Supplementary Material (ESI) for *Organic and Biomolecular Chemistry*

Convergent Synthesis of (+)-Carambolaflavone A, an Antidiabetic Agent using a Bismuth Triflate-Catalyzed *C*-Aryl Glycosylation

Arun K. Ghosh*, William L. Robinson,† John Gulliver, and Hannah Simpson

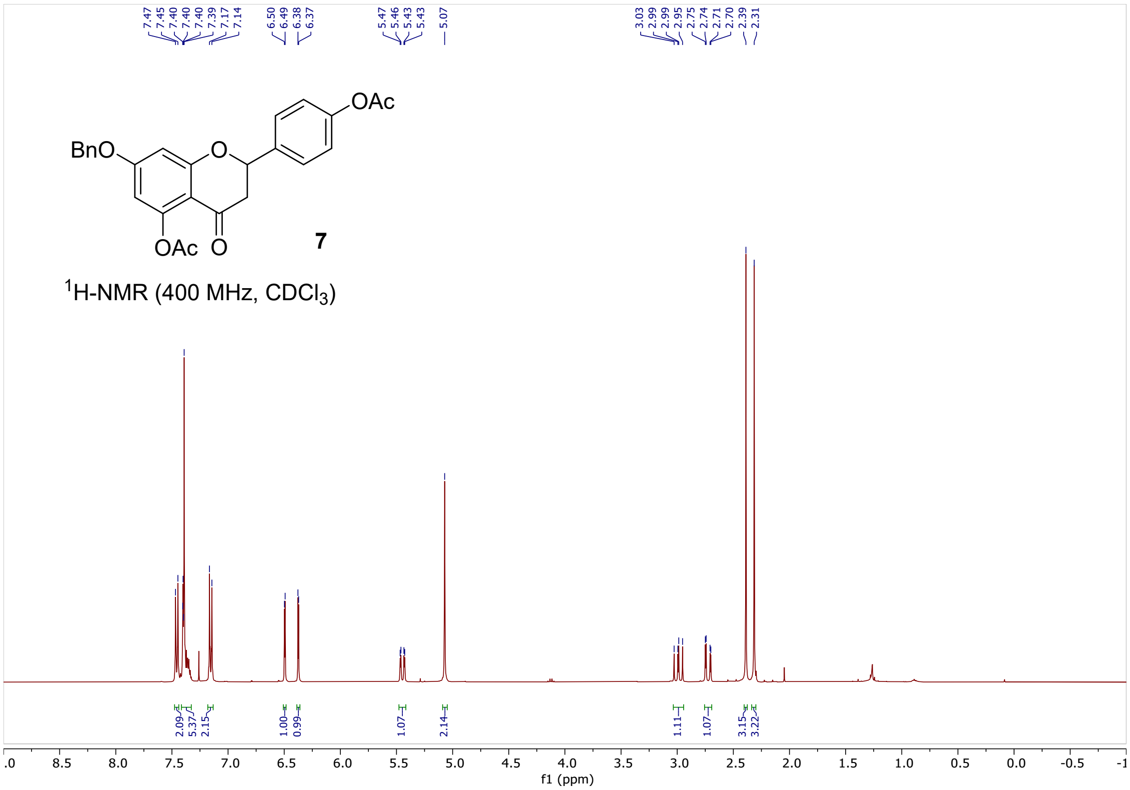
Department of Chemistry and Department of Medicinal Chemistry, Purdue University, 560 Oval Drive, West Lafayette, Indiana 47907

akghosh@purdue.edu

Table of Contents

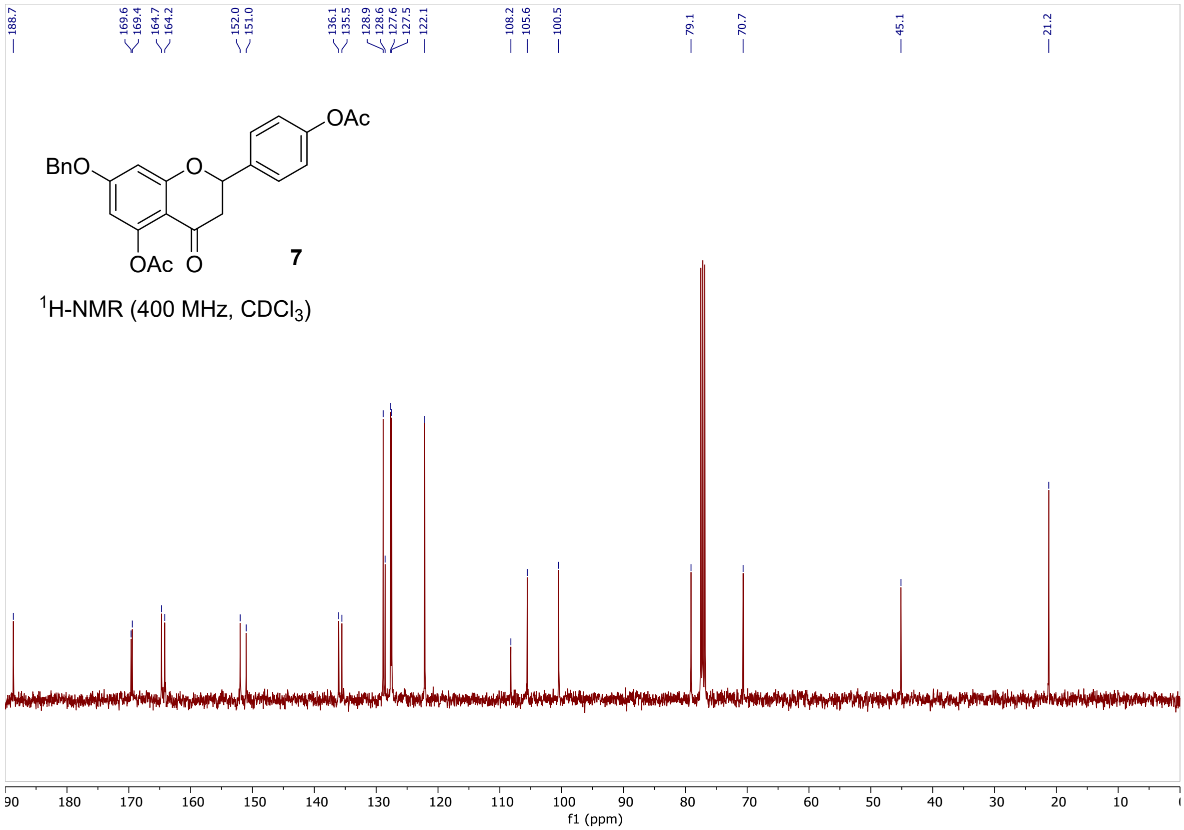
Experimental Procedures

General Methods. All chemical and reagents were purchased from commercial suppliers and used without further purification unless otherwise noted. Solvents (THF, CH_2Cl_2, and MeCN) were purchased in anhydrous, unstabilized form and were purified using a solvent purification system. Other solvents were purchased and used as is. Reactions were run under an argon atmosphere unless noted otherwise. Magnetic stirring was used for all reactions. Glassware used in reactions was oven-dried unless otherwise noted. Reactions were heated using an oil bath on a hot plate equipped with a temperature probe. TLC analysis was conducted using glass-backed thin-layer silica gel chromatography plates (60 Å, 250 μm thickness, F-254 indicator, 2 x 5 cm). Compound spots were visualized by using a combination of shortwave UV (254 nm) and/or various stains (Phosphomolybdic acid, $KMnO_4$, or 2,4-dinitrophenylhydrazine) followed by heating on a hot plate. Flash chromatography was done using 230−400 mesh, 60 Å silica gel. ^1H NMR spectra were recorded on 400 or 800 MHz spectrometers. ^{13}C NMR spectra were recorded on 100 or 200 MHz spectrometers. Chemical shifts are reported in parts per million and referenced to the deuterated residual solvent peak ($CDCl_3$, 7.26 ppm for ^1H and 77.16 ppm for ^{13}C). NMR data are reported as δ value (chemical shift), J-value (Hz), and integration, where s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, p = quintet, m = multiplet, dd = doublet doublets, and so on. Optical rotations were recorded on a Perkin Elmer 34l polarimeter. Low resolution mass spectra (LRMS) spectra were recorded using a quadrupole LCMS under positive electrospray ionization (ESI+). High-resolution mass spectrometry (HRMS) spectra were recorded at the Purdue University Department of Chemistry Mass Spectrometry Center. These experiments were performed under ESI+ and positive atmospheric pressure chemical ionization (APCI+) conditions using an Orbitrap XL Instrument.



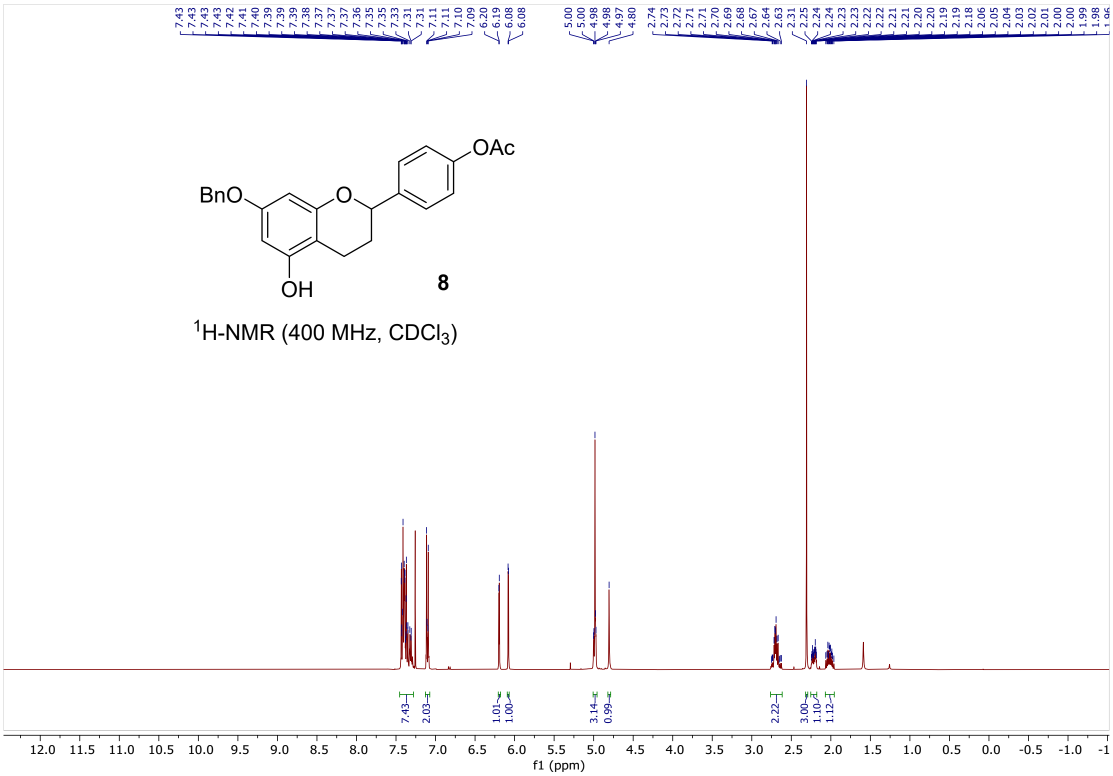
7

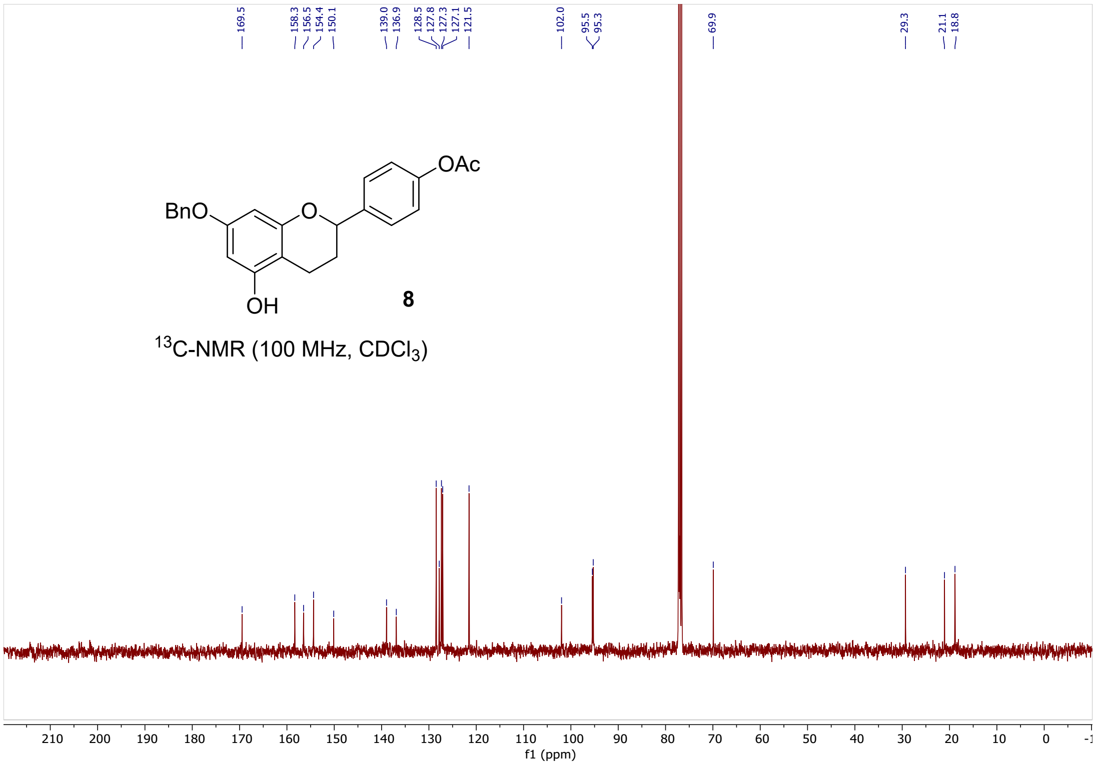
^{1}H-NMR (400 MHz, $CDCl_3$)

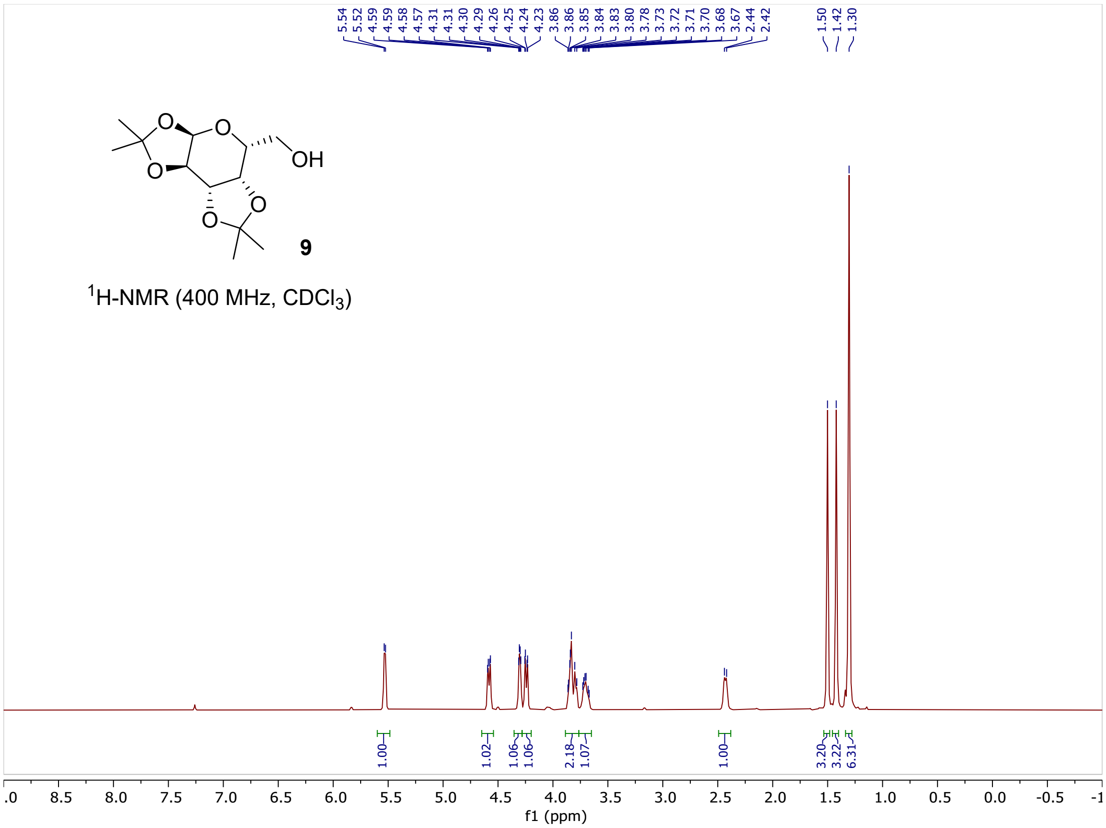


7

^{1}H-NMR (400 MHz, $CDCl_3$)

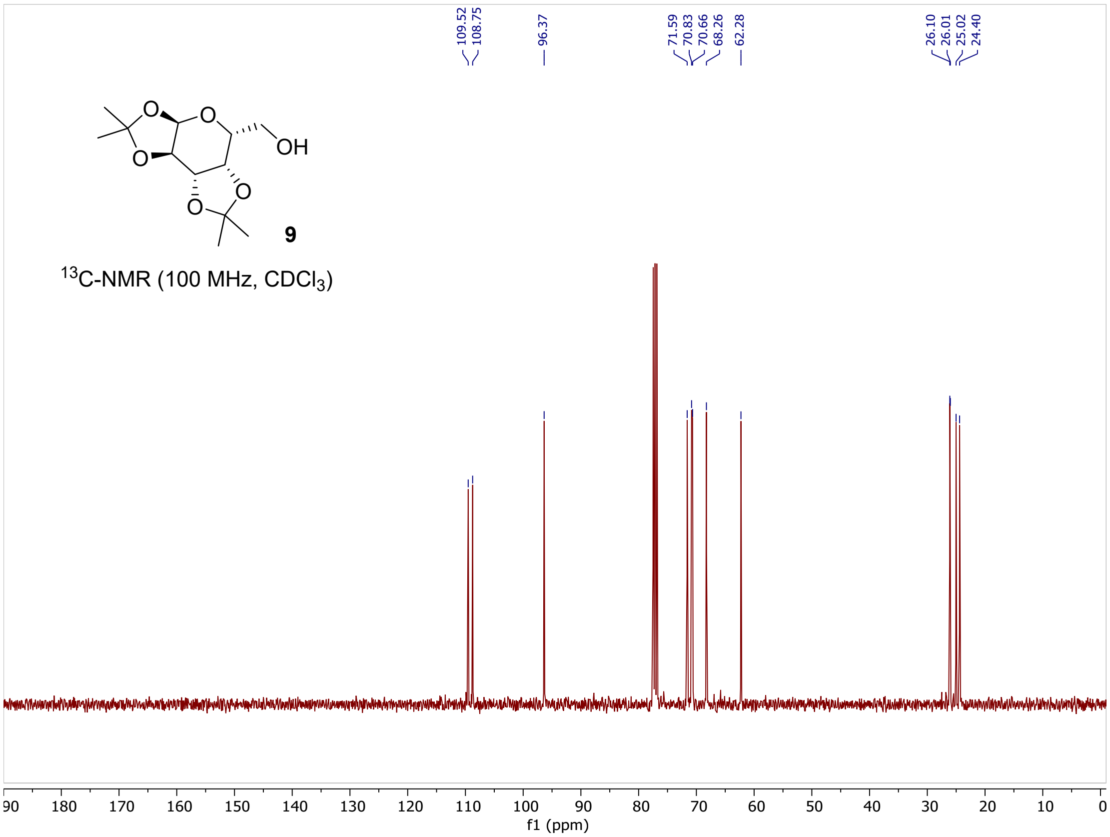

7.43
7.43
7.43
7.43
7.42
7.41
7.40
7.39
7.39
7.39
7.38
7.37
7.37
7.37
7.36
7.35
7.35
7.33
7.31
7.31
7.11
7.11
7.10
7.09
6.20
6.19
6.08
6.08
5.00
5.00
4.98
4.98
4.97
4.80
2.74
2.73
2.72
2.71
2.70
2.69
2.68
2.67
2.64
2.63
2.31
2.25
2.24
2.24
2.23
2.23
2.22
2.22
2.21
2.21
2.20
2.20
2.19
2.19
2.18
2.06
2.05
2.04
2.03
2.02
2.01
2.00
2.00
1.99
1.98
BnO
O
OAc
OH
8
^{1}H-NMR (400 MHz, CDCl$_3$)
7.43
2.03
1.01
1.00
3.14
0.99
2.22
3.00
1.10
1.12
12.0
11.5
11.0
10.5
10.0
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
0.0
-0.5
-1.0
f1 (ppm)


169.5
158.3
156.5
154.4
150.1
139.0
136.9
128.5
127.8
127.3
127.1
121.5
102.0
95.5
95.3
69.9
29.3
21.1
18.8
BnO
O
OAc
OH
8
^{13}C-NMR (100 MHz, CDCl$_3$)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



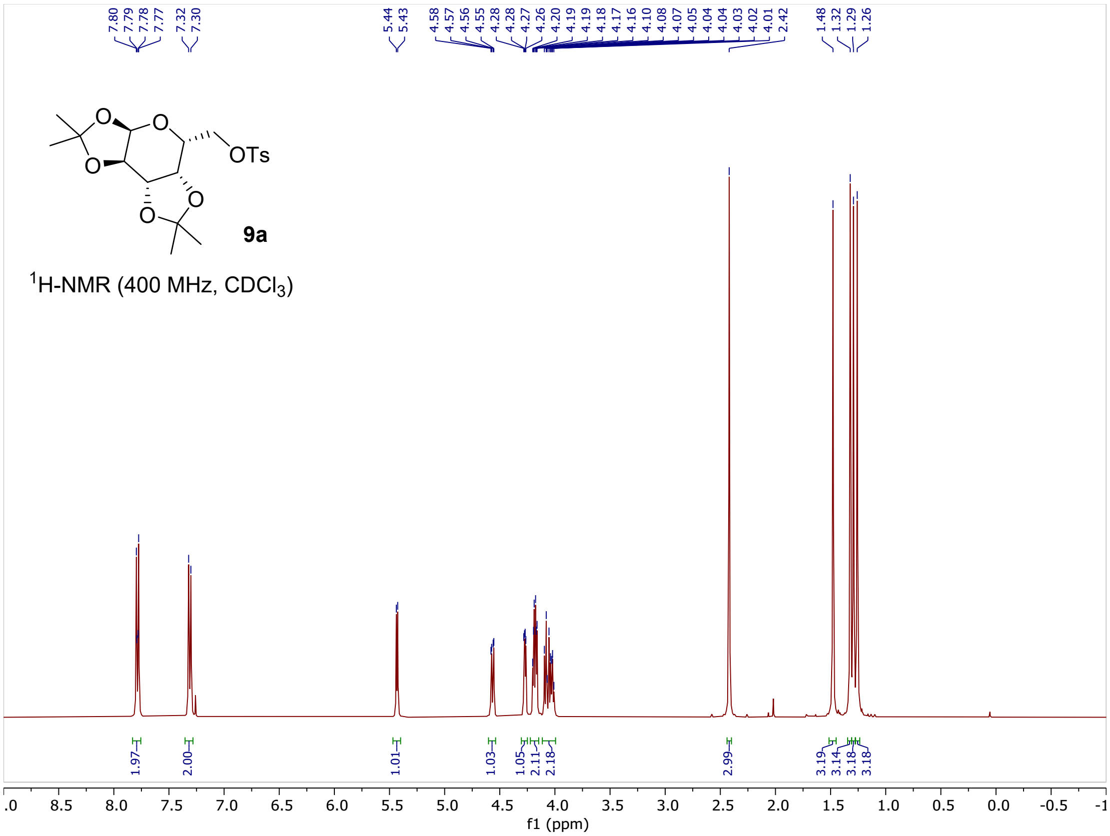
9

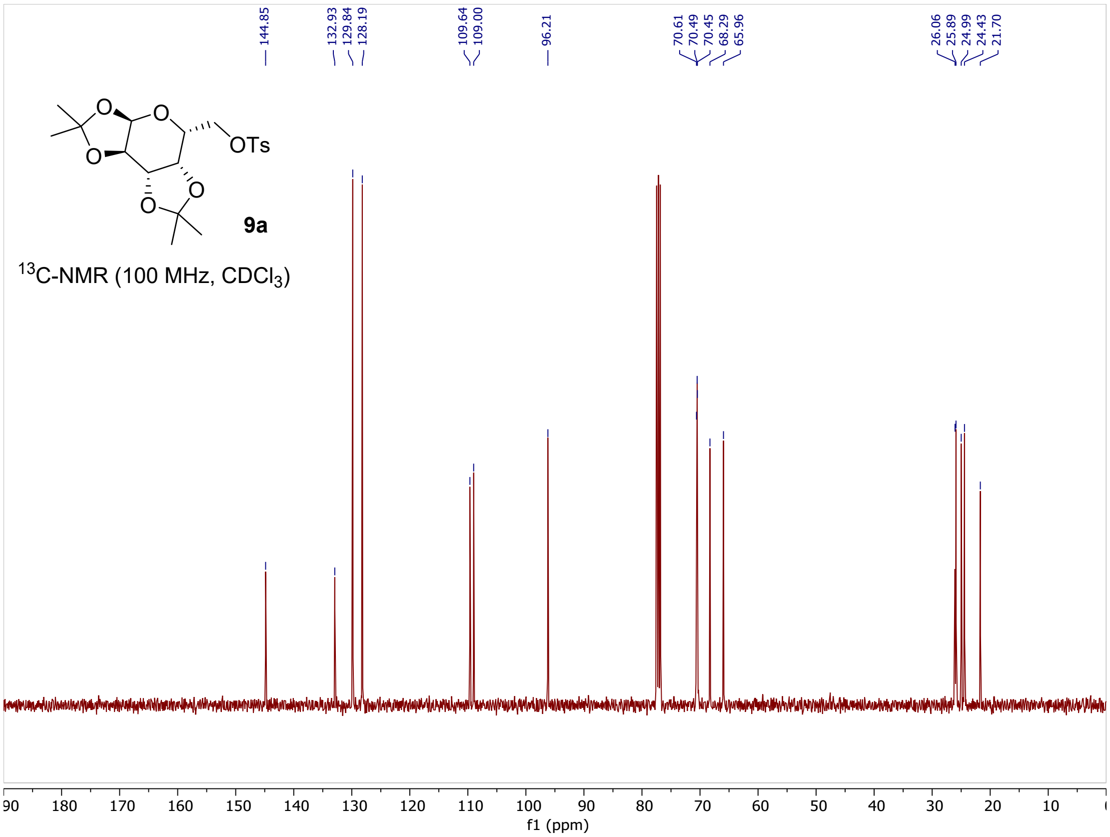
^{1}H-NMR (400 MHz, $CDCl_3$)

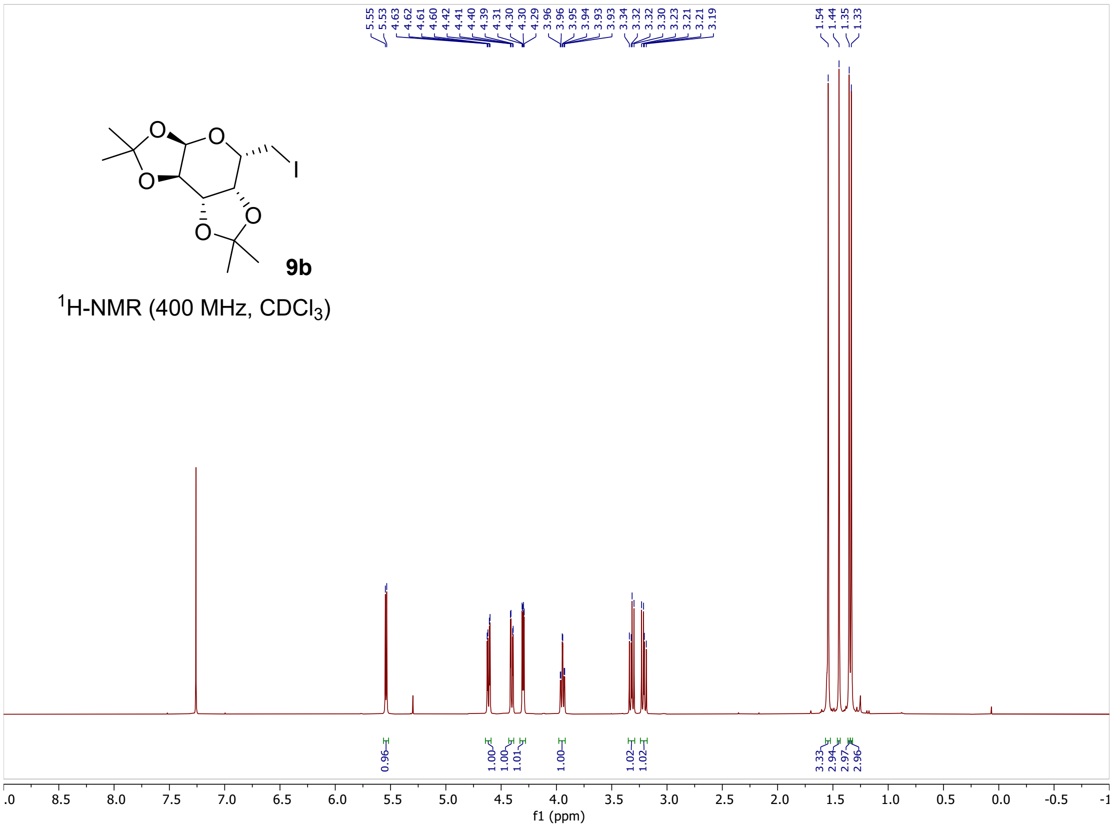


9

^{13}C-NMR (100 MHz, $CDCl_3$)

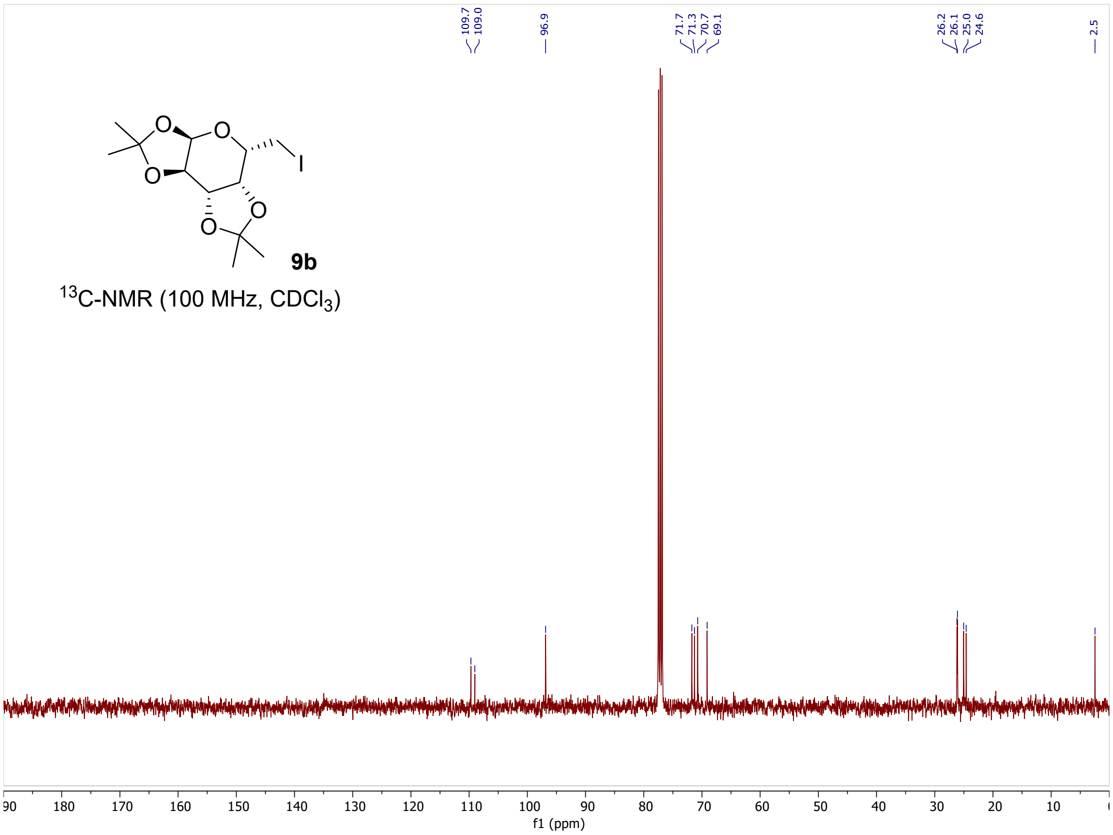

7.80
7.79
7.78
7.77
7.32
7.30
5.44
5.43
4.58
4.57
4.56
4.55
4.28
4.28
4.27
4.26
4.20
4.19
4.19
4.18
4.17
4.16
4.10
4.08
4.07
4.05
4.04
4.04
4.03
4.02
4.01
2.42
1.48
1.32
1.29
1.26
OTs
9a
^{1}H-NMR (400 MHz, CDCl$_3$)
1.97
2.00
1.01
1.03
1.05
2.11
2.18
2.99
3.19
3.14
3.18
3.18
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)


144.85
132.93
129.84
128.19
109.64
109.00
96.21
70.61
70.49
70.45
68.29
65.96
26.06
25.89
24.99
24.43
21.70
OTs
9a
^{13}C-NMR (100 MHz, CDCl$_3$)
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



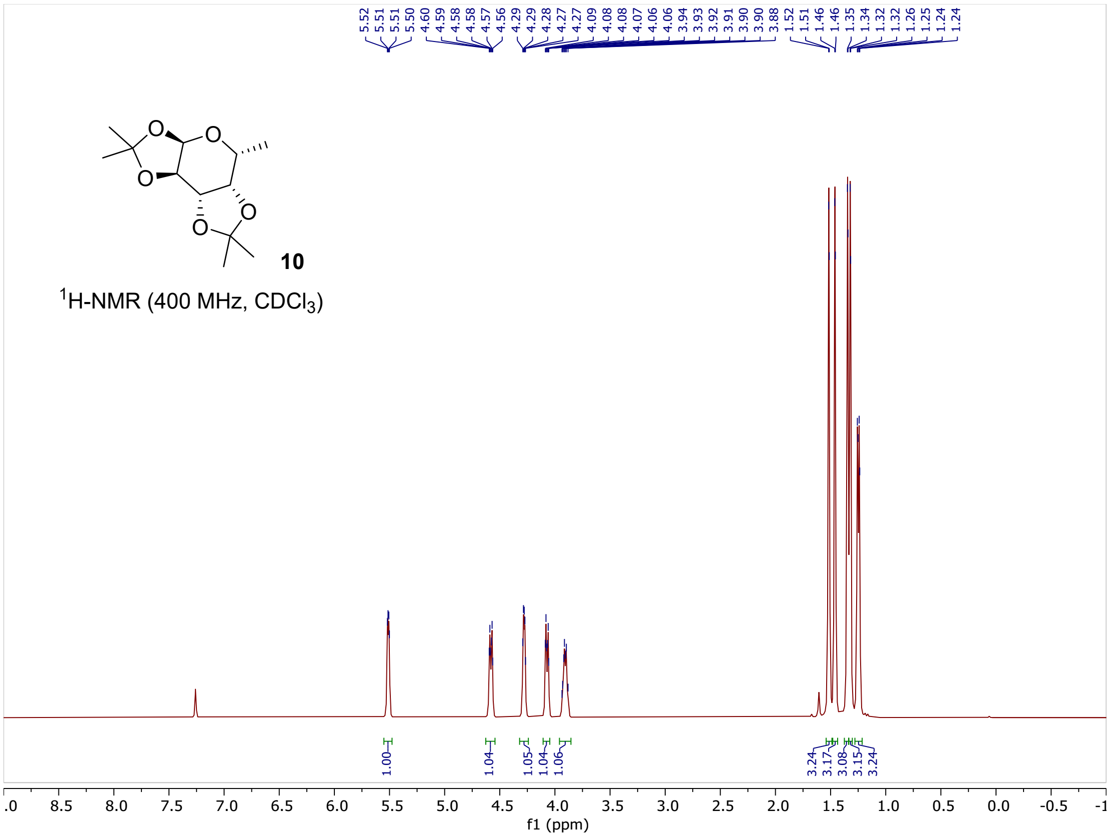
9b

^{1}H-NMR (400 MHz, CDCl$_3$)



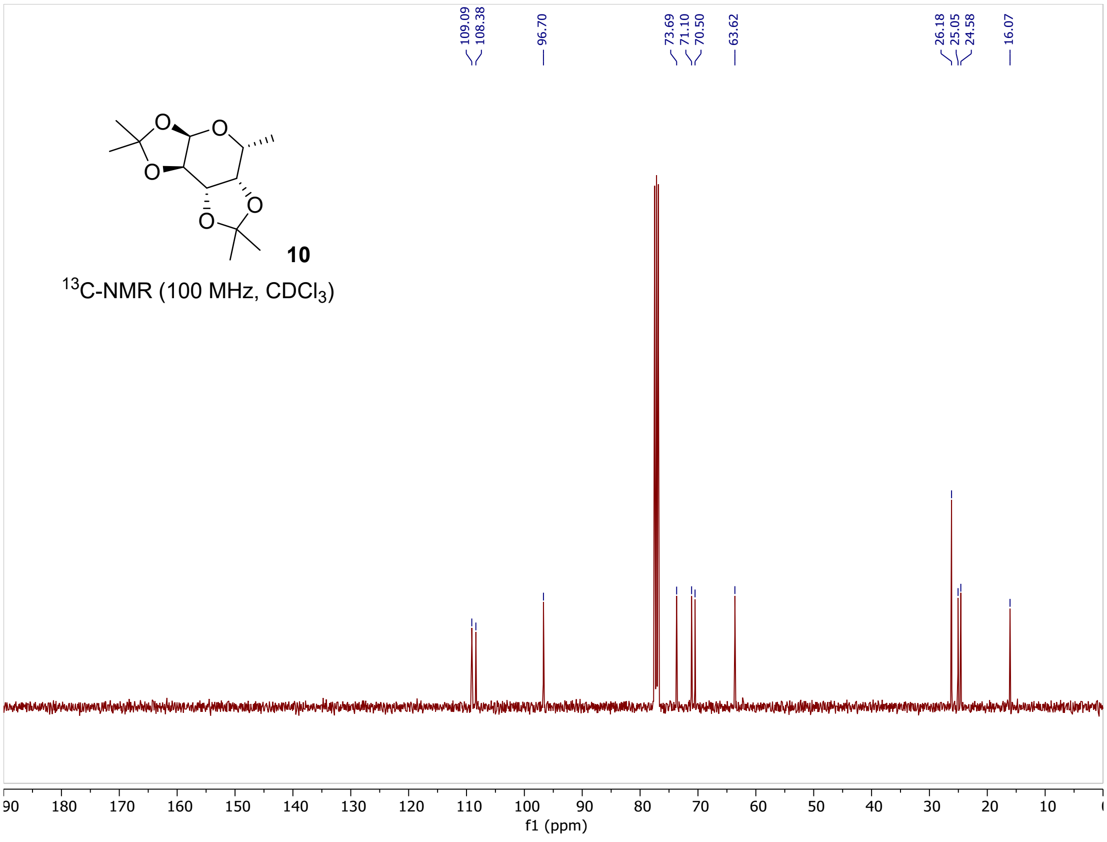
9b

^{13}C-NMR (100 MHz, CDCl$_3$)



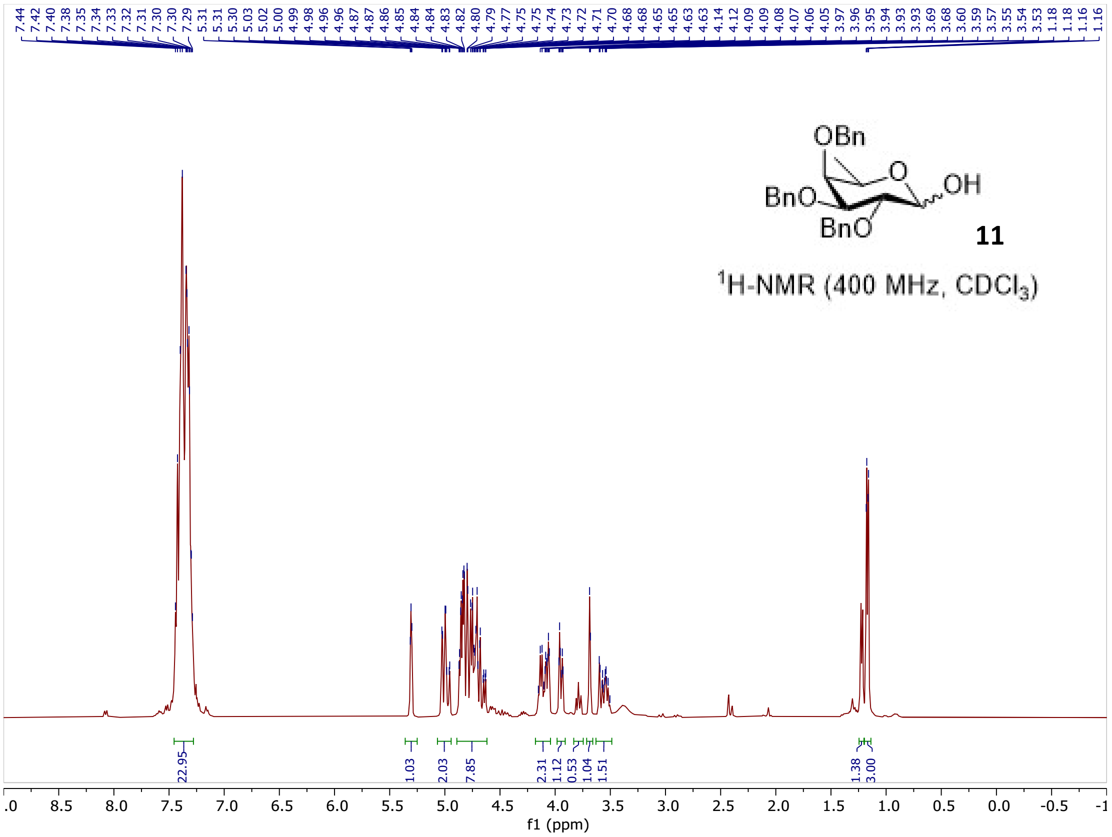
10

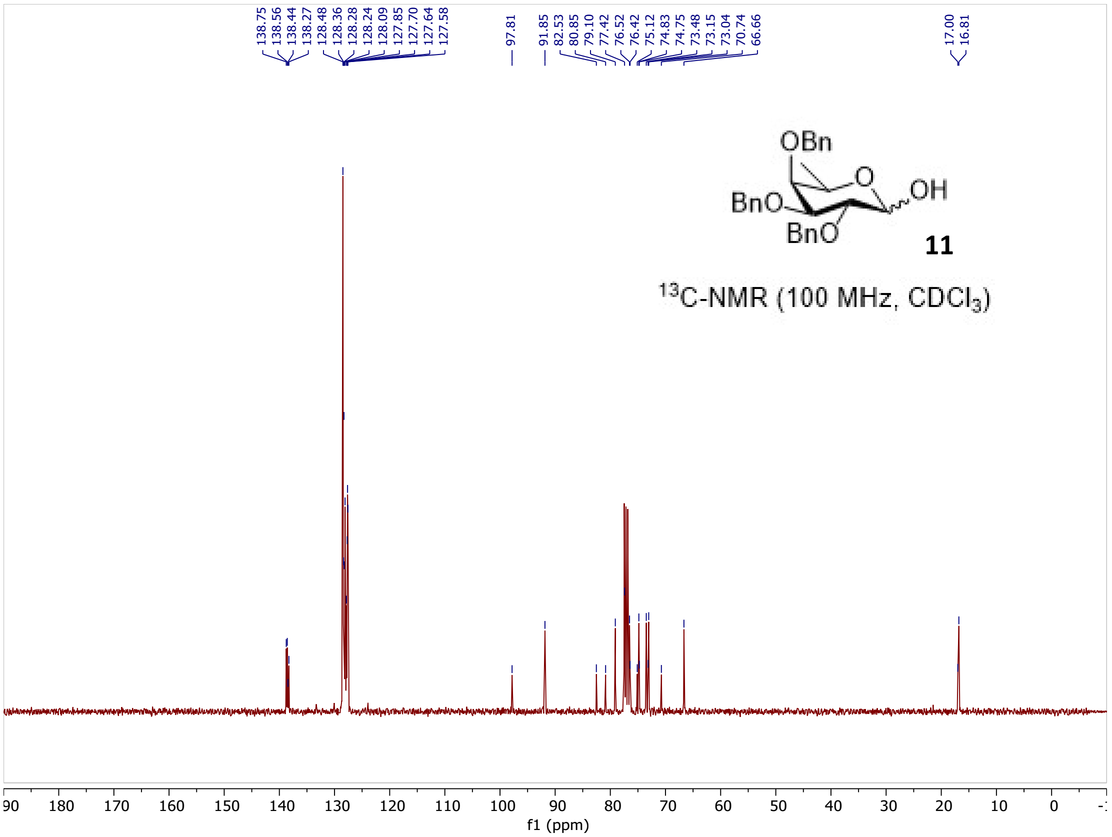
^{1}H-NMR (400 MHz, CDCl$_3$)

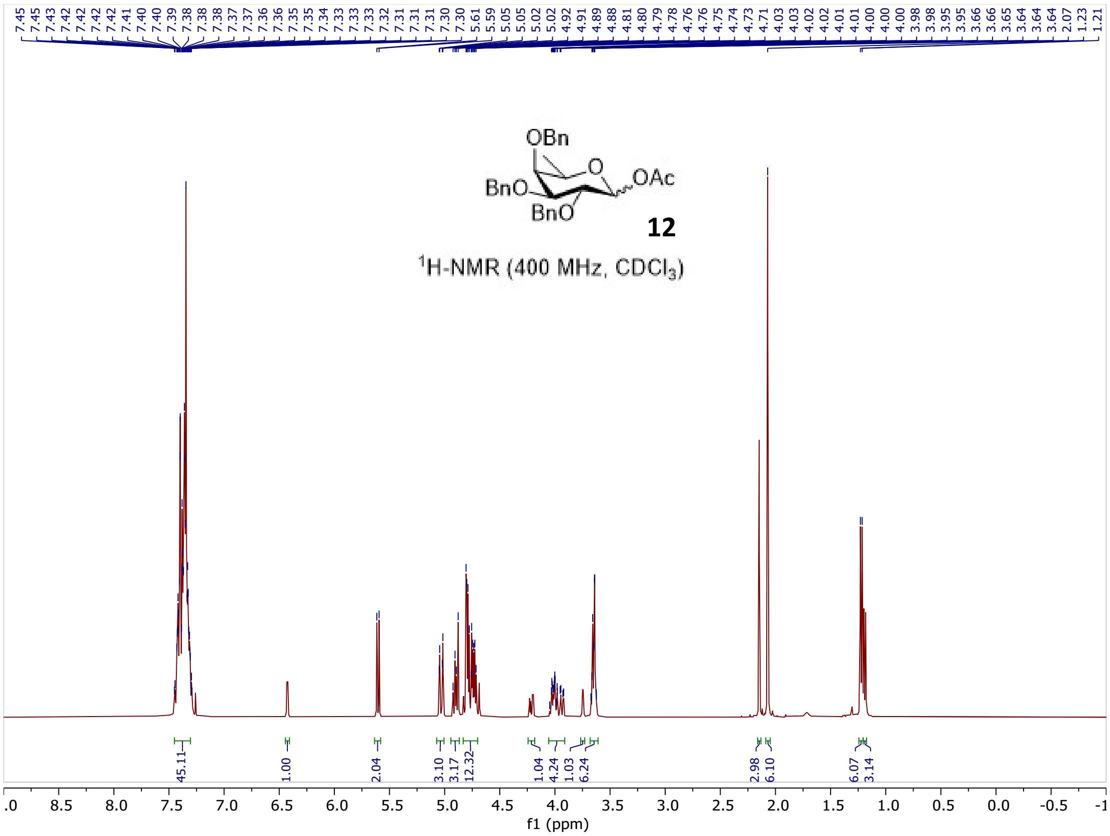


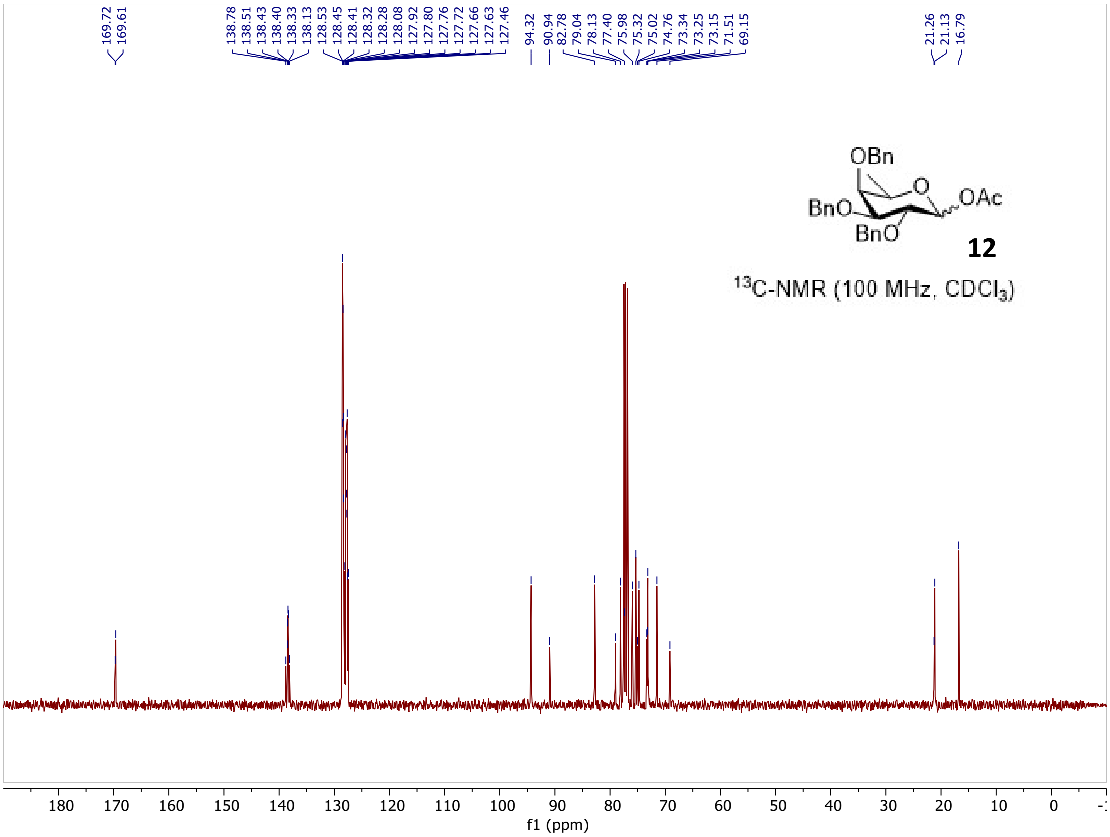
10

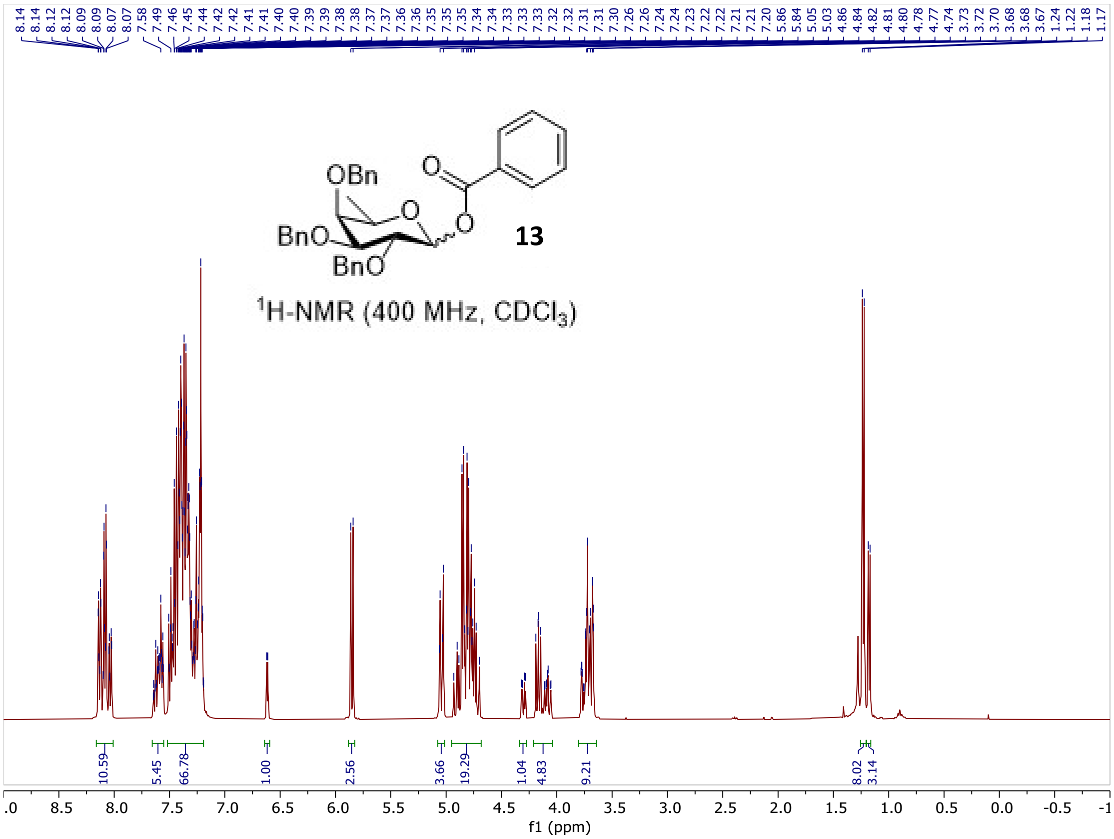
^{13}C-NMR (100 MHz, CDCl$_3$)


7.44
7.42
7.40
7.38
7.35
7.34
7.33
7.32
7.31
7.30
7.29
5.31
5.30
5.03
5.02
5.00
4.99
4.98
4.96
4.96
4.87
4.86
4.85
4.84
4.83
4.82
4.80
4.79
4.77
4.75
4.75
4.74
4.73
4.72
4.71
4.70
4.68
4.68
4.65
4.65
4.63
4.63
4.14
4.12
4.09
4.08
4.07
4.06
4.05
3.97
3.96
3.95
3.94
3.93
3.69
3.68
3.60
3.59
3.57
3.55
3.54
3.53
1.18
1.18
1.16
1.16
OBn
BnO
BnO
O
OH
11
^{1}H-NMR (400 MHz, CDCl$_3$)
22.95
1.03
2.03
7.85
2.31
1.12
0.53
1.04
1.51
1.38
3.00
.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
0.0
-0.5
-1
f1 (ppm)


138.75
138.56
138.44
138.27
128.48
128.36
128.28
128.24
128.09
127.85
127.70
127.64
127.58
97.81
91.85
82.53
80.85
79.10
77.42
76.52
76.42
75.12
74.83
74.75
73.48
73.15
73.04
70.74
66.66
17.00
16.81
OBn
BnO
BnO
O
OH
11
^{13}C-NMR (100 MHz, CDCl$_3$)
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

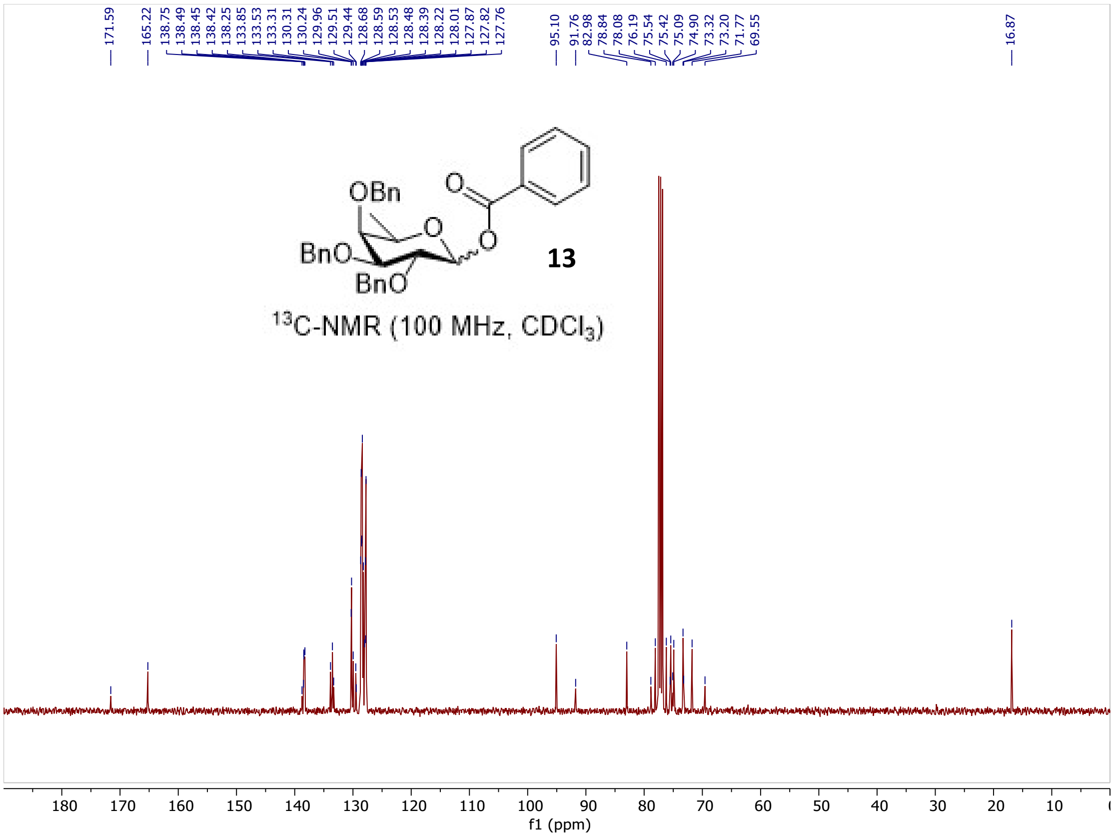

7.45 7.45 7.43 7.42 7.42 7.42 7.42 7.41 7.40 7.40 7.39 7.38 7.38 7.38 7.37 7.37 7.36 7.36 7.35 7.35 7.34 7.33 7.33 7.33 7.32 7.31 7.31 7.31 7.30 7.30 5.61 5.59 5.05 5.05 5.02 5.02 4.92 4.91 4.89 4.88 4.81 4.80 4.79 4.78 4.76 4.76 4.75 4.74 4.73 4.71 4.03 4.03 4.02 4.02 4.01 4.01 4.00 4.00 3.98 3.98 3.95 3.95 3.66 3.66 3.65 3.64 3.64 2.07 1.23 1.21
OBn
BnO
BnO
O
OAc
12
^{1}H-NMR (400 MHz, CDCl$_3$)
45.11
1.00
2.04
3.10
3.17
12.32
1.04
4.24
1.03
6.24
2.98
6.10
6.07
3.14
.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 0.0 -0.5 -1
f1 (ppm)


169.72 169.61
138.78 138.51 138.43 138.40 138.33 138.13 128.53 128.45 128.41 128.32 128.28 128.08 127.92 127.80 127.76 127.72 127.66 127.63 127.46
94.32 90.94 82.78 79.04 78.13 77.40 75.98 75.32 75.02 74.76 73.34 73.25 73.15 71.51 69.15
21.26 21.13 16.79
OBn
BnO
BnO
O
OAc
12
^{13}C-NMR (100 MHz, CDCl$_3$)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



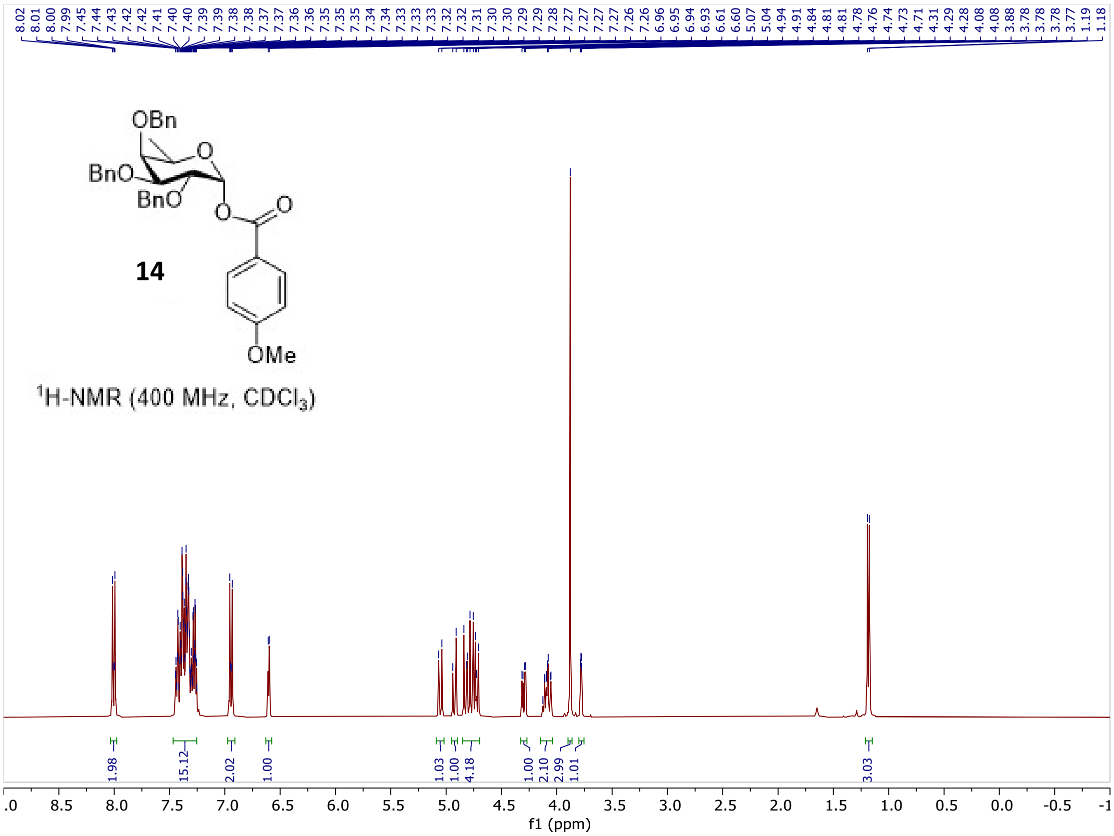
13

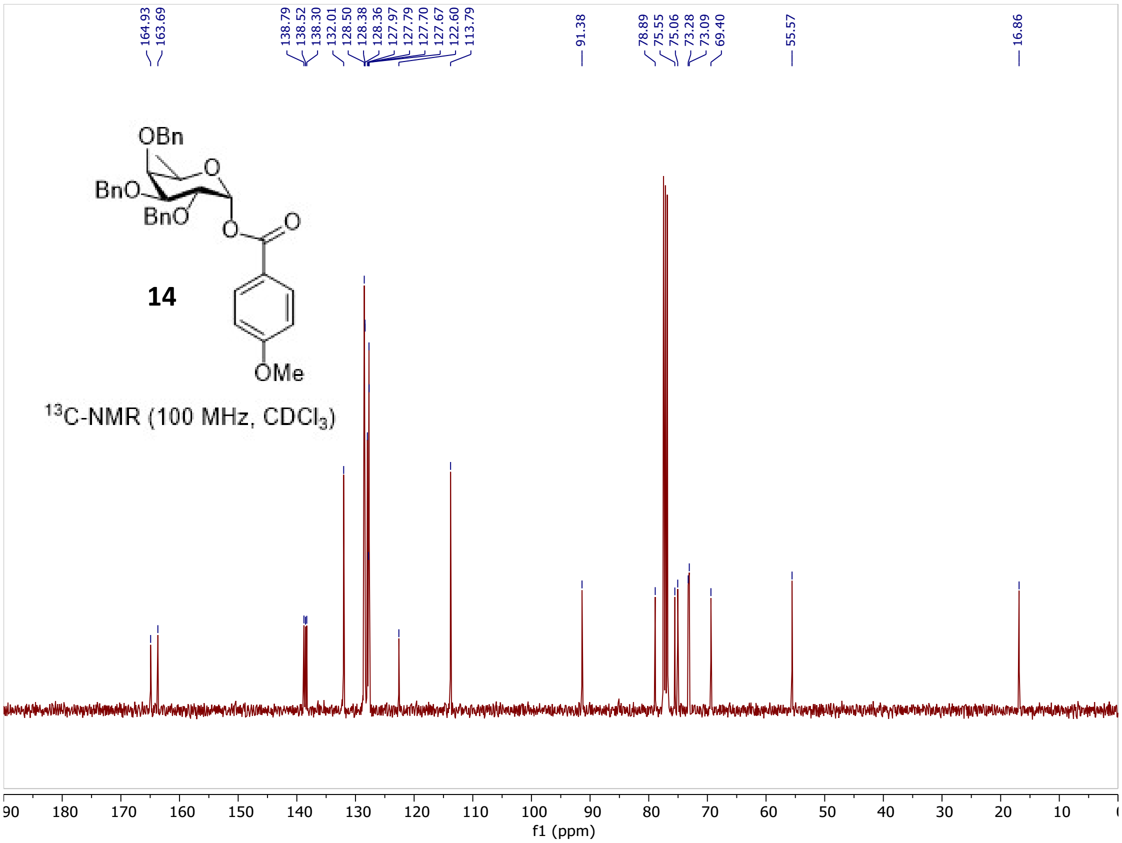
^{1}H-NMR (400 MHz, CDCl$_3$)

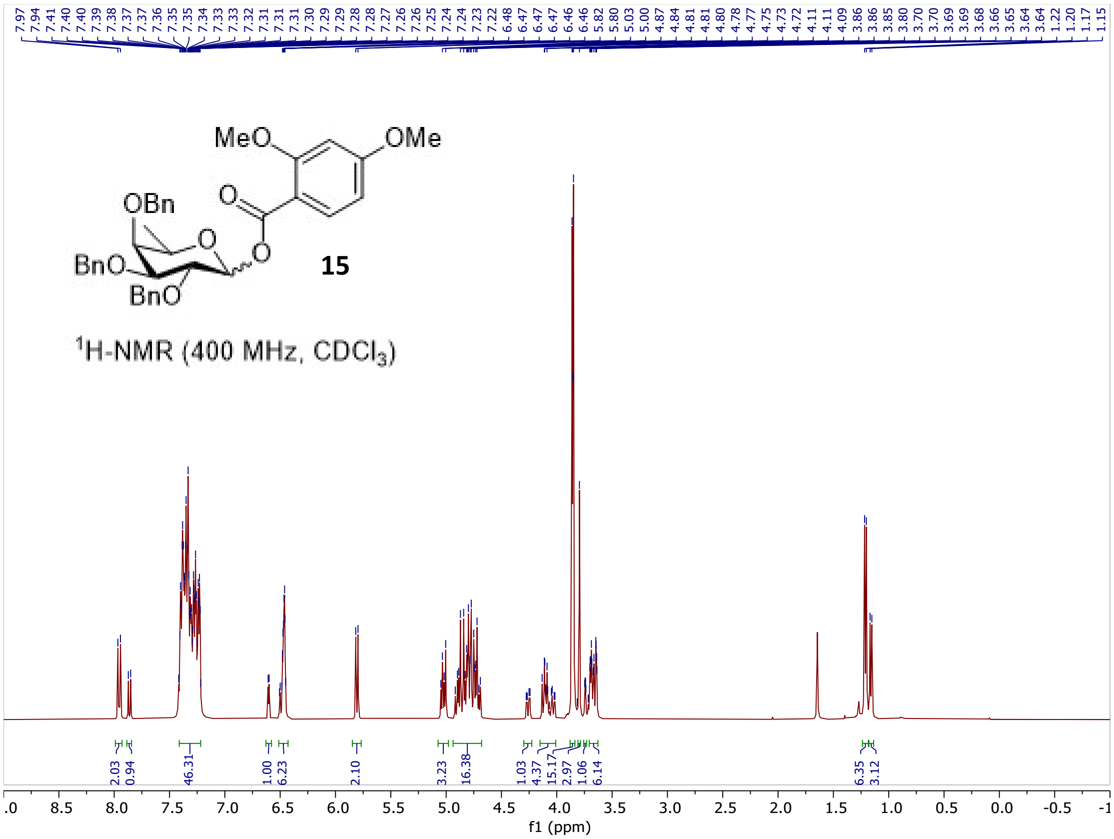


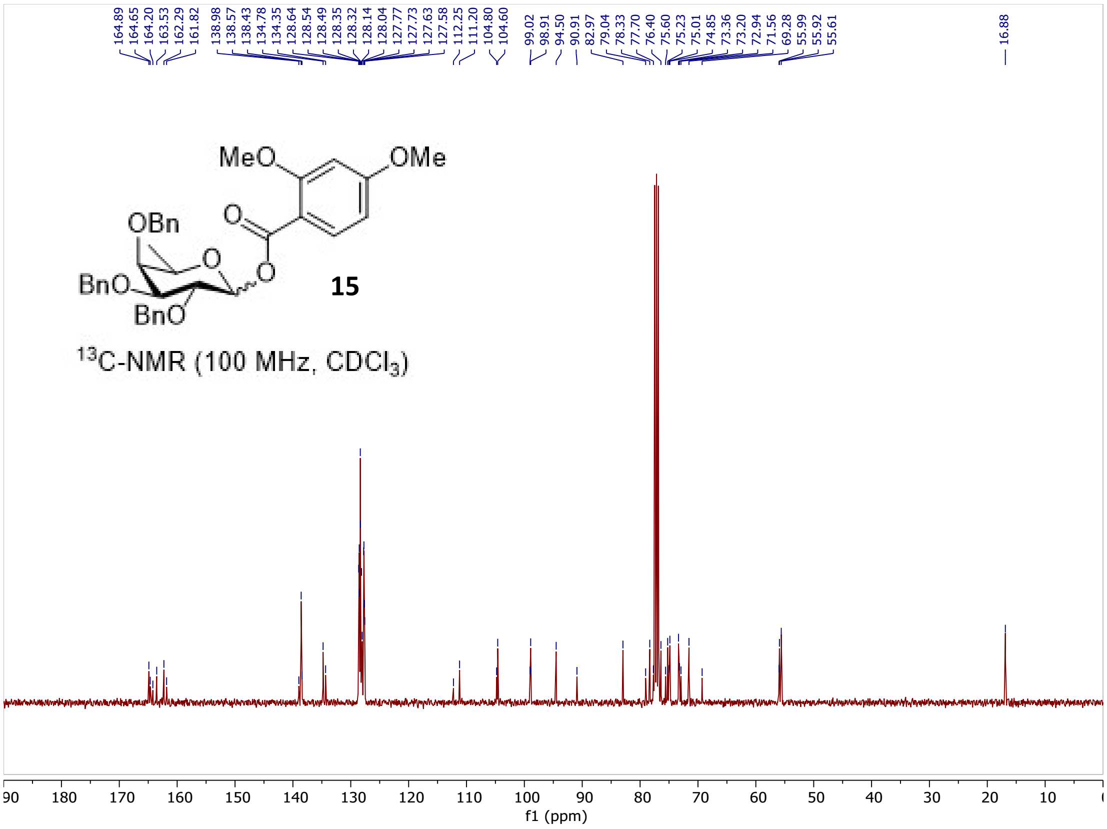
13

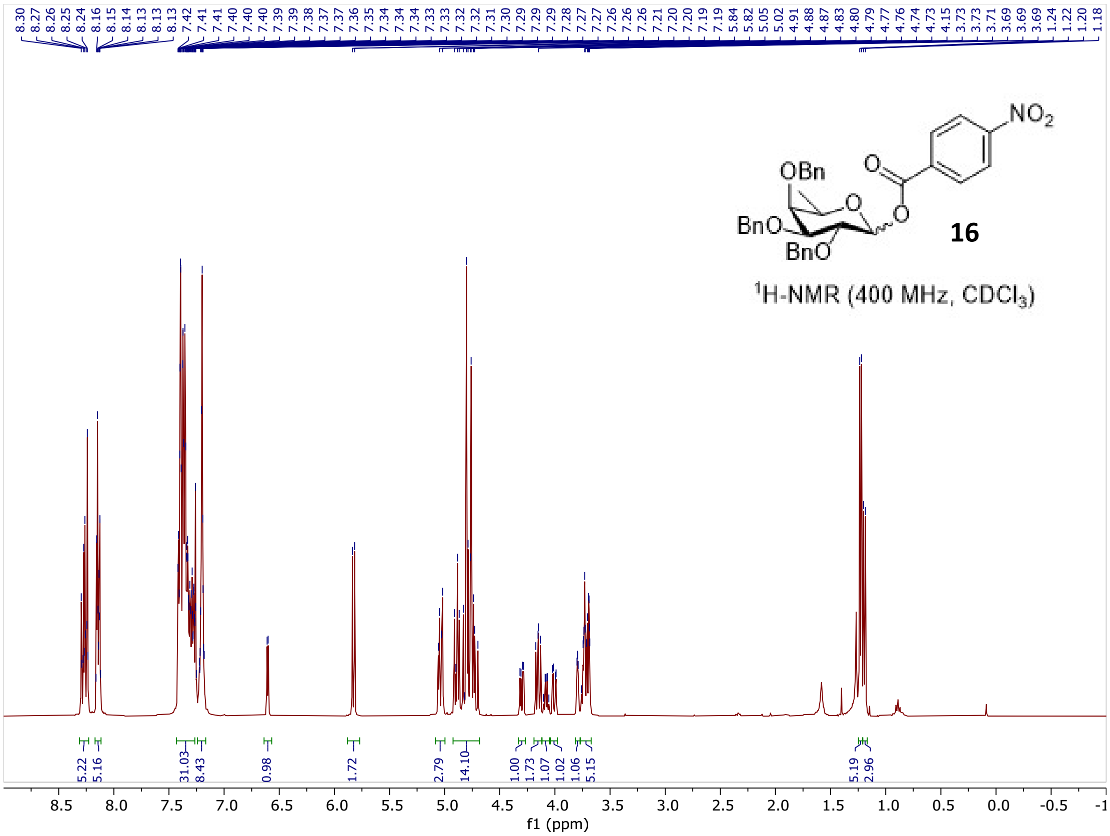
^{13}C-NMR (100 MHz, CDCl$_3$)


8.02
8.01
8.00
7.99
7.45
7.44
7.43
7.42
7.42
7.41
7.40
7.40
7.39
7.38
7.38
7.37
7.36
7.36
7.35
7.35
7.35
7.34
7.34
7.33
7.33
7.32
7.32
7.31
7.30
7.29
7.29
7.28
7.27
7.27
7.27
7.27
7.26
6.96
6.95
6.94
6.93
6.61
6.60
5.07
5.04
4.94
4.91
4.84
4.81
4.81
4.78
4.76
4.74
4.73
4.71
4.31
4.29
4.28
4.08
3.88
3.78
3.78
3.77
1.19
1.18
OBn
BnO
BnO
O
O
O
OMe
14
^{1}H-NMR (400 MHz, CDCl$_3$)
1.98
15.12
2.02
1.00
1.03
1.00
4.18
1.00
2.10
2.99
1.01
3.03
.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
0.0
-0.5
-1
f1 (ppm)


164.93
163.69
138.79
138.52
138.30
132.01
128.50
128.36
127.97
127.79
127.70
127.67
122.60
113.79
91.38
78.89
75.55
75.06
73.28
73.09
69.40
55.57
16.86
OBn
BnO
BnO
O
O
O
OMe
14
^{13}C-NMR (100 MHz, CDCl$_3$)
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

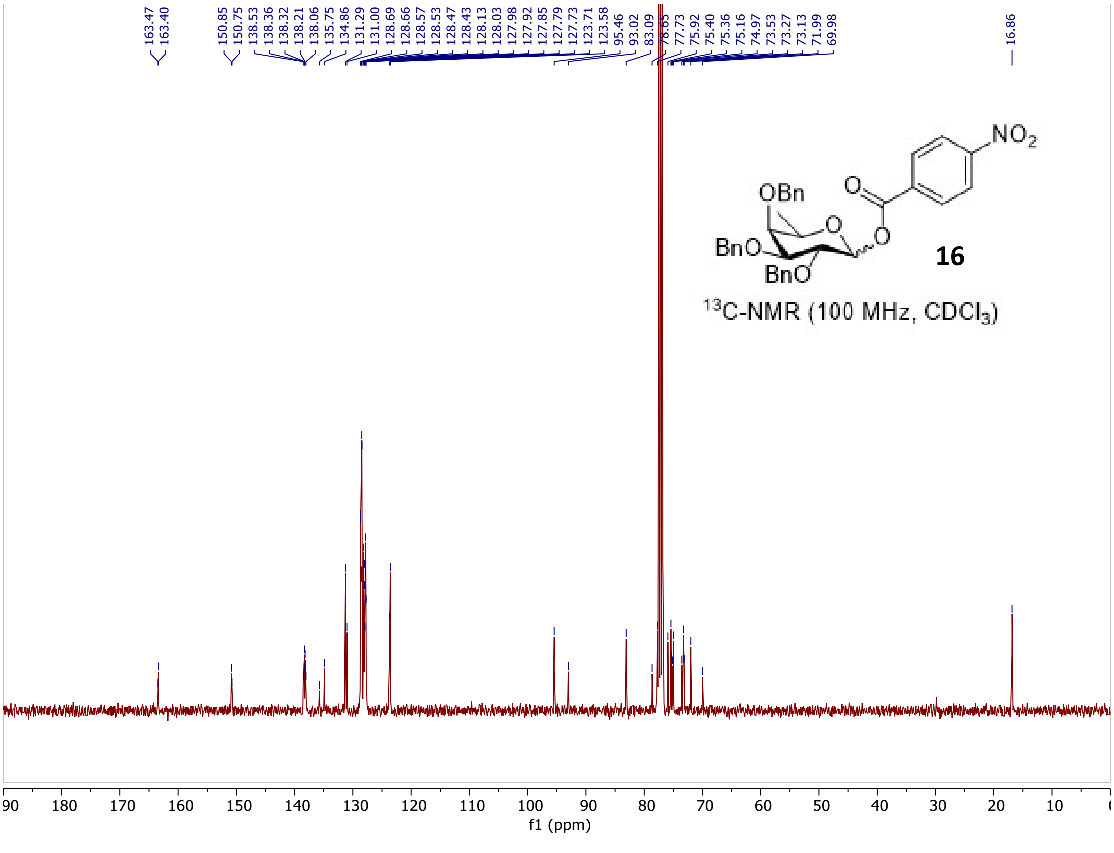

7.97
7.94
7.41
7.40
7.40
7.39
7.38
7.37
7.37
7.36
7.35
7.35
7.34
7.33
7.33
7.32
7.31
7.31
7.31
7.30
7.29
7.29
7.28
7.28
7.27
7.26
7.26
7.25
7.24
7.24
7.23
7.22
6.48
6.47
6.47
6.47
6.46
6.46
5.82
5.80
5.03
5.00
4.87
4.84
4.81
4.81
4.80
4.78
4.77
4.75
4.73
4.72
4.11
4.11
4.09
3.86
3.86
3.85
3.80
3.70
3.69
3.69
3.68
3.66
3.65
3.64
1.22
1.20
1.17
1.15
MeO
OMe
O
OBn
O
O
BnO
BnO
15
^{1}H-NMR (400 MHz, CDCl$_3$)
2.03
0.94
46.31
1.00
6.23
2.10
3.23
16.38
1.03
4.37
15.17
2.97
1.06
6.14
6.35
3.12
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
0.0
-0.5
-1
f1 (ppm)


164.89
164.65
164.20
163.53
162.29
161.82
138.98
138.57
138.43
134.78
134.35
128.64
128.54
128.49
128.35
128.32
128.14
128.04
127.77
127.73
127.63
127.58
112.25
111.20
104.80
104.60
99.02
98.91
94.50
90.91
82.97
79.04
78.33
77.70
76.40
75.60
75.23
75.01
74.85
73.36
73.20
72.94
71.56
69.28
55.99
55.92
55.61
16.88
MeO
OMe
O
OBn
O
O
BnO
BnO
15
^{13}C-NMR (100 MHz, CDCl$_3$)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



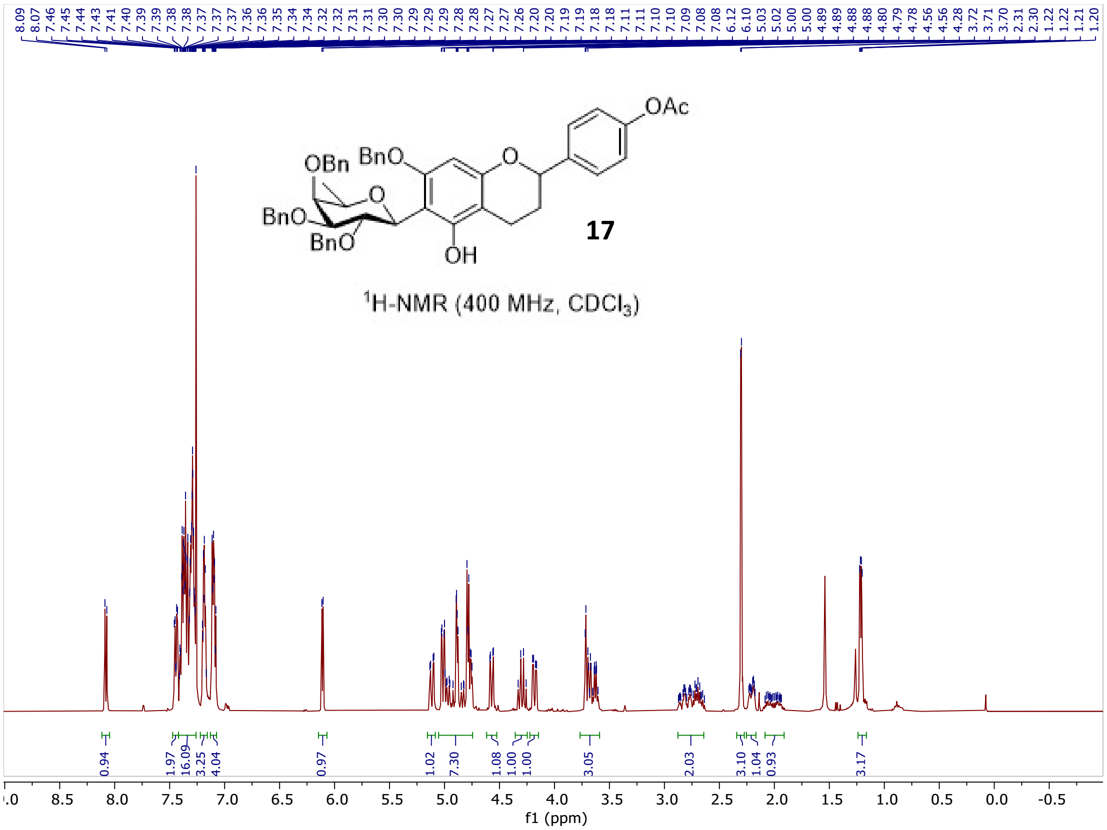
16

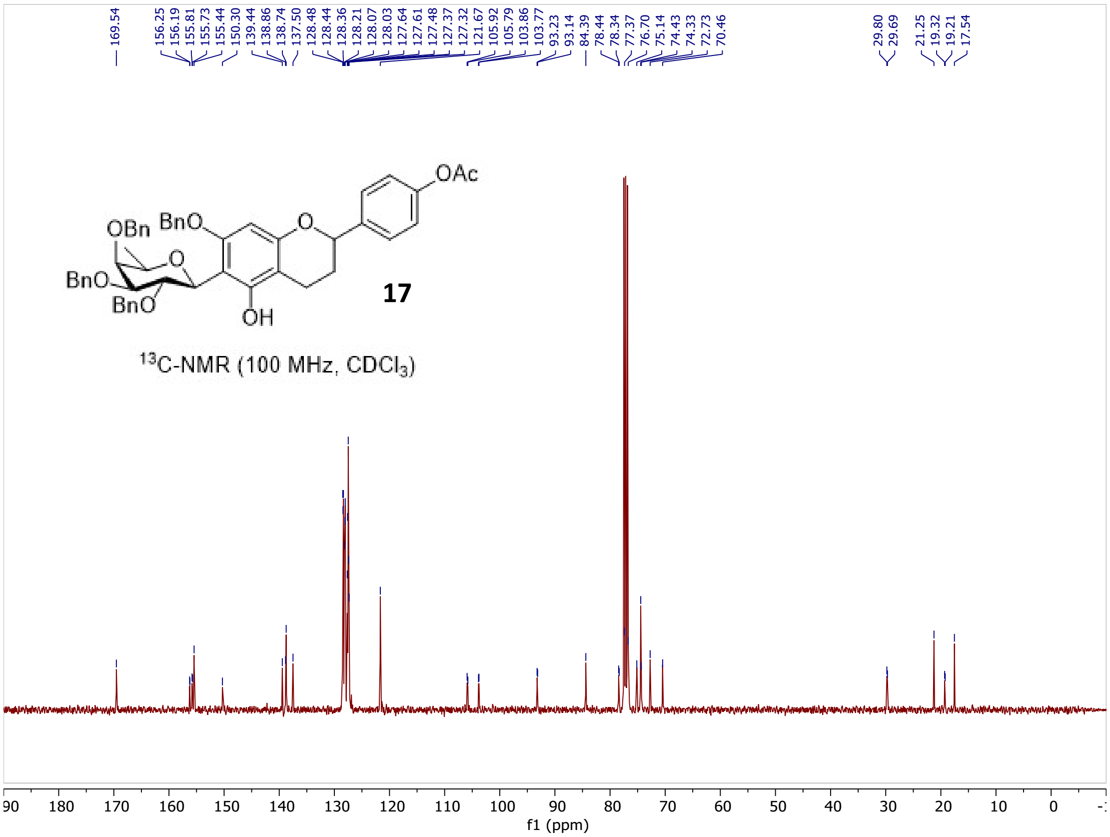
^{1}H-NMR (400 MHz, CDCl$_3$)

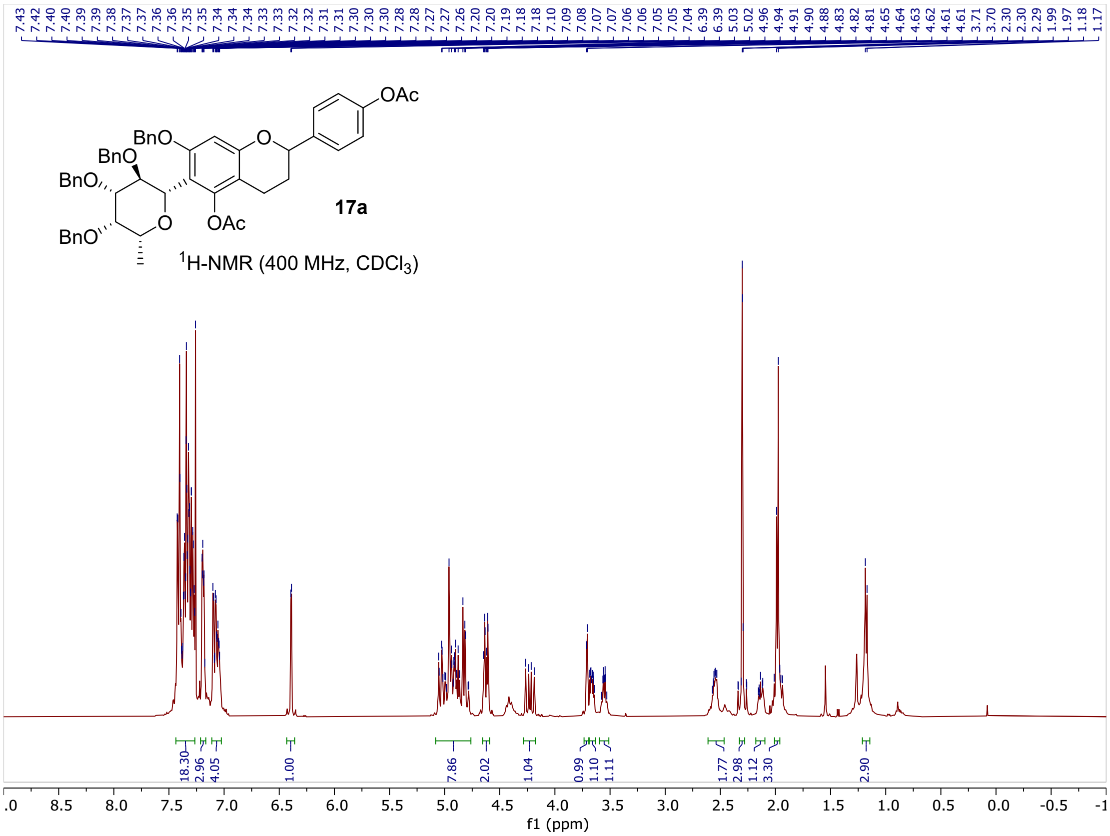


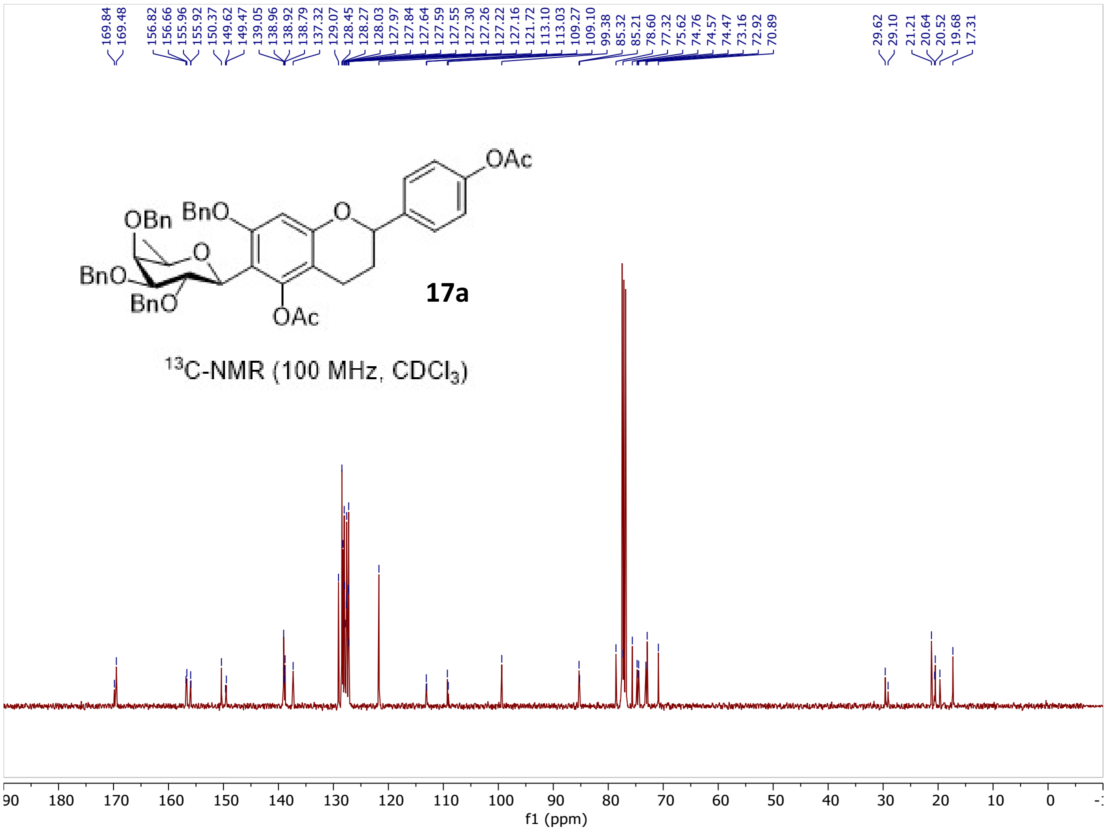
16

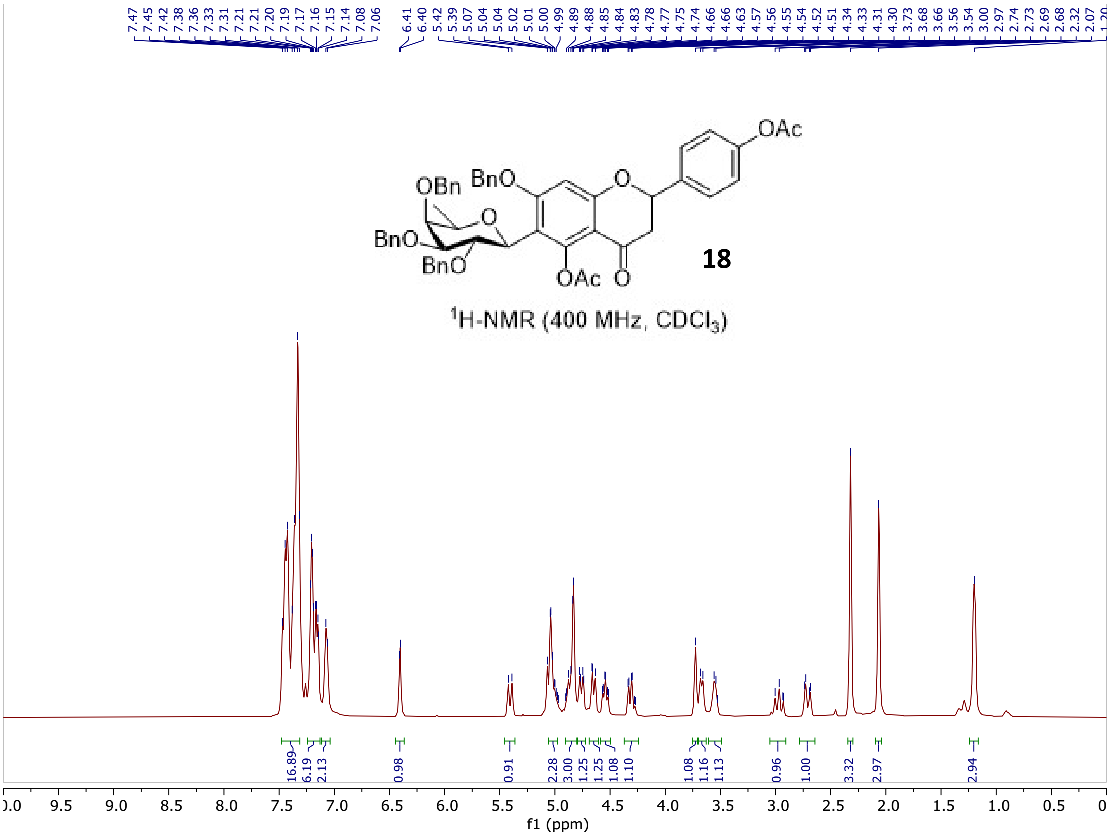
^{13}C-NMR (100 MHz, CDCl$_3$)

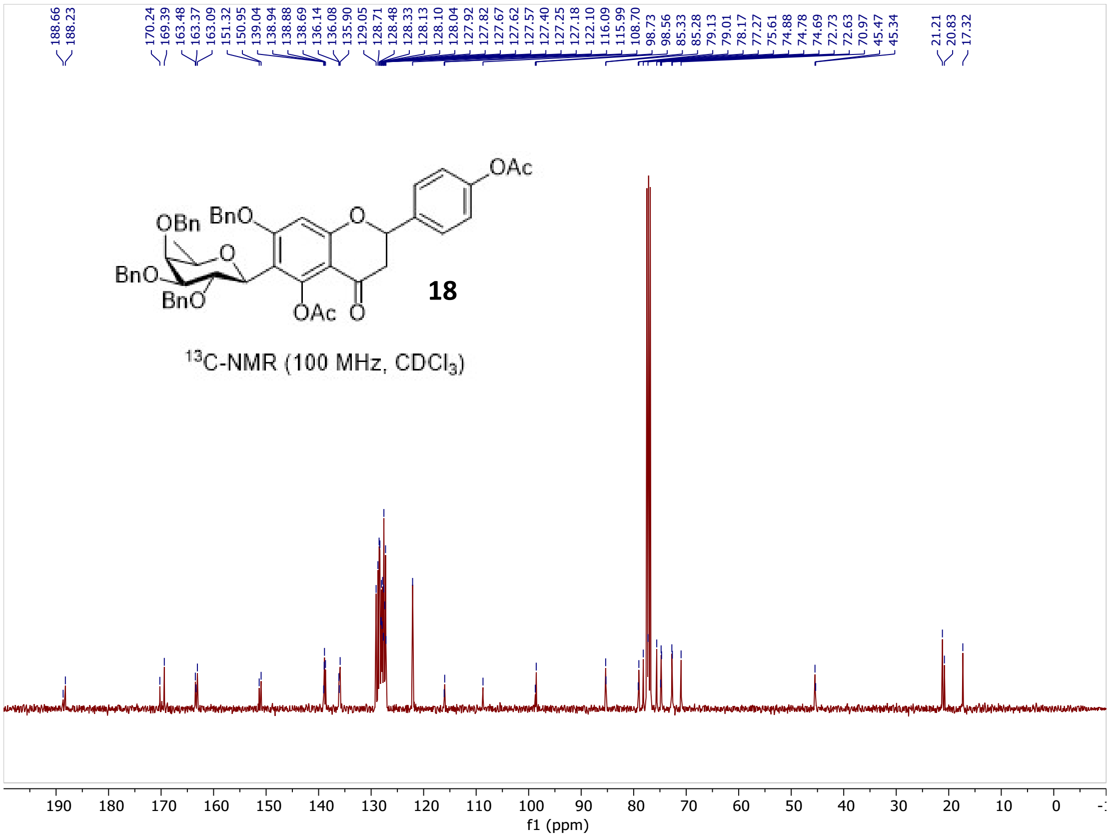

8.09
8.07
7.46
7.45
7.44
7.43
7.41
7.40
7.39
7.39
7.38
7.38
7.37
7.37
7.36
7.36
7.35
7.34
7.34
7.32
7.32
7.31
7.30
7.30
7.29
7.29
7.28
7.28
7.27
7.27
7.26
7.20
7.20
7.19
7.19
7.18
7.18
7.11
7.11
7.10
7.10
7.09
7.08
7.08
6.12
6.10
5.03
5.02
5.00
5.00
4.89
4.89
4.88
4.88
4.80
4.79
4.78
4.56
4.28
3.72
3.71
3.70
2.31
2.30
1.22
1.22
1.21
1.20
OAc
OBn
BnO
O
BnO
BnO
O
OH
17
^{1}H-NMR (400 MHz, CDCl$_3$)
0.94
1.97
16.09
3.25
4.04
0.97
1.02
7.30
1.08
1.00
1.00
3.05
2.03
3.10
1.04
0.93
3.17
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
0.0
-0.5
f1 (ppm)

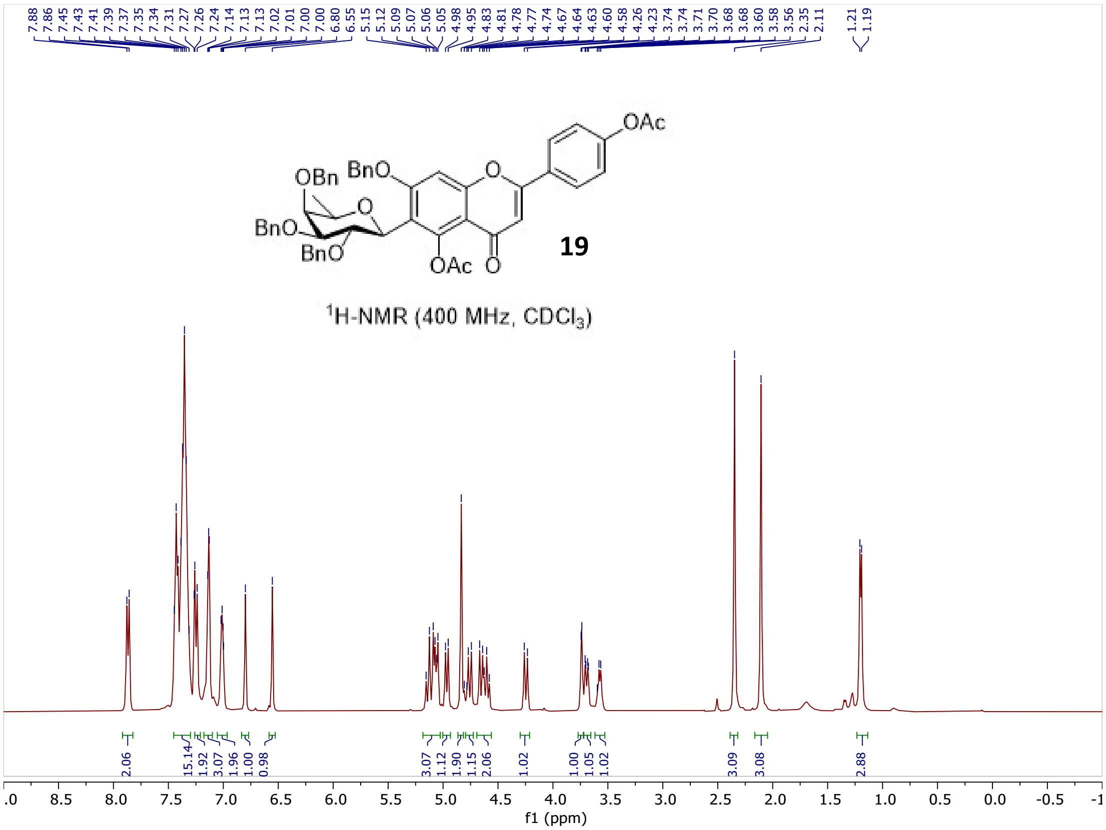

169.54
156.25
156.19
155.81
155.73
155.44
150.30
139.44
138.86
138.74
137.50
128.48
128.44
128.36
128.21
128.07
128.03
127.64
127.61
127.48
127.37
127.32
121.67
105.92
105.79
103.86
103.77
93.23
93.14
84.39
78.44
78.34
77.37
76.70
75.14
74.43
74.33
72.73
70.46
29.80
29.69
21.25
19.32
19.21
17.54
OAc
OBn
BnO
O
BnO
BnO
O
OH
17
^{13}C-NMR (100 MHz, CDCl$_3$)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

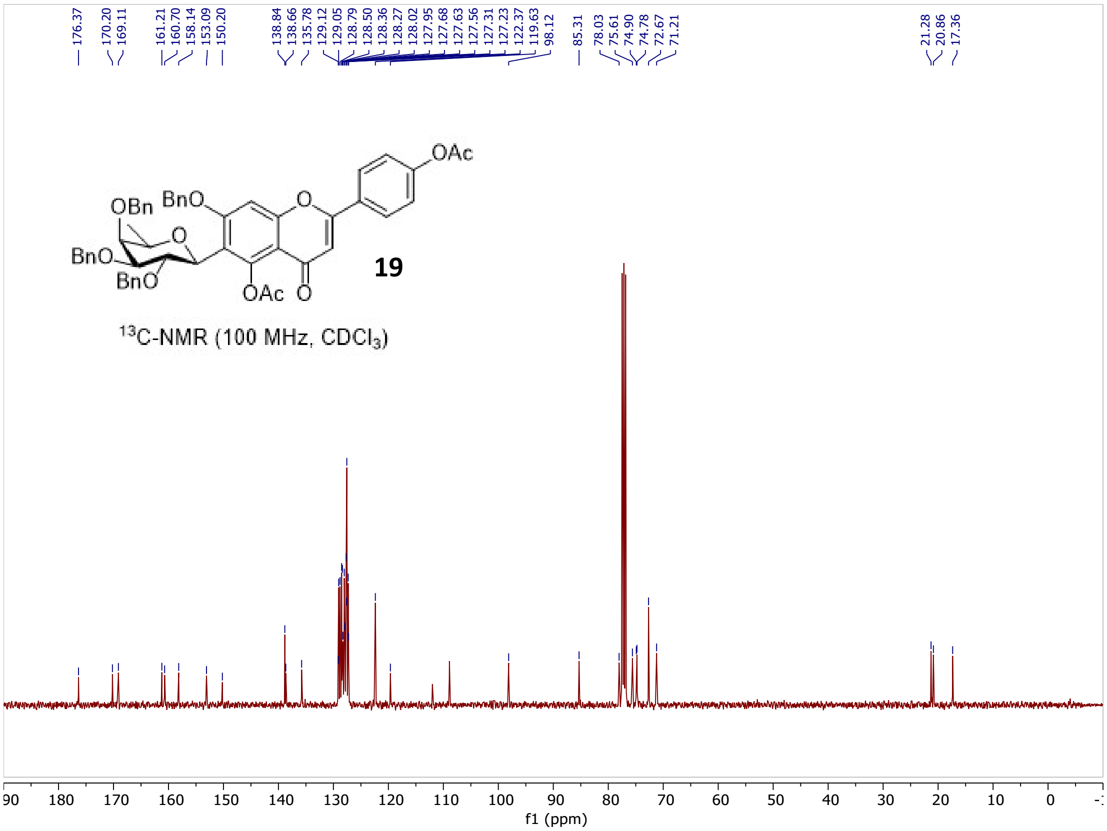

7.43
7.42
7.40
7.39
7.39
7.38
7.37
7.37
7.36
7.35
7.35
7.34
7.34
7.33
7.33
7.32
7.32
7.31
7.31
7.30
7.30
7.30
7.28
7.27
7.27
7.26
7.20
7.20
7.19
7.18
7.10
7.09
7.08
7.07
7.07
7.06
7.06
7.05
7.05
7.04
6.39
6.39
5.03
5.02
4.96
4.94
4.91
4.90
4.88
4.83
4.82
4.81
4.65
4.64
4.63
4.62
4.61
4.61
3.71
3.70
2.30
2.30
2.29
1.99
1.97
1.18
1.17
BnO
BnO
BnO
BnO
O
O
OAc
OAc
17a
^{1}H-NMR (400 MHz, CDCl$_3$)
18.30
2.96
4.05
1.00
7.86
2.02
1.04
0.99
1.10
1.11
1.77
2.98
1.12
3.30
2.90
.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
0.0
-0.5
-1
f1 (ppm)

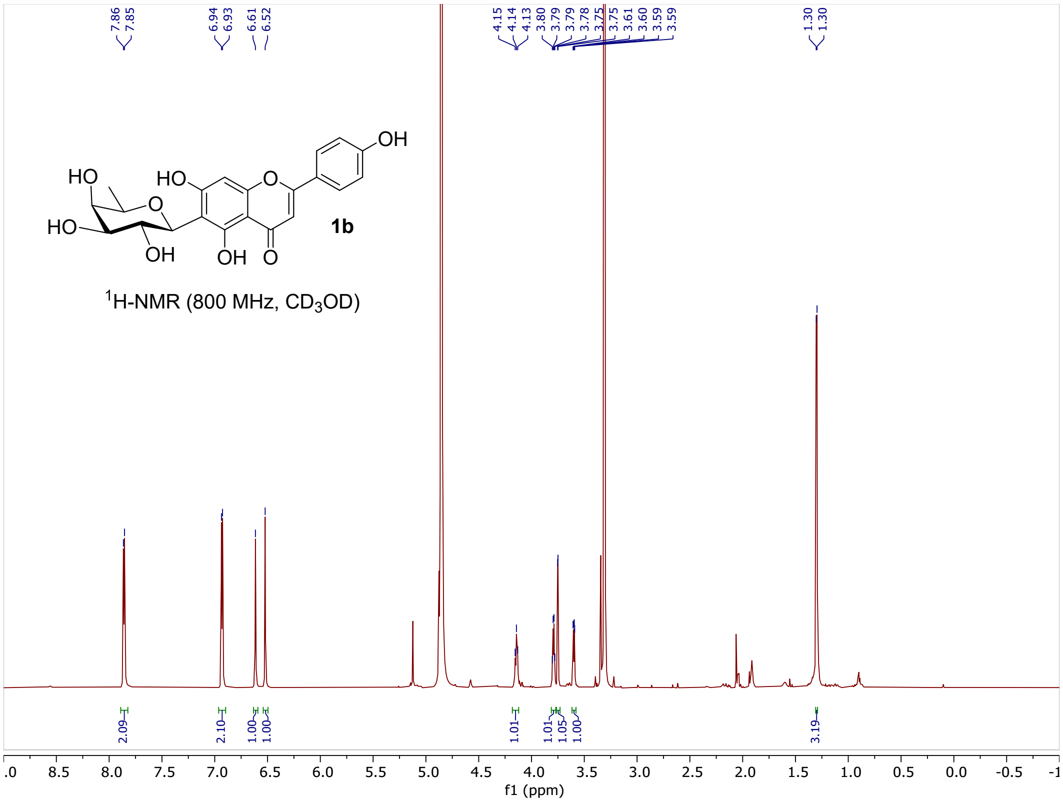

169.84
169.48
156.82
156.66
155.96
155.92
150.37
149.62
149.47
139.05
138.96
138.92
138.79
137.32
129.07
128.45
128.27
128.03
127.97
127.84
127.64
127.59
127.55
127.30
127.26
127.22
127.16
121.72
113.10
113.03
109.27
109.10
99.38
85.32
85.21
78.60
77.32
75.62
74.76
74.57
74.47
73.16
72.92
70.89
29.62
29.10
21.21
20.64
20.52
19.68
17.31
OAc
OBn
BnO
O
O
BnO
BnO
OAc
17a
^{13}C-NMR (100 MHz, CDCl$_3$)
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-:
f1 (ppm)

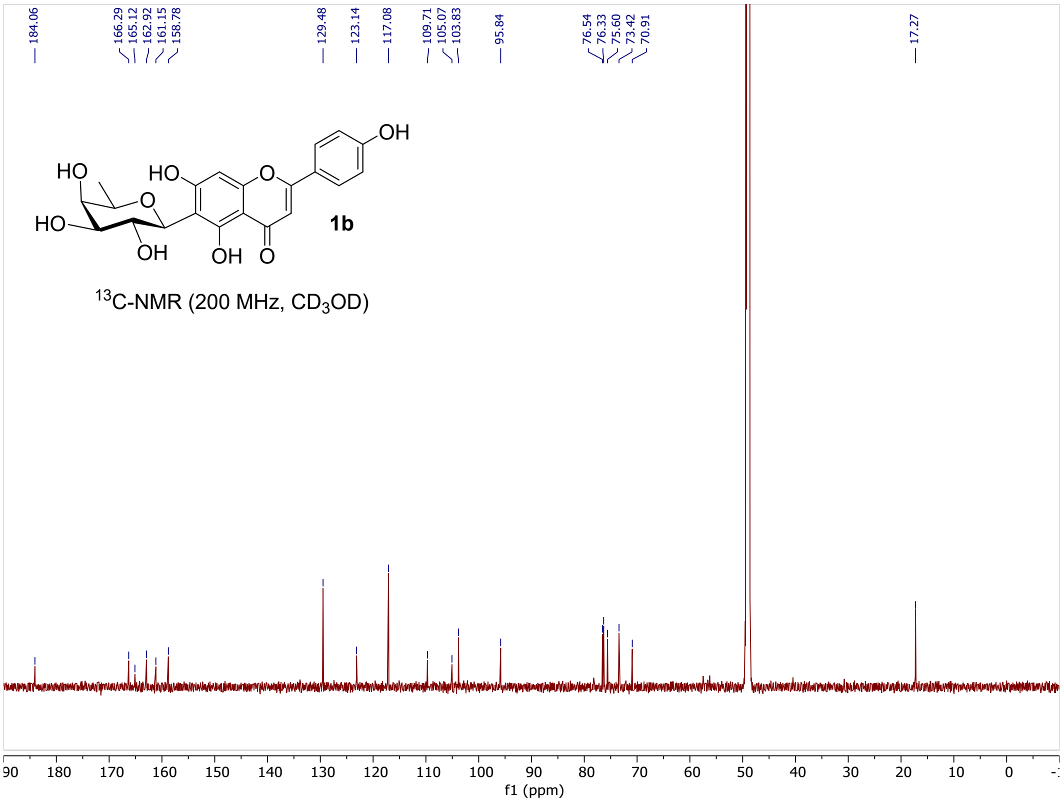

7.47
7.45
7.42
7.38
7.36
7.33
7.31
7.21
7.20
7.19
7.17
7.16
7.15
7.14
7.08
7.06
6.41
6.40
5.42
5.39
5.07
5.04
5.04
5.02
5.01
5.00
4.99
4.89
4.88
4.85
4.84
4.83
4.78
4.77
4.75
4.74
4.66
4.66
4.63
4.57
4.56
4.55
4.54
4.52
4.51
4.34
4.33
4.31
4.30
3.73
3.68
3.66
3.56
3.54
3.00
2.97
2.74
2.73
2.69
2.68
2.32
2.07
1.2
OAc
OBn
BnO
O
O
BnO
BnO
OAc
O
18
^{1}H-NMR (400 MHz, CDCl$_3$)
16.89
6.19
2.13
0.98
0.91
2.28
3.00
1.25
1.25
1.08
1.10
1.08
1.16
1.13
0.96
1.00
3.32
2.97
2.94
.0
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
0
f1 (ppm)


188.66
188.23
170.24
169.39
163.48
163.37
163.09
151.32
150.95
139.04
138.94
138.88
138.69
136.14
136.08
135.90
129.05
128.71
128.48
128.33
128.13
128.10
128.04
127.92
127.82
127.67
127.62
127.57
127.40
127.25
127.18
122.10
116.09
115.99
108.70
98.73
98.56
85.33
85.28
79.13
79.01
78.17
77.27
75.61
74.88
74.78
74.69
72.73
72.63
70.97
45.47
45.34
21.21
20.83
17.32
OAc
OBn
BnO
O
O
BnO
BnO
OAc
O
18
^{13}C-NMR (100 MHz, CDCl$_3$)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.88
7.86
7.45
7.43
7.41
7.39
7.37
7.35
7.34
7.31
7.27
7.26
7.24
7.14
7.13
7.13
7.02
7.01
7.00
7.00
6.80
6.55
5.15
5.12
5.09
5.07
5.06
5.05
4.98
4.95
4.83
4.81
4.78
4.77
4.74
4.67
4.64
4.63
4.60
4.58
4.26
4.23
3.74
3.74
3.71
3.70
3.68
3.60
3.58
3.56
2.35
2.11
1.21
1.19
OAc
OBn
BnO
BnO
BnO
O
O
OAc
O
19
^{1}H-NMR (400 MHz, CDCl$_3$)
2.06
15.14
1.92
3.07
1.96
1.00
0.98
3.07
1.12
1.90
1.15
2.06
1.02
1.00
1.05
1.02
3.09
3.08
2.88
.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
0.0
-0.5
-1
f1 (ppm)


176.37
170.20
169.11
161.21
160.70
158.14
153.09
150.20
138.84
138.66
135.78
129.12
129.05
128.79
128.50
128.36
128.27
128.02
127.95
127.68
127.63
127.56
127.31
127.23
122.37
119.63
98.12
85.31
78.03
75.61
74.90
74.78
72.67
71.21
21.28
20.86
17.36
OAc
OBn
BnO
BnO
BnO
O
O
OAc
O
19
^{13}C-NMR (100 MHz, CDCl$_3$)
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)





Comparison of the natural, Sun, and our ^{1}H NMR data for carambolaflavone A.[1, 2]

Natural	**Sun et al.**	**Current synthesis**
^{1}H NMR (400 MHz, CD$_3$OD)	^{1}H NMR (400 MHz, CD$_3$OD)	^{1}H NMR (800 MHz, CD$_3$OD)
7.84 (d, J = 8.8 Hz, 2H)	7.84 (d, J = 8.0 Hz, 2H)	7.86 (d, J = 8.3 Hz, 2H)
6.92 (d, J = 8.0 Hz, 2H)	6.93 (d, J = 7.6 Hz, 2H)	6.93 (d, J = 8.3 Hz, 2H)
6.61 (s, 1H)	6.59 (s, 1 H)	6.61 (s, 1H)
6.53 (s, 1H)	6.51 (d, J = 2.0 Hz, 1H)	6.52 (s, 1H)
4.64 (d, J = 8.4 Hz, 1H)	--[a]	--[a]
4.03 (t, J = 8.7 Hz, 1H)	4.17 (t, J = 9.2 Hz, 1H)	4.14 (t, J = 9.6 Hz, 1H)
3.97 (dd, J = 3.0, 6.5 Hz, 1H)	3.62 (dd, J = 3.2, 9.2 Hz, 1H)	3.60 (dd, J = 3.0, 9.4, Hz, 1H)
3.50 (d, J = 3.0 Hz, 1H)	3.76 (d, J = 2.8 Hz, 1H)	3.75 (d, J = 3.0 Hz, 1H)
3.17 (m, 1H)	3.80 (m, 1H)	3.75 (d, J = 3.0 Hz, 1H)
1.44 (d, J = 6.2 Hz, 3H)	1.31 (d, J = 6.0 Hz, 3H)	1.30 (d, J = 6.4 Hz, 3H)

[a] Peak was obscured by water.

†Passed away on September 13, 2021.

1. Wang, Y.; Liu, M.; Liu, L.; Xia, J.-H.; Du, Y.-G.; The Structural Revision and Total Synthesis of Carambolaflavone A. *J. Org. Chem.* **2018**, *83*, 4111-4118.
2. Cazarolli, L. H.; KIappel, V. D.; Pereira, D. F.; Moresco, H. H.; Brighente, I. M. C.; Pizzolatti, M. G.; Silva, F. R. M. B. Anti-hyperglycemic Action of Apigenin-6-C-β-fucopyranoside from *Averrhoa Carambola*. *Fitoterapia*. **2012**, *83*, 1176-1183.