CHAPTER 2

Synthesis of 2-C-Branched Oligo-glyco-amino acids (OGAAs) by Ring Opening of 1,2-Cyclopropanecarboxylated Sugar Donors

ABSTRACT: 1,2-Cyclopropanecarboxylated sugars were used as glycosyl donors, for the first time, in the synthesis of 2-C-branched oligo-glyco-amino acids (OGAAs), carbohydrates decorated with the α-amino acids. The method was applied to acceptor-reactivity-based stereo- and regioselective glycosylation reactions towards the preparation of several disaccharide-based glyco-amino acid derivatives.

2.1 Introduction

Carbohydrates decorated with amino acids are becoming an important area of glycochemistry research. Possessing the architecture of a sugar and an amino acid in a single molecule, these glyco-amino acids (GAAs) are expected to exhibit the characteristics of both carbohydrates and amino acids, which are both biological polymer precursors. Glyco-amino acids are the most important building blocks for the glycopeptides and glycoproteins which play essential roles in cell-cell recognition, fertilization and etc. In this aspect, C-glycopeptides, in which sugar and peptide are connected through the C-glycosidic linkage,
have been explored significantly due to the stability and resistance exhibited towards enzymatic hydrolysis. Moreover, C-branched glyco-α-amino acid moieties are found in a variety of nucleoside antibiotics, such as polyoxins, miharamycins, nikkomycin and amipuramycin (Figure 2.1).

Figure 2.1: Nucleoside antibiotics containing glyco-amino acid moiety

Very few methods are available in literature for the synthesis of monosaccharide-derived C-branched GAA derivatives. The synthetic methods available for the synthesis of 2-C-branched GAAs is discussed in detail in chapter 1 of this thesis (section 1.3). It has been found to be very difficult to link a an α-amino acid at C-2 or C-4 through a C-C bond. For this reason, the biological importance of these GAAs is not yet fully understood. It has been shown that the unnatural 2-C-acetonylsugars serve as the metabolic substrates for cell surface engineering by mimicking 2-N-acetyl sugars. Similarly, a 2-C-N-hydroxy acetamide mimic of GlcNAc was synthesized and shown to be an inhibitor of the biosynthesis of lipid A.

The high reactivity and regioselectivity of donor–acceptor cyclopropanes has been well documented in literature. 1,2-Cyclopropanecarboxylated sugars have been used as donor-acceptor cyclopropanes in the synthesis of 2-C-branched monosaccharides through electrophilic C1–C7 cyclopropane ring opening or by transition-metal-catalyzed glycosylation. Detailed ring opening reactions of 1,2-cyclopropanated sugar derivatives is described in chapter 1 of this thesis (vide supra section 1.2.1, section 1.3.1, section 1.5.1).
Recently, a four-component Pavarov reaction and a transition-metal-mediated radical reaction were developed for the direct synthesis of the 2-C-branched carbohydrate derivatives from glucals, which were further derivatized to bicyclic carbohydrate 1,2-lactones. Glucal-derived donor–acceptor cyclopropanes have also been used as 1,3-dipoles under acidic conditions, which result in (3+2) cycloaddition reactions in presence of dipolarophiles.

1,2-Cyclopropanated sugars have the ability to undergo electrophilic ring opening reaction assisted by the adjacent oxygen in presence of an electrophile. Utilizing this potentiality of these cyclopropanated sugars, in this chapter we described the N-iodosuccinimide (NIS)/trimethylsilyl trifluoromethanesulfonate (TMSOTf) mediated ring opening of 1,2-cyclopropanecarboxylated glycosyl donors with the carbohydrate derived O-nucleophilic glycosyl bond acceptors.

### 2.2 Results and Discussion

1,2-Cyclopropanecarboxylated sugar donors used in the glycosylation reaction, were prepared from the readily available carbohydrates (D-glucose, D-galactose and L-rhamnose) using the previously reported methods. The conversion of L-rhamnose to L-rhamnal involved the use of the methodology pioneered by Fisher and refined by others. The peracetylation of L-rhamnose 1 with acetic anhydride and catalytic perchloric acid gave the clear solution of tetra-O-acetyl-L-rhamnose, which was directly treated in the same pot with hydrobromic acid to provide the tri-O-acetyl-bromo-L-rhamnoside 2. The reductive elimination of 2 with Zinc.

**Reagents and Conditions:**

(i) (a) HClO₄, Ac₂O, 0 °C to rt, 30 min, (b) 33% HBr/AcOH, rt, 90 min; (ii) Zn, satd. NaH₂PO₄, EtOAc, 3 h, rt; (iii) KO₂CO₃, MeOH, rt, 1 h; (iv) NaH, BnBr, DMF, TBAI, 0 °C to rt, 16 h.

**Scheme 2.1:** Preparation of the 3,4-di-O-benzyl-L-rhamnal from the L-rhamnose

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and saturated NaH₂PO₄ gave the 3,4-di-O-acetyl-L-rhamnal 3 in good yield. To incorporate the stable protecting groups in 3, acetyl groups were deprotected using K₂CO₃ in methanol to give L-rhamnal 4 which upon benzylation with benzyl bromide and sodium hydride provided the 3,4-di-O-benzyl-L-rhamnal 5 (Scheme 2.1).

Similarly, using the above protocol 3,4,6-tri-O-benzyl-D-galactal 8 and 3,4,6-tri-O-benzyl-D-glucal 11 were synthesized in good yields from the D-galactose 6 and D-glucose 9 respectively. These three protected glycals were used as substrates for the transition-metal catalyzed cyclopropanation reaction.

**Scheme 2.2**: Synthesis of tri-O-benzyl-D-galactal 8 and tri-O-benzyl-D-glucal 11

The cyclopropanation of 3,4-di-O-benzyl-L-rhamnal 5 with methyl diazoacetate (MDA) in presence of dirhodium tetraacetate Rh₂(OAc)₄ in dichloromethane gave the 1,5-anhydro-

**Reagents and Conditions**: (i) Methyl diazoacetate, Rh₂(OAc)₄, CH₂Cl₂, rt, 1 h.

**Scheme 2.3**: Rhodium (II) catalyzed cyclopropanation of glycals with methyl diazoacetate
-2,6-dideoxy-1,2-(exo-carbomethoxy-methylene)-3,4-di-O-benzyl-α-L-rhamnal 12 with 45% yield as a major diastereomer. The benzyl protected D-galactal 8 and D-glucal 11 were also cyclopropanated using same protocol to obtain 1,2-cyclopropanecarboxylates 13 and 14 respectively in moderate yield (scheme 2.3).

The model glycosyl acceptors used for the glycosylation reaction, were synthesized from D-galactose 6 and D-fructose 16 in one step. Treatment of D-galactose 6 with dry acetone in presence of catalytic concentrated sulfuric acid gave the 1,2;3,4-di-O-isopropylidene-α-D-galactose 15 in 70% yield. Similarly, the other acceptor 17 was synthesized by treating fructose 16 with zinc chloride and catalytic conc. sulfuric acid in acetone (Scheme 2.4).

Reagents and Conditions: (i) H$_2$SO$_4$, acetone, rt, 2 h; (ii) H$_2$SO$_4$, ZnCl$_2$, acetone, rt, 3 h.

Scheme 2.4: Synthesis of D-galactose diacetonide and D-fructose diacetonide

2.2.1 Discovery and Optimization of the Novel Glycosylation Reaction

The glycosylation studies began with L-rhamnose-derived cyclopropane 12 as donor and 1,2;3,4-di-O-isopropylidene-α-D-galactose 15 as acceptor in presence of NIS as the electrophile at 0 °C in acetonitrile. However, no expected disaccharide was observed under these reaction conditions, even with an excess of acceptor (>3 equiv). Similar reaction conditions with various solvents did not provide the glycosylation reaction (Scheme 2.5).

Reagents and Conditions: (i) NIS, CH$_3$CN, 0 °C; (ii) NIS, CH$_2$Cl$_2$, 0 °C.

Scheme 2.5: Attempts for the glycosylation reaction
On screening several promoters and after several attempts, we found that TMSOTf (20 mol%) as the best promoter for this glycosylation reaction. Treatment of 12 and 15 with NIS/TMSOTf in dichloromethane (0-28 °C, 8 h) yielded 2′-C-branched disaccharide 18 in 74% as a single diastereomer in which two new stereocenters were introduced at C1′ and C7′ in a single reaction. It is worth noting that only 1.1 equivalents of acceptor, with respect to the donor, were used for this glycosylation reaction. The substitution of α-iodide in α-iodocarboxylate 18 with NaN₃/DMF (28 °C, 24 h) afforded azidocarboxylate 19 in 96% yield. Reduction of the azide 19 under Staudinger reaction conditions (Ph₃P/THF/H₂O) produced disaccharide-based glyco-amino acid derivative 20 in 91% yield (Scheme 2.6).

Scheme 2.6: Synthesis of 2-C-branched GAA disaccharide by ring-opening of 1,2-cyclopropanecarboxylated sugar donor

2.2.2 Plausible Mechanistic Pathway

The plausible mechanism of NIS-mediated ring opening involves a stereospecific “edge attack” of iodide on 1,2-cyclopropanecarboxylate 12 to generate an oxocarbenium ion that is immediately trapped with triflate. The triflate is released by neighbouring-group participation of the C7-carboxylate to generate a second oxocarbenium ion intermediate 21, which is sufficiently long lived that it can be intercepted with a carbohydrate-based O-nucleophile 15. Nucleophilic attack by glycosyl acceptor oxygen at the anomeric carbon gives the disaccharide product 18 (Scheme 2.7).
2.2.3 Scope of the Reaction

The generality of this methodology has been proved successfully by applying it to a number of 1,2-cyclopropanated glycosyl donors and differentially protected sugar acceptors. Thus, the reaction of cyclopropanecarboxylates 12, 13 and 14 with acceptors 17 and 15 gave the ring-opened 2-C-branched disaccharide derivatives 22, 25 and 28, respectively, in good yields with very high diastereoselectivity at the newly formed C1' and C7' stereocenters.

The structures of the 2-C-branched disaccharide iodides were assigned on the basis of NMR spectra. The stereochemistry at C1' was confirmed by observing a large coupling constant ($J = 8.8$ Hz) for the C1' proton, which indicates a 1,2-trans configuration for all the ring-opened disaccharide derivatives. The stereochemistry at C2' was defined on the basis of the stereochemistry present in the 1,2-cyclopropanecarboxylated sugar precursor. The stereochemistry at C7' was assigned based on the proposed mechanism and further confirmed by X-ray crystallographic data of one of the GAA derivative. The substitution of iodide functionality in disaccharide derivatives 22, 25 and 28 with azide using NaN₃/DMF afforded the 23, 26 and 29 respectively. The 2-C-branched GAA derivatives 24, 27 and 30
were obtained from the azides 23, 26 and 29 using Staudinger reaction conditions in excellent yield (Table 1, entries 1, 2 and 3).

Table 2.1: Ring-opening of the 1,2-cyclopropanecarboxylated sugar donors with glycosyl acceptors: synthesis of 2-C-branched GAA derivatives

<table>
<thead>
<tr>
<th>Entry</th>
<th>Donor cycpropane</th>
<th>Acceptor</th>
<th>Iodide (%)</th>
<th>Azide (%)</th>
<th>GAA (%) derivative</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>![Donor 1]</td>
<td>![Acceptor 1]</td>
<td>22 (75)</td>
<td>23 (95)</td>
<td>![GAA 1]</td>
</tr>
<tr>
<td>2</td>
<td>![Donor 2]</td>
<td>![Acceptor 2]</td>
<td>25 (72)</td>
<td>26 (96)</td>
<td>![GAA 2]</td>
</tr>
<tr>
<td>3</td>
<td>![Donor 3]</td>
<td>![Acceptor 3]</td>
<td>28 (72)</td>
<td>29 (92)</td>
<td>![GAA 3]</td>
</tr>
</tbody>
</table>

2.2.4 Regioselectivity of the Reaction

Our next investigation focused on the regioselective glycosylation reactions based on the relative reactivity between two hydroxyls on a single sugar acceptor. The glycosyl acceptors containing two free hydroxyl groups were synthesized using standard procedures from D-glucose and D-galactose in excellent yields. Initially, methyl 4,6-\(\text{O}\)-benzylidene-\(\alpha\)-D-glucopyranoside 32\textsuperscript{27} was prepared by formation of methyl glucoside followed by benzylidene protection from the D-glucose. The crystalline methyl \(\alpha\)-D-glucopyranoside 31 was obtained by heating D-glucose with methanolic hydrogen chloride. The benzylidene protection of C4 and C6 hydroxyl groups in 31 with benzaldehyde dimethyl acetal in presence of \(p\)-toluenesulfonic acid gave the glycosyl acceptor 32, which upon benzylation of C2 and C3 hydroxyl groups followed by deprotection of 4,6-\(\text{O}\)-benzylidene group provided
another glycosyl acceptor, namely, methyl 2,3-di-\(O\)-benzyl-\(\alpha\)-D-glucopyranoside \(34^{26}\) (Scheme 2.8).

Reagents and Conditions: (i) MeOH/HCl, reflux, 16 h; (ii) PhCH(OMe)\(_2\), PTSA, DMF, 60 °C, 2 h; (iii) BnBr, NaH, DMF, TBAI, 10 h; (iv) PTSA, MeOH, 5 h.

Scheme 2.8: Synthesis of acceptors for regioselective glycosylation

Like the above strategy, the preparation of methyl-2,6-di-\(O\)-benzyl-\(\beta\)-D-galactopyranoside \(38^{29}\) mainly consists of few protecting group transformations in D-galactose derivatives. The protection of C3 and C4 hydroxyl groups in methyl \(\beta\)-D-galactopyranoside \(35\) with acetone in presence of copper sulphate and catalytic sulfuric acid gave the \(36\). Benzylation of C2 and C4 hydroxyl groups of \(36\) followed by deprotection of acetonide gave the acceptor \(38\) in good yield.

Reagents and Conditions: (i) CuSO\(_4\), H\(_2\)SO\(_4\), acetone, 3 h; (ii) BnBr, NaH, DMF, 10 h; (iii) aq. AcOH, 50 °C 3 h.

Scheme 2.9: Synthesis of D-galactose-based acceptor for regioselective glycosylation
To investigate the regioselectivity of the novel glycosylation reaction, 1,2-cyclopropanecarboxylate 14 was treated with methyl 2,3-di-O-benzyl-α-D-glucopyranoside 34\textsuperscript{26} in the presence of NIS/TMSOTf in dichloromethane at 0 °C. The reaction produced a single product 39, which was converted to azide 40. The regioselectivity at the 6-O position was confirmed by acetylating the free hydroxyl group in 40 with Ac\textsubscript{2}O/pyridine and observing a downfield shift in the signal of the C4 proton in acetylated disaccharide derivative 41. The reaction of 40 using the Staudinger reaction conditions provided the 2-C-branched GAA derivative 42 in 85% yield (Scheme 2.10).

**Scheme 2.10**: Ring-opening of 1,2-cyclopropanecarboxylated sugar donor with glycosyl acceptor having two hydroxyl groups.

Similarly, reactivity-based glycosylation of 1,2-cyclopropanecarboxylates 12 and 13 with methyl-4,6-O-benzylidene-α-D-glucopyranoside 32\textsuperscript{27} produced the 2-C-branched disaccharide derivatives 43 and 47, respectively, in good yield. Interestingly, C3-OH of acceptor 32 was involved in the glycosylation reactions\textsuperscript{28} (Table 2, entry 1 and 2).

The aforementioned acceptor-reactivity-based glycosylation of 1,2-cyclopropanecarboxylated sugar donors could also be extended to the other sugar derivatives. Thus, treatment of cyclopropanecarboxylated donors 12, 13 and 14 with methyl-2,6-di-O-benzyl-β-D-
galactopyranoside 38 gave disaccharide derivatives 50, 54 and 57, respectively, in good yields. In these reactions, C3-OH of the glycosyl acceptor 38 was participated in glycosylation reactions to give the 2-C-branched disaccharides as a single regioisomer. All the disaccharide α-iodocarboxylates (43, 47, 50, 54 and 57) were converted to the corresponding azides (45, 48, 51, 55 and 58, respectively) by using NaN₃/DMF to give excellent yields (90%). All these azides were further converted to the corresponding 2-C-branched GAA derivatives 46, 49, 53, 56 and 59, respectively, under Staudinger reaction conditions (Table 2, entries 1, 2, 3, 4, and 5).

**Table 2.2:** Ring-opening of 1,2-cyclopropanecarboxylated sugar donors with glycosyl acceptors having the two hydroxyl groups: Synthesis of 2-C-branched GAA derivatives.

<table>
<thead>
<tr>
<th>entry</th>
<th>donor cyclopropane</th>
<th>acceptor</th>
<th>iodide (%)</th>
<th>azide (%)</th>
<th>GAA (%) derivative</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>Ph</td>
<td>43 (67)</td>
<td>45 (92)</td>
<td>46 (94)</td>
</tr>
<tr>
<td>2</td>
<td>Ph</td>
<td>MeO</td>
<td>44 (96)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Ph</td>
<td>OMe</td>
<td>47 (63)</td>
<td>48 (90)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Ph</td>
<td>OMe</td>
<td>50 (70)</td>
<td>51 (93)</td>
<td>52 (97)</td>
</tr>
<tr>
<td>5</td>
<td>Ph</td>
<td>OMe</td>
<td>54 (69)</td>
<td>55 (92)</td>
<td>56 (90)</td>
</tr>
</tbody>
</table>

*a* The free hydroxyl group of iodide 43 was acetylated. *b* The free hydroxyl group of azide 51 was acetylated.
2.2.5 Synthesis of Oligo-Glyco-Amino Acid (OGAA) Derivative

Keeping the above-mentioned acceptor-reactivity-based regio- and stereoselective glycosylation of 1,2-cyclopropanecarboxylated sugar donors in mind, we further planned to synthesize an OGAA derivative. Towards this goal, the benzylidene protecting group in α-iodocarboxylate 43 was deprotected by using p-TsOH·H₂O/MeOH to give the disaccharide triol 60. A second acceptor-reactivity-based glycosylation was performed by treating 12 with triol 60 in presence of NIS/TMSOTf to give trisaccharide 61 in good yield as the only isolated product. Treatment of 61 with NaN₃/DMF gave diazide 62. The free hydroxyls were acetylated to give compound 63, which gave OGAA derivative 64 under Staudinger reaction conditions (Scheme 2.11).

![Reaction scheme](image_url)

**Reagents and Conditions:**
(i) p-TsOH·H₂O, MeOH rt, 4 h,
(ii) NIS, TMSOTf, CH₂Cl₂, 0 °C to rt, 16 h,
(iii) NaN₃, DMF, rt, 24 h,
(iv) Ac₂O, Py, rt, 10 h,
(v) (a) PPh₃, THF, rt, 6 h,
(b) H₂O, reflux, 8 h.

**Scheme 2.11:** Synthesis of 2-C-branched OGAA derivatives
2.3 Summary and Conclusion

A new glycosylation method that uses carbohydrate-derived donor-acceptor cyclopropanes as glycosyl acceptors has been developed. To the best of our knowledge, this is the first method of the use of 1,2-cyclopropanecarboxylated sugars as donors in traditional oligosaccharide synthesis. The novel glycosylation method was successfully applied to the synthesis of a number of 2-C-branched GAA disaccharides by using various glycosyl donors and acceptors. The high regioselectivity was attained in the glycosylation reaction with the glycosyl acceptors having the competing hydroxyl groups. The acceptor-reactivity based regio- and stereoselective glycosylation was utilized for the preparation of an OGAA derivative. Mimicking natural glycosides with carbon-branched GAAs and determining the biological importance of these hybrid biomolecules are in progress.

2.4 Experimental Section

2.4.1 Materials and Methods

Chemicals and solvents were purchased from the local suppliers and Sigma-Aldrich® chemical company. Solvents were used in the reactions after distilled over the dehydrating agents. 4 Å Molecular sieves were used in the reactions after crushed and activated at 400 °C for 1 h. All the reactions were carried out under N₂ or Ar conditions and monitored by the thin layer chromatography (TLC) using silica-gel on aluminum plates (GF₂₅₄) by charring with 5% (v/v) H₂SO₄ in methanol or by phosphomolybdic acid (PMA) stain or by ultra violet (UV) detection. Silica-gel (100-200 mesh) was used for column chromatography to purify the all the compounds. ¹H, ¹³C, DEPT spectra were recorded on Bruker® 400 Avance MHz spectrometer in CDCl₃. ¹H NMR chemical shifts were reported in parts per million (ppm) (δ) with TMS as an internal standard (δ 0.00) and ¹³C NMR were reported in chemical shifts with solvent reference (CDCl₃, δ 77.00).
2.4.2 Experimental Procedures and Spectral Data

(2.4.2.1) 1,5-anhydro-2,6-dideoxy-1,2-(exo-carbomethoxy-methylene)-3,4-di-O-benzyl-α-L-rhamnal (12):

\[
\begin{align*}
\text{Reagents and Conditions:} & \quad (i) \text{ Rh}_2(O\text{Ac})_4, \text{CH}_2\text{Cl}_2, \text{rt}, 1\ h.
\end{align*}
\]

A solution of methyl diazoacetate (MDA) (1.0 mL, 9.66 mmol) in CH$_2$Cl$_2$ (32 mL) was slowly added dropwise to the stirred solution of 3,4-di-O-benzyl-L-rhamnal 5 (1 g, 3.22 mmol) and Rh$_2$(OAc)$_4$ (29 mg, 0.064 mmol) in CH$_2$Cl$_2$ (7 mL) in dropwise fashion for 1 hour at ambient temperature. After cessation of the nitrogen evolution, the reaction mixture was concentrated under vacuo and purified by silica-gel column chromatography (EtOAc in hexane (1:9)) to provide the 12 as a white solid (45% yield).

(2.4.2.2) 1,5-Anhydro-2-deoxy-1,2-C-(exo-carbomethoxymethylene)-3,4,6-tri-O-benzyl-α-D-galactal (13):

\[
\begin{align*}
\text{Reagents and Conditions:} & \quad (i) \text{ Rh}_2(O\text{Ac})_4, \text{CH}_2\text{Cl}_2, \text{rt}, 1\ h.
\end{align*}
\]

The compound 13 was synthesized using the 3,4,5-tri-O-benzyl-D-galactal 8 (1.0 g, 2.4 mmol), Rh$_2$(OAc)$_4$ (21 mg, 0.048 mmol) and methyl diazoacetate (0.76 mL, 7.2 mmol) in dichloromethane according to the procedure in (2.4.2.1). The crude product was purified by silica-gel column chromatography with ethyl acetate/hexane (1:9) to provide the 13 as a light yellow oil (61% yield).

(2.4.2.3) 1,5-Anhydro-2-deoxy-1,2-C-(exo-carbomethoxymethylene)-3,4,6-tri-O-benzyl-α-D-glucal (14):

\[
\begin{align*}
\text{Reagents and Conditions:} & \quad (i) \text{ Rh}_2(O\text{Ac})_4, \text{CH}_2\text{Cl}_2, \text{rt}, 1\ h.
\end{align*}
\]
The compound 14 was synthesized using the 3,4,5-tri-O-benzyl-D-glucal 11 (1.5 g, 3.6 mmol), Rh$_2$(OAc)$_4$ (32 mg, 0.072 mmol) and methyl diazoacetate (1.15 mL, 10.8 mmol) in dichloromethane according to procedure in (2.4.2.1). The crude product was purified by silica-gel column chromatography with ethyl acetate/hexane (1:9) to provide the 14 as a light yellow solid (59% yield).

(2.4.2.4) General procedure for the glycosylation reaction of 1,2-cyclopropanecarboxylated sugar donor with glycosyl acceptor:

To a stirred suspension of 1,2-cyclopropanecarboxylated sugar (0.1 mmol), glycosyl acceptor (0.11 mmol) and 4 Å molecular sieves (MS) in dichloromethane (5 mL) at 0 °C, under nitrogen atmosphere, was added NIS (0.11 mmol) and TMSOTf (0.02 mmol). The temperature was slowly raised to 25 °C and the mixture was stirred for a period of 10 h (the reaction was monitored by TLC). The reaction mixture was diluted with dichloromethane and filtered, washed with 5% aqueous sodium thiosulphate solution and the organic layer was dried over anhydrous sodium sulphate and concentrated. Column chromatography of the crude product with ethyl acetate/hexane afforded the pure 2-C-branched disaccharide derivative.

(2.4.2.5) Compound (18):

The compound 18 was synthesized using L-rhamnose-derived 1,2-cyclopropanecarboxylate 12 (100 mg, 0.26 mmol), 1,2;3,4-di-O-isopropylidene-α-D-galactopyranoside 15 (75 mg, 0.28 mmol), NIS (64.3 mg, 0.28 mmol), TMSOTf (9.3 μL, 0.05 mmol) and 4 Å MS in dichloromethane (10 mL) by following the general procedure in (2.4.2.4). The reaction mixture was stirred for overnight at ambient temperature. The obtained crude product was purified by silica-gel column chromatography (EtOAc/hexane 3:7 to 2:3) to provide the 18 as a thick gum (74% yield).
1H NMR (CDCl3, 400 MHz): δ 7.23 – 7.32 (m, 10 H), 5.51 (d, 1H, J = 5.2 Hz), 5.16 (d, 1H, J = 2.0 Hz), 4.93 (d, 1H, 10.8 Hz), 4.79 (d, 2H, J = 10.8 Hz), 4.65 (d, 1H, J = 10.4 Hz), 4.61 (dd, 1H, J = 2.0 Hz, J = 7.8 Hz), 4.34 (d, 1H, J = 8 Hz), 4.30 – 4.32 (m, 2H), 3.98 – 4.06 (m, 2H), 3.42 (m, 2H), 3.35 (s, 3H), 1.90 (dtd, 1H, J = 2 Hz, J = 2 Hz, J = 8.4 Hz), 1.53 (s, 3H), 1.46 (s, 3H), 1.32 – 1.35 (m, 9H).

13C NMR (CDCl3, 100 MHz): δ 167.9, 138.2, 137.7, 128.4, 128.0, 127.8, 127.7, 127.6, 127.3, 109.1, 108.5, 103.4, 96.1, 85.8, 81.4, 75.1, 74.6, 71.4, 70.6, 70.5, 70.4, 68.5, 65.9, 65.7, 53.3, 50.4, 29.2, 26.1, 25.9, 24.8, 24.5, 17.9.

(2.4.2.6) Compound (19):

Reagents and Conditions: (i) NaN3, DMF, rt, 24 h.

To a stirred solution of iodide 18 (80 mg, 0.10 mmol) in dry dimethylformamide (5 mL) was added sodium azide (13.5 mg, 0.20 mmol) (excess of NaN3 (upto 10 eq) will fast up the reaction). The reaction mixture was stirred for 24 h at 25 °C. Once the reaction was completed most of the dimethylformamide (DMF) was removed under vacuum and the pale yellow paste was extracted with dichloromethane (3 X 10 mL). The organic layer was washed with water (10 mL), dried over sodium sulphate and filtered. Concentration of organic layer followed by purification of the residue over silica gel column chromatography (EtOAc/hexane 2:3) furnished the pure azide 19 as a colorless oil (96% yield).

1H NMR (CDCl3, 400 MHz, TMS): δ 7.26 – 7.38 (m, 10H), 5.51 (d, 1H, J = 5.2 Hz), 4.94 (d, 1H, J = 11.2 Hz), 4.86 (d, 1H, J = 11.2 Hz), 4.69 (d, 1H, J = 11.2 Hz), 4.63 (d, 1H, J = 11.2 Hz), 4.58 (dd, 1H, J = 2.4 Hz, J = 8 Hz), 4.38 (d, 1H, J = 8.4 Hz), 4.27 – 4.29 (m, 3H), 3.85 – 3.91 (m, 2H), 3.76 (s, 3H), 3.55 – 3.61 (m, 2H), 3.32 – 3.35 (m, 1H), 3.23 (t, 1H, J = 9.2 Hz), 2.37 (dtd, 1H, J = 1.6 Hz, J = 2.4 Hz, J = 8.8 Hz), 1.56 (s, 3H), 1.42 (s, 3H), 1.26 – 1.33 (m, 9H).

13C NMR (CDCl3, 100 MHz): δ 170.4, 137.9, 128.6, 128.5, 128.1, 127.9, 127.8, 109.0, 108.3, 100.2, 96.3, 85.6, 78.6, 75.1, 75.1, 71.3, 70.8, 70.6, 70.4, 68.9, 66.1, 58.1, 52.6, 48.9, 25.9, 25.9, 24.9, 24.4, 17.8.
(2.4.2.7) Compound (20):

Reagents and Conditions: (i) PPh₃, THF, rt, 6 h, (ii) H₂O, reflux, 8 h.

Triphenyl phosphine (27 mg, 0.10 mmol) was added to a solution of azide 19 (70 mg, 0.10 mmol) in dry THF (5 mL) maintained under nitrogen. The solution was stirred for 8 h after which complete formation of iminophosphorane was confirmed by infrared spectroscopy (disappearance of azide stretching frequency at 2100 cm⁻¹). At this stage water (0.2 mL) was added and the solution was refluxed for 6 h. The reaction mixture was washed with brine solution (10 mL) and extracted with chloroform (2 X 10 mL). The organic extract was dried over anhydrous sodium sulphate and concentrated under vacuo. The crude product was purified by column chromatography on silica gel using ethyl acetate/hexane (2:3 to 1:1) as eluent to give the 2-C-branched disaccharide GAA derivative 20 as a colorless oil (91% yield).

¹H NMR (CDCl₃, 400 MHz): δ 7.29 – 7.33 (m, 10H), 5.48 (d, 1H, J = 5.2 Hz), 4.93 (d, 1H, J = 11.6 Hz), 4.88 (d, 1H, J = 11.2 Hz), 4.70 (bs, 1H), 4.67 (bs, 1H), 4.60 (dd, 1H, J = 2 Hz, J = 8 Hz), 4.42 (d, 1H, J = 8.8 Hz), 4.28 – 4.32 (m, 2H), 3.85 – 3.88 (m, 2H), 3.60 (dd, 1H, J = 2 Hz, J = 9.2 Hz), 3.68 (s, 3H), 3.63 (s, 1H), 3.50 – 3.55 (m, 1H), 3.31 – 3.41 (m, 1H), 1.52 (s, 3H), 1.41 (s, 3H), 1.34 (s, 3H), 1.30 (s, 3H), 1.27 (d, 3H, J = 6 Hz).

¹³C NMR (CDCl₃, 100 MHz): δ 176.5, 138.3, 138.2, 128.5, 128.5, 128.4, 128.2, 128.2, 109.0, 108.4, 100.7, 96.2, 85.9, 78.9, 78.8, 75.9, 74.7, 71.4, 70.5, 68.1, 65.6, 52.1, 52.0, 50.1, 50.0, 26.0, 25.9, 24.9, 24.5, 18.0.

(2.4.2.8) Compound (22):

Reagents and Conditions: (i) NIS, TMSOTf, CH₂Cl₂, 0 °C to rt, 16 h.
The compound 22 was synthesized using L-rhamnose-derived 1,2-cyclopropanecarboxylate 12 (150 mg, 0.39 mmol), 2,3;4,5-di-O-isopropylidene-α-D-fructopyranose 17 (111 mg, 0.42 mmol), NIS (96.5 mg, 0.42 mmol), TMSOTf (14.0 μL, 0.07 mmol) and 4 Å MS in dichloromethane (15 mL) by following the general procedure in (2.4.2.4). The reaction mixture was stirred for overnight at ambient temperature. The obtained crude product was purified by silica-gel column chromatography (EtOAc/hexane 3:7 to 2:3) to provide the 22 as a colorless oil (75% yield).

**1H NMR (CDCl₃, 400 MHz):** δ 7.23 – 7.32 (m, 10 H), 5.08 (d, 1H, J = 2.4 Hz), 4.94 (d, 1H, 10.8 Hz), 4.79 (d, 1H, J = 10.8 Hz), 4.78 (d, 1H, J = 10.8 Hz), 4.65 (d, 1H, J = 10.8 Hz), 4.59 (dd, 1H, J = 2.4 Hz, J = 7.8 Hz), 4.39 (d, 1H, J = 8 Hz), 4.33 (d, 1H, J = 2.4 Hz), 4.23 (bd, 1H, J = 7.6 Hz), 4.08 (d, 1H, J = 10.4 Hz), 3.90 (dd, 1H, J = 1.6 Hz, J = 12.8 Hz), 3.69 – 3.79 (m, 2H), 3.58 (d, 1H, J = 10.4 Hz), 3.41 – 3.44 (m, 2H), 3.34 (s, 3H), 1.96 (dtd, 1H, J = 2 Hz, J = 2 Hz, J = 8.4 Hz), 1.53 (s, 3H), 1.48 (s, 3H), 1.41 (s, 3H), 1.35 (bs, 6 H).

**13C NMR (CDCl₃, 100 MHz):** δ 167.7, 138.2, 137.7, 128.4, 128.0, 127.8, 127.7, 127.6, 127.3, 108.9, 108.5, 102.3, 102.0, 85.8, 81.3, 75.1, 74.6, 71.5, 70.9, 70.7, 70.3, 70.1, 61.0, 53.4, 50.0, 29.2, 26.6, 25.9, 25.5, 24.0, 17.9.

(2.4.2.9) **Compound (23):**

Reagents and Conditions: (i) NaN₃, DMF, rt, 24 h.

The compound 23 was synthesized using disaccharidyl iodide 22 (120 mg, 0.15 mmol) and NaN₃ (20 mg, 0.31 mmol) in DMF (10 mL) by following the same procedure in (2.4.2.6). The reaction mixture was stirred for 24 h at room temperature. Crude product was purified by silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to provide the disaccharide-based azide 23 as a thick gum (95% yield).

**1H NMR (CDCl₃, 400 MHz):** δ 7.29 – 7.36 (m, 10H), 4.95 (d, 1H, J = 11.6 Hz), 4.85 (d, 1H, J = 10.82 Hz), 4.69 (d, 1H, J = 10.8 Hz), 4.63 (d, 1H, J = 11.6 Hz), 4.55 (dd, 1H, J = 2.8 Hz, J = 7.8 Hz), 4.39 (d, 1H, J = 8.4 Hz), 4.29 (d, 1H, J = 2 Hz), 4.20 (dd, 1H, J = 1.2 Hz, J = 8...
Hz), 4.13 (d, 1H, $J = 2.8$ Hz), 3.86 (d, 1H, $J = 10$ Hz), 3.84 (dd, 1H, $J = 2$ Hz, $J = 13$ Hz), 3.79 (s, 3H), 3.70 (d, 1H, $J = 13$ Hz), 3.56 – 3.62 (m, 2H), 3.25 – 3.38 (m, 2H), 2.39 (dt, 1H, $J = 2$ Hz, $J = 2.4$ Hz, $J = 8.4$ Hz), 1.52 (s, 3H), 1.48 (s, 3H), 1.37 (s, 3H), 1.33 (s, 3H), 1.28 (d, 3H, $J = 5.6$ Hz).

$^{13}$C NMR (CDCl$_3$, 100 MHz): δ 170.0, 137.9, 137.9, 128.5, 128.4, 128.0, 127.9, 127.8, 109.0, 108.5, 101.9, 99.2, 85.5, 78.7, 75.0, 75.0, 71.6, 71.2, 71.1, 70.2, 70.2, 61.0, 58.6, 52.6, 49.0, 26.5, 25.8, 25.4, 24.3, 17.8.

(2.4.2.10) Compound (24):

![Chemical Structure](image)

Reagents and Conditions: (i) PPh$_3$, THF, rt, 6 h, (ii) H$_2$O, reflux, 8 h.

The compound 24 was synthesized using the azide 23 (90 mg, 0.13 mmol) and PPh$_3$ (35 mg, 0.13 mmol) in THF (5 mL) by following the same procedure in (2.4.2.7). The resulted crude product was purified by careful silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to furnish the 2-C-branched GAA derivative 24 as a colorless oil (92% yield).

$^1$H NMR (CDCl$_3$, 400 MHz): δ 7.28 – 7.34 (m, 10H), 4.95 (d, 1H, $J = 11.6$ Hz), 4.86 (d, 1H, $J = 10.8$ Hz), 4.69 (d, 1H, $J = 10.8$ Hz), 4.68 (d, 1H, $J = 10.8$ Hz), 4.58 (dd, 1H, $J = 2.4$ Hz, $J = 8$ Hz), 4.49 (d, 1H, $J = 8.8$ Hz), 4.25 (d, 1H, $J = 2.4$ Hz), 4.21 (d, 1H, $J = 8$ Hz), 3.97 (d, 1H, $J = 10.4$ Hz), 3.88 (d, 1H, $J = 13.2$ Hz), 3.73 (s, 3H), 3.67 – 3.72 (m, 3H), 3.49 (d, 1H, $J = 10.4$ Hz), 3.35 – 3.40 (m, 1H), 3.28 (t, 1H, $J = 8.8$ Hz), 2.30 (t, 1H, $J = 9.6$ Hz), 1.50 (s, 3H), 1.46 (s, 3H), 1.35 (s, 3H), 1.33 (s, 3H), 1.28 (d, 3H, $J = 5.6$ Hz).

$^{13}$C NMR (CDCl$_3$, 100 MHz): δ 176.1, 138.2, 138.1, 128.5, 128.4, 128.1, 127.9, 127.8, 108.9, 108.4, 101.9, 99.9, 85.8, 79.2, 74.9, 74.6, 71.4, 71.1, 71.0, 70.2, 69.9, 61.0, 52.0, 50.7, 50.0, 26.5, 25.9, 25.4, 24.2, 17.9.

(2.4.2.11) Compound (25):

The compound 25 was synthesized using D-galactose-derived 1,2-cyclopropanecarboxylate 13 (170 mg, 0.34 mmol), 1,2,3,4-di-O-isopropylidene-α-D-galactopyranoside 15 (99 mg, 0.38 mmol), NIS (86 mg, 0.38 mmol), TMSOTf (12.2 μL, 0.068 mmol) and 4 Å MS in
dichloromethane (20 mL) by following the general procedure in (2.4.2.4). The reaction mixture was stirred for overnight at ambient temperature. The obtained crude product was purified by silica-gel column chromatography (EtOAc/hexane 3:7 to 2:3) to provide the 25 as a yellowish oil (72% yield).

\[(\text{13}) + \text{HO} + (\text{15}) \rightarrow (\text{25}) \quad \text{72%} \]

**Reagents and Conditions:** (i) NIS, TMSOTf, CH₂Cl₂, 0 °C to rt, 16 h.

**¹H NMR (CDCl₃, 400 MHz):** δ 7.24 – 7.35 (m, 15 H), 5.53 (d, 1H, J = 4.8 Hz), 5.24 (d, 1H, J = 2.0 Hz), 4.82 (d, 1H, 11.6 Hz), 4.64 (d, 1H, J = 10.4 Hz), 4.59 (dd, 1H, J = 2.4 Hz, J = 8 Hz), 4.48 – 4.56 (m, 4H), 4.34 (d, 1H, J = 8 Hz), 4.29 (dd, 1H, J = 2.4 Hz, J = 8.8 Hz), 4.22 (dd, 1H, J = 1.6 Hz, J = 8 Hz), 4.05 (dd, 1H, J = 4.8 Hz, J = 10.4 Hz), 3.99 (dt, 1H, J = 1.6 Hz, J = 6.4 Hz), 3.95 (d, 1H, J = 2 Hz), 3.69 – 3.72 (m, 2H), 3.56 – 3.67 (m, 3H), 3.42 (s, 3H), 2.42 (ddt, 1H, J = 2 Hz, J = 2 Hz, J = 8.4 Hz), 1.51 (s, 3H), 1.44 (s, 3H), 1.32 (bs, 6H).

**¹³C NMR (CDCl₃, 100 MHz):** δ 168.1, 138.7, 137.9, 137.2, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.3, 109.2, 108.5, 103.9, 96.2, 81.5, 74.3, 73.5, 73.4, 72.1, 71.3, 71.1, 70.7, 70.5, 68.8, 68.6, 66.9, 50.0, 45.1, 30.5, 26.1, 25.9, 24.9, 24.4.

**(2.4.2.12) Compound (26):**

\[(\text{25}) \rightarrow (\text{26}) \quad \text{96%} \]

**Reagents and Conditions:** (i) NaN₃, DMF, rt, 24 h.

The compound 26 was synthesized using disaccharidyl iodide 25 (130 mg, 0.14 mmol) and NaN₃ (18.8 mg, 0.29 mmol) in DMF (10 mL) by following the same procedure in (2.4.2.6). The reaction mixture was stirred for 24 h at room temperature. Crude product was purified by silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to provide the disaccharide-based azide 26 as a thick gum (96% yield).
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1H NMR (CDCl3, 400 MHz): δ 7.27 – 7.39 (m, 15 H), 5.50 (d, 1H, J = 5.2 Hz), 4.89 (d, 1H, 11.6 Hz), 4.69 (d, 1H, J = 11.6 Hz), 4.63 (d, 1H, J = 11.6 Hz), 4.53 – 4.53 (dd, 1H, J = 2 Hz, J = 8 Hz), 4.52 (bs, 1H), 4.46 (d, 2H, J = 2 Hz), 4.41 (d, 1H, J = 2 Hz), 4.38 (d, 1H, J = 4.8 Hz), 4.26 (dd, 1H, J = 2.4 Hz, J = 9.2 Hz), 4.20 (dd, 1H, J = 2 Hz, J = 8 Hz), 3.97 (d, 1H, J = 2 Hz), 3.94 (dd, 1H, J = 6 Hz, J = 10 Hz), 3.89 (dt, 1H, J = 1.6 Hz, J = 5.6 Hz), 3.74 (s, 3H), 3.65 (dd, 1H, J = 8 Hz, J = 9.2 Hz), 3.54 – 3.60 (m, 2H), 3.47 – 3.51 (m, 2H), 2.80 (ddt, 1H, J = 2 Hz, J = 2.4 Hz, J = 8.4 Hz), 1.56 (s, 3H), 1.40 (s, 3H), 1.29 (s, 3H), 1.26 (s, 3H).

13C NMR (CDCl3, 100 MHz): δ 170.4, 138.4, 137.9, 137.3, 128.6, 128.4, 128.3, 128.2, 128.1, 127.8, 127.7, 127.6, 108.9, 108.4, 100.3, 96.2, 74.5, 73.5, 73.4, 71.5, 71.0, 70.6, 70.5, 70.4, 68.5, 68.3, 66.5, 58.5, 52.3, 44.1, 25.9, 25.8, 24.9, 24.3.

(2.4.2.13) Compound (27):

The compound 27 was synthesized using the azide 26 (100 mg, 0.12 mmol) and PPh3 (33 mg, 0.12 mmol) in THF (7 mL) by following the same procedure in (2.4.2.7). The resulted crude product was purified by careful silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to furnish the 2-C-branced GAA derivative 27 as a colorless oil (92% yield).

1H NMR (CDCl3, 400 MHz): δ 7.25-7.35 (m, 15 H), 5.54 (d, 1H, J = 12.0 Hz), 4.71 (d, 1H, J = 11.6 Hz), 4.62 (dd, 2H, J = 1.2 Hz, J = 10.0 Hz), 4.53 (dd, 1H, J = 2.4 Hz, J = 8.0 Hz), 4.41 – 4.49 (m, 3H), 4.27 (dd, 1H, J = 2.4 Hz, J = 4.8 Hz), 4.14 (dd, 1H, J = 2 Hz, J = 8 Hz), 3.92 – 3.96 (m, 2H), 3.87 (d, 1H, J = 1.6 Hz), 3.82 (dd, 1H, J = 3.2 Hz, J = 12 Hz), 3.70 – 3.76 (m, 2H), 3.67 (s, 3H), 3.52 – 3.66 (m, 4H), 2.74 (dd, 1H, J = 2 Hz, J = 8.4 Hz), 1.60 (s, 3H), 1.39 (s, 3H), 1.31 (s, 3H), 1.25 (s, 3H).

13C NMR (CDCl3, 100 MHz): δ 176.4, 138.7, 138.0, 137.9, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 109.1, 108.5, 100.3, 96.1, 78.1, 74.4, 73.6, 73.5, 71.7, 71.1, 71.0, 70.5, 70.1, 68.9, 67.8, 67.6, 51.9, 50.1, 45.3, 25.9, 25.8, 24.8, 24.3.
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(2.4.2.14) Compound (28):

![Chemical Structure of 28]

**Reagents and Conditions:** (i) NIS, TMSOTf, CH₂Cl₂, 0 °C to rt, 16 h.

The compound 28 was synthesized using d-glucose-derived 1,2-cyclopropanecarboxylate 14 (150 mg, 0.30 mmol), 1,2:3,4-di-O-isopropylidene-α-D-galactopyranoside 15 (87 mg, 0.33 mmol), NIS (75.9 mg, 0.33 mmol), TMSOTf (10.8 μL, 0.06 mmol) and 4 Å MS in dichloromethane (15 mL) by following the general procedure in (2.4.2.4). The reaction mixture was stirred for overnight at ambient temperature. The obtained crude product was purified by silica-gel column chromatography (EtOAc/hexane 3:7 to 2:3) to provide the 28 as a colorless oil (72% yield).

**¹H NMR (CDCl₃, 400 MHz):** δ 7.10 – 7.20 (m, 2H), 7.21 – 7.42 (m, 13H), 5.55 (d, 1H, J = 4.8 Hz), 5.17 (d, 1H, J = 2 Hz), 4.94 (d, 1H, J = 10.4 Hz), 4.80 (d, 1H, J = 10.8 Hz), 4.74 (d, 1H, J = 10.4 Hz), 4.66 (d, 1H, J = 12 Hz), 4.58-4.62 (m, 3H), 4.38 (d, 1H, J = 8 Hz), 4.32 (dd, 1H, J = 2.4 Hz, J = 4.8 Hz), 4.27 (dd, 1H, J = 2 Hz, J = 7.6 Hz), 4.08 – 4.12 (m, 1H), 4.05 (td, 1H, J = 4.8 Hz, J = 1.6 Hz), 3.73 – 3.89 (m, 5H), 3.47-3.50 (m, 1H), 3.37 (s, 3H), 1.98 (dtd, 1H, J = 2.4 Hz, J = 2 Hz, J = 8.0 Hz), 1.54 (s, 3H), 1.46 (s, 3H), 1.43 (bs, 6H).

**¹³C NMR (CDCl₃, 100 MHz):** δ 167.8, 138.2, 138.0, 137.7, 128.3, 128.3, 128.0, 127.8, 127.7, 127.6, 127.5, 127.3, 109.3, 108.5, 103.4, 96.2, 81.6, 80.0, 75.0, 74.7, 74.6, 73.4, 71.0, 70.6, 70.5, 68.7, 68.5, 66.8, 56.3, 49.9, 29.3, 26.0, 25.9, 24.9, 24.4.

(2.4.2.15) Compound (29):

![Chemical Structure of 29]

**Reagents and Conditions:** (i) NaN₃, DMF, rt, 24 h.

The compound 29 was synthesized using disaccharidyl iodide 28 (120 mg, 0.13 mmol) and NaN₃ (17.8 mg, 0.27 mmol) in DMF (10 mL) by following the same procedure in (2.4.2.6). The reaction mixture was stirred for 24 h at room temperature. Crude product was purified by
silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to provide the disaccharide-based azide 29 as a thick gum (92% yield).

\(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.20 – 7.37 (m, 15H), 5.51 (d, 1H, \(J = 5.2\) Hz), 4.94 (d, 1H, \(J = 11.2\) Hz), 4.80 (d, 1H, \(J = 10.8\) Hz), 4.53-4.66 (m, 5H), 4.44 (d, 1H, \(J = 8.4\) Hz), 4.30 (d, 1H, \(J = 1.6\) Hz), 4.28 (dd, 1H, \(J = 2.4\) Hz, \(J = 5.2\) Hz), 4.23 (dd, 1H, \(J = 1.6\) Hz, \(J = 8\) Hz), 3.96 – 4.00 (m, 1H), 3.92 (dt, 1H, \(J = 1.6\) Hz, \(J = 5.6\) Hz), 3.75 (s, 3H), 3.58 – 3.73 (m, 5H), 3.38 – 3.40 (m, 1H), 2.38 (dtd, 1H, \(J = 2\) Hz, \(J = 2.4\) Hz, \(J = 8.8\) Hz), 1.58 (s, 3H), 1.43 (s, 3H), 1.32 (s, 3H), 1.30 (s, 3H).

\(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 170.1, 138.0, 137.9, 137.9, 128.5, 128.4, 128.3, 128.0, 127.9, 127.7, 127.6, 127.6, 109.0, 108.5, 100.0, 96.27, 79.7, 78.8, 75.0, 74.99, 74.6, 73.5, 70.9, 70.5, 70.4, 68.4, 68.2, 66.3, 58.3, 52.4, 48.6, 25.9, 25.8, 24.9, 24.4.

(2.4.2.16) Compound (30):

\[\text{Reagents and Conditions: (i) PPh}_3, \text{THF, rt, 6 h, (ii) H}_2\text{O, reflux, 8 h.}\]

The compound 30 was synthesized using the azide 29 (90 mg, 0.11 mmol) and PPh\(_3\) (30 mg, 0.11 mmol) in THF (7 mL) by following the same procedure in (2.4.2.7). The resulted crude product was purified by careful silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to furnish the 2-C-branched GAA derivative 30 as a colorless oil (89% yield).

\(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.20 – 7.36 (m, 15H), 5.54 (d, 1H, \(J = 5.2\) Hz), 4.93 (d, 1H, \(J = 11.6\) Hz), 4.82 (d, 1H, \(J = 11.2\) Hz), 4.53-4.71 (m, 6H), 4.29 (dd, 1H, \(J = 2.4\) Hz, \(J = 5.2\) Hz), 4.18 (dd, 1H, \(J = 1.6\) Hz, \(J = 8\) Hz), 3.93 – 3.95 (m, 1H), 3.81 – 3.89 (m, 2H), 3.67 (s, 3H), 3.44 – 3.47 (m, 1H), 2.32 (dtd, 1H, \(J = 2\) Hz, \(J = 2\) Hz, \(J = 8\) Hz), 1.64 (s, 3H), 1.41 (s, 3H), 1.32 (s, 3H), 1.29 (s, 3H).

\(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 176.4, 138.3, 138.2, 129.0, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 127.6, 127.6, 127.5, 109.1, 108.2, 108.5, 100.3, 96.1, 80.1, 79.2, 75.0, 74.7, 74.4, 73.4, 71.1, 70.5, 70.1, 68.8, 67.7, 67.6, 51.8, 50.3, 49.9, 25.9, 25.8, 24.8, 24.3.
(2.4.2.17) Compound (39):

\[ \text{Reagents and Conditions: } (i) \text{ NIS, TMSOTf, CH}_2\text{Cl}_2, 0 \degree \text{C to rt, 16 h.} \]

The compound 39 was synthesized using D-glucose-derived 1,2-cyclopropanecarboxylate 14 (150 mg, 0.30 mmol), methyl 2,3-di-\(O\)-benzyl-\(\alpha\)-D-glucopyranoside 34 (126 mg, 0.33 mmol), NIS (75.9 mg, 0.33 mmol), TMSOTf (10.8 \(\mu\)L, 0.06 mmol) and 4 Å MS in dichloromethane (15 mL) by following the general procedure in (2.4.2.4). The reaction mixture was stirred for overnight at ambient temperature. The obtained crude product was purified by silica-gel column chromatography (EtOAc/hexane 3:7 to 2:3) to provide the 39 as a thick gum (70% yield).

\(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.12 – 7.24 (m, 23H), 6.97 – 6.98 (m, 2H), 4.93 (d, 1H, \(J = 2\) Hz), 4.88 (d, 1H, \(J = 11.2\) Hz), 4.82 (d, 1H, \(J = 10.4\) Hz), 4.39 – 4.66 (m, 9H), 4.82 (d, 1H, \(J = 10.4\) Hz), 4.39 – 4.66 (m, 9H), 4.25 (d, 1H, \(J = 8\) Hz), 4.00 (d, 1H, \(J = 8.8\) Hz), 3.59 – 3.72 (m, 7H), 3.47 (m, 1H), 3.41 (dd, 1H, \(J = 3.2\) Hz, \(J = 9.6\) Hz), 3.27 (s, 3H), 3.23 (s, 3H), 2.41 (bs, 1H), 1.89 (ddt, 1H, \(J = 2\) Hz, \(J = 2\) Hz, \(J = 8.4\) Hz). \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 167.6, 138.7, 138.1, 138.0, 137.9, 137.6, 128.5, 128.4, 128.3, 128.3, 127.9, 127.8, 127.7, 127.7, 127.6, 127.3, 103.2, 98.1, 81.4, 79.8, 79.5, 75.4, 75.0, 74.7, 74.7, 73.4, 73.1, 70.2, 69.9, 68.7, 68.5, 55.2, 53.3, 49.7, 28.9.

(2.4.2.18) Compound (40):

\[ \text{Reagents and Conditions: } (i) \text{ NaN}_3, \text{ DMF, rt, 24 h.} \]

The compound 40 was synthesized using disaccharidyl iodide 39 (100 mg, 0.10 mmol) and NaN\(_3\) (13.1 mg, 0.20 mmol) in DMF (10 mL) by following the same procedure in (2.4.2.6). The reaction mixture was stirred for 24 h at room temperature. Crude product was purified by silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to provide the disaccharide-based azide 40 as a thick gum (95% yield).
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1H NMR (CDCl₃, 400 MHz): δ 7.17–7.39 (m, 25H), 4.70 – 4.94 (m, 5H), 4.50 – 4.63 (m, 6H), 4.39 (d, 1H, J = 8.4 Hz), 4.26 (s, 1H), 3.89 (dd, 1H, J = 2.4 Hz, J = 10.4 Hz), 3.72 – 3.79 (m, 2H), 3.63 – 3.70 (m, 5H), 3.55 – 3.60 (m, 3H), 3.42 – 3.46 (m, 1H), 3.43 (dd, 1H, J = 3.6 Hz, J = 9.6 Hz), 3.39 (m, 1H), 3.34 (s, 3H), 2.98 (d, 1H, J = 3.6 Hz), 2.33 (t, 1H, J = 8.8 Hz).

13C NMR (CDCl₃, 100 MHz): δ 171.3, 139.2, 138.0, 138.0, 137.7, 128.5, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 127.8, 127.7, 127.7, 127.5, 127.5, 127.3, 99.6, 98.3, 81.3, 79.7, 79.0, 78.5, 75.2, 75.1, 75.0, 74.7, 73.9, 73.5, 70.2, 69.6, 68.7, 68.6, 58.4, 55.1, 52.8, 48.6.

(2.4.2.19) Compound (41):

Reagents and Conditions: (i) Ac₂O, Py, rt, 10 h

To the stirred solution of disaccharide-based azide 40 (60 mg, 0.06 mmol) in pyridine (2 mL) was added acetic anhydride (12.5 µL, 0.13 mmol) at 0 °C. The reaction mixture was stirred for 10 h at room temperature. After completion of reaction, the solution was concentrated under vacuo and purified by silica-gel column chromatography in ethyl acetate/hexane (1:9) to afford the acetylated 2-C-branched disaccharide derivative 41 as a colorless oil (98% yield).

1H NMR (CDCl₃, 400 MHz): δ 7.20 – 7.37 (m, 25H), 4.93 (d, 1H, J = 11.6 Hz), 4.87 (d, 1H, J = 11.6 Hz), 4.76 – 4.81 (m, 3H), 4.60 – 4.64 (m, 5H), 4.50 – 4.55 (m, 2H), 4.37 (d, 1H, J = 8.4 Hz), 4.30 (s, 1H), 3.90 (t, 1H, J = 9.2 Hz), 3.74 – 3.79 (m, 1H), 3.71 (dd, 1H, J = 3.6 Hz, J = 10.8 Hz), 3.62 – 3.68 (m, 6H), 3.59 (bs, 1H), 3.55 (dd, 1H, J = 3.2 Hz, J = 9.6 Hz), 3.48 (dd, 1H, J = 6.4 Hz, J = 11.2 Hz), 3.44 (s, 3H), 3.35 (bd, 1H, J = 7.6 Hz), 2.28 (dtd, 1H, J = 2 Hz, J = 2 Hz, J = 8.4 Hz), 1.84 (s, 3H).

13C NMR (CDCl₃, 100 MHz): δ 170.1, 169.9, 138.6, 138.1, 138.0, 137.9, 137.8, 128.5, 128.4, 128.3, 128.3, 128.1, 127.9, 127.7, 127.7, 127.6, 127.5, 99.9, 98.0, 79.7, 79.4, 79.0, 78.7, 75.0, 74.9, 74.6, 73.5, 73.4, 71.1, 69.1, 68.9, 68.6, 58.3, 55.5, 52.2, 48.8, 20.7.
(2.4.2.20) Compound (42):

\[
\begin{array}{c}
\text{MeOOC} \quad \text{N₃} \\
\text{OBn} \quad \text{OBn} \\
\text{OBn} \\
\text{OMe} \\
\text{HO} \\
\text{OBn} \\
\text{OBn} \\
\end{array}
\quad \xrightarrow{(i) \& (ii)} \\
\begin{array}{c}
\text{MeOOC} \quad \text{NH₂} \\
\text{OBn} \\
\text{OBn} \\
\text{OMe} \\
\text{HO} \\
\text{OBn} \\
\text{OBn} \\
\end{array}
\]

Reagents and Conditions: (i) PPh₃, THF, rt, 6 h, (ii) H₂O, reflux, 8 h.

The compound 42 was synthesized using the azide 40 (70 mg, 0.07 mmol) and PPh₃ (20 mg, 0.07 mmol) in THF (5 mL) by following the same procedure in (2.4.2.7). The resulted crude product was purified by silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to furnish the 2-C-branched GAA derivative 42 as a colorless oil (85% yield).

**¹H NMR (CDCl₃, 400 MHz):** δ 7.13 – 7.25 (m, 25H), 4.39 – 4.86 (m, 11H), 3.86 (dd, 1H, \(J = 1.6\) Hz, \(J = 10.4\) Hz), 3.61 – 3.73 (m, 4H), 3.58 – 3.60 (m, 5H), 3.36 – 3.39 (m, 4H), 3.27 (s, 3H), 2.21 (t, 1H, \(J = 9.2\) Hz).

**¹³C NMR (CDCl₃, 100 MHz):** δ 177.0, 138.3, 138.2, 138.1, 137.9, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.5, 127.3, 99.9, 98.4, 81.4, 80.0, 79.1, 78.5, 75.2, 75.1, 74.6, 74.5, 73.4, 73.1, 70.0, 69.6, 69.0, 68.2, 55.2, 52.3, 50.1, 49.8.

(2.4.2.21) Compound (43):

\[
\begin{array}{c}
\text{BnO} \\
\text{MeOOC} \quad \Phi \\
\text{OBn} \\
\text{OBn} \\
\text{OMe} \\
\text{HO} \\
\end{array}
\quad \xrightarrow{0} \\
\begin{array}{c}
\text{BnO} \\
\text{MeOOC} \quad \Phi \\
\text{OBn} \\
\text{OBn} \\
\text{OMe} \\
\text{HO} \\
\end{array}
\]

Reagents and Conditions: (i) NIS, TMSOTf, CH₂Cl₂, 0 °C to rt, 16 h

The compound 43 was synthesized using D-rhamnose-derived 1,2-cyclopropanecarboxylate 12 (150 mg, 0.39 mmol), methyl 4,6-O-benzylidene-α-D-glucopyranoside 32 (121 mg, 0.43 mmol), NIS (97 mg, 0.43 mmol), TMSOTf (14.1 μL, 0.078 mmol) and 4 Å MS in dichloromethane (15 mL) according to general procedure (2.4.2.4). The reaction mixture was stirred for overnight at ambient temperature. The obtained crude product was purified by silica-gel column chromatography (EtOAc/hexane 3:7 to 2:3) to provide the 43 as a thick gum (67% yield).
**Synthesis of 2-C-Branch Oligo-glyco-amino acids**

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### 1H NMR (CDCl₃, 400 MHz): δ 7.45 – 7.47 (m, 2H), 7.21 – 7.32 (m, 13H), 5.52 (s, 1H), 5.19 (d, 1H, J = 1.6 Hz), 4.91 (d, 1H, J = 10.8 Hz), 4.88 (d, 1H, J = 4.5 Hz), 4.78 (d, 1H, J = 10.8 Hz), 4.76 (d, 1H, J = 10.8 Hz), 4.63 (d, 1H, J = 10.8 Hz), 4.50 (d, 1H, J = 8.4 Hz), 4.48 (bs, 1H), 4.30 (dd, 1H, J = 4.8 Hz, J = 10 Hz), 4.86 – 4.94 (m, 3H), 4.77 (d, 1H, J = 10.8 Hz), 4.73 (d, 1H, J = 8.4 Hz), 4.57 – 4.62 (m, 2H), 4.33 (t, 1H, J = 8.8 Hz), 4.29 (dd, 1H, J = 4.4 Hz, J = 10.4 Hz), 3.89 (dt, 1H, J = 4.8 Hz, J = 9.6 Hz), 3.77 (t, 1H, J = 10.4 Hz), 3.69 (t, 2H, J = 9.6 Hz), 3.41 (s, 3H), 3.35 – 3.36 (m, 2H), 3.23 (s, 3H), 2.14 (s, 3H), 1.82 (dtd, 1H, J = 2 Hz, J = 2 Hz, J = 8.4 Hz), 1.34 (d, 3H, J = 4.8 Hz).

**13C NMR (CDCl₃, 100 MHz): δ 167.6, 137.9, 137.3, 136.7, 128.9, 128.3, 128.0, 128.0, 127.9, 127.8, 127.6, 127.5, 127.2, 126.1, 103.3, 101.6, 99.7, 84.9, 82.7, 81.4, 79.2, 75.1, 74.6, 71.8, 71.4, 68.9, 62.2, 55.2, 53.2, 50.8, 28.6, 17.5.**

**2.4.2.22 Compound (44):**

To the stirred solution of disaccharidyl iodide 43 (80 mg, 0.10 mmol) in pyridine (3 mL) was added acetic anhydride (19 μL, 0.20 mmol) at 0 °C. The reaction mixture was stirred for 10 h at room temperature. After completion of reaction, the solution was concentrated under vacuo and purified by silica-gel column chromatography by ethyl acetate in hexane (1:9) to afford the acetylated 2-C-branched disaccharide derivative 44 as a colorless gum (96% yield).

**1H NMR (CDCl₃, 400 MHz): δ 7.45 – 7.47 (m, 2H), 7.21 – 7.34 (m, 13H), 5.54 (s, 1H), 5.26 (d, 1H, J = 1.6 Hz), 4.86 – 4.94 (m, 3H), 4.77 (d, 1H, J = 10.8 Hz), 4.73 (d, 1H, J = 8.4 Hz), 4.57 – 4.62 (m, 2H), 4.33 (t, 1H, J = 8.8 Hz), 4.29 (dd, 1H, J = 4.4 Hz, J = 10.4 Hz), 3.89 (dt, 1H, J = 4.8 Hz, J = 9.6 Hz), 3.77 (t, 1H, J = 10.4 Hz), 3.69 (t, 2H, J = 9.6 Hz), 3.41 (s, 3H), 3.35 – 3.36 (m, 2H), 3.23 (s, 3H), 2.14 (s, 3H), 1.82 (dtd, 1H, J = 2 Hz, J = 2 Hz, J = 8.4 Hz), 1.34 (d, 3H, J = 4.8 Hz).

**13C NMR (CDCl₃, 100 MHz): δ 170.1, 167.8, 138.2, 137.6, 136.8, 129.1, 128.5, 128.2, 128.0, 127.9, 127.7, 127.6, 127.3, 126.3, 102.6, 102.1, 97.7, 85.7, 81.4, 81.0, 75.6, 75.2, 74.6, 72.2, 71.2, 68.9, 61.9, 55.3, 53.2, 51.4, 29.5, 21.0, 18.1.
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(2.4.2.23) Compound (45):

The compound 45 was synthesized using disaccharidyl iodide 43 (120 mg, 0.15 mmol) and NaN₃ (19.7 mg, 0.30 mmol) in DMF (10 mL) by following the same procedure in (2.4.2.6). The reaction mixture was stirred for 24 h at room temperature. Crude product was purified by silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to provide the disaccharide-based azide 45 as a semi solid (92% yield).

¹H NMR (CDCl₃, 400 MHz): δ 7.64 – 7.66 (m, 2H), 7.30 – 7.42 (m, 13H), 5.65 (s, 1H), 4.96 (d, 1H, J = 11.6 Hz), 4.87 (d, 1H, J = 10.8 Hz), 4.83 (d, 1H, J = 3.6 Hz), 4.74 (d, 1H, J = 8.4 Hz), 4.69 (d, 1H, J = 10.8 Hz), 4.62 (d, 1H, J = 11.2 Hz), 4.40 (d, 1H, J = 2 Hz), 4.29 (d, 1H, J = 5.6 Hz), 3.99 (t, 1H, J = 9.2 Hz), 3.79 – 3.81 (m, 2H), 3.74 (s, 3H), 3.48 – 3.62 (m, 4 H), 3.45 (s, 3H), 3.37 – 3.41 (m, 1H), 3.27 (t, 1H, J = 8.2 Hz), 2.33 (dtd, 1H, J = 2 Hz, J = 2 Hz, J = 8.8 Hz), 1.35 (d, 3H, J = 6 Hz).

¹³C NMR (CDCl₃, 100 MHz): δ 170.2, 137.7, 137.6, 137.3, 128.6, 128.5, 128.4, 128.0 (3), 127.9, 127.8, 125.9, 101.3, 99.5, 98.8, 85.2, 80.1, 78.3, 77.7, 75.1, 75.0, 71.1, 68.8, 62.1, 58.1, 55.1, 52.0, 48.7, 17.7.

(2.4.2.24) Compound (46):

The compound 46 was synthesized using the azide 45 (75 mg, 0.10 mmol) and PPh₃ (27.8 mg, 0.07 mmol) in THF (5 mL) by following the same procedure in (2.4.2.7). The resulted crude product was purified by silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to furnish the 2-C-branched GAA derivative 46 as a colorless oil (94% yield).
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**1H NMR (CDCl₃, 400 MHz):** δ 7.57 – 7.60 (m, 2H), 7.24 – 7.38 (m, 13H), 5.66 (s, 1H), 4.83 – 4.88 (m, 3H), 4.65 (d, 1H, J = 11.2 Hz), 4.58 (d, 1H, J = 11.2 Hz), 4.44 (d, 1H, J = 8.8 Hz), 4.27 (dd, 1H, J = 4 Hz, J = 9.6 Hz), 3.71 – 3.83 (m, 5H), 3.69 (s, 3H), 3.53 – 3.56 (m, 2H), 3.46 (s, 3H), 3.36 – 3.44 (m, 2H), 3.24 (t, 1H, J = 8.2 Hz), 2.31 (dt, 1H, J = 1.6 Hz, J = 2 Hz, J = 8.8 Hz), 1.30 (d, 3H, J = 6 Hz).

**13C NMR (CDCl₃, 100 MHz):** δ 176.8, 138.2, 138.0, 137.1, 129.3, 128.4, 128.2, 128.0, 127.9, 127.8, 127.7, 126.6, 102.5, 100.8, 99.7, 85.3, 80.6, 79.7, 79.0, 75.0, 74.9, 71.6, 71.2, 69.1, 62.5, 55.3, 51.8, 50.4, 50.0, 17.9.

(2.4.2.25) Compound (47):

![Chemical Structure](image)

**Reagents and Conditions:** (i) NIS, TMSOTf, CH₂Cl₂, 0 °C to rt, 16 h

The compound 47 was synthesized using D-galactose-derived 1,2-cyclopropanecarboxylate 13 (160 mg, 0.32 mmol), methyl 4,6-O-benzylidene-α-D-glucopyranoside 32 (101 mg, 0.36 mmol), NIS (81 mg, 0.36 mmol), TMSOTf (11.5 μL, 0.064 mmol) and 4 Å MS in dichloromethane (15 mL) by following the general procedure in (2.4.2.4). The reaction mixture was stirred for overnight at ambient temperature. The obtained crude product was purified by silica-gel column chromatography (EtOAc/hexane 3:7 to 2:3) to provide the 47 as a colorless oil (63% yield).

**1H NMR (CDCl₃, 400 MHz):** δ 7.35 – 7.37 (m, 2H), 7.16 – 7.22 (m, 18H), 5.50 (s, 1H), 5.40 (s, 1H), 4.72 (d, 1H, J = 10.4 Hz), 4.71 (d, 1H, J = 4.8 Hz), 4.49 – 4.54 (m, 2H), 4.43 (d, 1H, J = 6.4 Hz), 4.41 (d, 1H, J = 7.6 Hz), 4.28 (d, 1H, J = 12 Hz), 4.20 (d, 1H, J = 12 Hz), 4.18 (dd, 1H, J = 4.8 Hz, J = 10 Hz), 4.01 (t, 1H, J = 9.6 Hz), 3.86 (bs, 1H), 3.62 – 3.75 (m, 3H), 3.49 – 3.58 (m, 3H), 3.44 (t, 1H, J = 6 Hz), 3.36 (s, 3H), 3.28 – 3.30 (m, 1H), 3.26 (s, 3H), 3.01 (d, 1H, J = 6.8 Hz), 2.40 (dt, 1H, J = 2 Hz, J = 2 Hz, J = 8.4 Hz).

**13C NMR (CDCl₃, 100 MHz):** δ 167.8, 138.6, 137.7, 137.2, 137.0, 128.8, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.3, 126.1, 101.6, 101.3, 99.9, 81.7, 79.4, 78.8, 74.2, 73.4, 73.4, 72.1, 71.1, 70.8, 68.9, 68.3, 62.6, 55.3, 53.0, 45.3, 31.8.
(2.4.2.26) Compound (48):

Reagents and Conditions: (i) NaN₃, DMF, rt, 24 h

The compound 48 was synthesized using disaccharidyl iodide 47 (120 mg, 0.13 mmol) and NaN₃ (17.3 mg, 0.26 mmol) in DMF (10 mL) by following the same procedure in (2.4.2.6). The reaction mixture was stirred for 24 h at room temperature. Crude product was purified by silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to provide the disaccharide-based azide 48 as a thick gum (90% yield).

¹H NMR (CDCl₃, 400 MHz): δ 7.40 – 7.42 (m, 2H), 7.13 – 7.30 (m, 18H), 5.37 (s, 1H), 4.81 (d, 1H, J = 11.6 Hz), 4.73 (d, 1H, J = 3.6 Hz), 4.61 (d, 1H, J = 11.6 Hz), 4.57 (d, 1H, J = 1.6 Hz), 4.55 (d, 1H, J = 11.6 Hz), 4.52 (d, 1H, J = 8.4 Hz), 4.32 (d, 1H, J = 11.6 Hz), 4.29 (d, 1H, J = 11.6 Hz), 4.23 (d, 1H, J = 11.6 Hz), 3.93 (d, 1H, J = 2 Hz), 3.83 (t, 1H, J = 9.2 Hz), 3.77 (m, 1H), 3.70 (s, 3H), 3.63 (dd, 1H, J = 3.6 Hz, J = 10 Hz), 3.61 (dd, 1H, J = 3.2 Hz, J = 20 Hz), 3.49-3.53 (m, 1H), 3.36-3.40 (m, 3H), 3.35 (s, 3H), 3.29 (t, 1H, J = 9.2 Hz), 2.71 (dtd, 1H, J = 2 Hz, J = 2 Hz, J = 8.4 Hz).

¹³C NMR (CDCl₃, 100 MHz): δ 173.2, 138.7, 137.9, 137.5, 137.2, 128.6, 128.5, 128.4, 128.2, 128.1, 127.8, 127.8, 127.7, 127.7, 127.4, 127.3, 100.7, 100.6, 100.2, 80.1, 79.1, 77.2, 74.4, 73.5, 73.0, 71.3, 70.4, 68.9, 68.2, 62.9, 59.4, 55.2, 52.9, 44.3.

(2.4.2.27) Compound (49):

Reagents and Conditions: (i) PPh₃, THF, rt, 6 h, (ii) H₂O, reflux, 8 h.

The compound 49 was synthesized using the azide 48 (90 mg, 0.11 mmol) and PPh₃ (29 mg, 0.11 mmol) in THF (7 mL) by following the same procedure in (2.4.2.7). The resulted crude
product was purified by silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to furnish the 2-C-branched GAA derivative 49 as a colorless oil (92% yield).

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.46 (d, 2H, $J = 7.2$ Hz), 7.21 – 7.34 (m, 18H), 5.43 (s, 1H), 4.88 (d, 1H, $J = 11.6$ Hz), 4.74 (d, 1H, $J = 3.6$ Hz), 4.64 – 4.69 (m, 2H), 4.46 (d, 1H, $J = 11.6$ Hz), 4.36 (d, 1H, $J = 11.6$ Hz), 4.30 (d, 1H, $J = 11.6$ Hz), 4.20 (dd, 1H, $J = 4.4$ Hz, $J = 9.6$ Hz), 3.99 (bs, 1H), 3.95 (bs, 1H), 3.89 (t, 1H, $J = 9.2$ Hz), 3.64 – 3.71 (m, 6H), 3.53 (m, 2H), 3.41 (m, 1H), 3.39 (s, 3H), 3.31 (t, 1H, $J = 9.2$ Hz), 2.91 (bt, 1H, 9.6 Hz).

$^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 175.8, 138.6, 138.0, 137.5, 137.3, 128.7, 128.2, 128.1, 127.7, 127.7, 127.5, 101.2, 100.9, 100.3, 80.2, 78.8, 75.9, 74.5, 73.6, 71.4, 70.6, 70.4, 68.9, 68.5, 62.8, 55.2, 52.1, 49.6, 44.2.

(2.4.2.28) Compound (50):

\[
\begin{align*}
12 & \quad + \quad 38 & \rightarrow & \quad 50 \\
(1) & \quad \text{Reagents and Conditions: (i) NIS, TMSOTf, CH}_2\text{Cl}_2, 0 \ ^\circ \text{C to rt, 16 h}
\end{align*}
\]

The compound 50 was synthesized using L-rhamnose-derived 1,2-cyclopropanecarboxylate 12 (180 mg, 0.47 mmol), methyl 2,6-di-O-benzyl-β-D-galactopyranoside 38 (193 mg, 0.51 mmol), NIS (116 mg, 0.51 mmol), TMSOTf (17 μL, 0.094 mmol) and 4 Å MS in dichloromethane (20 mL) by following the general procedure in (2.4.2.4). The reaction mixture was stirred for overnight at ambient temperature. The obtained crude product was purified by silica-gel column chromatography (EtOAc/hexane 3:7 to 2:3) to provide the 50 as a light yellowish gum (70% yield).

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.24 – 7.41 (m, 20H), 5.23 (d, 1H, $J = 1.6$ Hz), 4.95 (d, 1H, $J = 10.8$ Hz), 4.59 – 4.82 (m, 7H), 4.55 (d, 1H, $J = 8.4$ Hz), 4.30 (d, 1H, $J = 8$ Hz), 4.19 (bs, 1H), 3.90 (dd, 1H, $J = 2.8$ Hz, $J = 9.6$ Hz), 3.81 (dd, 1H, $J = 6.4$ Hz, $J = 9.6$ Hz), 3.71 – 3.76 (m, 2H), 3.56 – 3.62 (m, 3H), 3.55 (s, 3H), 3.42 – 3.48 (m, 2H), 3.36 (s, 3H), 2.50 (d, 1H, $J = 4$ Hz), 2.03 (t, 1H, $J = 8.8$ Hz), 1.26 (d, 3H, $J = 4.8$ Hz).
13C NMR (CDCl3, 100 MHz): δ 168.0, 138.8, 138.2, 137.9, 137.7, 128.5, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 127.4, 104.6, 99.4, 85.9, 81.4, 78.6, 77.3, 75.3, 74.8, 74.7, 73.8, 72.8, 71.6, 69.1, 66.5, 57.1, 53.4, 50.4, 28.7, 18.0.

(2.4.2.29) Compound (51):

Reagents and Conditions: (i) NaN3, DMF, rt, 24 h

The compound 51 was synthesized using disaccharidyl iodide 50 (130 mg, 0.14 mmol) and NaN3 (19 mg, 0.29 mmol) in DMF (12 mL) by following the same procedure in (2.4.2.6). The reaction mixture was stirred for 24 h at room temperature. Crude product was purified by silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to provide the disaccharide-based azide 51 as a colorless gum (93% yield).

1H NMR (CDCl3, 400 MHz): δ 7.29 – 7.49 (m, 20H), 5.03 (d, 1H, J = 11.6 Hz), 4.93 (d, 1H, J = 11.2 Hz), 4.78 (d, 1H, J = 10.8 Hz), 4.76 (d, 1H, J = 10.8 Hz), 4.64 – 4.71 (m, 4H), 4.58 (d, 1H, J = 8 Hz), 4.39 (d, 1H, J = 1.2 Hz), 4.31 (d, 1H, J = 7.6 Hz), 4.07 (s, 1H), 3.87 – 3.91 (m, 2H), 3.70 (s, 3H), 3.58 – 3.65 (m, 5H), 3.49 (dd, 1H, J = 8 Hz, J = 9.6 Hz), 3.30 – 3.38 (m, 3H), 2.35 (t, 1H, J = 9.2 Hz), 1.36 (d, 3H, J = 5.6 Hz).

13C NMR (CDCl3, 100 MHz): δ 172.6, 138.9, 138.1, 137.6, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 127.6, 127.2, 104.1, 95.2, 85.8, 78.6, 78.1, 77.5, 75.1, 74.9, 74.6, 73.6, 73.0, 71.3, 69.1, 65.1, 58.6, 56.7, 52.9, 49.2, 17.8.

(2.4.2.30) Compound (52):

Reagents and Conditions: (i) Ac2O, Py, rt, 10 h

To the stirred solution of disaccharide-based azide 51 (85 mg, 0.10 mmol) in pyridine (4 mL) was added acetic anhydride (20 μL, 0.21 mmol) at 0 °C. The reaction mixture was stirred for 10 h at room temperature. After completion of reaction, the solution was concentrated under
vacuo and purified by silica-gel column chromatography in ethyl acetate in hexane (1:9 to 1:4) to afford the acetylated 2-C-branched disaccharide derivative 52 as a colorless oil (97% yield).

**1H NMR (CDCl₃, 400 MHz):** \( \delta 7.26 \text{ – 7.43 (m, 20H)}, \ 5.44 \text{ (d, 1H, } J = 3.2 \text{ Hz)}, \ 4.95 \text{ (d, 1H, } J = 11.2 \text{ Hz)}, \ 4.88 \text{ (d, 1H, } J = 11.2 \text{ Hz)}, \ 4.61 \text{ – 4.73 (m, 4H)}, \ 4.57 \text{ (d, 1H, } J = 8.4 \text{ Hz)}, \ 4.50 \text{ (bs, 2H)}, \ 4.32 \text{ (d, 1H, } J = 1.6 \text{ Hz)}, \ 4.29 \text{ (d, 1H, } J = 7.6 \text{ Hz)}, \ 4.17 \text{ (dd, 1H, } J = 3.6 \text{ Hz, } J = 10 \text{ Hz)}, \ 3.58 \text{ – 3.65 m, 5H)}, \ 3.54 \text{ (s, 3H)}, \ 3.36 \text{ – 3.52 (m, 5H)}, \ 3.24 \text{ (t, 1H, } J = 9.2 \text{ Hz)}, \ 2.31 \text{ (dtd, 1H, } J = 1.6 \text{ Hz, } J = 2 \text{ Hz, } J = 9.2 \text{ Hz)}, \ 2.24 \text{ (s, 3H)} \) 1.29 (d, 3H, } J = 6.4 \text{ Hz}).

**13C NMR (CDCl₃, 100 MHz):** \( \delta 170.8, \ 170.0, \ 138.8, \ 137.9, \ 137.8, \ 137.6, \ 128.6, \ 128.5, \ 128.4, \ 128.2, \ 128.1, \ 128.1, \ 128.0, \ 127.9, \ 127.8, \ 127.7, \ 127.6, \ 127.4, \ 104.4, \ 94.2, \ 85.9, \ 78.4, \ 75.2, \ 75.0, \ 74.6, \ 73.9, \ 73.8, \ 72.7, \ 72.7, \ 71.3, \ 68.8, \ 64.9, \ 58.0, \ 57.4, \ 52.2, \ 49.0, \ 20.8, \ 17.9 \)

(2.4.2.31) Compound (53):

![Diagram of compound 53]

**Reagents and Conditions:** (i) PPh₃, THF, rt, 6 h, (ii) H₂O, reflux, 8 h.

The compound 53 was synthesized using the azide 51 (75 mg, 0.09 mmol) and PPh₃ (24 mg, 0.11 mmol) in THF (5 mL) by following the same procedure in (2.4.2.7). The resulted crude product was purified by silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to furnish the 2-C-branched GAA derivative 53 as a colorless oil (97% yield).

**1H NMR (CDCl₃, 400 MHz):** \( \delta 7.26 \text{ – 7.46 (m, 20H)}, \ 4.96 \text{ (d, 1H, } J = 11.6 \text{ Hz)}, \ 4.92 \text{ (d, 1H, } J = 10.8 \text{ Hz)}, \ 4.69 \text{ – 4.78 (m, 4H)}, \ 4.65 \text{ (d, 1H, } J = 8.4 \text{ Hz)}, \ 4.50 \text{ (bs, 2H)}, \ 4.26 \text{ (d, 1H, } J = 7.6 \text{ Hz)}, \ 4.00 \text{ (d, 1H, } J = 2.8 \text{ Hz)}, \ 3.91 \text{ (dd, 1H, } J = 2.8 \text{ Hz, } J = 9.6 \text{ Hz)}, \ 3.82 \text{ (dd, 1H, } J = 6 \text{ Hz, } J = 9.6 \text{ Hz)}, \ 3.72 \text{ – 3.75 (m, 2H)}, \ 3.67 \text{ (dd, 1H, } J = 8.4 \text{ Hz, } J = 11.2 \text{ Hz)}, \ 3.61 \text{ – 3.64 (m, 1H)}, \ 3.60 \text{ (s, 3H)}, \ 3.55 \text{ (m, 1H)}, \ 3.53 \text{ (s, 3H)}, \ 3.43 \text{ (dd, 1H, } J = 7.6 \text{ Hz, } J = 1.6 \text{ Hz)}, \ 3.32 \text{ – 3.39 (m, 2H)}, \ 2.29 \text{ (dtd, 1H, } J = 1.6 \text{ Hz, } J = 2 \text{ Hz, } J = 8.4 \text{ Hz)}, \ 1.32 \text{ (d, 3H, } J = 5.6 \text{ Hz}).

**13C NMR (CDCl₃, 100 MHz):** \( \delta 177.6, \ 139.0, \ 138.1, \ 138.0, \ 128.6, \ 128.5, \ 128.5, \ 128.4, \ 128.1, \ 128.0, \ 127.9, \ 127.9, \ 127.8, \ 127.8, \ 127.6, \ 127.3, \ 104.1, \ 94.9, \ 86.1, \ 77.9, \ 77.8, \ 77.7, \ 75.1, \ 74.7, \ 74.4, \ 73.7, \ 73.1, \ 71.3, \ 69.3, \ 65.0, \ 56.8, \ 52.3, \ 50.3, \ 49.8, \ 18.0 \)
(2.4.2.32) Compound (54):

Reagents and Conditions: (i) NIS, TMSOTf, CH₂Cl₂, 0 °C to rt, 16 h

The compound 54 was synthesized using D-galactose-derived 1,2-cyclopropanecarboxylate 13 (160 mg, 0.32 mmol), methyl 2,6-di-O-benzyl-β-D-galactopyranoside 38 (134 mg, 0.36 mmol), NIS (80.9 mg, 0.51 mmol), TMSOTf (11.5 μL, 0.064 mmol) and 4 Å MS in dichloromethane (15 mL) according to general procedure (2.4.2.4). The reaction mixture was stirred for overnight at ambient temperature. The obtained crude product was purified by silica-gel column chromatography (EtOAc/hexane 3:7 to 2:3) to provide the 54 as a colorless oil (69% yield).

\(^1\)H NMR (CDCl₃, 400 MHz): δ 7.13 – 7.25 (m, 25H), 4.97 (s, 1H), 4.84 (d, 1H, \(J = 11.2\) Hz), 4.72 (d, 1H, \(J = 11.2\) Hz), 4.31 – 4.54 (m, 10H), 4.24 (m, 1H), 3.99 (bs, 1H), 3.81 (bs, 1H), 3.70 (d, 2H, \(J = 5.6\) Hz), 3.47 – 3.55 (m, 9H), 3.28 (s, 3H), 2.77 (bs, 1H), 2.31 (t, 1H, \(J = 8.4\) Hz).

\(^{13}\)C NMR (CDCl₃, 100 MHz): δ 167.5, 138.5, 138.3, 138.2, 137.7, 137.0, 128.4, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.6, 127.6, 127.3, 104.6, 104.0, 83.7, 81.2, 77.8, 75.0, 74.4, 73.7, 73.6, 73.4, 73.0, 72.3, 71.2, 69.4, 68.8, 67.6, 56.7, 53.0, 45.6, 30.6.

(2.4.2.33) Compound (55):

Reagents and Conditions: (i) NaN₃, DMF, rt, 24 h

The compound 55 was synthesized using disaccharidyl iodide 54 (150 mg, 0.15 mmol) and NaN₃ (19.7 mg, 0.30 mmol) in DMF (12 mL) by following the same procedure in (2.4.2.6). The reaction mixture was stirred for 24 h at room temperature. Crude product was purified by
silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to provide the disaccharide-based azide 55 as a colorless gum (92% yield).

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.21 – 7.33 (m, 25H), 4.82 – 4.92 (m, 4H), 4.65 (d, 1H, $J = 11.2$ Hz) 4.49 – 4.66 (m, 4H), 4.38 (bs, 2H), 4.32 (d, 1H, $J = 11.6$ Hz), 4.16 (dd, 1H, $J = 2.8$ Hz, $J = 7.6$ Hz), 3.90 (bs, 1H), 3.86 (bs, 1H), 3.65 – 3.75 (m, 6H), 3.48 – 3.57 (m, 7H), 3.38 – 3.41 (m, 2H), 2.74 (t, 1H, $J = 8.4$ Hz), 2.25 (bs, 1H).

$^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 171.0, 139.4, 138.3, 138.1, 137.8, 137.2, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.4, 127.1, 105.2, 99.6, 78.8, 76.7, 74.5, 73.8, 73.6, 73.4, 73.3, 73.2, 71.5, 70.5, 69.3, 69.1, 68.4, 58.6, 56.8, 52.5, 44.3.

(2.4.2.34) Compound (56):

The compound 56 was synthesized using the azide 55 (95 mg, 0.10 mmol) and PPh$_3$ (27 mg, 0.11 mmol) in THF (7 mL) by following the same procedure in (2.4.2.7). The resulted crude product was purified by silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to furnish the 2-C-branched GAA derivative 56 as a colorless oil (97% yield).

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.17 – 7.29 (m, 25H), 4.96 (d, 1H, $J = 11.2$ Hz), 4.82 (d, 1H, $J = 11.2$ Hz), 4.73 (d, 1H, $J = 11.2$ Hz), 4.61 (bs, 1H), 4.59 (d, 1H, $J = 4$ Hz), 4.45 – 4.52 (m, 3H), 4.32 – 4.35 (m, 3H), 4.16 (d, 1H, $J = 7.6$ Hz), 3.89 (d, 1H, $J = 2.4$ Hz), 3.81 (bs, 1H), 3.72 (bs, 1H), 3.66 (d, 2H, $J = 5.6$ Hz), 3.59 (s, 3H), 3.55 (d, 1H, $J = 2.8$ Hz), 3.45 – 3.52 (m, 4H), 3.41 (s, 3H), 3.38 (t, 1H, $J = 6$ Hz), 2.68 (t, 1H, $J = 9.2$ Hz).

$^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 176.8, 139.3, 138.5, 138.2, 137.9, 137.7, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.2, 105.1, 101.7, 79.8, 78.2, 78.1, 74.4, 73.7, 73.6, 73.5, 73.4, 73.3, 71.8, 71.0, 69.5, 69.1, 69.0, 56.6, 51.8, 50.5, 45.6.
(2.4.2.35) Compound (57):

The compound 57 was synthesized using D-glucose-derived 1,2-cyclopropanecarboxylate 14 (180 mg, 0.36 mmol), methyl 2,6-di-O-benzyl-β-D-galactopyranoside 38 (151 mg, 0.40 mmol), NIS (91 mg, 0.51 mmol), TMSOTf (13 μL, 0.072 mmol) and 4 Å MS in dichloromethane (15 mL) by following the general procedure in (2.4.2.4). The reaction mixture was stirred for overnight at ambient temperature. The obtained crude product was purified by silica-gel column chromatography (EtOAc/hexane 3:7 to 2:3) to provide the 57 as a glassy solid (65% yield).

\[ {\text{1H NMR (CDCl}_3, 400 MHz):} \delta 7.17 – 7.26 (m, 25H), 5.04 (d, 1H, J = 1.6 Hz), 4.99 (d, 1H, J = 11.6 Hz), 4.95 (d, 1H, J = 10.8 Hz), 4.80 (m, 2H, 4.51 – 4.68 (m, 7H), 4.38 (m, 1H), 4.16 (s, 1H), 3.80 – 3.83 (m, 4H), 3.68 – 3.74 (m, 5H), 3.61 (s, 3H), 3.54 (bs, 1H), 3.33 (s, 3H), 2.94 (s, 1H), 2.02 (bt, 1H, J = 8 Hz). \]

\[ {\text{13C NMR (CDCl}_3, 100 MHz):} \delta 167.2, 138.4, 138.0, 137.9, 137.7, 137.4, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 27.6, 127.5, 127.3, 104.6, 103.3, 83.6, 81.4, 79.7, 77.8, 74.9, 74.8, 74.7, 74.7, 73.5, 73.5, 73.3, 72.9, 69.3, 68.6, 67.5, 56.7, 53.1, 50.4, 29.5. \]

(2.4.2.36) Compound (58):

The compound 58 was synthesized using disaccharidyl iodide 57 (160 mg, 0.16 mmol) and NaN₃ (21 mg, 0.32 mmol) in DMF (12 mL) by following the same procedure in (2.4.2.6). The reaction mixture was stirred for 24 h at room temperature. Crude product was purified by silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to provide the disaccharide-based azide 58 as a thick gum (88% yield).
1H NMR (CDCl₃, 400 MHz): δ 7.12 – 7.32 (m, 25H), 4.79 – 4.88 (m, 4H), 4.71 (d, 1H, J = 11.2 Hz), 4.39 – 4.55 (m, 7H), 4.34 (d, 1H, J = 1.6 Hz), 4.14 (d, 1H, J = 8 Hz), 3.86 (bs, 1H), 3.74 (dd, 1H, J = 3.2 Hz, J = 9.6 Hz), 3.71 (s, 3H), 3.47 – 3.70 (m, 9H), 3.45 (s, 3H), 3.22 (bd, 1H, J = 9.6 Hz), 2.24 (t, 1H, J = 8.4 Hz), 2.22 (bs, 1H).

13C NMR (CDCl₃, 100 MHz): δ 170.7, 139.2, 138.1, 137.9, 137.8, 128.5, 128.4, 128.3, 128.2, 128.1, 127.0, 127.8, 127.7, 127.6, 127.6, 127.4, 127.2, 105.2, 99.3, 79.7, 78.8, 78.6, 76.9, 75.0, 74.7, 74.6, 73.9, 73.6, 73.3, 73.2, 69.3, 69.3, 68.3, 58.5, 56.9, 52.6, 48.9.

(2.4.2.37) Compound (59):

![Diagram of Compound 59]

Reagents and Conditions: (i) PPh₃, THF, rt, 6 h, (ii) H₂O, reflux, 8 h.

The compound 59 was synthesized using the azide 58 (90 mg, 0.09 mmol) and PPh₃ (26.1 mg, 0.11 mmol) in THF (7 mL) by following the same procedure in (2.4.2.7). The resulted crude product was purified by silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to furnish the 2-C-branched GAA derivative 59 as a colorless oil (88% yield).

1H NMR (CDCl₃, 400 MHz): δ 7.22 – 7.32 (m, 25H), 5.08 (d, 1H, J 11.2 Hz), 4.93 (d, 1H, J = 11.6 Hz), 4.84 (d, 1H, J = 10.8 Hz), 4.83 (d, 1H, J = 10.8 Hz), 4.76 (d, 1H, J = 8.4 Hz), 4.49 – 4.68 (m, 6H), 4.29 (d, 1H, J = 7.6 Hz), 4.05 (d, 1H, J = 2.4 Hz), 3.56 – 3.82 (m, 12H), 3.53 (s, 3H), 3.40 (bd, 1H, J = 9.6 Hz), 2.38 (t, 1H, J = 8.4 Hz).

13C NMR (CDCl₃, 100 MHz): δ 176.5, 1391, 138.2, 138.1, 137.9, 128.4, 128.3, 128.2, 127.8, 127.7, 127.6, 127.5, 127.3, 127.2, 105.1, 101.1, 79.7, 79.5, 79.2, 78.0, 74.8, 74.7, 74.5, 73.6, 73.5, 73.3, 69.4, 69.3, 68.7, 56.6, 51.9, 50.6, 50.1.

(2.4.2.38) Compound (60):

![Diagram of Compound 60]

Reagents and Conditions: (i) p-TsOH.H₂O, MeOH, rt, 4 h.

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To the stirred solution of benzylidene-protected disaccharide 43 (200 mg, 0.28 mmol) in methanol (10 mL), was added p-toluenesulfonic acid monohydrate (10 mg, 0.05 mmol) at 0 °C. The solution was stirred for 4 h at ambient temperature and concentrated under vacuo. The resulted crude product was purified by silica-gel column chromatography with ethyl acetate/hexane (1:1 to 4:1) to afford the disaccharide triol derivative 60 as a glassy solid (92% yield).

$^1$H NMR (CDCl$_3$, 400 MHz): δ 7.22 – 7.34 (m, 10H), 5.24 (d, 1H, $J = 2.4$ Hz), 4.95 (d, 1H, $J = 10.4$ Hz), 4.84 (d, 1H, $J = 3.6$ Hz), 4.81 (d, 1H, $J = 10.8$ Hz), 4.76 (d, 1H, $J = 10.8$ Hz), 4.64 (d, 1H, $J = 10.4$ Hz), 4.55 (d, 1H, $J = 8.4$ Hz), 4.25 (d, 1H, $J = 2$ Hz), 3.78 – 3.89 (m, 3H), 3.64 – 3.73 (m, 3H), 3.58 – 3.61 (m, 1H), 3.51 – 3.56 (m, 1H), 3.46 (s, 3H), 3.39 (s, 3H), 2.95 (bs, 1H), 2.08 (ddt, 1H, $J = 2$ Hz, $J = 2$ Hz, $J = 8.4$ Hz), 1.37 (d, 3H, $J = 6$ Hz).

$^{13}$C NMR (CDCl$_3$, 100 MHz): δ 168.4, 138.0, 137.5, 137.4, 128.6, 128.6, 128.3, 128.1, 127.9, 127.8, 127.7, 127.7, 127.6, 102.8, 99.4, 85.6, 85.2, 81.2, 75.4, 75.0, 71.9, 70.9, 70.7, 69.6, 62.5, 55.3, 53.6, 50.9, 29.4, 17.8.

(2.4.2.39) Compound (61):

Reagents and Conditions: (i) NIS, TMSOTf, CH$_2$Cl$_2$, 0 °C to rt, 16 h

The compound 61 was synthesized using L-rhamnose-derived 1,2-cyclopropanecarboxylate 12 (190 mg, 0.49 mmol), glycosyl acceptor 60 (273 mg, 0.39 mmol), NIS (121 mg, 0.53 mmol), TMSOTf (17.7 μL, 0.072 mmol) and 4 Å MS in dichloromethane (20 mL) by following the general procedure in (2.4.2.4). The reaction mixture was stirred for overnight at ambient temperature. The obtained crude product was purified by silica-gel column chromatography (EtOAc/hexane 2:3 to 1:1) to provide the 61 as yellowish a thick gum (62% yield).

$^1$H NMR (CDCl$_3$, 400 MHz): δ 7.13 – 7.22 (m, 20H), 5.29 (d, 1H, $J = 1.6$ Hz), 5.01 (d, 1H, $J = 2$ Hz), 4.87 (d, 1H, $J = 10.8$ Hz), 4.86 (d, 1H, $J = 10.8$ Hz), 4.78(d, 1H, $J = 3.6$ Hz), 4.54
- 4.75 (m, 6H), 4.45 (d, 1H, J = 8.4 Hz), 4.31 (d, 1H, J = 8 Hz), 4.15 (bs, 1H), 3.99 (dd, 1H, J = 2.8 Hz, J = 12 Hz), 3.91 (d, 1H, J = 12 Hz), 3.65 – 3.72 (m, 4H), 3.56 – 3.60 m, 2H), 3.38 – 3.48 (m, 3H), 3.35 (s, 3H), 3.33 (s, 3H), 3.27 (s, 3H), 3.22 (bs, 1H), 1.97 (dtd, 1H, J = 1.6 Hz, J = 2 Hz, J = 8.4 Hz), 1.89 (dtd, 1H, J = 1.6 Hz, J = 2 Hz, J = 8.4 Hz), 1.30 (d, 3H, J = 6 Hz), 1.26 (d, 3H, J = 6.4 Hz).

$^{13}$C NMR (CDCl$_3$, 100 MHz): δ 168.1, 167.6, 138.2, 138.1, 137.6, 137.5, 128.5, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 127.4, 127.3, 103.2, 103.1, 99.4, 85.4, 85.3, 85.2, 81.4, 81.2, 75.3, 75.2, 74.8, 74.6, 71.7, 71.6, 71.1, 70.6, 68.4, 68.2, 55.3, 53.5, 53.4, 50.9, 50.0, 28.8, 28.2, 17.8, 17.7.

(2.4.2.40) Compound (62):

Reagents and Conditions: (i) NaN$_3$, DMF, rt, 24 h

The compound 62 was synthesized using trisacharide-based diiodide 61 (170 mg, 0.14 mmol) and NaN$_3$ (36.4 mg, 0.56 mmol) in DMF (15 mL) by following the same procedure in (2.4.2.6). The reaction mixture was stirred for 24 h at room temperature. Crude product was purified by silica-gel column chromatography (EtOAc in hexane 2:3 to 1:1) to provide the trisasaccharide-based diazide 62 as a thick gum (85% yield).

$^1$H NMR (CDCl$_3$, 400 MHz): δ 7.29 – 7.39 (m, 20H), 4.98 (d, 1H, J = 12 Hz), 4.95 (d, 1H, J = 12 Hz), 4.85 – 4.89 (m, 2H), 4.75 (d, 1H, J = 3.6 Hz), 4.62 - 4.71 (m, 4H), 4.50 (d, 1H, J = 8.4 Hz), 4.43 (d, 1H, J = 8.4 Hz), 4.40 (d, 1H, J = 1.6 Hz), 4.30 (d, 1H, J = 2 Hz), 4.13 (s, 1H), 3.82 – 3.90 (m, 2H), 3.79 (s, 3H), 3.74 (s, 3H), 3.54 – 3.62 (m, 4H), 3.35 – 3.47 (m, 6H), 3.24 – 3.28 (m, 3H), 2.31 – 2.35 (m, 2H), 1.35 (d, 6H, J = 6 Hz).

$^{13}$C NMR (CDCl$_3$, 100 MHz): δ 172.5, 170.1, 137.9, 137.6, 137.5, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 100.4, 99.4, 99.0, 86.7, 85.6, 85.2, 78.6, 78.0, 75.3, 75.2, 75.1, 71.6, 71.3, 70.4, 70.0, 68.5, 68.4, 58.7, 58.4, 55.4, 53.1, 52.4, 49.1, 48.8, 17.8, 17.7.
(2.4.2.41) Compound (63):

![Chemical Structure of 62 and 63]

Reagents and Conditions: (i) Ac₂O, Py, rt, 10 h

To the stirred solution of trisaccharide-based azide 62 (120 mg, 0.11 mmol) in pyridine (8 mL) was added acetic anhydride (43 μL, 0.46 mmol) at 0 °C. The reaction mixture was stirred for 10 h at room temperature. After completion of reaction, the solution was concentrated under vacuo and purified by silica-gel column chromatography in ethyl acetate in hexane (1:4 to 3:7) to afford the acetylated trisaccharide derivative 63 as a colorless gum (93% yield).

^1H NMR (CDCl₃, 400 MHz): δ 7.17 – 7.30 (m, 20H), 4.87 (d, 1H, J = 11.6 Hz), 4.76 (d, 1H, J = 10.8 Hz), 4.67 (dd, 1H, J = 3.6 Hz, J = 10 Hz), 4.52 – 4.63 (m, 5H), 4.42 (d, 1H, J = 7.6 Hz), 4.24 (d, 1H, J = 8.8 Hz), 4.21 (s, 1H), 4.11 – 4.15 (m, 2H), 3.78 (t, 1H, J = 8.8 Hz), 3.67 (s, 3H), 3.66 (s, 3H), 3.60 (t, 1H, J = 8.8 Hz), 3.35 – 3.49 (m, 3H), 3.31 (s, 3H), 3.21 – 3.28 (m, 2H), 3.16 (t, 1H, J = 8.4 Hz), 3.09 (t, 1H, J = 8.8 Hz), 2.22 – 2.27 (m, 2H), 2.05 (s, 3H), 1.98 (s, 3H), 1.27 (d, 3H, J = 5.2 Hz), 1.24 (d, 3H, J = 5.2 Hz).

^13C NMR (CDCl₃, 100 MHz): δ 17.2, 169.9, 169.9, 169.4, 137.8, 137.7, 128.5, 128.5, 128.4, 128.3, 128.1, 127.9, 127.8, 127.8, 99.9, 98.1, 96.9, 85.9, 85.3, 78.5, 78.4, 75., 75.1, 75.0, 72.8, 71.7, 71.4, 71.1, 69.9, 68.9, 58.1, 58.0, 55.6, 52.4, 49.0, 48.7, 20.9, 20.8, 18.1, 17.7.

(2.4.2.42) Compound (64):

![Chemical Structure of 63 and 64]

Reagents and Conditions: (i) PPh₃, THF, rt, 6 h, (ii) H₂O, reflux, 8 h.
The compound 64 was synthesized using the trisaccharide-based diazide 63 (95 mg, 0.08 mmol) and PPh₃ (44.2 mg, 0.16 mmol) in THF (10 mL) by following the same procedure in (2.4.2.7). The resulted crude product was purified by silica-gel column chromatography (EtOAc in hexane 1:1 to 7:3) to furnish the trisaccharide-based bisamino acid adduct 64 as a colorless thick gum (80% yield).

**1H NMR (CDCl₃, 400 MHz):** δ 7.18 – 7.24 (m, 20H), 4.76 – 4.85 (m, 6H), 4.67 (d, 1H, J = 3.2 Hz), 4.58 – 4.61 (m, 3H), 4.54 (d, 1H, J = 11.6 Hz), 4.48 (d, 1H, J = 8 Hz), 4.31 (d, 1H, J = 8.4 Hz), 4.20 (t, 1H, J = 9.2 Hz), 3.71 (s, 3H), 3.66 – 3.68 (m, 1H), 3.56 – 3.63 (m, 5H), 3.52 (bs, 2H), 3.35 (d, 1H, J = 10.2 Hz), 3.28 (s, 3H), 3.19 -3.27 (m, 3H), 3.13 (t, 1H, J = 8.8 Hz), 2.19 (t, 1H, J = 9.2 Hz), 2.00 (bs, 4H), 1.95 (s, 3H), 1.42 (bs, 4H), 1.27 (d, 3H, J = 6 Hz), 1.21 (d, 3H, J = 5.6 Hz).

**13C NMR (CDCl₃, 100 MHz):** δ 176.1, 175.5, 169.9, 169.5, 138.2, 138.1, 138.1, 137.9, 128.4, 128.5, 128.3, 128.2, 127.9, 127.8, 127.7, 127.7, 100.8, 98.5, 97.1, 86.2, 85.5, 78.8, 78.7, 75.0, 74.9, 74.5, 72.1, 71.3, 71.1, 70.1, 68.6, 68.1, 54.4, 52.2, 52.0, 51.1, 50.1, 50.0, 49.8, 21.2, 20.9, 18.2, 17.8.

2.5 References


23. TMSOTf has been used as an activator in various reactions of donor-acceptor cyclopropanes.

24. Based on \(^1\)H and \(^{13}\)C NMR spectra.


28. The site of reactivity was found by acetylating the free hydroxyl group in disaccharide 24 and observing a downfield shift in the signal of the C-2 proton in compound 25.

2.6 NMR Spectra
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[Image of a chemical structure and an NMR spectrum]

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Synthesis of 2-C-Branched Oligo-glyco-amino acids...
Synthesis of 2-C-Branched Oligo-glyco-amino acids...
Synthesis of 2-C-Branched Oligo-glyco-amino acids....
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Synthesis of 2-C-Branched Oligo-glyco-amino acids....

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