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S_N2-Type glycosylation with unprotected pyranoses

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Abstract

An S_N2 mechanism was proposed for highly stereoselective glycosylation of benzoic acid with unprotected α -D-glucose under Mitsunobu conditions in dioxane, while an S_N1 mechanism seems to be responsible for non-stereoselective glycosylation in DMF. The S_N2-type glycosylation can be applicable to various unprotected pyranoses as glycosyl donors and a wide range of carboxylic acids, phenols, and imides as glycosyl acceptors, retaining its high stereoselectivity (34 examples). Glycosylation of a carboxylic acid with unprotected α -D-mannose proceeded also in an S_N2 manner to directly afford a usually less accessible 1,2-*cis*-mannoside. An extremely short-step total synthesis of a middle molecule (1874 Da) natural glycoside with antitumor activity, coriariin A, was achieved via a double S_N2 glycosylation strategy with two molecules of unprotected α -D-glucose.

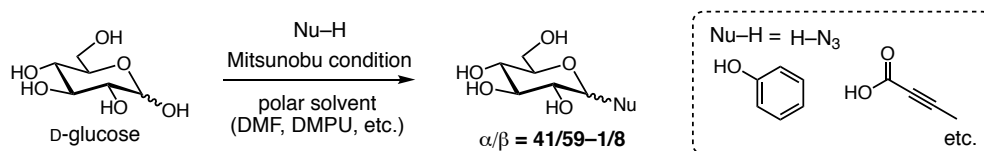
Main text

Since natural glycosides show a wide range of biological activities, much efforts have been

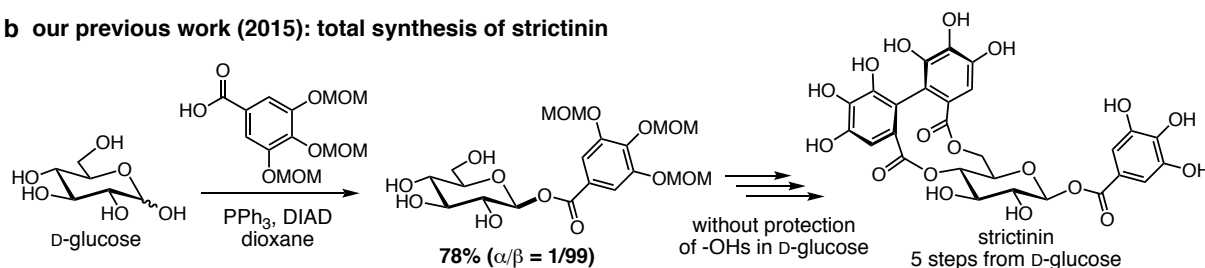
28 devoted to their synthesis toward the development of glycoside-based therapeutics.¹⁻⁹ For the
29 chemical synthesis of carbohydrates and glycosides, stereoselective glycosylation plays a
30 pivotal role.¹⁰⁻¹⁵ Properly protected saccharides with an activating group at the anomeric carbon
31 are generally employed as glycosyl donors to control the reacting site and stereochemistry of
32 the glycosylation.¹⁰⁻¹⁵ In contrast to the prevailing strategies, stereoselective chemical
33 glycosylation using unprotected saccharides as glycosyl donors remains a challenge, because
34 of the expected difficulties associated with chemoselective activation of the anomeric hydroxy
35 group and the stereocontrol of the glycosylation without neighboring group participation of the
36 protective group at the C(2)-OH. We recently developed highly β -selective glycosylation of a
37 gallic acid derivative using unprotected D-glucose as a glycosyl donor under Mitsunobu
38 conditions.¹⁶ Total synthesis of a natural antiviral glycoside, strictinin, was achieved in an
39 extremely short overall steps (5 steps)¹⁶ from D-glucose by virtue of the above-mentioned
40 glycosylation and organocatalytic site-selective introduction of galloyl groups^{17,18} (Figure 1b).
41 The advantage of the present glycosylation was obvious when the overall steps (5 steps) was
42 compared with those (11 and 13 steps)^{19,20} of the previously reported total synthesis of strictinin.
43 In order to clarify the origin of the high β -selectivity of the glycosylation, we investigated the
44 mechanism of the glycosylation using unprotected D-glucose. Here we report that the β -
45 selectivity of the present glycosylation in dioxane is resulting from the S_N2 -type displacement
46 of the commercially readily available α -D-glucose (Fig. 1c). On the other hand, glycosylation
47 in DMF was found to proceed via an S_N1 mechanism, responsible for the non-stereoselective
48 glycosylation. Therefore, the solvent was found to play a crucial role on the stereochemical
49 course of the glycosylation using unprotected D-glucose as a glycosyl donor. The observed non-
50 stereoselectivity in DMF was well consistent with the stereochemistry in the reported

51 pioneering examples of glycosylation reactions using unprotected monosaccharides under
 52 Mitsunobu conditions (Figure 1a).^{21–24} The present S_N2-type glycosylation was applicable to
 53 various unprotected saccharides including mannose to directly afford 1,2-*cis*-mannosides
 54 (Table 1, 2).^{25,26} One or two-step total syntheses of several simple natural glycosides were
 55 demonstrated by the present glycosylation strategy using unprotected pyranoses (Fig. 3). Total
 56 synthesis of coriariin A^{27,28} (Fig. 4) with a large molecular weight (1874 Da) and molecular size
 57 (~3 nm, Fig. S4) was also achieved by only eight steps from commercial unprotected D-glucose.
 58

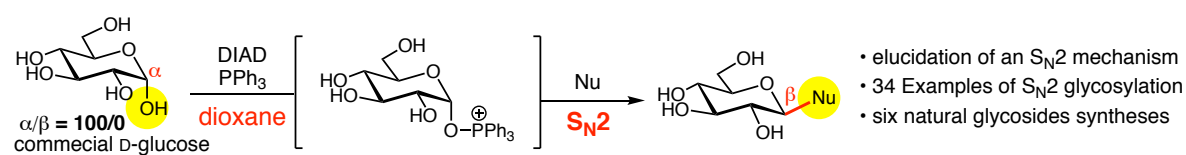
a pioneering examples of glycosylation using D-glucose as a glycosyl donor under Mitsunobu conditions



b our previous work (2015): total synthesis of strictinin



c this work

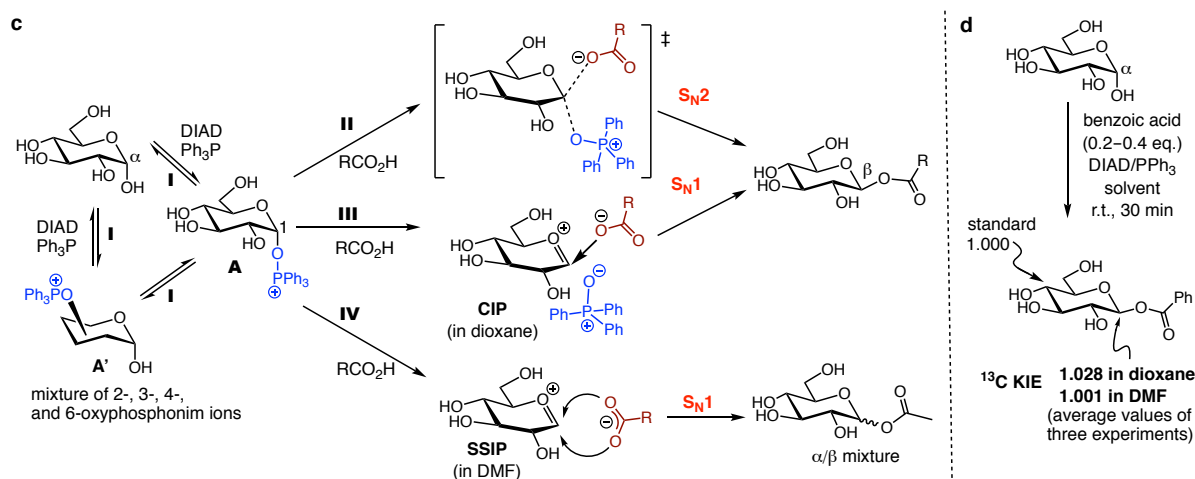
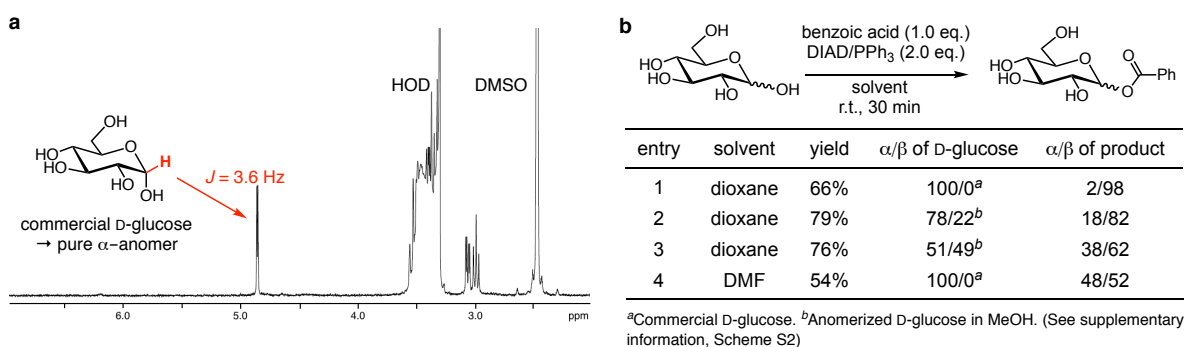


59
 60
 61 **Fig. 1 | Backgrounds and outlines.** **a**, Pioneering examples of glycosylation using D-glucose
 62 under Mitsunobu conditions (references 21–24). Merits of the method: direct use of unprotected
 63 D-glucose as a glycosyl donor. Demerit: formation of anomeric mixtures. **b**, Five-step total
 64 synthesis of strictinin from unprotected D-glucose via β -selective glycosylation and site-
 65 selective introduction of galloyl groups without employing protective groups for the glucose
 66 moiety (reference 16). **c**, This work: Elucidation of an S_N2 mechanism for the displacement of
 67 the anomeric hydroxy group of α -D-glucose (commercial D-glucose) in dioxane. 34 Examples
 68 of S_N2 glycosylation using commercial pyranoses as glycosyl donors. Total syntheses of six
 69 natural glycosides based on S_N2 glycosylation strategy with unprotected pyranoses. DMF =
 70 *N,N*-dimethylformamide; DMPU = *N,N'*-dimethylpropyleneurea; DIAD = diisopropyl
 71 azodicarboxylate; MOM = methoxymethyl.

72 **Results and discussion**

73 The first example of glycosylation using unprotected monosaccharides under Mitsunobu
74 conditions has been reported in 1979 by Gryniewicz²¹ (Figure 1a). Since then, the related
75 glycosylation reactions using unprotected saccharides as glycosyl donors under the Mitsunobu
76 conditions have been reported.²¹⁻²⁴ All of these glycosylation reactions, however, gave the
77 anomeric mixtures of glycosides ($\alpha/\beta=1/8$ ²¹, $1/3$ ²², $5/2$ ²³, $41/59$ ²⁴). In these examples, DMF and
78 the related polar solvents have been extensively employed, probably due to the expected
79 solubility of the unprotected saccharides. On the other hand, we found that the use of dioxane
80 was the key to the high β -selectivity of the glycosylation even though unprotected glucose
81 seemed to be hardly soluble in dioxane (Fig. 1b).¹⁶ During the course of the study on
82 glycosylation with unprotected glucose, we noticed that commercial D-glucose is supplied as a
83 pure or an almost pure α -anomer in most cases (Fig. 2a and Table S1).²⁹ Considering the
84 contrastive stereochemical results of the glycosylation depending on the solvent and the
85 stereochemistry of commercial D-glucose, we hypothesized that the observed β -selectivity in
86 the glycosylation reaction in dioxane might be the result from S_N2 displacement of an α -D-
87 glucose, while S_N1 displacement of D-glucose might be responsible for the poorly selective
88 glycosylation in DMF. We then reinvestigated the solvent effects of the glycosylation using
89 benzoic acid as a glycosyl acceptor (Table S2), and found that stereochemistry was highly
90 dependent on the solvent polarity. The glycosylation with α -D-glucose proceeds in high β -
91 selectivity in dioxane ($\alpha/\beta=1/99$), toluene ($\alpha/\beta=0/100$), and THF ($\alpha/\beta=2/98$), while it does in
92 non-stereoselective manner in DMF ($\alpha/\beta=48/52$). The observed stereochemistry and the
93 solvent-dependency seem consistent with the general aspects of Mitsunobu reaction that
94 strongly favors S_N2 displacement and phenomena that S_N2 reactions proceed more smoothly in

95 less polar solvents. To further test the S_N2 hypothesis, the glycosylation was examined with
 96 partially epimerized anomeric mixtures ($\alpha/\beta=78/22$ and $51/49$) of D-glucose (Scheme S2 and
 97 Fig. 2b). Glycosylation of benzoic acid using pure α -glucose in dioxane gave the β -glycoside
 98 in a ratio of $\alpha/\beta=2/98$ (Fig. 2b, entry 1). A decrease in the α -anomer contents in D-glucose
 99 resulted in a decrease in the β -isomer ratio of the glycoside (entries 2 and 3). These results
 100 suggest that the β -glycoside was generated selectively from α -D-glucose via formal inversion
 101 at the anomeric stereogenic center. In contrast, the reaction of pure α -D-glucose with benzoic
 102 acid in DMF gave the glycoside as an α/β mixture (entry 4, $\alpha/\beta=48/52$). The observed α/β ratios
 103 were assumed to be resulting solely from the glycosylation step because no epimerization of
 104 glucose itself took place in DMF or dioxane under the reaction conditions.³⁰



108

109 **Figure 2 Mechanistic investigation of β -selective glycosylation using D-glucose.** **a**, ^1H NMR
110 of commercial α -D-glucose (400 MHz, 298 K, $\text{DMSO-}d_6+\text{D}_2\text{O}$). **b**, Effects of the α/β ratio of
111 D-glucose on stereochemistry of glycosylation. **c**, Possible reaction paths. Path **I**: Generation
112 and interconversion of regioisomeric oxyphosphonium ions **A** and **A'** under equilibrium
113 conditions. Path **II**: $\text{S}_{\text{N}}2$ -type displacement of oxyphosphonium ion **A** to afford the β -anomer.
114 Path **III**: $\text{S}_{\text{N}}1$ -type displacement of oxyphosphonium ion **A** via contact ion pair (CIP) to afford
115 the β -anomer. Path **IV**: $\text{S}_{\text{N}}1$ -type displacement of oxyphosphonium ion **A** via solvent separated
116 ion pair (SSIP) to afford the anomeric mixture. **d**, ^{13}C -Kinetic isotope effects of the
117 glycosylation reaction. DMSO = dimethylsulfoxide.

118

119 Possible reaction paths for β -selective glycosylation in dioxane and non-stereoselective
120 glycosylation in DMF are shown in Fig. 2c. The regioisomeric mixture of oxyphosphonium
121 ions **A** and **A'** are assumed to be generated from α -D-glucose in non-regioselective manner
122 under equilibrium conditions (path **I**). Oxyphosphonium ion **A** generated at the anomeric
123 position is expected to be the most reactive among the oxyphosphonium ions, and it would
124 preferentially react with a benzoate anion under Curtin-Hammett situations. The β -selective
125 glycosylation is assumed to take place via an $\text{S}_{\text{N}}2$ displacement of the oxyphosphonium ion **A**
126 with α -configuration by the benzoate anion (path **II**). Alternatively, the β -selectivity could be
127 explained by an $\text{S}_{\text{N}}1$ -type displacement via a contact ion pair (CIP)-like intermediate
128 preferentially formed in a less polar solvent, 1,4-dioxane, where the α -face of the oxonium
129 cation is shielded by the oxyphosphonium zwitter ion (path **III**). On the other hand, non-
130 stereoselective glycosylation in DMF could be explained by the intervention of a solvent
131 separated ion pair (SSIP) (path **IV**). To elucidate the probability of the proposed mechanisms,
132 the ^{13}C kinetic isotope effect (KIE)³¹ of the present glycosylation reactions was measured (Fig.
133 2d). The ^{13}C KIE experiments were performed using α -D-glucose with natural ^{13}C abundance
134 by the Singleton method^{32,33} [200 MHz for ^{13}C measurement (800 MHz NMR instrument) with
135 cryogenic probe, S/N ratio=1860–2660, see Figure S3]. Reproducible KIEs were obtained in

136 the range between 1.026 and 1.033 for the reactions in dioxane (see, Table S3). Based on these
137 data, the KIE at C(1) in dioxane was determined to be 1.028 (an average value of three
138 experiments). The primary ^{13}C KIE at the anomeric carbon of glycosyl donors has been
139 extensively studied in both chemical and enzymatic glycosylation reactions.^{34–37} It has been
140 claimed that smaller (≤ 1.01) and larger (1.02–1.06) KIEs are responsible for $\text{S}_{\text{N}}1$ and $\text{S}_{\text{N}}2$
141 displacement, respectively.³⁵ Taking both the observed and the reported KIE data into
142 considerations, we concluded that the present glycosylation reactions take place via an $\text{S}_{\text{N}}2$
143 mechanism in dioxane (Fig. 2c, path **II**), while it does via an $\text{S}_{\text{N}}1$ mechanism in DMF (Fig. 2c,
144 path **IV**) based on the observed ^{13}C KIE (1.001) (Fig. 2d).

145 We next examined the scope of the $\text{S}_{\text{N}}2$ -type glycosylation of 2,6-dimethylbenzoic acid
146 with various unprotected pyranoses (Table 1). Glycosylation of 2,6-dimethylbenzoic acid with
147 α -D-glucose (**1a**, $\alpha/\beta=100/0$) under Mitsunobu conditions in dioxane gave β -glycoside **2a**
148 ($\alpha/\beta=1/99$, 92%) (entry 1). On the other hand, the same treatment of β -D-glucose (**1b**, $\alpha/\beta=4/96$)
149 gave α -glycoside **2b** ($\alpha/\beta=89/11$, 94% yield) (entry 2). These results are well compatible with
150 the $\text{S}_{\text{N}}2$ process. Similarly, α -D-galactose (**1c**, $\alpha/\beta=96/4$) and α -D-xylose (**1d**, $\alpha/\beta=100/0$) gave
151 β -glycosides **2c** ($\alpha/\beta=2/98$, 58%) and **2d** ($\alpha/\beta=4/96$, 52%), respectively, by the treatment with
152 2,6-dimethylbenzoic under Mitsunobu conditions (entries 3,4). Glycosylation with β -D-
153 arabinose (**1e**, $\alpha/\beta=4/96$) also gave α -glycoside **2e** ($\alpha/\beta=95/5$, 87%) (entry 5). Stereo-inversion
154 at the anomeric carbon was observed in each case. It is worthy to note that glycosylation even
155 with α -D-mannose (**1f**, $\alpha/\beta=100/0$) proceeded with inversion of stereochemistry at the anomeric
156 carbon to give β -glycoside **2f** ($\alpha/\beta=13/87$, 66%) (entry 6). The 1,2-*cis*-configuration of **2f** was
157 determined by single crystal X-ray analysis. Thus, glycosylation with unprotected D-mannose
158 possessing β -axial C(2)-OH took place in a usually unfavorable β -selective manner to directly

159 afford 1,2-*cis*-mannoside.^{25,26} All of these observed phenomena are consistent with the
 160 proposed S_N2-type glycosylation.

161

162

Table 1. Scope of glycosyl donors in S_N2-type glycosylation

commercial pyranoses **1** (3.0 eq.) + ArCOOH $\xrightarrow[\text{dioxane, r.t., 30 min}]{\text{DIAD (2.0 eq.), Ph}_3\text{P (2.0 eq.)}}$ **2**

entry	substrate	product	yield (α/β ratio)
1	<p>α-D-Glc (1a) $\alpha/\beta = 100/0$</p>	<p>2a</p>	92% ($\alpha/\beta = 1/99$)
2	<p>β-D-Glc (1b) $\alpha/\beta = 4/96$</p>	<p>2b</p>	94% ($\alpha/\beta = 89/11$)
3 ^a	<p>D-Gal (1c) $\alpha/\beta = 96/4$</p>	<p>2c</p>	58% ($\alpha/\beta = 2/98$) ^b
4	<p>D-Xyl (1d) $\alpha/\beta = 100/0$</p>	<p>2d</p>	52% ($\alpha/\beta = 4/96$)
5	<p>D-Ara (1e) $\alpha/\beta = 4/96$</p>	<p>2e</p>	87% ($\alpha/\beta = 95/5$)
6 ^a	<p>D-Man (1f) $\alpha/\beta = 100/0$</p>	<p>2f</p>	66% ($\alpha/\beta = 13/87$)

^aDIAD/Ph₃P (4.0 equiv.), 1,4-dioxane, r.t. ^bThe observed β -selectivity was higher than the original α -content. This seems to be due to the faster reaction of the α -anomer of **1c**.

163

164

165 The scope of glycosyl acceptors in the present glycosylation with α -D-glucose was shown
166 in Table 2. Aliphatic carboxylic acids and aromatic carboxylic acids with various functional
167 groups were well tolerated in the glycosylation reactions to give the corresponding glycosides
168 in a highly β -selective manner (Table 2, glycosides **4a-4p**). Glycosylation of acids with an α -
169 chiral center took place without any trace of epimerization of the chiral center (glycoside **4d**).
170 Because β -glycosylation is one of the metabolic pathways of medicines,³⁸ formation of the
171 drug-glucose conjugate was also examined. Oxaprozin (nonsteroidal anti-inflammatory),
172 naproxen (nonsteroidal anti-inflammatory), gemfibrozil (anti-hypertensive), chlorambucil
173 (anti-cancer), and probenecid (treatment of hyperuricemia) successfully gave the corresponding
174 β -glycosides under the standard conditions (**4l-4p**). Phenol derivatives and imides also
175 underwent glycosylation in moderate to good yields (**4q-4u**).

176 One-step syntheses of natural glycosides with simple structure was performed (Fig. 3).
177 Natural glycosides such as thotneoside C (**5**),³⁹ tecomin (**6**)⁴⁰ (gram-scale synthesis), perilloside
178 B (**7**)⁴¹, and skimmin (**9**)⁴² were obtained from α -D-glucose and commercially available
179 reagents in one-step under Mitsunobu conditions. β -Glucogallin (**8**)⁴³ was prepared in 67%
180 yield in two steps from α -D-glucose.

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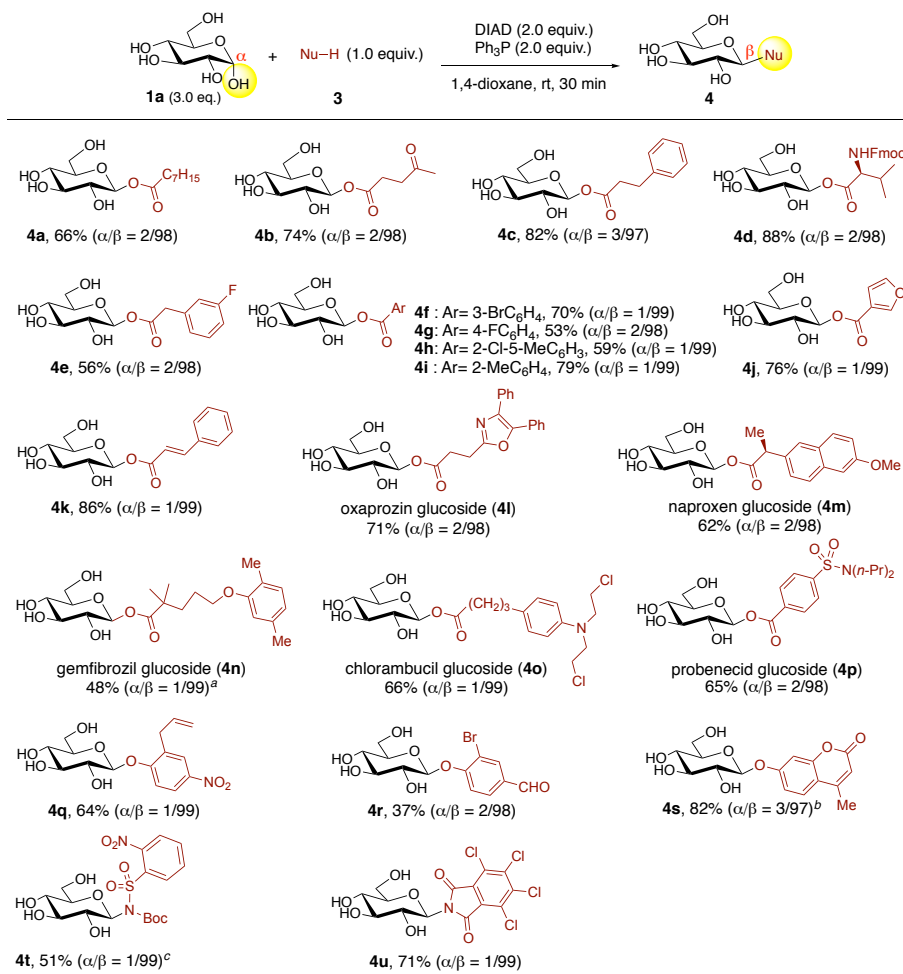
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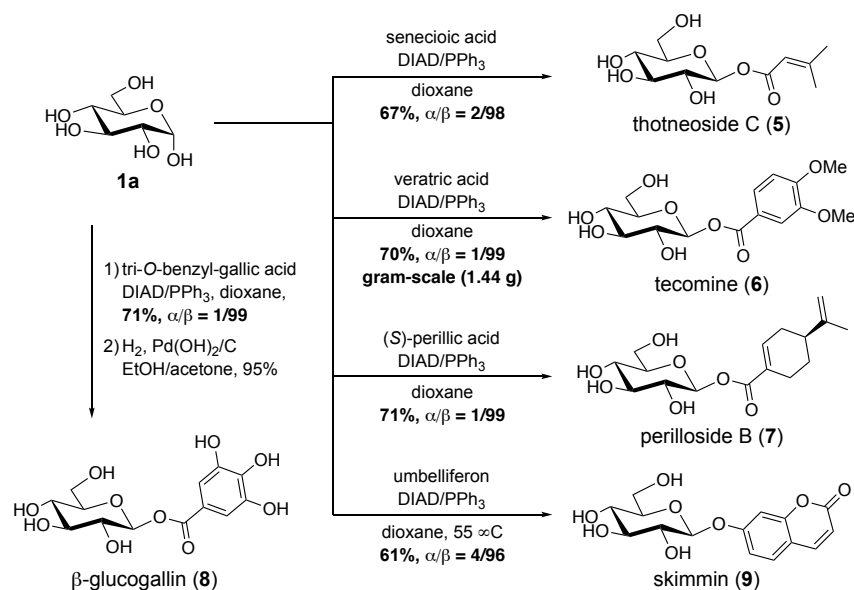
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Table 2. Scope of glycosyl acceptors for the S_N2-type glycosylation

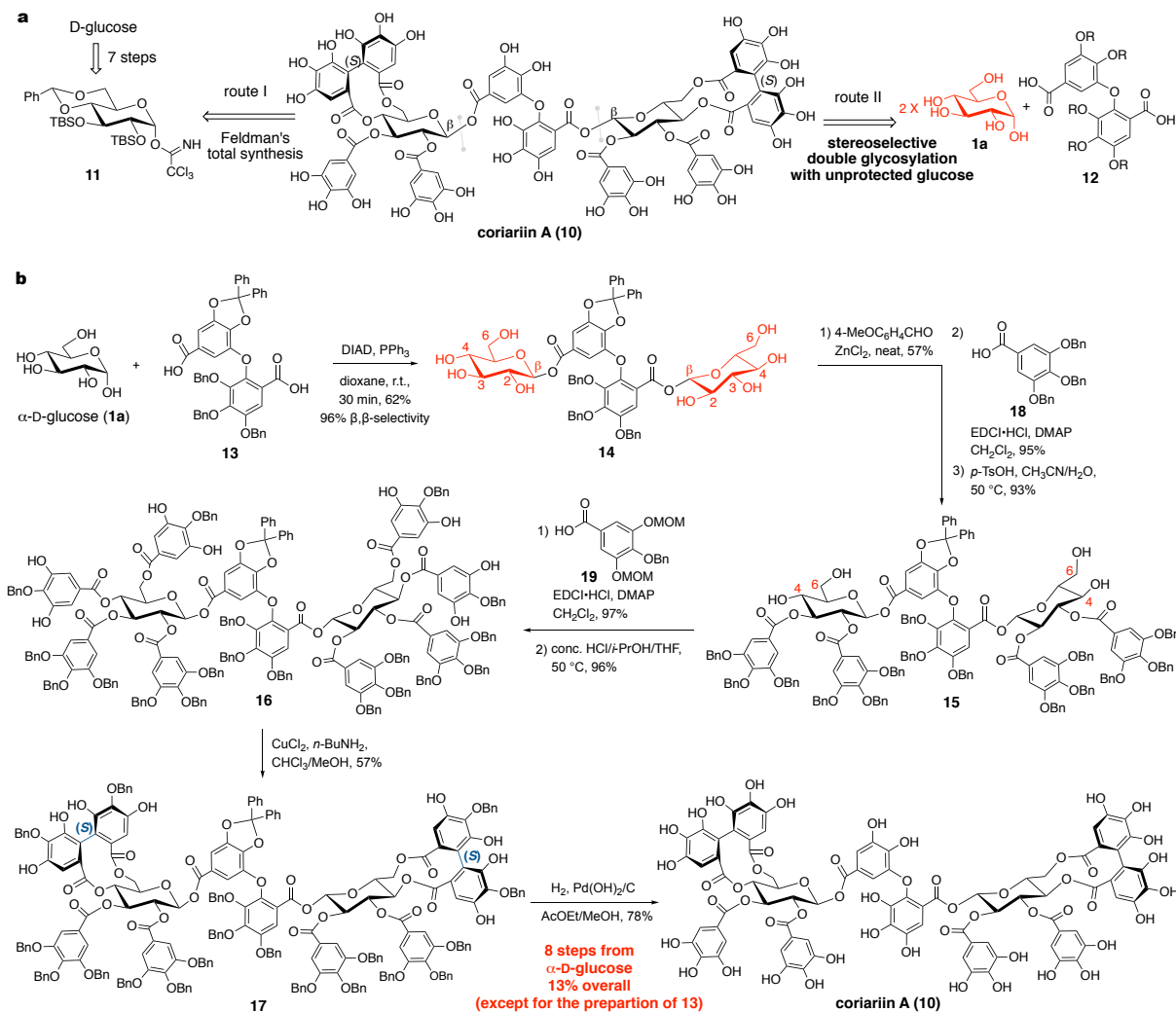
^aDIAD/Ph₃P (3.0 equiv.), 1,4-dioxane, rt. ^bDIAD/Ph₃P (4.0 equiv.), 55 °C. ^cDIAD/Ph₃P (4.0 equiv.), rt.

**Fig. 3 | One- or two-step syntheses of natural glycosides.**

193 This method was applied to a short-step total synthesis of coriariin A (**10**)^{27,28} (Fig. 4).
194 Outlines of the synthetic scheme are shown Fig. 4a. The pioneering first total synthesis of **10**
195 was achieved by Feldman in 15 overall steps, in which 7 steps were devoted to the preparation
196 of properly protected and activated glycosyl donor **11**⁴⁴(Fig. 4a, route I). We envisaged that
197 total synthesis of **10** would be achievable in much shorter overall steps if unprotected glucose
198 can be used for the glycosylation step. Our strategy is shown in route II of Fig. 4a, in which
199 double glycosylation of dicarboxylic acid **12** with two molecules of unprotected α -D-glucose
200 (**1a**) is a key step. Actual synthesis commenced with bis-gallic acid ether **13** prepared according
201 to the reported procedure.⁴⁵ Treatment of a suspension of **13** and α -D-glucose in 1,4-dioxane
202 with DIAD/Ph₃P gave β,β -diglycoside **14** in 62% yield and 96% stereoselectivity. After
203 purification, the pure β,β -diglycoside **14** was converted to **15** via 3 step sequences consisting
204 of protection of the C(4)-OH and C(6)-OH of the glucose moiety, esterification of the remaining
205 C(2)-OH and C(3)-OH with **18**, and removal of the 4,6-*O*-benzylidene acetal. Esterification of
206 the resulting C(4)-OH and C(6)-OH of **15** with **19** followed by removal of the MOM groups
207 gave octa-gallate **16** in 93% yield. Intramolecular double oxidative coupling between the
208 phenolic moieties of **16** with CuCl₂/*n*-BuNH₂ (Yamada's protocol)²⁰ proceeded to give **17**
209 possessing complete skeleton required for the synthesis of **10** in 57% yield. Chirality of two
210 newly formed chiral axes of the hexahydroxydiphenoyl moieties in **17** was totally controlled
211 by virtue of the Yamada's protocol. Removal of benzyl groups and a diphenylene acetal group
212 in **17** yielded coriariin A (**10**) in 78% yield. Thus, an extremely short-step total synthesis of an
213 antitumor natural glycoside, coriariin A, was accomplished. Only eight steps were required for
214 the synthesis of the middle molecule from naturally abundant α -D-glucose in 13% overall yield,
215 except for the steps for the preparation of dicarboxylic acid **13**. Separately, five steps were

216 required to prepare **13** from commercially available gallic acid (see SI, S24-25).

217



218

219 **Fig. 4 | Total synthesis of coriariin A.** **a**, Retrosynthetic analysis: route I; Feldman's total
220 synthesis. route II; our strategy. **b**, Total synthesis of coriariin A via eight-steps from α -D-
221 glucose, except for the preparation of **13**. Dicarboxylic acid **13** was separately prepared from
222 commercial gallic acid in five steps. TBS = *t*-butyldimethylsilyl; Bn = benzyl; EDCI·HCl = 1-
223 ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride; DMAP = *N,N*-demethyl-4-
224 aminopyridine; *p*-TsOH = *p*-toluenesulfonic acid.

225

226

227 Conclusion

228 We have developed S_N2-type stereoselective glycosylation using commercial unprotected
229 pyranoses as glycosyl donors. Glycosylation of a variety of carboxylic acids, phenols, and

230 imides under Mitsunobu conditions proceeded stereoselectively in dioxane via direct S_N2-type
231 displacement at the anomeric carbon. Mechanistic investigation clarified that glycosylation of
232 benzoic acid with α -D-glucose underwent via direct S_N2 mechanism in dioxane, while it does
233 in a non-stereoselective manner in DMF via an S_N1 mechanism. This protocol was applied to a
234 short-step total synthesis of coriariin A from naturally abundant glucose. The direct
235 glycosylation method using unprotected sugars is expected to be applicable to
236 glycodiversification of medicinally important molecules.^{46,47}

237

238 **Method**

239 **The representative procedure for the S_N2-type glycosylation (Table 1, entry 1).** Commercial
240 D-glucose was grinded with a mortar in open-air for 5 min. A round-bottom flask was charged
241 with the powdered α -D-glucose (200 mg, 1.11 mmol, 3.0 equiv.) and dehydrated 1,4-dioxane
242 (37 mL) under an Ar atmosphere. After ultrasound irradiation of the suspension of α -D-glucose
243 in 1,4-dioxane for 15 min, 2,6-dimethylbenzoic acid (55.6 mg, 0.37 mmol, 1.0 equiv.) and Ph₃P
244 (194 mg, 0.74 mmol, 2.0 equiv.) were added. DIAD (146 μ L, 0.74 mmol, 2.0 equiv.) was added
245 to the solution dropwise by a syringe and the resulting mixture was stirred vigorously at room
246 temperature for 30 min. The reaction mixture was quenched with MeOH, stirred for 5 min, and
247 concentrated *in vacuo* at 40 °C to give a residue. The residue was directly purified by flash
248 column chromatography (SiO₂, CHCl₃/MeOH 50:1 to 5:1 v/v) to give glucoside **2a** (106 mg,
249 92%, $\alpha/\beta=1/99$) as a white amorphous powder.

250

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369

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379

380 **Author contributions**

381 H.T. and Y.F. made equal contributions to this work. H.T., Y.F., H.S., M.N. and Y.U. carried out
382 experiments under the supervision of T.K., aided by Y.U., T.Y., and T.F. X-ray crystallography
383 of **2f** was carried out by T.S. and N.T. H.T. and T.K. conceived and designed the project. The
384 manuscript was written by H.T., Y.U. and T.K.

385

386 **Competing financial interests**

387 The authors declare no competing financial interests.

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S_N2-Type Glycosylation using Unprotected Pyranoses

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I. GENERAL EXPERIMENTAL CONSIDERATIONS

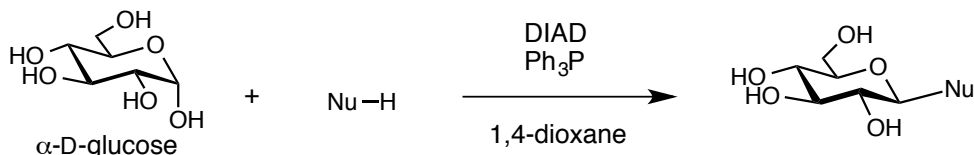
All reactions were carried out in an argon atmosphere under anhydrous conditions, and were stirred with Teflon-coated magnetic stir bars. Anhydrous acetonitrile (CH₃CN), 1,4-dioxane, tetrahydrofuran (THF), *N,N*-dimethylformamide (DMF), methanol (MeOH), chloroform (CHCl₃), dichloromethane (CH₂Cl₂), isopropanol (*i*-PrOH) were purchased from commercial suppliers and stored over activated molecular sieves. All other solvents were used as received unless otherwise noted. Yields were referred to isolated yield of analytically pure material unless otherwise noted. Reactions were magnetically stirred and monitored by thin-layer chromatography (TLC) using Silica gel 60 F254 precoated plates (0.25 mm, Merk). Visualization was accomplished with UV light and *p*-anisaldehyde stain followed by heating. Purification of the reaction products was carried out by flash column chromatography using Ultra Pure Silica Gel (230–400 mesh) purchased from SILYCYCLE, unless otherwise noted. Infrared (IR) spectra were recorded using a JASCO FT-IR 4200 spectrometer and are reported in reciprocal centimeters (cm⁻¹). ¹H NMR spectra were recorded on JEOL ECX-400 (400 MHz), JEOL ECA-600 (600 MHz), Bruker Avance 800 (800 MHz), and are reported in ppm using solvent resonance as the internal standard (acetone-*d*₆ at 2.05 ppm, CDCl₃ at 7.26 ppm, CD₃CN at 1.94 ppm, DMSO-*d*₆ at 2.49 ppm, MeOH-*d*₄ at 3.31 ppm). ¹H NMR data are reported as follows: chemical shift; multiplicity; coupling constants (Hz); number of hydrogen. Multiplicity is abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, dd = double doublet, ddt = double double triplet, m = multiplet, br = broad. Proton-decoupled ¹³C NMR spectra were recorded on ECX-400 (100 MHz), ECA-600 (150 MHz), Bruker Avance 800 (200 MHz), and are reported in ppm using solvent resonance as the internal standard (acetone-*d*₆ at 29.84 ppm, CDCl₃ at 77.16 ppm, CD₃CN at 118.26 ppm, DMSO-*d*₆ at 39.52 ppm, MeOH-*d*₄ at 49.00 ppm). High-resolution mass spectra (HRMS) were obtained using JEOL-DX 700 mass spectrometer for FAB and Impact HD (Bruker Daltonics) for ESI. Specific rotations were measured with JASCO P-2200 digital polarimeter using the sodium D line and are reported as follows: [α]_D^t (c = 10 mg/mL, solvent). Melting points were measured with Micro Melting Point Apparatus PM-500 (Yanagimoto) and are reported in degree Celsius (°C).

II. REAGENTS

α-D-Glucose was purchased from Becton Dickinson Inc. or Nacalai tesque Inc. and used after grinding (see: Preparation and properties of powdered D-glucose in Figure S1). β-D-Glucose, D-xylose, and D-mannose were purchased from TCI and used after grinding. D-Galactose was purchased from Kanto Chemical Co. Inc. and used after grinding. 3,4,5-Tris(benzyloxy)benzoic acid,¹ 2-allyl-4-nitrophenol,² 3-bromo-4-hydroxybenzaldehyde,³ and NsNHBoc⁴ were prepared according to literature procedures. Dicarboxylic acid **13** was prepared using the literature procedure⁵ (see: Access to aglycone **13**). Cu was activated using I₂ and conc. HCl aq. prior to use.⁶ *n*-Butylamine was distilled from CaH₂ prior to use. All other reagents were purchased from commercial sources and used without further purification.

III. EXPERIMENTAL PROCEDURES AND CHARACTERIZATION DATA

General procedures for β -selective glycosylation (Scheme S1)



General procedure A

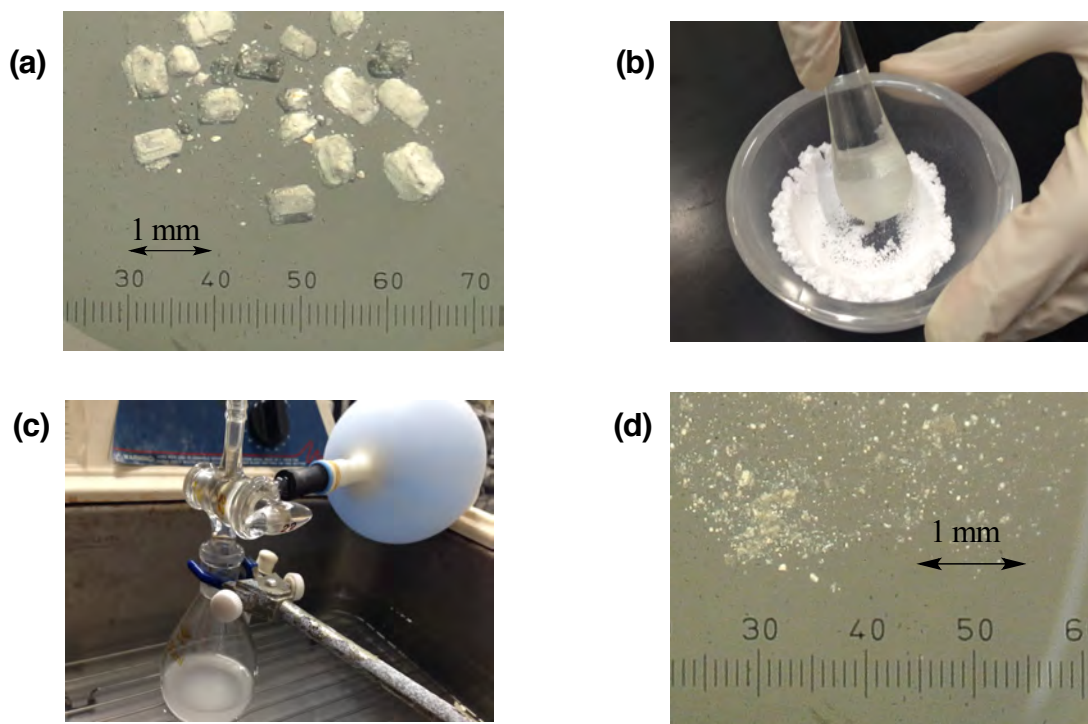
A round-bottom flask was charged with powdered α -D-glucose (3.0 equiv.) and dehydrated 1,4-dioxane (0.03 M of α -D-glucose) under an Ar atmosphere (Note 1). After ultrasound irradiation of the suspension of α -D-glucose in 1,4-dioxane for 15 min, glycosyl acceptor (NuH) (1.0 equiv.) and Ph_3P (2.0 equiv.) were added. DIAD (2.0 equiv.) was added dropwise by syringe and the resulting mixture was stirred vigorously at rt for 30 min (Note 2). The reaction mixture was quenched with MeOH, stirred for 5 min, and concentrated in vacuo at 40 °C to give a residue. The residue was directly purified by flash column chromatography (SiO_2 , $\text{CHCl}_3/\text{MeOH}$ 50:1 to 5:1 v/v) to give the corresponding β -glycoside (Note 3).

Notes

1. Reagent-grade D-glucose from Becton Dickinson Inc. was used after grinding procedures (See S-4).
2. DIAD should be added dropwise by syringe (ca. 1 drop / 3 sec) after the orange color of each DIAD drop disappeared in the reaction mixture to avoid possible side reactions.
3. The product is a highly polar compound so that the extraction procedures should be avoided to prevent product loss.

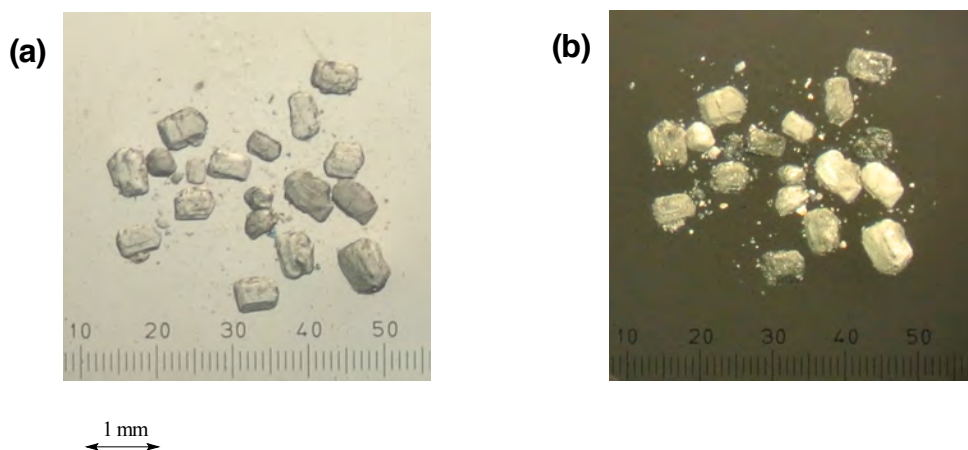
Preparation and properties of powdered D-glucose (Figure S1)

(a) Particle sizes of commercial D-glucose from Becton Dickinson Inc. (Difco™ Dextrose) were around 1 mm. (b) About 5 g of commercial D-glucose was grinded with an 8 cm-diameter mortar in open-air for 5 min. (c) A suspension of the powdered glucose in 1,4-dioxane was irradiated with ultrasound by an ordinary laboratory cleaner for 10 min prior to the reaction. (d) Powders of grinded glucose was not uniform, whose particle sizes were <0.1 mm.



Polarization microscope image of commercial D-glucose (Figure S2)

We noticed that D-glucose we used was identified as single crystals by polarization microscope (OLYMPUS SZ60 microscope with the polarizer SZ-PO) as shown below, while we measured the particle size of commercial D-glucose. Interestingly, this single crystal consisted of α -anomer of D-glucose. (See S-5) (a) Microscope image of D-glucose. (b) Polarization microscope image of D-glucose.



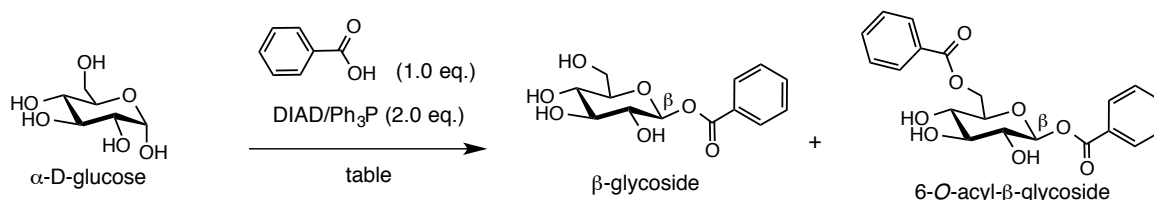
Anomeric ratios of several commercially available D-glucose (Table S1)

The anomeric ratio of D-glucose was determined by ¹H-NMR in DMSO-*d*₆ (ca. 0.6 mL) + 2 drops of D₂O at 293 K immediately after D-glucose was dissolved. While D-glucose epimerizes easily in protic polar solvent, the epimerization of anomeric hydroxyl group of D-glucose in aprotic solvent is known to be slow.⁷

Reagent	Supplier	Cat. No.	α/β ratio
Difco™ Dextrose	Becton Dickinson	215530	α/β = 100/0
D-(+)-Glucose, Anhydrous	Nacalai tesque	168-06	α/β = 100/0
D-(+)-Glucose	KANTO CHEMICAL	10017-30	α/β = 99/1
D-(+)-Glucose, ACS reagent	SIGMA-ALDRICH	G5767-25G	α/β = 96/4

Optimization of the reaction conditions for β-selective glycosylation using α-D-glucose (Table S2)

Procedure: A round-bottom flask was charged with α-D-glucose and solvent (0.03 M of α-D-glucose). Benzoic acid (1.0 equiv.) and Ph₃P (2.0 equiv.) were added. DIAD (2.0 equiv.) was slowly added by syringe causing the orange color to immediately disappear in every drops and the resulting mixture was stirred vigorously. The reaction mixture was quenched with MeOH. Major byproducts in this glycosylation reaction were 6-*O*-acyl-β-D-glucoside and benzoic anhydride.

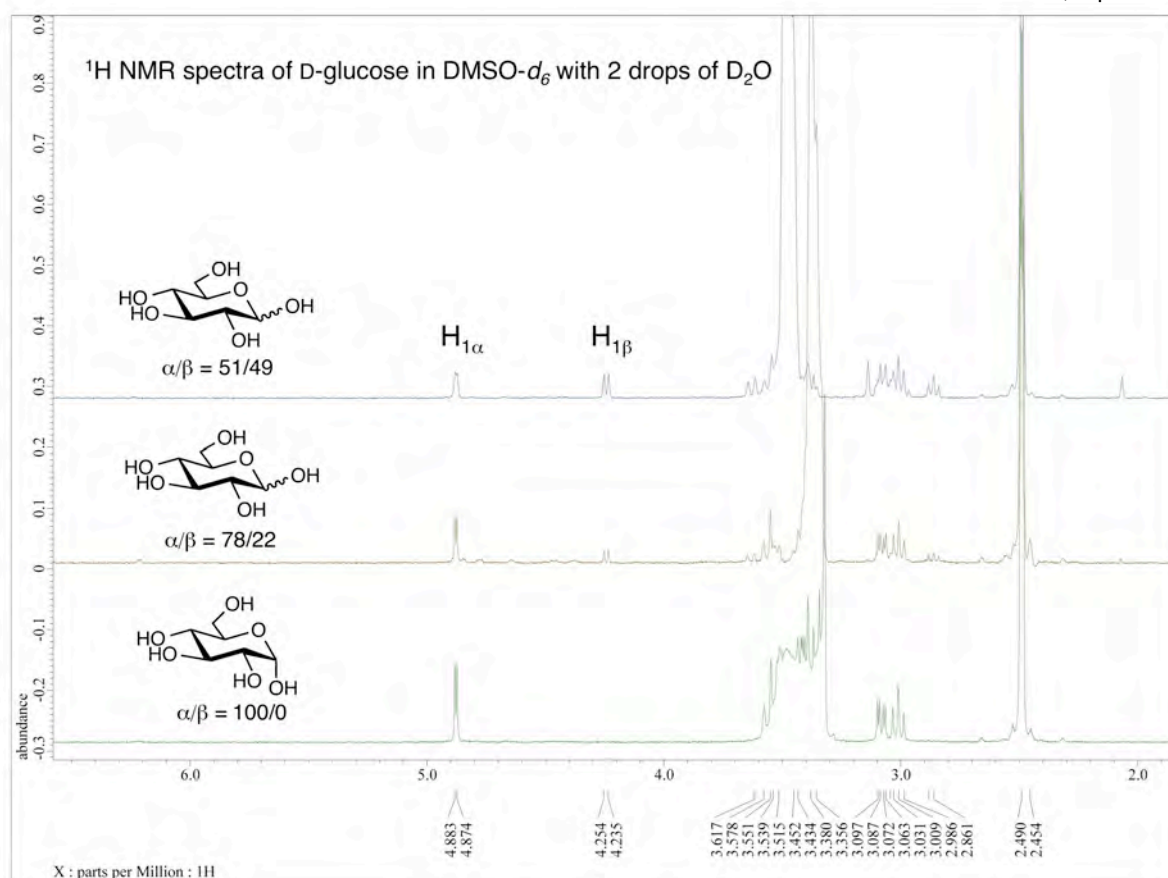
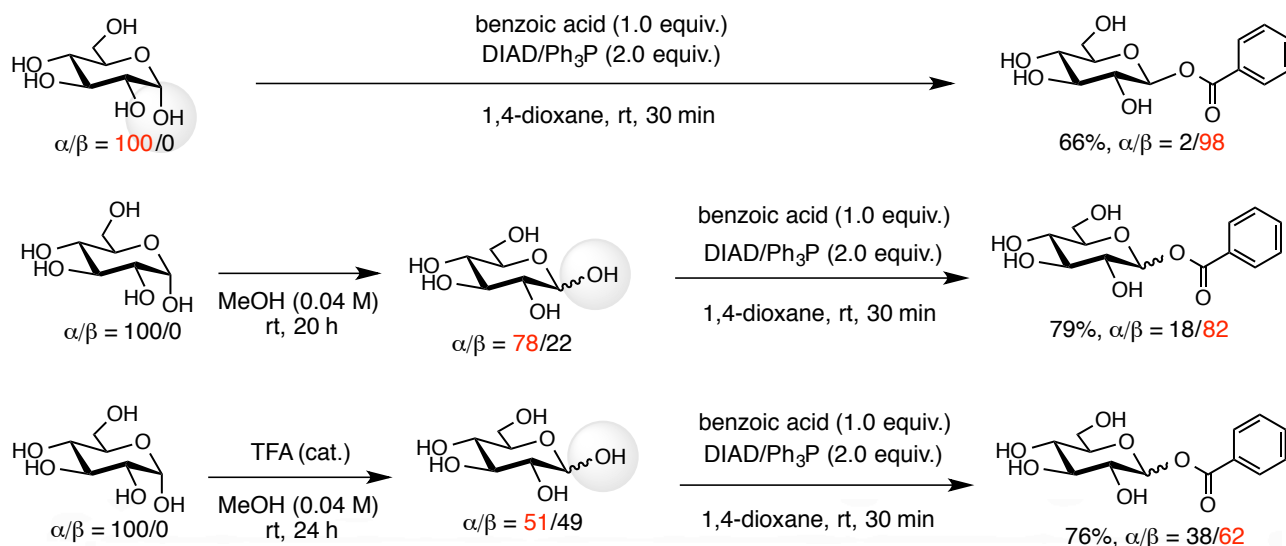


entry	solvent	E _T ^N ^a	time (min)	Glc (eq.)	β-glycoside (%) ^b	α/β ^b	6- <i>O</i> -acyl-β-glycoside (%) ^b
1	DMF	0.386	30	1.0	54	48/51	–
2	THF	0.207	30	1.0 (grinded)	11	2/98	24 (β only)
3	toluene	0.099	30	1.0 (grinded)	–	–	3 (β only)
4	1,4-dioxane	0.164	10	1.0 (grinded)	51	1/99	7 (β only)
5	1,4-dioxane	0.164	10	3.0 (grinded)	66 ^c	2/98	–

^anormalized polarity parameter. ^bNMR yield using 1,3-dinitrobenzene as an internal standard. ^cisolated yield

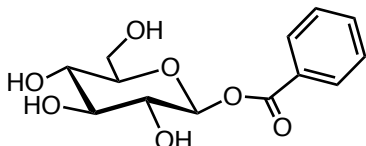
Mechanistic insights using epimerized D-glucose (Scheme S2)

A solution of α -D-glucose in MeOH (with catalytic amount of TFA) was stirred at rt for 20–24 h and concentrated in vacuo to give a white powder. The powder was dried well to give a partially epimerized D-glucose ($\alpha/\beta = 78/22$, 51/49 ; see below ^1H NMR spectra) as a white powder. Model reactions were examined using these epimerized D-glucose as a glycosyl donor. A decrease in the α -anomer content in the substrate resulted in a decrease in the β -anomer content of the glycoside. These results indicated that the β -glycoside was generated selectively from α -D-glucose.



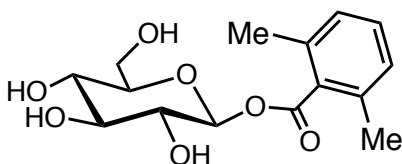
Specific procedures and characterization data of the glycosides in Figure 2, Table 1 and 2

(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl benzoate.



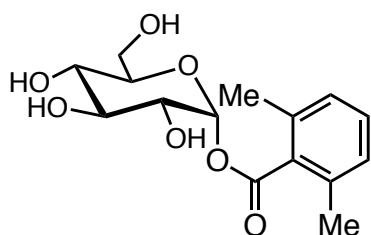
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (2.0 g, 11.1 mmol, 3.0 equiv.), benzoic acid (452 mg, 3.7 mmol, 1.0 equiv.), DIAD (4.4 mL, 22.2 mmol, 2.0 equiv.), and Ph_3P (5.82 g, 22.2 mmol, 2.0 equiv.) in 1,4-dioxane (222 mL) for 1 h, affording the glucoside (694 mg, 66%, $\alpha/\beta=2/98$) as a white powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: **m.p.** 188–191 °C; $[\alpha]_{\text{D}}^{21} = -5.6$ (*c* 0.71, acetone); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.17$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 8.10–8.07 (m, 2H), 7.69–7.66 (m, 1H), 7.56–7.52 (m, 2H), 5.73 (d, $J = 8.4$ Hz, 1H), 3.82 (dd, $J = 11.6, 1.6$ Hz, 1H), 3.68 (dd, $J = 12.0, 5.2$ Hz, 1H), 3.55–3.45 (m, 4H); **$^{13}\text{C NMR}$** (100 MHz, $\text{DMSO}-d_6$) δ : 164.7, 133.9, 129.6, 129.2, 128.8, 95.0, 78.0, 76.4, 72.5, 69.5, 60.6; **IR** (KBr, cm^{-1}): 3550, 3307, 2925, 1714, 1594, 1451, 1395, 1316, 1281, 1077, 1021, 711; **HRMS-ESI** (m/z): Calcd. for $\text{C}_{13}\text{H}_{16}\text{O}_7\text{Cl}$ $[\text{M}+\text{Cl}]^-$ 319.0579; found, 319.0575.

(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl 2,6-dimethylbenzoate (**2a**).



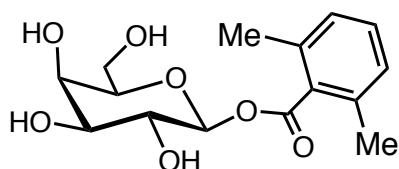
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (200 mg, 1.11 mmol, 3.0 equiv.), 2,6-dimethylbenzoic acid (55.6 mg, 0.37 mmol, 1.0 equiv.), DIAD (146 μL , 0.74 mmol, 2.0 equiv.), and Ph_3P (194 mg, 0.74 mmol, 2.0 equiv.) in 1,4-dioxane (37 mL) for 30 min, affording glucoside **2a** (106 mg, 92%, $\alpha/\beta=1/99$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{21} = +4.1$ (*c* 1.0, acetone); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.30$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 7.23 (t, $J = 8.0$ Hz, 1H), 7.08 (d, $J = 7.6$ Hz, 2H), 5.76 (d, $J = 8.4$ Hz, 1H), 3.85 (dd, $J = 12.0, 2.8$ Hz, 1H), 3.71 (dd, $J = 12.0, 4.4$ Hz, 1H), 3.54 (t, $J = 8.4$ Hz, 1H), 3.52–3.48 (m, 1H), 3.45–3.37 (m, 2H), 2.32 (s, 6H); **$^{13}\text{C NMR}$** (150 MHz, acetone- d_6) δ : 168.9, 135.9, 134.6, 130.3, 128.3, 95.8, 78.5, 78.1, 73.8, 71.3, 62.6, 19.7; **IR** (KBr, cm^{-1}): 3570, 3355, 2937, 2861, 1750, 1706, 1468, 1427, 1260, 1244, 1101, 1077, 1057, 1-34, 894, 782.; **HRMS-ESI** (m/z): Calcd. for $\text{C}_{15}\text{H}_{20}\text{O}_7\text{Cl}$ $[\text{M}+\text{Cl}]^-$ 347.0896; found, 347.0903.

**(2R,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl
2,6-dimethylbenzoate (2b).**



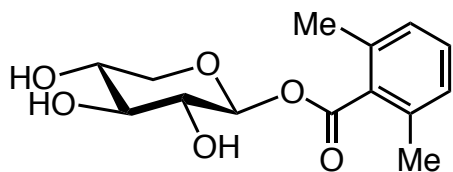
General procedure A for the synthesis of glycoside was followed, starting with β -D-glucose (purchased from TCI, $\alpha/\beta=4:96$, 105 mg, 0.58 mmol, 3.0 equiv.), 2,6-dimethylbenzoic acid (29.0 mg, 0.19 mmol, 1.0 equiv.), DIAD (70 μ L, 0.39 mmol, 2.0 equiv.), and Ph_3P (101 mg, 0.39 mmol, 2.0 equiv.) in 1,4-dioxane (19 mL) for 30 min, affording glycoside **2b** (57 mg, 94%, $\alpha/\beta=89:11$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (10:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{20} = +103.8$ (*c* 0.5, acetone); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5/1 v/v): $R_f=0.22$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 7.21 (t, $J = 7.8$ Hz, 1H), 7.05 (d, $J = 7.8$ Hz, 2H), 6.38 (d, $J = 3.7$ Hz, 1H), 3.80–3.60 (m, 5H), 3.57–3.38 (m, 1H), 2.31 (s, 6H); **$^{13}\text{C NMR}$** (100 MHz, acetone- d_6 + D_2O) δ : 169.5, 135.3, 134.9, 130.1, 128.1, 93.6, 76.1, 74.4, 71.6, 70.4, 61.9, 19.6; **IR** (KBr, cm^{-1}): 3346, 2911, 2334, 1744, 1464, 1265, 1080, 776; **HRMS-ESI $^+$** (m/z): Calcd. for $\text{C}_{15}\text{H}_{20}\text{O}_7\text{Na}$ $[\text{M}+\text{Na}]^+$ 335.1101; found, 335.1115.

**(2S,3R,4R,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl
2,6-dimethylbenzoate (2c).**



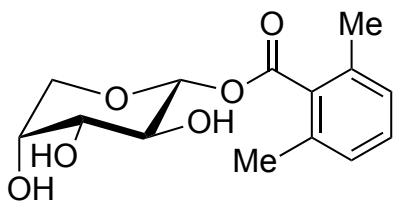
Modified general procedure A for the synthesis of glycoside was followed, starting with α -D-galactose (purchased from TCI, $\alpha/\beta=96:4$, 101 mg, 0.56 mmol, 3.0 equiv.), 2,6-dimethylbenzoic acid (28.1 mg, 0.19 mmol, 1.0 equiv.), DIAD (70 μ L, 0.37 mmol, 2.0 equiv.), and Ph_3P (98.1 mg, 0.37 mmol, 2.0 equiv.) in 1,4-dioxane (56 mL) for 30 min. The reaction mixture was quenched with 3 mL of MeOH, stirred for 5 min, and concentrated in vacuo at 40 $^{\circ}\text{C}$ to give a residue. The residue was directly purified by flash column chromatography (SiO_2 , $\text{CHCl}_3/\text{MeOH}$ 10:1 to 5:1 v/v) to give **2c** (33.6 mg, 58%, $\alpha/\beta=2:98$) as a white amorphous powder. Analytical data: $[\alpha]_{\text{D}}^{19} = +17.1$ (*c* 0.5, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5/1 v/v): $R_f=0.17$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 7.21 (t, $J = 7.8$ Hz, 1H), 7.05 (d, $J = 7.8$ Hz, 2H), 5.69 (d, $J = 7.8$ Hz, 1H), 3.98 (d, $J = 3.2$ Hz, 1H), 3.78–3.64 (m, 5H), 2.29 (s, 6H); **$^{13}\text{C NMR}$** (100 MHz, acetone- d_6 + D_2O) δ : 169.4, 135.6, 134.3, 130.2, 128.1, 96.1, 76.9, 74.4, 70.6, 69.0, 61.3, 19.5; **IR** (KBr, cm^{-1}): 3409, 2947, 1748, 1260, 1076, 769; **HRMS-ESI $^+$** (m/z): Calcd. for $\text{C}_{15}\text{H}_{20}\text{O}_7\text{Na}$ $[\text{M}+\text{Na}]^+$ 335.1101; found, 335.1117.

(2S,3R,4S,5R)-3,4,5-Trihydroxytetrahydropyran-2-yl 2,6-dimethylbenzoate (2d).



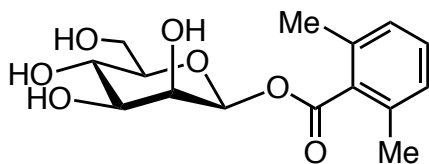
General procedure A for the synthesis of glycoside was followed, starting with α -D-xylose (purchased from TCI, $\alpha/\beta=100/0$, 300 mg, 2.00 mmol, 3.0 equiv.), 2,6-dimethylbenzoic acid (100 mg, 0.67 mmol, 1.0 equiv.), DIAD (262 μ L, 1.34 mmol, 2.0 equiv.), Ph_3P (349 mg, 1.34 mmol, 2.0 equiv.) in 1,4-dioxane (67 mL) for 30 min, affording **2d** (99.6 mg, 53%, $\alpha/\beta=4/96$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (20:1 to 10:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{21} = -5.9$ (*c* 0.62, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.32$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 7.23 (t, $J = 7.2$ Hz, 1H), 7.08 (d, $J = 7.6$ Hz, 2H), 5.70 (d, $J = 7.2$ Hz, 1H), 3.94 (dd, $J = 11.6, 4.8$ Hz, 1H), 3.60–3.54 (m, 1H), 3.51 (t, $J = 8.0$ Hz, 1H), 3.43–3.38 (m, 2H), 2.30 (s, 6H); **$^{13}\text{C NMR}$** (150 MHz, acetone- d_6) δ : 168.9, 135.7, 134.7, 130.3, 128.3, 96.5, 77.5, 73.3, 70.6, 67.3, 19.6; **IR** (KBr, cm^{-1}): 3303, 2921, 2893, 1746, 1591, 1471, 1427, 1363, 1264, 1240, 1089, 1049, 770; **HRMS-FAB $^-$** (m/z): Calcd. for $\text{C}_{14}\text{H}_{17}\text{O}_6$ $[\text{M}-\text{H}]^-$ 281.1025; found, 281.1018.

(2R,3S,4R,5R)-3,4,5-Trihydroxytetrahydropyran-2-yl 2,6-dimethylbenzoate (2e).



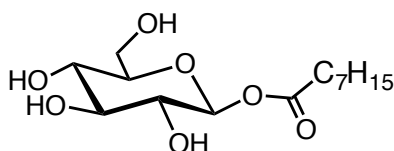
General procedure A for the synthesis of glycoside was followed, starting with α -D-xylose (purchased from TCI, $\alpha/\beta=4/96$, 90 mg, 0.60 mmol, 3.0 equiv.), 2,6-dimethylbenzoic acid (30 mg, 0.20 mmol, 1.0 equiv.), DIAD (79.0 μ L, 0.40 mmol, 2.0 equiv.), Ph_3P (105 mg, 0.40 mmol, 2.0 equiv.) in 1,4-dioxane (20 mL) for 30 min, affording **2e** (49.1 mg, 87%, $\alpha/\beta=95/5$) as a white amorphous after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (20:1 to 10:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{19} = -20$ (*c* 1.0, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.35$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 7.21 (t, $J = 7.6$ Hz, 1H), 7.06 (d, $J = 7.6$ Hz, 2H), 5.68 (d, $J = 6.8$ Hz, 1H), 3.96–3.88 (m, 2H), 3.79–3.67 (m, 3H), 2.30 (s, 6H); **$^{13}\text{C NMR}$** (100 MHz, acetone- d_6) δ : 168.7, 135.1, 134.3, 129.8, 127.8, 95.8, 73.1, 70.4, 67.9, 66.5, 19.2; **IR** (neat, cm^{-1}): 3389, 1744, 1260, 1243, 1055; **HRMS-ESI $^+$** (m/z): Calcd. for $\text{C}_{14}\text{H}_{18}\text{O}_6\text{Na}$ $[\text{M}+\text{Na}]^+$ 305.0996; found, 305.1039.

**(2S,3R,4R,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl
2,6-dimethylbenzoate (2f).**



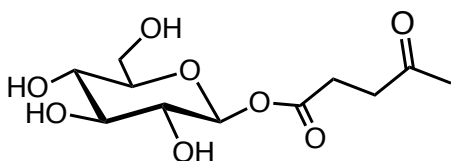
Modified general procedure A for the synthesis of glycoside was followed, starting with α -D-mannose (purchased from TCI, $\alpha/\beta=100/0$, 100 mg, 0.555 mmol, 3.0 equiv.), 2,6-dimethylbenzoic acid (27.8 mg, 0.185 mmol, 1.0 equiv.), DIAD (109 μ L, 0.555 mmol, 3.0 equiv.), Ph_3P (146 mg, 0.555 mmol, 3.0 equiv.) in 1,4-dioxane (10 mL) for 30 min. The reaction mixture was quenched with 2 mL of MeOH, stirred for 10 min, and concentrated in vacuo at 40 $^\circ\text{C}$ to give a residue. The residue was directly purified by flash column chromatography (SiO_2 , $\text{CHCl}_3/\text{MeOH}$ 50:1 to 5:1 v/v) to give the mannopyranoside (66%, $\alpha/\beta=13/87$) as a pale yellow amorphous powder. Pure **2f** was isolated by recrystallization from CH_3CN as a colorless prism crystal ($\alpha/\beta=0/100$). Analytical data: **m.p.** 183–185 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{21} = +12.6$ (c 0.25, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.39$; **$^1\text{H NMR}$** (400 MHz, methanol- d_4) δ : 7.22 (t, $J = 7.6$ Hz, 1H), 7.06 (d, $J = 7.6$ Hz, 2H), 5.96 (br s, 1H), 4.02 (d, $J = 2.4$ Hz, 1H), 3.90 (dd, $J = 12.4, 2.4$ Hz, 1H), 3.78 (dd, $J = 12.0, 5.2$ Hz, 1H), 3.70–3.60 (m, 2H), 3.44–3.40 (m, 1H), 2.35 (s, 6H); **$^{13}\text{C NMR}$** (100 MHz, methanol- d_4) δ : 169.6, 136.5, 134.3, 130.8, 128.6, 94.9, 79.4, 75.0, 71.7, 67.9, 62.6, 19.9; **IR** (KBr, cm^{-1}): 3463, 3244, 2885, 1746, 1591, 1427, 1268, 1065, 1010, 890, 782; **HRMS-ESI $^+$** (m/z): Calcd. for $\text{C}_{15}\text{H}_{20}\text{O}_7\text{Na}$ $[\text{M}+\text{Na}]^+$ 335.1101; found, 335.1114.

(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl octanoate (4a).



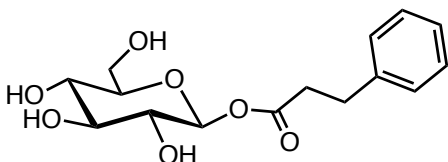
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (270 mg, 1.50 mmol, 3.0 equiv.), octanoic acid (79.2 μ L, 0.50 mmol, 1.0 equiv.), DIAD (197 μ L, 1.00 mmol, 2.0 equiv.), and Ph_3P (262 mg, 1.00 mmol, 2.0 equiv.) in 1,4-dioxane (50 mL) for 30 min, affording the glucoside (101 mg, 66%, $\alpha/\beta=2/98$) as a white powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{21} = -0.7$ (c 1.0, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.36$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6) δ : 5.50 (d, $J = 8.2$ Hz, 1H), 4.48 (d, $J = 4.6$ Hz, 1H), 4.37 (d, $J = 4.1$ Hz, 1H), 4.26 (d, $J = 4.1$ Hz, 1H), 3.83–3.78 (m, 1H), 3.70–3.64 (m, 1H), 3.59 (t, $J = 6.2$ Hz, 1H), 3.50–3.29 (m, 4H), 2.35 (dt, $J = 7.4, 2.3$ Hz, 2H), 1.61 (quint, $J = 7.3$ Hz, 2H), 1.38–1.26 (m, 8H), 0.88 (t, $J = 6.9$ Hz, 3H); **$^{13}\text{C NMR}$** (100 MHz, methanol- d_4) δ : 174.1, 95.5, 78.7, 77.9, 73.9, 71.0, 62.2, 34.8, 32.8, 30.07, 30.05, 25.6, 23.6, 14.4; **IR** (KBr, cm^{-1}): 3359, 2932, 2857, 1734, 1464, 1359, 1179, 885, 495; **HRMS-FAB $^+$** (m/z): Calcd. for $\text{C}_{14}\text{H}_{27}\text{O}_7$ $[\text{M}+\text{H}]^+$ 307.1757; found, 307.1756.

**(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl
4-oxopentanoate (4b).**



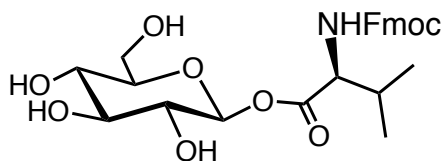
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (650 mg, 3.61 mmol, 3.0 equiv.), 4-oxopentanoic acid (140 mg, 1.21 mmol, 1.0 equiv.), DIAD (474 μ L, 2.41 mmol, 2.0 equiv.), and Ph_3P (630 mg, 2.40 mmol, 2.0 equiv.) in 1,4-dioxane (120 mL) for 30 min, affording the glucoside (248 mg, 74%, $\alpha/\beta=2/98$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{21} = -2.1$ (c 1.0, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.27$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 5.45 (d, $J = 8.3$ Hz, 1H), 3.81–3.76 (m, 1H), 3.67–3.62 (m, 1H), 3.48–3.29 (m, 4H), 2.78 (t, $J = 6.4$ Hz, 2H), 2.66–2.52 (m, 2H), 2.14 (s, 3H); **$^{13}\text{C NMR}$** (100 MHz, methanol- d_4) δ : 209.5, 173.3, 95.7, 78.7, 77.8, 73.8, 70.9, 62.3, 38.3, 29.7, 28.8; **IR** (KBr, cm^{-1}): 3358, 2932, 1750, 1710, 1513, 1421, 1367, 1171, 1065, 889; **HRMS-FAB $^+$** (m/z): Calcd. for $\text{C}_{11}\text{H}_{19}\text{O}_8$ $[\text{M}+\text{H}]^+$ 279.1080; found, 279.1082.

**(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl
3-phenylpropanoate (4c).**



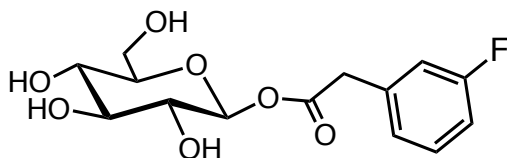
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (270 mg, 1.50 mmol, 3.0 equiv.), 3-phenylpropanoic acid (75.1 mg, 0.50 mmol, 1.0 equiv.), DIAD (197 μ L, 1.00 mmol, 2.0 equiv.), and Ph_3P (262 mg, 1.00 mmol, 2.0 equiv.) in 1,4-dioxane (50 mL) for 30 min, affording the glucoside (133 mg, 82%, $\alpha/\beta=3/97$) as a white powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{21} = +4.1$ (c 1.0, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.38$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6) δ : 7.29–7.19 (m, 5H), 5.52 (d, $J = 8.2$ Hz, 1H), 4.48 (d, $J = 4.6$ Hz, 1H), 4.38 (d, $J = 4.2$ Hz, 1H), 4.27 (d, $J = 3.7$ Hz, 1H), 3.84–3.79 (m, 1H), 3.71–3.64 (m, 1H), 3.58 (t, $J = 6.0$ Hz, 1H), 3.51–3.31 (m, 4H), 2.93 (t, $J = 7.8$ Hz, 2H), 2.68 (dt, $J = 7.6, 3.2$ Hz, 2H); **$^{13}\text{C NMR}$** (100 MHz, acetone- d_6) δ : 171.9, 141.6, 129.2, 127.0, 95.3, 78.3, 77.8, 73.8, 71.0, 62.4, 36.3, 31.1 (One sp^2 carbon signal missing, possibly due to signal overlap.); **IR** (KBr, cm^{-1}): 3347, 2931, 1754, 1455, 1373, 1203, 1076, 896, 752, 699; **HRMS-FAB $^+$** (m/z): Calcd. for $\text{C}_{15}\text{H}_{20}\text{O}_7\text{Na}$ $[\text{M}+\text{Na}]^+$ 335.1107; found, 335.1107.

**(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl
(2S)-2-(9H-fluoren-9-ylmethoxycarbonylamino)-3-methylbutanoate (4d).**



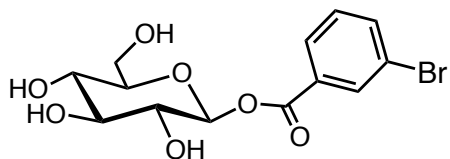
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (108 mg, 0.60 mmol, 3.0 equiv.), Fmoc-Val-OH (67.9 mg, 0.20 mmol, 1.0 equiv.), DIAD (78.8 μ L, 0.40 mmol, 2.0 equiv.), and Ph_3P (105 mg, 0.40 mmol, 2.0 equiv.) in 1,4-dioxane (20 mL) for 30 min, affording the glucoside (88.5 mg, 88%, $\alpha/\beta=2/98$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{21} = -44$ (c 0.5, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.41$; **$^1\text{H NMR}$** (400 MHz, methanol- d_4) δ : 7.80 (d, $J = 7.8$ Hz, 2H), 7.68 (t, $J = 7.8$ Hz, 2H), 7.39 (t, $J = 7.8$ Hz, 2H), 7.32 (t, $J = 7.8$ Hz, 2H), 5.50 (d, $J = 7.8$ Hz, 1H), 4.45–4.33 (m, 2H), 4.28–4.17 (m, 2H), 3.81 (dd, $J = 11.9, 1.8$ Hz, 1H), 3.65 (dd, $J = 11.9, 4.6$ Hz, 1H), 3.45–3.33 (m, 4H), 2.23 (sext, $J = 5.5$ Hz, 1H), 0.99 (d, $J = 6.9$ Hz, 3H), 0.95 (d, $J = 6.9$ Hz, 3H); **$^{13}\text{C NMR}$** (100 MHz, acetone- d_6) δ : 171.8, 157.6, 144.9, 144.7, 141.9, 128.5, 128.0, 127.9, 126.15, 126.08, 120.7, 95.9, 78.4, 77.2, 73.3, 70.7, 67.4, 62.1, 60.1, 47.8, 31.2, 19.4, 17.9; **IR** (KBr, cm^{-1}): 3358, 2965, 1750, 1702, 1538, 1513, 1453, 1250, 1076, 1027, 738; **HRMS-FAB $^+$** (m/z): Calcd. for $\text{C}_{26}\text{H}_{31}\text{NO}_9\text{Na}$ $[\text{M}+\text{Na}]^+$ 524.1897; found, 524.1899.

**(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl
3-(fluorophenyl)acetate (4e).**



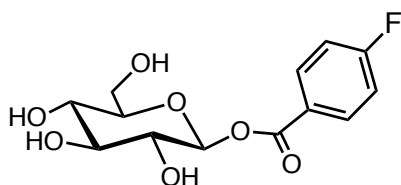
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (300 mg, 1.67 mmol, 3.0 equiv.), 3-fluorophenyl acetic acid (85.9 mg, 0.58 mmol, 1.0 equiv.), DIAD (164 μ L, 0.84 mmol, 2.0 equiv.), and Ph_3P (219 mg, 0.84 mmol, 2.0 equiv.) in 1,4-dioxane (56 mL) for 30 min, affording the glucoside (99 mg, 56%, $\alpha/\beta=1/99$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{21} = +8.3$ (c 0.81, acetone); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.24$ **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 7.39–7.34 (m, 1H), 7.17–7.13 (m, 2H), 7.07–7.02 (m, 1H), 5.53 (d, $J = 8.0$ Hz, 1H), 3.81–3.78 (m, 3H), 3.66 (dd, $J = 12.8, 4.8$ Hz, 1H), 3.48–3.39 (m, 3H), 3.35 (t, $J = 8.8$ Hz, 1H); **$^{13}\text{C NMR}$** (150 MHz, acetone- d_6) δ : 170.4, 163.6 (d, $J_{\text{CF}} = 241.4$ Hz), 137.7 (d, $J_{\text{CF}} = 8.7$ Hz), 130.9 (d, $J_{\text{CF}} = 8.7$ Hz), 126.4 (d, $J_{\text{CF}} = 2.9$ Hz), 117.2 (d, $J_{\text{CF}} = 21.5$ Hz), 114.5 (d, $J_{\text{CF}} = 21.6$ Hz), 95.8, 78.5, 77.9, 73.8, 71.1, 62.5, 40.7; **IR** (KBr, cm^{-1}): 3606, 3542, 2937, 1742, 1619, 1587, 1491, 1447, 1344, 1252, 1141, 1073, 1049, 1010, 894, 791, 679; **HRMS-ESI $^-$** (m/z): Calcd. for $\text{C}_{14}\text{H}_{17}\text{O}_7\text{FCl}$ $[\text{M}+\text{Cl}]^-$ 351.0624; found, 351.0641.

(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl 3-bromobenzoate (4f).



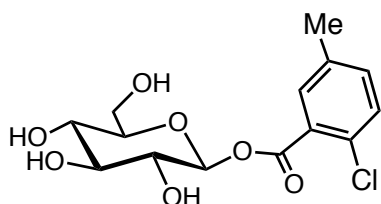
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (270 mg, 1.50 mmol, 3.0 equiv.), 3-bromobenzoic acid (101 mg, 0.50 mmol, 1.0 equiv.), DIAD (197 μ L, 1.00 mmol, 2.0 equiv.), and Ph_3P (262 mg, 1.00 mmol, 2.0 equiv.) in 1,4-dioxane (50 mL) for 30 min, affording the glucoside (128 mg, 70%, $\alpha/\beta=1/99$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{20} = -19$ (c 1.0, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.42$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 8.20 (t, $J = 1.8$ Hz, 1H), 8.10–8.06 (m, 1H), 7.88–7.84 (m, 1H), 7.52 (t, $J = 8.2$ Hz, 1H), 5.72 (d, $J = 8.2$ Hz, 1H), 3.82 (dd, $J = 12.4, 1.8$ Hz, 1H), 3.68 (dd, $J = 11.9, 5.0$ Hz, 1H), 3.56–3.42 (m, 4H); **$^{13}\text{C NMR}$** (100 MHz, acetone- d_6 + D_2O) δ : 164.3, 137.3, 133.2, 132.7, 131.6, 129.5, 122.9, 96.3, 78.6, 77.7, 73.8, 71.0, 62.4; **IR** (KBr, cm^{-1}): 3343, 1717, 1429, 1391, 1288, 1254, 1079, 746, 646; **HRMS-FAB $^+$** (m/z): Calcd. for $\text{C}_{13}\text{H}_{15}\text{BrO}_7\text{Na}$ $[\text{M}+\text{Na}]^+$ 384.9899; found, 384.9898.

(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl 4-fluorobenzoate (4g).



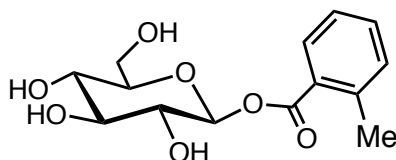
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (300 mg, 1.67 mmol, 3.0 equiv.), 4-fluorobenzoic acid (78.0 mg, 0.58 mmol, 1.0 equiv.), DIAD (164 μ L, 0.84 mmol, 2.0 equiv.), and Ph_3P (219 mg, 0.84 mmol, 2.0 equiv.) in 1,4-dioxane (56 mL) for 30 min, affording the glucoside (89.3 mg, 53%, $\alpha/\beta=1/99$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{21} = -5.5$ (c 1.0, acetone); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.22$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 8.18–8.14 (m, 2H), 7.33–7.29 (m, 2H), 5.72 (d, $J = 8.0$ Hz, 1H), 3.82 (dd, $J = 12.0, 2.0$ Hz, 1H), 3.68 (dd, $J = 12.0, 4.4$ Hz, 1H), 3.58–3.45 (m, 4H); **$^{13}\text{C NMR}$** (150 MHz, acetone- d_6) δ : 166.9 (d, $J_{\text{CF}} = 249.9$ Hz), 164.7, 133.5 (d, $J_{\text{CF}} = 10.1$ Hz), 127.2, 116.5 (d, $J_{\text{CF}} = 23.0$ Hz), 96.1, 78.6, 77.9, 73.9, 71.2, 62.5; **IR** (KBr, cm^{-1}): 3463, 3331, 2925, 1718, 1603, 1507, 1412, 1380, 1284, 1236, 1101, 1077, 858, 782; **HRMS-ESI $^-$** (m/z): Calcd. for $\text{C}_{13}\text{H}_{15}\text{O}_7\text{FCl}$ $[\text{M}+\text{Cl}]^-$ 337.0469; found, 337.0485.

**(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl
2-chloro-5-methylbenzoate (4h).**



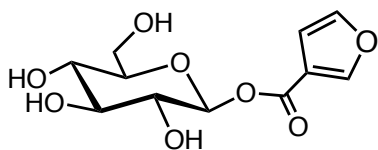
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (200 mg, 1.11 mmol, 3.0 equiv.), 2-chloro-5-methylbenzoic acid (63.1 mg, 0.37 mmol, 1.0 equiv.), DIAD (146 μ L, 0.74 mmol, 2.0 equiv.), and Ph_3P (194 mg, 0.74 mmol, 2.0 equiv.) in 1,4-dioxane (37 mL) for 30 min, affording the glucoside (73 mg, 59%, $\alpha/\beta=1/99$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{21} = -4.5$ (*c* 1.1, acetone); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.26$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 7.82 (br s, 1H), 7.44–7.38 (m, 2H), 5.71 (d, $J = 8.0$ Hz, 1H), 3.83 (dd, $J = 12.0, 2.0$ Hz, 1H), 3.70 (dd, $J = 12.0, 4.4$ Hz, 1H), 3.58–3.43 (m, 4H), 2.37 (s, 3H); **$^{13}\text{C NMR}$** (150 MHz, acetone- d_6) δ : 164.2, 138.1, 135.0, 133.0, 131.8, 131.4, 129.9, 96.2, 78.6, 78.0, 73.9, 71.1, 62.5, 20.6; **IR** (KBr, cm^{-1}): 3590, 3331, 3192, 2877, 2307, 1754, 1714, 1642, 1479, 1399, 1292, 1244, 1197, 1109, 1025, 894, 810, 778, 639; **HRMS-ESI $^-$** (m/z): Calcd. for $\text{C}_{14}\text{H}_{17}\text{O}_7\text{Cl}_2$ $[\text{M}+\text{Cl}]^-$ 367.0333; found, 367.0346.

**(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl
2-methylbenzoate (4i).**



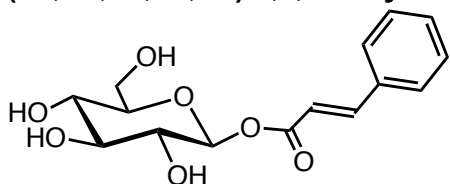
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (540 mg, 3.00 mmol, 3.0 equiv.), 2-methylbenzoic acid (136 mg, 1.00 mmol, 1.0 equiv.), DIAD (394 μ L, 2.00 mmol, 2.0 equiv.), and Ph_3P (525 mg, 2.00 mmol, 2.0 equiv.) in 1,4-dioxane (100 mL) for 30 min, affording the glucoside (238 mg, 79%, $\alpha/\beta=1/99$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{21} = -16$ (*c* 0.5, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.28$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 7.99 (d, $J = 7.4$ Hz, 1H), 7.48 (t, $J = 6.8$ Hz, 1H), 7.34–7.29 (m, 2H), 5.71 (d, $J = 8.2$ Hz, 1H), 3.83 (dd, $J = 11.2, 2.3$ Hz, 1H), 3.68 (dd, $J = 12.4, 4.6$ Hz, 1H), 3.58–3.42 (m, 4H), 2.55 (s, 3H); **$^{13}\text{C NMR}$** (100 MHz, acetone- d_6 + D_2O) δ : 166.5, 141.3, 133.4, 132.5, 131.6, 129.7, 126.7, 95.6, 78.4, 77.6, 73.6, 70.8, 62.1, 21.7; **IR** (KBr, cm^{-1}): 3491, 3355, 2925, 1714, 1459, 1380, 1253, 1069, 738; **HRMS-FAB $^+$** (m/z): Calcd. for $\text{C}_{14}\text{H}_{19}\text{O}_7$ $[\text{M}+\text{H}]^+$ 299.1131; found, 299.1131.

(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl furan-3-carboxylate (4j).



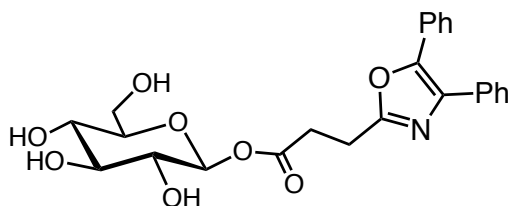
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (100 mg, 0.56 mmol, 3.0 equiv.), 3-furoic acid (20.7 mg, 0.185 mmol, 1.0 equiv.), DIAD (72.9 μ L, 0.37 mmol, 2.0 equiv.), and Ph_3P (97.0 mg, 0.37 mmol, 2.0 equiv.) in 1,4-dioxane (19 mL) for 30 min, affording the glucoside (38.7 mg, 76%, $\alpha/\beta=1/99$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{20} = -12.2$ (c 0.5, MeOH); TLC ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.17$; $^1\text{H NMR}$ (400 MHz, $\text{CD}_3\text{CN}+\text{D}_2\text{O}$) δ : 8.35 (d, $J = 1.2$ Hz, 1H), 7.70 (t, $J = 1.6$ Hz, 1H), 6.92 (d, $J = 1.6$ Hz, 1H), 5.69 (d, $J = 7.6$ Hz, 1H), 3.83 (dd, $J = 12.0, 2.4$ Hz, 1H), 3.69 (dd, $J = 12.4, 5.6$ Hz, 1H), 3.57–3.38 (m, 4H); $^{13}\text{C NMR}$ (100 MHz, acetone- d_6) δ : 162.0, 149.7, 145.5, 119.9, 110.5, 95.5, 78.5, 77.9, 73.8, 71.1, 62.5; IR (KBr, cm^{-1}): 3542, 3435, 2917, 1722, 1511, 1308, 1169, 1077, 1041, 763, 603; HRMS-FAB $^-$ (m/z): Calcd. for $\text{C}_{11}\text{H}_{13}\text{O}_7$ $[\text{M}-\text{H}]^-$ 273.0610; found, 273.0607.

(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl cinnamate (4k).



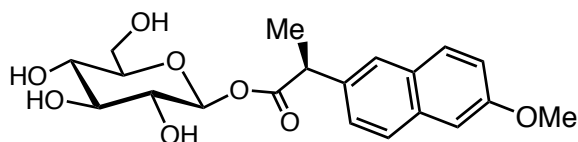
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (100 mg, 0.555 mmol, 3.0 equiv.), *trans*-cinnamic acid (27.4 mg, 0.19 mmol, 1.0 equiv.), DIAD (72.9 μ L, 0.37 mmol, 2.0 equiv.), and Ph_3P (97 mg, 0.37 mmol, 2.0 equiv.) in 1,4-dioxane (19 mL) for 30 min, affording the glucoside (51.0 mg, 86%, $\alpha/\beta=1/99$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{21} = +1.2$ (c 0.67, acetone); TLC ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.32$; $^1\text{H NMR}$ (400 MHz, acetone- d_6 + D_2O) δ : 7.78 (d, $J = 16.0$ Hz, 1H), 7.73–7.70 (m, 2H), 7.46–7.44 (m, 3H), 6.58 (d, $J = 16.0$ Hz, 1H), 5.61 (d, $J = 8.0$ Hz, 1H), 3.83–3.80 (m, 1H), 3.67 (dd, $J = 12.0, 4.8$ Hz, 1H), 3.53–3.40 (m, 4H); $^{13}\text{C NMR}$ (150 MHz, acetone- d_6) δ : 165.8, 146.6, 135.3, 131.5, 129.9, 129.2, 118.6, 95.5, 78.5, 78.0, 73.9, 71.2, 62.5; IR (KBr, cm^{-1}): 3491, 3060, 2933, 1702, 1634, 1582, 1455, 1376, 1340, 1281, 1133, 1077, 1013, 862, 763, 679; HRMS-FAB $^+$ (m/z): Calcd. for $\text{C}_{15}\text{H}_{18}\text{O}_7\text{Na}$ $[\text{M}+\text{Na}]^+$ 333.0950; found, 333.0955.

(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl 3-(4,5-diphenyloxazol-2-yl)propanoate (4l).



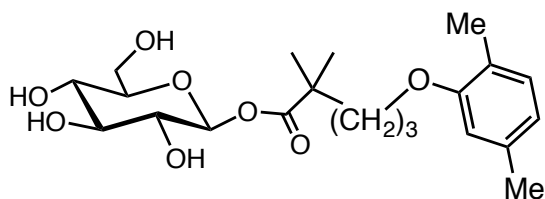
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (432 mg, 2.40 mmol, 3.0 equiv.), oxaprozin (235 mg, 0.80 mmol, 1.0 equiv.), DIAD (315 μ L, 1.60 mmol, 2.0 equiv.), and Ph_3P (420 mg, 1.60 mmol, 2.0 equiv.) in 1,4-dioxane (80 mL) for 30 min, affording the glycoside (257 mg, 71%, $\alpha/\beta=2/98$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{20} = +4.0$ (*c* 1.0, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.46$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 7.65–7.58 (m, 4H), 7.46–7.34 (m, 6H), 5.55 (d, $J = 8.4$ Hz 1H), 3.82–3.78 (m, 1H), 3.69–3.65 (m, 1H), 3.50–3.41 (m, 2H), 3.36 (t, $J = 8.4$ Hz, 1H), 3.21–3.17 (m, 1H), 3.04–2.95 (m, 4H); **$^{13}\text{C NMR}$** (100 MHz, acetone- d_6) δ : 171.7, 163.1, 146.0, 135.6, 133.2, 129.7, 129.6, 129.5, 129.3, 128.9, 128.5, 127.3, 95.5, 78.3, 77.3, 73.4, 70.6, 62.0, 31.2, 23.5; **IR** (KBr, cm^{-1}): 3367, 1753, 1570, 1443, 1363, 1328, 1173, 1077, 1029, 763, 690; **HRMS-FAB $^+$** (m/z): Calcd. for $\text{C}_{24}\text{H}_{25}\text{NO}_8\text{Na}$ $[\text{M}]^+$ 478.1478; found, 478.1480.

(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl (S)-2-(6-methoxynaphthalen-2-yl)propanoate (4m).



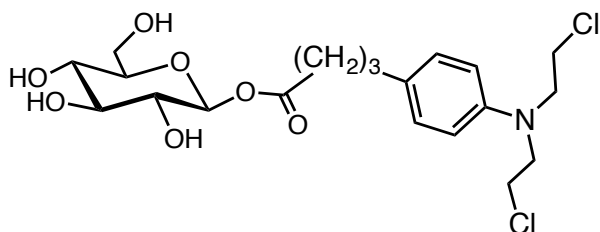
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (1.0 g, 5.55 mmol, 3.0 equiv.), naproxen (426 mg, 1.85 mmol, 1.0 equiv.), DIAD (728 μ L, 3.7 mmol, 2.0 equiv.), and Ph_3P (970 mg, 3.7 mmol, 2.0 equiv.) in 1,4-dioxane (185 mL) for 1 h, affording the glycoside (452 mg, 62%, $\alpha/\beta=1/99$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{20} = +21$ (*c* 1.0, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.38$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 7.79–7.76 (m, 3H), 7.45 (dd, $J = 8.0, 1.2$ Hz, 1H), 7.27 (d, $J = 2.4$ Hz, 1H), 7.13 (dd, $J = 8.8, 2.8$ Hz, 2H), 5.52 (d, $J = 7.6$ Hz, 1H), 3.97 (q, $J = 7.2$ Hz, 1H), 3.89 (s, 3H), 3.73 (dd, $J = 11.6, 2.0$ Hz, 1H), 3.58 (dd, $J = 12.0, 5.2$ Hz, 1H), 3.49–3.29 (m, 4H), 1.52 (d, $J = 7.2$ Hz, 3H); **$^{13}\text{C NMR}$** (100 MHz, acetone- d_6) δ : 174.0, 158.6, 136.5, 134.7, 130.1, 129.8, 128.0, 127.2, 126.9, 119.7, 106.4, 95.6, 78.4, 77.6, 73.5, 70.8, 62.1, 55.6, 45.8, 19.4; **IR** (KBr, cm^{-1}): 3390, 3191, 2976, 1742, 1626, 1606, 1268, 1225, 1189, 1101, 1065, 1025, 858, 822; **HRMS-FAB $^+$** (m/z): Calcd. for $\text{C}_{20}\text{H}_{24}\text{O}_8$ $[\text{M}]^+$ 392.1471; found, 392.1468.

**(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl
5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (4n).**



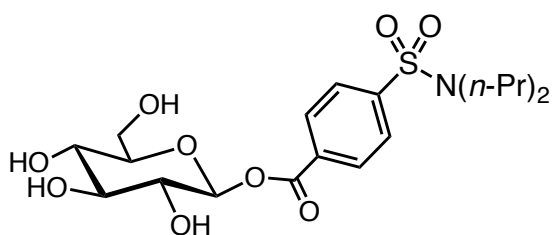
Modified general procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (200 mg, 1.11 mmol, 3.0 equiv.), gemfibrozil (92.6 mg, 0.37 mmol, 1.0 equiv.), DIAD (291 μ L, 1.48 mmol, 4.0 equiv.), and Ph_3P (388 mg, 1.48 mmol, 4.0 equiv.) in 1,4-dioxane (37 mL) for 1 h, affording the glucoside (74 mg, 48%, $\alpha/\beta=1/99$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{20} = -0.2$ (*c* 1.0, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.54$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 6.96 (d, $J = 7.2$ Hz, 1H), 6.70 (br s, 1H), 6.62 (d, $J = 7.2$ Hz, 1H), 5.50 (d, $J = 8.0$ Hz, 1H), 3.95–3.93 (m, 2H), 3.79 (dd, $J = 11.6, 2.0$ Hz, 1H), 3.68–3.64 (m, 1H), 3.47–3.29 (m, 4H), 2.25 (s, 3H), 2.12 (s, 3H), 1.79–1.76 (m, 2H), 1.23 (s, 3H), 1.22 (s, 3H); **$^{13}\text{C NMR}$** (100 MHz, acetone- d_6) δ : 177.2, 157.5, 137.0, 130.7, 123.5, 121.2, 112.6, 95.0, 77.9, 77.0, 73.0, 70.3, 68.4, 61.7, 42.5, 37.3, 25.3, 25.1, 24.9, 21.2, 15.8; **IR** (KBr, cm^{-1}): 3386, 2933, 1734, 1615, 1510, 1471, 1419, 1387, 1268, 1120, 1073, 806; **HRMS-ESI $^-$** (m/z): Calcd. for $\text{C}_{21}\text{H}_{32}\text{O}_8\text{Cl}$ $[\text{M}+\text{Cl}]^-$ 447.1777; found, 447.1780.

**(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl
4-{4-[bis(2-chloroethyl)amino]phenyl}butanoate (4o).**



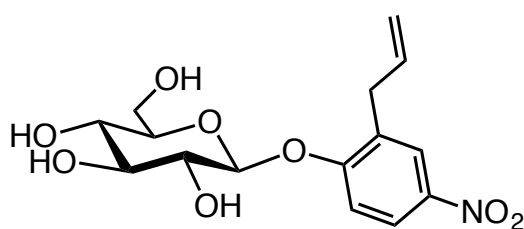
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (711 mg, 3.95 mmol, 3.0 equiv.), chlorambucil (400 mg, 1.32 mmol, 1.0 equiv.), DIAD (518 μ L, 2.63 mmol, 2.0 equiv.), and Ph_3P (690 mg, 2.63 mmol, 2.0 equiv.) in 1,4-dioxane (132 mL) for 30 min, affording the glucoside (405 mg, 66%, $\alpha/\beta=1/99$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{21} = +3.2$ (*c* 1.14, acetone); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.48$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 7.09 (d, $J = 8.8$ Hz, 2H), 6.73 (d, $J = 6.4$ Hz, 2H), 5.50 (d, $J = 8.0$ Hz, 1H), 3.80–3.70 (m, 9H), 3.67–3.63 (m, 1H), 3.49–3.38 (m, 3H), 3.32 (t, $J = 8.4$ Hz, 1H), 2.56 (t, $J = 7.6$ Hz, 2H), 2.39–2.34 (m, 2H), 1.86 (quint, $J = 7.2$ Hz, 2H); **$^{13}\text{C NMR}$** (100 MHz, acetone- d_6) δ : 172.8, 145.6, 131.0, 130.4, 113.0, 95.1, 78.3, 77.6, 73.5, 70.8, 62.2, 53.8, 41.6, 34.4, 33.9, 27.4; **IR** (KBr, cm^{-1}): 3550, 3307, 2925, 1714, 1594, 1451, 1395, 1316, 1281, 1077, 1021, 711; **HRMS-ESI $^-$** (m/z): Calcd. for $\text{C}_{20}\text{H}_{29}\text{NO}_7\text{Cl}_2$ $[\text{M}+\text{Cl}]^-$ 500.1005; found, 500.1015.

**(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl
4-(*N,N*-Dipropylsulfamoyl)benzoate (4p).**



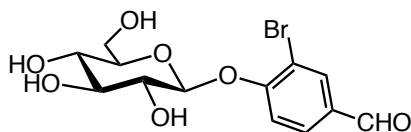
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (200 mg, 1.11 mmol, 3.0 equiv.), probenecid (105 mg, 0.37 mmol, 1.0 equiv.), DIAD (146 μ L, 0.74 mmol, 2.0 equiv.), and Ph_3P (194 mg, 0.74 mmol, 2.0 equiv.) in 1,4-dioxane (37 mL) for 30 min, affording the glucoside (107 mg, 65%, $\alpha/\beta=2/98$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{20} = -6.0$ (*c* 1.0, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.38$; **$^1\text{H NMR}$** (600 MHz, acetone- d_6 +D $_2$ O) δ : 8.27 (d, $J = 9.0$ Hz, 2H), 7.99 (d, $J = 9.0$ Hz, 2H), 5.76 (d, $J = 8.4$ Hz, 1H), 3.83 (dd, $J = 12.0, 3.0$ Hz, 1H), 3.69 (dd, $J = 12.0, 4.8$ Hz, 1H), 3.56–3.45 (m, 4H), 3.14 (t, $J = 7.8$ Hz, 4H), 1.55 (sext, $J = 7.8$ Hz, 4H), 0.85 (t, $J = 7.2$ Hz, 6H); **$^{13}\text{C NMR}$** (150 MHz, acetone- d_6) δ : 164.7, 145.7, 133.8, 131.4, 128.1, 96.4, 78.6, 77.6, 73.7, 70.9, 62.2, 50.7, 22.6, 11.3; **IR** (KBr, cm^{-1}): 3406, 2933, 2877, 1742, 1464, 1404, 1335, 1268, 1157, 1085, 989, 862, 750, 611; **HRMS-FAB $^+$** (m/z): Calcd. for $\text{C}_{19}\text{H}_{29}\text{NO}_9\text{SNa}$ $[\text{M}]^+$ 470.1461; found, 470.1464.

**(2S,3R,4S,5S,6R)-2-(2-Allyl-4-nitrophenoxy)-6-(hydroxymethyl)tetrahydropyran-3,4,5-triol
(4q).**



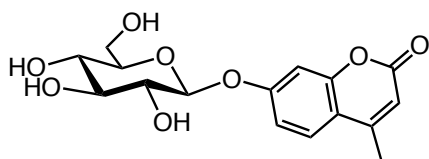
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (108 mg, 0.60 mmol, 3.0 equiv.), 2-allyl-4-nitrophenol³ (35.8 mg, 0.20 mmol, 1.0 equiv.), DIAD (78.8 μ L, 0.40 mmol, 2.0 equiv.), Ph_3P (105 mg, 0.40 mmol, 2.0 equiv.) in 1,4-dioxane (20 mL) for 30 min, affording the glucoside (43.7 mg, 64%, $\alpha/\beta=1/99$) as a pale yellow powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{21} = -76$ (*c* 1.0, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.44$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 +D $_2$ O) δ : 8.09 (dd, $J = 9.2, 2.7$ Hz, 1H), 8.04 (d, $J = 2.8$ Hz, 1H), 7.37 (d, $J = 9.2$ Hz, 1H), 6.05 (ddt, $J = 18.6, 10.1, 6.9$ Hz, 1H), 5.21–5.08 (m, 3H), 3.89 (dd, $J = 12.0, 2.8$ Hz, 1H), 3.67 (dd, $J = 12.0, 4.4$ Hz, 1H), 3.62–3.42 (m, 6H); **$^{13}\text{C NMR}$** (100 MHz, acetone- d_6 +D $_2$ O) δ : 161.1, 142.9, 136.5, 131.5, 125.5, 124.4, 117.2, 115.5, 101.5, 77.9, 77.5, 74.3, 70.8, 62.2, 34.5; **IR** (KBr, cm^{-1}): 3279, 2937, 1591, 1515, 1358, 1243, 1972, 1044, 673; **HRMS-FAB $^+$** (m/z): Calcd. for $\text{C}_{15}\text{H}_{20}\text{NO}_8$ $[\text{M}+\text{H}]^+$ 342.1189; found, 342.1191.

3-Bromo-4-[[[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl]oxy]benzaldehyde (4r).



General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (108 mg, 0.60 mmol, 3.0 equiv.), 3-bromo-4-hydroxybenzaldehyde⁴ (40.2 mg, 0.20 mmol, 1.0 equiv.), DIAD (78.8 μ L, 0.40 mmol, 2.0 equiv.), Ph₃P (105 mg, 0.40 mmol, 2.0 equiv.) in 1,4-dioxane (20 mL) for 30 min, affording the glucoside (26.9 mg, 37%, $\alpha/\beta=2/98$) as a white powder after purification by flash chromatography, eluting with CHCl₃/MeOH (50:1 to 5:1 v/v). Analytical data: $[\alpha]_D^{21} = -63$ (*c* 1.0, MeOH); **TLC** (CHCl₃/MeOH 5:1 v/v): *R_f* = 0.34; **¹H NMR** (400 MHz, acetone-*d*₆+D₂O) δ : 9.90 (s, 1H), 8.10 (d, *J* = 1.8 Hz, 1H), 7.89 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.45 (d, *J* = 8.7 Hz, 1H), 5.25 (d, *J* = 7.3 Hz, 1H), 3.87 (dd, *J* = 11.7, 2.5 Hz, 1H), 3.68 (dd, *J* = 11.9, 5.5 Hz, 1H), 3.63–3.43 (m, 4H); **¹³C NMR** (100 MHz, acetone-*d*₆+D₂O) δ : 190.7, 159.4, 134.9, 132.8, 131.6, 116.8, 113.2, 101.3, 78.0, 77.7, 74.2, 70.7, 62.2; **IR** (KBr, cm⁻¹): 3414, 2889, 1674, 1593, 1494, 1264, 1080, 1053, 881, 818, 657, 630; **HRMS-ESI⁻** (*m/z*): Calcd. for C₁₃H₁₄BrO₇ [M-H]⁻ 360.9928; found, 360.9917.

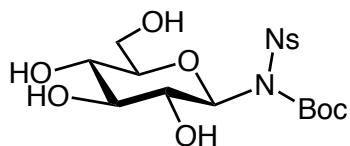
4-Methyl-7-[[[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl]oxy]-2H-chromen-2-one (4s).



A round-bottom flask was charged with α -D-glucose (216 mg, 1.20 mmol, 3.0 equiv.) and dehydrated 1,4-dioxane (40 mL) under an Ar atmosphere. After ultrasound irradiation of the suspension of α -D-glucose in 1,4-dioxane for 15 min, the suspension was warmed to 55 °C and 4-methylumbelliferone (70.5 mg, 0.40 mmol, 1.0 equiv.) and Ph₃P (210 mg, 0.80 mmol, 2.0 equiv.) were added. DIAD (158 μ L, 0.80 mmol, 2.0 equiv.) was added dropwise by syringe and the reaction mixture was stirred at 55 °C. After stirring vigorously for 15 min, Ph₃P (210 mg, 0.80 mmol, 2.0 equiv.) and DIAD (158 μ L, 0.80 mmol, 2.0 equiv.) were added again in the same manner and stirred at 55 °C for 45 min. The reaction mixture was quenched with MeOH, stirred for 5 min, and concentrated in vacuo at 40 °C to give a residue. The residue was directly purified by flash column chromatography (SiO₂, CHCl₃/MeOH 50:1 to 5:1 v/v) to give the glucoside (111 mg, 82%, $\alpha/\beta=3/97$). Analytical data: $[\alpha]_D^{20} = -92$ (*c* 0.5, MeOH); **TLC** (CHCl₃/MeOH 5:1 v/v): *R_f* = 0.28; **¹H NMR** (400 MHz, acetone-*d*₆+D₂O) δ : 7.69 (d, *J* = 8.7 Hz, 1H), 7.06 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.01 (d, *J* = 2.8 Hz, 1H), 6.17 (s, 1H), 5.10 (d, *J* = 7.3 Hz, 1H), 3.89 (dd, *J* = 11.9, 2.3 Hz, 1H), 3.68 (dd, *J* = 11.9, 5.5 Hz, 1H), 3.64–3.42 (m, 4H), 2.44 (s, 3H); **¹³C NMR** (100 MHz, acetone-*d*₆+D₂O) δ : 161.4, 161.2, 155.7, 153.9, 127.0, 115.4, 114.3, 112.8, 104.4, 101.5, 77.8, 77.5, 74.3, 70.9, 62.2, 18.5; **IR** (KBr, cm⁻¹): 3407, 2897, 1713, 1620, 1393, 1296, 1089, 1038, 855, 644; **HRMS-FAB⁺** (*m/z*): Calcd. for C₁₆H₁₉O₈ [M+H]⁺ 339.1080; found, 339.1079.

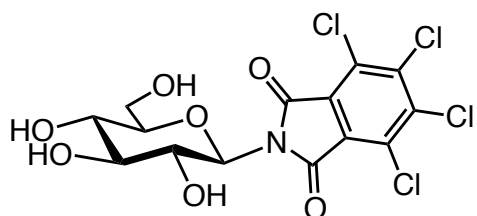
tert-Butyl

[(2-nitrophenyl)sulfonyl][(2R,3S,4S,5S)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl]carbamate (4t).



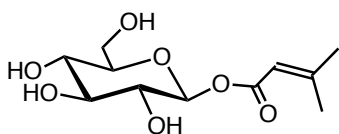
Modified general procedure A was followed, starting with α -D-glucose (1.79 g, 9.9 mmol, 3.0 equiv.), NsNHBOc⁴ (1.0 g, 3.3 mmol, 1.0 equiv.), DIAD (2.6 mL, 13.2 mmol, 2.0 equiv.), Ph₃P (3.5g, 13.2 mmol, 2.0 equiv.) in 1,4-dioxane (330 mL) at rt for 5 min, adding extra DIAD (2.6 mL, 13.2 mmol, 2.0 equiv.) and Ph₃P (3.5g, 13.2 mmol, 2.0 equiv.) at rt for 25 min, affording the glucoside (631 mg, 41%, $\alpha/\beta=1/99$) as a white amorphous powder after purification by two-time flash chromatography, eluting with (1st) CHCl₃/MeOH (50:1 to 5:1 v/v) and then (2nd) CH₃CN/CHCl₃ (2:1 v/v). Analytical data: $[\alpha]_D^{21} = +321$ (*c* 0.55, acetone); TLC (CHCl₃/MeOH 5:1 v/v): *R_f* = 0.33; ¹H NMR (400 MHz, acetone-*d*₆+D₂O) δ : 8.62 (d, *J* = 7.6 Hz, 1H), 7.95–7.84 (m, 3H), 5.28 (d, *J* = 9.2 Hz, 1H), 4.35 (t, *J* = 9.2 Hz, 1H), 3.92 (dd, *J* = 12.0, 2.4 Hz, 1H), 3.70 (dd, *J* = 12.0, 6.0 Hz, 1H), 3.52–3.38 (m, 3H), 1.23 (s, 9H); ¹³C NMR (100 MHz, acetone-*d*₆) δ : 149.9, 149.3, 134.95, 134.90, 133.3, 130.7, 125.1, 87.6, 85.6, 80.7, 79.5, 71.4, 71.2, 62.7, 27.7; IR (KBr, cm⁻¹): 3395, 2980, 1742, 1705, 1543, 1455, 1372, 1284, 1260, 1180, 1145, 1077, 742; HRMS-ESI⁺ (*m/z*): Calcd. for C₁₇H₂₄N₂O₁₁SNa [M+Na]⁺ 487.0993; found, 487.1001.

4,5,6,7-Tetrachloro-2-[(2R,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl]isoindoline-1,3-dione (4u).



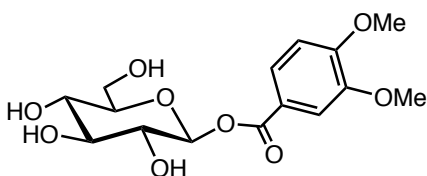
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (200 mg, 1.11 mmol, 3.0 equiv.), 3,4,5,6-tetrachlorophthalimide (105 mg, 0.37 mmol, 1.0 equiv.), DIAD (146 μ L, 0.74 mmol, 2.0 equiv.), Ph₃P (194 mg, 0.74 mmol, 2.0 equiv.) in 1,4-dioxane (37 mL) for 30 min, affording the glucoside (117 mg, 71%, $\alpha/\beta=1/99$) as a white amorphous powder after purification by flash chromatography, eluting with CHCl₃/MeOH (50:1 to 5:1 v/v). Analytical data: $[\alpha]_D^{21} = -3.1$ (*c* 0.74, acetone); TLC (CHCl₃/MeOH 5:1 v/v): *R_f* = 0.40; ¹H NMR (400 MHz, acetone-*d*₆+D₂O) δ : 5.16 (d, *J* = 9.6 Hz, 1H), 4.38 (t, *J* = 9.2 Hz, 1H), 3.85 (dd, *J* = 12.0, 2.0 Hz, 1H), 3.65 (dd, *J* = 12.4, 5.2 Hz, 1H), 3.58–3.45 (m, 3H); ¹³C NMR (100 MHz, acetone-*d*₆) δ : 163.3, 140.3, 130.2, 128.7, 81.8, 80.6, 78.9, 71.2, 69.6, 62.7; IR (KBr, cm⁻¹): 3323, 2980, 1790, 1726, 1388, 1372, 1145, 1077, 1045, 905, 742; HRMS-ESI⁻ (*m/z*): Calcd. for C₁₄H₁₁NO₇Cl₅ [M+Cl]⁻ 479.8966; found, 479.8984.

Thotneoside C (5).



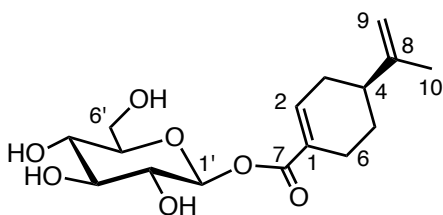
General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (270 mg, 1.50 mmol, 3.0 equiv.), 3-phenylpropanoic acid (50.1 mg, 0.50 mmol, 1.0 equiv.), DIAD (197 μ L, 1.00 mmol, 2.0 equiv.), and Ph_3P (262 mg, 1.00 mmol, 2.0 equiv.) in 1,4-dioxane (50 mL) for 30 min, affording thotneoside C (4) (88.4 mg, 67%, $\alpha/\beta=2/98$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{21} = -36$ (c1.0, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.35$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 5.71–5.69 (m, 1H), 5.51 (d, $J = 8.2$ Hz, 1H), 3.79 (dd, $J = 11.9, 1.8$ Hz, 1H), 3.68–3.62 (m, 1H), 3.49–3.31 (m, 4H), 2.16 (s, 3H), 1.93 (s, 3H); **$^{13}\text{C NMR}$** (100 MHz, acetone- d_6 + D_2O) δ : 165.2, 159.8, 116.2, 94.6, 78.3, 78.0, 73.8, 71.1, 62.4, 27.3, 20.3; **IR** (KBr, cm^{-1}): 3364, 2928, 1739, 1646, 1454, 1382, 1227, 1142, 1073, 847; **HRMS-FAB $^+$** (m/z): Calcd. for $\text{C}_{11}\text{H}_{18}\text{O}_7\text{Na}$ $[\text{M}+\text{Na}]^+$ 285.0950; found, 285.0952.

Tecomin (6).



General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (3.24 g, 18.0 mmol, 3.0 equiv.), 3,4-dimethoxybenzoic acid (1.09 mg, 5.98 mmol, 1.0 equiv.), DIAD (2.36 mL, 12.0 mmol, 2.0 equiv.), and Ph_3P (3.15 g, 12.0 mmol, 2.0 equiv.) in 1,4-dioxane (600 mL) for 30 min, affording tecomin (5) (1.44 g, 70%, $\alpha/\beta=1/99$) as a white powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{20} = -15$ (c 1.0, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.39$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 7.71 (dd, $J = 8.7, 2.3$ Hz, 1H), 7.58 (d, $J = 1.8$ Hz, 1H), 7.08 (d, $J = 8.7$ Hz, 1H), 5.71 (d, $J = 7.8$ Hz, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 3.86–3.80 (m, 1H), 3.71–3.66 (m, 1H), 3.55–3.45 (m, 4H); **$^{13}\text{C NMR}$** (100 MHz, acetone- d_6 + D_2O) δ : 165.5, 154.8, 149.8, 124.8, 122.6, 113.1, 111.6, 95.8, 78.4, 77.6, 73.6, 70.8, 62.2, 56.2, 56.1; **IR** (KBr, cm^{-1}): 3367, 1705, 1600, 1517, 1276, 1223, 1083, 1023, 761; **HRMS-FAB $^+$** (m/z): Calcd. for $\text{C}_{15}\text{H}_{21}\text{O}_9$ $[\text{M}+\text{H}]^+$ 345.1186; found, 345.1187.

Perilloside B (7).



General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (200 mg, 1.11 mmol, 3.0 equiv.), (*S*)-(-)-perillic acid (61.5 mg, 0.37 mmol, 1.0 equiv.), DIAD (145 μ L, 0.74 mmol, 2.0

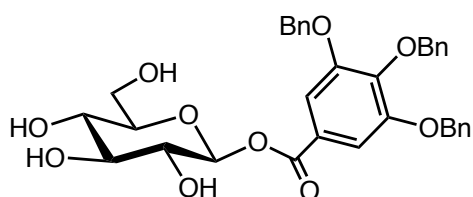
equiv.), and Ph_3P (194 mg, 0.74 mmol, 2.0 equiv.) in 1,4-dioxane (37 mL) for 30 min affording perilloside B (**4**) (74 mg, 48%, $\alpha/\beta=1/99$) as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). Analytical data: $[\alpha]_{\text{D}}^{20} = -52$ (c 0.6, MeOH), reported $[\alpha]_{\text{D}}^{22} = -57.1$ (c 0.645, MeOH)⁸; **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.35$; **$^1\text{H NMR}$** (400 MHz, methanol- d_4) δ : 7.15 (br s, 1H), 5.53 (d, $J = 7.2$ Hz, 1H), 4.77–4.74 (m, 2H), 3.83 (dd, $J = 10.4, 2.0$ Hz, 1H), 3.70–3.66 (m, 1H), 3.44–3.36 (m, 4H), 2.49–2.10 (m, 5H), 1.92–1.88 (m, 1H), 1.76 (s, 3H), 1.54–1.48 (m, 1H); **$^{13}\text{C NMR}$** (100 MHz, methanol- d_4) δ : 167.3, 150.0, 142.3, 130.5, 109.8, 95.7, 78.8, 78.1, 74.0, 71.1, 62.3, 41.4, 32.2, 28.2, 25.4, 20.9; **IR** (KBr, cm^{-1}): 3390, 2933, 1718, 1698, 1647, 1376, 1256, 1081, 890, 739, 703; **HRMS-FAB⁺** (m/z): Calcd. for $\text{C}_{16}\text{H}_{25}\text{O}_7$ $[\text{M}+\text{H}]^+$ 329.1600; found, 329.1603.

Comparison of $^{13}\text{C NMR}$ between isolated⁸ and synthetic perilloside B (**7**).

Synthetic 4 (100 MHz, methanol- d_4)	Isolated sample ⁸ (67.8 MHz, methanol- d_4)
20.9	20.9 (C10)
25.4	25.3 (C6)
28.2	28.1 (C5)
32.2	32.2 (C3)
41.4	41.2 (C4)
62.3	62.2 (C6')
71.1	70.9 (C4')
74.0	73.9 (C2')
78.1	77.9 (C5')
78.8	78.6 (C3')
95.7	95.7 (C1')
109.8	109.8 (C9)
130.5	130.4 (C1)
142.3	142.3 (C2)
150.0 (correct)	159.9 (C8) (error)
167.3	167.2 (C7)

The ^{13}C chemical shift that differs significantly from that of the reported natural product is shown in bold. This difference comes from a human careless mistake in the assignment of isolated natural product.

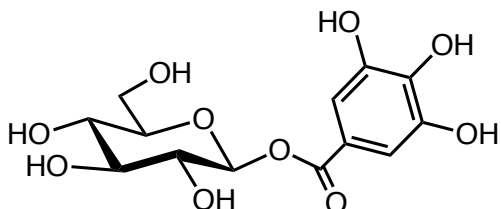
(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl 3,4,5-tris(benzyloxy)benzoate (**S1**).



General procedure A for the synthesis of glycoside was followed, starting with α -D-glucose (300 mg, 1.67

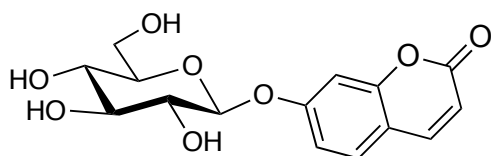
mmol, 3.0 equiv.), 3,4,5-tris(benzyloxy)benzoic acid¹ (244 mg, 0.555 mmol, 1.0 equiv.), DIAD (219 μ L, 1.11 mmol, 2.0 equiv.), and Ph₃P (291 mg, 1.11 mmol, 2.0 equiv.) in 1,4-dioxane (55 mL) for 1 h, affording corresponding the glucoside (237 mg, 71%, $\alpha/\beta=1/99$) as a white amorphous powder after purification by flash chromatography, eluting with CHCl₃/MeOH (50:1 to 5:1 v/v). Analytical data: $[\alpha]_D^{21} = -4.1$ (*c* 1.0, acetone); **TLC** (CHCl₃/MeOH 5:1 v/v): *R_f* = 0.43; **¹H NMR** (400 MHz, acetone-*d*₆+D₂O) δ : 7.55–7.26 (m, 17H), 5.70 (d, *J* = 7.6 Hz, 1H), 5.23 (s, 4H), 5.14 (s, 2H), 3.84–3.81 (m, 1H), 3.71–3.67 (m, 1H), 3.55–3.53 (m, 2H), 3.48–3.46 (m, 2H); **¹³C NMR** (150 MHz, acetone-*d*₆) δ : 165.1, 153.6, 143.6, 138.7, 138.0, 129.4, 129.2, 129.0, 128.8, 128.69, 128.65, 125.7, 110.1, 96.1, 78.6, 78.0, 75.5, 73.9, 71.8, 71.2, 62.5; **IR** (KBr, cm⁻¹): 3331, 3203, 2367, 1714, 1647, 1591, 1503, 1427, 1335, 1252, 1217, 1133, 1085, 985, 858, 730, 690; **HRMS-ESI⁻** (*m/z*): Calcd. for C₃₄H₃₄O₁₀Cl [M+Cl]⁻ 637.1840; found, 637.1835.

β -Glucogallin (8).



A 10 mL round-bottom flask was charged with **S1** (200 mg, 0.33 mmol, 1.0 equiv.) and Pd(OH)₂/C (10 wt.%, 20.0 mg). 3.3 mL of EtOH/acetone (4/1) was added and the atmosphere was replaced by H₂ (balloon). The reaction mixture was stirred at rt for 4 h until TLC analysis indicated complete consumption of the starting material. The resulting suspension was filtered and washed with acetone. The filtrate was concentrated in vacuo to give β -glucogallin (**7**) (105 mg, 95%) as a pale gray amorphous powder. Analytical data: $[\alpha]_D^{21} = -9.8$ (*c* 1.0, MeOH), reported $[\alpha]_D^{20} = -8.0$ (*c* 0.1, MeOH)⁹; **¹H NMR** (600 MHz, methanol-*d*₄) δ : 7.12 (s, 2H), 5.65 (d, *J* = 7.8 Hz, 1H), 3.85 (dd, *J* = 12.0 Hz, 2.4 Hz, 1H), 3.70 (dd, *J* = 12.6, 4.8 Hz, 1H), 3.48–3.47 (m, 2H), 3.43–3.40 (m, 2H); **¹³C NMR** (150 MHz, methanol-*d*₄) δ : 167.1, 146.5, 140.3, 120.8, 110.5, 96.0, 78.8, 78.2, 74.1, 71.1, 62.3; **IR** (KBr, cm⁻¹): 3550, 3307, 2925, 1714, 1594, 1451, 1395, 1316, 1281, 1077, 1021, 711; **HRMS-ESI⁻** (*m/z*): Calcd. for C₁₃H₁₅O₁₀ [M-H]⁻ 331.0658; found, 331.0660.

Skimmin (9).

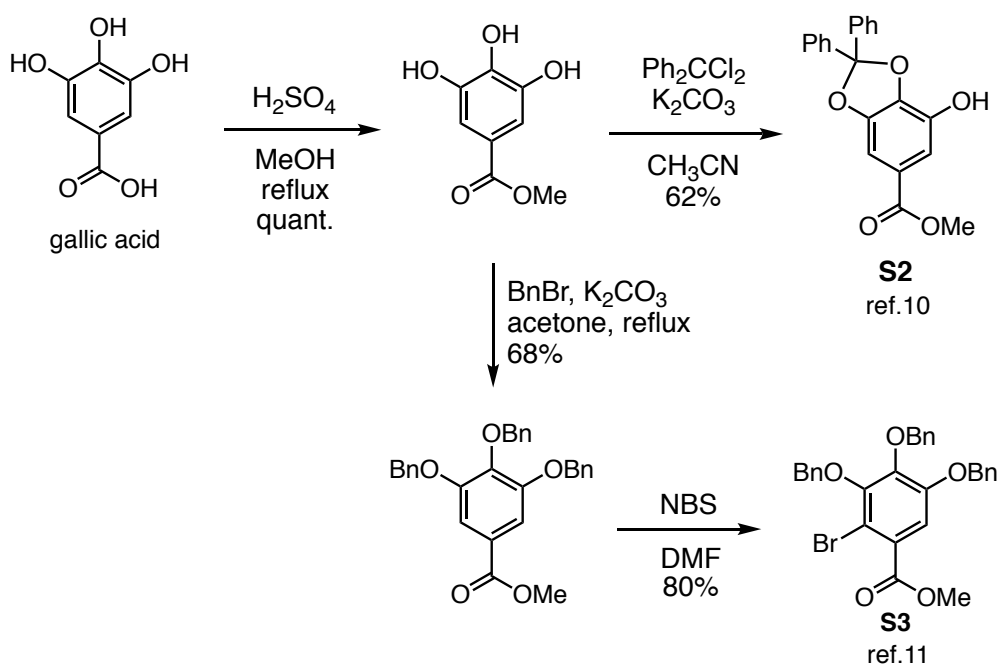


A round-bottom flask was charged with α -D-glucose (101 mg, 0.56 mmol, 3.0 equiv.) and dehydrated 1,4-dioxane (19 mL) under an Ar atmosphere. After ultrasound irradiation of the suspension of α -D-glucose in 1,4-dioxane for 15 min, umbelliferone (30.5 mg, 0.19 mmol, 1.0 equiv.) and Ph₃P (98.6 mg, 0.38 mmol, 2.0 equiv.) were added. DIAD (74 μ L, 0.38 mmol, 2.0 equiv.) was added dropwise by syringe and the reaction mixture was stirred at 55 °C. After stirring vigorously for 15 min, DIAD (74 μ L, 0.38 mmol, 2.0

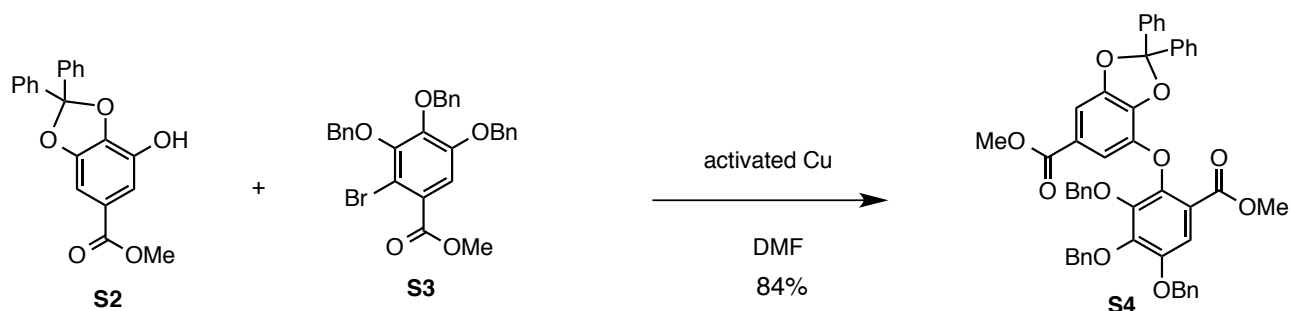
equiv.) and Ph_3P (98.6 mg, 0.38 mmol, 2.0 equiv.) were added again in the same manner and stirred at 55 °C for 45 min. The reaction mixture was quenched with 3 mL of MeOH, stirred for 5 min, and concentrated in vacuo at 40 °C to give a residue. The residue was directly purified by flash column chromatography (SiO_2 , $\text{CHCl}_3/\text{MeOH}$ 10:1 to 5:1 v/v) to give the skimmin (**1z**) (37.2 mg, 61%, $\alpha/\beta=4:96$) as a white amorphous powder. Analytical data: $[\alpha]_D^{19} = -177$ (*c* 0.1, MeOH); TLC ($\text{CHCl}_3/\text{MeOH}$ 5/1 v/v): $R_f=0.29$; $^1\text{H NMR}$ (400 MHz, $\text{DMSO}-d_6$) δ : 8.01 (d, $J = 9.6$ Hz, 1H), 7.65 (d, $J = 8.7$ Hz, 1H), 7.05 (d, $J = 2.3$ Hz, 1H), 7.01 (dd, $J = 11.0, 2.3$ Hz, 1H), 6.33 (d, $J = 9.6$ Hz, 1H), 5.43 (brs, 1H), 5.19 (d, $J = 4.6$ Hz, 1H), 5.11 (d, $J = 5.5$ Hz, 1H), 5.03 (d, $J = 7.3$ Hz, 1H), 4.61 (t, $J = 6.0$ Hz, 1H), 3.70 (dd, $J = 10.1, 5.0$ Hz, 1H), 3.47–3.42 (m, 2H), 3.28–3.13 (m, 3H); $^{13}\text{C NMR}$ (100 MHz, $\text{DMSO}-d_6$) δ : 160.3, 160.2, 155.1, 144.3, 129.5, 113.7, 113.3, 113.2, 103.2, 100.0, 77.2, 76.5, 73.1, 69.6, 60.6; **IR** (KBr, cm^{-1}): 3356, 2915, 1717, 1621, 1404, 1281, 1073, 1016, 838; **HRMS-ESI**⁺ (*m/z*): Calcd. for $\text{C}_{15}\text{H}_{17}\text{O}_8$ $[\text{M}+\text{H}]^+$ 325.0918; found, 325.0895.

Access to aglycone **13**

Methyl 3-hydroxy-4,5-(diphenylmethylene)dioxybenzoate (**S2**) and methyl 2-bromo-3,4,5-tris(benzyloxy)benzoate (**S3**) were prepared according to the reported methods.^{10,11}

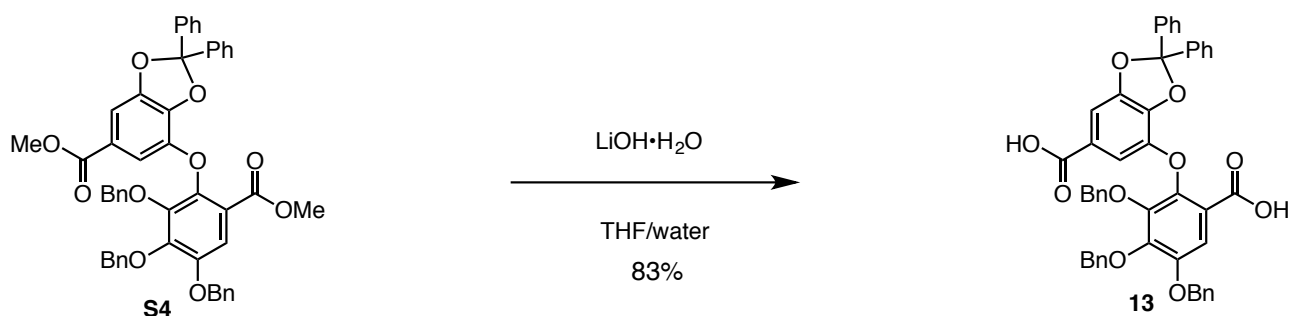


Dimethylester **S4**



A mixture of **S2** (2.00 g, 5.74 mmol, 1.0 equiv.), **S3** (7.66 g, 14.3 mmol, 2.5 equiv.) and activated Cu (1.82 g, 28.6 mmol, 5.0 equiv.) in DMF (82 mL) was stirred under reflux for 12 h. The reaction mixture was cooled to room temperature and filtered through a pad of Celite. The filtrate was diluted with hexane/AcOEt (1/1) and washed with water (2 times) and brine. The organic layer was dried over Na₂SO₄ and concentrated in vacuo to give a residue. The residue was purified by flash chromatography (SiO₂, hexane/AcOEt 10:1 to 1:1 v/v) to give the product **S4** (3.87 g, 84%) as a yellow solid. Analytical data: **TLC** (hexane/AcOEt 3:1 v/v): R_f = 0.38; **¹H NMR** (400 MHz, CDCl₃) δ: 7.56–7.06 (m, 27H), 7.01 (d, *J* = 1.4 Hz, 1H), 5.14 (s, 2H), 5.07 (s, 2H), 4.90 (s, 2H), 3.78 (s, 3H), 3.56 (s, 3H); **¹³C NMR** (100 MHz, CDCl₃) δ: 166.3, 165.4, 150.1, 148.7, 147.0, 146.8, 142.7, 142.1, 139.7, 138.9, 136.9, 136.8, 136.3, 129.4, 128.72, 128.69, 128.43, 128.39, 128.32, 128.29, 128.1, 128.0, 127.8, 126.3, 124.3, 119.8, 118.8, 112.4, 110.9, 104.4, 75.9, 75.7, 71.4, 52.3, 52.2 (One sp² carbon signal missing, possibly due to a signal overlap.); **IR** (KBr, cm⁻¹): 3033, 2949, 1712, 1631, 1504, 1434, 1203, 1078, 752, 697; **HRMS-FAB⁺** (*m/z*): Calcd. for C₅₀H₄₀O₁₀Na [M+Na]⁺ 823.2519; found, 823.2518.

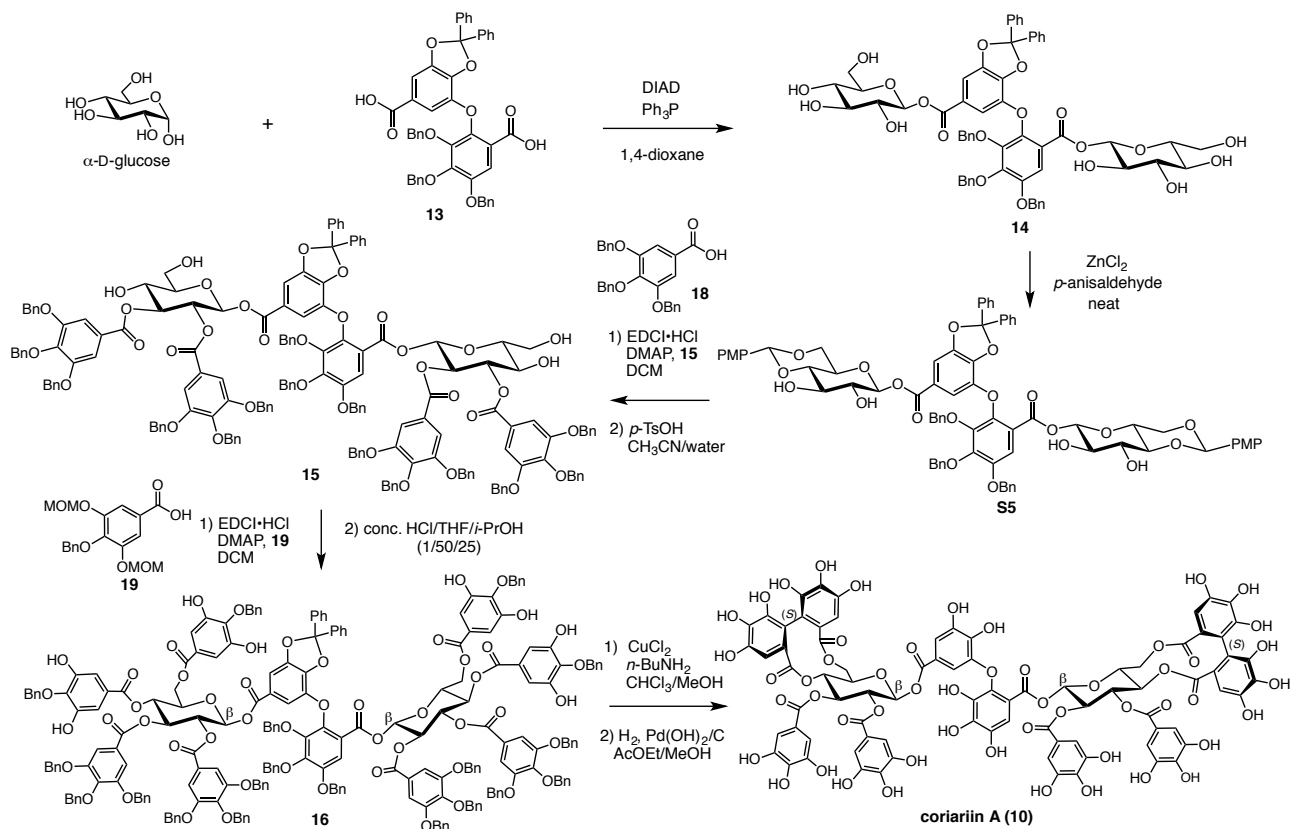
Dicarboxylic acid **13**



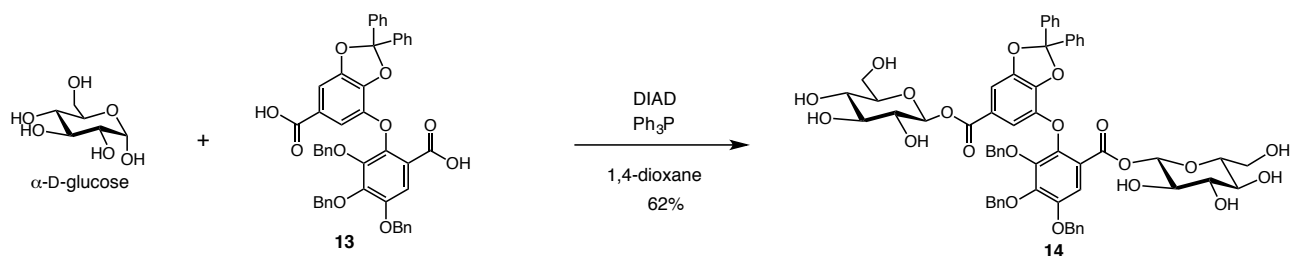
LiOH·H₂O (770 mg, 18.4 mmol, 5.0 equiv.) was added to a solution of **S4** (2.94 g, 3.67 mmol, 1.0 equiv.) in 40 mL of THF/H₂O (3/1). After stirred at 50 °C for 21 h, the reaction mixture was concentrated in vacuo (removal of THF) to give an aqueous residue. The aqueous residue was acidified to around pH=2 by saturated citric acid aq. and extracted with AcOEt (2 times). The combined organic layer was washed with brine, dried over Na₂SO₄ and concentrated in vacuo to give a residue. The residue was purified by flash chromatography (SiO₂, CHCl₃/MeOH 40:1 to 10:1 v/v) to give **13** (2.34 g, 83%) as a pale yellow amorphous powder. Analytical data: **TLC** (CHCl₃/MeOH 10:1 v/v): R_f = 0.43; **¹H NMR** (400 MHz, acetone-*d*₆+D₂O) δ:

7.60–7.06 (m, 28H), 5.29 (s, 2H), 5.15 (s, 2H), 4.92 (s, 2H); ¹³C NMR (100 MHz, acetone-*d*₆+D₂O) δ: 166.6, 165.7, 151.0, 149.5, 147.4, 147.3, 143.3, 143.2, 140.8, 139.5, 138.1, 137.79, 137.76, 130.2, 129.4, 129.3, 129.1, 129.0, 128.8, 128.7, 126.8, 125.5, 121.2, 119.3, 113.5, 111.6, 104.6, 76.2, 76.0, 71.8 (Four carbon signals missing, possibly due to signal overlaps.); IR (KBr, cm⁻¹): 3032, 2945, 2873, 1690, 1631, 1439, 1205, 1091, 1016, 743, 695; HRMS-FAB⁺ (*m/z*): Calcd. for C₄₈H₃₇O₁₀ [M+H]⁺ 773.2387; found, 773.2387.

Total synthesis of coriariin A (10)



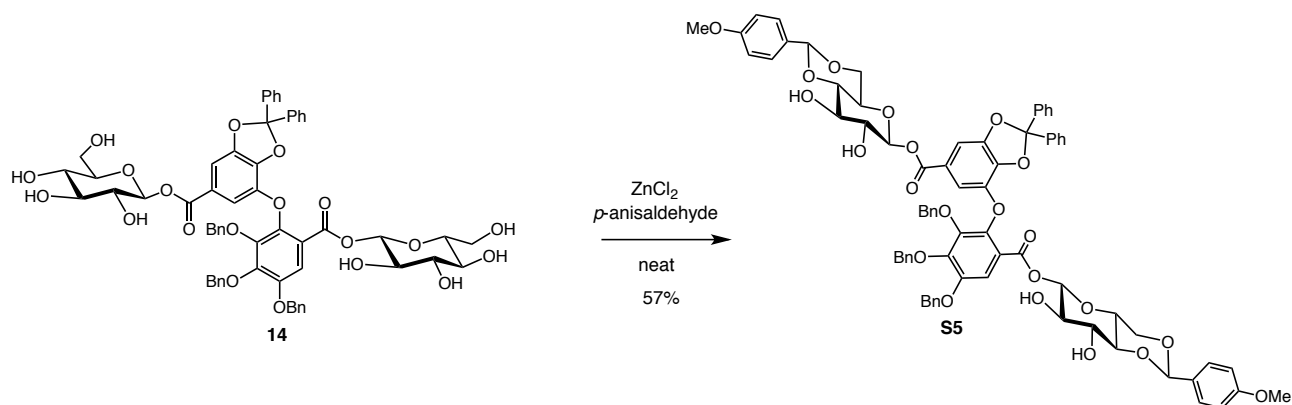
Diglucoside 13



General procedure A for the synthesis of glycoside was followed, starting with α-D-glucose (139 mg, 0.77 mmol, 6.0 equiv.), dicarboxylic acid **13** (100 mg, 0.13 mmol, 1.0 equiv.), DIAD (100 μL, 0.52 mmol, 4.0 equiv.), and Ph₃P (135 mg, 0.51 mmol, 4.0 equiv.). The reaction mixture was stirred for 30 min in 1,4-dioxane (4.3 mL). Desired β,β-diglucoside **14** containing small amount of α,β- or β,α-diglucosides

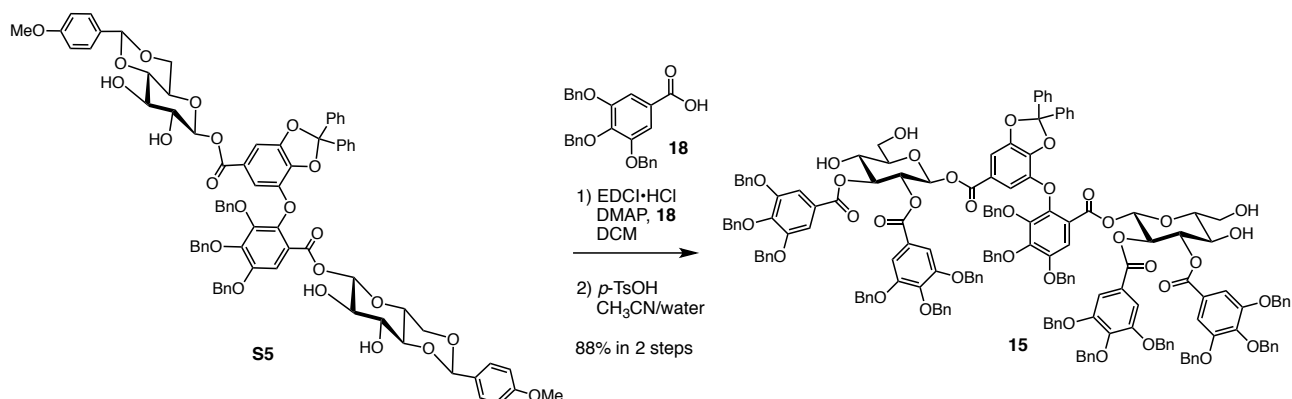
(β,β /other stereoisomers = 96/4) was obtained as a white amorphous powder after purification by flash chromatography, eluting with $\text{CHCl}_3/\text{MeOH}$ (50:1 to 5:1 v/v). It was further purified with recycle HPLC ($\text{CHCl}_3:\text{MeOH}$ 7:1) to give β,β -diglucoside **13** as a white amorphous powder (87.5 mg, 62%). Analytical data: $[\alpha]_{\text{D}}^{21} = +5.4$ (c 0.5, MeOH); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 5:1 v/v): $R_f = 0.20$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 7.67–7.08 (m, 28H), 5.64 (d, $J = 7.8$ Hz, 1H), 5.61 (d, $J = 8.2$ Hz, 1H), 5.28 (s, 2H), 5.13 (s, 2H), 4.92–4.89 (m, 2H), 3.80–3.34 (m, 12H); **$^{13}\text{C NMR}$** (100 MHz, acetone- d_6 + D_2O) δ : 164.7, 163.2, 151.0, 149.6, 147.9, 147.6, 144.0, 143.1, 140.6, 140.5, 139.9, 138.0, 137.65, 137.57, 130.2, 129.4, 129.3, 129.1, 129.01, 128.97, 128.8, 126.9, 124.6, 120.1, 119.6, 114.2, 111.8, 104.9, 96.0, 95.9, 79.2, 78.5, 78.3, 77.8, 77.7, 76.3, 76.1, 73.7, 72.0, 71.0, 70.9, 62.4, 62.3 (Three carbon signals missing, possibly due to signal overlaps.); **IR** (KBr, cm^{-1}): 3331, 1715, 1631, 1502, 1436, 1380, 1312, 1205, 1077, 1015, 741, 697; **HRMS-ESI $^+$** (m/z): Calcd. for $\text{C}_{60}\text{H}_{56}\text{O}_{20}\text{Na}$ $[\text{M}+\text{Na}]^+$ 1119.3257; found, 1119.3263.

Tetraol S5



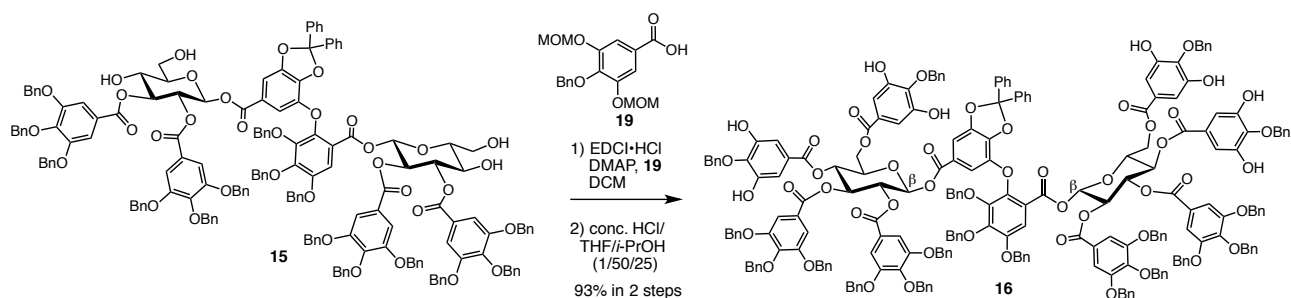
A mixture of *p*-anisaldehyde (10.2 mL, 83.8 mmol, 100 equiv.), ZnCl_2 (1.14 g, 8.36 mmol, 10 equiv.), and **14** (920 mg, 0.84 mmol, 1.0 equiv.) was stirred at rt for 2 h. Excess aldehyde was quenched with 15% w/v NaHSO_3 aq. and the resulting mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4 , and concentrated in vacuo to give a residue. The residue was purified by flash column chromatography (SiO_2 , hexane/AcOEt 5:1 to 1:1 v/v) to give tetraol **S5** (633 mg, 57%) as a white amorphous powder. Analytical data: $[\alpha]_{\text{D}}^{21} = -11$ (c 1.0, acetone); **TLC** ($\text{CHCl}_3/\text{MeOH}$ 10:1 v/v): $R_f = 0.37$; **$^1\text{H NMR}$** (400 MHz, acetone- d_6 + D_2O) δ : 7.67–7.08 (m, 32H), 6.90 (dd, $J = 8.7, 3.2$ Hz, 4H), 5.78 (d, $J = 7.8$ Hz, 1H), 5.73 (d, $J = 8.2$ Hz, 1H), 5.51 (s, 1H), 5.44 (s, 1H), 5.29 (s, 2H), 5.12 (s, 2H), 4.92–4.85 (m, 2H), 4.19 (dd, $J = 9.6, 4.6$ Hz, 1H), 4.08–4.05 (m, 1H), 3.80–3.48 (m, 16H); **$^{13}\text{C NMR}$** (100 MHz, acetone- d_6 + D_2O) δ : 164.5, 163.2, 160.9, 151.1, 149.7, 148.0, 147.6, 144.0, 143.1, 140.62, 140.56, 140.0, 138.0, 137.63, 137.57, 131.32, 131.30, 130.2, 129.41, 129.37, 129.1, 129.01, 128.96, 128.92, 128.8, 128.6, 126.84, 126.79, 124.4, 119.9, 119.6, 114.4, 114.0, 111.7, 104.9, 102.14, 102.07, 96.2, 96.0, 81.6, 81.4, 76.3, 76.1, 74.6, 74.5, 74.3, 74.2, 72.0, 68.91, 68.87, 67.9, 67.7, 55.5 (Five carbon signals missing, possibly due to signal overlaps.); **IR** (KBr, cm^{-1}): 3459, 2873, 1731, 1614, 1437, 1381, 1307, 1252, 1197, 1074, 830, 752, 695; **HRMS-ESI $^+$** (m/z): Calcd. for $\text{C}_{76}\text{H}_{68}\text{O}_{22}\text{Na}$ $[\text{M}+\text{Na}]^+$ 1355.4094; found, 1355.4077.

Tetraol **S6**.



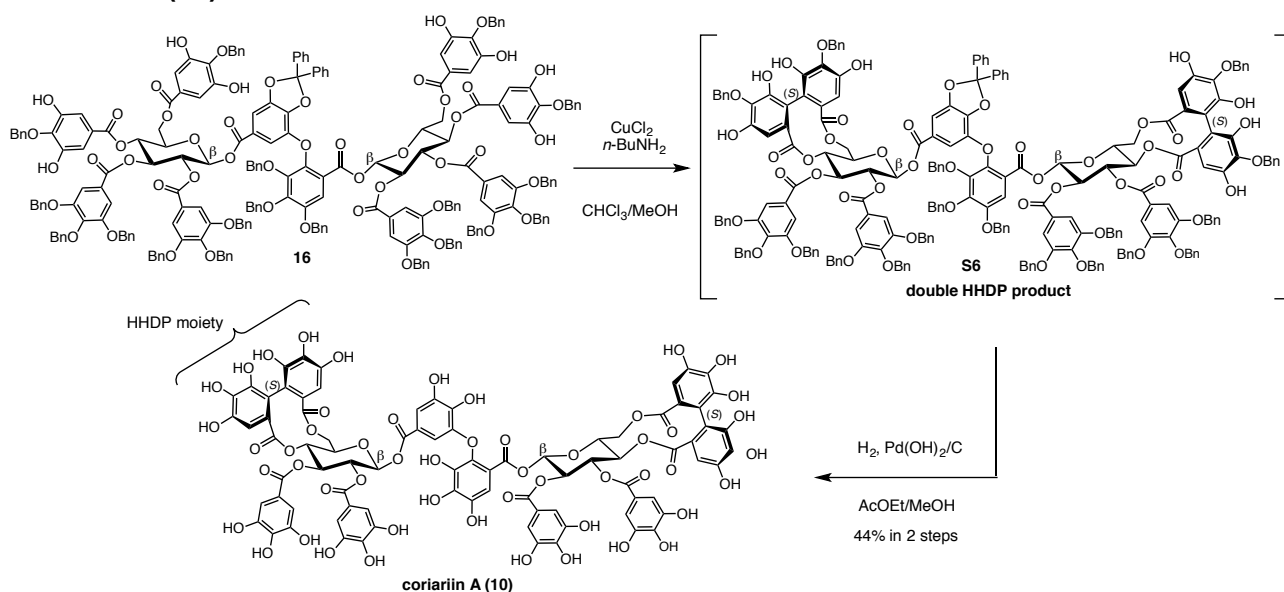
3,4,5-Tris(benzyloxy)benzoic acid **18** (2.09 g, 4.75 mmol, 4.4 equiv.), DMAP (264 mg, 2.16 mmol, 2.0 equiv.), and EDCI·HCl (1.24 g, 6.48 mmol, 6.0 equiv.) were added to a solution of **S5** in DCM (40 mL). The resulting mixture was stirred at rt for 6 h. The reaction mixture was concentrated, dissolved in AcOEt, and washed with saturated NH₄Cl aq., water, and brine. The organic layer was dried over Na₂SO₄ and concentrated in vacuo to give a residue. The residue was purified by flash chromatography (SiO₂, hexane/AcOEt 2:1 to 1:1 v/v) to give sufficiently pure tetra-gallate (3.11 g, 95%) for the next reaction. To a solution of the tetra-gallate (500 mg, 0.17 mmol, 1.0 equiv.) in 10.5 mL of CH₃CN/water (20/1) was added *p*-toluenesulfonic acid monohydrate (6.3 mg, 0.033 mmol, 0.19 equiv.). The resulting mixture was warmed to 50 °C and stirred at the same temperature for 2.5 h. The reaction mixture was concentrated in vacuo to give a residue. The residue was purified by flash chromatography (SiO₂, CHCl₃/MeOH 30:1 to 20:1 v/v) to give tetraol **15** (430 mg, 93%) as a white amorphous. Analytical data: $[\alpha]_D^{21} = +51$ (*c* 1.0, CHCl₃); **TLC** (CHCl₃/MeOH 30:1 v/v): *R_f* = 0.41; **¹H NMR** (400 MHz, acetonitrile-*d*₃+D₂O, 50 °C) δ : 7.48 (s, 1H), 7.43–7.10 (m, 92H), 7.04–6.99 (m, 1H), 6.91 (t, *J* = 7.8 Hz, 1H), 6.83–6.80 (m, 1H), 6.08 (d, *J* = 8.3 Hz, 1H), 6.01 (d, *J* = 8.2 Hz, 1H), 5.60–5.52 (m, 2H), 5.38–5.28 (m, 2H), 5.13–4.66 (m, 30H), 3.87–3.61 (m, 8H); **¹³C NMR** (100 MHz, acetone-*d*₆+D₂O) δ : 166.5, 166.0, 165.7, 164.4, 162.4, 153.3, 150.9, 149.8, 148.2, 147.6, 144.2, 143.5, 143.4, 143.32, 143.29, 142.9, 140.4, 140.3, 140.2, 138.6, 138.5, 137.8, 137.7, 137.6, 137.5, 137.4, 137.3, 137.2, 130.1, 129.4, 129.2, 129.04, 129.01, 128.9, 128.8, 128.74, 128.69, 128.6, 128.5, 128.4, 128.3, 126.8, 126.7, 125.7, 125.0, 124.9, 123.8, 119.7, 118.7, 114.5, 111.5, 109.7, 109.6, 109.5, 105.1, 93.7, 78.3, 77.1, 76.12, 76.08, 75.4, 73.0, 72.7, 71.9, 71.5, 71.35, 71.26, 69.1, 69.0, 61.6, 61.5 (Thirty-five carbon signals missing, possibly due to signal overlaps.); **IR** (KBr, cm⁻¹): 3410, 3063, 3032, 2931, 2875, 1729, 1588, 1497, 1429, 1374, 1335, 1195, 1108, 1016, 749, 696, 486; **HRMS-ESI⁺** (*m/z*): Calcd. for C₁₇₂H₁₄₄O₃₆Na₂ [M+2Na]²⁺ 1415.9628; found, 1415.9600.

Octaphenol 16



3,5-Bis(methoxymethoxy)-4-benzyloxybenzoic acid **19** (186 mg, 0.53 mmol, 4.4 equiv.), DMAP (14.9 mg, 0.12 mmol, 1.0 equiv.), EDCI·HCl (140 mg, 0.73 mmol, 6.1 equiv.) were added to a solution of **15** (339 mg, 0.12 mmol, 1.0 equiv.) in DCM (10 mL). The resulting mixture was stirred for 26 h. The reaction mixture was concentrated, then dissolved in AcOEt and washed with saturated NH₄Cl aq., water, and brine. The organic layer was dried over Na₂SO₄ and concentrated in vacuo to give a residue. The residue was purified by flash chromatography (SiO₂, hexane/AcOEt 1:1 v/v) to afford sufficiently pure octagallate (485 mg, 97%) for the next reaction. The octagallate (109 mg, 0.027 mmol, 1.0 equiv.) was dissolved in 3.0 mL of 2-propanol/THF (2/1) containing conc. HCl aq. (40 μL). The resulting mixture was warmed to 50 °C and stirred at the same temperature for 12 h. The reaction mixture was quenched with saturated NaHCO₃ aq. and concentrated in vacuo to give an aqueous residue. The aqueous residue was diluted with AcOEt, washed with water and brine. The organic layer was dried over Na₂SO₄ and concentrated in vacuo to give a residue. The residue was purified by flash chromatography (SiO₂, CHCl₃/MeOH 30:1 to 20:1 v/v) and oven-dried (70 °C) to give the octaphenol **16** (96.1 mg, 96%) as a white amorphous. Analytical data: $[\alpha]_D^{20} = +8.9$ (*c* 0.5, acetone); **TLC** (CHCl₃/MeOH 30:1 v/v): *R_f* = 0.33; **¹H NMR** (400 MHz, acetone-*d*₆) δ : 8.50–8.42 (m, 8H), 7.69 (s, 1H), 7.61–6.88 (m, 115H), 6.38 (d, *J* = 8.2 Hz, 1H), 6.35 (d, *J* = 8.2 Hz, 1H), 6.15–6.09 (m, 2H), 5.85 (t, *J* = 9.2 Hz, 1H), 5.78–5.68 (m, 3H), 5.30–4.93 (m, 36H), 4.76–4.45 (m, 8H); **¹³C NMR** (150 MHz, acetone-*d*₆) δ : 166.1, 165.9, 165.6, 165.5, 164.1, 162.1, 153.4, 151.31, 151.27, 151.24, 150.9, 149.8, 148.3, 147.4, 144.7, 143.7, 143.6, 143.4, 142.9, 140.41, 140.35, 140.2, 139.6, 139.1, 138.54, 138.49, 138.4, 137.8, 137.55, 137.45, 137.3, 130.2, 129.4, 129.2, 129.11, 129.08, 129.0, 128.9, 128.8, 128.73, 128.69, 128.6, 128.5, 126.7, 126.6, 126.0, 125.9, 125.2, 125.0, 124.9, 124.7, 123.6, 119.7, 118.5, 115.3, 111.5, 110.3, 110.24, 110.18, 109.8, 109.7, 109.6, 105.1, 93.6, 93.5, 76.1, 76.0, 75.5, 75.4, 74.6, 74.4, 74.3, 73.7, 72.9, 72.6, 72.0, 71.6, 69.6, 69.5, 63.2, 62.9 (Sixty-five carbon signals missing, possibly due to signal overlaps.); **IR** (KBr, cm⁻¹): 3512, 3032, 2949, 1729, 1591, 1499, 1432, 1338, 1195, 1099, 1011, 752, 695; **HRMS-ESI⁺** (*m/z*): Calcd. for C₂₂₈H₁₈₄O₅₂Na₂ [*M*+2Na]²⁺ 1900.5803; found, 1900.5771.

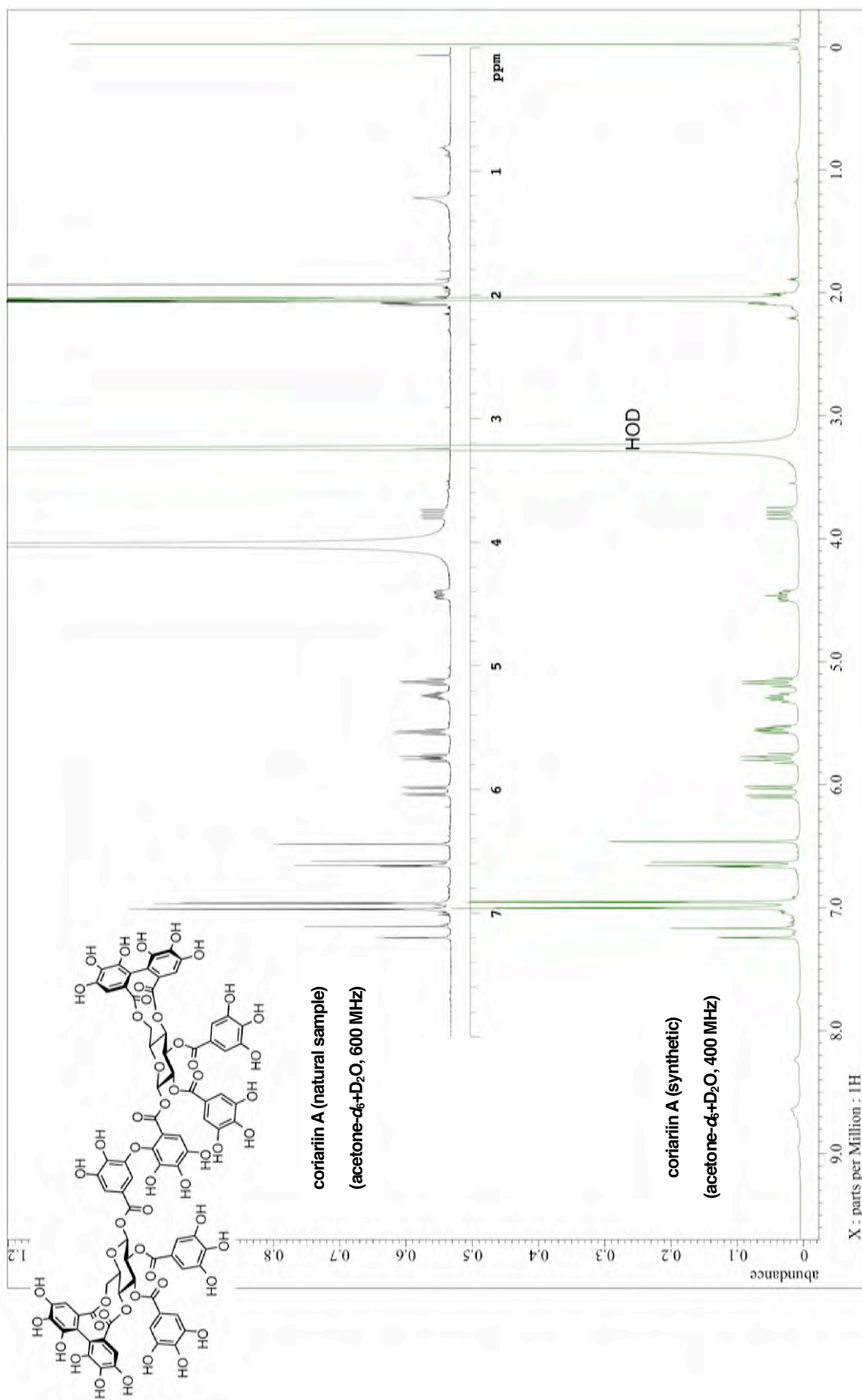
Coriariin A (10)



A solution of CuCl_2 (14.0 mg, 0.10 mmol, 3.7 equiv.) and $n\text{-BuNH}_2$ (105 μL , 1.06 mmol, 39 equiv.) in MeOH (2.0 mL) was stirred for 30 min at rt to prepare a blue solution of $\text{CuCl}_2/n\text{-BuNH}_2$ complex under Ar atmosphere. A 20 mL round-bottom flask was charged with octaphenol **16** (100 mg, 0.027 mmol, 1.0 eq.) and CHCl_3 (2.0 mL). Then a blue solution of $\text{CuCl}_2/n\text{-BuNH}_2$ complex was added in one portion. The resulting solution was stirred at rt under Ar atmosphere for 1 h. The reaction mixture was quenched with saturated NH_4Cl aq. The layers were separated and the aqueous layer was extracted with CHCl_3 . The combined organic extracts were washed with water and brine, dried over Na_2SO_4 and concentrated in vacuo to give a residue. The residue was purified by flash chromatography (SiO_2 , $\text{CHCl}_3/\text{MeOH}$ 30:1 to 20:1 v/v) to give sufficiently pure double HHDP product (57.0 mg, 57%) for next reaction. (Note: Compound **16** was not able to be separated from the desired product **S6**. When octaphenol **16** remained in this coupling reaction, the crude mixture was further treated with the coupling conditions until full conversion to the double HHDP product **S6**.) A mixture of **S6** (131 mg, 0.035 mmol, 1.0 equiv.) and $\text{Pd(OH)}_2/\text{C}$ (65.5 mg, 50 wt.%) in AcOEt (5.0 mL) and MeOH (2.0 mL) was stirred under H_2 atmosphere (H_2 balloon) for 15 h. The resulting suspension was filtered and washed with MeOH. The filtrate was concentrated in vacuo to give a residue. To complete the removal of diphenyleneacetal moiety, a mixture of the crude material and fresh $\text{Pd(OH)}_2/\text{C}$ (65.5 mg, 50 wt.%) in MeOH (3.5 mL) was stirred under H_2 atmosphere (H_2 balloon) for 15 h. The resulting suspension was filtered and washed with MeOH, and the filtrate was concentrated in vacuo to give a brown solid. The brown solid was grinded with a spatula, suspended in Et_2O and triturated by sonication for 2 h to dissolve diphenylmethane derived from the protecting group. Et_2O was then removed by decantation and the resulting powder was dried well in vacuo to give coriariin A (**10**) (50.8 mg, 78%) as a brown powder. Analytical data: $[\alpha]_{\text{D}}^{20} = +80$ (c 0.1, acetone); $^1\text{H NMR}$ (400 MHz, acetone- d_6 + D_2O) δ : 7.24 (d, $J = 1.8$ Hz, 1H), 7.17 (s, 1H), 7.01 (s, 2H), 7.00 (s, 2H), 6.96 (s, 2H), 6.95 (s, 2H), 6.67 (d, $J = 1.8$ Hz, 1H), 6.66 (s, 1H), 6.63 (s, 1H), 6.46 (s, 2H), 6.10 (d, $J = 8.2$ Hz, 1H), 6.02 (d, $J = 8.2$ Hz, 1H), 5.82–5.75 (m, 2H), 5.59–5.53 (m, 2H), 5.33–5.26 (m, 2H), 5.20–5.14 (m, 2H), 4.50–4.42 (m, 2H), 3.82 (d, $J = 13.3$ Hz, 1H), 3.76 (d, $J = 13.3$ Hz, 1H); $^{13}\text{C NMR}$ (150 MHz, acetone- d_6 + D_2O) δ : 168.1, 168.0, 167.6, 166.4, 165.9, 165.6, 164.7,

162.1, 147.9, 146.3, 145.81, 145.78, 145.7, 145.1, 145.0, 144.2, 143.2, 141.0, 140.7, 140.3, 139.3, 139.2, 139.0, 137.5, 136.4, 136.21, 136.19, 126.2, 125.59, 125.56, 120.2, 120.0, 119.9, 119.1, 115.70, 115.67, 115.52, 115.50, 112.7, 112.1, 110.0, 109.8, 108.04, 107.96, 107.7, 93.5, 93.0, 73.2, 73.1, 72.8, 72.7, 71.6, 71.5, 70.52, 70.47, 62.92, 62.88; **IR** (KBr, cm^{-1}): 3371, 1729, 1614, 1349, 1205, 1032, 740; **HRMS-ESI⁺** (m/z): Calcd. for $\text{C}_{82}\text{H}_{58}\text{O}_{52}\text{Na}$ $[\text{M}+\text{Na}]^{1+}$ 1897.1786; found, 1897.184

Comparison of ¹H NMR Spectrum of coriariin A (10)



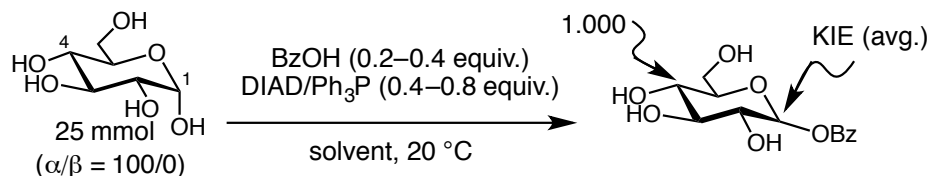
Comparison of ¹³C NMR between synthetic coriariin A (10) and the literature data^{12,13}.

Synthetic 10 (150 MHz, acetone- <i>d</i> ₆ +D ₂ O) ^a	Reported-1 (isolated) ¹² (50.1 MHz, acetone- <i>d</i> ₆ +D ₂ O) ^a	Reported-2 (synthetic) ¹³ (90 MHz, acetone- <i>d</i> ₆ +D ₂ O) ^a
62.88	63.3 (2C)	62.8
63.92		62.9
70.47	70.8 (2C)	70.5
70.52		70.5
71.5	71.7 (2C)	71.5
71.6		71.5
72.7	72.8 (2C)	72.8
72.8		72.8
73.1	73.5 (2C)	73.0
73.2		73.1
93.0	93.1	93.1
93.5	93.6	93.5
107.7	107.8	107.6
107.96	108.2 (4C)	108.0
108.04		108.1
109.8	110.3	109.9
110.0	110.3 (8C)	110.0
		110.1
112.1	112.5	112.1
112.7	115.8	112.2
115.50	116.1 (4C)	115.5
115.52		
115.67		115.6
115.70		
119.1	118.7	– ^b
119.9	119.8 (4C)	120.1
120.0		120.2
120.2		120.2
		120.3
125.56	125.4 (2C)	125.7
125.59		125.7
126.2	125.9 (2C)	126.3
–	–	126.6 ^c
–	–	129.0 ^c

Synthetic 10 (150 MHz, acetone- <i>d</i> ₆ +D ₂ O) ^a	Reported-1 (isolated) ¹² (50.1 MHz, acetone- <i>d</i> ₆ +D ₂ O) ^a	Reported-2 (synthetic) ¹³ (90 MHz, acetone- <i>d</i> ₆ +D ₂ O) ^a
–	–	129.1 ^c
–	–	129.1 ^c
–	–	129.5 ^c
136.19	136.5 (2C)	136.2
136.21		
136.5	136.8 (2C)	136.3
137.5	138.0	138.9
139.0	139.6 (2C)	139.1
139.2	139.8 (2C)	139.1
139.3		139.2
140.3	140.4	140.3
140.7	141.3	140.7
141.0	141.8	141.0
143.2	143.3	143.2
144.2	144.6 (4C)	144.3
145.0	145.2 (4C)	145.0
145.1		145.0
145.7	145.9 (8C)	145.6
145.78		145.7
145.81		145.7
146.3	145.9	146.3
147.9	148.1	147.8
–	–	161.6 ^d
162.1	162.6	162.0
164.7	165.1	164.7
165.6	165.5 (2C)	165.6
165.9		
166.4	167.0 (2C)	166.2
167.6	168.0 (2C)	167.5
168.0	168.8 (2C)	167.9
168.1		168.0

^a1,4-Dioxane (67.4 ppm) was used as an internal standard. ^bThe signal (Reported-2) corresponds to 119.1 ppm (synthetic **10**) and 118.7 ppm (Reported-1) was not assigned. ^cThese signals (Reported-2) might come from the impurity (diphenylmethane) from the final deprotection step.¹³ ^dThis signal (Reported-2) might also come from some impurities.

IV. KIE MEASUREMENTS (Table S3)



Entry	Solvent	BzOH (eq.)	DIAD/Ph ₃ P (eq.)	Conversion (%) ^a	α/β	KIE (20 °C)
1	1,4-dioxane	0.2	0.4	14.6	1/99	1.026
2	1,4-dioxane	0.2	0.4	16.6	1/99	1.033
3	1,4-dioxane	0.4	0.8	25.7	1/99	1.026
average						1.028

4	DMF	0.2	0.4	8.9	60/40	1.005
5	DMF	0.2	0.4	6.2	63/37	1.000
6	DMF	0.4	0.8	9.4	58/42	0.998
average						1.001

^aDetermined by crude ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard.

Primary ¹³C KIE was determined for the formation of glycoside using natural abundance NMR method.¹⁴ A round-bottom flask was charged with powdered α -D-glucose and dehydrated 1,4-dioxane (0.03 M of α -D-glucose) under an Ar atmosphere. After ultrasound irradiation of the suspension of α -D-glucose in 1,4-dioxane for 15 min, benzoic acid and Ph₃P were added. DIAD was added dropwise by syringe and the resulting mixture was stirred vigorously at rt for 30 min. The reaction mixture was quenched with MeOH, stirred for 5 min, and concentrated in vacuo at 40 °C to give a residue. The residue was directly purified by flash column chromatography (SiO₂, CHCl₃/MeOH 50:1 to 5:1 v/v) to give the glycoside.

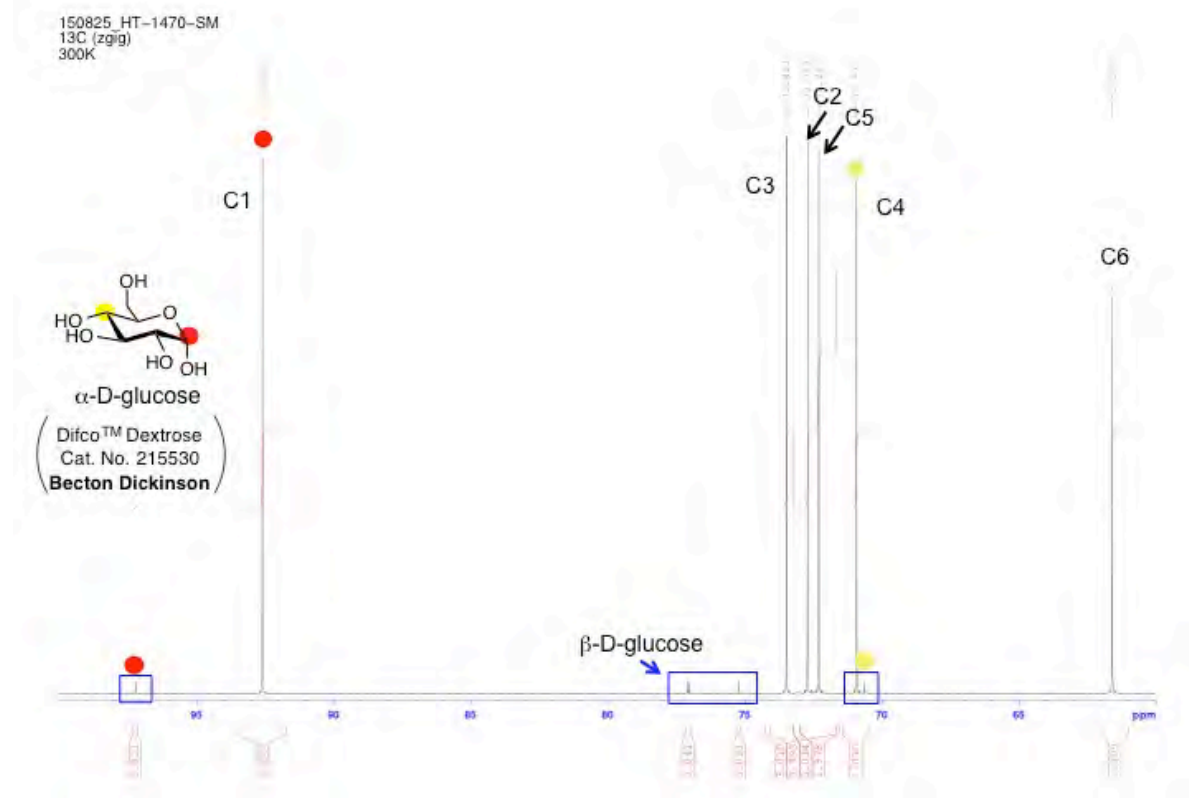
$$\text{KIE} = \frac{\ln(1-F)}{\ln[1-(FR_p/R_0)]} \quad (1)$$

Primary ¹³C KIE of product was calculated from equation (1).¹⁵ *F* is the conversion of α -D-glucose into the glycoside determined by crude ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard. *R_p* is the molar activity of the minor isotope (¹³C) in the product, which was determined by integration of anomeric carbon (C1) of the glycoside against the C4 carbon of it. *R₀* is the molar activity of the minor isotope (¹³C) in the starting material (α -D-glucose), determined by integration of the sum of anomeric carbon (C1) in α - and β -D-glucose against the C4 carbon of them, because a small amount of α -D-glucose was epimerized to β -D-glucose during the acquisition of ¹³C NMR spectra in DMSO-*d*₆ at 300 K (4 h 40 min). Assuming that KIE at C4 of glucopyranoside ring is relatively small in glycosylation,¹⁶ we chose the C4 carbon as an internal standard of ¹³C concentration. The determined α -primary ¹³C KIE was the average of three runs.

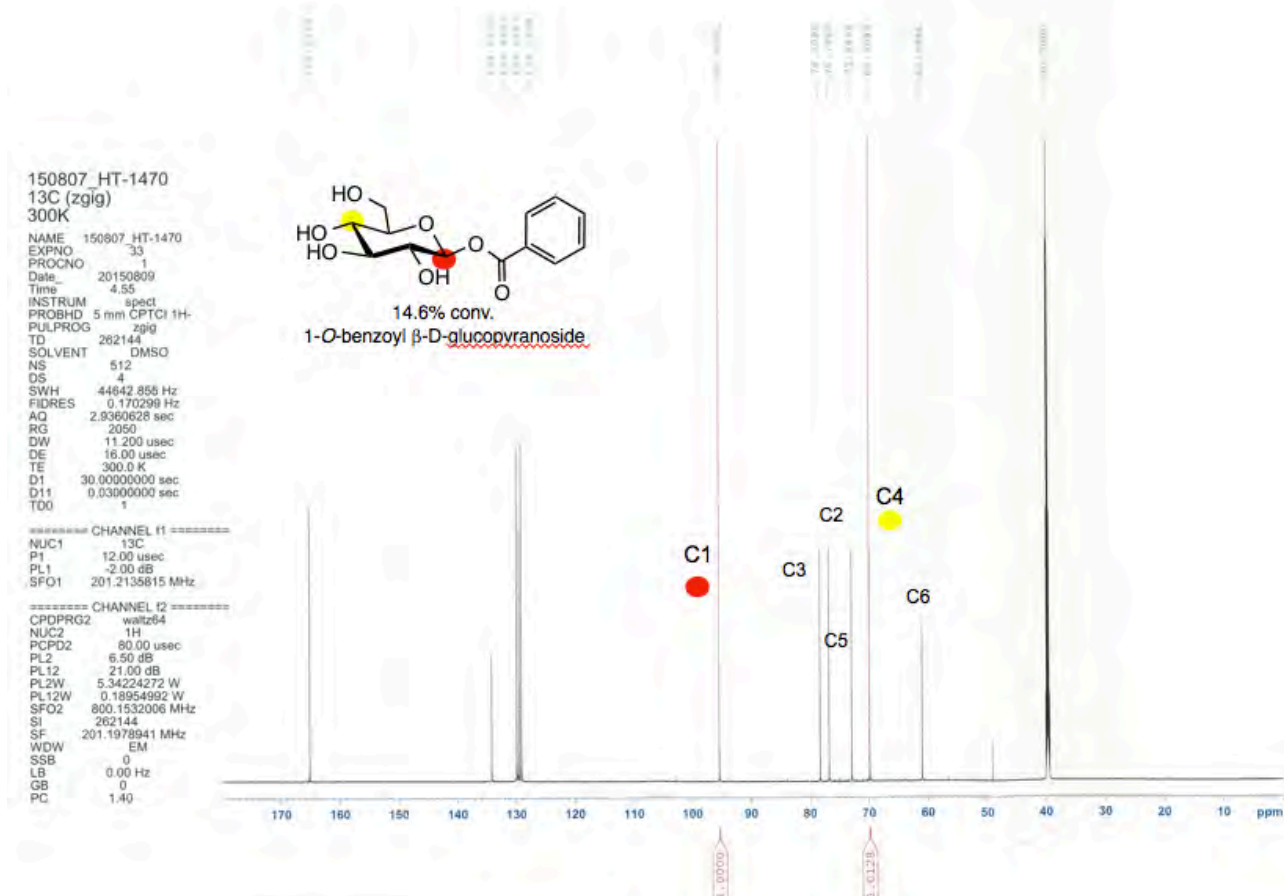
V. NMR EXPERIMENTS (Figure S3)

Carbon NMR spectra were recorded on a Bruker Avance 800 (200 MHz operating frequency for ^{13}C measurement), equipped with a 5 mm-TCI 800 MHz cryogenic probe. Shigemi 5 mm NMR tubes (PS-003) were used. Samples of α -D-glucose (200 mg) and 1-*O*-benzoyl-D-glucopyranoside (200–250 mg) were dissolved in $\text{DMSO-}d_6$ (D 99.9%, Cambridge isotope Laboratories, Inc.). The temperature was set to 300 K. For the acquisition of the quantitative ^{13}C -NMR spectra, direct carbon detection was obtained using 90° pulse with their carrier frequency adjusted at the middle of the peaks of sugar carbons (78.05 ppm) to equilibrate offset effects. Inverse gated bi-level decoupling via Waltz-64 sequence was applied with carrier frequency between the neighboring protons, to avoid creation of heteronuclear Overhauser effect and to eliminate decoupling sidebands. Long enough acquisitions (2.93 s) and relaxation delays (30 s) were employed. The signal-to-noise ratios were between 1863 and 2658.

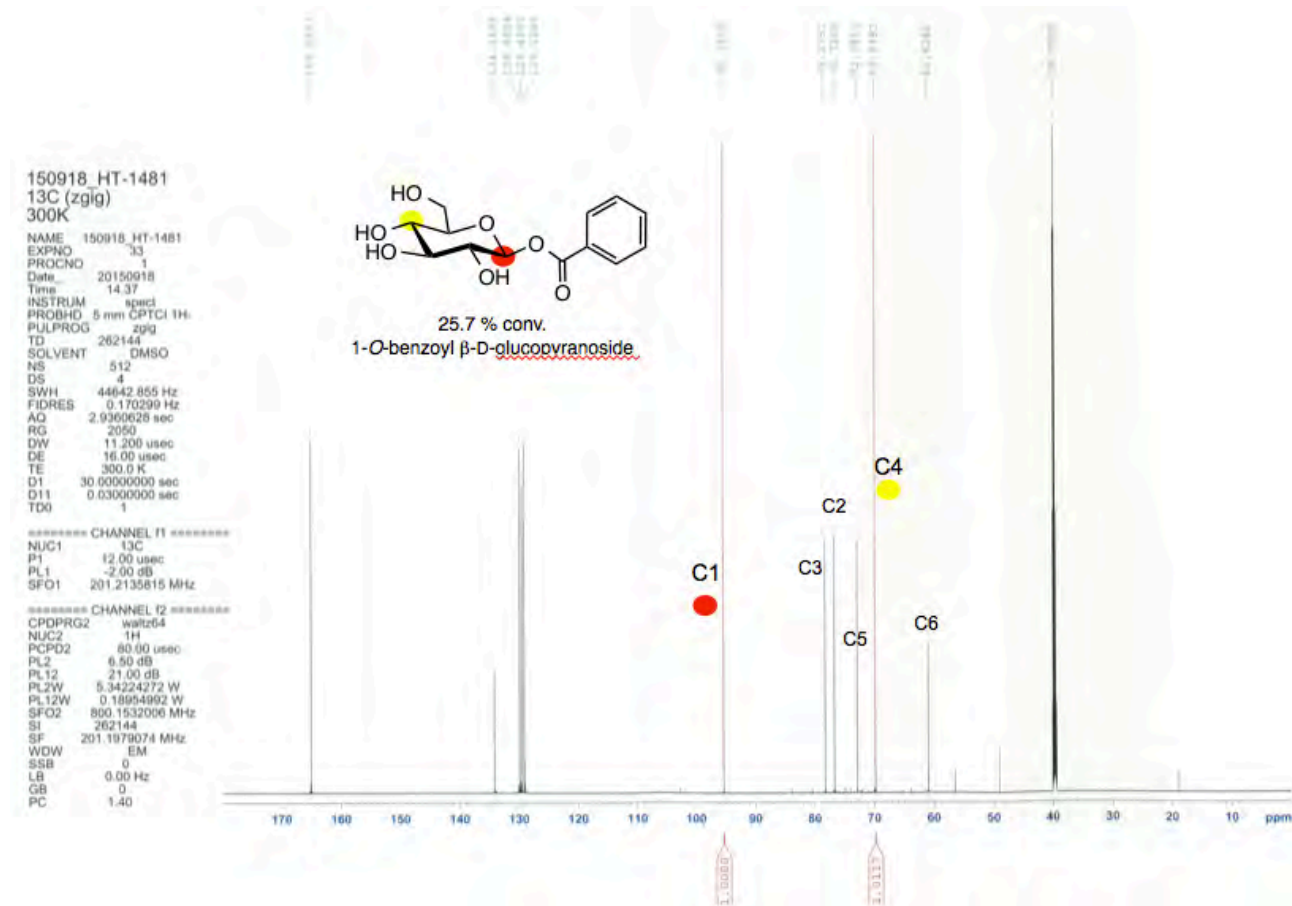
Quantitative ^{13}C NMR spectrum of α -D-glucose, SINO = 2658.



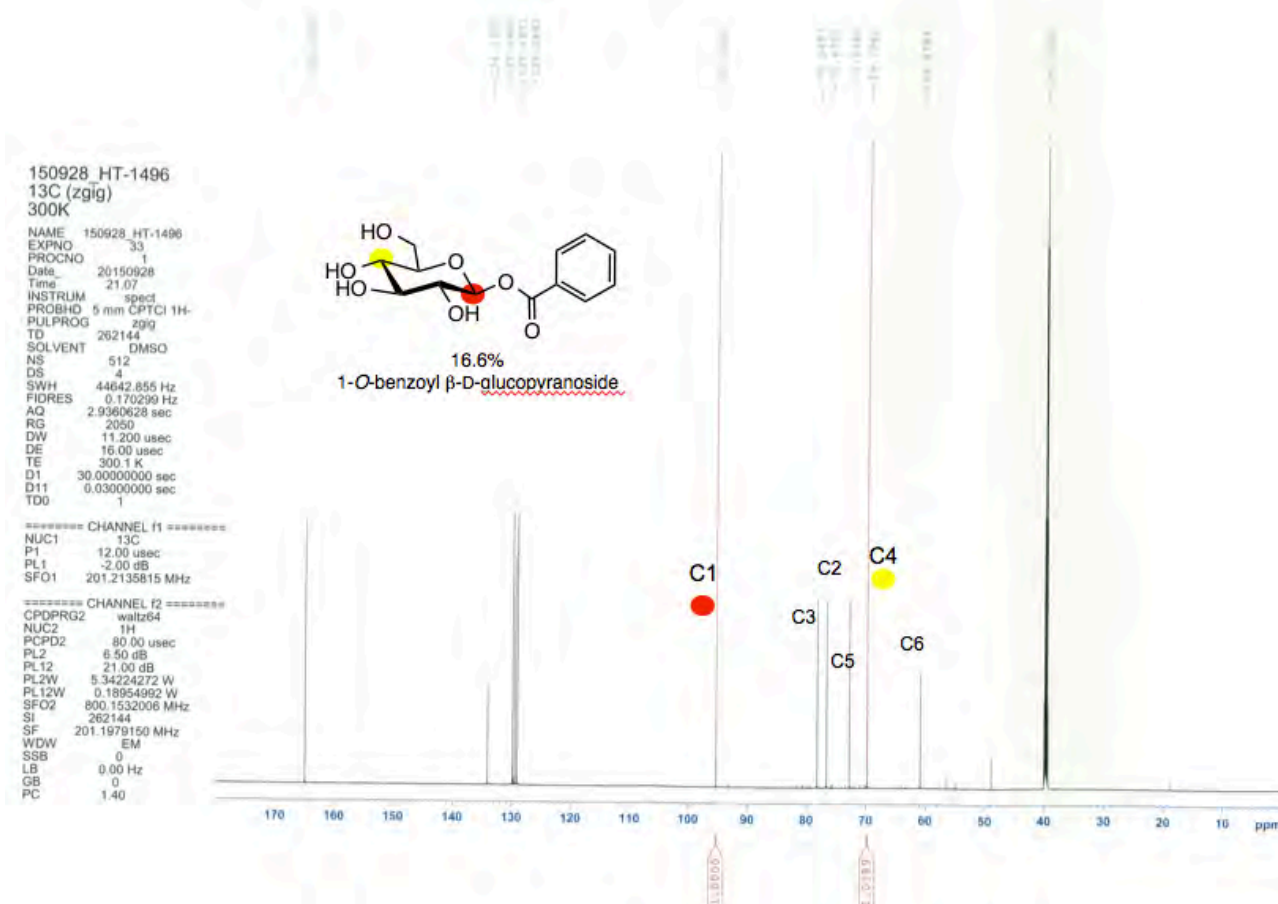
Quantitative ^{13}C NMR spectrum of the glycoside (Table S3, entry 1, 14.6% conv.), SINO = 1863.



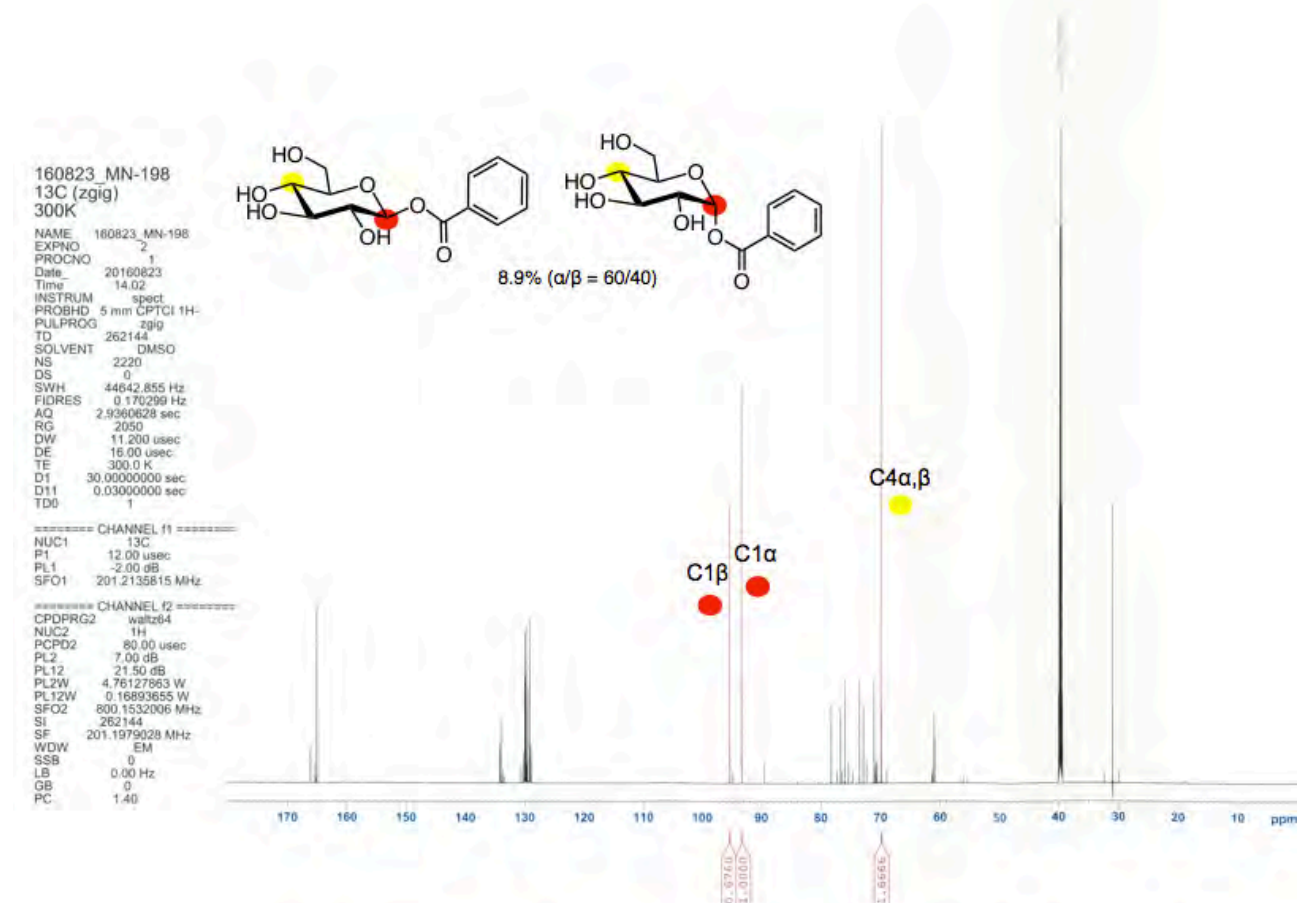
Quantitative ^{13}C NMR spectrum of the glycoside (Table S3, entry 3, 25.7% conv.), SINO = 2418.



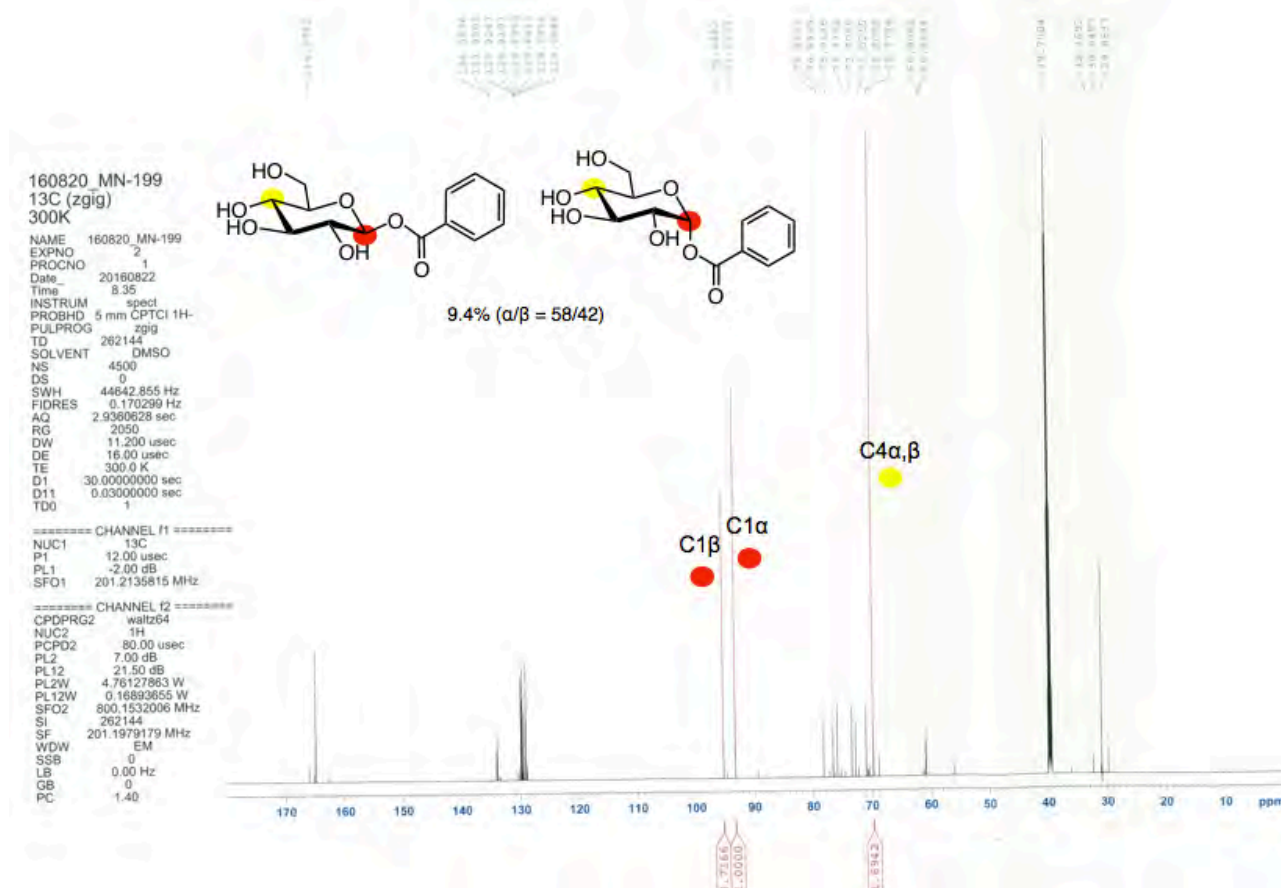
Quantitative ¹³C NMR spectrum of the glycoside (Table S3, entry 2, 16.6% conv.), SINO = 1913.



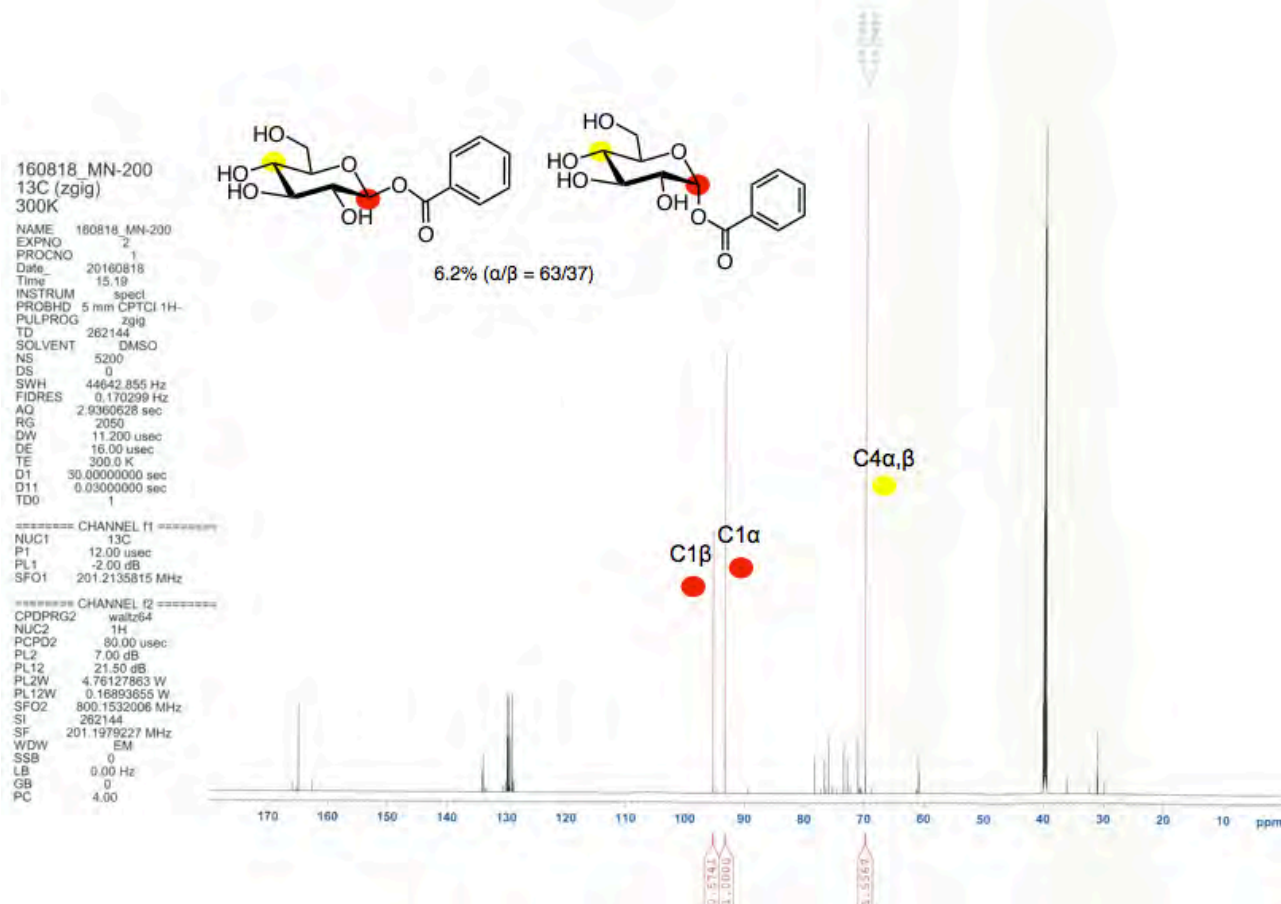
Quantitative ¹³C NMR spectrum of the glycosides (Table S3, entry 4, 8.9% conv.), SINO = 2397.



Quantitative ¹³C NMR spectrum of the glycosides (Table S3, entry 6, 9.4% conv.), SINO = 2439.



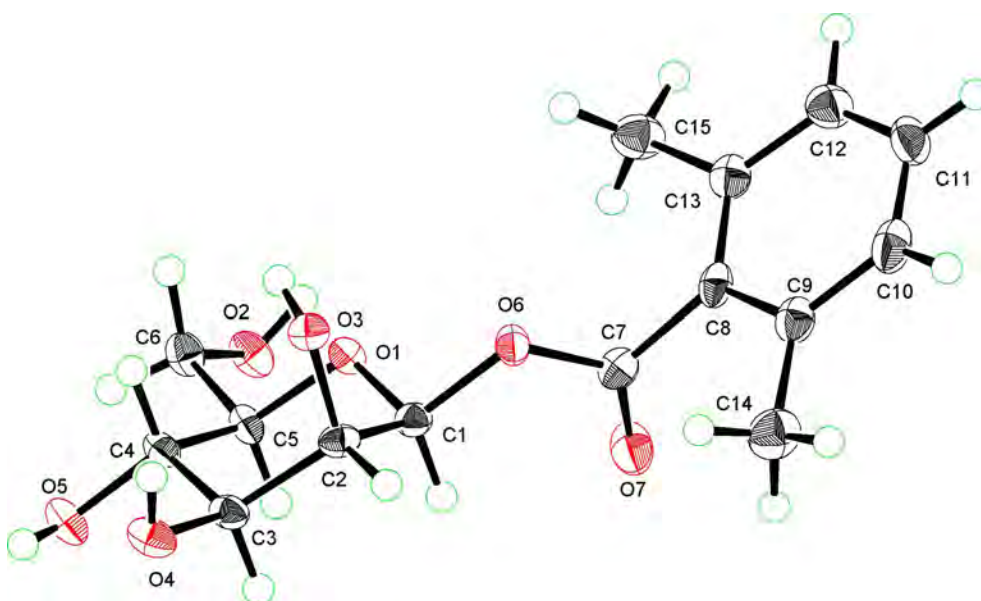
Quantitative ¹³C NMR spectrum of the glycosides (Table S3, entry 5, 6.2% conv.), SINO = 1925.



VI. X-RAY CRYSTAL STRUCTURAL ANALYSIS OF 2f

X-ray crystallography

Single crystal of **2f** was obtained by cooling its saturated hot solution in CH₃CN to 15 °C. The crystal data of **2f** was collected on a Rigaku Saturn 70 CCD diffractometer with a VariMax Mo Optic System using a Mo K α radiation ($\lambda=0.71070$ Å). The reflection data for **2f** was integrated, scaled, and averaged by using the HKL-2000.¹⁷ Semi-empirical absorption correction was applied using the program of MULABS.¹⁸ The structure was solved by a direct method (SIR2004)¹⁹ and refined by full-matrix least square method of F^2 for all reflections with the Shelx program package (SHELXL-97).²⁰ All hydrogen atoms were refined isotropically, while all other atoms were refined anisotropically. CCDC-1445049 (**2f**) contains the supplementary crystallographic data for this paper. This data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.



Crystal structure of **2e** (50% probability).

Table 1. Crystal data and structure refinement for HT1557 (Compound **2f**)

CCDC No.	1445049	
Identification code	ht1557	
Empirical formula	C ₁₅ H ₂₀ O ₇	
Formula weight	312.31	
Temperature	103(2) K	
Wavelength	0.71075 Å	
Crystal system	Orthorhombic	
Space group	<i>P</i> 2 ₁ 2 ₁ 2 ₁ (#19)	
Unit cell dimensions	a = 7.9924(2) Å	α = 90°.
	b = 8.9411(3) Å	β = 90°.
	c = 20.9681(7) Å	γ = 90°.
Volume	1498.40(8) Å ³	
Z	4	
Density (calculated)	1.384 Mg/m ³	
Absorption coefficient	0.110 mm ⁻¹	
F(000)	664	
Crystal size	0.30 x 0.05 x 0.04 mm ³	
Theta range for data collection	1.94 to 27.50°.	
Index ranges	-10 ≤ h ≤ 10, -11 ≤ k ≤ 11, -27 ≤ l ≤ 27	
Reflections collected	20303	
Independent reflections	3454 [R(int) = 0.0874]	
Completeness to theta = 27.50°	99.9 %	
Max. and min. transmission	0.9956 and 0.9677	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	3454 / 0 / 279	
Goodness-of-fit on F ²	1.021	
Final R indices [I > 2σ(I)]	R1 = 0.0391, wR2 = 0.0644	
R indices (all data)	R1 = 0.0637, wR2 = 0.0710	
Absolute structure parameter	0.7(9)	
Largest diff. peak and hole	0.174 and -0.178 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for HT1557. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	$U(\text{eq})$
O(1)	796(1)	2646(1)	6677(1)	18(1)
C(1)	1933(2)	2851(2)	6168(1)	18(1)
C(2)	3628(2)	3333(2)	6411(1)	18(1)
C(3)	4273(2)	2122(2)	6855(1)	18(1)
C(4)	3017(2)	1807(2)	7375(1)	18(1)
C(5)	1310(2)	1438(2)	7081(1)	18(1)
C(6)	-4(2)	1228(2)	7586(1)	21(1)
O(2)	-1481(2)	546(2)	7341(1)	24(1)
O(3)	3580(1)	4754(1)	6713(1)	19(1)
O(4)	5879(1)	2462(2)	7115(1)	23(1)
O(5)	3493(2)	550(2)	7750(1)	24(1)
O(6)	1260(1)	4032(1)	5791(1)	20(1)
C(7)	382(2)	3637(2)	5267(1)	21(1)
O(7)	153(2)	2357(2)	5112(1)	34(1)
C(8)	-268(2)	4942(2)	4906(1)	20(1)
C(9)	618(2)	5483(2)	4383(1)	24(1)
C(10)	-104(3)	6597(2)	4020(1)	30(1)
C(11)	-1669(3)	7168(2)	4166(1)	30(1)
C(12)	-2515(2)	6645(2)	4694(1)	28(1)
C(13)	-1825(2)	5540(2)	5077(1)	23(1)
C(14)	2340(3)	4884(3)	4228(1)	34(1)
C(15)	-2702(3)	5021(3)	5672(1)	32(1)

Table 3. Bond lengths [Å] and angles [°] for HT1557.

O(1)-C(1)	1.413(2)	C(14)-H(16)	0.94(2)
O(1)-C(5)	1.433(2)	C(14)-H(17)	0.96(3)
C(1)-O(6)	1.425(2)	C(15)-H(18)	0.93(3)
C(1)-C(2)	1.511(2)	C(15)-H(19)	0.98(2)
C(1)-H(1)	0.999(18)	C(15)-H(20)	1.01(3)
C(2)-O(3)	1.420(2)		
C(2)-C(3)	1.517(3)	C(1)-O(1)-C(5)	111.08(12)
C(2)-H(2)	0.937(17)	O(1)-C(1)-O(6)	105.85(13)
C(3)-O(4)	1.428(2)	O(1)-C(1)-C(2)	111.05(15)
C(3)-C(4)	1.509(3)	O(6)-C(1)-C(2)	108.31(15)
C(3)-H(3)	0.981(19)	O(1)-C(1)-H(1)	108.6(10)
C(4)-O(5)	1.423(2)	O(6)-C(1)-H(1)	110.8(10)
C(4)-C(5)	1.532(2)	C(2)-C(1)-H(1)	112.0(9)
C(4)-H(4)	0.996(19)	O(3)-C(2)-C(1)	112.38(14)
C(5)-C(6)	1.504(3)	O(3)-C(2)-C(3)	111.98(16)
C(5)-H(5)	1.011(18)	C(1)-C(2)-C(3)	107.93(15)
C(6)-O(2)	1.425(2)	O(3)-C(2)-H(2)	106.6(11)
C(6)-H(6)	0.995(19)	C(1)-C(2)-H(2)	107.6(10)
C(6)-H(7)	0.93(2)	C(3)-C(2)-H(2)	110.2(10)
O(2)-H(8)	0.81(2)	O(4)-C(3)-C(4)	111.25(15)
O(3)-H(9)	0.84(2)	O(4)-C(3)-C(2)	112.83(15)
O(4)-H(10)	0.83(2)	C(4)-C(3)-C(2)	110.52(14)
O(5)-H(11)	0.83(2)	O(4)-C(3)-H(3)	107.7(10)
O(6)-C(7)	1.350(2)	C(4)-C(3)-H(3)	108.1(10)
C(7)-O(7)	1.204(2)	C(2)-C(3)-H(3)	106.2(11)
C(7)-C(8)	1.485(3)	O(5)-C(4)-C(3)	111.62(14)
C(8)-C(9)	1.393(3)	O(5)-C(4)-C(5)	106.87(14)
C(8)-C(13)	1.401(2)	C(3)-C(4)-C(5)	109.98(16)
C(9)-C(10)	1.380(3)	O(5)-C(4)-H(4)	111.2(11)
C(9)-C(14)	1.512(3)	C(3)-C(4)-H(4)	109.4(11)
C(10)-C(11)	1.385(3)	C(5)-C(4)-H(4)	107.7(10)
C(10)-H(12)	0.95(2)	O(1)-C(5)-C(6)	108.07(14)
C(11)-C(12)	1.379(3)	O(1)-C(5)-C(4)	109.32(14)
C(11)-H(13)	0.91(2)	C(6)-C(5)-C(4)	111.42(16)
C(12)-C(13)	1.387(3)	O(1)-C(5)-H(5)	109.4(10)
C(12)-H(14)	0.994(19)	C(6)-C(5)-H(5)	109.5(9)
C(13)-C(15)	1.505(3)	C(4)-C(5)-H(5)	109.1(9)
C(14)-H(15)	0.98(3)	O(2)-C(6)-C(5)	112.23(17)

O(2)-C(6)-H(6)	112.7(9)	C(12)-C(11)-C(10)	119.7(2)
C(5)-C(6)-H(6)	108.4(10)	C(12)-C(11)-H(13)	121.0(12)
O(2)-C(6)-H(7)	107.7(12)	C(10)-C(11)-H(13)	119.2(12)
C(5)-C(6)-H(7)	108.4(11)	C(11)-C(12)-C(13)	120.74(19)
H(6)-C(6)-H(7)	107.2(16)	C(11)-C(12)-H(14)	122.1(12)
C(6)-O(2)-H(8)	108.6(15)	C(13)-C(12)-H(14)	117.1(12)
C(2)-O(3)-H(9)	113.0(15)	C(12)-C(13)-C(8)	118.50(19)
C(3)-O(4)-H(10)	107.3(14)	C(12)-C(13)-C(15)	120.94(17)
C(4)-O(5)-H(11)	110.5(18)	C(8)-C(13)-C(15)	120.54(18)
C(7)-O(6)-C(1)	116.98(14)	C(9)-C(14)-H(15)	113.7(15)
O(7)-C(7)-O(6)	123.24(18)	C(9)-C(14)-H(16)	109.5(13)
O(7)-C(7)-C(8)	123.77(18)	H(15)-C(14)-H(16)	107(2)
O(6)-C(7)-C(8)	112.99(15)	C(9)-C(14)-H(17)	112.4(13)
C(9)-C(8)-C(13)	121.37(18)	H(15)-C(14)-H(17)	111(2)
C(9)-C(8)-C(7)	119.77(17)	H(16)-C(14)-H(17)	102.5(18)
C(13)-C(8)-C(7)	118.72(17)	C(13)-C(15)-H(18)	112.2(16)
C(10)-C(9)-C(8)	118.20(18)	C(13)-C(15)-H(19)	109.3(13)
C(10)-C(9)-C(14)	121.2(2)	H(18)-C(15)-H(19)	107(2)
C(8)-C(9)-C(14)	120.61(19)	C(13)-C(15)-H(20)	109.6(14)
C(9)-C(10)-C(11)	121.4(2)	H(18)-C(15)-H(20)	105(2)
C(9)-C(10)-H(12)	119.2(14)	H(19)-C(15)-H(20)	113(2)
C(11)-C(10)-H(12)	119.4(13)		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for HT1557. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	16(1)	17(1)	20(1)	3(1)	0(1)	1(1)
C(1)	21(1)	15(1)	18(1)	-1(1)	1(1)	1(1)
C(2)	16(1)	18(1)	20(1)	-1(1)	6(1)	0(1)
C(3)	15(1)	17(1)	23(1)	-3(1)	-3(1)	1(1)
C(4)	19(1)	14(1)	22(1)	2(1)	-4(1)	2(1)
C(5)	19(1)	16(1)	20(1)	4(1)	-4(1)	0(1)
C(6)	16(1)	26(1)	23(1)	4(1)	-1(1)	-2(1)
O(2)	16(1)	25(1)	31(1)	7(1)	-1(1)	-1(1)
O(3)	17(1)	18(1)	22(1)	-2(1)	1(1)	-1(1)
O(4)	14(1)	20(1)	36(1)	0(1)	-3(1)	-1(1)
O(5)	19(1)	21(1)	31(1)	9(1)	-5(1)	-1(1)
O(6)	24(1)	18(1)	17(1)	1(1)	-4(1)	-1(1)
C(7)	22(1)	22(1)	20(1)	-2(1)	1(1)	-4(1)
O(7)	49(1)	20(1)	31(1)	-1(1)	-16(1)	-3(1)
C(8)	25(1)	20(1)	15(1)	-1(1)	-5(1)	-6(1)
C(9)	30(1)	21(1)	20(1)	0(1)	-2(1)	-5(1)
C(10)	46(1)	25(1)	19(1)	3(1)	-2(1)	-8(1)
C(11)	43(1)	21(1)	26(1)	4(1)	-10(1)	2(1)
C(12)	32(1)	22(1)	31(1)	-1(1)	-2(1)	0(1)
C(13)	27(1)	20(1)	23(1)	-1(1)	-2(1)	-5(1)
C(14)	34(1)	37(1)	32(1)	2(1)	9(1)	-2(1)
C(15)	31(1)	29(1)	35(2)	2(1)	8(1)	2(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for HT1557.

	x	y	z	U(eq)
H(1)	1995(19)	1900(20)	5918(8)	9(4)
H(2)	4340(20)	3430(19)	6058(9)	10(4)
H(3)	4390(20)	1220(20)	6595(9)	15(5)
H(4)	2880(20)	2720(20)	7644(9)	22(5)
H(5)	1412(18)	490(20)	6819(8)	10(4)
H(6)	-226(19)	2210(20)	7790(8)	13(4)
H(7)	430(20)	600(20)	7900(10)	24(5)
H(8)	-2070(30)	1190(20)	7189(11)	33(7)
H(9)	2830(30)	4820(20)	6989(10)	35(7)
H(10)	5900(30)	3370(30)	7192(11)	35(7)
H(11)	4460(30)	650(30)	7883(12)	51(8)
H(12)	490(30)	6990(30)	3662(12)	43(7)
H(13)	-2120(20)	7900(20)	3914(9)	27(6)
H(14)	-3610(20)	7070(20)	4829(10)	33(6)
H(15)	2360(30)	3810(30)	4134(13)	59(8)
H(16)	3050(30)	5040(30)	4578(11)	39(7)
H(17)	2880(30)	5440(30)	3895(11)	46(7)
H(18)	-2640(30)	3990(30)	5725(12)	52(8)
H(19)	-3890(20)	5280(20)	5644(10)	32(6)
H(20)	-2130(30)	5460(30)	6058(12)	55(8)

Table 6. Torsion angles [°] for HT1557.

C(5)-O(1)-C(1)-O(6)	177.86(13)	O(1)-C(1)-O(6)-C(7)	-98.15(17)
C(5)-O(1)-C(1)-C(2)	-64.80(18)	C(2)-C(1)-O(6)-C(7)	142.69(15)
O(1)-C(1)-C(2)-O(3)	-64.3(2)	C(1)-O(6)-C(7)-O(7)	-0.1(2)
O(6)-C(1)-C(2)-O(3)	51.6(2)	C(1)-O(6)-C(7)-C(8)	179.92(14)
O(1)-C(1)-C(2)-C(3)	59.72(19)	O(7)-C(7)-C(8)-C(9)	-83.4(2)
O(6)-C(1)-C(2)-C(3)	175.54(15)	O(6)-C(7)-C(8)-C(9)	96.6(2)
O(3)-C(2)-C(3)-O(4)	-55.77(19)	O(7)-C(7)-C(8)-C(13)	92.4(2)
C(1)-C(2)-C(3)-O(4)	-179.98(15)	O(6)-C(7)-C(8)-C(13)	-87.65(19)
O(3)-C(2)-C(3)-C(4)	69.50(19)	C(13)-C(8)-C(9)-C(10)	-2.2(3)
C(1)-C(2)-C(3)-C(4)	-54.7(2)	C(7)-C(8)-C(9)-C(10)	173.51(18)
O(4)-C(3)-C(4)-O(5)	-61.22(19)	C(13)-C(8)-C(9)-C(14)	176.54(19)
C(2)-C(3)-C(4)-O(5)	172.62(15)	C(7)-C(8)-C(9)-C(14)	-7.8(3)
O(4)-C(3)-C(4)-C(5)	-179.67(15)	C(8)-C(9)-C(10)-C(11)	-0.1(3)
C(2)-C(3)-C(4)-C(5)	54.2(2)	C(14)-C(9)-C(10)-C(11)	-178.9(2)
C(1)-O(1)-C(5)-C(6)	-176.69(14)	C(9)-C(10)-C(11)-C(12)	1.6(3)
C(1)-O(1)-C(5)-C(4)	61.87(19)	C(10)-C(11)-C(12)-C(13)	-0.7(3)
O(5)-C(4)-C(5)-O(1)	-177.77(15)	C(11)-C(12)-C(13)-C(8)	-1.5(3)
C(3)-C(4)-C(5)-O(1)	-56.44(19)	C(11)-C(12)-C(13)-C(15)	176.8(2)
O(5)-C(4)-C(5)-C(6)	62.8(2)	C(9)-C(8)-C(13)-C(12)	3.0(3)
C(3)-C(4)-C(5)-C(6)	-175.82(15)	C(7)-C(8)-C(13)-C(12)	-172.73(17)
O(1)-C(5)-C(6)-O(2)	73.8(2)	C(9)-C(8)-C(13)-C(15)	-175.34(19)
C(4)-C(5)-C(6)-O(2)	-166.05(15)	C(7)-C(8)-C(13)-C(15)	8.9(3)

Symmetry transformations used to generate equivalent atoms:

VII. CALCULATION OF A STABLE CONFORMER OF 10 (Figure S4)

The most stable structure of coriariin A (**10**) was calculated with the GB/SA solvation model for water, using MacroModel V 9.0 with OPLS2005 force field (20,000 steps MCMM), and is shown below. Most hydrogens were removed for clarity. The longest molecular length of **10** was ~ 3 nm.

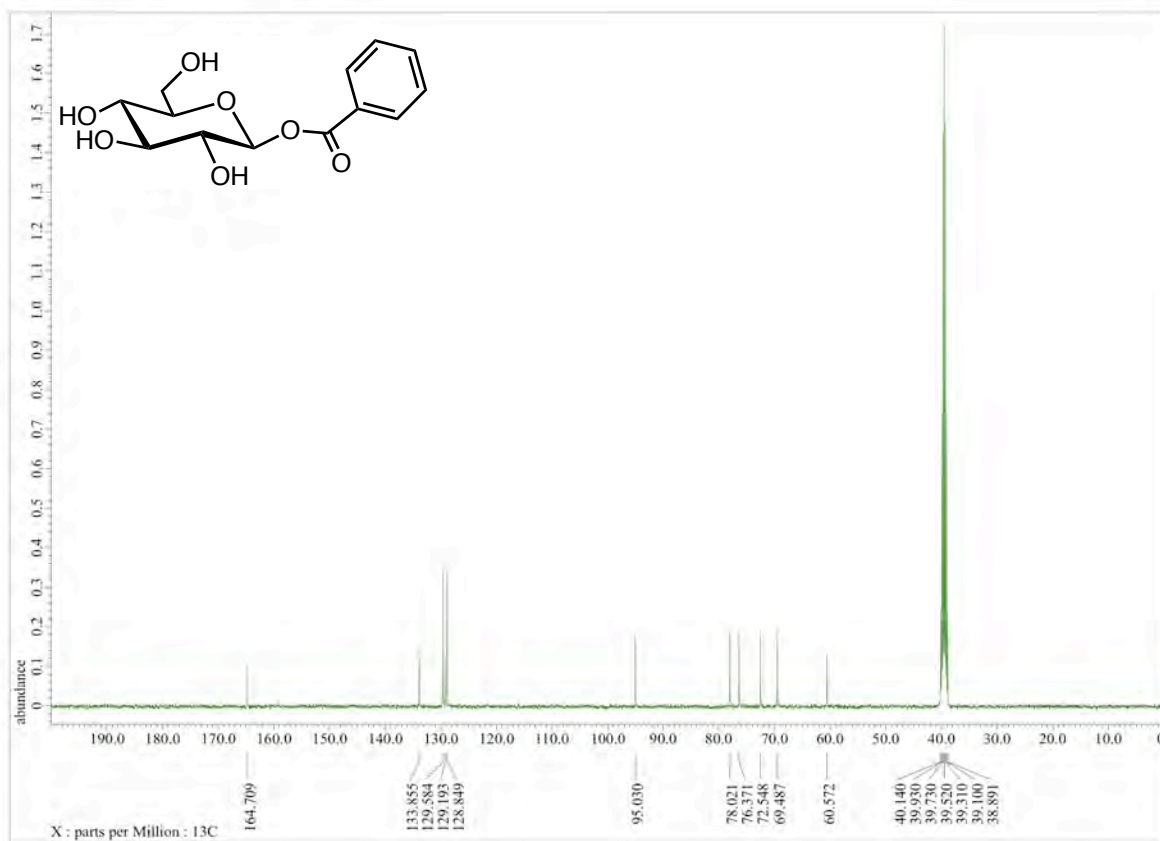
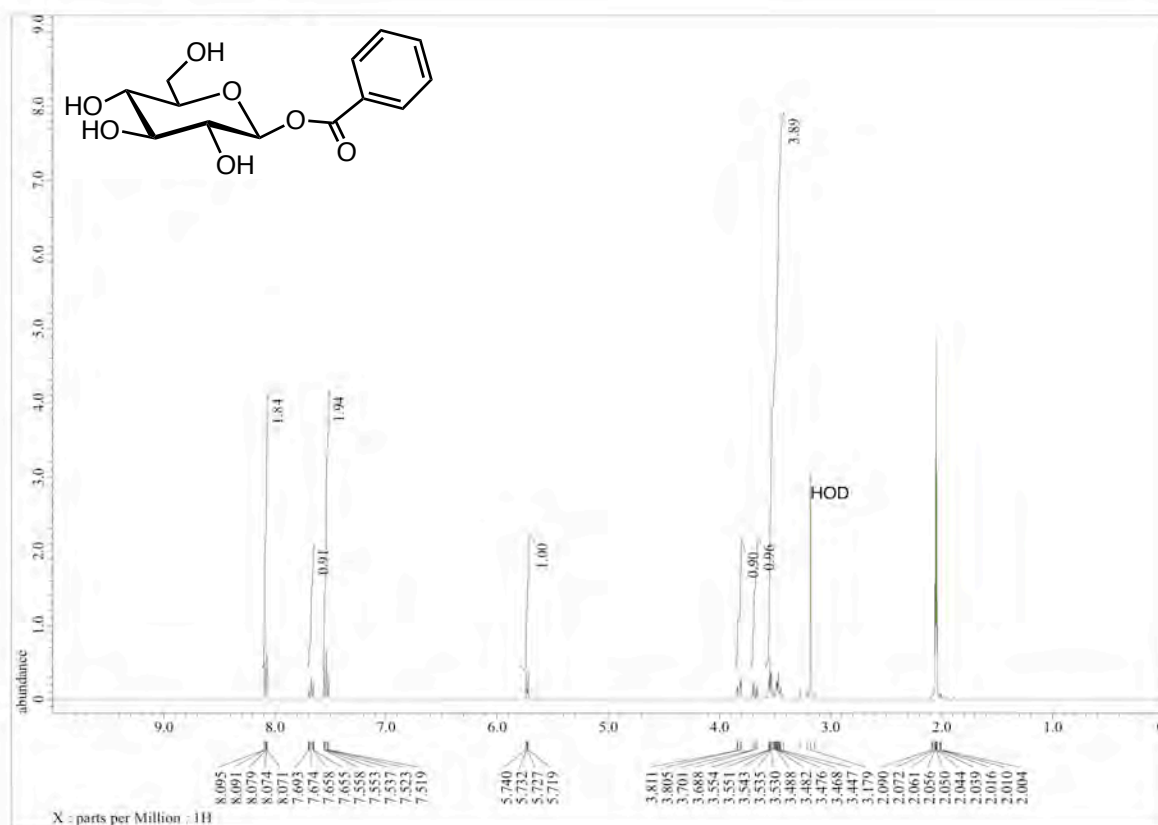


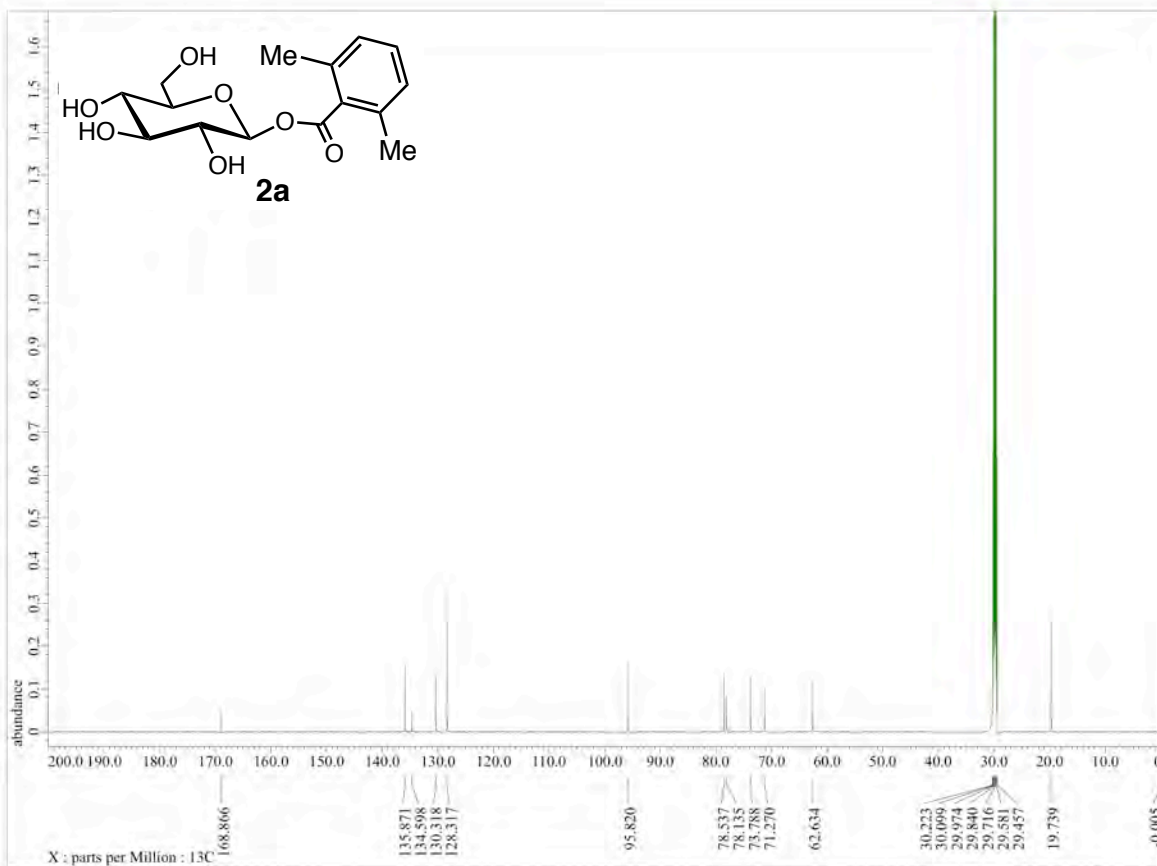
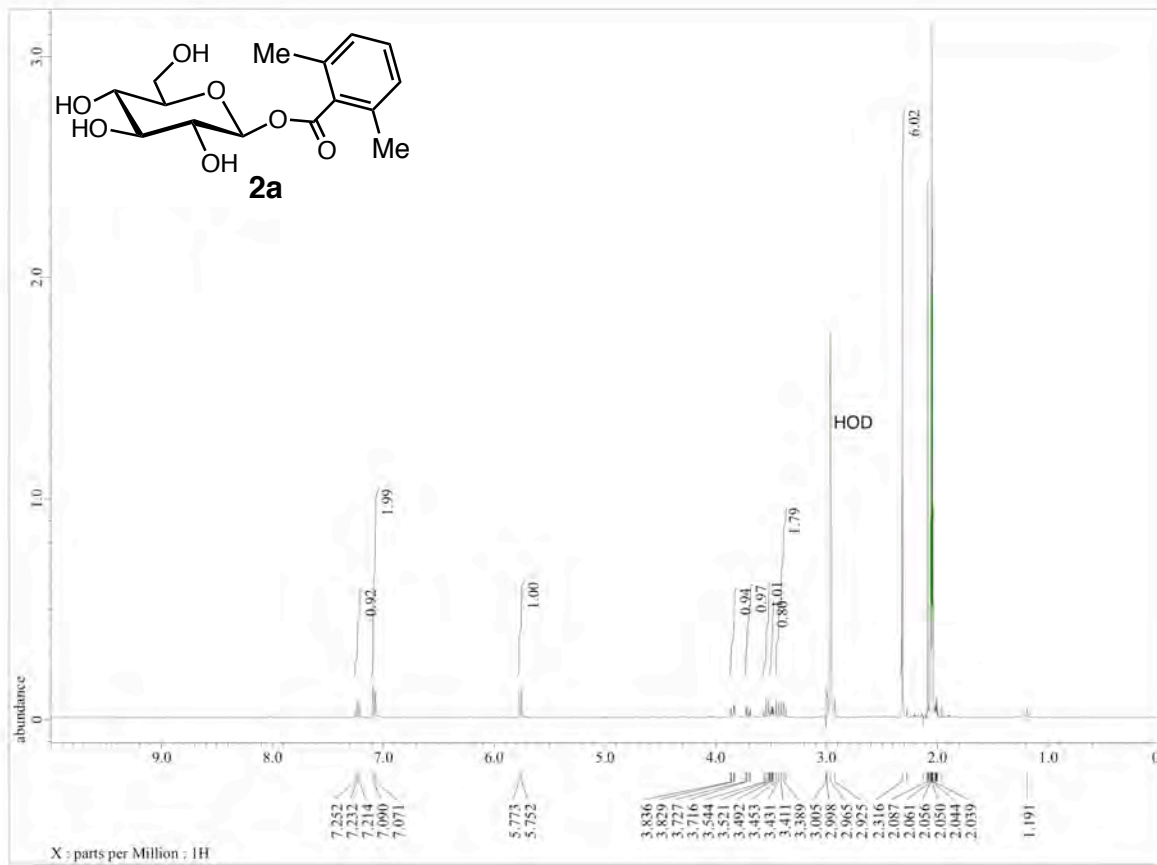
Calculated structure of coriariin A (**10**).

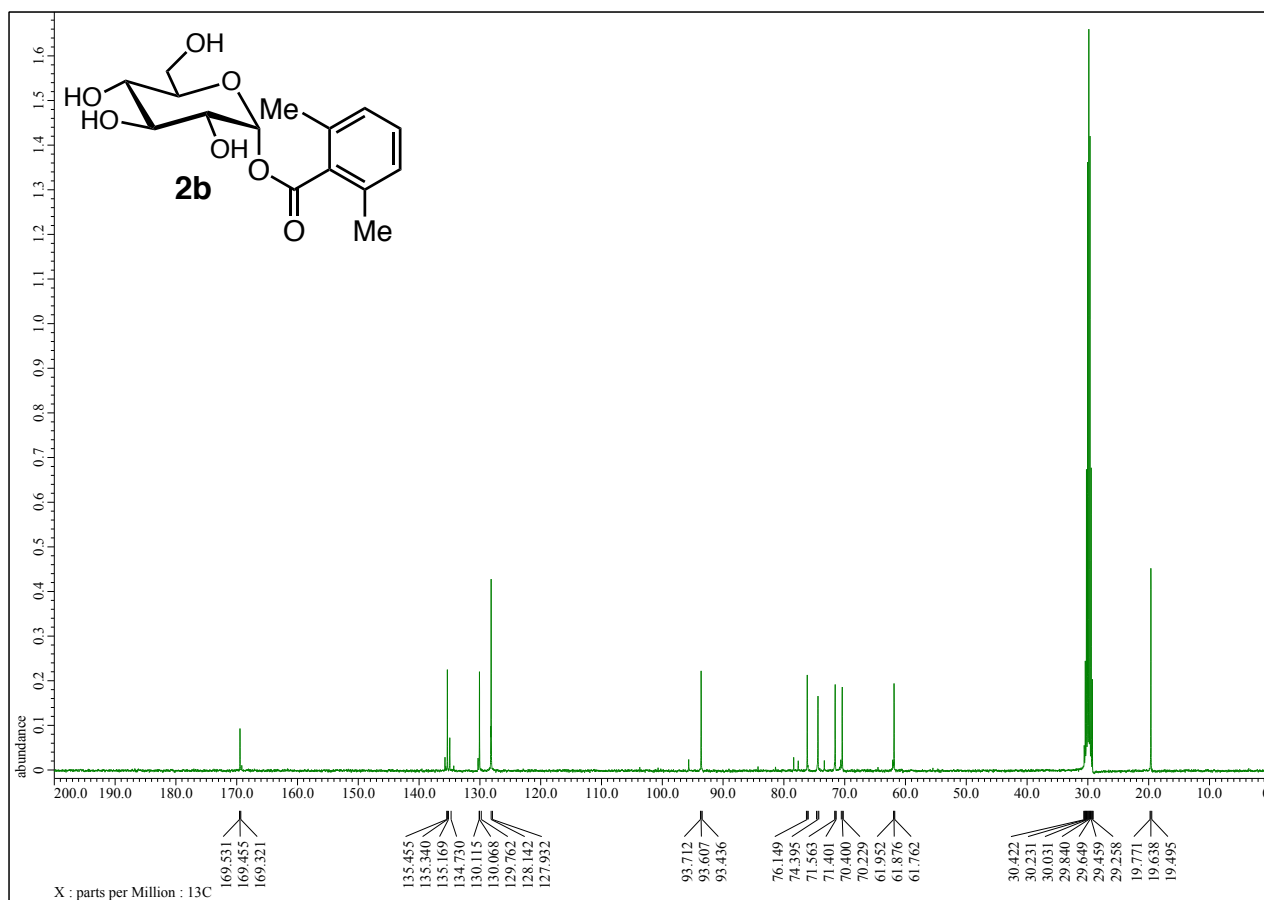
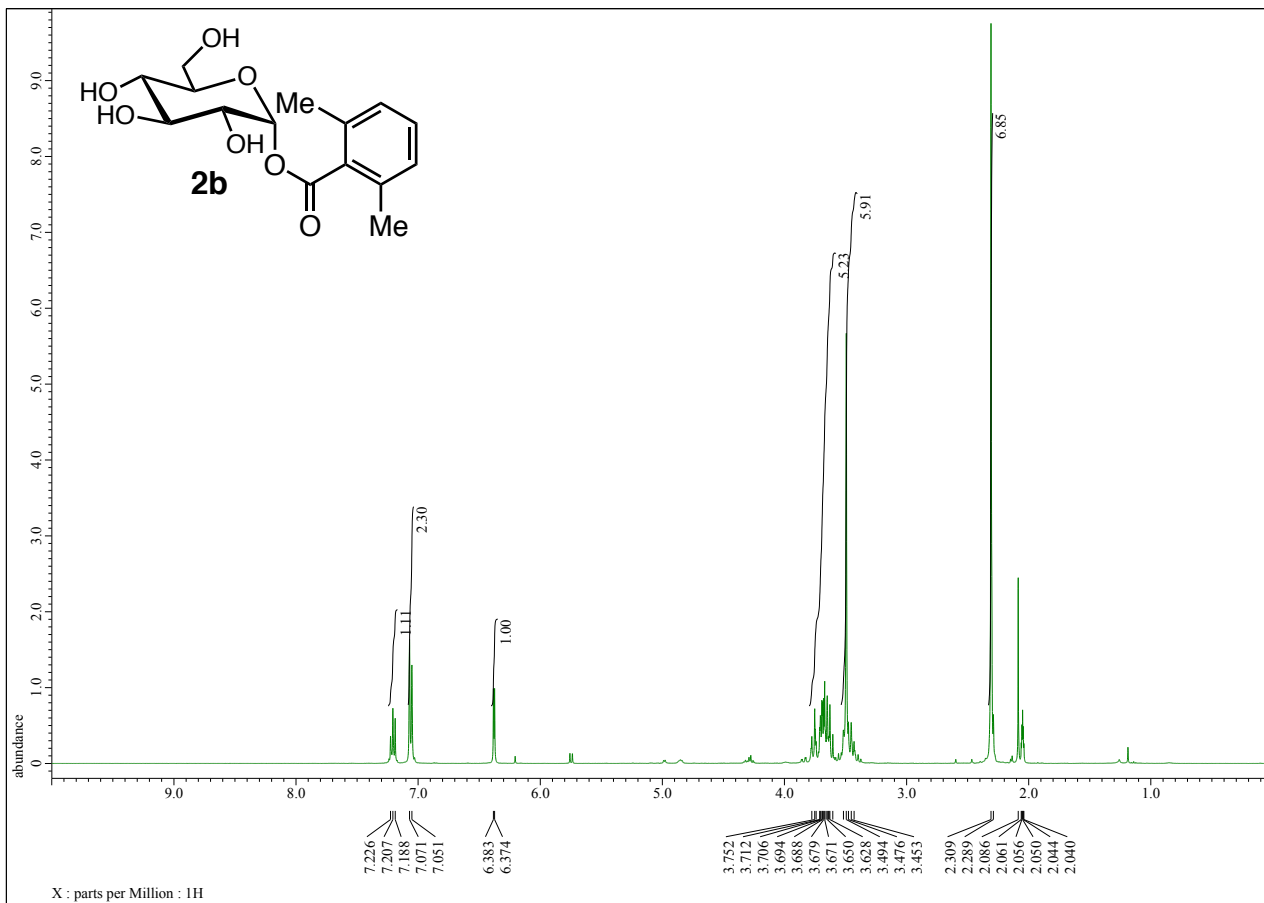
VIII. REFERENCES

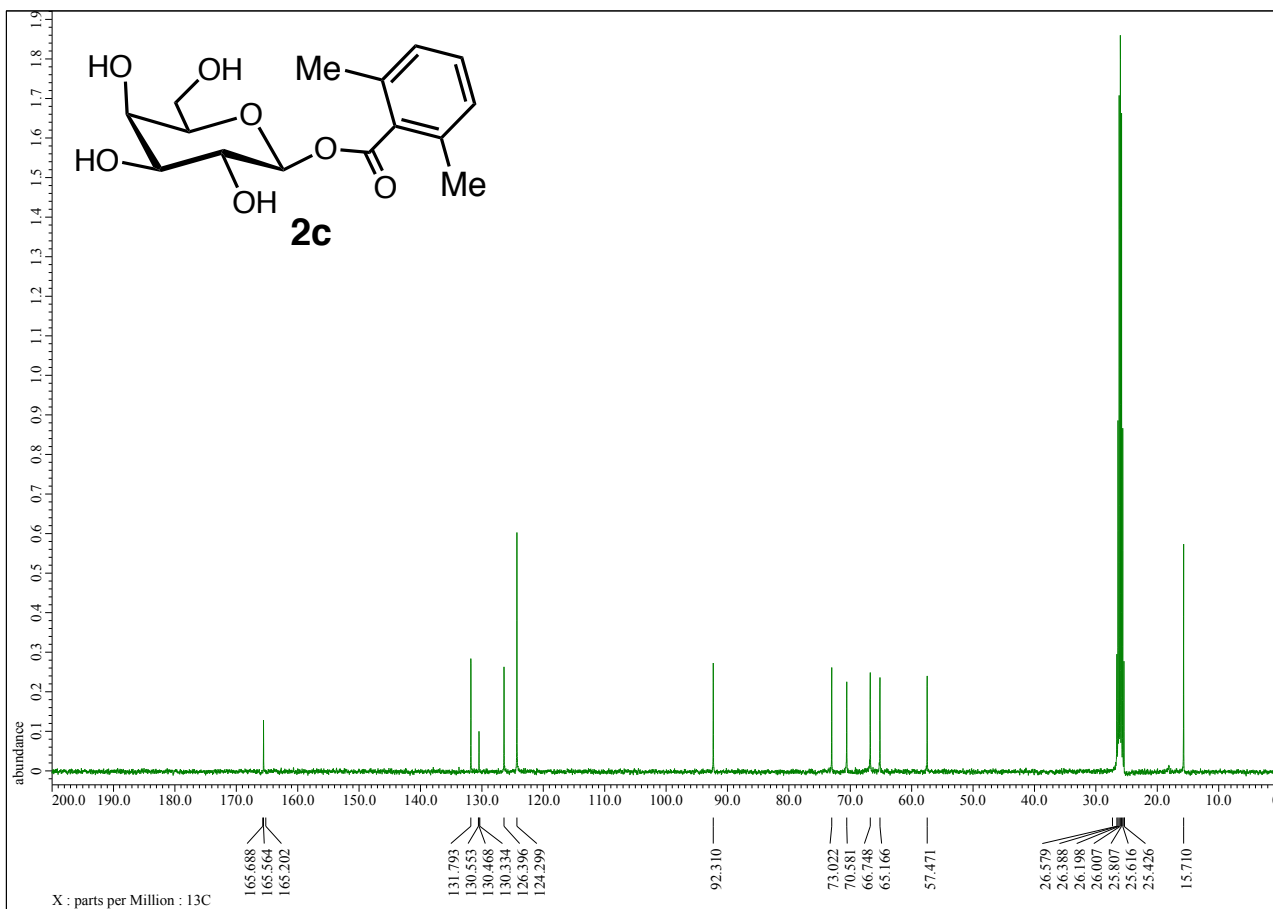
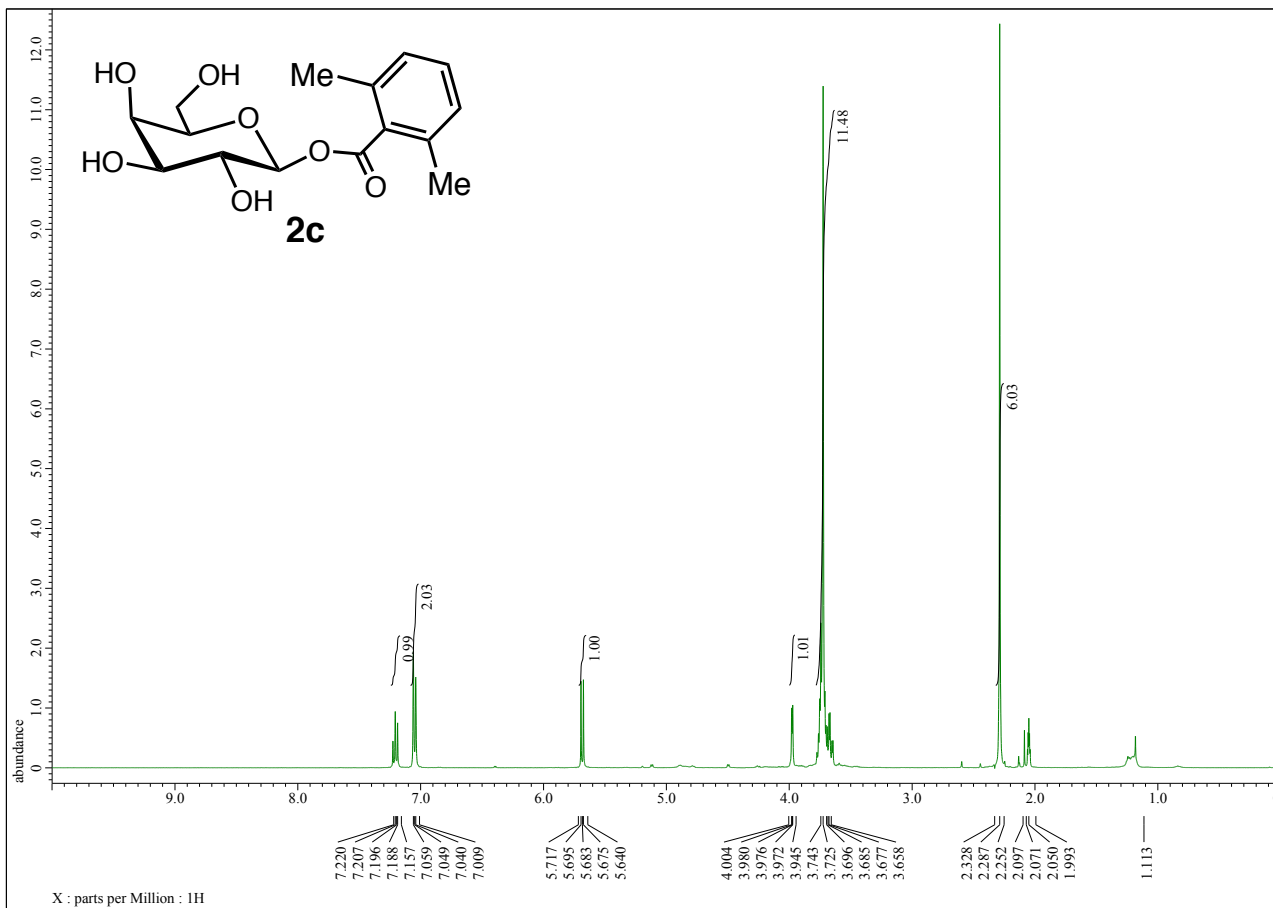
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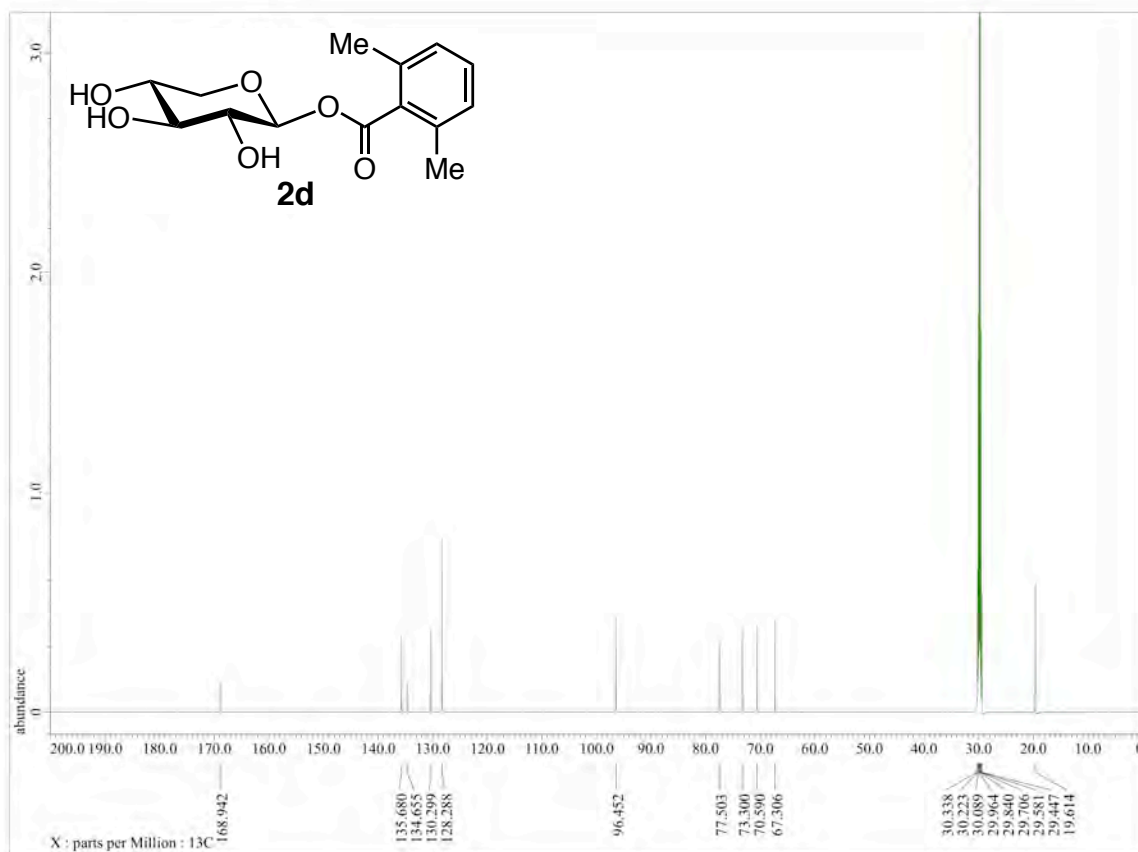
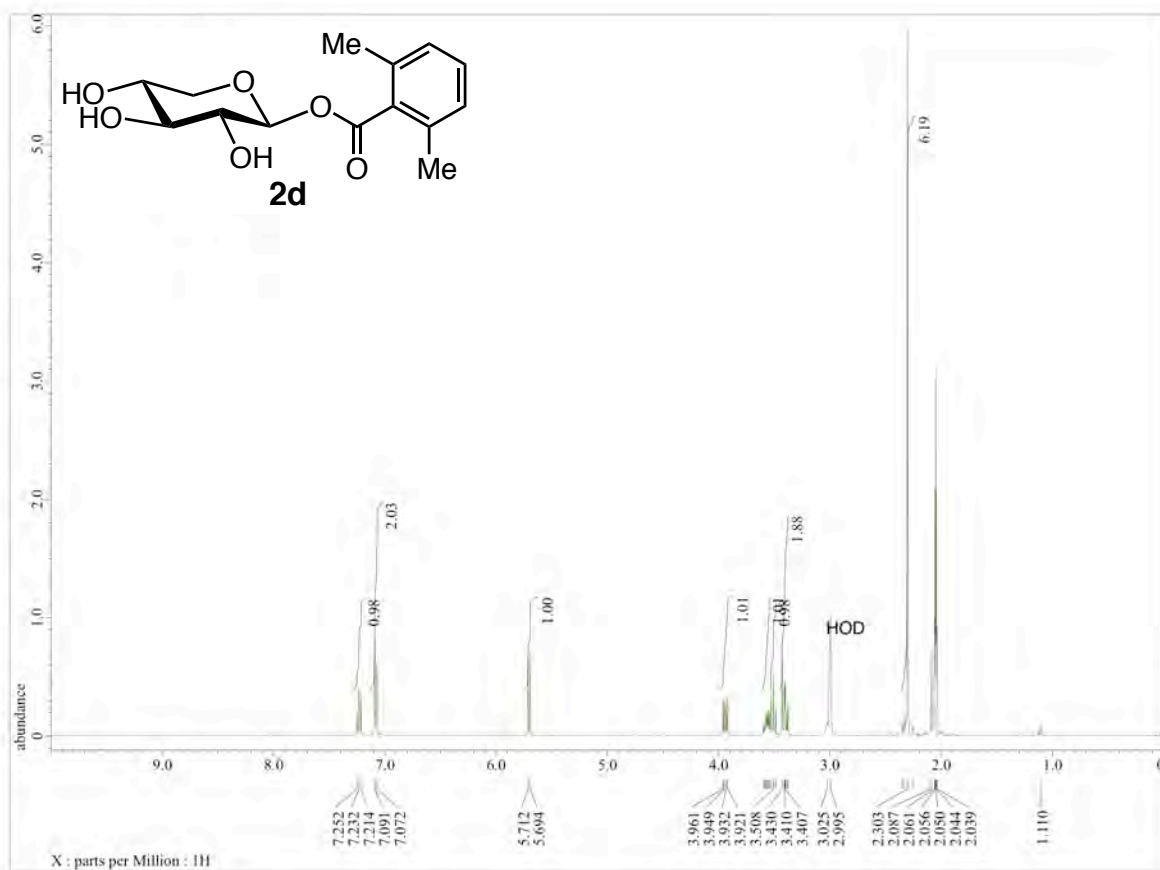
IX. ¹H-NMR and ¹³C-NMR SPECTRA REPRINTS

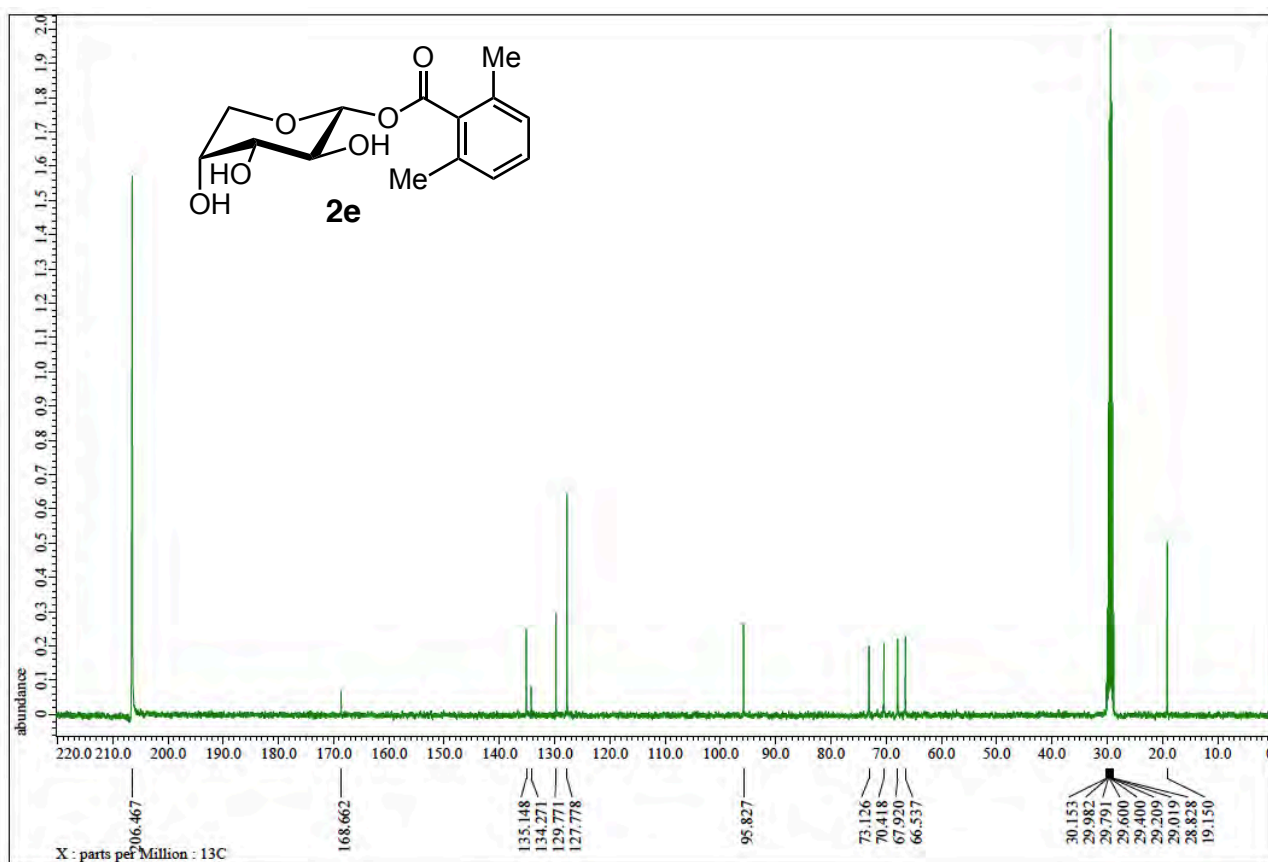
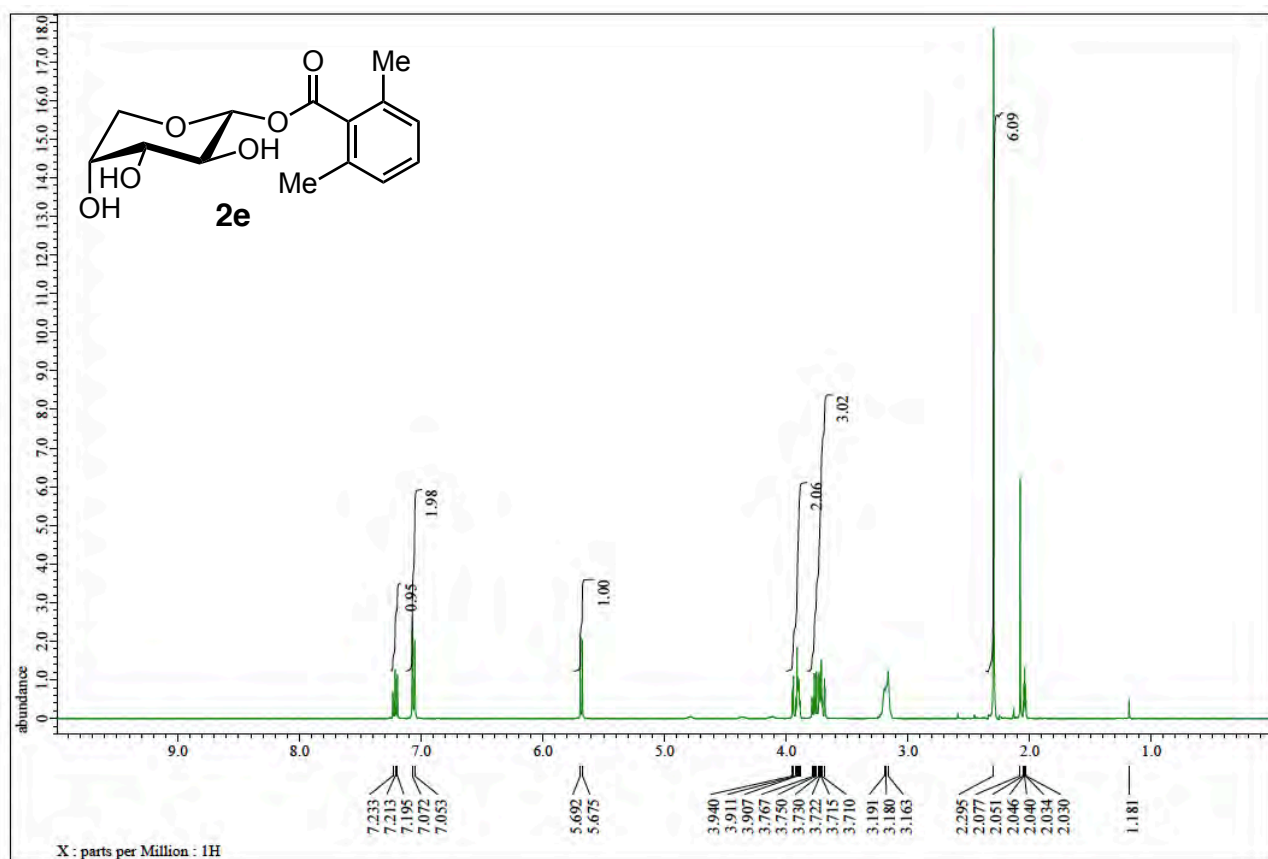


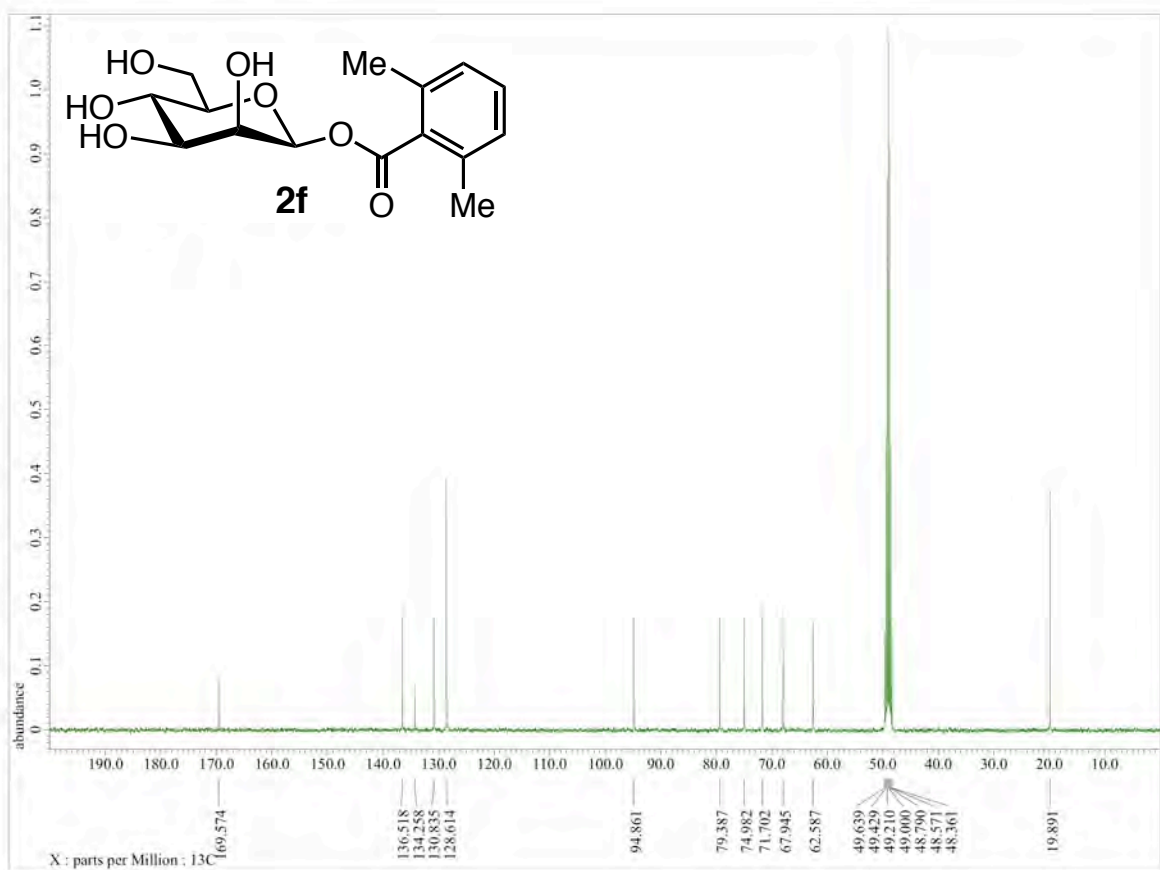
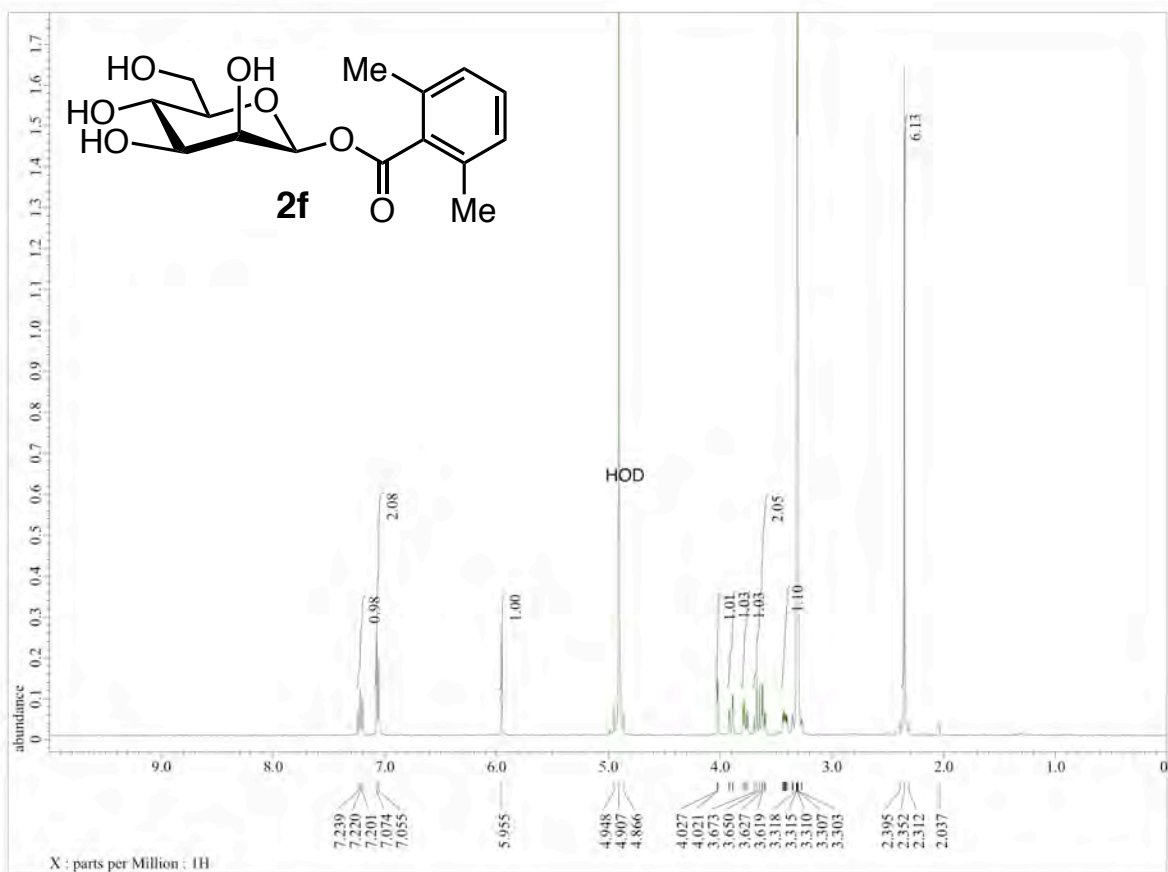


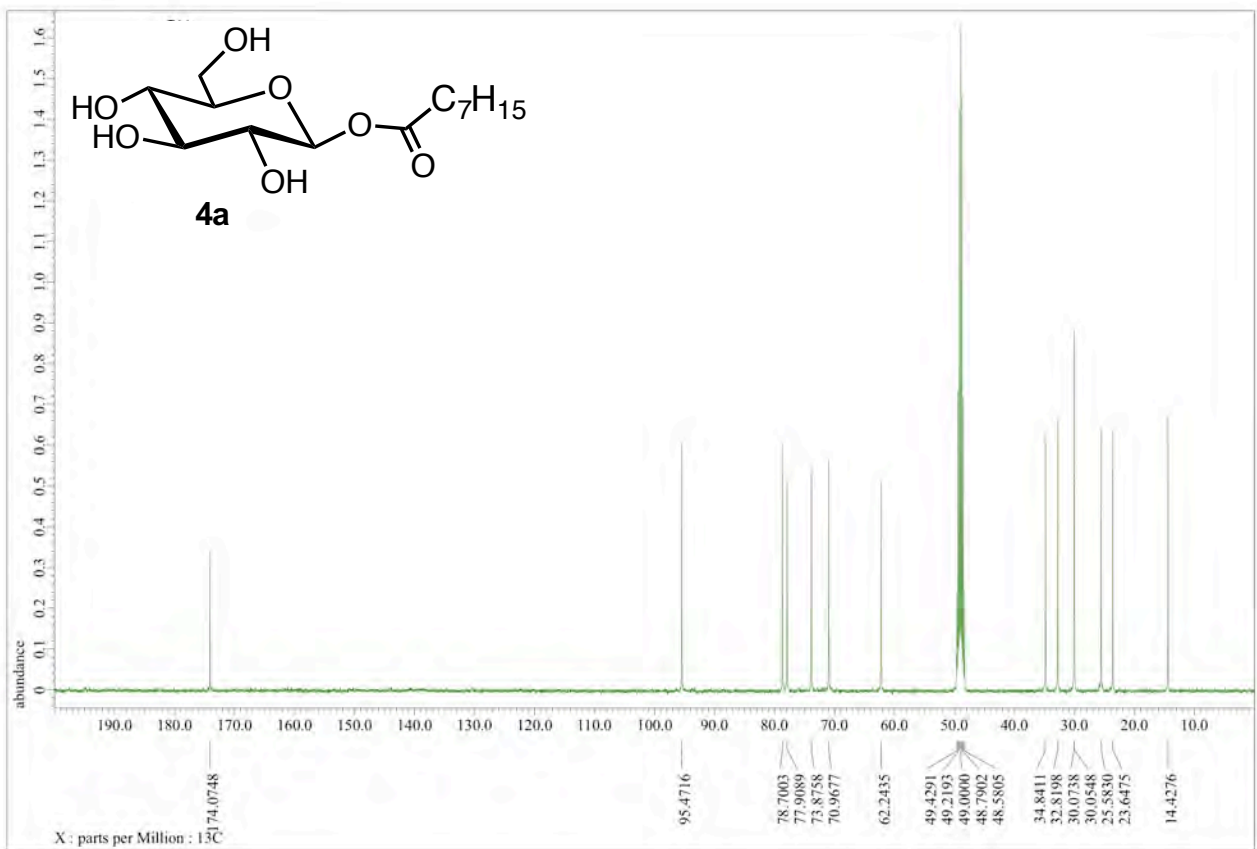
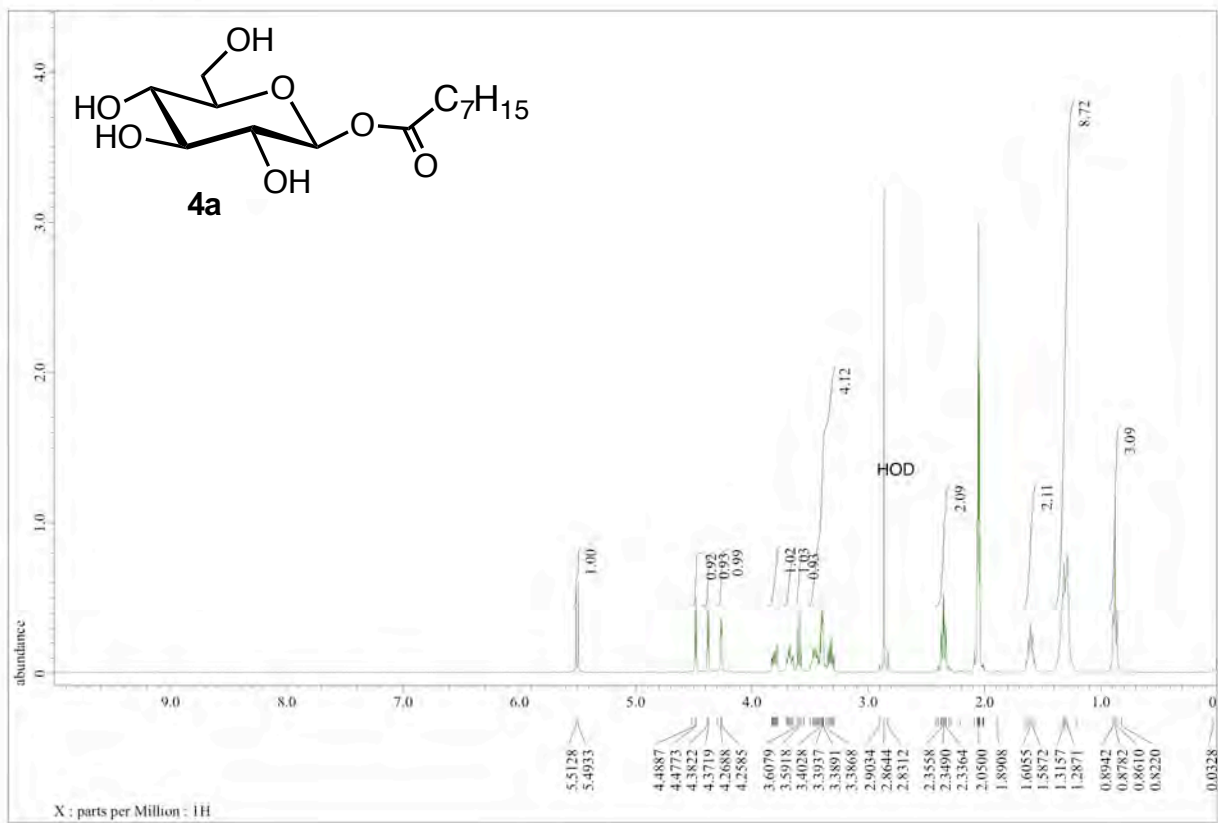


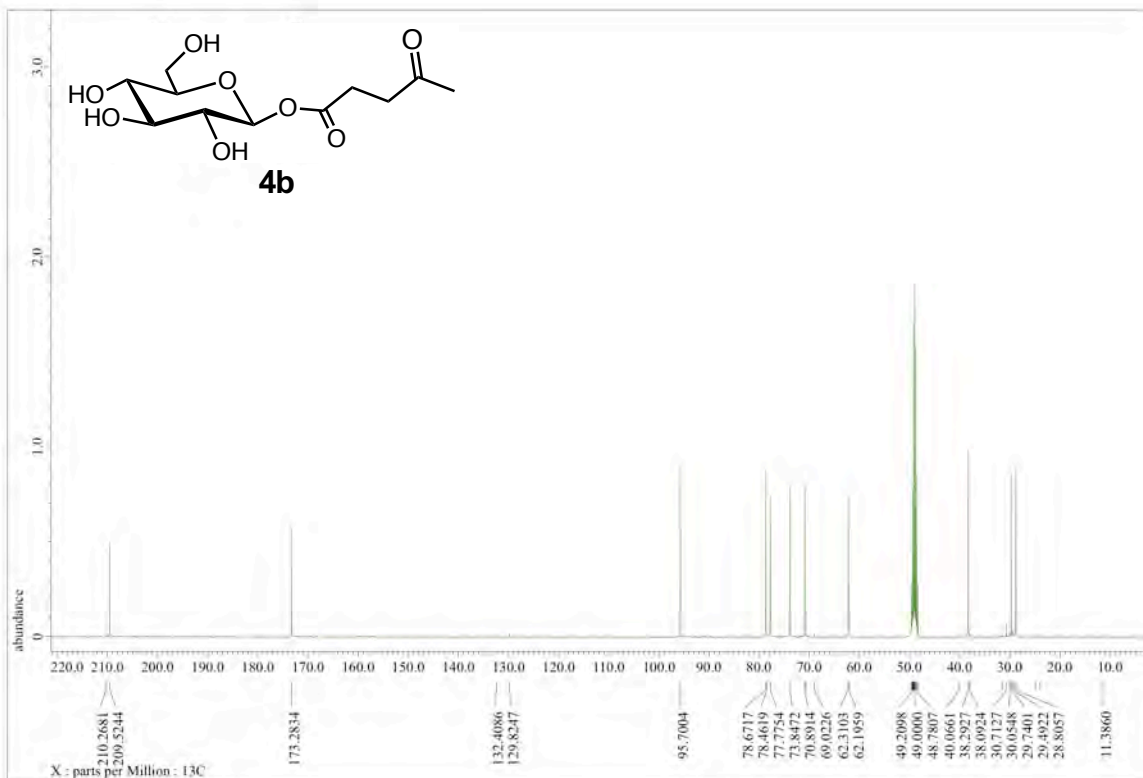
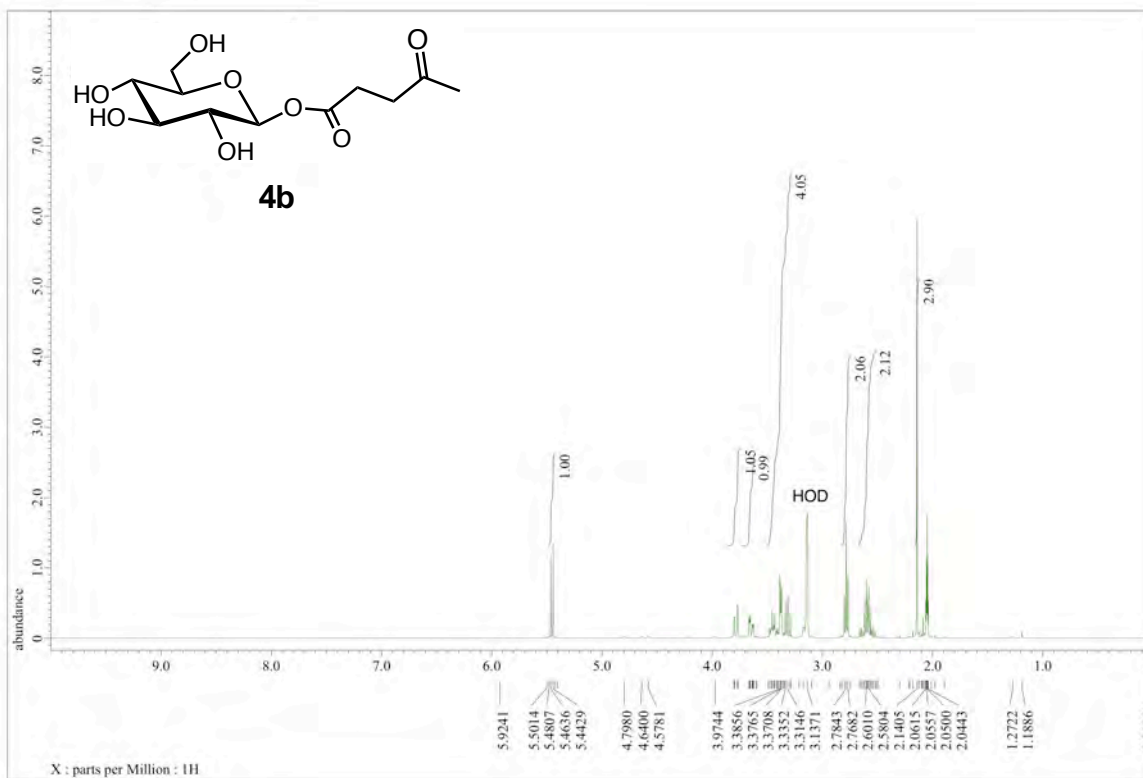


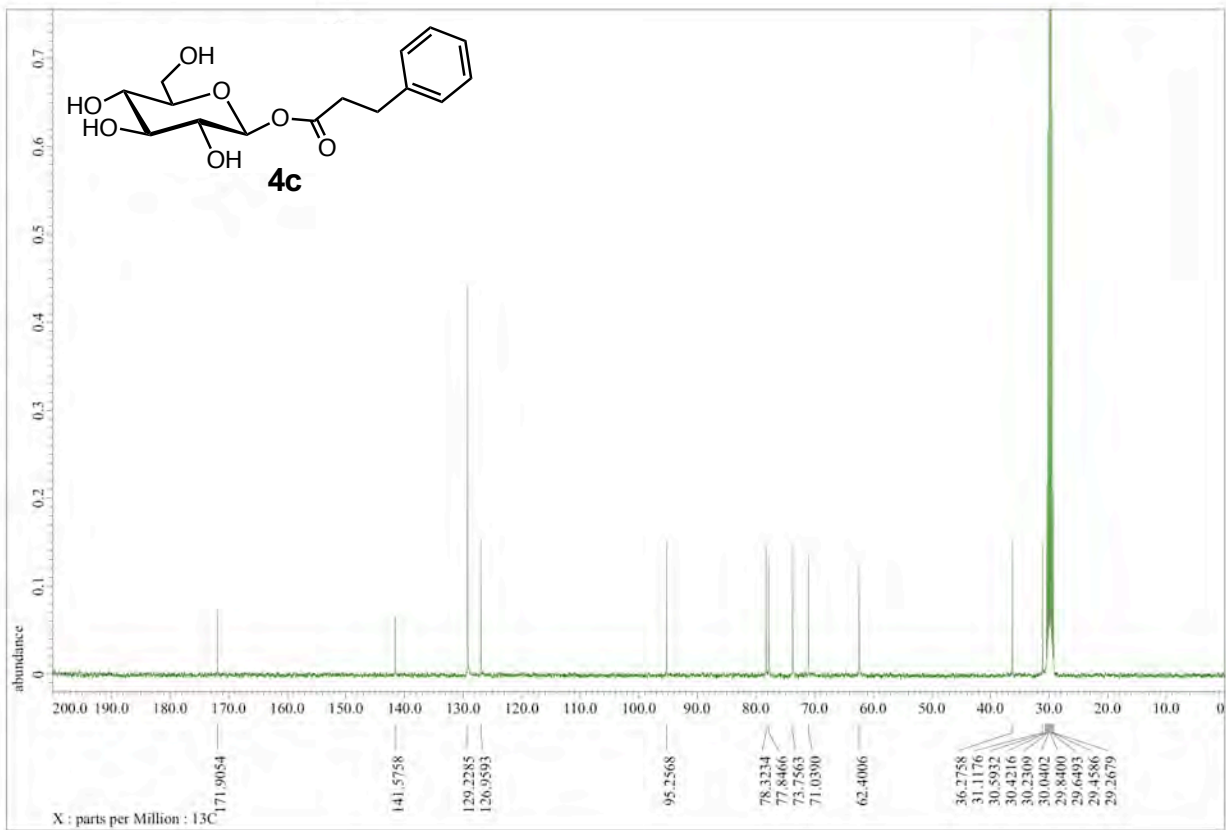
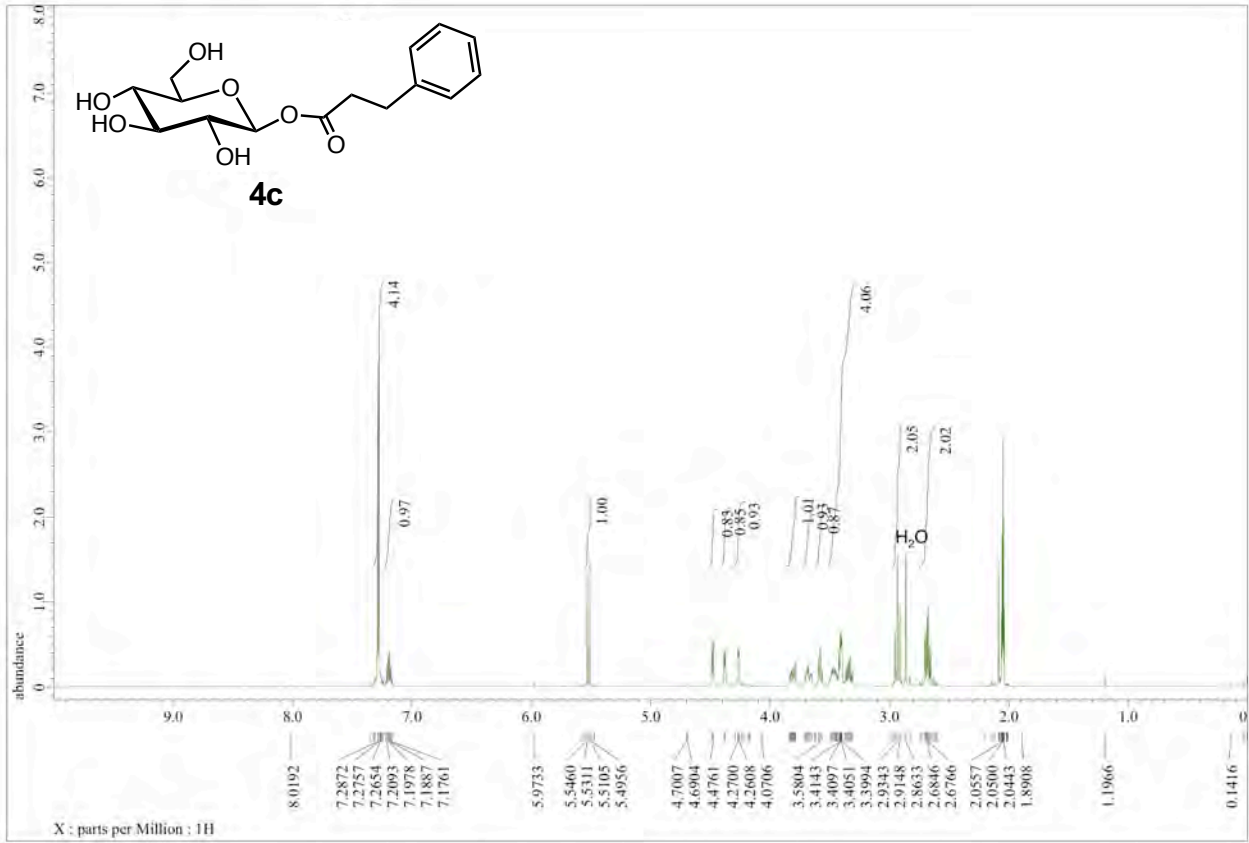


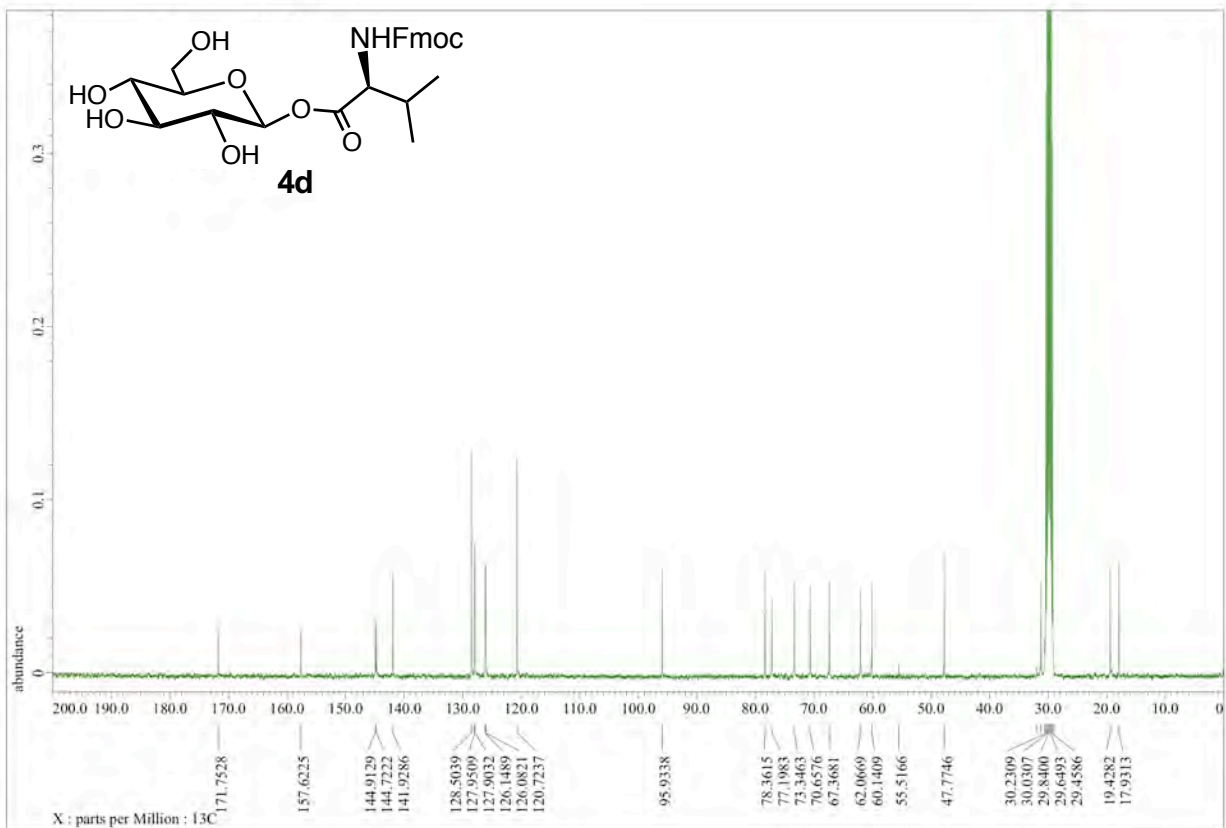
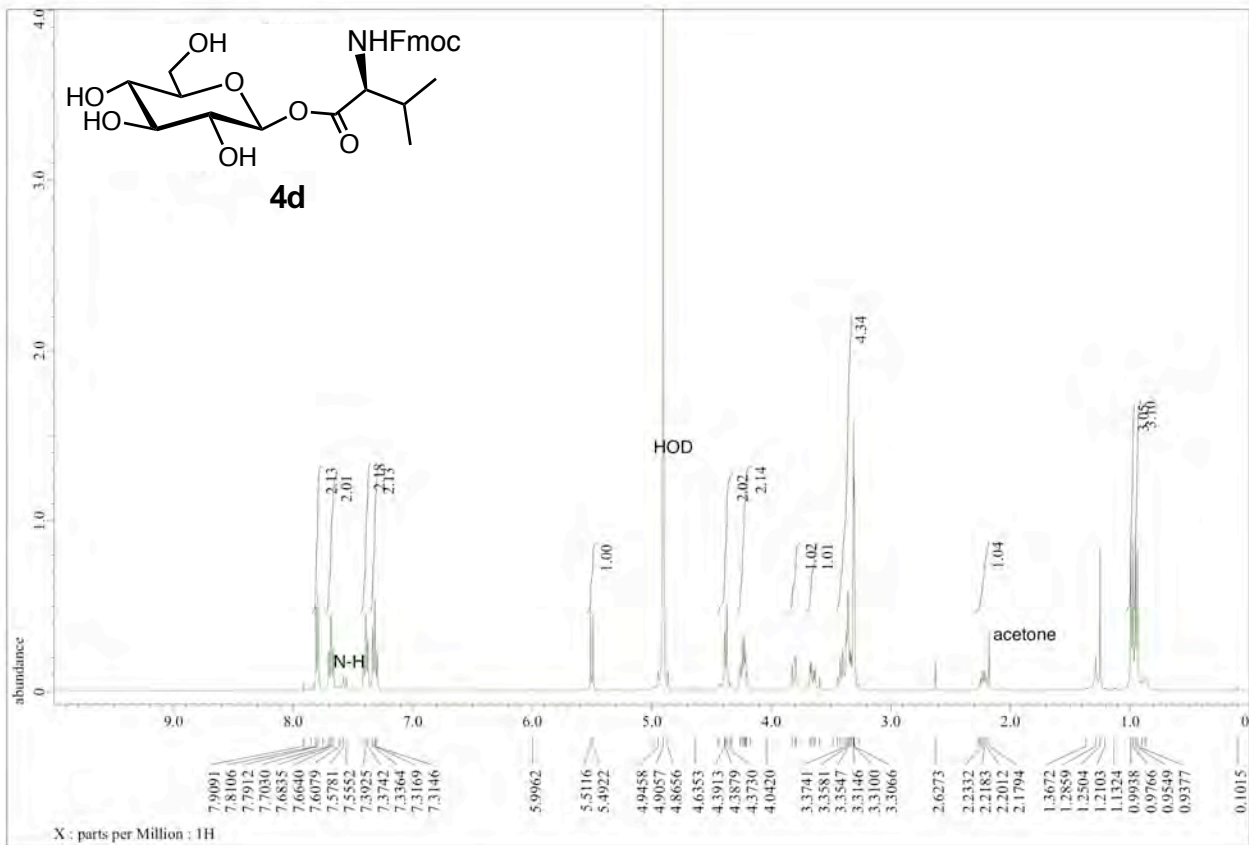


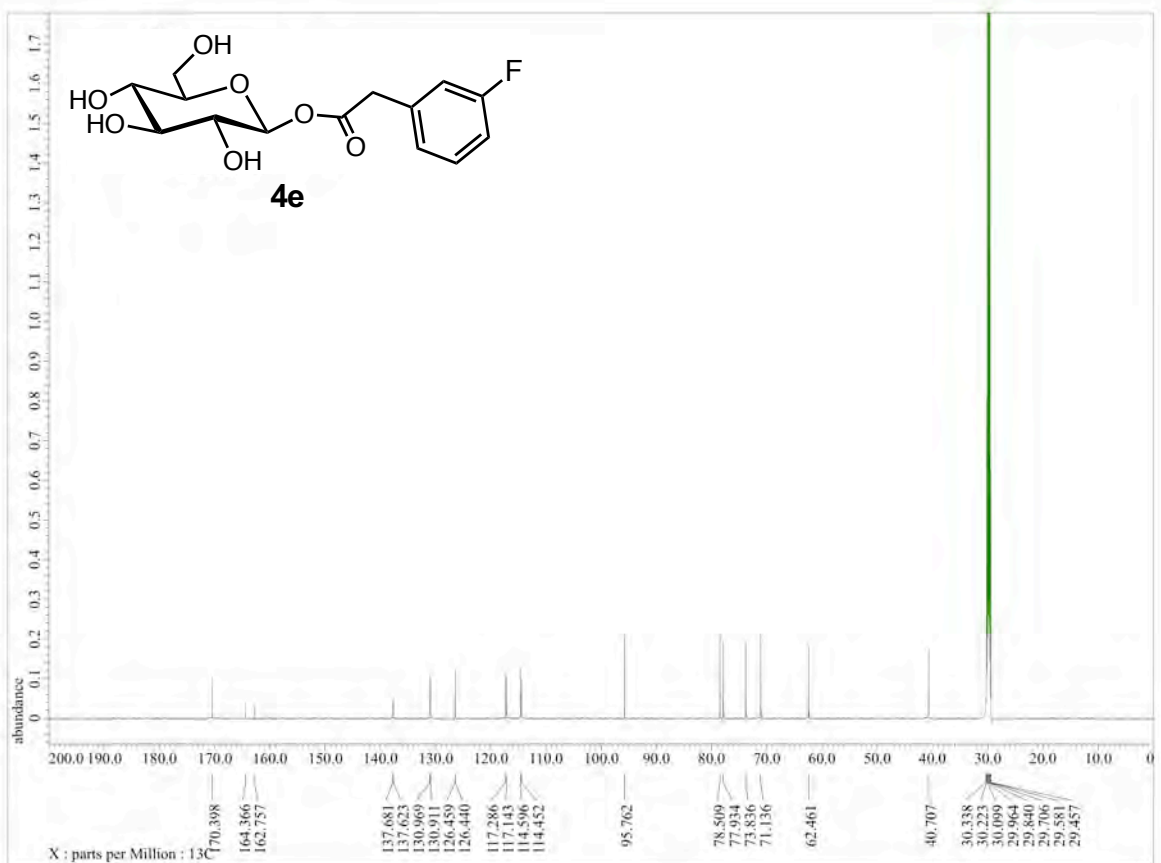
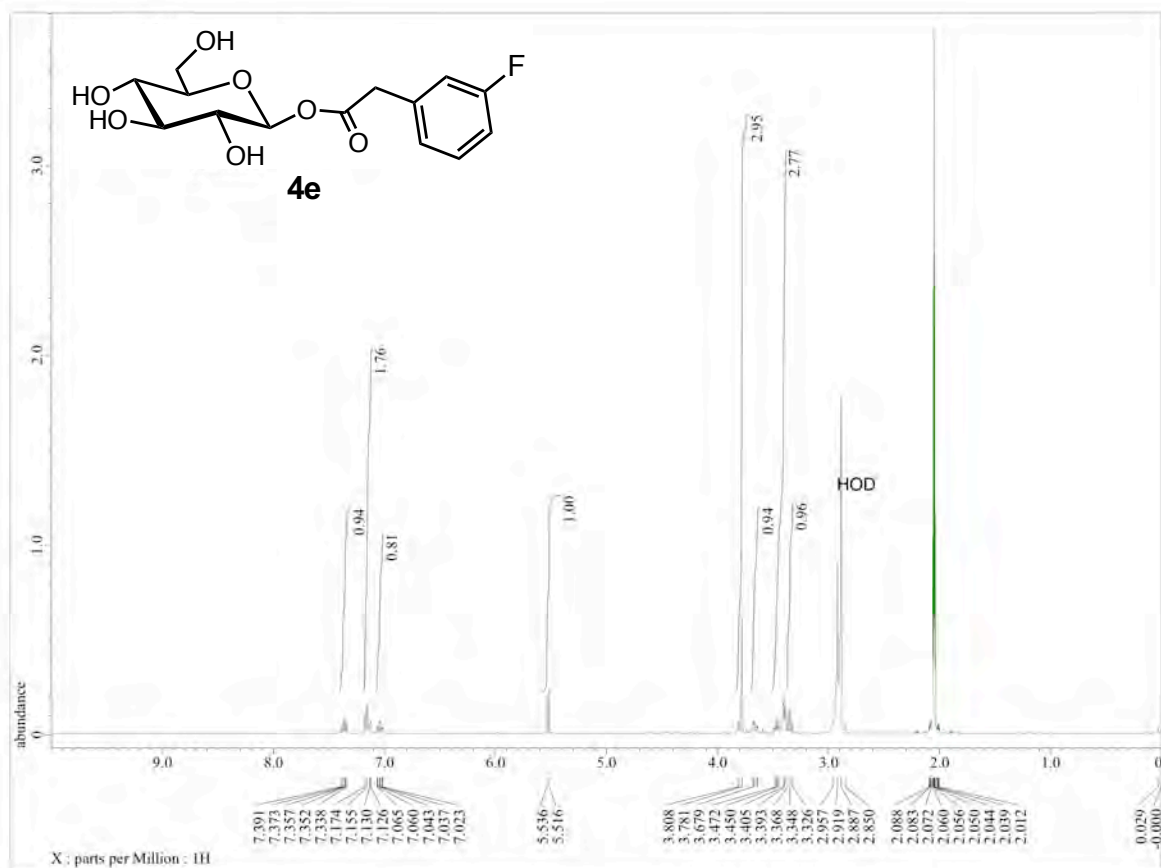


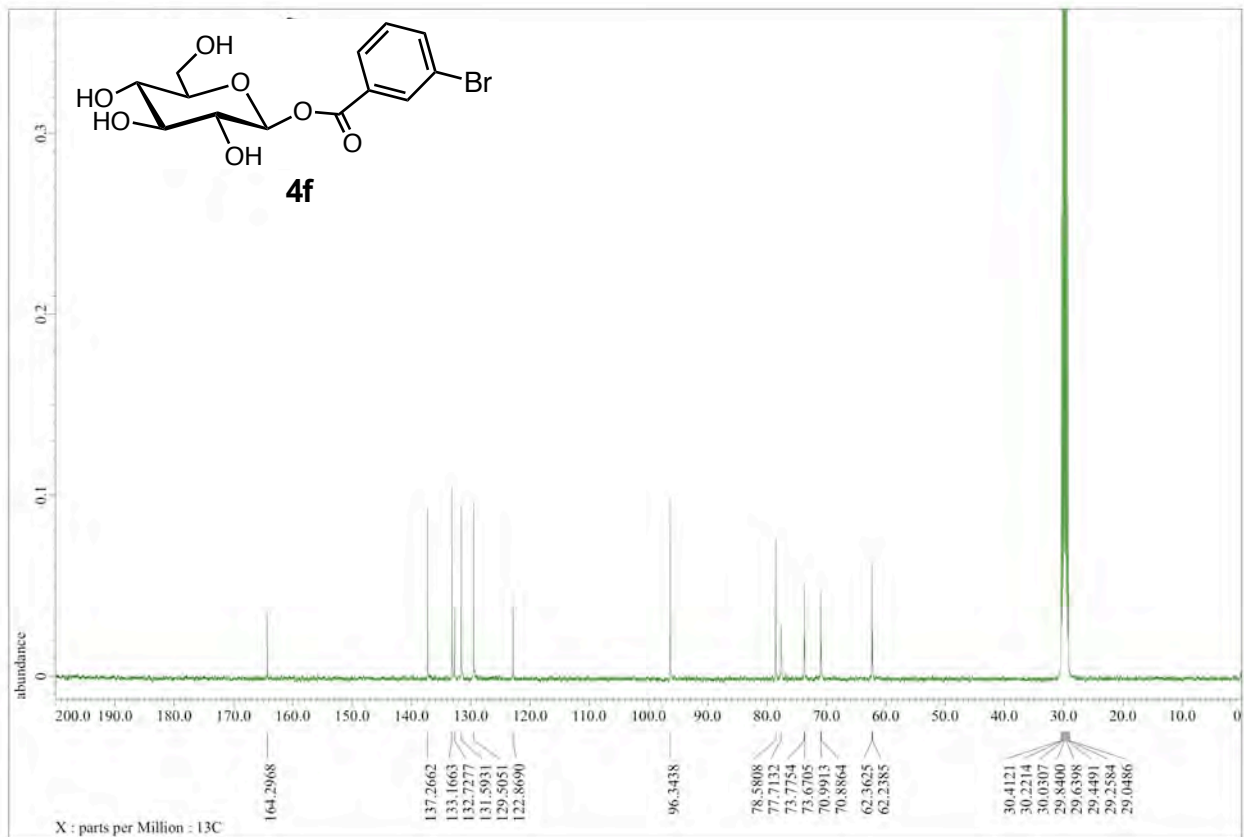
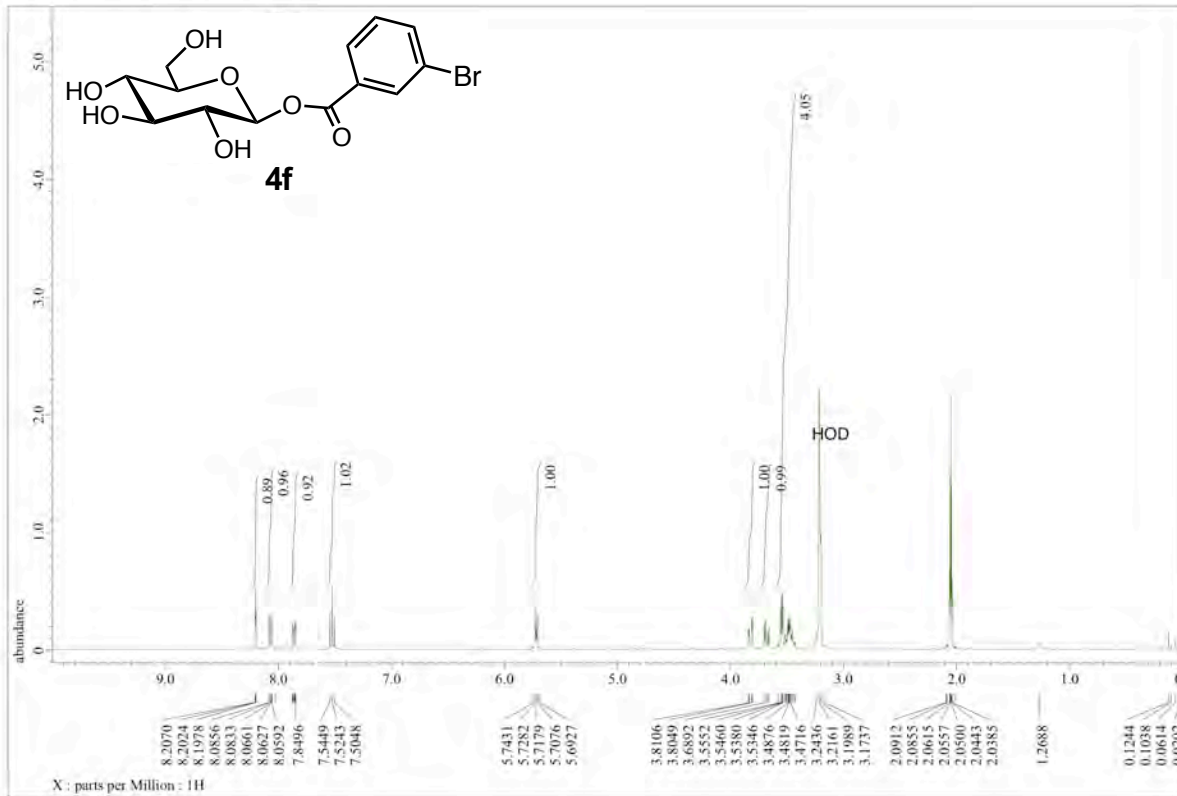


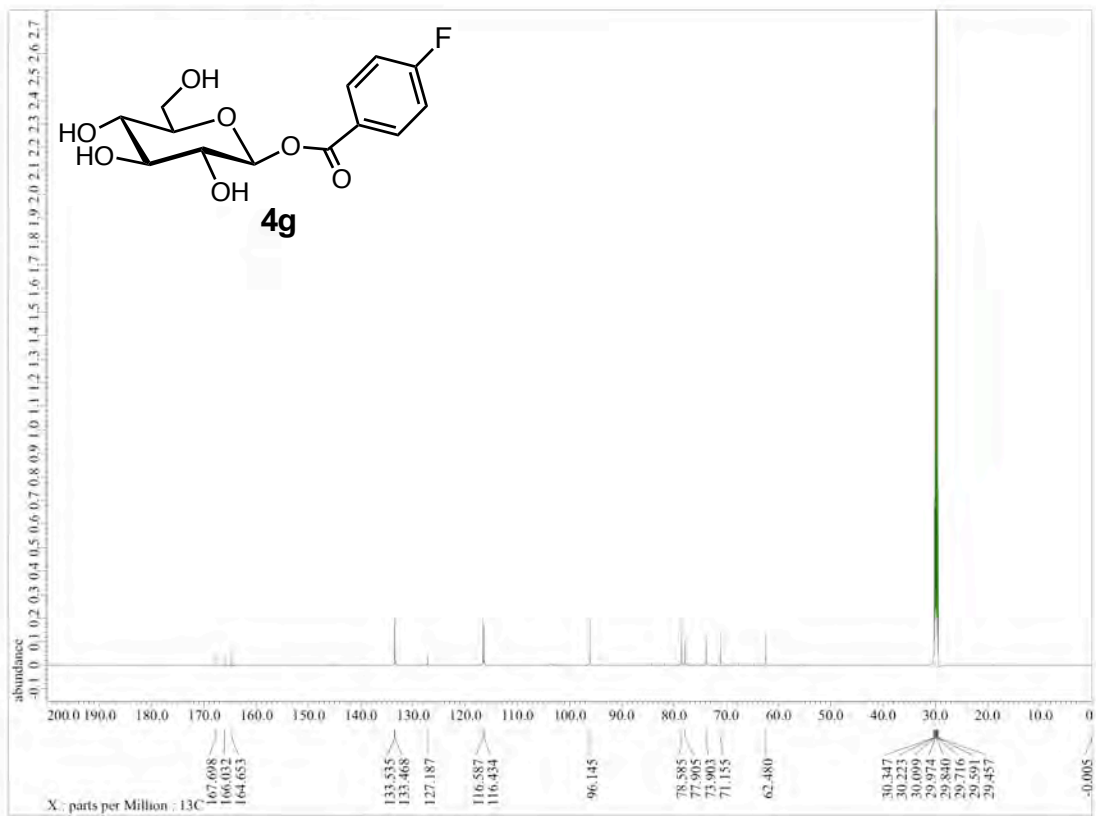
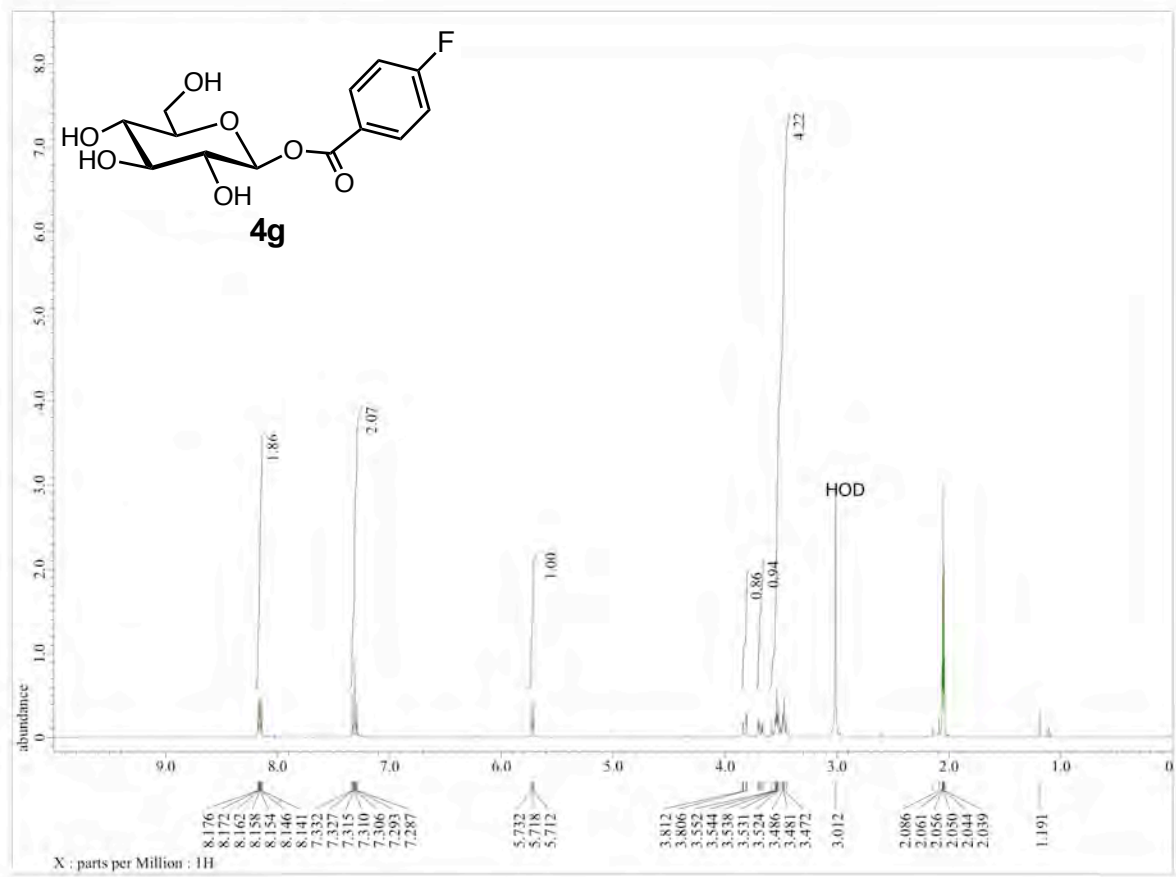


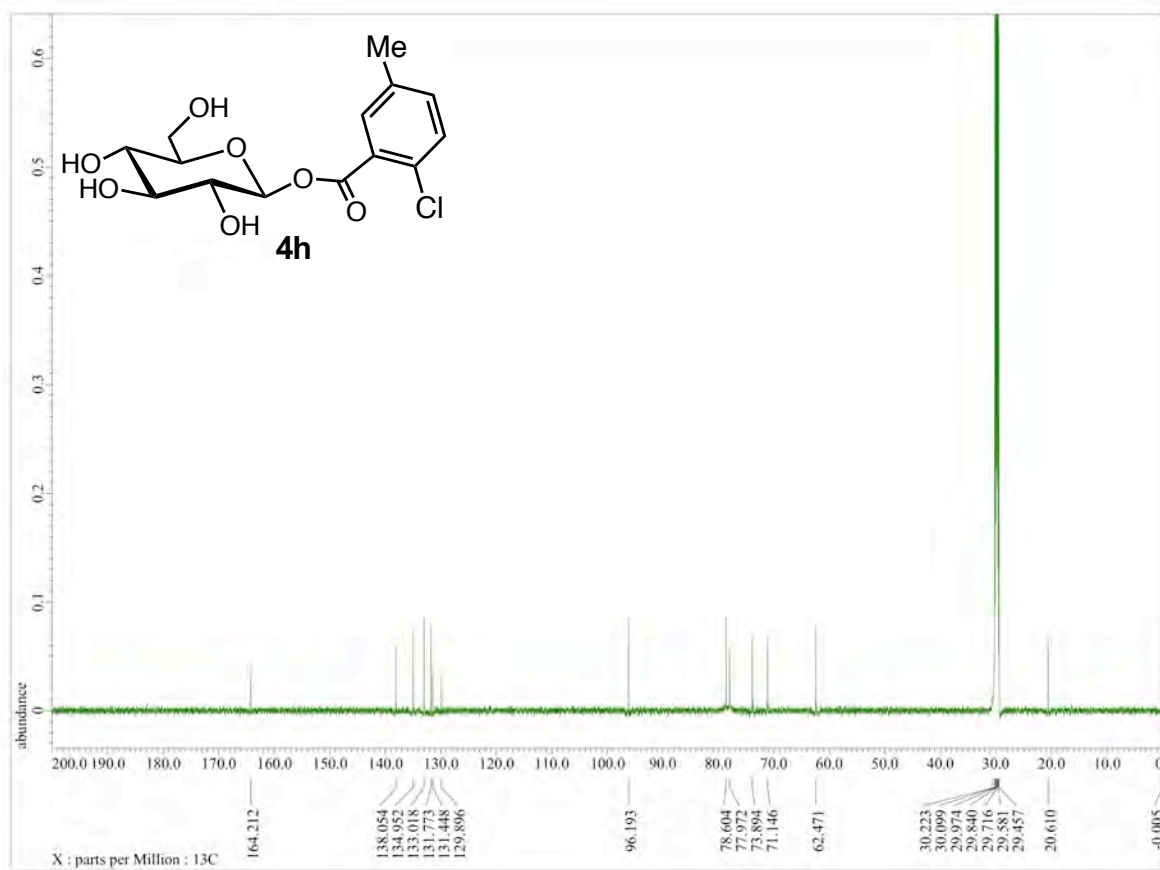
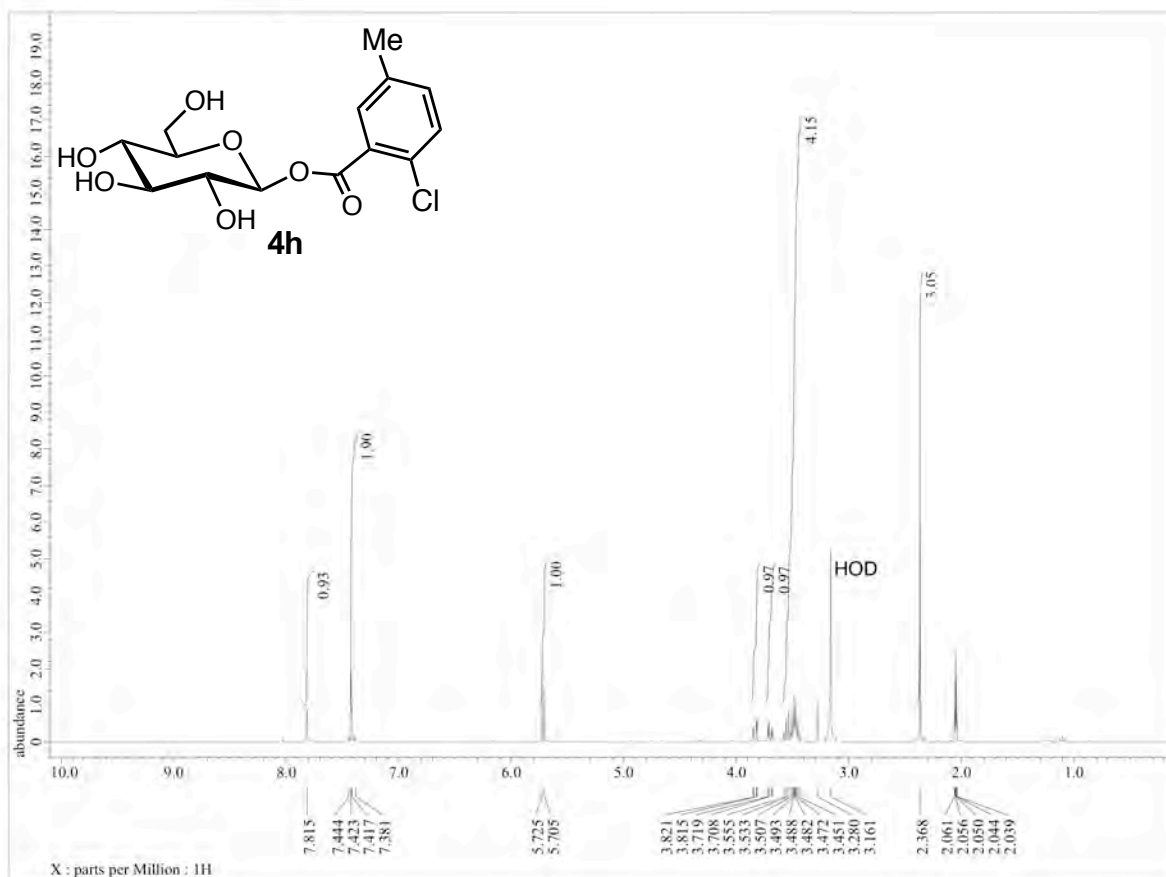


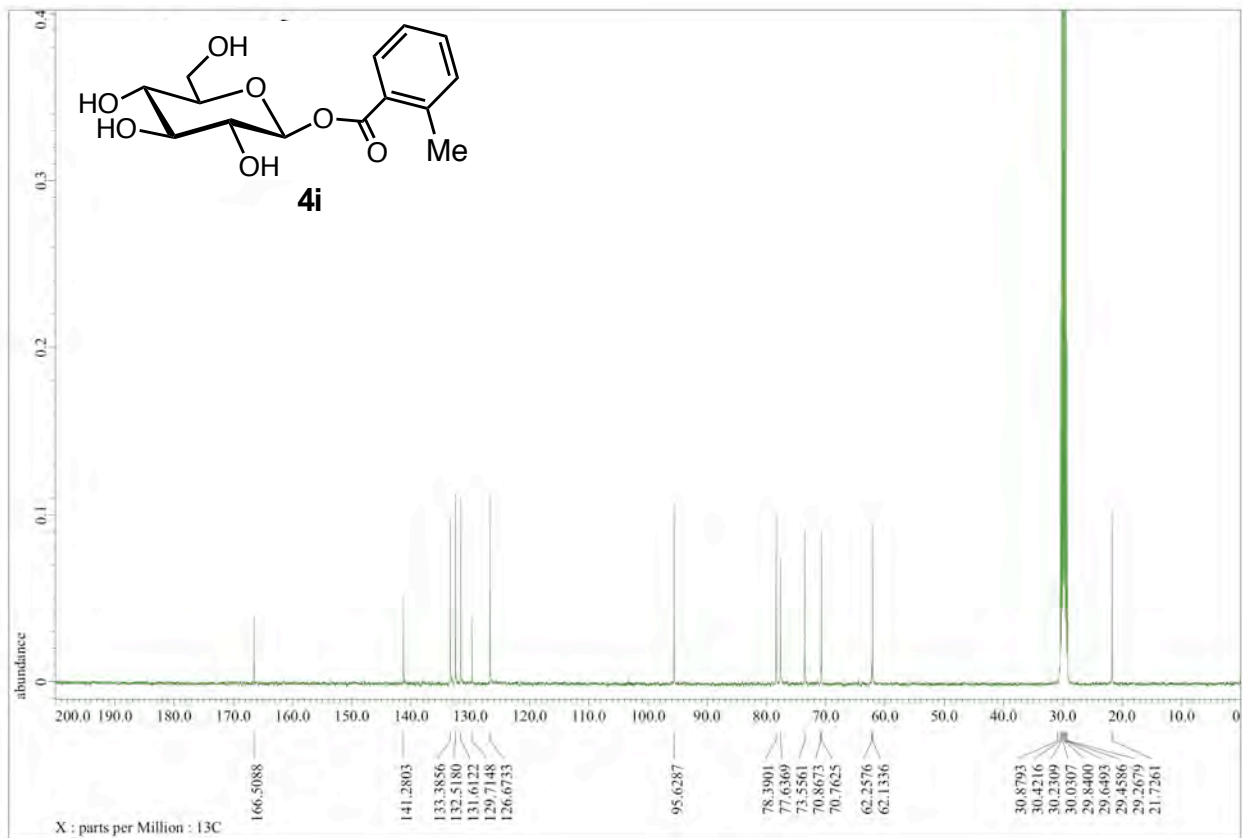
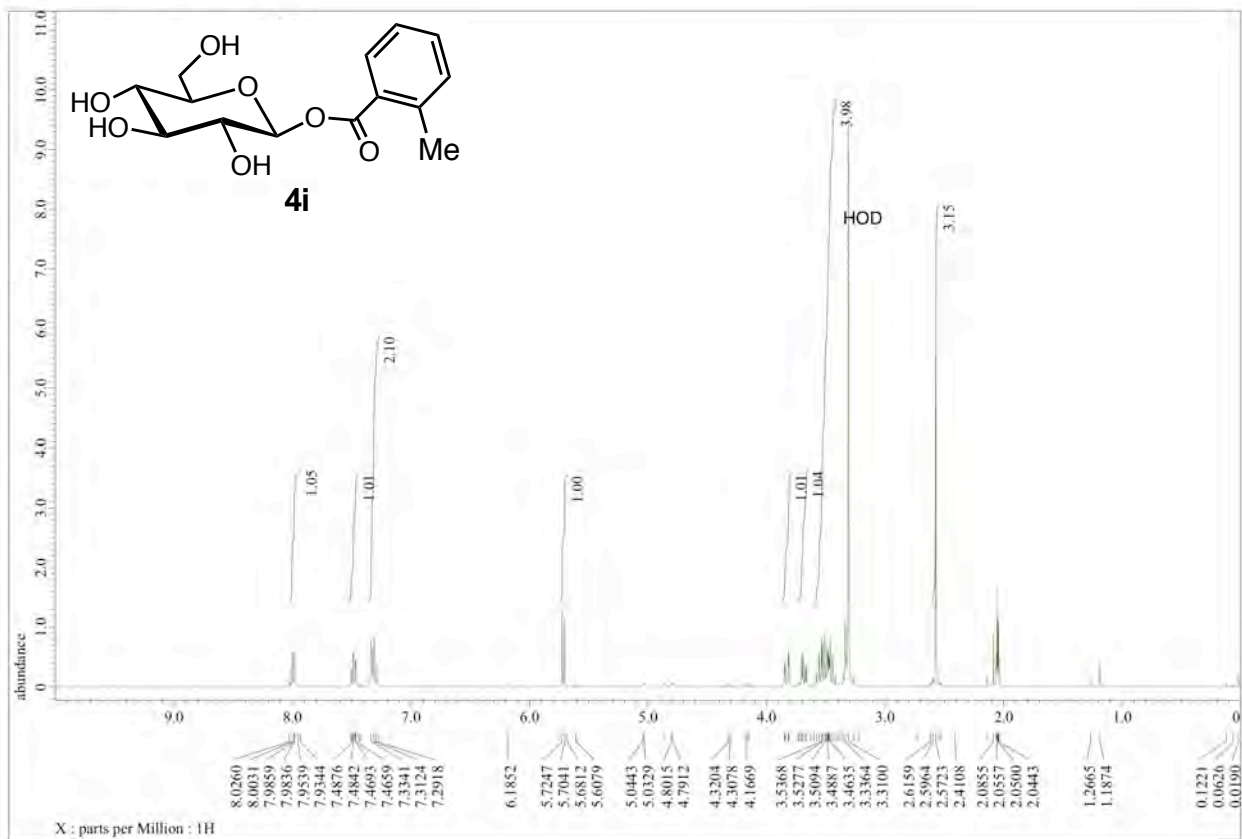


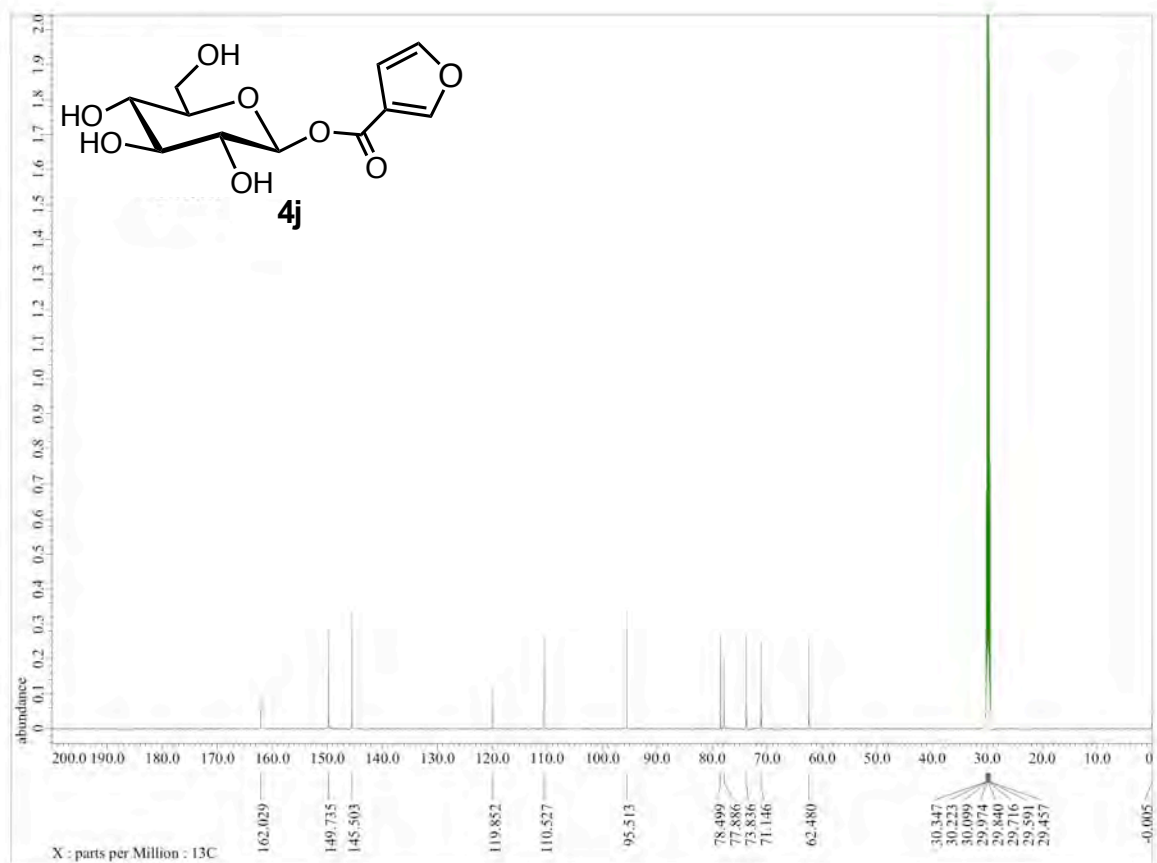
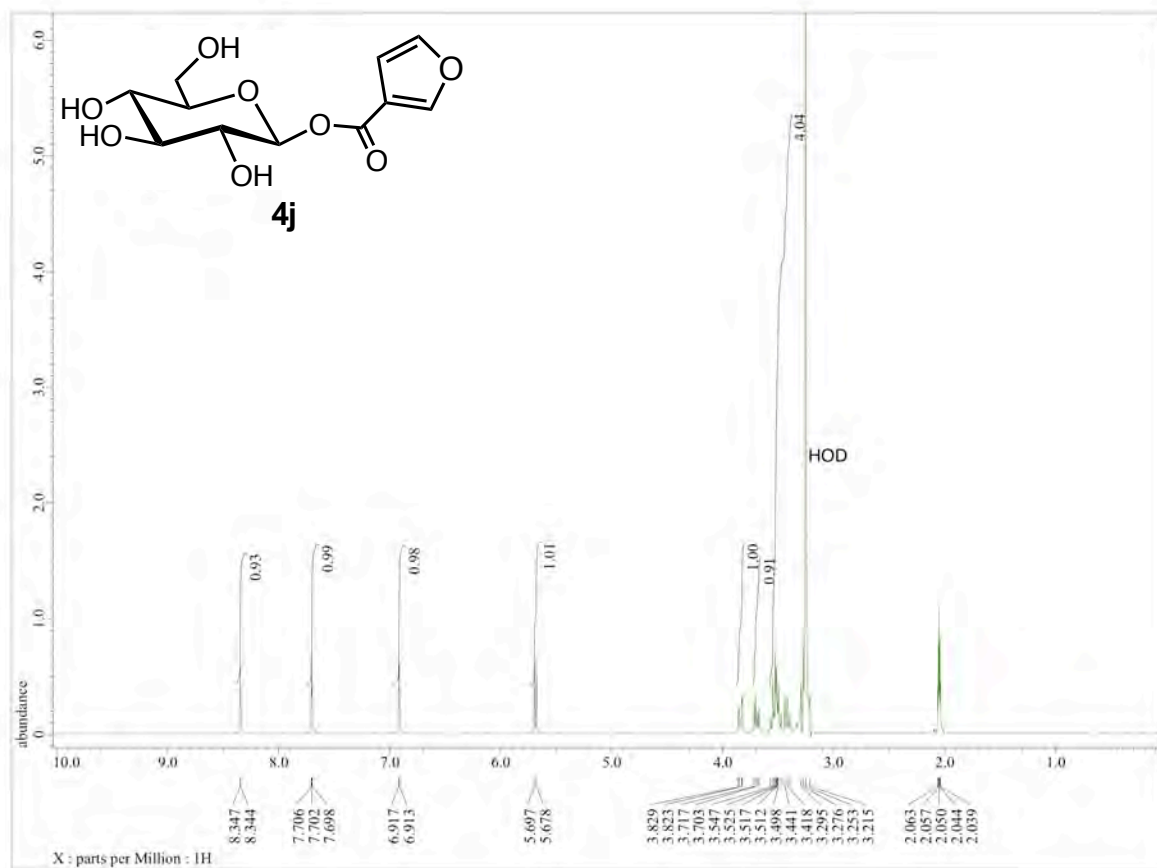


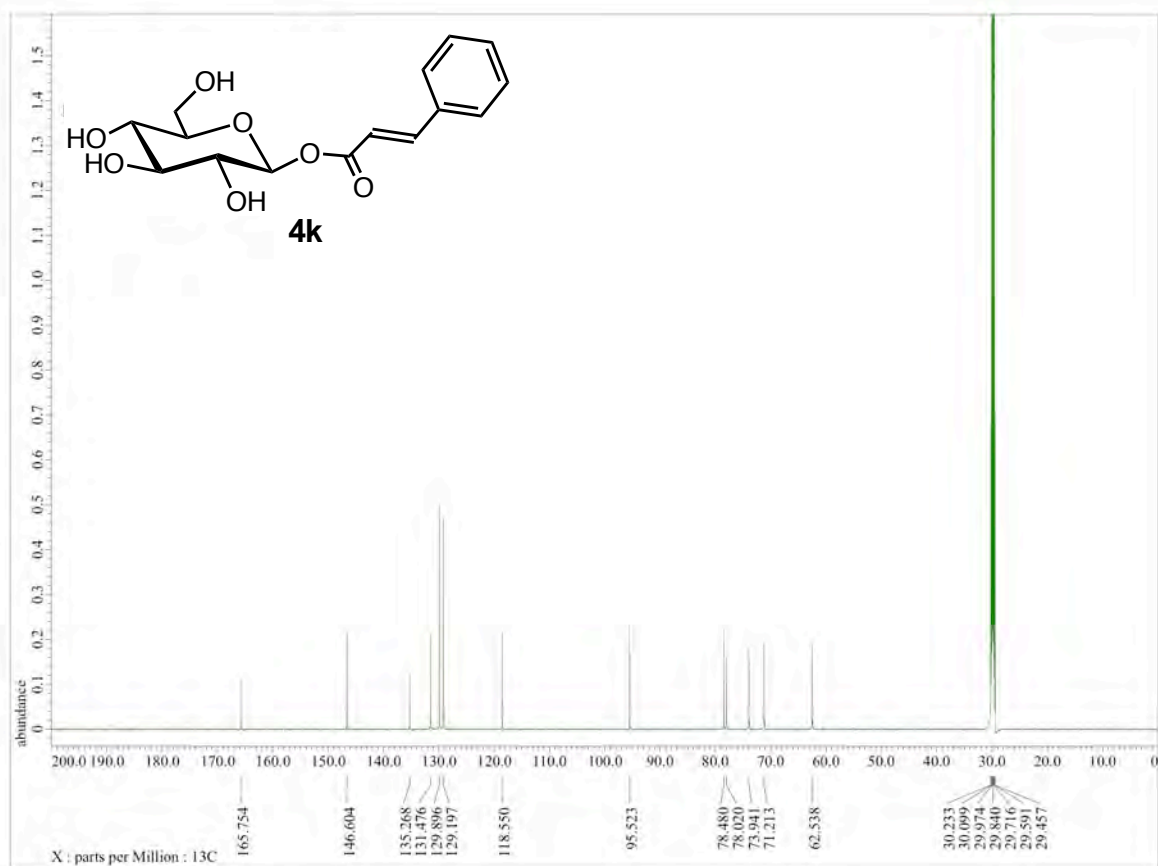
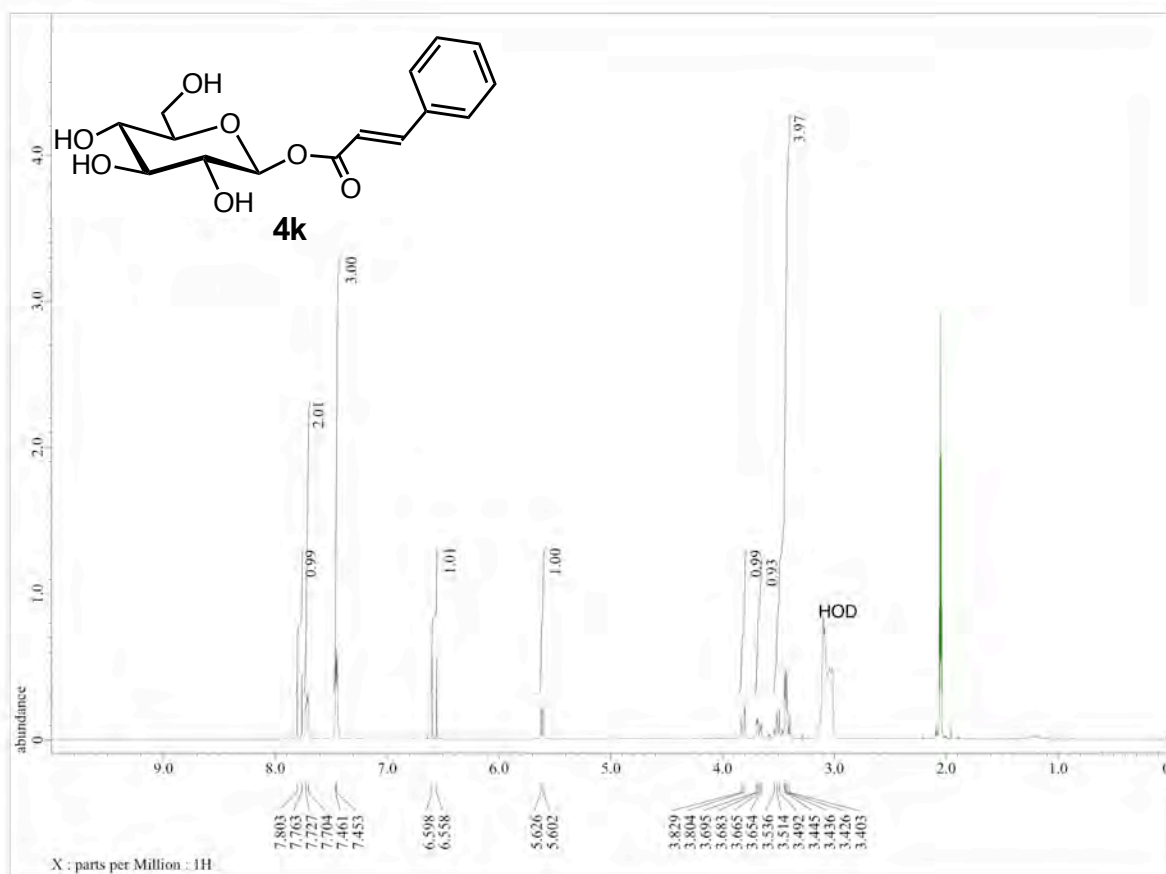


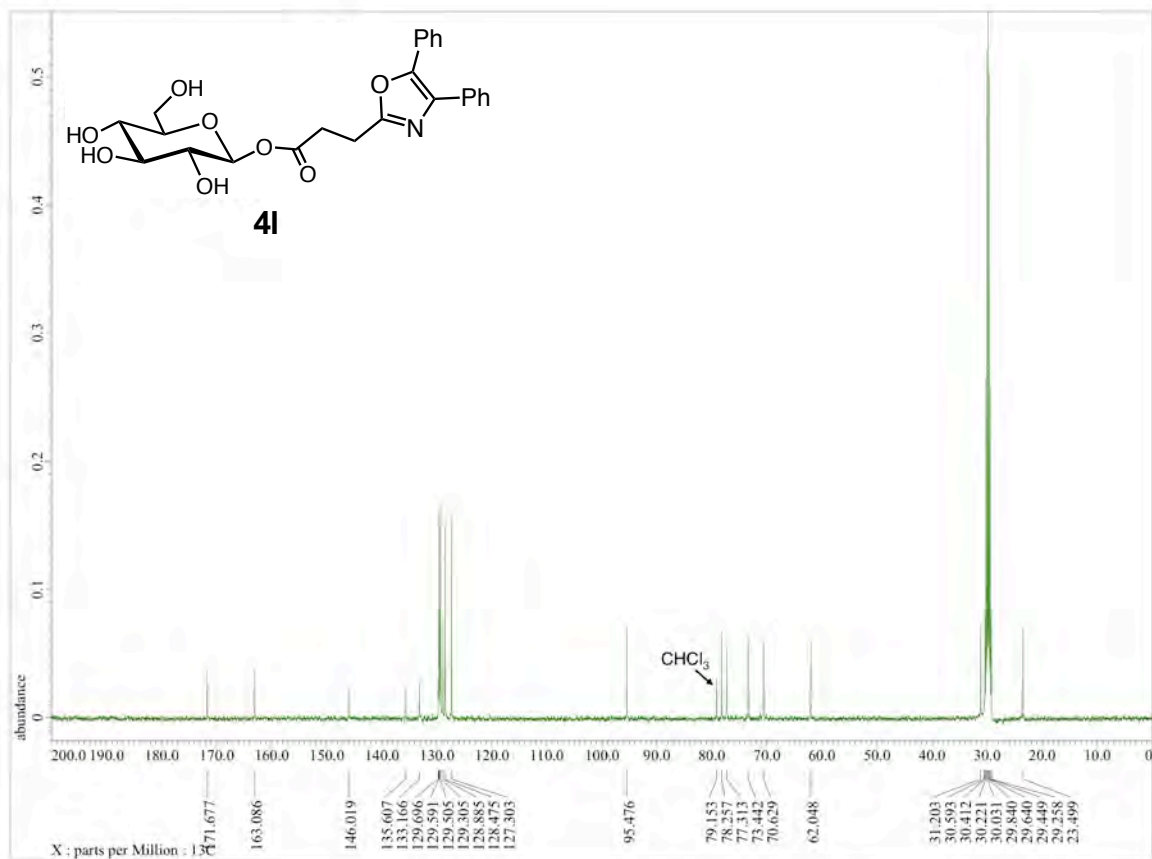
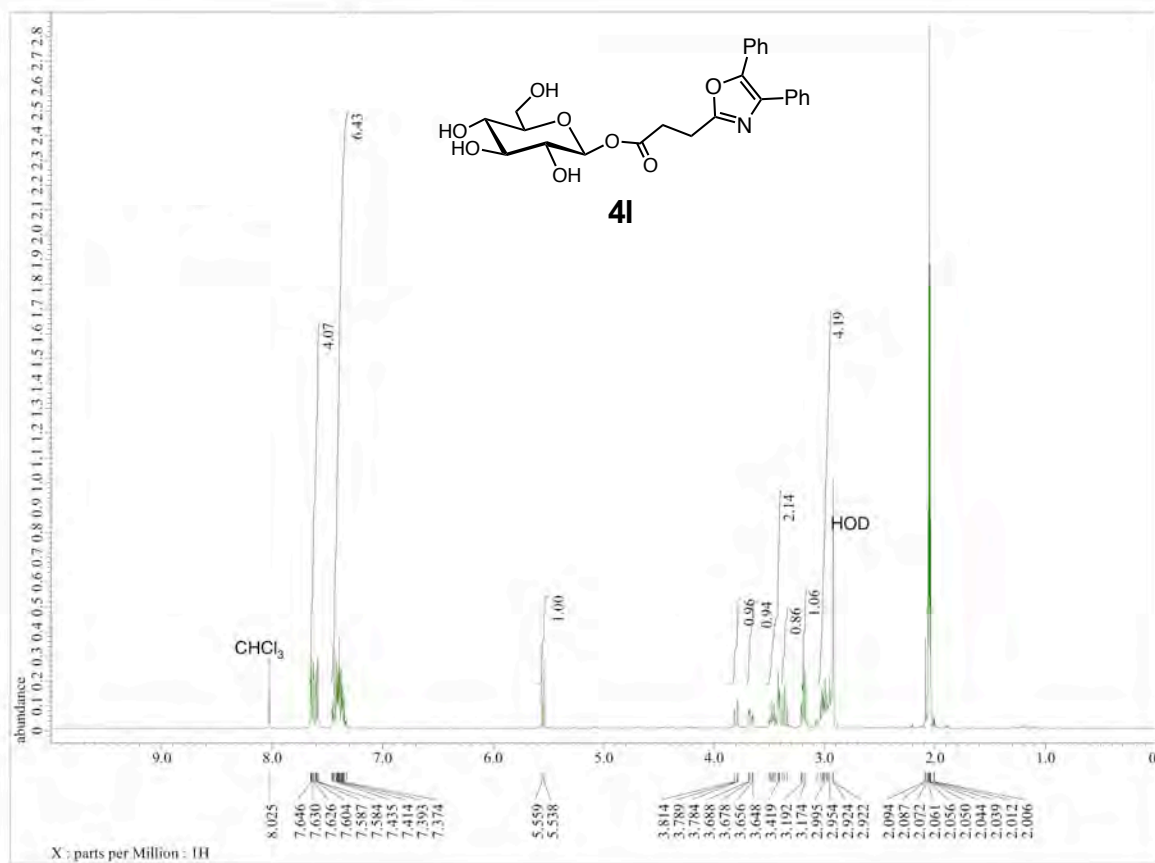


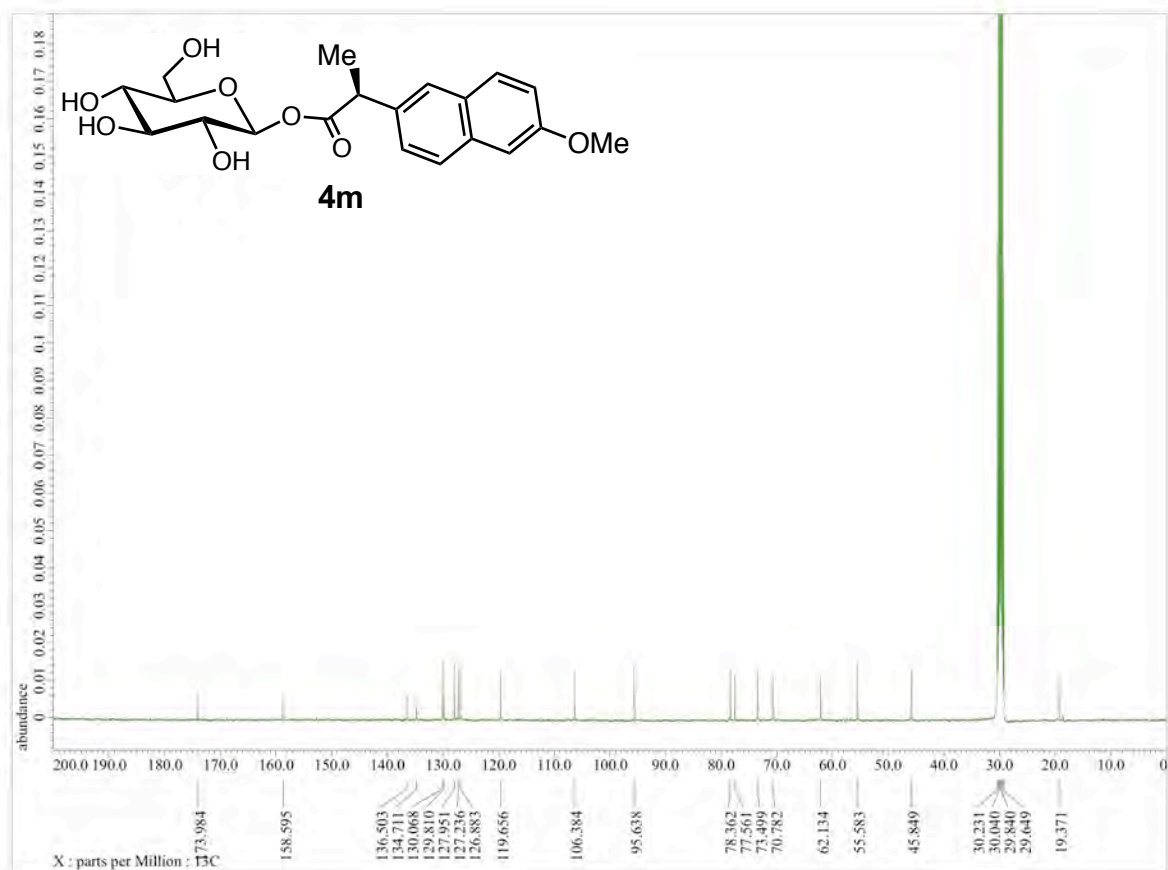
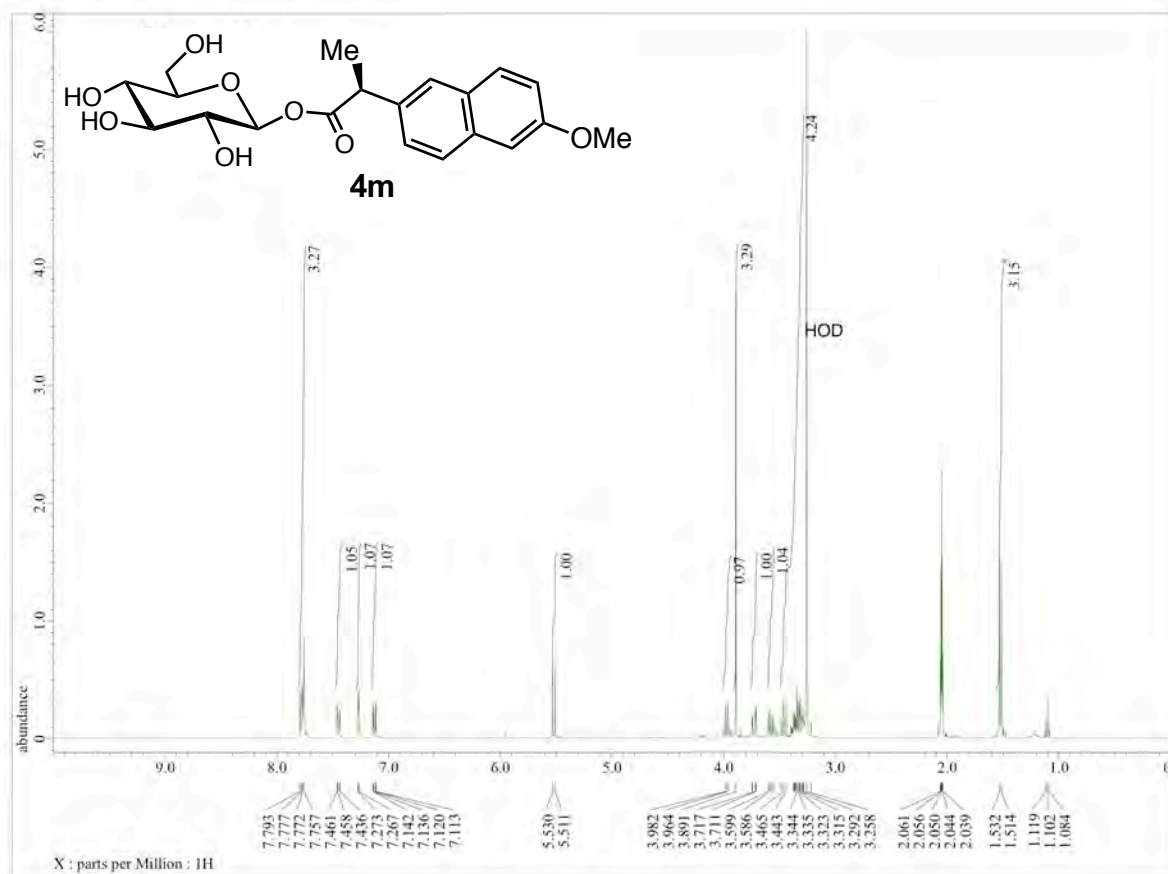


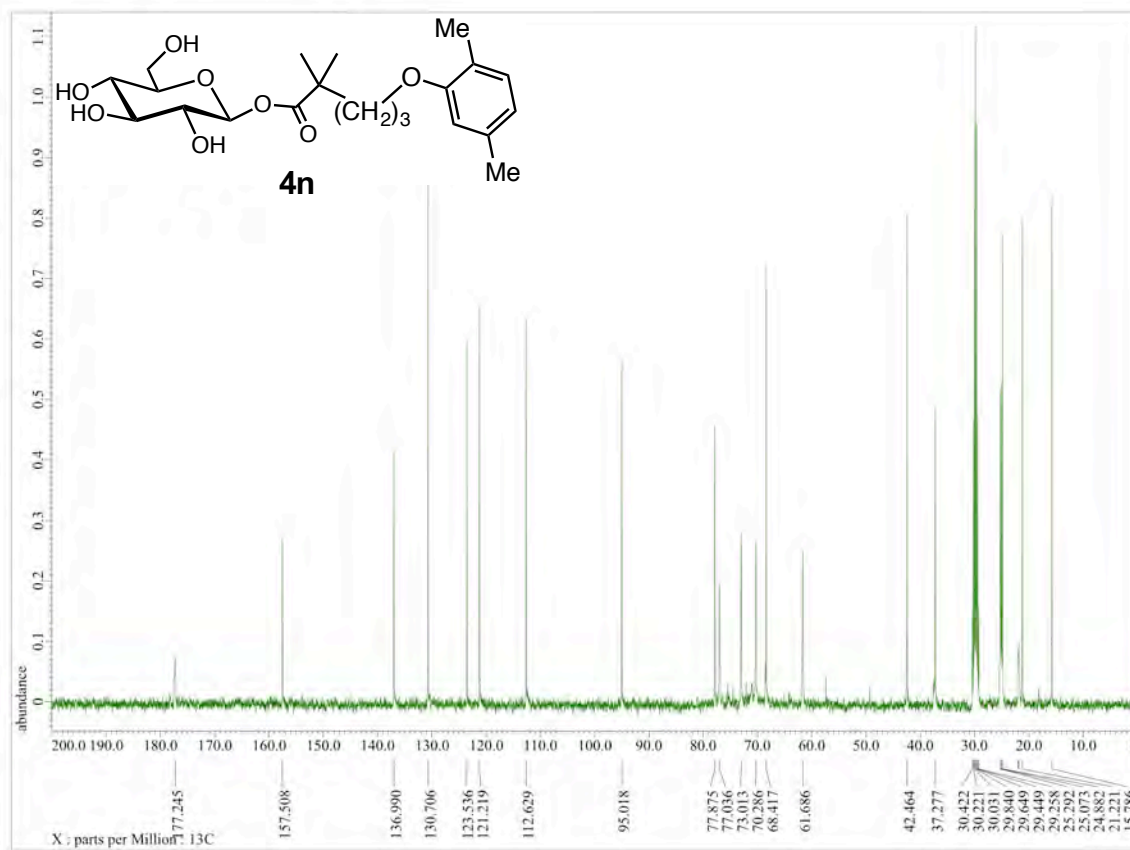
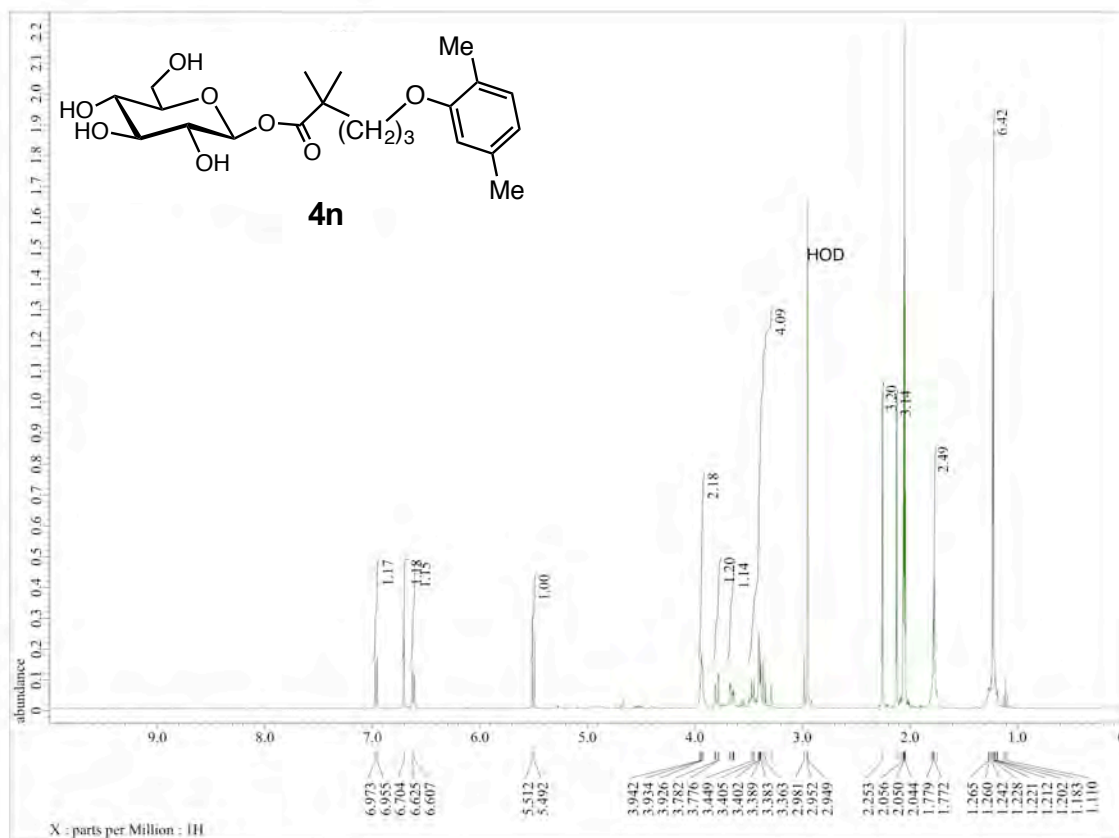


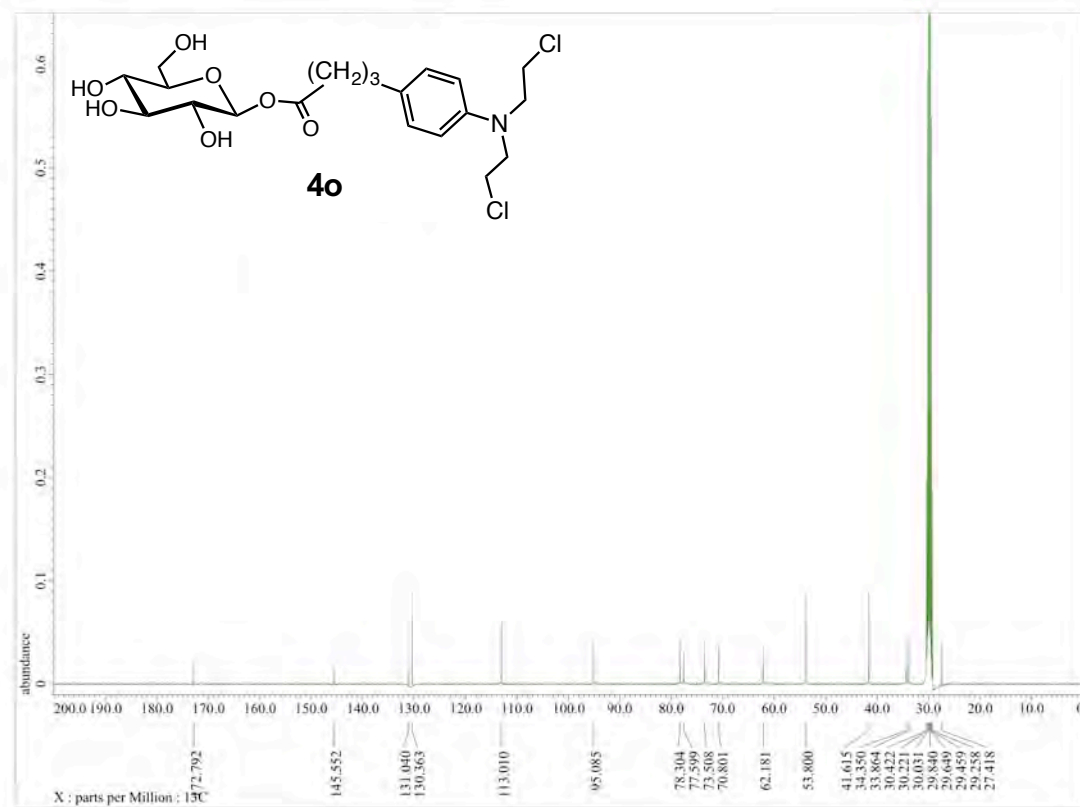
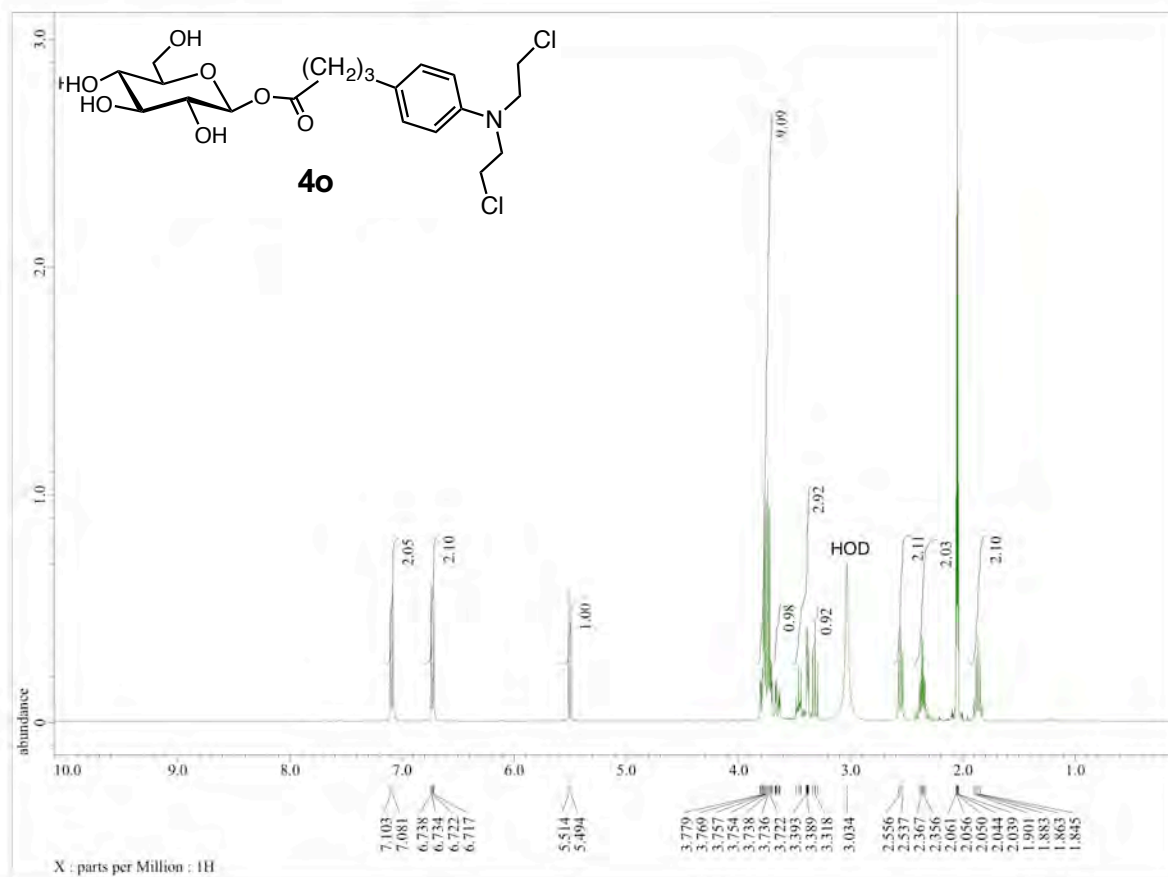


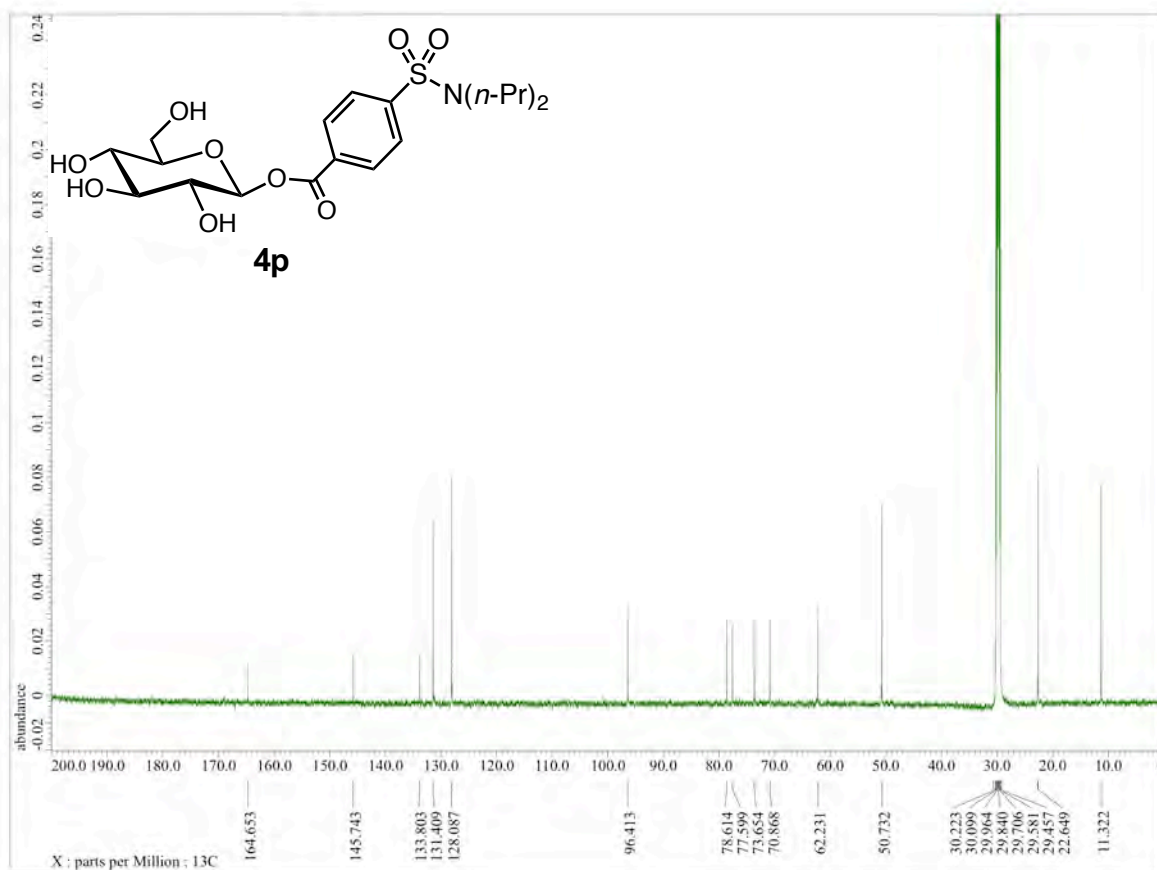
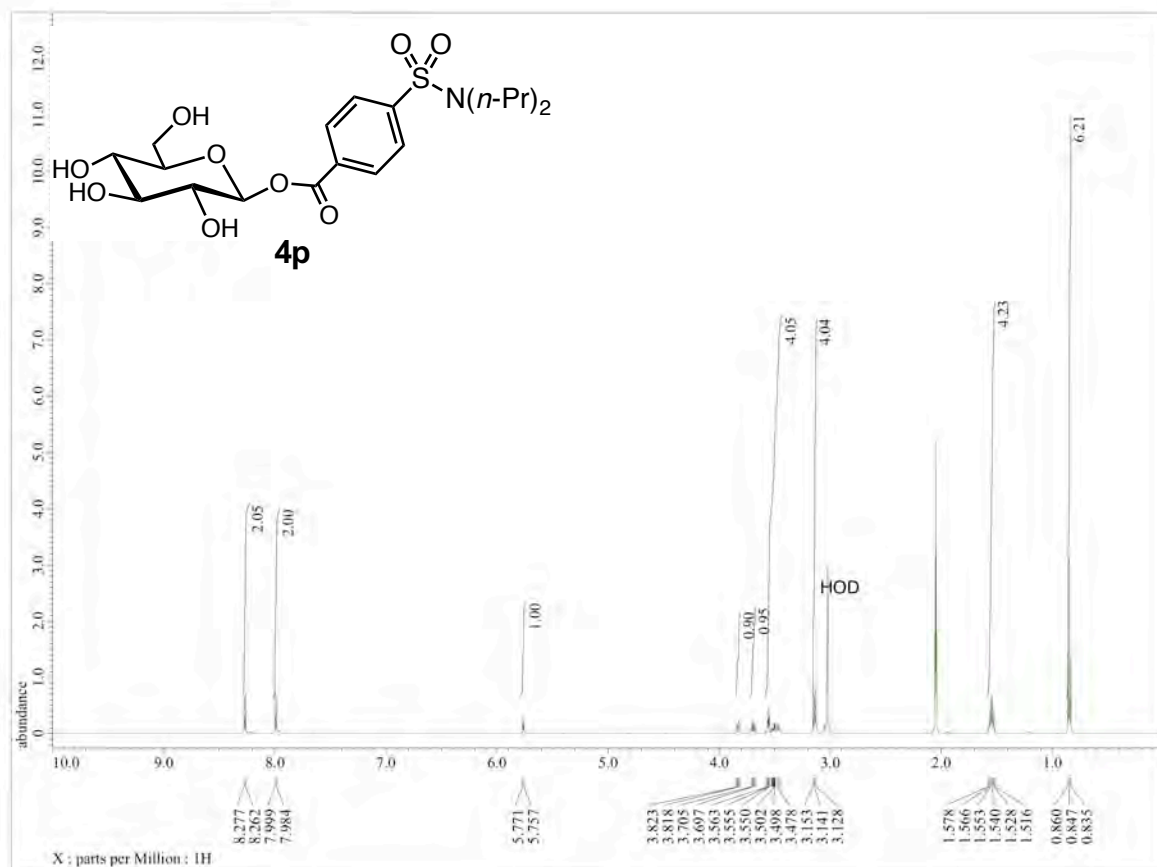


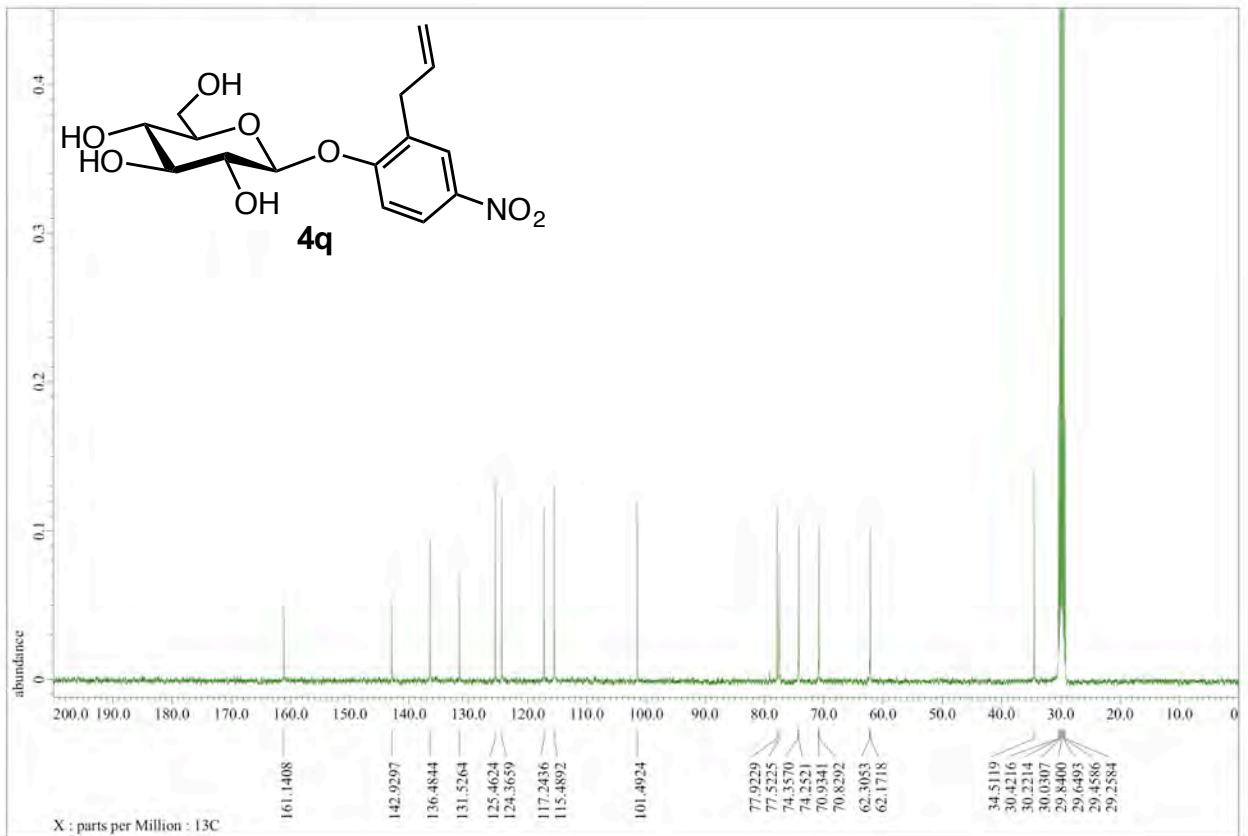
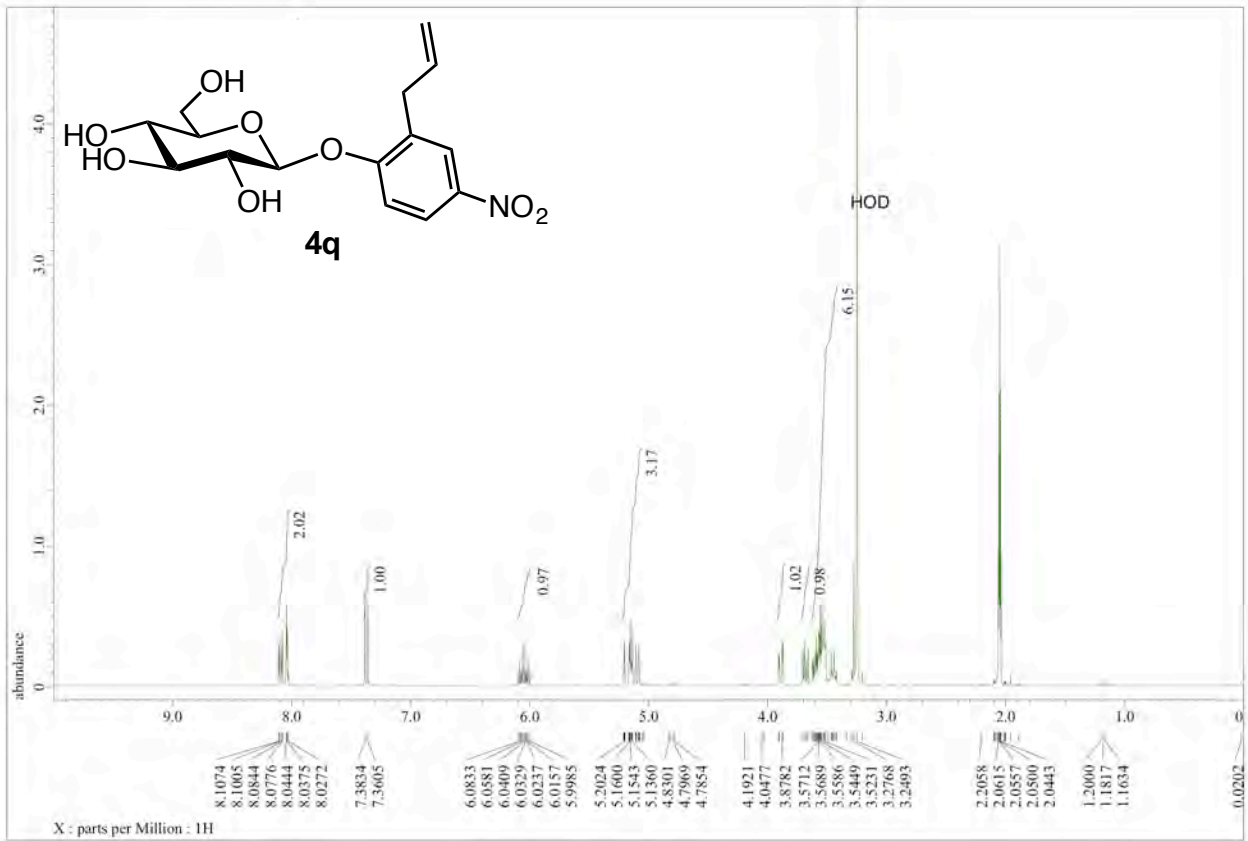


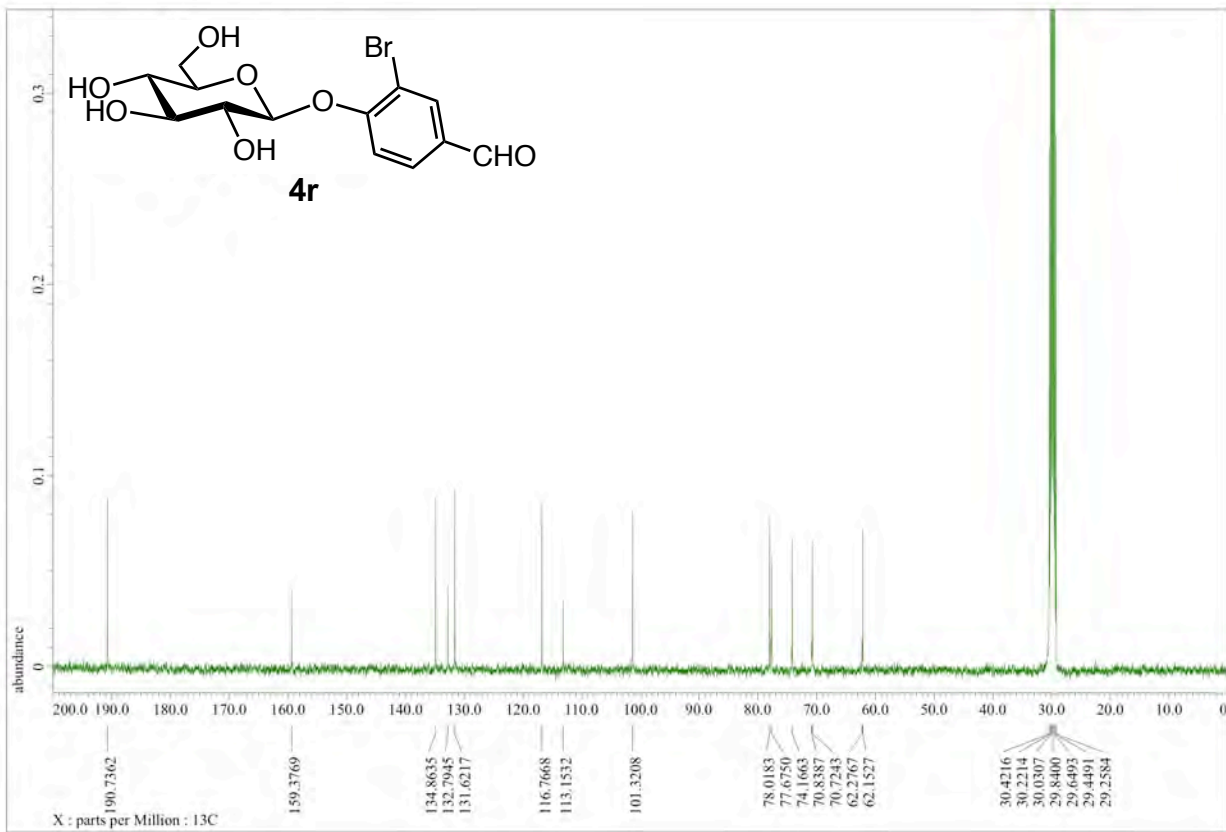
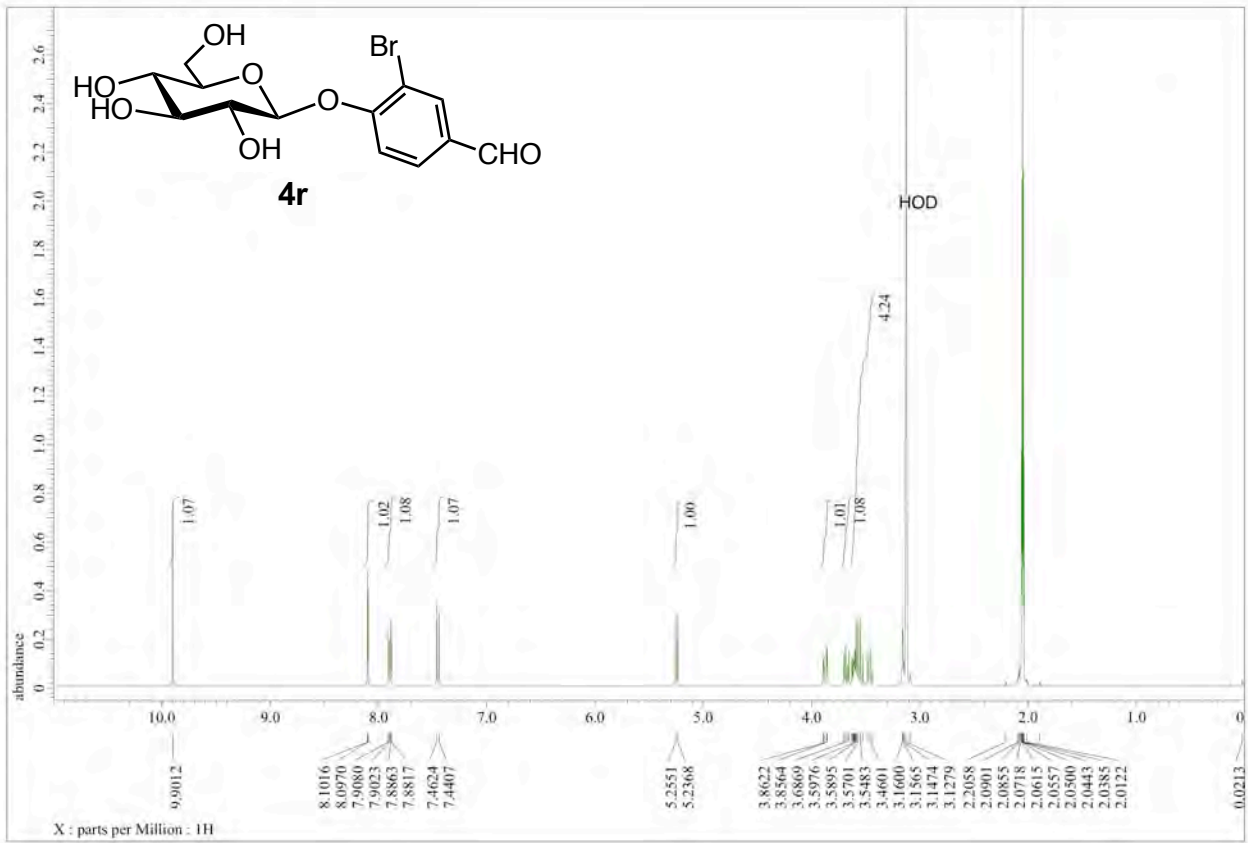


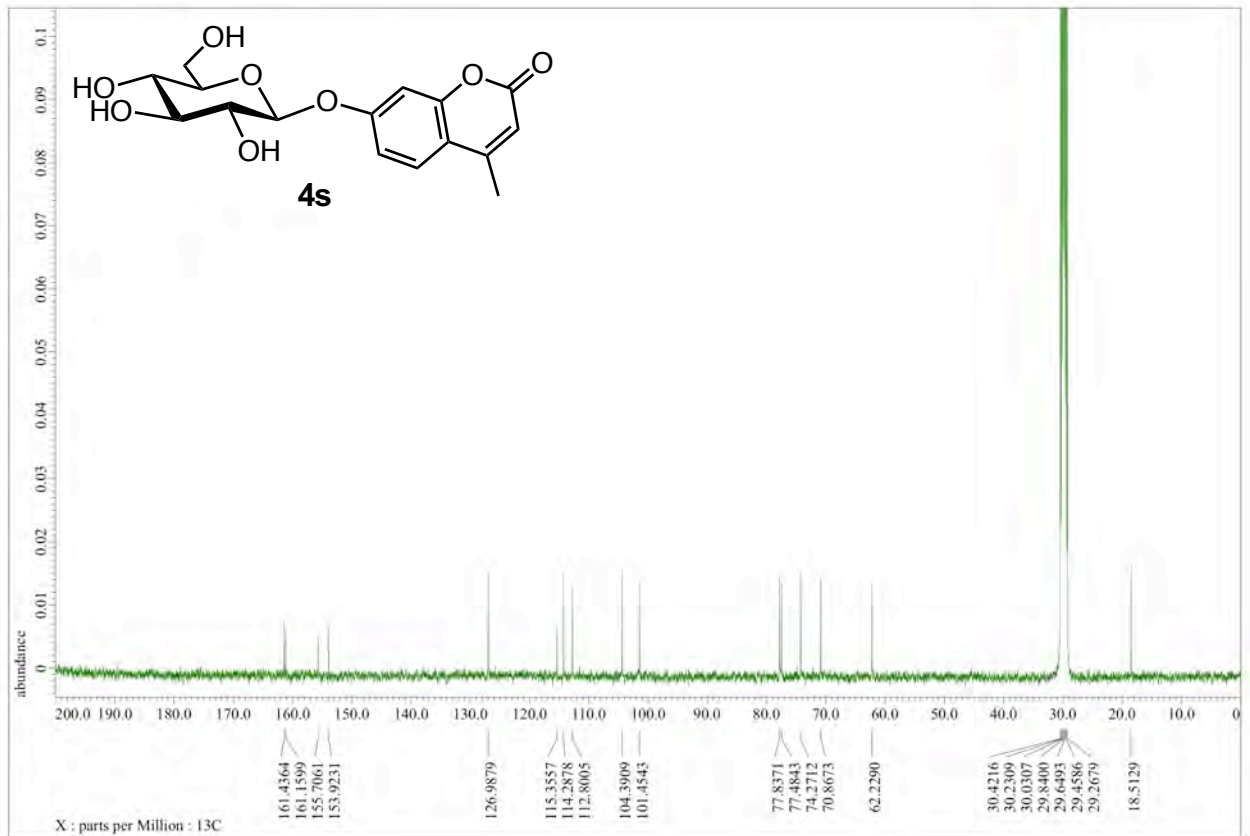
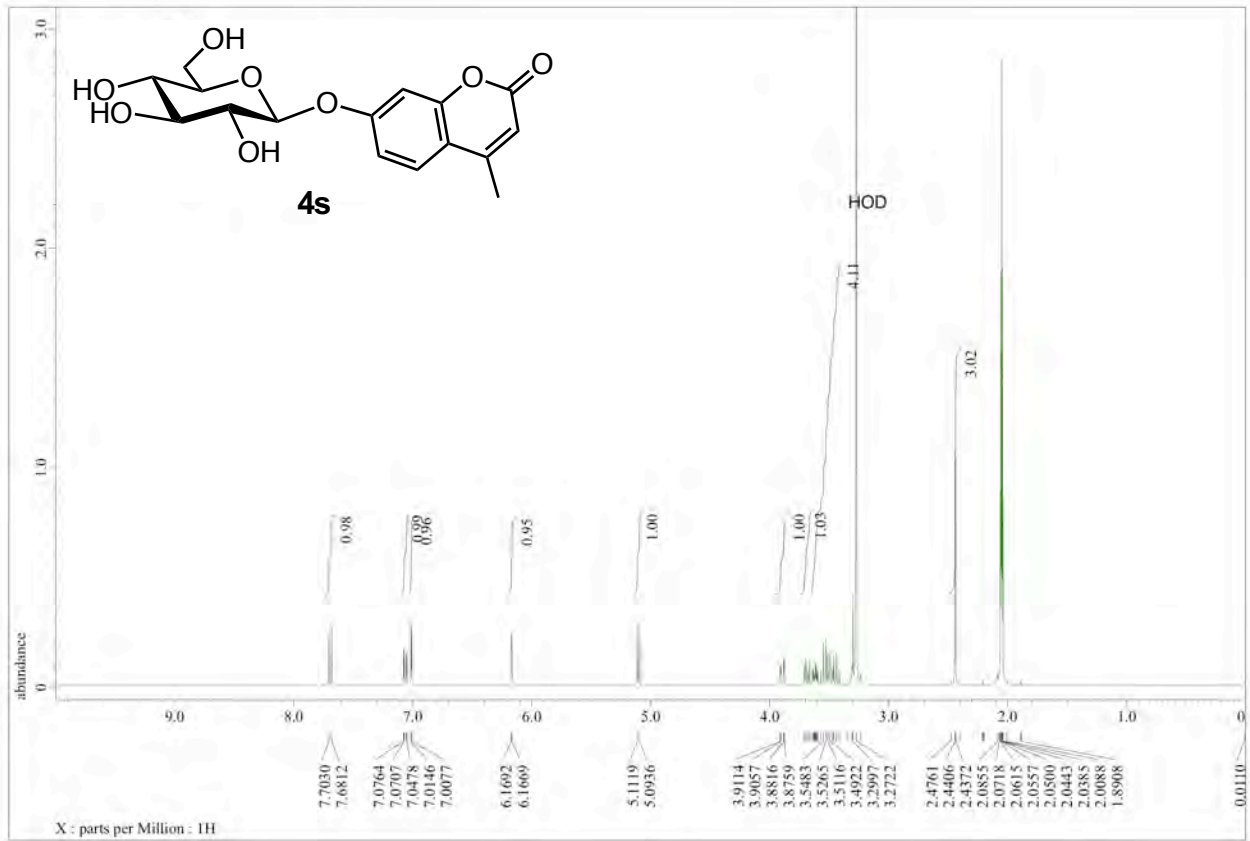


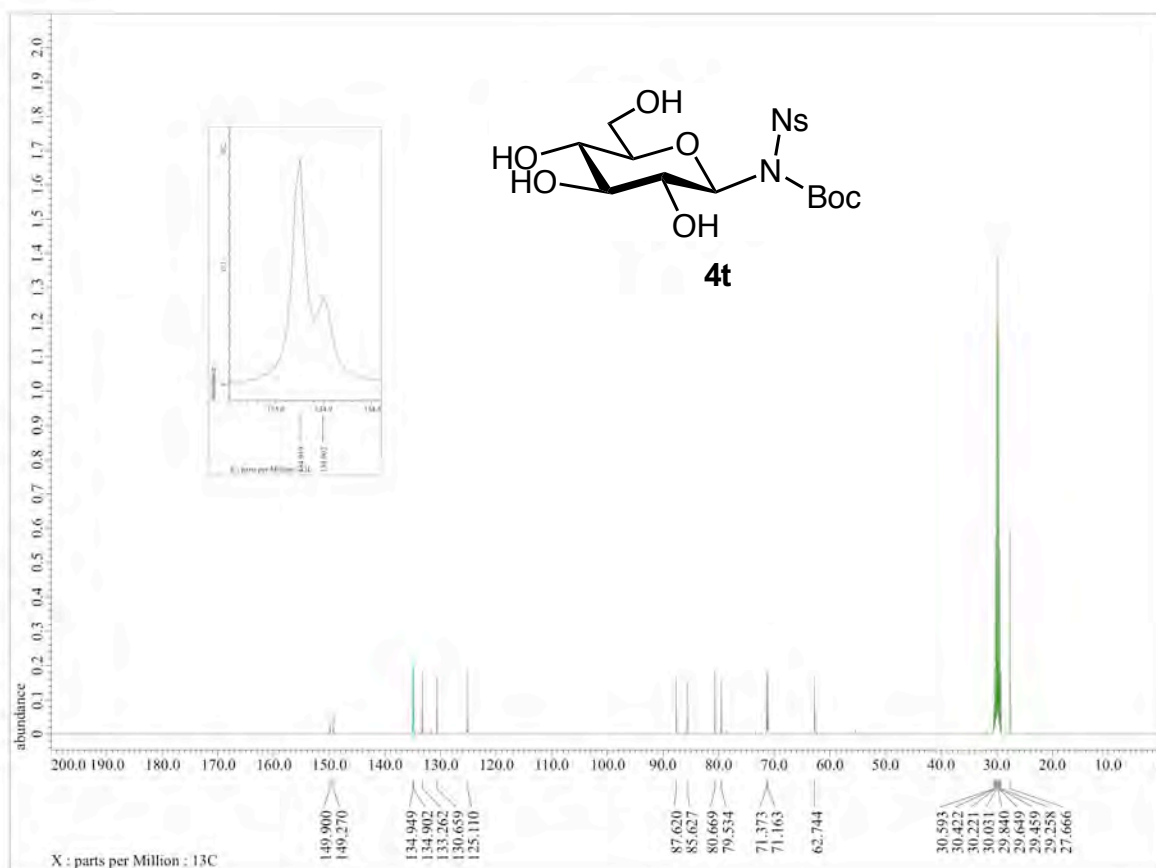
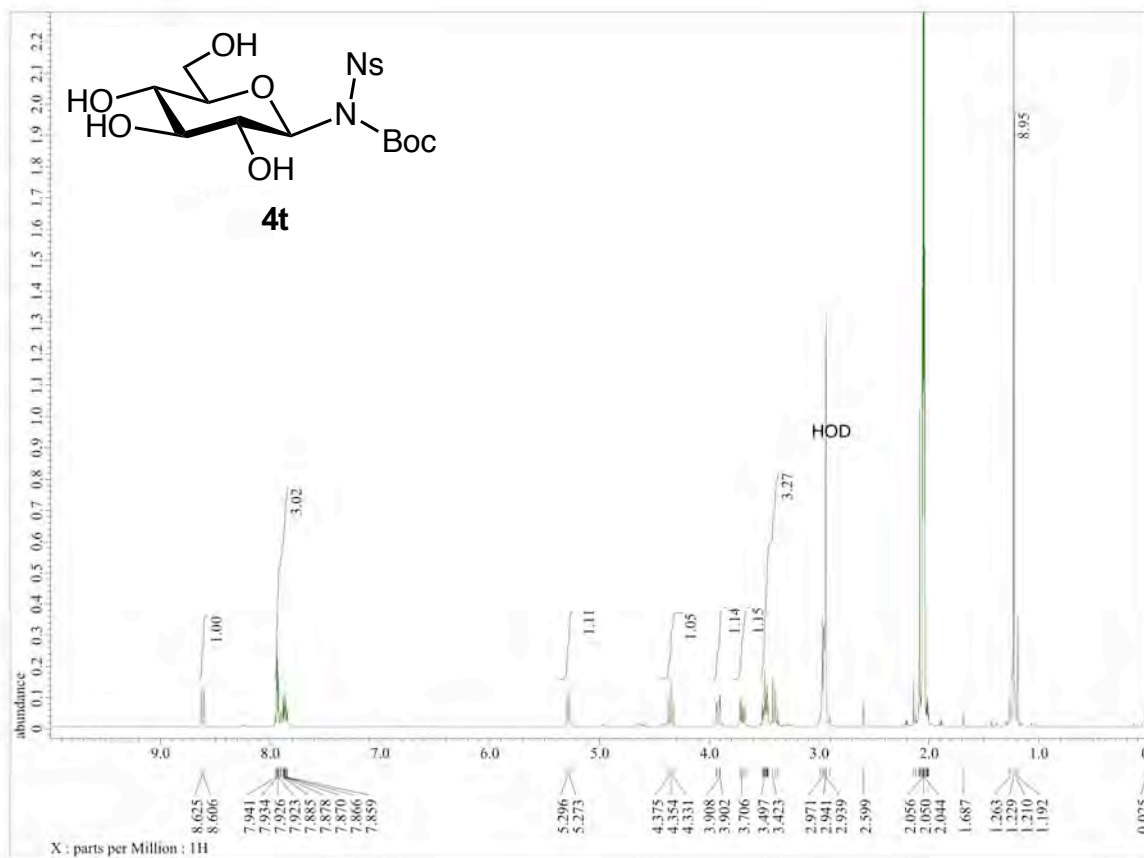


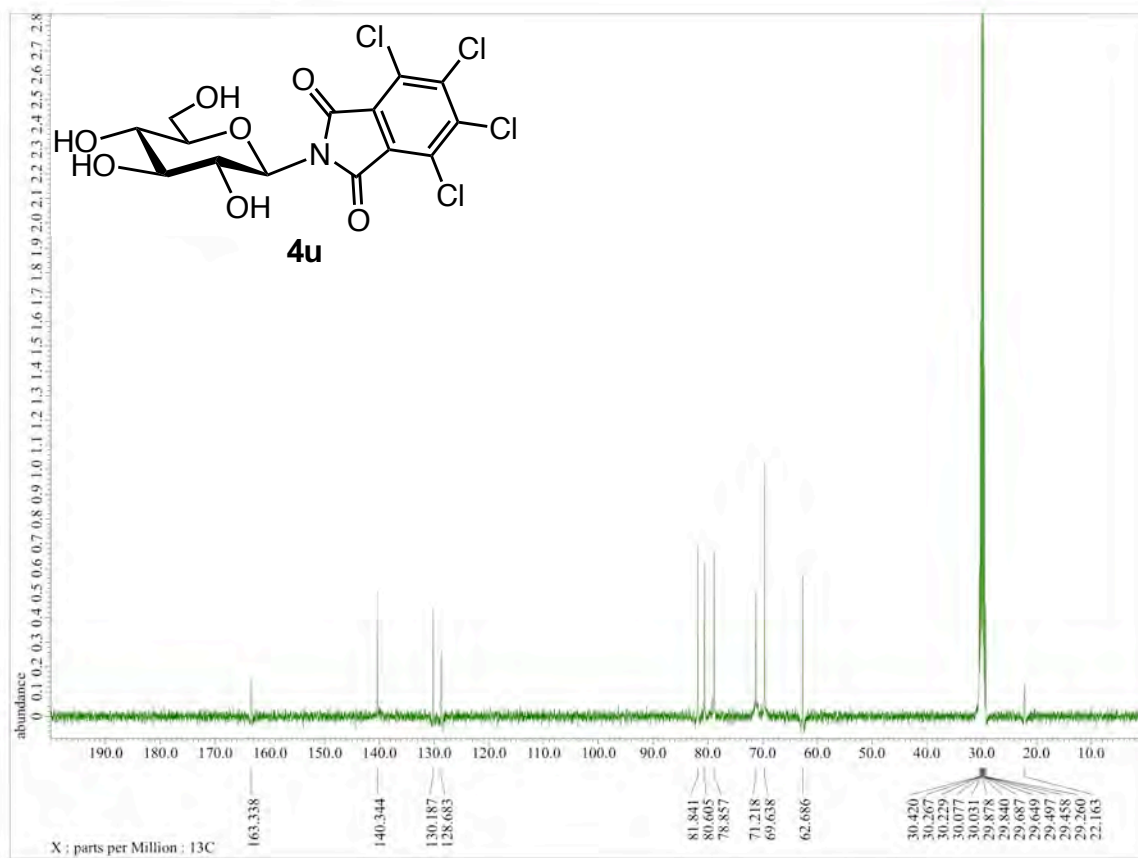
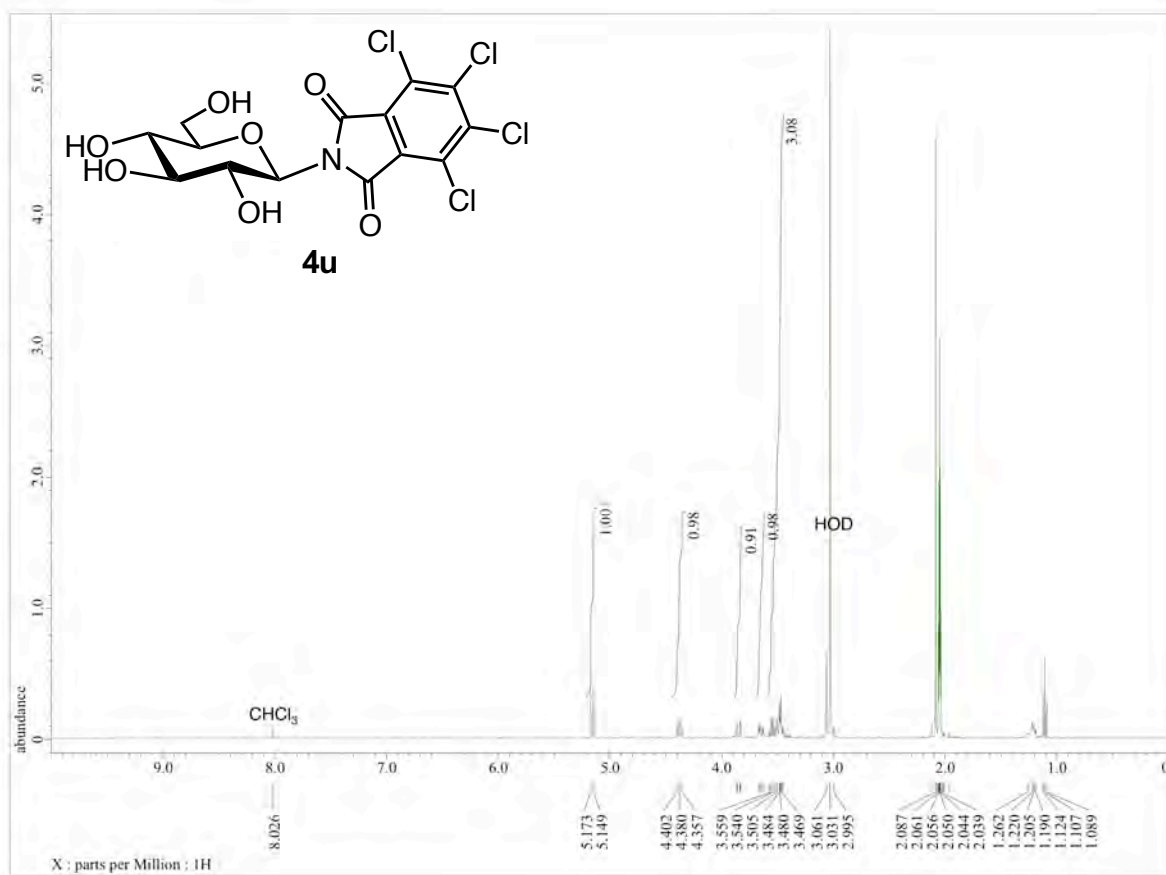


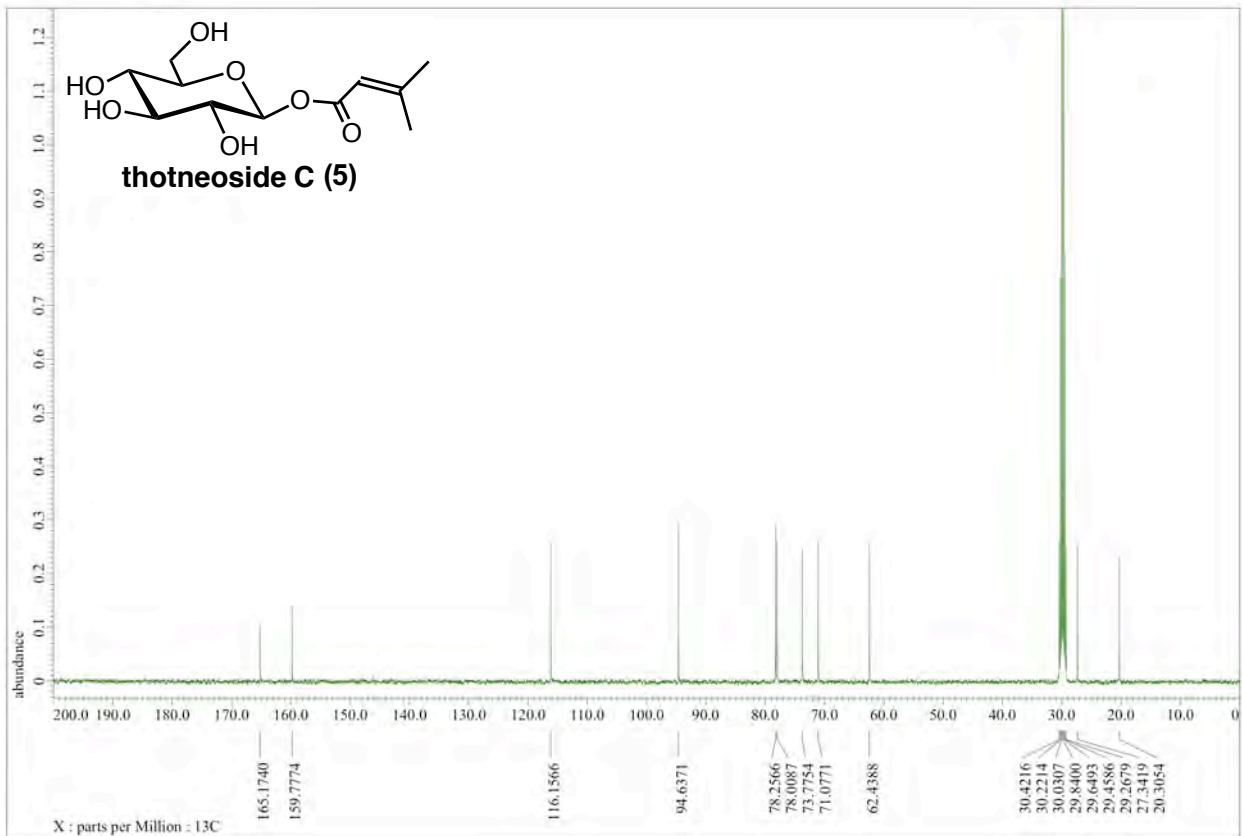
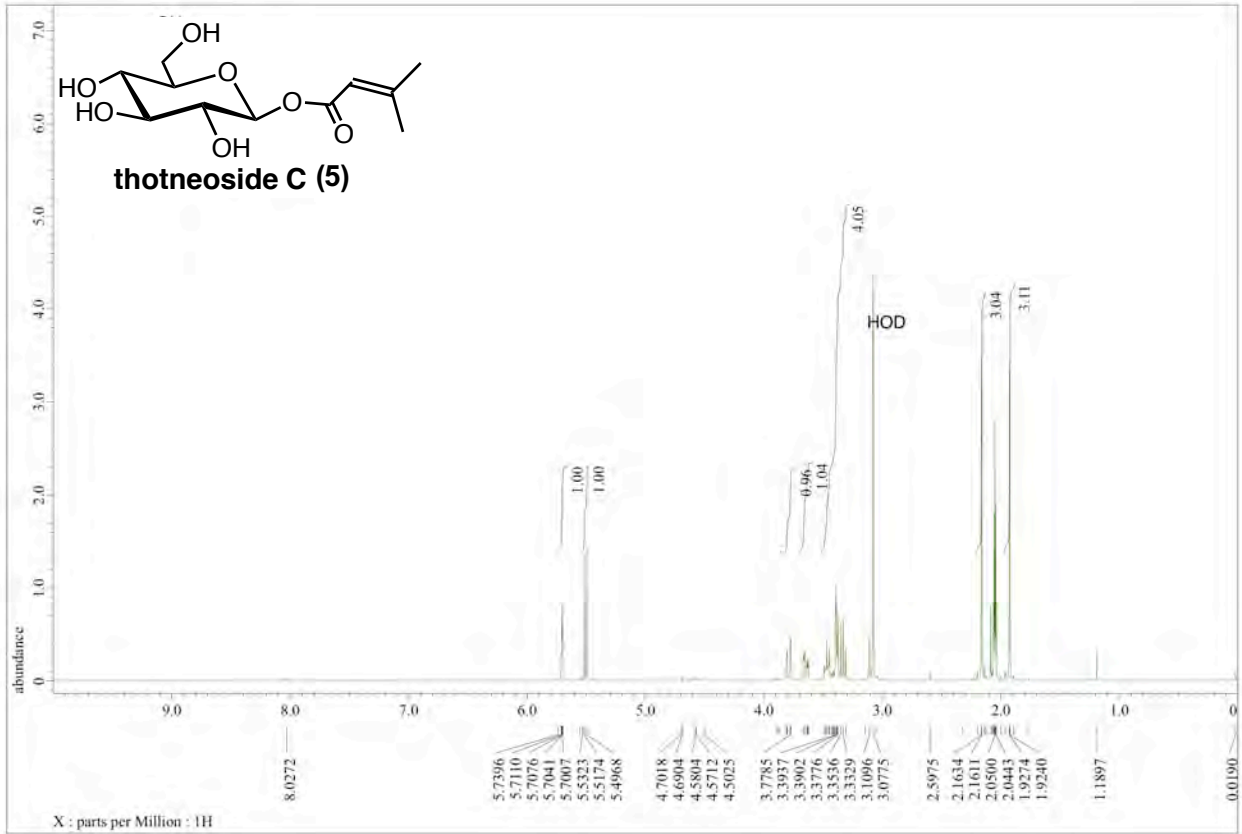


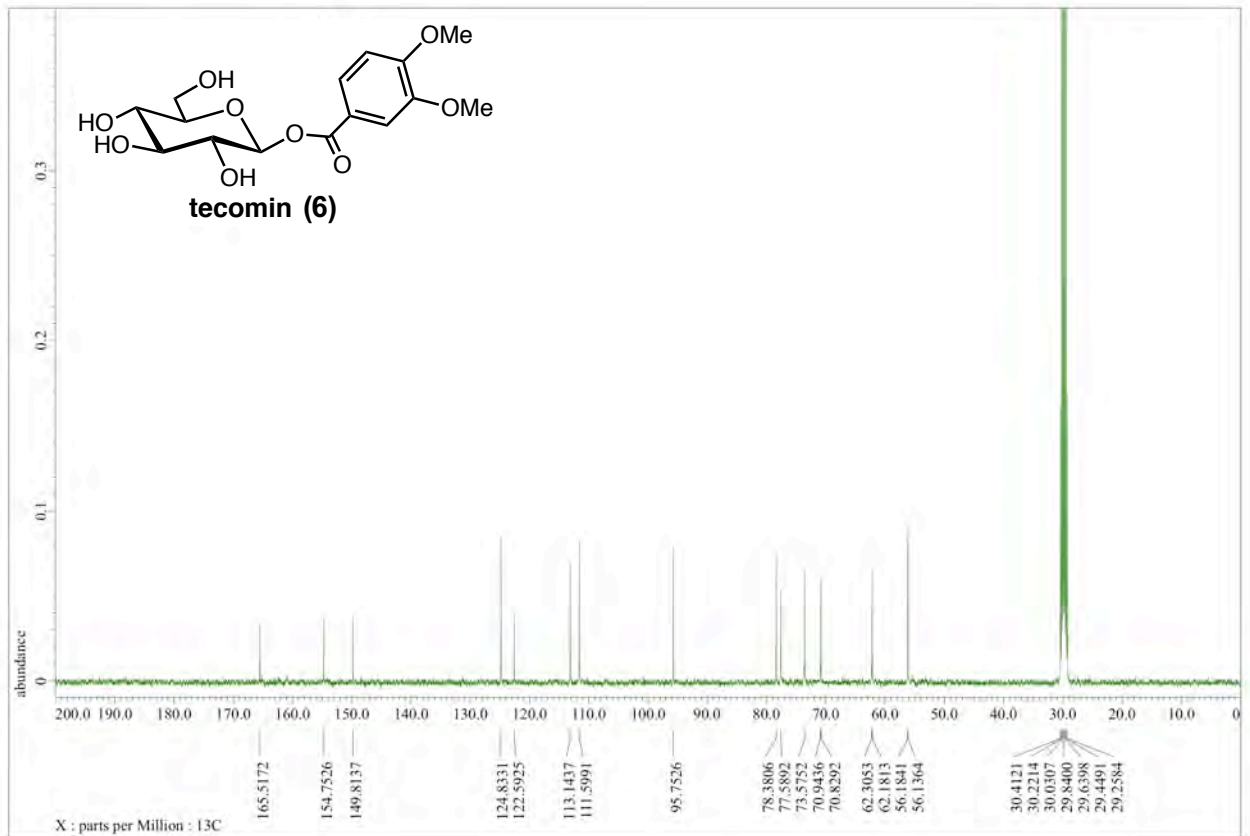
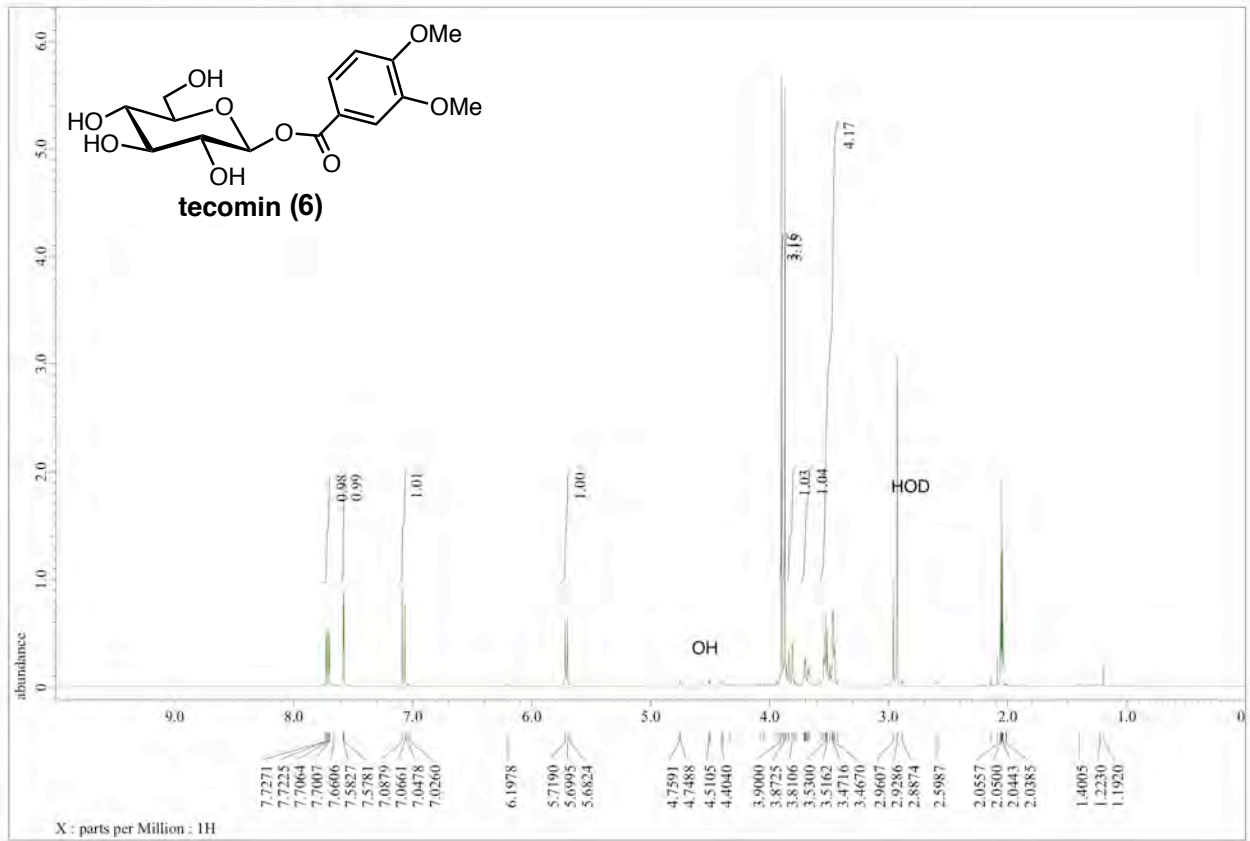


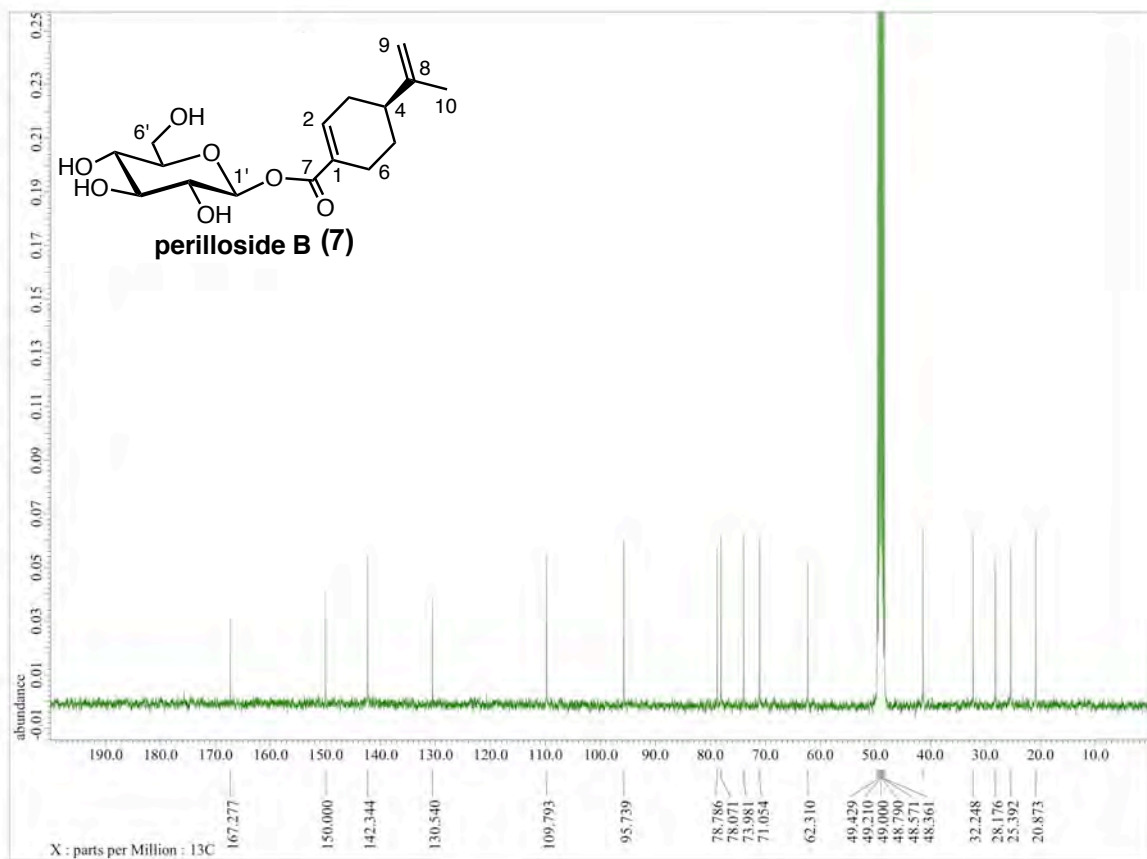
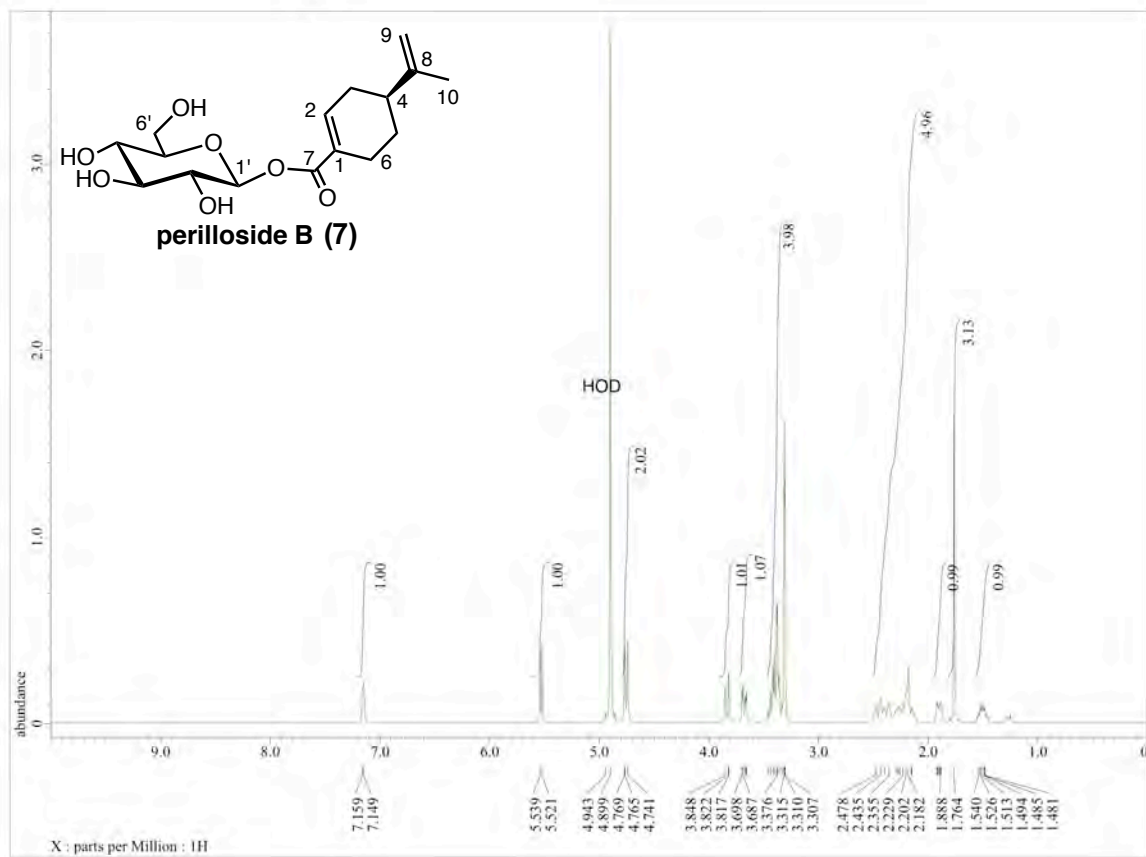


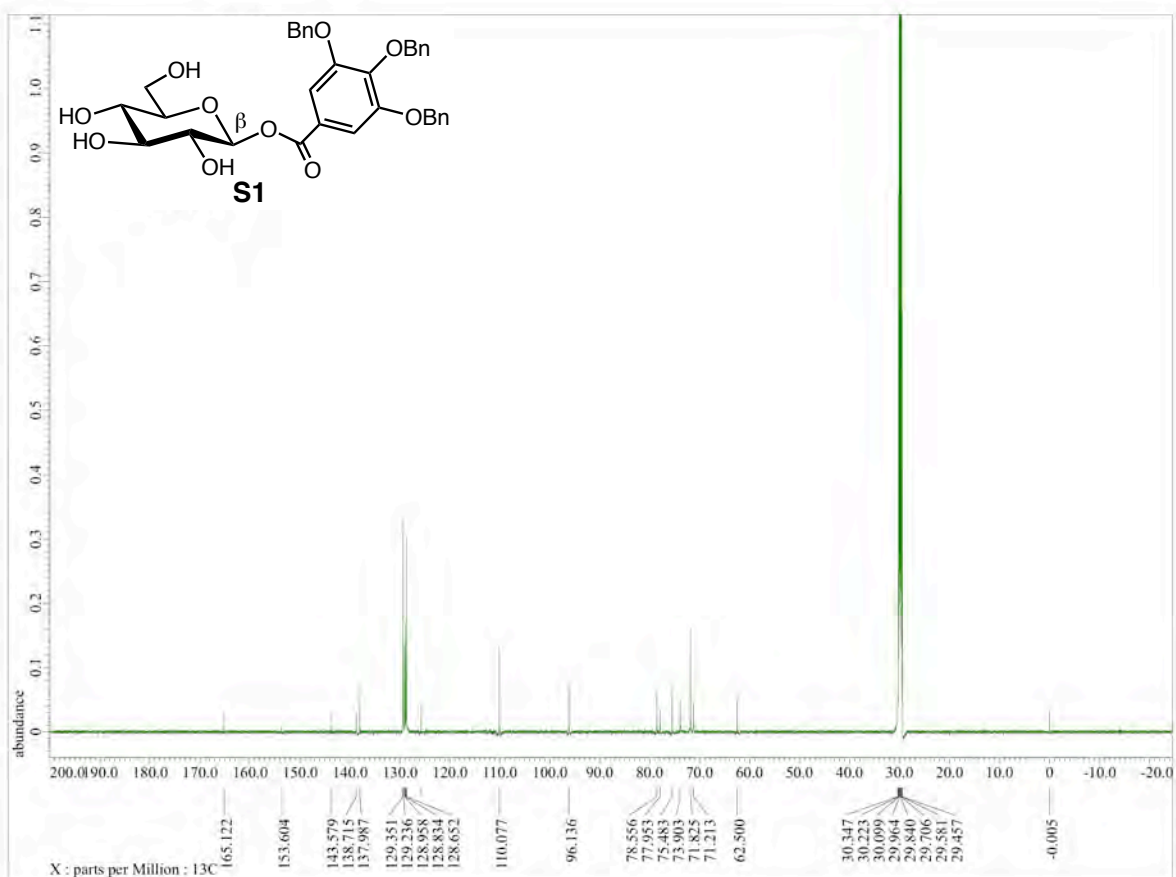
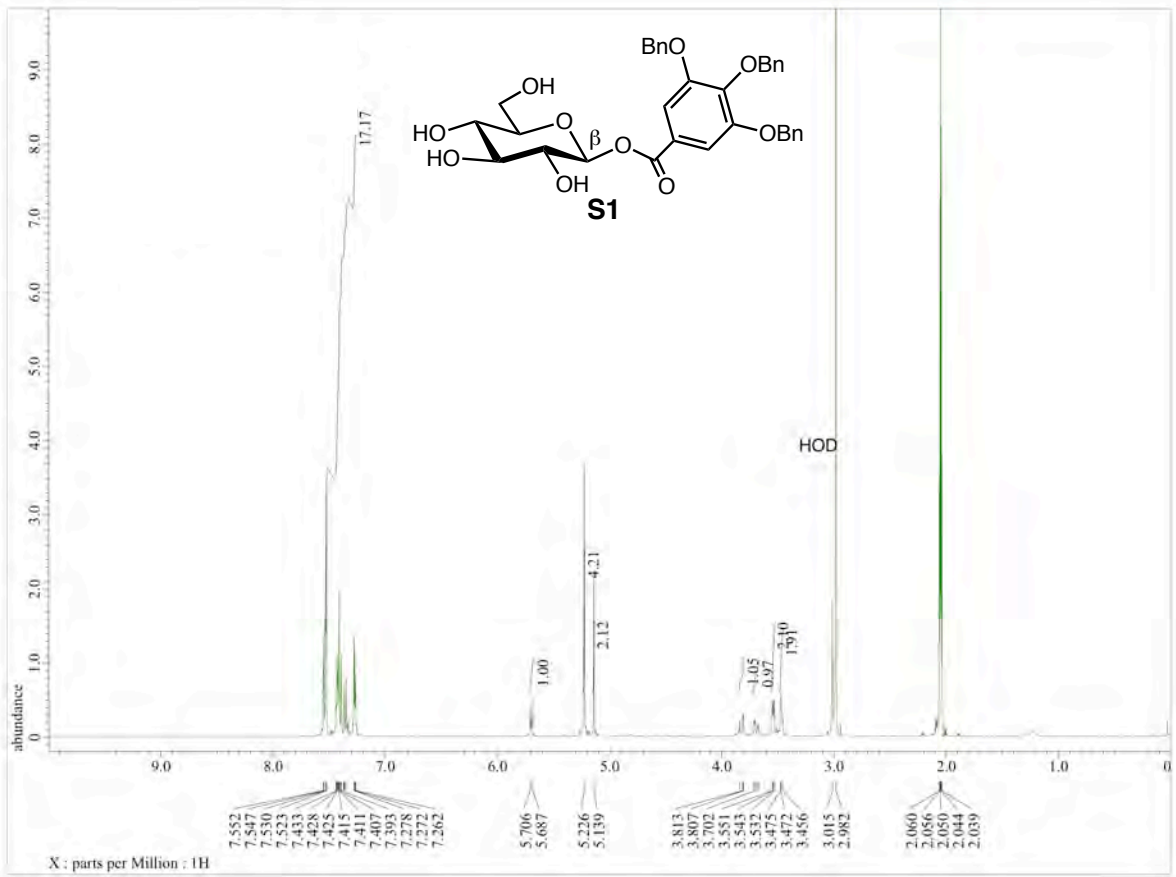


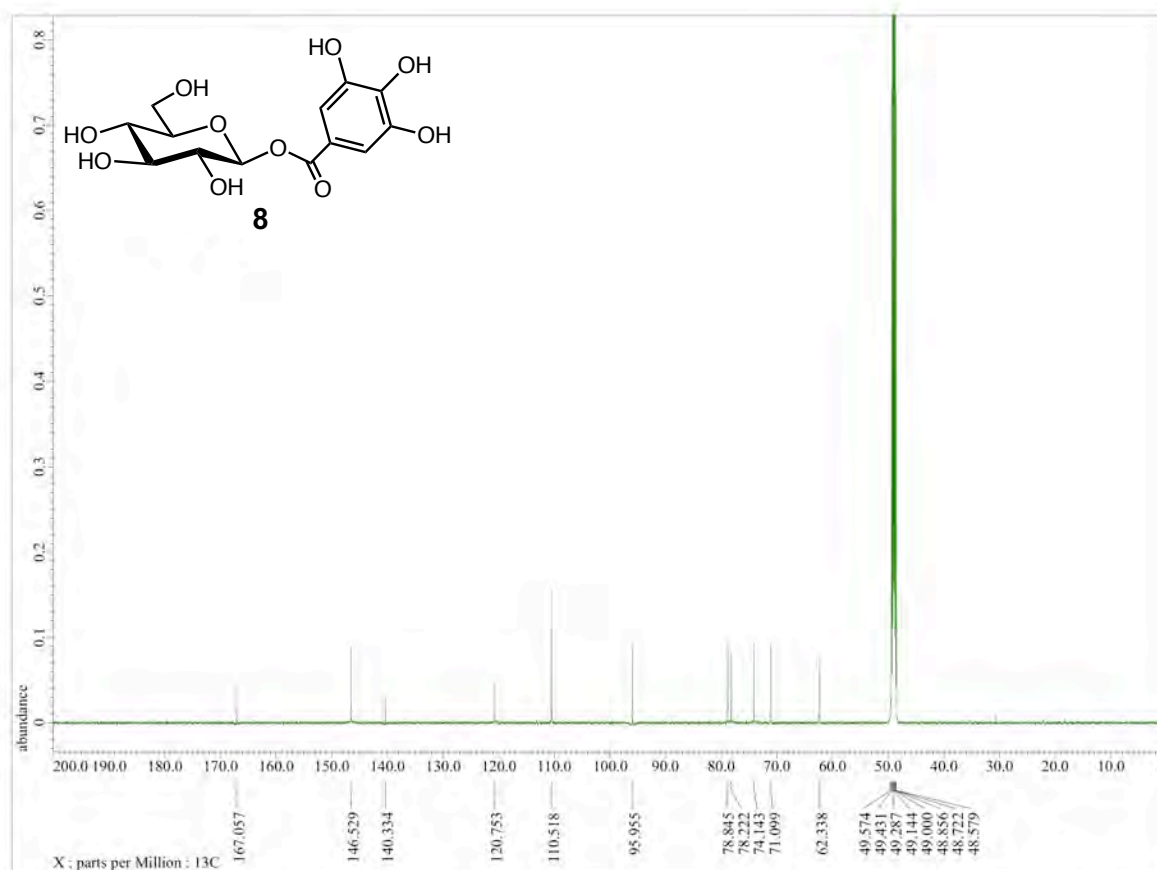
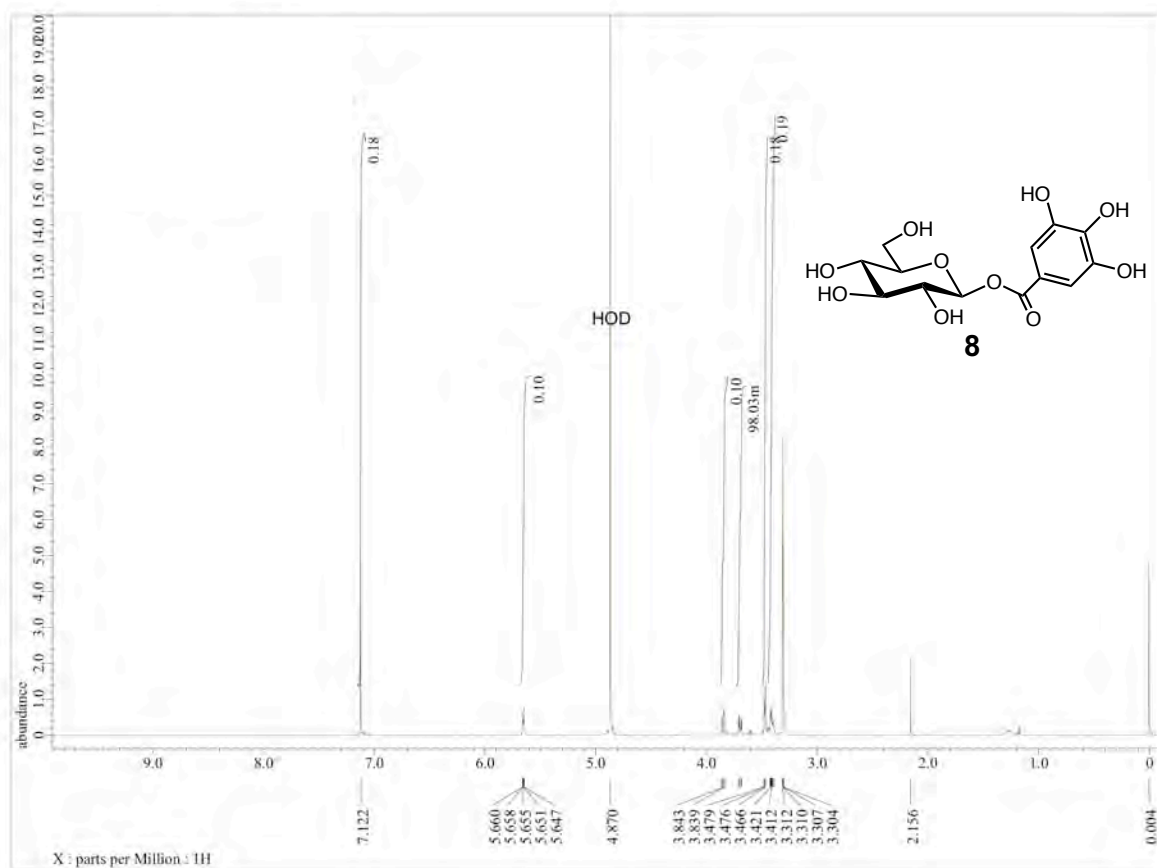


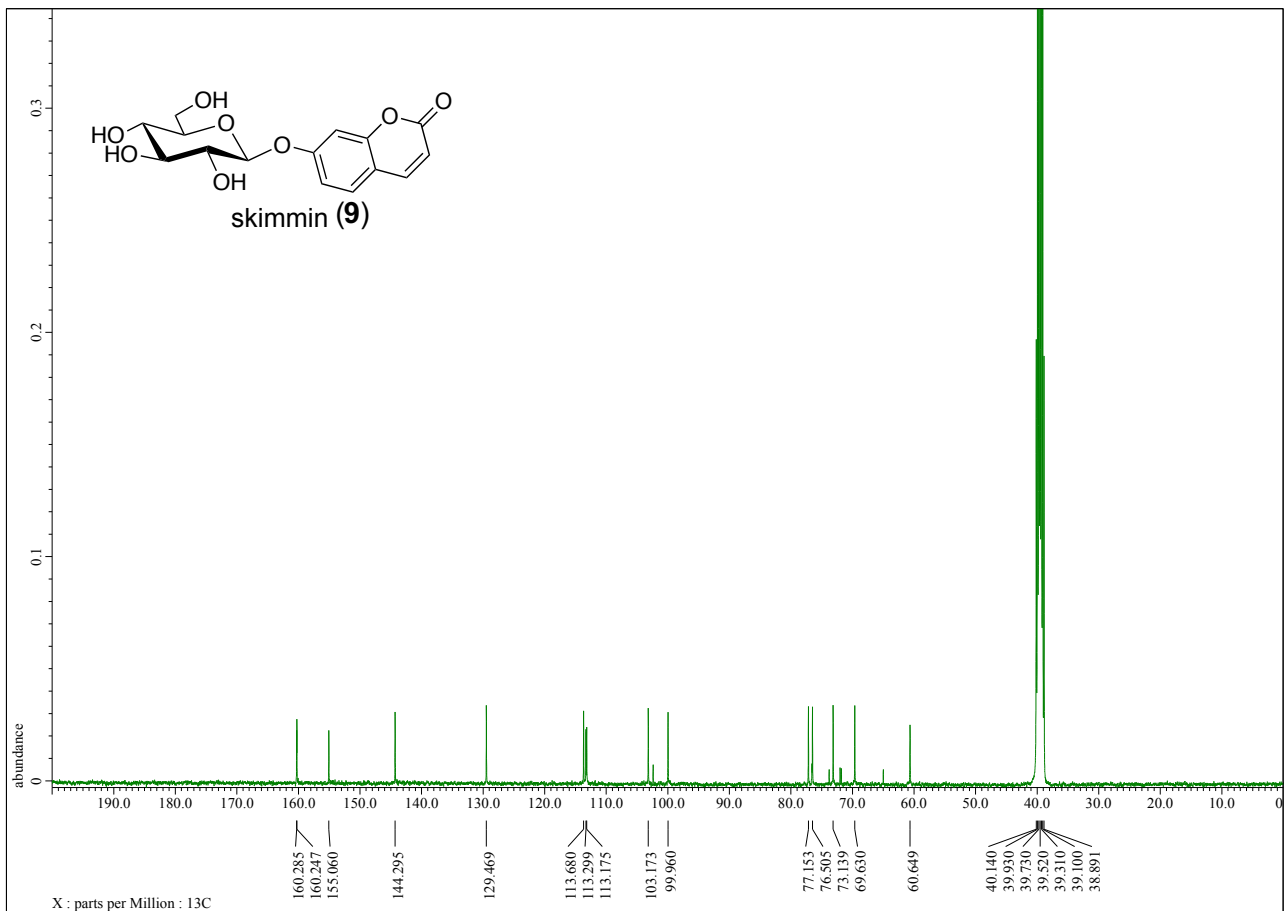
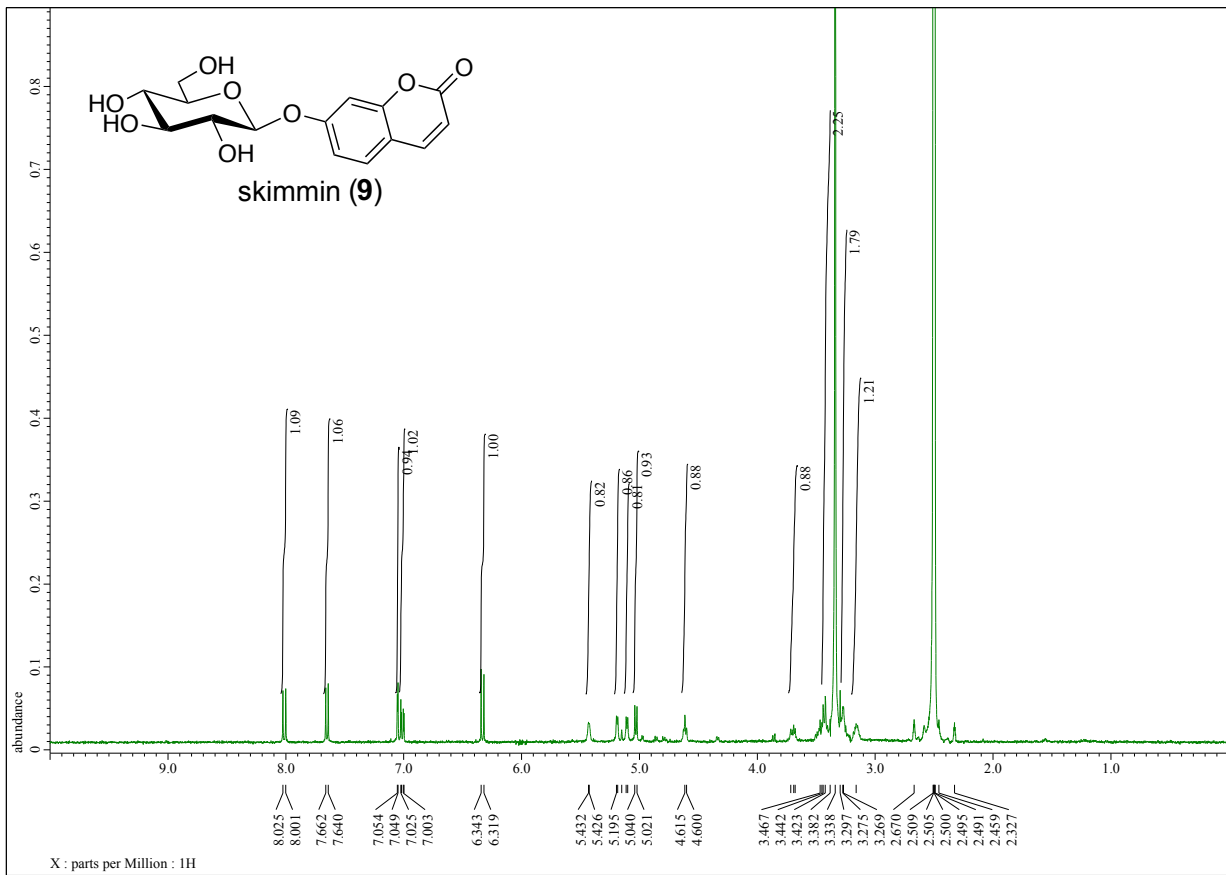


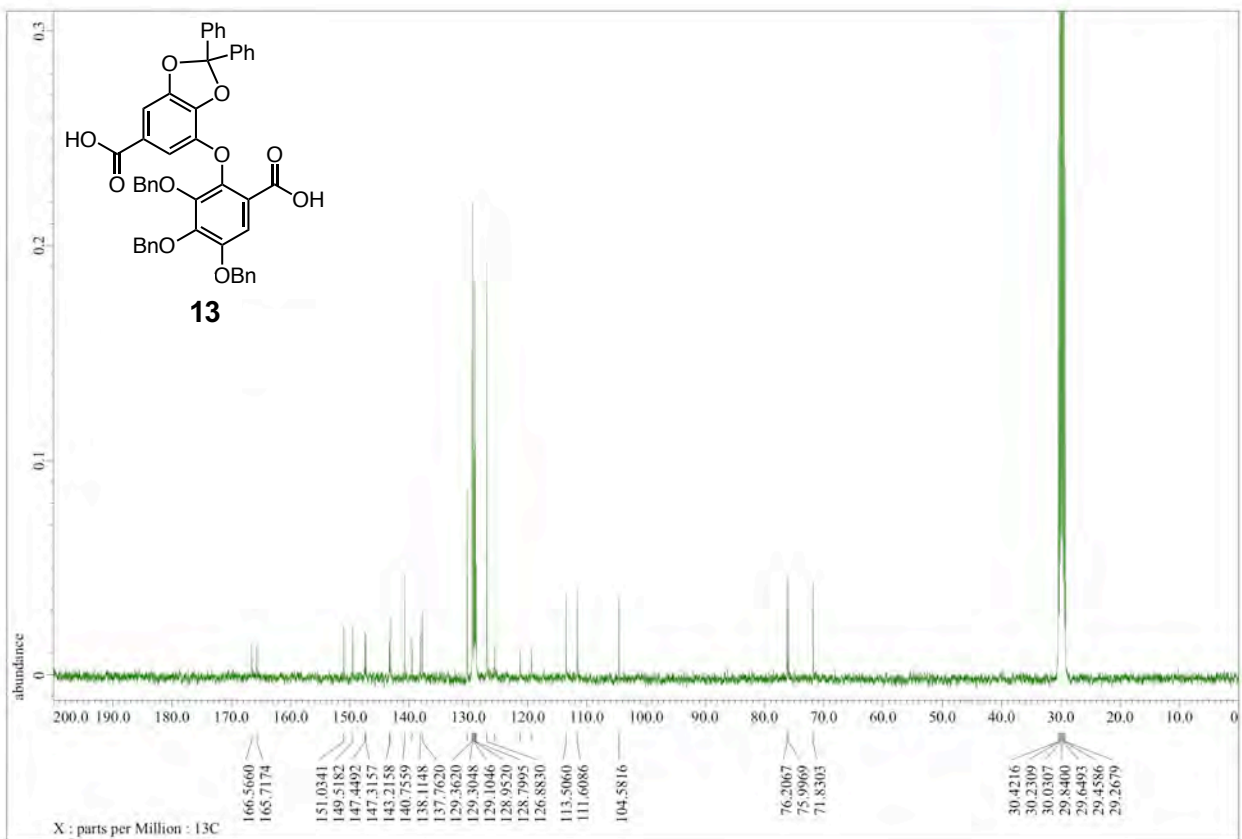
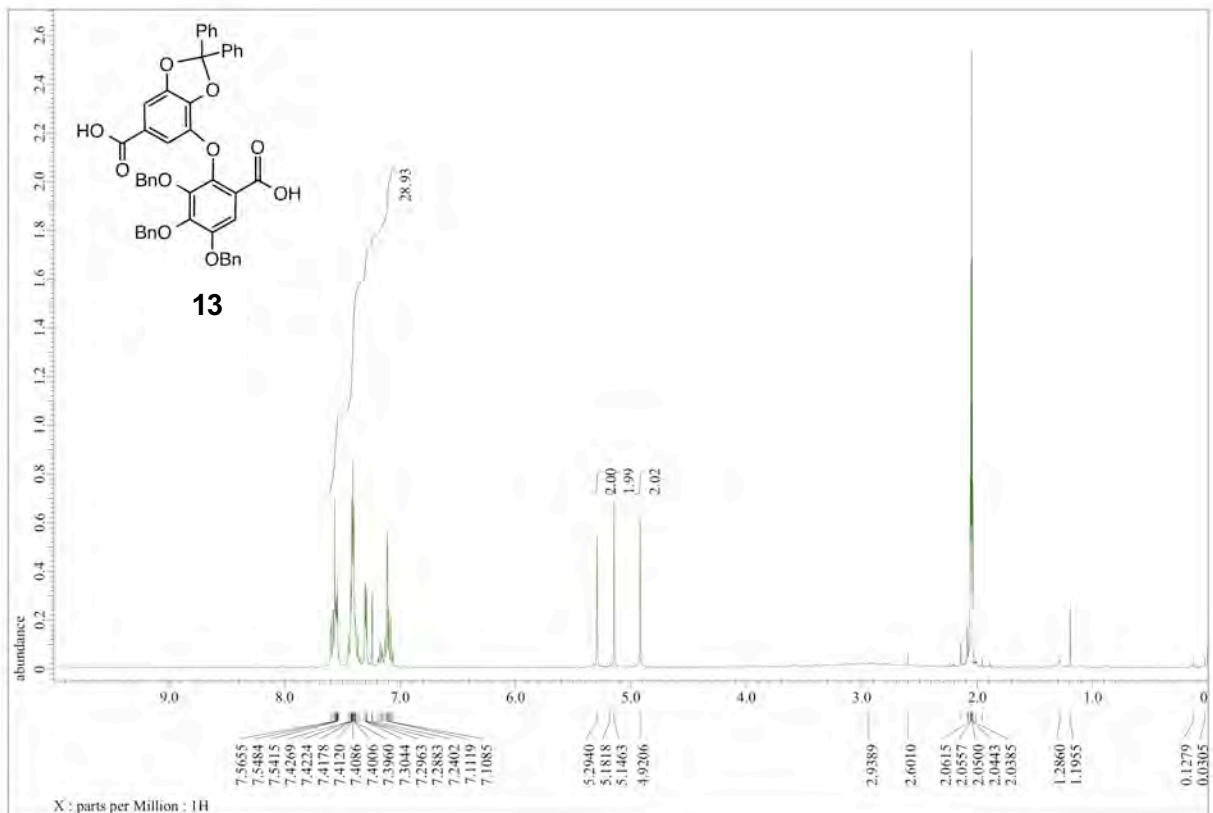


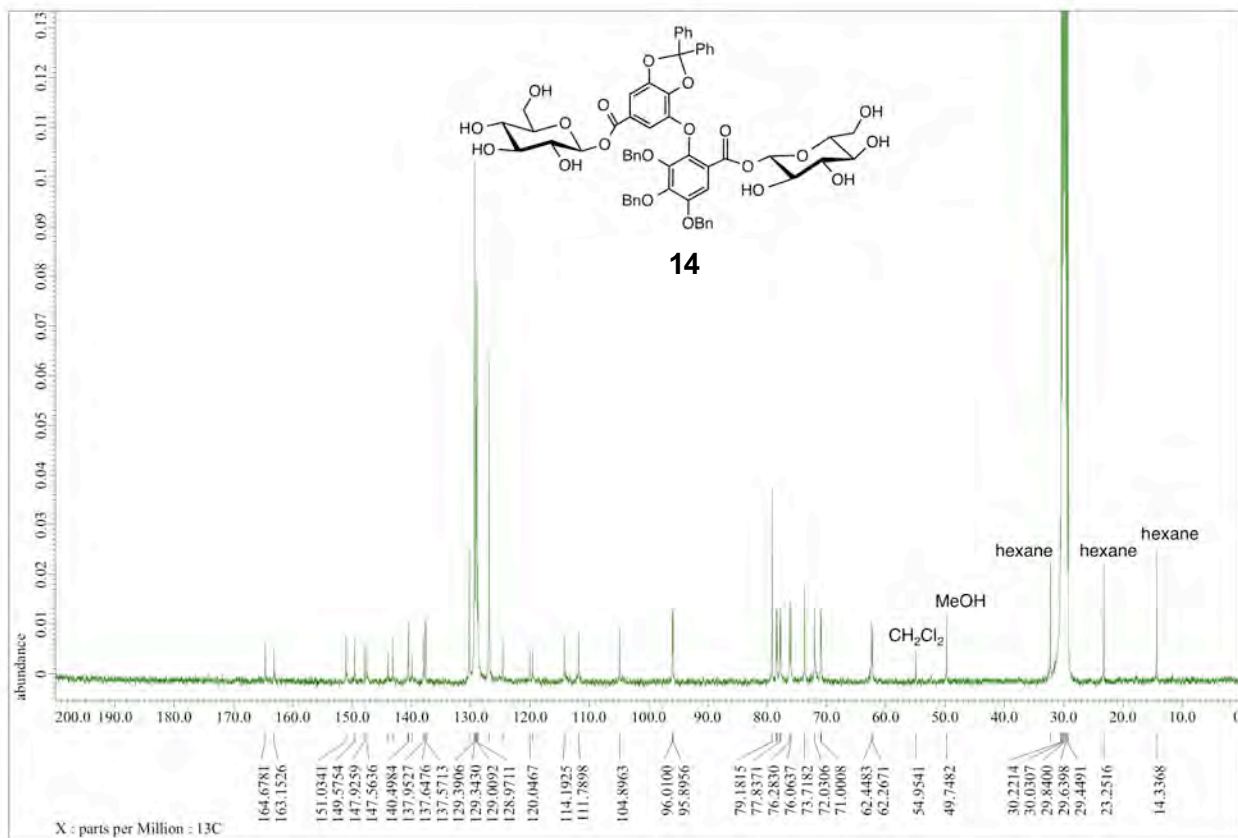
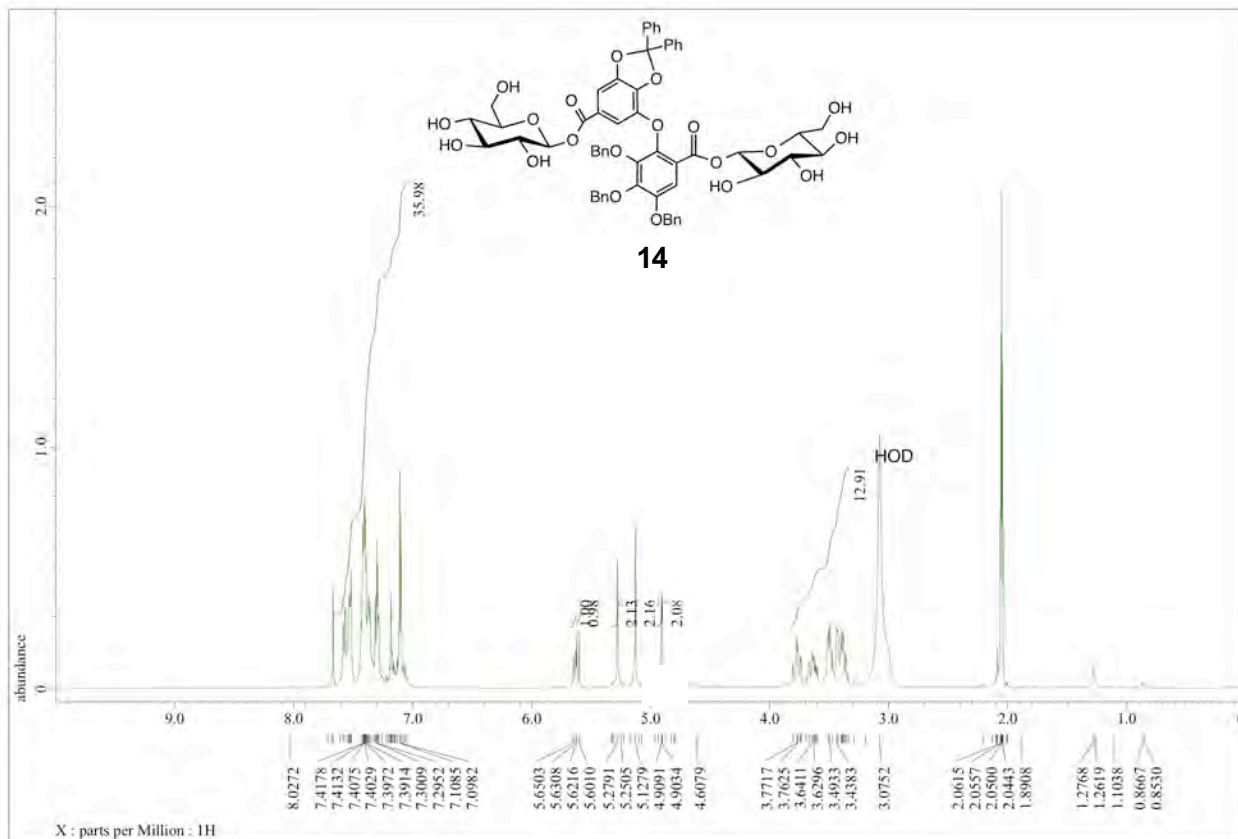


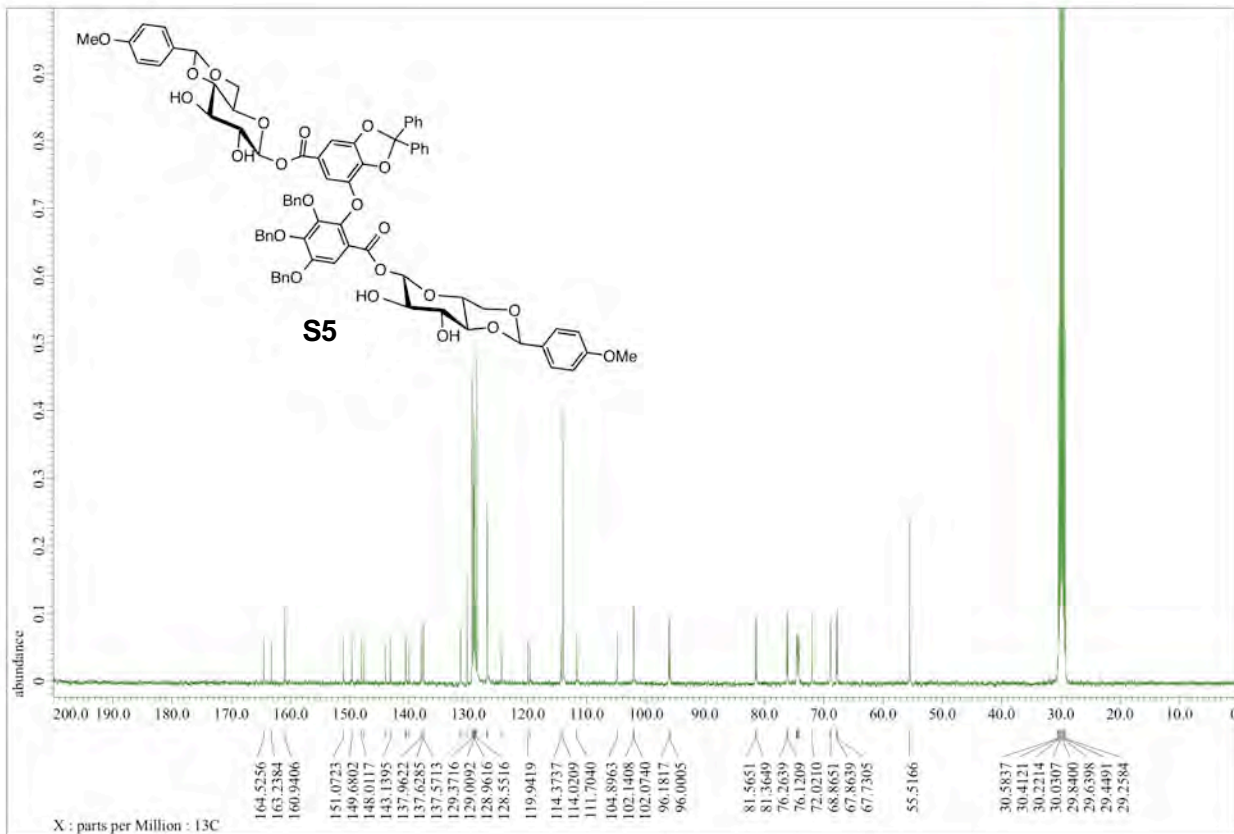
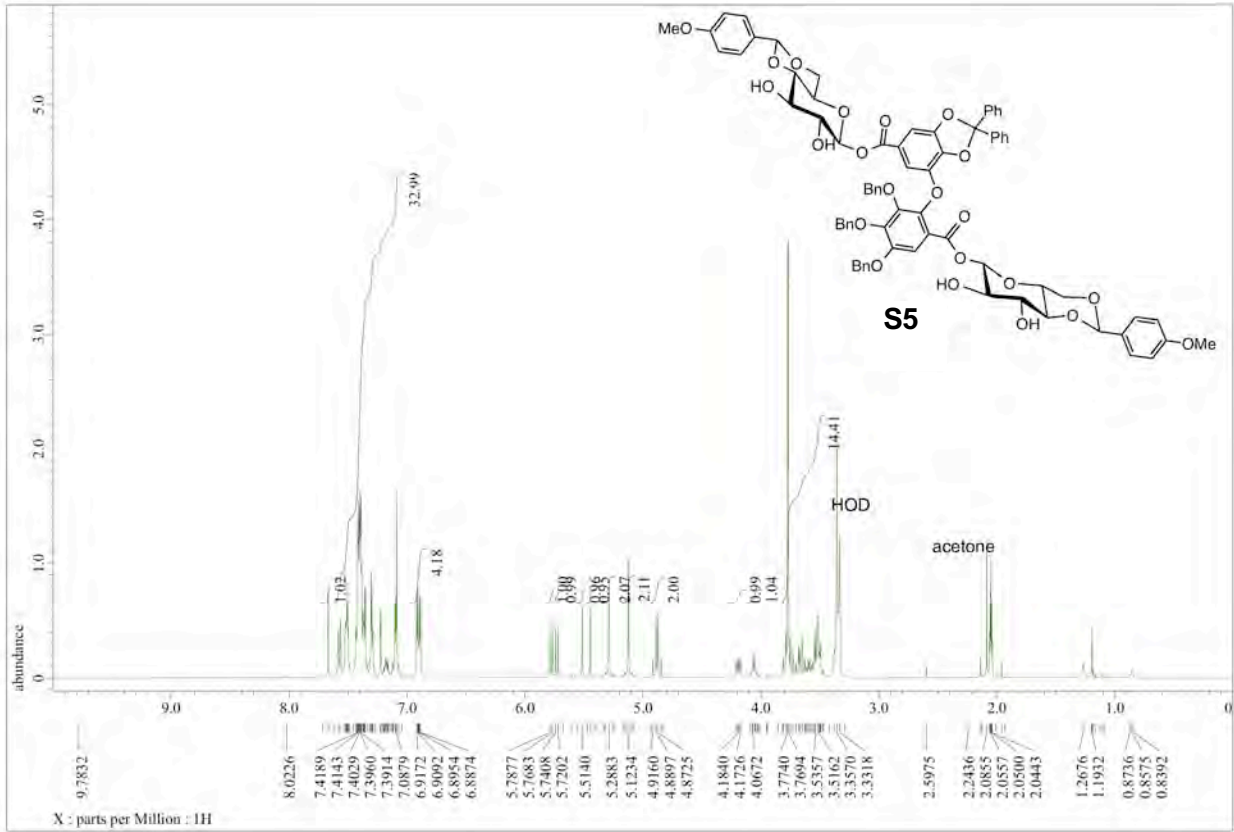


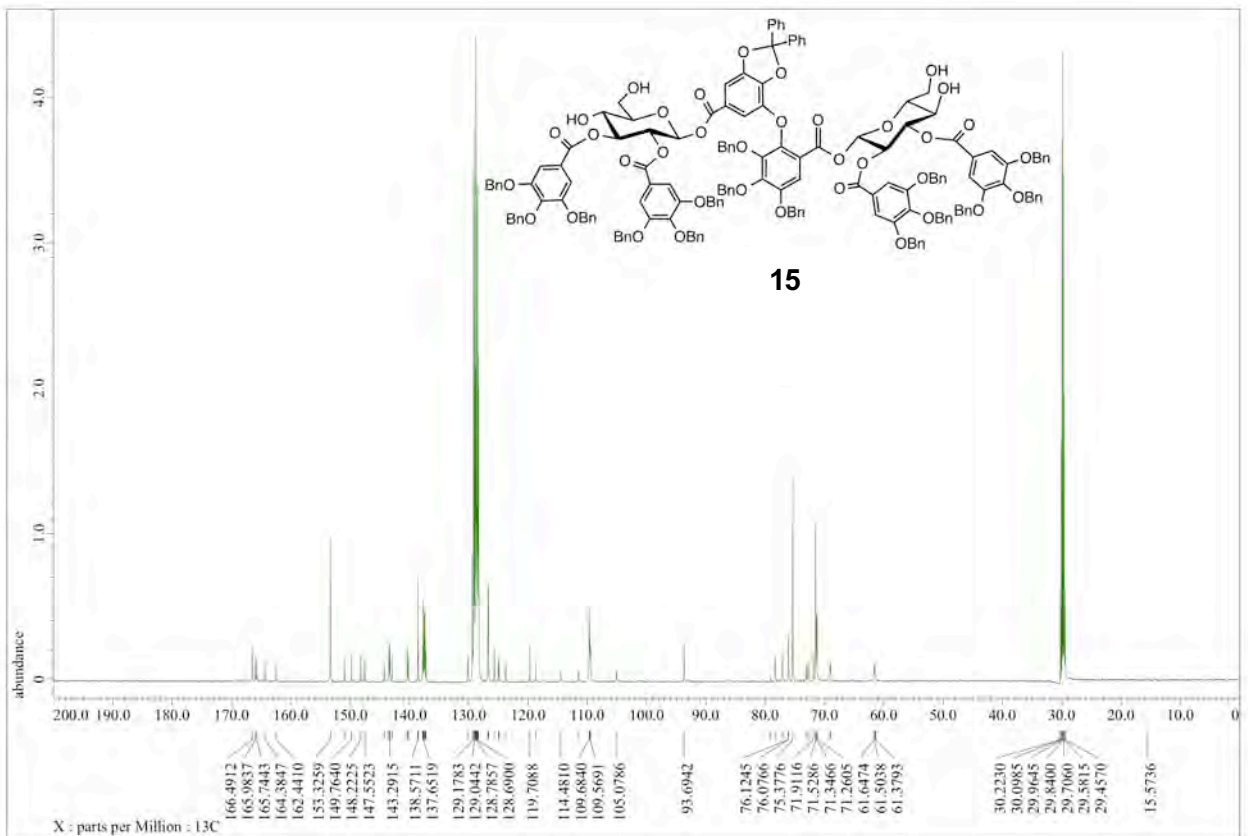
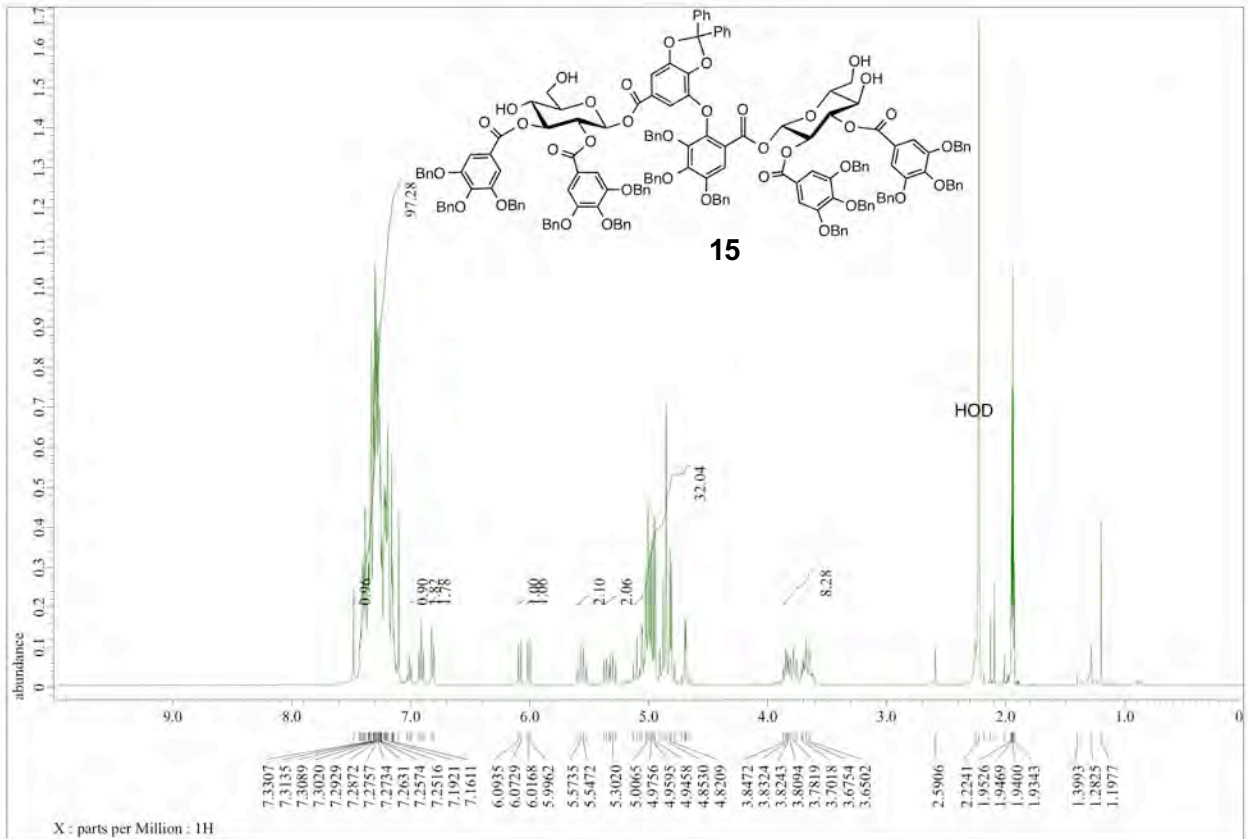


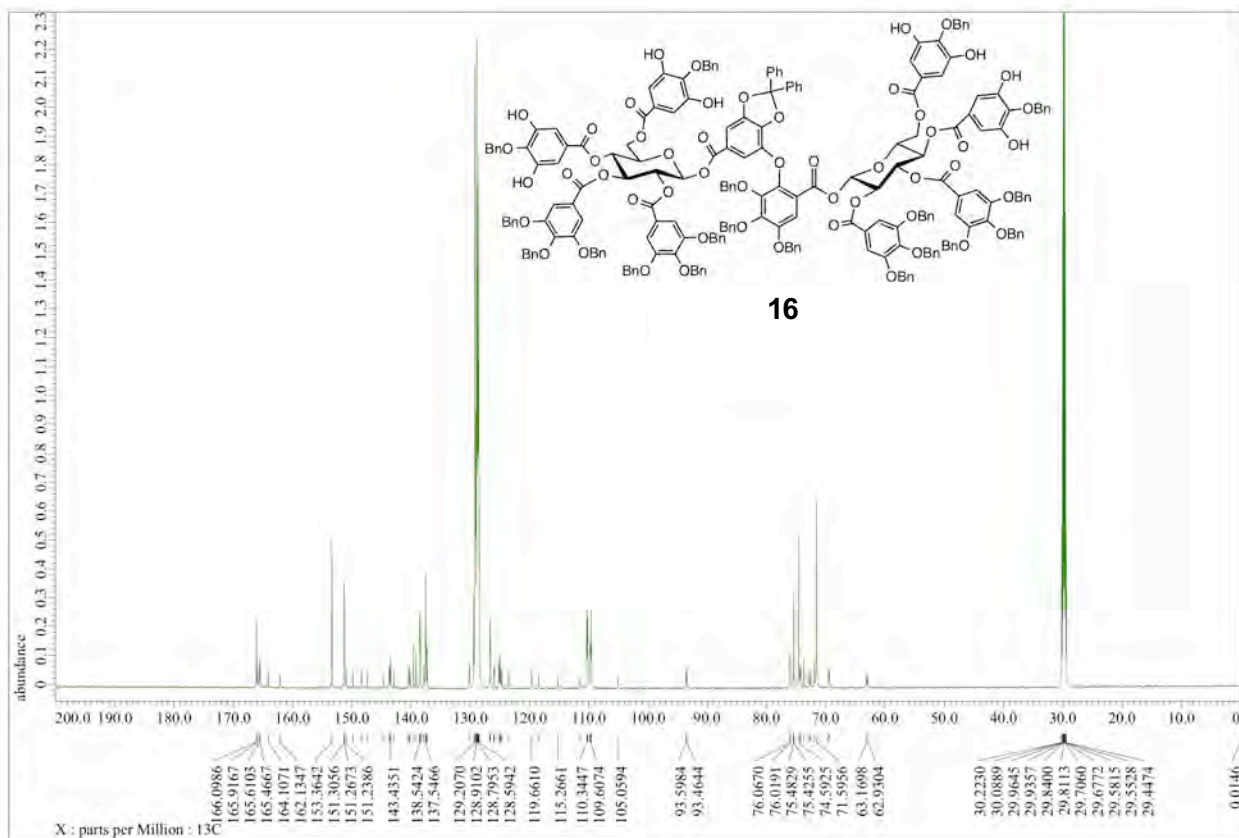
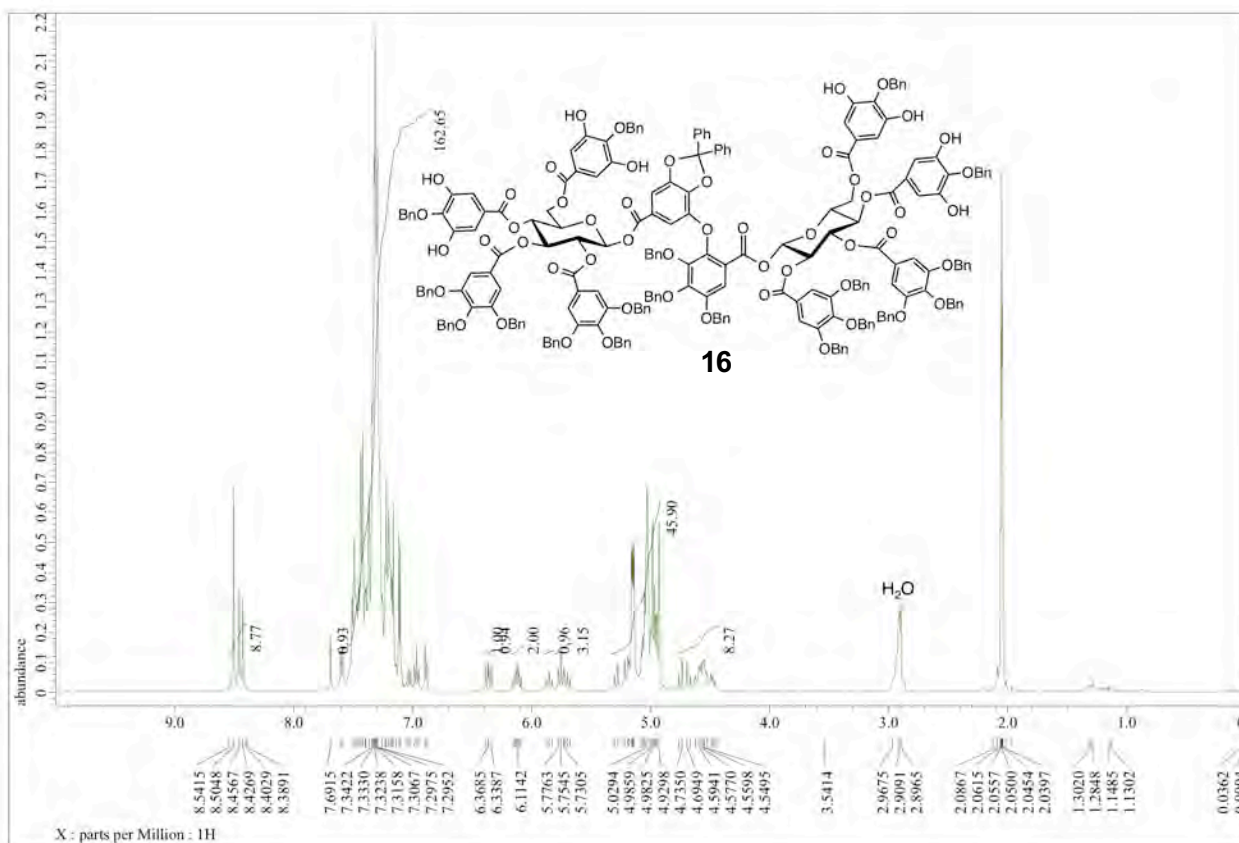


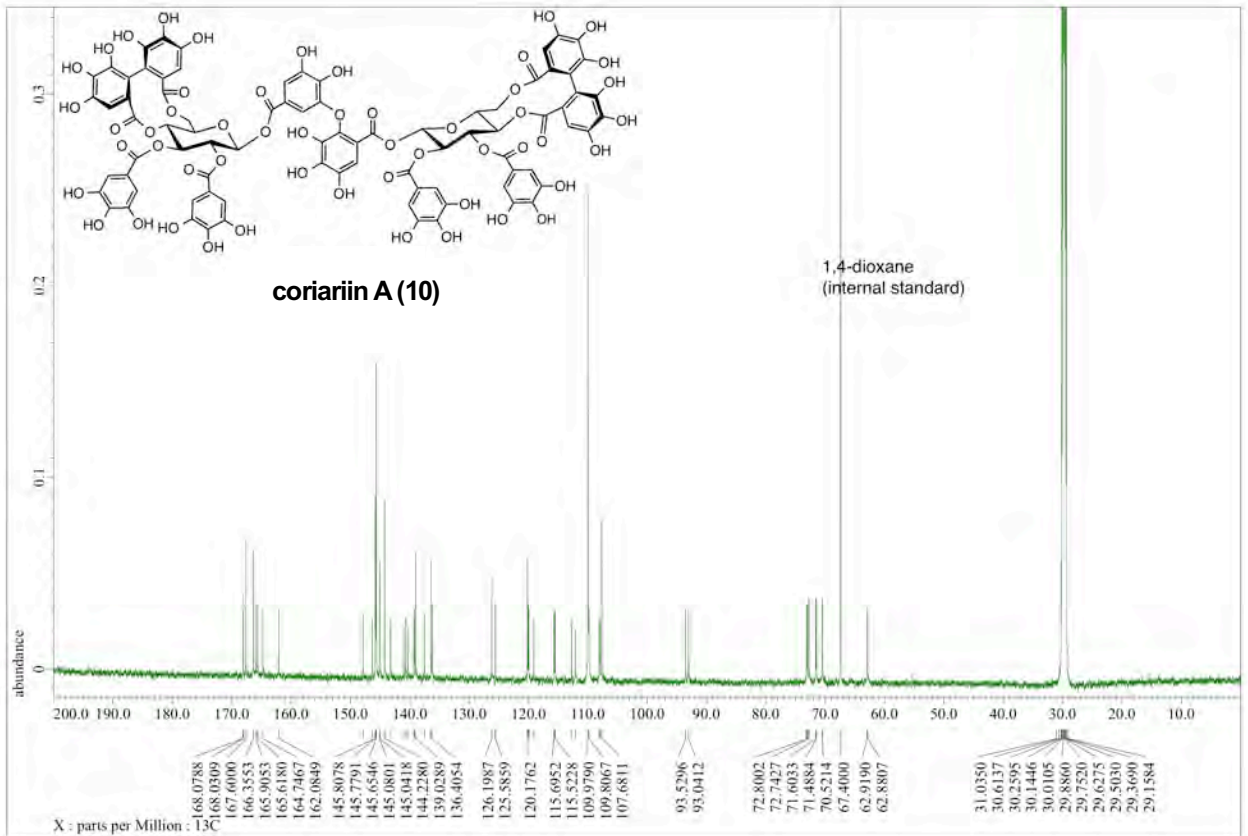
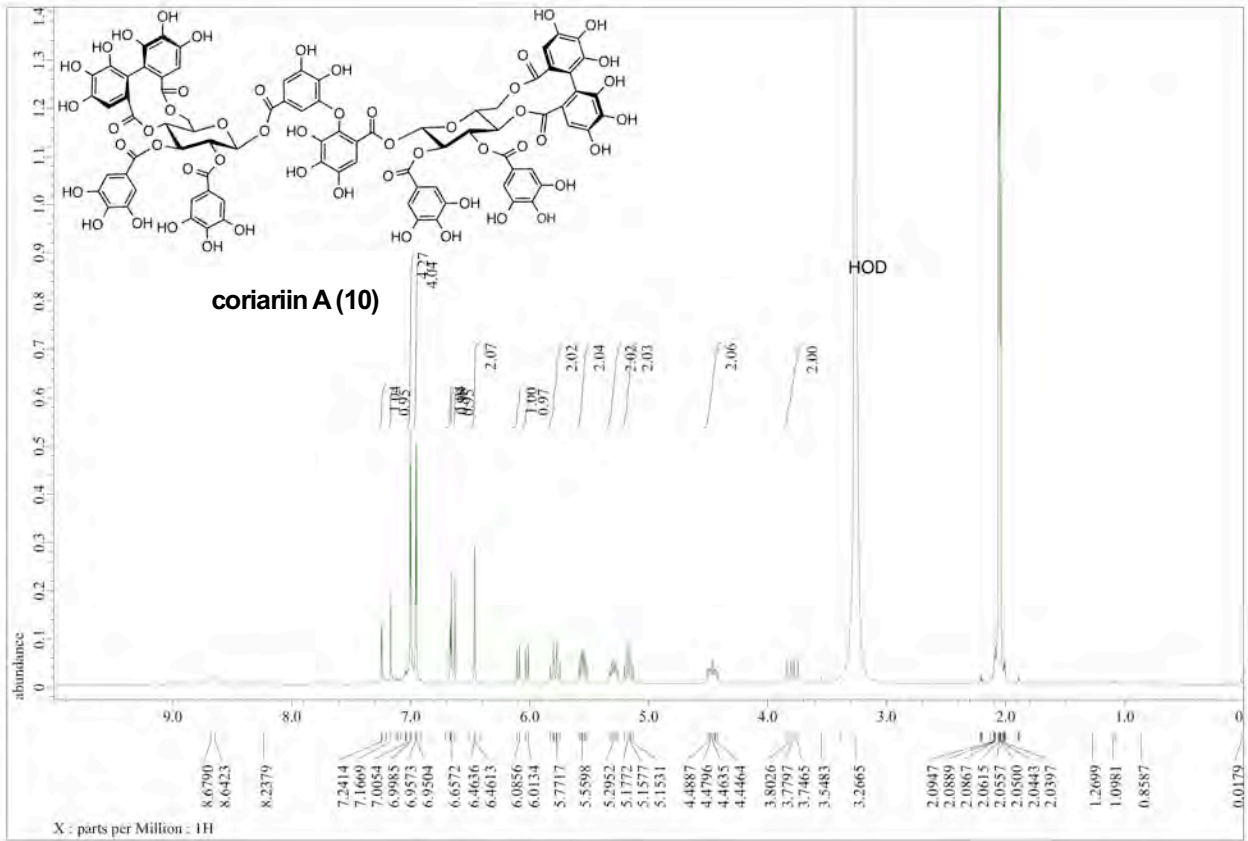












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