

Supplementary Materials

A Study on Bisphosphonic Derivatives Coming from the Pudovik Reaction of Dialkyl α -Oxophosphonates and $>\text{P}(\text{O})\text{H}$ Reagents: X-Ray Structure and Bioactivity

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1. Geometrical data for compounds 2d, 2e and 6 obtained from the X-ray measurements

SI Table S1. Selected bond lengths (Å) of compound **2d**, **2e** and **6**.

2d		2e		6	
P1 – O1	1.493(1)	P1 – O1	1.485(1)	P1 – O1	1.488(1)
P1 – C7	1.801(2)	P1 – C1	1.809(2)	P1 – C7	1.807(1)
P1 – C1	1.811(2)	P1 – C8	1.809(2)	P1 – C1	1.809(1)
P1 – C13	1.863(2)	P1 – C15	1.862(2)	P1 – C13	1.860(1)
P2 – O5	1.463(1)	C1 – C2	1.393(2)	P2 – O5	1.476(1)
P2 – O3	1.572(1)	C1 – C6	1.396(2)	P2 – O3	1.568(1)
P2 – O4	1.574(1)	O4A – C17A	1.425(5)	P2 – O4	1.570(1)
P2 – C13	1.831(2)	O4A – P2	1.524(2)	P2 – C13	1.841(1)
O4 – C16	1.438(2)	P2 – O3	1.466(1)	O3 – C15	1.457(1)
O2 – C13	1.424(2)	P2 – O5A	1.642(3)	O4 – C17	1.464(1)
C7 – C8	1.398(2)	P2 – C15	1.834(2)	C1 – C2	1.394(1)
C7 – C12	1.400(2)	O2 – C15	1.424(2)	C1 – C6	1.398(1)
C12 – C11	1.389(2)	C2 – C3	1.385(2)	O2 – C13	1.427(1)
C5 – C4	1.384(3)	O5A – C18A	1.415(7)	C8 – C9	1.395(2)
C5 – C6	1.391(2)	C4 – C3	1.394(3)	C2 – C3	1.390(2)
C8 – C9	1.390(2)	C4 – C7	1.512(2)	C17 – C18	1.490(2)
C11 – C10	1.386(3)	C5 – C6	1.391(2)	C9 – C10	1.385(2)
C10 – C9	1.384(3)	O6 – C20	1.176(4)	C15 – C16	1.495(2)
O3 – C15	1.440(2)	C15 – C16	1.528(2)	C10 – C11	1.389(2)
C1 – C6	1.390(2)	C8 – C13	1.389(2)	C13 – C14	1.536(1)
C1 – C2	1.403(2)	C8 – C9	1.397(2)	C7 – C12	1.396(2)
C14 – C13	1.535(2)	C19 – C20	1.482(3)	C7 – C8	1.397(2)
C3 – C4	1.385(3)	C9 – C10	1.390(2)	C6 – C5	1.392(2)
C3 – C2	1.385(2)	C10 – C11	1.391(2)	C5 – C4	1.392(2)
		C11 – C12	1.391(2)	C4 – C3	1.384(2)
		C11 – C14	1.511(2)	C12 – C11	1.387(2)
		C12 – C13	1.388(2)		
		C4 – C5	1.389(3)		

SI Table S2. Selected bond angles (°) of compound **2d**, **2e** and **6**.

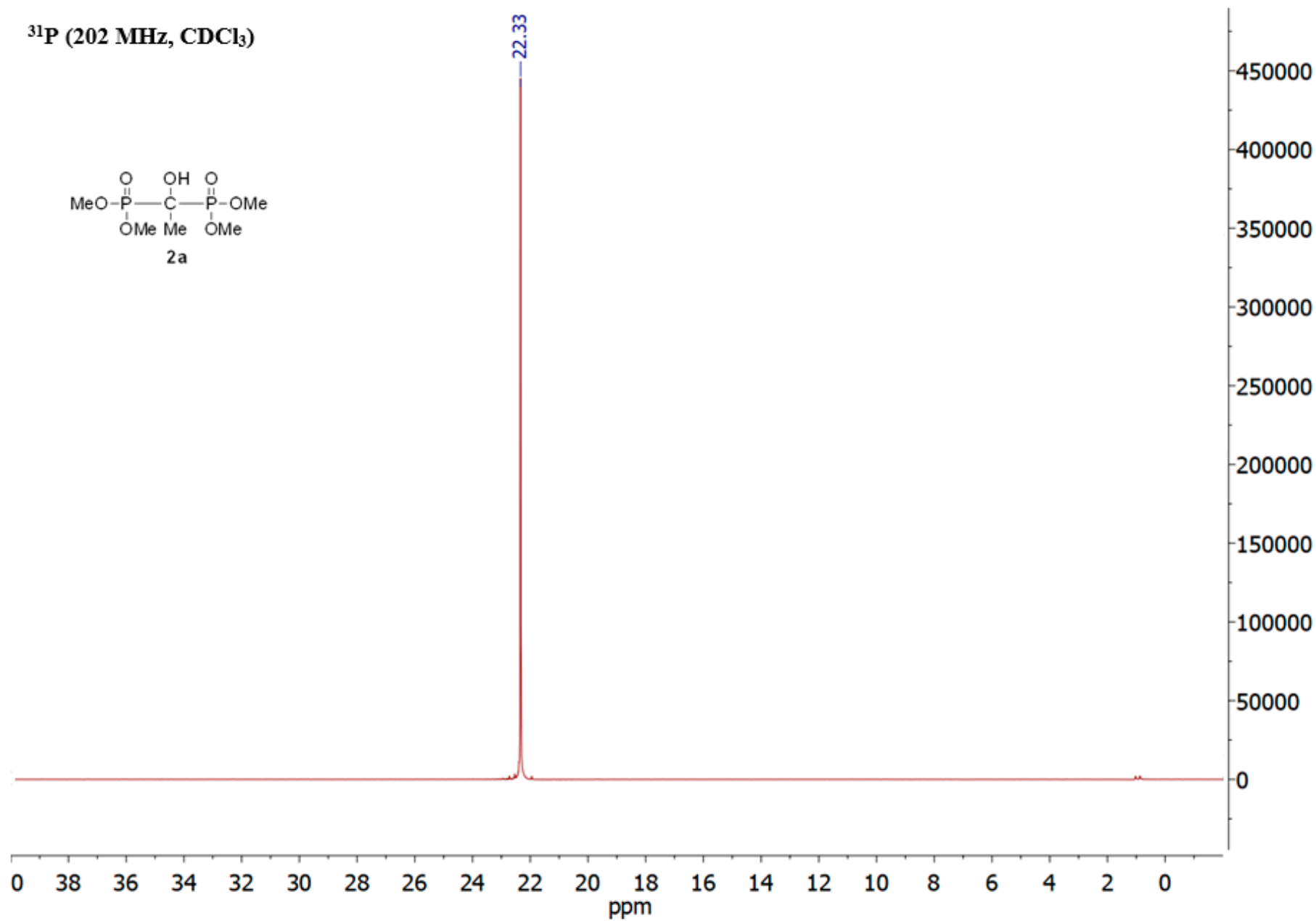
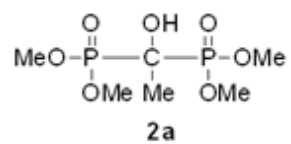
2d		2e (i = 1-x, y, 0.5-z; acetone molecule)		6	
O1 – P1 – C7	112.0(1)	O1 – P1 – C1	112.2(1)	O1 – P1 – C7	112.1(1)
O1 – P1 – C1	111.9(1)	O1 – P1 – C8	111.3(1)	O1 – P1 – C1	112.3(1)
C7 – P1 – C1	107.1(1)	C1 – P1 – C8	107.4(1)	C7 – P1 – C1	105.3(1)
O1 – P1 – C13	111.4(1)	O1 – P1 – C15	111.7(1)	O1 – P1 – C13	111.2(1)
C7 – P1 – C13	109.5(1)	C1 – P1 – C15	108.2(1)	C7 – P1 – C13	104.6(1)
C1 – P1 – C13	104.6(1)	C8 – P1 – C15	105.8(1)	C1 – P1 – C13	111.0(1)
O5 – P2 – O3	116.5(1)	C2 – C1 – C6	118.7(2)	O5 – P2 – O3	115.9(1)
O5 – P2 – O4	114.1(1)	C2 – C1 – P1	124.3(1)	O5 – P2 – O4	109.2(1)
O3 – P2 – O4	102.3(1)	C6 – C1 – P1	117.0(1)	O3 – P2 – O4	107.7(1)
O5 – P2 – C13	115.4(1)	C17A – O4A – P2	121.8(4)	O5 – P2 – C13	111.1(1)
O3 – P2 – C13	101.7(1)	O3 – P2 – O4A	118.3(1)	O3 – P2 – C13	103.1(1)
O4 – P2 – C13	105.1(1)	O3 – P2 – O5A	111.3(1)	O4 – P2 – C13	109.6(1)
C16 – O4 – P2	122.4(1)	O4A – P2 – O5A	101.4(2)	C15 – O3 – P2	123.0(1)
C8 – C7 – C12	119.6(2)	O3 – P2 – C15	113.2(1)	C17 – O4 – P2	125.0(1)
C8 – C7 – P1	116.4(1)	O4A – P2 – C15	109.7(1)	C2 – C1 – C6	119.3(1)
C12 – C7 – P1	123.9(1)	O5A – P2 – C15	100.8(1)	C2 – C1 – P1	115.3(1)
C15 – O3 – P2	118.6(1)	C3 – C2 – C1	120.5(2)	C6 – C1 – P1	125.4(1)
C6 – C1 – C2	119.1(2)	C18A – O5A – P2	119.5(4)	O2 – C13 – C14	112.4(1)
C6 – C1 – P1	123.7(1)	C5 – C4 – C3	118.2(2)	O2 – C13 – P2	106.7(1)
O2 – C13 – C14	111.7(1)	C5 – C4 – C7	121.3(2)	C4 – C3 – C2	120.1(1)
O2 – C13 – P2	103.7(1)	C3 – C4 – C7	120.5(2)	O4 – C17 – C18	108.0(1)
C14 – C13 – P2	110.3(1)	C2 – C3 – C4	121.2(2)	C10 – C9 – C8	120.1(1)
O2 – C13 – P1	109.7(1)	C4 – C5 – C6	121.1(2)	O3 – C15 – C16	109.3(1)
C14 – C13 – P1	108.8(1)	C5 – C6 – C1	120.3(2)	C9 – C10 – C11	120.2(1)
P2 – C13 – P1	112.6(1)	O2 – C15 – C16	112.1(1)	C12 – C11 – C10	120.0(1)
C9 – C8 – C7	119.9(2)	O2 – C15 – P2	108.2(1)	C14 – C13 – P1	107.2(1)
C10 – C11 – C12	120.0(2)	C16 – C15 – P2	108.4(1)	P2 – C13 – P1	115.7(1)
C9 – C10 – C11	120.5(2)	O2 – C15 – P1	106.5(1)	C12 – C7 – C8	119.3(1)
C1 – C6 – C5	120.2(2)	C16 – C15 – P1	110.2(1)	C12 – C7 – P1	123.0(1)
C5 – C4 – C3	120.3(2)	P2 – C15 – P1	111.4(1)	C8 – C7 – P1	117.7(1)
C10 – C9 – C8	120.0(2)	C13 – C8 – C9	118.7(1)	C5 – C6 – C1	120.0(1)
C10 – C9 – H9	120.000	C13 – C8 – P1	114.8(1)	C6 – C5 – C4	120.3(1)
C4 – C5 – C6	120.1(2)	C9 – C8 – P1	126.5(1)	C3 – C4 – C5	119.9(1)
C3 – C2 – C1	120.5(2)	O6 – C20 – C19	121.8(2)	C11 – C12 – C7	120.4(1)
C2 – C1 – P1	117.1(1)	O6 – C20 – C19ⁱ	121.8(2)	C9 – C8 – C7	120.0(1)
C4 – C3 – C2	119.8(2)	C19 – C20 – C19ⁱ	116.4(3)	C3 – C2 – C1	120.5(1)
C11 – C12 – C7	119.9(2)	C10 – C9 – C8	120.3(2)	C14 – C13 – P2	107.9(1)
		C9 – C10 – C11	120.9(2)	O2 – C13 – P1	107.1(1)
		C12 – C11 – C10	118.7(2)		
		C12 – C11 – C14	119.9(2)		
		C10 – C11 – C14	121.4(2)		
		C13 – C12 – C11	120.5(2)		
		C12 – C13 – C8	120.9(2)		

SI Table S3. Selected torsion angles (°) of compound **2d**, **2e** and **6**.

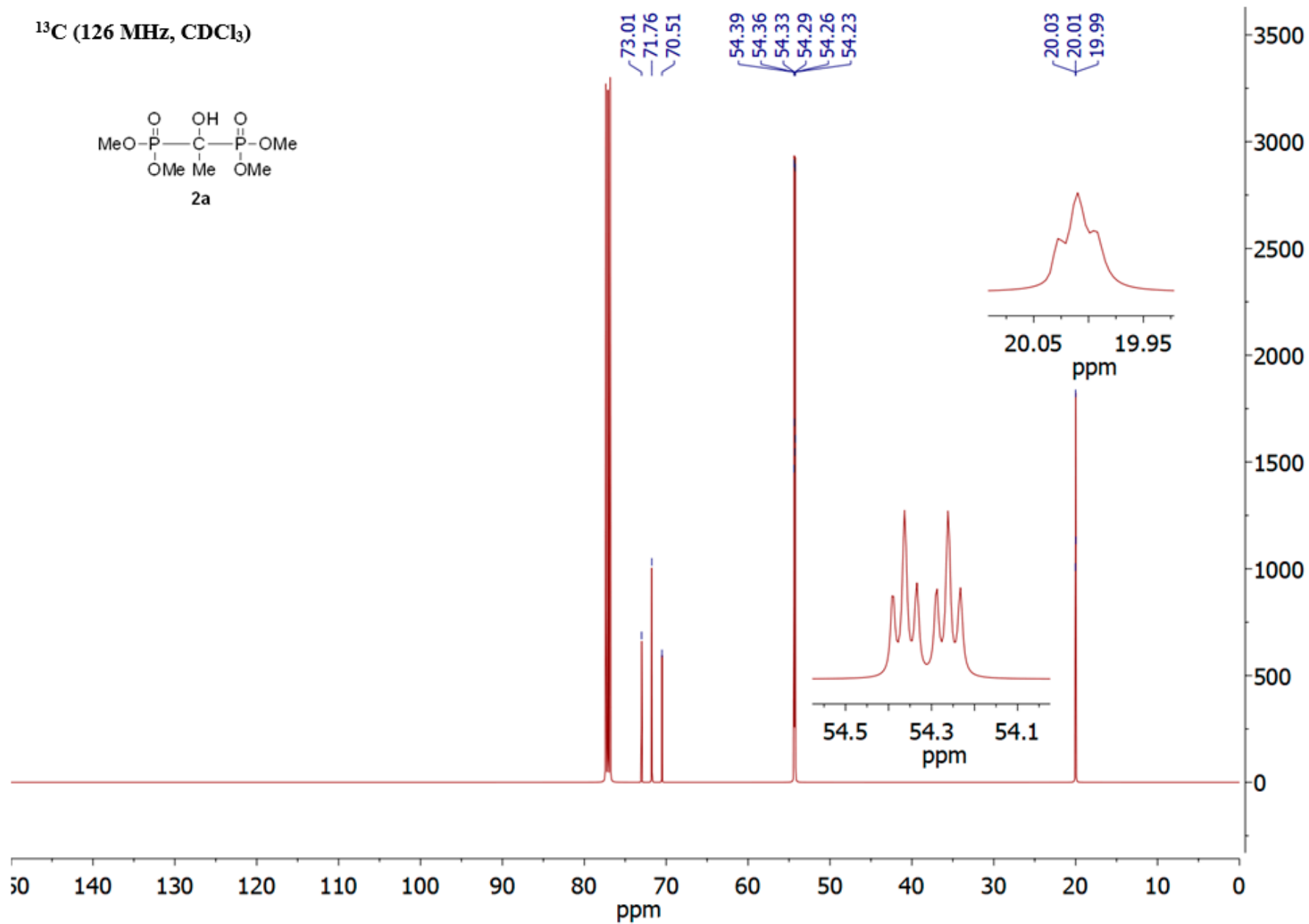
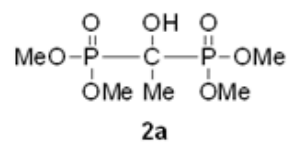
2d		2e		6	
O5 – P2 – O4 – C16	-27.4(2)	O1 – P1 – C1 – C2	174.2(1)	O5 – P2 – O3 – C15	-32.3(1)
O3 – P2 – O4 – C16	-154.1(2)	C8 – P1 – C1 – C2	51.6(2)	O4 – P2 – O3 – C15	90.3(1)
C13 – P2 – O4 – C16	100.1(2)	C15 – P1 – C1 – C2	-62.2(2)	C13 – P2 – O3 – C15	-153.9(1)
O1 – P1 – C7 – C8	-11.0(2)	O1 – P1 – C1 – C6	-3.9(2)	O5 – P2 – O4 – C17	145.3(1)
C1 – P1 – C7 – C8	112.1(1)	C8 – P1 – C1 – C6	-126.5(1)	O3 – P2 – O4 – C17	18.7(1)
C13 – P1 – C7 – C8	-135.1(1)	C15 – P1 – C1 – C6	119.7(1)	C13 – P2 – O4 – C17	-92.8(1)
O1 – P1 – C7 – C12	172.4(1)	C17A – O4A – P2 – O3	-25.6(5)	O1 – P1 – C1 – C2	-19.3(1)
C1 – P1 – C7 – C12	-64.6(2)	C17A – O4A – P2 – O5A	-147.6(5)	C7 – P1 – C1 – C2	103.0(1)
C13 – P1 – C7 – C12	48.3(2)	C17A – O4A – P2 – C15	106.4(4)	C13 – P1 – C1 – C2	-144.4(1)
O5 – P2 – O3 – C15	-56.5(2)	C6 – C1 – C2 – C3	-1.1(2)	O1 – P1 – C1 – C6	163.5(1)
O4 – P2 – O3 – C15	68.7(2)	P1 – C1 – C2 – C3	-179.2(1)	C7 – P1 – C1 – C6	-74.3(1)
C13 – P2 – O3 – C15	177.1(2)	O3 – P2 – O5A – C18A	-64.2(5)	C13 – P1 – C1 – C6	38.4(1)
O1 – P1 – C1 – C6	144.9(2)	O4A – P2 – O5A – C18A	62.5(5)	O5 – P2 – C13 – O2	-52.0(1)
C7 – P1 – C1 – C6	21.9(2)	C15 – P2 – O5A – C18A	175.4(5)	O3 – P2 – C13 – O2	72.8(1)
C13 – P1 – C1 – C6	-94.3(2)	C1 – C2 – C3 – C4	1.2(3)	O4 – P2 – C13 – O2	-172.8(1)
O1 – P1 – C1 – C2	-35.0(2)	C5 – C4 – C3 – C2	-0.5(3)	O5 – P2 – C13 – C14	69.0(1)
C7 – P1 – C1 – C2	-158.1(1)	C7 – C4 – C3 – C2	179.0(2)	O3 – P2 – C13 – C14	-166.3(1)
C13 – P1 – C1 – C2	85.8(1)	C3 – C4 – C5 – C6	-0.2(3)	O4 – P2 – C13 – C14	-51.8(1)
C8 – C7 – C12 – C11	-2.5(2)	C7 – C4 – C5 – C6	-179.7(2)	O5 – P2 – C13 – P1	-171.0(1)
P1 – C7 – C12 – C11	174.0(1)	C4 – C5 – C6 – C1	0.3(3)	O3 – P2 – C13 – P1	-46.3(1)
C4 – C3 – C2 – C1	-0.7(3)	C2 – C1 – C6 – C5	0.4(2)	O4 – P2 – C13 – P1	68.2(1)
C6 – C1 – C2 – C3	0.9(3)	P1 – C1 – C6 – C5	178.6(1)	O1 – P1 – C13 – O2	179.8(1)
P1 – C1 – C2 – C3	-179.2(1)	O3 – P2 – C15 – O2	44.3(1)	C7 – P1 – C13 – O2	58.6(1)
O5 – P2 – C13 – O2	56.1(1)	O4A – P2 – C15 – O2	-90.4(2)	C1 – P1 – C13 – O2	-54.5(1)
O3 – P2 – C13 – O2	-176.8(1)	O5A – P2 – C15 – O2	163.3(2)	O1 – P1 – C13 – C14	59.0(1)
O4 – P2 – C13 – O2	-70.5(1)	O4B – P2 – C15 – O2	-63.0(3)	C7 – P1 – C13 – C14	-62.2(1)
O5 – P2 – C13 – C14	175.9(1)	O5B – P2 – C15 – C16	68.6(5)	C1 – P1 – C13 – C14	-175.3(1)
O3 – P2 – C13 – C14	-57.0(1)	C9 – C8 – C13 – C12	0.5(2)	O1 – P1 – C13 – P2	-61.4(1)
O4 – P2 – C13 – C14	49.3(1)	P1 – C8 – C13 – C12	-180.0(1)	C7 – P1 – C13 – P2	177.4(1)
O5 – P2 – C13 – P1	-62.4(1)	O3 – P2 – C15 – C16	-77.5(1)	C1 – P1 – C13 – P2	64.3(1)
O3 – P2 – C13 – P1	64.7(1)	O4A – P2 – C15 – C16	147.9(2)	O1 – P1 – C7 – C12	164.6(1)
O4 – P2 – C13 – P1	171.0(1)	O5A – P2 – C15 – C16	41.5(2)	C1 – P1 – C7 – C12	42.3(1)
O1 – P1 – C13 – O2	-179.5(1)	O3 – P2 – C15 – P1	161.0(1)	C13 – P1 – C7 – C12	-74.8(1)
C7 – P1 – C13 – O2	-55.1(1)	O4A – P2 – C15 – P1	26.4(2)	O1 – P1 – C7 – C8	-13.7(1)
C1 – P1 – C13 – O2	59.4(1)	O5A – P2 – C15 – P1	-80.0(2)	C1 – P1 – C7 – C8	-136.0(1)
O1 – P1 – C13 – C14	58.0(1)	O1 – P1 – C15 – O2	163.7(1)	C13 – P1 – C7 – C8	106.9(1)
C7 – P1 – C13 – C14	-177.6(1)	C1 – P1 – C15 – O2	39.8(1)	C2 – C1 – C6 – C5	0.5(2)
C1 – P1 – C13 – C14	-63.1(1)	C8 – P1 – C15 – O2	-75.1(1)	P1 – C1 – C6 – C5	177.6(1)
O1 – P1 – C13 – P2	-64.6(1)	O1 – P1 – C15 – C16	-74.5(1)	C1 – C6 – C5 – C4	0.4(2)
C7 – P1 – C13 – P2	59.9(1)	C1 – P1 – C15 – C16	161.6(1)	C6 – C5 – C4 – C3	-1.0(2)
C1 – P1 – C13 – P2	174.3(1)	C8 – P1 – C15 – C16	46.7(1)	C8 – C7 – C12 – C11	-0.8(2)
C12 – C7 – C8 – C9	1.6(2)	O1 – P1 – C15 – P2	45.9(1)	P1 – C7 – C12 – C11	-179.1(1)
P1 – C7 – C8 – C9	-175.1(1)	C1 – P1 – C15 – P2	-78.0(1)	C12 – C7 – C8 – C9	0.7(2)
C7 – C12 – C11 – C10	1.3(3)	C8 – P1 – C15 – P2	167.1(1)	P1 – C7 – C8 – C9	179.1(1)
C12 – C11 – C10 – C9	0.8(3)	O1 – P1 – C8 – C13	-7.4(2)	C6 – C1 – C2 – C3	-0.8(2)
C2 – C1 – C6 – C5	-0.6(3)	C1 – P1 – C8 – C13	115.7(1)	P1 – C1 – C2 – C3	-178.2(1)
P1 – C1 – C6 – C5	179.5(1)	C15 – P1 – C8 – C13	-128.9(1)	C5 – C4 – C3 – C2	0.6(2)
C4 – C5 – C6 – C1	0.1(3)	O1 – P1 – C8 – C9	172.1(2)	C1 – C2 – C3 – C4	0.3(2)
C6 – C5 – C4 – C3	0.1(3)	C1 – P1 – C8 – C9	-64.7(2)	P2 – O4 – C17 – C18	172.8(1)
C2 – C3 – C4 – C5	0.2(3)	C15 – P1 – C8 – C9	50.7(2)	C7 – C8 – C9 – C10	-0.1(2)
C11 – C10 – C9 – C8	-1.6(3)	C13 – C8 – C9 – C10	-0.4(3)	P2 – O3 – C15 – C16	108.6(1)
C7 – C8 – C9 – C10	0.4(3)	P1 – C8 – C9 – C10	-179.9(1)	C8 – C9 – C10 – C11	-0.4(2)
		C8 – C9 – C10 – C11	-0.5(3)	C7 – C12 – C11 – C10	0.4(2)
		C9 – C10 – C11 – C12	1.2(3)	C9 – C10 – C11 – C12	0.2(2)
		C9 – C10 – C11 – C14	-178.2(2)		
		C10 – C11 – C12 – C13	-1.1(3)		
		C14 – C11 – C12 – C13	178.3(2)		
		C11 – C12 – C13 – C8	0.3(3)		

2. Spectra of the compounds 2a-f, 3a, 3b-1 + 3b-2, 3c-1 + 3c-2, 5d-1 + 5d-2, 5e-1 and 5f-1 synthesized

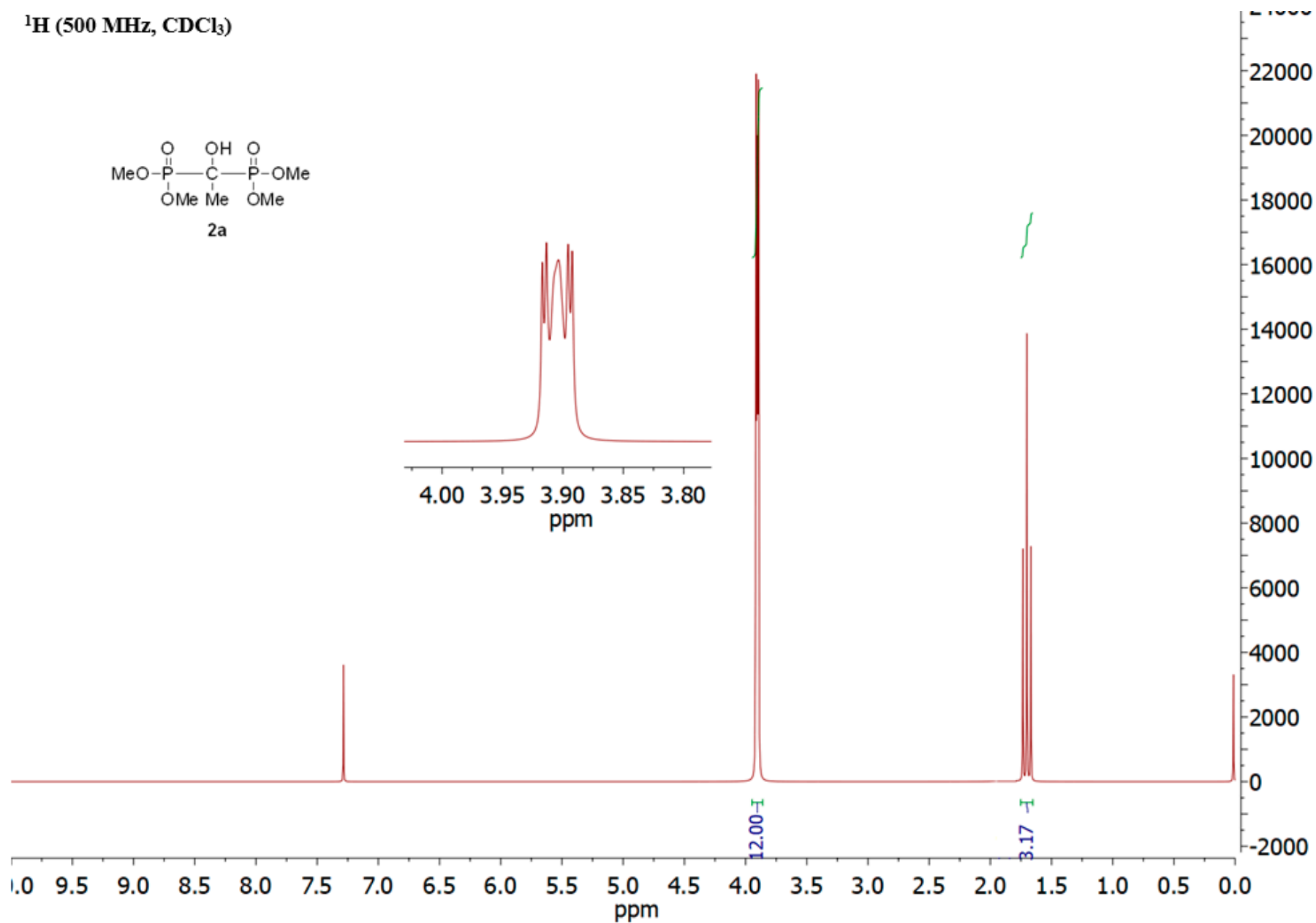
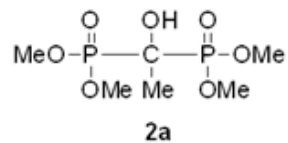
³¹P (202 MHz, CDCl₃)



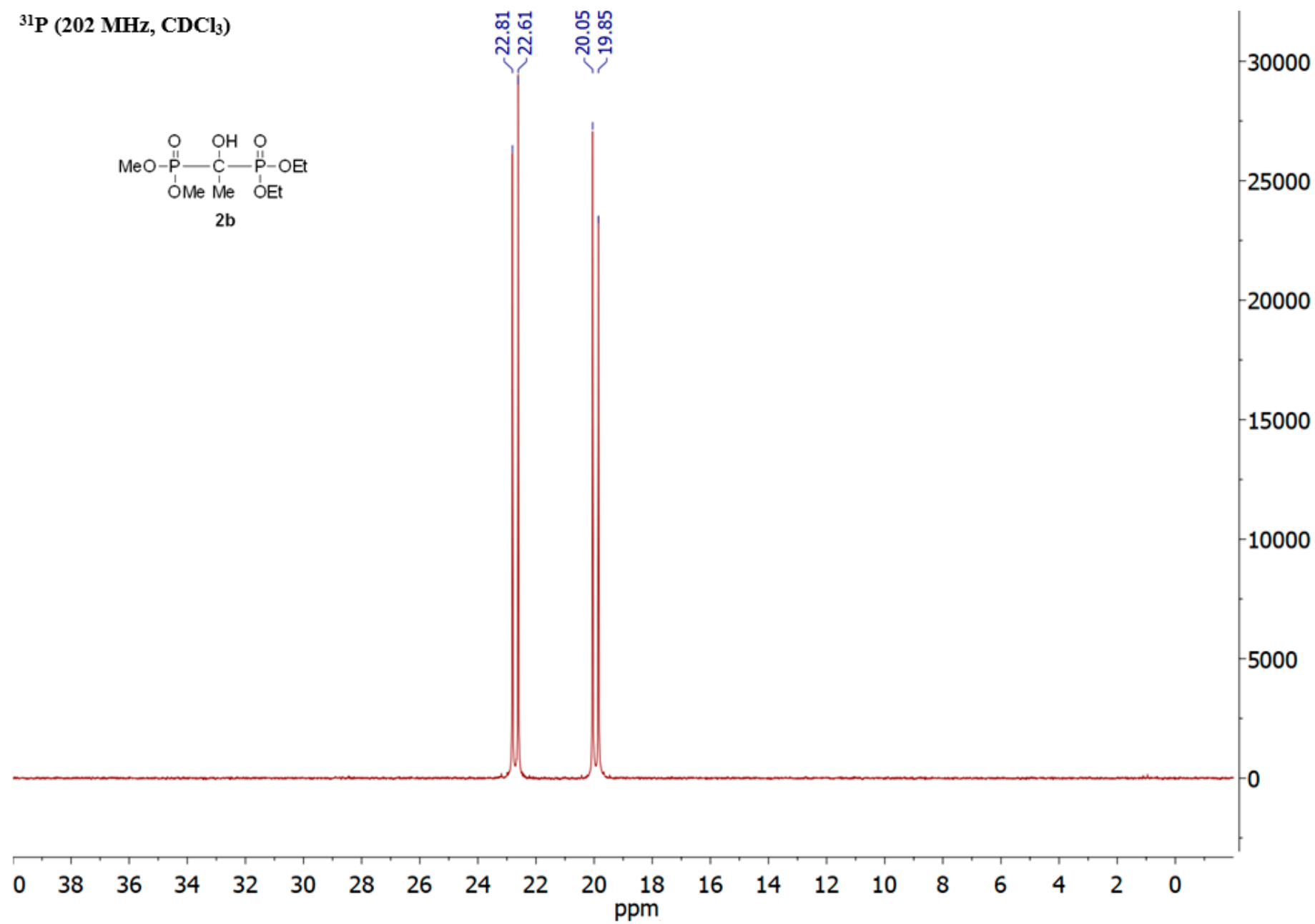
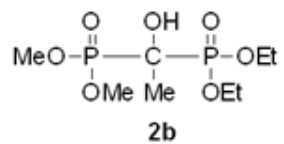
^{13}C (126 MHz, CDCl_3)



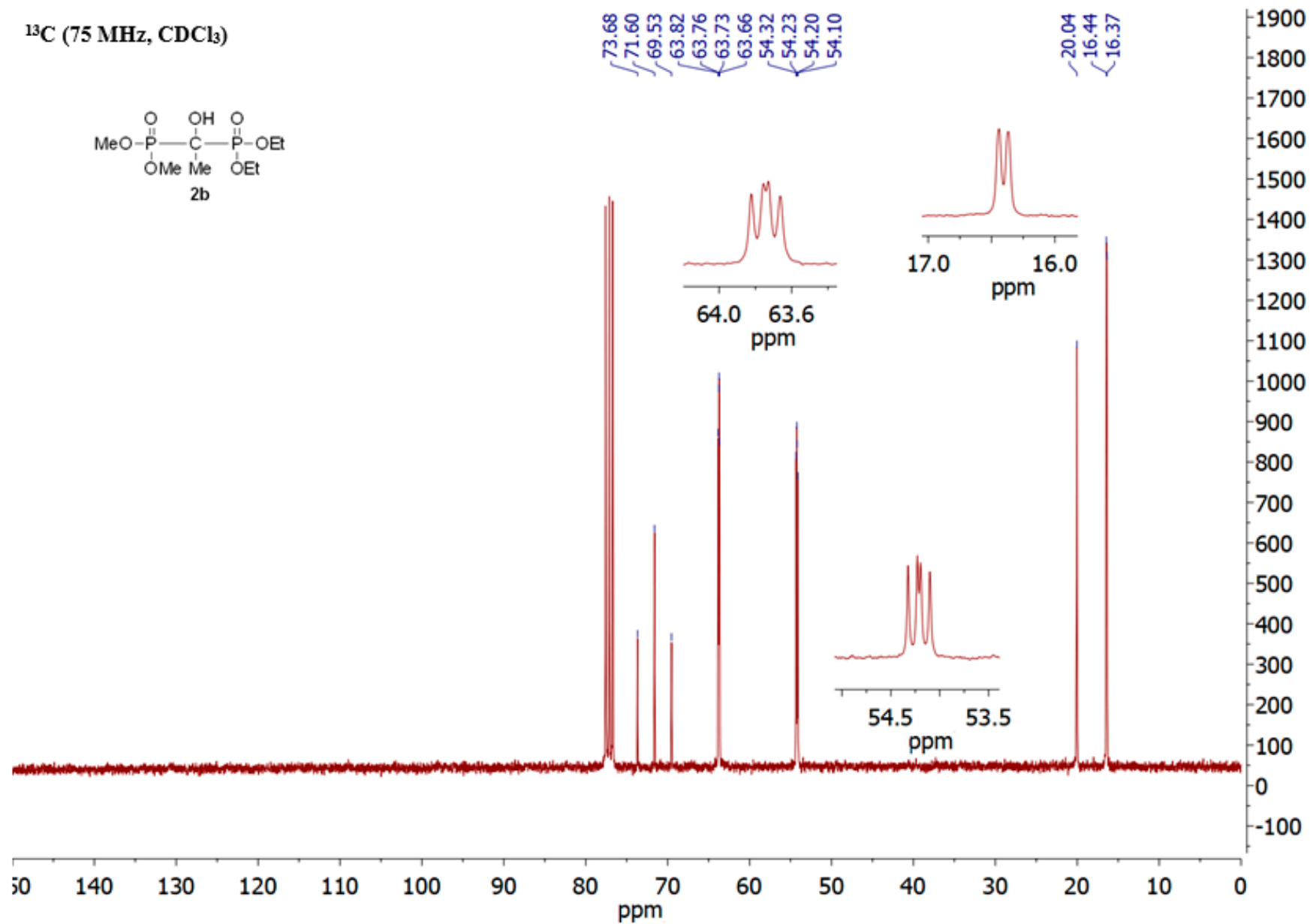
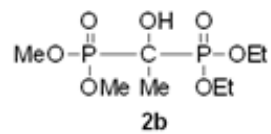
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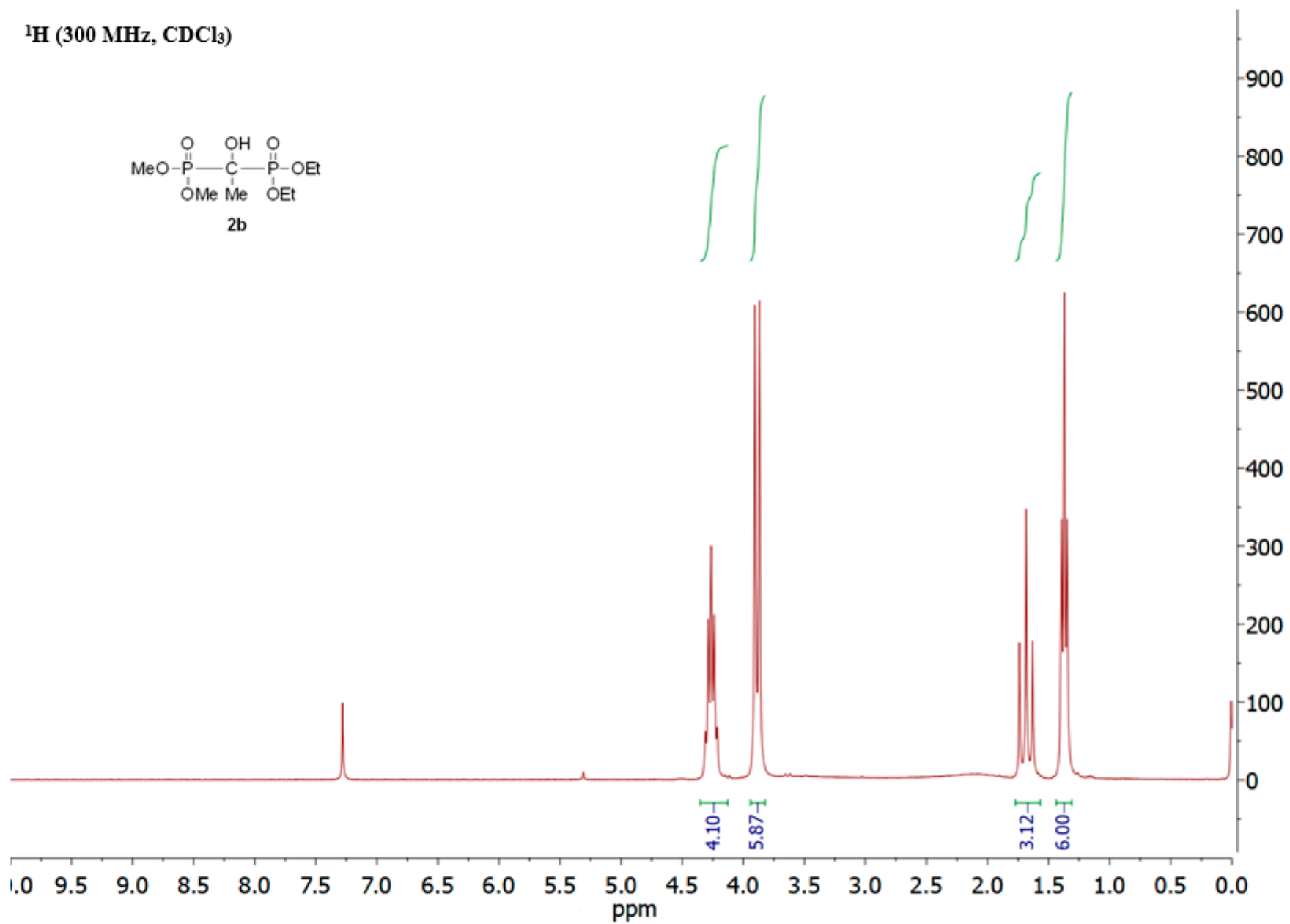
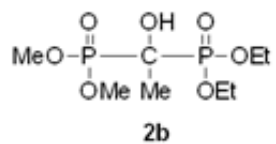
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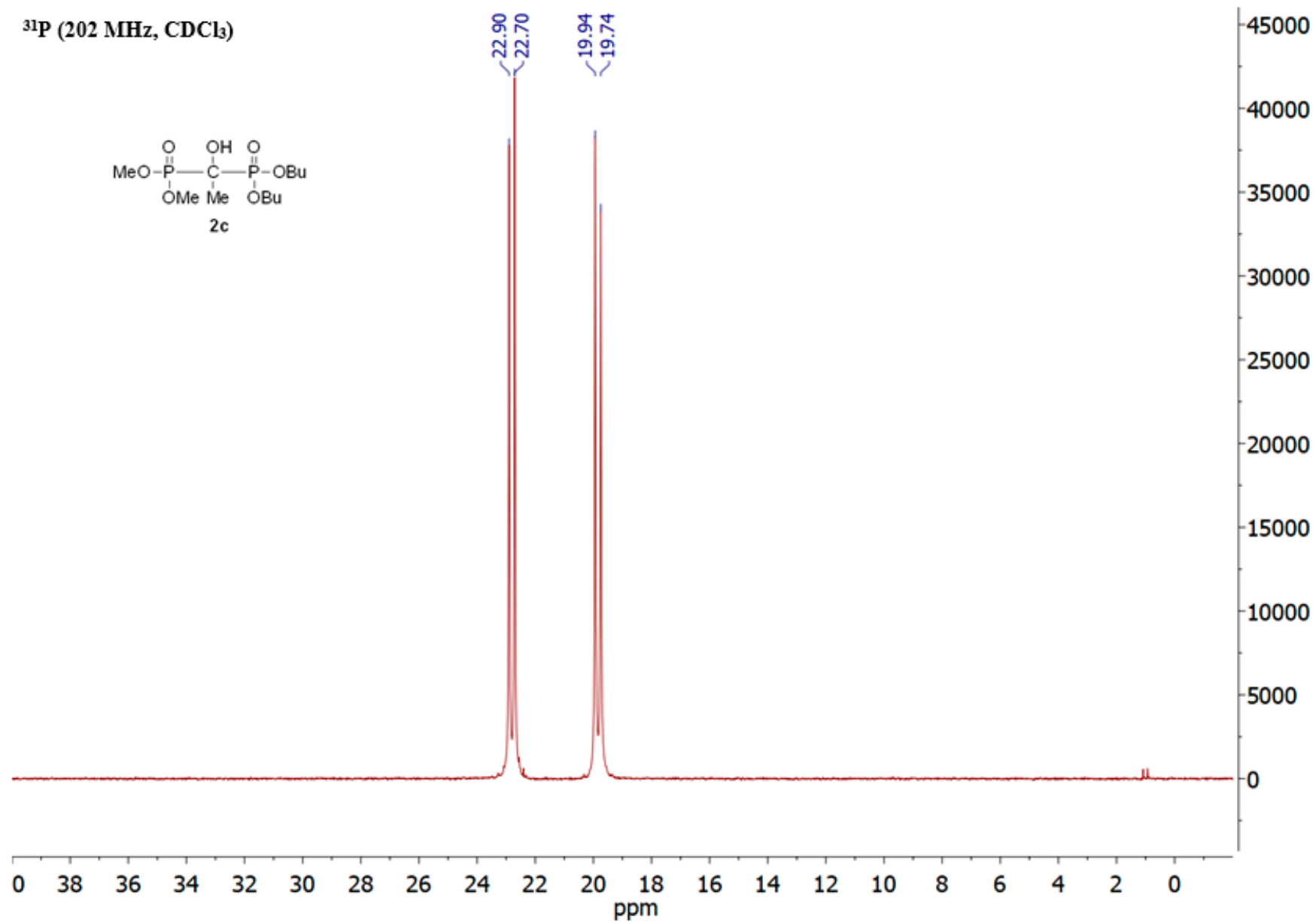
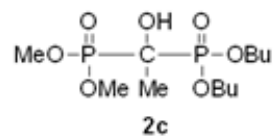
^{13}C (75 MHz, CDCl_3)



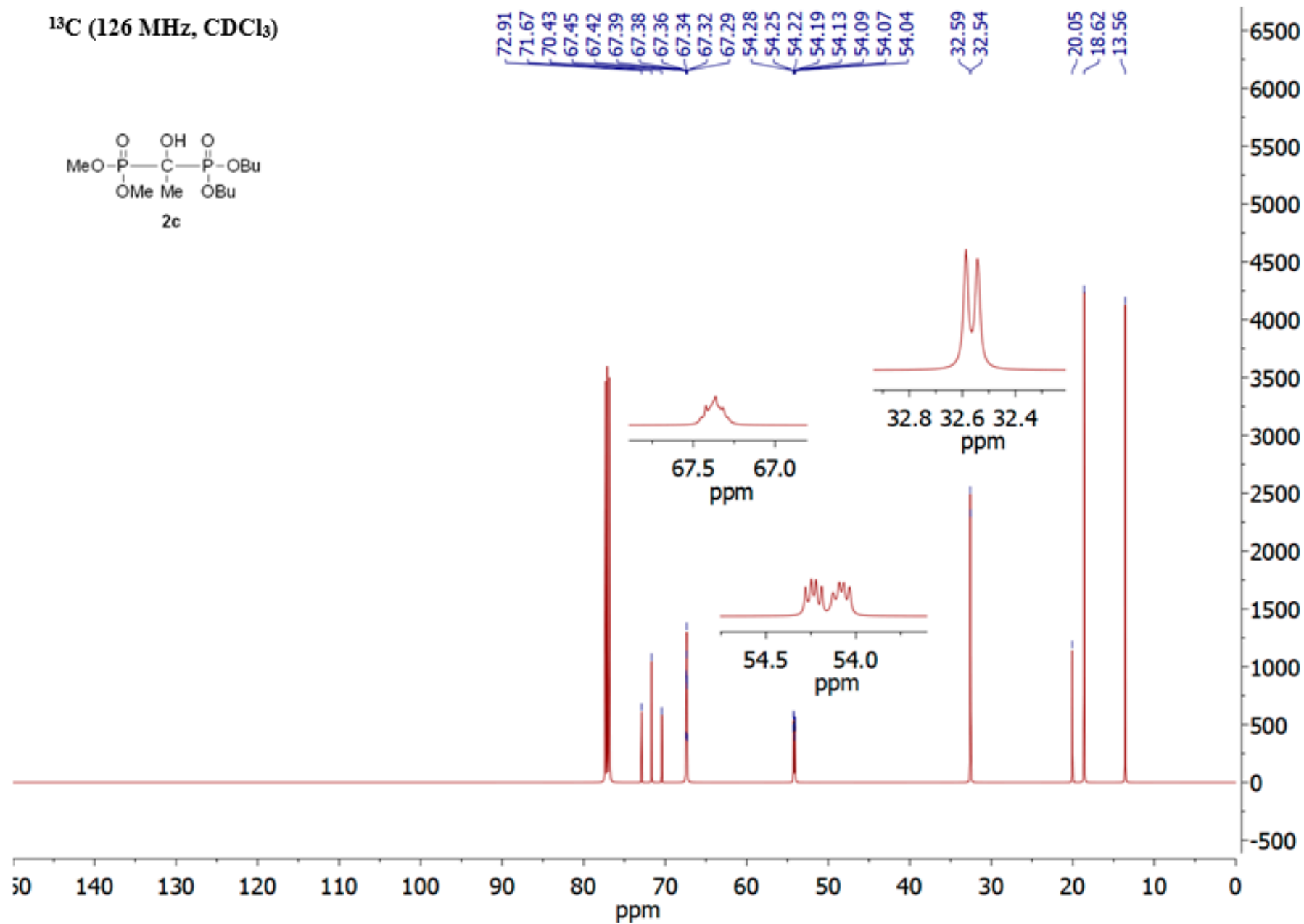
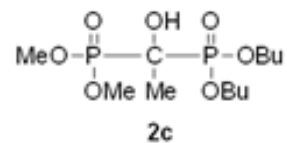
^1H (300 MHz, CDCl_3)



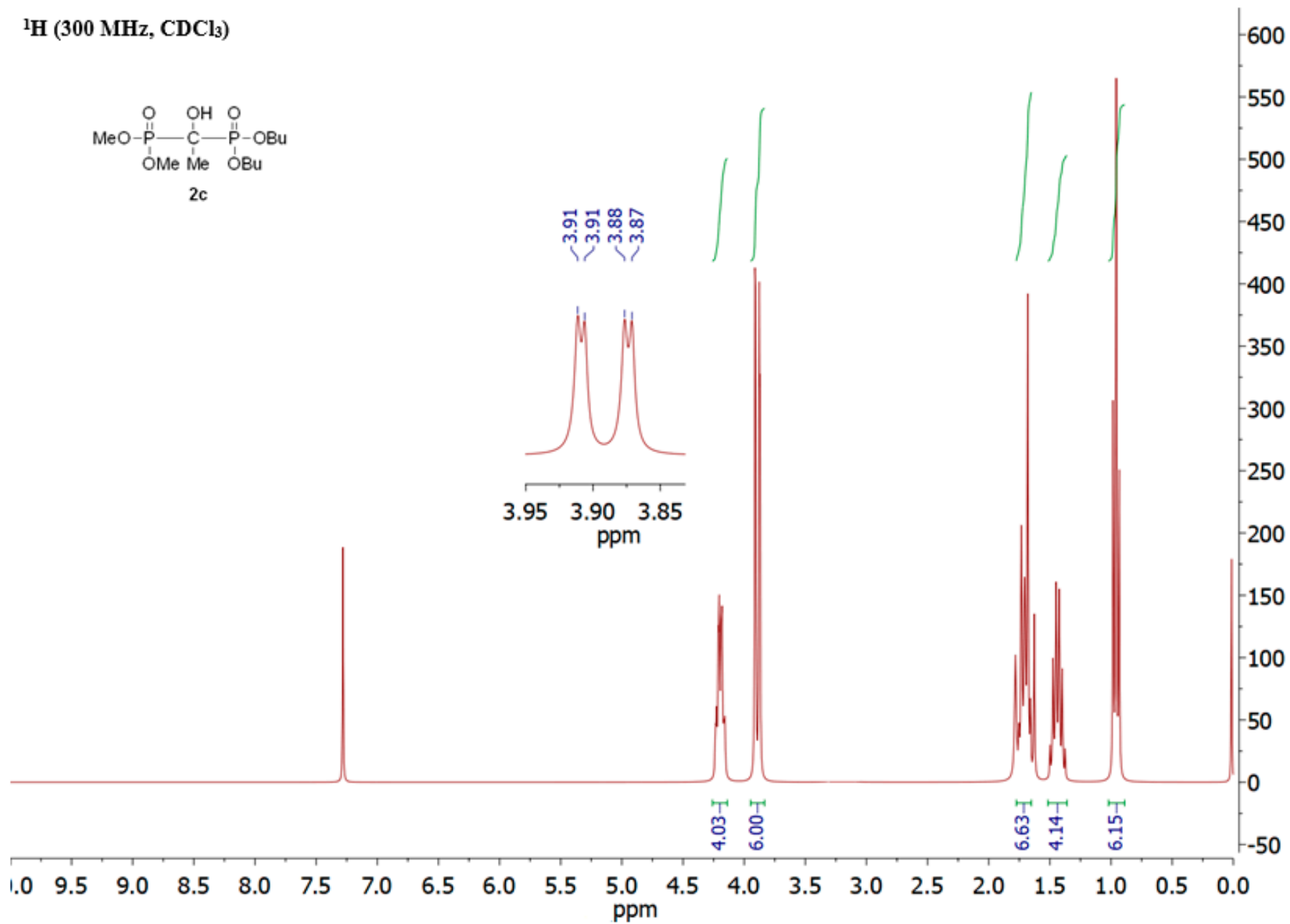
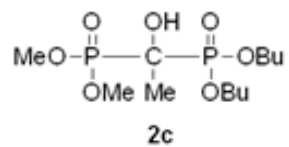
³¹P (202 MHz, CDCl₃)



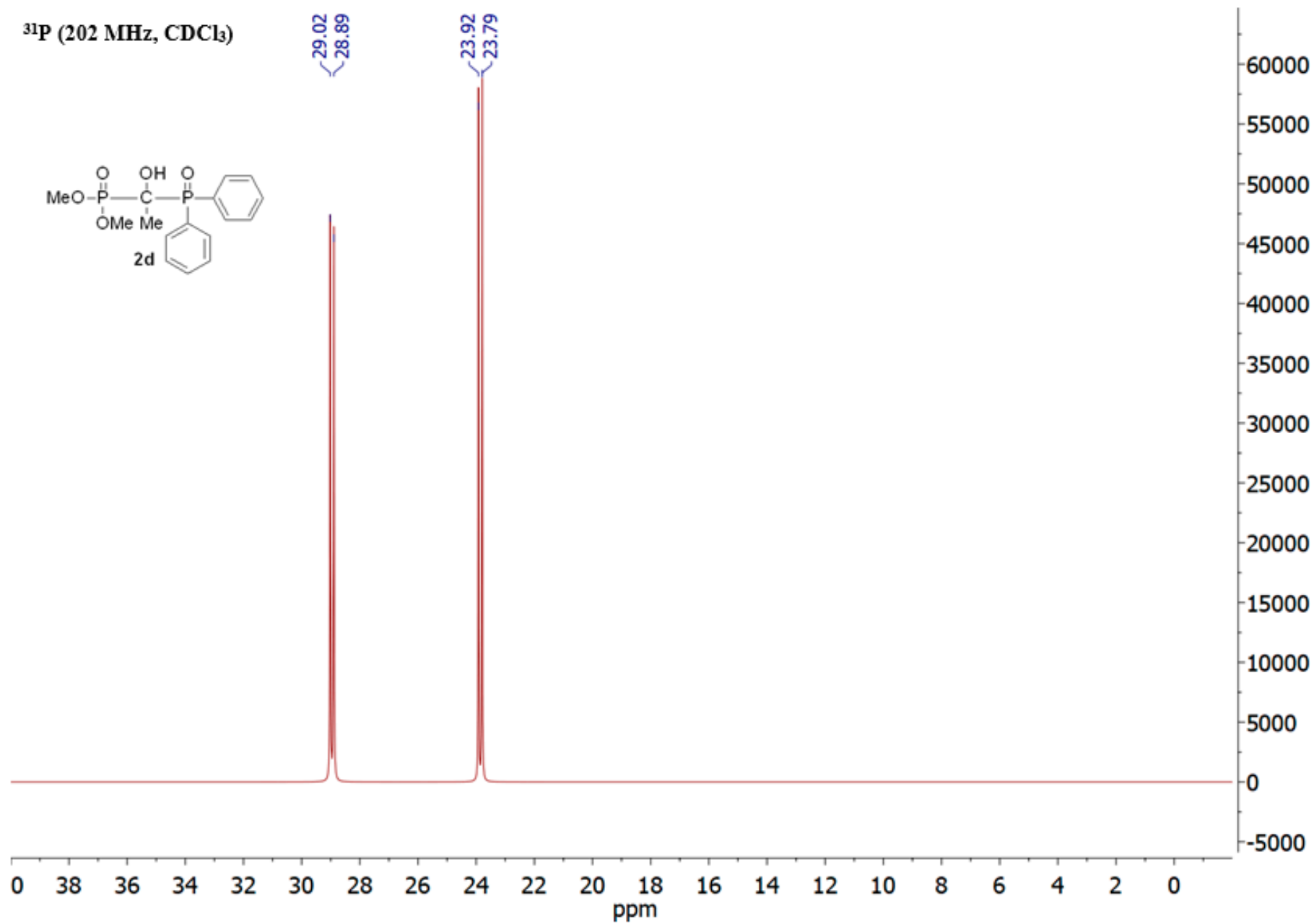
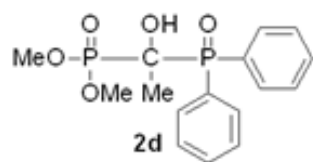
^{13}C (126 MHz, CDCl_3)

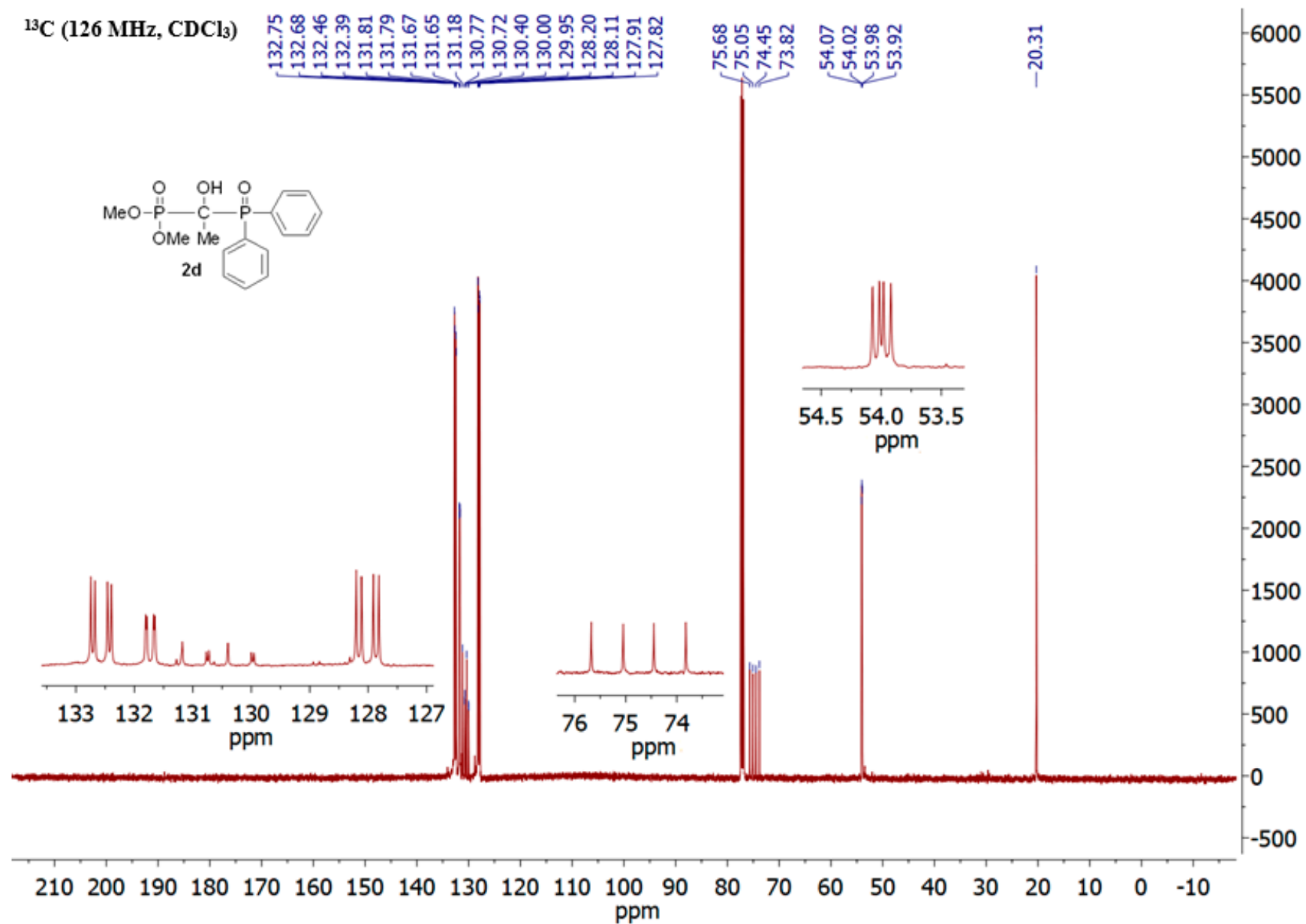


^1H (300 MHz, CDCl_3)

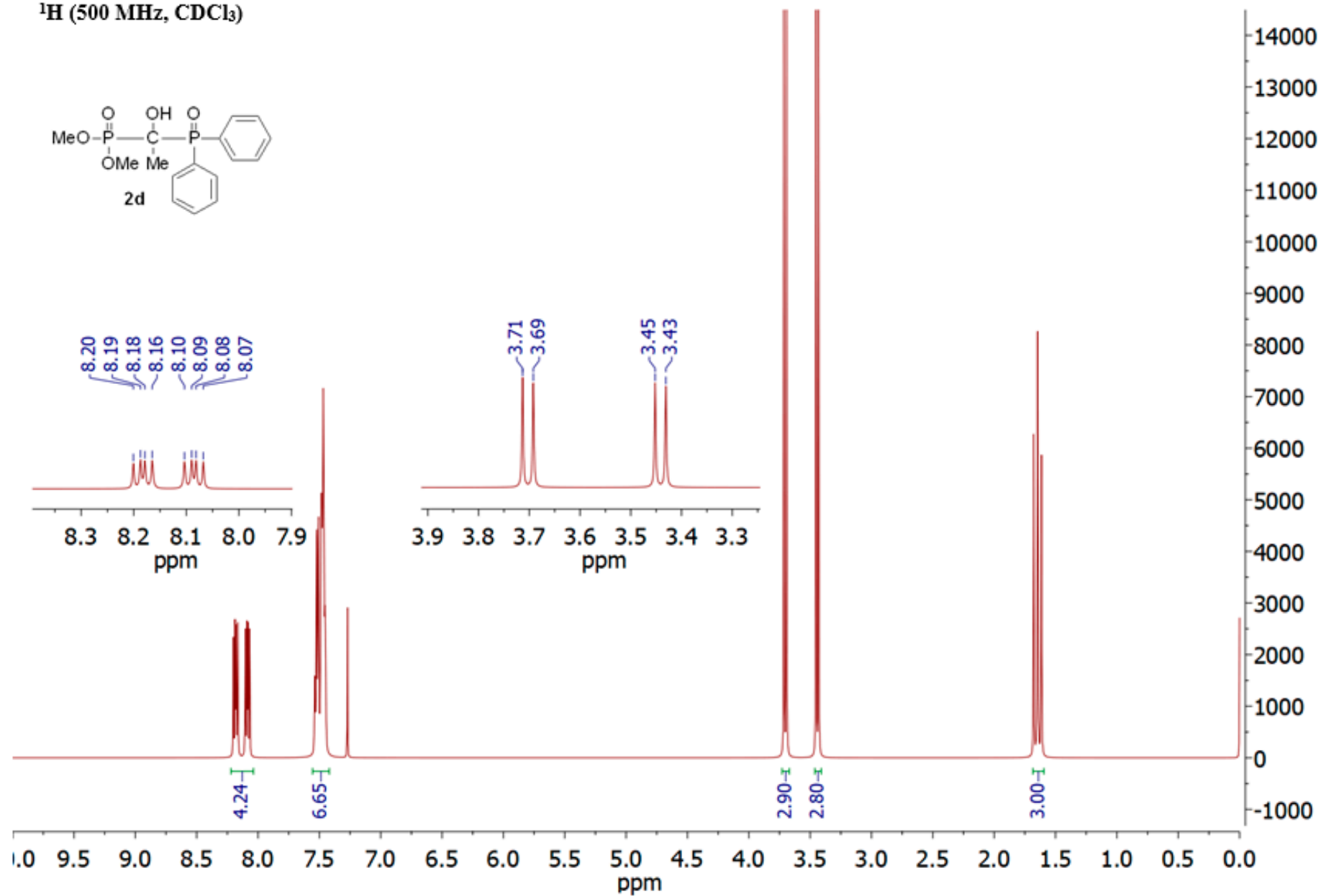
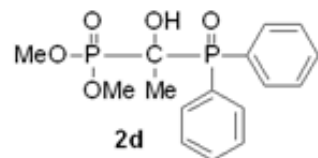


³¹P (202 MHz, CDCl₃)

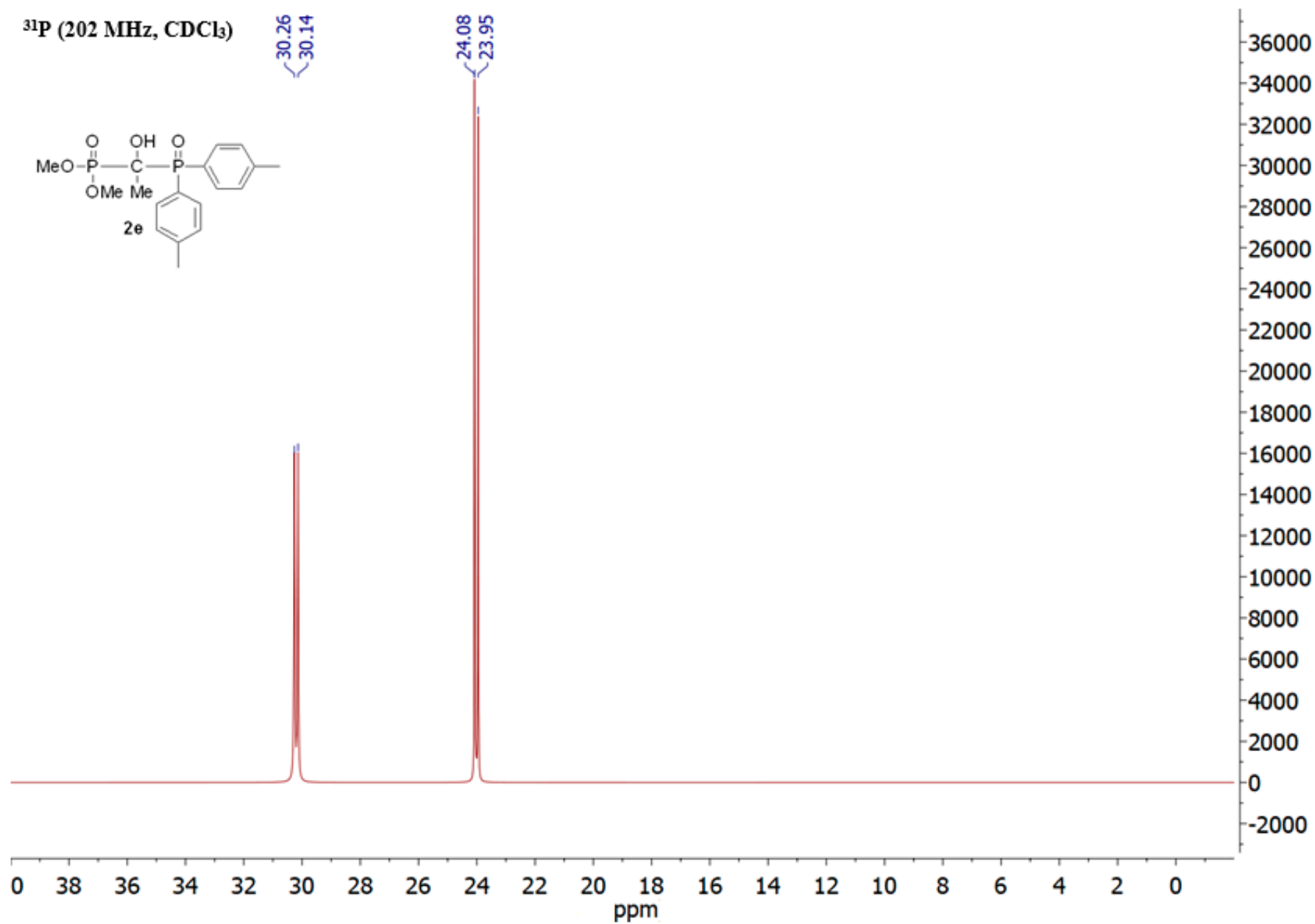
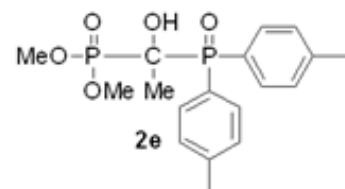


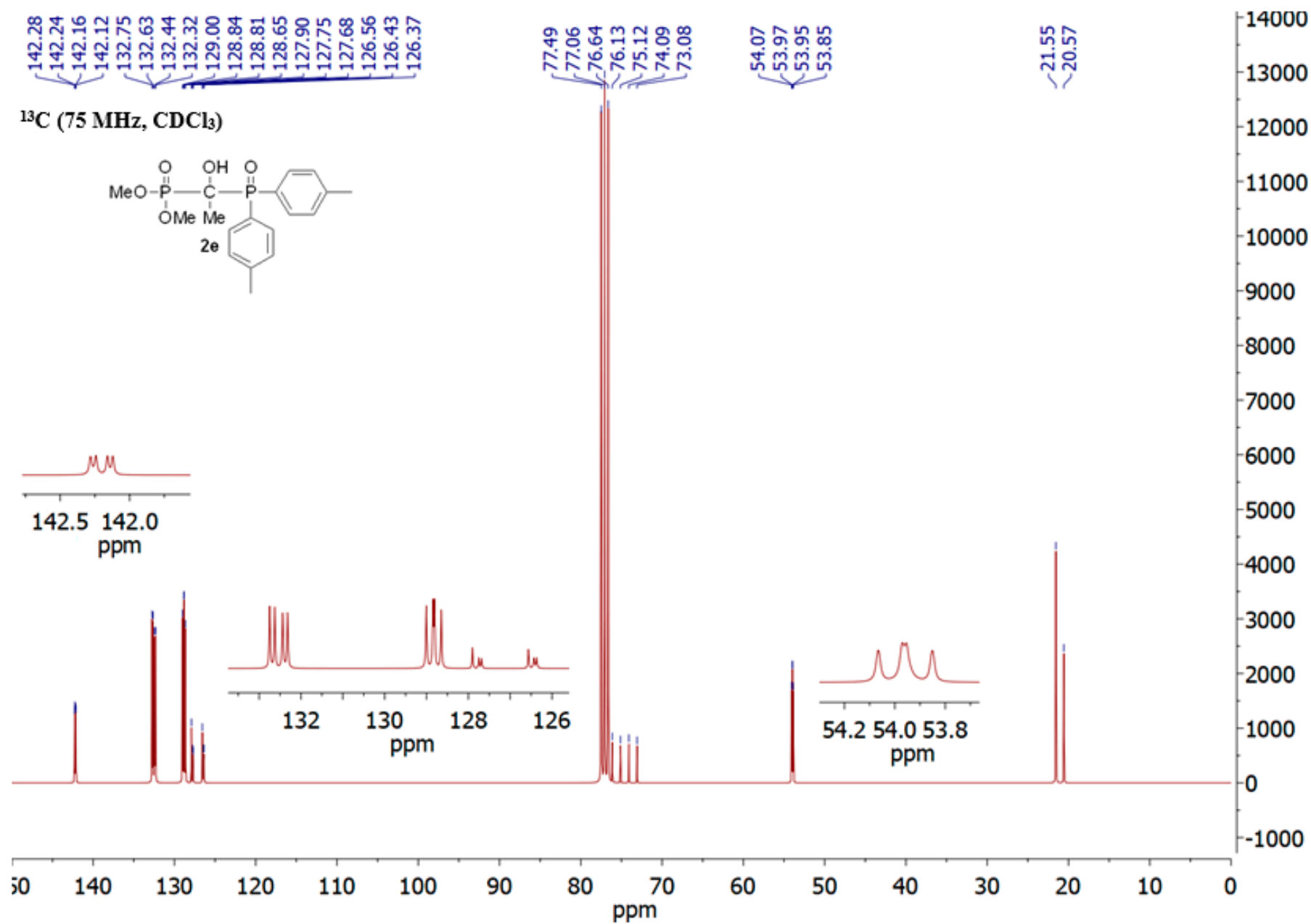


^1H (500 MHz, CDCl_3)

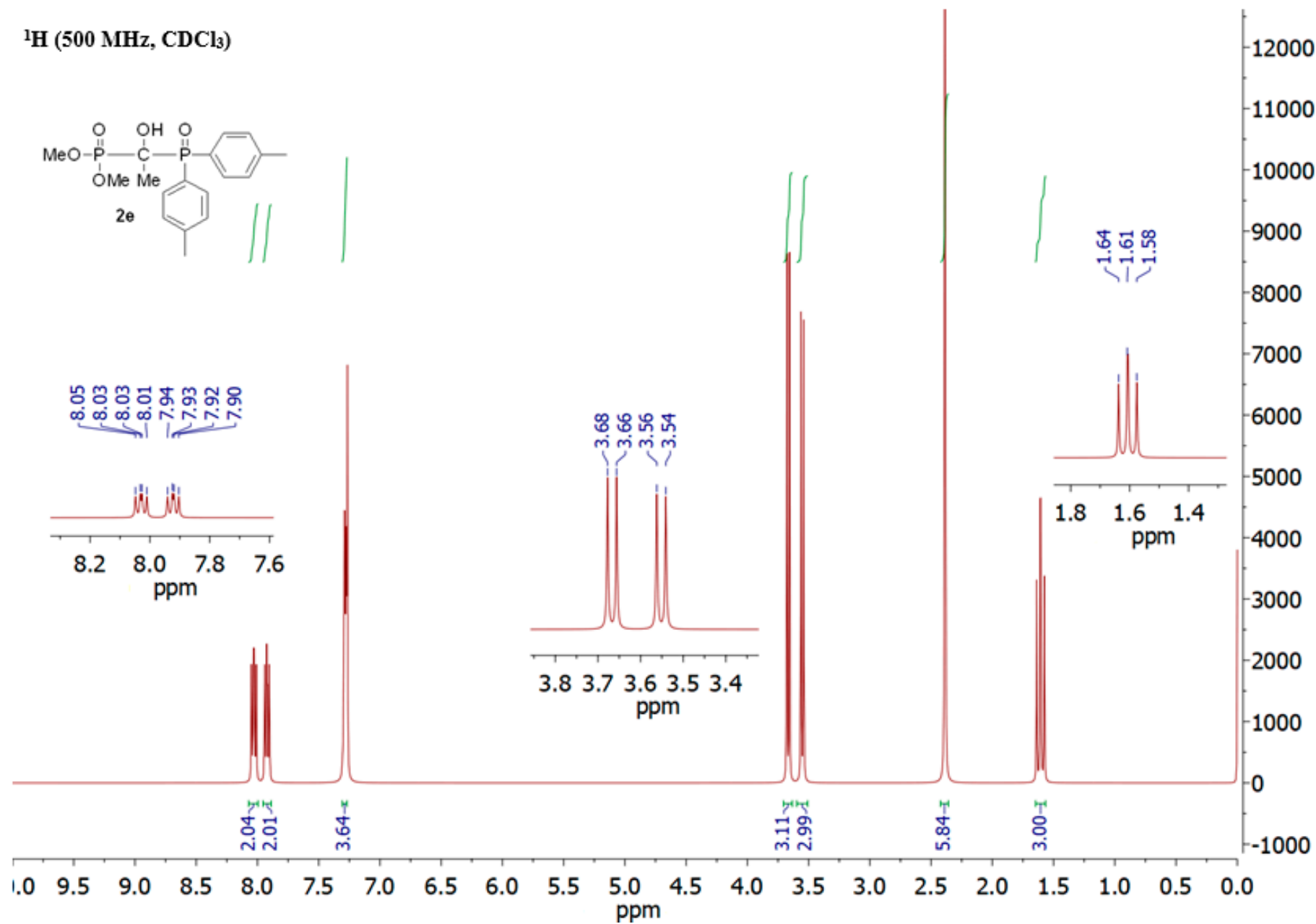
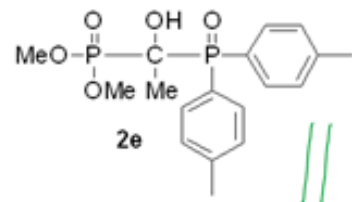


^{31}P (202 MHz, CDCl_3)

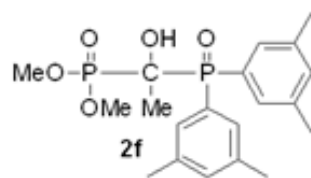




^1H (500 MHz, CDCl_3)

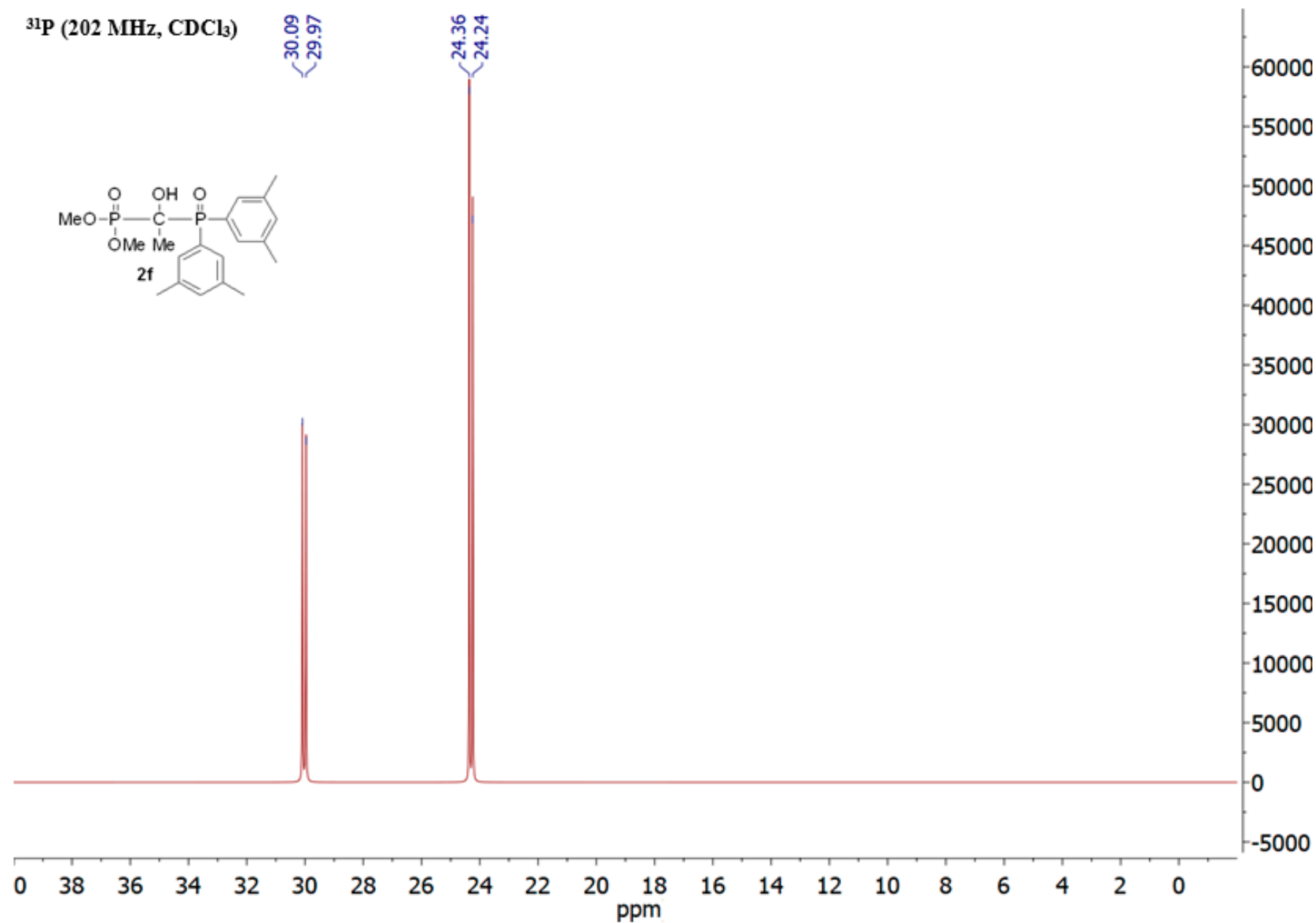


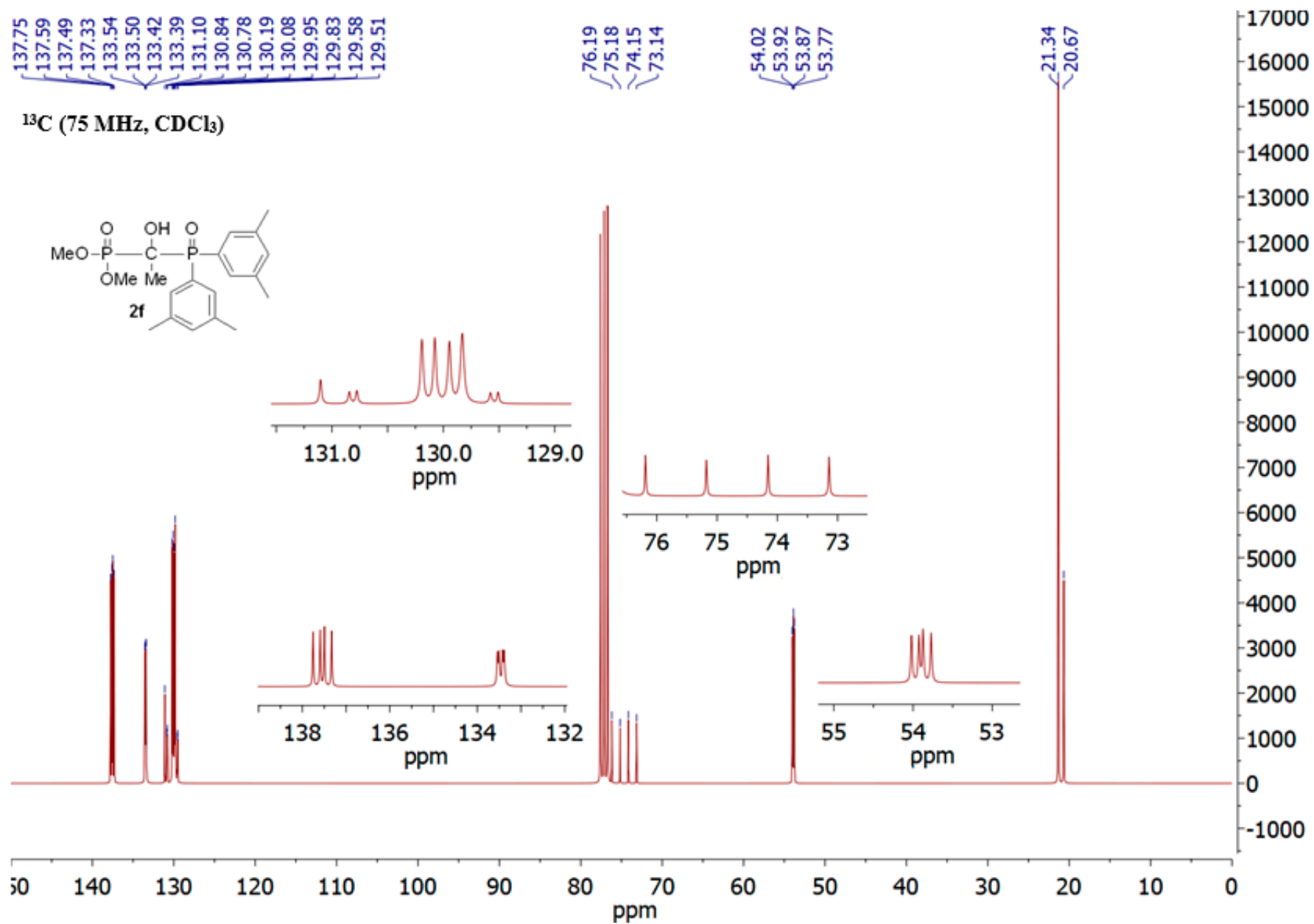
³¹P (202 MHz, CDCl₃)



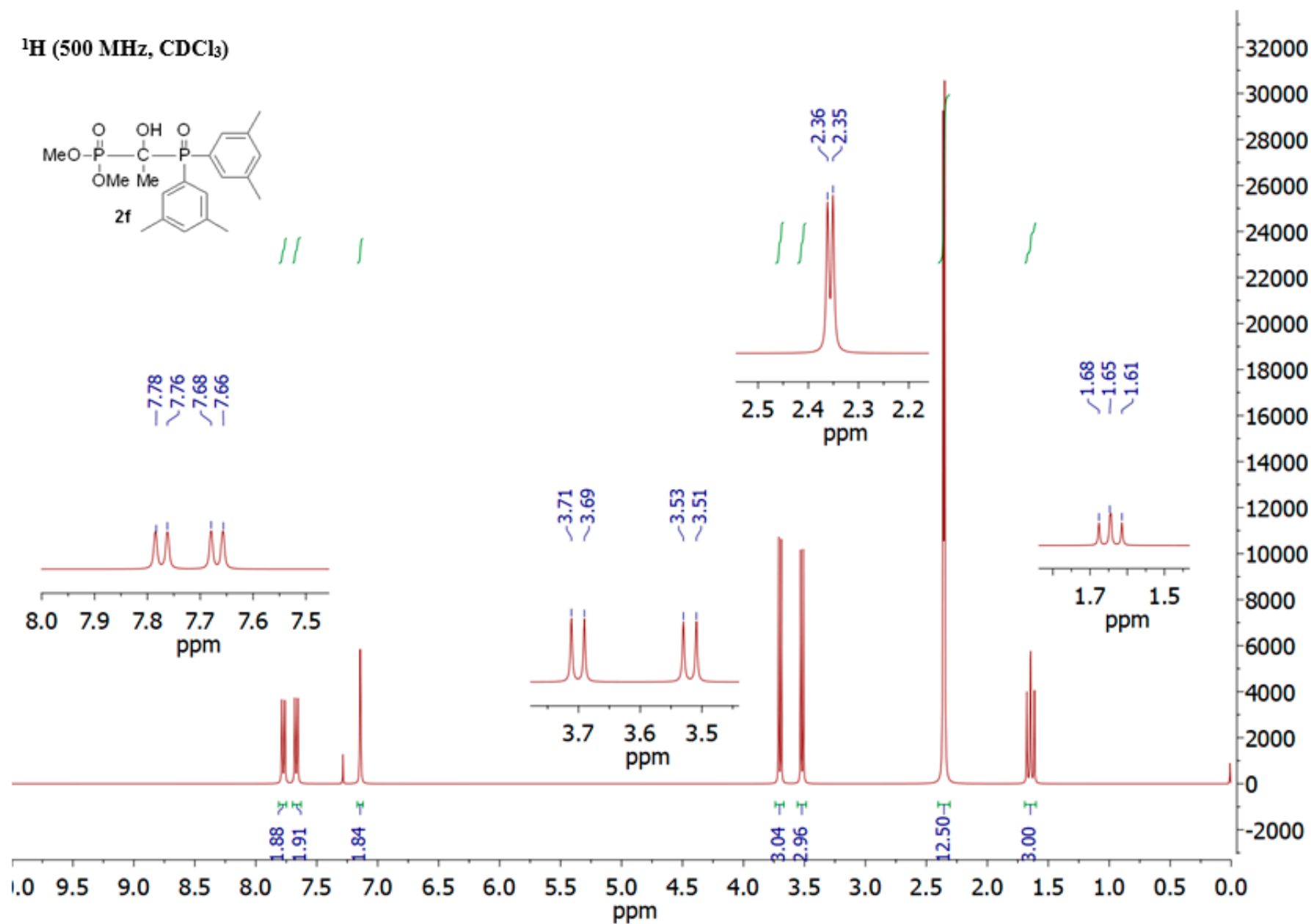
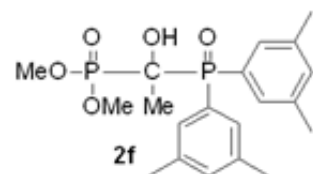
30.09
29.97

24.36
24.24

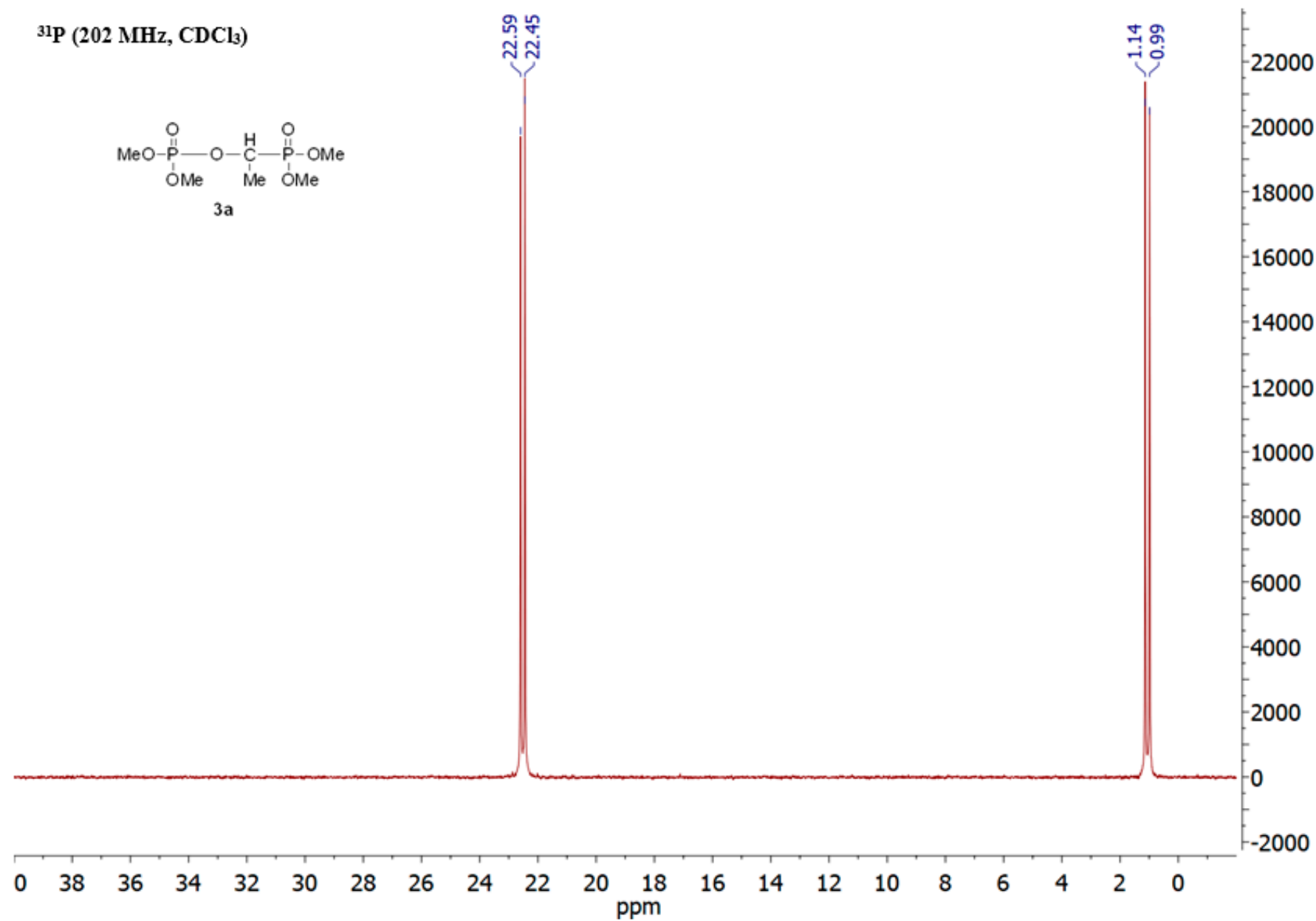
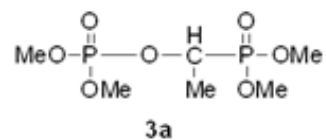




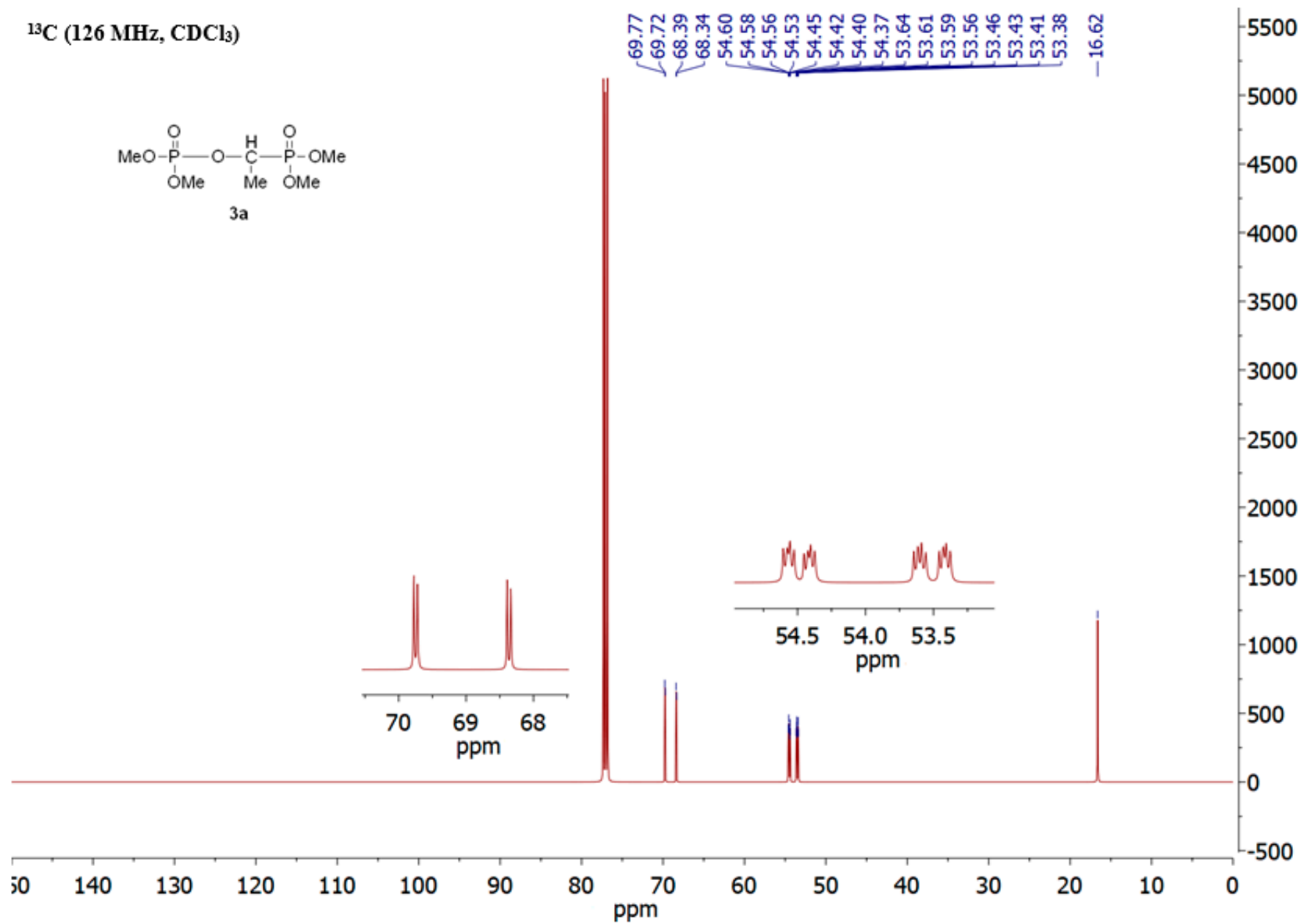
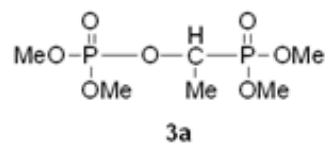
^1H (500 MHz, CDCl_3)



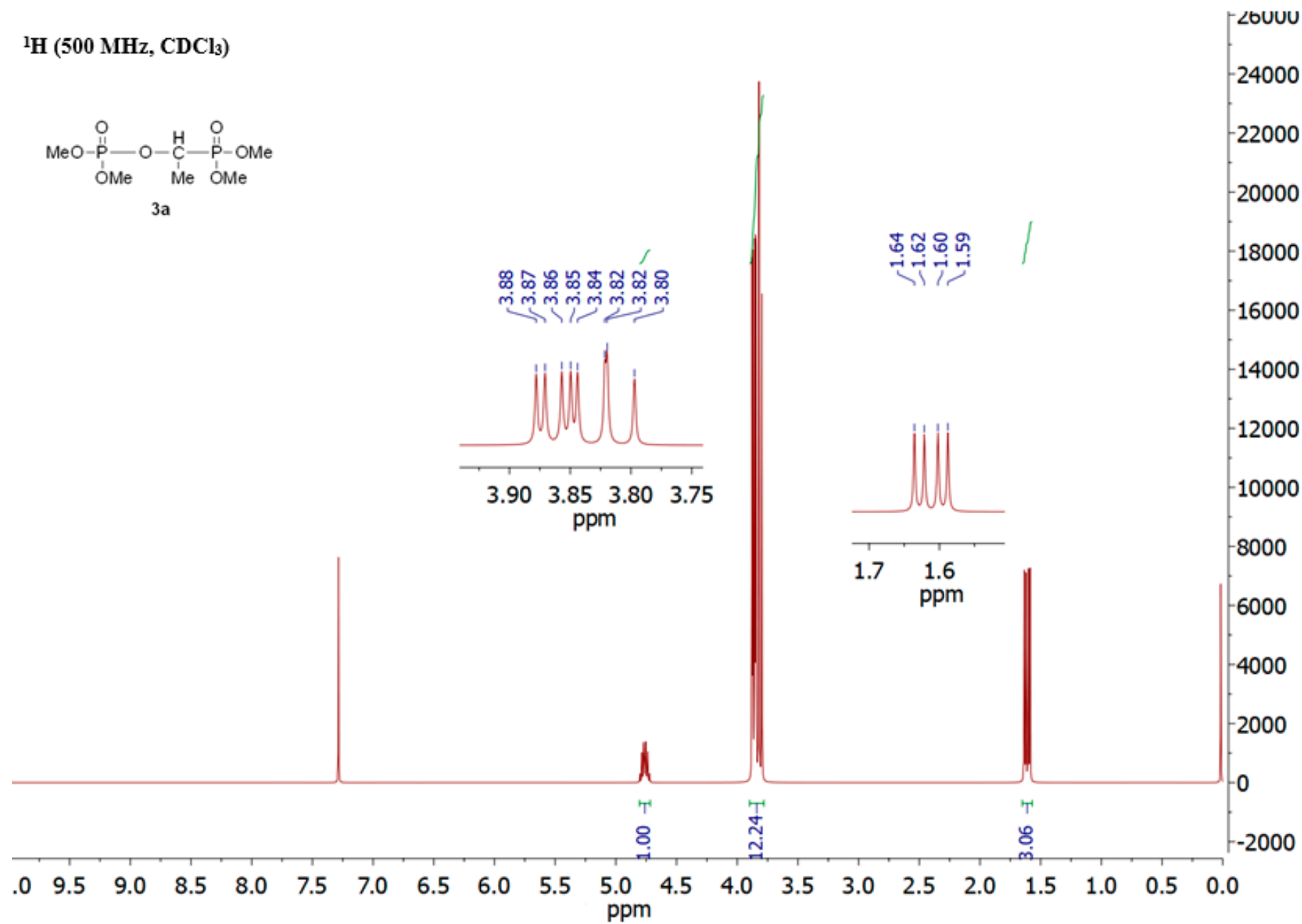
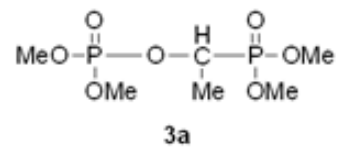
^{31}P (202 MHz, CDCl_3)



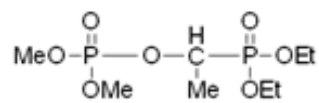
^{13}C (126 MHz, CDCl_3)



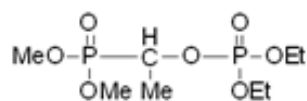
^1H (500 MHz, CDCl_3)



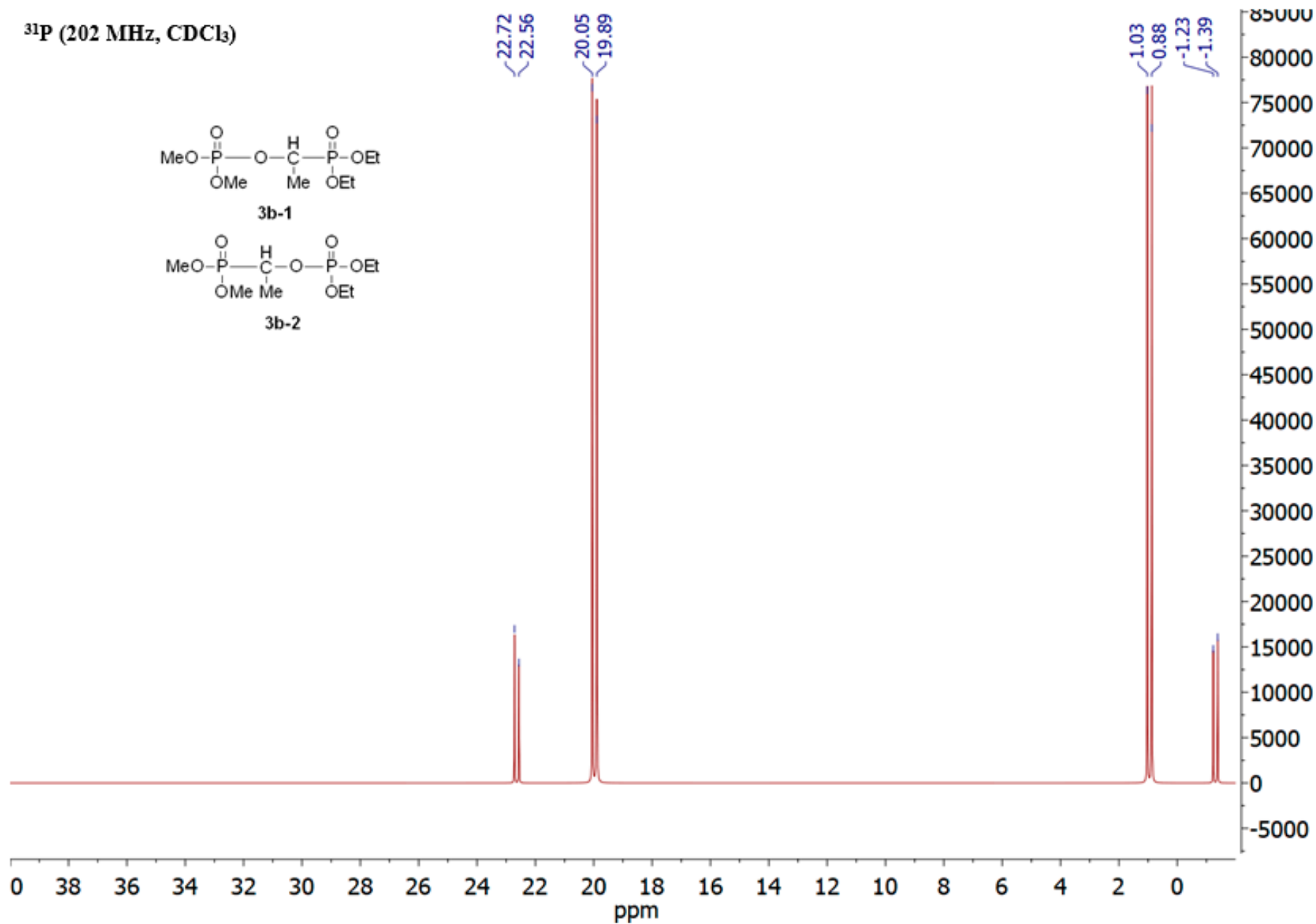
³¹P (202 MHz, CDCl₃)



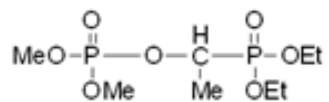
3b-1



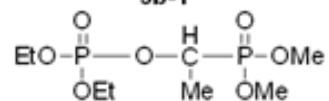
3b-2



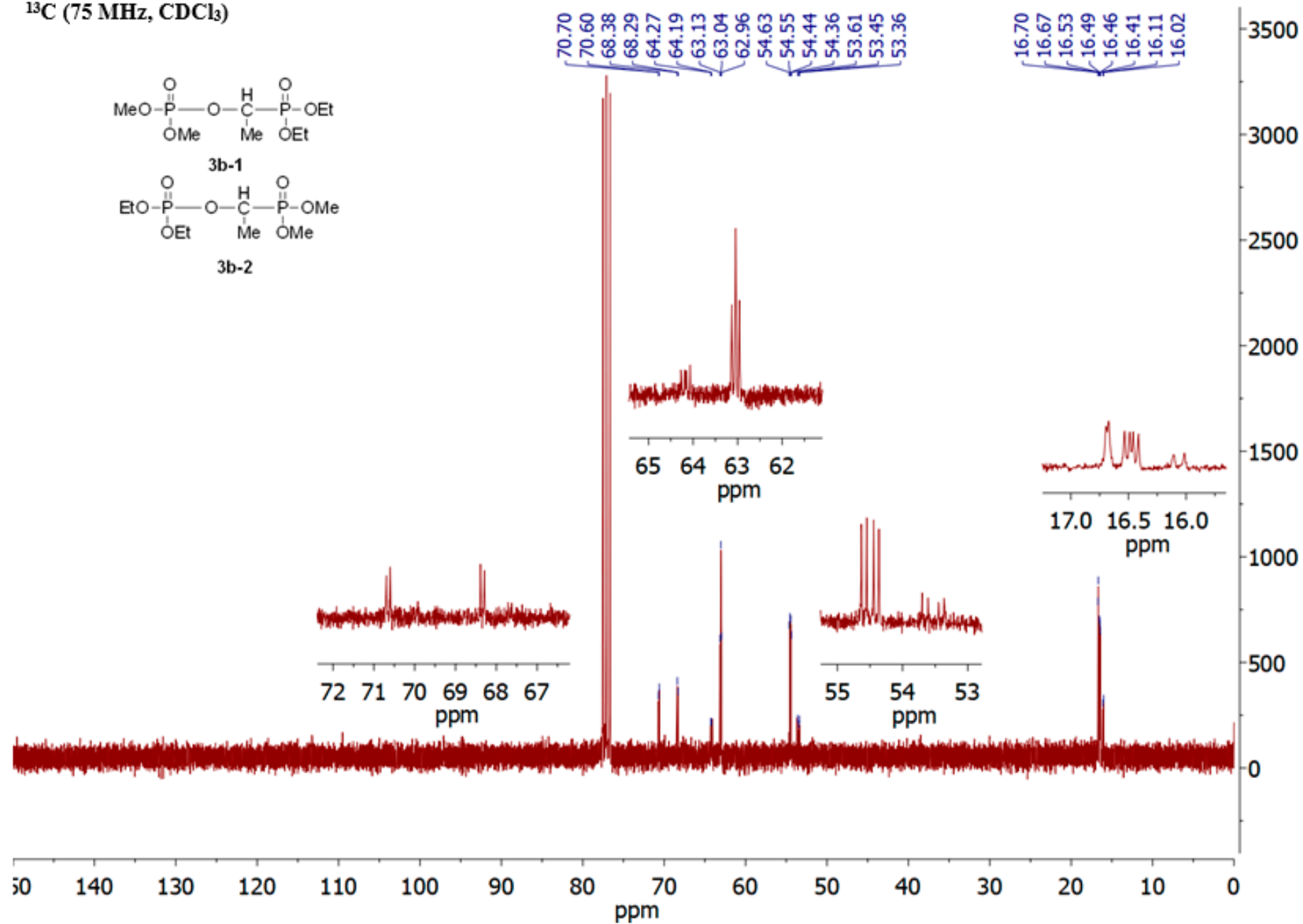
^{13}C (75 MHz, CDCl_3)



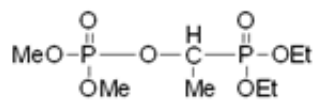
3b-1



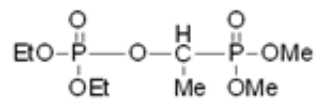
3b-2



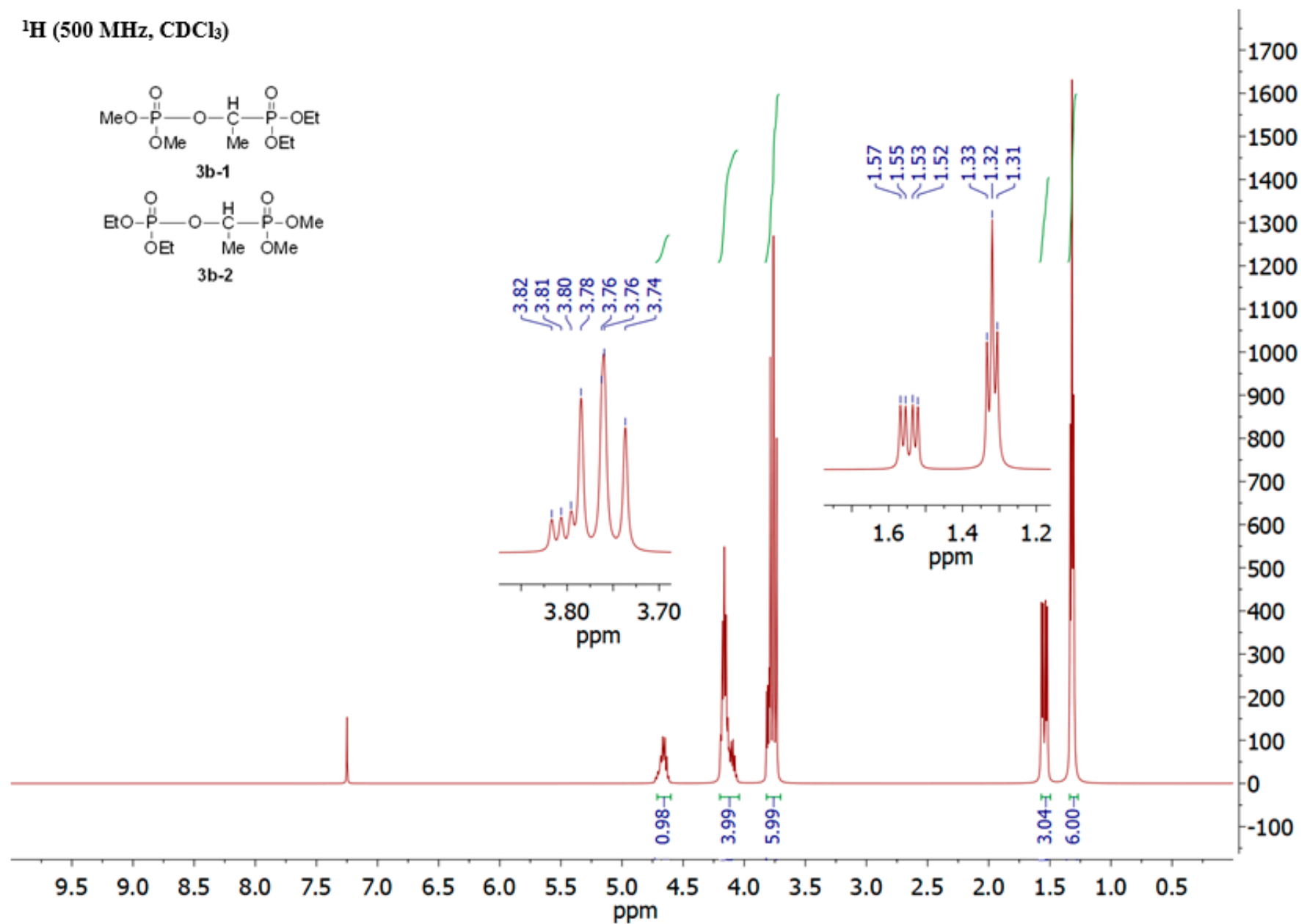
^1H (500 MHz, CDCl_3)



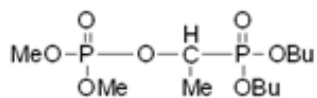
3b-1



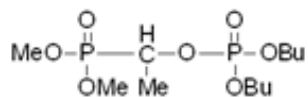
3b-2



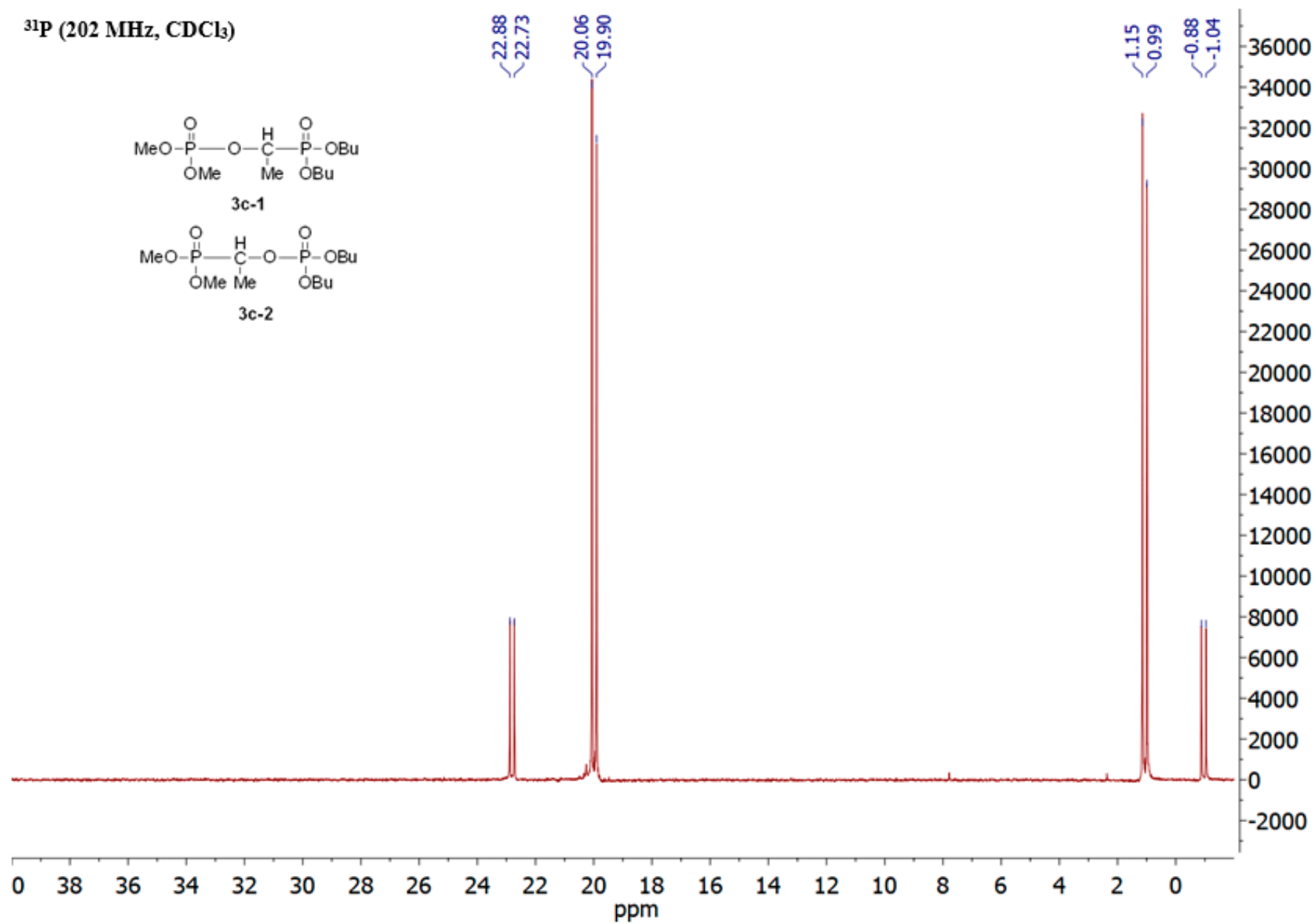
³¹P (202 MHz, CDCl₃)



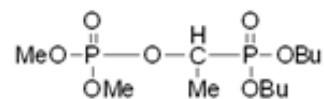
3c-1



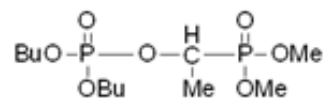
3c-2



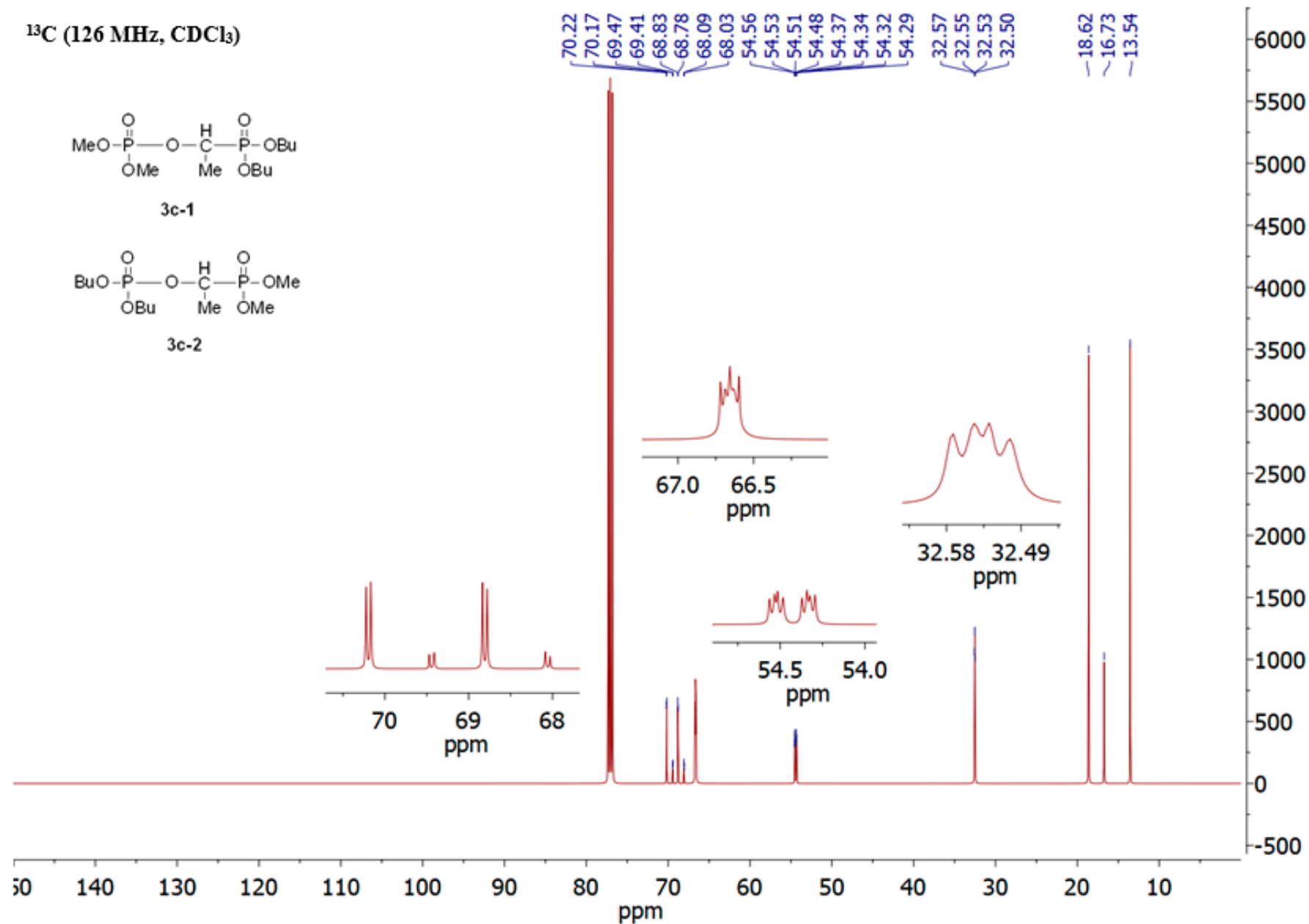
^{13}C (126 MHz, CDCl_3)



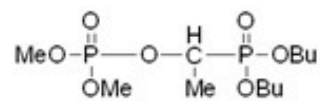
3c-1



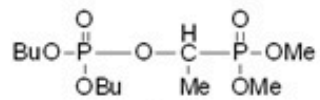
3c-2



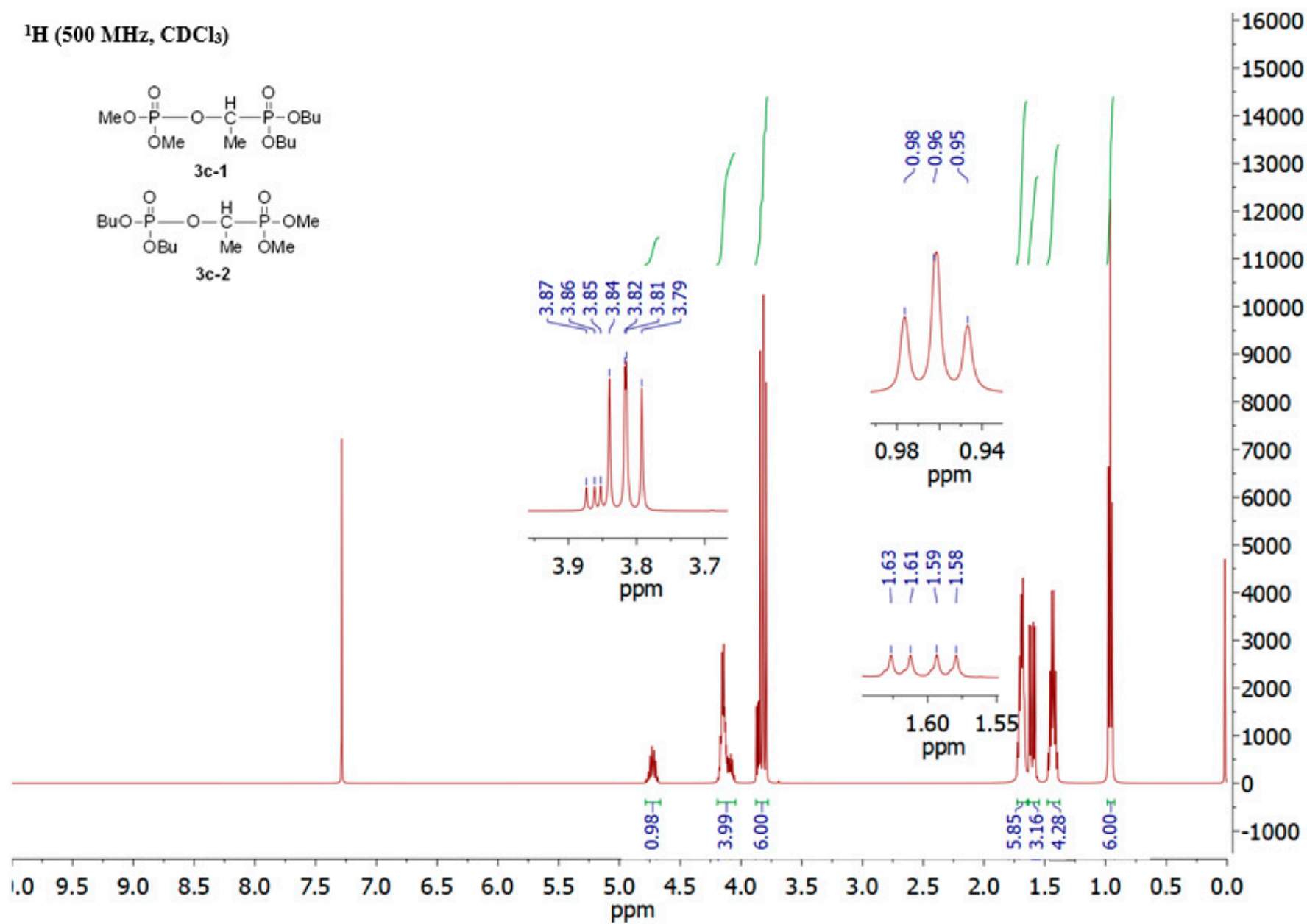
^1H (500 MHz, CDCl_3)

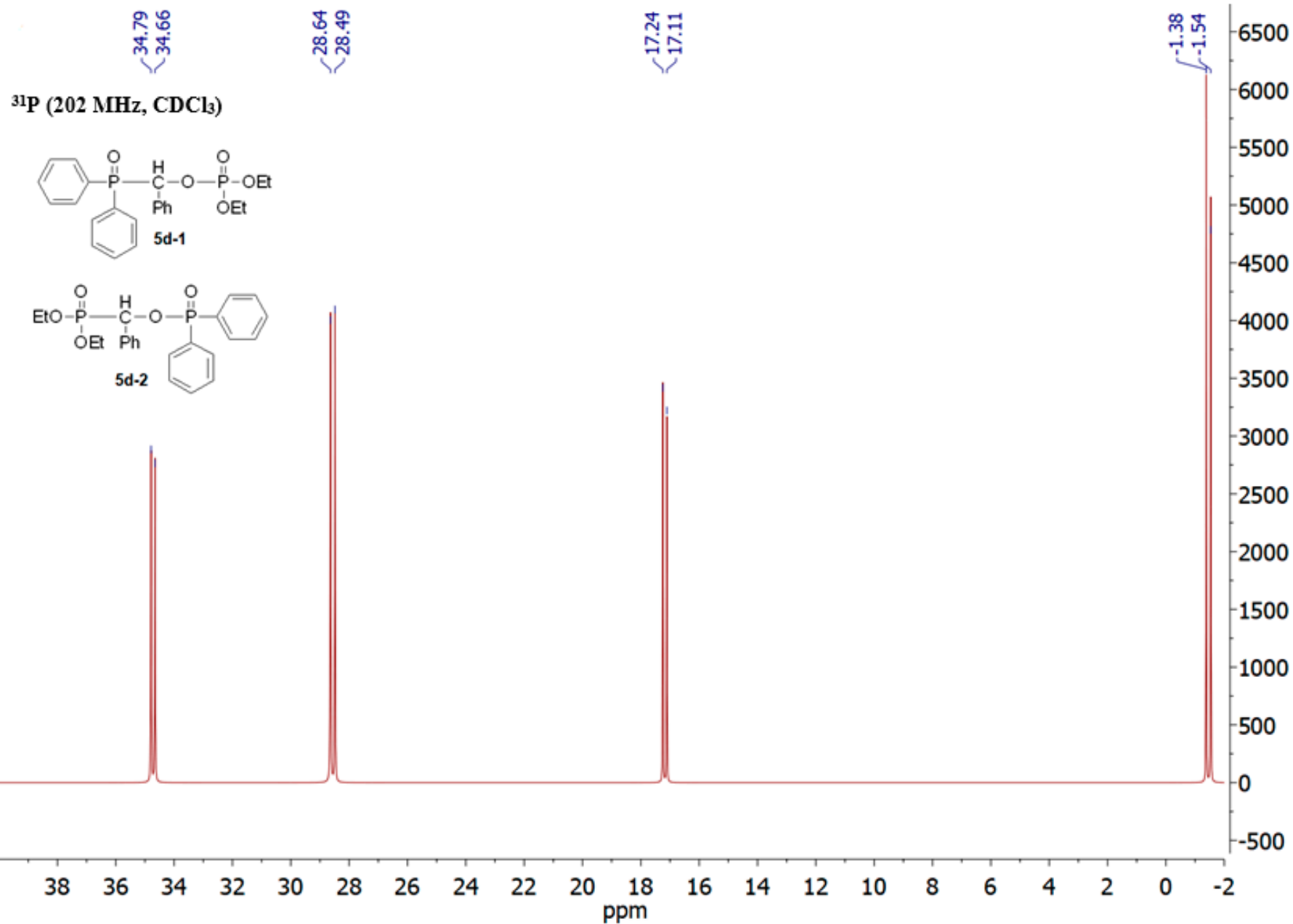


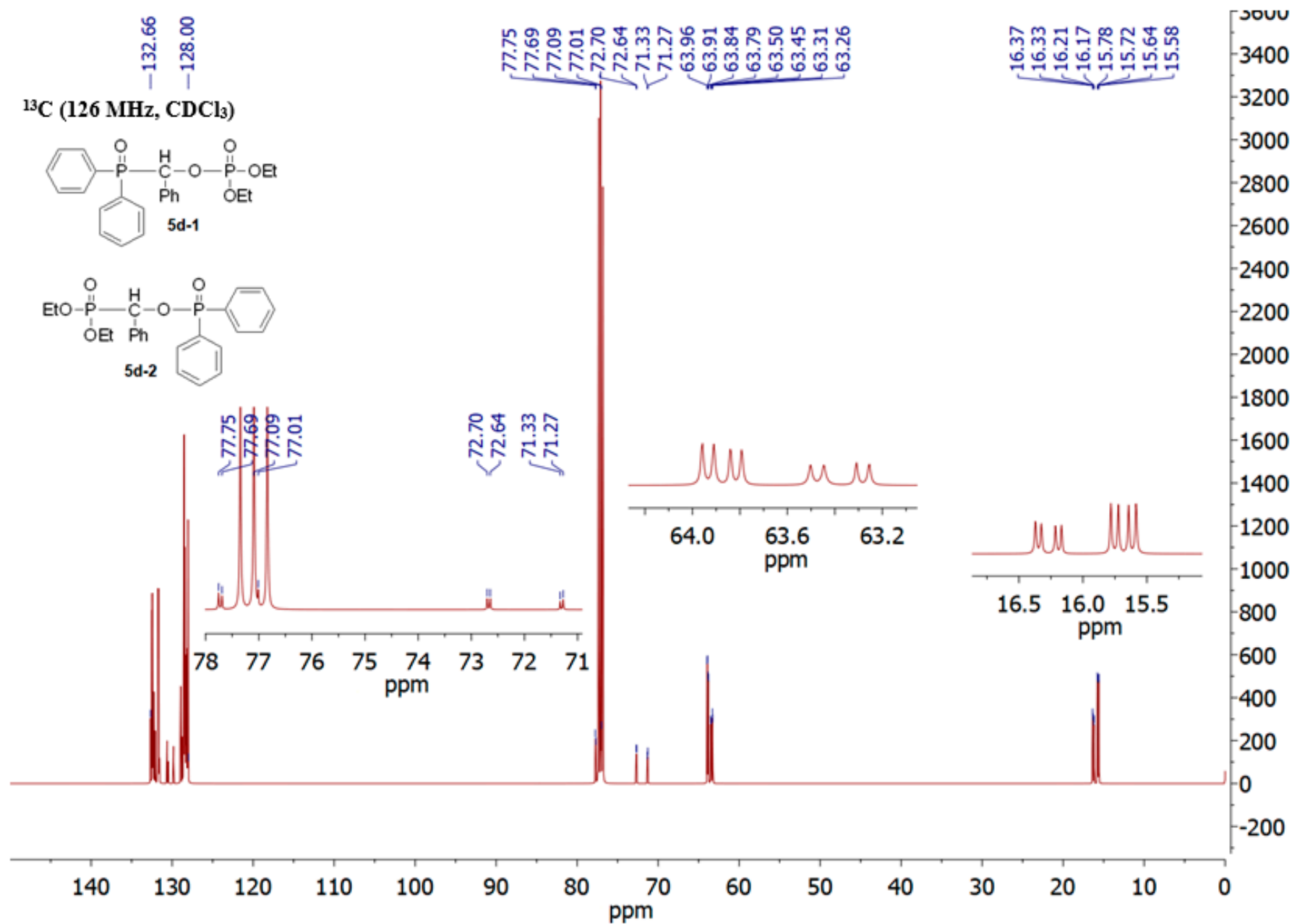
3c-1



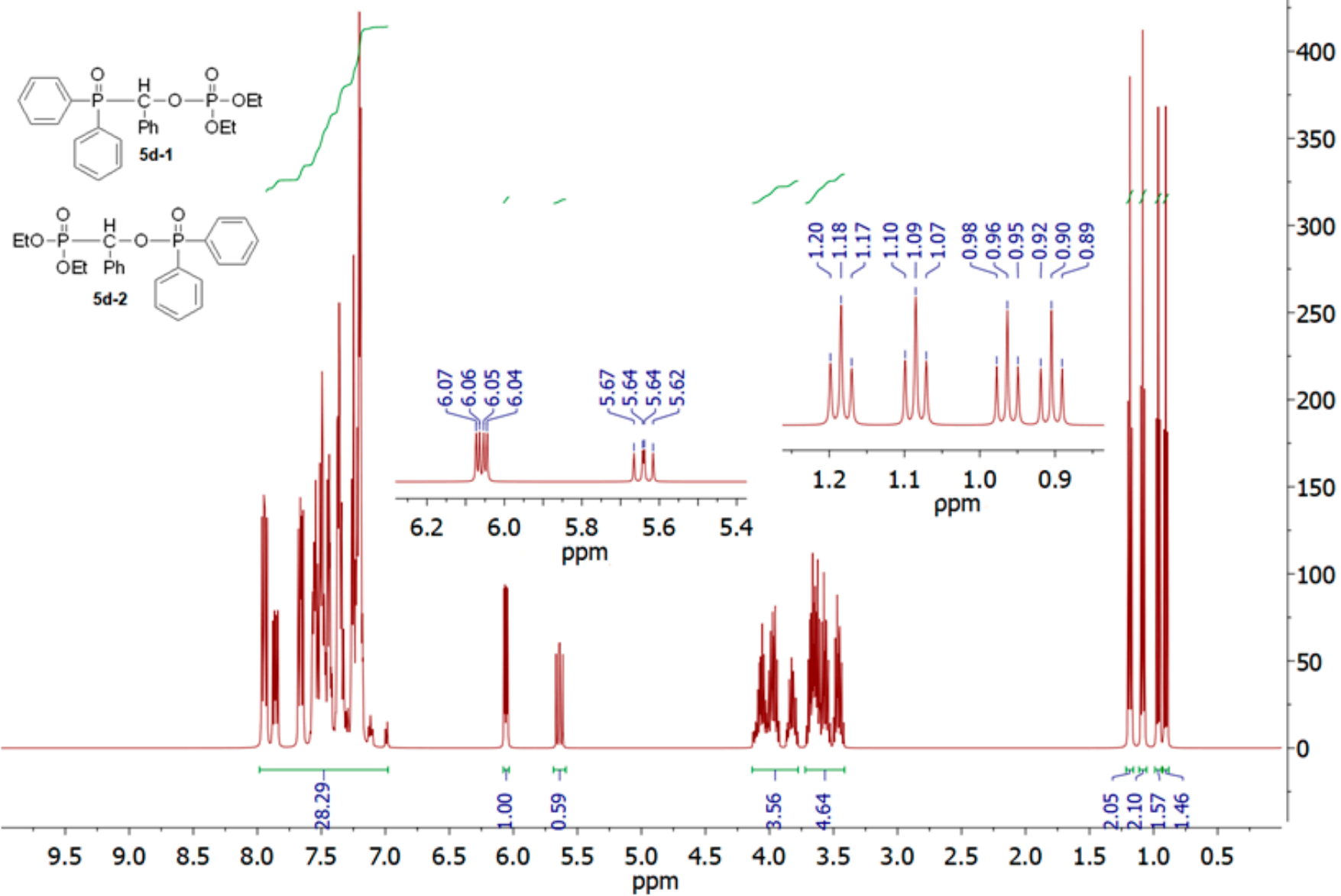
3c-2





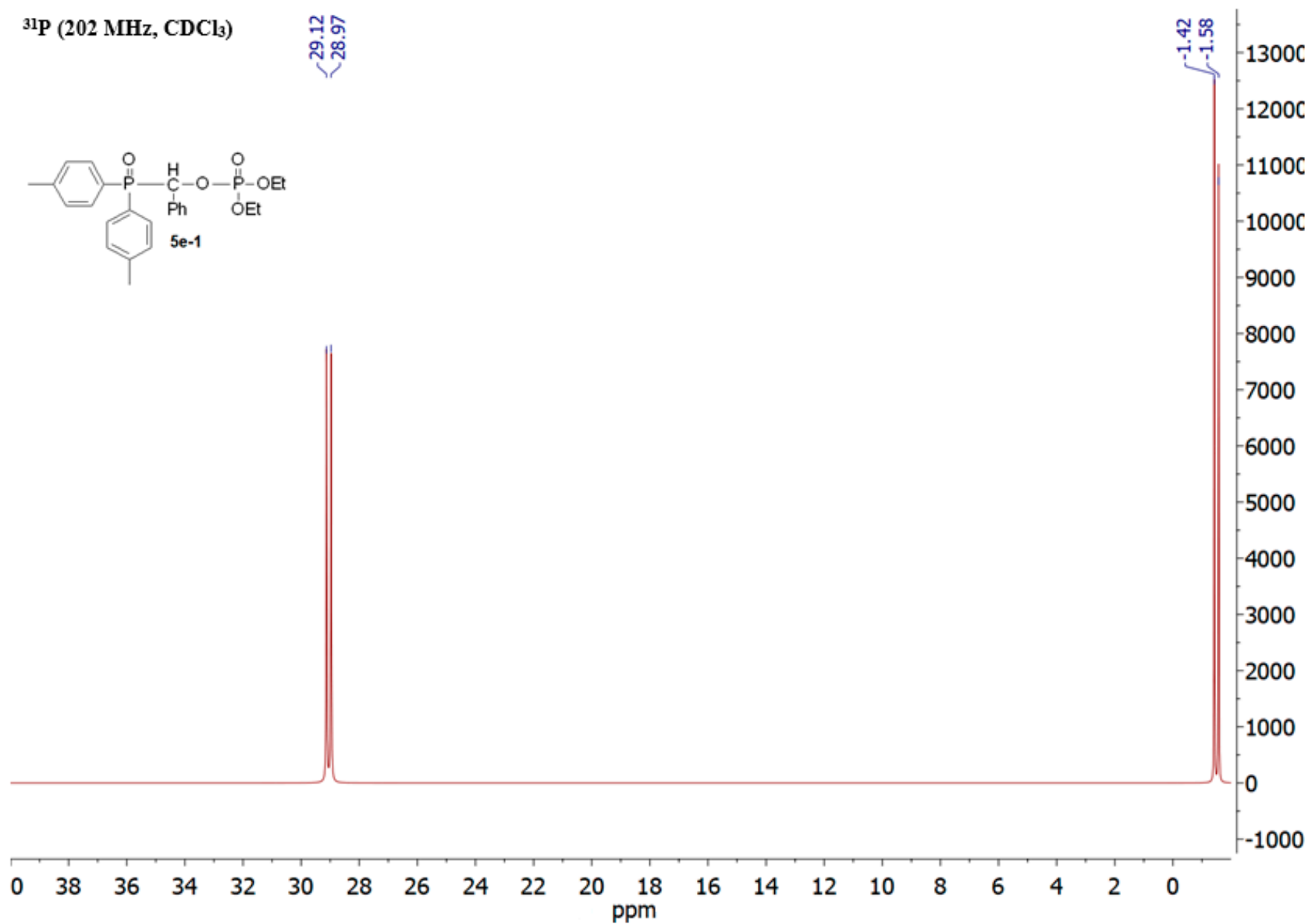
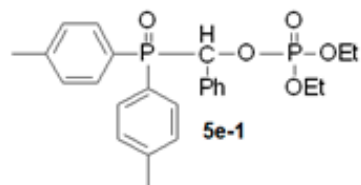


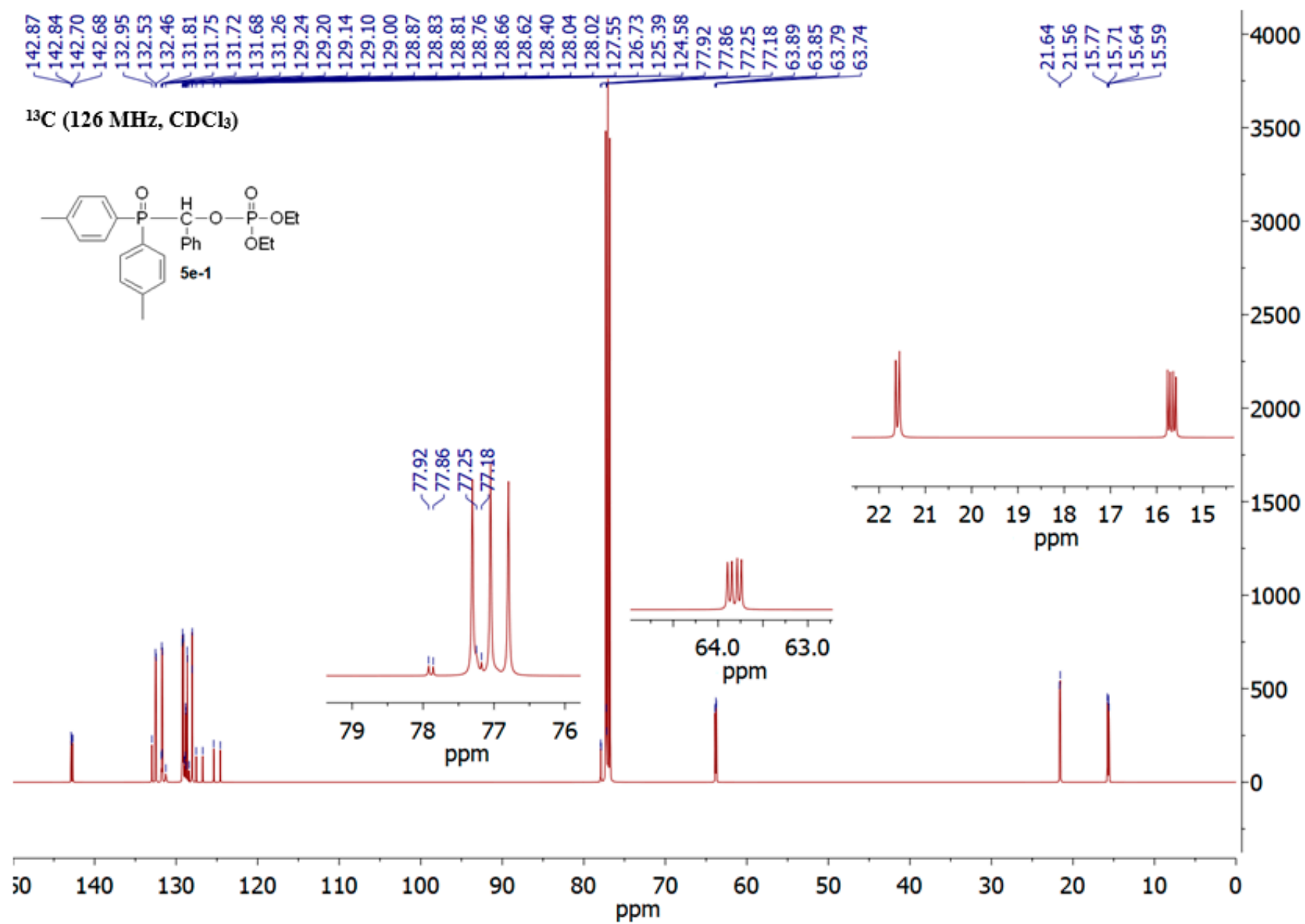
^1H (500 MHz, CDCl_3)



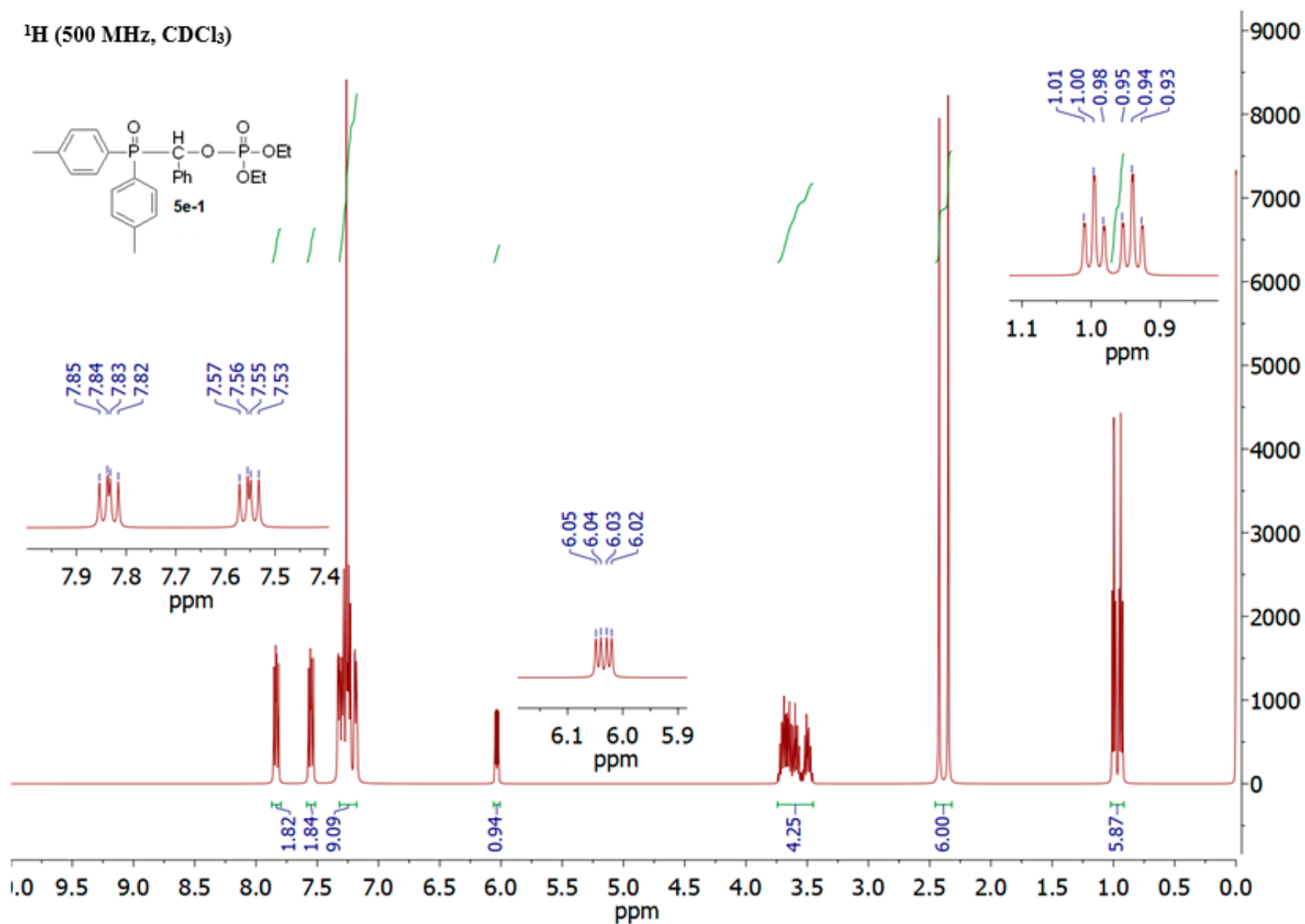
^{31}P (202 MHz, CDCl_3)

29.12
28.97

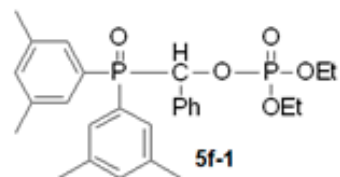




^1H (500 MHz, CDCl_3)



^{31}P (202 MHz, CDCl_3)



5f-1

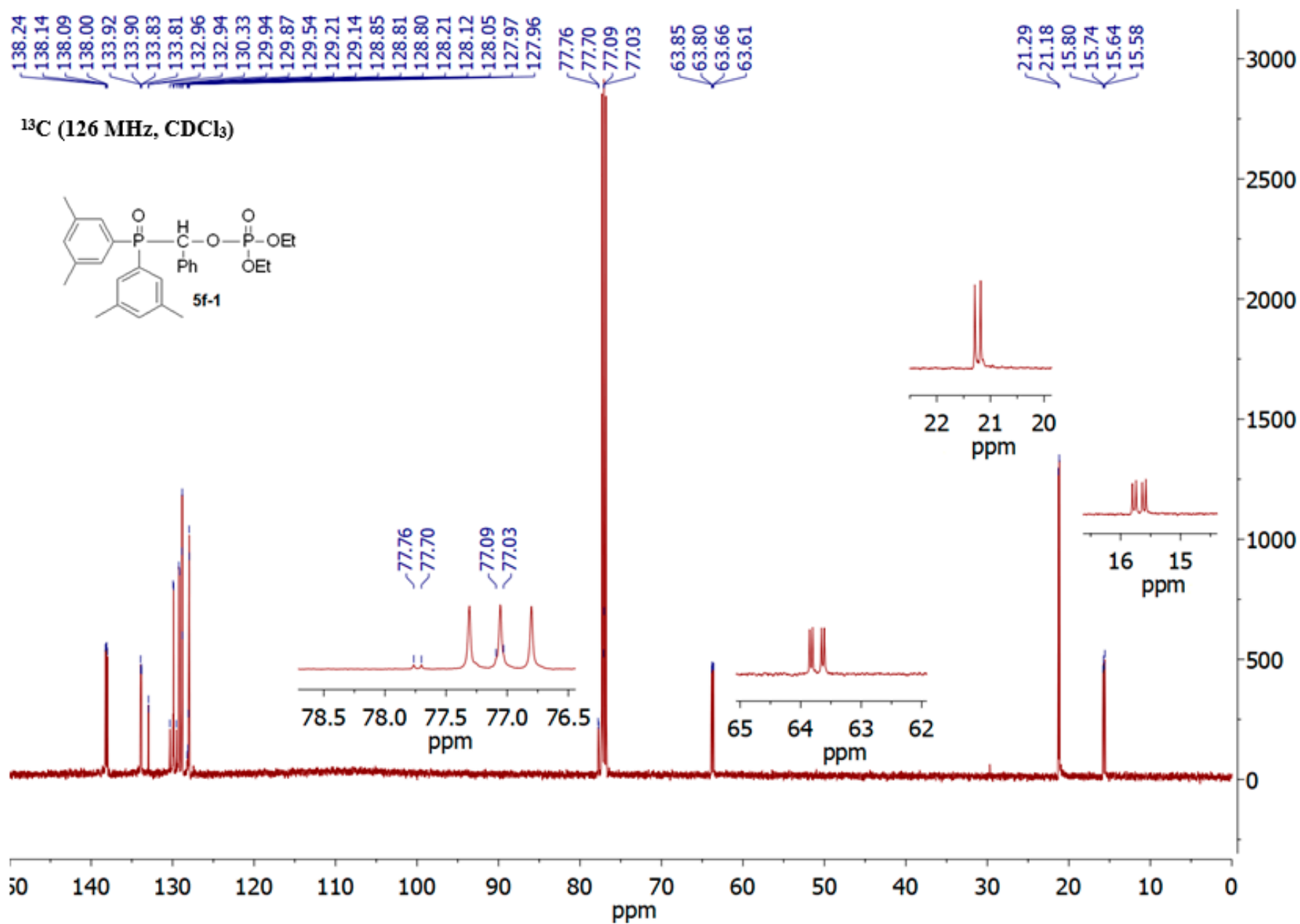
29.10
28.95

-1.19
-1.34

16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000

0 38 36 34 32 30 28 26 24 22 20 18 16 14 12 10 8 6 4 2 0

ppm



^1H (500 MHz, CDCl_3)

