

# Synthesis and antiviral evaluation of (1,4-disubstituted-1,2,3-triazol)-(E)-2-methyl-but-2-enyl nucleosides phosphonate prodrugs

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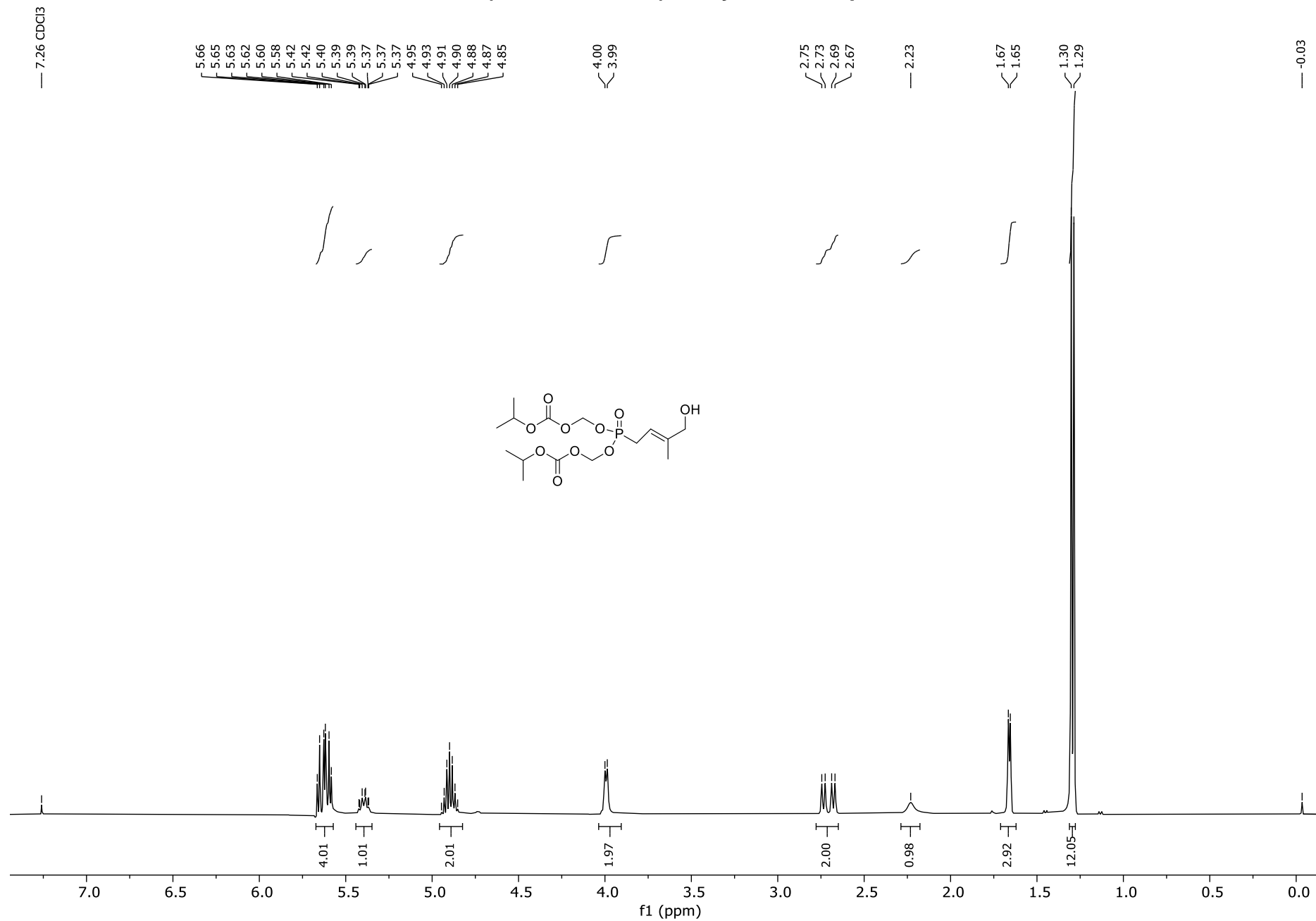
<sup>4</sup>Center for AIDS Research, Laboratory of Biochemical Pharmacology, Department of Pediatrics, Emory University School of Medicine and Children's Healthcare of Atlanta, Atlanta, Georgia, USA

Corresponding authors : [vincent.roy@univ-orleans.fr](mailto:vincent.roy@univ-orleans.fr); [luigi.agrofoglio@univ-orleans.fr](mailto:luigi.agrofoglio@univ-orleans.fr)

## Supplementary Informations

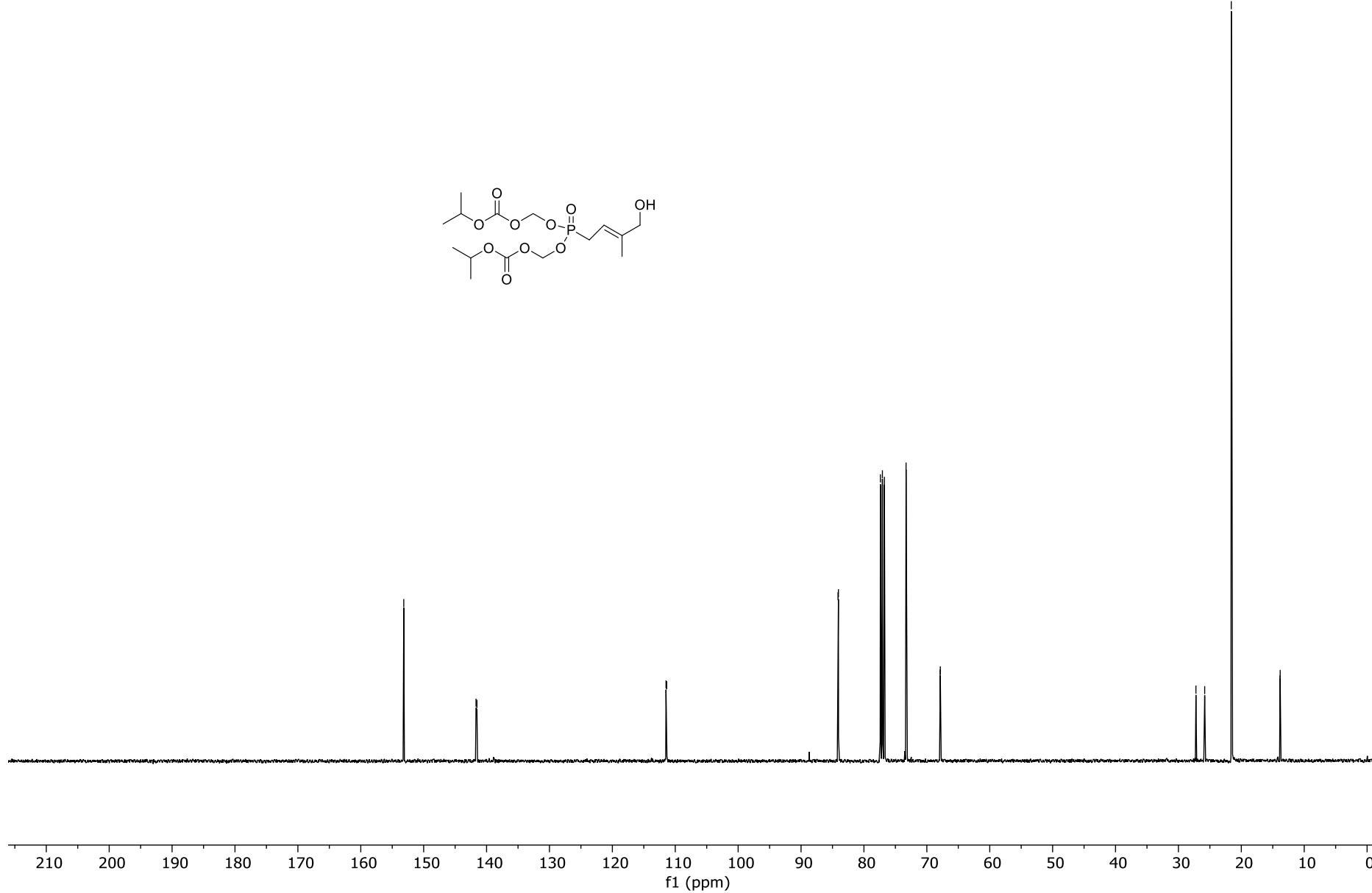
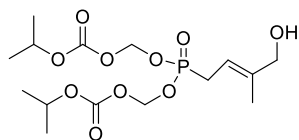
Copies of <sup>1</sup>H-, <sup>13</sup>C- and <sup>1</sup>H-<sup>13</sup>C HMBC NMR spectra of representative molecules

# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) Analysis of Compound 9

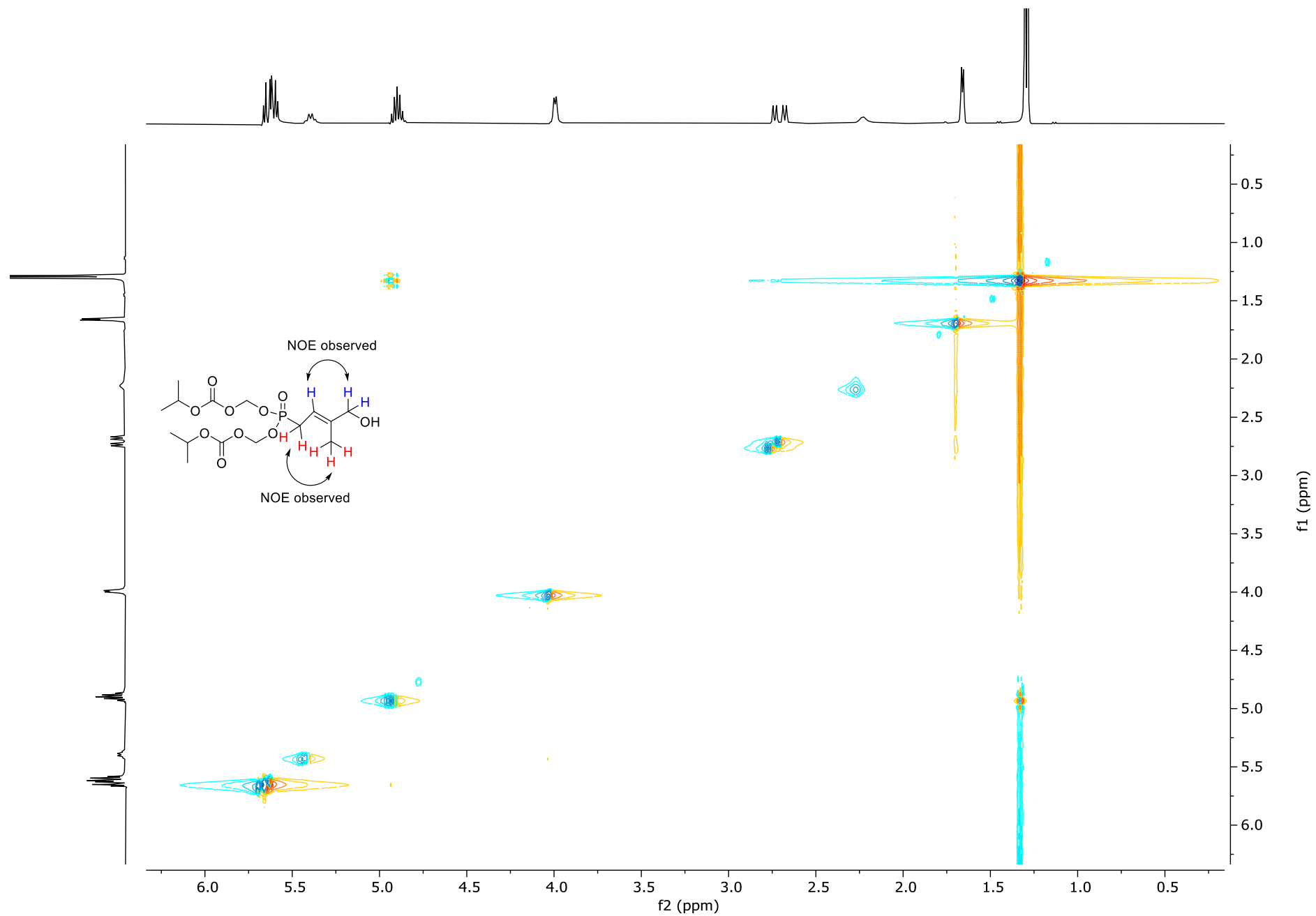


# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 9

153.17  
141.68  
141.53  
111.47  
111.35  
84.12  
84.06  
77.38  
77.06  
76.74  
73.30  
67.89  
67.86  
27.22  
25.82  
21.59  
13.85  
13.82

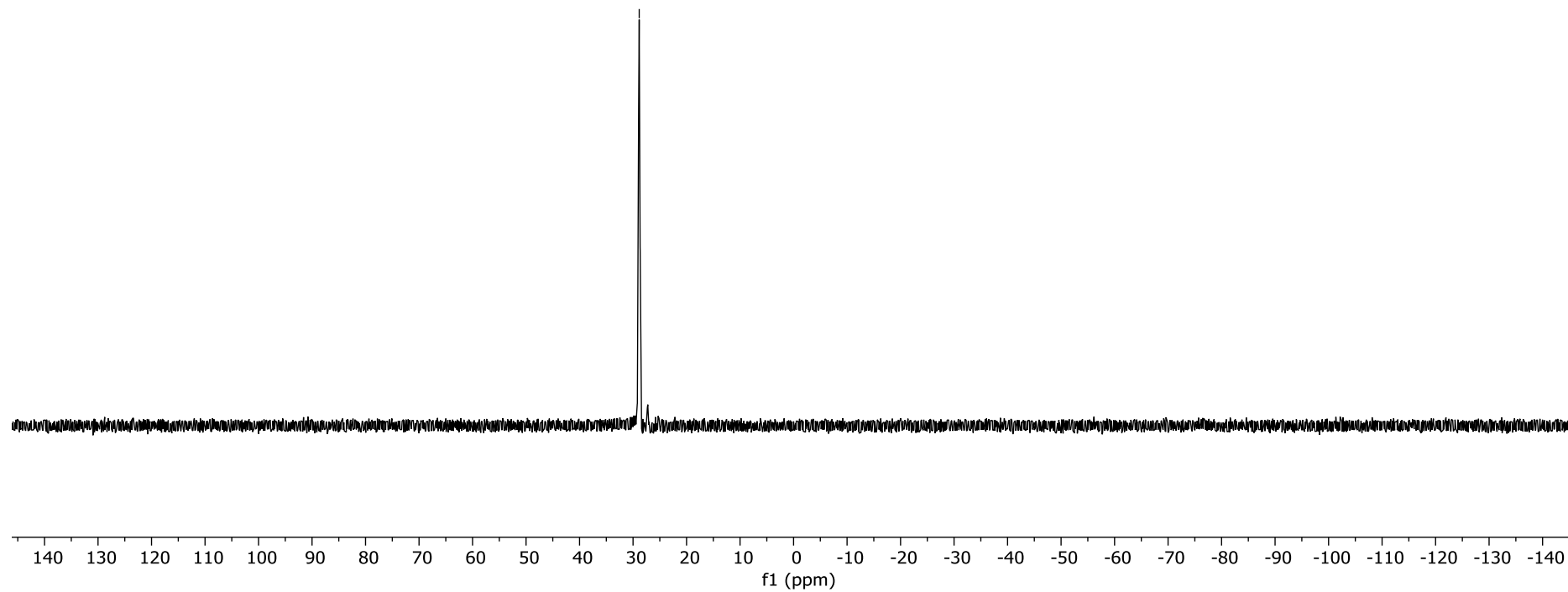
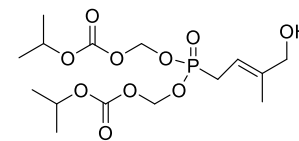


# NOESY of Compound 9

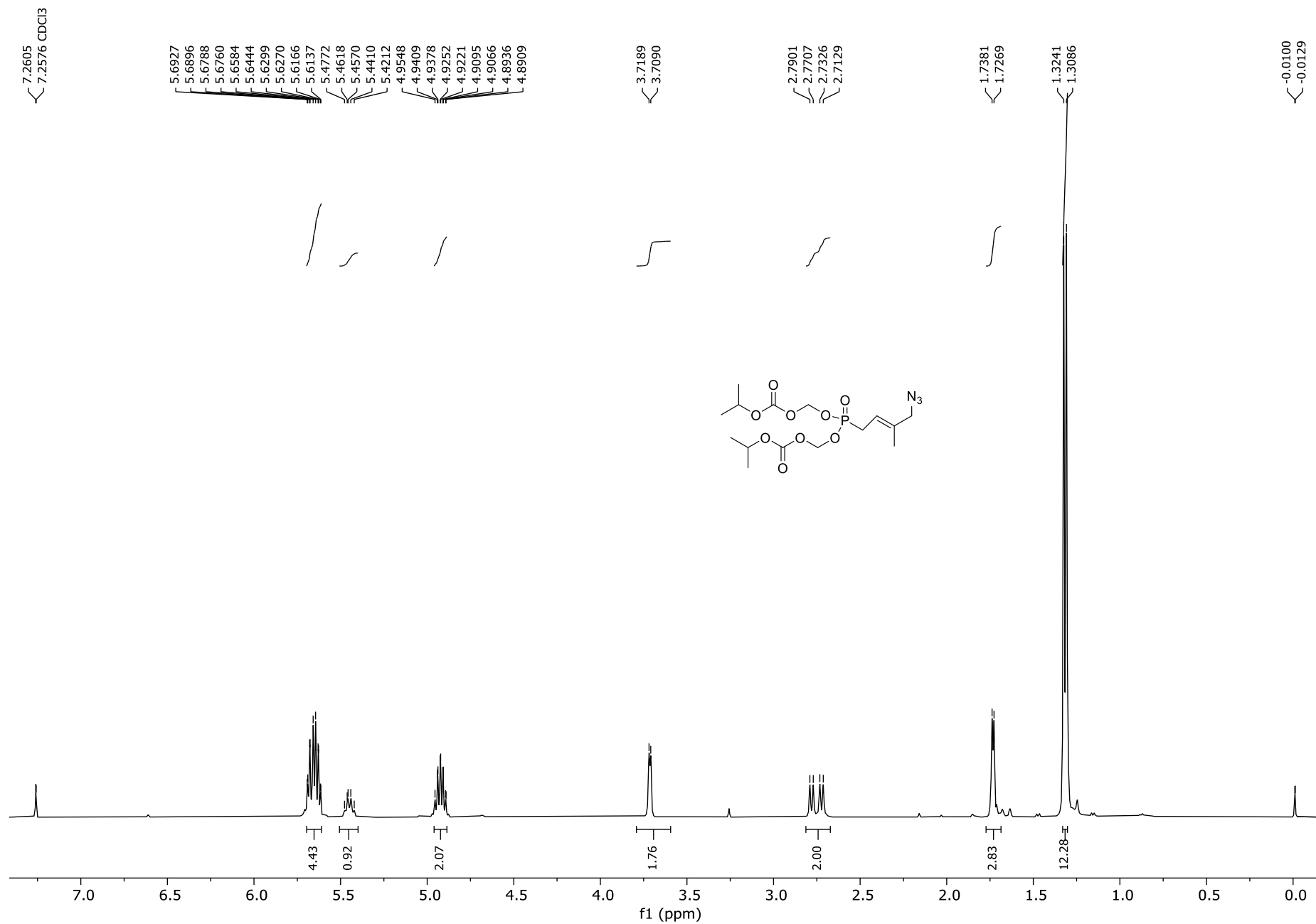


# <sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 9

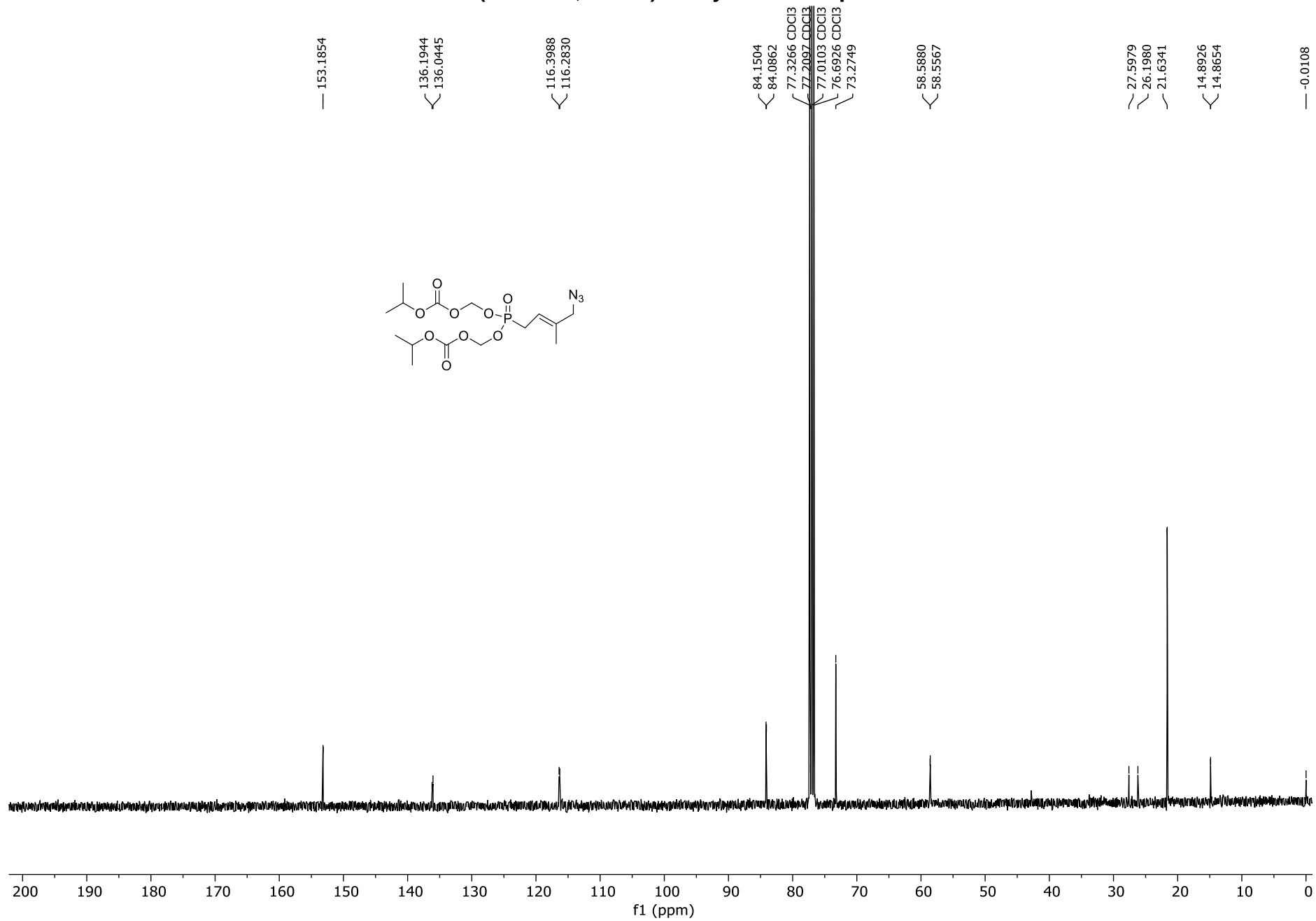
— 28.85



# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) Analysis of Compound 10

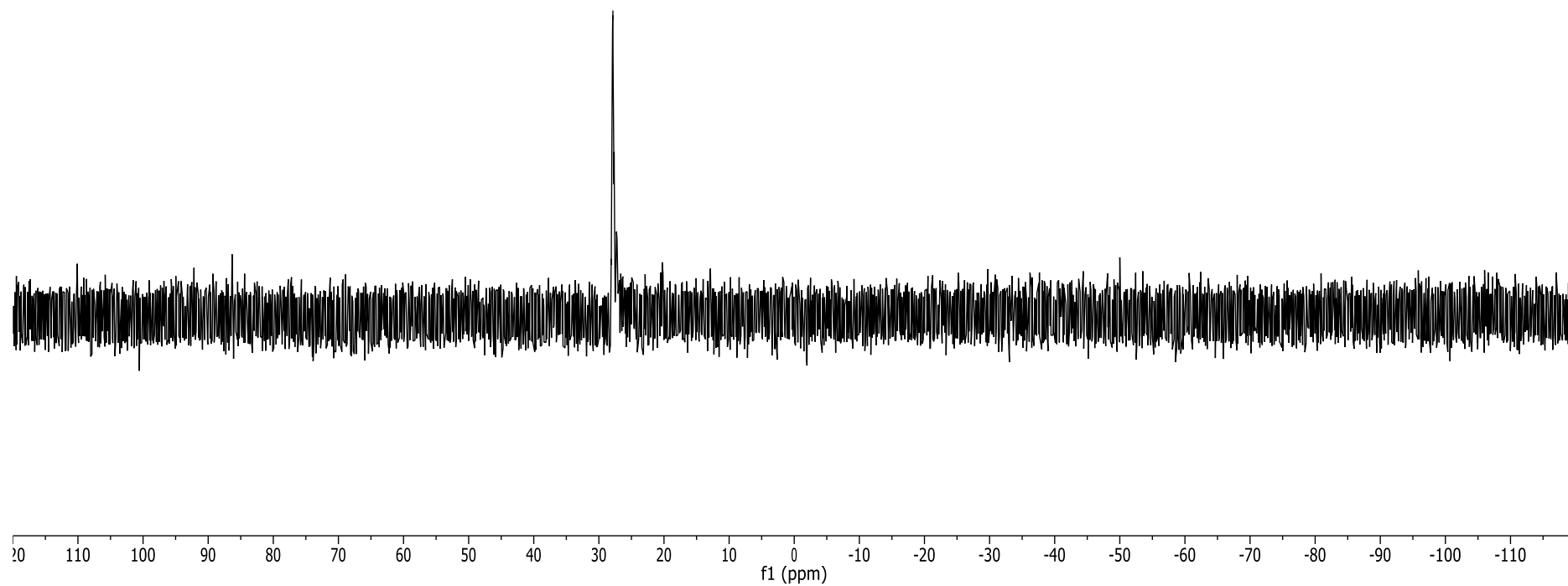
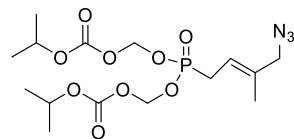


# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 10



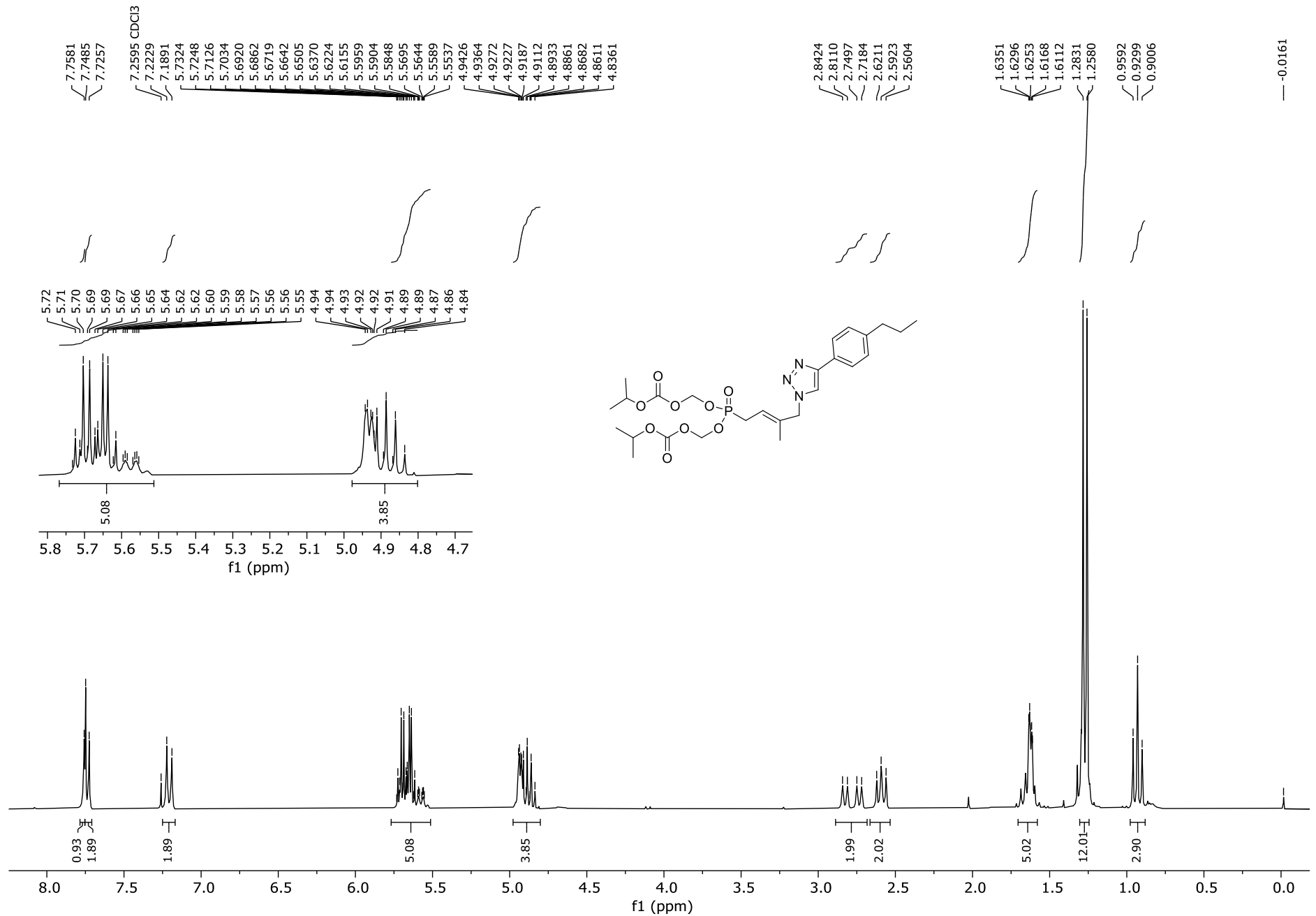
**<sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 10**

27.85

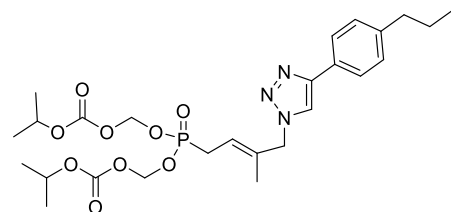




# <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>) Analysis of Compound 11a



# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 11a



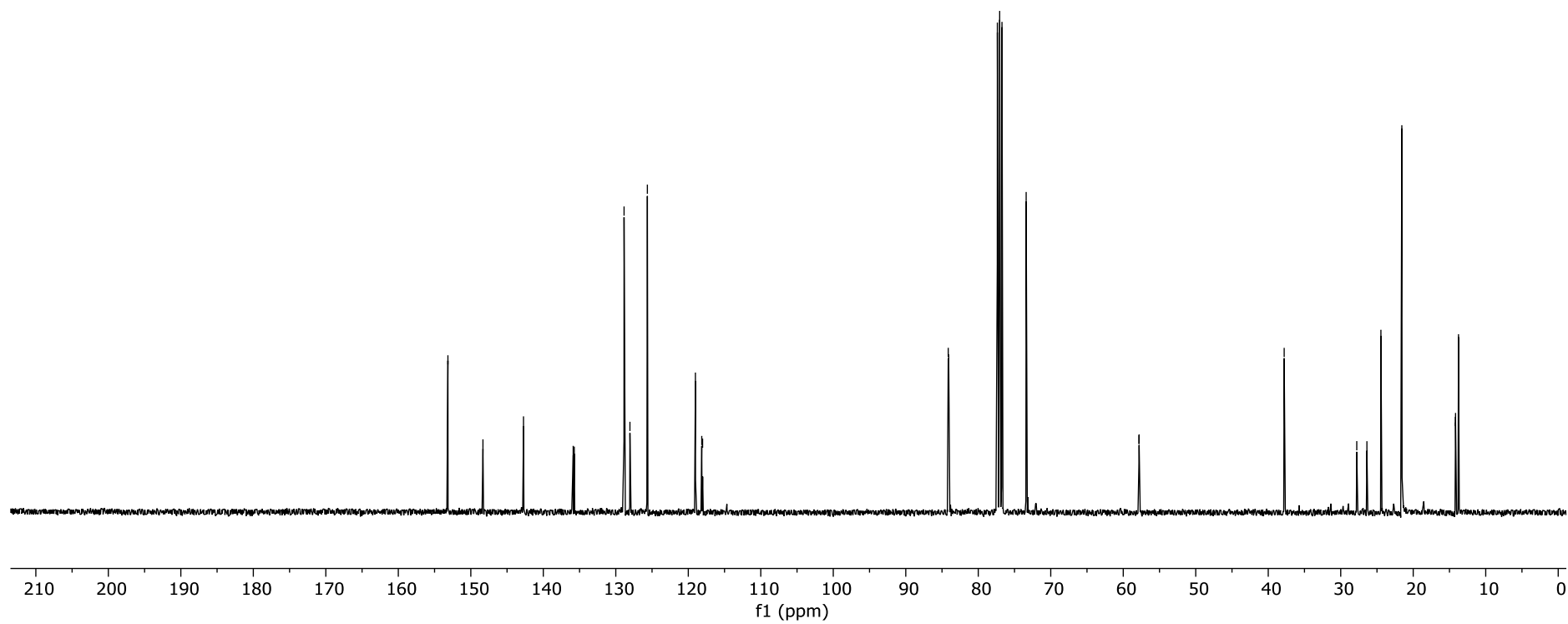
— 153.1585  
— 148.3262  
— 142.7307  
{ 135.8779  
{ 135.7278  
{ 128.8582  
{ 128.0489  
{ 125.6433  
{ 119.0169  
{ 118.1425  
{ 118.0257

{ 84.1417  
{ 84.0778  
{ 77.3644  
{ 77.0463 CDCl<sub>3</sub>  
{ 76.7287 CDCl<sub>3</sub>  
{ 73.3917

{ 57.8379  
{ 57.8080

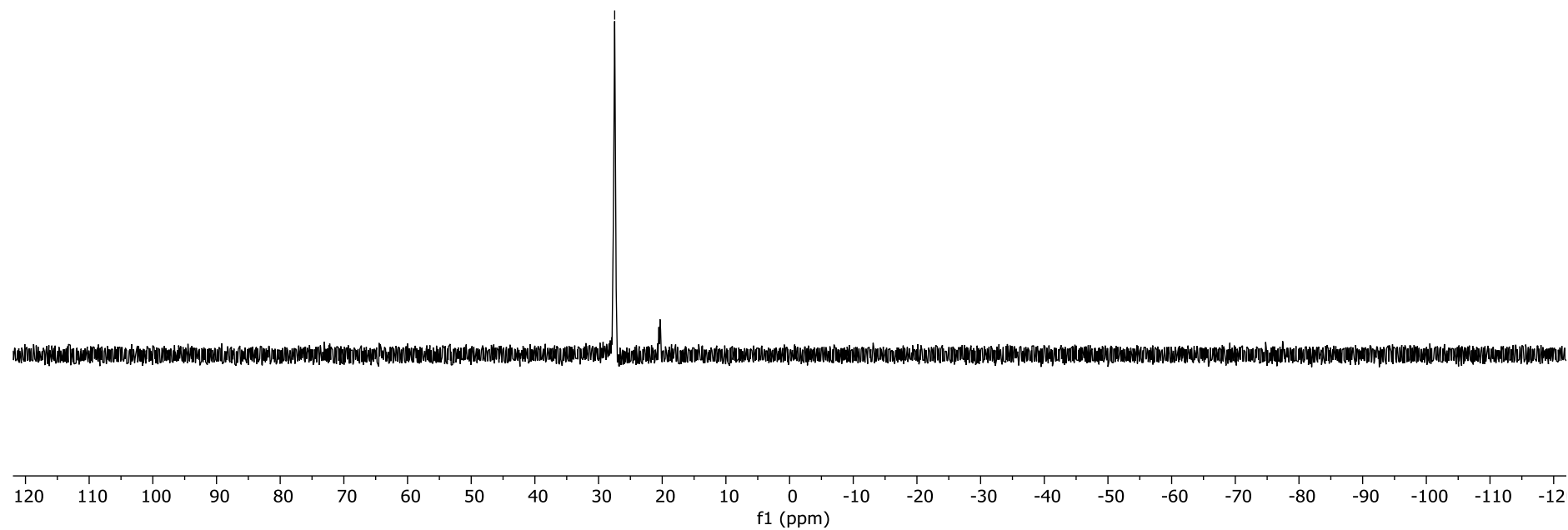
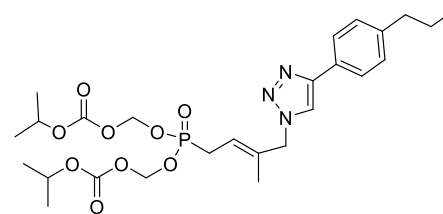
— 37.8004

{ 27.7871  
{ 26.3884  
— 24.4572  
{ 21.5993  
{ 21.5722  
{ 14.1877  
{ 14.1609  
{ 13.7531

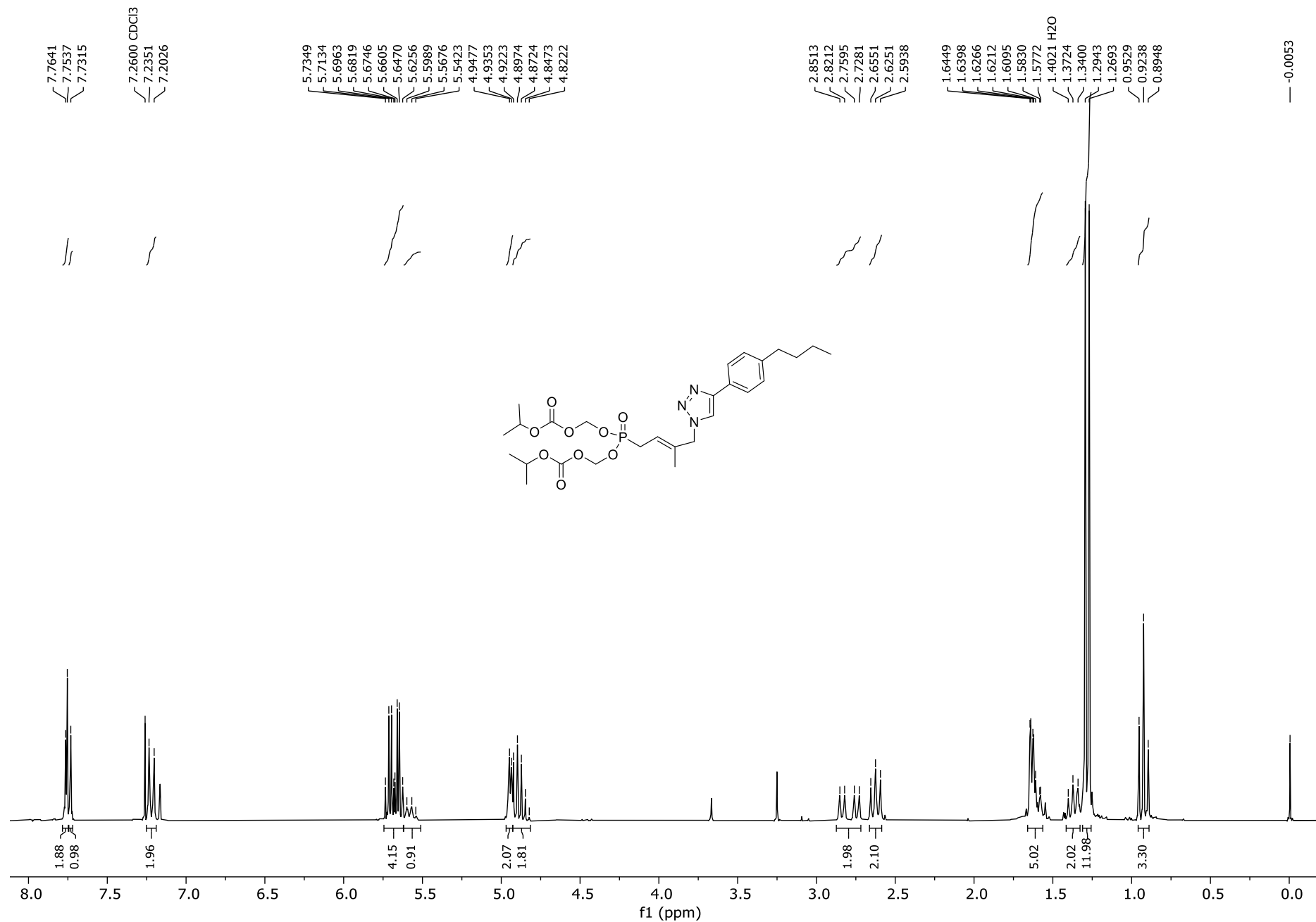


**<sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 11a**

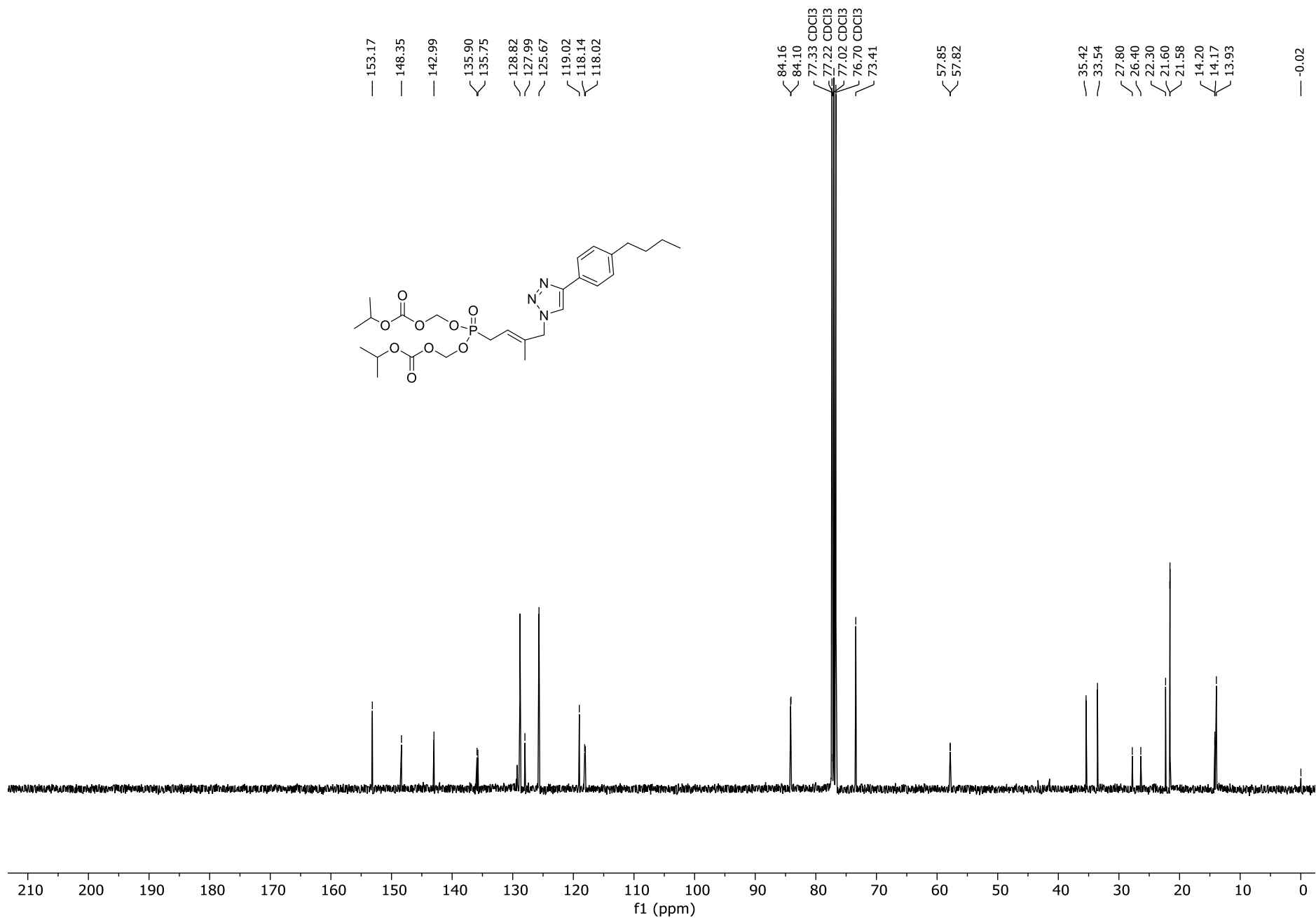
— 27.47



# <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>) Analysis of Compound 11b

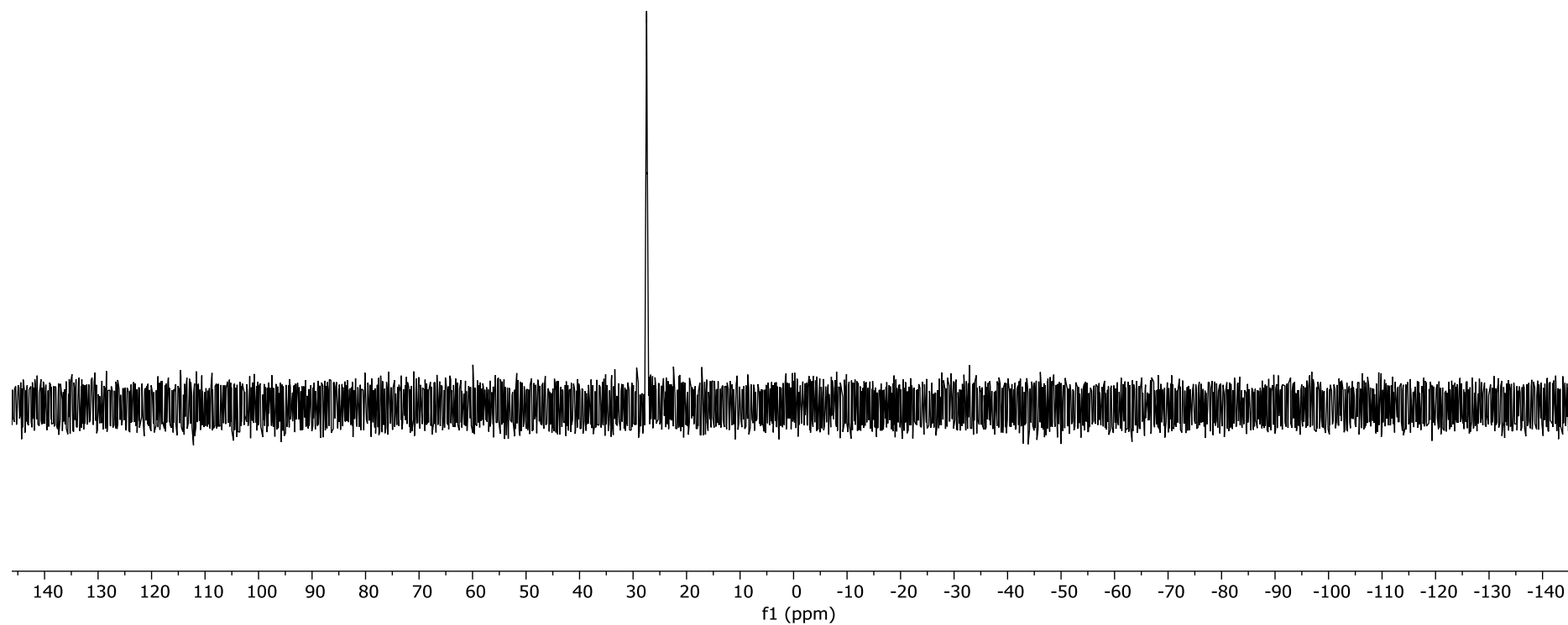
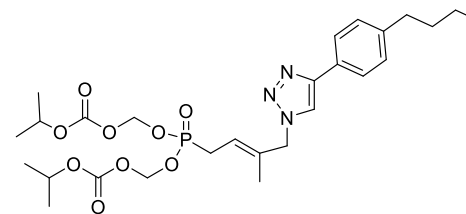


# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 11b

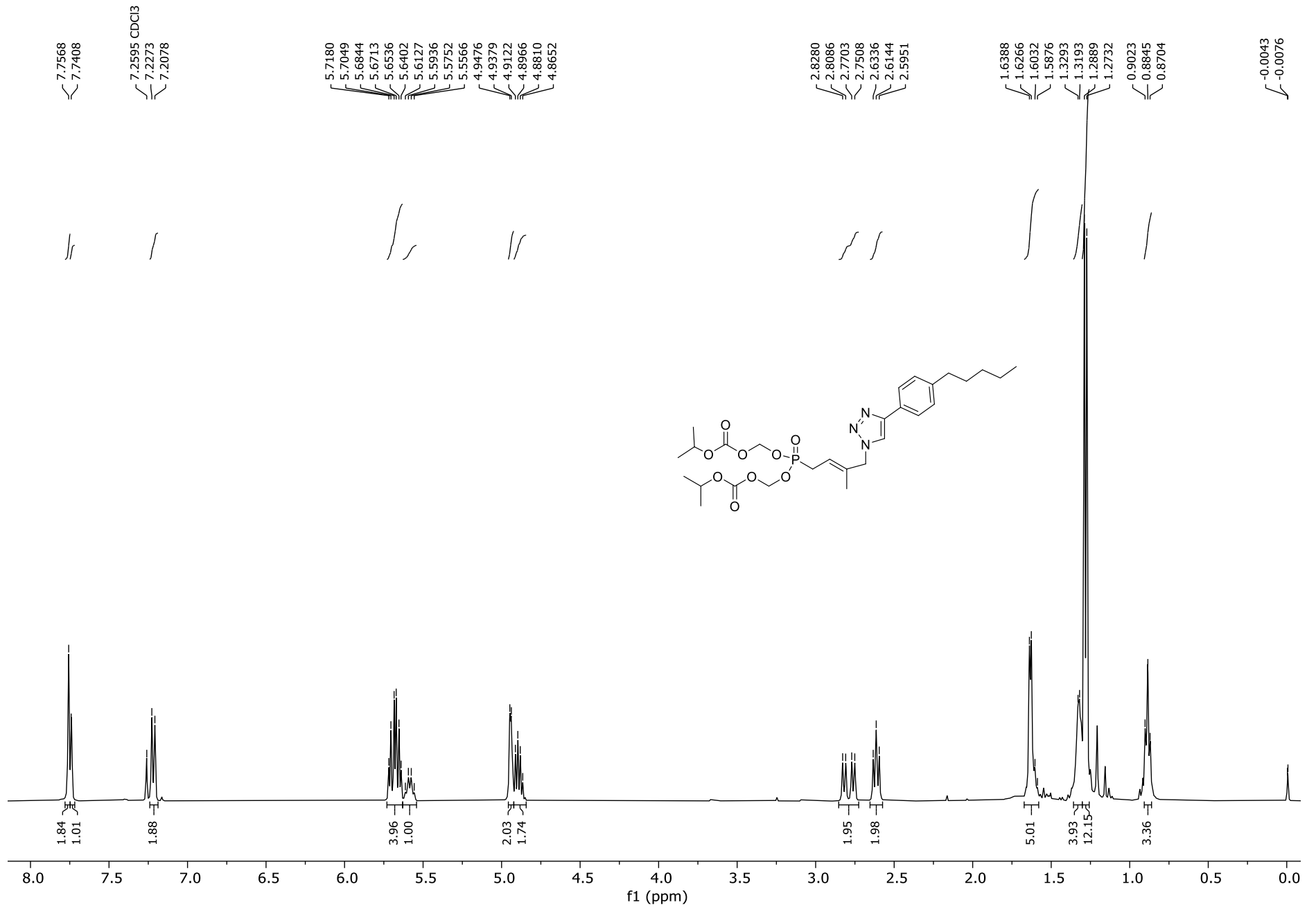


# <sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 11b

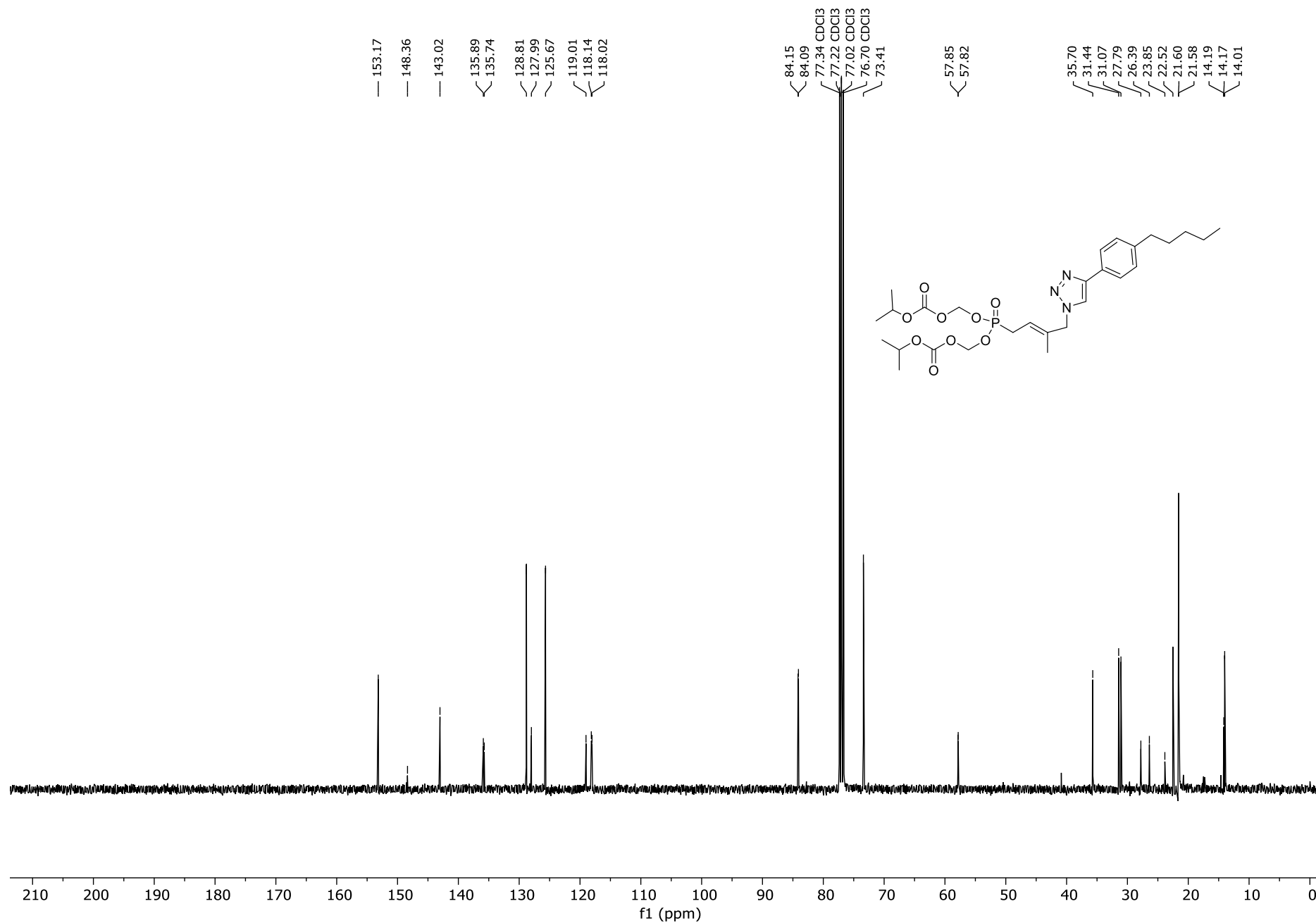
— 27.46



# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) Analysis of Compound 11c



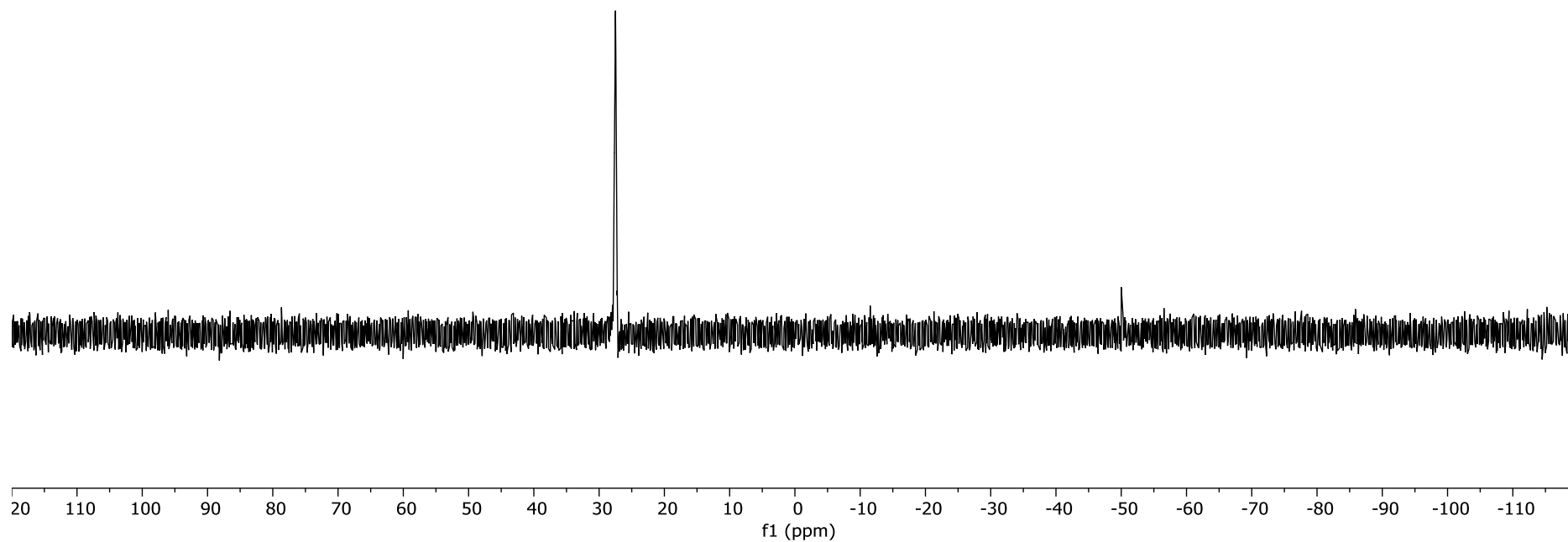
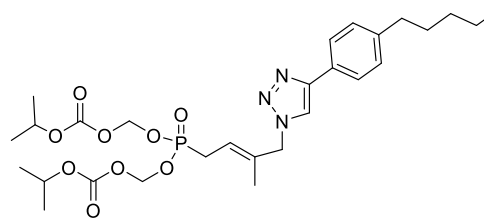
# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 11c



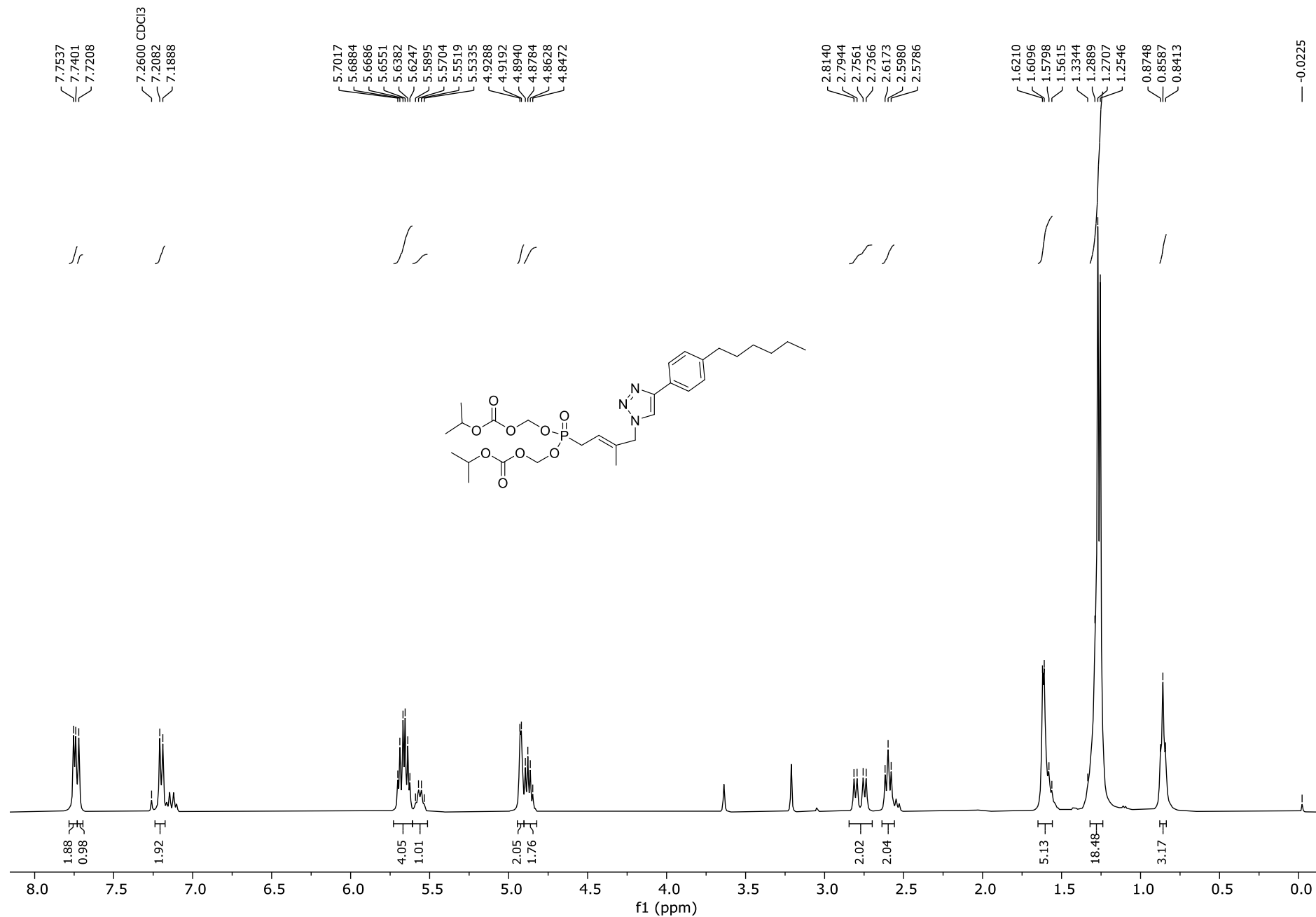


**<sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 11c**

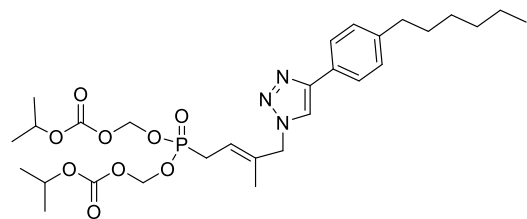
— 27.51



# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) Analysis of Compound 11d



# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 11d

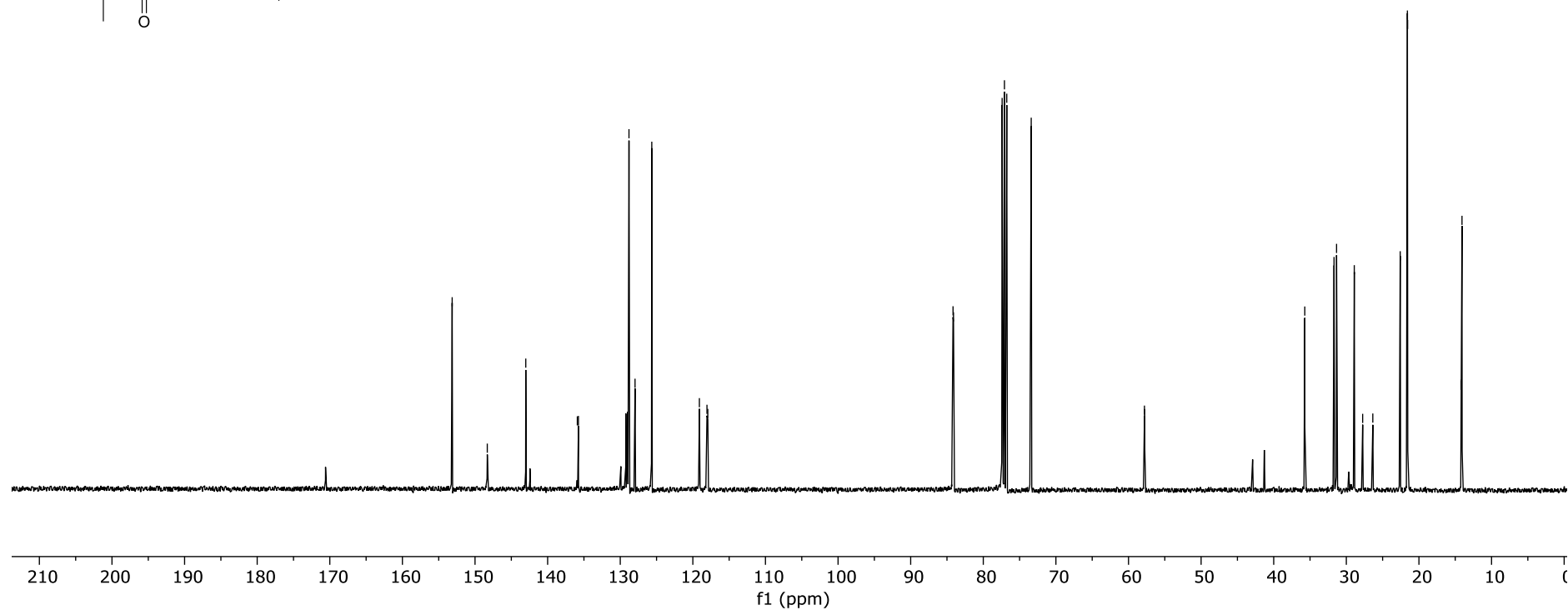


— 153.15  
— 148.31  
— 143.01  
∠ 135.91  
∠ 135.76  
∠ 128.80  
∠ 127.96  
∠ 125.66  
∠ 119.10  
∠ 118.05  
∠ 117.94

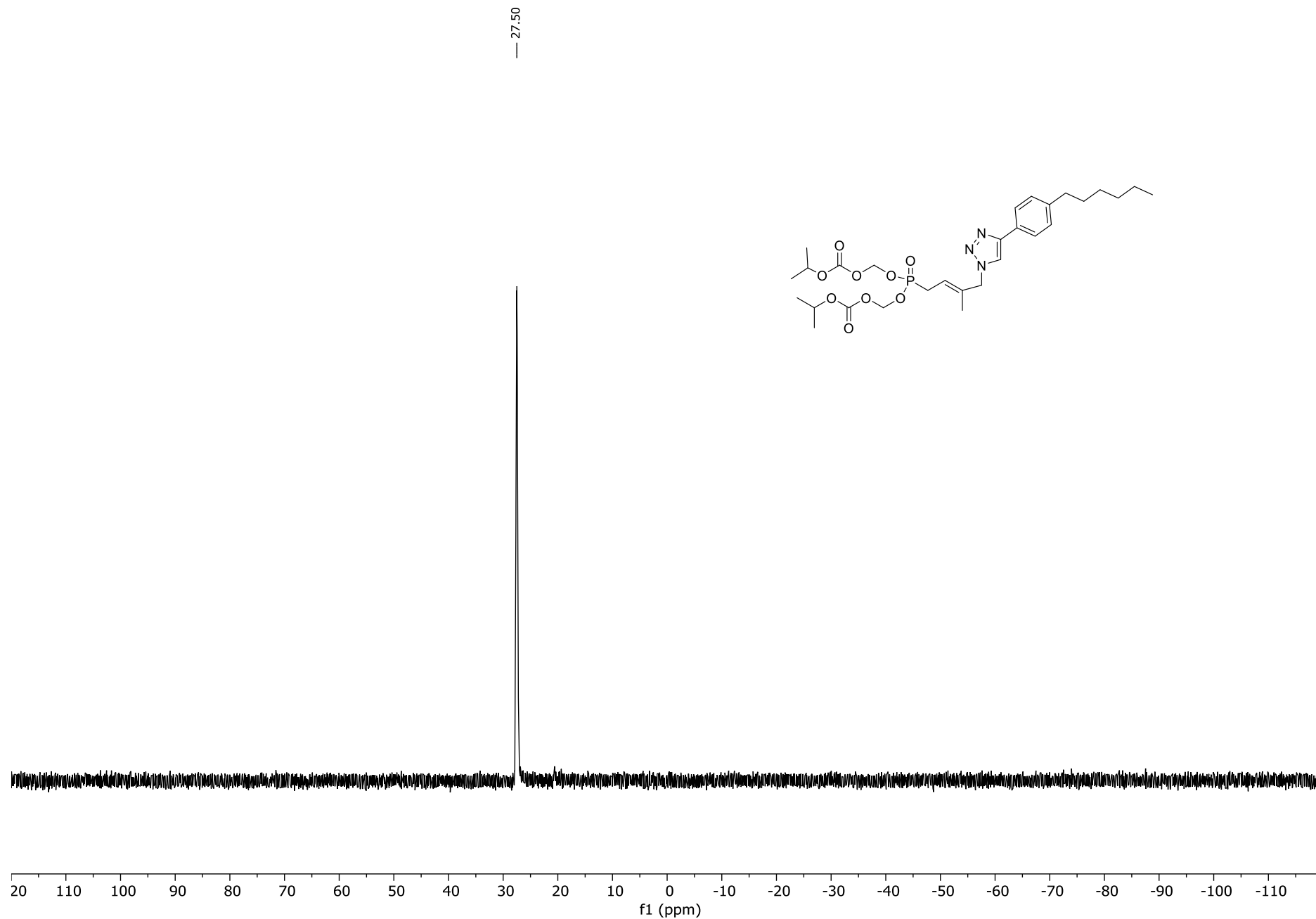
∠ 84.17  
∠ 84.10  
∠ 77.40  
∠ 77.08  
∠ 76.77  
∠ 73.40

∠ 57.80  
∠ 57.78

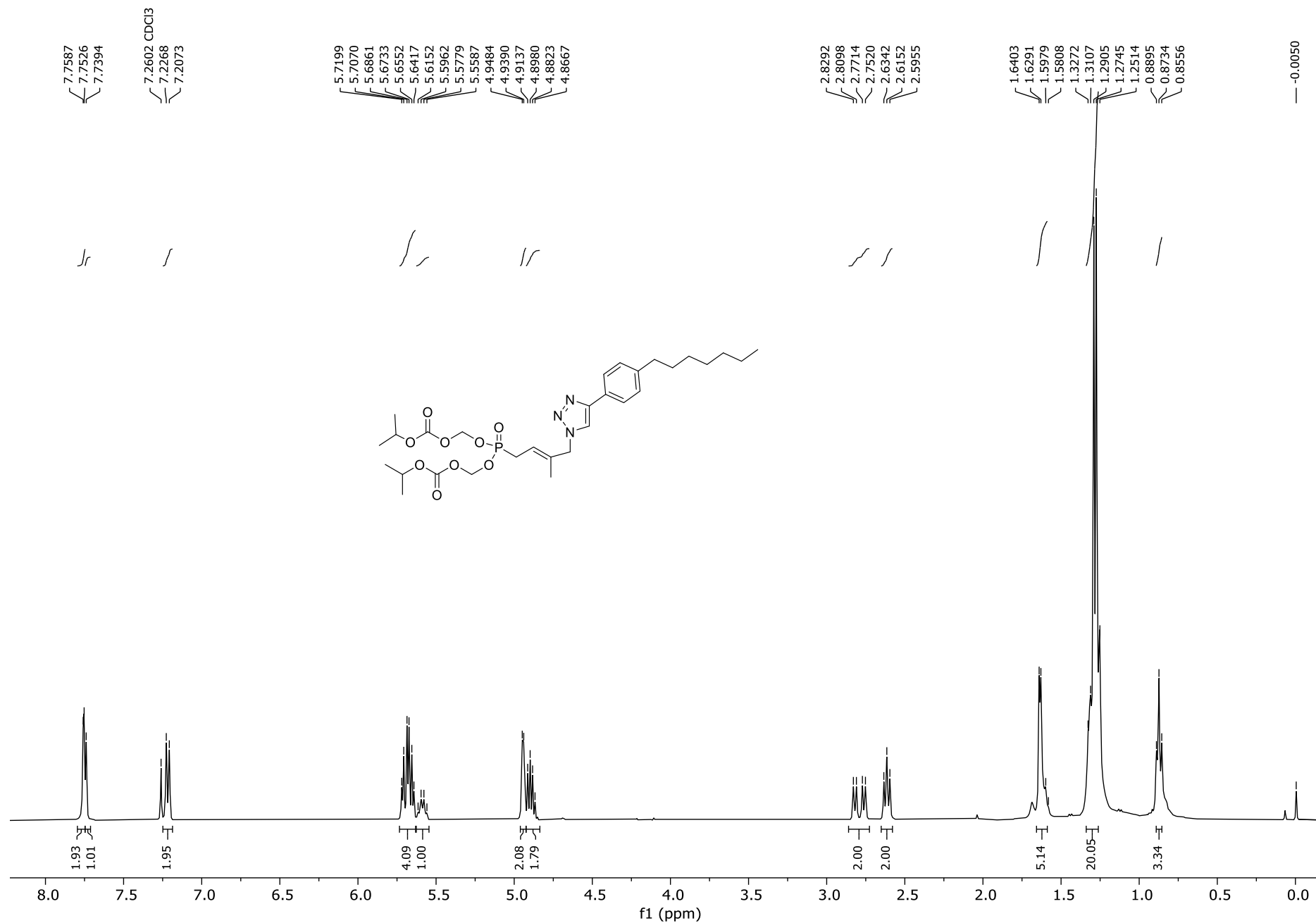
∠ 35.72  
∠ 31.69  
∠ 31.34  
∠ 28.91  
∠ 27.75  
— 26.35  
∠ 22.58  
∠ 21.59  
∠ 21.56  
∠ 14.18  
∠ 14.16  
∠ 14.07



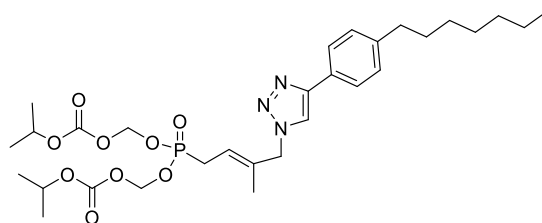
**<sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 11d**



# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) Analysis of Compound 11e



# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 11e

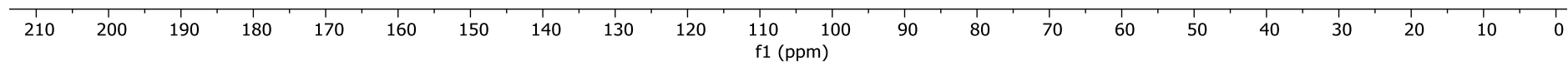


153.17  
148.36  
143.03  
135.89  
135.74  
128.81  
127.99  
125.66  
119.00  
118.16  
118.04

84.15  
84.08  
77.34 CDCl<sub>3</sub>  
77.22 CDCl<sub>3</sub>  
77.02 CDCl<sub>3</sub>  
76.70 CDCl<sub>3</sub>  
73.40

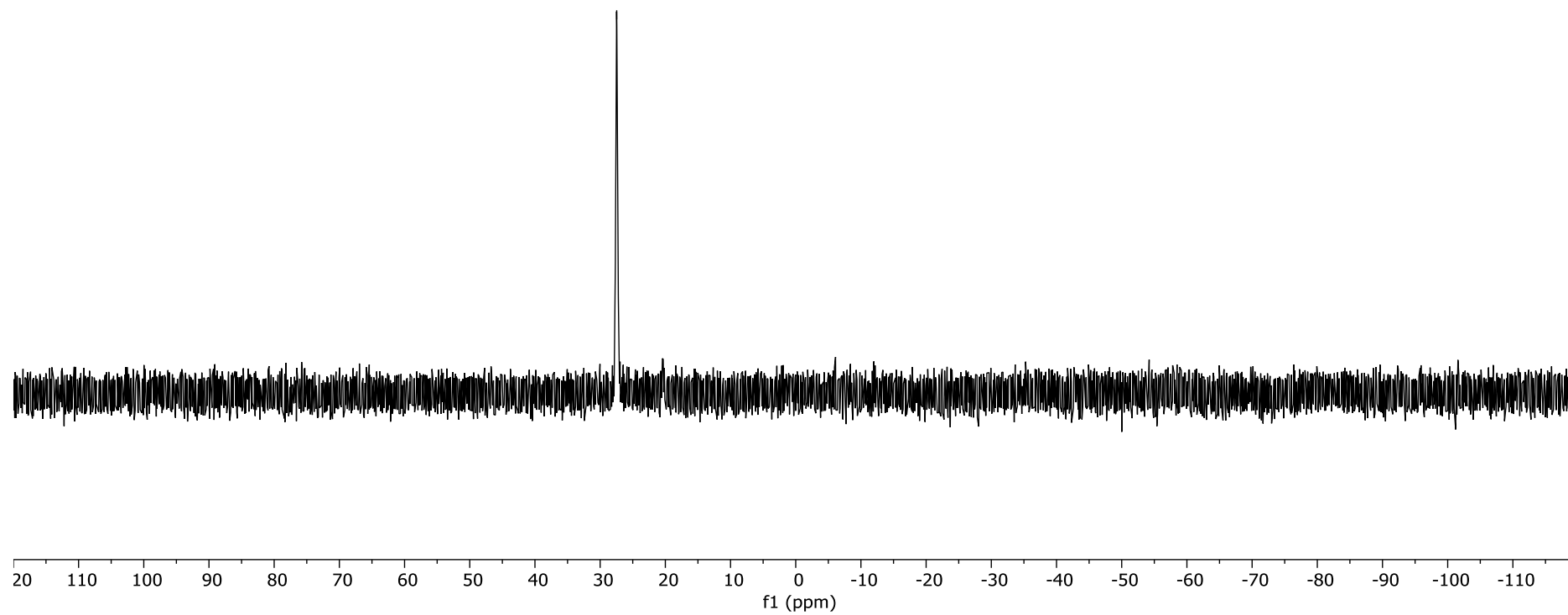
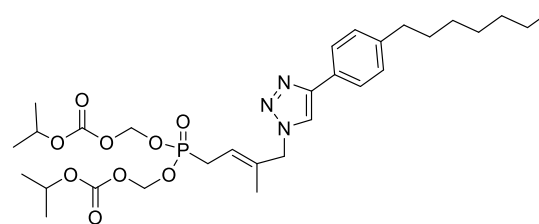
57.86  
57.83

35.74  
31.81  
31.40  
29.70  
29.22  
29.17  
27.80  
26.40  
22.65  
21.61  
21.58  
14.20  
14.17  
14.08

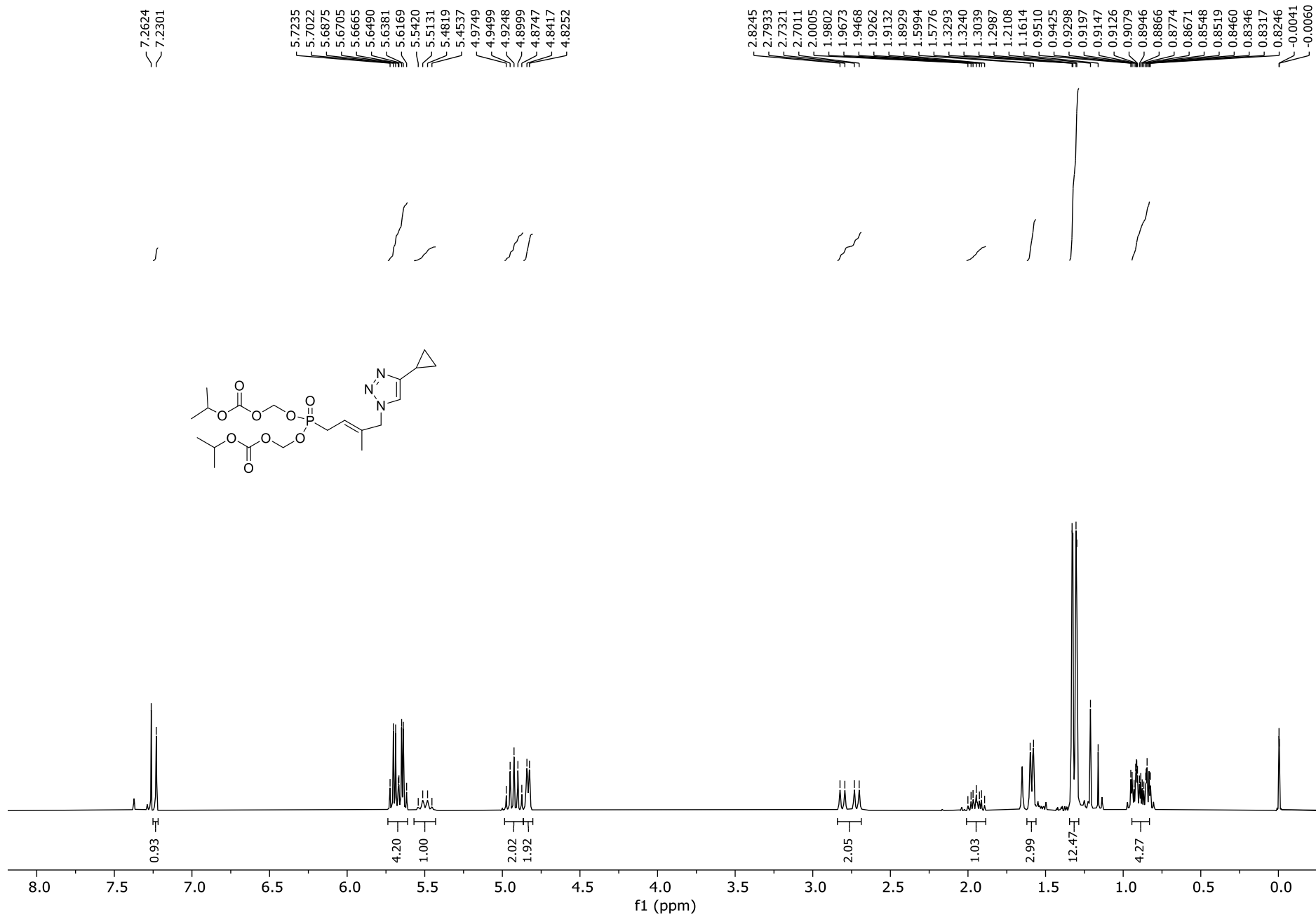


**$^{31}\text{P}$  NMR (161 MHz,  $\text{CDCl}_3$ ) Analysis of Compound 11e**

— 27.46

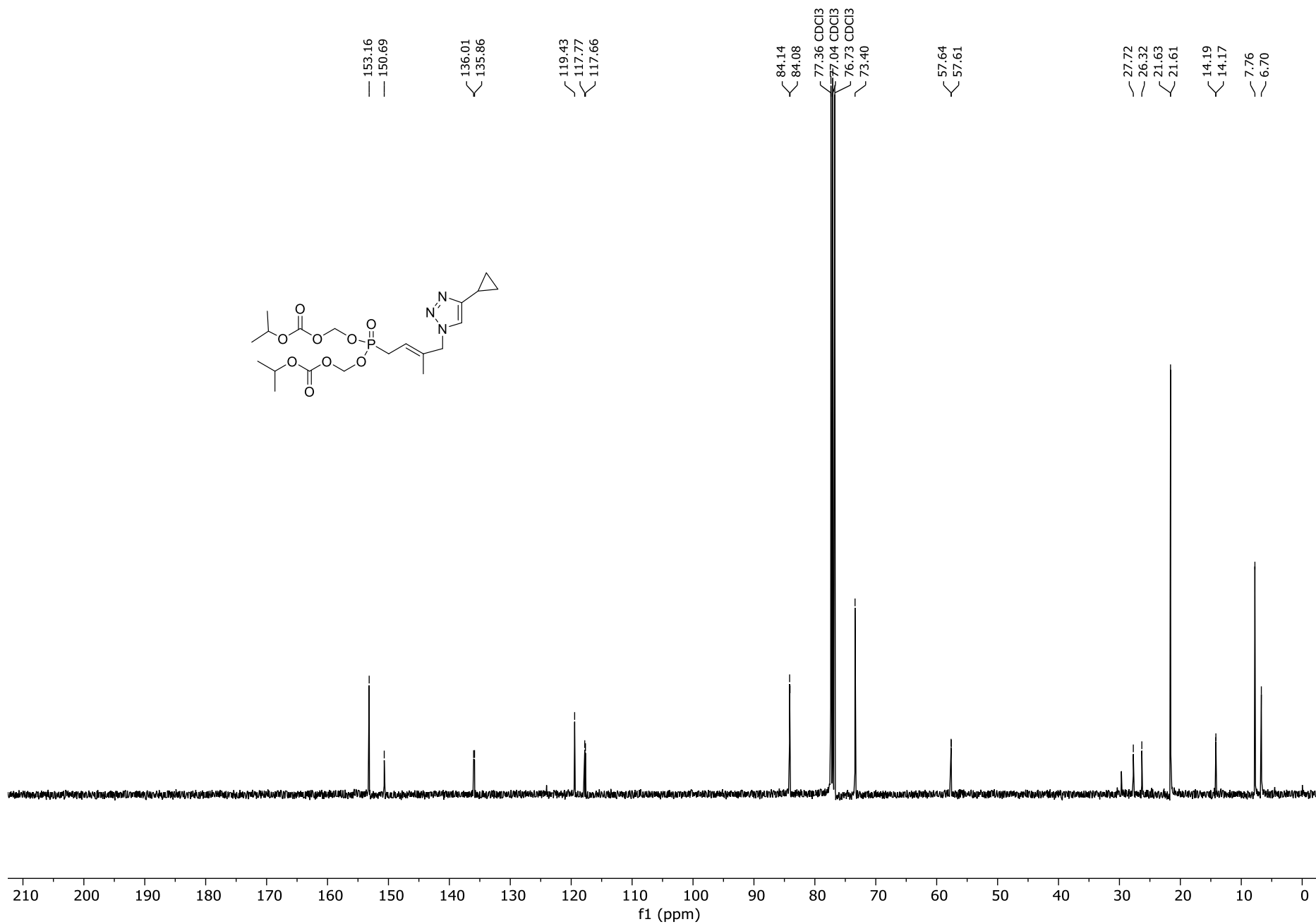
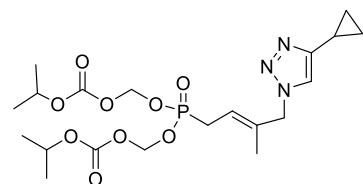


# <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>) Analysis of Compound 11f



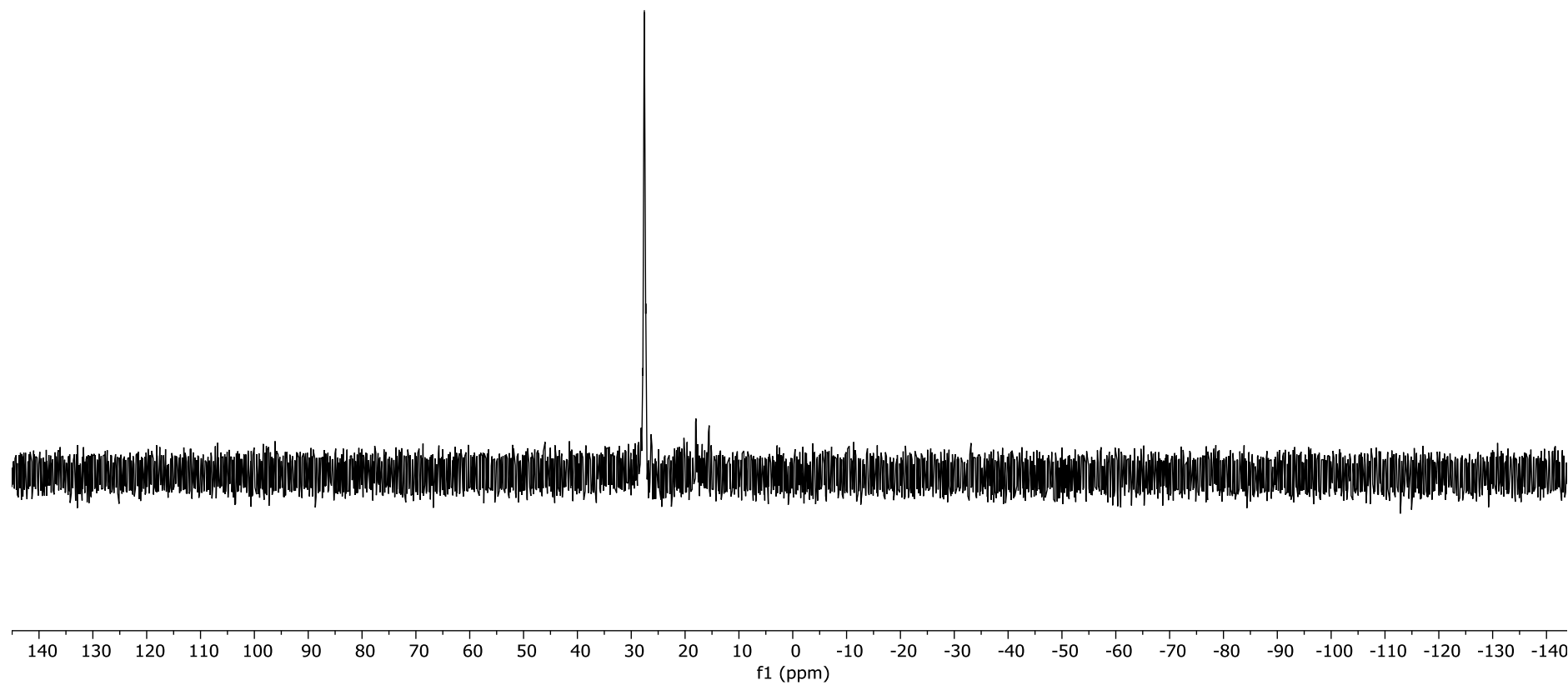
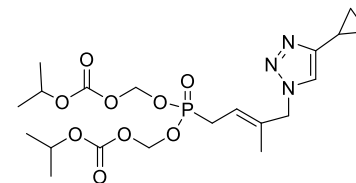


# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 11f

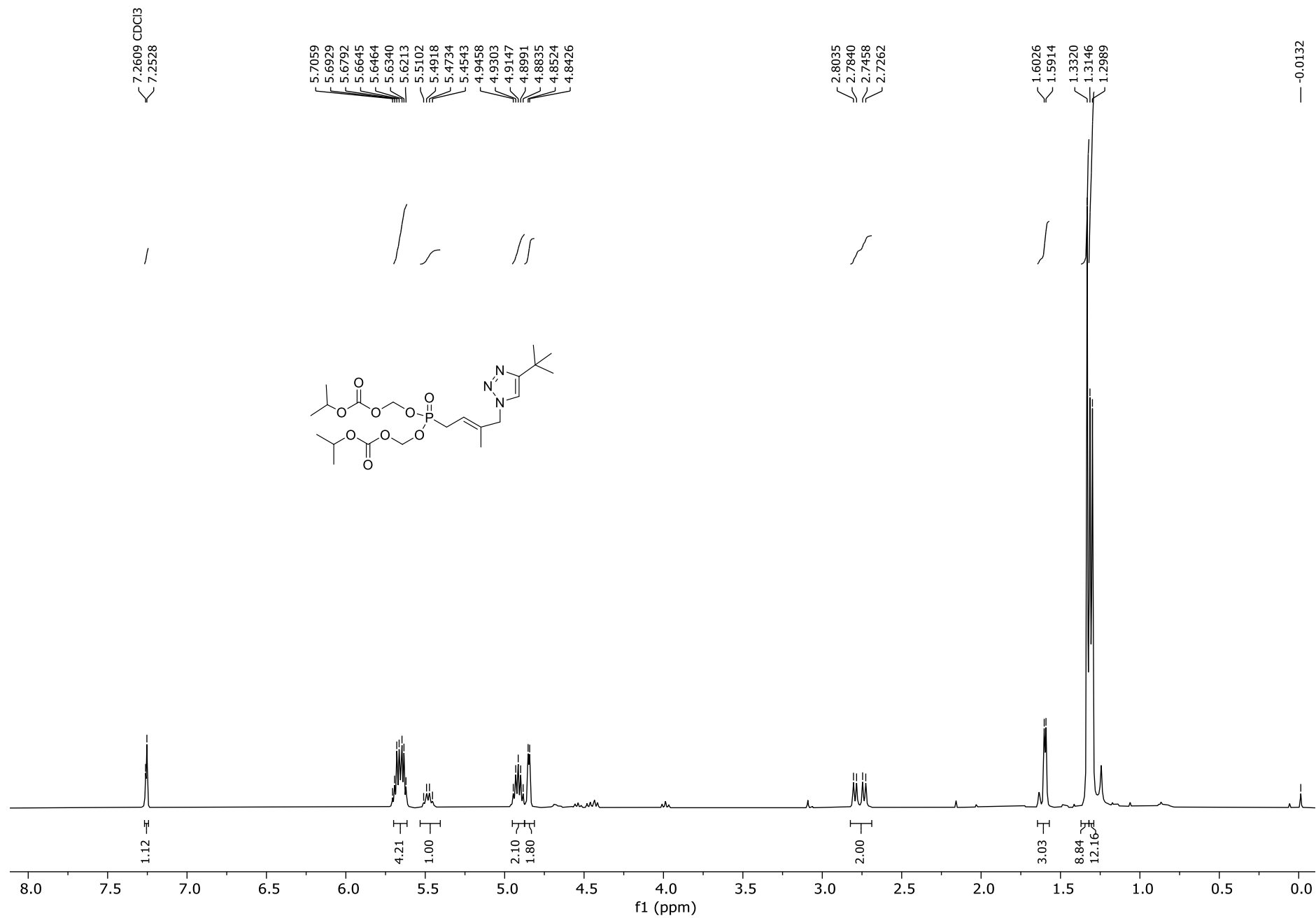


**<sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 11f**

— 27.56



# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) Analysis of Compound 11g



# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 11g

— 153.15

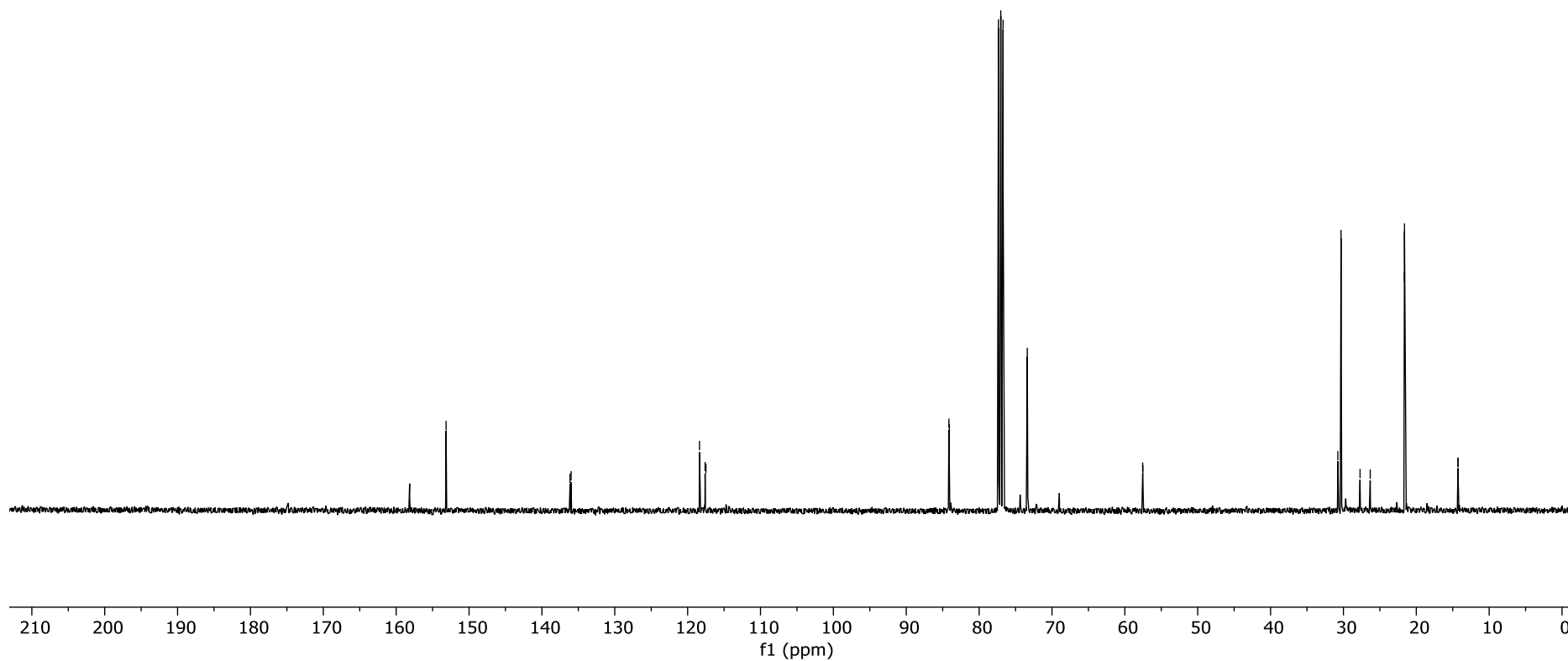
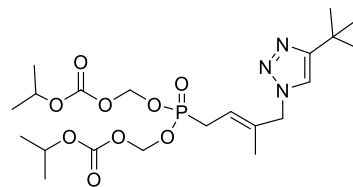
136.14  
135.99

118.37  
117.61  
117.49

84.15  
84.08  
77.34 CDCl<sub>3</sub>  
77.03 CDCl<sub>3</sub>  
76.71 CDCl<sub>3</sub>  
73.39

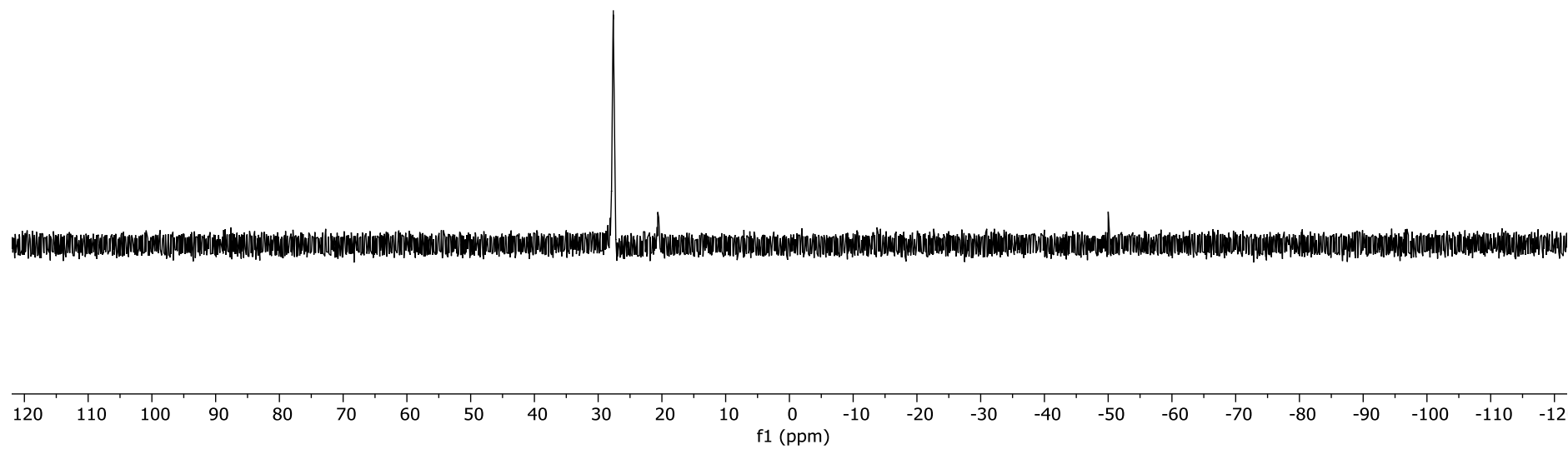
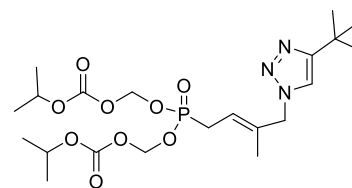
57.56  
57.53

30.76  
30.33  
27.72  
26.32  
21.64  
21.62  
14.29  
14.26

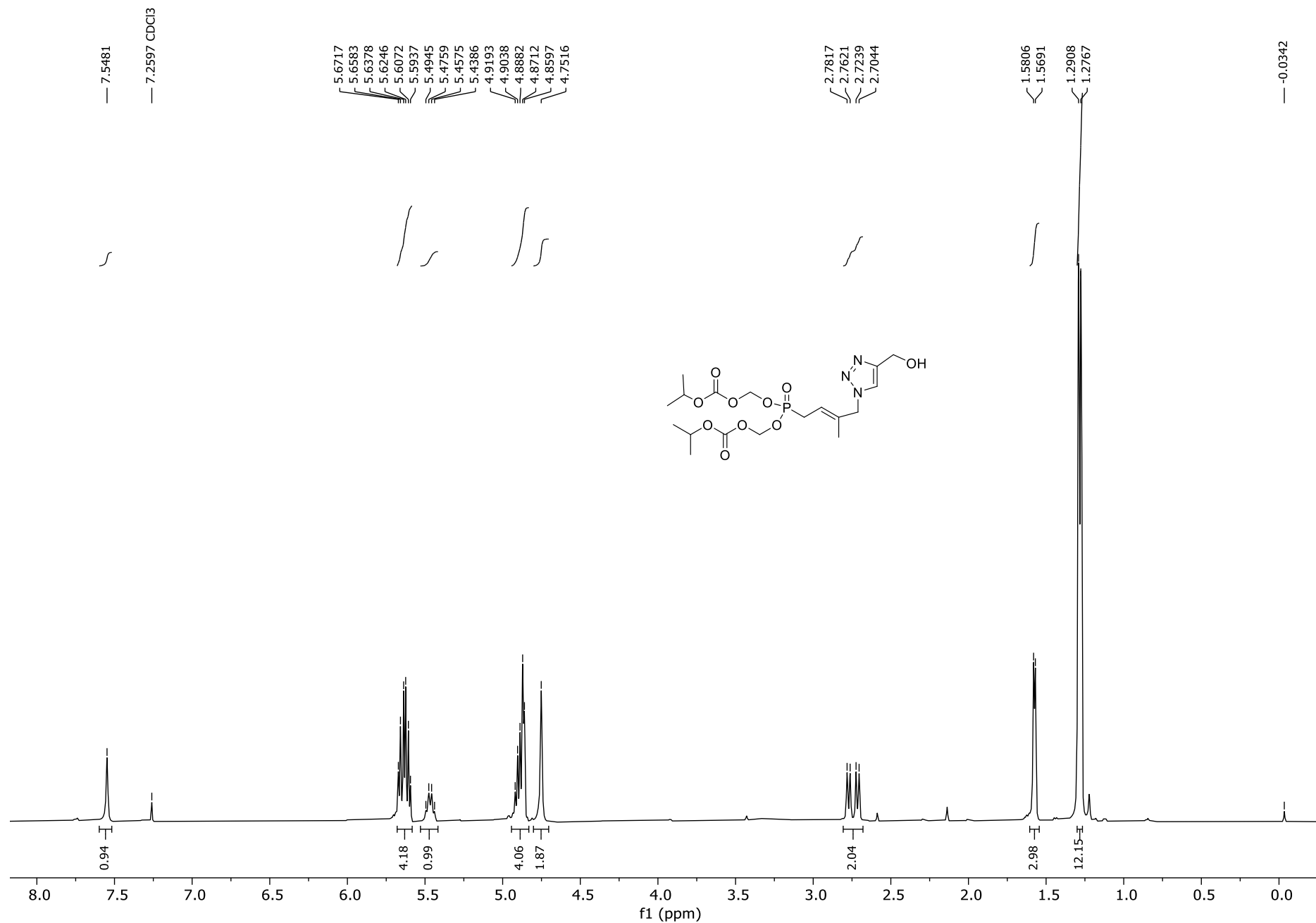


**$^{31}\text{P}$  NMR (161 MHz,  $\text{CDCl}_3$ ) Analysis of Compound 11g**

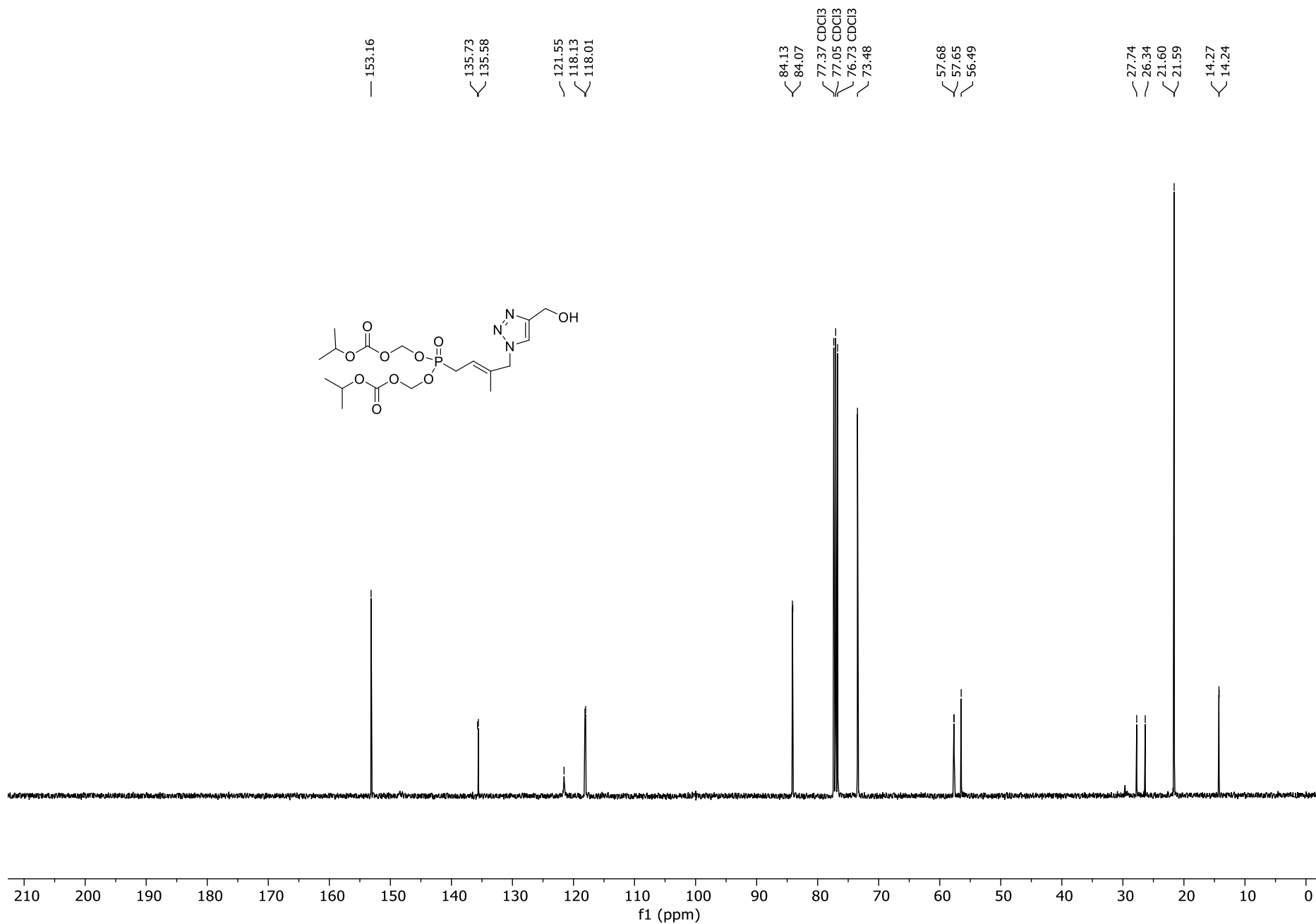
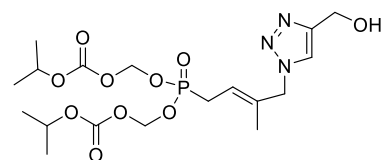
— 27.62



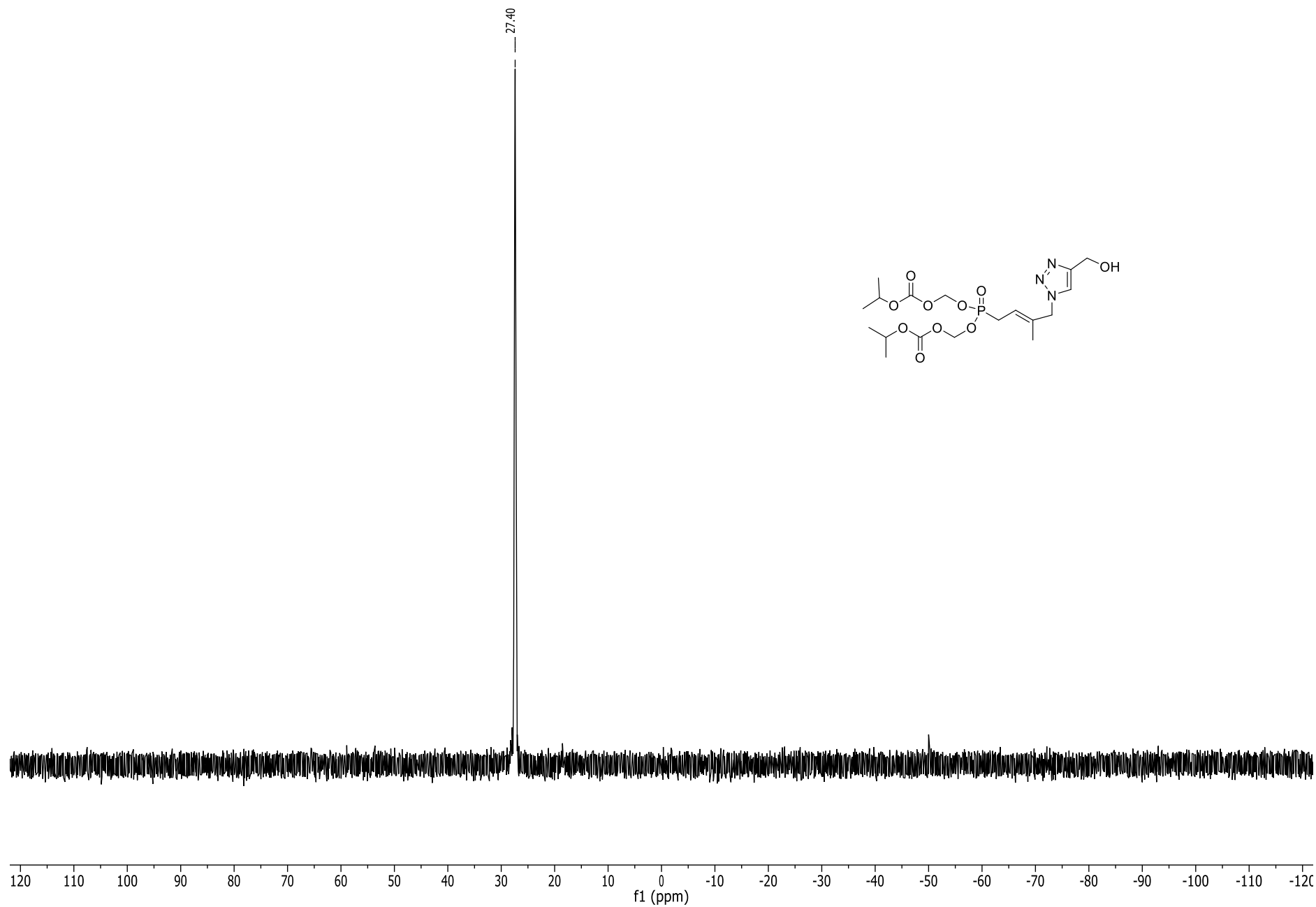
# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) Analysis of Compound 11h



# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 11h

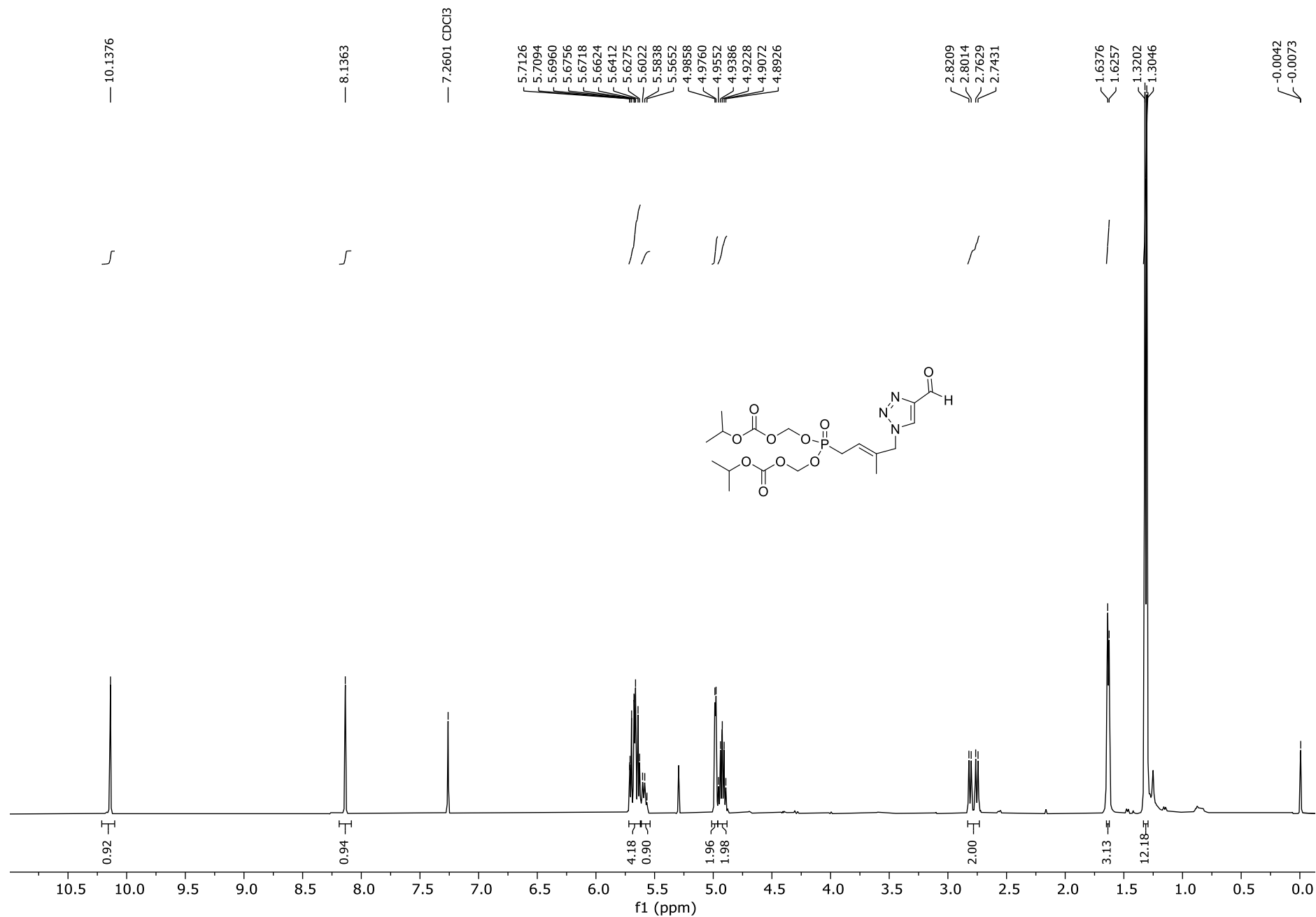


**<sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 11h**

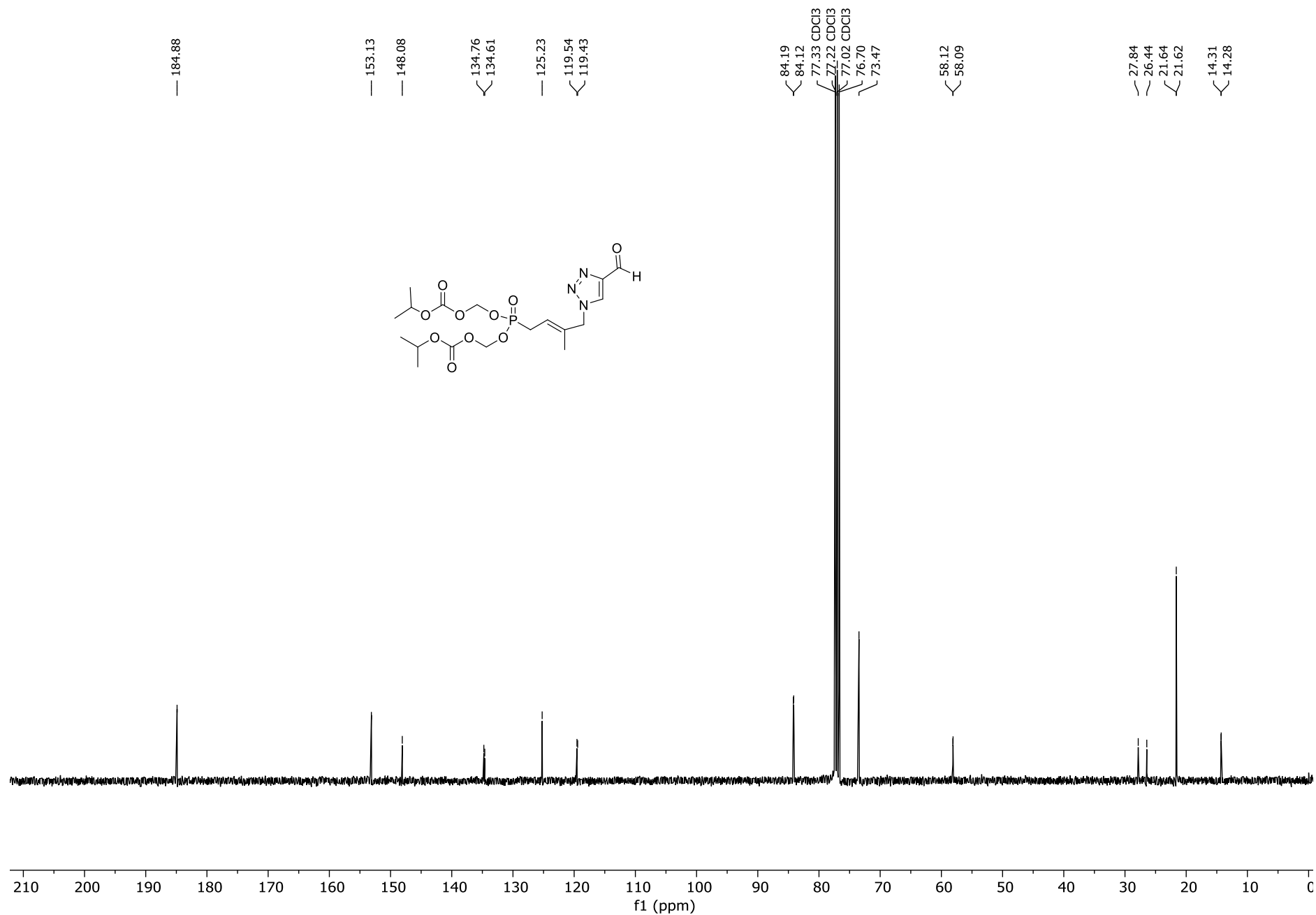




# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) Analysis of Compound 11i

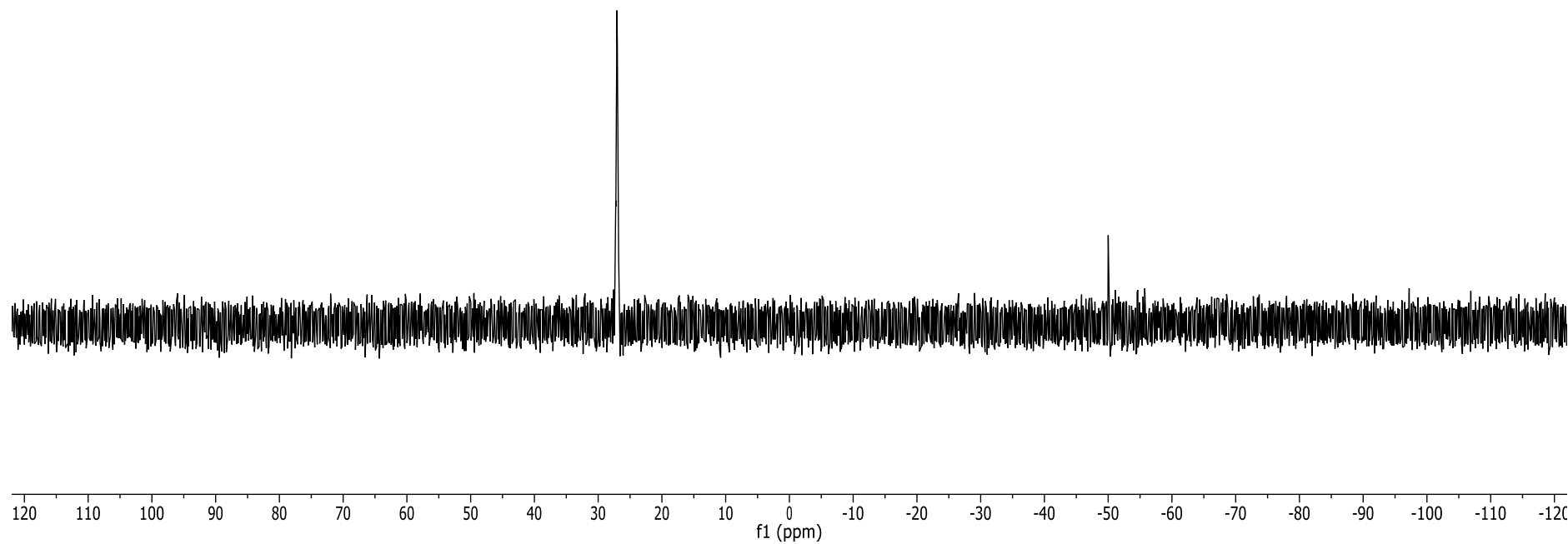
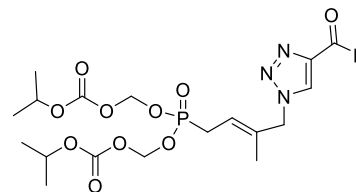


# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 11i

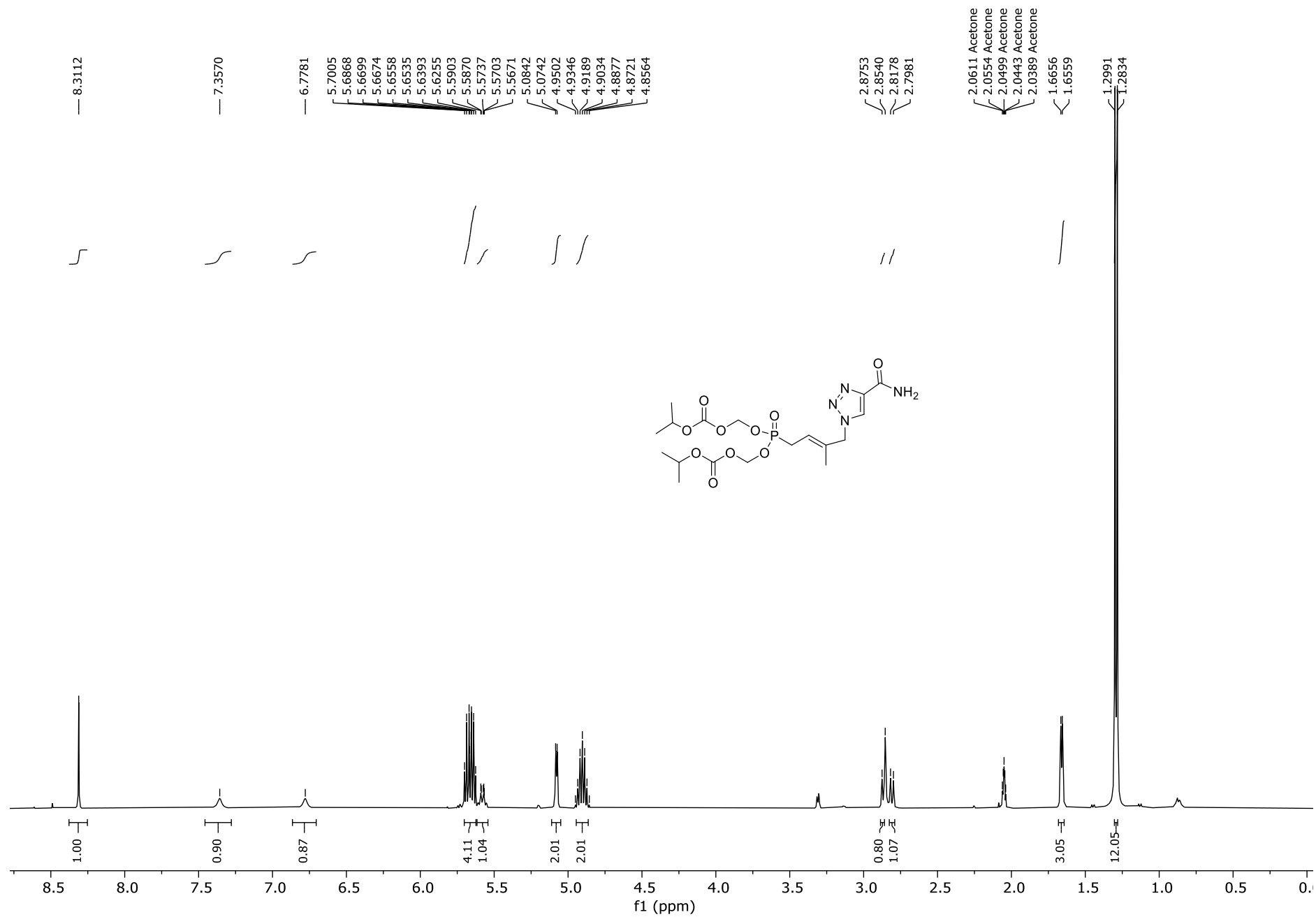


**<sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 11i**

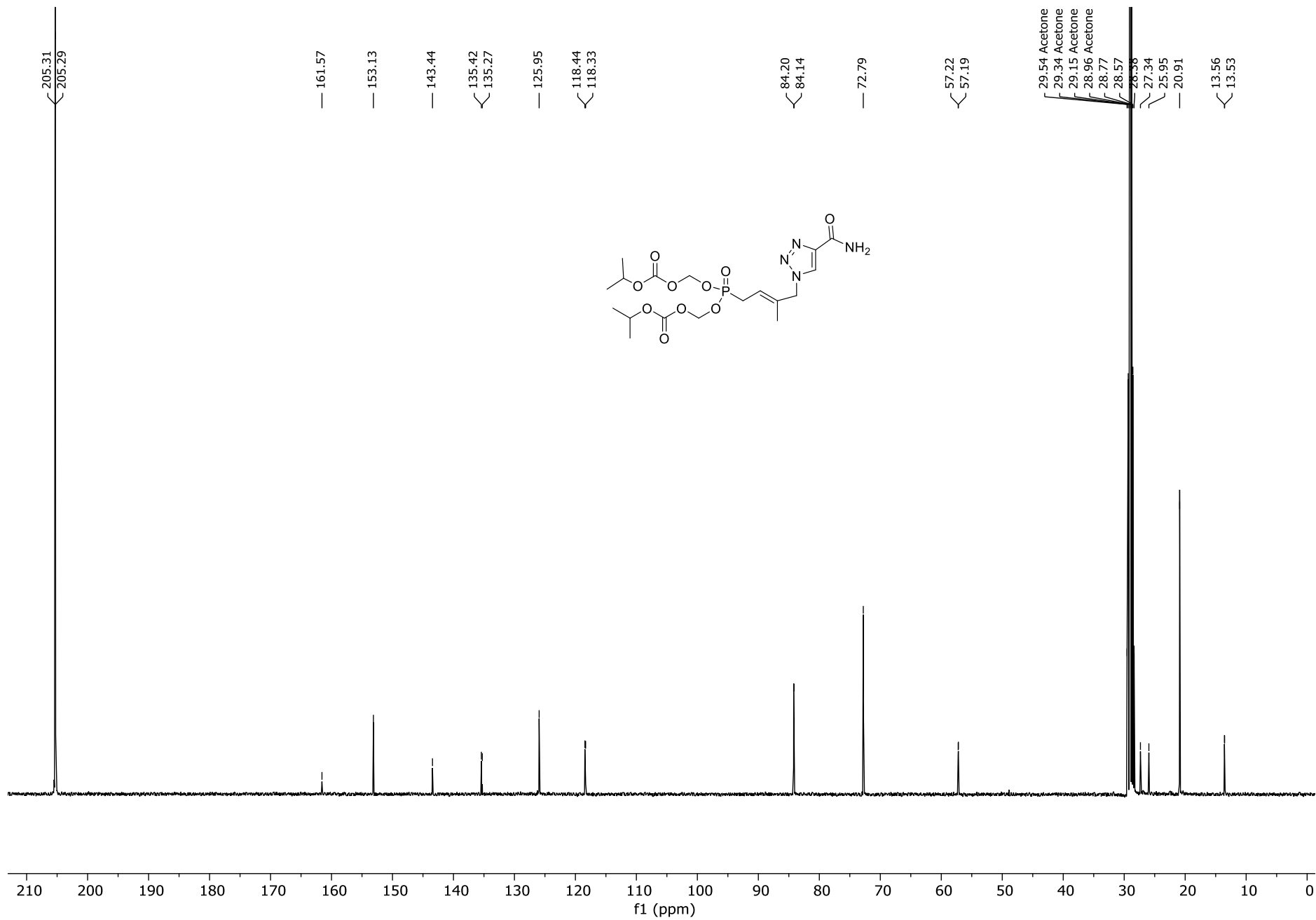
27.04



# <sup>1</sup>H NMR (400 MHz, Acetone-d<sub>6</sub>) Analysis of Compound 11j



# <sup>13</sup>C NMR (101 MHz, Acetone-d<sub>6</sub>) Analysis of Compound 11j



205.31  
205.29

161.57

153.13

143.44

135.42  
135.27

125.95

118.44  
118.33

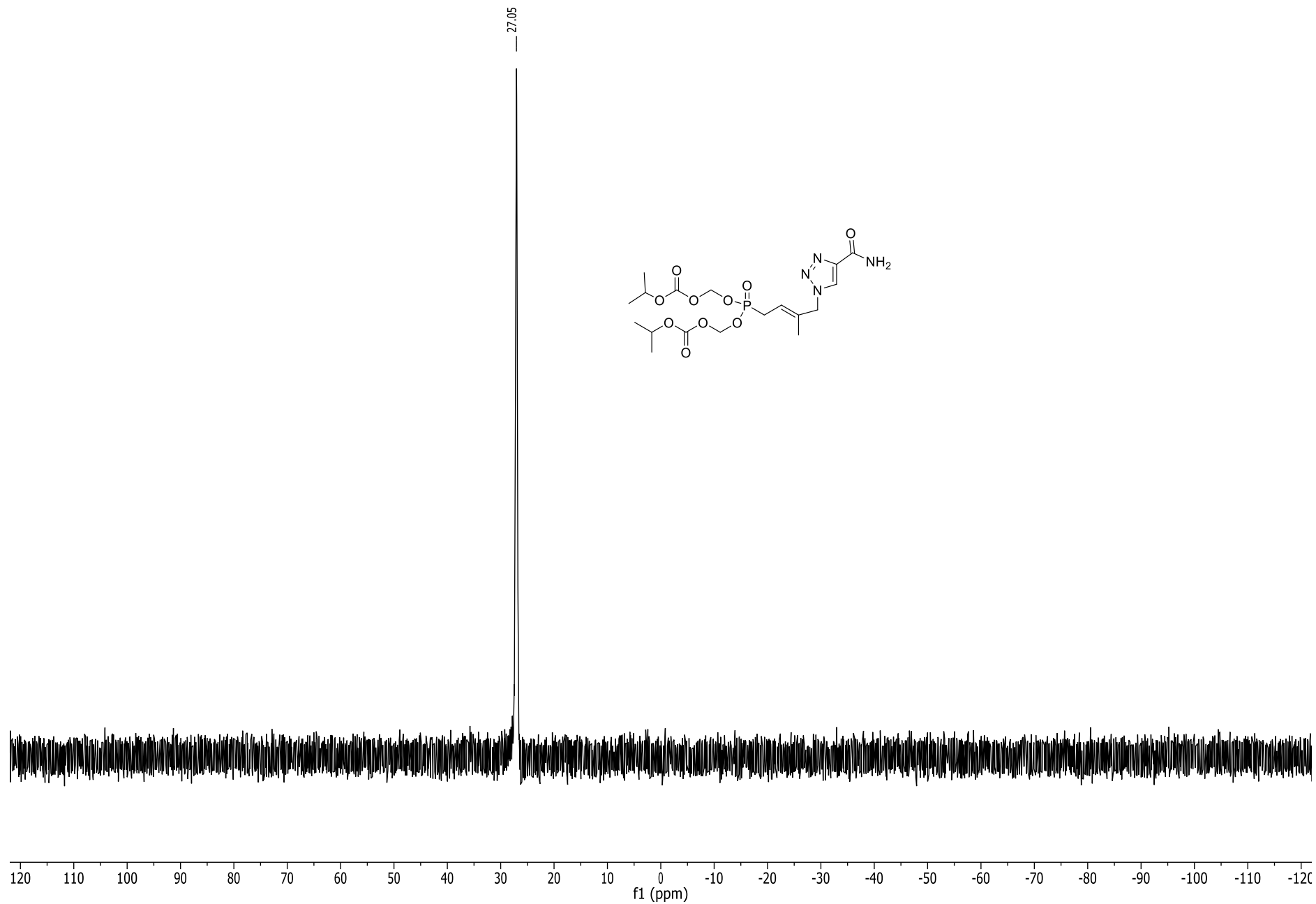
84.20  
84.14

72.79

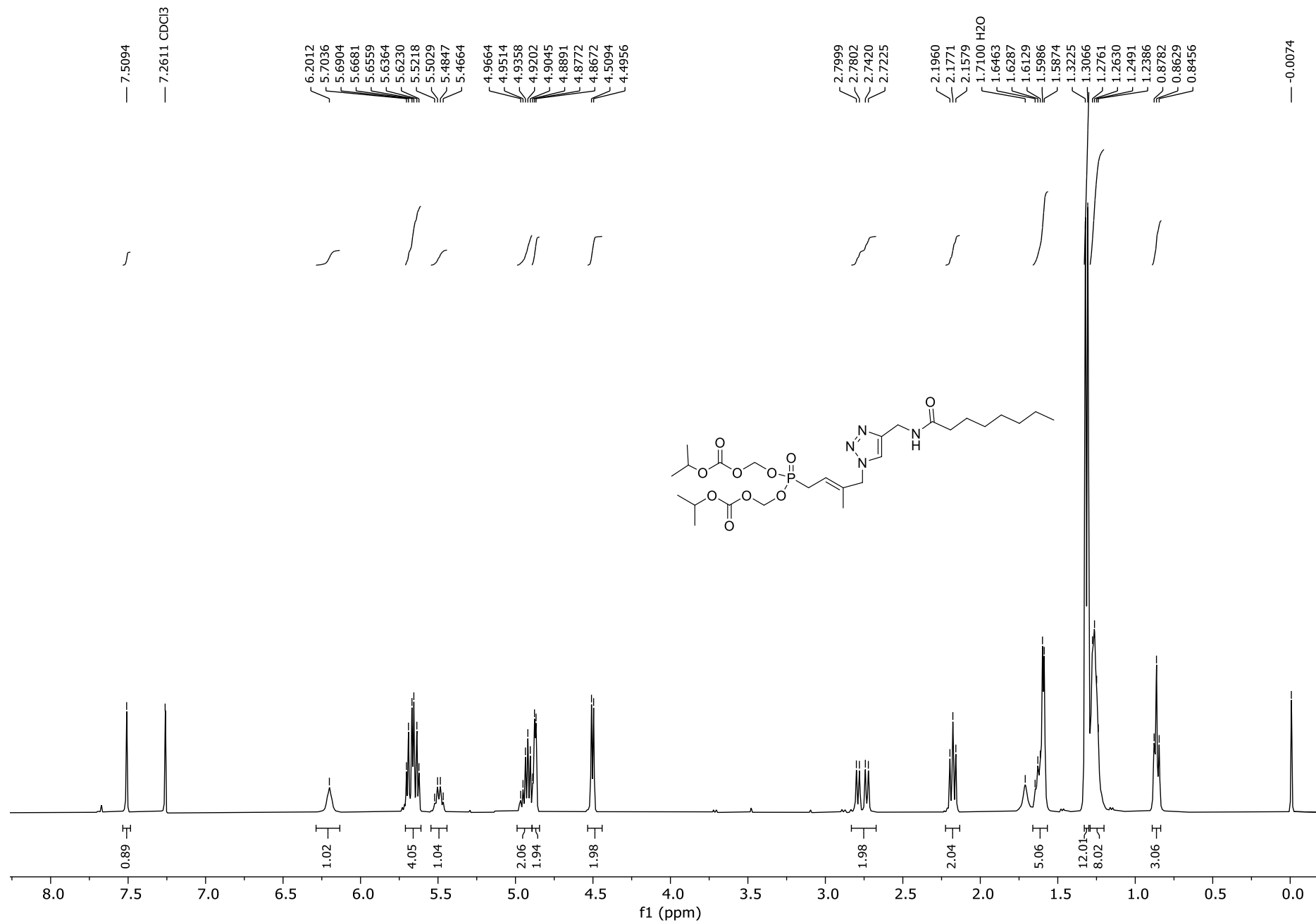
57.22  
57.19

29.54 Acetone  
29.34 Acetone  
29.15 Acetone  
28.96 Acetone  
28.77  
28.57  
28.36  
27.34  
25.95  
20.91  
13.56  
13.53

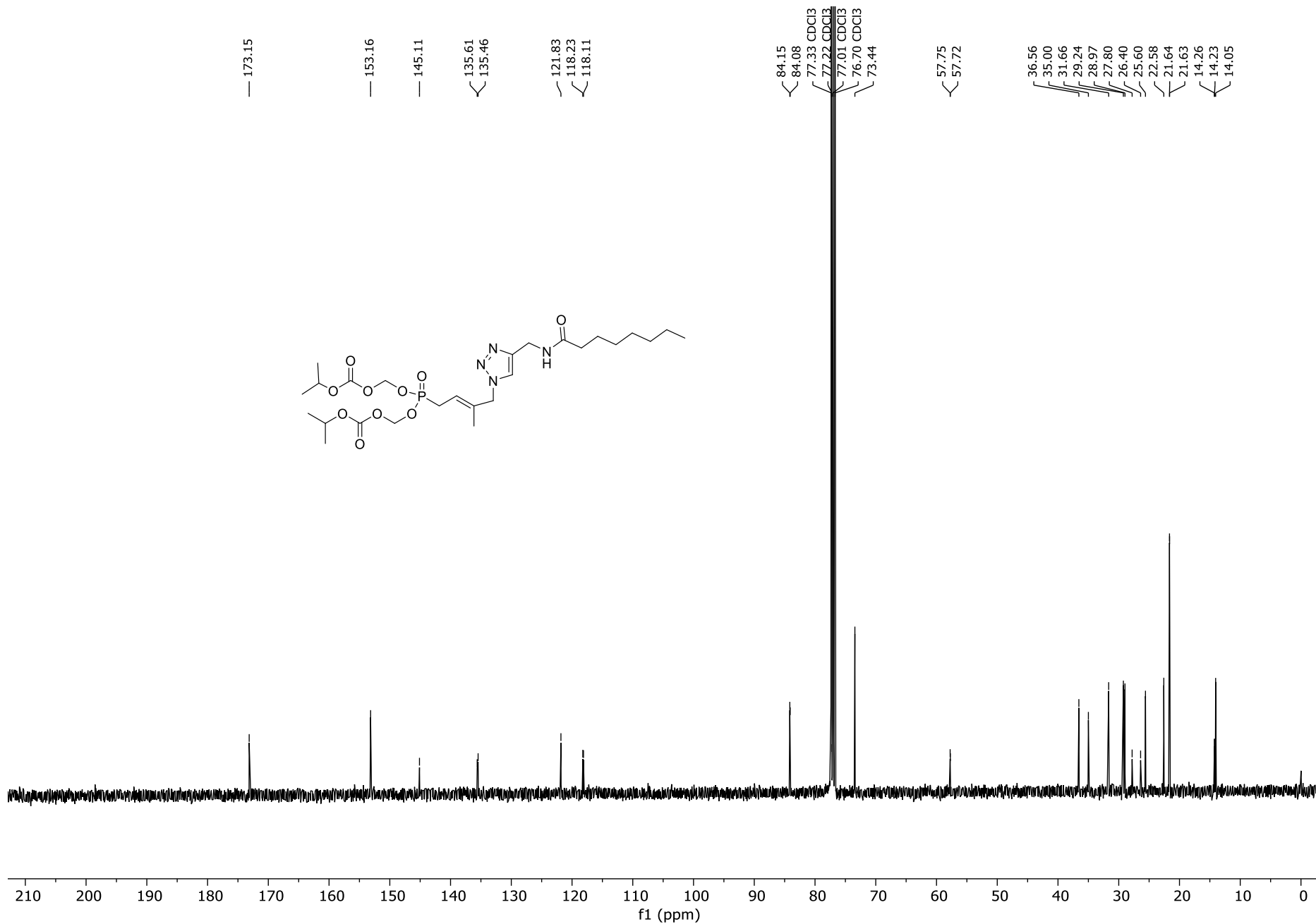
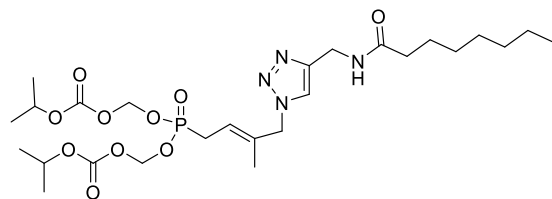
**<sup>31</sup>P NMR (161 MHz, Acetone-d<sub>6</sub>) Analysis of Compound 11j**



# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) Analysis of Compound 11k



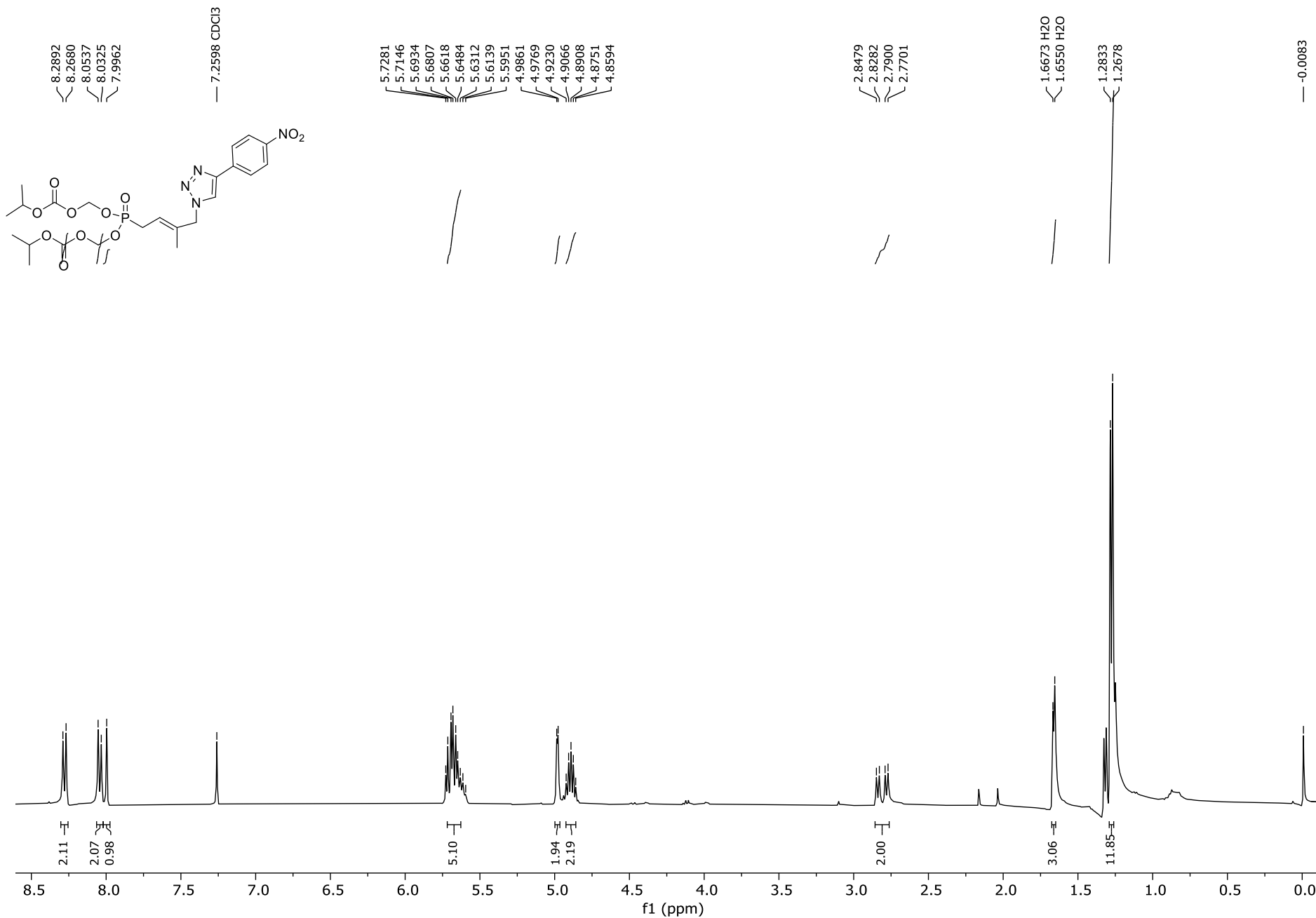
# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 11k



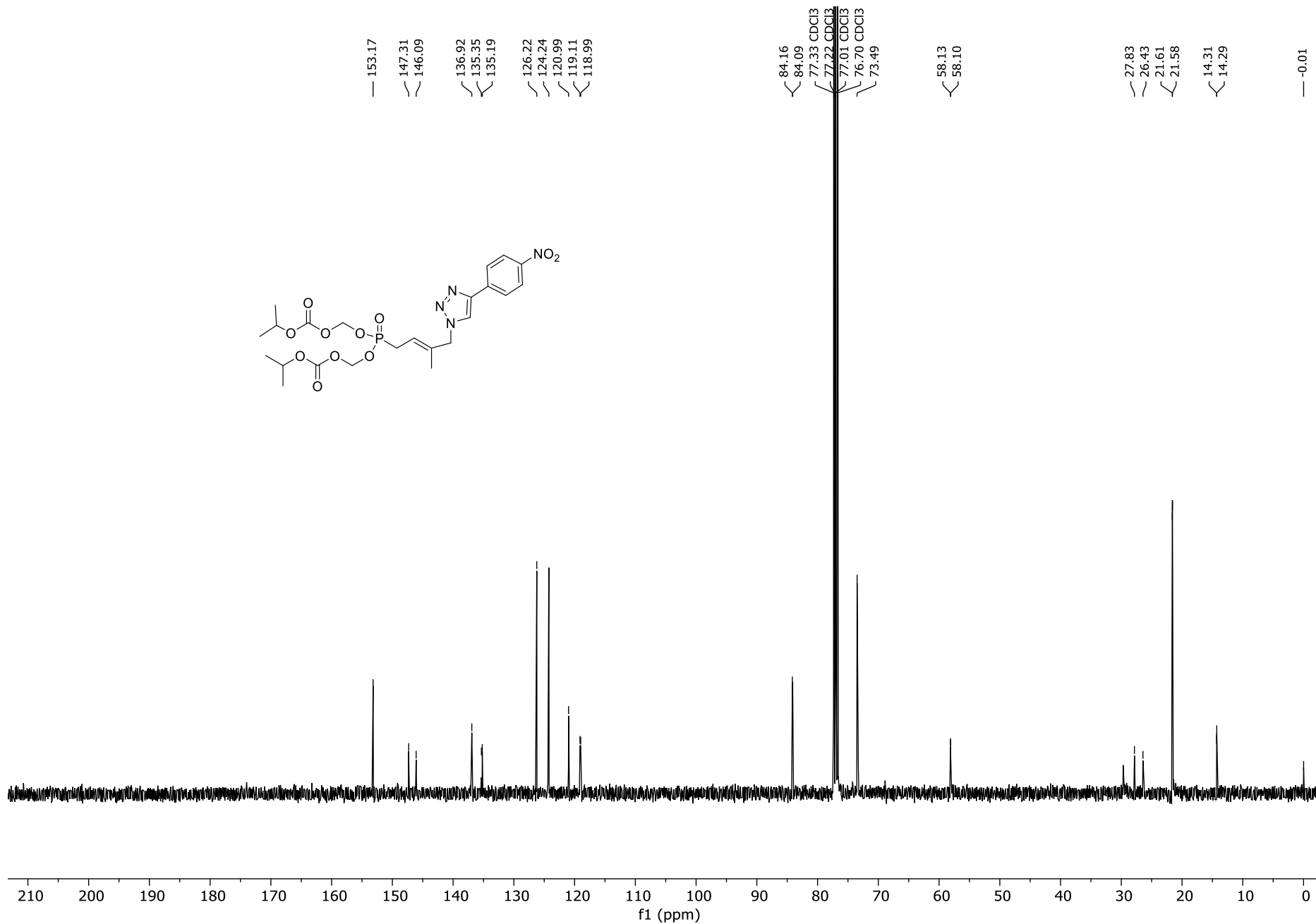
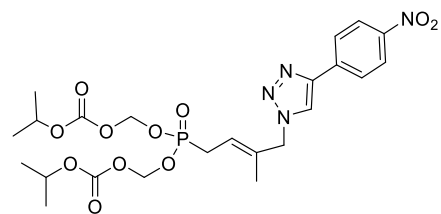




# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) Analysis of Compound 11I

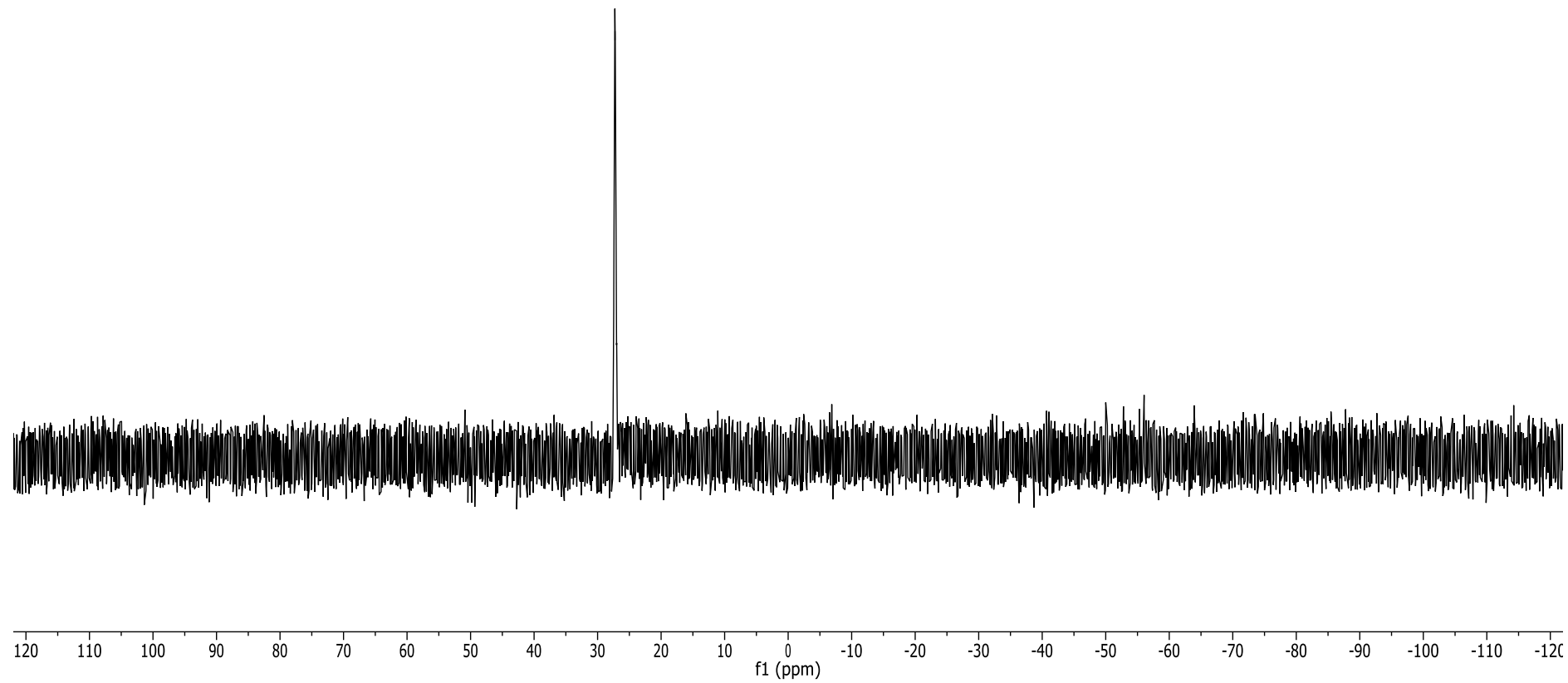
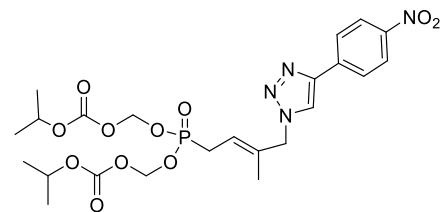


# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 11I

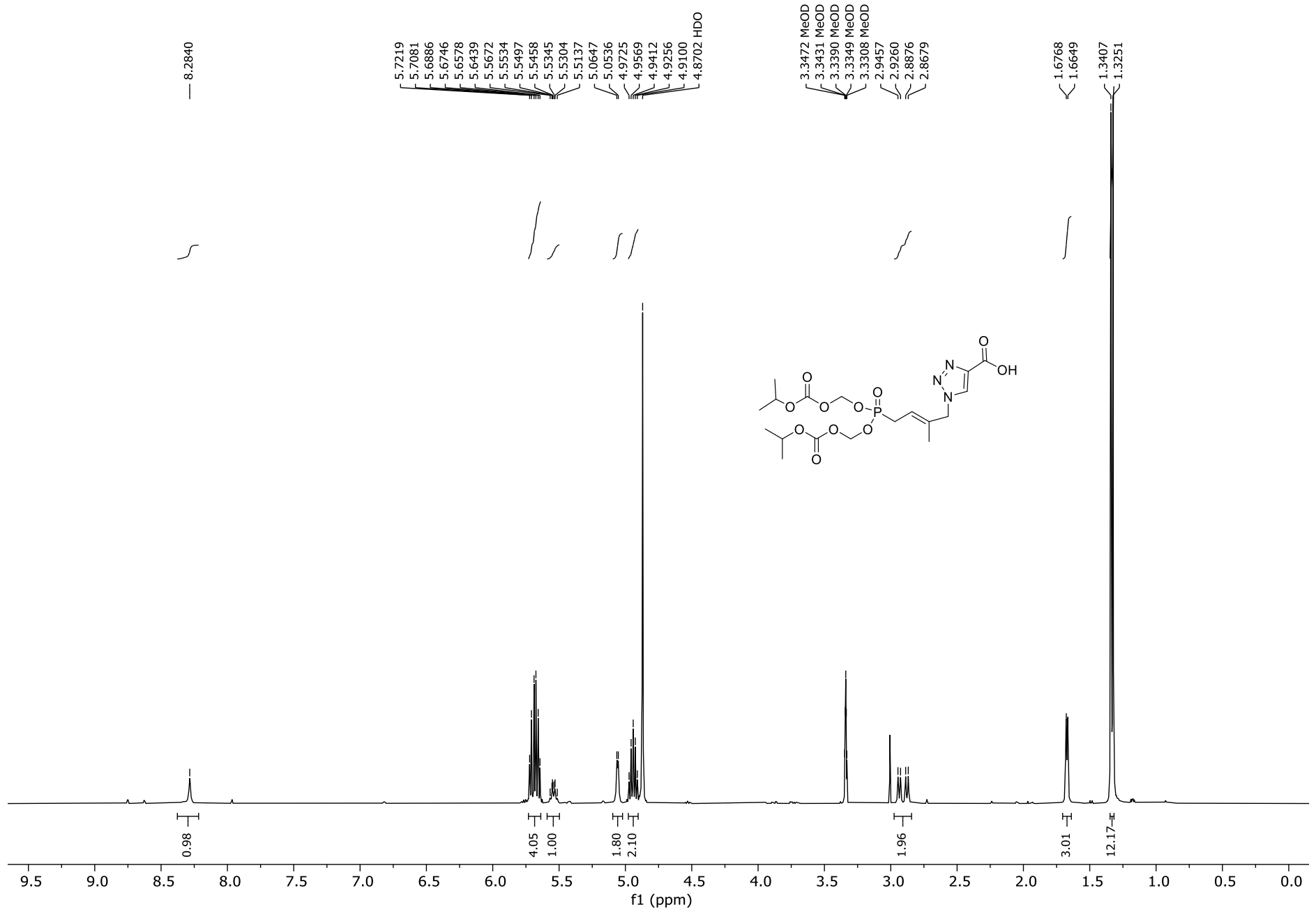


# <sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 11I

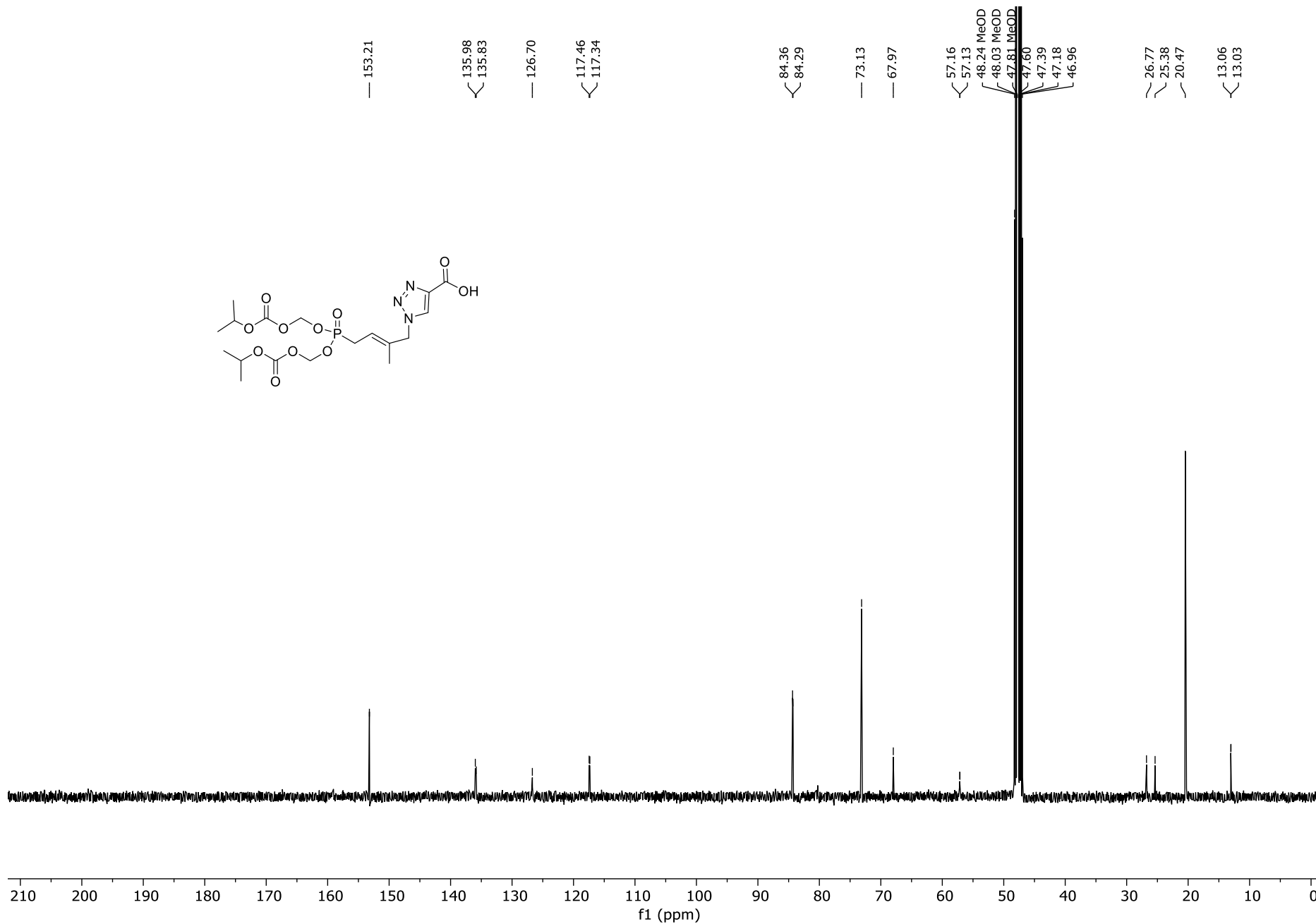
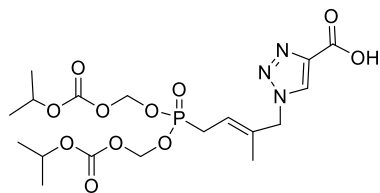
— 27.26



# <sup>1</sup>H NMR (400 MHz, MeOD) Analysis of Compound 11m

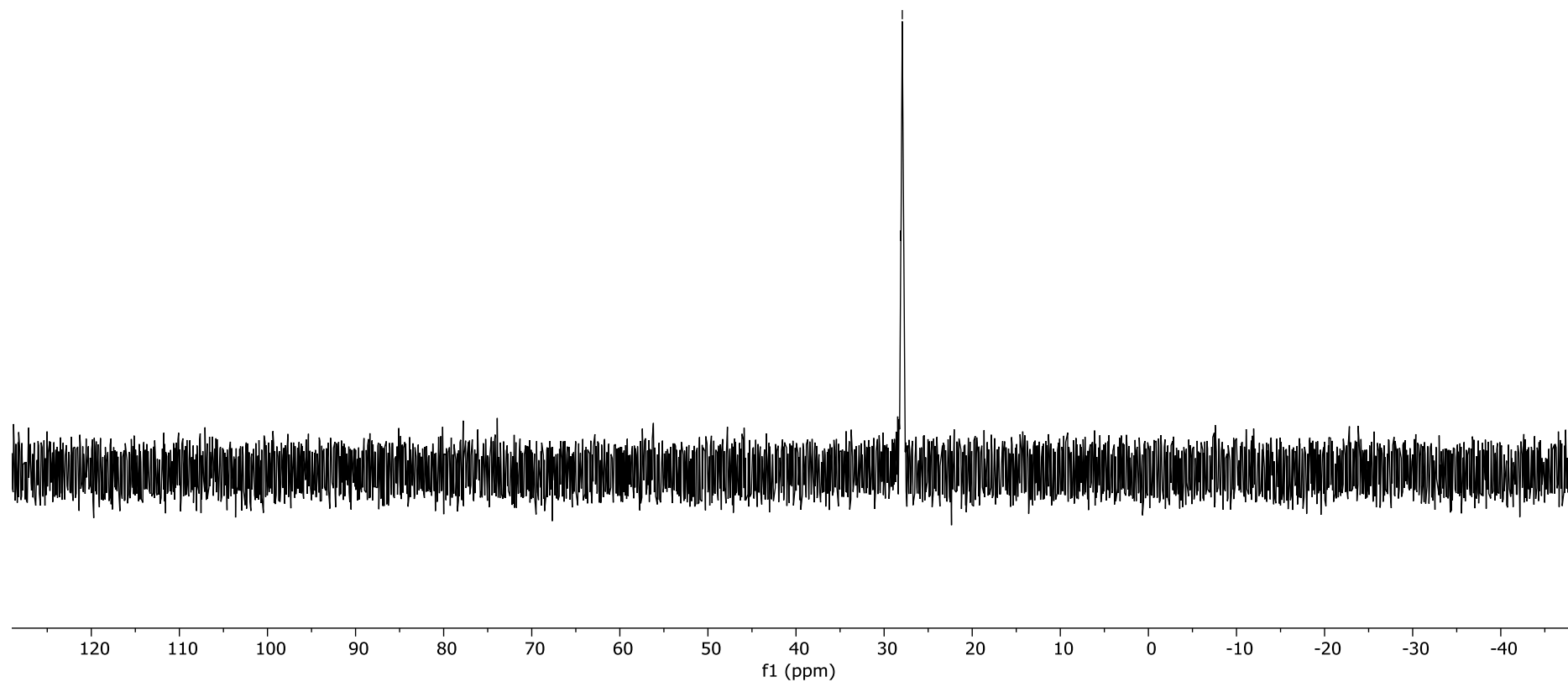
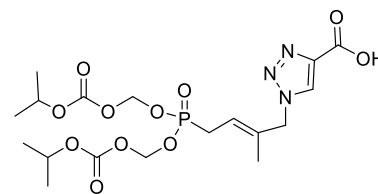


# <sup>13</sup>C NMR (101 MHz, MeOD) Analysis of Compound 11m

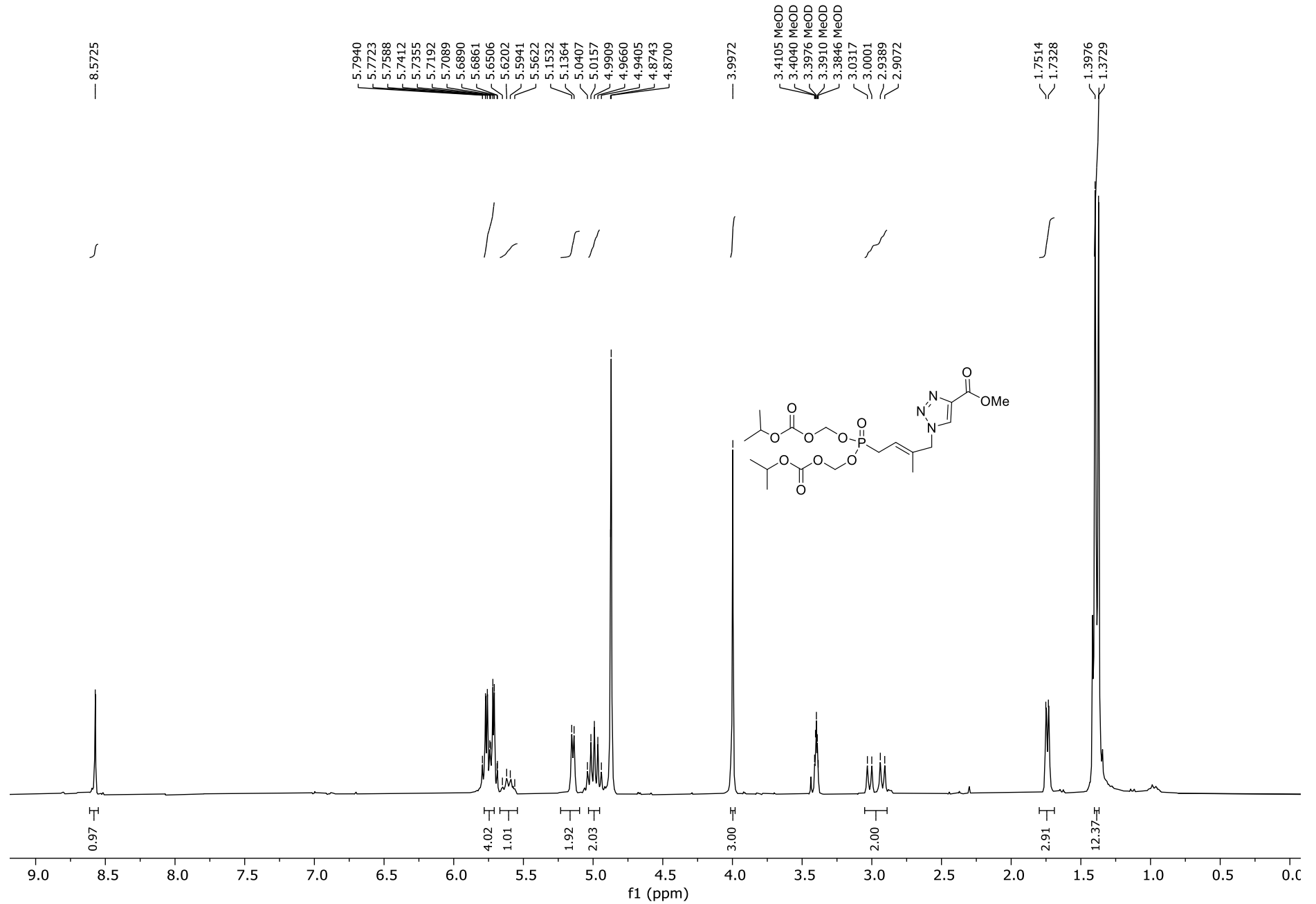


**<sup>31</sup>P NMR (161 MHz, MeOD) Analysis of Compound 11m**

— 27.94

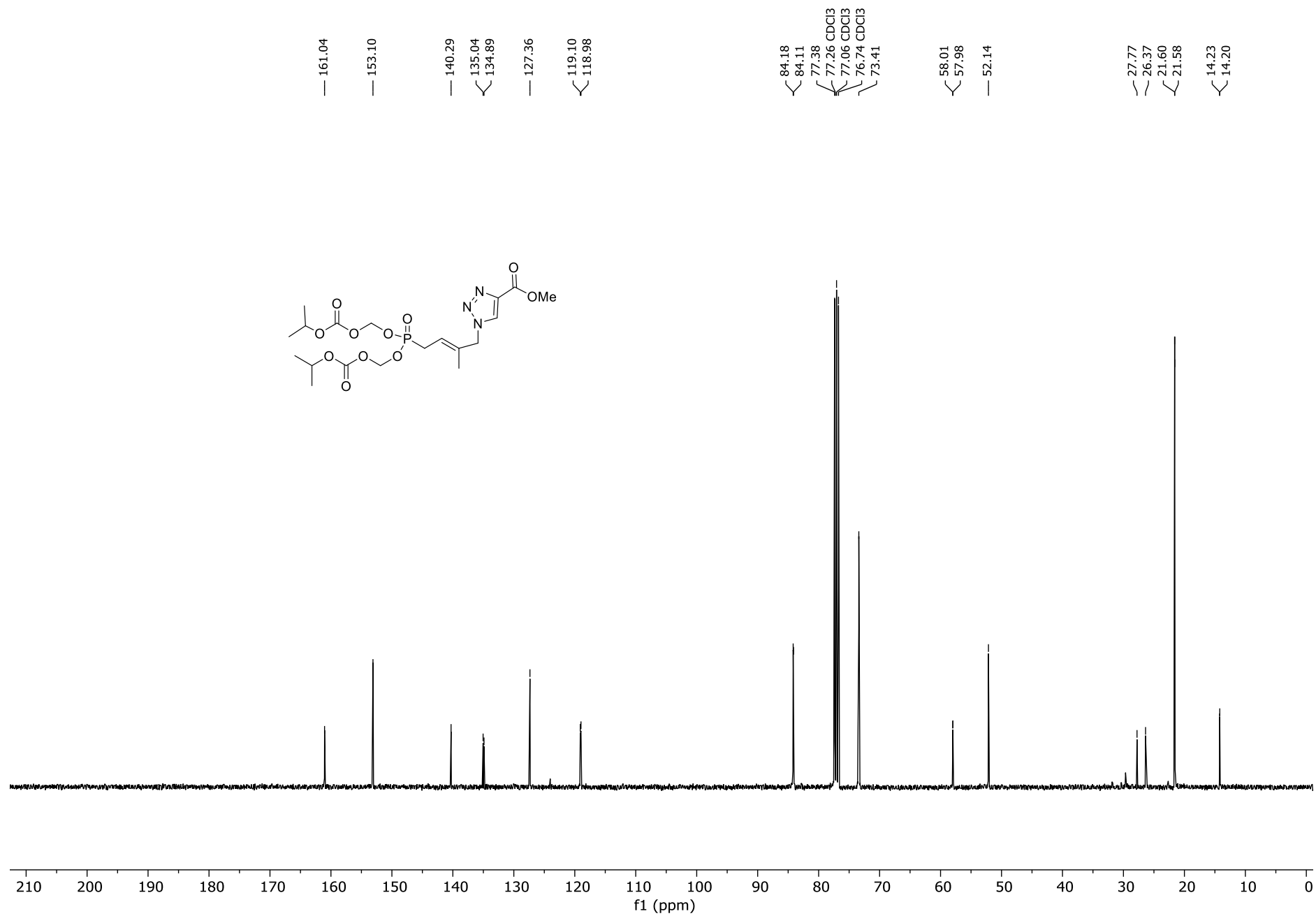
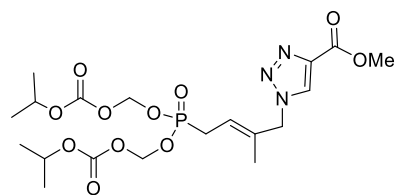


# <sup>1</sup>H NMR (250 MHz, MeOD) Analysis of Compound 11n



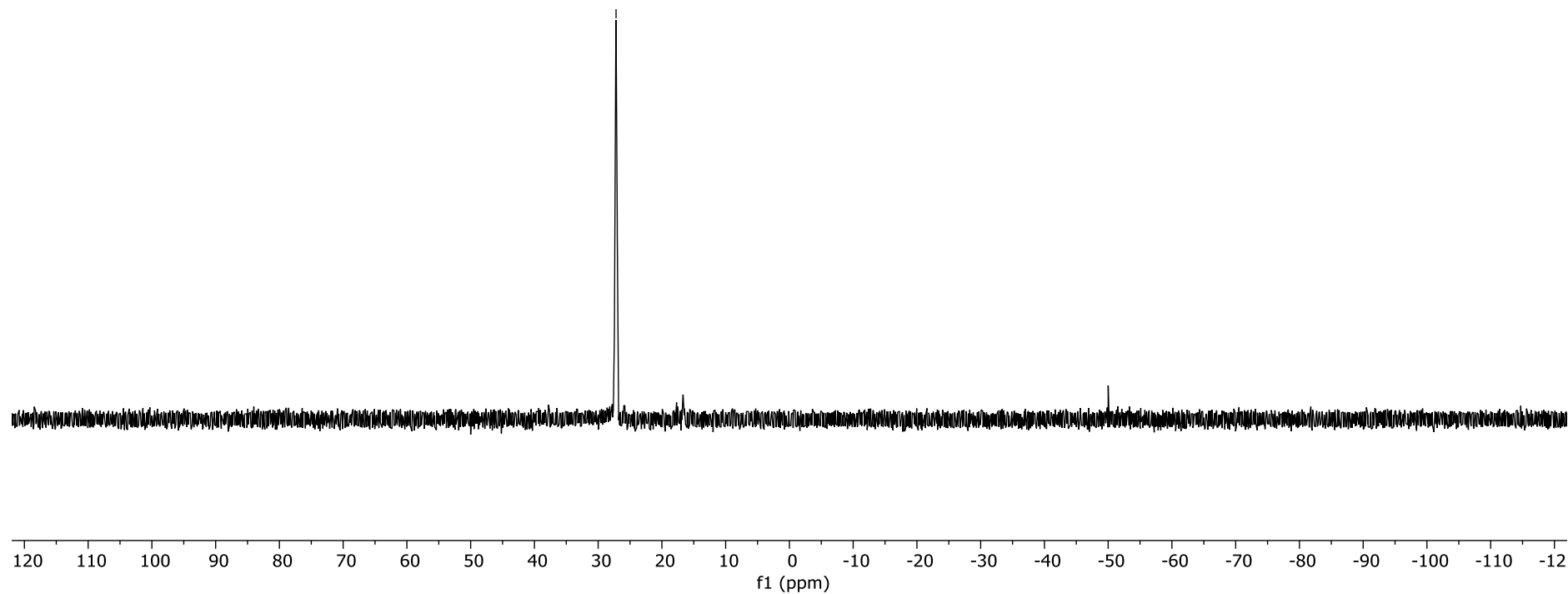
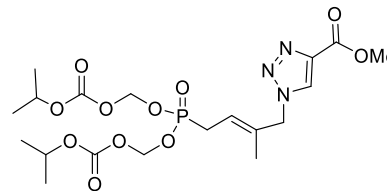


# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 11n

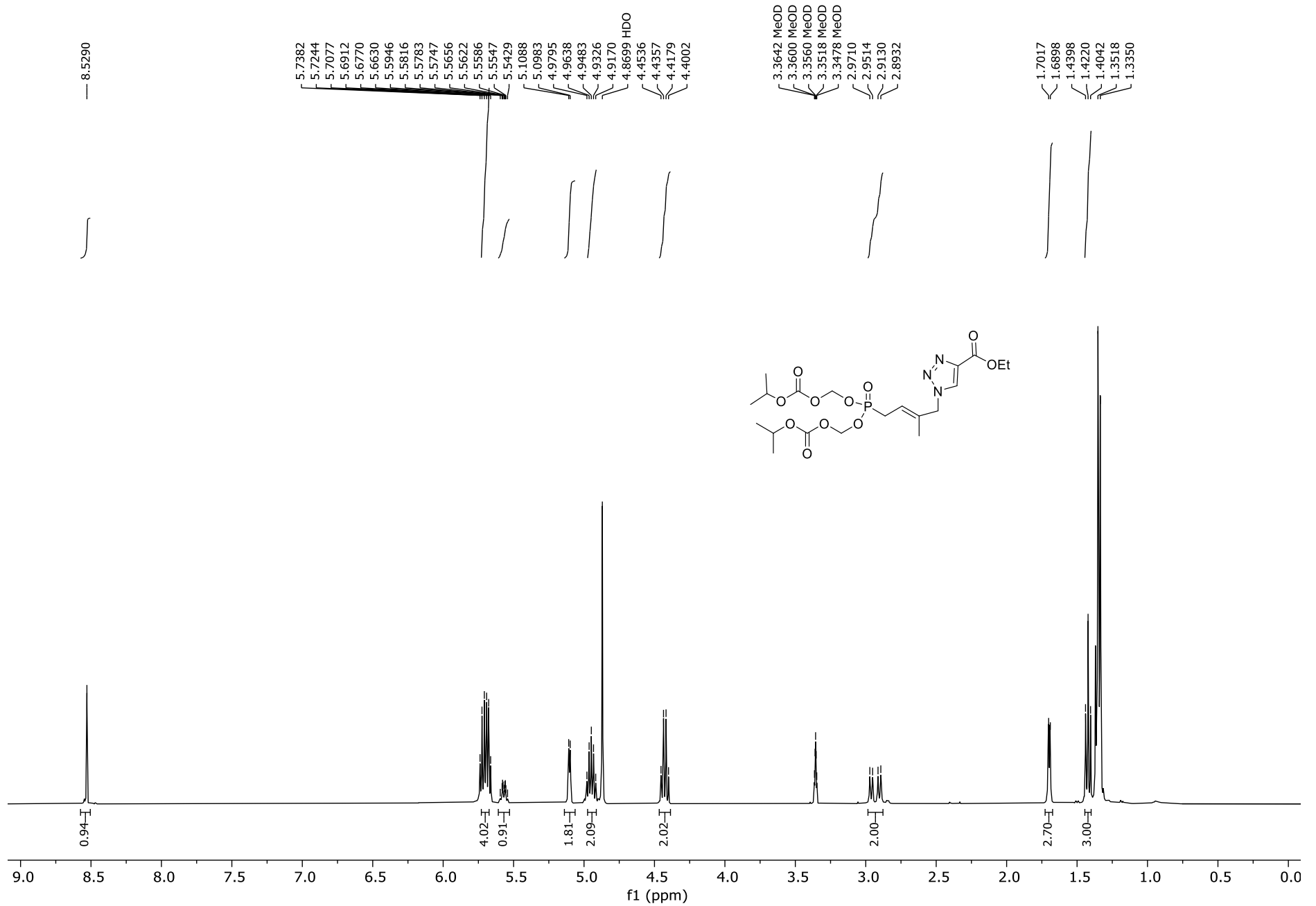


**<sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 11n**

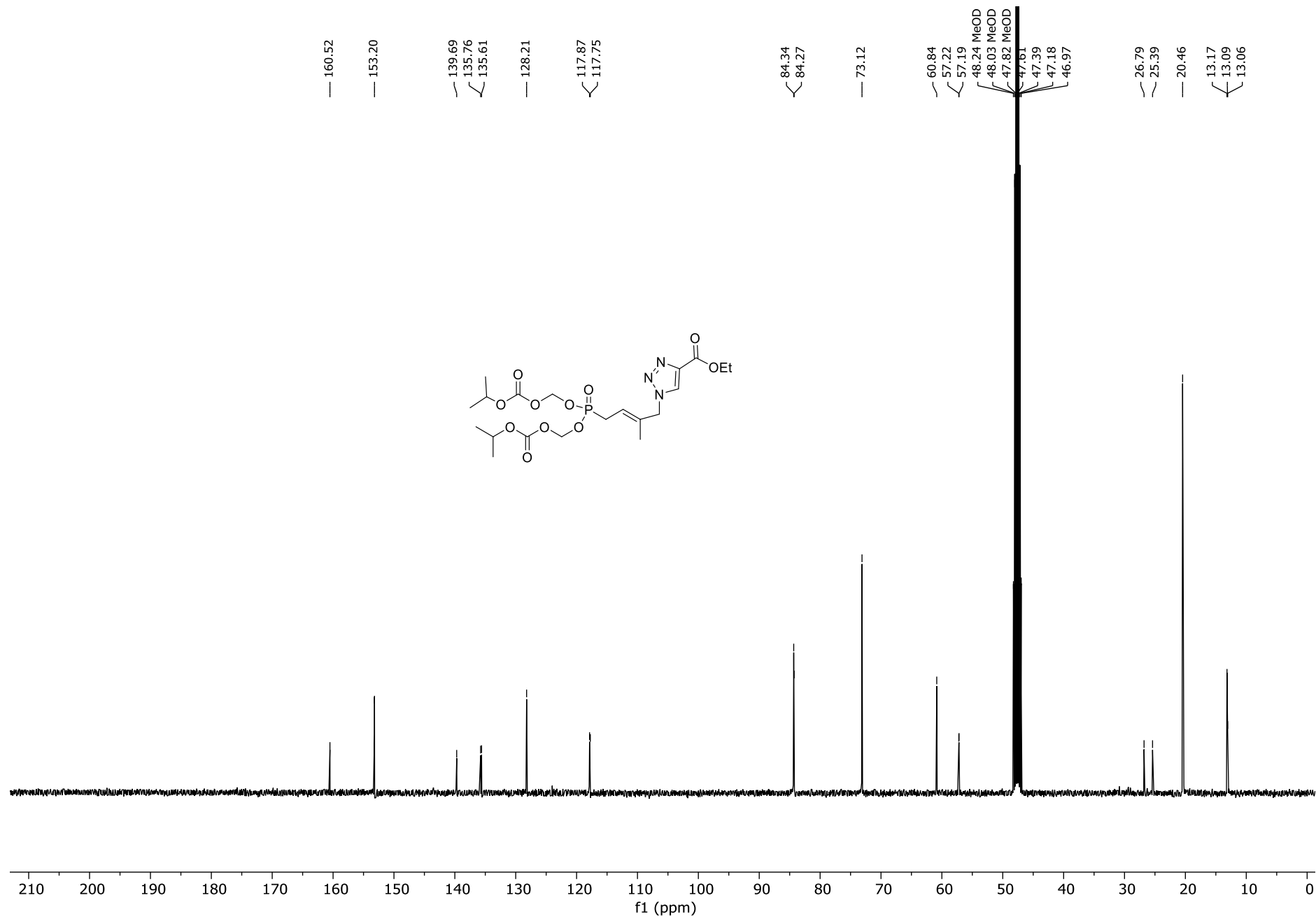
— 27.19



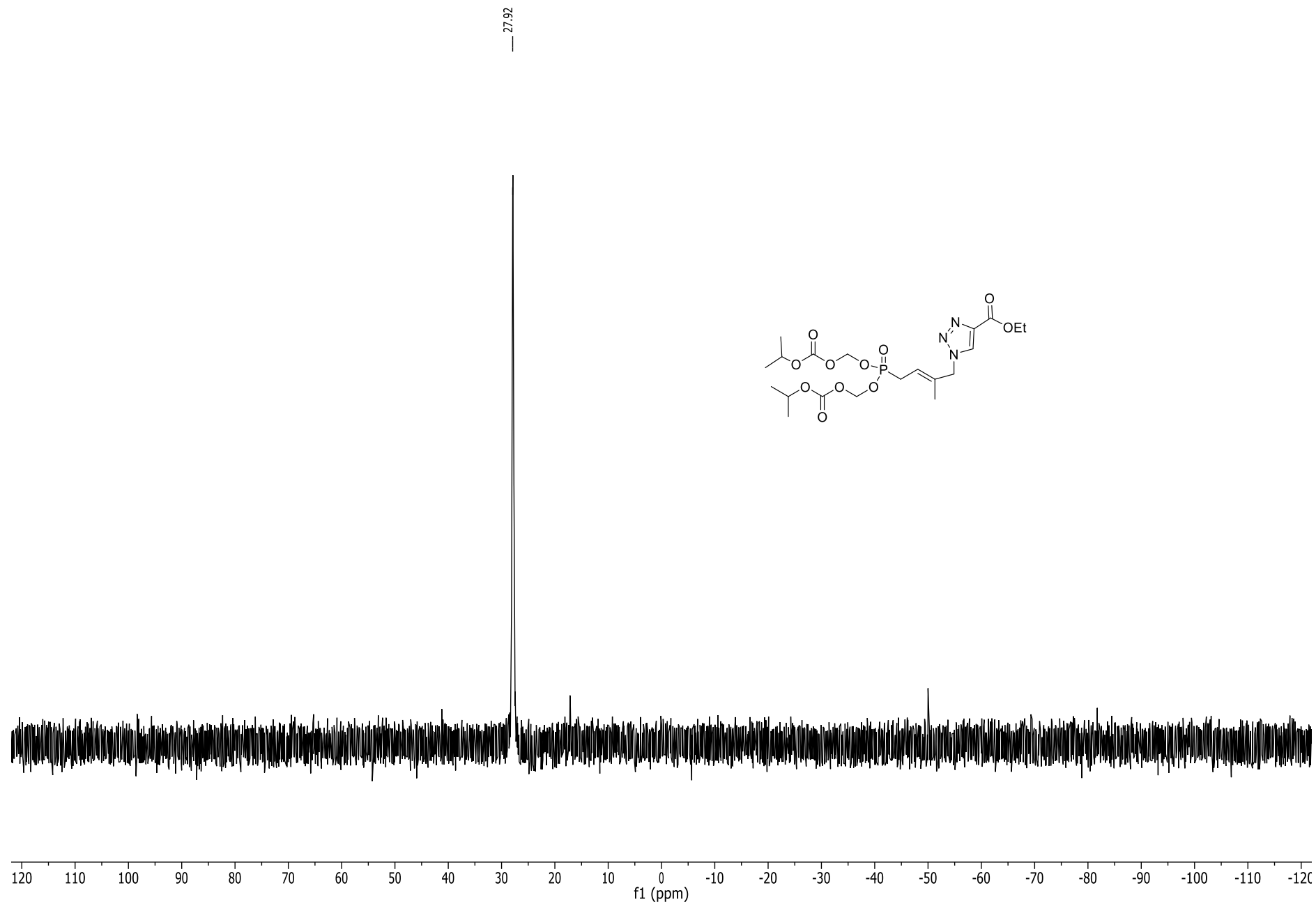
# <sup>1</sup>H NMR (400 MHz, MeOD) Analysis of Compound 11o



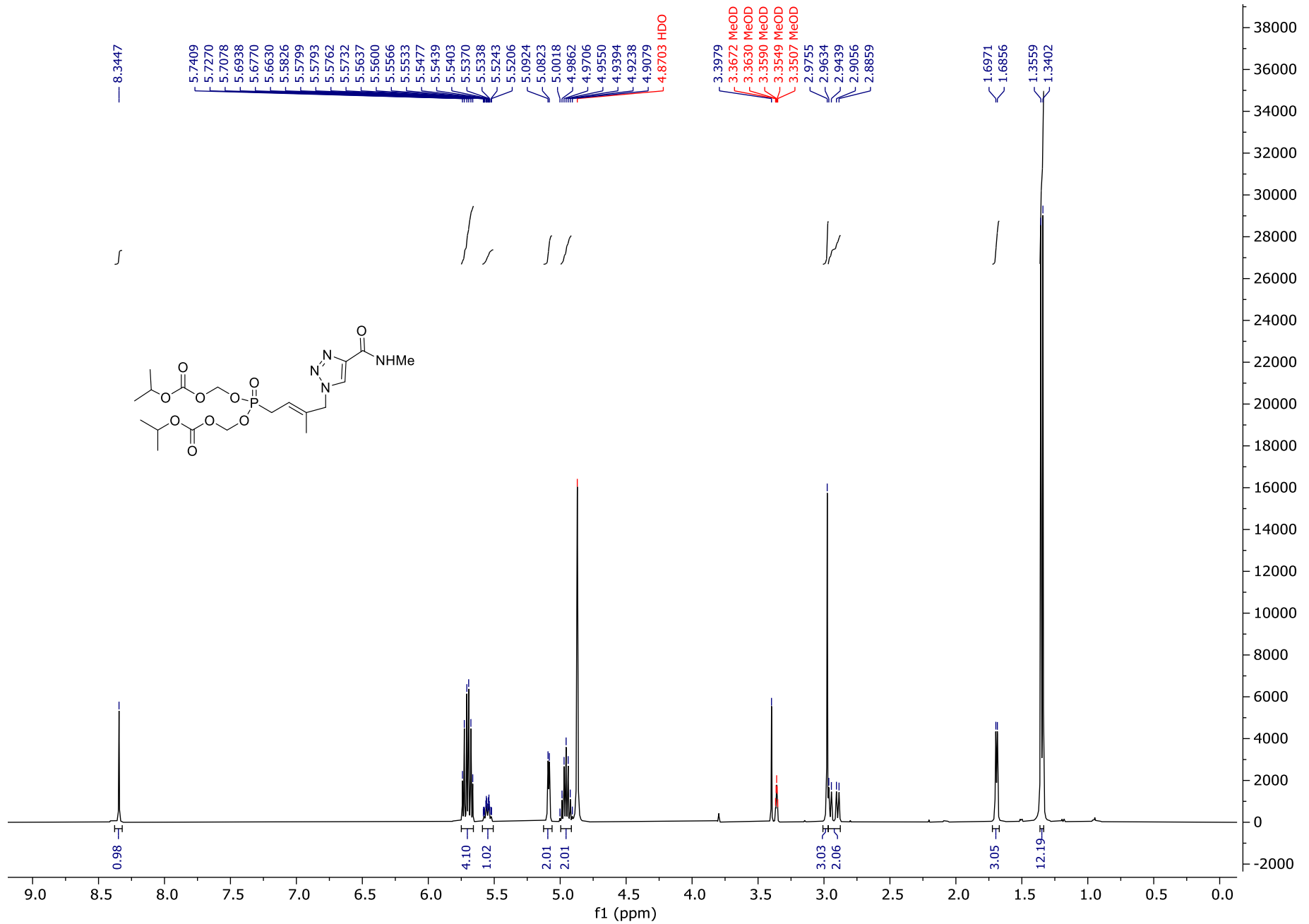
# <sup>13</sup>C NMR (101 MHz, MeOD) Analysis of Compound 11o



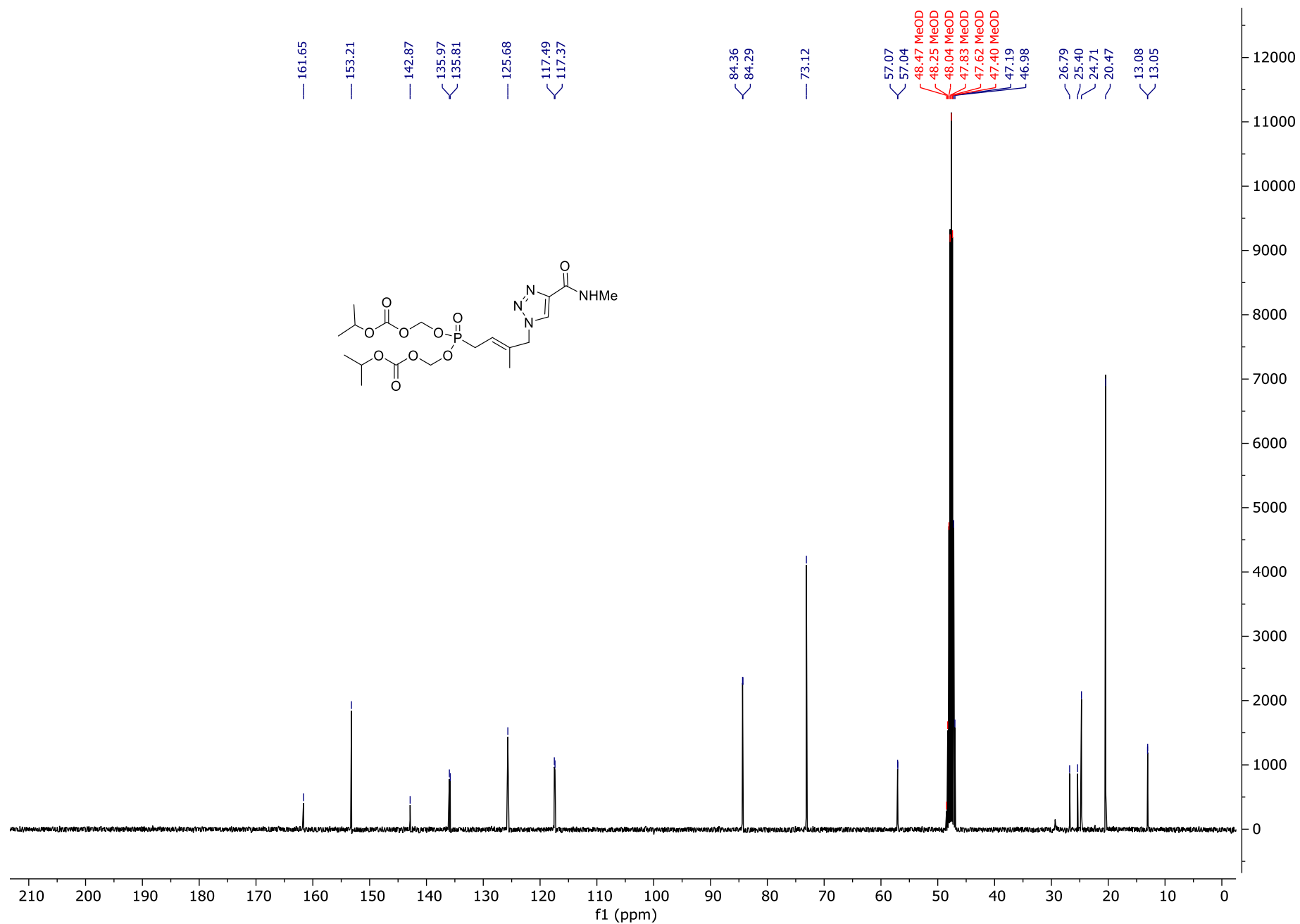
**<sup>31</sup>P NMR (161 MHz, MeOD) Analysis of Compound 11o**



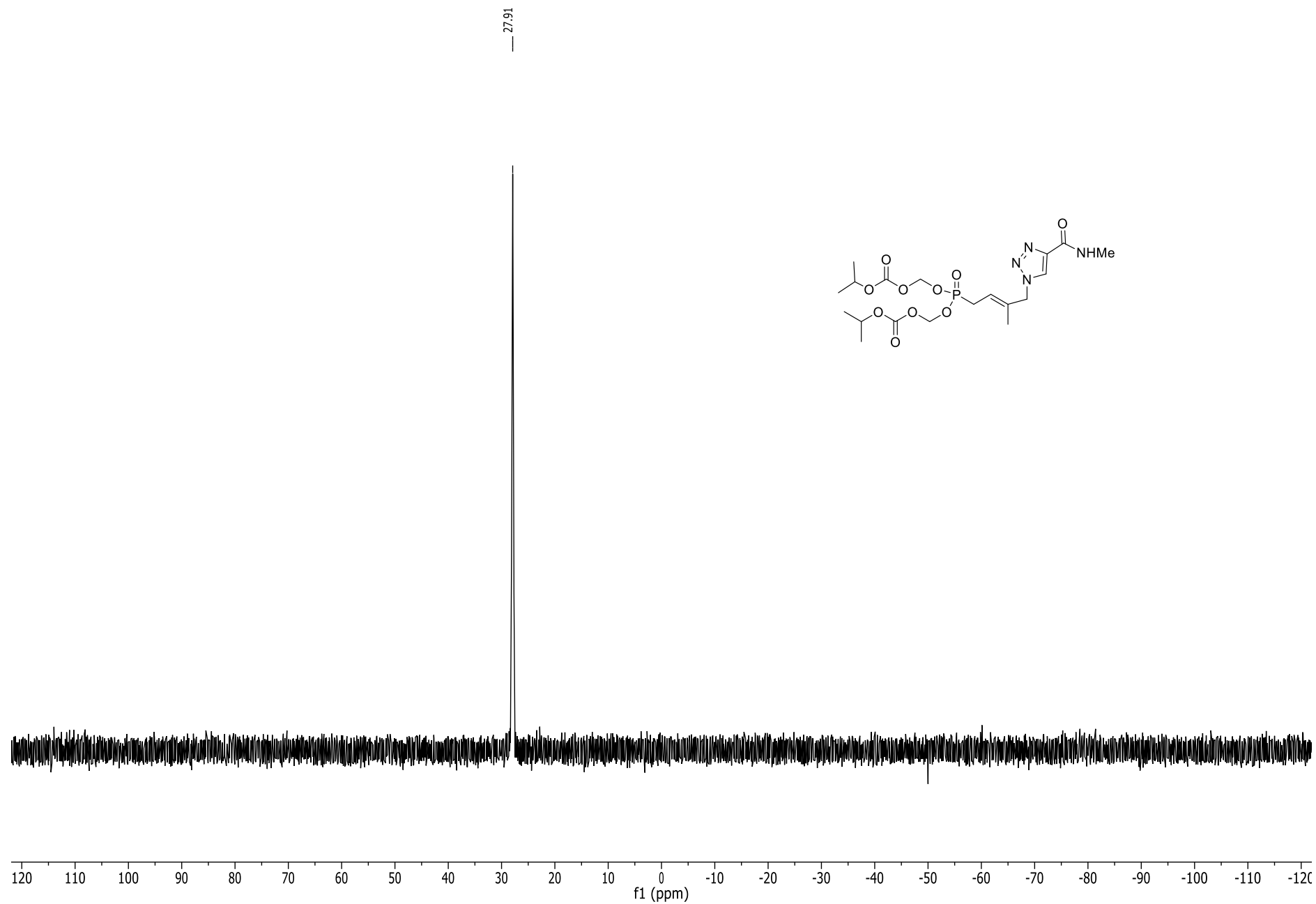
# <sup>1</sup>H NMR (400 MHz, MeOD) Analysis of Compound 11p



# <sup>13</sup>C NMR (101 MHz, MeOD) Analysis of Compound 11p

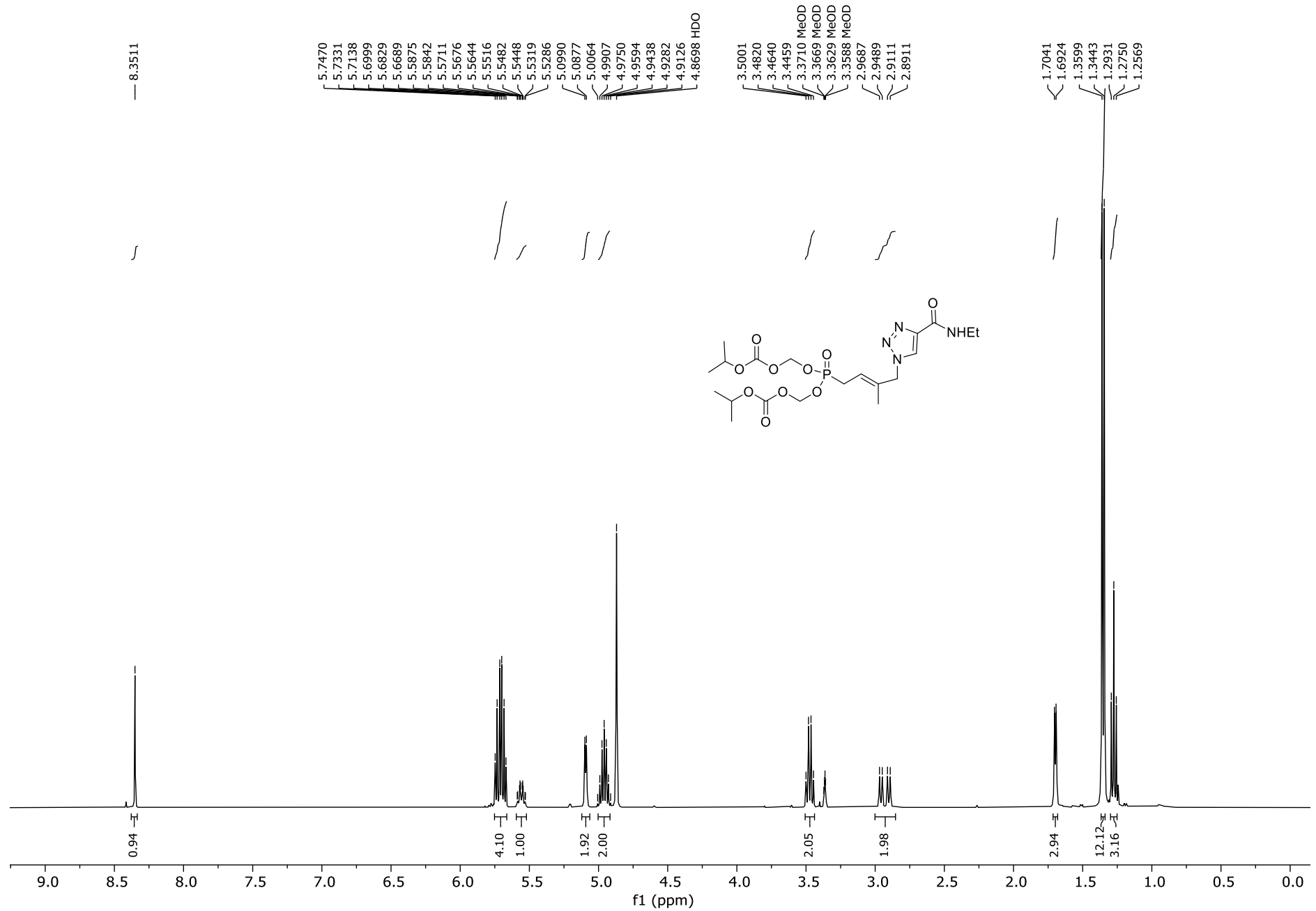


**<sup>31</sup>P NMR (161 MHz, MeOD) Analysis of Compound 11p**

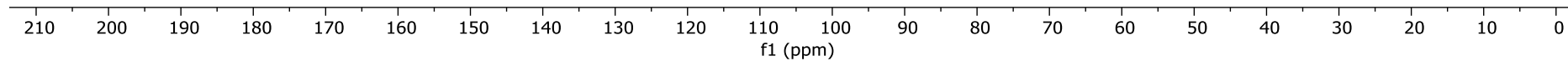
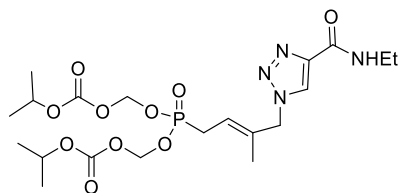
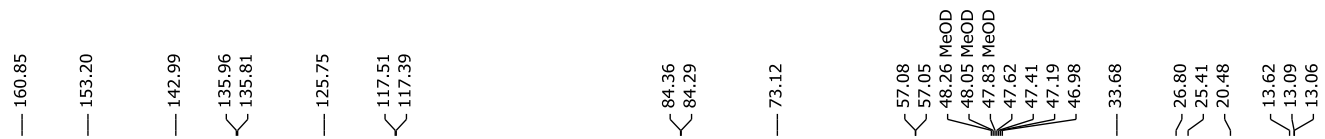




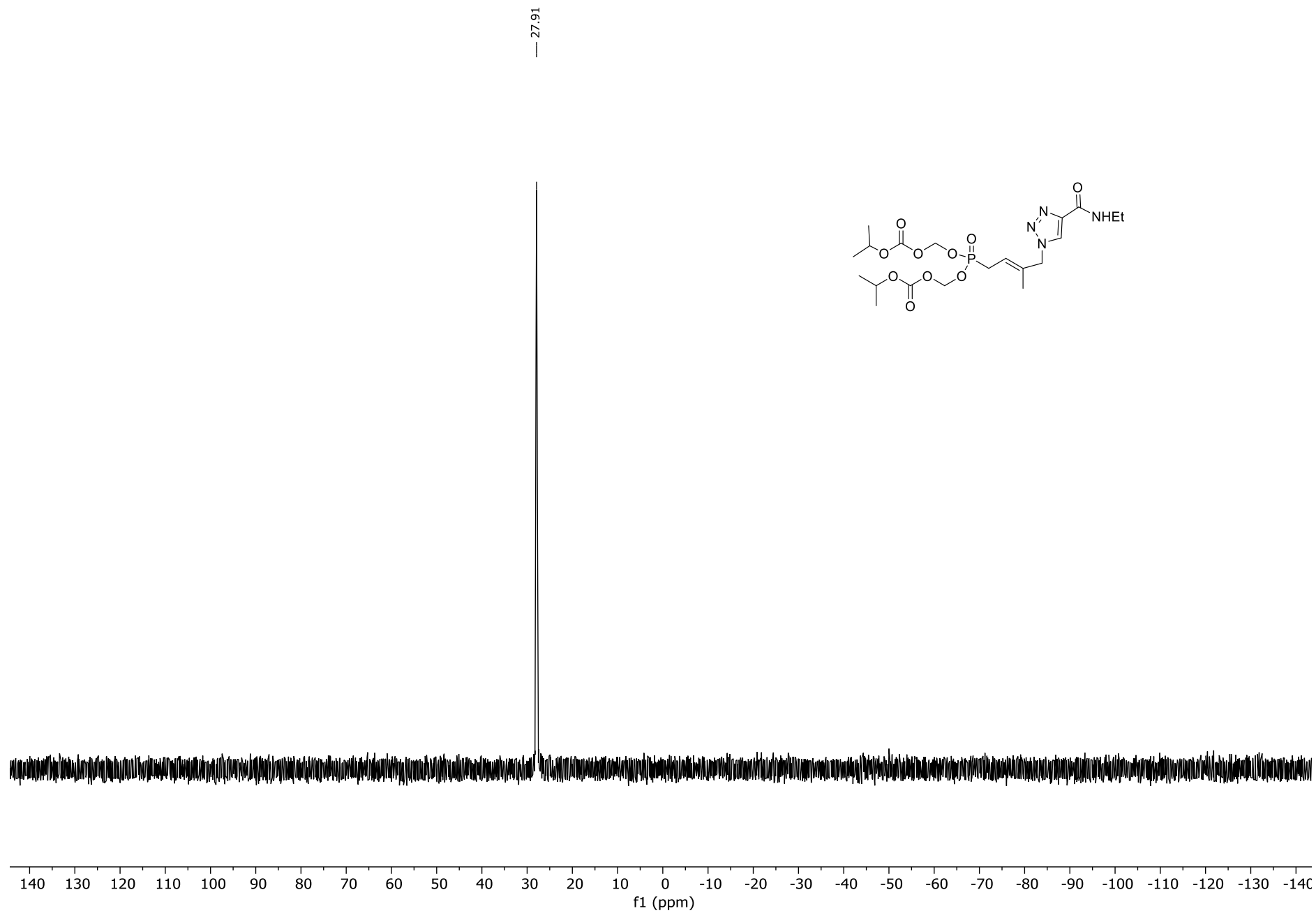
# <sup>1</sup>H NMR (400 MHz, MeOD) Analysis of Compound 11q



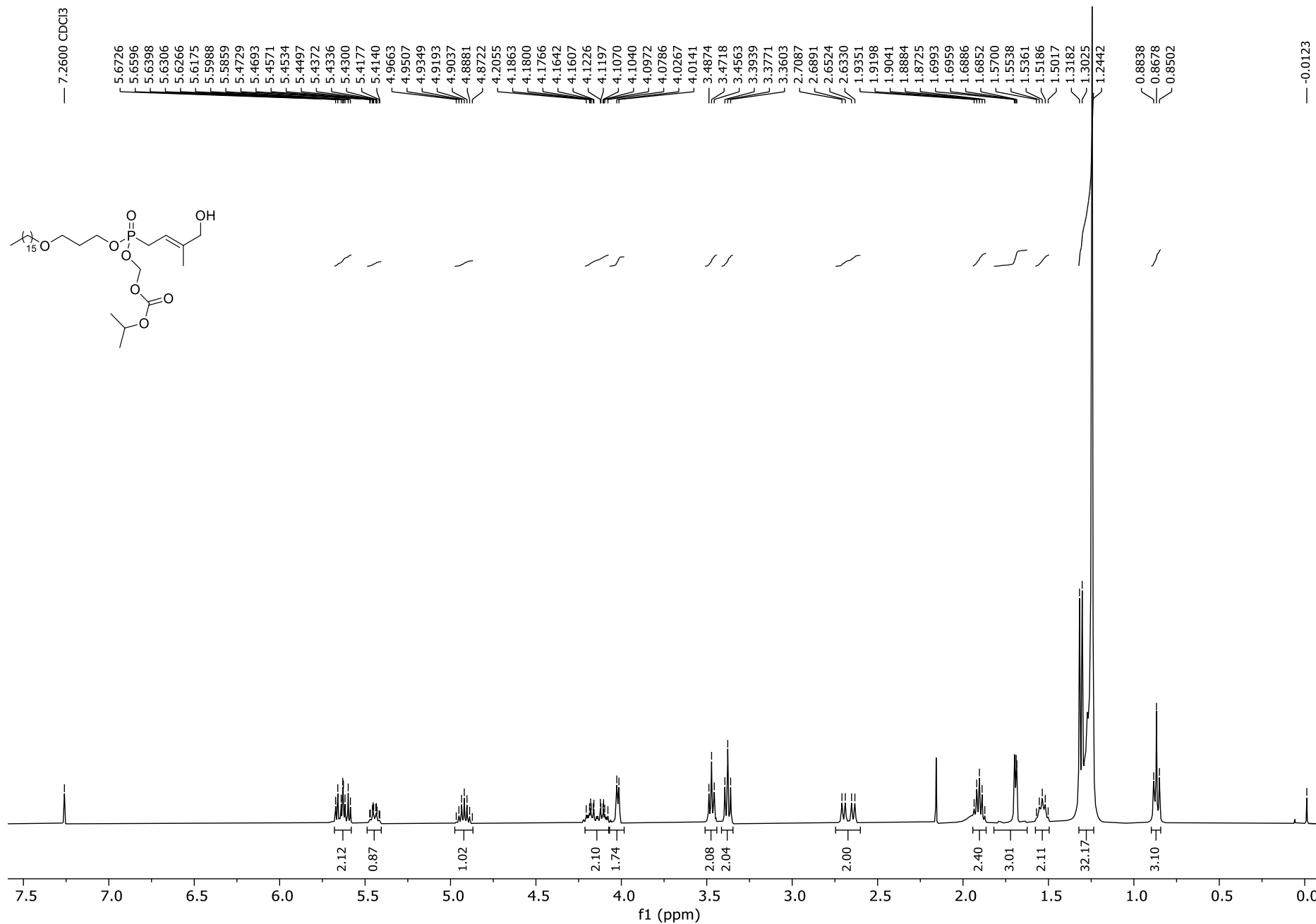
# <sup>13</sup>C NMR (101 MHz, MeOD) Analysis of Compound 11q



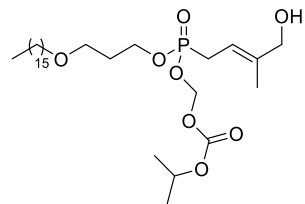
**<sup>31</sup>P NMR (161 MHz, MeOD) Analysis of Compound 11q**



# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) Analysis of Compound 13



# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 13



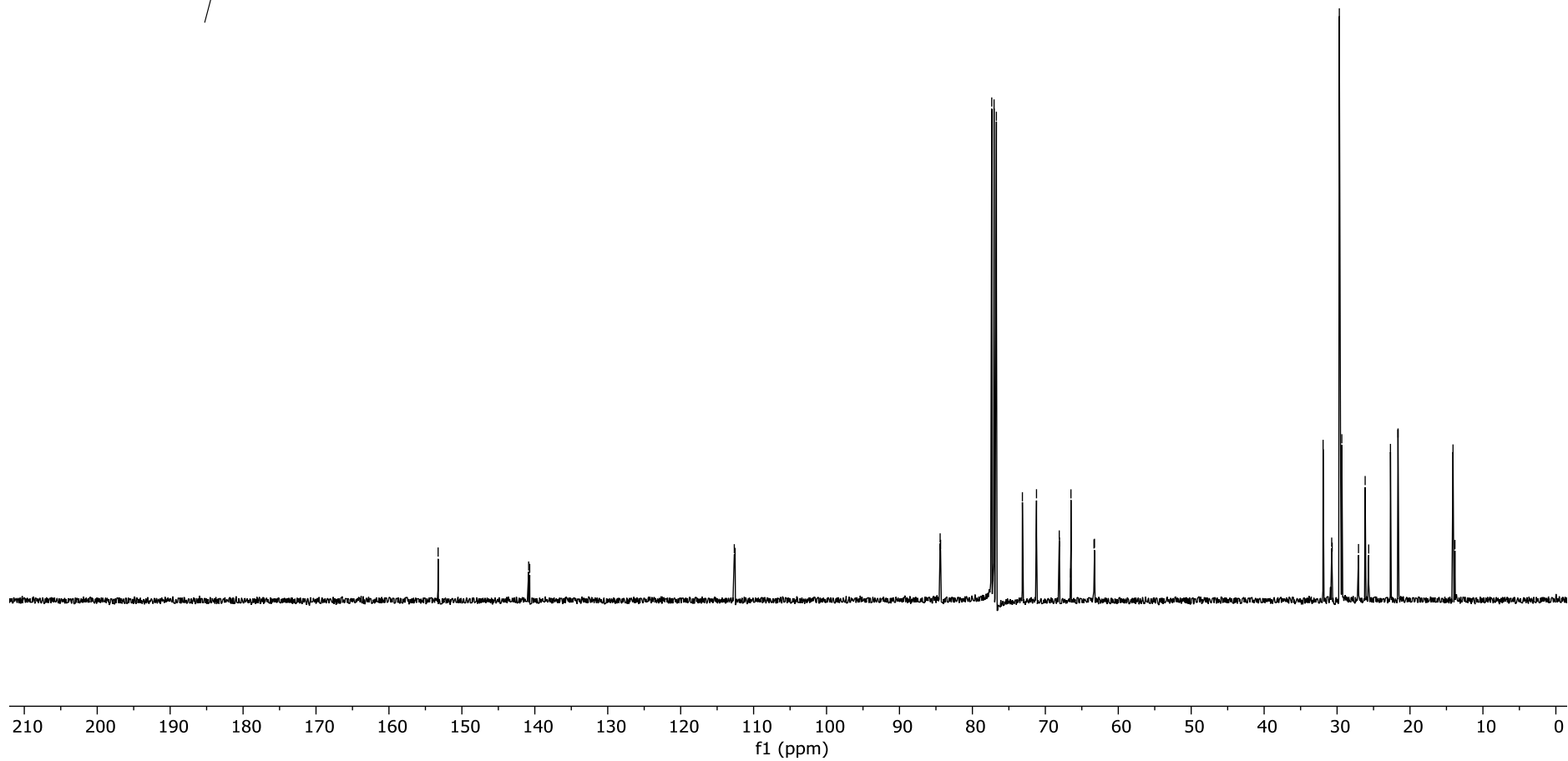
153.26

140.84  
140.70

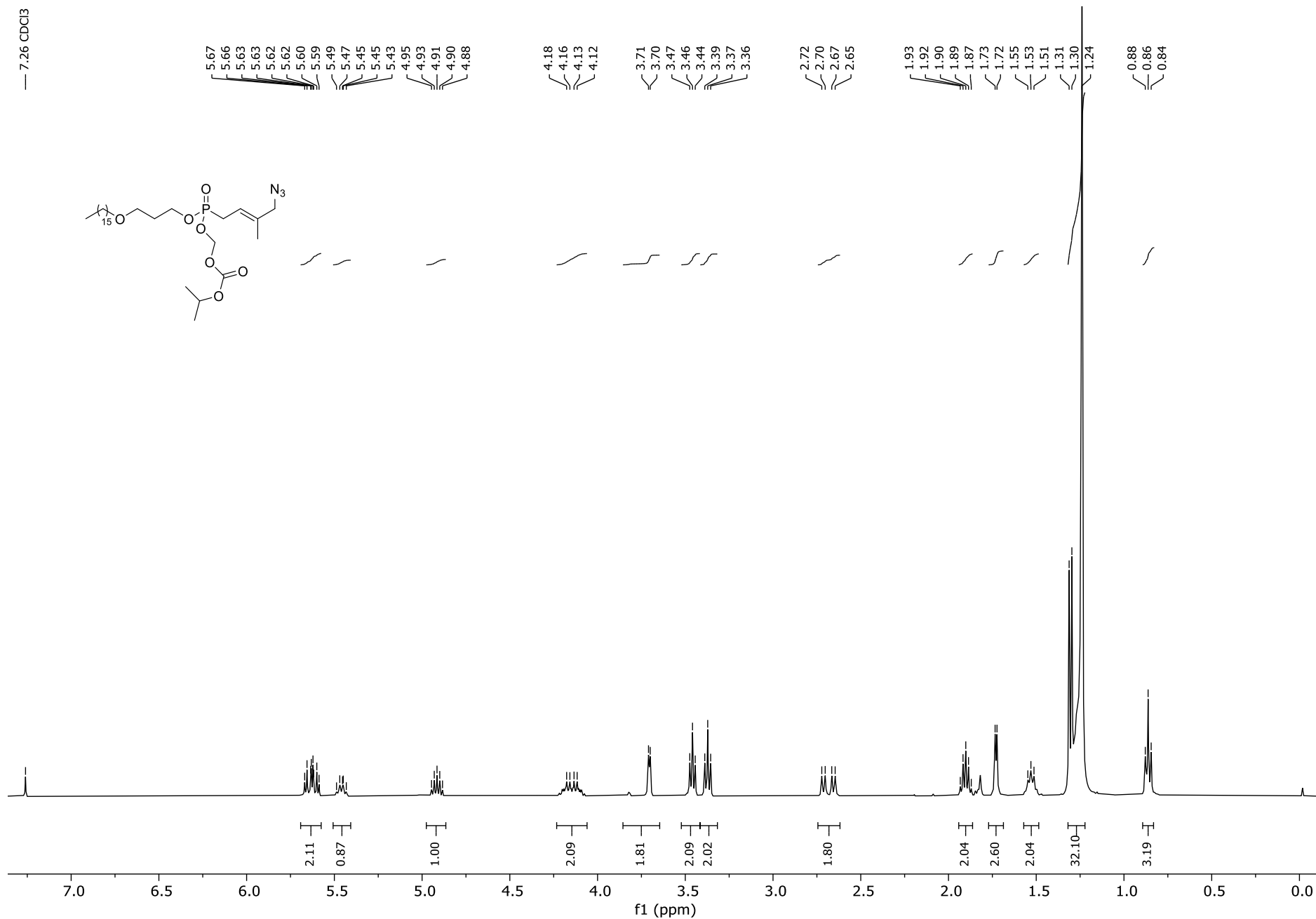
112.65  
112.54

84.42  
84.36  
77.35  
77.23  
77.03  
76.71  
73.14  
71.21  
68.09  
68.06  
66.52  
66.49  
63.33  
63.26

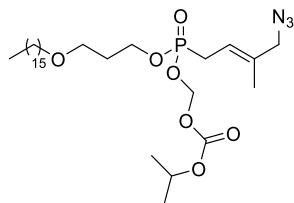
31.92  
30.73  
30.67  
29.69  
29.51  
29.35  
27.06  
26.15  
25.66  
22.68  
21.64  
14.10  
13.87  
13.84



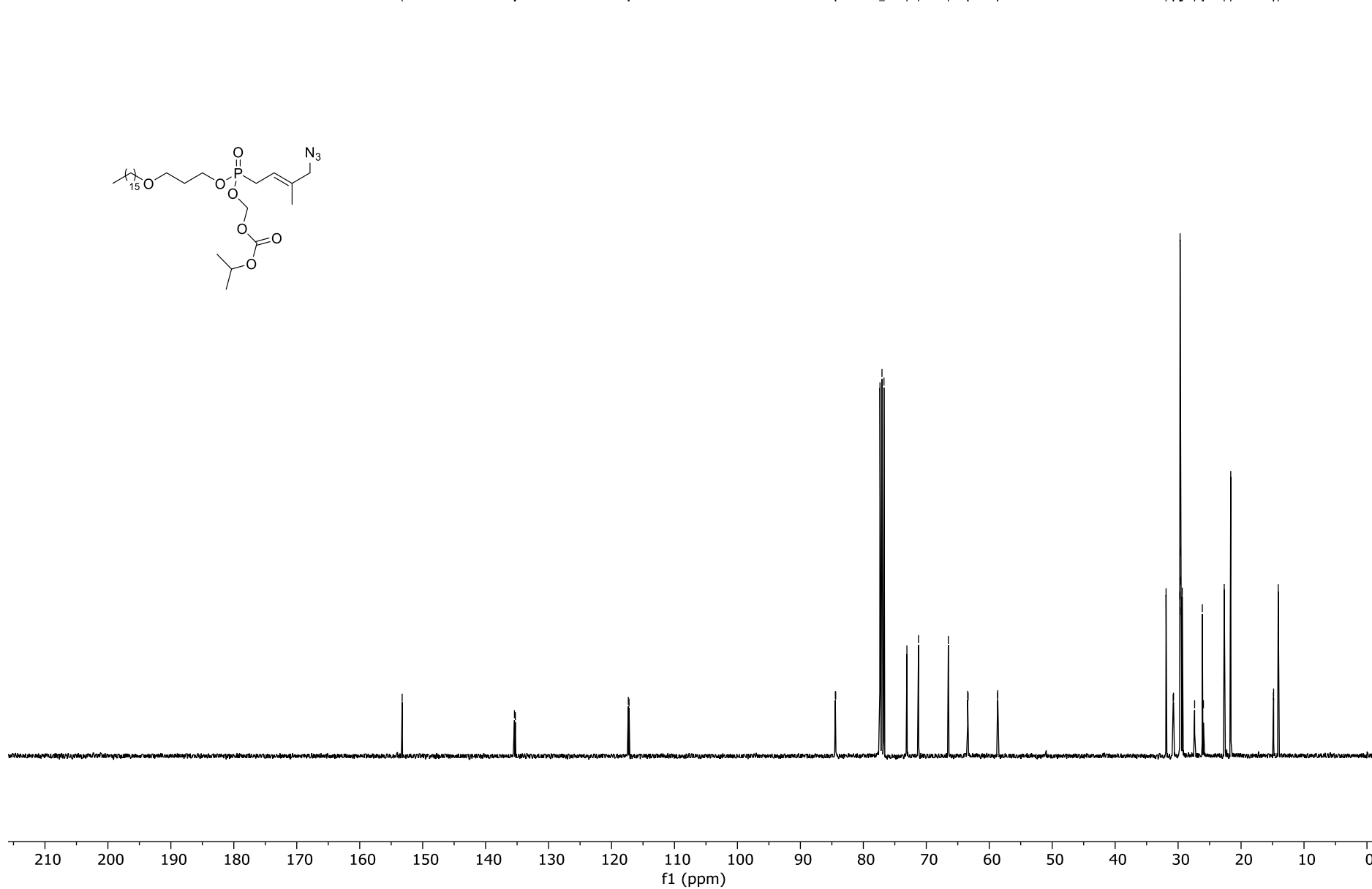
# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) Analysis of Compound 14



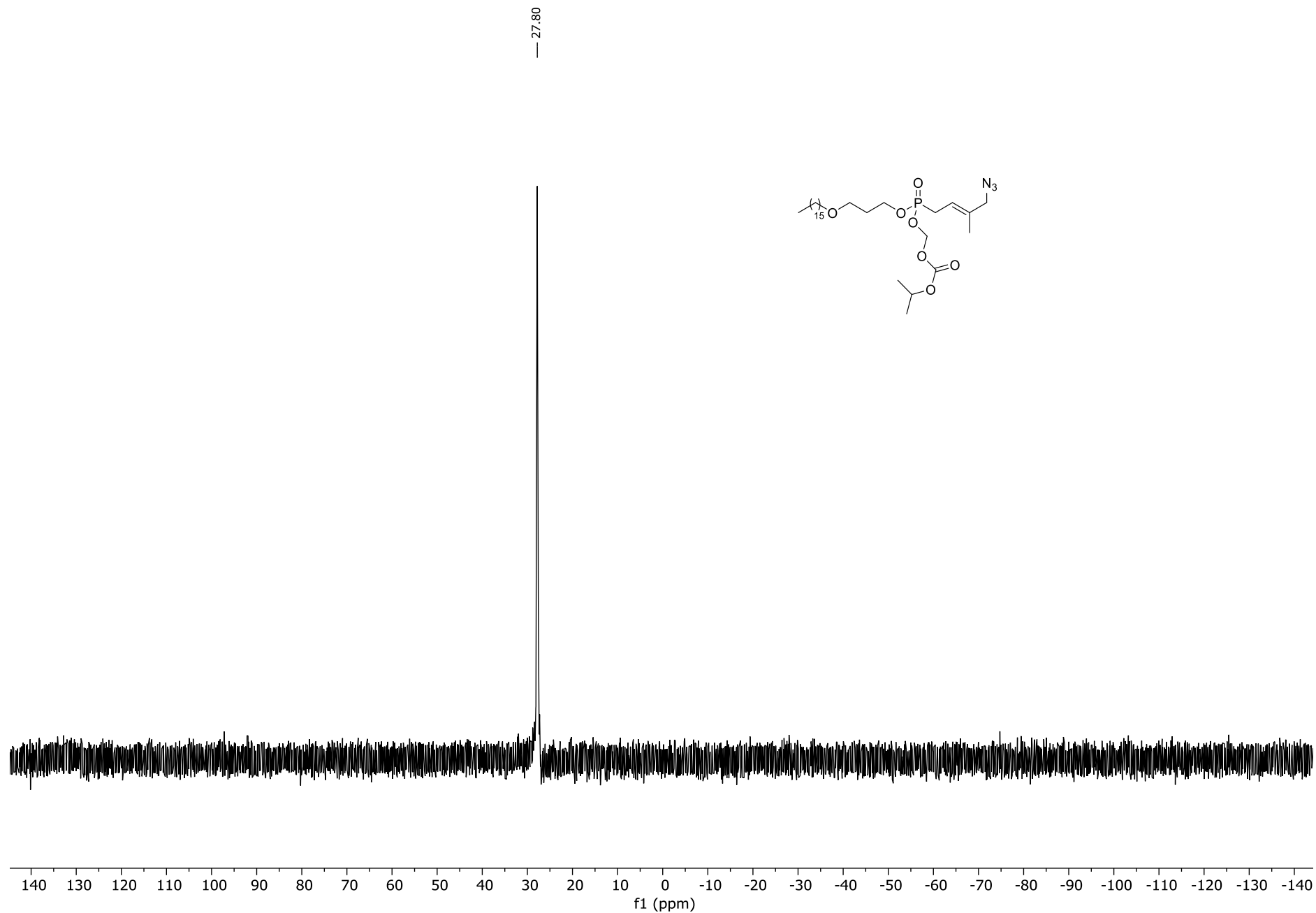
# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 14



153.26  
135.42  
135.28  
117.33  
117.22  
84.45  
84.39  
77.36  
77.04  
76.72  
73.08  
71.23  
66.50  
63.43  
63.36  
58.67  
58.64  
31.91  
30.78  
30.72  
29.71  
29.68  
29.67  
29.64  
29.63  
29.60  
29.51  
29.34  
27.38  
26.16  
25.98  
22.67  
21.64  
14.85  
14.83  
14.10

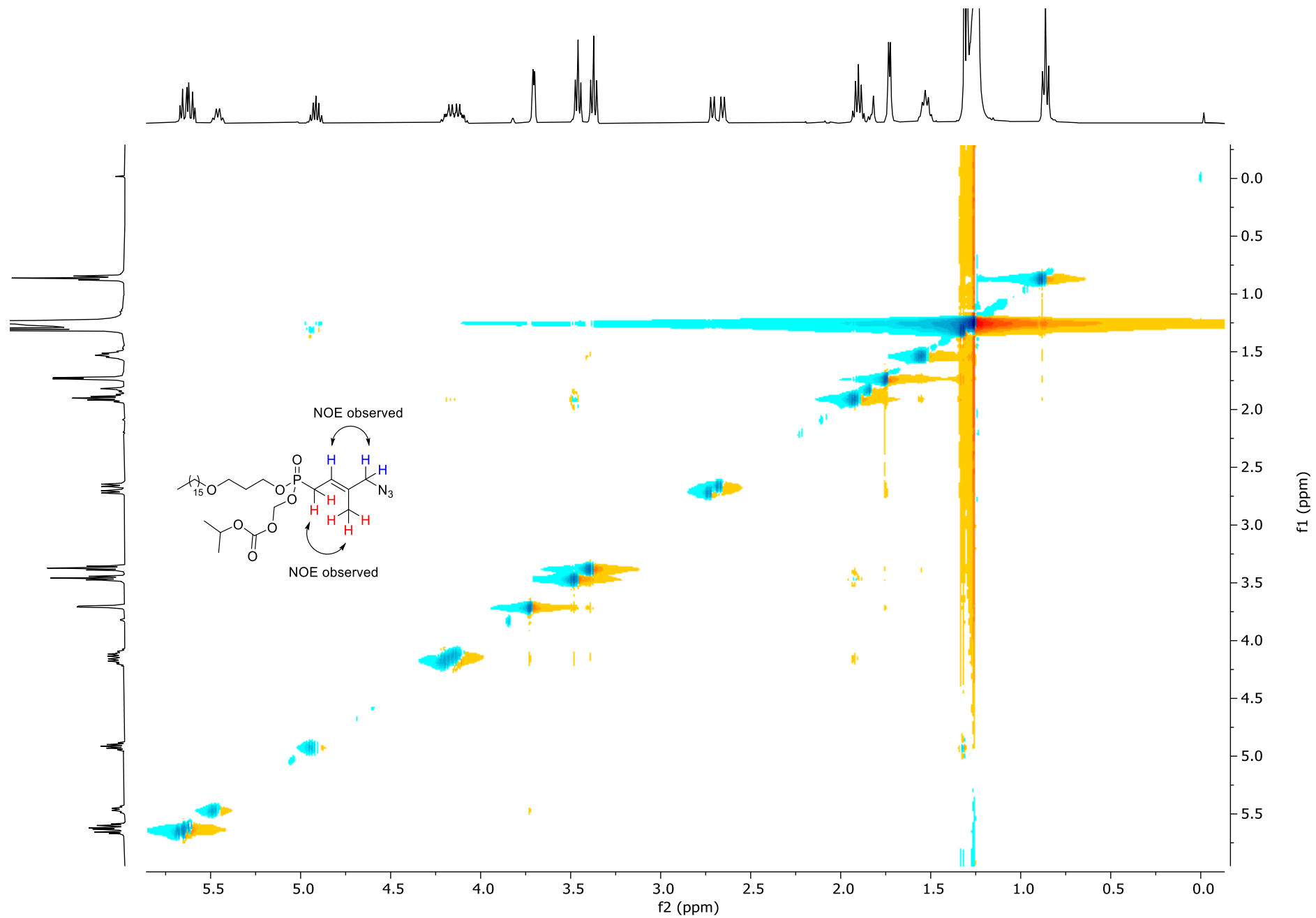


**<sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 14**

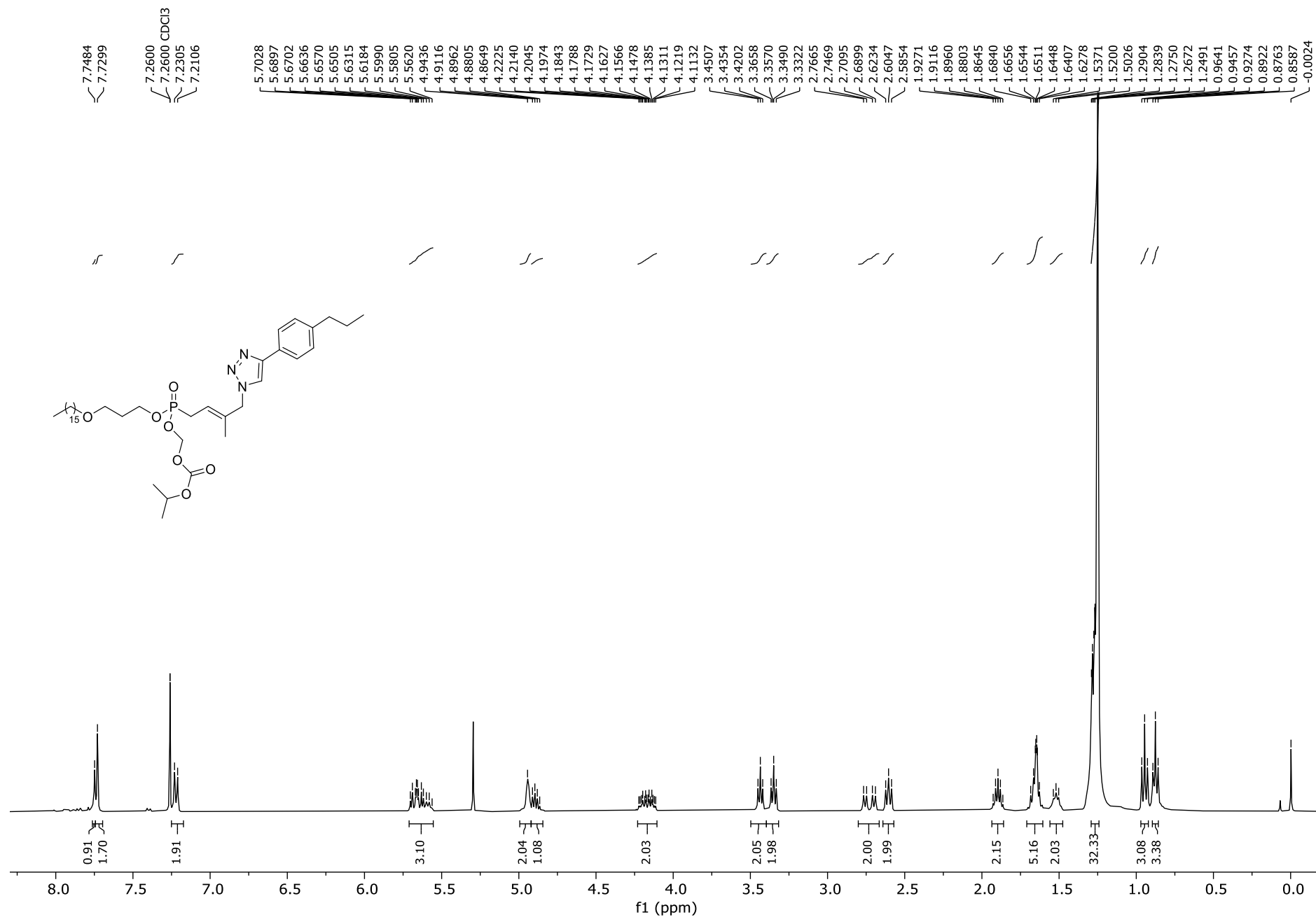




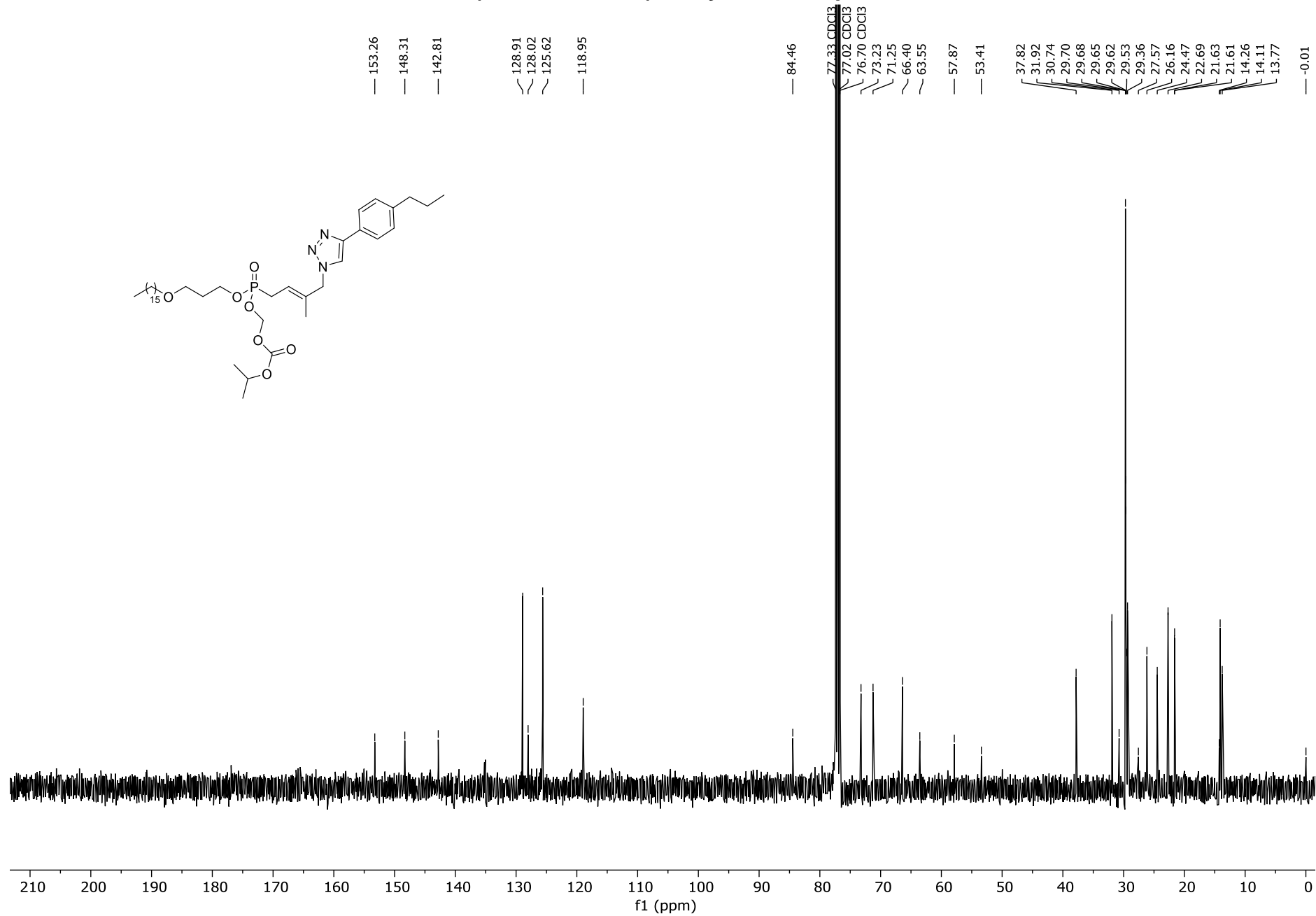
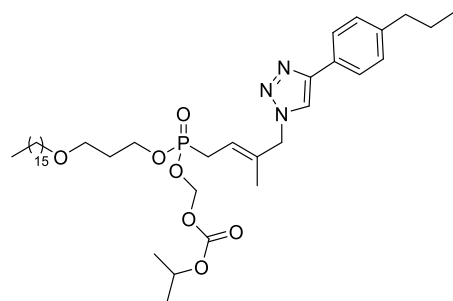
# NOESY of Compound 14



# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) Analysis of Compound 15a

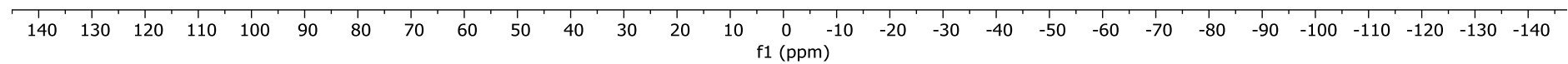
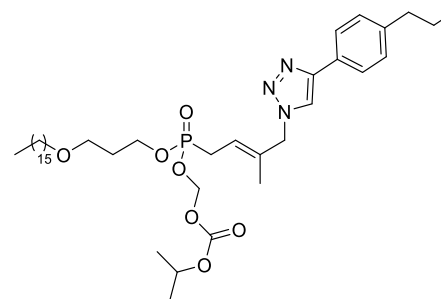


# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 15a



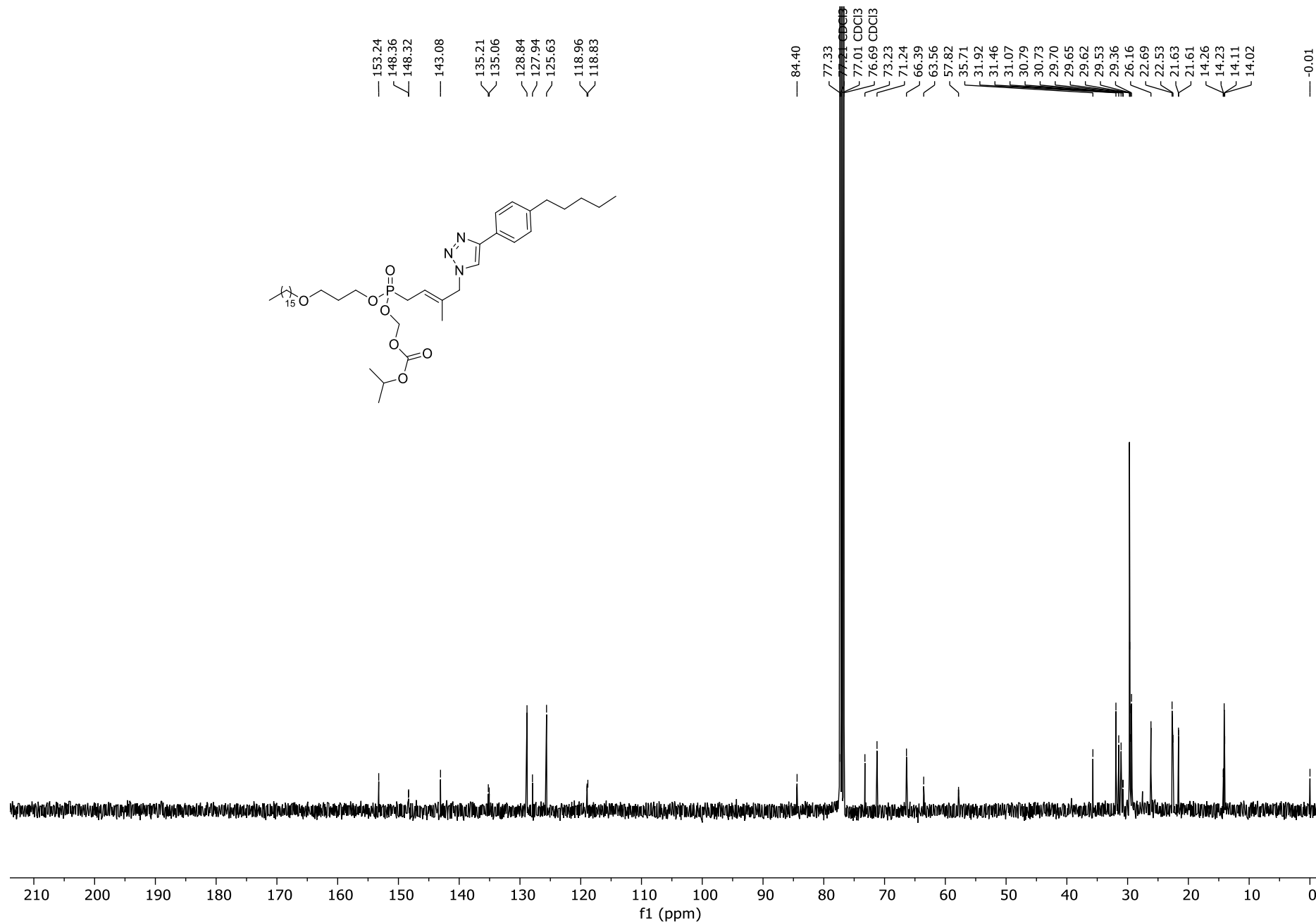
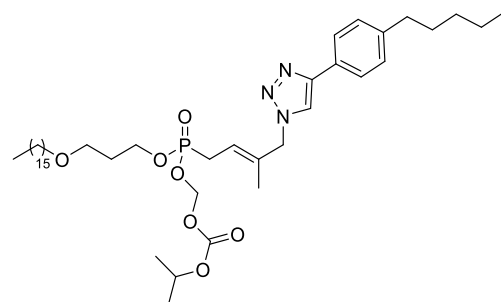
**<sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 15a**

— 27.46



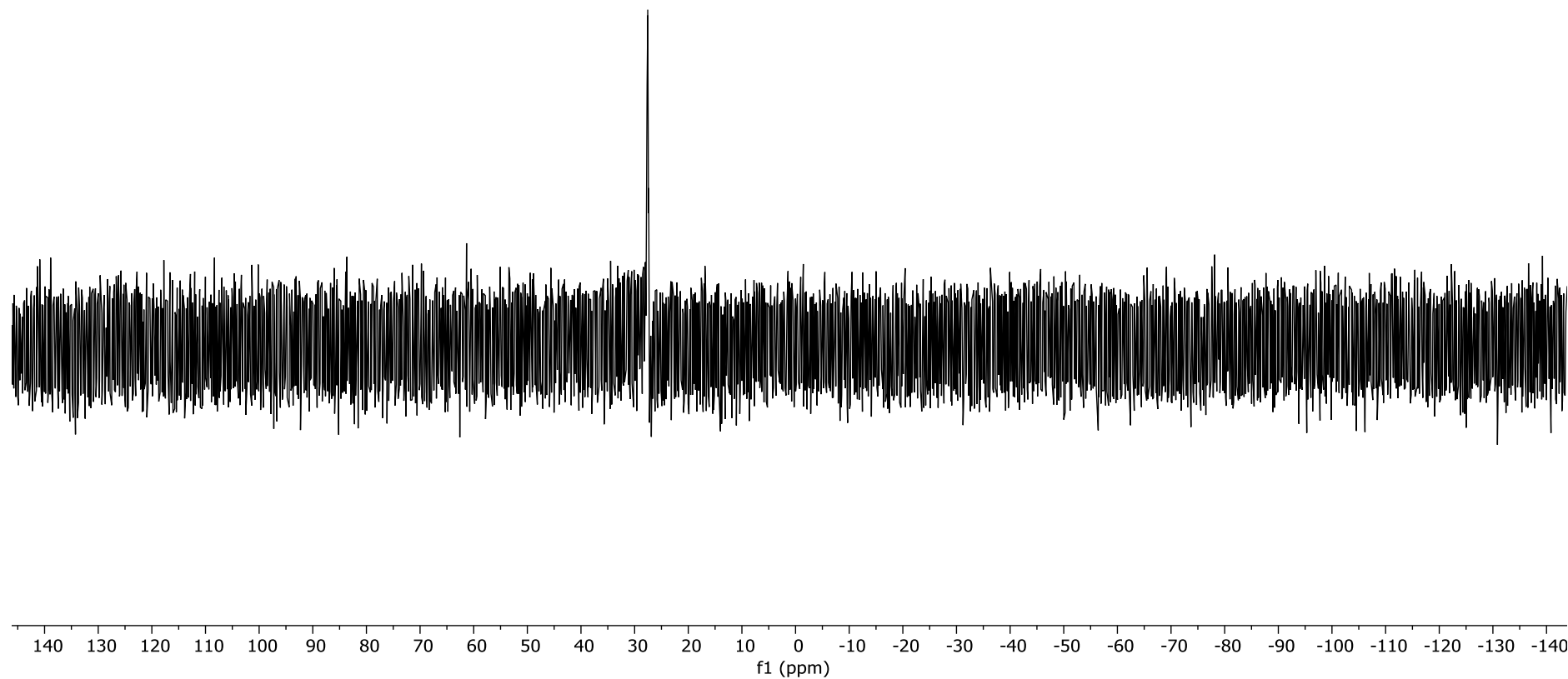
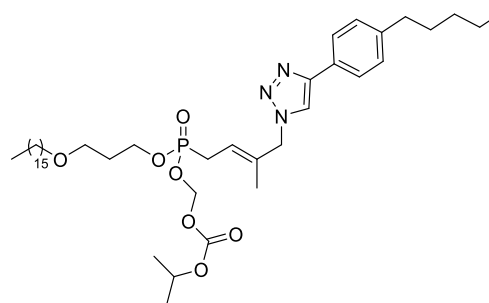


# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 15c

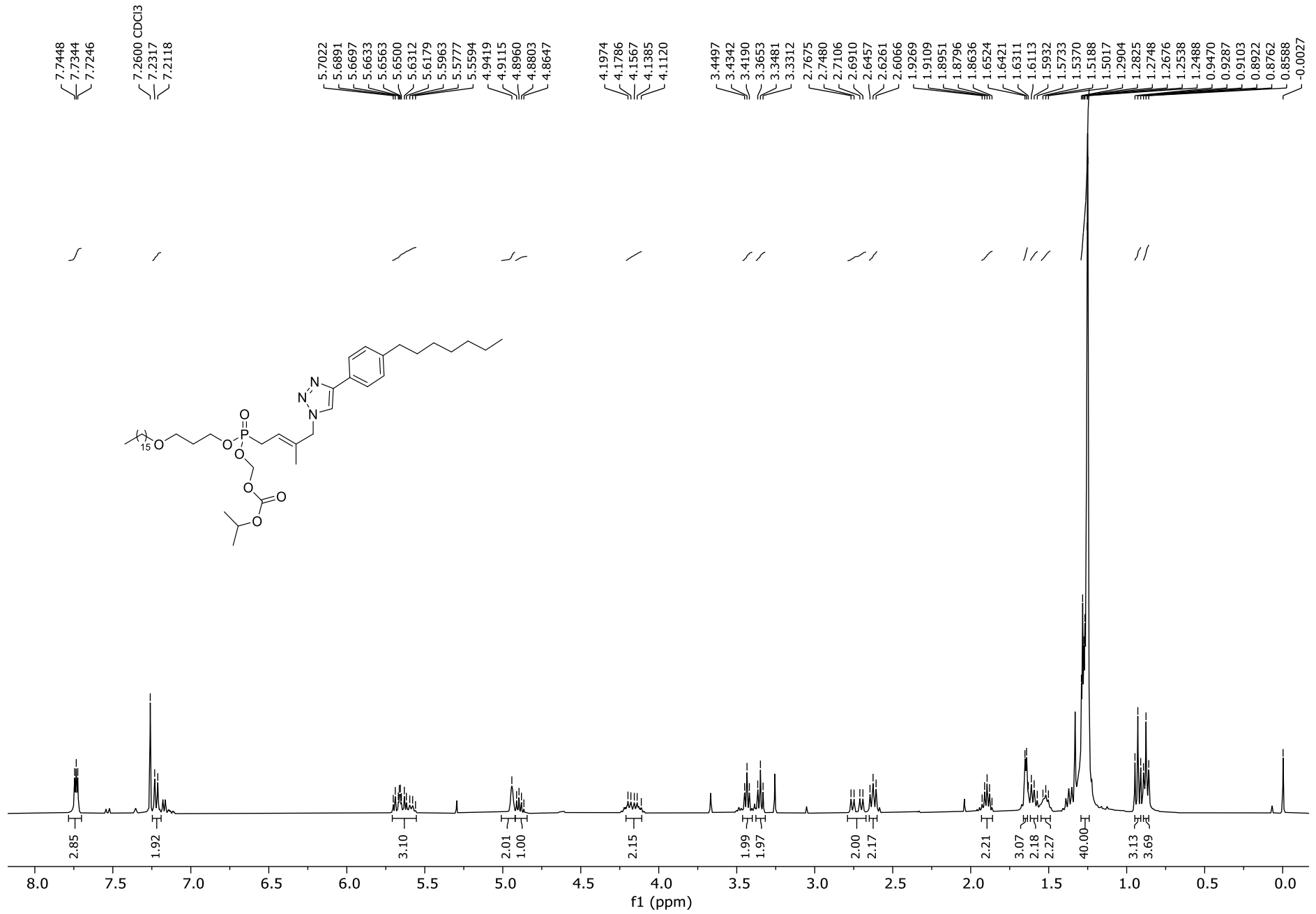


**<sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 15c**

— 27.56

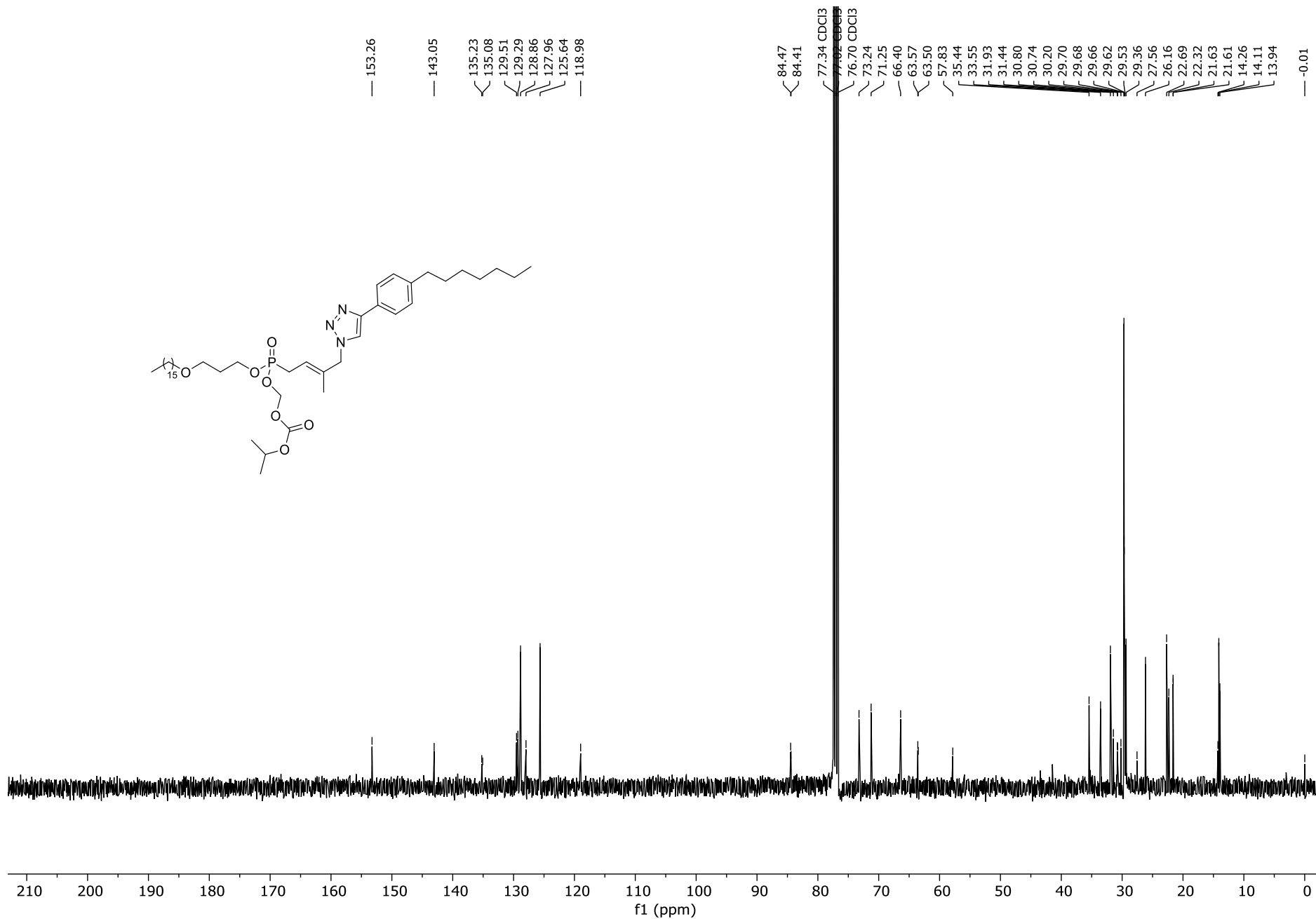
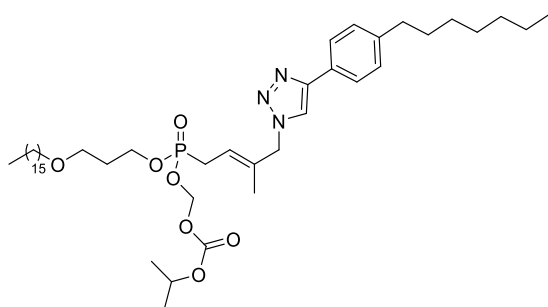


# <sup>1</sup>H NMR (400 MHz, MeOD) Analysis of Compound 15e

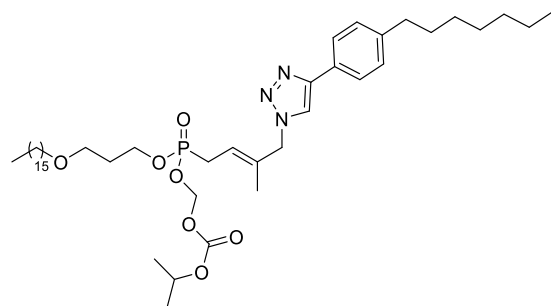




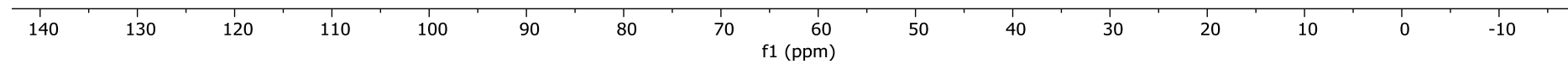
# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 15e



**<sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 15e**

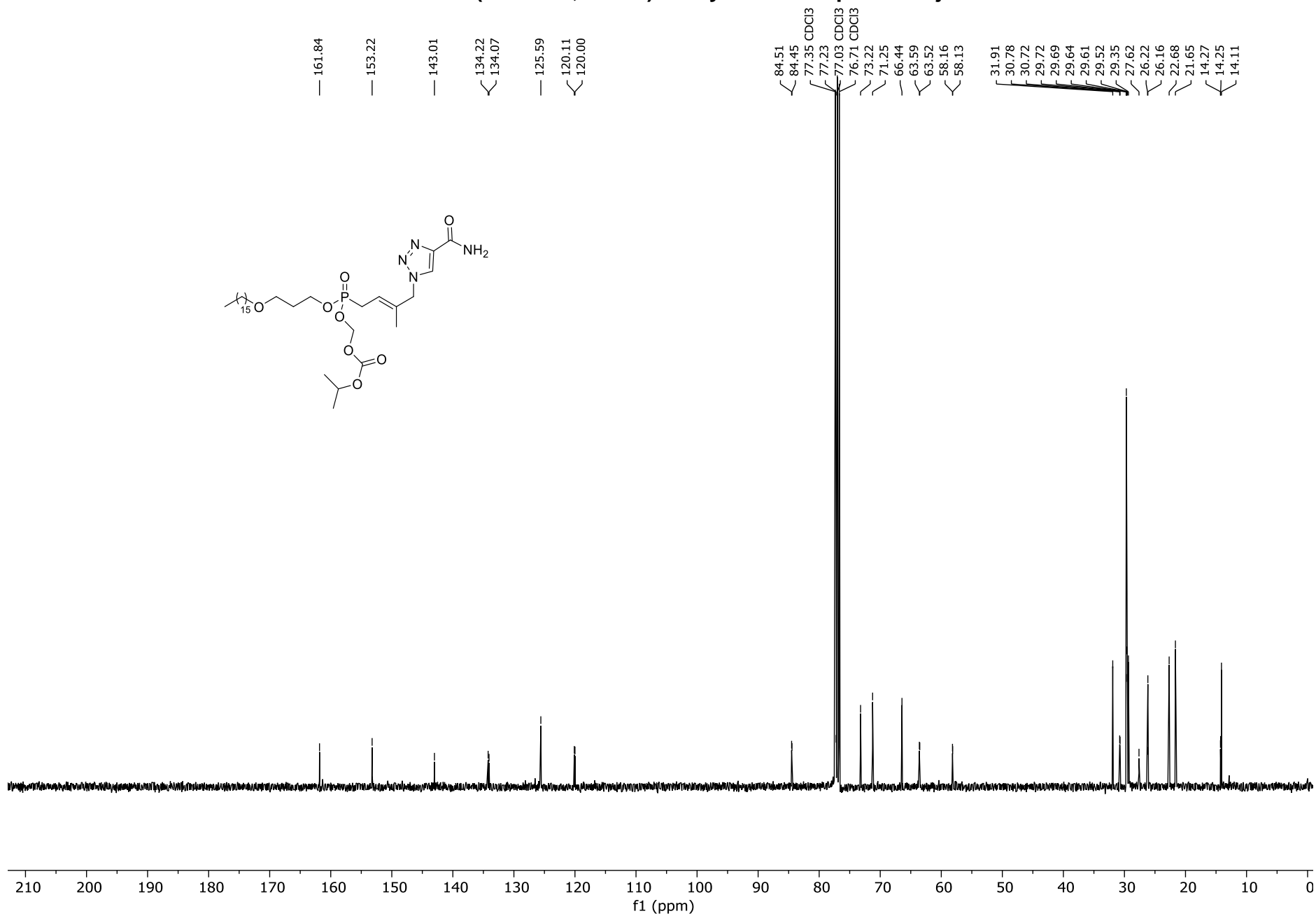
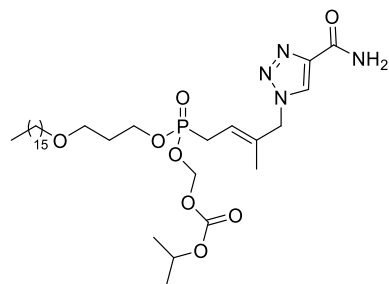


— 27.49



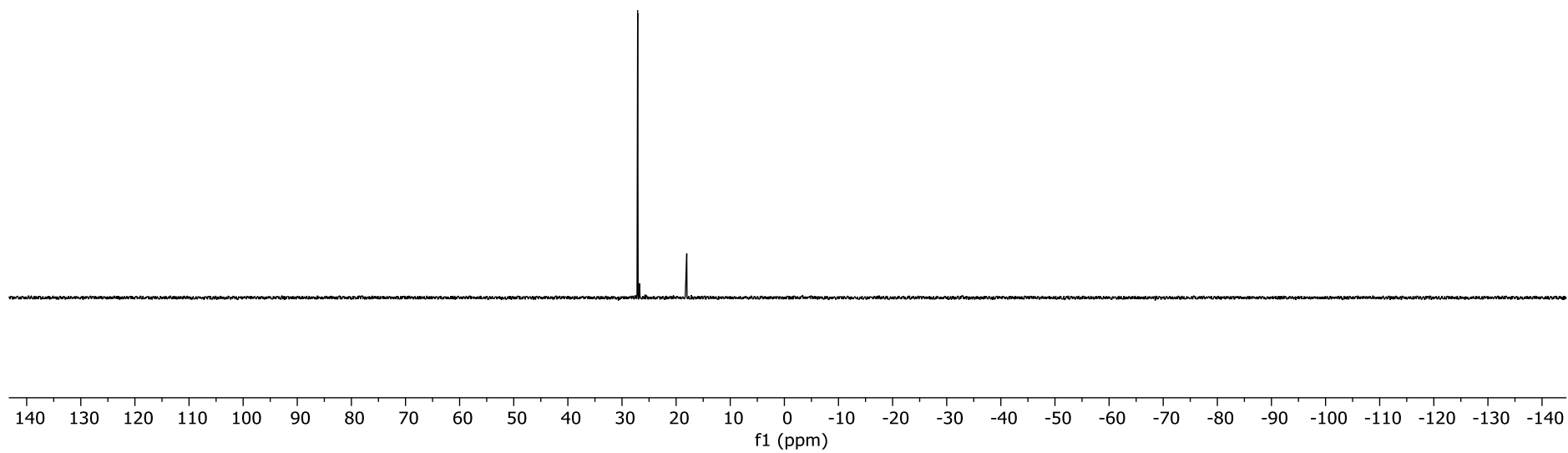
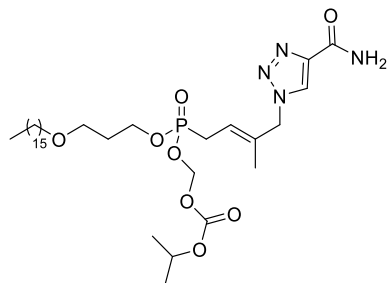


# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 15j

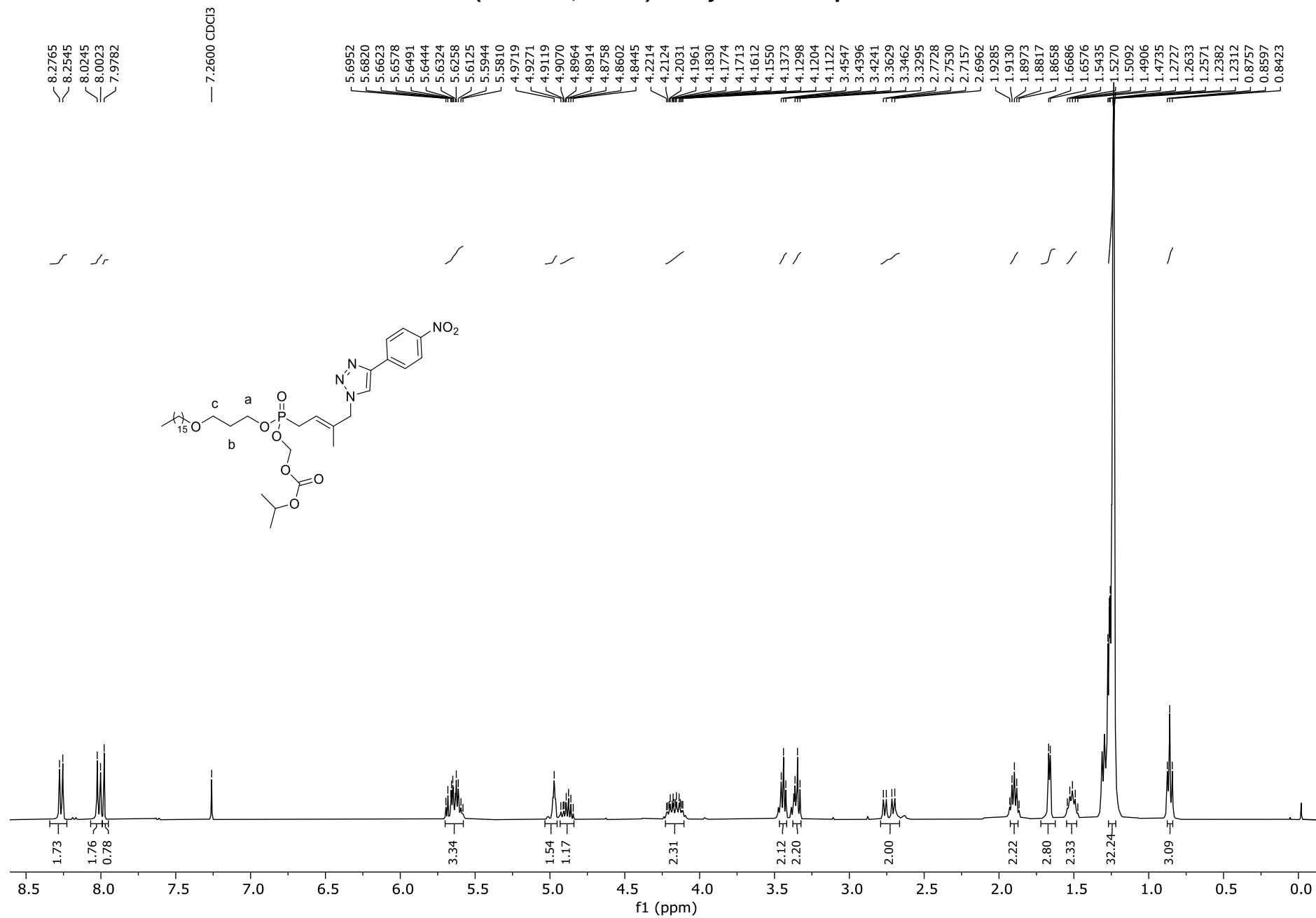


**<sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 15j**

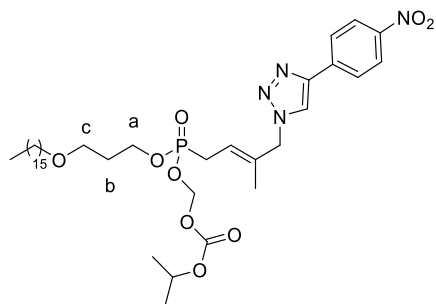
— 27.11



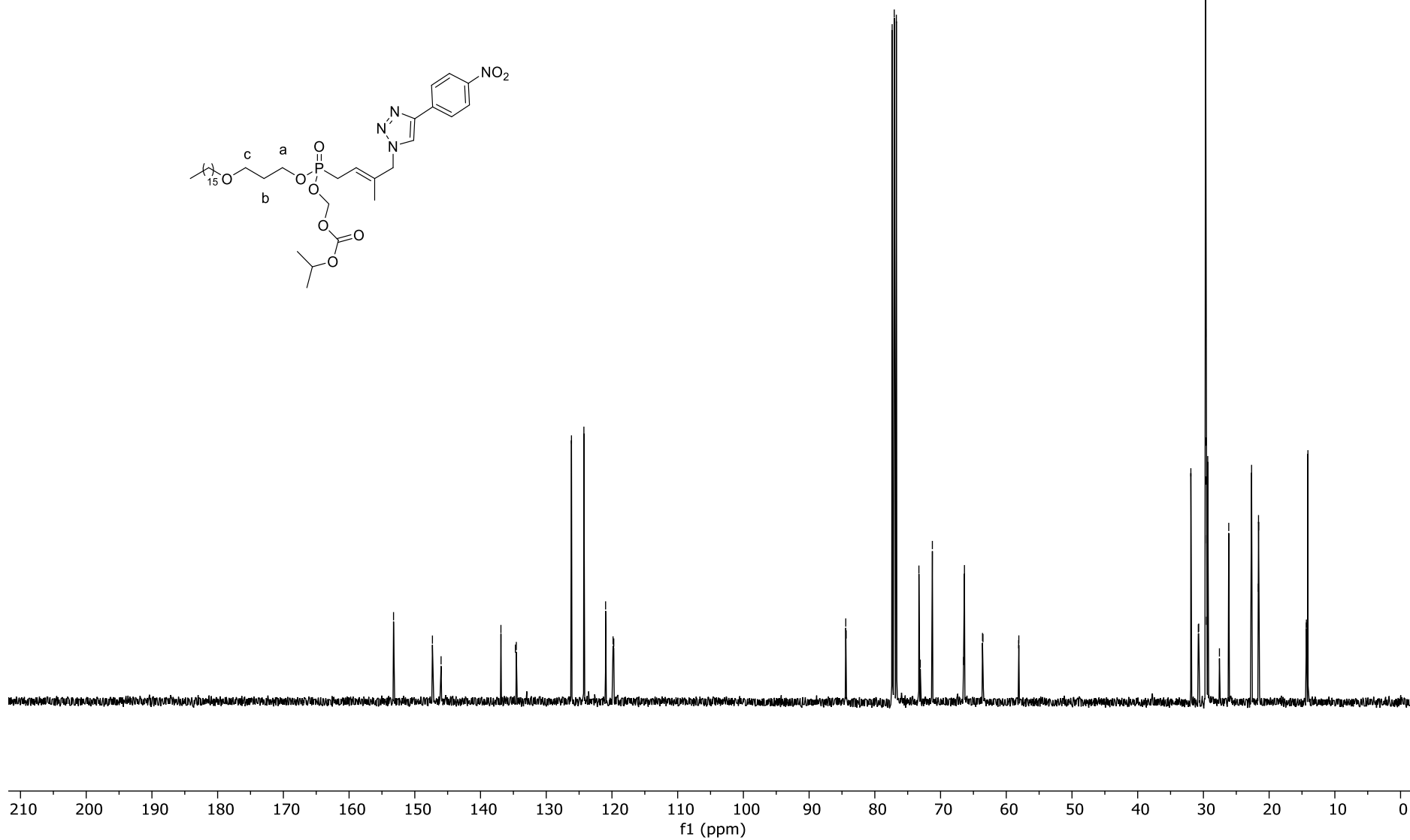
# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) Analysis of Compound 15I



# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) Analysis of Compound 15I



- 153.23
- 147.32
- 146.00
- 136.89
- 134.70
- 134.55
- 126.16
- 124.27
- 120.97
- 119.83
- 119.72
- 84.42
- 84.36
- 77.36
- 77.25
- 77.04
- 76.72
- 73.29
- 73.08
- 71.24
- 66.51
- 66.36
- 63.61
- 63.54
- 58.11
- 58.09
- 31.91
- 30.78
- 30.72
- 29.68
- 29.64
- 29.62
- 29.60
- 29.53
- 29.50
- 29.34
- 27.56
- 26.16
- 26.14
- 22.67
- 21.65
- 21.61
- 21.59
- 14.35
- 14.33
- 14.10



**<sup>31</sup>P NMR (161 MHz, CDCl<sub>3</sub>) Analysis of Compound 15I**

— 27.31

