Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Synthesis of 4-thiol-furanosidic uronate *via* hydrothiolation reaction

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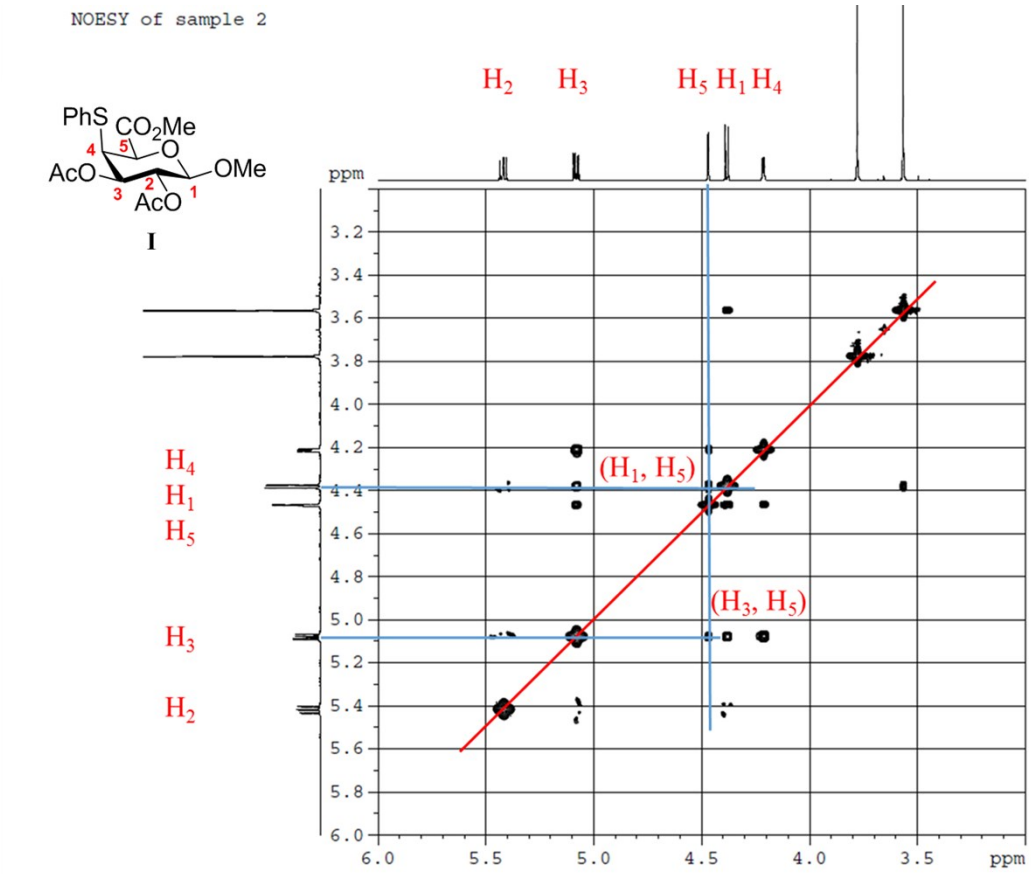
(A)



(B)

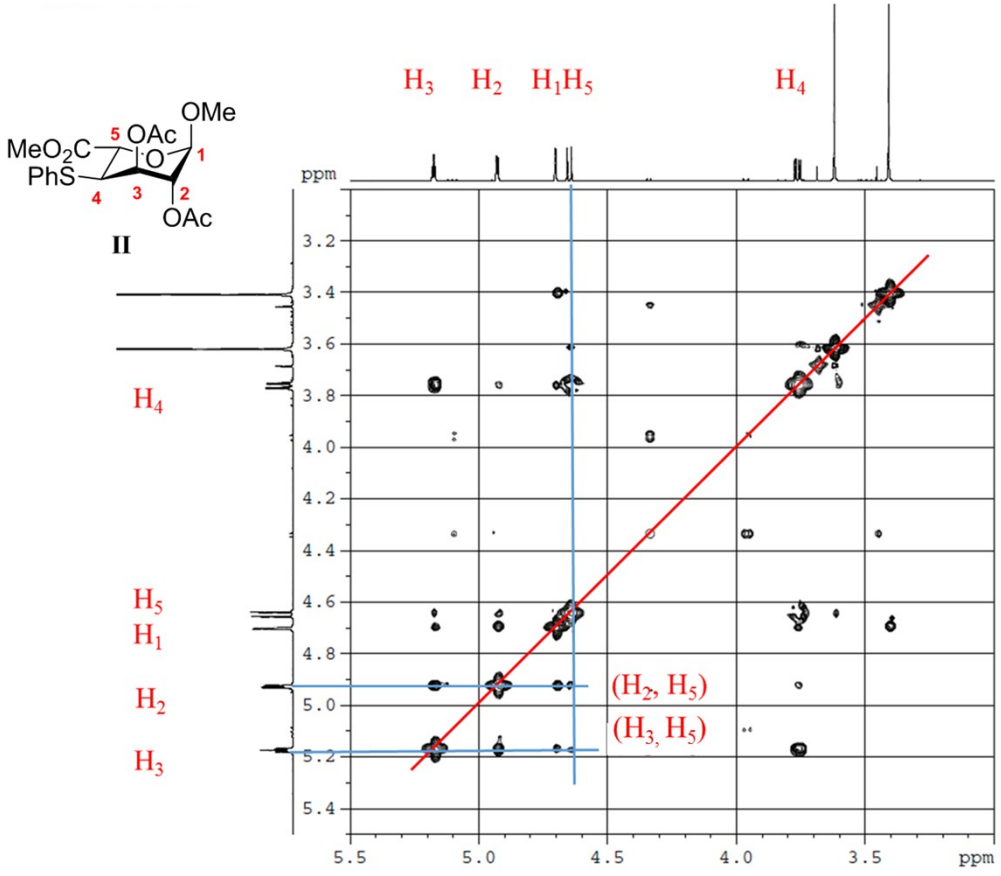


Figure S1. The NOESY spectra of compound **I** (A) and **II** (B).

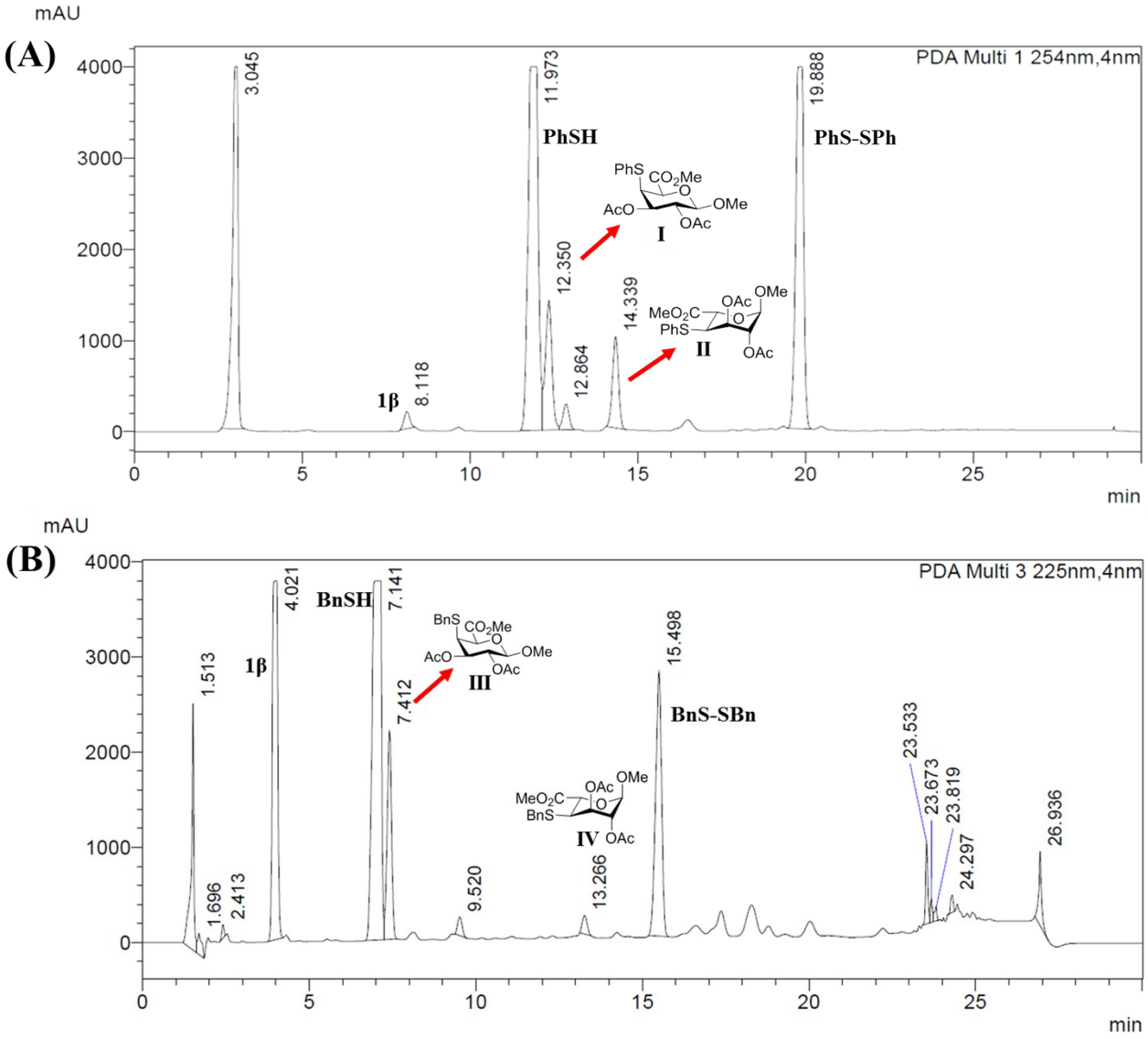
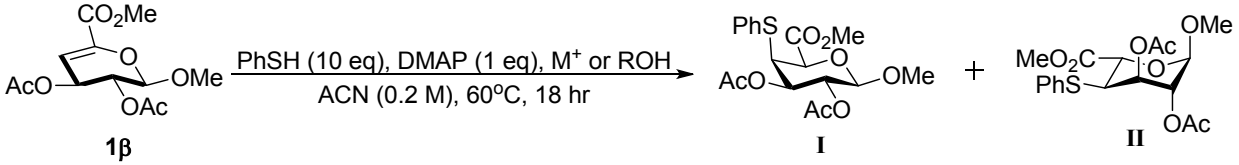


Figure S2. The ratio of desired products was determined by HPLC analysis. Using PhS (A) and BnSH (B), respectively, as nucleophiles for base-mediate thiol-Michael addition, the reaction crude mixture was diluted with acetonitrile and that was immediately analyzed by HPLC.

Table S1. 1β with metallic salts and alcohols containing bulky alkyl group.

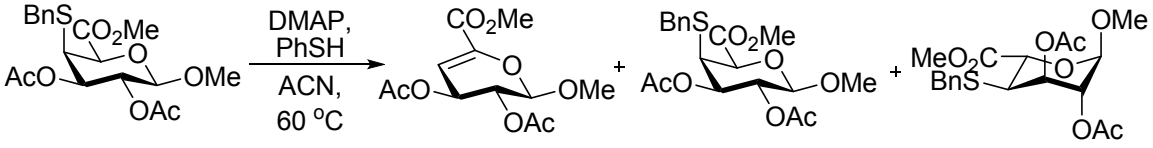


1β **I** **II**

Entry	Additives (equiv.)	Yield[a]	I:II[a]
1	none	72 %	1.6:1
2	$MgBr_2.OEt_2$ (0.1 eq)	73 %	1.1:1
3	$Mg(ClO_4)_2$ (0.1 eq)	78 %	1.1:1
4	$Mg(OTf)_2$ (0.1 eq)	76 %	1.1:1
5	NaBr (0.1 eq)	73 %	1.2:1
6	$ZnCl_2$ (0.1 eq)	65 %	1.3:1
7	IPA (1 eq)	75 %	1.3:1
8	t-BuOH (1 eq)	76 %	1.3:1

[a] yield percentage and the ratio of products were determined by high performance liquid chromatography (HPLC) analysis.

Table S2. Retro thiol-Michael addition.

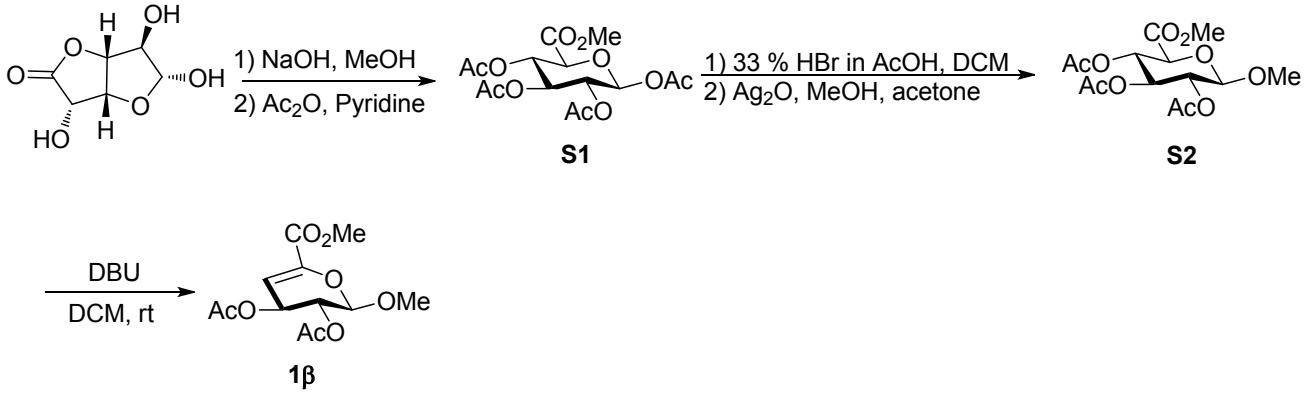


III **1β** **III** **IV**

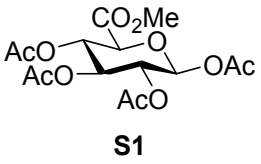
Entry	Thiol (Eq.)	Time	Result[a]
1	-	1 hr	**III** (100)
2	-	3 hr	**III** (100)
3	-	12 hr	**1β** + **III** + **IV** (1 : 97 : 2)
4	BnSH (10)	1 hr	**III** (100)
5	BnSH (10)	3 hr	**1β** + **III** (1: 99)
6	BnSH (10)	12 hr	**1β** + **III** + **IV** (2 : 96 : 2)

[a] The ratio of products was determined by HPLC analysis.

Synthesis of compound 1β:



Scheme S1. Synthesis of methyl (methyl 2,3-di-O-acetyl-4-deoxy-α-L-threo-hex-4-enopyranosid)uronate (**1β**).

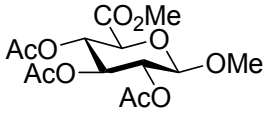


S1

β-D-Glucopyranuronic acid, methyl ester, 1,2,3,4-tetraacetate (S1)

To a solution of D-Glucurono-6,3-lactone (10.0 g, 56.8 mmol) in MeOH (30.0 mL) was added NaOH/MeOH (0.01 wt%, 90.0 mL) at 0 °C for 20 min, then the reaction mixture was allowed to warm up to room temperature. After another 16 hr stirring at room temperature, the solvent of this reaction mixture was removed under vacuums and acetic anhydride (47.2 mL) and pyridine (113.6 mL) was added to this crude residue at 0 °C. The reaction was stirred at 0 °C for overnight, then quenched in ice/water. Thereafter, the reaction mixture was diluted with EtOAc and the organic layer was washed with 1 N $HCl_{(aq)}$, and brine to remove pyridine. The organic layer was dried over $MgSO_4$, and the organic layer was concentrated under reduced pressure. The crude product was recrystallized from methanol to give a slightly pale yellow powder (45.0 g, 0.1 mol, 52%). R_f = 0.33 (EtOAc : *n*-Hex = 1 : 3 v/v). ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ = 5.76 (d, J = 7.8 Hz, 1H), 5.30 (dd, $J_1 = J_2$ = 9.2 Hz, 1H,), 5.23 (dd, $J_1 = J_2$ = 9.3 Hz, 1H), 5.13 (dd, $J_1 = J_2$ = 8.3 Hz, 1H), 4.17 (d, J = 9.3 Hz, 1H), 3.74 (s, 3H), 2.11 (s, 3H), 2.03 (s, 6H), 2.02 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 298 K): δ = 170.03,

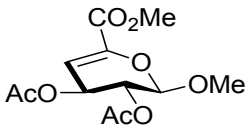
169.54, 169.31, 168.96, 166.93, 91.48, 73.11, 71.94, 70.27, 69.04, 53.15, 20.89, 20.68, 20.66, 20.59 ppm. ^{1}H and ^{13}C NMR spectra were agreed with reported literature[S1].



S2

β-D-Glucopyranosiduronic acid, methyl, methyl ester, 2,3,4-triacetate (S2)

To a solution of **S1** (2.0 g, 5.3 mmol) in dry dichloromethane (24.4 mL) was added 33% HBr in acetic acid (12.4 mL). The reaction was stirred at 0 °C for 20 min then left at 4 °C until the starting material was finished. After which, the reaction was quenched in cool sat. $NaHCO_3$ and the aqueous layer was extracted with dichloromethane. The combined organic layer was quickly washed with cold water, cold sat. $NaHCO_3$ and brine. After drying over $MgSO_4$, the organic layer was concentrated *via* reduce pressure and the concentrated residue was directly used for next step without purification. To a solution of crude product in dry acetone (43.7 mL) was added Ag_2O (3.7 g, 16.0 mmol) and dry MeOH (19.6 mL, 483.3 mmole) under nitrogen. The reaction mixture was vigorously stirred at room temperature in the dark. After an overnight stirring, the reaction mixture was filtered through a plug of celite and the filtrate was concentrated under reduced pressure. The concentrated residue was diluted with EtOAc, and then it was washed with sat. $NaHCO_3$, water and brine, sequentially. Thereafter, the organic layer was dried over $MgSO_4$, concentrated *via* reduce pressure, and purified by flash column chromatography to yield desired product (1.4 g, 4.0 mmol, 76 %). R_f = 0.20 (EtOAc : *n*-Hex = 1 : 1.5 v/v). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.29-5.19 (m, 2H), 5.00 (td, J_1 = 8.2 Hz, J_2 = 3.1 Hz, 1H), 4.48 (d, J = 7.7 Hz, 1H), 4.04 (dd, J_1 = 6.6 Hz, J_2 = 3.0 Hz, 1H), 3.77 (s, 3H), 3.52 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 298 K): δ = 170.28, 169.53, 169.47, 167.41, 101.82, 72.77, 72.23, 71.29, 69.61, 57.46, 53.05, 20.82, 20.75, 20.65 ppm. ^{1}H and ^{13}C NMR spectra were agreed with reported literature[S1].



1β

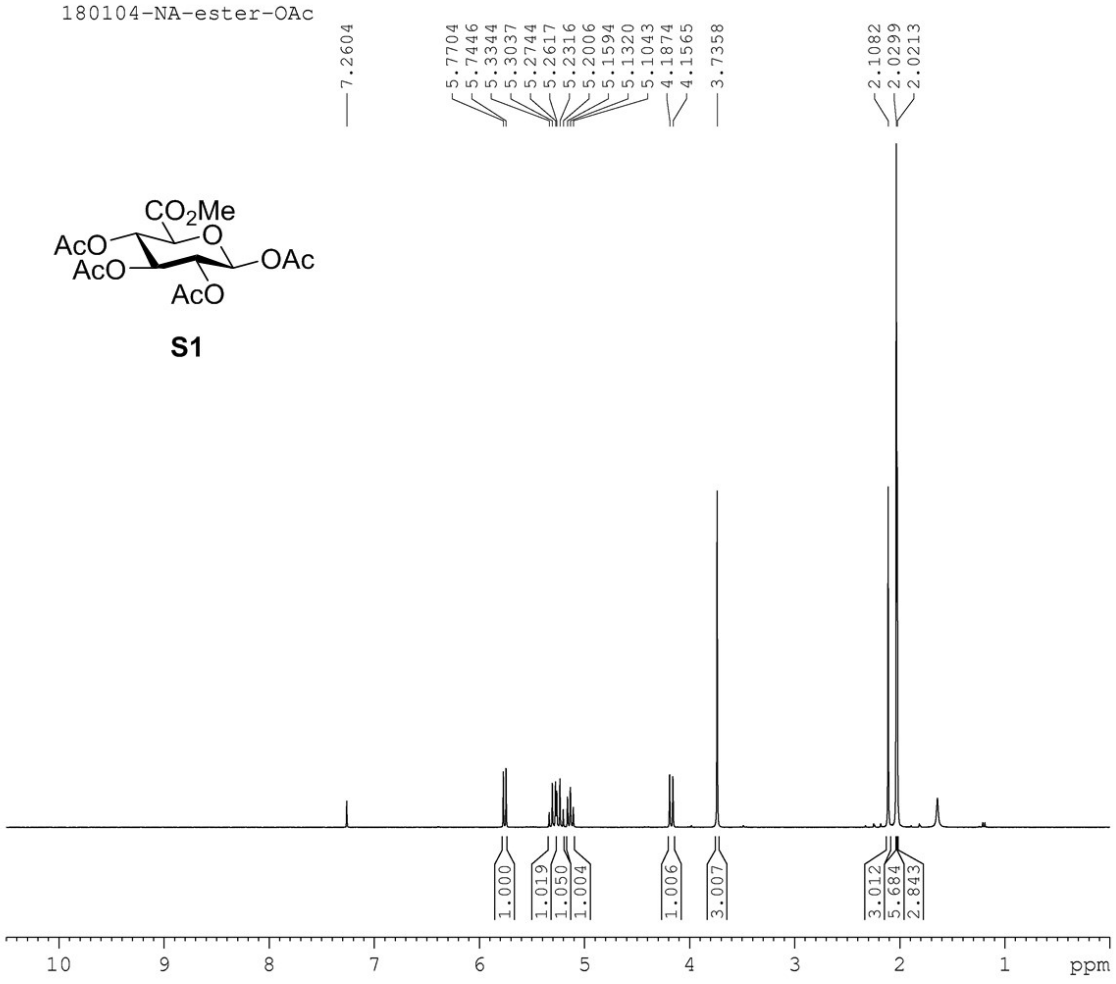
methyl (methyl 2,3-di-O-acetyl-4-deoxy-α-L-threo-hex-4-enopyranosid)uronate (1β)

To a solution of compound **S3** (30.0 mg, 0.1 mmol) in dry dichloromethane (0.8 mL) was slowly added DBU (66.0 μL, 0.7 mmol) under $Ar_{(g)}$. After 4 hr stirring at room temperature, the reaction was quenched by sat. $NH_4Cl_{(aq)}$ and diluted with dichloromethane. The organic layer was washed with water and brine, sequentially. Thereafter, the organic layer was dried over $MgSO_4$, concentrated under reduced pressure, then purification by flash column chromatography giving a white powder (21.6 mg, 0.07 mmol, 89 %). R_f = 0.30 (EtOAc : *n*-Hex = 1 : 2 v/v). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.22 (dd, J_1 = 4.5 Hz, J_2 = 1.2 Hz, 1H), 5.19 (ddd, J_1 = 0.7 Hz, J_2 = 2.0 Hz, J_3 = 4.5 Hz, 1H), 5.13 (dd, J_1 = 2.8 Hz, J_2 = 0.6 Hz, 1H), 5.09-5.07 (m, 1H), 3.84 (s, 3H), 3.52 (s, 3H), 2.10 (s, 3H), 2.09 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 298 K): δ = 170.08, 169.50, 142.31, 107.34, 97.74, 68.74, 64.34, 57.06, 52.68, 20.99, 20.81 ppm. ^{1}H and ^{13}C spectra were agreed with reported literature[S1].

References:

S1. Jongkees, S. A. K.; Withers, S. G., Glycoside Cleavage by a New Mechanism in Unsaturated Glucuronyl Hydrolases. *J. Am. Chem. Soc.* **2011,** *133*, 19334-19337.

Appendix ^{1}H and ^{13}C NMR spectra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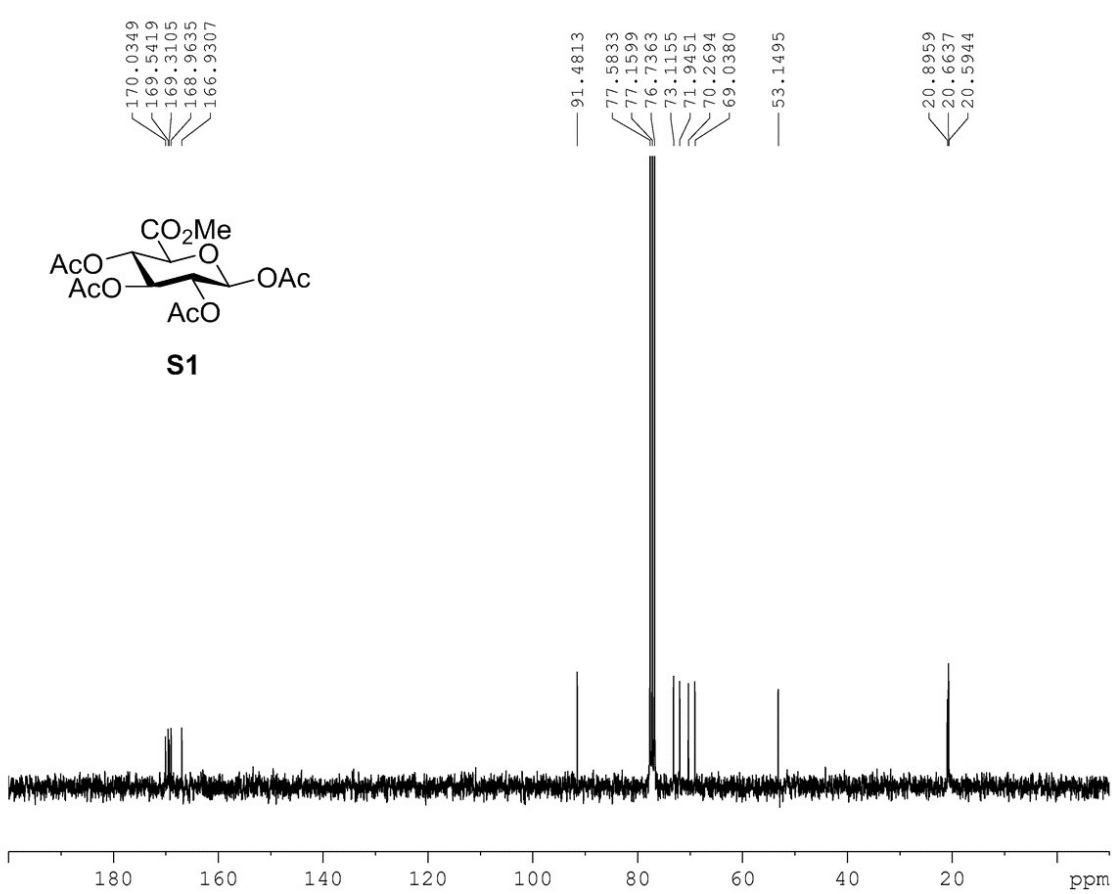
5.1594
5.1320
5.1043
4.1874
4.1565
3.7358
2.1082
2.0299
2.0213
CO2Me
AcO
AcO
AcO
OAc
1.000
1.019
1.050
1.004
1.006
3.007
3.012
5.684
2.843
10
9
8
7
6
5
4
3
2
1
ppm

S1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73.1155
71.9451
70.2694
69.0380
53.1495
20.8959
20.6637
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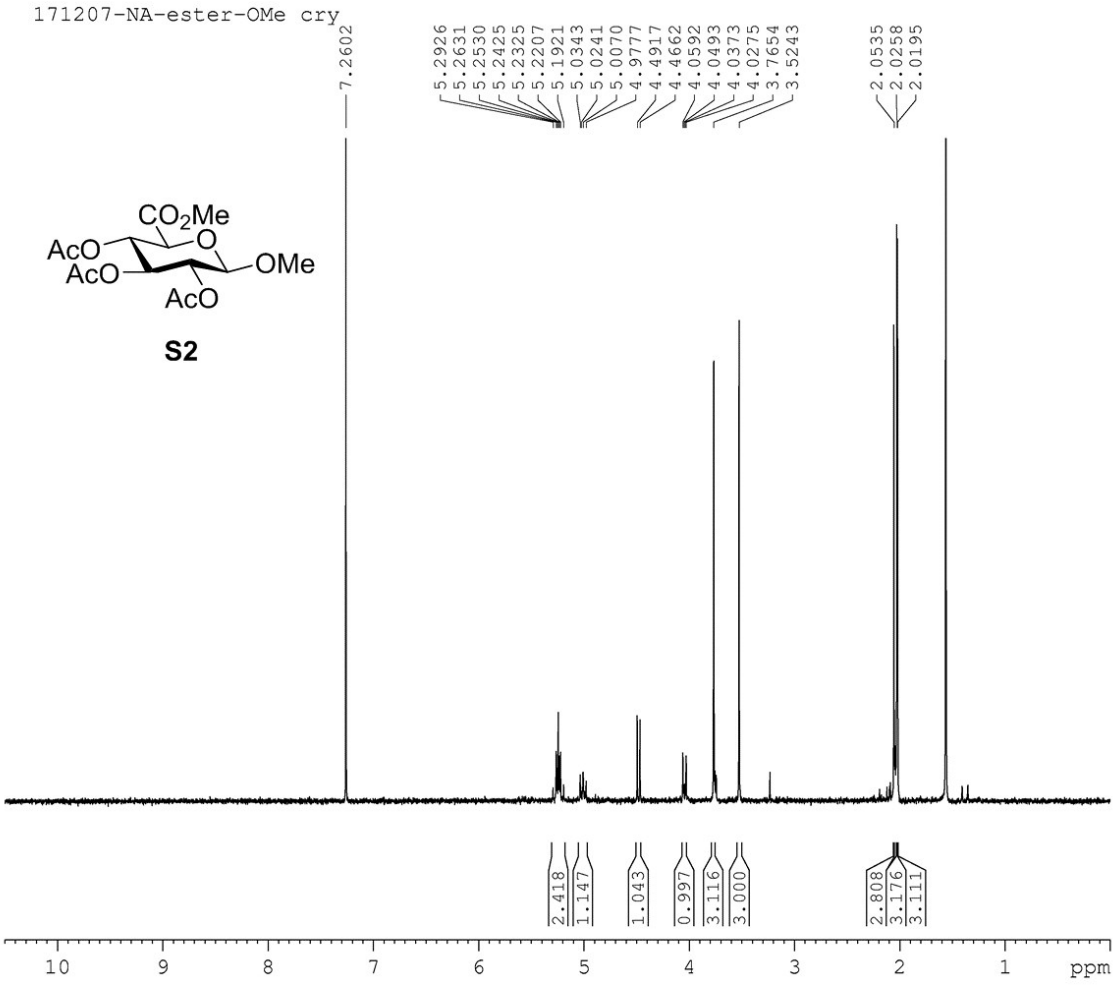
120
100
80
60
40
20
ppm

S1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5.0241
5.0070
4.9777
4.4917
4.4662
4.0592
4.0493
4.0373
4.0275
3.7654
3.5243
2.0535
2.0258
2.0195
CO2Me
AcO
AcO
AcO
OMe
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1.043
0.997
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5
4
3
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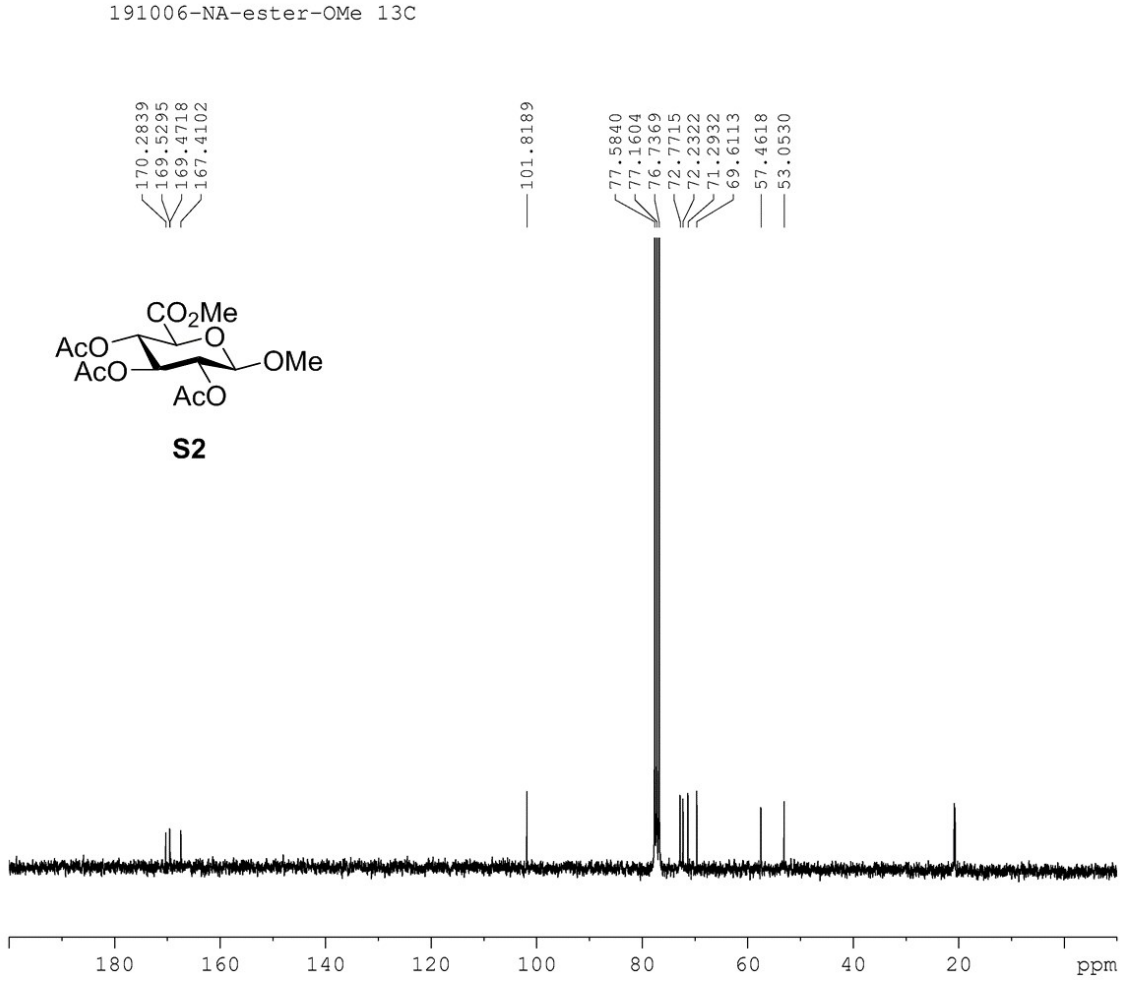
ppm

S2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69.6113
57.4618
53.0530
CO2Me
AcO
AcO
AcO
OMe
180
160
140
120
100
80
60
40
20
ppm

S2

171208-NA-ester

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6.2271
6.2160
6.2118
5.2040
5.2011
5.1969
5.1947
5.1862
5.1793
5.1319
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3.5172
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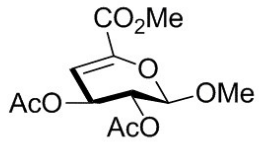
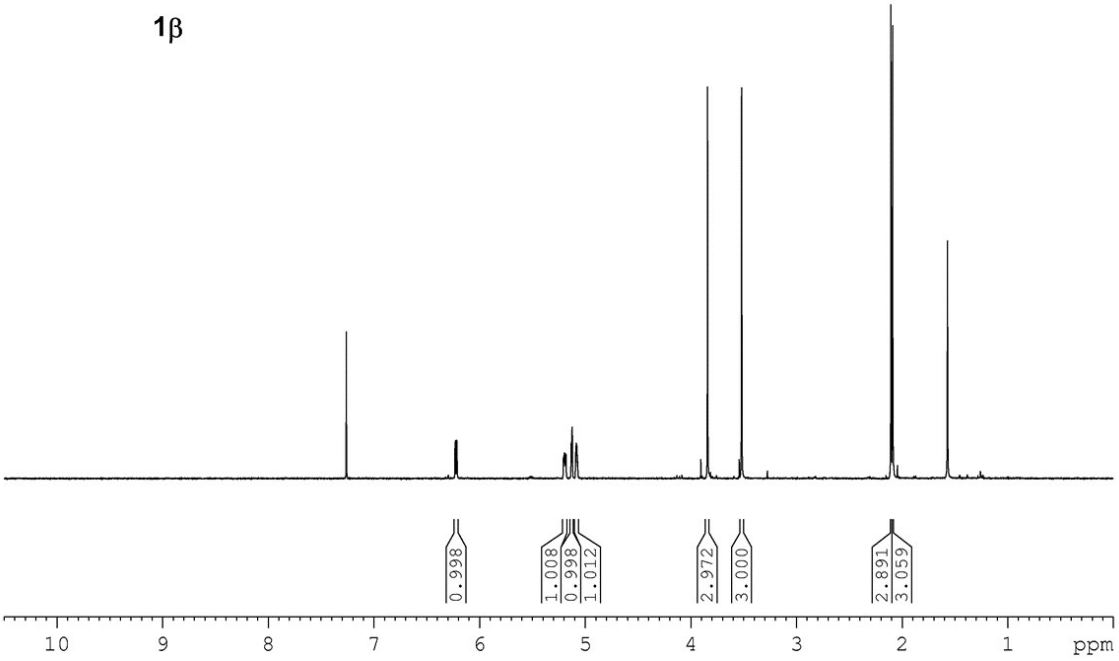
2.0877



1β



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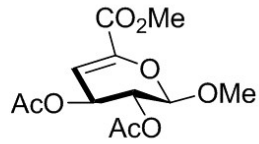
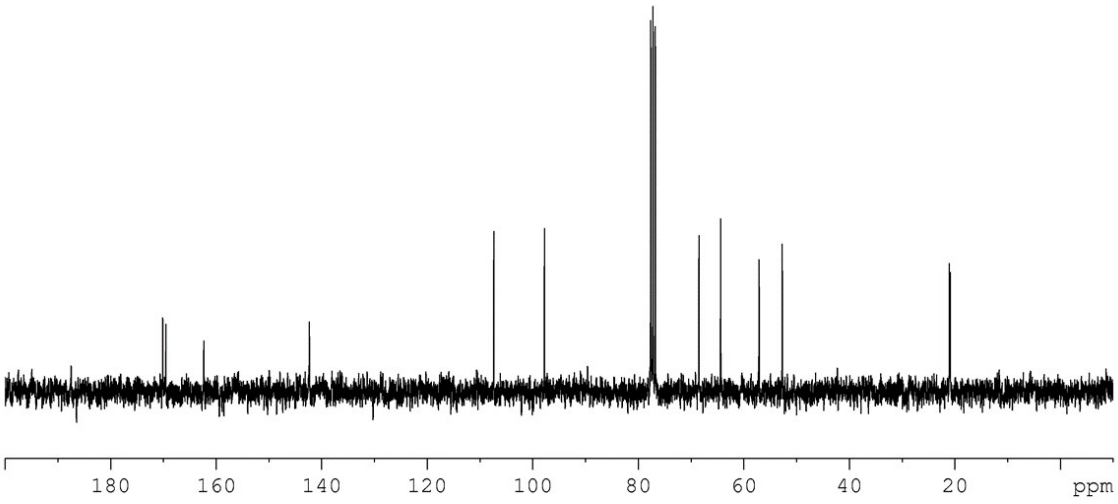
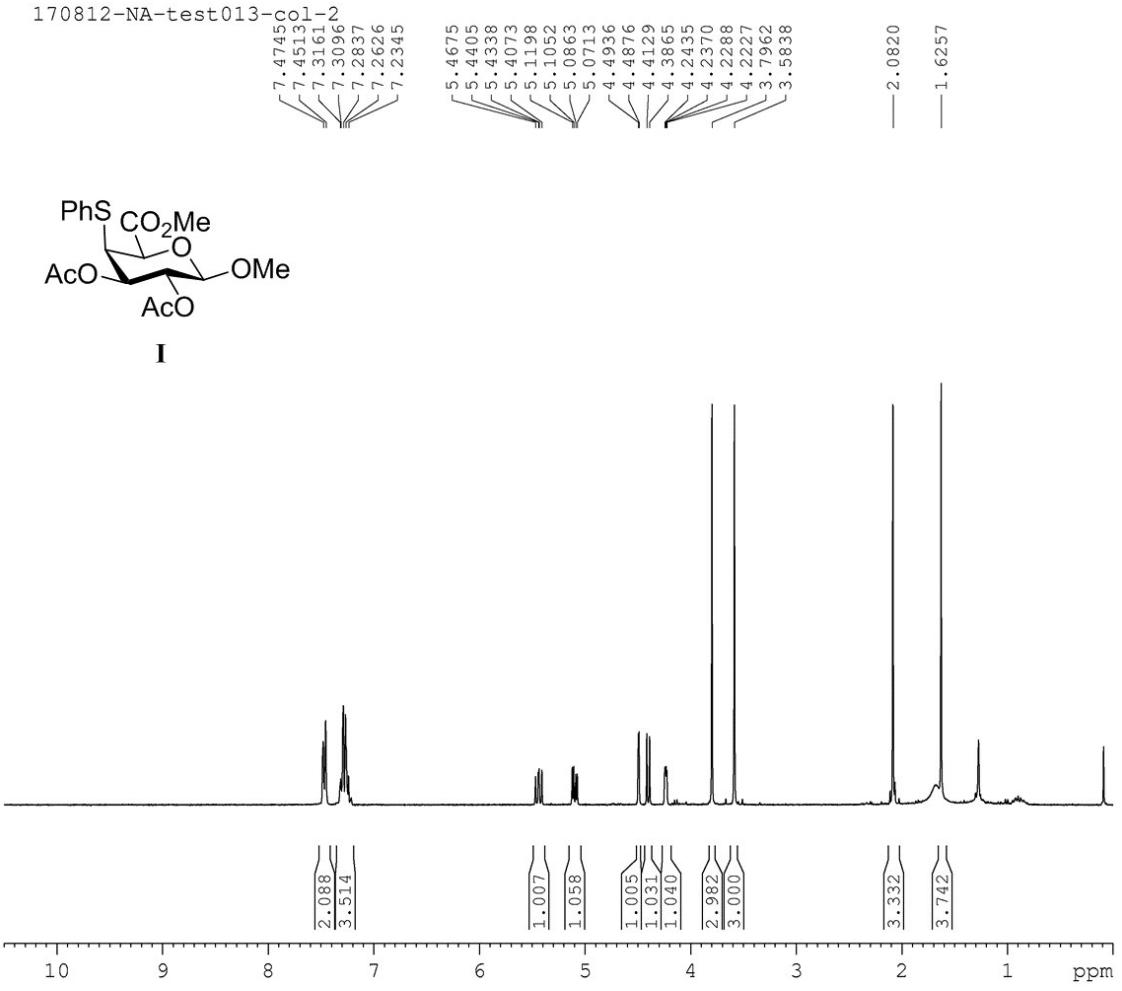


1β

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4.4129
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4.2435
4.2370
4.2288
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3.7962
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1.6257
PhS
CO2Me
O
AcO
OMe
AcO
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3.514
1.007
1.058
1.005
1.031
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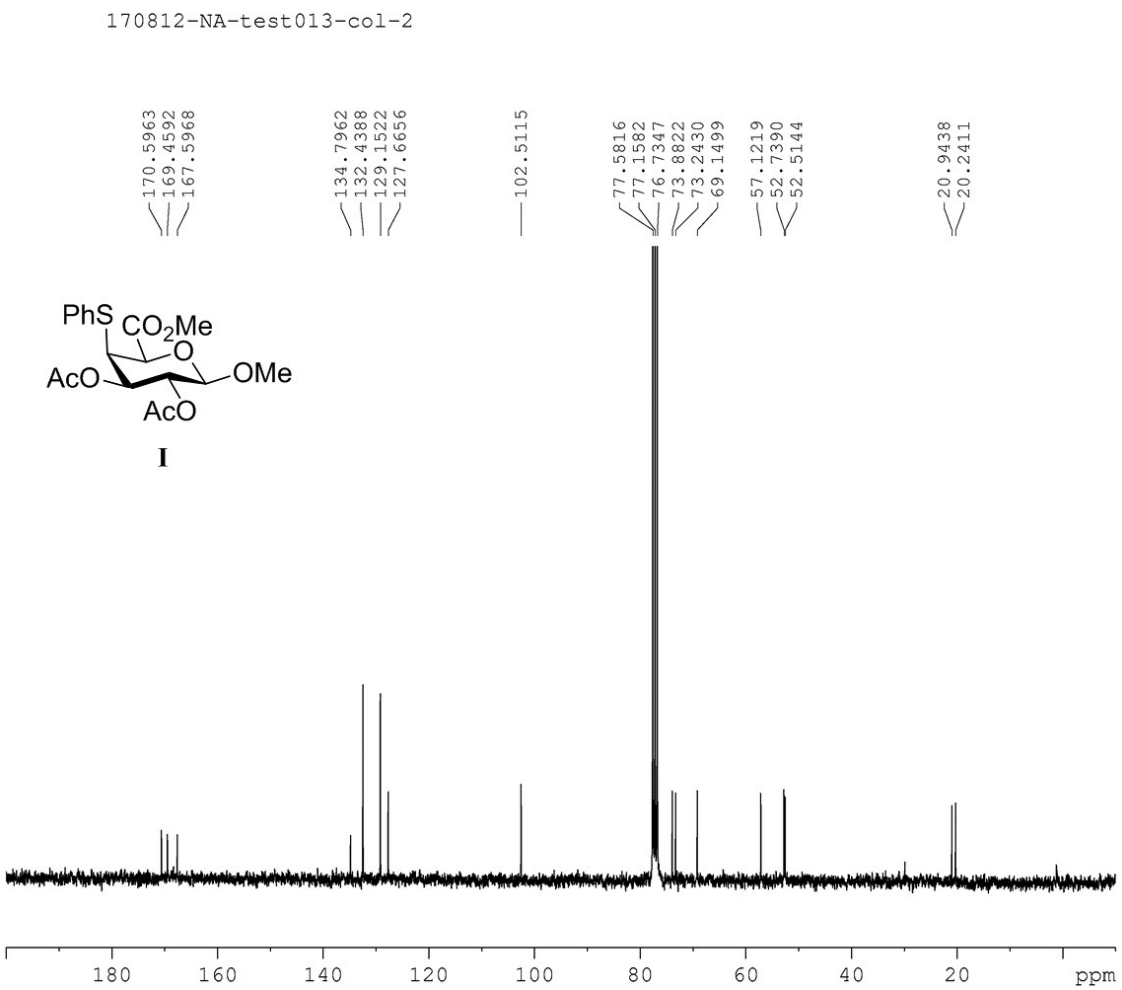
8
7
6
5
4
3
2
1
ppm

I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77.1582
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73.8822
73.2430
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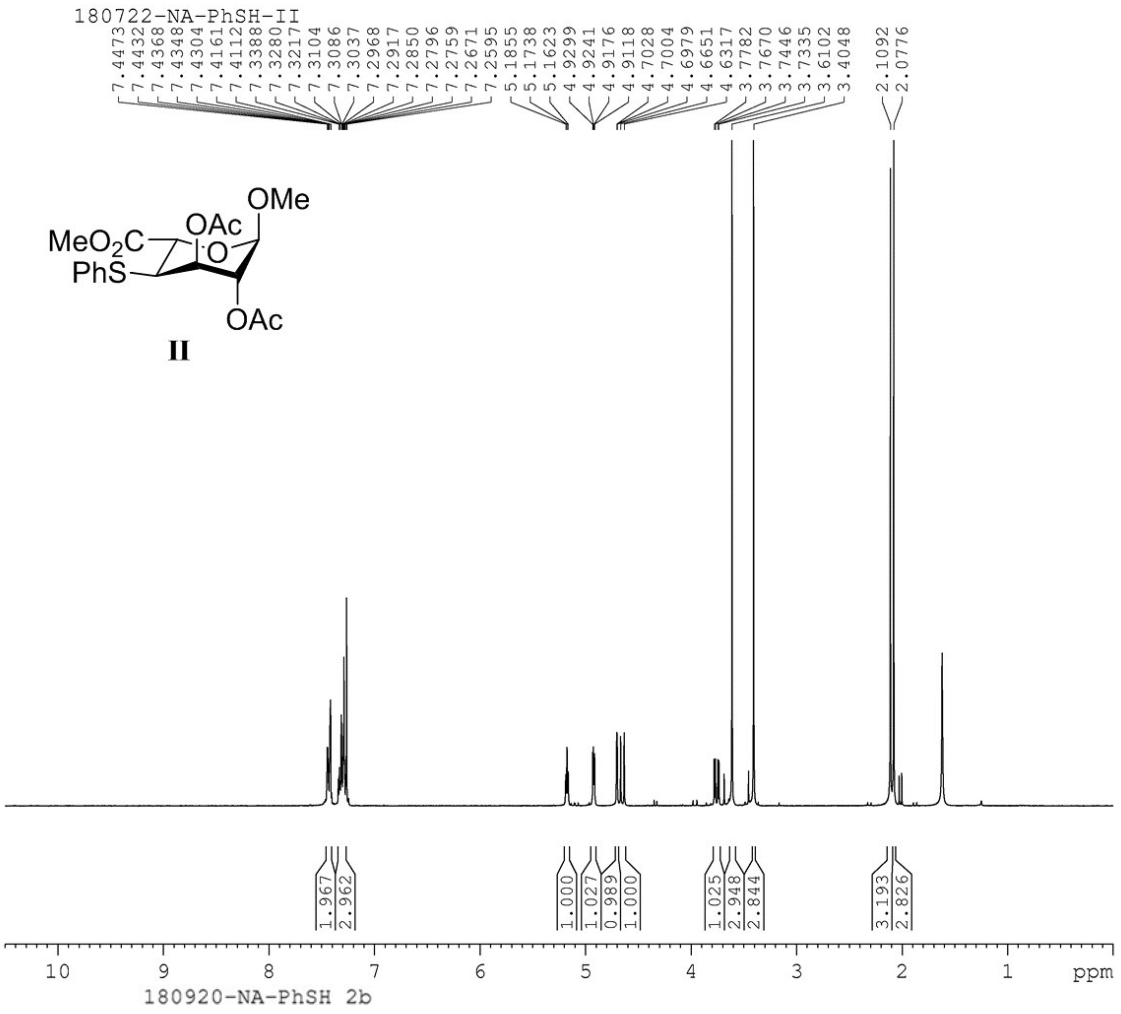
20
ppm

I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7.3037
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7.2850
7.2796
7.2759
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7.2595
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5.1738
5.1623
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3.7446
3.7335
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3.4048
2.1092
2.0776
OMe
OAc
MeO2C
O
PhS
OAc
II
1.967
2.962
1.000
1.027
0.989
1.000
1.025
2.948
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ppm
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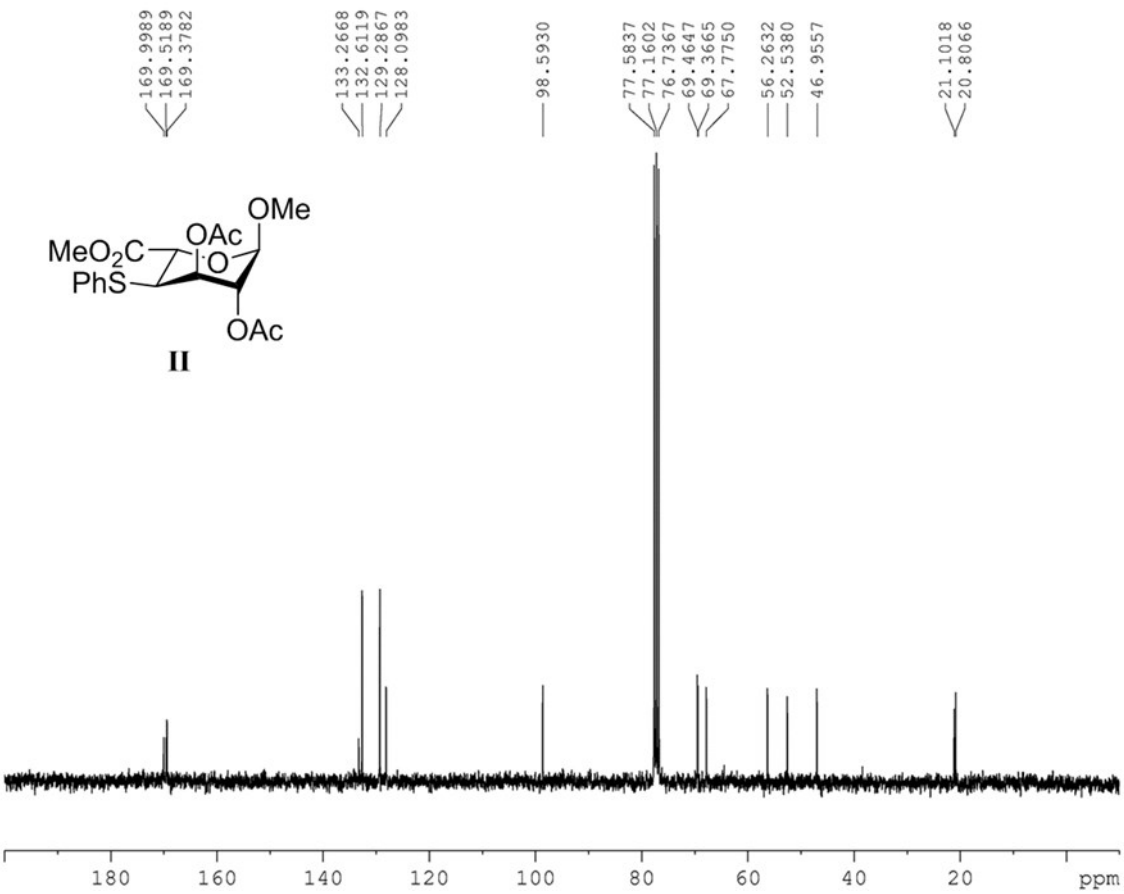
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67.7750
56.2632
52.5380
46.9557
21.1018
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OAc
MeO2C
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ppm

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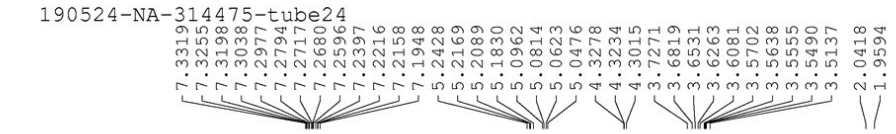

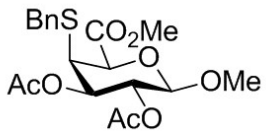

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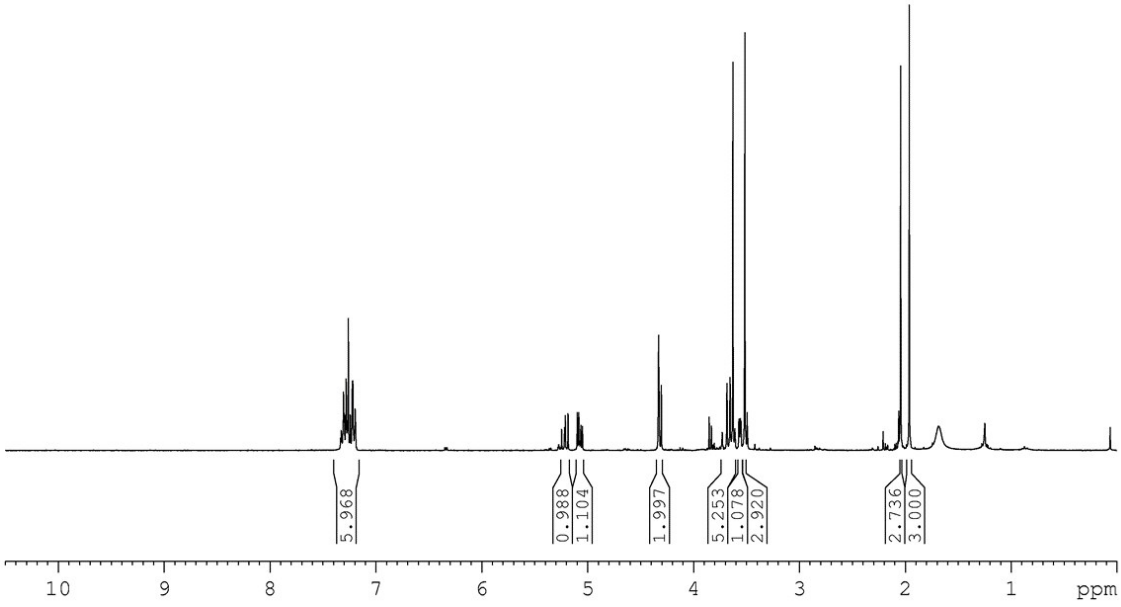

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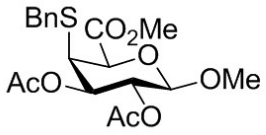

III

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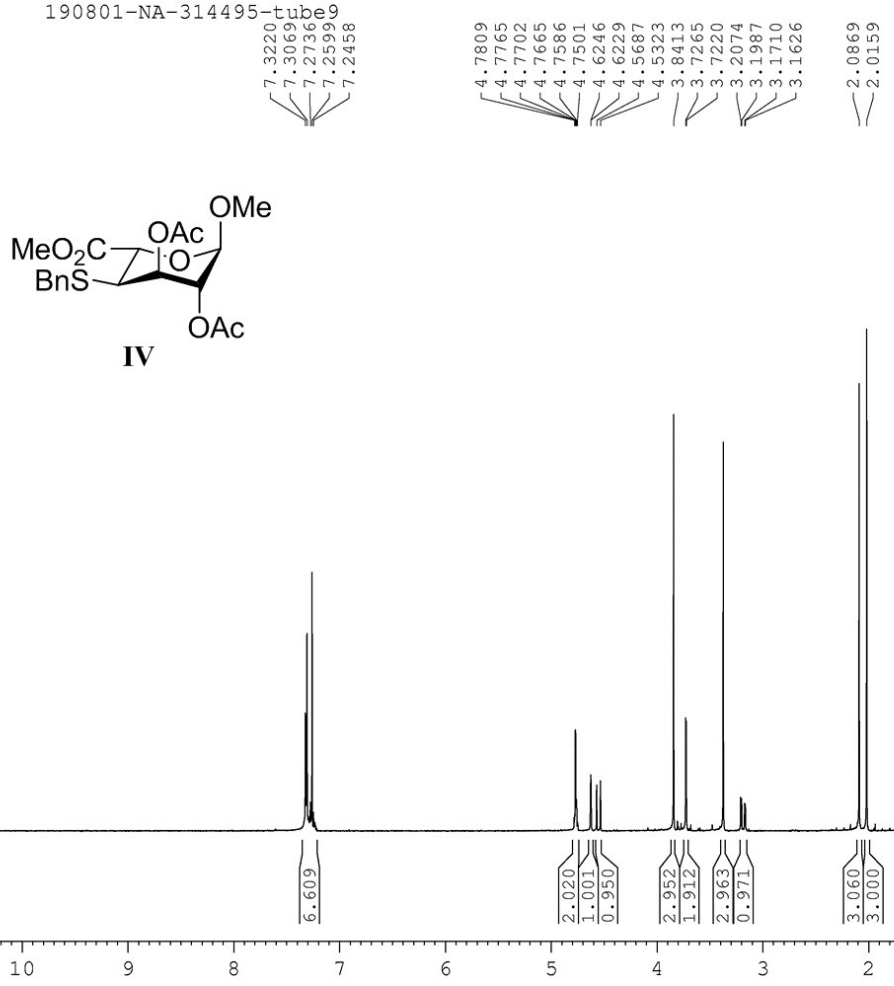

IV

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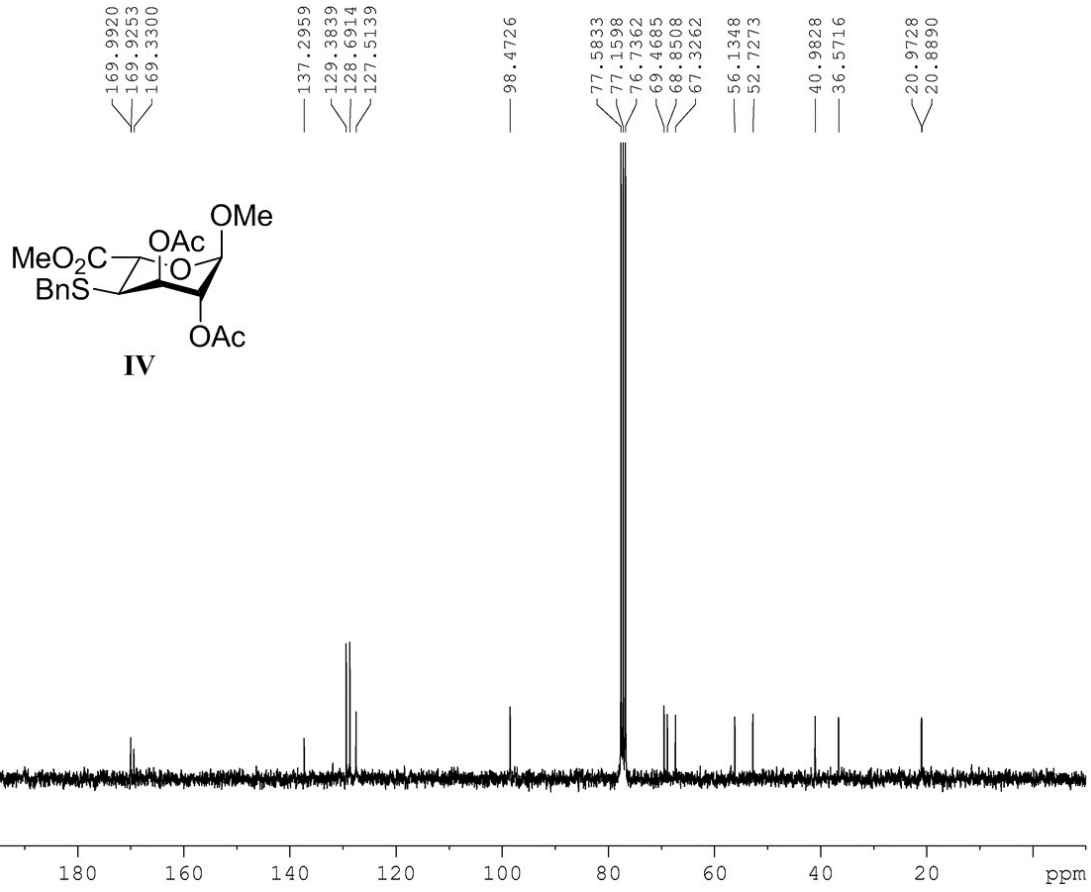
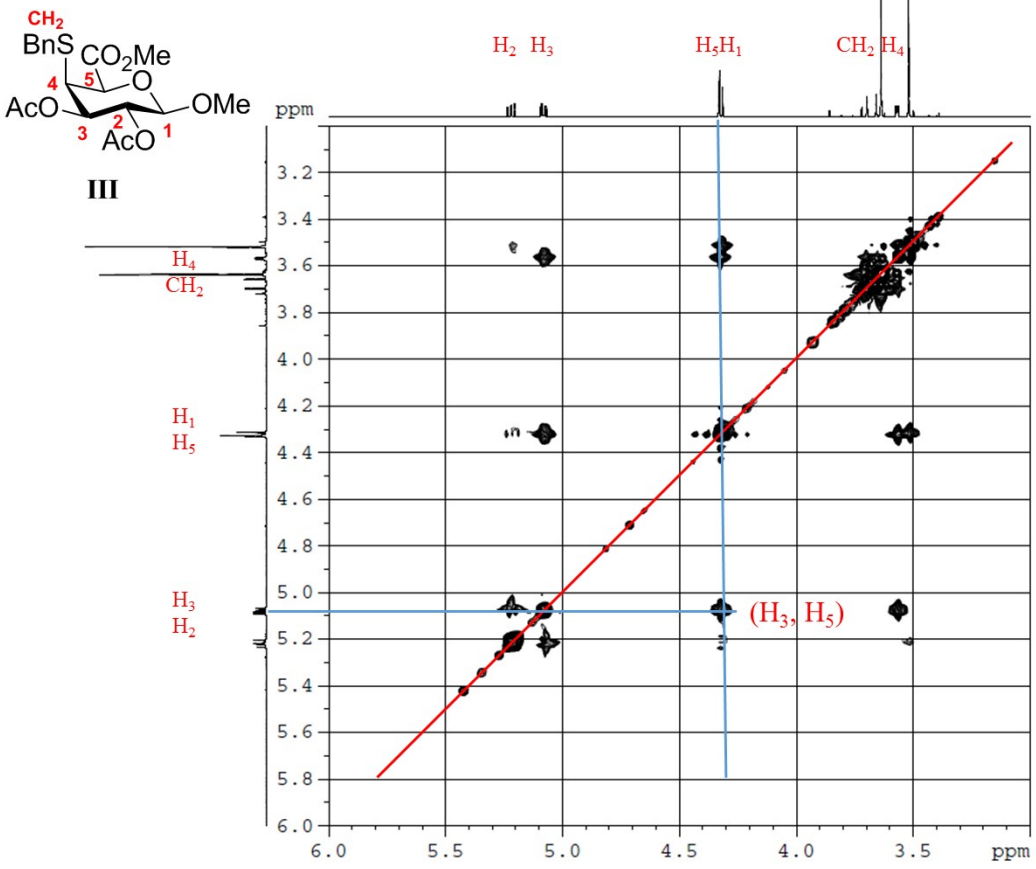
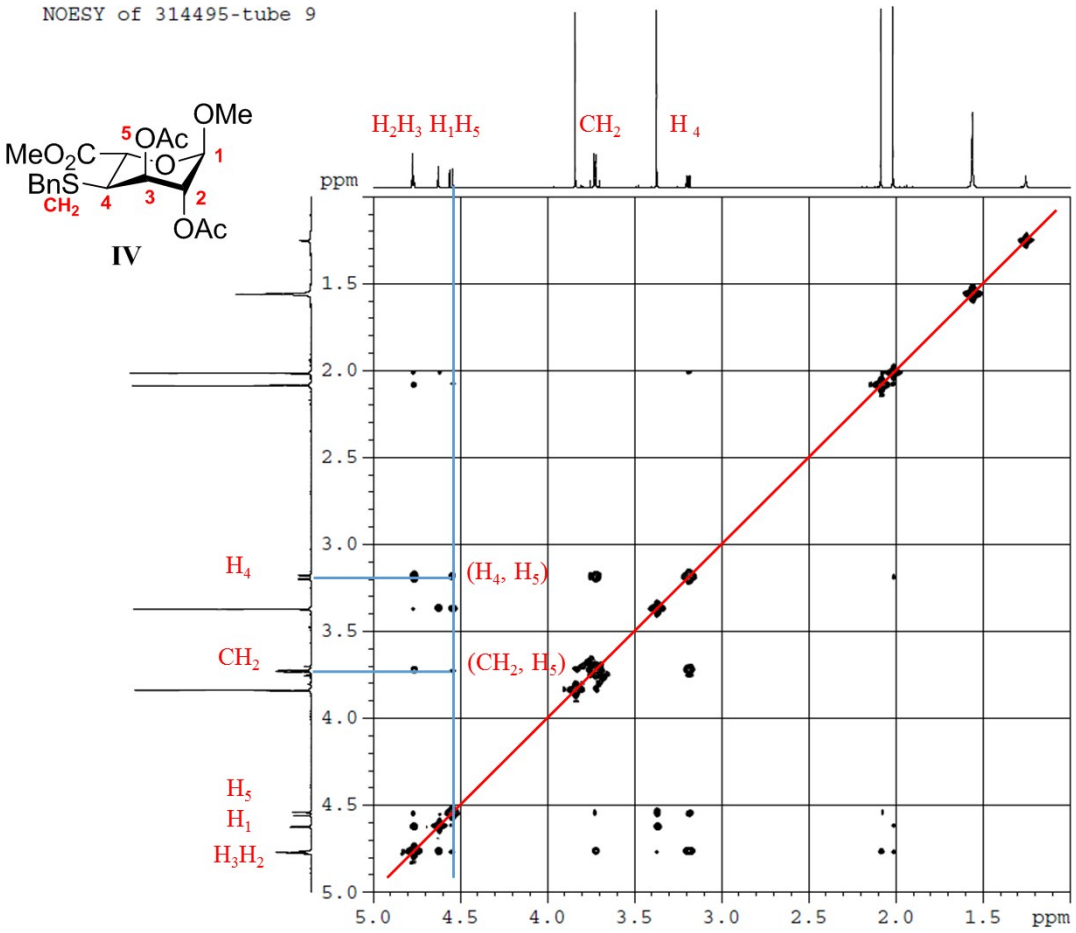


IV

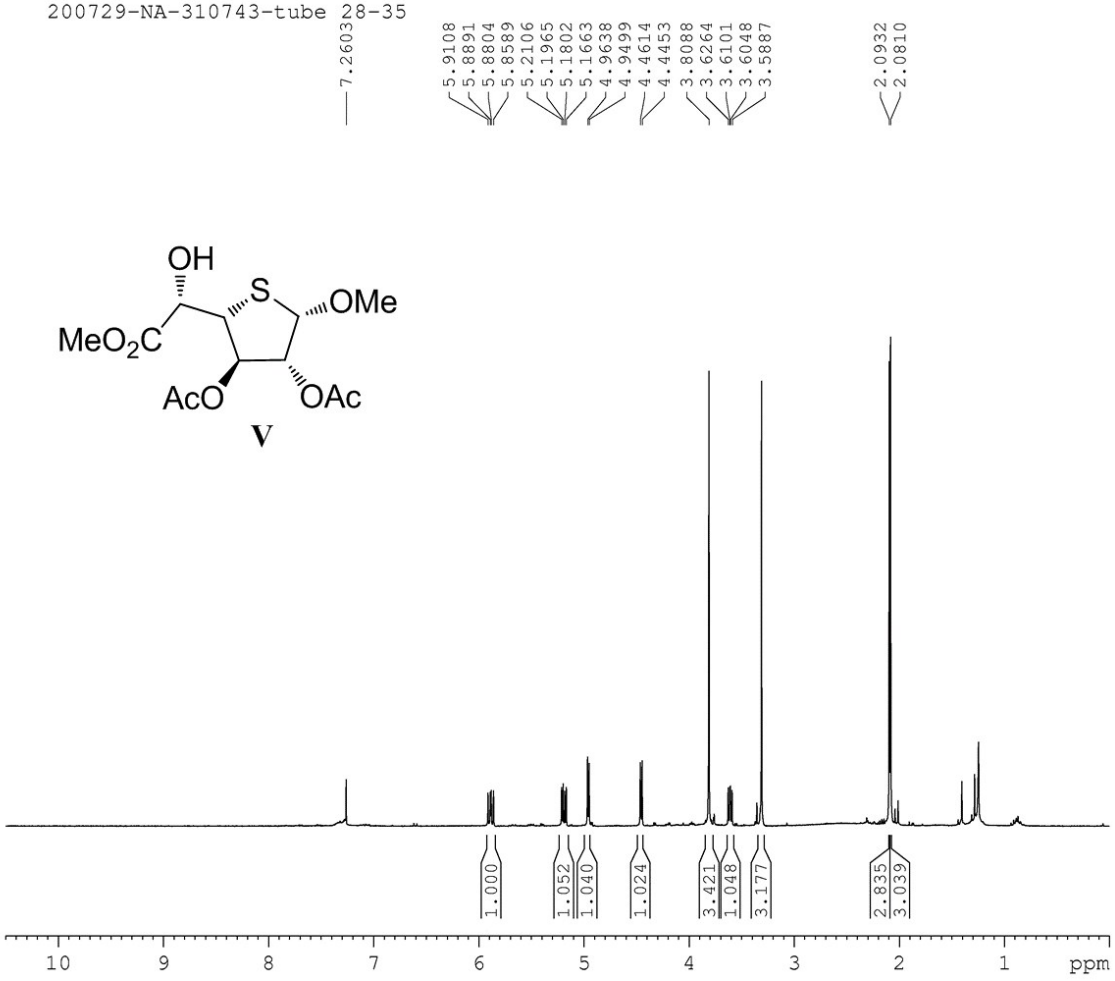
NOESY of 314495-tube 22



NOESY of 314495-tube 9

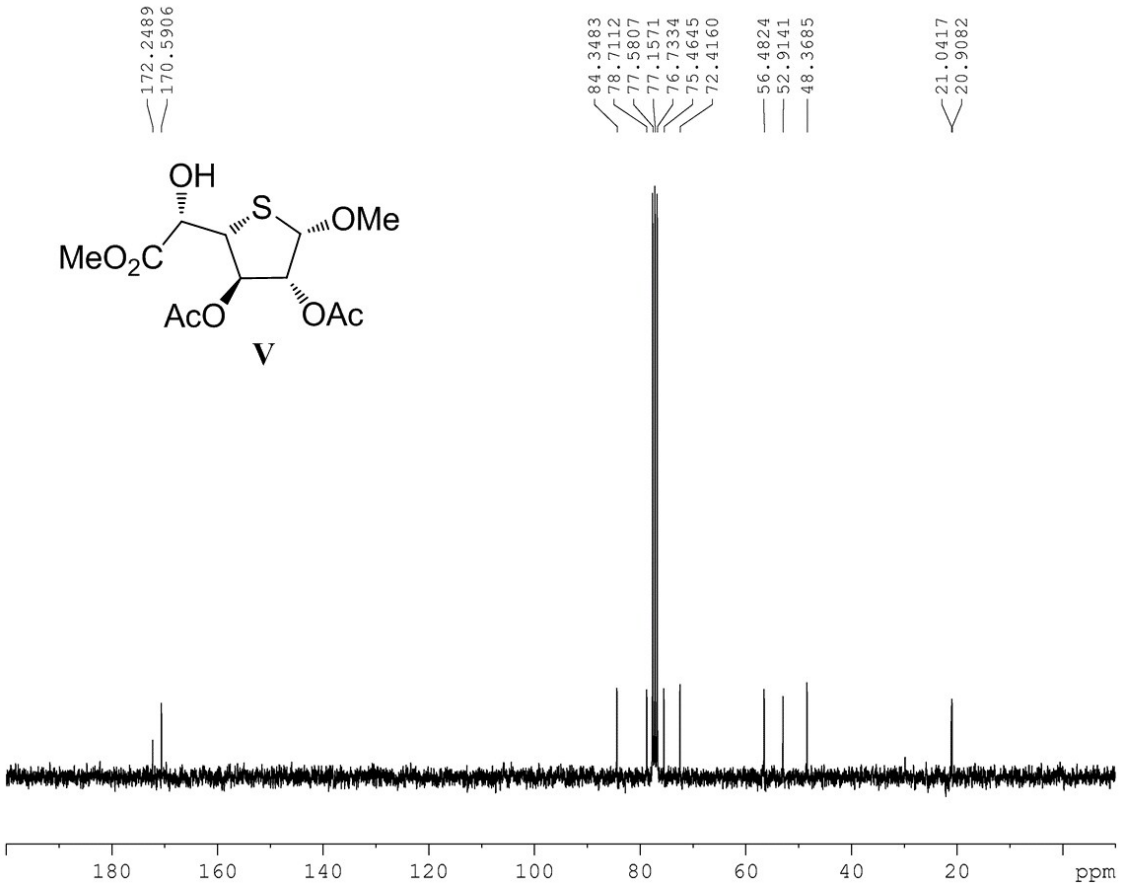


200729-NA-310743-tube 28-35

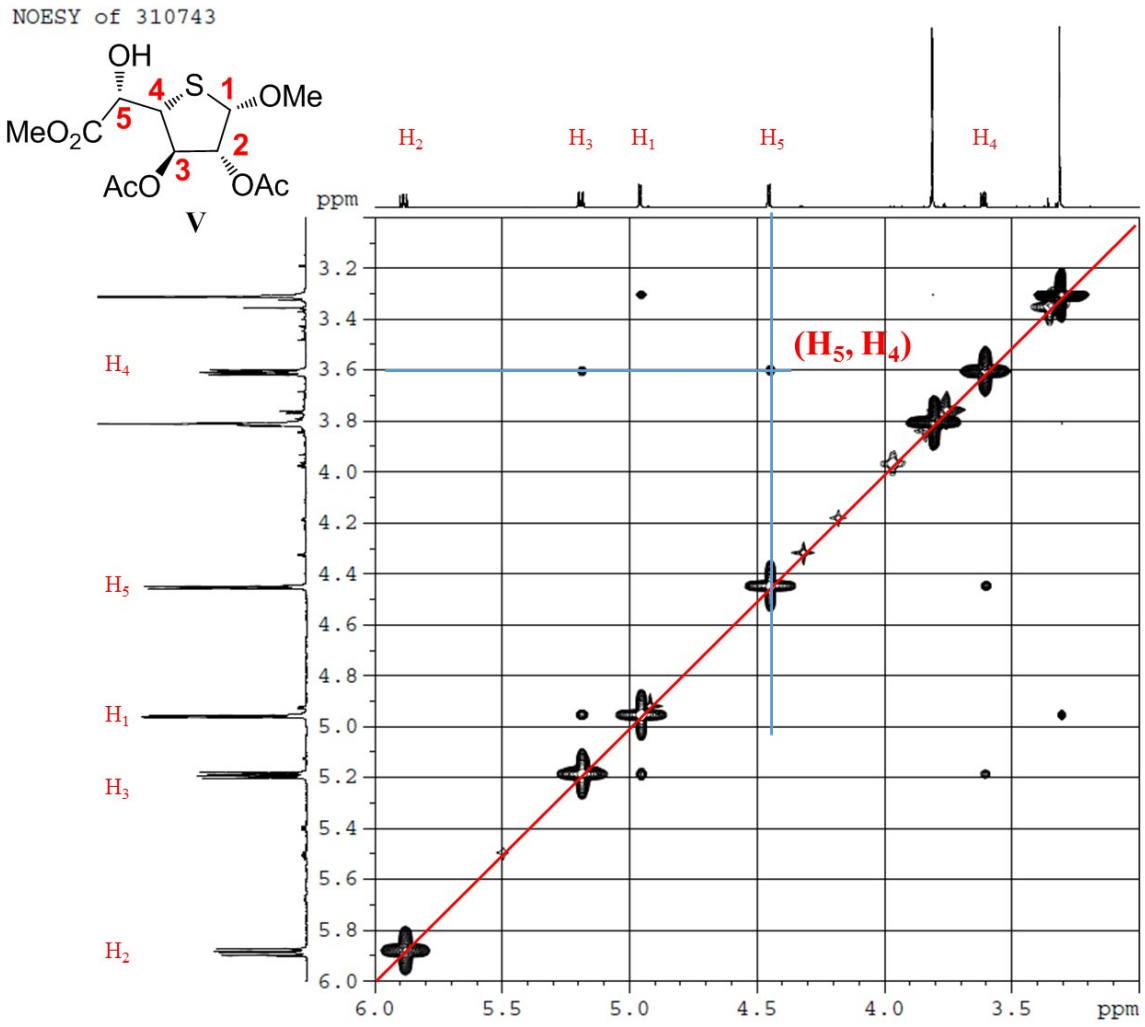


V

200729-NA-310743-tube 28-35 13C



V


NOESY of 310743
OH
4
S
1
OMe
MeO2C
5
2
AcO
3
OAc
V
H2
H3
H1
H5
H4
ppm
3.2
3.4
3.6
3.8
4.0
4.2
4.4
4.6
4.8
5.0
5.2
5.4
5.6
5.8
6.0
(H5, H4)
6.0
5.5
5.0
4.5
4.0
3.5
ppm