Supporting Information for

Polyhydroxylated GdDTPA-derivatives as high relaxivity Magnetic Resonance Imaging contrast agents

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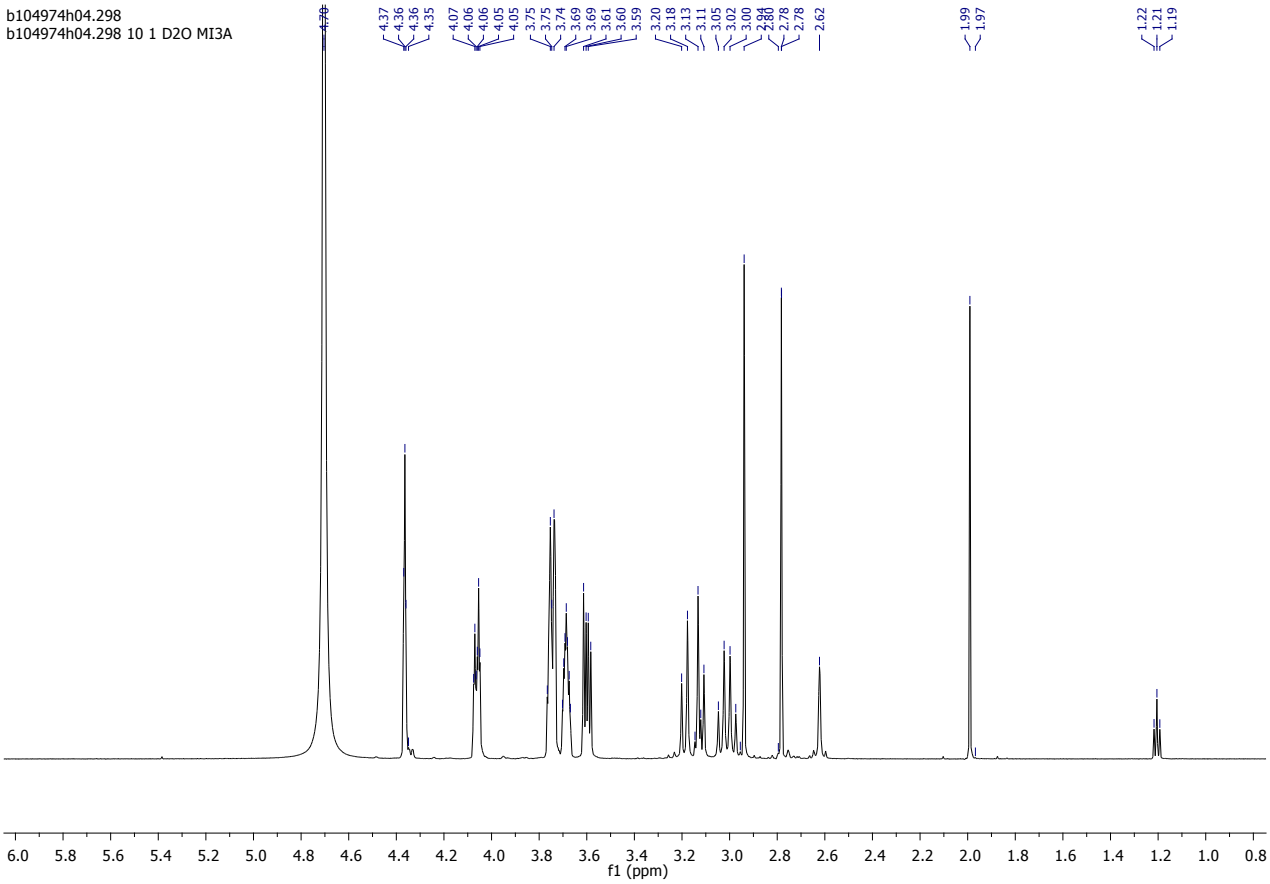
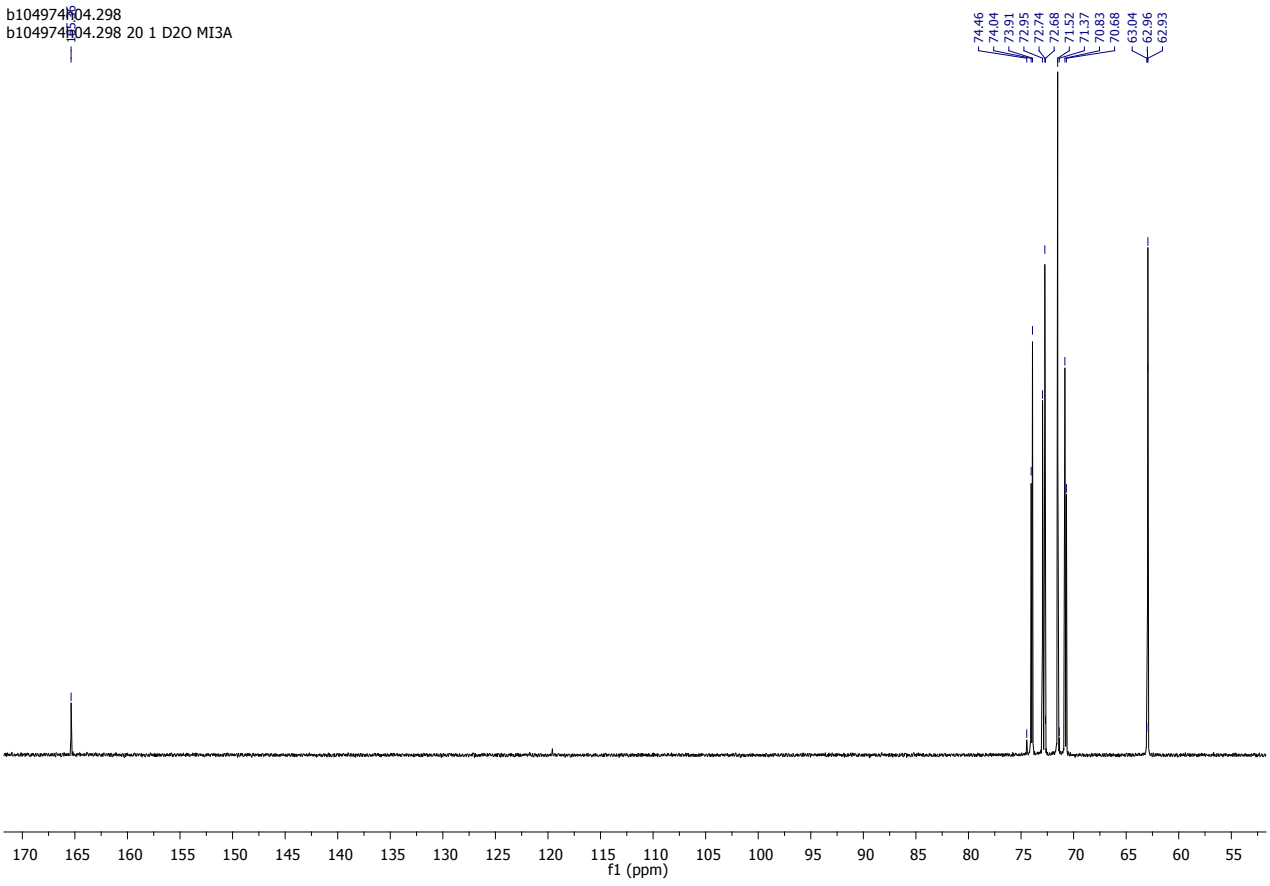
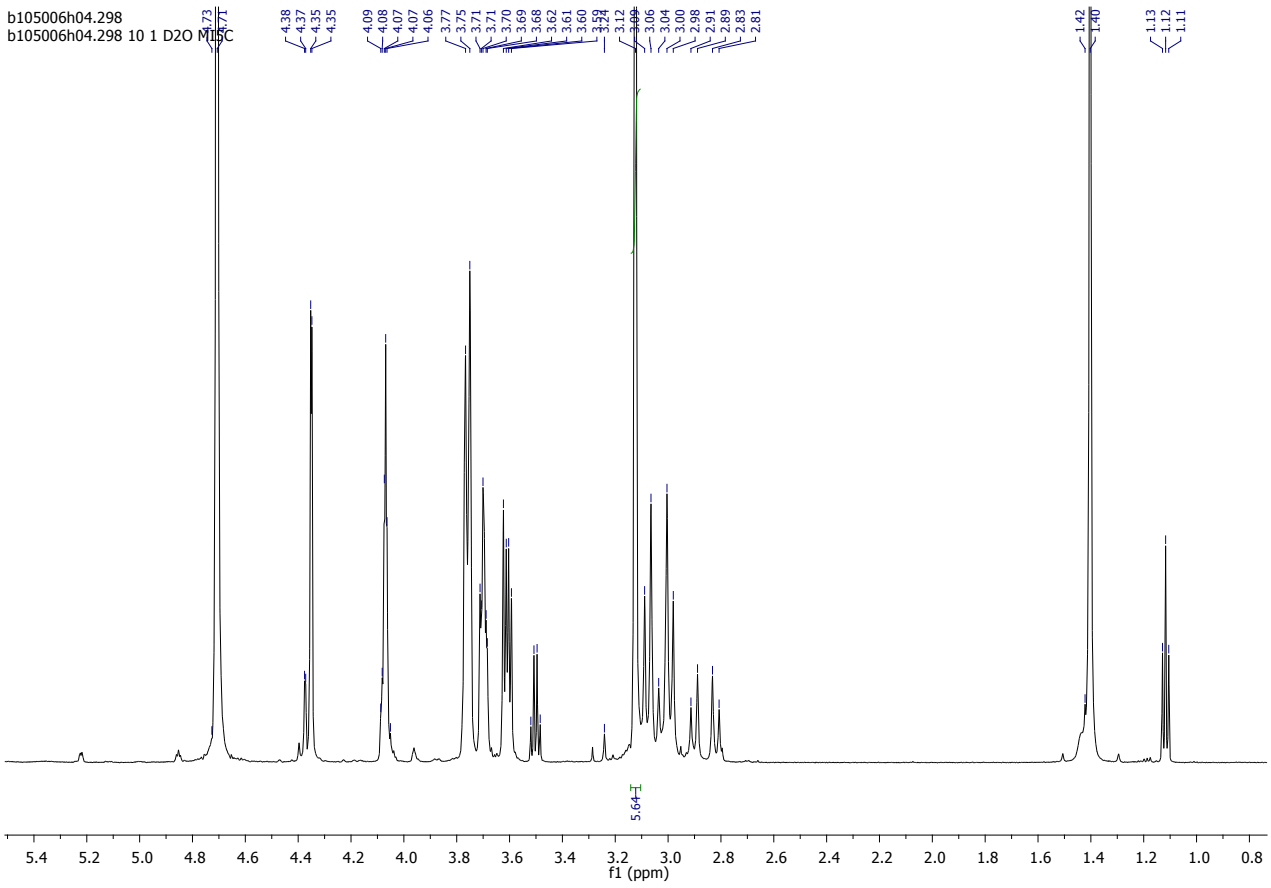
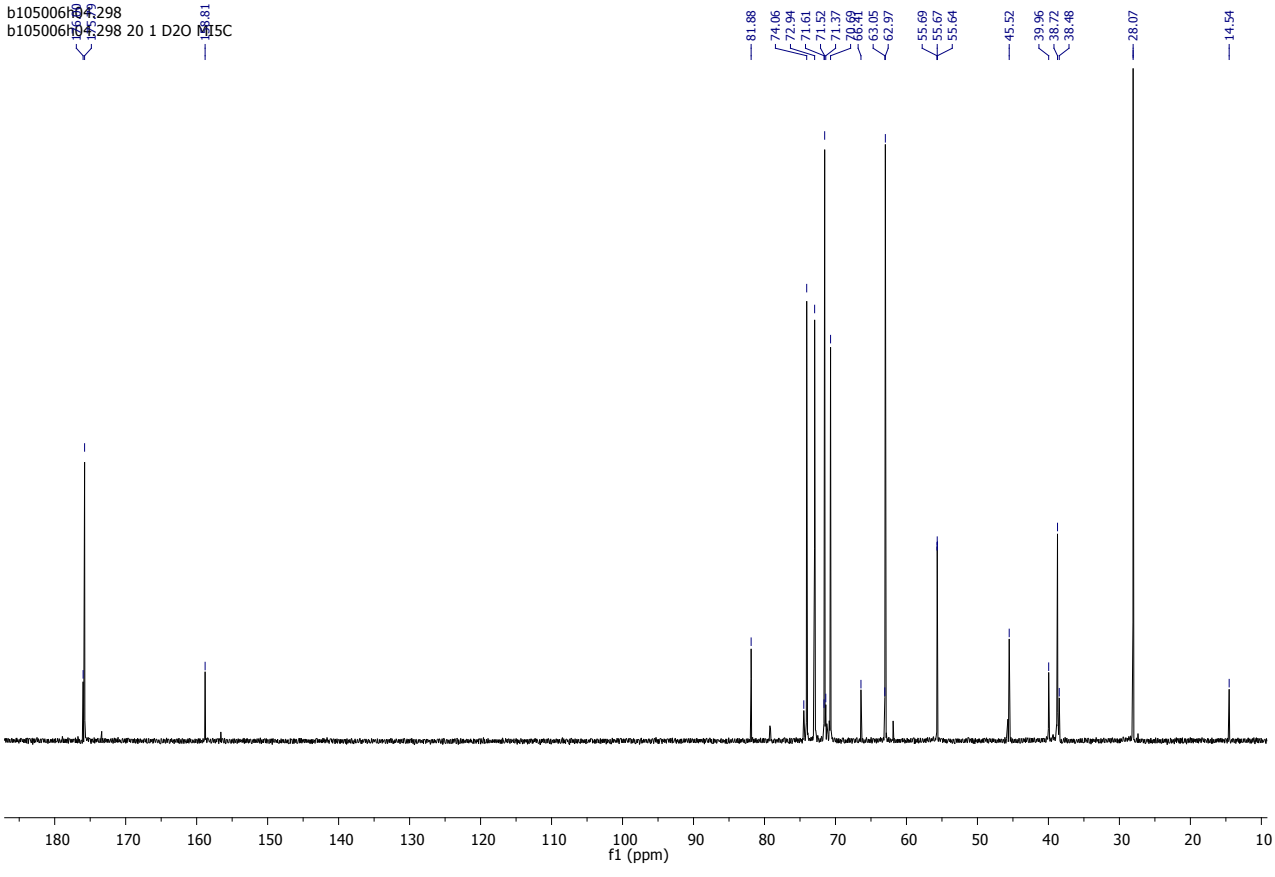
Compound 6


b104974h04.298
b104974h04.298 10 1 D2O MI3A
4.37
4.36
4.36
4.35
4.07
4.06
4.06
4.05
4.05
3.75
3.75
3.74
3.69
3.69
3.61
3.60
3.59
3.20
3.18
3.13
3.11
3.05
3.02
3.00
2.94
2.80
2.78
2.78
2.62
1.99
1.97
1.22
1.21
1.19
f1 (ppm)

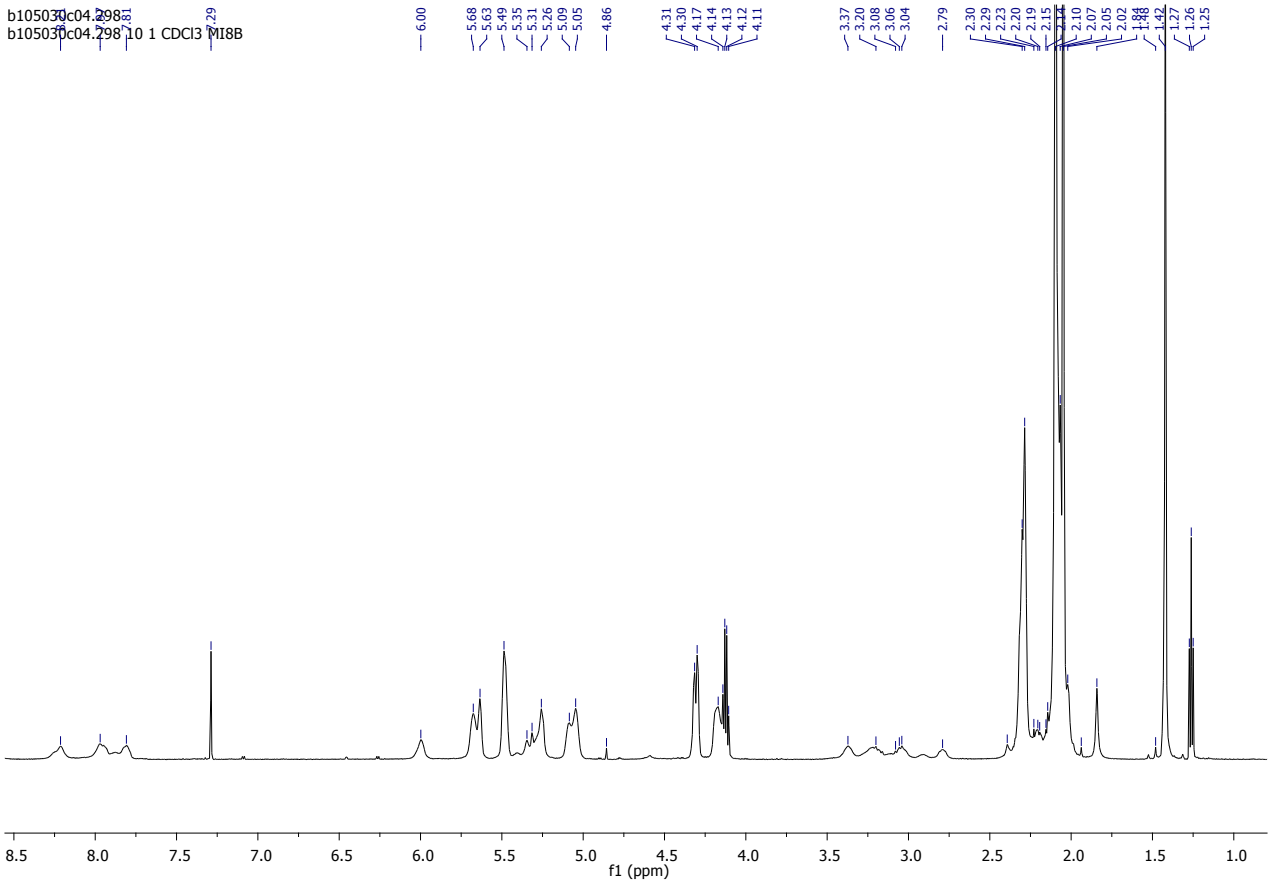

b104974h04.298
b104974h04.298 20 1 D2O MI3A
74.46
74.04
73.91
72.95
72.74
72.68
71.52
71.37
70.83
70.68
63.04
62.96
62.93
f1 (ppm)

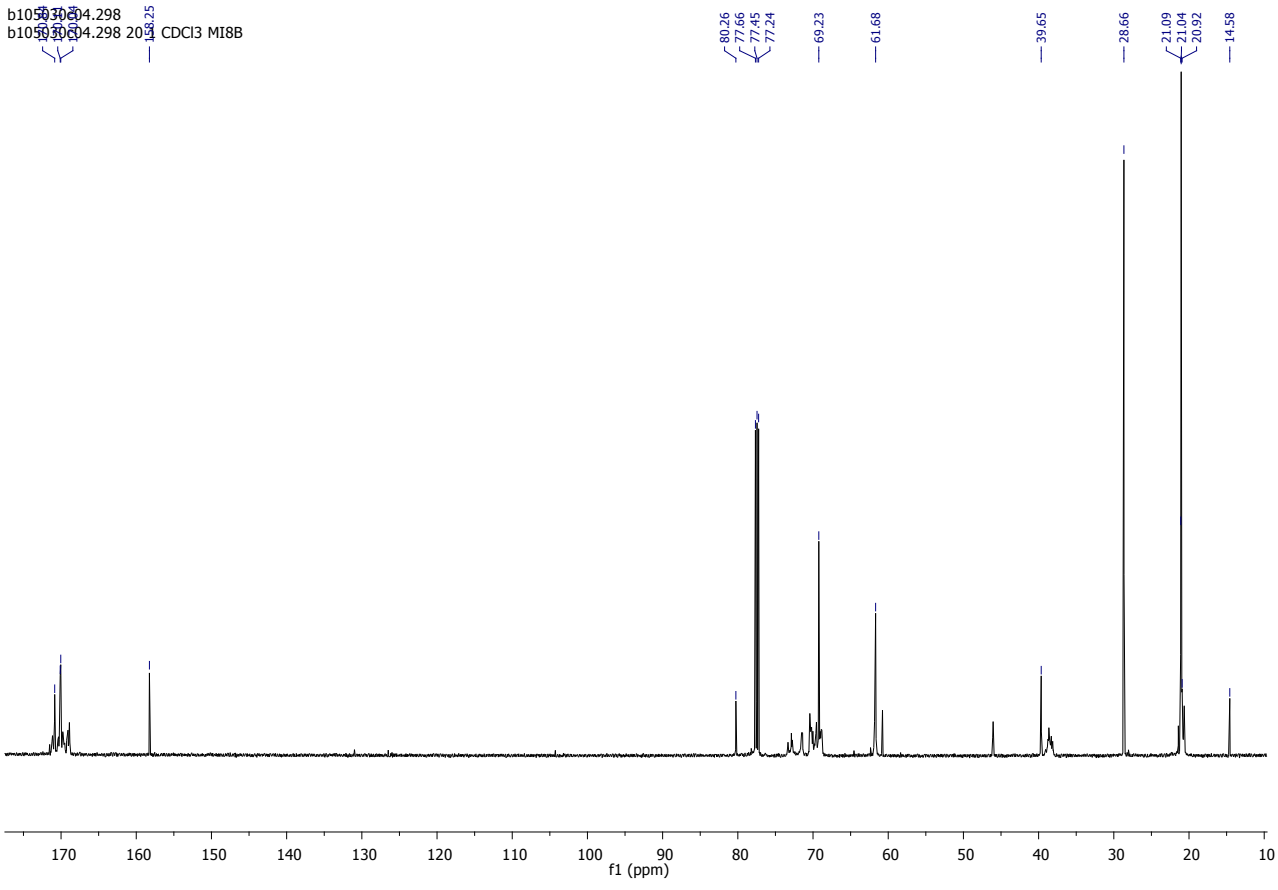
Compound 7


b105006h04.298
b105006h04.298 10 1 D2O M15C
4.73
4.71
4.38
4.37
4.35
4.35
4.09
4.08
4.07
4.07
4.06
3.77
3.75
3.71
3.71
3.70
3.69
3.68
3.62
3.61
3.60
3.59
3.24
3.12
3.09
3.06
3.04
3.00
2.98
2.91
2.89
2.83
2.81
1.42
1.40
1.13
1.12
1.11
5.64
5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8
f1 (ppm)

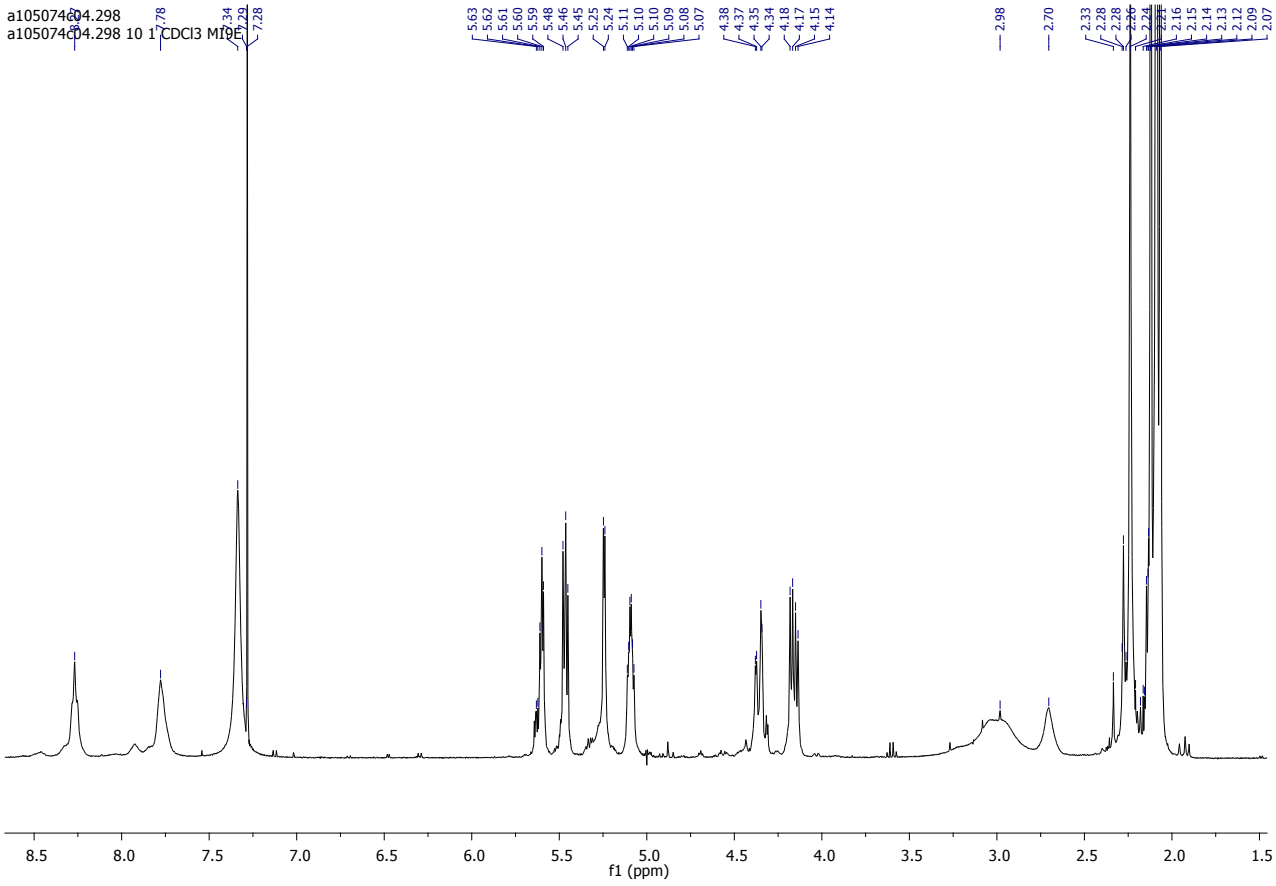

b105006h04.298
b105006h04.298 20 1 D2O M15C
174.92
174.81
81.88
74.06
72.94
71.61
71.52
71.37
70.68
70.41
63.05
62.97
55.69
55.67
55.64
45.52
39.96
38.72
38.48
28.07
14.54
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

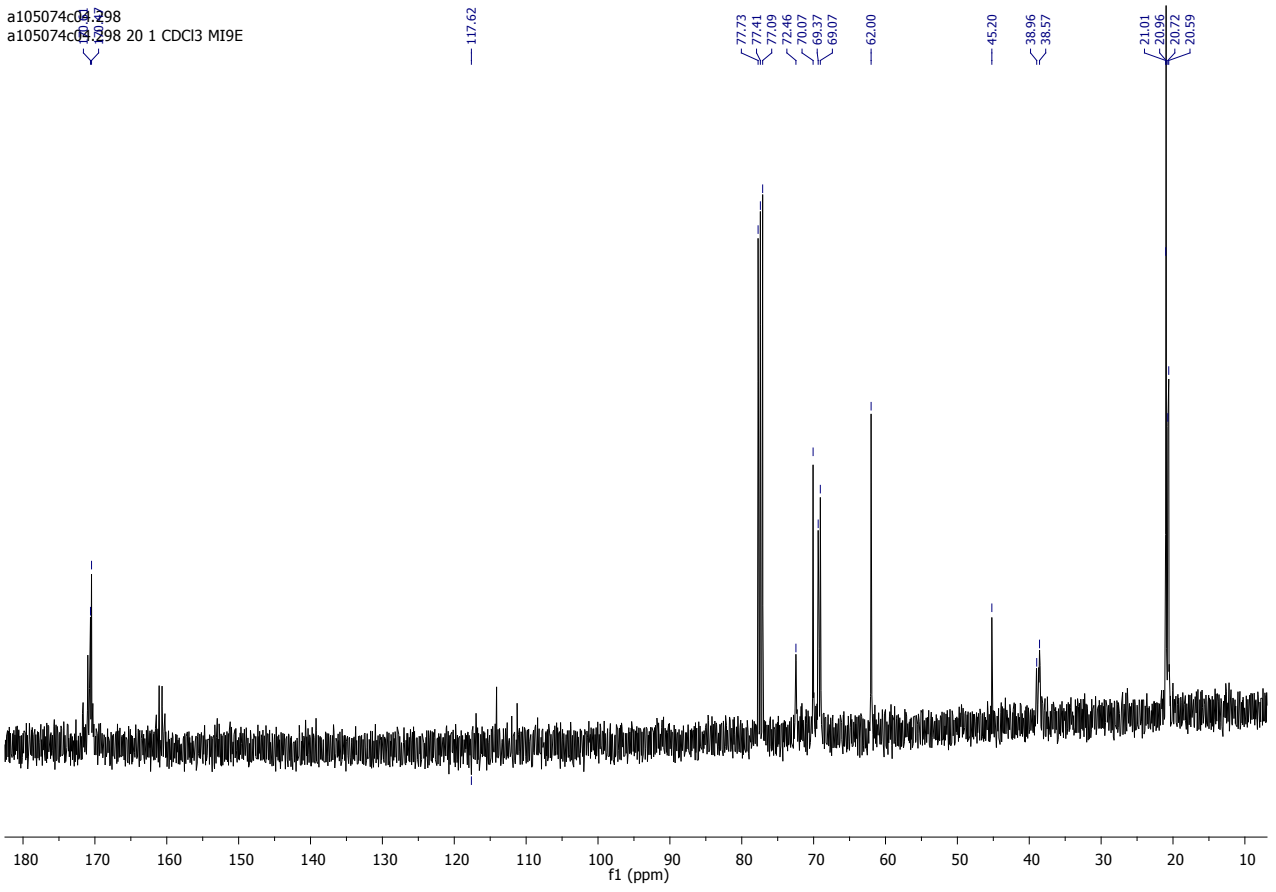
Compound 8


b105030c04.298
b105030c04.298 10 1 CDCl3 MI8B
7.81
7.29
6.00
5.68
5.63
5.49
5.35
5.31
5.26
5.09
5.05
4.86
4.31
4.30
4.17
4.14
4.13
4.12
4.11
3.37
3.20
3.08
3.06
3.04
2.79
2.30
2.29
2.23
2.20
2.19
2.15
2.10
2.07
2.05
2.02
1.84
1.48
1.42
1.27
1.26
1.25
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
f1 (ppm)

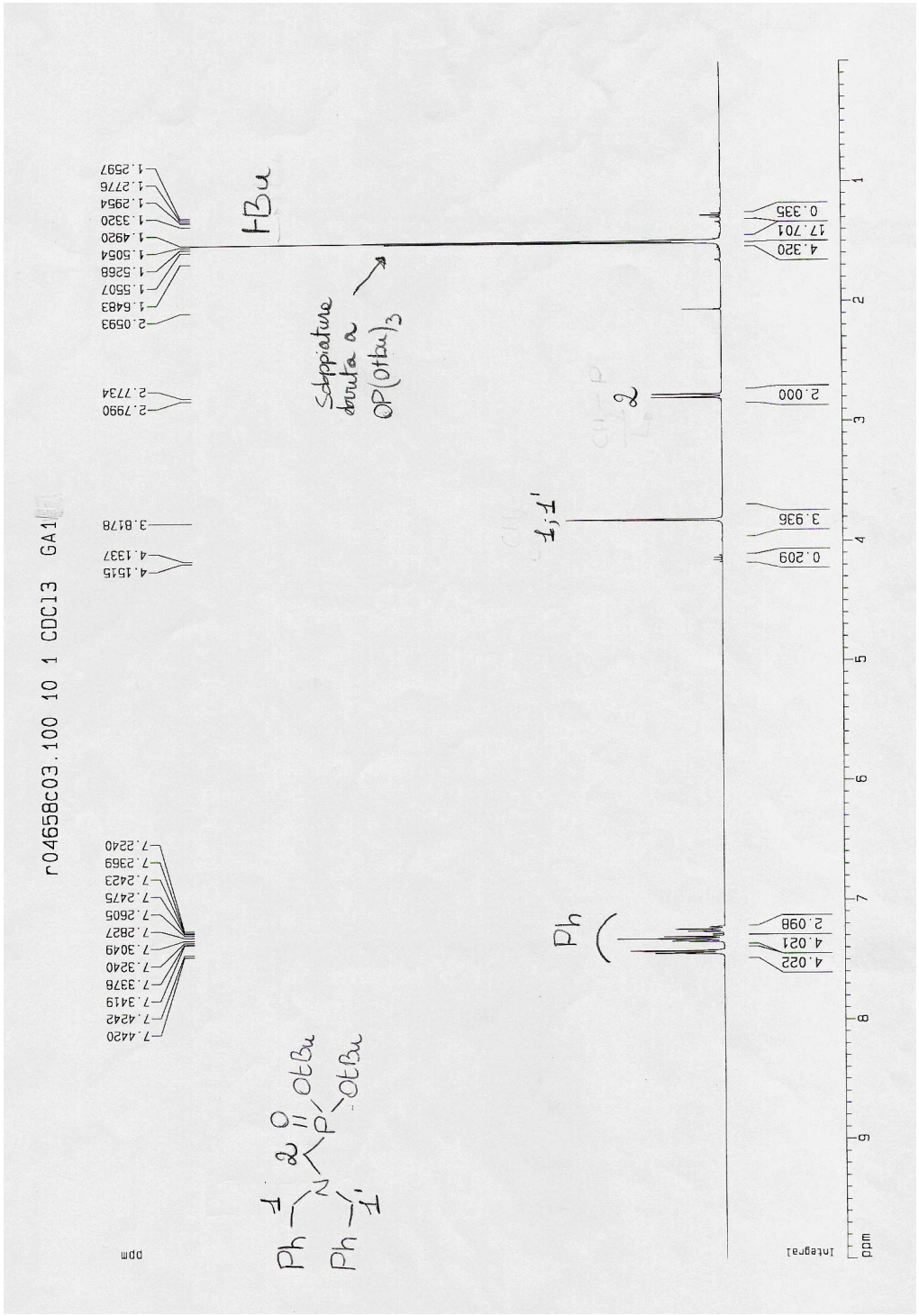

b105030c04.298
b105030c04.298 20 1 CDCl3 MI8B
158.25
80.26
77.66
77.45
77.24
69.23
61.68
39.65
28.66
21.09
21.04
20.92
14.58
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

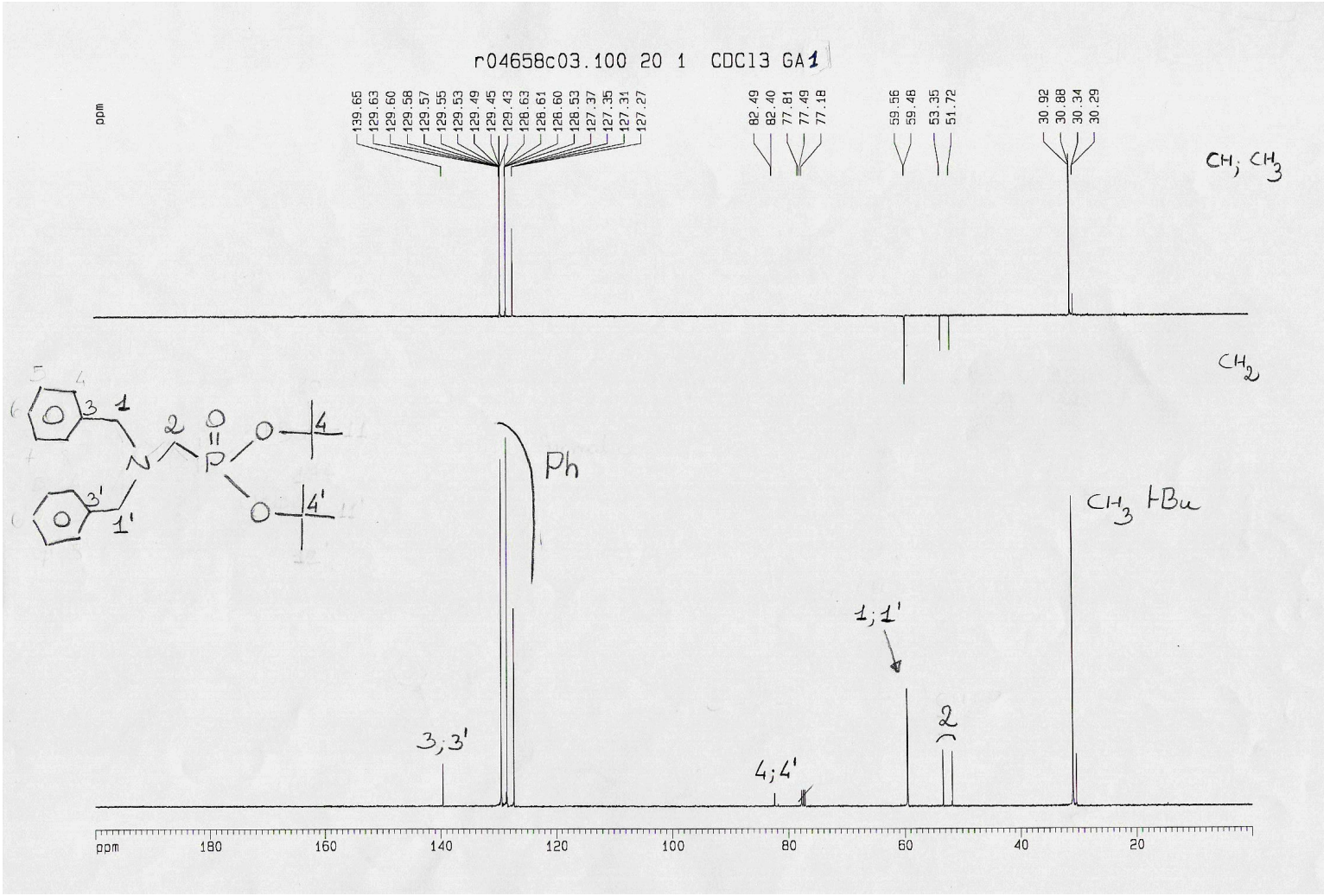
Compound 9

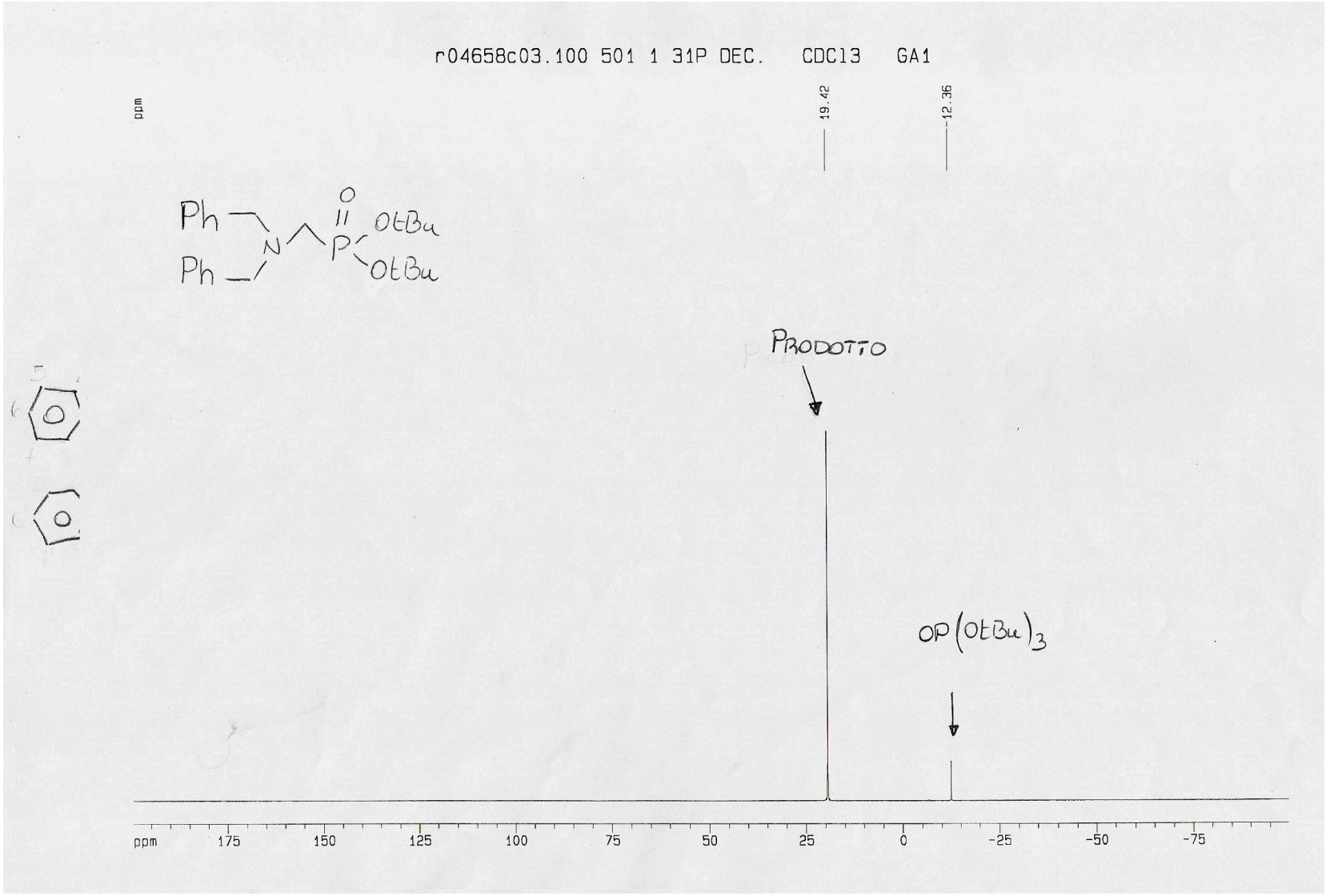

a105074c04.298
a105074c04.298 10 1 CDCl3 MI9E
7.78
7.34
7.29
7.28
5.63
5.62
5.61
5.60
5.59
5.48
5.46
5.45
5.25
5.24
5.11
5.10
5.10
5.09
5.08
5.07
4.38
4.37
4.35
4.34
4.18
4.17
4.15
4.14
2.98
2.70
2.33
2.28
2.28
2.26
2.24
2.16
2.15
2.14
2.13
2.12
2.09
2.07
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)


a105074c04.298
a105074c04.298 20 1 CDCl3 MI9E
117.62
77.73
77.41
77.09
72.46
70.07
69.37
69.07
62.00
45.20
38.96
38.57
21.01
20.96
20.72
20.59
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

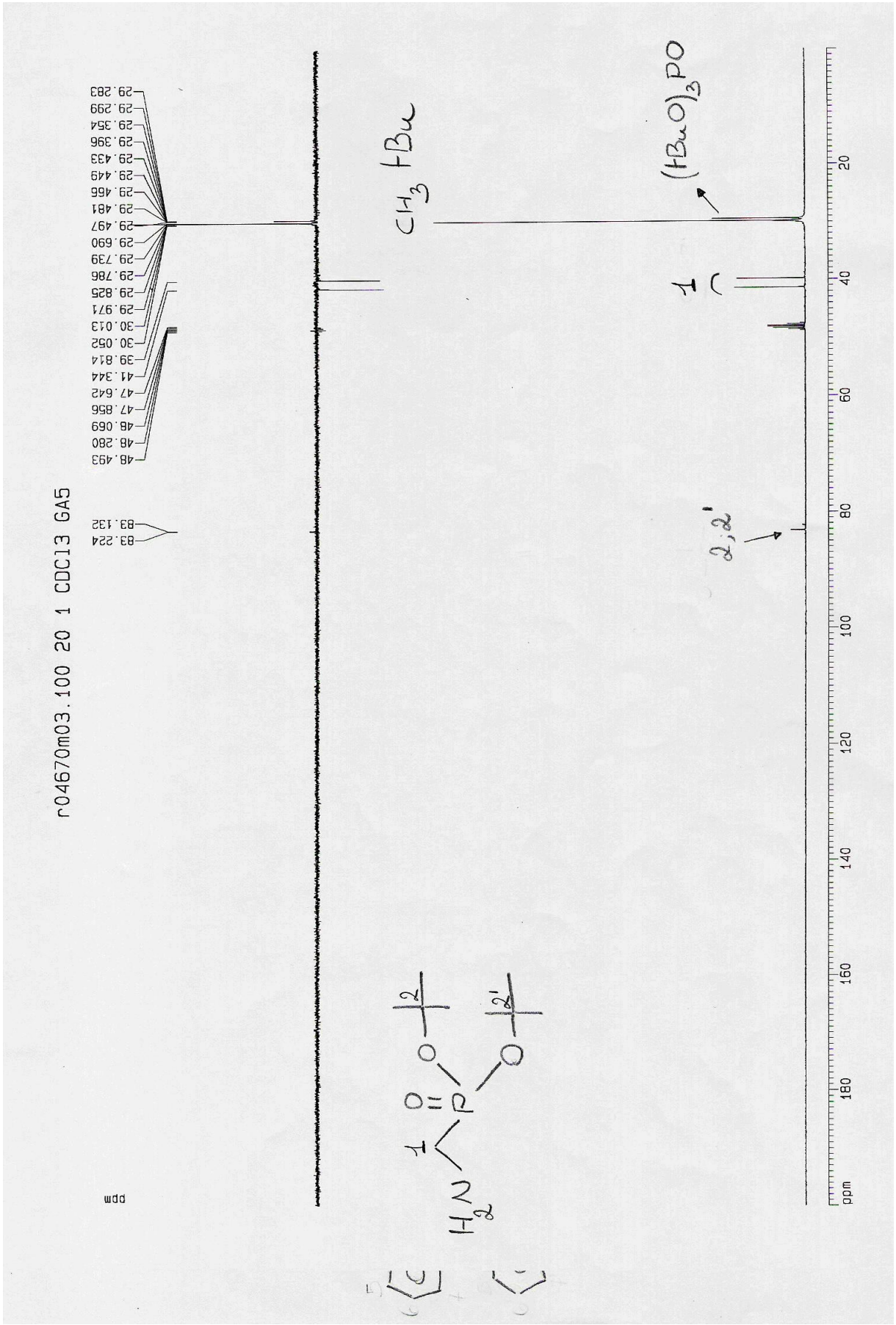
Compound 18

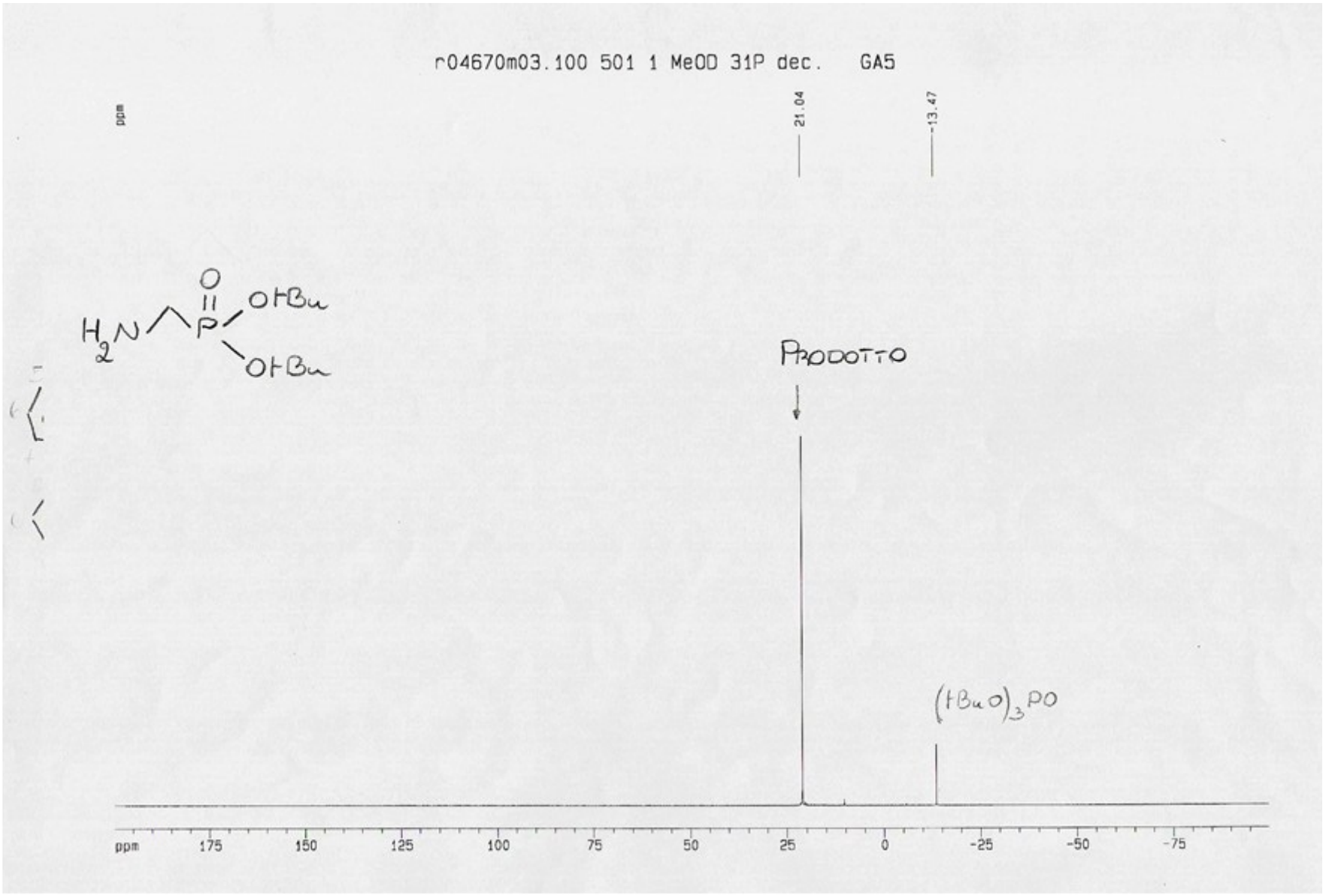

r04658c03.100 10 1 CDC13 GA1
7.4420
7.4242
7.3419
7.3378
7.3240
7.3049
7.2827
7.2605
7.2475
7.2423
7.2369
7.2240
3.8178
4.1337
4.1515
2.7990
2.7734
2.0593
1.6483
1.5507
1.5268
1.5054
1.4920
1.3320
1.2954
1.2776
1.2597
tBu
Soppiatura
dovuta a
OP(OtBu)3
1;1'
2
Ph
Ph
1
2
1'
OtBu
OtBu
4.022
4.021
2.098
0.209
3.936
2.000
4.320
17.701
0.335
ppm
Integral


r04658c03.100 20 1 CDCl3 GA1
ppm
139.65
129.63
129.60
129.58
129.57
129.55
129.53
129.49
129.45
129.43
128.63
128.61
126.60
128.53
127.37
127.35
127.31
127.27
82.49
82.40
77.81
77.49
77.18
59.56
59.48
53.35
51.72
30.92
30.88
30.34
30.29
CH; CH3
CH2
Ph
CH3 tBu
1;1'
2
3;3'
4;4'
ppm
180
160
140
120
100
80
60
40
20

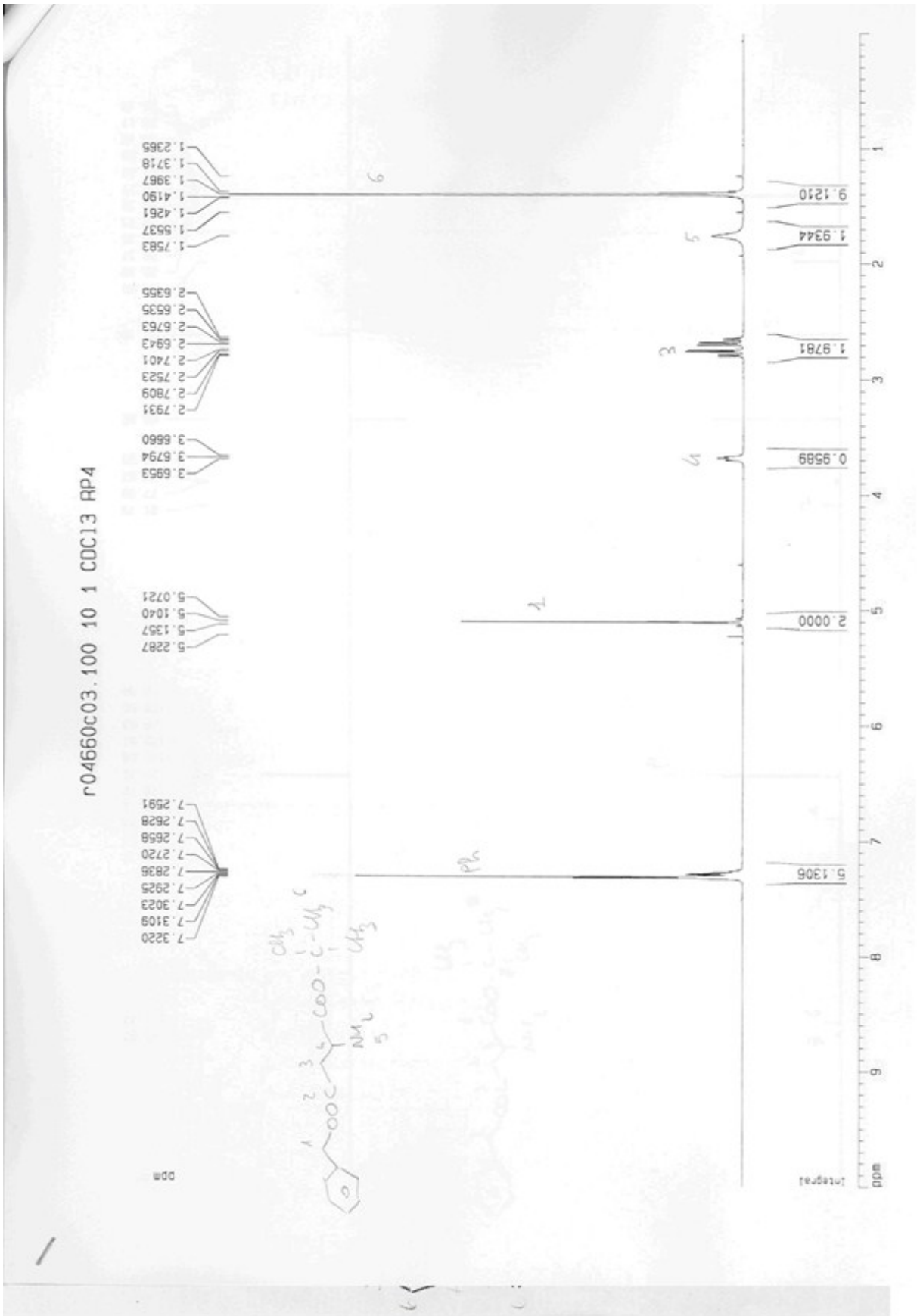

r04658c03.100 501 1 31P DEC. CDCl3 GA1
ppm
19.42
12.36
Ph
Ph
N
O
P
OtBu
OtBu
PRODOTTO
OP(OtBu)3
ppm
175
150
125
100
75
50
25
0
-25
-50
-75

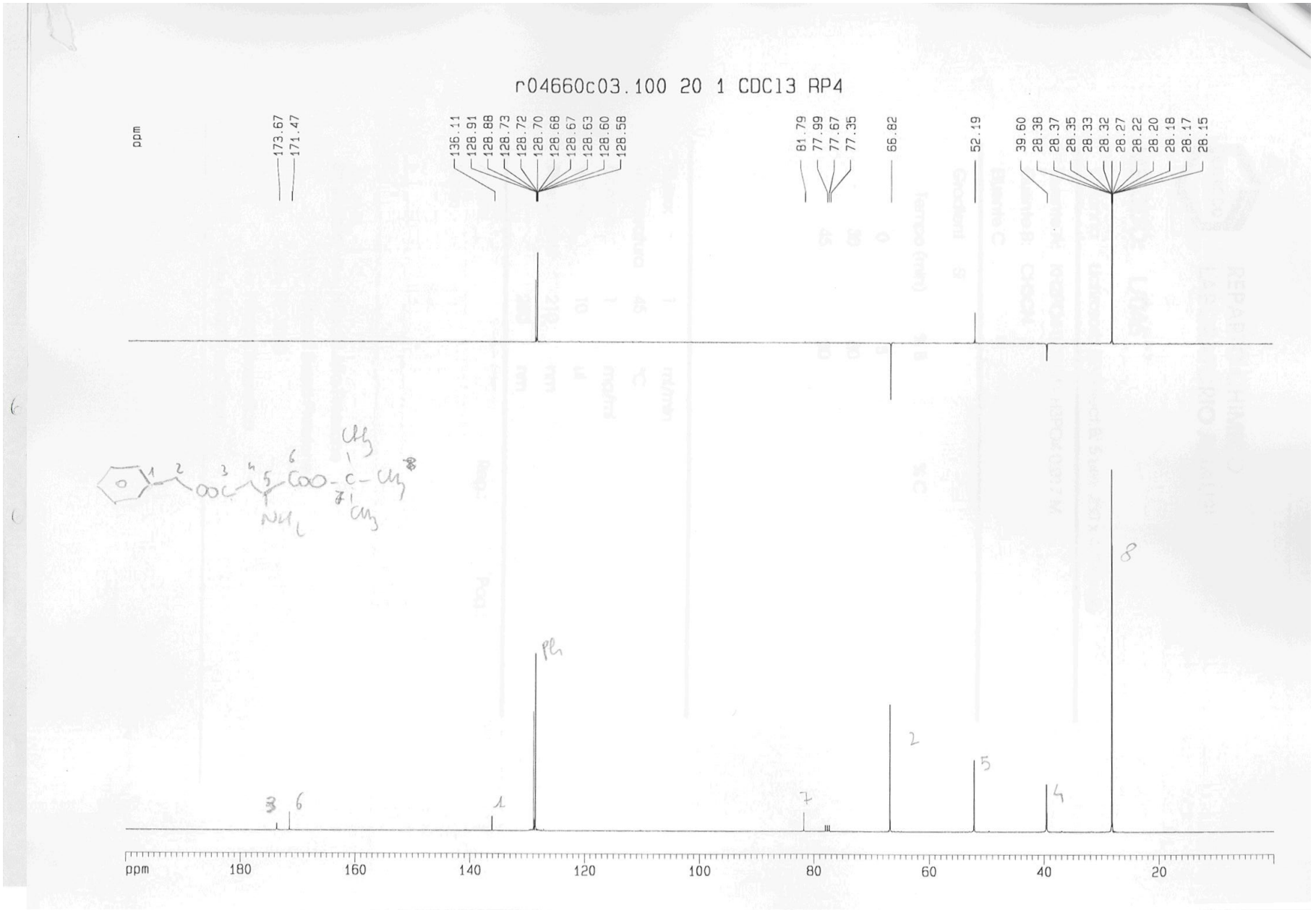
Compound 19


r04670m03.100 20 1 CDC13 GA5
ppm
29.283
29.299
29.354
29.396
29.433
29.449
29.466
29.481
29.497
29.690
29.739
29.786
29.825
29.971
30.013
30.052
39.814
41.344
47.642
47.856
48.069
48.280
48.493
83.132
83.224
CH_3 tBu
$(tBuO)_3PO$
1
2,2'
1
2
2'
H_2N
P
O
O
O
O

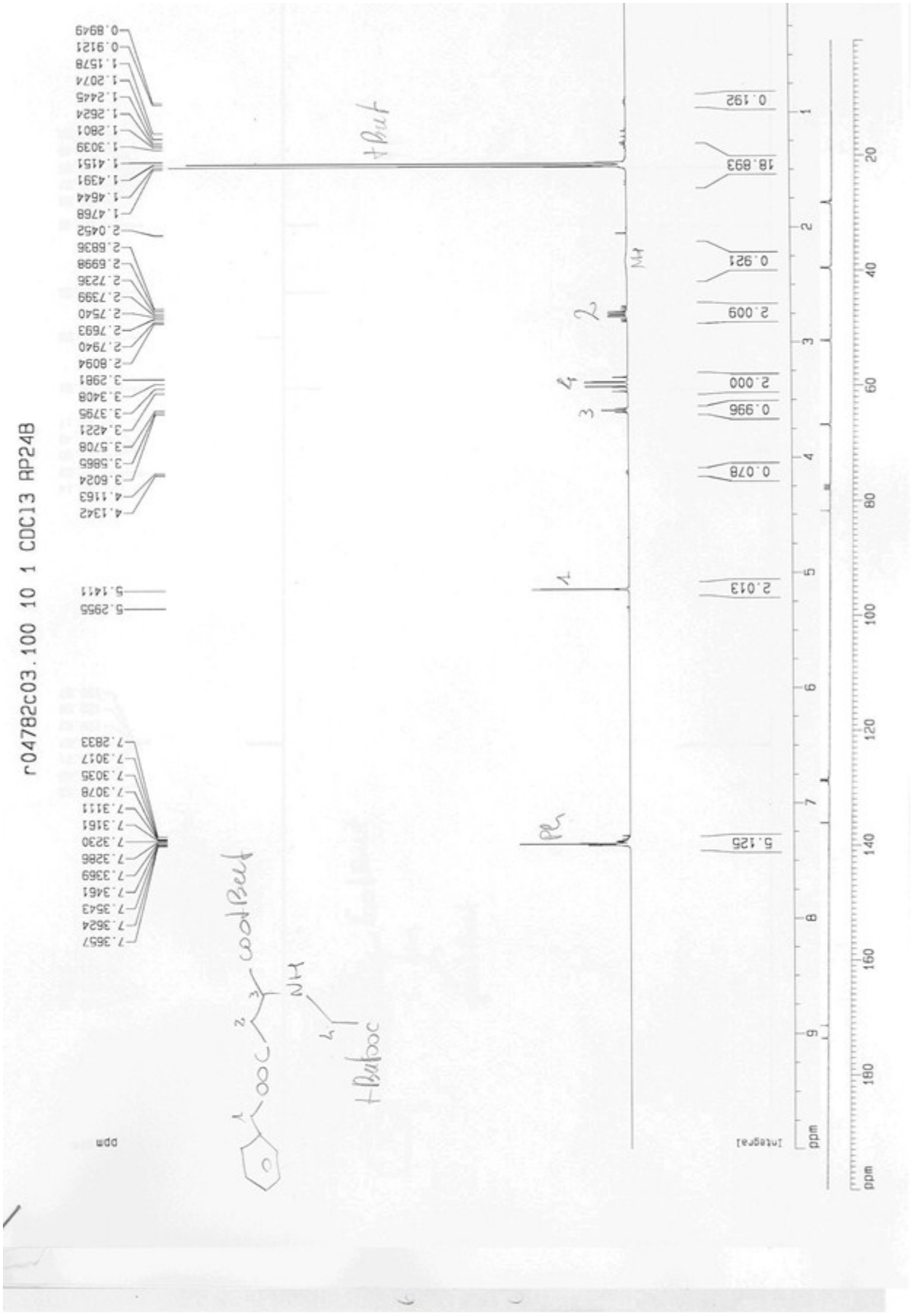

r04670m03.100 501 1 MeOD 31P dec. GA5
ppm
21.04
-13.47
PRODOTTO
(tBuO)3PO
ppm 175 150 125 100 75 50 25 0 -25 -50 -75

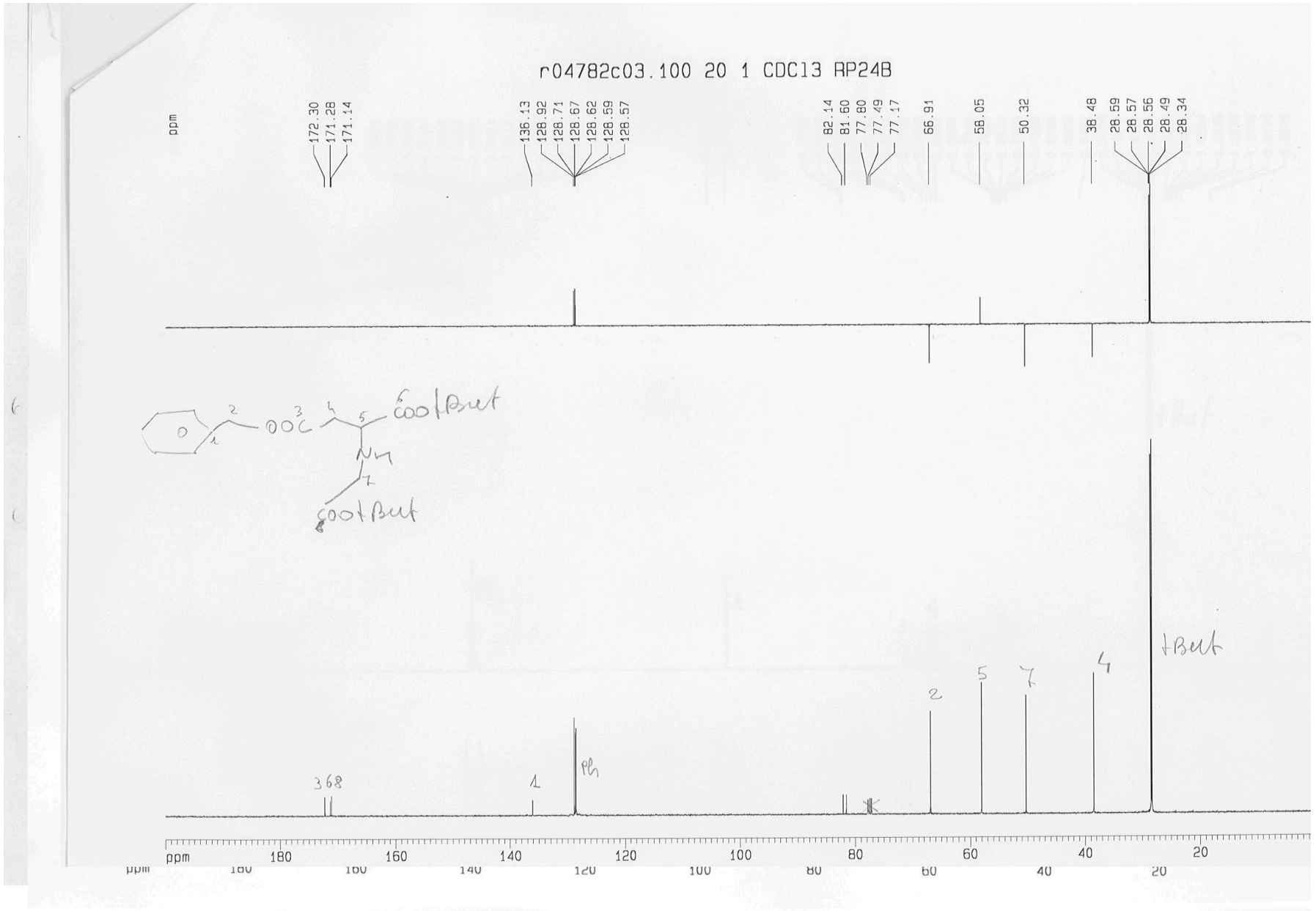
Compound 11


r04660c03.100 10 1 CDCl3 RP4
7.3220
7.3109
7.3023
7.2925
7.2836
7.2720
7.2658
7.2628
7.2581
5.2287
5.1357
5.1040
5.0721
3.6953
3.6794
3.6660
2.7931
2.7809
2.7523
2.7401
2.6943
2.6763
2.6535
2.6355
1.7583
1.5537
1.4261
1.4190
1.3967
1.3718
1.2365
5.1306
2.0000
0.9589
1.9781
1.9344
9.1210
integral
ppm

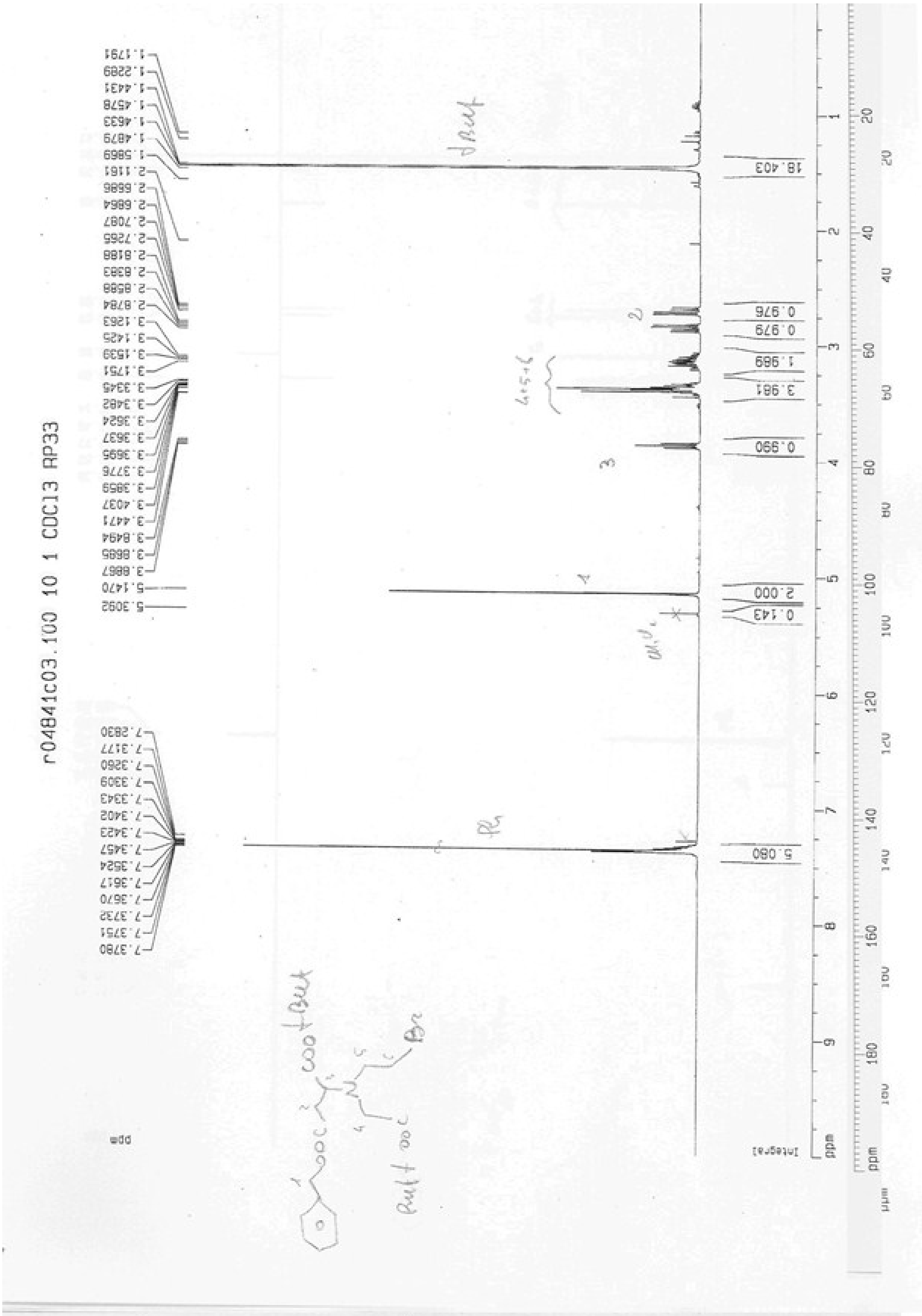

r04660c03.100 20 1 CDCl3 RP4
ppm
173.67
171.47
136.11
128.91
128.88
128.73
128.72
128.70
128.68
128.67
128.63
128.60
128.58
81.79
77.99
77.67
77.35
66.82
52.19
39.60
28.38
28.37
28.35
28.33
28.32
28.27
28.22
28.20
28.18
28.17
28.15
Ph
8
2
5
4
1
7
3
6
ppm
180
160
140
120
100
80
60
40
20

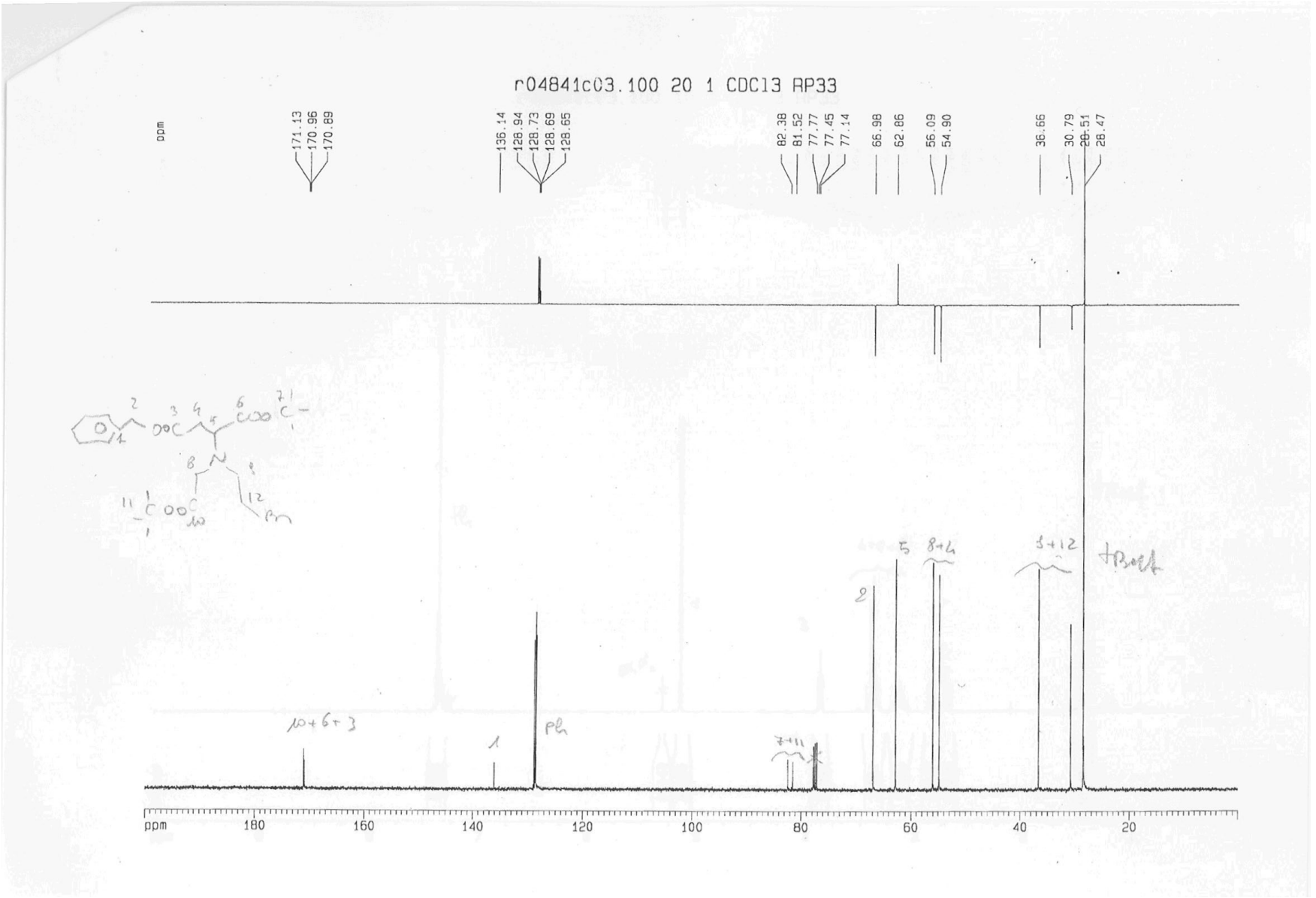
Compound 12



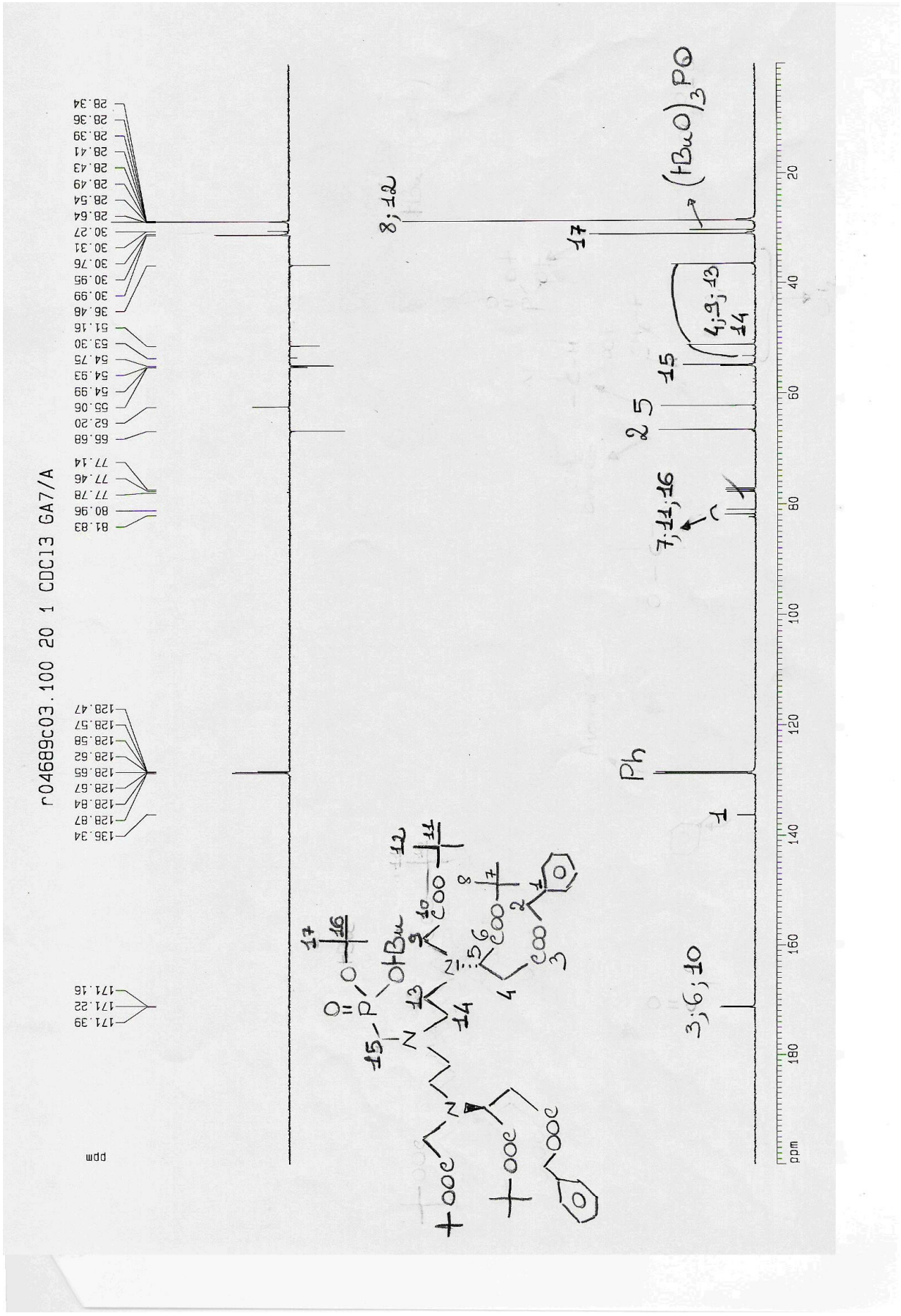

r04782c03.100 20 1 CDCl3 RP24B
ppm
172.30
171.28
171.14
136.13
128.92
128.71
128.67
128.62
128.59
128.57
82.14
81.60
77.80
77.49
77.17
66.91
58.05
50.32
38.48
28.59
28.57
28.56
28.49
28.34
COOtBut
COOtBut
tBut
2
5
7
4
1
Ph
3 6 8
ppm
180
160
140
120
100
80
60
40
20

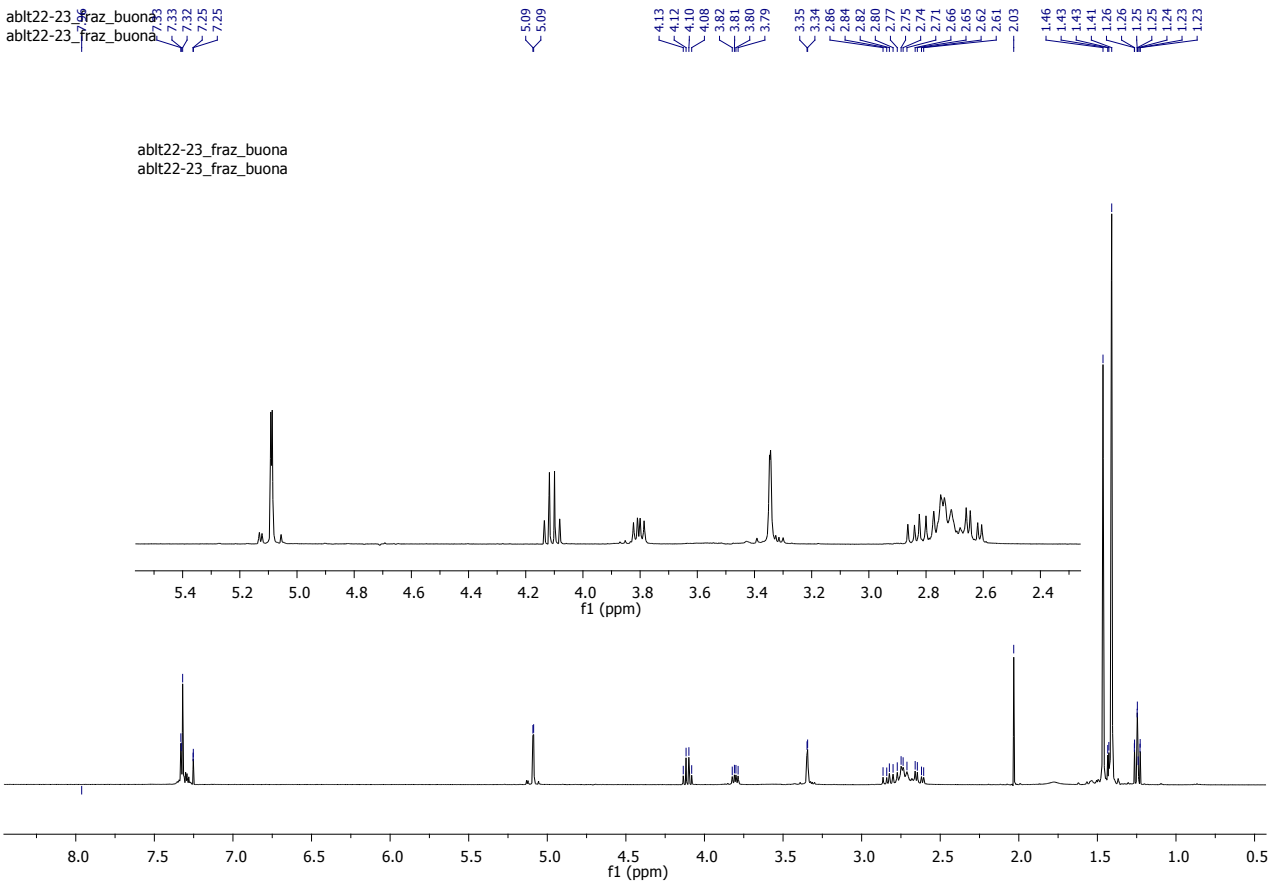
Compound 13



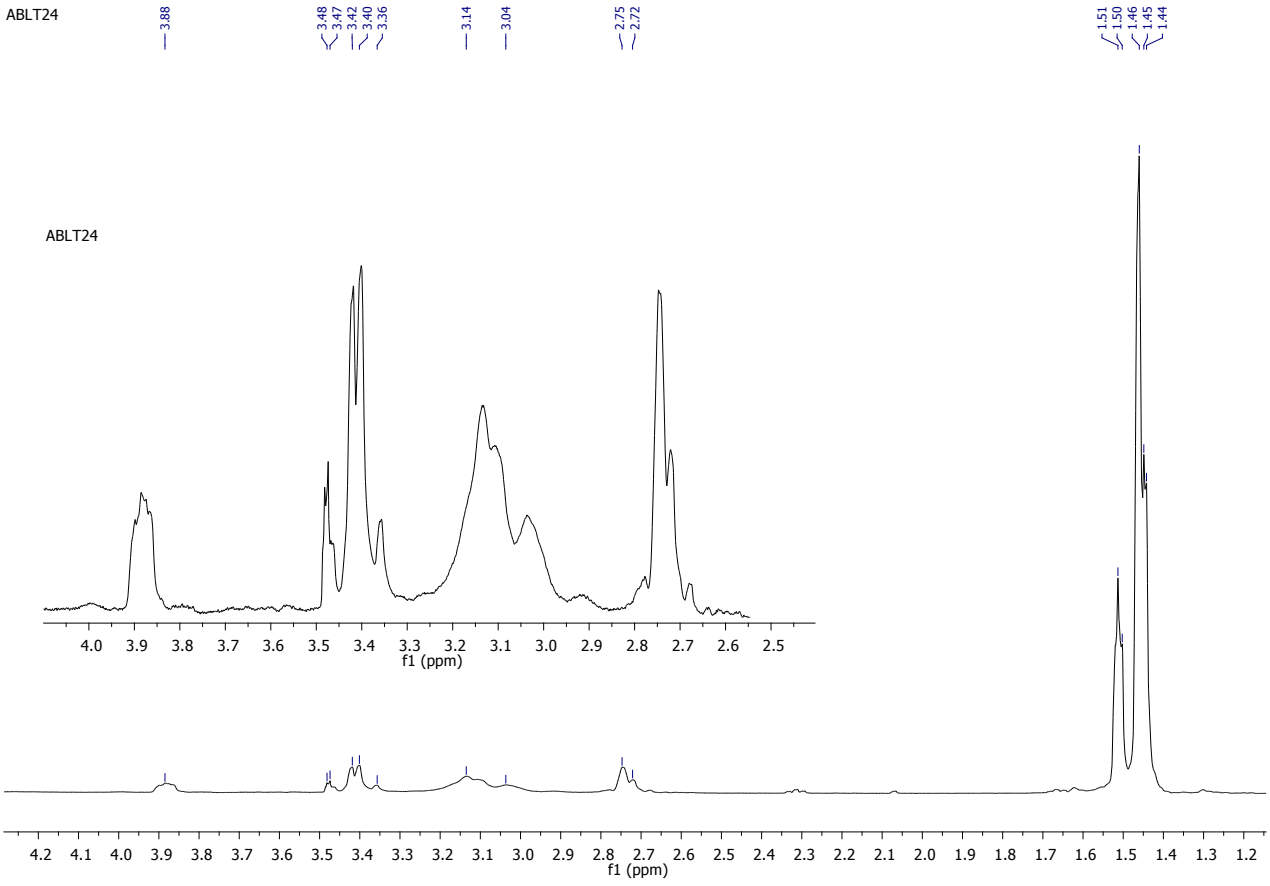

r04841c03.100 20 1 CDCl3 RP33
ppm
171.13
170.96
170.89
136.14
128.94
128.73
128.69
128.65
82.38
81.52
77.77
77.45
77.14
66.98
62.86
56.09
54.90
36.66
30.79
28.51
28.47
10+6+3
1
Ph
7+11
2
5
8+4
3+12
tBu
ppm
180
160
140
120
100
80
60
40
20

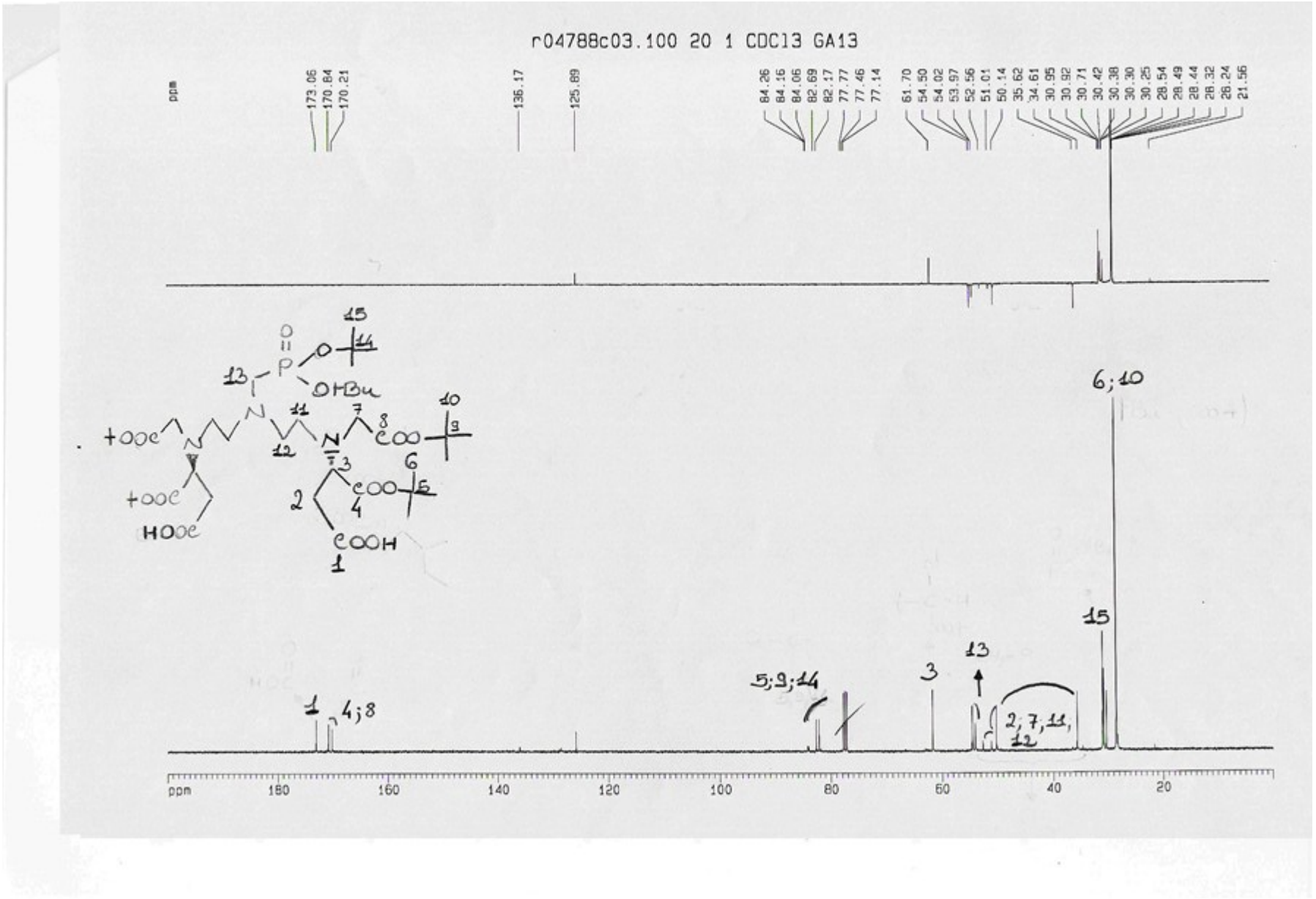
Compound 14


r04689c03.100 20 1 CDCl3 GA7/A
ppm
(tBuO)3PO
Ph
8;12
17
7;11;16
2 5
15
4;9;13
14
3;6;10
1
12
11
10
9
8
7
6
5
4
3
2
1
13
14
15
16
17

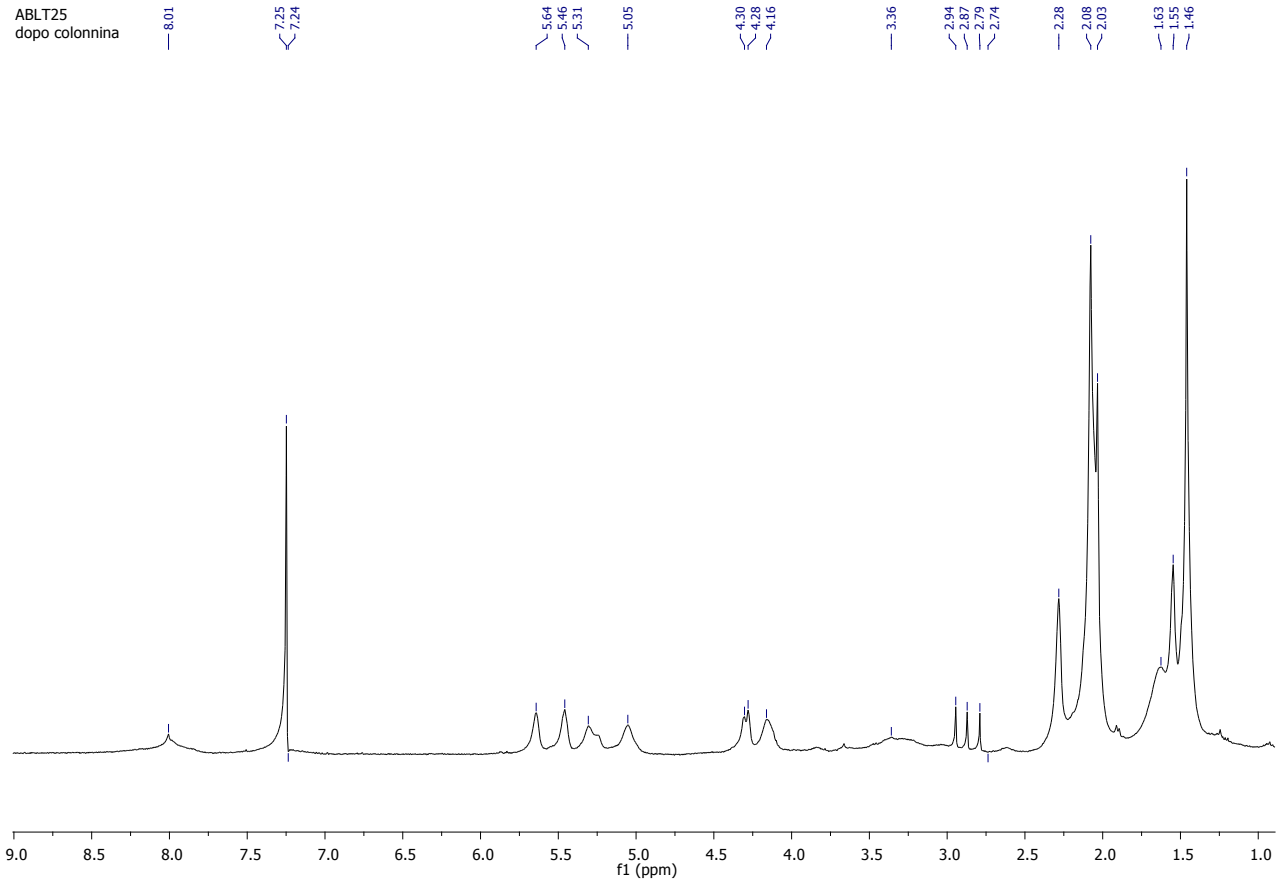

ablt22-23_fraz_buona
ablt22-23_fraz_buona
f1 (ppm)

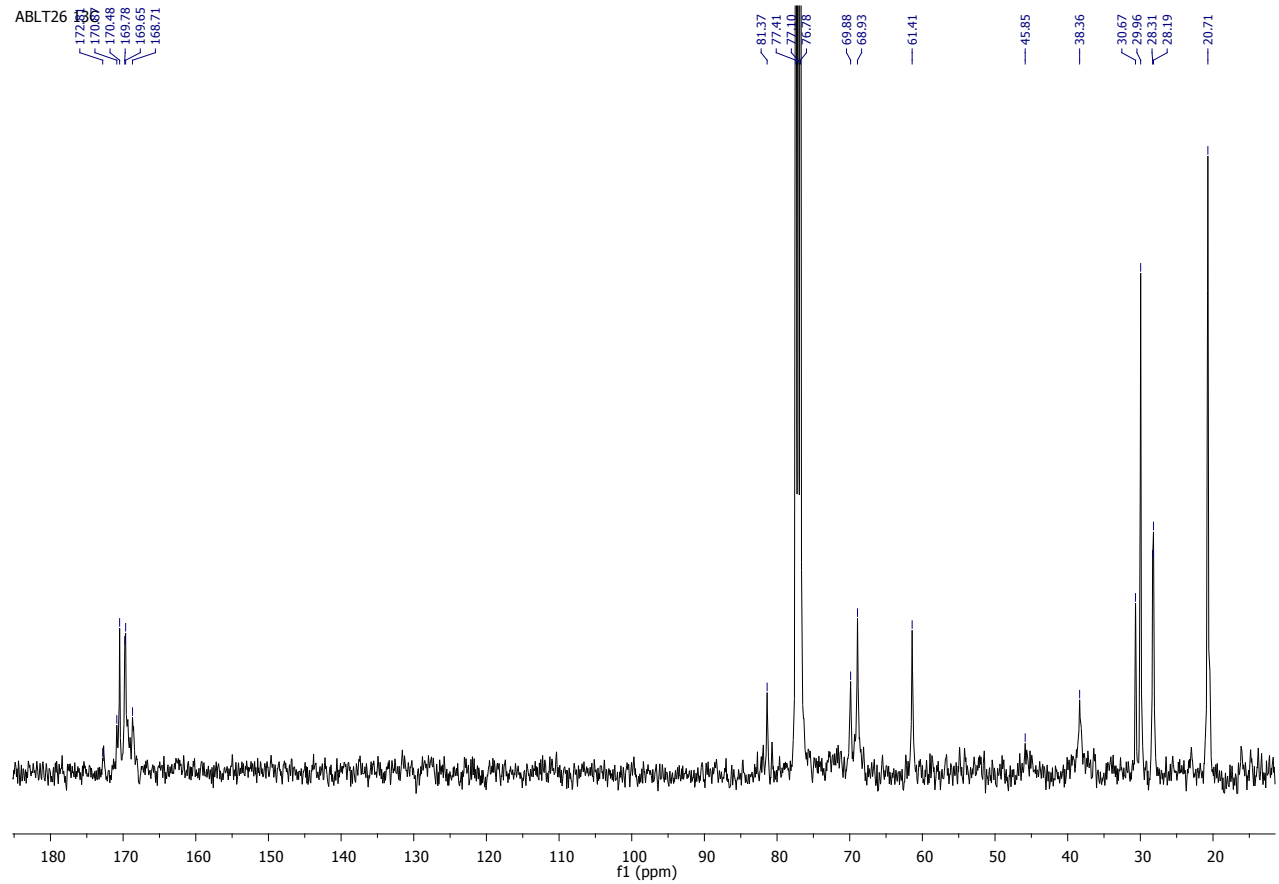
Compound 15


ABLT24
ABLT24
f1 (ppm)

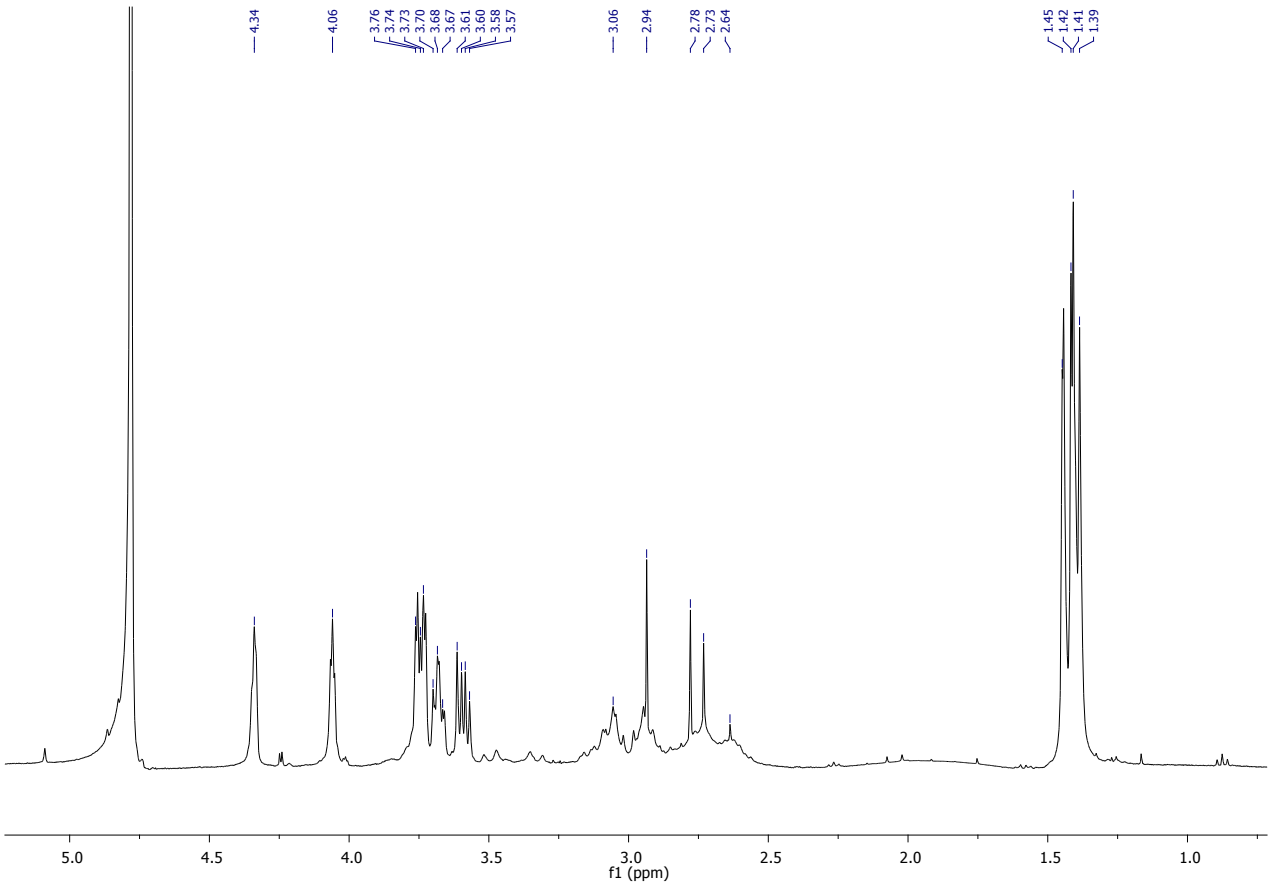

r04788c03.100 20 1 CDCl3 GA13
ppm
173.06
170.84
170.21
136.17
125.89
84.26
84.16
84.06
82.69
82.17
77.77
77.46
77.14
61.70
54.50
54.02
53.97
52.56
51.01
50.14
35.62
34.61
30.95
30.92
30.71
30.42
30.38
30.30
30.25
28.54
28.49
28.44
28.32
28.24
21.56
6;10
15
13
5;9;14
3
1
4;8
2;7;11;12
ppm
180
160
140
120
100
80
60
40
20

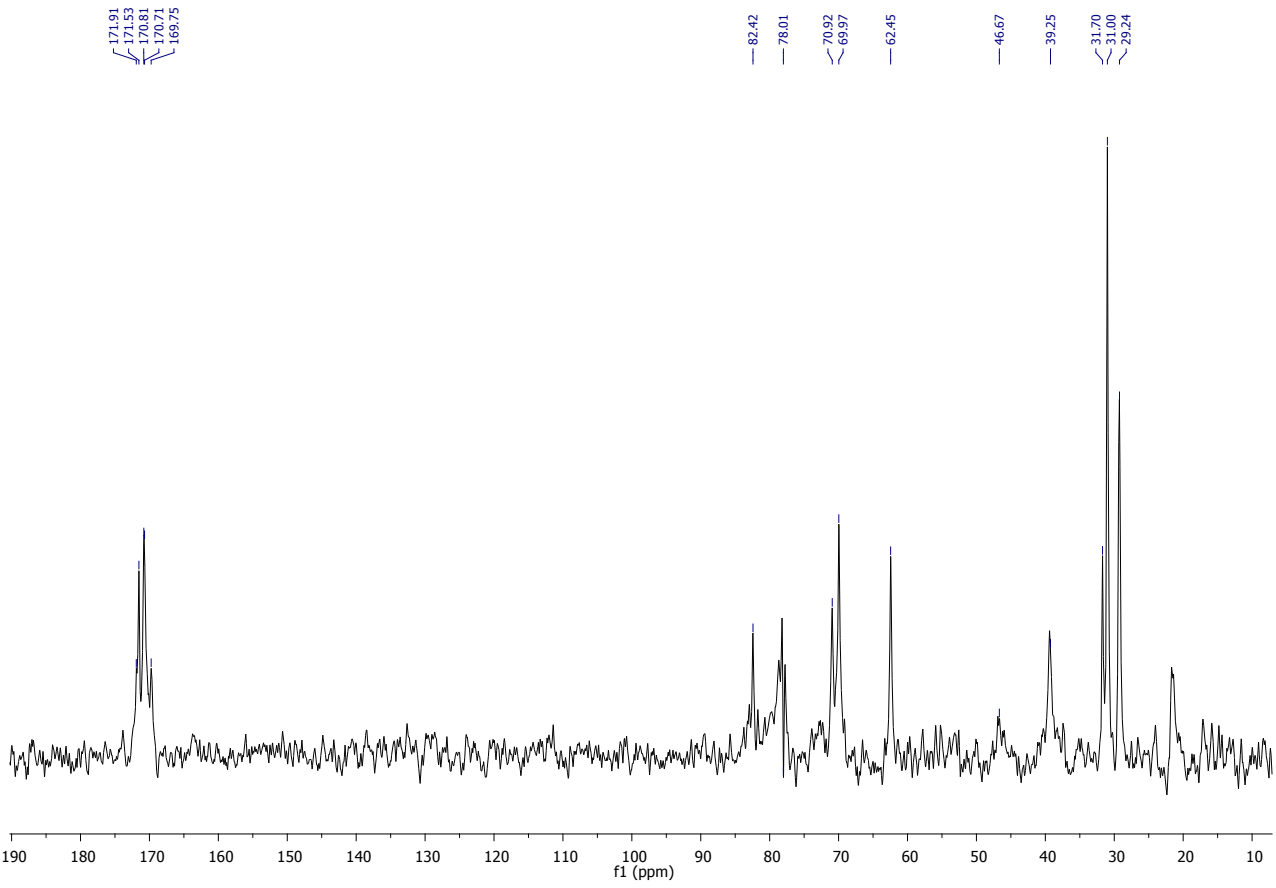
Compound 16


ABLT25
dopo colonnina
8.01
7.25
7.24
5.64
5.46
5.31
5.05
4.30
4.28
4.16
3.36
2.94
2.87
2.79
2.74
2.28
2.08
2.03
1.63
1.55
1.46
f1 (ppm)

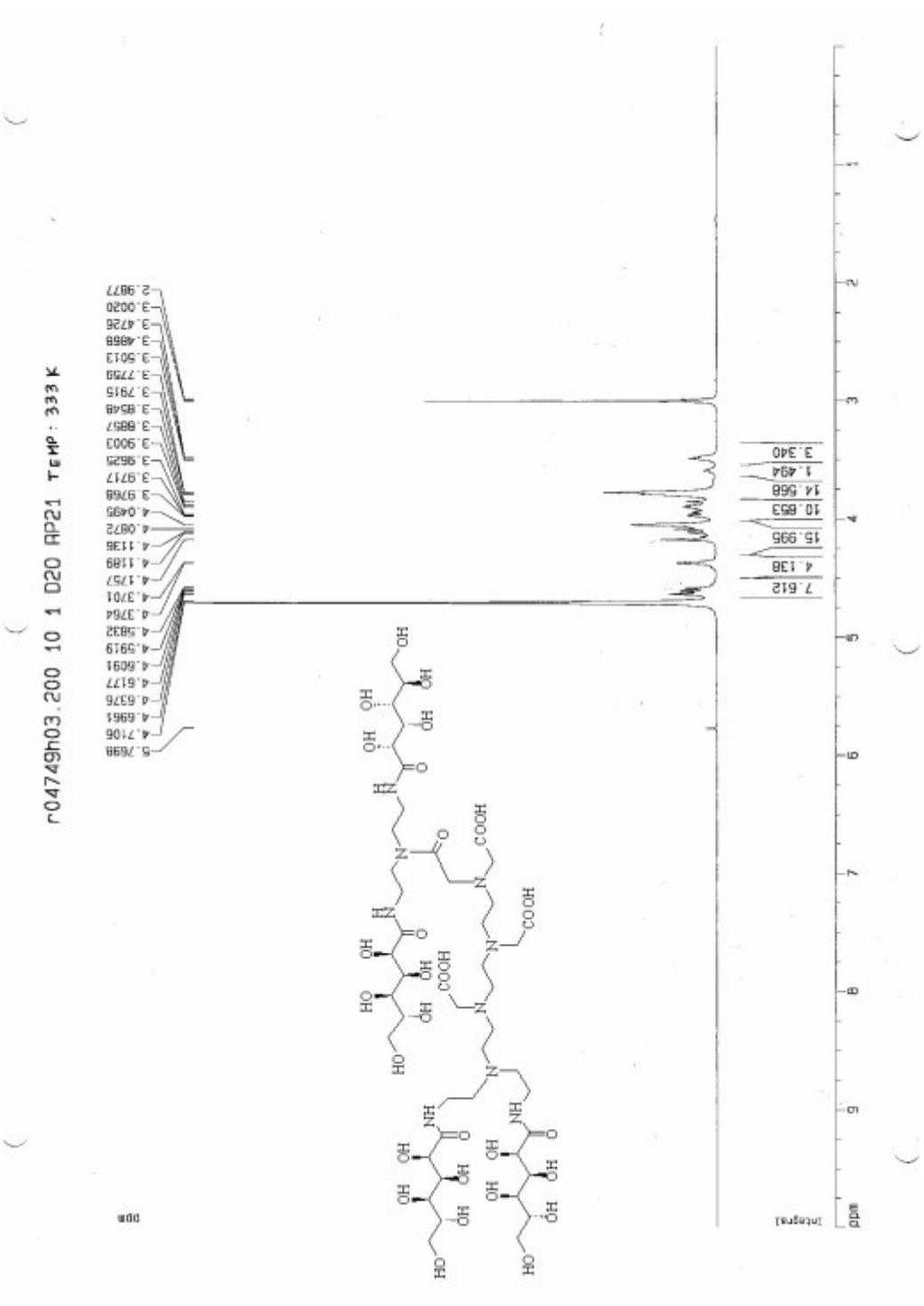

ABLT26
172.87
170.67
170.48
169.78
169.65
168.71
81.37
77.41
77.10
76.78
69.88
68.93
61.41
45.85
38.36
30.67
29.96
28.31
28.19
20.71
f1 (ppm)

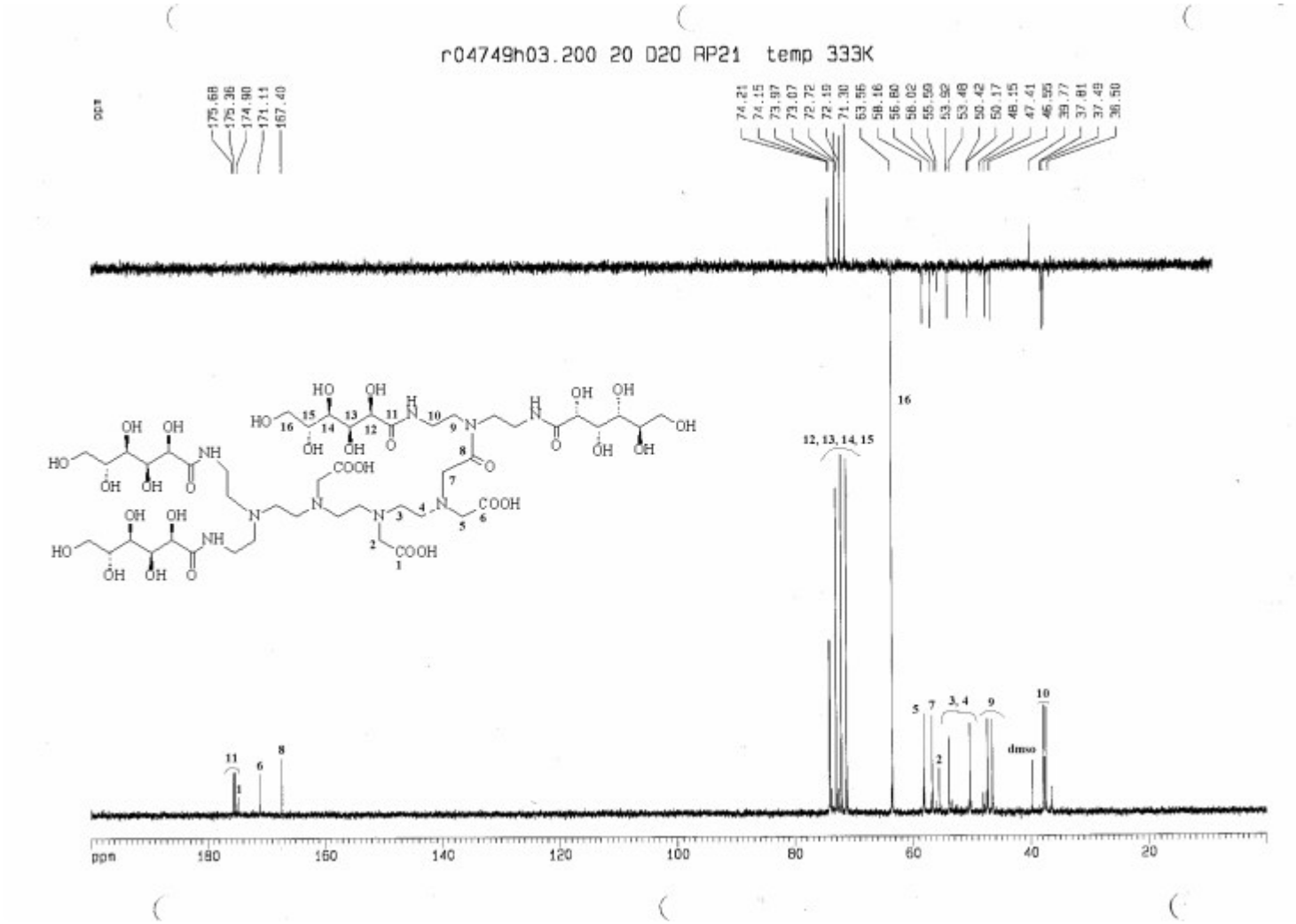
Compound 17


4.34
4.06
3.76
3.74
3.73
3.70
3.68
3.67
3.61
3.60
3.58
3.57
3.06
2.94
2.78
2.73
2.64
1.45
1.42
1.41
1.39
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


171.91
171.53
170.81
170.71
169.75
82.42
78.01
70.92
69.97
62.45
46.67
39.25
31.70
31.00
29.24
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

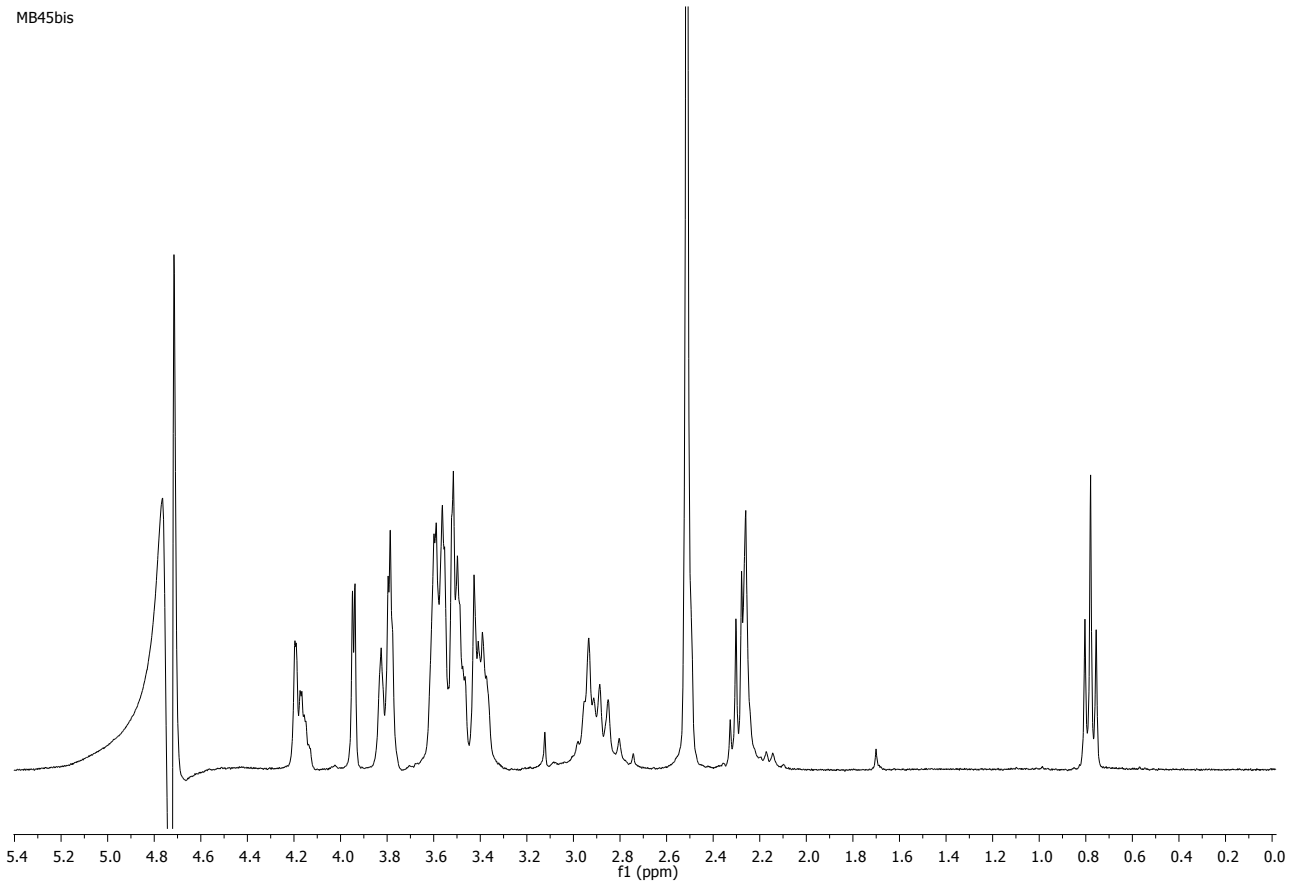
Compound L1

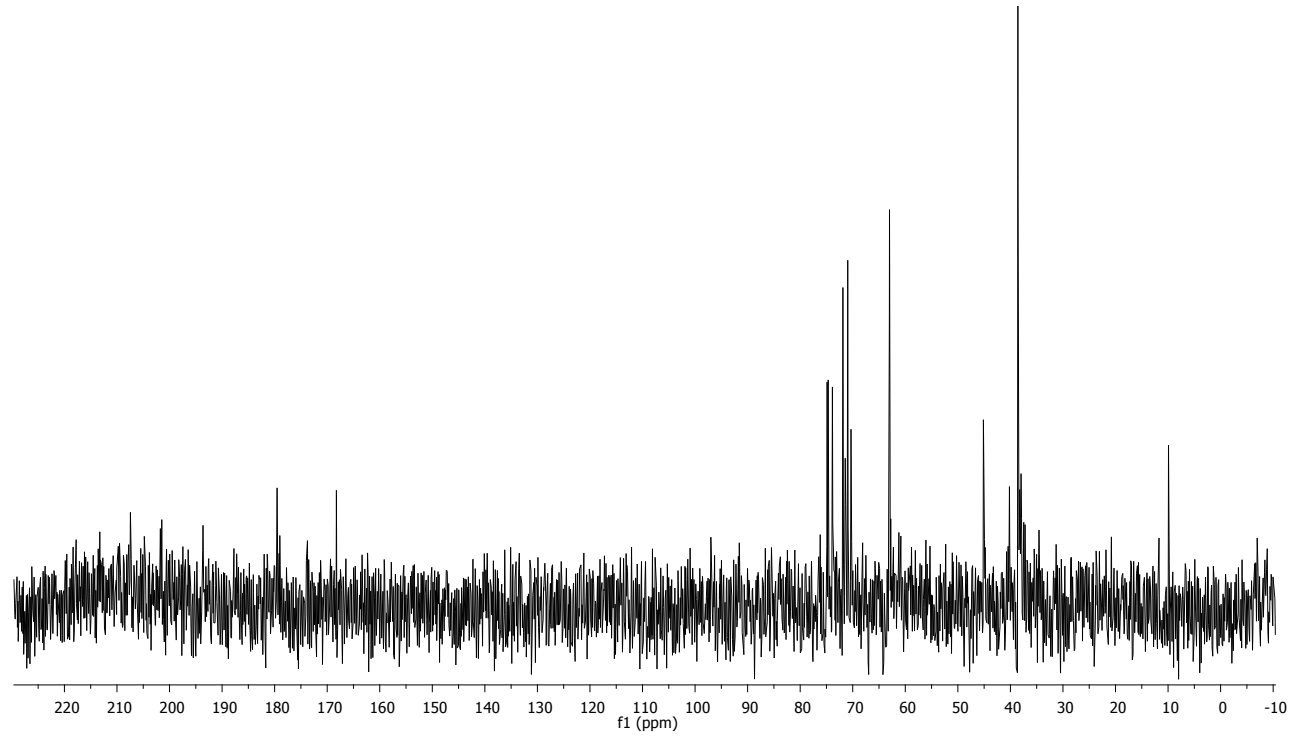

r04749h03.200 10 1 D2O AP21 TEMP: 333 K
5.7698
4.7106
4.6961
4.6376
4.6177
4.6091
4.5919
4.5832
4.3764
4.3701
4.1757
4.1189
4.1136
4.0872
4.0495
3.9768
3.9717
3.9625
3.9003
3.8857
3.8548
3.7915
3.7758
3.5013
3.4868
3.4726
3.0020
2.9877
7.612
4.138
15.995
10.853
14.568
1.494
3.340
ppm
Integral
ppm
OH
HO
HN
O
N
COOH


r04749h03.200 20 D20 RP21 temp 333K
ppm
175.68
175.36
174.90
171.11
167.40
74.21
74.15
73.97
73.07
72.72
72.19
71.30
63.56
58.16
56.80
56.02
55.59
53.92
53.48
50.42
50.17
48.15
47.41
46.95
39.77
37.81
37.49
36.50
16
12, 13, 14, 15
11
6
8
1
5
7
3, 4
9
2
dmso
10
180
160
140
120
100
80
60
40
20

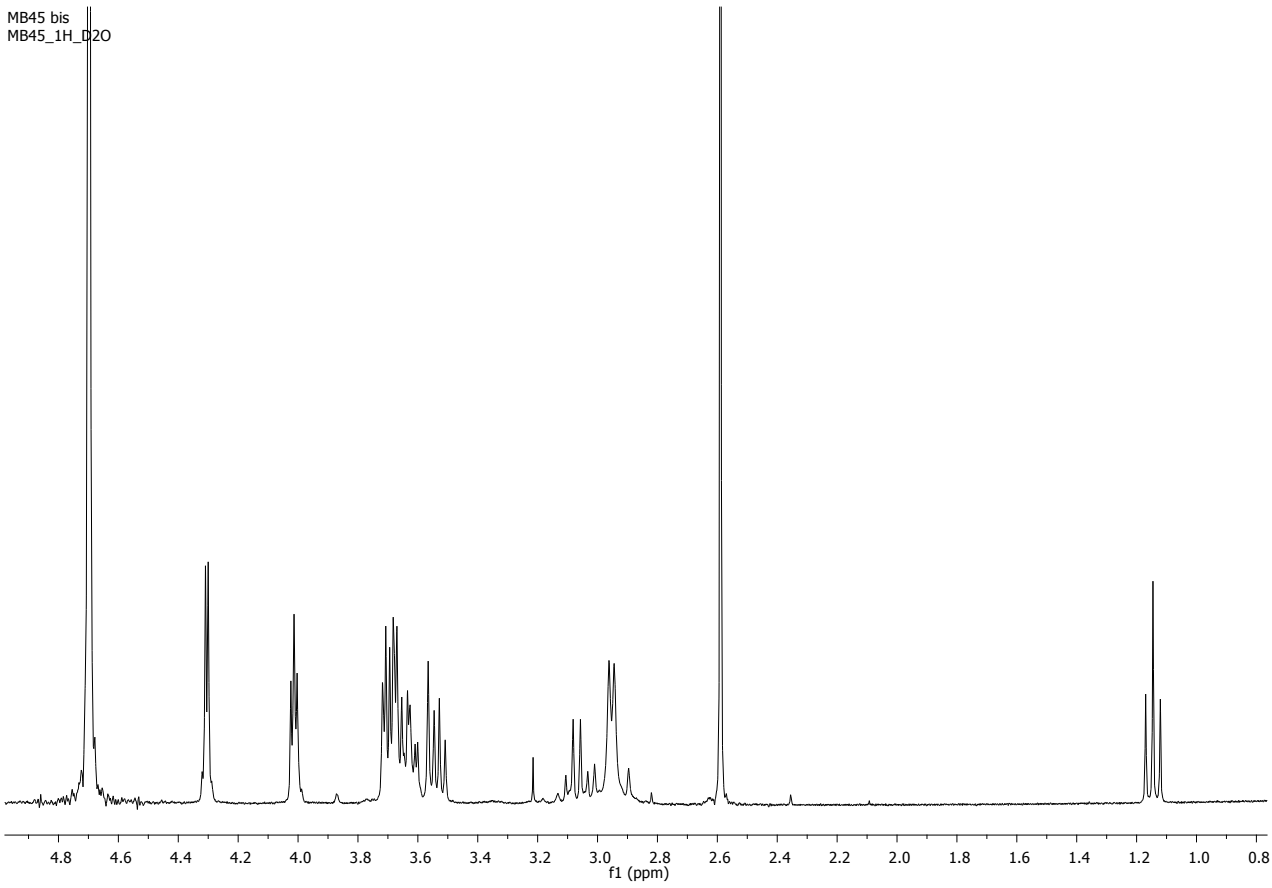
Compound L2

^{1}H-NMR, basic pH

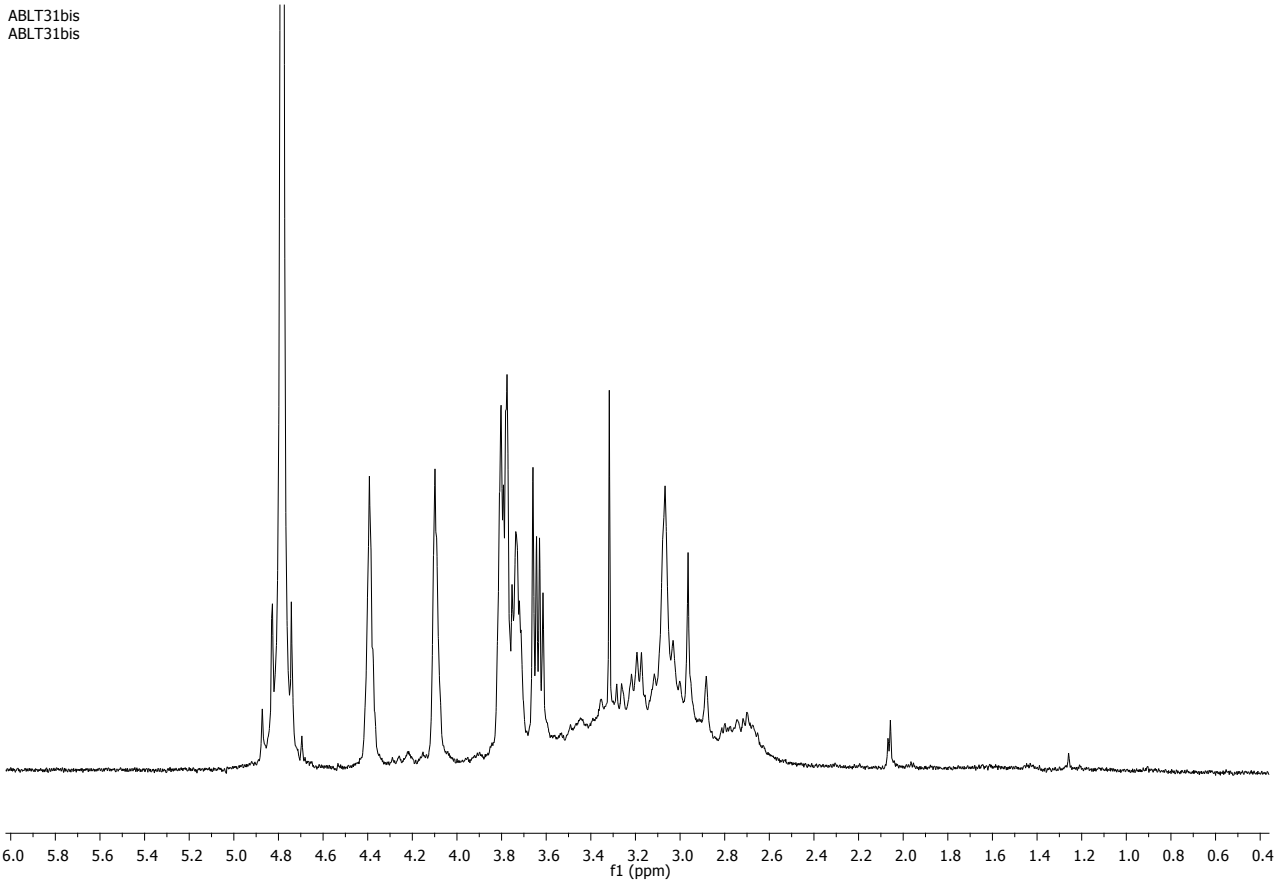


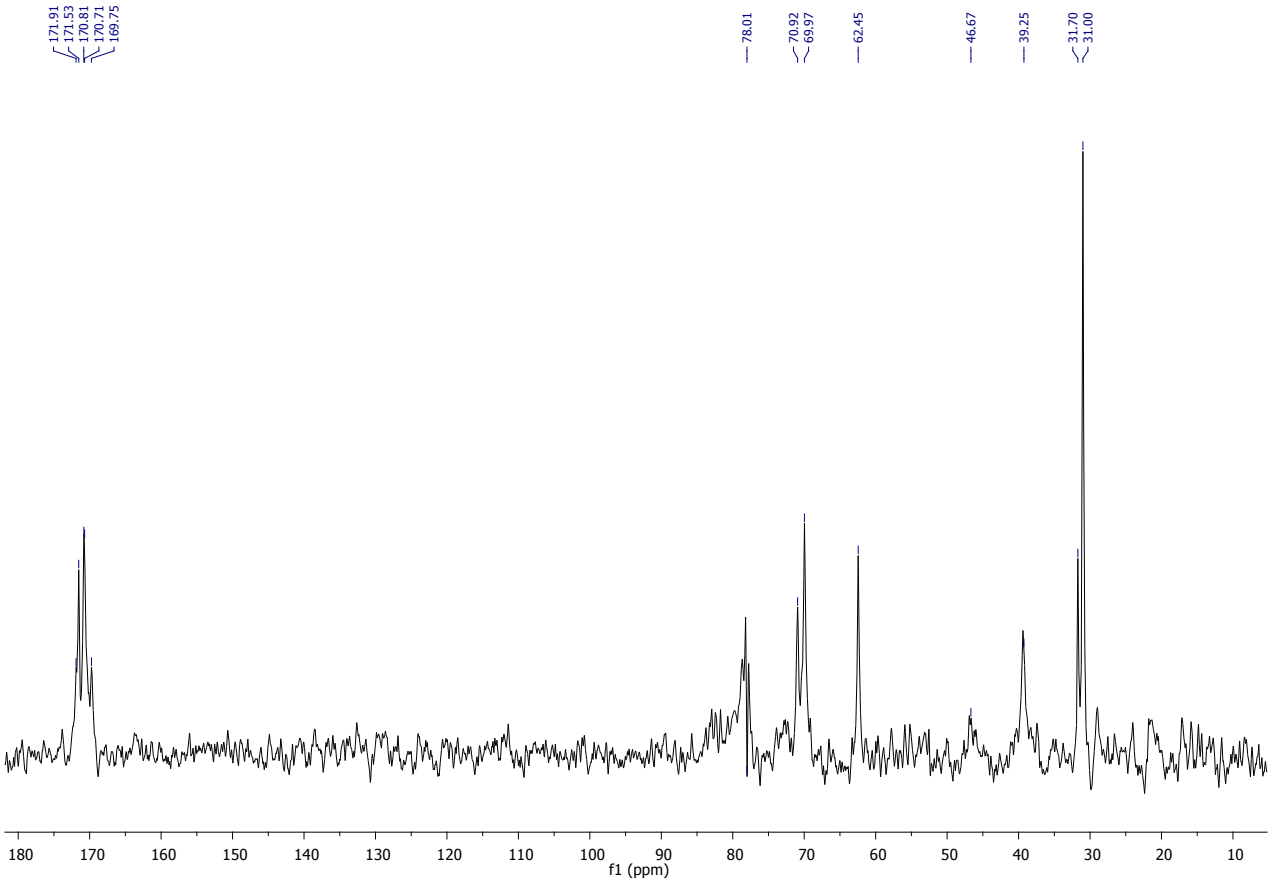


^{1}H-NMR acid pH



Compound L3


ABLT31bis
ABLT31bis
6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 0.6 0.4
f1 (ppm)


171.91
171.53
170.81
170.71
169.75
78.01
70.92
69.97
62.45
46.67
39.25
31.70
31.00
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)