

Impact of α -modifications on the activity of triazole bisphosphonates as geranylgeranyl
diphosphate synthase inhibitors

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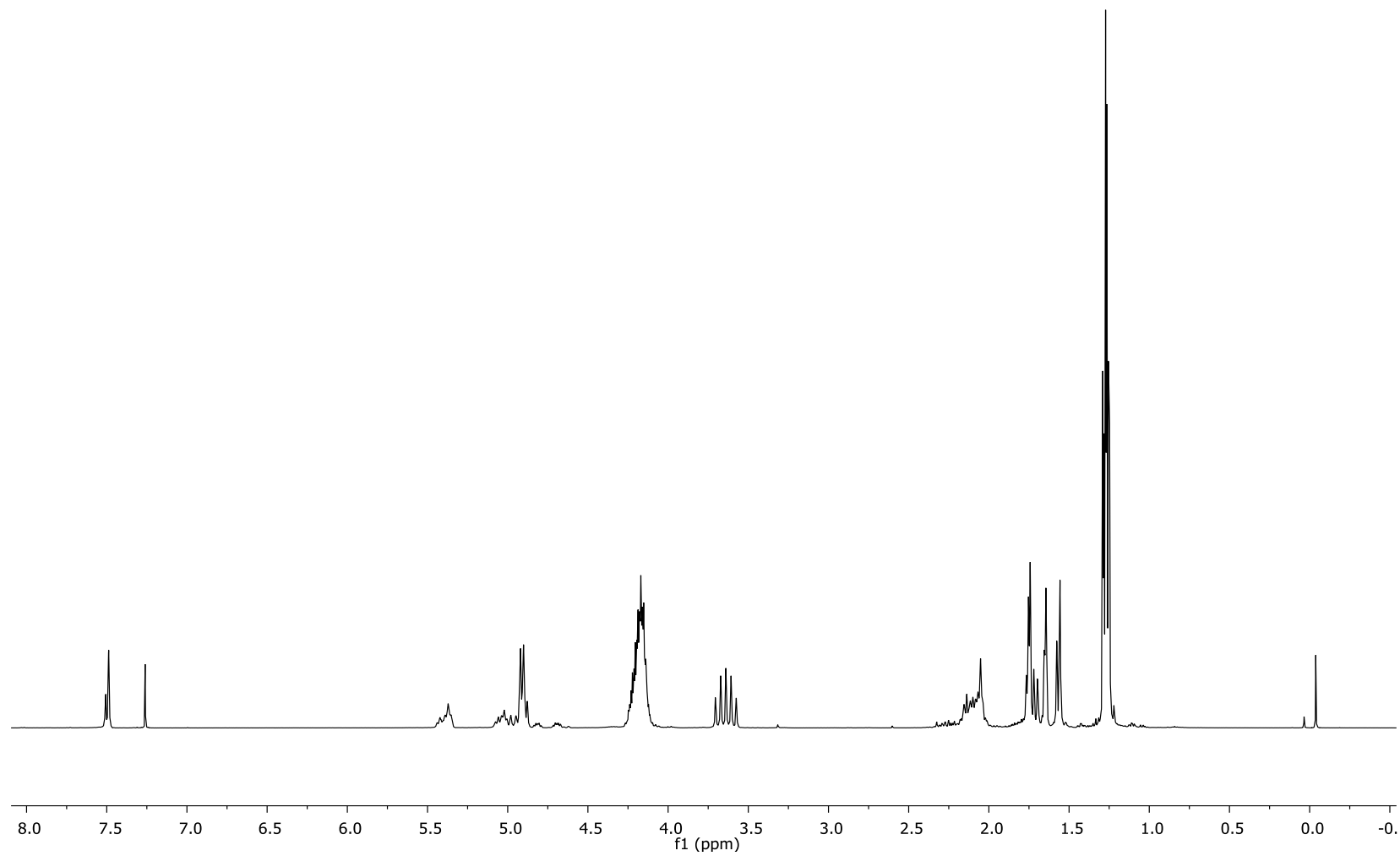
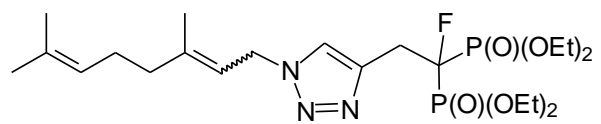
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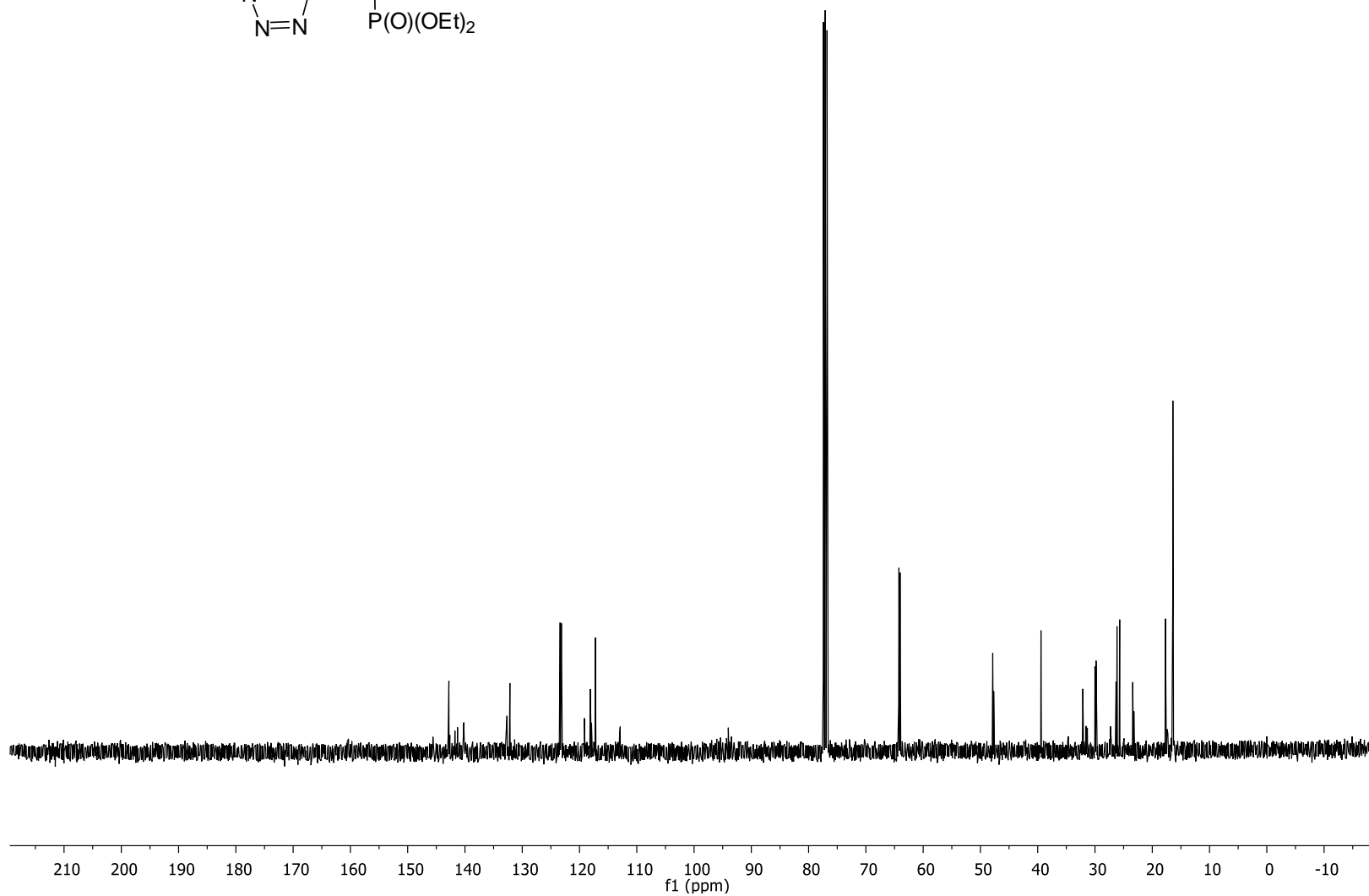
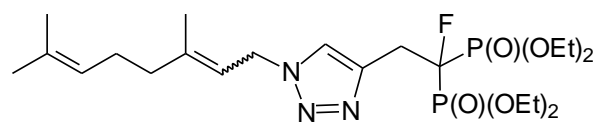
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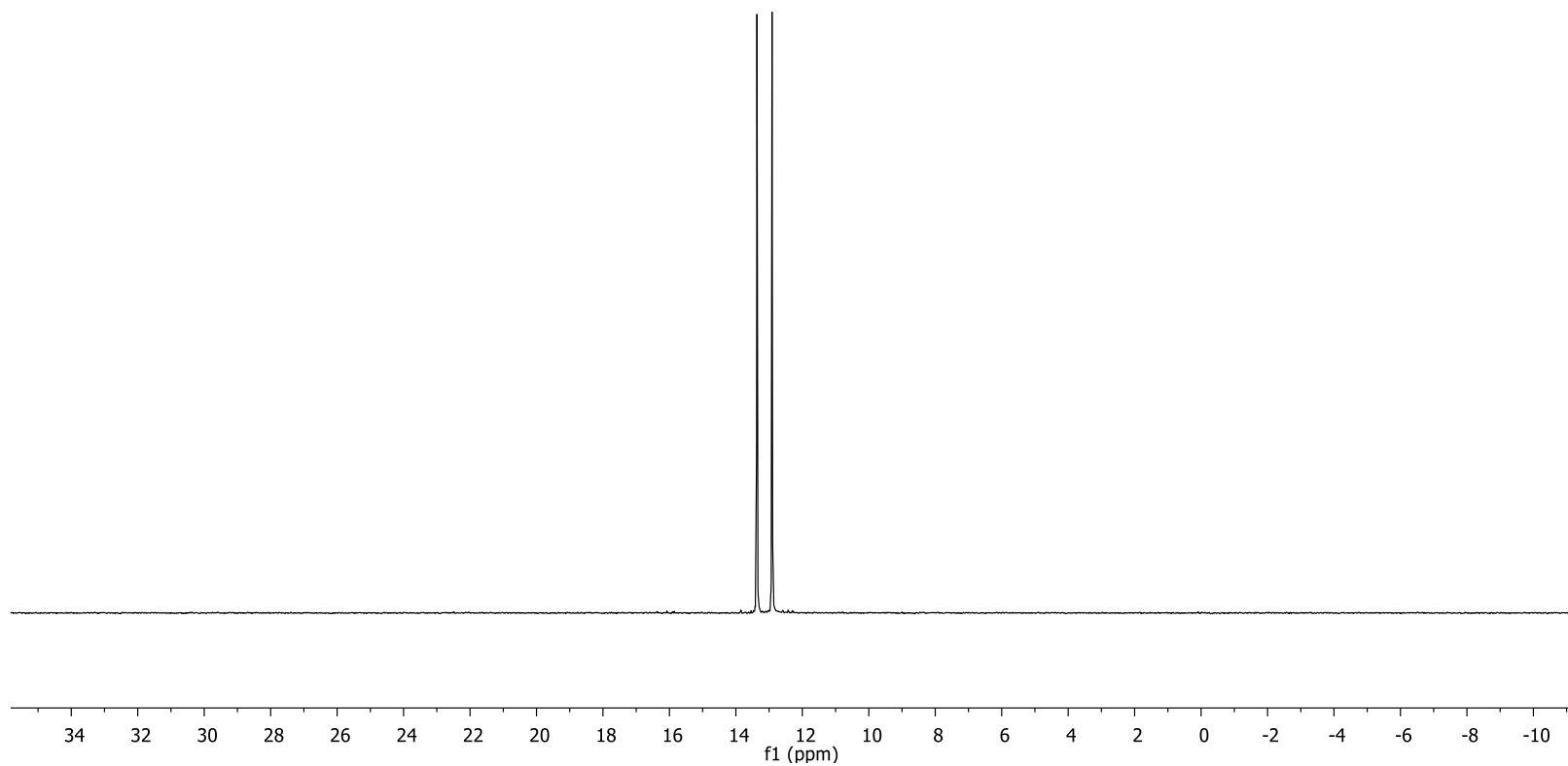
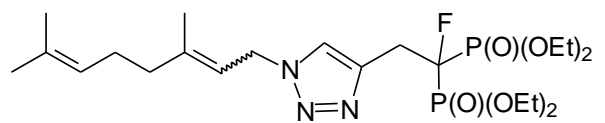
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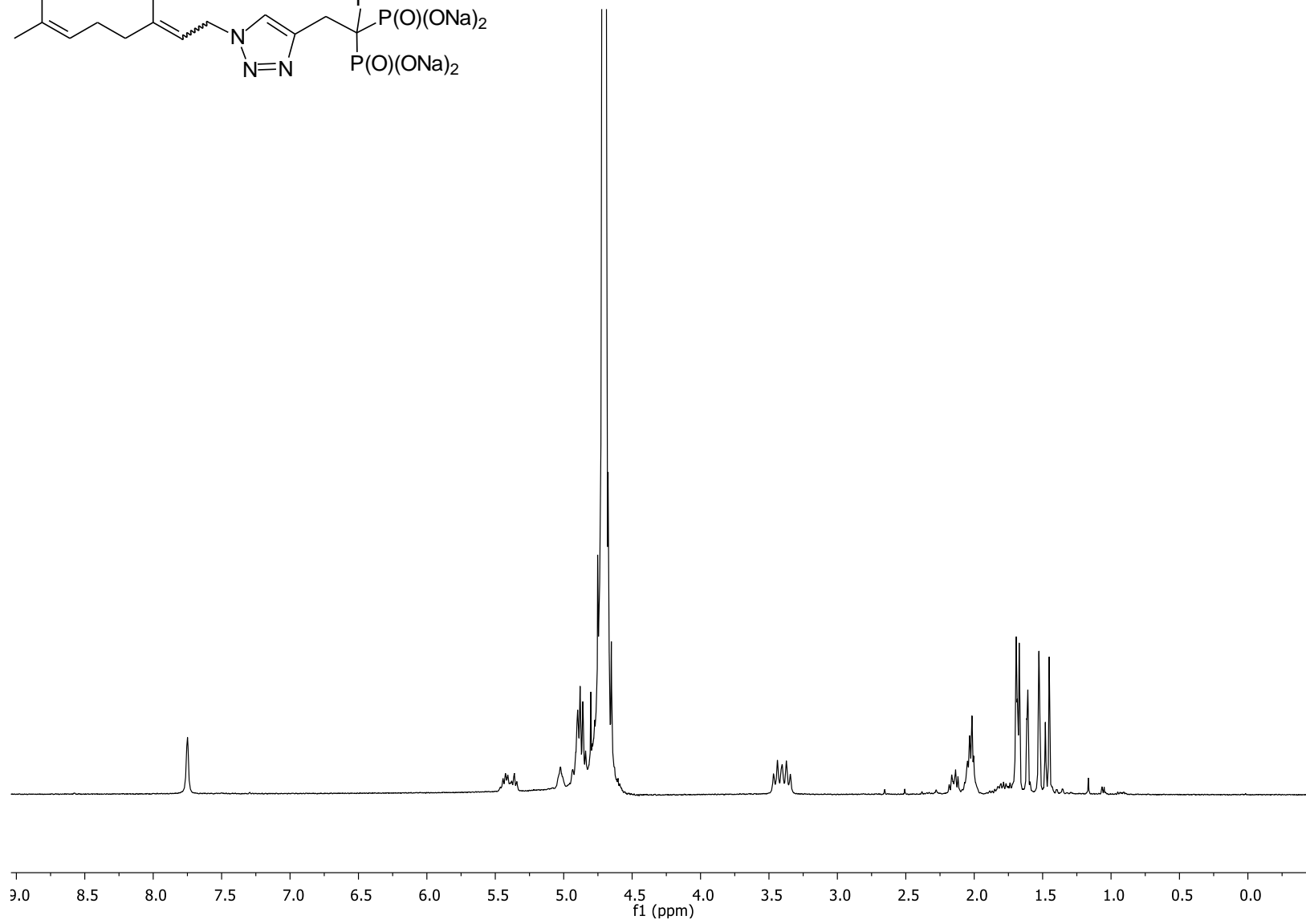
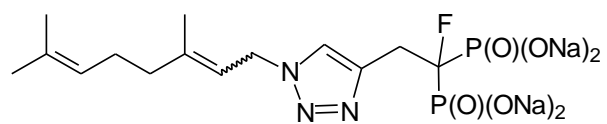
^1H NMR Spectrum of Compound **6** (CDCl_3 , 400 MHz)



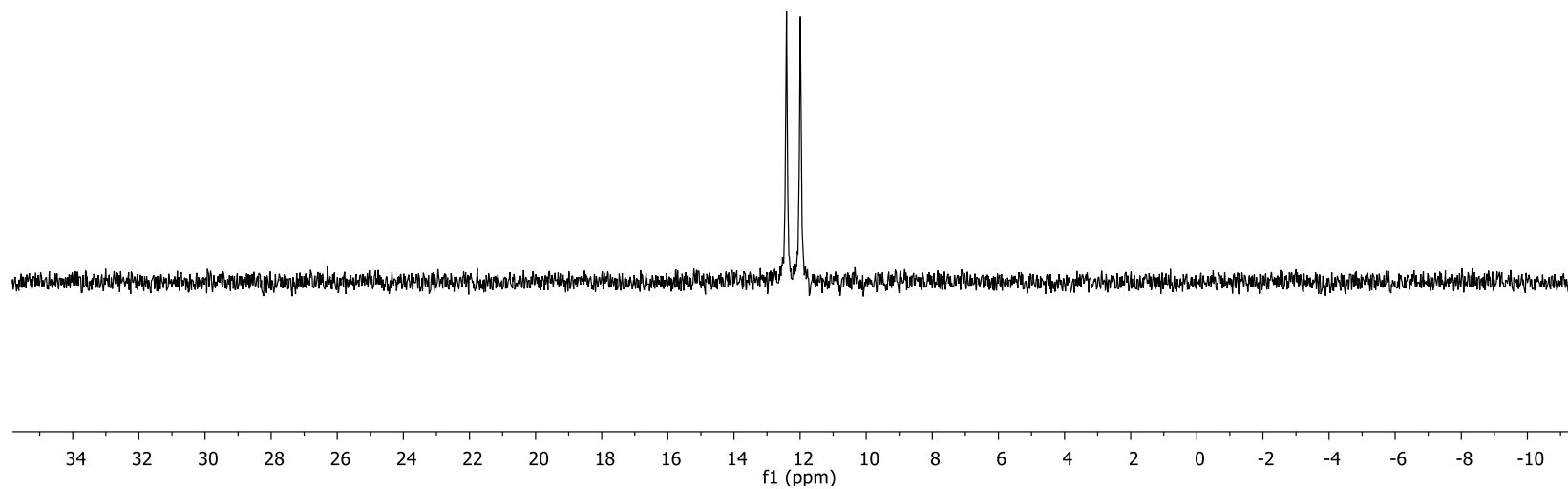
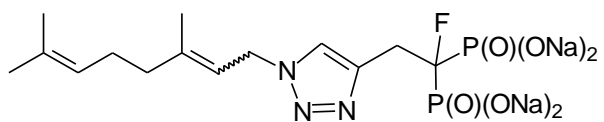
¹³C NMR Spectrum of Compound 6 (CDCl₃, 100 MHz)



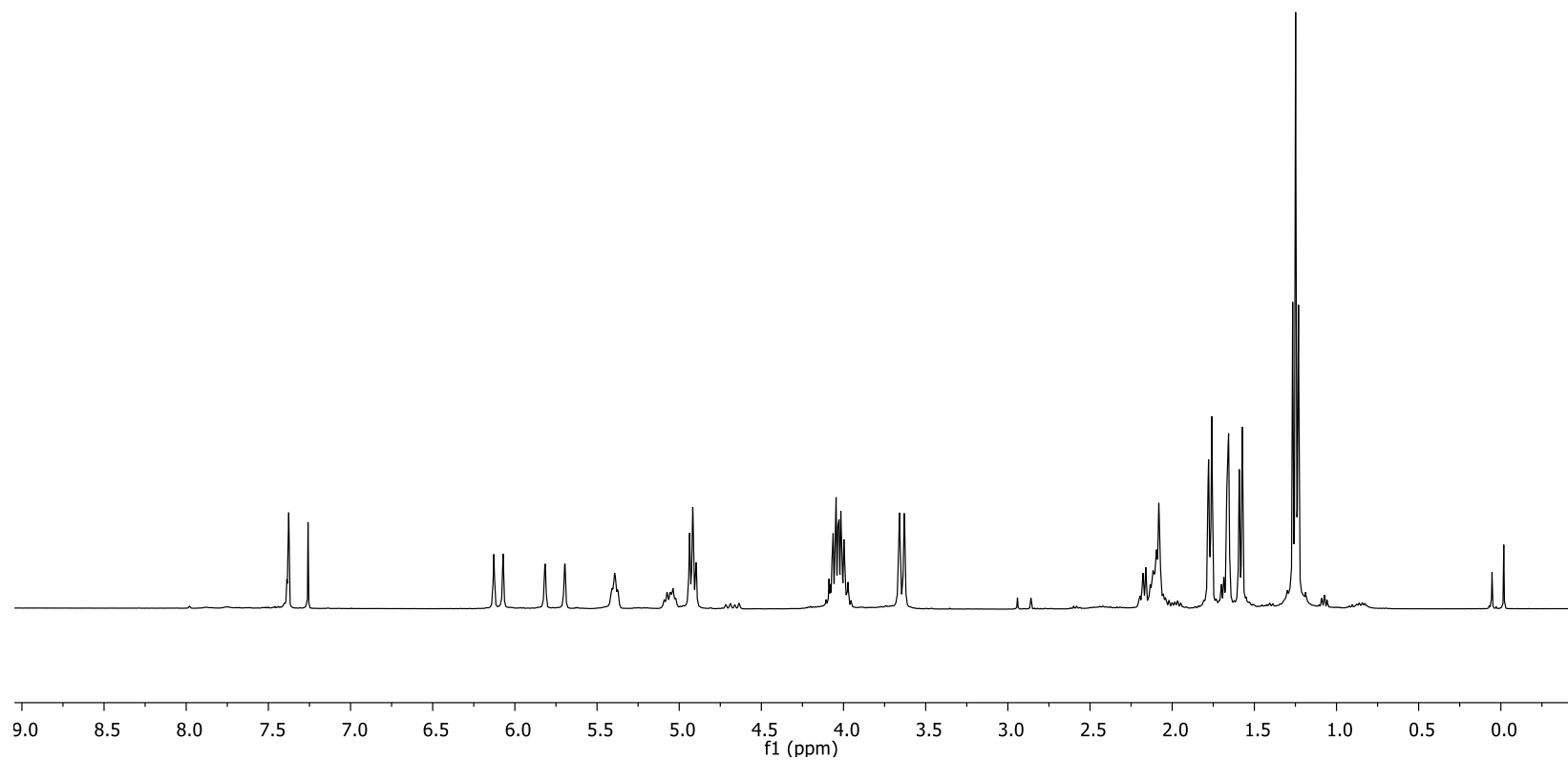
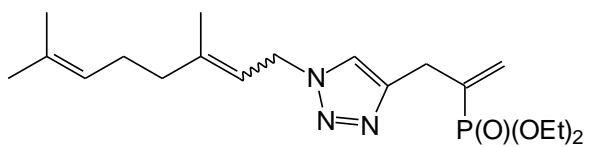
^{31}P NMR Spectrum of Compound **6** (CDCl_3 , 162 MHz)



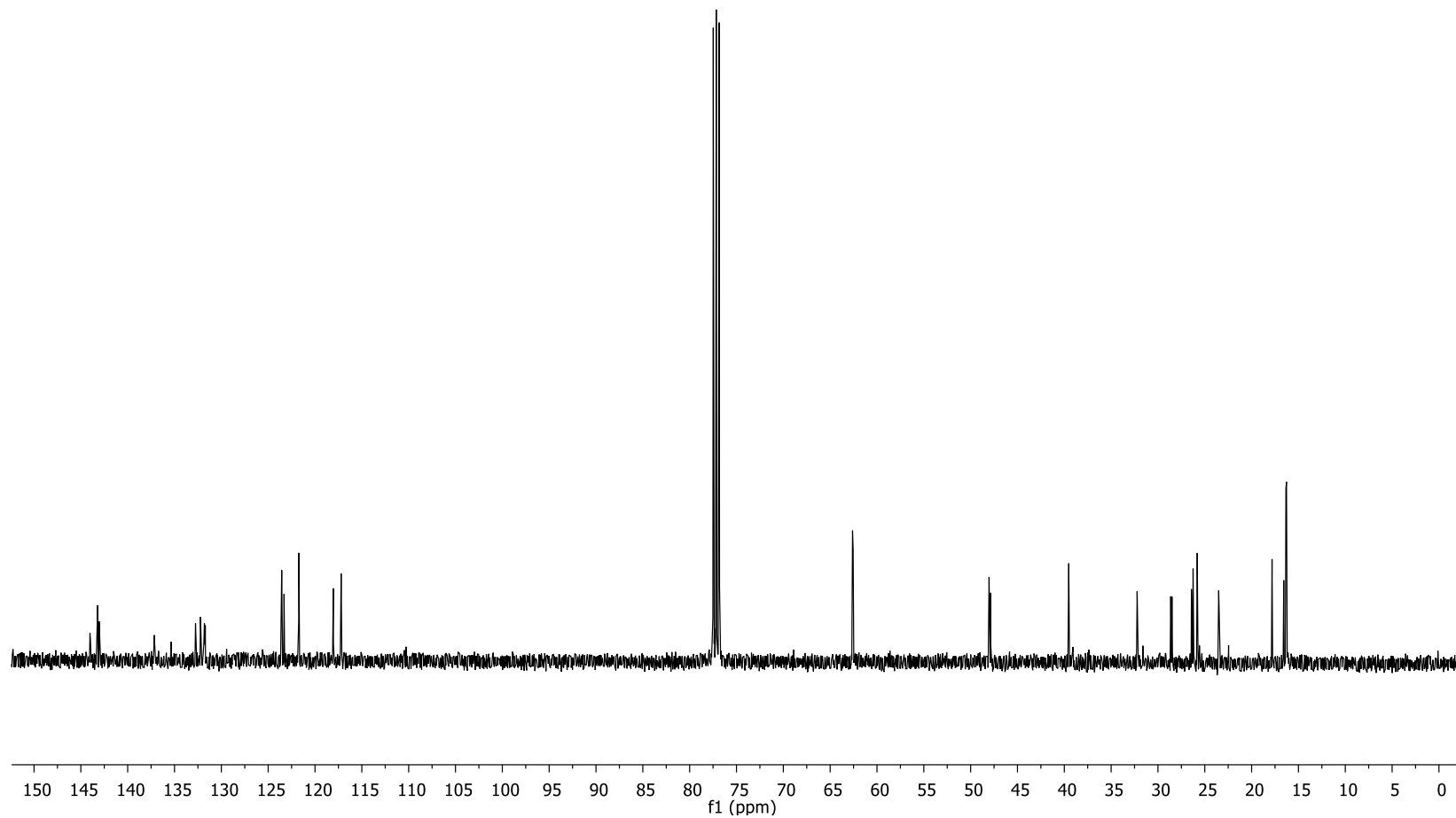
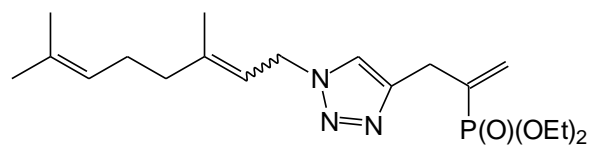
¹H NMR Spectrum of Compound 7 (D₂O, 400 MHz)



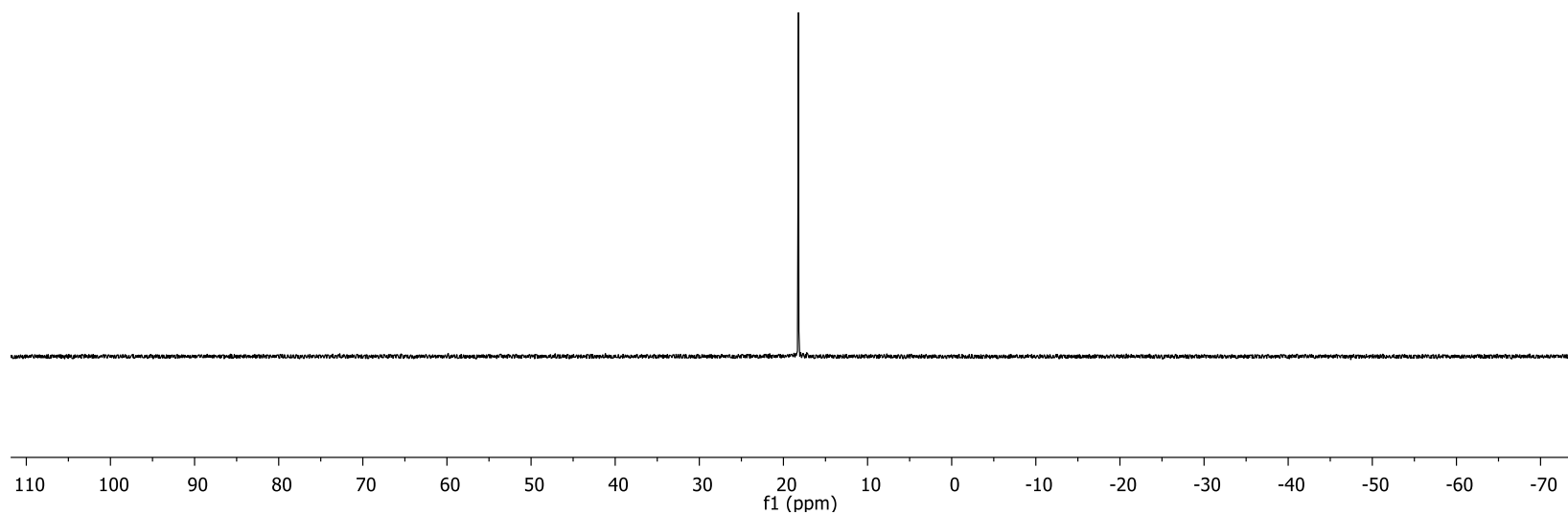
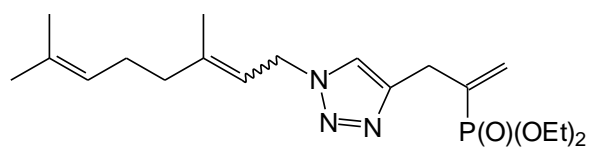
^{31}P NMR Spectrum of Compound 7 (D_2O , 400 MHz)



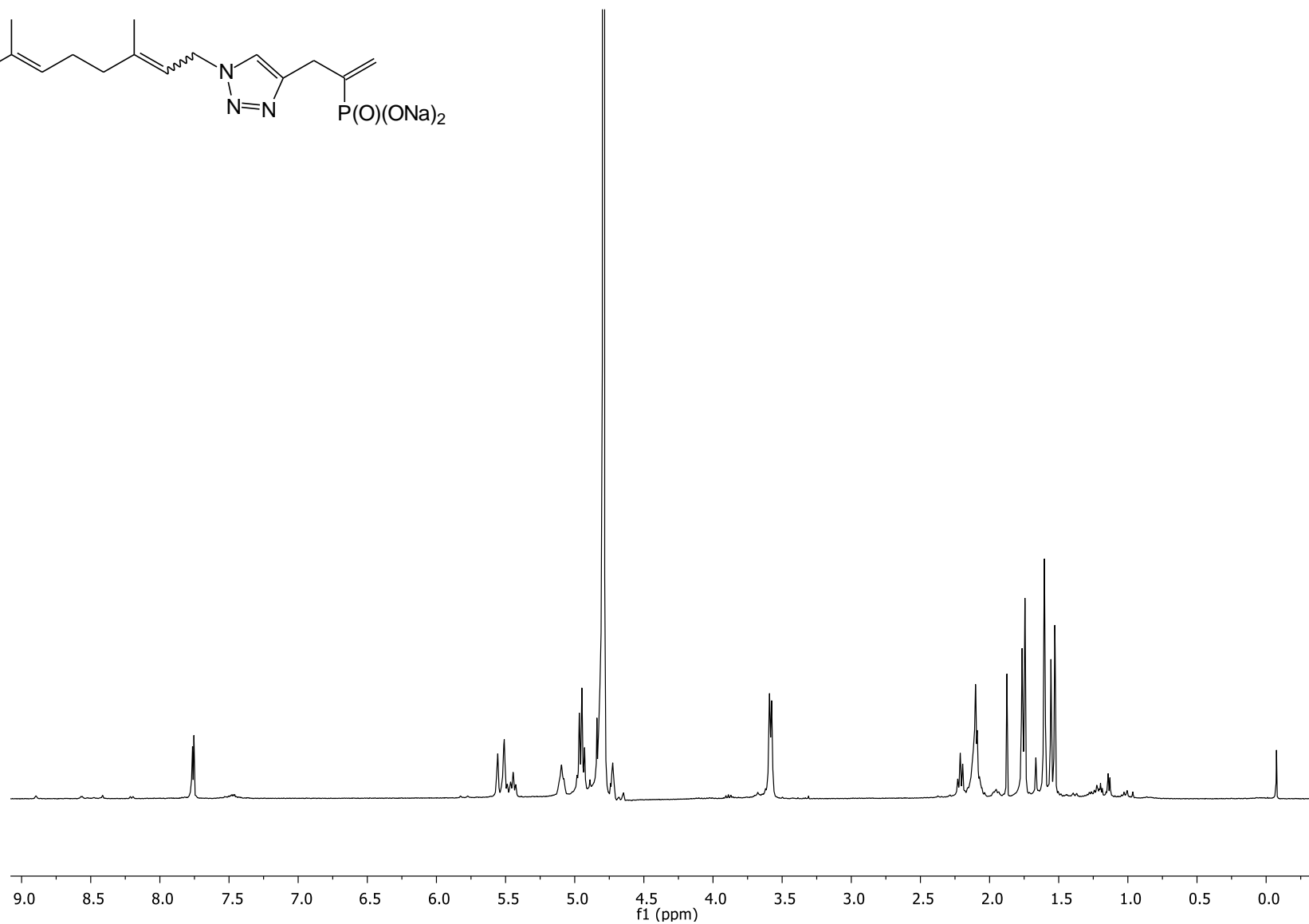
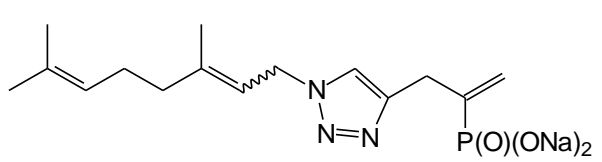
¹H NMR Spectrum of Compound **10** (CDCl₃, 400 MHz)



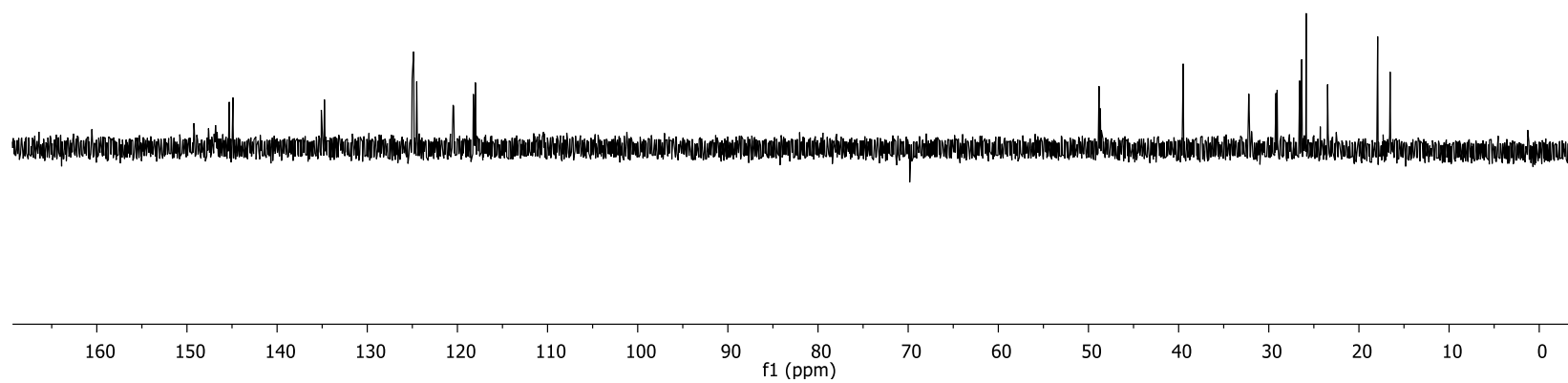
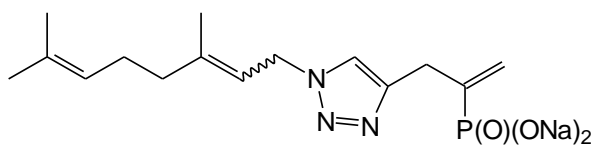
¹³C NMR Spectrum of Compound **10** (CDCl₃, 100 MHz)



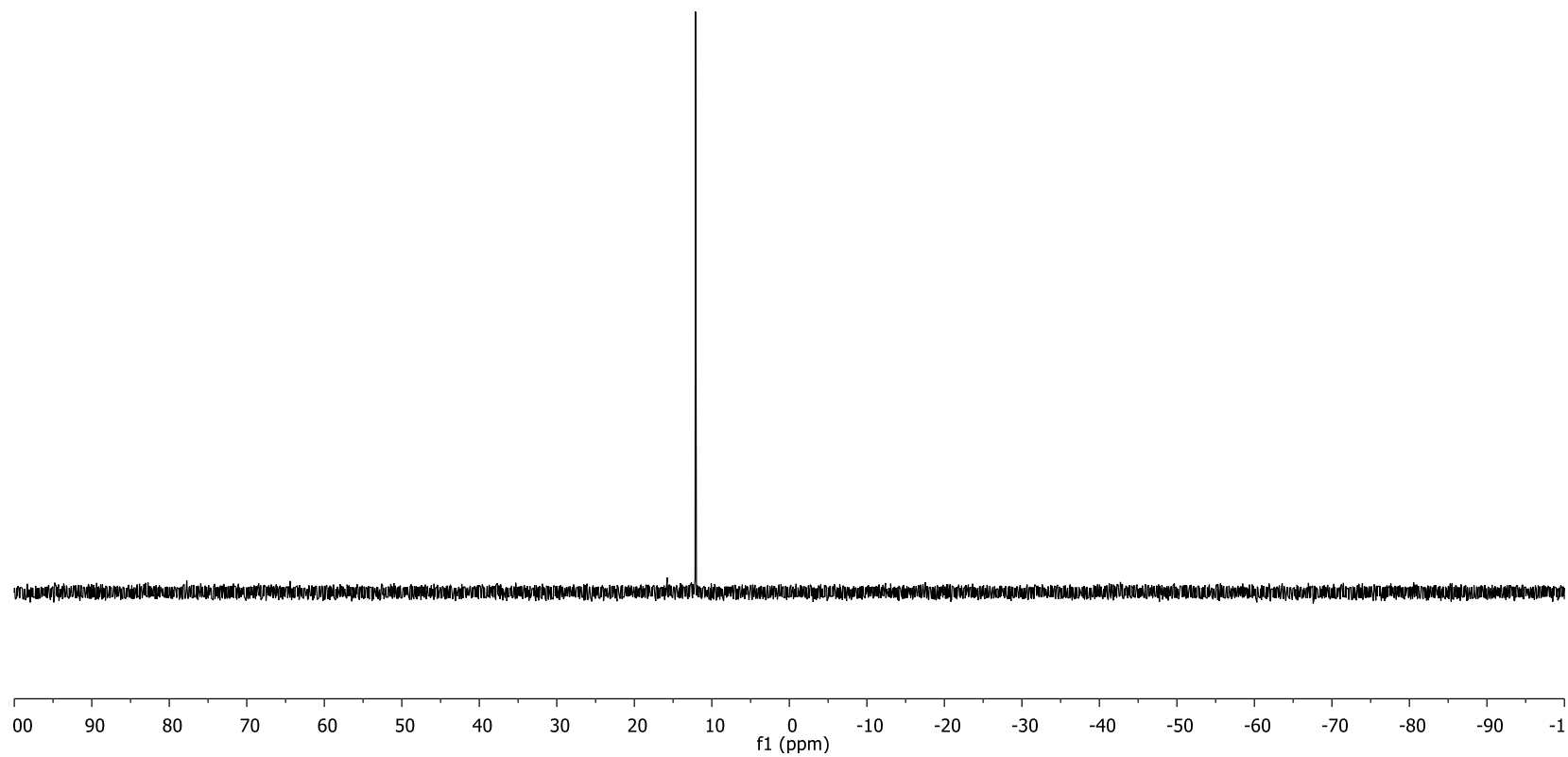
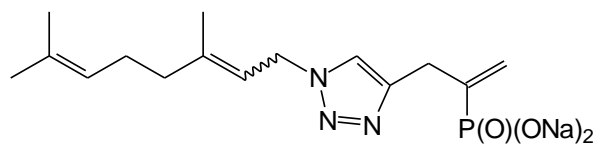
^{31}P NMR Spectrum of Compound **10** (CDCl_3 , 162 MHz)



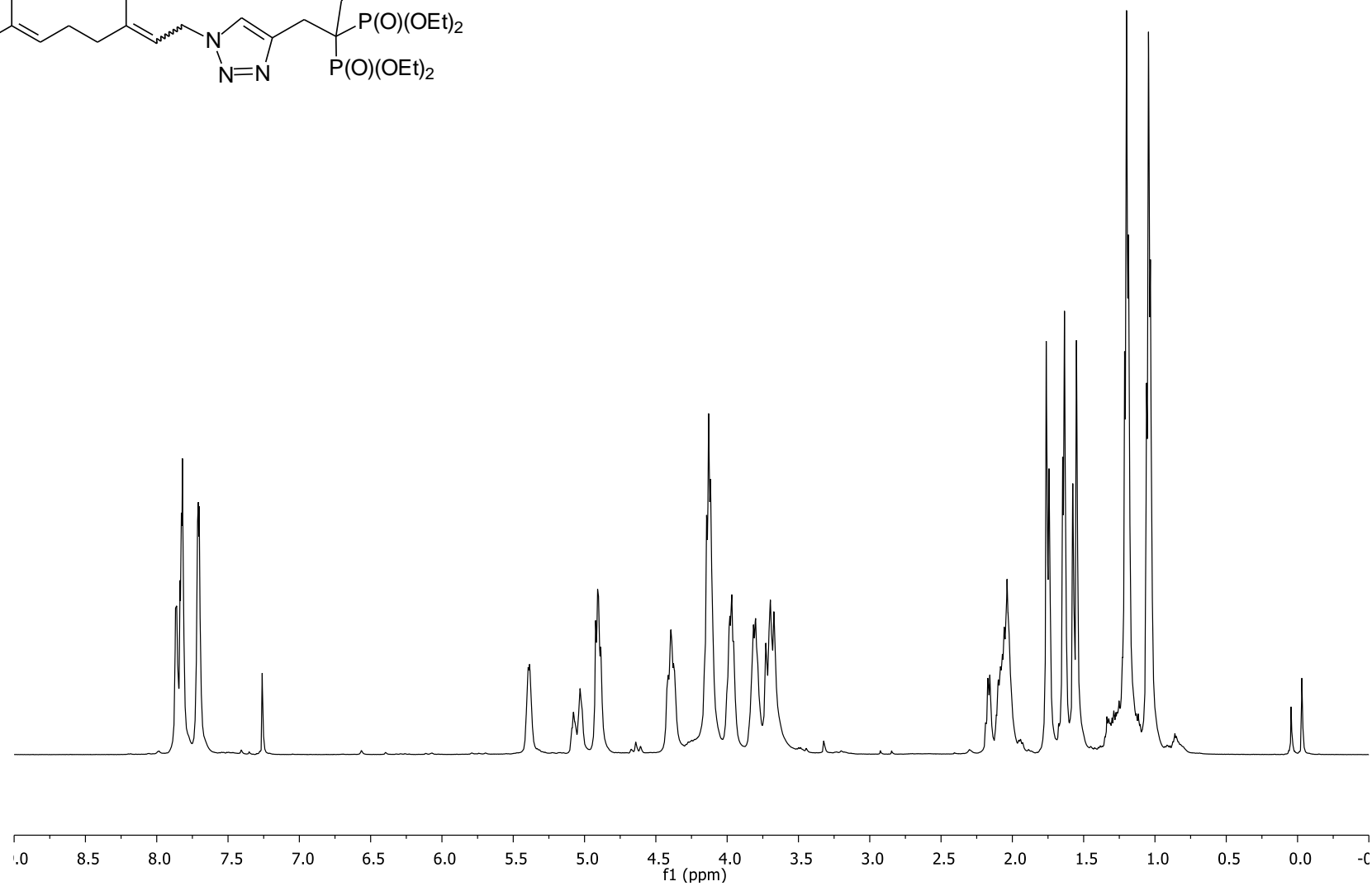
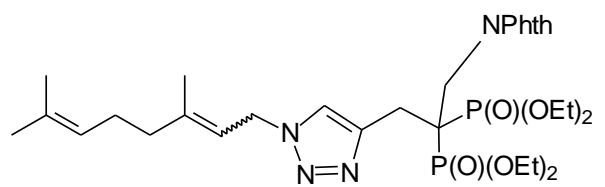
¹H NMR Spectrum of Compound **11** (D₂O, 400 MHz)



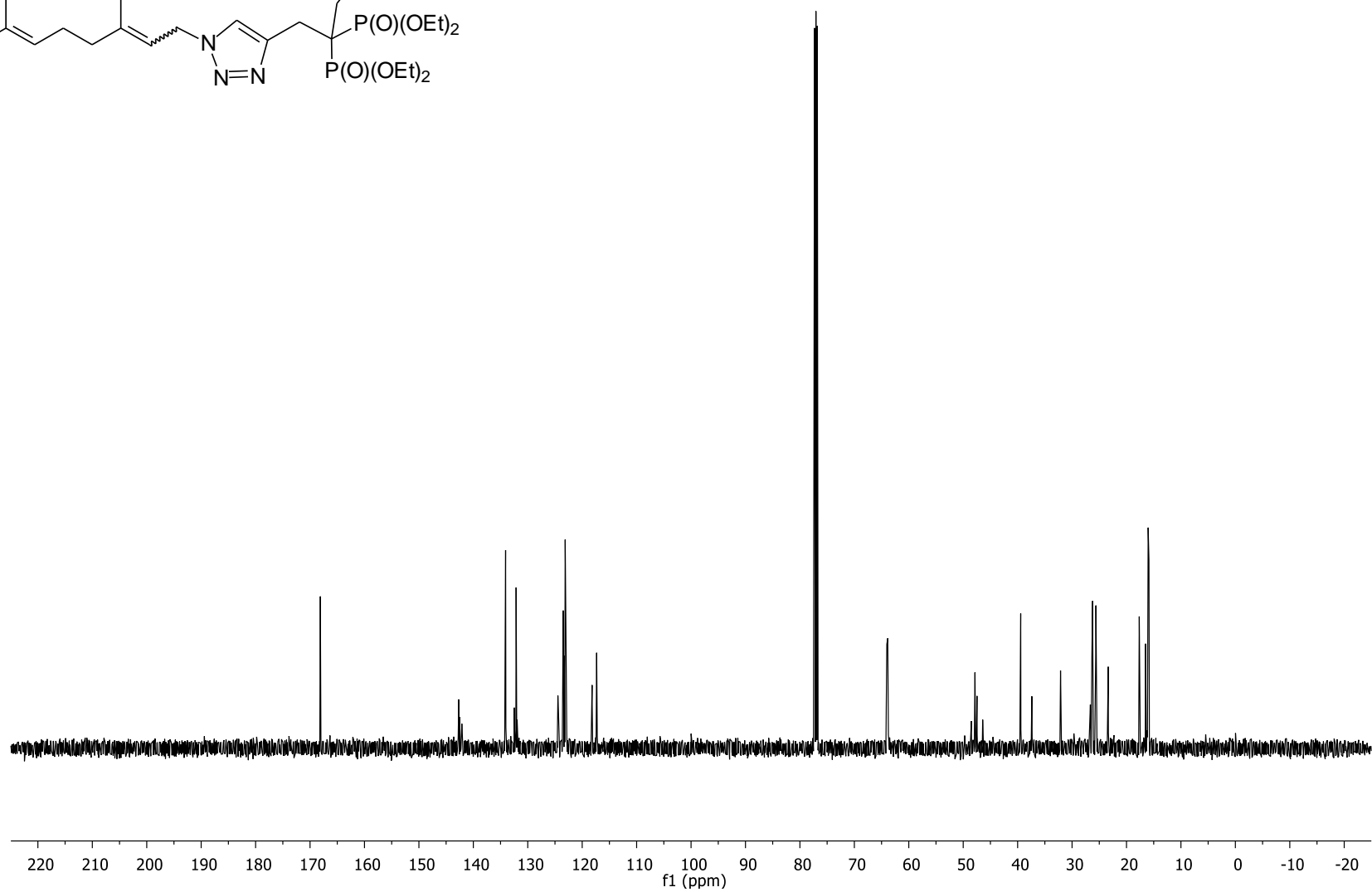
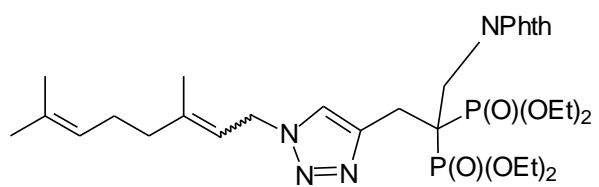
¹³C NMR Spectrum of Compound 11 (D₂O, 100 MHz)



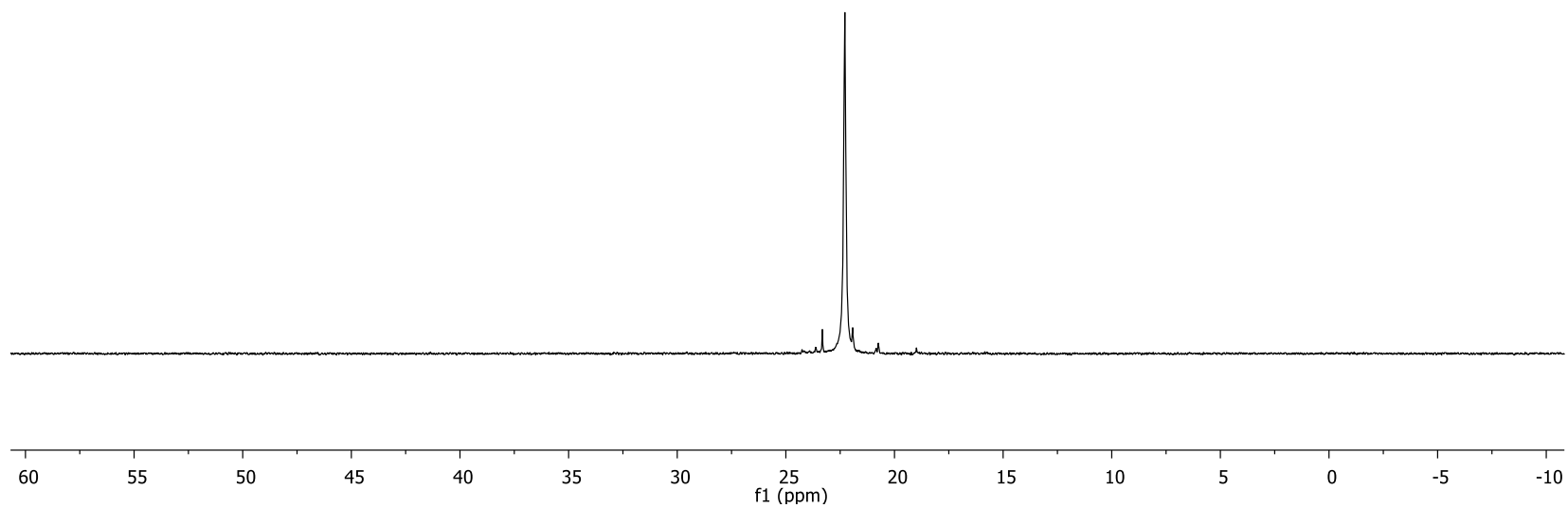
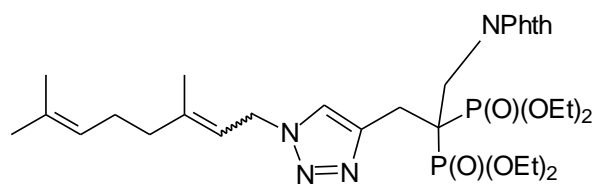
³¹P NMR Spectrum of Compound 11 (D₂O, 162 MHz)



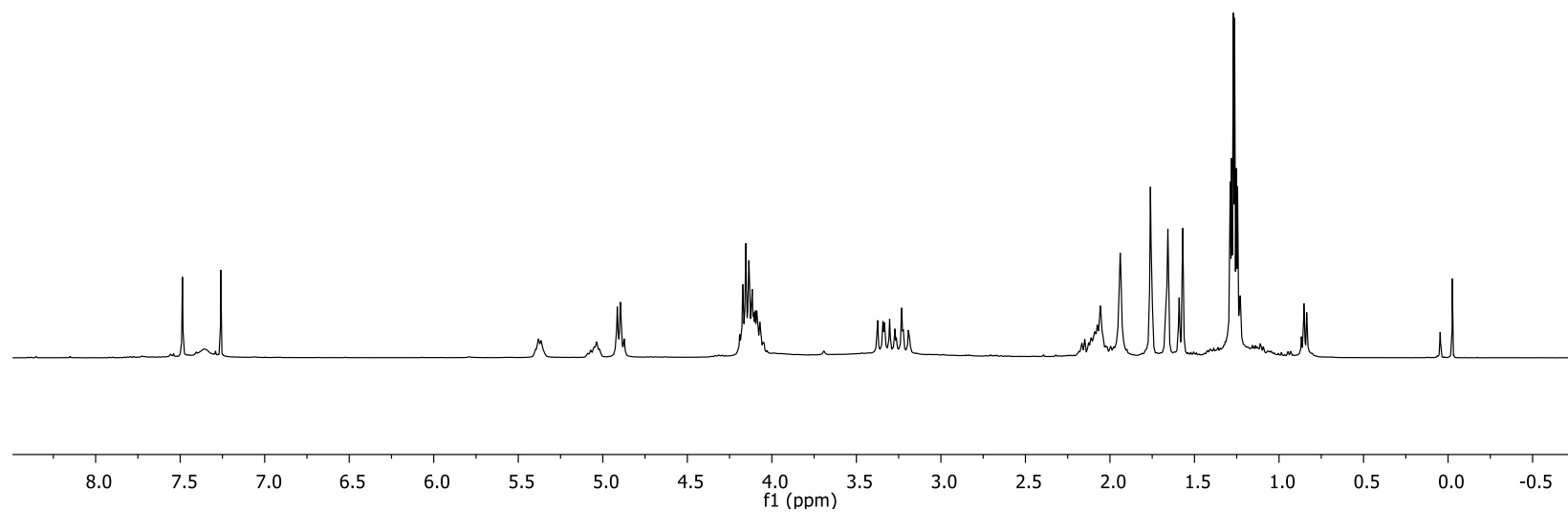
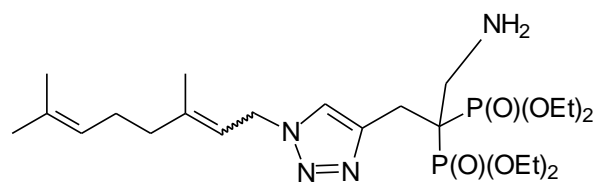
¹H NMR Spectrum of Compound 9 (CDCl₃, 500 MHz)



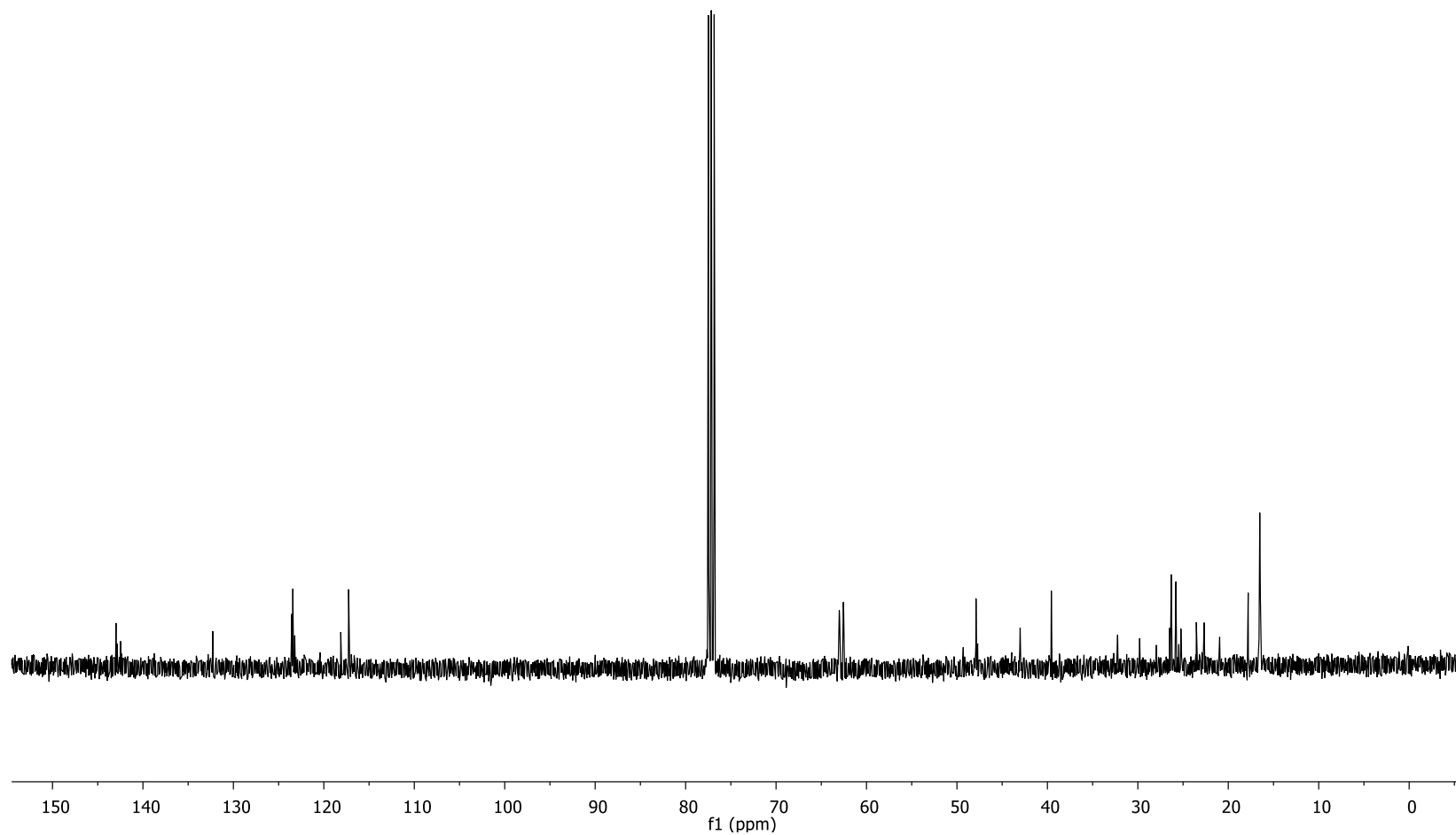
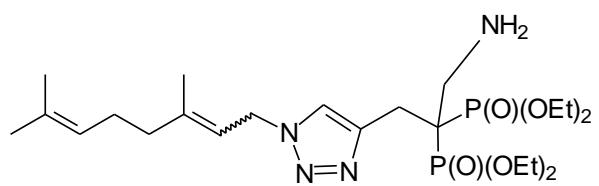
¹³C NMR Spectrum of Compound 9 (CDCl₃, 126 MHz)



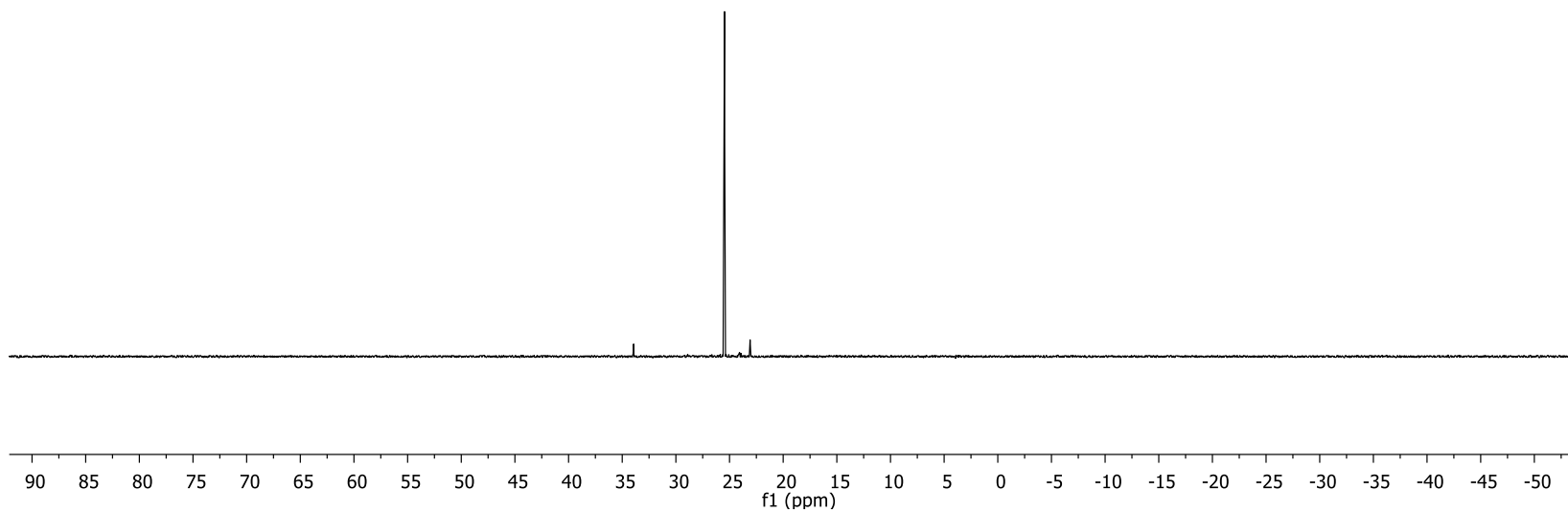
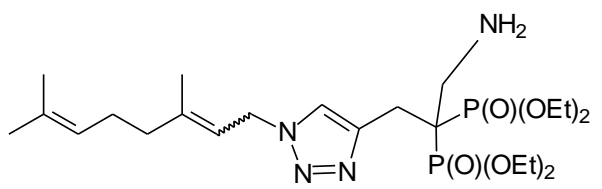
³¹P NMR Spectrum of Compound 9 (CDCl₃, 202 MHz)



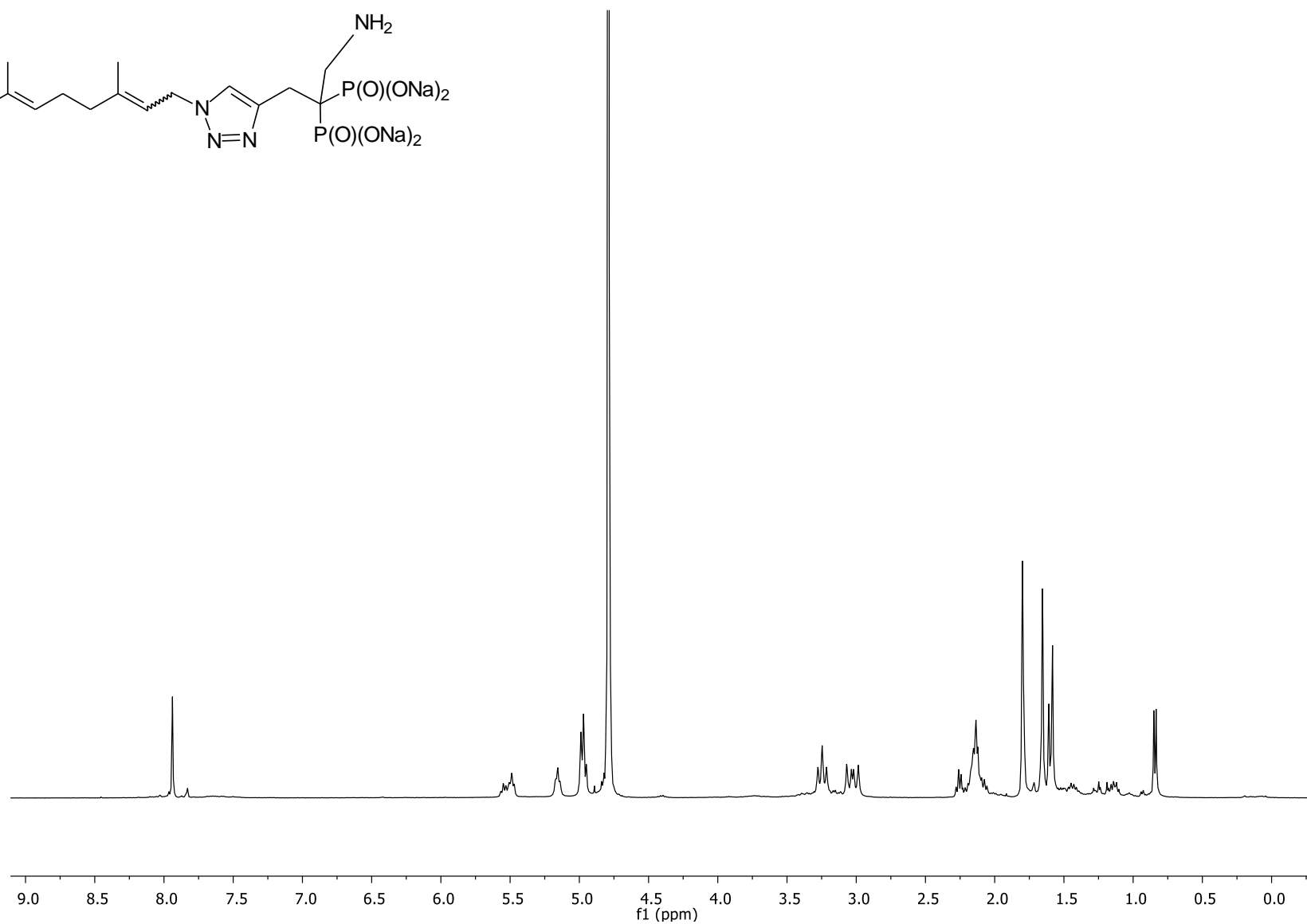
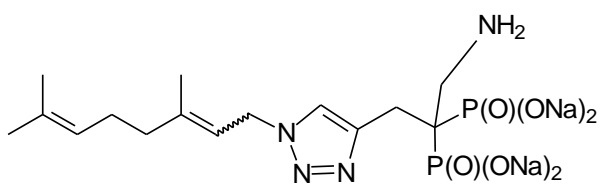
¹H NMR Spectrum of Compound **16** (CDCl₃, 400 MHz)



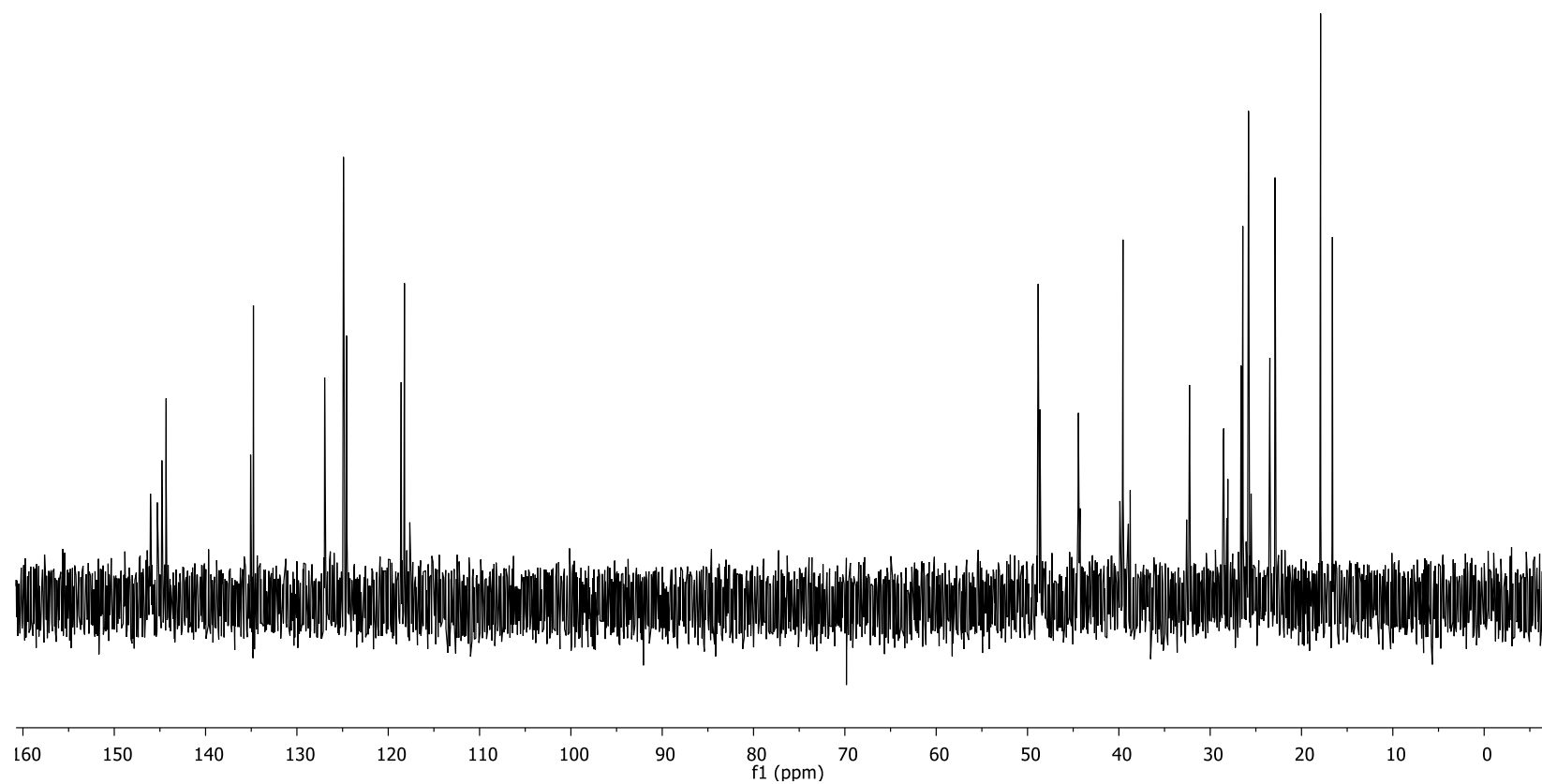
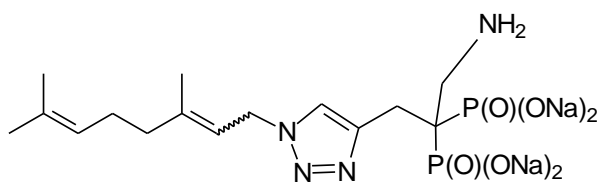
¹³C NMR Spectrum of Compound **16** (CDCl₃, 100 MHz)



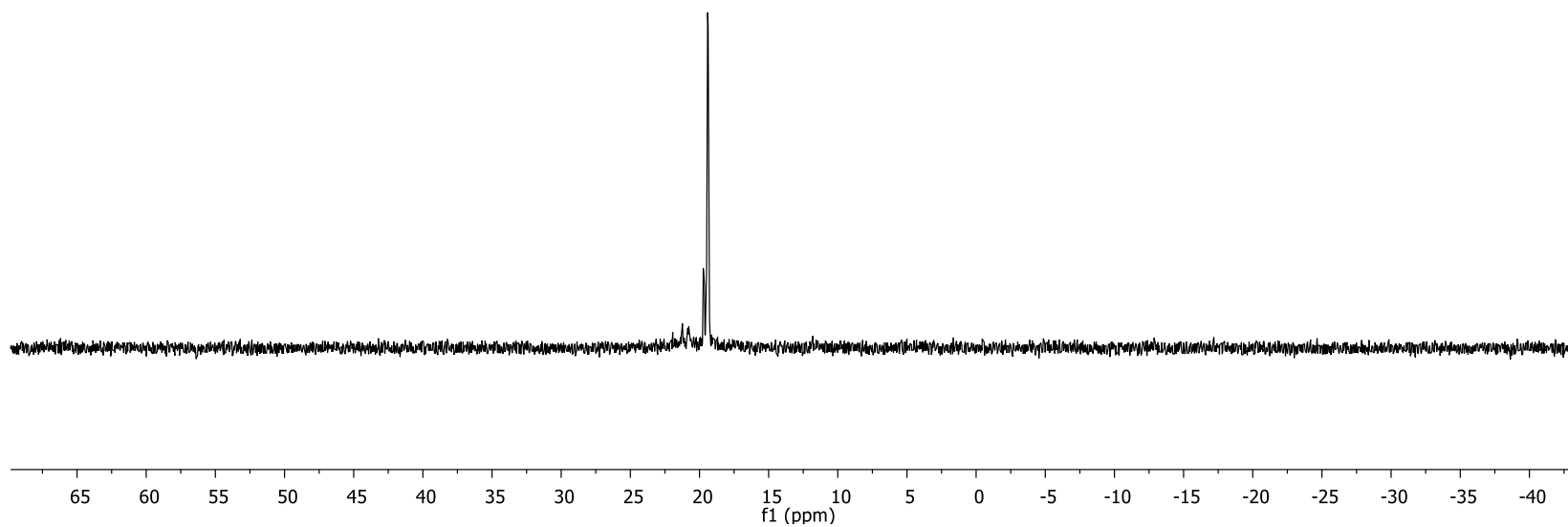
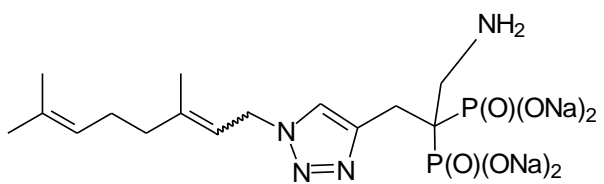
^{31}P NMR Spectrum of Compound **16** (CDCl_3 , 162 MHz)



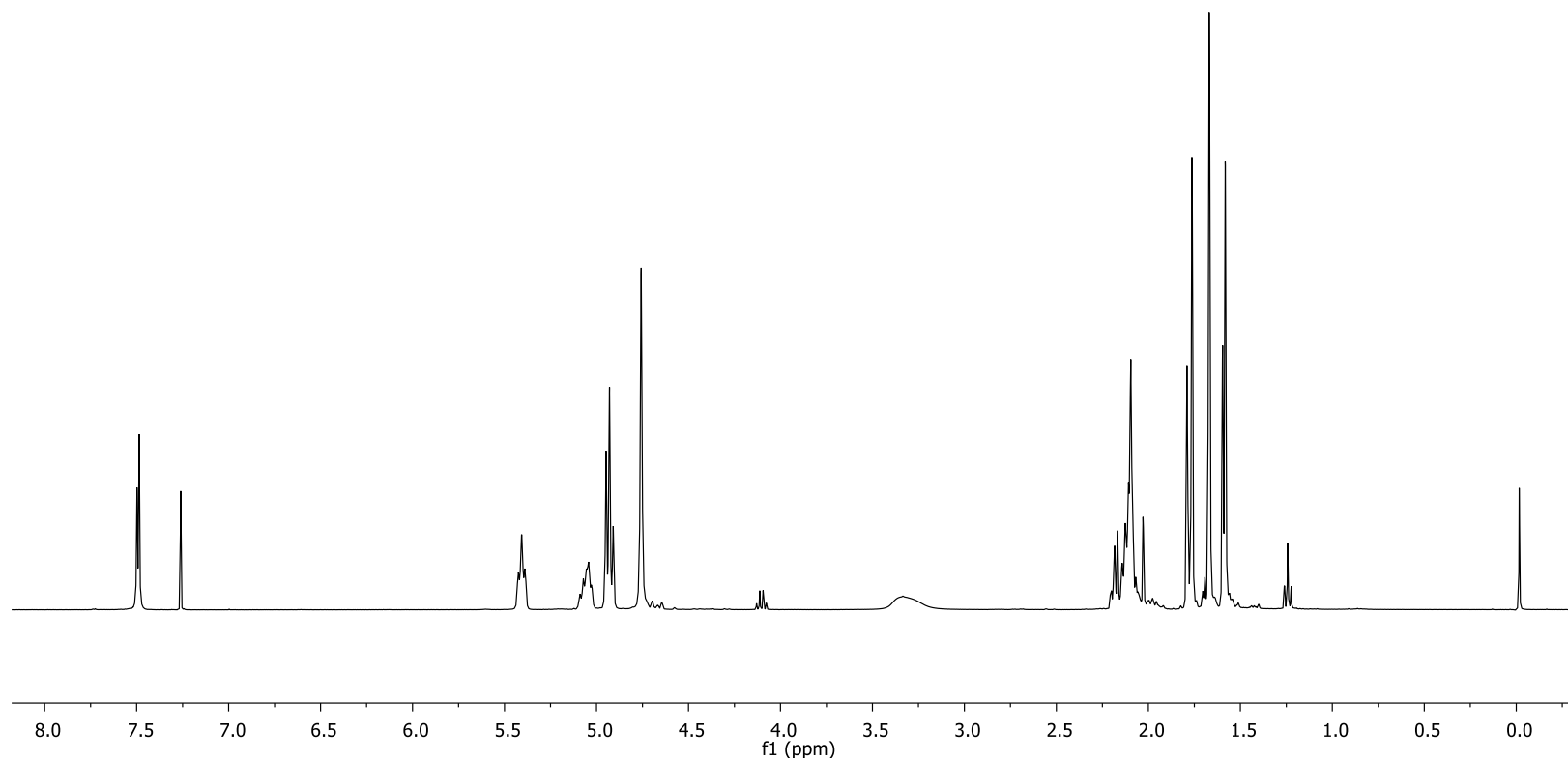
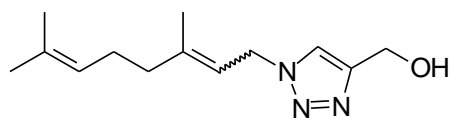
^1H NMR Spectrum of Compound 17 (D_2O , 400 MHz)



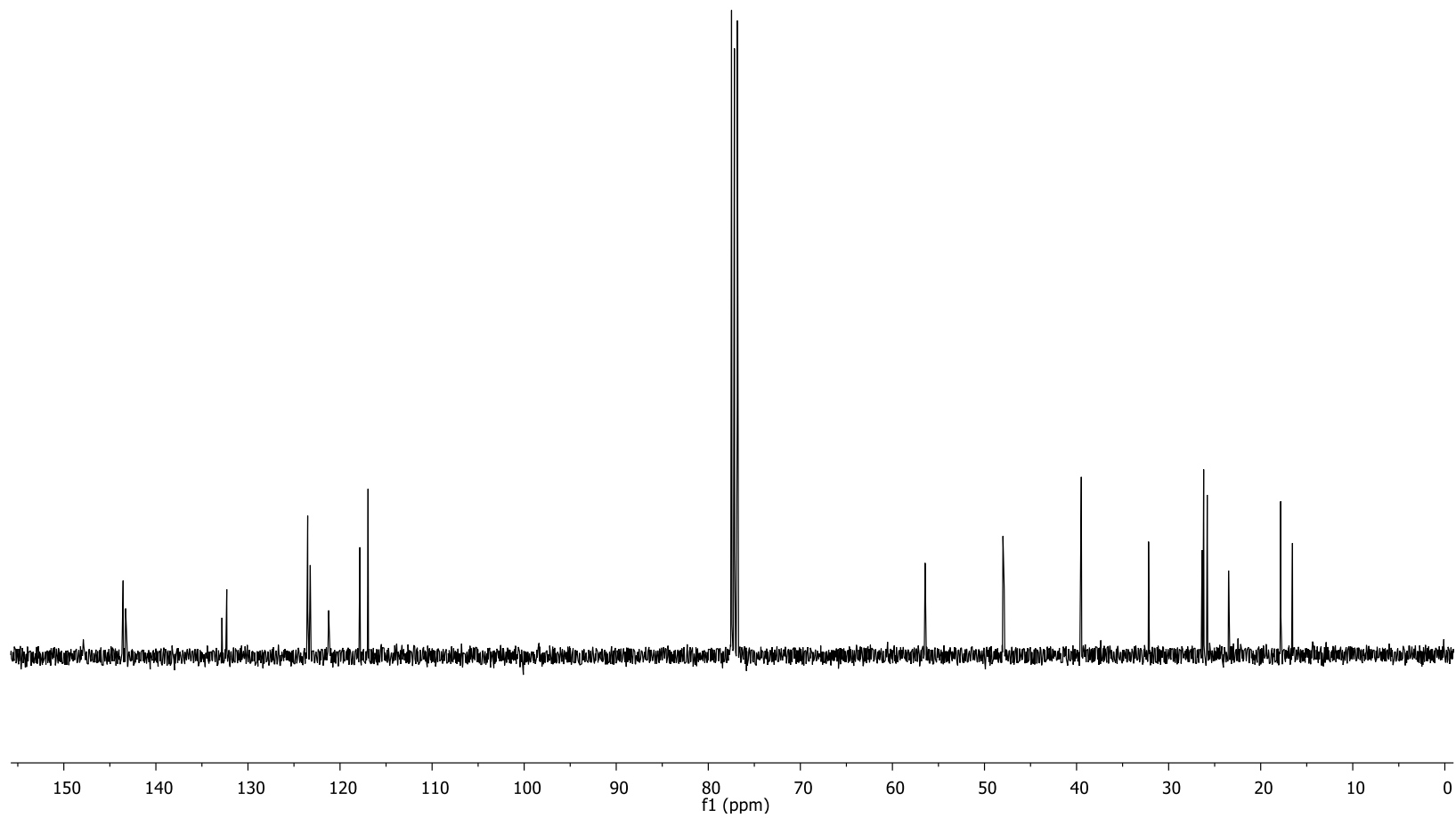
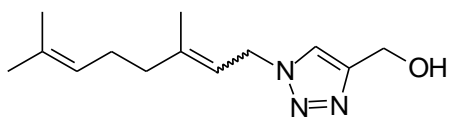
^{13}C NMR Spectrum of Compound 17 (D_2O , 100 MHz)



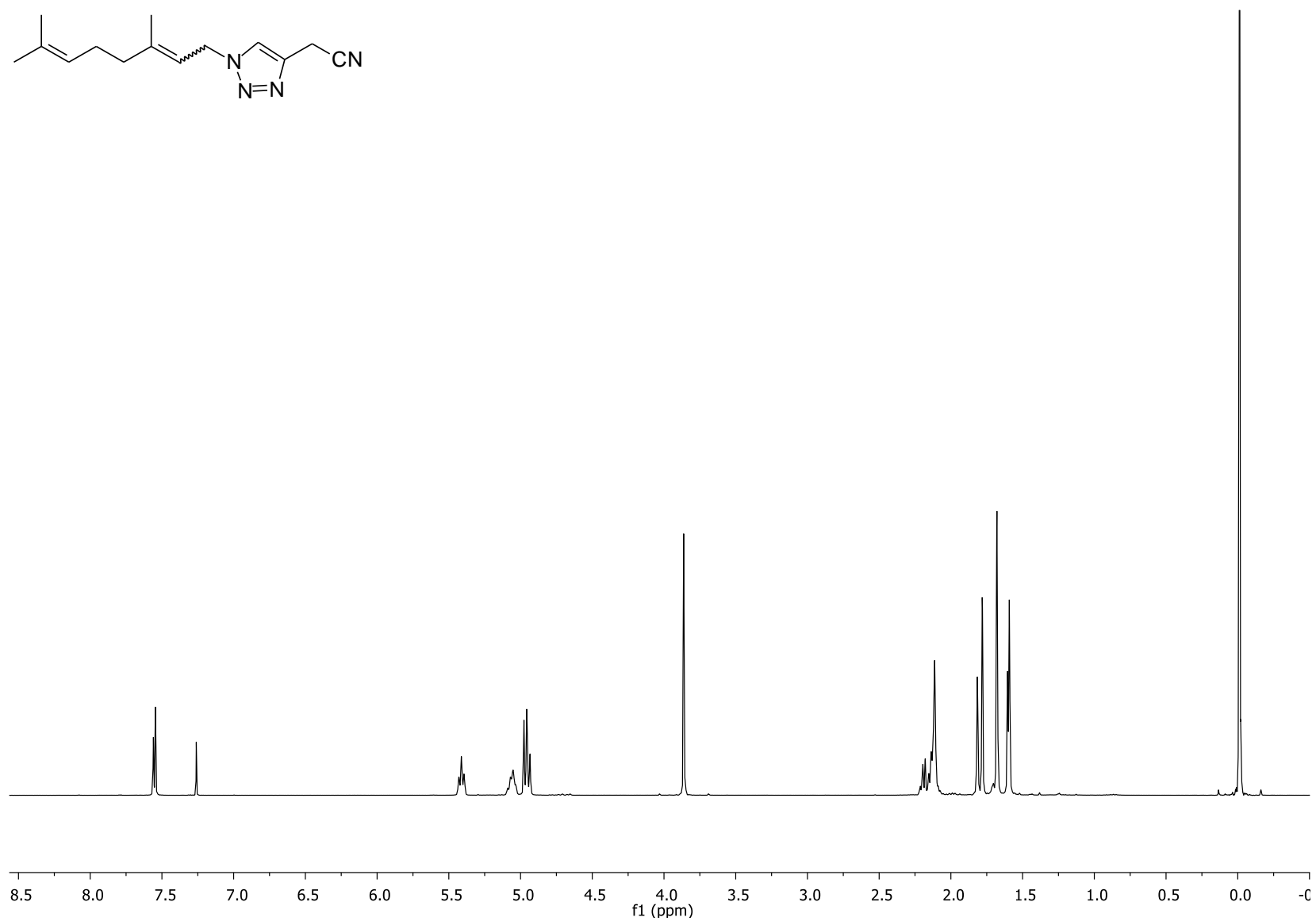
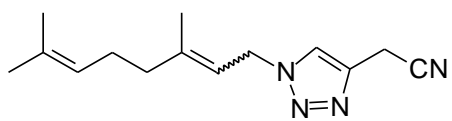
^{31}P NMR Spectrum of Compound 17 (D_2O , 162 MHz)



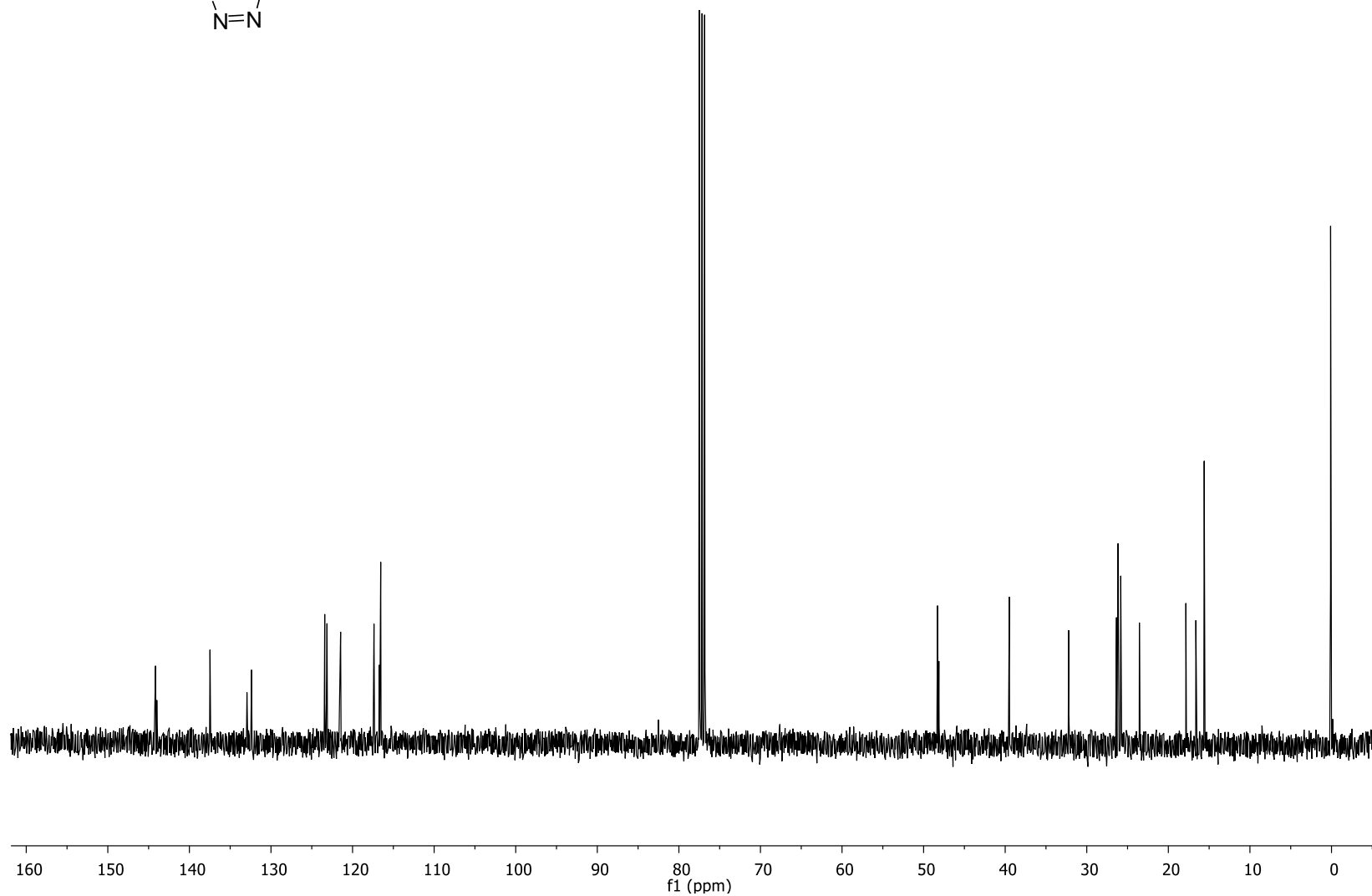
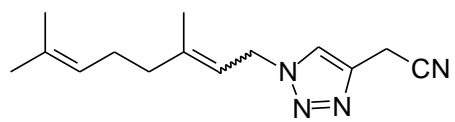
¹H NMR Spectrum of Compound **19** (CDCl₃, 400 MHz)



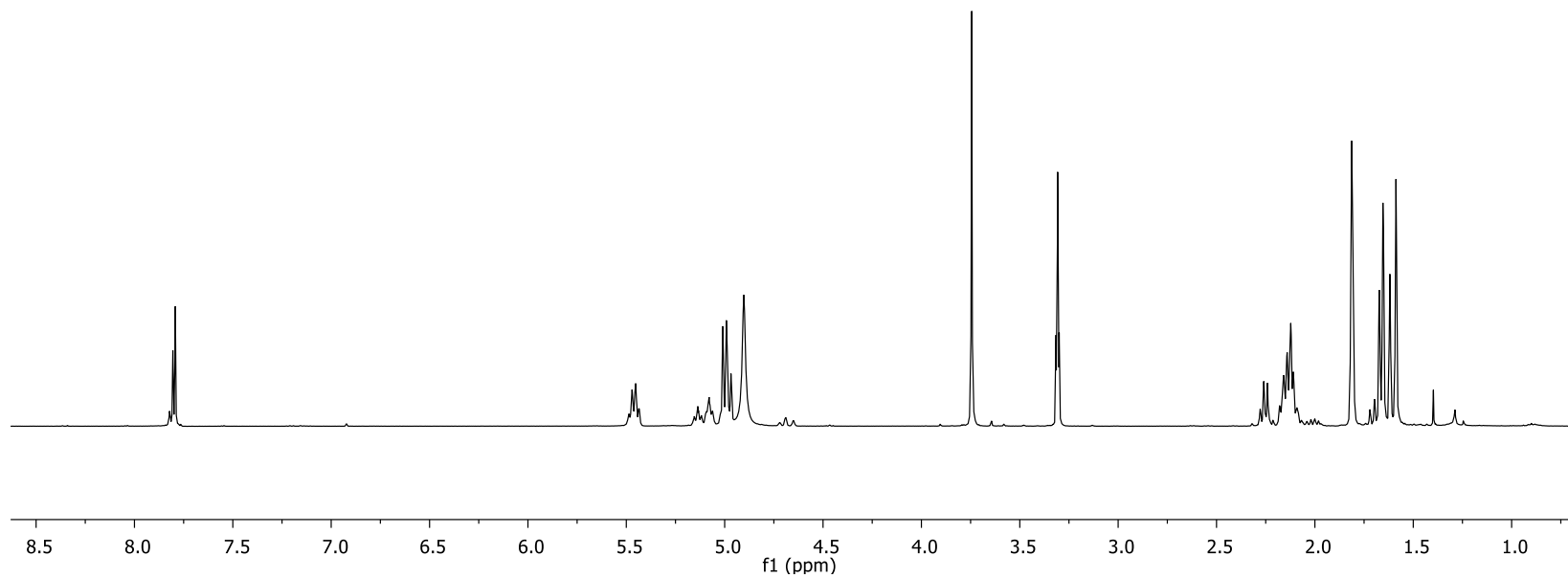
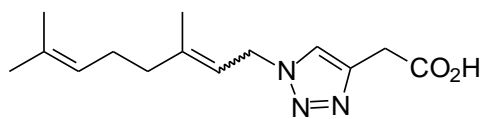
^{13}C NMR Spectrum of Compound 19 (CDCl_3 , 100 MHz)



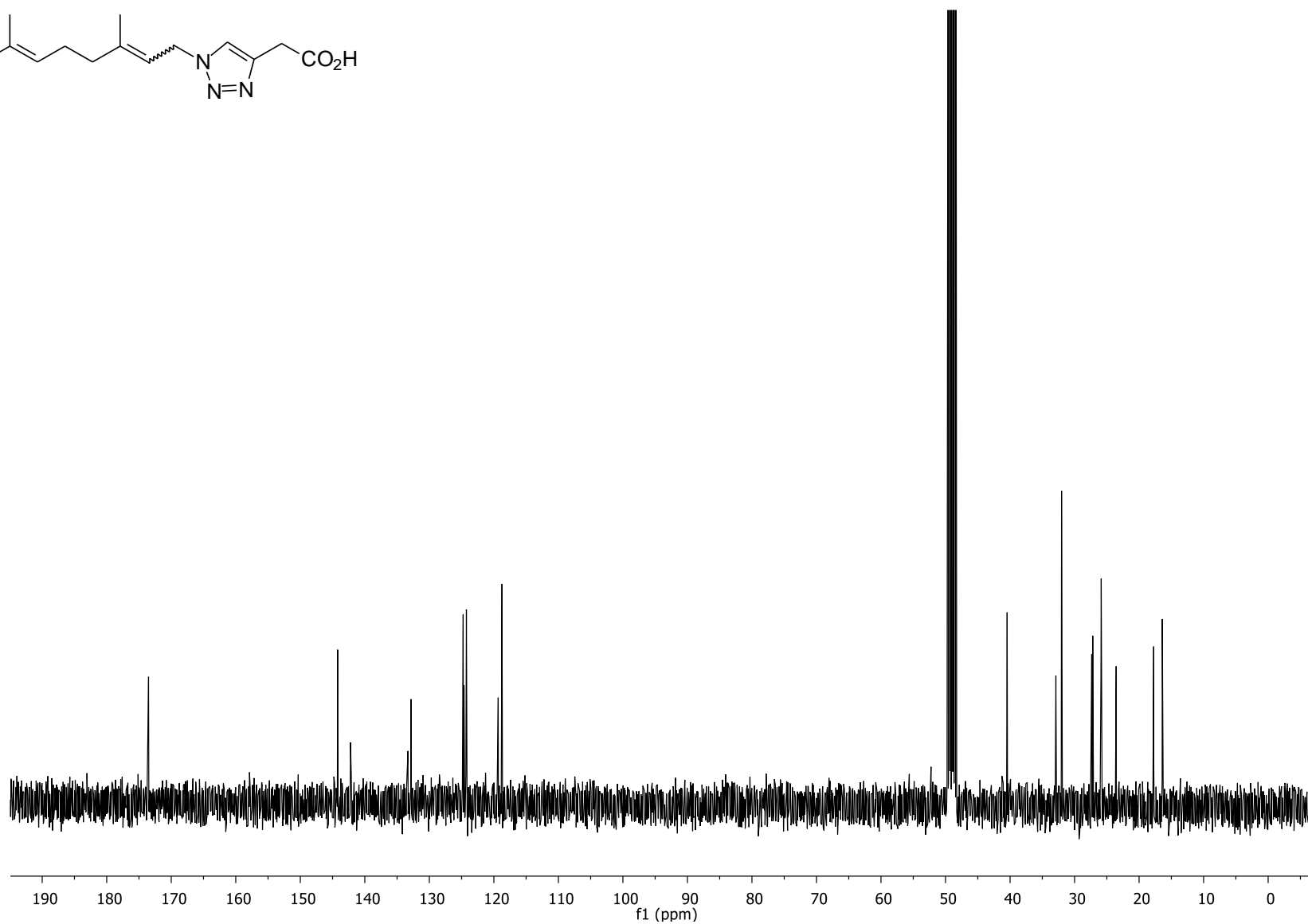
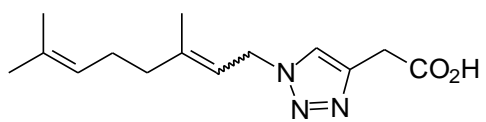
¹H NMR Spectrum of Compound **20** (CDCl₃, 400 MHz)



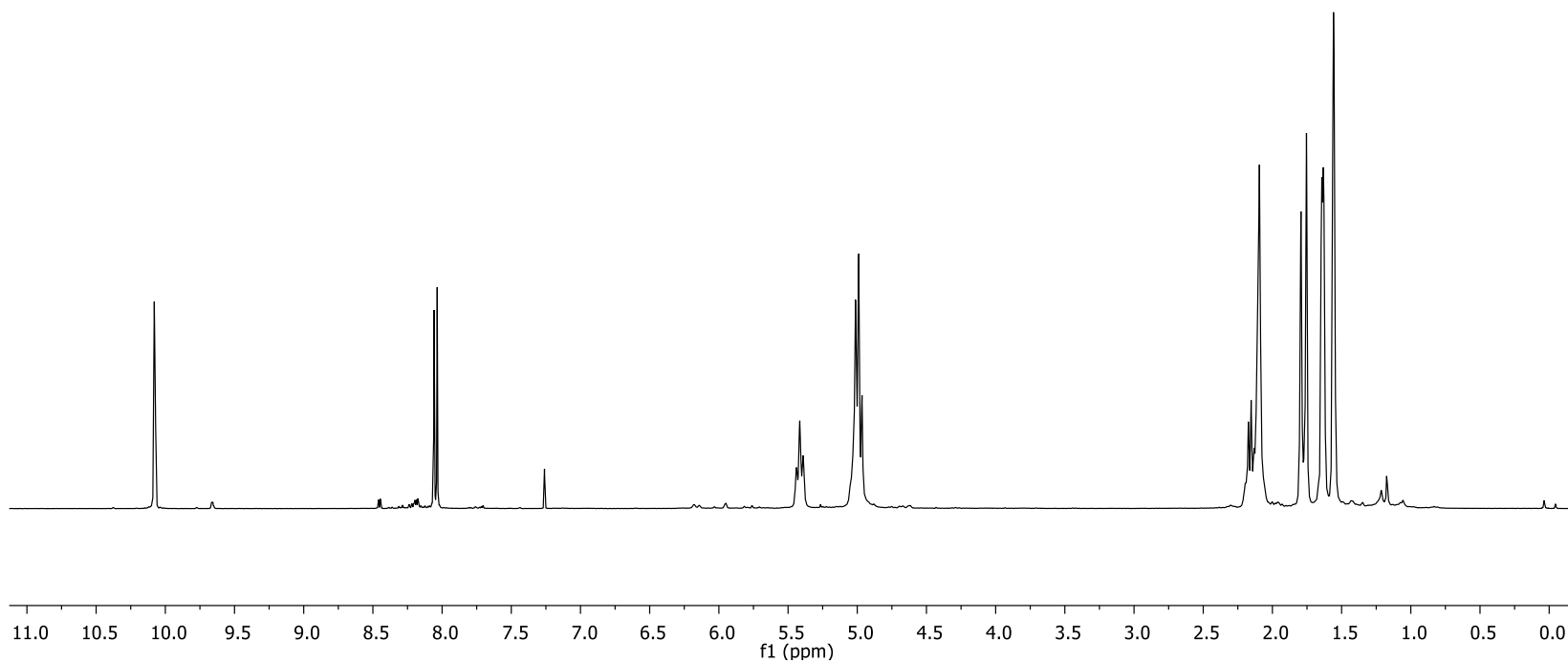
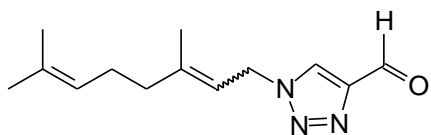
^{13}C NMR Spectrum of Compound **20** (CDCl_3 , 100 MHz)



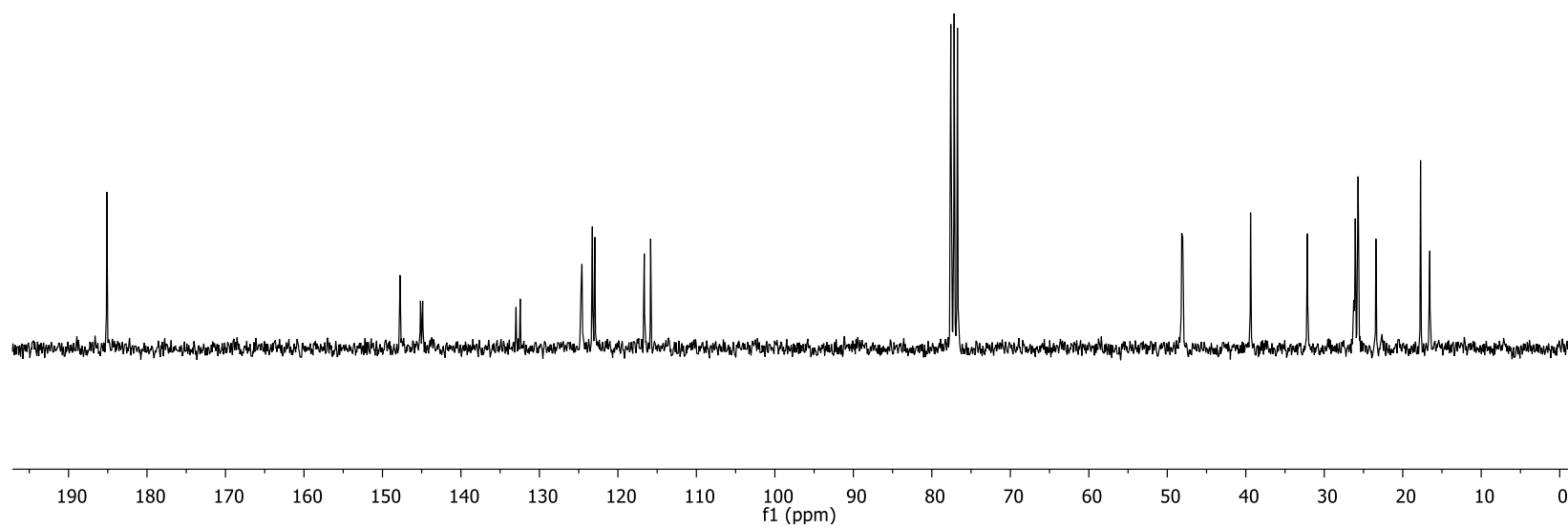
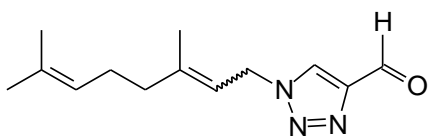
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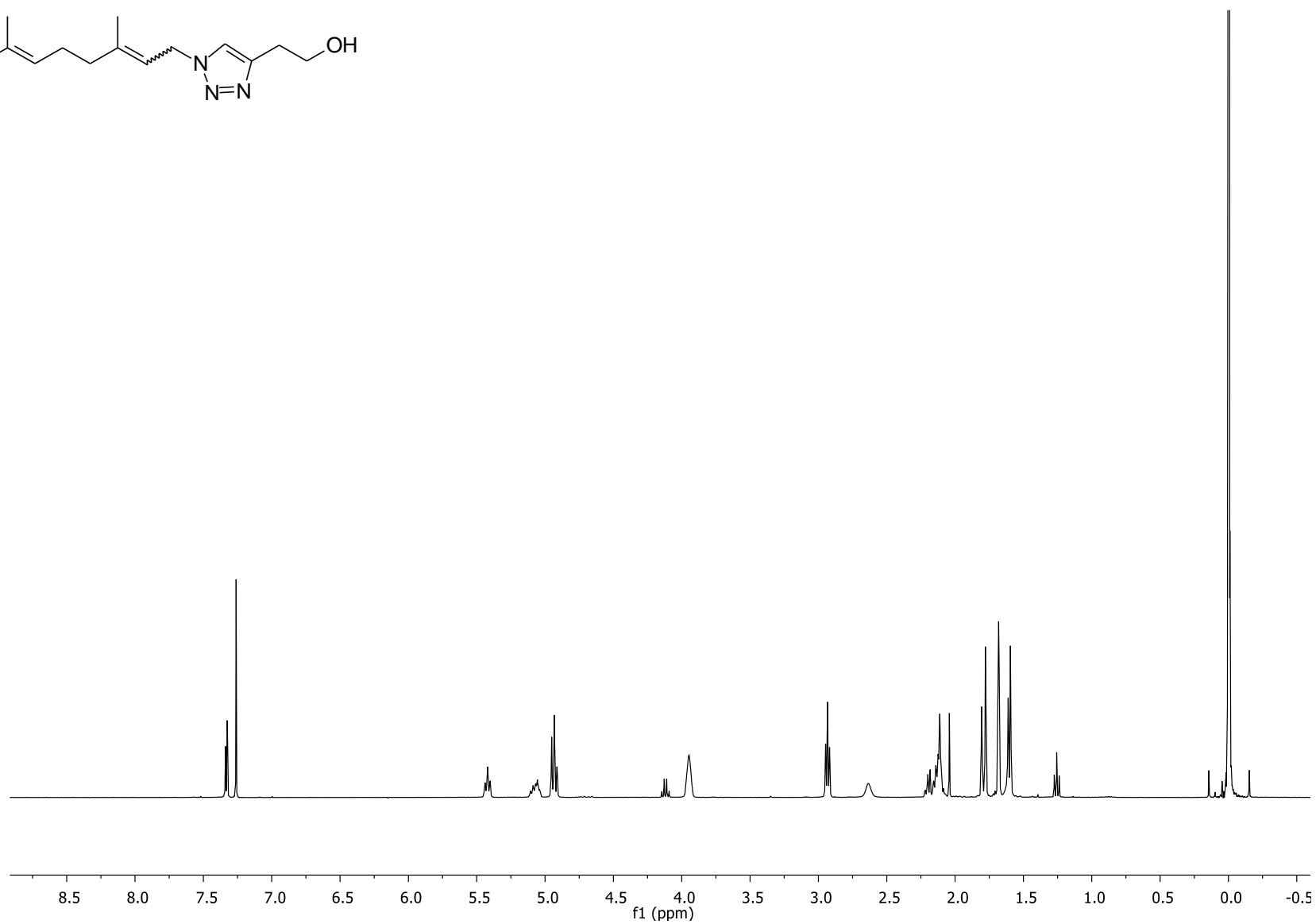
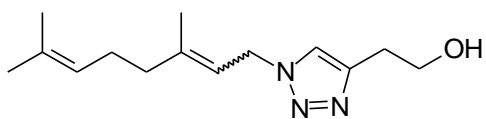
¹³C NMR Spectrum of Compound 21 (MeOD, 100 MHz)



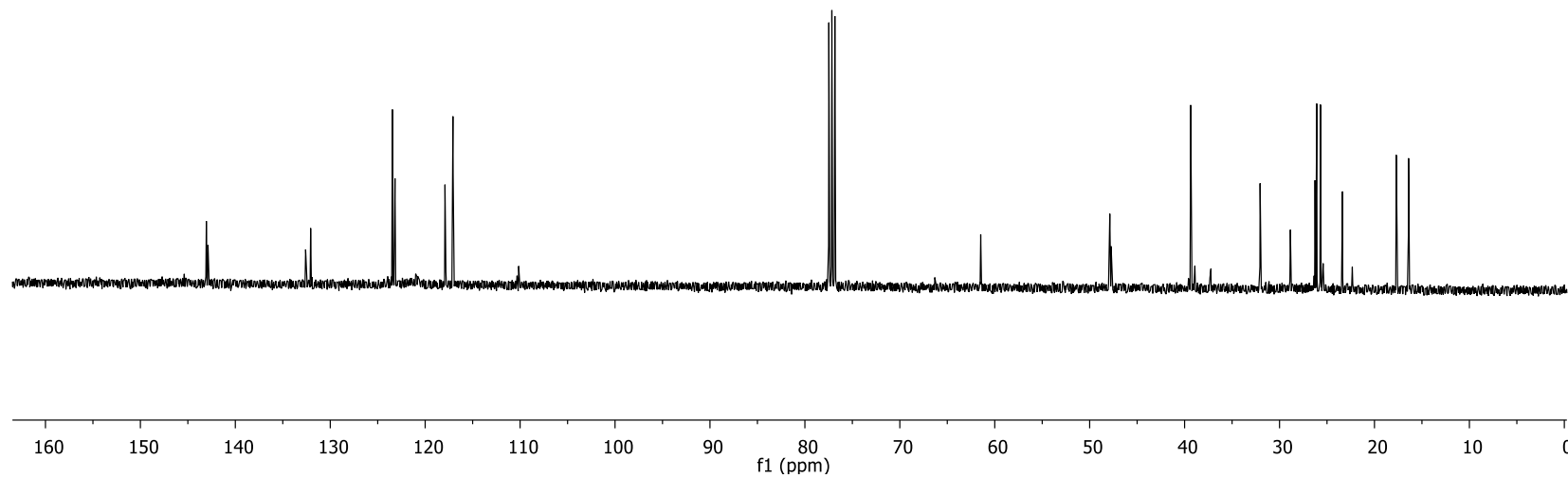
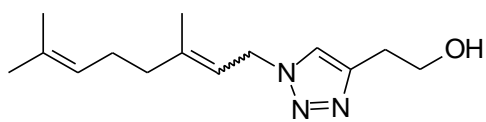
¹H NMR Spectrum of Compound 22 (CDCl₃, 400 MHz)



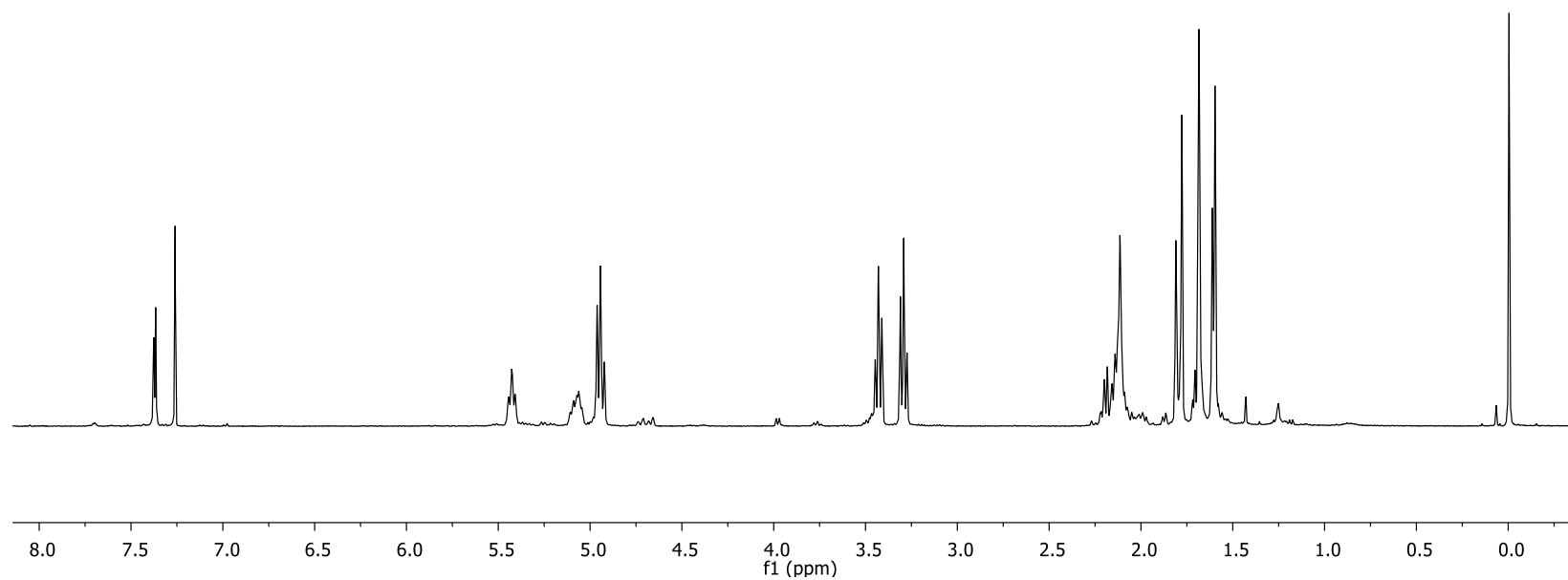
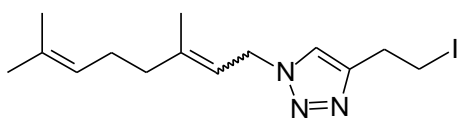
¹³C NMR Spectrum of Compound **22** (CDCl₃, 75.5 MHz)



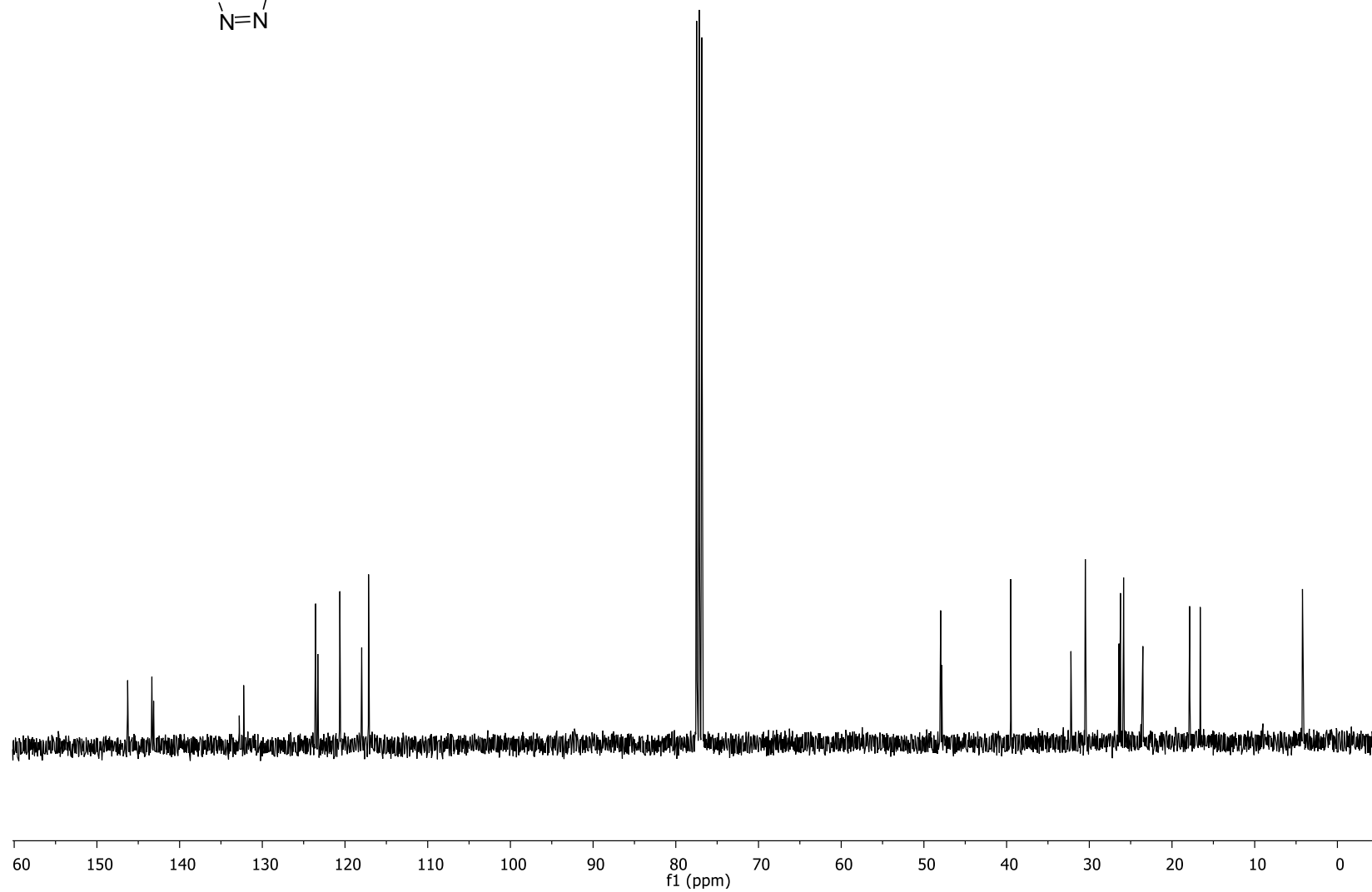
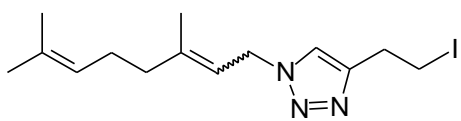
¹H NMR Spectrum of Compound **24** (CDCl₃, 400 MHz)



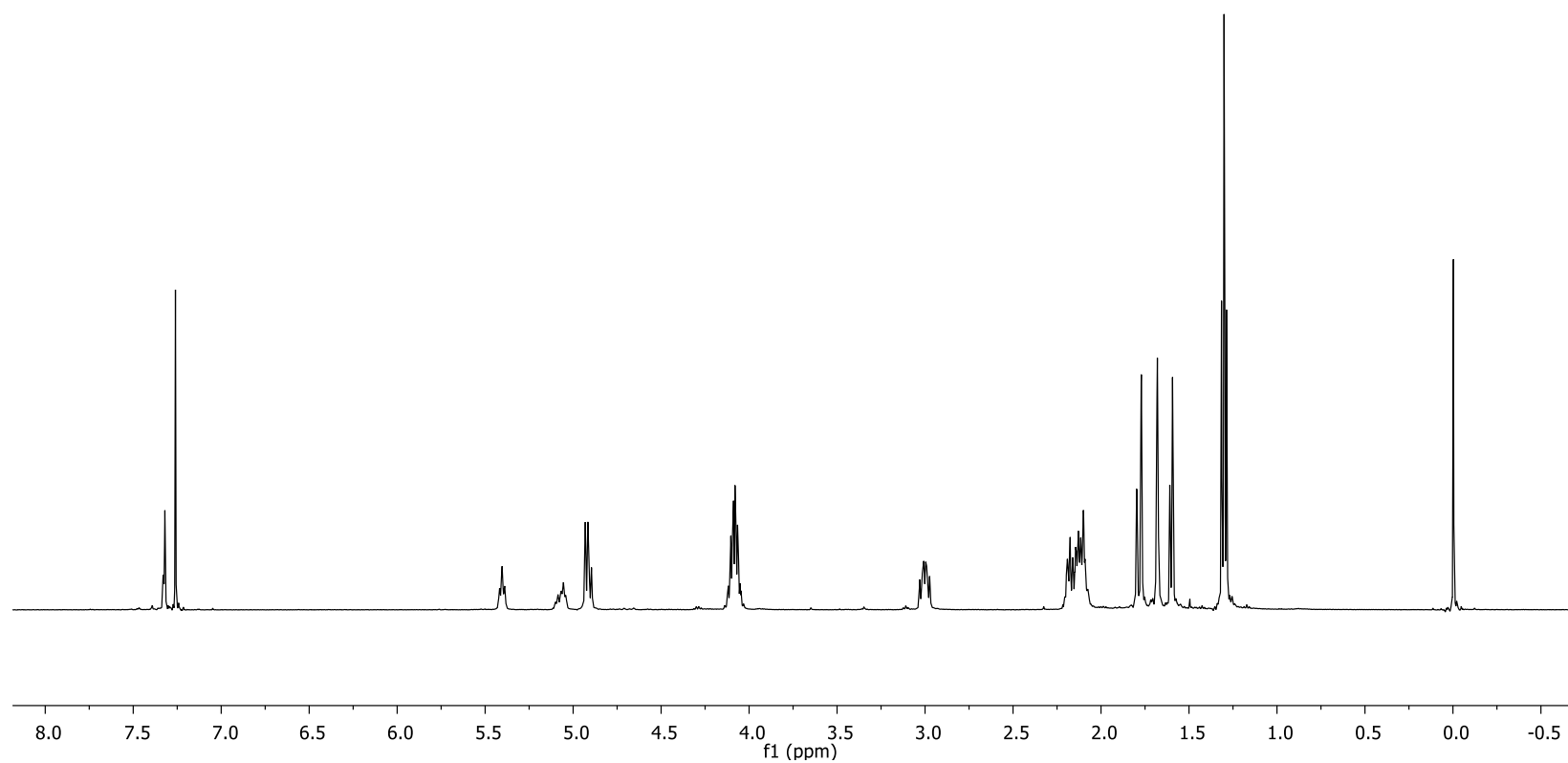
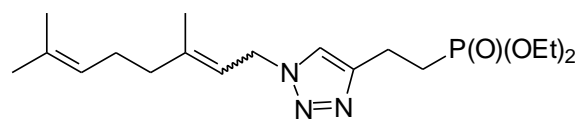
¹³C NMR Spectrum of Compound **24** (CDCl₃, 100 MHz)



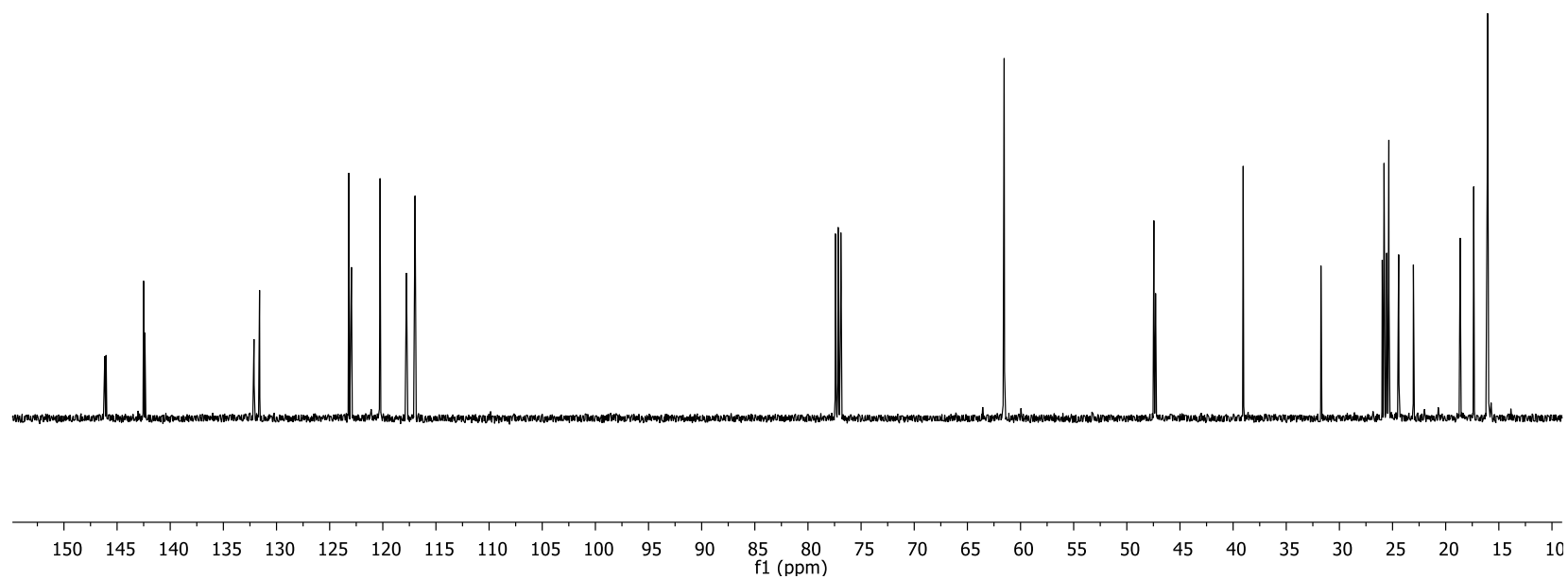
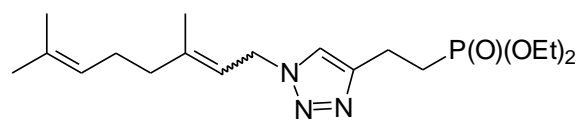
¹H NMR Spectrum of Compound **25** (CDCl₃, 400 MHz)



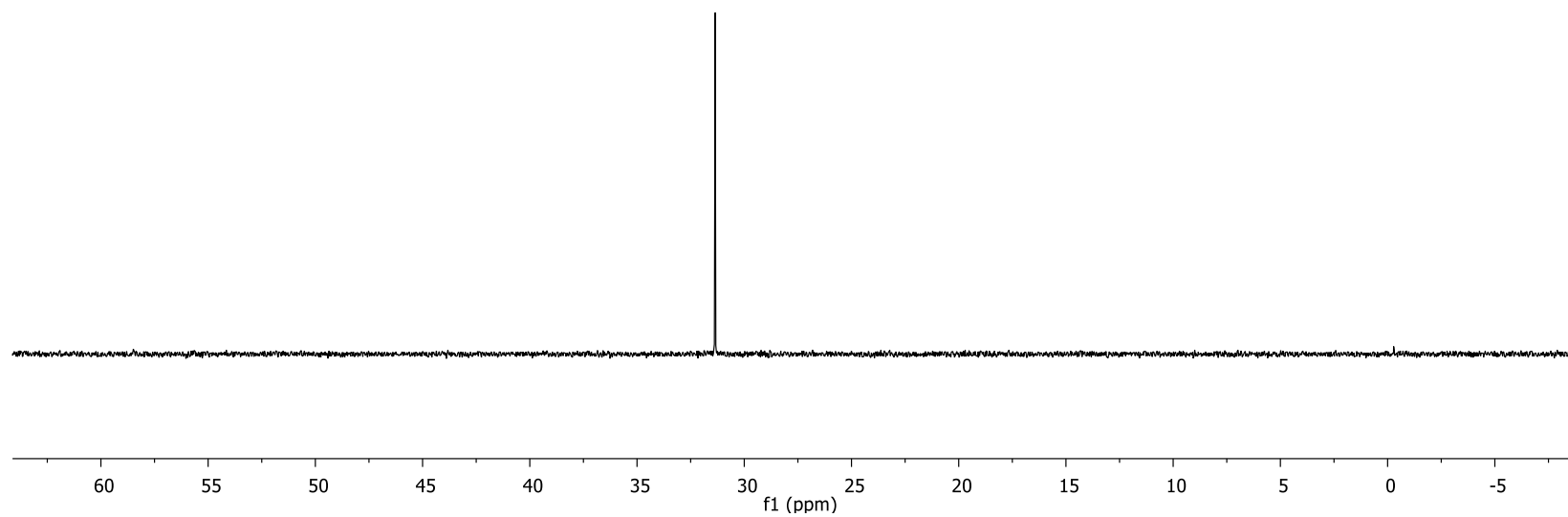
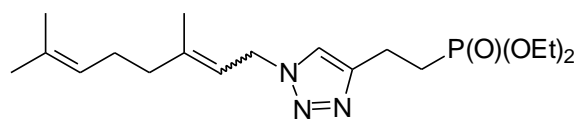
^{13}C NMR Spectrum of Compound **25** (CDCl_3 , 100 MHz)



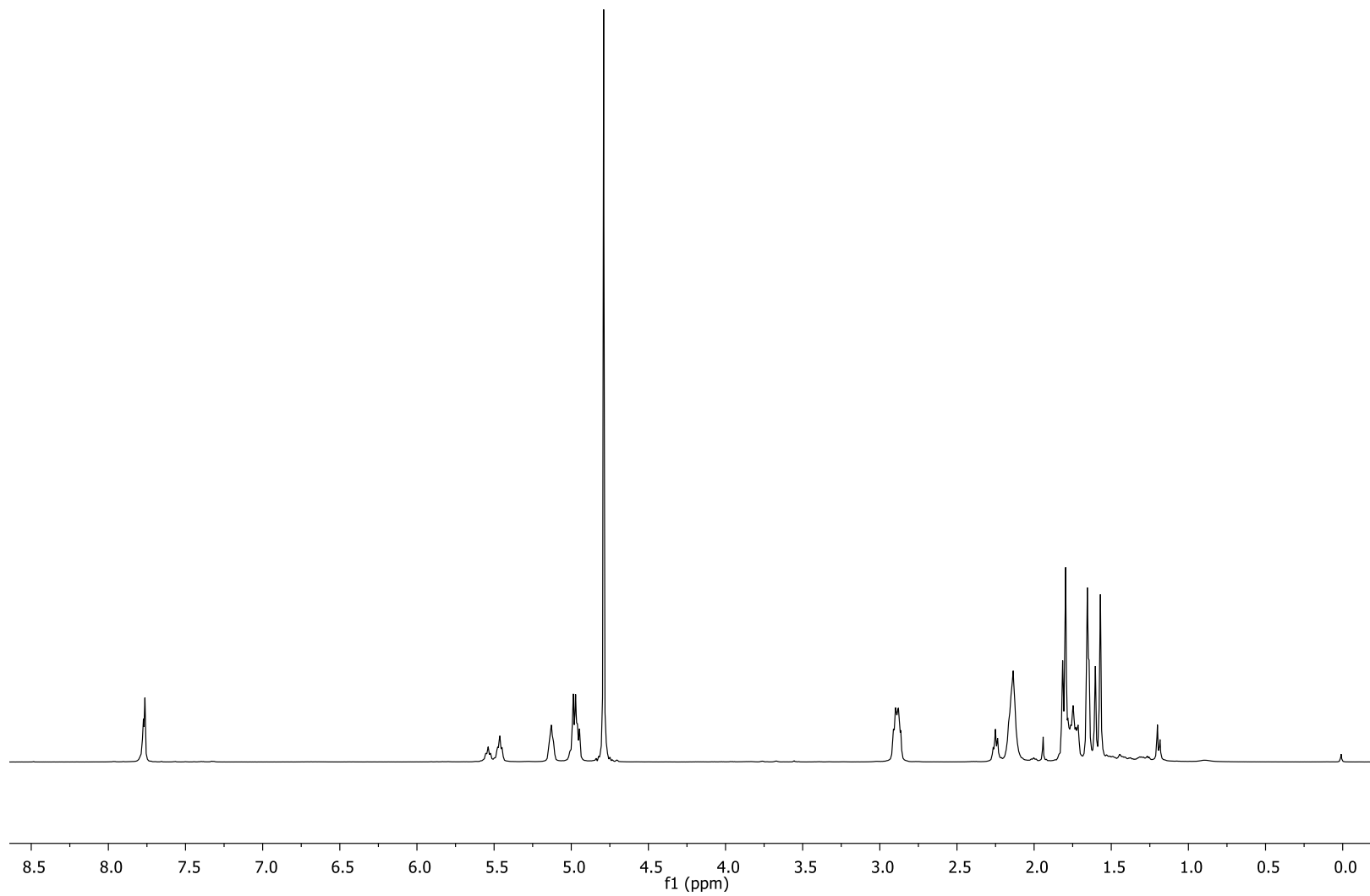
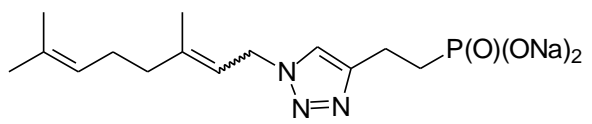
¹H NMR Spectrum of Compound **26** (CDCl₃, 500 MHz)



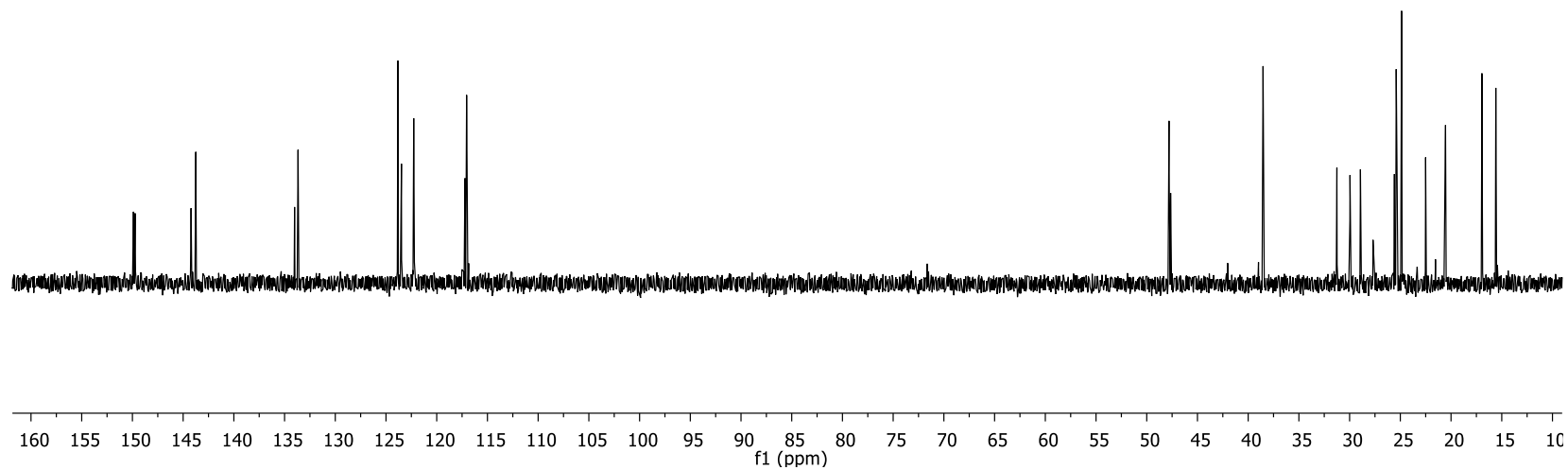
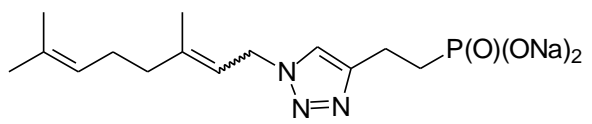
¹³C NMR Spectrum of Compound **26** (CDCl₃, 126 MHz)



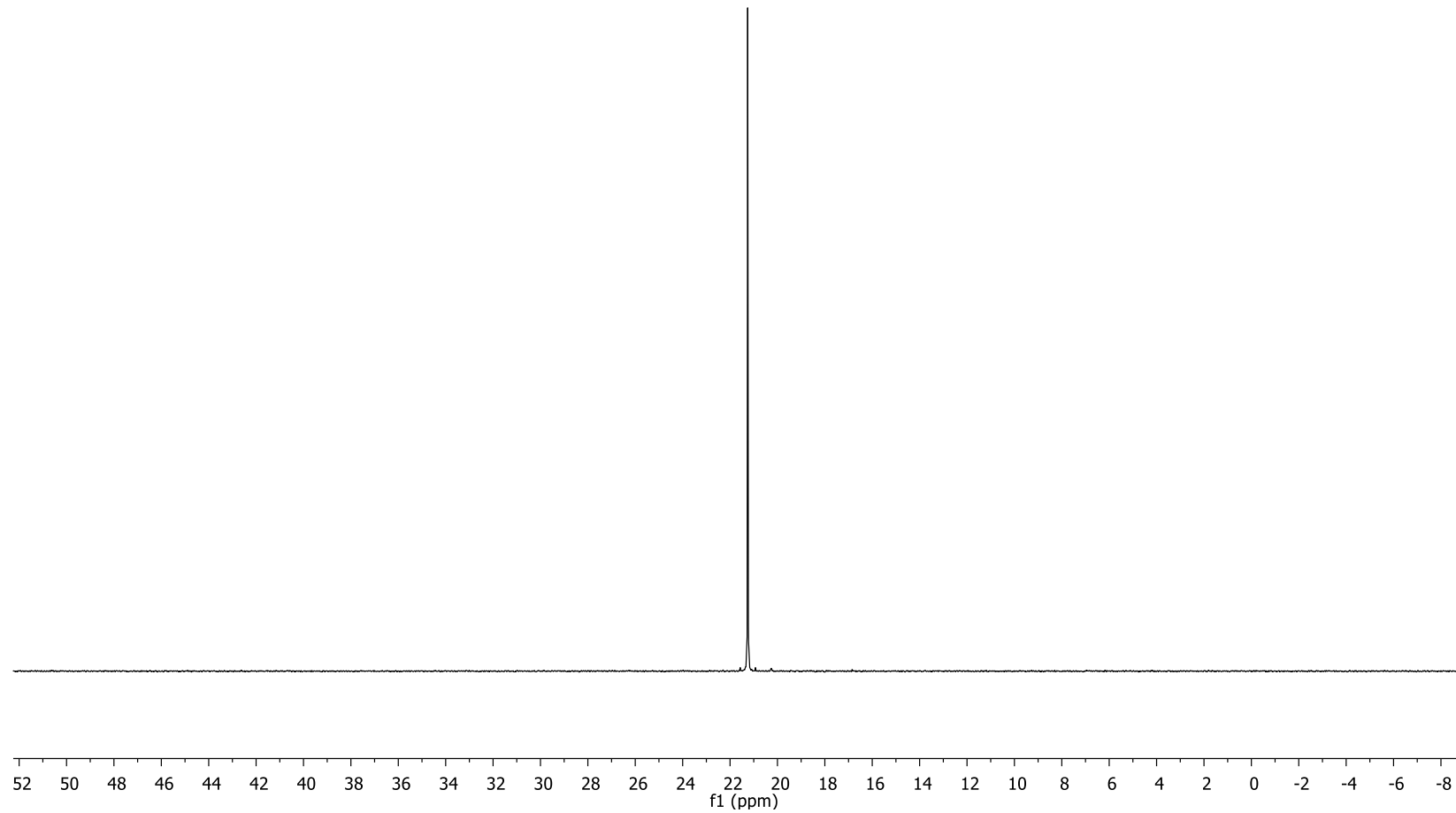
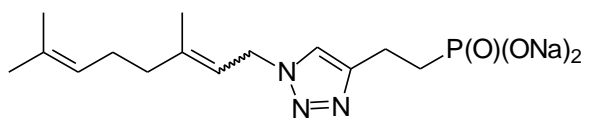
³¹P NMR Spectrum of Compound **26** (CDCl₃, 202 MHz)



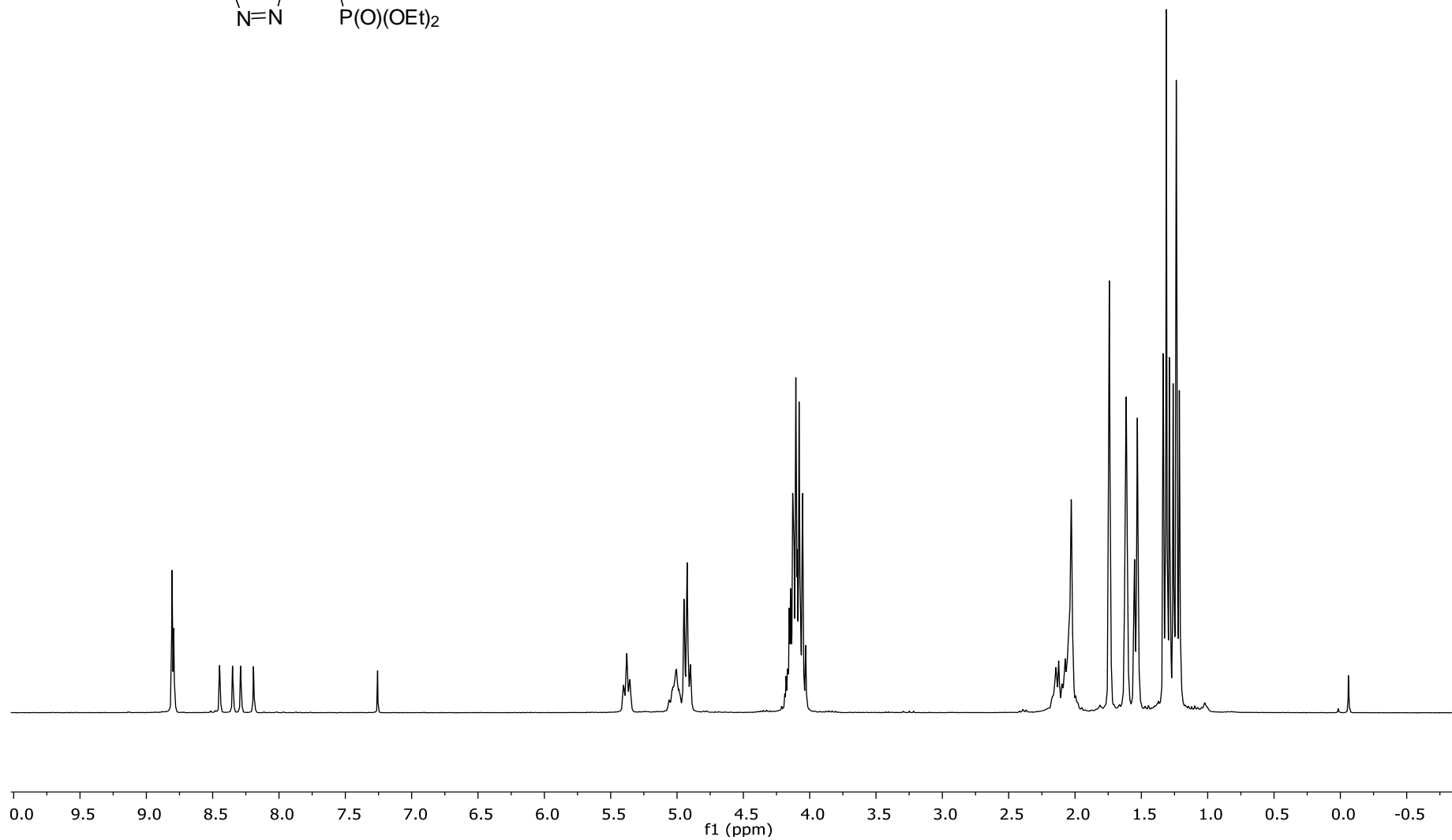
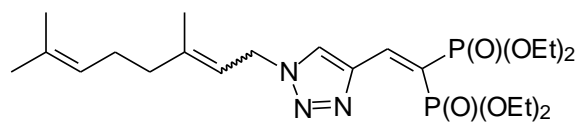
¹H NMR Spectrum of Compound **27** (D₂O, 500 MHz)



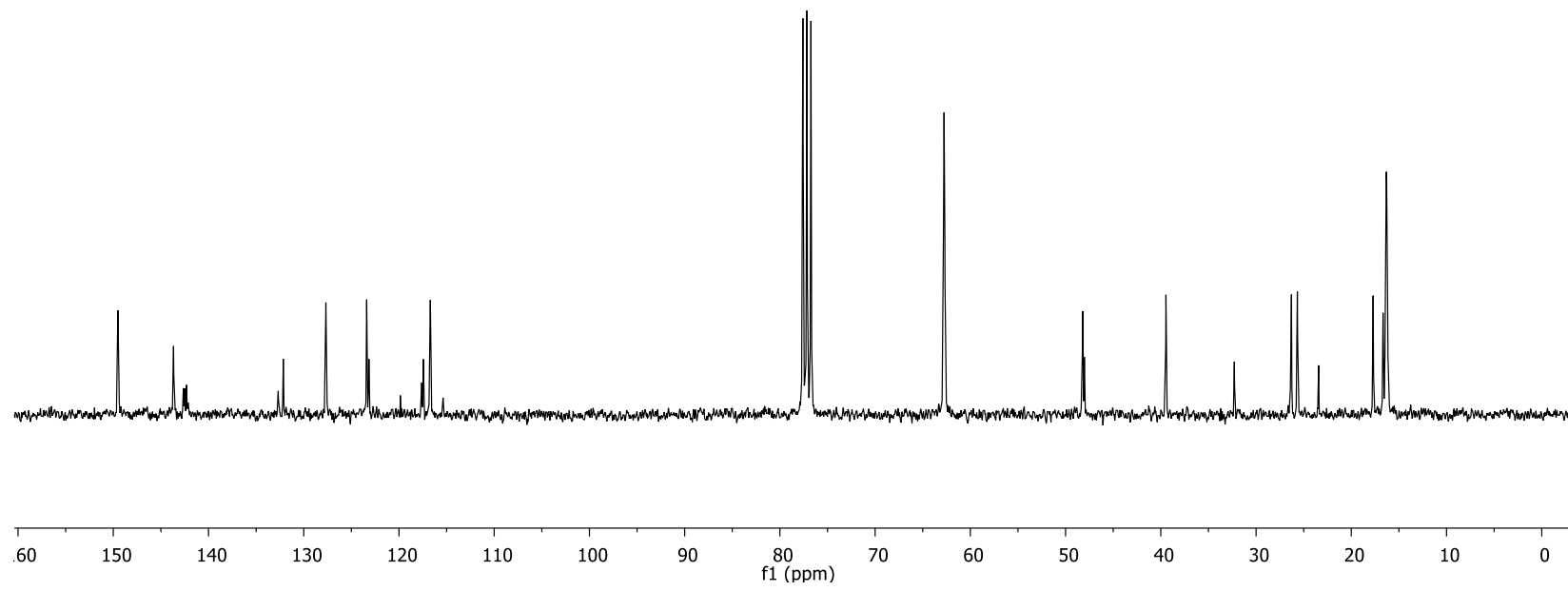
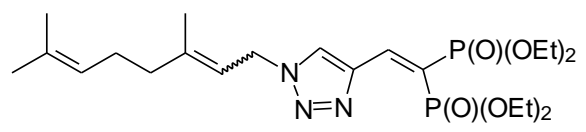
^{13}C NMR Spectrum of Compound **27** (D_2O , 126 MHz)



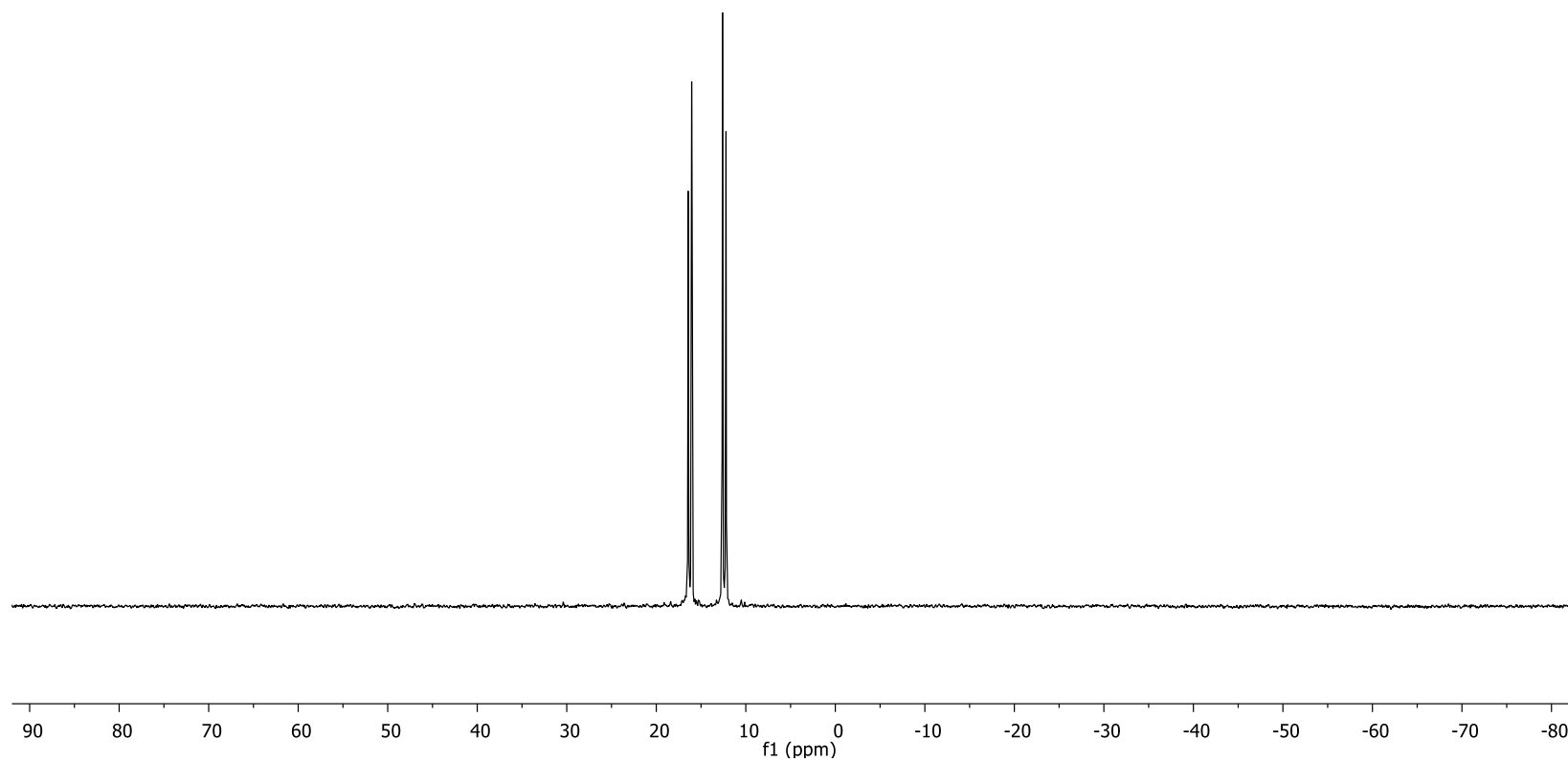
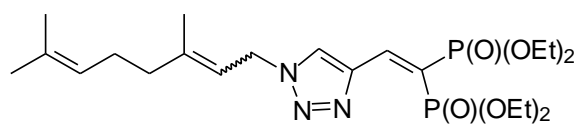
³¹P NMR Spectrum of Compound **27** (D₂O, 202 MHz)



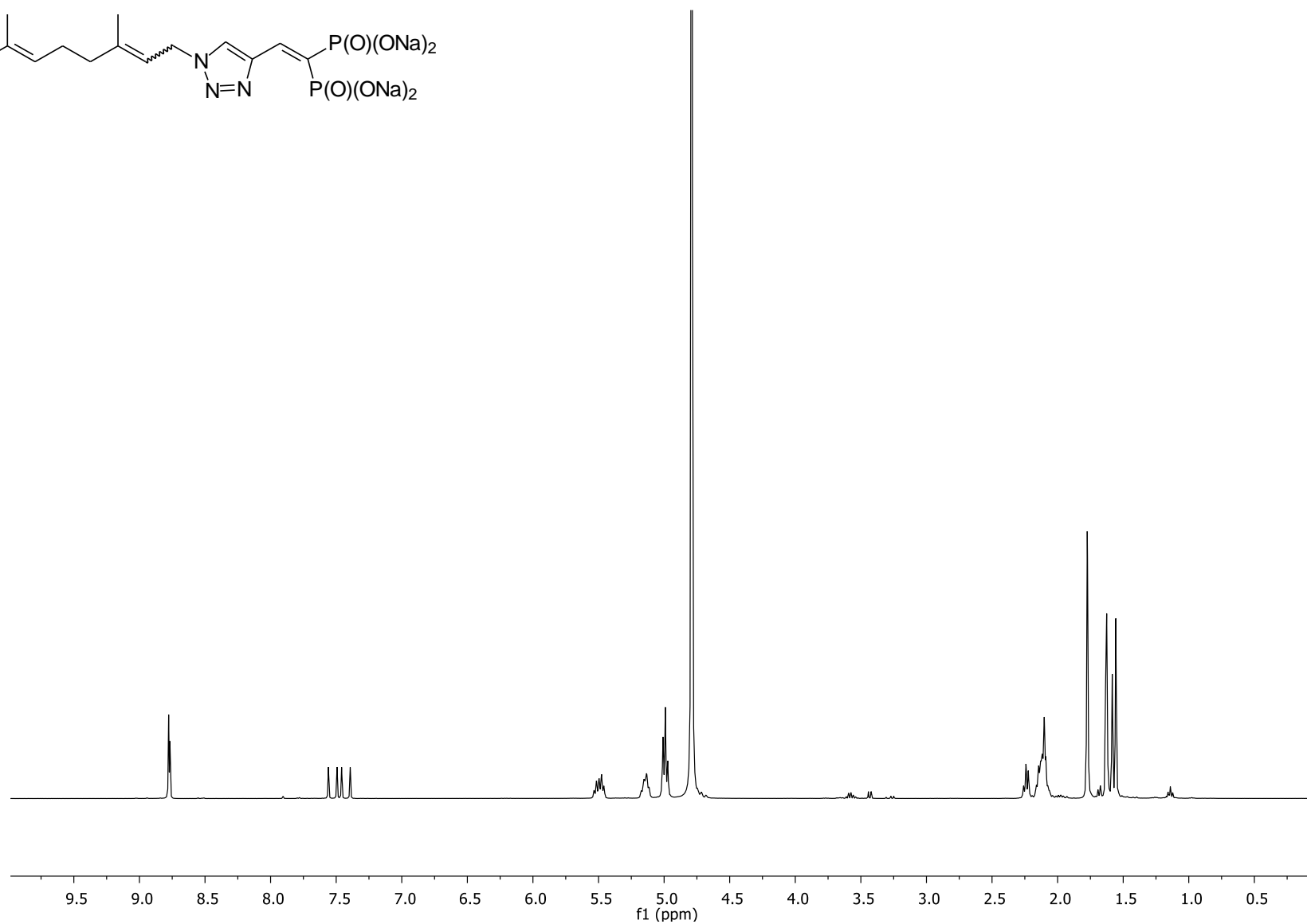
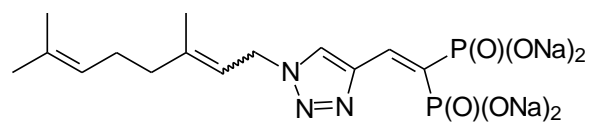
¹H NMR Spectrum of Compound **28** (CDCl₃, 300 MHz)



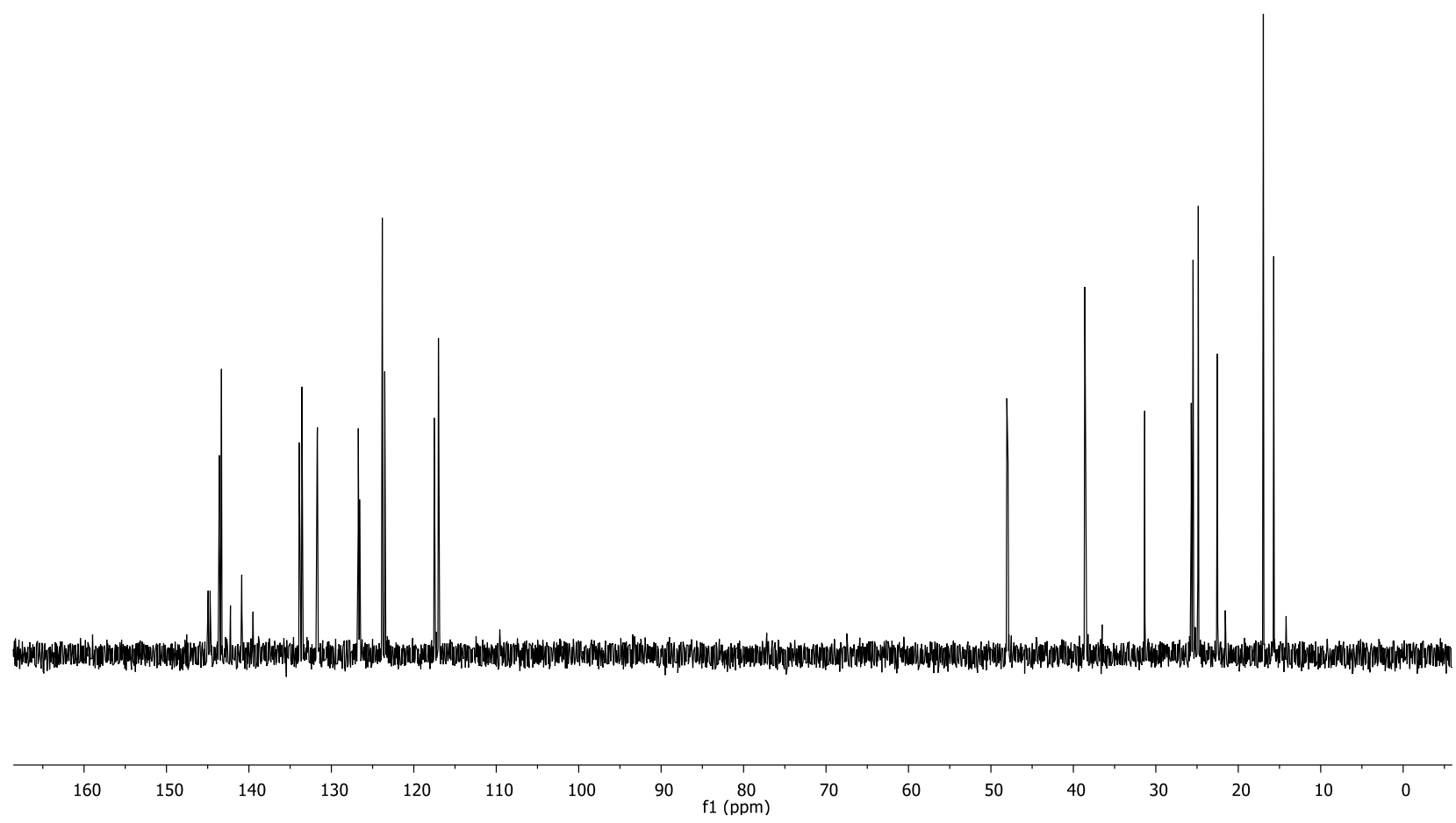
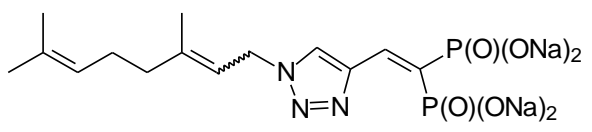
¹³C NMR Spectrum of Compound **28** (CDCl₃, 75.5 MHz)



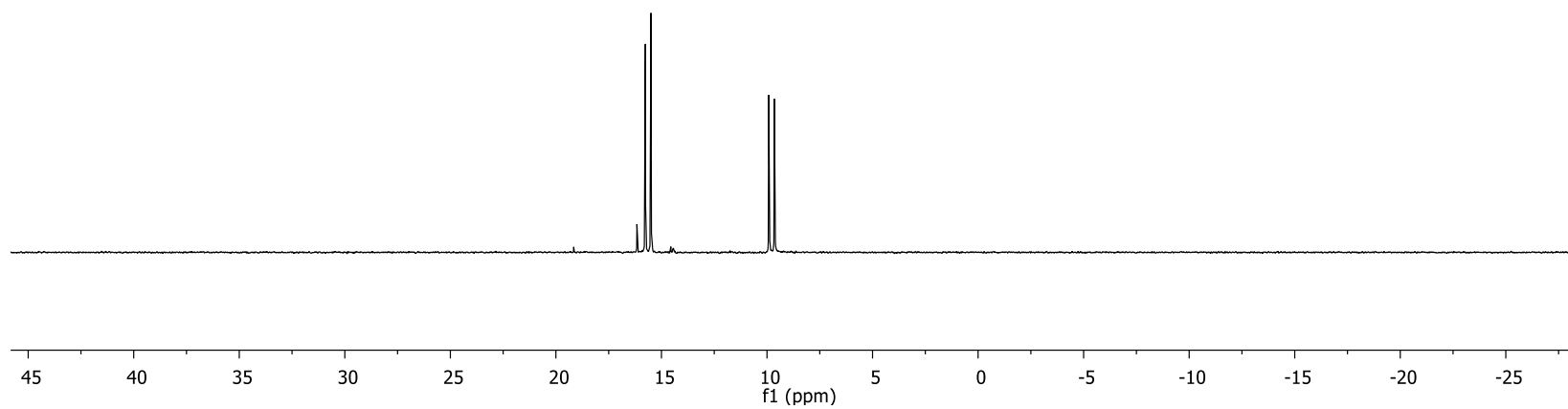
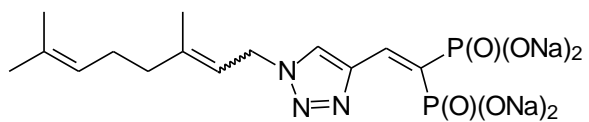
^{31}P NMR Spectrum of Compound **28** (CDCl_3 , 122 MHz)



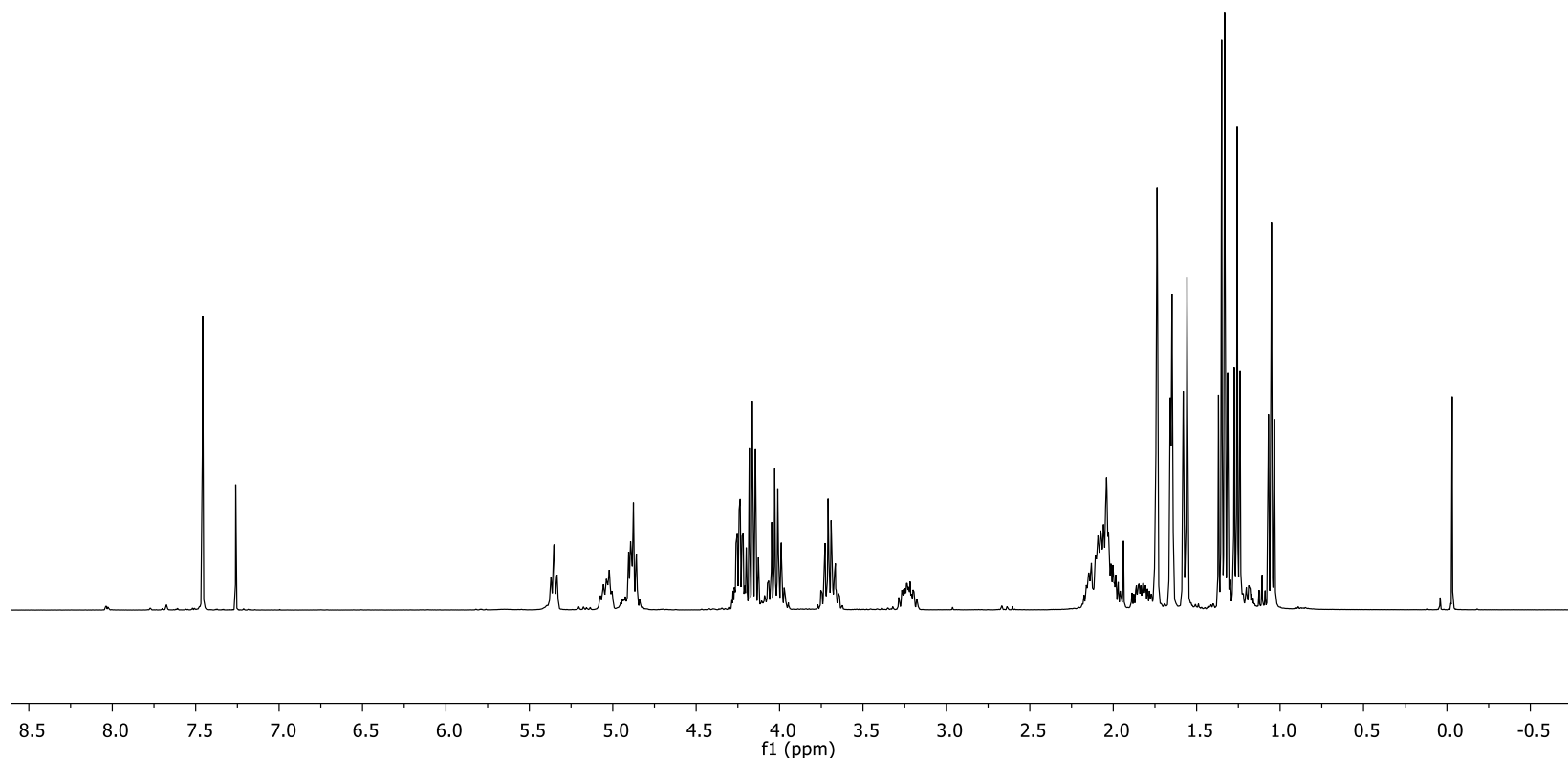
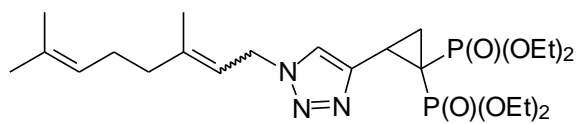
¹H NMR Spectrum of Compound **29** (D₂O, 400 MHz)



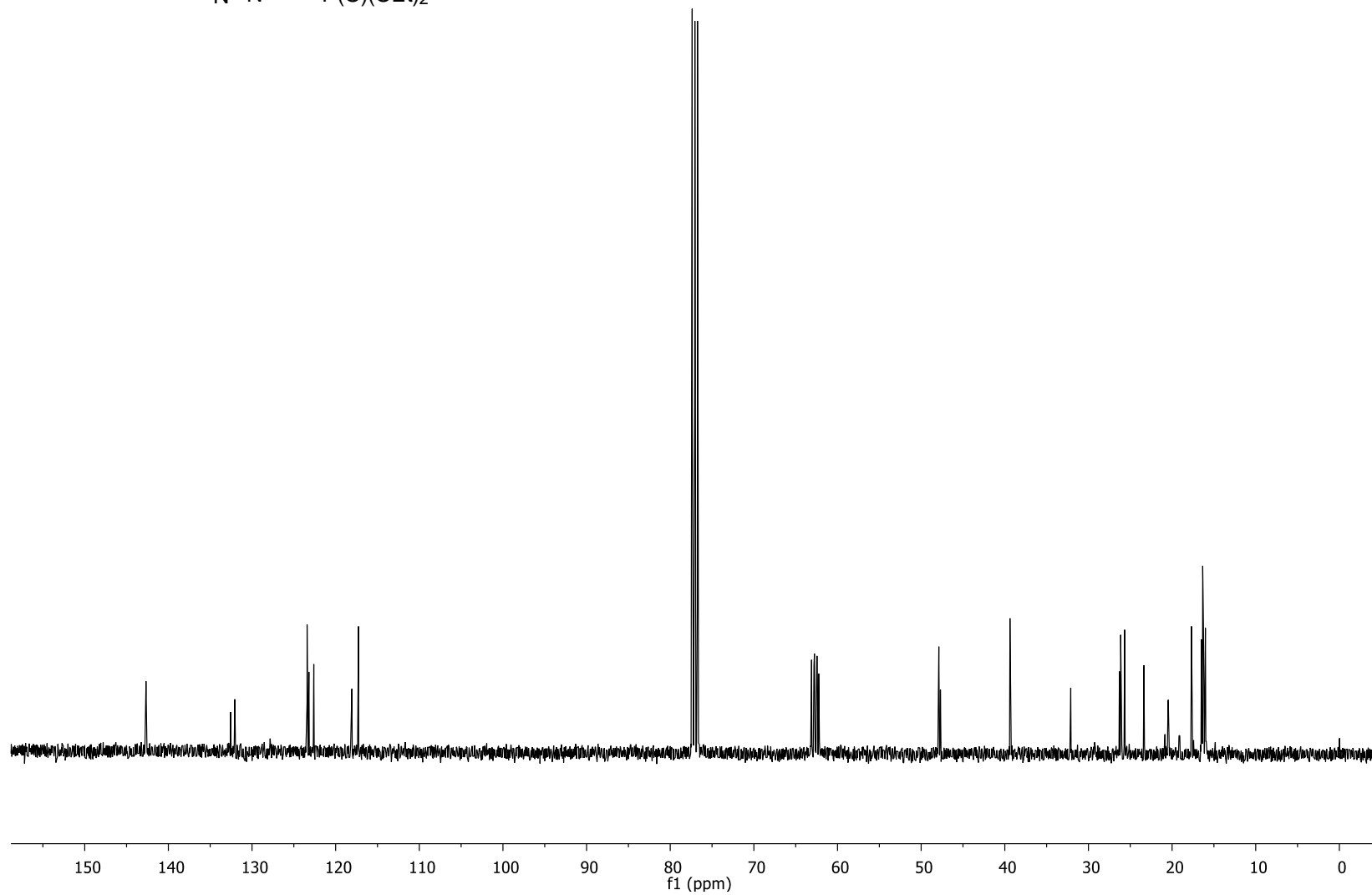
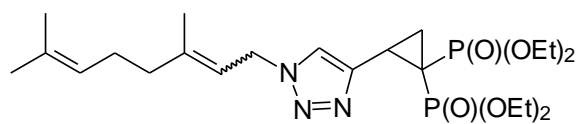
¹³C NMR Spectrum of Compound **29** (D₂O, 100 MHz)



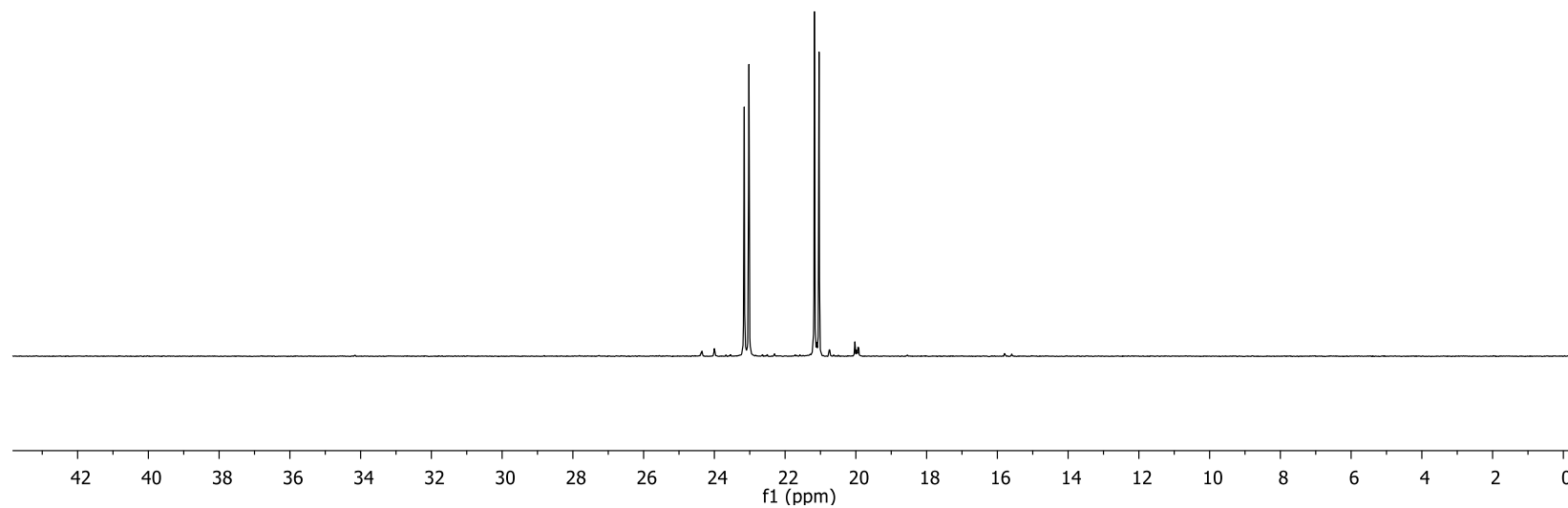
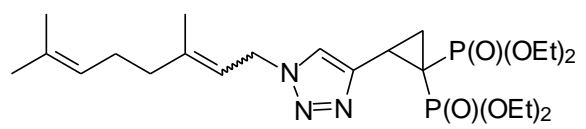
^{31}P NMR Spectrum of Compound **29** (D_2O , 162 MHz)



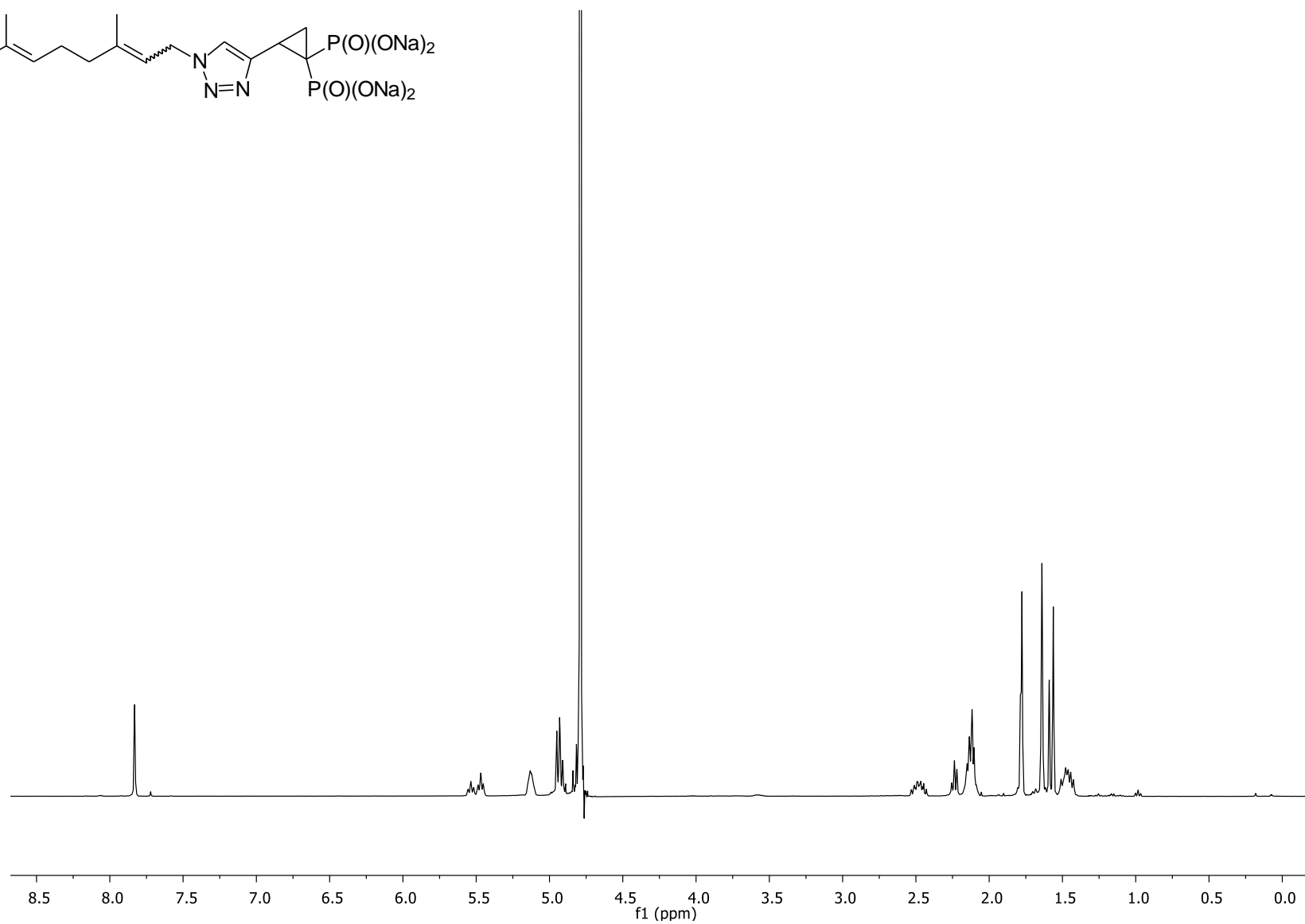
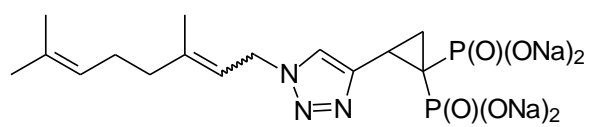
¹H NMR Spectrum of Compound **30** (CDCl₃, 400 MHz)



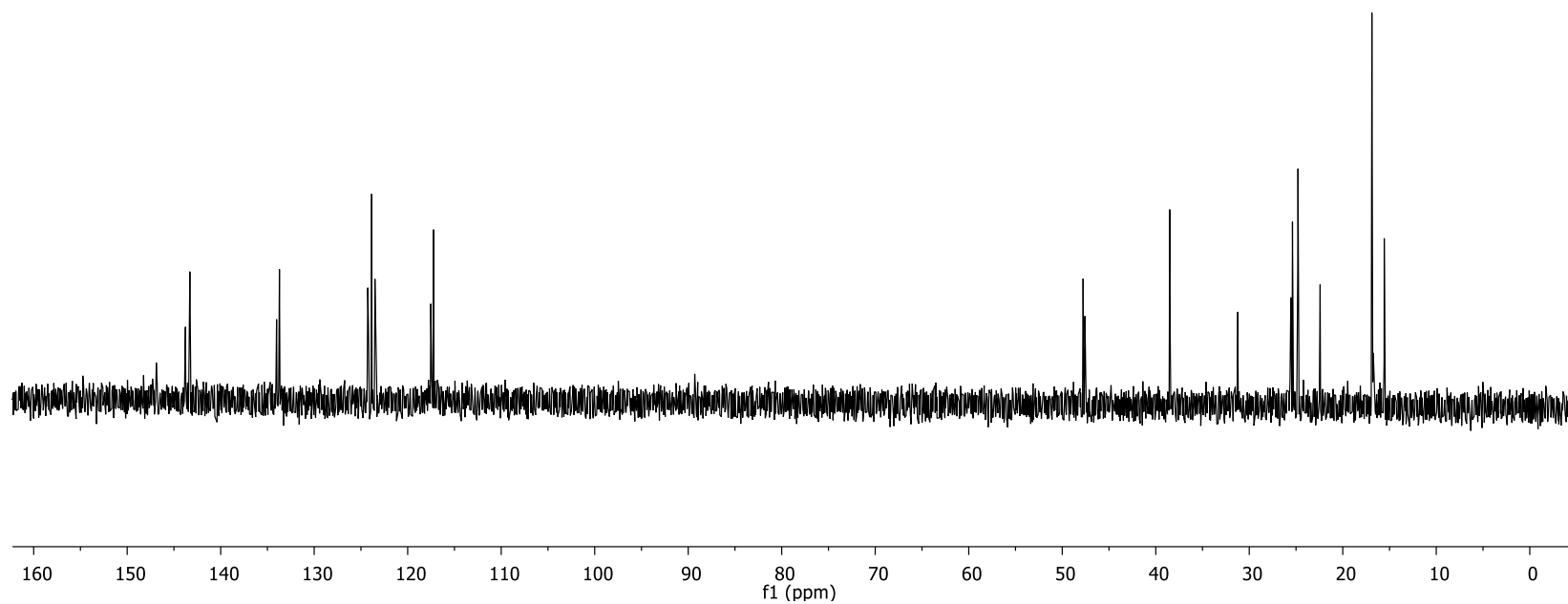
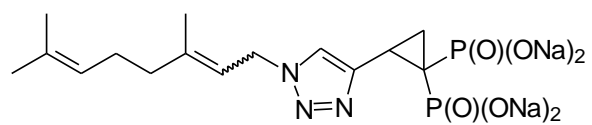
¹³C NMR Spectrum of Compound **30** (CDCl₃, 100 MHz)



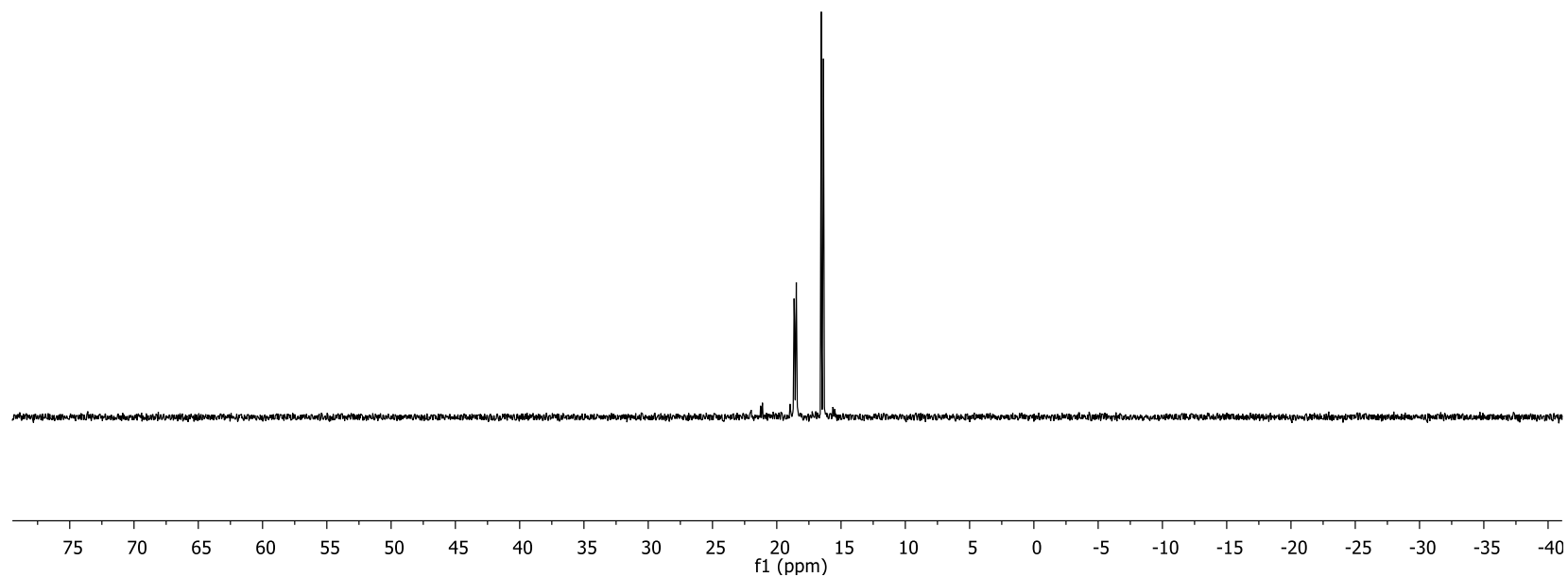
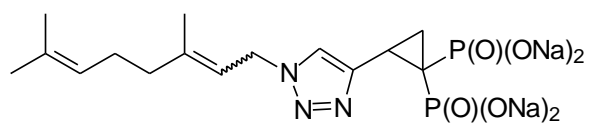
^{31}P NMR Spectrum of Compound **30** (CDCl_3 , 162 MHz)



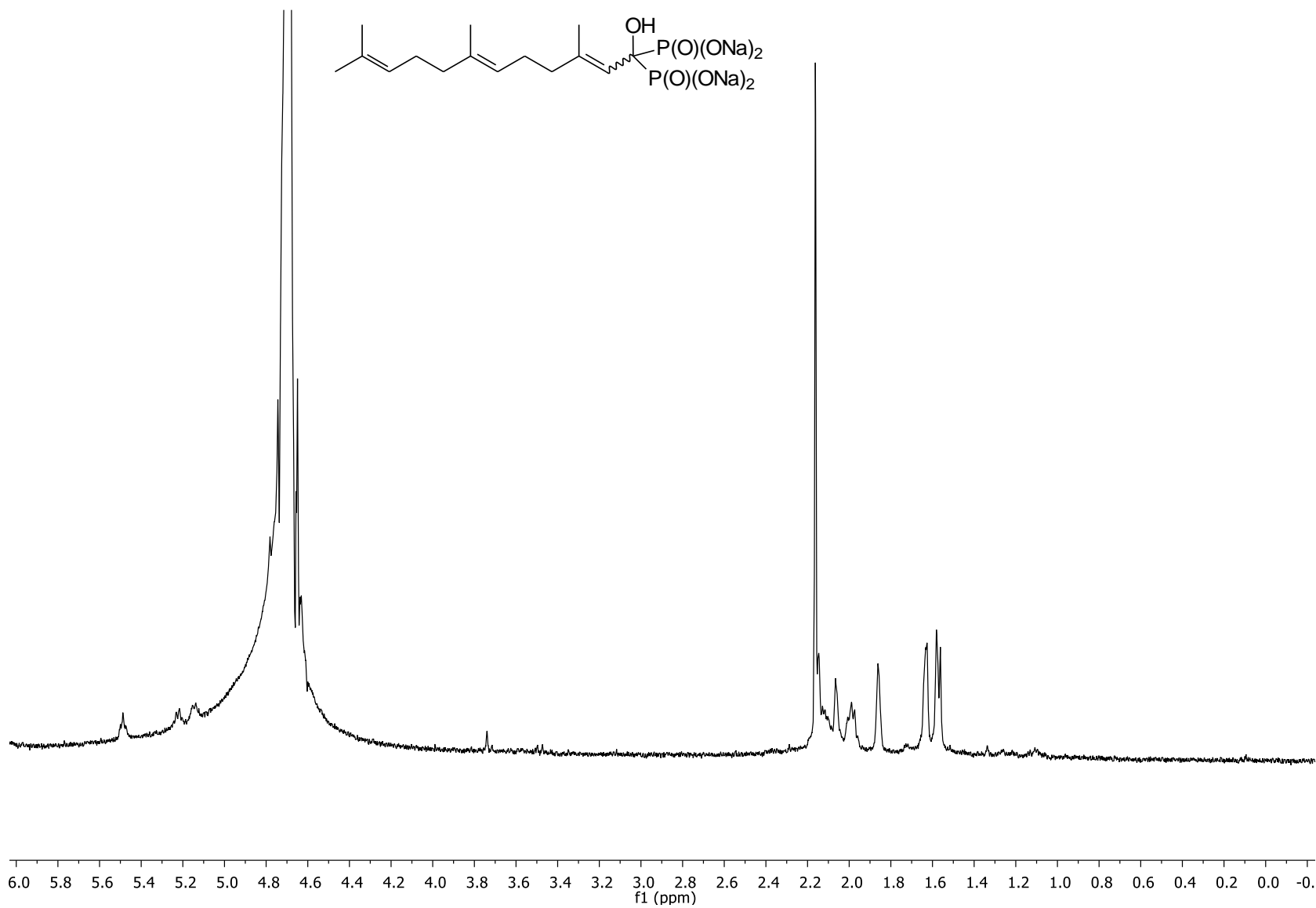
^1H NMR Spectrum of Compound **31** (D_2O , 400 MHz)



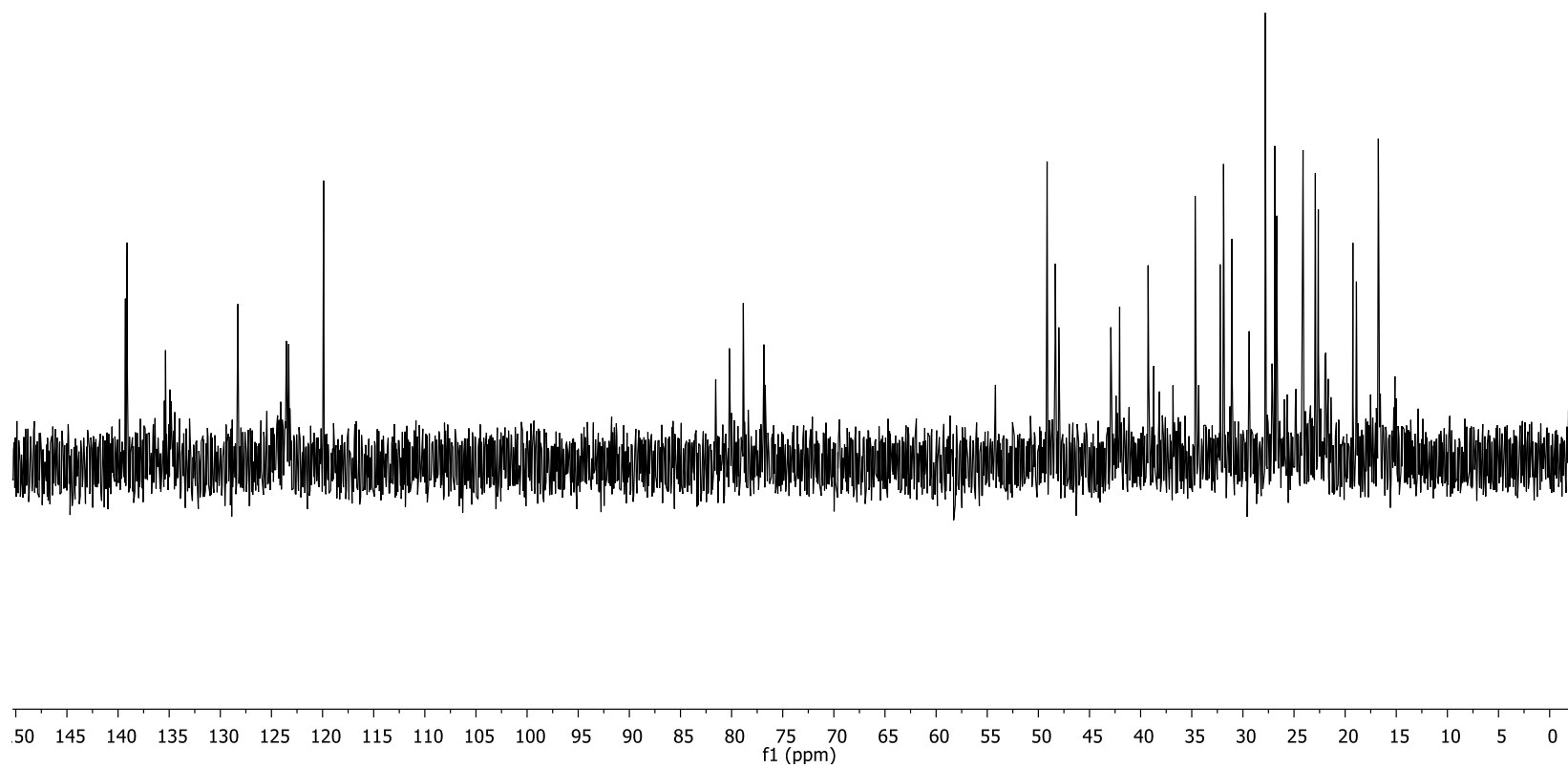
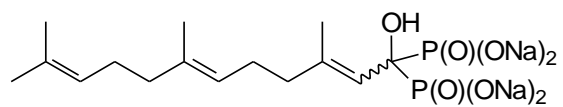
¹³C NMR Spectrum of Compound 31 (D₂O, 100 MHz)



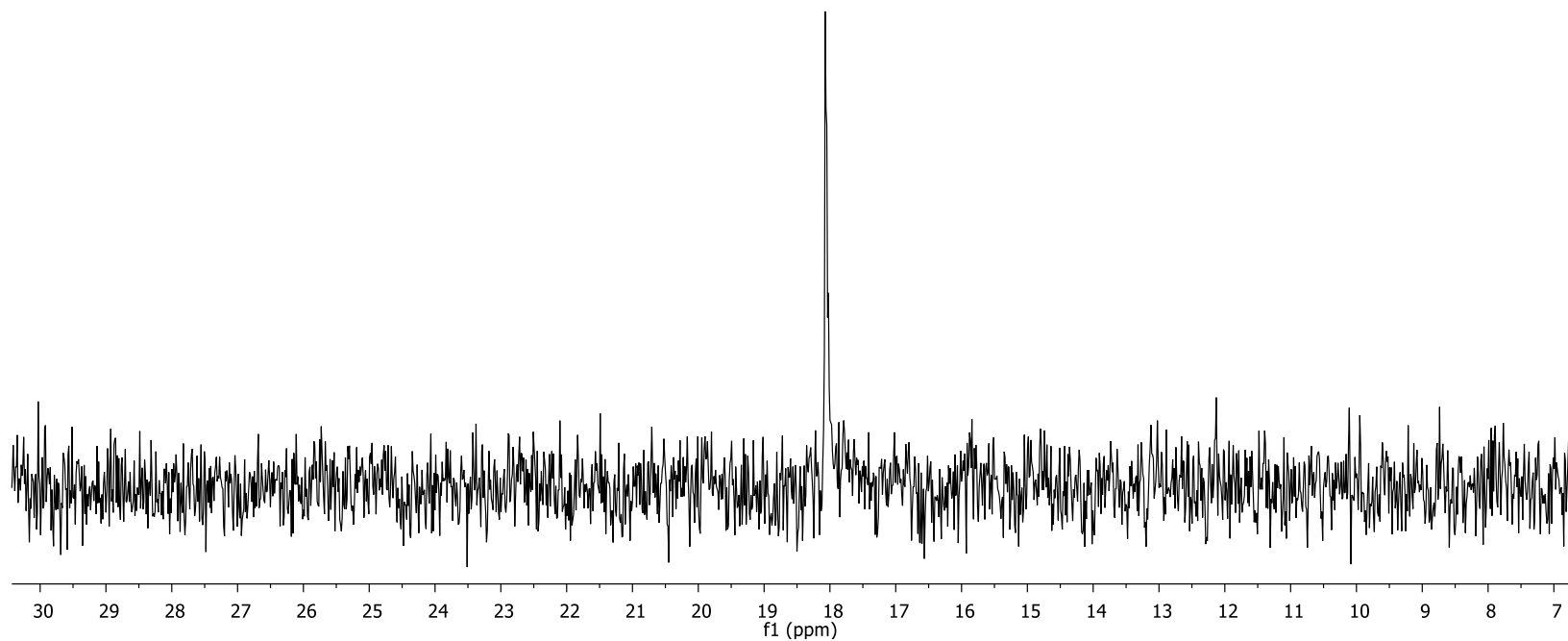
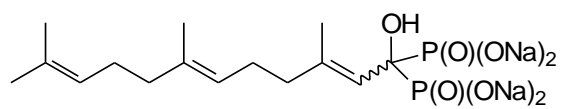
^{31}P NMR Spectrum of Compound **31** (D_2O , 162 MHz)



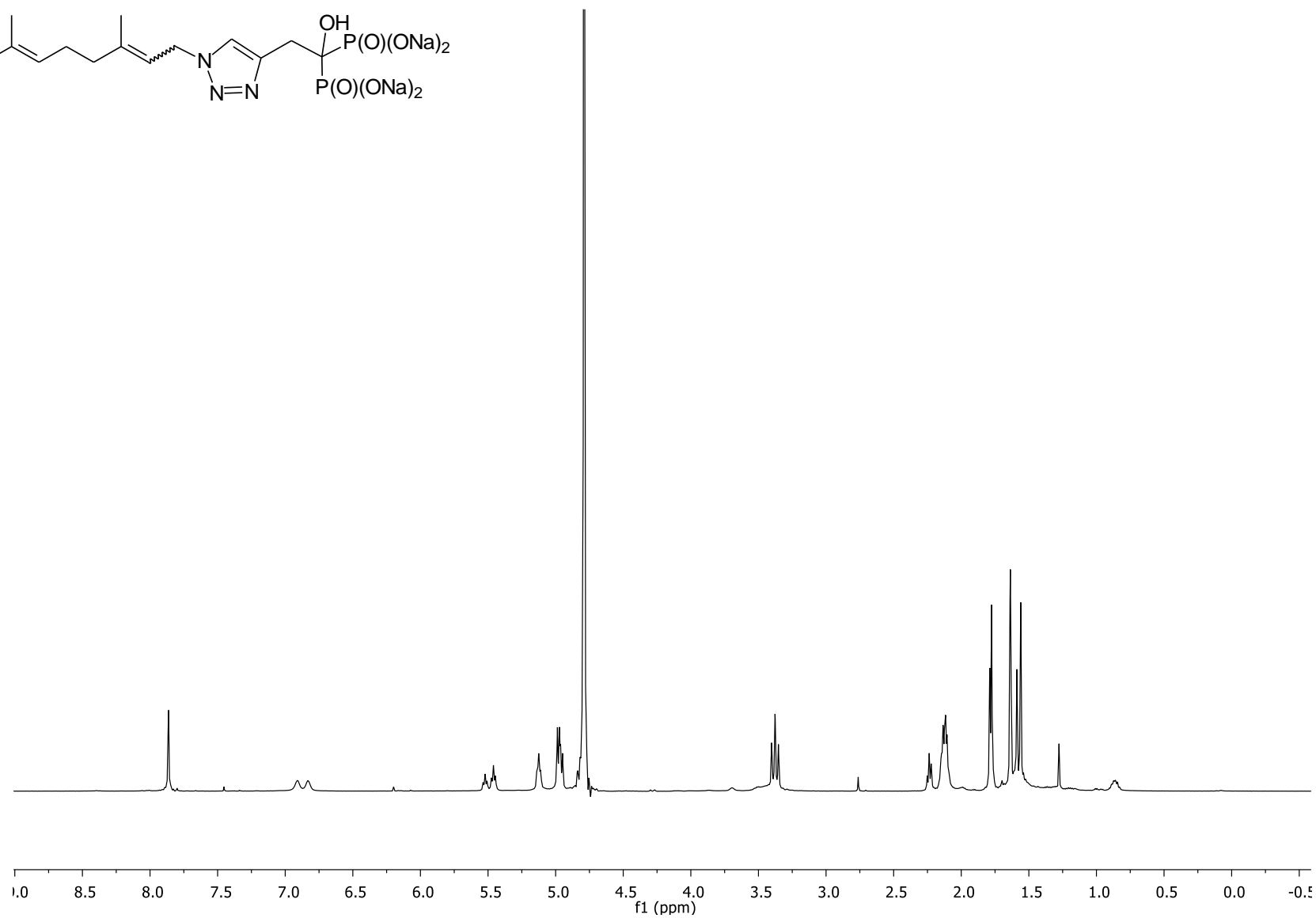
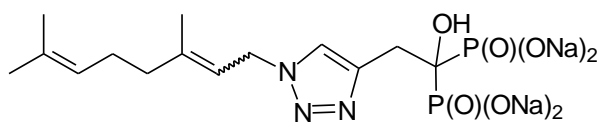
^1H NMR Spectrum of Compound **34** (D_2O , 500 MHz)



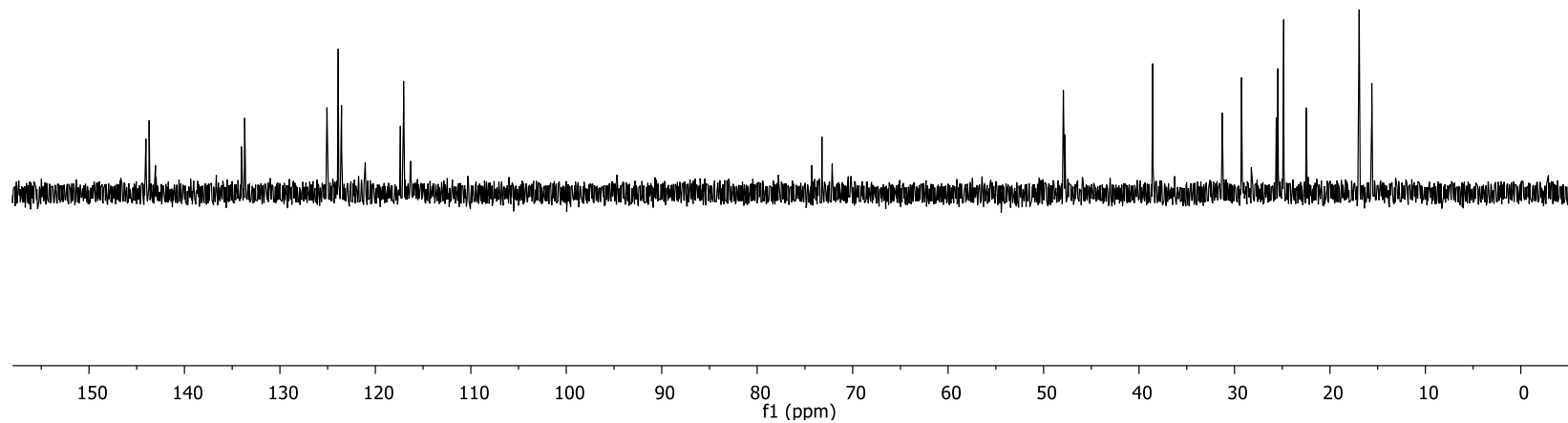
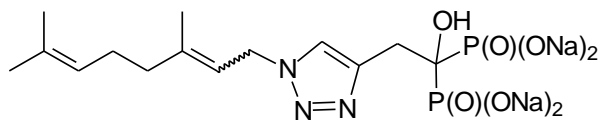
¹³C NMR Spectrum of Compound **34** (D₂O, 100 MHz)



³¹P NMR Spectrum of Compound **34** (D₂O, 162 MHz)



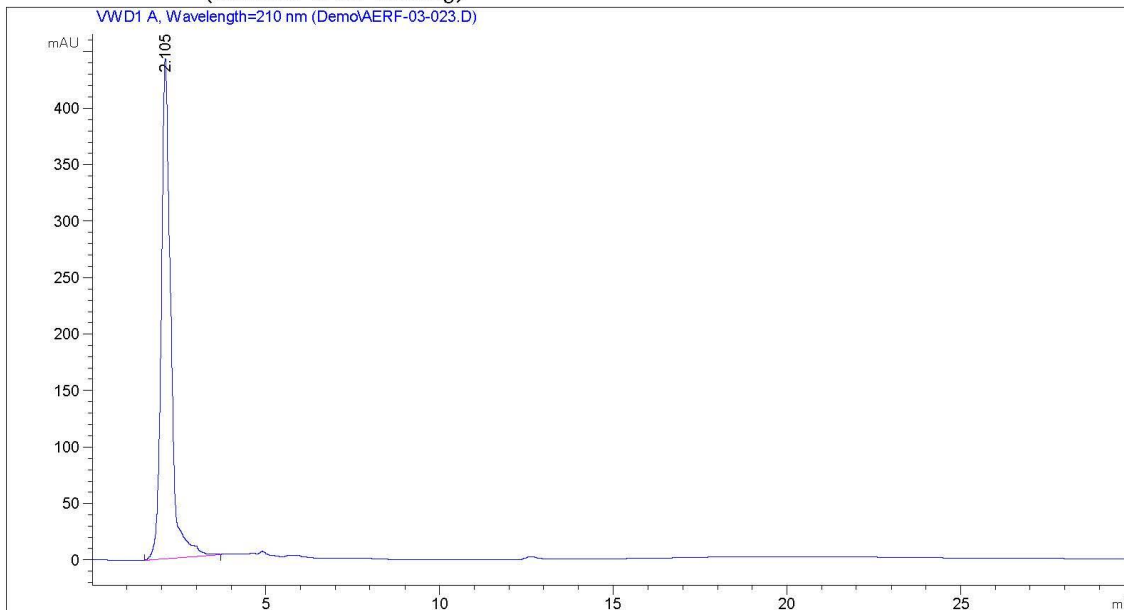
^1H NMR Spectrum of Compound **37** (D_2O , 500 MHz)



¹³C NMR Spectrum of Compound 37 (D₂O, 126 MHz)

Data File C:\Users\Public\Documents\ChemStation\1\Data\Demo\AERF-03-023.D
Sample Name:

```
=====
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : Shared 1220           Location : 1
Injection Date  : 12/2/2020 10:29:34 AM Inj       : 1
                                           Inj Volume: No inj
Method          : C:\Users\Public\Documents\ChemStation\1\Methods\AERF_LC.M
Last changed    : 12/2/2020 10:28:53 AM by SYSTEM
                  (modified after loading)
=====
```



```
=====
                          Area Percent Report
=====
```

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: VWD1 A, Wavelength=210 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.105	BV R	0.2686	8444.32617	442.47632	100.0000

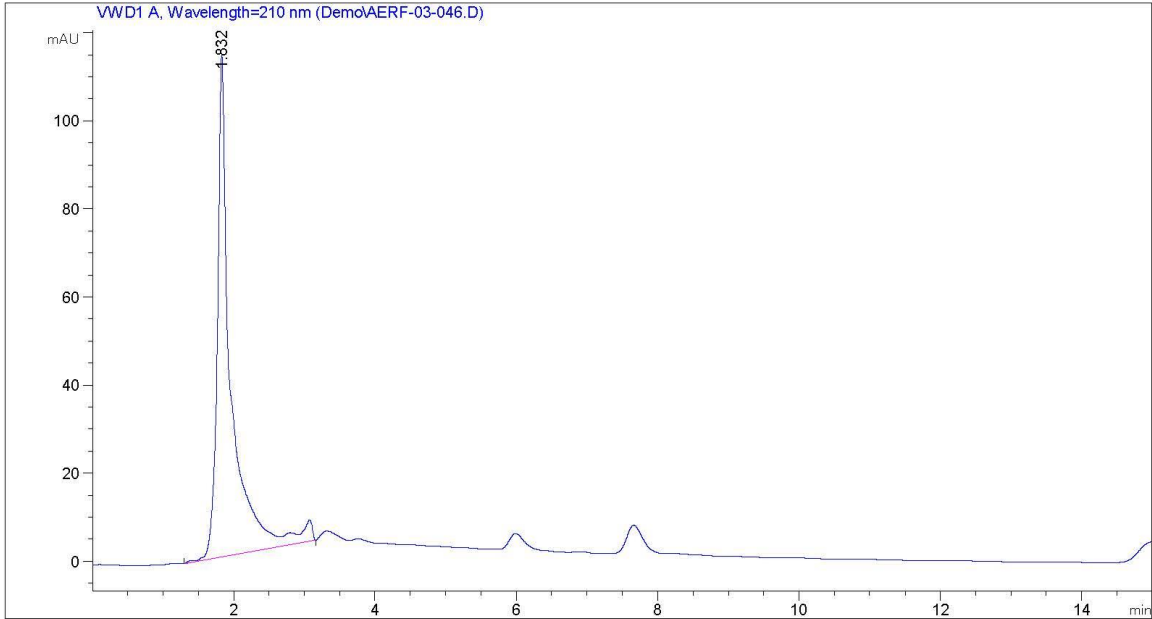
```
Totals :                8444.32617  442.47632
```

```
=====
*** End of Report ***
```

HPLC trace of Compound 11

Data File C:\Users\Public\Documents\ChemStation\1\Data\Demo\AERF-03-046.D
Sample Name:

```
=====
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : Shared 1220           Location : 1
Injection Date  : 1/5/2021 2:48:19 PM Inj       : 1
                                           Inj Volume : No inj
Acq. Method     : C:\Users\Public\Documents\ChemStation\1\Methods\DEF_LC.M
Last changed    : 1/5/2021 2:47:56 PM by SYSTEM
                 (modified after loading)
Analysis Method : C:\Users\Public\Documents\ChemStation\1\Methods\DEF_LC.M
Last changed    : 1/5/2021 2:46:30 PM by SYSTEM
                 (modified after loading) (Current integration events modified)
=====
```



=====
Area Percent Report
=====

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: VWD1 A, Wavelength=210 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.832	BV R	0.1763	1524.75305	113.84121	100.0000

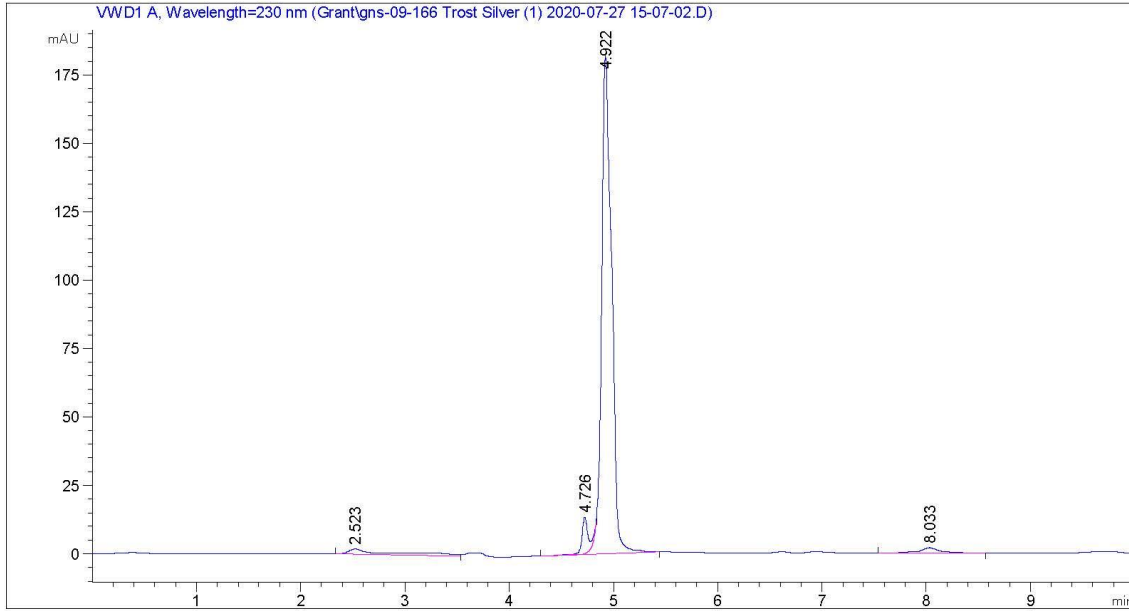
Totals : 1524.75305 113.84121

HPLC trace of Compound 17

Data File C:\Users\P...tion\1\Data\Grant\gns-09-166 Trost Silver (1) 2020-07-27 15-07-02.D
 Sample Name: gns-09-166 Trost Silver

```

=====
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : Shared 1220           Location : 1
Injection Date  : 7/27/2020 3:07:03 PM Inj       : 1
                                           Inj Volume: No inj
Method          : C:\Users\Public\Documents\ChemStation\1\Methods\DEF_LC.M
Last changed    : 7/27/2020 3:16:31 PM by SYSTEM
                 (modified after loading)
Sample Info     : Asymmetric Reaction Analysis. Chiracel OJ-H 5:95 IPA:Hex 2mL/min
  
```



=====
 Area Percent Report
 =====

```

Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs
  
```

Signal 1: WVD1 A, Wavelength=230 nm

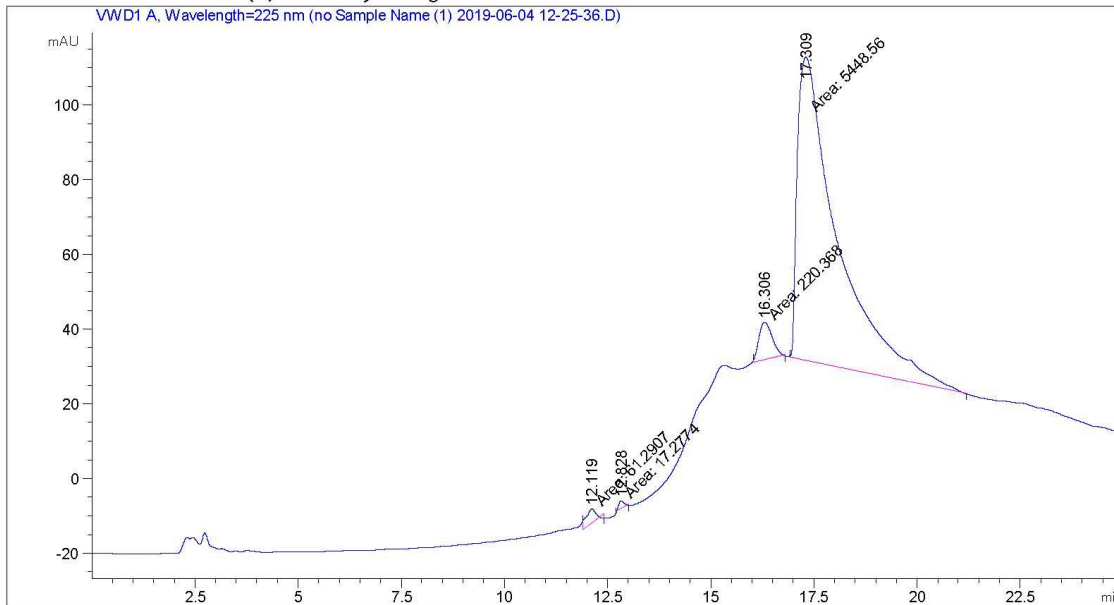
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.523	BV	0.3786	54.47862	1.84451	4.0237
2	4.726	BV E	0.0599	55.05247	13.41618	4.0661
3	4.922	VB R	0.0941	1220.58765	182.37109	90.1507
4	8.033	BB	0.1812	23.82263	1.83874	1.7595

Totals : 1353.94137 199.47052

HPLC trace of Compound 27

```

=====
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : Shared 1220           Location : 1
Injection Date  : 6/4/2019 12:25:37 PM Inj       : 1
                                           Inj Volume: No inj
Acq. Method     : C:\Users\Public\Documents\ChemStation\1\Methods\HILIC_analytical_run.M
Last changed    : 6/4/2019 12:22:13 PM by SYSTEM
                 (modified after loading)
Analysis Method : C:\Users\Public\Documents\ChemStation\1\Methods\HILIC_analytical_run.M
Last changed    : 6/4/2019 12:57:31 PM by SYSTEM
Additional Info : Peak(s) manually integrated
  
```



=====
 Area Percent Report
 =====

```

Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs
  
```

Signal 1: VWD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.119	MM	0.2725	61.29074	3.74926	1.0664
2	12.828	MM	0.1398	17.27742	2.05988	0.3006
3	16.306	MM	0.3701	220.36827	9.92279	3.8342
4	17.309	MM	1.1195	5448.56006	81.11897	94.7988

Totals : 5747.49649 96.85090

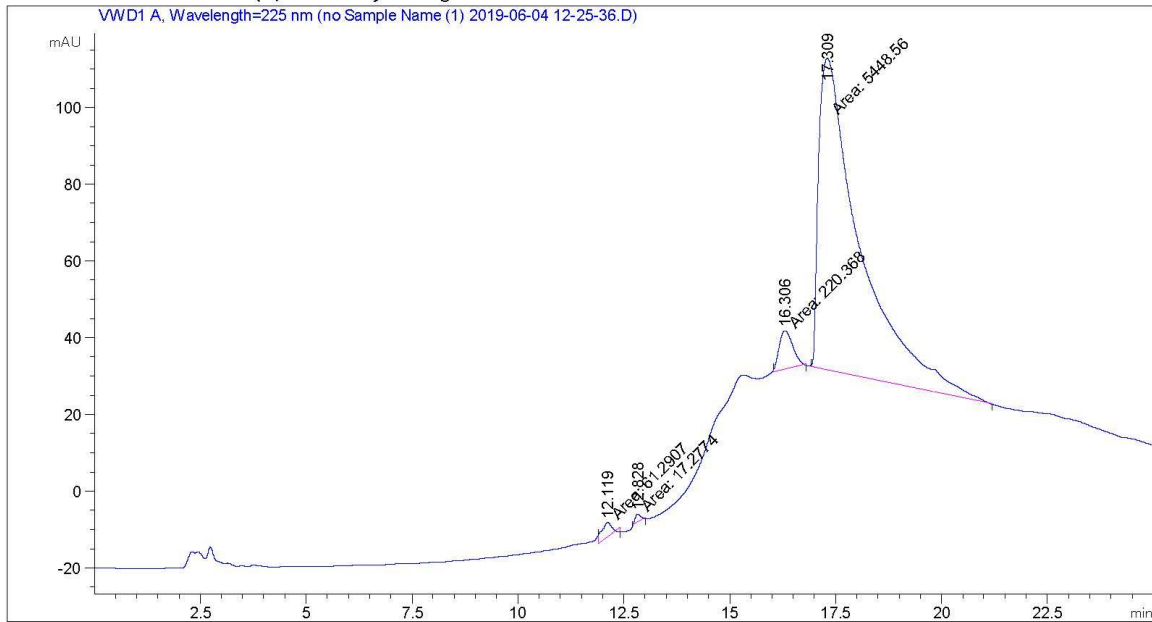
HPLC trace of Compound 29

Data File C:\Users\Public\Documents\ChemStation\1\Data\no Sample Name (1) 2019-06-04 12-25-36.D
 Sample Name:

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=====
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : Shared 1220           Location : 1
Injection Date  : 6/4/2019 12:25:37 PM      Inj : 1
                                           Inj Volume : No inj

Acq. Method     : C:\Users\Public\Documents\ChemStation\1\Methods\HILIC_analytical_run.M
Last changed    : 6/4/2019 12:22:13 PM by SYSTEM
                 (modified after loading)
Analysis Method : C:\Users\Public\Documents\ChemStation\1\Methods\HILIC_analytical_run.M
Last changed    : 6/4/2019 12:57:31 PM by SYSTEM
Additional Info  : Peak(s) manually integrated
  
```



Area Percent Report

```

Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs
  
```

Signal 1: VWD1 A, Wavelength=225 nm

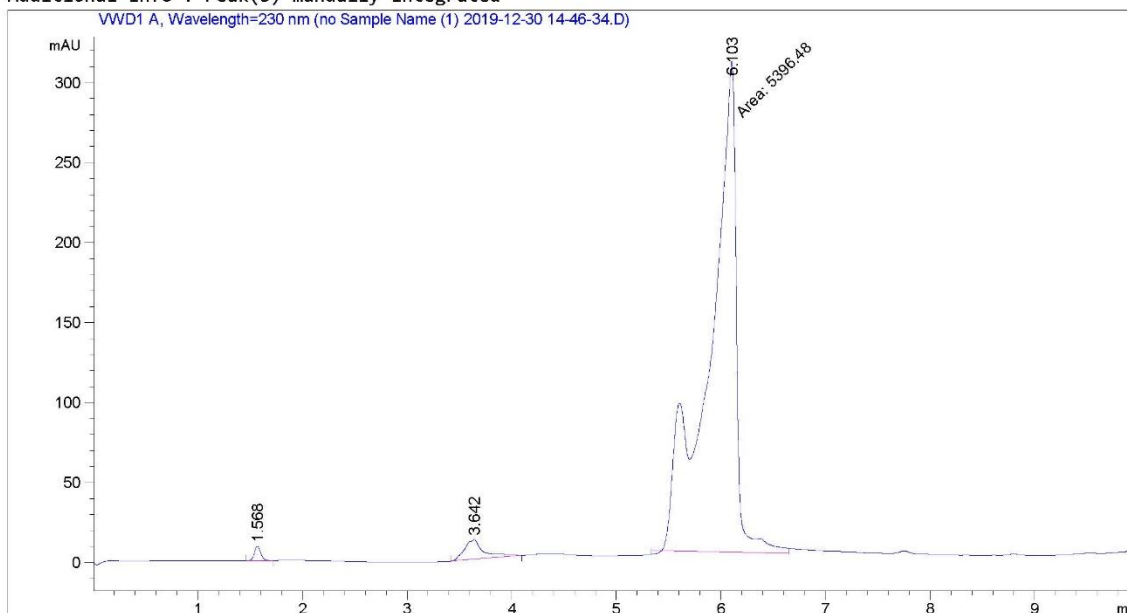
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.119	MM	0.2725	61.29074	3.74926	1.0664
2	12.828	MM	0.1398	17.27742	2.05988	0.3006
3	16.306	MM	0.3701	220.36827	9.92279	3.8342
4	17.309	MM	1.1195	5448.56006	81.11897	94.7988

Totals : 5747.49649 96.85090

HPLC trace of Compound 31

Data File C:\Users\P...cuments\ChemStation\1\Data\no Sample Name (1) 2019-12-30 14-46-34.D
Sample Name:

```
=====
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : Shared 1220           Location : 1
Injection Date  : 12/30/2019 2:46:35 PM Inj       : 1
                                           Inj Volume: No inj
Acq. Method     : C:\Users\Public\Documents\ChemStation\1\Methods\CMS-C18A.M
Last changed    : 12/30/2019 2:53:18 PM by SYSTEM
                 (modified after loading)
Analysis Method : C:\USERS\PUBLIC\DOCUMENTS\CHEMSTATION\1\METHODS\BMD TTI918.M
Last changed    : 12/30/2019 2:39:49 PM by SYSTEM
                 (modified after loading)
Additional Info : Peak(s) manually integrated
=====
```



```
=====
                          Area Percent Report
=====
```

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Do not use Multiplier & Dilution Factor with ISTDs
```

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.568	BB	0.0629	36.81658	8.96037	0.6590
2	3.642	BB	0.1597	153.17264	12.18526	2.7418
3	6.103	MM	0.2932	5396.48389	306.72931	96.5991

Totals : 5586.47311 327.87493

HPLC trace of Compound 37