New Linear Precursors of cIDPR Derivatives as Stable Analogs of cADPR: A Potent Second Messenger with Ca^{2+}-Modulating Activity Isolated from Sea Urchin Eggs

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4 Dipartimento di Scienze Biomediche, Università degli Studi di Padova, via Ugo Bassi 58/b, 35131 Padova, Italy
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6 Istituto Veneto di Medicina Molecolare, via Orus 2, 35129 Padova, Italy
7 Dipartimento di Scienze Chimiche, Università degli Studi di Napoli Federico II, via Cintia 26, 80126 Napoli, Italy

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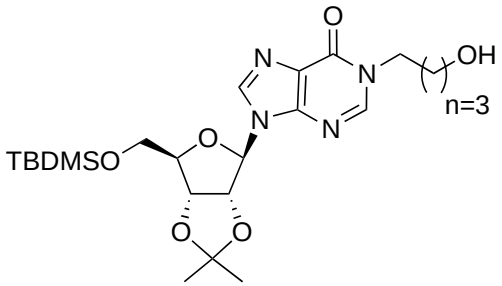
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N
OH
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TBDMSO
O
O
O

8a


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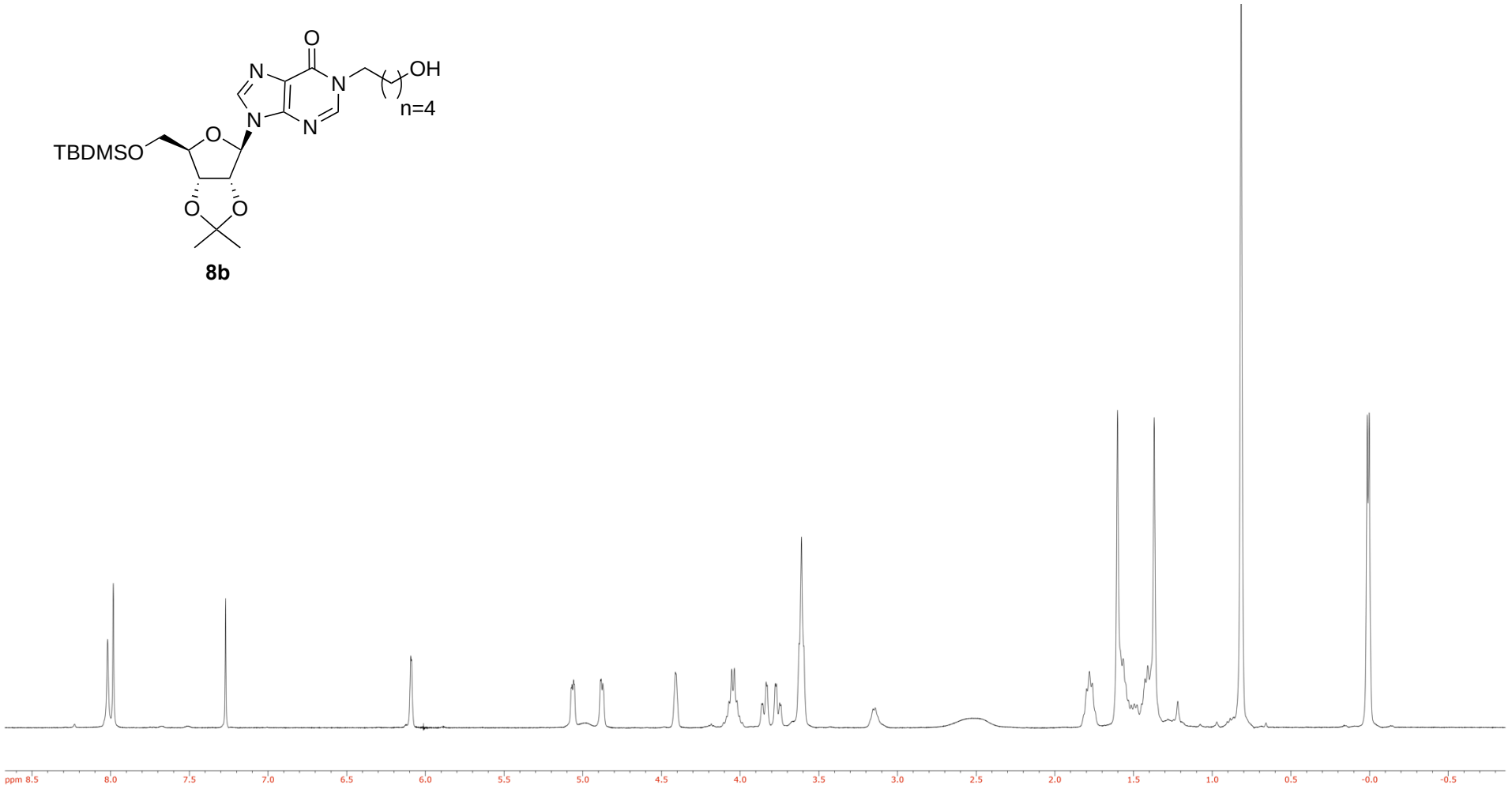
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
-0.0
-0.5

O
N
N
N
N
OH
n=4
TBDMSO
O
O
O

8b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2.5
2.0
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1.0
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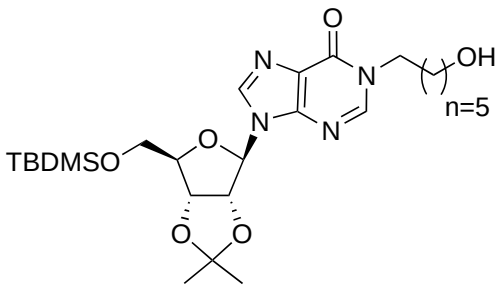
-0.5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N
N
N
N
OH
n=5
TBDMSO
O
O
O

8c


ppm
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8.0
7.5
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6.5
6.0
5.5
5.0
4.5
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3.5
3.0
2.5
2.0
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1.0
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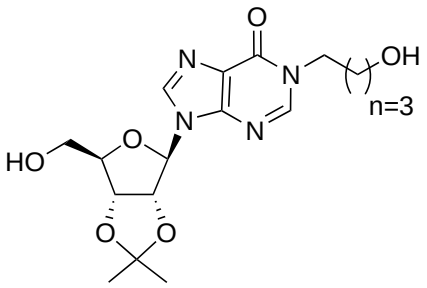
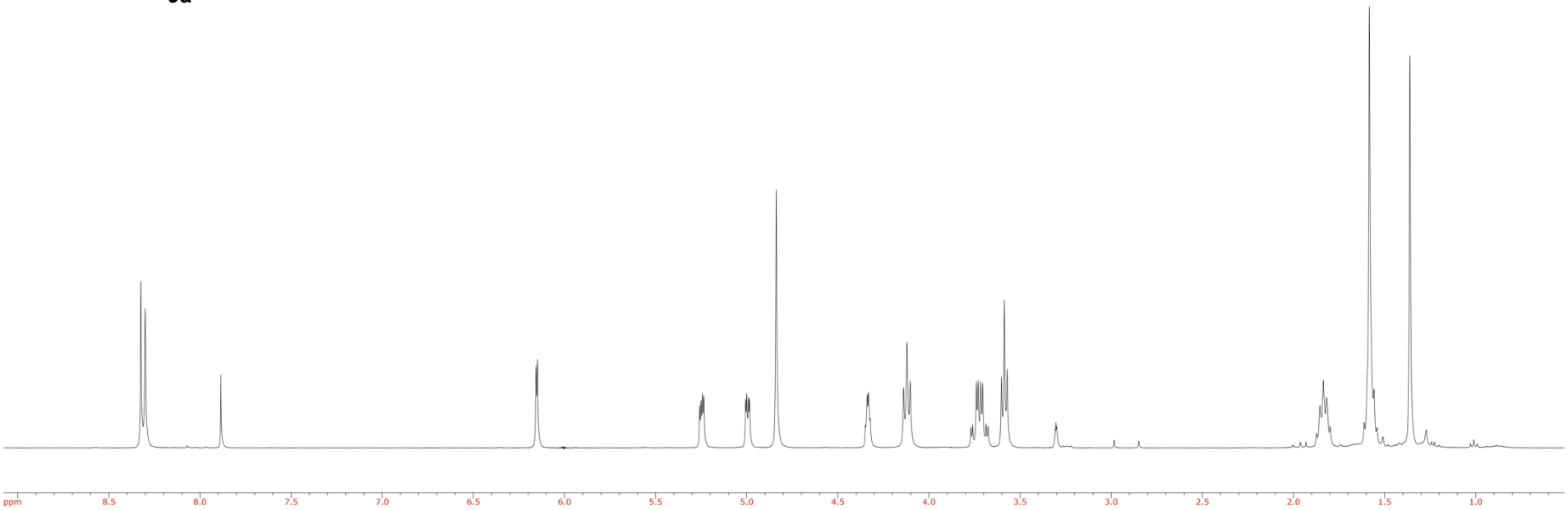
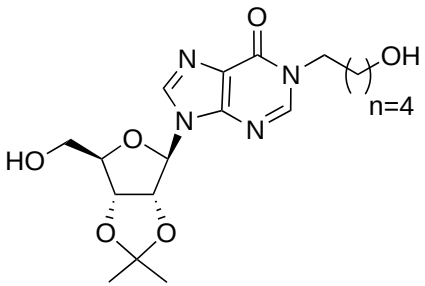
-0.0
-0.5



9a

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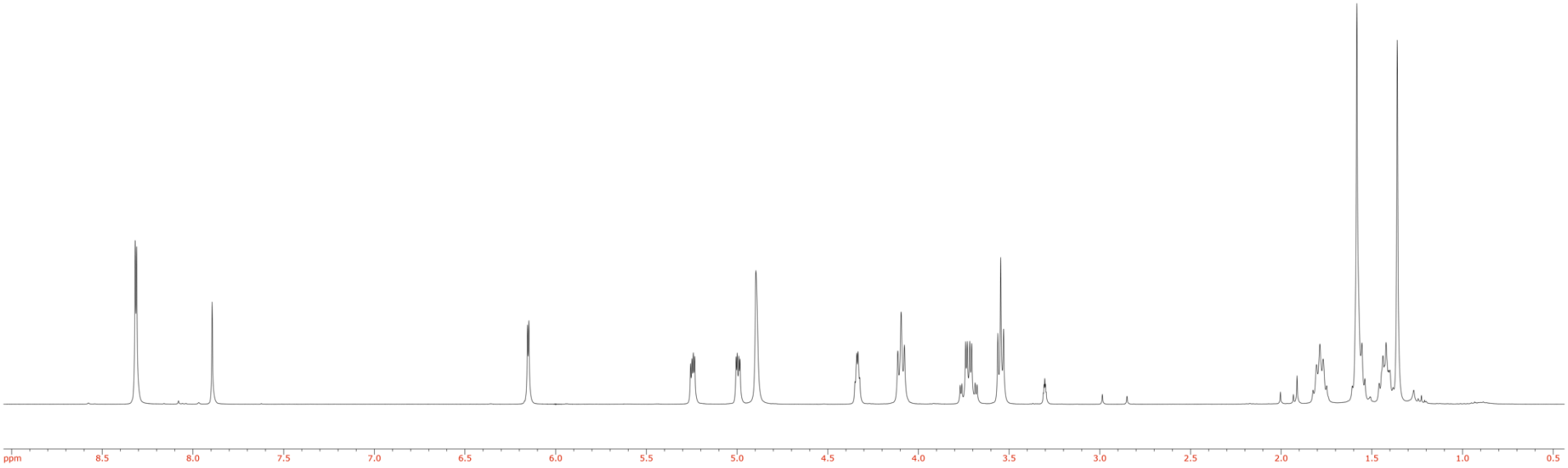
N
OH
n=4
N
N
HO
O
O
O

9b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6.5
6.0
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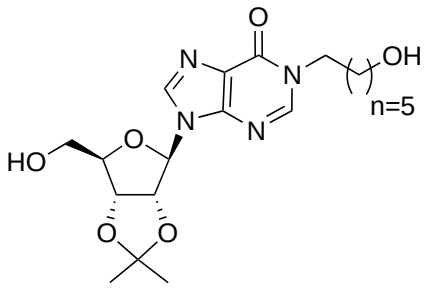
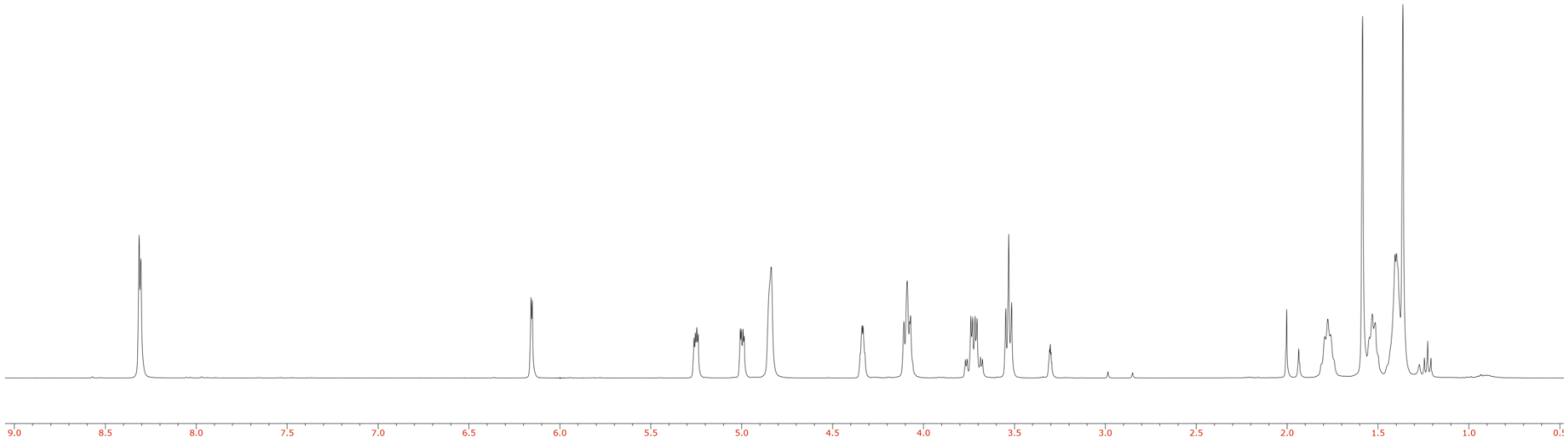
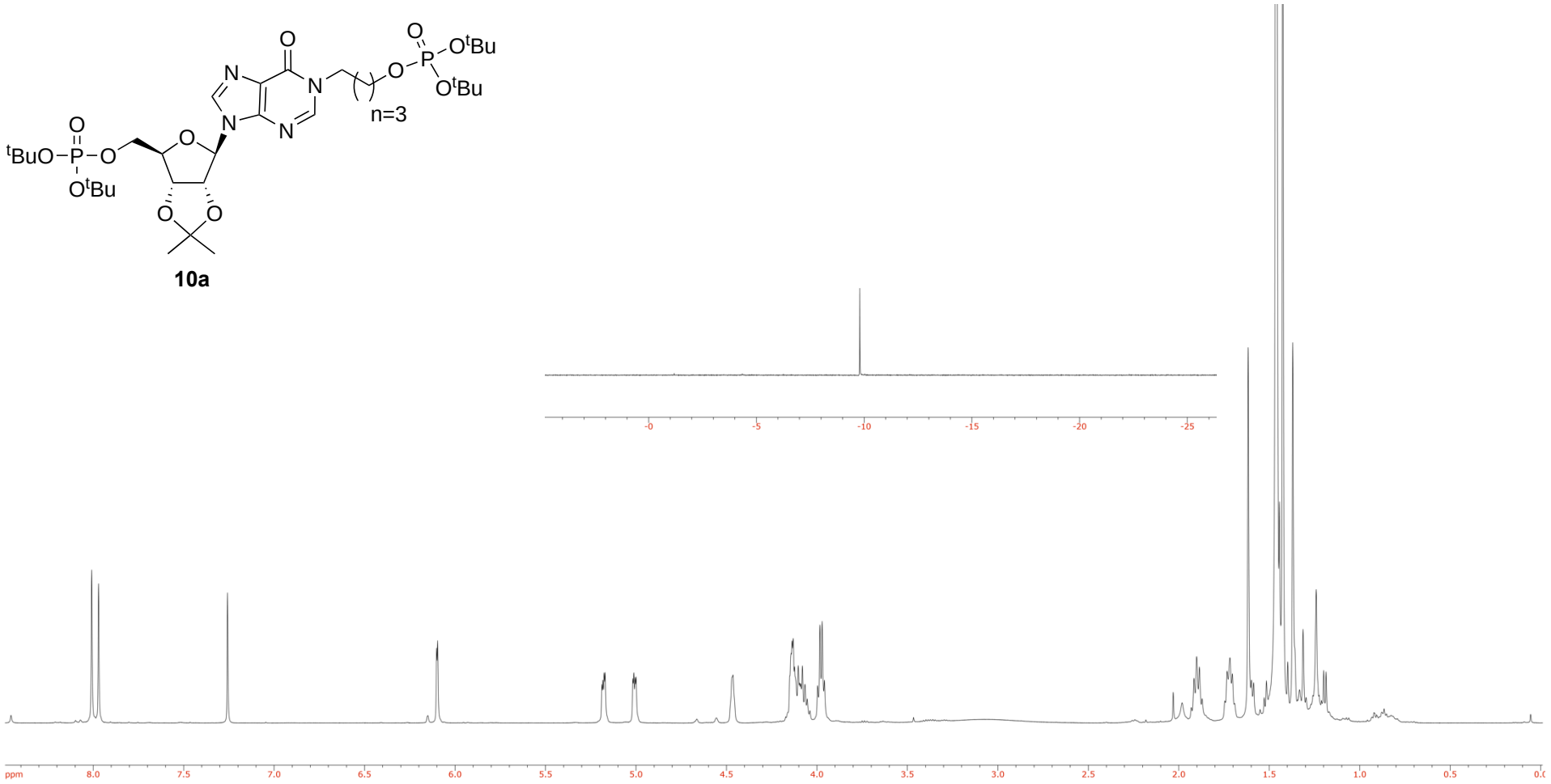
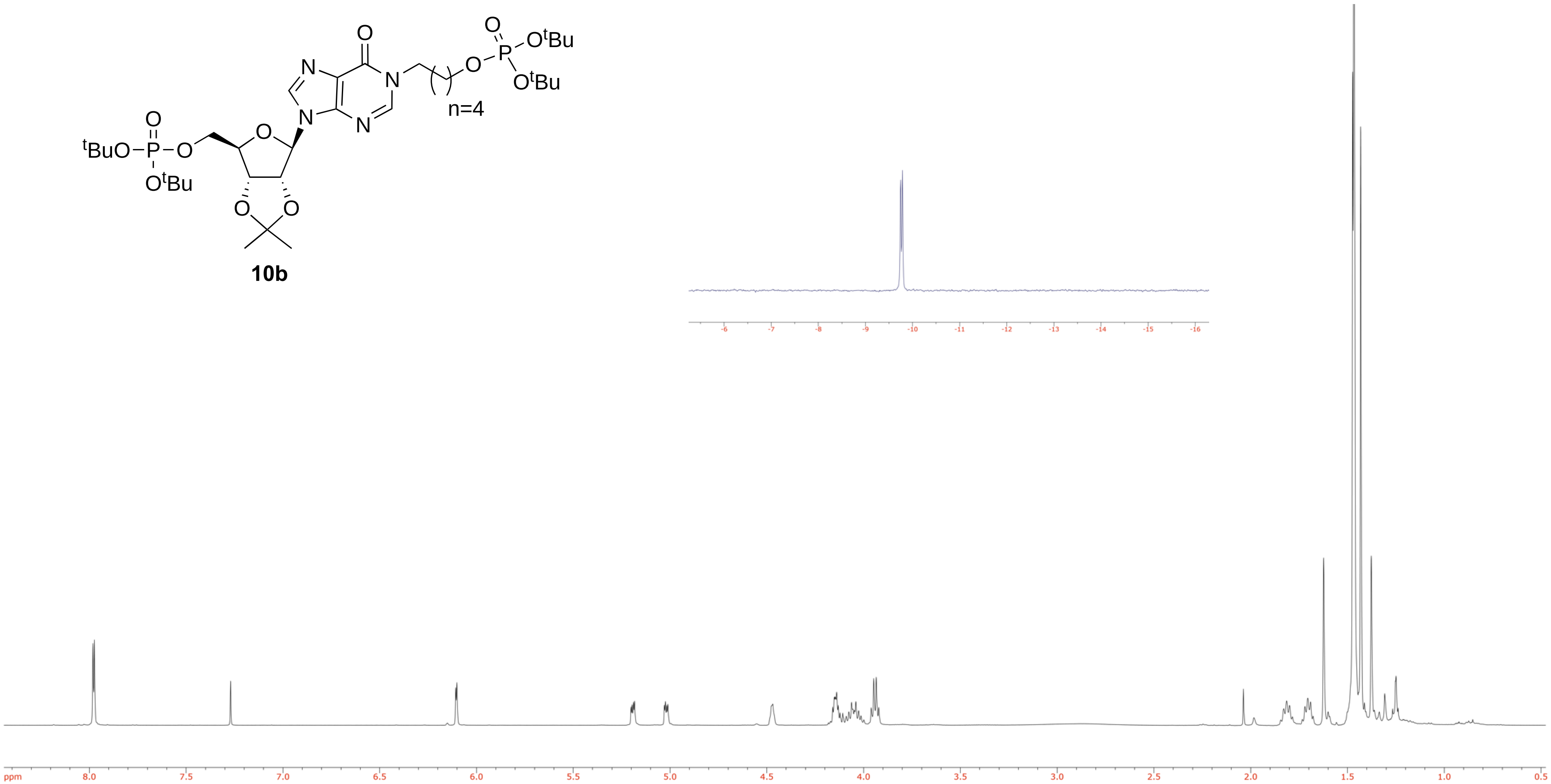
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5



9c




n=3
10a
ppm



O
O
O
N
N
N
N
O
O
O
P
P
O
O
O^tBu
O^tBu
^tBuO
O^tBu
n=4
-6
-7
-8
-9
-10
-11
-12
-13
-14
-15
-16
ppm
8.0
7.5
7.0
6.5
6.0
5.5
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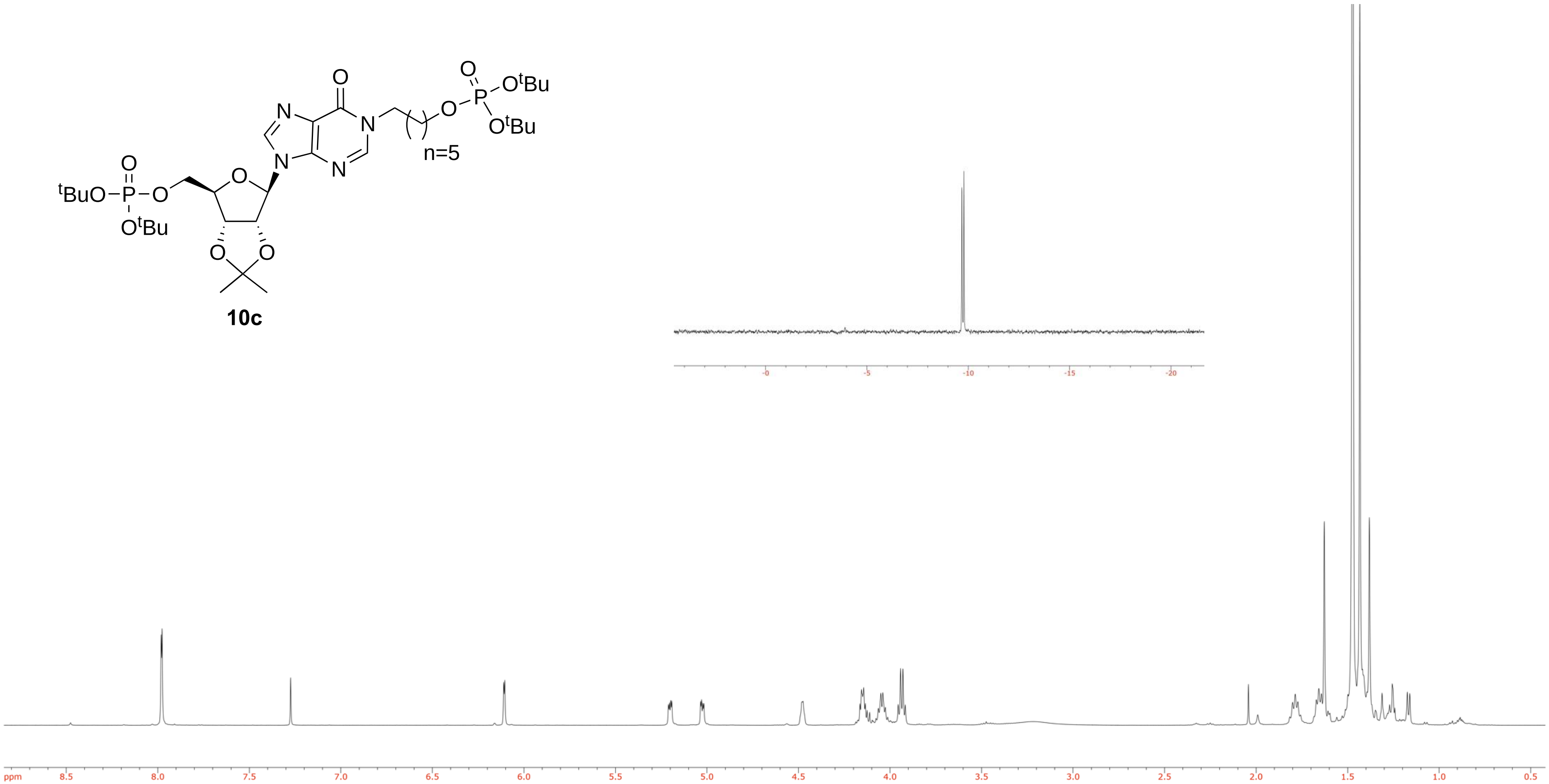
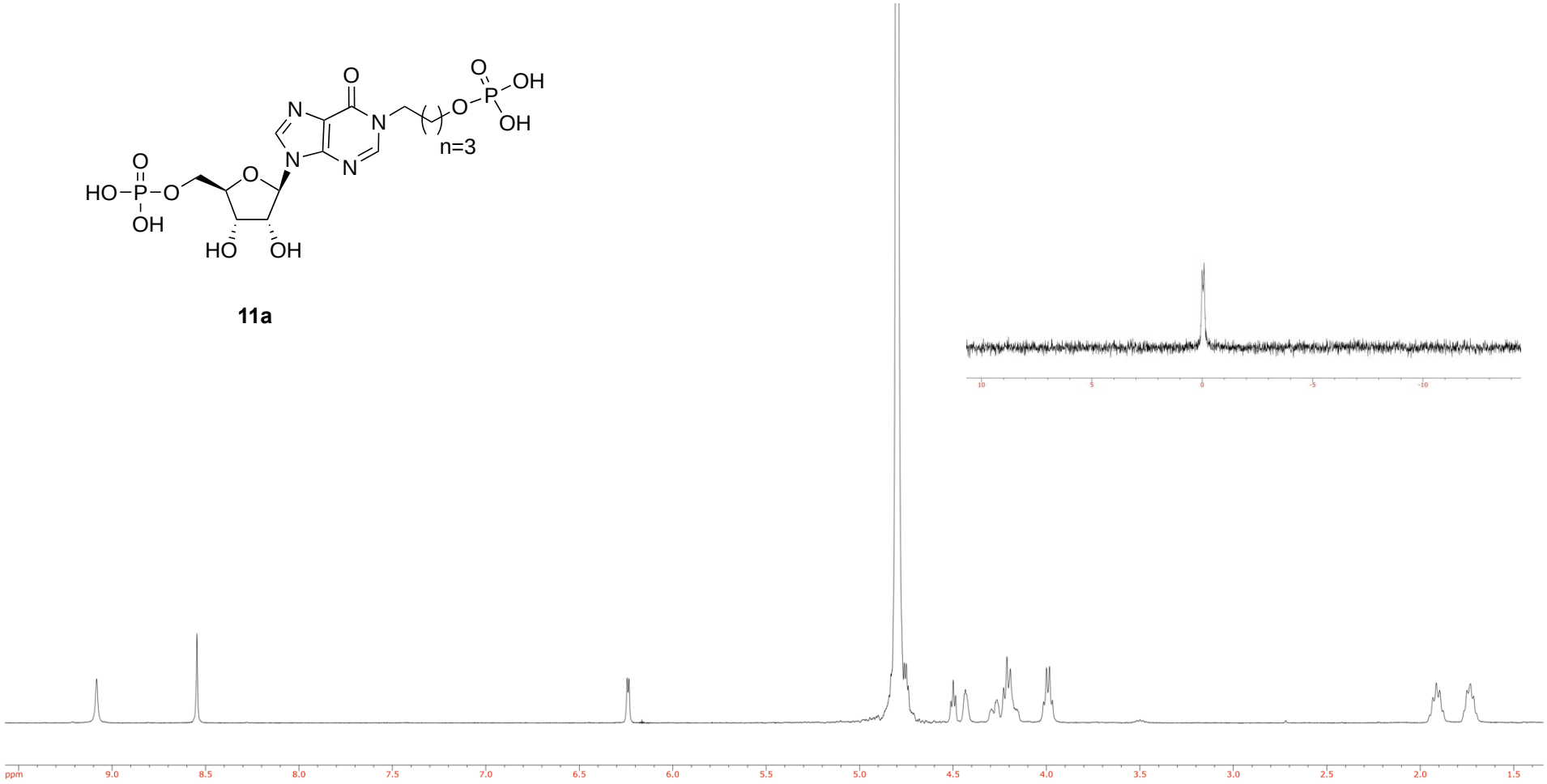
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

10b



10c


O
N
N
N
N
O
O
P
OH
OH
n=3
HO
P
O
OH
O
HO
OH
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

11a

O
N
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N
O
O
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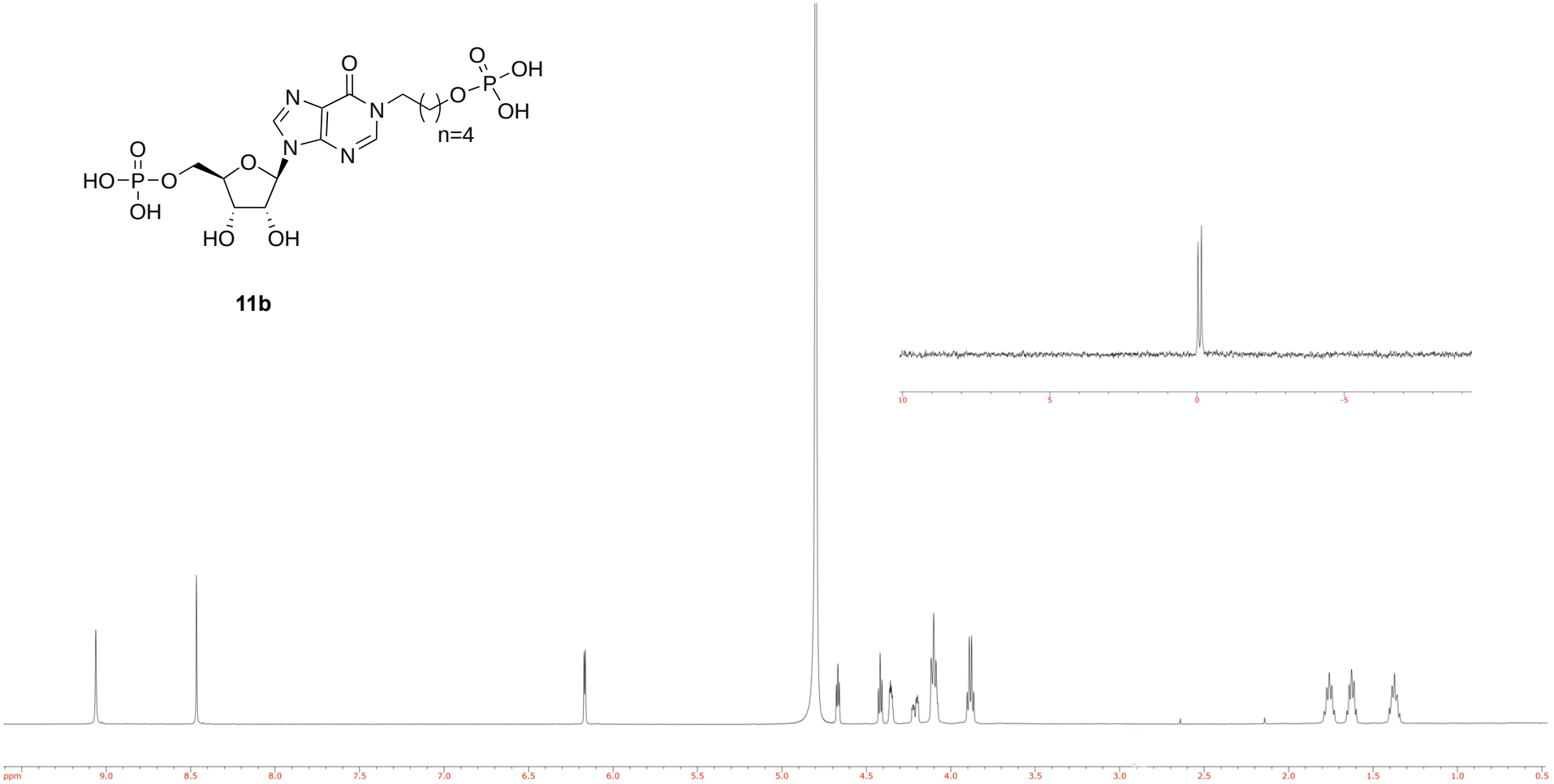
OH
n=4
HO
P
O
OH
O
HO
OH

11b


ppm
9.0
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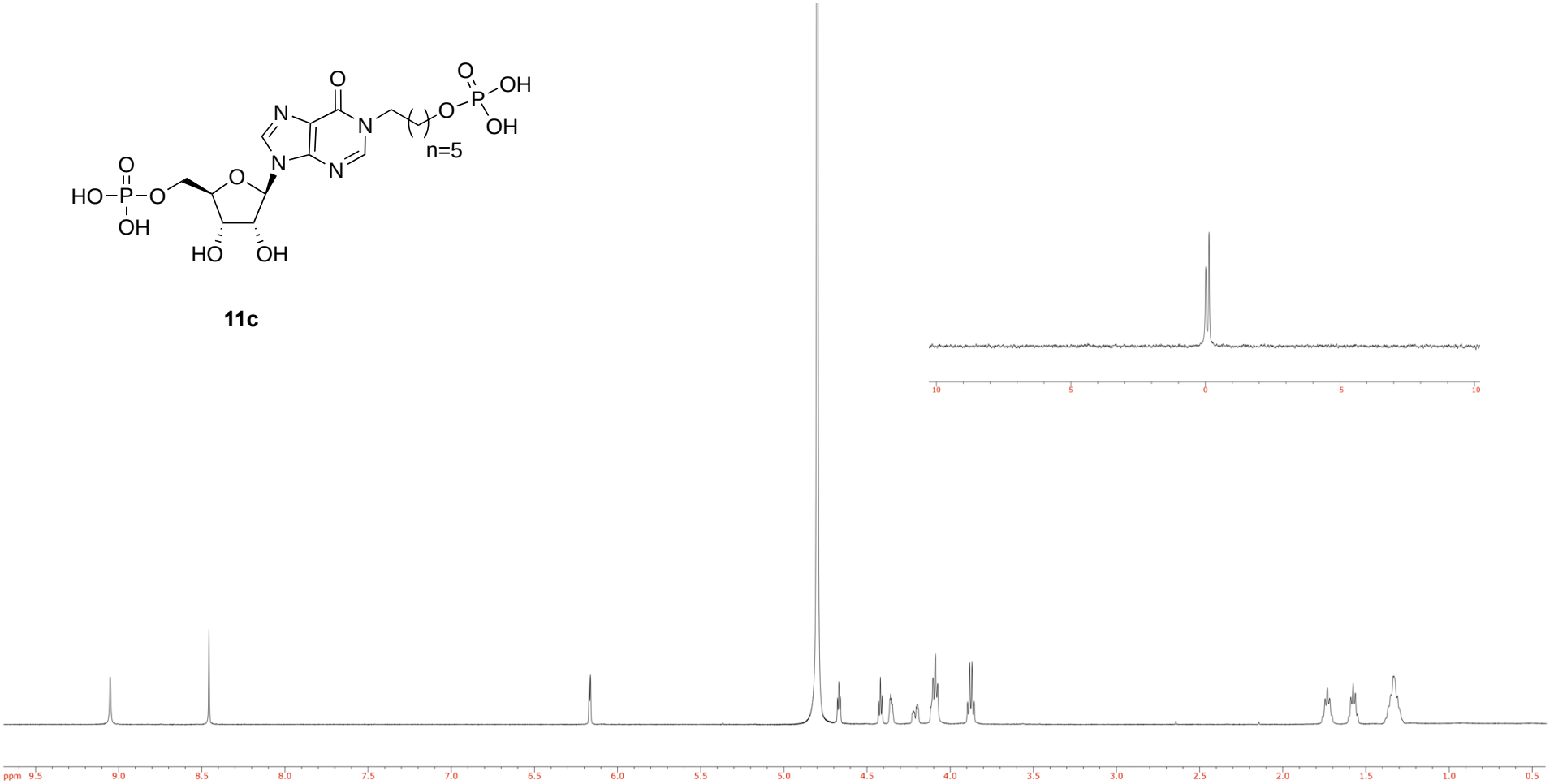
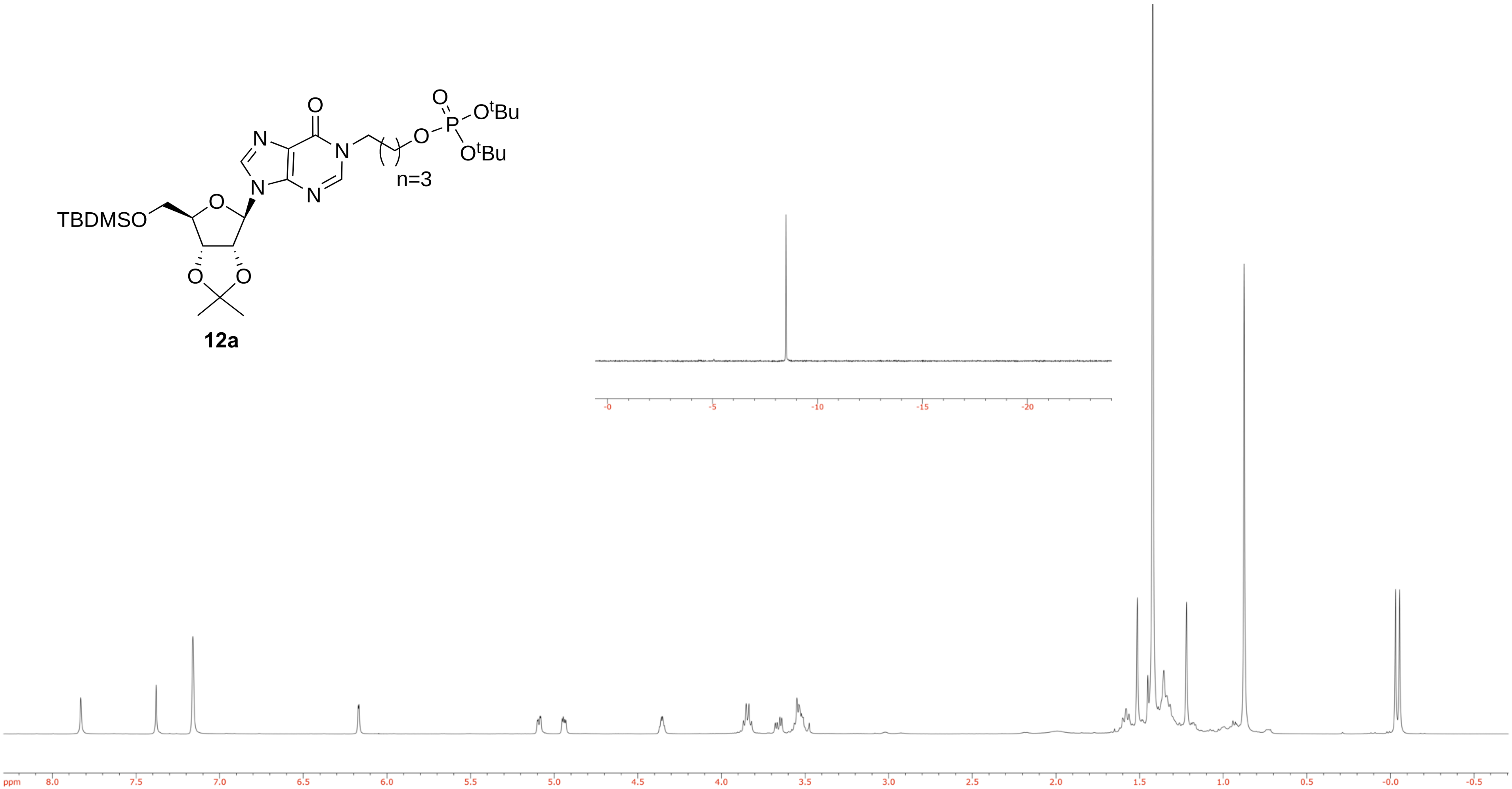
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

O
N
N
N
N
O
O
P
OH
OH
n=5
HO
P
O
OH
O
HO
OH

11c


10
5
0
-5
-10
ppm 9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5


O
N
N
N
N
O
O
P
O
O^{t}Bu
O^{t}Bu
n=3
TBDMSO
O
O
O
-0
-5
-10
-15
-20
ppm
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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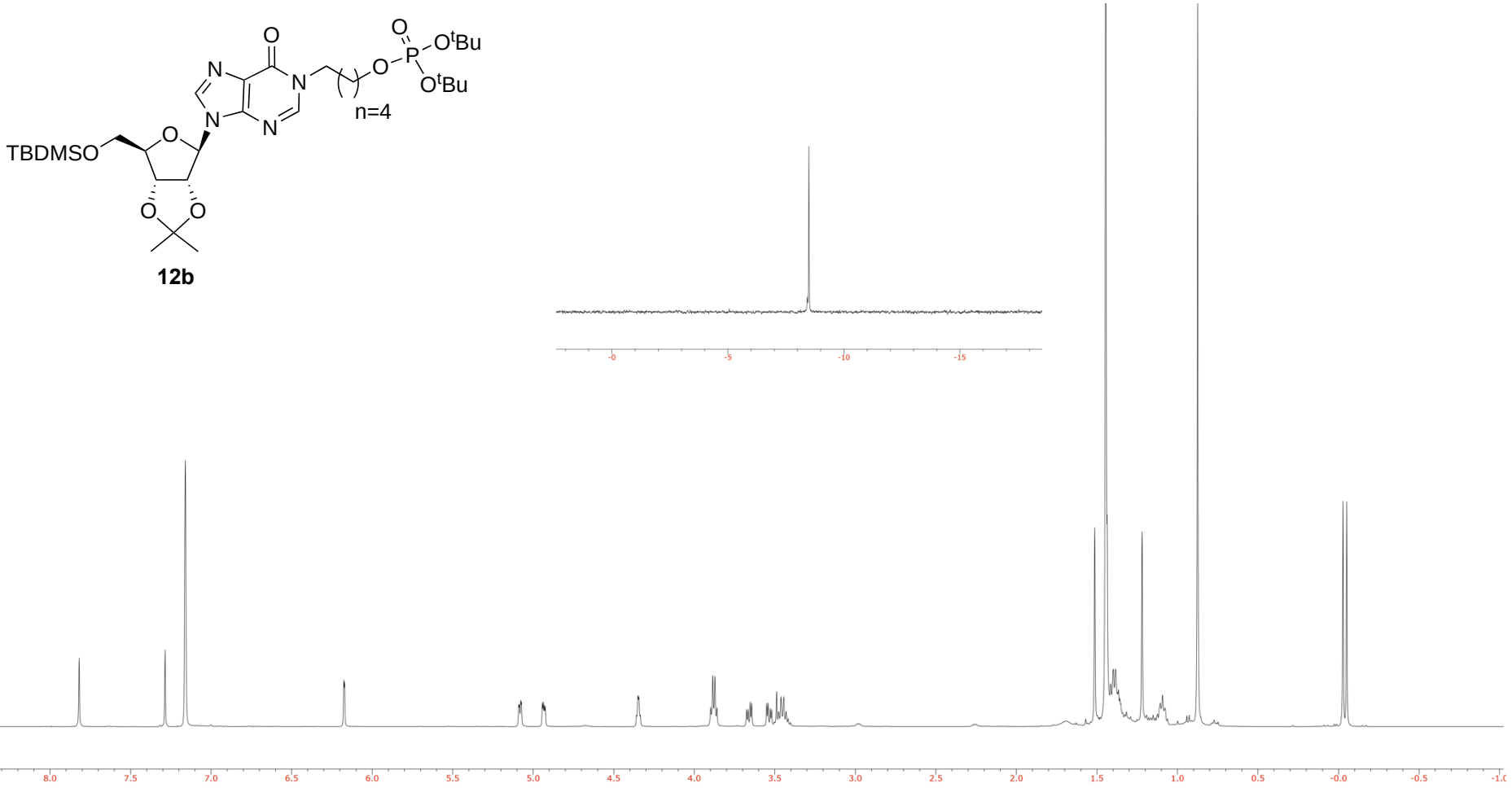
3.0
2.5
2.0
1.5
1.0
0.5
-0.0
-0.5

12a


TBDMSO
O
N
N
N
N
O
O
O
O
P
O^{t}Bu
O^{t}Bu
n=4
ppm
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7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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1.5
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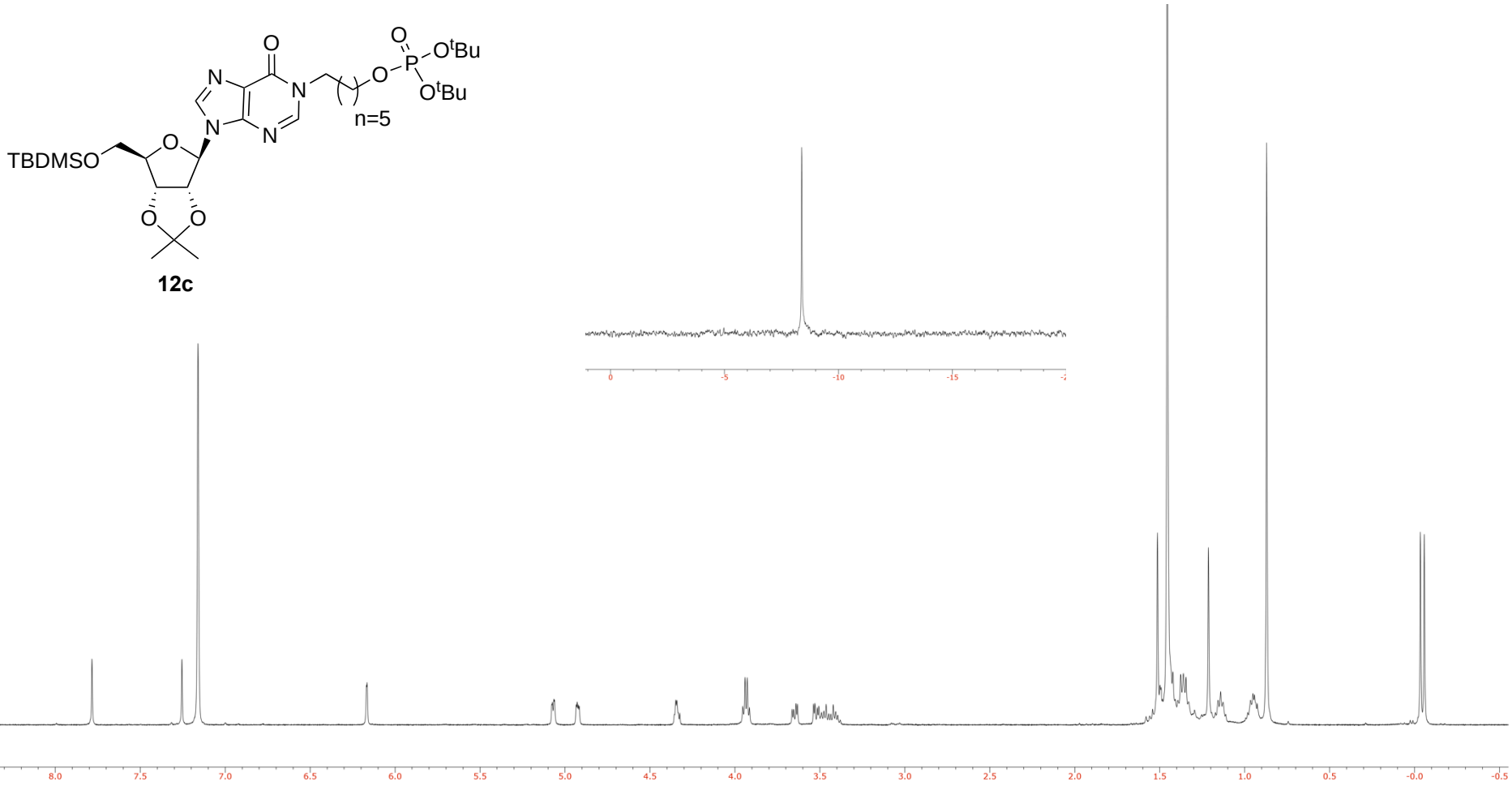
-0.0
-0.5
-0
-5
-10
-15

12b


TBDMSO
O
N
N
N
N
O
O
O
O
P
O^{t}Bu
O^{t}Bu
n=5
12c
ppm
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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3.0
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2.0
1.5
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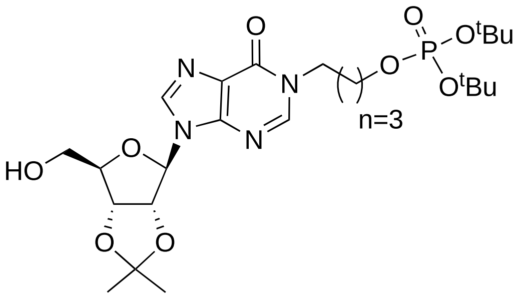
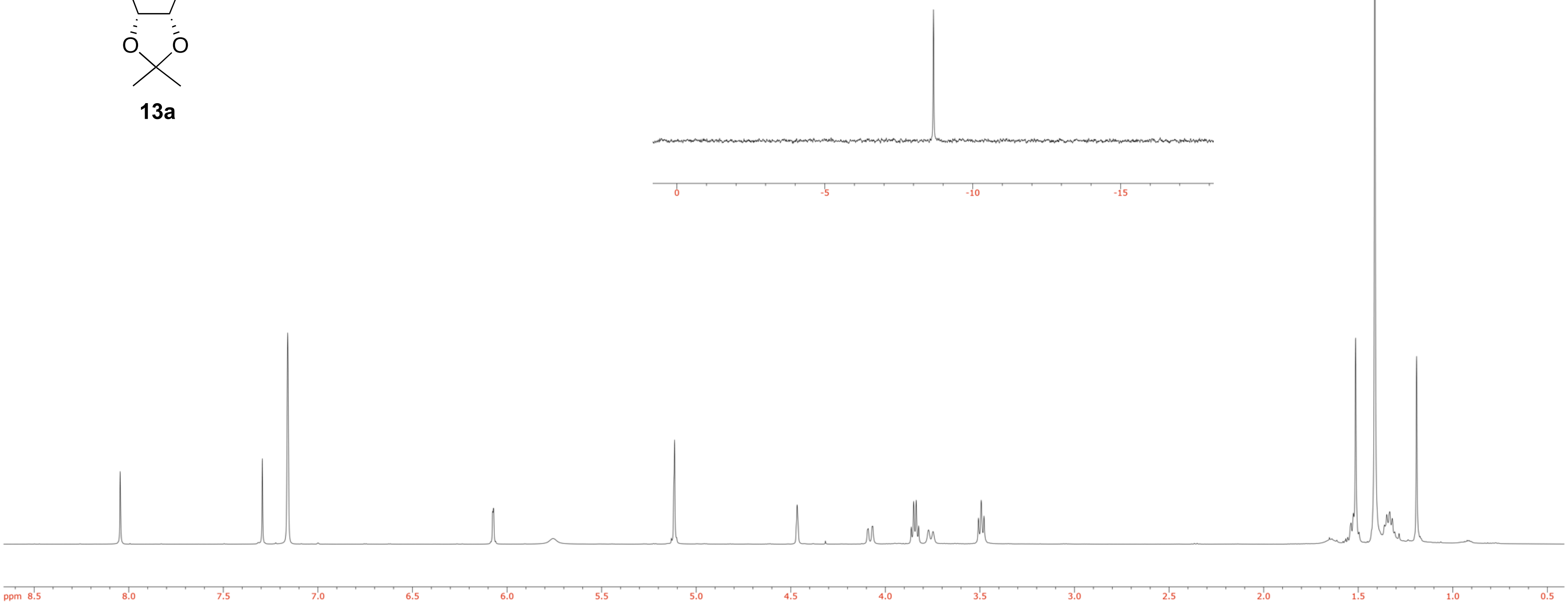
0
-5
-10
-15



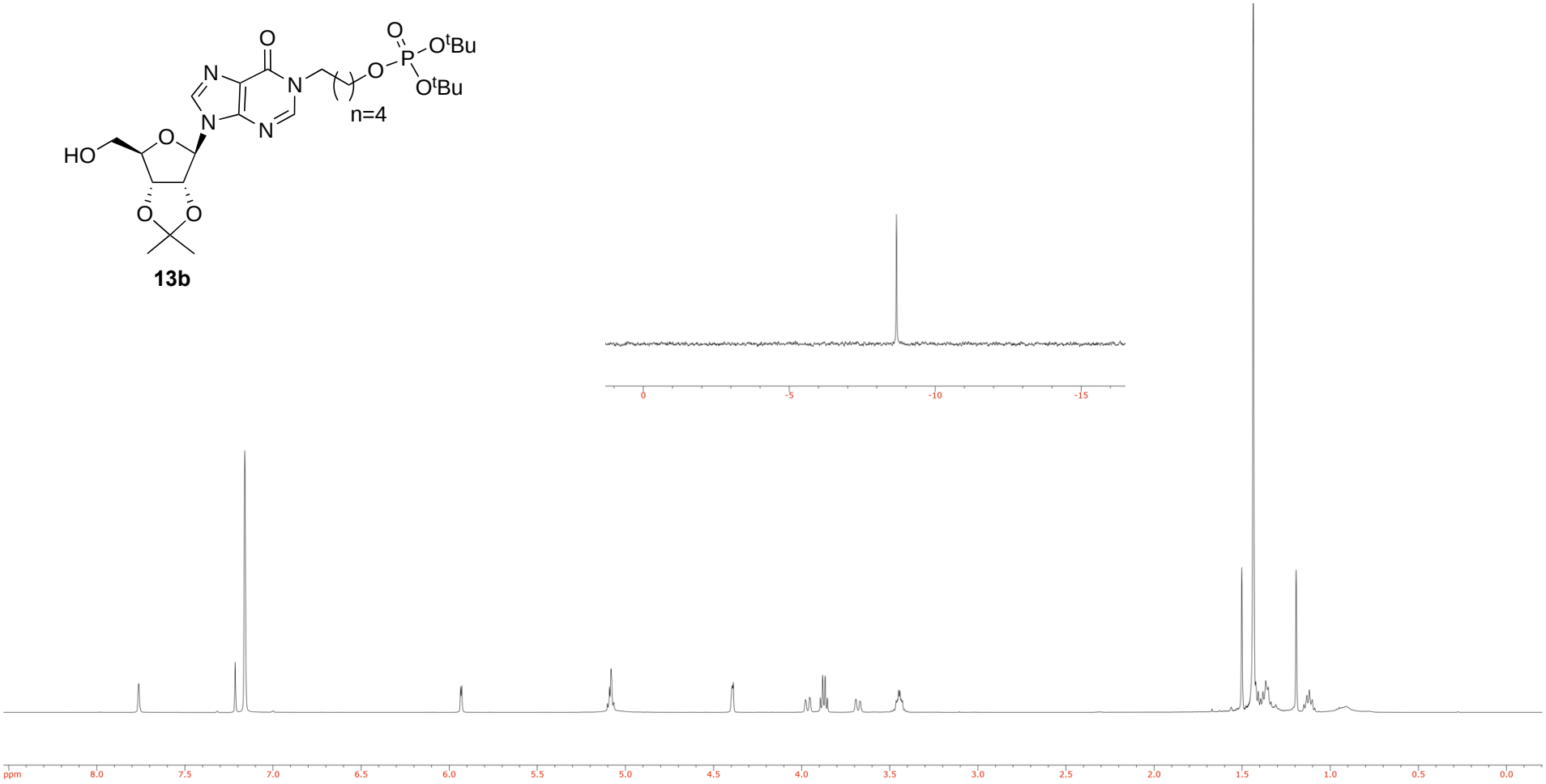
13a



O
N
N
N
N
O
O
P
O^{t}Bu
O^{t}Bu
n=4
HO
O
O
O

13b

0
-5
-10
-15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4.5
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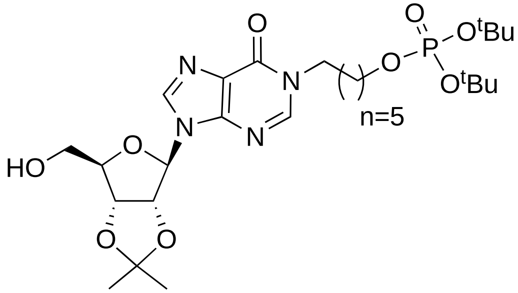
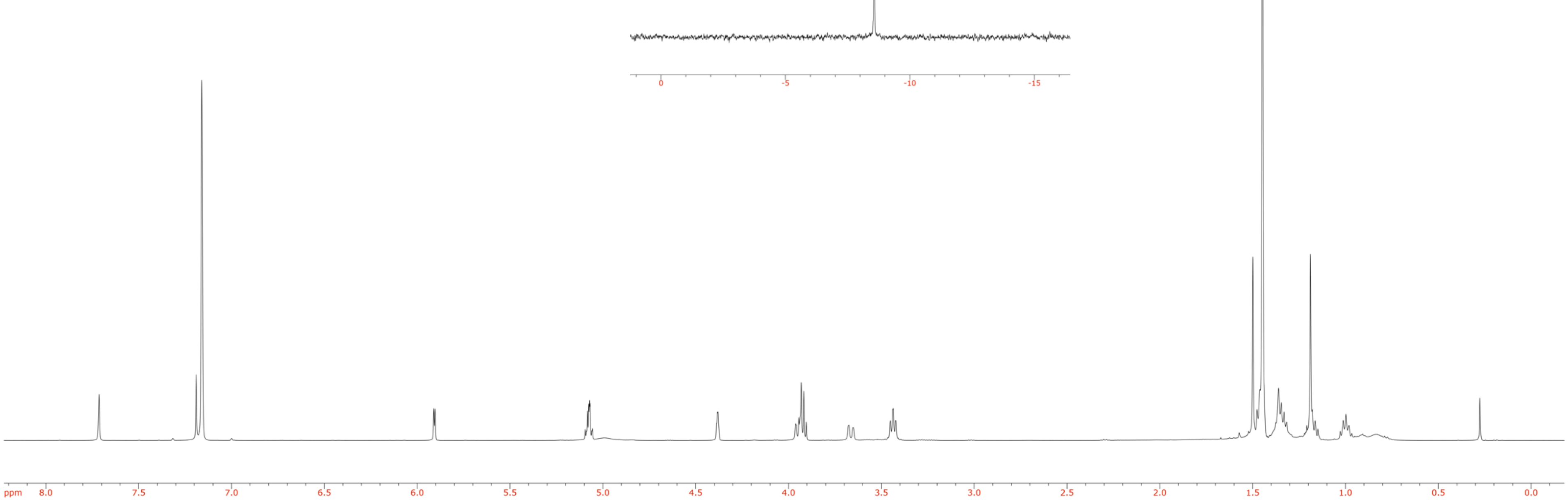
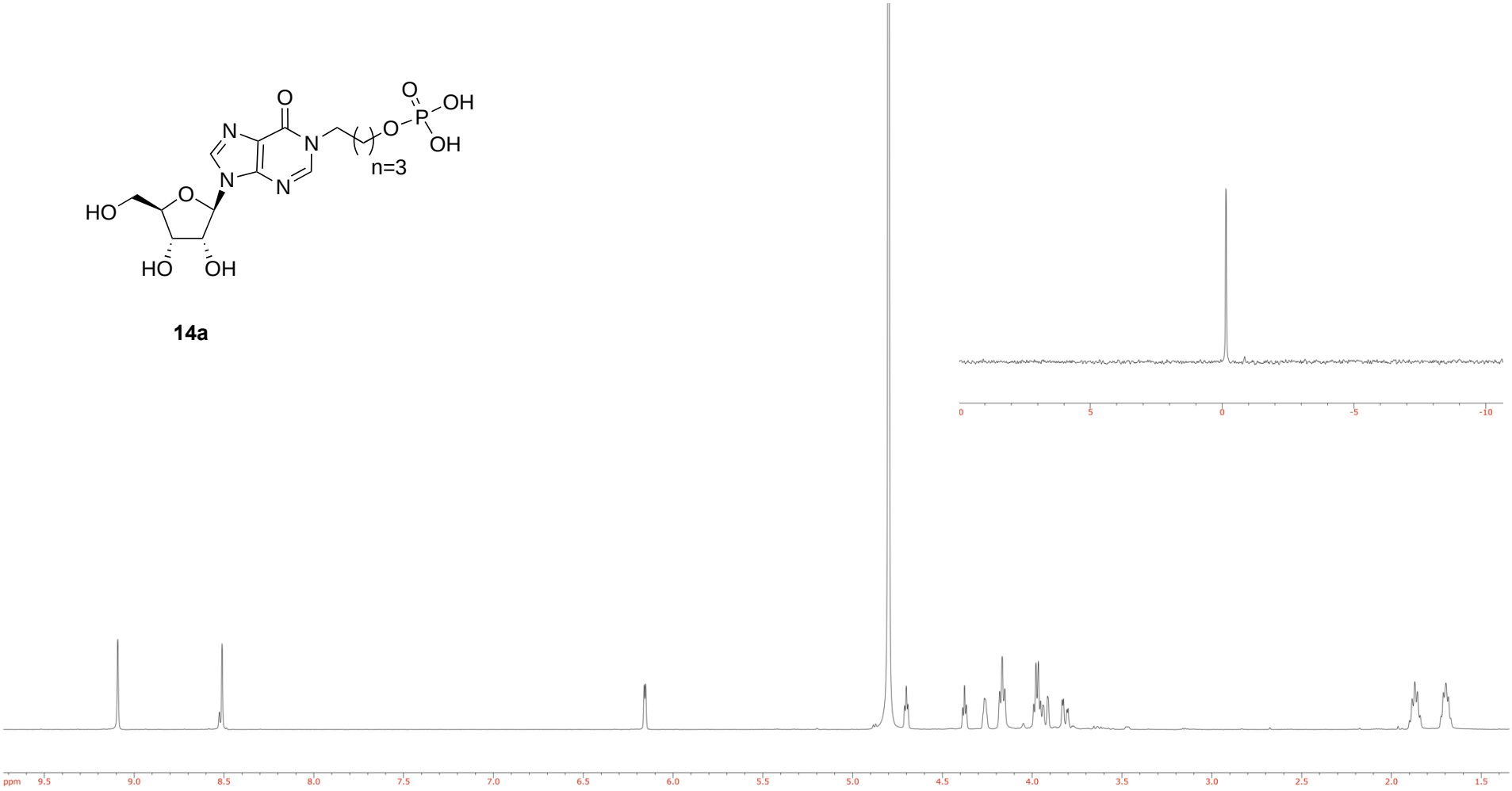


13c



O
N
N
N
N
O
O
P
OH
OH
n=3
HO
HO
OH

14a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1.5
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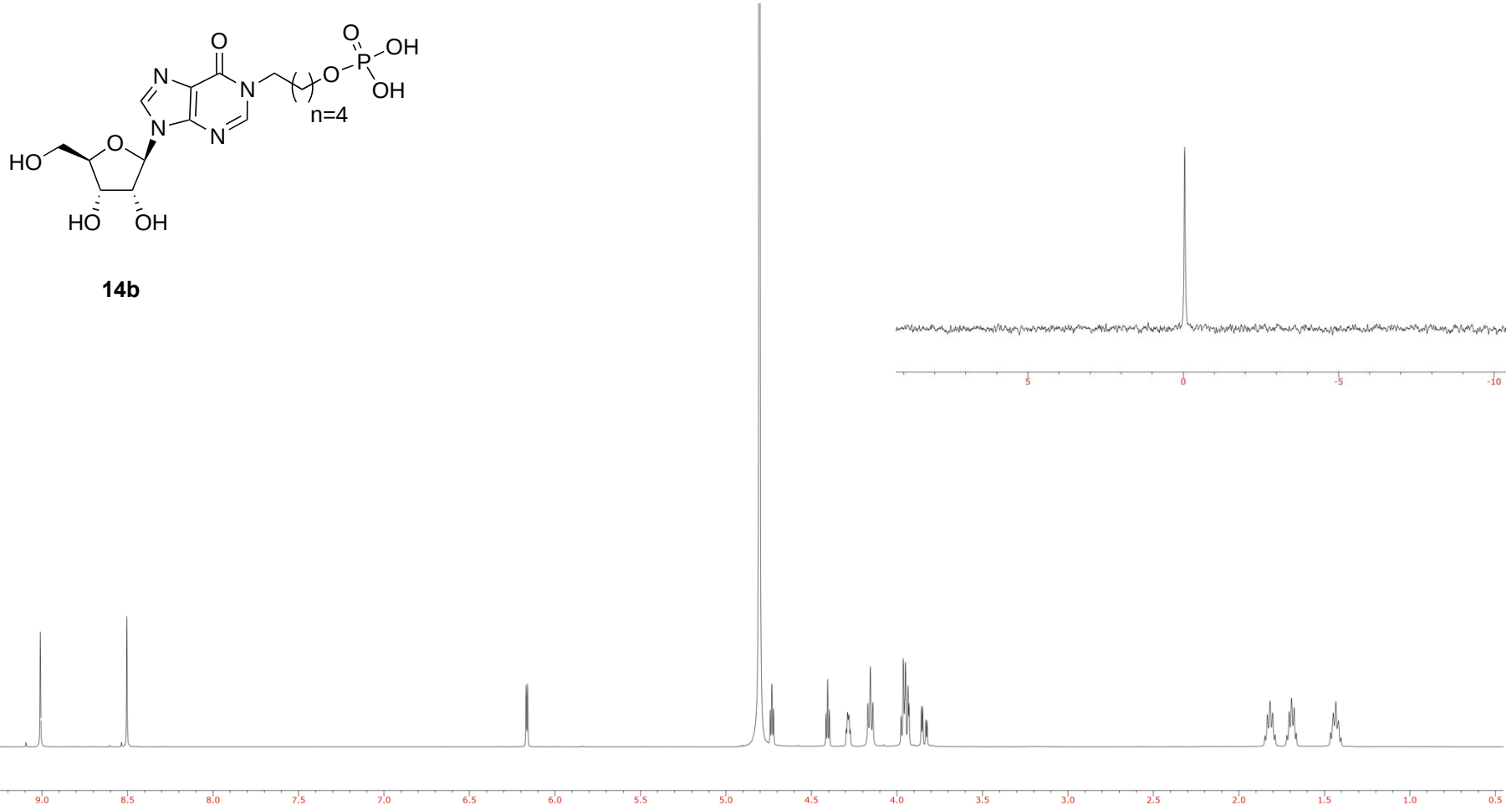
0
-5
-10


O
N
N
N
N
O
O
P
OH
OH
n=4
HO
HO
OH
ppm
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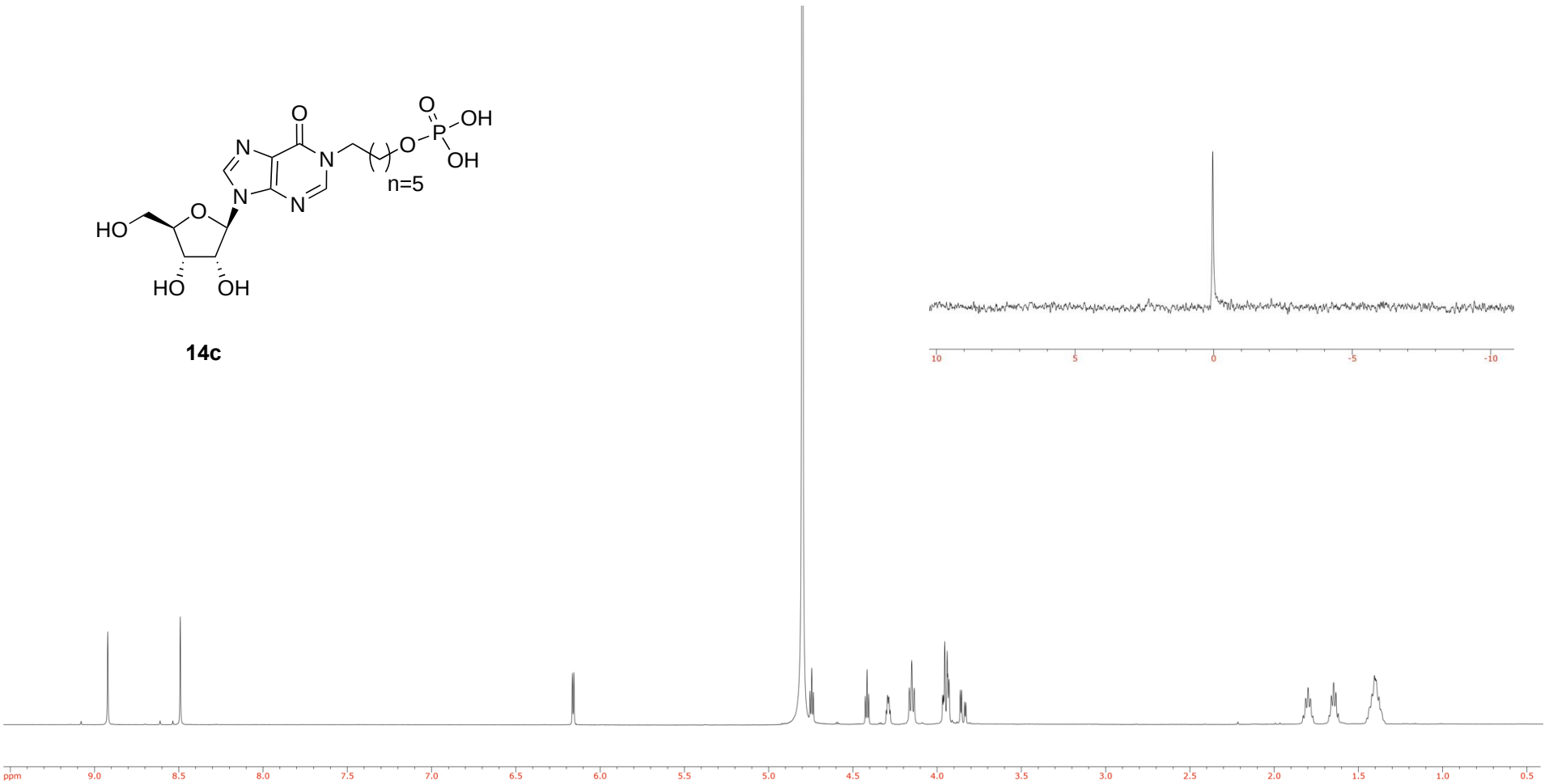
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
5
0
-5
-10

14b

O
N
N
N
N
O
O
P
OH
OH
n=5
HO
HO
OH

14c

10
5
0
-5
-10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4.5
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3.5
3.0
2.5
2.0
1.5
1.0
0.5

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N
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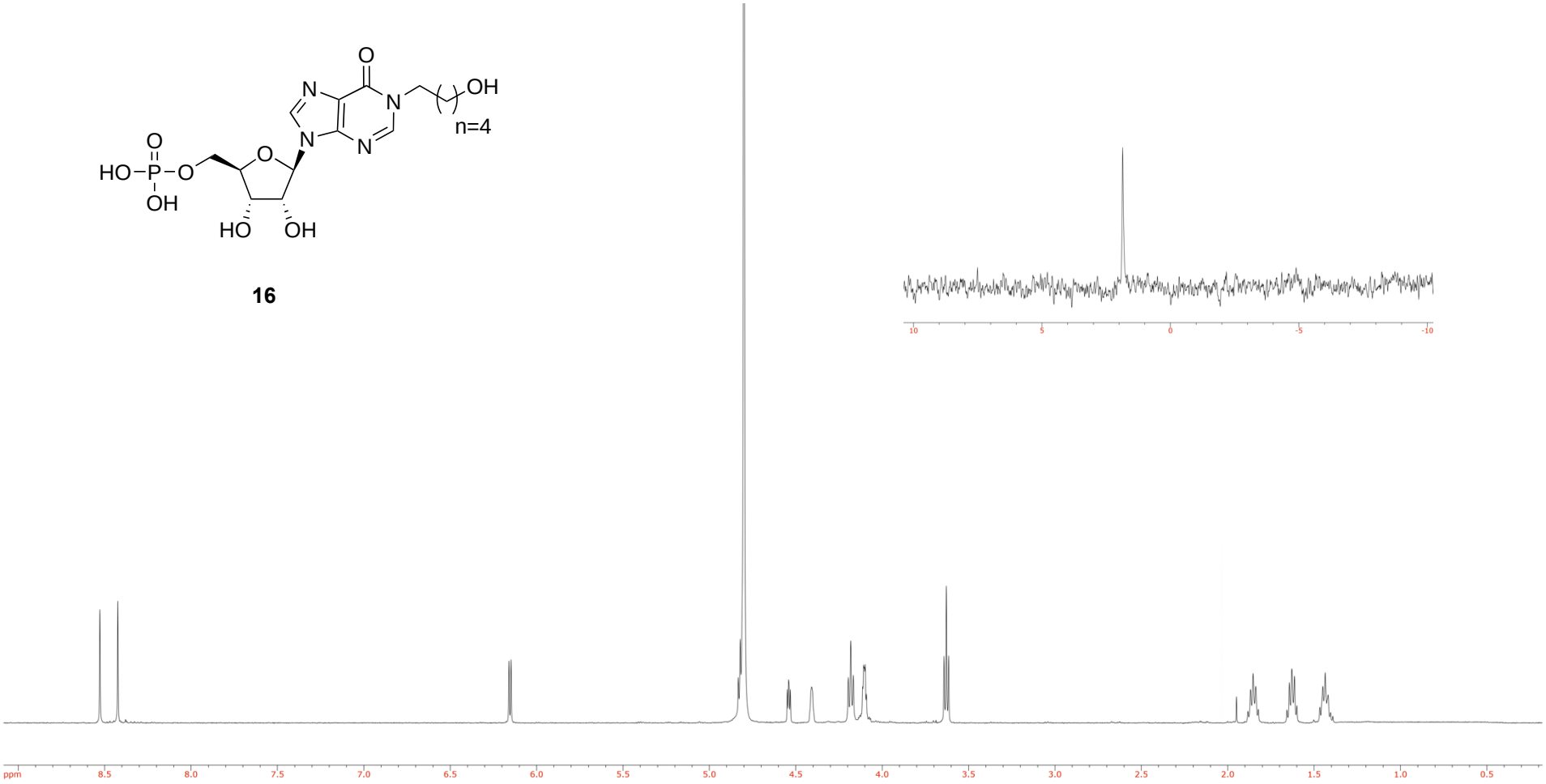
OH
n=4
O
HO–P–O
OH
O
HO
OH

16

10
5
0
-5
-10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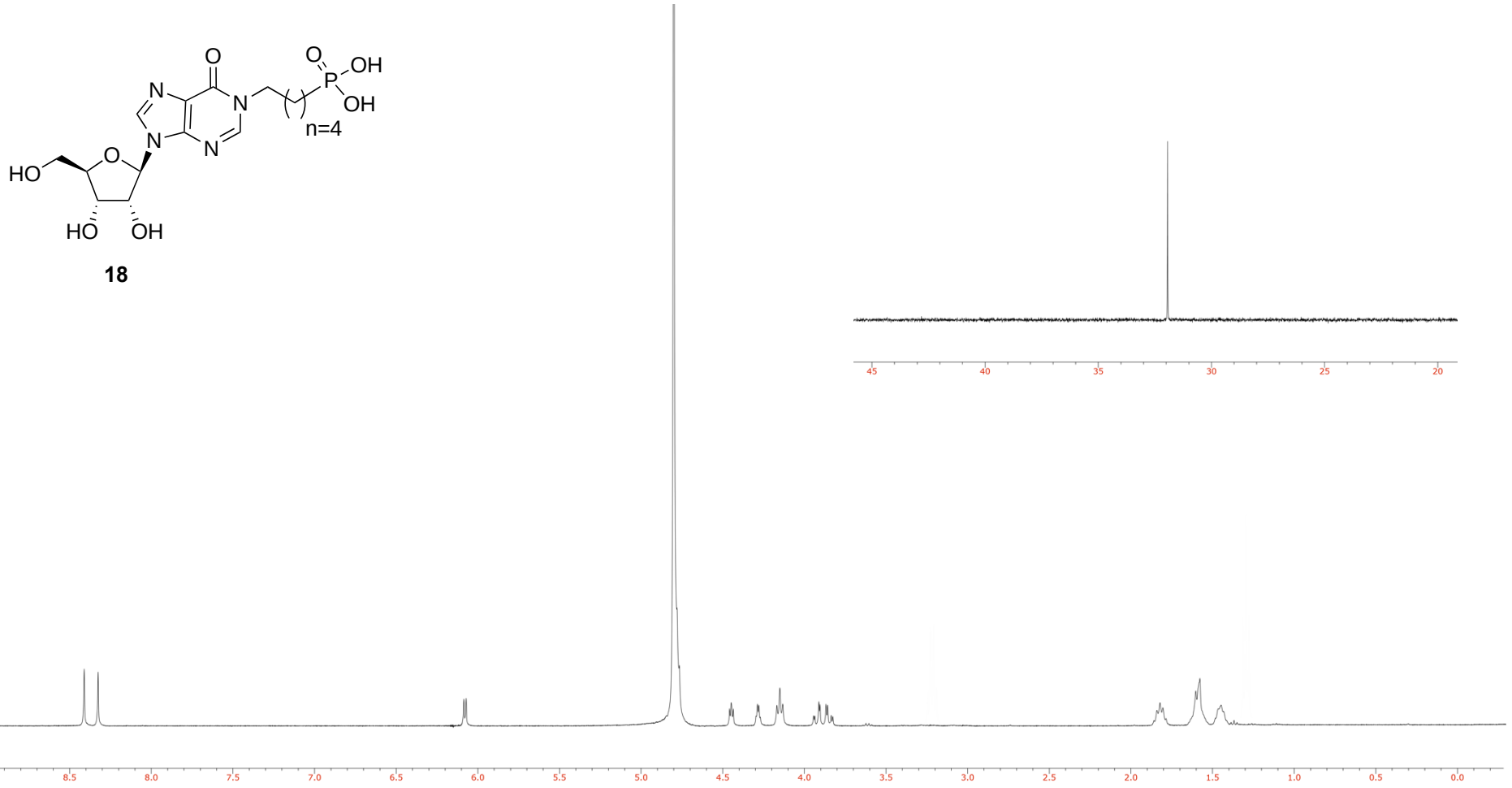
O
N
N
N
N
O
P
OH
OH
n=4
HO
O
HO
OH
18
45
40
35
30
25
20
ppm
8.5
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7.0
6.5
6.0
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2.0
1.5
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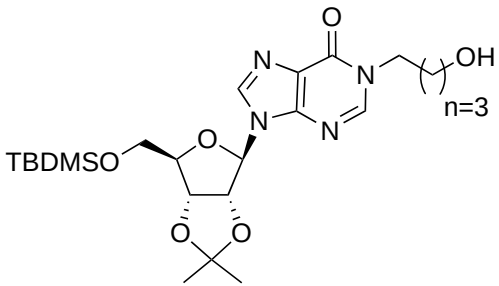
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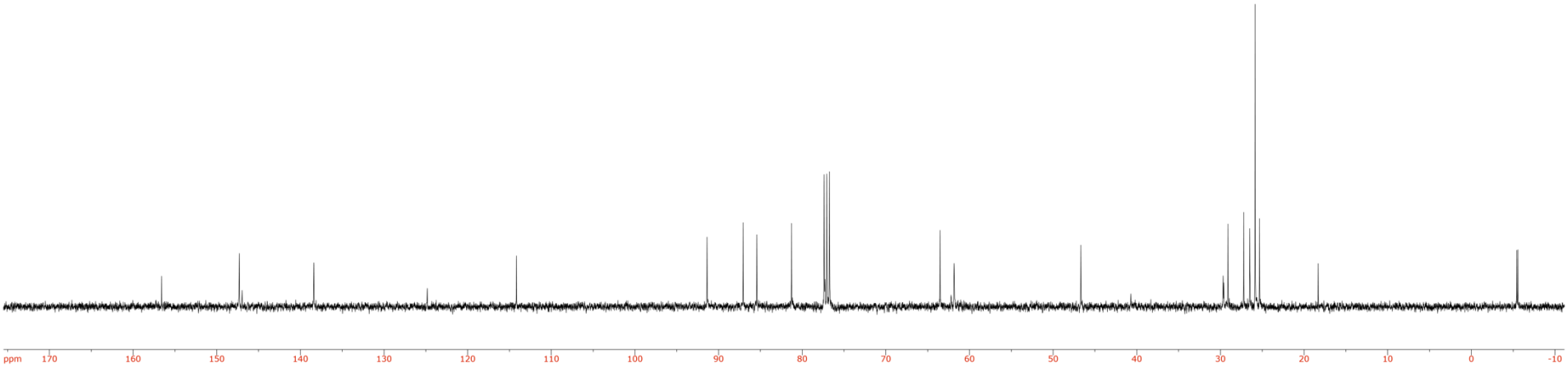
N
N
N
N
OH
n=3
TBDMSO
O
O
O

8a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140
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120
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100
90
80
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60
50
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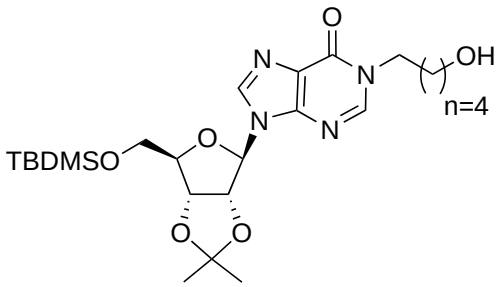
30
20
10
0
-10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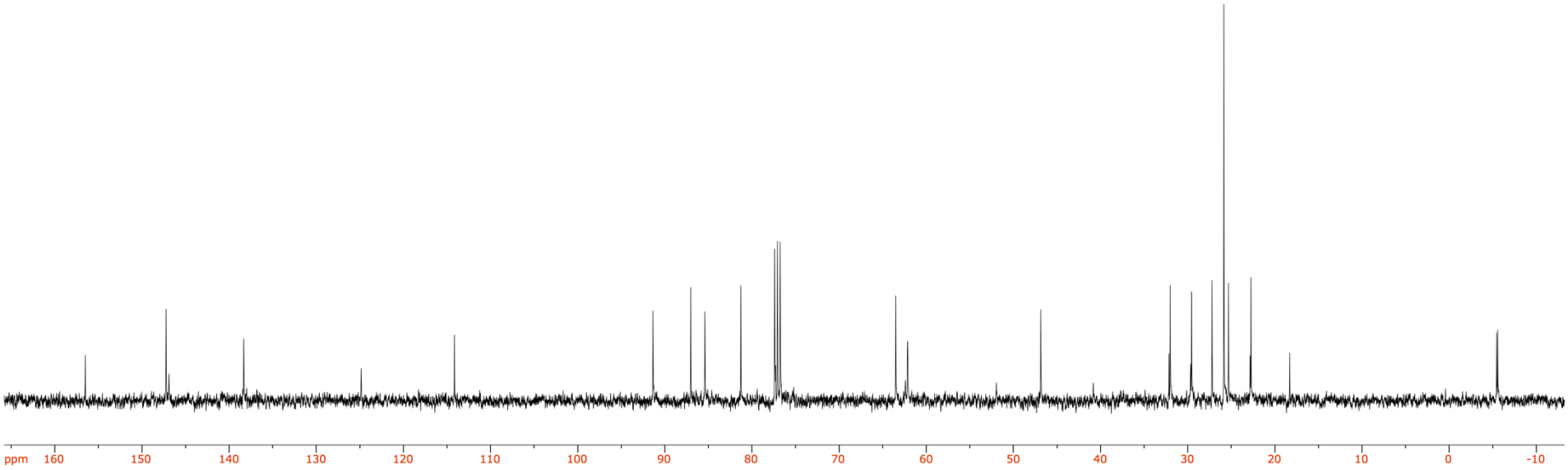
N
N
N
N
OH
n=4
TBDMSO
O
O
O

8b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90
80
70
60
50
40
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20
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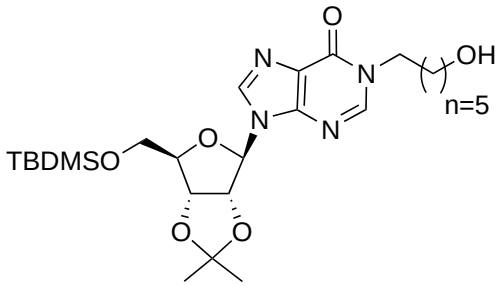
0
-10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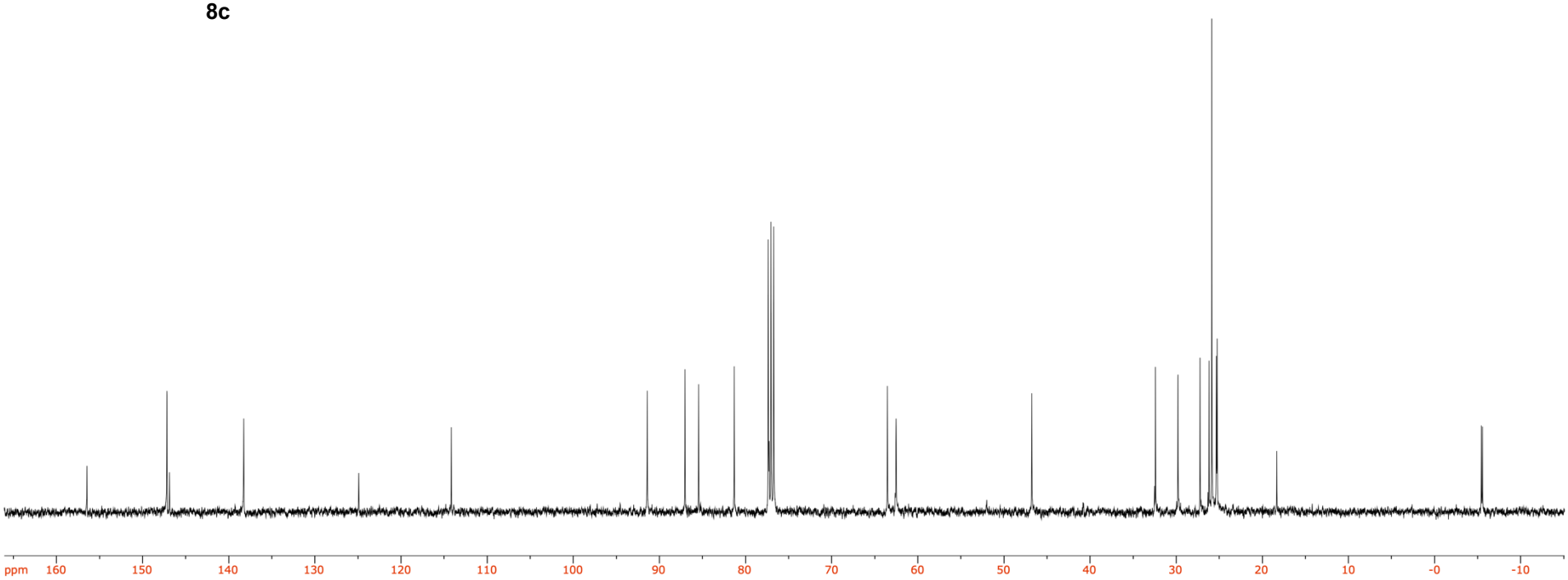
N
N
N
N
OH
n=5
TBDMSO
O
O
O

8c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80
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50
40
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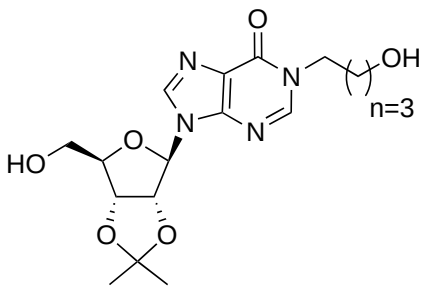
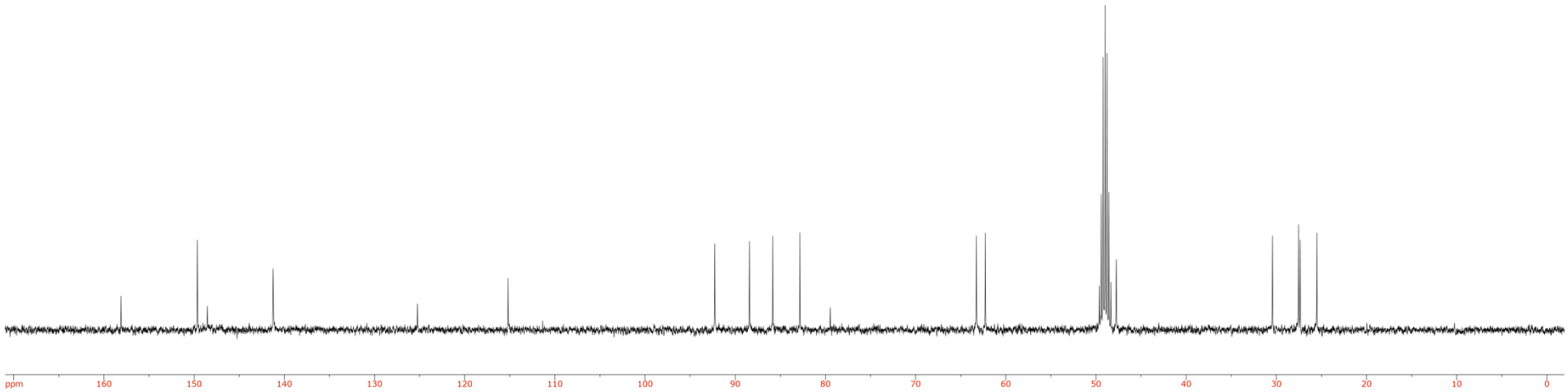
20
10
-0
-10


O
N
N
OH
n=3
N
N
HO
O
O
O

9a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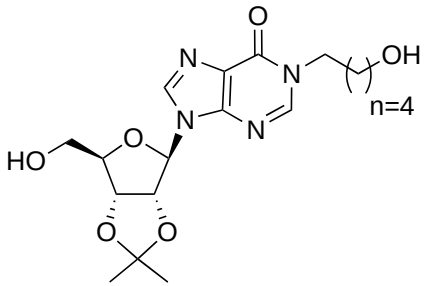
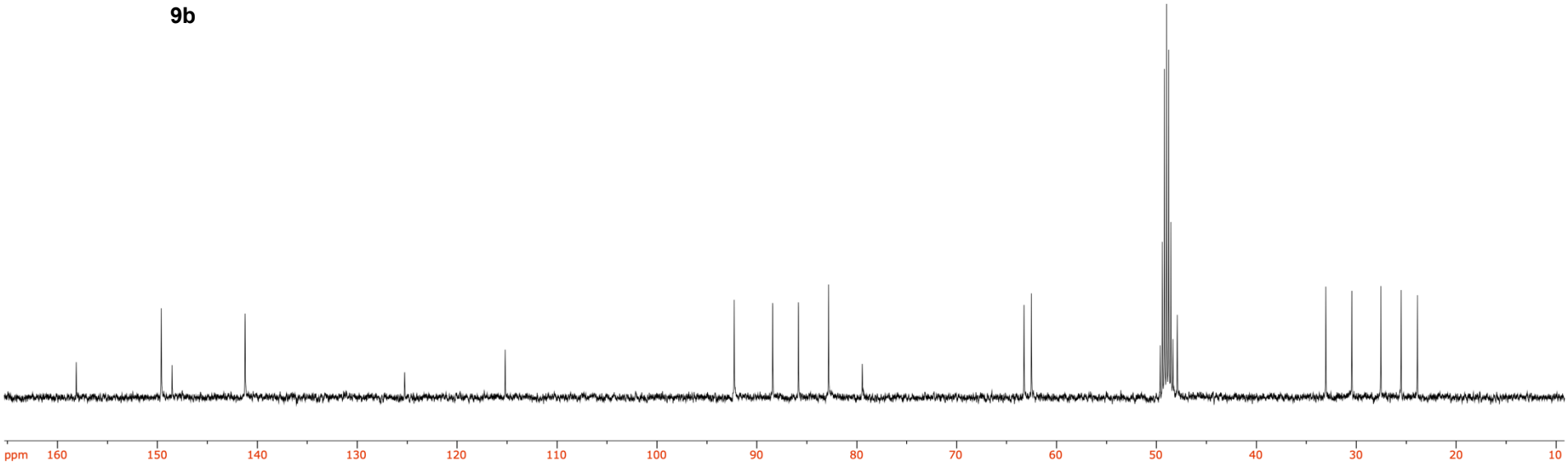
10
0


O
N
N
N
N
OH
n=4
HO
O
O
O

9b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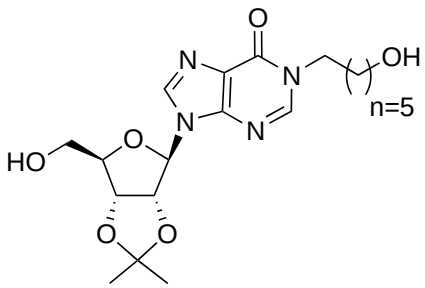
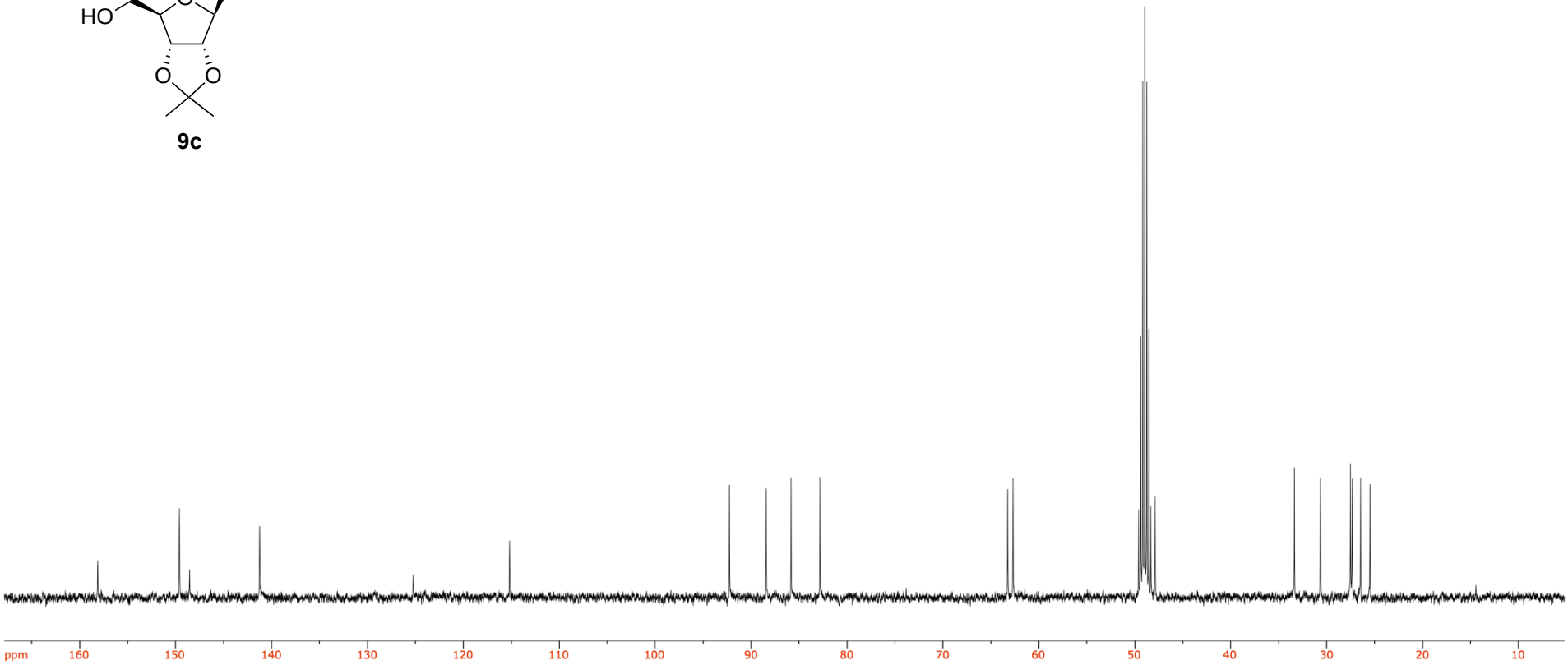

O
N
N
N
N
OH
n=5
HO
O
O
O

9c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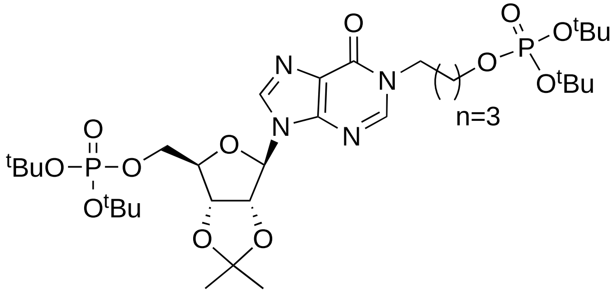
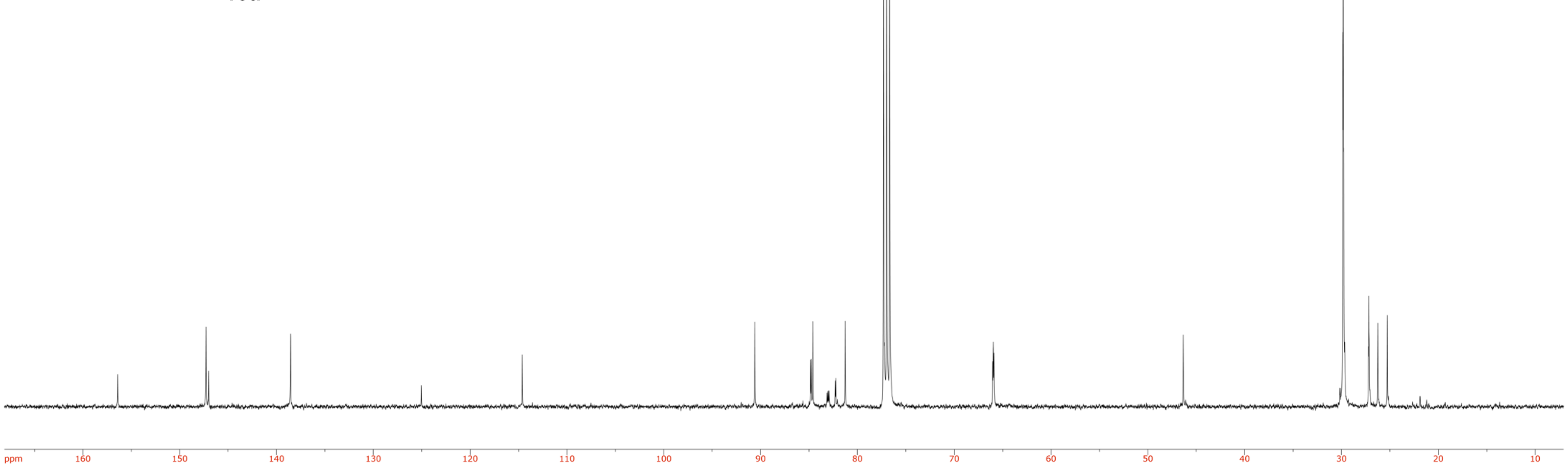


O
N
N
N
N
n=3
O
P
O
OᵗBu
OᵗBu
O
ᵗBuO
P
O
OᵗBu
O
O
O

10a



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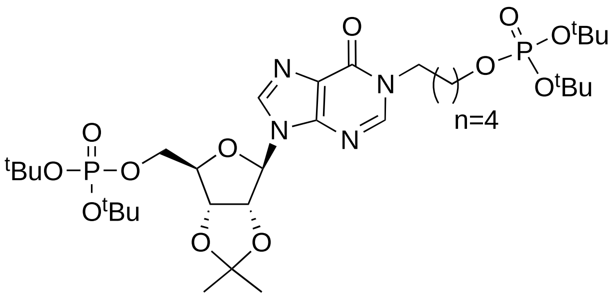
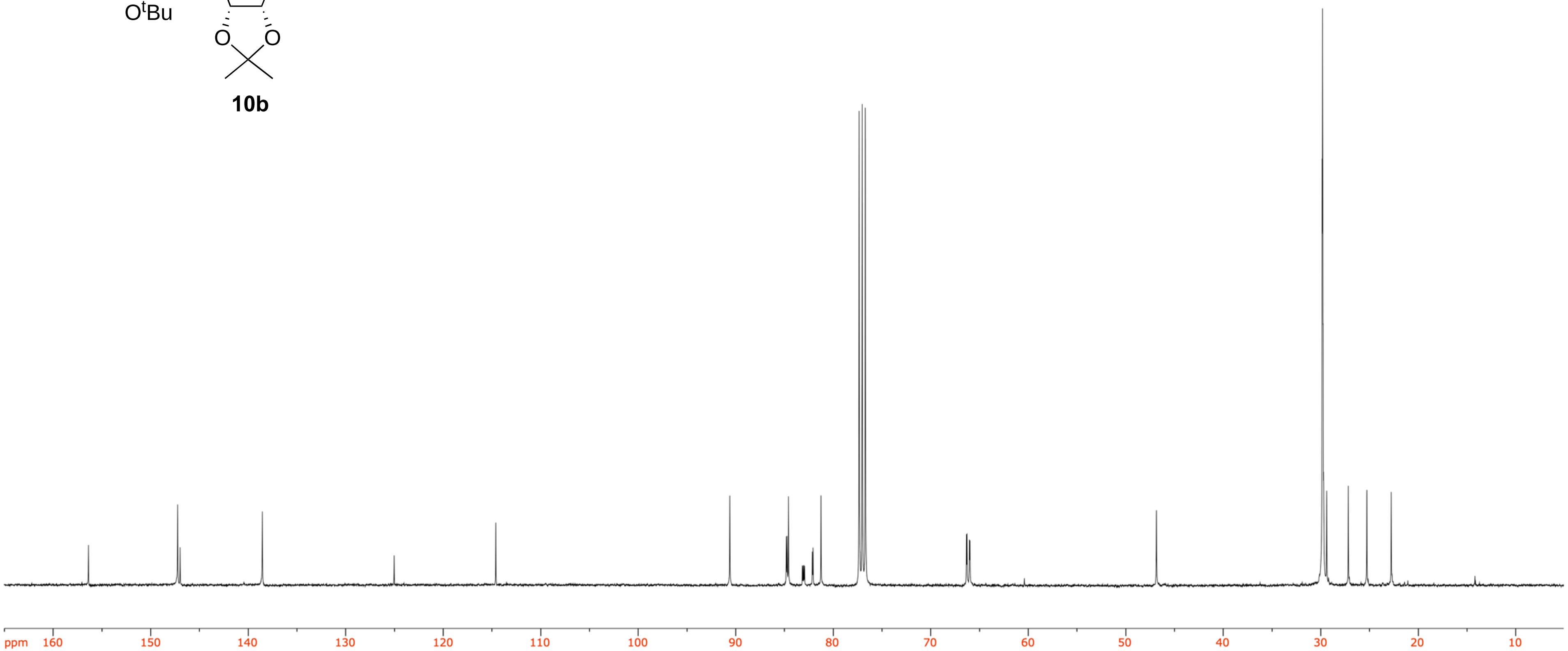


O
N
N
N
N
O
P
O
O^{t}Bu
O^{t}Bu
n=4
O
^{t}BuO
P
O
O
O^{t}Bu
O
O

10b



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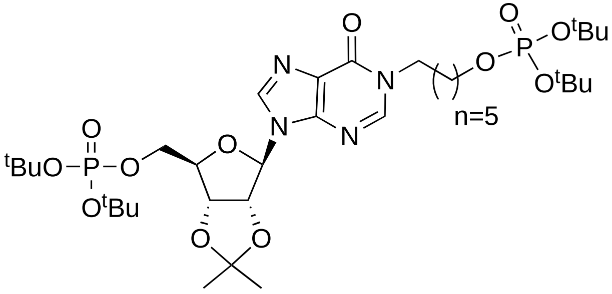
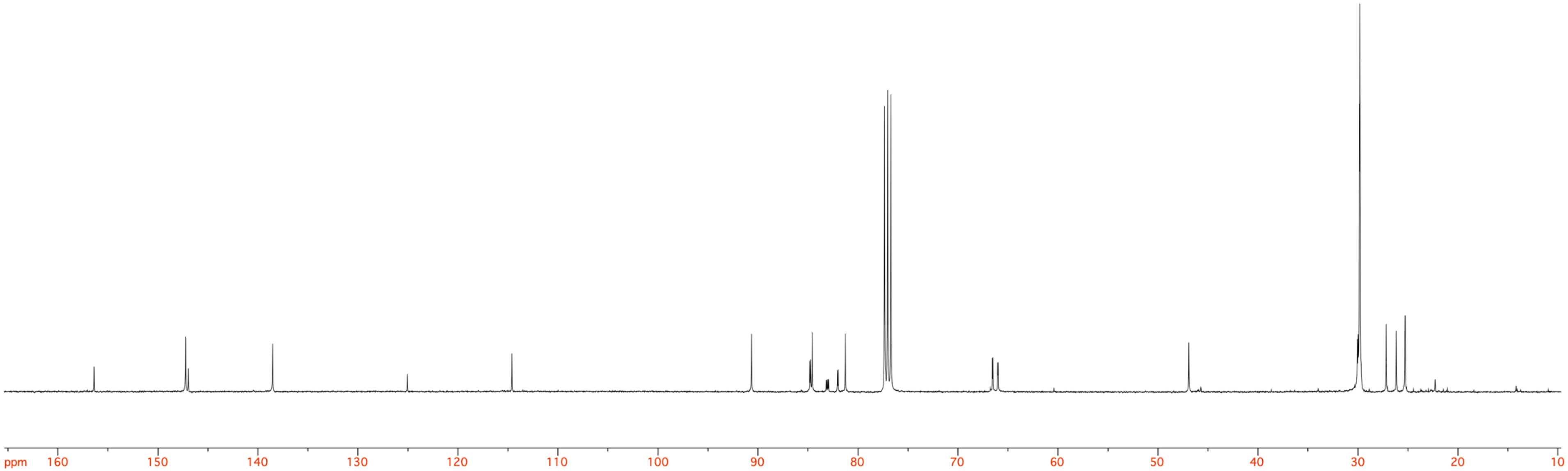
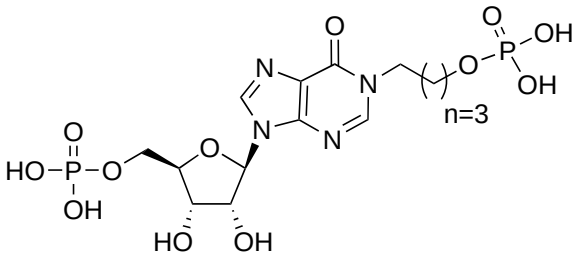
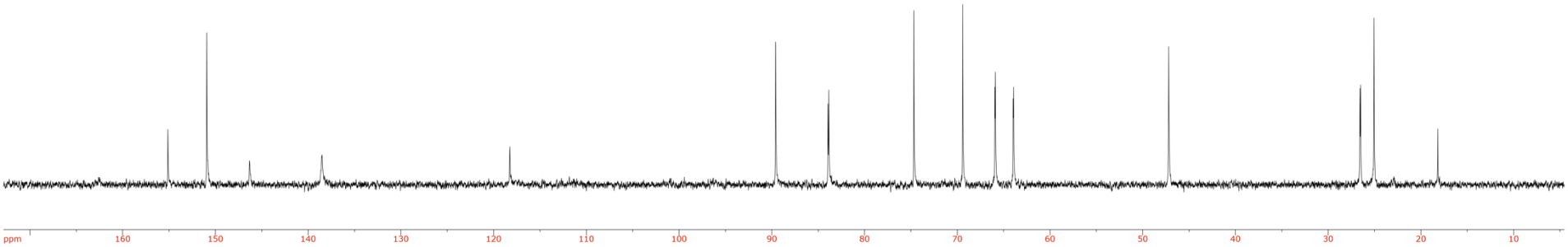


10c




O
N
N
N
N
O
O
P
OH
OH
n=3
HO
P
O
OH
O
HO
OH

11a


ppm
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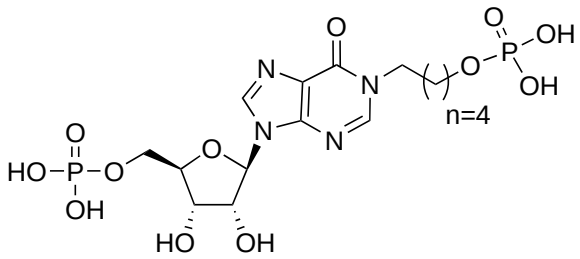
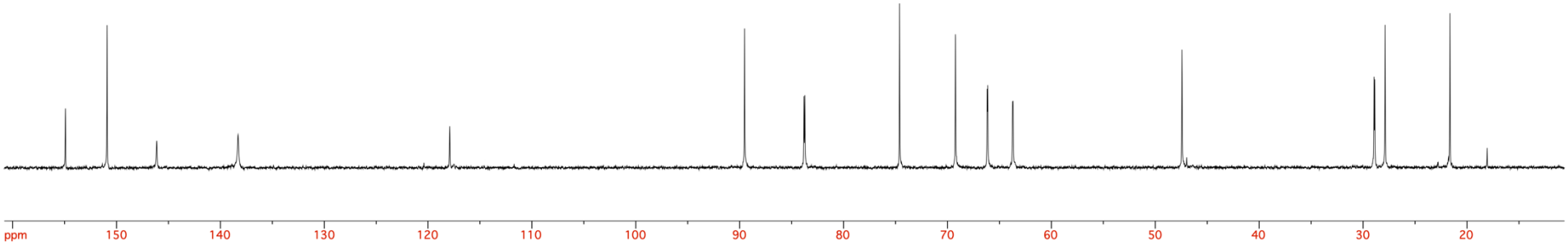

O
N
N
N
O
N
O
P
OH
OH
n=4
HO
P
O
OH
O
HO
OH

11b


ppm
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90
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50
40
30
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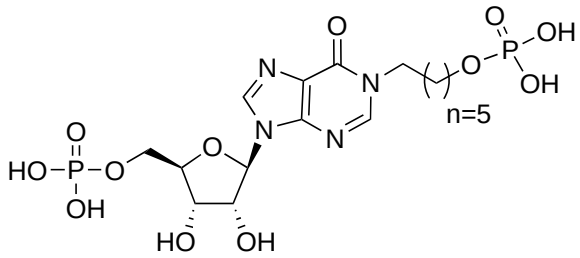
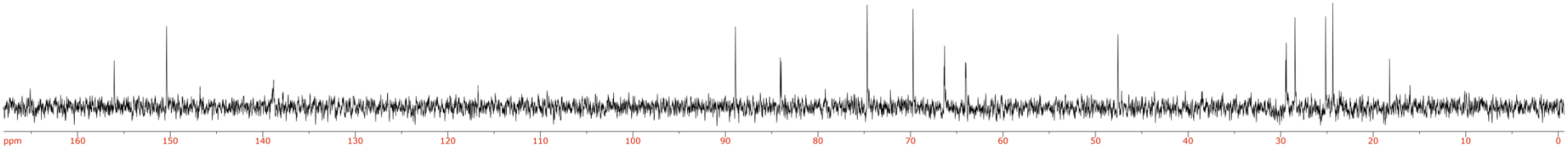

O
N
N
N
N
O
O
P
OH
OH
n=5
HO
P
O
O
OH
HO
OH

11c


ppm
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150
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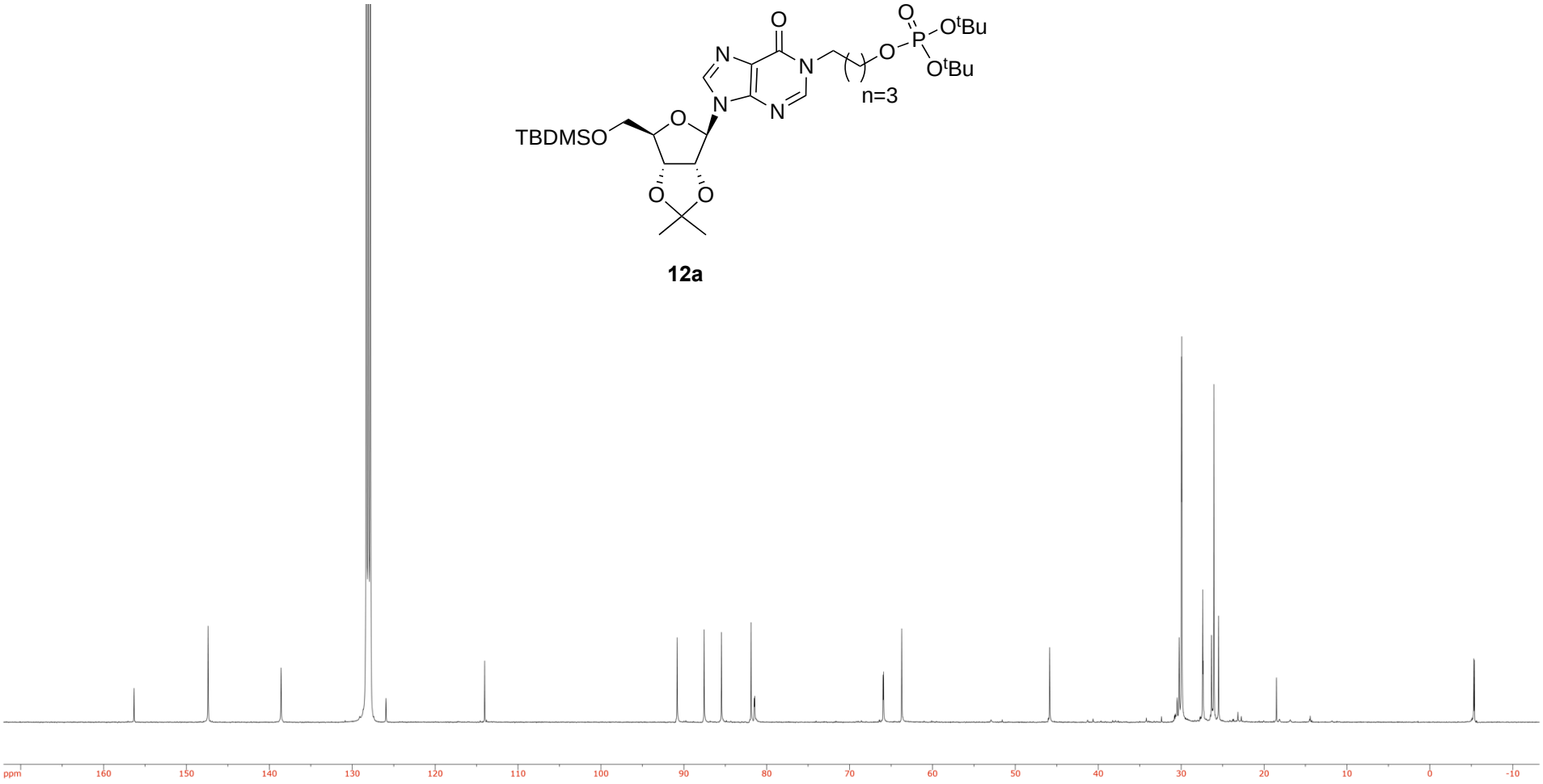
130
120
110
100
90
80
70
60
50
40
30
20
10
0

O
N
N
N
N
O
O
P
O^{t}Bu
O^{t}Bu
n=3
TBDMSO
O
O

12a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20
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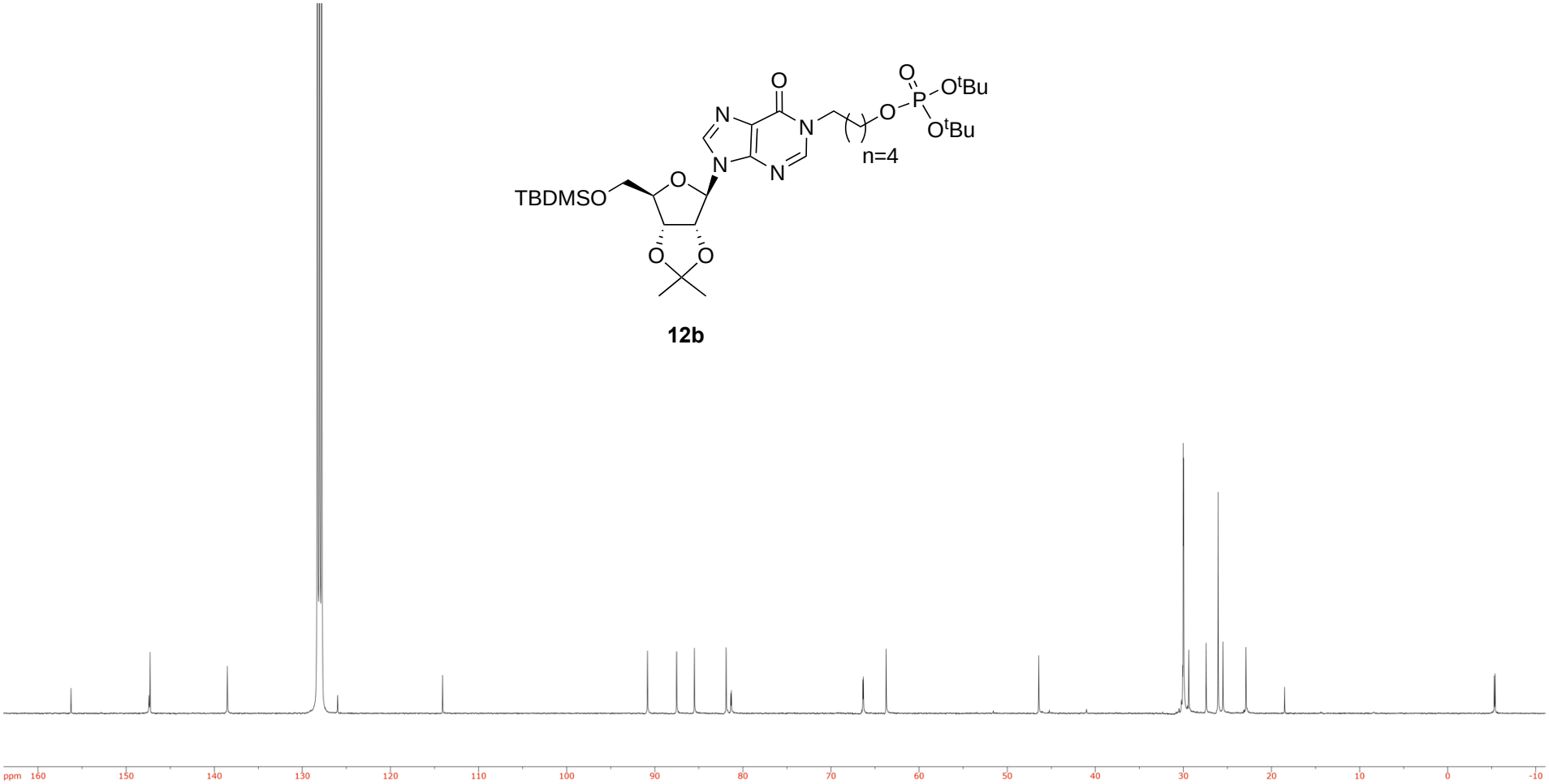
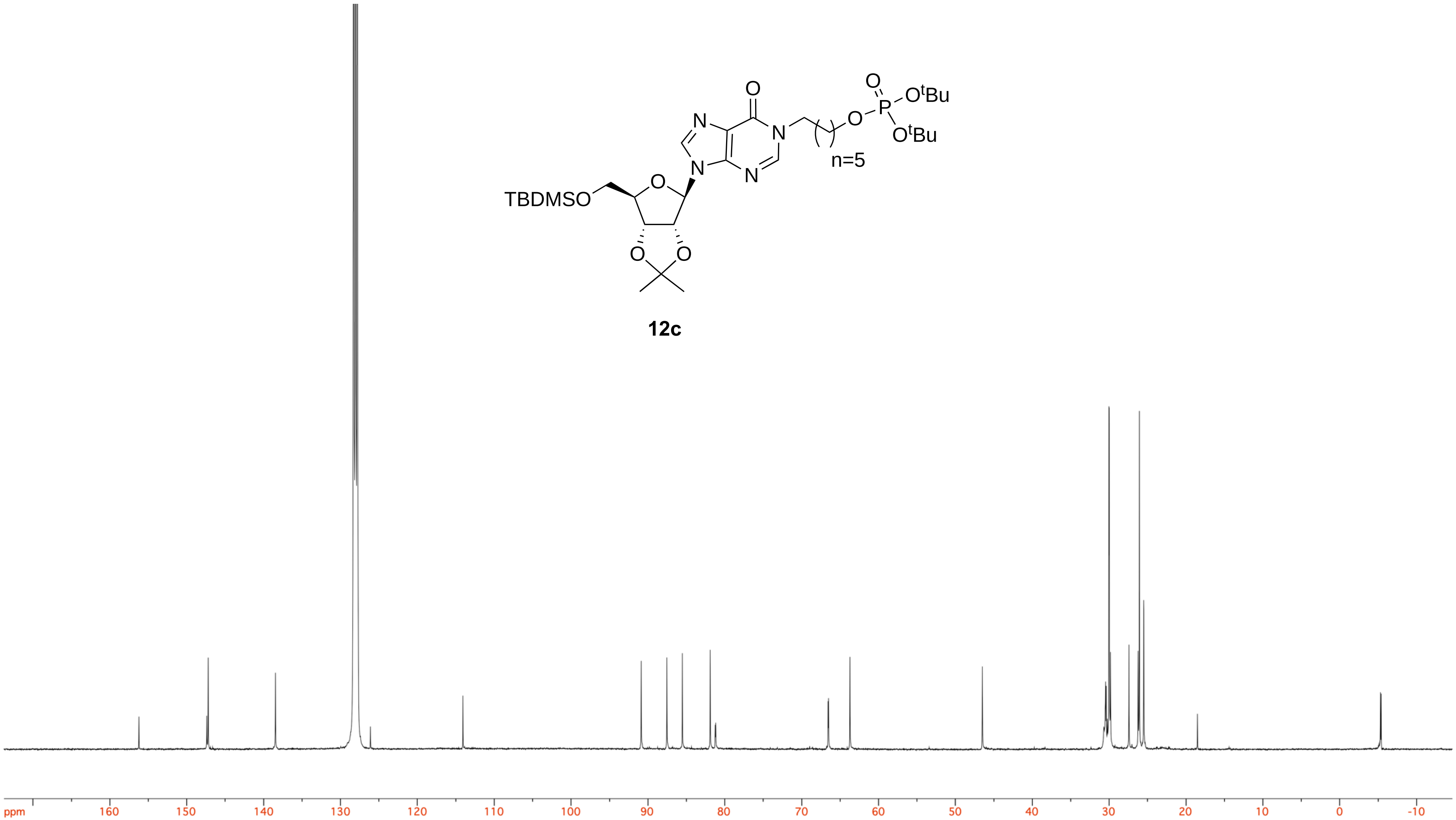
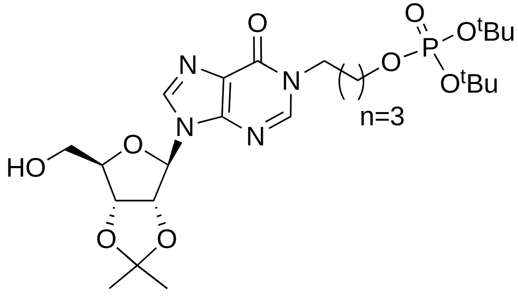
0
-10


TBDMSO
O
N
N
N
N
O
O
O
O
P
O^{t}Bu
O^{t}Bu
n=4
ppm 160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

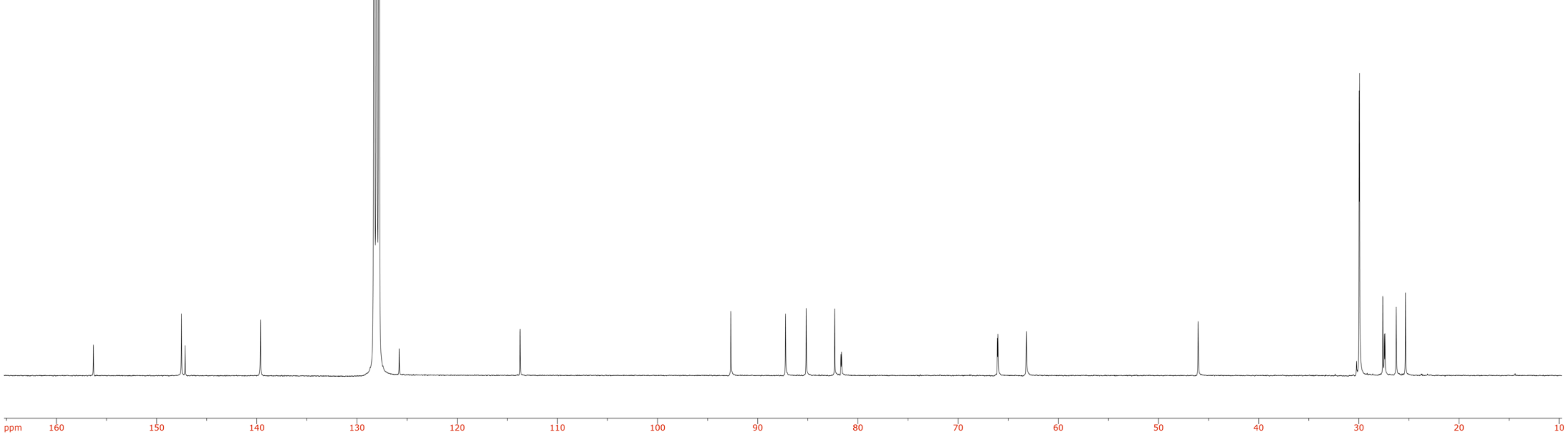
12b


TBDMSO
n=5
O^{t}Bu
12c
ppm
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10



O
N
N
N
N
HO
O
O
O
N
O
P
O
OᵗBu
OᵗBu
n=3

13a



ppm
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150
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120
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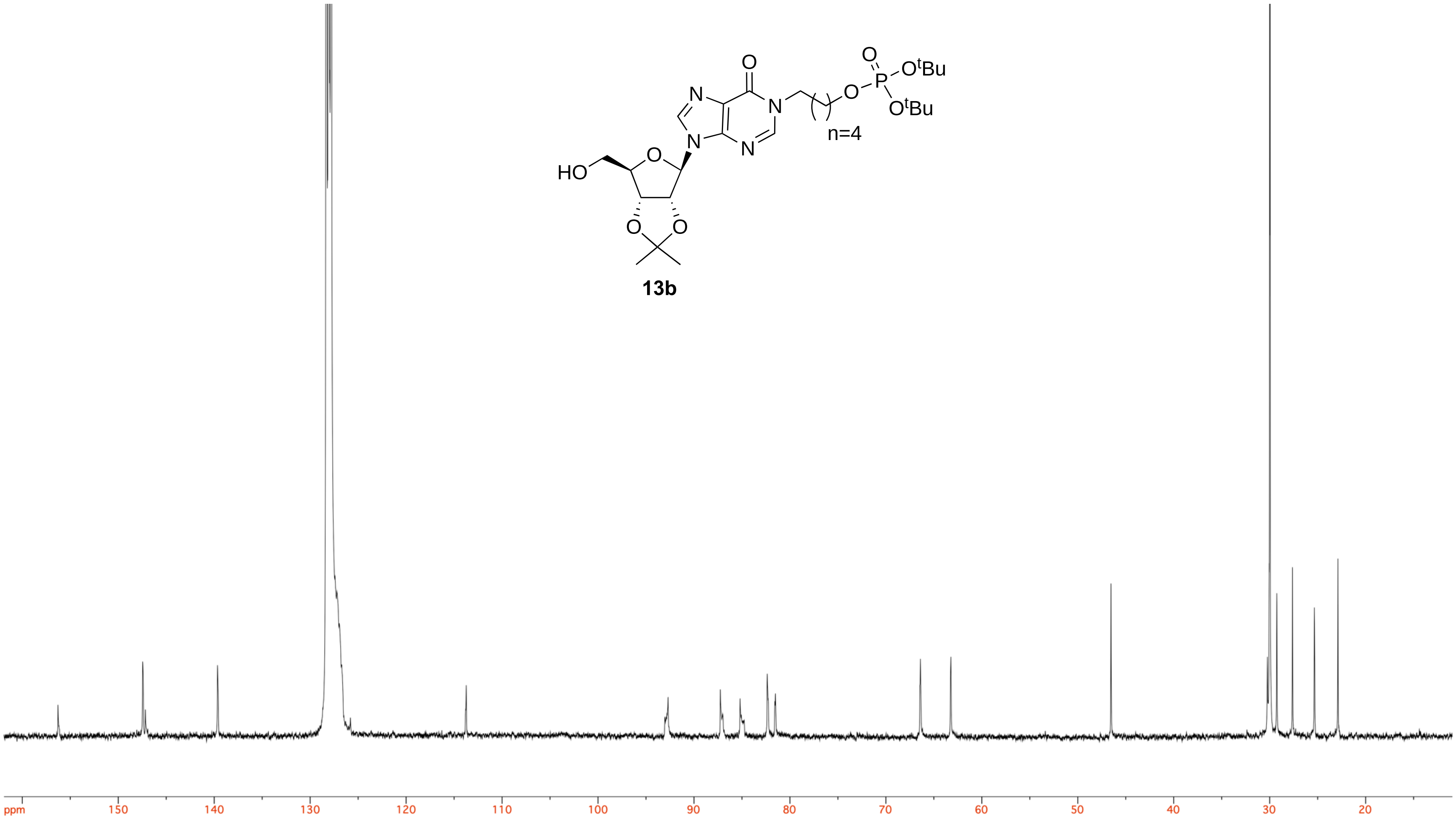
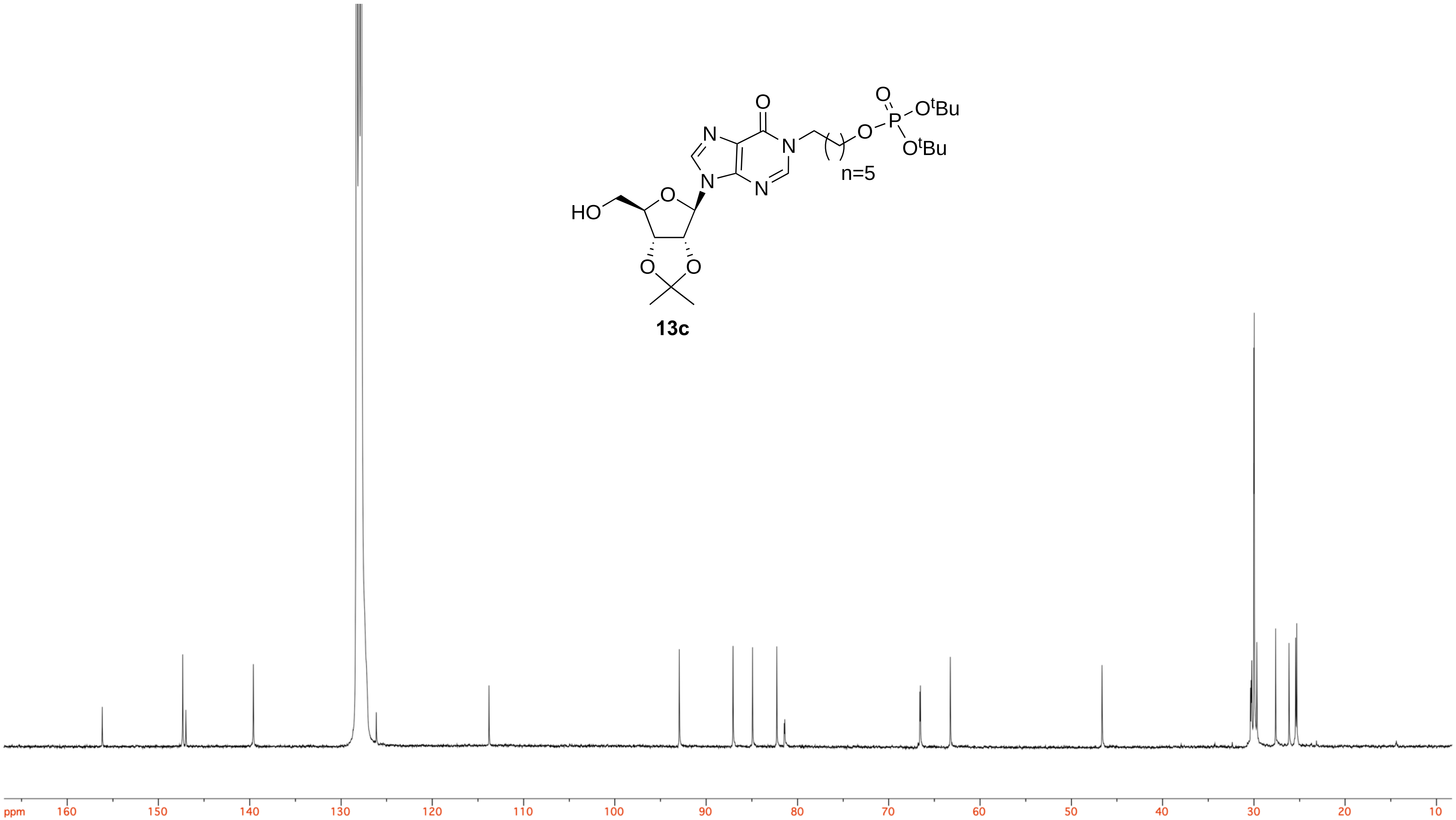
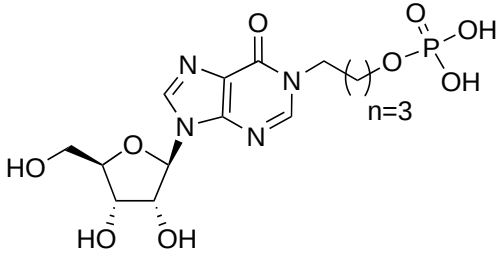

O
N
N
N
N
HO
O
O
O
O
O
P
O^{t}Bu
O^{t}Bu
n=4
ppm
150
140
130
120
110
100
90
80
70
60
50
40
30
20

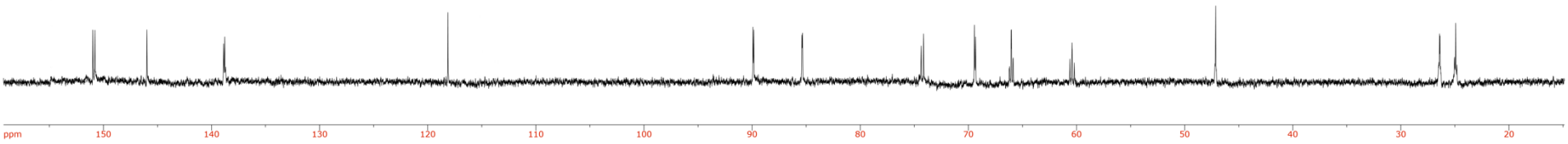
13b



O
N
N
N
N
O
O
P
O^tBu
O^tBu
n=5
HO
O
O
O
13c
ppm
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10


O
N
N
N
N
O
P
OH
OH
n=3
HO
HO
OH

14a


ppm
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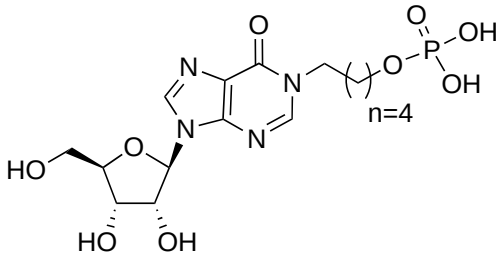
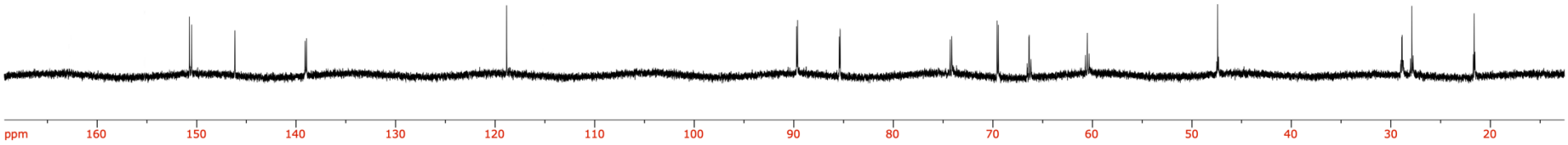

O
N
N
N
N
O
O
P
OH
OH
n=4
HO
HO
OH

14b


ppm
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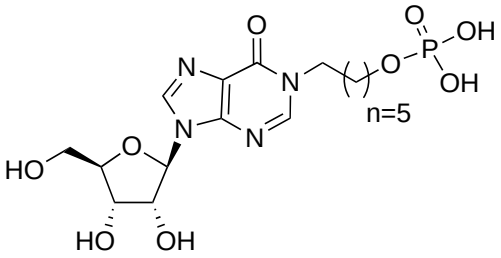
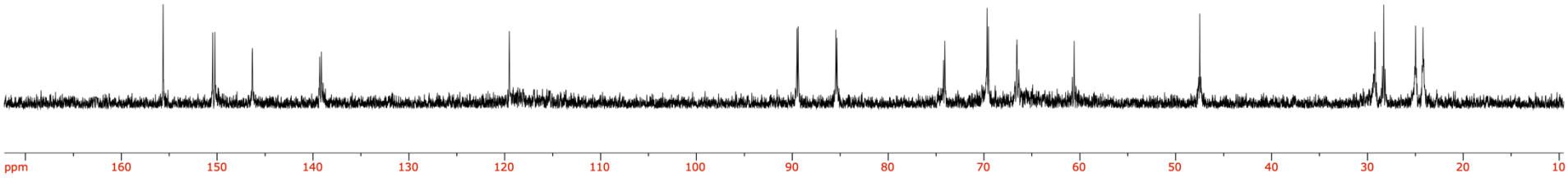
50
40
30
20


O
N
N
N
N
O
O
P
OH
OH
n=5
HO
HO
OH

14c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20
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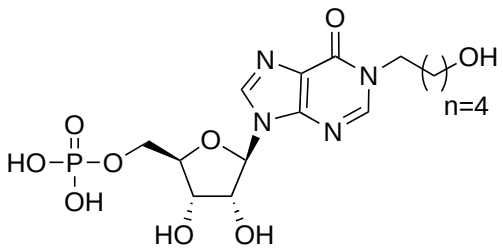
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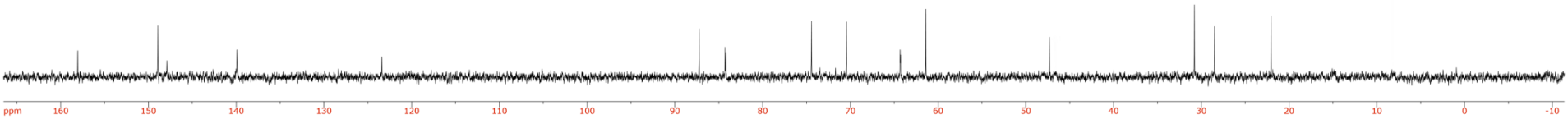
N
N
N
N
OH
n=4
O
HO–P–O
OH
O
HO
OH

16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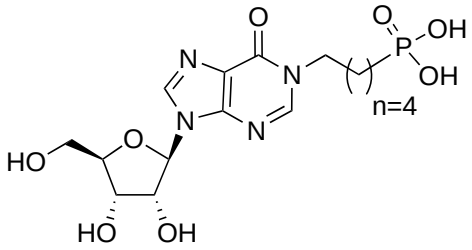
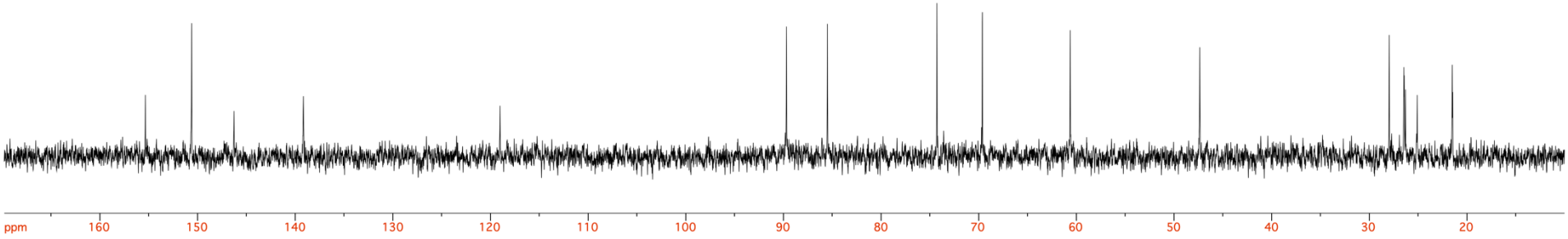
10
0
-10


O
O
OH
P
OH
N
N
N
N
n=4
HO
O
HO
OH

18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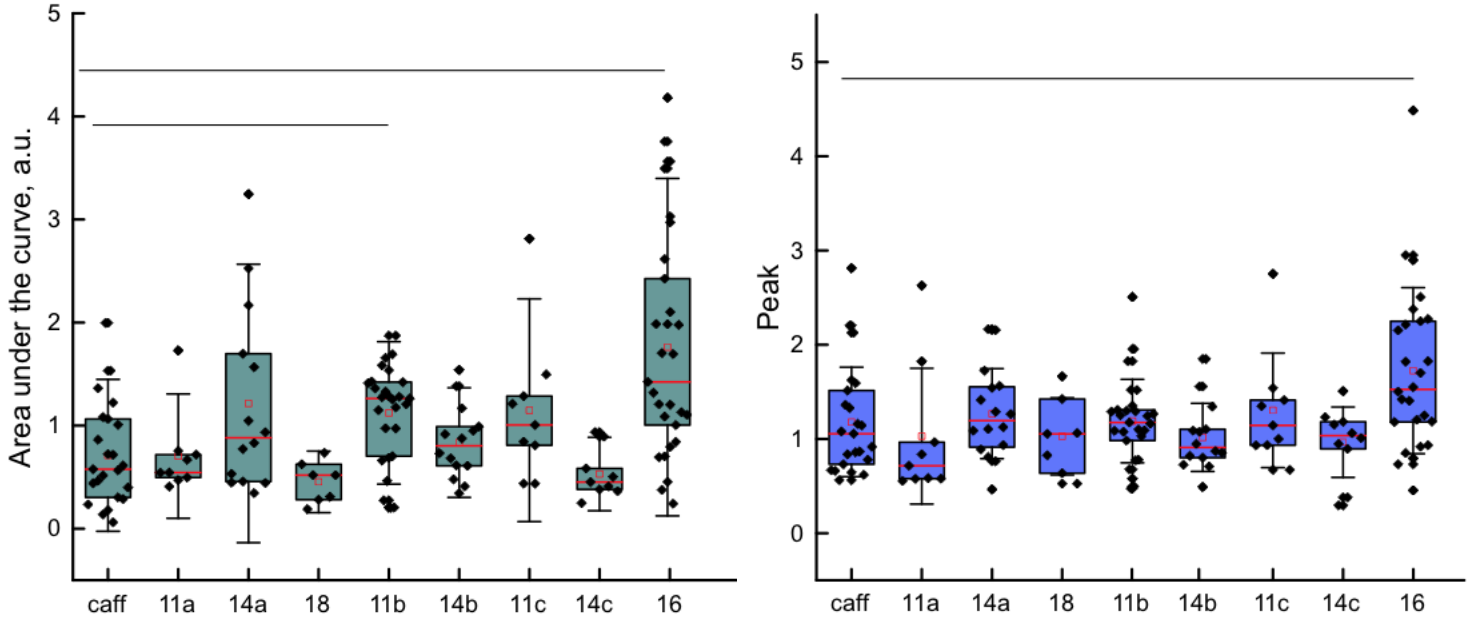

Figure 3. Average area (left panel) and peak values (right panel), above the baseline, in response to 20 mM caffeine addition, or to caffeine added 5 min after the addition of 1 μM of the indicated compound. Box size 25-75 percentile, red square: mean values, red bar: median, whiskers: standard deviation, each symbol represents an individual cell. Only cells responding to caffeine were included in this calculation. P 0.05