

Water Enhanced Synthesis of *gem*-Bisphosphonates via Rh(I) Mediated 1,4-Conjugate Addition of Aryl Boronic Acids to Vinlydenbisphosphonate Esters

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Reagents and Materials

General. ¹H NMR, ³¹P{¹H} NMR, spectra were run on a Bruker Avance 300 spectrometer operating at 300.15, 121.5, MHz, respectively, at 298 K, unless otherwise stated. δ values in ppm are relative to Si(CH₃)₄, 85% H₃PO₄. GC-MS analyses were performed on a GC Trace GC 2000 coupled with a quadrupole MS Thermo Finnigan Trace MS with *Full Scan* method. Experimental conditions are reported in the following table.

Experimental conditions for GC-MS analysis	
Capillary column:	HP5-MS 30 m, 0.25 mm x 0.25 μm
Initial T, °C:	80°C for 5 min
Rate, °C/min:	30°C/min
Final T, °C:	280°C for 30 min
Injector T (split), °C:	280°C
GAs carier flow, mL/min.	0.8 mL/min
Injected volume, μL	0.8-1 μL
Solvent delay, min.	4 min.
Mass range, amu:	35-500 amu
Detector voltage, V:	350 V
Interface T, °C	280°C
Source T, °C:	200°C

Vinilyldenbisphosphonate tetraethyl ester (VBP) was prepared as reported in the literature.¹ All the synthetic work was carried out with the exclusion of atmospheric oxygen under nitrogen atmosphere using standard Schlenk techniques. Solvents were dried and purified according to standard methods.

Catalytic Studies: general procedure for the catalytic addition of boronic acid to VBP

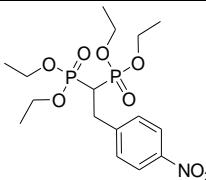
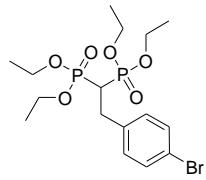
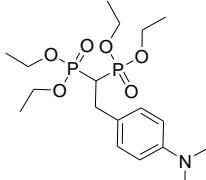
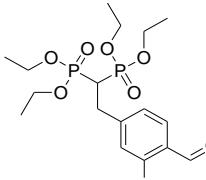
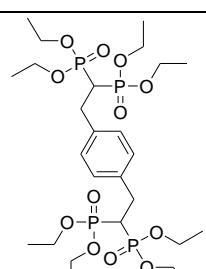
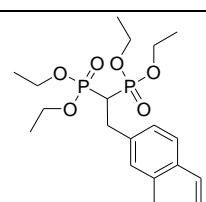
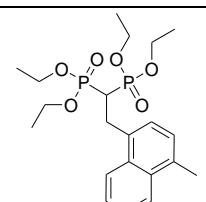
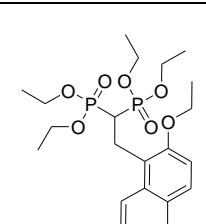
In a Schlenk reactor 0.2 mmol (50 µL) of VBP and 0.6 mmol of the proper boronic acid were added. To this, 1.50 mL of degassed water and 150 µL of a solution containing 24 mg of [RhCl(COD)]₂ in 1.5 mL of 1,4-dioxane were added. The resulting solution was tightly closed and thermostatted at 110°C for 6-18 h under vigorous stirring. The solution was cooled to room temperature, diluted with 5 mL of water and extracted with ethyl acetate (2 X 5 mL) leading to the isolation of the crude product. This was further purified with column chromatography (hexane:acetone 1:1) and characterized with ¹H, ³¹P and GC-MS analysis.

General procedure for the ester deprotection of the BP

The tetraethyl ester of the bisphosphonic acid (0.2 mmol) was introduced in a vial under anhydrous condition. To this 12 equivalents of bromotrimethylsilane (2.4 mmol) were added. The vial was then sealed and stirred under inert atmosphere at rt for 18 h. The crude mixture was concentrated under reduced pressure, diluted with bidistilled water, stirred for 4 h at room temperature and dried. The free bisphosphonic acid was obtained in quantitative yield and was characterized by ¹H and ³¹P NMR.

Table 1. New BP tetraethylester derivatives prepared by Rh(I) aryl boronic addition to VBP.

1BA		¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.21-1.31 (m, 12H), 2.65 (tt, J = 24.0, 6.3 Hz, 1H), 3.24 (td, J = 16.5, 6.3 Hz, 2H), 3.97-4.21 (m, 8H), 7.15-7.28 (m, 5H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 24.20 (s)
2BA		¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.28 (td, J = 7.2, 3.0 Hz, 12H), 2.59 (tt, J = 23.7, 6.0 Hz, 1H), 3.19 (td, J = 16.5, 6.0 Hz, 2H), 3.78 (s, 3H), 4.02 – 4.19 (m, 8H), 6.81 (d, J = 8.7 Hz, 2H), 7.19 (d, J = 8.7 Hz, 2H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 24.33 (s).
3BA		¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.27 (td, J = 6.9, 2.7 Hz, 12H), 2.46 (s, 3H), 2.60 (tt, J = 24.0, 6.3 Hz, 1H), 3.20 (td, J = 16.5, 6.3 Hz, 2H), 4.00 – 4.20 (m, 8H), 7.19 (s, 4H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 24.14 (s).

4BA		¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.27 (td, <i>J</i> = 7.2, 2.4 Hz, 12H), 2.62 (tt, <i>J</i> = 23.7, 6.3 Hz, 1H), 3.33 (td, <i>J</i> = 16.5, 6.3 Hz, 2H), 4.00 – 4.20 (m, 8H), 7.45 (d, <i>J</i> = 8.7 Hz, 2H), 8.14 (d, <i>J</i> = 8.7 Hz, 2H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 23.38 (s).
5BA		¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.27 (td, <i>J</i> = 6.9 , 3.0 Hz, 12H), 2.57 (tt, <i>J</i> = 23.7, 6.3 Hz, 1H), 3.19 (td, <i>J</i> = 16.5, 6.3 Hz, 2H), 4.00 – 4.21 (m, 8H), 7.15 (d, <i>J</i> = 8.4 Hz, 2H), 7.39 (d, <i>J</i> = 8.4 Hz, 2H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 23.89(s).
6BA		¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.28 (td, <i>J</i> = 6.9, 4.2 Hz, 12H), 2.59 (tt, <i>J</i> = 23.7, 6.0 Hz, 1H), 2.90 (s, 6H), 3.16 (td, <i>J</i> = 16.7, 6.0 Hz, 2H), 4.00 – 4.30 (m, 8H), 6.67 (d, <i>J</i> = 8.7 Hz, 2H), 7.14 (d, <i>J</i> = 8.7 Hz, 2H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 24.59 (s).
7BA		¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.28 (td, <i>J</i> = 6.9, 2.7 Hz, 12H), 2.61 (tt, <i>J</i> = 24.0, 6.6 Hz, 1H), 3.28 (td, <i>J</i> = 16.5, 6.6 Hz, 2H), 4.02 – 4.25 (m, 8H), 7.12 (d, <i>J</i> = 11.4 Hz, 1H), 7.18 (d, <i>J</i> = 7.8 Hz, 1H), 7.78 (t, <i>J</i> = 7.8 Hz, 1H), 10.31 (s, 1H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 23.34 (s).
1BAbis		¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.28 (td, <i>J</i> = 6.9, 3.0 Hz, 12H), 2.59 (tt, <i>J</i> =23.4, 6.6 Hz, 1H), 3.20 (td, <i>J</i> =15.0, 6.0 Hz, 2H), 4.00 - 4.22 (m, 8H), 7.26 – 7.30 (bs, 5H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 24.20 (s).
ω	8BA 	¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.23 (td, <i>J</i> = 6.9, 3.3 Hz, 12H), 2.75 (tt, <i>J</i> = 24.0, 6.3 Hz, 1H), 3.41 (td, <i>J</i> = 16.5, 6.3 Hz, 2H), 4.00-4.22 (m, 8H), 7.36 – 7.48 (m, 3H), 7.69-7.82 (m, 4H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 24.21 (s).
	9BA 	¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.16-1.28 (m, 12H), 2.66 (s, 3H), 2.87 (tt, <i>J</i> = 23.4, 6.6 Hz, 1H), 3.70 (td, <i>J</i> = 15.9, 6.6 Hz, 2H), 3.94 – 4.24 (m, 8H), 7.22 (d, <i>J</i> = 7.2 Hz, 1H), 7.38 (d, <i>J</i> = 7.2 Hz, 1H), 7.50 – 7.55 (m, 2H), 7.97 – 8.05 (m, 1H), 8.10 – 8.17 (m, 1H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 24.21 (s).
	10BA 	¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.14 (dt, <i>J</i> = 20.4, 7.2 Hz, 12H), 1.49 (t, <i>J</i> = 6.9 Hz, 3H), 3.18 (tt, <i>J</i> = 23.4, 7.2 Hz, 1H), 3.64-3.80 (m, 2H), 3.87-4.10 (m, 8H), 4.19 (q, <i>J</i> = 7.2 Hz, 2H), 7.21 (d, <i>J</i> = 9.0 Hz, 1H), 7.34-7.27 (m, 1H), 7.51-7.42 (m, 1H), 7.73 (m, 2H), 8.17 (d, <i>J</i> = 8.4 Hz, 1H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 24.70 (s).

11BA		¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.23 (td, <i>J</i> = 7.2, 3.3 Hz, 12H), 2.72 (tt, <i>J</i> = 23.7, 6.3 Hz, 1H), 3.37 (td, <i>J</i> = 16.5, 6.3 Hz, 2H), 3.90 (s, 3H), 4.02 – 4.18 (m, 8H), 7.07 – 7.15 (m, 2H), 7.33 – 7.38 (m, 1H), 7.63-7.70 (m, 3H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 24.29 (s).
12BA		¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.25 (td, <i>J</i> = 6.9, 3.3 Hz, 12H), 2.77 (tt, <i>J</i> = 24.0, 6.3 Hz, 1H), 3.38 (td, <i>J</i> = 16.5, 6.3 Hz, 2H), 4.00 – 4.24 (m, 8H), 6.97-7.08 (m, 2H), 7.29 (d, <i>J</i> = 9.6 Hz, 1H), 7.48 (d, <i>J</i> = 8.4 Hz, 1H), 7.52 (d, <i>J</i> = 8.7 Hz, 1H), 7.61 (s, 1H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 24.66 (s).
13BA		¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.28 (td, <i>J</i> = 7.2, 2.4 Hz, 12H), 2.57 (tt, <i>J</i> = 24.0, 6.0 Hz, 1H), 3.09-3.25 (m, 4H), 4.00 – 4.22 (m, 8H), 4.54 (t, <i>J</i> = 8.7 Hz, 2H), 6.68 (d, <i>J</i> = 8.1 Hz, 1H), 7.00 (d, <i>J</i> = 8.4 Hz, 1H), 7.12 (s, 1H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 24.42 (s).
14BA		¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.24-1.33 (m, 12H), 2.57 (tt, <i>J</i> = 23.7, 6.0 Hz, 1H), 3.13 (td, <i>J</i> = 16.5, 6.0 Hz, 2H), 4.02 – 4.19 (m, 8H), 4.22 (s, 4H), 6.77 – 6.70 (m, 3H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 24.26 (s).
15BA		¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.24-1.35 (m, 12H), 2.51 (tt, <i>J</i> = 23.7, 6.0 Hz, 1H), 3.07 (td, <i>J</i> = 16.5, 6.0 Hz, 2H), 4.06 – 4.22 (m, 8H), 6.35-6.37 (m, 1H), 7.31-7.35 (m, 2H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 24.16 (s).
16BA		¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.28 (td, <i>J</i> = 7.2, 2.4 Hz, 12H), 2.61 (tt, <i>J</i> = 23.7, 6.0 Hz, 1H), 3.27 (td, <i>J</i> = 16.5, 6.0 Hz, 2H), 4.04-4.20 (m, 8H), 7.01 (dd, <i>J</i> = 4.9, 1.2 Hz, 1H), 7.10 (bs, 1H), 7.23 (dd, <i>J</i> = 4.9, 3.0 Hz, 1H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 24.10 (s).
17BA		¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.20-1.31 (m, 12H), 2.80 (tt, <i>J</i> = 23.7, 6.3 Hz, 1H), 3.51 (td, <i>J</i> = 16.1, 6.4 Hz, 2H), 4.00-4.22 (m, 8H), 7.31 (s, 1H), 7.33-7.42 (m, 2H), 7.81-7.90 (m, 2H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 23.99 (s).
18BA		¹ H-NMR (300.15 MHz, CDCl ₃): δ 1.29 (t, <i>J</i> = 12.3 Hz, 12H), 2.70 (tt, <i>J</i> = 24.0, 5.4 Hz, 1H), 3.18 (td, <i>J</i> = 16.5, 5.4 Hz, 2H), 4.014.–24 (m, 8H), 6.60-6.70 (m, 2H), 7.03 (td, <i>J</i> = 7.6, 1.6 Hz, 1H), 7.12 (dd, <i>J</i> = 7.5, 1.5 Hz, 1H). ³¹ P { ¹ H}-NMR (121.5 MHz, CDCl ₃): δ 25.28 (s).

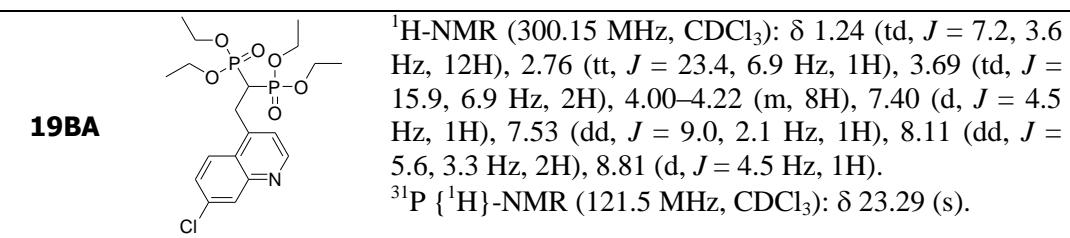
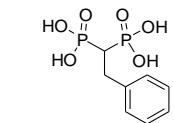
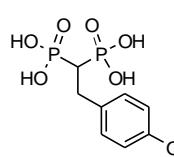
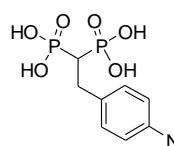
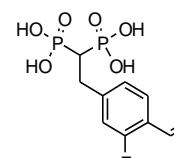
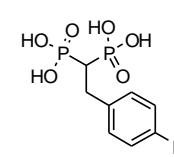
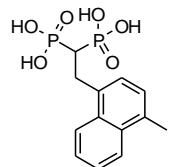


Table 2. New bisphosphonic acids prepared by deprotection of the BP tetraethylester derivatives with trimethylsilylbromide and water.

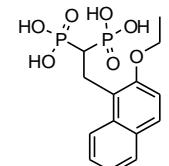
#	Product	NMR
1		¹ H-NMR (300.15 MHz, D ₂ O): δ 2.63 (tt, <i>J</i> = 22.8, 6.6 Hz, 1H), 3.20 (td, <i>J</i> = 16.2, 6.6 Hz, 2H), 7.23-7.32 (m, 1H), 7.32-7.40 (m, 3H). ³¹ P { ¹ H}-NMR (121.5 MHz, D ₂ O): δ 24.02 (s)
2		¹ H-NMR (300 MHz, D ₂ O): δ 2.40-2.70 (bs, 1H), 3.15 (btd, <i>J</i> = 16.5, 5.7 Hz, 2H), 3.82 (s, 3H), 6.95 (d, <i>J</i> = 8.4 Hz, 2H), 7.31 (d, <i>J</i> = 8.4 Hz, 2H). ³¹ P { ¹ H}-NMR (121.5 MHz, D ₂ O): δ 22.61 (s)
3		¹ H-NMR (300 MHz, D ₂ O): δ 2.64 (tt, <i>J</i> = 22.2, 7.2 Hz, 1H), 3.30 (td, <i>J</i> = 15.6, 7.2 Hz, 2H), 7.56 (d, <i>J</i> = 8.7 Hz, 2H), 8.18 (d, <i>J</i> = 8.7 Hz, 2H). ³¹ P { ¹ H}-NMR (121.5 MHz, D ₂ O): δ 21.42 (s)
4		¹ H-NMR (300 MHz, D ₂ O): δ 2.50-2.76 (btt, <i>J</i> = 22.8, 7.2 Hz, 1H), 3.23 (td, <i>J</i> = 15.9, 6.3 Hz, 2H), 7.05-7.30 (m, 2H), 7.85 (t, <i>J</i> = 7.8 Hz, 1H), 10.11 (s, 1H). ³¹ P { ¹ H}-NMR (121.5 MHz, D ₂ O): δ 21.69
5		¹ H-NMR (δ , 300 MHz, D ₂ O): δ 2.45-2.69 (bt, <i>J</i> = 24.0 Hz, 1H), 3.15 (btd, <i>J</i> = 15.6, 5.4 Hz, 2H), 7.26 (d, <i>J</i> = 8.4 Hz, 2H), 7.50 (d, <i>J</i> = 8.4 Hz, 2H). ³¹ P { ¹ H}-NMR (121.5 MHz, D ₂ O): d 22.38 (s)

6



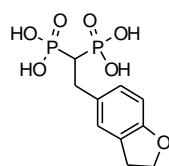
^1H -NMR (300.15 MHz, D_2O): d 2.67 (s, 3H),
2.77 (tt, $J= 22.8, 6.6$ Hz, 1H), 2.65 (td, $J=$
16.2, 7.2 Hz, 2H), 7.34 (d, $J= 6.9$ Hz, 1H),
7.47 (d, $J= 6.9$ Hz, 1H), 7.58-7.70 (m, 2H),
8.10-8.23 (m, 2H).
 $^{31}\text{P} \{^1\text{H}\}$ -NMR (121.5 MHz, D_2O): d 22.19 (s)

7



^1H -NMR (300 MHz, D_2O): δ 1.47 (t, $J= 6.6$ Hz, 3H), 2.80-3.05 (bt, $J= 22.2$ Hz, 1H), 3.68 (td, $J= 14.7, 6.6$ Hz, 2H), 4.30 (q, $J= 6.9$ Hz, 2H), 7.40-7.47 (m, 2H), 7.56-7.63 (m, 1H), 7.84-7.93 (m, 2H), 8.13-8.20 (m, 1H).
 $^{31}\text{P} \{^1\text{H}\}$ -NMR (MHz, D_2O): δ 22.55

8



^1H -NMR (300 MHz, D_2O): δ 2.35-2.60 (bt, $J= 23.1$ Hz, 1H), 3.12 (td, $J= 15.6, 5.4$ Hz, 2H), 3.22 (t, $J= 8.7$ Hz, 2H), 4.58 (t, $J= 8.7$ Hz, 2H), 6.77 (d, $J= 8.1$ Hz, 1H), 7.11 (d, $J= 8.1$ Hz, 1H), 7.27 (s, 1H).
 $^{31}\text{P} \{^1\text{H}\}$ -NMR (121.5 MHz, D_2O): δ 22.23 (s)

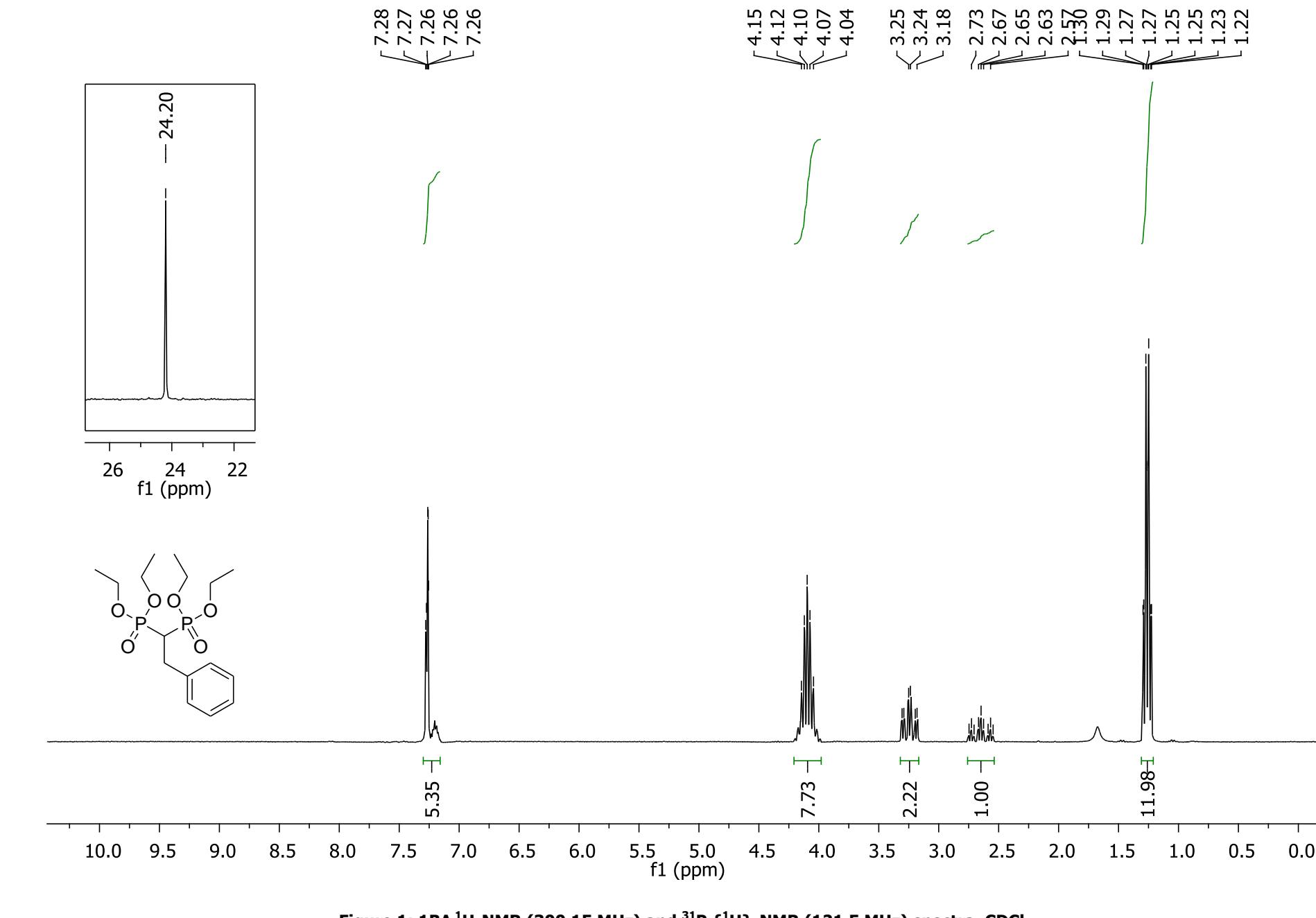


Figure 1: 1BA ^1H -NMR (300.15 MHz) and $^{31}\text{P}\{^1\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

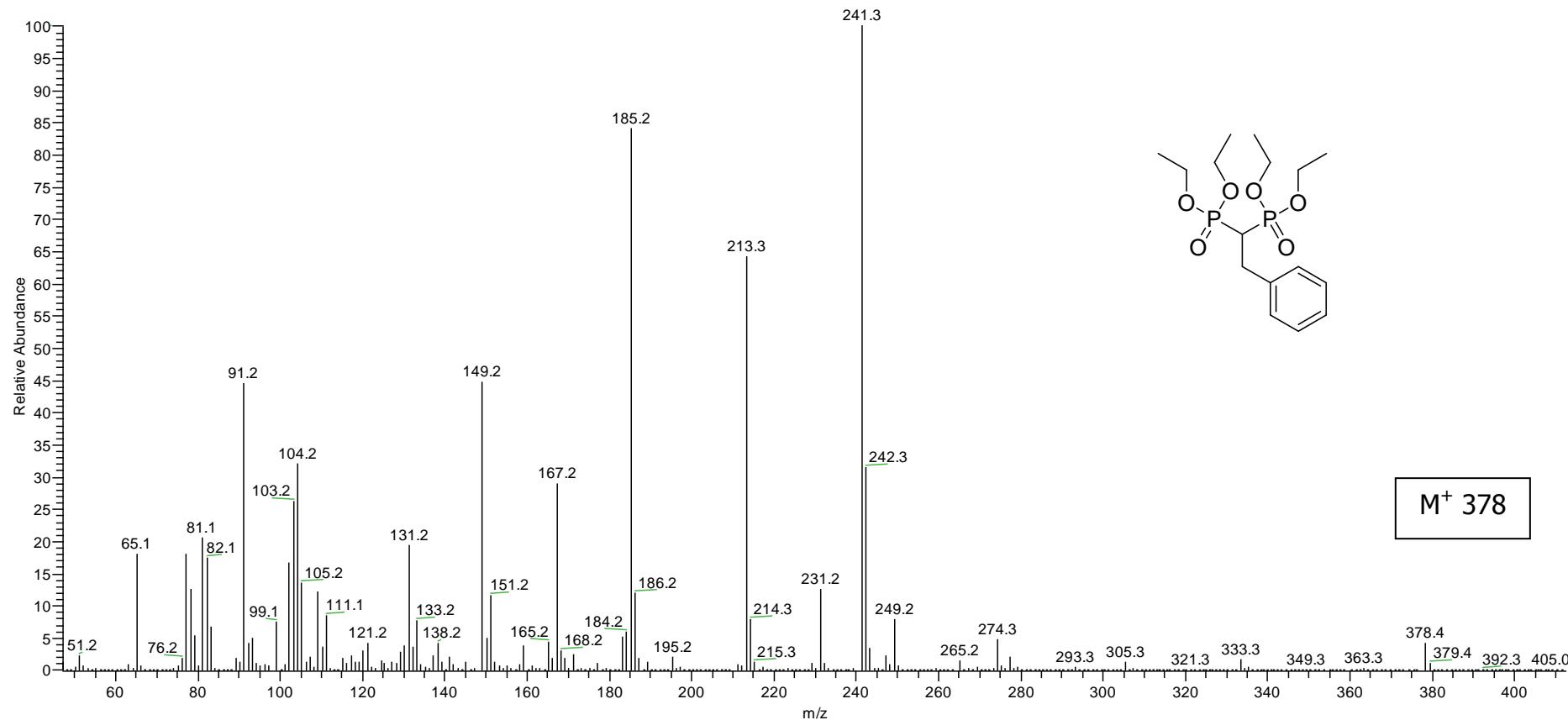


Figure 2: 1BA mass spectrum

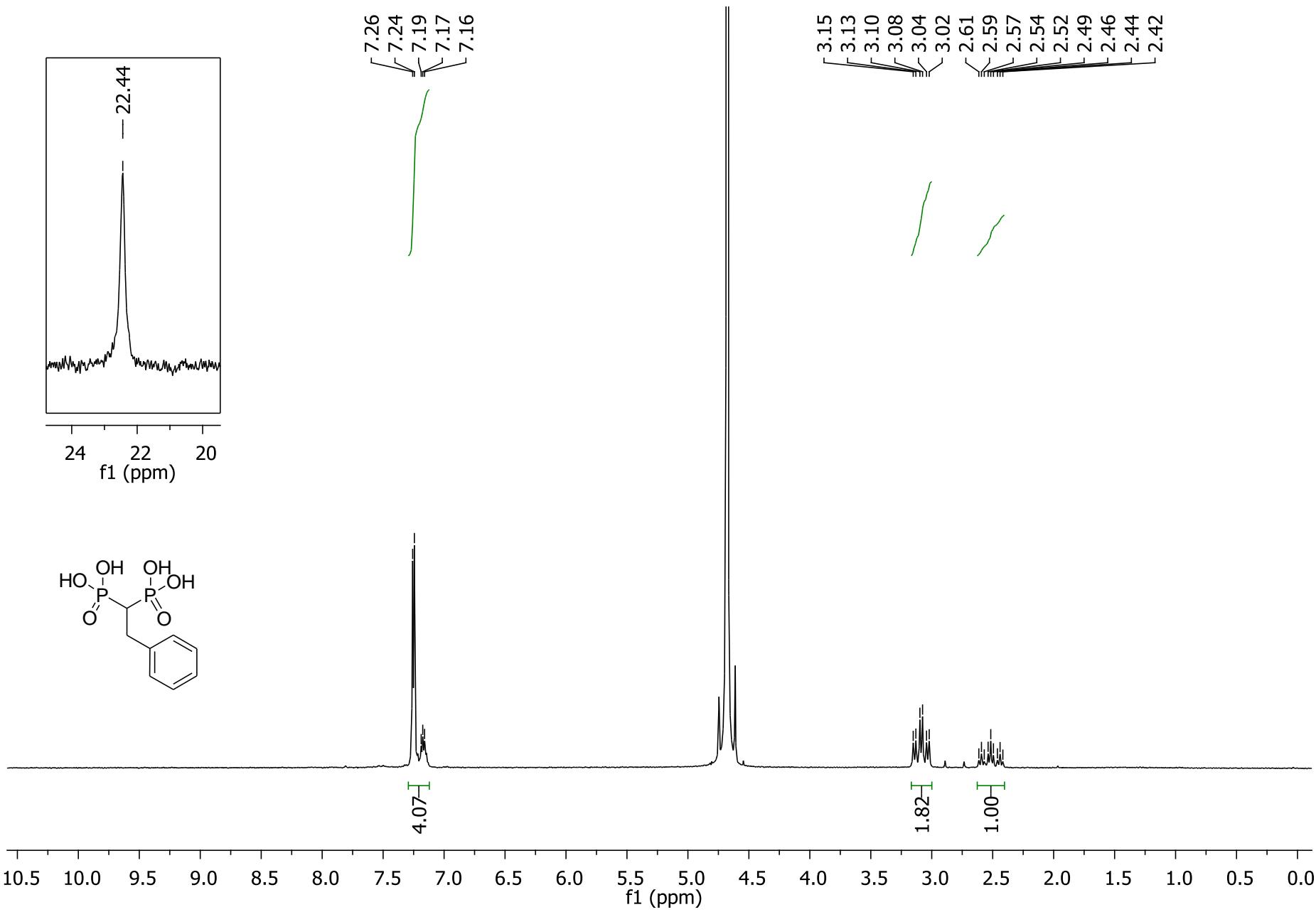


Figure 3: Deprotected 1BA ^1H -NMR (300.15 MHz) and $^{31}\text{P}\{^1\text{H}\}$ -NMR (121.5 MHz) spectra, D_2O .

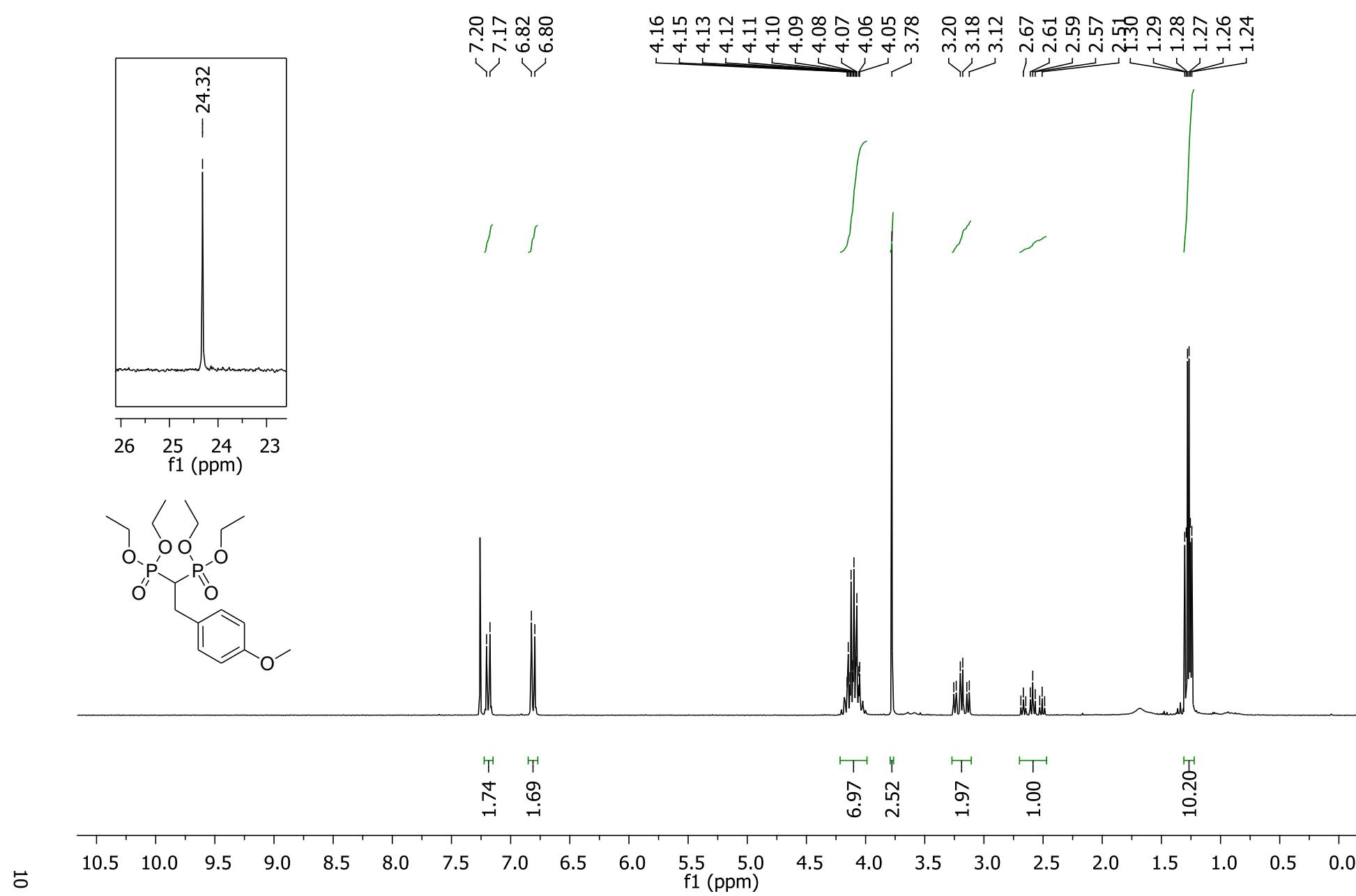


Figure 4: 2BA ^1H -NMR (300.15 MHz) and $^{31}\text{P} \{^1\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

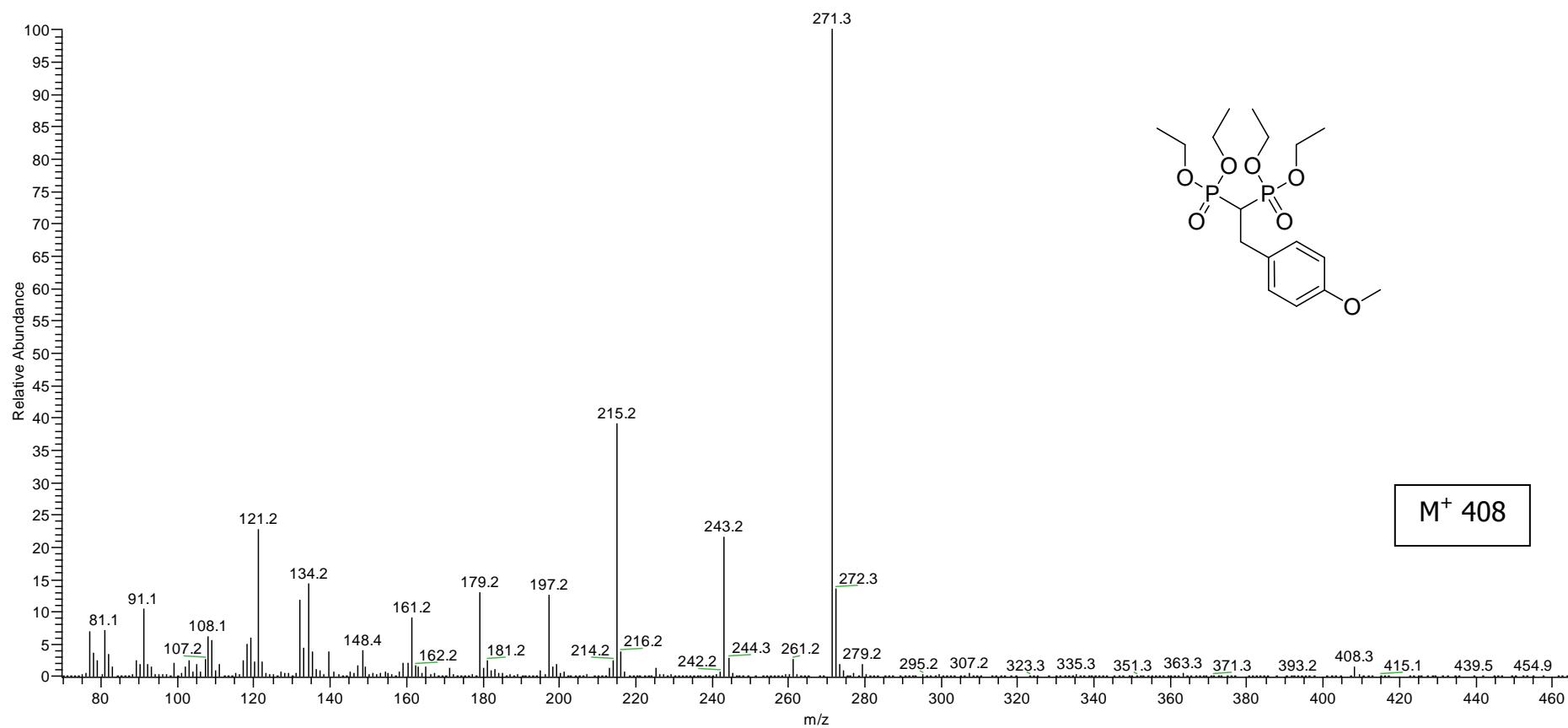


Figure 5: 2BA mass spectrum.

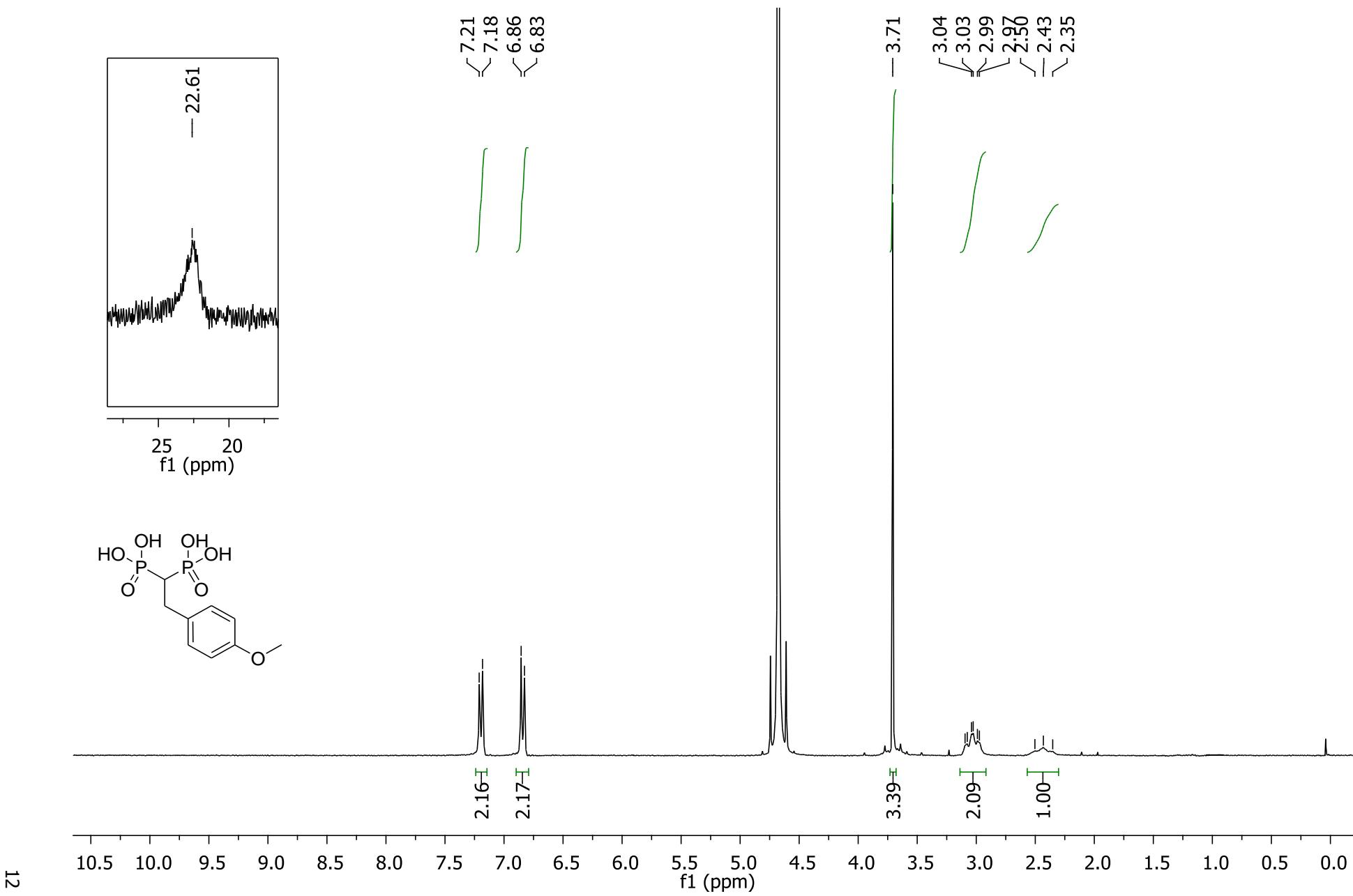


Figure 6: Deprotected 2BA ^1H -NMR (300.15 MHz) and $^{31}\text{P} \{^1\text{H}\}$ -NMR (121.5 MHz) spectra, D_2O .

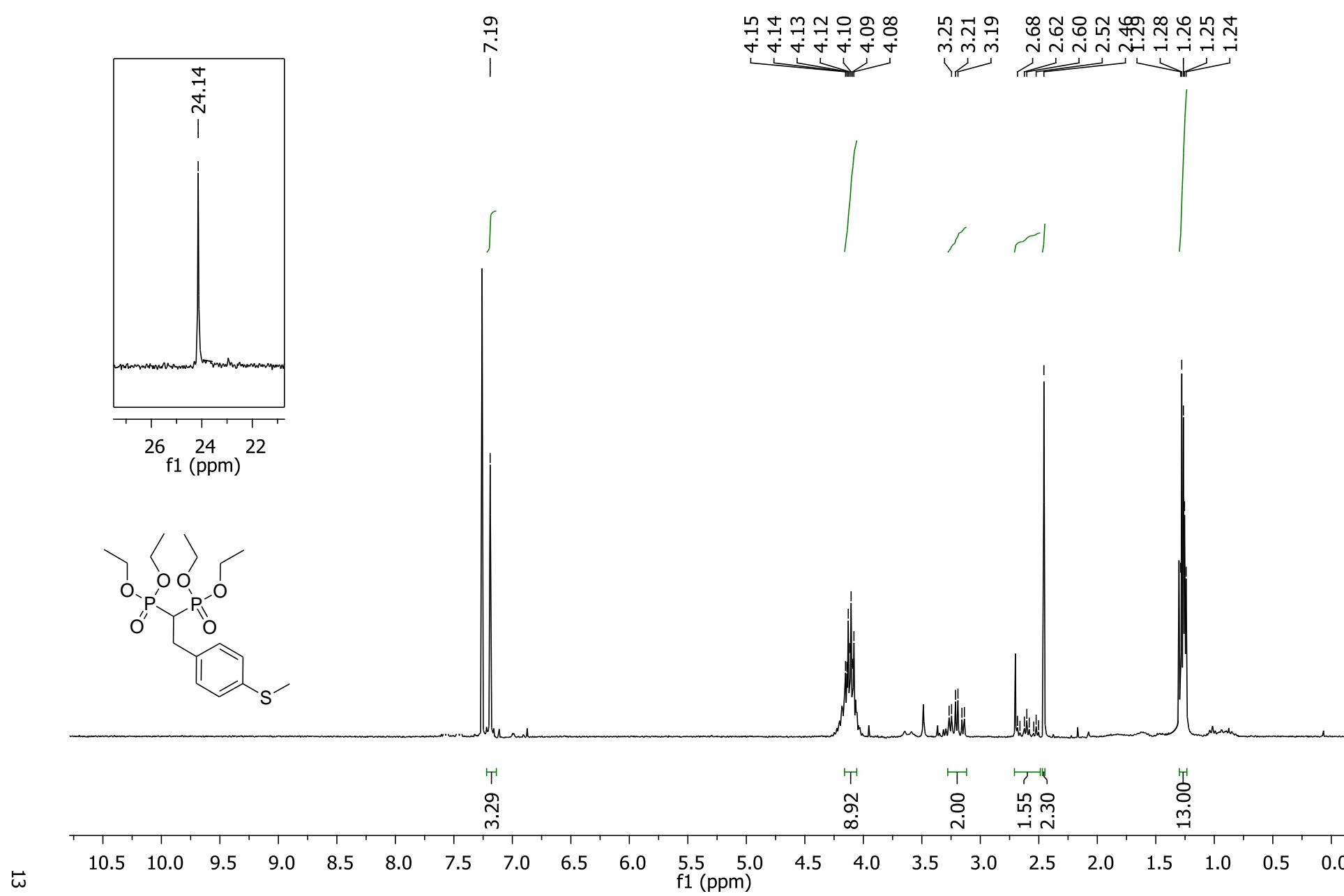


Figure 7: 3BA ^1H -NMR (300.15 MHz) e $^{31}\text{P}\{\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

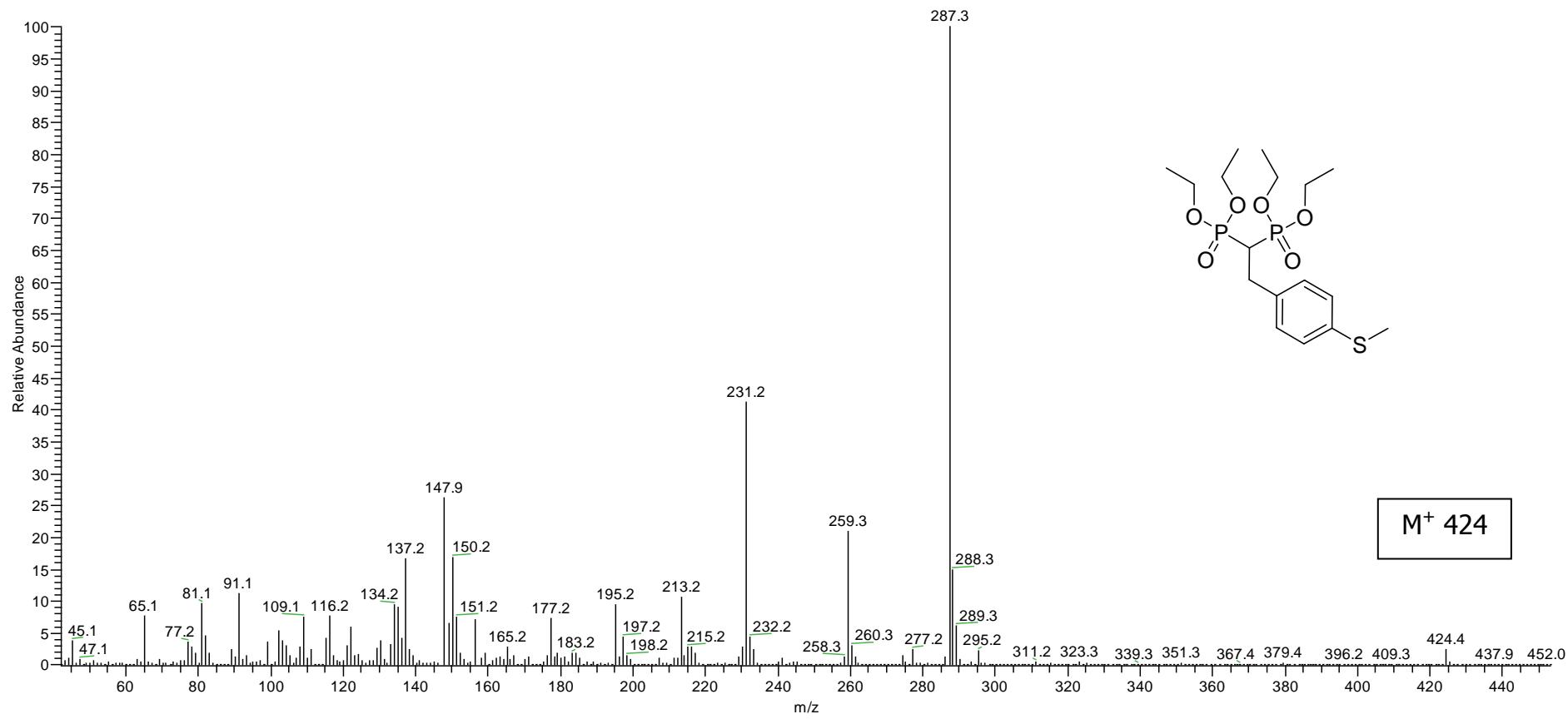


Figure 8: 3BA mass spectrum.

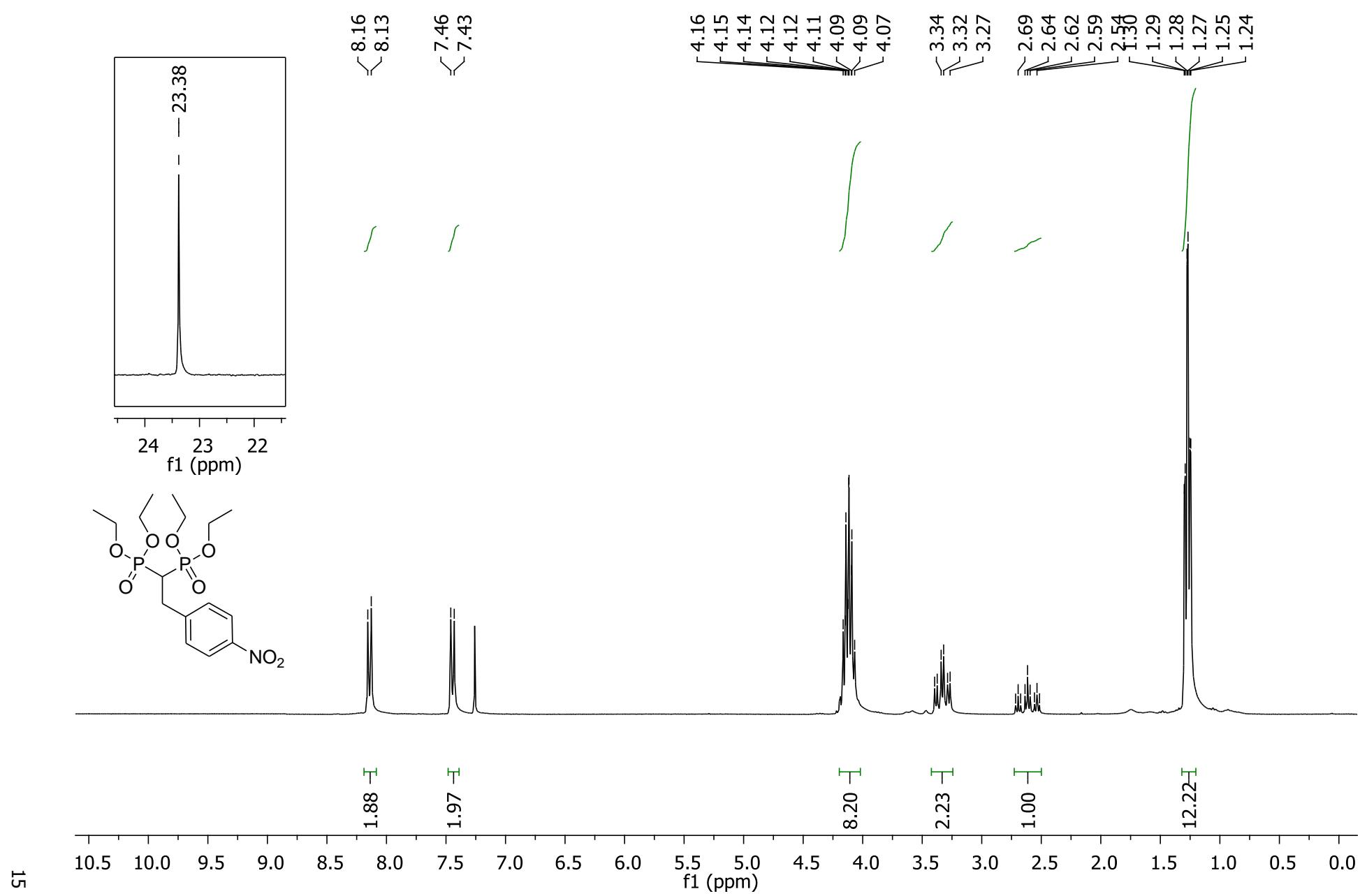


Figure 9: 4BA ^1H -NMR (300.15 MHz) and $^{31}\text{P} \{^1\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

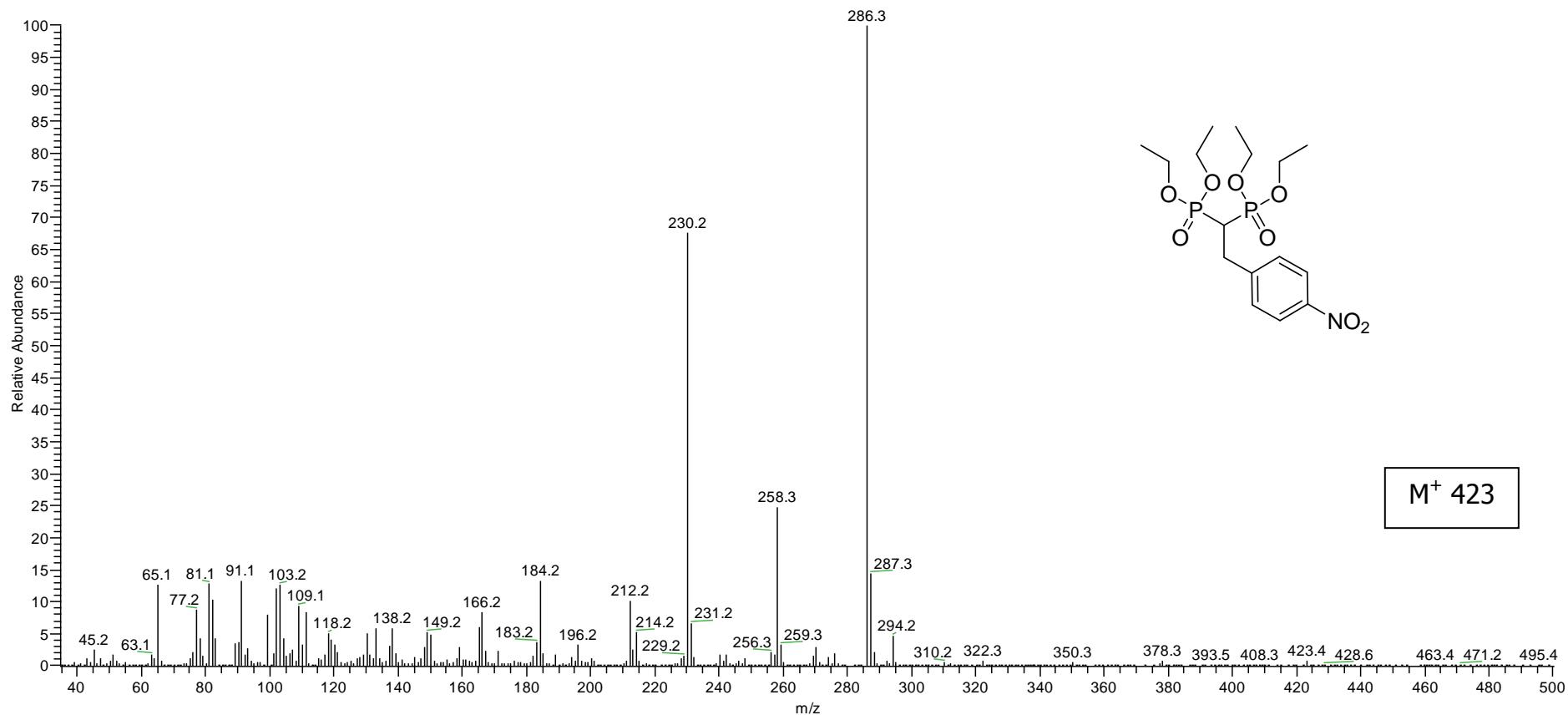


Figure 10: 4BA mass spectrum.

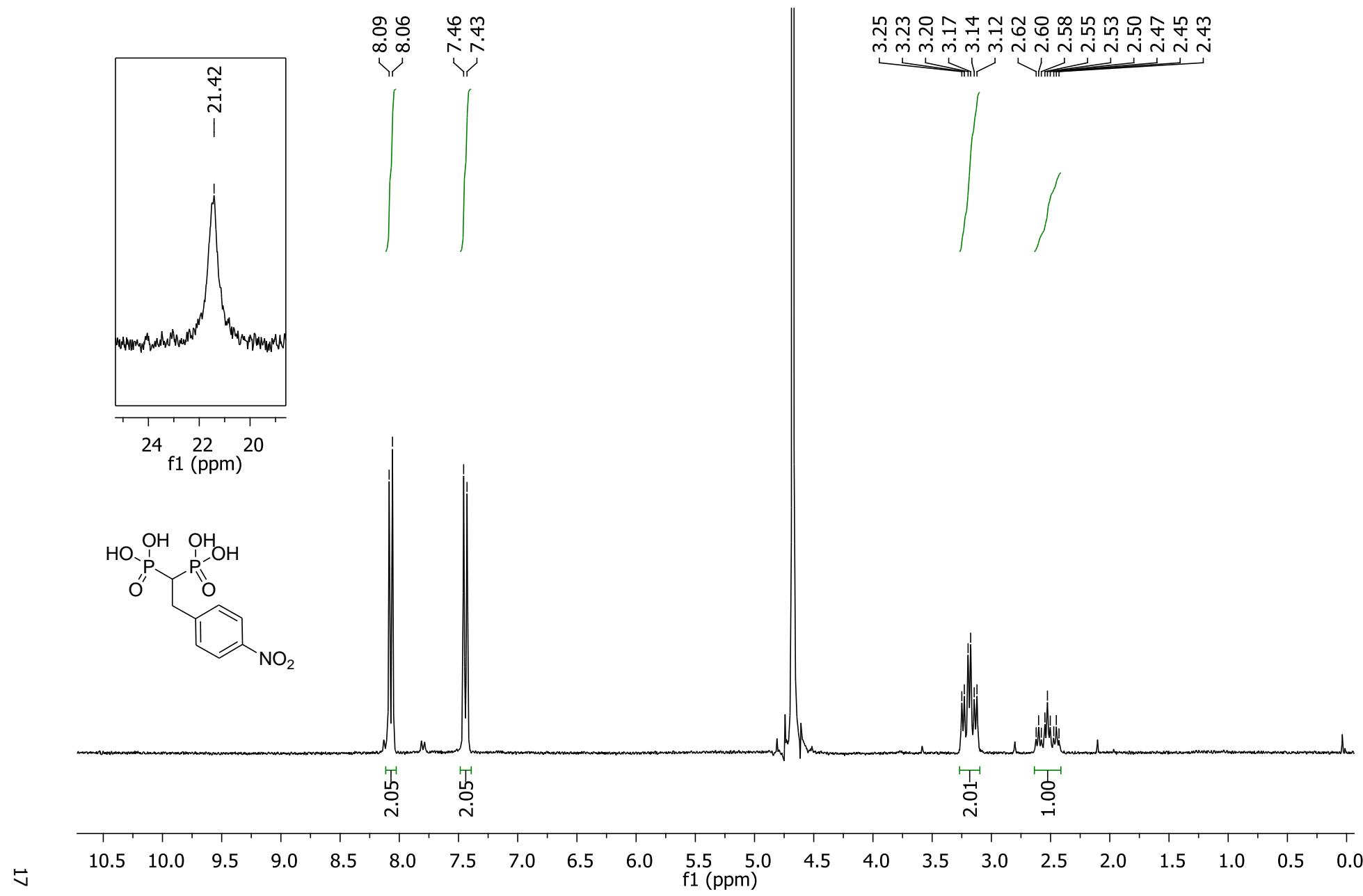


Figure 11: Deprotected 4BA ^1H -NMR (300.15 MHz) and $^{31}\text{P}\{^1\text{H}\}$ -NMR (121.5 MHz) spectra, D_2O .

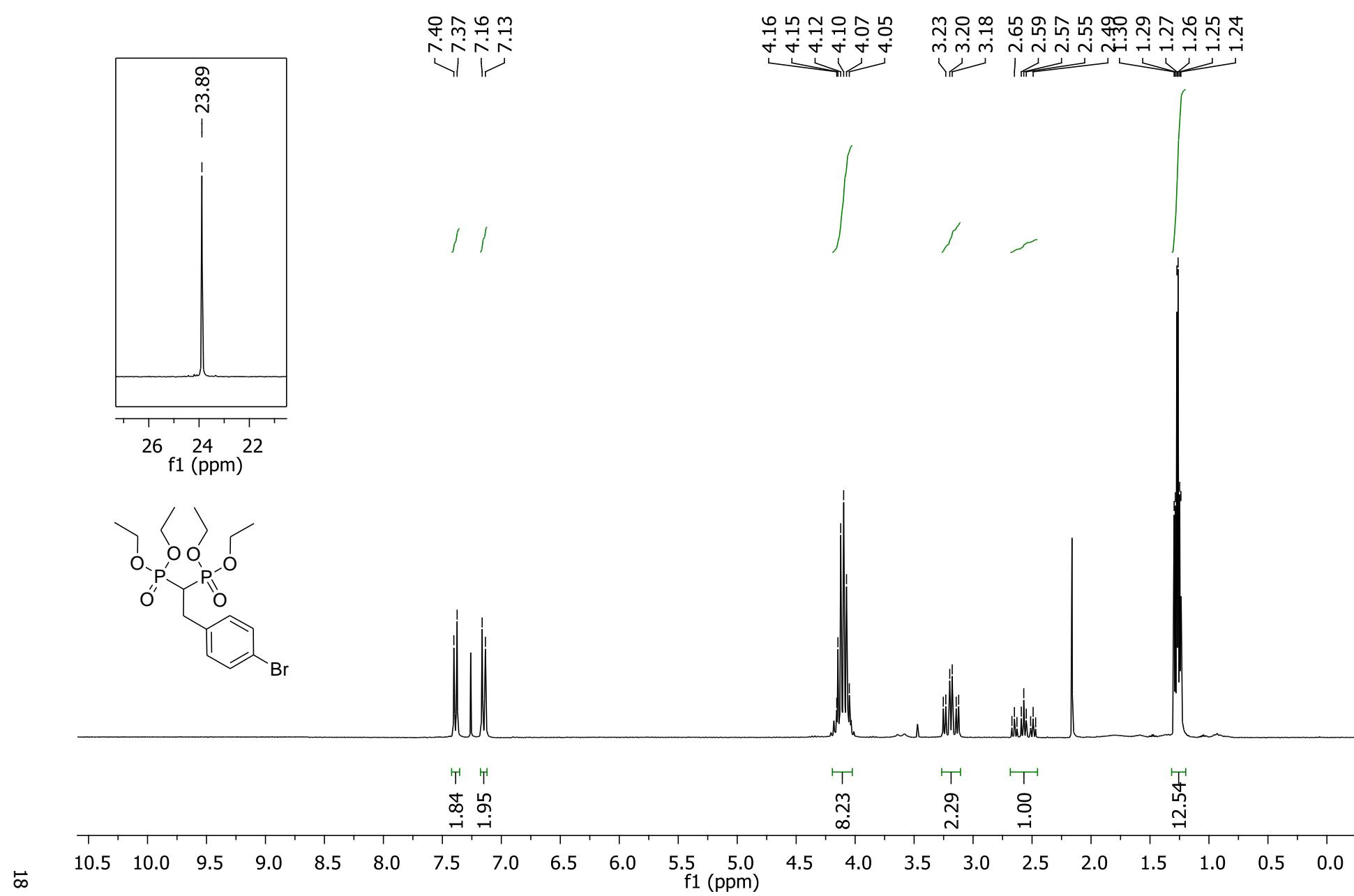


Figure 12: 5BA ^1H -NMR (300.15 MHz) and $^{31}\text{P}\{^1\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

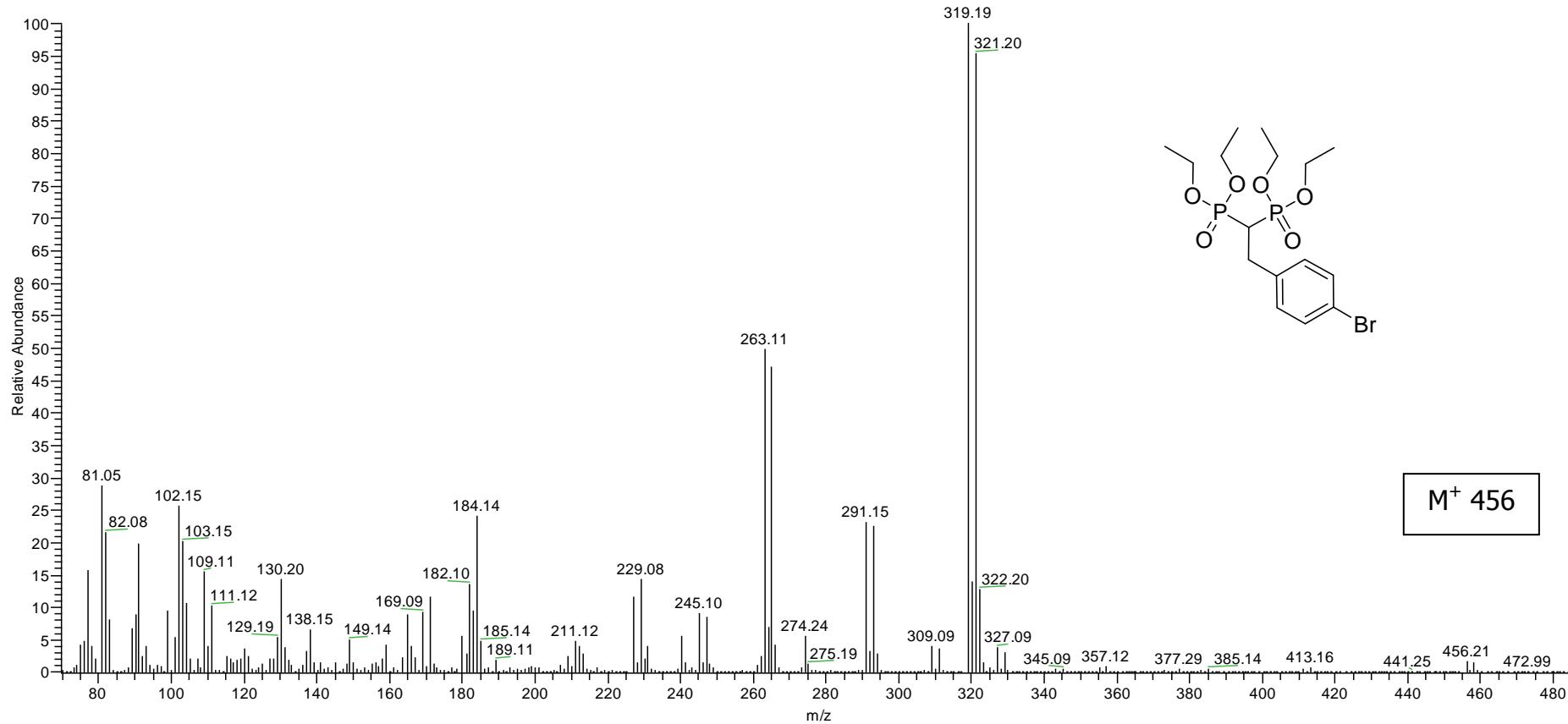
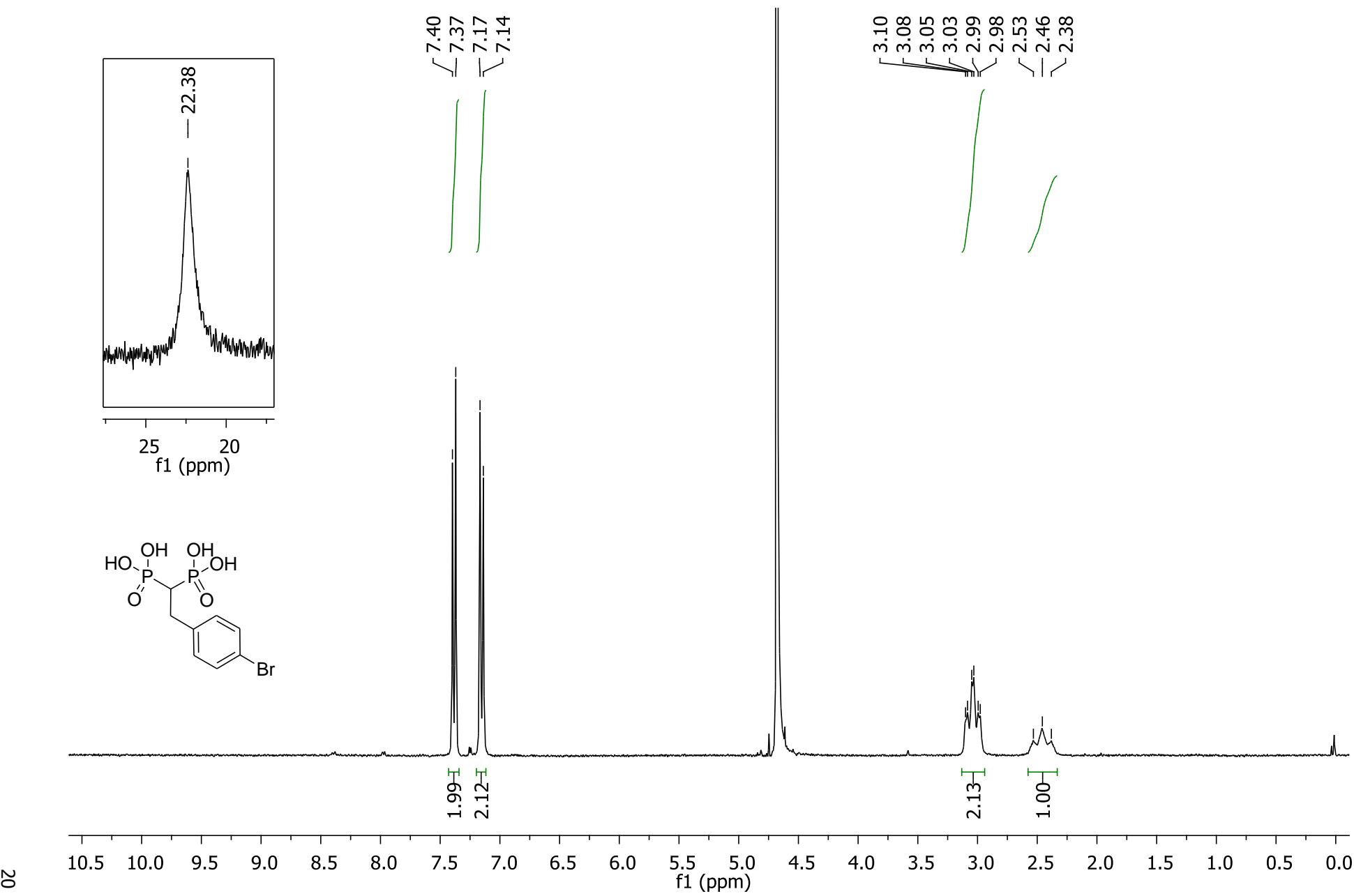


Figure 13: 5BA mass spectrum.



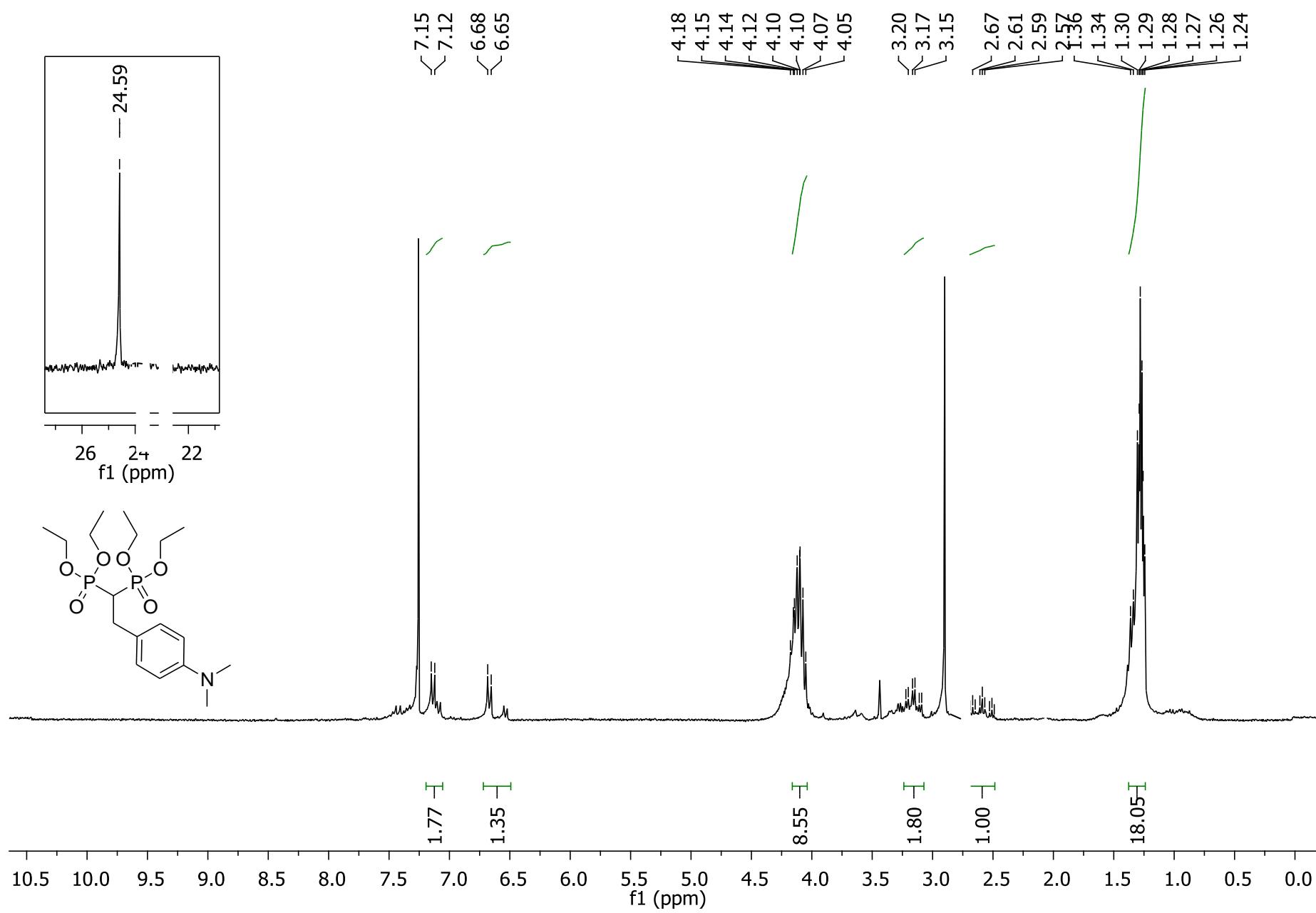


Figure 15: 6BA ^1H -NMR (300.15 MHz) and $^{31}\text{P}\{^1\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

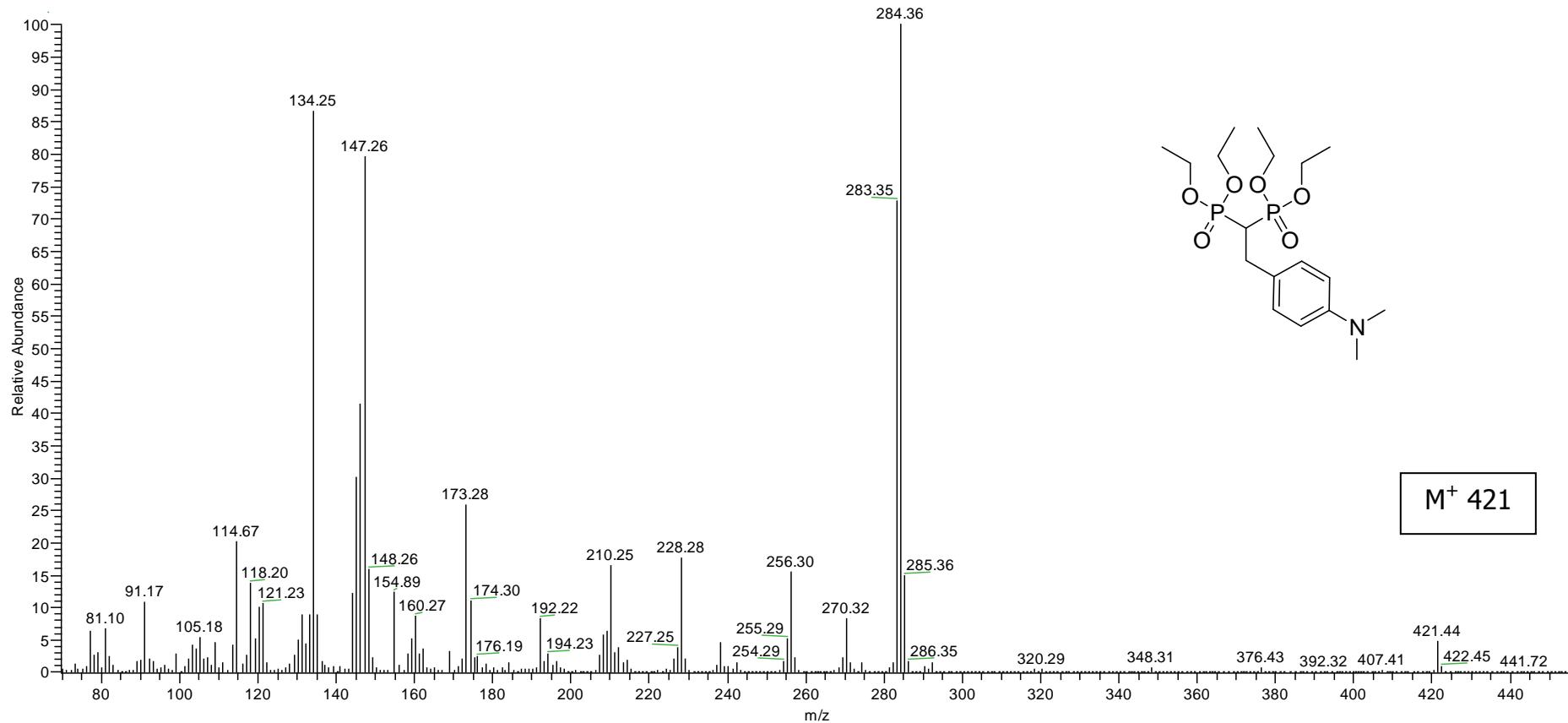


Figure 16: 6BA mass spectrum.

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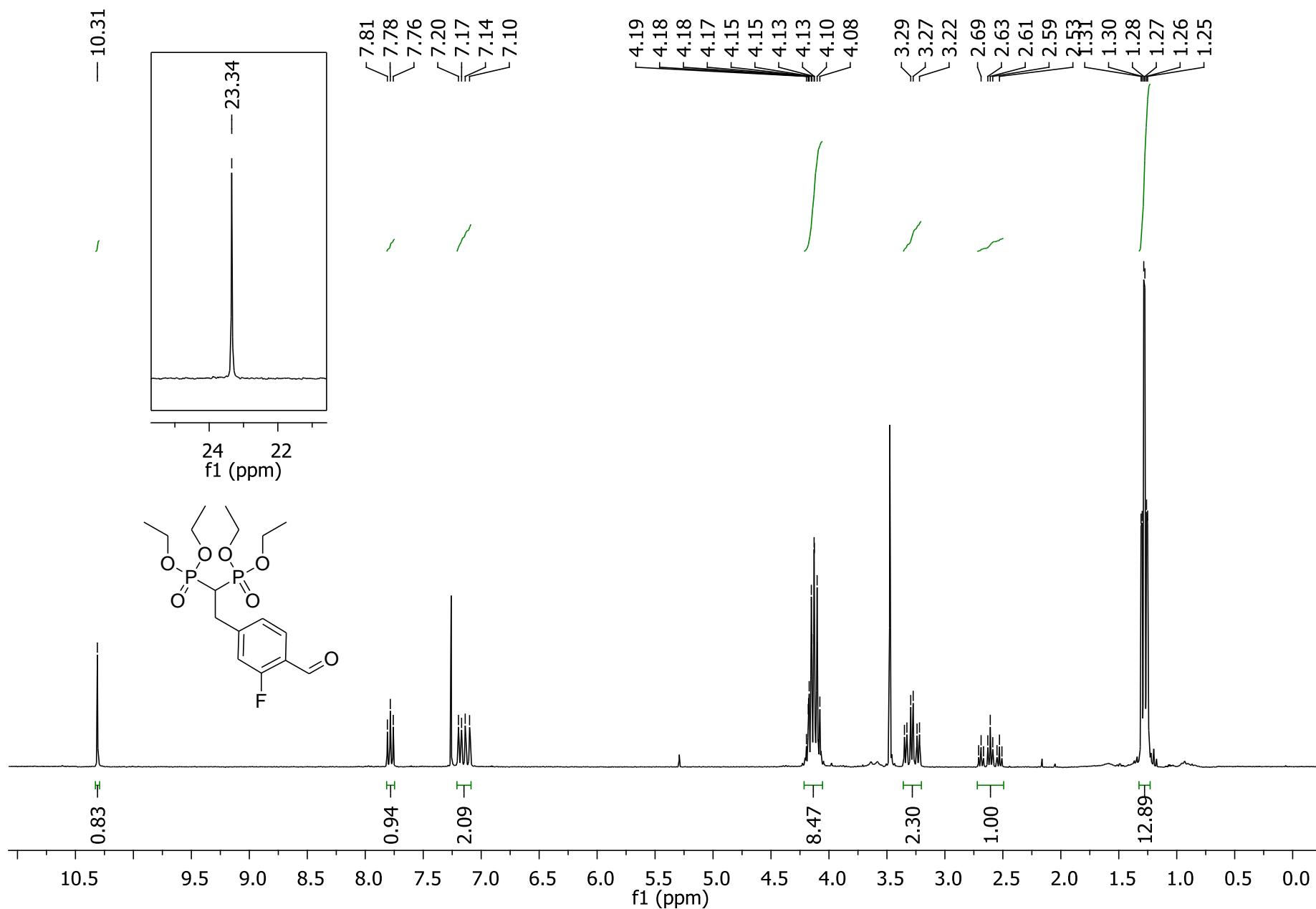


Figure 17: 7BA ^1H -NMR (300.15 MHz) and $^{31}\text{P}\{^1\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

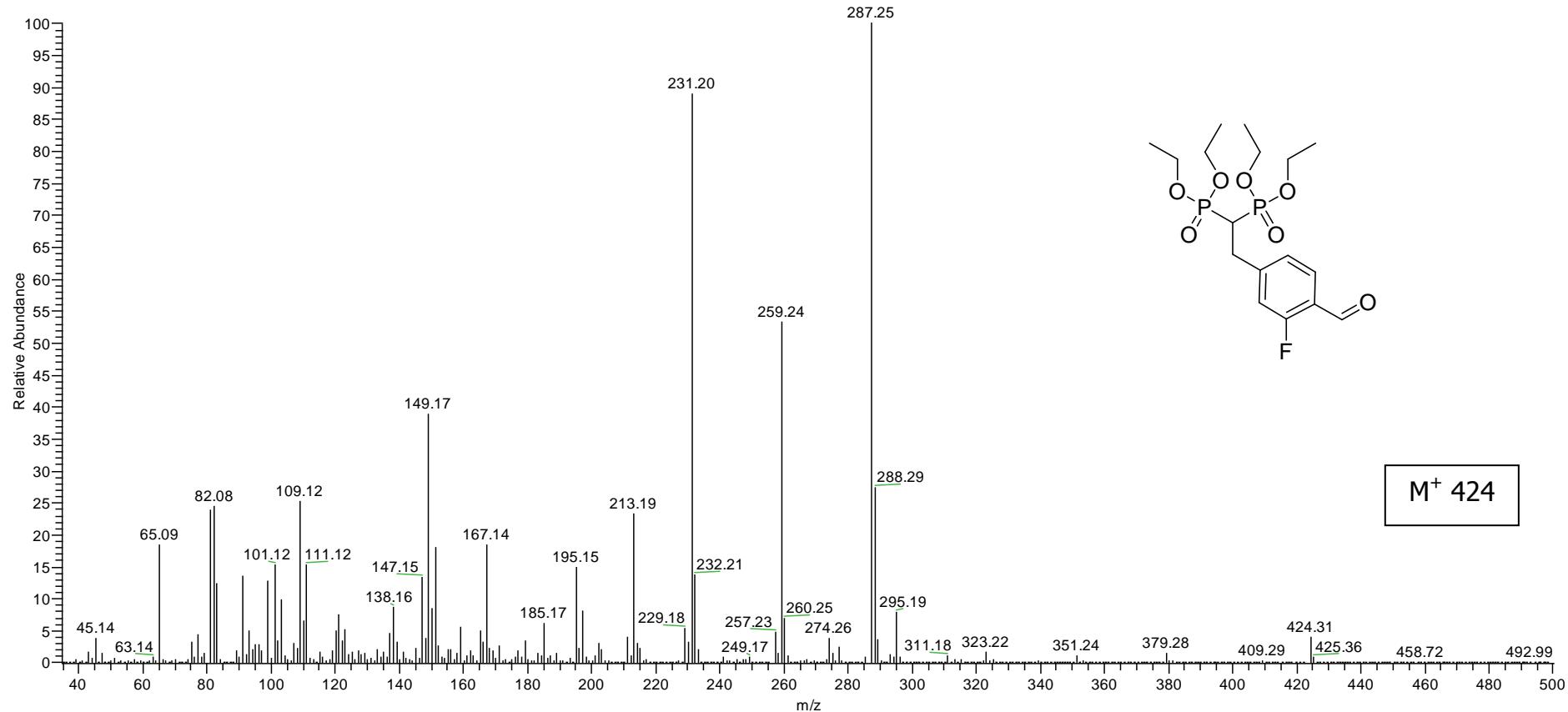


Figure 18: 7BA mass spectrum.

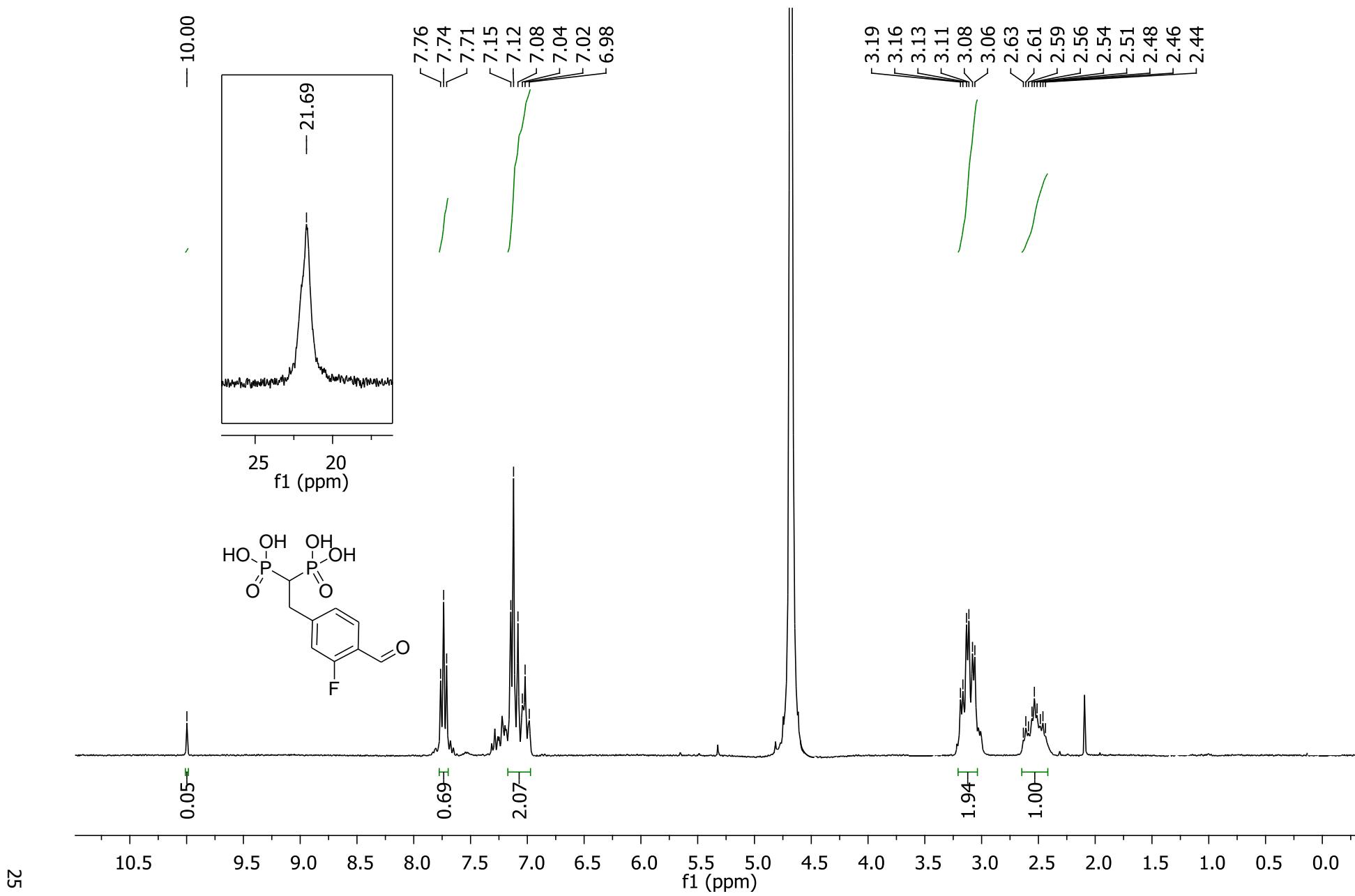


Figure 19: Deprotected 7BA ^1H -NMR (300.15 MHz) and $^{31}\text{P}\{^1\text{H}\}$ -NMR (121.5 MHz) spectra, D_2O .

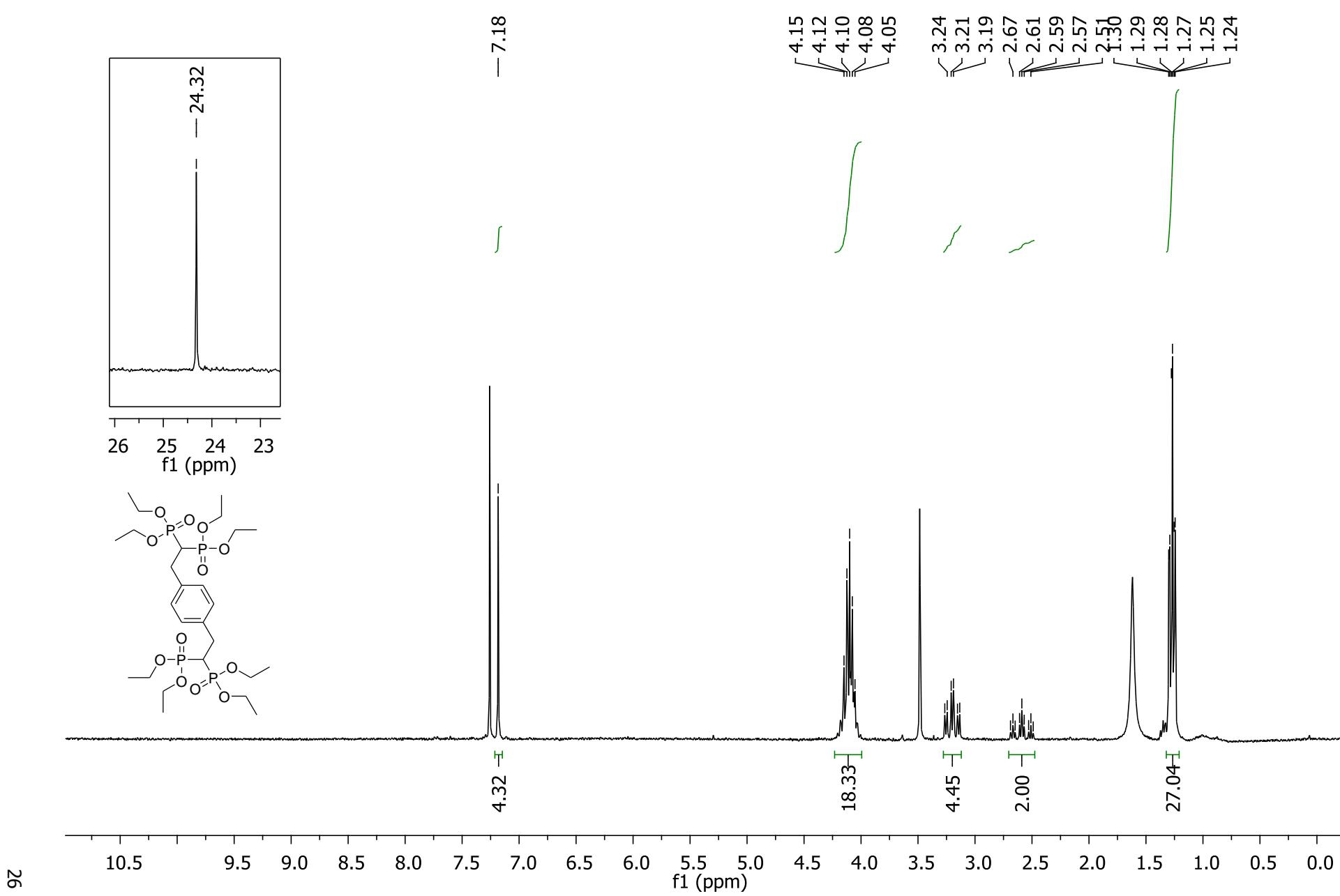


Figure 20: 1BAbis ^1H -NMR (300.15 MHz) and $^{31}\text{P}\{^1\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

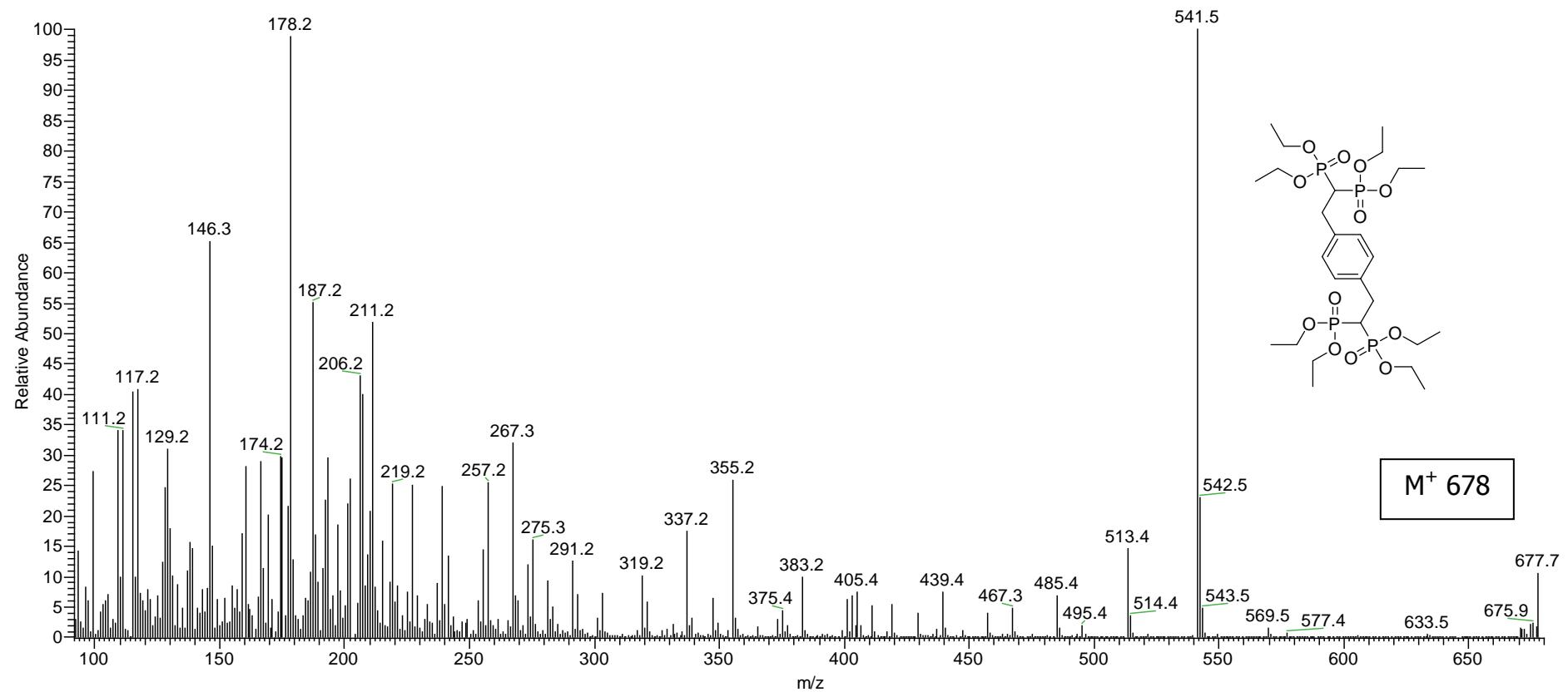


Figure 21: 1Babis mass spectrum.

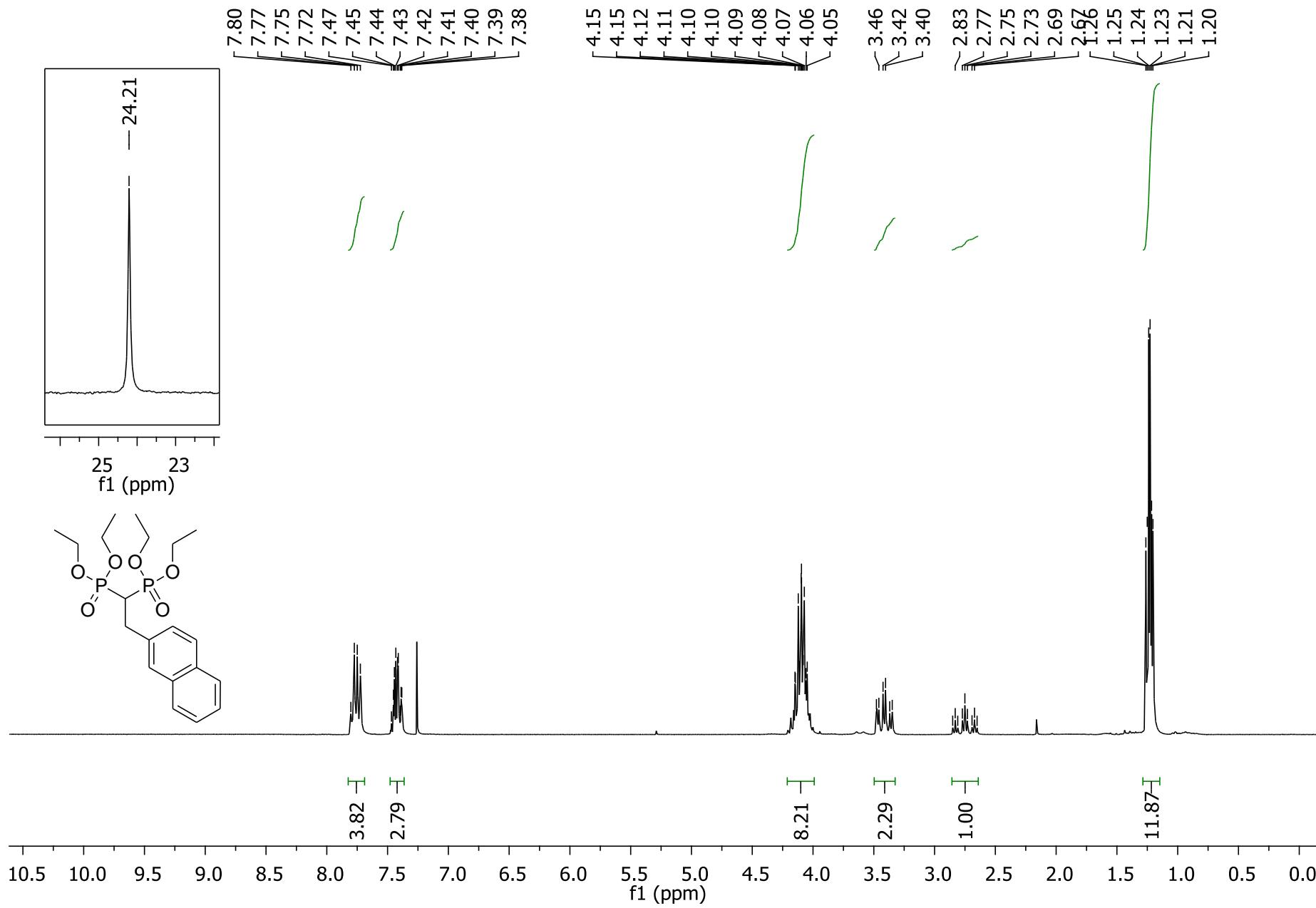


Figure 22: 8BA ^1H -NMR (300.15 MHz) and $^{31}\text{P}\{^1\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

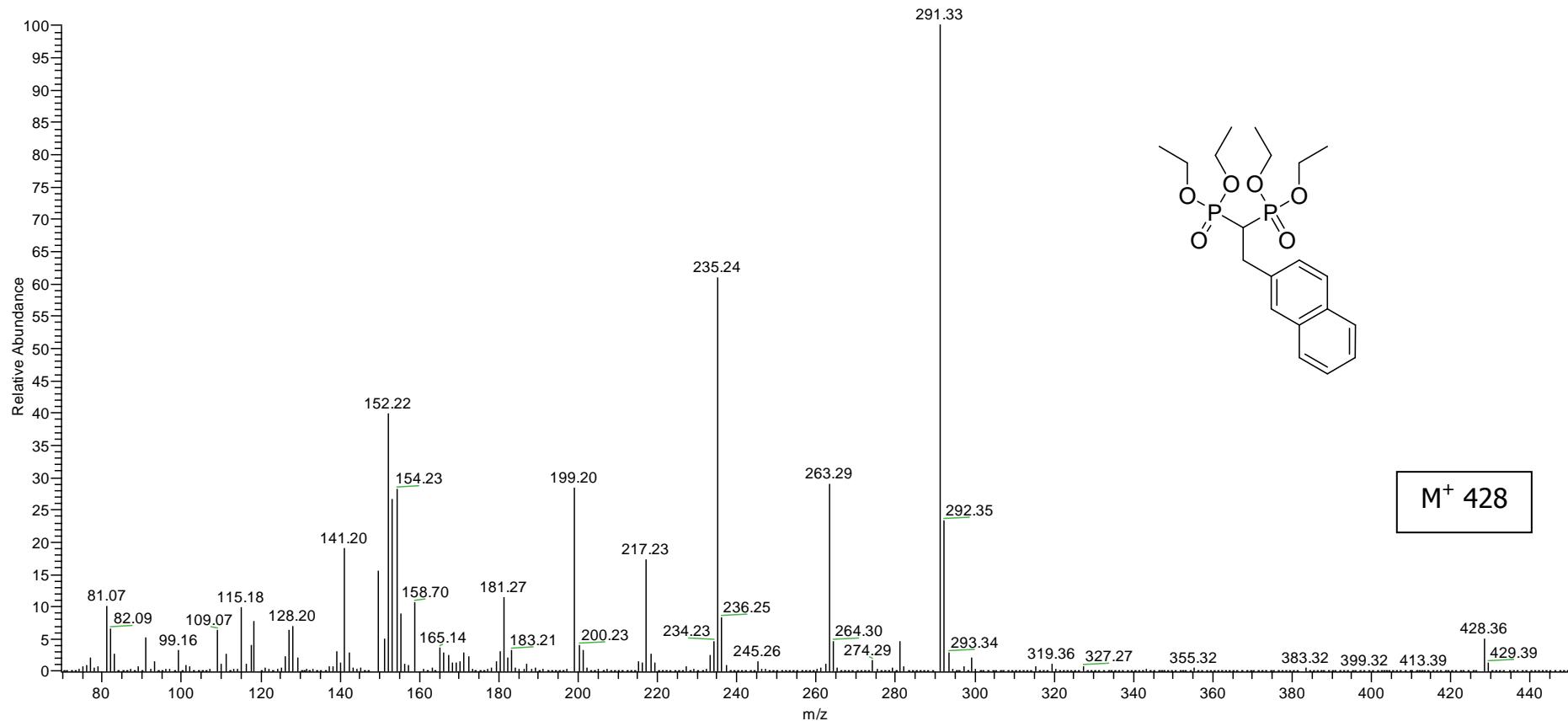


Figure 23: 8BA mass spectrum.

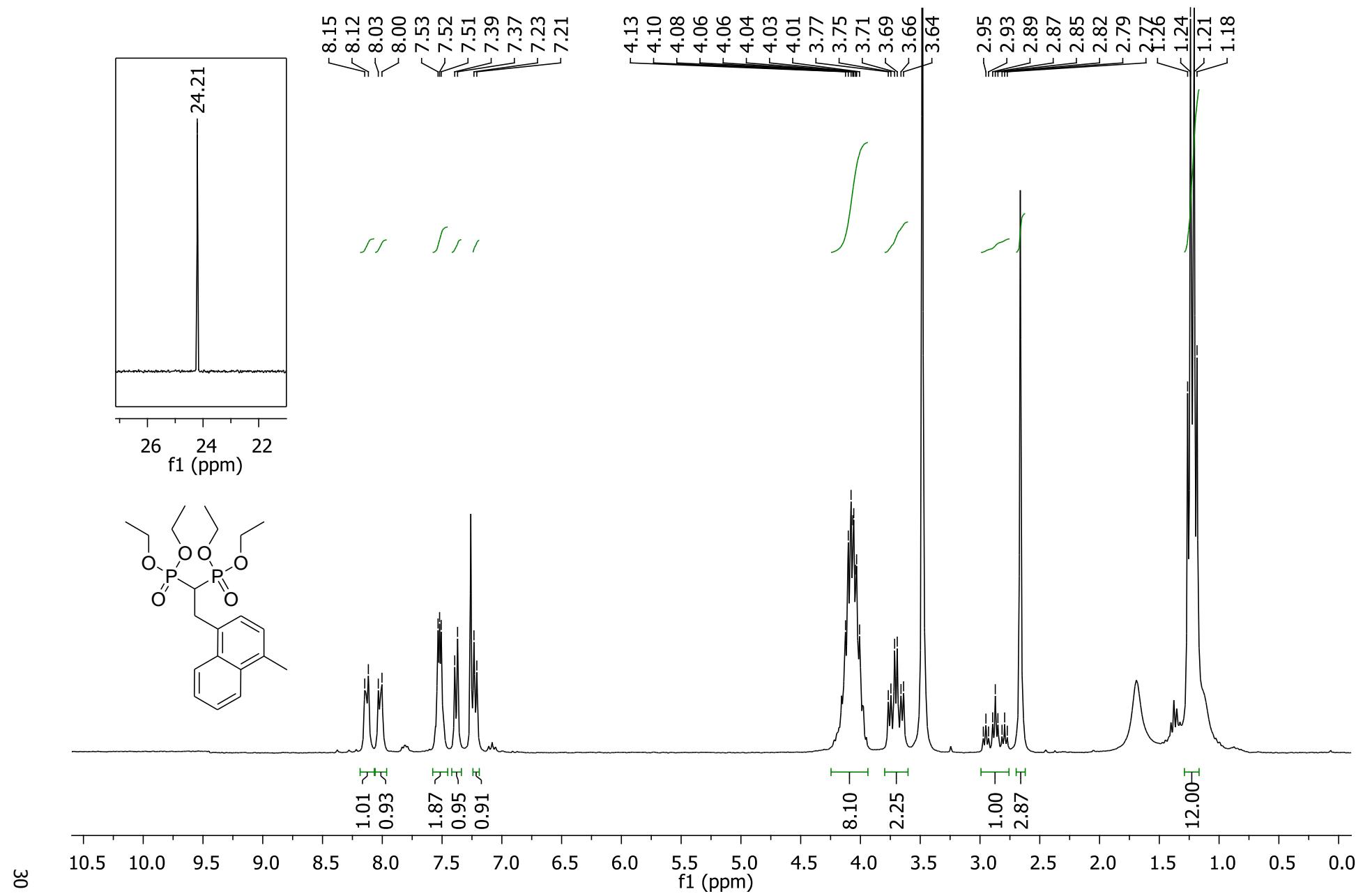


Figure 24: 9BA ^1H -NMR (300.15 MHz) and $^{31}\text{P} \{^1\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

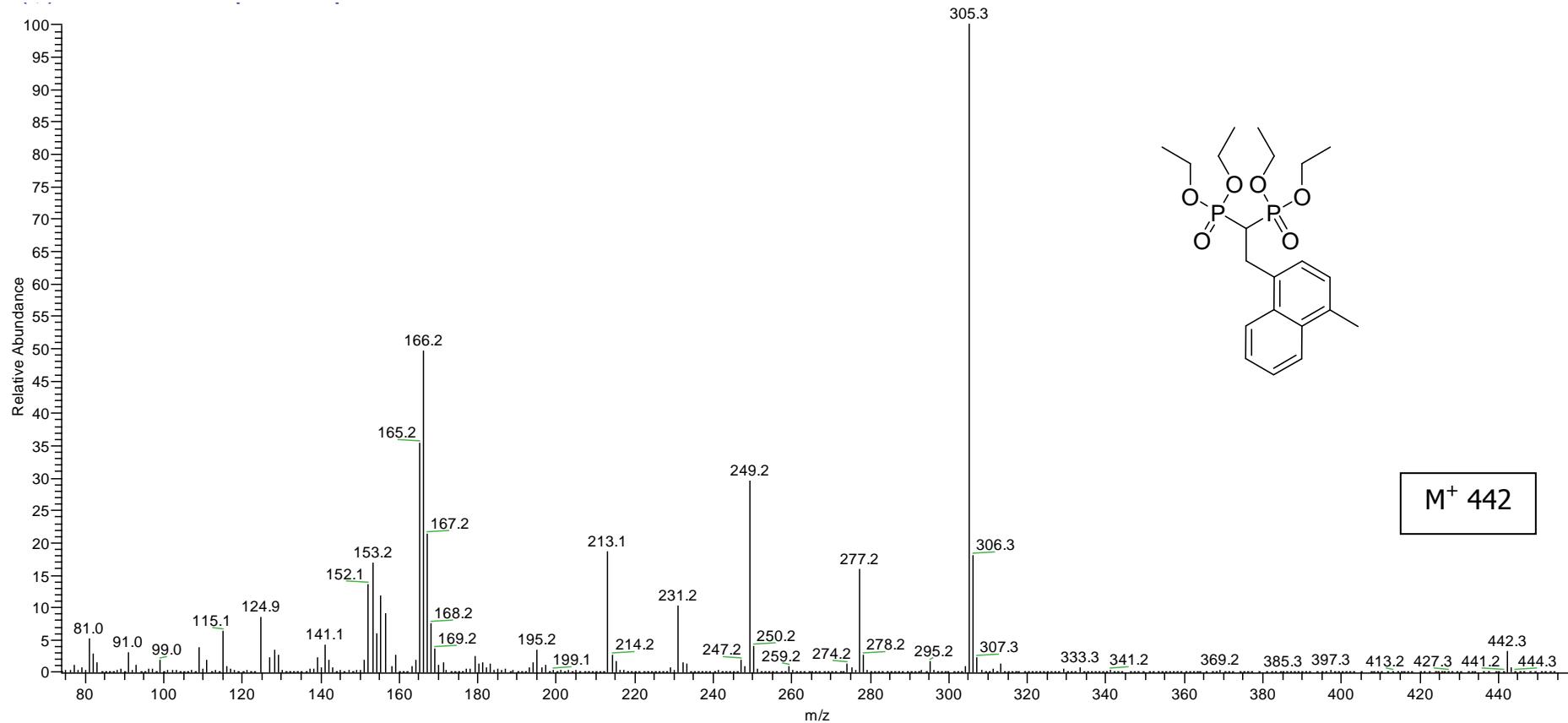


Figure 25: 9BA mass spectrum.

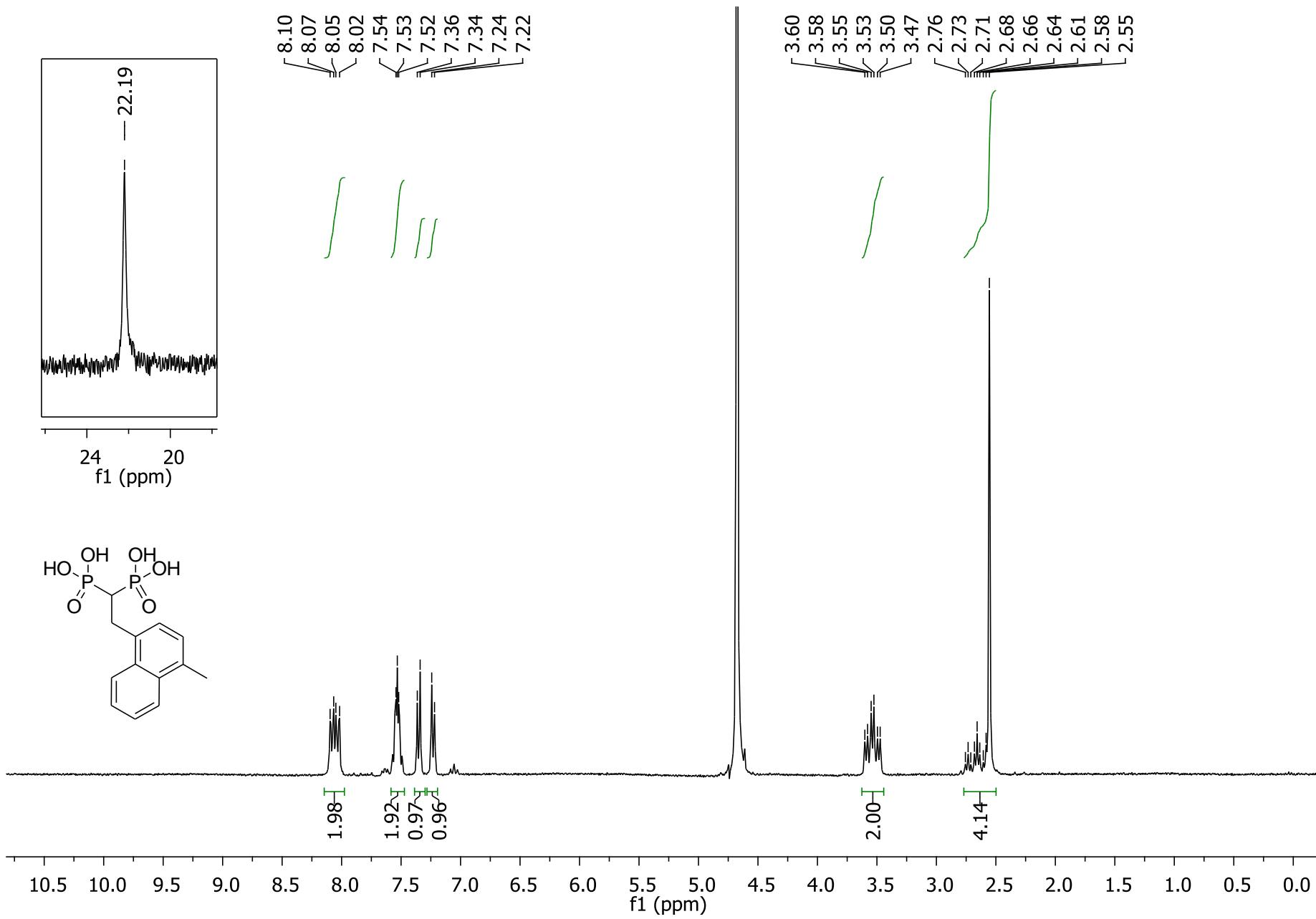


Figure 26: 9BA ^1H -NMR (300.15 MHz) and $^{31}\text{P} \{^1\text{H}\}$ -NMR (121.5 MHz) spectra, D_2O .

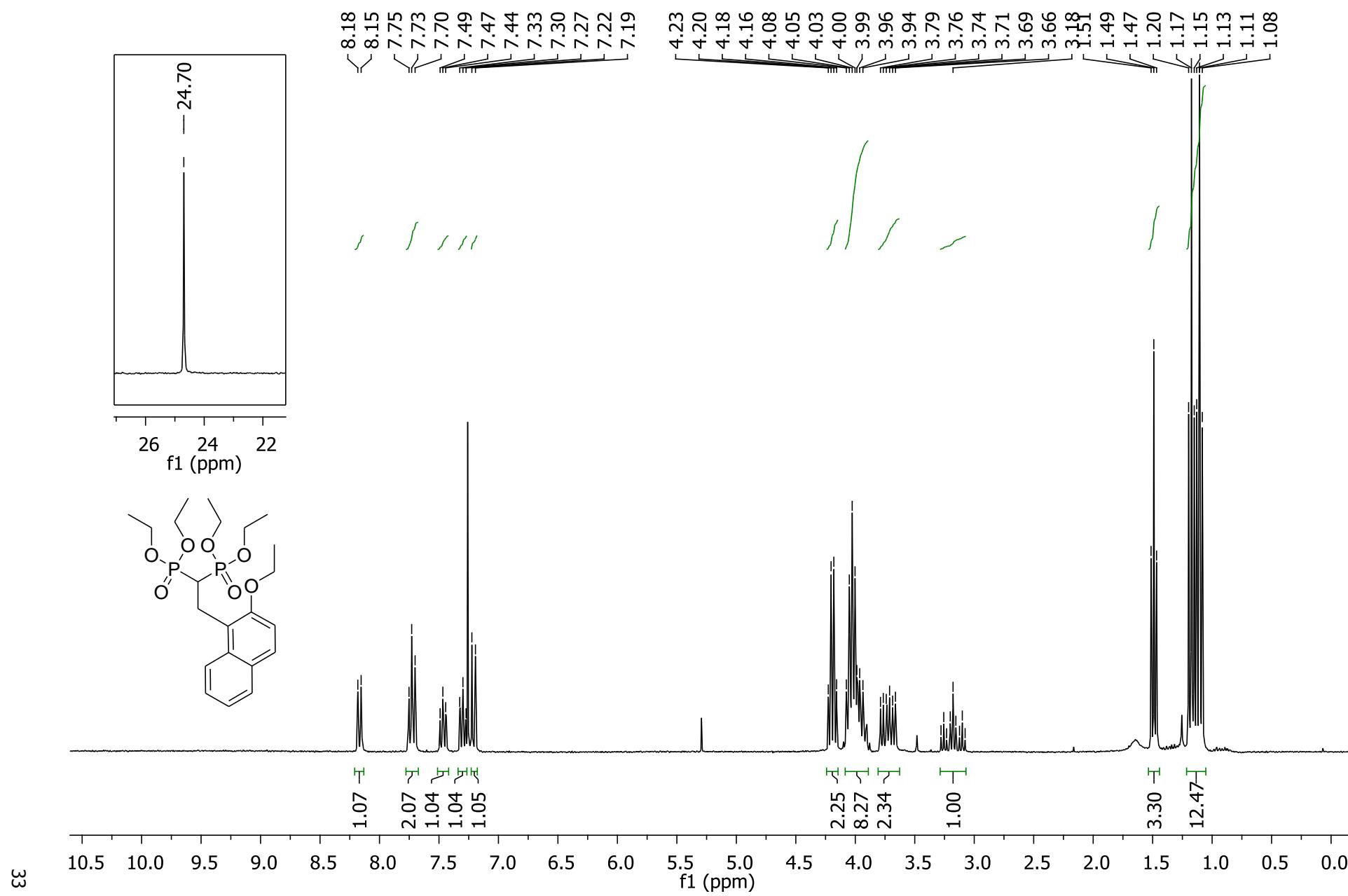


Figure 27: 10BA ^1H -NMR (300.15 MHz) and $^{31}\text{P}\{^1\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

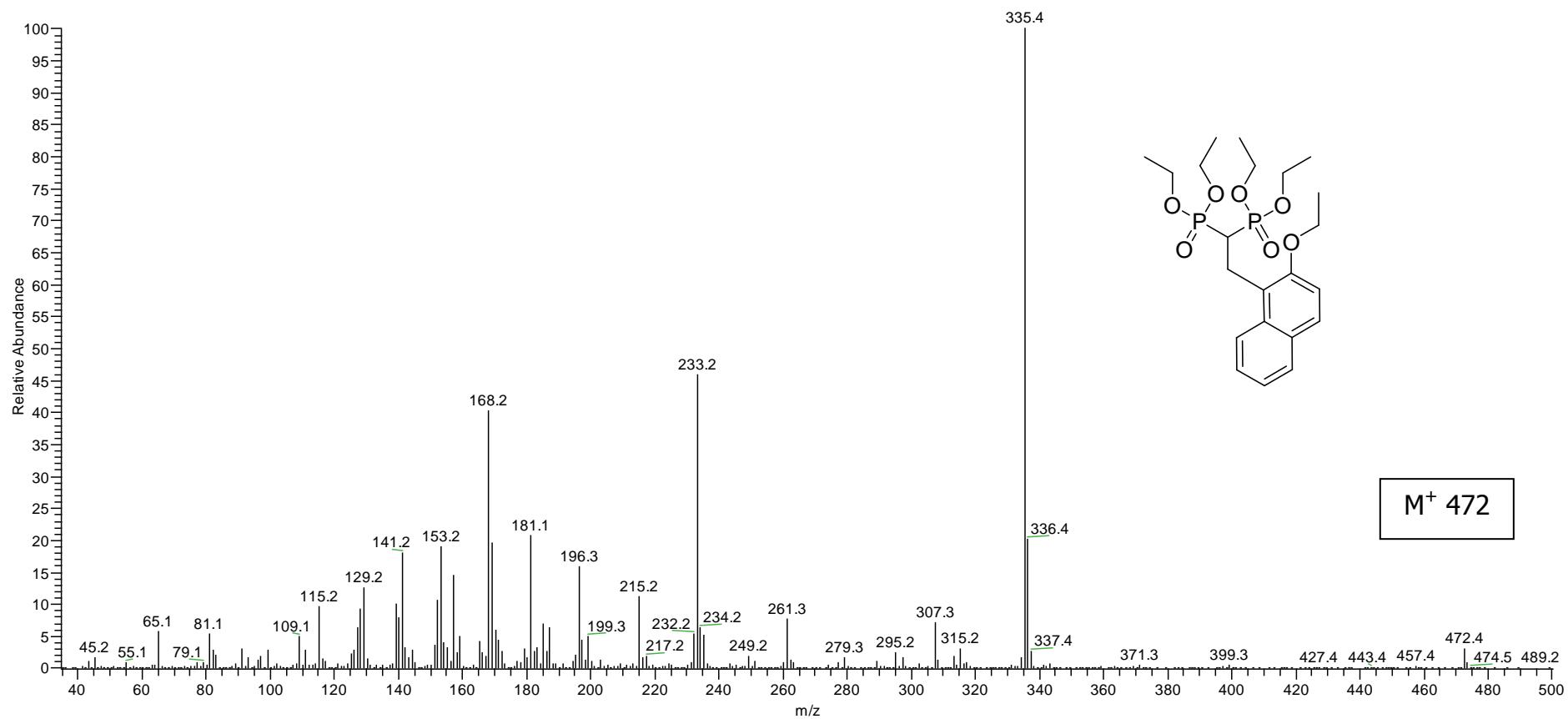


Figure 28: 10BA spectrum.

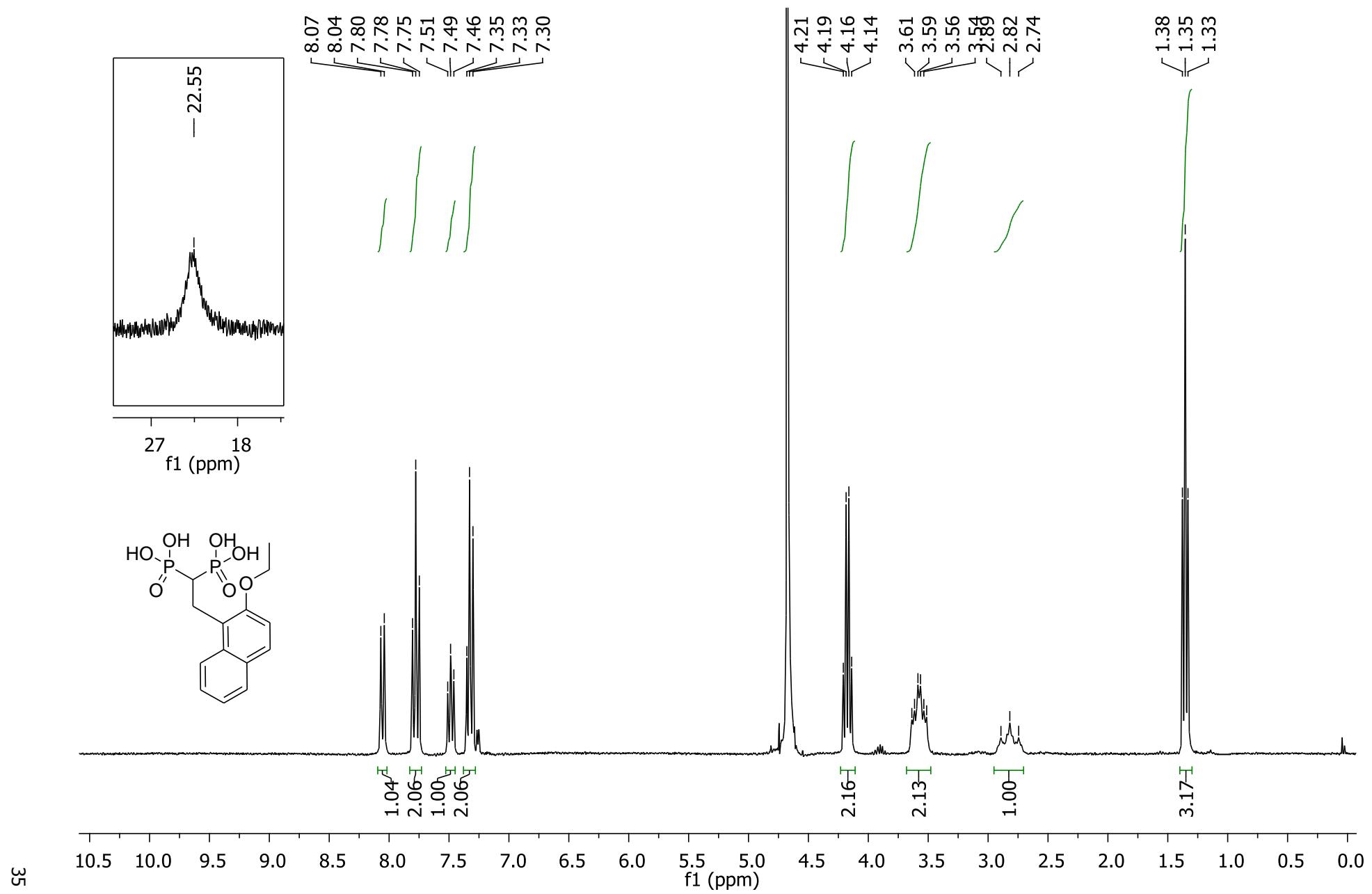


Figure 29: Deprotected 10BA ^1H -NMR (300.15 MHz) and $^{31}\text{P}\{^1\text{H}\}$ -NMR (121.5 MHz) spectra, D_2O .

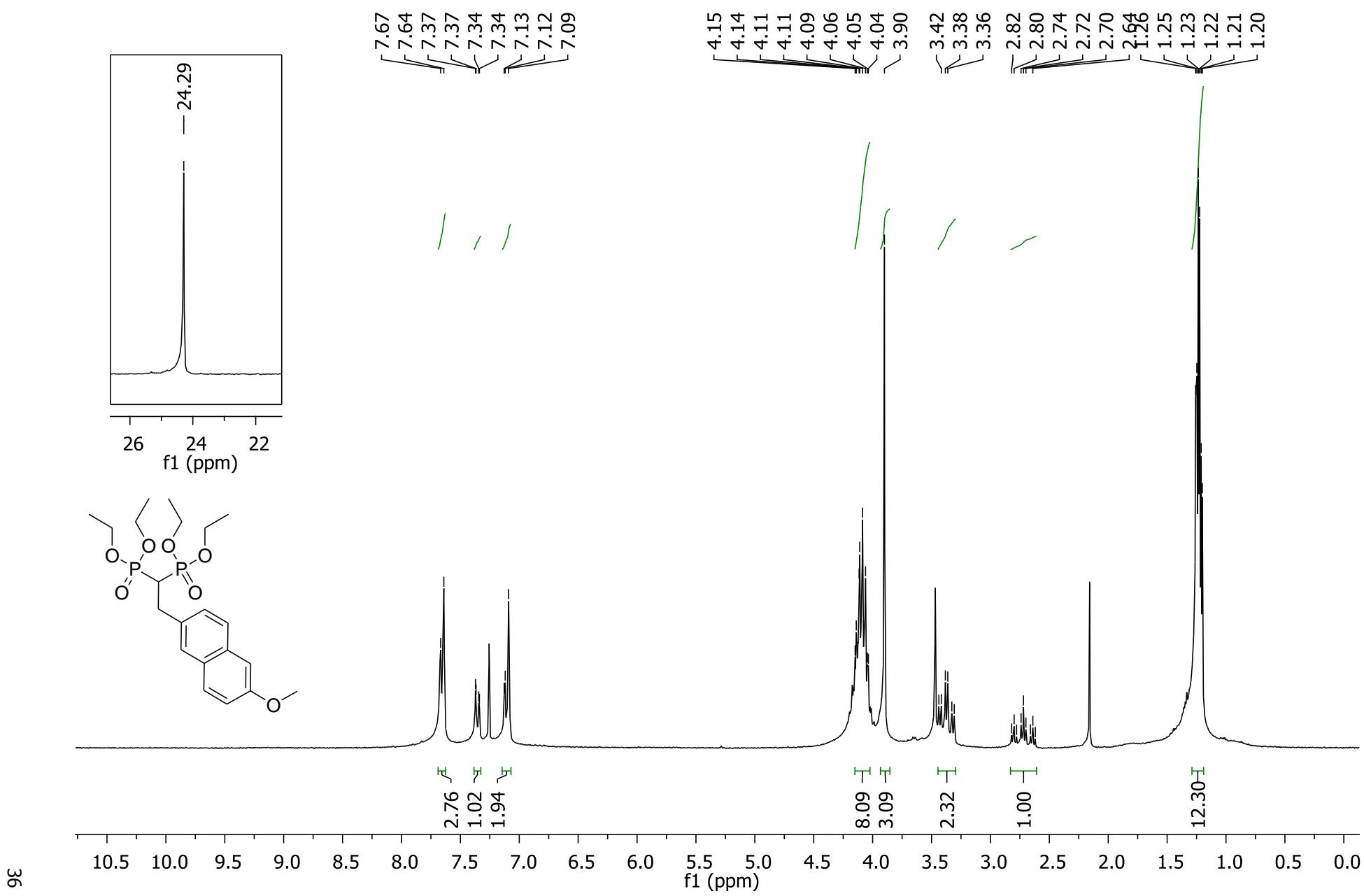


Figure 30: 11BA ^1H -NMR (300.15 MHz) and $^{31}\text{P}\{^1\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

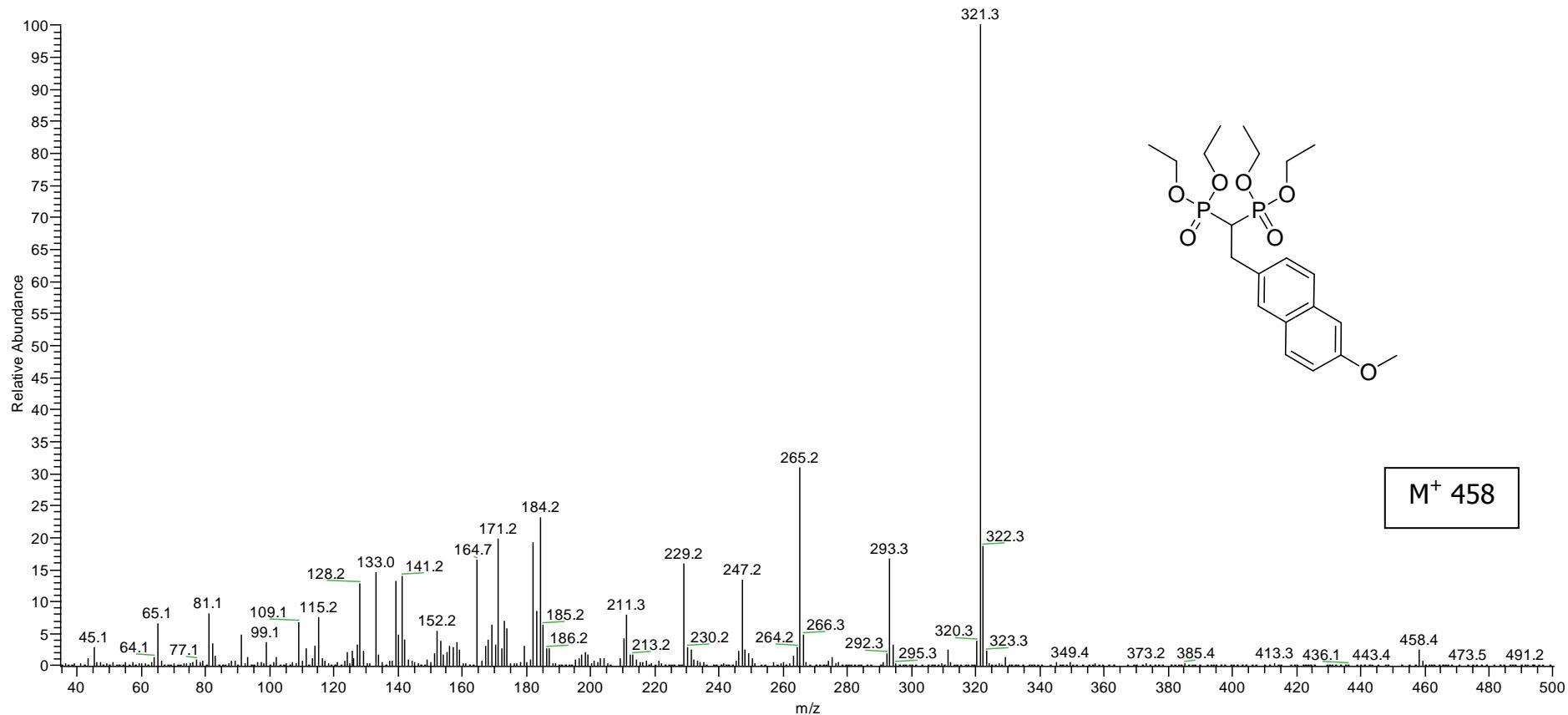


Figure 31: 11BA mass spectrum.

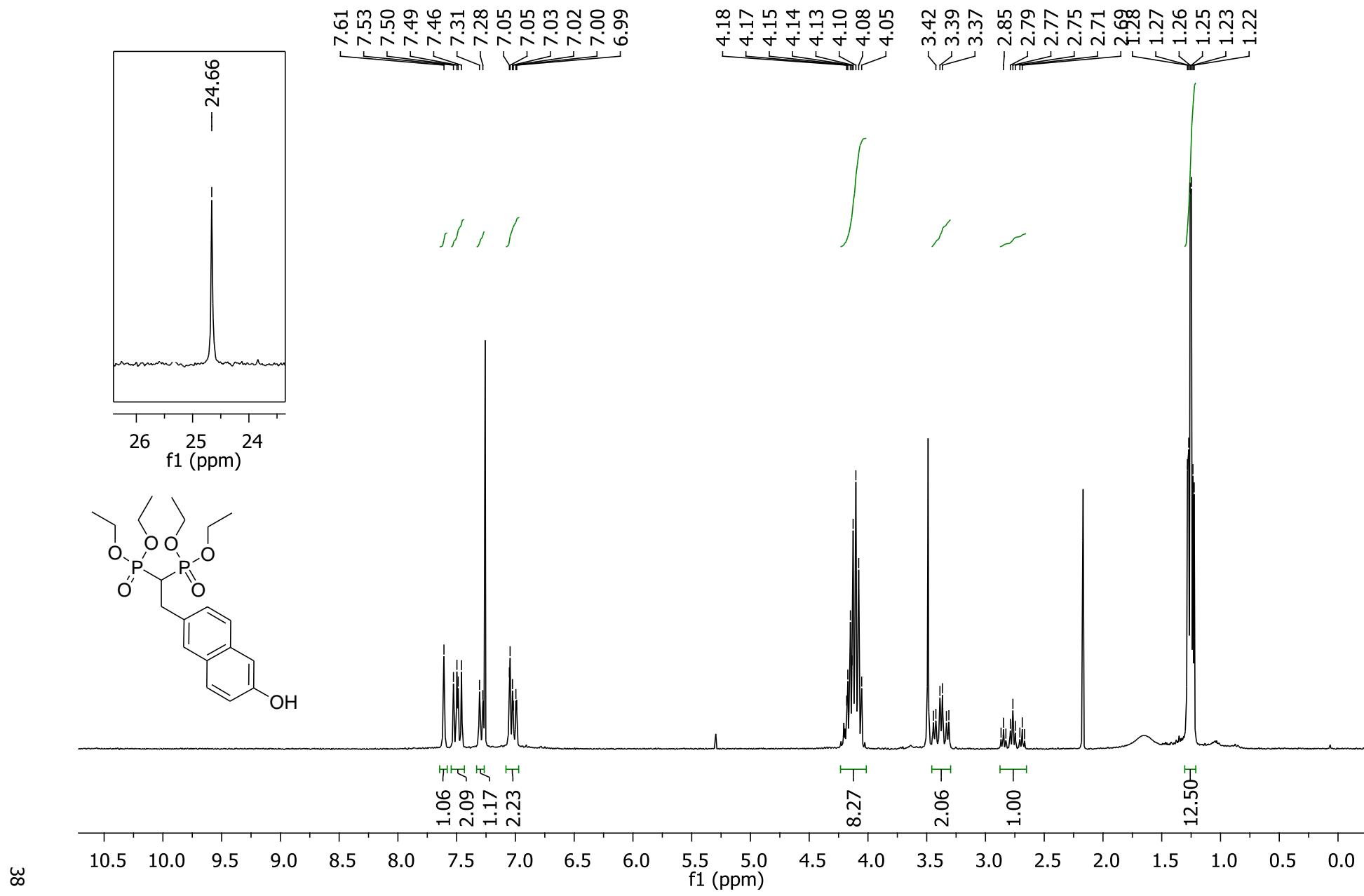


Figure 32: 12BA ^1H -NMR (300.15 MHz) and $^{31}\text{P} \{^1\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

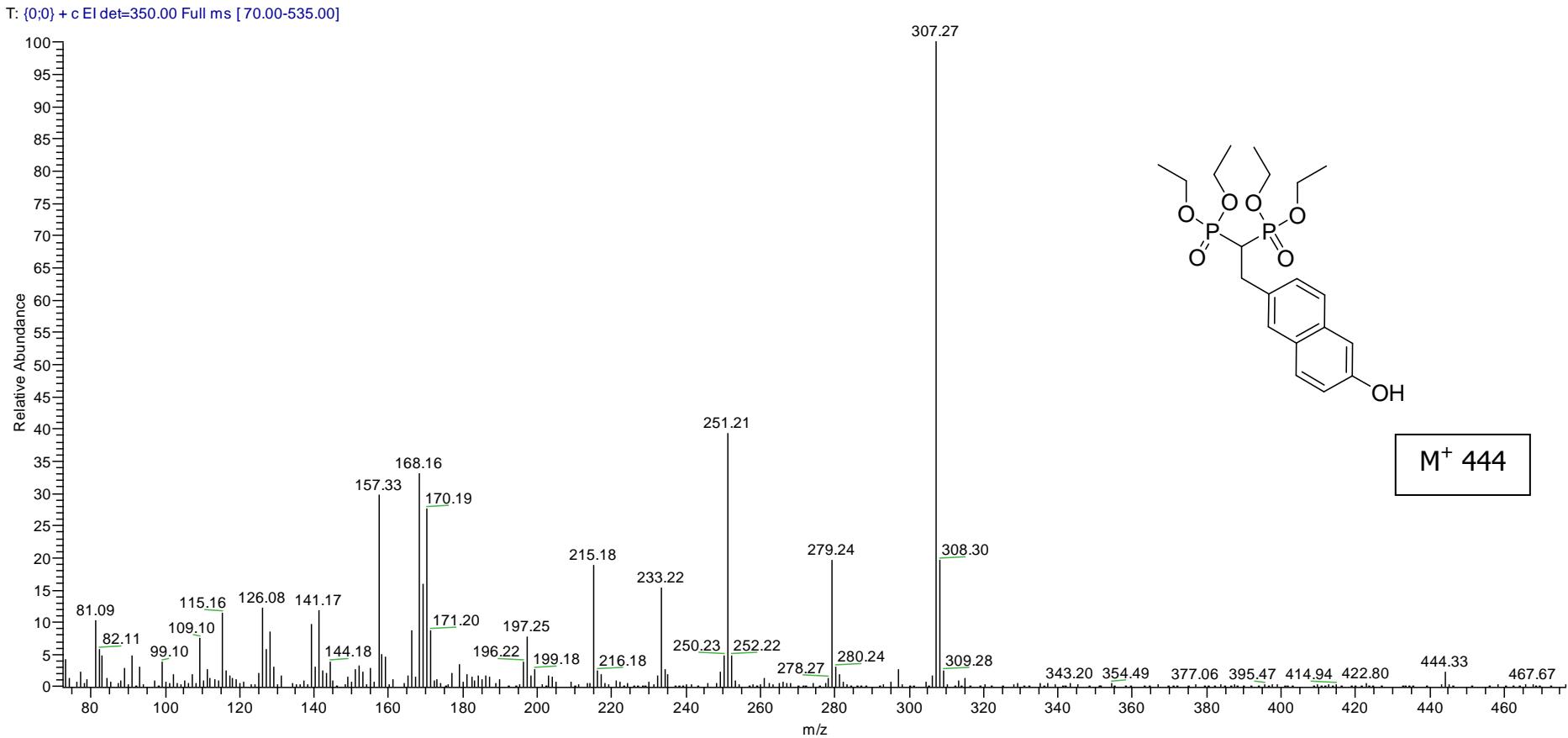


Figure 33: 12BA mass spectrum.

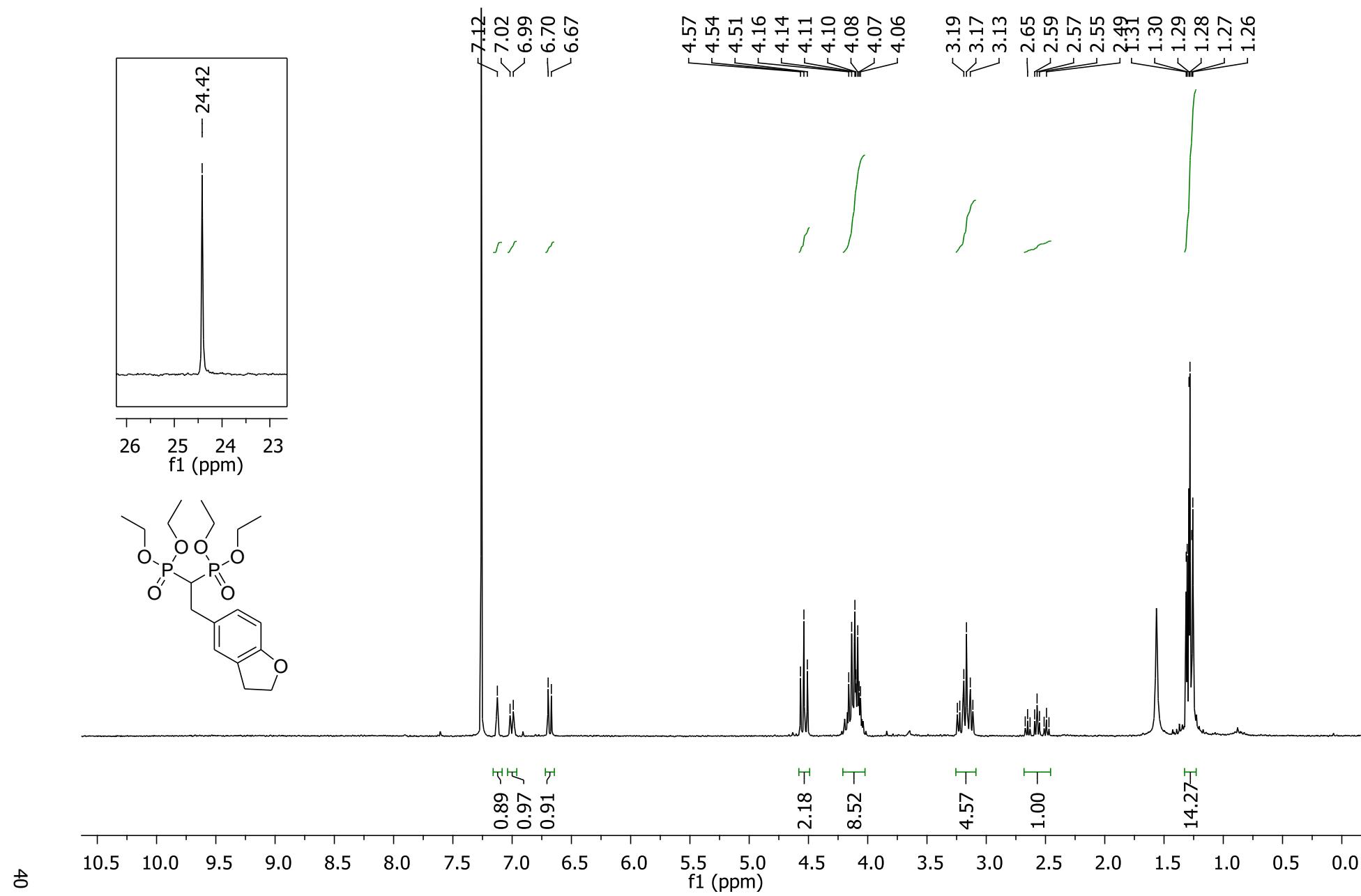


Figure 34: 13BA ^1H -NMR (300.15) MHz and $^{31}\text{P}\{^1\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

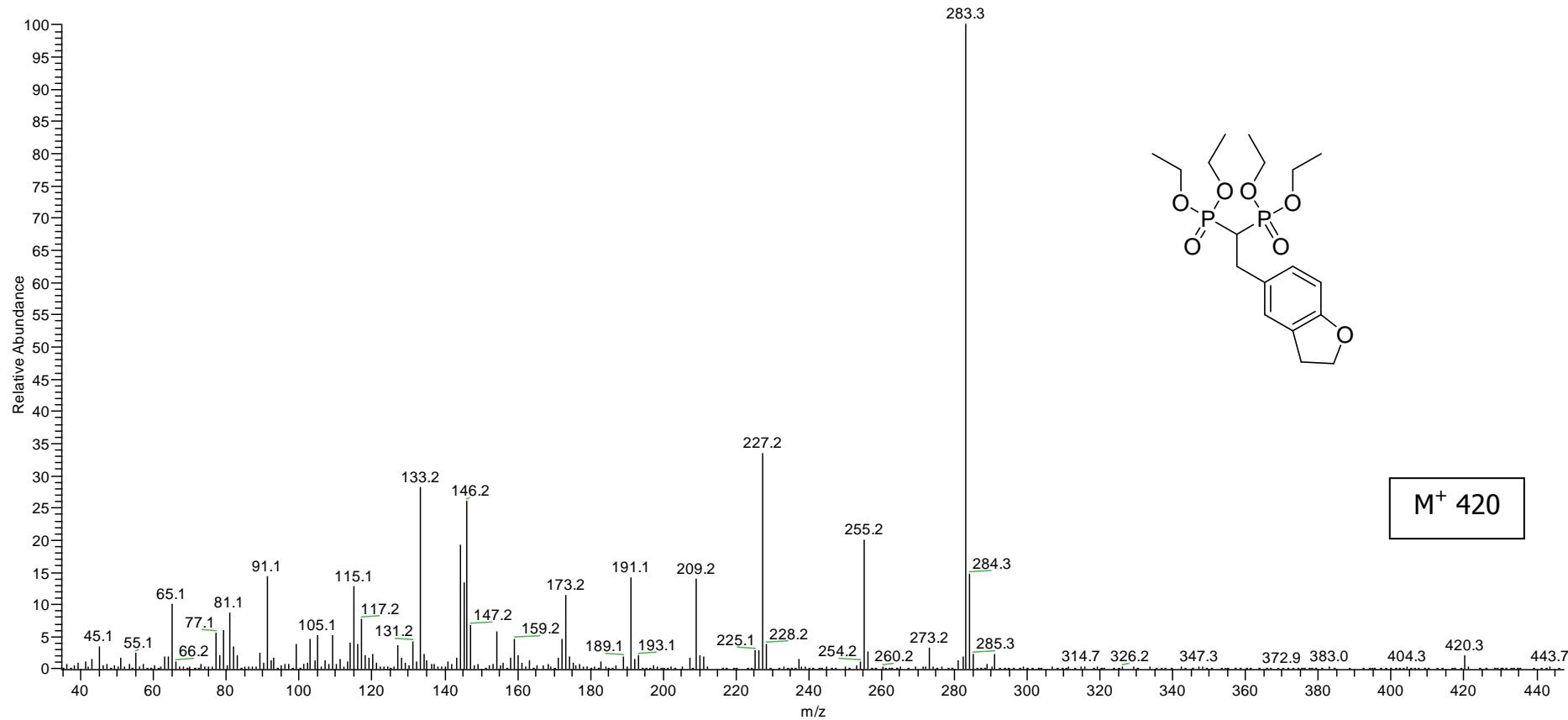


Figure 35: 13BA spectrum.

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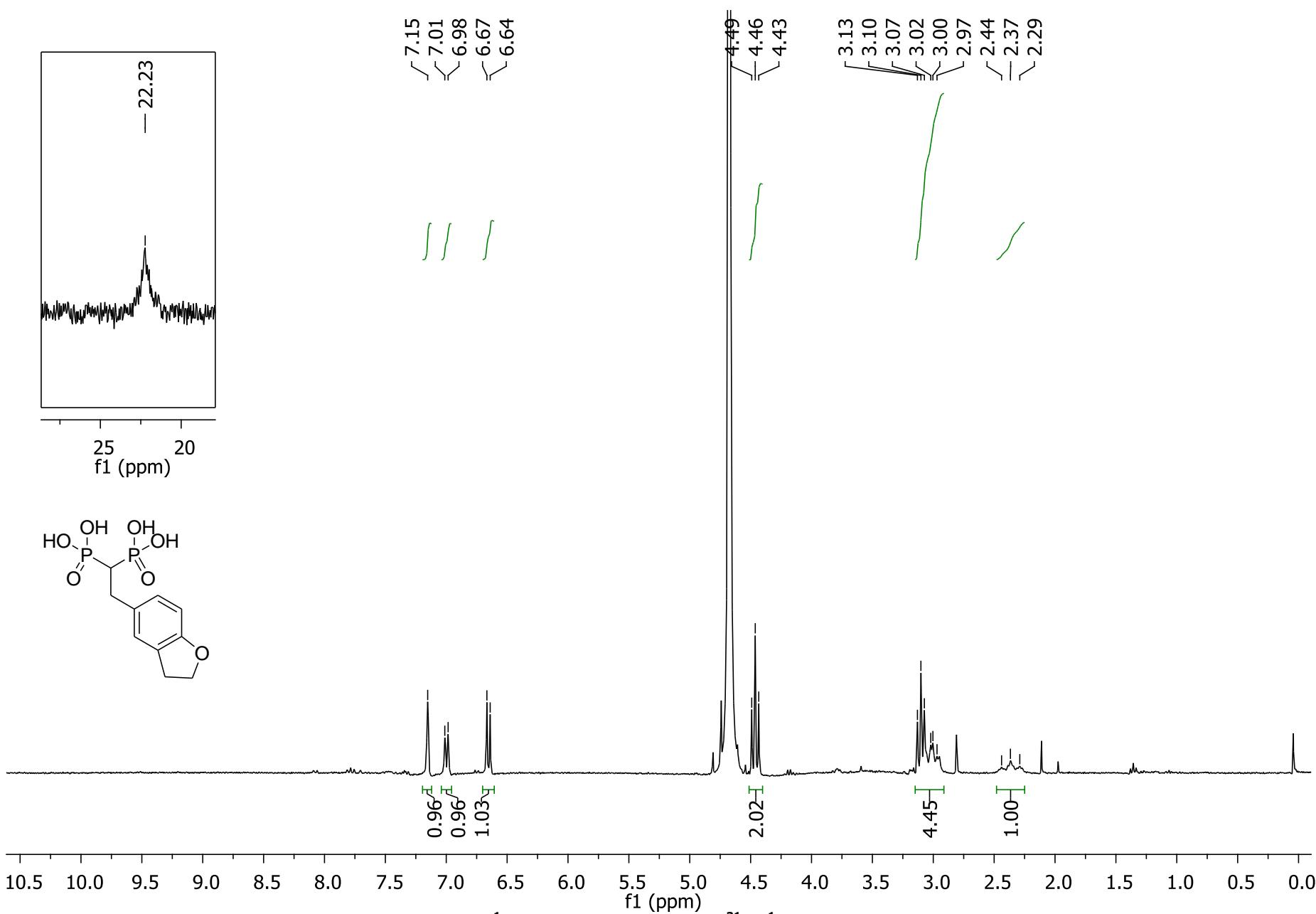


Figure 36: Deprotected 13BA ^1H -NMR (300.15 MHz) and $^{31}\text{P}\{^1\text{H}\}$ -NMR (121.5 MHz) spectra, D_2O .

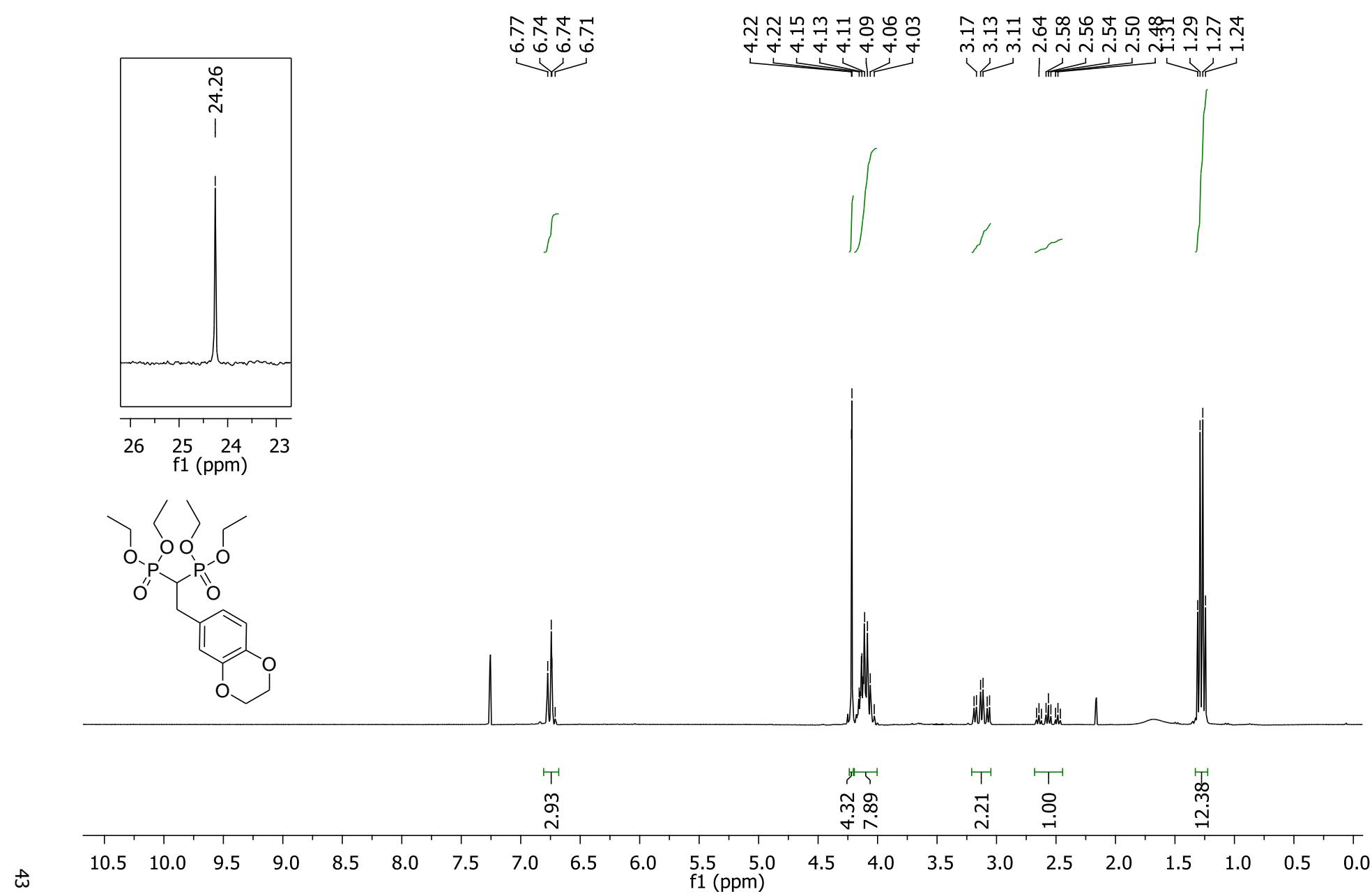


Figure 37: 14BA ^1H -NMR (300.15 MHz) and $^{31}\text{P} \{^1\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

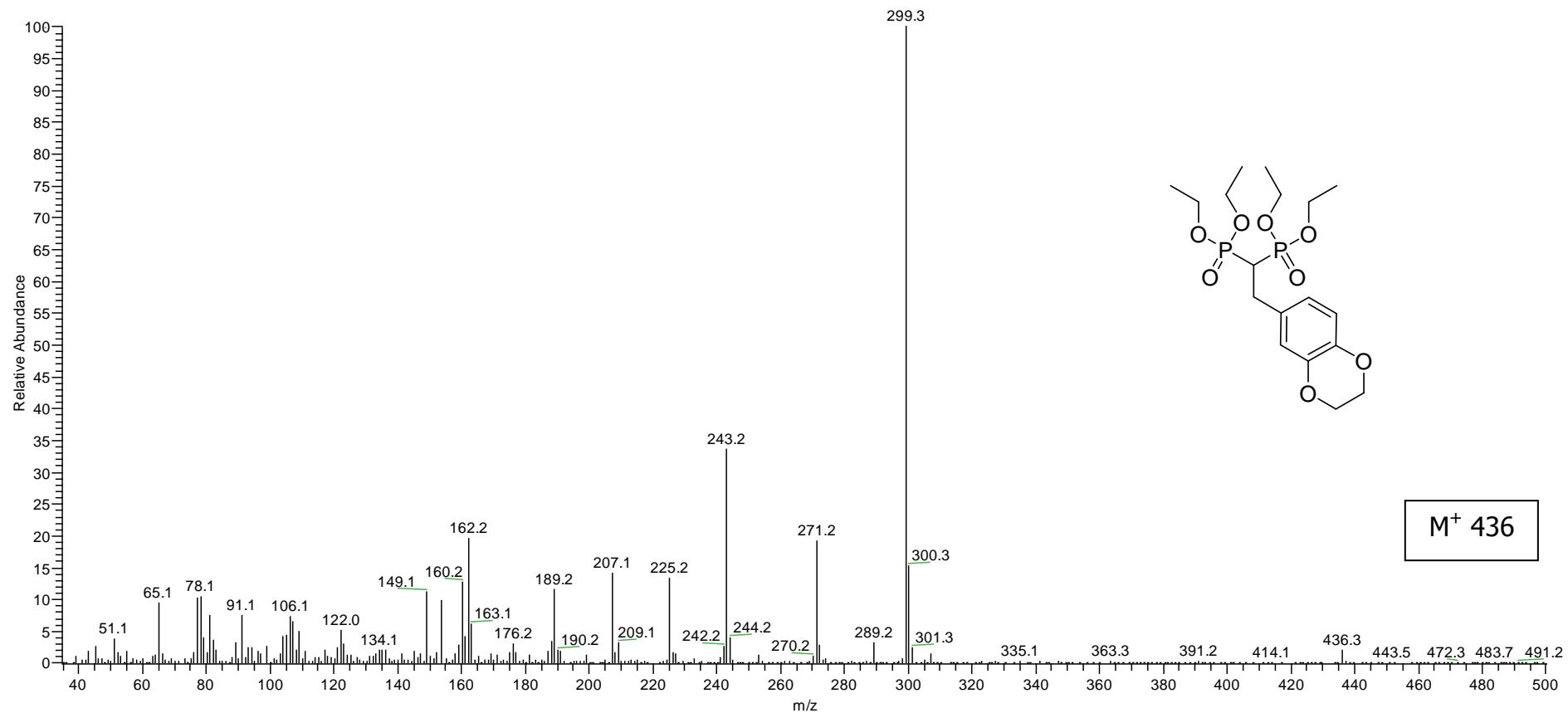


Figure 38: 14BA mass spectrum.

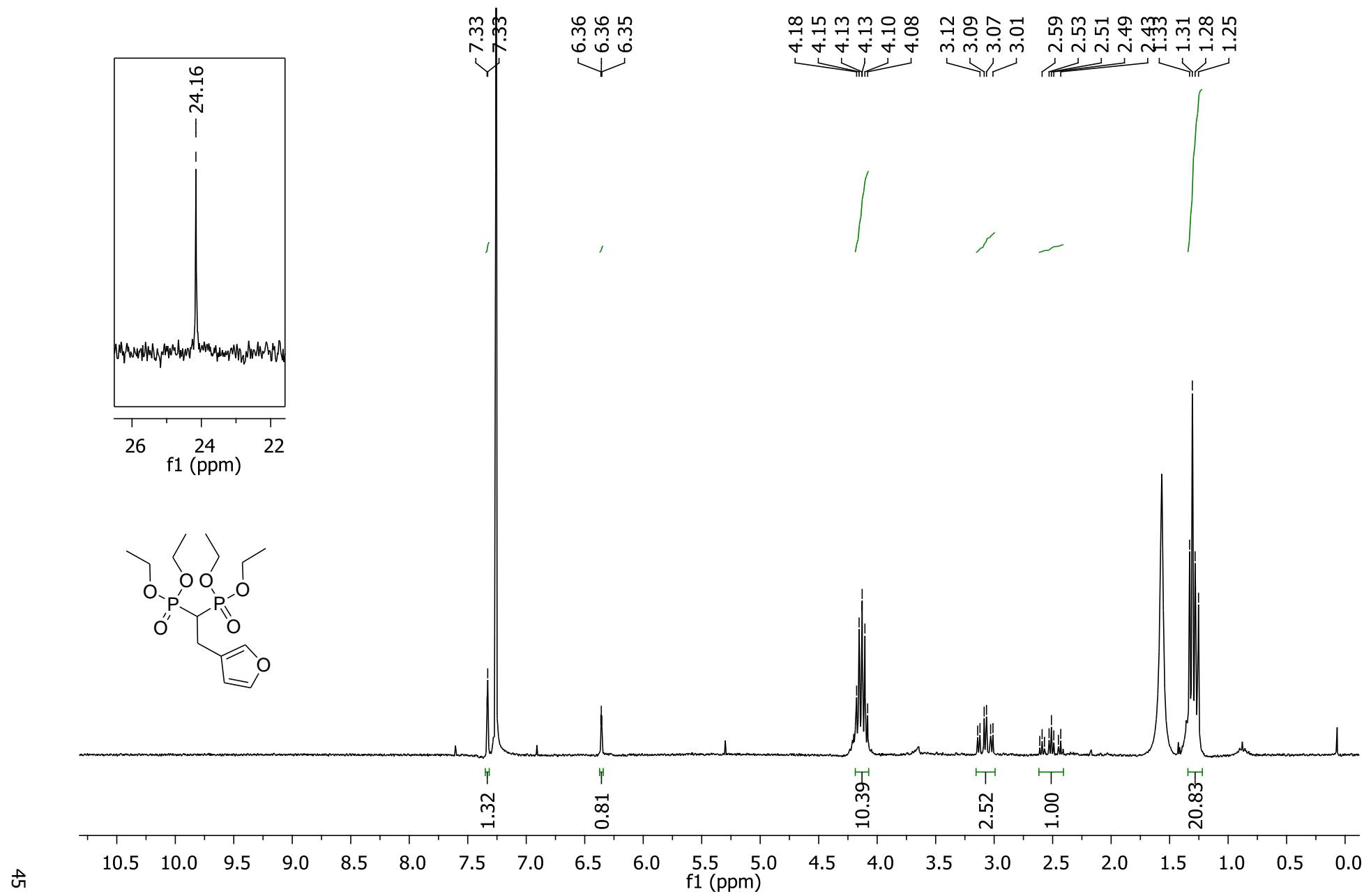


Figure 39: 15BA ^1H -NMR (300.15 MHz) and $^{31}\text{P}\{\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

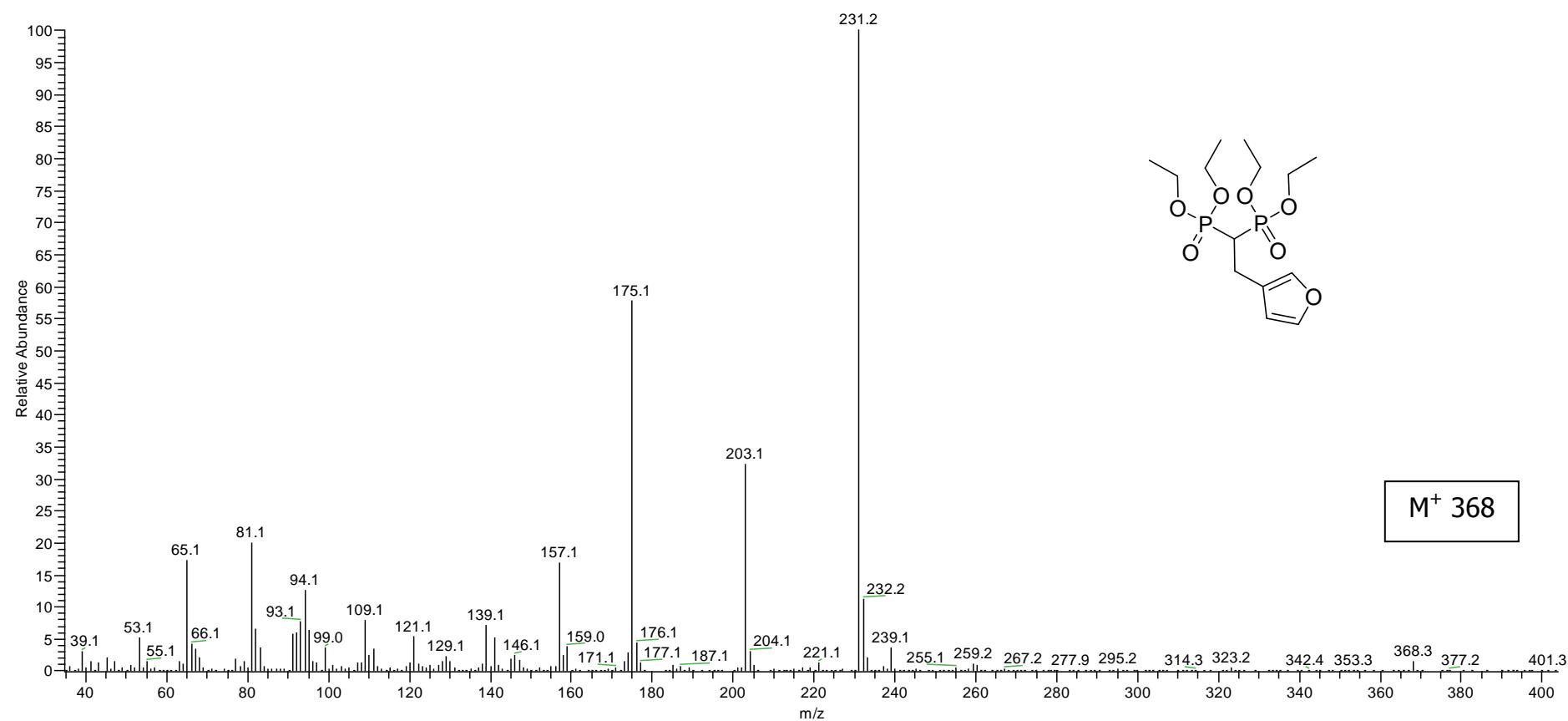


Figure 40: 15BA mass spectrum.

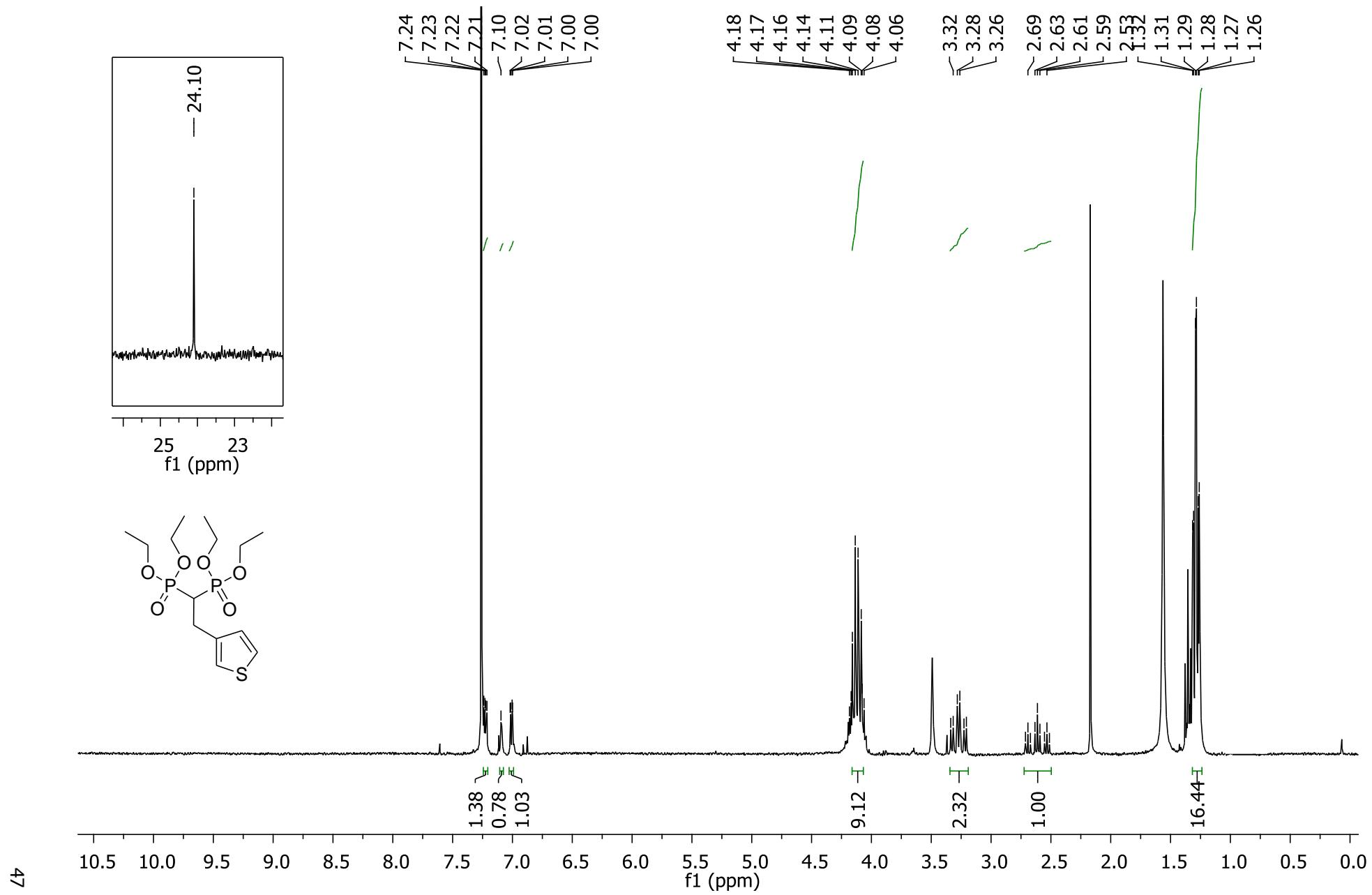


Figure 41: 16BA ^1H -NMR (300.15 MHz) and $^{31}\text{P}\{\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

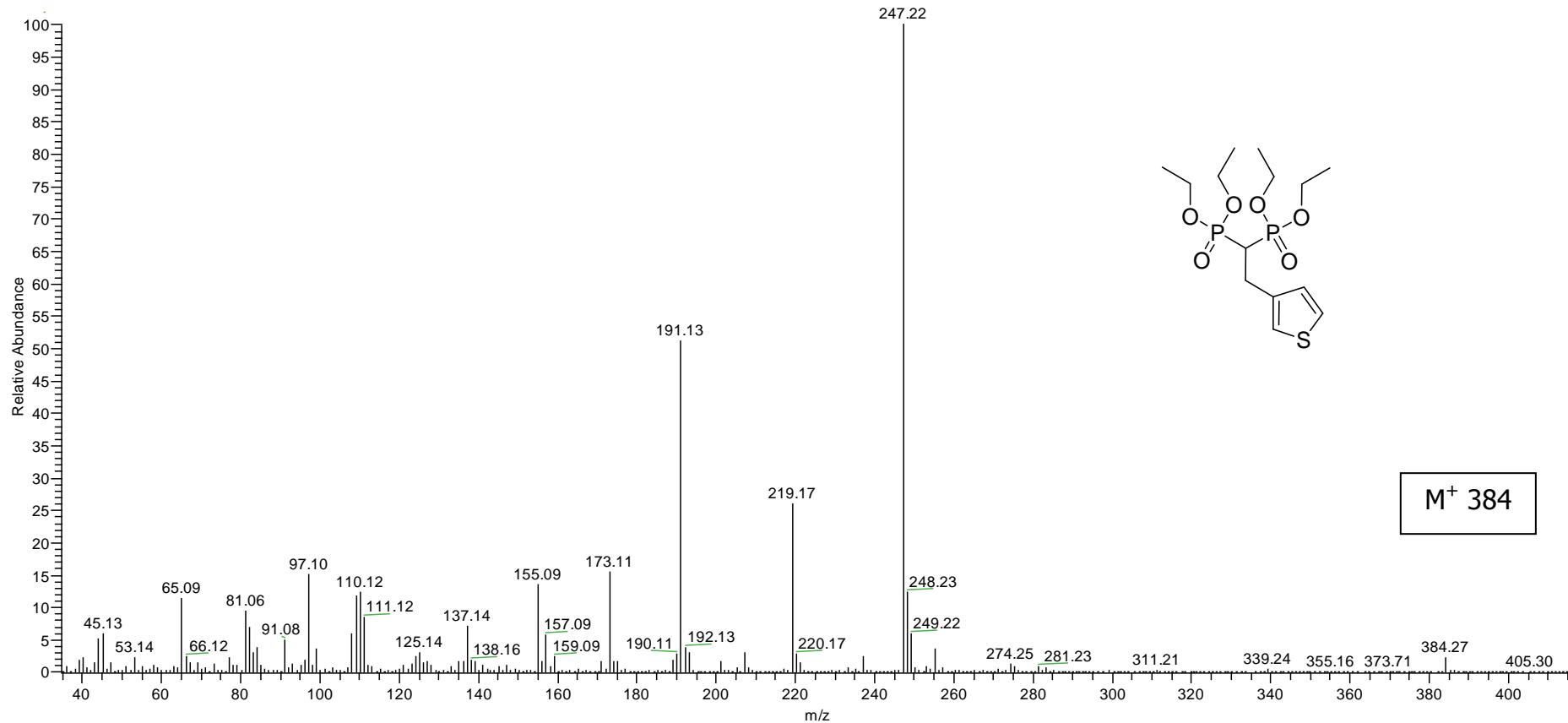


Figure 42: 16BA mass spectrum.

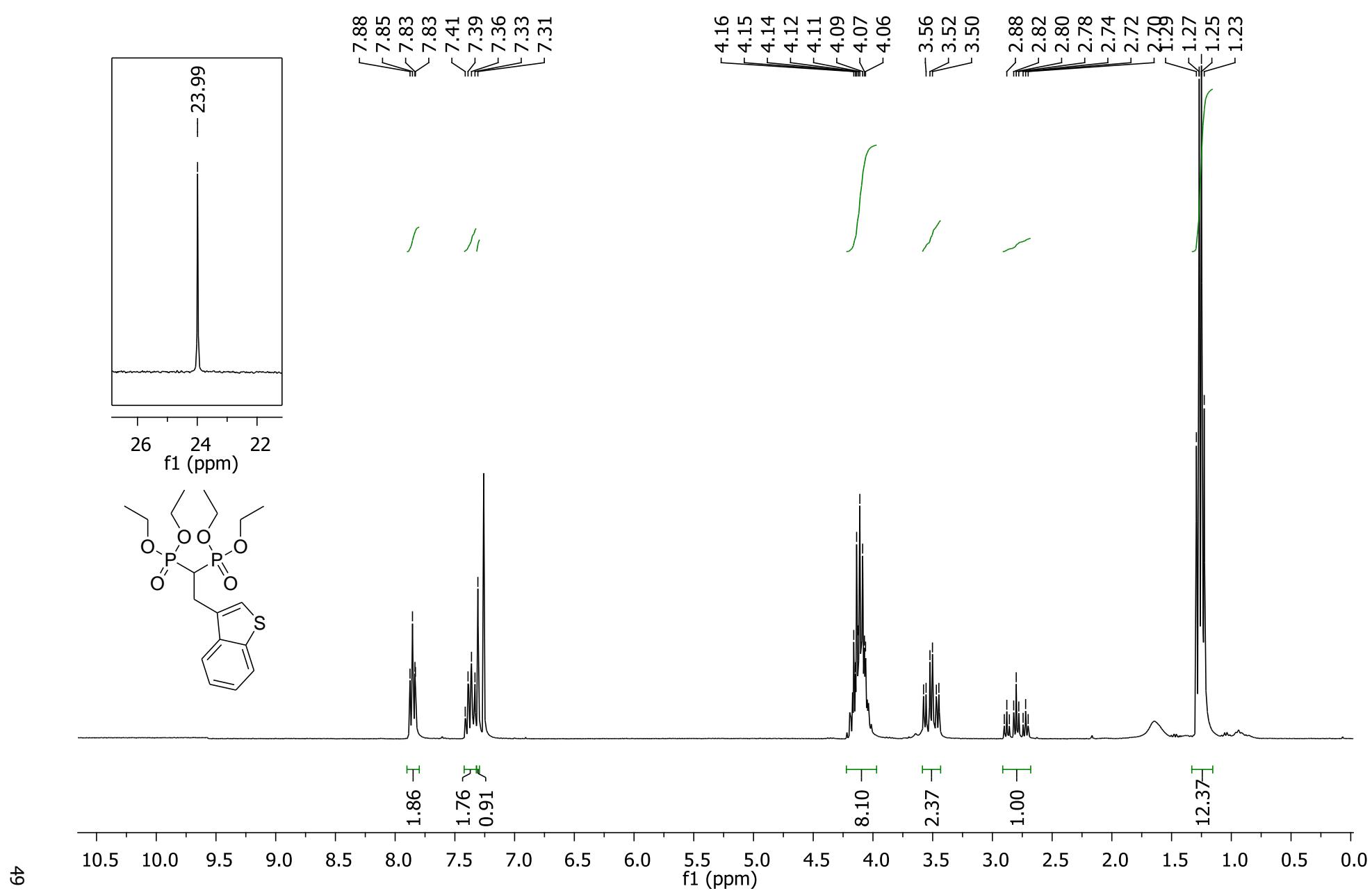


Figure 43: 17BA ^1H -NMR (300.15 MHz) and $^{31}\text{P} \{^1\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

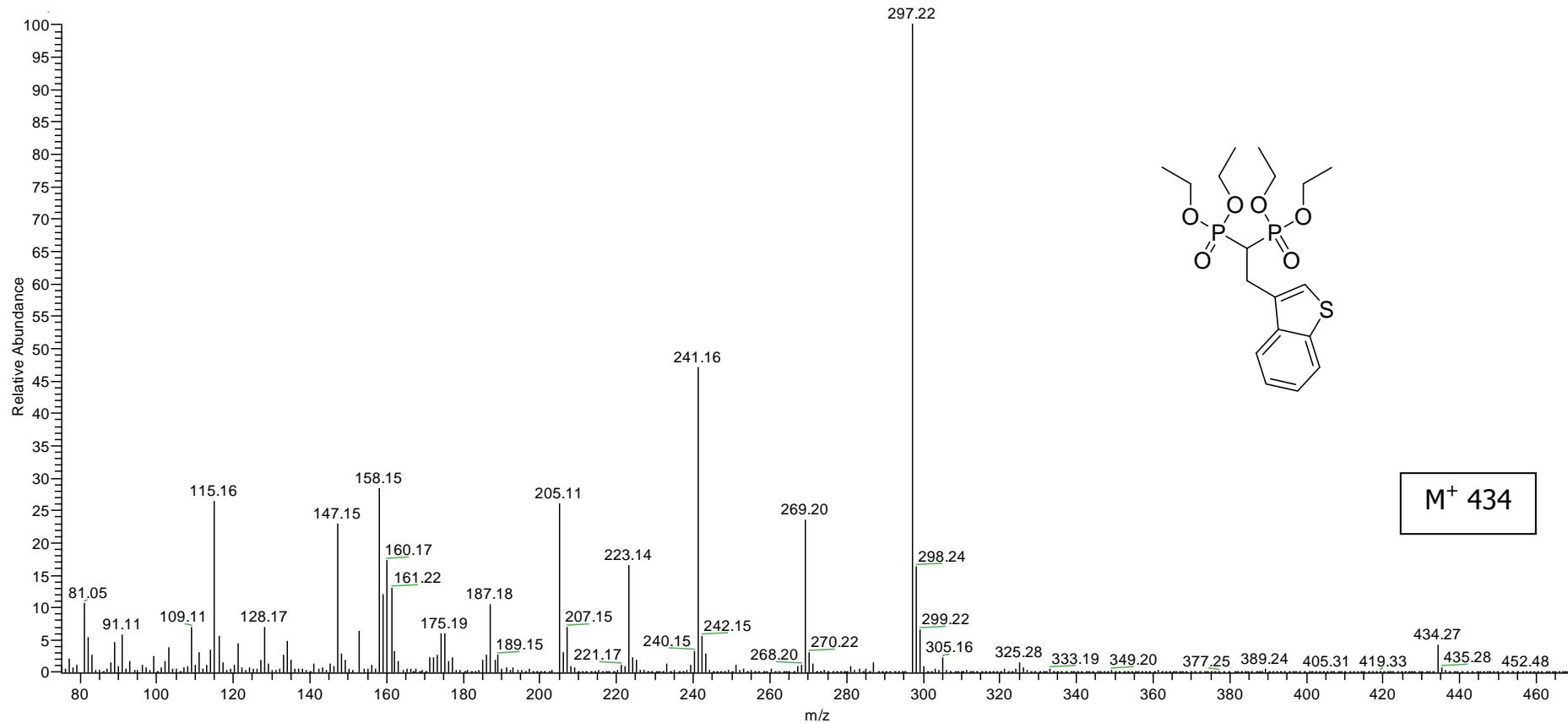


Figure 44: 17BA mass spectrum.

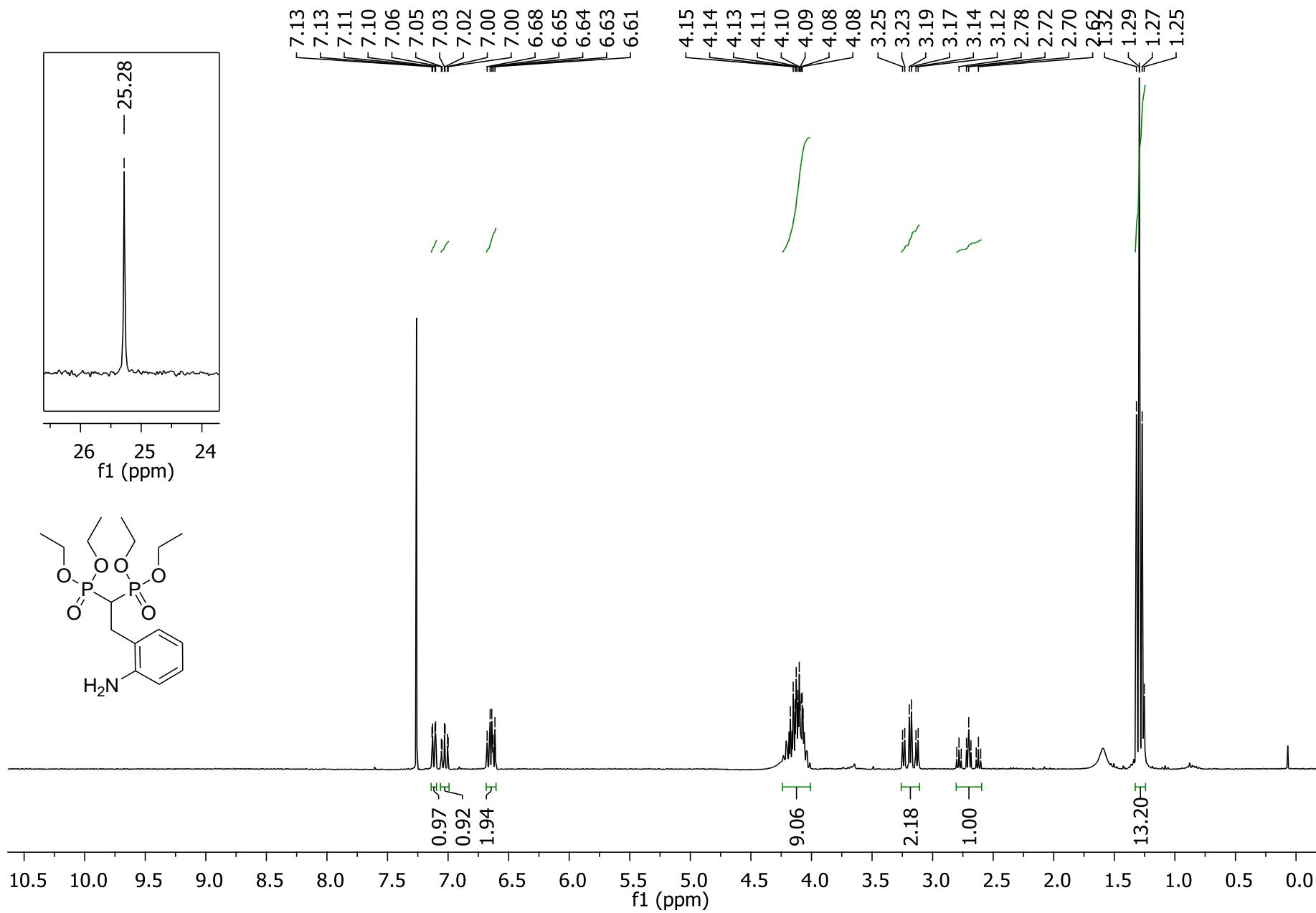


Figure 45: 18BA mass spectrum.

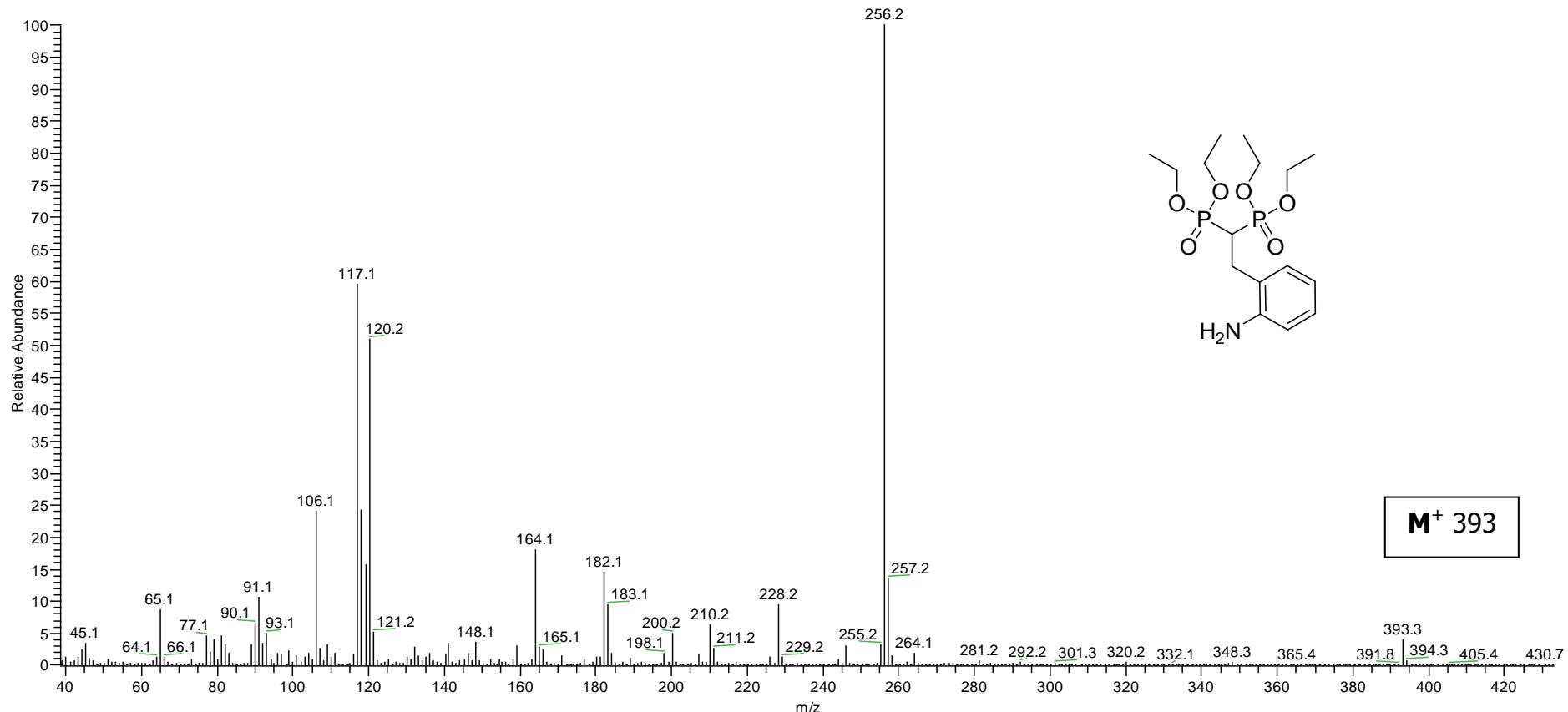


Figure 46: 18BA mass spectrum.

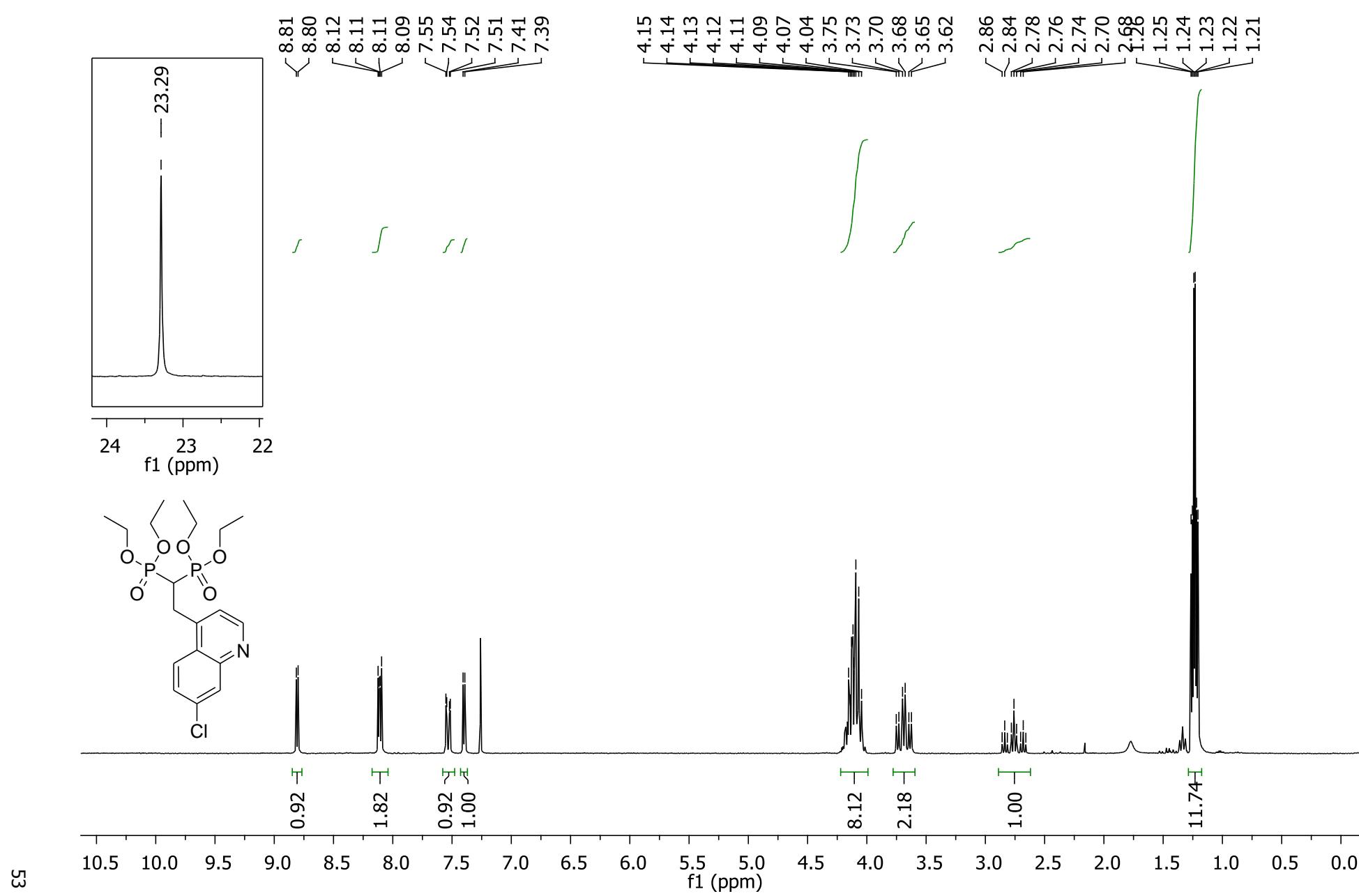


Figure 47: 19BA ^1H -NMR (300.15 MHz) and $^{31}\text{P}\{^1\text{H}\}$ -NMR (121.5 MHz) spectra, CDCl_3 .

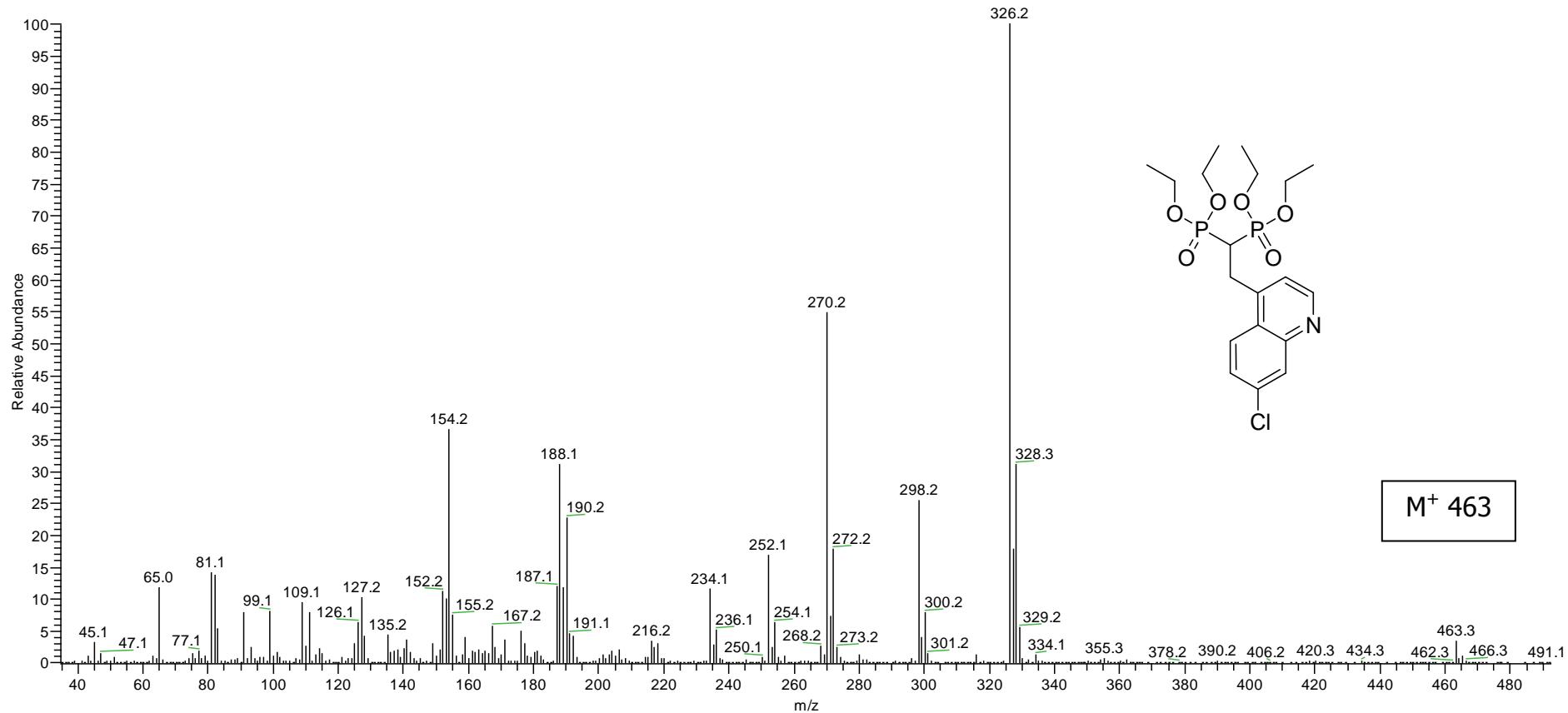


Figure 48: 19BA mass spectrum.

1 R.A. Nugent, M. Murphy, S.T. Schlatchter, C.J. Dunn, R.J. Smith, N.D. Staite, L.A. Galinet, S.K. Shields, D.G. Aspar, K.A. Richard, N.A. Rohloff, *J. Med. Chem.*, **1993**, *36*, 134-139