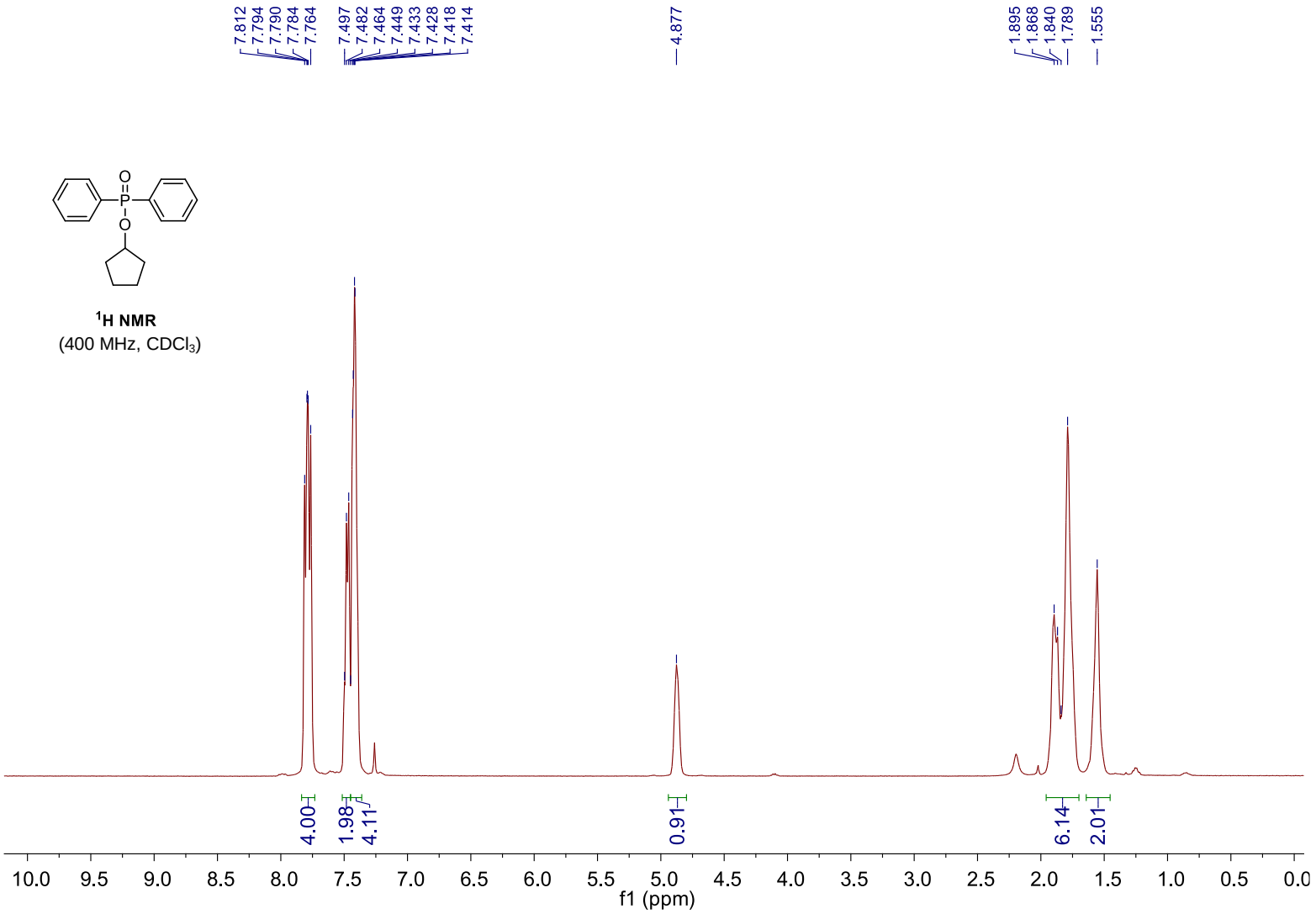
^{31}P NMR
(162 MHz, $CDCl_3$)

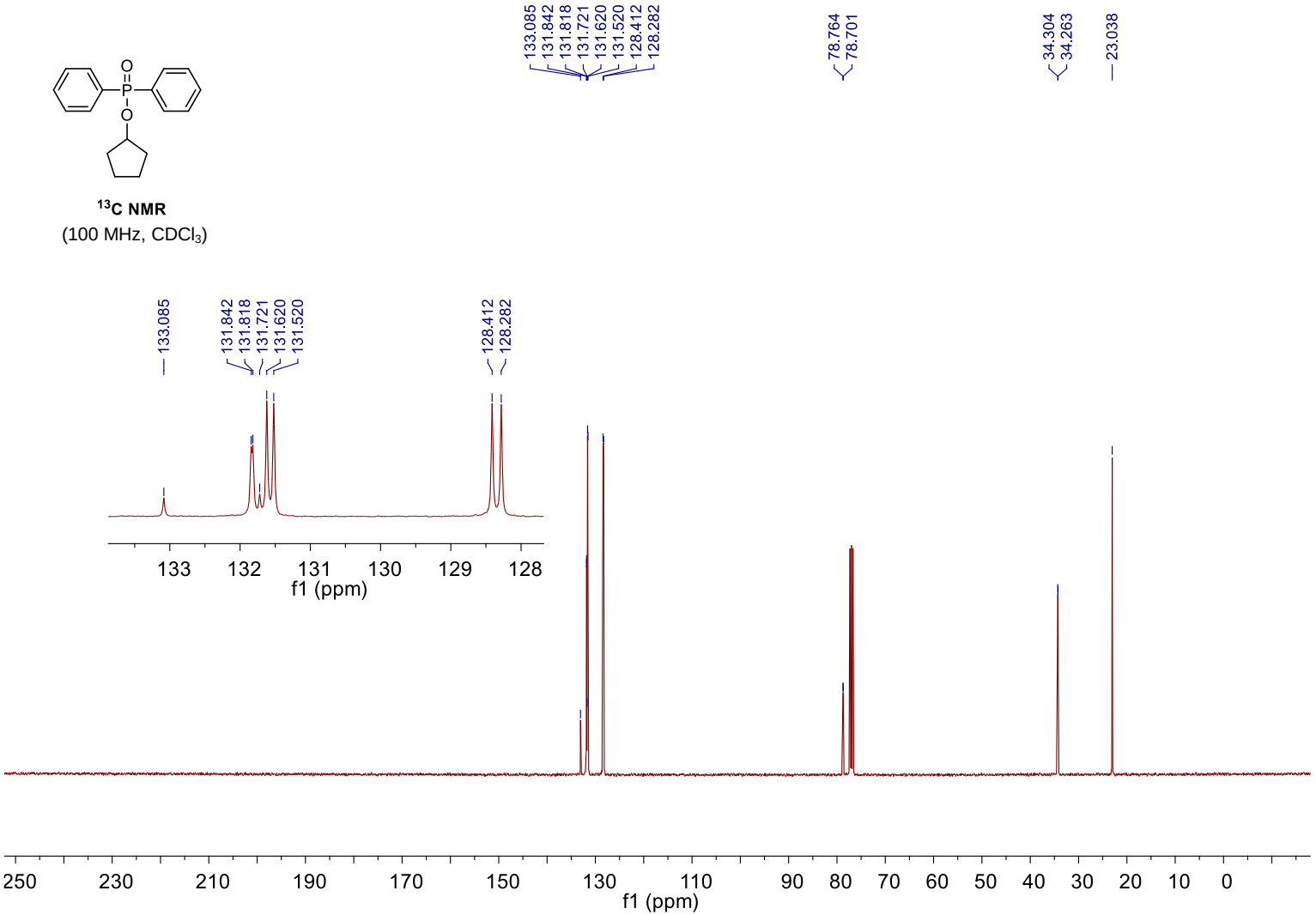

7.803
7.800
7.796
7.788
7.783
7.779
7.772
7.769
7.758
7.752
7.748
7.475
7.461
7.457
7.448
7.428
7.419
7.413
7.410
7.405
7.401
7.392
7.383
3.910
3.902
3.894
3.887
3.878
3.871
3.862
3.855
0.824
0.821
0.553
0.552
0.543
0.539
0.509
O
P
O
1H NMR
(400 MHz, CDCl3)
4.00
2.07
4.05
0.91
2.00
1.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


132.109
132.083
131.986
131.565
131.463
130.623
128.451
128.320
49.784
49.724
5.691
5.650
O
P
O
13C NMR
(100 MHz, CDCl3)
132.0
130.5
129.0
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



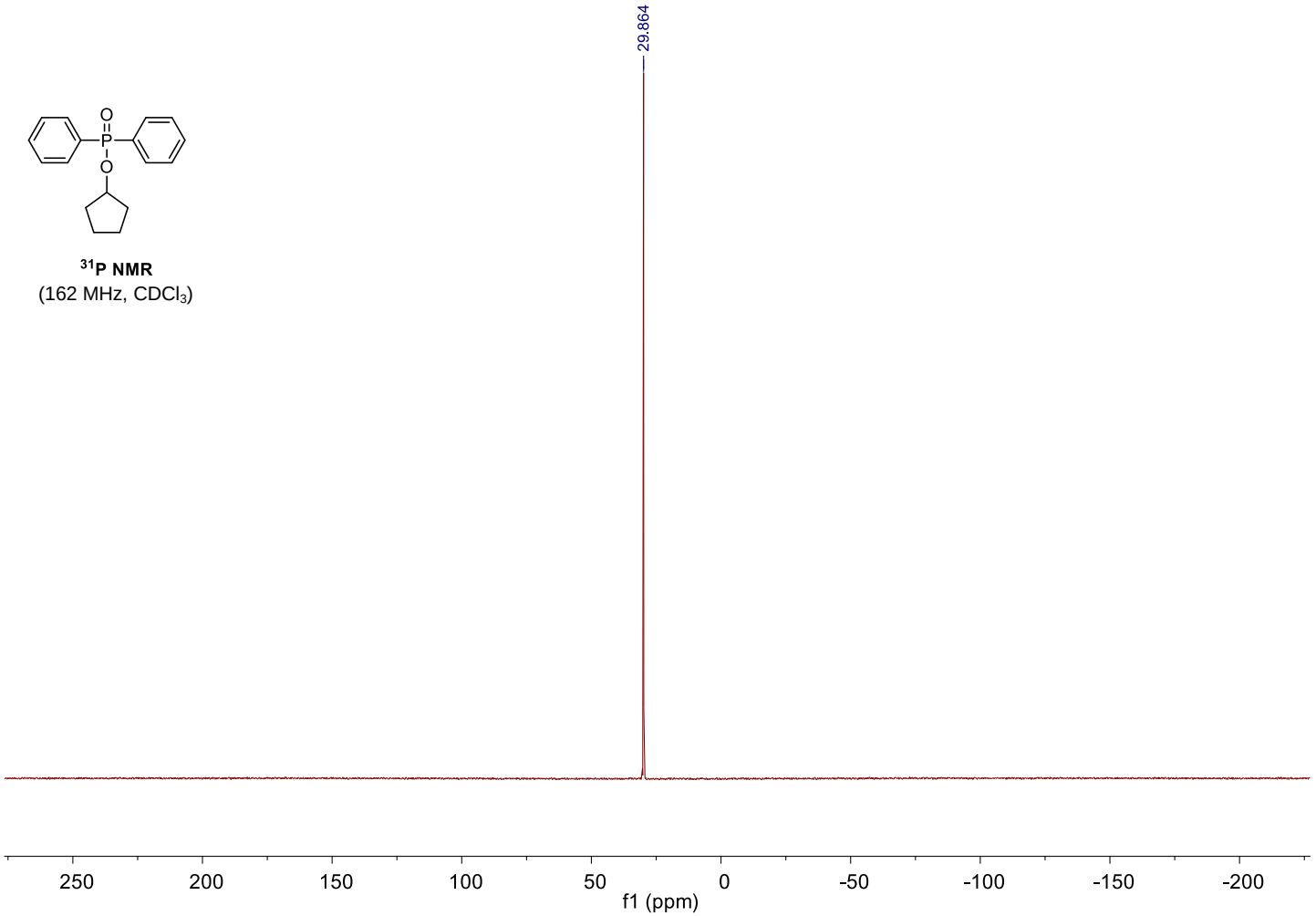
^{31}P NMR
(162 MHz, $CDCl_3$)


7.812
7.794
7.790
7.784
7.764
7.497
7.482
7.464
7.449
7.433
7.428
7.418
7.414
4.877
1.895
1.868
1.840
1.789
1.555
O
P
O
1H NMR
(400 MHz, CDCl3)
4.00
1.98
4.11
0.91
6.14
2.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

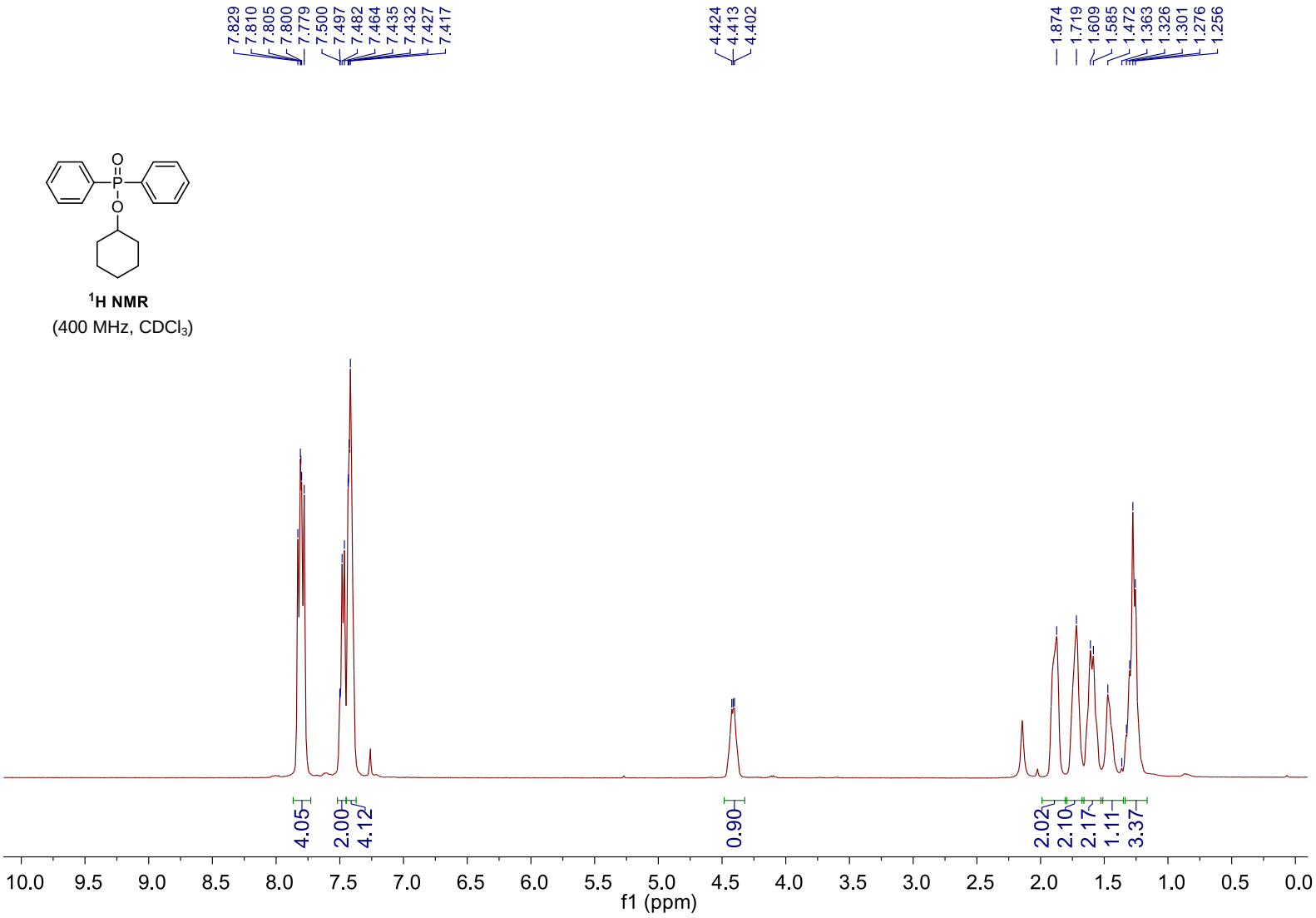


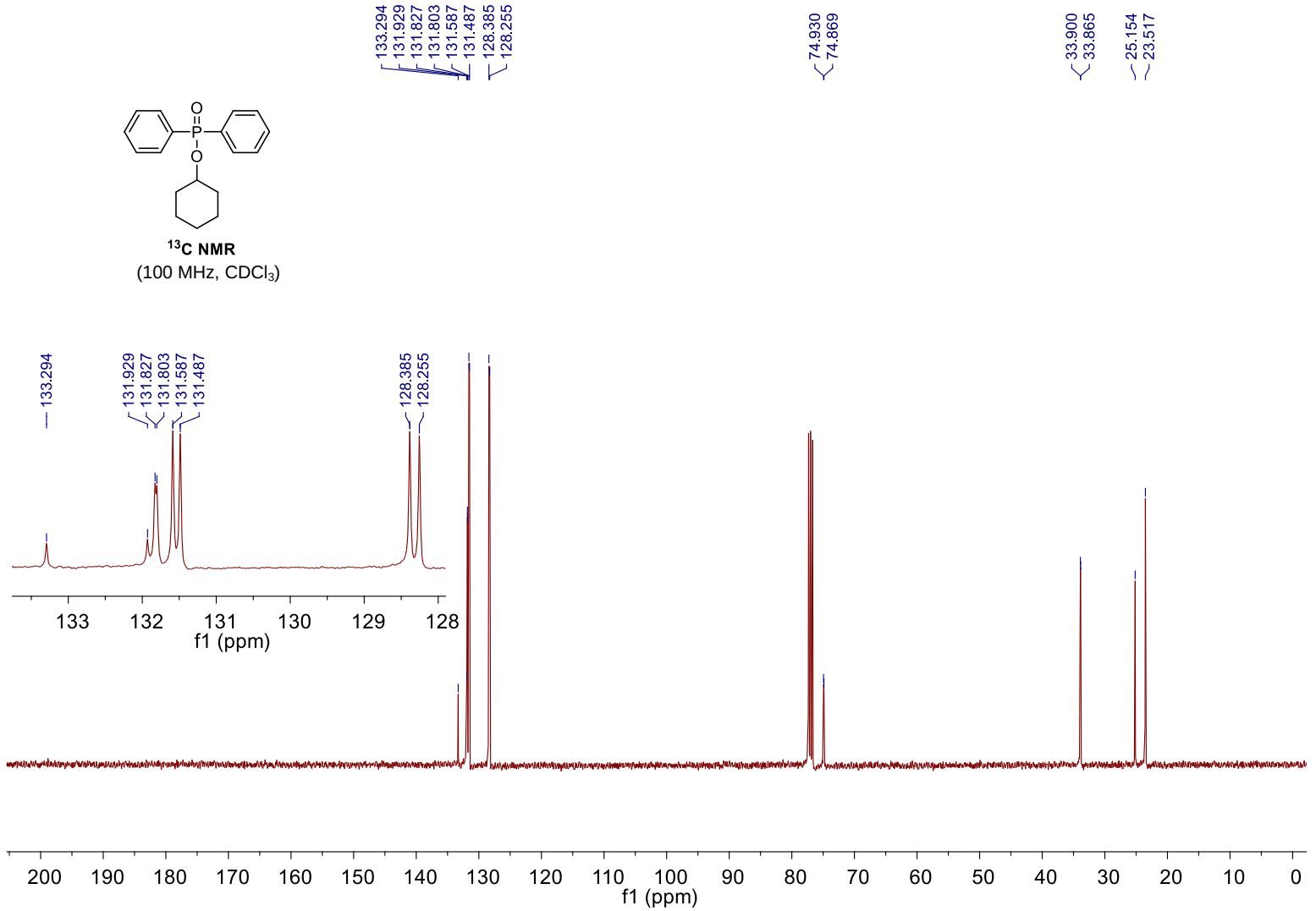
^{13}C NMR

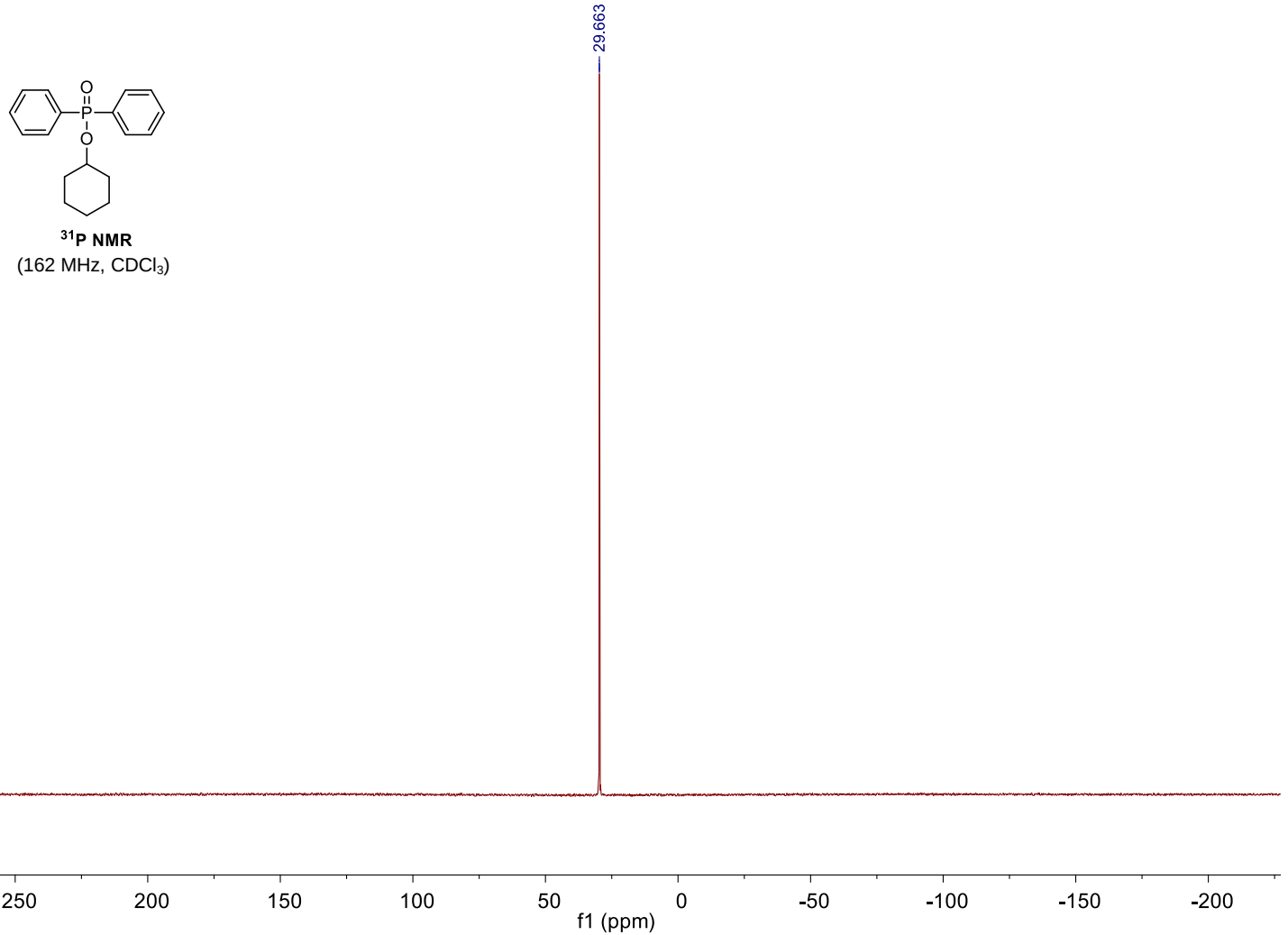
(100 MHz, $CDCl_3$)



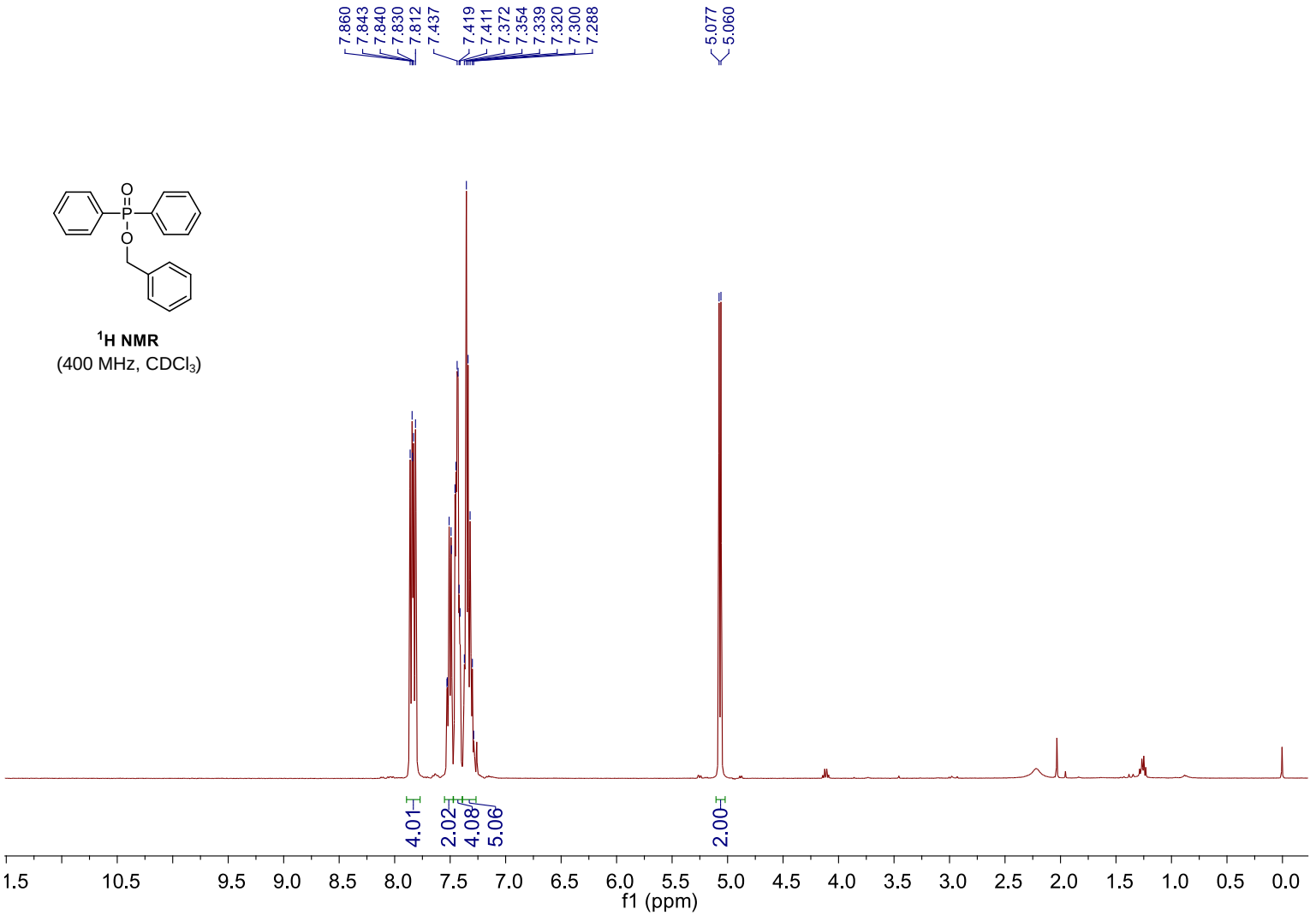
^{31}P NMR
(162 MHz, $CDCl_3$)

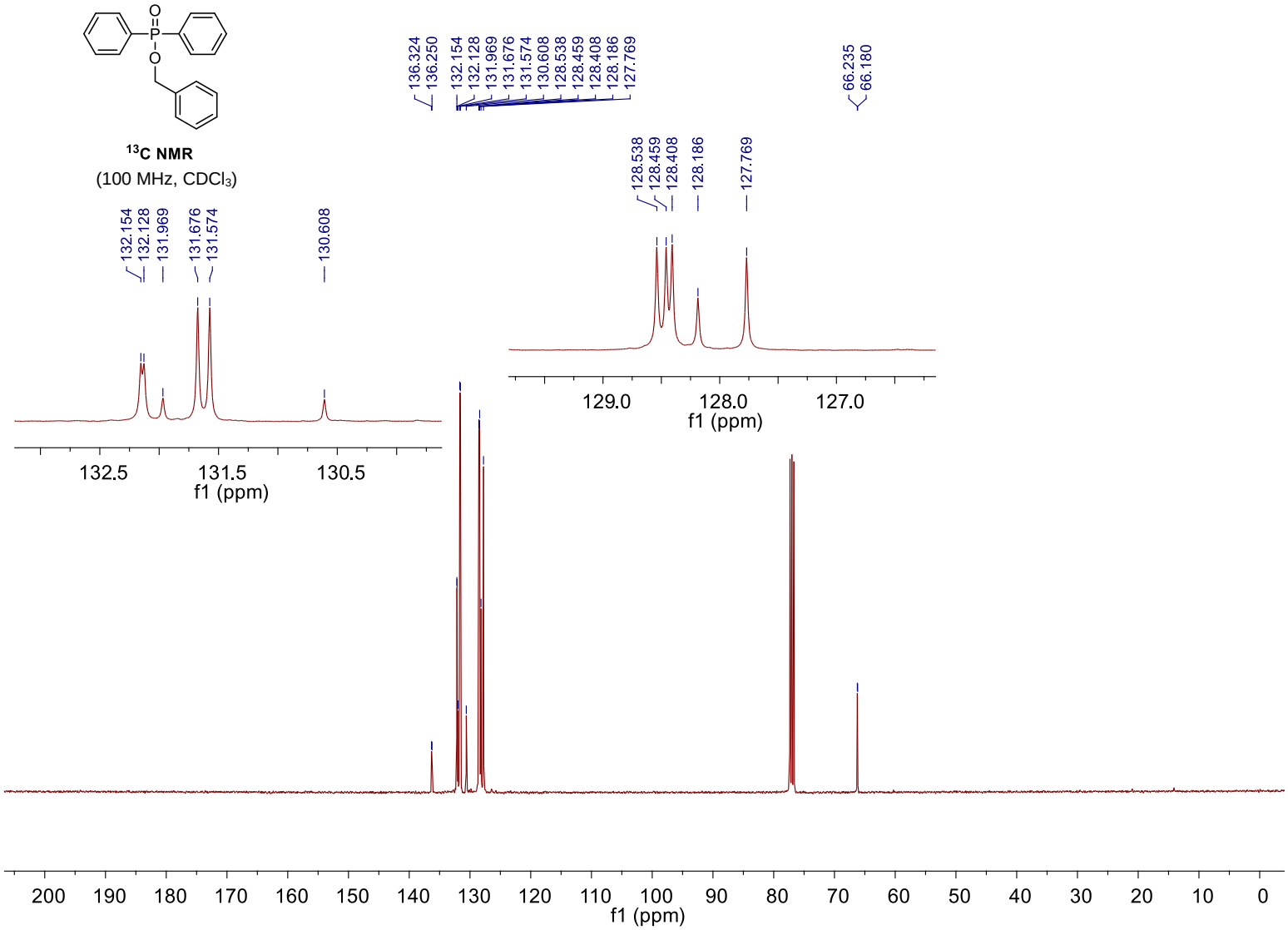

7.829
7.810
7.805
7.800
7.779
7.500
7.497
7.482
7.464
7.435
7.432
7.427
7.417
4.424
4.413
4.402
1.874
1.719
1.609
1.585
1.472
1.363
1.326
1.301
1.276
1.256
O
P
O
¹H NMR
(400 MHz, CDCl3)
4.05
2.00
4.12
0.90
2.02
2.10
2.17
1.11
3.37
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

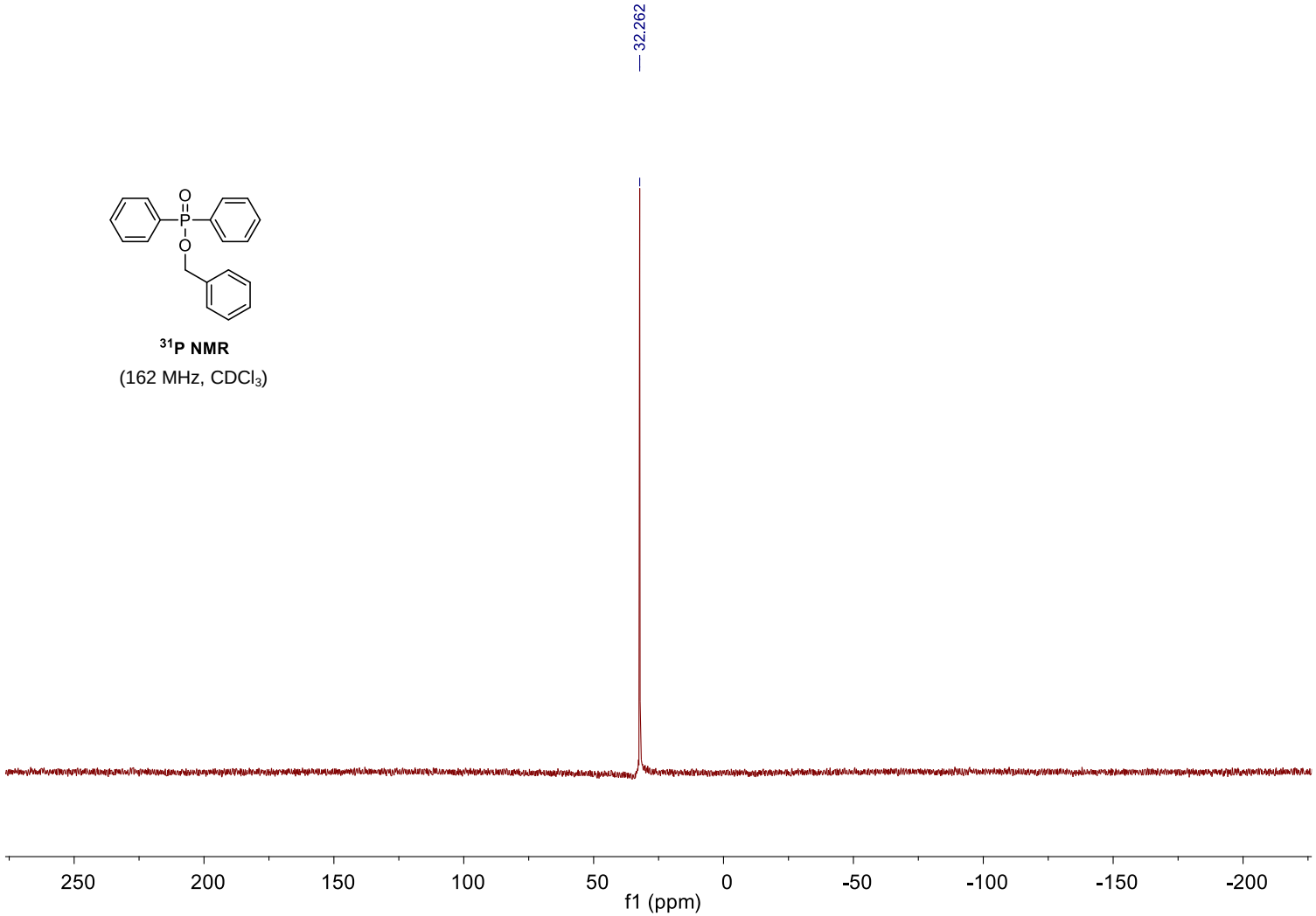

133.294
131.929
131.827
131.803
131.587
131.487
128.385
128.255
74.930
74.869
33.900
33.865
25.154
23.517
^{13}C NMR
(100 MHz, $CDCl_3$)
f1 (ppm)
f1 (ppm)



^{31}P NMR
(162 MHz, $CDCl_3$)

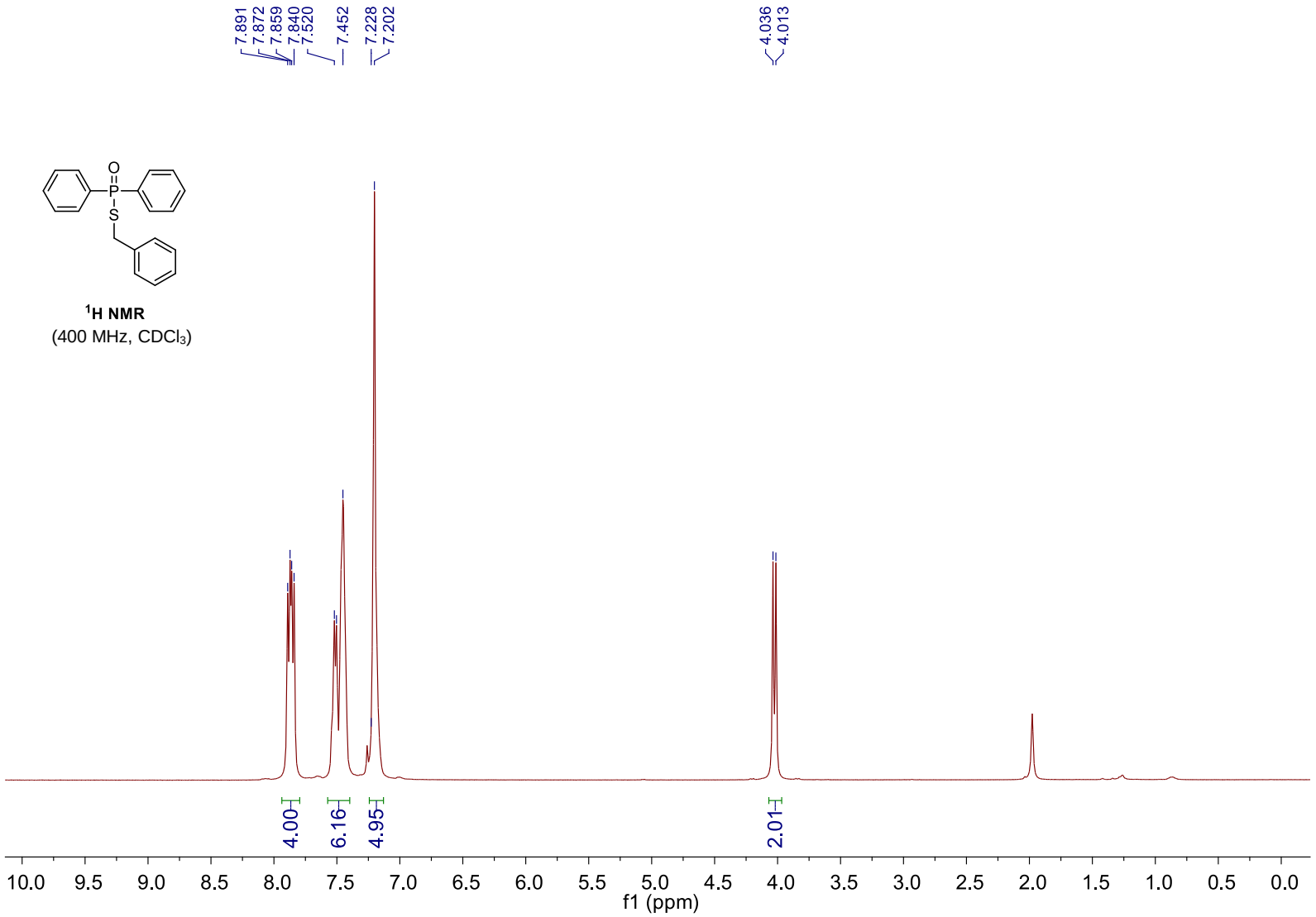

7.860
7.843
7.840
7.830
7.812
7.437
7.419
7.411
7.372
7.354
7.339
7.320
7.300
7.288
5.077
5.060
O
P
O
¹H NMR
(400 MHz, CDCl3)
4.01
2.02
4.08
5.06
2.00
1.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

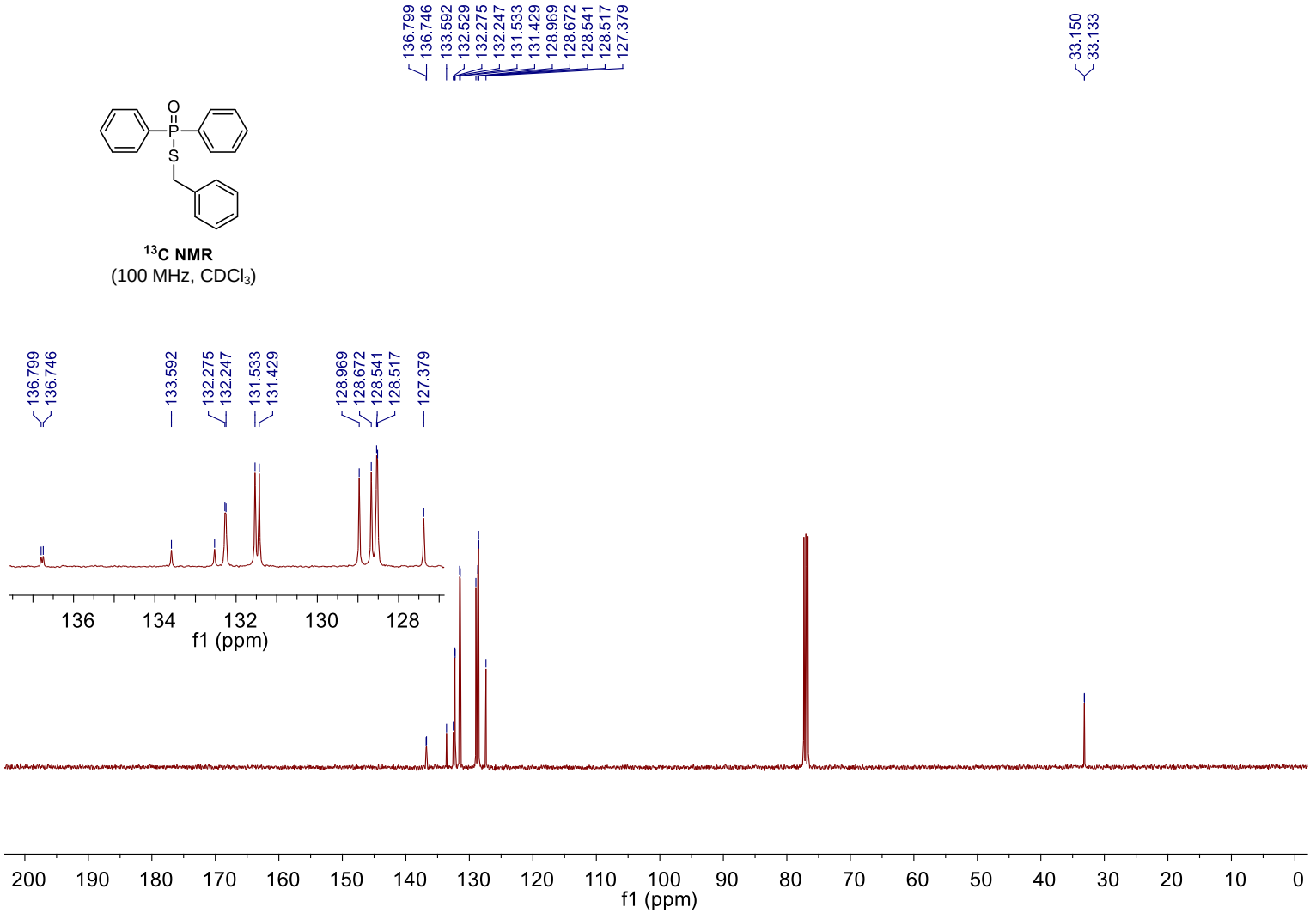

^{13}C NMR
(100 MHz, $CDCl_3$)
136.324
136.250
132.154
132.128
131.969
131.676
131.574
130.608
128.538
128.459
128.408
128.186
127.769
66.235
66.180
f1 (ppm)

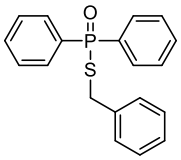


^{31}P NMR

(162 MHz, $CDCl_3$)

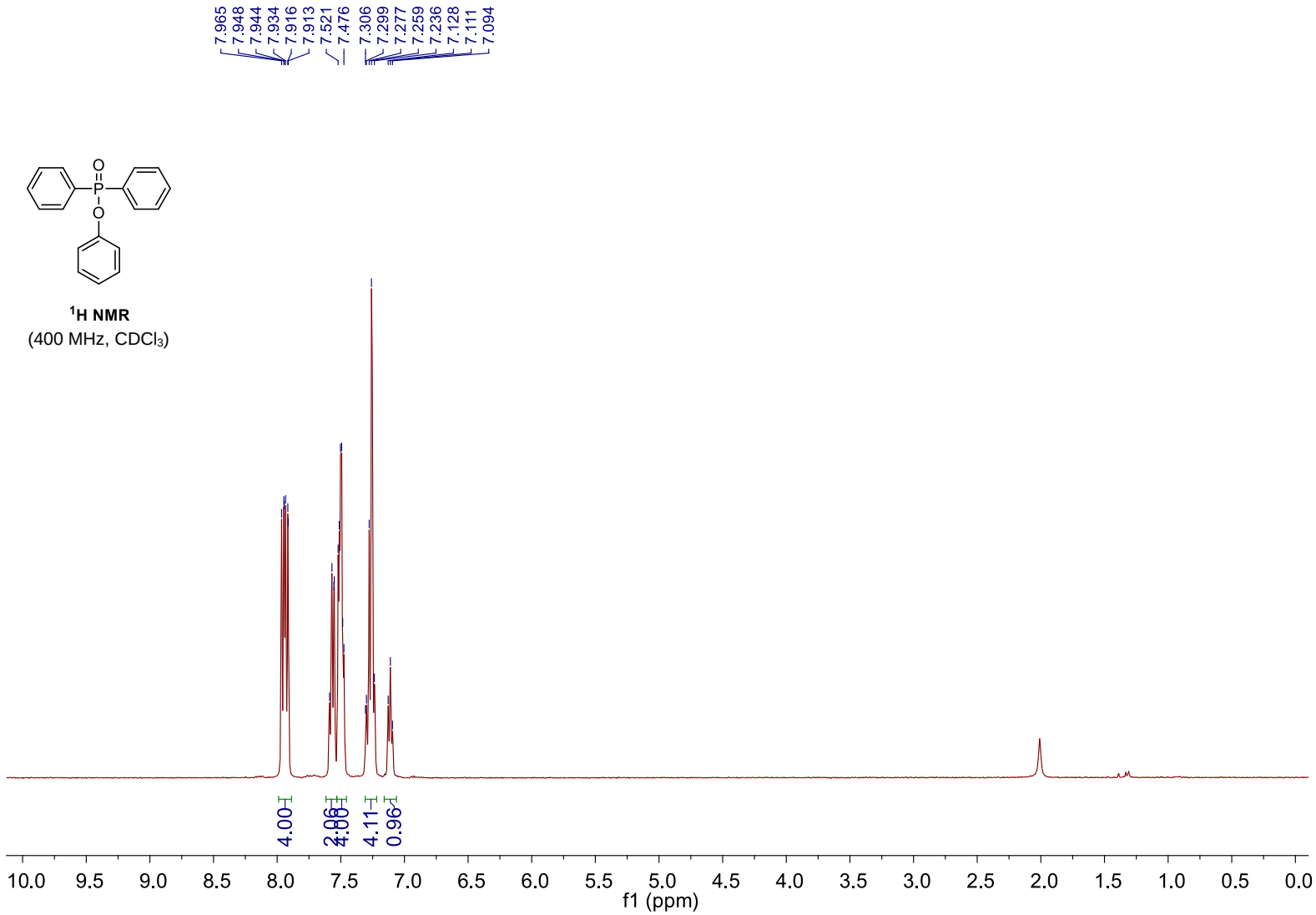

7.891
7.872
7.859
7.840
7.520
7.452
7.228
7.202
4.036
4.013
O
P
S
1H NMR
(400 MHz, CDCl3)
4.00
6.16
4.95
2.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

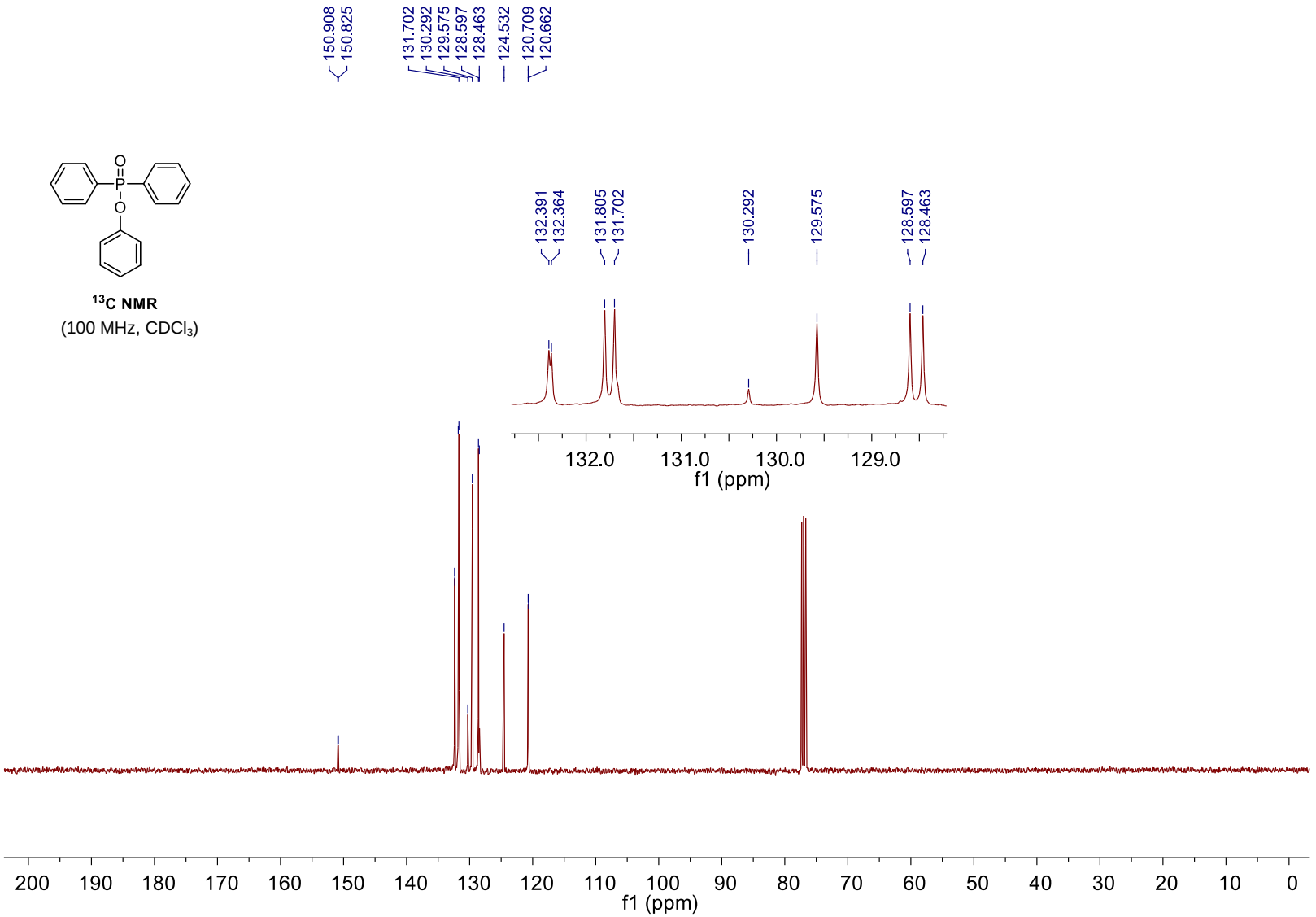

136.799
136.746
133.592
132.529
132.275
132.247
131.533
131.429
128.969
128.672
128.541
128.517
127.379
33.150
33.133
O
P
S
13C NMR
(100 MHz, CDCl3)
f1 (ppm)
f1 (ppm)



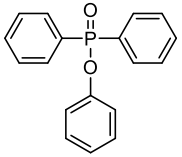
^{31}P NMR

(162 MHz, $CDCl_3$)


7.965
7.948
7.944
7.934
7.916
7.913
7.521
7.476
7.306
7.299
7.277
7.259
7.236
7.128
7.111
7.094
O
P
O
1H NMR
(400 MHz, CDCl3)
4.00
2.06
4.00
4.11
0.96
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

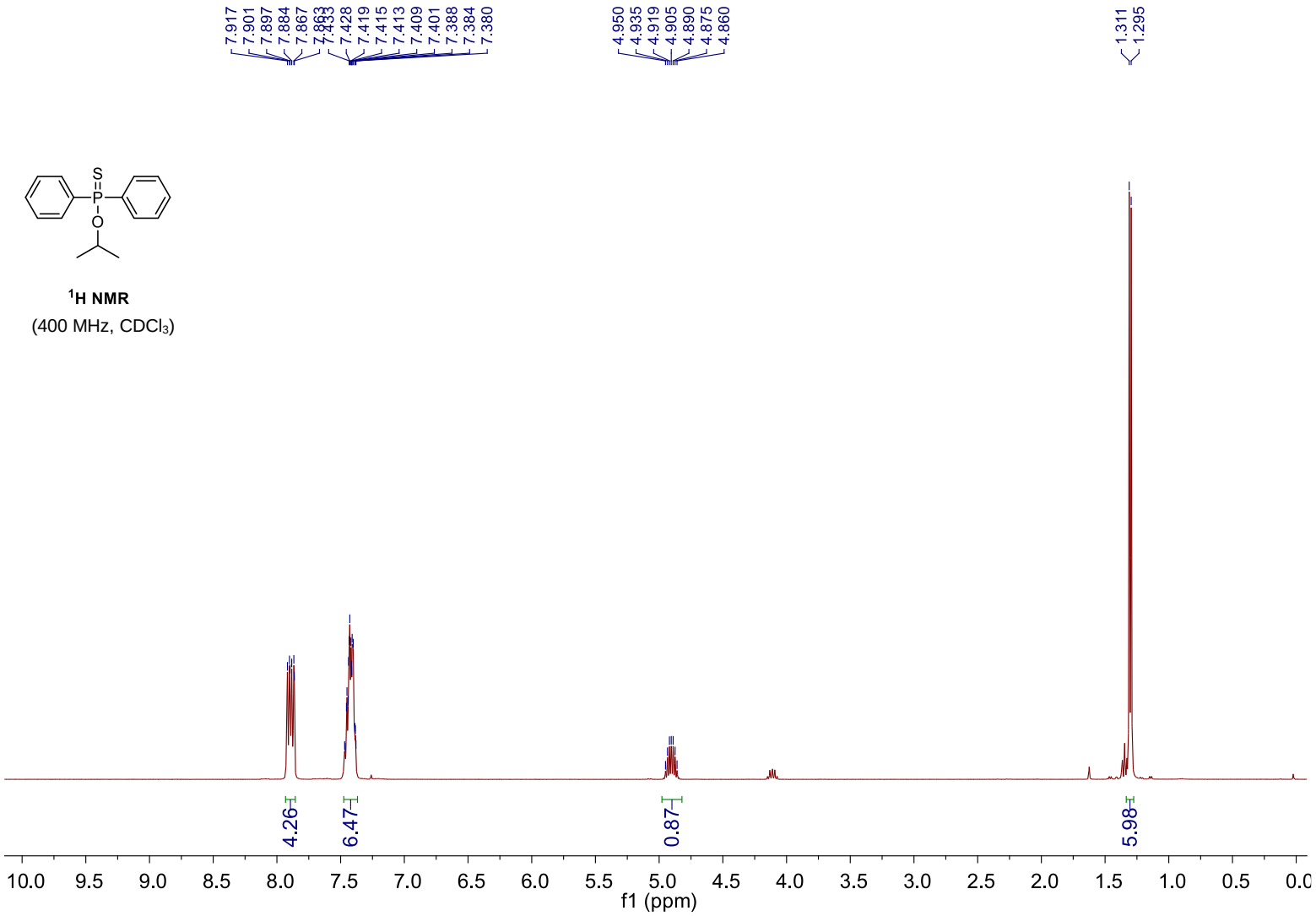


^{13}C NMR
(100 MHz, $CDCl_3$)



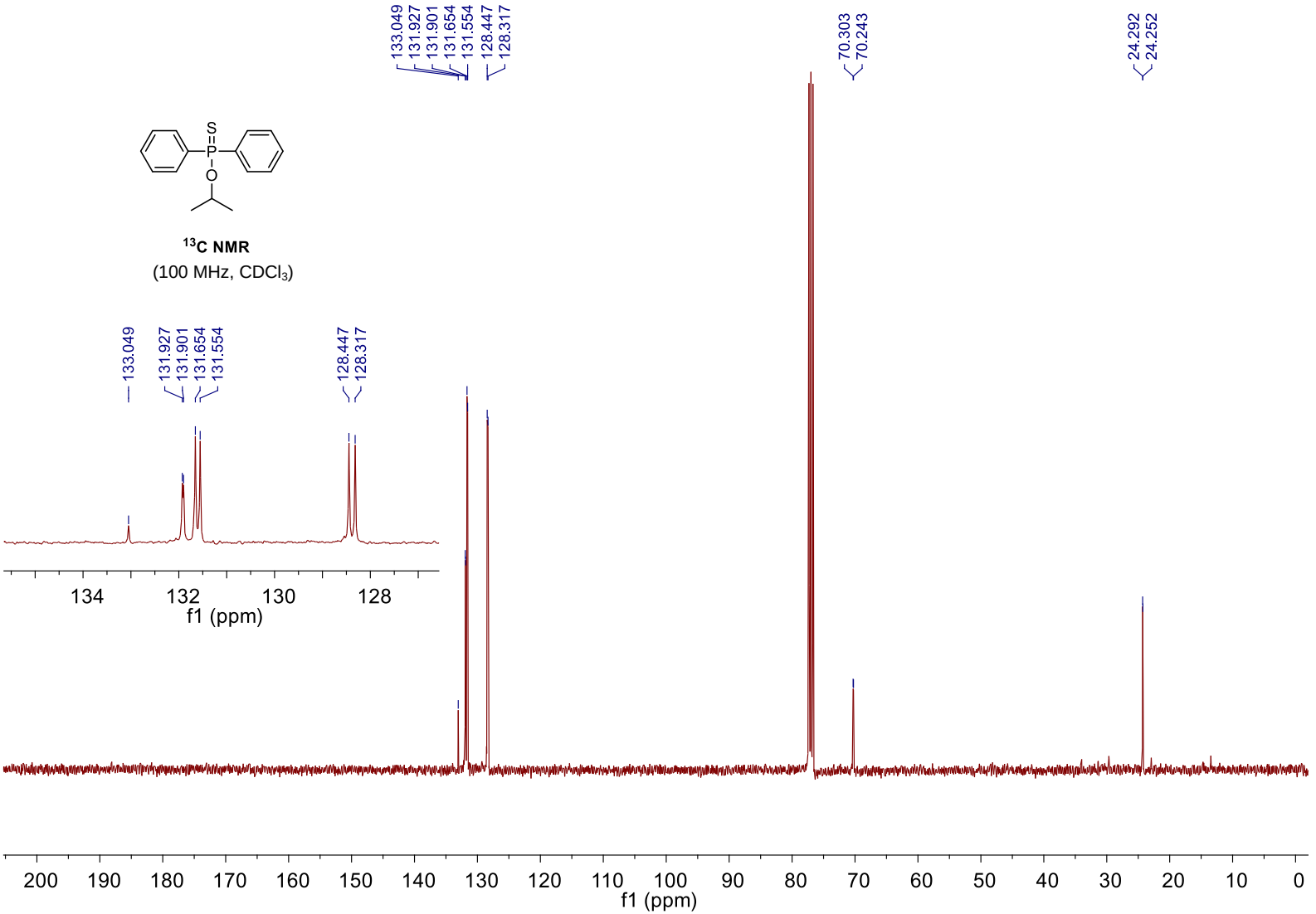
^{31}P NMR

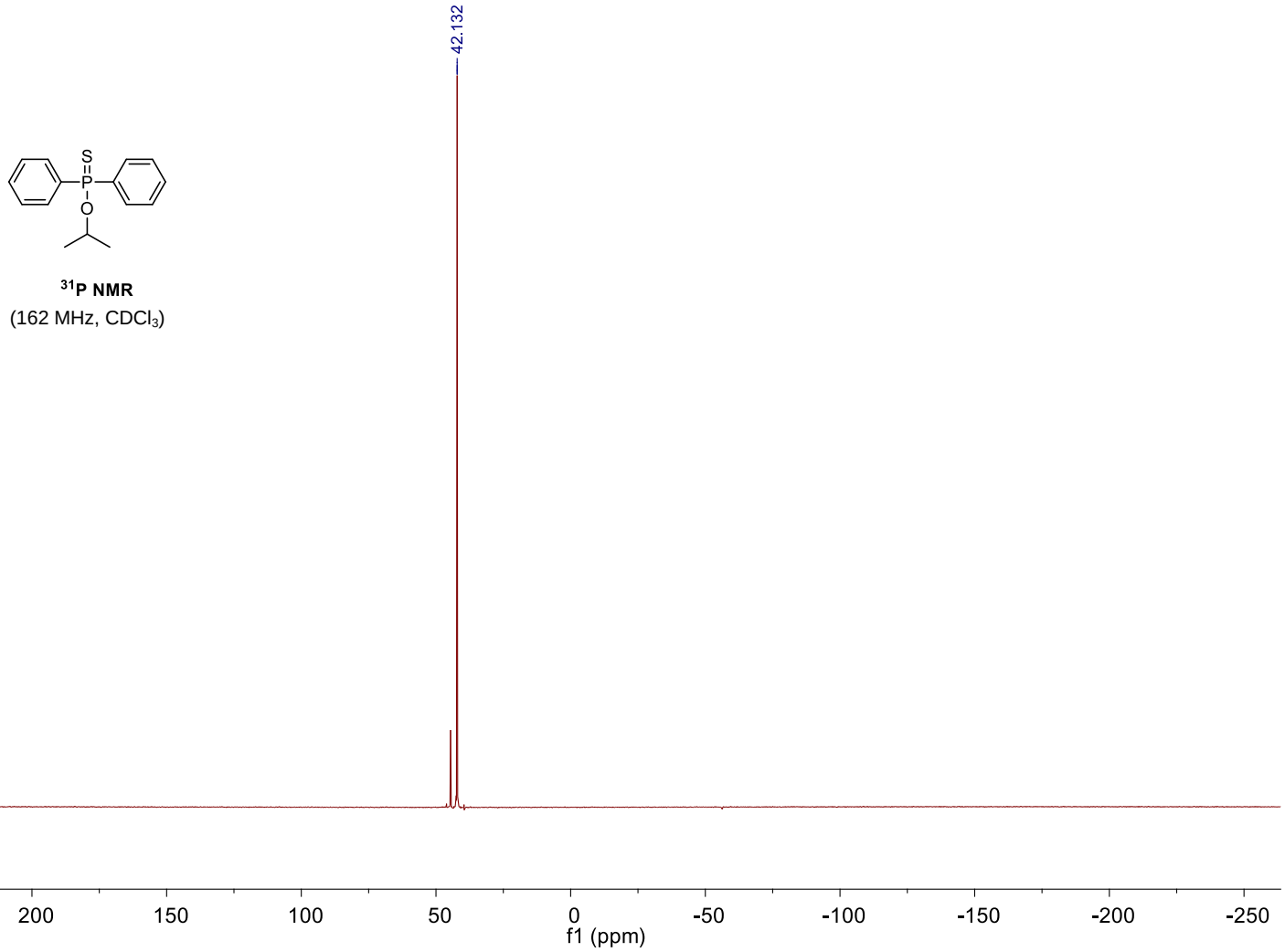
(162 MHz, $CDCl_3$)



^{1}H NMR

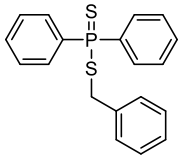
(400 MHz, $CDCl_3$)


133.049
131.927
131.901
131.654
131.554
128.447
128.317
70.303
70.243
24.292
24.252
S
P
O
13C NMR
(100 MHz, CDCl3)
134
132
130
128
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

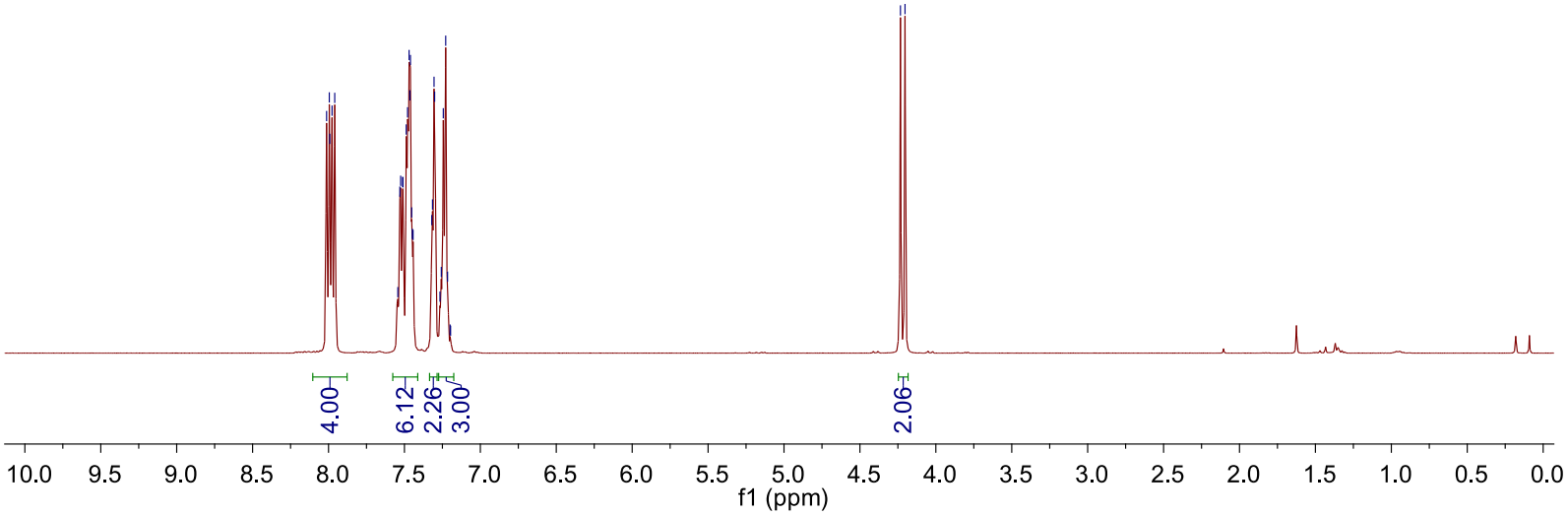


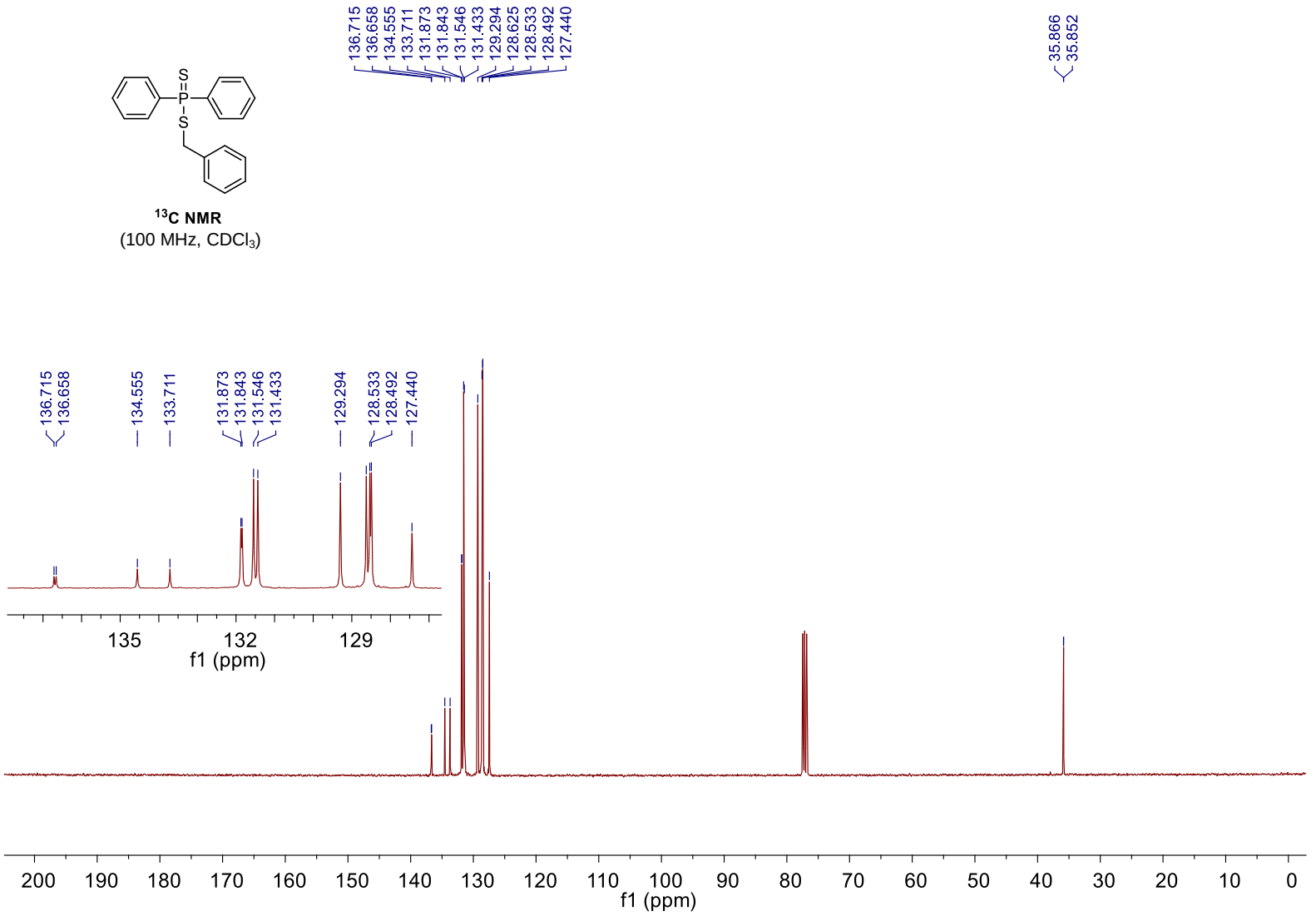
^{31}P NMR

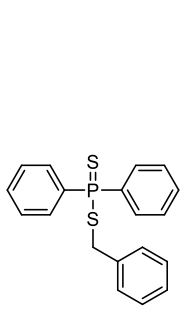
(162 MHz, $CDCl_3$)



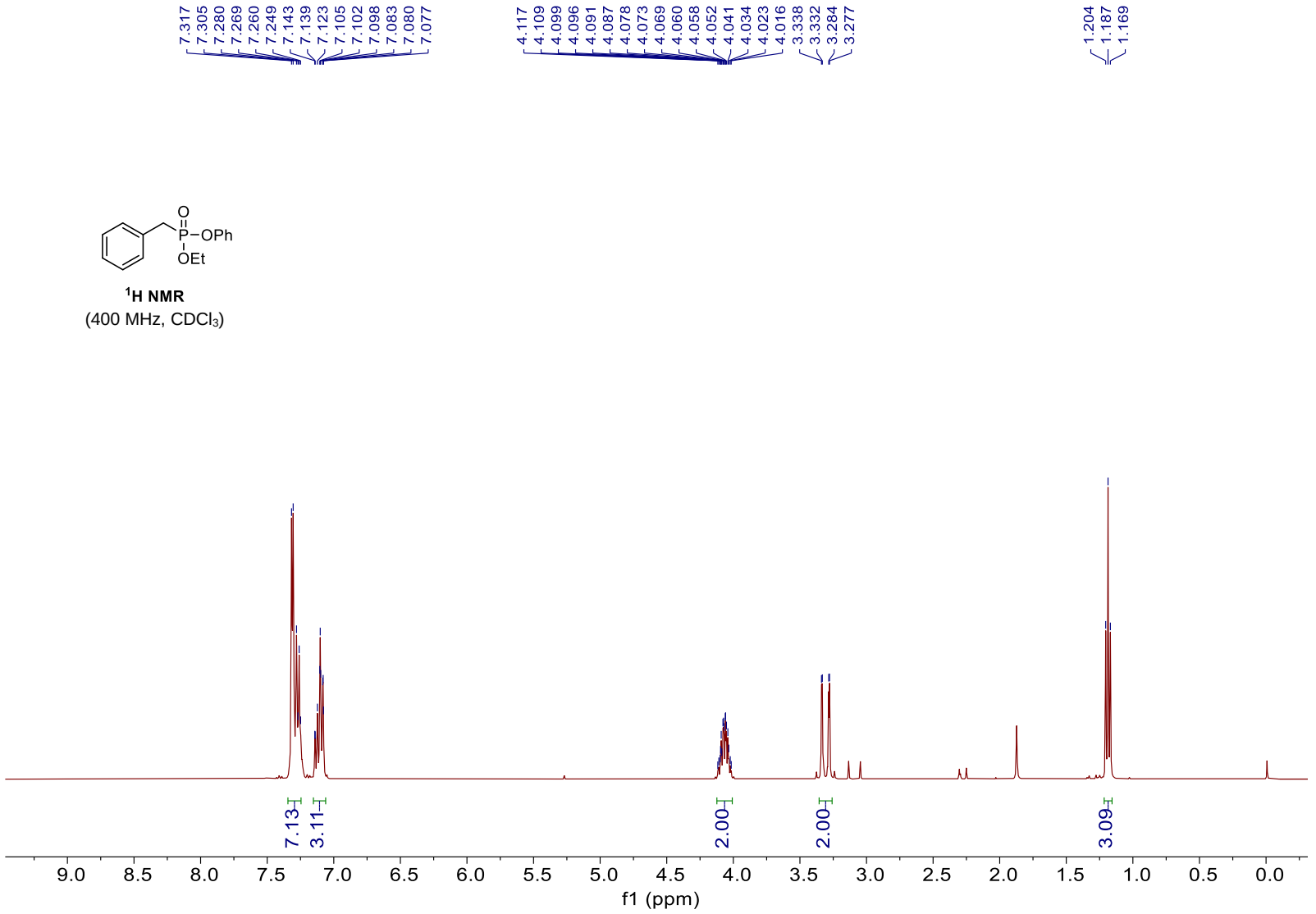
^{1}H NMR
(400 MHz, $CDCl_3$)



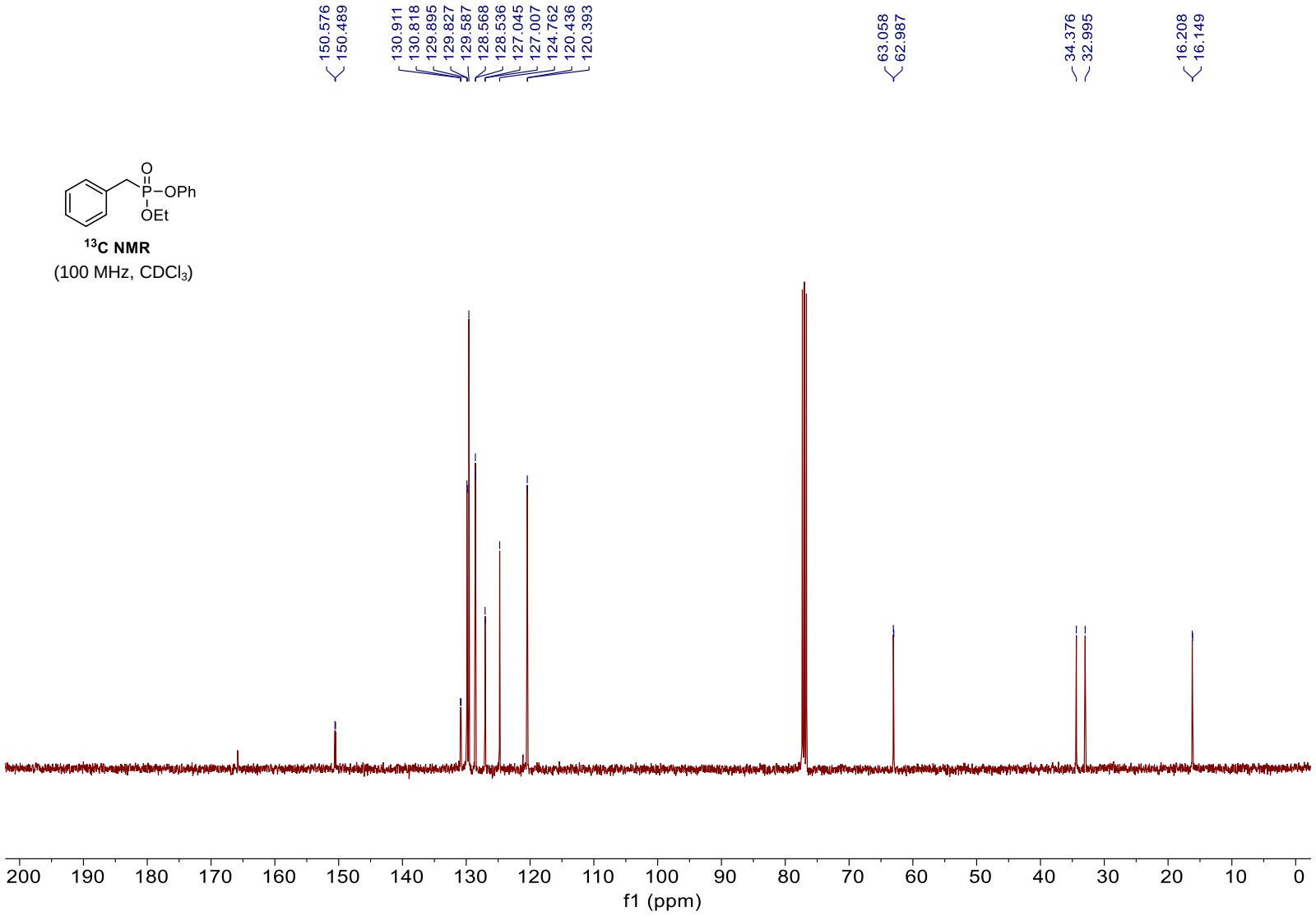

136.715
136.658
134.555
133.711
131.873
131.843
131.546
131.433
129.294
128.625
128.533
128.492
127.440
35.866
35.852
S
P
S
^{13}C NMR
(100 MHz, CDCl$_3$)
135
132
129
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

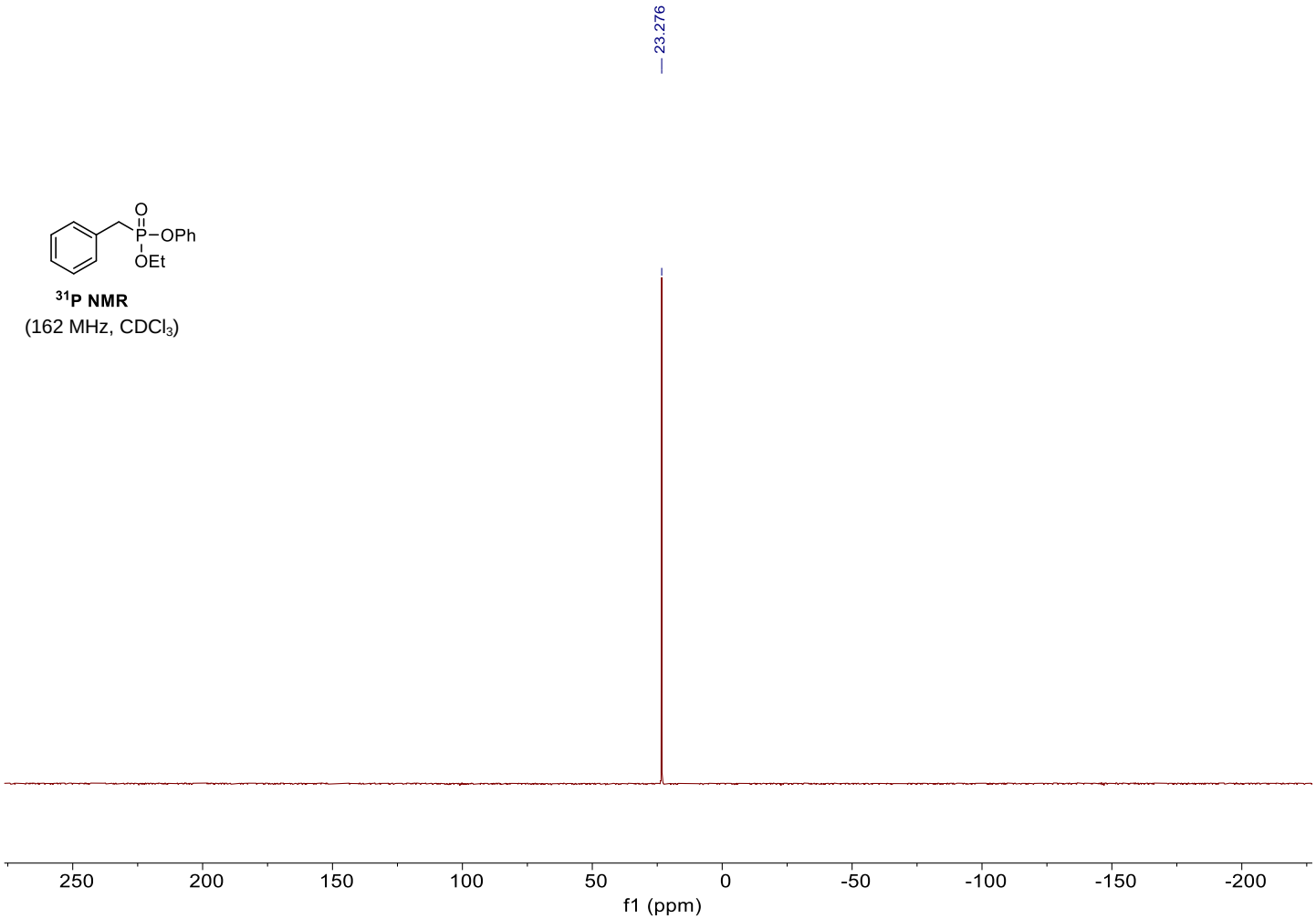


^{31}P NMR
(162 MHz, $CDCl_3$)

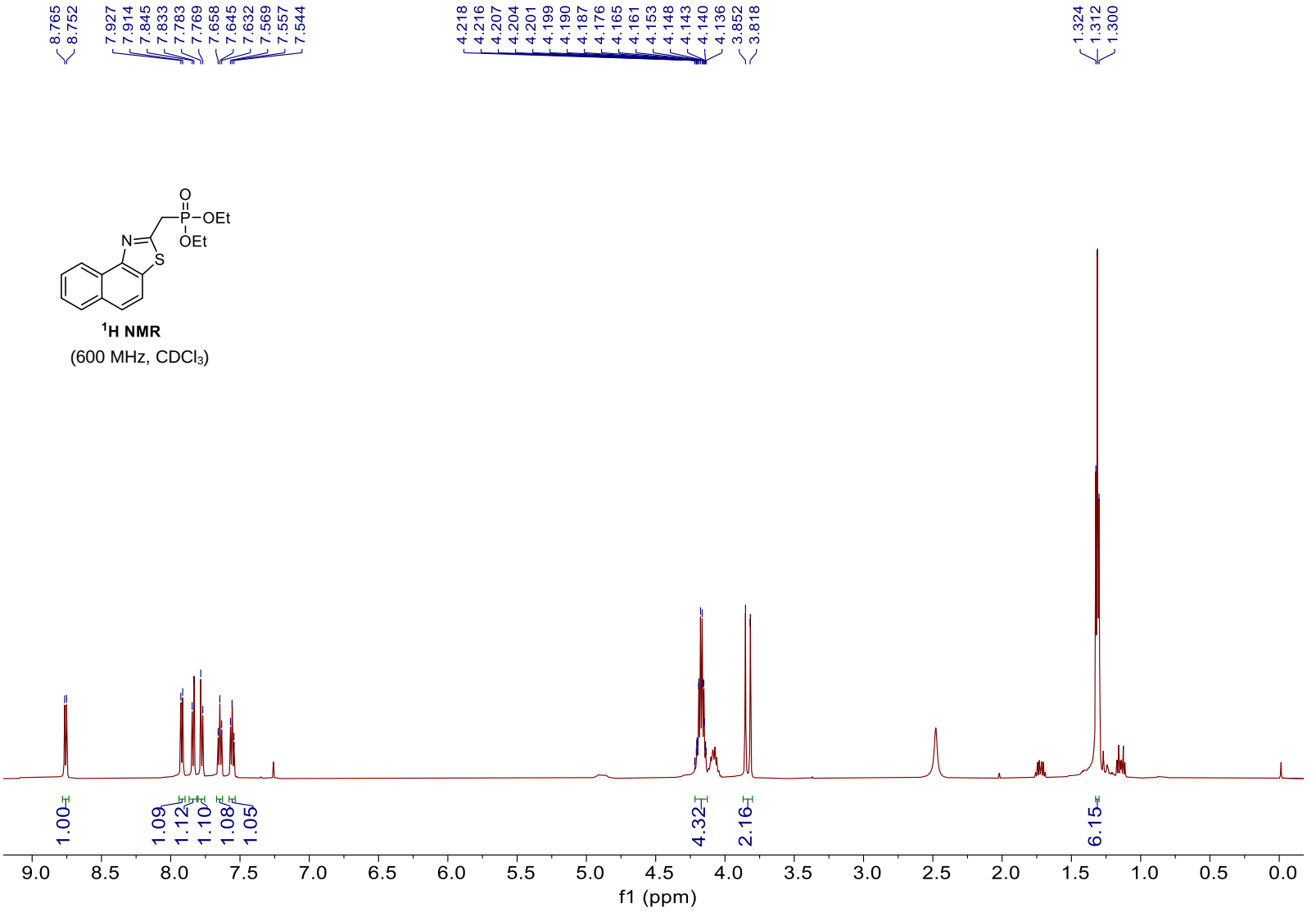


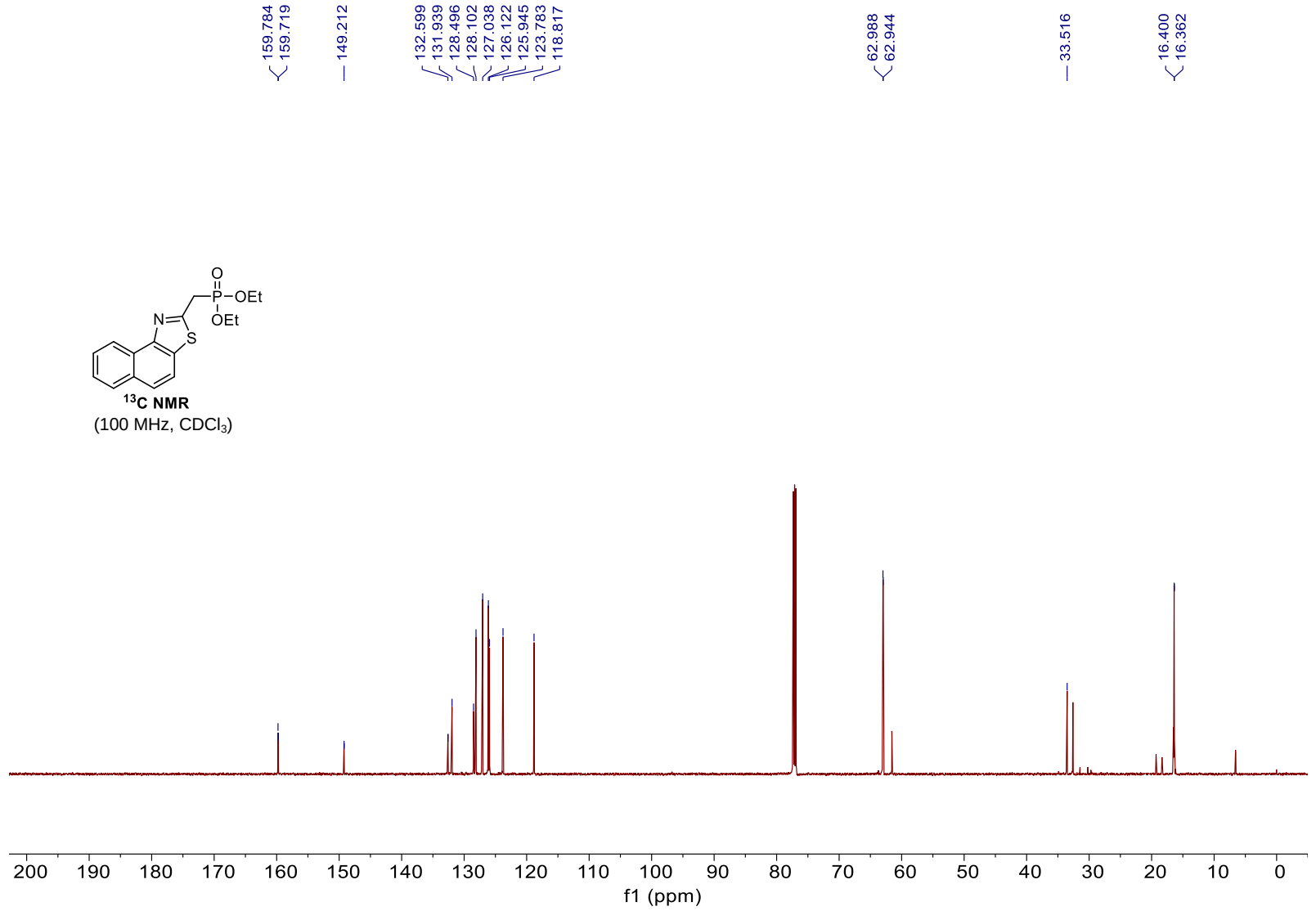
^{1}H NMR
(400 MHz, $CDCl_3$)


150.576
150.489
130.911
130.818
129.895
129.827
129.587
128.568
128.536
127.045
127.007
124.762
120.436
120.393
63.058
62.987
34.376
32.995
16.208
16.149
O
P–OPh
OEt
13C NMR
(100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

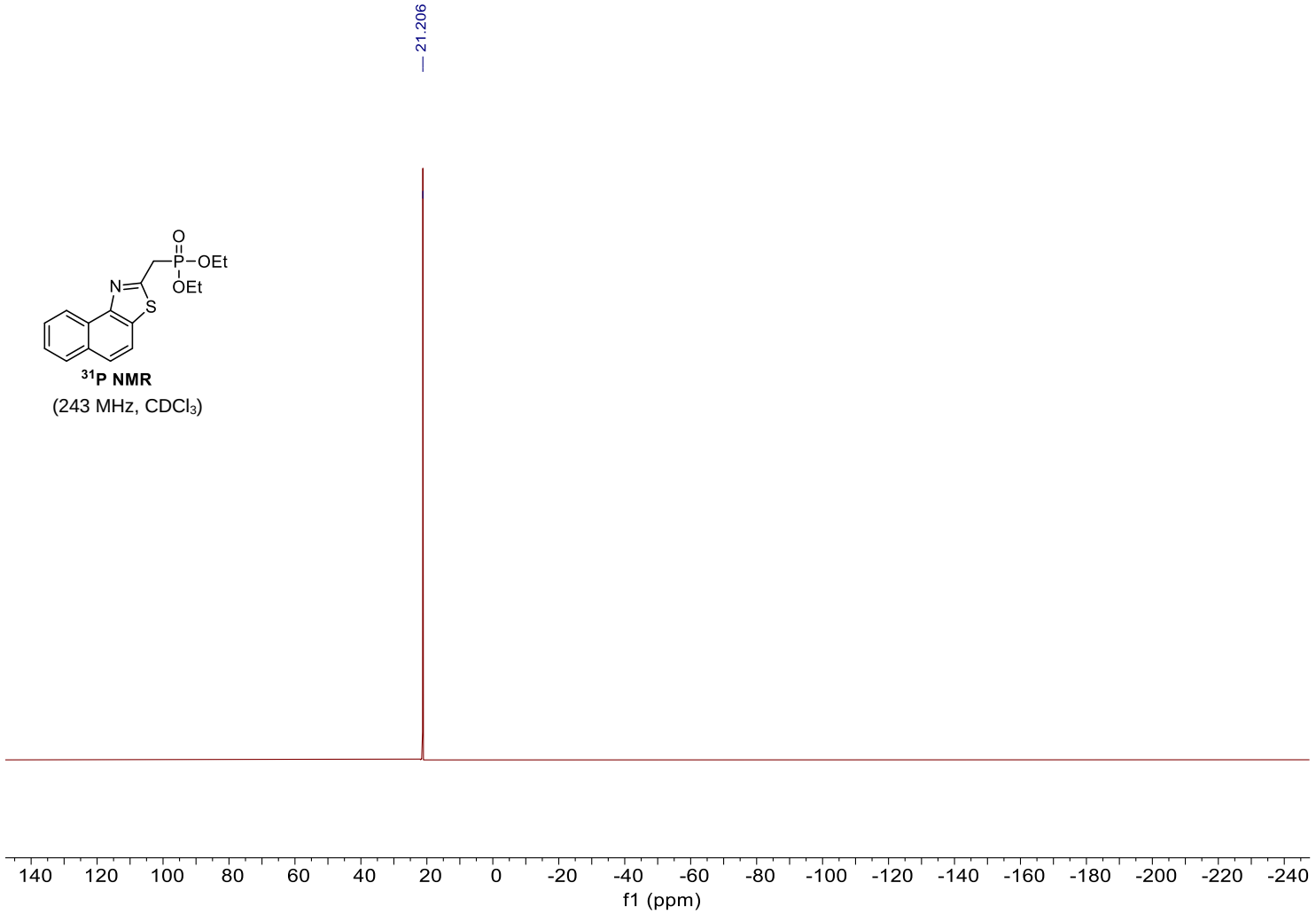


^{31}P NMR
(162 MHz, $CDCl_3$)


8.765
8.752
7.927
7.914
7.845
7.833
7.783
7.769
7.658
7.645
7.632
7.569
7.557
7.544
4.218
4.216
4.207
4.204
4.201
4.199
4.190
4.187
4.176
4.165
4.161
4.153
4.148
4.143
4.140
4.136
3.852
3.818
1.324
1.312
1.300
O
P
OEt
OEt
N
S
1H NMR
(600 MHz, CDCl3)
1.00
1.09
1.12
1.10
1.08
1.05
4.32
2.16
6.15
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

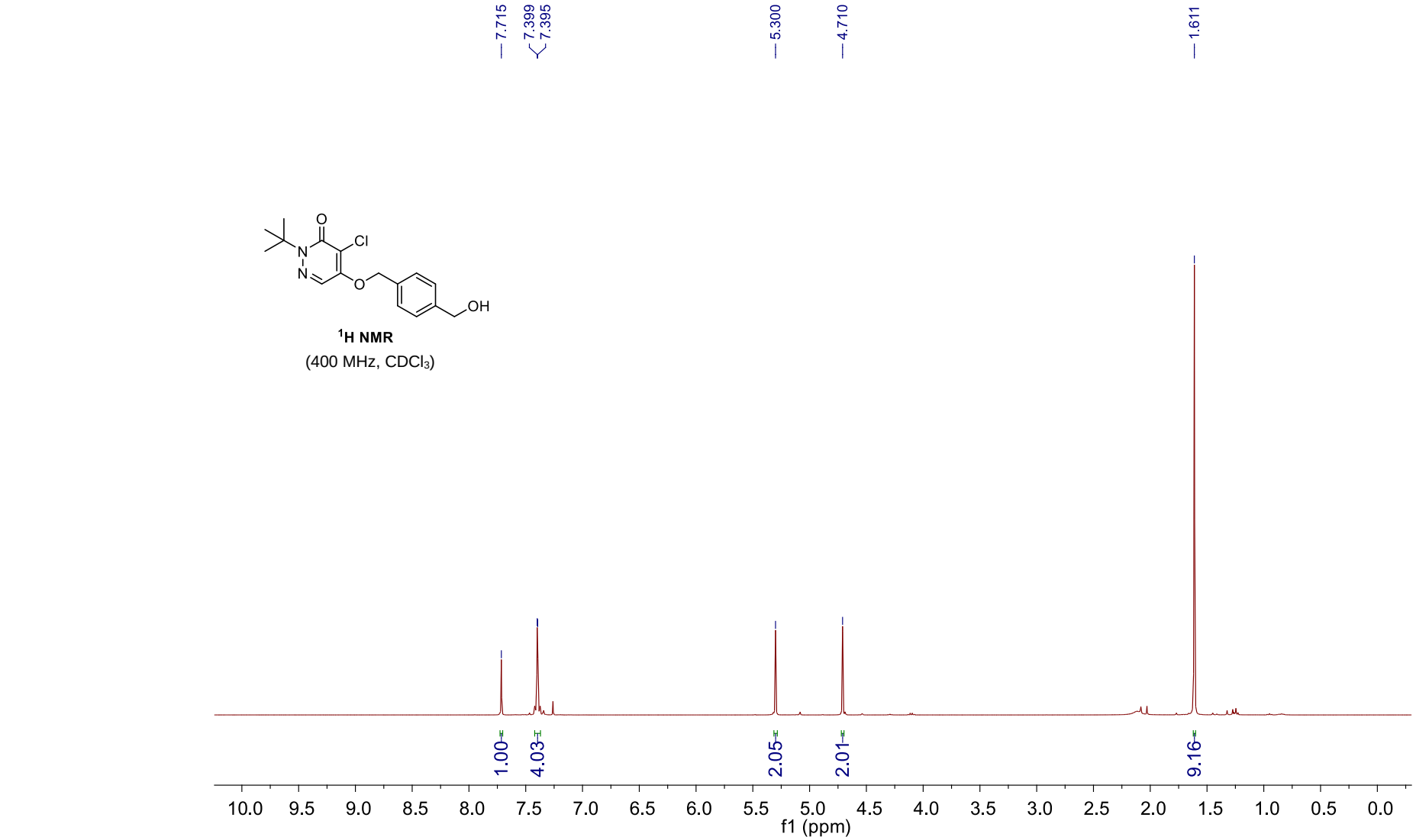


^{13}C NMR
(100 MHz, $CDCl_3$)



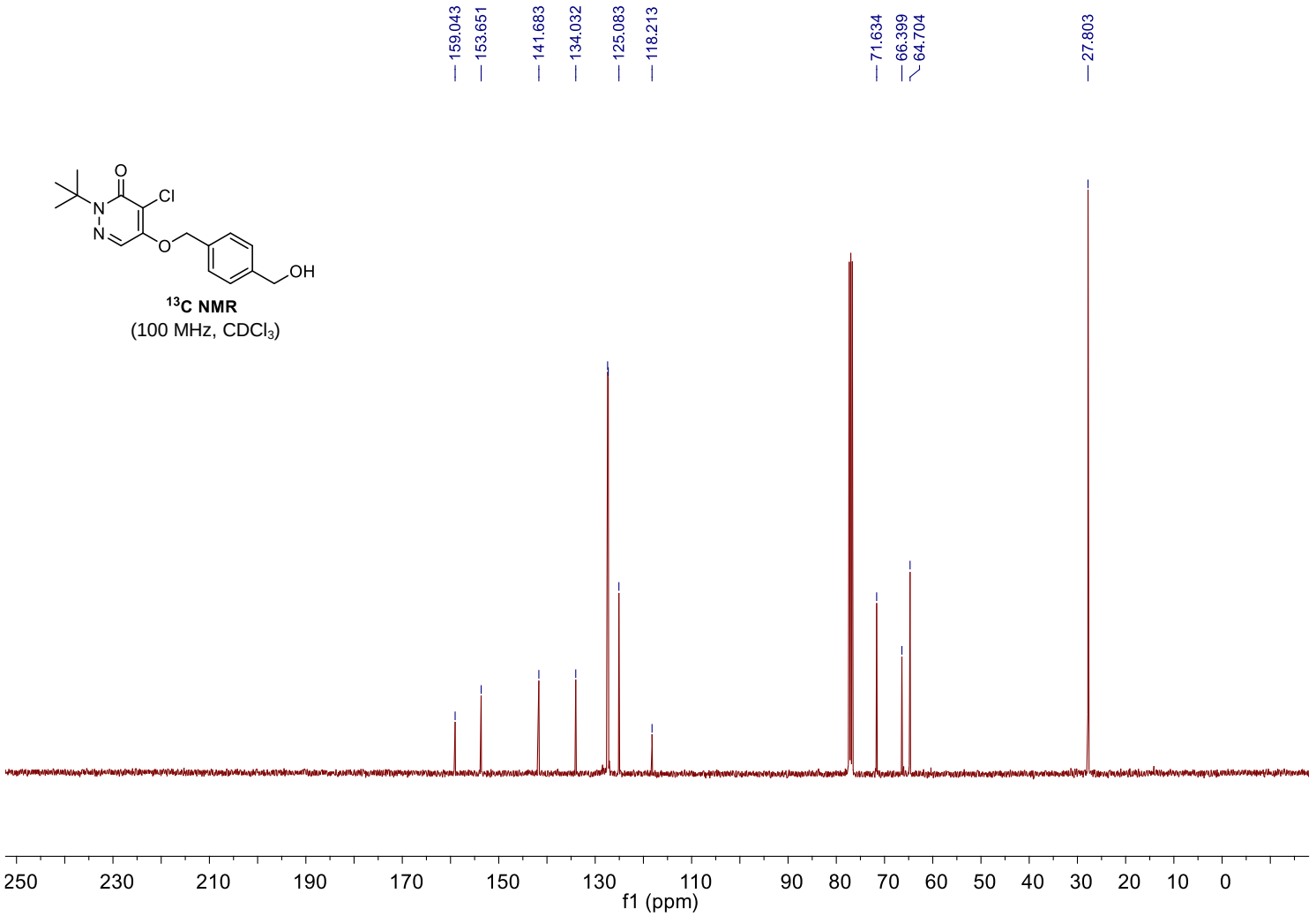
^{31}P NMR

(243 MHz, $CDCl_3$)

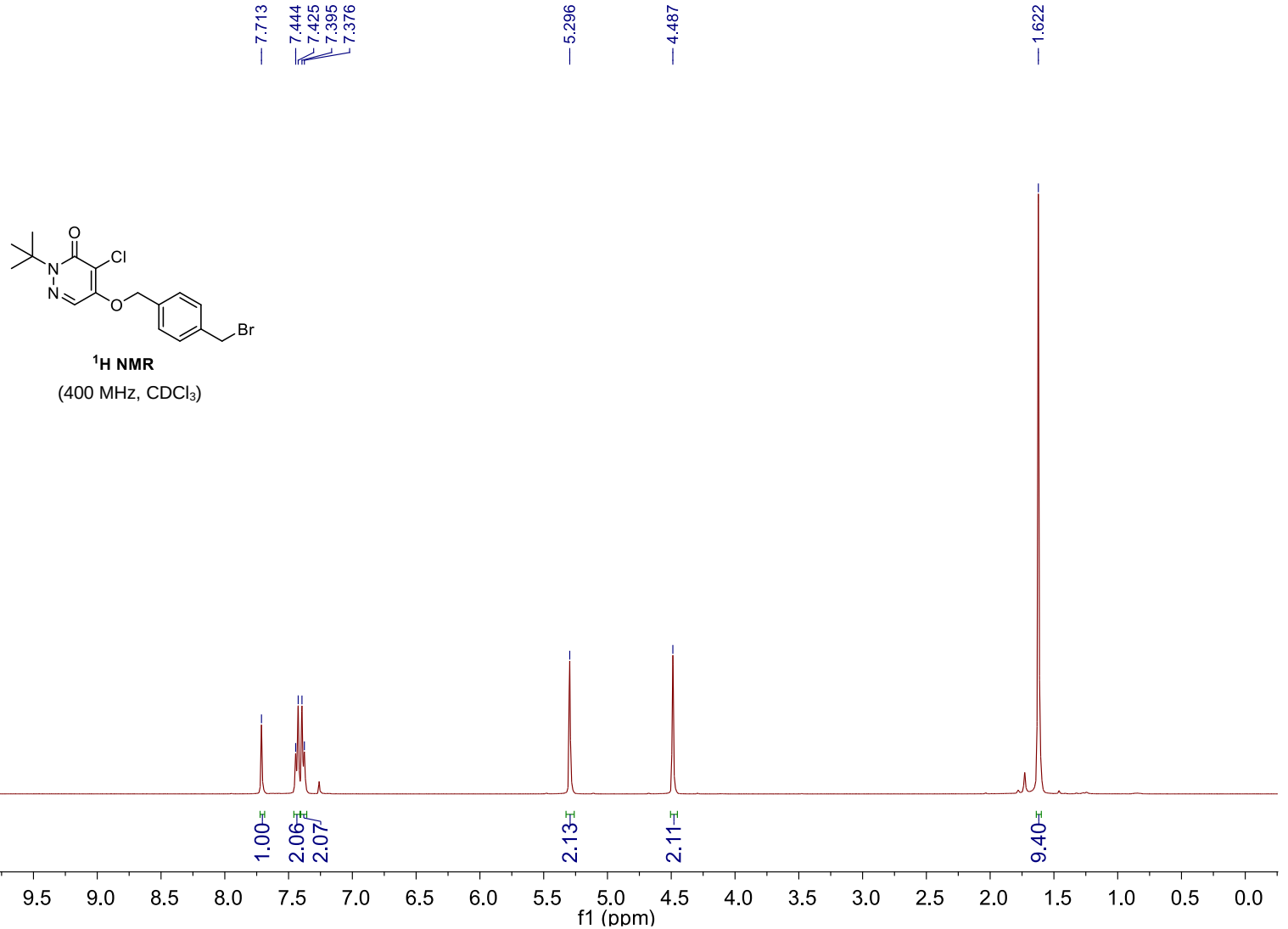


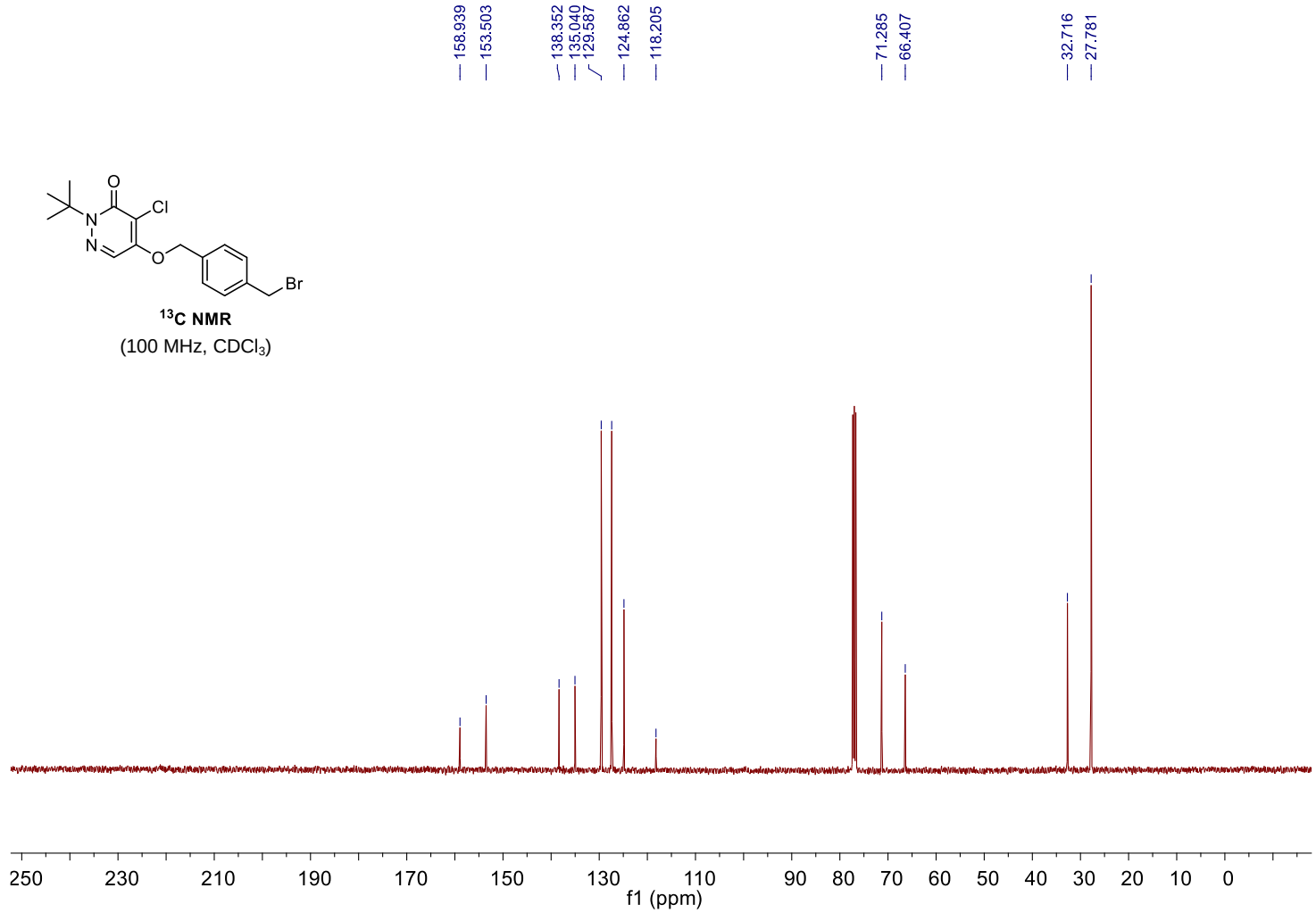
^{1}H NMR

(400 MHz, $CDCl_3$)



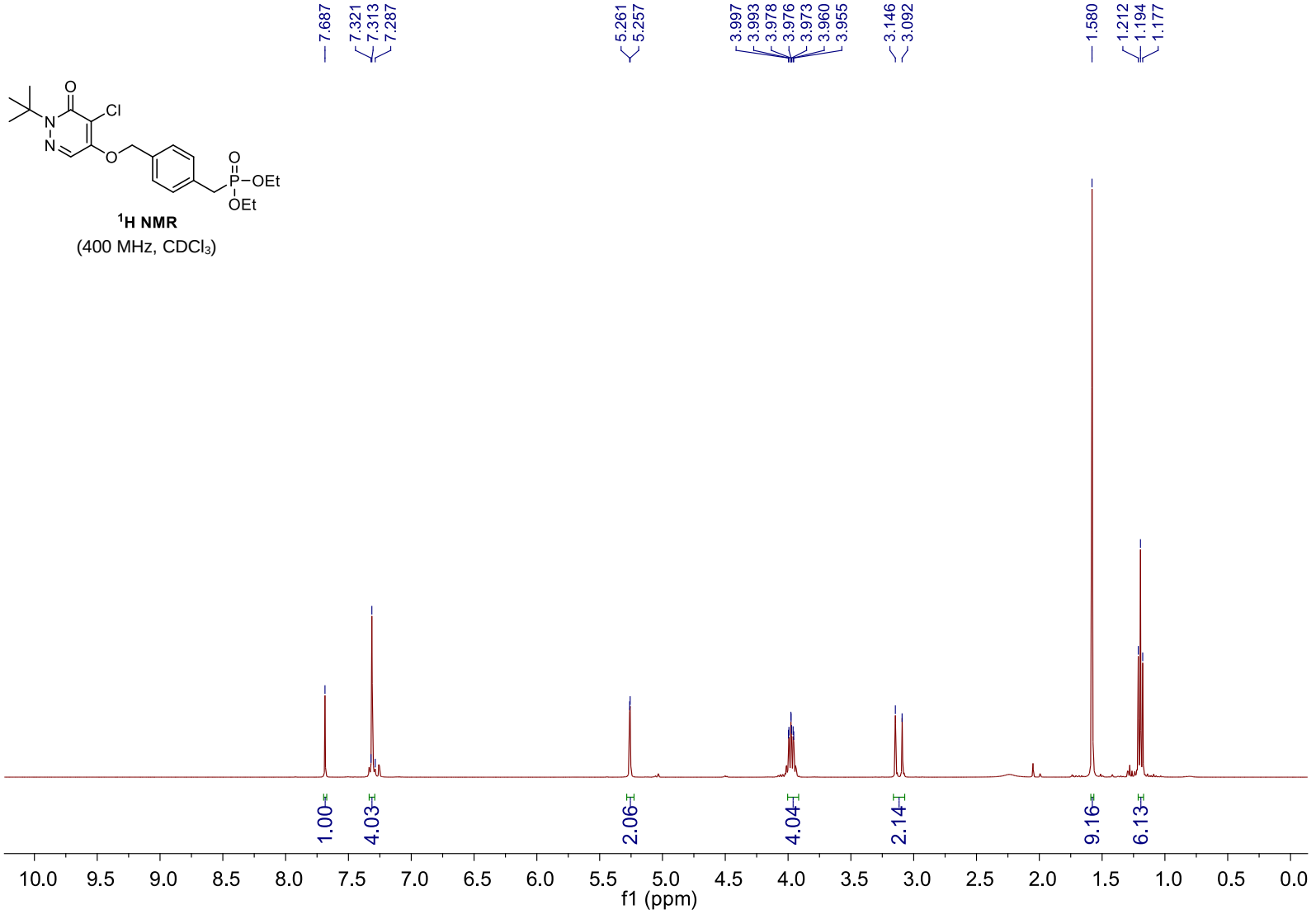
^{13}C NMR
(100 MHz, $CDCl_3$)

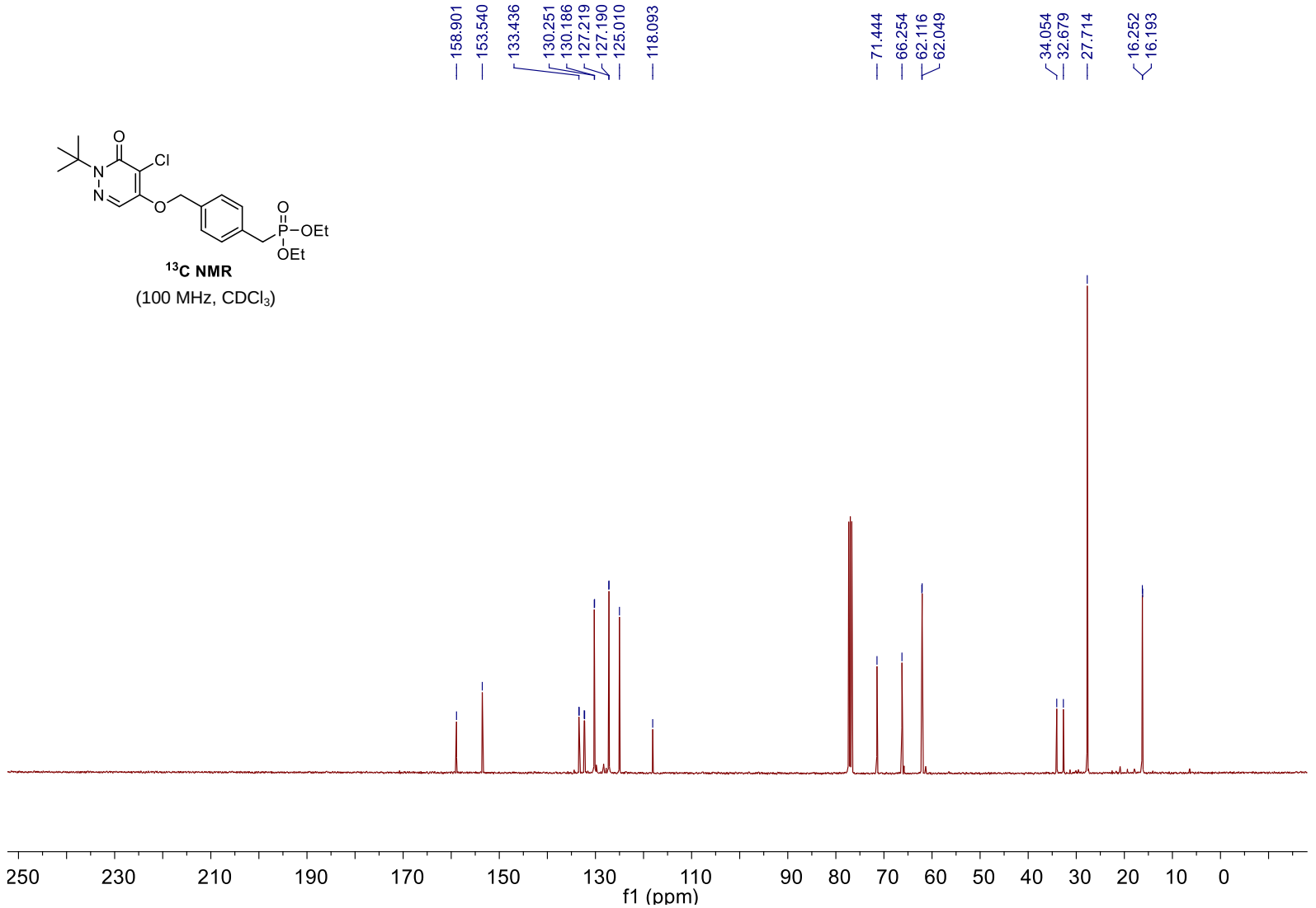

7.713
7.444
7.425
7.395
7.376
5.296
4.487
1.622
O
N
N
Cl
O
Br
1H NMR
(400 MHz, CDCl3)
1.00
2.06
2.07
2.13
2.11
9.40
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



^{13}C NMR

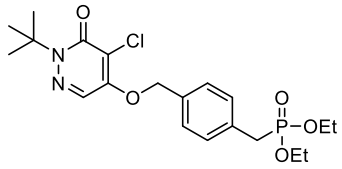
(100 MHz, $CDCl_3$)


7.687
7.321
7.313
7.287
5.261
5.257
3.997
3.993
3.978
3.976
3.973
3.960
3.955
3.146
3.092
1.580
1.212
1.194
1.177
O
N
N
Cl
O
O
P
OEt
OEt
1H NMR
(400 MHz, CDCl3)
1.00
4.03
2.06
4.04
2.14
9.16
6.13
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



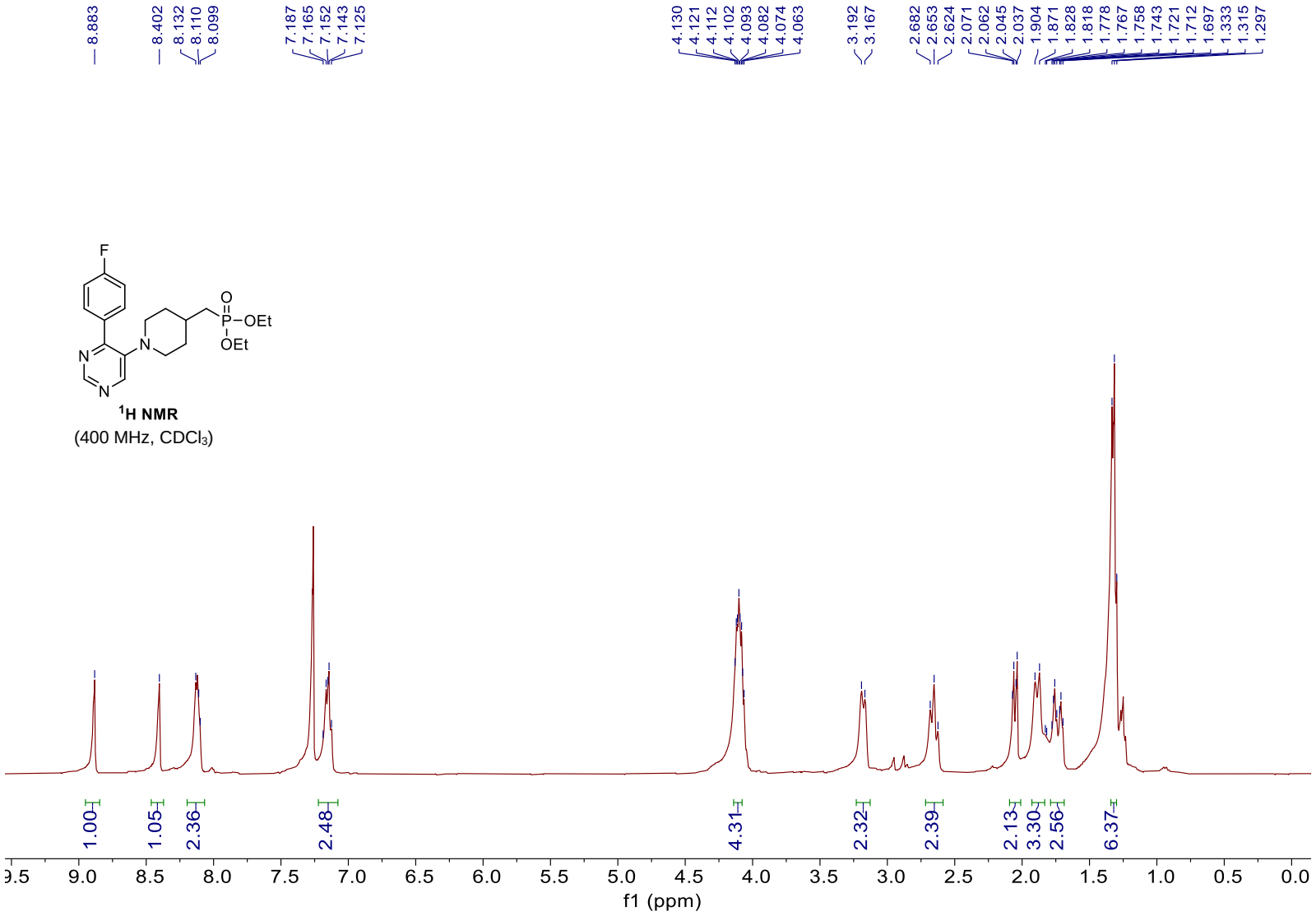
^{13}C NMR

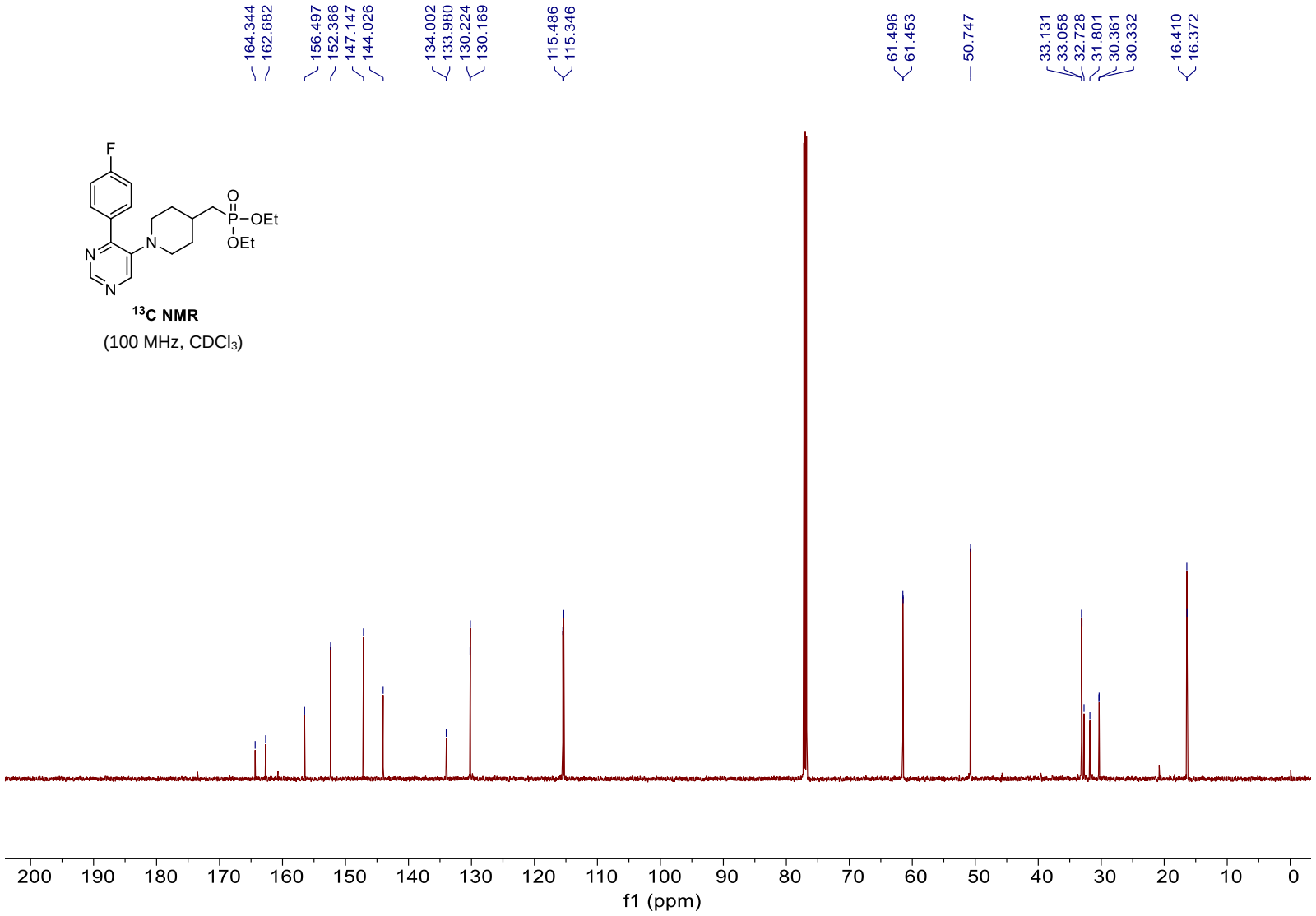
(100 MHz, $CDCl_3$)



^{31}P NMR

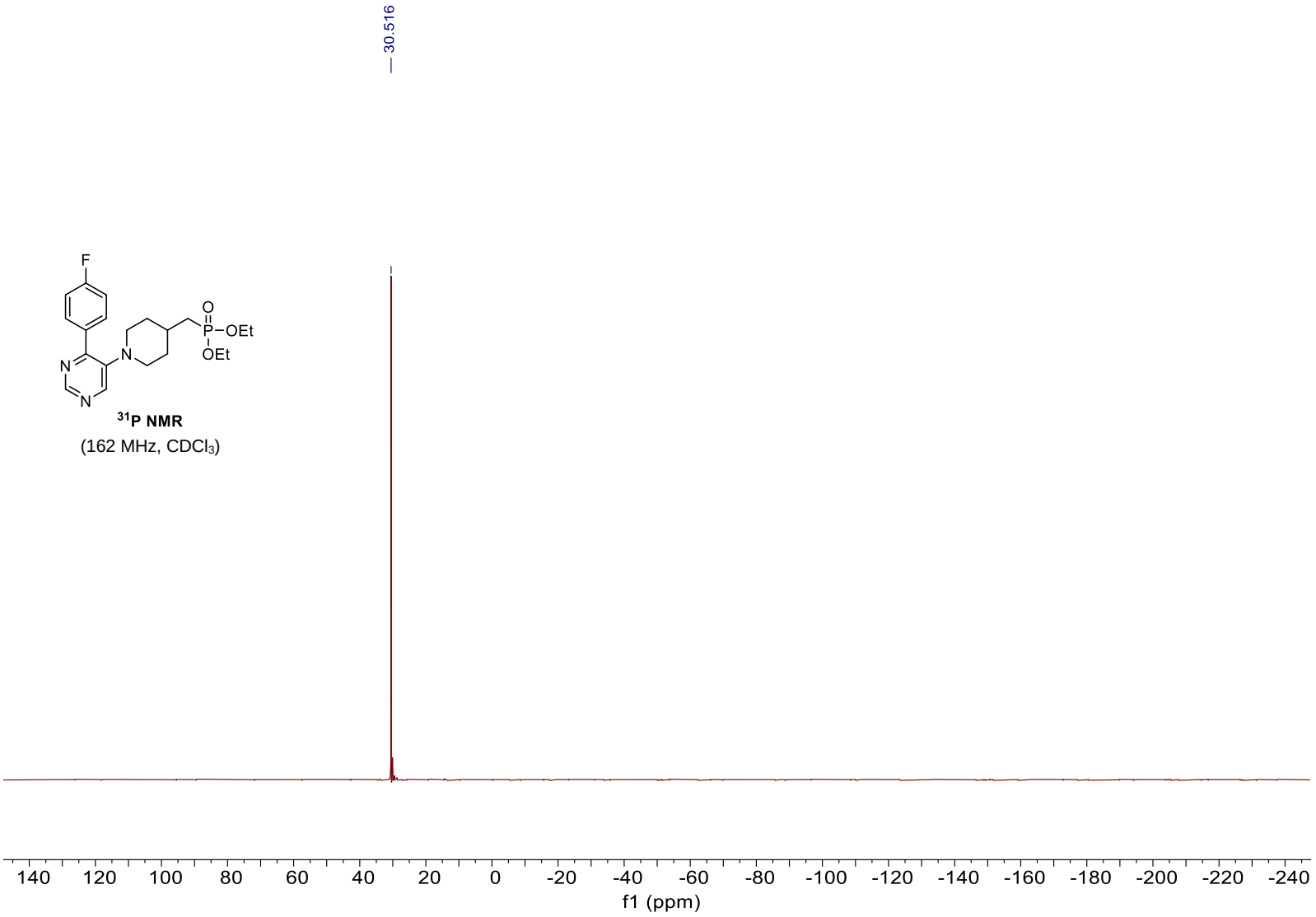
(162 MHz, $CDCl_3$)


8.883
8.402
8.132
8.110
8.099
7.187
7.165
7.152
7.143
7.125
4.130
4.121
4.112
4.102
4.093
4.082
4.074
4.063
3.192
3.167
2.682
2.653
2.624
2.071
2.062
2.045
2.037
1.904
1.871
1.828
1.818
1.778
1.767
1.758
1.743
1.721
1.712
1.697
1.333
1.315
1.297
F
O
P–OEt
OEt
N
N
N
1H NMR
(400 MHz, CDCl3)
1.00
1.05
2.36
2.48
4.31
2.32
2.39
2.13
3.30
2.56
6.37
f1 (ppm)



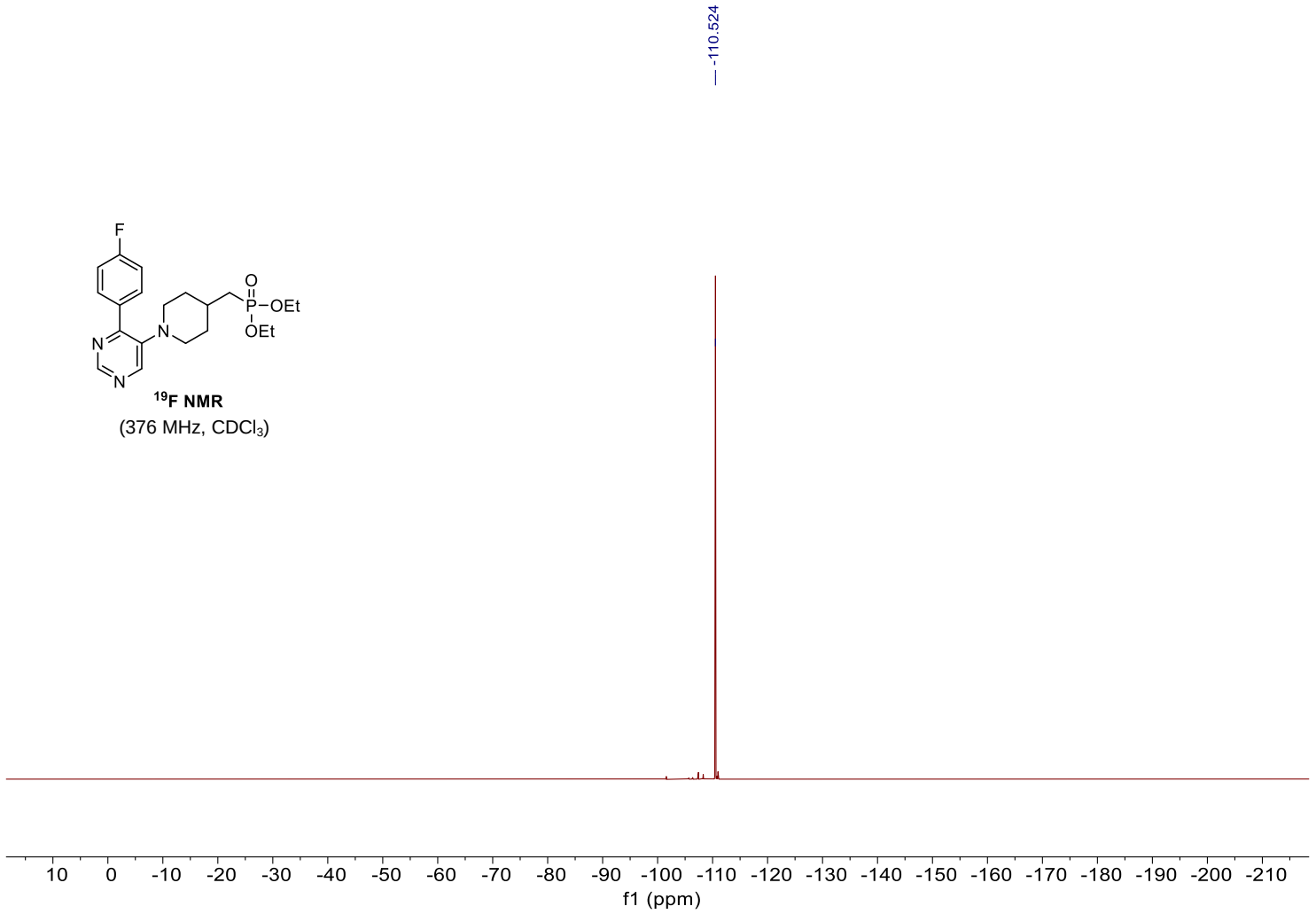
^{13}C NMR

(100 MHz, $CDCl_3$)



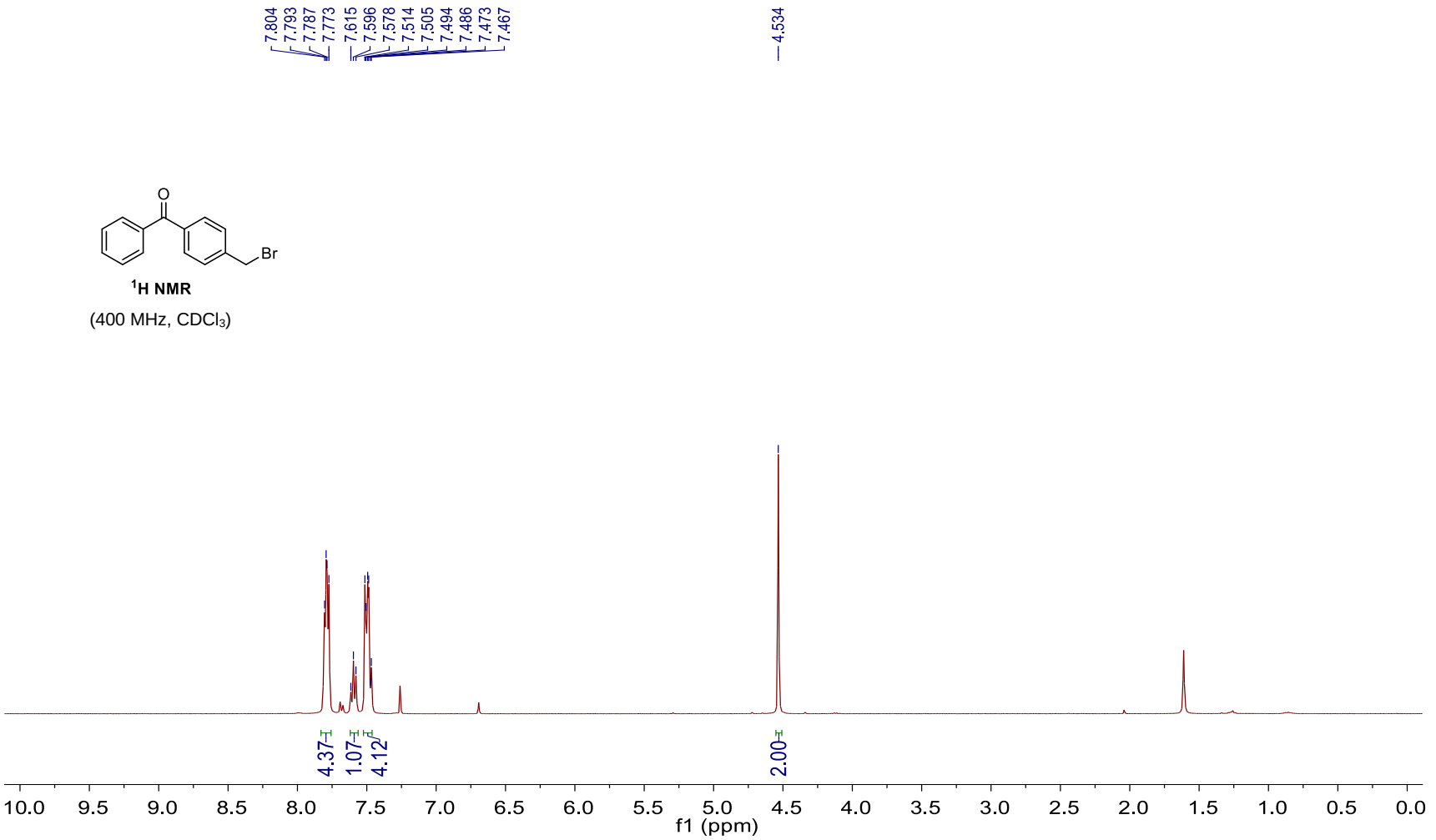
^{31}P NMR

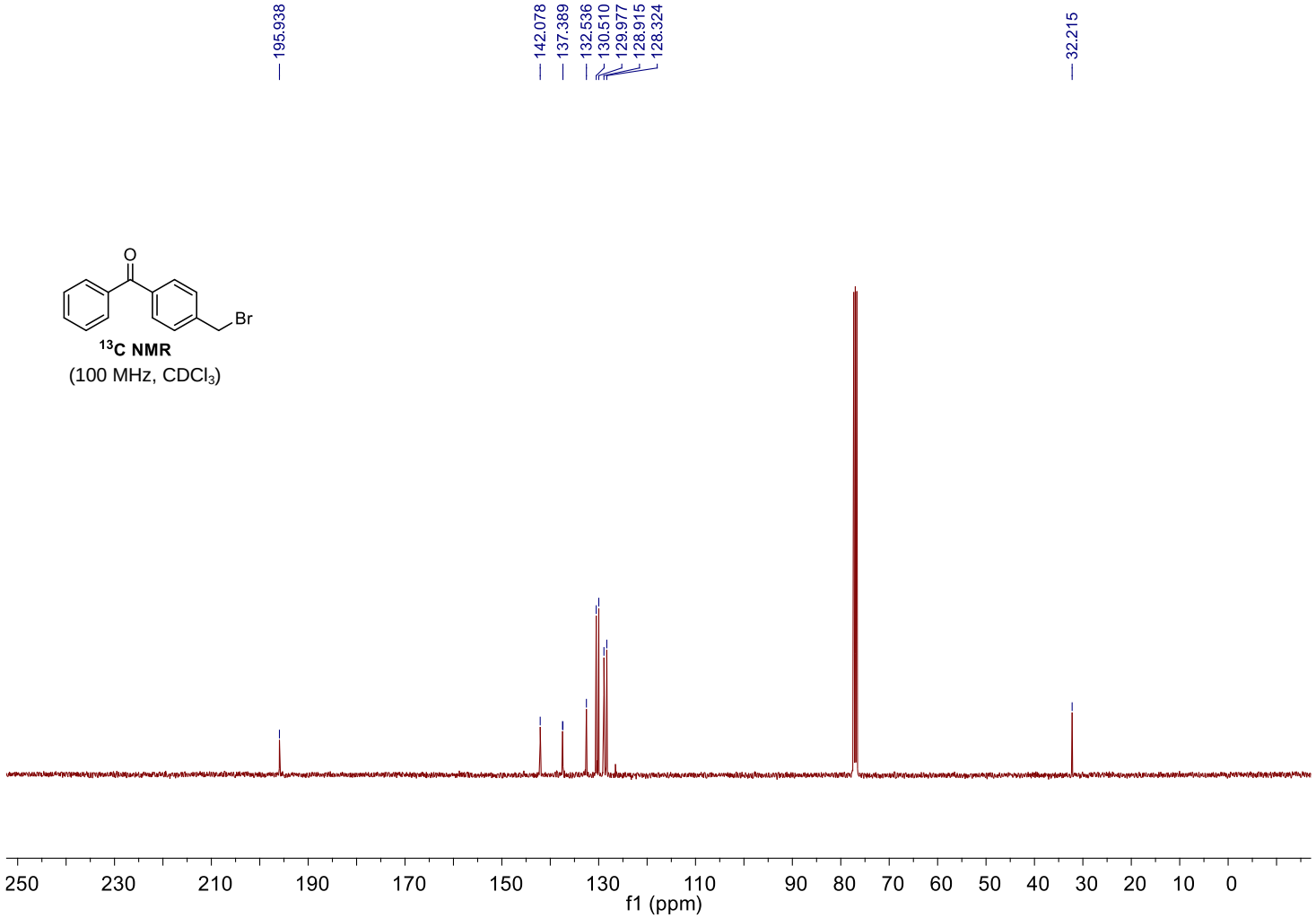
(162 MHz, $CDCl_3$)

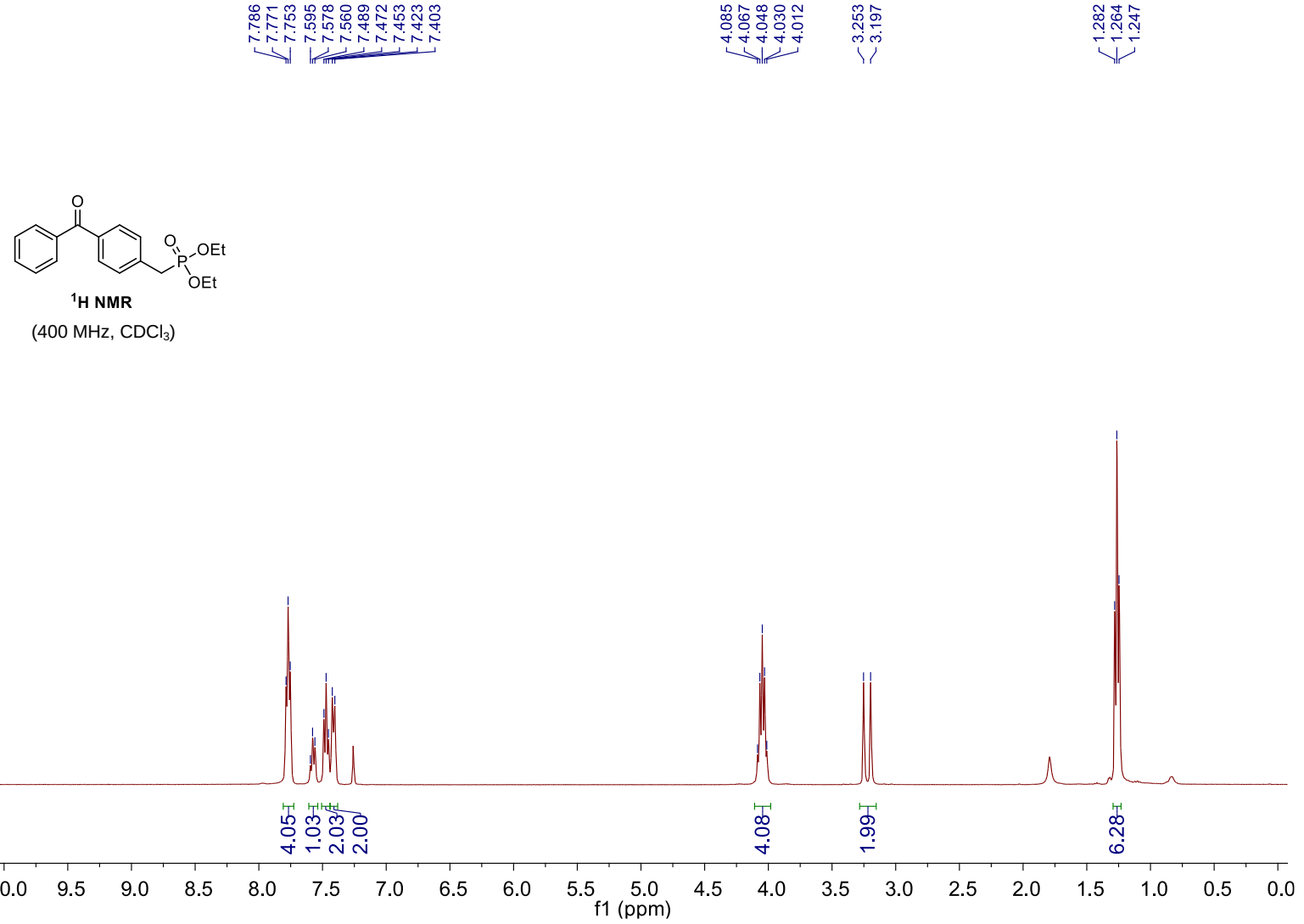


^{19}F NMR

(376 MHz, $CDCl_3$)

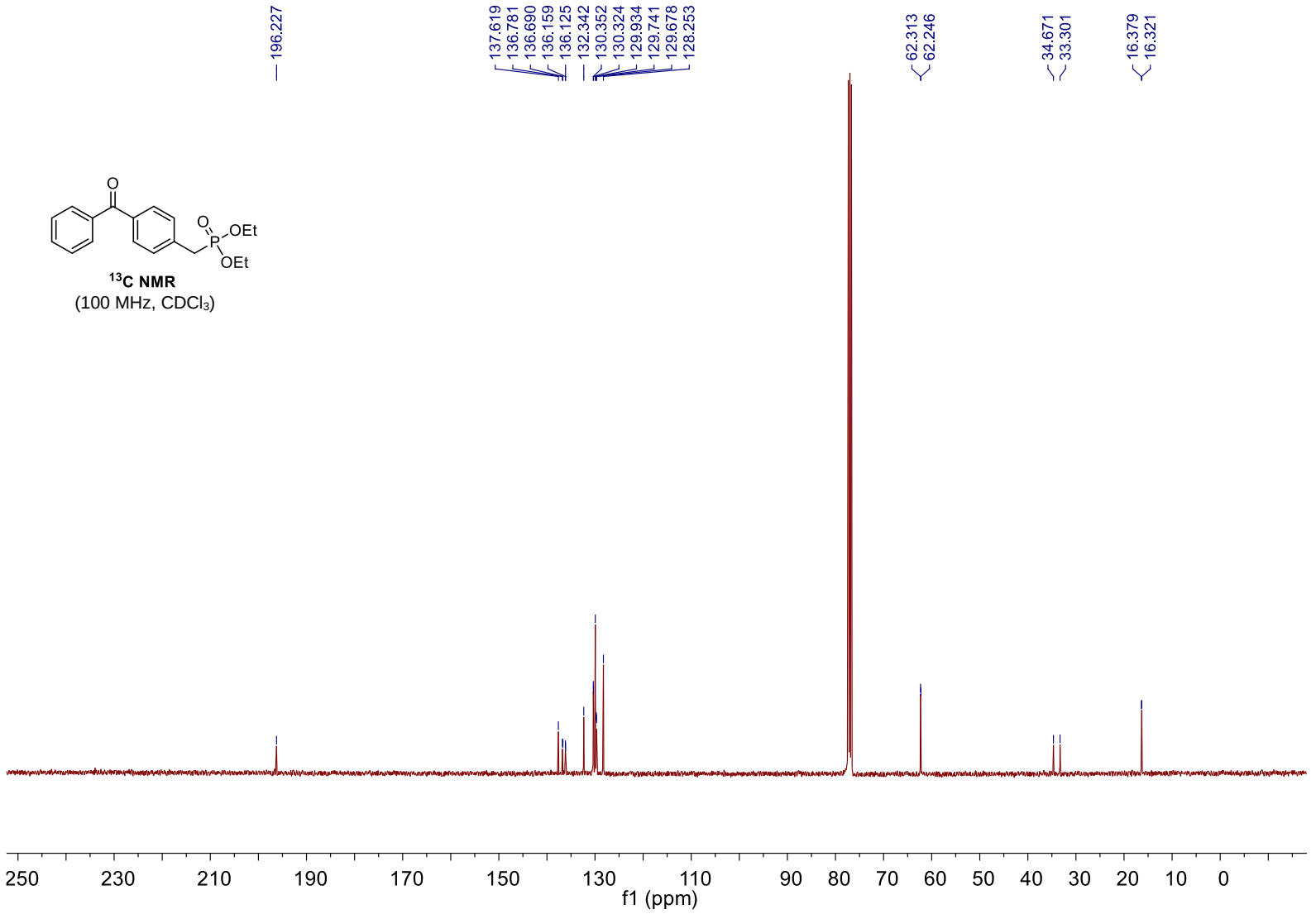

7.804
7.793
7.787
7.773
7.615
7.596
7.578
7.514
7.505
7.494
7.486
7.473
7.467
4.534
O
Br
¹H NMR
(400 MHz, CDCl₃)
4.37
1.07
4.12
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

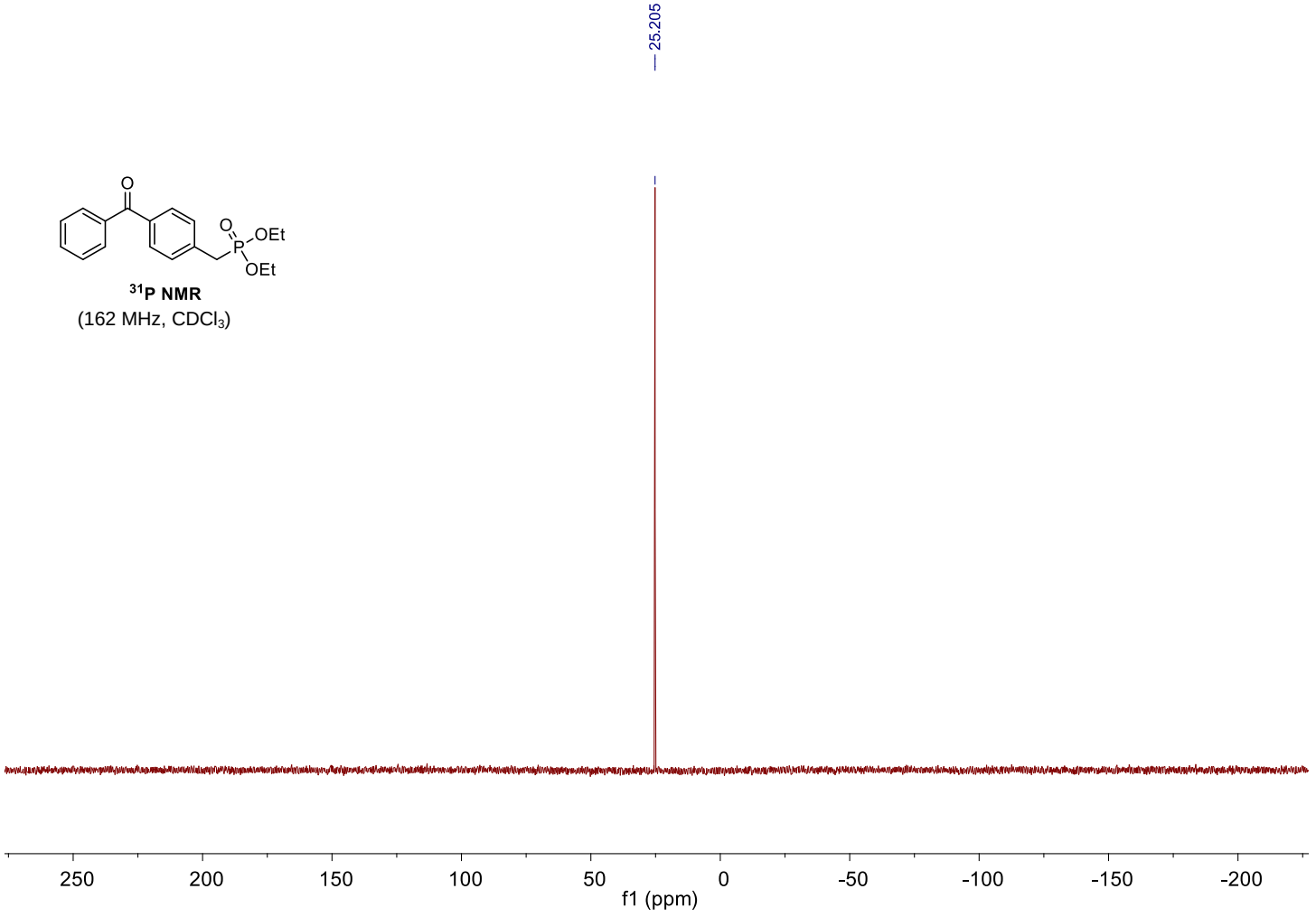

195.938
142.078
137.389
132.536
130.510
129.977
128.915
128.324
32.215
O
Br
13C NMR
(100 MHz, CDCl3)
250
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



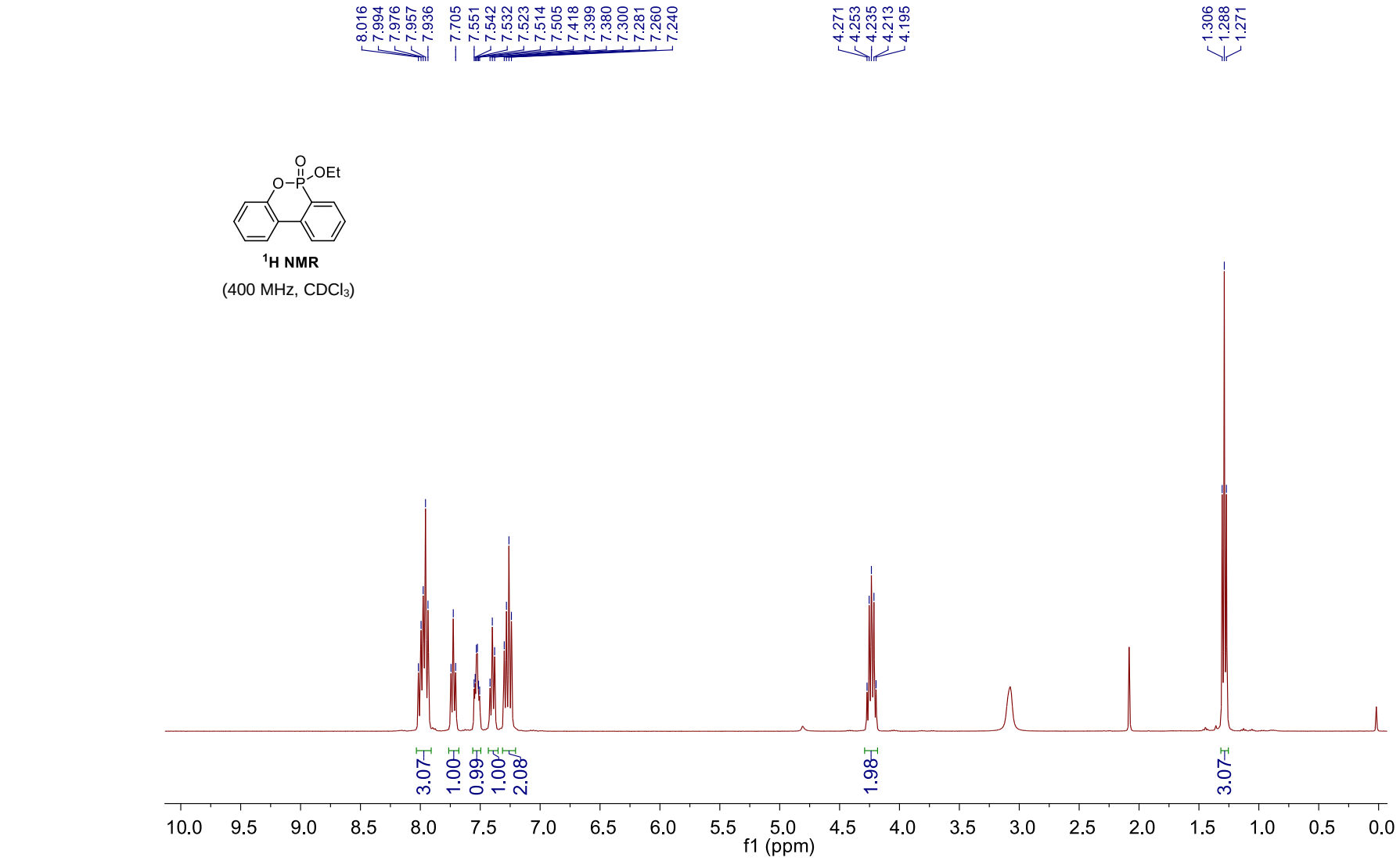
^{1}H NMR

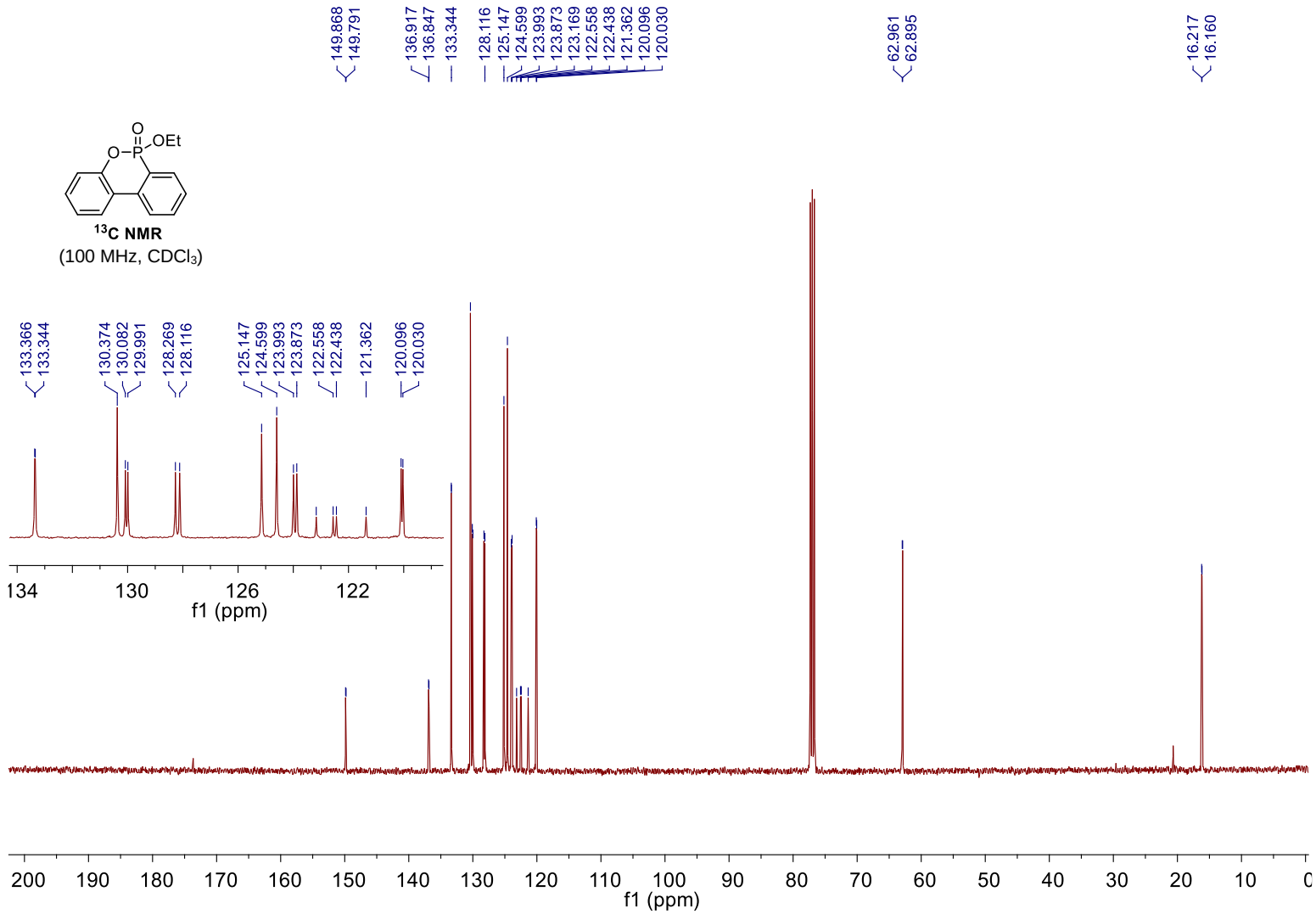
(400 MHz, $CDCl_3$)

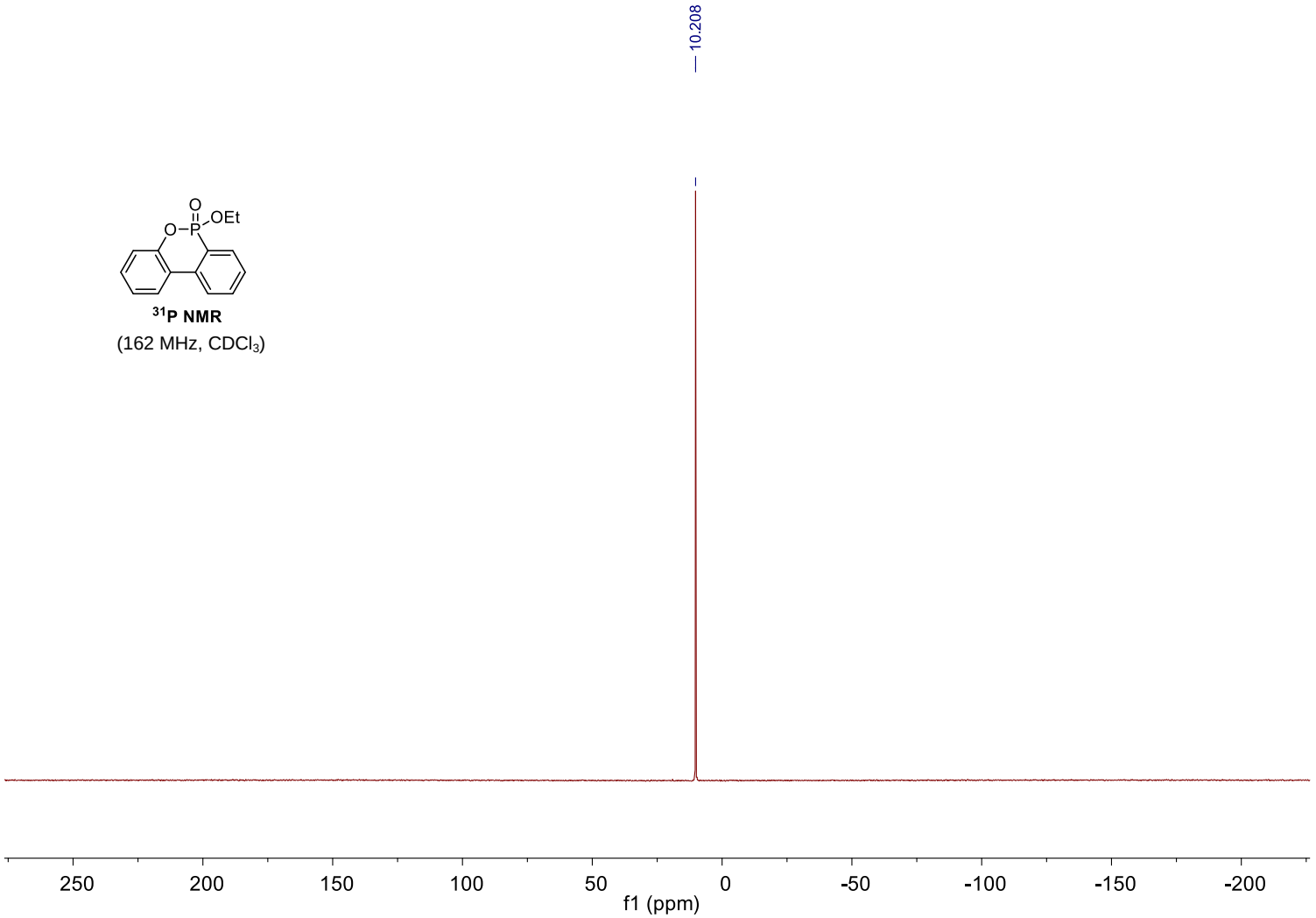

196.227
137.619
136.781
136.690
136.159
136.125
132.342
130.352
130.324
129.934
129.741
129.678
128.253
62.313
62.246
34.671
33.301
16.379
16.321
O
O
P
OEt
OEt
13C NMR
(100 MHz, CDCl3)
250
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



^{31}P NMR
(162 MHz, $CDCl_3$)

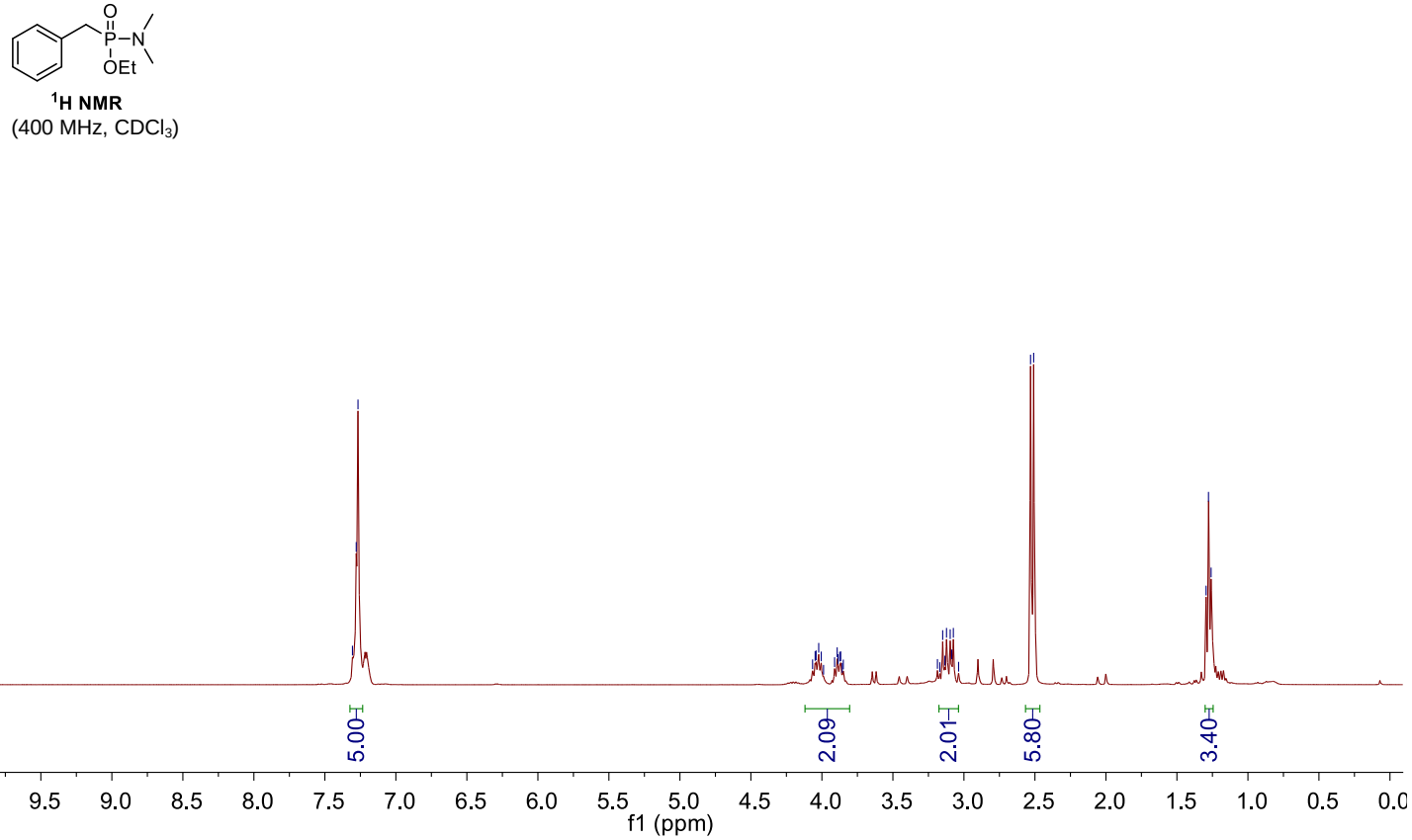

8.016
7.994
7.976
7.957
7.936
7.705
7.551
7.542
7.532
7.523
7.514
7.505
7.418
7.399
7.380
7.300
7.281
7.260
7.240
4.271
4.253
4.235
4.213
4.195
1.306
1.288
1.271
O
O
P
OEt
1H NMR
(400 MHz, CDCl3)
3.07
1.00
0.99
1.00
2.08
1.98
3.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


149.868
149.791
136.917
136.847
133.344
128.116
125.147
124.599
123.993
123.873
123.169
122.558
122.438
121.362
120.096
120.030
62.961
62.895
16.217
16.160
O
O–P
OEt
13C NMR
(100 MHz, CDCl3)
133.366
133.344
130.374
130.082
129.991
128.269
128.116
125.147
124.599
123.993
123.873
122.558
122.438
121.362
120.096
120.030
134
130
126
122
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

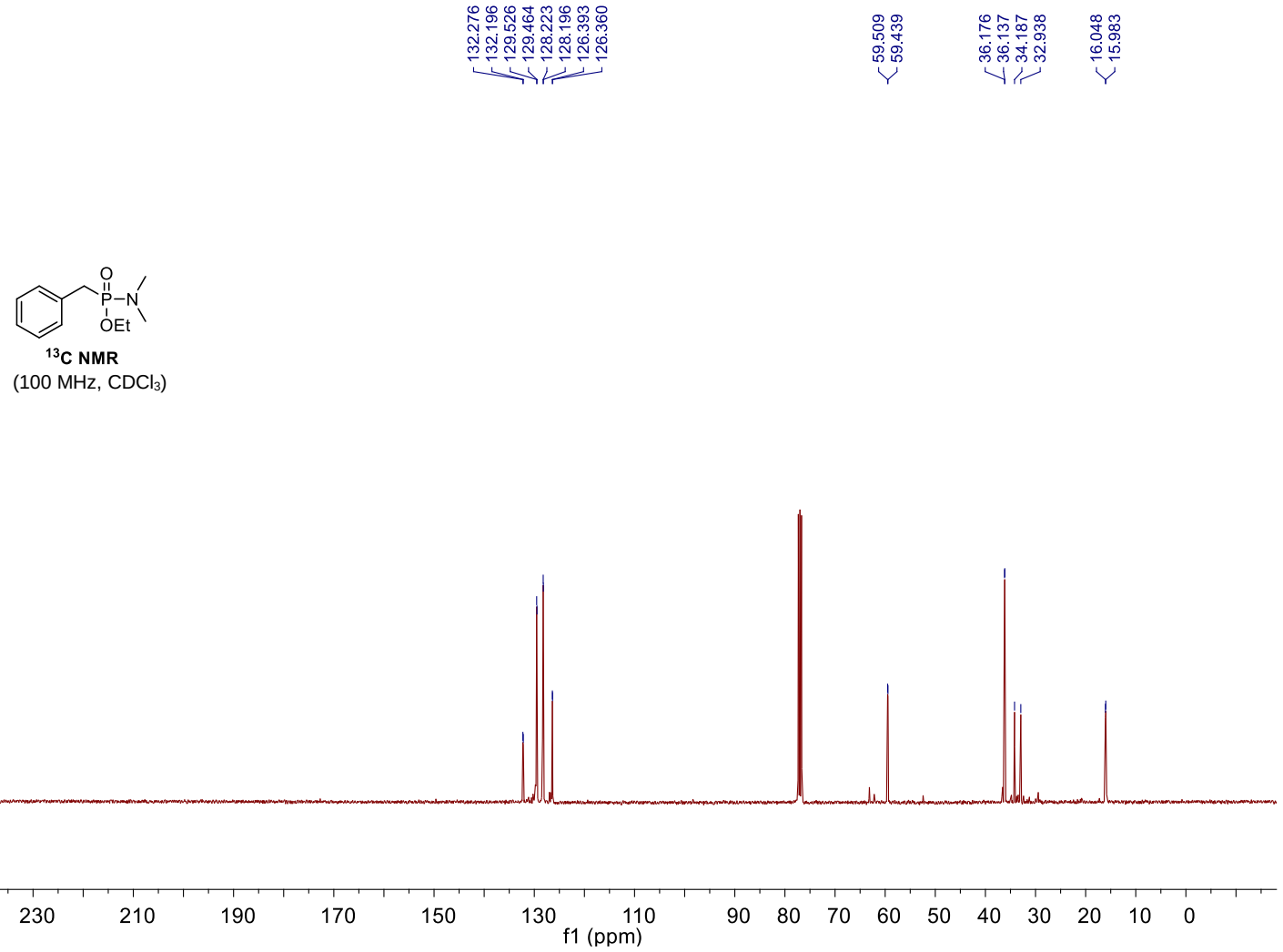


^{31}P NMR

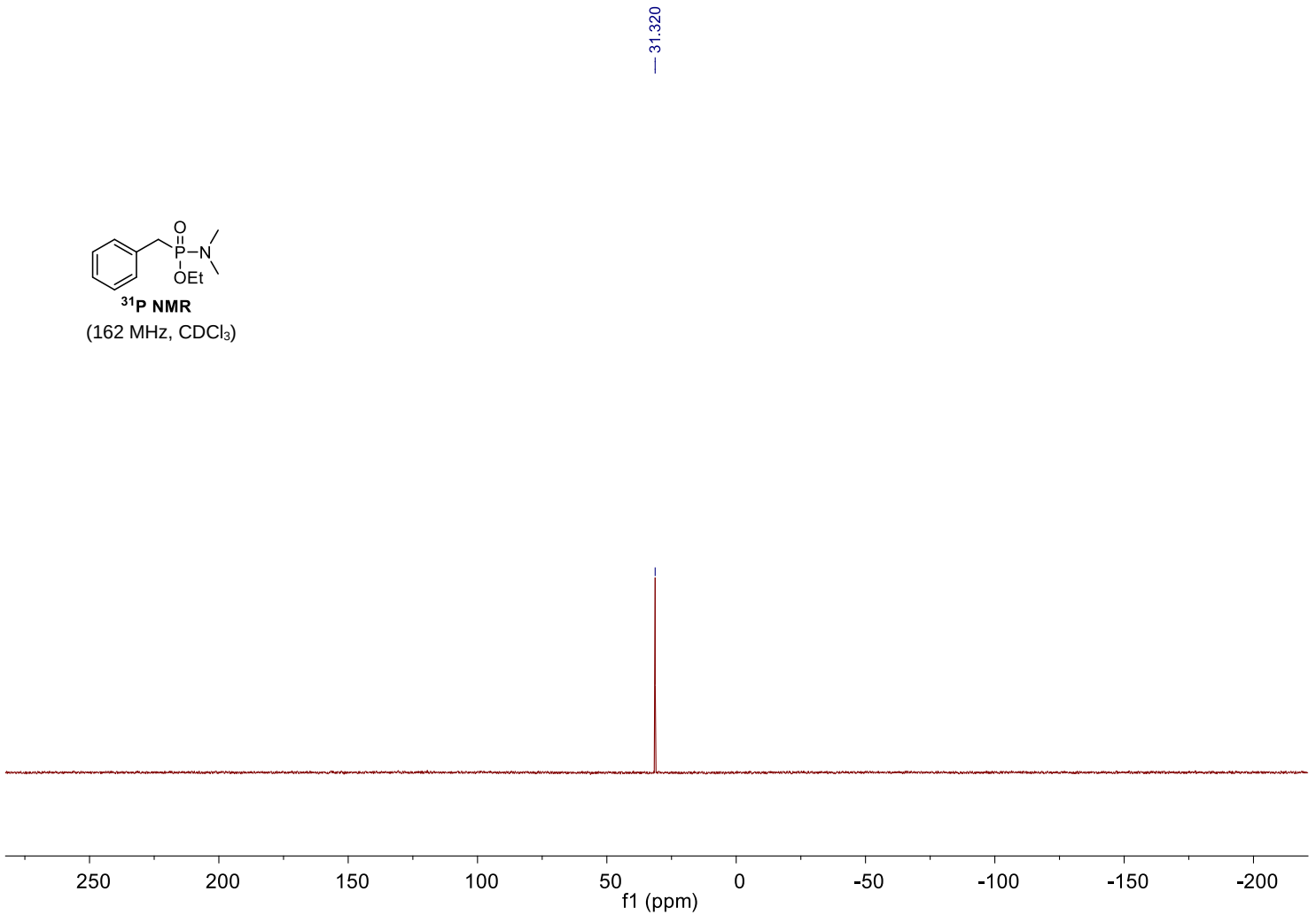
(162 MHz, $CDCl_3$)



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

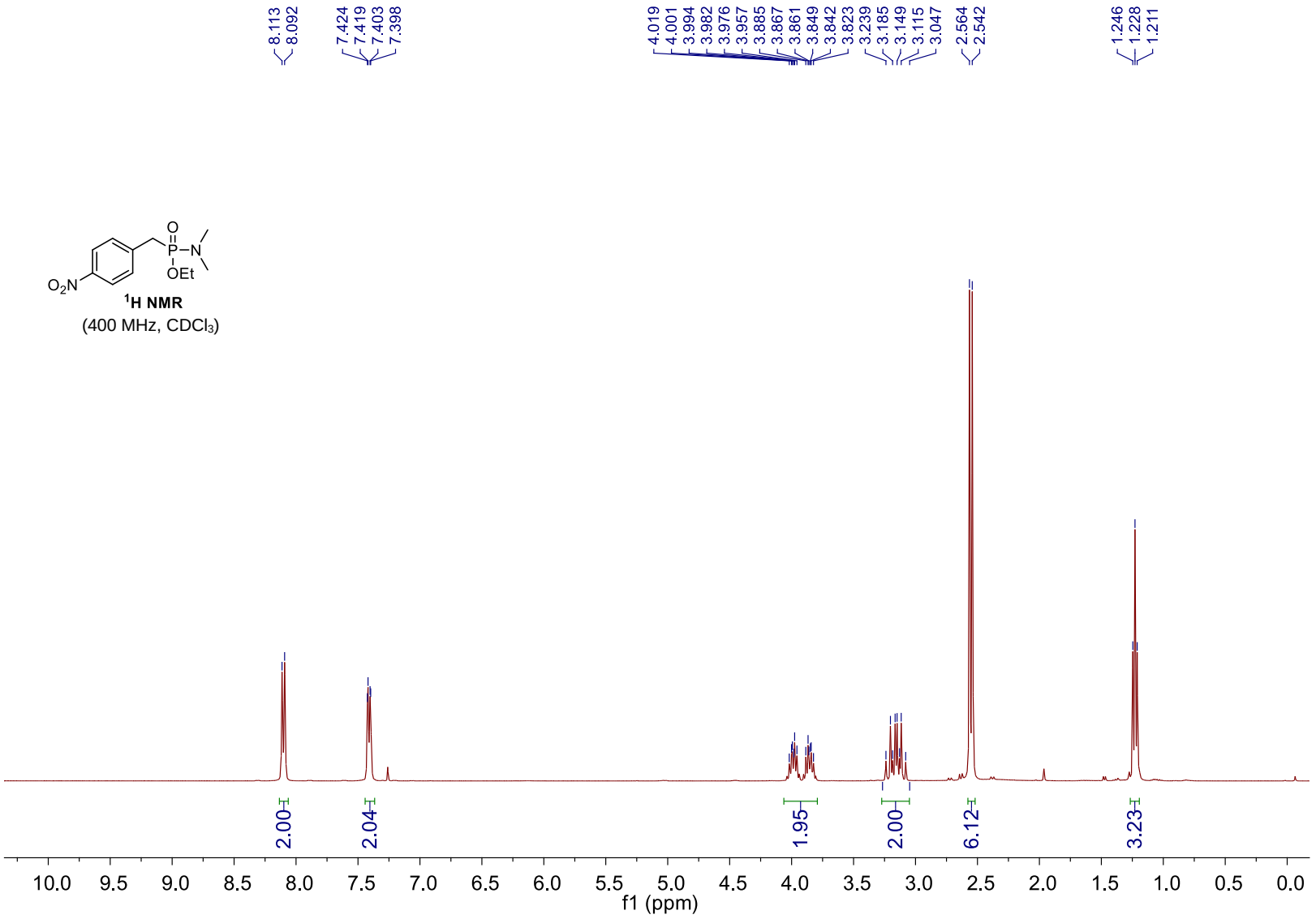


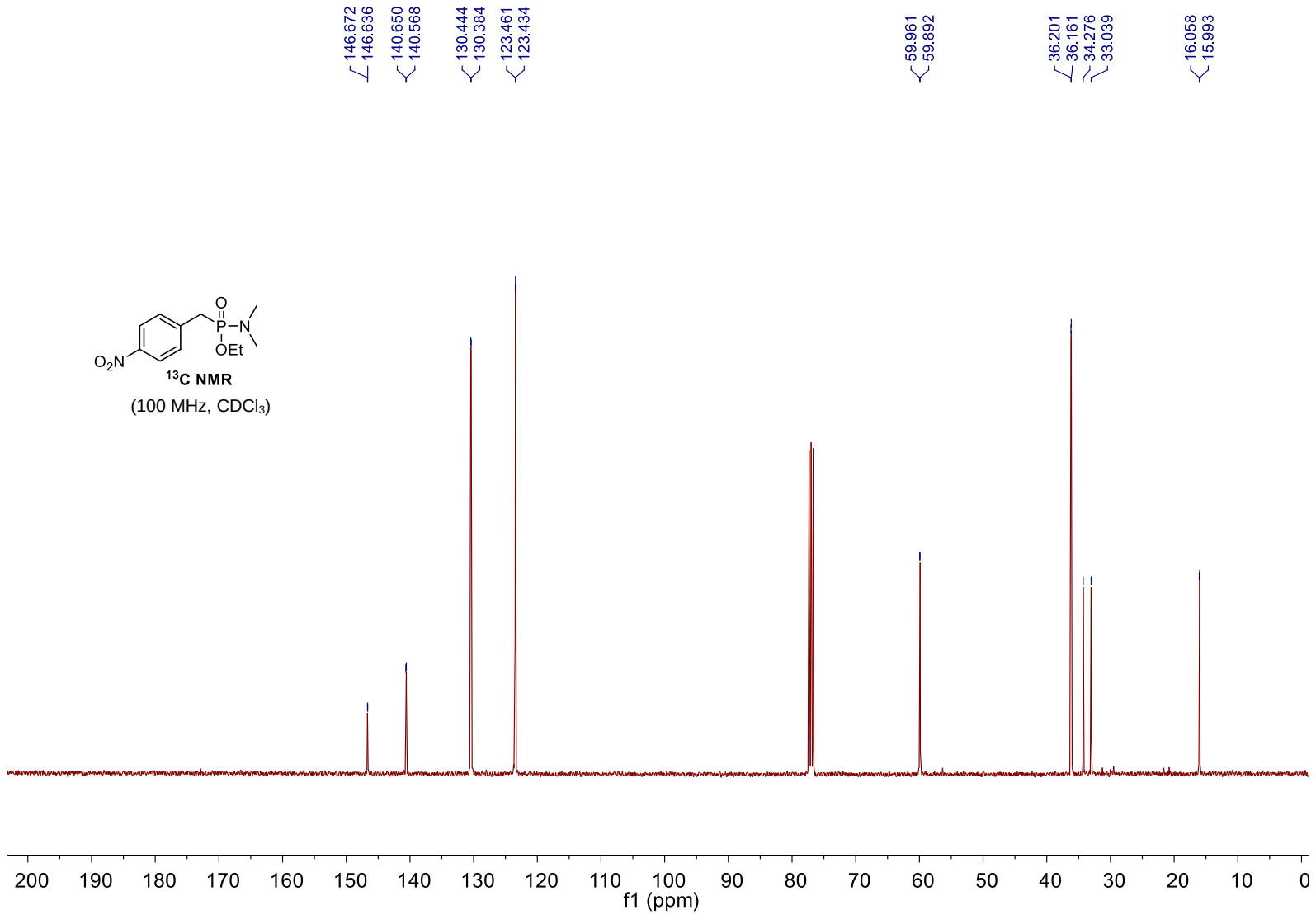
^{13}C NMR
(100 MHz, $CDCl_3$)

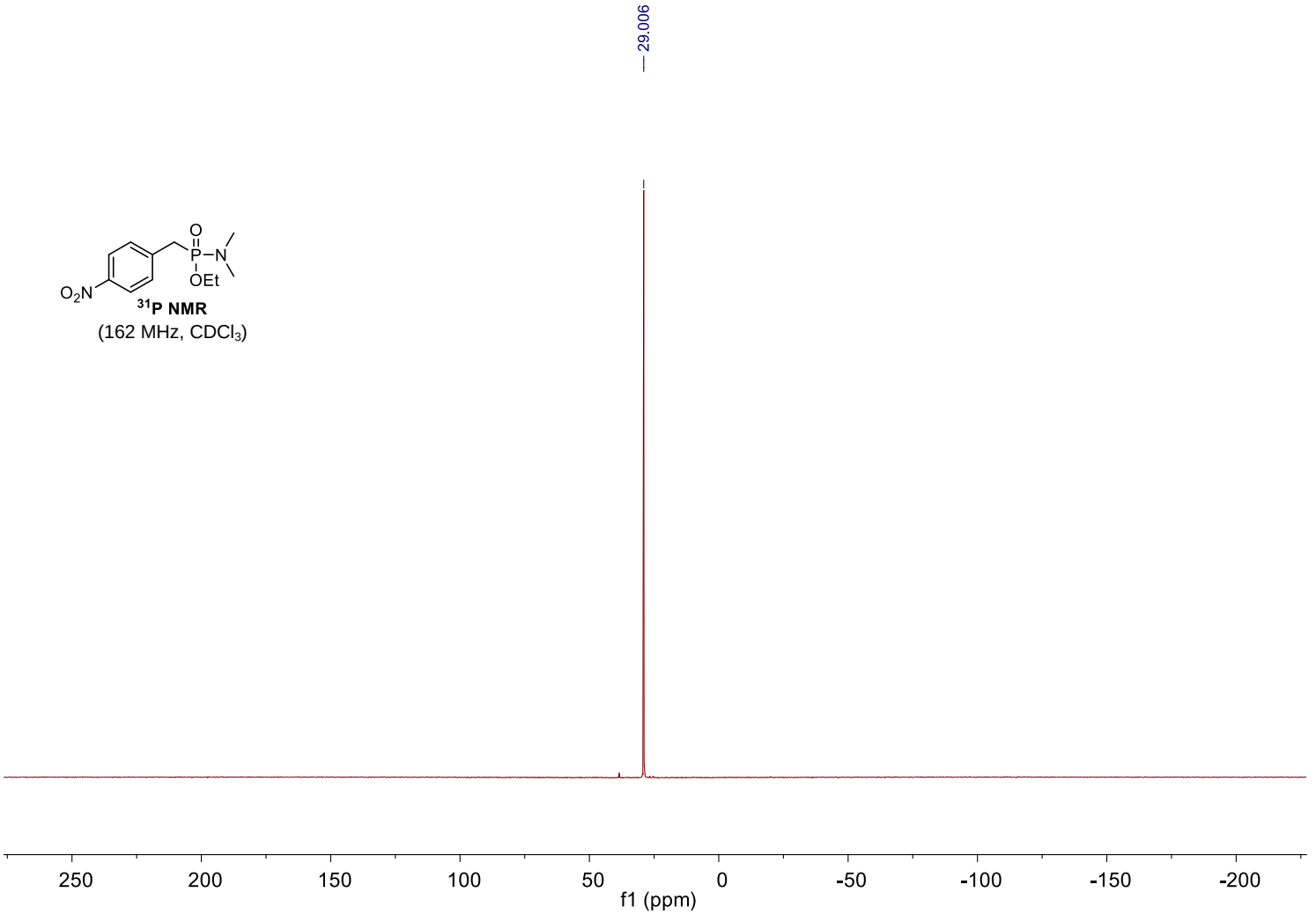


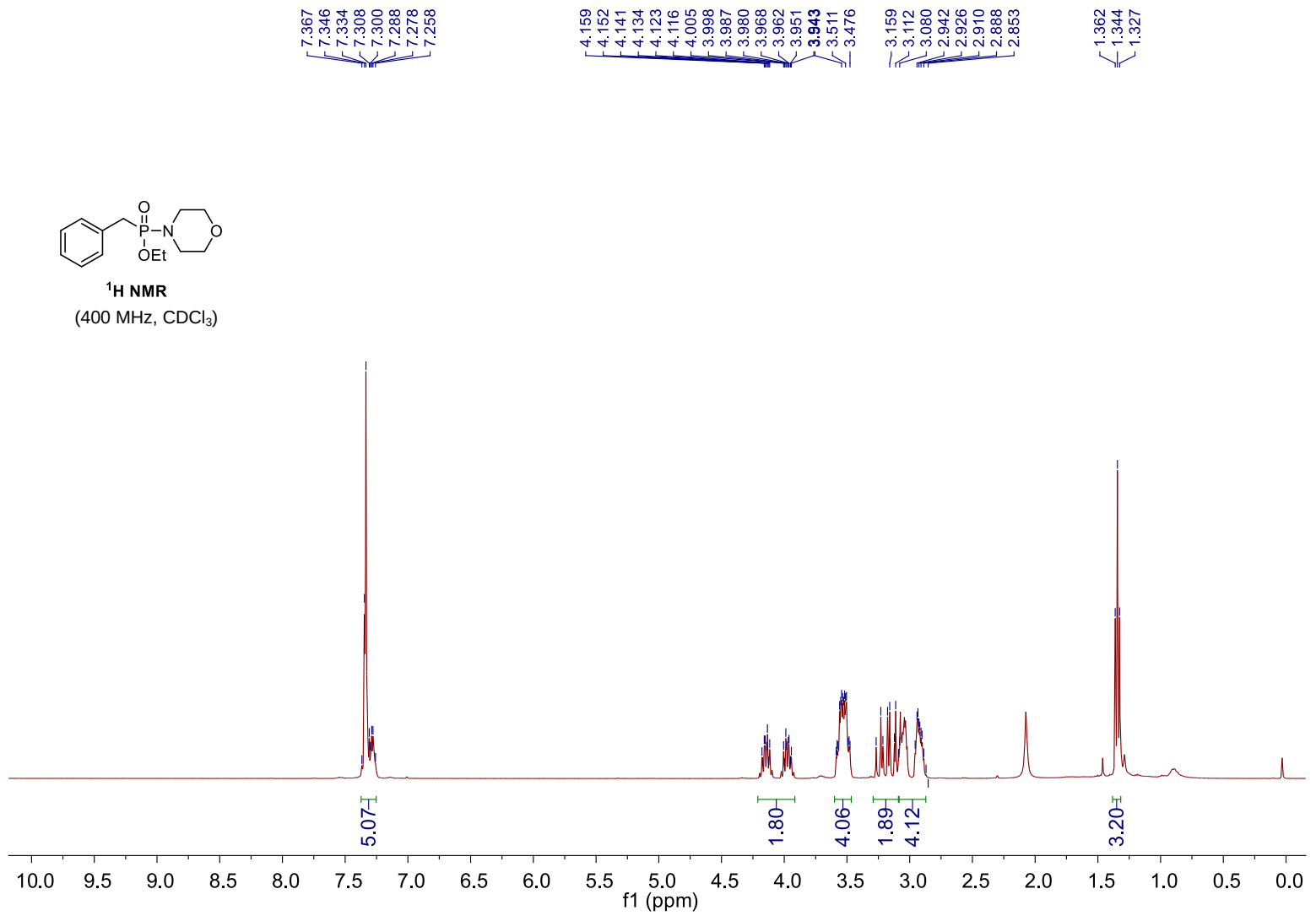
^{31}P NMR

(162 MHz, $CDCl_3$)


8.113
8.092
7.424
7.419
7.403
7.398
4.019
4.001
3.994
3.982
3.976
3.957
3.885
3.867
3.861
3.849
3.842
3.823
3.239
3.185
3.149
3.115
3.047
2.564
2.542
1.246
1.228
1.211
O
P
N
OEt
O2N
1H NMR
(400 MHz, CDCl3)
2.00
2.04
1.95
2.00
6.12
3.23
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

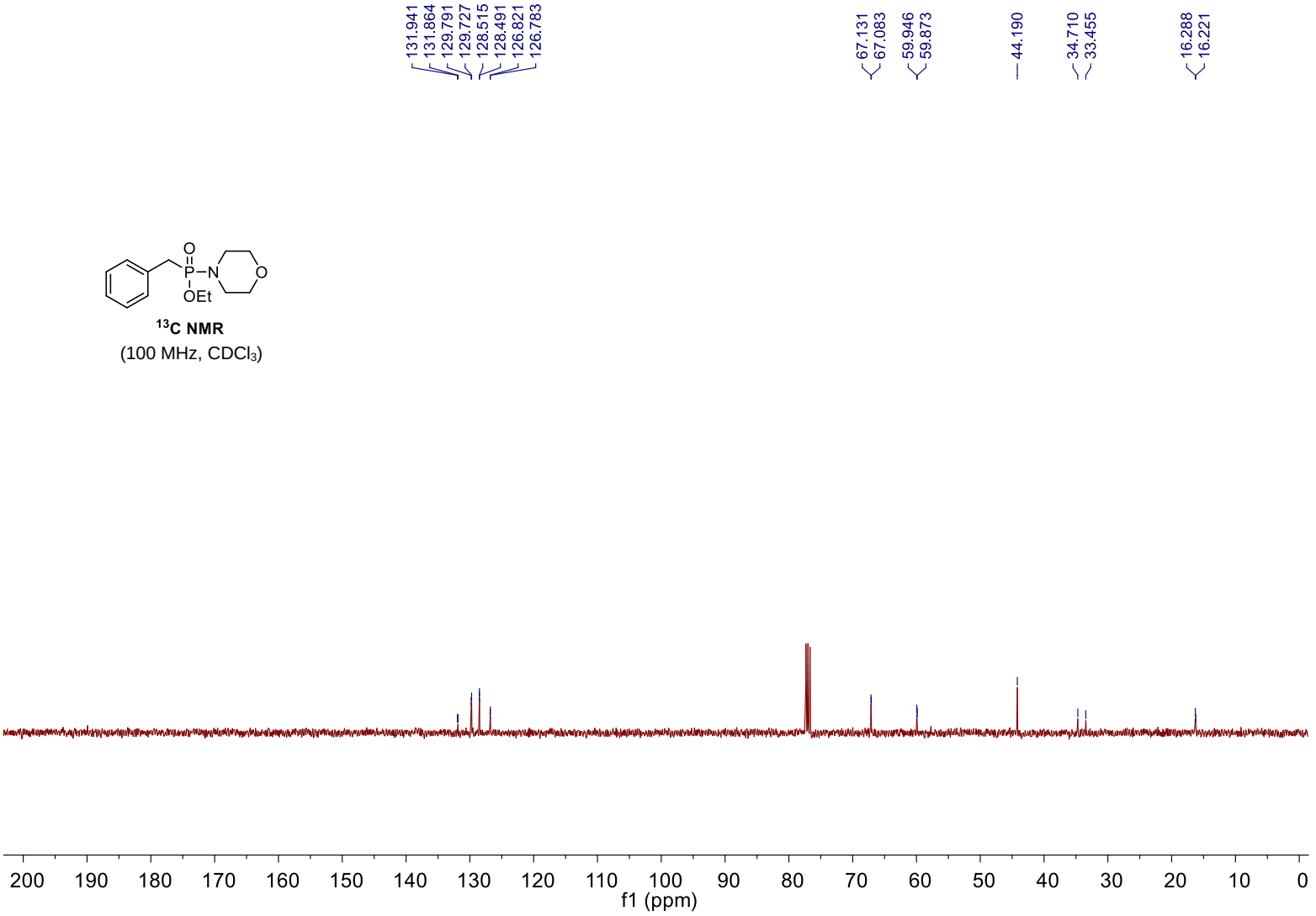

146.672
146.636
140.650
140.568
130.444
130.384
123.461
123.434
59.961
59.892
36.201
36.161
34.276
33.039
16.058
15.993
O
P
N
OEt
O2N
13C NMR
(100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


29.006
O
P
N
OEt
O2N
31P NMR
(162 MHz, CDCl3)
250
200
150
100
50
0
-50
-100
-150
-200
f1 (ppm)



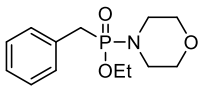
^{1}H NMR

(400 MHz, $CDCl_3$)



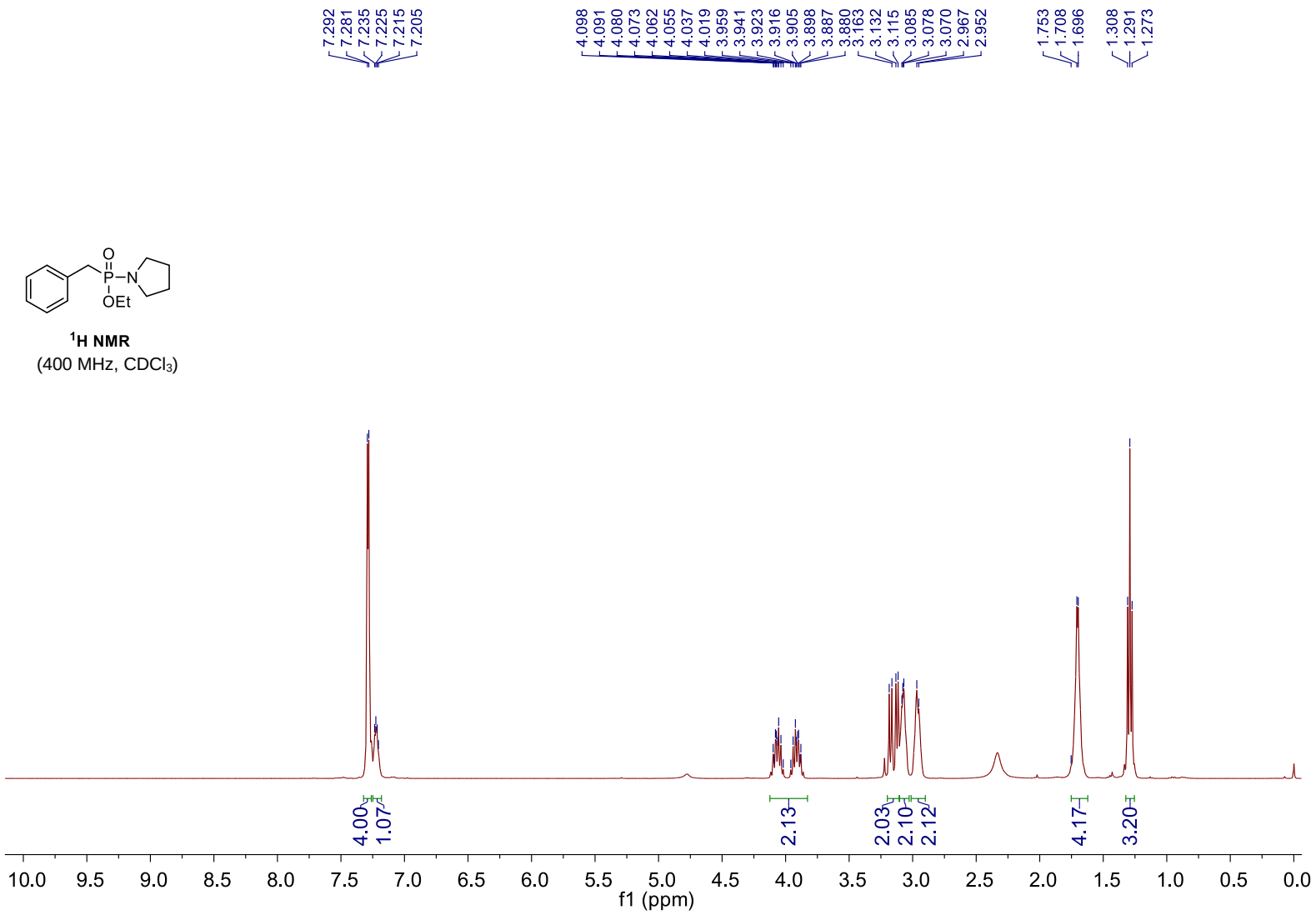
^{13}C NMR

(100 MHz, $CDCl_3$)

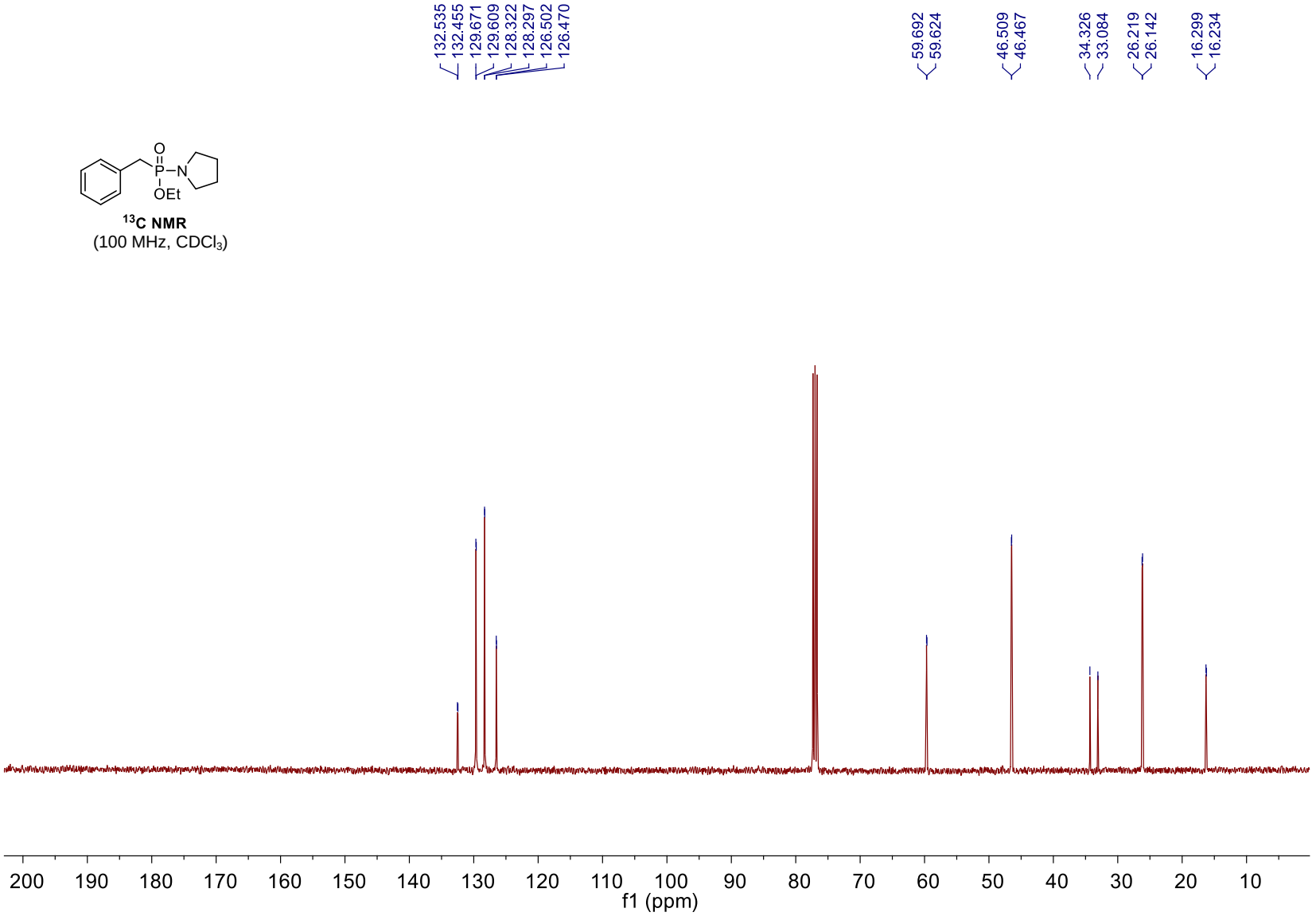


^{31}P NMR

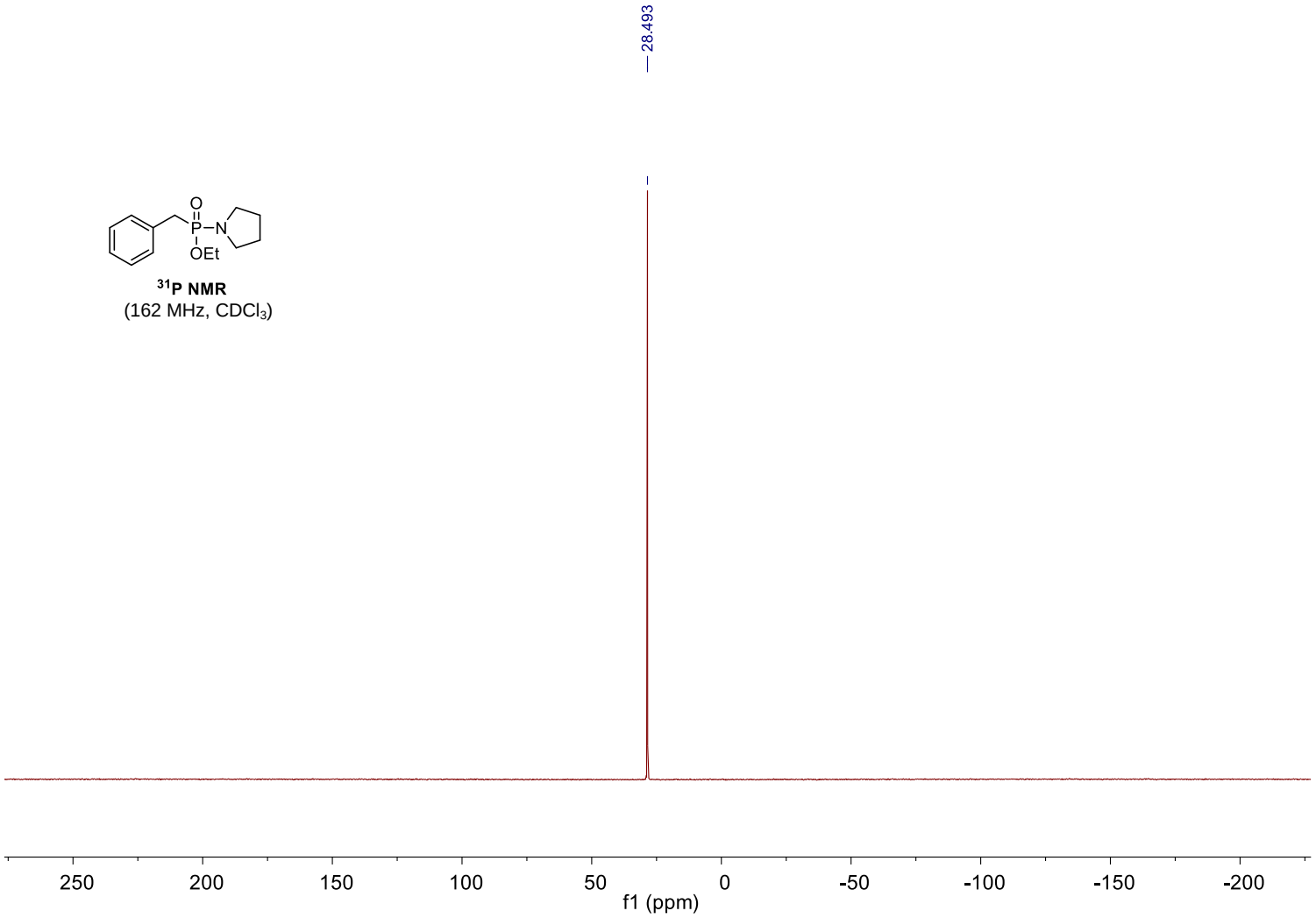
(162 MHz, $CDCl_3$)



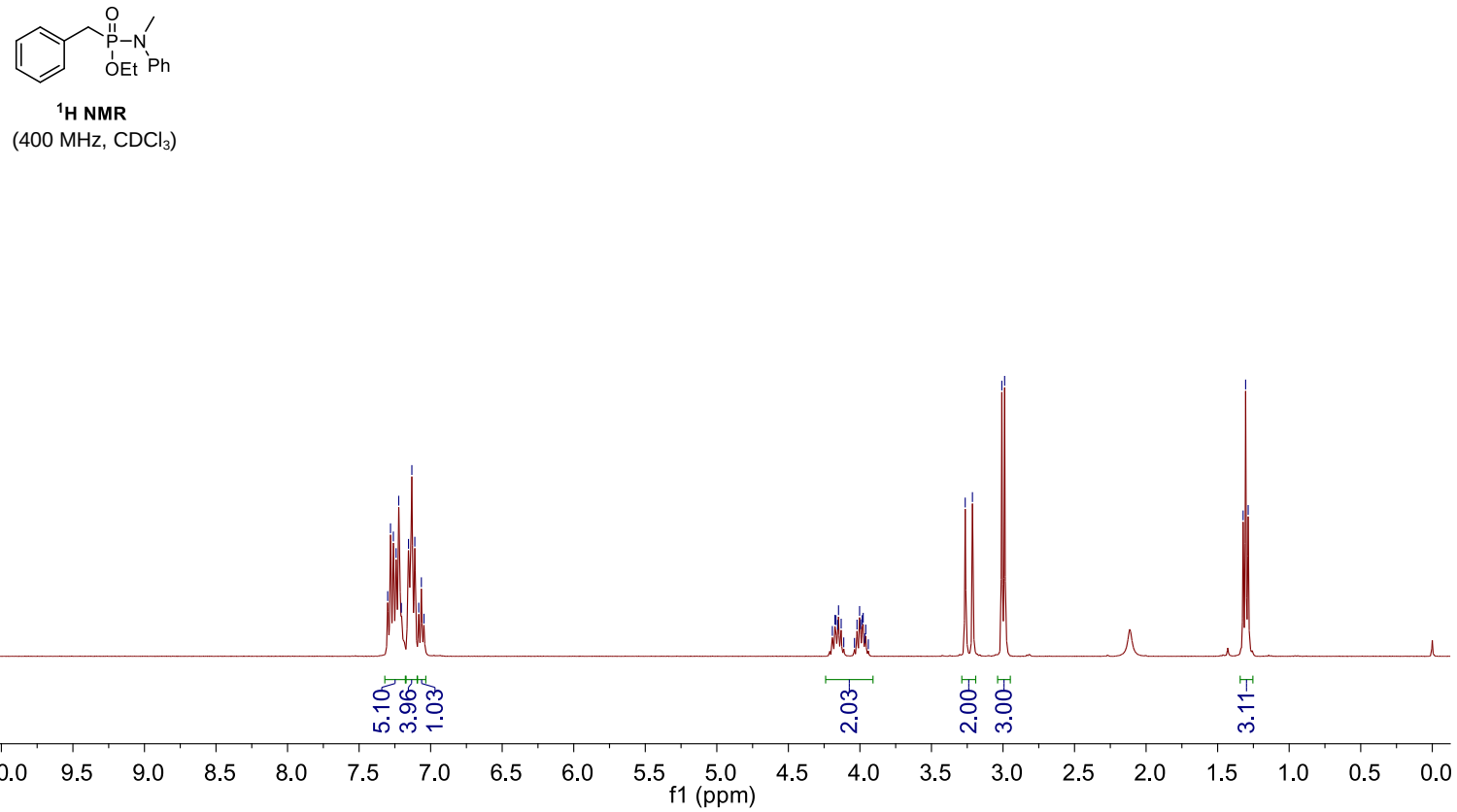
^{1}H NMR
(400 MHz, $CDCl_3$)



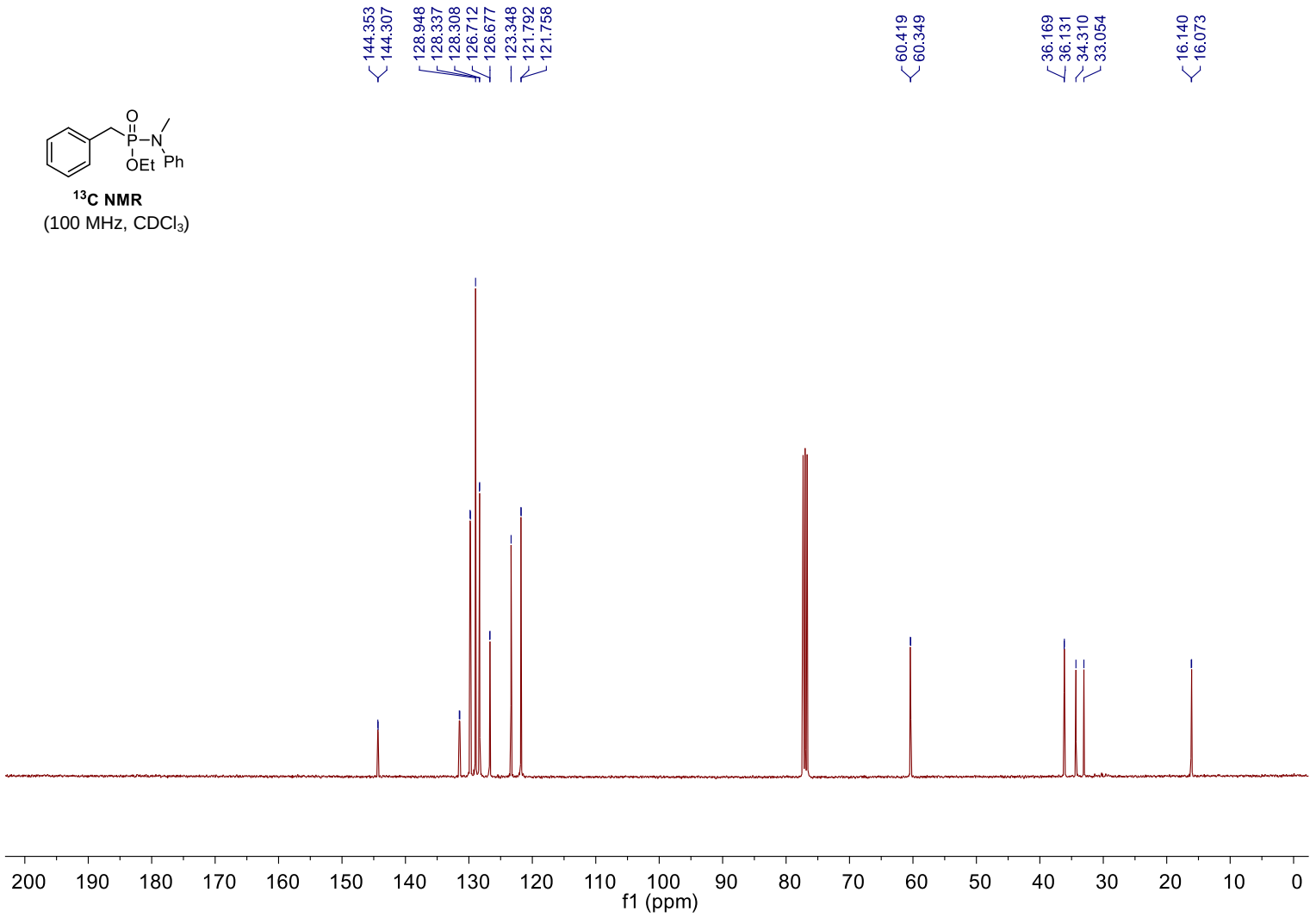
^{13}C NMR
(100 MHz, $CDCl_3$)



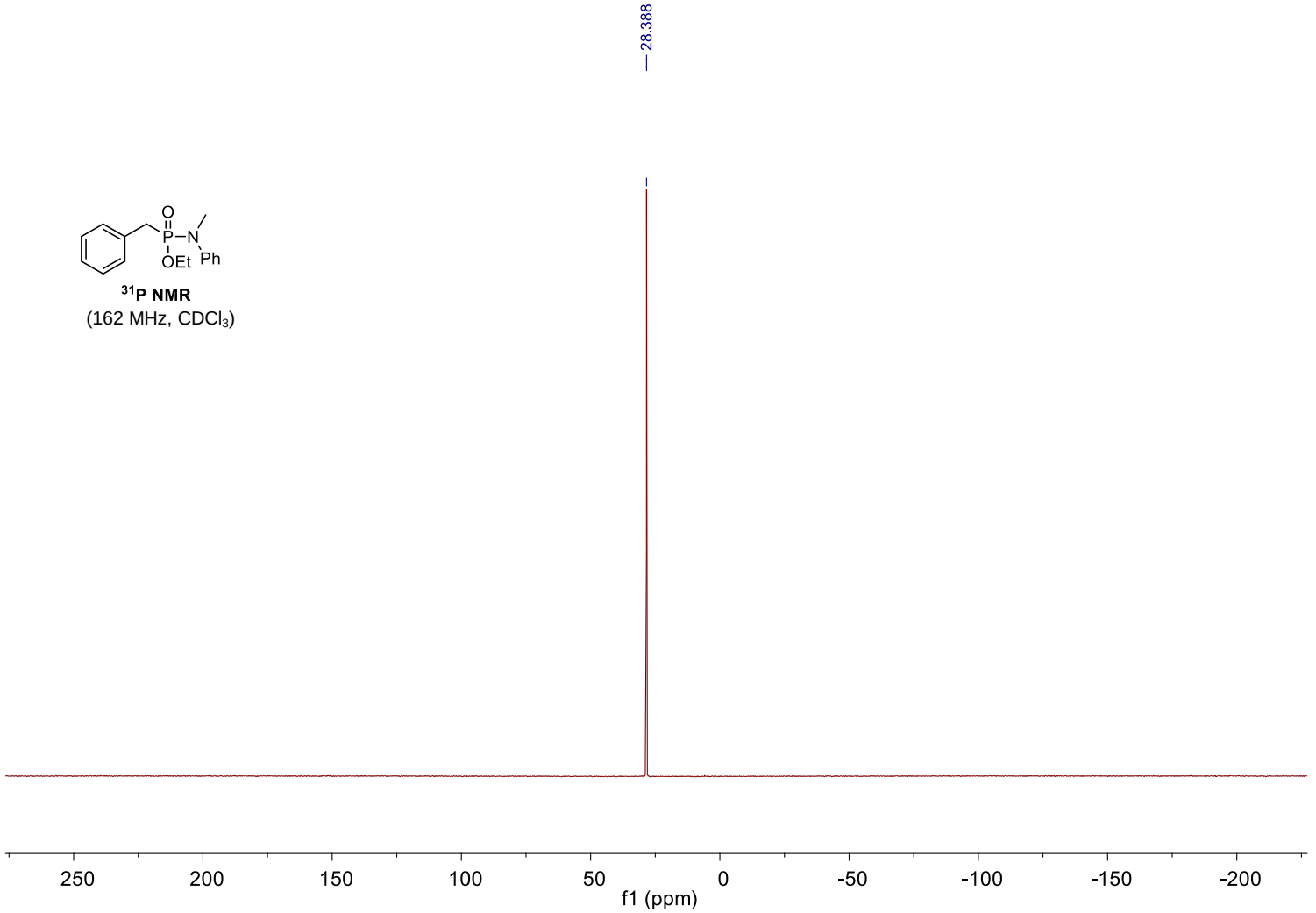
^{31}P NMR
(162 MHz, $CDCl_3$)



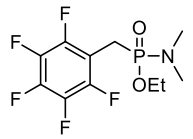
^{1}H NMR
(400 MHz, $CDCl_3$)



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

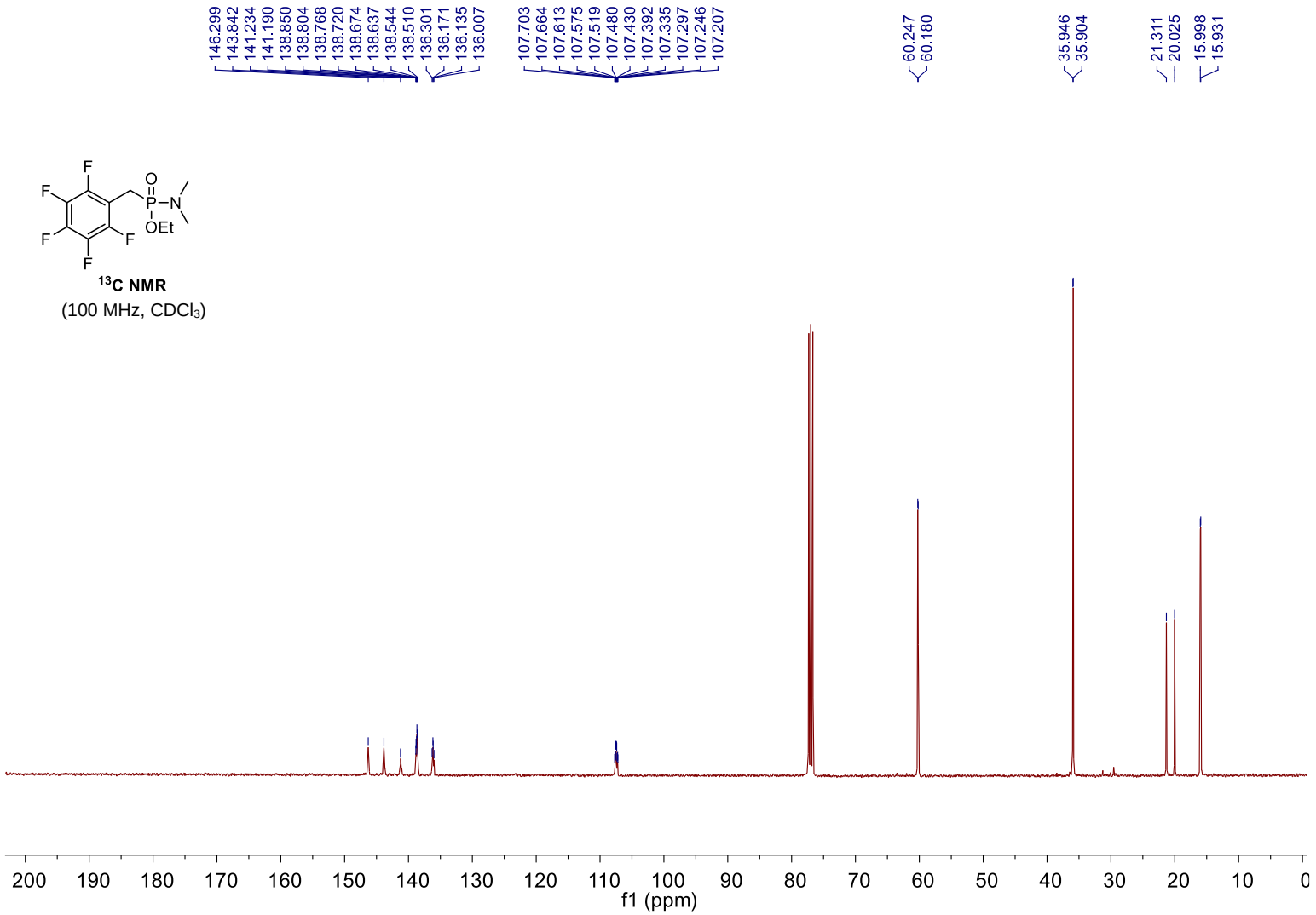


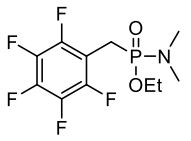
^{31}P NMR
(162 MHz, $CDCl_3$)



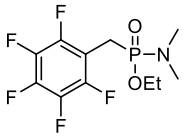
^{1}H NMR

(400 MHz, $CDCl_3$)


146.299
143.842
141.234
141.190
138.850
138.804
138.768
138.720
138.674
138.637
138.544
138.510
136.301
136.171
136.135
136.007
107.703
107.664
107.613
107.575
107.519
107.480
107.430
107.392
107.335
107.297
107.246
107.207
60.247
60.180
35.946
35.904
21.311
20.025
15.998
15.931
F
F
F
F
F
O
P
N
OEt
13C NMR
(100 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

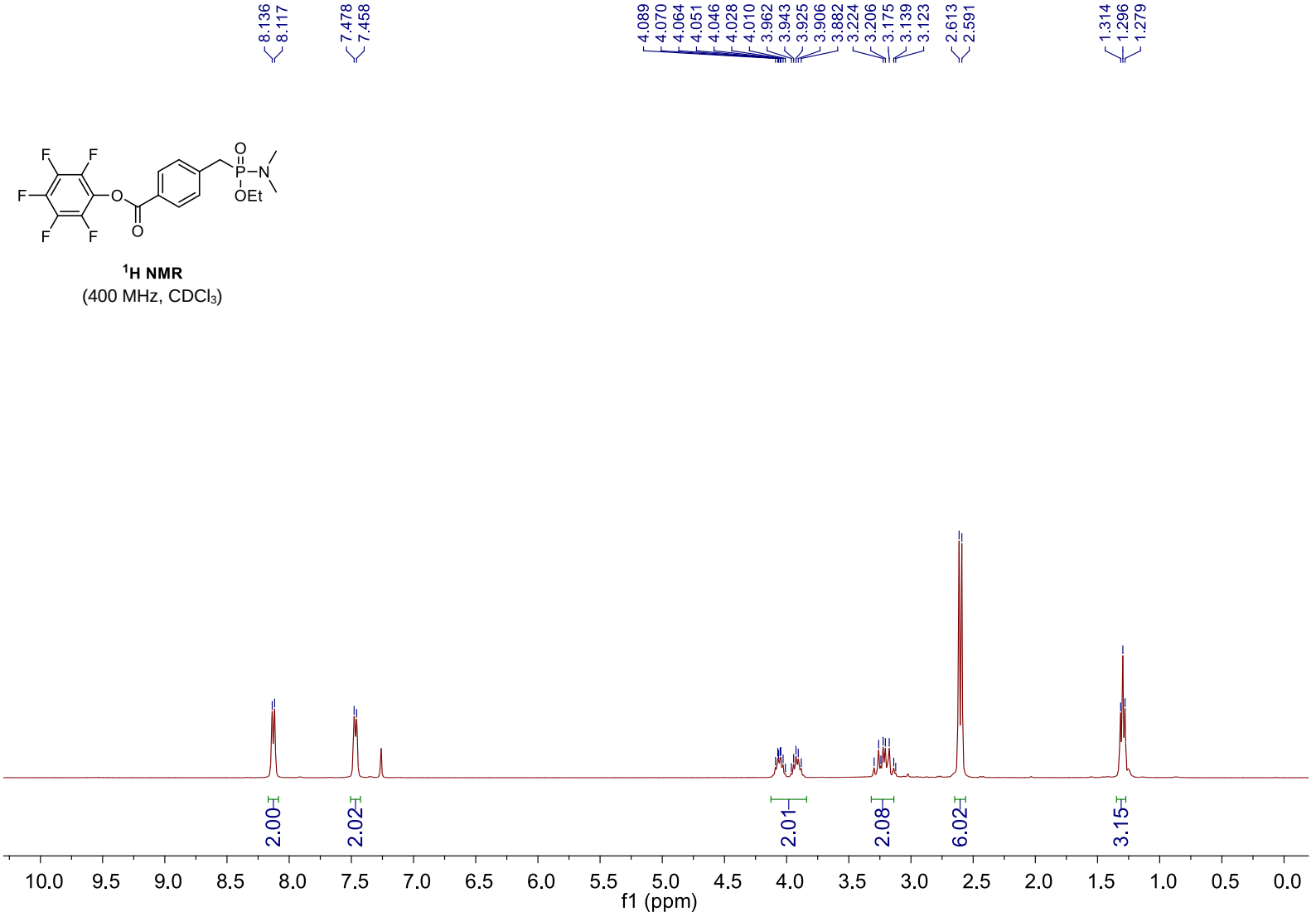


^{31}P NMR
(162 MHz, $CDCl_3$)

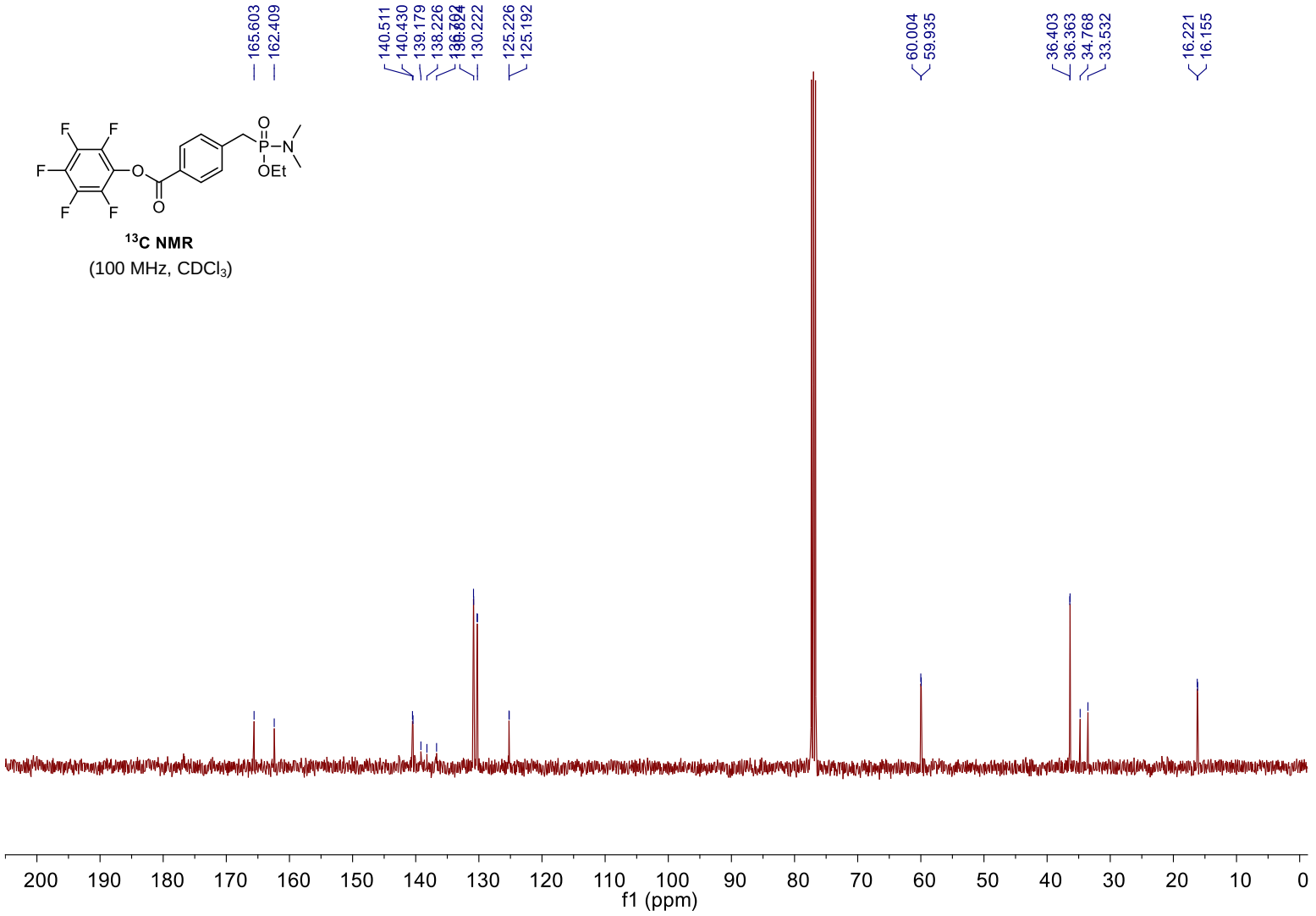


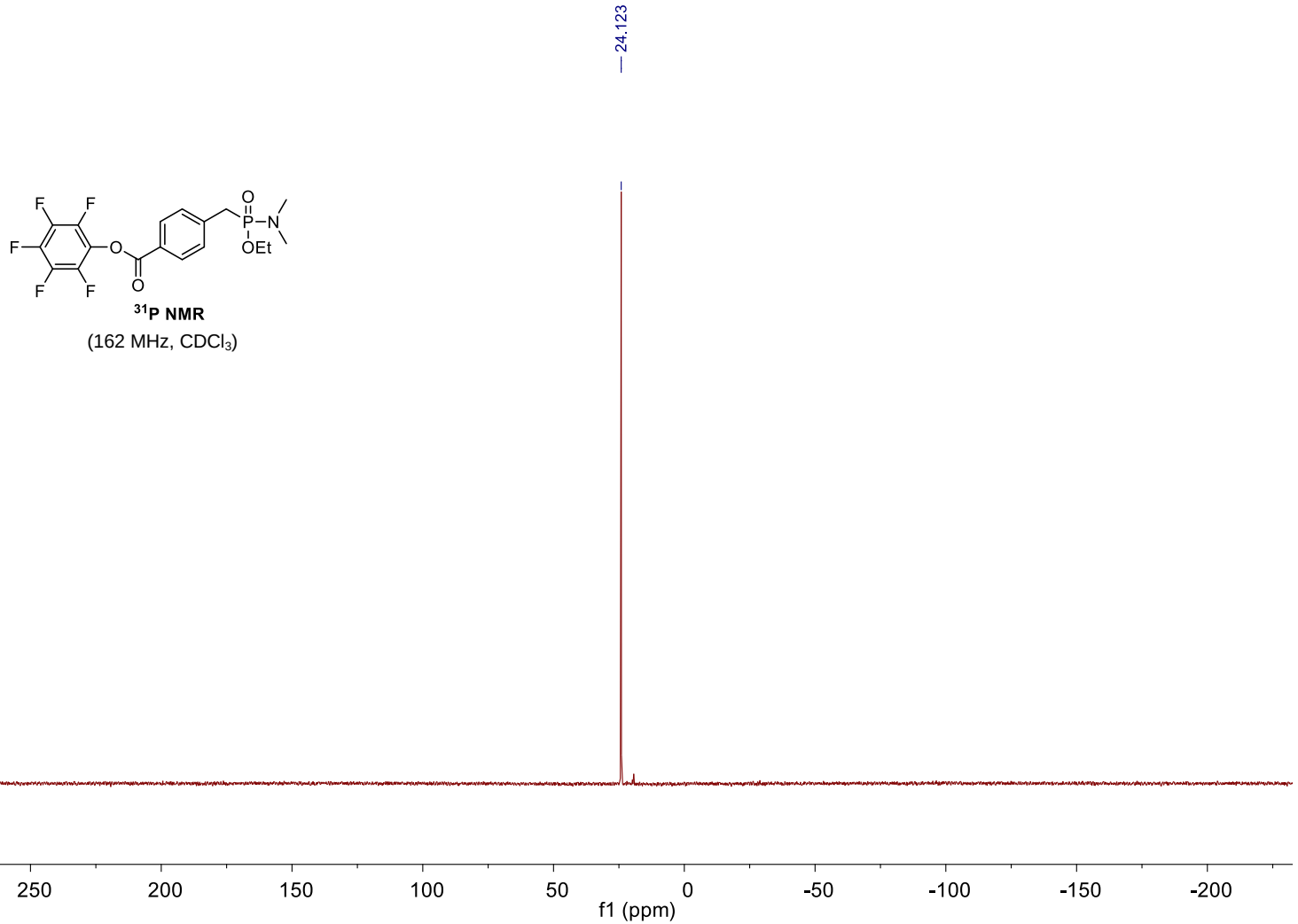
^{19}F NMR

(376 MHz, $CDCl_3$)



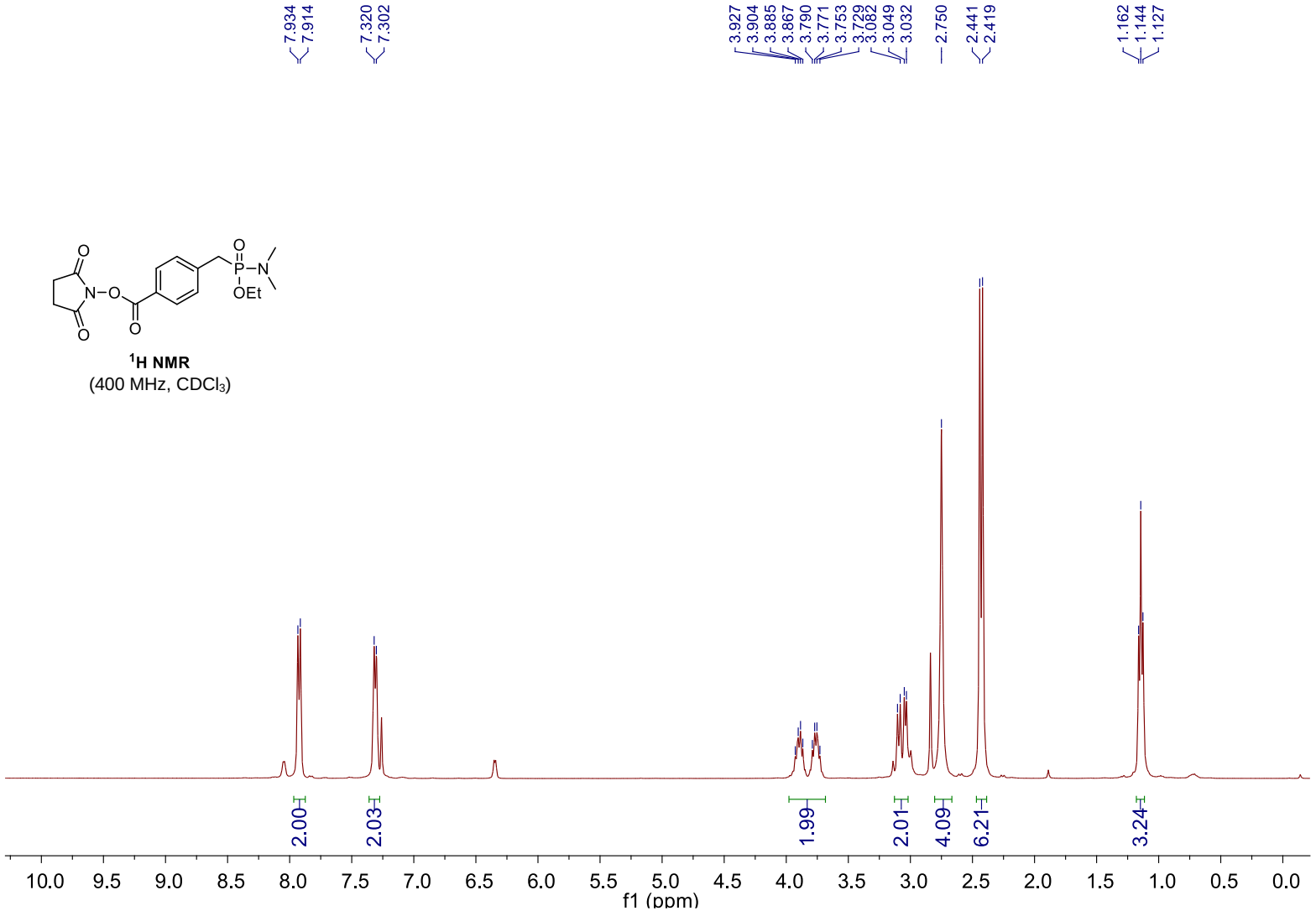
^{1}H NMR
(400 MHz, $CDCl_3$)


165.603
162.409
140.511
140.430
139.179
138.226
130.222
125.226
125.192
60.004
59.935
36.403
36.363
34.768
33.532
16.221
16.155
F
F
F
F
F
O
O
O
P
N
OEt
13C NMR
(100 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

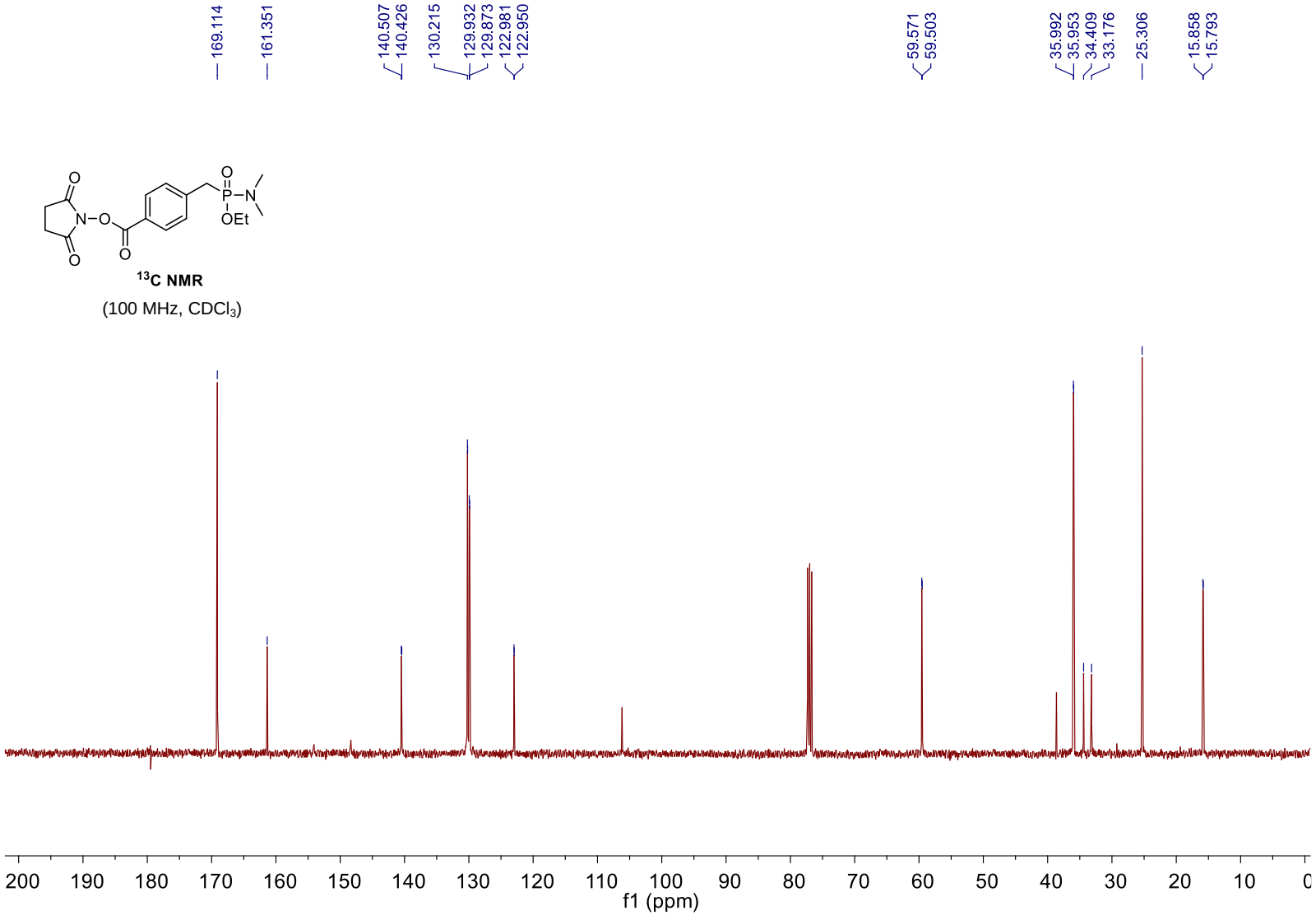


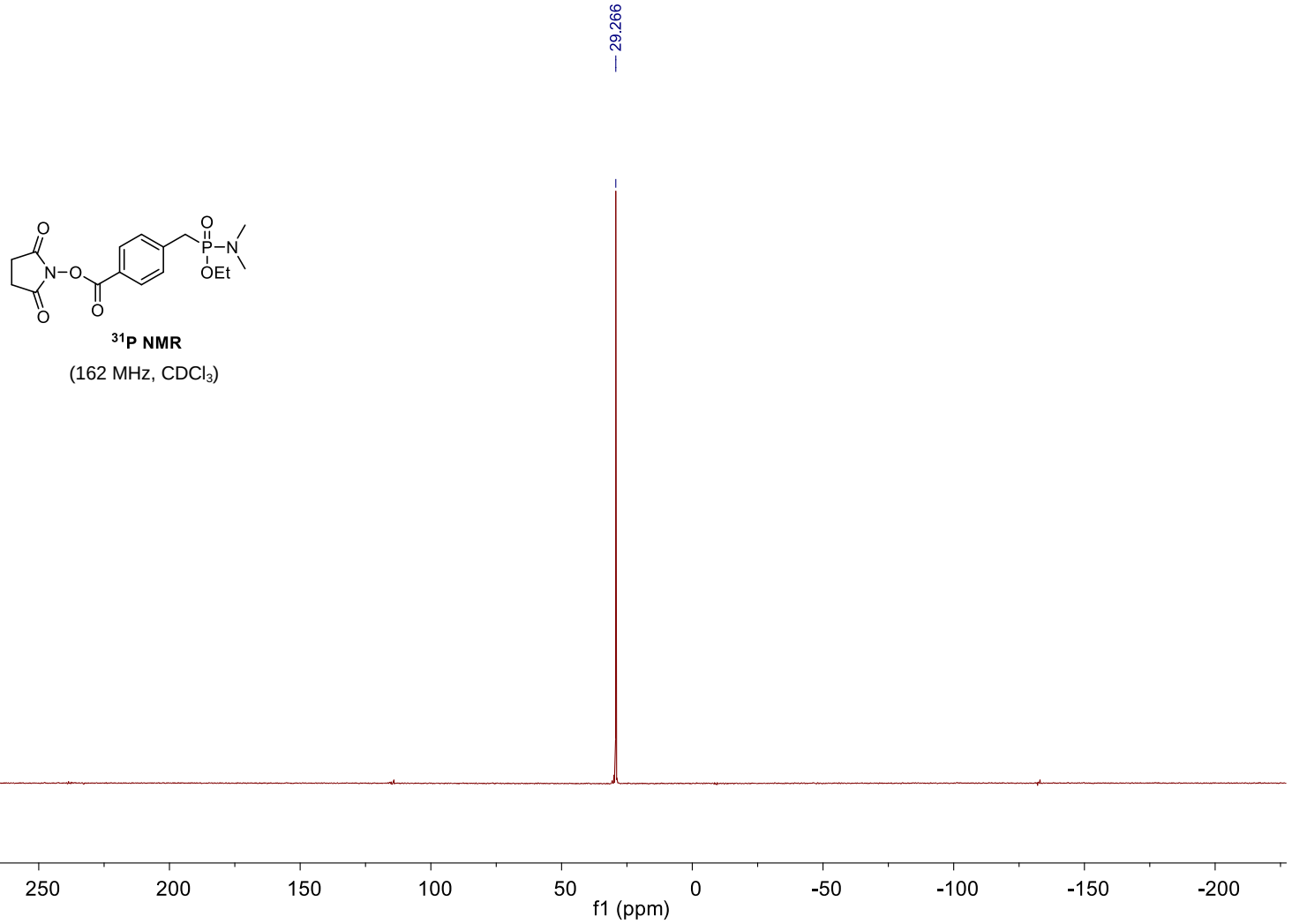
^{31}P NMR

(162 MHz, $CDCl_3$)



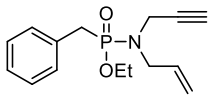
^{1}H NMR
(400 MHz, $CDCl_3$)


169.114
161.351
140.507
140.426
130.215
129.932
129.873
122.981
122.950
59.571
59.503
35.992
35.953
34.409
33.176
25.306
15.858
15.793
O
O
N
O
O
O
P
N
OEt
^{13}C NMR
(100 MHz, $CDCl_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



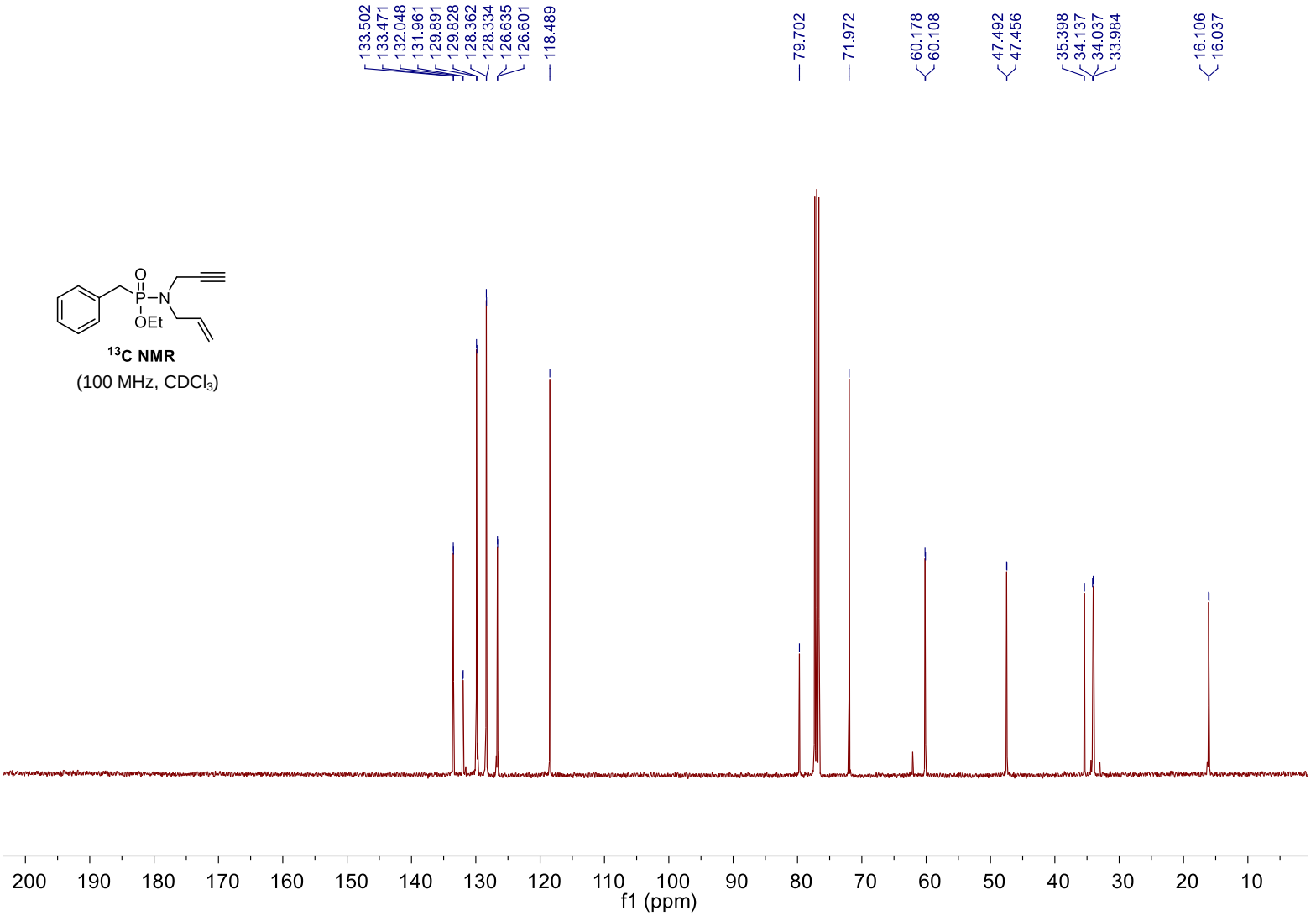
^{31}P NMR

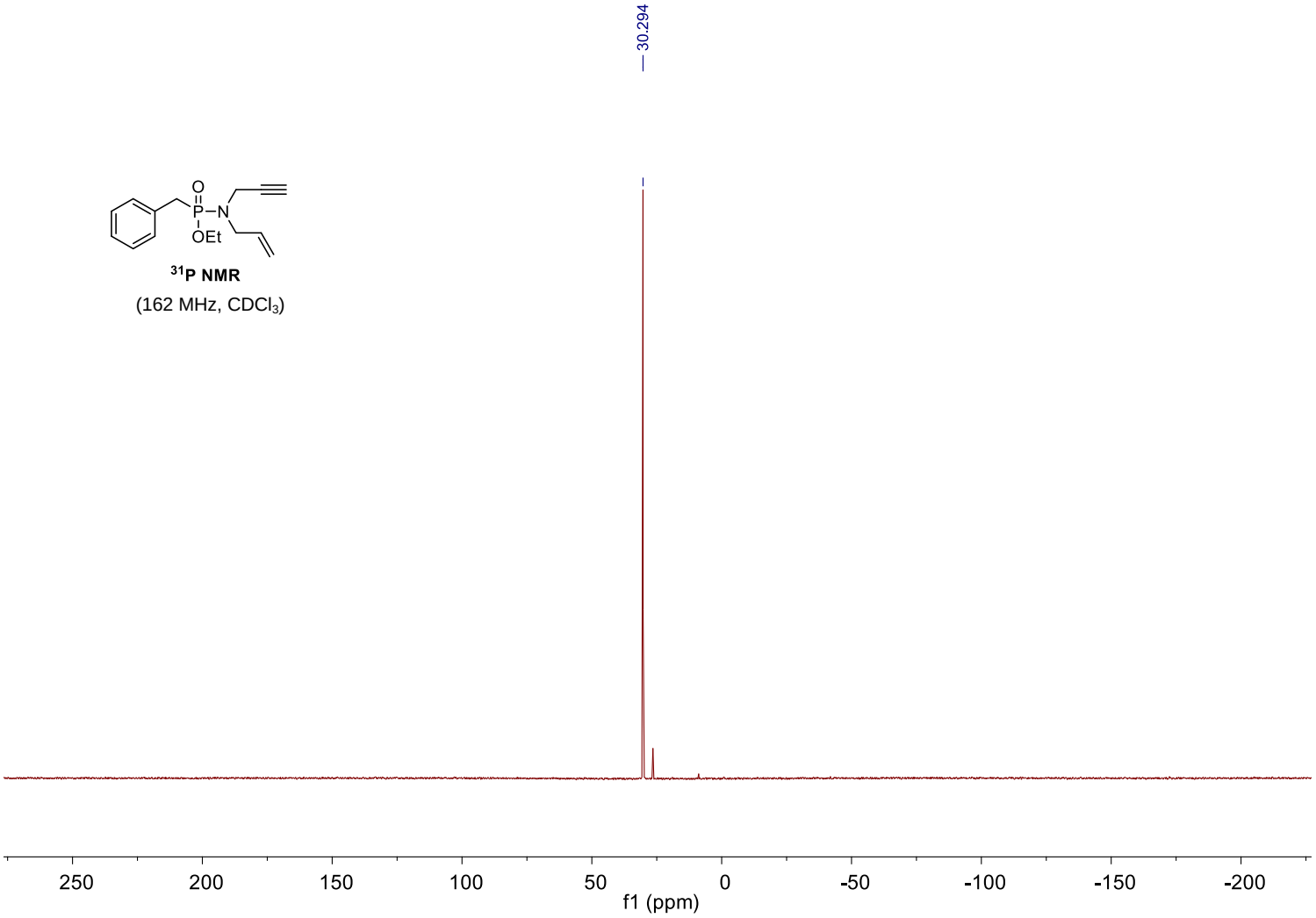
(162 MHz, $CDCl_3$)



^{1}H NMR

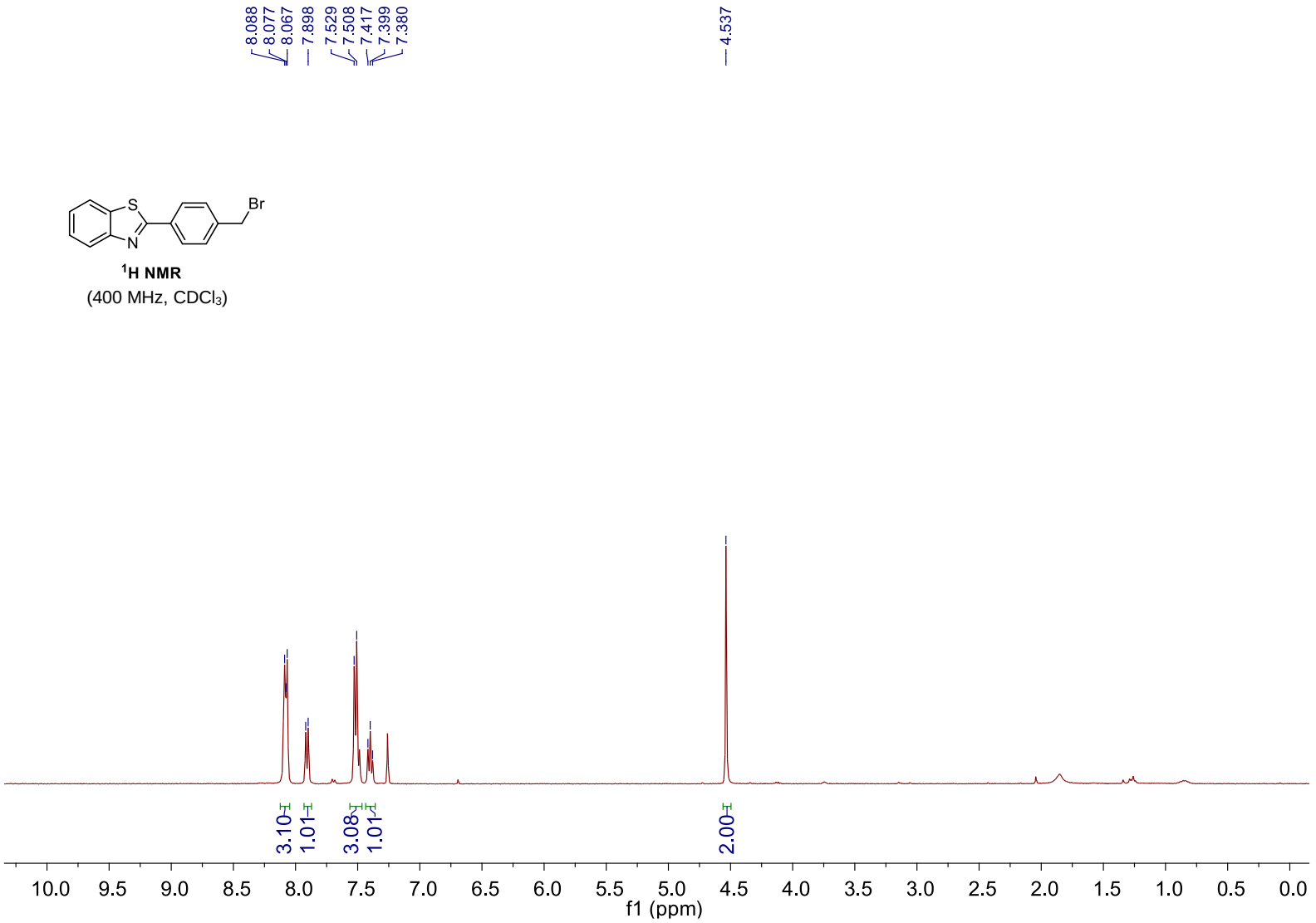
(400 MHz, $CDCl_3$)


133.502
133.471
132.048
131.961
129.891
129.828
128.362
128.334
126.635
126.601
118.489
79.702
71.972
60.178
60.108
47.492
47.456
35.398
34.137
34.037
33.984
16.106
16.037
O
P
N
OEt
13C NMR
(100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

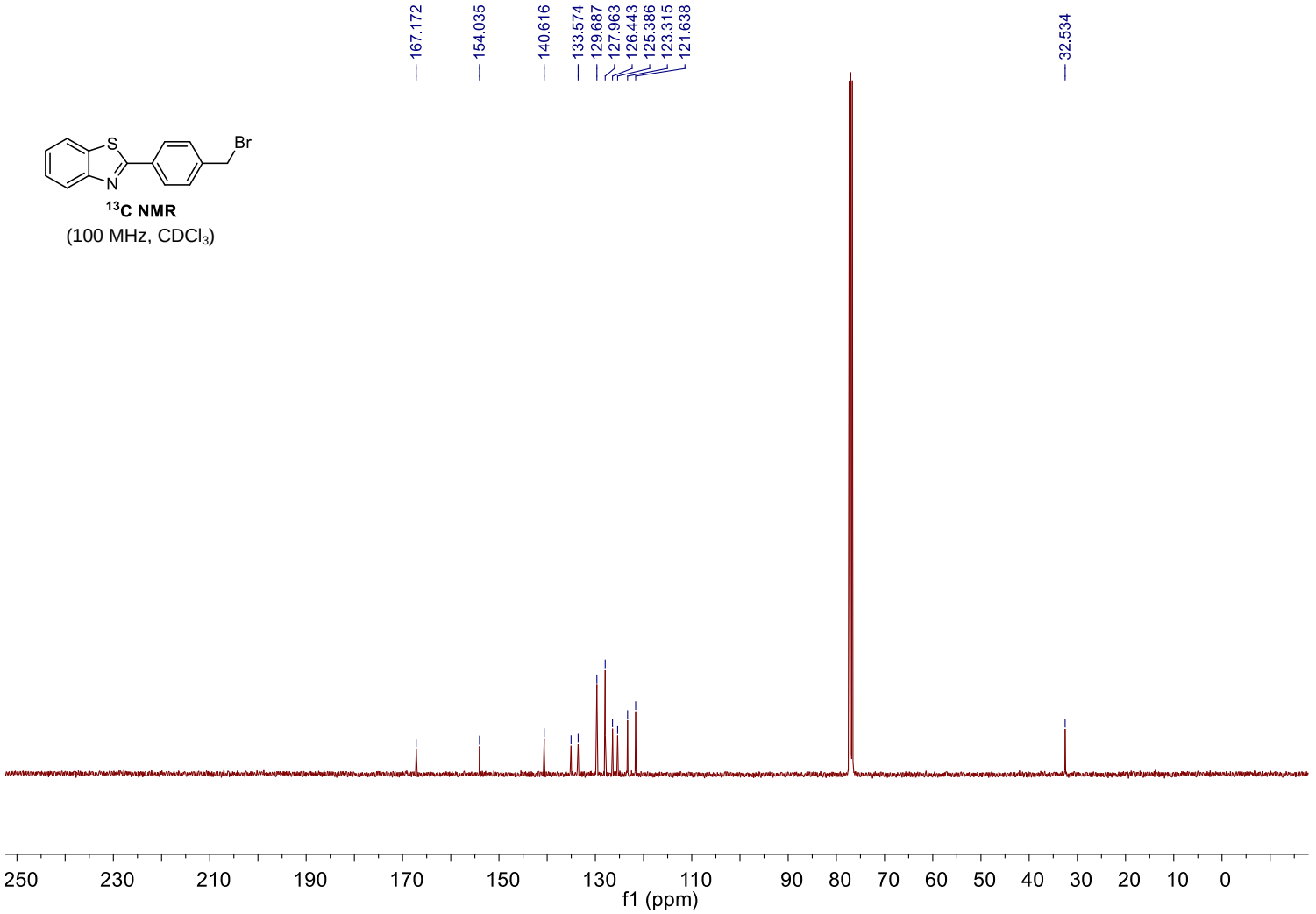


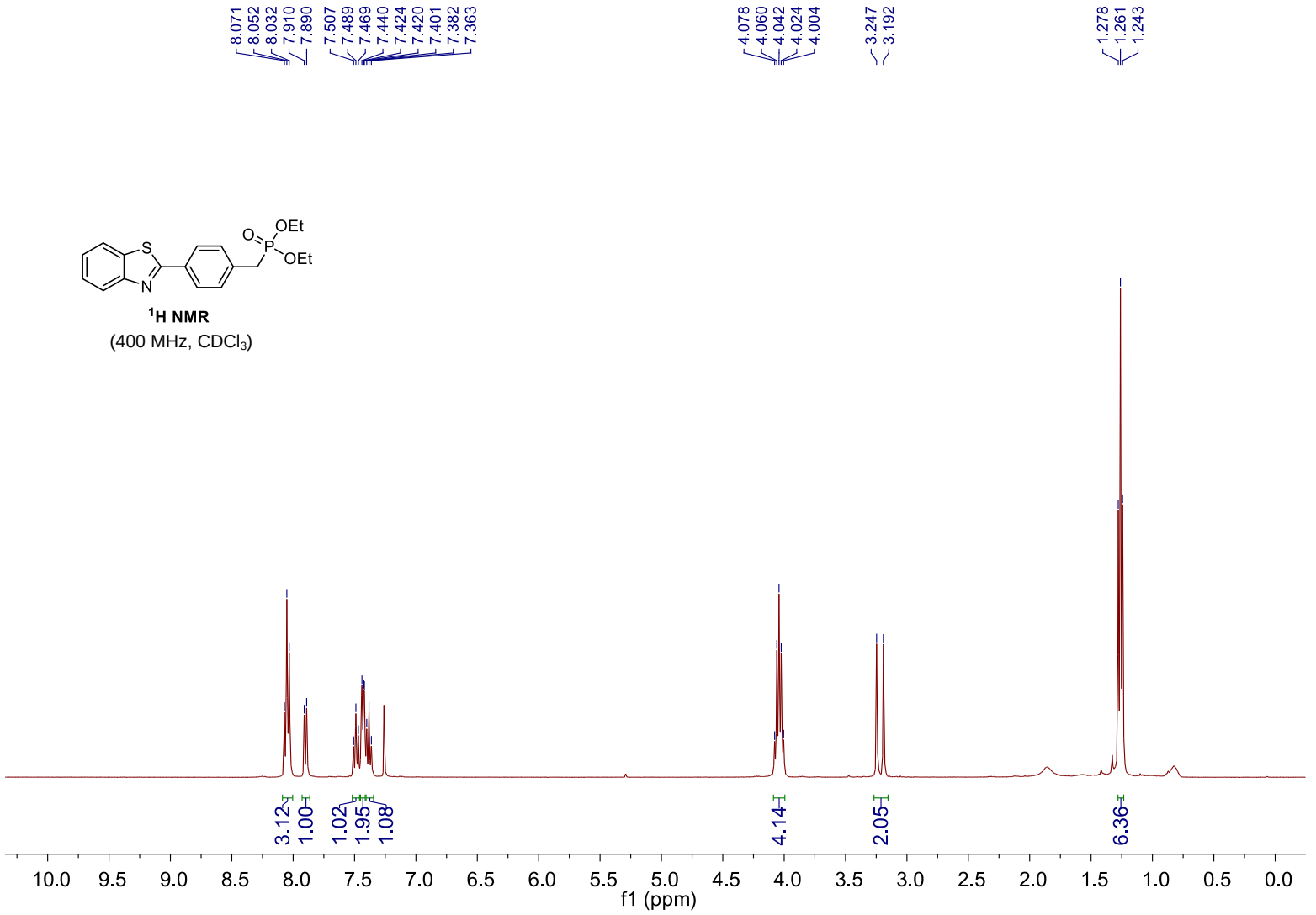
^{31}P NMR

(162 MHz, $CDCl_3$)

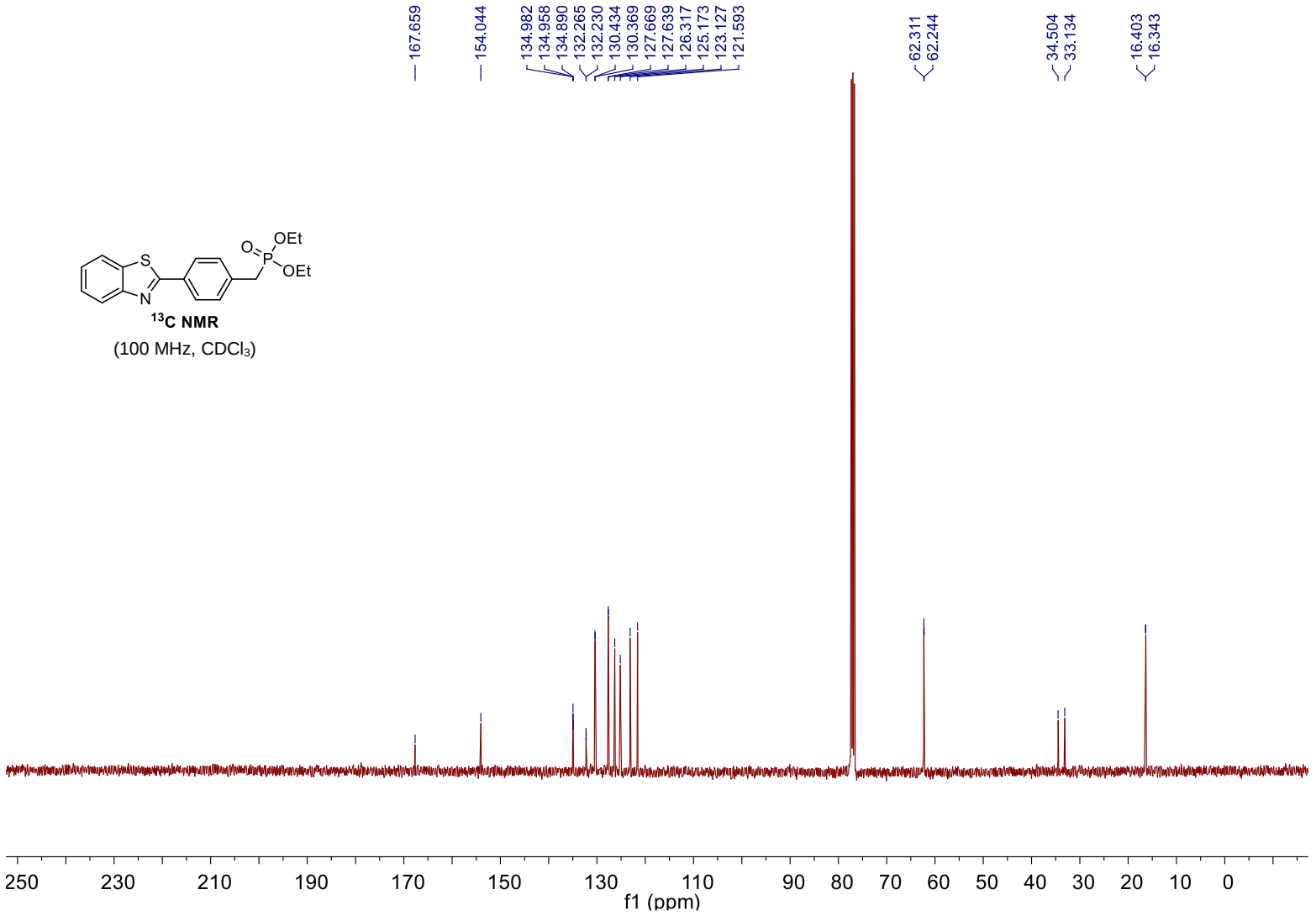


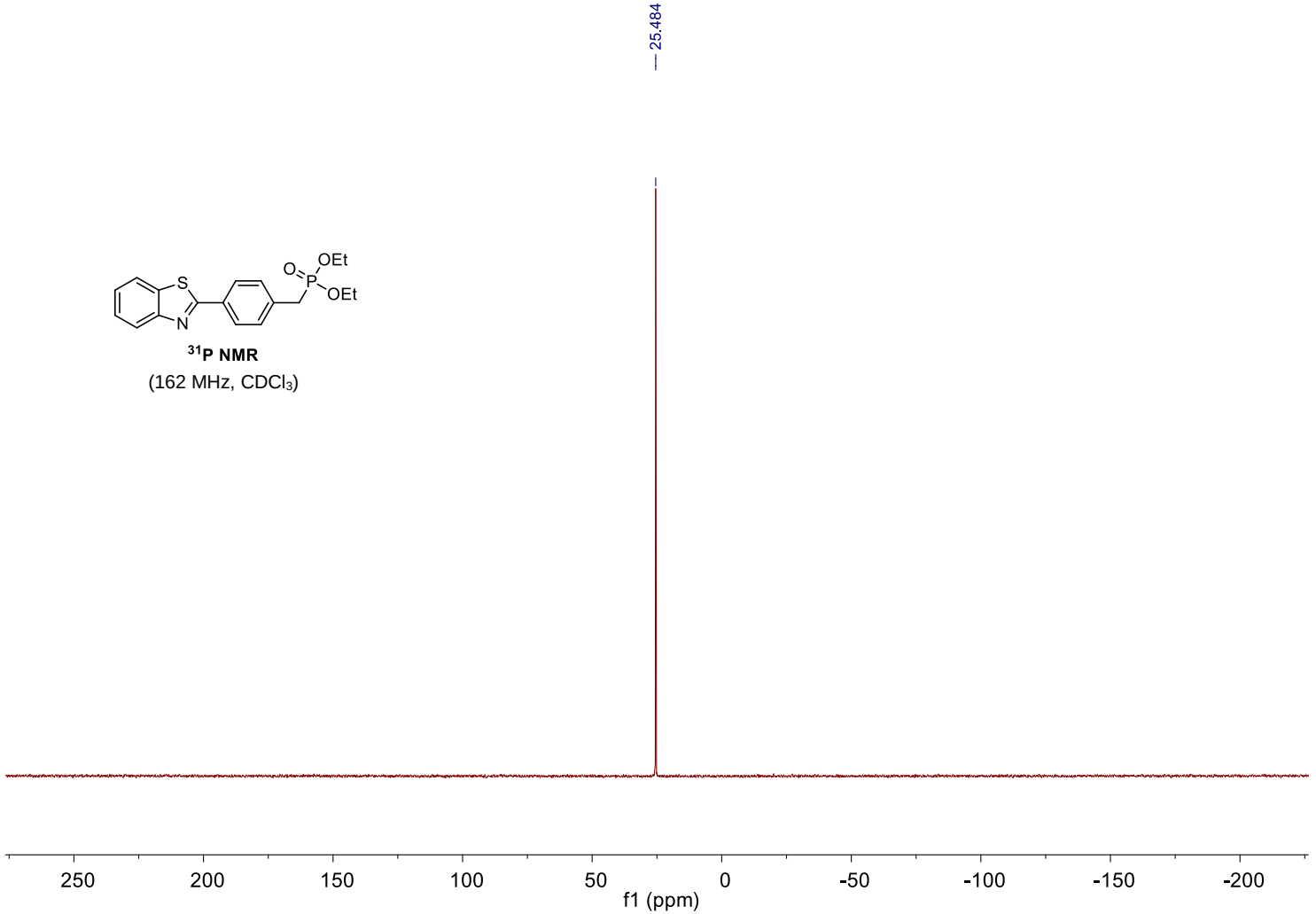
^{1}H NMR
(400 MHz, $CDCl_3$)


167.172
154.035
140.616
133.574
129.687
127.963
126.443
125.386
123.315
121.638
32.534
S
N
Br
13C NMR
(100 MHz, CDCl3)
250
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



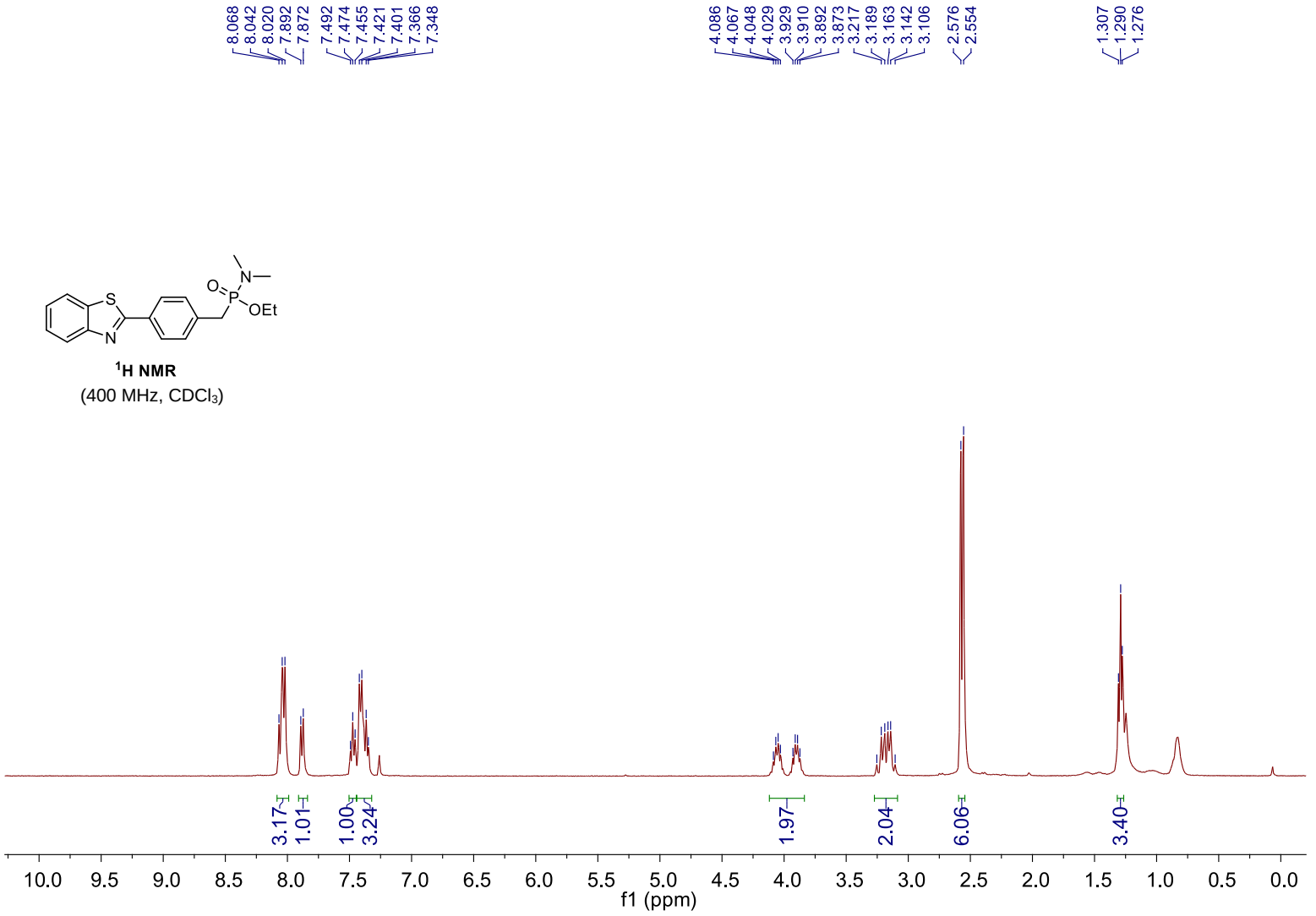
^{1}H NMR
(400 MHz, $CDCl_3$)


167.659
154.044
134.982
134.958
134.890
132.265
132.230
130.434
130.369
127.669
127.639
126.317
125.173
123.127
121.593
62.311
62.244
34.504
33.134
16.403
16.343
OEt
OEt
S
N
O
P
13C NMR
(100 MHz, CDCl3)
250
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



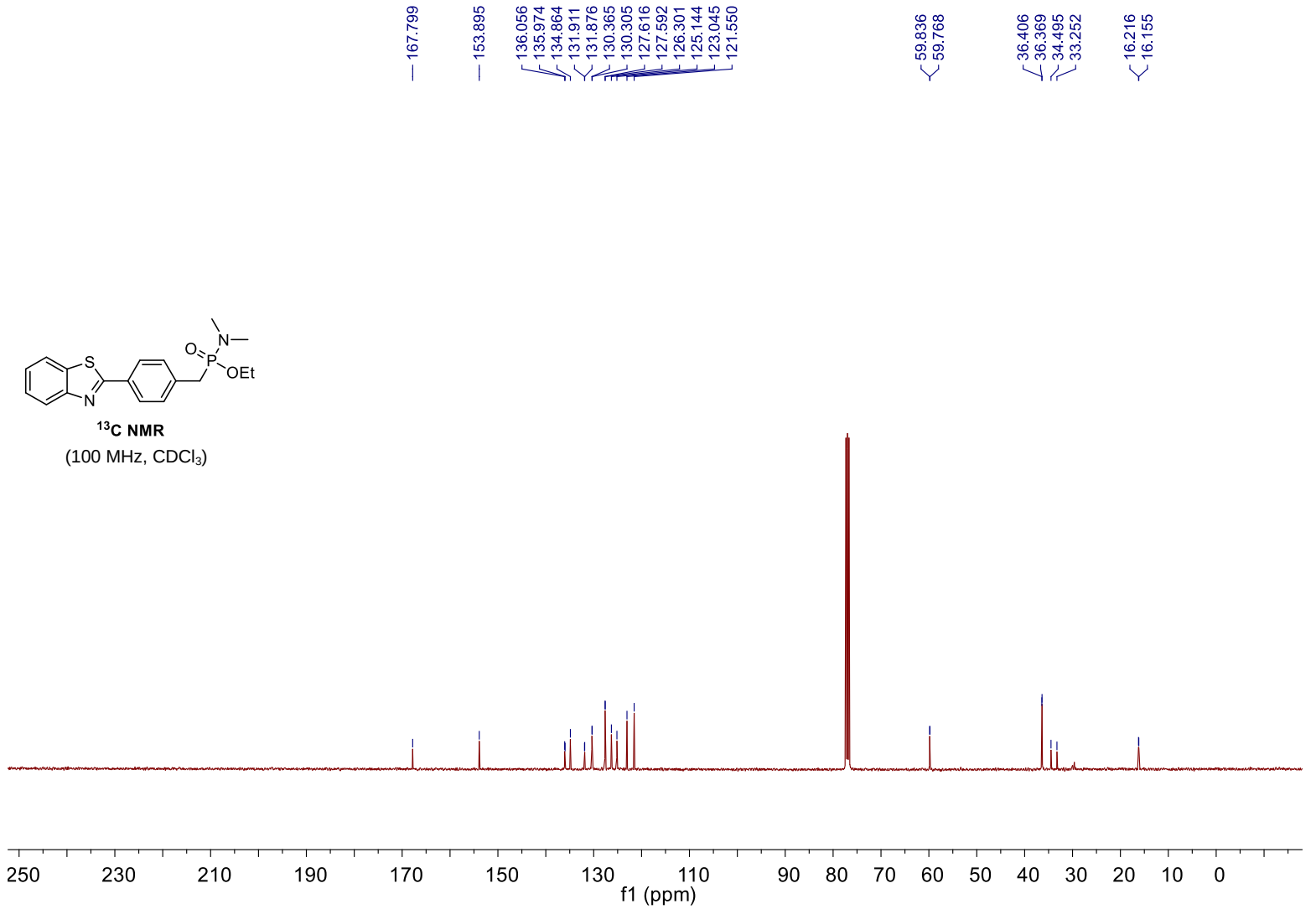
^{31}P NMR

(162 MHz, $CDCl_3$)



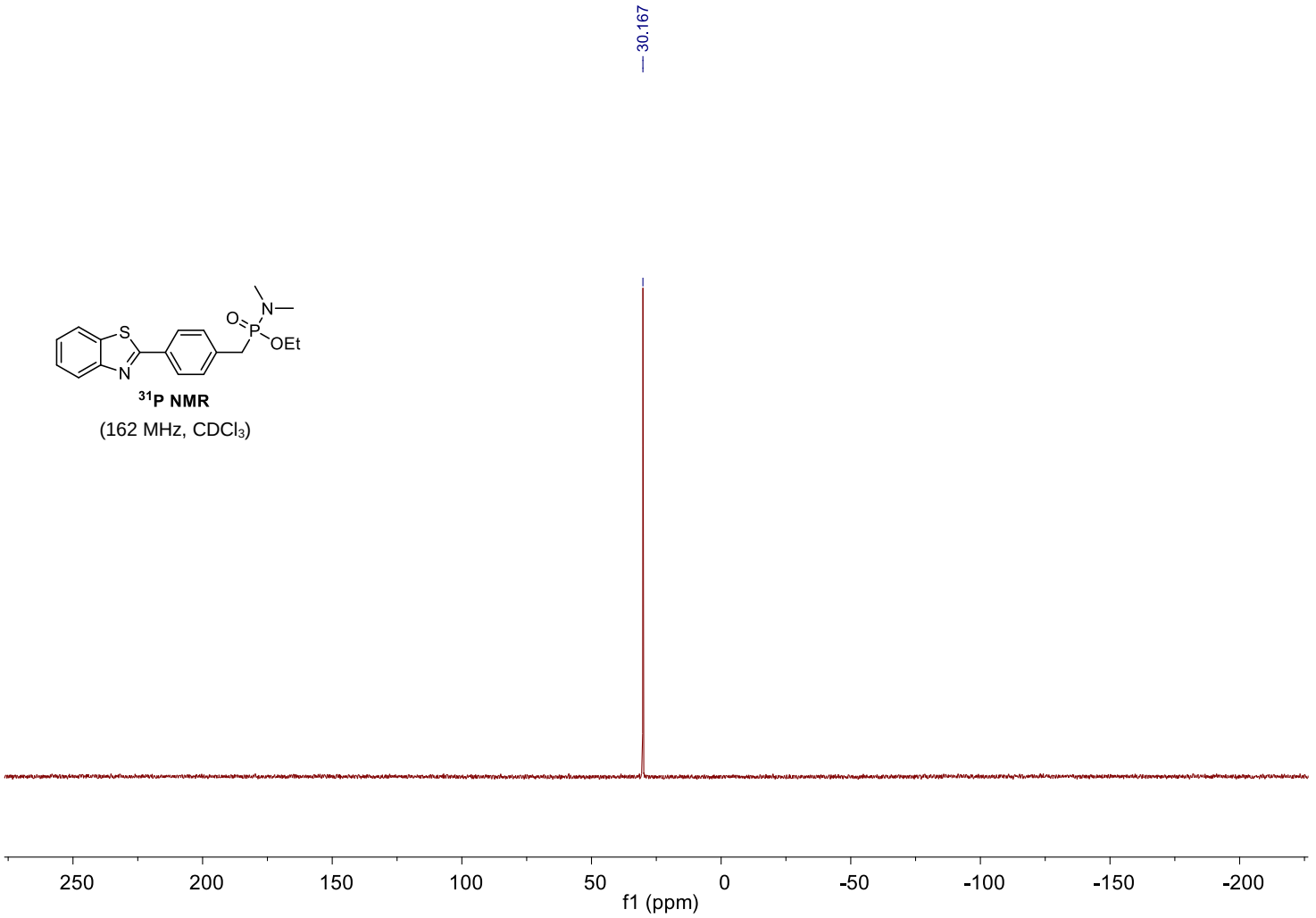
^{1}H NMR

(400 MHz, $CDCl_3$)



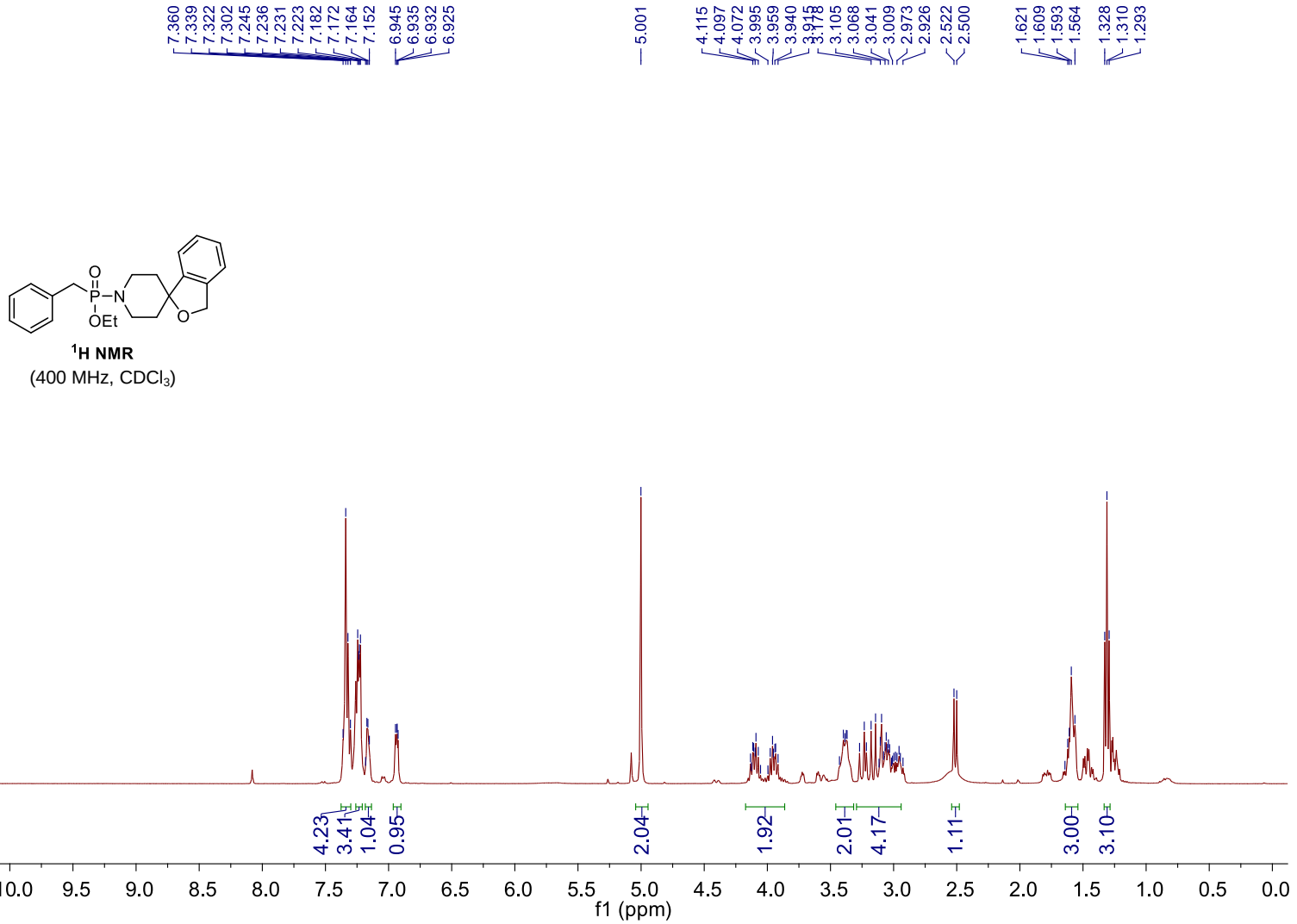
^{13}C NMR

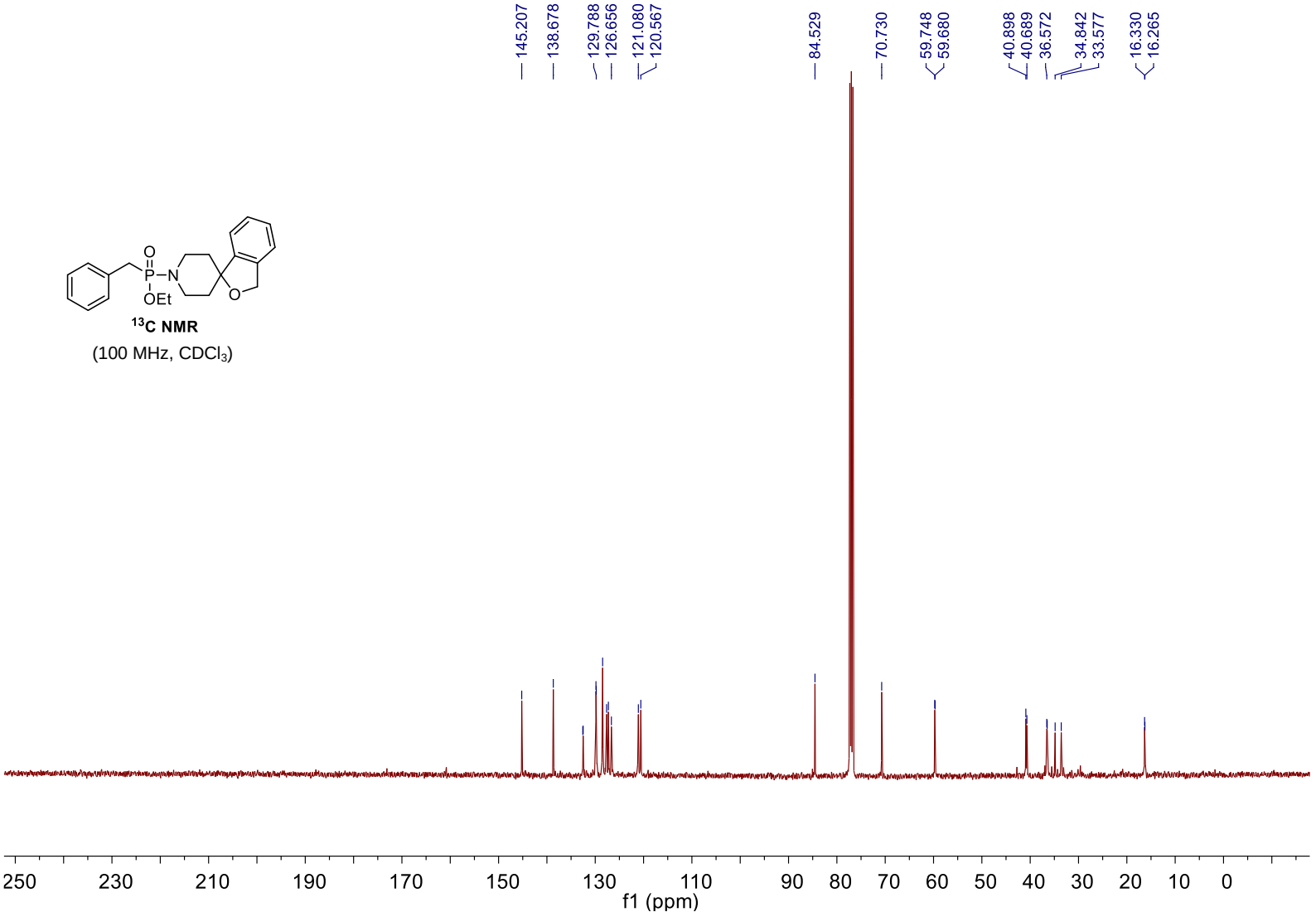
(100 MHz, $CDCl_3$)



^{31}P NMR

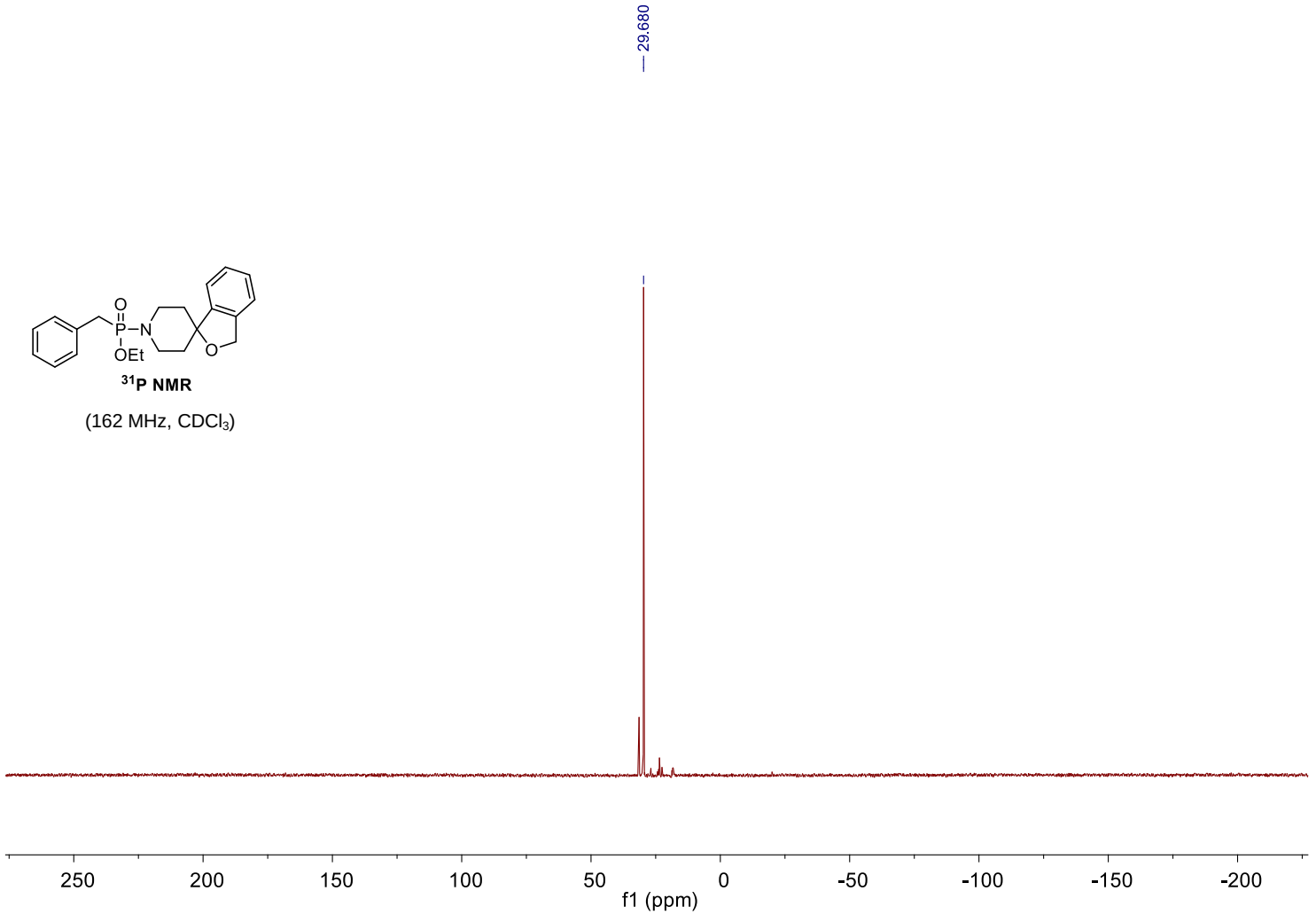
(162 MHz, $CDCl_3$)


7.360
7.339
7.322
7.302
7.245
7.236
7.231
7.223
7.182
7.172
7.164
7.152
6.945
6.935
6.932
6.925
5.001
4.115
4.097
4.072
3.995
3.959
3.940
3.915
3.178
3.105
3.068
3.041
3.009
2.973
2.926
2.522
2.500
1.621
1.609
1.593
1.564
1.328
1.310
1.293
O
P
N
OEt
O
1H NMR
(400 MHz, CDCl3)
4.23
3.41
1.04
0.95
2.04
1.92
2.01
4.17
1.11
3.00
3.10
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



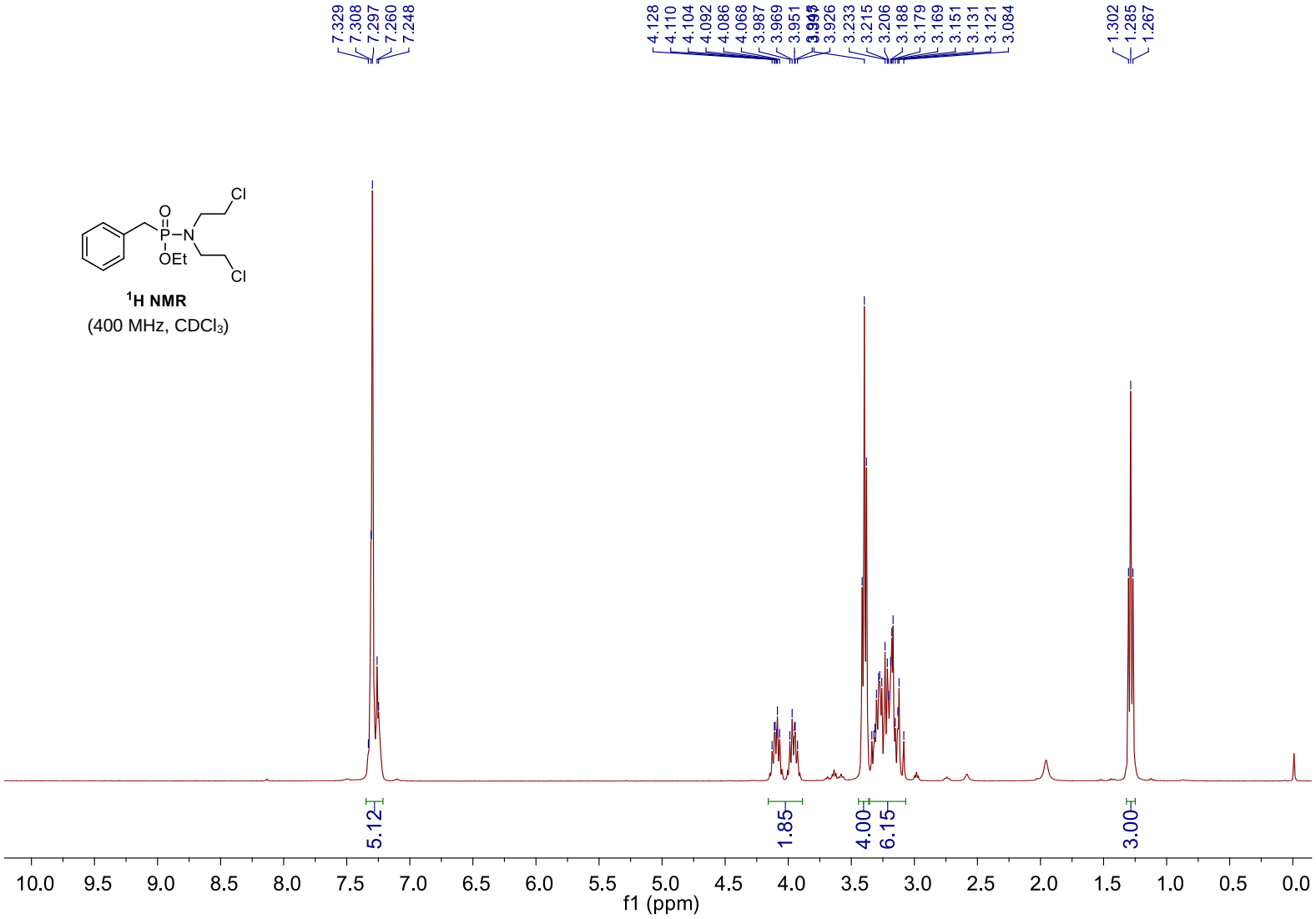
^{13}C NMR

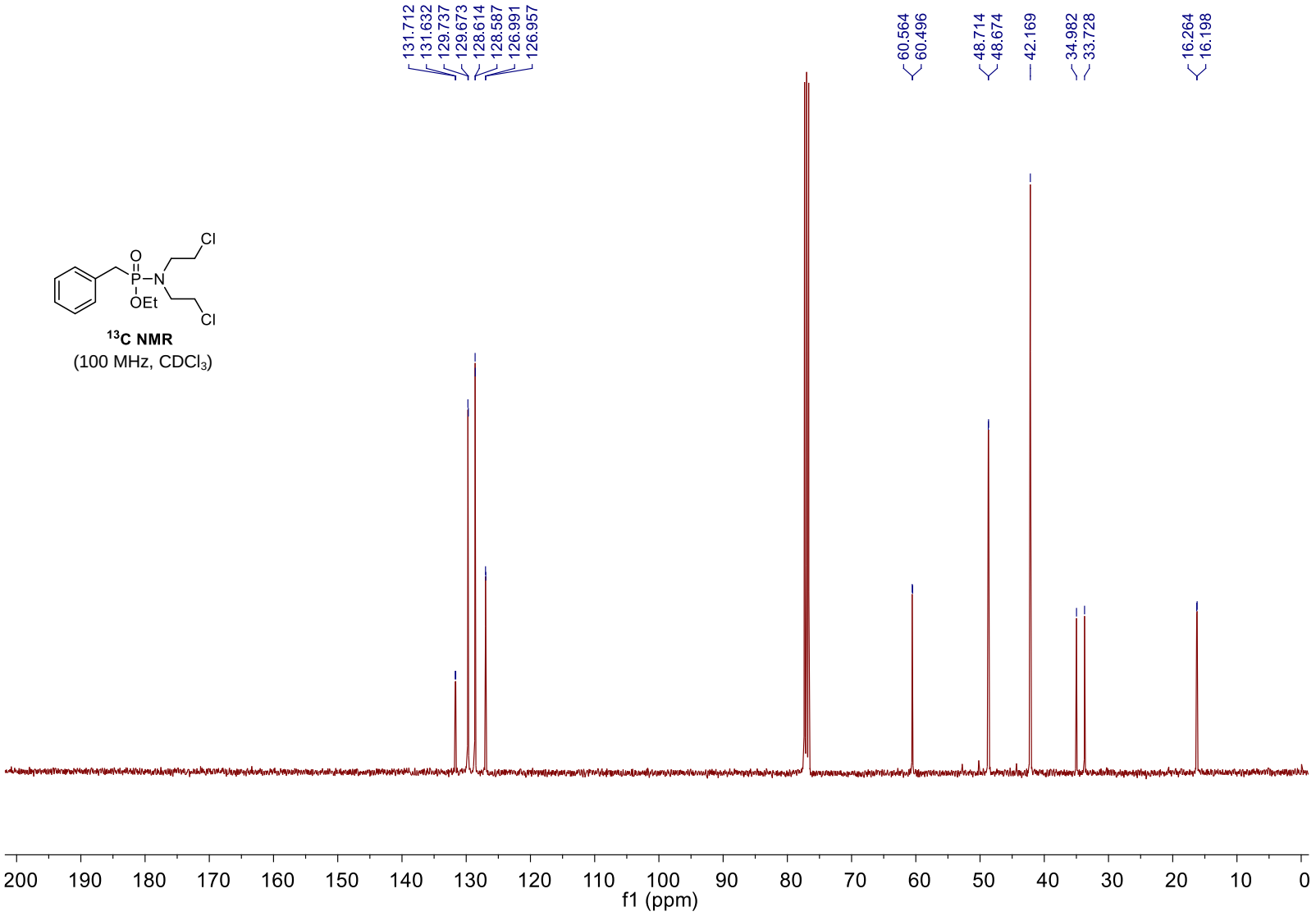
(100 MHz, $CDCl_3$)

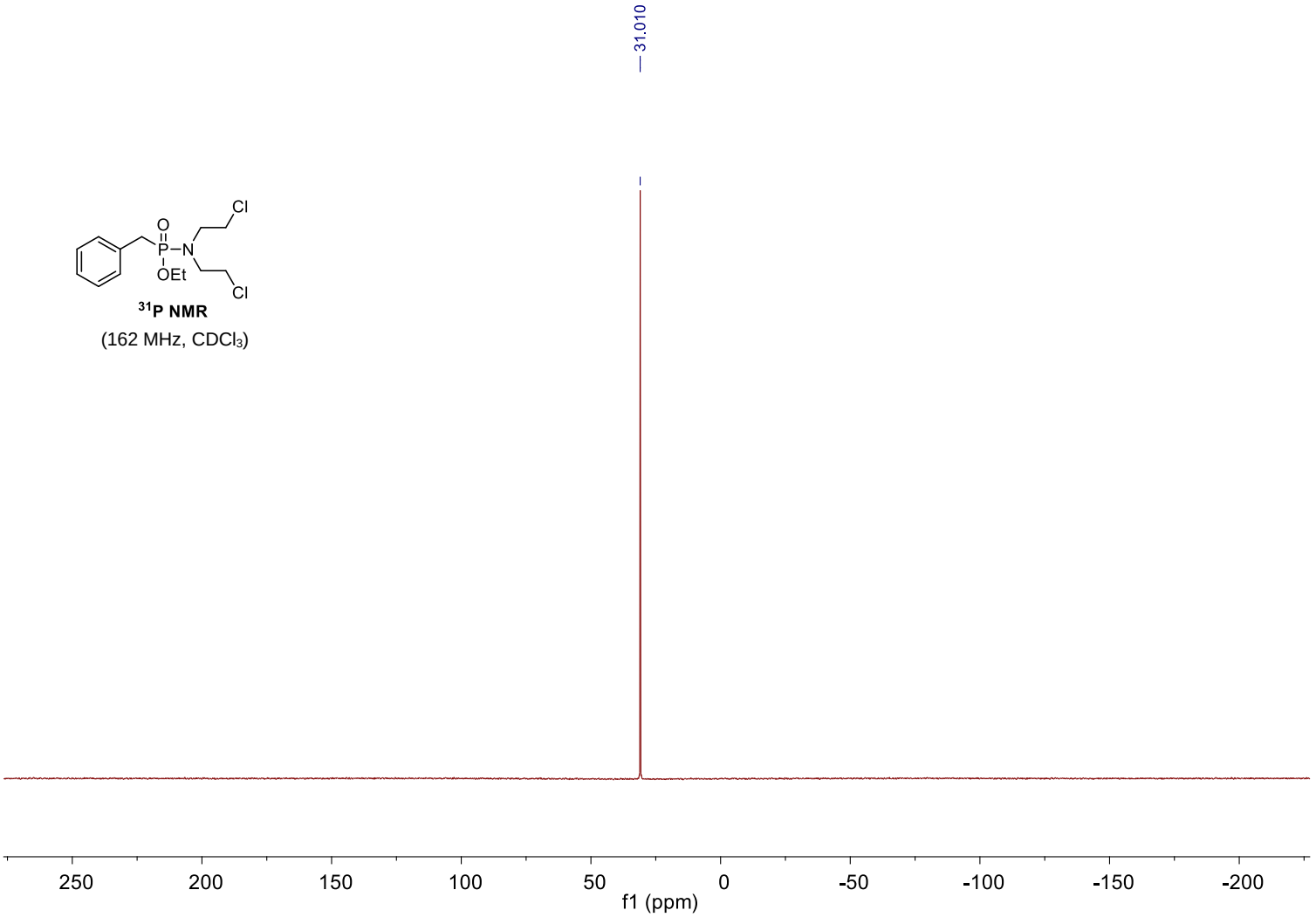


^{31}P NMR

(162 MHz, $CDCl_3$)

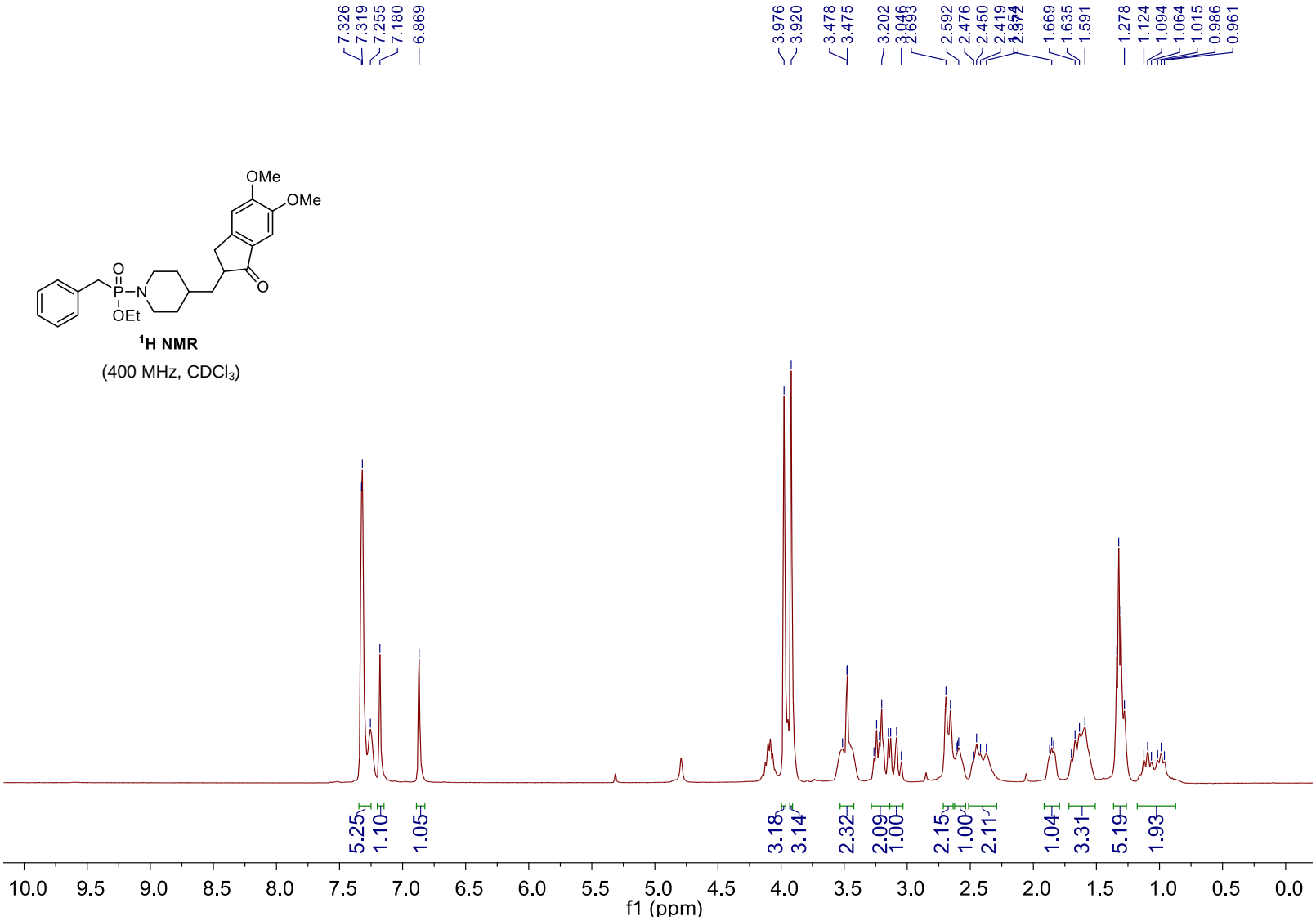

7.329
7.308
7.297
7.260
7.248
4.128
4.110
4.104
4.092
4.086
4.068
3.987
3.969
3.951
3.926
3.233
3.215
3.206
3.188
3.179
3.169
3.151
3.131
3.121
3.084
1.302
1.285
1.267
Cl
O
P
N
OEt
Cl
1H NMR
(400 MHz, CDCl3)
5.12
1.85
4.00
6.15
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


131.712
131.632
129.737
129.673
128.614
128.587
126.991
126.957
60.564
60.496
48.714
48.674
42.169
34.982
33.728
16.264
16.198
Cl
O
P
N
OEt
Cl
13C NMR
(100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



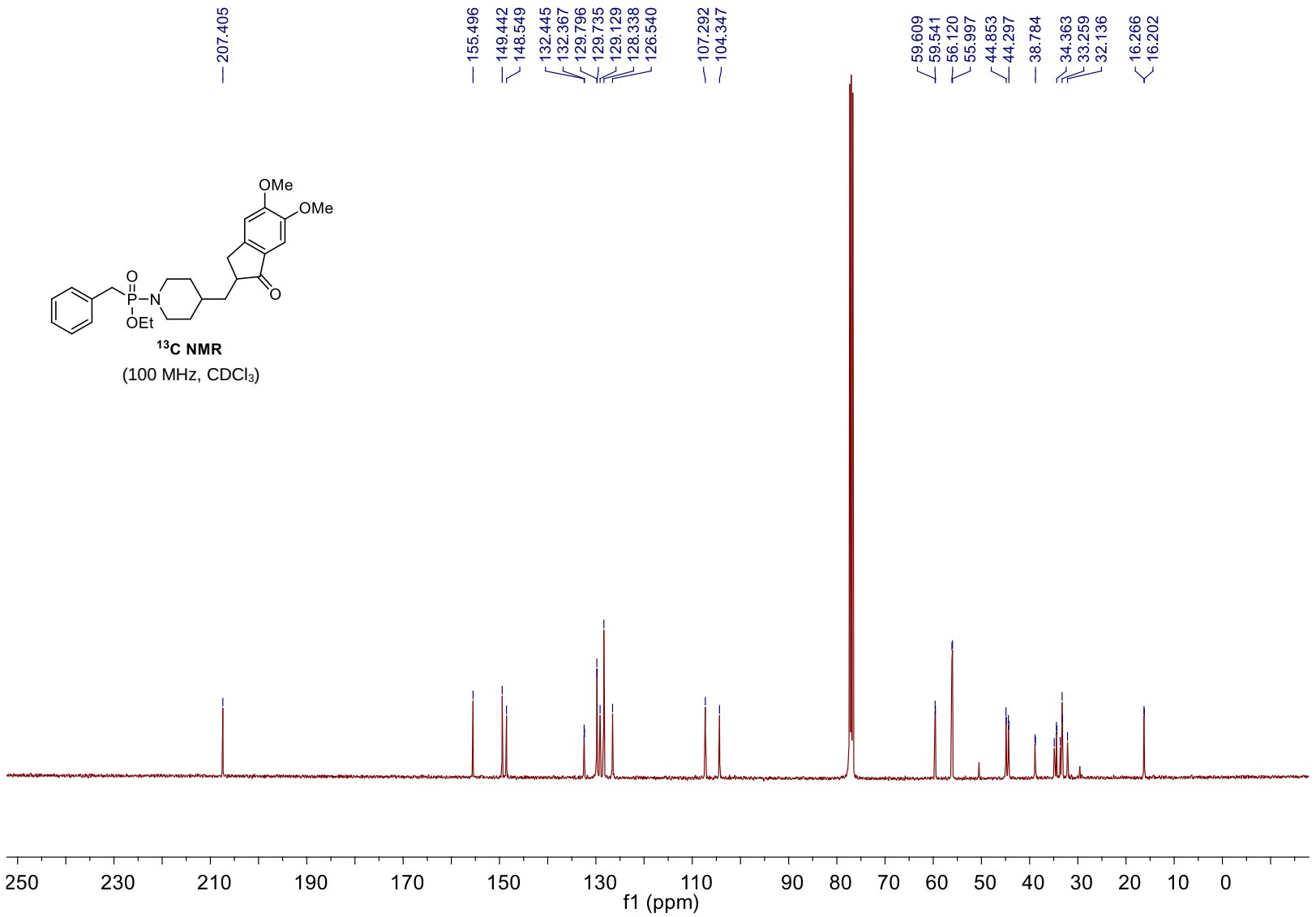
^{31}P NMR

(162 MHz, $CDCl_3$)



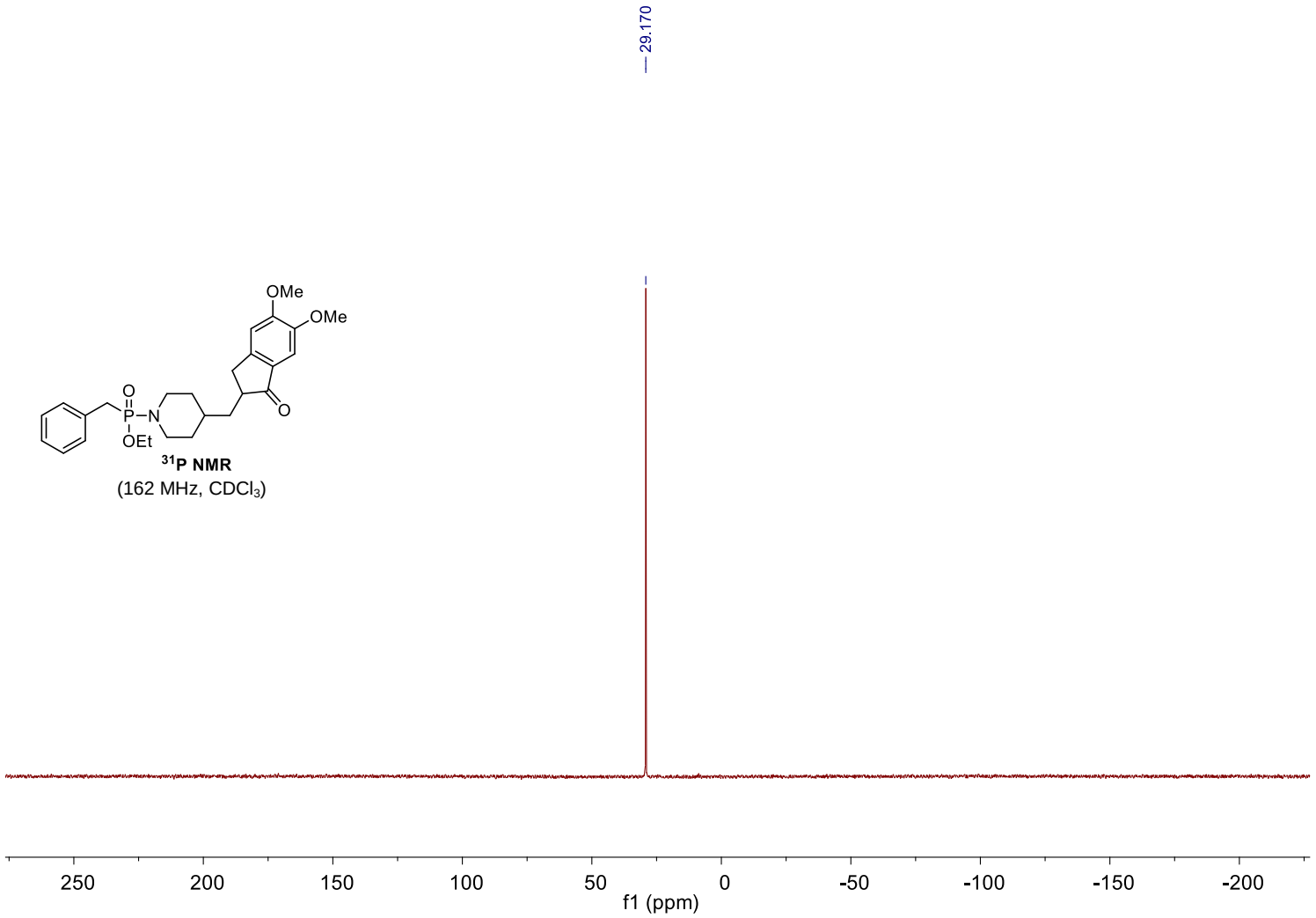
^{1}H NMR

(400 MHz, $CDCl_3$)

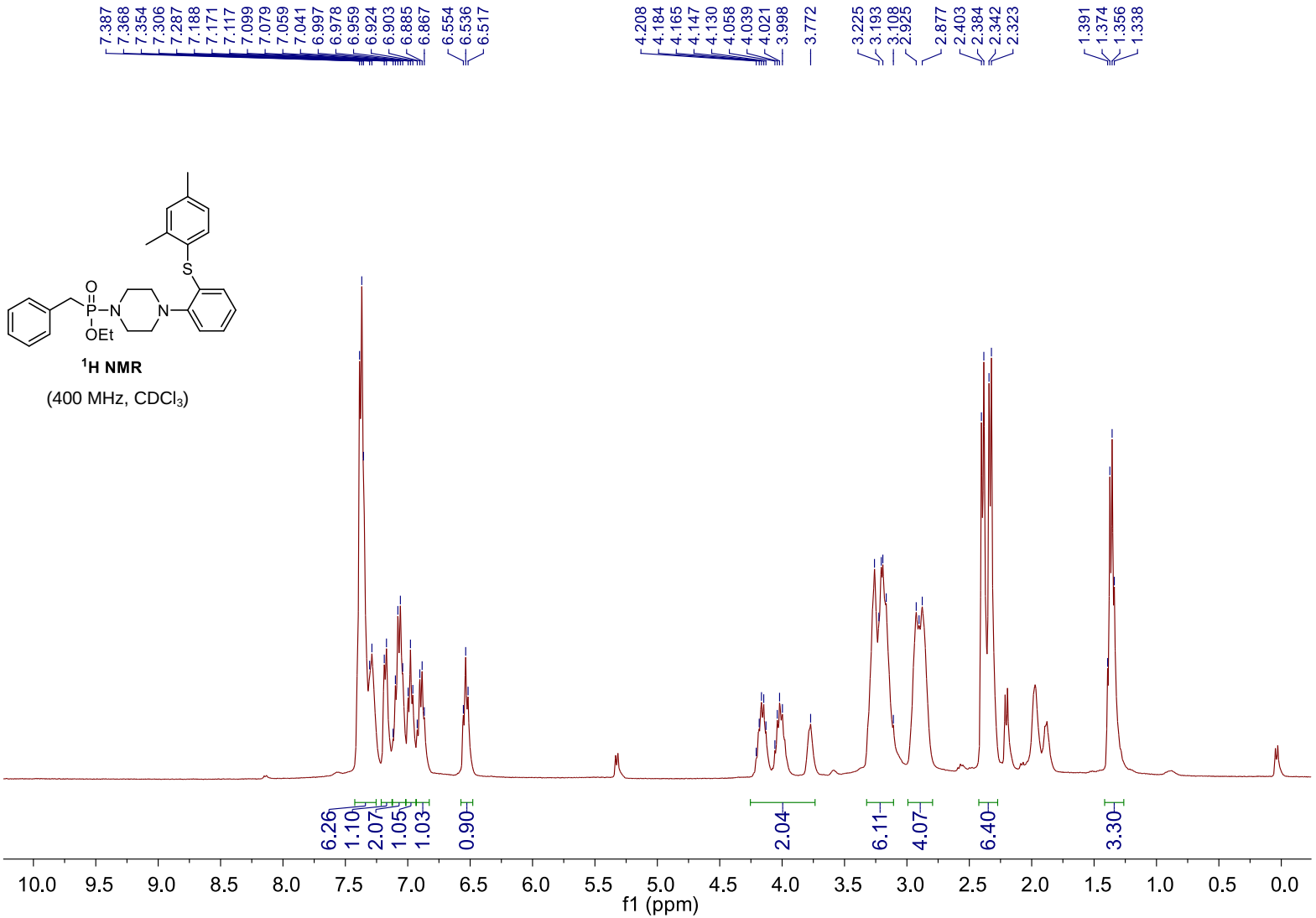


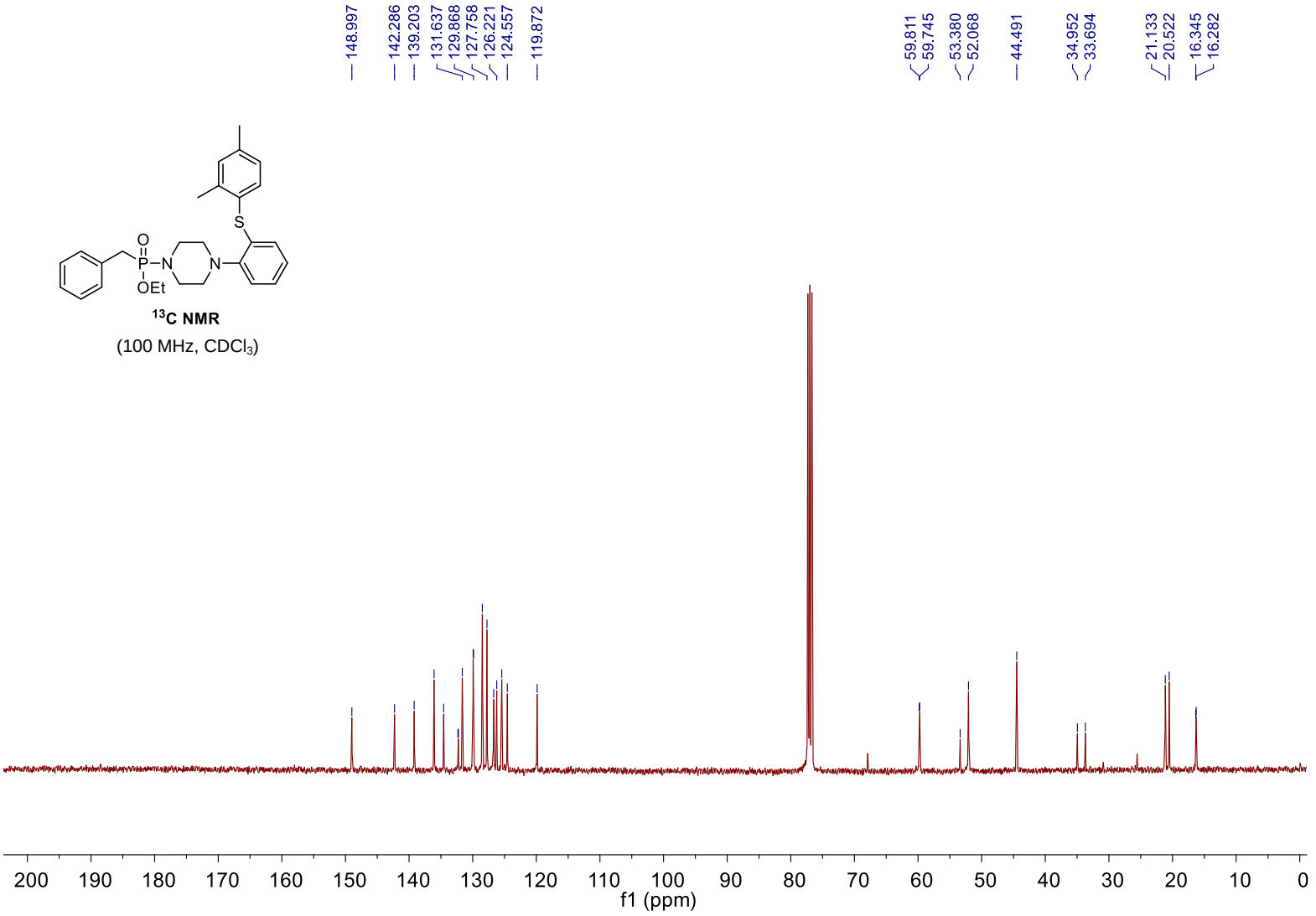
^{13}C NMR

(100 MHz, $CDCl_3$)



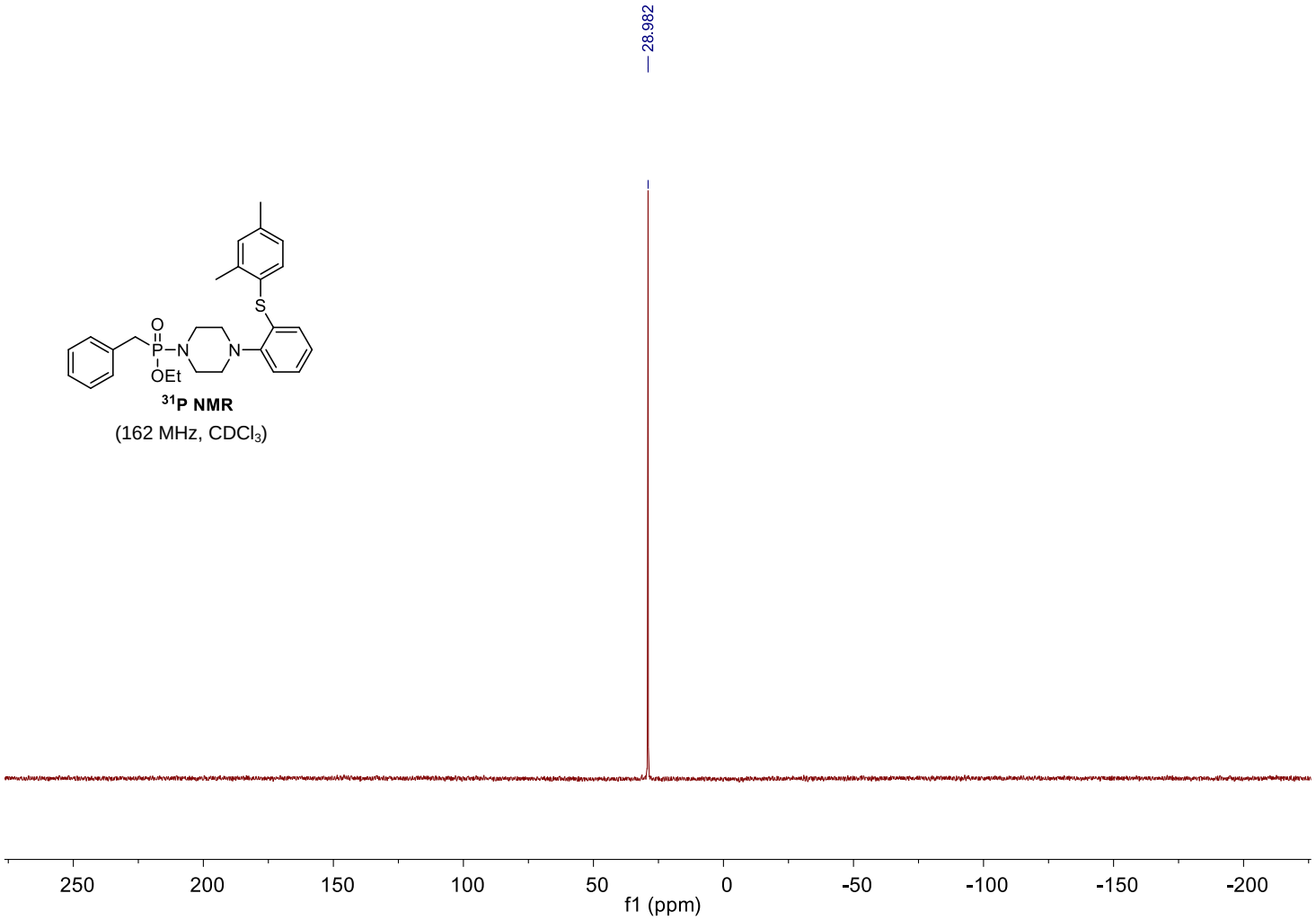
^{31}P NMR
(162 MHz, $CDCl_3$)


7.387
7.368
7.354
7.306
7.287
7.188
7.171
7.117
7.099
7.079
7.059
7.041
6.997
6.978
6.959
6.924
6.903
6.885
6.867
6.554
6.536
6.517
4.208
4.184
4.165
4.147
4.130
4.058
4.039
4.021
3.998
3.772
3.225
3.193
3.108
2.925
2.877
2.403
2.384
2.342
2.323
1.391
1.374
1.356
1.338
O
P
N
N
S
OEt
1H NMR
(400 MHz, CDCl3)
6.26
1.10
2.07
1.05
1.03
0.90
2.04
6.11
4.07
6.40
3.30
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



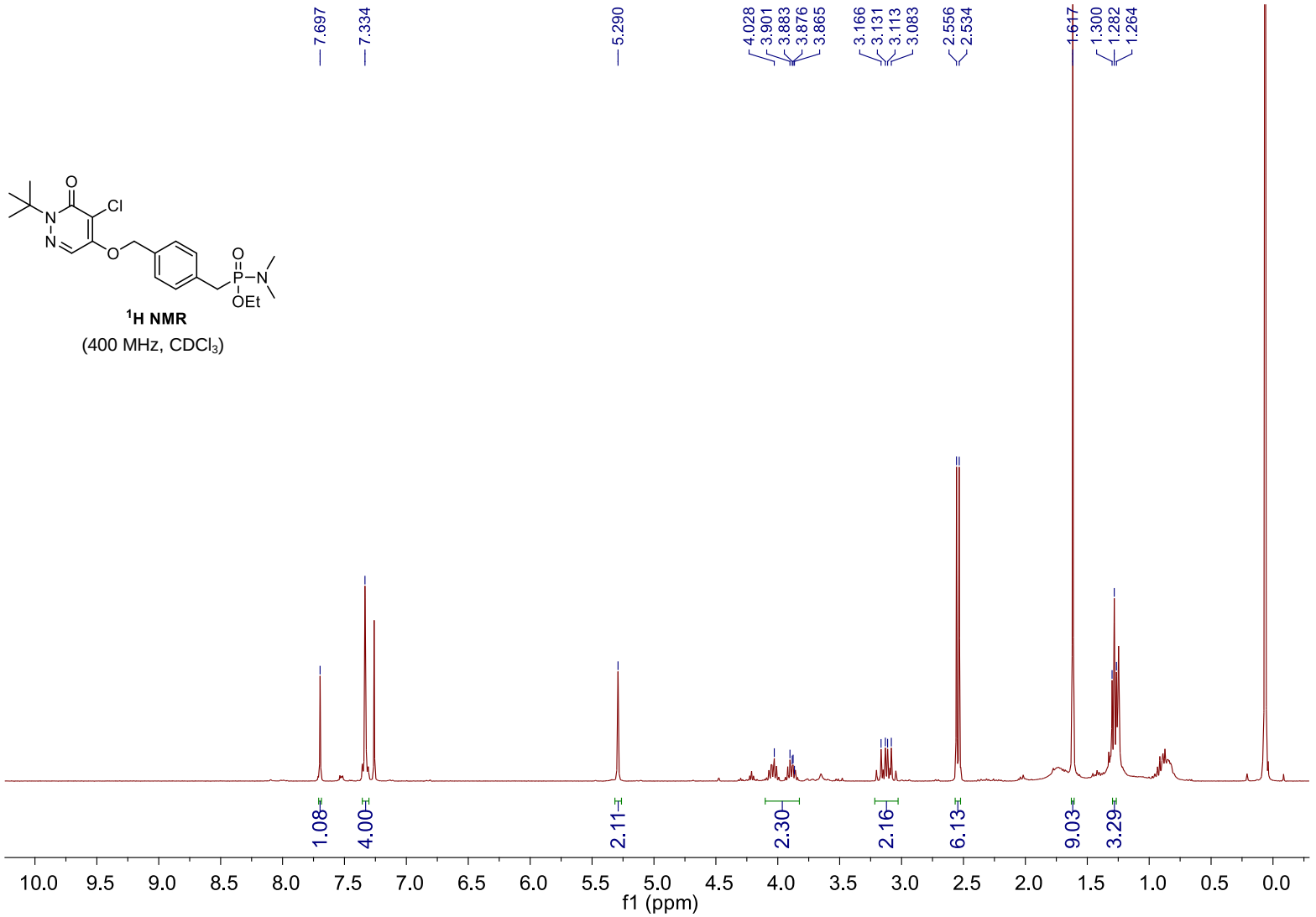
^{13}C NMR

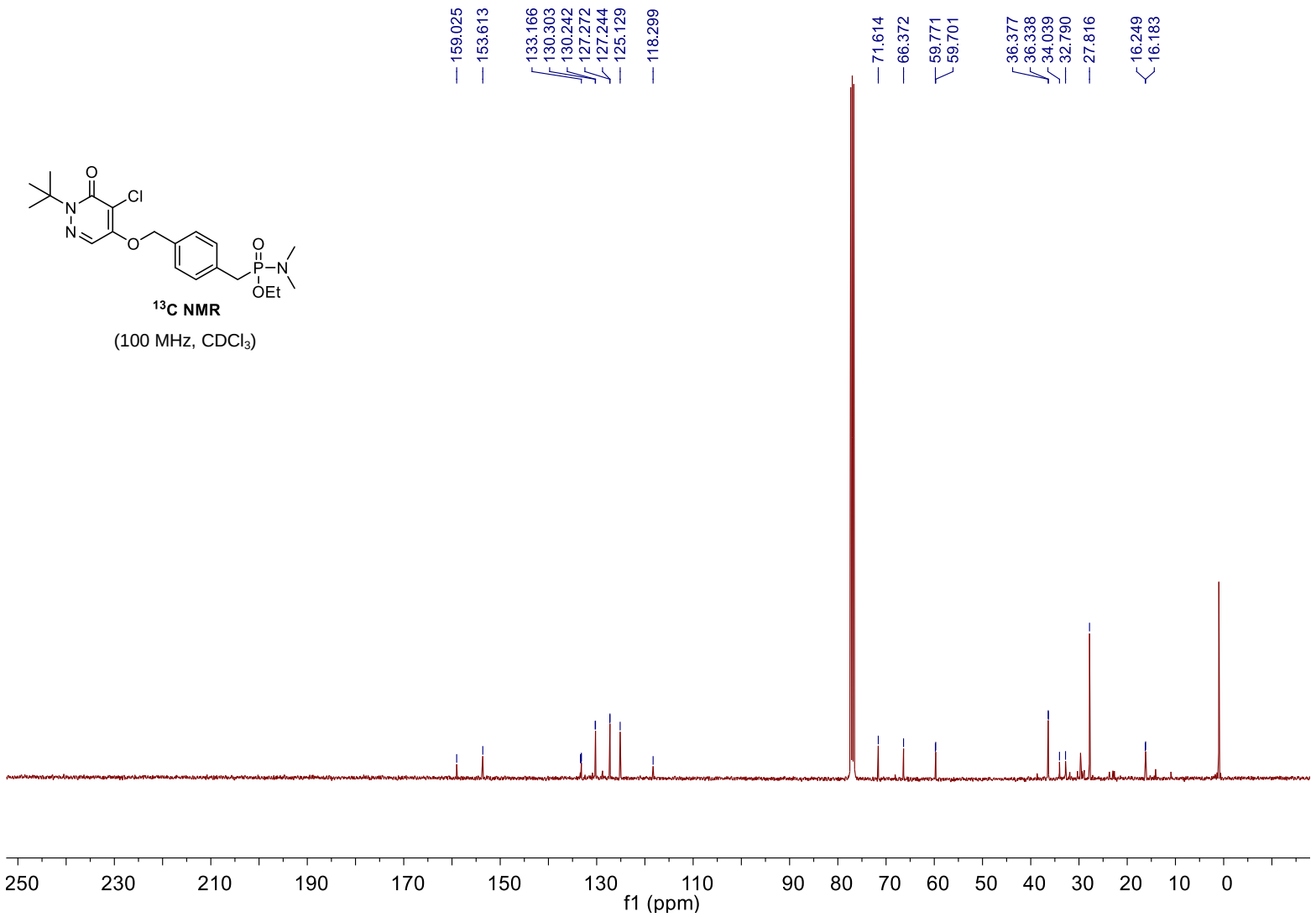
(100 MHz, $CDCl_3$)



^{31}P NMR

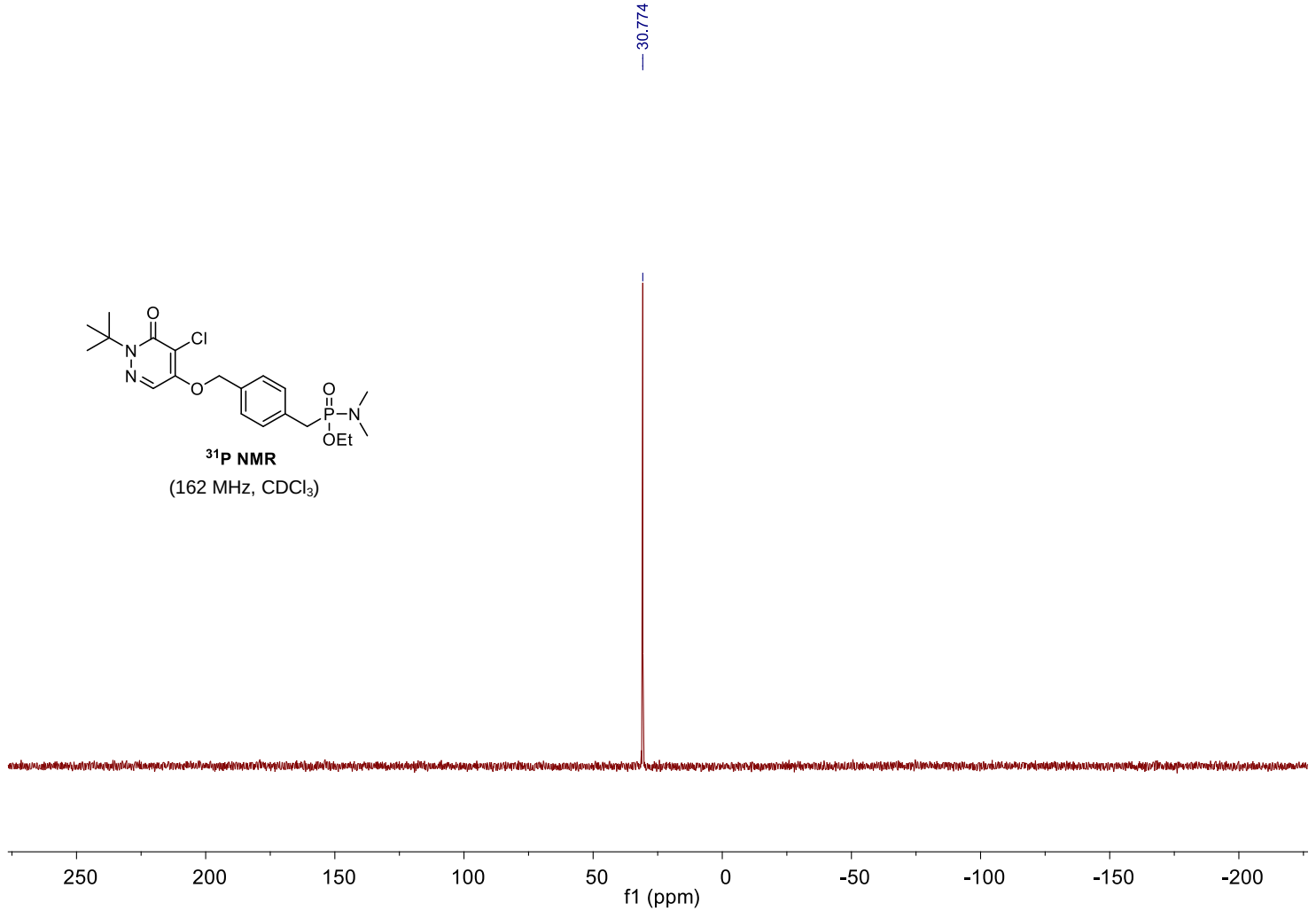
(162 MHz, $CDCl_3$)


7.697
7.334
5.290
4.028
3.901
3.883
3.876
3.865
3.166
3.131
3.113
3.083
2.556
2.534
1.617
1.300
1.282
1.264
Cl
O
N
N
O
O
P
N
OEt
1H NMR
(400 MHz, CDCl3)
1.08
4.00
2.11
2.30
2.16
6.13
9.03
3.29
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



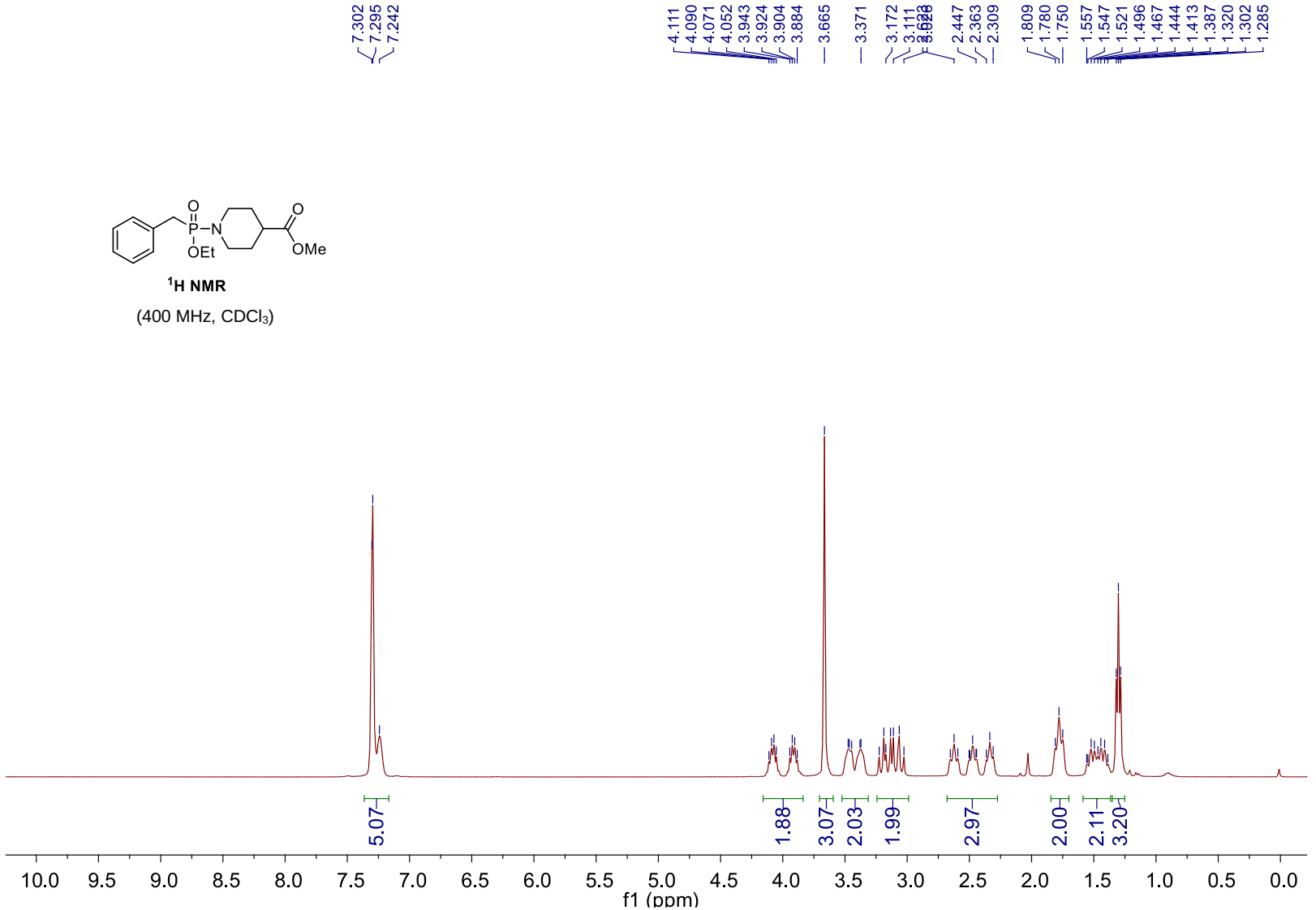
^{13}C NMR

(100 MHz, $CDCl_3$)



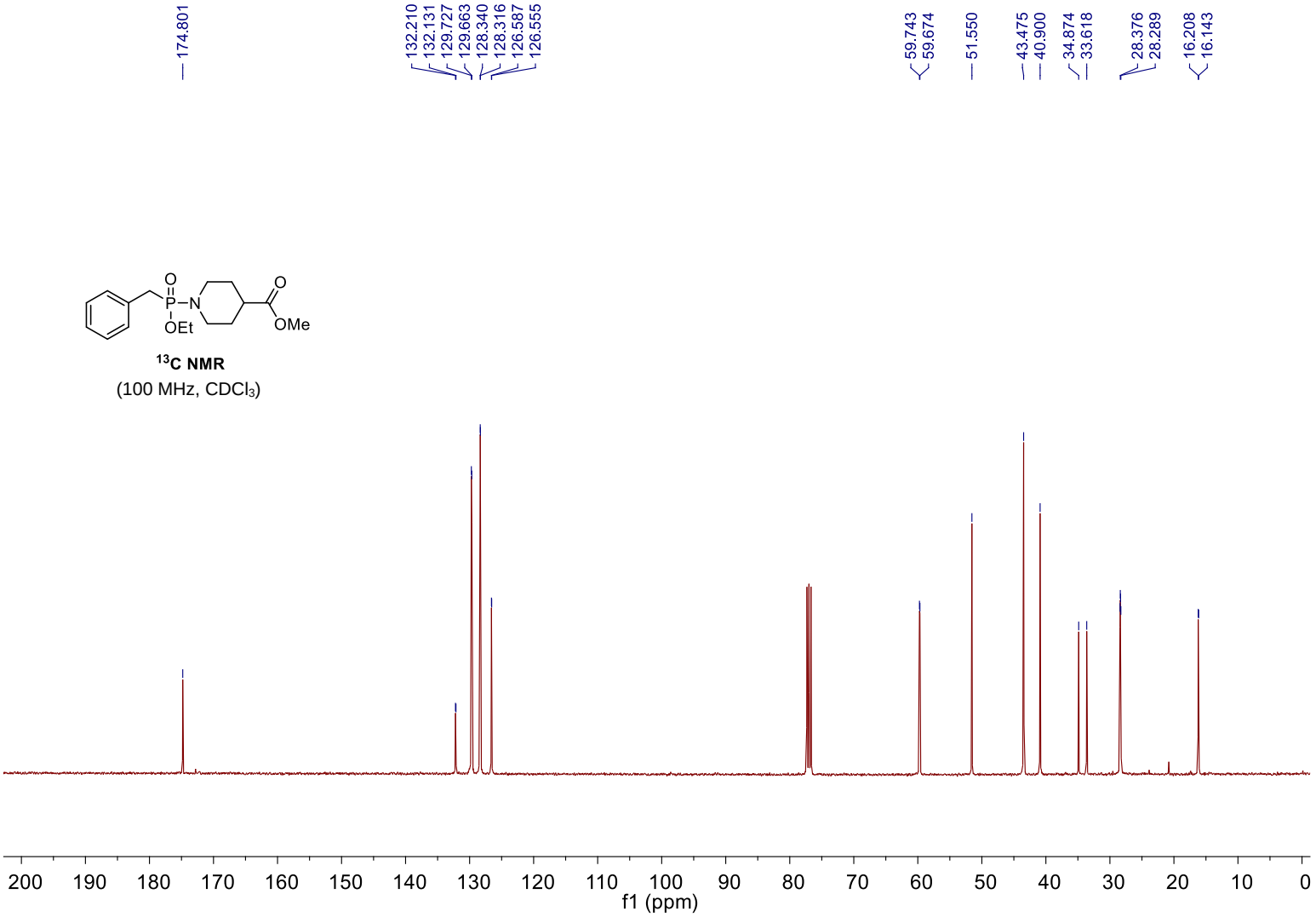
^{31}P NMR

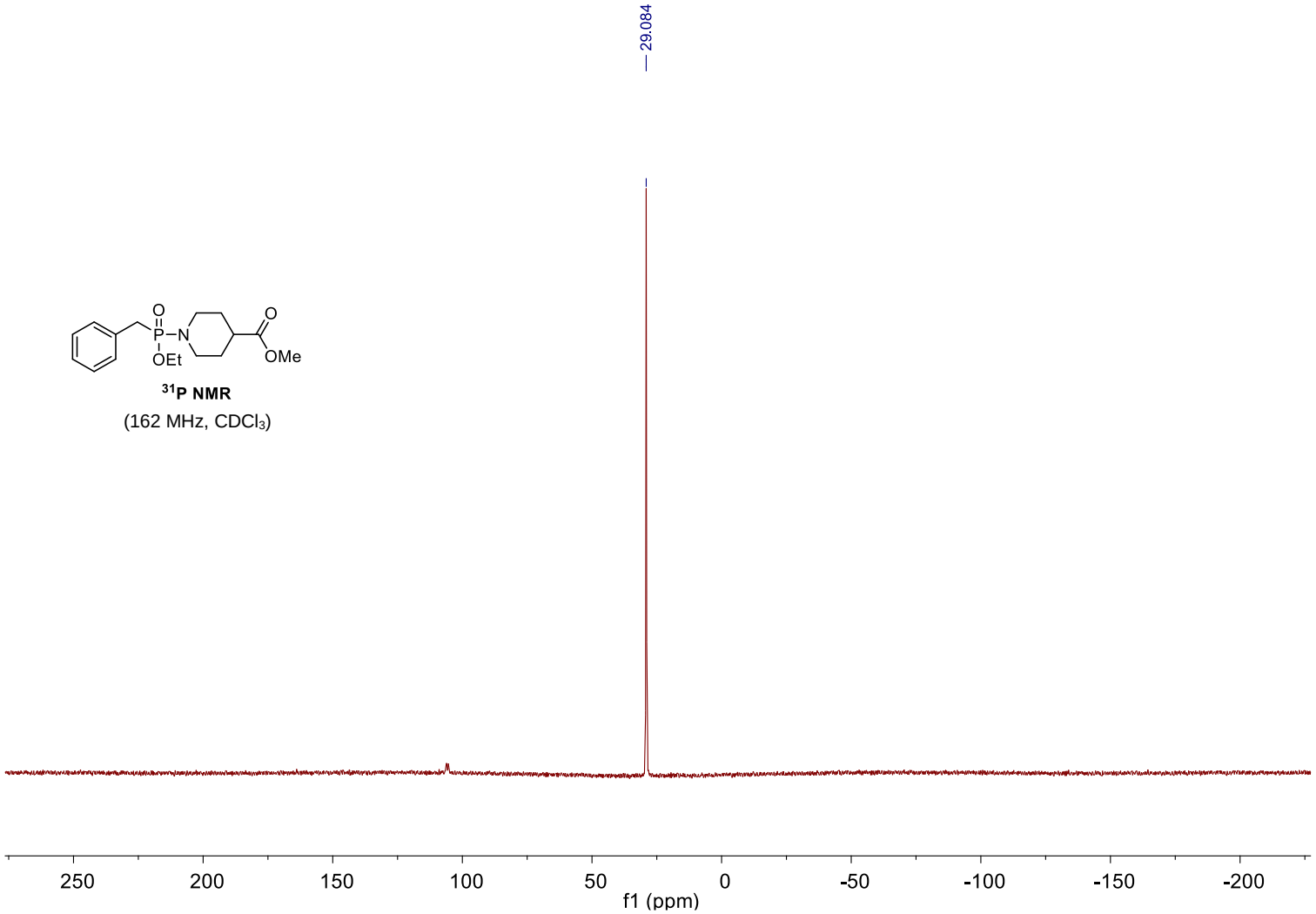
(162 MHz, $CDCl_3$)



^{1}H NMR

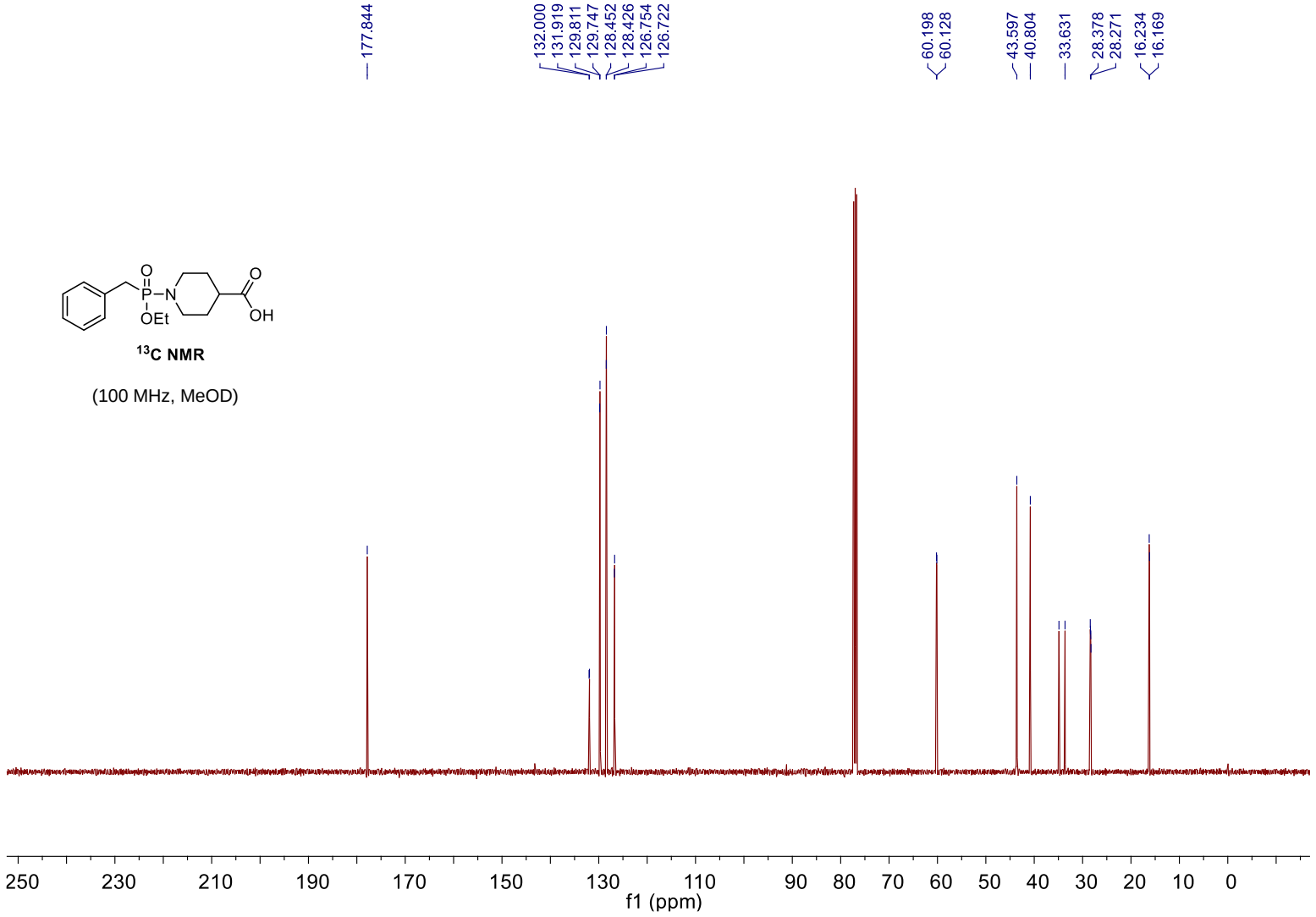
(400 MHz, $CDCl_3$)

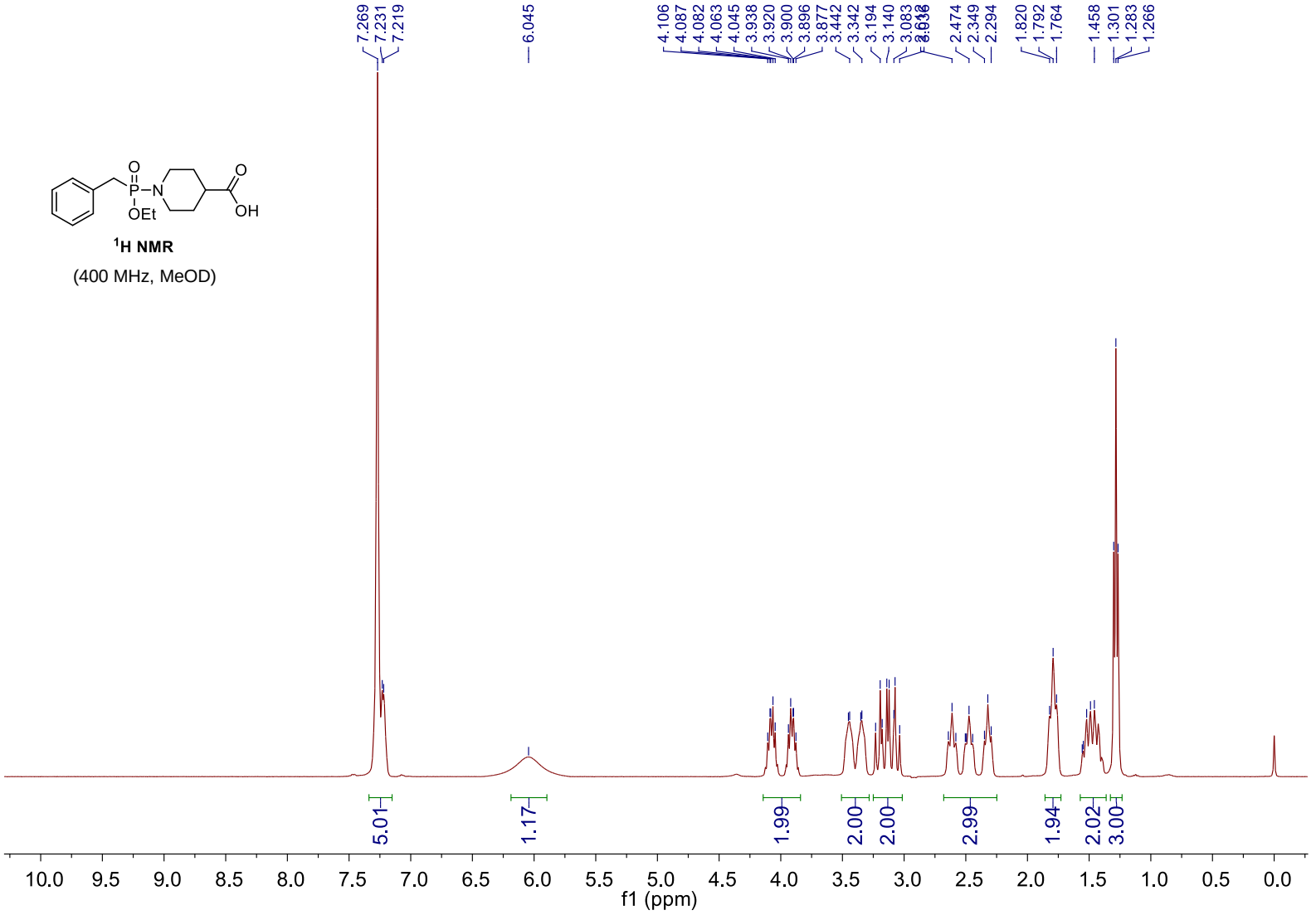

174.801
132.210
132.131
129.727
129.663
128.340
128.316
126.587
126.555
59.743
59.674
51.550
43.475
40.900
34.874
33.618
28.376
28.289
16.208
16.143
O
P
N
OEt
O
OMe
13C NMR
(100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



^{31}P NMR

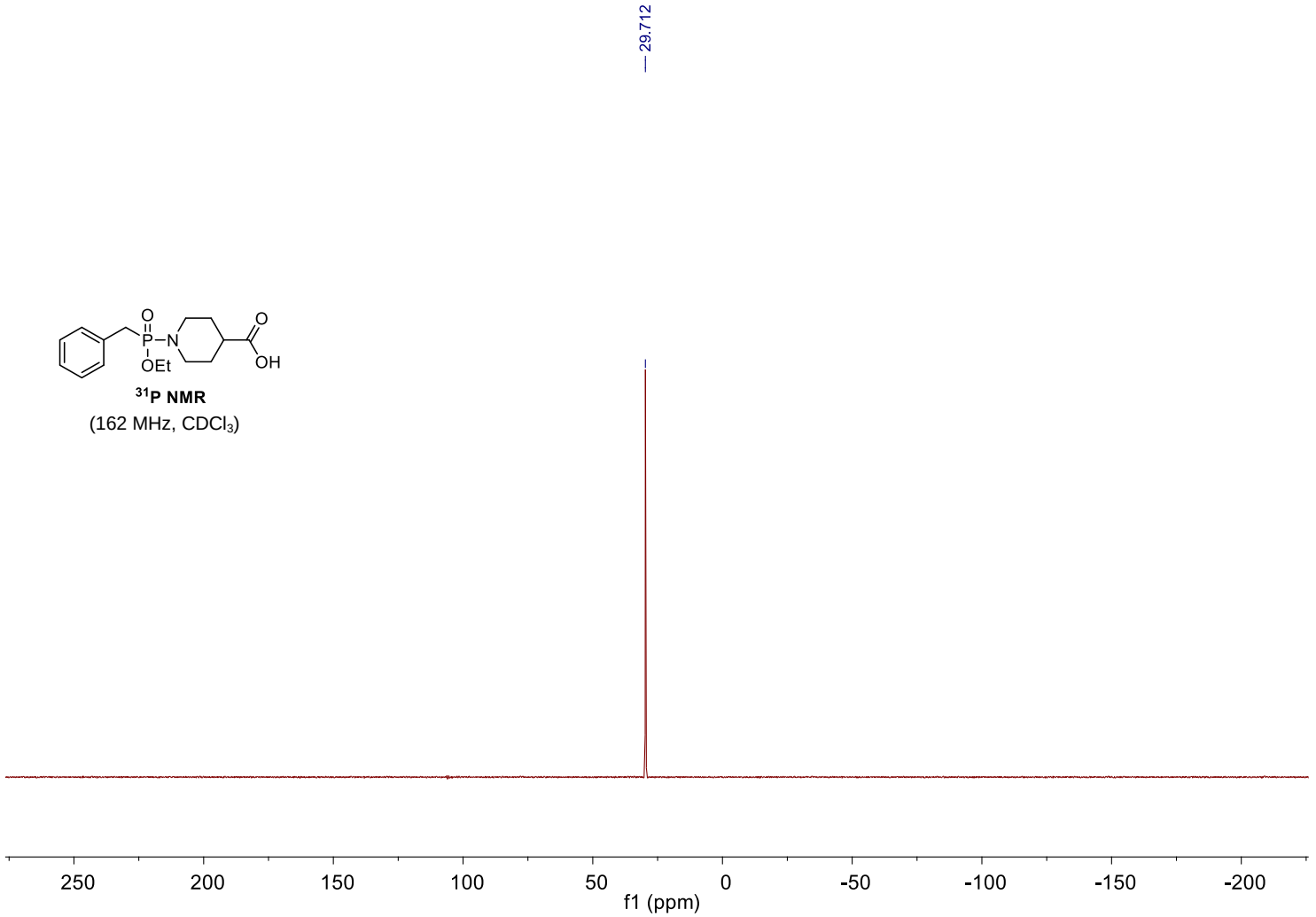
(162 MHz, $CDCl_3$)


177.844
132.000
131.919
129.811
129.747
128.452
128.426
126.754
126.722
60.198
60.128
43.597
40.804
33.631
28.378
28.271
16.234
16.169
O
P
N
OEt
O
OH
13C NMR
(100 MHz, MeOD)
250
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



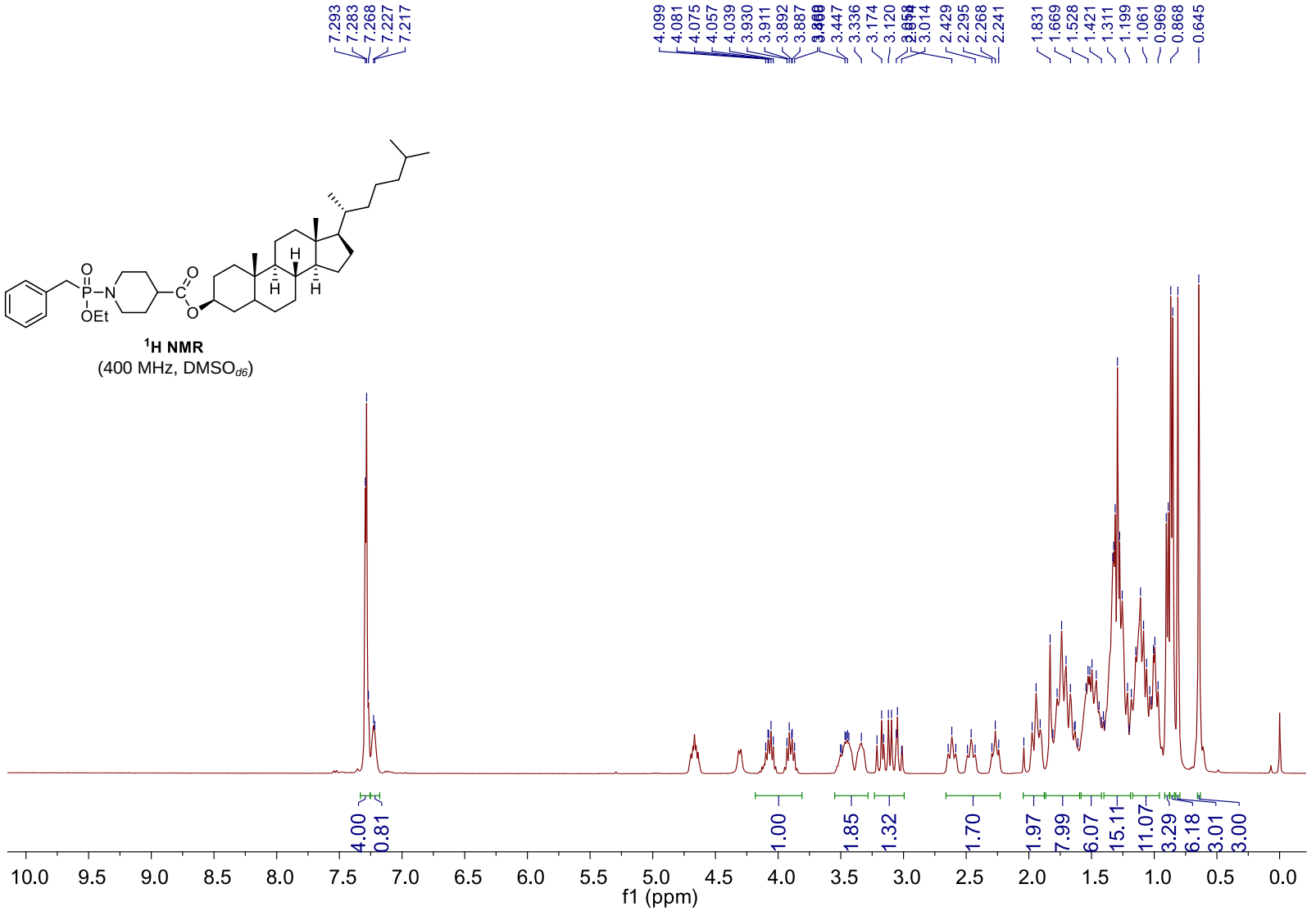
^{1}H NMR

(400 MHz, MeOD)

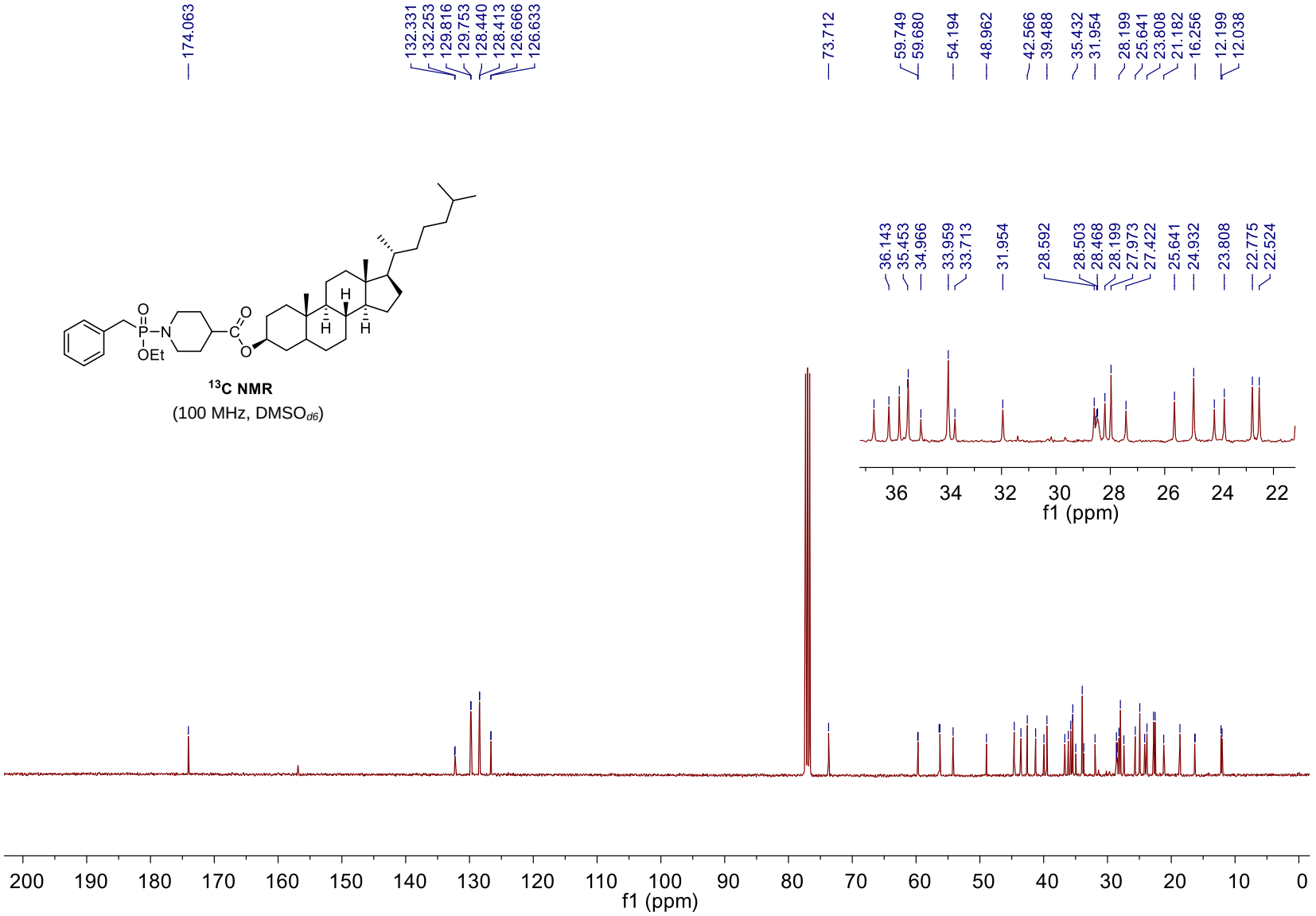


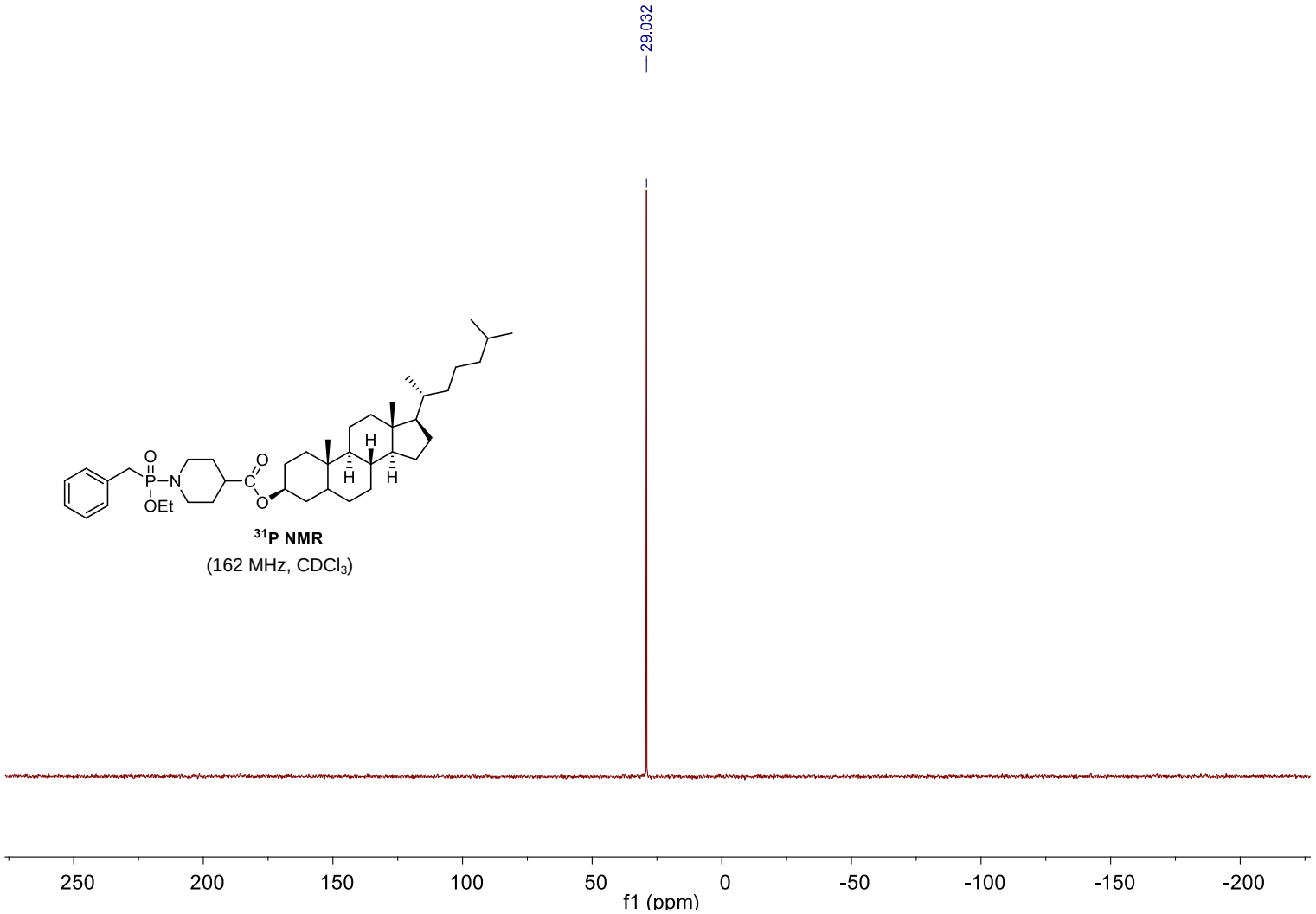
^{31}P NMR

(162 MHz, $CDCl_3$)



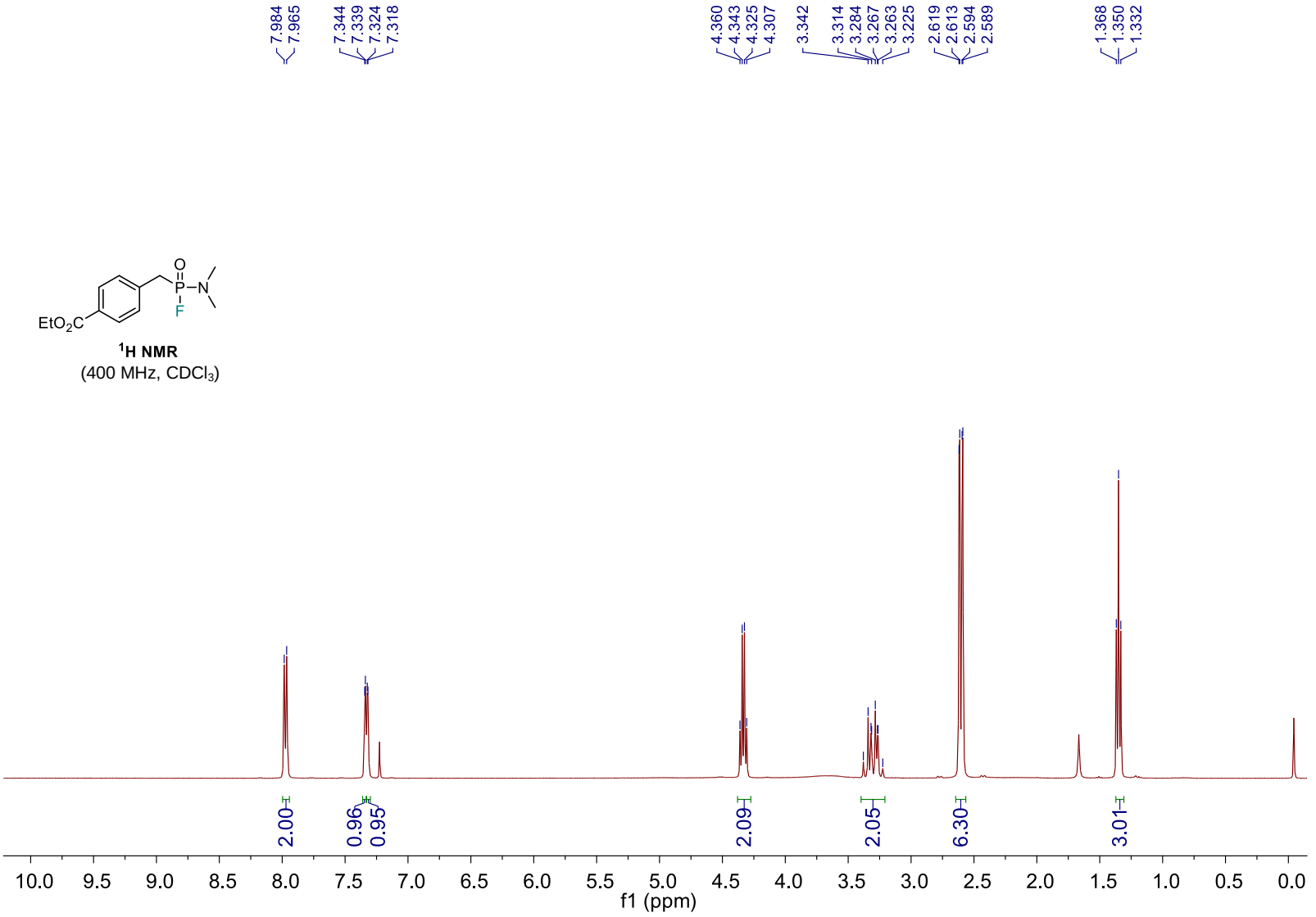
^{1}H NMR
(400 MHz, $DMSO_{d6}$)


174.063
132.331
132.253
129.816
129.753
128.440
128.413
126.666
126.633
73.712
59.749
59.680
54.194
48.962
42.566
39.488
35.432
31.954
28.199
25.641
23.808
21.182
16.256
12.199
12.038
36.143
35.453
34.966
33.959
33.713
31.954
28.592
28.503
28.468
28.199
27.973
27.422
25.641
24.932
23.808
22.775
22.524
O
P
N
OEt
O
C
O
H
H
H
13C NMR
(100 MHz, DMSOd6)
36 34 32 30 28 26 24 22
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

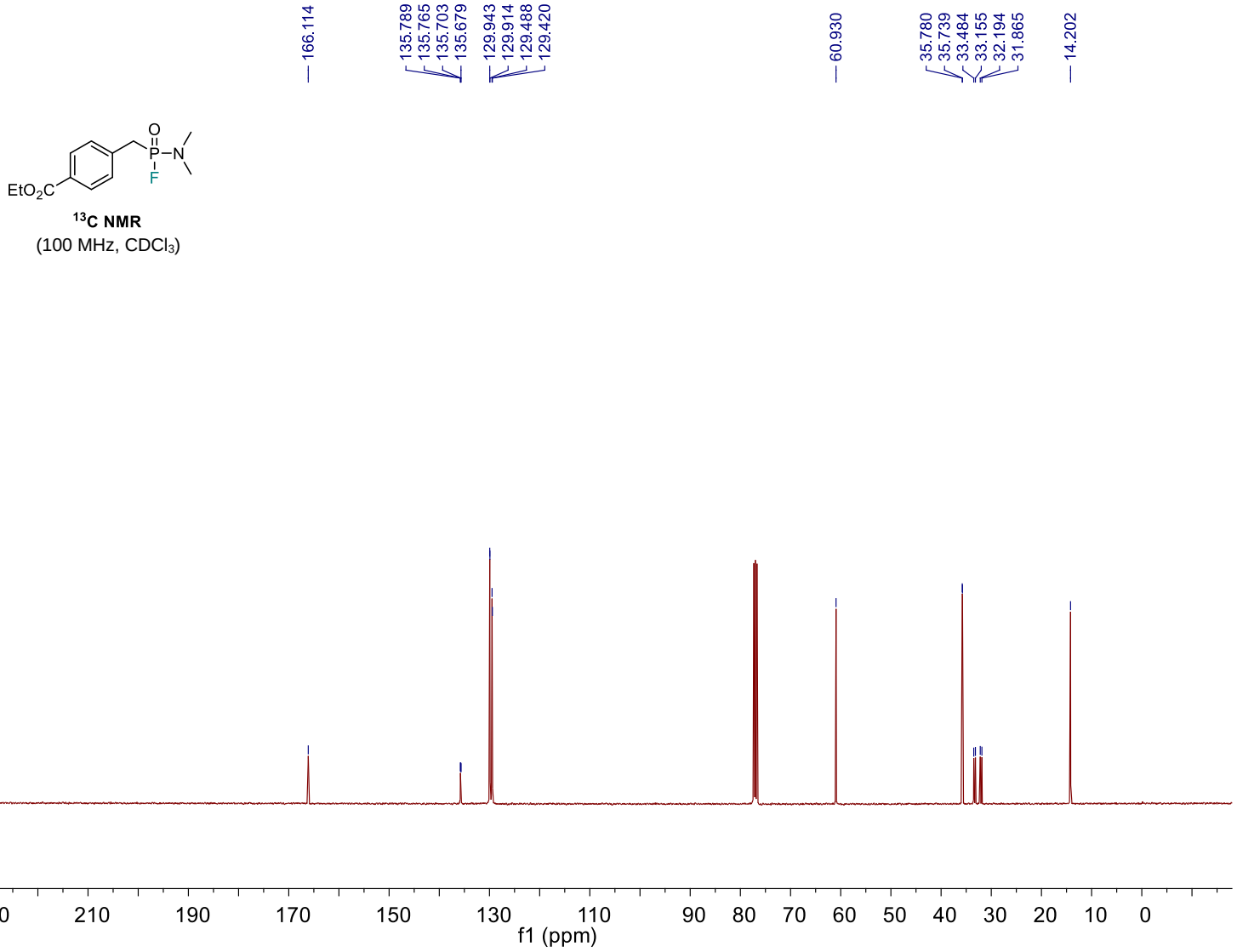


^{31}P NMR

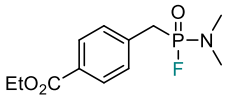
(162 MHz, $CDCl_3$)



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

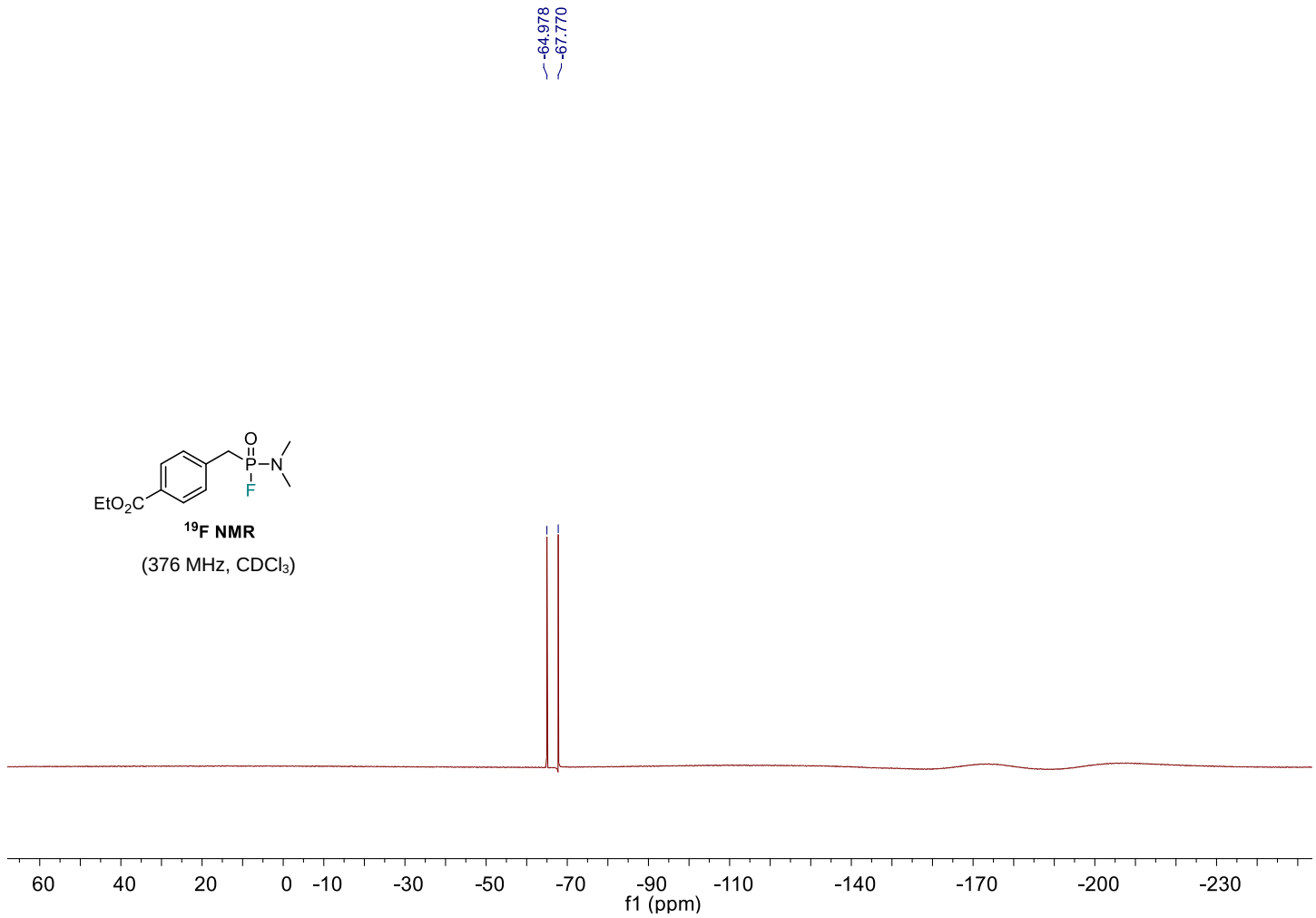


^{13}C NMR
(100 MHz, $CDCl_3$)



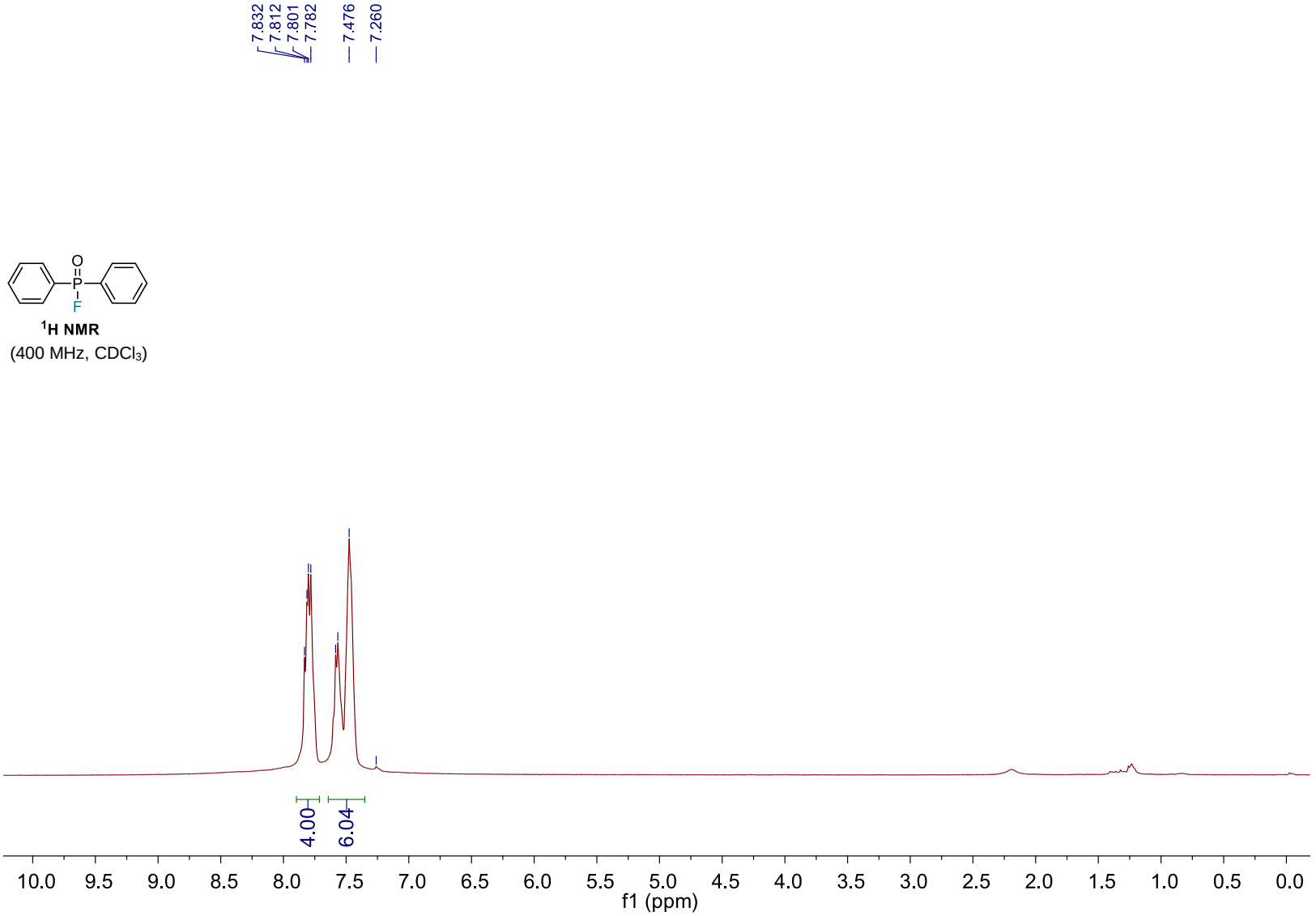
^{31}P NMR

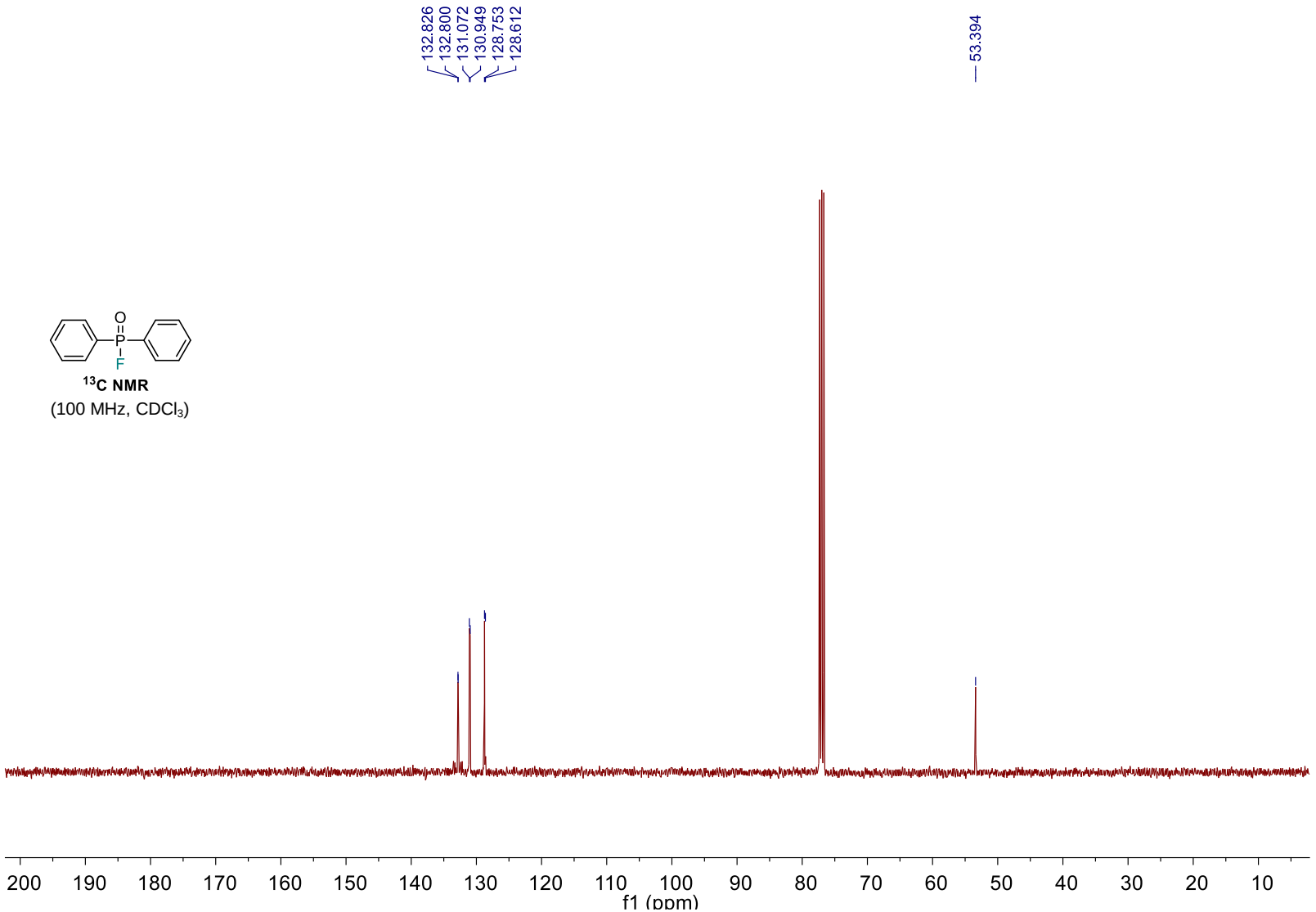
(162 MHz, $CDCl_3$)



^{19}F NMR

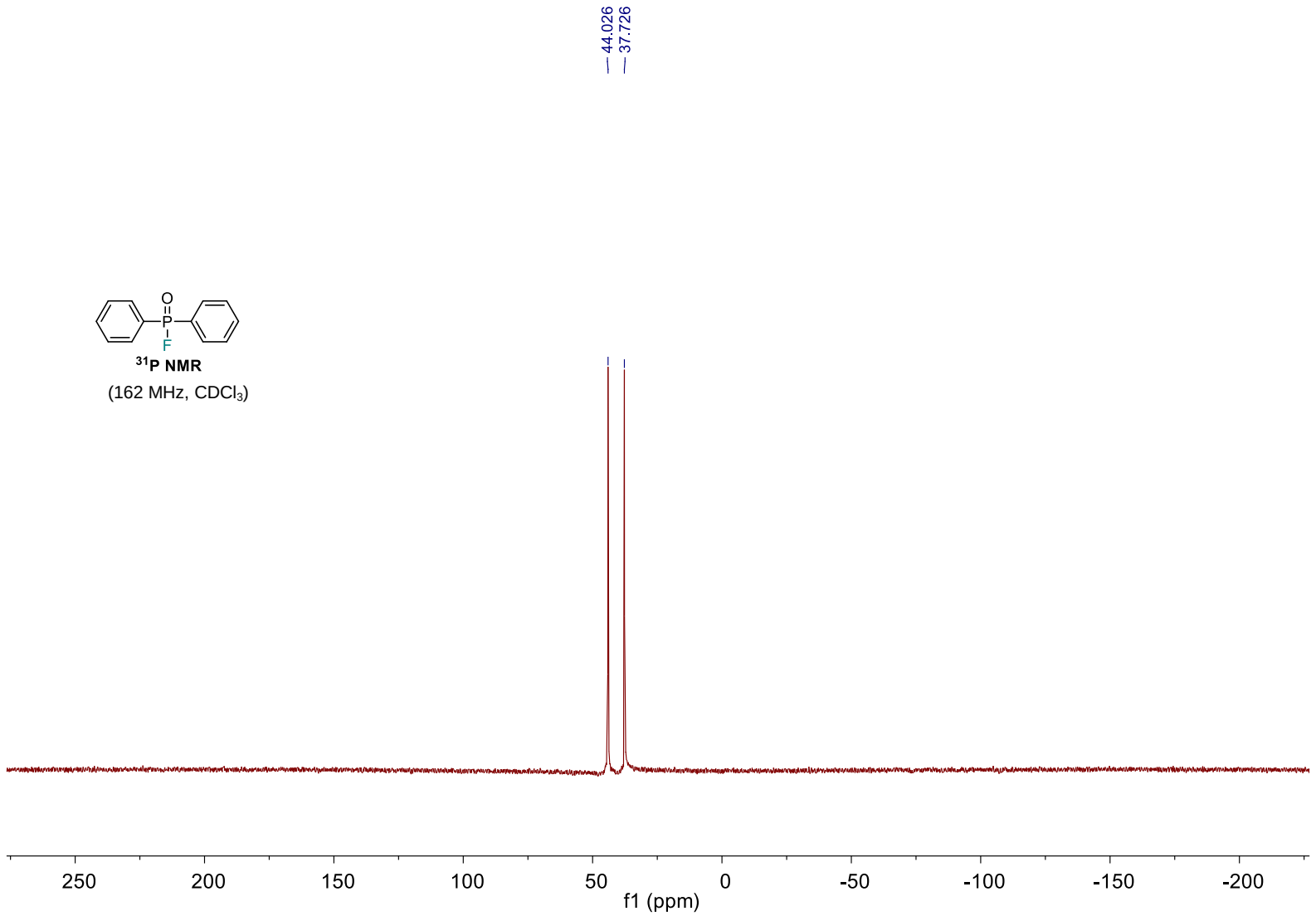
(376 MHz, $CDCl_3$)

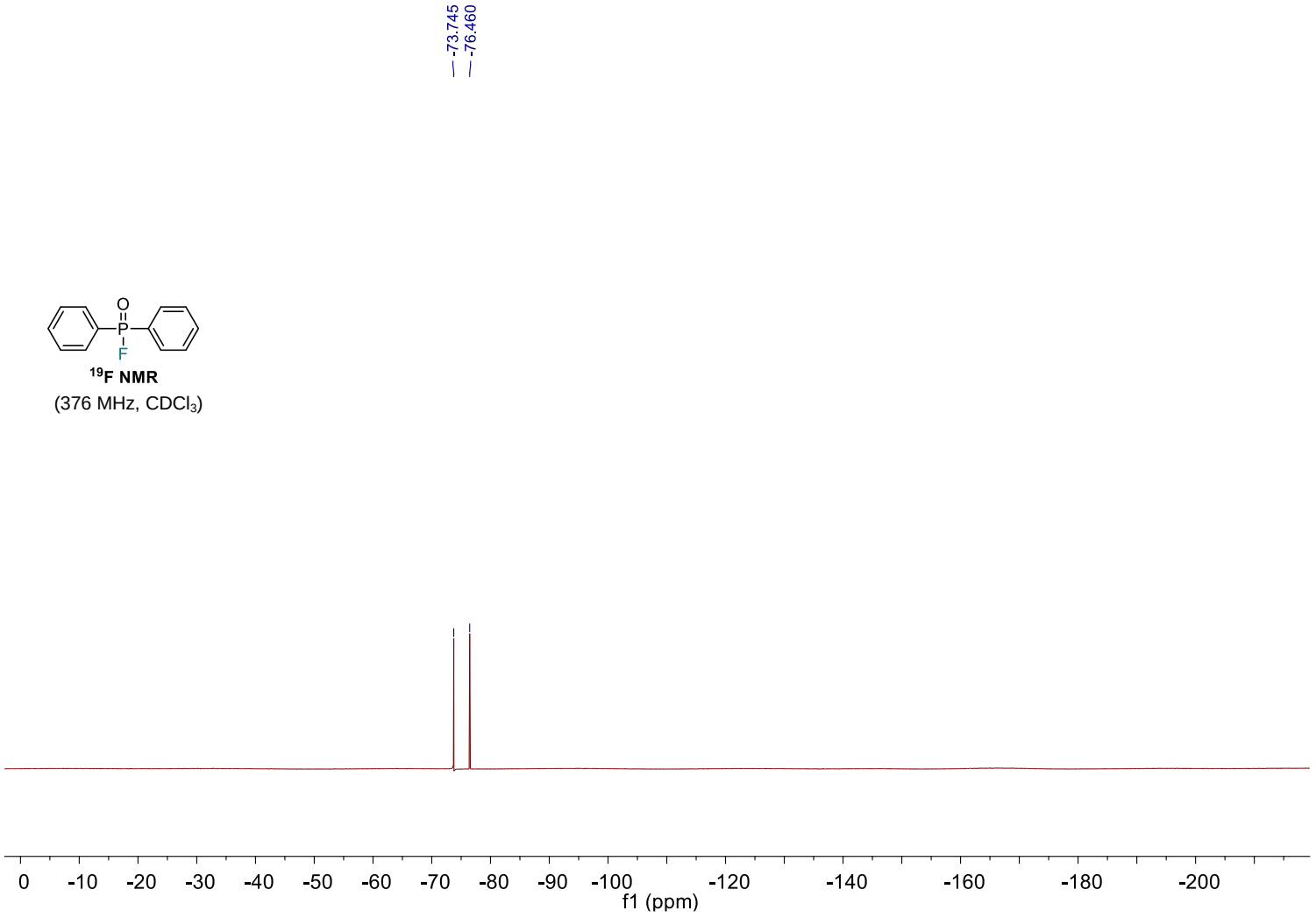

7.832
7.812
7.801
7.782
7.476
7.260
O
P
F
1H NMR
(400 MHz, CDCl3)
4.00
6.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



^{13}C NMR

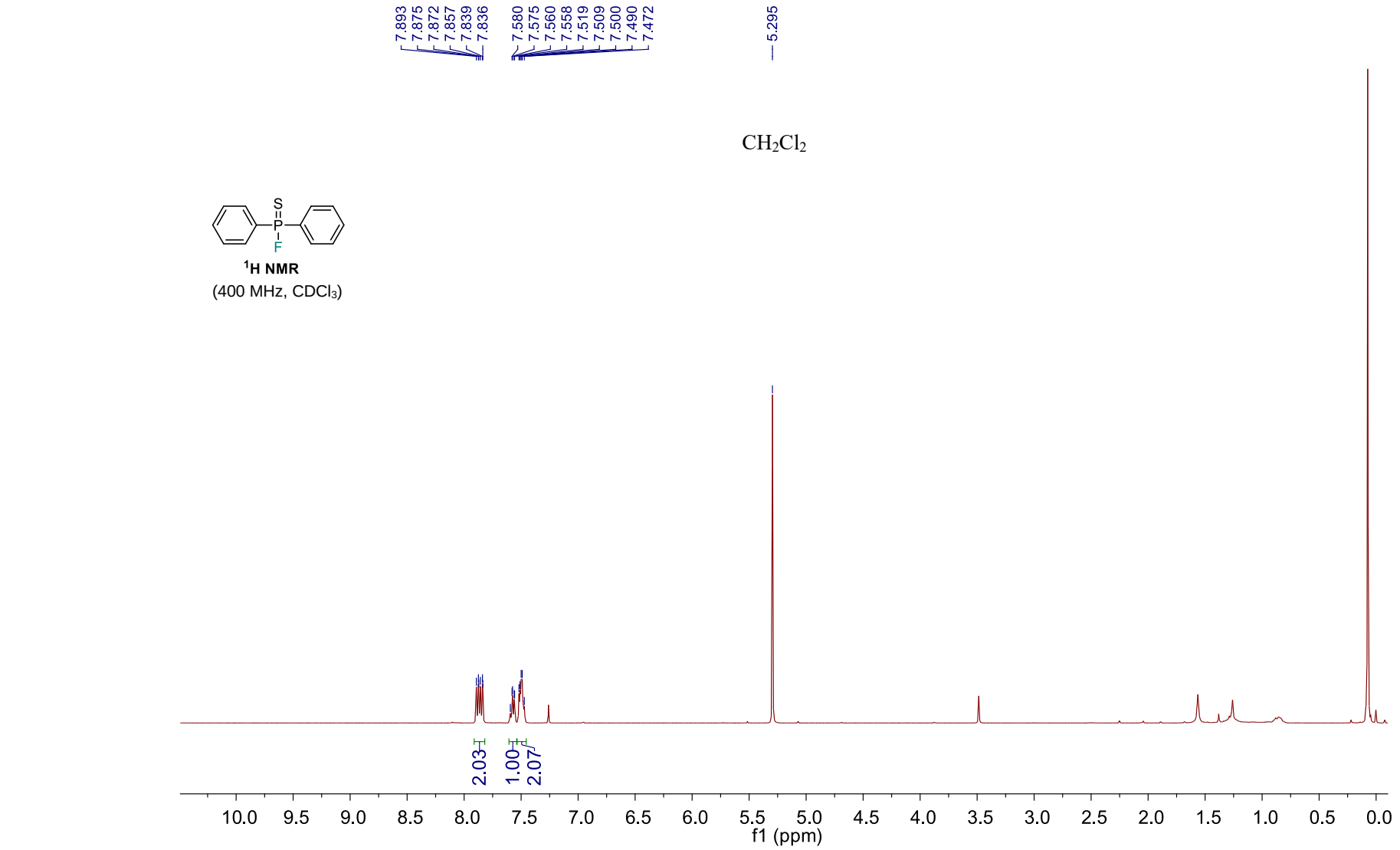
(100 MHz, $CDCl_3$)

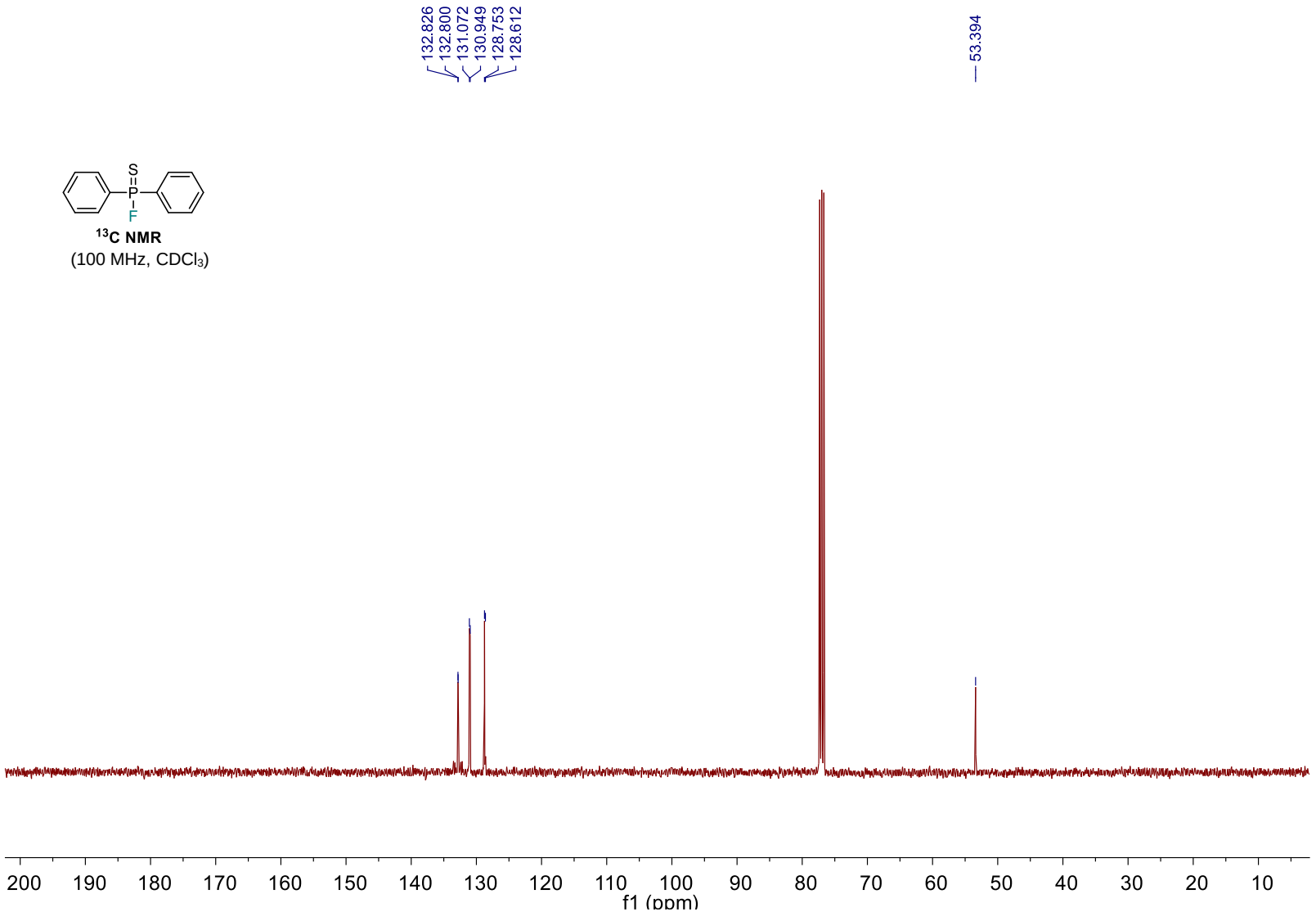

44.026
37.726
O
P
F
31P NMR
(162 MHz, CDCl3)
250
200
150
100
50
0
-50
-100
-150
-200
f1 (ppm)

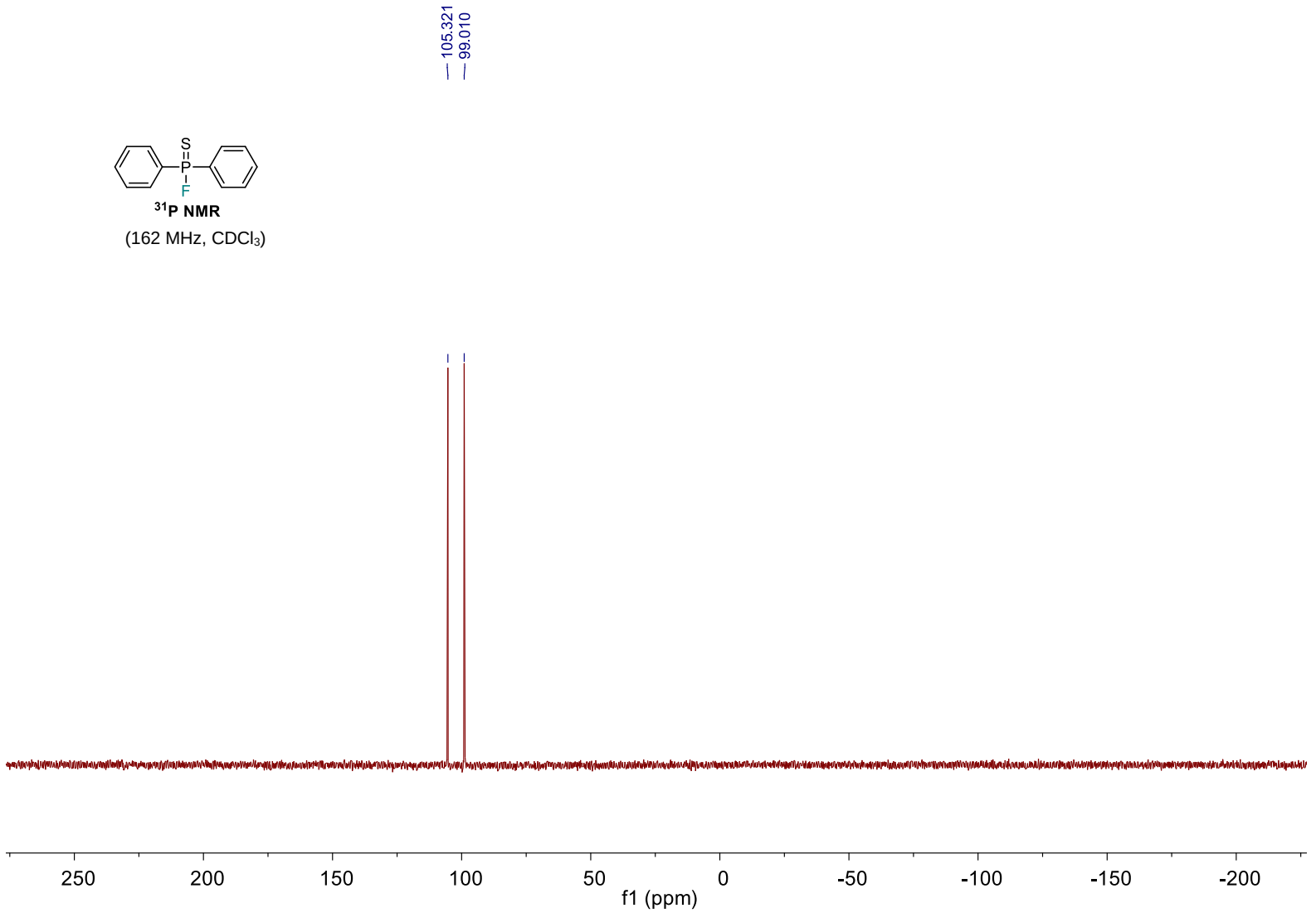


^{19}F NMR

(376 MHz, $CDCl_3$)

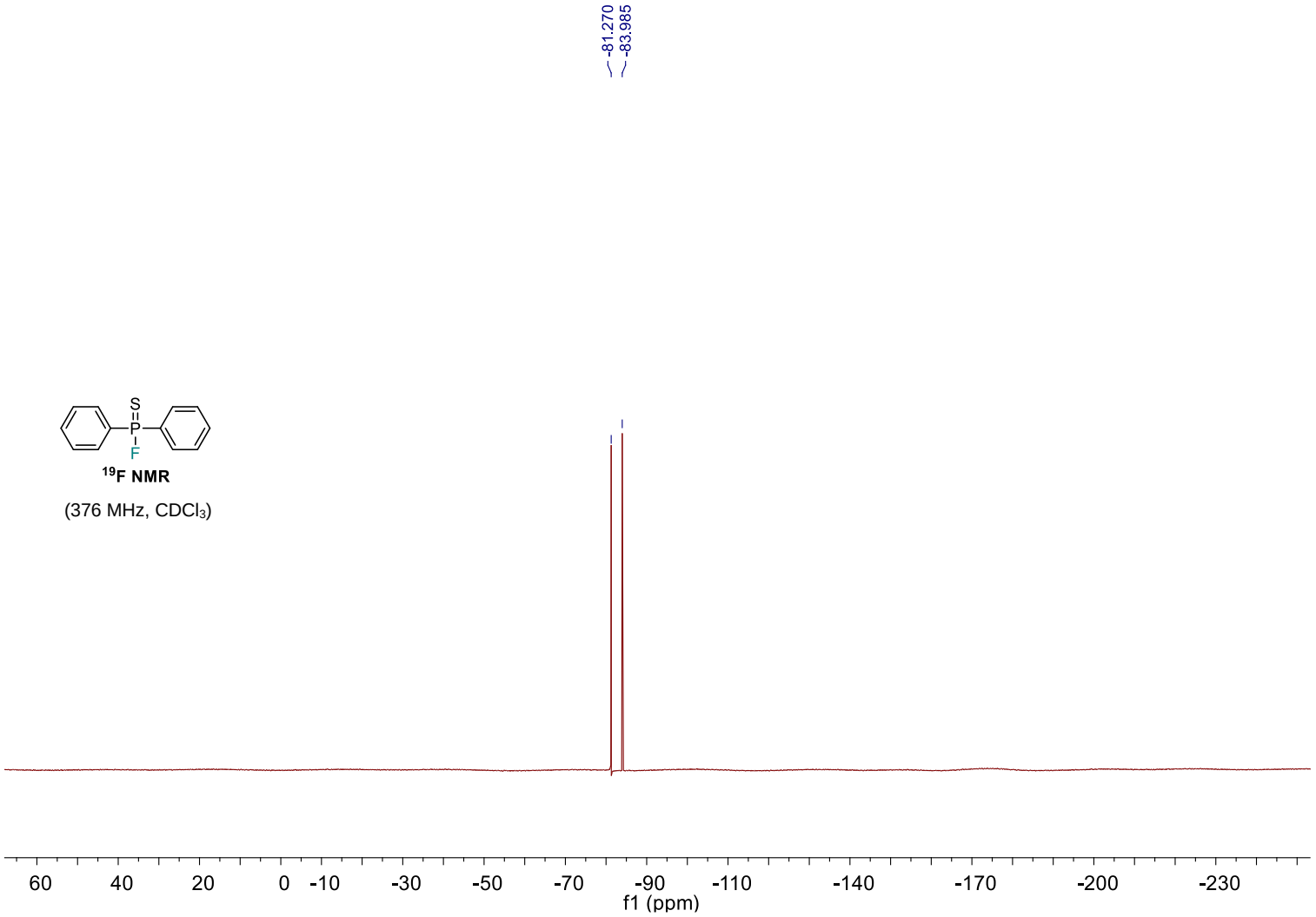

7.893
7.875
7.872
7.857
7.839
7.836
7.580
7.575
7.560
7.558
7.519
7.509
7.500
7.490
7.472
5.295
CH2Cl2
S
P
F
1H NMR
(400 MHz, CDCl3)
2.03
1.00
2.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


132.826
132.800
131.072
130.949
128.753
128.612
53.394
S
P
F
13C NMR
(100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



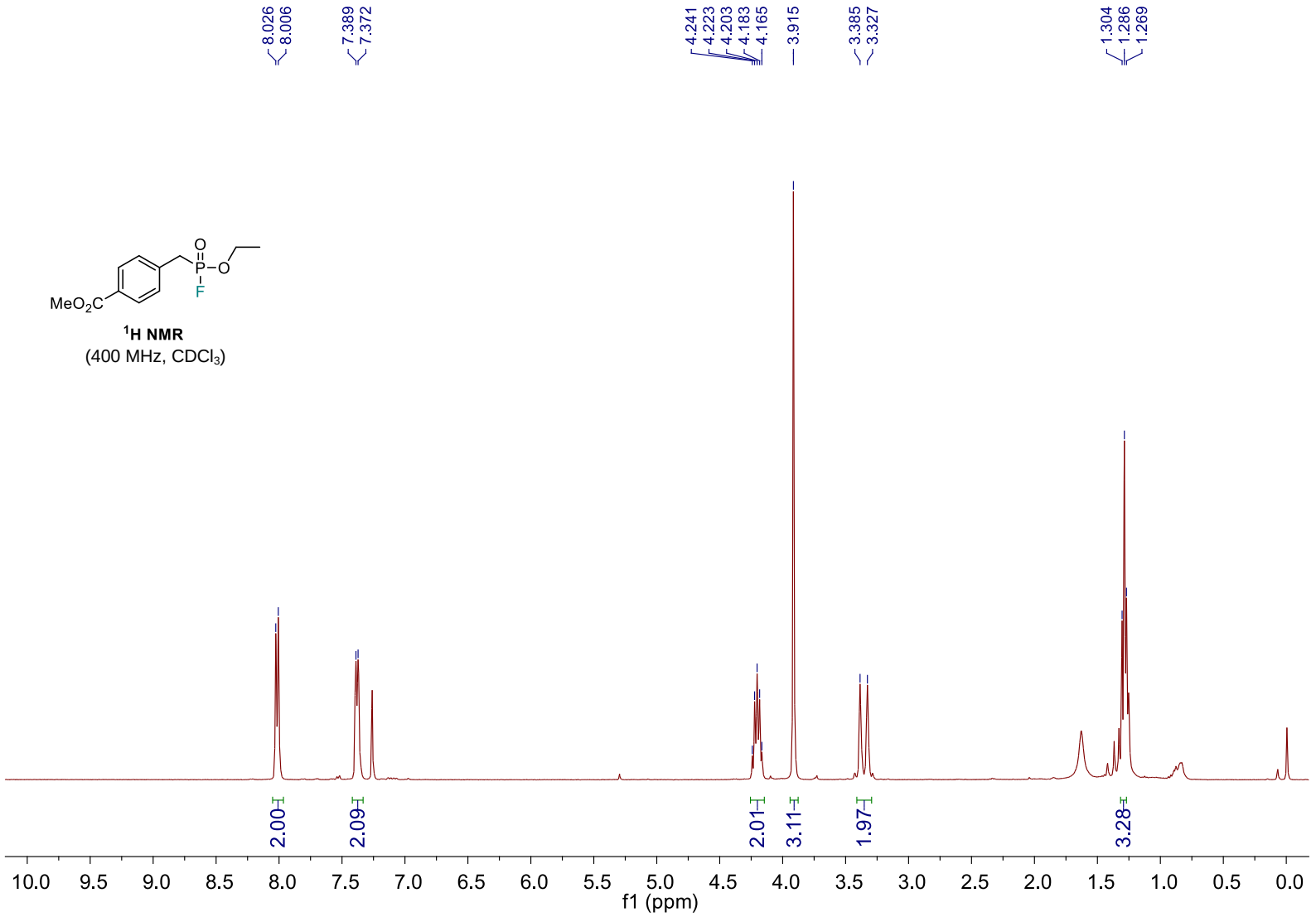
^{31}P NMR

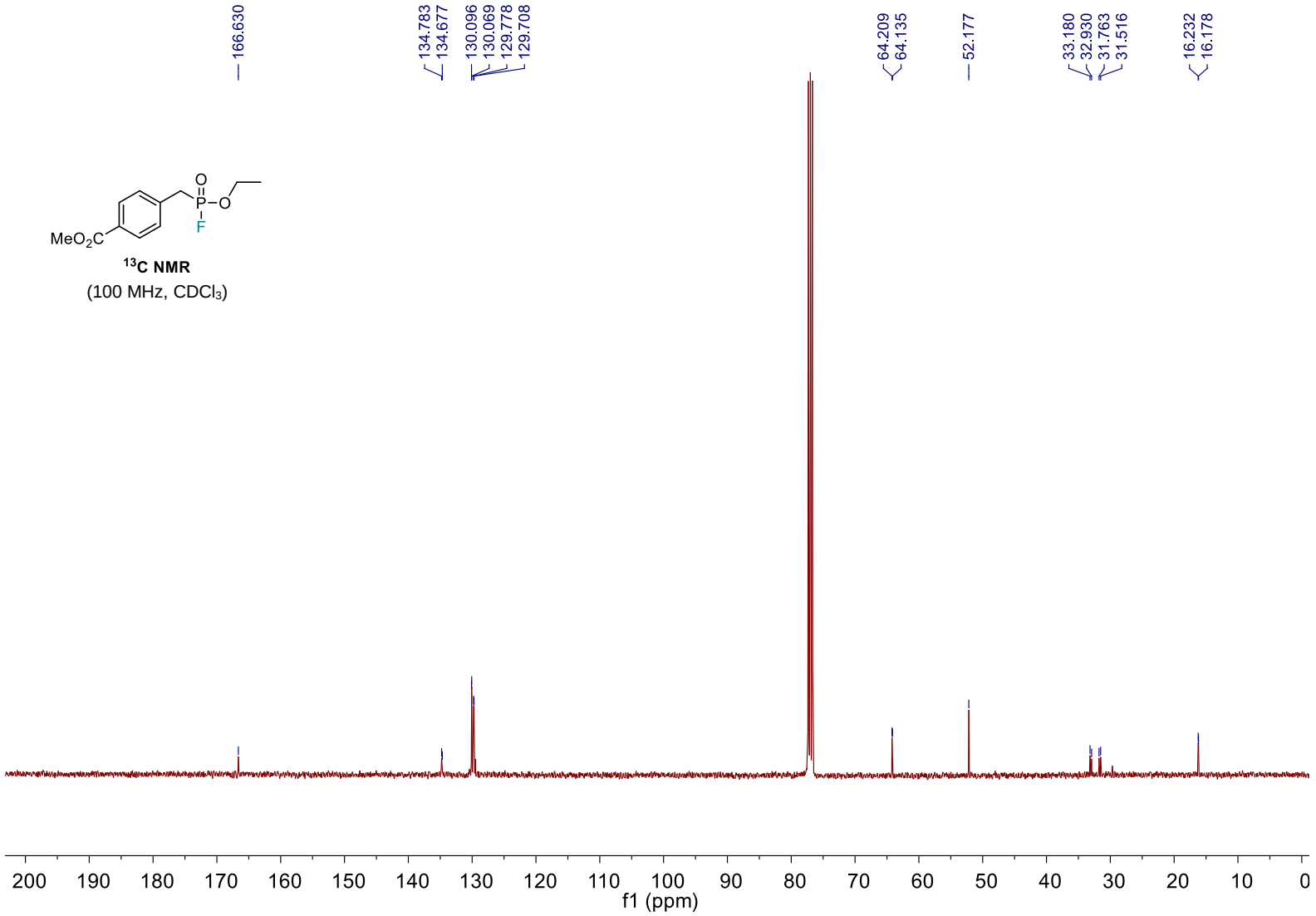
(162 MHz, $CDCl_3$)

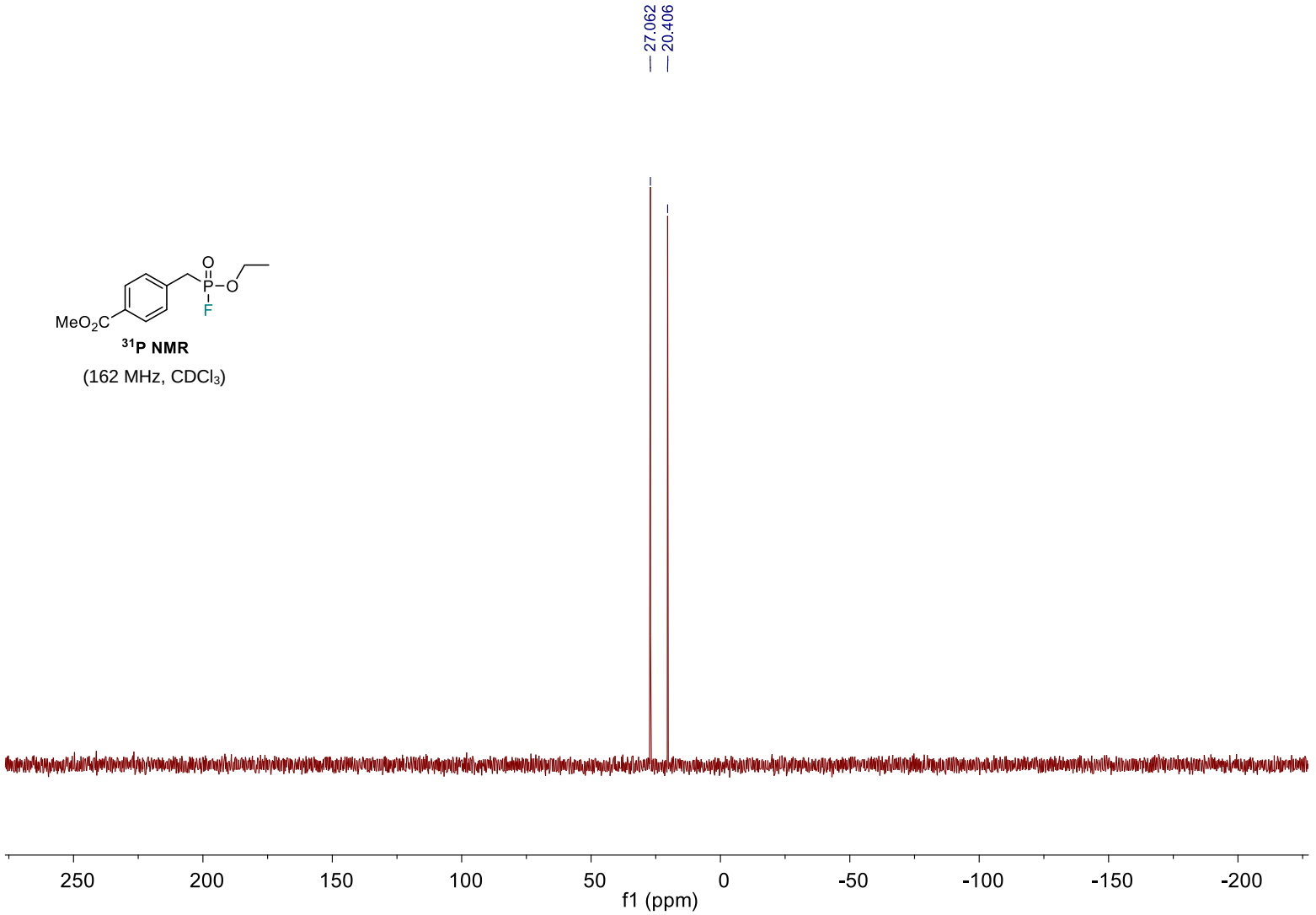


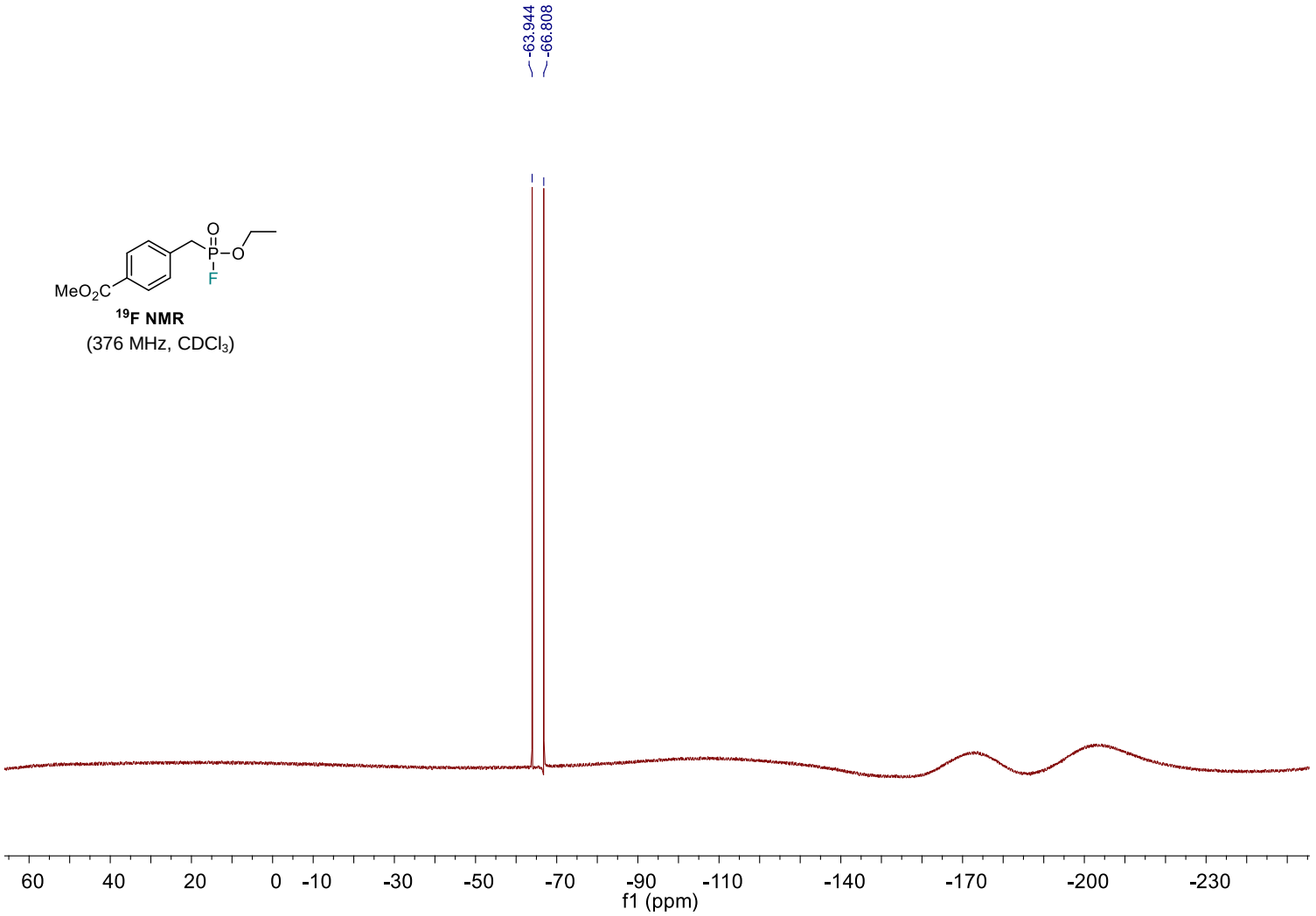
^{19}F NMR

(376 MHz, $CDCl_3$)


8.026
8.006
7.389
7.372
4.241
4.223
4.203
4.183
4.165
3.915
3.385
3.327
1.304
1.286
1.269
MeO2C
O
P
O
F
1H NMR
(400 MHz, CDCl3)
2.00
2.09
2.01
3.11
1.97
3.28
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

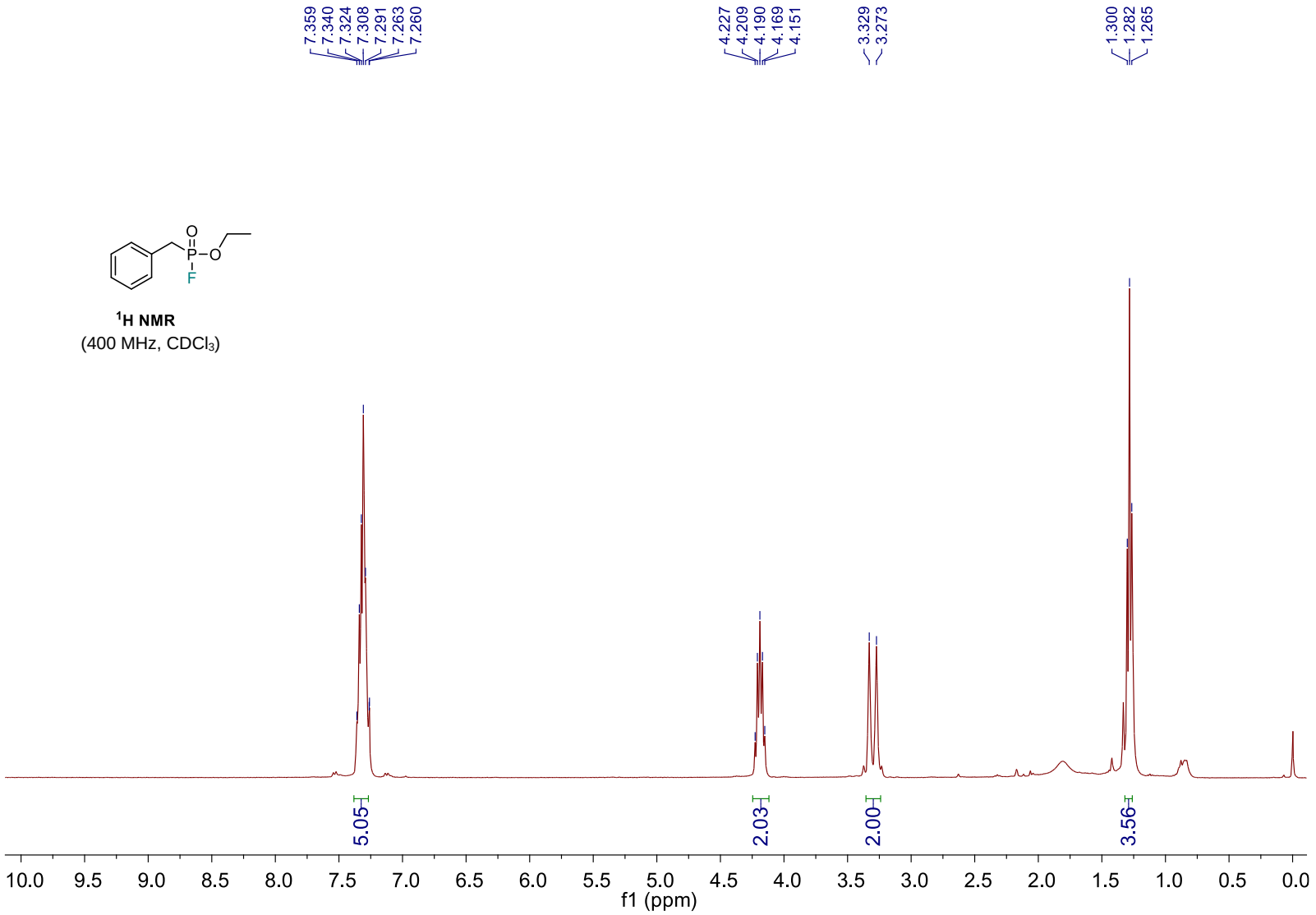

166.630
134.783
134.677
130.096
130.069
129.778
129.708
64.209
64.135
52.177
33.180
32.930
31.763
31.516
16.232
16.178
MeO2C
O
P
O
F
13C NMR
(100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

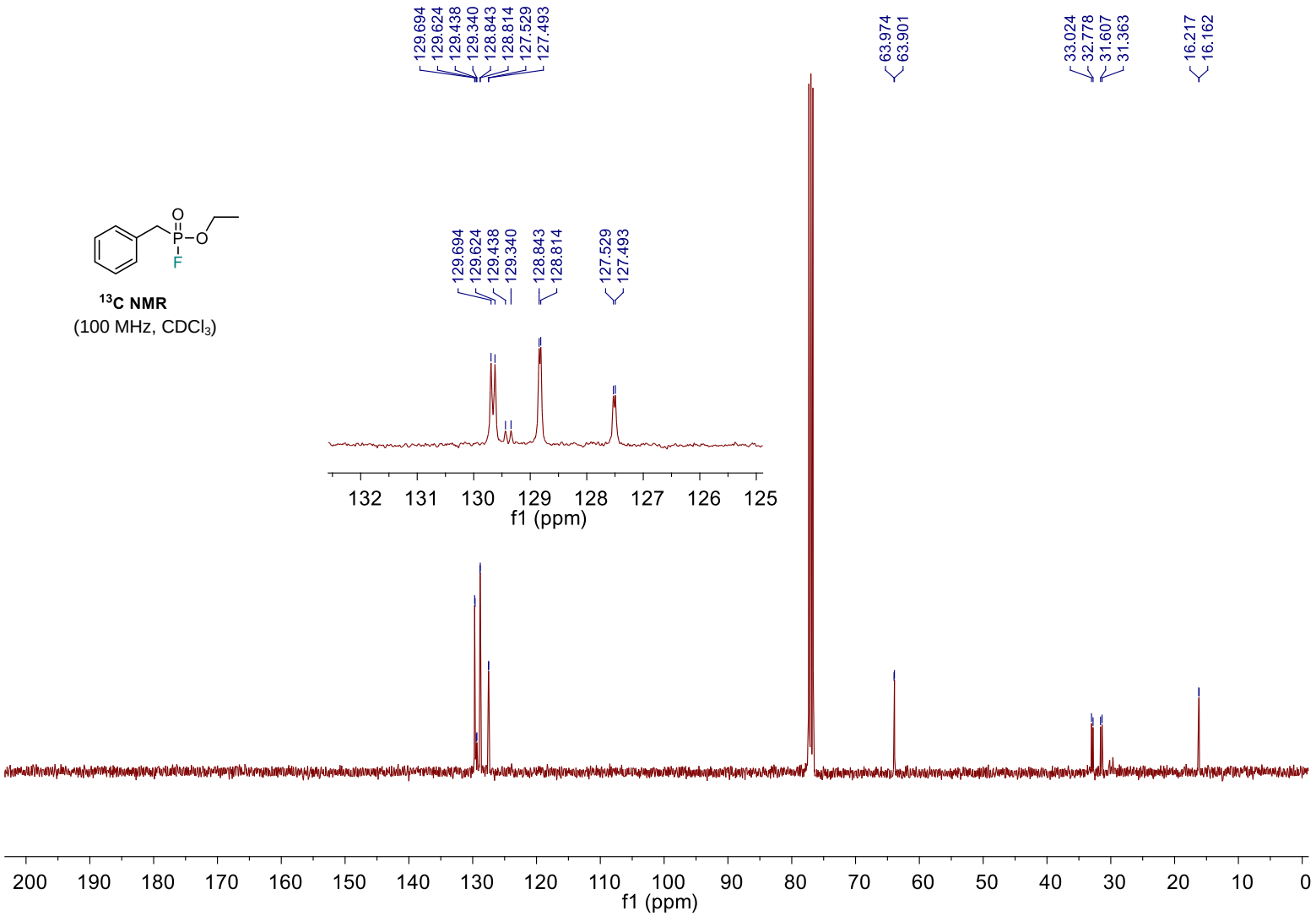

27.062
20.406
MeO2C
O
P
O
F
31P NMR
(162 MHz, CDCl3)
250
200
150
100
50
0
-50
-100
-150
-200
f1 (ppm)

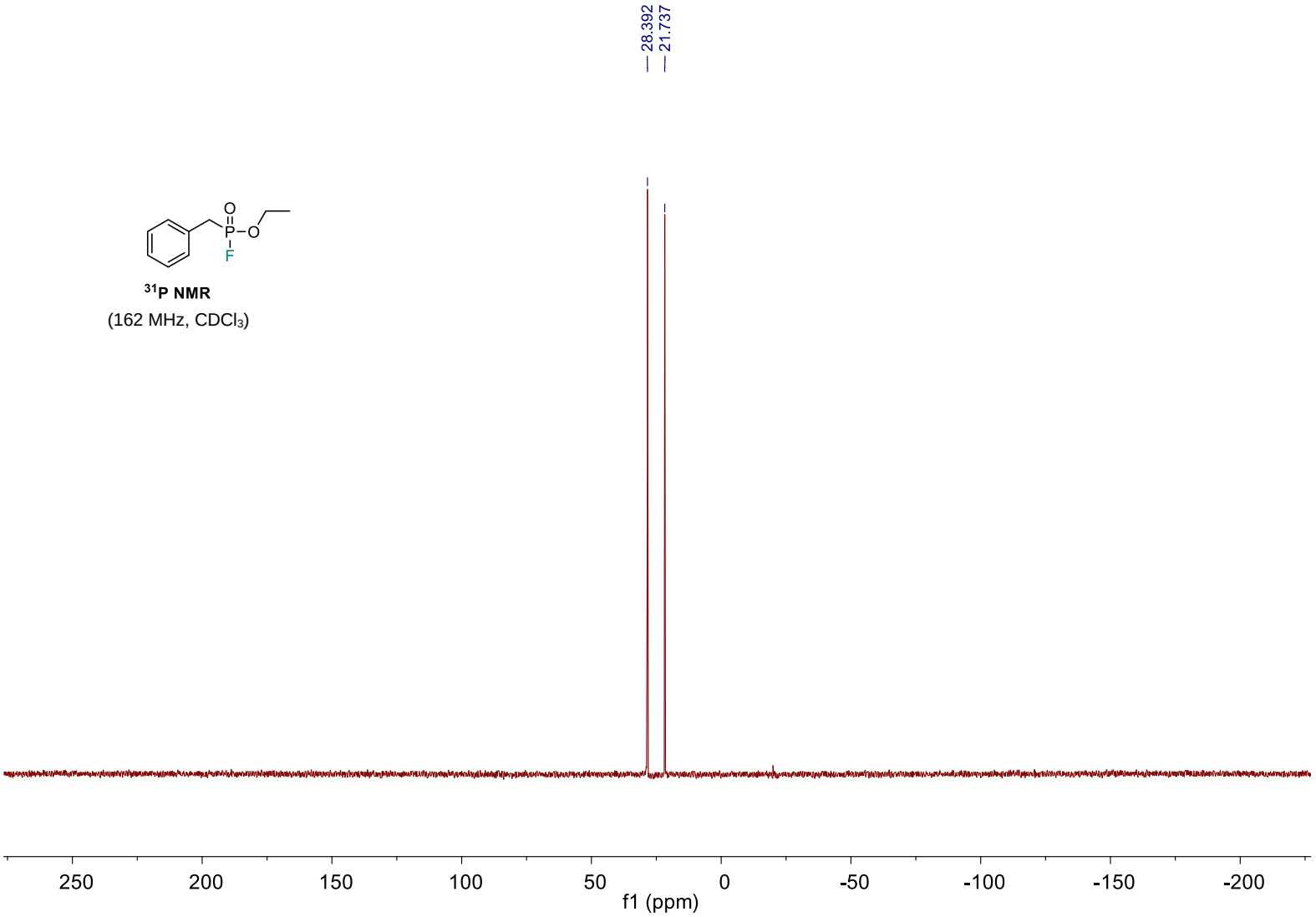


^{19}F NMR

(376 MHz, $CDCl_3$)

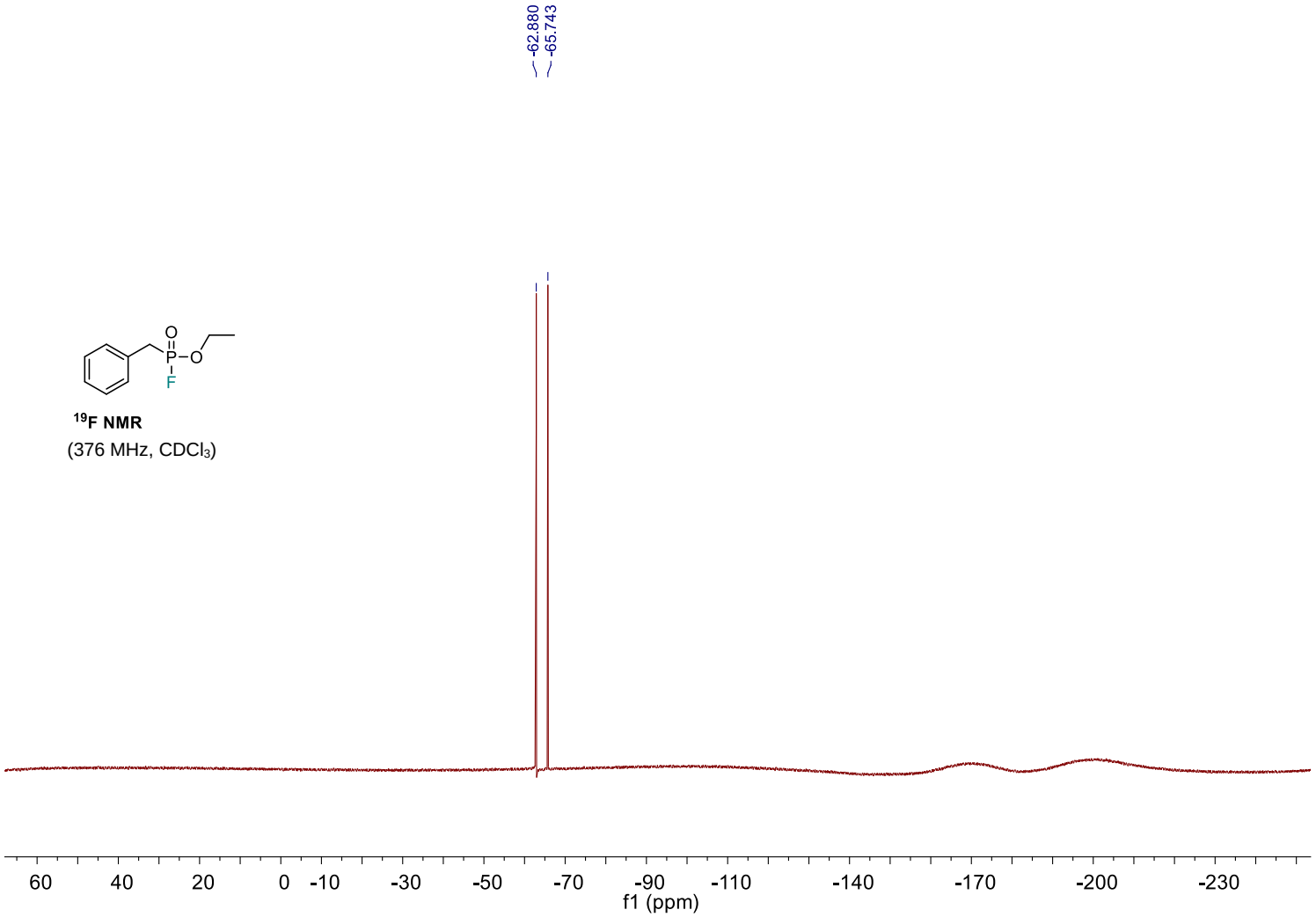

7.359
7.340
7.324
7.308
7.291
7.263
7.260
4.227
4.209
4.190
4.169
4.151
3.329
3.273
1.300
1.282
1.265
O
P
O
F
1H NMR
(400 MHz, CDCl3)
5.05
2.03
2.00
3.56
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


129.694
129.624
129.438
129.340
128.843
128.814
127.529
127.493
63.974
63.901
33.024
32.778
31.607
31.363
16.217
16.162
O
P
O
F
13C NMR
(100 MHz, CDCl3)
132 131 130 129 128 127 126 125
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



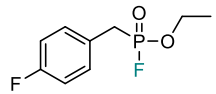
^{31}P NMR

(162 MHz, $CDCl_3$)

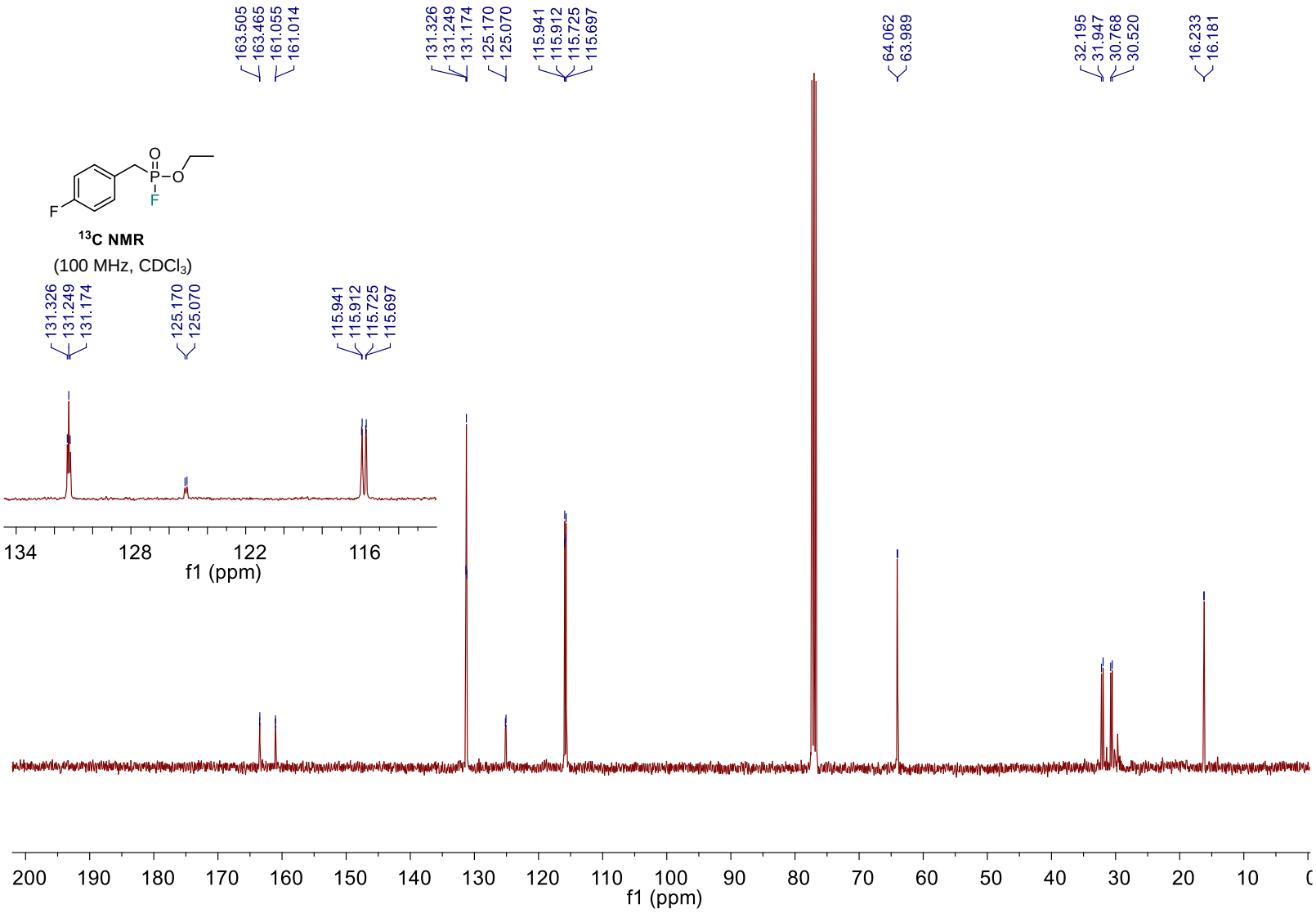


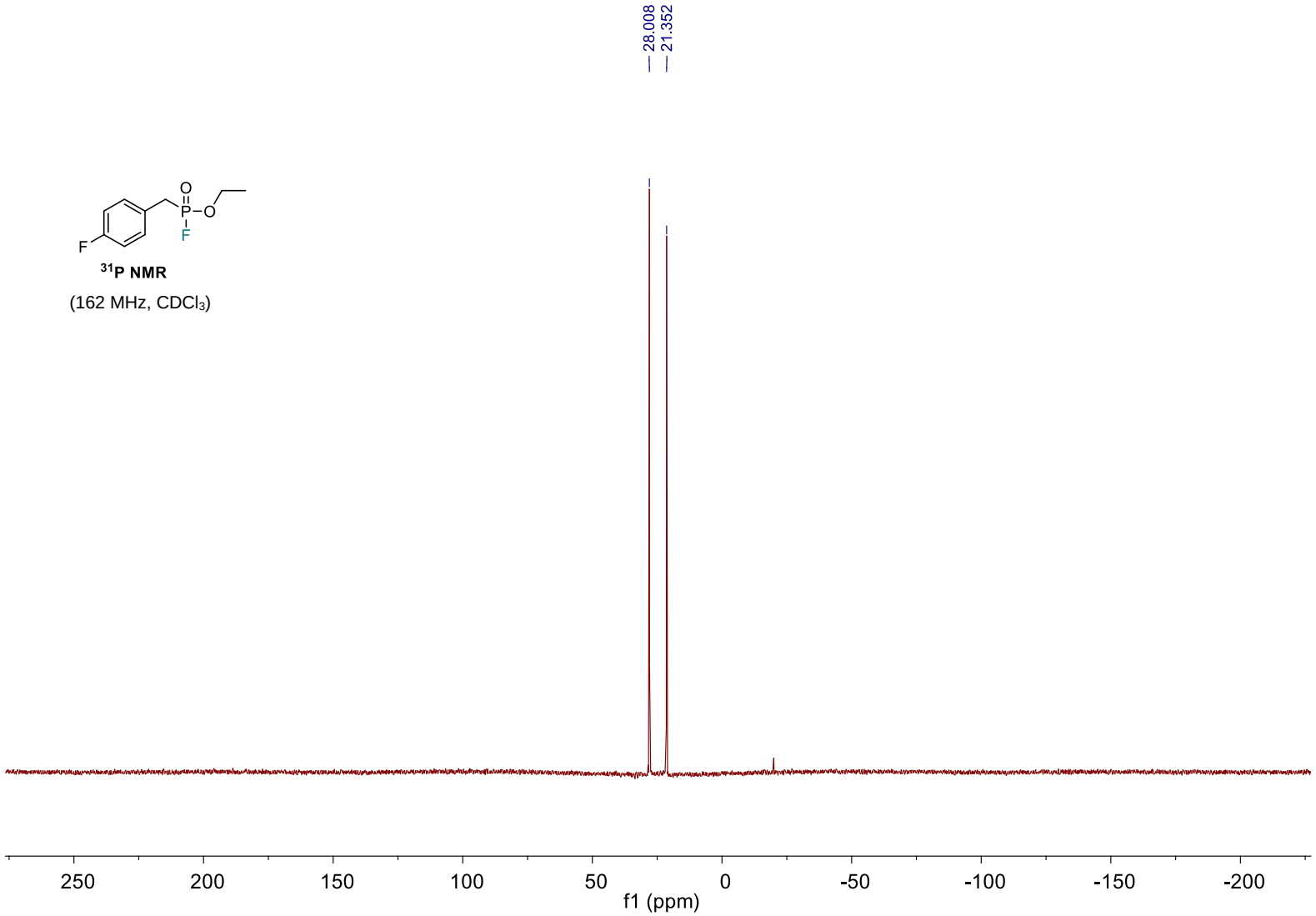
^{19}F NMR

(376 MHz, $CDCl_3$)



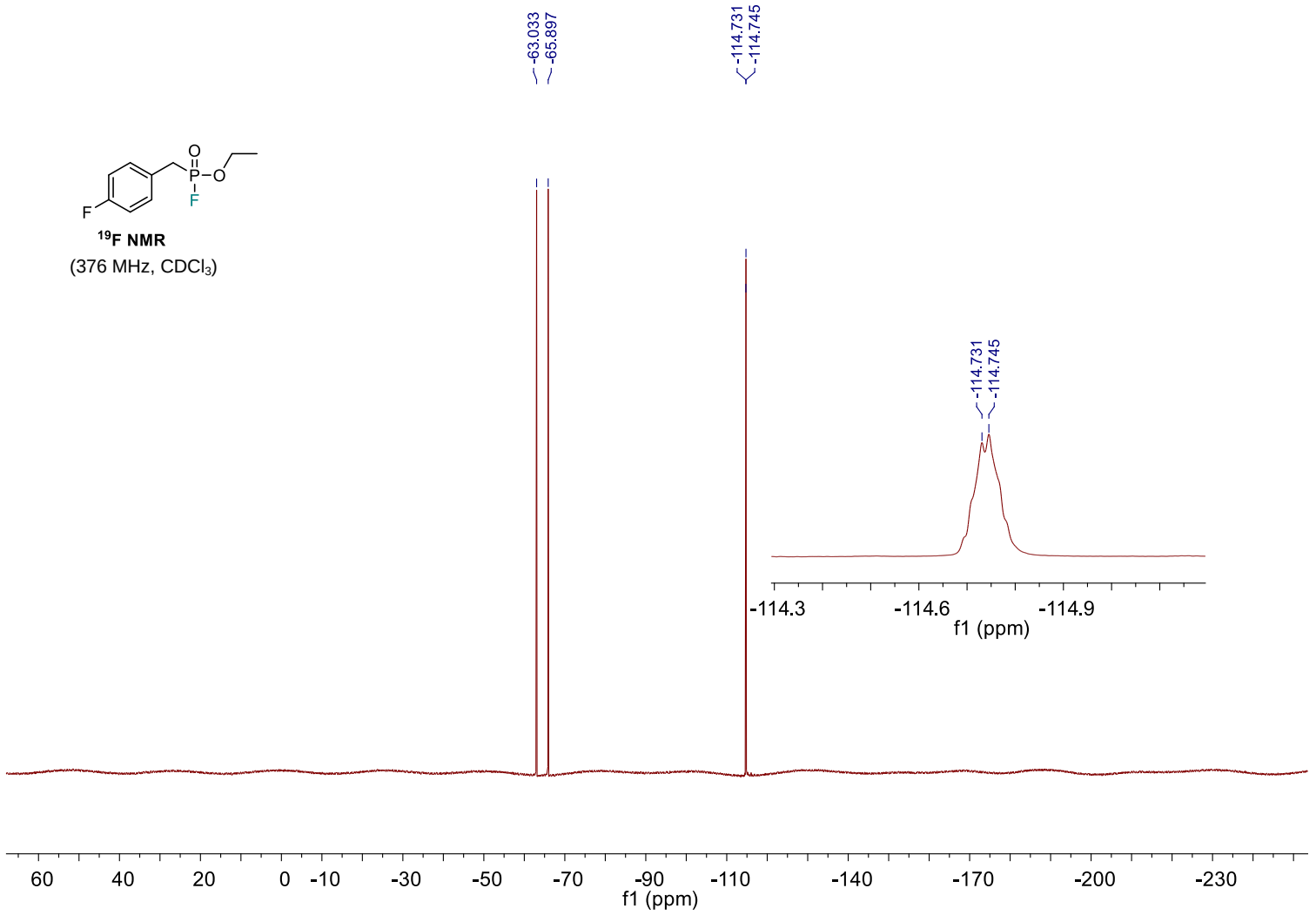
^{1}H NMR
(400 MHz, $CDCl_3$)

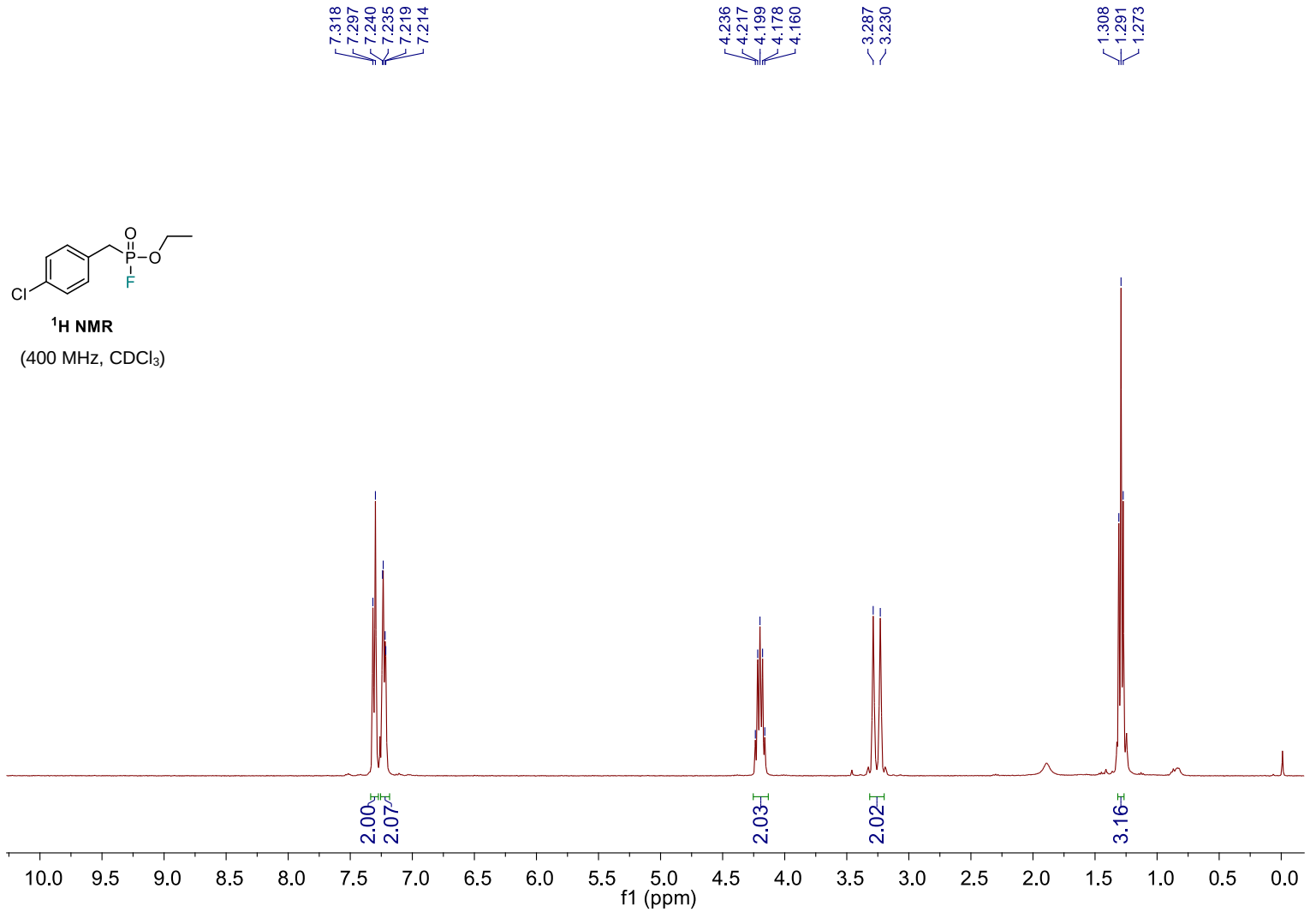

163.505
163.465
161.055
161.014
131.326
131.249
131.174
125.170
125.070
115.941
115.912
115.725
115.697
64.062
63.989
32.195
31.947
30.768
30.520
16.233
16.181
O
P
O
F
F
13C NMR
(100 MHz, CDCl3)
131.326
131.249
131.174
125.170
125.070
115.941
115.912
115.725
115.697
134
128
122
116
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

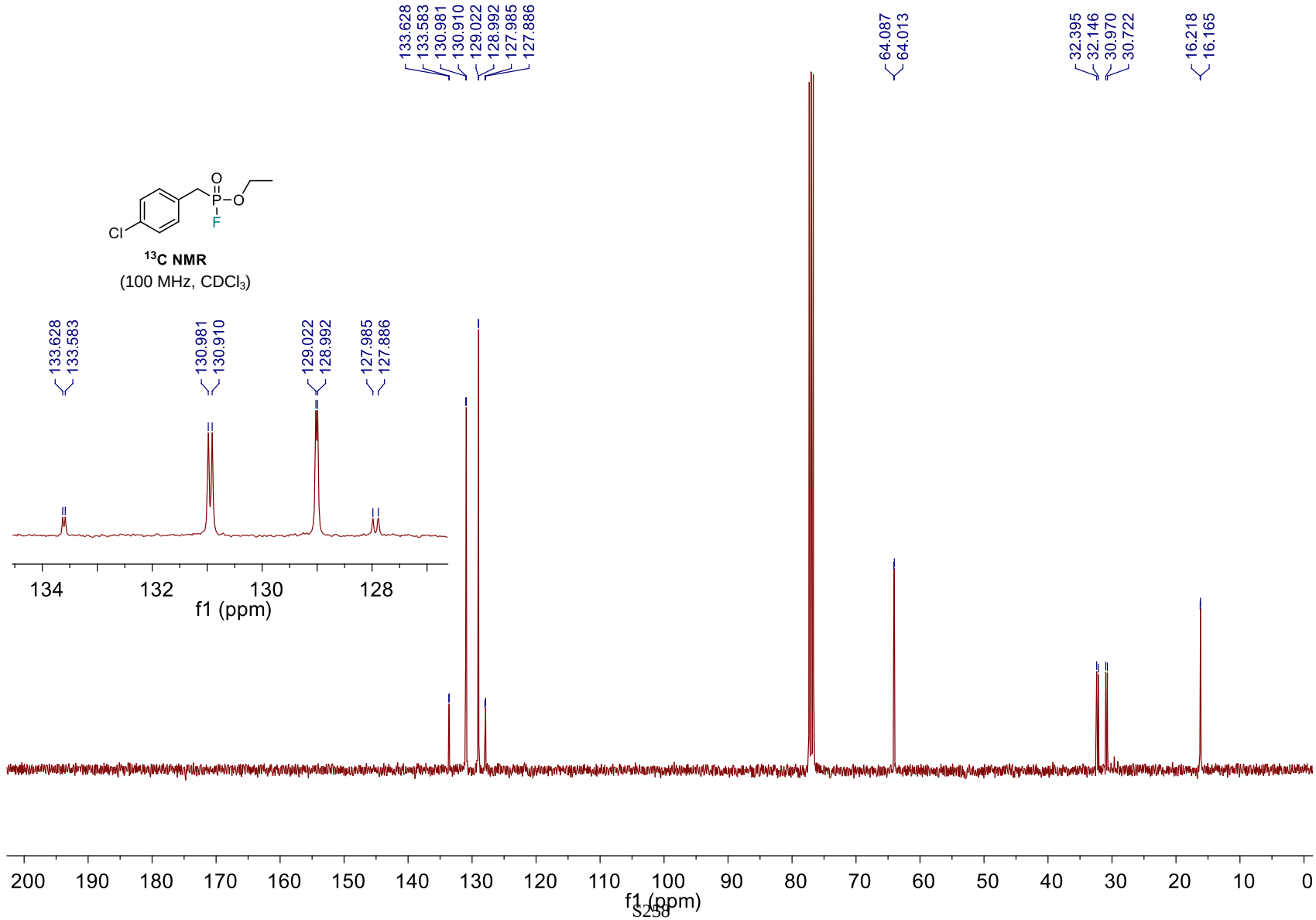


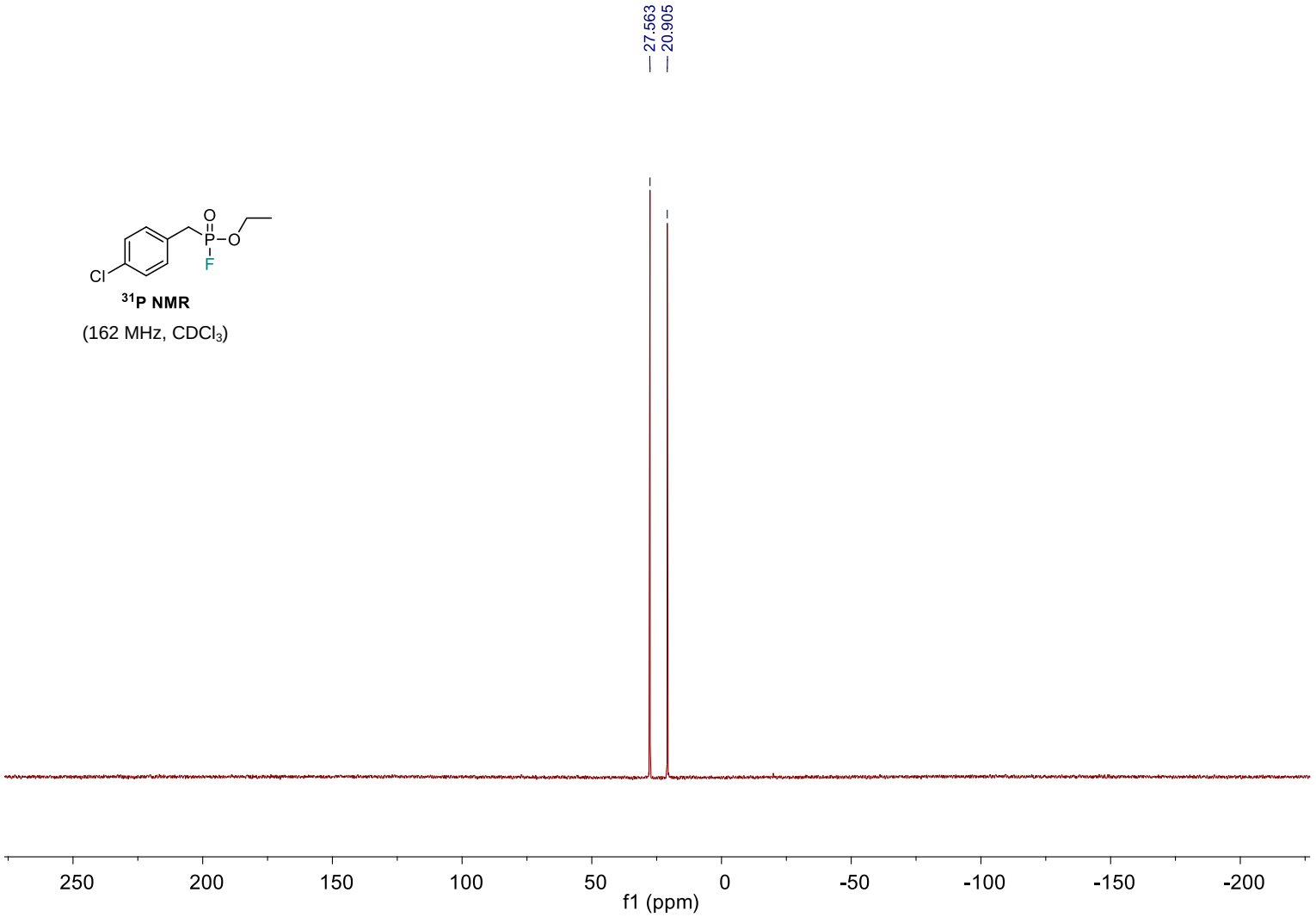
^{31}P NMR

(162 MHz, $CDCl_3$)


-63.033
-65.897
-114.731
-114.745
F
O
P
O
F
19F NMR
(376 MHz, CDCl3)
-114.731
-114.745
-114.3
-114.6
-114.9
f1 (ppm)
60
40
20
0
-10
-30
-50
-70
-90
-110
-140
-170
-200
-230
f1 (ppm)

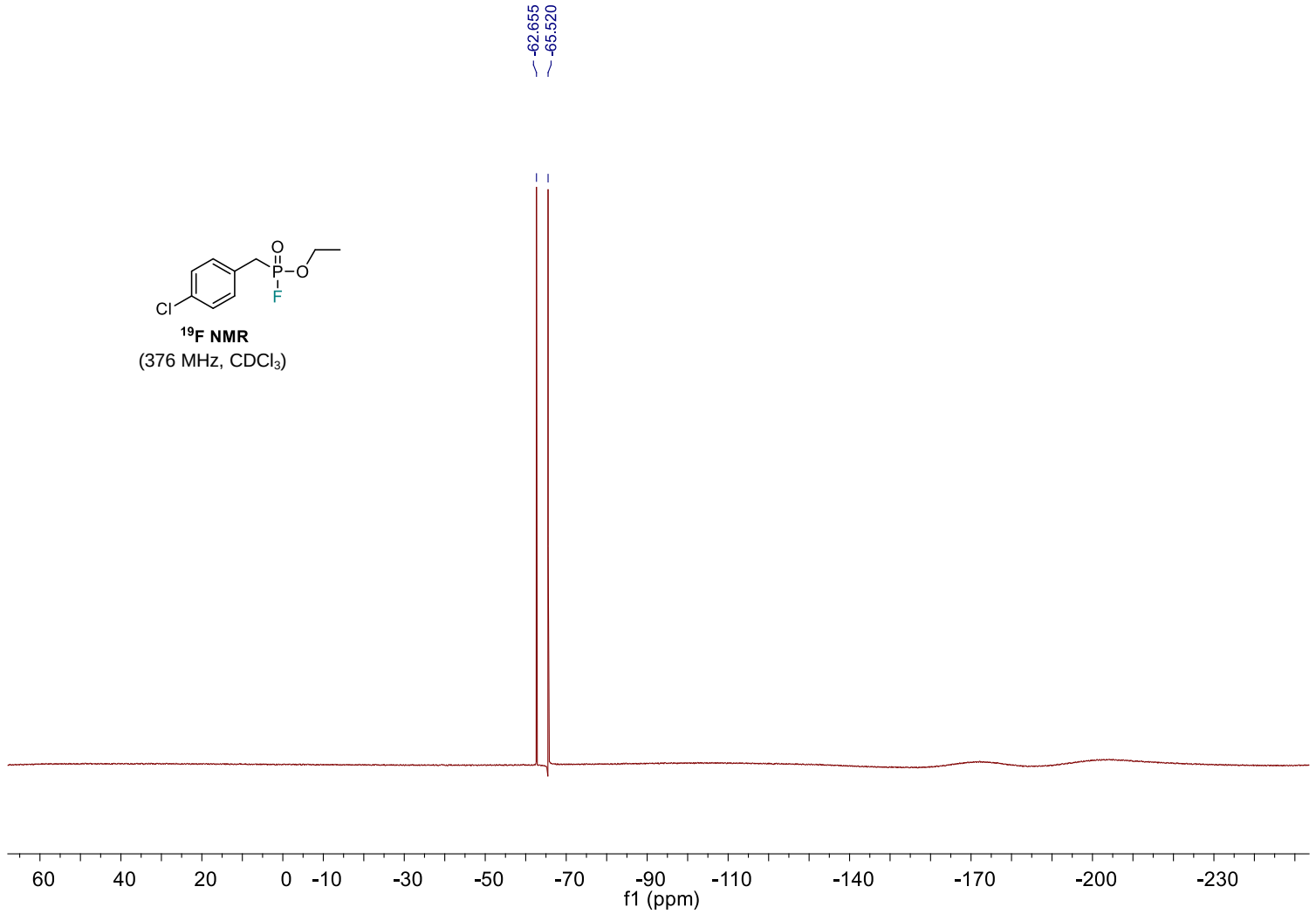

7.318
7.297
7.240
7.235
7.219
7.214
4.236
4.217
4.199
4.178
4.160
3.287
3.230
1.308
1.291
1.273
Cl
O
P
O
F
1H NMR
(400 MHz, CDCl3)
2.00
2.07
2.03
2.02
3.16
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


133.628
133.583
130.981
130.910
129.022
128.992
127.985
127.886
64.087
64.013
32.395
32.146
30.970
30.722
16.218
16.165
Cl
O
P
O
F
13C NMR
(100 MHz, CDCl3)
f1 (ppm)
f1 (ppm)

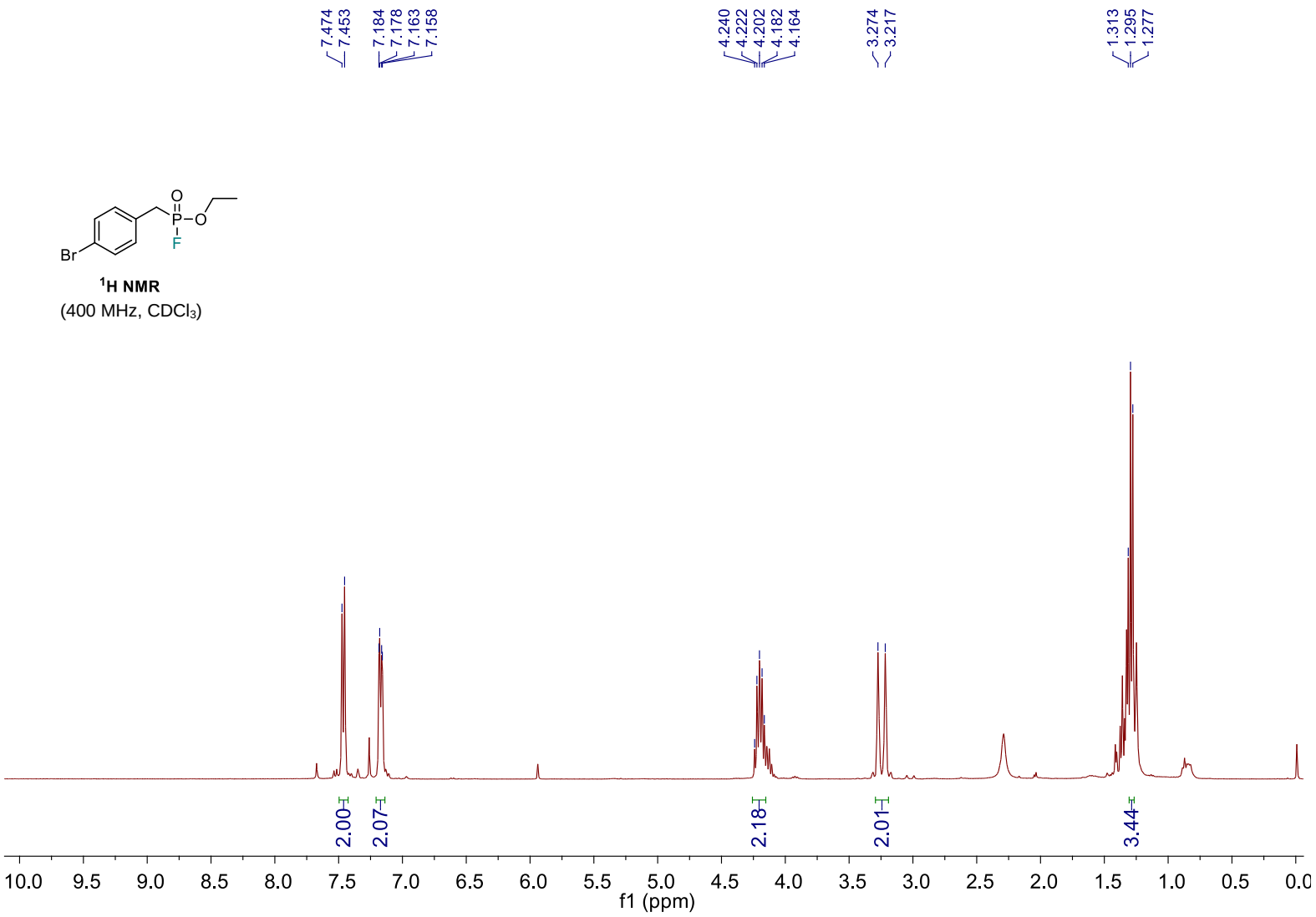


^{31}P NMR

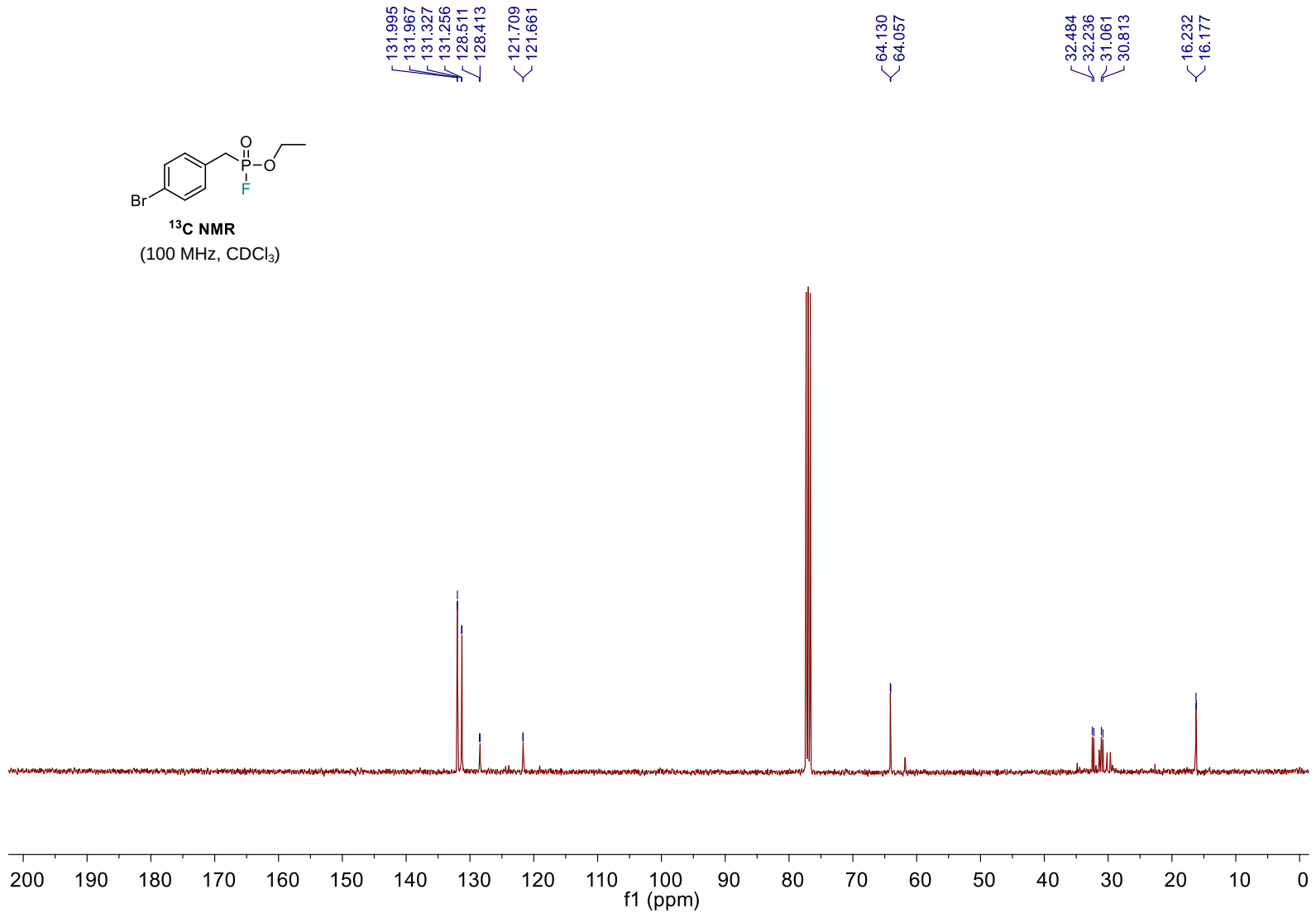
(162 MHz, $CDCl_3$)



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

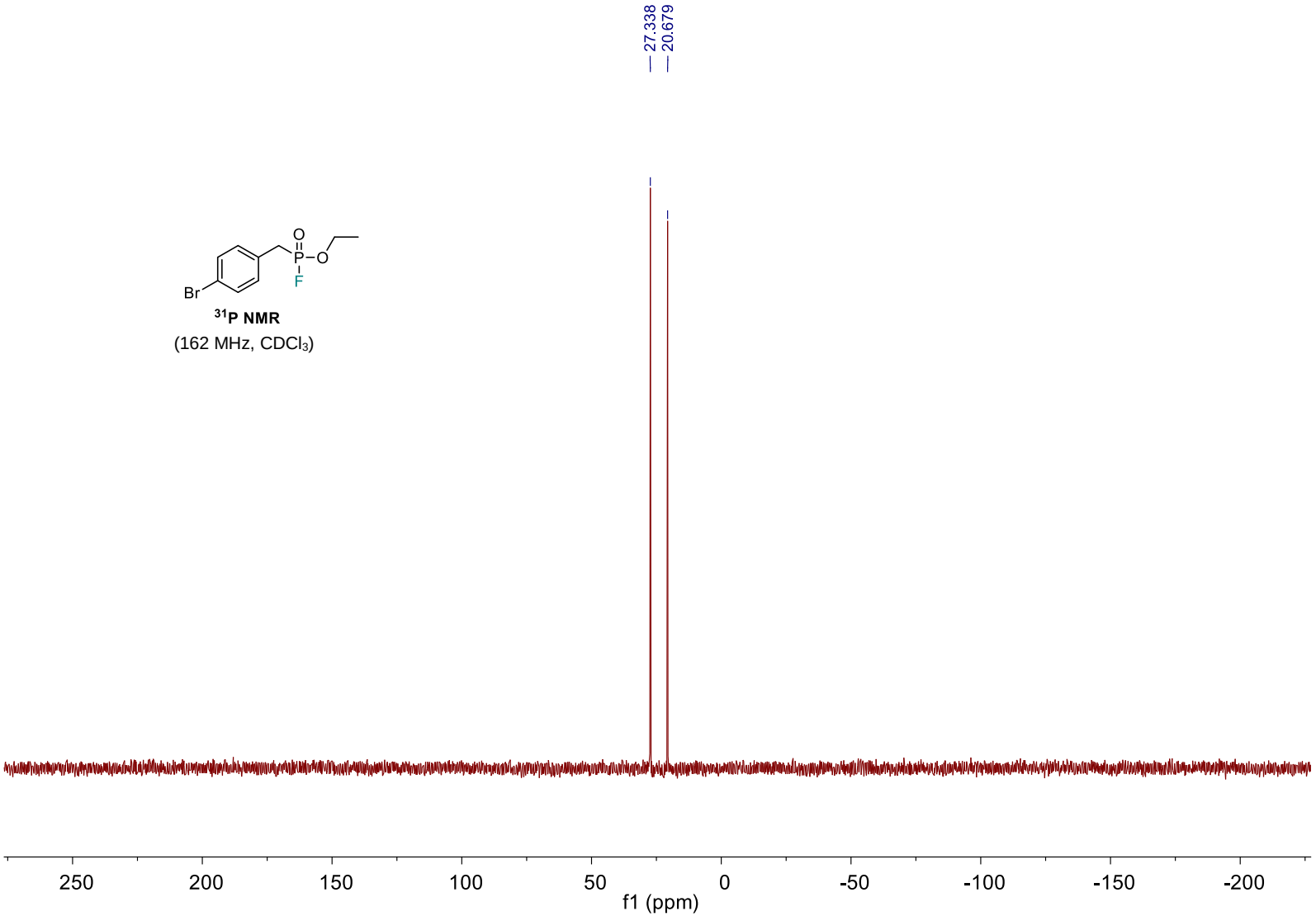


^{1}H NMR
(400 MHz, $CDCl_3$)



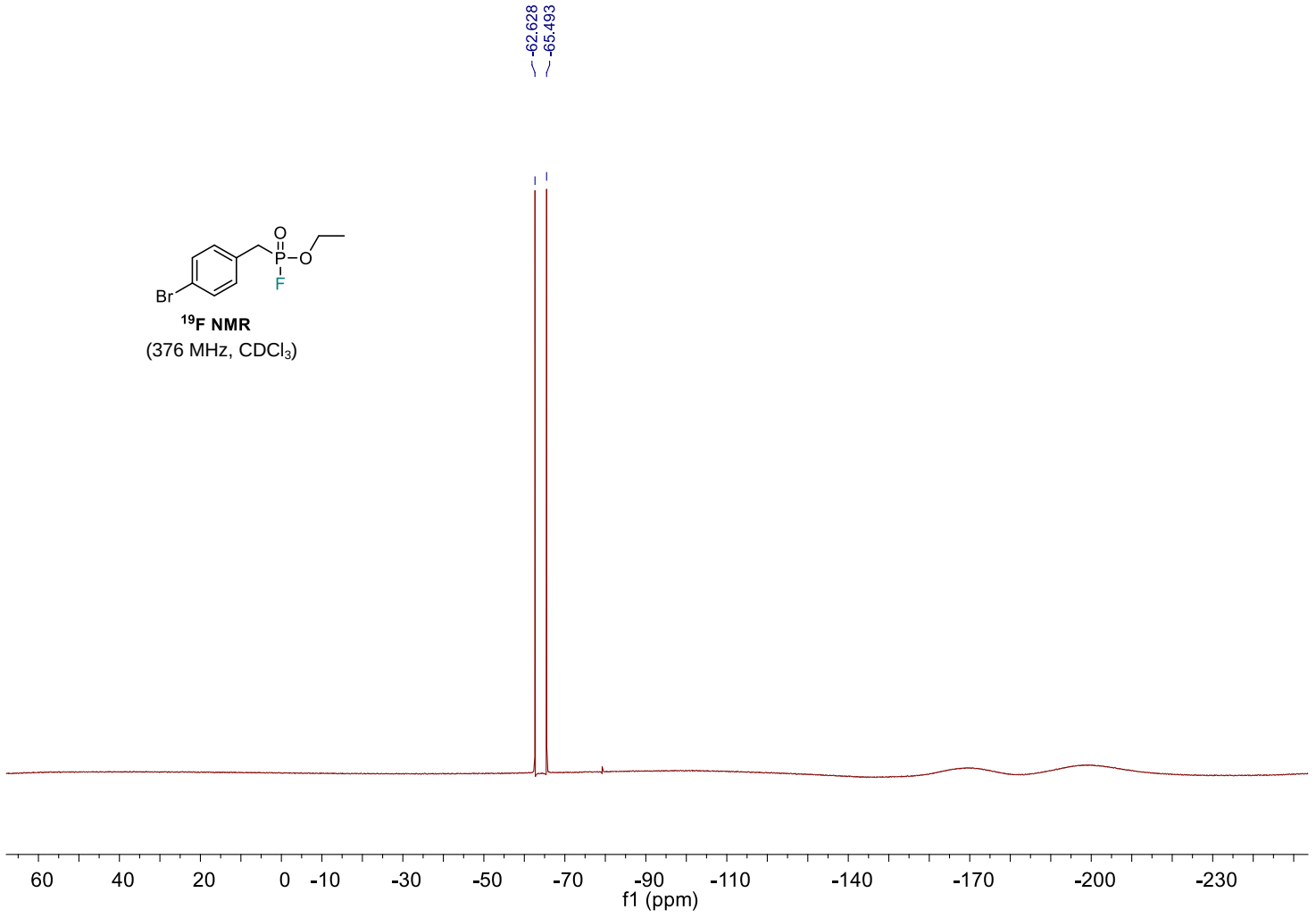
^{13}C NMR

(100 MHz, $CDCl_3$)



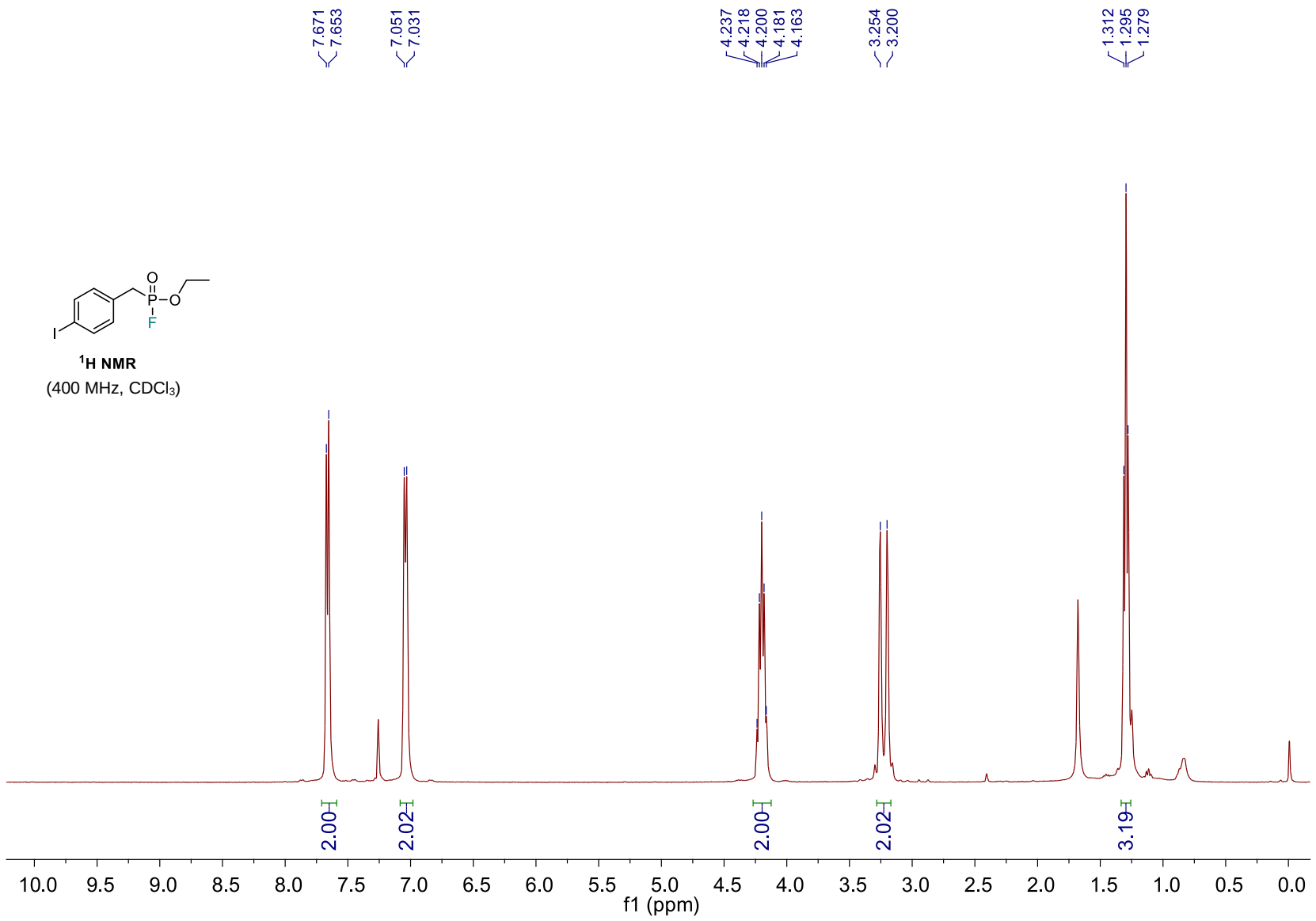
^{31}P NMR

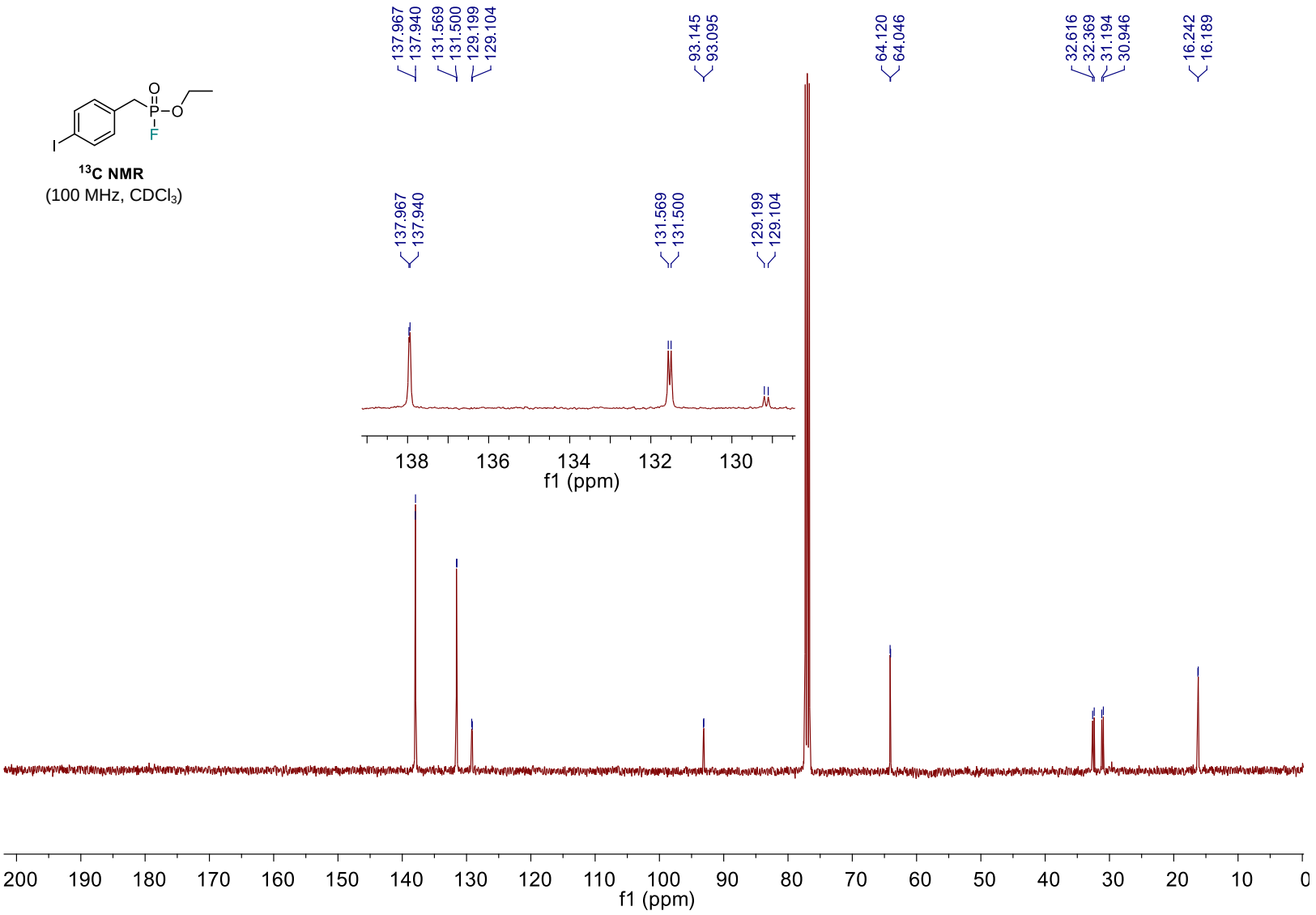
(162 MHz, $CDCl_3$)

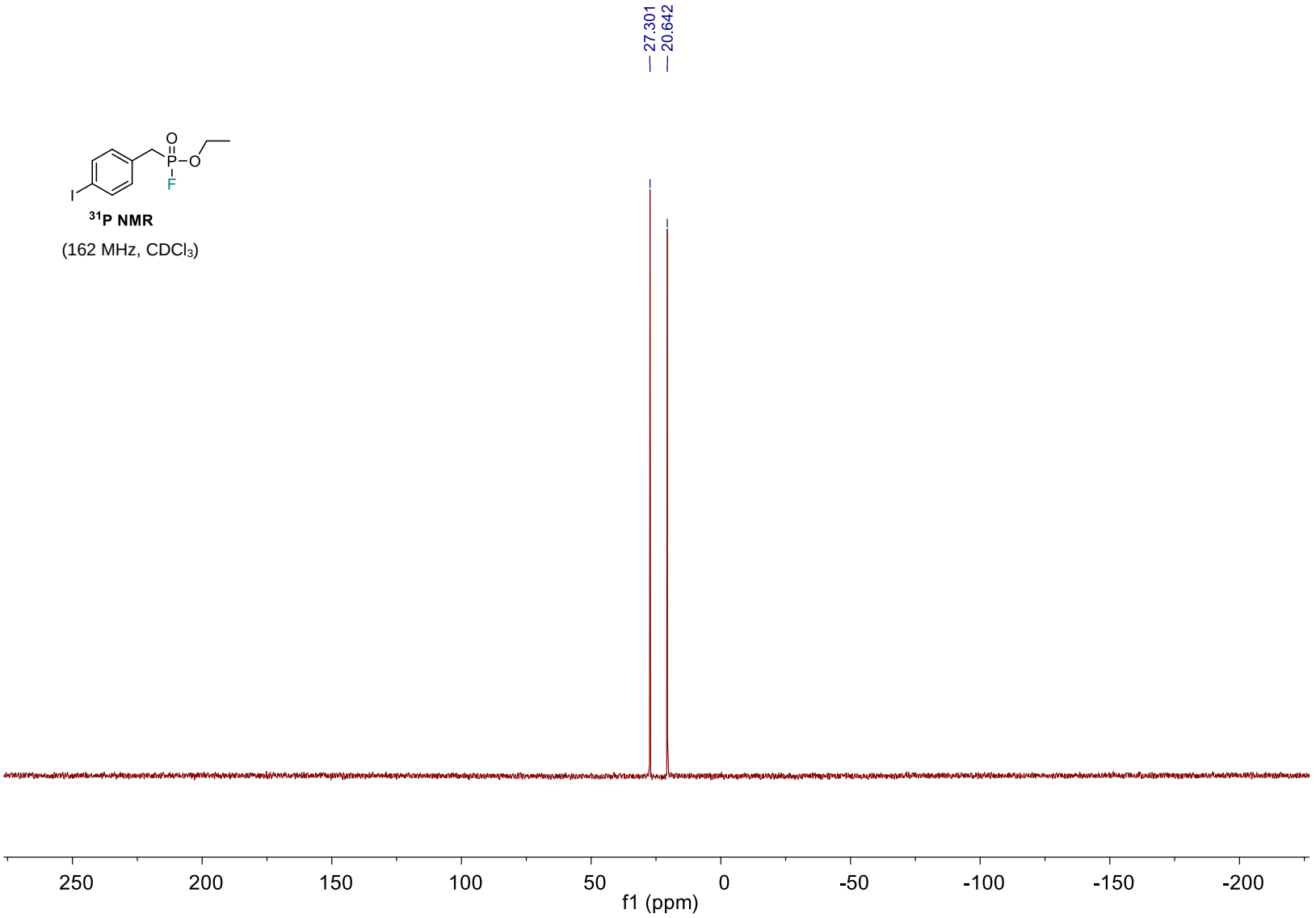


^{19}F NMR

(376 MHz, $CDCl_3$)

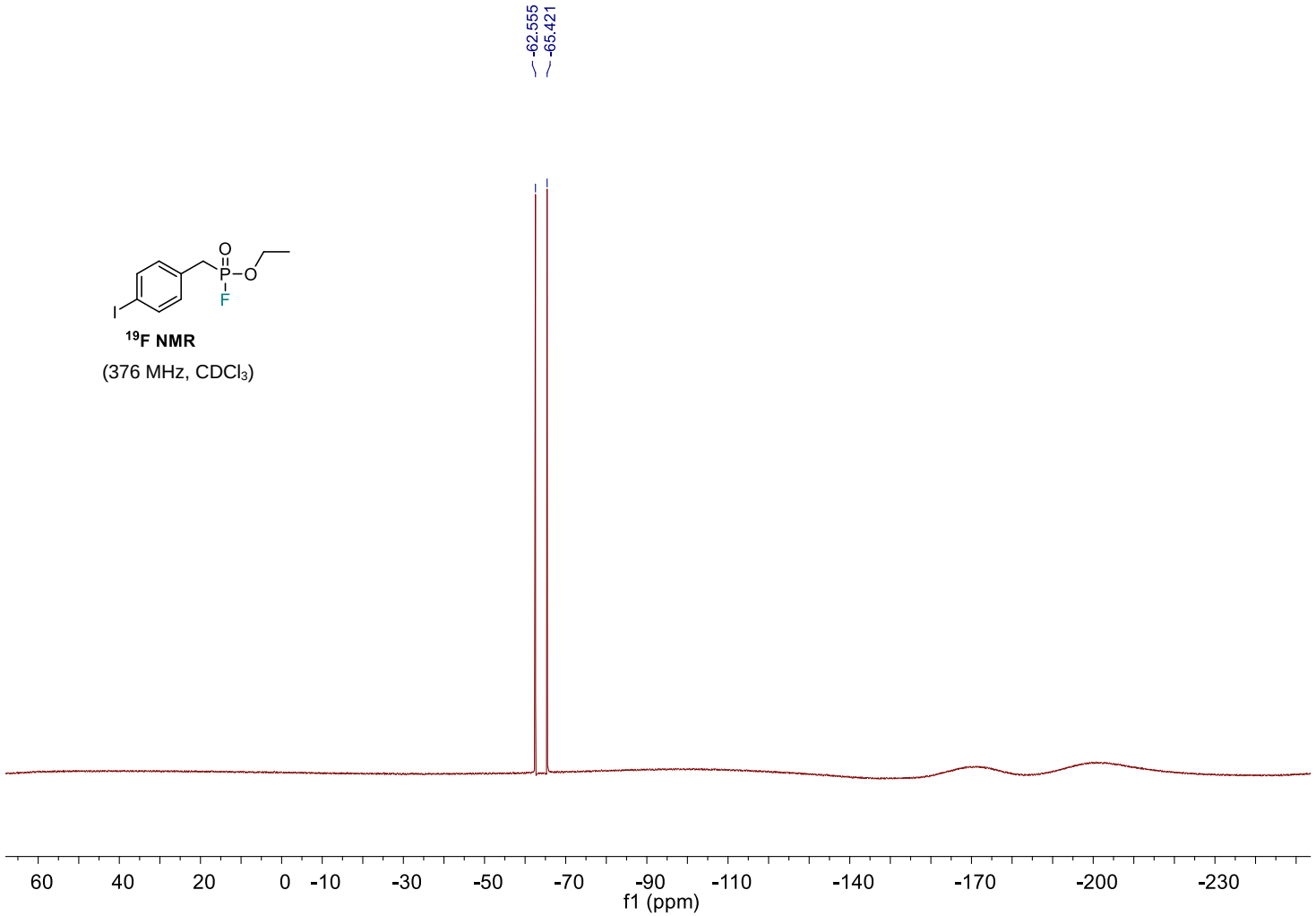

7.671
7.653
7.051
7.031
4.237
4.218
4.200
4.181
4.163
3.254
3.200
1.312
1.295
1.279
O
P
O
F
I
^{1}H NMR
(400 MHz, CDCl$_3$)
2.00
2.02
2.00
2.02
3.19
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


137.967
137.940
131.569
131.500
129.199
129.104
93.145
93.095
64.120
64.046
32.616
32.369
31.194
30.946
16.242
16.189
O
P
O
F
I
13C NMR
(100 MHz, CDCl3)
138
136
134
132
130
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



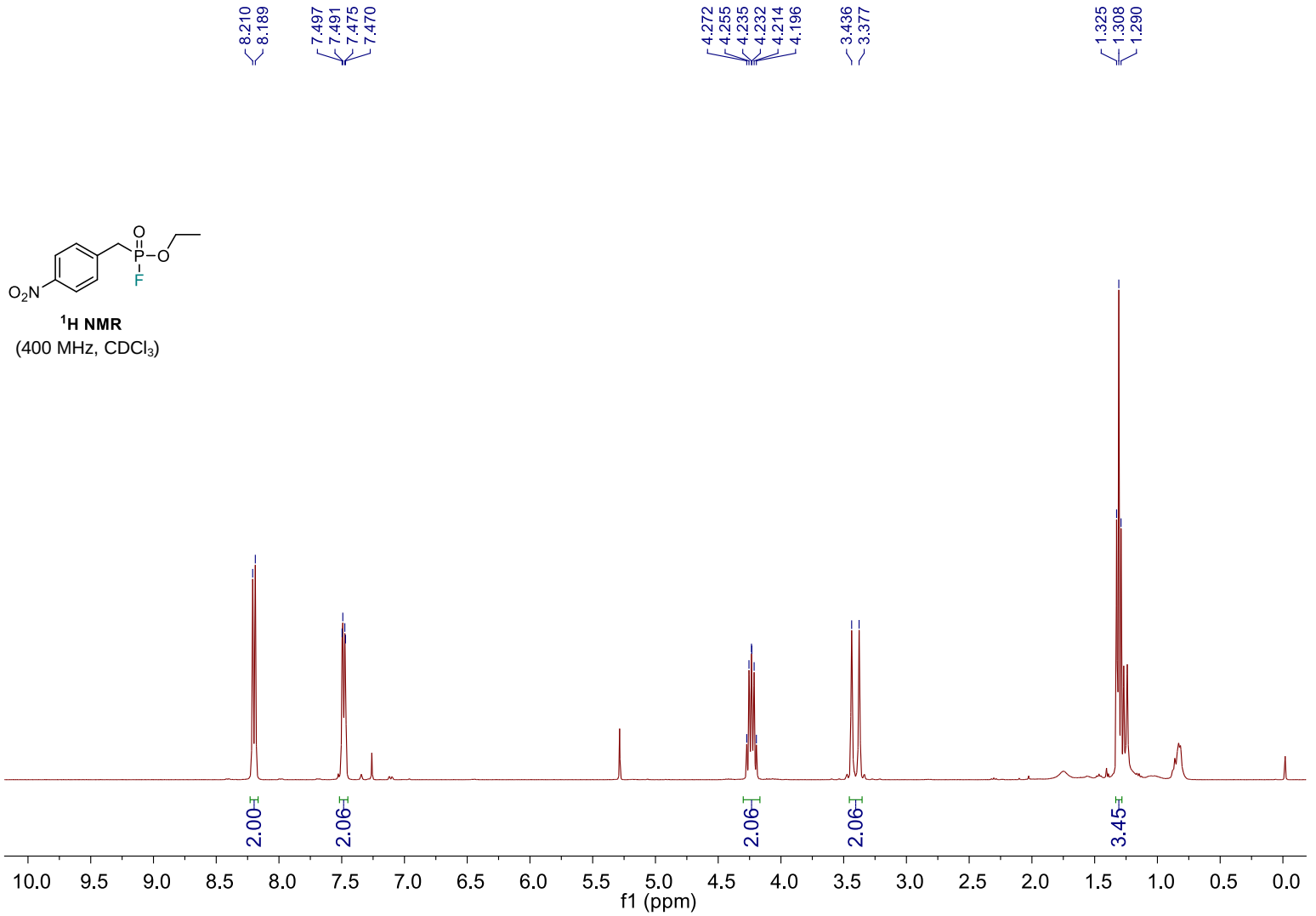
^{31}P NMR

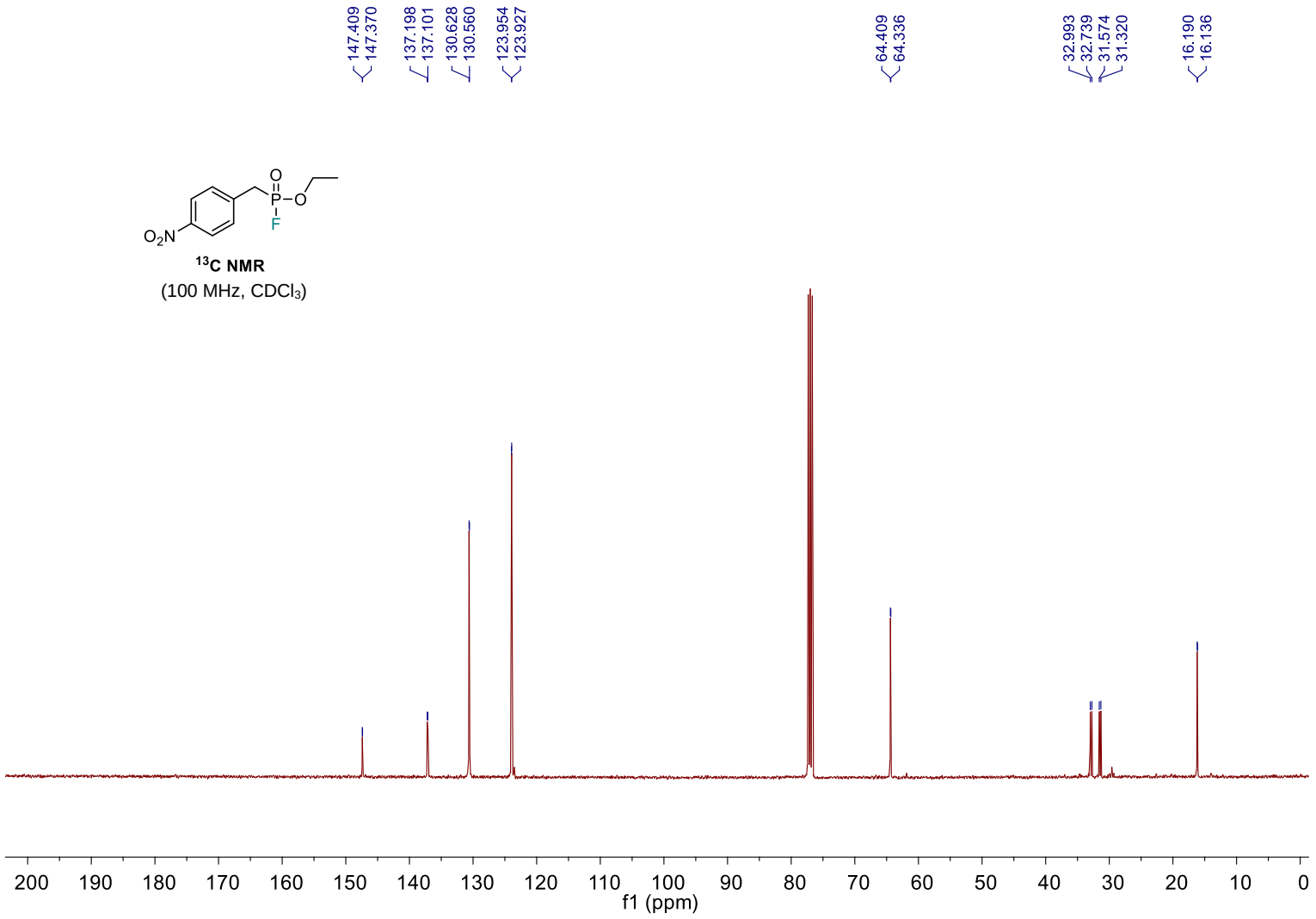
(162 MHz, $CDCl_3$)

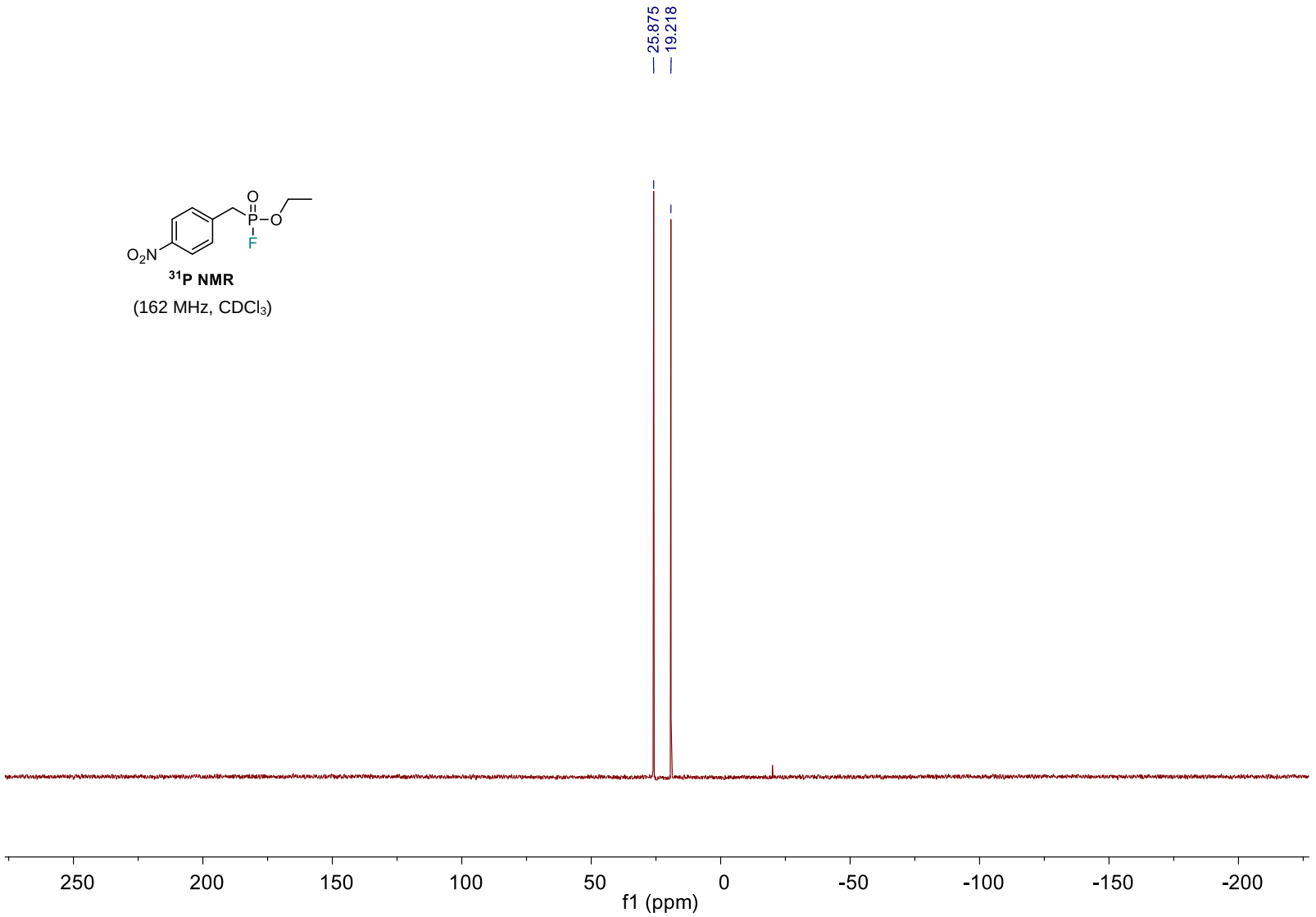


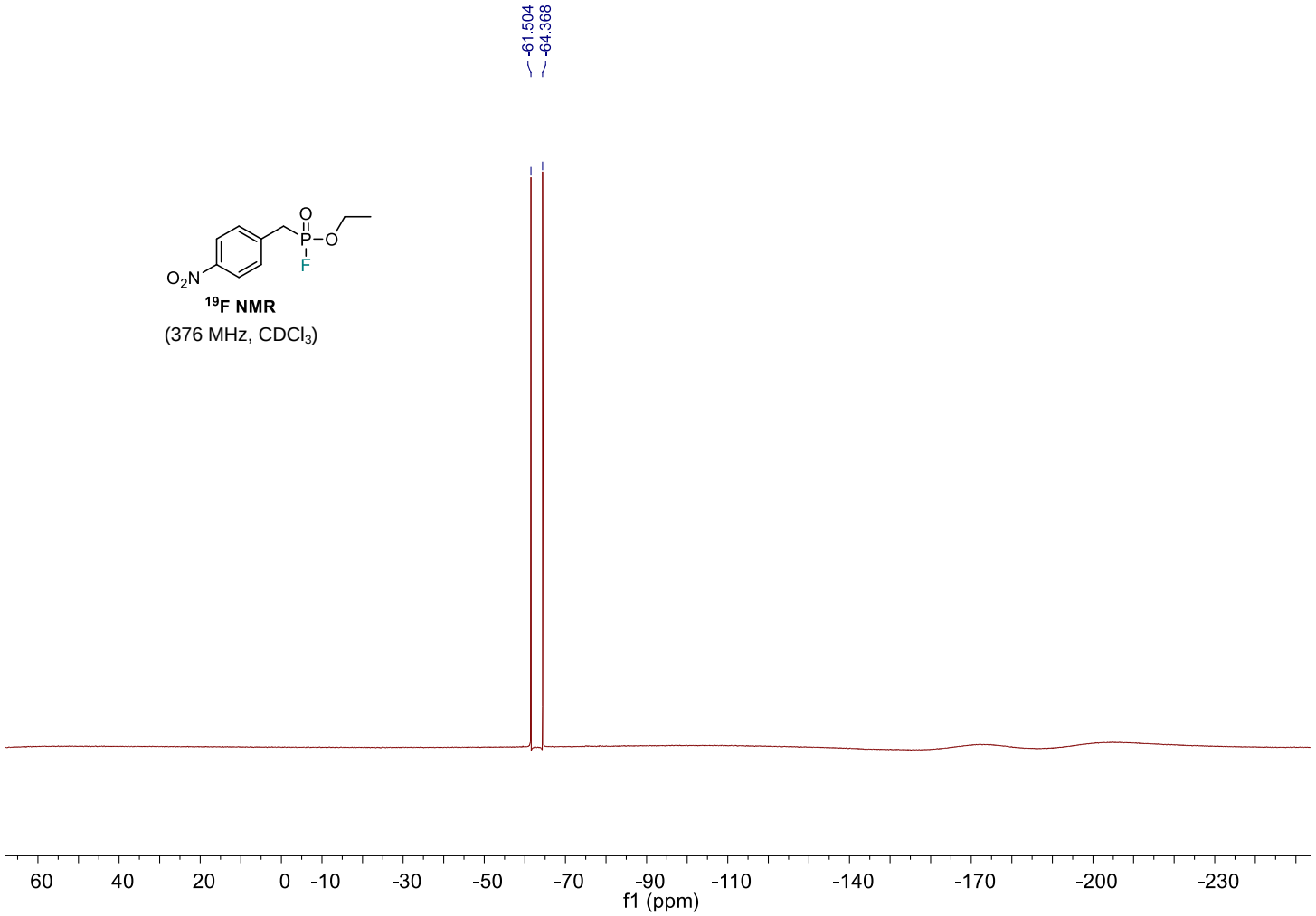
^{19}F NMR

(376 MHz, $CDCl_3$)


8.210
8.189
7.497
7.491
7.475
7.470
4.272
4.255
4.235
4.232
4.214
4.196
3.436
3.377
1.325
1.308
1.290
O
P
O
F
O2N
1H NMR
(400 MHz, CDCl3)
2.00
2.06
2.06
2.06
3.45
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

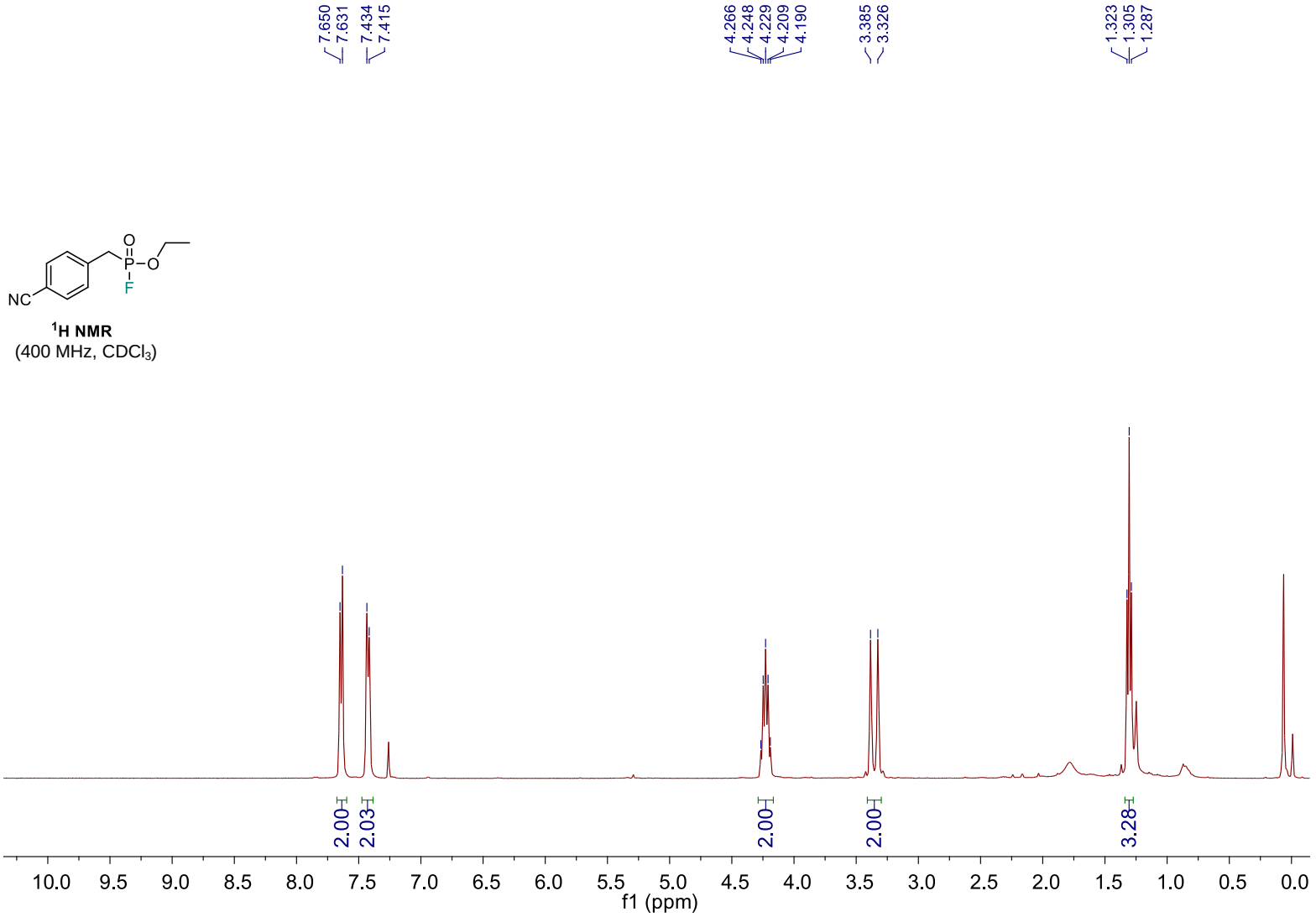

147.409
147.370
137.198
137.101
130.628
130.560
123.954
123.927
64.409
64.336
32.993
32.739
31.574
31.320
16.190
16.136
O
P
O
F
O2N
13C NMR
(100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


25.875
19.218
O
P
O
F
O2N
31P NMR
(162 MHz, CDCl3)
250
200
150
100
50
0
-50
-100
-150
-200
f1 (ppm)

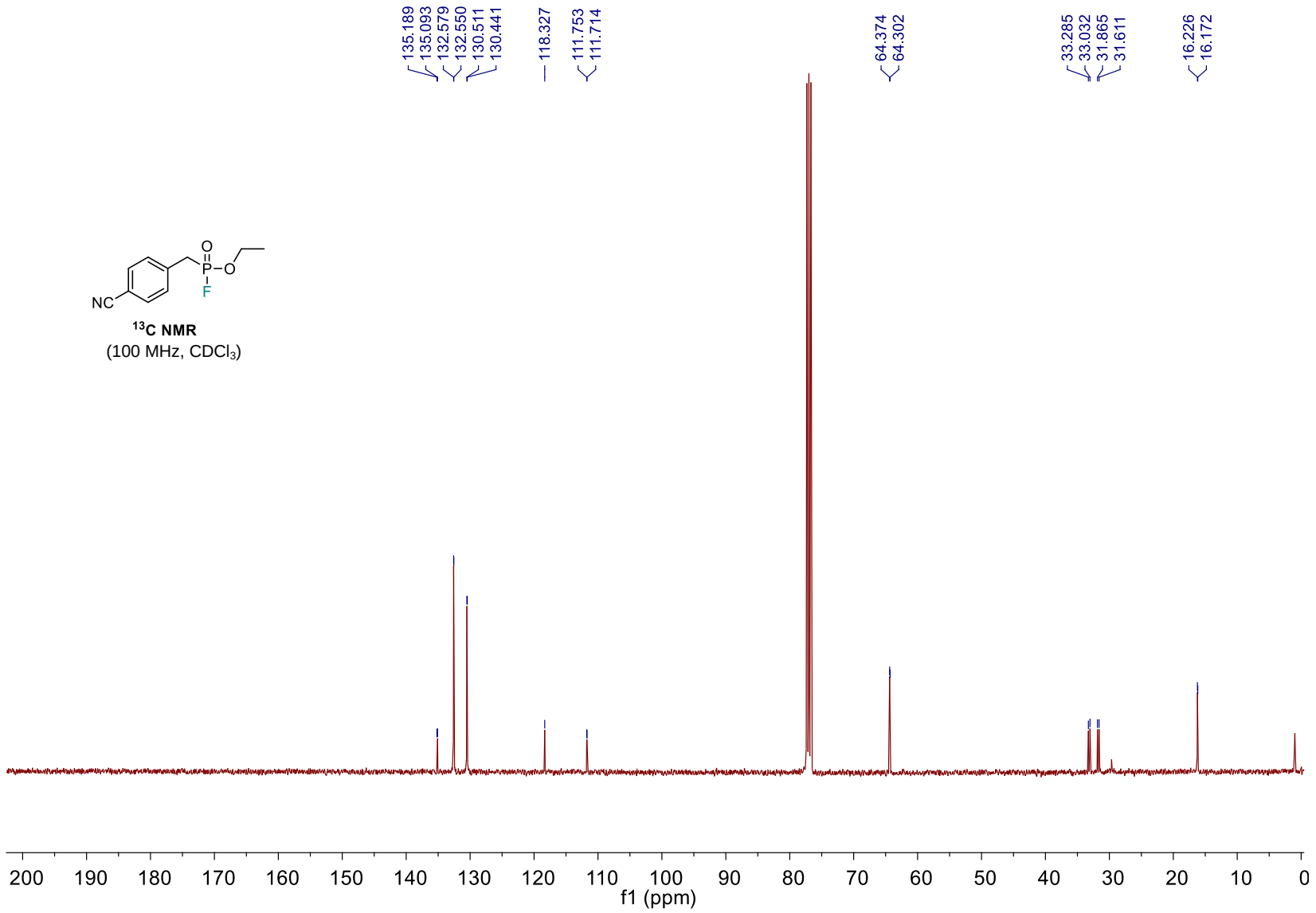


^{19}F NMR

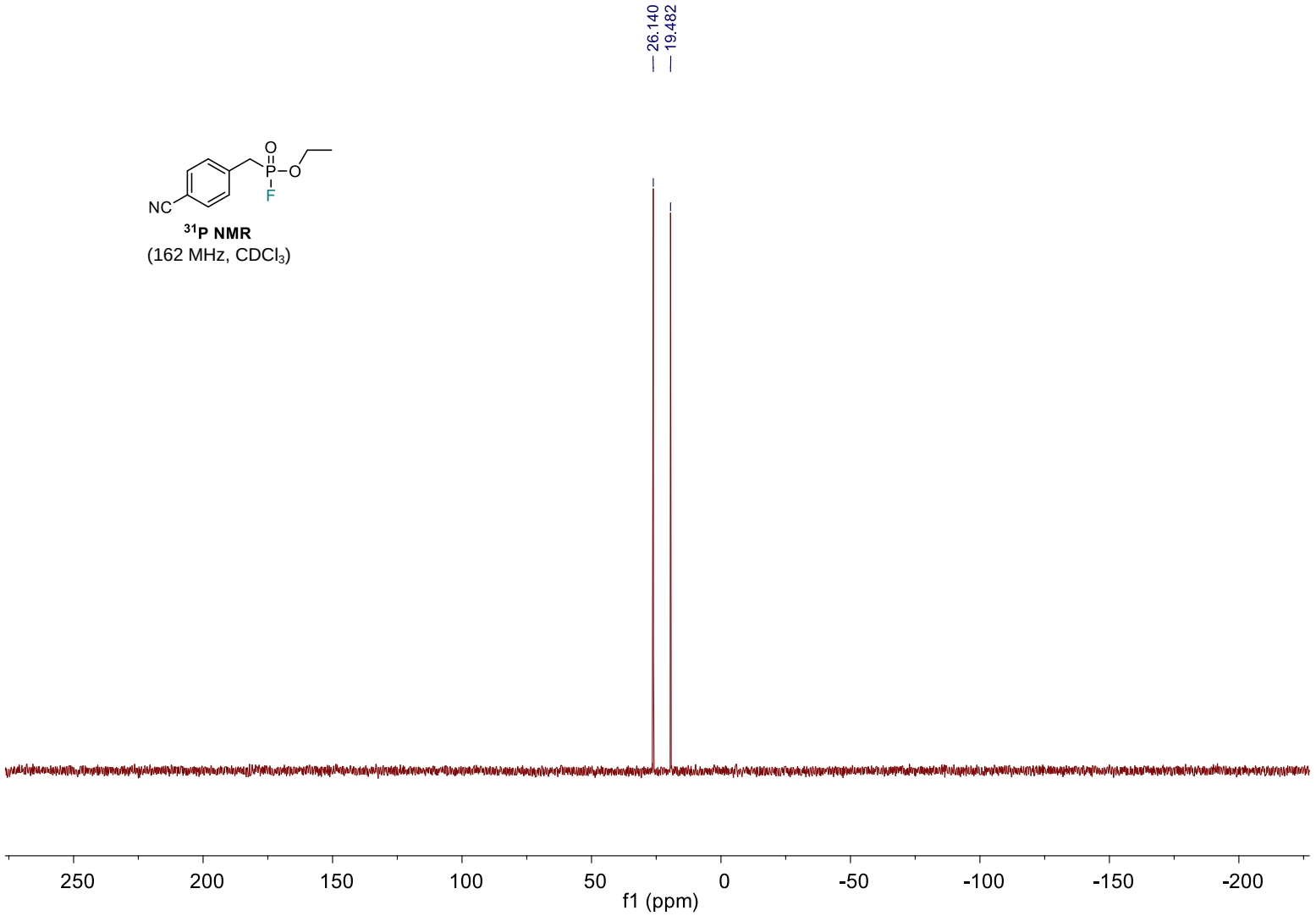
(376 MHz, $CDCl_3$)



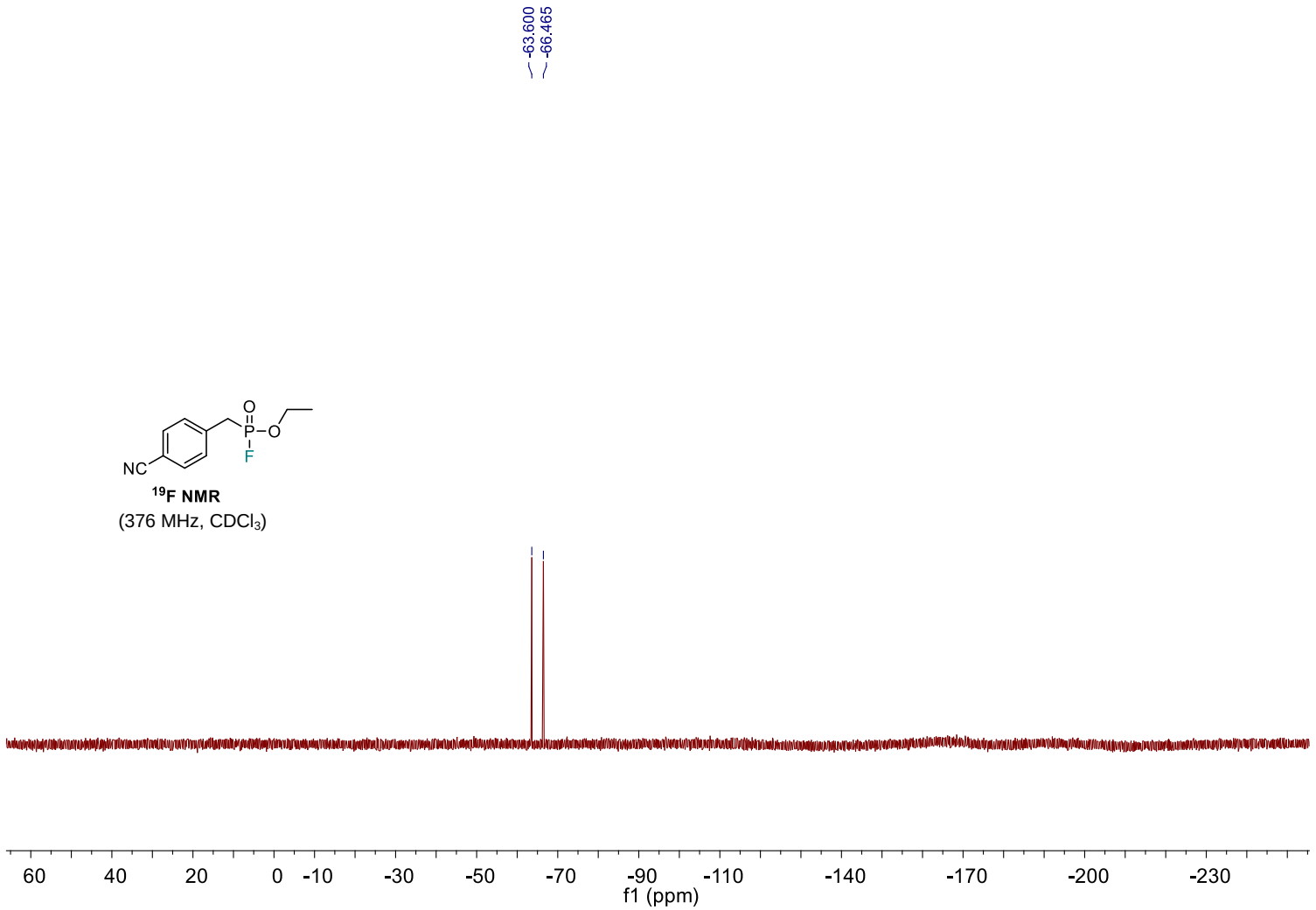
^{1}H NMR
(400 MHz, $CDCl_3$)



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

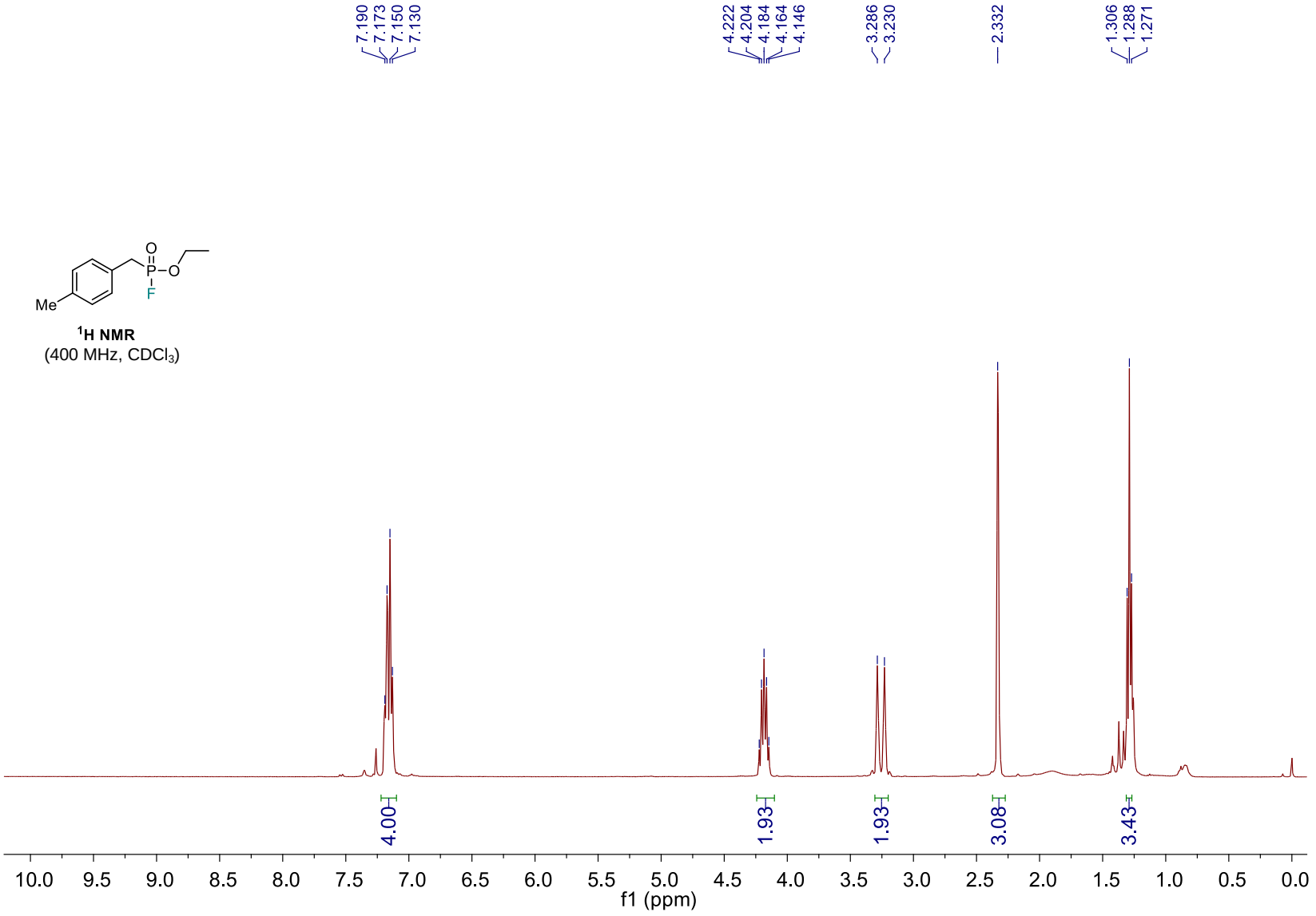


^{31}P NMR
(162 MHz, $CDCl_3$)

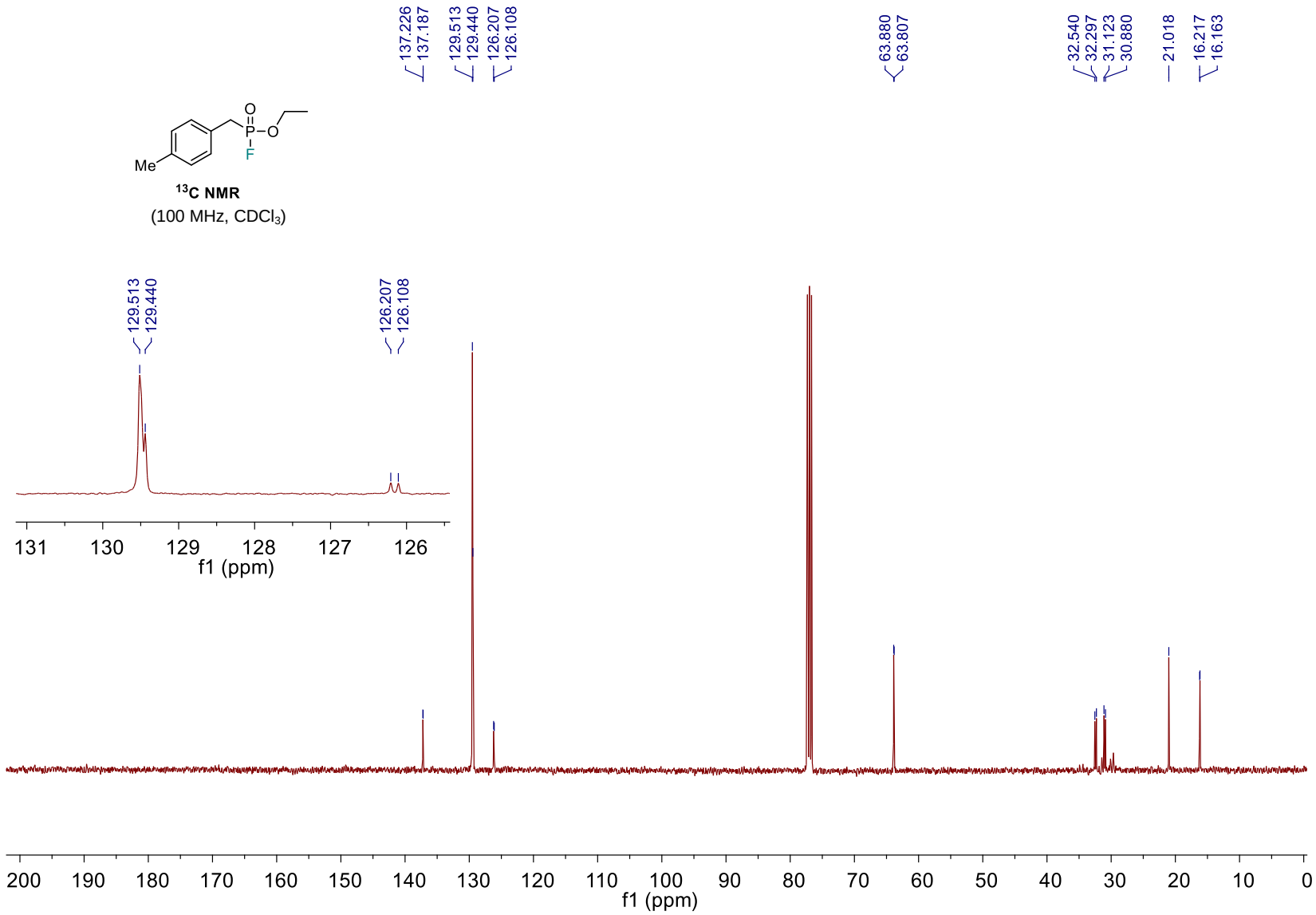


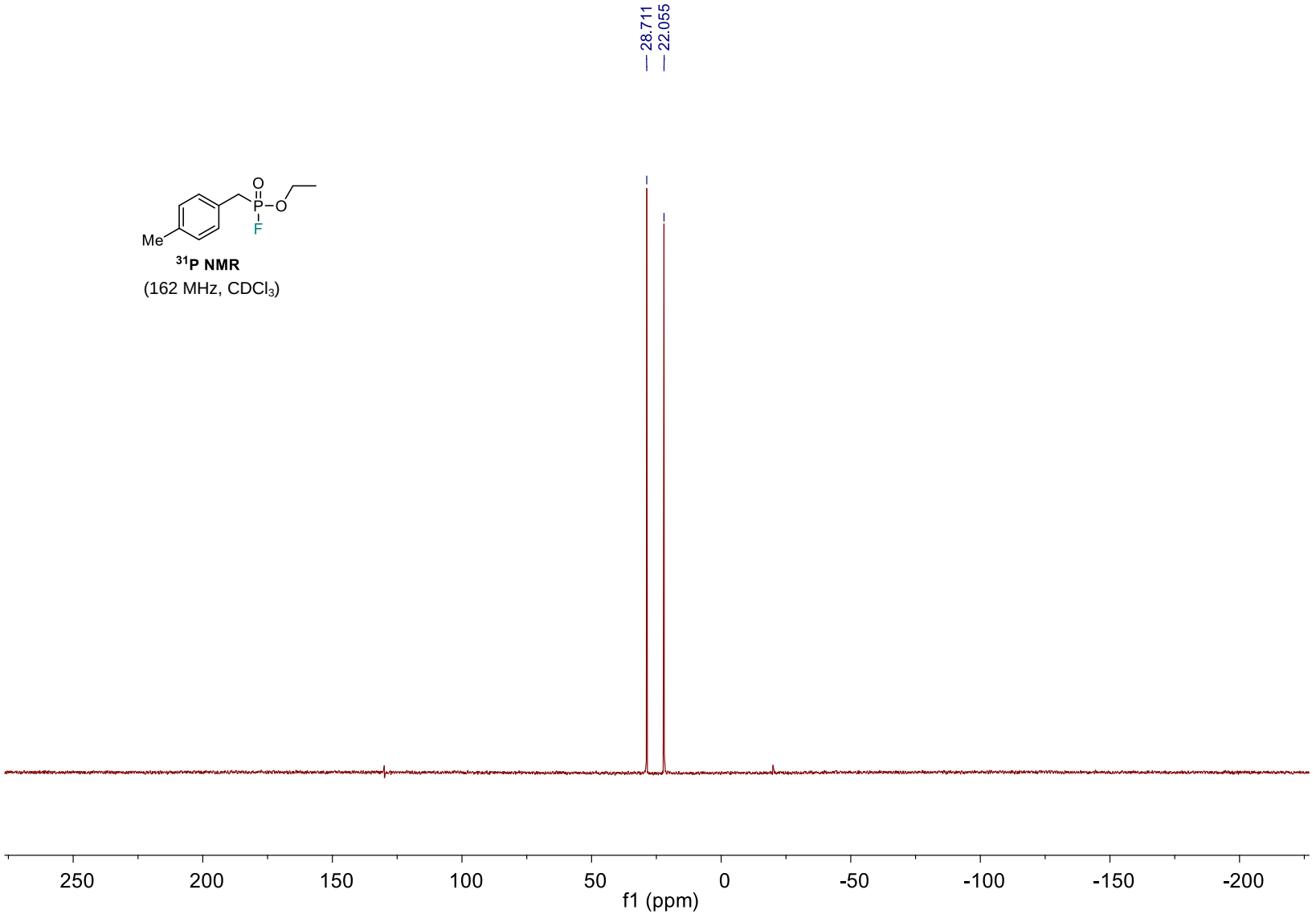
^{19}F NMR

(376 MHz, $CDCl_3$)



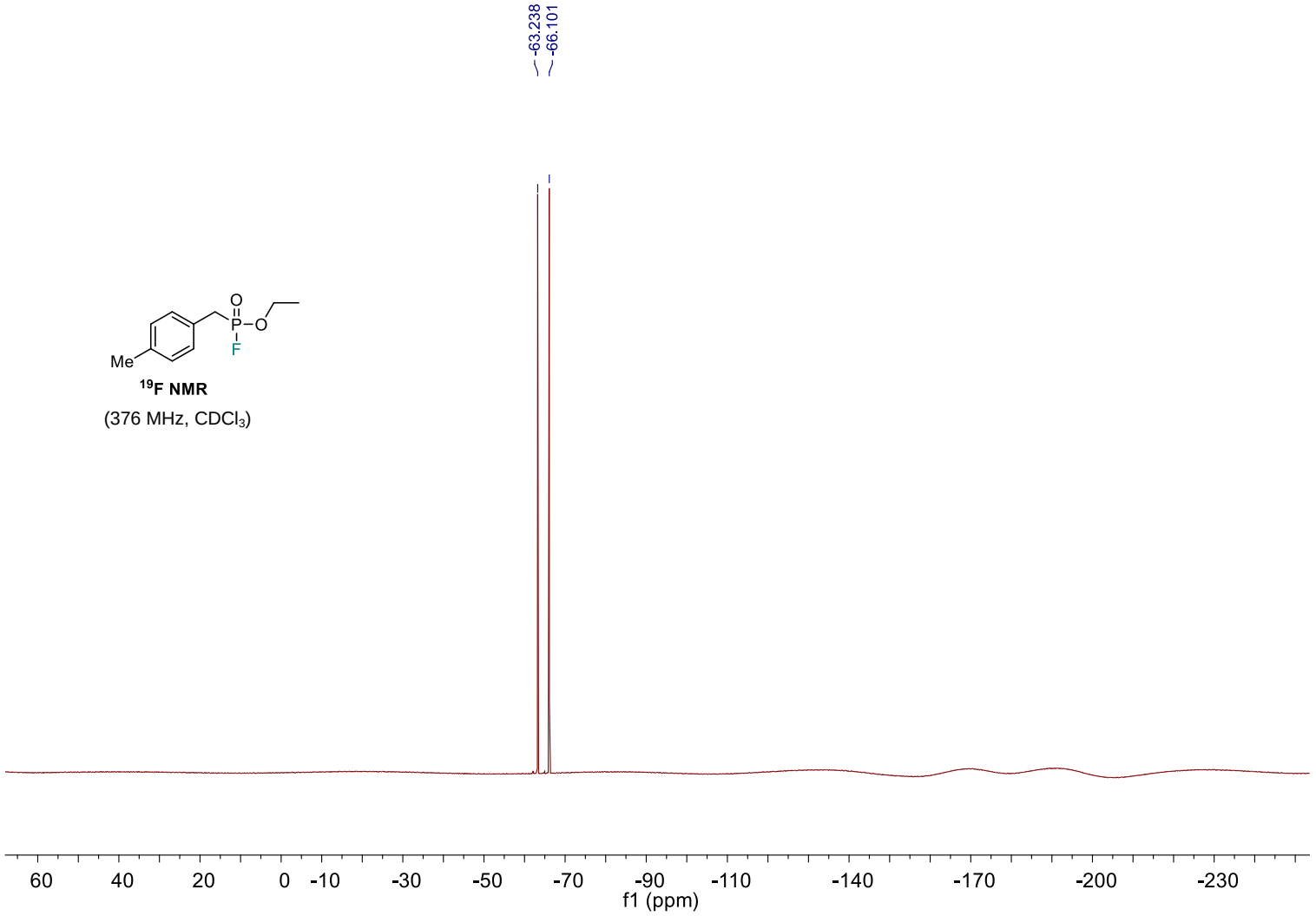
^{1}H NMR
(400 MHz, $CDCl_3$)


137.226
137.187
129.513
129.440
126.207
126.108
63.880
63.807
32.540
32.297
31.123
30.880
21.018
16.217
16.163
Me
O
P
O
F
13C NMR
(100 MHz, CDCl3)
129.513
129.440
126.207
126.108
131
130
129
128
127
126
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



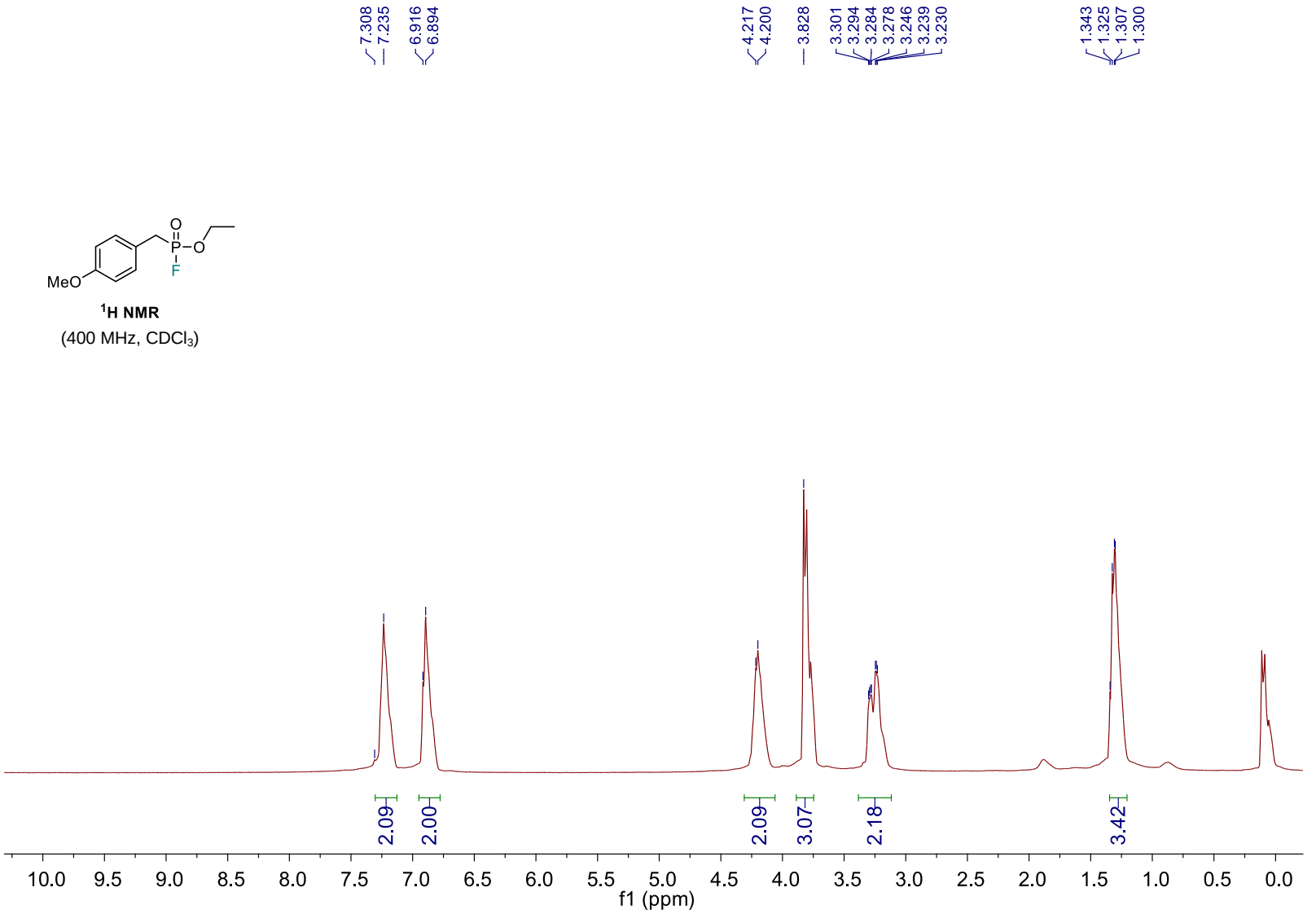
^{31}P NMR

(162 MHz, $CDCl_3$)



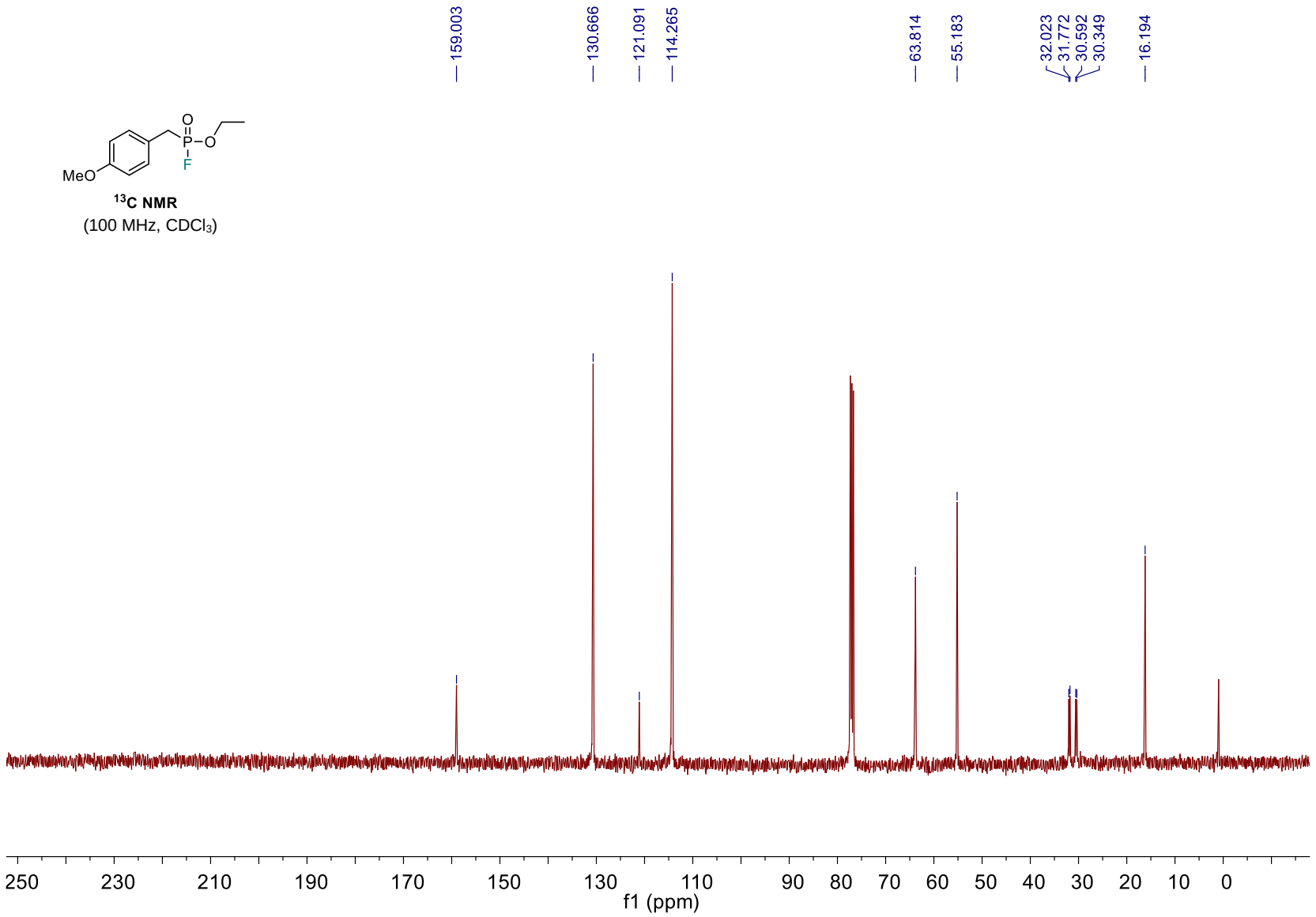
^{19}F NMR

(376 MHz, $CDCl_3$)



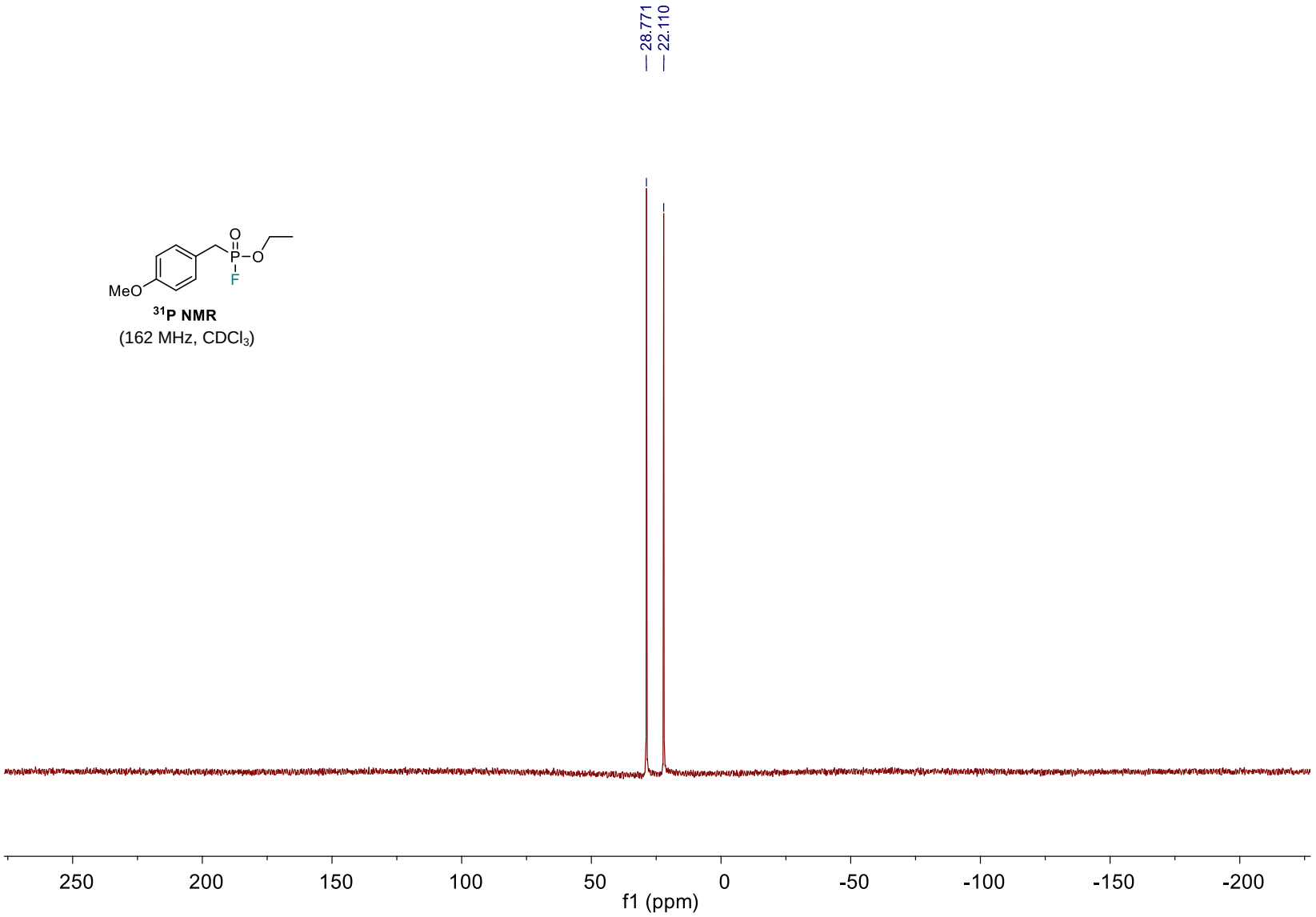
^{1}H NMR

(400 MHz, $CDCl_3$)



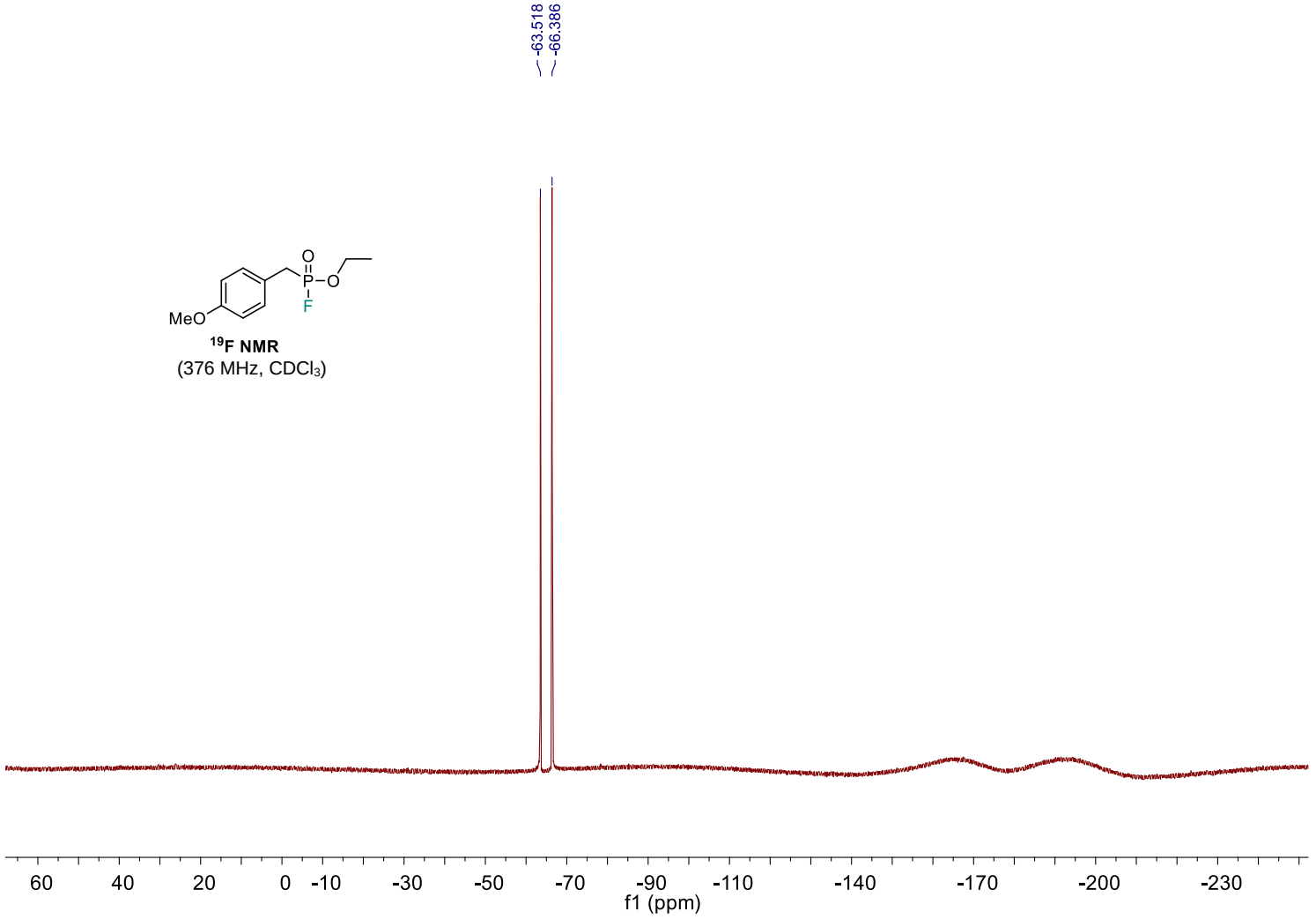
^{13}C NMR

(100 MHz, $CDCl_3$)

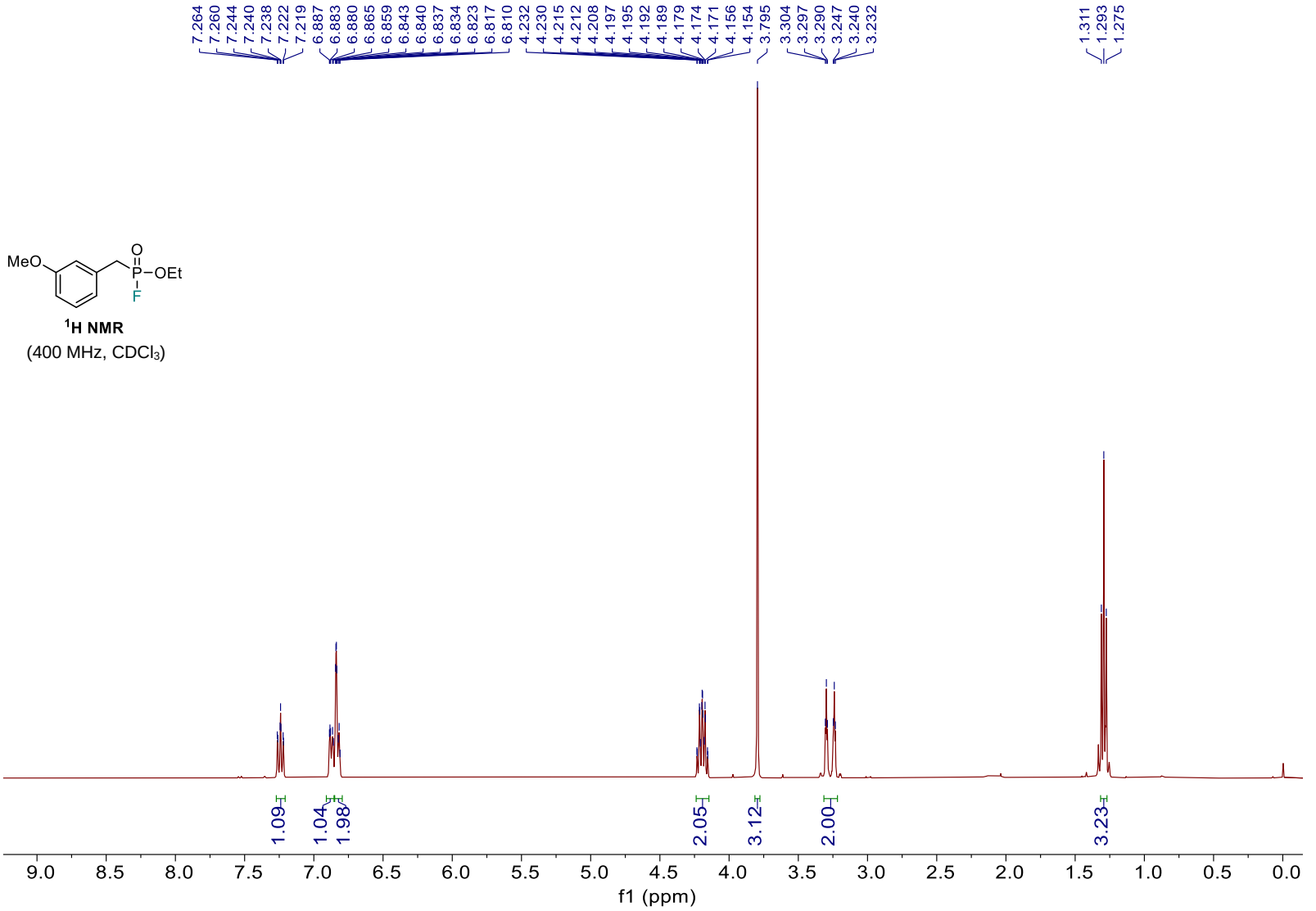


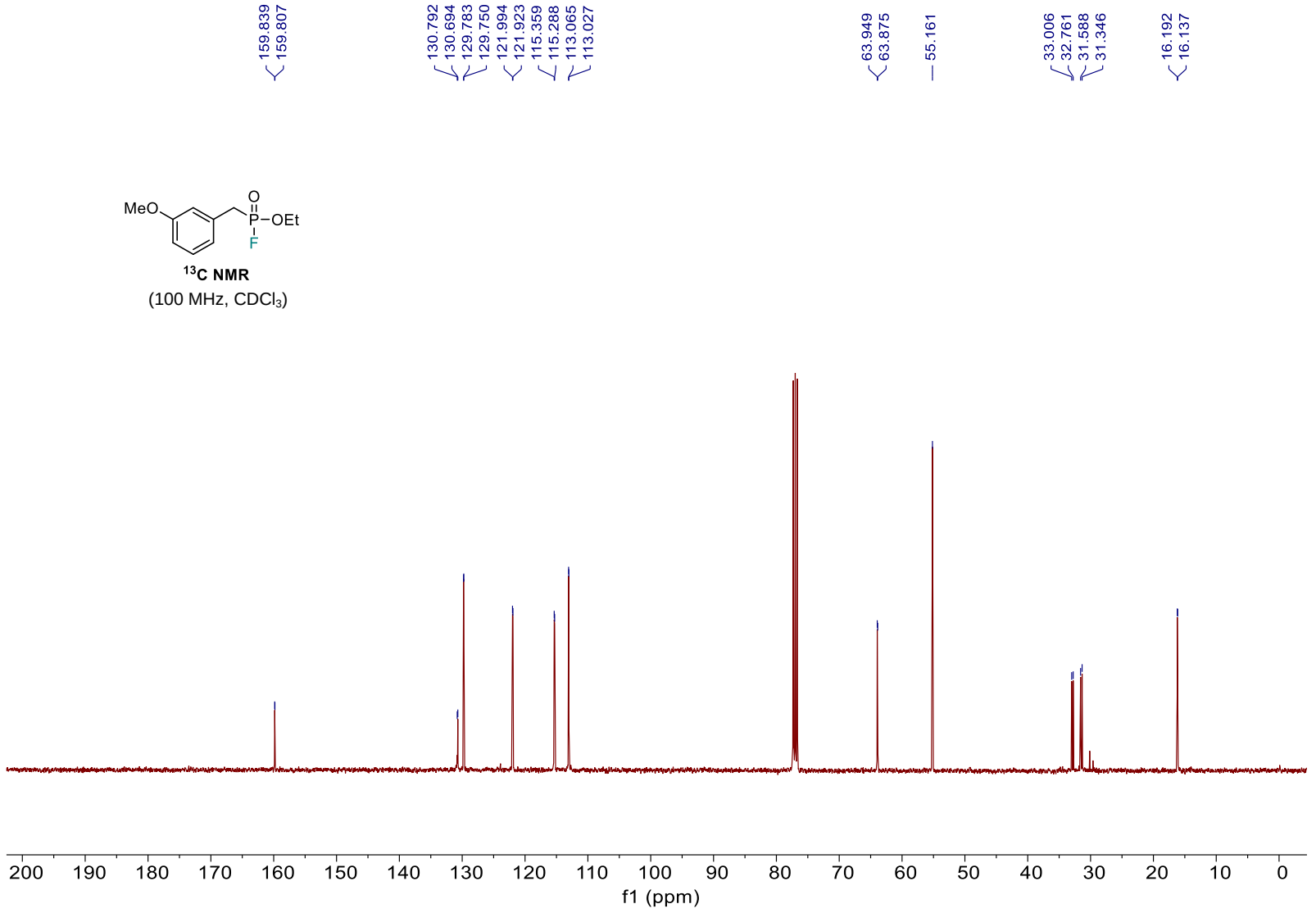
^{31}P NMR

(162 MHz, $CDCl_3$)



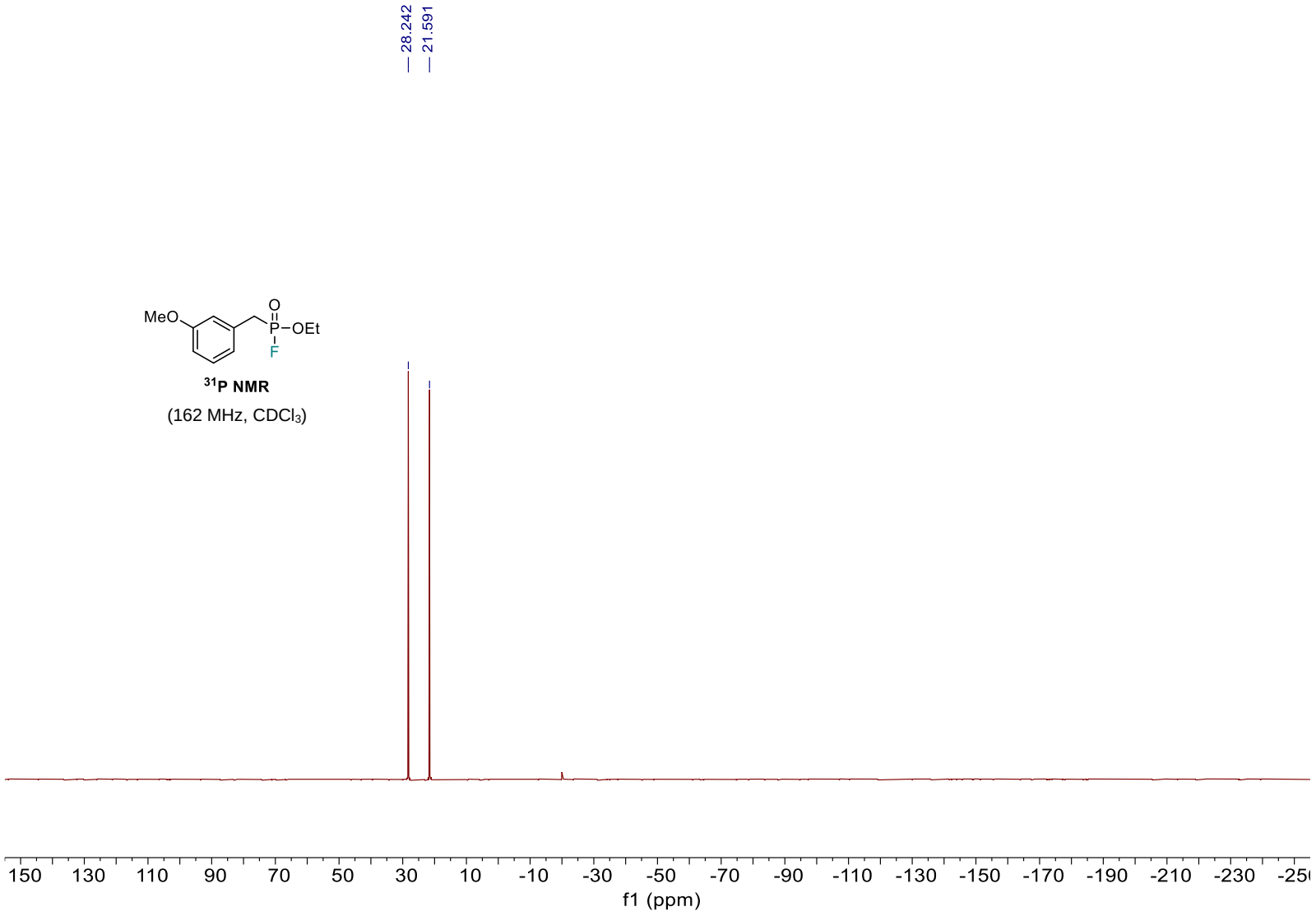
^{19}F NMR
(376 MHz, $CDCl_3$)

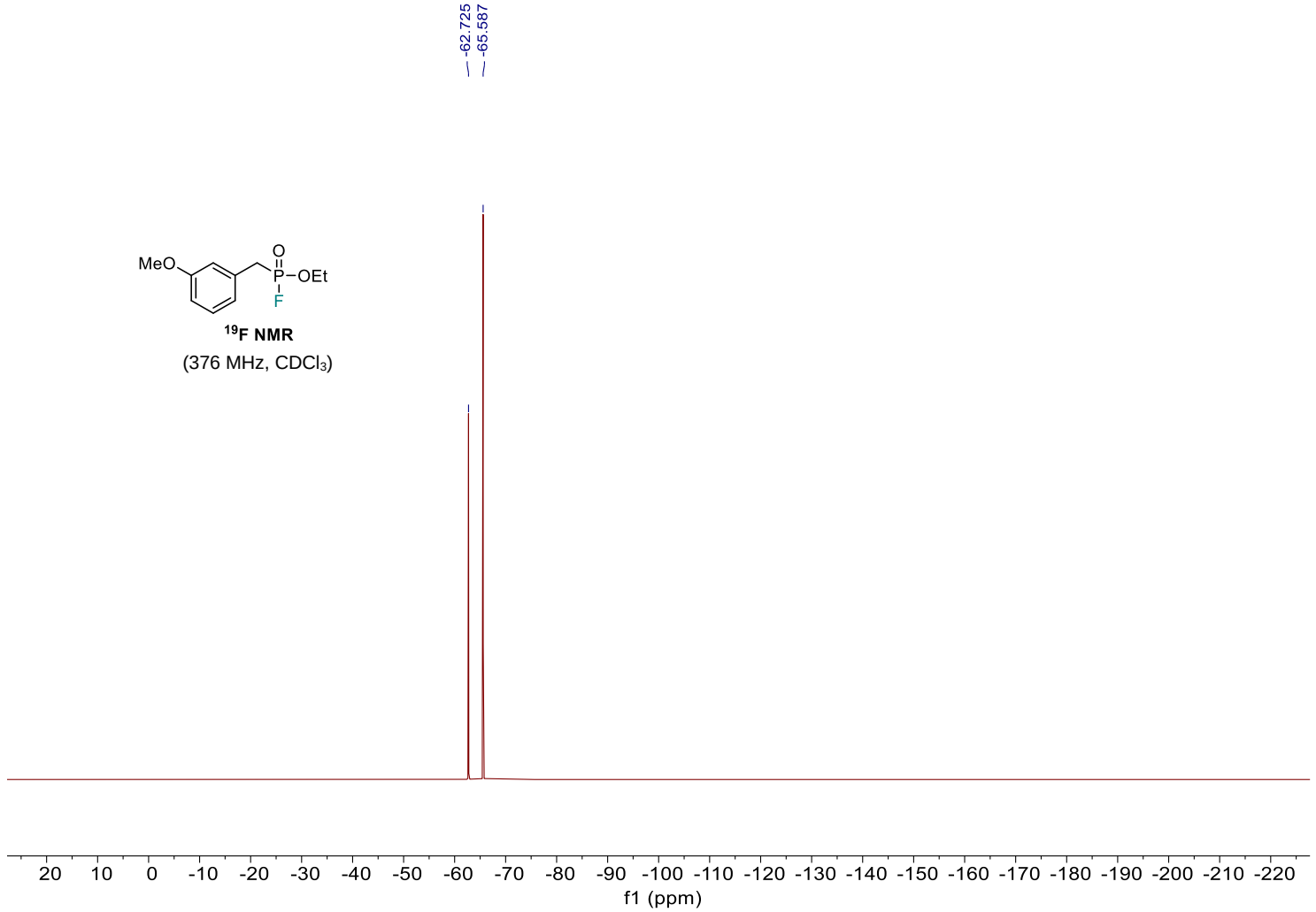

7.264
7.260
7.244
7.240
7.238
7.222
7.219
6.887
6.883
6.880
6.865
6.859
6.843
6.840
6.837
6.834
6.823
6.817
6.810
4.232
4.230
4.215
4.212
4.208
4.197
4.195
4.192
4.189
4.179
4.174
4.171
4.156
4.154
3.795
3.304
3.297
3.290
3.247
3.240
3.232
1.311
1.293
1.275
MeO
O
P
OEt
F
1H NMR
(400 MHz, CDCl3)
1.09
1.04
1.98
2.05
3.12
2.00
3.23
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



^{13}C NMR

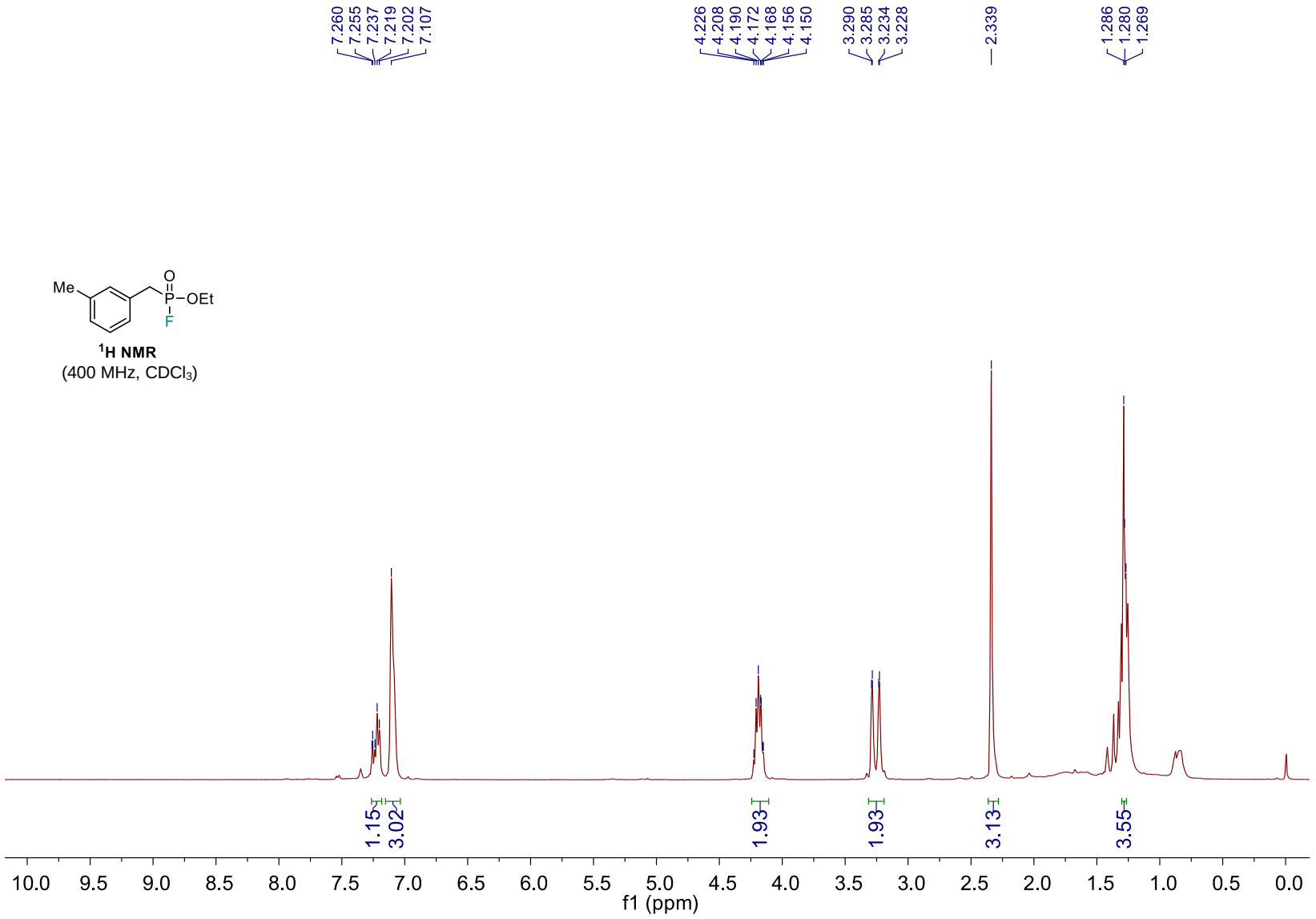
(100 MHz, $CDCl_3$)

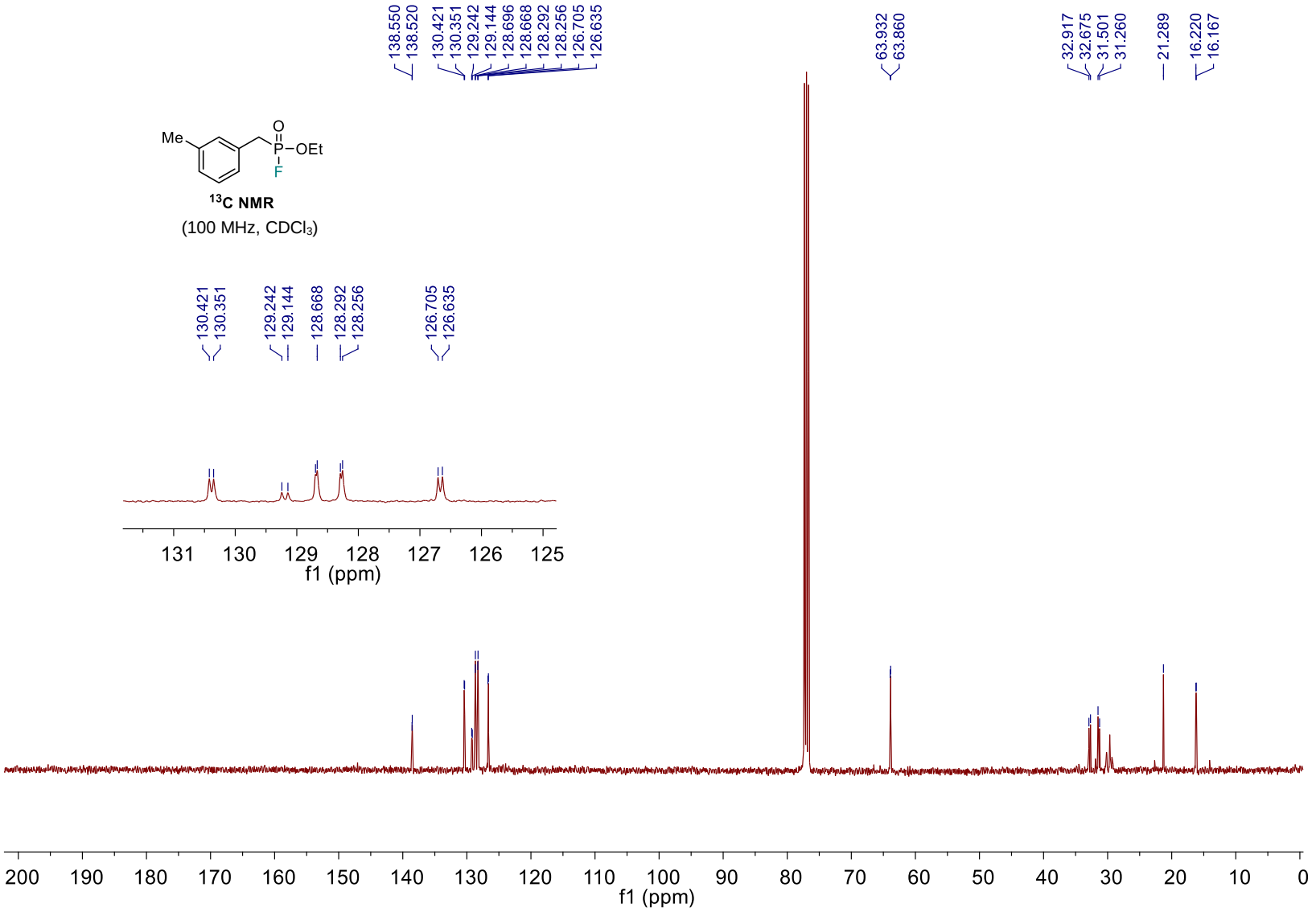

28.242
21.591
MeO
O
P
OEt
F
31P NMR
(162 MHz, CDCl3)
150 130 110 90 70 50 30 10 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190 -210 -230
f1 (ppm)

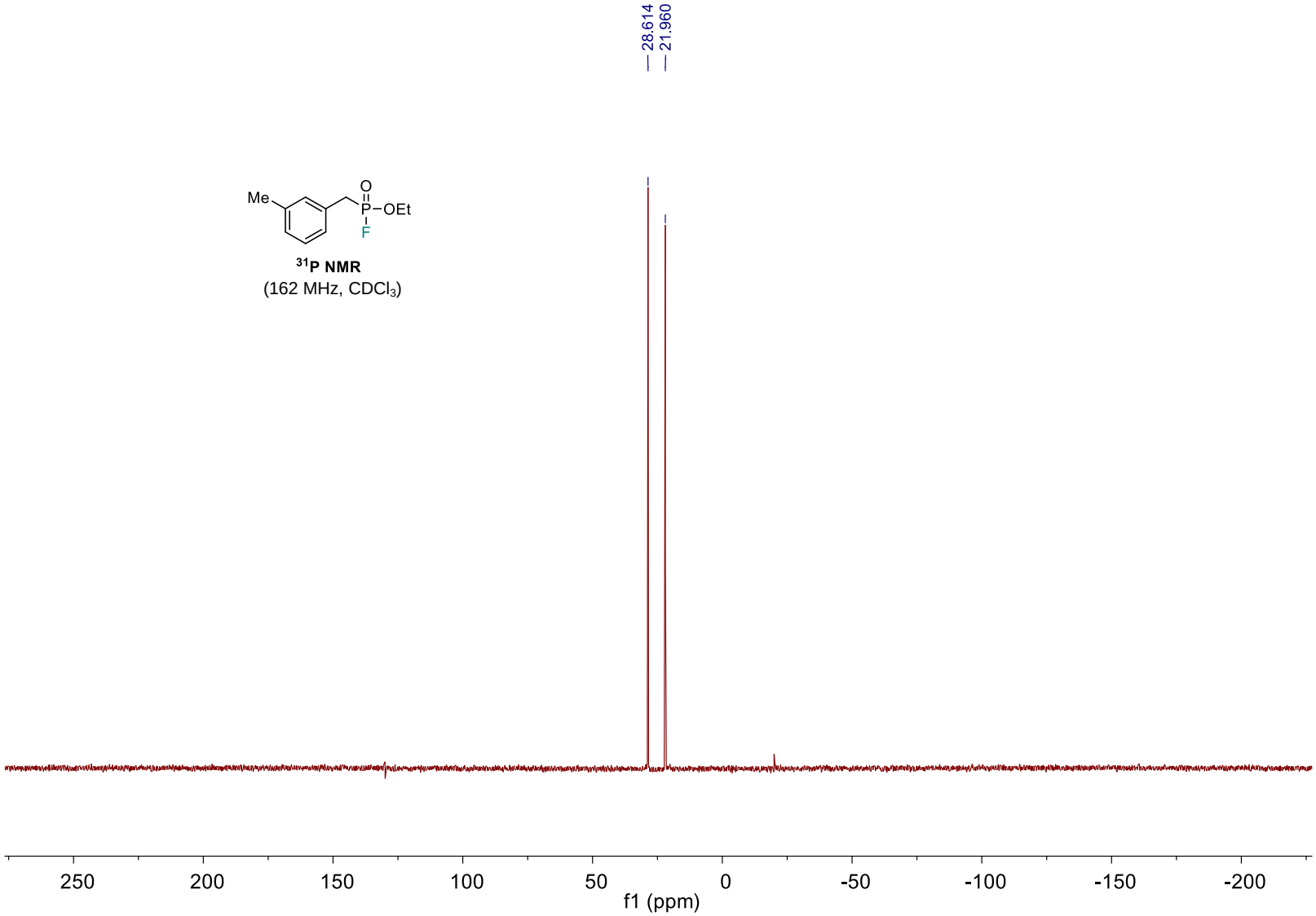


^{19}F NMR

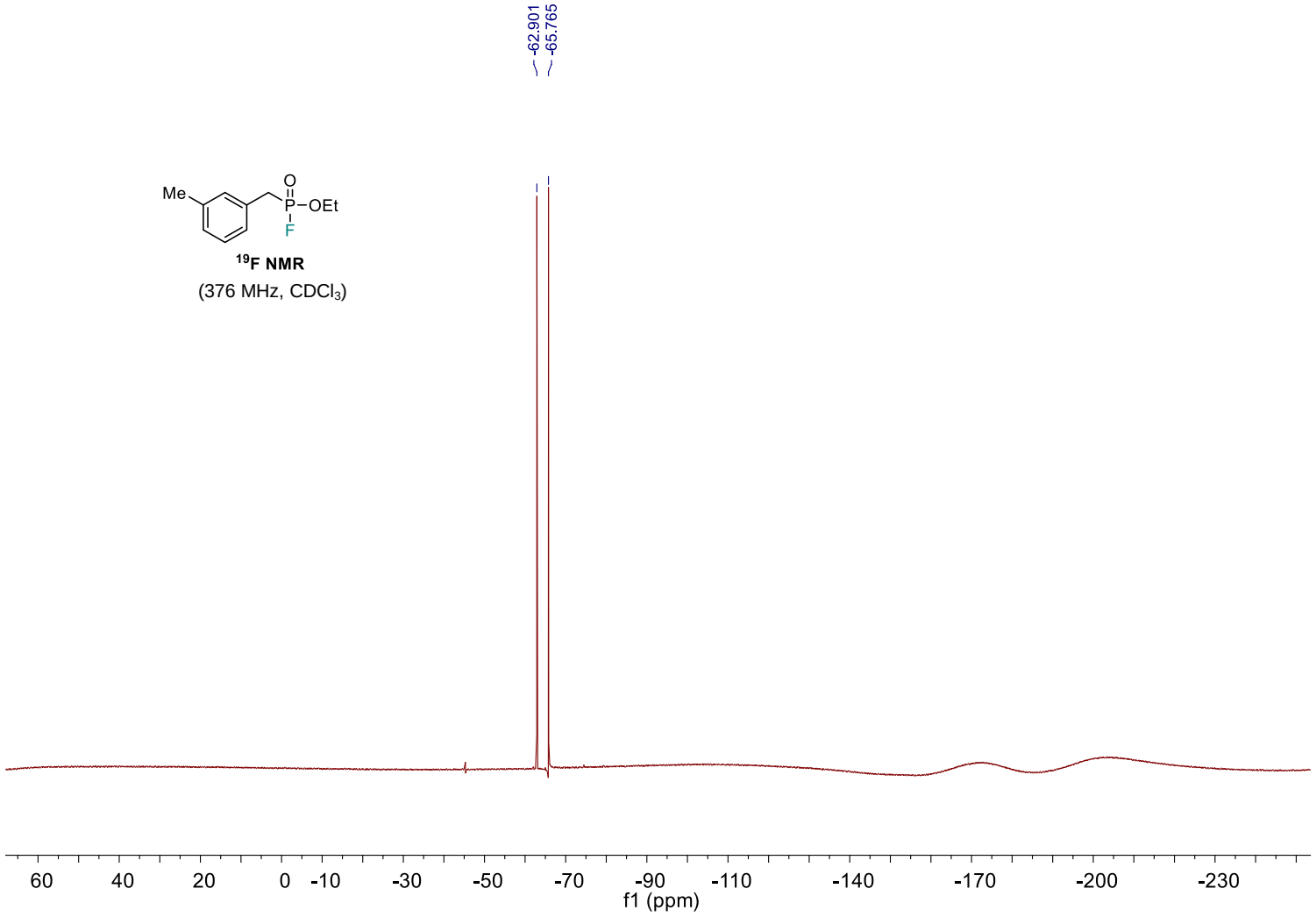
(376 MHz, $CDCl_3$)


7.260
7.255
7.237
7.219
7.202
7.107
4.226
4.208
4.190
4.172
4.168
4.156
4.150
3.290
3.285
3.234
3.228
2.339
1.286
1.280
1.269
Me
O
P
OEt
F
1H NMR
(400 MHz, CDCl3)
1.15
3.02
1.93
1.93
3.13
3.55
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


138.550
138.520
130.421
130.351
129.242
129.144
128.696
128.668
128.292
128.256
126.705
126.635
63.932
63.860
32.917
32.675
31.501
31.260
21.289
16.220
16.167
Me
O
P–OEt
F
13C NMR
(100 MHz, CDCl3)
130.421
130.351
129.242
129.144
128.668
128.292
128.256
126.705
126.635
131
130
129
128
127
126
125
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

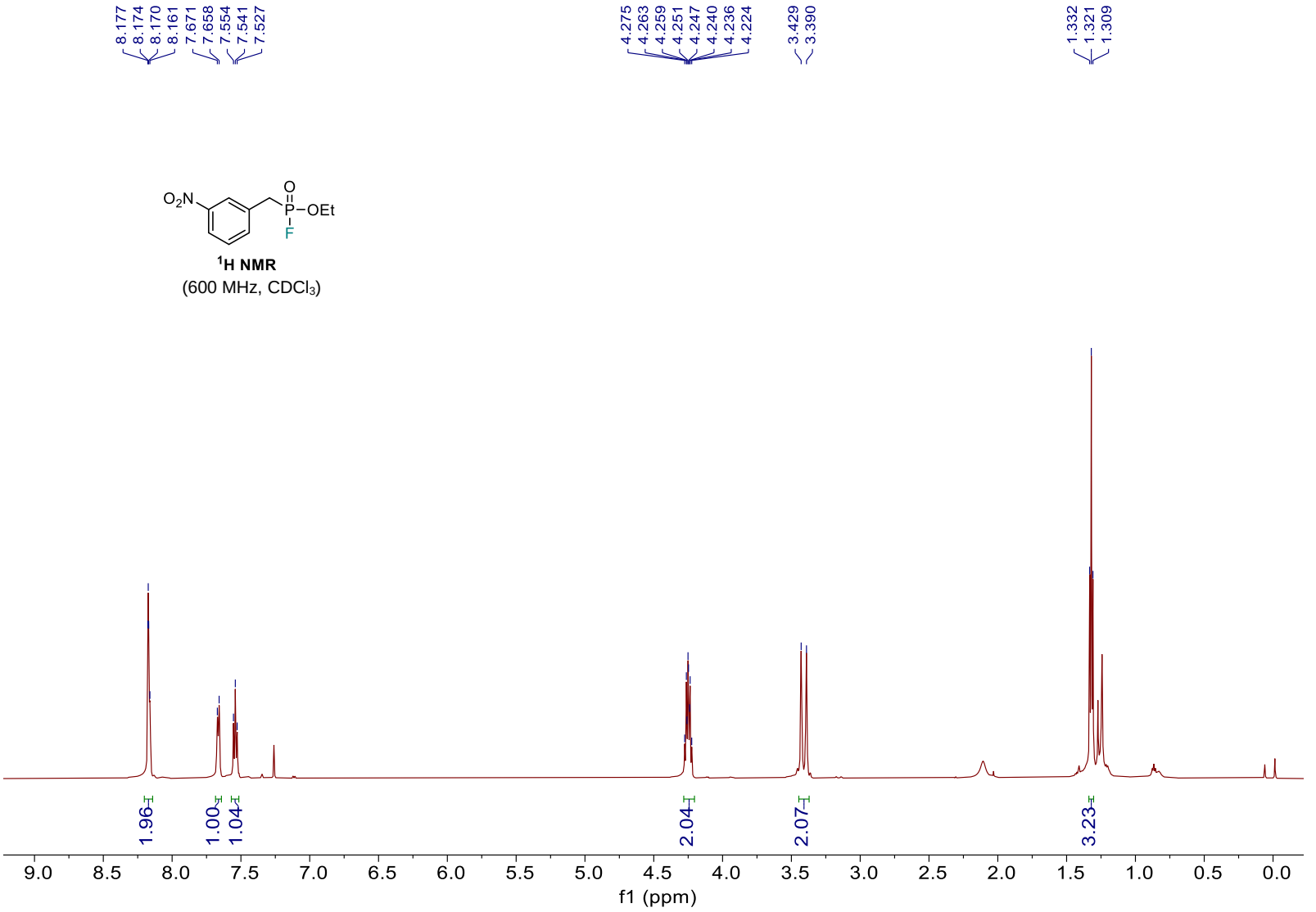


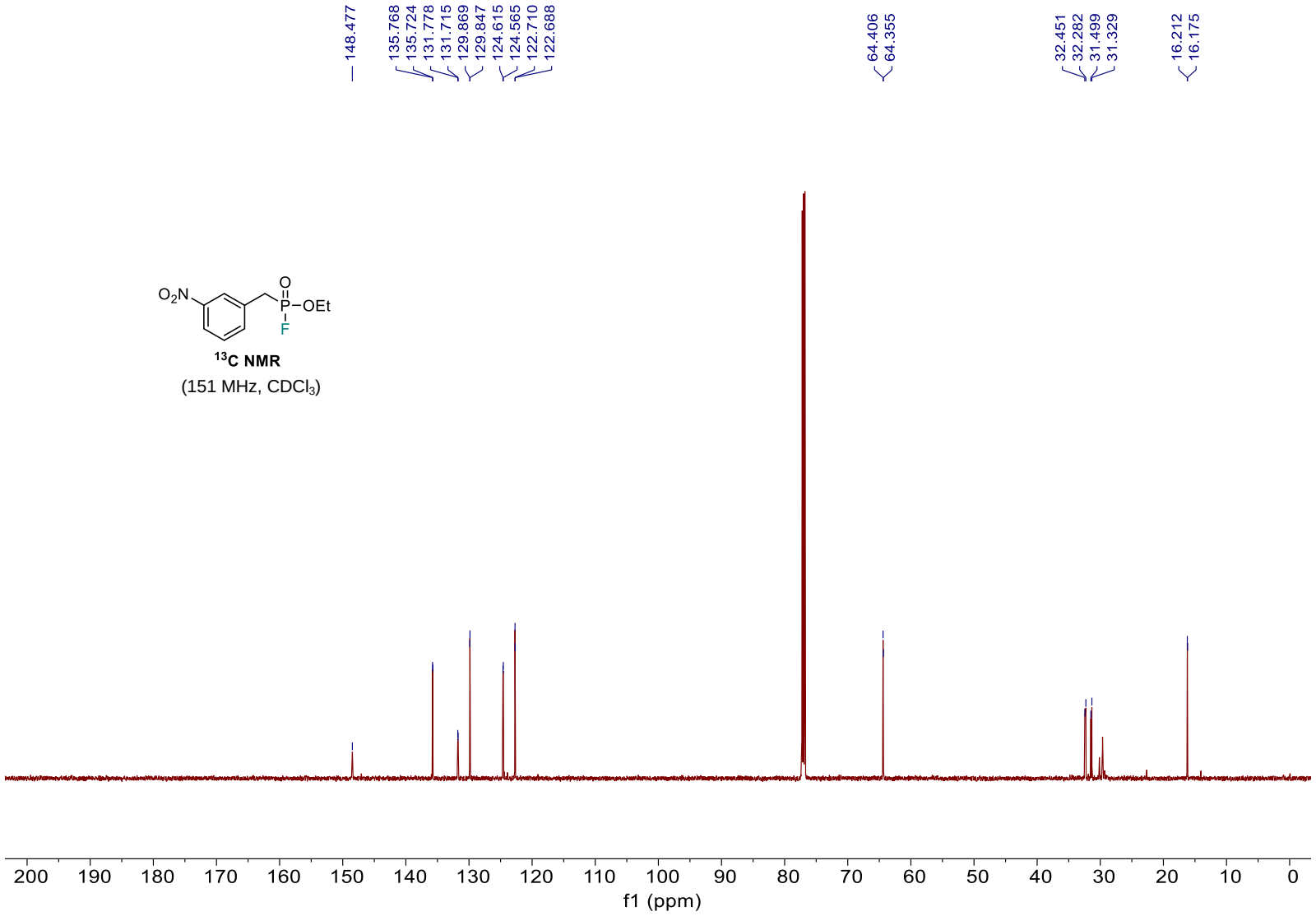
^{31}P NMR
(162 MHz, $CDCl_3$)

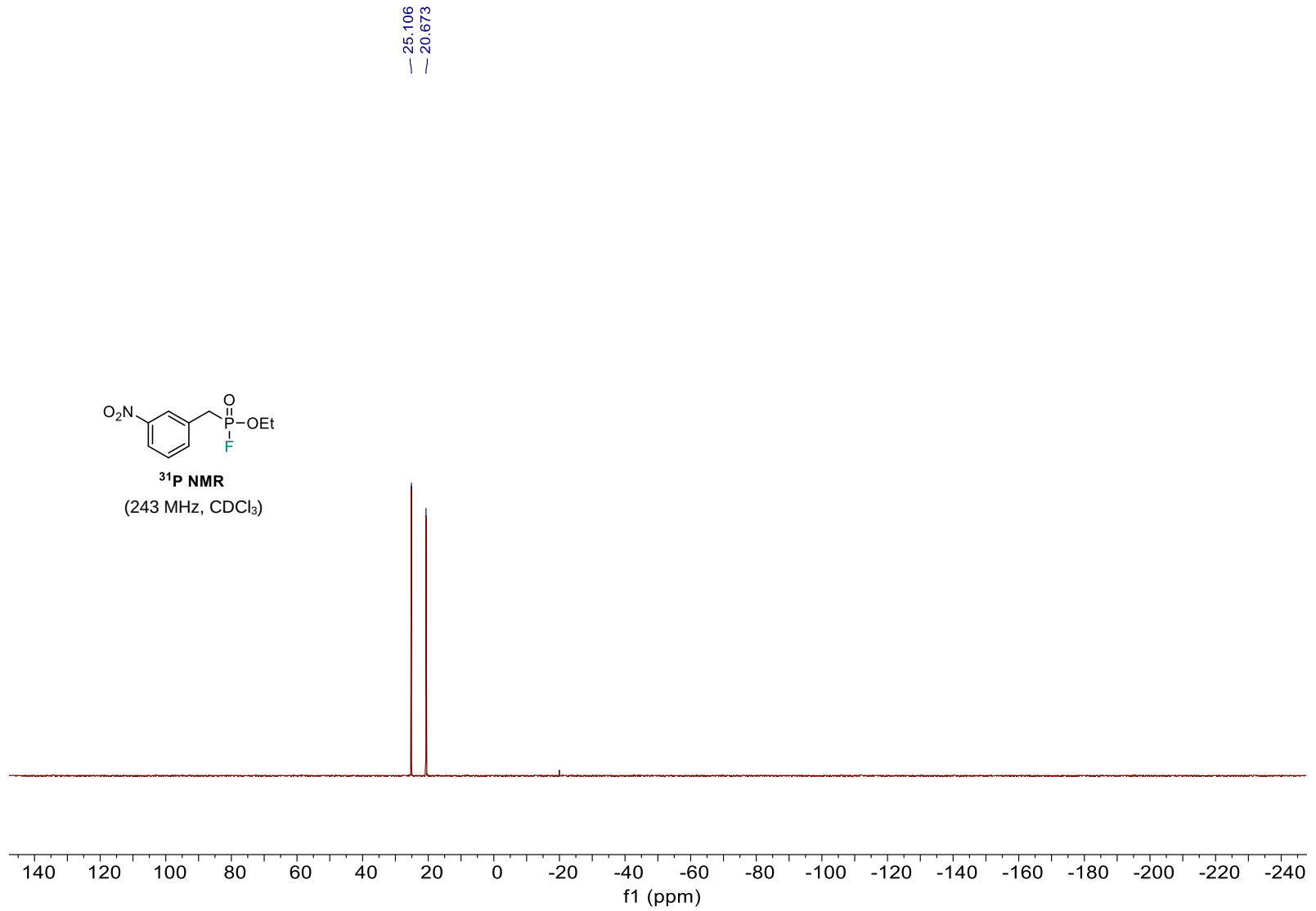


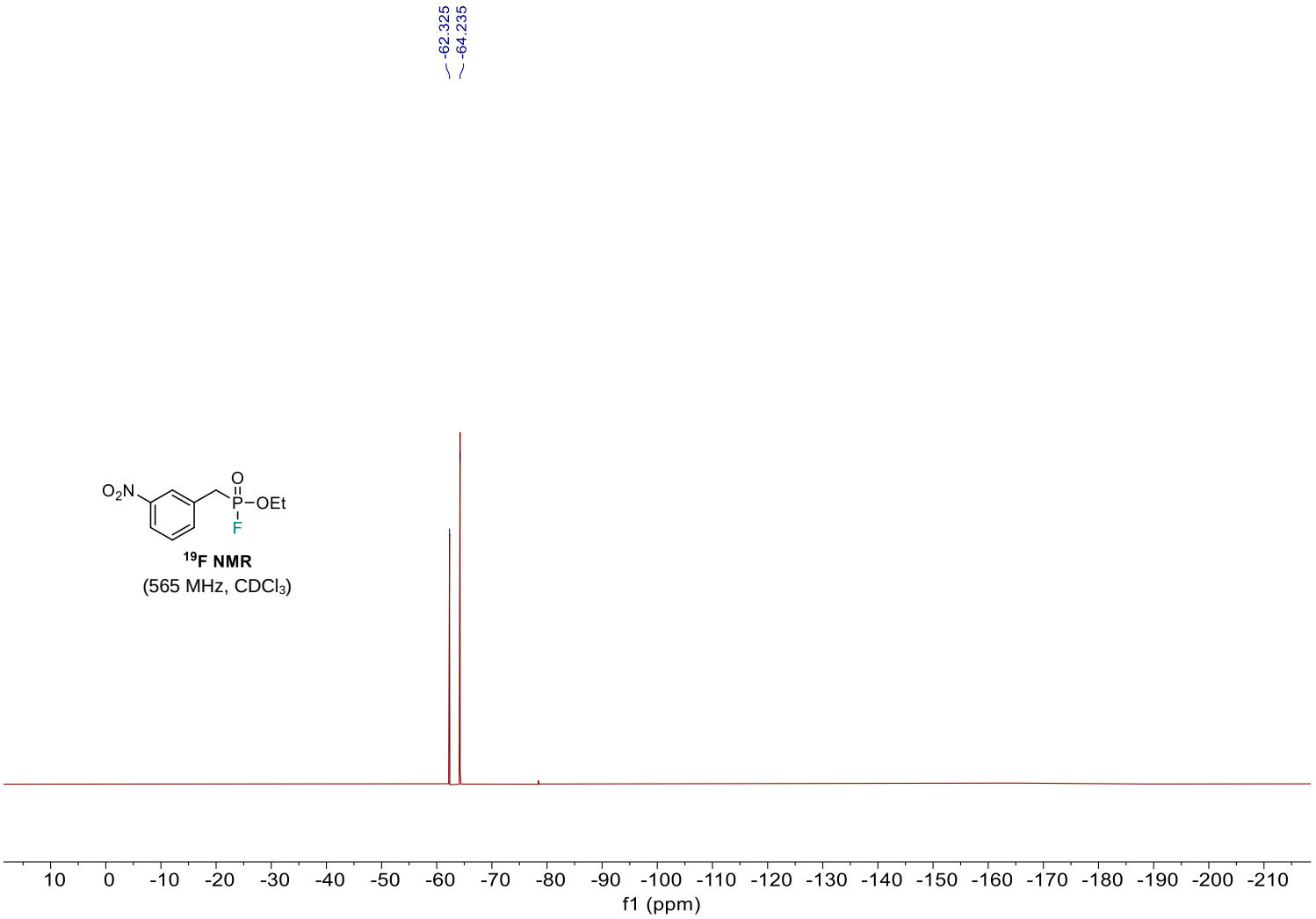
^{19}F NMR

(376 MHz, $CDCl_3$)


8.177
8.174
8.170
8.161
7.671
7.658
7.554
7.541
7.527
4.275
4.263
4.259
4.251
4.247
4.240
4.236
4.224
3.429
3.390
1.332
1.321
1.309
O2N
O
P
OEt
F
1H NMR
(600 MHz, CDCl3)
1.96
1.00
1.04
2.04
2.07
3.23
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

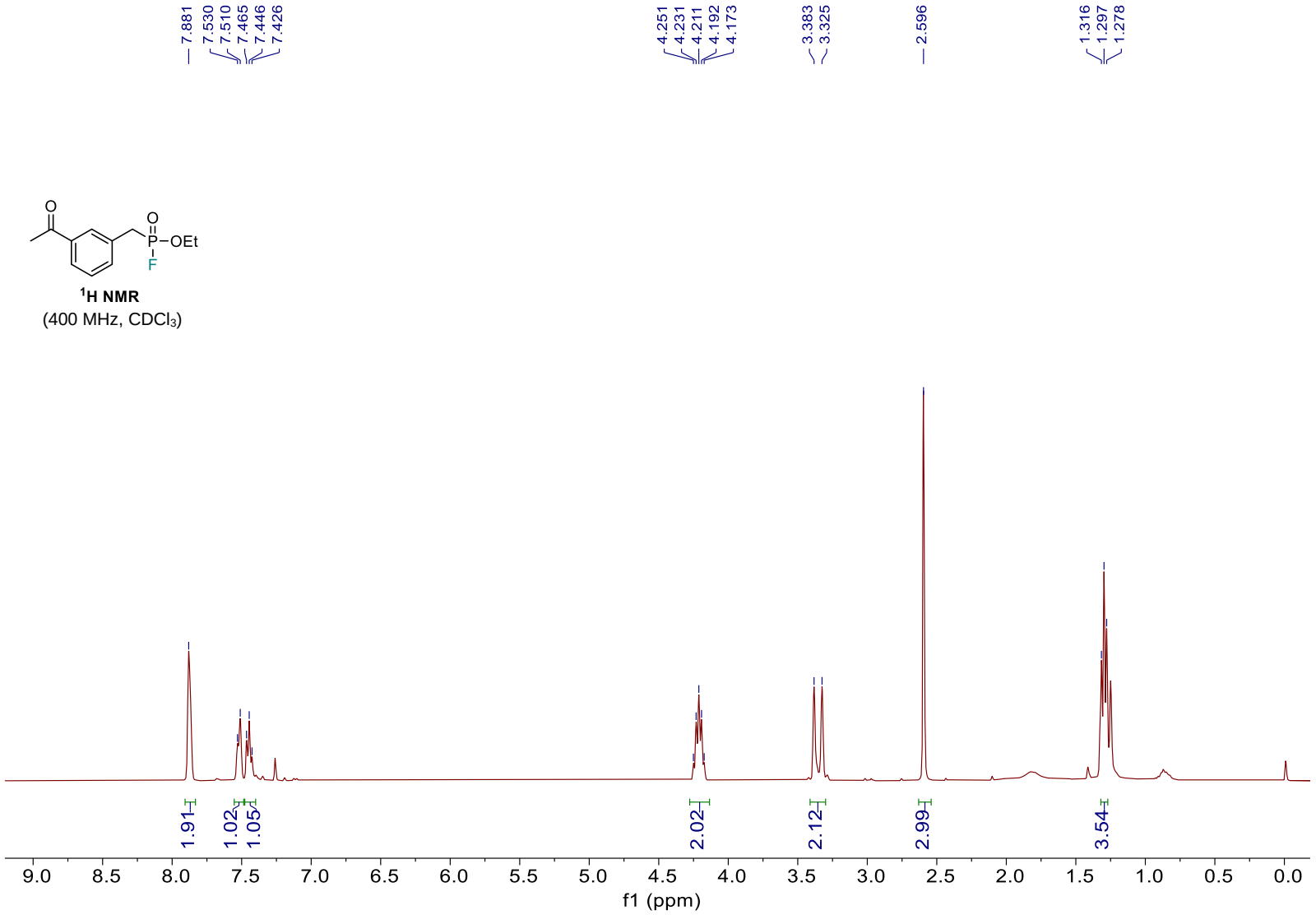

148.477
135.768
135.724
131.778
131.715
129.869
129.847
124.615
124.565
122.710
122.688
64.406
64.355
32.451
32.282
31.499
31.329
16.212
16.175
O2N
O
P
OEt
F
13C NMR
(151 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

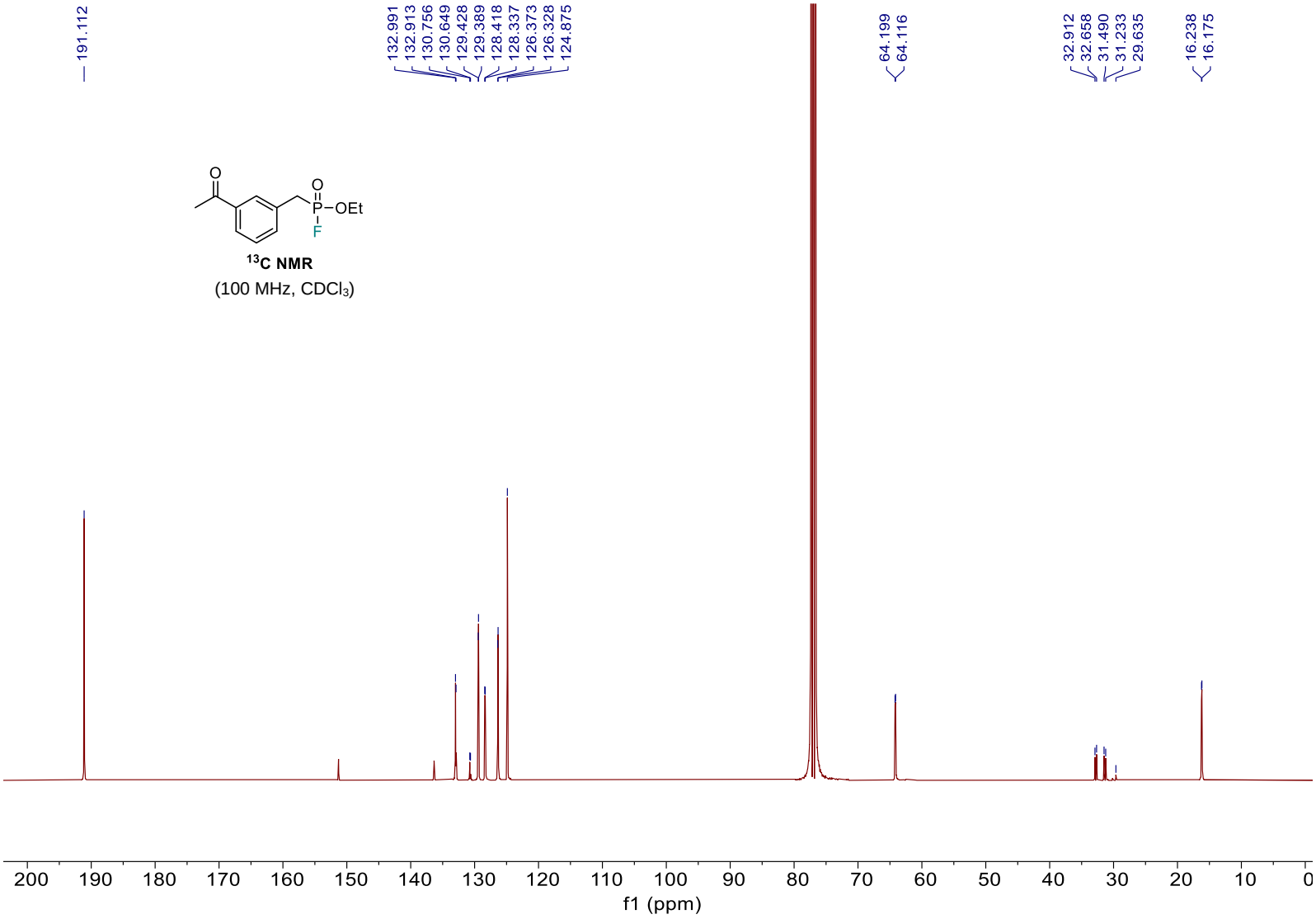

25.106
20.673
O2N
O
P–OEt
F
31P NMR
(243 MHz, CDCl3)
140 120 100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240
f1 (ppm)

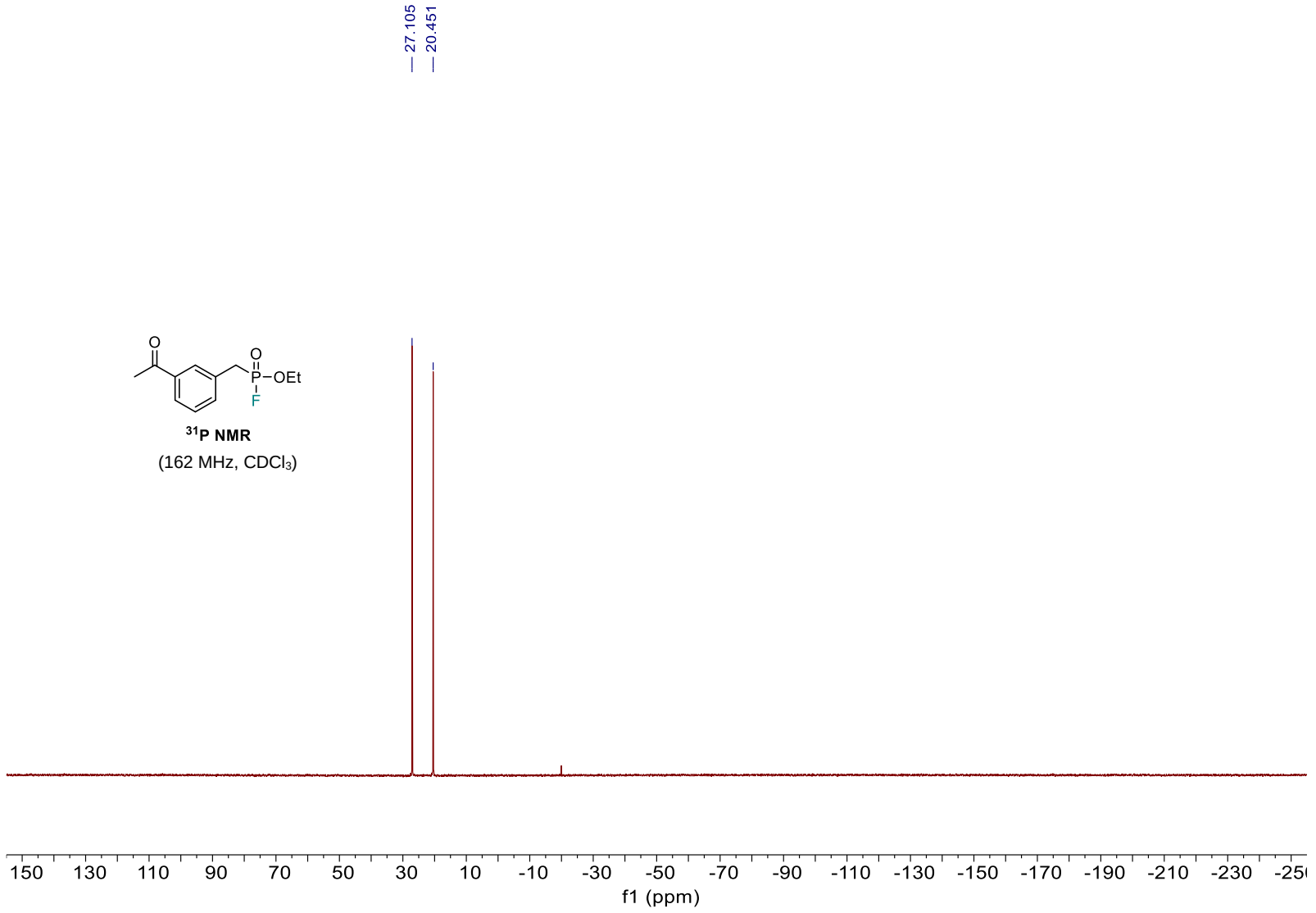


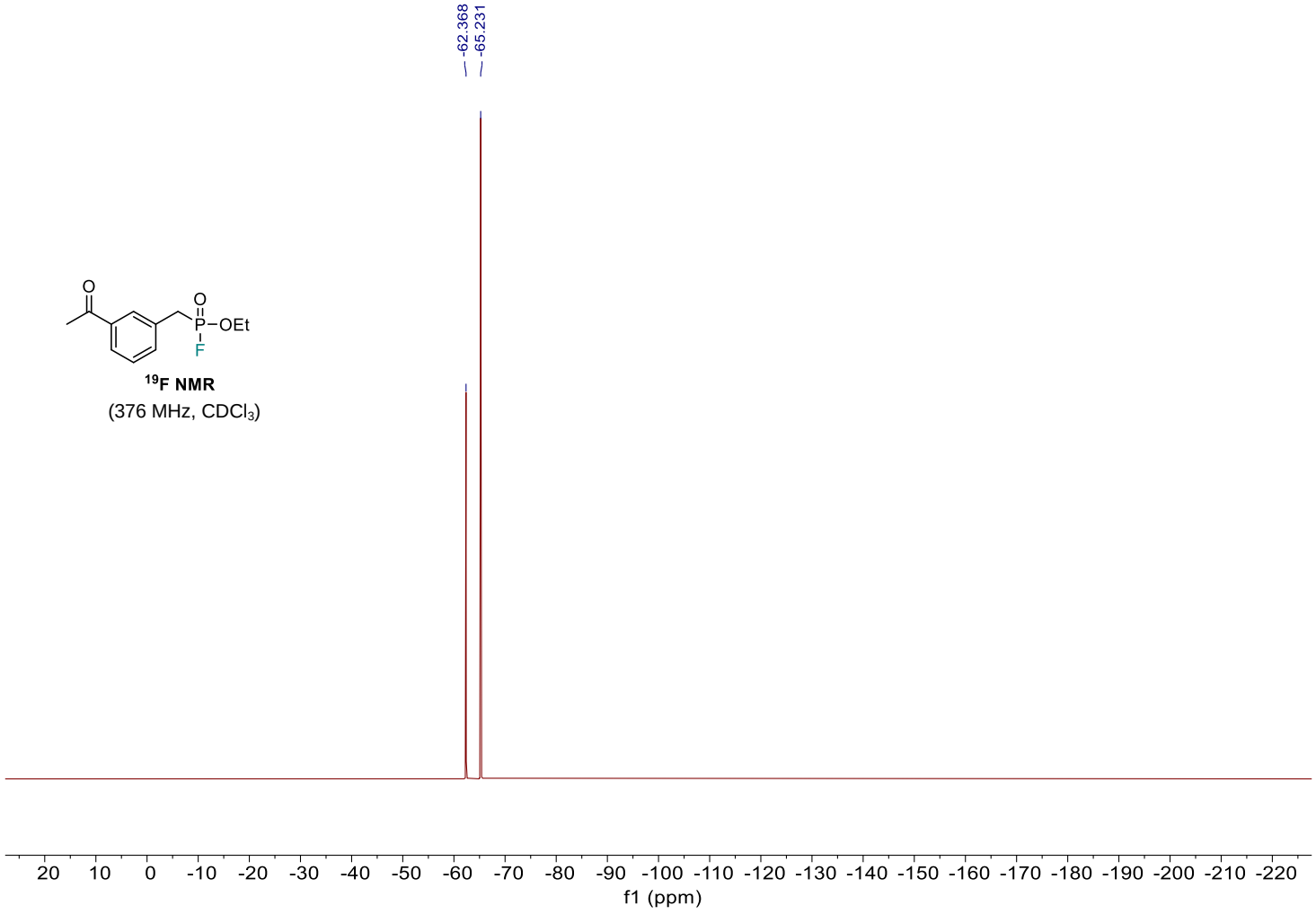
^{19}F NMR

(565 MHz, $CDCl_3$)


7.881
7.530
7.510
7.465
7.446
7.426
4.251
4.231
4.211
4.192
4.173
3.383
3.325
2.596
1.316
1.297
1.278
O
O
P
OEt
F
1H NMR
(400 MHz, CDCl3)
1.91
1.02
1.05
2.02
2.12
2.99
3.54
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

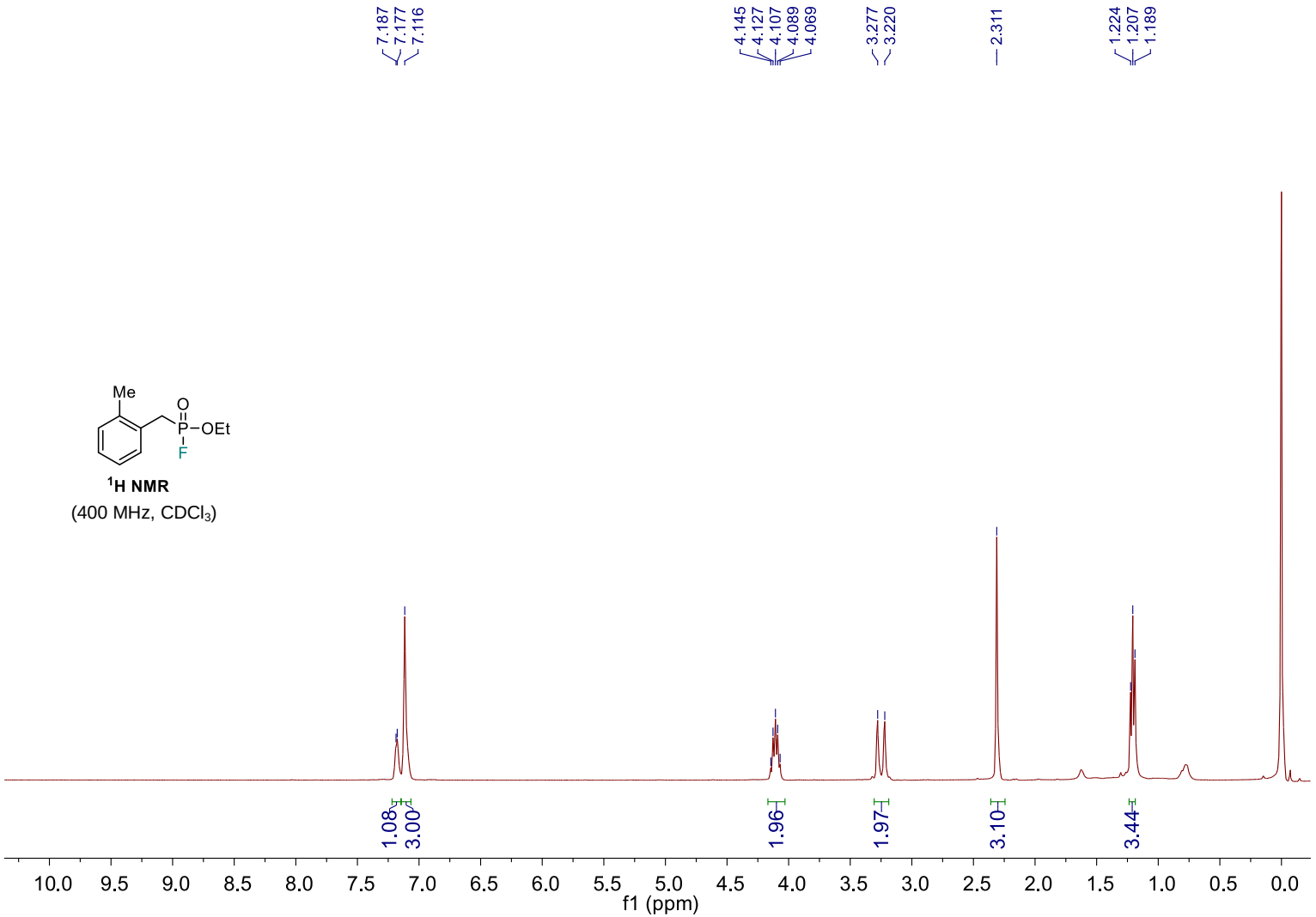

191.112
132.991
132.913
130.756
130.649
129.428
129.389
128.418
128.337
126.373
126.328
124.875
64.199
64.116
32.912
32.658
31.490
31.233
29.635
16.238
16.175
O
O
P–OEt
F
13C NMR
(100 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

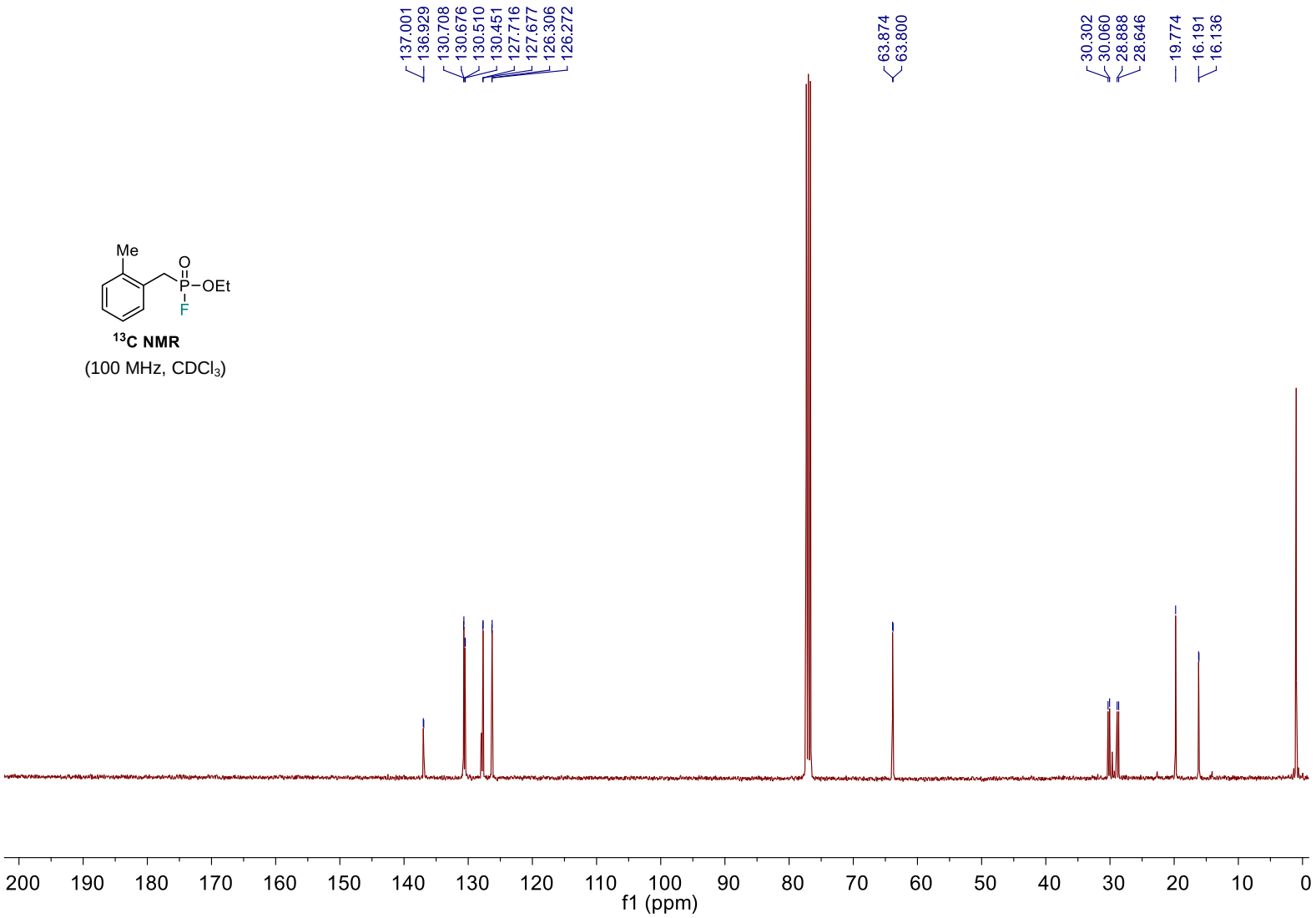

27.105
20.451
O
O
P
OEt
F
31P NMR
(162 MHz, CDCl3)
150 130 110 90 70 50 30 10 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190 -210 -230
f1 (ppm)

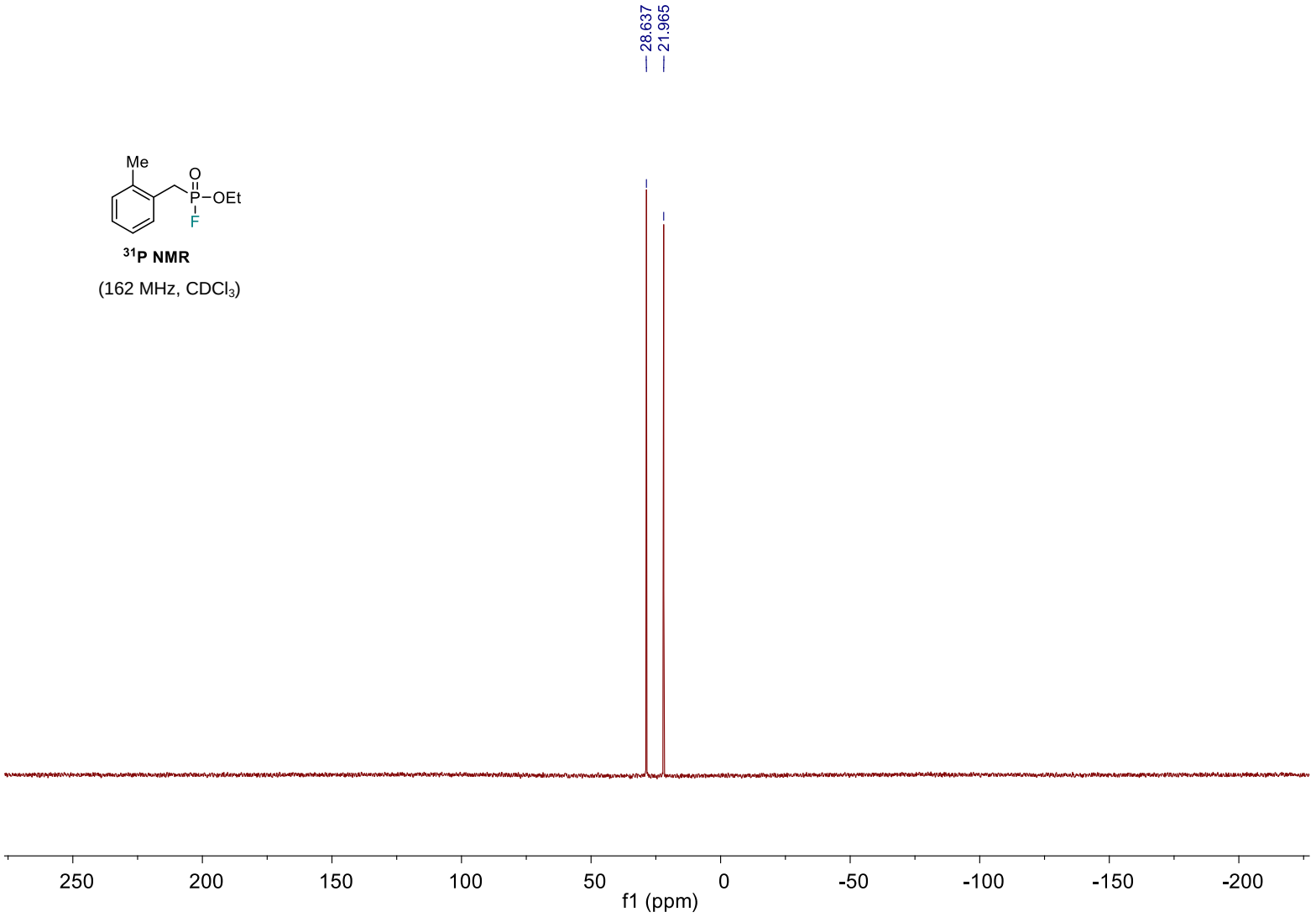


^{19}F NMR

(376 MHz, $CDCl_3$)

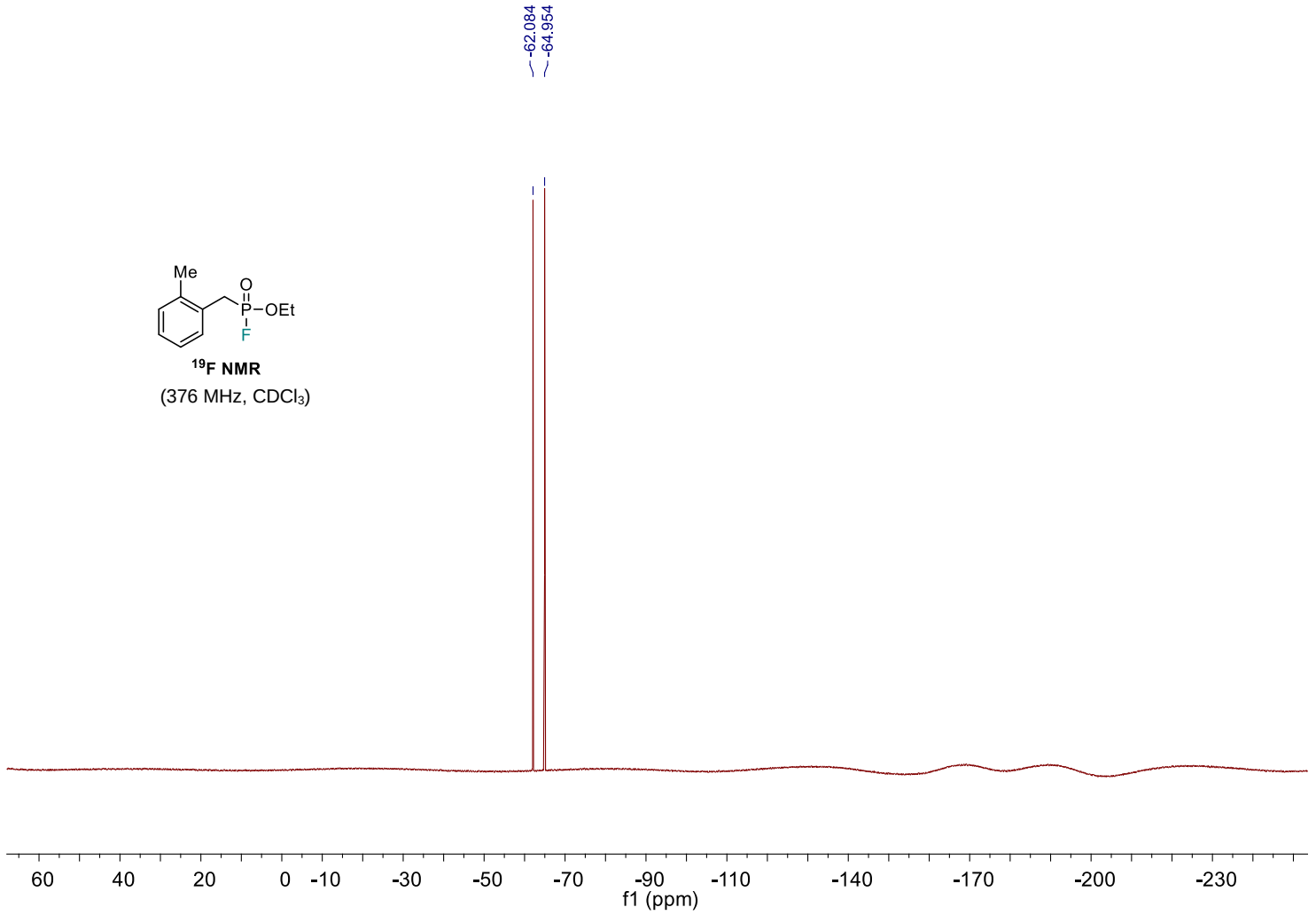

7.187
7.177
7.116
4.145
4.127
4.107
4.089
4.069
3.277
3.220
2.311
1.224
1.207
1.189
Me
O
P
OEt
F
1H NMR
(400 MHz, CDCl3)
1.08
3.00
1.96
1.97
3.10
3.44
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


137.001
136.929
130.708
130.676
130.510
130.451
127.716
127.677
126.306
126.272
63.874
63.800
30.302
30.060
28.888
28.646
19.774
16.191
16.136
Me
O
P–OEt
F
13C NMR
(100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



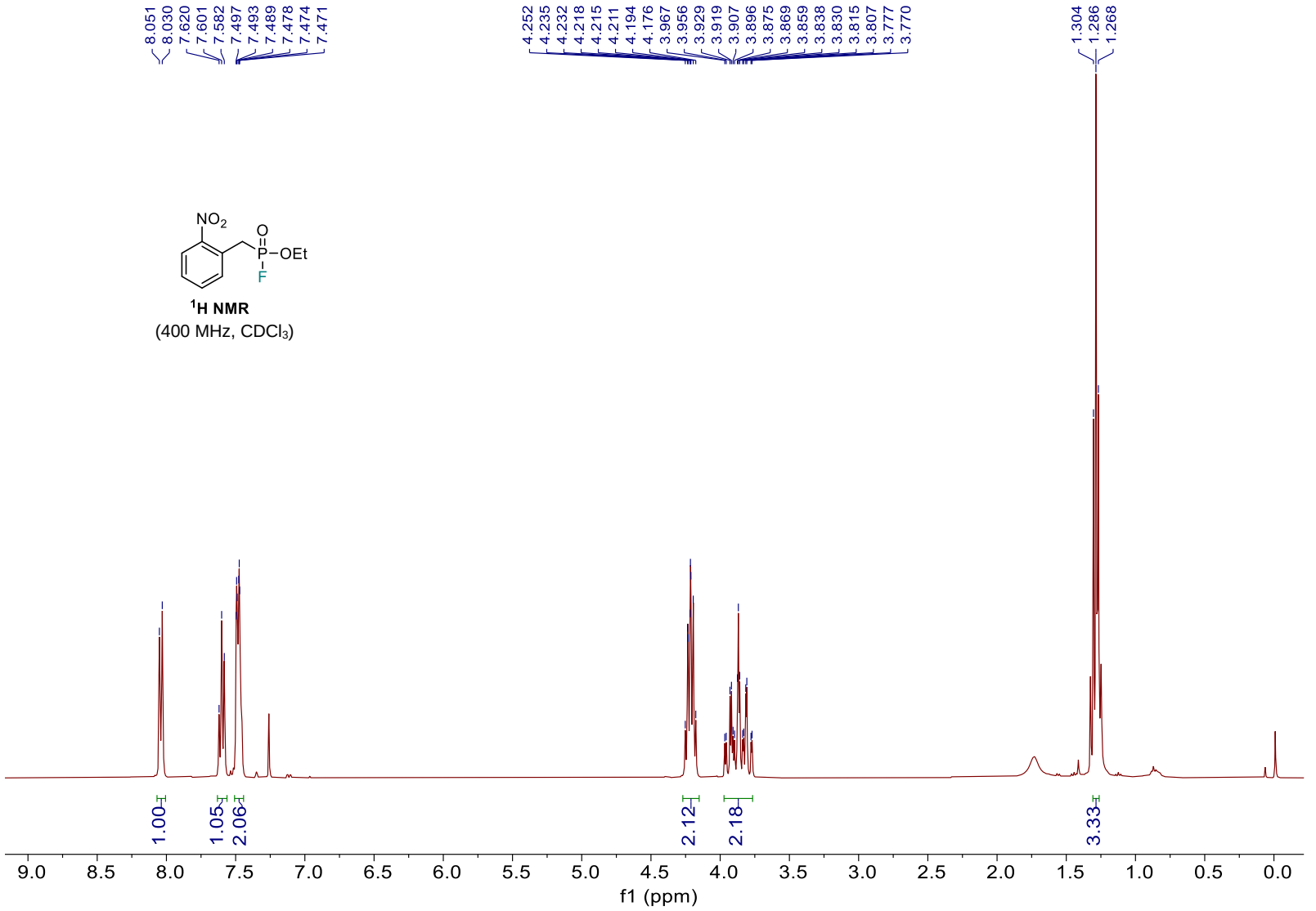
^{31}P NMR

(162 MHz, $CDCl_3$)

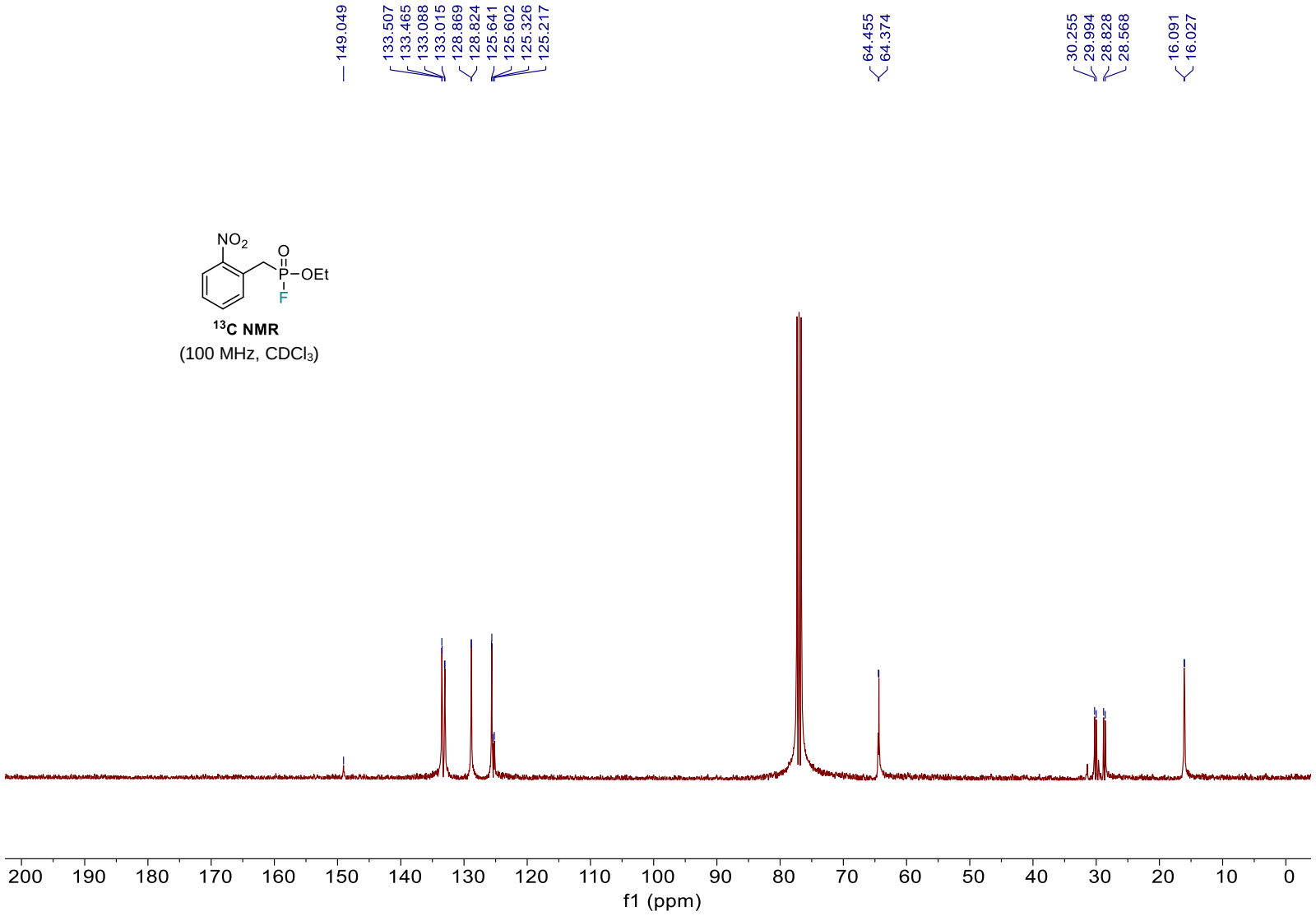


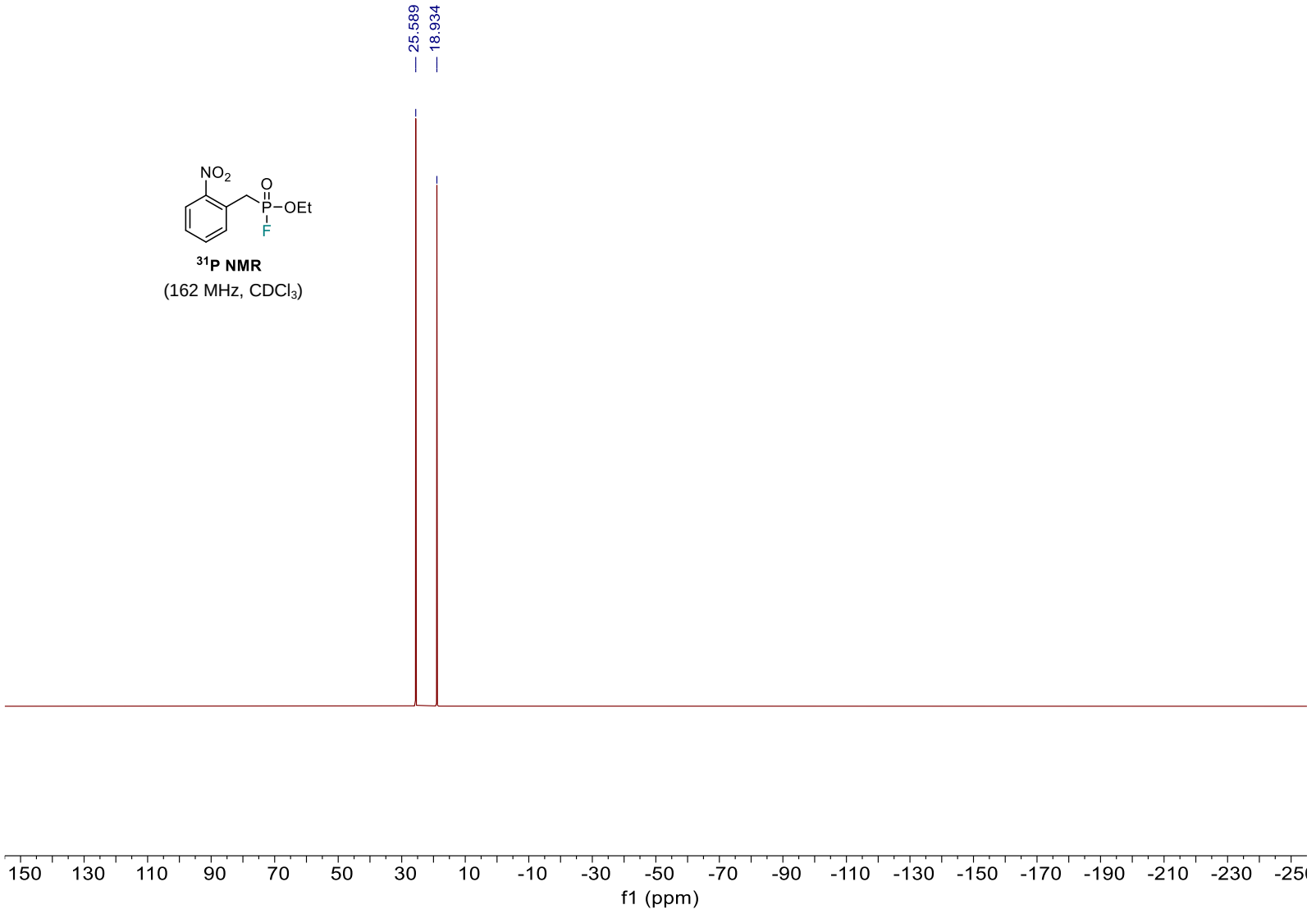
^{19}F NMR

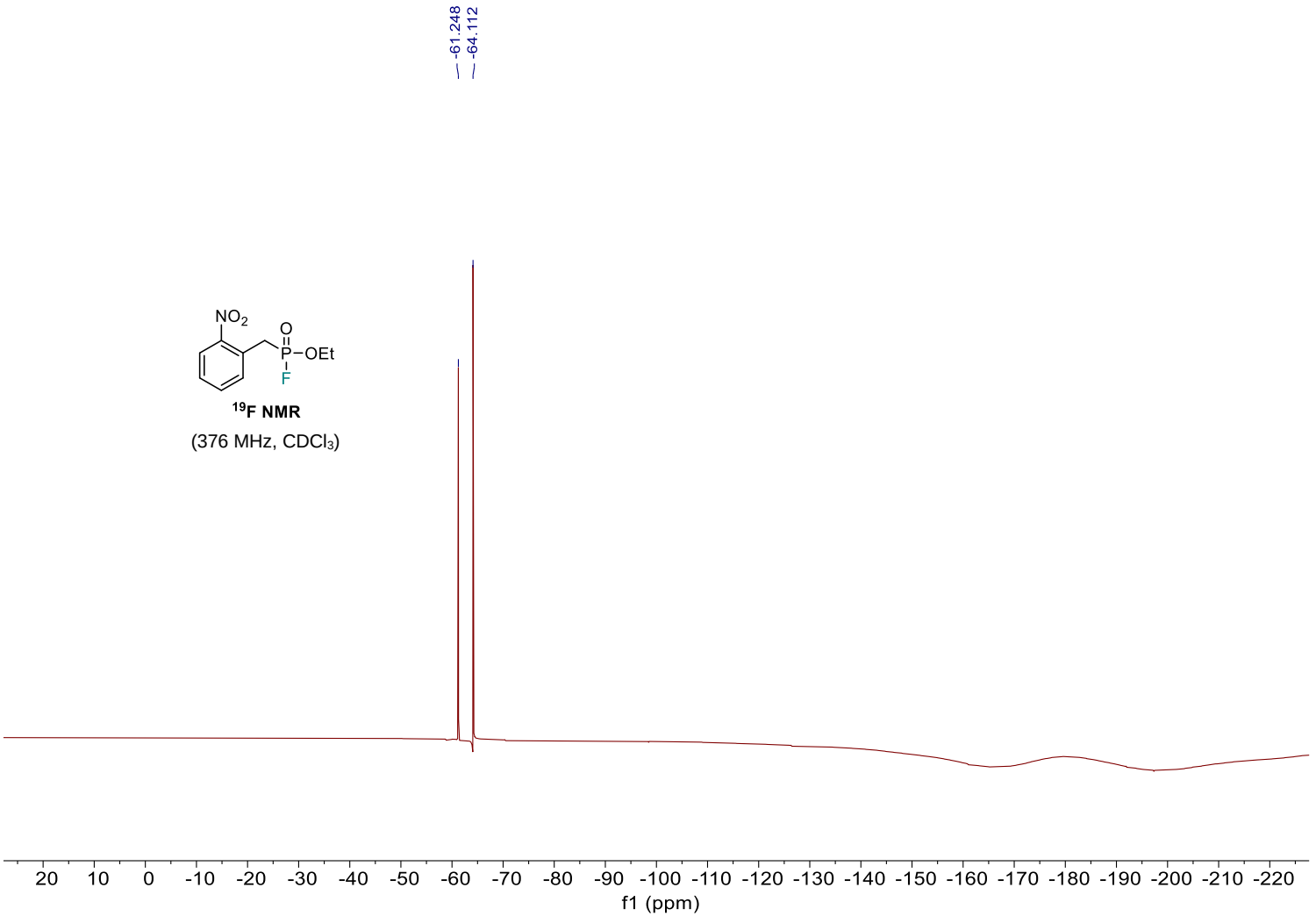
(376 MHz, $CDCl_3$)

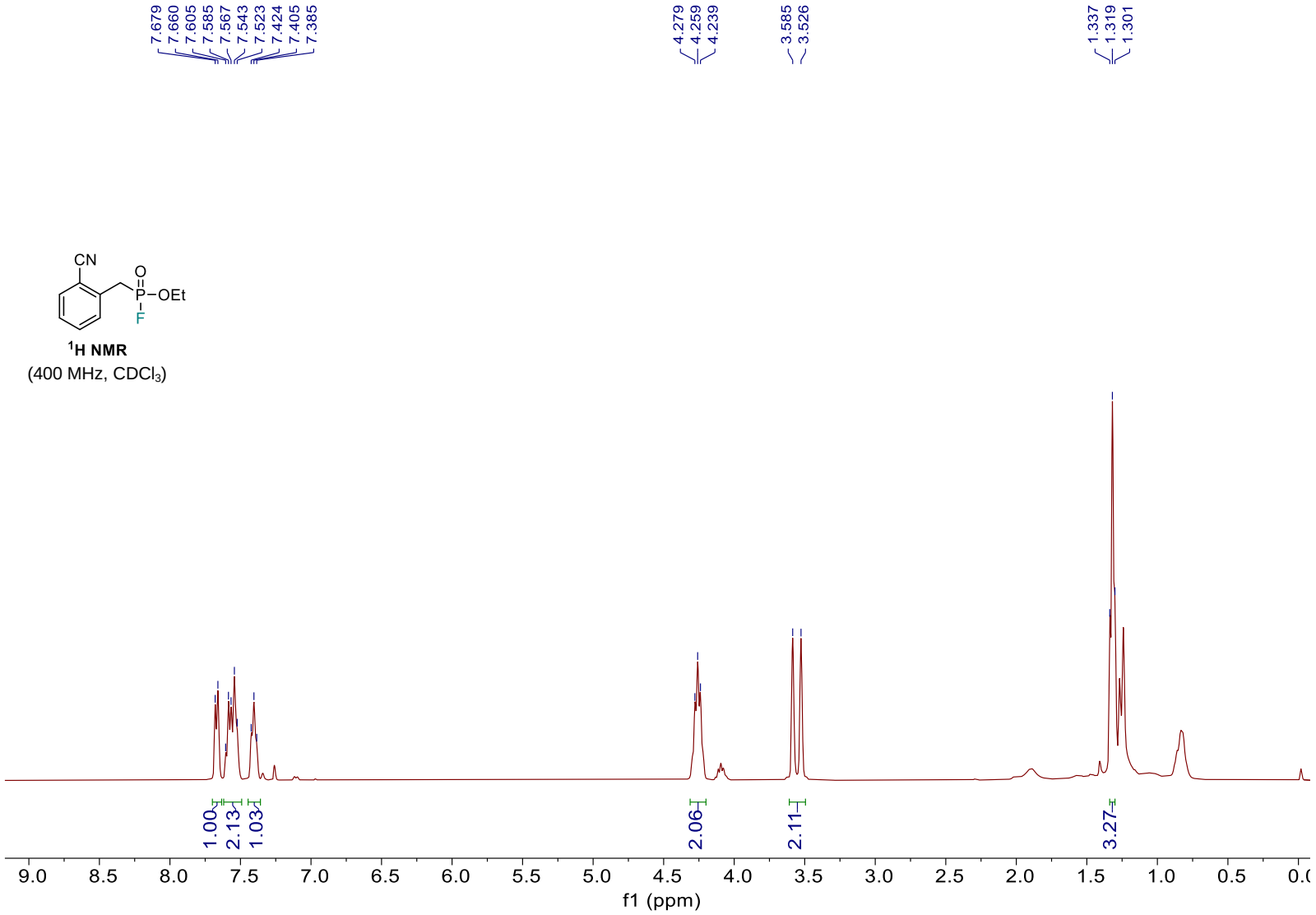


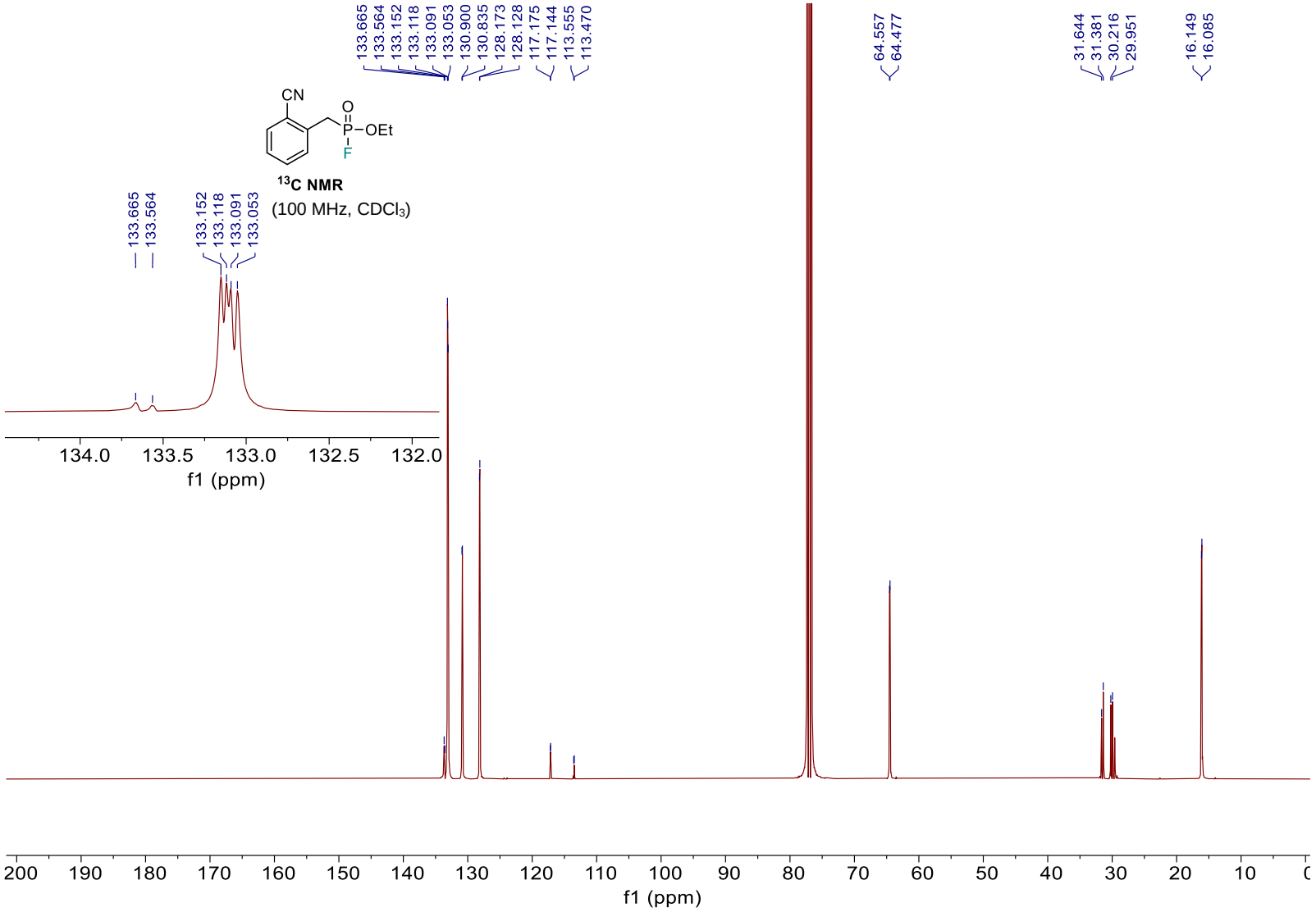
^{1}H NMR
(400 MHz, $CDCl_3$)

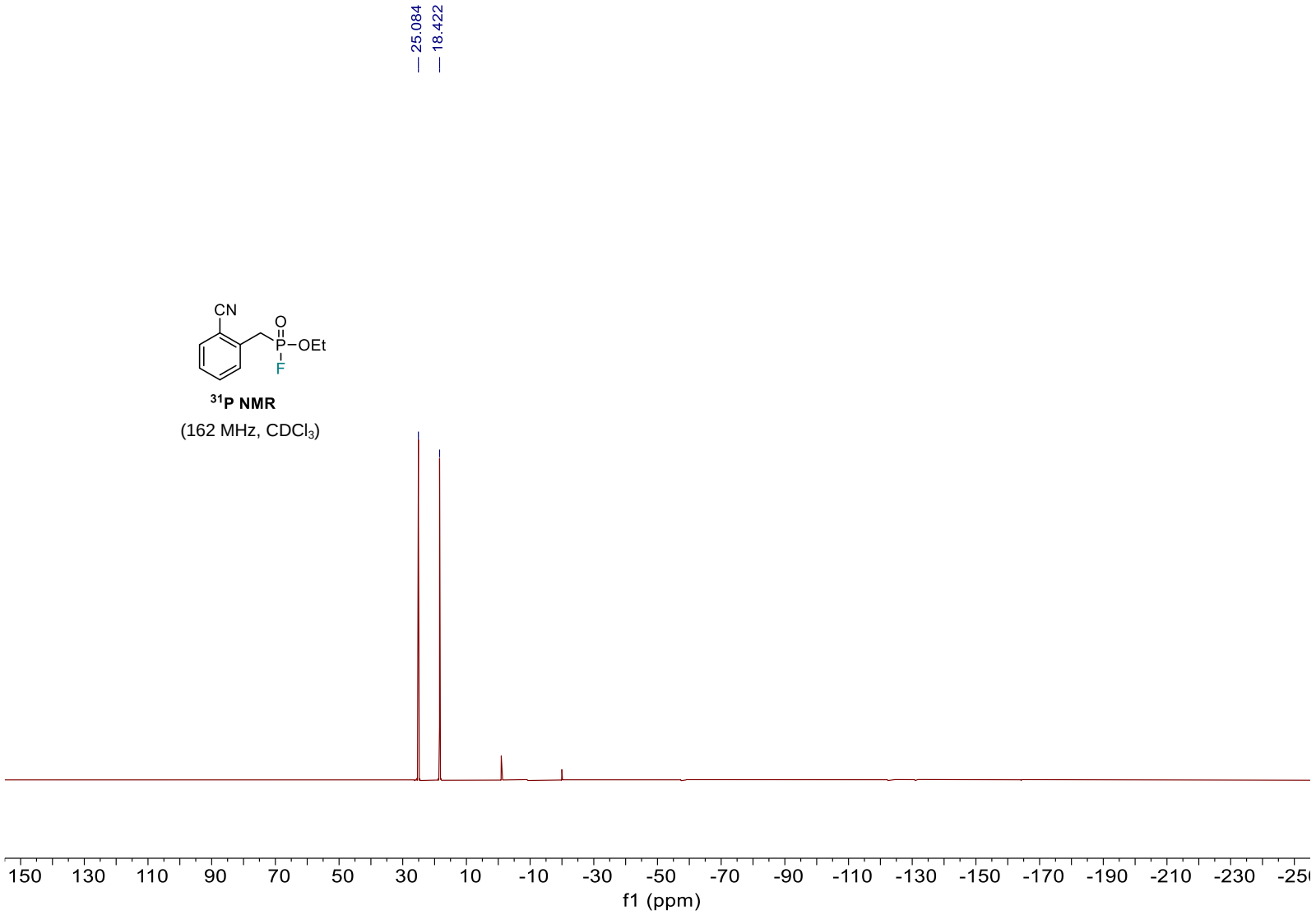

149.049
133.507
133.465
133.088
133.015
128.869
128.824
125.641
125.602
125.326
125.217
64.455
64.374
30.255
29.994
28.828
28.568
16.091
16.027
NO2
O
P–OEt
F
13C NMR
(100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

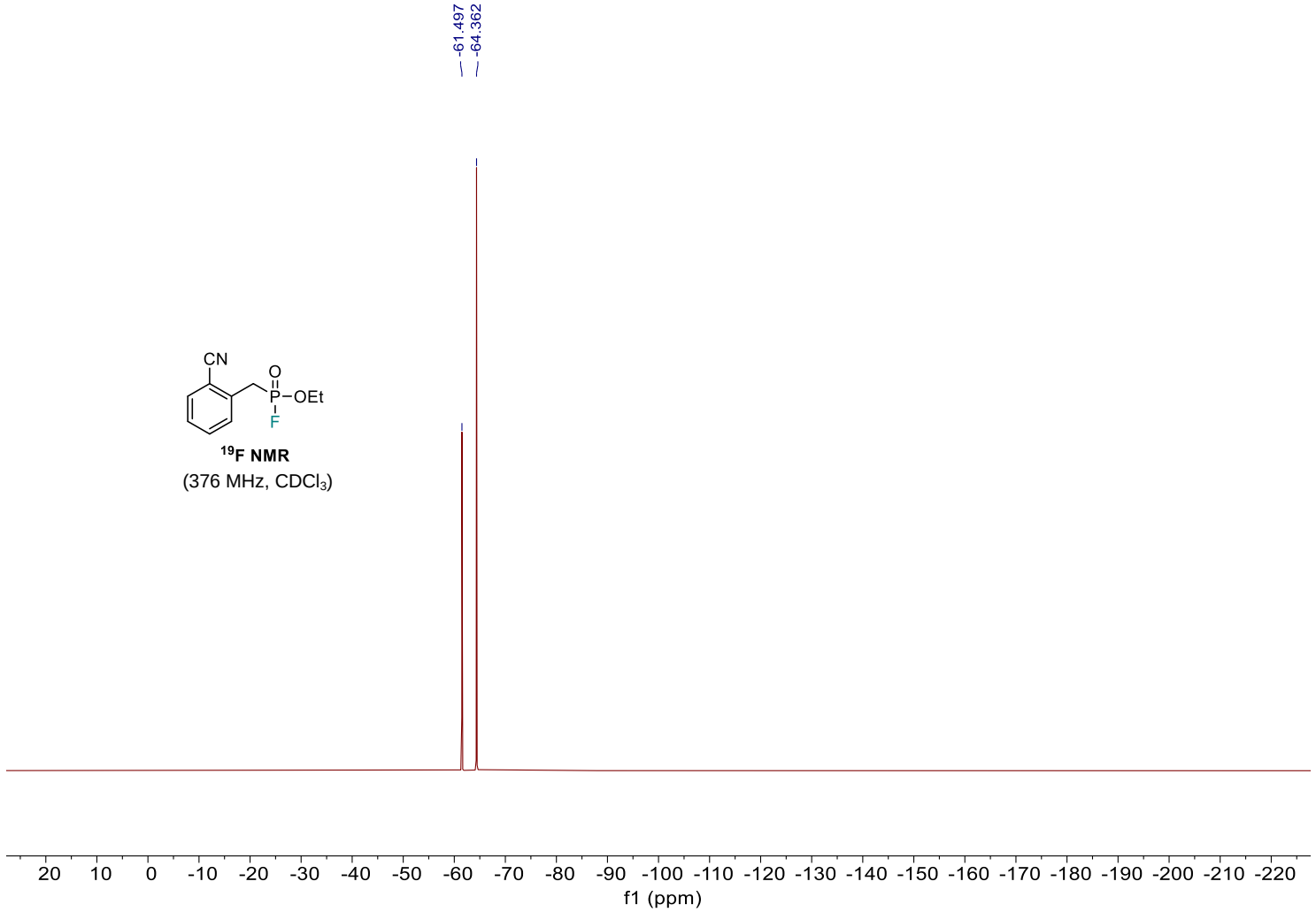

25.589
18.934
NO2
O
P
OEt
F
31P NMR
(162 MHz, CDCl3)
150 130 110 90 70 50 30 10 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190 -210 -230
f1 (ppm)


-61.248
-64.112
NO2
O
P
OEt
F
19F NMR
(376 MHz, CDCl3)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)


7.679
7.660
7.605
7.585
7.567
7.543
7.523
7.424
7.405
7.385
4.279
4.259
4.239
3.585
3.526
1.337
1.319
1.301
CN
O
P
OEt
F
1H NMR
(400 MHz, CDCl3)
1.00
2.13
1.03
2.06
2.11
3.27
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

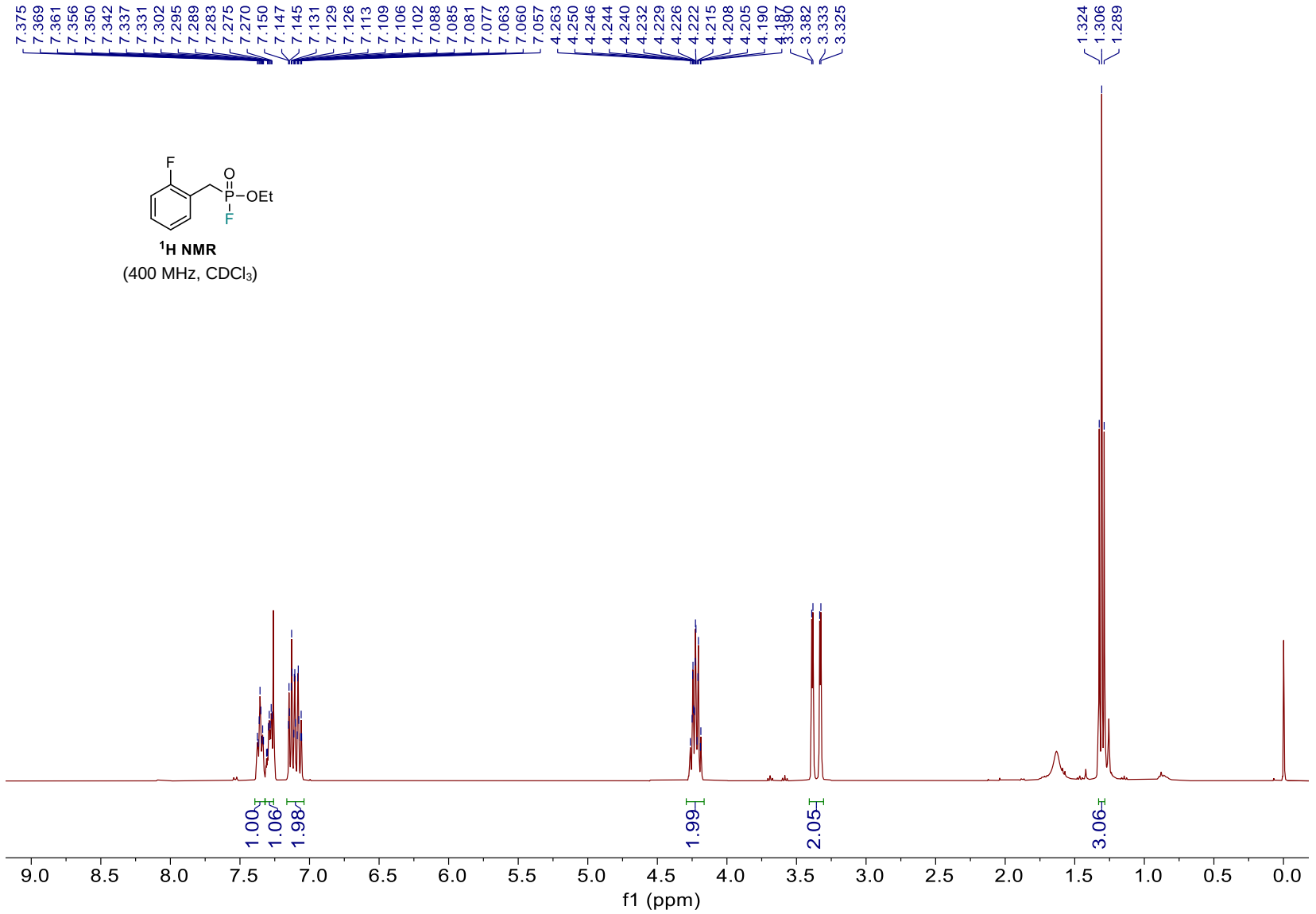

133.665
133.564
133.152
133.118
133.091
133.053
130.900
130.835
128.173
128.128
117.175
117.144
113.555
113.470
64.557
64.477
31.644
31.381
30.216
29.951
16.149
16.085
CN
O
P
OEt
F
13C NMR
(100 MHz, CDCl3)
f1 (ppm)
f1 (ppm)

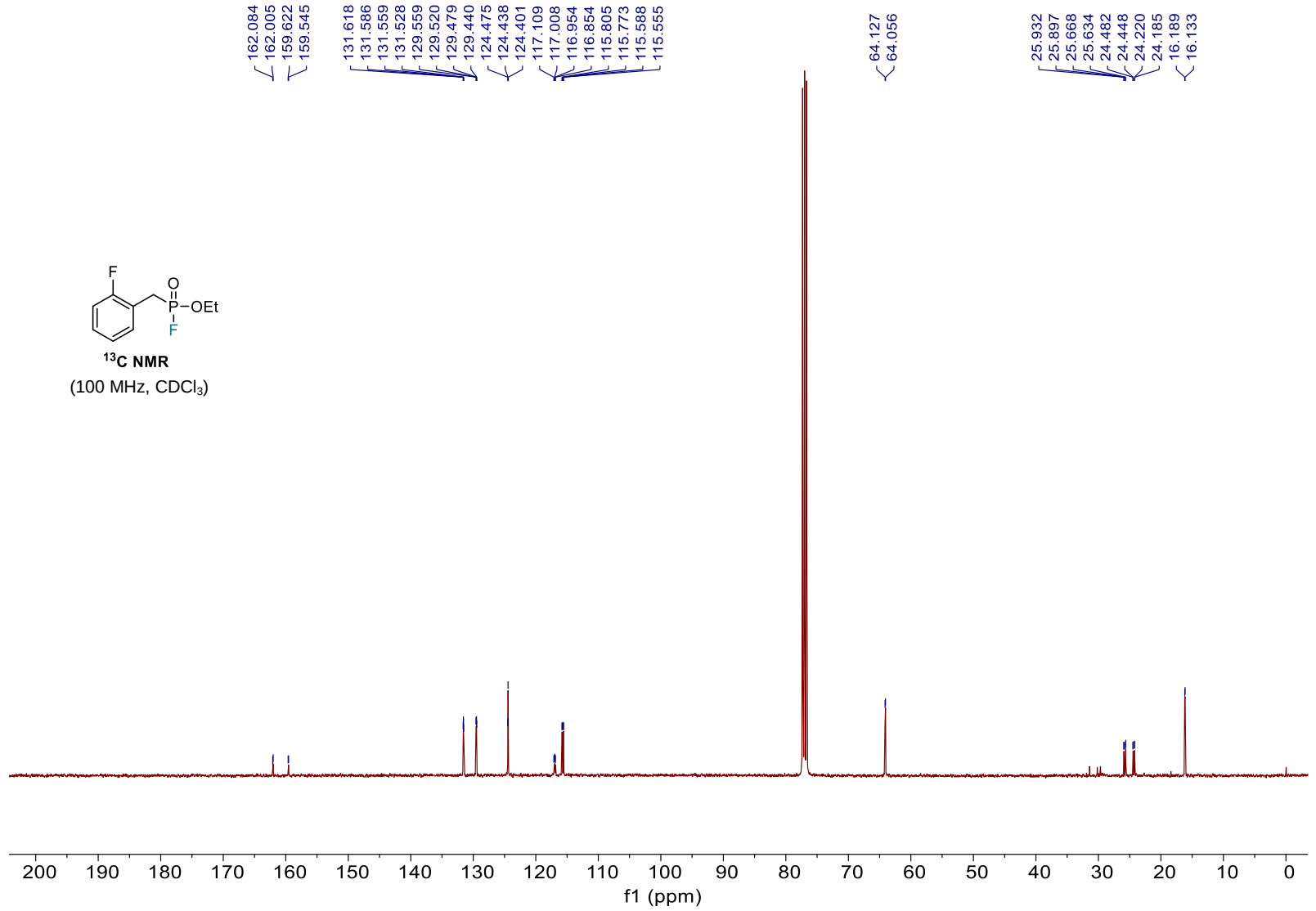

25.084
18.422
CN
O
P
OEt
F
31P NMR
(162 MHz, CDCl3)
150 130 110 90 70 50 30 10 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190 -210 -230
f1 (ppm)



^{19}F NMR

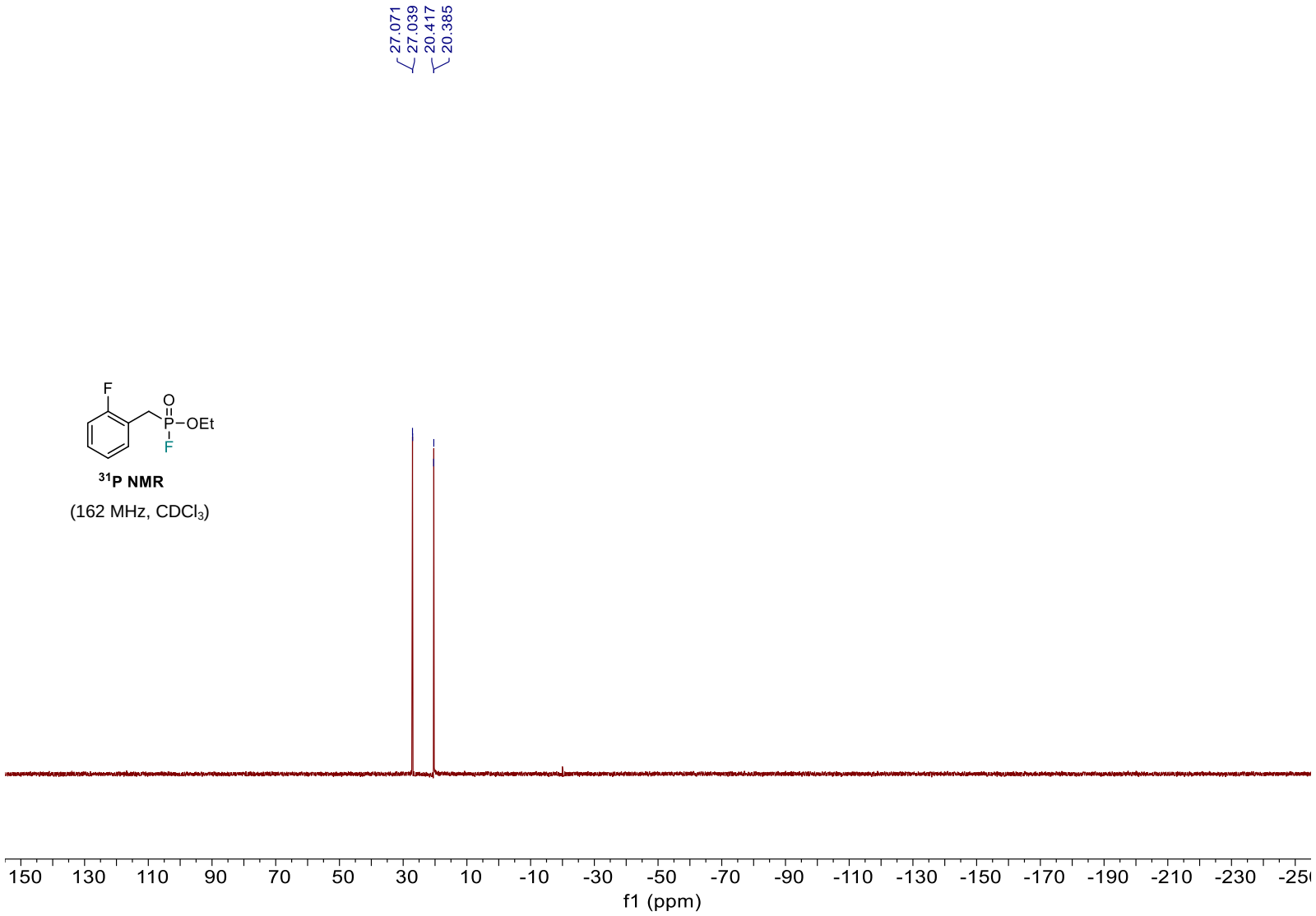
(376 MHz, $CDCl_3$)


7.375
7.369
7.361
7.356
7.350
7.342
7.337
7.331
7.302
7.295
7.289
7.283
7.275
7.270
7.150
7.147
7.145
7.131
7.129
7.126
7.113
7.109
7.106
7.102
7.088
7.085
7.081
7.077
7.063
7.060
7.057
4.263
4.250
4.246
4.244
4.240
4.232
4.229
4.226
4.222
4.215
4.208
4.205
4.190
4.187
3.380
3.382
3.333
3.325
1.324
1.306
1.289
F
O
P
OEt
F
1H NMR
(400 MHz, CDCl3)
1.00
1.06
1.98
1.99
2.05
3.06
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



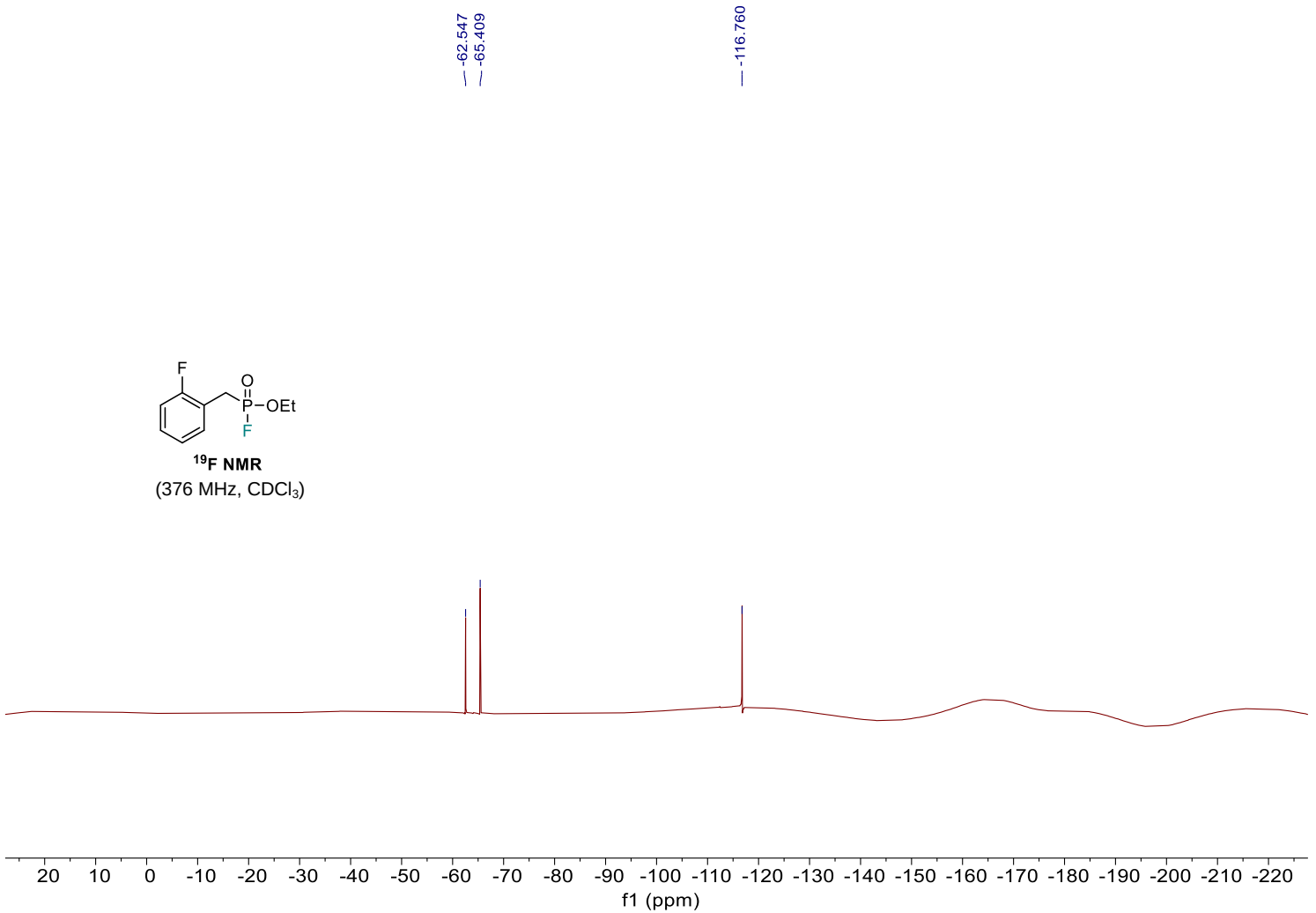
^{13}C NMR

(100 MHz, $CDCl_3$)



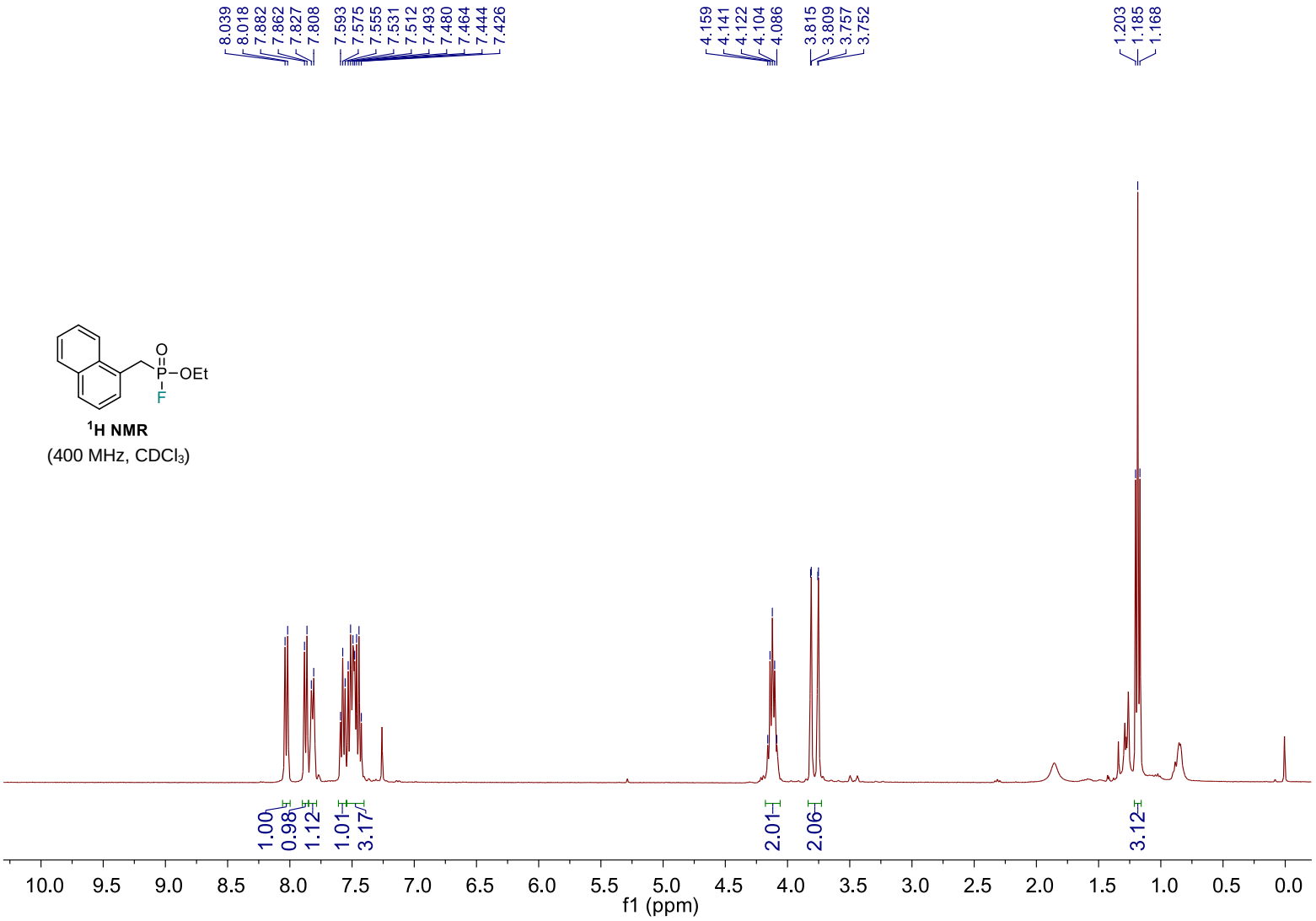
^{31}P NMR

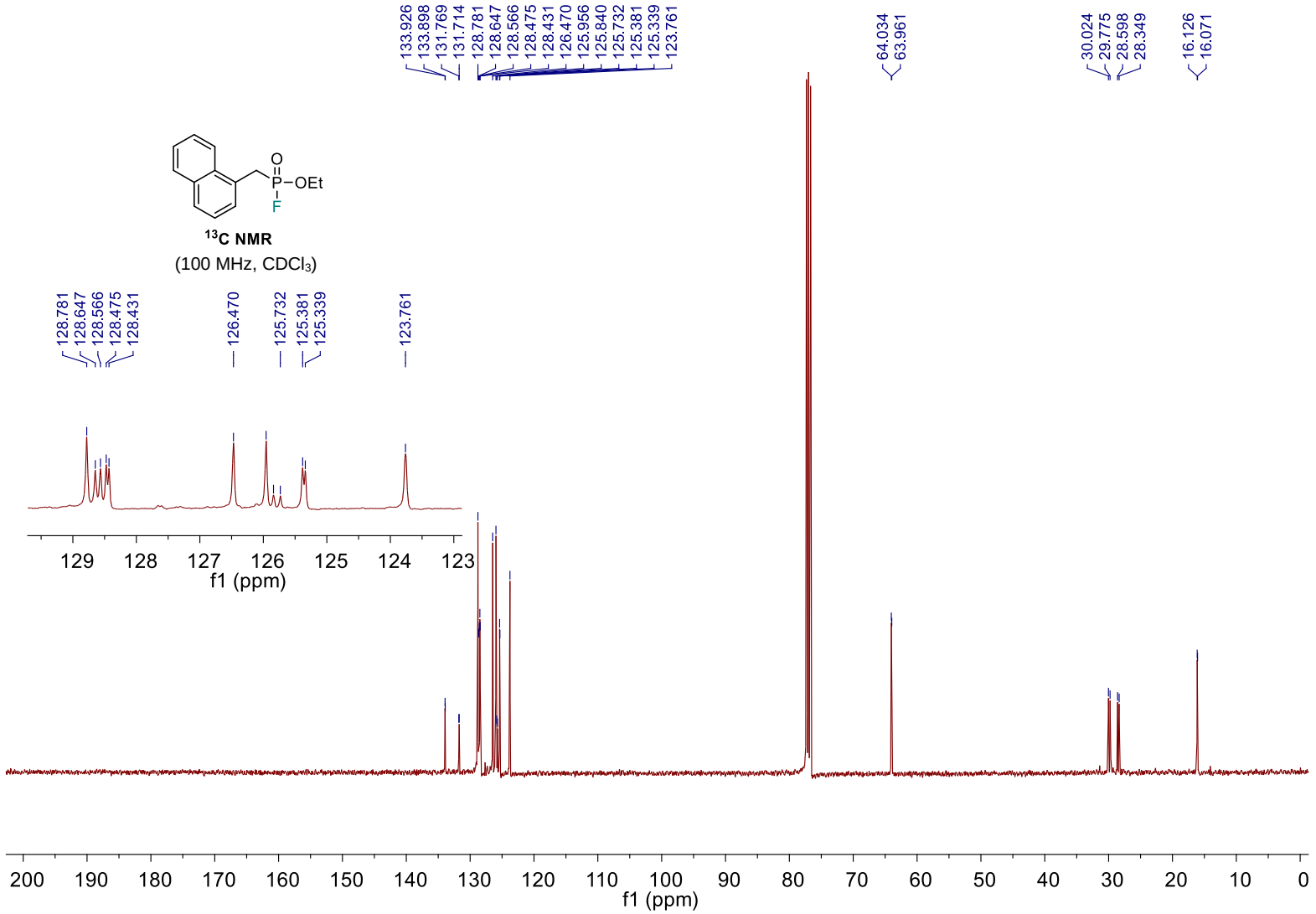
(162 MHz, $CDCl_3$)

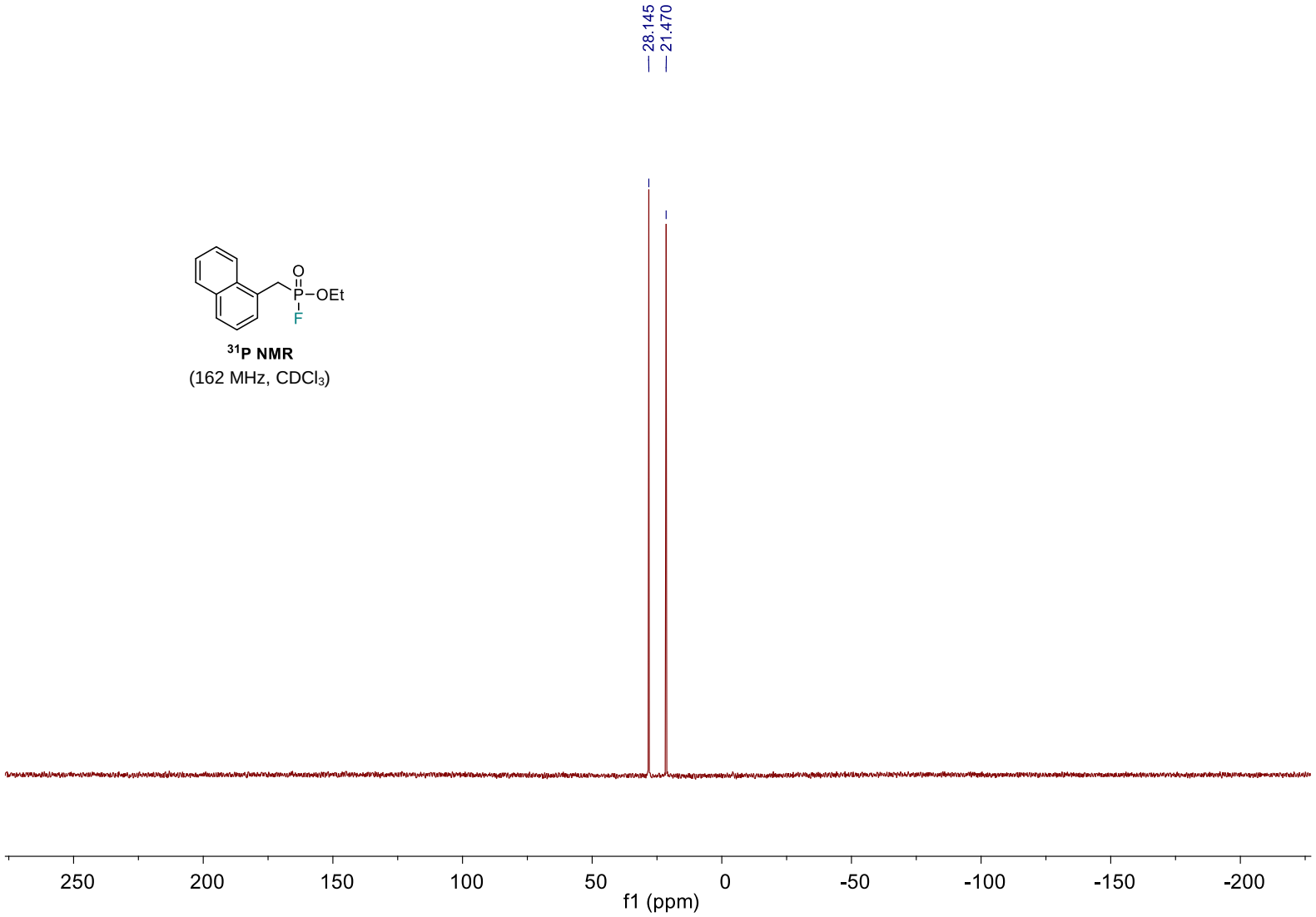


^{19}F NMR

(376 MHz, $CDCl_3$)

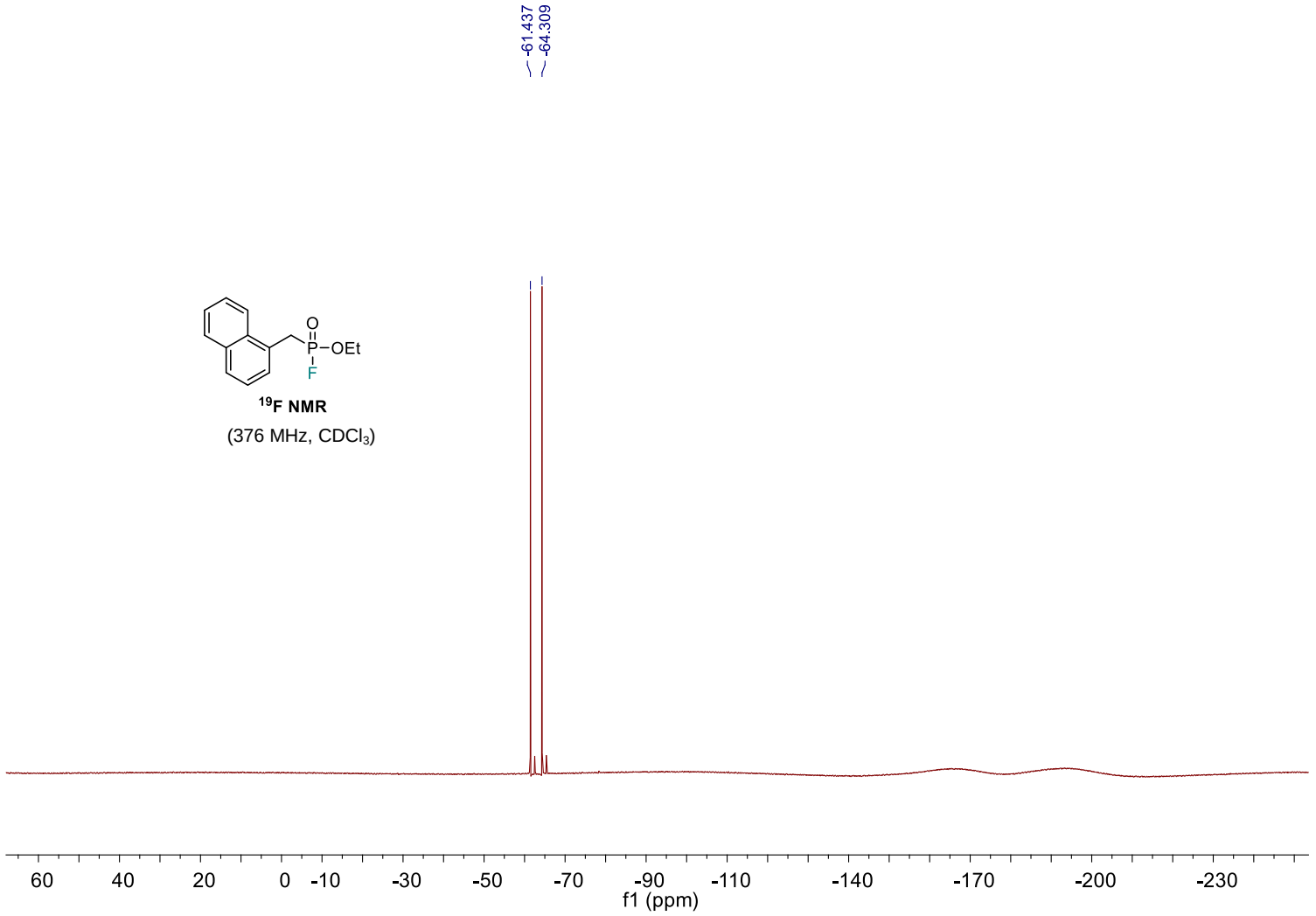

8.039
8.018
7.882
7.862
7.827
7.808
7.593
7.575
7.555
7.531
7.512
7.493
7.480
7.464
7.444
7.426
4.159
4.141
4.122
4.104
4.086
3.815
3.809
3.757
3.752
1.203
1.185
1.168
O
P–OEt
F
1H NMR
(400 MHz, CDCl3)
1.00
0.98
1.12
1.01
3.17
2.01
2.06
3.12
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


133.926
133.898
131.769
131.714
128.781
128.647
128.566
128.475
128.431
126.470
125.956
125.840
125.732
125.381
125.339
123.761
64.034
63.961
30.024
29.775
28.598
28.349
16.126
16.071
O
P
OEt
F
13C NMR
(100 MHz, CDCl3)
f1 (ppm)
f1 (ppm)



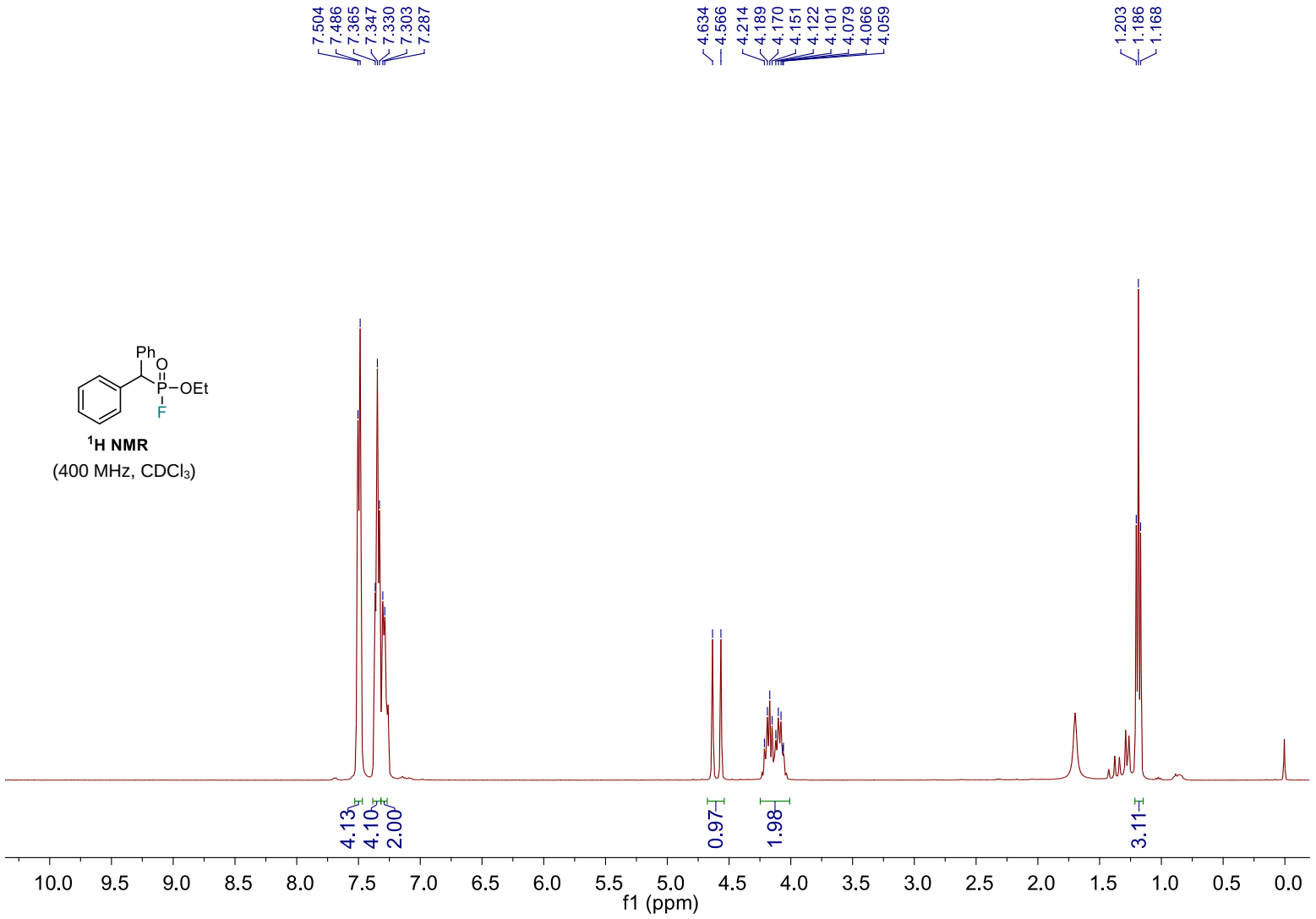
^{31}P NMR

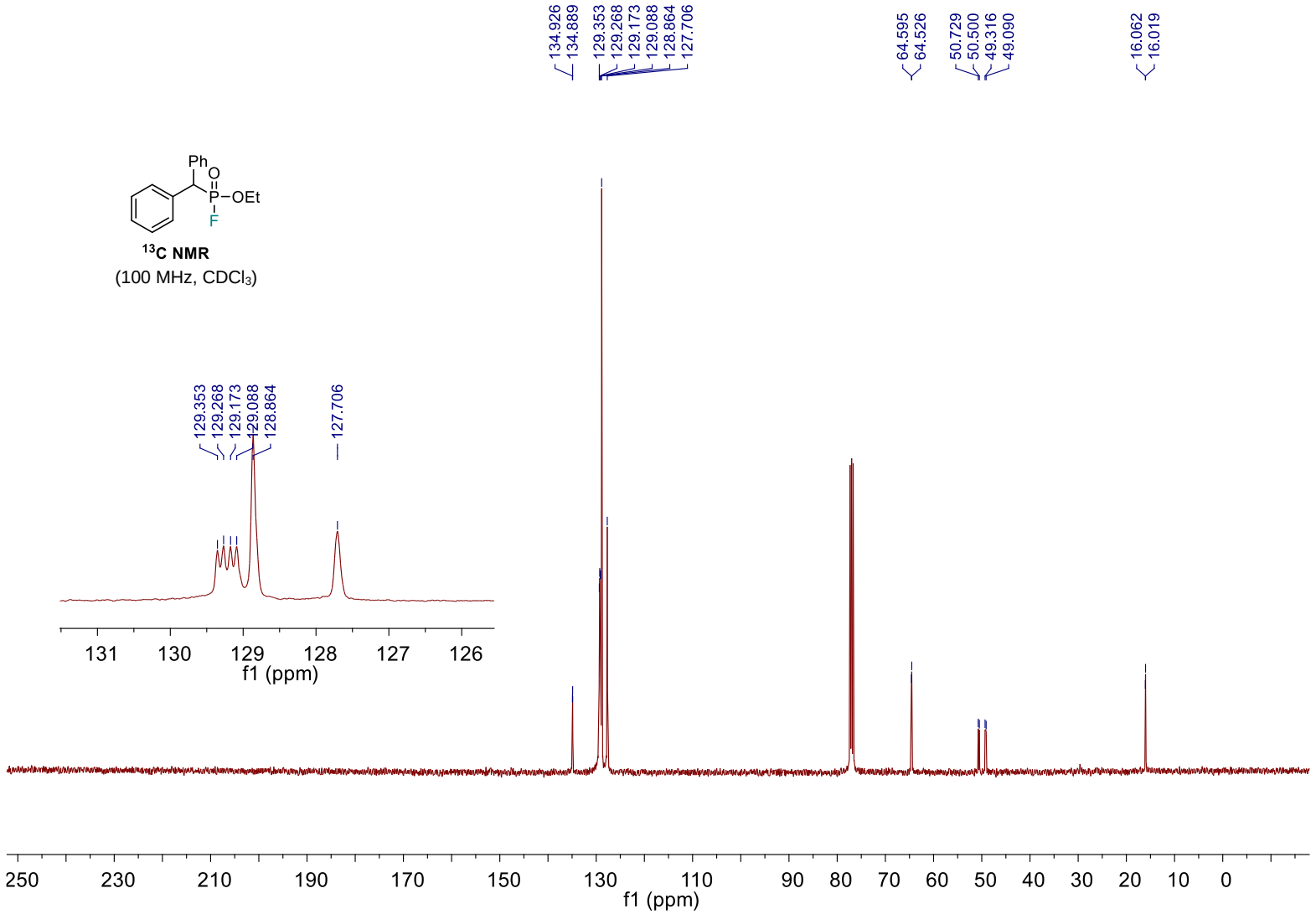
(162 MHz, $CDCl_3$)

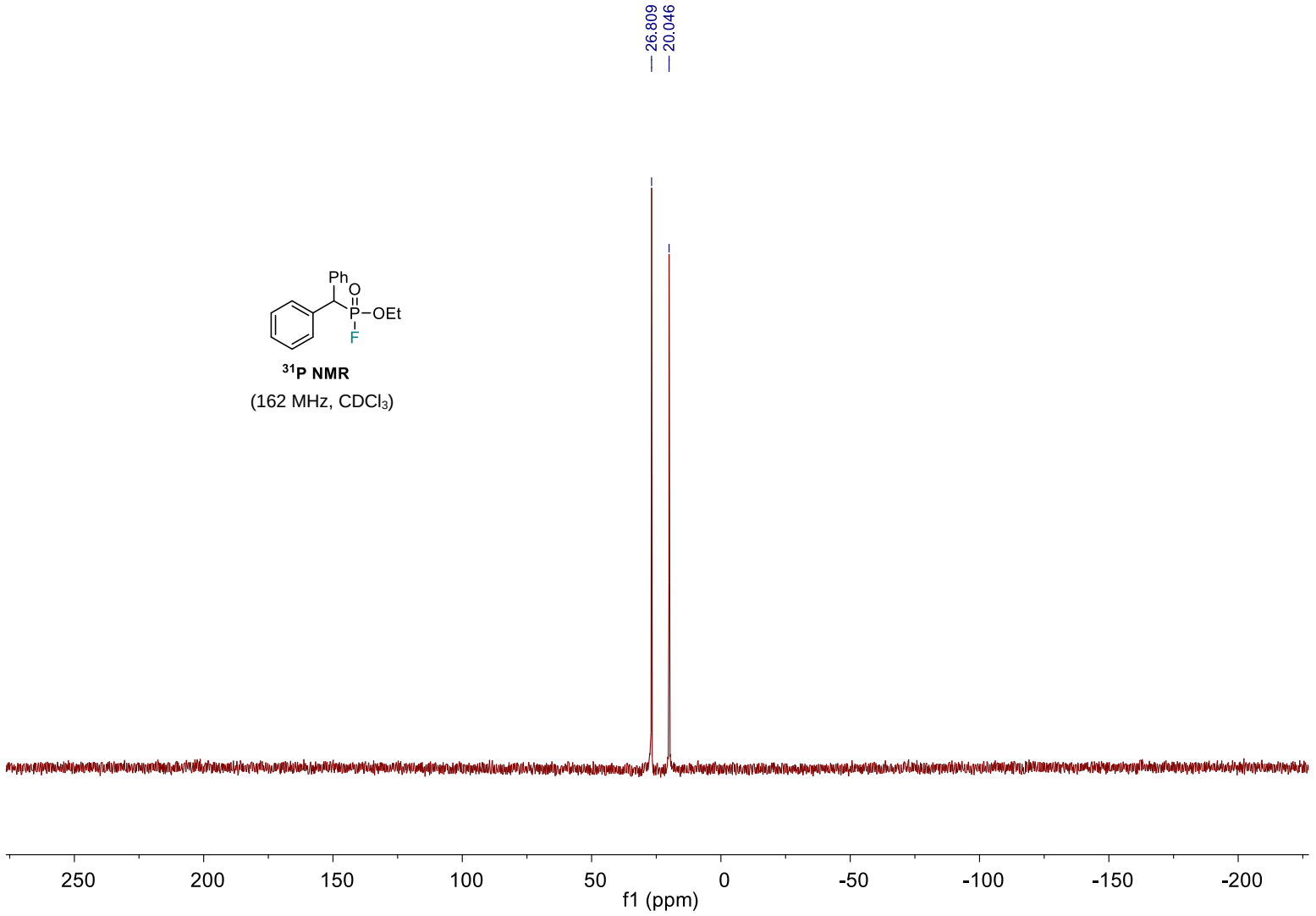


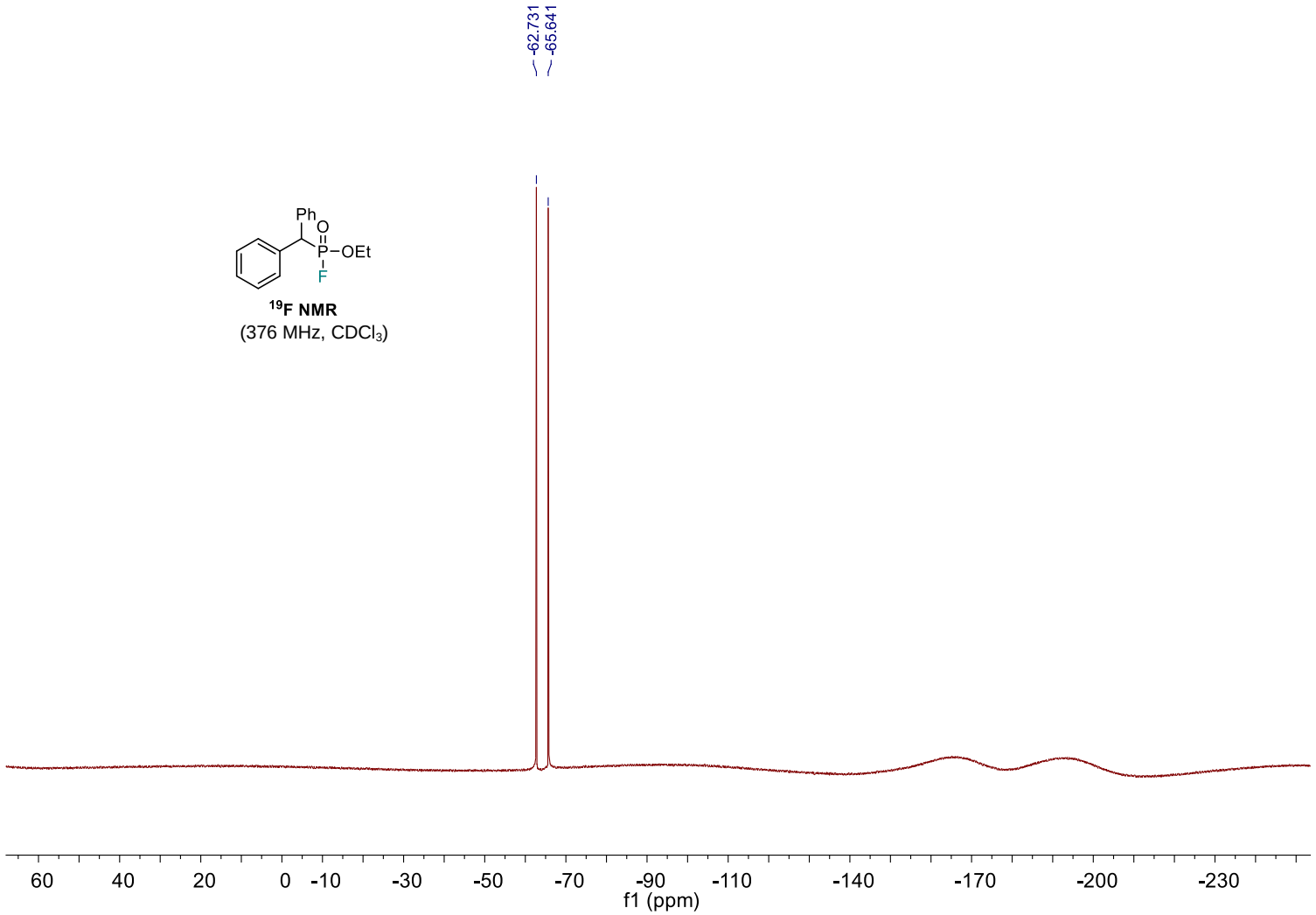
^{19}F NMR

(376 MHz, $CDCl_3$)

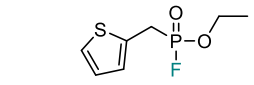

7.504
7.486
7.365
7.347
7.330
7.303
7.287
4.634
4.566
4.214
4.189
4.170
4.151
4.122
4.101
4.079
4.066
4.059
1.203
1.186
1.168
Ph
O
P–OEt
F
1H NMR
(400 MHz, CDCl3)
4.13
4.10
2.00
0.97
1.98
3.11
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


134.926
134.889
129.353
129.268
129.173
129.088
128.864
127.706
64.595
64.526
50.729
50.500
49.316
49.090
16.062
16.019
Ph
O
P–OEt
F
13C NMR
(100 MHz, CDCl3)
129.353
129.268
129.173
129.088
128.864
127.706
131
130
129
128
127
126
f1 (ppm)
250
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

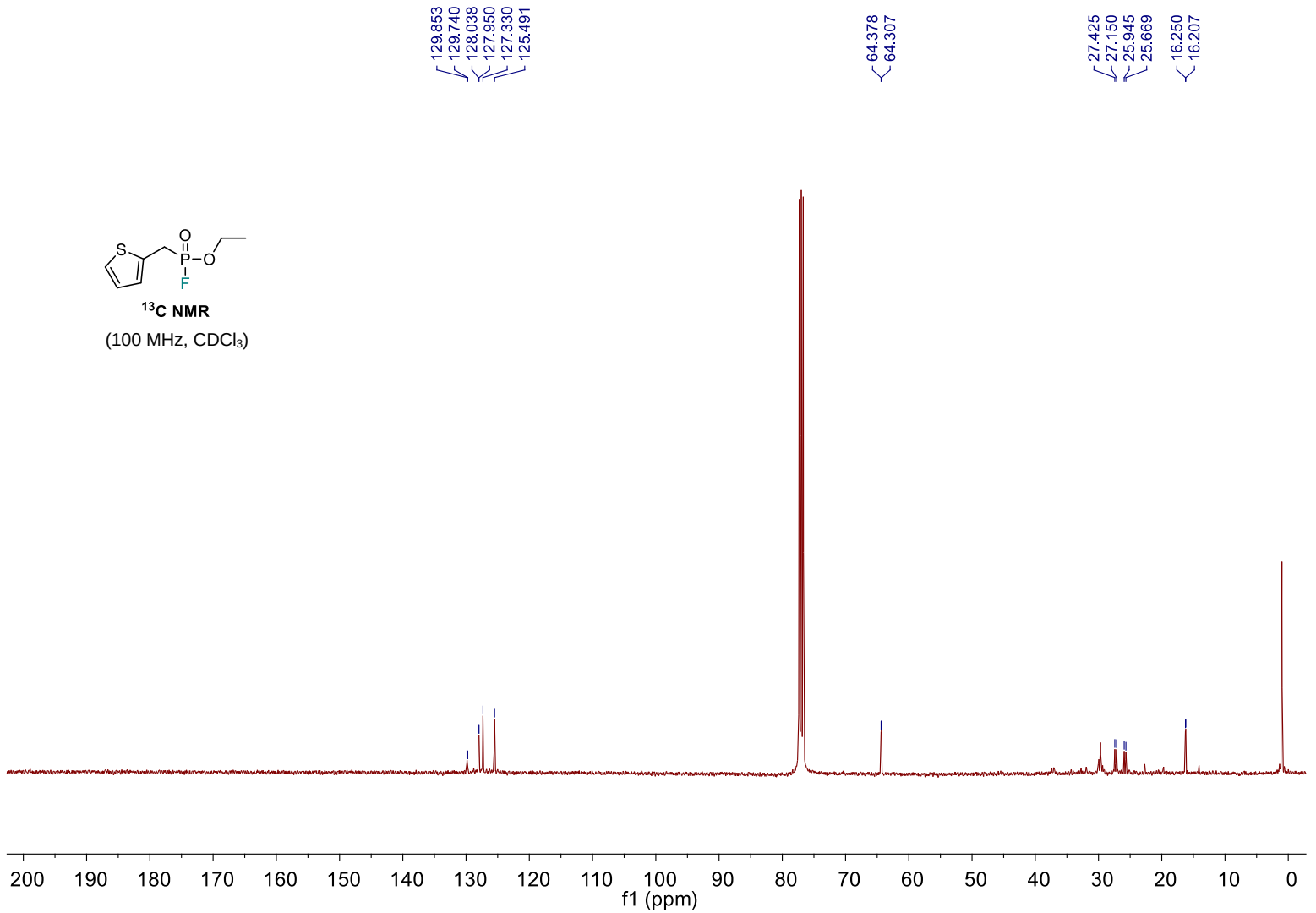

26.809
20.046
Ph
O
P–OEt
F
31P NMR
(162 MHz, CDCl3)
250
200
150
100
50
0
-50
-100
-150
-200
f1 (ppm)



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

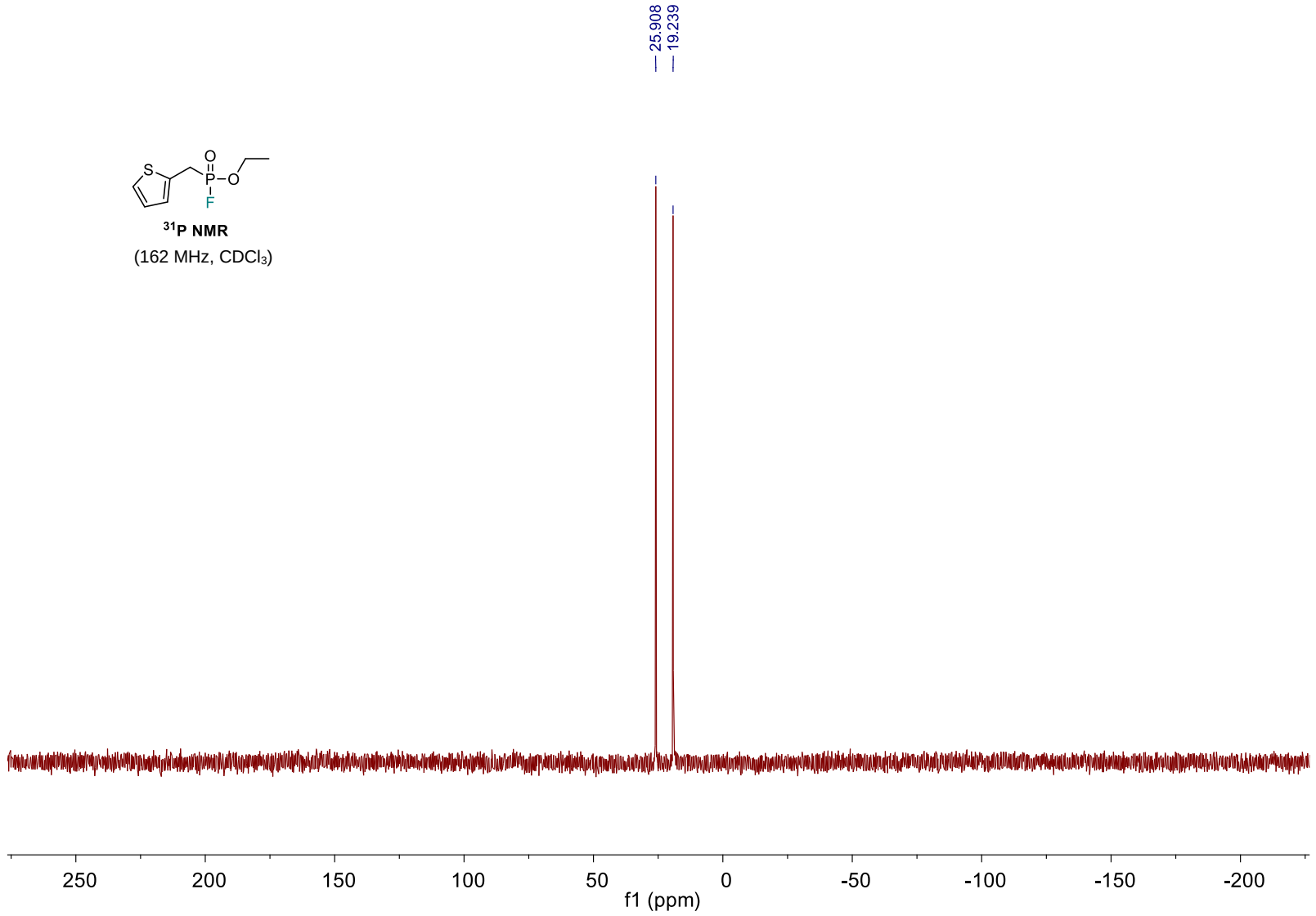


^{1}H NMR
(400 MHz, $CDCl_3$)



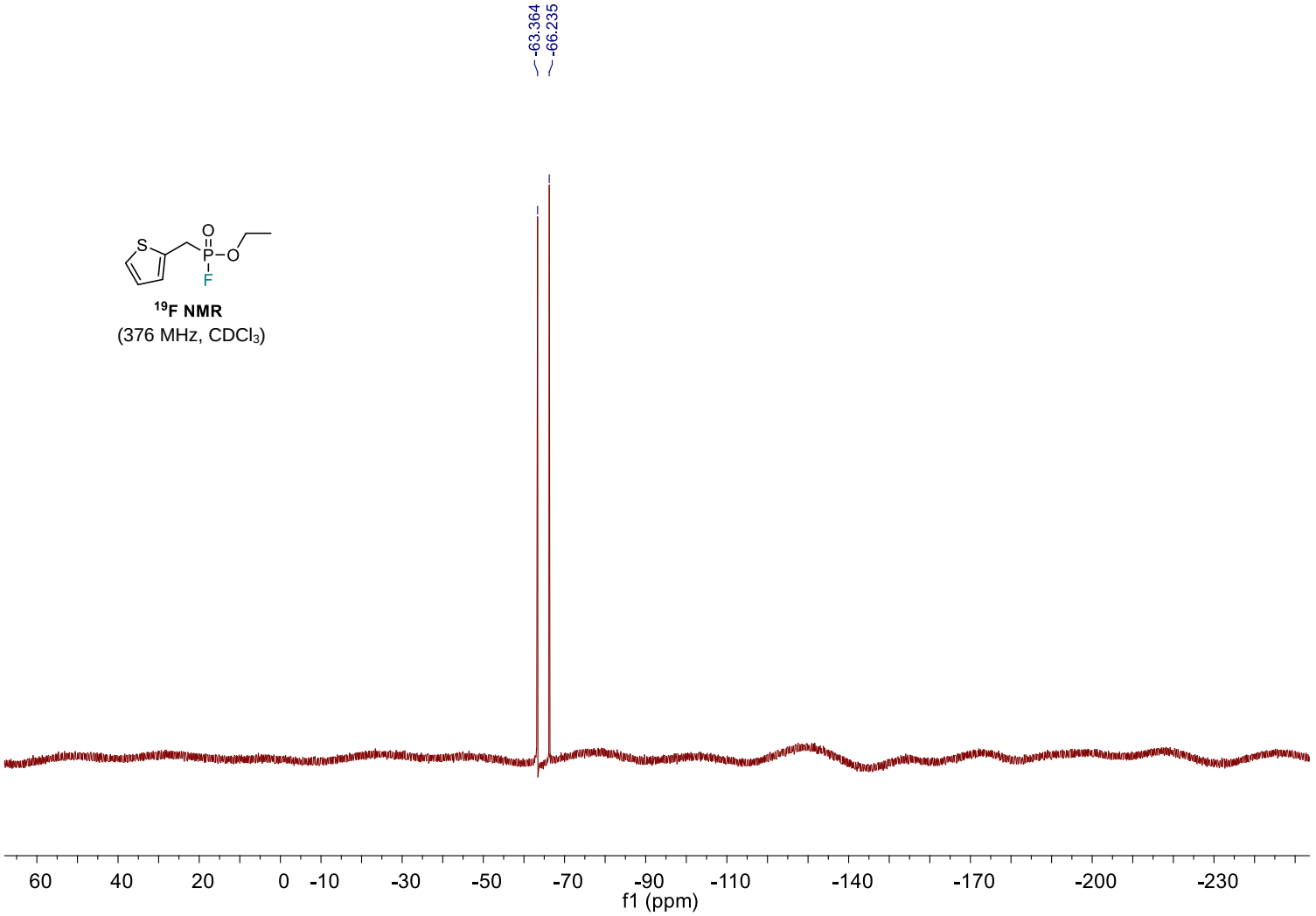
^{13}C NMR

(100 MHz, $CDCl_3$)

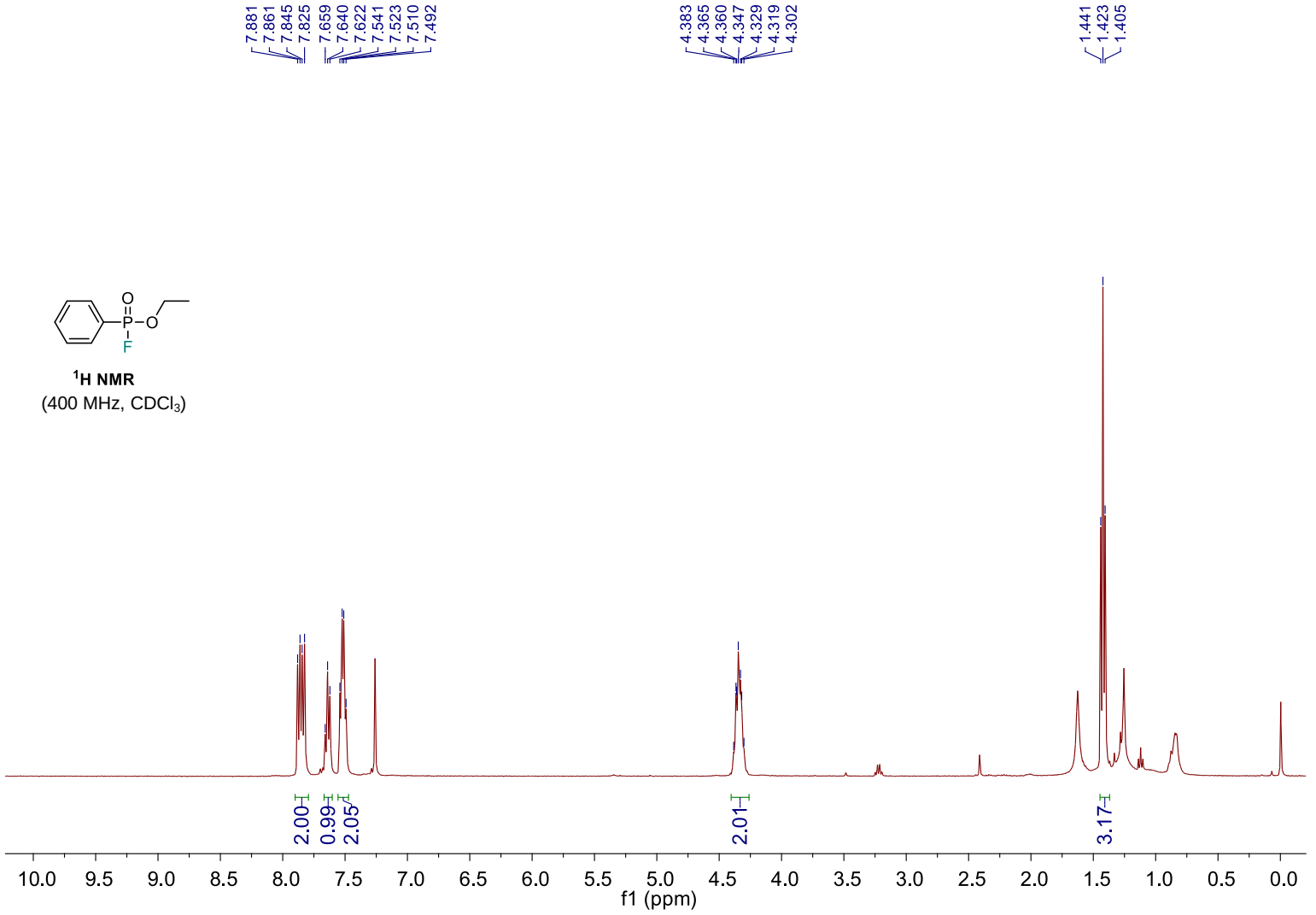


^{31}P NMR

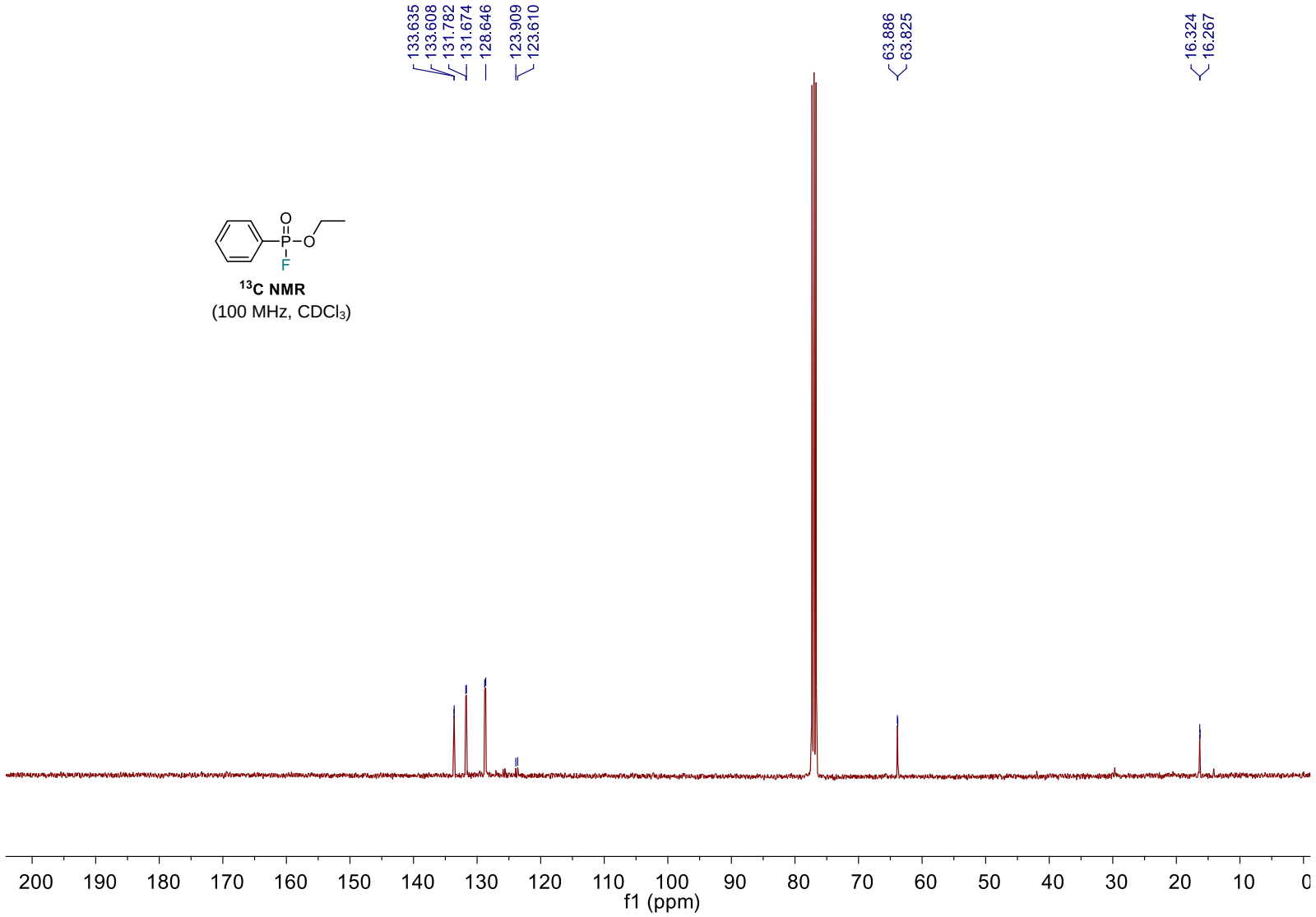
(162 MHz, $CDCl_3$)

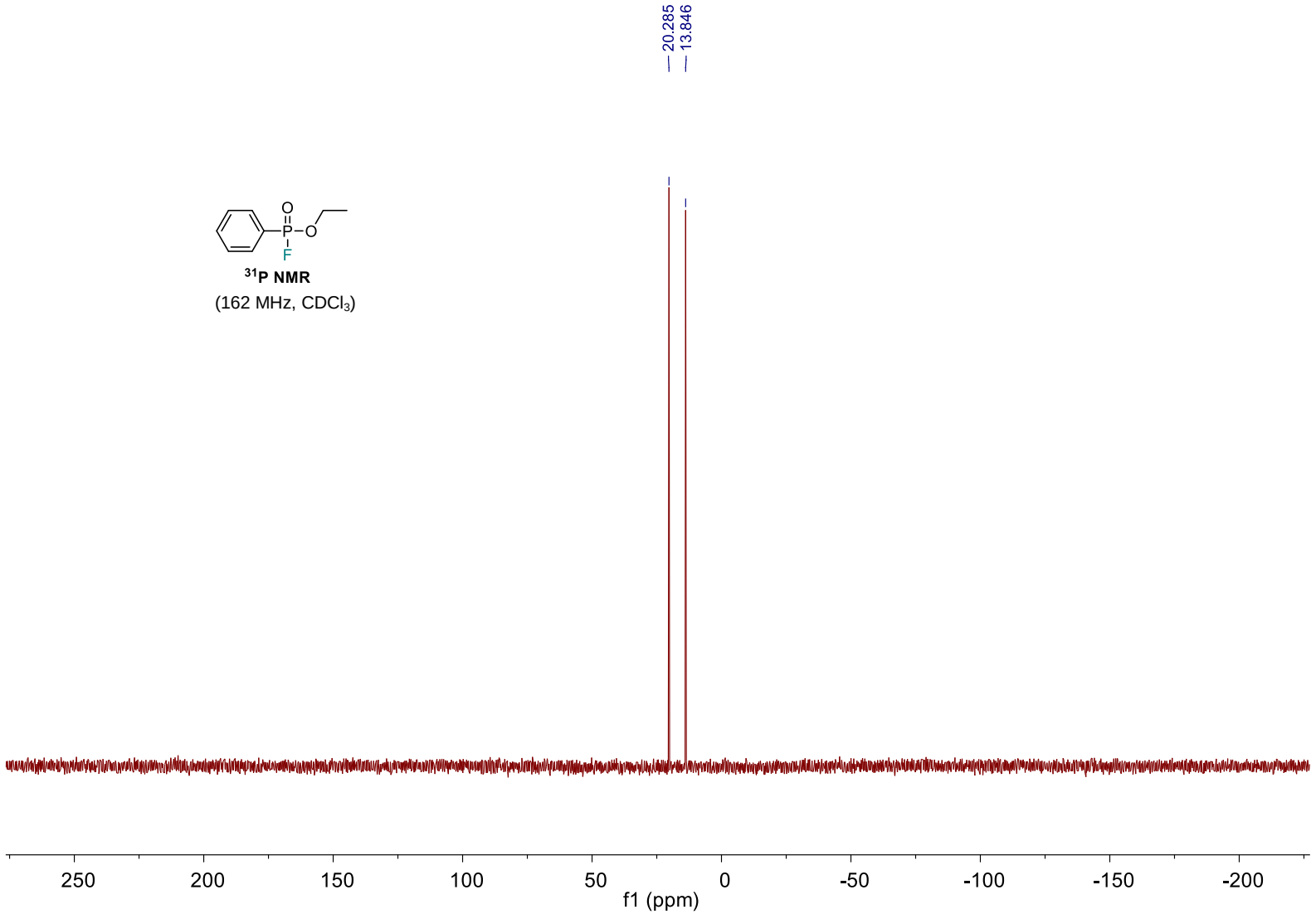


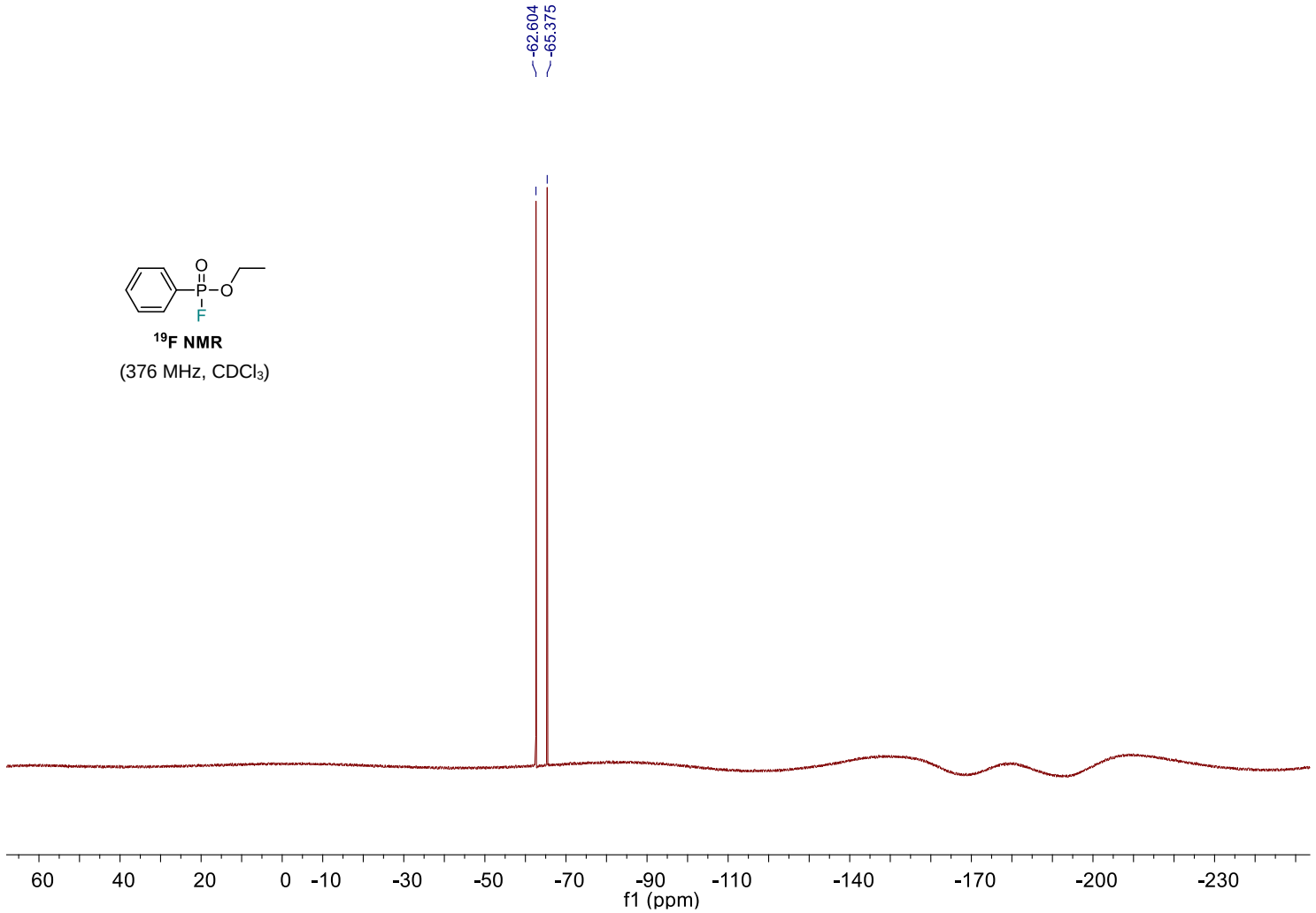
^{19}F NMR
(376 MHz, $CDCl_3$)



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

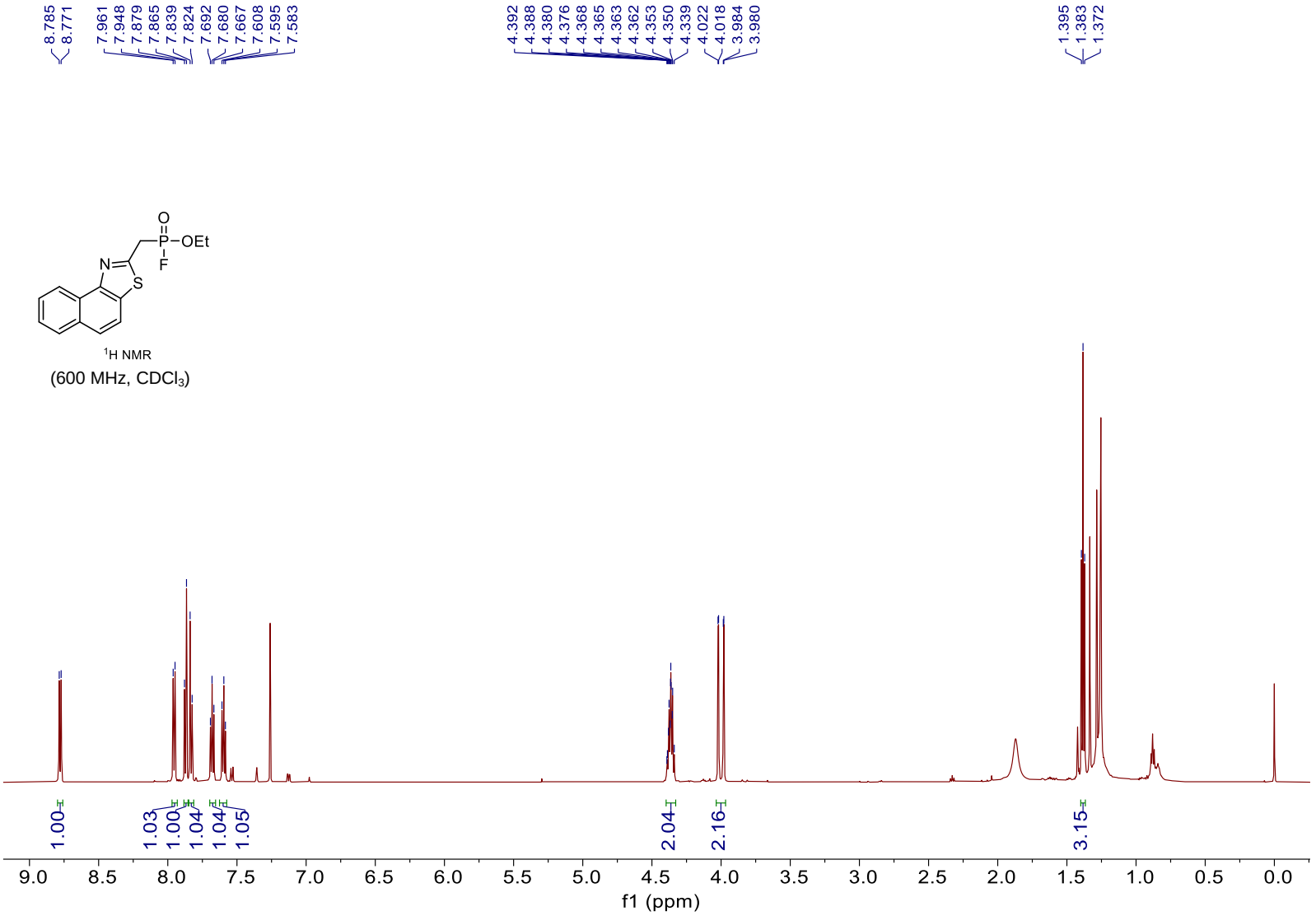

133.635
133.608
131.782
131.674
128.646
123.909
123.610
63.886
63.825
16.324
16.267
O
P
O
F
^{13}C NMR
(100 MHz, CDCl$_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

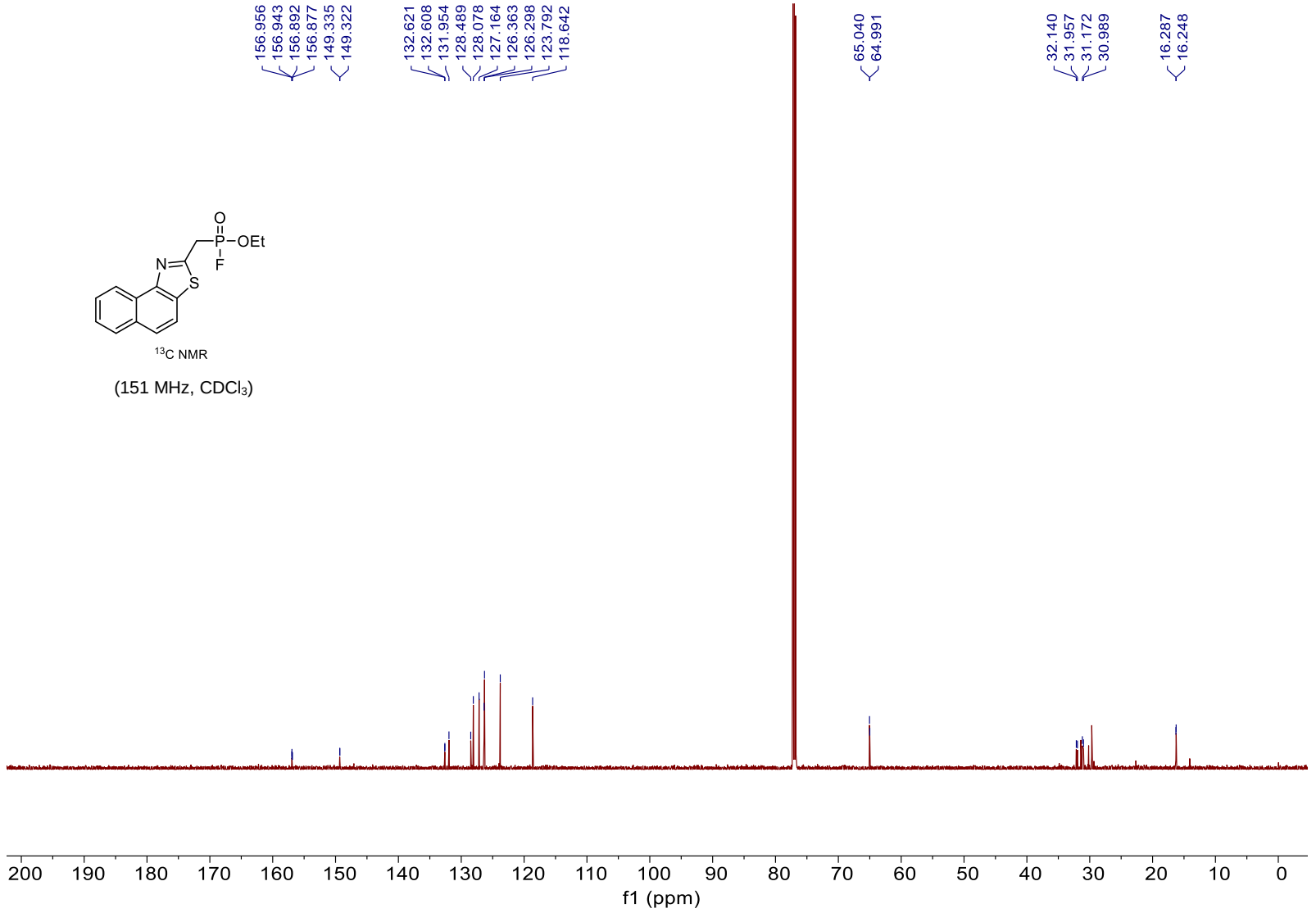

20.285
13.846
O
P
O
F
31P NMR
(162 MHz, CDCl3)
250
200
150
100
50
0
-50
-100
-150
-200
f1 (ppm)

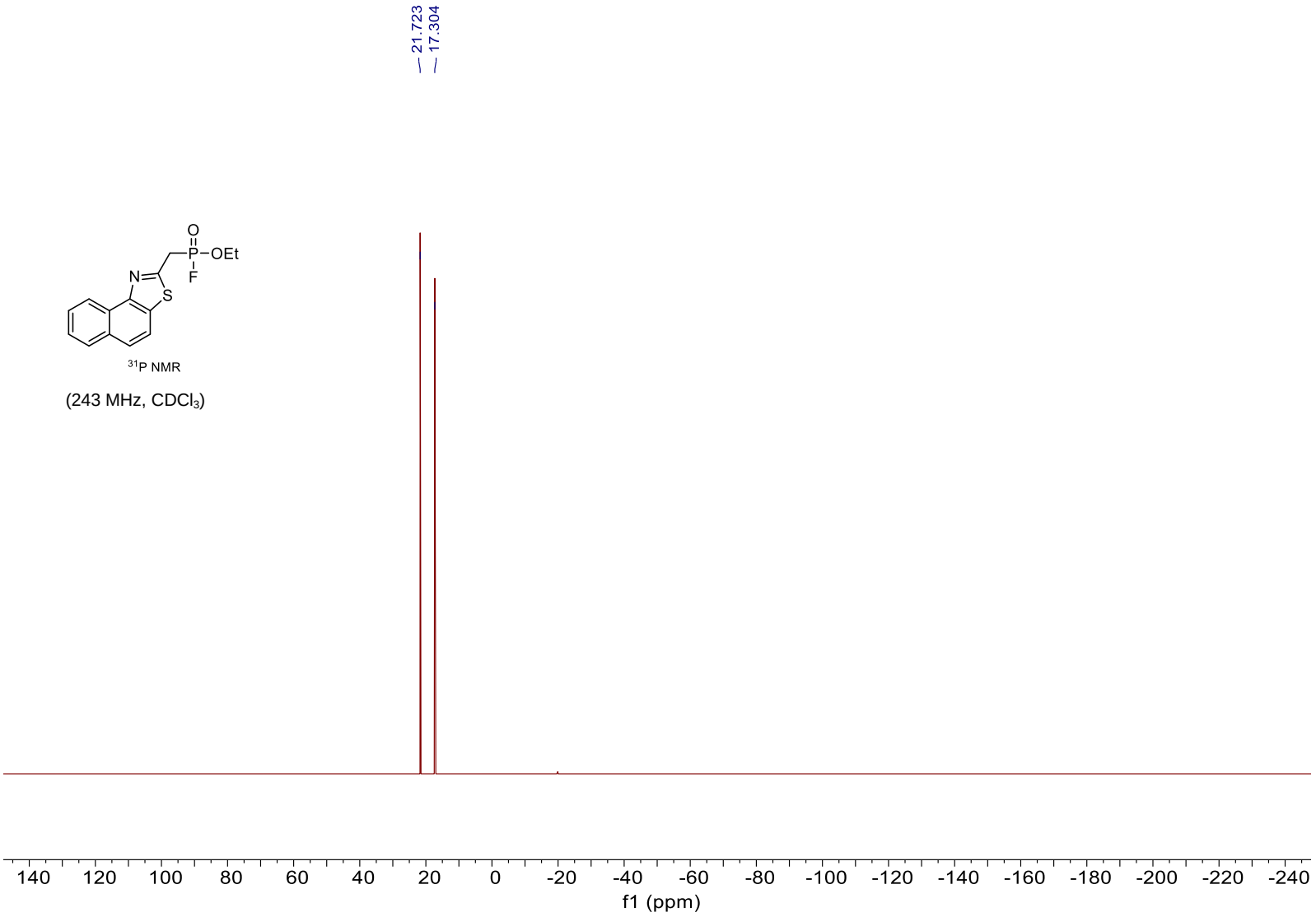


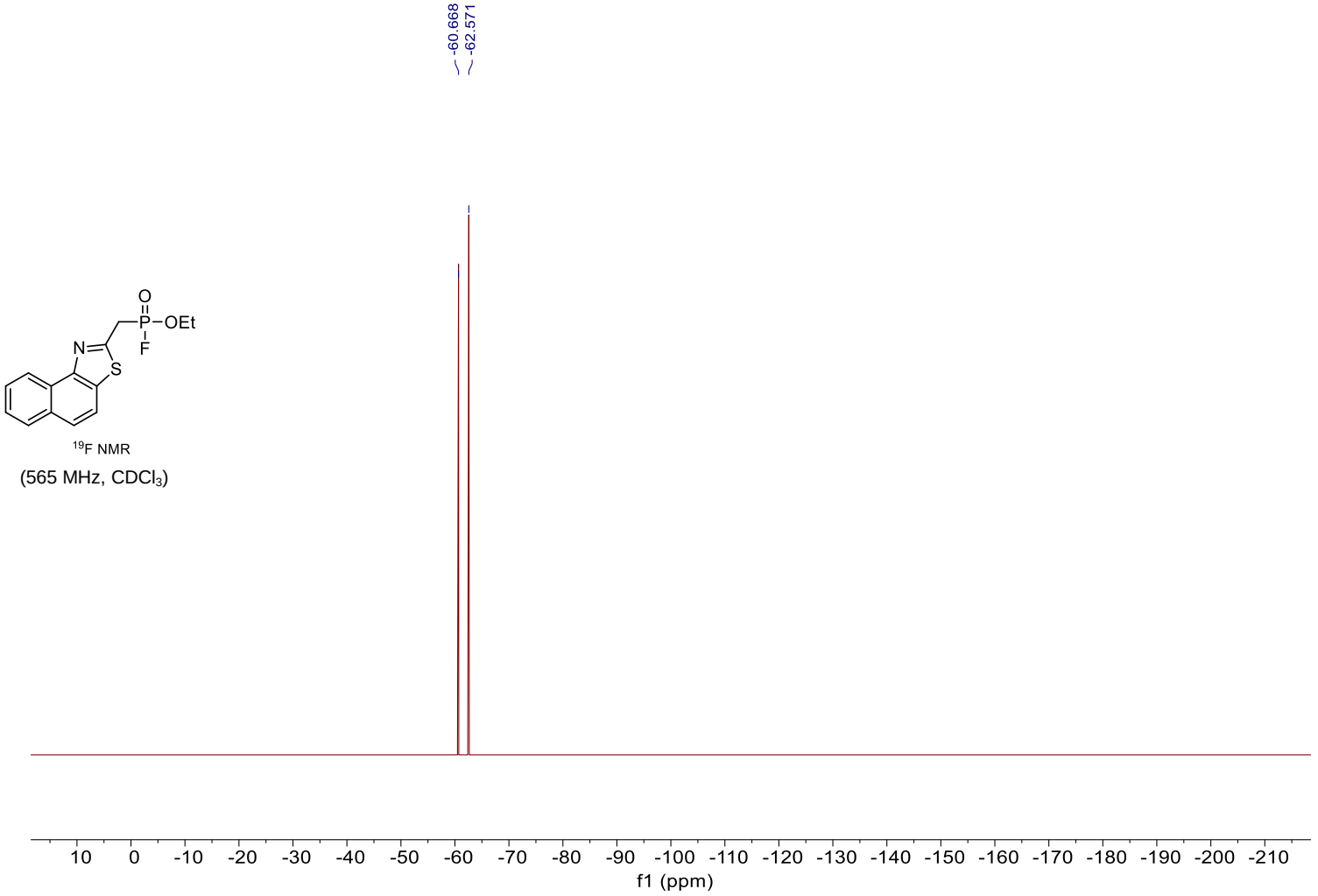
^{19}F NMR

(376 MHz, $CDCl_3$)


8.785
8.771
7.961
7.948
7.879
7.865
7.839
7.824
7.692
7.680
7.667
7.608
7.595
7.583
4.392
4.388
4.380
4.376
4.368
4.365
4.363
4.362
4.353
4.350
4.339
4.022
4.018
3.984
3.980
1.395
1.383
1.372
O
P
OEt
F
N
S
1H NMR
(600 MHz, CDCl3)
1.00
1.03
1.00
1.04
1.04
1.05
2.04
2.16
3.15
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

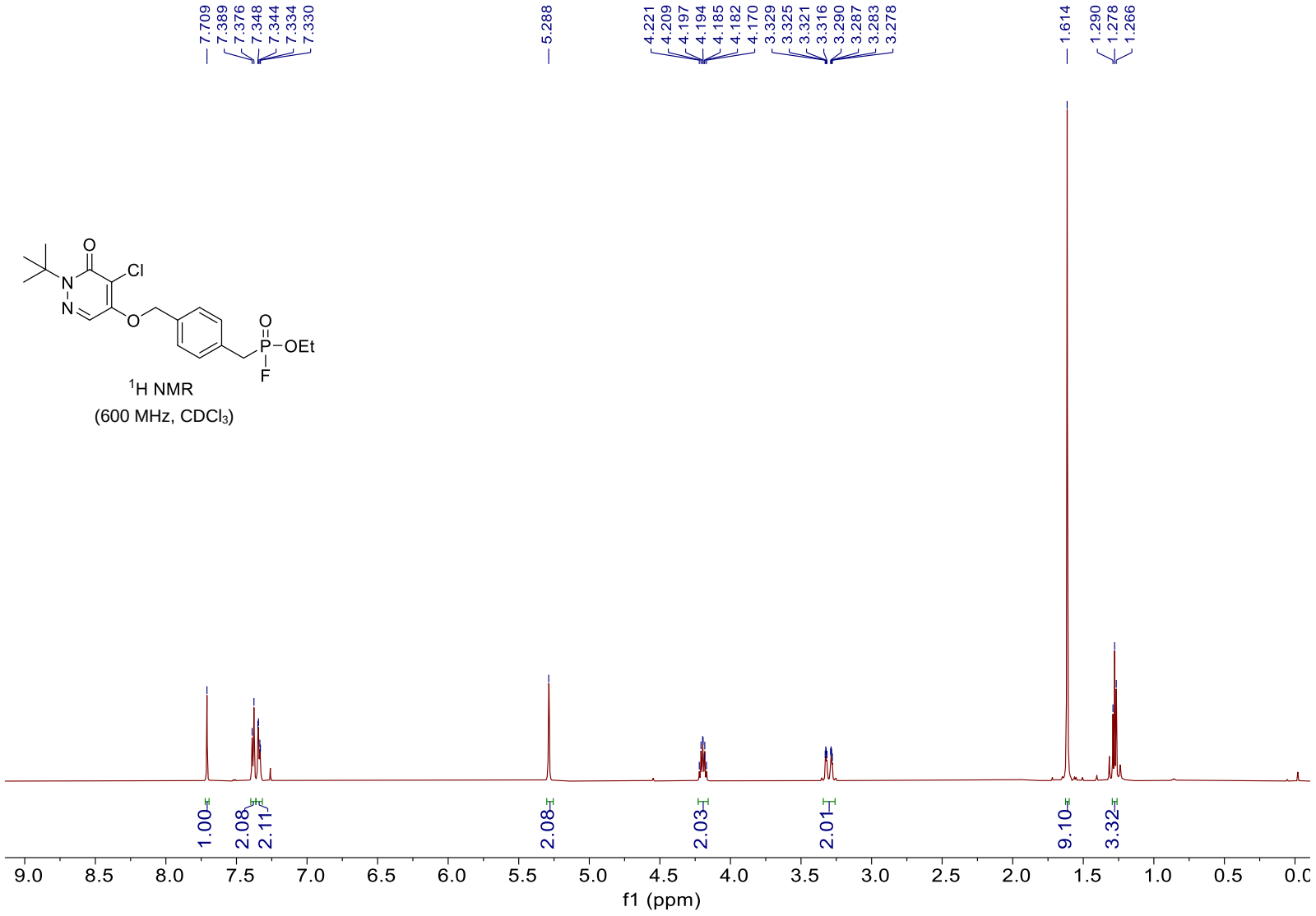

156.956
156.943
156.892
156.877
149.335
149.322
132.621
132.608
131.954
128.489
128.078
127.164
126.363
126.298
123.792
118.642
65.040
64.991
32.140
31.957
31.172
30.989
16.287
16.248
O
P
OEt
F
N
S
13C NMR
(151 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

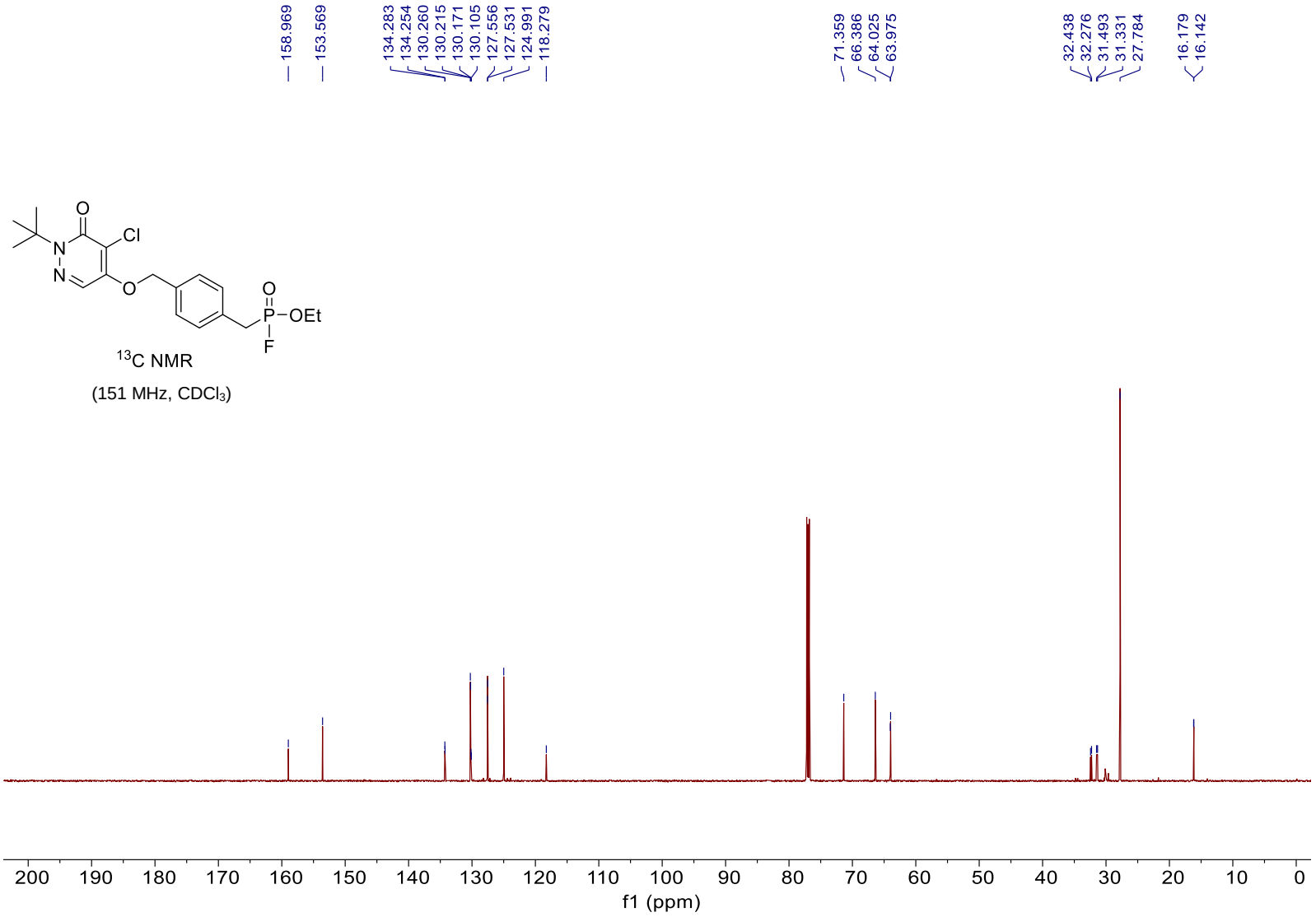

21.723
17.304
O
P–OEt
F
N
S
31P NMR
(243 MHz, CDCl3)
140 120 100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240
f1 (ppm)



^{19}F NMR

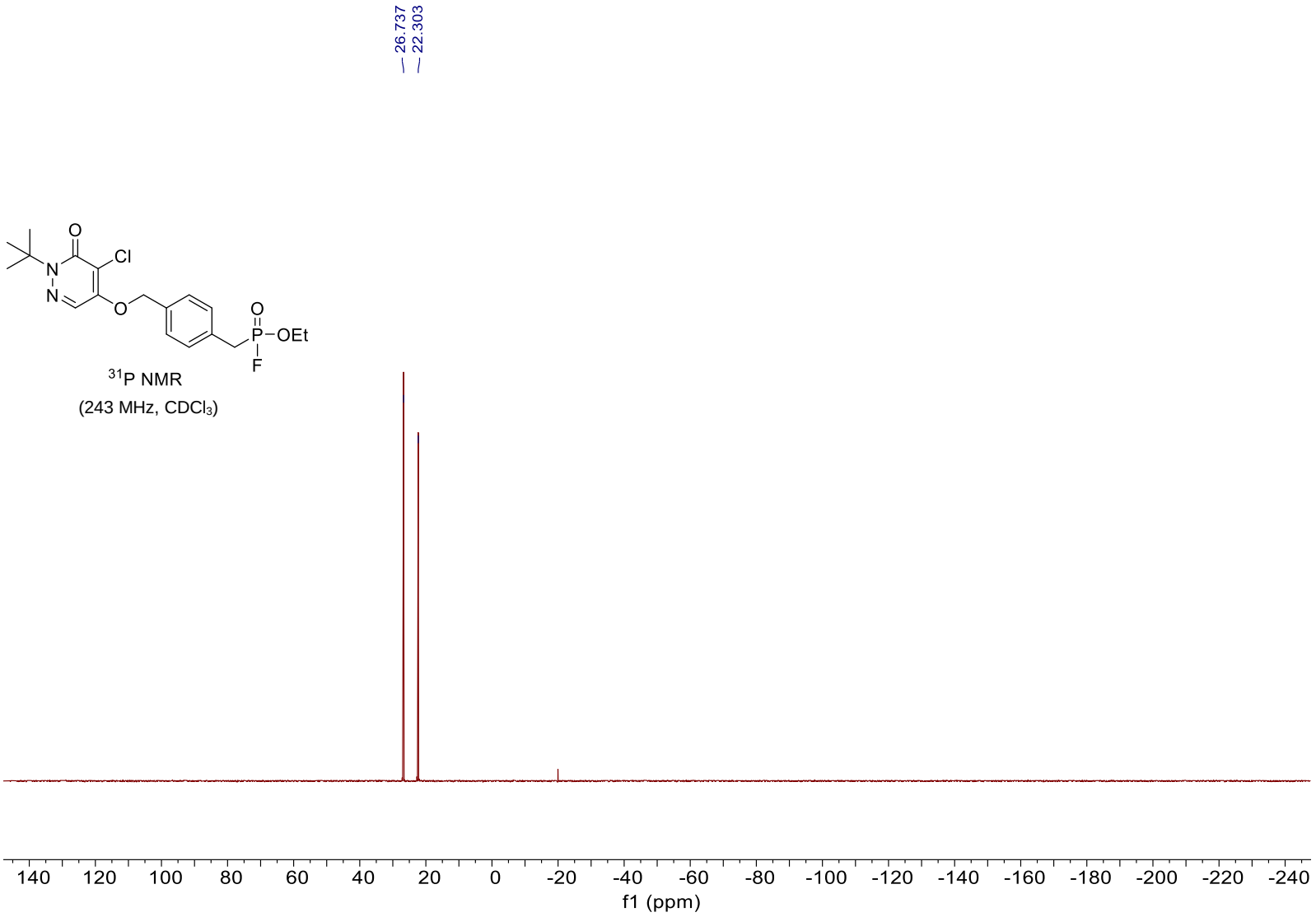
(565 MHz, $CDCl_3$)

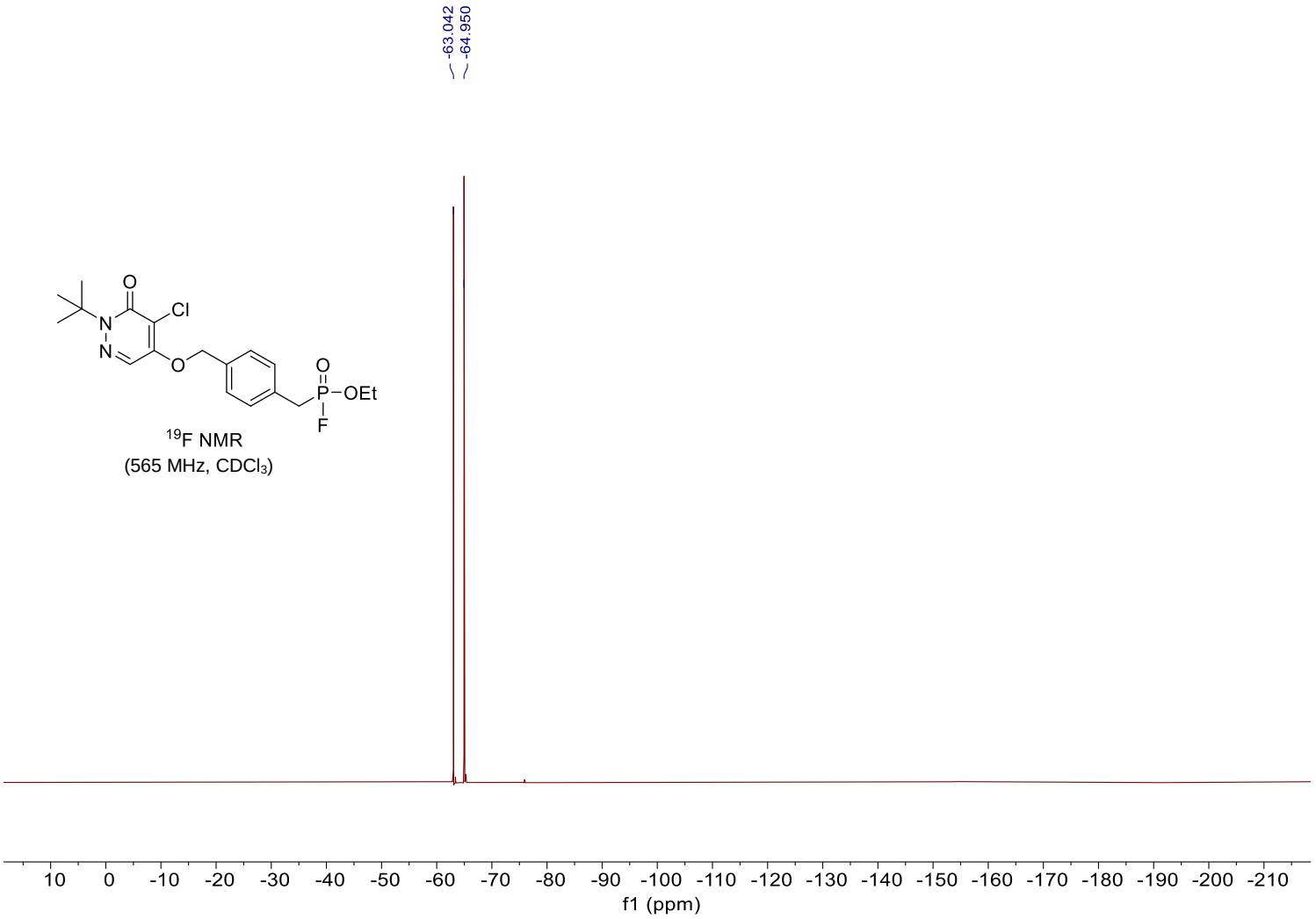

7.709
7.389
7.376
7.348
7.344
7.334
7.330
5.288
4.221
4.209
4.197
4.194
4.185
4.182
4.170
3.329
3.325
3.321
3.316
3.290
3.287
3.283
3.278
1.614
1.290
1.278
1.266
O
N
N
Cl
O
O
P
OEt
F
1H NMR
(600 MHz, CDCl3)
1.00
2.08
2.11
2.08
2.03
2.01
9.10
3.32
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)



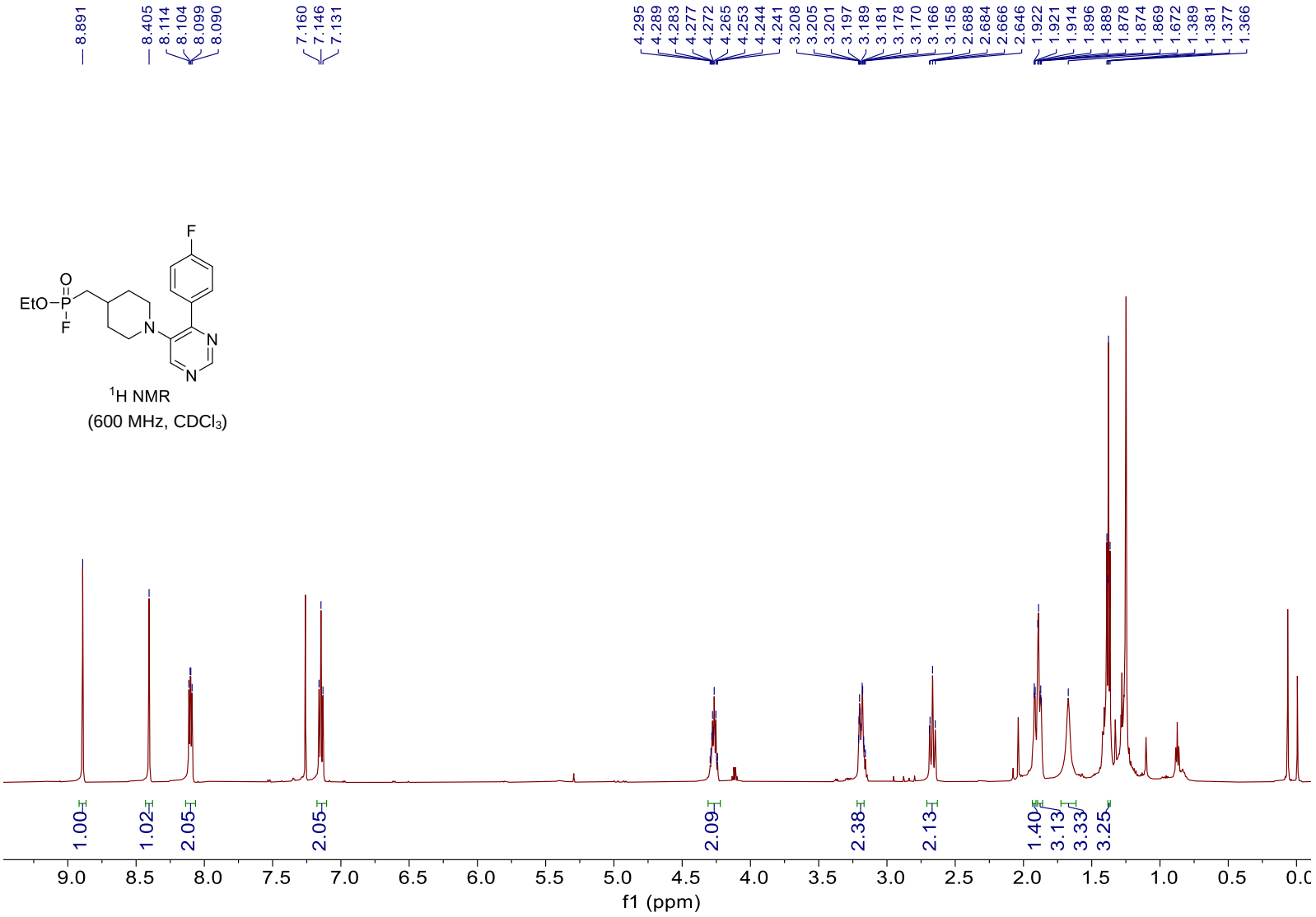
^{13}C NMR

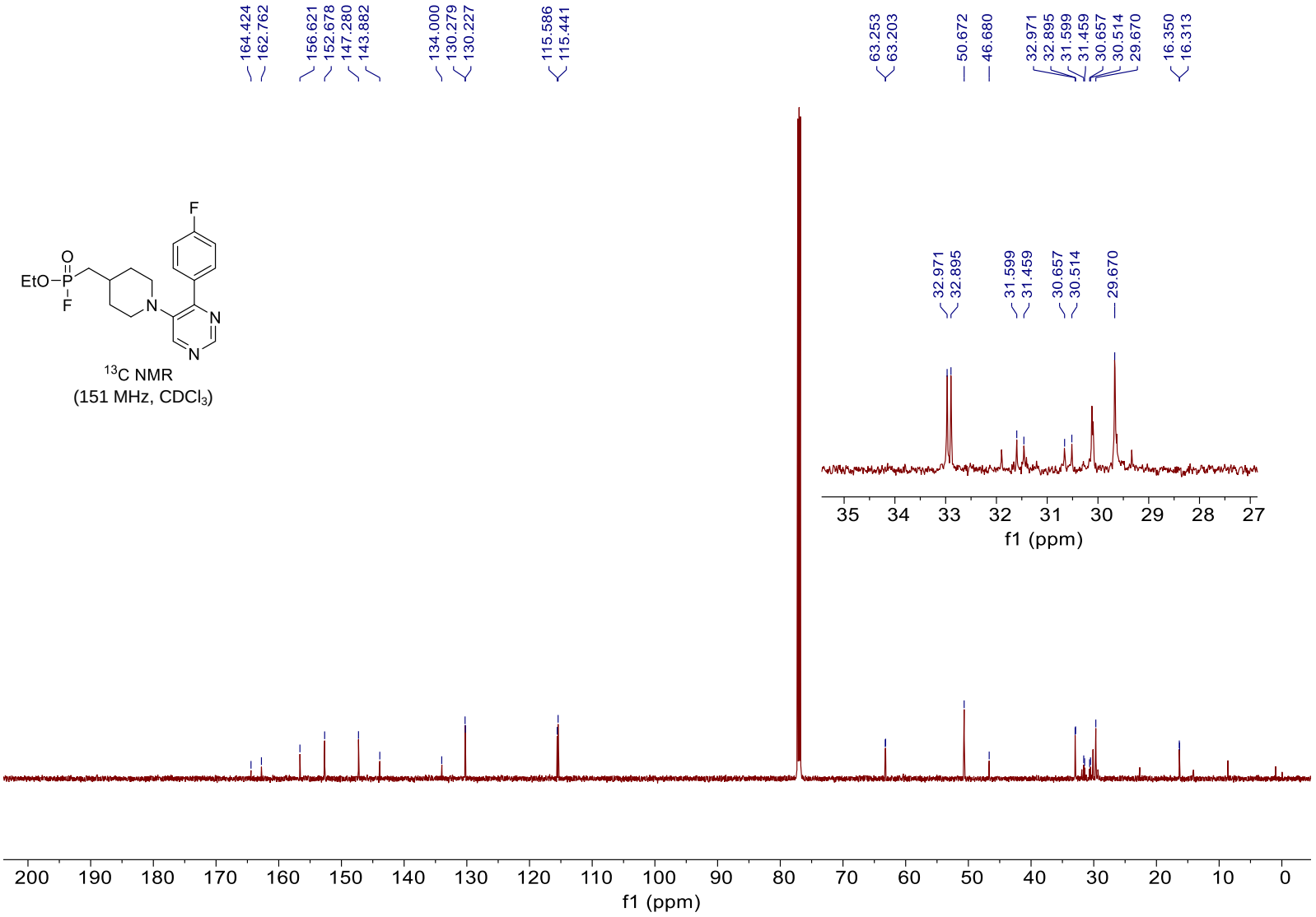
(151 MHz, $CDCl_3$)

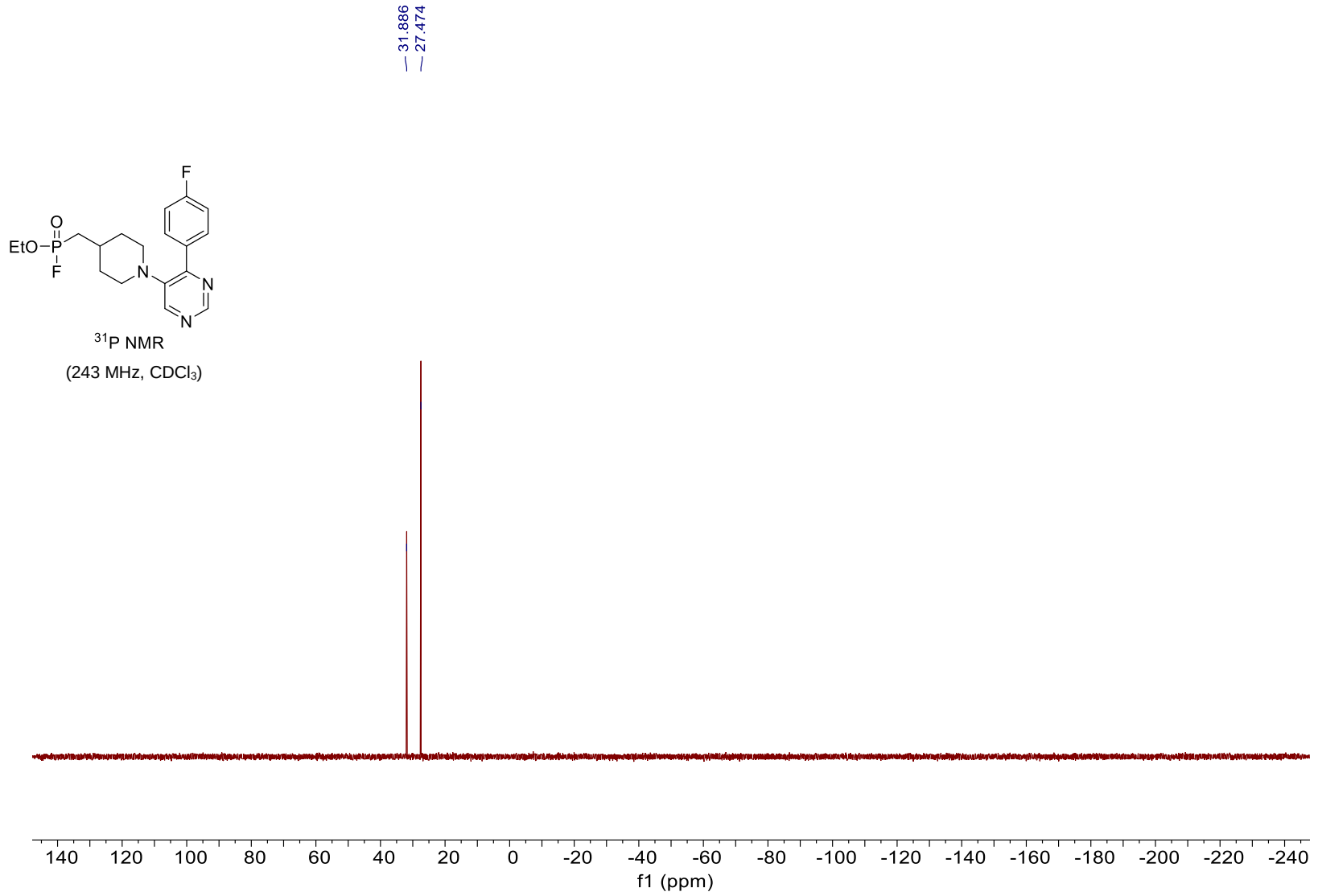

26.737
22.303
O
Cl
N
N
O
O
P
OEt
F
31P NMR
(243 MHz, CDCl3)
140
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
f1 (ppm)

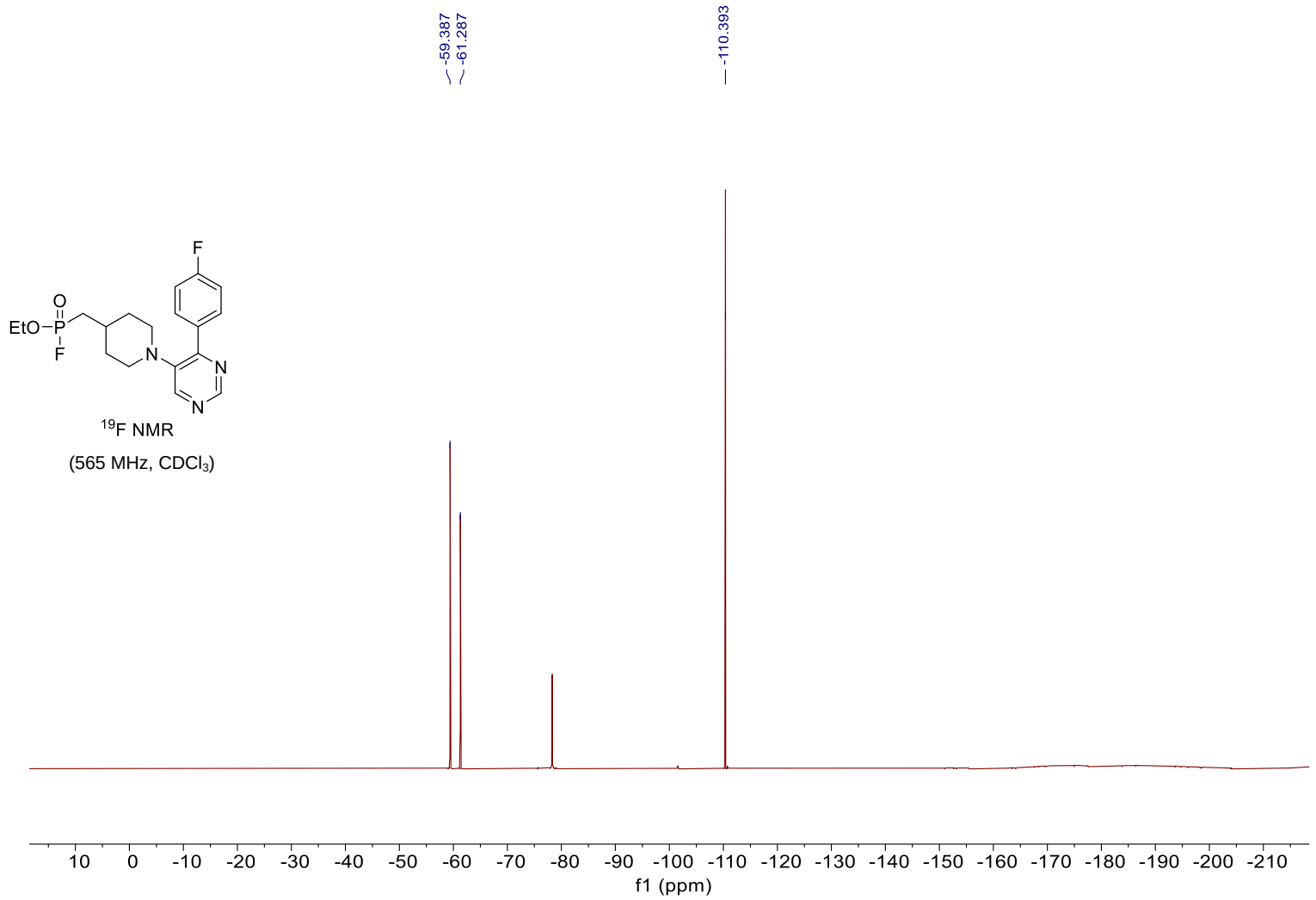


^{19}F NMR
(565 MHz, $CDCl_3$)


8.891
8.405
8.114
8.104
8.099
8.090
7.160
7.146
7.131
4.295
4.289
4.283
4.277
4.272
4.265
4.253
4.244
4.241
3.208
3.205
3.201
3.197
3.189
3.181
3.178
3.170
3.166
3.158
2.688
2.684
2.666
2.646
1.922
1.921
1.914
1.896
1.889
1.878
1.874
1.869
1.672
1.389
1.381
1.377
1.366
F
O
EtO
P
F
N
N
N
1H NMR
(600 MHz, CDCl3)
1.00
1.02
2.05
2.05
2.09
2.38
2.13
1.40
3.13
3.33
3.25
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

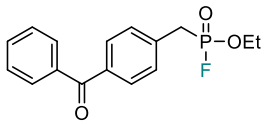

164.424
162.762
156.621
152.678
147.280
143.882
134.000
130.279
130.227
115.586
115.441
63.253
63.203
50.672
46.680
32.971
32.895
31.599
31.459
30.657
30.514
29.670
16.350
16.313
F
EtO
P
O
F
N
N
N
13C NMR
(151 MHz, CDCl3)
f1 (ppm)
f1 (ppm)


31.886
27.474
F
O
EtO–P
F
N
N
N
31P NMR
(243 MHz, CDCl3)
140 120 100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240
f1 (ppm)

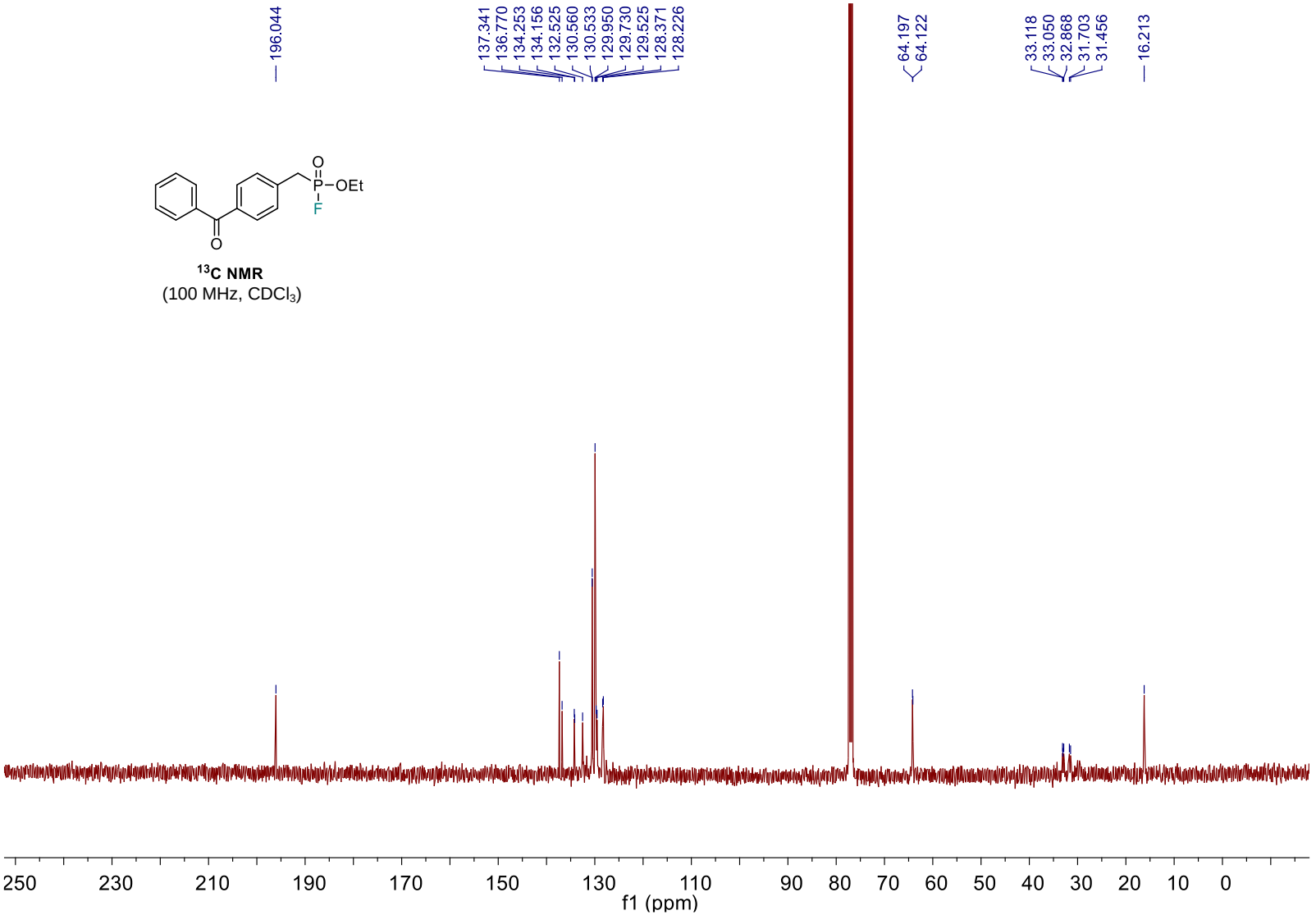


^{19}F NMR

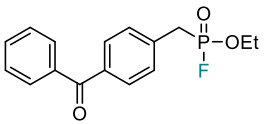
(565 MHz, $CDCl_3$)



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

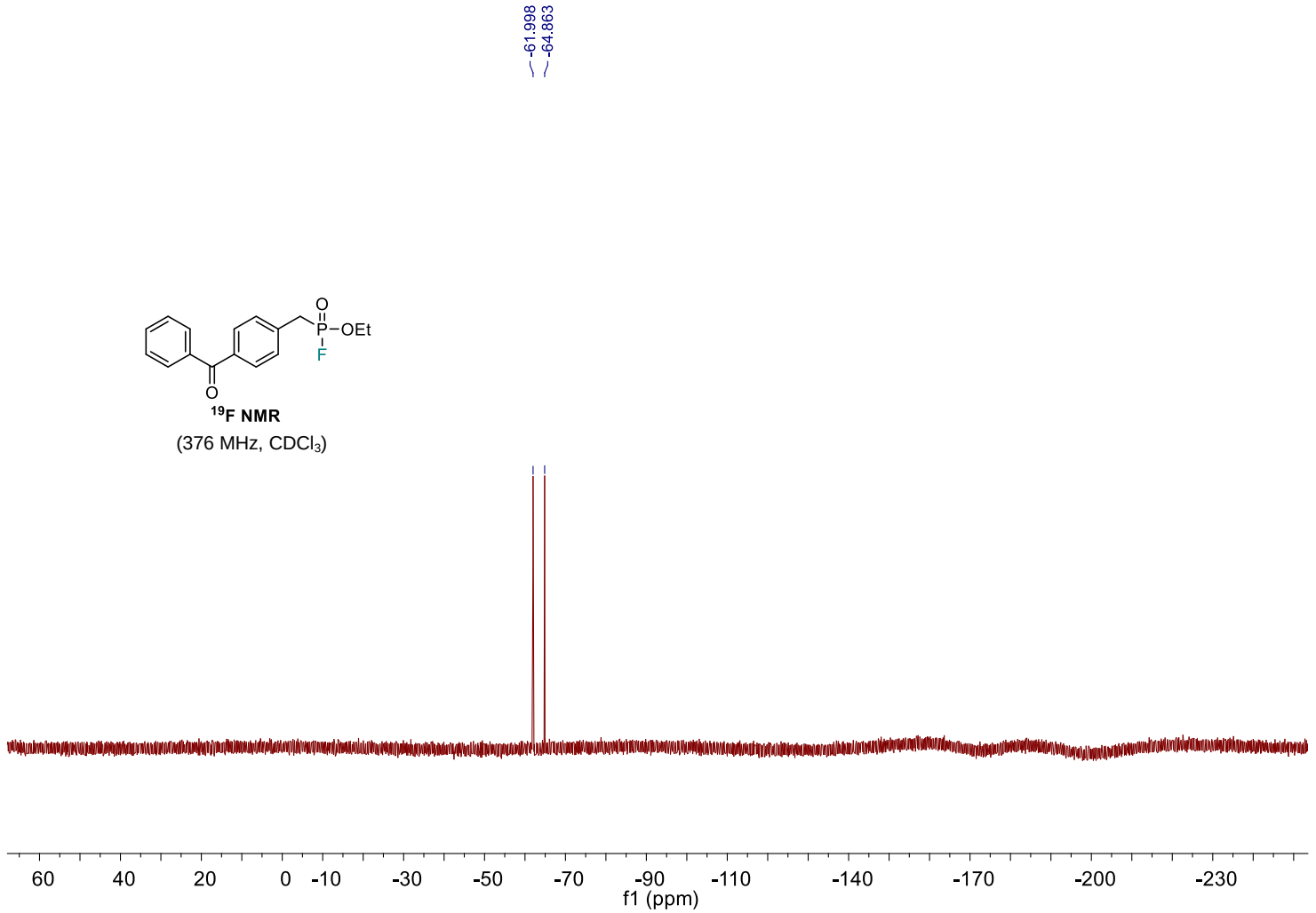


^{13}C NMR
(100 MHz, $CDCl_3$)



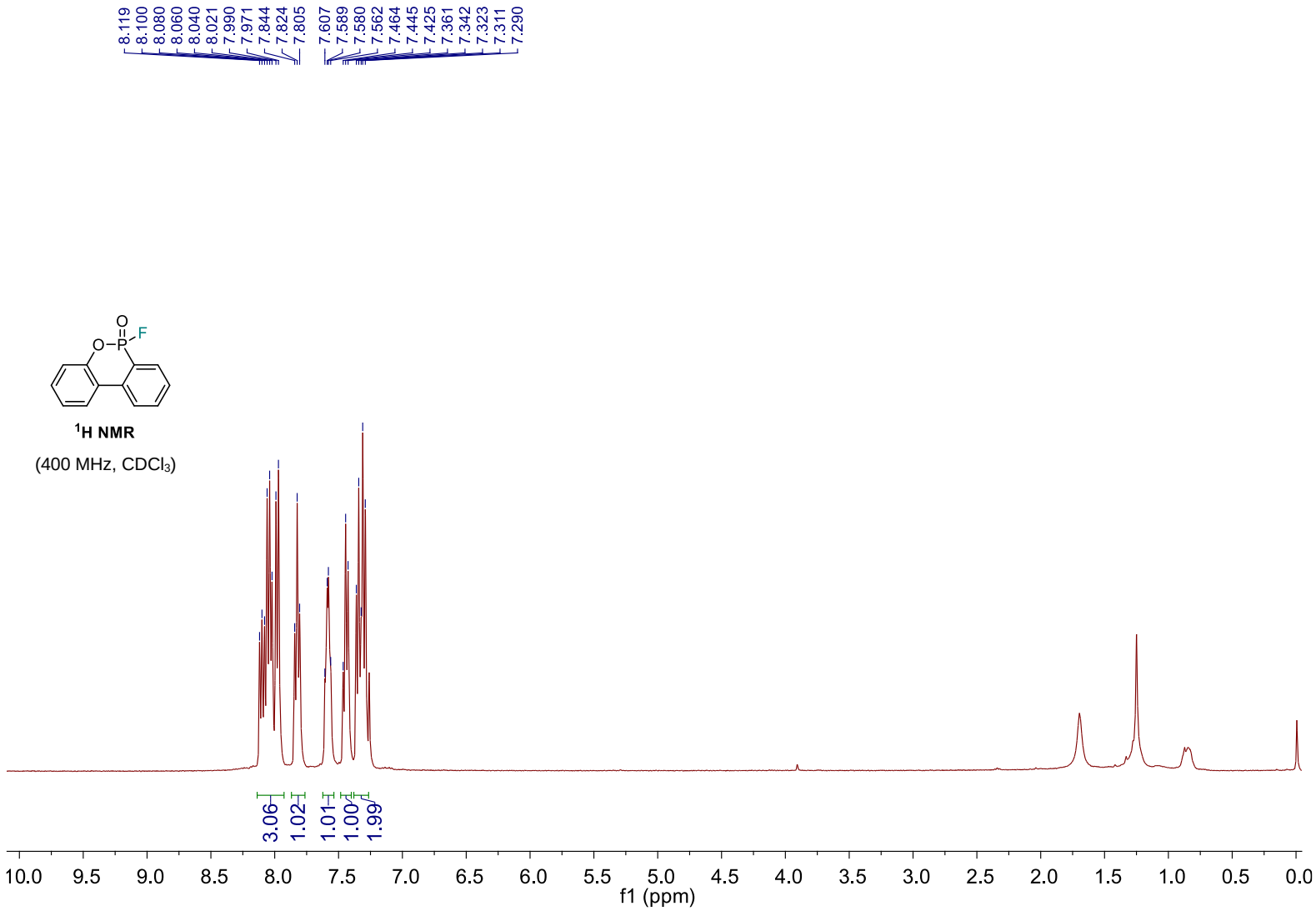
^{31}P NMR

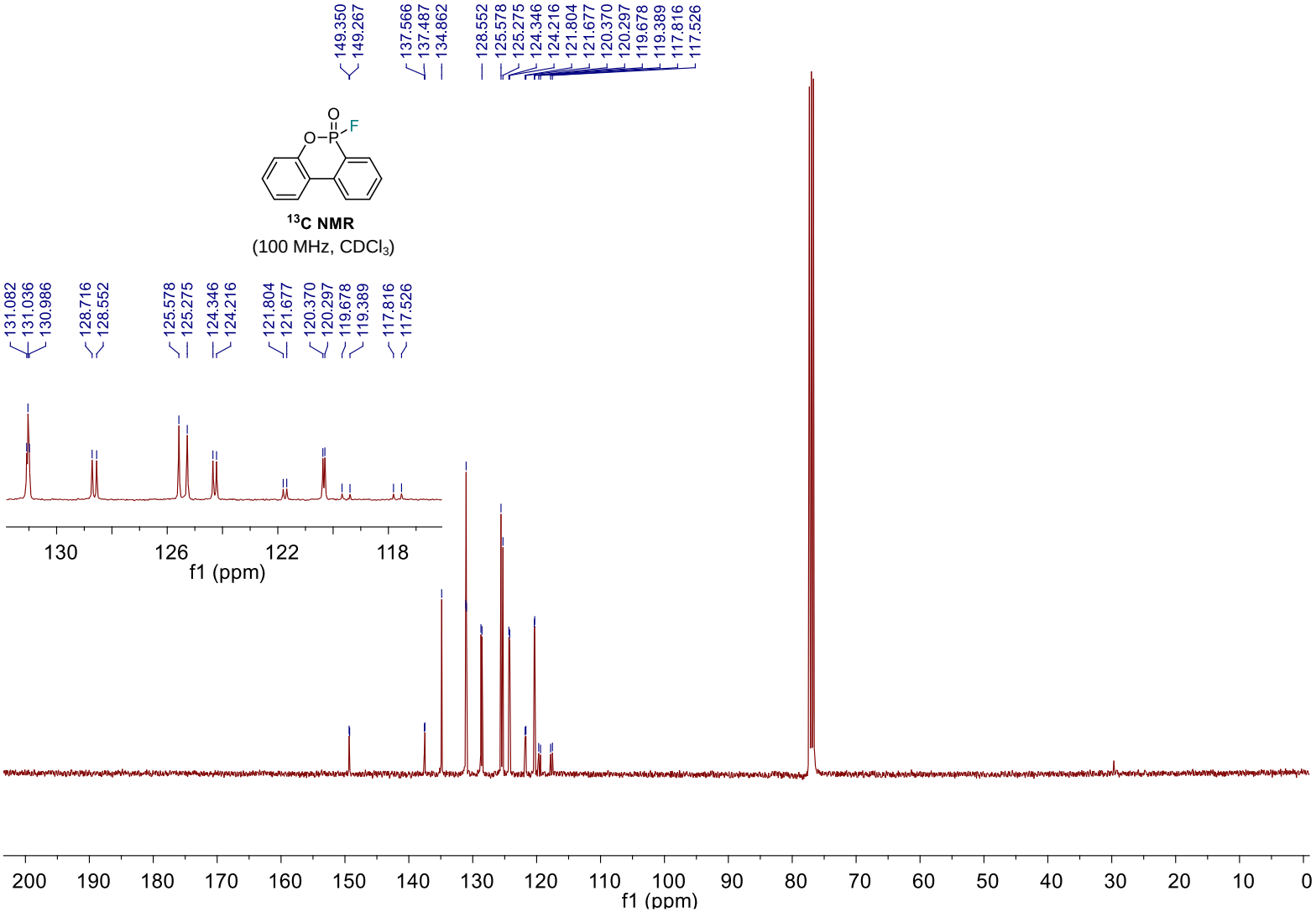
(162 MHz, $CDCl_3$)

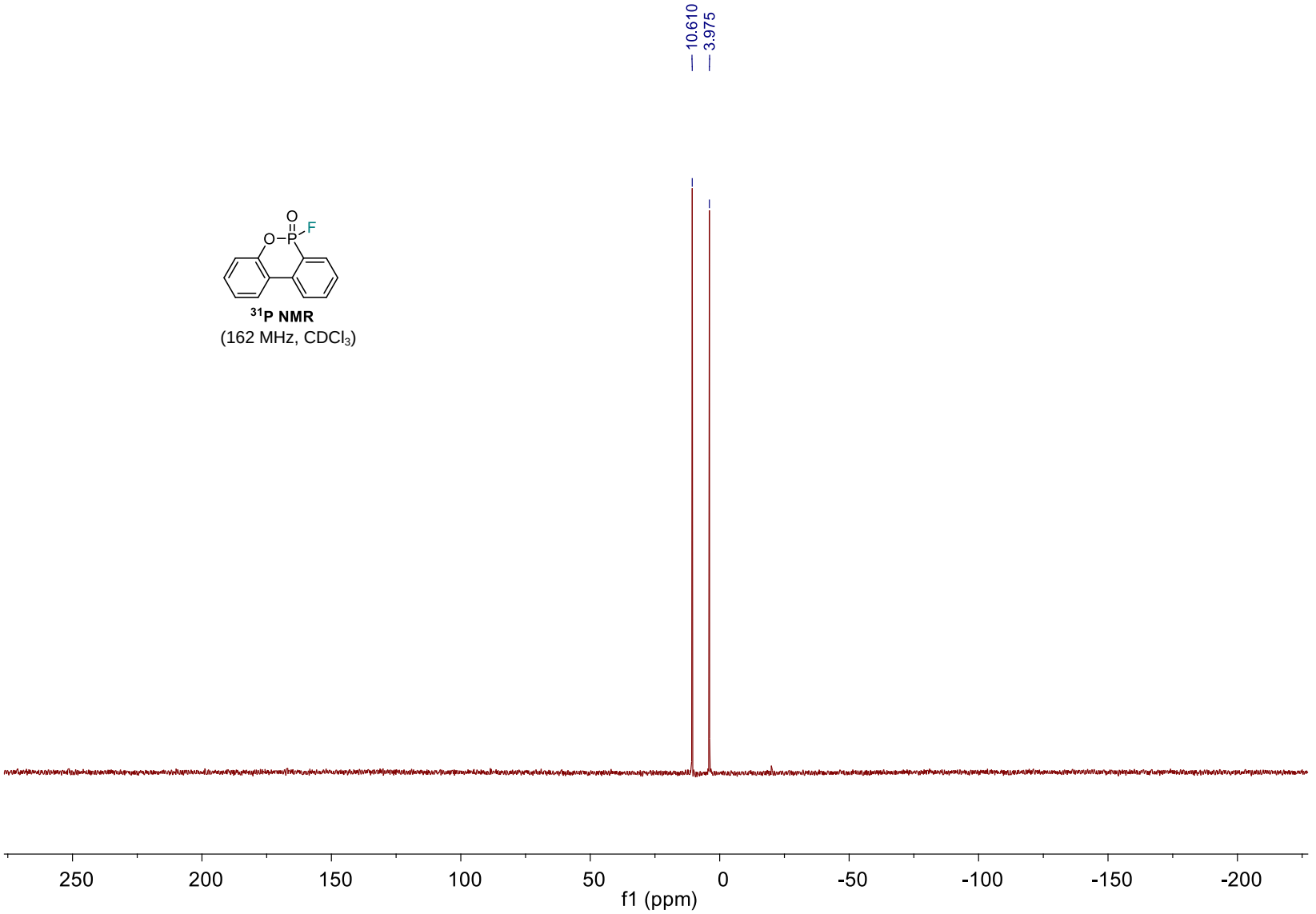


^{19}F NMR

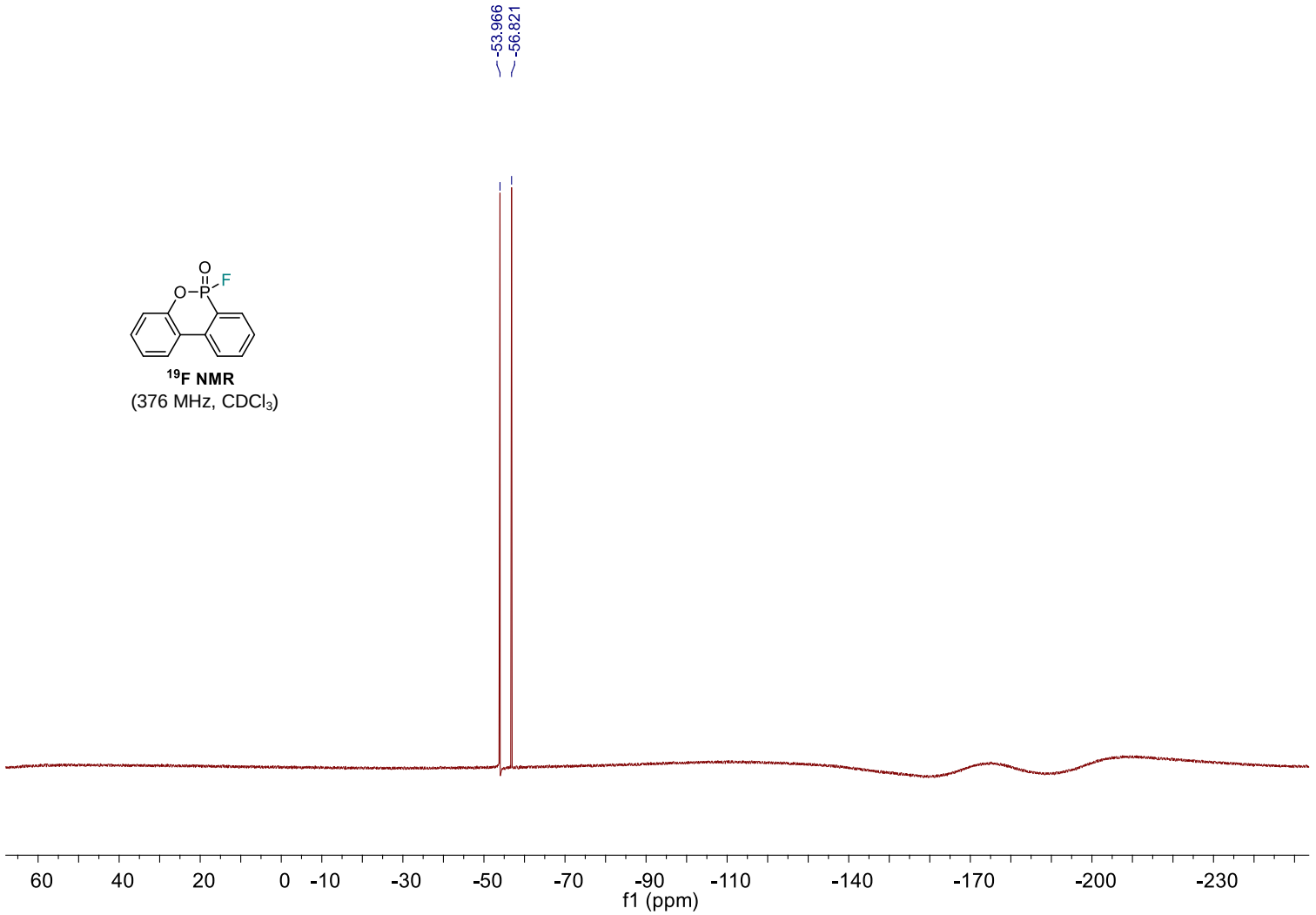
(376 MHz, $CDCl_3$)


8.119
8.100
8.080
8.060
8.040
8.021
7.990
7.971
7.844
7.824
7.805
7.607
7.589
7.580
7.562
7.464
7.445
7.425
7.361
7.342
7.323
7.311
7.290
O
O
P
F
^{1}H NMR
(400 MHz, CDCl$_3$)
3.06
1.02
1.01
1.00
1.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

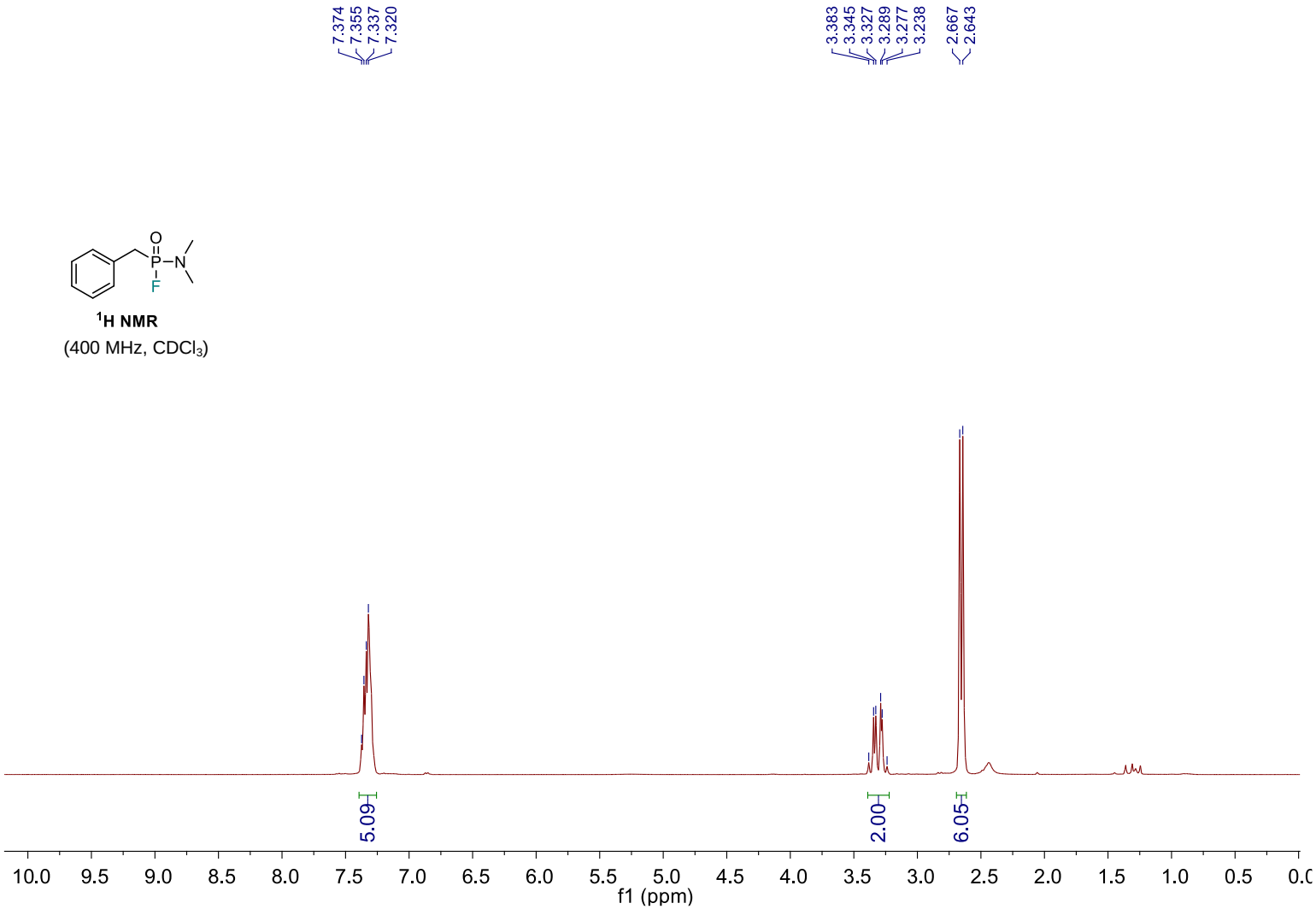

149.350
149.267
137.566
137.487
134.862
128.552
125.578
125.275
124.346
124.216
121.804
121.677
120.370
120.297
119.678
119.389
117.816
117.526
O
O–P
F
13C NMR
(100 MHz, CDCl3)
131.082
131.036
130.986
128.716
128.552
125.578
125.275
124.346
124.216
121.804
121.677
120.370
120.297
119.678
119.389
117.816
117.526
130
126
122
118
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



^{31}P NMR
(162 MHz, $CDCl_3$)

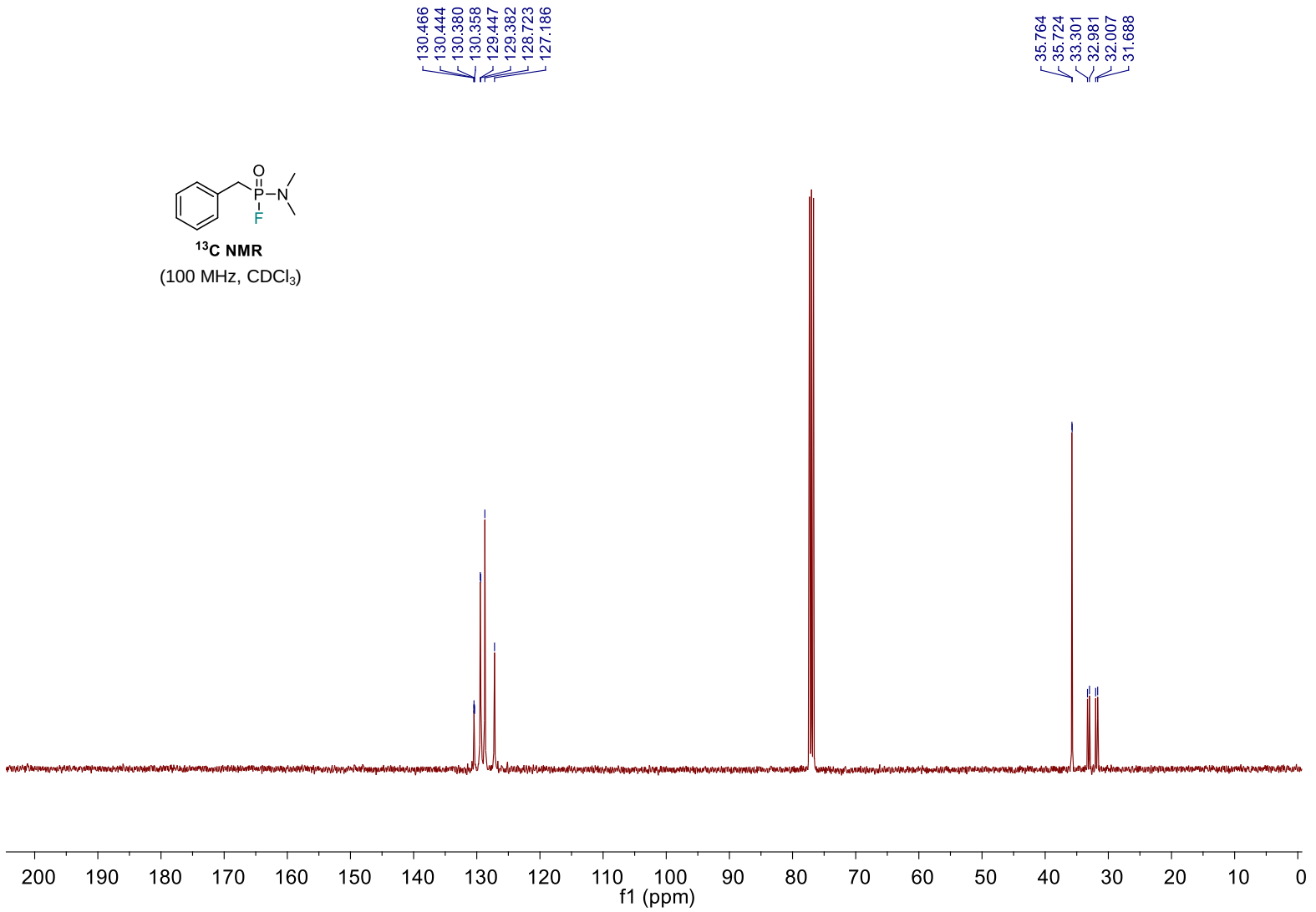


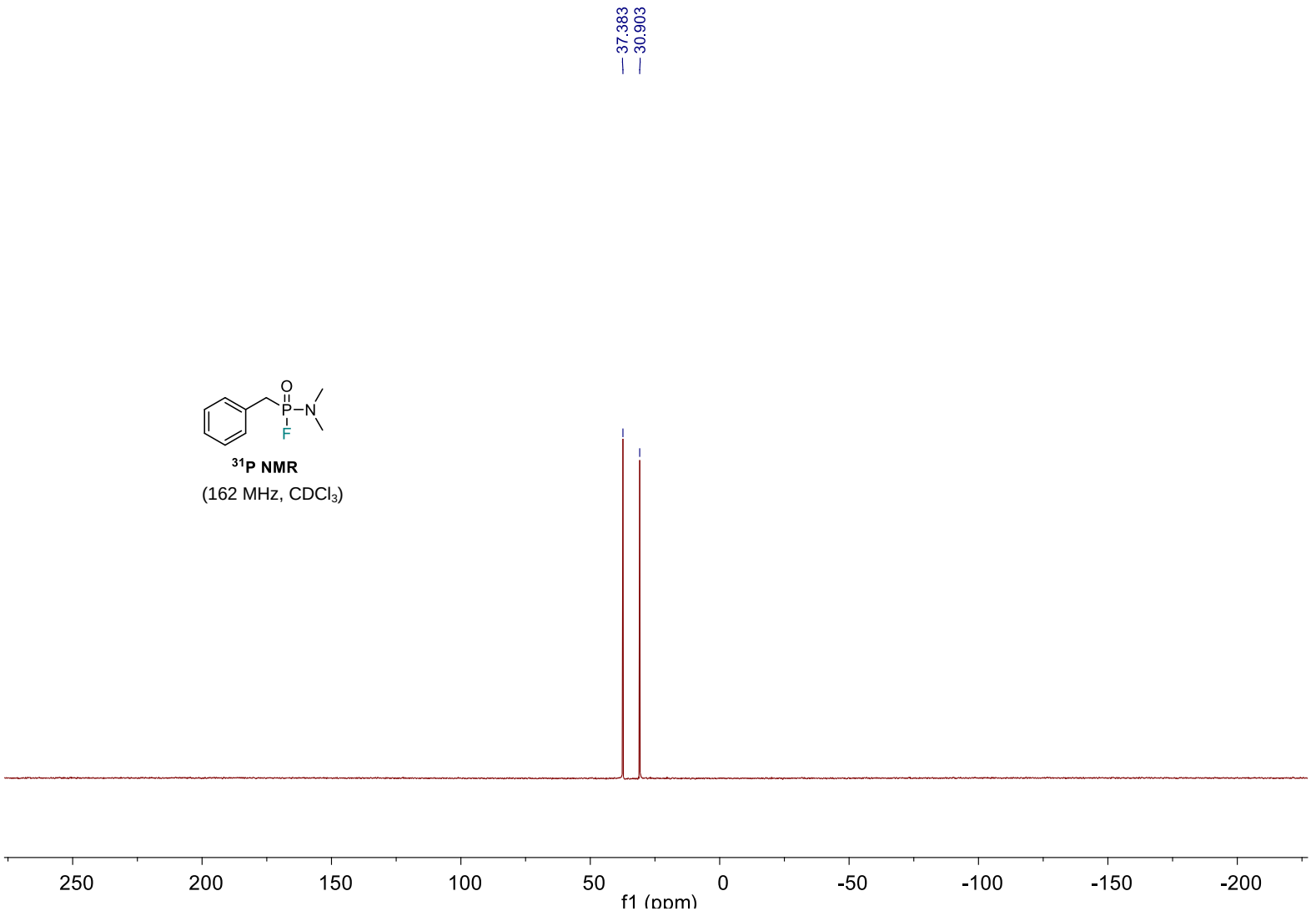
^{19}F NMR
(376 MHz, $CDCl_3$)



^{1}H NMR

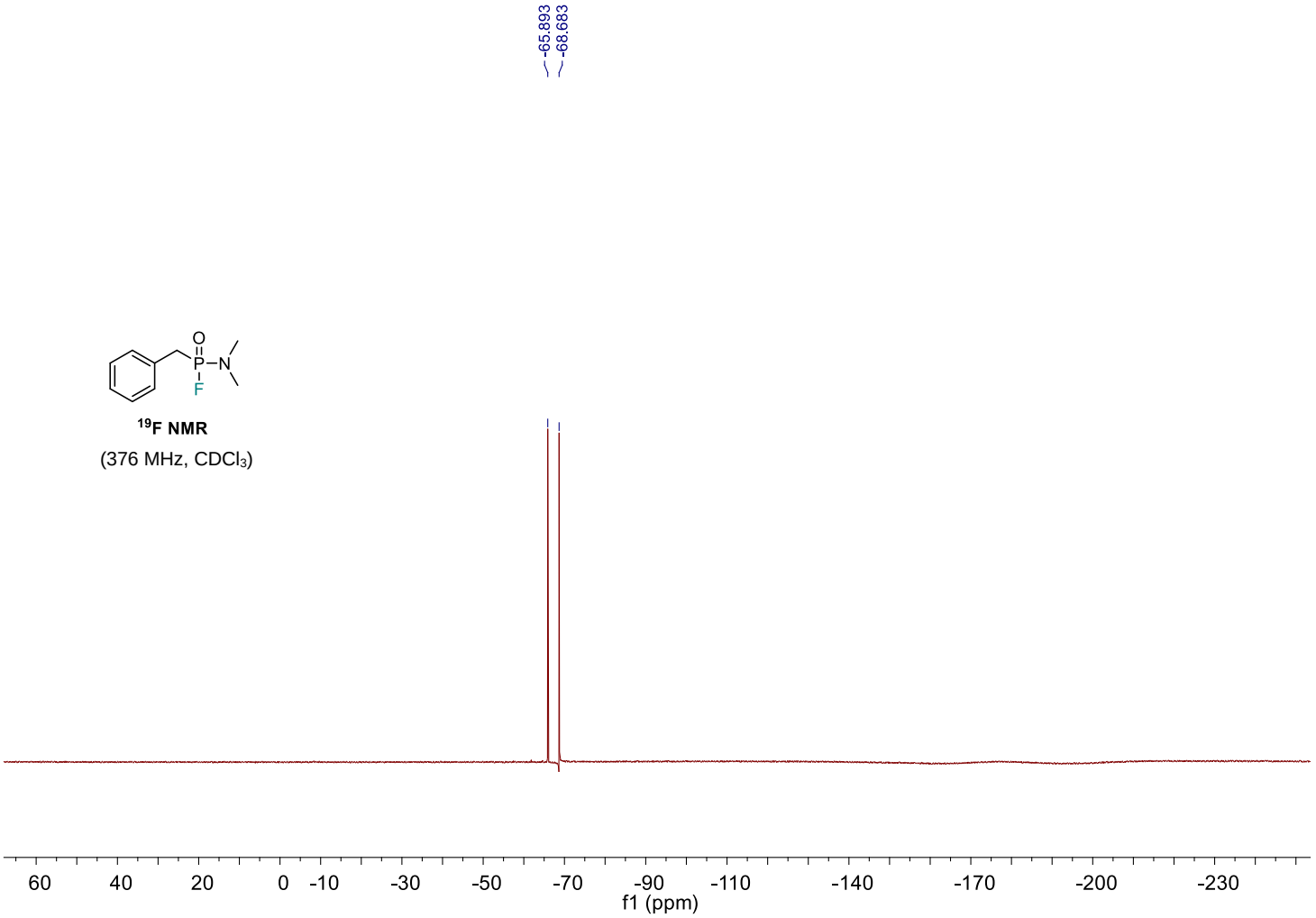
(400 MHz, $CDCl_3$)


130.466
130.444
130.380
130.358
129.447
129.382
128.723
127.186
35.764
35.724
33.301
32.981
32.007
31.688
O
P
N
F
^{13}C NMR
(100 MHz, $CDCl_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



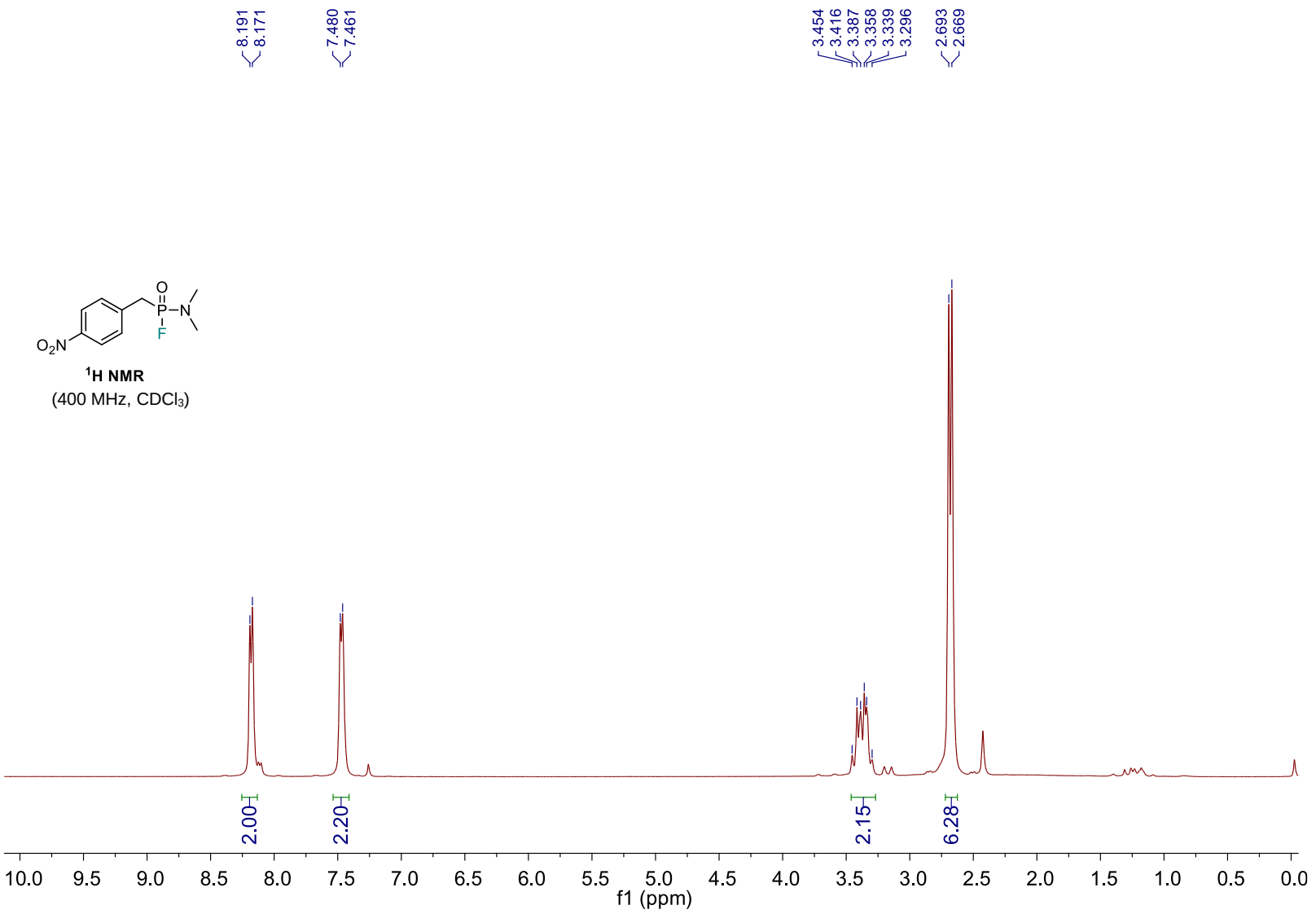
^{31}P NMR

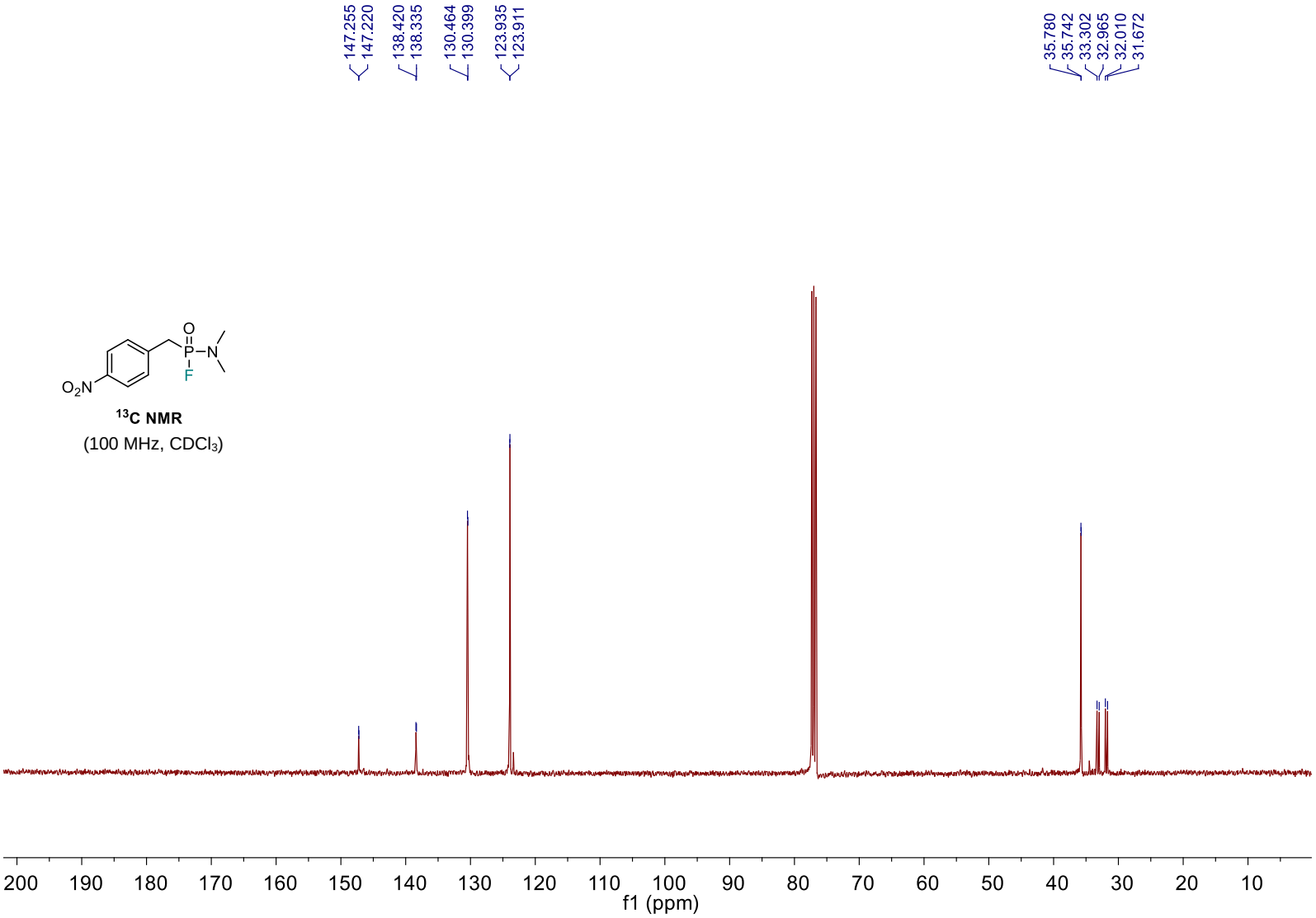
(162 MHz, $CDCl_3$)

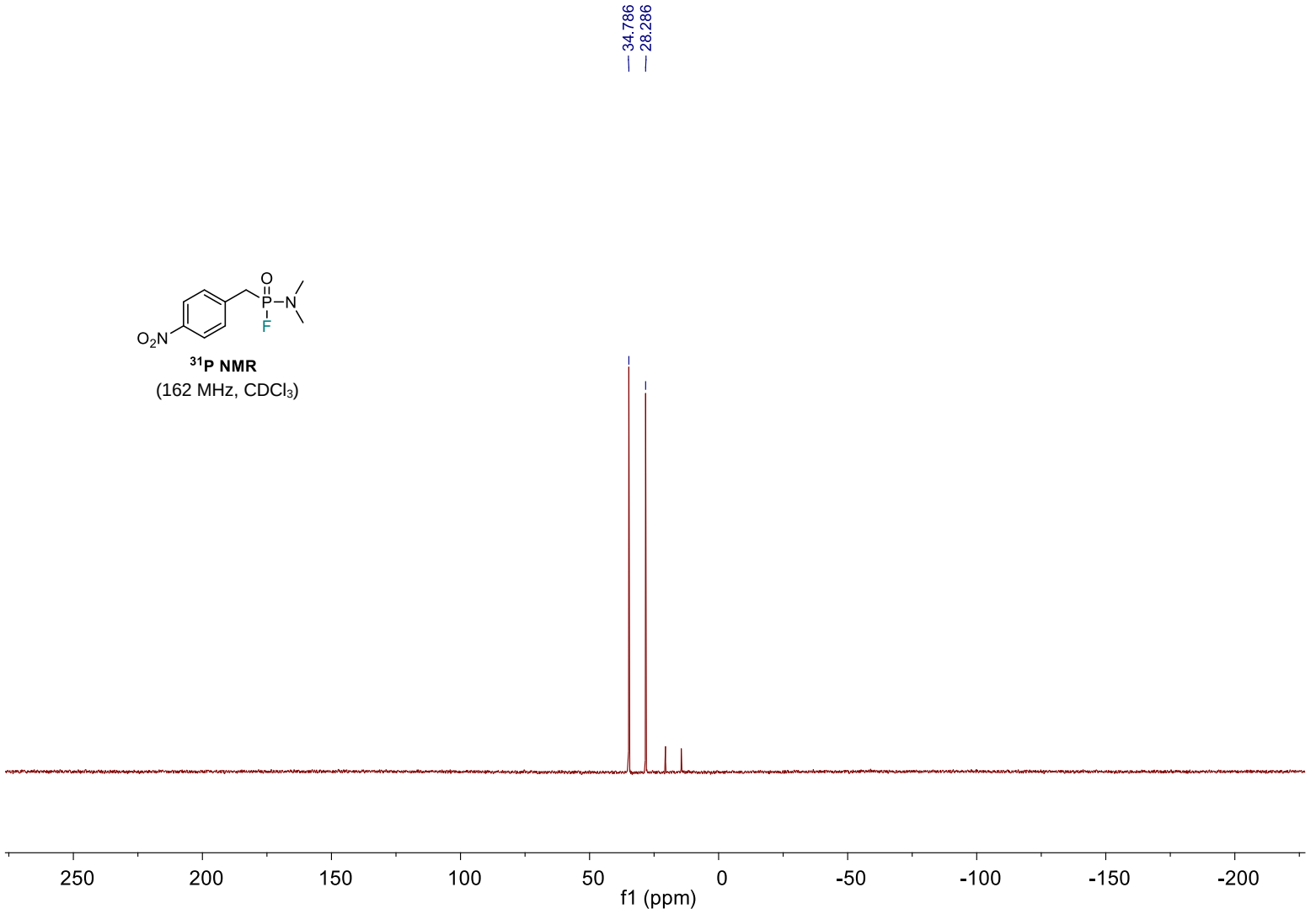


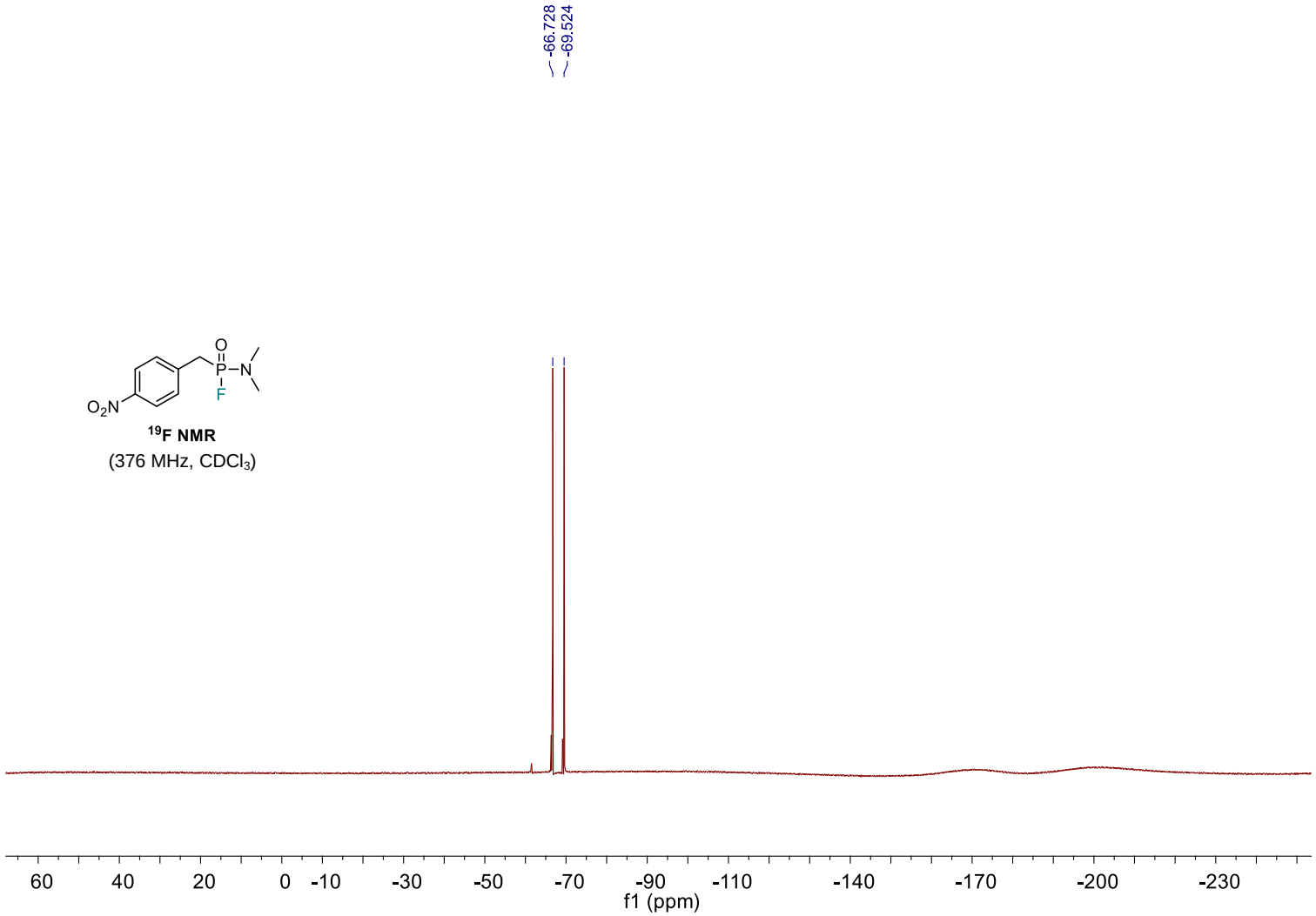
^{19}F NMR

(376 MHz, $CDCl_3$)


8.191
8.171
7.480
7.461
3.454
3.416
3.387
3.358
3.339
3.296
2.693
2.669
O
P
N
F
O_2N
^{1}H NMR
(400 MHz, $CDCl_3$)
2.00
2.20
2.15
6.28
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

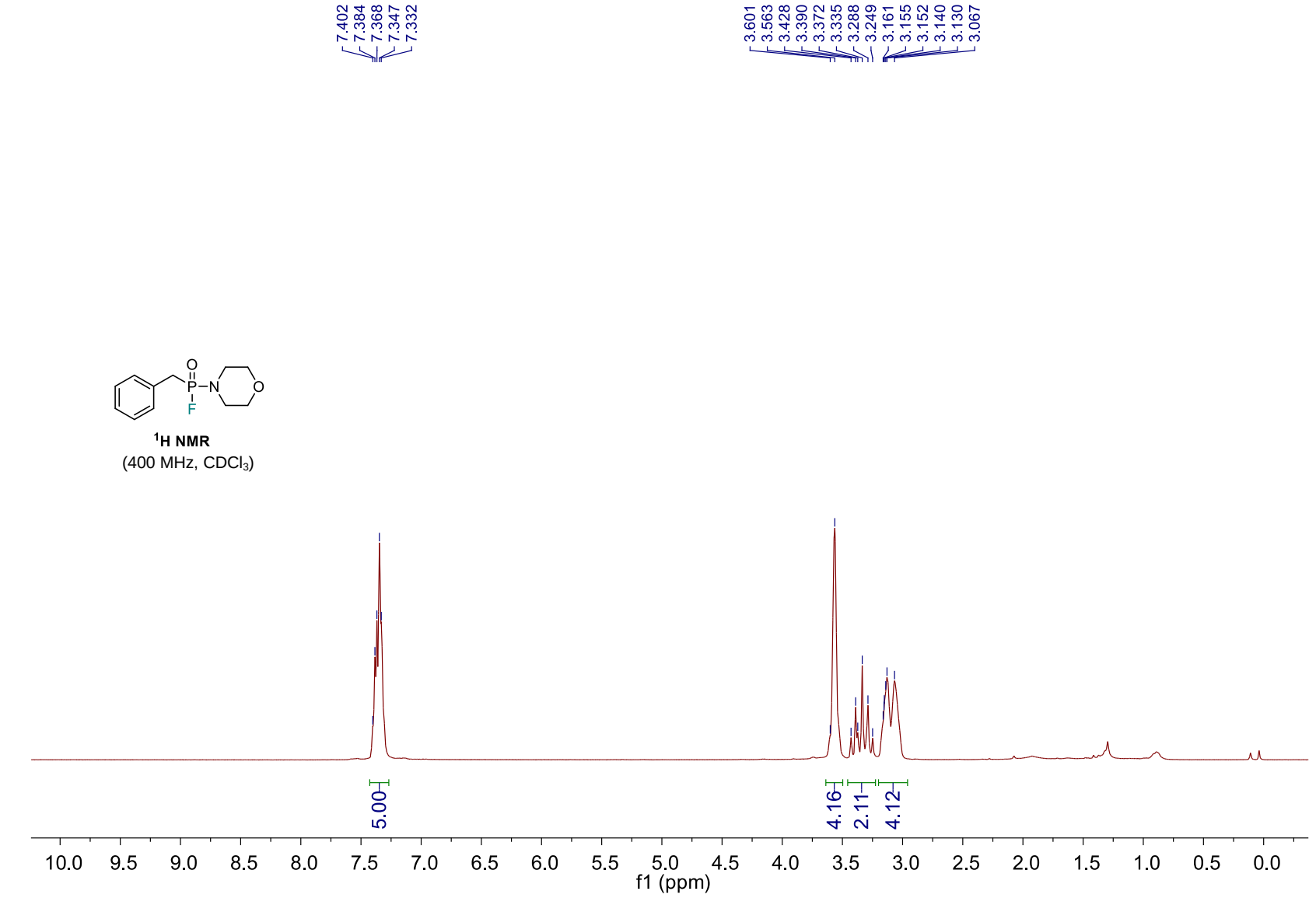

147.255
147.220
138.420
138.335
130.464
130.399
123.935
123.911
35.780
35.742
33.302
32.965
32.010
31.672
O
P
N
F
O2N
13C NMR
(100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


34.786
28.286
O
P
N
F
O2N
31P NMR
(162 MHz, CDCl3)
250
200
150
100
50
0
-50
-100
-150
-200
f1 (ppm)

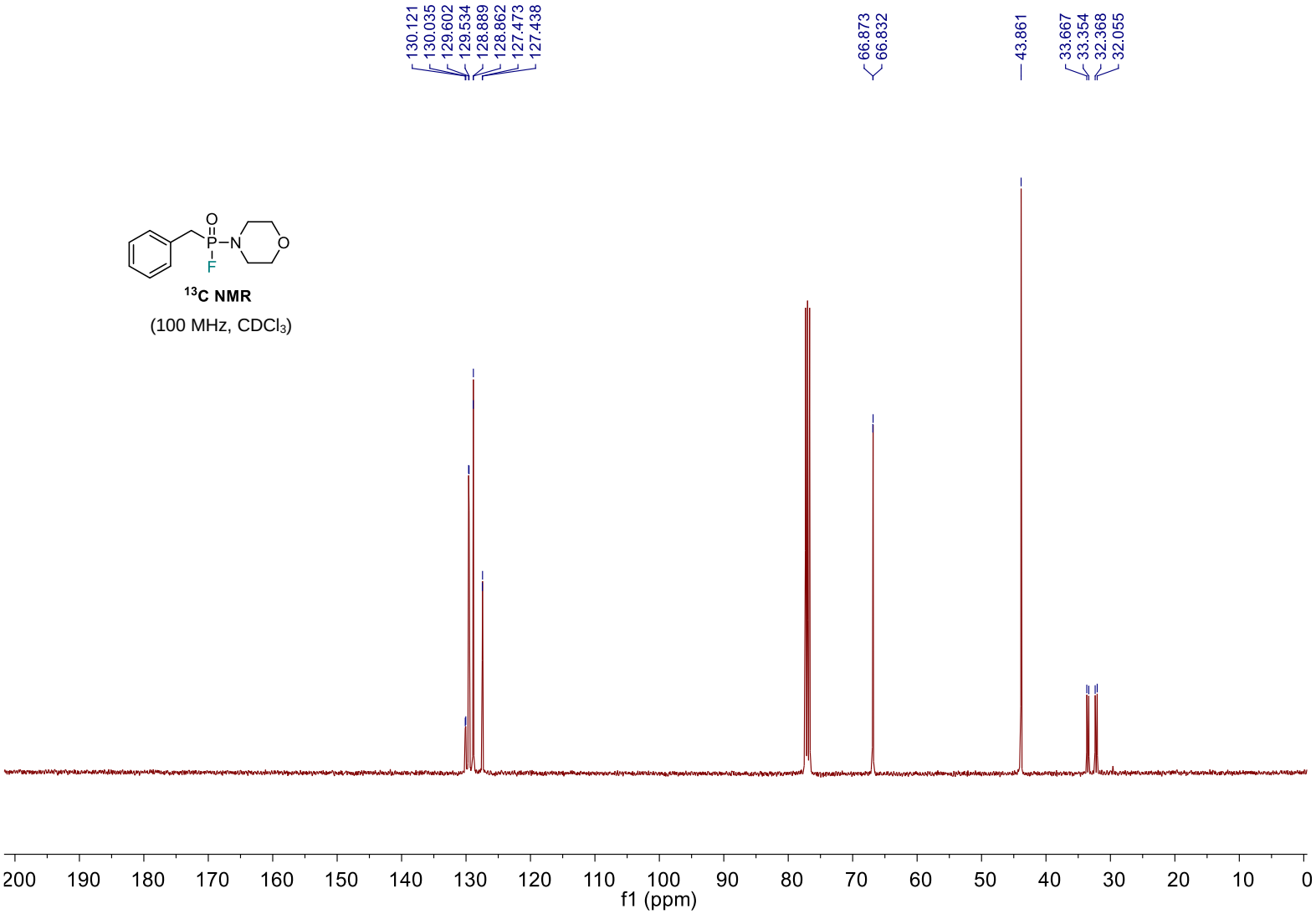


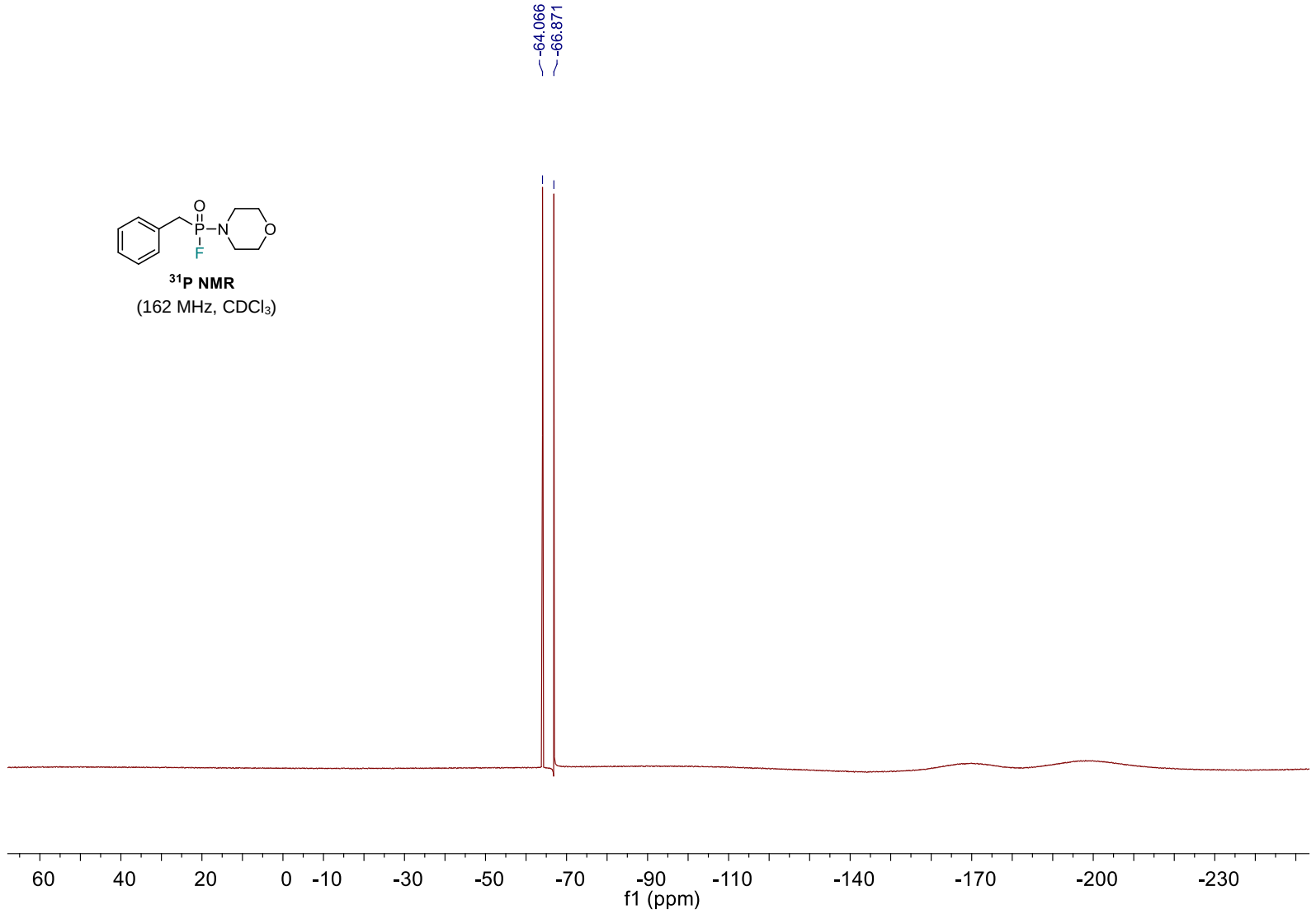
^{19}F NMR

(376 MHz, $CDCl_3$)

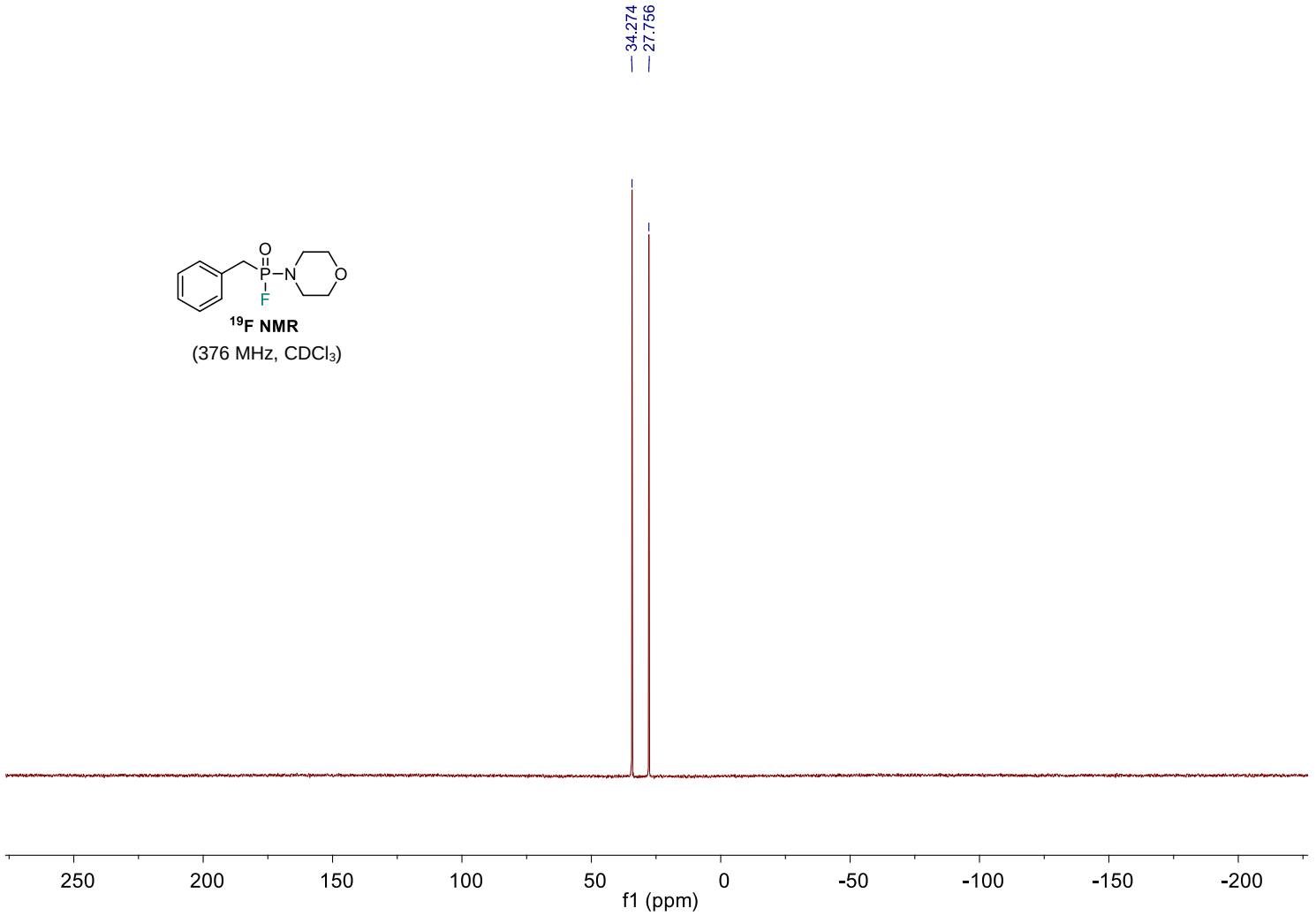


^{1}H NMR
(400 MHz, $CDCl_3$)


130.121
130.035
129.602
129.534
128.889
128.862
127.473
127.438
66.873
66.832
43.861
33.667
33.354
32.368
32.055
O
P
N
O
F
13C NMR
(100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

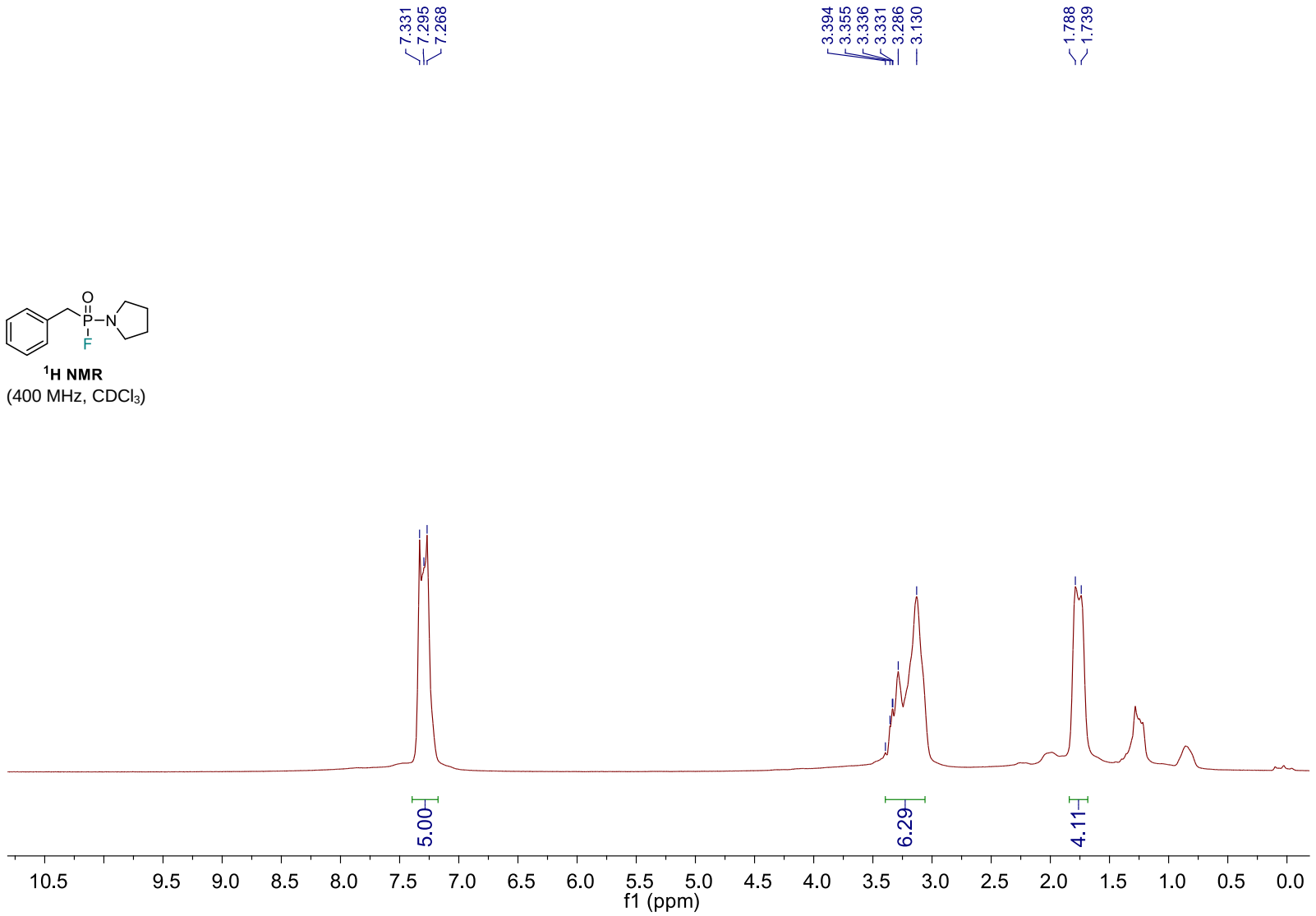


^{31}P NMR
(162 MHz, $CDCl_3$)

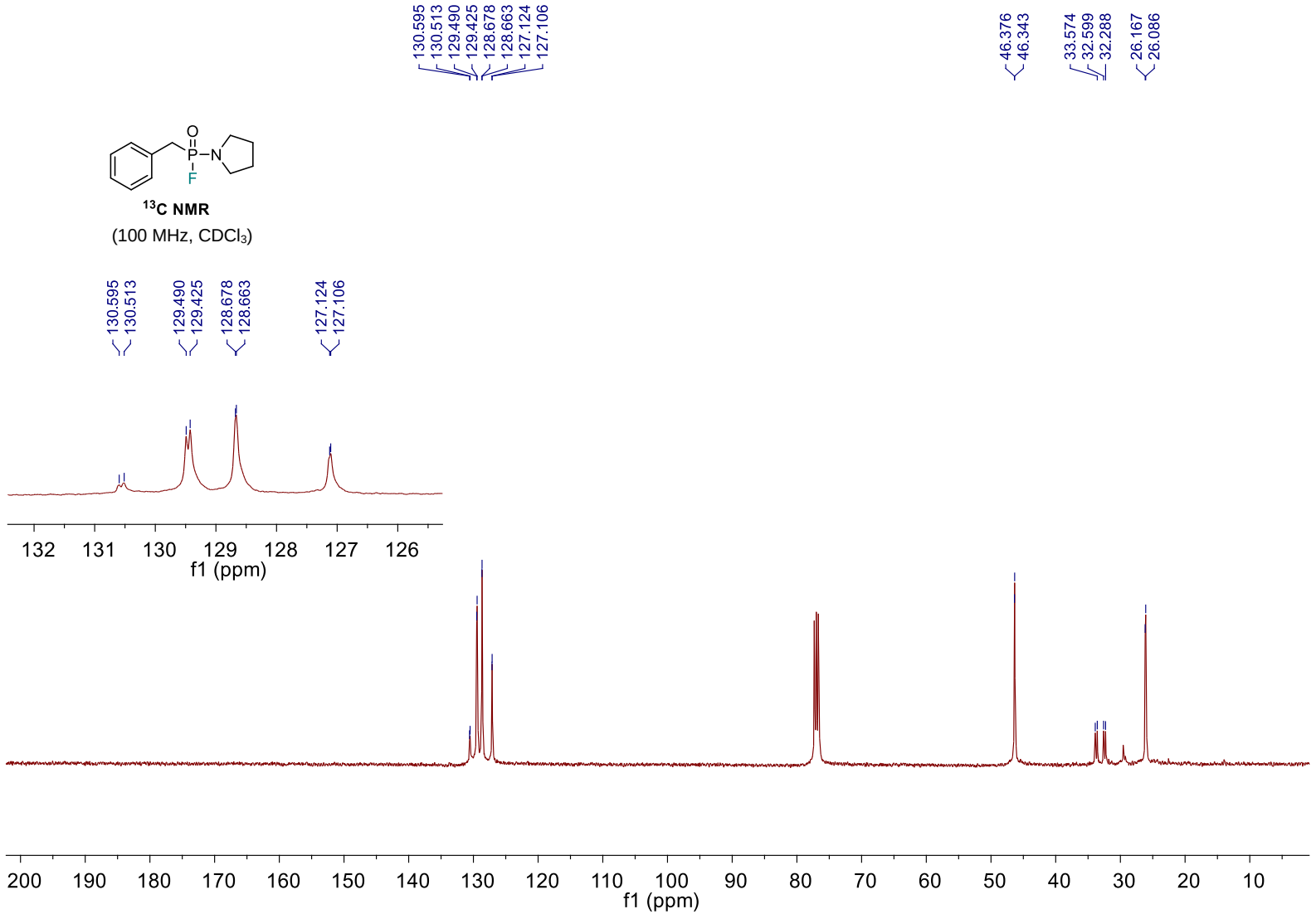


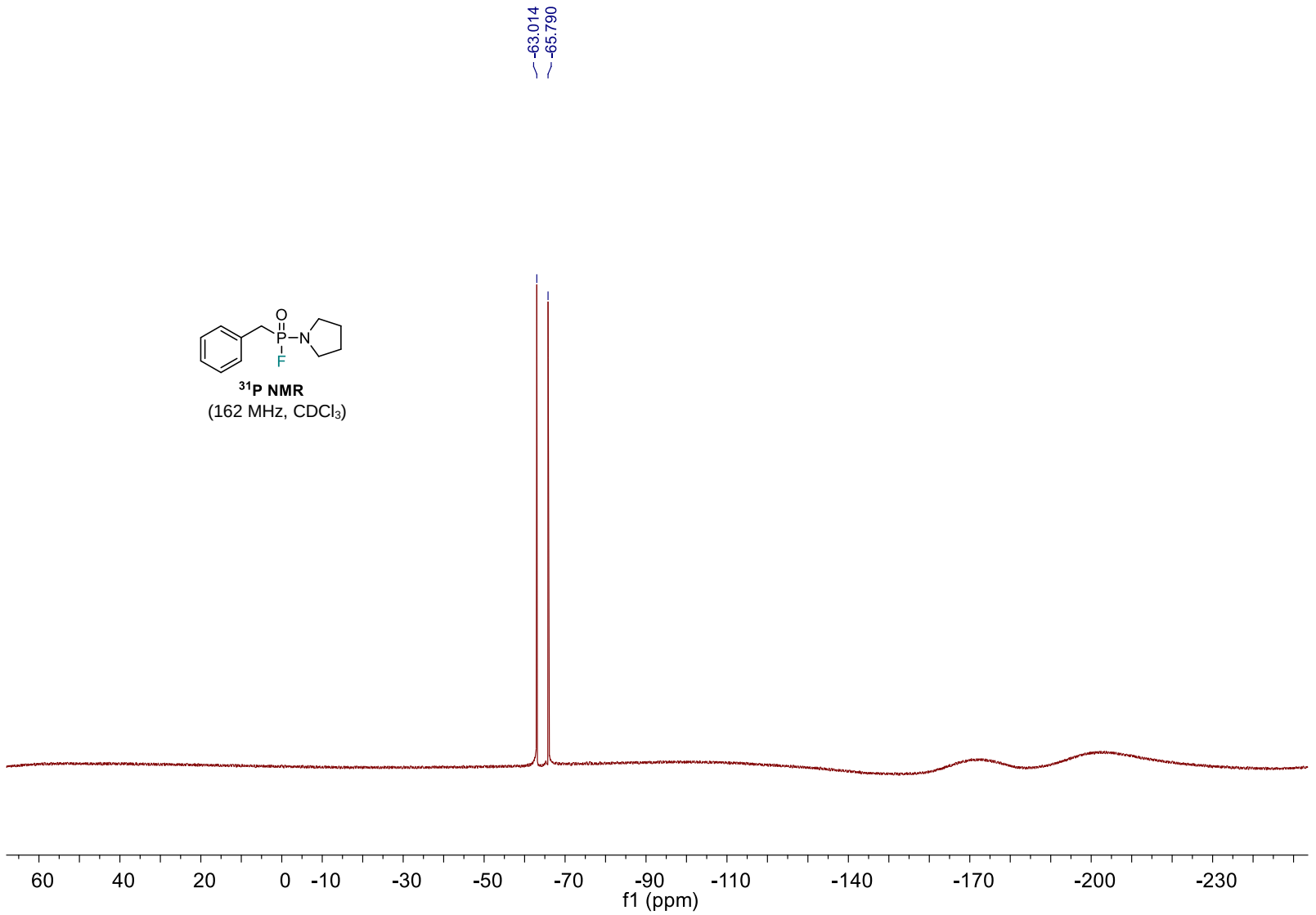
^{19}F NMR

(376 MHz, $CDCl_3$)

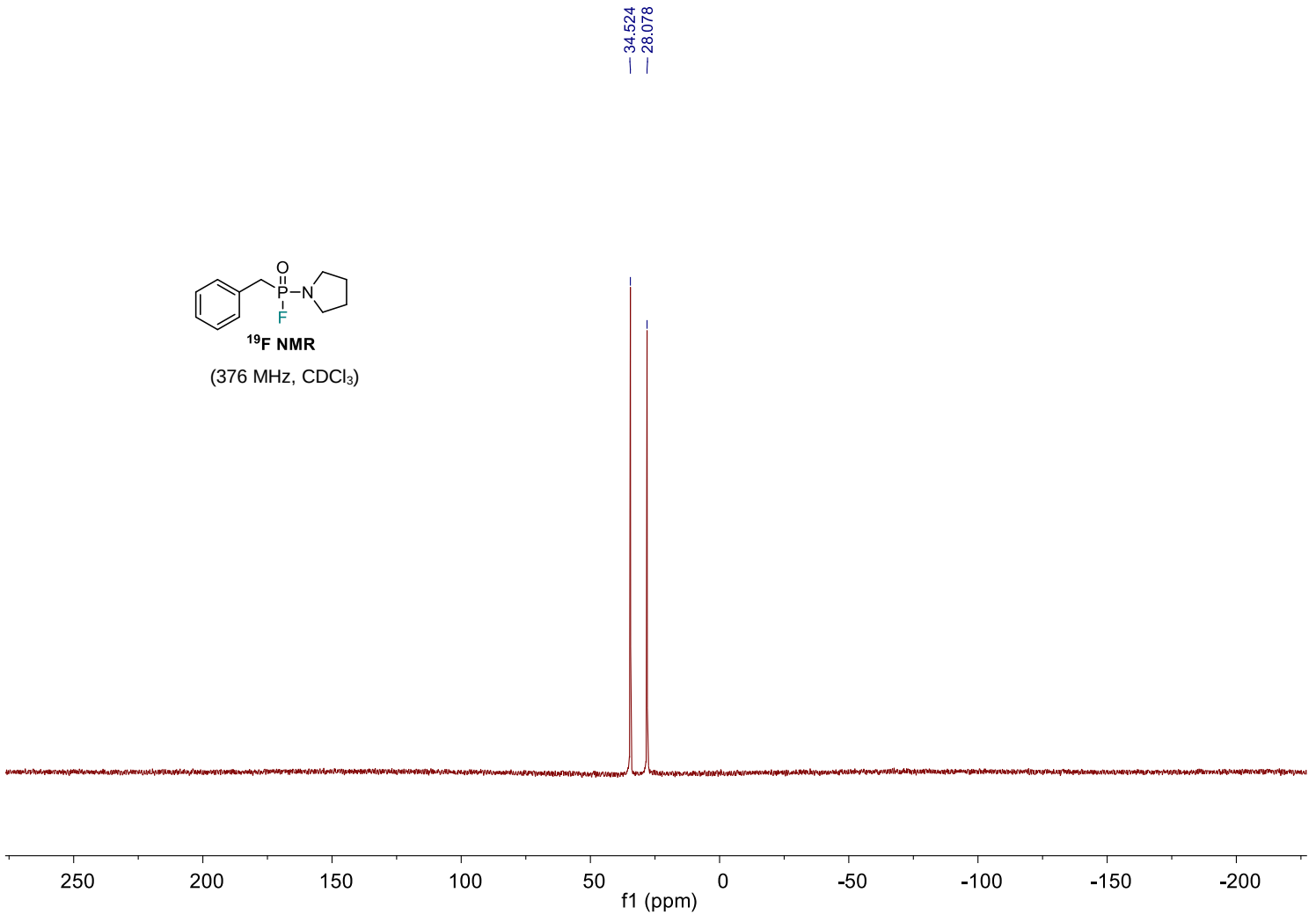


^{1}H NMR
(400 MHz, $CDCl_3$)


130.595
130.513
129.490
129.425
128.678
128.663
127.124
127.106
46.376
46.343
33.574
32.599
32.288
26.167
26.086
O
P
N
F
13C NMR
(100 MHz, CDCl3)
f1 (ppm)
f1 (ppm)

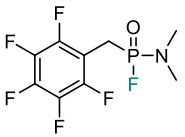


^{31}P NMR
(162 MHz, $CDCl_3$)

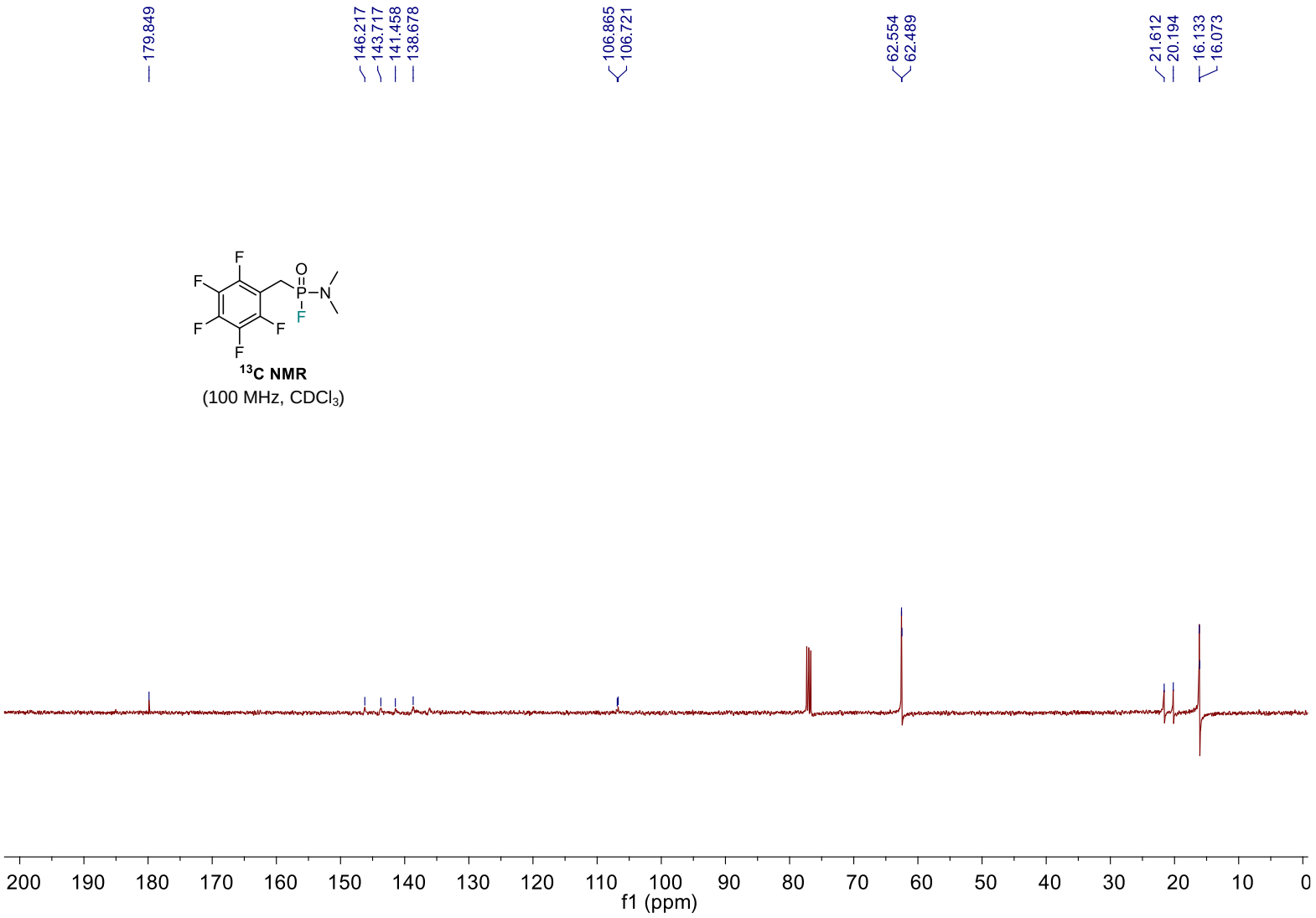


^{19}F NMR

(376 MHz, $CDCl_3$)

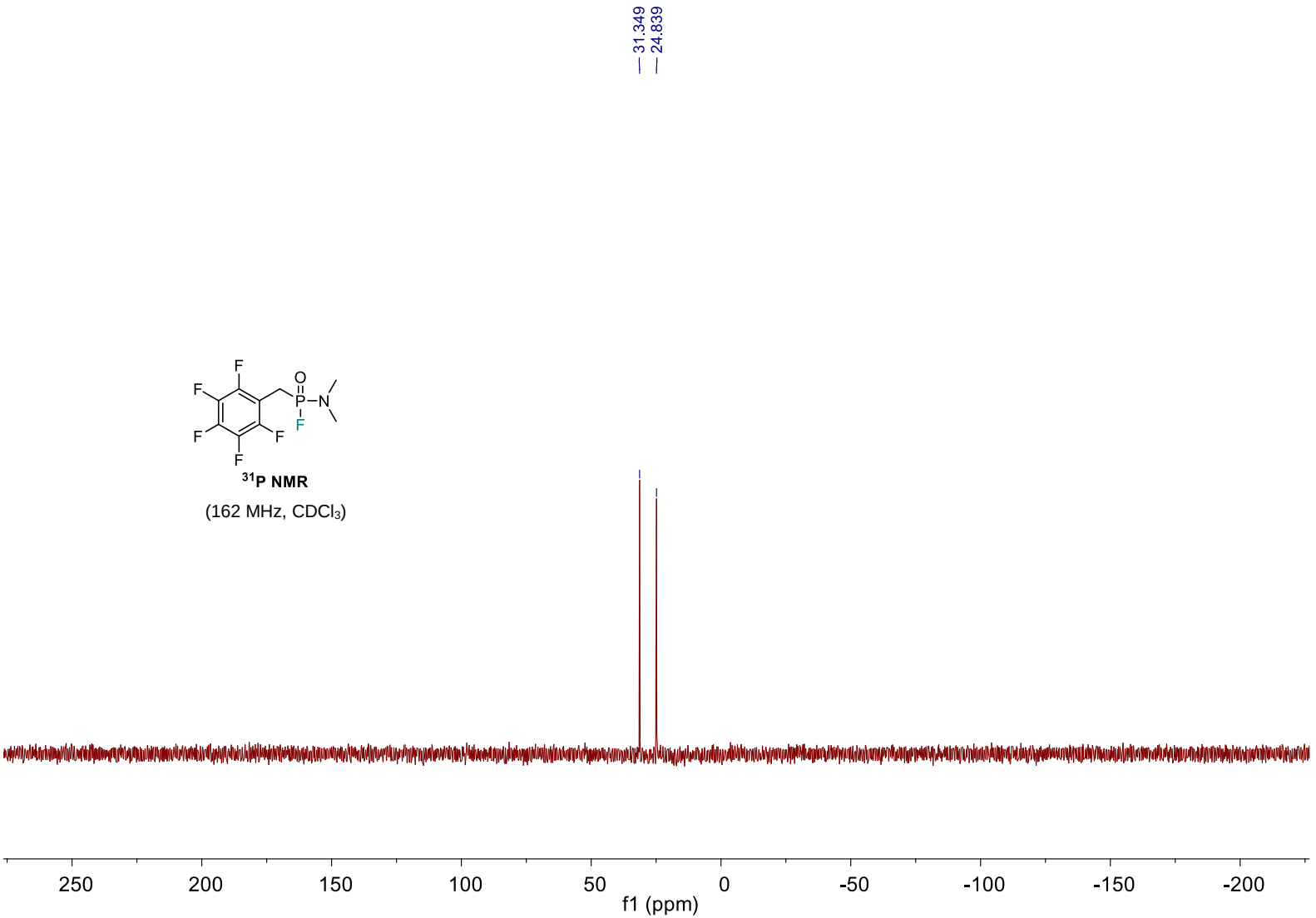


^{1}H NMR
(400 MHz, $CDCl_3$)



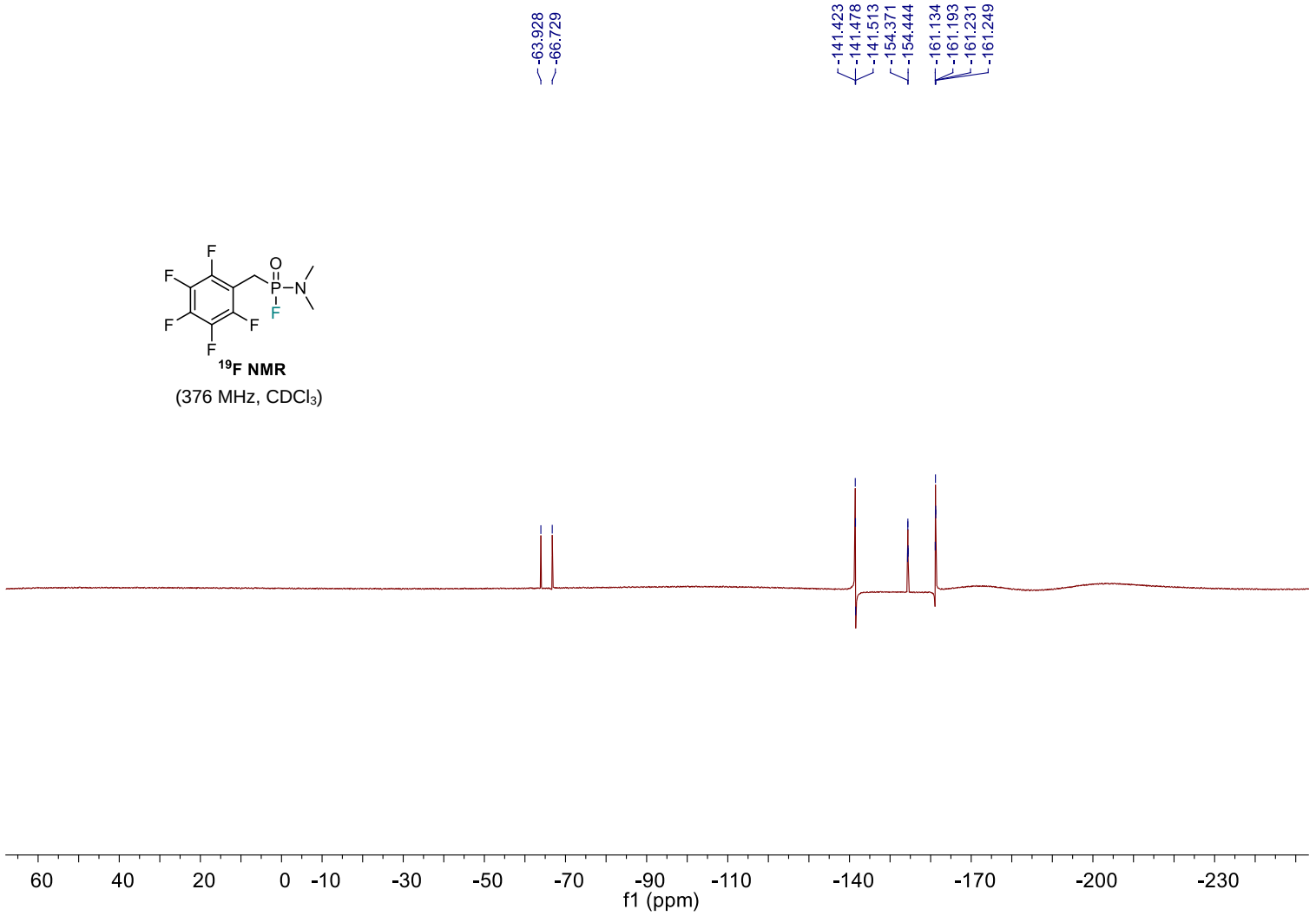
^{13}C NMR

(100 MHz, $CDCl_3$)



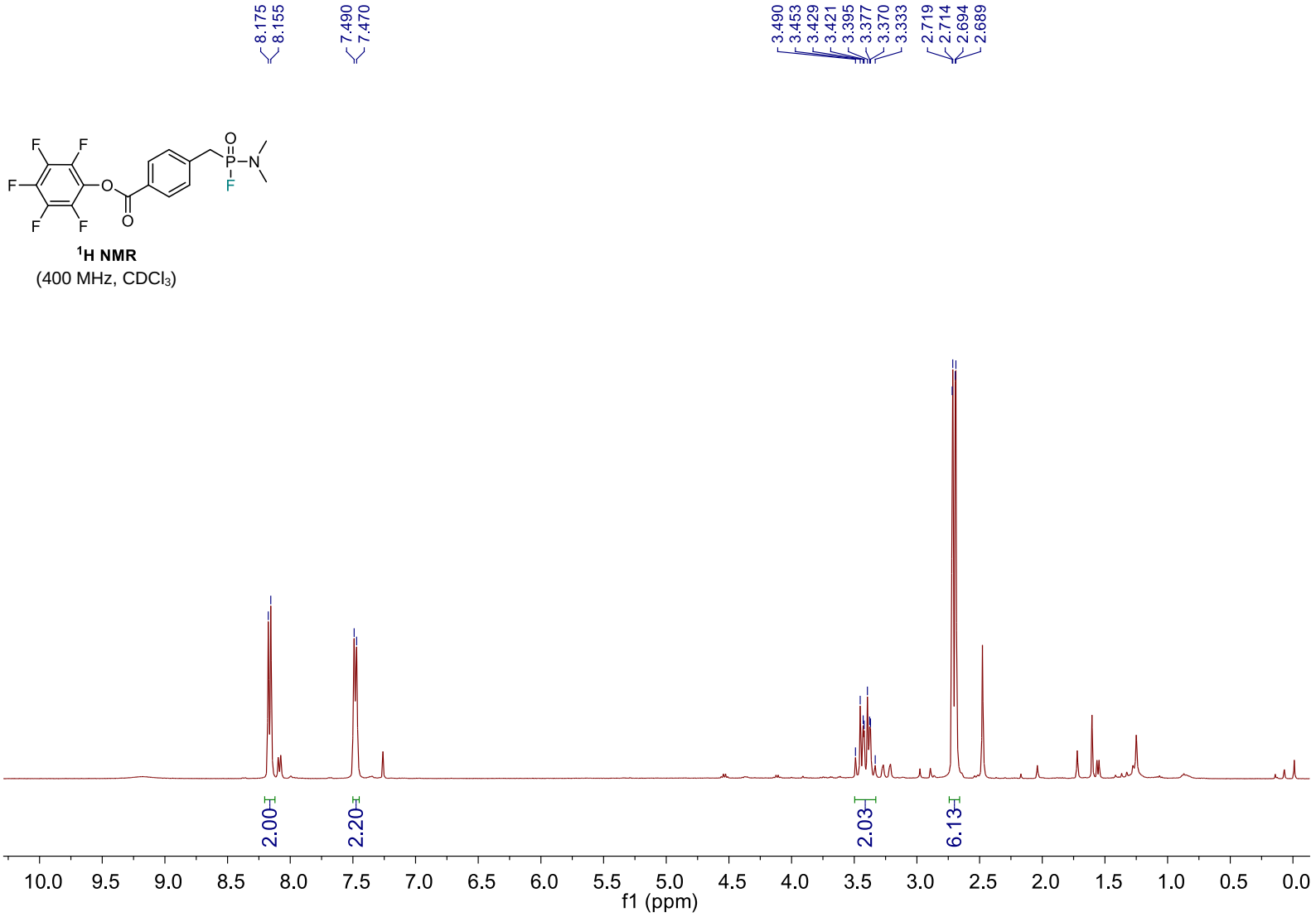
^{31}P NMR

(162 MHz, $CDCl_3$)

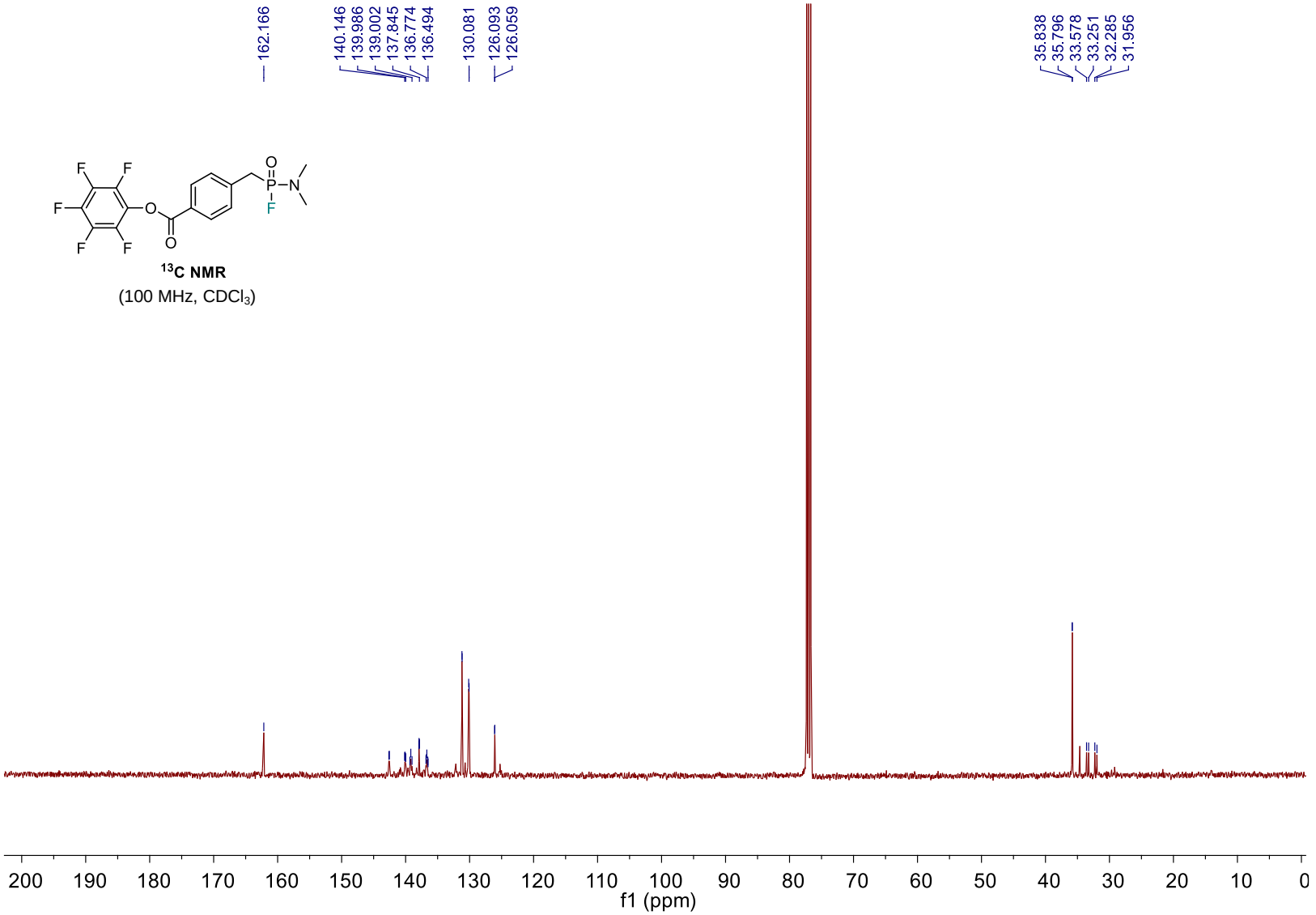


^{19}F NMR

(376 MHz, $CDCl_3$)

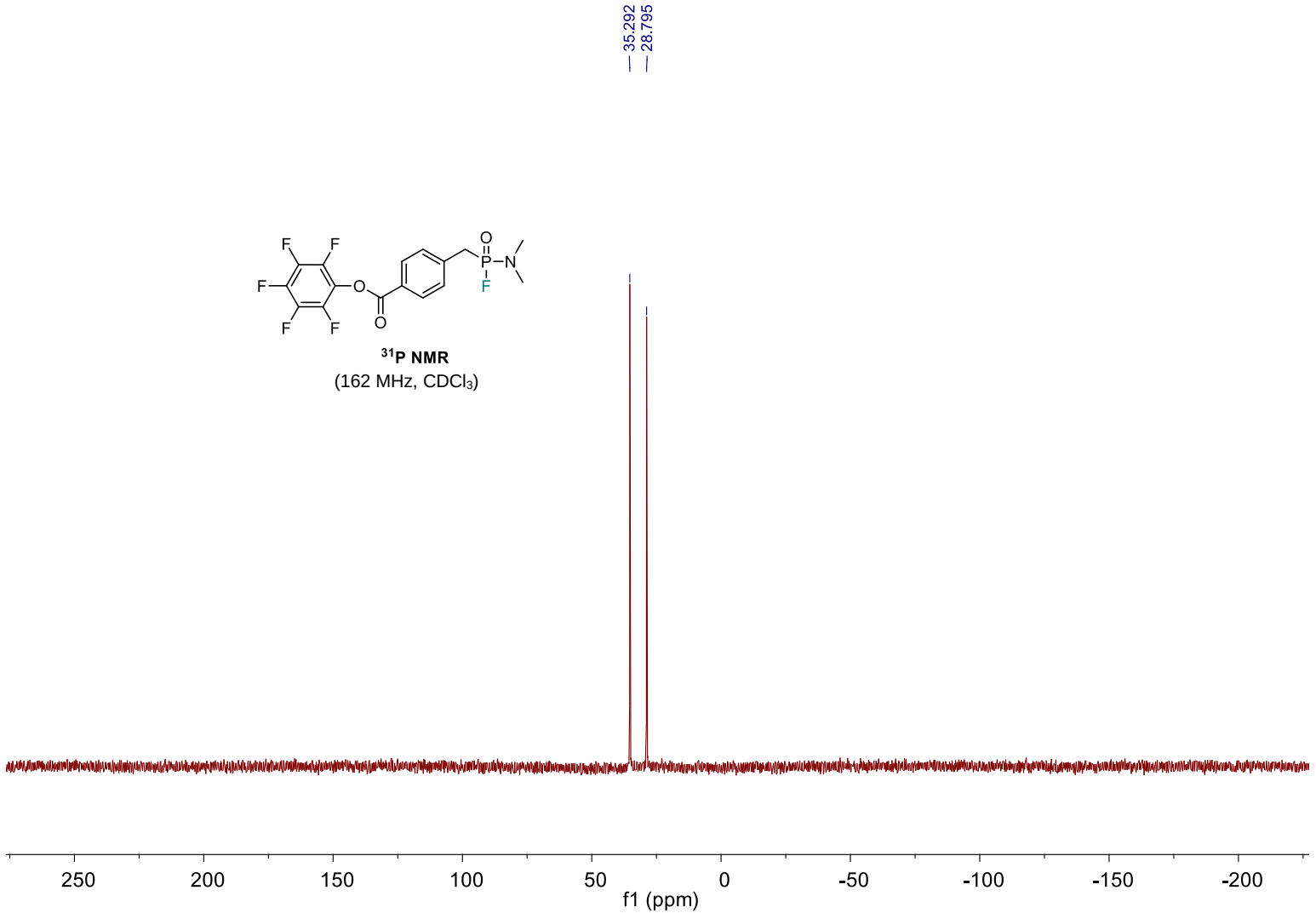


^{1}H NMR
(400 MHz, $CDCl_3$)

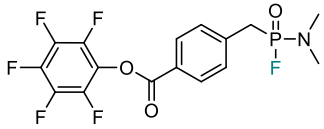


^{13}C NMR

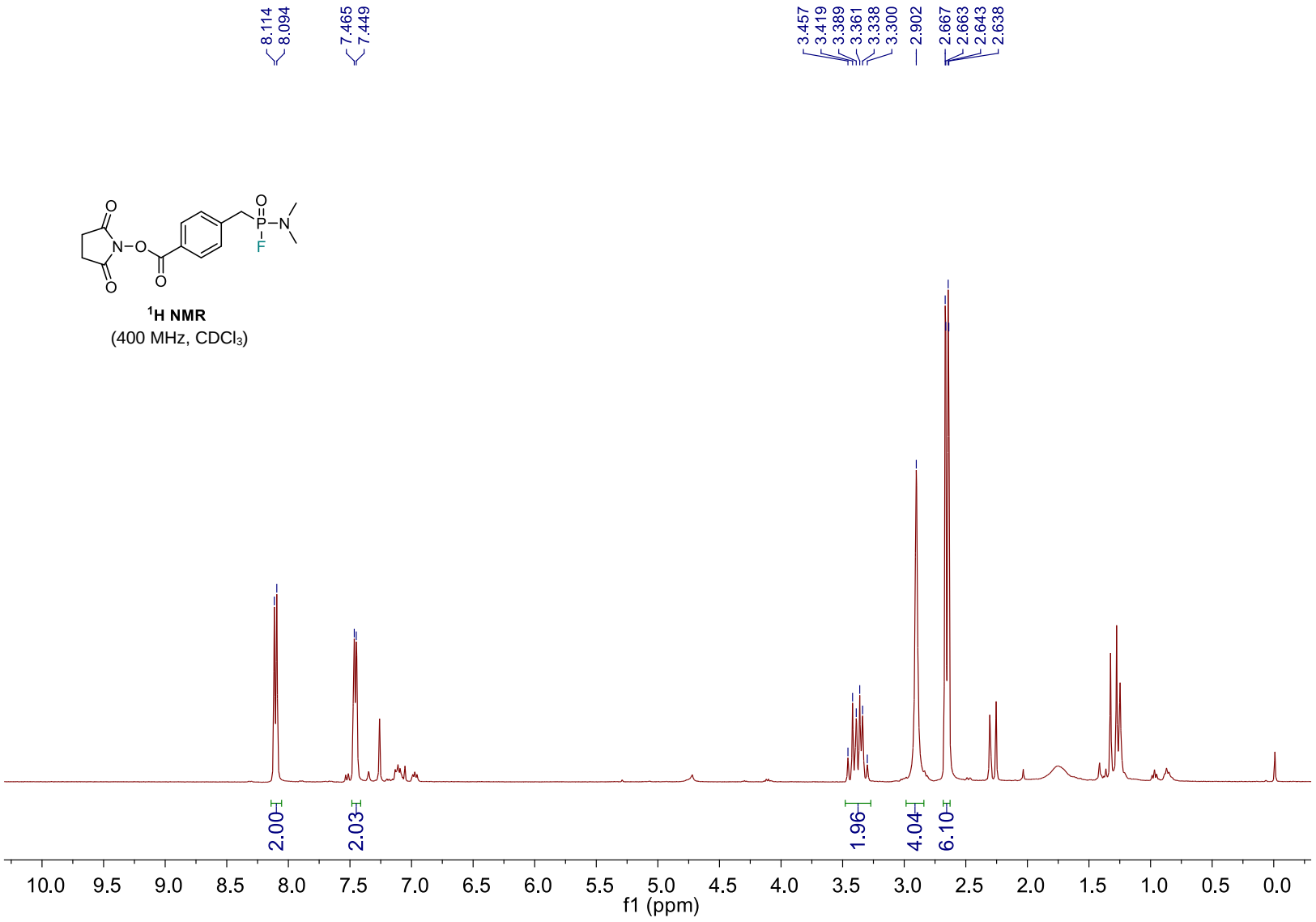
(100 MHz, $CDCl_3$)



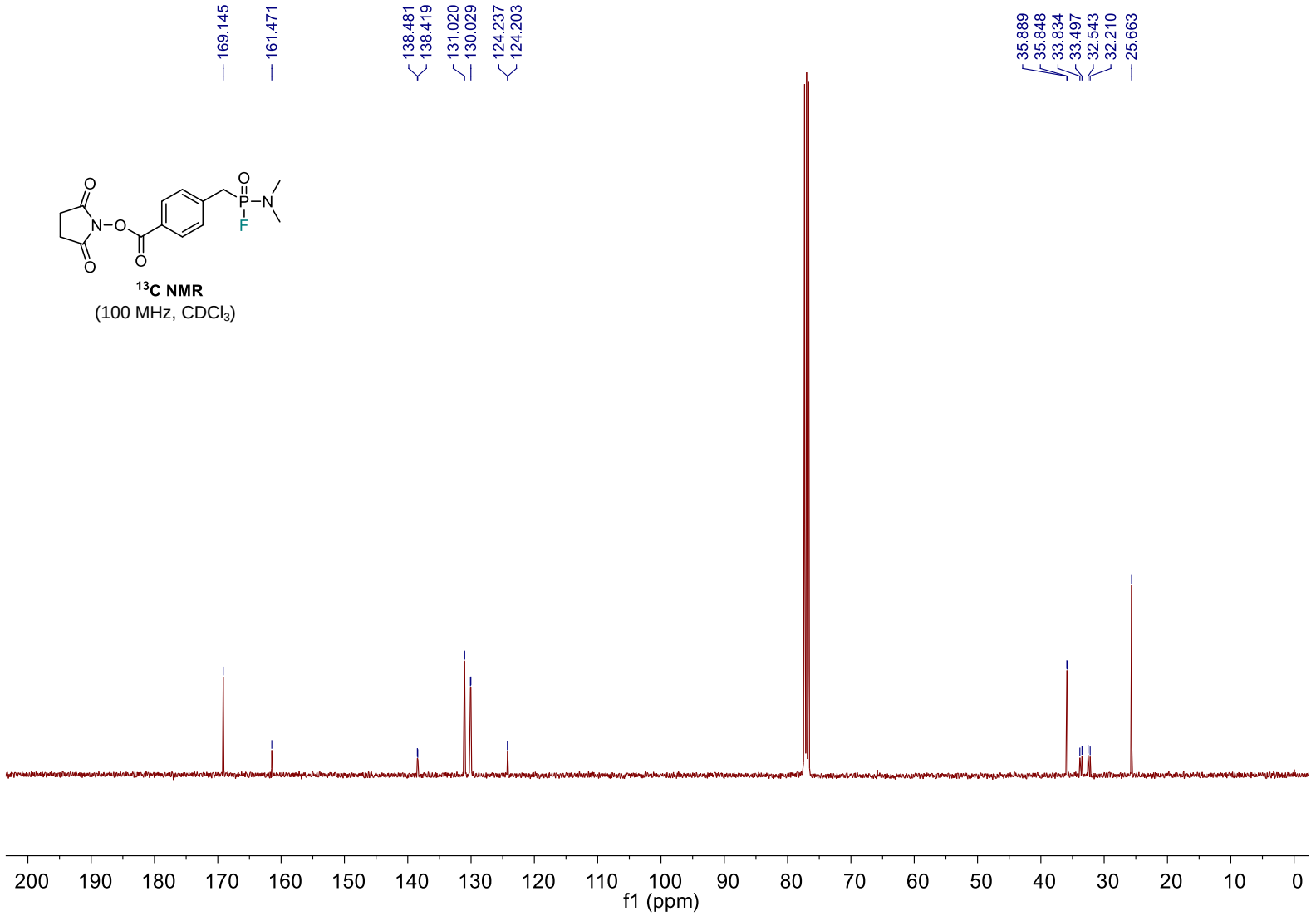
^{31}P NMR
(162 MHz, $CDCl_3$)



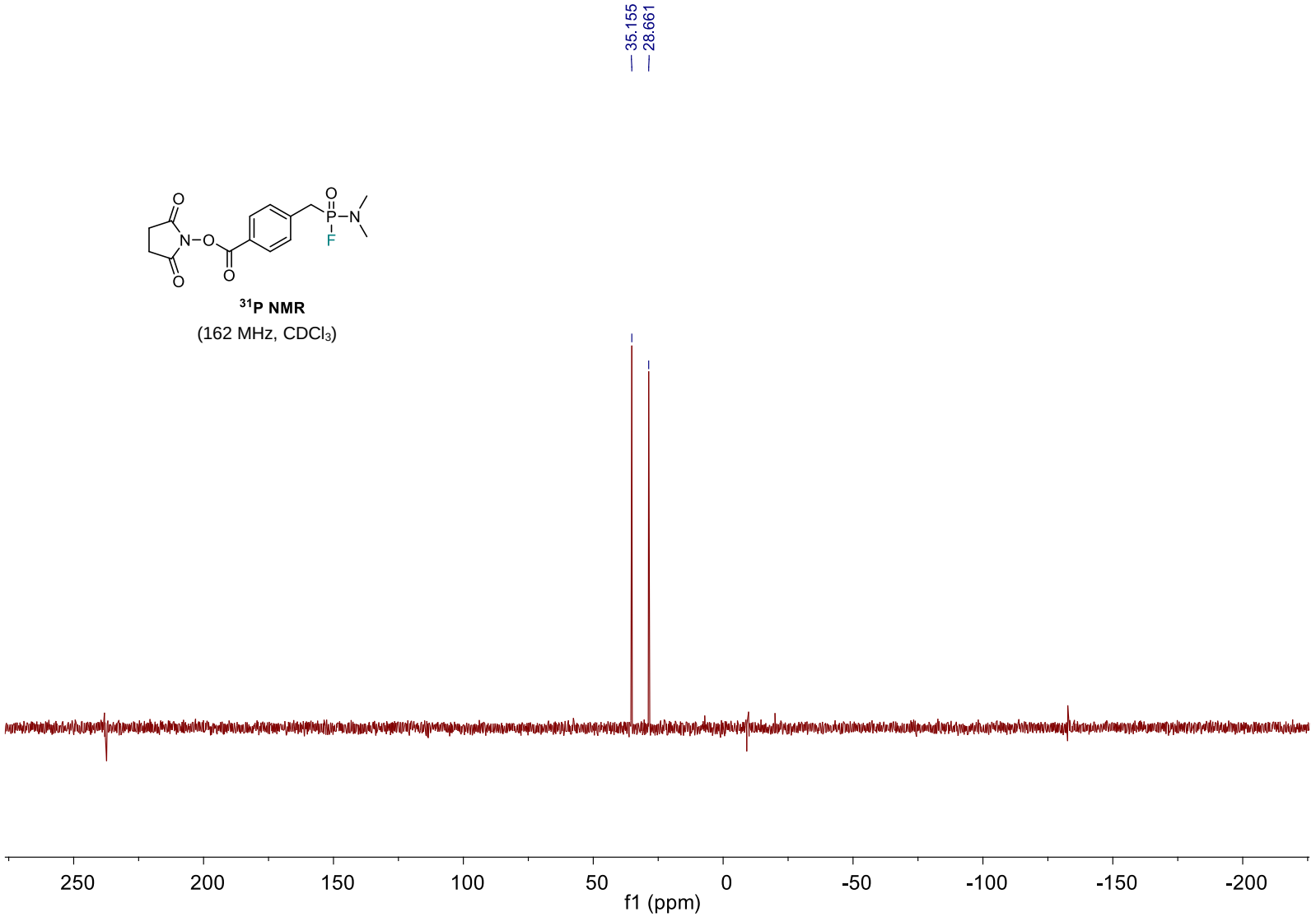
^{19}F NMR
(376 MHz, $CDCl_3$)



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

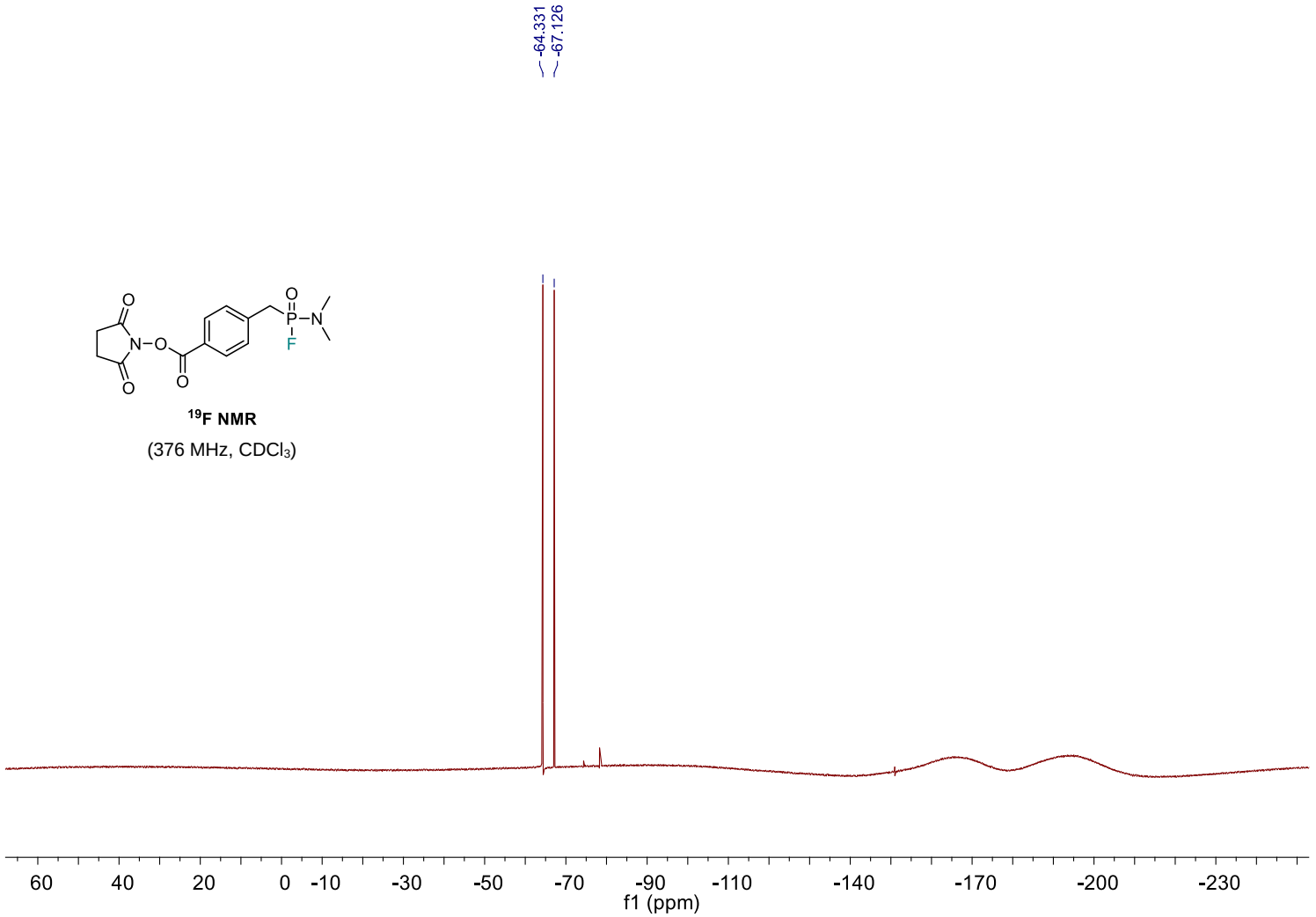


^{13}C NMR
(100 MHz, $CDCl_3$)



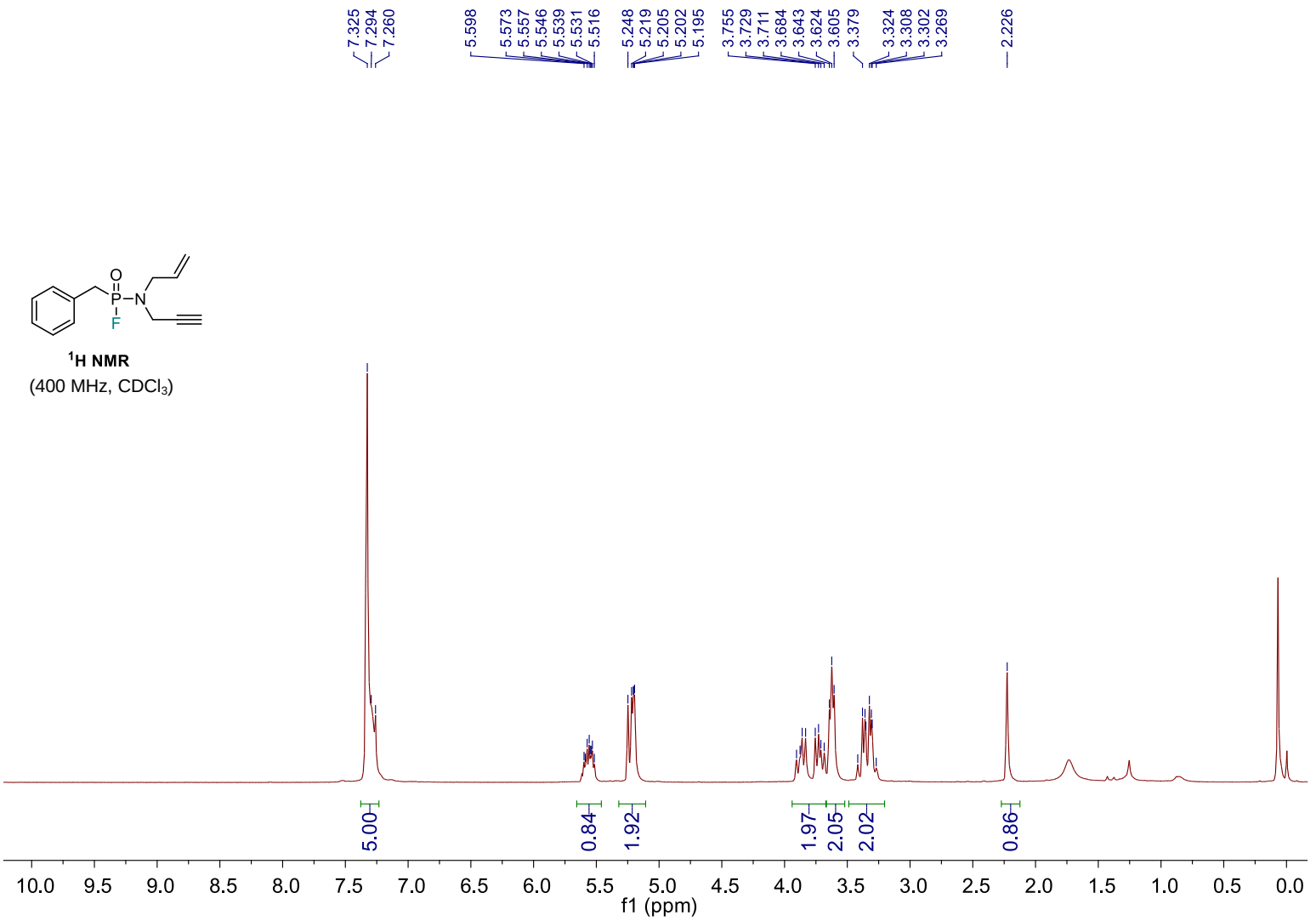
^{31}P NMR

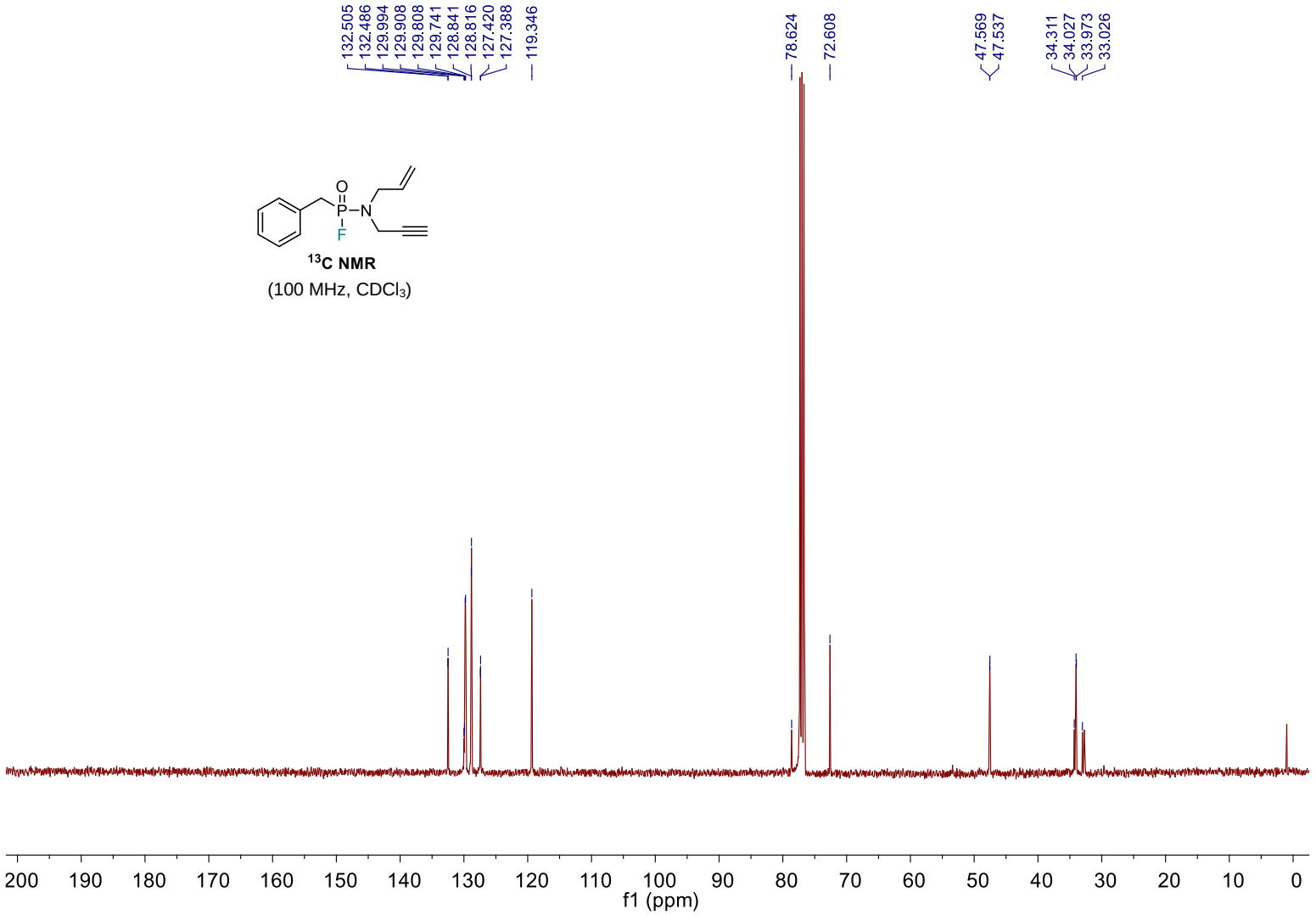
(162 MHz, $CDCl_3$)



^{19}F NMR

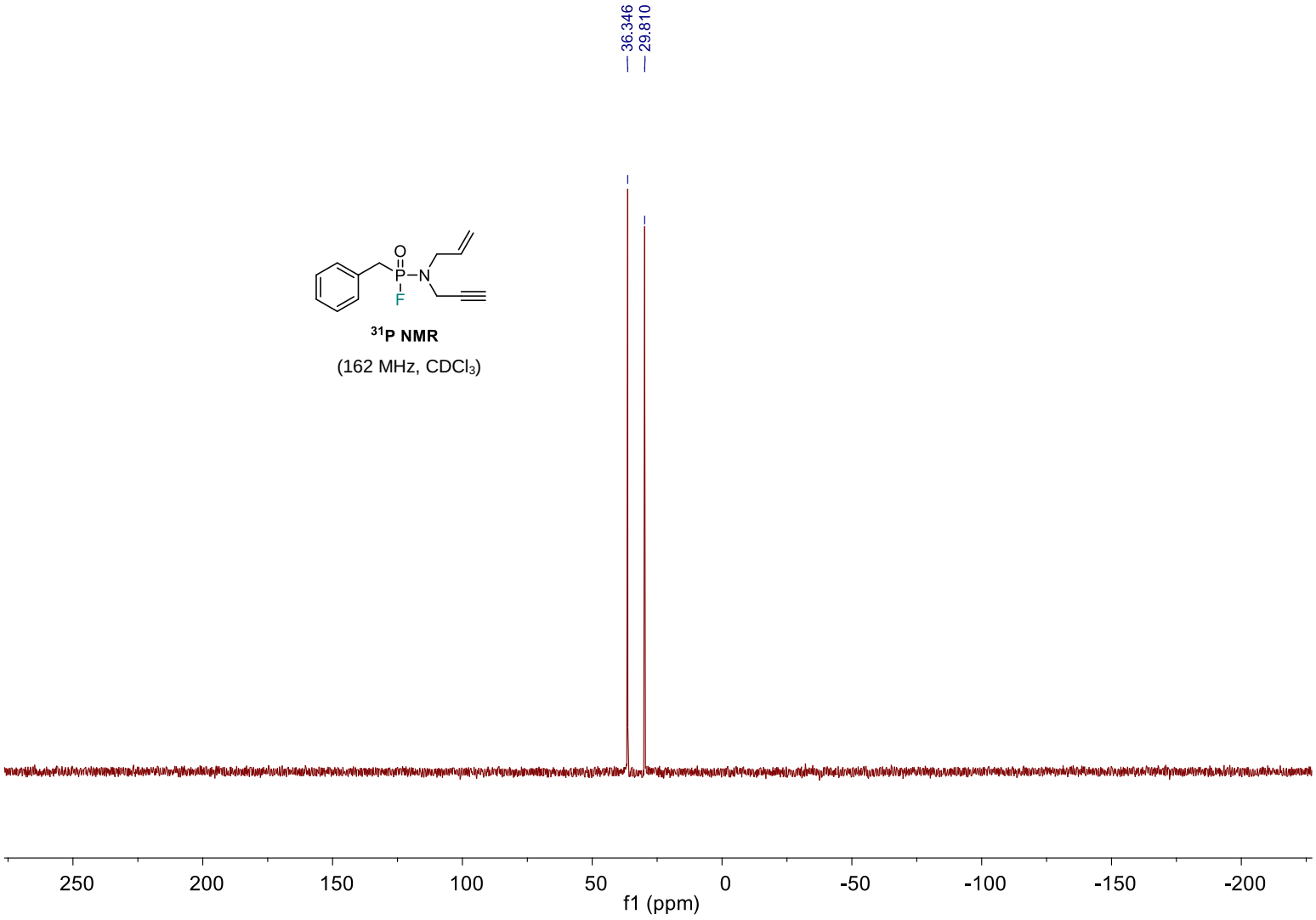
(376 MHz, $CDCl_3$)


7.325
7.294
7.260
5.598
5.573
5.557
5.546
5.539
5.531
5.516
5.248
5.219
5.205
5.202
5.195
3.755
3.729
3.711
3.684
3.643
3.624
3.605
3.379
3.324
3.308
3.302
3.269
2.226
O
P
N
F
1H NMR
(400 MHz, CDCl3)
5.00
0.84
1.92
1.97
2.05
2.02
0.86
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



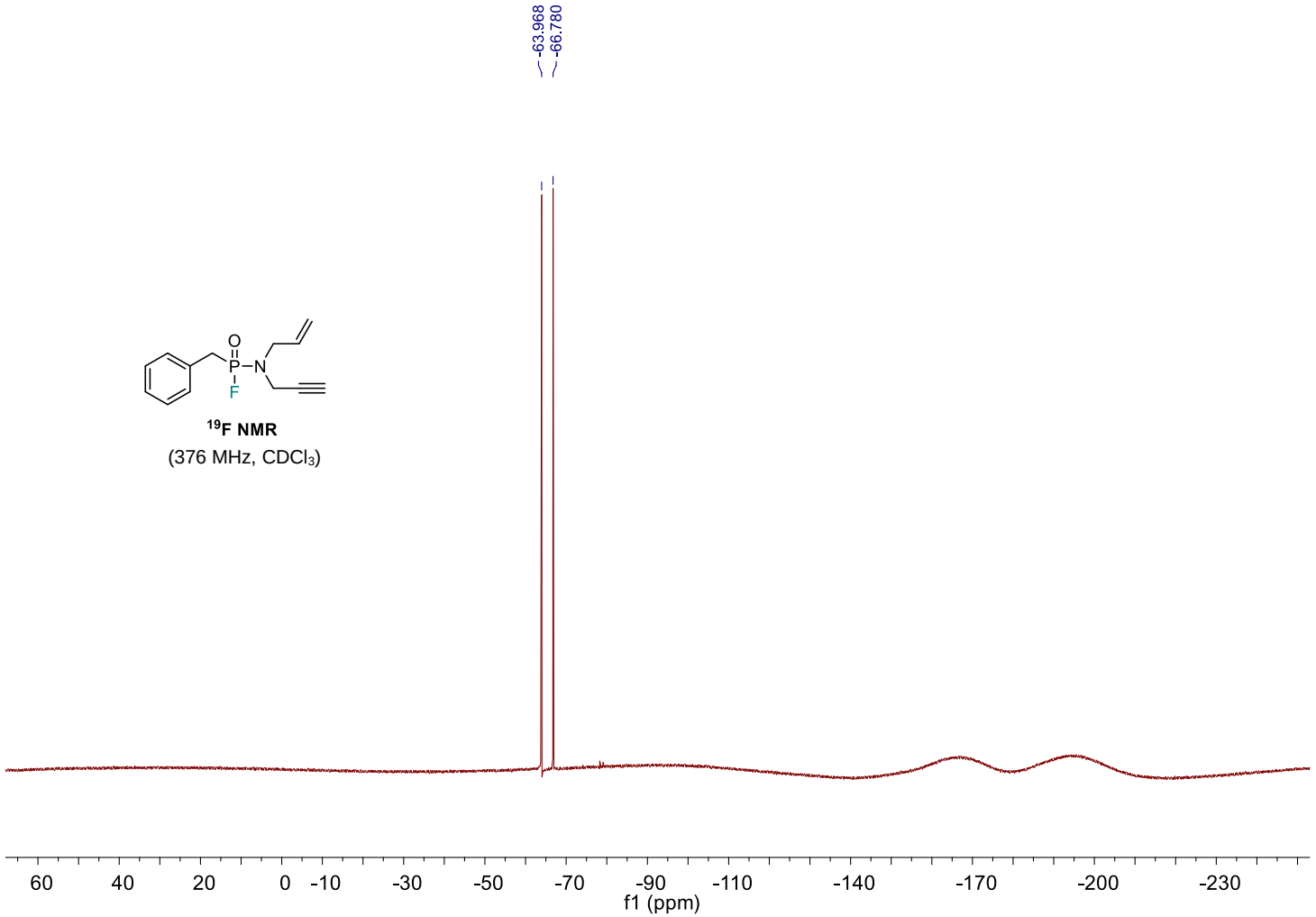
^{13}C NMR

(100 MHz, $CDCl_3$)



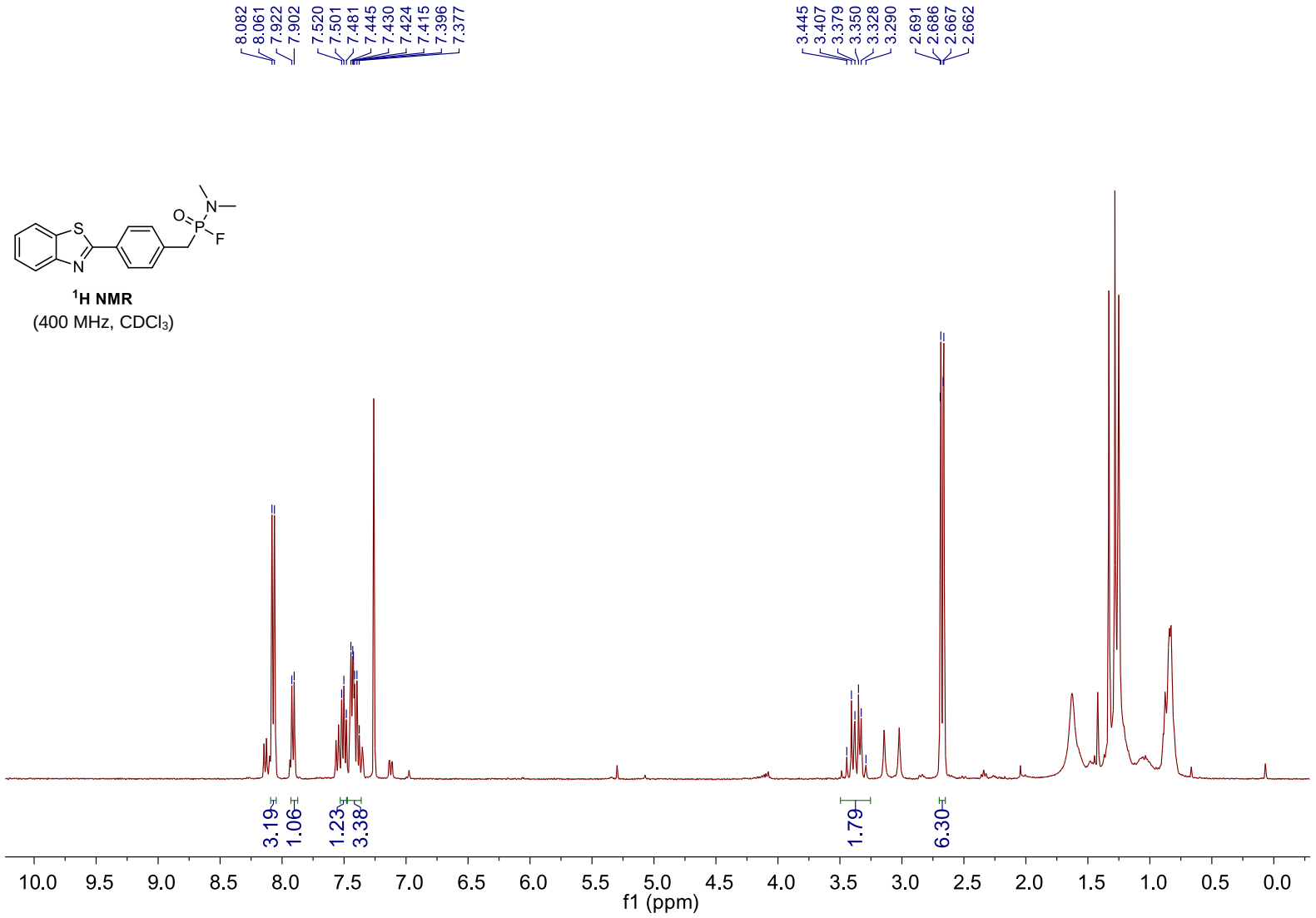
^{31}P NMR

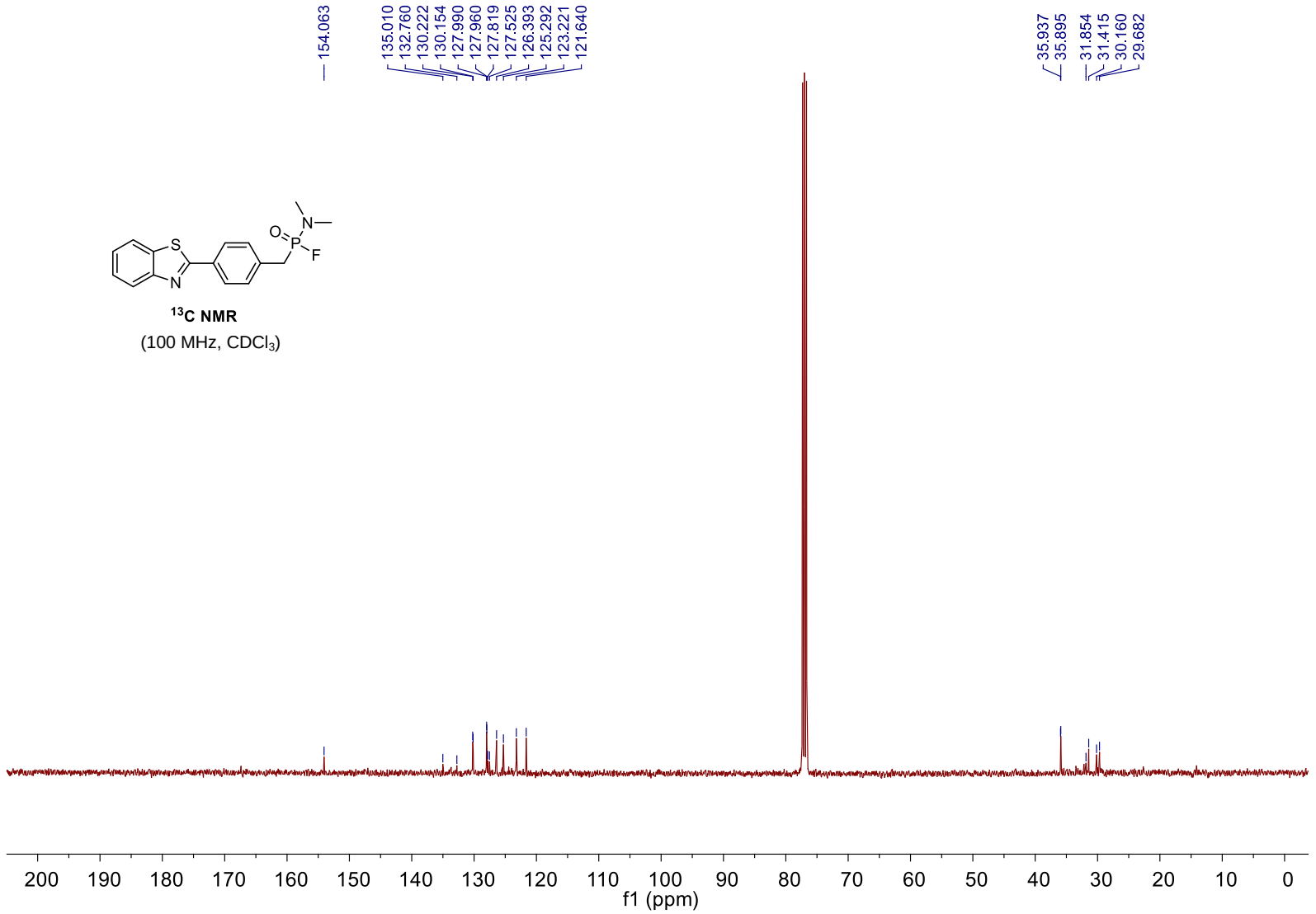
(162 MHz, $CDCl_3$)



^{19}F NMR

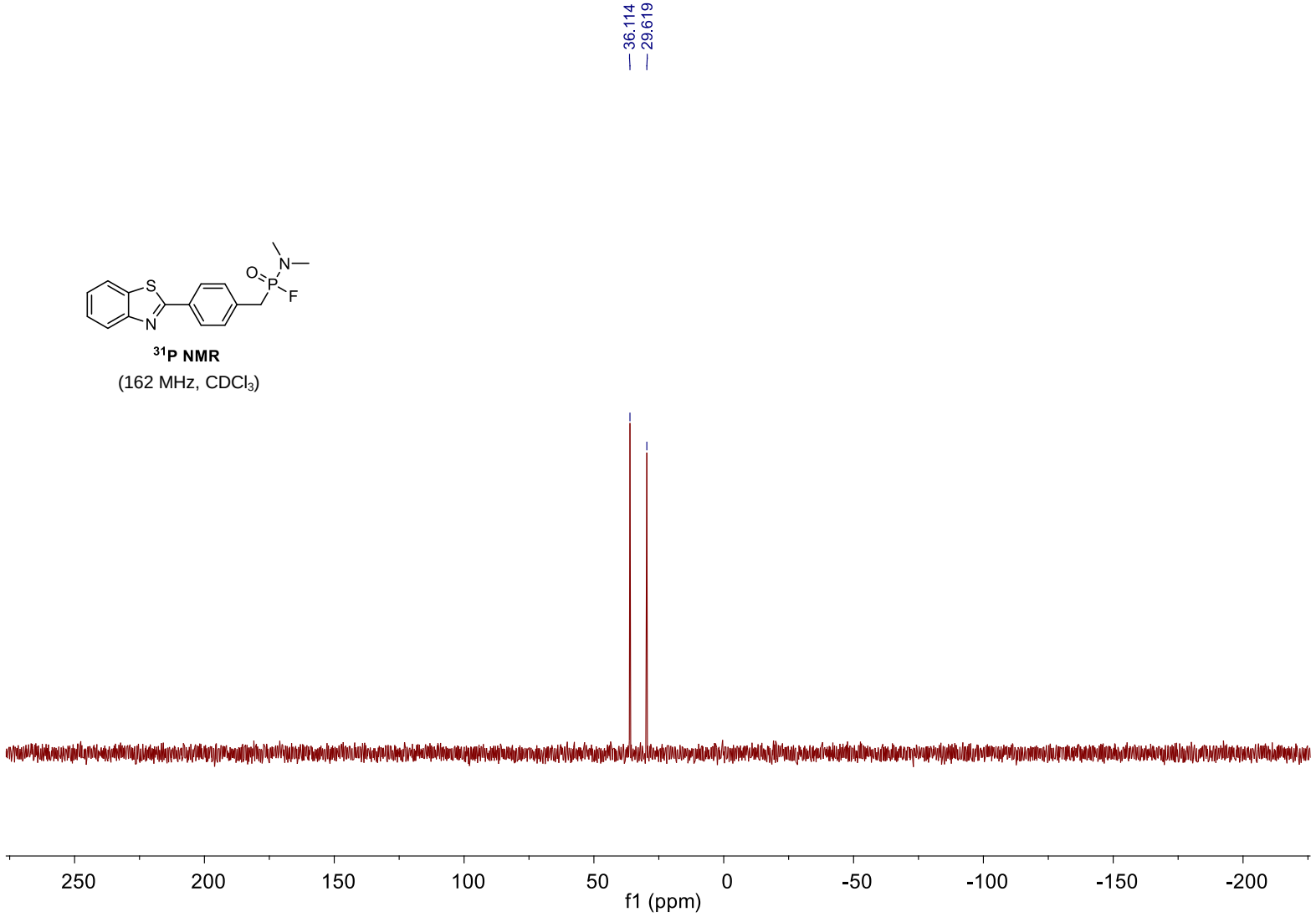
(376 MHz, $CDCl_3$)

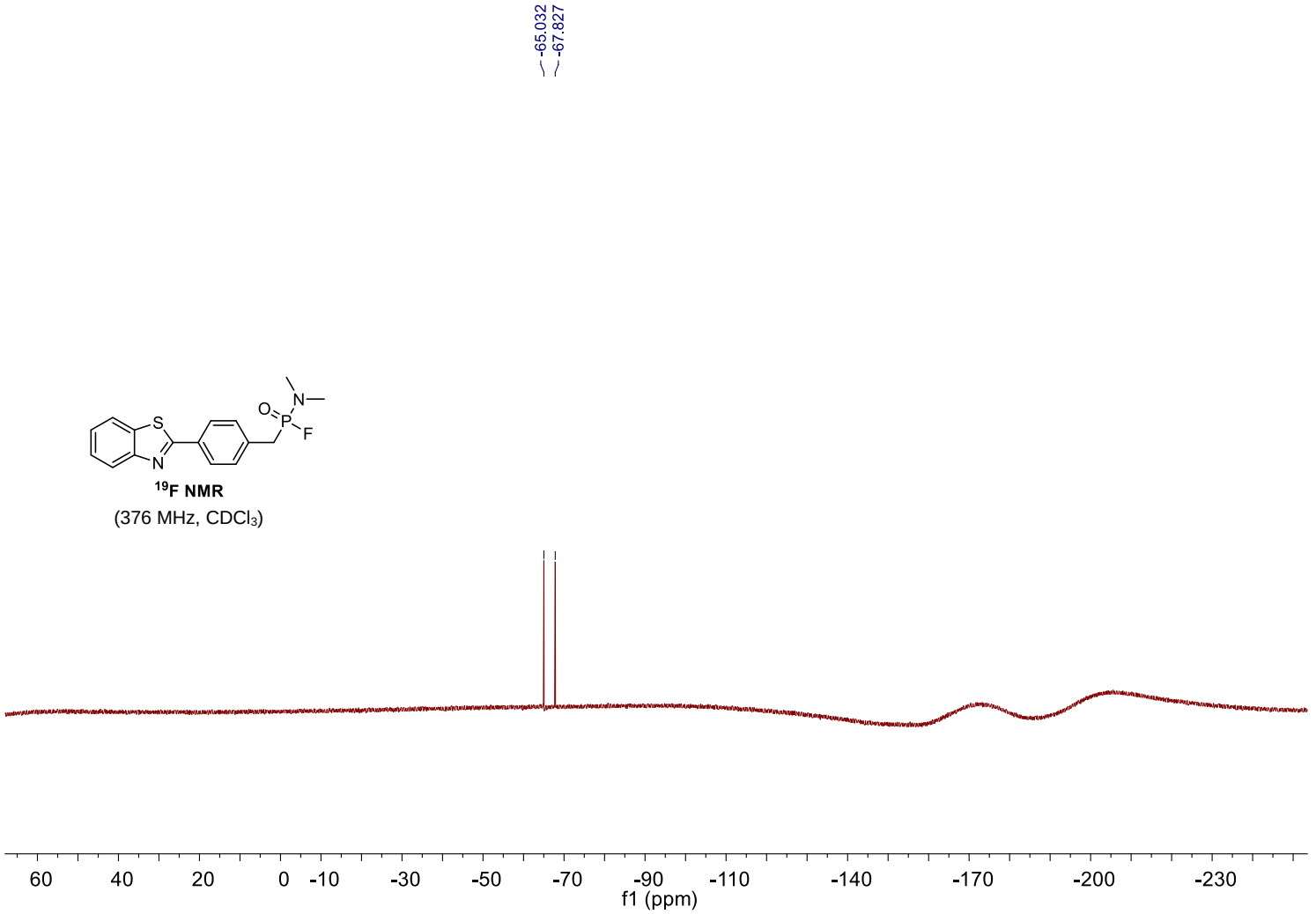

8.082
8.061
7.922
7.902
7.520
7.501
7.481
7.445
7.430
7.424
7.415
7.396
7.377
3.445
3.407
3.379
3.350
3.328
3.290
2.691
2.686
2.667
2.662
S
N
O
P
N
F
1H NMR
(400 MHz, CDCl3)
3.19
1.06
1.23
3.38
1.79
6.30
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



^{13}C NMR

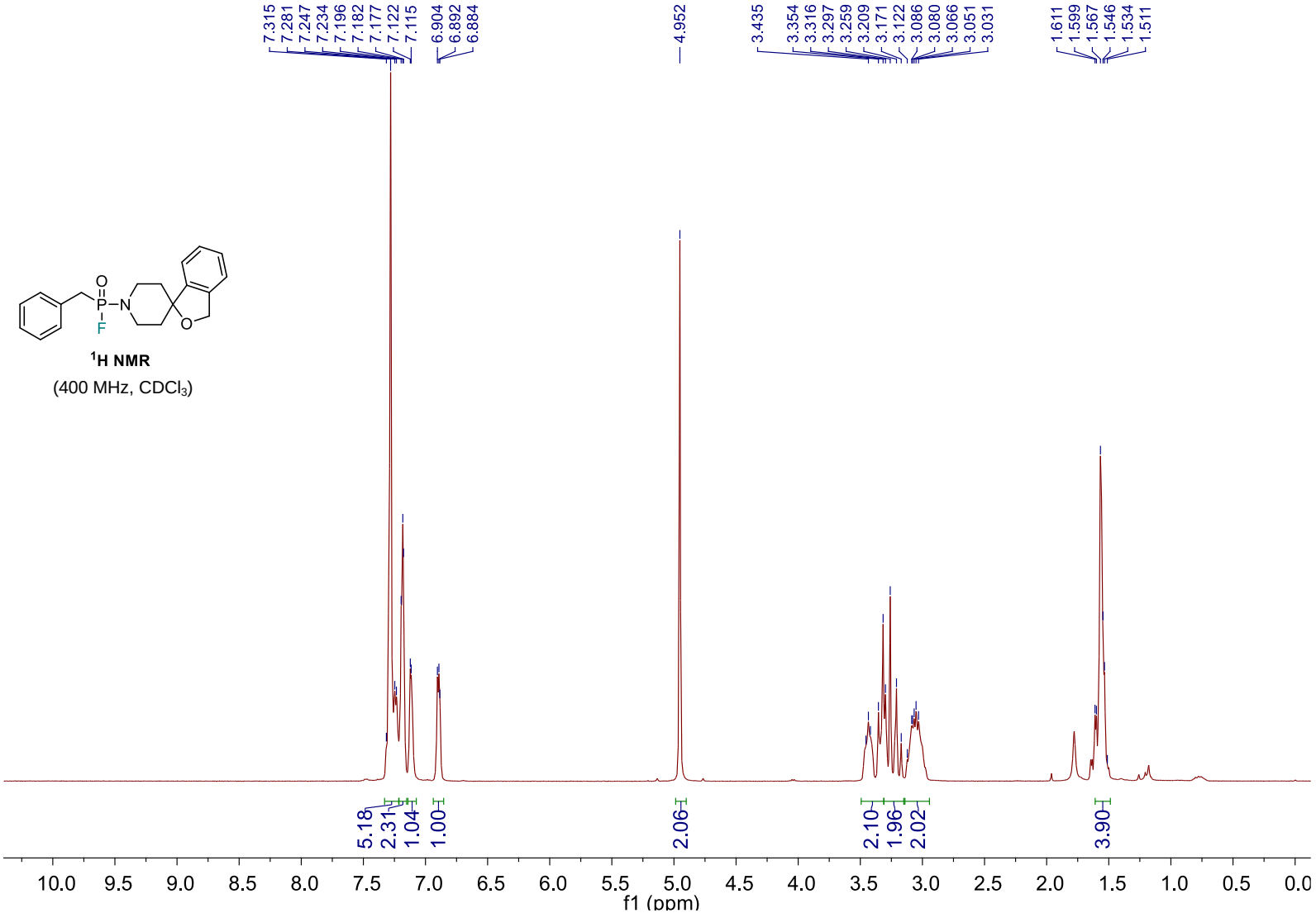
(100 MHz, $CDCl_3$)


36.114
29.619
S
N
O
P
F
N
31P NMR
(162 MHz, CDCl3)
250
200
150
100
50
0
-50
-100
-150
-200
f1 (ppm)



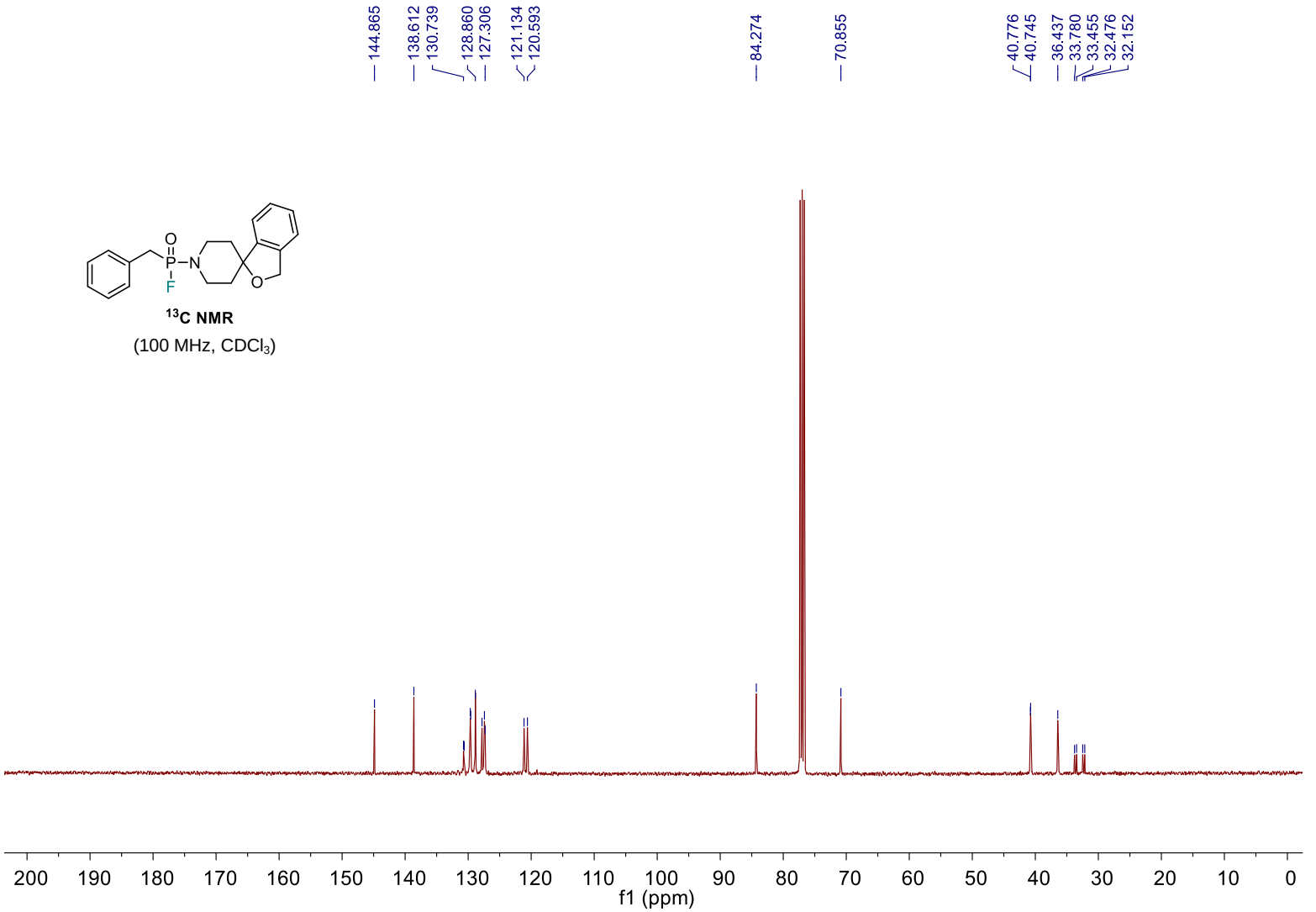
^{19}F NMR

(376 MHz, $CDCl_3$)



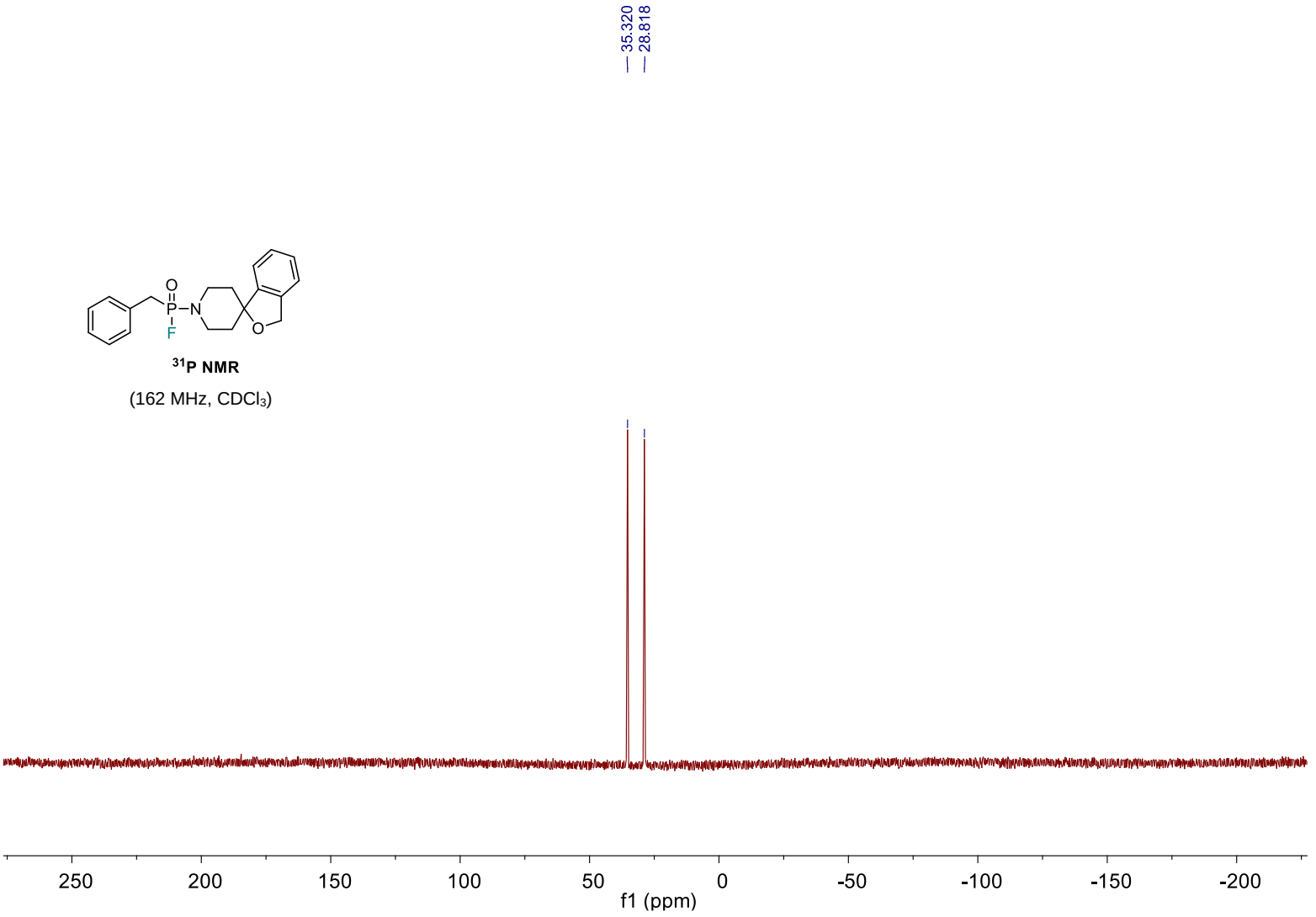
^{1}H NMR

(400 MHz, $CDCl_3$)



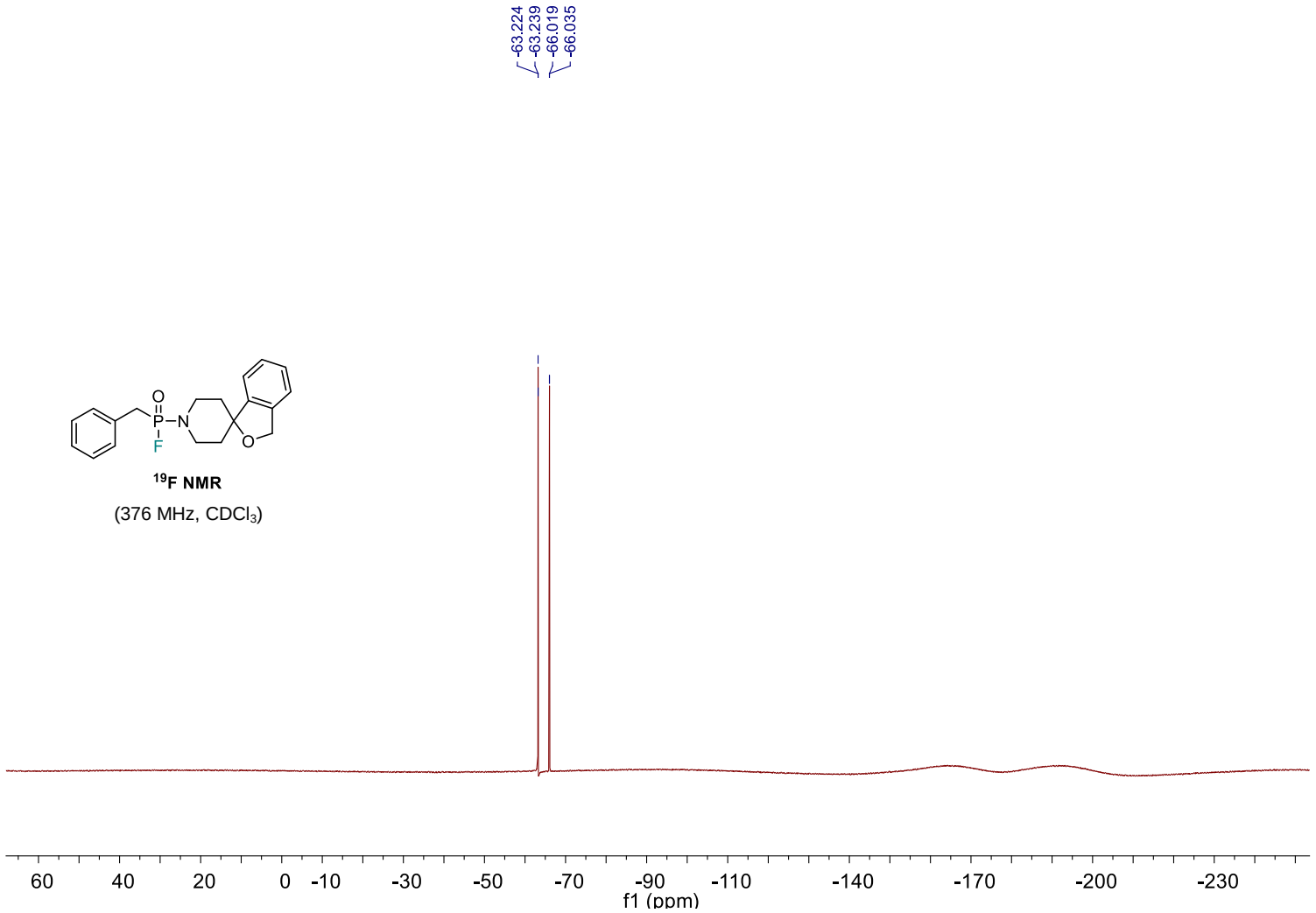
^{13}C NMR

(100 MHz, $CDCl_3$)



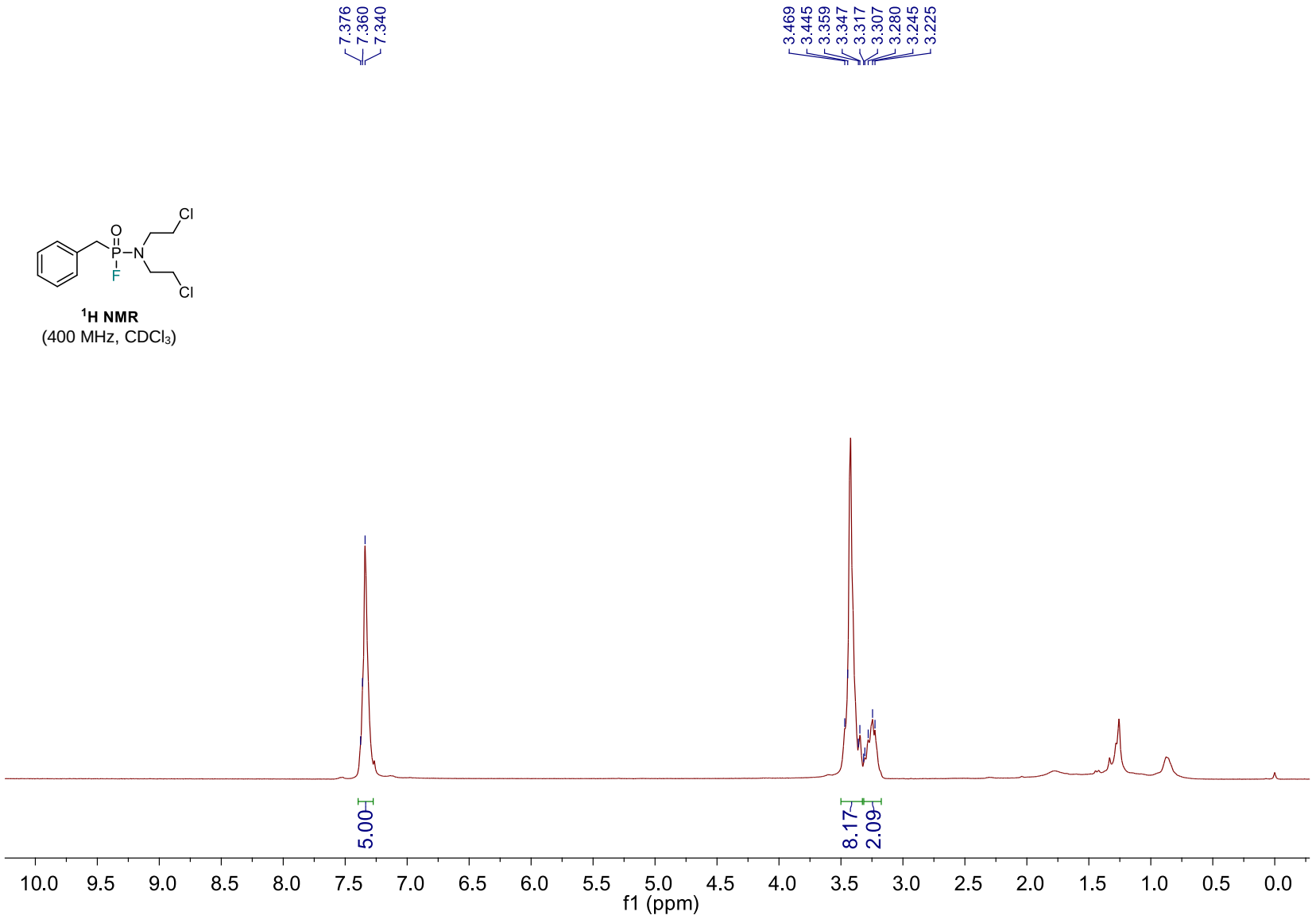
^{31}P NMR

(162 MHz, $CDCl_3$)

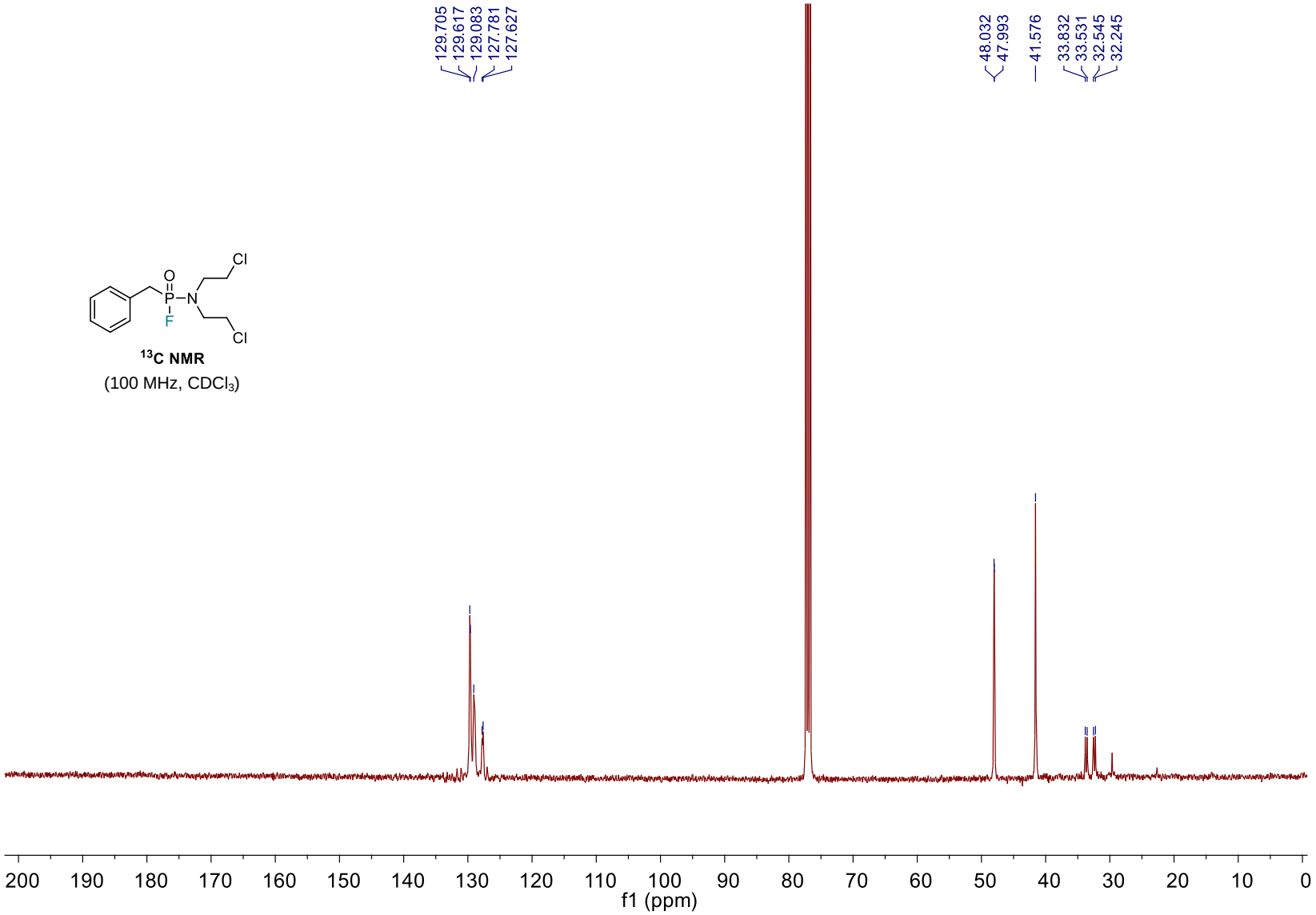


^{19}F NMR

(376 MHz, $CDCl_3$)

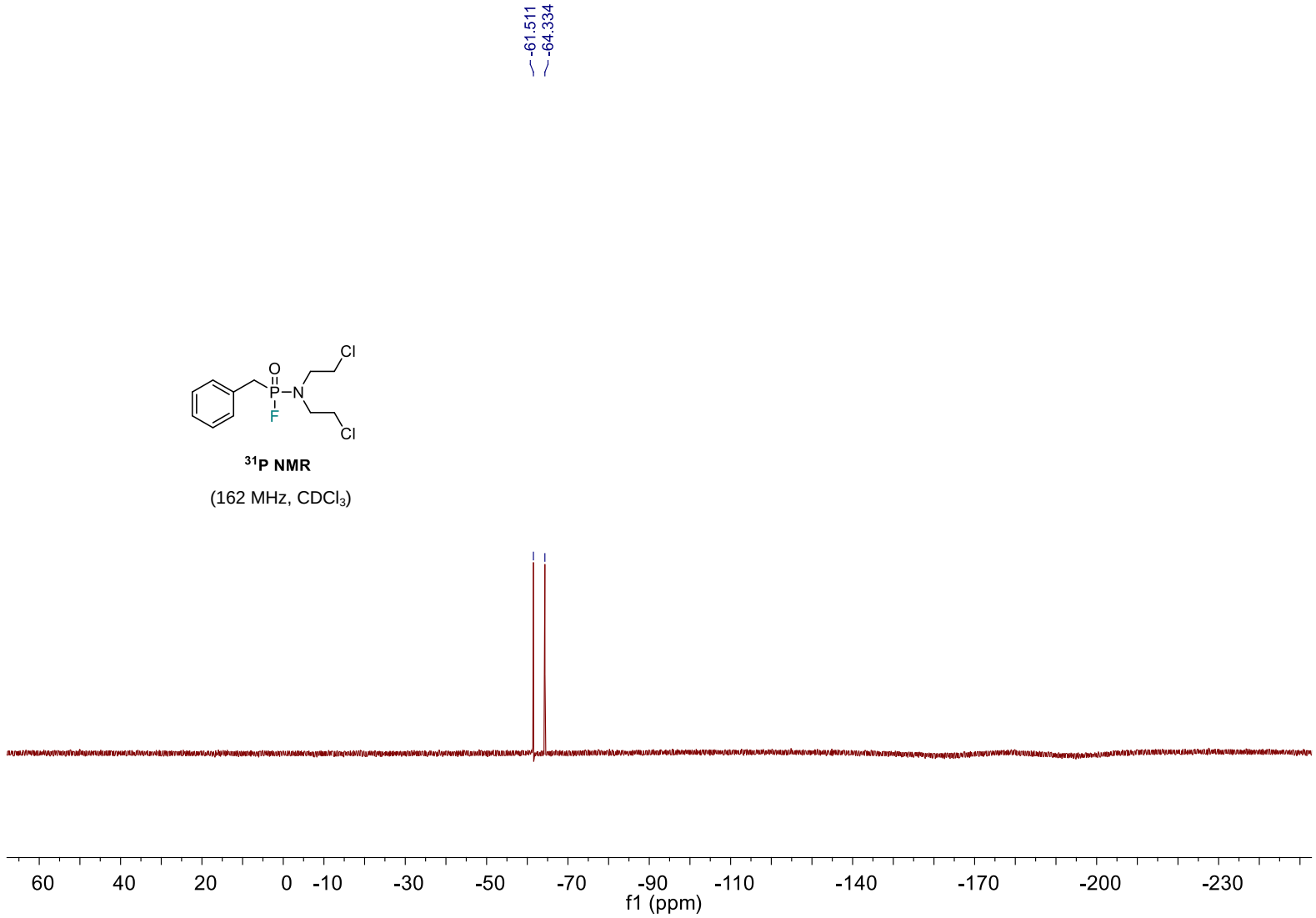


^{1}H NMR
(400 MHz, $CDCl_3$)



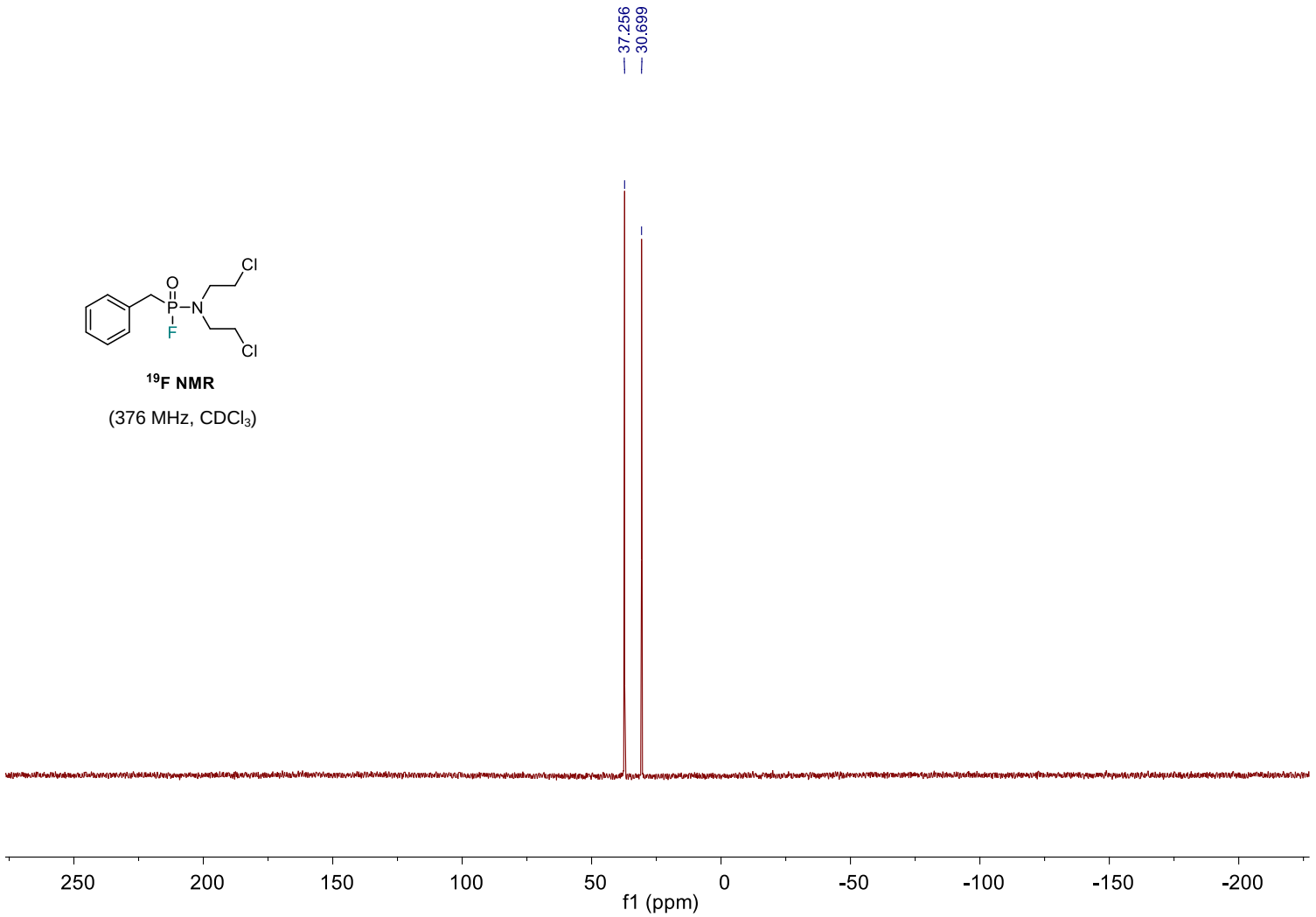
^{13}C NMR

(100 MHz, $CDCl_3$)



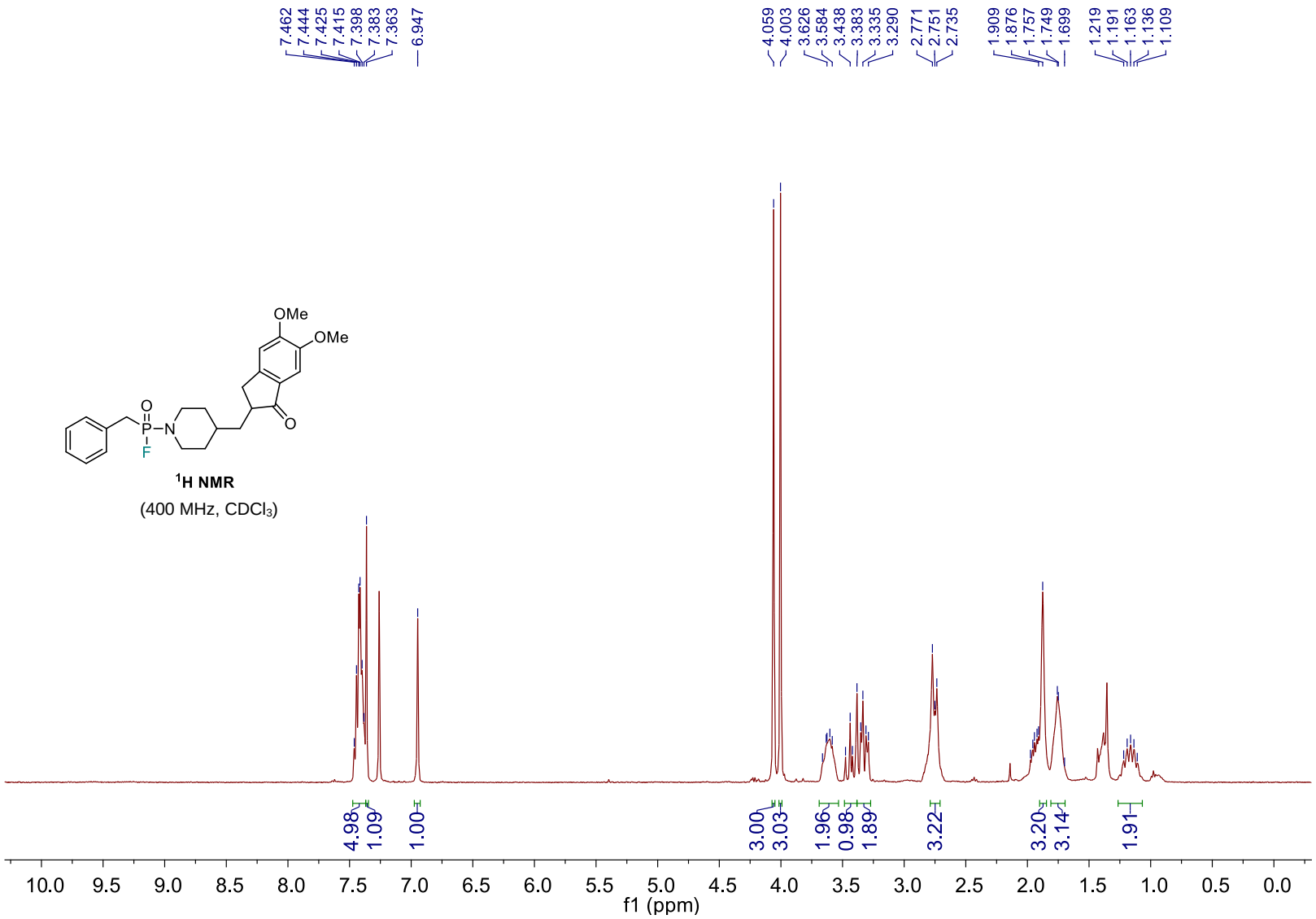
^{31}P NMR

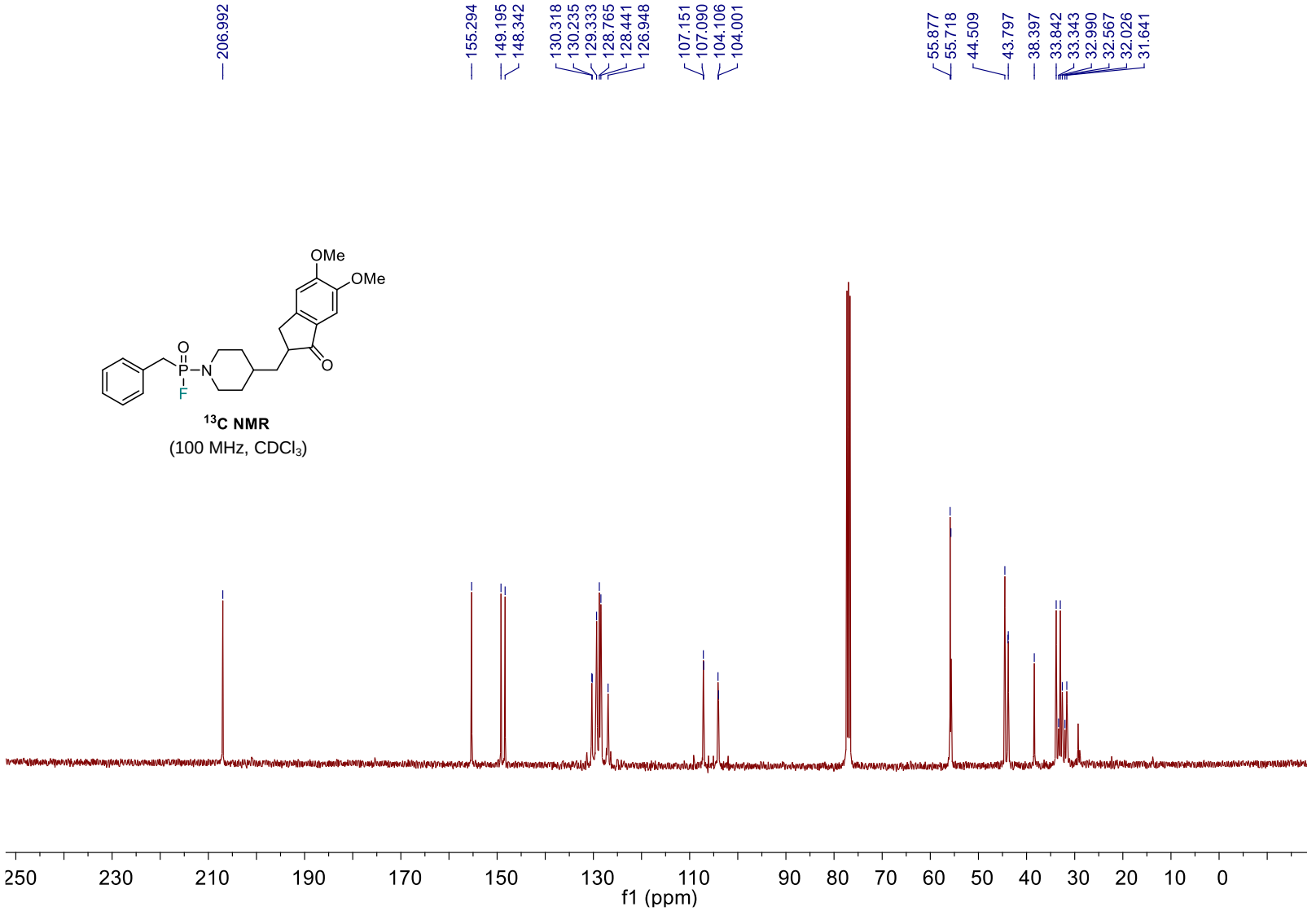
(162 MHz, $CDCl_3$)



^{19}F NMR

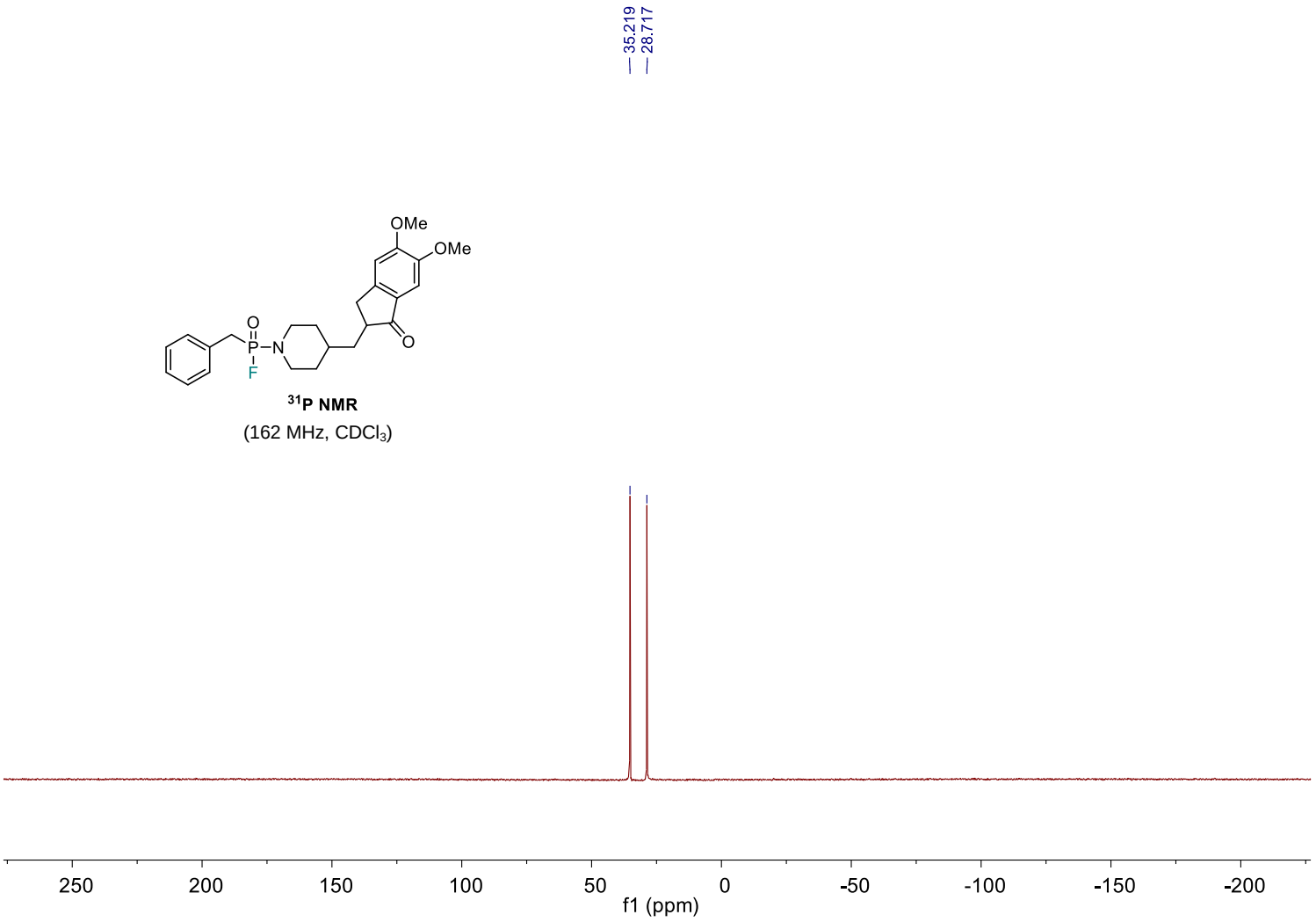
(376 MHz, $CDCl_3$)


7.462
7.444
7.425
7.415
7.398
7.383
7.363
6.947
4.059
4.003
3.626
3.584
3.438
3.383
3.335
3.290
2.771
2.751
2.735
1.909
1.876
1.757
1.749
1.699
1.219
1.191
1.163
1.136
1.109
OMe
OMe
O
P
N
F
O
1H NMR
(400 MHz, CDCl3)
4.98
1.09
1.00
3.00
3.03
1.96
0.98
1.89
3.22
3.20
3.14
1.91
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



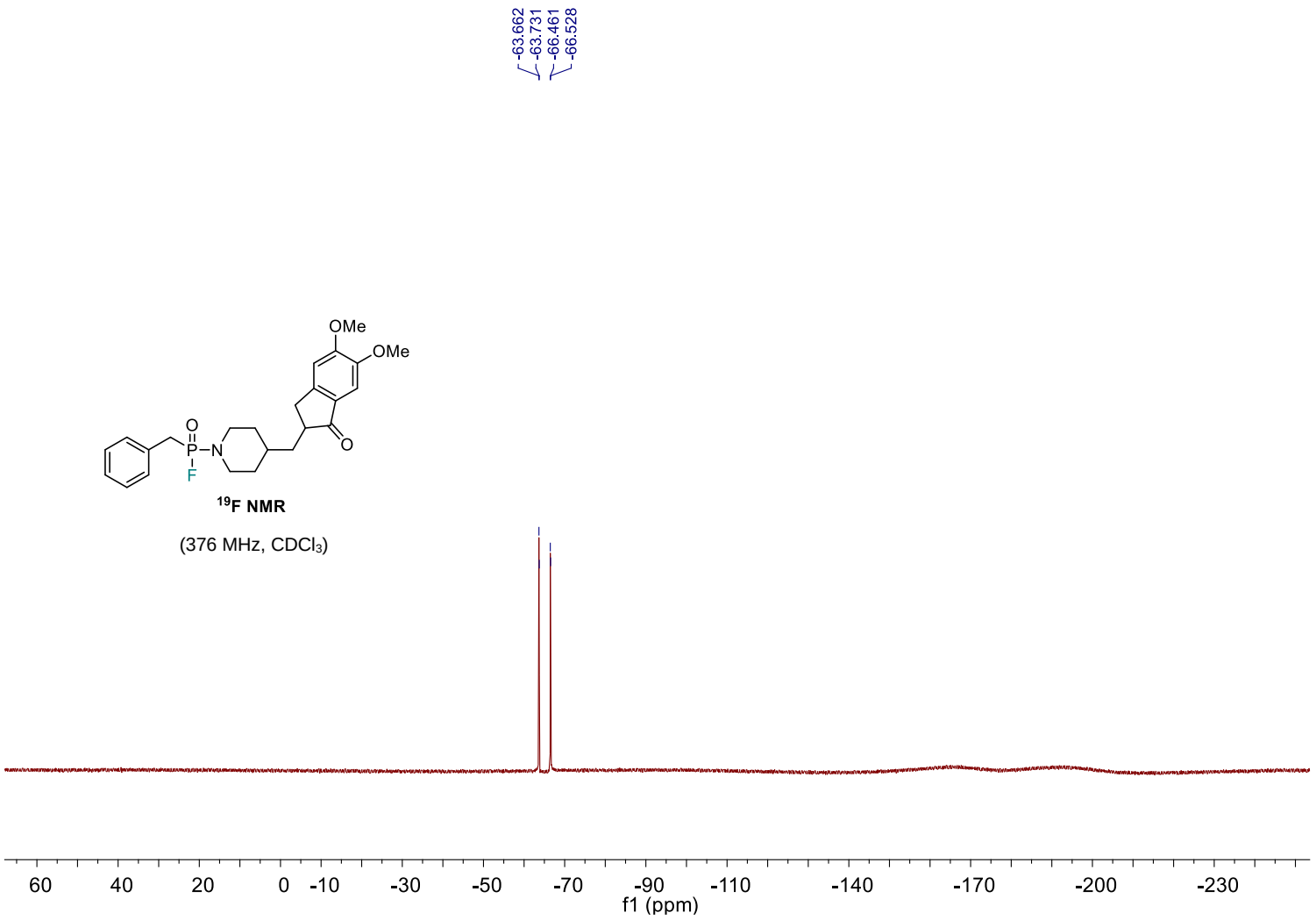
^{13}C NMR

(100 MHz, $CDCl_3$)



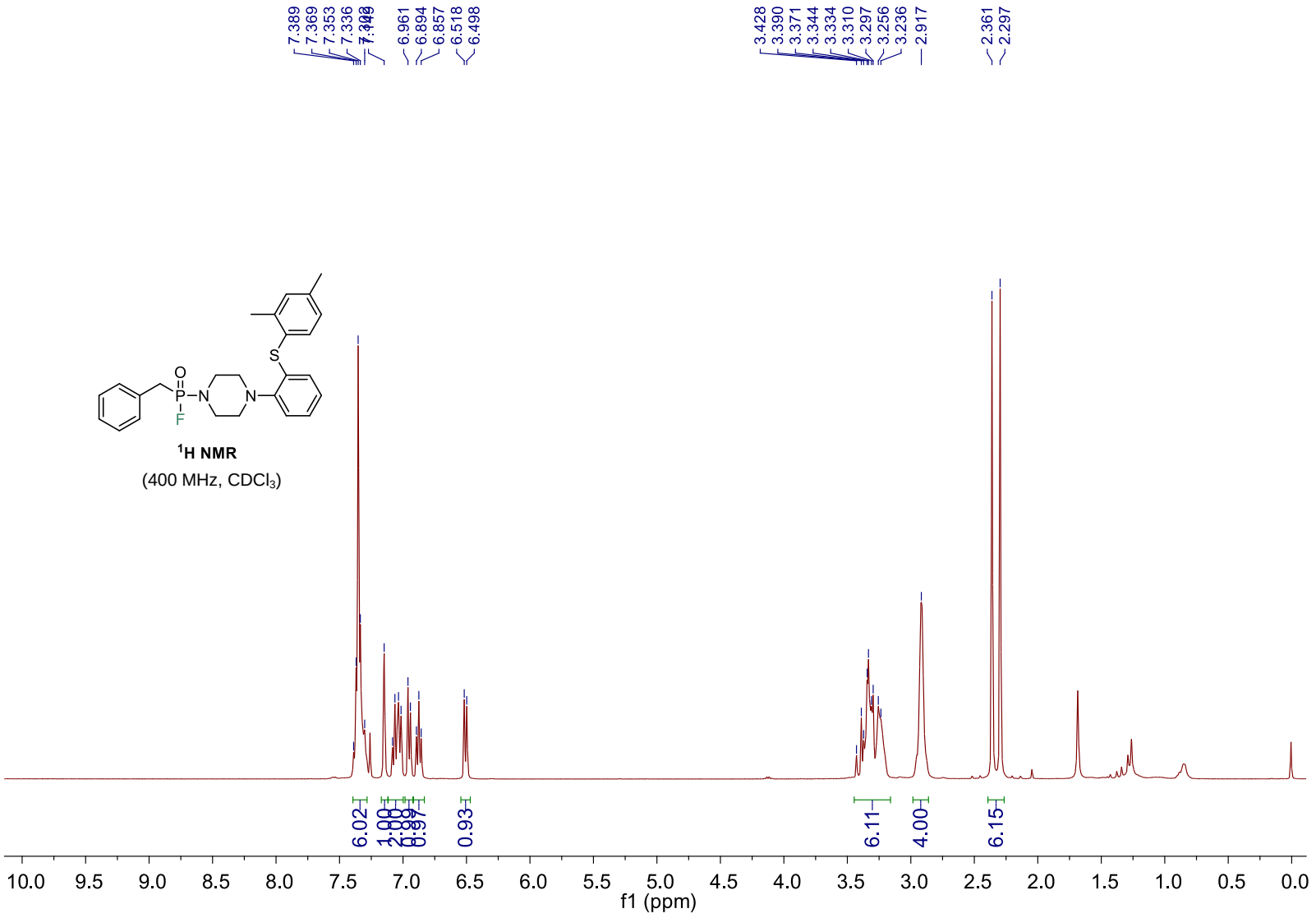
^{31}P NMR

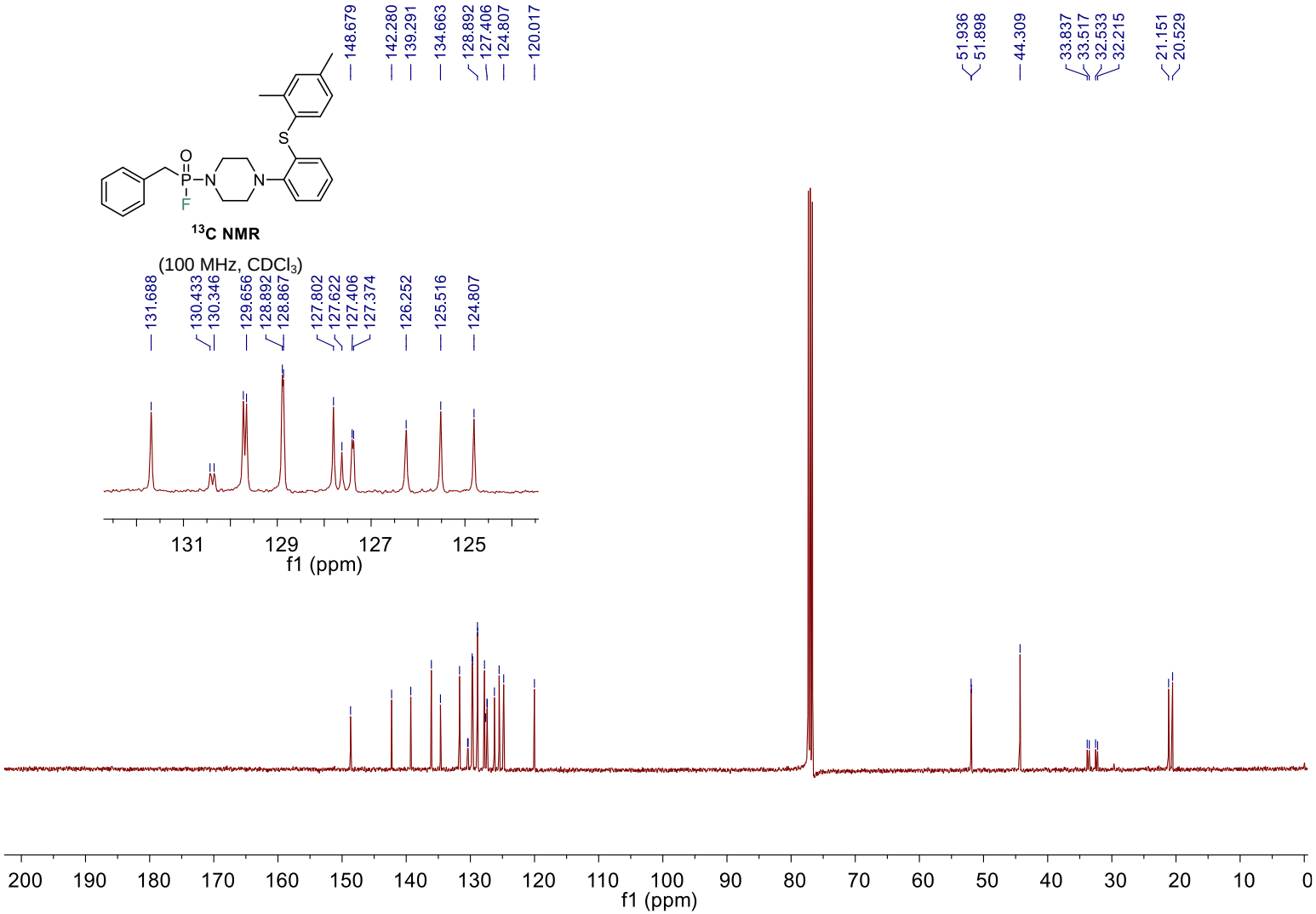
(162 MHz, $CDCl_3$)

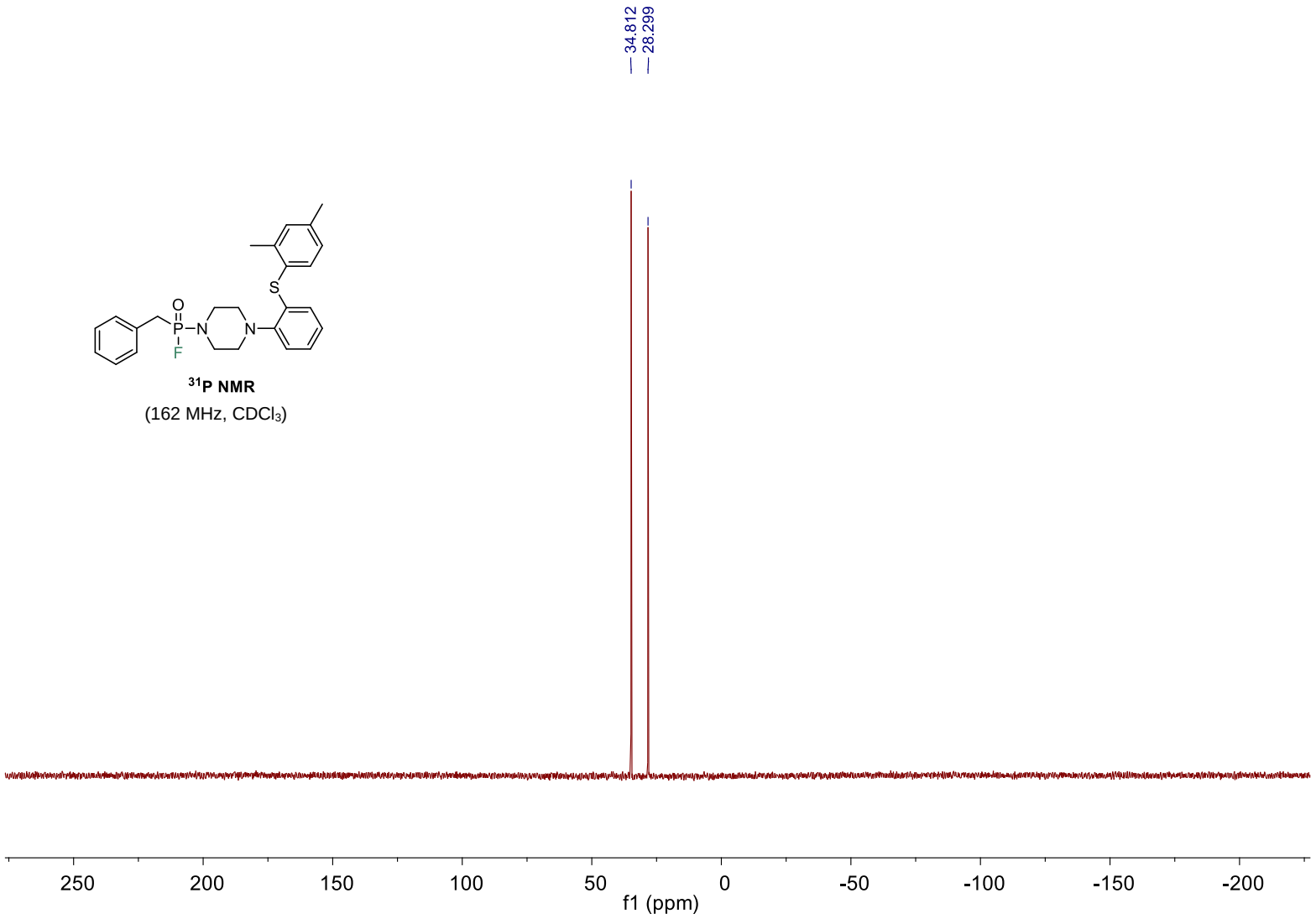


^{19}F NMR

(376 MHz, $CDCl_3$)

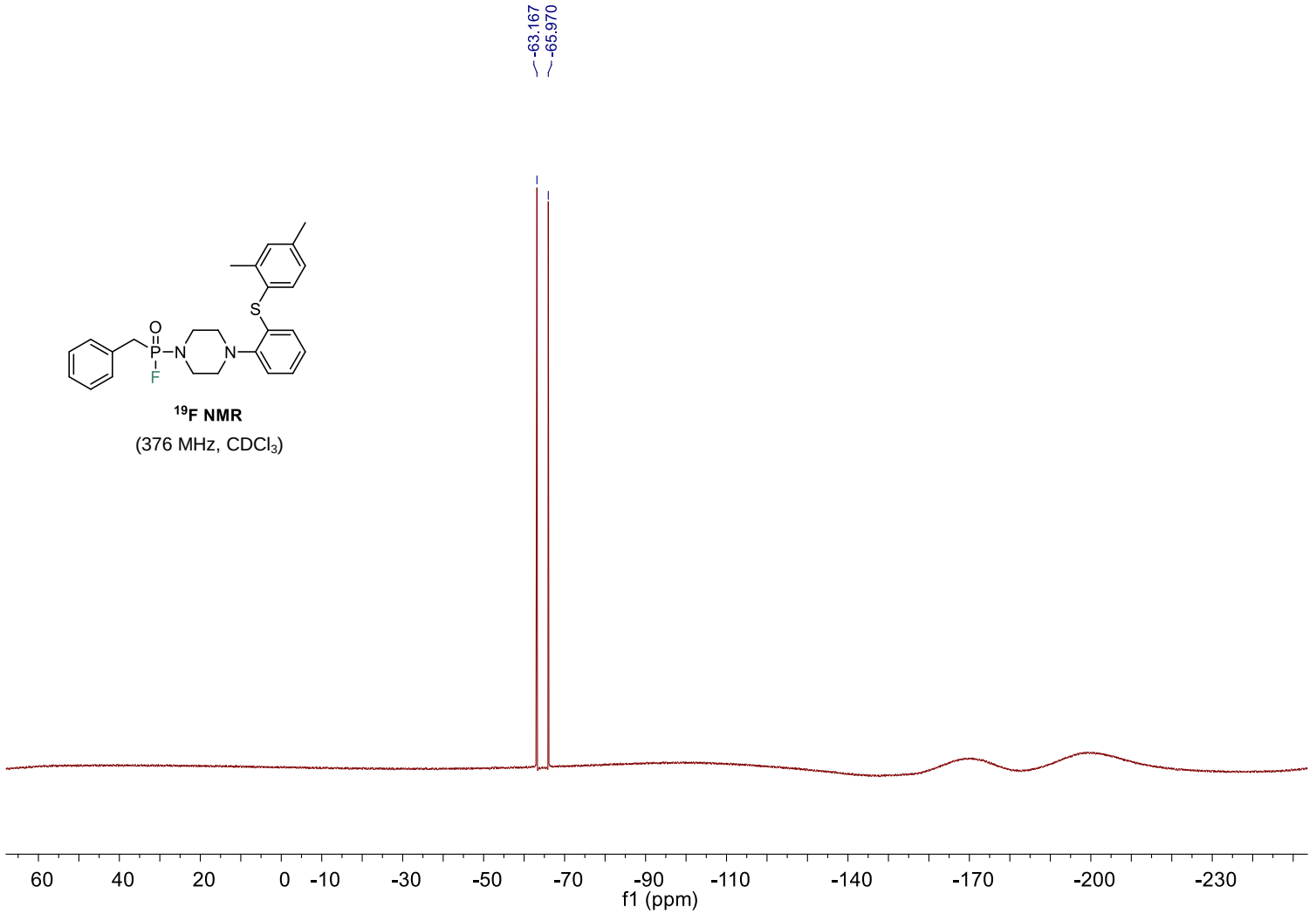

7.389
7.369
7.353
7.336
6.961
6.894
6.857
6.518
6.498
3.428
3.390
3.371
3.344
3.334
3.310
3.297
3.256
3.236
2.917
2.361
2.297
O
P
N
N
S
F
1H NMR
(400 MHz, CDCl3)
6.02
1.00
2.08
0.97
0.93
6.11
4.00
6.15
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


148.679
142.280
139.291
134.663
128.892
127.406
124.807
120.017
51.936
51.898
44.309
33.837
33.517
32.533
32.215
21.151
20.529
O
P
N
N
S
F
13C NMR
(100 MHz, CDCl3)
131.688
130.433
130.346
129.656
128.892
128.867
127.802
127.622
127.406
127.374
126.252
125.516
124.807
131
129
127
125
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



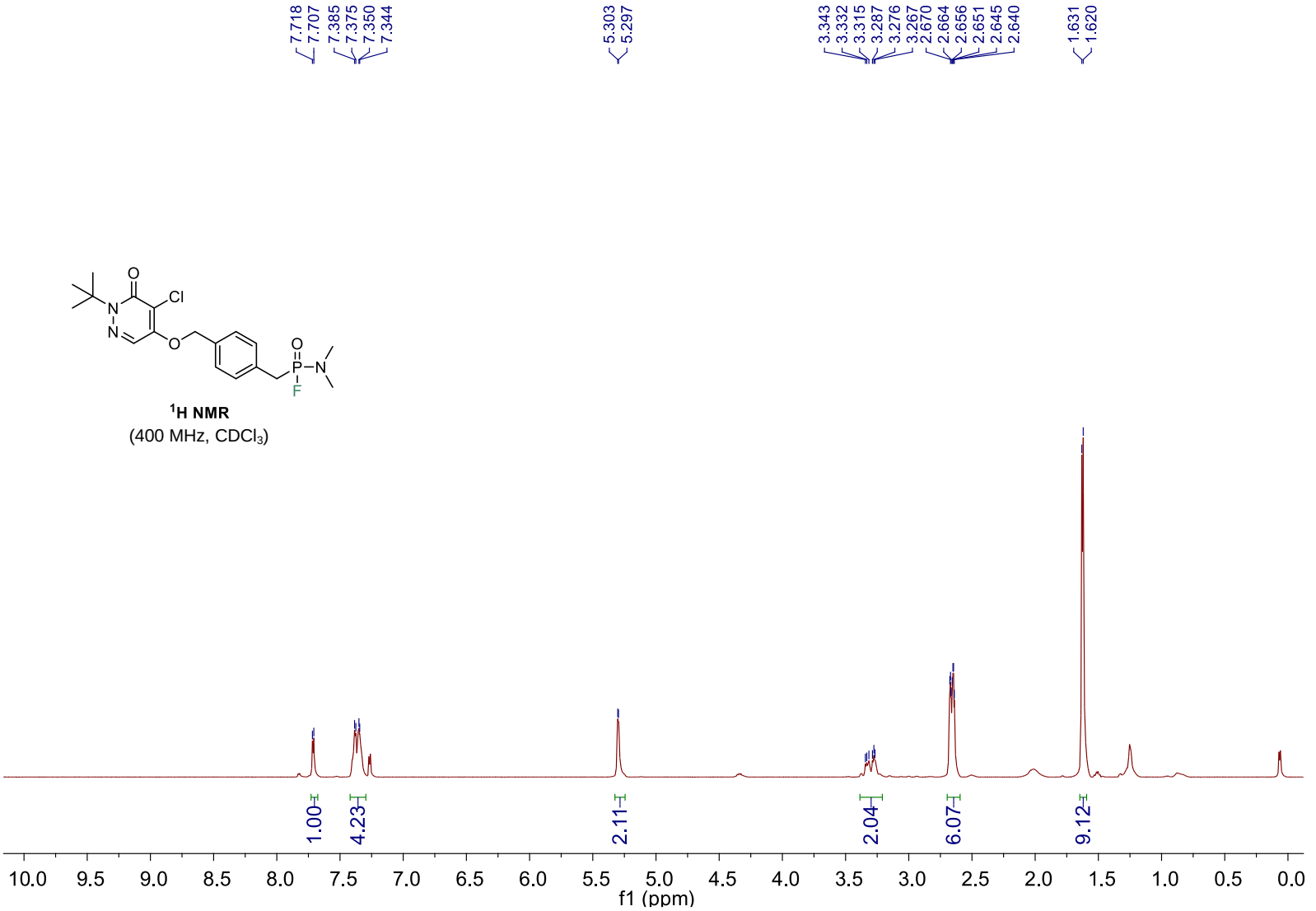
^{31}P NMR

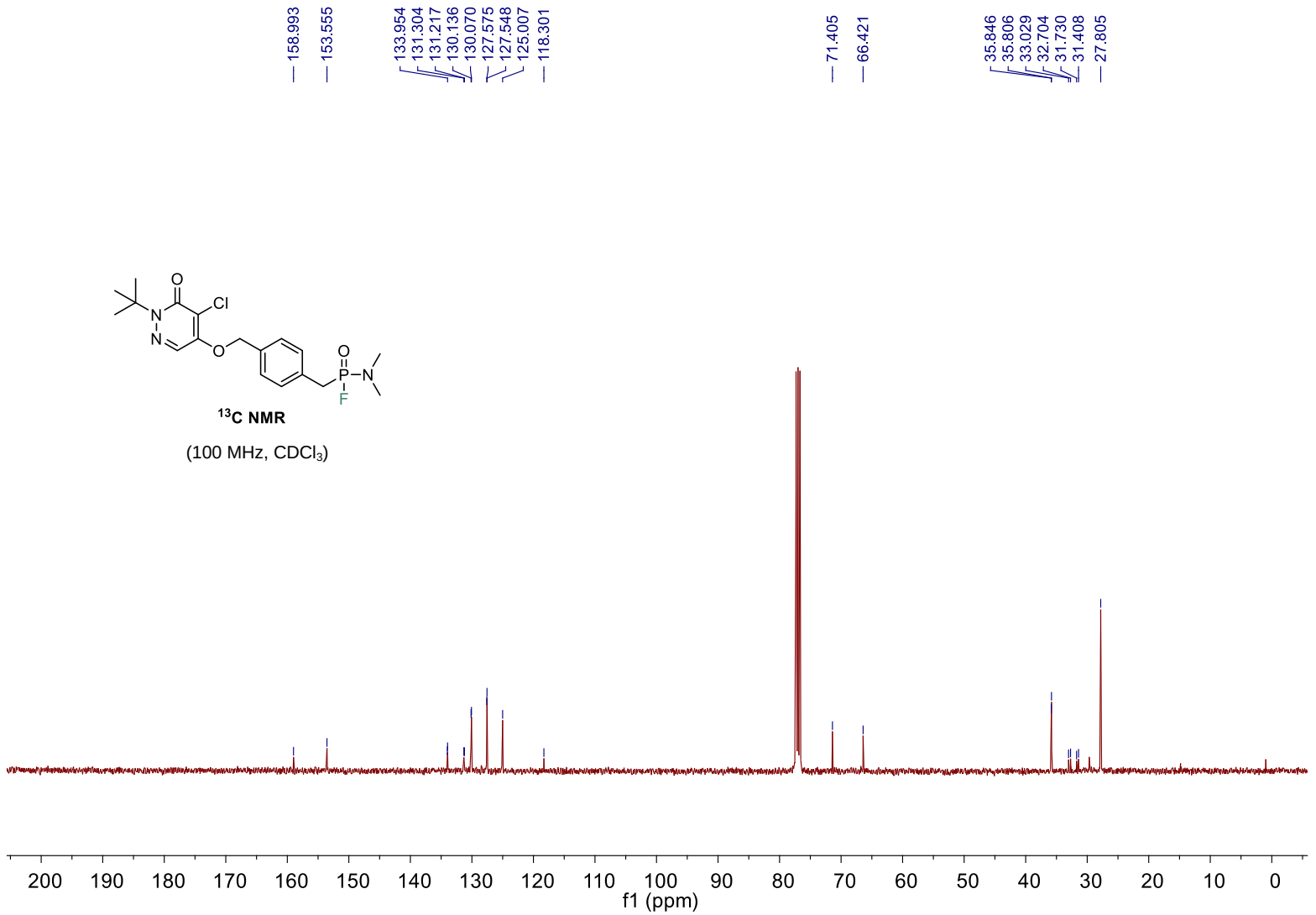
(162 MHz, $CDCl_3$)



^{19}F NMR

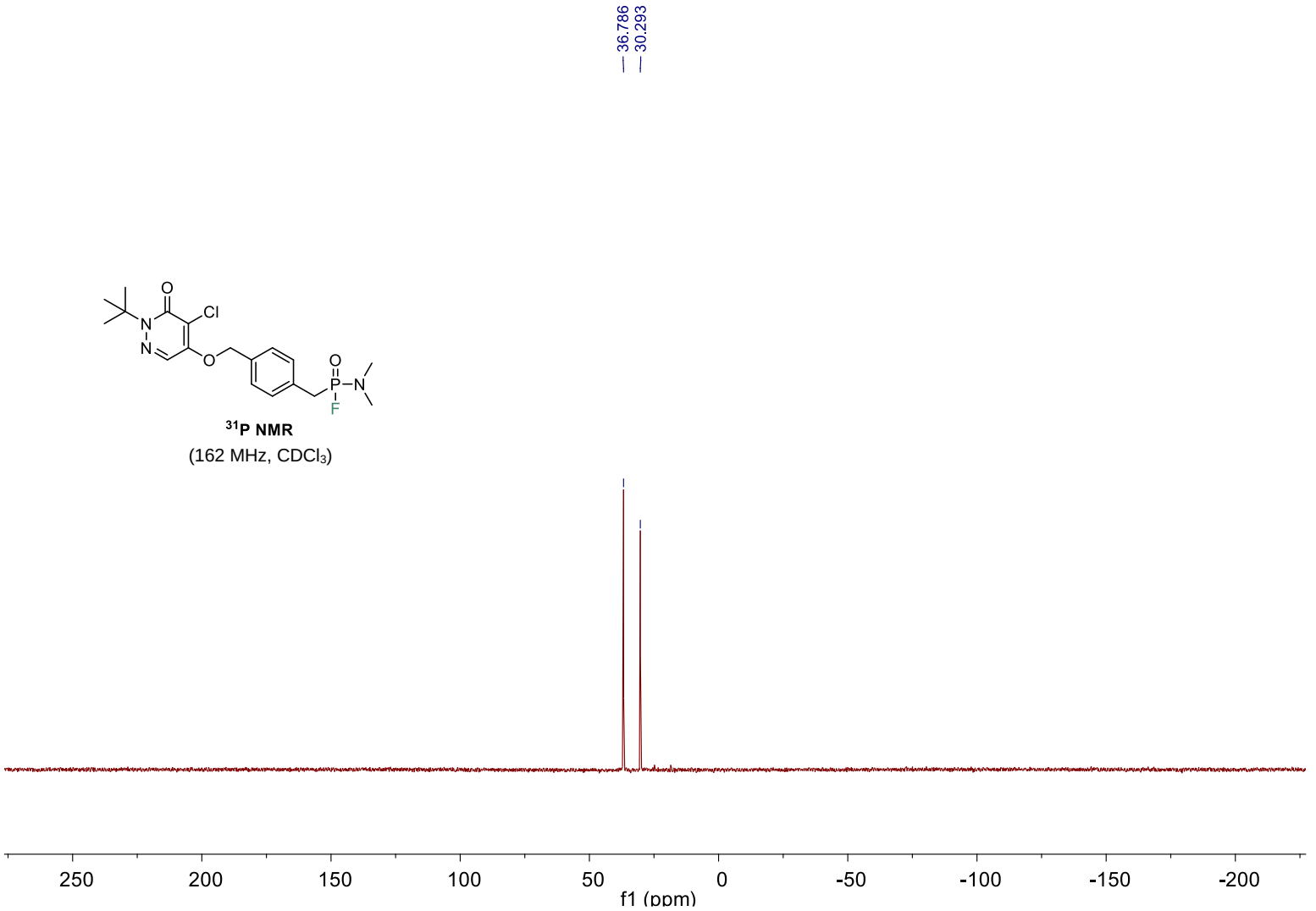
(376 MHz, $CDCl_3$)


7.718
7.707
7.385
7.375
7.350
7.344
5.303
5.297
3.343
3.332
3.315
3.287
3.276
3.267
2.670
2.664
2.656
2.651
2.645
2.640
1.631
1.620
O
Cl
N
N
O
O
P
N
F
1H NMR
(400 MHz, CDCl3)
1.00
4.23
2.11
2.04
6.07
9.12
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



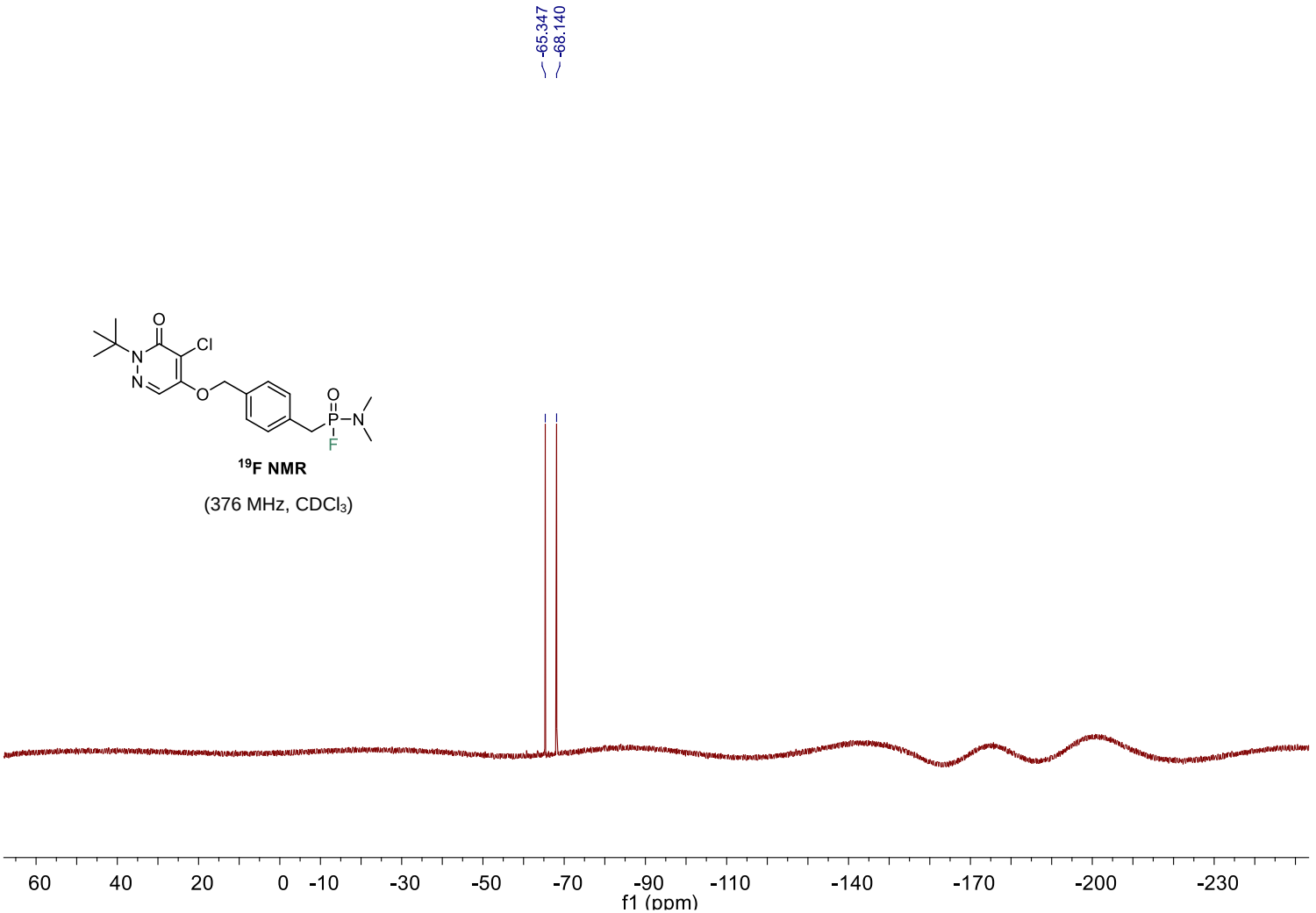
^{13}C NMR

(100 MHz, $CDCl_3$)



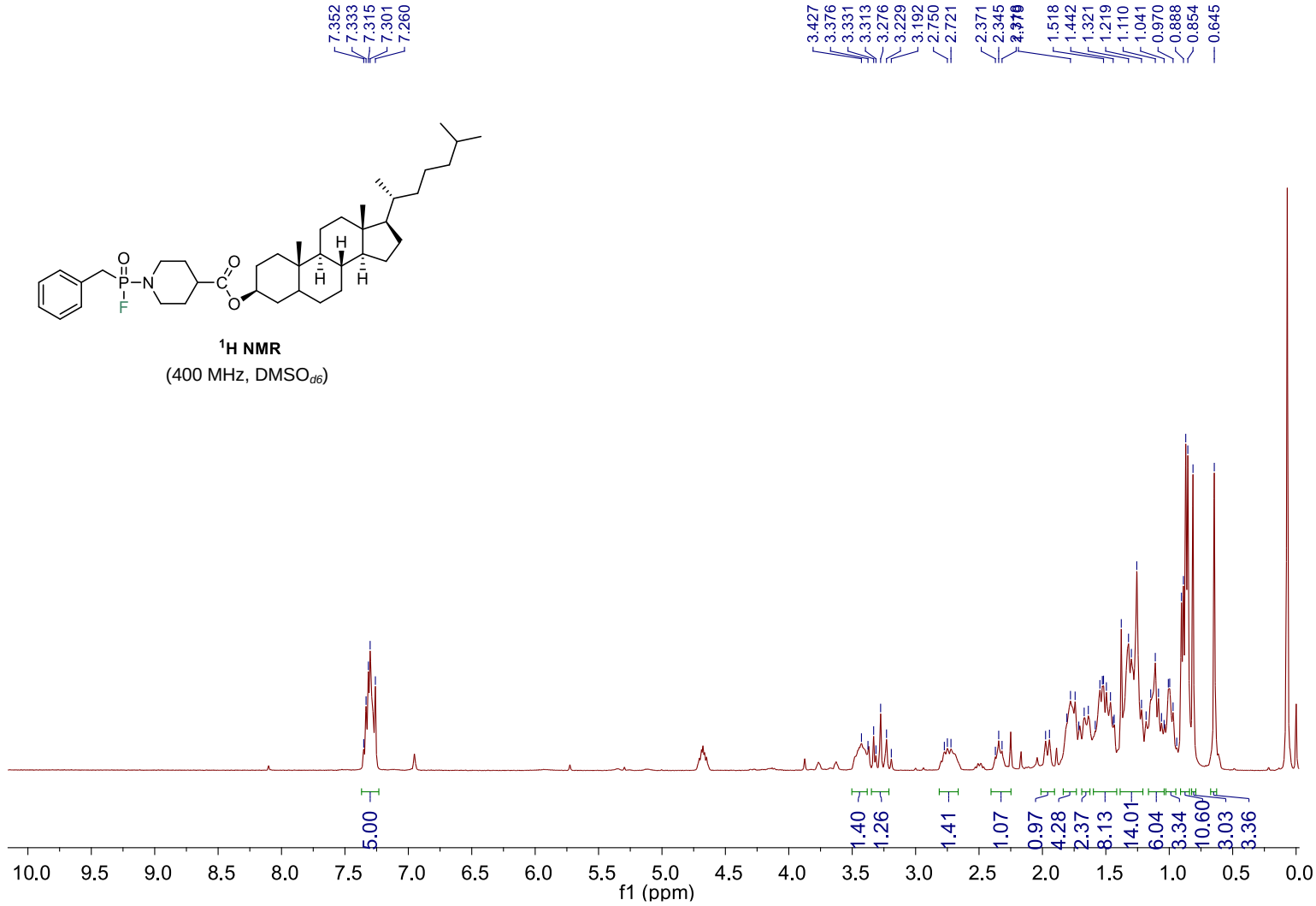
^{31}P NMR

(162 MHz, $CDCl_3$)



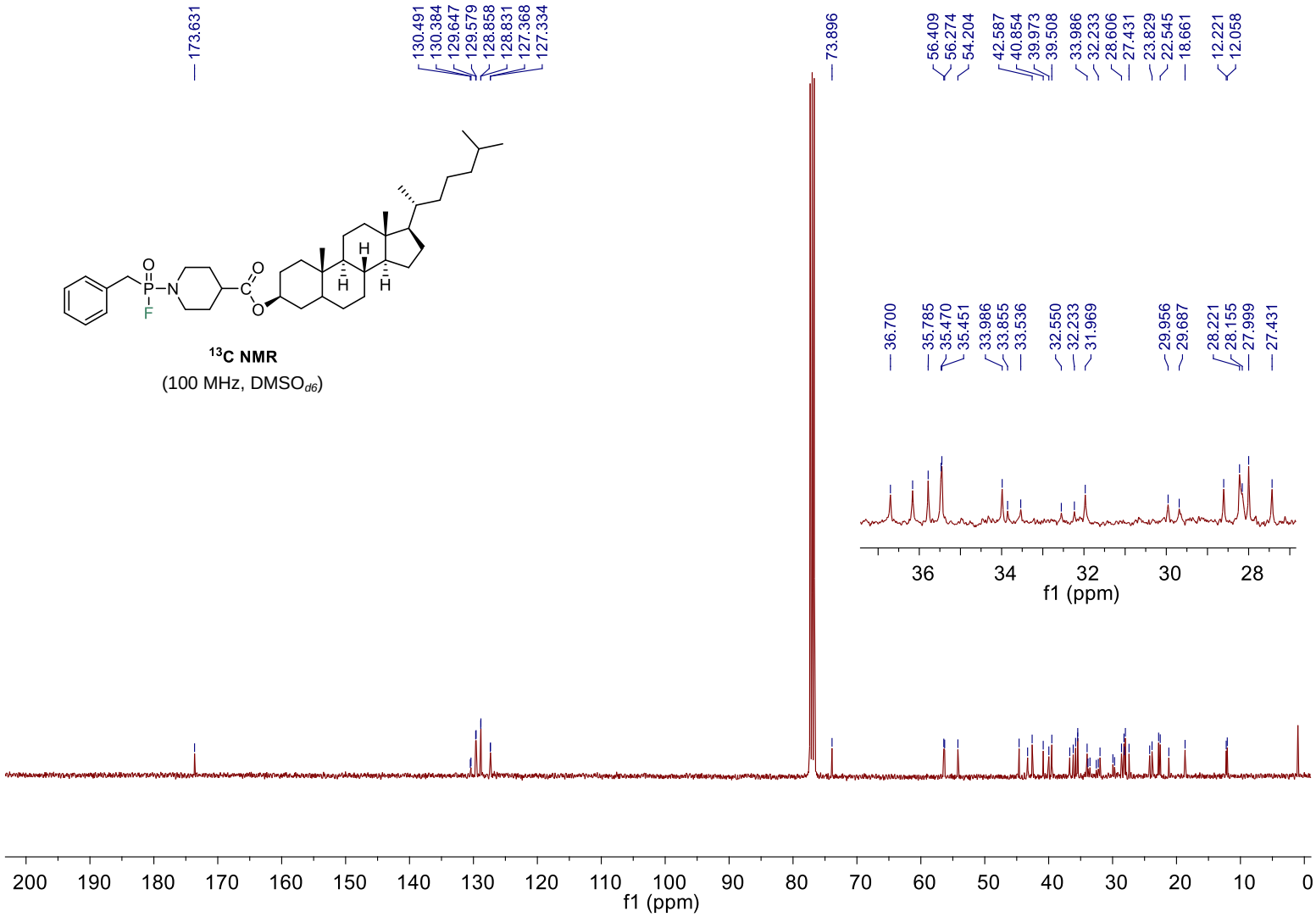
^{19}F NMR

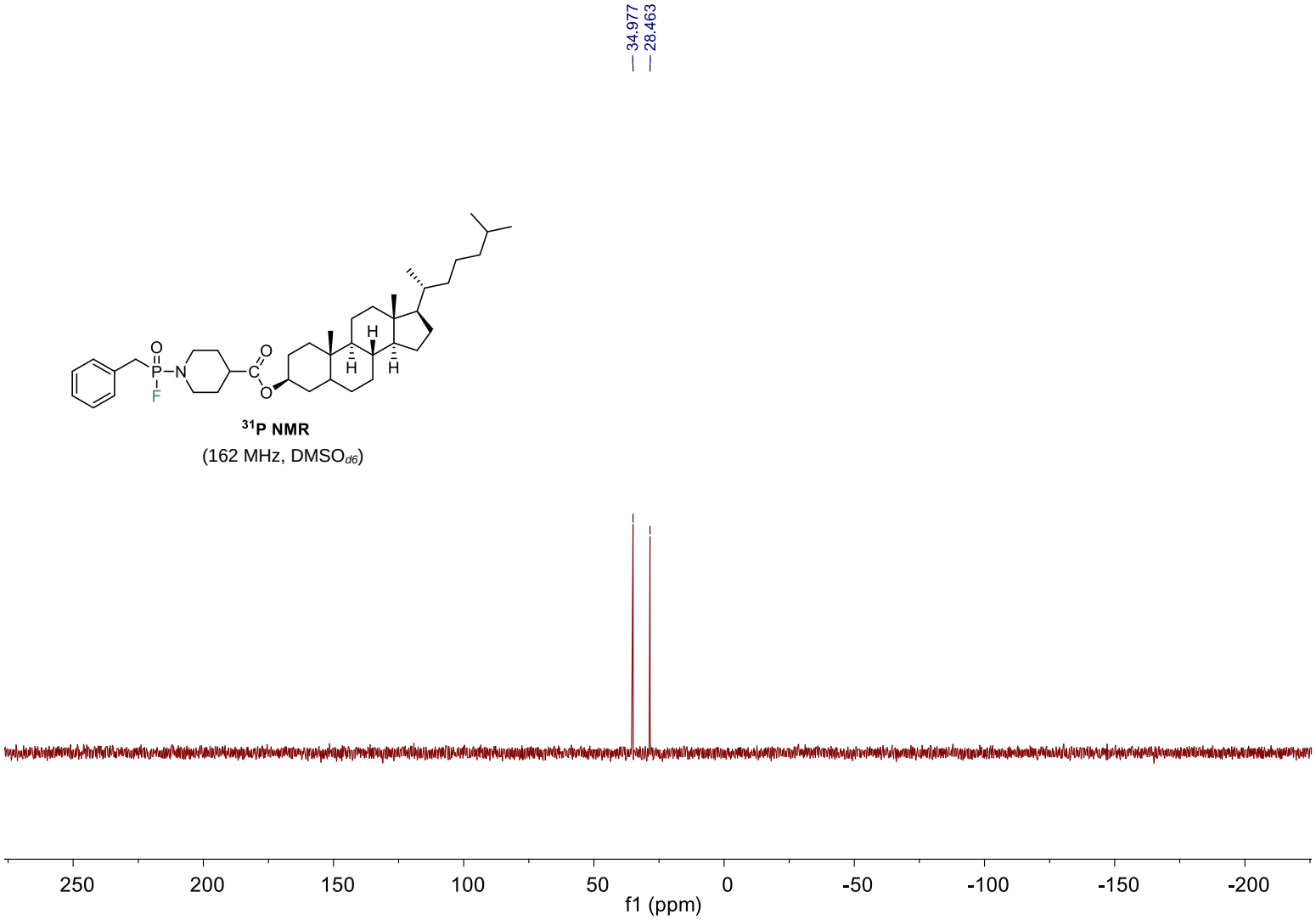
(376 MHz, $CDCl_3$)



^{1}H NMR

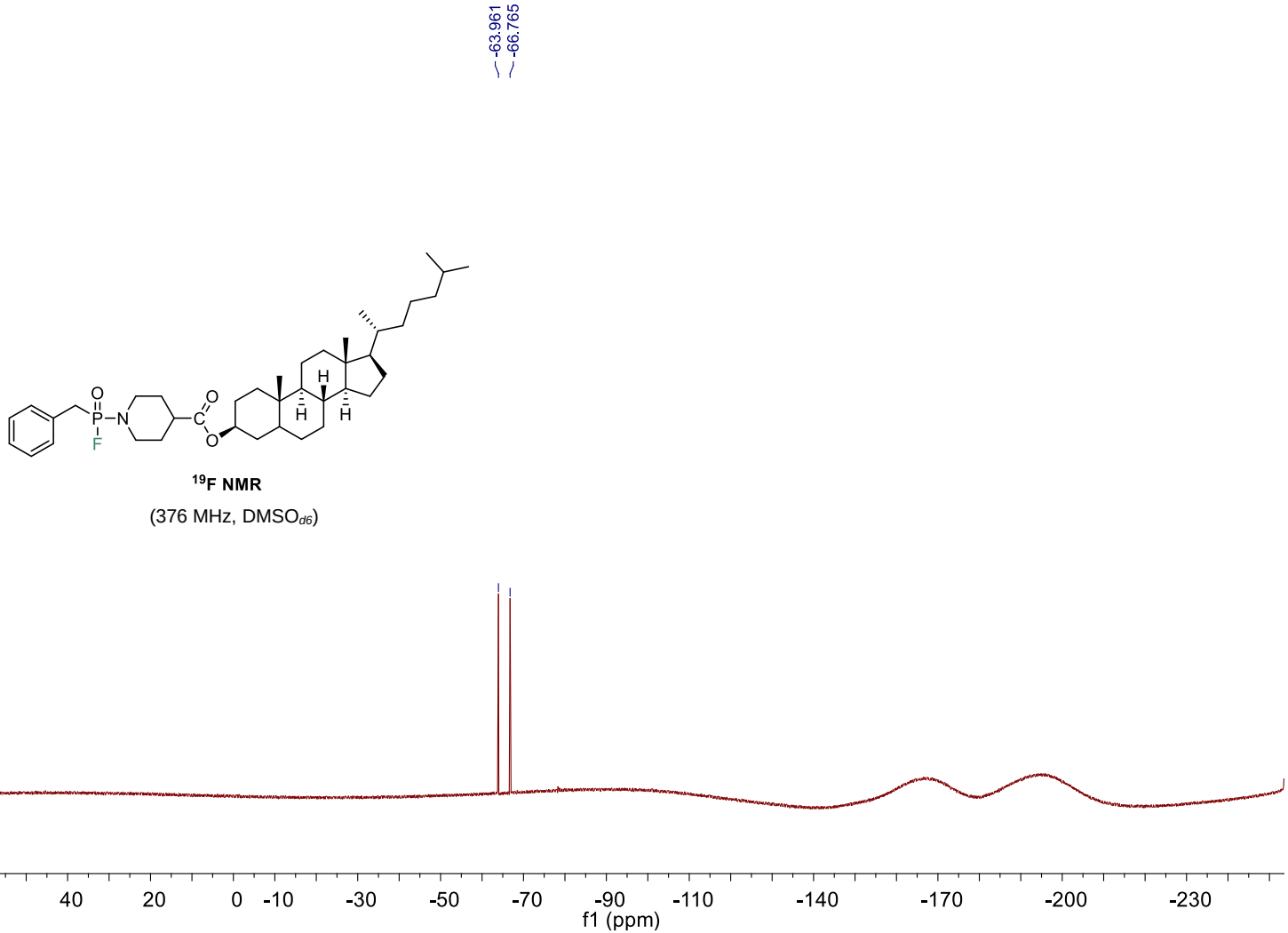
(400 MHz, $DMSO_{d6}$)


173.631
130.491
130.384
129.647
129.579
128.858
128.831
127.368
127.334
73.896
56.409
56.274
54.204
42.587
40.854
39.973
39.508
33.986
32.233
28.606
27.431
23.829
22.545
18.661
12.221
12.058
36.700
35.785
35.470
35.451
33.986
33.855
33.536
32.550
32.233
31.969
29.956
29.687
28.221
28.155
27.999
27.431
O
P
N
F
C
O
O
H
H
H
13C NMR
(100 MHz, DMSOd6)
36
34
32
30
28
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



^{31}P NMR

(162 MHz, $DMSO_{d6}$)



^{19}F NMR

(376 MHz, DMSO$_{d6}$)

4 Supplementary references

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