

Supporting Information File 2

for

Synthesis of medronic acid monoesters and their purification by high-performance countercurrent chromatography or by hydroxyapatite

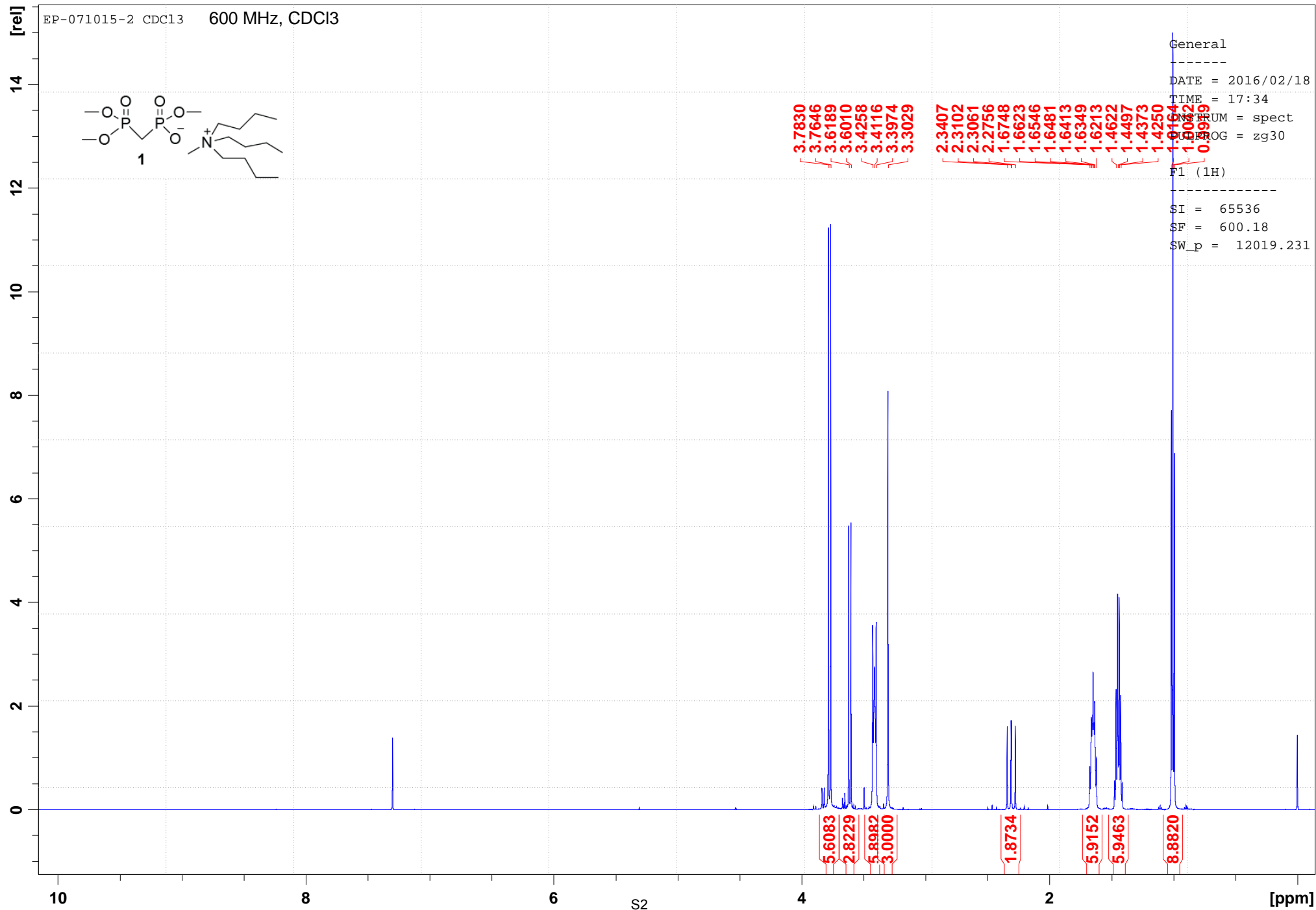
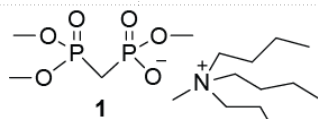
Elina Puljula*, Jouko Vepsäläinen and Petri A. Turhanen

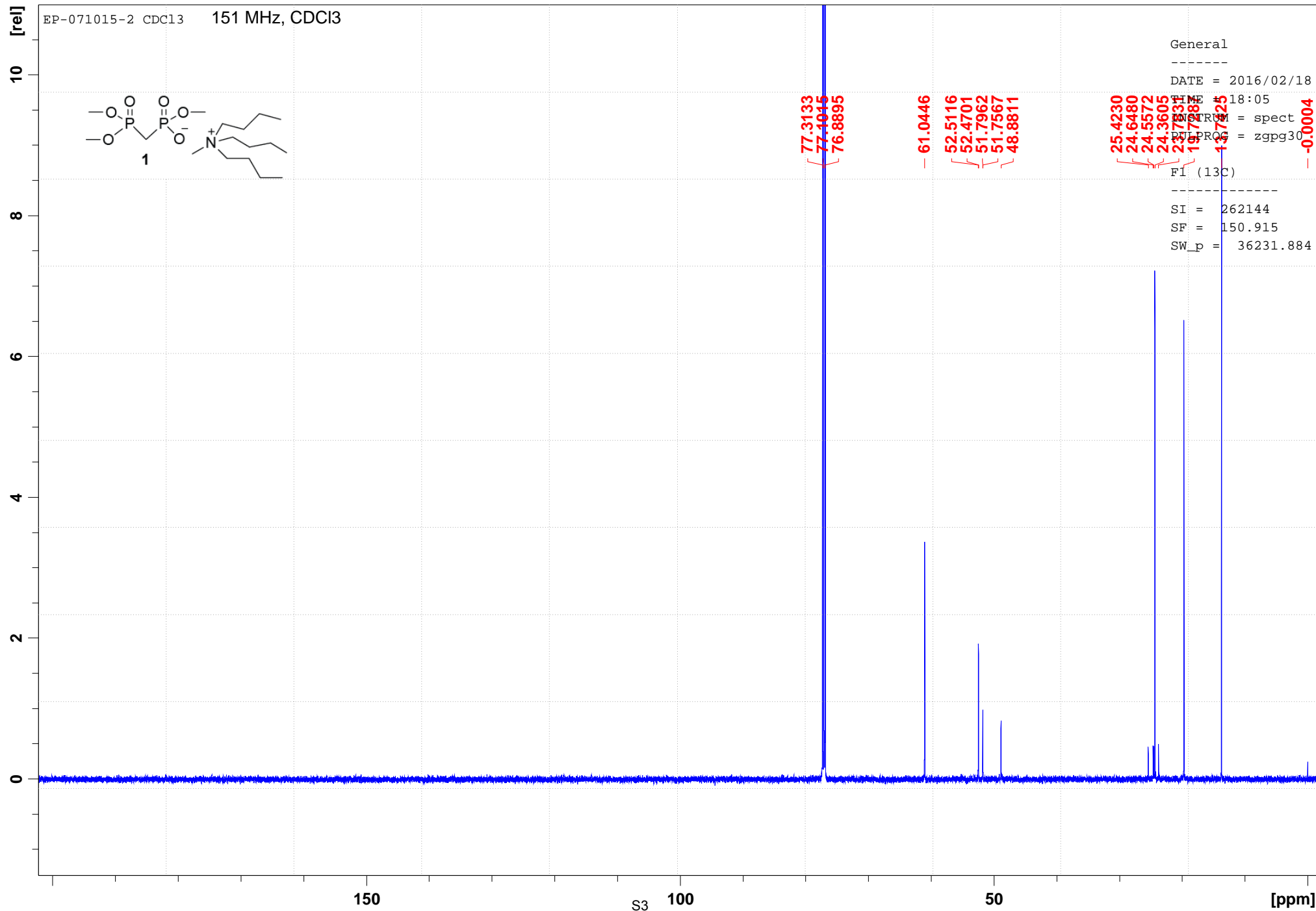
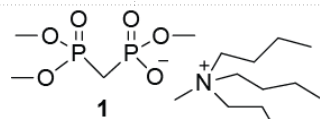
Address: School of Pharmacy, University of Eastern Finland, Biocenter Kuopio,
P.O.Box 1627, FI-70211 Kuopio, Finland

Email: Elina Puljula - elina.puljula@uef.fi

* Corresponding author

^1H , ^{13}C , and ^{31}P NMR spectra and an example of HPLC chromatogram



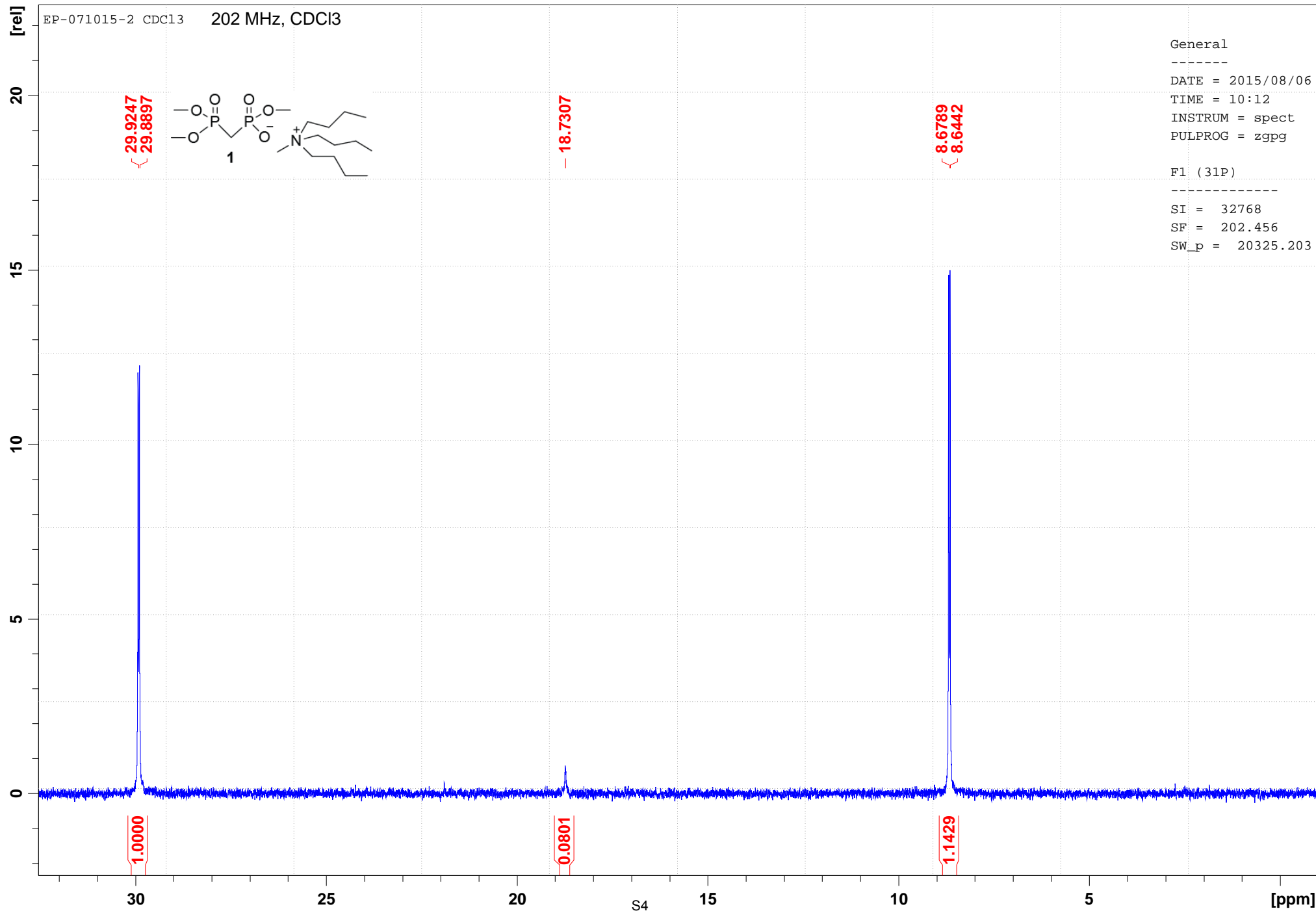


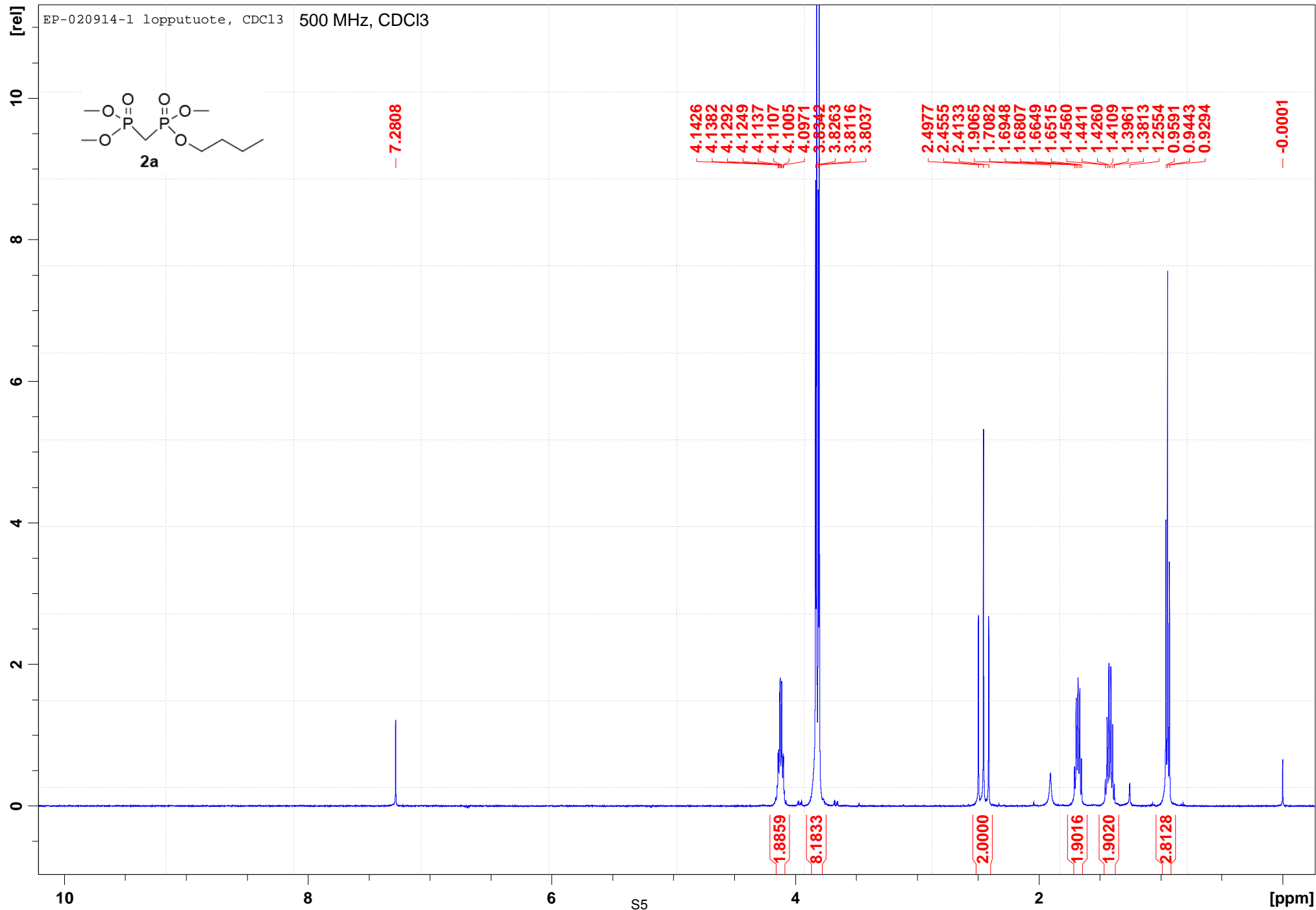
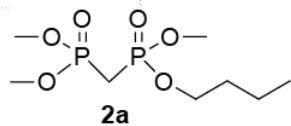
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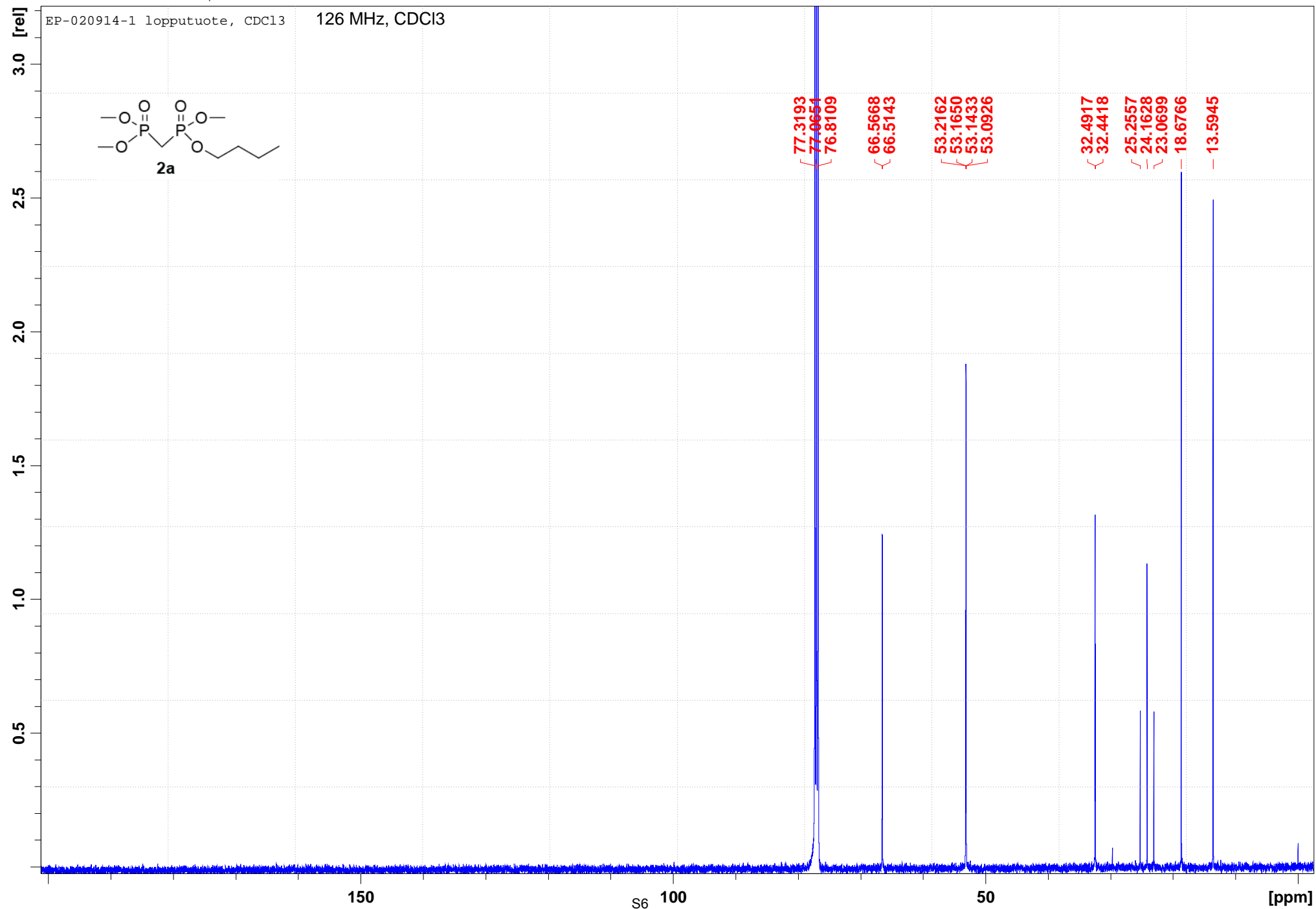
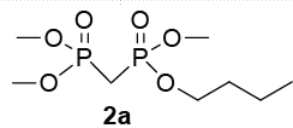
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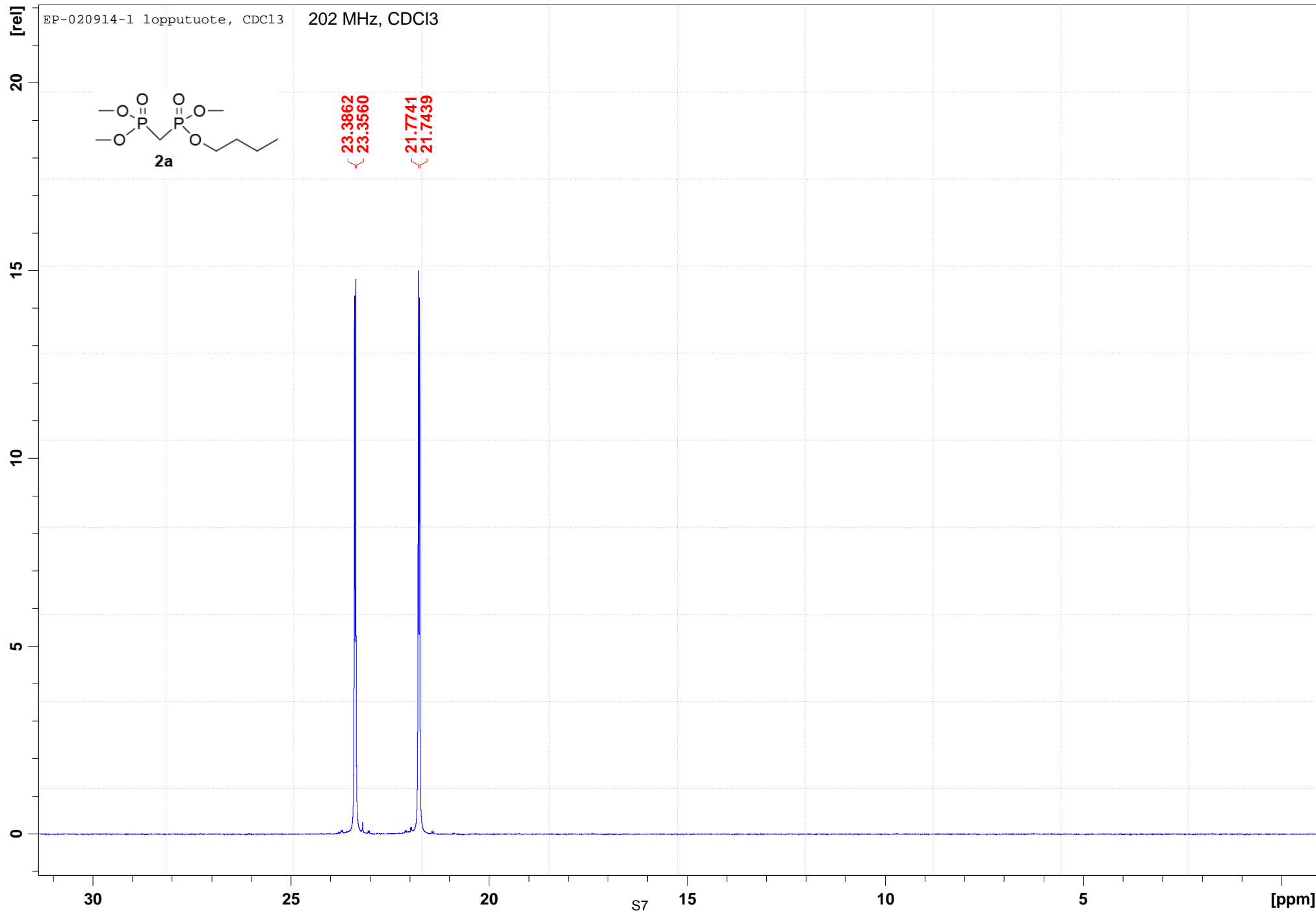
F1 (31P)

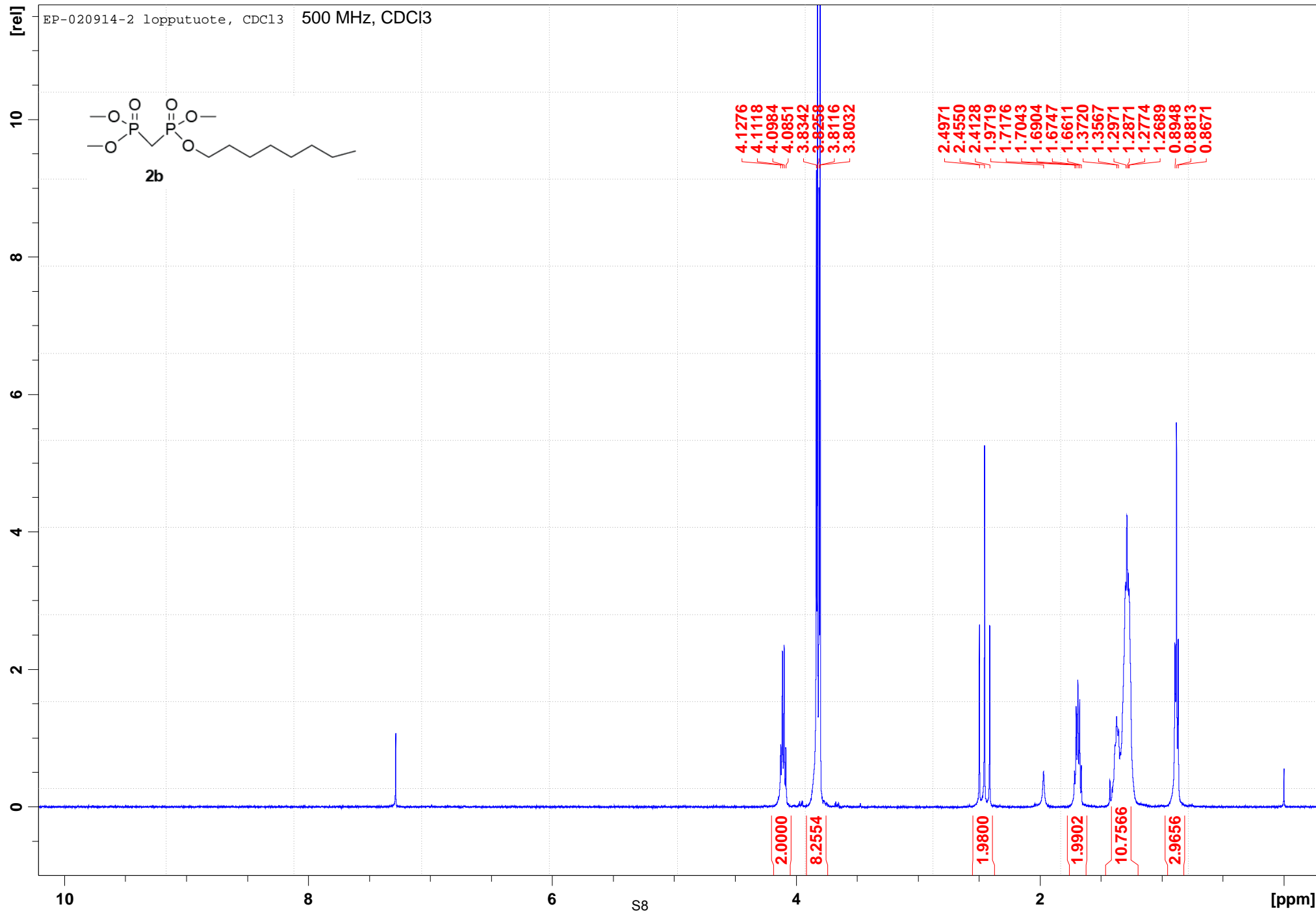
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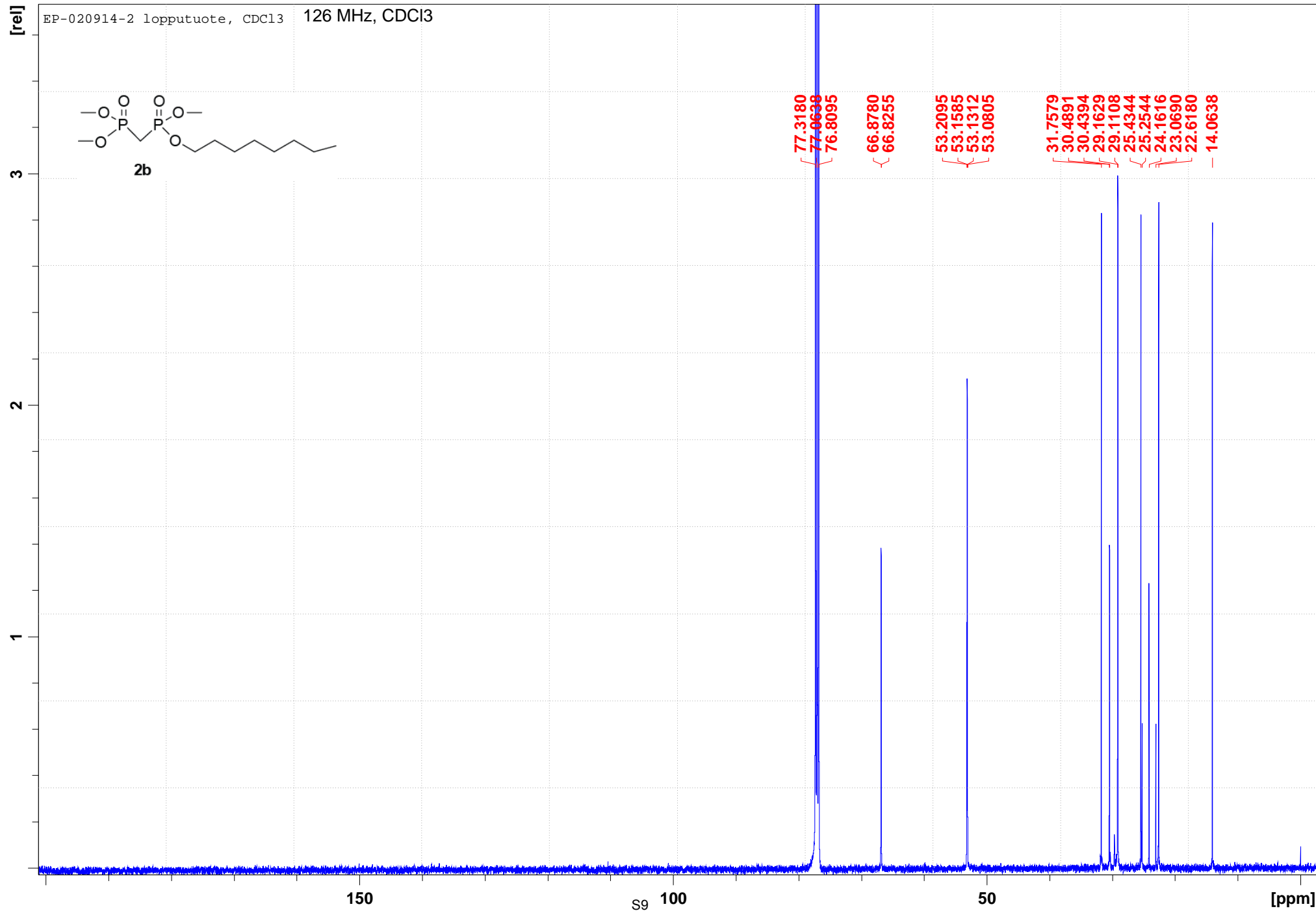


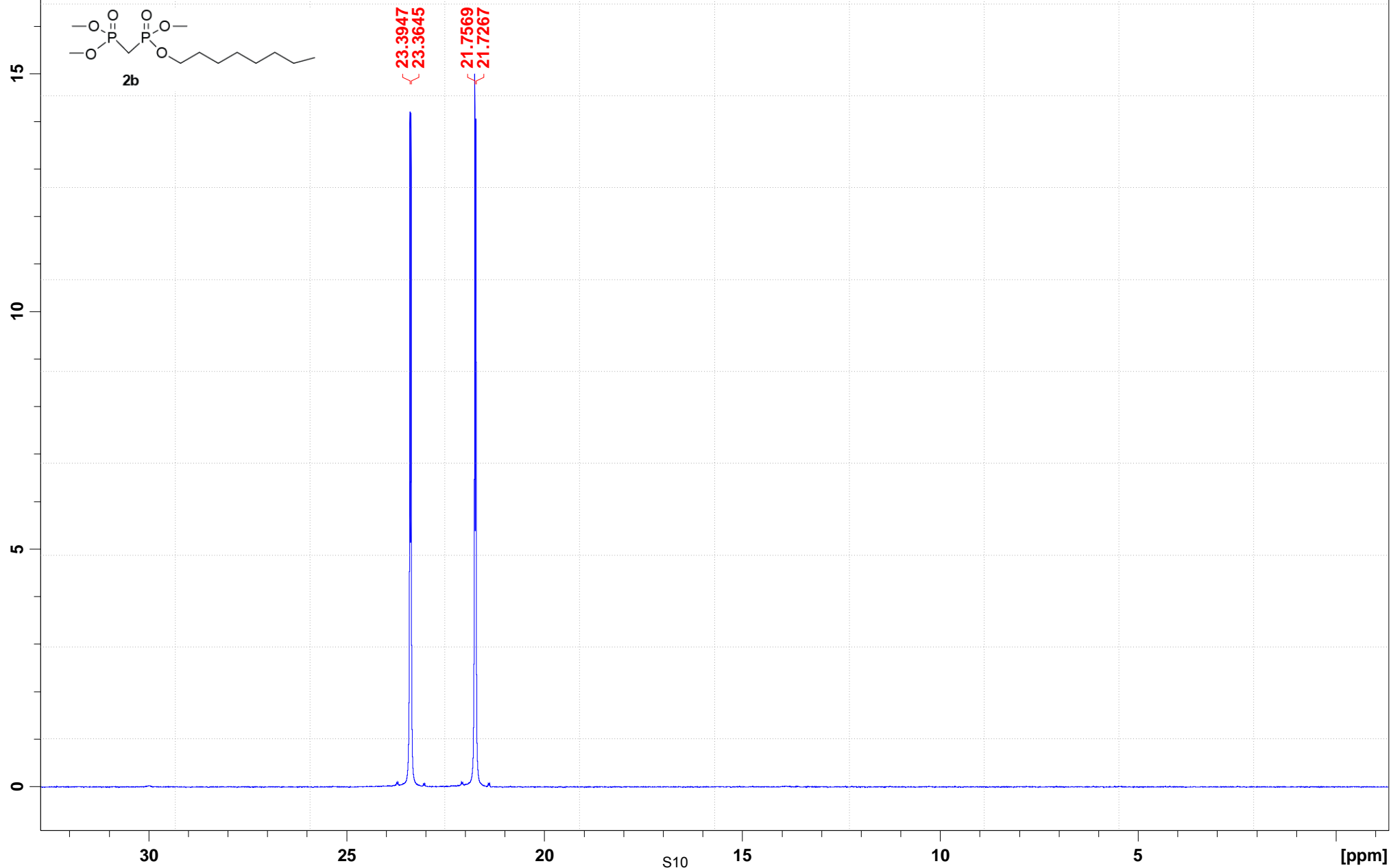


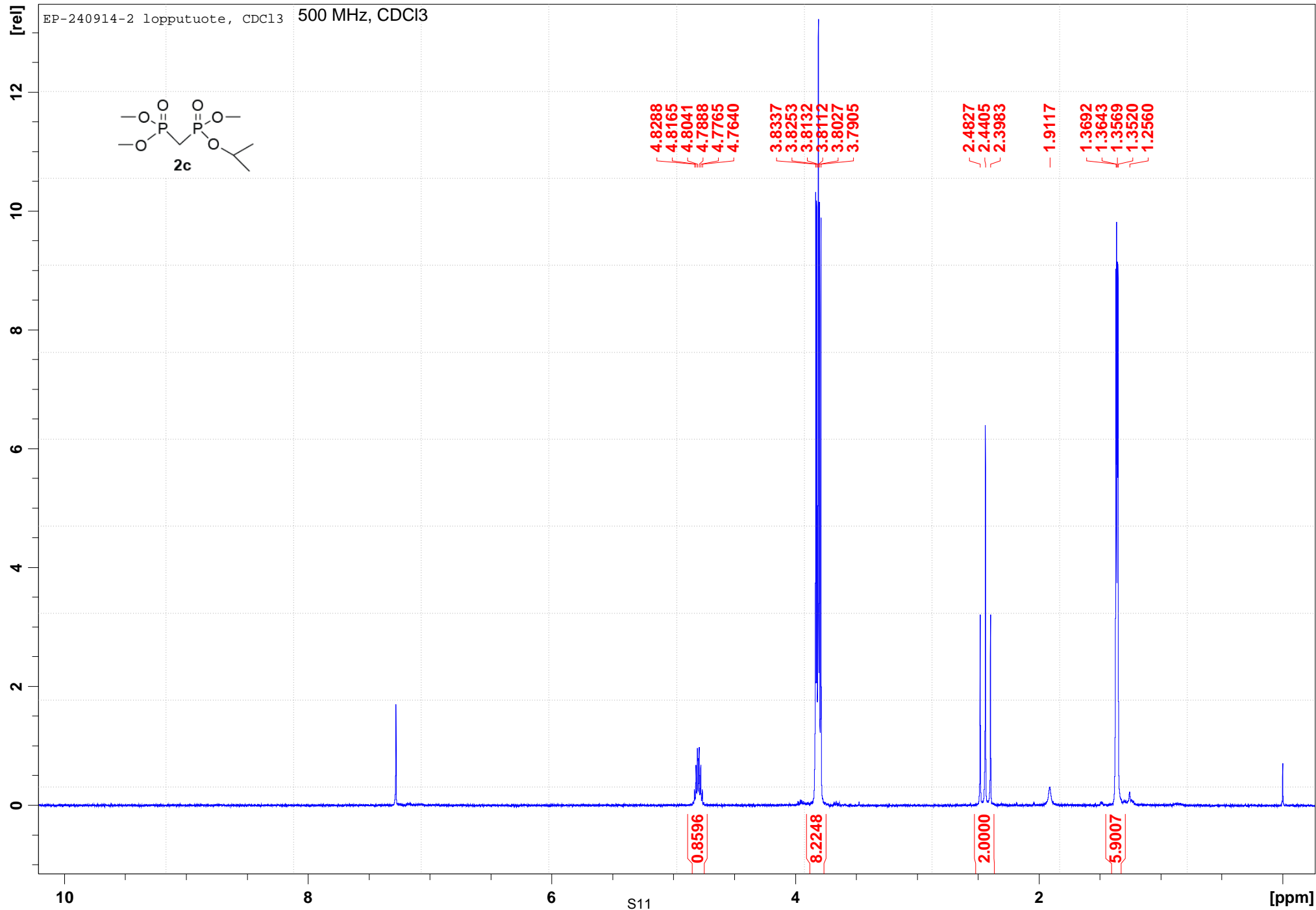
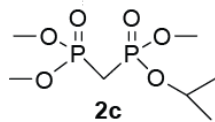


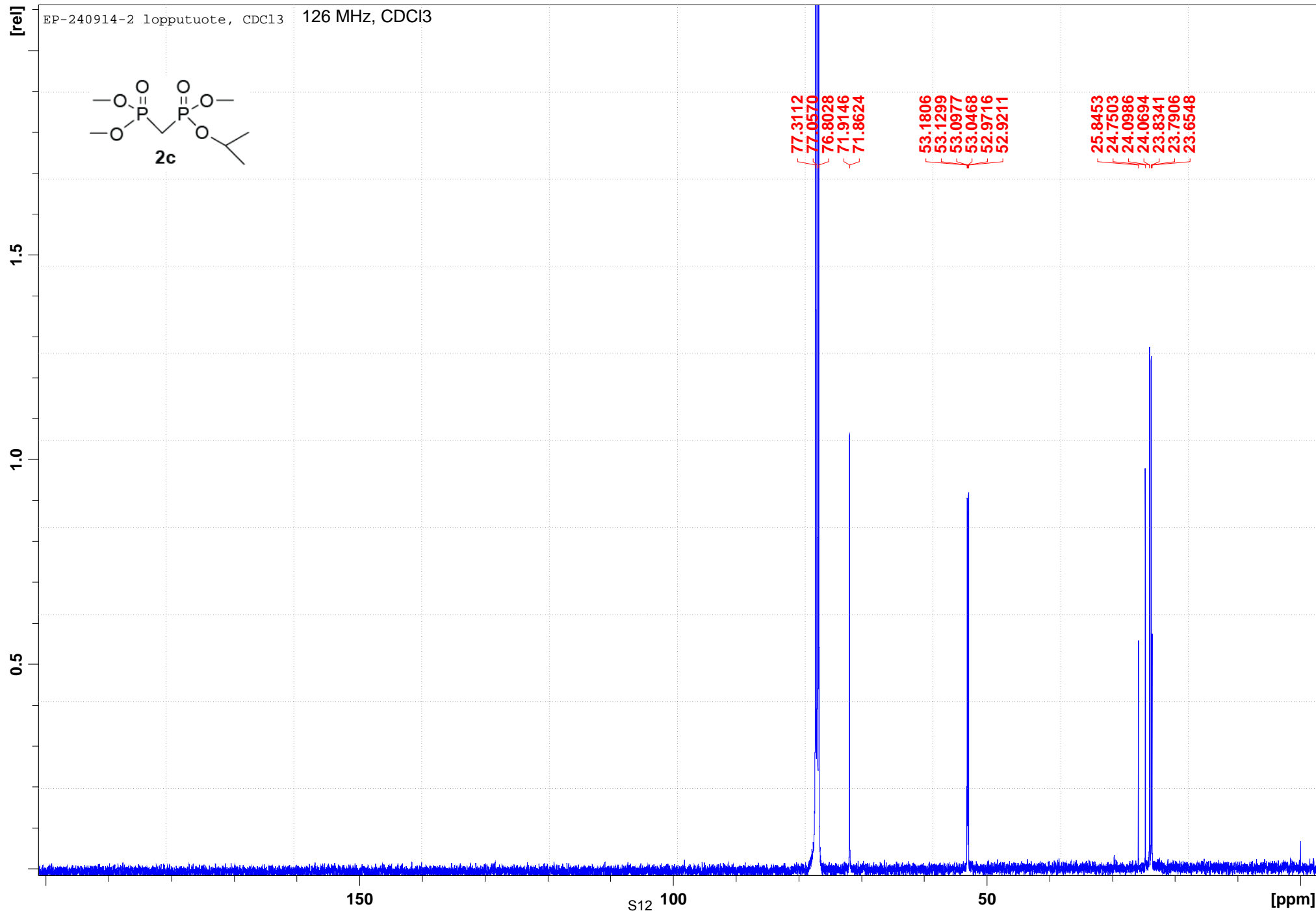
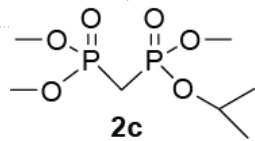


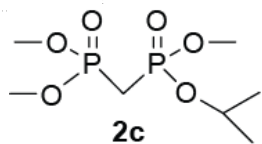






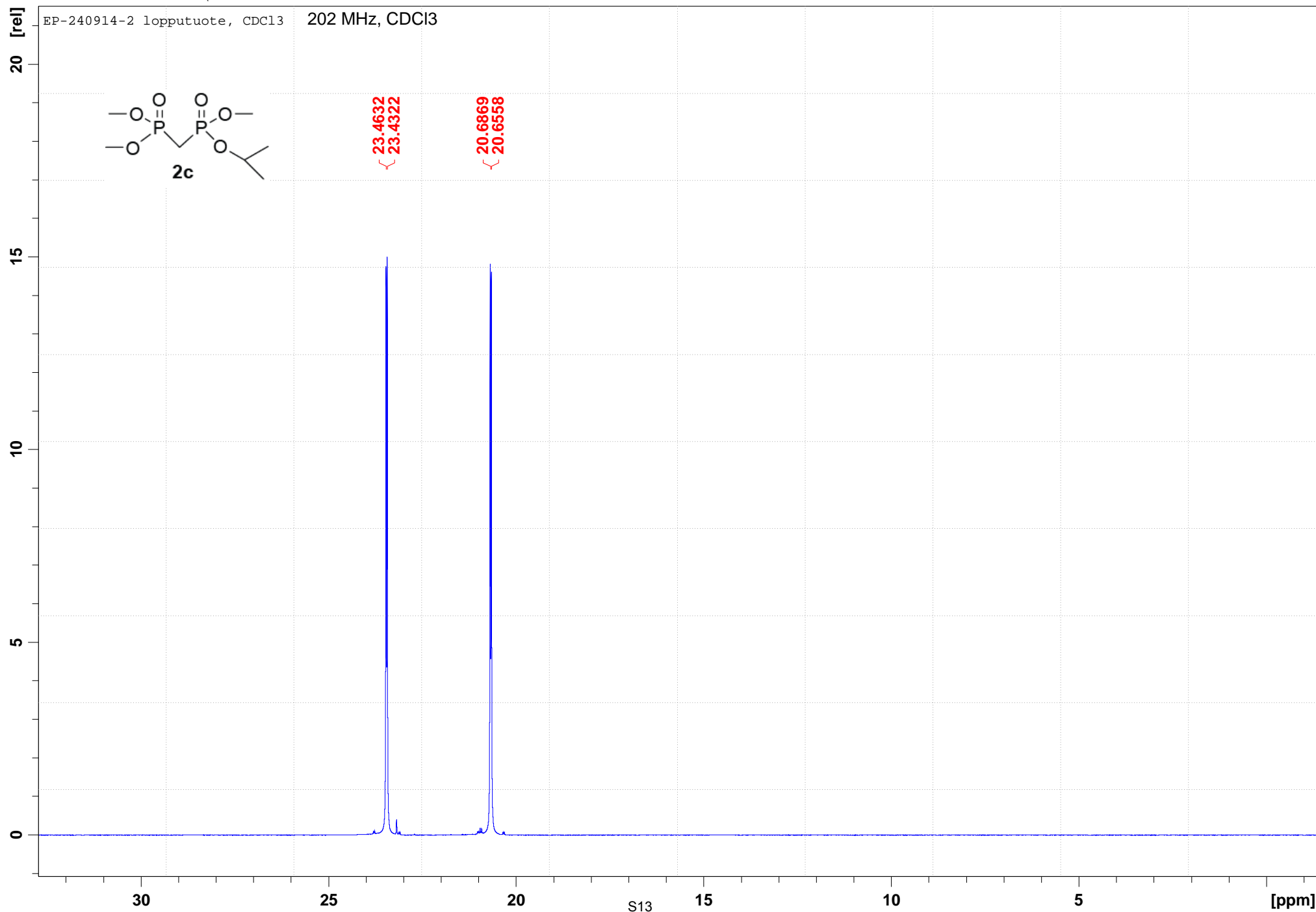


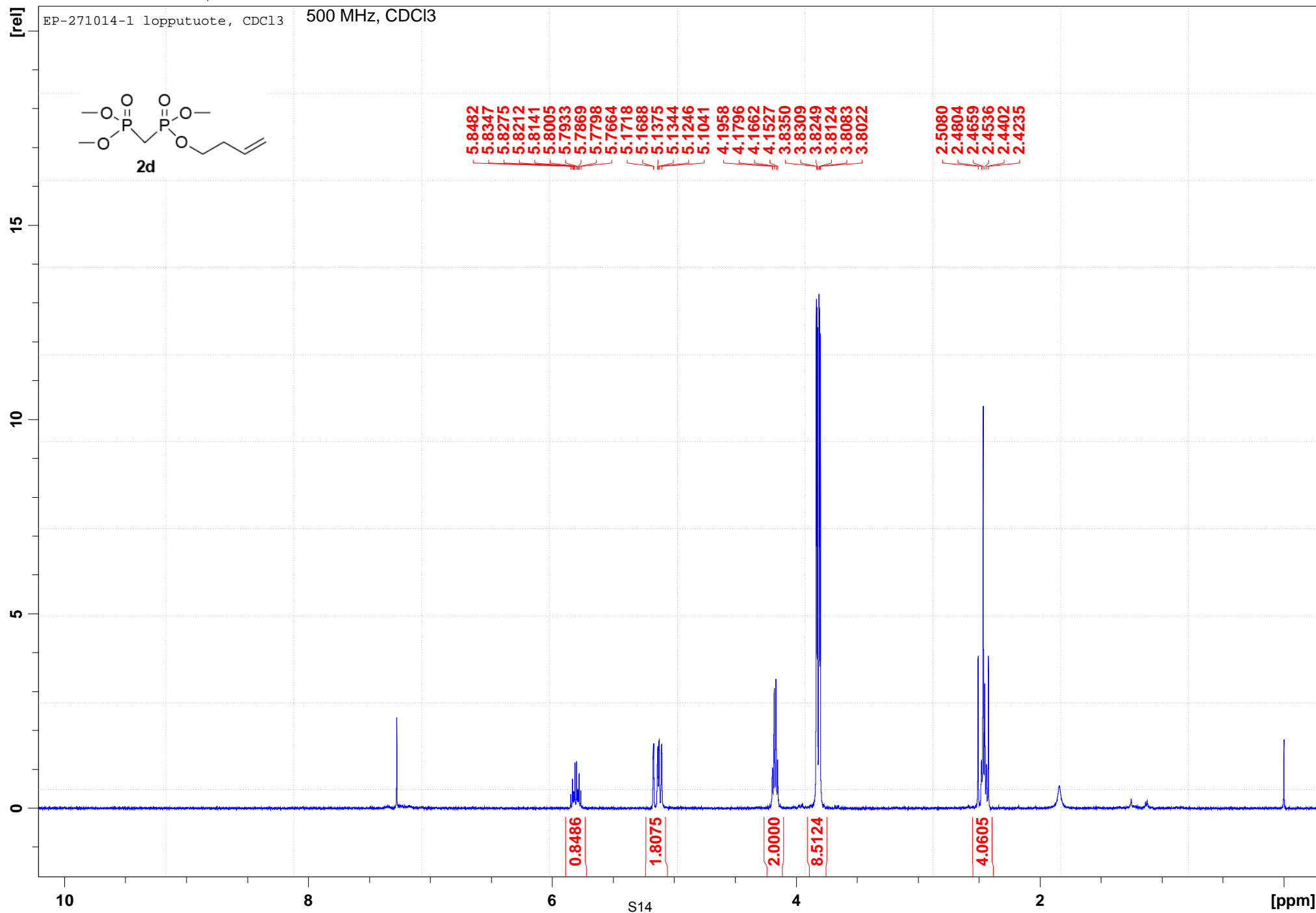
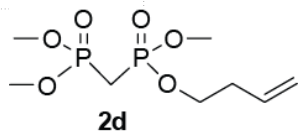


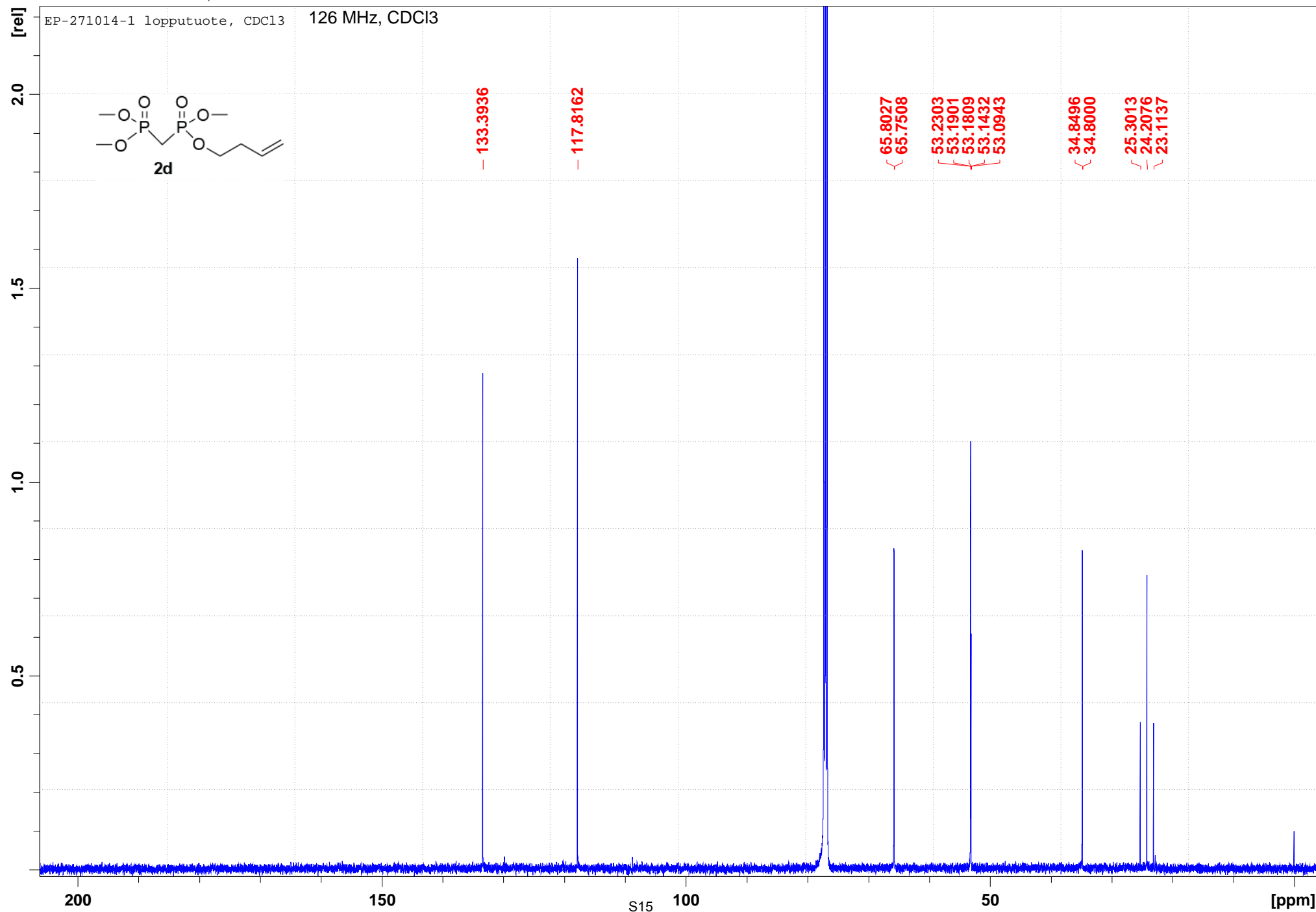
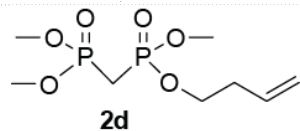


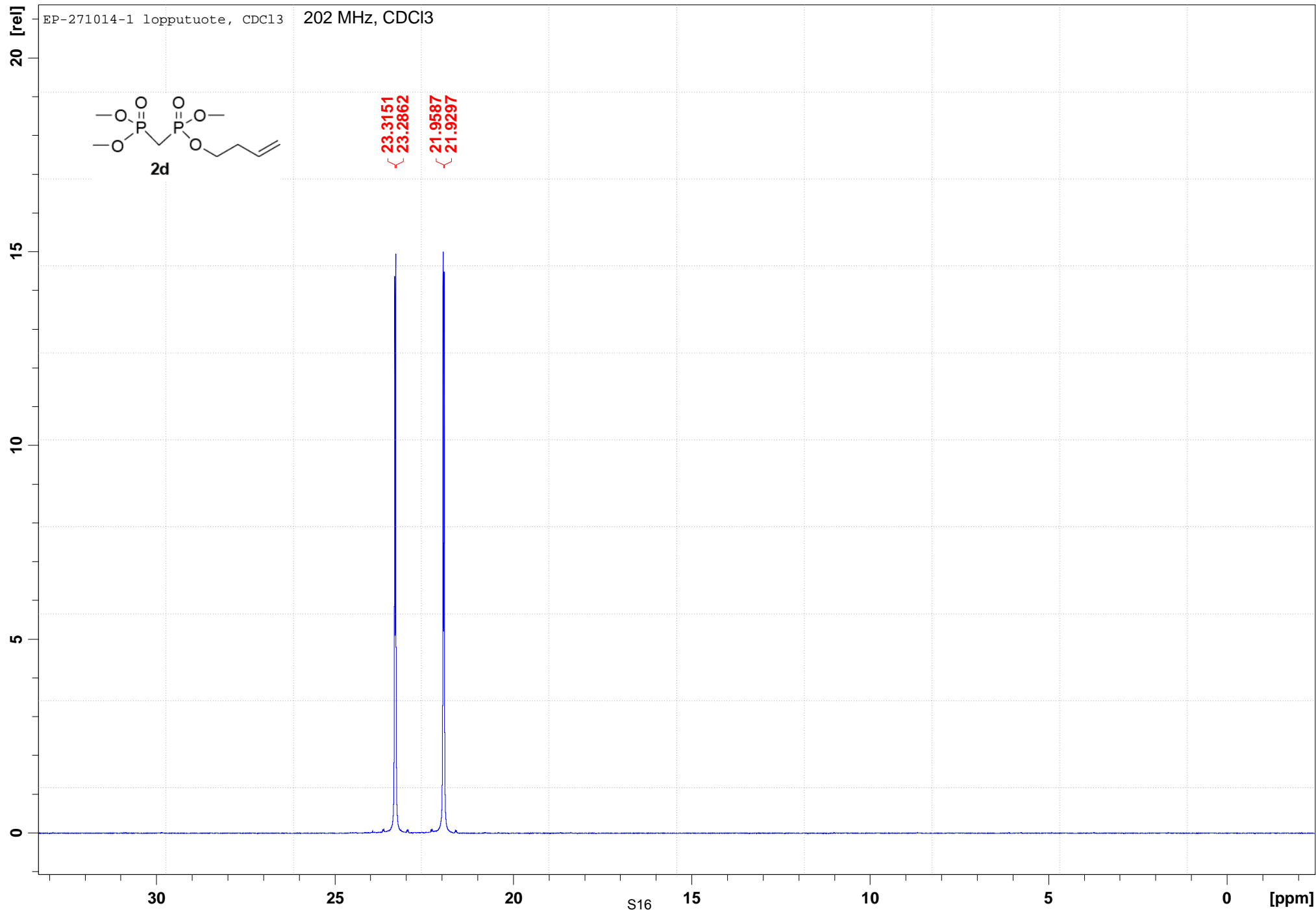
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23.4322

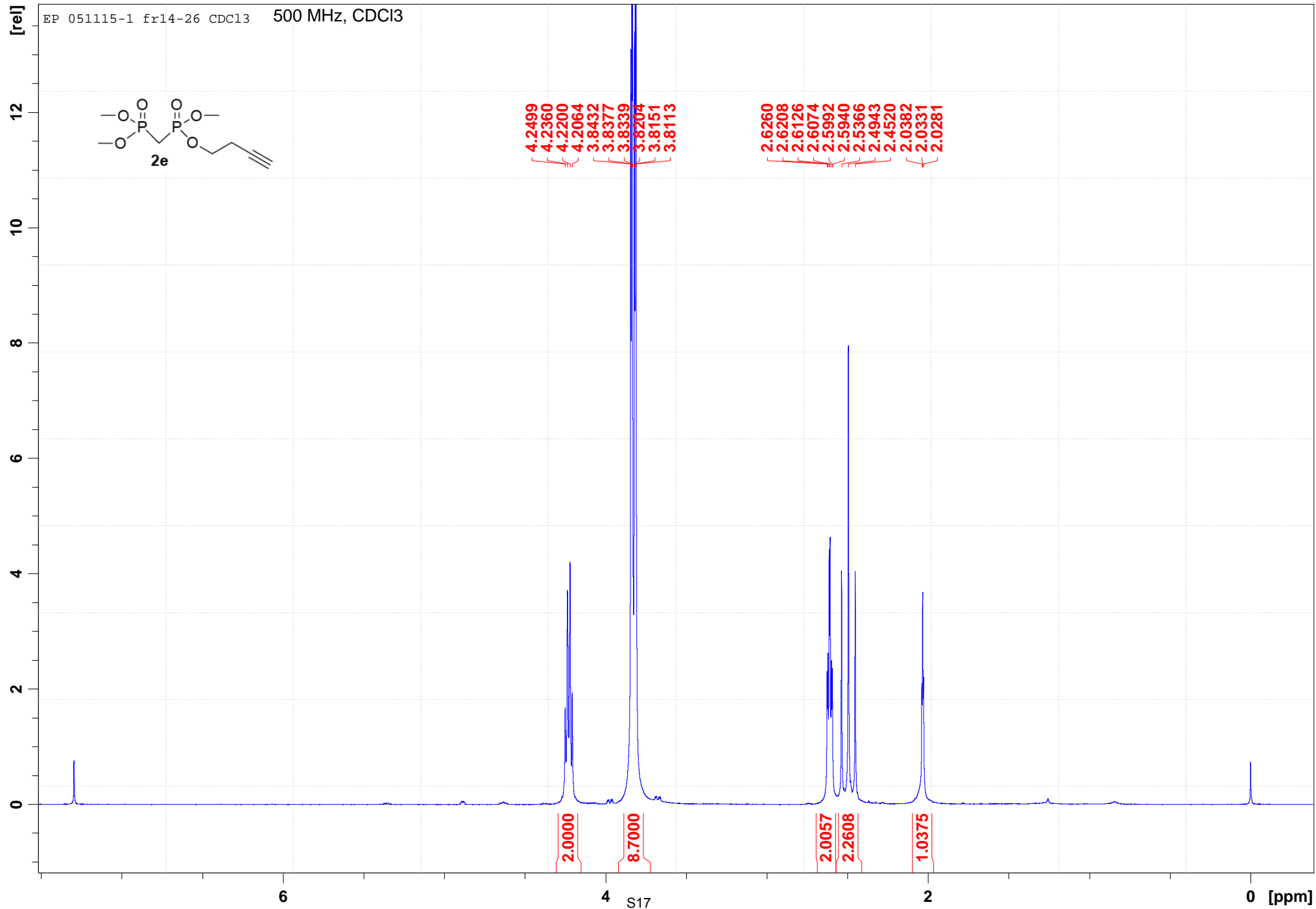
20.6869
20.6558











6

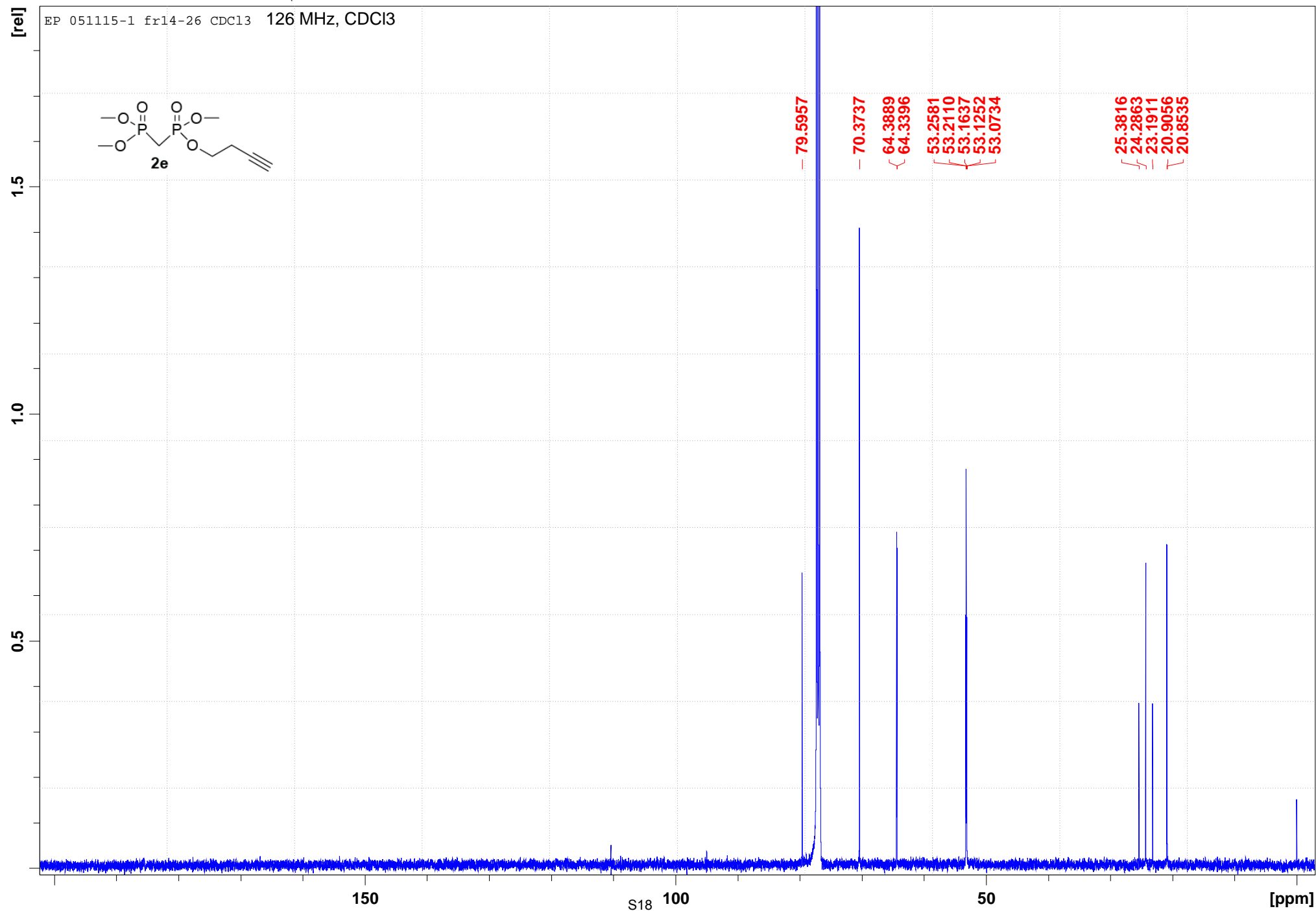
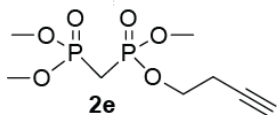
4 S17

2

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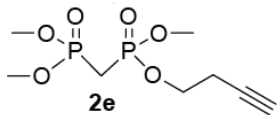
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EP 051115-1 fr14-26 CDCl3 126 MHz, CDCl3

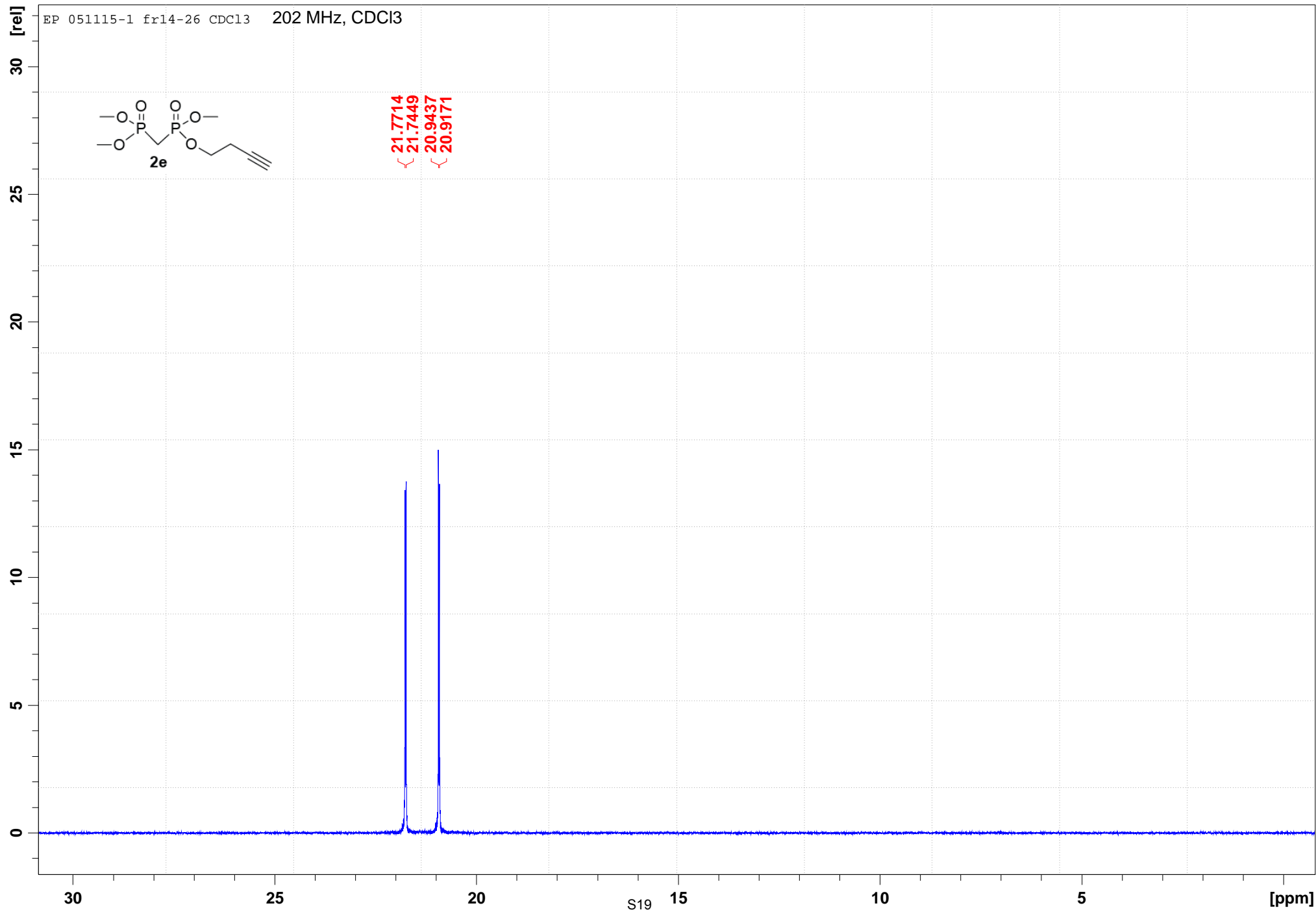


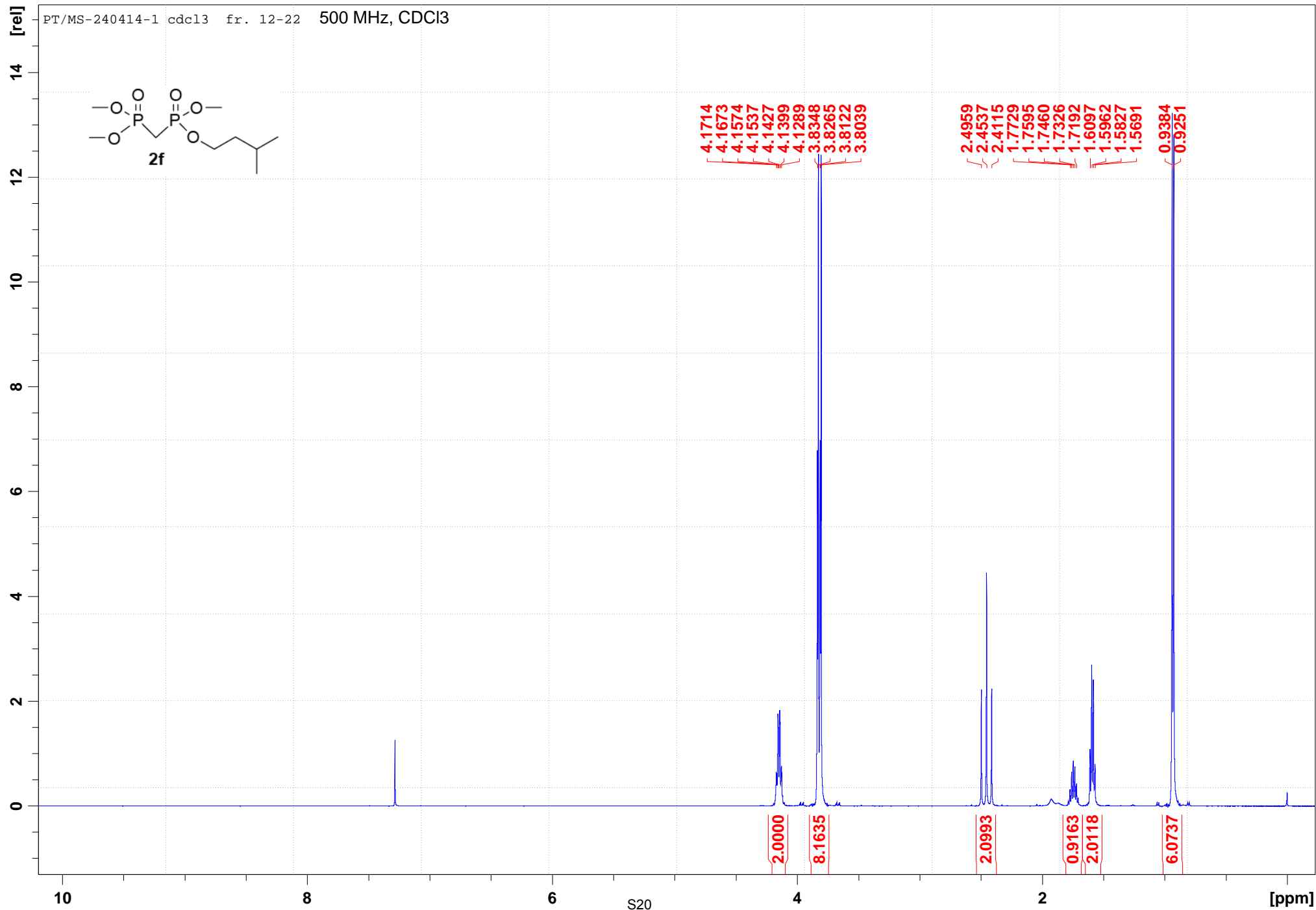
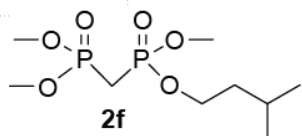
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EP 051115-1 fr14-26 CDCl3 202 MHz, CDCl3



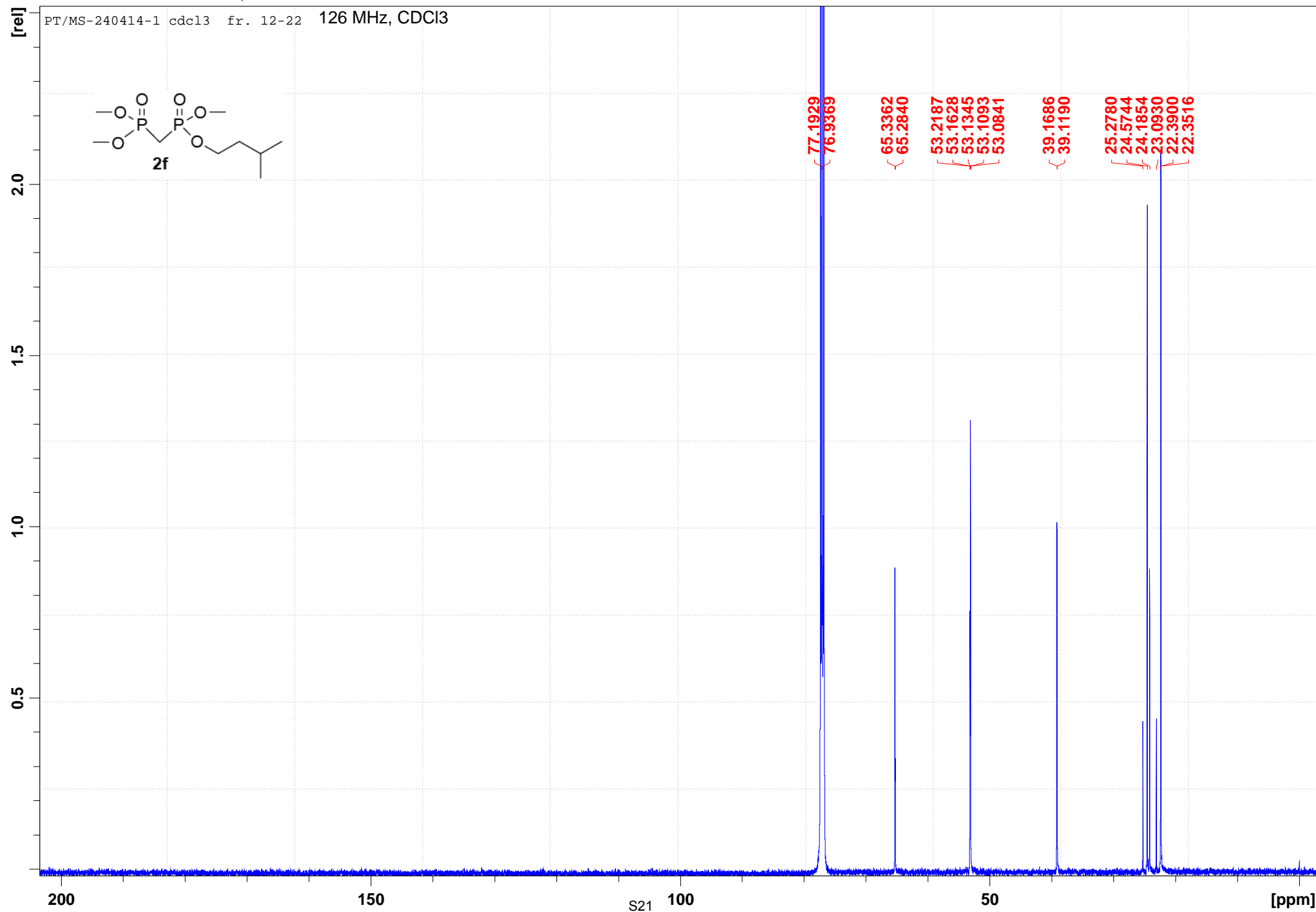
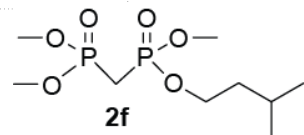
21.7714
21.7449
20.9437
20.9171





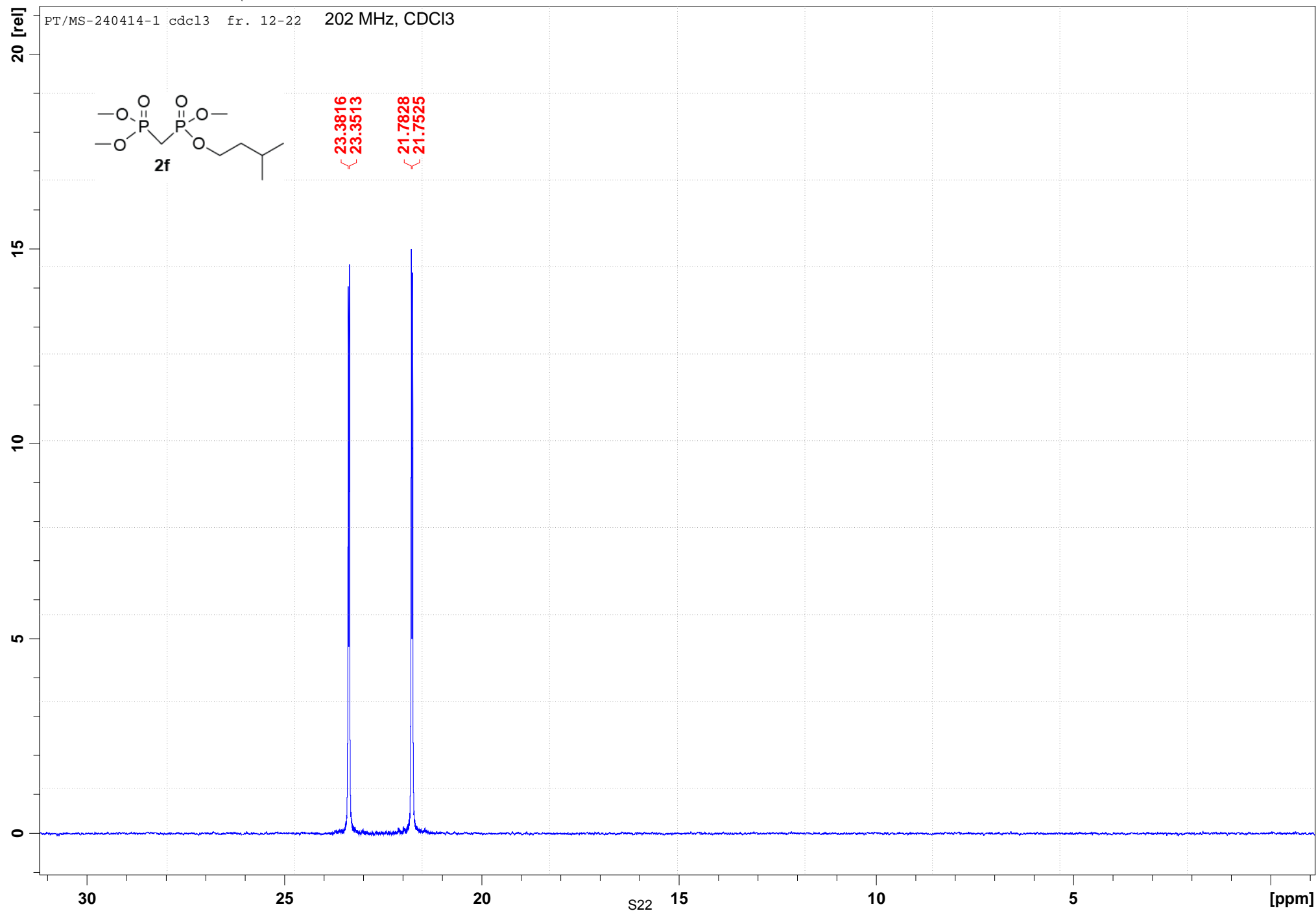
MS-240414-1 33 1 "E:\NMR 2015"

PT/MS-240414-1 cdcl3 fr. 12-22 126 MHz, CDCl3



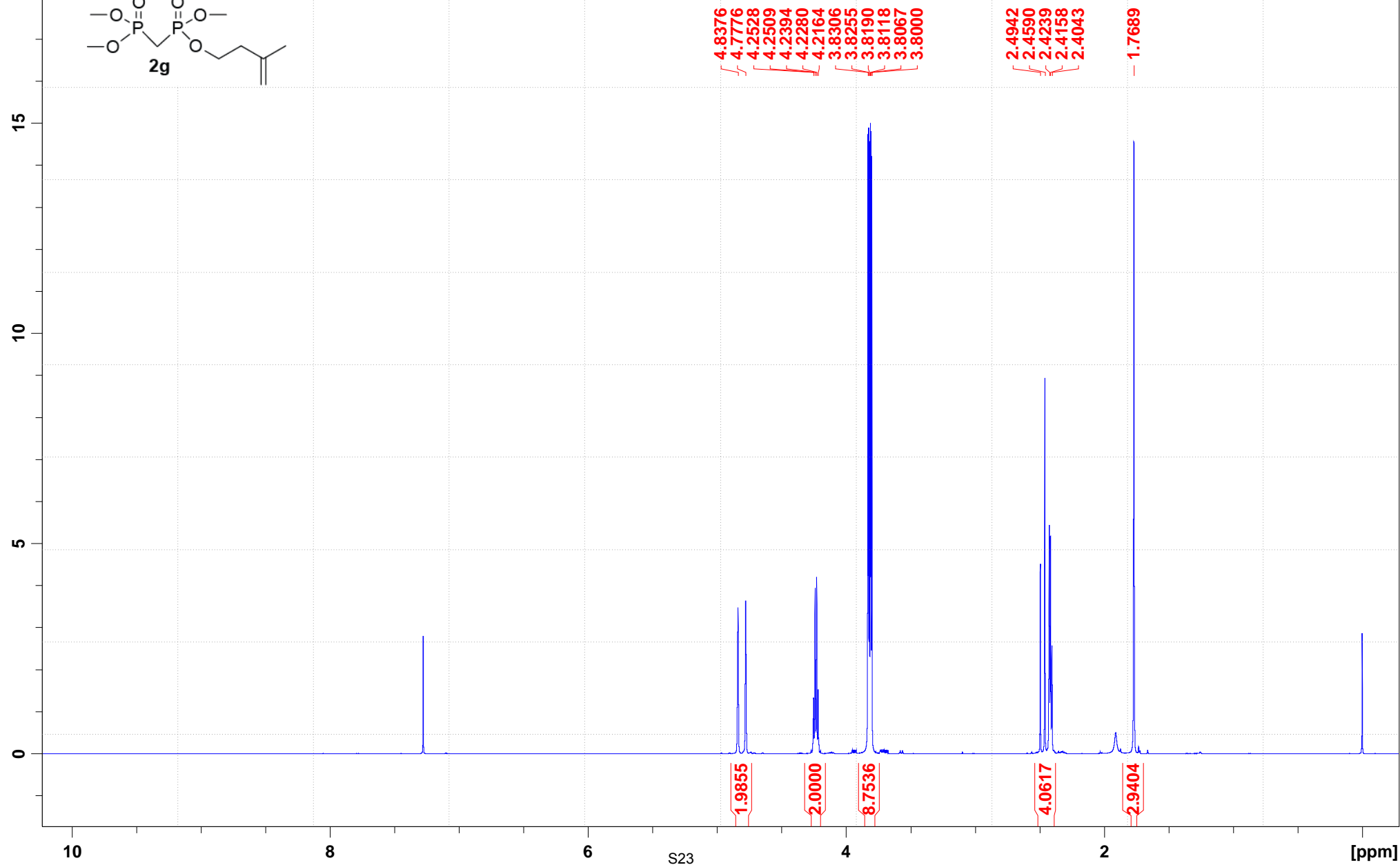
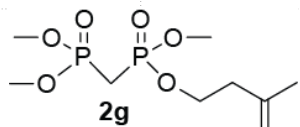
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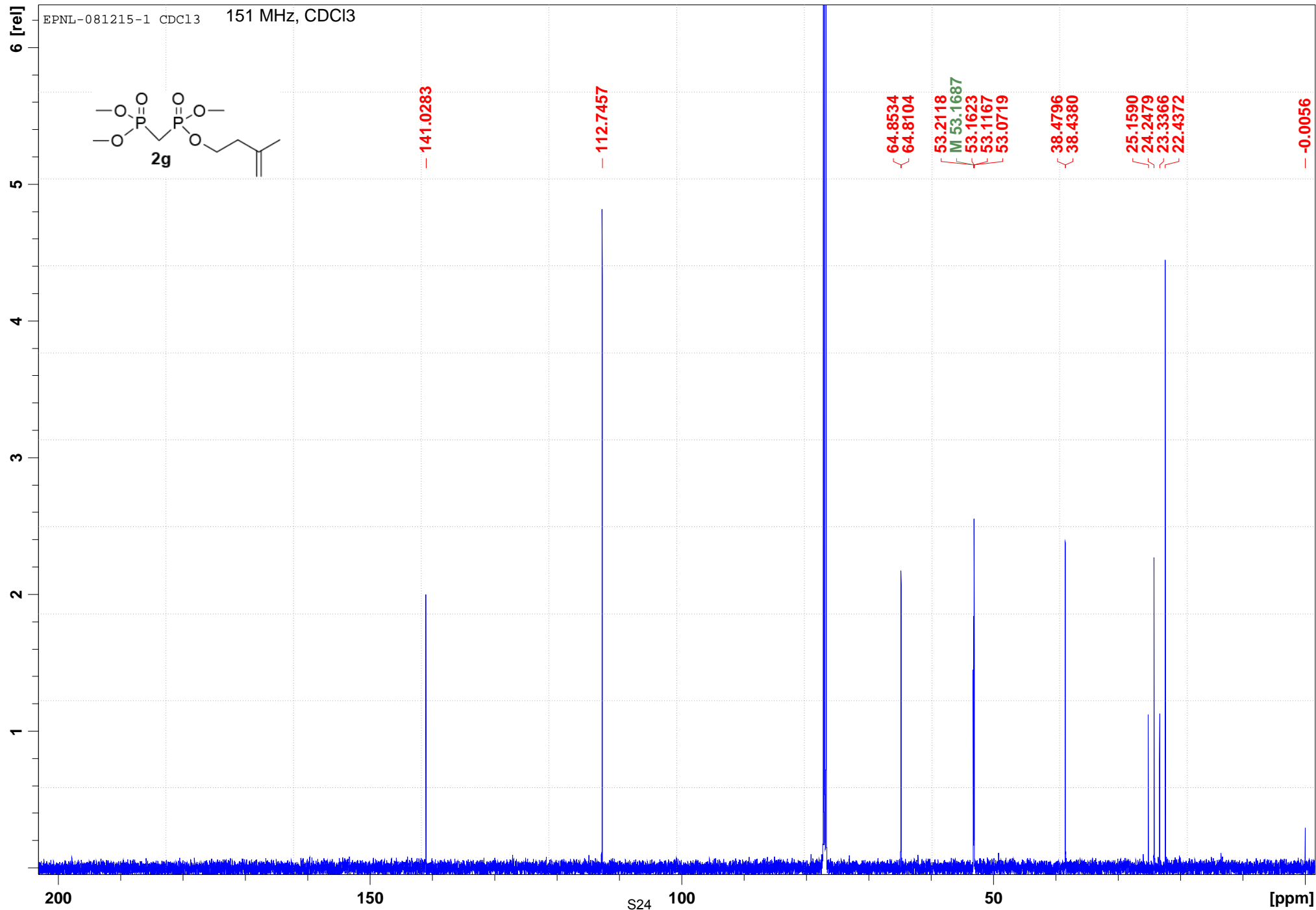
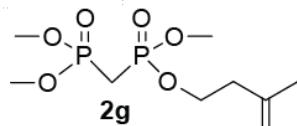
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EPNL-081215-1 10 1 "E:\NMR 2015"

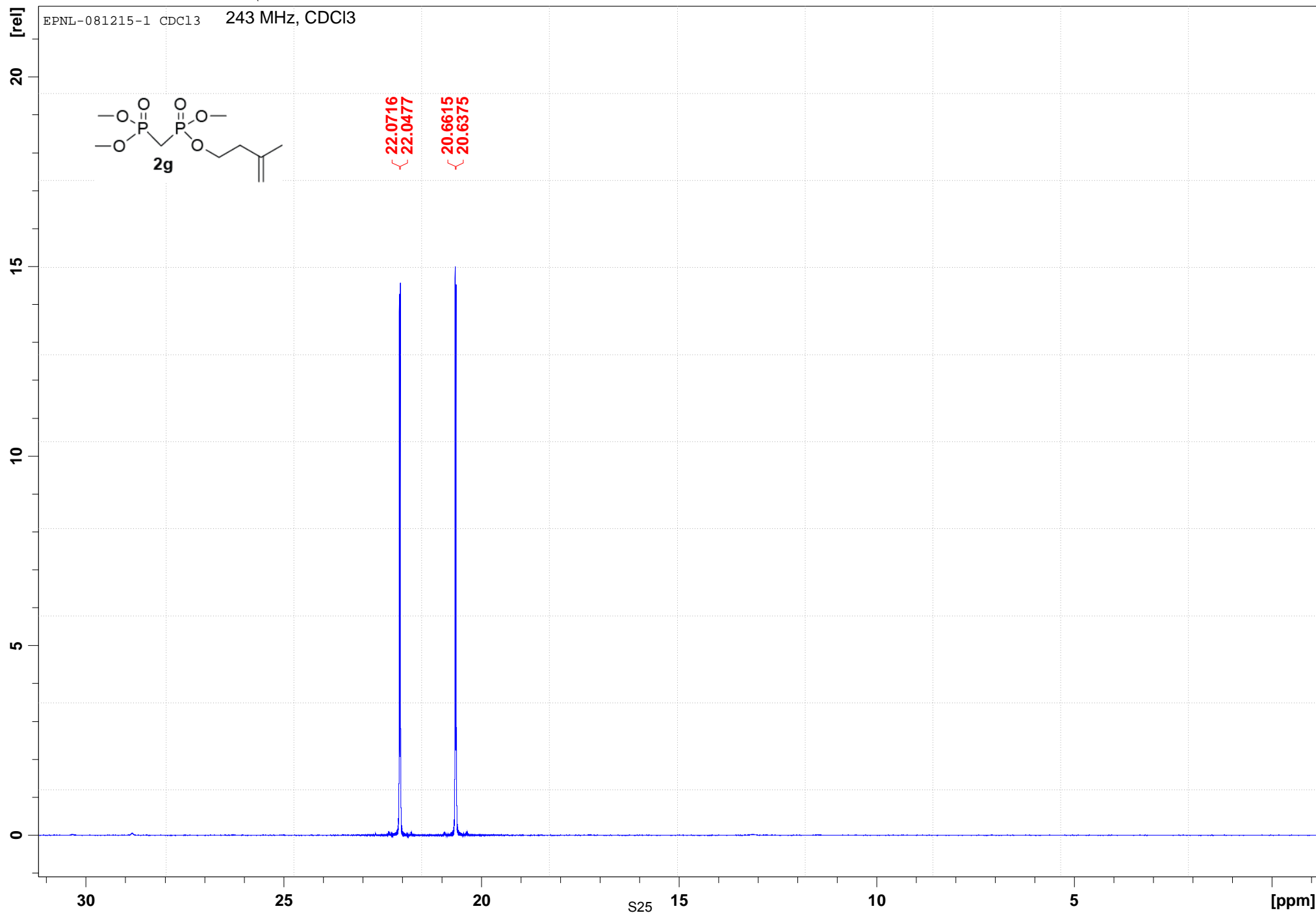
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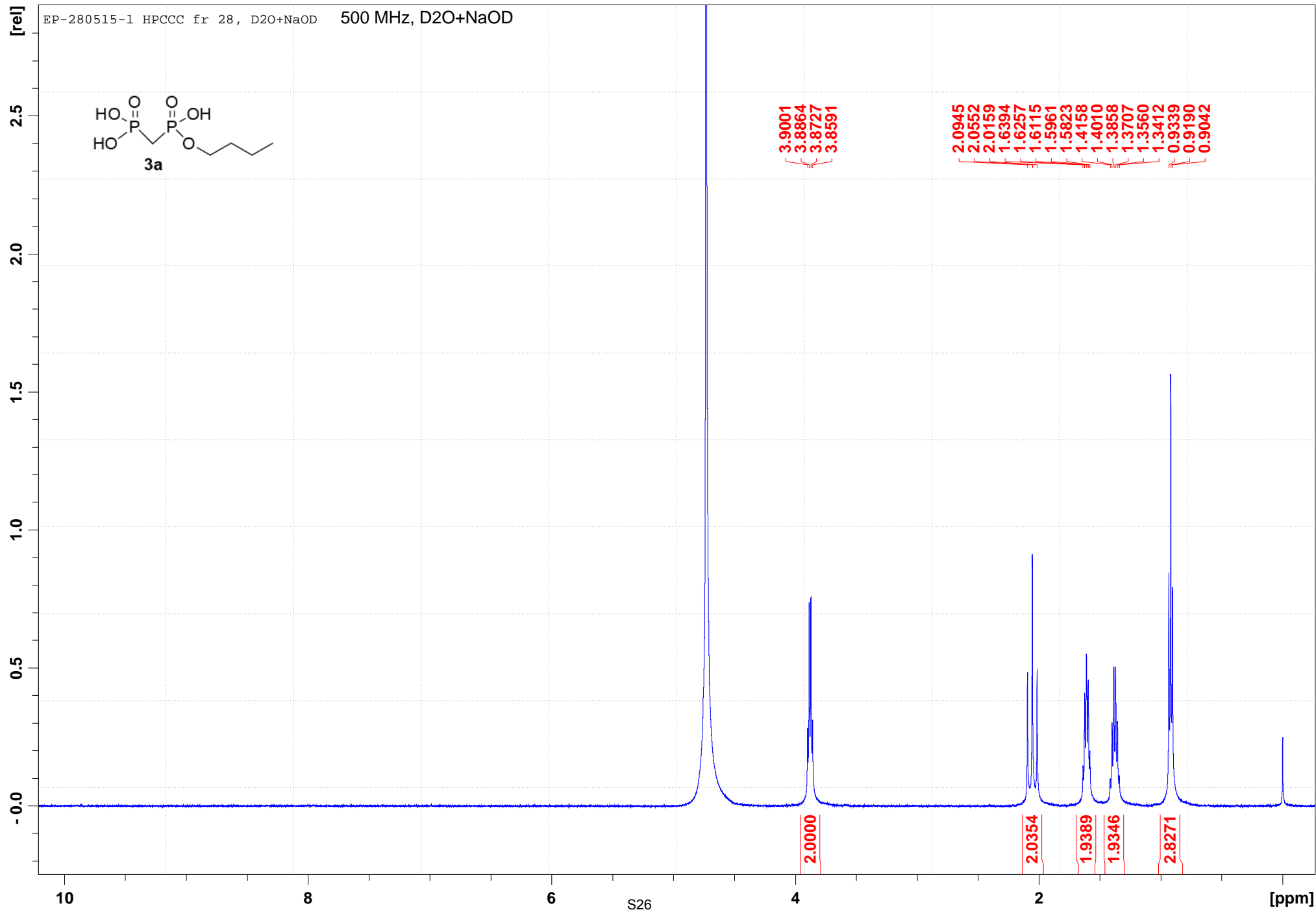
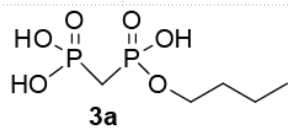




EPNL-081215-1 11 1 "E:\NMR 2015"

EPNL-081215-1 CDC13 243 MHz, CDCl3





10

8

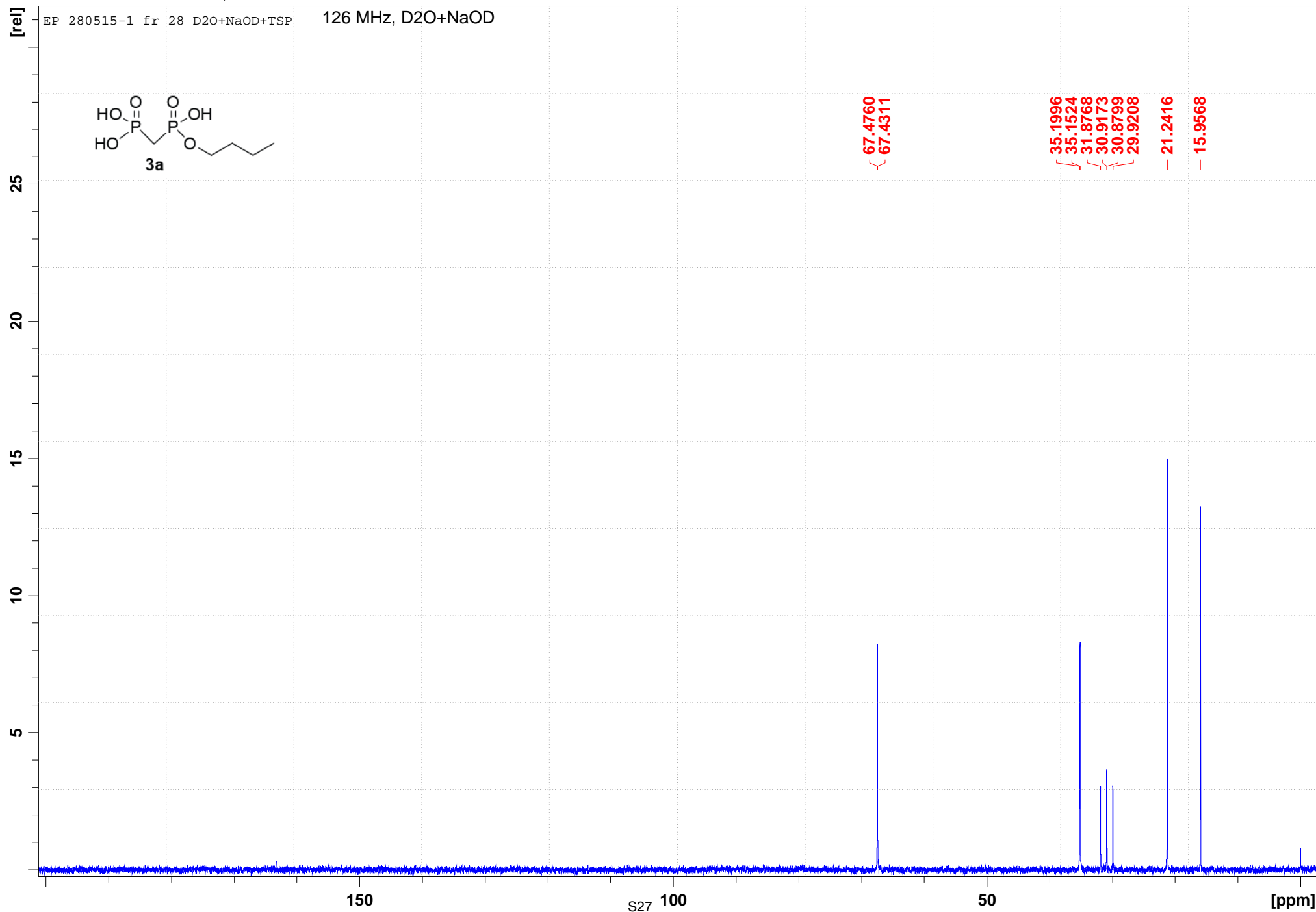
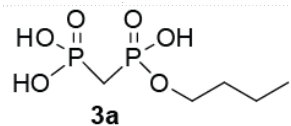
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S26

4

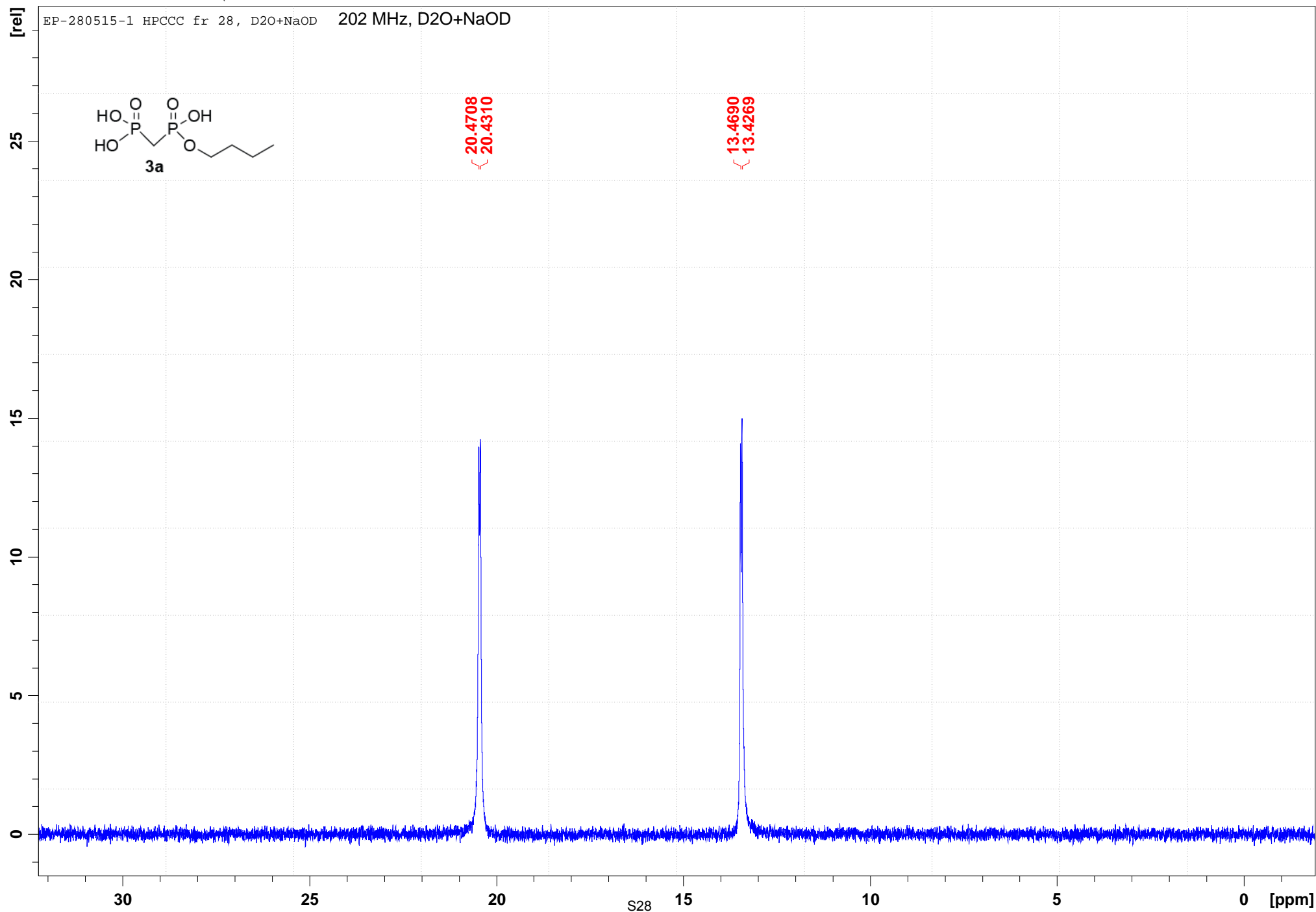
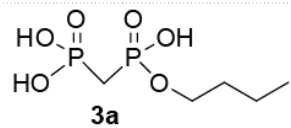
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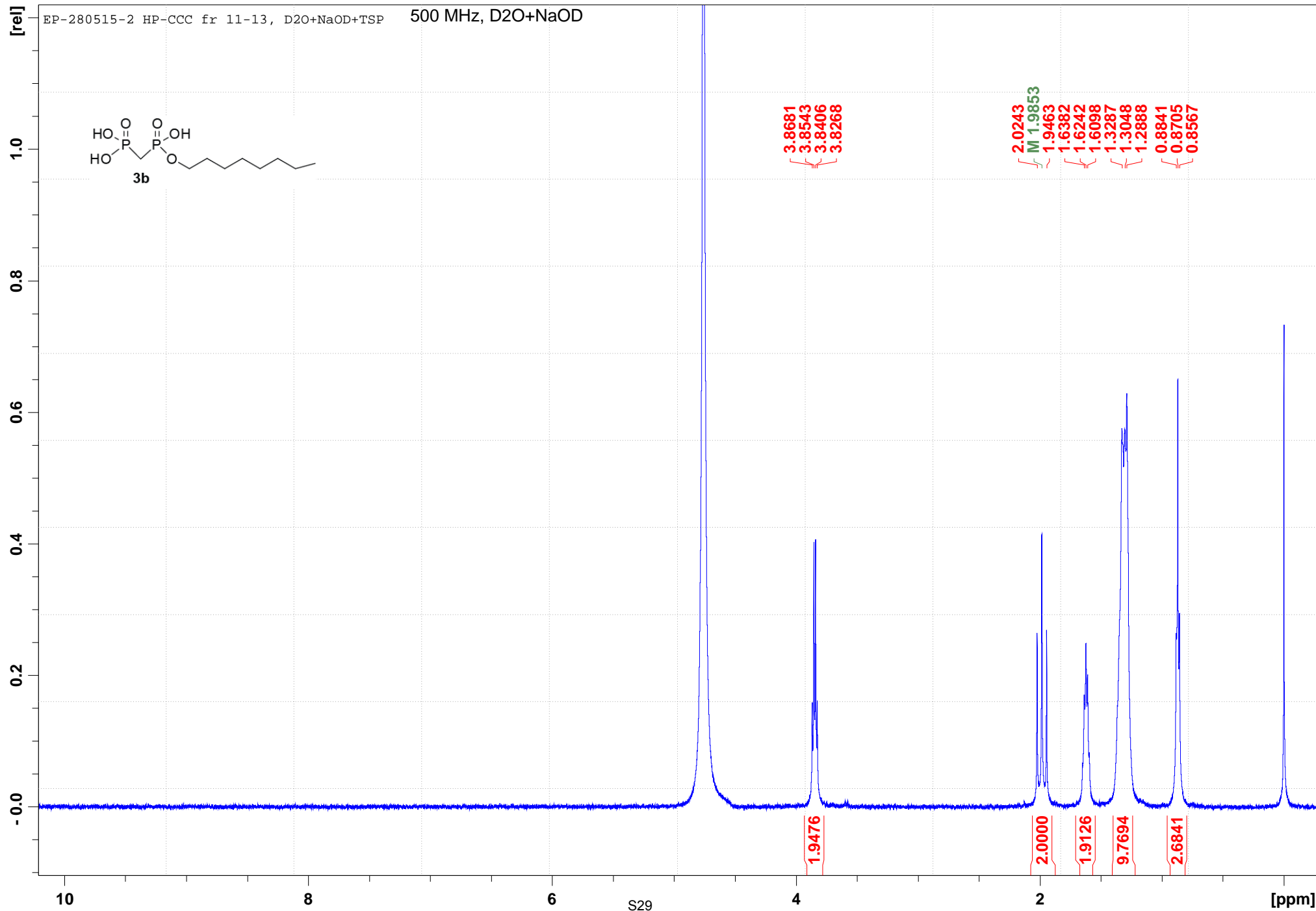
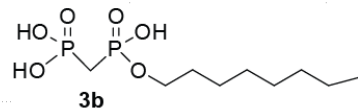
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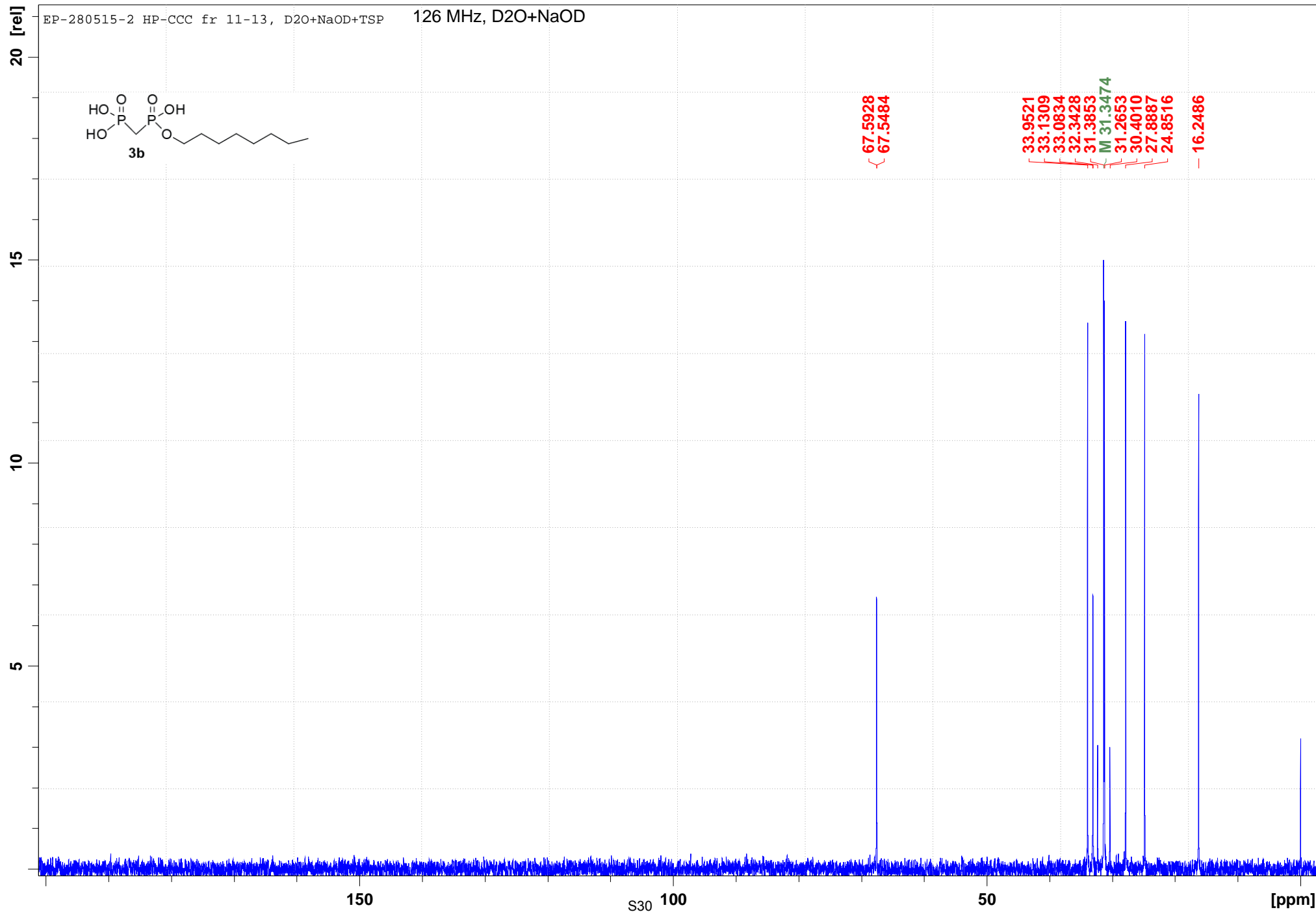
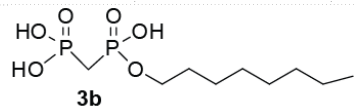


150528-1 112 1 "E:\NMR 2015"

EP-280515-1 HPLCC fr 28, D2O+NaOD 202 MHz, D2O+NaOD

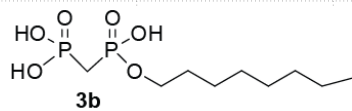






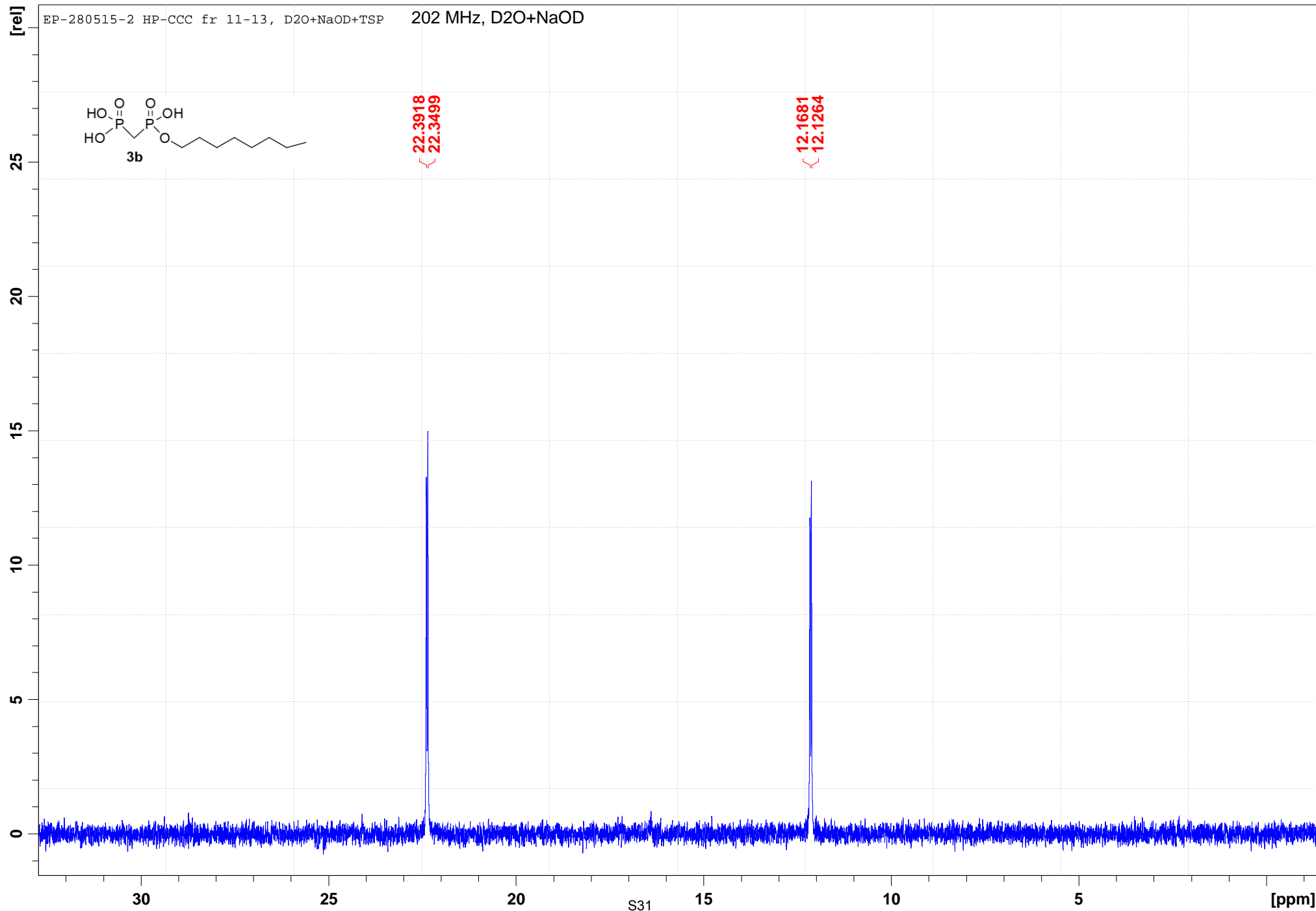
150528-2 92 1 "E:\NMR 2015"

EP-280515-2 HP-CCC fr 11-13, D2O+NaOD+TSP 202 MHz, D2O+NaOD



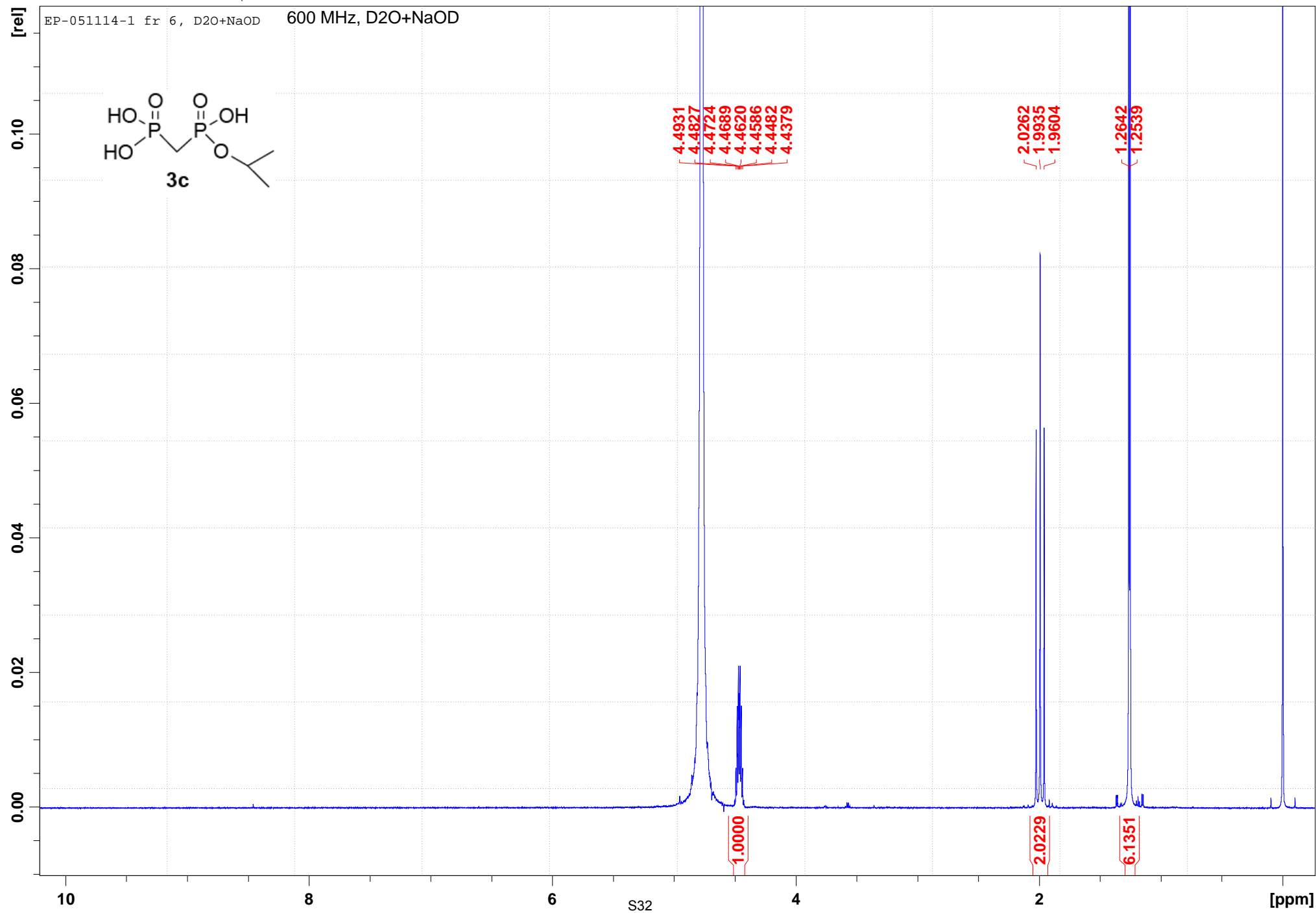
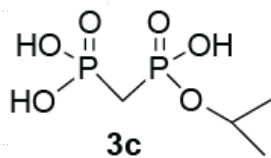
22.3918
22.3499

12.1681
12.1264



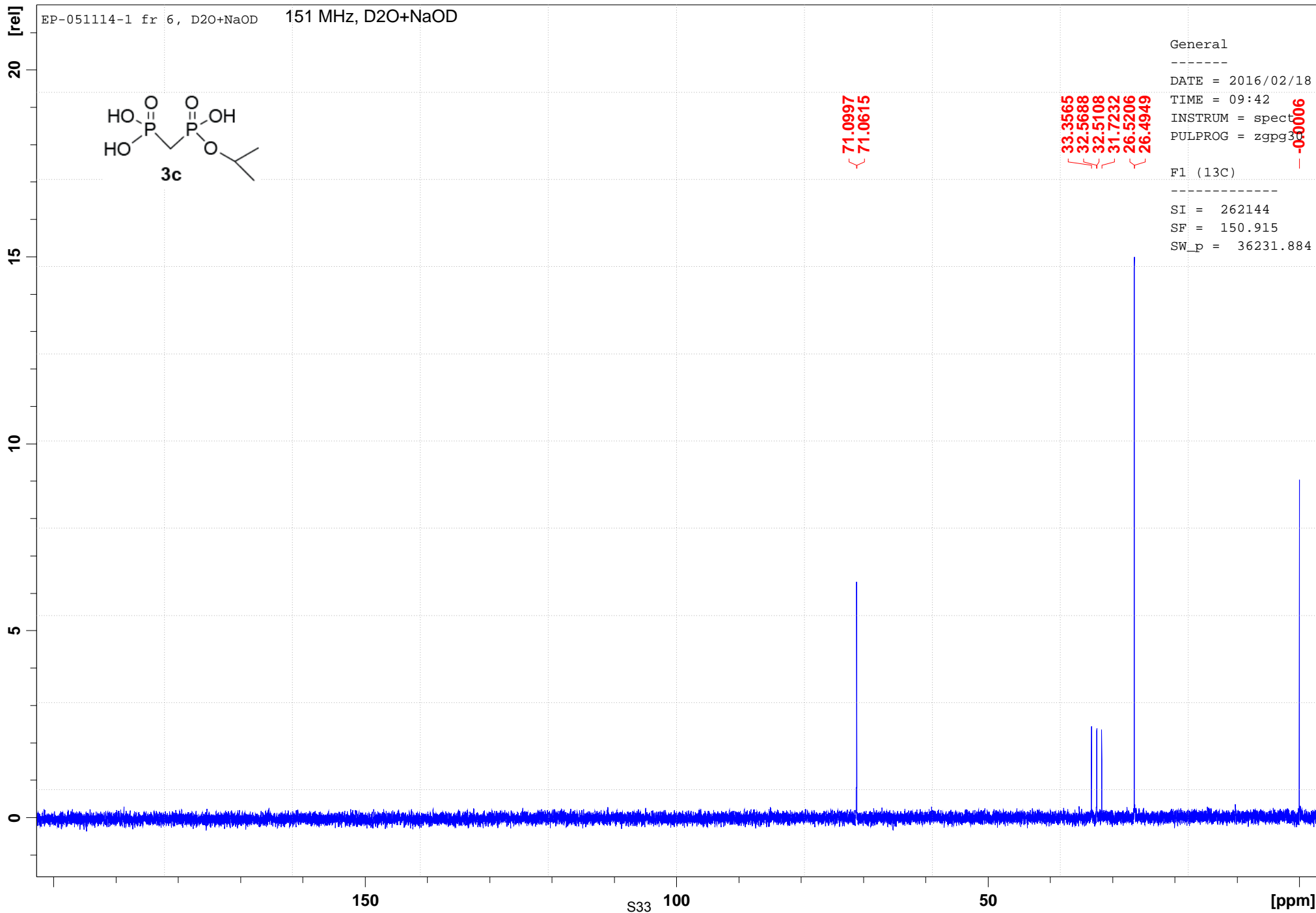
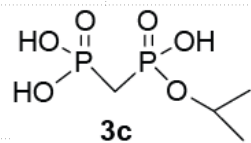
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EP-051114-1 fr 6, D2O+NaOD 600 MHz, D2O+NaOD



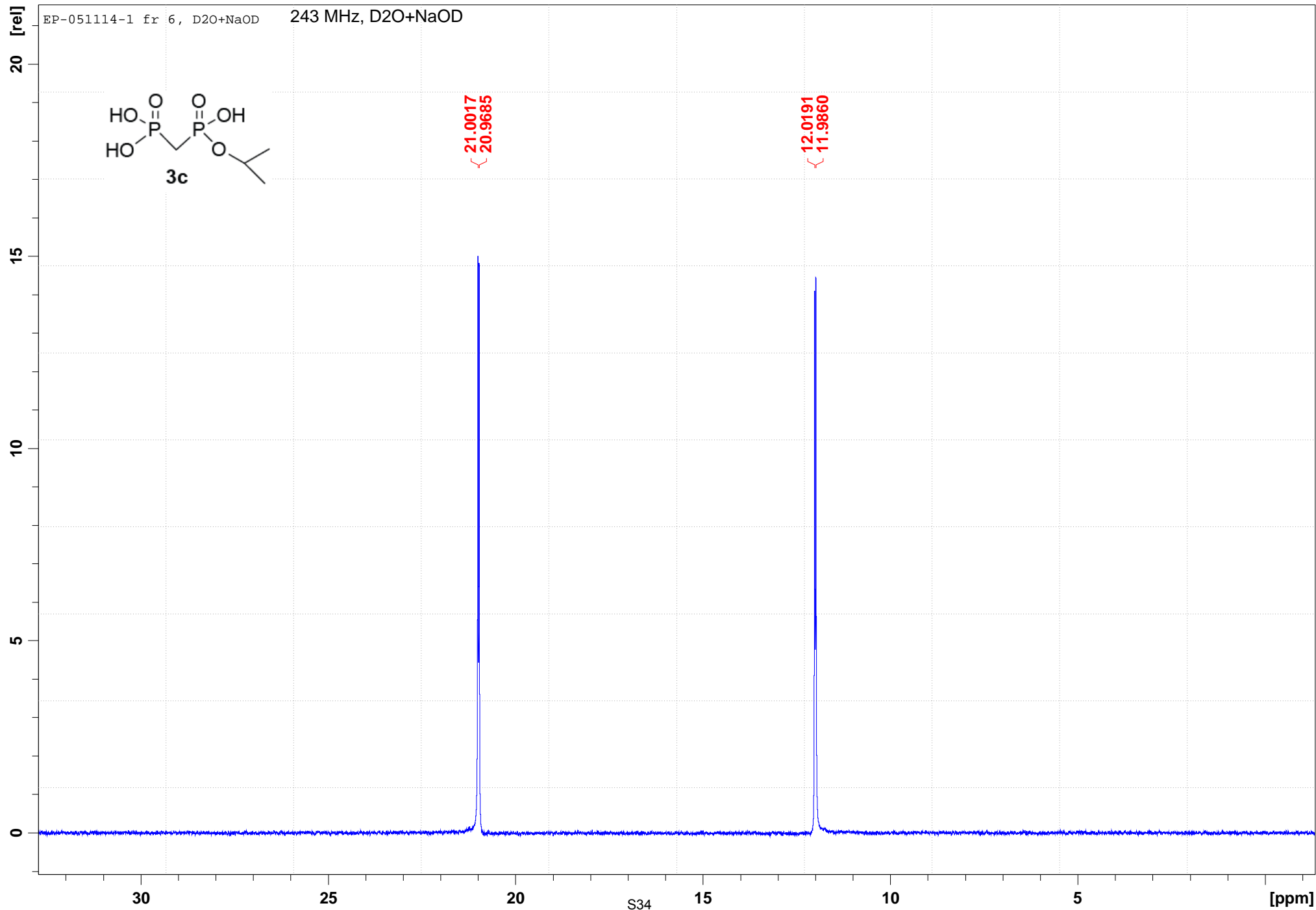
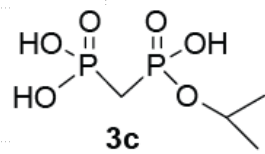
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EP-051114-1 fr 6, D2O+NaOD 151 MHz, D2O+NaOD



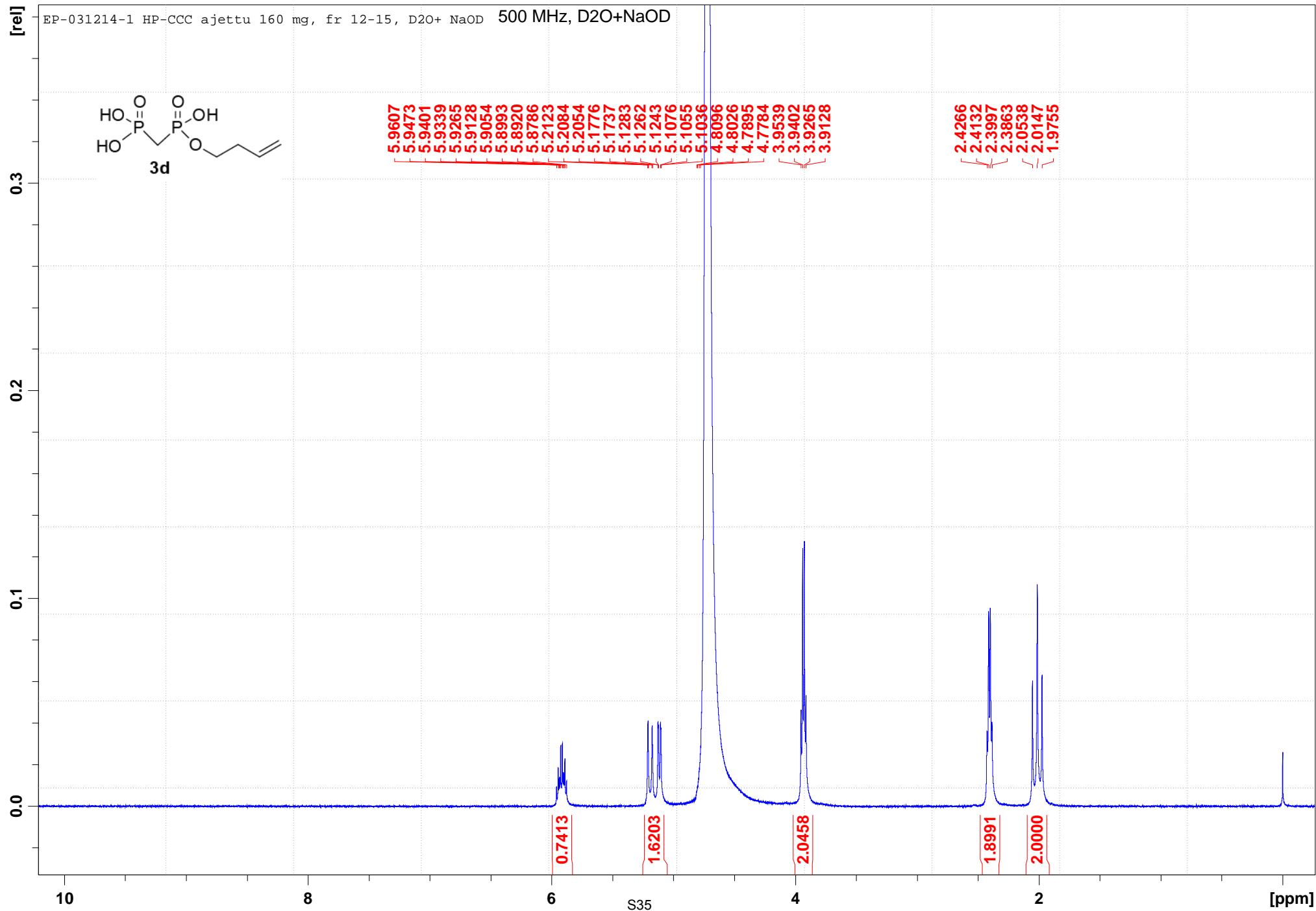
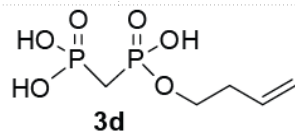
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EP-051114-1 fr 6, D2O+NaOD 243 MHz, D2O+NaOD



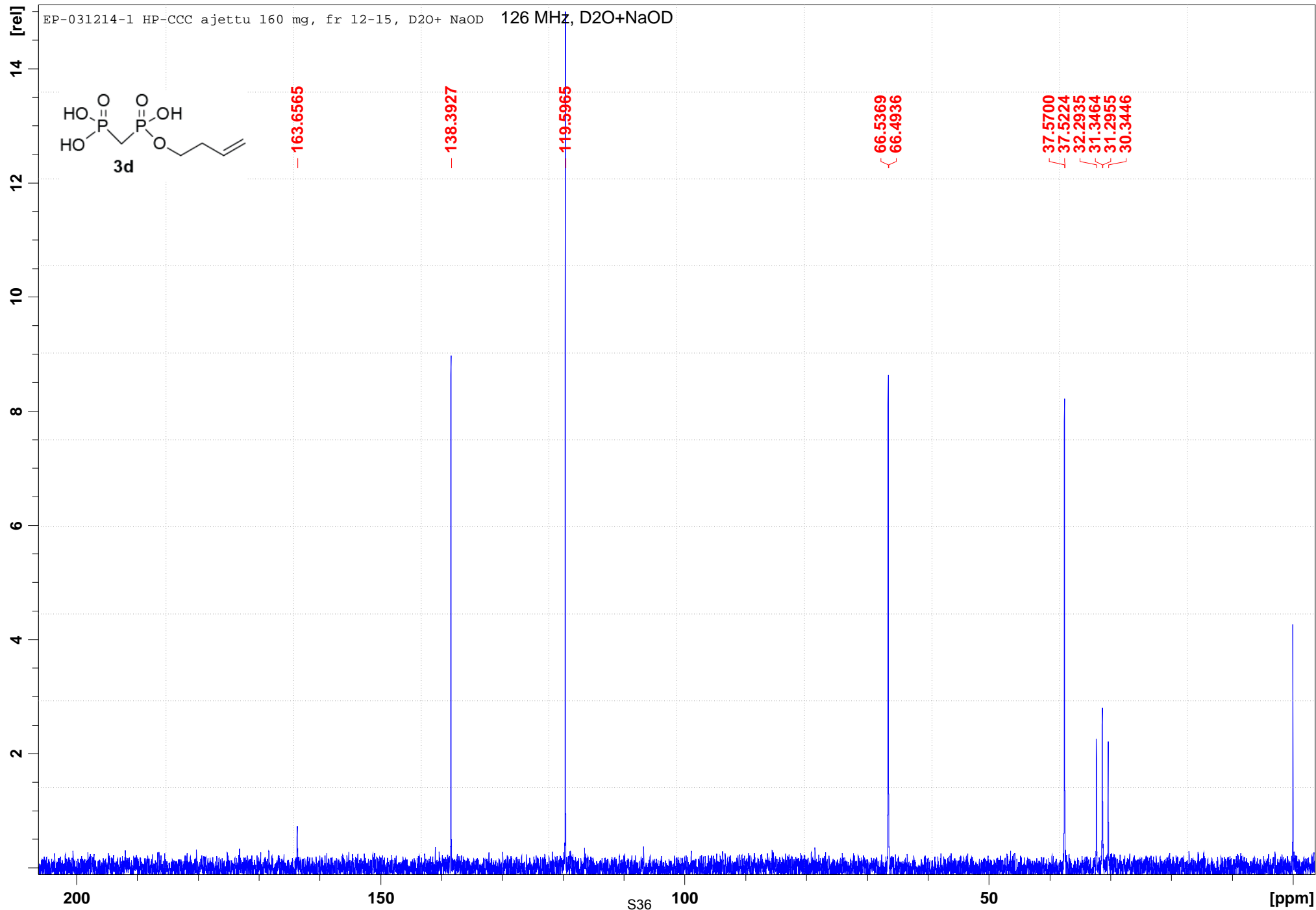
141027-1 31 1 "E:\NMR 2015"

EP-031214-1 HP-CCC ajettu 160 mg, fr 12-15, D2O+ NaOD 500 MHz, D2O+NaOD



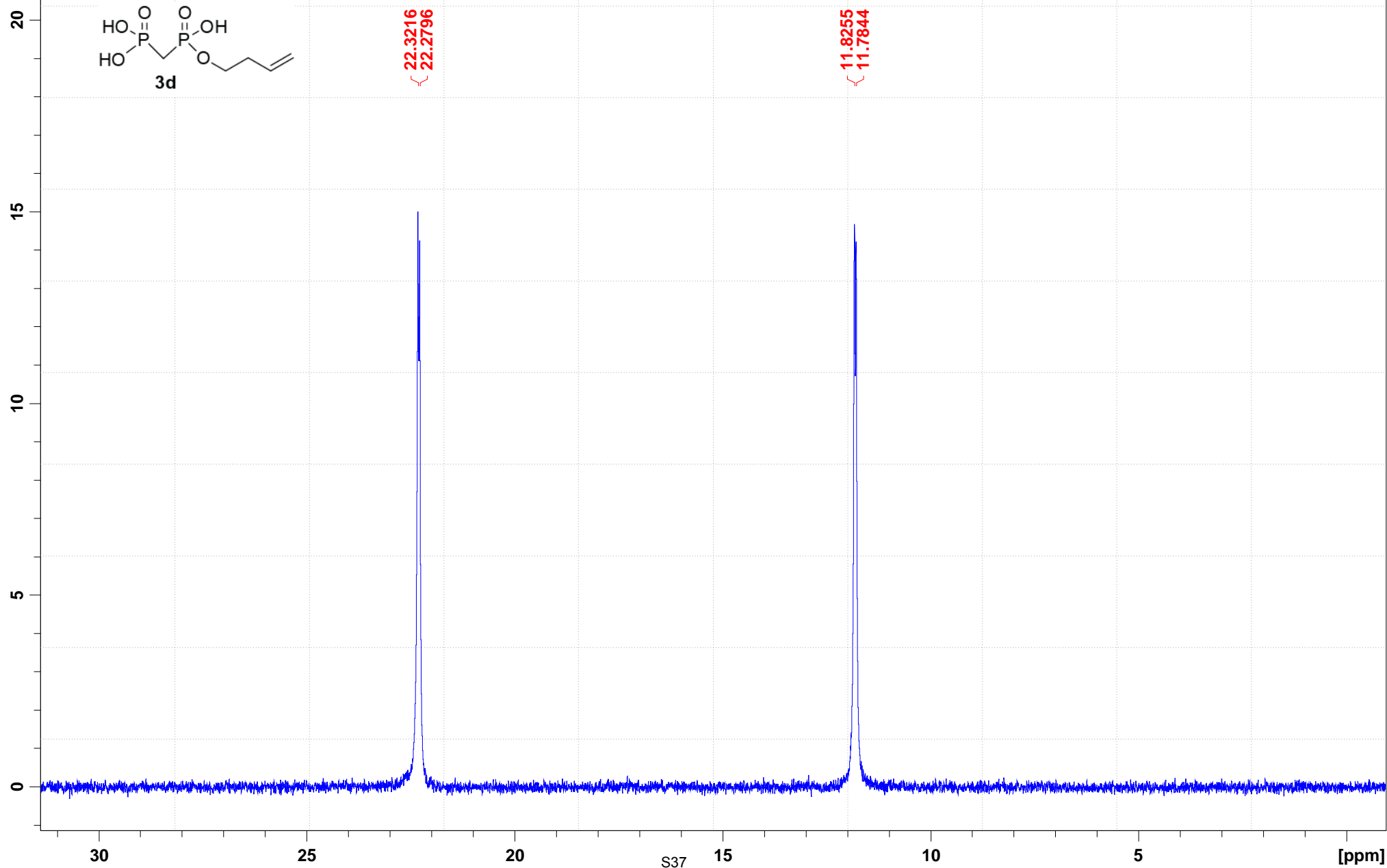
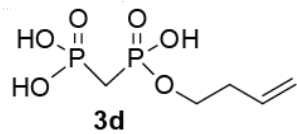
141027-1 36 1 "E:\NMR 2015"

EP-031214-1 HP-CCC ajettu 160 mg, fr 12-15, D2O+ NaOD 126 MHz, D2O+NaOD



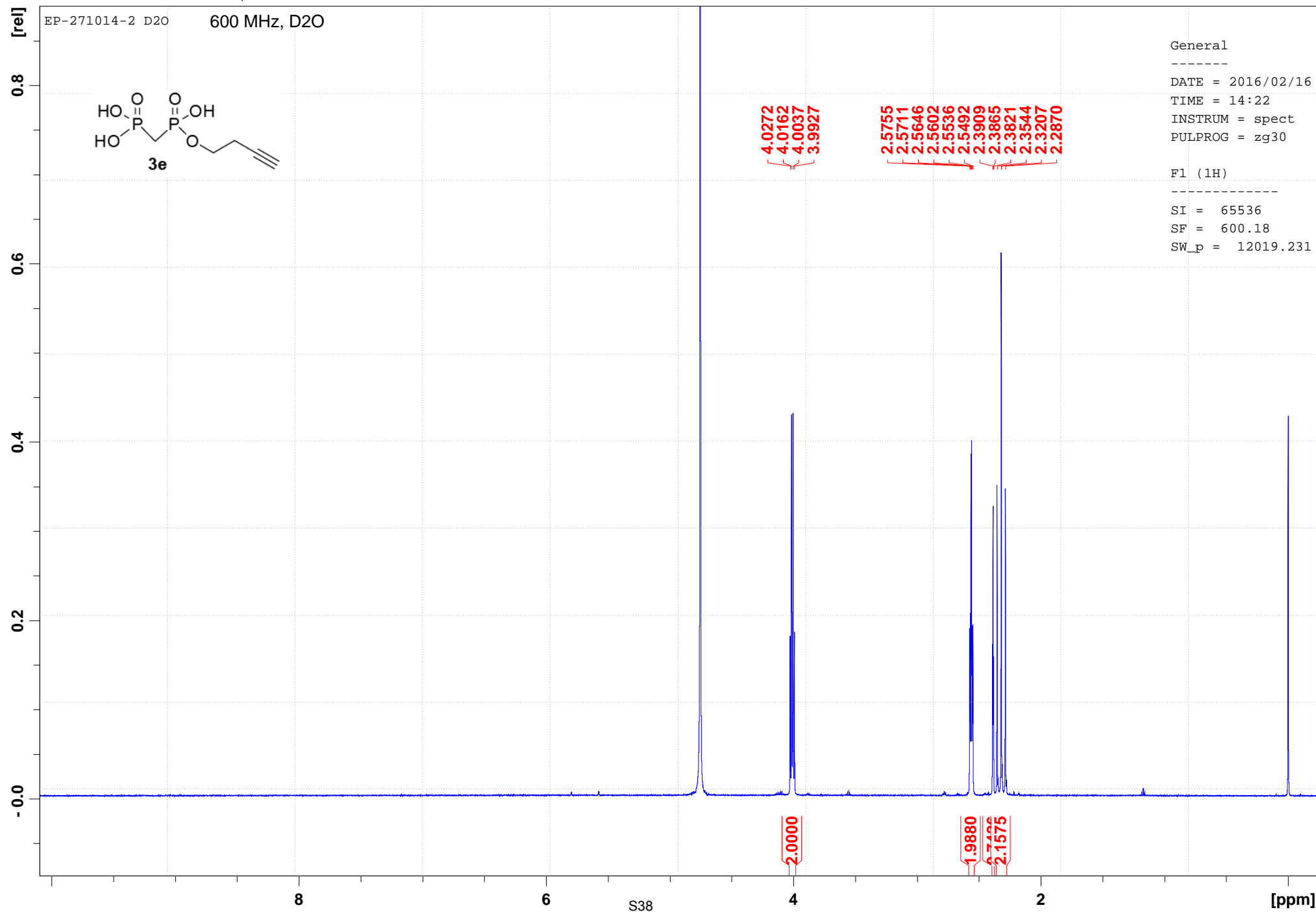
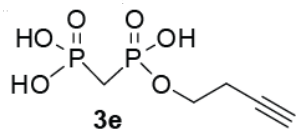
141203-1 122 1 "E:\NMR 2015"

EP-031214-1 HP-CCC ajettu 160 mg, fr 12-15, D2O+ NaOD 202 MHz, D2O+NaOD



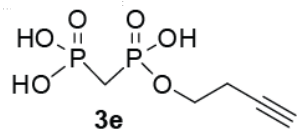
EP-271014-2 20 1 "E:\NMR 2015"

EP-271014-2 D2O 600 MHz, D2O



EP-271014-2 80 1 "E:\NMR 2015"

EP-271014-2 D2O 151 MHz, D2O



General

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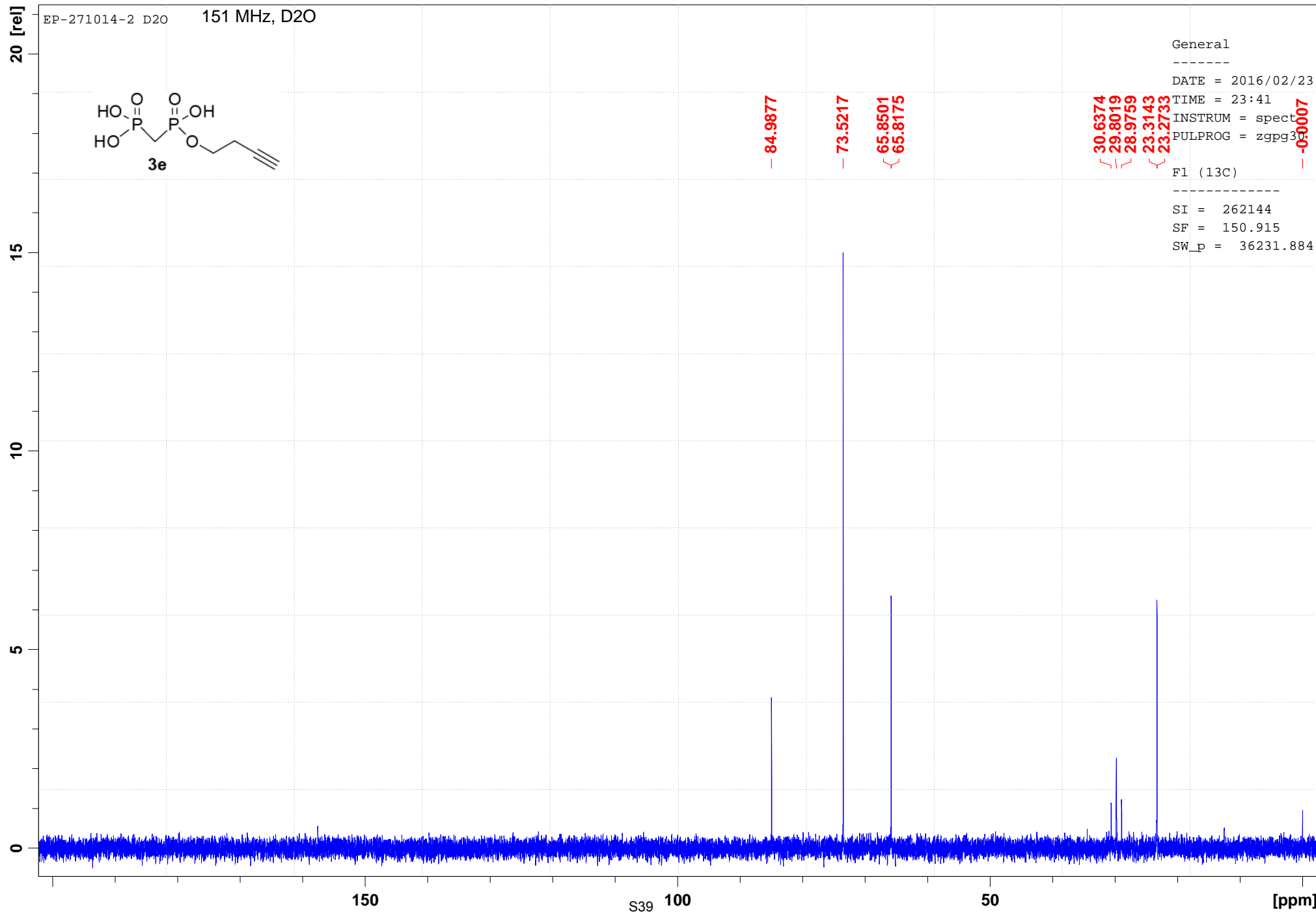
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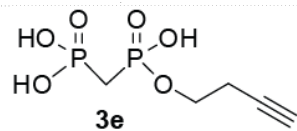
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EP-271014-2 11 1 "E:\NMR 2015"

EP-271014-2 D2O+NaOD 243 MHz, D2O+NaOD



General

DATE = 2016/02/16

TIME = 13:24

INSTRUM = spect

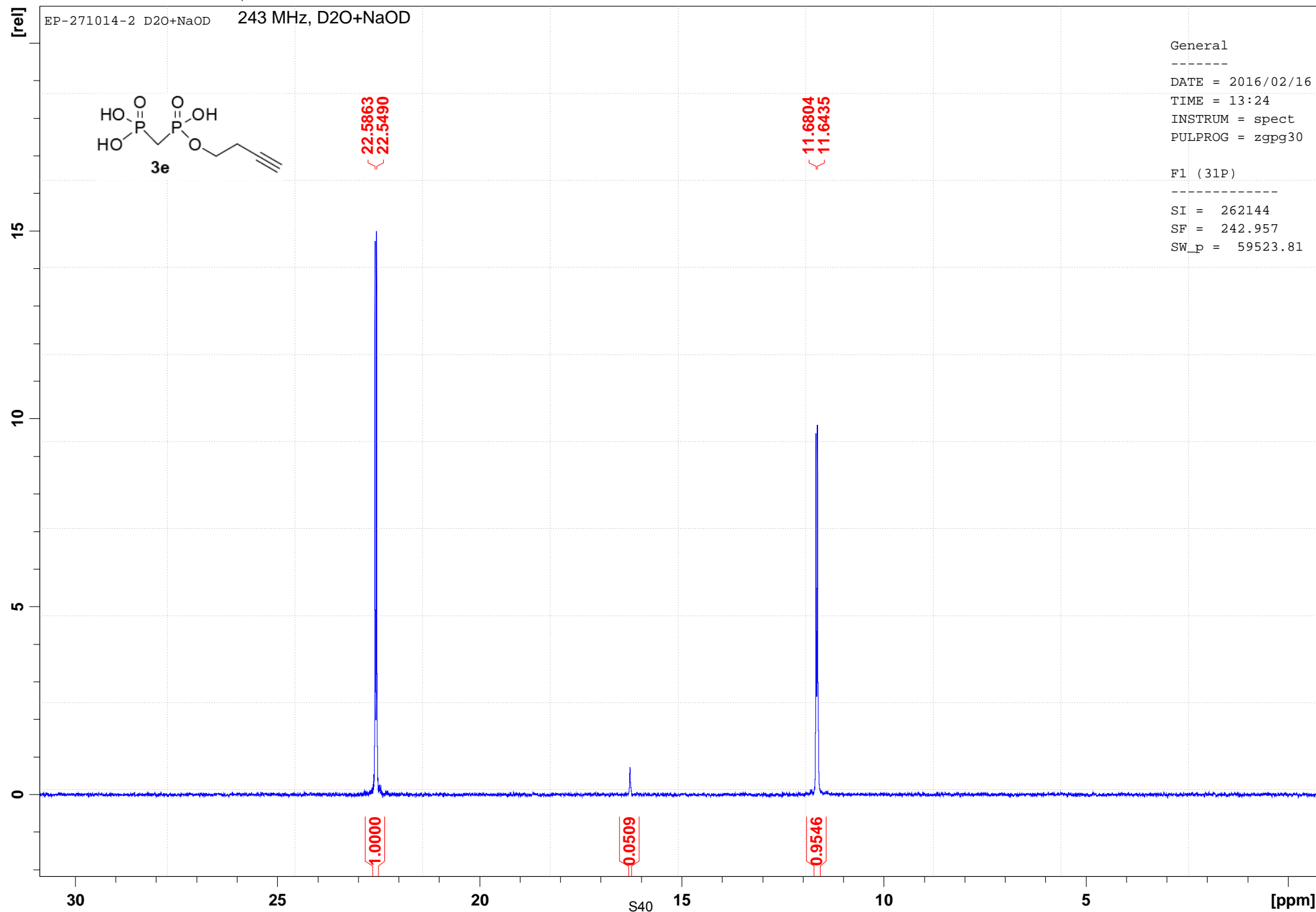
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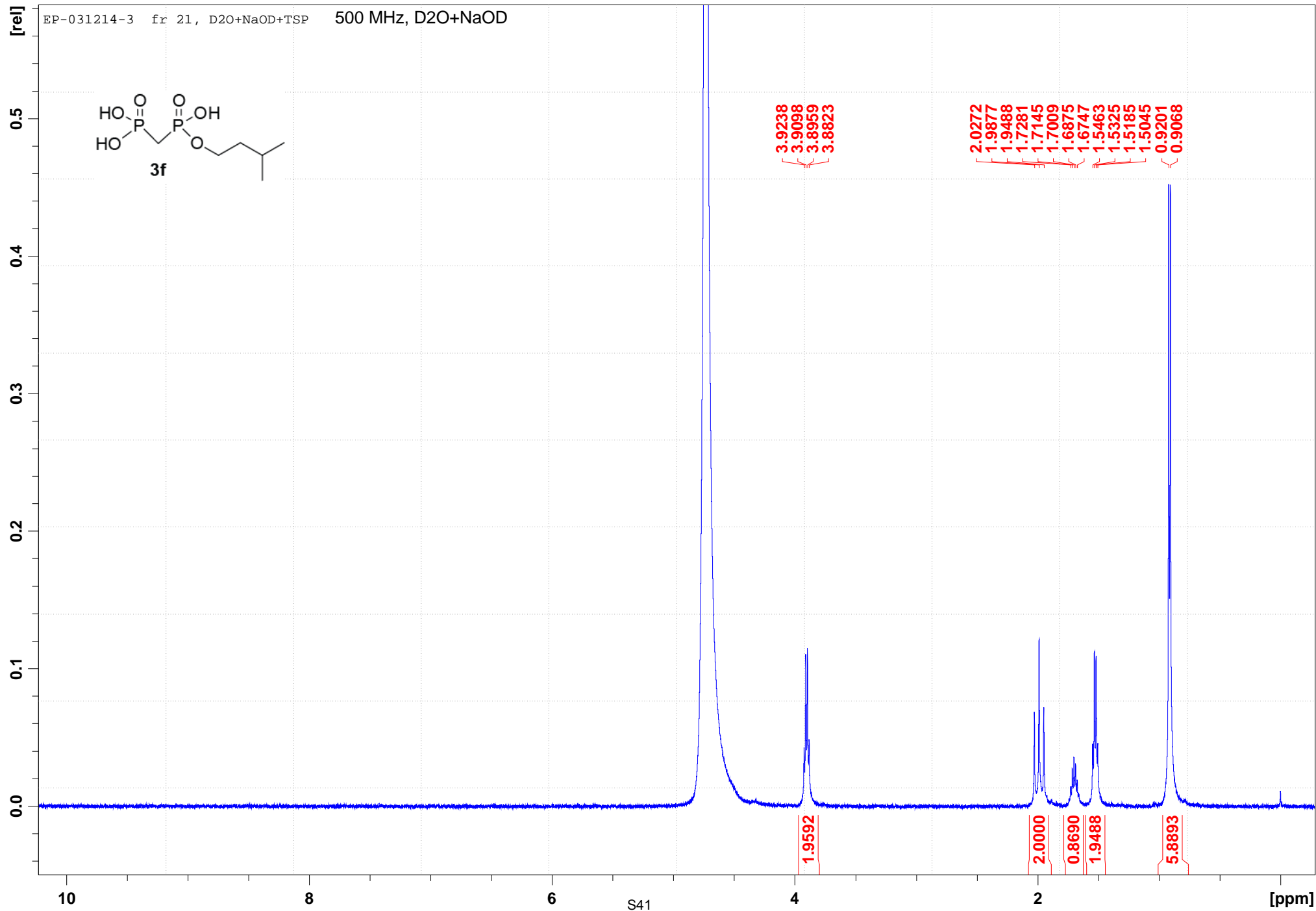
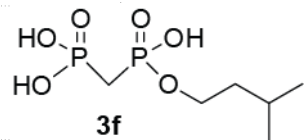
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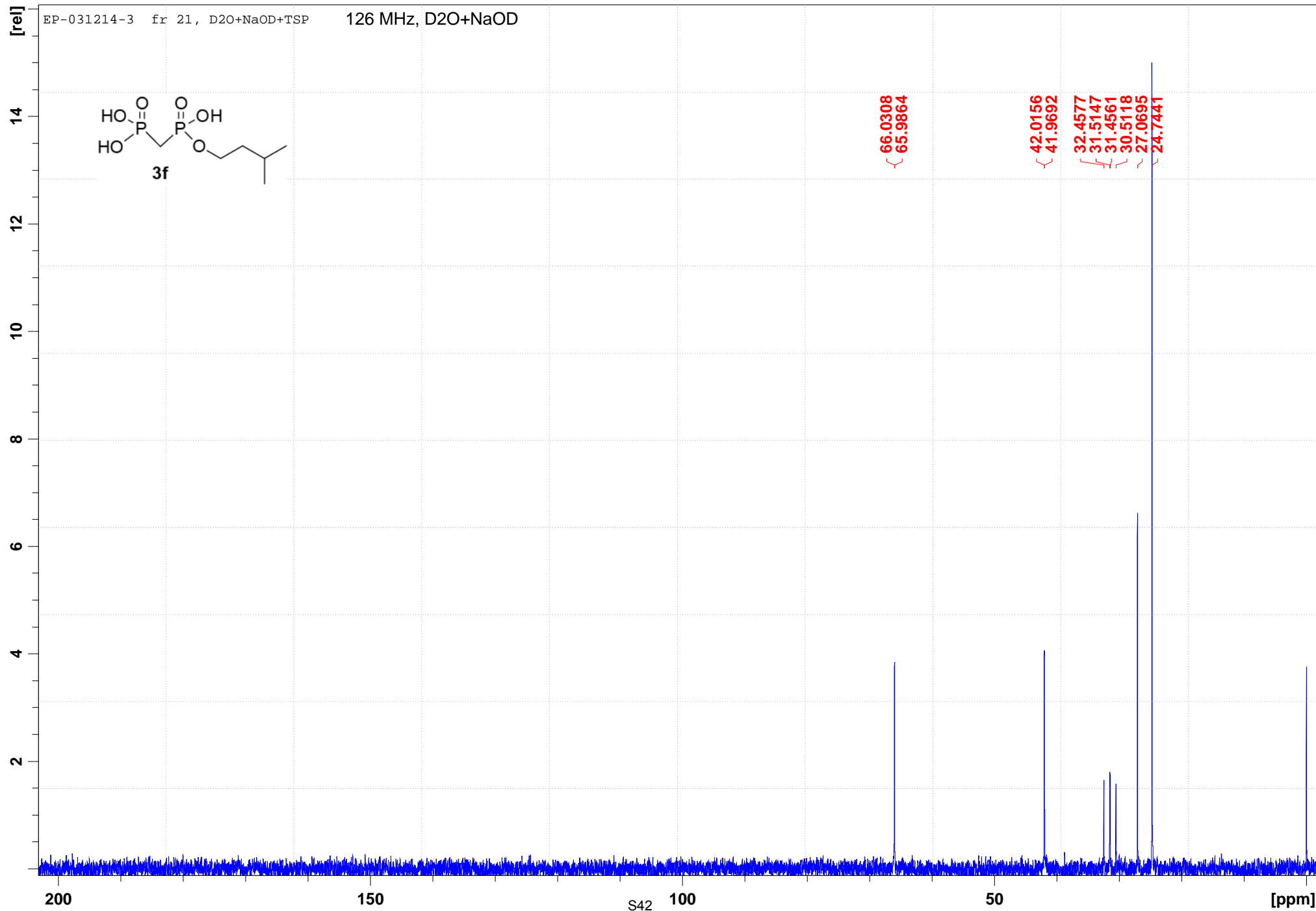




141203-3 76 1 "E:\NMR 2015"

EP-031214-3 fr 21, D2O+NaOD+TSP

126 MHz, D2O+NaOD



200

150

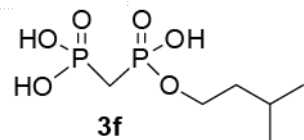
S42 100

50

[ppm]

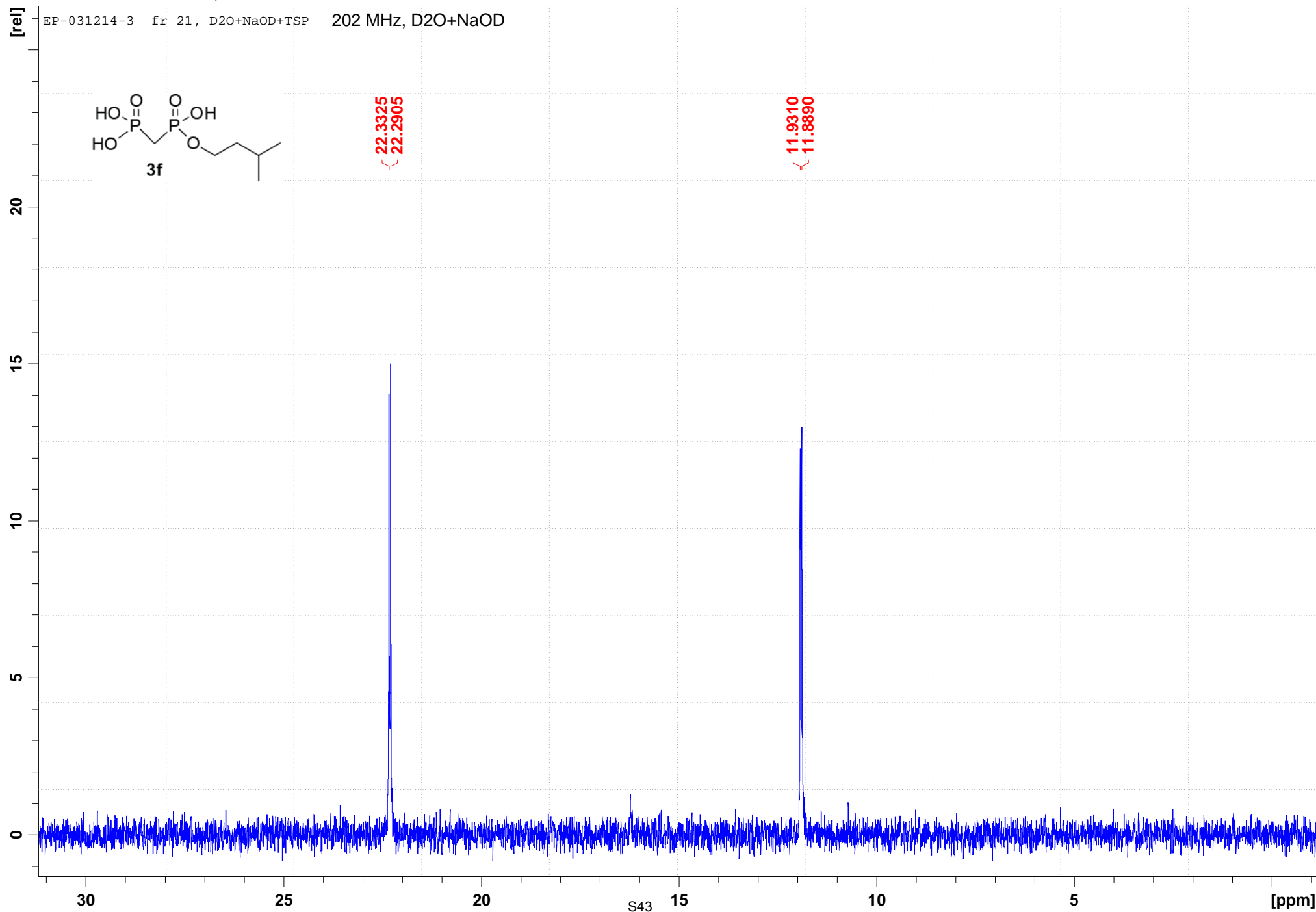
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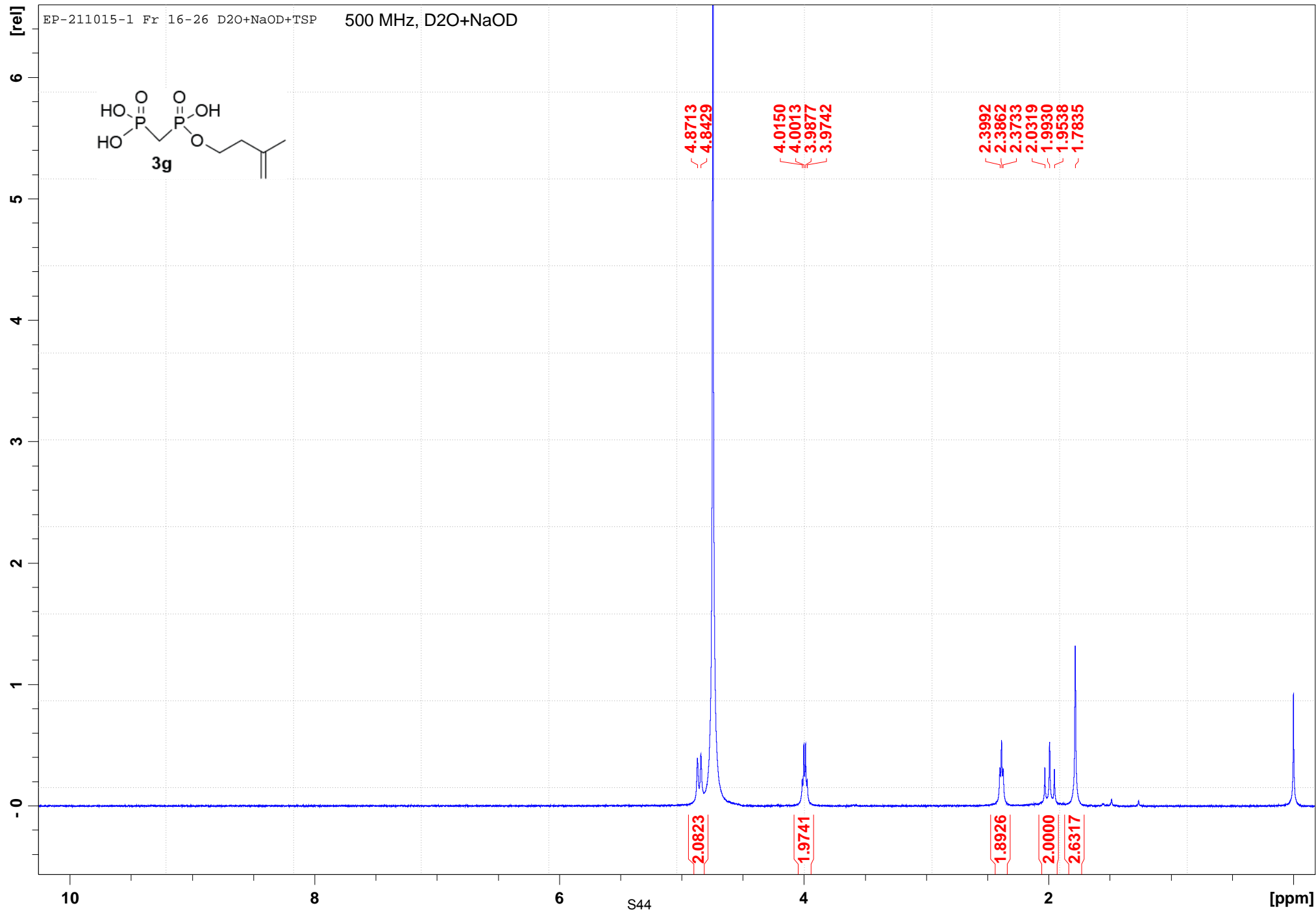
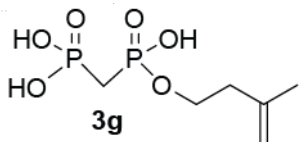
EP-031214-3 fr 21, D2O+NaOD+TSP 202 MHz, D2O+NaOD



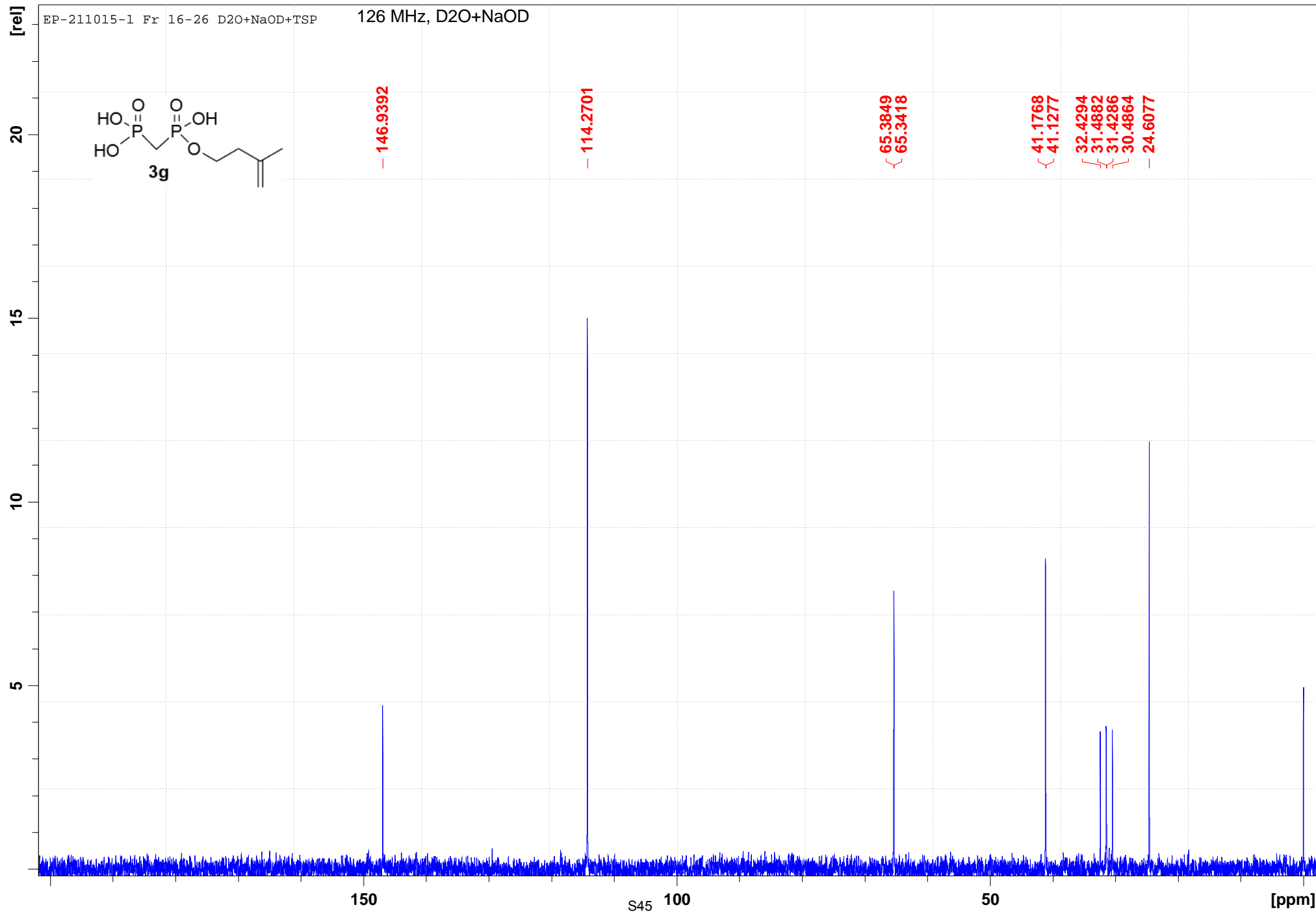
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22.2905

11.9310
11.8890



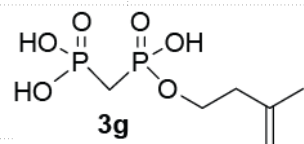


[ppm]



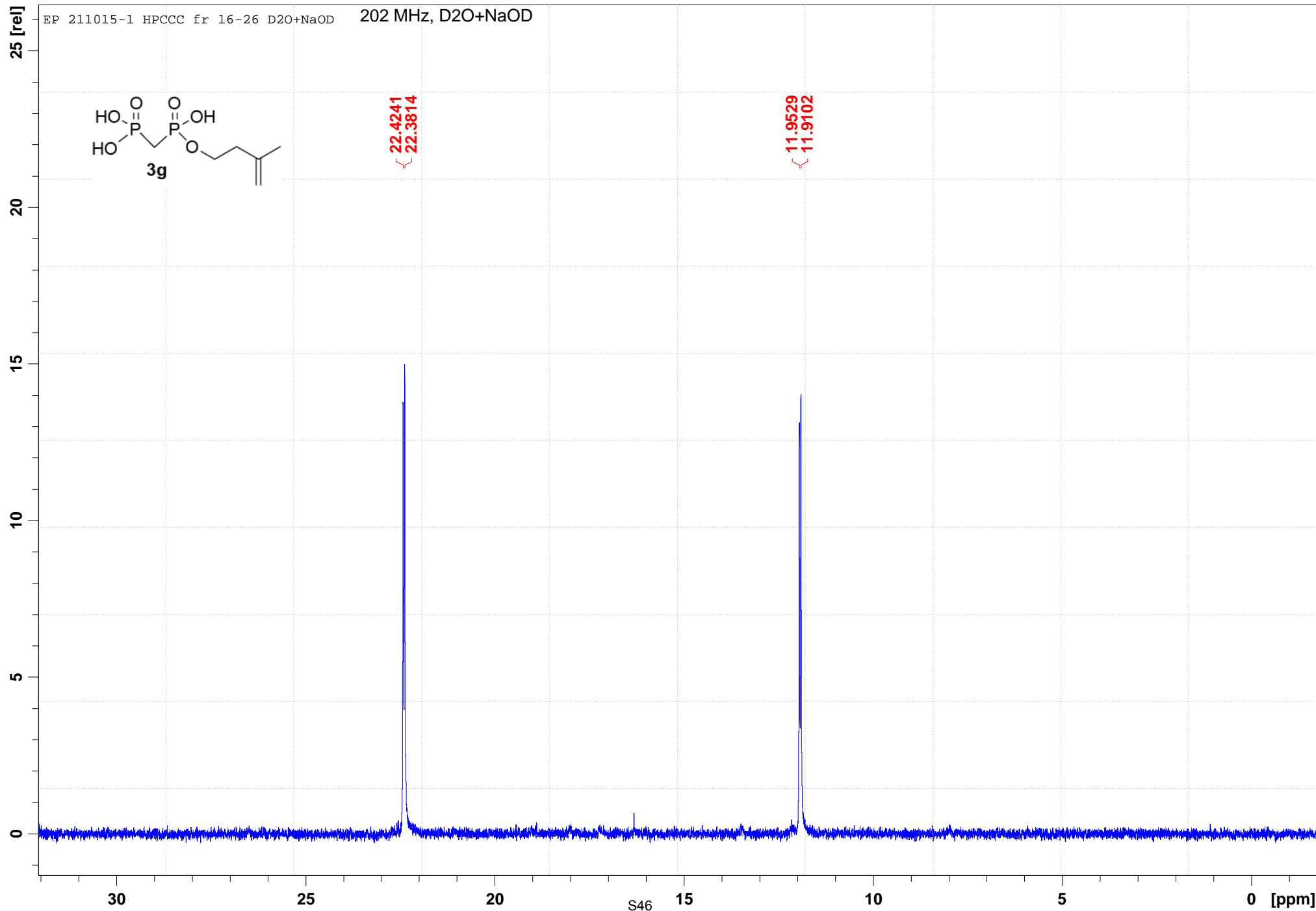
151021-1 72 1 "E:\NMR 2015"

EP 211015-1 HPLCC fr 16-26 D2O+NaOD 202 MHz, D2O+NaOD



22.4241
22.3814

11.9529
11.9102



HPCCC chromatogram from the purification of **3g**

Detection by UV at 200 (red), 220 (blue) and 254 (green) nm.

Fractions 1-8: **3g** and medronic acid

Fractions 9-23: **3g**

Fractions 24-26: **3g** and **3g** with one methyl ester remaining

