Coupling Reactions of Anhydro-Aldose Tosylhydrazones with Boronic Acids

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Abstract: A catalyst-free coupling reaction between O-peracetylated, O-perbenzoylated, O-permethylated, and O-permethoxymethylated 2,6-anhydro-aldose tosylhydrazones (C-(β-D-glycopyranosyl)formaldehyde tosylhydrazones) and aromatic boronic acids is reported. The base-promoted reaction is operationally simple and exhibits a broad substrate scope. The main products in most of the transformations were open-chain 1-C-aryl-hept-1-enitol type compounds while the expected β-D-glycopyranosylmethyl arylamines (benzyl C-glycosides) were formed in subordinate yields only. A mechanistic rationale is provided to explain how a complex substrate may change the well-established course of the reaction.

Keywords: coupling; anhydro-aldose tosylhydrazones; C-glycosides; heptenitols

1. Introduction

N-Tosylhydrazones have extensively been used in organic synthesis for more than half a century. In the past decade N-tosylhydrazones were generally applied in a variety of carbon–carbon and carbon–heteroatom bond forming reactions [1–6]. These transition metal catalyzed or catalyst-free cross-coupling reactions proceed through the in situ generated diazo compounds, followed by the formation of metal–carbene or carbene intermediates, which lead to the corresponding coupled products. Carbohydrate tosylhydrazones are also known, but their application in coupling reactions is poorly investigated.

In our research group an easy, one-step method was worked out for the synthesis of anhydro-aldose tosylhydrazones from readily accessible glycosyl cyanides [7–9]. We began a systematic study aimed at the investigation of the applicability of anhydro-aldose-tosylhydrazones in coupling reactions. In this project C-O [10], C-S [11], and C-N [12] bonds were successfully formed under metal-free conditions, while C-C bonds [13,14] were obtained in Pd-catalyzed reactions (Scheme 1).

The metal-free reaction between the diazo precursor N-tosylhydrazones and alkyl, allyl, and arylboronic acids has been established in recent years as a powerful C(sp³)-C bond-forming transformation (Scheme 2a) that avoids the application of precious metal catalysts and highly air/moisture-sensitive or expensive coupling partners [15,16]. However, this reaction was primarily limited to benzylic, α-heterocyclic, and/or aldehyde-derived tosylhydrazones at the substrate level, with lower yields observed for substrates that differed from these [15,17–20]. Dai and coworkers expanded this reductive coupling to acylferrocene tosylhydrazones, producing highly substituted α-arylalkylferrocenes [21]. N-Tosylhydrazones derived from 2-, 3-, and 4-substituted cyclohexanones and 4-substituted cyclopentanone were also used in couplings with alkyl boronic acids [22]. The reductive coupling of N-tosylhydrazones under the standard reaction conditions was also examined with diarylborinic acids (Ar₂B(OH)) to give diarylmethanes with good yields [23]. Kirschning developed a flow protocol for the reductive coupling reaction of N-tosylhydrazones...
with aryl boronic acids. To increase the practical applicability of the reaction, a two-step continuous flow protocol, starting with carbonyl compounds and tosylhydrazide, was also developed [24]. Nakagawa and coworkers expanded the scope of the transformation to a set of challenging heterocycle-containing aldehyde tosylhydrazones, such as those of protected azetidine, imidazole, and azaindole derivatives. These couplings resulted in low to good yields of drug-like molecules, bicyclic products, with a methylene linker between the rings (Scheme 2b) [25]. This type of coupling of indole-3-carbaldehyde tosylhydrazone with boronic acids was used for the synthesis of biologically important 3-benzyl indole derivatives (Scheme 2b) [26]. Ley and coworkers used the procedure for the metal-free coupling of 4-, 5-, and 6-membered saturated heterocyclic p-methoxyphenyl (PMP) sulfonylhydrazones with (het)aryl boronic acids to form sp$^3$C(sp$^3$)-linked bicyclic building blocks, including oxetanes, piperidines, and azetidines, from their parent ketones (Scheme 2c) [27]. The reductive coupling was also applied for the synthesis of 9-arylfluorenes (Scheme 2d) [28]. Thus, a wide range of 9-arylfluorenes was prepared in a one-pot process from 9-fluorenones by treatment with N-tosylhydrazide, followed by the reductive coupling of (het)aryl and alkyl boronic acids in the presence of potassium carbonate. A similar protocol was applied for the synthesis of triarylmethanes from less reactive diaryl ketones (Scheme 2d) [29] and 1(or 2)-(1-phenylethyl)naphthalenes from acetyl naphthalene derivatives [30]. Wang and coworkers developed a three-component transition-metal-free reaction from α-halo-N-tosylhydrazones in the presence of N-alkylindoles and arylboronic acids to form a range of 3-substituted indoles [31]. A new type of cascade cyclization by reaction of alkenylboronic acids with 2-cyanoethyl or 3-cyanopropylcyclohexanone N-tosylhydrazones was developed by Valdés et al. [32,33]. A similar reaction between γ-azido-N-tosylhydrazones and boronic acids led to the formation of 2,2-disubstituted pyrrolidines in a domino process under microwave activation [34].

Scheme 1. Synthetic applications of anhydro-aldose tosylhydrazones in coupling reactions.

As the tosylhydrazone-boronic acid coupling can be of a great potential to avoid the utility of costly and poisonous metals and ligands, metal-free coupling reactions of boronic acids with anhydro-aldose tosylhydrazones were examined as a new type of substrate with higher complexity in comparison to the previous ones (Scheme 2e). This transformation offers a simple possibility for the formation of C-glycosylmethyl derivatives whose preparation is rather cumbersome in the literature [13,35–43]. Herein we disclose our experiences with this reaction using various sugar configurations, protecting groups and boronic acids.
Scheme 2. Selected examples of N-tosylhydrazone-boronic acid coupling (a–d) and the reaction studied in this work (e).

2. Results and Discussion

We started our study with the reaction between O-perbenzoylated C-(β-D-glucopyranosyl)formaldehyde tosylhydrazone 1a [7–9] and phenylboronic acid (Table 1). First, the literature conditions [15] were applied using 1.5 equivalents of boronic acid and 1.5 equivalents of K₂CO₃ as the base in dry dioxane at reflux temperature (entry 1). The transformation resulted in a complex mixture, containing heptenitols 3a and 4a and exo-glucal 5 [8,44,45] but we did not observe the formation of the expected C-glucoside 2a [13]. However, it can be assumed that the formation of the open chain compounds might occur by a base mediated ring-opening process, whose driving force could be the resonance stabilization of styrene 3a. Similar heptenitols were obtained by the Wittig reaction [46,47]. Migration of a benzoyl protecting group could result in 4a, and intramolecular carbene insertion into the C-2-H bond yielded exo-glucal 5 [8,44,45]. With other bases (Bu₄NF, LiO₂Bu, and K₃PO₄) the formation of the coupled product 2a could also not be observed (entries 2–4). Instead, we obtained variable amounts of the heptenitols 3a and 4a, and exo-glucal 5. Increasing the amount of K₃PO₄ raised the yield of heptenitol 3a to 43% (entry 5). The effects of solvents other than dioxane were also studied, but in each case, complex reaction mixtures were obtained (entries 6–8). On the other hand, performing the reaction in the presence of five equivalents of phenylboronic acid with three or four equivalents of K₃PO₄ gave the...
C-glucoside 2a in a very low yield beside 3a, while 4a and 5 were also isolated (entries 9 and 10). Raising the base excess gave exo-glucal 5 in moderate yield and heptenitols 3a and 4a in traces (entry 11). The best result was achieved with 20-fold excess of phenylboronic acid and 10-fold excess of K₃PO₄, to give heptenitol 3a in 70% yield (entry 12). Thus, instead of the expected C-glycosylmethylarene derivative 2a, an open chain compound, 3a, proved to be the main product of the transformation.

Table 1. Optimization of the coupling reaction of 1 with phenylboronic acid.

| Entry | PhB(OH)₂ (Equiv.) | Base (Equiv.) | Solvent | T (°C) | t (h) | 2a | 3a | 4a | 5 |
|-------|--------------------|---------------|---------|--------|------|----|----|----|---|
| 1     | a 1.5              | K₂CO₃ (1.5)   | 1,4-dioxane | 101    | 3    | -  | -  | 28 | - |
| 2     | a 1.5              | Bu₄NF (1.5)   | 1,4-dioxane | 101    | 3    | complex reaction mixture |
| 3     | a 1.5              | LiO/Bu (1.5)  | 1,4-dioxane | 101    | 3    | -  | + a | -  | 16 |
| 4     | a 1.5              | K₃PO₄ (1.5)   | 1,4-dioxane | 101    | 3    | -  | + a | -  | 38 |
| 5     | a 1.5              | K₃PO₄ (3)     | 1,4-dioxane | 101    | 3    | -  | 43 | -  | -  |
| 6     | a 1.5              | K₃PO₄ (3)     | fluorobenzene | 85    | 3.5  | complex reaction mixture |
| 7     | a 1.5              | K₃PO₄ (3)     | acetonitrile | 82     | 3    | complex reaction mixture |
| 8     | a 1.5              | K₃PO₄ (3)     | toluene    | 111    | 3.5  | complex reaction mixture |
| 9     | a 5                | K₃PO₄ (3)     | 1,4-dioxane | 101    | 3.5  | 2  | 36 b | 11 b | 2 b |
| 10    | a 5                | K₃PO₄ (4)     | 1,4-dioxane | 101    | 3    | 4  | 38 b | 12 b | -  |
| 11    | a 5                | K₃PO₄ (10)    | 1,4-dioxane | 101    | 3    | -  | + a | + a | 39 |
| 12    | a 20               | K₃PO₄ (10)    | 1,4-dioxane | 101    | 2.5  | -  | 70 | -  | -  |
| 13    | b 2                | -             | 1,4-dioxane | 101    | 2    | + a | -  | -  | -  |
| 14    | b 5                | -             | 1,4-dioxane | 101    | 2    | + a | 19 | -  | -  |
| 15    | b 10               | -             | 1,4-dioxane | 101    | 2    | 7 b | 17 b | 15 b | 15 b |

a Compounds were detected in the mixture. b Yields were calculated on the basis of the ¹H NMR spectra of the worked-up reaction mixture.

To avoid base mediated side reactions, such as the acyl migration, C-(β-D-glucopyranosyl)formaldehyde tosylhydrazone Li-salt 1b [10,12] was used for the couplings, where no added base is needed. Attempted reactions under UV irradiation (λ = 254 nm and 368 nm) carried out in a quartz tube proved to be totally ineffective, resulting in complex reaction mixtures. However, thermic conditions gave, generally, 3a as the main product, besides C-glucoside 2a and exo-glucal 5 (entries 13 and 14). Although the application of 10 equivalents of boronic acid significantly increased the yields (entry 15), the Li-salt...
reactions appeared less effective. Thus, tosylhydrazone 1a and 1.5 or 20-fold excess of a boronic acid and 3 or 10-fold excesses of K$_3$PO$_4$ were used in further transformations.

The coupling reaction of 1a was also examined with a variety of aryl boronic acids under the conditions selected above. These reactions resulted in varying yields of compound types 2–5, among which the heptenitols 3 and 4 were the main products (Table 2). Application of higher excess of boronic acids and K$_3$PO$_4$ improved the yields in couplings with 4-(dibenzofuranyl) and 4-methoxyphenyl boronic acids (compare entries 3–4 and 6–7), but in other cases, this had no significant effect on the reaction outcome (compare entries 1–2, 10–11 and 12–13). The coupling was found to be significantly affected by the substituents on the aromatic ring; boronic acids with electron-releasing (entries 1–7) and chloro (entries 8 and 9)-substituents gave better yields. However, with the strong electron-withdrawing nitro group (entries 10–13) exo-glucal 5 was the main product, the coupled compound 2h was observed in only one case. Isolation of the products in pure state often encountered difficulties. Due to very similar mobilities in silica gel column chromatography, C-glucosyl compounds 2 were polluted with the exo-glucal 5, and heptenitols 3 and 4 polluted each other, therefore the yields were generally calculated on the basis of the $^1$H NMR spectra (Supplementary Materials).

### Table 2. Reactions of tosylhydrazone 1a with aryl boronic acids.

| Entry | Reaction Conditions | Yield (%) |
|-------|---------------------|-----------|
|       | Ar                  | Boronic Acid (Equiv.) | K$_3$PO$_4$ (Equiv.) | t (h) | 2     | 3     | 4     | 5     |
| 1     | b 2-naphthyl        | 1.5        | 3        | 2     | 7      | 39    | 14    | 3     |
| 2     | 2-naphthyl          | 20         | 10       | 1.5   | 4      | 44    | 31    | -     |
| 3     | c 4-(dibenzofuranyl)| 1.5        | 3        | 2     | 3      | 16    | 4    | 18    |
| 4     | 4-(dibenzofuranyl)  | 20         | 10       | 2     | 19     | 9     | 47    | 15    |
| 5     | d 4-MeC$_6$H$_4$     | 1.5        | 3        | 2     | -      | 31    | 12    | -     |
| 6     | e 4-MeOC$_6$H$_4$    | 1.5        | 3        | 3     | -      | 34    | 14    | -     |
| 7     | 4-MeOC$_6$H$_4$      | 20         | 10       | 3     | -      | +     | 42    | -     |
| 8     | f 3-CIC$_6$H$_4$     | 1.5        | 3        | 1.5   | 5      | 34    | 18    | 11    |
| 9     | g 4-CIC$_6$H$_4$     | 1.5        | 3        | 2     | -      | 68    | -     | 4     |
| 10    | h 4-NO$_2$C$_6$H$_4$ | 1.5        | 3        | 2     | -      | -     | -     | 63    |
| 11    | 4-NO$_2$C$_6$H$_4$   | 20         | 10       | 2.5   | 10     | -     | -     | 12    |
| 12    | i 3-NO$_2$C$_6$H$_4$ | 1.5        | 3        | 2     | complex reaction mixture | 22 |
| 13    | 3-NO$_2$C$_6$H$_4$   | 20         | 10       | 2     | complex reaction mixture | 62 |

a Yields were calculated on the basis of the $^1$H NMR spectra of the worked-up reaction mixture. b Compounds were detected in the mixture.

The coupling of O-peracetylated C-(β-D-galactopyranosyl)formaldehyde tosylhydrazone (6, Table 3) with phenylboronic acid was also investigated. With 1.5 equivalents of phenylboronic acid and 3 equivalents of potassium carbonate, only traces of the known compound types 7, 8, and 10 [8,44,45] were detected in the complex product mixture (entry 1), but with a 20-fold excess of the boronic acid C-(galactosyl)phenylmethane 7 was formed in low yield and heptenitols 8 and 9 proved to be the main products (entry 2). A compound
with a free 6-OH (analogue of 3), though might be formed, could not be detected possibly due to a faster acetyl migration to give 8 and 9.

Table 3. Reactions of tosylhydrazone 6 with phenyl boronic acids.

| Entry | Reaction Conditions | Isolated Yield (%) |
|-------|---------------------|--------------------|
|       | PhB(OH)$_2$ (Equiv.) | Base (Equiv.) | t (h) | 7 | 8 | 9 | 10 |
| 1     | 1.5                 | K$_2$CO$_3$ (3)   | 3.5   | 3$^a$ | 6 | -  | 2$^a$ |
| 2     | 20                  | K$_3$PO$_4$ (10)  | 1.5   | 4   | 5 | 75 | -  |

$^a$ Yields were calculated on the basis of the $^1$H NMR spectra of the worked-up reaction mixture.

The NMR analysis provided evidence for the structure of all of the above derivatives and these are illustrated here by the examples of compounds 2, 3, and 4. Anhydro-heptitol 2a, synthesized in our group earlier [13], showed characteristic $^1$H NMR resonances for the C-1 methylene (δ 2.96 ppm (H-1a), 2.92 ppm (H-1b), with a great geminal coupling constant (12.3 Hz) between them) and the H-2 (‘anomeric’) protons (4.00 ppm). The characteristic $^{13}$C NMR resonances were δ 38.0 ppm (C-1) and 79.2 ppm (C-2). $^1$H and $^{13}$C NMR analysis of C-glycosyl derivatives 2b,c,f,h showed similar chemical shifts for H-1a (2.92–3.44 ppm), H-1b (2.90–3.29 ppm), H-2 (3.98–4.33 ppm), C-1 (32.1–38.1), and C-2 (77.9–79.2) with geminal coupling constants of H-1a-H-1b in the range of 14.3–15.0 Hz. These data indicated the similar structure of the C-glycosyl derivatives 2. Ring-opened heptenitols 3 and 4 showed quite different spectral data. Signals characteristic for C-1 and C-2 of compounds 2 in the above ranges were missing in the $^{13}$C NMR spectra of 3 and 4, instead resonances for –CH$_2$ type carbons in the ranges 130.8–136.9 ppm (for C-1) and 119.6–125.9 ppm (for C-2) appeared to prove the presence of a double bond in the molecules. The acyclic form was evidenced by the small vicinal coupling constants (in the range of 0.8–8.9 Hz). The great values (14.9–16.3 Hz) of coupling constant $^3$J$_{1,2}$ proved the $E$-configured double bond C-1=C-2 in these structures. The position of the free OH groups of heptenitols 3 and 4 were confirmed by observing cross peaks between OH and H-6 in heptenitols 3 and OH and H-5 in molecules 4 in their $^3$H--$^3$H COSY spectra.

To further prove the formation of heptenitols and acyl group migration, benzylation/acetylation of the corresponding compounds under standard conditions were carried out. Benzoylation [47] of the mixture of heptenitols 3 and 4 resulted in a single product 11 (Table 4) while acetylation [48] of heptenitol 9 gave O-peracetylated product 12 in good to excellent yields (Scheme 3).

Scheme 3. Acetylation of heptenitol 9.
Table 4. Benzoylation of heptenitols 3 and 4.

| Entry | Reaction Conditions | Yield of 11 (%) |
|-------|---------------------|-----------------|
| 1     | Ph                  | 90              |
| 2     | 4-(dibenzo[b]furan)  | 54              |

To get an insight into the effect of hydrolytically resistant ether type protecting groups on the outcome of the studied coupling reactions, O-permethylated (β-D-glucopyranosyl) formaldehyde tosylhydrazone 17 was synthesized. Methyl glucoside 13 was O-permethylated to get 14 [49] which was converted to the acetate derivative 15 [50] (Scheme 4). On reacting 15 with trimethylsilyl cyanide in the presence of boron trifluoride etherate, cyanide 16 [51] was obtained. The anomers were separated by column chromatography. Then, β-cyanide 16β was reduced in the presence of tosylhydrazide to give β-D-glucosyl tosylhydrazone 17 as a mixture of E and Z isomers.

Couplings with 17 gave cleaner product mixtures in better yields, and resulted in C-glucosides 18 (Table 5, entries 2, 4, and 8) or open-chain heptenitols 19 and 20 as the main products (entries 1, 5, 6, 7, 9, 10). Exo-glucal 21 [52] was always formed as a by-product. Compounds 18 and 21 proved inseparable, similar to open chain isomers 19 and 20.

The transformation was extended to the acetal protected galactose derivative 24, which was synthesized from the galactosyl cyanide 22 in two steps. Compound 22 was reacted with methoxymethyl chloride to obtain cyanide 23 [53], then a reduction step in the presence of tosylhydrazide gave a mixture of E and Z isomers of 24 (Scheme 5).

Scheme 4. Synthesis of O-permethylated (β-D-glucopyranosyl) formaldehyde tosylhydrazone 17.

Scheme 5. Synthesis of O-permethoxymethylated (β-D-galactopyranosyl) formaldehyde tosylhydrazone 24.
Table 5. Reactions of tosylhydrazone 17 with aryl boronic acids.

| Entry | Ar          | Boronic Acid (Equiv.) | K₃PO₄ (Equiv.) | t (h) | Yield (%) |
|-------|-------------|-----------------------|----------------|-------|-----------|
| 1     | a           | Ph                    | 1.5            | 3     | 17ᵃ       |
| 2     | b           | 4-(dibenzofuranyl)    | 1.5            | 3     | 17ᵃ       |
| 3     | c           | 4-CF₃C₆H₄             | 1.5            | 3     | 45        |
| 4     | d           | 4-FC₆H₄               | 1.5            | 3     | 14        |
| 5     | e           | 3-CIC₆H₄              | 1.5            | 3     | 2.5       |
| 6     | f           | 4-BrC₆H₄              | 1.5            | 3     | 1.5       |
| 7     | g           | 4-NO₂C₆H₄             | 1.5            | 3     | 15        |
| 8     | h           | 4-BrC₆H₄              | 1.5            | 3     | 1.5       |
| 9     | i           | 4-BrC₆H₄              | 1.5            | 3     | 15        |

ᵃ Yields calculated on the basis of the ¹H NMR spectra of the worked-up reaction mixture. b Compounds were detected in the mixture.

The coupling of 24 with phenylboronic acid resulted in E heptenitol 26 as the main product and an inseparable mixture of C-(galactopyranosyl)phenylmethane 25 and exo-galactal 28 [53]. The Z isomer 27 was also detected in the mixture (Scheme 6).

![Scheme 6](image)

For the structure elucidation of Me (18–20) and MOM (25–27), protected derivatives 1D-NMR (¹H, ¹³C) and 2D-NMR (¹H–¹H COSY, HSQC, and HMBC) spectra were recorded. The characteristic chemical shifts of C-1 (32.0–38.1 ppm vs. 132.3–134 ppm) and C-2 (79.0–80.9 ppm vs. 124.3–130.4 ppm) clearly revealed the structures of the anhydro-heptitols 18, 25, and heptenitols 19, 20, 26, 27, respectively.

In contrast to the transformations of acylated derivatives 2 and 7, those of tosylhydrazones 17 and 24 possessing ether-type protecting groups (Me, MOM) resulted in no migration of the protecting groups as expected, but the E and Z isomers of the acyclic derivatives were isolated. The configuration of the double bonds was identified by the vicinal coupling constants being 16.0 Hz for the E and 11.4–12.1 Hz for the Z isomers. The measured vicinal coupling constants showed high variety for heptenitols 19 and 20, in contrast to the cyclic ⁴C₂₁ conformers 18, where these values were 8.7 and 9.8 Hz for the trans diaxial protons. The position of the free OH groups of heptenitols 19, 20, 26, and 27 were confirmed by observing cross peaks between OH and H-6 in their ¹H–¹H COSY spectra.
Examination of possible ring opening of some anhydro-heptitols.

Table 6: Examination of possible ring opening of some anhydro-heptitols.

| Entry | PG | Ar | Boronic Acid (Equiv.) | K3PO4 (Equiv.) | t (h) | Experience       |
|-------|----|----|-----------------------|----------------|------|------------------|
| 1     | 2a | Bz | Ph                    | -              | 10   | 22               |
| 2     | 18g | Me | 4-NO2C6H4              | -              | 3    | 21               |
| 3     | 18g | Me | 4-NO2C6H4              | 1.5            | -    | 21               |
| 4     | 18c | Me | 4-CF3C6H4              | 1.5            | 3    | 21               |

Table 7: Examination of possible ring closing of heptenitols.

| Entry | PG | Ar | Boronic Acid (Equiv.) | K3PO4 (Equiv.) | t (h) | Experience       |
|-------|----|----|-----------------------|----------------|------|------------------|
| 1     | 19c, 20c | Bz | 4-CF3C6H4              | 1.5            | 3    | 21               |
| 2     | 19d, 20d | Bz | 4-FC6H4               | -              | 3    | 21               |
| 3     | 19e, 20e | Bz | 4-ClC6H4              | 1.5            | -    | 21               |

To obtain more information about the formation of the open-chain heptenitols, first we checked the possibility of the ring opening of the anhydro-heptitols under the reaction conditions. Thus, 2a was reacted with K3PO4 but partial deprotection of 2a was observed only, without the formation of 3a (Table 6, entry 1). The methyl protected derivatives 18c or 18g reacted neither in the presence of K3PO4, nor of a boronic acid or both (entries 2–4).

Next, formation of C-(glycosyl)arylmethane derivatives 18c,d,e was examined from the corresponding heptenitols 19c,d,e and 20c,d,e. Attempted reactions in the presence of base and/or boronic acid resulted in no conversion (Table 7).

Based on these observations, it can be concluded that the cyclic C-glycosylmethyl derivatives and the open-chain heptenitols are not interconvertible under the applied conditions, they must be formed from the same intermediate during the reaction.

To explain these experiences, the following mechanistic possibilities can be considered (Scheme 7). Loss of a sulfinate ion from tosylhydrazones I upon deprotonation or from Li-salt V may lead to the diazo intermediate VI which can give rise to carbene VII by eliminating a nitrogen molecule. The zwitterionic intermediate VIII, which arises from carbene VII (path a) or boronate complex X, formed from the diazo compound VI (path b), may lead to intermediate IX. Then, protodeboronation of IX under basic conditions can give anhydro-heptitol type products III (path c). Nevertheless, in intermediate IX, the ring
oxygen, as a Lewis base, can attack the electron deficient boron atom to form the open chain heptenitol borate XI (path e) which, upon hydrolysis, can lead to the isolated heptenitols IV. The driving force of this rearrangement may be the conjugation of the double bond with the aromatic system, leading to an energetically more stable species. The standard by-product exo-glycal II can be formed by an intramolecular insertion reaction of carbene VII (path d).

Scheme 7. Mechanistic possibilities for the coupling reactions.

3. Conclusions

This study on the metal-free coupling reactions of C-(β-D-glycopyranosyl)formaldehyde (2,6-anhydro-aldose) tosylhydrazones with aromatic boronic acids revealed that the main reaction pathway was the formation of ring-opened hept-1-enitol derivatives, while the expected C-glycopyranosyl compounds (benzyl C-glycosides) were formed only in low to moderate yields. The corresponding exo-glycals always appeared as unavoidable by-products. O-Acyl protecting groups on the carbohydrate moieties underwent migrations which further increased the number of products in the otherwise rather complex reaction mixtures. Tosylhydrazones with ether type
derivatives and the open-chain heptenitols are not interconvertible under the applied conditions, they must be formed from the same intermediate during the reaction.

4. Experimental

4.1. General Methods

Optical rotations were determined with a Perkin–Elmer 241 polarimeter or Jasco P-2000 (Easton, MD, USA) at room temperature. NMR spectra were recorded with a Bruker AM Avance DRX 360 MHz (360/90 MHz for 1H/13C) or Bruker AM Avance I 400 MHz (400/100 MHz for 1H/13C) or Bruker AM Avance II 500 MHz (500/125 MHz for 1H/13C) spectrometers. Chemical shifts are referenced to TMS as the internal reference (1H), or to the residual solvent signals (13C). The assignments of the 1H and 13C NMR signals of compounds 2–4, 7–9, 11, 12, 18–20, and 25–27 were performed by their COSY (2a, 3a,c, 4a,e, 7, 8, 9, 11a,b, 12, 18b,f,i, 19a,c,h,i, 20a,d,i, 25, 26, 27), HSQC (2a, 3a,c, 4a,e, 7, 8, 9, 11a,b, 12, 18b,f,i, 19a,c,h,i, 20a,d,i, 25, 26, 27), or HMBC (3a,c, 4a,e, 7, 8, 9, 11a,b, 12, 18b,e,f,i, 19a,c,h,i, 20a,d,i, 25, 26, 27) spectra. Mass spectra were recorded with maXis II UHR ESI-
reaction pathway. We think that this study also highlights the importance of transformation.

4.1. General Methods

A boronic acid (1.5 or 20 mmol, specified with the particular reactions) and K$_3$PO$_4$ (3 or 10 mmol, specified with the particular reactions) were suspended in dry 1,4-dioxane (15 mL). The suspension was stirred and heated to reflux, and then a solution of a tosylhydrazone (17 or 24, 1 mmol) in dry 1,4-dioxane (15 mL) was added dropwise over ~20 min. When TLC (1:2 EtOAc–hexane for 1 and 17, 1:1 EtOAc–hexane for 24) indicated complete consumption of the starting compound (20 min–4 h), the mixture was cooled down and the insoluble material was filtered off and washed thoroughly with dry 1,4-dioxane (3 × 20 mL). The solvent was removed under reduced pressure, and the residue was purified by column chromatography, with eluents indicated for the particular compounds to give anhydro heptitols and hept-1-enitols.

4.2. General Procedure 1: Conditions for the Reaction of Anhydro-Aldehyde Tosylhydrazones with Boronic Acids

A boronic acid (1.5 or 20 mmol, specified with the particular reactions) and K$_3$PO$_4$ (3 or 10 mmol, specified with the particular reactions) were suspended in dry 1,4-dioxane (15 mL). The suspension was stirred and heated to reflux, and then a solution of a tosylhydrazone (1, 17 or 24, 1 mmol) in dry 1,4-dioxane (15 mL) was added dropwise over ~20 min. When TLC (1:2 EtOAc–hexane for 1 and 17, 1:1 EtOAc–hexane for 24) indicated complete consumption of the starting compound (20 min–4 h), the mixture was cooled down and the insoluble material was filtered off and washed thoroughly with dry 1,4-dioxane (3 × 20 mL). The solvent was removed under reduced pressure, and the residue was purified by column chromatography, with eluents indicated for the particular compounds to give anhydro heptitols and hept-1-enitols.

4.3. Characterization of Anhydro-Heptitols 2

4.3.1. 2,6-Anhydro-3,4,5,7-Tetra-O-Benzoyl-1-Deoxy-1-Phenyl-d-glycero-d-gulo-Heptitol (2a)

Isolated from a reaction of tosylhydrazone 1a (0.10 g, 0.13 mmol), phenylboronic acid (1.5 equiv., 0.02 g, 0.19 mmol), and K$_3$PO$_4$ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:2 EtOAc–hexane) to yield 3 mg (4%) of 2a as a white amorphous product. Optical rotation, NMR and MS spectra are identical with those reported [13].

![Structure of 2a](image)

4.3.2. 2,6-Anhydro-3,4,5,7-Tetra-O-Benzoyl-1-Deoxy-1-(Naphth-2-yl)-d-glycero-d-gulo-Heptitol (2b)

Isolated from a reaction of tosylhydrazone 1a (0.10 g, 0.13 mmol), naphthalen-2-ylboronic acid (20 equiv., 0.44 g, 2.57 mmol), and K$_3$PO$_4$ (10 equiv., 0.27 g, 1.29 mmol) according to General procedure I by column chromatography (1:4 EtOAc–hexane) to yield 4 mg (4%) of 2b as a pale brown amorphous solid. R$_f$: 0.42 (1:2 EtOAc–hexane); [α]$_D^+ + 6$ (c 0.16, CH$_2$Cl$_2$). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.99–7.19 (27H, m, aromatics), 5.90 (1H, pseudo t, $J_{4,5}$ 9.6 Hz, H-4), 5.62 (1H, pseudo t, $J_{5,6}$ 9.7 Hz, H-5), 5.52 (1H, pseudo t, $J_{3,4}$ 9.6 Hz, H-3), 4.57 (1H, dd, $J_{7a,7b}$ 12.0 Hz, H-7$_a$), 4.41 (1H, dd, H-7$_b$), 4.09 (1H, ddd, $J_{1a,2}$ 5.1, $J_{1b,2}$ 6.6, $J_{2,3}$ 9.8 Hz, H-2), 4.04 (1H, ddd, $J_{5,6,7a}$ 2.7, $J_{6,7b}$ 6.3 Hz, H-6), 3.12 (1H, ddd, $J_{1a,1b}$ 14.8 Hz, H-1$_a$), 3.08 (1H, dd, H-1$_b$). $^{13}$C NMR (90 MHz, CDCl$_3$) δ 166.3, 166.1, 165.6, 165.5 (4 × CO), 136.6–124.7 (aromatics), 79.2 (C-2), 76.3 (C-6), 74.7 (C-4), 72.6 (C-3), 70.1 (C-5), 63.6 (C-7), 38.3 (C-1). HR-ESI-MS positive mode (m/z): calc. for [M + Na]$^+ = 743.2252$, found: [M + Na]$^+ = 743.2253$; C$_{48}$H$_{36}$O$_9$ (720.24).
4.3.3. 2,6-Anhydro-3,4,5,7-Tetra-O-Benzoyl-1-(4-Dibenzo[b,d]furanyl)-1-Deoxy-D-glycero-D-gulo-Heptitol (2c)

Isolated from a reaction of tosylhydrazone 1a (0.10 g, 0.13 mmol), dibenzo[b,d]furanyl-4-yboronic acid (20 equiv., 0.55 g, 2.57 mmol), and K$_3$PO$_4$ (10 equiv., 0.27 g, 1.29 mmol) according to General procedure I by column chromatography (1:3 EtOAc–hexane) to yield 30 mg pale brown amorphous solid containing 2c and 5 in 1:1 ratio. R$_f$: 0.50 (1:2 EtOAc–hexane). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.21–6.93 (27H, m, aromatics), 5.91 (1H, pseudo t, J$_{4,5}$ 9.5 Hz, H-4), 5.64 (1H, pseudo t, J$_{5,6}$ 9.8 Hz, H-5), 5.52 (1H, pseudo t, J$_{3,4}$ 9.8 Hz, H-3), 4.56 (1H, dd, J$_{7a,7b}$ 12.0 Hz, H-7a), 4.42 (1H, dd, H-7b), 4.33 (1H, ddd, J$_{1a,2}$ 3.2, J$_{1b,2}$ 8.0, J$_{2,3}$ 9.8 Hz, H-2), 4.07 (1H, ddd, $\delta$$_{6,7a}$ 2.9, $\delta$$_{6,7b}$ 5.9 Hz, H-6), 3.44 (1H, dd, J$_{1a,1b}$ 14.6 Hz, H-1a), 3.29 (1H, dd, H-1b). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 166.3, 166.1, 165.5 (4 $\times$ CO), 135.6–110.4 (aromatics), 77.9 (C-2), 76.2 (C-6), 74.8 (C-4), 72.5 (C-3), 70.1 (C-5), 63.5 (C-7), 32.1 (C-1). HR-ESI-MS positive mode (m/z): calc. for [M + H]$^+$ = 761.2381, found: [M + H]$^+$ = 761.2379; C$_{47}$H$_{50}$O$_{10}$ (760.23).

4.3.4. 2,6-Anhydro-3,4,5,7-Tetra-O-Benzoyl-1-(3-Chlorophenyl)-1-Deoxy-D-glycero-D-gulo-Heptitol (2f)

Isolated from a reaction of tosylhydrazone 1a (0.10 g, 0.13 mmol), 3-chlorophenylboronic acid (1.5 equiv., 0.03 g, 0.19 mmol), and K$_3$PO$_4$ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:4 EtOAc–hexane) to yield 3 mg white amorphous solid containing 2f and 5 in 1:2 ratio. R$_f$: 0.48 (1:2 EtOAc–hexane). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.13–7.76 (12H, m, aromatics), 7.63–6.94 (12H, m, aromatics), 5.89 (1H, pseudo t, J$_{4,5}$ 9.7 Hz, H-4), 5.60 (1H, pseudo t, J$_{5,6}$ 9.7 Hz, H-5), 5.45 (1H, pseudo t, J$_{3,4}$ 9.5 Hz, H-3), 4.57 (1H, dd, J$_{7a,7b}$ 12.1 Hz, H-7a), 4.42 (1H, dd, H-7b), 4.05 (1H, ddd, J$_{6,7a}$ 2.8, J$_{6,7b}$ 6.2 Hz, H-6), 3.98 (1H, ddd, J$_{1a,1b}$ 5.3, J$_{1b,2}$ 6.6, J$_{2,3}$ 9.7 Hz, H-2), 2.92 (1H, dd, J$_{1a,1b}$ 15.0 Hz, H-1a), 2.90 (1H, dd, H-1b). $^{13}$C NMR (90 MHz, CDCl$_3$) $\delta$ 166.3, 166.1, 165.7, 165.6 (4 $\times$ CO), 156.3–125.7 (aromatics), 78.8 (C-2), 76.4 (C-4), 74.6 (C-6), 72.6 (C-3), 70.1 (C-5), 63.5 (C-7), 37.4 (C-1). HR-ESI-MS positive mode (m/z): calc. for [M + Na]$^+$ = 727.1705, found: [M + Na]$^+$ = 727.1708; C$_{41}$H$_{34}$O$_{9}$ (670.22).

4.3.5. 2,6-Anhydro-3,4,5,7-Tetra-O-Benzoyl-1-Deoxy-1-(4-Nitrophenyl)-D-glycero-D-gulo-Heptitol (2h)

Isolated from a reaction of tosylhydrazone 1a (0.30 g, 0.39 mmol), 4-nitrophenylboronic acid (20 equiv., 1.30 g, 7.72 mmol), and K$_3$PO$_4$ (10 equiv., 0.82 g, 3.86 mmol) according to General procedure I by column chromatography (1:3 EtOAc–hexane) to yield 32 mg pale brown amorphous solid containing 2h and 5 in 4:1 ratio. R$_f$: 0.44 (1:2 EtOAc–hexane). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.32–7.72 (8H, m, aromatics), 7.69–7.16 (16H, m, aromatics), 5.90 (1H, pseudo t, J$_{4,5}$ 9.5 Hz, H-4), 5.58 (1H, pseudo t, J$_{5,6}$ 9.8 Hz, H-5), 5.45 (1H, pseudo t, J$_{3,4}$ 9.7 Hz, H-3), 4.53 (1H, dd, J$_{7a,7b}$ 12.2 Hz, H-7a), 4.48 (1H, dd, H-7b), 4.05 (1H, ddd, J$_{6,7a}$ 3.2, J$_{6,7b}$ 6.6 Hz, H-6), 3.99 (1H, ddd, J$_{1a,1b}$ 5.1, J$_{1b,2}$ 7.0, J$_{2,3}$ 9.7 Hz, H-2), 3.03 (1H, dd, J$_{1a,1b}$ 14.3 Hz, H-1a), 3.02 (1H, dd, H-1b). $^{13}$C NMR (90 MHz, CDCl$_3$) $\delta$ 166.4, 166.2, 165.7, 165.6 (4 $\times$ CO), 161.7–115.1 (aromatics), 78.3 (C-2), 76.4 (C-6), 74.5 (C-4), 72.5 (C-3), 70.0 (C-5), 63.3 (C-7), 37.8 (C-1). HR-ESI-MS positive mode (m/z): calc. for [M + Na]$^+$ = 738.1946, found: [M + Na]$^+$ = 738.1950; C$_{41}$H$_{33}$N$_{10}$O$_{11}$ (715.21).

![Structure of 2c](image-url)

![Structure of 2f](image-url)

![Structure of 2h](image-url)
4.4. Characterization of Hept-1-Enitol 3 and 4

4.4.1. (E)-3,4,5,7-Tetra-O-Benzoyl-1,2-Dideoxy-1-Phenyl-D-gluc-Hept-1-Enitol (3a)

Prepared from tosylhydrazone 1a (0.80 g, 1.03 mmol), phenylboronic acid (20 equiv., 2.51 g, 20.60 mmol), and K3PO4 (10 equiv., 2.19 g, 10.30 mmol) according to General procedure I by column chromatography (1:2 EtOAc–hexane) to yield 16 mg (16%) of 3a as a white amorphous solid. Rf: 0.36 (1:2 EtOAc–hexane); [α]D + 21 (c 0.20, CH2Cl2).

1H NMR (400 MHz, CDCl3) δ 8.18–7.82 (8H, m, aromatics), 7.64–7.15 (17H, m, aromatics), 6.78 (1H, d, J1,2 15.9 Hz, H-1), 6.32 (1H, dd, J2,3 6.9 Hz, H-2), 6.14–6.02 (2H, m, H-3, H-4), 5.76 (1H, dd, J4,5 0.8, J5,6 8.9 Hz, H-5), 4.53 (1H, dd, J6,7a 2.6, J7a,7b 11.9 Hz, H-7a), 4.34 (1H, dd, J6,7b 5.7 Hz, H-7b), 4.21–4.11 (1H, m, H-6), 3.58 (1H, d, J6,OH 4.3 Hz, OH). 13C NMR (100 MHz, CDCl3) δ 167.3, 166.7, 165.6, 165.4 (4 × CO), 136.7 (C-1), 136.3–125.9 (aromatics), 122.1 (C-2), 73.9 (C-3), 73.3 (C-4), 71.3 (C-5), 68.6 (C-6), 65.5 (C-7). HR-ESI-MS positive mode (m/z): calc. for [M + Na]+ = 693.2095, found: [M + Na]+ = 693.2096; C41H34O9 (670.22).

4.4.2. (E)-3,4,6,7-Tetra-O-Benzoyl-1,2-Dideoxy-1-Phenyl-D-gluc-Hept-1-Enitol (4a)

Isolated from a reaction of tosylhydrazone 1a (0.30 g, 0.39 mmol), phenylboronic acid (20 equiv., 0.94 g, 7.72 mmol), and K3PO4 (10 equiv., 0.80 g, 3.86 mmol) in 1.5:1 ratio. Rf: 0.25 (1:2 EtOAc–hexane).

1H NMR (400 MHz, CDCl3) δ 8.22–7.77 (8H, m, aromatics), 7.63–7.06 (17H, m, aromatics), 6.99 (1H, d, J1,2 15.6 Hz, H-1), 6.31 (1H, dd, J2,3 8.0 Hz, H-2), 6.23 (1H, pseudo t, J3,4 8.6 Hz, H-3), 5.82 (1H, dd, J4,5 1.3 Hz, H-4), 5.44 (1H, ddd, J6,7a 3.5, J6,7b 4.4, J5,6 8.0 Hz, H-6), 4.81 (1H, dd, J7a,7b 12.4 Hz, H-7a), 4.74 (1H, dd, H-7b), 4.39 (1H, pseudo t, H-5), 3.25 (1H, d, J5,OH 8.4 Hz, OH). 13C NMR (100 MHz, CDCl3) δ 167.3, 166.7, 165.7, 165.4 (4 × CO), 136.9 (C-1), 136.3–124.1 (aromatics), 122.7 (C-2), 74.6 (C-3), 74.2 (C-4), 71.7 (C-5), 68.5 (C-6), 65.4 (C-7). HR-ESI-MS positive mode (m/z): calc. for [M + Na]+ = 693.2095, found: [M + Na]+ = 693.2096; C41H34O9 (670.22).

4.4.3. (E)-3,4,5,7-Tetra-O-Benzoyl-1,2-Dideoxy-1-Naphth-2-yl-D-gluc-Hept-1-Enitol (3b) and (E)-3,4,6,7-Tetra-O-Benzoyl-1,2-Dideoxy-1-Naphth-2-yl-D-gluc-Hept-1-Enitol (4b)

Isolated from a reaction of tosylhydrazone 1a (0.10 g, 0.13 mmol), naphthalen-2-ylboronic acid (20 equiv., 0.44 g, 2.57 mmol), and K3PO4 (10 equiv., 0.27 g, 1.29 mmol) according to General procedure I by column chromatography (1:4 EtOAc–hexane) to yield 70 mg pale brown amorphous solid containing 3b and 4b in 1.5:1 ratio. Rf: 0.25 (1:2 EtOAc–hexane).

3b: 1H NMR (400 MHz, CDCl3) δ 8.20–7.03 (27H, m, aromatics), 6.94 (1H, d, J1,2 15.9 Hz, H-1), 6.45 (1H, dd, J2,3 6.7 Hz, H-2), 6.19–6.09 (2H, m, H-3, H-4), 5.82 (1H, dd, J4,5 1.2, J5,6 8.9 Hz, H-5), 4.54 (1H, dd, J6,7a 3.0, J7a,7b 11.9 Hz, H-7a), 4.35 (1H, dd, J6,7b
5.7 Hz, H-7b), 4.24–4.13 (1H, m, H-6), 3.66 (1H, bs, OH). 13C NMR (100 MHz, CDCl3) δ 167.2, 166.7, 165.6, 165.4 (4 × CO), 136.6 (C-1), 136.4–132.3 (aromatics), 122.4 (C-2), 73.9 (C-3), 73.2 (C-4), 71.3 (C-5), 68.5 (C-6), 65.5 (C-7). HR-ESI-MS positive mode (m/z): calc. for [M + Na]⁺ = 743.2252, found: [M + Na]⁺ = 743.2250; C43H34O10 (720.24).

4b: 1H NMR (400 MHz, CDCl3) δ 8.20–7.03 (28H, m, aromatics, H-1), 6.44 (1H, dd, J1,2 15.8, J1,2 8.4 Hz, H-2), 6.31 (1H, pseudo t, J2,3 8.9 Hz, H-3), 5.88 (1H, dd, J4,5 1.4 Hz, H-4), 5.48 (1H, ddd, J6,7a 3.3, J6,7a 4.4, J3,4 8.0 Hz, H-6), 4.82 (1H, dd, J7a,7b 12.4 Hz, H-7a), 4.75 (1H, dd, H-7b), 4.44 (1H, d, H-5), 3.57 (1H, bs, OH). 13C NMR (100 MHz, CDCl3) δ 166.9, 166.3, 165.8, 165.4 (4 × CO), 136.9 (C-1), 136.4–132.0 (aromatics), 123.1 (C-2), 74.8 (C-3), 72.5 (C-4), 71.6 (C-6), 68.4 (C-5), 63.4 (C-7). HR-ESI-MS positive mode (m/z): calc. for [M + Na]⁺ = 743.2252, found: [M + Na]⁺ = 743.2254; C43H34O10 (720.24).

4.4.4. (E)-3,4,5,7-Tetra-O-Benzoyl-1-(4-Dibenzofuran-4-ylboronic acid (1.5 equiv., 0.04 g, 0.19 mmol) and K3PO4 (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I. Purified by column chromatography (1:2 EtOAc–hexane) to yield 16 mg (16%) of 3c as a pale brown amorphous solid. Rf: 0.32 (1:2 EtOAc–hexane); [α]D + 5 (c 0.11, CH2Cl2). 1H NMR (400 MHz, CDCl3) δ 8.38–7.68 (12H, m, aromatics), 7.64–7.16 (15H, m, aromatics), 7.15–6.92 (2H, m, H-1, H-2), 6.22 (1H, dd, J2,3 5.5, J3,4 8.0 Hz, H-3), 6.16 (1H, dd, J4,5 1.7 Hz, H-4), 5.87 (1H, dd, J5,6 8.9 Hz, H-5), 4.54 (1H, dd, J6,7a 3.0, J7a,7b 11.9 Hz, H-7a), 4.35 (1H, dd, J6,7b 5.7 Hz, H-7b), 4.23–4.15 (1H, m, H-6), 3.60 (1H, d, J6,OH 5.3 Hz, OH). 13C NMR (100 MHz, CDCl3) δ 167.2, 166.7, 165.6, 165.4 (4 × CO), 130.8 (C-1), 156.5–111.9 (aromatics), 125.9 (C-2), 74.1 (C-3), 73.3 (C-4), 71.3 (C-5), 68.6 (C-6), 65.5 (C-7). C44H36O10 (760.23). HR-ESI-MS positive mode (m/z): calc. for [M + Na]⁺ = 783.2201, found: [M + Na]⁺ = 783.2202; C47H36O10 (760.23).

4.4.5. (E)-3,4,6,7-Tetra-O-Benzoyl-1-(4-Dibenzofuran-4-ylboronic acid (20 equiv., 0.55 g, 2.57 mmol), and K3PO4 (10 equiv., 0.27 g, 1.29 mmol) according to General procedure I. Purified by column chromatography (1:3 EtOAc–hexane) to yield 29 mg (30%) of 4c as a yellow amorphous solid. Rf: 0.32 (1:2 EtOAc–hexane); [α]D + 5 (c 0.11, CH2Cl2). 1H NMR (400 MHz, CDCl3) δ 8.23–6.76 (27H, m, aromatics), 7.02 (1H, d, J1,2 16.2 Hz, H-1), 6.97 (1H, dd, J2,3 8.2 Hz, H-2), 6.29 (1H, pseudo t, J3,4 9.0 Hz, H-3), 5.91 (1H, dd, J4,5 1.5 Hz, H-4), 5.44 (1H, ddd, J6,7a 3.5, J6,7a 4.4, J5,6 8.0 Hz, H-5), 4.77 (1H, dd, J7a,7b 12.4 Hz, H-7a), 4.68 (1H, dd, H-7b), 4.50–4.41 (1H, m, H-6), 3.28 (1H, d, J5,OH 6.0 Hz, OH). 13C NMR (100 MHz, CDCl3) δ 167.1, 166.9, 165.9, 165.8 (4 × CO), 131.7 (C-1), 156.3–111.0 (aromatics), 120.6 (C-2), 75.1 (C-3), 72.5 (C-4), 71.7 (C-6), 68.4 (C-5), 63.3 (C-7). HR-ESI-MS positive mode (m/z): calc. for [M + Na]⁺ = 783.2201, found: [M + Na]⁺ = 783.2202; C44H36O10 (760.23).
4.4.6. (E)-3,4,5,7-Tetra-O-Benzoyl-1,2-Dideoxy-1-(4-Methylphenyl)-D-glucopyranosyl-Hept-1-Enitol (3d) and (E)-3,4,6,7-Tetra-O-Benzoyl-1,2-Dideoxy-1-(4-Methylphenyl)-D-glucopyranosyl-Hept-1-enitol (4d)

Isolated from a reaction of tosylhydrazide 1a (0.10 g, 0.13 mmol), 4-methylphenylboronic acid (1.5 equiv., 0.03 g, 0.19 mmol), and K$_3$PO$_4$ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:2 EtOAc–hexane) to yield 44 mg pale yellow amorphous solid containing 3d and 4d in 2:1 ratio. R$_f$: 0.38 (1:2 EtOAc–hexane).

![3d and 4d](image)

**3d:** $^1$H NMR (400 MHz, CDCl$_3$) δ 8.20–7.81 (8H, m, aromatics), 7.64–7.01 (16H, m, aromatics), 6.74 (1H, dd, $J_{1,2}$ 15.9 Hz, H-1), 6.26 (1H, dd, $J_{2,3}$ 6.7 Hz, H-2), 6.12–6.02 (2H, m, H-3, H-4), 5.75 (1H, bd, $J_{5,6}$ 8.9 Hz, H-5), 4.52 (1H, dd, $J_{6,7a}$ 2.9, $J_{7a,7b}$ 11.9 Hz, H-6), 4.34 (1H, dd, $J_{6,7b}$ 5.9 Hz, H-7b), 4.20–4.10 (1H, m, H-6), 3.60 (1H, d, $J_{6,HO}$ 5.2 Hz, OH), 2.33 (3H, s, CH$_3$). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 167.3, 167.2, 165.5, 165.4 (4 × CO), 136.8 (C-1), 139.5–126.1 (aromatics), 120.9 (C-2), 74.0 (C-3), 73.4 (C-4), 71.4 (C-5), 68.6 (C-6), 65.5 (C-7), 21.4 (CH$_3$). HR-ESI-MS positive mode (m/z): calc. for [M + Na]$^+$ = 707.2252, found: [M + Na]$^+$ = 707.2251; C$_{42}$H$_{36}$O$_{10}$ (684.24).

**4d:** $^1$H NMR (400 MHz, CDCl$_3$) δ 8.21–7.73 (8H, m, aromatics), 7.72–7.01 (16H, m, aromatics), 6.96 (1H, d, $J_{1,2}$ 14.9 Hz, H-1), 6.25 (1H, dd, $J_{2,3}$ 6.6 Hz, H-2), 6.21 (1H, pseudo t, $J_{2,3}$ 8.6 Hz, H-3), 5.81 (1H, dd, $J_{4,5}$ 1.3 Hz, H-4), 5.44 (1H, ddd, $J_{6,7a}$ 3.4, $J_{6,7b}$ 4.5, $J_{5,6}$ 8.5 Hz, H-6), 4.79 (1H, dd, $J_{7a,7b}$ 12.4 Hz, H-7a), 4.74 (1H, dd, H-7b), 4.39 (1H, pseudo t, $J_{5,OH}$ 8.8 Hz, H-5), 3.16 (1H, bs, OH). 2.35 (3H, s, CH$_3$). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 167.1, 166.9, 165.9, 165.3 (4 × CO), 135.9 (C-1), 139.5–115.0 (aromatics), 121.6 (C-2), 74.7 (C-3), 72.5 (C-4), 71.7 (C-6), 68.5 (C-5), 63.4 (C-7), 21.4 (CH$_3$). HR-ESI-MS positive mode (m/z): calc. for [M + Na]$^+$ = 707.2252, found: [M + Na]$^+$ = 707.2254; C$_{42}$H$_{36}$O$_{10}$ (684.24).

4.4.7. (E)-3,4,5,7-Tetra-O-Benzoyl-1,2-Dideoxy-1-(4-Methoxyphenyl)-D-glucopyranosyl-Hept-1-Enitol (3e) and (E)-3,4,6,7-Tetra-O-Benzoyl-1,2-Dideoxy-1-(4-Methoxyphenyl)-D-glucopyranosyl-Hept-1-Enitol (4e)

Isolated from a reaction of tosylhydrazide 1a (0.10 g, 0.13 mmol), 4-methoxyphenylboronic acid (1.5 equiv., 0.03 g, 0.19 mmol), and K$_3$PO$_4$ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:2 EtOAc–hexane) to yield 43 mg yellow amorphous solid containing 3e and 4e in 2:5.1 ratio. R$_f$: 0.31 (1:2 EtOAc–hexane).

![3e and 4e](image)

**3e:** $^1$H NMR (400 MHz, CDCl$_3$) δ 8.28–7.67 (8H, m, aromatics), 7.65–7.09 (14H, m, aromatics), 6.81 (2H, d, $J_{4,5}$ 8.8 Hz, aromatics), 6.71 (1H, d, $J_{1,2}$ 15.7 Hz, H-1), 6.25–6.11 (1H, m, H-2), 6.10–6.02 (2H, m, H-3, H-4), 5.75 (1H, dd, $J_{5,6}$ 1.0, $J_{5,6}$ 8.9 Hz, H-5), 4.52 (1H, dd, $J_{6,7a}$ 3.0, $J_{7a,7b}$ 11.9 Hz, H-6), 4.34 (1H, dd, $J_{6,7b}$ 5.9 Hz, H-7b), 4.21–4.09 (1H, m, H-6), 3.80 (3H, s, OCH$_3$), 3.63 (1H, bs, OH). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 167.3, 166.7, 165.6, 165.4 (4 × CO), 136.5 (C-1), 160.9–112.7 (aromatics), 119.6 (C-2), 74.2 (C-3), 73.4 (C-4), 71.4 (C-5), 68.5 (C-6), 65.5 (C-7), 55.4 (OCH$_3$). HR-ESI-MS positive mode (m/z): calc. for [M + Na]$^+$ = 723.2201, found: [M + Na]$^+$ = 723.2204; C$_{42}$H$_{36}$O$_{10}$ (700.23).

**4e:** $^1$H NMR (400 MHz, CD$_2$OD) δ 8.19–7.74 (8H, m, aromatics), 7.65–7.12 (14H, m, aromatics), 6.96 (1H, d, $J_{1,2}$ 15.8 Hz, H-1), 6.90 (1H, d, $J_{1,2}$ 8.7 Hz, aromatics), 6.32 (1H, dd, $J_{2,3}$ 8.2 Hz, H-2), 6.21 (1H, pseudo t, $J_{3,4}$ 9.1 Hz, H-3), 5.82 (1H, dd, $J_{4,5}$ 1.5 Hz, H-4), 5.45 (1H, ddd, $J_{6,7a}$ 2.5, $J_{6,7b}$ 5.1 Hz, H-6), 4.93 (1H, dd, $J_{7a,7b}$ 12.2 Hz, H-7a), 4.57 (1H, dd, H-7b), 4.52 (1H, dd, $J_{6,7b}$ 9.1 Hz, H-5), 3.80 (3H, s, OCH$_3$), 3.58 (1H, bs, OH). $^{13}$C NMR (90 MHz, CDCl$_3$) δ 167.0, 166.9, 165.8, 165.4 (4 × CO), 136.6 (C-1), 160.9–112.7 (aromatics), 120.3 (C-2), 74.5
(C-3), 72.5, 71.7 (C-4, C-6), 68.8 (C-5), 63.4 (C-7), 55.5 (OCH3). HR-ESI-MS positive mode (m/z): calc. for [M + H]+ = 707.2252, found: [M + H]+ = 707.2254; C42H36O9 (684.24).

4.4.8. (E)-3,4,5,7-Tetra-O-Benzoyl-1-(3-Chlorophenyl)-1,2-Dideoxy-D-glucopyranose (3f) and (E)-3,4,6,7-Tetra-O-Benzoyl-1-(3-Chlorophenyl)-1,2-Dideoxy-D-galactopyranose (4f)

Isolated from a reaction of tosylhydrazone 1a (0.10 g, 0.13 mmol), 3-chlorophenylboronic acid (1.5 equiv., 0.03 g, 0.19 mmol), and K3PO4 (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:4 EtOAc–hexane) to yield 6 mg (7%) of 3f and 4f in 2:1 ratio with two unidentified species. Rf: 0.35 (1:2 EtOAc–hexane).

3f: 1H NMR (400 MHz, CDCl3) δ 8.18–7.82 (8H, m, aromatics), 7.64–7.02 (16H, m, aromatics), 6.70 (1H, d, J1,2 15.9 Hz, H-1), 6.34 (1H, dd, J2,3 6.9 Hz, H-2), 6.12–6.04 (2H, m, H-3, H-4), 5.76 (1H, dd, J4,5 0.6, J5,6 8.9 Hz, H-5), 4.54 (1H, dd, J6,7a 3.0, J7a,7b 11.9 Hz, H-7a), 4.34 (1H, dd, J6,7b 5.7 Hz, H-7b), 4.23–4.14 (1H, m, H-6), 3.64 (1H, d, J5,6OH 3.9 Hz, OH). 13C NMR (90 MHz, CDCl3) δ 167.1, 166.7, 165.7, 165.5 (4 × CO), 134.9 (C-1), 138.4–123.4 (aromatics), 123.7 (C-2), 73.5 (C-3), 73.0 (C-4), 71.2 (C-5), 68.5 (C-6), 65.5 (C-7). HR-ESI-MS positive mode (m/z): calc. for [M + Na]+ = 727.1705, found: [M + Na]+ = 727.1706; C41H33ClO9 (704.18).

4f: 1H NMR (400 MHz, CDCl3) δ 8.18–7.79 (8H, m, aromatics), 7.69–7.06 (16H, m, aromatics), 6.91 (1H, d, J1,2 15.8 Hz, H-1), 6.32 (1H, dd, J2,3 8.0 Hz, H-2), 6.21 (1H, pseudo t, J3,4 8.4 Hz, H-3), 5.81 (1H, dd, J4,5 1.5 Hz, H-4), 5.43 (1H, dd, J5,6a 3.3, J5,6b 4.3, J5,6 8.0 Hz, H-5, H-6), 4.84 (1H, dd, J7a,7b 12.4 Hz, H-7a), 4.73 (1H, dd, H-7b), 4.38–4.27 (1H, m, H-6), 3.34 (1H, d, J5,OH 8.4 Hz, OH). 13C NMR (90 MHz, CDCl3) δ 167.1, 166.8, 165.8, 165.4 (4 × CO), 135.2 (C-1), 153.1–123.4 (aromatics), 124.4 (C-2), 74.4 (C-3), 72.4 (C-4), 71.7 (C-5), 68.4 (C-6), 63.4 (C-7). HR-ESI-MS positive mode (m/z): calc. for [M + Na]+ = 727.1705, found: [M + Na]+ = 727.1706; C41H33ClO9 (704.18).

4.4.9. 3,4,5,7-Tetra-O-Benzoyl-1-(4-Chlorophenyl)-1,2-Dideoxy-D-glucopyranose (3g)

Prepared from tosylhydrazone 1a (0.10 g, 0.13 mmol), 4-chlorophenylboronic acid (1.5 equiv., 0.03 g, 0.19 mmol), and K3PO4 (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:2 acetone–hexane) to yield 62 mg (68%) of 3g as a white amorphous solid. Rf: 0.36 (1:2 EtOAc–hexane); [α]D0 + 9 (c 0.57, CH3Cl2).

1H NMR (400 MHz, CDCl3) δ 8.16–7.85 (8H, m, aromatics), 7.64–7.12 (16H, m, aromatics), 6.71 (1H, d, J1,2 16.0 Hz, H-1), 6.34–6.24 (1H, m, H-2), 6.10–6.02 (2H, m, H-3, H-4), 5.74 (1H, dd, J4,5 0.9, J5,6 8.9 Hz, H-5), 4.53 (1H, dd, J6,7a 2.9, J7a,7b 11.9 Hz, H-7a), 4.34 (1H, dd, J6,7b 5.7 Hz, H-7b), 4.21–4.10 (1H, m, H-6), 3.60 (1H, d, J5,6OH 5.1 Hz, OH). 13C NMR (100 MHz, CDCl3) δ 167.2, 166.8, 165.5, 165.4 (4 × CO), 135.2 (C-1), 134.7–127.2 (aromatics), 122.7 (C-2), 73.7 (C-3), 73.1 (C-4), 71.2 (C-5), 68.5 (C-6), 65.5 (C-7). HR-ESI-MS positive mode (m/z): calc. for [M + Na]+ = 727.1705, found: [M + Na]+ = 727.1703; C41H33ClO9 (704.18).

4.5. Characterization of Molecules 7–9 Isolated from the Reaction of Tosylhydrazone 6 and Phenylboronic Acid

4.5.1. 3,4,5,7-Tetra-O-Acetyl-2,6-Anhydro-1-Deoxy-1-Phenyl-D-mannopyranose (7)

Isolated from a reaction of tosylhydrazone 6 (0.10 g, 0.19 mmol), phenylboronic acid (20 equiv., 0.46 g, 3.78 mmol), and K3PO4 (10 equiv., 0.40 g, 1.89 mmol) according to General procedure I by column chromatography (1:4 EtOAc–hexane) to yield 6 mg (7%) of 7 as a...
white amorphous product. Optical rotation, NMR and MS spectra are identical with those reported [13].

![Structure](image)

4.5.2. (E)-3,5,6,7-Tetra-O-Acetyl-1,2-Dideoxy-1-Phenyl-β-galacto-Hept-1-Enitol (8)

Isolated from a reaction of tosylhydrazone 6 (0.30 g, 0.56 mmol), phenylboronic acid (20 equiv., 1.38 g, 11.35 mmol), and K₃PO₄ (10 equiv., 1.20 g, 5.68 mmol) according to General procedure I by column chromatography (1:4 EtOAc–hexane) to yield 12 mg (5%) of 8 as a white amorphous solid. Rf: 0.15 (1:2 EtOAc–hexane); [α]D + 40 (c 0.18, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.43–7.09 (5H, m, aromatics), 6.71 (1H, dd, J₁,₂ 16.0 Hz, H-1), 6.32 (1H, dd, J₂,₃ 7.6 Hz, H-2), 5.54 (1H, ddd, J₆,₇a 4.6, J₆,₇b 7.7 Hz, H-6), 5.48 (1H, dd, J₃,₄ 1.1 Hz, H-3), 5.19 (1H, dd, J₅,₆ 1.7 Hz, H-5), 4.26 (1H, dd, J₇a,₇b 11.8 Hz, H-7a), 4.05 (1H, dd, H-7b), 3.72 (1H, dd, J₄,₅ 9.6 Hz, H-4), 3.09 (1H, bs, OH), 2.16, 2.11, 2.10, 2.04 (12H, 4s, 4 × CH₃).

¹³C NMR (100 MHz, CDCl₃) δ 171.8, 170.6, 170.4, 170.0 (4 × CO), 134.9 (C-1), 136.7–123.2 (aromatics), 123.7 (C-2), 74.4 (C-3), 72.4 (C-4), 71.7 (C-6), 68.4 (C-5), 63.4 (C-7), 21.3, 21.0, 20.8 (4 × CH₃). HR-ESI-MS positive mode (m/z): calc. for [M + Na]⁺ = 445.1467, found: [M + Na]⁺ = 445.1469, found: [M + Na]⁺ = 445.1467; C₂₁H₂₆O₉ (422.16).

![Structure](image)

4.5.3. (E)-3,4,6,7-Tetra-O-Acetyl-1,2-Dideoxy-1-Phenyl-α-galacto-Hept-1-Enitol (9)

Prepared from tosylhydrazone 6 (0.30 g, 0.56 mmol), phenylboronic acid (20 equiv., 1.38 g, 11.35 mmol), and K₃PO₄ (10 equiv., 1.20 g, 5.68 mmol) according to General procedure I. Purified by column chromatography (1:4 EtOAc–hexane) to yield 180 mg (75%) of 9 as a white amorphous solid. Rf: 0.10 (1:2 EtOAc–hexane); [α]D + 37 (c 0.40, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.57–7.09 (5H, m, aromatics), 6.63 (1H, d, J₁,₂ 15.8 Hz, H-1), 6.03 (1H, dd, J₂,₃ 6.0 Hz, H-2), 5.88 (1H, dd, J₃,₄ 1.9 Hz, H-3), 5.22 (1H, dd, J₅,₆ 1.7 Hz, H-5), 5.17 (1H, dd, J₄,₅ 9.7 Hz, H-4), 4.43 (1H, dd, J₆,₇a 11.7 Hz, H-7a), 4.17 (1H, dd, H-7b), 3.85 (1H, dd, J₅,₆ 1.5 Hz, H-5), 3.53 (1H, bs, OH), 2.21, 2.07, 2.04, 2.01 (12H, 4s, 4 × CH₃).

¹³C NMR (100 MHz, CDCl₃) δ 171.5, 171.2, 170.7, 170.0 (4 × CO), 133.0 (C-1), 136.0–121.2 (aromatics), 123.4 (C-2), 72.5 (C-3), 71.6 (C-4), 69.0 (C-6), 67.9 (C-5), 63.4 (C-7), 21.1, 20.8, 20.7 (4 × CH₃). HR-ESI-MS positive mode (m/z): calc. for [M + Na]⁺ = 445.1469, found: [M + Na]⁺ = 445.1467; C₂₁H₃₂O₉ (422.16).

![Structure](image)

4.6. General Procedure II for the Synthesis of 1-Aryl-3,4,5,6,7-Penta-O-Benzoyl-1,2-Dideoxy-D-gluco-Hept-1-Enitols 11 and 12

A mixture of 1-aryl-tetra-O-benzoyl-1,2-dideoxy-D-gluco-hept-1-enitol (3 and 4, 1 mmol) and dry pyridine (6.3 mmol) were dissolved in dry chloroform (3 mL). Then, benzoyl chloride (7 mmol) was added dropwise to the solution. The reaction mixture was stirred and heated at 80 °C. When TLC (1:2 EtOAc–hexane) showed complete consumption of the starting compound (~2 h), the mixture was cooled down. The organic layer was washed with 2M aqueous hydrogen chloride solution (1 × 3 mL), cold, saturated sodium hydrogen carbonate solution (1 × 3 mL), water (1 × 3 mL), and then dried on anhydrous magnesium...
sulfate. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (1:2 EtOAc–hexane) to give hept-1-enitols.

4.6.1. (E)-3,4,5,6,7-Penta-O-Benzoyl-1,2-Dideoxy-1-Phenyl-D-gluc-Hept-1-Enitol (11a)

Prepared from (E)-3,4,5,7-tetra-O-benzoyl-1,2-dideoxy-1-phenyl-D-gluc-Hept-1-enitol 3a and (E)-3,4,6,7-tetra-O-benzoyl-1,2-dideoxy-1-phenyl-D-gluc-Hept-1-enitol 4a (0.10 g, 0.15 mmol) according to General procedure II. Purified by column chromatography (1:2 EtOAc–hexane) to yield 104 mg (92%) of 11a as a white amorphous solid. Rp: 0.41 (1:2 EtOAc–hexane); [α]D = −2 (c 0.50, CH2Cl2). 1H NMR (400 MHz, CDCl3) δ 8.24–7.84 (8H, m, aromatics), 7.66–7.17 (17H, m, aromatics), 6.80 (1H, d, J1,2 15.9 Hz, H-1), 6.40–6.29 (1H, m, H-2), 6.18 (1H, dd, J4,5 2.0 Hz, H-5), 6.12–6.04 (2H, m, H-3, H-4), 5.91 (1H, ddd, J6,7b 3.6, J5,6 5.9, J5,6 7.2 Hz, H-6), 4.82 (1H, dd, J7a,7b 12.3 Hz, H-7a), 4.55 (1H, dd, H-7b). 13C NMR (100 MHz, CDCl3) δ 170.5, 170.3, 170.1, 169.8 (5 × CO), 133.5 (C-1), 133.3 (C-2, C-6), 122.0 (C-2), 73.8 (C-3), 71.8 (C-4), 69.9, 69.7 (C-5, C-6), 62.8 (C-7). HR-ESI-MS positive mode (m/z): calc. for [M + Na]+ = 797.2357, found: [M + Na]+ = 797.2355; C48H38O10 (774.25).

4.6.2. (E)-3,4,5,6,7-Penta-O-Benzoyl-1-(4-Dibenzo[b,d]furananyl)-1,2-Dideoxy-D-gluc-Hept-1-Enitol (11b)

Prepared from (E)-3,4,5,7-tetra-O-benzoyl-1-(4-dibenzo[b,d]furananyl)-1,2-dideoxy-D-gluc-Hept-1-enitol 3c and (E)-3,4,6,7-tetra-O-benzoyl-1-(4-dibenzo[b,d]furananyl)-1,2-dideoxy-D-gluc-Hept-1-enitol 4c (0.05 g, 0.06 mmol), according to General procedure II. Purified by column chromatography (1:2 EtOAc–hexane) to yield 28 mg (55%) of 11b as a yellow amorphous solid. Rp: 0.39 (1:2 EtOAc–hexane); [α]D = −1 (c 0.48, CH2Cl2). 1H NMR (400 MHz, CDCl3) δ 8.44–6.81 (32H, m, aromatics), 7.08–7.04 (2H, m, H-1, H-2), 6.28 (1H, dd, J4,5 2.0 Hz, H-5), 6.12–6.04 (2H, m, H-3, H-4), 5.92 (1H, ddd, J5,6 7.1 Hz, H-6), 4.82 (1H, dd, J7a,7b 12.2 Hz, H-7a), 4.53 (1H, dd, H-7b). 13C NMR (100 MHz, CDCl3) δ 170.5, 170.3, 170.1, 169.8 (5 × CO), 133.5 (C-1), 133.3 (C-2, C-6), 122.0 (C-2), 73.8 (C-3), 71.8 (C-4), 69.9, 69.7 (C-5, C-6), 62.8 (C-7). HR-ESI-MS positive mode (m/z): calc. for [M + Na]+ = 887.2463, found: [M + Na]+ = 887.2460; C54H40O11 (864.26).

4.6.3. (E)-3,4,5,6,7-Penta-O-Acetyl-1,2-Dideoxy-1-Phenyl-D-galac-Hept-1-Enitol (12)

3,4,6,7-Tetra-O-acetyl-1,2-dideoxy-1-phenyl-D-galac-Hept-1-enitol (9, 0.12 g, 0.29 mmol) was dissolved in dry pyridine (1 mL) and cooled to 0 °C. Then, acetic anhydride (1.5 equiv., 0.04 mL, 0.04 g, 0.43 mmol) was added dropwise to the solution. The reaction mixture was stirred for a day at room temperature and the pyridine was evaporated. The residue was dissolved in dichloromethane and washed with water (1 × 2 mL), then dried on anhydrous magnesium sulfate. The solution was concentrated under reduced pressure and traces of pyridine were removed by repeated co-evaporations with toluene to yield 122 mg (91%) of 12 as a white amorphous solid. Rp: 0.36 (1:2 EtOAc–hexane); [α]D + 115 (c 0.02, CH2Cl2). 1H NMR (400 MHz, CDCl3) δ 7.57–7.06 (5H, m, aromatics), 6.58 (1H, dd, JAc1 0.7, J1,2 15.9 Hz, H-1), 5.97 (1H, dd, J2,3 6.1 Hz, H-2), 5.67–5.59 (1H, m, H-3), 5.45 (1H, dd, J5,6 1.8 Hz, H-5), 5.41–5.31 (1H, m, H-6), 5.37 (1H, dd, J3,4 2.5, J4,5 10.0 Hz, H-4), 4.29 (1H, dd, J6,7a 5.0, J7a,7b 11.6 Hz, H-7a), 3.88 (1H, dd, J6,7b 7.5 Hz, H-7b), 2.14, 2.10, 2.08, 2.04, 202 (15H, 5a, 5 × CH3).
13C NMR (90 MHz, CDCl3) δ 170.5, 170.3, 170.1, 169.8 (5 × CO), 133.5 (C-1), 136.5–122.2 (aromatics), 122.9 (C-2), 71.1 (C-3), 69.5 (C-4), 68.1 (C-5), 68.0 (C-6), 62.3 (C-7), 21.0, 20.8, 20.7 (5 × CH3). HR-ESI-MS positive mode (m/z): calc. for [M + Na]+ = 487.1575, found: [M + Na]+ = 487.11577; C23H28O10 (464.17).

4.7. General Procedure III for the Synthesis of Anhydro-Aldose Tosylhydrazones (C-(2,3,4,6-Tetra-O-Alkyl-β-D-Glycopyranosyl) Formaldehyde Tosylhydrazones) (17, 24)

Raney-nickel (1.5 g, an aqueous suspension, Merck) was added at room temperature to a vigorously stirred solution of pyridine (6 mL), acetic acid (4 mL), and water (4 mL). Then, sodium hypophosphite (0.75 g, 8.50 mmol), tosylhydrazine (0.37 g, 2.00 mmol), and nitrile (166 [52] or 23) (1.00 mmol) were added to the mixture. When TLC (2:1 EtOAc–hexane) indicated complete consumption of the starting compound, the insoluble material was filtered off through a pad of celite and washed with dichloromethane (10 mL). The organic layer of the filtrate was separated, washed with water (3 mL), 10% aqueous hydrazine (3 mL), and then dried on anhydrous magnesium sulfate. The solution was concentrated by column chromatography (1:2 EtOAc–hexane) to yield 18 mg amorphous tosylhydrazones (preaded co-evaporations with toluene. The residue was purified by silica gel column chromatography (1:2 EtOAc–hexane) indicated for the particular compounds to give anhydro-aldose tosylhydrazones (2,3,4,6-Tetra-O-Methyl-β-D-glycero-d-gulo-Heptose Tosylhydrazone (C-(2,3,4,6-Tetra-O-Methyl-β-D-Glycopyranosyl) Formaldehyde Tosylhydrazones) (17)

Prepared from cyanide 166 [52] (1.00 g, 4.08 mmol) according to General procedure III. Purified by column chromatography (1:2 EtOAc–hexane) to yield 1.02 g (60%) two unidentified isomers 17-1 and 17-2 in 1:3 ratio as a colourless oil.

17-1 Rf: 0.11 (1:1 EtOAc–hexane). 1H NMR (360 MHz, CDCl3) δ 7.92 (1H, bs, NH), 7.86–7.76 (2H, m, aromatics), 7.31 (2H, d, J 8.2 Hz, aromatics), 7.05 (1H, d, J1,2 6.0 Hz, H-1), 3.74 (1H, dd, J2,3 9.5 Hz, H-2), 3.61–3.45 and 3.32–3.00 (6H, m, H-3–H7b), 3.63, 3.52, 3.35, 3.25 (12H, 4s, 4 × CH3), 2.41 (3H, s, CH3-Ts). 13C NMR (90 MHz, CDCl3) δ 146.7 (C-1), 144.3–127.5 (aromatics), 88.5, 82.7, 79.4, 78.6, 74.1 (C-2–C-6), 71.0 (C-7), 60.9, 60.7, 60.6, 59.3 (4 × CH3), 21.6 (CH3-Ts). HR-ESI-MS positive mode (m/z): calcd. for [M + H]+ = 417.1692, found: [M + H]+ = 417.1694; C18H28N2O7S (416.16).

17-2 Rf: 0.10 (1:1 EtOAc–hexane). 1H NMR (360 MHz, CDCl3) δ 9.31 (1H, bs, NH), 7.83 (2H, d, J 8.2 Hz, aromatics), 7.31 (2H, d, J 8.2 Hz, aromatics), 6.80 (1H, d, J1,2 4.6 Hz, H-1), 4.02 (1H, dd, J2,3 10.3 Hz, H-2), 3.61–3.45 and 3.32–3.00 (6H, m, H-3–H7b), 3.63, 3.52, 3.41, 3.30 (4s, 12H, 4 × CH3), 2.41 (s, 3H, CH3-Ts). 13C NMR (90 MHz, CDCl3) δ 146.2 (C-1), 144.3–127.5 (aromatics), 87.9, 81.2, 79.4, 78.4, 77.9 (C-2–C-6), 71.3 (C-7), 60.8, 60.4, 59.8, 59.2 (4 × CH3), 21.6 (CH3-Ts). HR-ESI-MS positive mode (m/z): calcd. for [M + H]+ = 417.1692, found: [M + H]+ = 417.1694; C18H28N2O7S (416.16).

4.8. Characterization of Anhydro-Hepitols 18

4.8.1. 2,6-Anhydro-1-Deoxy-3,4,5,7-Tetra-O-Methyl-1-Phenyl-d-glycero-d-gulo-Heptitol (18a)

Isolated from a reaction of tosylhydrazine 17 (0.05 g, 0.13 mmol), phenylboronic acid (1.5 equiv., 0.02 g, 0.19 mmol), and K3PO4 (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:2 EtOAc–hexane) to yield 18 mg amorphous solid containing 18a and 21 in 1:3.1 ratio. Rf: 0.50 (1:2 EtOAc–hexane). 1H NMR (400 MHz, CDCl3) δ 8.34–6.74 (5H, m, aromatics), 3.65 (3H, s, CH3OC-4), 3.59 (3H, s, CH3OC-3), 3.53
4.8.2. 2,6-Anhydro-1-Deoxy-1-(4-Dibenzof[b,d]furan-4-yl)boronic acid (1.5 equiv., 0.04 g, 0.19 mmol), and K₃PO₄ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:4 EtOAc–hexane) to yield 4 mg (8%) of isolated as a white amorphous solid. Rf: 0.47 (1:2 EtOAc–hexane). ¹H NMR (500 MHz, CDCl₃) δ 7.93 (1H, d, J 7.7 Hz, aromatic), 7.80 (1H, dd, J 1.1, 7.7 Hz, aromatic), 7.58 (1H, d, J 8.2 Hz, aromatic), 7.47–7.39 (2H, m, aromatics), 7.35–7.30 (1H, m, aromatic), 7.29–7.23 (1H, m, aromatics), 3.67 (3H, s, CH₃OC-4), 3.62 (3H, s, CH₃OC-3), 3.58 (1H, ddd, J1a,2 2.9, J1b,2 8.9, J2,3 9.2 Hz, H-2), 3.54 (1H, dd, H-1a), 3.53 (3H, s, CH₃OC-5), 3.48 (1H, dd, H-1b), 3.46 (1H, dd, J7a,7b 11.2 Hz, H-7a), 3.28 (3H, s, CH₃OC-7), 3.26 (1H, pseudo t, J3,4 8.7 Hz, H-4), 3.21 (1H, pseudo t, J4,5 8.8 Hz, H-5), 3.14 (1H, ddd, J6,7a 2.5, J6,7b 3.4, J5,6 9.5 Hz, H-6), 3.09 (1H, dd, J1a,1b 14.4 Hz, H-1b) 3.02 (1H, pseudo t, J3,4 8.9 Hz, H-3). ¹³C NMR (90 MHz, CDCl₃) δ 129.4–110.9 (aromatics), 89.2 (C-4), 84.2 (C-3), 80.2 (C-5), 79.0, 78.9 (C-2, C-6), 71.5 (C-7), 60.9 (CH₃OC-3), 60.5 (CH₃OC-5), 59.5 (CH₃OC-4), 32.0 (C-1). HR-ESI-MS positive mode (m/z): calc. for [M + Na]⁺ = 423.1778, found: [M + Na]⁺ = 423.1777; C₁₈H₂₈O₆ (400.19).

4.8.3. 2,6-Anhydro-1-Deoxy-3,4,5,7-Tetra-O-Methyl-D-glycero-D-gulo-Heptitol (18c)

Prepared from tosylhydrazone 17 (0.05 g, 0.13 mmol), (4-trifluoromethyl)phenylboronic acid (0.05 g, 0.13 mmol), dibenzo[b,d]furan-4-ylboronic acid (1.5 equiv., 0.04 g, 0.19 mmol), and K₃PO₄ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:3 EtOAc–hexane) to yield 22 mg (45%) of 18c as a white amorphous solid. Rf: 0.50 (1:2 EtOAc–hexane); [α]D – 6 (c 0.30, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ 7.52 (2H, d, J 8.1 Hz, aromatics), 7.38 (2H, d, J 8.1 Hz, aromatics), 3.65 (3H, s, CH₃OC-4), 3.59 (3H, s, CH₃OC-3), 3.54 (1H, dd, H-7a), 3.53 (3H, s, CH₃OC-5), 3.50 (1H, dd, J7a,7b 11.1 Hz, H-7b), 3.56 (3H, s, CH₃OC-7), 3.29 (1H, ddd, J1a,2 2.3, J1b,2 8.9, J2,3 9.2 Hz, H-2), 3.24–3.08 (3H, m, H-1a, H-4, H-5), 3.13 (1H, ddd, J6,7a 2.0, J6,7b 3.9, J5,6 9.8 Hz, H-6), 2.88 (1H, pseudo t, J3,4 8.9 Hz, strongly coupled, H-3), 2.80 (1H, dd, J1a,1b 14.2 Hz, H-1b). ¹³C NMR (100 MHz, CDCl₃) δ 143.7–124.1 (aromatics), 89.2 (C-4), 83.6 (C-3), 80.0 (C-2), 79.8 (C-5), 78.8 (C-6), 71.4 (C-7), 60.8 (CH₃OC-4), 60.8 (CH₃OC-3), 60.5 (CH₃OC-5), 59.5 (CH₃OC-7), 37.7 (C-1). HR-ESI-MS positive mode (m/z): calc. for [M + H]⁺ = 379.1727, found: [M + H]⁺ = 379.1727; C₁₈H₂₅F₃O₅ (378.17).
4.8.4. 2,6-Anhydro-1-Deoxy-1-(4-Fluorophenyl)-3,4,5,7-Tetra-O-Methyl-D-glycero-D-gulo-Heptitol (18d)

Isolated from a reaction of tosylhydrazone 17 (0.05 g, 0.13 mmol), 4-fluorophenylboronic acid (1.5 equiv., 0.03 g, 0.19 mmol), and K₂PO₄ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:4 EtOAc–hexane) to yield 6 mg (14%) of 18d as a white amorphous solid. Rᵣ: 0.41 (1:2 EtOAc–hexane); [α]D + 0.5 (c 0.20, CH₂Cl₂).

1H NMR (400 MHz, CDCl₃) δ 7.22 (2H, dd, J 5.6, 8.6 Hz, aromatics), 6.94 (2H, t, J 8.8 Hz, aromatics), 3.65 (3H, s, CH₃OC-4), 3.58 (3H, s, CH₃OC-3), 3.54 (1H, dd, H-7a), 3.53 (3H, s, CH₂OC-5), 3.50 (1H, dd, J₇a,₇b 10.8 Hz, H-7ₐ), 3.37 (3H, s, CH₂OC-7), 3.24 (1H, ddd, Jₐ,₁₈ 2.1, J₁₈,₂ 8.8, J₂,₃ 9.1 Hz, H-2), 3.21–3.13 (2H, m, H-4, H-5), 3.12 (1H, ddd, J₆₇a 1.9, J₆₇b 3.6, J₅,₆ 8.7 Hz, H-6), 3.04 (1H, dd, J₆,₁₈ 14.3 Hz, H-1ₐ), 2.87 (1H, pseudo t, J₃₄ 9.0 Hz, strongly coupled, H-3), 2.71 (1H, dd, H-1ₐb).

13C NMR (90 MHz, CDCl₃) δ 131.4–109.0 (aromatics), 89.3 (C-4), 83.6 (C-3), 80.2 (C-2), 80.1 (C-5), 78.8 (C-6), 71.5 (C-7), 60.8 (CH₂OC-3, CH₂OC-4), 60.5 (CH₂OC-5), 59.5 (CH₂OC-7), 37.1 (C-1). HR-ESI-MS positive mode (m/z): calc. for [M + H]⁺ = 329.1759, found: [M + Na]⁺ = 329.1759; C₁₇H₂₅F₃O₅ (378.17).

4.8.5. 2,6-Anhydro-1-(3-Chlorophenyl)-1-Deoxy-3,4,5,7-Tetra-O-Methyl-D-glycero-D-gulo-Heptitol (18e)

Prepared from tosylhydrazone 17 (0.05 g, 0.13 mmol), 3-chlorophenylboronic acid (1.5 equiv., 0.03 g, 0.19 mmol), and K₂PO₄ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I. Purified by column chromatography (1:2 EtOAc–hexane) to yield 13 mg (29%) of 18e as a pale-yellow amorphous solid. Rᵣ: 0.48 (1:2 EtOAc–hexane); [α]D − 3 (c 0.24, CH₂Cl₂).

1H NMR (400 MHz, CDCl₃) δ 7.32–7.24 (1H, m, aromatic), 7.23–7.08 (3H, m, aromatics), 3.65 (3H, s, CH₂OC-4), 3.59 (3H, s, CH₂OC-3), 3.56 (1H, dd, J₇a,₇b 11.0 Hz, H-7ₐ), 3.53 (3H, s, CH₂OC-5), 3.51 (1H, dd, H-7ₐb), 3.37 (3H, s, CH₂OC-7), 3.27 (1H, ddd, J₁₈,₂ 2.3, J₁₈,₂ 8.8, J₂,₃ 9.1 Hz, H-2), 3.23–3.14 (2H, m, H-4, H-5), 3.13 (1H, ddd, J₆₇a 1.6, J₆₇b 3.4, J₅,₆ 8.6 Hz, H-6), 3.04 (1H, dd, J₁₈,₁₈b 14.3 Hz, H-1ₐ), 2.87 (1H, pseudo t, J₃₄ 8.8 Hz, H-3), 2.71 (1H, dd, H-1ₐb).

13C NMR (90 MHz, CDCl₃) δ 141.3–126.0 (aromatics), 89.2 (C-4), 83.5 (C-3), 80.1 (C-2), 79.9 (C-5), 78.8 (C-6), 71.5 (C-7), 60.9 (CH₂OC-4), 60.8 (CH₂OC-3), 60.5 (CH₂OC-5), 59.6 (CH₂OC-7), 37.6 (C-1). HR-ESI-MS positive mode (m/z): calc. for [M + H]⁺ = 345.1463, found: [M + H]⁺ = 345.1460; C₁₇H₂₅ClO₅ (344.14).

4.8.6. 2,6-Anhydro-1-(4-Bromophenyl)-1-Deoxy-3,4,5,7-Tetra-O-Methyl-D-glycero-D-gulo-Heptitol (18f)

Prepared from tosylhydrazone 17 (0.05 g, 0.13 mmol), 4-bromophenylboronic acid (1.5 equiv., 0.04 g, 0.19 mmol), and K₂PO₄ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I. Purified by column chromatography (1:4 EtOAc–hexane) to yield 11 mg (22%) of 18f as a white amorphous solid. Rᵣ: 0.53 (1:2 EtOAc–hexane); [α]D − 6 (c 0.21, CH₂Cl₂).

1H NMR (400 MHz, CDCl₃) δ 7.38 (2H, d, J 8.4 Hz, aromatics), 7.14 (2H, d, J 8.4 Hz, aromatics), 3.65 (3H, s, CH₂OC-4), 3.58 (3H, s, CH₂OC-3), 3.53 (3H, s, CH₂OC-5), 3.53 (1H, dd, H-7ₐ), 3.49 (1H, dd, J₇a,₇b 10.8 Hz, H-7ₐb), 3.37 (3H, s, CH₂OC-7), 3.24 (1H, ddd, J₁₈,₂ 2.2, J₁₈,₂ 8.9, J₂,₃ 9.1 Hz, H-2), 3.21–3.13 (2H, m, H-4, H-5), 3.11 (1H, ddd, J₆₇a 2.1, J₆₇b 3.5, J₅,₆ 8.7 Hz).
4.8.7. 2,6-Anhydro-1-Deoxy-3,4,5,7-Tetra-O-Methyl-1-(4-Nitrophenyl)-D-glycero-D-gulo-Heptitol (18g)

Prepared from tosylhydrazone 17 (0.05 g, 0.13 mmol), 4-nitrophenylboronic acid (1.5 equiv., 0.03 g, 0.19 mmol), and K$_3$PO$_4$ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I. Purified by column chromatography (1:2 EtOAc–hexane) to yield 4 mg (46%) of 18g as a yellow amorphous solid. R$_f$: 0.26 (1:2 EtOAc–hexane); [α]$_{D} + 5$ (c 0.22, CH$_2$Cl$_2$).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.13 (2H, d, $J_{2,3}$ = 9.0 Hz, aromatics), 7.43 (2H, d, $J_{2,3}$ = 9.8 Hz, aromatics), 3.66 (3H, s, CH$_3$OC-4), 3.60 (3H, s, CH$_3$OC-3), 3.53 (3H, s, CH$_3$OC-5), 3.53 (1H, dd, H-7a), 3.49 (1H, dd, H-7b), 10.8 Hz, H-7b), 3.37 (3H, s, CH$_3$OC-7), 3.29 (1H, ddd, $J_{1a,2}$ 2.4, $J_{1b,2}$ 9.0, $J_{2,3}$ 9.2 Hz, H-2), 3.23–3.14 (3H, m, H-1a, H-4, H-5), 3.12 (1H, ddd, $J_{6a,7a}$ 1.3, $J_{6a,7b}$ 3.1, $J_{6b,7a}$ 9.6 Hz, H-6), 2.89 (1H, pseudo t, $J_{3,4}$ 8.8 Hz, strongly coupled, H-3), 2.85 (1H, dd, H-1b).

$^{13}$C NMR (90 MHz, CDCl$_3$) $\delta$ 147.6–121.1 (aromatics), 89.2 (C-4), 83.5 (C-3), 80.0 (C-2), 79.6 (C-5), 78.8 (C-6), 71.4 (C-7), 60.9 (CH$_3$OC-4), 60.8 (CH$_3$OC-3), 60.5 (CH$_3$OC-5), 59.5 (CH$_3$OC-7), 37.3 (C-1). HR-ESI-MS positive mode (m/z): calc. for [M + H]$^+$ = 341.1959, found: [M + H]$^+$ = 341.1957; C$_{18}$H$_{28}$O$_5$ (340.42).

4.8.8. 2,6-Anhydro-1-Deoxy-3,4,5,7-Tetra-O-Methyl-1-(4-Methoxyphenyl)-D-glycero-D-gulo-Heptitol (18h)

Isolated from a reaction of tosylhydrazone 17 (0.05 g, 0.13 mmol), 4-methoxyphenylboronic acid (1.5 equiv., 0.03 g, 0.19 mmol), and K$_3$PO$_4$ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:2 EtOAc–hexane) to yield 4 mg (9%) of 18h as a pale-yellow amorphous solid. R$_f$: 0.41 (1:2 EtOAc–hexane); [α]$_{D} + 5$ (c 0.57, CH$_2$Cl$_2$).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.19 (2H, d, $J_{2,3}$ = 8.6 Hz, aromatics), 6.81 (2H, d, $J_{2,3}$ = 8.7 Hz, aromatics), 3.79 (3H, s, OCH$_3$), 3.65 (3H, s, CH$_3$OC-4), 3.59 (3H, s, CH$_3$OC-3), 3.55 (1H, dd, $J_{6a,7a}$ 10.9 Hz, H-7a), 3.53 (3H, s, CH$_3$OC-5), 3.50 (1H, dd, H-7b), 3.38 (3H, s, CH$_3$OC-7), 3.24 (1H, ddd, $J_{1a,2}$ 2.3, $J_{1b,2}$ 8.8, $J_{2,3}$ 9.1 Hz, H-2), 3.21–3.14 (2H, m, H-4, H-5), 3.12 (1H, ddd, $J_{6a,7a}$ 2.0, $J_{6a,7b}$ 3.9, $J_{6b,7a}$ 9.8 Hz, H-6), 3.01 (1H, dd, $J_{1a,1b}$ 14.3 Hz, H-1a), 2.88 (1H, pseudo t, $J_{3,4}$ 9.0 Hz, strongly coupled, H-3), 2.69 (1H, dd, H-1b).

$^{13}$C NMR (90 MHz, CDCl$_3$) $\delta$ 162.4–109.6 (aromatics), 89.3 (C-4), 83.7 (C-3), 80.5 (C-2), 80.1 (C-5), 78.8 (C-6), 71.6 (C-7), 60.8 (CH$_3$OC-3, CH$_3$OC-4), 60.5 (CH$_3$OC-5), 59.6 (CH$_3$OC-7), 55.4 (OCH$_3$), 37.0 (C-1). HR-ESI-MS positive mode (m/z): calc. for [M + H]$^+$ = 356.1704, found: [M + H]$^+$ = 356.1704; C$_{17}$H$_{25}$NO$_7$ (355.16).
4.8.9. 2,6-Anhydro-1-Deoxy-3,4,5,7-Tetra-O-Methyl-1-(4-Methylphenyl)-D-glycero-D-gulo-Heptitol (18i)

Isolated from a reaction of tosylhydrazone 17 (0.05 g, 0.13 mmol), 4-methylphenylboronic acid (1.5 equiv., 0.03 g, 0.19 mmol), and K$_3$PO$_4$ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:2 EtOAc–hexane) to yield 11 mg white amorphous solid containing 18i in 3:1 ratio. R$_f$: 0.48 (1:2 EtOAc–hexane); [α]$_D$ + 5 (c 0.08, CH$_2$Cl$_2$). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.16 (2H, d, J 7.9 Hz, aromatics), 7.07 (2H, d, J 7.9 Hz, aromatics), 3.65 (3H, s, CH$_3$OC-4), 3.59 (3H, s, CH$_3$OC-3), 3.53 (3H, s, CH$_3$OC-5), 3.55–3.50 (2H, m, H-7a, H-7b), 3.37 (3H, s, CH$_3$OC-7), 3.26 (1H, dd, J$_{1a,2}$ 2.1, J$_{1b,2}$ 8.8, J$_{2,3}$ 9.1 Hz, H-2), 3.23–3.14 (2H, m, H-4, H-5), 3.11 (1H, ddd, J$_{6,7a}$ 1.9, J$_{6,7b}$ 3.6, J$_{5,6}$ 9.7 Hz, H-6), 3.03 (1H, dd, J$_{1a,1b}$ 14.3 Hz, H-1a), 2.88 (1H, pseudo t, J$_{3,4}$ 9.0 Hz, strongly coupled, H-3), 2.70 (1H, dd, H-1b), 2.31 (3H, s, CH$_3$). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 134.0 (C-1), 137.0–126.3 (aromatics), 126.7 (C-2), 83.8 (C-4), 83.4 (C-3), 79.8 (C-5), 73.8 (C-7), 70.2 (C-6), 60.8 (CH$_3$OC-3, CH$_3$OC-4), 60.5 (CH$_3$OC-5), 59.6 (CH$_3$OC-7), 37.5 (C-1), 21.2 (CH$_3$). HR-ESI-MS positive mode (m/z): calc. for [M + H]$^+$ = 325.2010, found: [M + H]$^+$ = 325.2008; C$_{18}$H$_{28}$O$_5$ (324.42).

4.9. Characterization of Heptenitols 19 and 20

4.9.1. (E)-1,2-Dideoxy-3,4,5,7-Tetra-O-Methyl-1-Phenyl-D-gluco-Hept-1-Enitol (19a) and (Z)-1,2-Dideoxy-3,4,5,7-Tetra-O-Methyl-1-Phenyl-D-gluco-Hept-1-Enitol (20a)

Isolated from a reaction of tosylhydrazone 17 (0.05 g, 0.13 mmol), phenylboronic acid (1.5 equiv., 0.02 g, 0.19 mmol), and K$_3$PO$_4$ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:2 EtOAc–hexane) to yield 29 mg white amorphous solid containing 19a in 9:1 ratio. R$_f$: 0.16 (1:2 EtOAc–hexane), [α]$_D$ + 28 (c 0.16, CH$_2$Cl$_2$).

19a: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.42 (2H, d, J 7.6 Hz, aromatics), 7.38–7.30 (2H, m, aromatics), 7.29–7.23 (1H, m, aromatic), 6.63 (1H, d, J$_{1,2}$ 16.0 Hz, H-1), 6.16 (1H, dd, J$_{2,3}$ 8.2 Hz, H-2), 4.05 (1H, dd, J$_{3,4}$ 6.0 Hz, H-3), 3.96 (1H, ddd, J$_{6,7a}$ 3.9, J$_{6,7b}$ 5.5, J$_{5,6}$ 6.7 Hz, H-6), 3.60 (3H, s, CH$_3$OC-4), 3.59–3.50 (3H, m, H-4, H-7a, H-7b), 3.40 (6H, 2s, CH$_3$OC-5, CH$_3$OC-7), 3.40–3.37 (1H, m, H-5), 3.32 (3H, s, CH$_3$OC-3), 3.32 (1H, bs, OH). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 134.0 (C-1), 137.0–126.3 (aromatics), 126.7 (C-2), 83.8 (C-4), 83.4 (C-3), 79.8 (C-5), 73.8 (C-7), 70.2 (C-6), 60.8 (CH$_3$OC-4), 59.4 (CH$_3$OC-5), 59.2 (CH$_3$OC-7), 56.8 (CH$_3$OC-3). HR-ESI-MS positive mode (m/z): calc. for [M + Na]$^+$ = 333.1669; C$_{18}$H$_{26}$O$_5$ (310.39).

20a: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.45–7.38 (2H, m, aromatic), 7.38–7.30 (2H, m, aromatics), 7.29–7.23 (1H, m, aromatic), 6.77 (1H, d, J$_{1,2}$ 12.0 Hz, H-1), 5.58 (1H, dd, J$_{2,3}$ 10.0 Hz, H-2), 4.59 (1H, dd, J$_{3,4}$ 4.6 Hz, H-3), 3.99–3.91 (1H, m, H-6), 3.57 (3H, s, CH$_3$OC-4), 3.57–3.49 (3H, m, H-4, H-7a, H-7b), 3.45 (1H, dd, J$_{4,5}$ 3.6, J$_{5,6}$ 6.4 Hz, H-5), 3.40 (3H, s, CH$_3$OC-5), 3.32 (3H, s, CH$_3$OC-3), 3.23 (1H, bs, OH). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 133.9 (C-1), 137.0–126.3 (aromatics), 129.5 (C-2), 84.1 (C-4), 79.6 (C-5), 76.8 (C-3), 73.9 (C-7), 70.4 (C-6), 60.7 (CH$_3$OC-4), 59.2 (CH$_3$OC-7), 59.1 (CH$_3$OC-5), 56.4 (CH$_3$OC-3). HR-ESI-MS positive mode (m/z): calc. for [M + Na]$^+$ = 333.1672; C$_{18}$H$_{26}$O$_5$ (310.39).
4.9.2. (E)-1,2-Dideoxy-3,4,5,7-Tetra-O-Methyl-1-(4-Fluoromethylphenyl)-D-glucose-Hept-1-Enitol (19c)

Isolated from a reaction of tosylhydrazone 17 (0.05 g, 0.13 mmol), (4-trifluoromethyl)phenylboronic acid (1.5 equiv., 0.04 g, 0.39 mmol), and K$_2$PO$_4$ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:4 EtOAc–hexane) to yield 11 mg white amorphous solid containing 19c and an unidentified impurity in 3:1 ratio. R$_f$: 0.41 (1:2 EtOAc–hexane). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.40–7.40 (4H, aromatics), 5.66 (1H, s, H-1), 5.60 (1H, s, H-2), 4.56 (1H, d, $J_{2,3}$ 10.1 Hz, H-2), 4.54 (1H, d, $J_{3,4}$ 4.8 Hz, H-3), 3.98–3.91 (1H, m, H-6), 3.57 (3H, s, CH$_3$OC-4), 3.57–3.50 (3H, s, CH$_3$OC-7), 3.33 (3H, s, CH$_3$OC-5), 3.22 (3H, s, CH$_3$OC-3), 3.17 (1H, bs, OH). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 132.7 (C-1), 131.2–114.5 (aromatics), 129.4 (C-2), 84.1 (C-4), 79.6 (C-5), 76.8 (C-3), 73.9 (C-7), 70.4 (C-6), 60.7 (CH$_3$OC-4), 59.3 (CH$_3$OC-7), 58.0 (CH$_3$OC-5), 56.4 (CH$_3$OC-3). HR-ESI-MS positive mode (m/z): calc. for [M + Na]$^+$ = 351.1578; found: [M + Na]$^+$ = 351.1579; C$_{17}$H$_{25}$F$_{3}$O$_{5}$ (328.17).

4.9.3. (E)-1,2-Dideoxy-1-(4-Fluorophenyl)-3,4,5,7-Tetra-O-Methyl-D-glucose-Hept-1-Enitol (19d) and (Z)-1,2-Dideoxy-(4-Fluorophenyl)-3,4,5,7-Tetra-O-Methyl-D-glucose-Hept-1-Enitol (20d)

Isolated from a reaction of tosylhydrazone 17 (0.05 g, 0.13 mmol), 4-fluorophenylboronic acid (1.5 equiv., 0.03 g, 0.19 mmol), and K$_2$PO$_4$ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:4 EtOAc–hexane) to yield 31 mg white amorphous solid containing 19d and 20d in 3:1 ratio. R$_f$: 0.11 (1:2 EtOAc–hexane).

19d: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.39 (2H, dd, $J_{5,4}$ 8.7 Hz, aromatics), 7.03 (2H, t, $J_{5,4}$ 8.7 Hz, aromatics), 6.60 (1H, d, $J_{1,2}$ 16.0 Hz, H-1), 6.09 (1H, dd, $J_{2,3}$ 8.1 Hz, H-2), 4.04 (1H, dd, $J_{3,4}$ 5.9 Hz, H-3), 4.00–3.91 (1H, m, H-6), 3.59 (3H, s, CH$_3$OC-4), 3.59–3.49 (3H, m, H-4, H-7$_a$, H-7$_b$), 3.40 (6H, s, CH$_3$OC-5, CH$_3$OC-7), 3.38 (1H, dd, $J_{4,5}$ 3.1, $J_{5,6}$ 7.3 Hz, H-5), 3.36 (3H, s, CH$_3$OC-3), 3.03 (1H, bs, OH). $^{13}$C NMR (90 MHz, CDCl$_3$) $\delta$ 132.7 (C-1), 129.7–110.2 (aromatics), 126.4 (C-2), 83.7 (C-4), 83.2 (C-3), 79.8 (C-5), 73.7 (C-7), 70.2 (C-6), 60.8 (CH$_3$OC-4), 59.4 (CH$_3$OC-5), 59.2 (CH$_3$OC-7), 59.2 (CH$_3$OC-3), 57.1 (CH$_3$OC-3). HR-ESI-MS positive mode (m/z): calc. for [M + Na]$^+$ = 351.1578, found: [M + Na]$^+$ = 351.1579; C$_{17}$H$_{25}$F$_{3}$O$_{5}$ (318.17).

20d: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.34 (2H, dd, $J_{5,4}$ 5.5, 8.5 Hz, aromatics), 7.03 (2H, t, $J_{5,4}$ 8.7 Hz, aromatics), 6.72 (1H, d, $J_{1,2}$ 11.9 Hz, H-1), 5.66 (1H, dd, $J_{2,3}$ 10.1 Hz, H-2), 4.54 (1H, d, $J_{3,4}$ 4.8 Hz, H-3), 3.98–3.91 (1H, m, H-6), 3.57 (3H, s, CH$_3$OC-4), 3.57–3.50 (3H, m, H-4, H-7$_a$, H-7$_b$), 3.45 (1H, dd, $J_{4,5}$ 3.3, $J_{5,6}$ 6.6 Hz, H-5), 3.40 (3H, s, CH$_3$OC-7), 3.33 (3H, s, CH$_3$OC-5), 3.22 (3H, s, CH$_3$OC-3), 3.17 (1H, bs, OH). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 132.7 (C-1), 131.2–114.5 (aromatics), 129.4 (C-2), 84.1 (C-4), 79.6 (C-5), 76.8 (C-3), 73.9 (C-7), 70.4 (C-6), 60.7 (CH$_3$OC-4), 59.3 (CH$_3$OC-7), 59.0 (CH$_3$OC-5), 56.4 (CH$_3$OC-3). HR-ESI-MS positive mode (m/z): calc. for [M + Na]$^+$ = 351.1578, found: [M + Na]$^+$ = 351.1579; C$_{17}$H$_{25}$F$_{3}$O$_{5}$ (318.17).
4.9.4. (E)-1-(3-Chlorophenyl)-1,2-Dideoxy-3,4,5,7-Tetra-O-Methyl-D-gluco-Hept-1-Enitol (19e) and (Z)-1-(3-Chlorophenyl)-1,2-Dideoxy-3,4,5,7-Tetra-O-Methyl-D-gluco-Hept-1-Enitol (20e)

Isolated from a reaction of tosylhydrazone 17 (0.05 g, 0.13 mmol), 3-chlorophenylboronic acid (1.5 equiv., 0.03 g, 0.19 mmol), and K$_3$PO$_4$ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:2 EtOAc–hexane) to yield 18 mg pale yellow amorphous solid containing 19e and 20e in 9:1 ratio. R$_f$: 0.13 (1:2 EtOAc–hexane).

19e: $^1$H NMR (400 MHz, CDCl$_3$) δ 7.50–7.37 (1H, m, aromatic), 7.36–7.19 (3H, m, aromatics), 6.58 (1H, d, J$_{1,2}$ 16.0 Hz, H-1), 6.19 (1H, dd, J$_{2,3}$ 7.9 Hz, H-2), 4.06 (1H, dd, J$_{3,4}$ 6.2 Hz, H-3), 4.01–3.90 (1H, m, H-6), 3.60 (3H, s, CH$_3$OC-4), 3.59–3.44 (3H, m, H-4, H-7$_a$, H-7$_b$), 3.40 (6H, 2s, CH$_3$OC-5, CH$_3$OC-7), 3.38 (1H, dd, J$_{4,5}$ 2.6, J$_{5,6}$ 7.4 Hz, H-5), 3.37 (3H, s, CH$_3$OC-3), 3.11 (1H, bs, OH). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 132.5 (C-1), 130.7–120.5 (aromatics), 129.3 (C-2), 83.9 (C-4), 83.0 (C-3), 79.7 (C-5), 73.6 (C-7), 70.2 (C-6), 60.8 (CH$_3$OC-4), 59.4 (CH$_3$OC-5), 59.2 (CH$_3$OC-7), 57.0 (CH$_3$OC-3). HR-ESI-MS positive mode (m/z): calcd. for [M + Na]$^+$ = 367.1283, found: [M + Na]$^+$ = 367.1282; C$_{17}$H$_{25}$ClO$_5$ (344.14).

20e: (E)-1-(4-Bromophenyl)-1,2-Dideoxy-3,4,5,7-Tetra-O-Methyl-D-gluco-Hept-1-Enitol (19f) and (Z)-1-(4-Bromophenyl)-1,2-Dideoxy-3,4,5,7-Tetra-O-Methyl-D-gluco-Hept-1-Enitol (20f)

Isolated from a reaction of tosylhydrazone 17 (0.05 g, 0.13 mmol), 4-bromophenylboronic acid (1.5 equiv., 0.04 g, 0.19 mmol), and K$_3$PO$_4$ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure I by column chromatography (1:4 EtOAc–hexane) to yield 20 mg white amorphous solid containing 19f and 20f in 9:1 ratio. R$_f$: 0.10 (1:2 EtOAc–hexane).

19f: $^1$H NMR (400 MHz, CDCl$_3$) δ 7.46 (2H, d, J 8.5 Hz, aromatics), 7.28 (2H, d, J 8.5 Hz, aromatics), 6.57 (1H, d, J$_{1,2}$ 16.0 Hz, H-1), 6.18 (1H, dd, J$_{2,3}$ 7.9 Hz, H-2), 4.04 (1H, dd, J$_{3,4}$ 5.9 Hz, H-3), 3.99–3.90 (1H, m, H-6), 3.59 (3H, s, CH$_3$OC-4), 3.58–3.50 (3H, m, H-4, H-7$_a$, H-7$_b$), 3.40 (3H, s, CH$_3$OC-5), 3.39 (3H, s, CH$_3$OC-7), 3.37 (3H, s, CH$_3$OC-3), 3.37 (1H, dd, J$_{4,5}$ 2.8, J$_{5,6}$ 6.7 Hz, H-5), 3.00 (1H, bs, OH). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 132.4 (C-1), 136.1–117.1 (aromatics), 127.6 (C-2), 83.6 (C-4), 83.0 (C-3), 79.7 (C-5), 73.7 (C-7), 70.2 (C-6), 60.7 (CH$_3$OC-4), 59.4 (CH$_3$OC-5), 59.2 (CH$_3$OC-7), 57.0 (CH$_3$OC-3). HR-ESI-MS positive mode (m/z): calcd. for [M + Na]$^+$ = 411.0778, found: [M + Na]$^+$ = 411.0777; C$_{17}$H$_{25}$BrO$_5$ (389.29).

20f: $^1$H NMR (400 MHz, CDCl$_3$) δ 7.47 (2H, d, J 8.4 Hz, aromatics), 7.25 (2H, d, J 8.4 Hz, aromatics), 6.69 (1H, d, J$_{1,2}$ 11.9 Hz, H-1), 5.71 (1H, dd, J$_{2,3}$ 10.1 Hz, H-2), 4.53 (1H, dd, J$_{3,4}$
4.7 Hz, H-3), 3.99–3.90 (1H, m, H-6), 3.57 (3H, s, CH$_3$OC-4), 3.56–3.47 (3H, m, H-4, H-7$_a$, H-7$_b$), 3.45 (1H, dd, J$_{14,5}$ 3.3, J$_{5,6}$ 6.5 Hz, H-5), 3.40 (3H, s, CH$_3$OC-7), 3.34 (3H, s, CH$_3$OC-5), 3.21 (3H, s, CH$_3$OC-3), 3.00 (1H, bs, OH). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 132.6 (C-1), 136.1–117.1 (aromatics), 130.2 (C-2), 84.0 (C-4), 79.5 (C-5), 76.8 (C-6), 73.8 (C-7), 70.4 (C-6), 60.7 (CH$_3$OC-4), 59.3 (CH$_3$OC-7), 59.0 (CH$_3$OC-5), 56.4 (CH$_3$OC-3). HR-ESI-MS positive mode (m/z): calc. for [M + Na]$^+$ = 411.0778, found: [M + Na]$^+$ = 411.0777; C$_{17}$H$_{25}$BrO$_5$ (389.29).

4.9.6. (E)-1,2-Dideoxy-3,4,5,7-Tetra-O-Methyl-1-(4-Methoxyphenyl)-d-gluc-o-Hept-1-Enitol (19h) and (Z)-1,2-Dideoxy-3,4,5,7-Tetra-O-Methyl-1-(4-Methoxyphenyl)-d-gluc-o-Hept-1-Enitol (20h)

Isolated from a reaction of tosylhydrazone 17 (0.05 g, 0.13 mmol), 4-methoxyphenylboronic acid (1.5 equiv., 0.03 g, 0.19 mmol), and K$_3$PO$_4$ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure 1 by column chromatography (1:2 EtOAc-hexane) to yield 24 mg pale yellow amorphous solid containing 19h and 20h in 23:1 ratio. R$_f$: 0.13 (1:2 EtOAc–hexane).

![Image of 19h and 20h](image)

**19h:** $^1$H NMR (400 MHz, CDCl$_3$) δ 7.36 (2H, d, J 8.7 Hz, aromatics), 6.88 (2H, d, J 8.7 Hz, aromatics), 6.57 (1H, d, J$_{1,2}$ 16.0 Hz, H-1), 6.01 (1H, dd, J$_{2,3}$ 8.3 Hz, H-2), 4.02 (1H, dd, J$_{3,4}$ 6.0 Hz, H-3), 3.98–3.91 (1H, m, H-6), 3.82 (3H, s, OCH$_3$), 3.60 (3H, s, CH$_3$OC-4), 3.59–3.53 (2H, m, H-7$_a$, H-7$_b$), 3.54–3.49 (1H, m, H-4), 3.40 (3H, s, CH$_3$OC-5), 3.39 (3H, s, CH$_3$OC-7), 3.38 (1H, dd, J$_{4,5}$ 2.9, J$_{5,6}$ 6.9 Hz, H-5), 3.35 (3H, s, CH$_3$OC-3), 3.02 (1H, bs, OH). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 133.6 (C-1), 159.9–112.7 (aromatics), 124.3 (C-2), 83.9 (C-3), 83.6 (C-3), 79.8 (C-5), 73.8 (C-7), 70.3 (C-6), 60.8 (CH$_3$OC-4), 59.4 (CH$_3$OC-5), 59.2 (CH$_3$OC-7), 56.7 (CH$_3$OC-3), 55.5 (OCH$_3$). HR-ESI-MS positive mode (m/z): calc. for [M + Na]$^+$ = 363.1778, found: [M + Na]$^+$ = 363.1776; C$_{15}$H$_{27}$NO$_9$ (340.42).

**20h:** $^1$H NMR (400 MHz, CDCl$_3$) δ 7.32 (2H, d, J 8.7 Hz, aromatics), 6.88 (2H, d, J 8.7 Hz, aromatics), 6.69 (1H, d, J$_{1,2}$ 12.0 Hz, H-1), 5.56 (1H, dd, J$_{2,3}$ 10.0 Hz, H-2), 4.63 (1H, dd, J$_{3,4}$ 4.7 Hz, H-3), 3.99–3.90 (1H, m, H-6), 3.82 (3H, s, OCH$_3$), 3.58 (3H, s, CH$_3$OC-4), 3.57–3.49 (2H, m, H-4, H-7$_a$, H-7$_b$), 3.46 (1H, dd, J$_{4,5}$ 3.3, J$_{5,6}$ 6.6 Hz, H-5), 3.40 (3H, s, CH$_3$OC-7), 3.33 (3H, s, CH$_3$OC-5), 3.23 (3H, s, CH$_3$OC-3), 3.02 (1H, bs, OH). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 133.3 (C-1), 161.0–112.7 (aromatics), 130.4 (C-2), 84.2 (C-4), 79.6 (C-5), 77.0 (C-3), 73.9 (C-7), 70.4 (C-6), 60.7 (CH$_3$OC-4), 59.3 (CH$_3$OC-7), 59.0 (CH$_3$OC-5), 56.3 (CH$_3$OC-3), 55.4 (OCH$_3$). HR-ESI-MS positive mode (m/z): calc. for [M + Na]$^+$ = 363.1778, found: [M + Na]$^+$ = 363.1776; C$_{15}$H$_{28}$O$_5$ (340.42).

4.9.7. (E)-1,2-Dideoxy-3,4,5,7-Tetra-O-Methyl-1-(4-Methylphenyl)-d-gluc-o-Hept-1-Enitol (19i) and (Z)-1,2-Dideoxy-3,4,5,7-Tetra-O-Methyl-1-(4-Methylphenyl)-d-gluc-o-Hept-1-Enitol (20i)

Isolated from a reaction of tosylhydrazone 17 (0.05 g, 0.13 mmol), 4-methylphenylboronic acid (1.5 equiv., 0.03 g, 0.19 mmol), and K$_3$PO$_4$ (3 equiv., 0.08 g, 0.39 mmol) according to General procedure 1 by column chromatography (1:2 EtOAc–hexane) to yield 24 mg pale white amorphous solid containing 19i and 20i in 8:1 ratio. R$_f$: 0.13 (1:2 EtOAc–hexane), [a]$_D$ +28 (c 0.36, CH$_2$Cl$_2$).

![Image of 19i and 20i](image)
19i: \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.32 (2H, d, \( J \) 8.1 Hz, aromatics), 7.15 (2H, d, \( J \) 7.9 Hz, aromatics), 6.60 (1H, d, \( J_{12} \) 16.0 Hz, H-1), 6.10 (1H, dd, \( J_{23} \) 8.3 Hz, H-2), 4.03 (1H, dd, \( J_{34} \) 6.0 Hz, H-3), 3.98–3.90 (1H, m, H-4), 3.60 (3H, s, CH\(_3\)OC-4), 3.58–3.49 (3H, m, H-4, H-7a, H-7b), 3.39 (6H, s, CH\(_3\)OC-5, CH\(_3\)OC-6), 3.39–3.36 (1H, m, H-5), 3.35 (3H, s, CH\(_3\)OC-3), 3.03 (1H, bs, OH), 2.35 (3H, s, CH\(_3\)). 13C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 164.0 (C-1), 227.2 (C-16), 143.4 (C-21), 124.3 (C-31), 123.8 (C-32), 123.7 (C-33), 118.3 (C-34), 117.5 (C-1 = CN), 97.0, 95.9, 93.0, 77.7, 77.2, 72.3, 72.2, 66.6 (C-2=C-6), 66.2 (C-7), 56.1, 55.4, 55.3, 54.8 (4 \( \times \) CH\(_3\)). HR-ESI-MS positive mode (m/z): calcld. for [M + Na\(^+\)] = 433.2065, found: [M + Na\(^+\)] = 433.2063; C\(_{21}\)H\(_{35}\)NO\(_8\) (432.44).

20i: \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.28–7.23 (4H, m, aromatics), 6.73 (1H, d, \( J_{2.3} \) 12.1 Hz, H-1), 5.62 (1H, dd, \( J_{2.3} \) 10.0 Hz, H-2), 4.61 (1H, dd, \( J_{3.4} \) 4.6 Hz, H-3), 3.98–3.90 (1H, m, H-4), 3.57 (3H, s, CH\(_3\)OC-4), 3.58–3.49 (3H, m, H-4, H-7a, H-7b), 3.46 (1H, dd, \( J_{3.4} \) 3.4, \( J_{5.6} \) 6.5 Hz, H-5), 3.40 (3H, s, CH\(_3\)OC-7), 3.33 (3H, s, CH\(_3\)OC-5), 3.23 (3H, s, CH\(_3\)OC-3), 3.03 (1H, bs, OH), 2.36 (3H, s, CH\(_3\)). 13C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 169.7 (C-1), 151.9 (C-16), 151.2 (C-31), 142.5 (C-32), 130.2 (C-33), 129.3 (C-34), 123.5 (C-1 = CN), 118.3 (C-21), 98.0, 96.0, 92.0, 78.2 (C-2), 76.7 (C-5), 76.5 (C-7), 70.5 (C-6), 60.1 (CH\(_3\)OC-4), 59.2 (CH\(_3\)OC-5), 59.1 (CH\(_3\)OC-3), 21.3 (CH\(_3\)). HR-ESI-MS positive mode (m/z): calcld. for [M + Na\(^+\)] = 433.2065, found: [M + Na\(^+\)] = 433.2063; C\(_{21}\)H\(_{35}\)NO\(_8\) (432.44).

4.10. 2,6-Anhydro-3,4,5,7-Tetra-O-Methoxymethyl-D-glycero-L-manno-Heptonitrite (2,3,4,6-Tetra-O-Methoxymethyl-β-D-Galactopyranosyl Cyanide) (23)

β-D-Galactopyranosyl cyanide 22 (0.10 g, 0.53 mmol) was suspended in dichloromethane (7 mL). The suspension was stirred under nitrogen atmosphere and cooled to 0 °C, and then N-diisopropylethylamine (6.4 equiv. / OH, 2.3 mL, 1.75 g, 13.55 mmol) was added, followed by careful addition of chloromethyl methyl ether (10 equiv. / OH, 1.6 mL, 1.70 g, 21.13 mmol). The reaction mixture was stirred in the dark at room temperature. When TLC (1:1 EtOAc–hexane) indicated complete consumption of the starting compound (3 day), the mixture was cooled to 0 °C. Saturated aqueous NH\(_4\)Cl solution (1 mL) was added to the reaction mixture. The organic layer was separated, washed with water (1 mL), then the aqueous phase was washed with dichloromethane (3 × 3 mL). The combined organic phase was washed with water (1 mL) and dried on anhydrous magnesium sulfate. The solution was concentrated under reduced pressure and purified by column chromatography (1:1 EtOAc–hexane) to yield 163 mg (84%) of 23 as a colourless oil. [\( [\alpha]D \) = 40 (c 0.29, CHCl\(_3\)). \( ^1H \) NMR (400 MHz, DMSO-\( d_6 \)) \( \delta \) 4.86 (1H, d, \( J \) 6.7 Hz, CH\(_2\)), 4.77 (1H, d, \( J \) 6.7 Hz, CH\(_2\)), 4.72 (1H, d, \( J \) 6.6 Hz, CH\(_2\)), 4.71 (1H, d, \( J \) 6.6 Hz, CH\(_2\)), 4.65–4.58 (3H, m, H-2, CH\(_2\)), 4.57 (2H, s, \( 2 \times \) CH\(_2\)), 4.00 (1H, dd, \( J_{5.6} \) 0.6 Hz, H-5), 3.91 (1H, pseudo t, \( J_{2.3} \) 9.8, \( J_{3.4} \) 9.6 Hz, H-3), 3.85 (1H, ddd, \( J_{6.7a} \) 5.9, \( J_{6.7b} \) 5.9 Hz, H-6), 3.76 (1H, dd, \( J_{3.4} \) 2.7 Hz, H-4), 3.58 (1H, dd, \( J_{7a.7b} \) 11.0 Hz, H-7a), 3.56 (1H, dd, H-7b), 3.37, 3.32, 3.31, 3.26 (12H, 4s, 4 × CH\(_3\)). 13C NMR (100 MHz, DMSO-\( d_6 \)) \( \delta \) 117.5 (C-1 = CN), 97.0, 95.9, 94.6 (4 × CH\(_2\)), 77.7, 77.2, 72.3, 72.2, 66.6 (C-2=C-6), 66.2 (C-7), 56.1, 55.4, 55.3, 54.8 (4 \( \times \) CH\(_3\)). HR-ESI-MS positive mode (m/z): calcld. for [M + H\(^+\)] = 366.1759, found: [M + H\(^+\)] = 366.1761; C\(_{15}\)H\(_{27}\)NO\(_9\) (365.17).

4.11. 2,6-Anhydro-3,4,5,7-Tetra-O-Methoxymethyl-D-glycero-L-manno-Heptose Tosylhydrazone (C-(2,3,4,6-Tetra-O-Methoxymethyl-β-D-Galactopyranosyl) Formaldehyde Tosylhydrazone) (24)

Prepared from cyanide 23 (0.10 g, 0.27 mmol) according to General procedure III. Purified by column chromatography (2:1 EtOAc–hexane) to get two unidentified isomers 24-1 and 24-2.
4.12.1. Characterization of Anhydro-Heptitol 25 and Heptenitols 26 and 27

24-I yellow oil, 19 mg (13%); Rf: 0.33 (2:1 EtOAc–hexane). 1H NMR (360 MHz, CDCl3) δ 9.50 (1H, s, NH), 7.84–7.75 (2H, m, aromatics), 7.33–7.22 (2H, m, aromatics), 4.89 (1H, d, J = 6.8 Hz, CH2), 4.85 (1H, d, J = 6.5 Hz, CH2), 4.79 (1H, d, J = 6.8 Hz, CH2), 4.73–4.59 (4H, m, CH2), 4.57 (1H, d, J = 6.5 Hz, CH2), 4.03 (1H, dd, J = 4.5, 6.6 Hz, H-5), 4.03–3.99 (1H, m, H-2 or H-4), 3.98 (1H, pseudo t, J = 2.5, 7.3, 9.9 Hz, H-3), 3.78–3.65 (4H, m, H-2 or H-4, H-6, H-7α, H-7β), 3.41, 3.39, 3.21 (12H, 4s, 4 × CH3), 2.42 (3H, s, CH3-Ts). HR-ESI-MS positive mode (m/z): calcd. for [M + H]+ = 537.2113, found: [M + H]+ = 537.2111; C22H36N2O11Si (536.20).

24-2 yellow oil, 96 mg (65%); Rf: 0.19 (2:1 EtOAc–hexane). 1H NMR (360 MHz, CDCl3) δ 8.25 (1H, s, NH), 7.86–7.73 (2H, m, aromatics), 7.35–7.23 (2H, m, aromatics), 7.05 (1H, d, J = 4.4 Hz, H-1), 4.87 (1H, d, J = 6.7 Hz, CH2), 4.77 (1H, d, J = 6.6 Hz, CH2), 4.72–4.67 (2H, m, CH2), 4.65 (1H, d, J = 6.7 Hz, CH2), 4.60 (2H, s, CH2), 4.42 (1H, d, J = 6.7 Hz, CH2), 4.02 (1H, dd, J = 4.5, 2.6, J = 6.6 Hz, H-5), 3.88–3.78 (2H, m) and 3.75–3.55 (4H, m) and 3.46–3.19 (1H, m): (H-2, H-3, H-4, H-6, H-7α, H-7β), 3.39, 3.32, 3.05 (12H, 4s, 4 × CH3), 2.42 (3H, s, CH3-Ts). 13C NMR (90 MHz, CDCl3) δ 146.6 (C-1), 144.8–127.4 (aromatics), 98.2, 97.6, 96.9, 95.7 (4 × CH3-Ts), 79.1, 78.8, 77.3, 74.6, 72.9 (C-2–C-6), 66.9 (C-7), 56.2, 55.9, 55.6 (4 × CH3-Ts). HR-ESI-MS positive mode (m/z): calcd. for [M + Na]+ = 537.2113, found: [M + Na]+ = 537.2111; C22H36N2O11Si (536.20).

4.12.2. (E)-1,2-Dideoxy-3,4,5,7-Tetra-O-Methoxymethyl-1-Phenyl-D-gluco-Hept-1-Enitol (26) and (Z)-1,2-Dideoxy-3,4,5,7-Tetra-O-Methoxymethyl-1-Phenyl-D-gluco-Hept-1-Enitol (27)

Isolated from a reaction of tosylhydrazone 24 (0.10 g, 0.19 mmol), phenylboronic acid (1.5 equiv., 0.03 g, 0.28 mmol), and K3PO4 (3 equiv., 0.12 g, 0.56 mmol) according to General procedure I by column chromatography (1:6 EtOAc–hexane) to yield 19 mg white amorphous solid containing 26 and 27 in 100:1 ratio. Rf: 0.29 (1:2 EtOAc–hexane), [α]D + 1 (c 0.30, CH2Cl2).
26: ^1^H NMR (500 MHz, CDCl3) δ 7.39 (2H, d, J 8.7 Hz, aromatics), 7.35–7.29 (2H, m, aromatics), 7.29–7.23 (1H, m, aromatic), 6.65 (1H, d, J1,2 16.0 Hz, H-1), 6.15 (1H, dd, J2,3 8.1 Hz, H-2), 4.86 (1H, d, J 6.6 Hz, CH3OCH2OC-4), 4.84 (2H, d, J 6.7 Hz, CH3OCH2OC-4, CH2OCH2OC-5), 4.78 (1H, d, J 6.7 Hz, CH3OCH2OC-3), 4.71 (1H, d, J 6.8 Hz, CH3OCH2OC-5), 4.64 (1H, d, J 6.7 Hz, CH3OCH2OC-3), 4.62 (1H, d, J 6.5 Hz, CH3OCH2OC-7), 4.60 (1H, d, J 6.5 Hz, CH3OCH2OC-7), 4.47 (1H, dd, J3,4 5.4 Hz, H-3), 4.20–4.12 (1H, m, H-6), 4.00 (1H, pseudo t, J4,5 4.6 Hz, H-4), 3.89 (1H, dd, J5,6 2.1 Hz, H-5), 3.66 (1H, dd, J6,7a 6.4, J7a,7b 10.3 Hz, H-7a), 3.64 (1H, dd, J6,7b 6.1 Hz, H-7b), 3.49 (1H, dd, J6,OH 3.9 Hz, CH3OH), 3.46 (3H, s CH3OCH2OC-4), 3.44 (3H, s, CH3OCH2OC-5), 3.41 (3H, s, CH3OCH2OC-3), 3.31 (3H, s, CH3OCH2OC-7). ^1^C NMR (125 MHz, CDCl3) δ 134.6 (C-1), 136.4–125.5 (aromatics), 125.9 (C-2), 98.5 (CH3OCH2OC-4), 97.5 (CH3OCH2OC-5), 96.9 (CH3OCH2OC-7), 94.3 (CH3OCH2OC-3), 81.3 (C-4), 77.2 (C-3), 76.9 (C-5), 69.8 (C-6), 69.1 (C-7), 56.4 (CH3OCH2OC-4, CH3OCH2OC-5), 56.0 (CH3OCH2OC-3), 55.4 (CH3OCH2OC-7). HR-ESI-MS positive mode (m/z): calc. for [M + Na]^+ = 453.2095, found: [M + Na]^+ = 453.2099; C21H30O9 (430.49).

27: ^1^H NMR (500 MHz, CDCl3) δ 7.43–7.36 (2H, m, aromatics), 7.35–7.29 (2H, m, aromatics), 7.29–7.23 (1H, m, aromatic), 6.75 (1H, d, J1,2 11.4 Hz, H-1), 5.70 (1H, dd, J2,3 9.9 Hz, H-2), 4.93–4.22 (11H, m, H-3, H-4, H-5, 4 × CH3OCH2), 4.20–4.12 (1H, m, H-6), 3.96–3.83 (2H, m, H-7a, H-7b), 3.44, 3.35, 3.34 (12H, 4s, 4 × CH3OCH2). ^1^C NMR (125 MHz, CDCl3) δ 133.9 (C-1), 136.4–125.5 (aromatics), 129.2 (C-2), 98.9, 97.6, 97.0, 94.6 (4 × CH3OCH2), 81.6 (C-4), 76.9 (C-5), 71.7 (C-3), 69.5 (C-6), 65.7 (C-7), 56.6, 56.5, 55.9, 55.7 (4 × CH3OCH2). HR-ESI-MS positive mode (m/z): calc. for [M + Na]^+ = 453.2095, found: [M + Na]^+ = 453.2099; C21H34O9 (430.49).

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